Global Innovative Drugs Market Study

Independent Market Research Report

Confidential For

Date : Dec 2, 2025

For and on behalf of
Frost & Sullivan Limited

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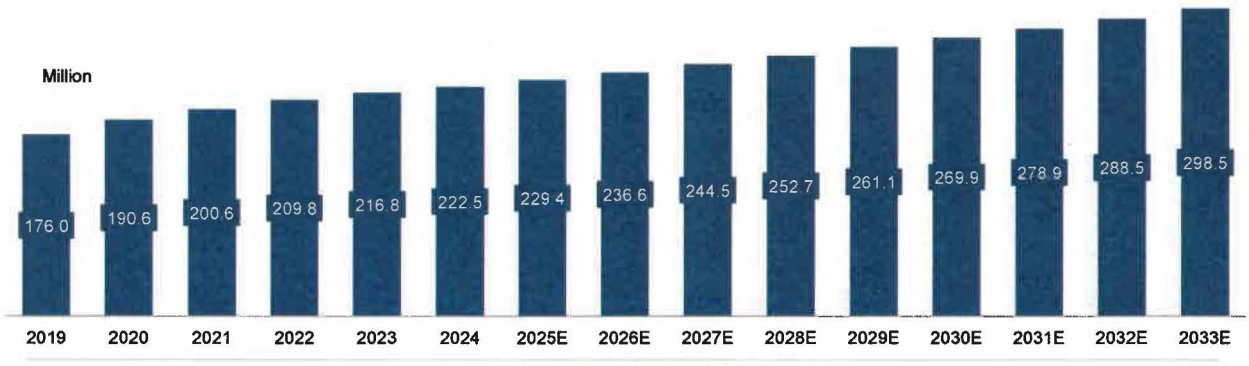
Frost & Sullivan
Nov 2025

Aging Population Trend in China, 2019-2033E

- With the implementation of the 'One Child Policy' and increasing life expectancy, China has entered an aging society. From 2019 to 2024, the population was aging rapidly in China with people aged above 65 growing at a CAGR of 4.8%. According to the National Bureau of Statistics of China (NBSC), individuals aged above 65 years old were 222.5 million in 2024. The number of individuals aged above 65 years old is growing at a fairly fast pace and is expected to continue its growth momentum into the future. This number of people is expected to reach 252.7 million by 2028, and 298.5 million by 2033.
- China's demographic shift offers immense opportunities for healthcare market, as elder people generally have a greater need for medications and scientific disease management.

Aging Population Trend in China, 2019-2033E

Period	CAGR
2019-2024	4.8%
2024-2028E	3.2%
2028E-2033E	3.4%



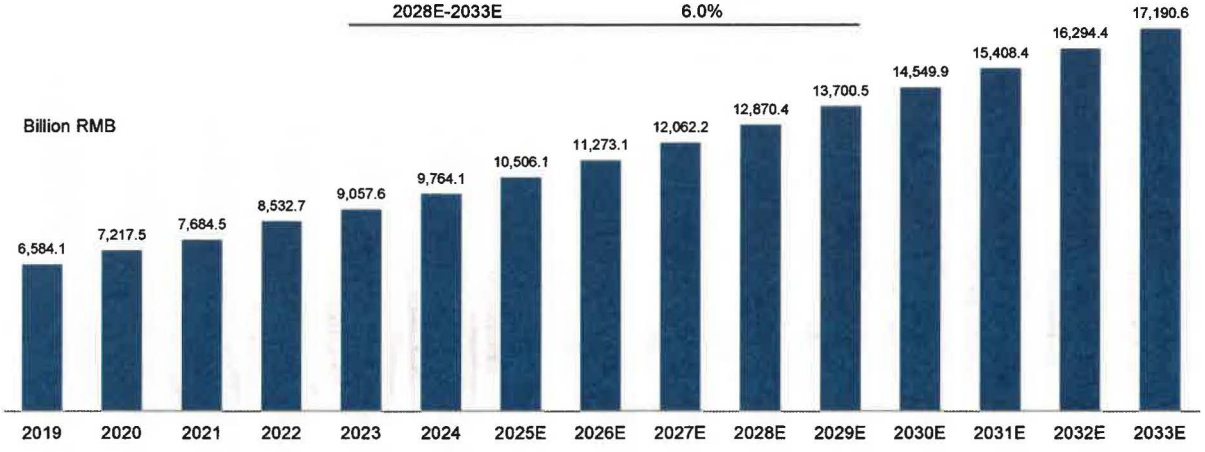
Source: NBSC, Frost & Sullivan Analysis

Total Healthcare Expenditure in China, 2019-2033E

- In 2024, China total expenditure was RMB 9,764.1 billion in total healthcare expenditure, compared to RMB 6,584.1 billion in 2019, a CAGR of 8.2% is presented over this period. With the increase of health awareness and personal disposable income, the total expenditure is projected to boost up to RMB 12,870.4 billion in 2028 and RMB 17,190.6 billion in 2033.

China Healthcare Expenditure, 2019-2033E

Period	CAGR
2019-2024	8.2%
2024-2028E	7.1%
2028E-2033E	6.0%



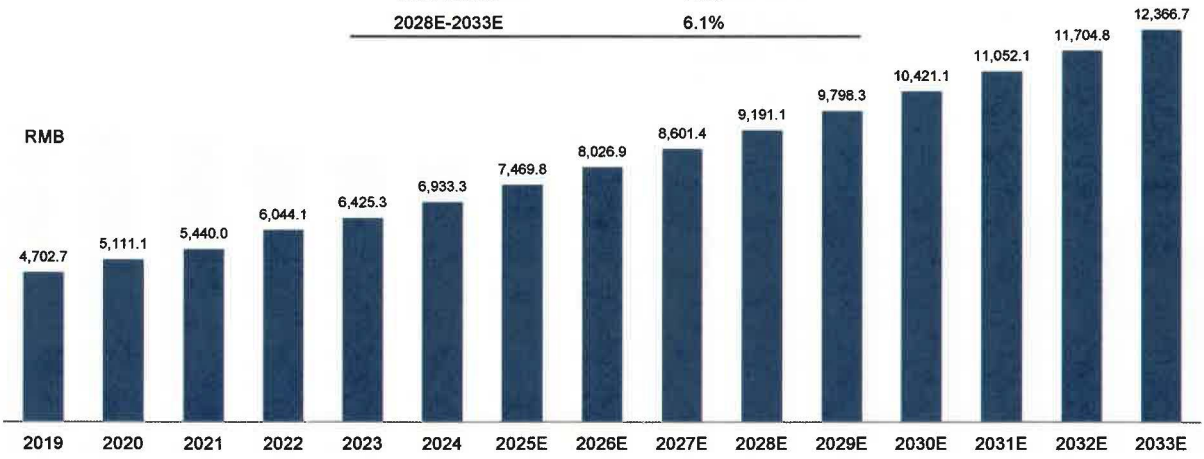
Source: NBSC, Frost & Sullivan Analysis

Per Capita Healthcare Expenditure in China, 2019-2033E

- The per capita healthcare expenditure in China has experienced steady growth. From 2019 to 2024, the per capita healthcare expenditure in China has increased from RMB 4,702.7 to RMB 6,933.3, representing a CAGR of 8.1%. Furthermore, the rapid increasing trend in healthcare expenditure per capita will continue in the near future. The per capita healthcare expenditure in China is forecasted to reach to RMB 9,191.1 by 2028 and RMB 12,366.7 by 2033.

Per Capita Healthcare Expenditure in China, 2019-2040E

Period	CAGR
2019-2024	8.1%
2024-2028E	7.3%
2028E-2033E	6.1%



Source: NBSC, Frost & Sullivan Analysis

Per Capita Disposable Income in China, 2019-2033E

- Along with the continuous growth in economy and urbanization, the average income level of the Chinese residents has also increased continuously in recent years. From 2019 to 2024, the per capita disposable income has increased from RMB 30,733 to RMB 41,314, representing a CAGR of 6.1%. Frost & Sullivan estimates that by 2033, the per capita disposable income will increase to RMB 64,733, with a CAGR of 4.9% during 2028 to 2033.

China Per Capita Disposable Income, 2019-2033E

Period	CAGR
2019-2024	6.1%
2024-2028E	5.4%
2028E-2033E	4.9%

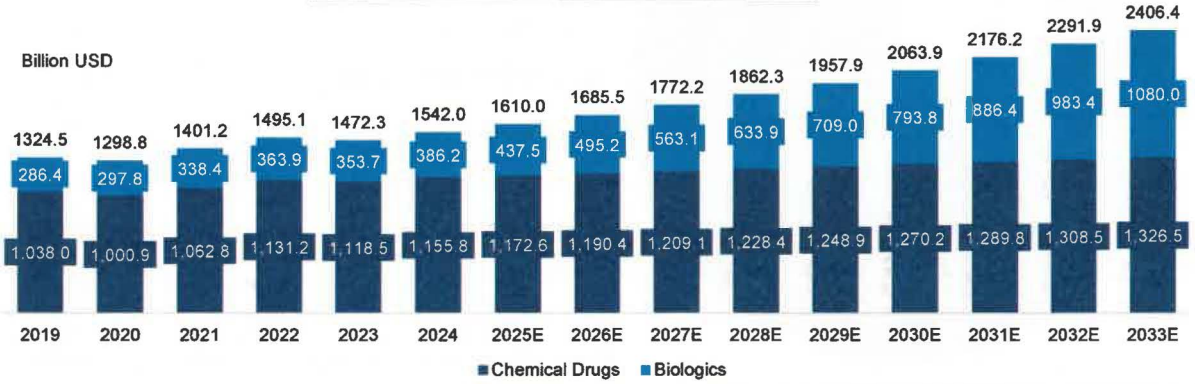
Source: NBSC, Frost & Sullivan Analysis

Global Pharmaceutical Market, 2019-2033E

- Global pharmaceutical market is composed by two segments, namely chemical drug and biologics. The size of global pharmaceutical market was USD 1,542.0 billion in 2024, and is expected to reach USD 1,862.3 billion and USD 2,406.4 billion in 2028 and 2033 respectively, representing a CAGR of 4.8% from 2024 to 2028 and 5.3% from 2028 to 2033.
- Comparing with chemical drugs, biologics has witnessed a faster growth in the past 5 years, increasing from USD 286.4 billion in 2019 to USD 386.2 billion in 2024 at a CAGR of 6.2%. Driven by factors as increasing demand, technology advancement, as well as growth revenue of new generation products, biologics is expected to further reach USD 633.9 billion and USD 1,080.0 billion in 2028 and 2033 respectively, representing a CAGR of 13.2% from 2024 to 2028 and 11.2% from 2028 to 2033.

Breakdown of Global Pharmaceutical Market by Chemical Drugs and Biologics, 2019-2033E

Period	CAGR		
	Chemical	Biologics	Total
2019-2024	2.2%	6.2%	3.1%
2024-2028E	1.5%	13.2%	4.8%
2028E-2033E	1.5%	11.2%	5.3%



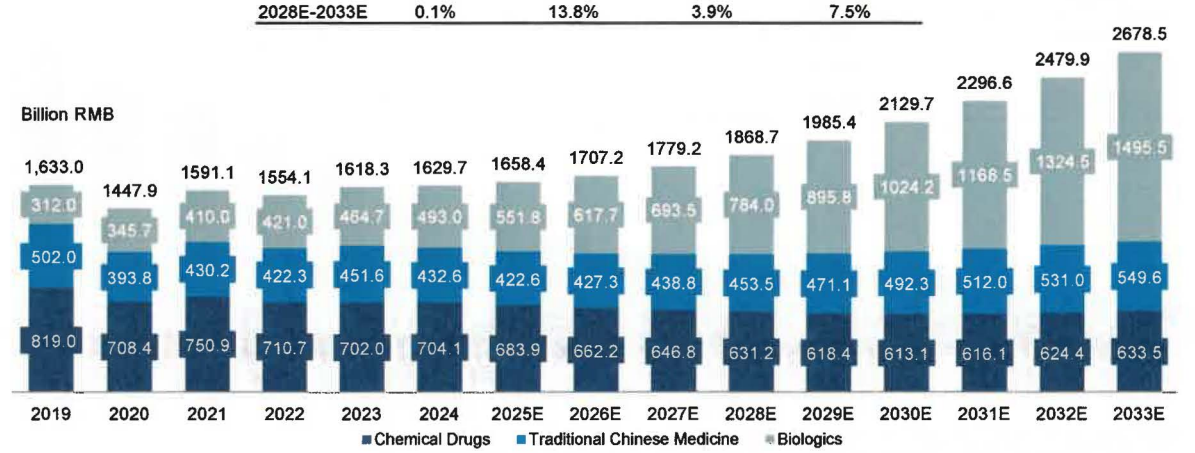
Source: Frost & Sullivan analysis

China Pharmaceutical Market, 2019-2033E

- China pharmaceutical market, accompanying with the growth of economy and healthcare demand, increased from RMB 1,626.7 billion in 2024 to RMB 1,868.7 billion in 2028 with a growth rate of 3.5%. The market is projected to be RMB 2,678.5 billion in 2033, representing a CAGR of 7.5% from 2028 to 2033.

Historical and Forecasted Market Size of China Pharmaceutical Market, 2019-2033E

Period	CAGR			
	Chemical	Biologics	TCM	Total
2019-2024	-3.0%	9.6%	-2.9%	0.0%
2024-2028E	-2.7%	12.3%	1.2%	3.5%
2028E-2033E	0.1%	13.8%	3.9%	7.5%



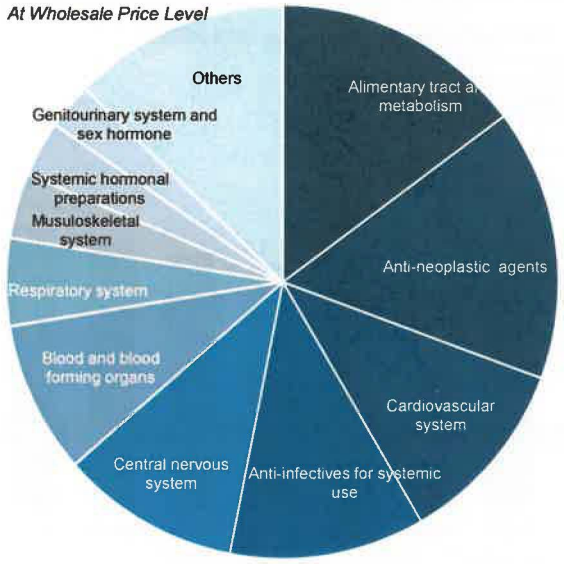
Source: Frost & Sullivan analysis

Breakdown of China Pharmaceutical Market by Therapeutic Area, 2024

- Anti-neoplastic agents, alimentary tract and metabolism and anti-infectives for systemic use are the top three therapeutic areas in the overall pharmaceutical market in China, of which the market share is 15.8%, 14.8%, and 11.5% respectively.

Billion RMB

At Wholesale Price Level



Therapeutic Area	Sales	Market Share
Anti-neoplastic agents	258.2	**15.8%**
Alimentary tract and metabolism	241.1	14.8%
Anti-infectives for systemic use	186.7	11.5%
Cardiovascular system	178.7	11.0%
Central nervous system	170.5	10.5%
Blood and blood forming organs	145.3	8.9%
Respiratory system	83.1	5.1%
Musuloskeletal system	62.2	3.8%
Systemic hormonal preparations	53.1	3.3%
Genitourinary system and sex hormone	44.5	2.7%
Others	206.6	12.7%

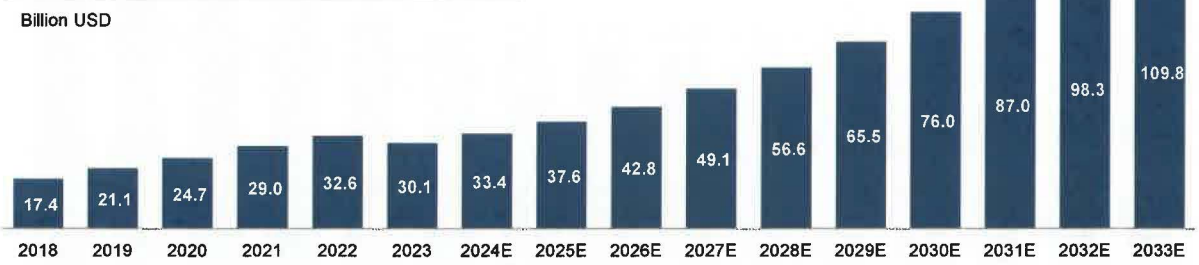
Source: Frost & Sullivan Analysis

China R&D Expenditure, 2018-2033E

- Since the encouragement from government, large pharmas in China has begun to strategize for new drug development. In addition, mid-size and small pharmas are devoting to drug innovation, expected to lead the trends of emerging biologics in China as well. The total R&D expenditure will rapidly grow in next few years.

China R&D Expenditure, 2018-2033E

Period	CAGR
2018-2023	11.5%
2023-2028E	13.5%
2028-2033E	14.2%



Notes: Large pharma refers to pharmaceutical companies with sales revenue over USD1 billion
Mid-sized pharma refers to pharmaceutical companies with sales revenue between USD100 million and USD1 billion.
Small Pharma including biotech companies and virtual pharmas refer to pharmaceutical companies with sales revenue lower than USD100 million.

Source: Frost & Sullivan Analysis

Comparison of Different Therapy Products

Characteristics	Cellular Therapy Products	Biologic Targeted Drugs	Small Molecule Targeted Drugs
Efficacy	• Cellular immunotherapy has also demonstrated efficacy in populations resistant to other targeted therapies, providing new treatment options for patients.	• With prolonged use, most patients will develop resistance.	• With prolonged use, most patients will develop resistance.
Safety	• By specifically recognizing antigens to target tumor cells, the likelihood of off-target effects causing side effects is low, though it may trigger an immune response.	• By specifically recognizing antigens to target tumor cells, the likelihood of off-target effects causing side effects is low. • It may trigger an immune response.	• Small molecule drugs are more likely to produce off-target effects, leading to greater side effects. • Low immunogenicity.
effectiveness	• Cellular immunotherapy can stimulate immune memory, prolonging the immune system's antitumor response and extending response duration. For instance, CAR-T cells can persist effectively in a patient's body for several weeks or even months. Some activated immune cells can become memory cells, retaining their ability to specifically recognize antigens and eliminating diseased cells upon future antigen invasion, providing significant advantages in preventing tumor recurrence.	• Drugs with a longer half-life, such as most antibody drugs, are typically administered via intravenous injection every 1-2 weeks.	• Drugs with a shorter half-life generally need to be taken daily.
Production	• Currently, all approved products are autologous CAR-T cell therapies, with a lengthy production process. This involves steps such as cell culture and purification, and the drug's activity must be maintained throughout the production process, leading to higher production costs.	• The process requires steps such as cell culture and purification, and it is essential to maintain the drug's activity throughout production, leading to higher production costs.	• The production process involves fewer steps compared to biologic drugs, leading to a shorter overall production time. It is also less sensitive to storage conditions, making storage and transportation more convenient.
Price	• The cost is relatively high, with approved products in China exceeding 1 million RMB per dose.	• The annual treatment cost typically ranges from several hundred thousand to over a million RMB, depending on the specific drug and type of cancer.	• The annual treatment cost varies greatly based on the drug and cancer type, generally ranging from tens of thousands to hundreds of thousands of RMB.

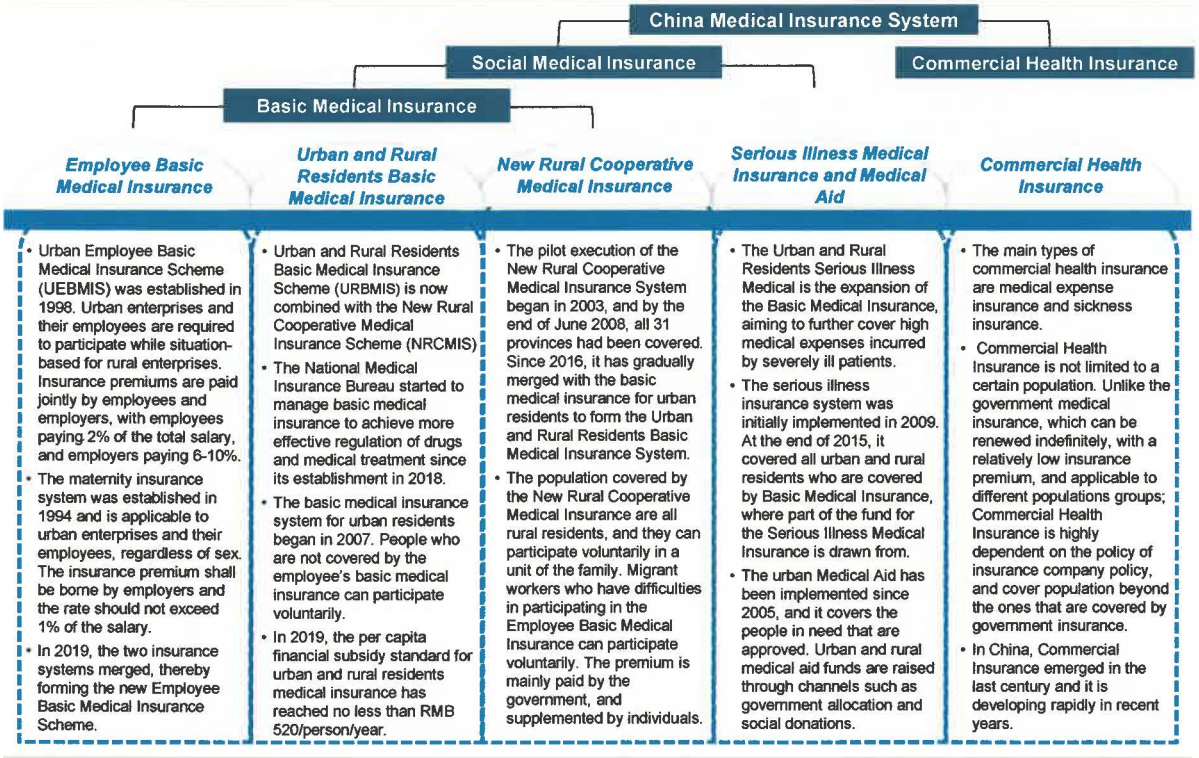
Source: Frost & Sullivan Analysis

Comparison of Different Antibody Types

Categories	Structure functions	Advantages	Limitations
Mono-antibody (mAb)	Antibodies that are made by identical immune cells that are all clones of a unique parent cell. mAb can have monovalent 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.	mAbs diffuse poorly and large tumor masses may be more difficult to treat by mAb therapy. Triggering of ADCC by therapeutic antibodies faces several limitations, especially for low affinity variant of the receptor.
Bispecific antibody (BsAb)	A bispecific monoclonal antibody (BsMAb, BsAb) is an artificial protein that can simultaneously bind to two different types of antigen.	Potential used in 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 doses and the number of injections that can be given to patients. Difficulties in chemical, manufacturing and control (CMC) development.
Heavy Chain Antibody (HCAb)	HCAb is an antibody which consists only of two heavy chains and lacks the two light chains usually found in antibodies.	Markedly more acid- and heat-resistant than conventional antibodies. Easier to express in a functional recombinant form. High affinities towards a large spectrum of antigens.	The development of nanobodies requires larger, more complicated housing and animal husbandry for obtaining the desired antibody. Short serum half-life reduces its efficacy in parenteral preparations.
Single-chain Variable Fragment (ScFV)	ScFV is a fusion protein of the variable regions of the heavy (VH) and light chains (VL) of immunoglobulins, connected with a short linker peptide of ten to about 25 amino acids.	Preservation of the binding activity of the parental antibody, efficient expression in a wide range of hosts (e.g., bacteria and mammalian cells), and great tumor tissue penetration.	Short in vivo half-life owing to the rapid blood clearance and poor retention time in the target tissues.
Single-domain Antibody (sdAb)	sdAb is an antibody fragment consisting of a single monomeric variable antibody domain.	Small size and low structural complexity which allows them to readily be produced as fusions in a variety formats.	The antigen-binding paratope of camelid HCAbs has been restricted to a single domain of about 110 amino acids will automatically put more weight on each and every residue in the VHH domain.
Antibody-drug Conjugate (ADC)	ADC is composed of an antibody linked to a biologically active cytotoxic payload or drug.	ADCs take advantage of the specificity of a monoclonal antibody to deliver a linked cytotoxic agent directly into a tumor cell, combining the unique and very sensitive targeting capabilities of antibodies allowing sensitive discrimination between healthy and cancer tissues with the cell-killing ability of cytotoxic drugs	ADCs encountered major obstacles including, low blood residency time, low penetration capacity to tumor microenvironment, low payload potency, immunogenicity, unusual off-target toxicity, drug resistance, and the lack of stable linkage in blood circulation.

Source: Literature review, Frost & Sullivan Analysis

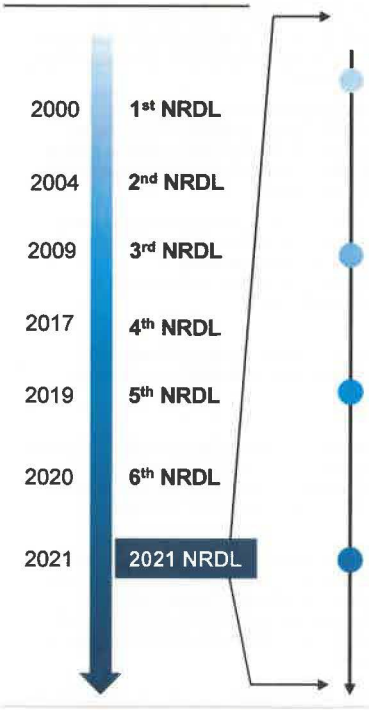
Overview of Medical Insurance System in China



Source: NMPA, Frost & Sullivan analysis

Analysis of Healthcare Reimbursement System in China
Recent Progress and Impact of the 2021 NRDL

Progression of NRDL



Recent Progression of 2021 NRDL

- In Dec 2021, NHSA and MOHRSS released the official work plan for the adjustment of the 2021 NRDL, enforced from January 1st, 2022. The latest NRDL negotiation aims to eliminate medications with unreasonably high prices, optimize clinical use of medications, and further lower prices of current drugs by inducing virtuous competition
- 117 kinds of drugs were involved in price negotiation, and 94 of them were smoothly negotiated. 74 kinds of drugs have been newly included in NRDL for the first time, leading to a 61.71% decline in prices.
- Affected by fair competition in the market, the drug list and payment standard should also be adjusted accordingly. Some drugs in previous NRDL occupied too many funds with a relatively high price. 11 previously included drugs were removed from the list due to substitutability, low clinical value and low utilization rate. This allows newer drugs and drugs with higher efficacies to be included in NRDL in the coming future.
- 20 drugs for chronic diseases such as hypertension, diabetes, and hyperlipidaemia have been newly included. Besides, 18 oncology drugs, 15 drugs for infectious diseases, 7 drugs for rare diseases, 2 drugs for covid-19 and 12 drugs for other indications have been newly included.

Implication for Innovation

The inclusion of NRDL promoted the sales of innovative drugs significantly. At the same time, pharmaceutical companies need to embrace continuous innovation and accelerate the pace. Only those pharmaceutical companies that develop drugs with independent IP rights can win the industrial competition and keep a higher margin.

2021 NRDL restricts the price of drugs strictly by introducing economic competition among different drugs with the same indication. The substitutability of drugs is now an important indicator, and only the most cost-effective drugs are expected to enter NRDL.

Numerous domestic innovative drugs were included by 2021 NRDL, marking the initiation of a rapid increase of sales and the rapid transformation of the Chinese pharmaceutical industry towards innovation.

Since the implementation of the self-declaration system of pharma, only drugs that meet the conditions of 2021 NRDL plans can be included in the adjustment scope.

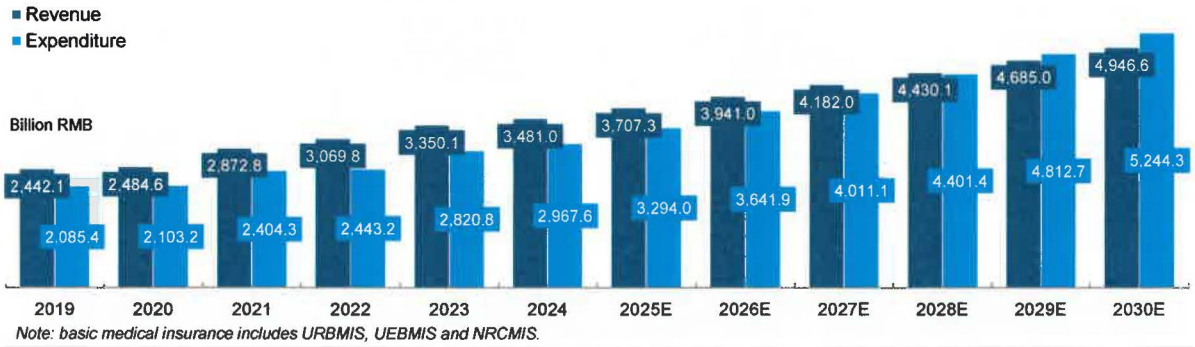
Source: MORHSS, Frost & Sullivan analysis

Basic Medical Insurance Fund in China, 2019-2030E

- The revenue of basic medical insurance fund has increased from RMB2,442.1 billion in 2019 to RMB3,481.0 billion in 2024, with a CAGR of 7.3%, while the expenditure has increased from RMB2,085.4 billion in 2019 to RMB2,967.6 billion in 2024, representing a CAGR of 7.3% during the indicated period.
- The revenue is expected to continue its growth while the expenditure will experience a much higher growth if no intervention is implemented. The expenditure will surpass the revenue in 2029 and reach RMB5,244.3 billion in 2030. Therefore, there is a high willingness to control the expenditure of basic medical insurance fund, which can be achieved through digital technologies.

Revenue and Expenditure of Basic Medical Insurance Fund, 2019-2030E

Period	CAGR	
	Revenue	Expenditure
2019-2024	7.3%	7.3%
2024-2030E	6.0%	10.0%



Note: basic medical insurance includes URBMIS, UEBMIS and NRCMIS.

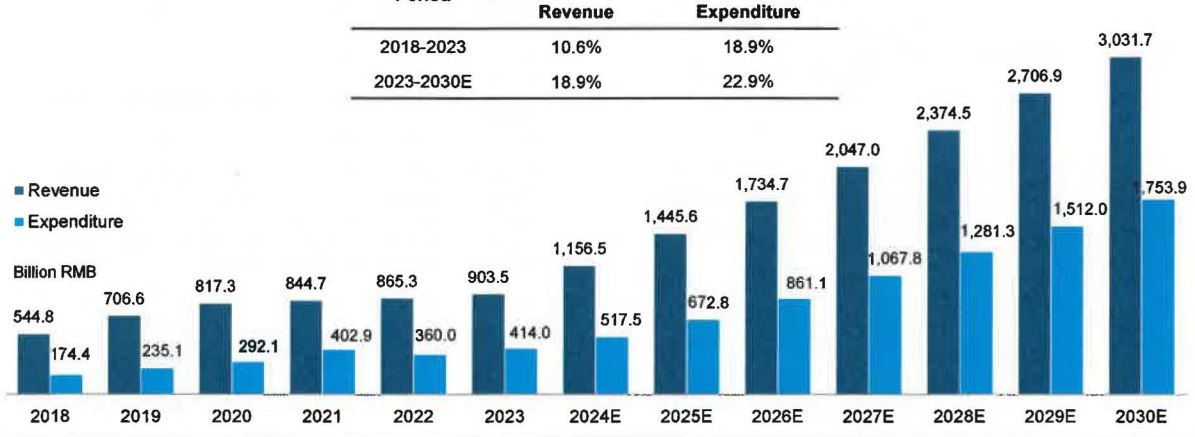
Source: NMPA, Frost & Sullivan Analysis

Commercial Health Insurance Fund in China, 2018-2030E

- According to China Insurance Regulatory Commission, the revenue of commercial health insurance fund has increased from RMB544.8 billion in 2018 to RMB903.5 billion in 2023, with a CAGR of 10.6%, while the expenditure has increased from RMB174.4 billion in 2018 to RMB414.0 billion in 2023, representing a CAGR of 18.9% during the indicated period.
- Commercial health insurance fund in China has shown explosive growth before 2017 due to the absence of regulation. After the introduction of a series of regulatory measures by China Insurance Regulatory Commission, commercial health insurance premiums began to reflect the real demand for health insurance. Along with demographic changes and increasing health awareness, the commercial health insurance is expected to continue its growth. The revenue and expenditure is forecasted to reach RMB 3,031.7 billion and RMB 1,753.9 billion by 2030.

Revenue and Expenditure of Commercial Health Insurance Fund, 2018-2030E

Period	CAGR	
	Revenue	Expenditure
2018-2023	10.6%	18.9%
2023-2030E	18.9%	22.9%

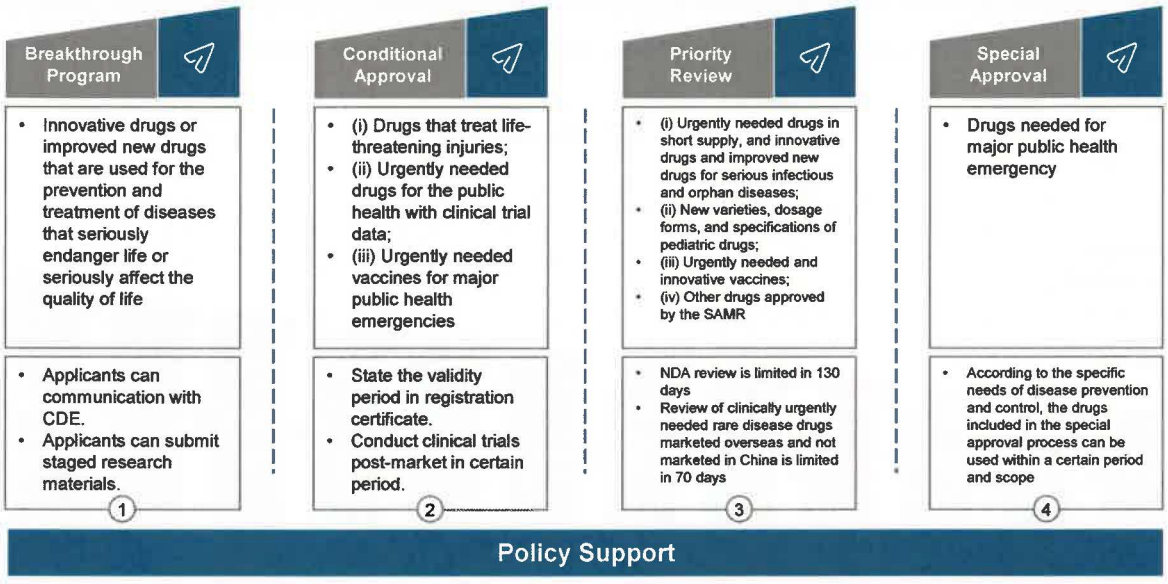


Source: CIRC, Frost & Sullivan Analysis

Favorable Policies/ Regulations

Review of market access

- On March 30, 2020, the State Administration for Market Regulation (SAMR), released a revised Drug Registration Regulation (Revised DRR) as part of its efforts to strengthen and streamline its regulation of the pharmaceutical industry. According to the revised DDR, four accelerated approval pathways would be established. The revised DRR went into effect on July 1, 2020.



Source: Frost & Sullivan Analysis

Favorable Government Policy of Medical Insurance (1/7)

Release Date	Issuing Authority	Policies	Comments
July 13, 2017	MOHRSS	*Notification on the Inclusion of 36 Drugs in the National Basic Medical Insurance, Work Injury Insurance, and Maternity Insurance Drug Catalogue Category B* 《人力资源社会保障部关于将36种药品纳入国家基本医疗保险、工伤保险和生育保险药品目录乙类范围的通知》	• Liraglutide injection and 35 other drugs have been newly included in the National Medical Insurance Category B catalogue. • The 2017 edition of the medical insurance catalogue has been updated to expand drug coverage and enhance the level of medical security.
September 13, 2018	State Council	*Opinions on Improving the National Essential Medicines System* 《关于完善国家基本药物制度的意见》	• Full-process management: From selection to monitoring, ensuring the quality and supply of essential medicines at all stages. • Dynamic catalog optimization: Implementing dynamic adjustments to ensure drug updates and optimization. • Payment policy optimization: Reducing the financial burden of medication for patients through policy adjustments. • Priority use and equipment: Fully equipping with essential medicines and giving priority to their use. • Enhancing safety levels: Raising standards for drug quality and safety.
September 30, 2018	NHC, SAMR, NATCM	Notification on Doing a Good Job in Implementing the National Essential Medicines Catalogue (2018 Edition) 《关于做好<国家基本药物目录（2018年版）>实施工作的通知》	• In accordance with the Opinions of the General Office of the State Council on Improving the National Essential Medicines System, dynamically adjust and optimize the catalogue, effectively ensure production and supply, fully equip and prioritize the use of essential medicines, reduce the financial burden of medication for the public, and strengthen organizational guarantees.
November 22, 2019	NHSA, MOHRSS	*Notification on Including the 2019 Negotiated Drugs in the National Basic Medical Insurance, Work Injury Insurance, and Maternity Insurance Drug Catalogue Category B* 《国家医保局人力资源社会保障部关于将2019年谈判药品纳入<国家基本医疗保险、工伤保险和生育保险药品目录>乙类范围的通知》	• Including drugs such as liraglutide and lixisenatide in the National Basic Medical Insurance, Work Injury Insurance, and Maternity Insurance Drug Catalogue Category B.

Source: Government Website, Frost & Sullivan Analysis

Favorable Government Policy of Medical Insurance (2/7)

Release Date	Issuing Authority	Policies	Comments
February 25, 2020	Central Committee of the Communist Party of China, State Council	*Opinions on Deepening the Reform of the Medical Insurance System* 《中共中央 国务院关于深化医疗保障制度改革的意见》	• By 2025, the medical insurance system will be more mature and standardized, with the basic completion of reform tasks in important mechanisms such as treatment protection, financing operation, medical insurance payment, and fund supervision, as well as key areas such as medical service supply and medical insurance management services. • By 2030, a medical insurance system will be fully established with basic medical insurance as the main body, medical assistance as the bottom line, and supplementary medical insurance, commercial health insurance, charitable donations, and medical mutual aid developing together, with fair and moderate treatment protection, stable and sustainable fund operation, optimized and convenient management services, and significantly improved modernization level of medical insurance governance, achieving the goal of better protection for the sick.
July 30, 2020	NHSA	*Interim Measures for the Administration of Medical Insurance Drug Use* 《基本医疗保险用药管理暂行办法》	• Functional positioning: Adhering to "protecting the basics," ensuring that the level of drug use matches the medical insurance fund and the affordability of the insured. • Graded management: Implementing graded management to clarify the responsibilities and powers at all levels. • Expert review: Through expert review, adapting to the development of clinical technology to achieve scientific, standardized, refined, and dynamic management. • Drug selection principles: Based on clinical necessity, safety and efficacy, reasonable pricing, convenience of use, sufficient market supply, and medical insurance affordability. • Dynamic adjustment mechanism: The State Council's medical insurance administrative department establishes a mechanism to adjust the drug catalogue once a year in principle.
December 28, 2020	NHSA, MOHRSS	*National Basic Medical Insurance, Work Injury Insurance, and Maternity Insurance Drug Catalogue* (2020) 《国家基本医疗保险、工伤保险和生育保险药品目录（2020年）》	• 119 drugs such as dulaglutide, bexagliptin, and polyethylene glycol loxenatide were added to the catalogue, and 29 drugs were removed.

Source: Government Website, Frost & Sullivan Analysis

Favorable Government Policy of Medical Insurance (3/7)

Release Date	Issuing Authority	Policies	Comments
September 9, 2021	NHSA, NHC	*Notification on Adapting to the Normalization of National Medical Insurance Negotiations and Continuously Doing a Good Job in the Implementation of Negotiated Drugs* 《关于适应国家医保谈判常态化持续做好谈判药品落地工作的通知》	• Rational drug use: Medical institutions are responsible for adjusting the drug equipment in a timely manner to synchronize with the medical insurance catalogue. • Clinical demand response: Establish a rapid response mechanism to provide temporary procurement and a green channel for urgently needed drugs. • Drug accessibility: Improve the convenience of drug acquisition through prescription circulation and "dual channels". • Supervision and assessment: Strengthen the supervision of drug use behavior and adjust assessment indicators to promote the rational use of negotiated drugs. • Policy support: Avoid restrictions such as the total amount of medical insurance to ensure the effective implementation of negotiated drugs.
November 15, 2021	NHC	*Announcement on Publicly Soliciting Opinions on the "National Essential Medicines Catalogue Management Method (Revised Draft)* 《关于就<国家基本药物目录管理办法（修订草案）>公开征求意见的公告》	• Further consolidate the national essential medicines system and establish a sound selection and adjustment mechanism for the national essential medicines catalogue.
November 24, 2021	NHSA, MOHRSS	*National Basic Medical Insurance, Work Injury Insurance, and Maternity Insurance Drug Catalogue (2021)* 《国家基本医疗保险、工伤保险和生育保险药品目录（2021年）》	• Require departments at all levels to standardize payment standards, adjust the scope of payment in a timely manner, and ensure that negotiated drugs are implemented on time and the digestion task is completed.
June 15, 2022	NHC	*Reply to the Suggestions No. 6347 and No. 9017 at the Fifth Session of the 13th National People's Congress* 《对十三届全国人大五次会议第6347、9017号建议的答复》	• Supply and guarantee: Improve the supply level of negotiated drugs to ensure the effective implementation of innovative drugs. • Responsibility and linkage: Medical institutions take the main responsibility and establish linkage with the adjustment of the medical insurance catalogue. • Timely response: Convene the drug committee quickly according to clinical needs to optimize drug equipment. • Procurement and circulation: Simplify the temporary procurement process and establish a prescription circulation mechanism to improve drug accessibility.

Source: Government Website, Frost & Sullivan Analysis

Favorable Government Policy of Medical Insurance (4/7)

Release Date	Issuing Authority	Policies	Comments
June 29, 2022	NHSA	*Announcement on the "2022 National Basic Medical Insurance, Work Injury Insurance, and Maternity Insurance Drug Catalogue Adjustment Work Plan" and Related Documents* 《关于公布<2022年国家基本医疗保险、工伤保险和生育保险药品目录调整工作方案>及相关文件的公告》	• In the "Negotiated Drug Renewal Rules," it is proposed to adopt a "simple renewal" rule for eligible exclusive drugs in the catalogue to be included in the medical insurance catalogue.
June 30, 2022	NHSA, MOF	*Notification on Further Doing a Good Job in Direct Settlement of Basic Medical Insurance for Out-of-Province Medical Treatment* 《关于进一步做好基本医疗保险跨省异地就医直接结算工作的通知》	• Out-of-province medical treatment settlement: By the end of 2025, achieve a comprehensive upgrade of the settlement system, with the settlement rate for inpatient expenses exceeding 70%. • Service network expansion: Double the number of outpatient network institutions to cover more chronic and special disease treatment costs. • Information platform support: Strengthen the national unified medical insurance information platform to improve settlement efficiency. • Record process optimization: Simplify the out-of-province medical treatment record process to improve service standardization and convenience.
July 14, 2022	NHSA	*Reply of the National Healthcare Security Bureau to the Suggestion No. 1599 at the Fifth Session of the 13th National People's Congress* 《国家医疗保障局对十三届全国人大五次会议第1599号建议的答复》	• Include new indications in the scope of simple renewal consideration.
December 23, 2022	NHSA	*Notification of the National Healthcare Security Bureau on Comprehensively Investigating and Canceling Unreasonable Restrictions of Medical Insurance* 《国家医疗保障局关于全面排查并取消医保不合理限制的通知》	• Focus on investigating whether there are unreasonable restrictions and requirements in the medical insurance management, causing inconvenience to medical institutions or harming the interests of insured personnel.

Source: Government Website, Frost & Sullivan Analysis

Favorable Government Policy of Medical Insurance (5/7)

Release Date	Issuing Authority	Policies	Comments
May 25, 2023	NHSA	*Notification on Implementing Sixteen People-Oriented Measures for Medical Insurance Services* 《关于实施医保服务十六项便民措施的通知》	• Online Registration and Emergency Support: Simplify the out-of-area registration process through the medical insurance App and mini-programs, with automatic registration protection for emergency patients. • Benefit Enjoyment and Transfer Continuation: Residents living across provinces enjoy bidirectional medical insurance benefits, with the transfer and continuation period significantly reduced. • Service Process and Digital Empowerment: Achieve "one-window handling" and "online handling" for medical insurance services, with digital technology making medical treatment and drug purchases more convenient.
July 26, 2023	NHSA, MOF, State Taxation Administration	*Notification on Doing a Good Job in Basic Medical Insurance for Urban and Rural Residents in 2023* 《关于做好2023年城乡居民基本医疗保障工作的通知》	• Medical insurance financing and subsidies: The standard for resident medical insurance financing in 2023 is 1020 yuan, with financial subsidies not less than 640 yuan, and personal payments of 380 yuan, ensuring that funds are allocated in a timely and full amount. • Financial subsidy policy: The central finance implements tiered subsidies for localities, with 80% for the western region, 60% for the central region, and proportional subsidies for the eastern region, coordinating major disease insurance funds to ensure that the level of benefits is not reduced.
December 13, 2023	NHSA, MOHRSS	*National Basic Medical Insurance, Work Injury Insurance, and Maternity Insurance Drug Catalogue (2023 Edition)* 《国家基本医疗保险、工伤保险和生育保险药品目录 (2023年) 》	• Drug catalogue update: 126 new drugs were added to the national medical insurance drug catalogue in 2023, and 1 was removed, with a negotiation success rate of 84.6%, an average price reduction of 61.7%, maintaining a level comparable to last year. • Total number of drugs in the catalogue: After adjustment, the total number of drugs in the catalogue reached 3088, including 1698 Western medicines, 1390 traditional Chinese patent medicines, and 892 traditional Chinese medicine decoctions.

Favorable Government Policy of Medical Insurance (6/7)

Release Date	Issuing Authority	Policies	Comments
January 1, 2024	NHSA	*Notification on Strengthening the Supply Guarantee of Selected Products in Centralized Volume Procurement of Medicines* 《关于加强医药集中带量采购中选产品供应保障工作的通知》	• The Healthcare Security Bureau strengthens enterprise performance through procurement agreements, establishes communication and coordination mechanisms between medical institutions and enterprises, guides medical institutions to effectively respond to surging demand and monitor the supply of selected drugs, and encourages the establishment of a supply evaluation mechanism to promote credit evaluation and procurement decisions, ensuring that healthcare security departments take responsibility in supply monitoring, rectification supervision, and breach handling, allowing the public to continue to benefit from the reforms of centralized procurement.
May 20, 2024	NHSA	*Notification on Strengthening Regional Coordination and Doing a Good Job in Centralized Procurement of Medicines in 2024* 《关于加强区域协同 做好2024年医药集中采购提质扩面的通知》	• Expand the scope of alliances to form a national alliance for centralized procurement. On the basis of the state's centralized volume procurement of drugs and high-value medical consumables, strengthen regional coordination, promote provincial alliance procurements that meet the conditions to a national level, and require the implementation of centralized procurement monitoring and management, treat all types of operators fairly, and strictly guard against "local protectionism".
June 6, 2024	State Council	*Key Tasks for Deepening the Reform of the Medical and Health System in 2024* 《深化医药卫生体制改革2024年重点工作任务》	• Increase the per capita financial subsidy standard for basic public health services by 5 yuan. Organize secondary and tertiary hospitals to improve the capabilities at the grassroots level through personnel decentralization, telemedicine, training, and mobile medical services. Recruit about 8,000 rural order-directed free undergraduate medical students for township health centers in central and western regions.

Source: Government Website, Frost & Sullivan Analysis

Favorable Government Policy of Medical Insurance (7/7)

Release Date	Issuing Authority	Policies	Comments
June 28, 2024	NHSA	*Announcement on the Publication of the "2024 National Basic Medical Insurance, Work Injury Insurance, and Maternity Insurance Drug Catalogue Adjustment Work Plan" and Application Guidelines* 《关于公布<2024年国家基本医疗保险、工伤保险和生育保险药品目录调整工作方案>及申报指南等文件的公告》	• Adjustment of application conditions: Relax the time requirements for drug applications, allowing applications for drugs marketed or with modified indications after January 1, 2019. • Supply guarantee management: Focus on adjusting regular drugs that have not been supplied to designated medical institutions in nearly three years and negotiated drugs that have not ensured market supply. • Strengthening expert supervision: Clarify the rules for expert participation, enhance professional training, improve the scientific and standardized review, and establish regulations for fair performance and confidentiality.
July 23, 2024	NHSA	*Notification on the Issuance of the 2.0 Version of the DRG Grouping Plan and Further Advancement of Related Work* 《关于印发按病组和病种分值付费2.0版分组方案并深入推进相关工作的通知》	• Optimization of DRG grouping: The new version of DRG core grouping is optimized for 13 disciplines including critical care medicine and combined surgery issues, increasing to 409 groups. • Adjustment of the DIP disease library: The new version of the DIP disease library core diseases is reduced to 9520 groups, which is streamlined compared to the previous version.
August 1, 2024	NHSA	*Guidance on Improving the Long-term Mechanism for Basic Medical Insurance Participation* 《关于健全基本医疗保险参保长效机制的指导意见》	• Relaxation of household registration restrictions: Relax the participation restrictions for primary and secondary school students and preschool children, and cancel the household registration restrictions for urban workers' medical insurance in megacities. Personal account sharing: The scope of personal account sharing in workers' medical insurance is expanded to close relatives. • Increase in critical illness insurance amount: After continuous participation in the resident medical insurance for four years, the limit for critical illness insurance increases year by year. • Reimbursement incentives: The cap for critical illness insurance for the following year is raised for those who did not claim reimbursement in the current year. • Grassroots designated points: Village health rooms are included in designated medical institutions, centralized procurement drugs are directly settled at the grassroots level, benefiting the grassroots level.

Source: Government Website, Frost & Sullivan Analysis

Favorable Government Policy of Pharmaceutical Industry

Review of Clinical Trial and New Drug Application

Release Date	Issuing Authority	Policies	Comments
Aug, 2015	State Council	*Opinions of the State Council on Reform of the System of Evaluation, Review and Approval of Drugs and Medical Devices* 《国务院关于改革药品医疗器械审评审批制度的意见》	• Accelerating the review and approval of innovative drug trials. • Implementing specific review, evaluation and approval system to accelerating the review and approval process for innovative drugs that are in use of prevention and treatment of AIDS, malignant tumors, major infectious diseases, rare diseases, as well as drugs listed in national science and technology projects and national key R&D programs.
Mar, 2016	State Council	*Guiding Opinions of the General Office of the State Council on Promoting the Sound Development of the Medical Industry* 《国务院办公厅关于促进医药产业健康发展的指导意见》	• Deepening review and approval system reforms. Establishing a more scientific and efficient review and approval system for drug and medical devices. • Strengthening the construction of review teams, and recruiting experts and scholars with international review and approval experience.
Oct, 2016	State Council	*Healthy China 2030* 《"健康中国2030"规划纲要》	• Strengthening drug safety supervision. • Deepening the reform of the review and approval system for pharmaceuticals (medical devices), establishing review and approval system based on clinical curative effects. • Improving the approval standards for drug (medical devices).
Dec, 2017	General Office of the CPC Central Committee and the General Office of the State Council	*Opinions of Encouraging Drug Innovation to Implement Priority Review and Approval* 《总局关于鼓励药品创新实行优先审评审批的意见》	Drug registration with obvious clinical value meets one of the following requirements: • Application for registration of innovative drugs not listed and sold in China or abroad. • Application for registration of innovative drugs transferred to China. • Drug registration applications with advanced preparation technology, innovative treatment methods and obvious therapeutic advantages.

Source: Government Website, Frost & Sullivan Analysis

Favorable Government Policy of Pharmaceutical Industry

Review of Clinical Trial and New Drug Application

Release Date	Issuing Authority	Policies	Comments
May, 2018	CFDA	*Notice for Optimizing the Examination, Assessment and Approval of Drug Registration* 《关于优化药品注册审评审批有关事宜的公告》	In order to improve the efficiency of review and approval of innovative drugs as well as simplify the procedure: • The review and approval for rare diseases that seriously endanger life with no effective treatment could be sped up through communication system between CDE and applicants. • The clinical data obtained overseas with no ethnic difference could directly apply for drug launch registration.
Jul, 2018	CFDA	*Technical Guidelines for Accepting Data from Overseas Clinical Trials of Drugs* 《接受药品境外临床试验数据的技术指导原则》	• In order to encourage the synchronous drug R&D both domestic and abroad, the acceptable overseas clinical trials data are clarified. • The overseas R&D of generic drug with complete and assessable bioequivalence data can also be used for registration applications.
Jul, 2018	CFDA	*Announcement on Adjusting the Examination and Approval Procedure of Drug Clinical Trials* 《关于调整药物临床试验审评审批程序的公告》	• Drug clinical trial filing system: The drug clinical trial can be carried out according to the submitted scheme if the applicant fails to receive the negative or doubtful opinions from CDE within 60 days from the accepted and payment date of the application.
Oct, 2018	CFDA	*Announcement on the urgent clinical need for approval of new drugs abroad* 《关于临床急需境外新药审评审批相关事宜的公告（2018年第79号）》	Establish a special channel for review and approval of overseas innovative drugs that are urgently needed, which has launched in the United States, the EU or Japan in the past 10 years but not in China, meeting one of the following circumstances: • Drugs for the treatment of rare diseases • Drugs for serious life-threatening diseases without effective treatment • Drugs have obvious clinical advantages for serious life-threatening diseases. The innovative drugs from abroad can be declared for manufacturing directly without domestic clinical data after demonstration of no ethnic difference.

Source: Government Website, Frost & Sullivan Analysis

Favorable Government Policy of Pharmaceutical Industry

Review of Clinical Trial and New Drug Application

Release Date	Issuing Authority	Policies	Comments
Sep, 2019	NHC, NHSA, NMPA	*Notice for the Publication of the Health China_ Implementation Plan for Cancer Prevention (2019-2022 edition)* 《关于印发健康中国行动——癌症防治实施方案（2019—2022年）的通知》	• Establish a comprehensive clinical evaluation system for anticancer drugs. • Speed up the approval of new anticancer drugs at home and abroad.
Nov, 2019	NMPA	*Notice on Soliciting Opinions on the Working Procedures of Breakthrough Therapeutics and the Priority Review and Approval Process* 《关于突破性治疗药物工作程序和优先审评审批工作程序征求意见的通知》	• For innovative drugs or improved new drugs that are used to prevent or treat severely life-threatening diseases, and that have no effective prevention measures or have sufficient evidence to show obvious clinical advantages compared with existing therapies, they can apply for Breakthrough Treatment Drugs. • Breakthrough Treatment Drugs can be reviewed and approved first.
Mar, 2020	NMPA, NHC	*Announcement on the Release of Administrative Regulations on Extended Clinical Trials of Medical Devices (Trial)* 《关于发布医疗器械拓展性临床试验管理规定（试行）的公告》	• Meet the public clinical needs and support clinical experimental on medical instruments as soon as possible. • Standardize the development of extended clinical trials and the collection of safety data for medical devices. • Safeguard the rights and interests of subjects.
Apr, 2020	NMPA, NHC	*Announcement on the Release of Quality Management Practices for Drug Clinical Trials* 《关于发布药物临床试验质量管理规范的公告》	• Deepen the reform of drug evaluation and approval system and encourage innovation. • Further promote standardized research and improve the quality of drug clinical trials in China.
Dec, 2020	NMPA	*Guidelines for Statistical Design of Antitumor Drug Clinical Trials (Trial)* 《抗肿瘤药物临床试验统计学设计指导原则（试行）》	• The statistical methods for the commonly used efficacy endpoints are proposed in the guidelines, and the statistical design requirements are putted forward from the perspectives of exploratory and confirmatory trials.

Source: Government Website, Frost & Sullivan Analysis

Favorable Government Policy of Pharmaceutical Industry

Review of Innovation Encouragement

Release Date	Issuing Authority	Policies	Comments
Mar, 2016	State Council	*Guiding Opinions of Promoting the Healthy Development of the Pharmaceutical Industry* 《国务院办公厅关于促进医药产业健康发展的指导意见》	• Accelerating the development of innovative drugs and biological products with major clinical needs; • Speeding up the promotion of green and intelligent pharmaceutical production technologies; • Strengthening scientific and efficient supervision; • Promoting the development of industrial internationalization.
Mar, 2016	CFDA	*Plan of the System of the Holders of Drug Marketing Licenses* 《药品上市许可持有人制度试点方案》	• Drug research and development institutions or scientific research personnel in the pilot administrative areas may serve as drug applicants for registration, and submit applications for drugs clinical trials and marketing.
Oct, 2016	State Council	*Healthy China 2030* 《"健康中国2030"规划纲要》	• Strengthening technical innovation by forming a Government-Industry-University-Research Cooperation efficient system; • Improving the quality control system of drug and medical devices. By 2030, quality standards for drugs and medical devices would be fully integrated with international standards.
Dec, 2016	State Council	*13th Five-Year Plan for National Strategic Emerging industry Development* 《"十三五"国家战略性新兴产业发展规划》	• Accelerating the innovation and industrialization of new drugs. • Promoting the development of high-tech biosimilar drugs such as monoclonal antibodies, long-acting recombinant proteins, and third-generation insulin, and increasing the accessibility of drugs to patients.
May, 2017	CFDA	*Policies of Encouraging Drug Medical Equipment Innovation to Implement Drug Medical Equipment Life Cycle Management* 《关于鼓励药品医疗器械创新实施药品医疗器械全生命周期管理的相关政策（征求意见稿）》	• Accelerating the informationization of review and approval system. • Formulating the technical requirements for the electronic submission of drug and medical device registration. • Improving the general electronic documentation system.

Source: Government Website, Frost & Sullivan Analysis

Favorable Government Policy of Pharmaceutical Industry

Review of Innovation Encouragement

Release Date	Issuing Authority	Policies	Comments
Oct, 2017	CFDA	*Reform of Review and Approval System for Drugs and Medical Devices to Encourage Innovation (the Opinion)* 《关于深化审评审批制度改革鼓励药品医疗器械创新的意见》	• Seek to streamline the clinical trial process and shorten the time line. • Provid for special fast-track approval for two kinds of drugs and medical devices: (i) new drugs and devices in urgent clinical need; (ii) drugs and devices for rare diseases. • Encouraging innovation and protect innovators through (i) the adoption of a patent linkage system, (ii) restoration of patent term, (iii) protection of innovator's data.
Dec, 2017	CFDA	*Opinions of Implementing Priority Review and Approval to Encourage Drug Innovation* 《总局关于鼓励药品创新实行优先审评审批的意见》	• Establish a comprehensive evaluation system with technical review as the core, in combination with risk-based on-site inspection and sample testing. • Accept foreign data to support MAA if meet China requirements; • Accept application of new dosage form based on clinical needs; • Implement conditional approvals
Jan, 2018	CFDA	*Reform of Review and Approval System for Drugs and Medical Devices to Encourage Innovation (the Opinion)* 《关于深化审评审批制度改革鼓励药品医疗器械创新的意见》	• Promote the integration of drug registration technical standards with international standards. • Accelerate the drug examination and approval process. • Strengthening the management for drug life cycle.
Jan, 2018	CFDA	*Opinions of Strengthening and Promoting Scientific and Technological Innovation in Food and Drugs* 《关于加强和促进食品药品科技创新工作的指导意见》	• Encourage innovation and protect innovators through (i) Improve the support of scientific and technological innovation in the field of food and drug. (ii) Establish and improve the supporting network for scientific research. (iii) Enhance companies' technological innovation capability. (iv) Strengthen the construction of major technological innovation platforms. (v) Establish incentive and reward mechanism for talents.

Source: Government Website, Frost & Sullivan Analysis

Favorable Government Policy of Pharmaceutical Industry

Review of Innovation Encouragement

Release Date	Issuing Authority	Policies	Comments
Mar, 2018	CFDA	*Guidance for Pharmaceutical Research in Phase III Clinical Trials of Innovative Drugs (Chemicals)* 《创新药(化学药) III期临床试验药学研究信息指南》	• Encourage R&D of new and innovative drugs. • Accelerate establishment of the standard system of technical guidelines for R&D and examination and approval process of innovative pharmaceuticals. • Improve the quality and efficiency new R&D review.
Feb, 2019	MoF	*Notice on VAT policy for rare disease drugs* 《关于罕见病药品增值税政策的通知》	• To encourage the development of the rare disease pharmaceutical industry and reduce the cost of medication for patients. VAT general taxpayers who produce, wholesale and retail rare disease drugs can pay VAT at a 3% levy rate according to the simple method, starting from March 1, 2019.
Jul, 2019	NMPA	*Announcement on Further Improving the Correlated Matters of Drug Related Evaluation, Approval and Supervision* 《关于进一步完善药品关联审评审批和监管工作有关事宜的公告》	• Encourage innovative drugs by optimizing the approval process. • Further clarifies the review, approval and supervision of the association between active pharmaceutical ingredients, excipients, and immediate packaging materials and containers as well as pharmaceutical products.
Aug, 2019	NMPA	*Pharmaceutical Administration Law of the People's Republic of China* 《中华人民共和国药品管理法》	• It is the second major systematic and structural amendment to the Pharmaceutical Administration Law since its first promulgation in 1984. • Focus on supporting clinical value-oriented drug innovations which have significant effects on human disease. Encourage the development of new medicines with new treatment mechanism on severely life-threatening diseases, rare diseases and children's diseases. • Establish related laws of clinical trial acquiescence system, clinical trial institution filing management system, priority review and approval system, conditional approval system, etc. • Established a listing authorization system to encourage innovation.

Source: Government Website, Frost & Sullivan Analysis

Favorable Government Policy of Pharmaceutical Industry

Review of Innovation Encouragement

Release Date	Issuing Authority	Policies	Comments
Jul, 2020	NMPA	*Announcement on the Release of Three Documents such as the Work Procedure for the Evaluation of Breakthrough Therapy Drugs (trial)* 《关于发布《突破性治疗药物审评工作程序（试行）》等三个文件的公告》	• To cooperate with the implementation of Drug Registration Administration Measures, hese work procedures are developed: (i) Review and Evaluation Procedures for Breakthrough Therapy Drugs (Trial) (ii) Review and Approval Procedures for conditionally approved marketing application of drugs (Trial) (iii) Procedure for Priority Evaluation and Approval of Drug Marketing Authorization (Trial)
Sep, 2020	MoF	*Announcement on the Release of the Second Batch on Anticancer Drugs and Orphan Drugs Applicable to the VAT Policy* 《关于发布第二批适用增值税政策的抗癌药品和罕见病药品清单的公告》	• In order to encourage the development of pharmaceutical industry, and reduce the cost of drugs for patients, the second list includes 39 pharmaceutical products, 6 active pharmaceutical ingredients of anticancer drugs and 14 pharmaceutical products of orphan drugs. VAT general taxpayers who produce, wholesale and retail those drugs can pay VAT at a 3% levy rate according to the simple method, starting from Octor 1, 2020.
Dec. 2020	NHSA	*Announcement on the "Internet + healthcare" "five one" service action* 《关于深入推进“互联网+医疗健康”“五个一”服务行动的通知》	• Support the pharmaceutical industry by making the payment process quicker and easier, simplifying the healthcare services and applying digitalization methods.
Sep. 2021	NHSA, NMPA	*The "14th Five-Year Plan" National Drug Safety and High-quality Development Plan Promotion* 《“十四五”国家药品安全及促进高质量发展规划印发》	• Support high-quality industrial development of the regulatory environment and system reform. • Approving many innovative drugs in urgent clinical need. • Accelerate the listing of innovative drugs with clinical value and innovative medical devices as soon as possible in the domestic market. • Formulate and revise 2650 standards and 480 new guidelines on drugs, medical devices, and cosmetics.

Source: Government Website, Frost & Sullivan Analysis

Favorable Government Policy of Pharmaceutical Industry

Review of Innovation Encouragement

Release Date	Issuing Authority	Policies	Comments
Dec. 2021	NHSA	*Guidance from the National Health Insurance Administration and the State Administration of Traditional Chinese Medicine on Medical Insurance Support for the Development of Traditional Chinese Medicine Inheritance and Innovation* 《国家医疗保障局和国家中医药管理局关于医保支持中医药传承创新发展的指导意见》	• Medical insurance to support the development of Chinese medicine heritage and innovation • Policy to include eligible TCM institutions into the medical insurance designated points and to include "Internet+" TCM services into the scope of medical insurance payment
Jun. 2022	MoF	*Support rare disease drugs for children, medical insurance negotiations are imminent, and competition rules will be improved* 《支持儿童用药罕见病用药 医保谈判在即竞争规则再完善》	• According to the policy, the 2022 medical insurance catalog adjustment will mainly include COVID-19 drugs, children's drugs and drugs for rare diseases. • Negotiated drugs that expire at the end of this year, or drugs with significant changes in indications or functionalities will have the opportunity to be re-included in the negotiation list. • It is expected that this year's medical insurance catalog will have a certain focus on pediatric drugs and rare disease drugs, and the medical insurance catalog will further expand the scope of disease coverage.

Source: Government Website, Frost & Sullivan Analysis

Favorable Government Policy of Pharmaceutical Industry

Review of Innovation Encouragement

Release Date	Issuing Authority	Policies	Comments
Aug. 2023	NMPA	*Work Process for Conditional Approval of Drug Marketing Authorization Applications (Trial) (Revised Draft for Solicitation of Comments)* 《药品附条件批准上市申请审评审批工作程序(试行)(修订稿征求意见稿)》	• After obtaining conditional marketing approval for a certain drug, it is generally not permissible to approve other similar drugs with the same mechanism, target, and indication for conducting clinical trials aimed at obtaining conditional marketing authorization.
Nov. 2021	CDE	*Guiding Principles for Clinical Development of Antitumor Drugs Oriented towards Clinical Value* 《以临床价值为导向的抗肿瘤药物临床研发指导原则》	• In the selection of control drugs, attention should be paid not only to safeguarding the rights and interests of trial subjects during clinical trials but also to ensuring the rights and interests of a wide range of patient populations after drug marketing. When selecting a positive drug as a control, consideration should be given to whether the positive control drug reflects and represents the best treatment choice for the target patients in clinical practice; when planning to select a placebo or best supportive care (BSC) as a control drug, it should be ensured that there is no standard treatment for the indication in clinical practice. When BSC is available, it should be preferred as the control over a placebo.
Jul. 2023	CDE	*Guiding Principles for Patient-Centric Drug Clinical Trial Design Techniques (Trial)* 《以患者为中心的药物临床试验设计技术指导原则（试行）》	• Selecting the best and accessible control for the subjects should avoid using inferior treatments as controls, which could impact the subjects' treatment choices.

Source: Government Website, Frost & Sullivan Analysis

Favorable Government Policy of Pharmaceutical Industry

Review of Innovation Encouragement

Release Date	Issuing Authority	Policies	Comments
Jul. 2023	Shanghai Healthcare Security Administration and other departments	*Several Measures to Further Improve the Diverse Payment Mechanisms in Shanghai to Support the Development of Innovative Drugs and Medical Devices* 《上海市进一步完善多元支付机制支持创新药械发展的若干措施》	• By strengthening measures such as commercial insurance, promote the affordability of innovative drugs.
Jan. 2024	General Office of the CPC Central Committee, General Office of the State Council	*Implementation Plan for Comprehensive Reform Pilot in Pudong New Area (2023-2027)* 《浦东新区综合改革试点实施方案(2023 - 2027年)》	• According to relevant regulations, the pricing of innovative biopharmaceutical products are allowed to refer to similar drugs overseas, supporting the development of innovative drug and medical device industries.
Jan. 2024	NMPA	*Announcement on Matters Related to Optimizing the Registration Application for the Transfer of Overseas Manufactured Drugs Already Marketed Domestically to Domestic Production* 《关于优化已在境内上市的境外生产药品转移至境内生产的药品上市注册申请相关事宜的公告》	• For the transfer of overseas manufactured drugs already marketed domestically to domestic production, relevant pharmaceutical, non-clinical, and clinical research data (where applicable) may be submitted based on the original registration application materials for the overseas manufactured drugs, along with the submission of related research data for the transfer to domestic production. Specific requirements for the application materials will be separately formulated and issued by the CDE. • For the marketing registration application of chemically synthesized drugs and biologics transferred from the original research to domestic production, the NMPA should include them in the scope of priority review and approval.

Source: Government Website, Frost & Sullivan Analysis

Growth Drivers of China Pharmaceutical Market

Increasing Disposable Income	• China resident annual disposable income has experienced fast growth in the past few years, increasing from RMB25,974.0 in 2017 to RMB35,128.0 in 2021 at a CAGR of 7.8% during this period. With the economic development, the per capita annual disposable income is expected to further grow to RMB47,262.0 in 2025. The growth of per capita annual income of Chinese residents has a positive effect on the purchasing power and the level of health awareness among the Chinese population.
Aging Population	• As the overall metabolic and immune capacities of elder people gradually decline, they are more likely to suffer from chronic diseases, and therefore incur high costs on long-term medication and scientific disease management. The aging population reached 200.6 million in 2021, accounting for 14.2% of the total population. The proportion is projected to further increase to 17.3%, representing a population 247.1 million in 2025.
Favorable Policies	• Chinese government promulgated a series of policies to encourage R&D, as well as strengthen the regulation on the pharmaceutical market. • For example, shortening the review and approval time span for innovative drugs IND and BLA applications will accelerate the process of drugs with the potential to address the urgent clinical needs to get into the market. Patent protection is greatly enhanced as well. All these reforms will attract MNC pharmas to launch more innovative drugs to China market. Furthermore, the government has issued favorable policies in terms of tax reduction, talents incentive programs and special public R&D funds to support R&D activities of domestic companies in particular. • A series of strengthening regulations, such as new GMP and two-invoice implementation, will lead to a more efficient and disciplined pharmaceutical market with healthy competition and sustainable development.
Improve Public Medical Insurance	• Public medical insurance is the largest single-payer for pharmaceuticals in China. The latest version of NRDL not only expand to include more drugs to be reimbursable but also adopt dynamic adjustment via price negotiation to include more advanced drugs in the List with a more economical price. Currently, there are 2,860 drugs in the NRDL

Source: Frost & Sullivan analysis

Future Trends of China Pharmaceutical Market

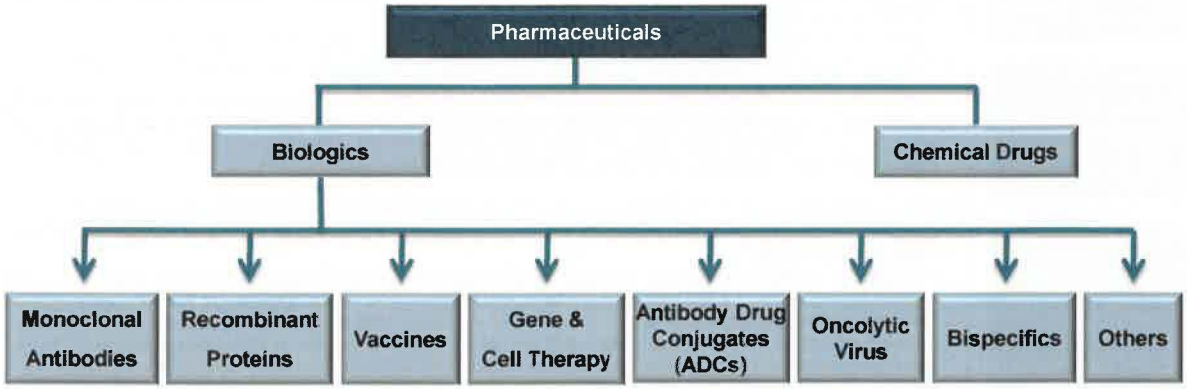
Expansion of Innovative Drug Market	• With the pilot scheme of centralized procurement of generics and inclusion of innovative drugs into NRDL, it is believed that China pharmaceutical market is shifting towards the innovation-driven market. Also, the government promulgated a series of policies to encourage R&D, such as accelerated drug review and approval, patent protection, tax reduction, etc. The development of innovative drugs is therefore encouraged and will lead to innovative drug market expansion in the future.
More Biotech Companies to Get Involved	• Due to the strong support from the government, capital investment and talent reserve, biotech companies are expected to play a more important role in the pharmaceutical market with their innovative drugs under clinical development and to be launched in the near future. For example, China market has launched 12 PD-1/PD-L1 drugs so far, with their sales revenue reaching tens of millions in a few months, showing the huge potential of innovative drugs in China pharmaceutical market. This will attract more biotech companies to get involved.
Alignment with International Standard	• In recent years, China has joined the ICH as the 8th number, which emblems the onset of alignment of the pharmaceutical industry practices with international standards, indicating an effort to realize a gradual transformation of drug application and registration process toward the higher and unified standard. It is expected that the drug review and approval system will be gradually improved.
Novel Therapies Available to Patients Sooner	• Historically, novel therapies usually have a gap of a few years in approval time between China and other major markets due to a less efficient approval process. The gap is narrowed through reform on the review and approval process as well as the ICH alignment. The approval process is further accelerated through enabling priority review and listing the drugs of clinically urgent, potentially bringing more novel drugs to China market in a more timely manner. In this way, effective novel therapies will benefit patients sooner.

Source: Frost & Sullivan analysis

Biologics Market Segmentation

- Segmentation is based on existing and emerging biologics products, which may vary across regions.

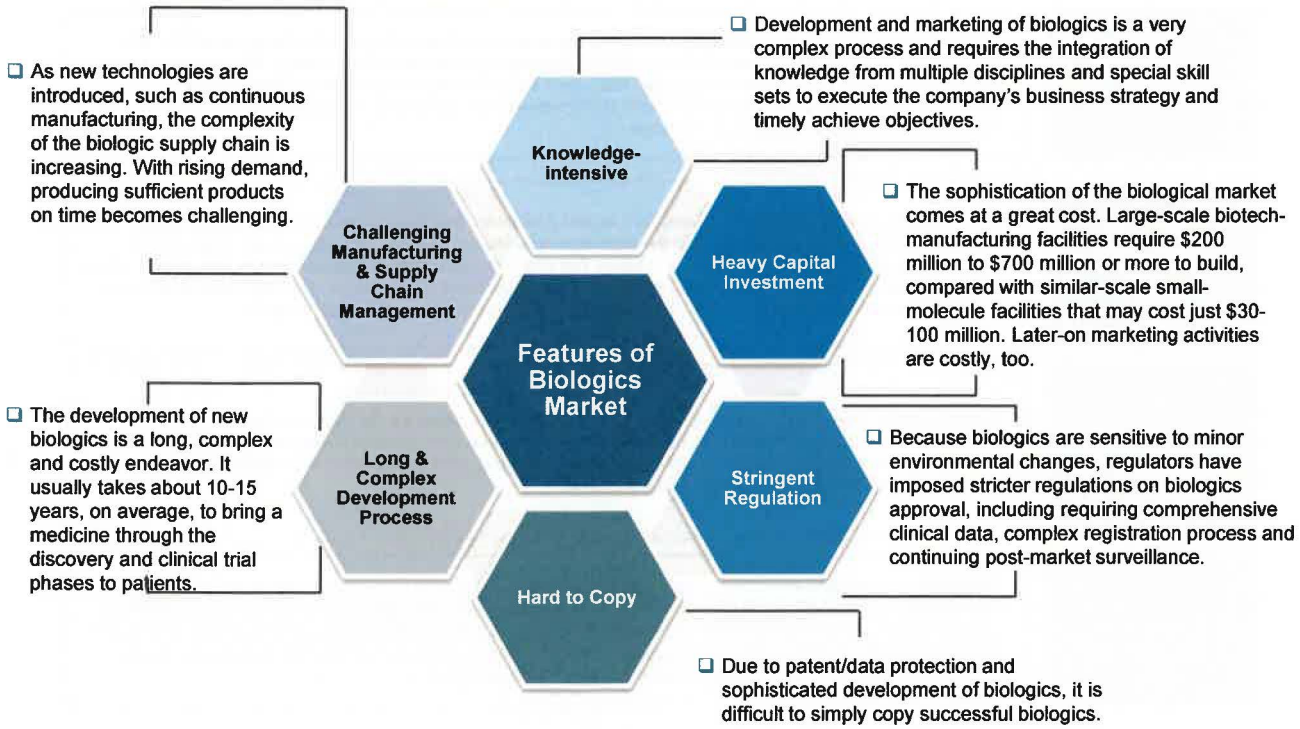
Total Biologics Market: Market Segmentation, Global



- **Definition:** The FDA is defining Biologics as products that include a wide range of products such as vaccines, blood and blood components, allergenic, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins. Biologics are isolated from a variety of natural sources - human, animal, or microorganism - and may be produced by biotechnology methods and other cutting-edge technologies. In addition, gene-based and cellular biologics often are at the forefront of biomedical research and emerging category such as ADCs and oncolytic virus have also been put in the spotlight.

Source: FDA, Frost & Sullivan analysis

Features of Biologics Market



Source: Frost & Sullivan analysis

Comparison of Manufacturing in Biologics and Small Molecule Drugs

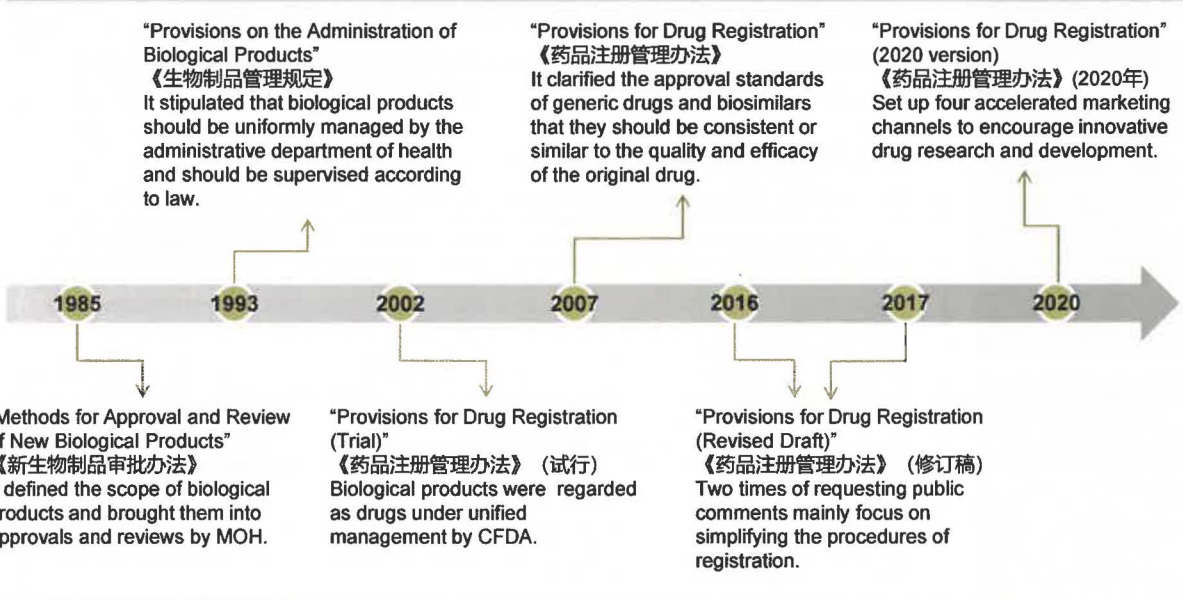
- Compared with chemical drugs, there are dozens of challenges that manufacturers have to deal with during biologics manufacturing. Such a large gap in the manufacturing process is attributed to the large and complex biologic molecule, which puts stringent requirements on harvest, formulation, environment control, etc.

	Small Molecule Drugs	Biologics
Methodology	• Chemical drugs are manufactured by chemical synthesis in laboratories.	• Biologics are expressed in mammalian cells (mice, rabbits, etc.) or micro-organisms (yeast, fungi, etc.).
Downstream	• Downstream processing is relatively simple, as it involves only a few steps, such as crystallisation, chromatography, or filtration.	• Downstream processing is highly complex, involving multiple steps depending upon the host or product manufactured.
Manufacturing Stage	• Different manufacturers at different stages of product manufacturing are available, such as APIs, intermediates, and finished formulation.	• All stages of product manufacturing are dealt with by a single manufacturer, only fill and finish activities can be decentralised.
Formulation	• Finished dose formulations are solids (capsules, tablets); semi-solids (ointments, creams, sprays, emulsions, gels); and liquids (syrups).	• Formulations are predominantly injectables, such as sterile, pre-filled syringes, or cartridges.
Others	• Manufacturing equipment is not designed for aseptic processes. • Manufacturing processes are less sensitive to changes in the environment.	• Manufacturing equipment is mainly designed for aseptic conditions. • Manufacturing processes are highly sensitive to changes in the manufacturing environment.

Source: Frost & Sullivan analysis

China Regulatory Regime of Biologics

- In 1985, the first regulation on the biological product was published, and in 2002, the "Provisions for Drug Registration (Trial)" first regulated biologics and chemical drugs with the same policy. In 2017, the fourth version of "Provisions for Drug Registration (Revised Draft) ", of which the regulations standard of biological products are adjusted to simplify the registration procedures was issued and the 2007 version was no longer effective after then.



Source: NMPA, Frost & Sullivan analysis

Analysis of Future Trends in the Biologics Market

The rise of cell and gene therapy	• Limitations of traditional cellular immunotherapy drive the development of combination cellular and gene therapy. Cell and gene therapy (CGT) is a new frontier in the treatment of cancer and genetic diseases and is currently a promising development in biomedicine. For example, CAR-T technology adds chimeric antigen receptors to T cells through gene editing, resulting in CAR-T cells that can effectively capture and kill tumor cells to achieve therapeutic effects. The core distinction of CGT therapy over traditional chemotherapy or antibody drugs is that it requires a single treatment with long-term benefits. In addition, because CGT therapy is designed to cure patients by changing their cell genes, it provides a new treatment option for some diseases that are ineffective and difficult to treat with traditional therapies and is a major trend in the future biologics market.
Innovative antibody therapies continue to advance	• While monoclonal antibodies continue to dominate the overall antibody drug landscape, as antibody drug technology continues to evolve, antibody drugs have generated many innovative strategies, such as dual antibodies and antibody-drug conjugates (ADCs). Compared to monoclonal antibodies, the bispecific antibodies are better at targeting and has a stronger potential therapeutic effect. ADC drugs combine the powerful killing power of small molecules with the high targeting and specificity of monoclonal antibodies, allowing for more precise delivery to tumor cells and less killing of normal cells. The evolution of innovative antibody therapies such as bispecific antibodies and ADC drugs (e.g., the selection and optimization of conjugation processes and small-molecule toxins) will be a major trend in the future of the biologics market.
Competitive biosimilar market improves drug accessibility	• With the expiration of patents on original biologics and the continuous development of biotechnology, the development of biosimilars based on the quality, safety and efficacy of the original biologics is accelerating and the competition getting fierce, with most of the developed products currently focused on rituximab, trastuzumab, bevacizumab, and adalimumab. The development and approval of more and more biosimilars also mean that the accessibility of related drugs will be improved, and patients will continue to benefit from the development of the biologics market in the future. At the same time, the possibility of biologics/biosimilars being included in pooled procurement will also create a new impact on the biologics market in the future.

Source: Frost & Sullivan Analysis

Key Growth Drivers of China Biologics Market

Growing Disease Incidence	• Driven by unhealthy lifestyles, pollution, and the aging population, the number of patients with chronic diseases in China continues to expand. For example, total annual cancer incidence in China increased from 4,061 thousand in 2016 to 4,596 thousand in 2020, and this number expected to reach 5,812 thousand in 2030. In the area of metabolic diseases, prevalence is also expected to increase. For example, the prevalence of type 2 diabetes in China increased from 116.6 million to 131.1 million in 2020, and this number is expected to reach 167.7 million in 2030. Biological drugs have excellent clinical effects on many chronic diseases, including cancer and diabetes, and the huge patient population pool will further drive market growth.
Increasing R&D Investments	• The biologics industry is capital-intensive and requires heavy investment in research and development. In China, the research and development spending on biologics increased from RMB 62.8 billion to RMB 126.3 billion with a CAGR of 19.1% from 2016 to 2020. R&D expenditure on biologics is expected to reach RMB 308.8 billion in 2030, indicating a promising future with more biologics approved and brought to the market.
Regulatory Reform and Favorable Government Policies	• The China government has established a set of regulations and policies to support the development of China's biologics market. Notably, in October 2017, the General Office of the CPC Central Committee and the General Office of the State Council issued the Opinions on Deepening the Reform of the Evaluation and Approval Systems and Encouraging Innovation on Drugs and Medical Devices (《关于深化审评审批制度改革鼓励药品医疗器械创新的意见》), which aims to improve the regulatory regime for the biologics industry, encourage the technological innovation for new drugs and enhance the competitiveness of the biologics industry. With respect to biosimilars, the Centre for Drug Evaluation (CDE) promulgated《生物类似药相似性评价和适应症外推技术指导原则》, which puts forward clear regulatory requirements for product development and indication extrapolation for biosimilars.
Increasing Affordability and Healthcare Awareness	• In China, the per capita disposable income has grown rapidly from 23,821 RMB in 2016 to 32,189 RMB in 2020. This increase in disposable income is reflected in the increase in healthcare expenditure, and this trend is expected to continue. In recent years, the inclusion of biologics into NRDL further increases accessibility and affordability of biologics. In addition, in November 2021, China's latest centralized drug procurement involved centralized purchase of insulin, which is the first biological drug involved in the centralized procurement program. After the centralized purchase, the average price cut and highest price cut are 48% and 74%, respectively, which sets an example for improvement in biologics affordability through centralized drug procurement. With the increasing biologics affordability and the improvement of health awareness, domestic demand for biological drugs will burgeon in the future.

Source: Frost & Sullivan Analysis

Global Top 10 Biologics by 2024 Sales Revenue

- By sales in 2024, the top ten biologics in the world mainly include antibodies, vaccines and peptide drugs, one of which is used to treat ophthalmic diseases.

Rank	Brand Name	Generic Name	Company	2024 Sales, Billion USD
1	Keytruda	Pembrolizumab	Merck & Co.	29.5
2	Ozempic	Semaglutide	Novo Nordisk	17.5
3	Dupixent	Dupilumab	Sanofi/Regeneron	14.1
4	Skyrizi	Risankuzumab-rzaa	Abbvie	11.7
5	Darzalex	Daratumumab	Johnson & Johnson	11.7
6	Mounjaro	Tirzepatide	Lilly	11.5
7	Stelara	Ustekinumab	Johnson & Johnson	10.4
8	Opdivo	Nivolumab	BMS/Ono pharmaceutical	10.2
9	Eylea	Aflibercept	Bayer/Regeneron/Santen	9.5
10	Humira	Adalimumab	AbbVie	9.0

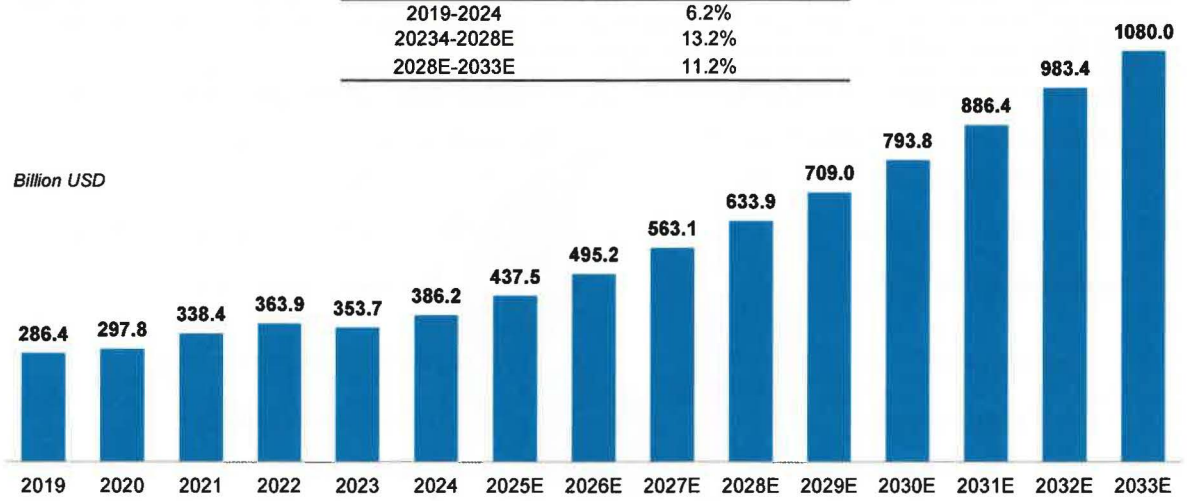
Source: Frost & Sullivan Analysis

Global Biologics Pharmaceutical Market Size and Forecast, 2019-2033E

- Global biologics market, accompanying with the growth of economy and healthcare demand, increased from USD 286.4 billion in 2019 to USD 386.2 billion in 2024, and then will further increase to USD 633.9 billion in 2028, with CAGR of 11.2% from 2024 to 2028.

Global Market Size and Forecast, 2019-2033E

Period	CAGR
2019-2024	6.2%
20234-2028E	13.2%
2028E-2033E	11.2%



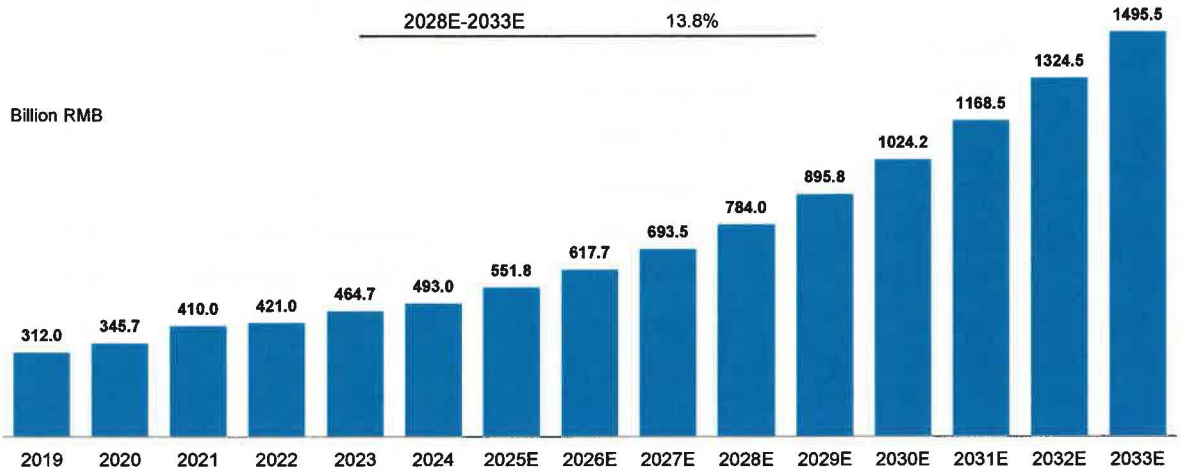
Source: Annual Reports of Listed Medical Companies, NMPA, CDE, NRDL, MOHRSS, FDA, Frost & Sullivan Analysis

Biologics Market Size and Forecast in China, 2019-2033E

- Chinese biologics market, accompanying with the growth of economy and healthcare demand, increased from RMB 312.0 billion in 2019 to RMB 464.7 billion in 2024, and then will further increase to RMB 784.0 billion in 2028, with CAGR of 12.3% from 2024 to 2028.

Biologics Market Size and Forecast in China, 2019-2033E

Period	CAGR
2019-2024	9.6%
20234-2028E	12.3%
2028E-2033E	13.8%

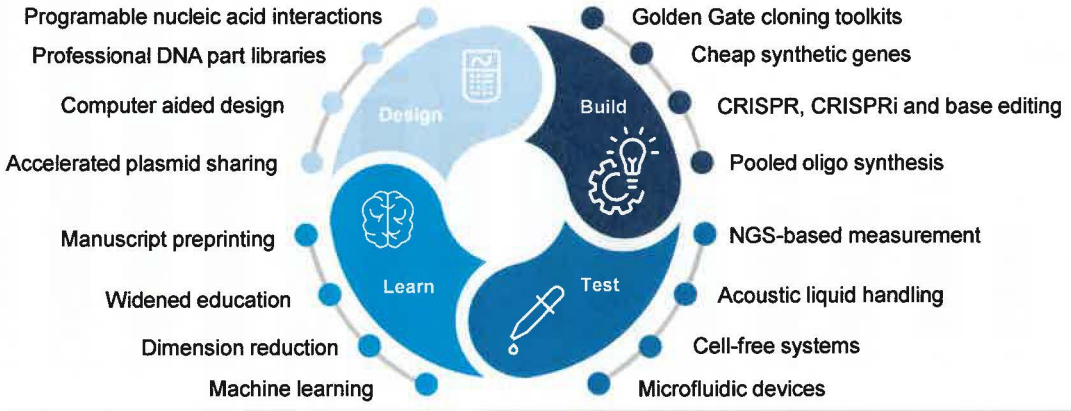


Source: Annual Reports of Listed Medical Companies, NMPA, CDE, NRDL, MOHRSS, Frost & Sullivan Analysis

Overview of Synthetic Biology

- Synthetic biology was first proposed by Hobom B. in 1980. However, with the continuous advancement of technology and technology, synthetic biology has gradually developed in recent years. Scientists can design components and modules according to specific needs, transform and optimize biological systems, and ultimately produce new, non-natural substances with unique structures. Through targeted editing of the genome and regulation of cellular metabolic pathways, synthetic biology technology can effectively increase the expression of major products. It also inhibits side metabolic pathways, increases production while reducing the generation of by-products, and has the advantages of less environmental pollution and low cost. Different from traditional chemical synthesis, biosynthetic products are more complex and diverse in chemical structure and can synthesize some substances that are difficult to chemically synthesize. The unique chemical structure of its products provides good targeting and biological activity. Therefore, it is of great significance in the drug development and production process.

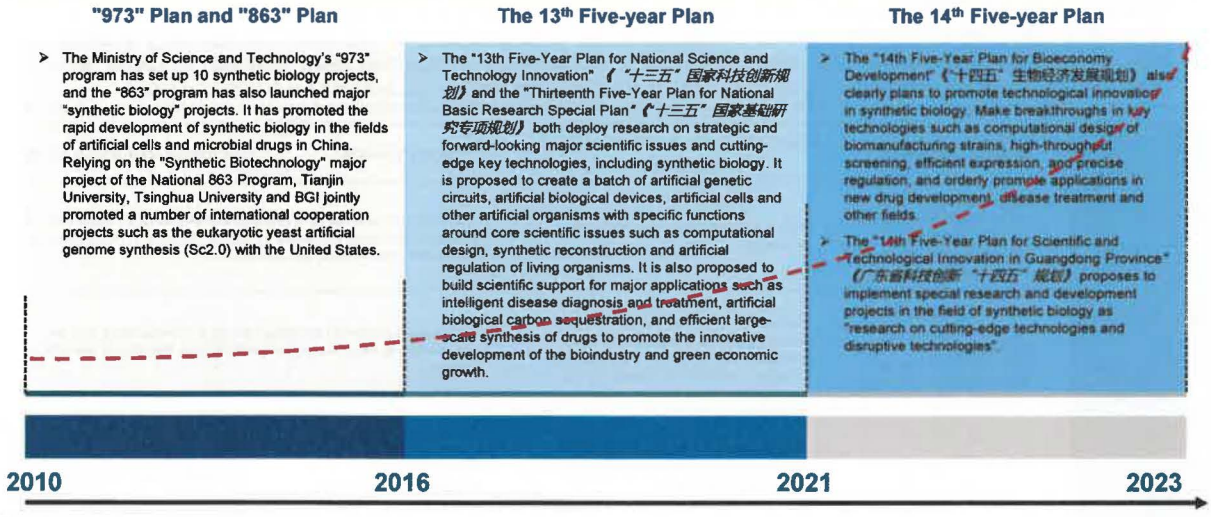
New Enabling Technologies and Ways of Working Accelerate Synthetic Biology's Design-build-test-learn Cycle



Source: Literature Review, Frost & Sullivan Analysis

Favorable Policies for Synthetic Biology

- In the healthcare field, most biopharmaceutical companies have established complete monoclonal antibody production systems, using mice or cell lines to mass-produce monoclonal antibody drugs with reliable quality. However, due to the high technical barriers of combinatorial biosynthesis, only a few companies are currently able to produce drugs through combinatorial biology platforms.
- In recent years, the Chinese government has vigorously supported innovation, continuously introduced relevant incentive policies, and continued to plan and deploy cutting-edge fields. As a result, synthetic biology has developed rapidly.



Source: Frost & Sullivan Analysis

Drug Manufacturing Platform Comparison

	Direct Extraction	Chemical Semi-synthesis/Total Synthesis	Biosynthesis	Combinatorial Biosynthesis
Technology Requirements	• No special technical requirements, easy to get started and universally applicable	• It has a complete industrial chain and clear synthesis route, and its existing experimental equipment and industrial equipment are very mature.	• Through methods such as gene editing, the required genes can be transferred into engineered bacteria or cell lines to produce drugs in large quantities.	• On the basis of biosynthesis, through the modification and recombination of foreign genes, the structure of the compound is modified in a targeted manner, the expression level of the product is optimized, and the metabolites are controlled, so as to synthesize a large number of new complex substances.
Raw Materials/Cost	• Extracted from plants, roots, stems and leaves. • High cost.	• A large number of semi-synthetic precursor substances exist in plants, and the cost is greatly reduced.	• The starting raw materials are all from readily available raw materials such as amino acids, sugars, and inorganic salts. No toxic low-boiling point organic solvents are involved, and the cost of raw materials is low.	
Purity	• The purity is low, there are a lot of impurities, and it takes a lot of time to detect and purify.	• Through chemical synthesis, the purity of the synthetic products is consistent and the types of impurities are limited, making it easy to control trace impurities and reducing inspection time.	• With the development of biotechnology, purification and separation efficiency are higher and high-purity products can be provided.	
Activity	• Lower purity and complex purification processes will affect the biological activity of the product.	• There is insufficient control over the spatial structure of the product, and the biological activity is moderate.	• Its unique chemical structure confers diverse biological activities and the ability to specifically combine with specific targets.	
Environmentally Friendly /Renewable	• Over-exploitation will cause irreversible damage to the environment.	• Although synthetic precursor substances exist in large quantities, overexploitation can also endanger ecology and species.	• Usually using renewable biological resources as raw materials, it has the advantages of high efficiency, green and sustainable. Most of the reaction steps in biosynthesis are carried out under the action of microorganisms or enzymes, and the reaction conditions are milder and the process is simpler.	

Source: Literature Review, Frost & Sullivan Analysis

Analysis of Technological Advantages, Disadvantages and Barriers Drug Manufacturing Platform

- Drug manufacturing methods use different platforms depending on the type of drug. Direct extraction is now rarely used in drug production due to its low yield, high impurities, and unfriendly environment.
- At present, the main drug synthesis methods are chemical semi-synthesis/total synthesis, which are widely used in the manufacture of most drugs. However, chemical synthesis still has many disadvantages, such as more complex synthesis steps, harsh reaction conditions, and greater environmental pollution.
- In recent years, biopharmaceuticals have developed rapidly, and biosynthetic platforms have gradually emerged and are widely used in the manufacture of biopharmaceuticals. Biosynthesis has the advantages of being green, environmentally friendly, and having mild reaction conditions, and is a new drug manufacturing method with great potential. The current development of combinatorial biosynthesis technology is still in its early stages, and there are still many bottlenecks. Only one innovative anti-tumor drug synthesized using combinatorial biology has been launched in China, and no overseas innovative anti-tumor drug synthesized using combinatorial biology has entered the Chinese market.

	Direct Extraction	Chemical Semi-synthesis/Total Synthesis	Biosynthesis	Combinatorial Biosynthesis
Advantages	• Due to the availability of raw materials, the purity of the product is low, requiring a lot of time to detect impurities and purify.	• High output and high manufacturing efficiency.	• It has high yield and can synthesize biological macromolecules with complex structures. Moreover, the synthesis method is low-cost, environmentally friendly, and has mild reaction conditions.	
Disadvantages	• Due to the availability of raw materials, the purity of the product is low, requiring a lot of time to detect impurities and purify.	• The synthesis steps are complicated and steric hindrance problems are prominent, making it difficult to produce complex biomacromolecule drugs. Moreover, the reaction conditions are violent and the environment is polluted.	• All production processes are completed by microorganisms, and the controllability of the production process is lower than that of chemical synthesis.	
Technical Barriers	• Technical barriers are low.	• The barriers are lower for drugs with simple structures and higher for drugs with complex structures.	• Involving genetic engineering, microbial culture and other technologies, the technical barriers are relatively high	• It not only involves genetic engineering and microbial culture, but also involves the recombination of gene clusters and the regulation of metabolic processes and signaling pathways. The technical barriers are extremely high.

Source: Literature Review, Frost & Sullivan Analysis

Entry Barriers of Synthetic Biology

High Technological Barriers

- Technological barriers are also a challenge for the development and expansion of synthetic biology products. Fundamentally, humans currently have a very limited understanding of DNA and its interactions in biological processes. How to write long and accurate DNA sequences and successfully transfer them into organisms still requires Continuous research. The synthetic biology industry requires long-term strategic layout and heavy capital investment in technologies such as gene editing, DNA synthesis, cellular immunity, and strain modification.
- In mechanical or chemical systems, the laws of interaction are already clear, and each link in the supply chain has honed mature traditional processes. But biological systems are highly complex and cell behavior is more difficult to predict. These factors are challenges for large-scale production. For these complex reasons, more than half of the startups said that they face challenges in pilot expansion. In addition, synthetic biology startups also need to continuously supplement technical solutions, such as laboratory automation and data analysis tools, to improve production efficiency.

Unclear Commercialization Path

- In the past decade, dozens of investment and financing events have occurred in the field of synthetic biology around the world, and the amount of investment and financing in the field of synthetic biology is increasing rapidly. From the perspective of financing rounds, investment and financing rounds in the field of synthetic biology are mainly concentrated in the seed round and the A round. The enthusiasm of capital has also brought many challenges. From the current development of the synthetic biology industry, due to the long R&D cycle, large capital investment, and high technical barriers, the industry threshold is high, so there are currently very few products that can truly be commercialized in the market. And there are also very few companies that can truly achieve commercial production.
- In addition, start-up synthetic biology companies often lack scale advantages, so it is difficult to finance large-scale production. In the absence of funds, they are forced to carry out small-scale production. As a result, costs remain high, and they are unable to prove that there is a solid market demand for synthetic biology products.

Improved Supervision Needed

- Existing regulations may not keep up with the rapid development of synthetic biology technology, resulting in regulatory lags and legal risks, which may bring safety issues on the one hand and affect the participation of synthetic biology products in market competition on the other. The acceleration of the approval cycle and the clarification of support policies will affect the landing of the synthetic biology industry. In contrast, the chemical synthesis path is more mature, with large volume and low cost. Taking peptide intermediates as an example, although biosynthesis is more advantageous and less costly in theory, in China, in order to speed up the approval process, many companies have chosen the method of chemical total synthesis. The current policy has affected the production method decision of enterprises to a certain extent, and also determined the speed of overall industrial transformation.

Source: Frost & Sullivan Analysis

Future Trends of Synthetic Biology

Technology Integration and Innovation	• In the future, synthetic biology will intensify its integration with other fields, such as artificial intelligence, big data, and materials science. This interdisciplinary collaboration has driven continuous innovation in synthetic biology technologies, enabling more efficient and precise gene editing and the design of biological systems. Upstream companies in the industry will focus on the development of enabling technologies, including read-write-edit-learn, automation/high-throughput, and biomanufacturing, paying attention to the disruption of underlying technologies and improving efficiency while reducing costs. In addition, as the biologics market continues to expand, the application of synthetic biology in biomedicine will also continue to expand.
Accelerated Industrial Transformation	• During the rapid growth stage of synthetic biology companies, key industry issues such as the commercialization and product selection of synthetic biology have been gradually taken seriously. In this process, some synthetic biology companies have provided "full-chain" solutions, covering the full-chain development model of "basic research, industrial transformation, and market transformation", which may be more suitable for the development requirements and characteristics of the synthetic biology industry and is expected to become a new industrial development trend. In the process of the full-chain development of synthetic biology, the importance of the "pilot" link has become increasingly prominent, and it is a key link for synthetic biology to cross the "valley of death". my country has currently built the world's largest synthetic biology pilot transformation platform, which is expected to further accelerate the transformation of my country's synthetic biology industry.
Industrial Clusters	• The United States has nurtured most of the world's synthetic biology companies, with a highly concentrated regional distribution. China's synthetic biology is rapidly catching up, with a multi-point bloom in enterprise distribution, forming industrial clusters represented by Shenzhen, Tianjin, and Shanghai. These industrial clusters facilitate communication and cooperation among enterprises, as well as collaboration with research institutions, making them an important part of strategic planning. In the future, China's synthetic biology industry will become more concentrated in industrial clusters or parks. As the application of synthetic biology in the field of biologics continues to deepen, related synthetic biology companies will also deepen cooperation with other biopharmaceutical companies.

Source: Frost & Sullivan Analysis

Overview of Enzyme Engineering Application Areas

• Enzyme engineering utilizes the catalytic function of enzymes to catalyze chemical reactions under certain conditions. It has now been applied to many fields, including life sciences, pharmaceutical industry, light industry, agriculture, food industry and environmental protection. Due to its high reaction efficiency, low pollution, low energy consumption and easy control, its application areas are still expanding.

Life Sciences
Enzyme engineering plays an important role in molecular biology and genetic engineering. For example, restriction endonucleases can recognize specific nucleotide sequences in double-stranded DNA molecules and cut them off; DNA polymerases can be used for DNA labeling, DNA sequence analysis, and amplification of DNA fragments.

Pharmaceutical Manufacturing
Enzyme engineering can replace some traditional pharmaceutical production technologies and reduce production costs. Enzyme engineering can be used to produce biological metabolites, antibiotics, amino acids, vitamins, etc.

Agriculture
Enzyme engineering is applied to the deep processing of agricultural products. The catalytic functions of α-amylase, glucoamylase and glucose isomerase are used to produce high fructose syrup using corn starch as raw materials. The processing of dairy products uses rennet and lactase.

Food Industry
The food industry is the earliest and most extensive industry to apply enzyme engineering technology. In the food field, it can be used for food processing, food preservation, and food measurement and analysis. In the field of food processing, it can be applied to the production process of foods such as starch, dairy products, and juice.

Light Industry
Enzyme engineering has a wide range of applications in light industry, including textile raw material processing, detergent manufacturing, collagen fiber manufacturing, toothpaste and cosmetics production, papermaking, etc. In textile raw material processing, cellulase can reduce the fiber weight or weight, and improve the feel and appearance.

Environmental Science
Enzyme engineering can also be applied to clean production, pollution control and environmental monitoring through effective biodegradation. For example, in wastewater purification for pollution control, enzymes can be used to convert organic matter in wastewater into usable small molecules, thereby achieving the purpose of purification.

Source: Frost & Sullivan Analysis

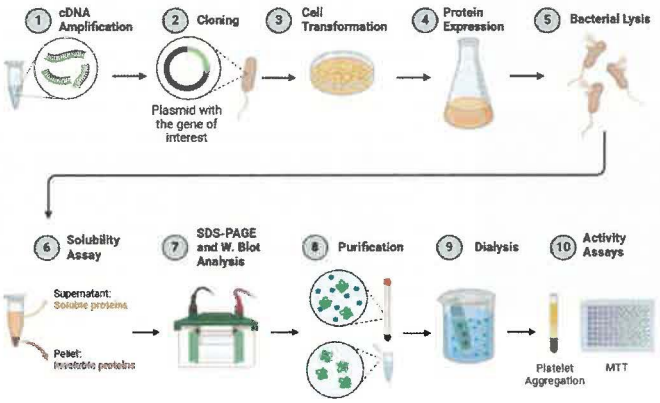
Overview of Recombinant Protein

- Recombinant protein uses gene recombination technology to insert DNA/RNA gene fragments that can be translated into the target protein into host cells that can express the target protein, thereby obtaining a recombinant vector. At present, recombinant protein drugs mainly include peptide hormones, cytokines, recombinant enzymes and other categories. Compared with traditional small molecule chemical drugs, they have more significant efficacy, stronger specificity, lower toxicity, fewer side effects, and clearer biological functions. It has irreplaceable therapeutic effects in the fields of anti-virus, tumor and immunity, and blood diseases.

The steps of this technique usually include:

- 1. Cloning the target gene: Clone the target gene through PCR or gene synthesis and insert it into an appropriate vector
- 2. Transfect host cells: Introduce the recombinant vector into appropriate host cells, such as Escherichia coli, yeast, mammalian cells, etc.
- 3. Express protein: Make the host cell express the target protein through appropriate induction conditions, such as adding chemicals or adjusting environmental factors.
- 4. Purify protein: Extract pure recombinant protein from host cells through appropriate separation and purification techniques, such as affinity chromatography, ion exchange chromatography and gel filtration

Recombinant Protein Manufacturing Process(in E.coli)



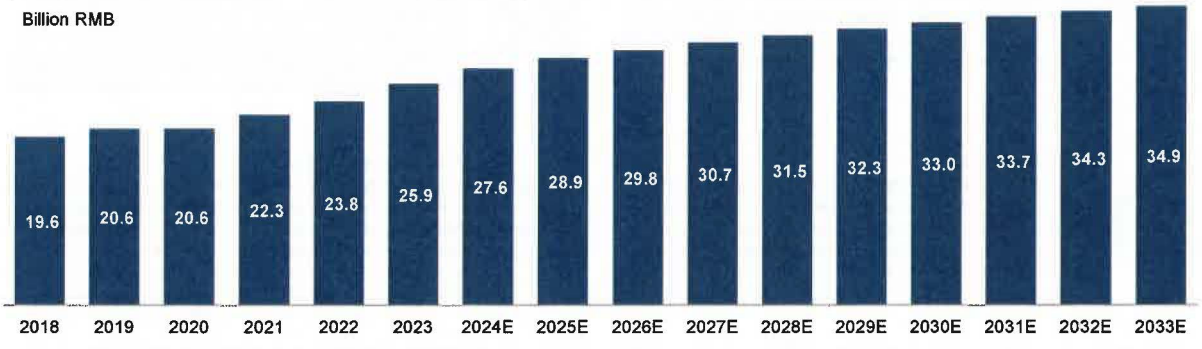
Source: Frost & Sullivan Analysis

Market Size of Recombinant Protein in China, 2018-2033E

- At present, China's recombinant protein market mainly includes interferon, cytokine, recombinant enzyme, etc. Among them, recombinant enzyme drugs are currently mainly used in cardiovascular and other disease fields. Approved drugs such as reteplase, tenecteplase, alteplase, and recombinant human thrombin are currently widely used in bleeding, myocardial infarction and other diseases.

Market Size of Recombinant Protein in China, 2018-2033E

Period	CAGR
2018-2023	5.7%
2023-2028E	4.0%
2028-2033E	2.1%

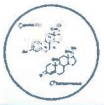


Source: Annual Reports of Listed Medical Companies, NMPA, CDE, Frost & Sullivan Analysis

The Main Types of Biologic Drugs Developed by Synthetic Biology

Recombinant Enzymes and Inhibitors

- Recombinant enzymes are the enzymes isolated from bacteria, yeast or fungus and are produced in huge quantities by being injected into host organisms, through recombinant DNA and protein technology. Most of the unique FDA-approved enzymes are recombinant human enzymes, which are primarily used in replacement therapy.
- They are used in supplement deficiencies in metabolism or digestion, management clotting which can be divided into coagulation and thrombolytic treatments, cancer treatment, toxin degradation and biosynthesizing critical endogenous compounds. They are also used as adjuvants to improve the delivery of antibiotics, chemotherapeutics, and even antibodies, and as antibacterials and antiparasitics.
- Enzyme inhibitors are molecules that interact with enzymes (temporary or permanent) in some way and reduce the rate of an enzyme-catalyzed reaction or prevent enzymes to work in a normal manner. The important types of inhibitors are competitive, noncompetitive, and uncompetitive inhibitors. The primary use of enzyme inhibitors is in medicine, where they target human enzymes to correct pathological conditions or inhibit essential enzymes used by foreign pathogens. Enzyme inhibitors can also serve as insecticides, such as malathion, and herbicides.



Sex Hormones

- Sex hormones are responsible for behavior and sexual differentiation, but also hold a key role in the normal function of various organs, including the brain. Synthetic sex hormones are used in medicine and include gestodene, norgestrel, levonorgestrel, medrogestone, 17α-ethynylestradiol and trimegestone. For instance, synthetic estrogens, most notably ethinylestradiol, in combination with synthetic progestins, are used in contraceptive and hormone replacement therapy formulations.

Antibody and Immunotherapy

- Synthetic biology has promoted the development of monoclonal antibody drugs, which are widely used in the treatment of cancer, immune diseases and infectious diseases. For example, trastuzumab targets breast cancer and adalimumab is used to treat rheumatoid arthritis. In recent years, bispecific antibodies and antibody-drug conjugates (ADCs) have been further enhanced through engineering design. In addition, synthetic cytokines (such as interleukins and interferons) can activate or inhibit immune responses, providing new means for the treatment of viral infections and autoimmune diseases.

Gene and Cell Therapy Products

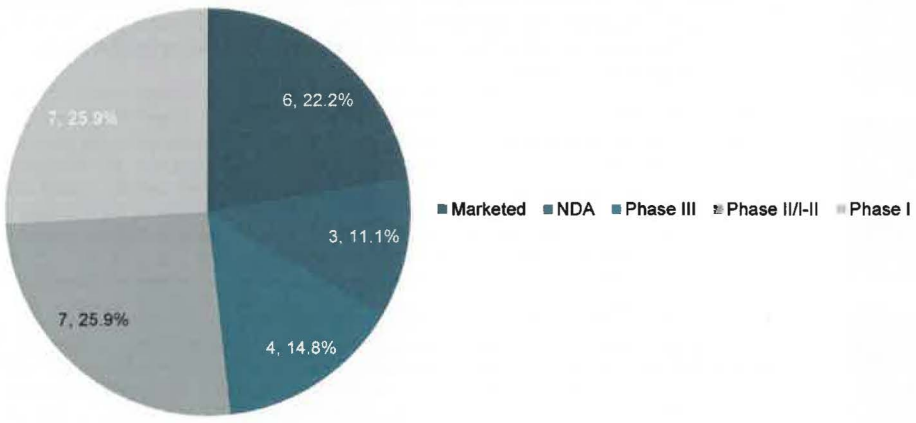
- Gene and cell therapy is a cutting-edge application of synthetic biology, which uses gene editing tools (e.g. CRISPR-Cas9 and TALENs) to accurately repair mutant genes or knock out pathogenic genes. Engineered T cells (e.g. CAR-T cells) provide a revolutionary approach to cancer treatment, while synthetic gene circuits can regulate cell behavior for the precise treatment of complex diseases. These technologies, combined with the advantages of large-scale production, make personalized and efficient treatment possible.

Source: Literature review, Frost & Sullivan analysis

Breakdown of Recombinant Enzymes Pipeline in China

- The pipeline for recombinant enzymes in China shows a strong focus on early-stage development. Among the candidates, 6 have been marketed, accounting for 20.7% of the total. Meanwhile, 3 (10.3%) are in the NDA stage, 4 (13.8%) are in Phase III, and the majority are in earlier phases, with 7 (24.1%) in Phase II/I-II and another 7 (24.1%) in Phase I. This highlights an emphasis on advancing candidates through initial clinical trials.

Breakdown of Recombinant Enzymes Pipeline in China



Note: As of 2025.01.14

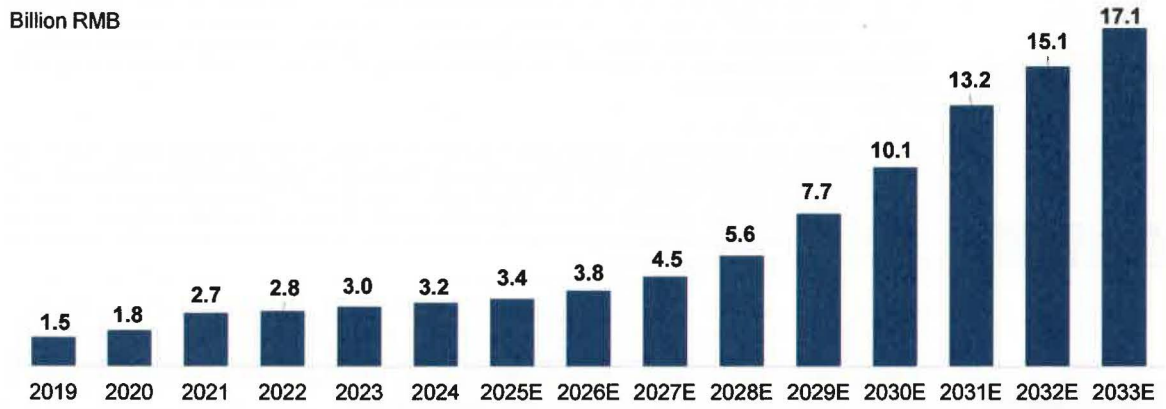
Source: Frost & Sullivan Analysis

Recombinant Enzymes Market in China, 2019-2033E

- From 2019-2024, the recombinant enzymes market in China grew from RMB 1.5 billion to RMB 3.2 billion, with a CAGR of 16.8% during this period. It is expected that by 2029, the market size will grow to RMB 7.7 billion, and by 2033, to RMB 17.1 billion.

Recombinant Enzymes Market in China, 2019-2033E

Period	CAGR
2019-2024	16.8%
2024-2029E	19.1%
2029E-2033E	22.0%



Source: Annual Reports, NMPA, CDE, Literature review, Frost & Sullivan analysis

Entry Barriers for Recombinant Enzymes

Technological Complexity	• Recombinant enzyme development requires advanced expertise in molecular biology, protein engineering, and bioprocessing. This knowledge is necessary to design, produce, and optimize enzymes with specific activity, stability, and functionality. Additionally, bioinformatics tools and techniques for genetic manipulation add to the complexity. Only organizations with cutting-edge R&D capabilities can effectively compete in this domain. Furthermore, enzyme expression often relies on intricate systems like bacteria, yeast, or mammalian cells, each requiring tailored protocols.
Regulatory Hurdles	• Stringent safety and efficacy standards imposed by regulatory authorities like the FDA or NMPA make market entry challenging. Each enzyme must undergo rigorous testing in preclinical and clinical trials to ensure safety and functionality. Regulatory compliance also extends to the production process, which must meet Good Manufacturing Practices (GMP) standards. Acquiring approvals is time-consuming and requires significant investment in documentation, auditing, and certification. Failing to meet these requirements can delay or block market access entirely.
High Initial Investment	• The development of recombinant enzymes demands substantial financial resources for research, production facilities, and quality control. State-of-the-art bioreactors, purification systems, and analytical equipment are costly but necessary for large-scale production. Additionally, companies need to invest in skilled personnel, including molecular biologists, biochemical engineers, and regulatory experts. Scaling up production from lab-scale to commercial-scale requires further capital expenditure. Small or new companies often struggle to secure the funds needed to compete with established players.
Market Dynamics and Competition	• The recombinant enzyme market is dominated by established players with strong brand recognition and proprietary technologies. Companies like Novozymes, Roche, and Amgen have extensive distribution networks and long-standing customer relationships. These incumbents also protect their market positions with extensive patent portfolios, creating legal barriers for newcomers. Additionally, pricing pressures and customer expectations for high-quality products create challenges for new entrants to differentiate themselves. Competing with well-resourced market leaders requires significant innovation or a niche focus, which is difficult to achieve without prior expertise.

Source: Frost & Sullivan Analysis

Drivers of the Recombinant Biologic Drugs Market in China

Increasing Demand For Targeted Therapies	• The shift towards precision medicine has boosted demand for recombinant biologics that can target specific pathways in diseases. Unlike traditional drugs, these biologics are highly specific and reduce off-target effects. For example, monoclonal antibodies can neutralize a single molecule or receptor linked to a disease. This precision improves therapeutic outcomes and patient compliance. With advancements in genomics and biomarkers, the need for such targeted therapies continues to grow.
Rising Prevalence of Chronic and Rare Diseases	• Chronic conditions like diabetes, cancer, and autoimmune disorders are on the rise, creating a larger market for recombinant biologics. Rare diseases, which often lack effective treatments, also benefit from recombinant enzymes and protein therapies. Governments incentivize drug development for rare diseases through orphan drug designations and tax benefits. For instance, recombinant enzyme replacement therapies have become life-changing for conditions like Pompe disease and Fabry disease. This trend highlights the unmet medical needs biologics address.
Expiration of Patents and Growth of Biosimilars	• The expiration of patents for blockbuster biologics has opened the door for biosimilar development. Biosimilars are cost-effective alternatives with similar efficacy and safety profiles as original biologics. Regulatory frameworks are now more supportive of biosimilar approvals, reducing barriers to entry. This has increased competition, making recombinant biologic drugs more affordable and accessible. Emerging markets, in particular, are driving biosimilar adoption to reduce healthcare costs.
Advancements in Bioprocessing Technologies	• Innovations in production technologies, such as single-use bioreactors and continuous manufacturing, have reduced costs and increased scalability. Modern cell lines like CHO cells are optimized for higher yields and stability in producing recombinant proteins. Downstream purification processes have also become more efficient, ensuring consistency and quality. These improvements make recombinant biologics more viable for large-scale production and broader use. This technological evolution enables faster time-to-market and cost-effective production.

Source: Frost & Sullivan Analysis

Development Trends of the Recombinant Biologic Drugs Market in China

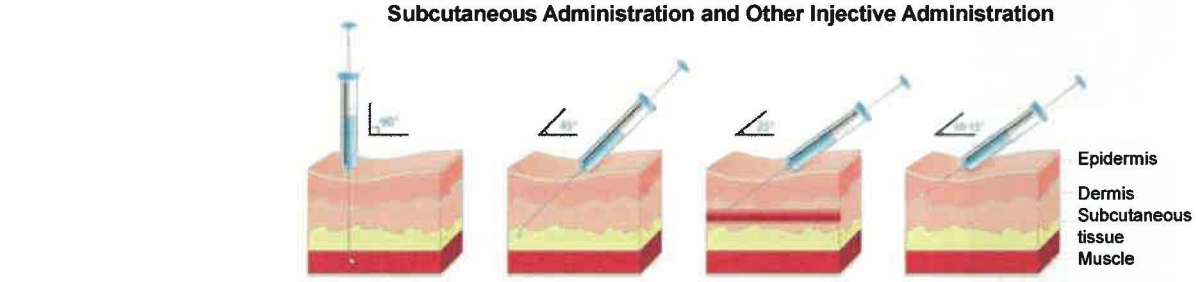
Transformation from Biochemical Drugs to Recombinant Biologic Drugs	• The transformation from biochemical drugs to recombinant biologic drugs represents a significant advancement in precision, safety, and scalability. Unlike biochemical drugs, which are often extracted from natural sources and can have variable quality, recombinant biologics are engineered to mimic human proteins, ensuring consistency and reducing immunogenicity. These biologics offer targeted mechanisms of action, improving efficacy and minimizing side effects, as seen with monoclonal antibodies and recombinant insulin. Additionally, recombinant production processes allow for scalable manufacturing, meeting growing demands without reliance on finite resources. This shift has expanded therapeutic applications, particularly for chronic and rare diseases, revolutionizing modern medicine.
Integration of Artificial Intelligence in Drug Development	• AI and machine learning are accelerating recombinant biologic drug discovery and optimization. AI can predict protein structures, design variants, and optimize manufacturing processes with greater accuracy. Machine learning algorithms help monitor bioprocesses, improving yield and consistency during production. Virtual screening of protein libraries reduces R&D timelines and costs significantly. The integration of AI is poised to revolutionize the efficiency and precision of biologic drug development.
Growth in Biosimilar and Biobetter Markets	• Biosimilars are gaining traction as patents for major biologics expire, especially in oncology and immunology. Biobetters, which improve upon original biologics in efficacy or stability, are emerging as premium alternatives. Both categories address the cost concerns of healthcare systems while maintaining quality. The rise of biosimilars is particularly significant in emerging markets where affordability is critical. The competition among biosimilars and biobetters is driving innovation and lowering overall costs.
Focus on Sustainable Biomanufacturing	• Sustainability in biologics production is becoming a priority for pharmaceutical companies. Advances in microbial and plant-based expression systems are reducing the environmental footprint of production. Single-use technologies and optimized fermentation processes minimize waste and energy use. These sustainable practices align with global goals to reduce industrial emissions and resource consumption. By adopting greener technologies, the industry aims to make biologics more eco-friendly and accessible.

Source: Frost & Sullivan Analysis

Overview and History of Subcutaneous Drug Delivery Systems

- A subcutaneous injection is administered as a bolus into the subcutis, the layer of skin directly below the dermis and epidermis, collectively referred to as the cutis. Subcutaneous tissue has few blood vessels and so drugs injected into it are intended for slow, sustained rates of absorption, often with some amount of depot effect. Compared with other routes of administration, it is slower than intramuscular injections but still faster than intradermal injections. Subcutaneous infusion (as opposed to subcutaneous injection) is similar but involves a continuous drip from a bag and line, as opposed to injection with a syringe.
- Subcutaneous administration has become a valuable alternative to intravenous administration in many disease areas. Although the pharmacokinetic profiles of subcutaneous and intravenous formulations differ, subcutaneous administration has been shown to be effective, safe, well tolerated, generally favored by patients and healthcare providers, and can reduce healthcare costs and resource use associated with drug delivery.

Subcutaneous Administration and Other Injective Administration



Development of Subcutaneous Administration

Intramuscular Injection	Subcutaneous Injection	Intravenous Injection	Intradermal Injection

1850s

Subcutaneous drug delivery began to develop gradually with the advent of hollow needles and hypodermic syringes.

1960s

Subcutaneous administration was used to deliver a variety of therapeutic substances, from **morphine and opium to insulin and heparin.**

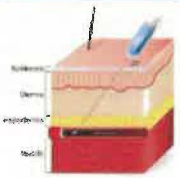
2000s

In recent years, subcutaneous administration has become the preferred choice for biologics that are usually injected intravenously. Biologics include peptides, proteins, cytokines, replacement enzymes, and monoclonal antibodies (mAbs).

Source: Frost & Sullivan analysis

Overview of Drug Injection Methods

Intravenous Injection (IV)



- **Location**: Vein
- **Methods**: Inserting a needle into a vein, allowing a substance to be delivered directly into the bloodstream.
- **Administration angle**: 25°
- **Suitable drugs**: blood products or electrolytes
- **Adverse effects**: Pain, infection and inflammation and infiltration and extravasation.
- **Purpose**:
  - Needs the quickest onset of the desired effects and quickly circulated to the rest of the body
  - Suitable for high concentration, irritant and large amount administration
  - For diagnosis and test use
  - Intravenous nutrition therapy

Subcutaneous Injection (SC)

- **Location**: subcutaneous tissue
- **Methods**: injecting a substance into the fat tissue between the skin and the muscle.
- **Administration angle**: 45° or 90°
- **Suitable drugs**: insulin, morphine, diacetylmorphine and goserelin.
- **Adverse effects**: combination of redness, swelling, itching, bruising, or other irritation
- **Purpose**:
  - Reach the efficacy immediately, while oral medication cannot be applied
  - Local anesthesia or preoperative medication
  - Vaccination

Other Injection

Intradermal Injection
- **Location**: Dermis
- **Methods**: Delivering the substance with the needle placed at a 5 to 15 degree angle into the dermis.

Intraosseous Injection
- **Location**: Bone marrow
- **Methods**: Injecting a needle with 90 degree angle to the injection site through the bone's hard cortex and into the soft marrow interior

Intramuscular Injection
- **Location**: Muscle
- **Methods**: Delivering a substance deep into a muscle, where they are quickly absorbed by the blood vessels into systemic circulation.

Source: Frost & Sullivan analysis

Comparison of Intravenous Injection and Subcutaneous Injection

	Intravenous Injection	Subcutaneous Injection
Location	Vein	Subcutaneous tissue
Administration Angle	25°	45° or 90°
Capacity for Osmolality	The upper limit for intraveneous injection is 1,000 mOsm/kg, making it more suitable for patients that require higher concentration and osmolality	The upper limit for subcutaneous injection is 600 mOsm/kg, and drugs with osmolality over 600 mOsm/kg cannot be injected subcutaneously
Injection Time	Typically 30-90 minutes	Typically 2-5 minutes
Absorption Speed	• Intravenous injection can enable drugs to access the entire body and release in a short period of time, rendering it to be more efficient in life-threatening situations.	• Subcutaneous injection is not suitable for emergency needs but is especially widely used in drug delivery systems that need the feature of slow-release and long work time, such as the injection of long-acting insulin.
Aseptic Conditions	• Intravenous injection imposes strict requirements on the aseptic conditions.	• As compared, subcutaneous injection imposes lighter requirements on the aseptic conditions as it poses relatively fewer risks.
Reservation Flexibility	• Low due to capacity limits of medical facilities	• High
Medical Staff Requirement	• According to Expert Rev. Pharmacoecon. Outcomes Res. 2019, as healthcare providers can treat multiple patients receiving intravenous injections simultaneously, they have the tendency of preferring providing intravenous injection to patients. • Nevertheless, the difference between intravenous and subcutaneous injections in terms of cumulative workload and time for healthcare providers associated with administration is insignificant.	
Costs	• According to Br J Cancer. 2021 Apr 12; 124(8):1346–1352, subcutaneous injection is more convenient than intravenous injection. Derived costs for healthcare providers' time and consumables per intravenous treatment were £132.05 and £12.92, respectively, compared with £31.99 and £1.17 per subcutaneous treatment, respectively. • According to a study comparing subcutaneous and intravenous formulation of trastuzumab in Eur J Obstet Gynecol Reprod Biol. 2018 Feb; 221: 46-51, the administration of trastuzumab subcutaneous was translated in a cost saving of C212.93 ($231.73) per patient episode compared to trastuzumab intravenous, which could lead to a total potential saving of C3,832.74 ($4,171.06) over a full course of treatment (18 cycles). • In addition, according to Breast. 2016 Oct; 29:140-6., British Journal of Cancer. 2021 Feb; 124(Suppl.2), the indirect cost (including transportation costs, accommodation costs and additional nutrition supply costs) of subcutaneous injection is lower than that of intravenous injection.	
Suited Patients	• Patients who are receiving chemotherapy or other intravenous therapies may prefer intravenous injections because they have already had a central venous port in place and tend to avoid having an additional injection; • Patients in emergency situations or situations that require immediate releases of drug effect; and • Patients that require high concentration and large amount administrations or continuous medication deliveries.	• For cancer patients who need to receive long-term treatments, subcutaneous injection could help them save time and is flexible in reservation (Geburtshilfe Frauenheilkd. 2015 Jun;75(6):566-573.); • Patients that require drug deliveries with slow release and long work time, as subcutaneous administration acts as a reservoir of drugs, allowing for sustained absorption and release. (Pharmaceuticals (Basel). 2020 Sep 2;13(9):231.); and • Approximately 10% of cancer patients who may be unsuitable for intravenous administration due to limited vein access caused by longterm and numerous drug treatments (Anticancer Res. 2014 Apr;34(4):1579-86.).

Note: (1) Osmolality refers to the concentration of dissolved particles of chemicals in the serum. Higher osmolality means more particles in the serum. Lower osmolality means the particles are more diluted.
(2) The comparison on reservation flexibility between the two injection methods is concluded according to Geburtshilfe Frauenheilkd. 2015;75:566-573.

Source: Int J Pharm. 2015 Jul 25;490(1-2):308-15., JA Clin Rep. 2021 Feb 27;7(1):18., Stud. Nat. Prod. Chem. 2018 Aug 14;58:161-212., Anticancer Res. 2014 Apr;34(4):1579-86., Patient Prefer Adherence. 2015; 9: 923–942., The Patient, 8 (2). pp. 145-153., Expert Rev. Pharmacoecon. Outcomes Res. 2019, Br J Cancer. 2021 Apr 12; 124(8):1346–1352, Breast. 2016 Oct; 29:140-6., British Journal of Cancer. 2021 Feb; 124(Suppl.2), Geburtshilfe Frauenheilkd. 2015;75:566-573, phase II PrefHER study of Roche's Herceptin Hylecta,Roche public presentation, Frost & Sullivan analysis

Comparable Advantage of Subcutaneous vs. Intravenous Injections

Subcutaneous injection is more convenient than intravenous injection. The subcutaneous administration usually only takes 2-5 min, while intravenous administration usually takes 30-90 mins or several hours And intravenous injection is mostly conducted in class 3 hospitals by experienced professionals, while subcutaneous injection can be conducted in county-level hospitals and medical clinics.

The cost of subcutaneous injection is lower from both direct and indirect perspectives. The direct cost of Herceptin Hylecta was $978.09 per unit which was cheaper than the price of Herceptin, $1,636.49 per unit. The indirect medical cost was saved from accommodation fee and transportation fee of traveling from home to class 3 hospitals in first-tier cities.

In the real world, customers are prefer the subcutaneous injection methods. In the PrefHER study, 86% of patients preferred subcutaneous administration of Herceptin HYLECTA over intravenous injection for the treatment of HER2+ breast cancer.

The subcutaneous administration of Herceptin Hylecta has a higher efficacy advantage compared with intravenous Herceptin. The pathological complete response of Herceptin Hylecta was higher than the complete response rate of Herceptin (45.4% VS 40.7%).

Subcutaneous injection has a higher safety compared with intravenous injection. Intravenous injection usually company with large volume and strong irritation. Patients have a high possibility of developing infusion reaction. About 10% of cancer patients will have intravenous intolerance of whom cannot accept intravenous administration.

Source: Frost & Sullivan analysis

Overview of Hyaluronidase(HAase) Development

- Hyaluronic acid (HA) is widely present in human tissues such as the intercellular matrix, and plays an important role in wound healing, joint lubrication, and electrolyte transport regulation. However, it also limits the diffusion of water and other extracellular substances, thus restricting the fluidity of subcutaneous fluid.
- Hyaluronidase (HAase) can degrade hyaluronic acid, a component of the extracellular matrix, to generate small molecule hyaluronic acid or oligosaccharides, thereby improving tissue permeability and fluid penetration. It has demonstrated application potential and clinical value in many fields of the healthcare industry.

Discovery of HAase

- Hyaluronidase was first discovered in 1929 and is derived from mammalian testicular extracts. In 1940, Chain and Duthie determined that this "diffusible factor" was an enzyme and named it hyaluronidase because it promotes the diffusion of vaccines, dyes, toxins, etc. Due to the difficulty in isolating and purifying hyaluronidase and the lack of knowledge about its function, the research on hyaluronidase has been relatively stagnant for a long time.
- China officially put hyaluronidase into production in 1965 by Shanghai Biochemical Pharmaceutical Factory, and it was included in the 1977 edition of the Chinese Pharmacopoeia.

Development of HAase

- In the past few decades, hyaluronidase has been widely used in many fields such as orthopedics, surgery, ophthalmology, internal medicine, dermatology, and gynecology. Because hyaluronidase has a depolymerization effect on hyaluronic acid in tissues, hyaluronidase has a good effect of promoting drug diffusion, so it can be used as a drug injection additive to enhance the body's absorption efficiency of drugs, and it can also promote the dissipation of local blood or fluid accumulation to achieve the effect of eliminating hematoma and edema. The half-life of HA in the skin stroma is less than two days, which means that the skin stroma at the injection site will recover within 24-48 hours without any tissue changes or inflammatory manifestations. At the same time, hyaluronidase has substrate specificity and has no effect on combined drugs and other proteins in tissues, ensuring the safety of clinical use.

Innovation of HAase

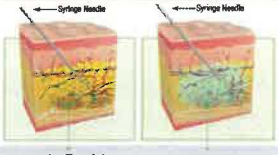
- In 2005, Halozyme Therapeutics developed Enhanze drug delivery technology based on recombinant human hyaluronidase PH20 (rHuPH20) and it was rapidly promoted in the United States. Before that, hyaluronidase preparations were mostly extracted from testicular tissue of animals (cattle and sheep). The prepared HA often had disadvantages such as low purity, excessive impurity protein content, low activity and strong immunogenicity. Side effects included allergic reactions. Skin allergy tests were required before injection, which limited the application of promoting the absorption of nutritional factors and drugs. The recombinant human hyaluronidase developed by Halozyme Therapeutics does not contain animal-derived ingredients, has high purity, high activity, no immunogenicity, and few side effects.

1929 — 1980 — 2000 — 2024

Source: Frost & Sullivan analysis

Comparison of SC Drug Delivery (Recombinant Human Hyaluronidase SC vs. Traditional SC)

- The subcutaneous (SC) drug delivery market is rapidly evolving, driven by the increasing demand for patient-friendly administration methods and the growing portfolio of biological therapies, including monoclonal antibodies, insulin analogues, and vaccines. Innovative modalities such as recombinant human hyaluronidase have expanded the market by overcoming traditional SC delivery limitations, enabling larger injection volumes and improving drug absorption.

Drug Category	Traditional Subcutaneous Injection 	Recombinant Human Hyaluronidase Injection 
Monoclonal Antibodies (mAbs)	- Small volumes (≤2mL), requiring multiple injections - Slower absorption, potentially affecting efficacy	- Supports large volumes (>5mL) - Enhances bioavailability, reduces injection frequency
Insulin and Analogues	- Widely used for diabetes management - Single small-dose injections, suitable for traditional methods	- Rarely used but applicable for high-dose or novel insulin formulations
Vaccines	- Suitable for standard-dose and multiple-dose vaccines	- Potentially applicable to novel vaccines, improving absorption efficiency
Fusion Proteins	- Used for conditions like rheumatoid arthritis and cancer, but limited by injection volume and efficiency	- Supports large-volume, high-concentration injections, improving therapeutic outcomes
Gene Therapy and Cell Therapy	- Limited to small-scale clinical trials, with low delivery efficiency	- Improves diffusion and absorption of gene or cell products in local tissues
Chemical Drugs	- Generally not used for SC delivery, requiring optimized formulations	- Enhances permeability for chemical drugs, aiding in new drug development
Large Molecule Drugs (e.g., ADCs)	- Restricted by molecular size, limiting efficient SC delivery	- Provides effective subcutaneous diffusion and absorption for large molecules

Source: Literature review, Frost & Sullivan analysis

Competitive Landscape of Approved Biologics Based on Hyaluronidase Subcutaneous Drug Delivery System in China

- In addition to insulin, heparin, and some vaccines, subcutaneous administration of large-molecule biological drugs such as antibody drugs has also been gradually realized through new technologies such as recombinant human hyaluronidase. Through subcutaneous administration, patients can self-administer drugs in outpatient clinics or even at home, greatly improving the comfort and compliance of patients, especially cancer patients, thereby improving the quality of life.
- In addition, subcutaneous administration can also be rapidly diffused under the action of rHuPH20, and large doses of drugs injected subcutaneously will not appear on the skin. And because the half-life of hyaluronic acid is less than 2 days, the effect of hyaluronidase is reversible within 24-48 hours and will not cause long-term changes in the injection site.
- At present, China has approved a number of biological preparations based on subcutaneous drug delivery systems, with tumors as the main indication.

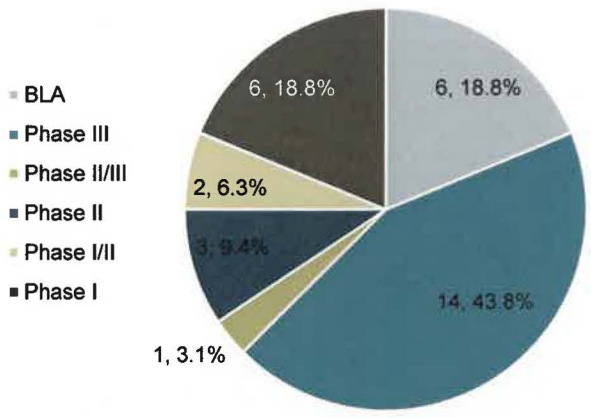
Generic Name	Company	Approval Date	Approved Indications	SC Drug Delivery		IV Single Dose Duration	Treatment Cost of SC (RMB/year)	Treatment Cost of IV (RMB/year)
				Subcutaneous Drug Delivery System	SC Single Dose Duration			
Daratumumab Subcutaneous Injection	Johnson & Johnson	2021-09-30	AL amyloidosis, multiple myeloma	PH20 (Enhanze™)	3-5min	3-7h	457,600	203,394
Trastuzumab+hyaluronidase	Roche	2022-09-30	HER2-positive breast cancer	PH20 (Enhanze™)	2-5min	30-90min	76,800	77,000
Pertuzumab Trastuzumab and Hyaluronidase-zzxf	Roche	2023-12-26	HER2+ Breast Cancer	PH20 (Enhanze™)	5-8min	30-90min	235,314	No IV dosage form
Rituximab+hyaluronidase	Roche	2024-04-02	Diffuse large B-cell lymphoma, follicular lymphoma	PH20 (Enhanze™)	5min	2-3h	-	123,900
Efgartigimod PH20 SC	Argenx	2024-07-19	Chronic inflammatory demyelinating polyneuropathy, myasthenia gravis	PH20 (Enhanze™)	0.5-1.5min	1h	83,088/ treatment cycle [2]	82,400/ treatment cycle [2]

Note: 1. As of 2025.11.22; 2. Clinical assessment of whether a subsequent treatment cycle is needed.
Source: NMPA, Frost & Sullivan analysis

Competitive Landscape of Subcutaneous Biologics under Clinical Stage in China

- At present, the main types of subcutaneous biologics under development in China are still antibody drugs (monoclonal antibodies), and most products are in the clinical phase III stage, accounting for 43.8%. The indications of subcutaneous biologics under development are still mainly tumors and immune diseases, in addition to digestive system diseases and respiratory system diseases.

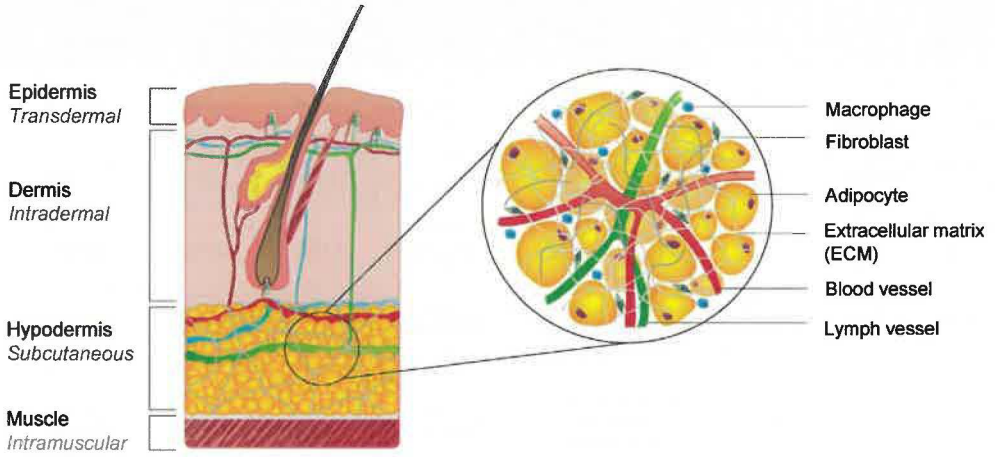
Subcutaneous Biologics under Clinical Stage in China



Note: As of 2025.01.14. Only original drugs are included.
Source: NMPA, CDE, Frost & Sullivan analysis

MOA of Subcutaneous Biologics

- The skin tissue structure can be divided into epidermis, dermis, subcutaneous tissue and muscle tissue from the outside to the inside. At the same time, the skin also has accessory organs such as hair follicles, sweat glands, sebaceous glands and nails, and also contains abundant nerves, blood vessels, lymphatic vessels and muscle tissue.
- Subcutaneous tissue is mainly composed of fat, with capillaries and lymphatic capillaries shuttling through it, and the extracellular matrix (ECM) provides support for it. ECM is composed of various proteins and polysaccharides, including collagen, hyaluronic acid (HA) and chondroitin sulfate (CS). At physiological pH, HA and CS are both negatively charged. These highly negative charges control the fluid conductivity in ECM and become the first line of defense for subcutaneous preparations to break through. Studies have shown that in the human body, ECM limits the subcutaneous injection volume to no more than 2 ml, otherwise pain, bulging and other phenomena will occur.



Source: Frost & Sullivan analysis

MOA of Subcutaneous Biologics

- Normally, the dosage of biologics, especially anti-tumor monoclonal antibodies, is usually large. For example, the subcutaneous dosage of trastuzumab is 600 mg, while the dosage of adalimumab, a monoclonal antibody for the treatment of immune diseases, is only 40 mg (0.8 mL). Therefore, for subcutaneous administration of large doses of biologics, it is necessary to increase the drug concentration and improve the method of administration to break through the skin tissue defense line.

Solutions to the Problem of Subcutaneous Biologic Injection

- **Developing high-concentration formulations** allows high-dose subcutaneous administration within the 2-3 ml volume limit, but this method often reduces the distance between molecules and increases the frequency of protein-protein contact, thereby increasing the possibility of drug aggregation. In the development of monoclonal antibody drugs, antibody aggregation is one of the most important issues to pay attention to, because it not only reduces the therapeutic effect of the drug, but also may be immunogenic. In addition, high-concentration formulations also mean high viscosity, which will increase injection time and pain during administration.

- **Multiple small-dose injections.** Large doses of medication are divided into multiple small subcutaneous injections to avoid adverse reactions caused by a single large dose. Although this approach may increase the injection burden on patients, it can effectively help avoid the risks and discomfort that may be associated with a single large-dose injection. Multiple injections require the cooperation of the patient or caregiver, and may need to be injected in different sites to reduce the risk of reactions and pain.

- **Innovative drug delivery technology.** Hyaluronic acid in the subcutaneous tissue is the backbone of defense, and using hyaluronidase to degrade it can greatly increase the limit on infusion volume. rHuPH20 can increase the permeability and fluid conductivity of subcutaneous tissue, allowing larger volumes of drugs to enter the subcutaneous tissue, successfully helping monoclonal antibody anti-tumor drugs break through the skin tissue defense line. Under the action of rHuPH20, large doses of drugs injected subcutaneously can diffuse rapidly, and no obvious bulges will appear on the skin. And because the half-life of hyaluronic acid is less than 2 days, the effect of hyaluronidase is reversible within 24-48 hours and will not cause long-term changes to the injection site.

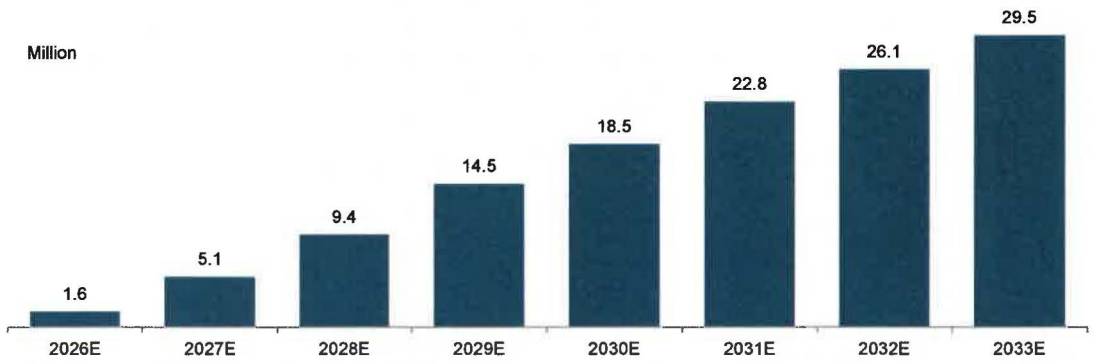
Source: Frost & Sullivan analysis

The Number of SC Infusion Administrations in China, 2026E-2033E

- From 2026-2033, the number of subcutaneous large-volume infusion administrations in China is expected to experience rapid and sustained growth. In 2026, the total number is estimated at 1.59 million, increasing significantly to 5.09 million by 2027E and further reaching 9.38 million in 2028E. From 2028-2033, the market is projected to expand at a CAGR of 25.8%, with the number of SC administrations rising to 29.53 million in 2033.

The Number of SC Infusion Administrations in China, 2026E-2033E

Period	CAGR
2028E-2033E	25.8%



Source: Annual Reports, NMPA, CDE, Literature review, Frost & Sullivan analysis

Overview of Recombinant Human Hyaluronidase

- Naturally derived hyaluronidase, i.e., animal-derived hyaluronidase, is mainly extracted and purified from the testicular tissue of animals (cows or sheep). Due to the complexity and diversity of its sources, it is prone to allergies, immunogenicity, and even zoonotic infectious diseases, which limits its clinical use scenarios.
- The human genome contains 6 types of hyaluronidases, including HYAL-1, HYAL-2, HYAL-3, HYAL-4, HYAL-P1 and PH20/SPAM1. PH20 is the main enzyme that degrades hyaluronic acid in the human body and is also the main clinical research direction.
- Recombinant human hyaluronidase (rHuPH20) is a human hyaluronidase synthesized in vitro by genetic engineering technology. Compared with naturally extracted hyaluronidase, the recombinant enzyme has higher purity, fewer impurities, better safety and stability, and therefore has broad application prospects in medical and other fields.
- HYLENEX ®(rHuPH20) was approved by the U.S. Food and Drug Administration (FDA) in 2005 based in part on the FDA's findings of hyaluronidase effectiveness in a 1970 Drug Efficacy Study Implementation (DESI) review and studies evaluating allergic reactions in healthy volunteers. The DESI review determined the efficacy of three animal-derived hyaluronidases based on years of clinical use, which formed the basis for the HYLENEX labeling. Based on the DESI review, the safety information in the HYLENEX labeling was consistent with the safety information of the animal-derived hyaluronidases marketed at the time: VITRASE® (a sheep-derived hyaluronidase) and AMPHADASE® (a bovine-derived hyaluronidase).

	Recombinant Human Hyaluronidase	Animal-derived hyaluronidase
Product raw materials	E. coli, yeast, or mammalian cell lines and culture media	Animal (cow or sheep) testicular tissue
Approval date	2005	1948
Immunogenicity	Low	High, prone to allergic reactions
Product purity	High	Low, high protein content
Manufacturing Method	Through synthetic biology and other methods, it is expressed in modified engineered cells or bacteria and then isolated and purified. It is highly efficient and has low impurity content.	Extraction and purification, the steps are complicated due to the large number of natural impurities

Source: Frost & Sullivan analysis

Competitive Landscape of Recombinant Human Hyaluronidase (rHuPH20) Globally

- Since 2005, Halozyme Therapeutic has been leading the development of recombinant human hyaluronidase worldwide, and has developed the single-drug product HYLENEX and the ENHANZE drug delivery platform based on recombinant human hyaluronidase, and has extensively cooperated with major multinational pharmaceutical companies on blockbuster products, enjoying a considerable annual revenue share.
- As the first and only recombinant human hyaluronidase in China to enter the clinical stage, Bao Pharma's KJ017 is expected to show great commercial potential during the period of vigorous development of biologics and rapid development of subcutaneous preparations in China.

Competitive Landscape of Recombinant Human Hyaluronidase (rHuPH20) Globally

Drug Name	Company	R&D Progress	Approval Date/ First Posted Date	Indication
rHuPH20 (Hylenex)	Halozyme Therapeutic	Approved by FDA	2005.12	Subcutaneous infusion vehicle
Tergase	Alteogen	Approved in South Korea	2024.07	Subcutaneous infusion vehicle
KJ017	Bao Pharma	BLA (NMPA)	2024.09	Subcutaneous infusion vehicle
BMI2004	BMI Korea	Phase I (South Korea)	2023.06	Subcutaneous infusion vehicle
HLB3-002	Huons Korea	Phase I (South Korea)	2024.12	Subcutaneous injection
Recombinant human hyaluronidase	Aimeike Biotech	Phase I (China)	2025.05	Subcutaneous infusion vehicle

Halozyme's business model features: Exclusivity

- According to publicly disclosed information from Halozyme's collaboration agreements with Roche, Janssen, Pfizer and Argenx etc., the collaborative clients have exclusive rights to the collaborative targets, which means that **only the corresponding client company has the exclusive right to use the target of its target choice and develop corresponding drugs based on Halozyme's rHuPH20 product or drug delivery system.**

Market opportunities for other competitors

- A large number of other innovative drugs with the same target (such as HER2 target) have the need for cooperation on subcutaneous delivery systems, including potential best-in-class drugs, but due to the exclusivity of Halozyme, they can only seek cooperation with other rHuPH20 manufacturers, especially in China where the development of innovative drugs started late.
- For biosimilars of target drugs that have cooperated with Halozyme and commercialized products, such as many trastuzumab biosimilar products, there is also a need to switch the dosage form from intravenous injection to subcutaneous administration.

Note: As of 2025.11.22

Source: NMPA, FDA, Frost & Sullivan analysis

Analysis of Application Fields of Hyaluronidase

- Hyaluronic acid (HA) is widely present in human tissues such as the intercellular matrix, and plays an important role in wound healing, joint lubrication, and electrolyte transport regulation. However, it also limits the diffusion of water and other extracellular substances, thus restricting the fluidity of subcutaneous fluid. Hyaluronidase can degrade HA, a component of the extracellular matrix, to generate small molecule HA or oligosaccharides, thereby improving tissue permeability and fluid penetration. It has demonstrated application potential and clinical value in many fields of the medical industry.

Subcutaneous injection
Hyaluronidase can locally and temporarily degrade hyaluronic acid to enhance the dispersion and permeability of drugs in tissues, including **antibodies, antibiotics**, etc.
Advantages: Increase the utilization of drugs, realize the conversion from intravenous administration of antibodies to subcutaneous administration and dosage optimization

Medical cosmetic services
Hyaluronidase can decompose medical cosmetic fillers such as hyaluronic acid.
Advantages: Alleviate or even reverse potential complications after injection (vascular occlusion, overcorrection, blue eyes, lower eyelid edema) and other adverse reactions and complications, and improve prognosis.

Anesthesia aid
Hyaluronidase helps spread the permeate and reduces infusion pressure.
Advantages: As an auxiliary drug for tumescent anesthesia or other surgical anesthetics, it can significantly reduce postoperative pain.

Tumor treatment
Hyaluronidase can decompose a large amount of collagen and hyaluronic acid in the dense extracellular matrix of solid tumors.
Advantages: Enhance the ability of chemotherapy molecules and cell therapy to penetrate deep areas of infiltrated tumors to improve efficacy.

Assisted reproduction
When using intracytoplasmic sperm injection for assisted reproduction, hyaluronidase is required to digest the hyaluronic acid between the cumulus cells.
Advantages: It can remove the cumulus cells and corona cells around the oocytes, reducing oocyte damage.

Osteoarthritis treatment
Hyaluronidase can promote the diffusion of locally accumulated exudate or blood, reducing tissue tension or pain.
Advantages: It is conducive to the absorption of edema and inflammatory exudates, and relieves the patient's pain.

Source: Frost & Sullivan analysis

Analysis of Technical Route and Advantages of Combined Drug Delivery of Recombinant Human Hyaluronidase and Antibiotics

- At present, antibiotics are the core of bacterial infection treatment, among which intravenous β-lactam antibiotics have always been the cornerstone of antibacterial infection treatment due to their broad antibacterial spectrum and good tolerance. The bactericidal activity of β-lactam antibiotics has been proven to be time-dependent, and the ability to eliminate bacteria is directly related to the time that the free drug concentration is maintained above the minimum inhibitory concentration (MIC) during the dosing interval. In order to better exert the bactericidal properties, β-lactam antibiotics can be infused (PIs) for a long time (extending the infusion time and continuous infusion) to increase the time that the blood drug concentration is above the MIC.
- However, intravenous administration and prolonged administration time will also reduce patient compliance, and direct subcutaneous infusion will cause adverse reactions such as pain at the injection site. There is an urgent need for an antibiotic administration method that can improve the medication experience of patients using antibiotics.

- Ceftriaxone is a β-lactam antibiotic. As a third-generation cephalosporin drug, ceftriaxone produces bactericidal activity by inhibiting cell wall synthesis. It has bactericidal effects on many Gram-negative and Gram-positive bacteria in vitro, and has high stability against most β-lactamases (penicillinase and cephalosporinase) of Gram-positive and Gram-negative bacteria. Ceftriaxone is mainly used for infections caused by pathogenic bacteria that are sensitive to this product, such as lung inflammation, peritonitis, respiratory tract infection, Lyme disease, Neisseria gonorrhoeae infection, urinary tract infection, meningitis, sepsis, reproductive system infection, gastrointestinal infection and other infectious diseases.

Intravenous injection

Direct subcutaneous injection

Subcutaneous injection based on rHuPH20

- According to a clinical trial and related studies, by comparing three administration methods of ceftriaxone, namely intravenous injection of ceftriaxone, direct subcutaneous injection of ceftriaxone and normal saline, and subcutaneous administration of ceftriaxone based on rHuPH20, their pharmacokinetics were compared and the relationship between their bioavailability was explored.

Route of administration	Intravenous injection	Direct subcutaneous injection	Subcutaneous injection based on rHuPH20
AUC(Area Under Curve)	No significant difference		
$t_{1/2}$ (Drug half-life)	No significant difference		
Cmax tmax	lower Cmax and longer tmax plasma ceftriaxone values were seen following SC infusion (with or without rHuPH20) than after IV administration, indicating a slower rate of ceftriaxone delivery with SC administration. Median tmax was 1 hour earlier and mean Cmax was 12% higher after rHuPH20- facilitated SC administration than after SC ceftriaxone.		
Adverse event	Infusion site pain was reported with both SC and IV infusions, but adverse events tended to be mild or moderate in intensity and most resolved within 1 day without sequelae.		

This means that the subcutaneous and intravenous routes have the potential to be bioequivalent, and rHuPH20-based subcutaneous injections also have the potential to improve the treatment experience of patients using antibiotics.

Source: Literature, Frost & Sullivan analysis

Competitive Landscape of rHuPH20 and Antibiotic Combination

- Currently, there are no rHuPH20-based combination antibiotic drugs approved for marketing or in clinical trials worldwide. With the increase in the number of patients using antibiotics in the future, the gradual emphasis on treatment experience, and the approval of more rHuPH20 products, more antibiotics are expected to be converted to subcutaneous administration based on rHuPH20.

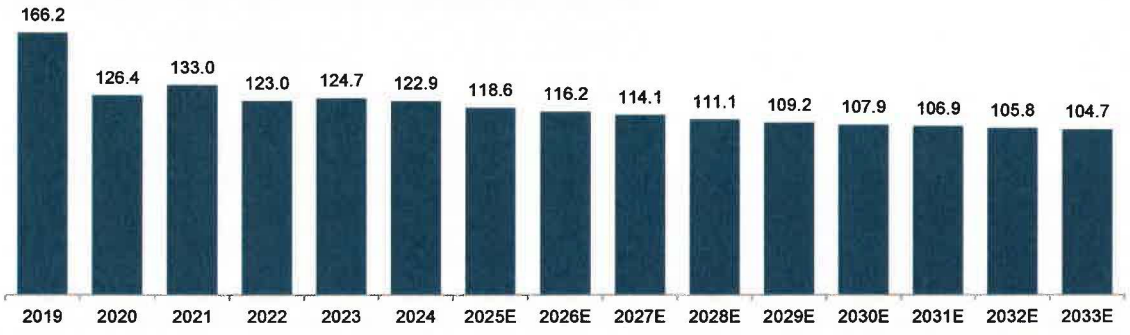
Source: Frost & Sullivan analysis

Antibiotic Drug Market Size in China, 2019-2033E

- The antibiotic drugs market is facing undergone significant changes from 2019 to 2033, due to the Centralized Procurement. In 2019, the market size was RMB 166.2 billion, but it declined sharply to RMB 122.9 billion in 2024, representing a CAGR of -5.9%. During 2024-2029, the market is expected to decline further but at a slower pace, with a CAGR of -2.3%. From 2029 to 2033, the market is expected to decline further, dropping from RMB 109.2 billion to RMB 104.7 billion at a CAGR of -1.1%.

Antibiotic Drugs Market Size in China, 2019-2033E

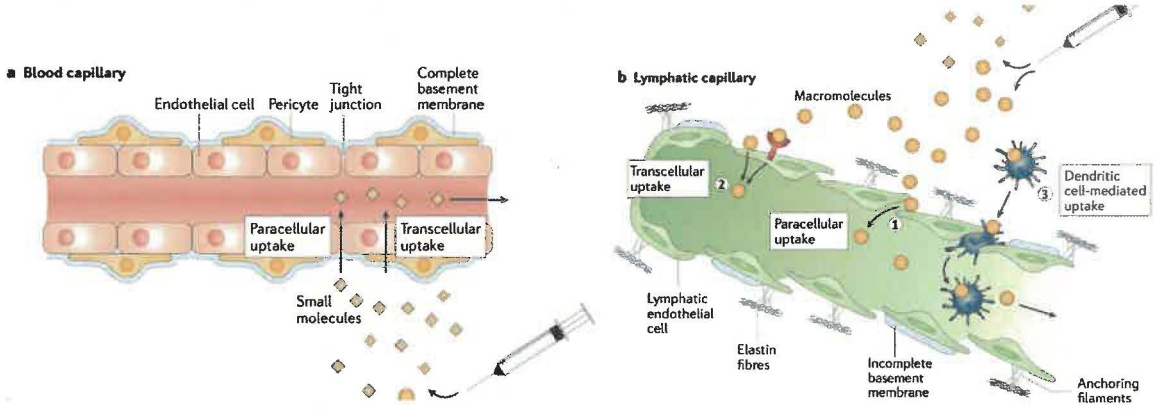
Period	CAGR
2019-2024	-5.9%
2024-2029E	-2.3%
2029E-2033E	-1.1%



Source: Annual Reports, NMPA, CDE, Literature review, Frost & Sullivan analysis

MOA of SC Antibody

- Several studies have shown that there is a linear relationship between the molecular weight of a drug and the amount of it absorbed by the capillaries. Specifically, small molecule drugs or medium-sized drugs less than 10nm (proteins are about 16-20kDa) are preferentially absorbed by capillaries. Therapeutic proteins and macromolecules of 20-30 kda, as well as particles of 10-100nm, tend to be absorbed through the capillaries.
- The structure of capillaries is relatively dense and has a strong basement membrane. The structure of capillaries is not so dense, and the basement membrane is intermittent. Therefore, small molecular weight drugs can freely pass through capillaries and capillaries, but because the exchange rate of fluid in the former is 100~500 times that of the latter, small molecular weight drugs are mainly absorbed through capillaries. As the molecular weight increases, capillaries become the preferred absorption route.
- Therefore, for subcutaneous preparations of anti-tumor monoclonal antibodies, the main absorption route is lymphatic capillaries. During absorption through the lymphatic system, drug size, chemical modifications, interactions with immune cells, and injection site, as well as individual differences, can affect the drug's absorption process.



Source: Literature, Frost & Sullivan analysis

Analysis of Technical Route and Advantages of Combined Drug Delivery of Recombinant Human Hyaluronidase and Antibody

- When rHuPH20 is used to facilitate subcutaneous drug administration, it is not therapeutically active as a single agent. Therefore, the pharmacodynamic profile of rHuPH20 is assessed by its effect on absorption of the co-administered active drug, or changes in flux rate, pharmacokinetics (PK)/bioavailability, tolerability, and general ability to rapidly deliver large quantities of drug subcutaneously. Studies have shown that co-administration of rHuPH20 with a co-administered SC drug may affect its PK properties, including increased absorption rate, increased bioavailability, increased maximum concentration (Cmax), and accelerated time to reach Cmax (tmax), compared to SC treatment without rHuPH20. Co-administration of rHuPH20 may also reduce intra- and inter-individual PK variability.
- When administered subcutaneously, rHuPH20 has no measurable systemic exposure at doses used in currently approved products. In a series of Phase Ib dose-ranging studies of rHuPH20 administered subcutaneously in combination with various monoclonal antibody therapies in healthy volunteers, plasma concentrations of rHuPH20 remained below the limit of quantitation for all rHuPH20 doses used (1350 U to 30,000 U). Clinical observations showed that no measurable systemic exposure was observed at the doses tested, a result consistent with the low subcutaneous bioavailability observed in non-human primates (<10%) and modeling studies that predicted low systemic exposure in humans after subcutaneous administration. This suggests that subcutaneous administration of rHuPH20 does not result in systemic distribution and its potential adverse effects. In addition, a study in healthy volunteers showed that even intravenous rHuPH20 was rapidly cleared from plasma.
- Currently, based on clinical studies and real-world studies and patient data based on marketed products, rHuPH20-mediated subcutaneous administration of monoclonal antibodies has been shown to be highly similar to intravenous administration in terms of pharmacokinetics, efficacy and safety, but with lower immunogenicity, and is currently widely used in antibody therapy for tumors.

Good safety profile
Subcutaneously administered rHuPH20 was generally well tolerated in different study populations, including healthy volunteers, the elderly, and patients in hospice and palliative care, as well as patients with cancer, primary immunodeficiency, type 1 and type 2 diabetes, rheumatoid arthritis, hereditary angioedema, and hyperlipidemia. Adverse events generally reflected the safety of the combined medication or were related to the rapid infusion of relatively large amounts of fluid into the subcutaneous cavity and multiple subcutaneous injections, and extensive clinical data and experience have not demonstrated any long-term safety issues with repeated injections.

Mild local reactions
The most common adverse events were mild, transient and self-limited local administration site reactions. In clinical studies of rHuPH20 in combination with other drugs, local administration site reactions were more common with subcutaneous injection than with intravenous injection, but most were mild to moderate reactions, such as swelling, erythema and mild pain.

No significant allergic reactions
For approved products that use rHuPH20 in combination with other drugs, the incidence of infusion-related reactions (IRR) and/or administration-related reactions (ARR) is similar for intravenous and subcutaneous routes of administration, and there are no clinical trial reports indicating that severe hypersensitivity reactions or allergic reactions occur when rHuPH20 is used alone.

Immunogenicity Comparable to IV Administration
In the absence of rHuPH20 exposure, approximately 5% of adults have rHuPH20-reactive antibodies, while 1-21% of individuals have developed treatment-emergent rHuPH20-reactive antibodies when rHuPH20 is administered subcutaneously in combination with a monoclonal antibody product. However, in studies of the potential immunogenicity of rHuPH20, no clinical signs or symptoms associated with positive rHuPH20 antibody responses have been identified, and rHuPH20-reactive antibodies capable of neutralizing hyaluronidase activity have not been demonstrated. In addition, there was no clinical difference in the immunogenicity of the co-formulated monoclonal antibody delivered subcutaneously compared to intravenous administration.

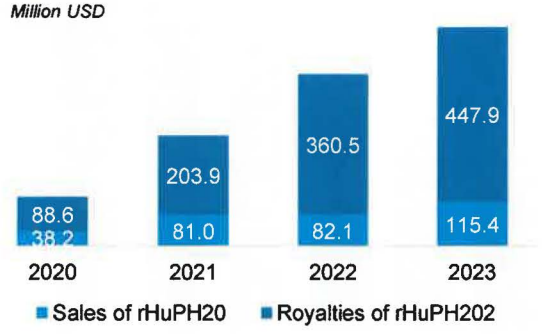
Source: Literature, Frost & Sullivan analysis

Competitive Landscape of rHuPH20 and Antibody Combination

- Currently, only Halozyme's Enhanze technology has been approved for subcutaneous injection of biopharmaceuticals such as combination antibodies, while South Korea's Alteogen and China's Bao Pharma are currently actively working with other biopharmaceutical companies to develop subcutaneous antibody drugs based on rHuPH20.

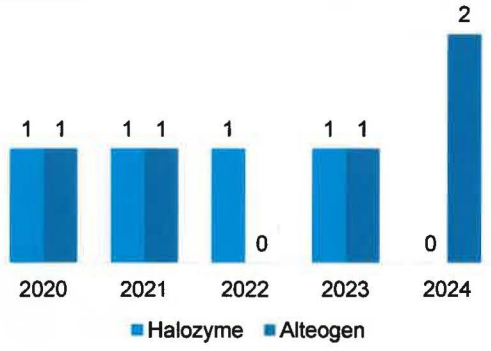
Financial Performance of Halozyme

As it was approved the earliest, Halozyme has started early cooperation with well-known pharmaceutical companies such as Roche, Janssen, BMS, Argenx, etc. on subcutaneous drug delivery products based on rHuPH20, and many of its cooperative products have been approved for marketing, providing Halozyme with considerable royalties. In addition, the single-drug sales of rHuPH20 also contribute to Halozyme's continuously growing revenue every year.



Authorization/Cooperation amount of rHuPH20, 2020-2024

Although it started late, Alteogen has carried out extensive cooperation with well-known pharmaceutical companies in recent years, such as cooperation with MSD on the subcutaneous formulation of pembrolizumab (Keytruda), the product with the highest global drug sales in 2023, and cooperation with Daiichi Sankyo on the subcutaneous formulation of trastuzumab deruxtecan (Enhertu), the product with the highest global ADC sales in 2023.



Note: As of 2024.11.30; Opdivo was approved by FDA on 2024.12.27

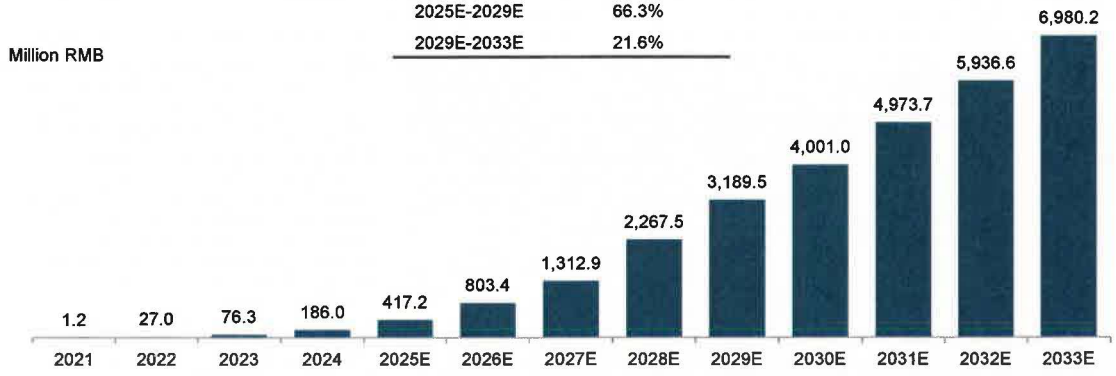
Source: Annual Reports, Literature review, Frost & Sullivan analysis

Recombinant Human Hyaluronidase Market in China, 2021-2033E

- From 2021-2024, the recombinant human hyaluronidase market grew from RMB 1.2 million to RMB186.0 million. It is expected that by 2029, the market size will grow to RMB 3189.5 million. And by 2033, to RMB 6980.2 million, with a CAGR of 21.6% from 2029 to 2033.
- Chinese market is expected to show robust growth. For recombinant human hyaluronidase monotherapy market, it is expected to have a CAGR of 12.3% from 2029 to 2033, expanding from RMB 948.6 million to RMB 1,506.9 million. And for recombinant human hyaluronidase combined with antibiotics market, it is expected to have a CAGR of 47.6% from 2029 to 2033, expanding from RMB 474.5 million to RMB 2,254.7 million.

Recombinant Human Hyaluronidase Market in China , 2021-2033E

Period	CAGR
2025E-2029E	66.3%
2029E-2033E	21.6%



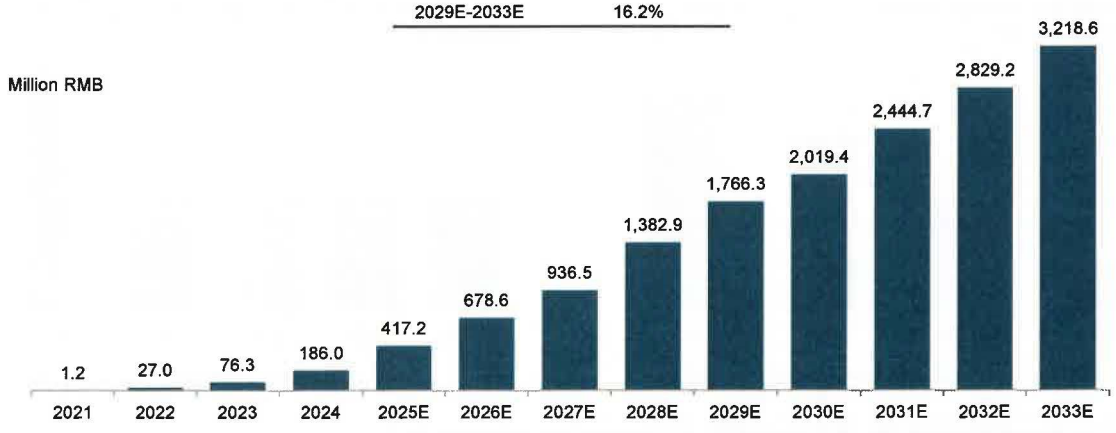
Source: Annual Reports, NMPA, CDE, Literature review, Frost & Sullivan analysis

Recombinant Human Hyaluronidase Combined with Antibodies Market in China, 2021-2033E

- From 2021-2024, the recombinant human hyaluronidase combined with antibodies market grew from RMB 1.2 million to RMB 186.0 million. It is expected that by 2029, the market size will grow to RMB 1,766.3 million, with a CAGR of 43.4% form 2025 to 2029, and by 2033, to RMB 3,218.6 million, with a CAGR of 16.2%.

Recombinant Human Hyaluronidase Combined with Antibodies Market in China , 2021-2033E

Period	CAGR
2025E-2029E	43.4%
2029E-2033E	16.2%



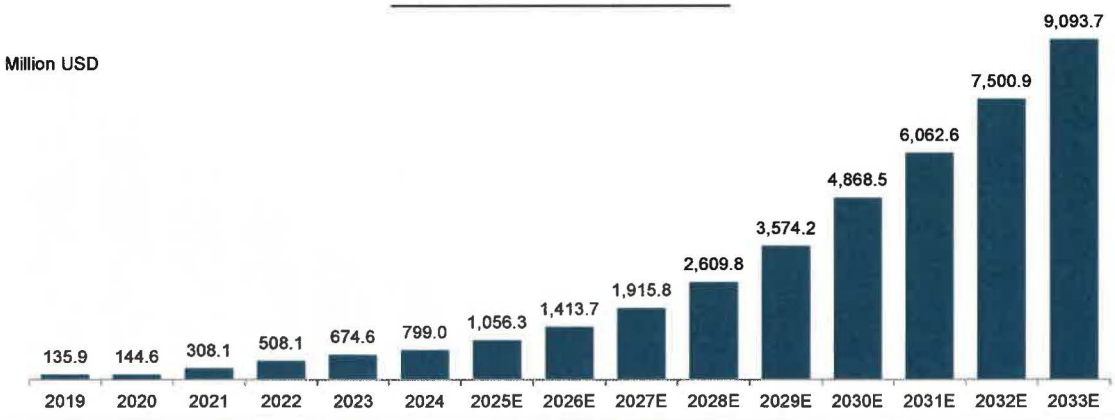
Source: Annual Reports, NMPA, CDE, Literature review, Frost & Sullivan analysis

Global Recombinant Human Hyaluronidase Market Size, 2019-2033E

- From 2019-2024, global recombinant human hyaluronidase market grew from USD 135.9 million to USD 799.0 million, with a CAGR of 42.5% during this period. It is expected that by 2029, the market size will grow to USD 3,574.2 million, and by 2033, to USD 9,093.7 million.

Global Recombinant Human Hyaluronidase Market Size, 2019-2033E

Period	CAGR
2019-2024	42.5%
2025E-2029E	35.6%
2029E-2033E	26.3%



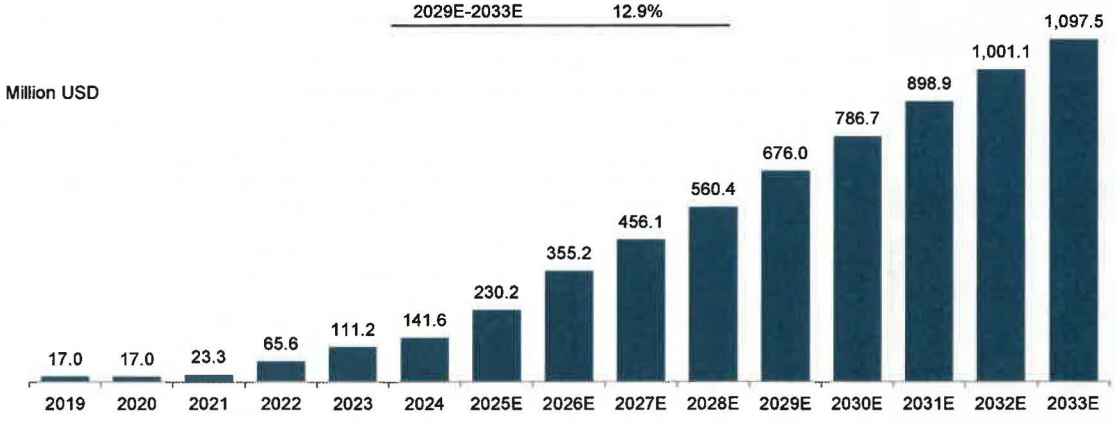
Source: Annual Reports, NMPA, CDE, Literature review, Frost & Sullivan analysis

Global Recombinant Human Hyaluronidase Monotherapy Market, 2019-2033E

- From 2019-2024, the global recombinant human hyaluronidase single therapy market grew from USD 17.0 million to USD 141.6 million, with a CAGR of 52.8% during this period. It is expected that by 2029, the market size will grow to USD 676.0 million, and by 2033, to USD 1,097.5 million.

Global Recombinant Human Hyaluronidase Monotherapy Market, 2019-2033E

Period	CAGR
2019-2024	52.8%
2025E-2029E	30.9%
2029E-2033E	12.9%



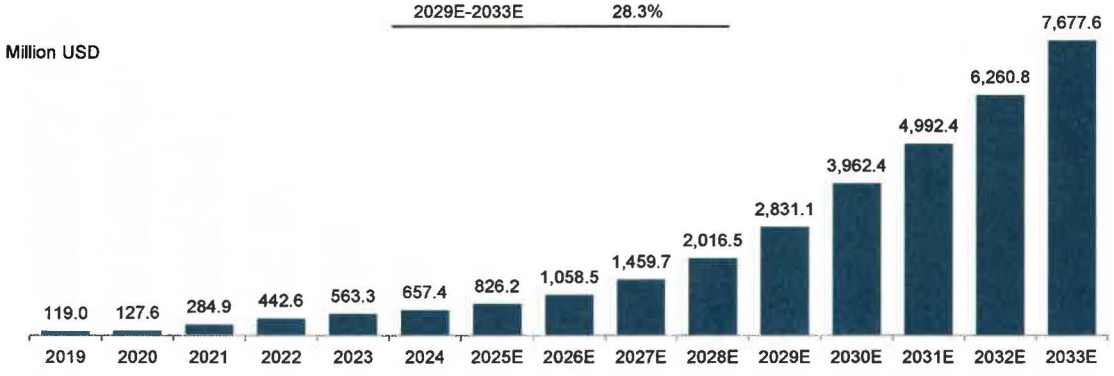
Source: Annual Reports, NMPA, CDE, Literature review, Frost & Sullivan analysis

Global Recombinant Human Hyaluronidase Combined with Antibodies Market, 2019-2033E

- From 2019-2024, the recombinant human hyaluronidase combined with antibodies market grew from USD 119.0 million to RMB 657.4 million. It is expected that by 2029, the market size will grow to RMB 2,831.1 million, with a CAGR of 36.1%, and by 2033, to RMB 7,677.6 million, with a CAGR of 28.3%.

Global Recombinant Human Hyaluronidase Combined with Antibodies Market, 2019-2033E

Period	CAGR
2019-2024	40.8%
2025E-2029E	36.1%
2029E-2033E	28.3%



Source: Annual Reports, NMPA, CDE, Literature review, Frost & Sullivan analysis

Unmet Needs and Limitations of Combined Drug Delivery System and HER2 Antibody Market

High-Cost Limitation	• HER2 antibody therapies are expensive to develop and manufacture, making them expensive for patients, especially in markets with limited healthcare reimbursement structures. High costs limit accessibility for some patients and affect further market expansion. Using recombinant human hyaluronidase subcutaneous injection technology, the drug administration route and dosage can be optimized, and the drug utilization efficiency can be improved, thereby reducing treatment costs to a certain extent. In addition, companies can also reduce costs through economies of scale and process optimization, making HER2 antibody treatment affordable for more patients.
Adverse Side Effects Limitation	• Despite the targeted effects of HER2 antibodies, some patients experience adverse reactions, such as cardiac toxicity. Concerns about side effects may hinder their widespread adoption, limiting the scope of application of HER2 antibodies and the expansion of the patient population. • Through innovative drug research and development, HER2 antibody drugs with better safety and lower toxic side effects are developed. Additionally, combined with recombinant human hyaluronidase subcutaneous injection technology, the aggregation and distribution of drugs in the body can be reduced, reducing local and systemic side effects.
Improve Convenience and Compliance of Medical Administration	• The treatment of HER2-positive breast cancer and other diseases requires long-term medication. Traditional intravenous injection is inconvenient for patients, affecting compliance. However, subcutaneous injection with recombinant human hyaluronidase can make drugs more easily break through the physical barriers of subcutaneous tissue, enabling HER2 antibodies and other drugs to be administered subcutaneously more conveniently. This reduces the number of times patients need to visit hospitals and improves the convenience and compliance of treatment.
Expand Combination Therapy Schemes	• At present, combination therapy is an important means to improve the efficacy of HER2-targeted treatment, but there are limitations in the compatibility and administration methods of existing combination schemes. Subcutaneous injection with recombinant human hyaluronidase can provide a new administration route for the combination of HER2 antibodies with other drugs, helping to develop more innovative combination therapy schemes and further improve treatment outcomes. • For example, new clinical studies of different drug combinations are being carried out, including the combination of bispecific antibodies, TKIs, ADCs, immunotherapy and anti-HER2 targeted therapy, showing certain improvements in efficacy. Recombinant human hyaluronidase subcutaneous injection is expected to play an important role in these combination therapy schemes.

Source: Frost & Sullivan analysis

Growth Drivers of China's Subcutaneous Drug Delivery System Market/Recombinant Human Hyaluronidase Market

Improves SC Dosage Limitation	• Generally speaking, the maximum injection volume of subcutaneous injections is about 1-2 ml. However, the subcutaneous injection volume depends on many factors, including injection speed, injection site, injection volume, leakage/tissue back pressure, drug formulation composition and individual patient characteristics, including the patient's pain sensitivity. By using rHuPH20, hyaluronic acid is locally decomposed at the injection site and the barrier is temporarily cleared, so a large amount of fluid can be injected into the subcutaneous space and dispersed. Hyaluronic acid can be restored under the skin within 24 hours. Therefore, the use rHuPH20 technology can break through the natural subcutaneous barrier that limits the dosage to 2 ml, allowing larger doses of drugs to be delivered through a single subcutaneous injection.
Improve Patient Compliance	• Tumor antibody drugs can be converted from intravenous (IV) to SC dosage forms based on rHuPH20, which can be completed in less than 10 minutes instead of several hours of injection time. Compared with patients with conventional chronic diseases, cancer patients are often in worse physical condition and have shorter survival. For regular antibody treatment (usually once every three weeks), if patients can self-administer in outpatient clinics or even at home, it will undoubtedly greatly improve patient comfort and compliance, thereby improving the quality of life.
Broad Application Areas of Drugs	• In the past, the main application areas of subcutaneous drug delivery included drugs such as insulin, heparin, and some vaccines, and the usage scenarios were relatively limited. At present, the drugs approved for marketing based on the rHuPH20 subcutaneous drug delivery system worldwide mainly include antibodies and proteins, and its main application areas have expanded to anti-tumor drugs, autoimmune diseases, etc.

Source: Frost & Sullivan analysis

Analysis of Future Trends in the China's Subcutaneous Drug Delivery System Market/Recombinant Human Hyaluronidase Market

Continuous Innovation of Technology Platform	• From animal-derived hyaluronidase to recombinant human hyaluronidase, the technology platform of hyaluronidase has changed from biochemical extraction to a production path based on genetic engineering and modern biological culture technology. On the one hand, it reduces impurities in the product to reduce immunogenicity, and on the other hand, the standardized modern biopharmaceutical production path reduces production costs. In addition, based on the continuous development of current biotechnology, the production technology of recombinant human hyaluronidase is also continuously innovating. New technologies such as synthetic biology are expected to provide a stable and economical supply chain for recombinant human hyaluronidase in the future when it is applied on a large scale due to its advantages such as high efficiency, environmental friendliness, and low production costs.
Gradually Expanding the Application Field	• At present, subcutaneous drug delivery systems based on recombinant human hyaluronidase are mainly used for antibody and protein drugs, and new macromolecular drugs such as antibody-drug conjugates are also trying to achieve subcutaneous delivery through recombinant human hyaluronidase to further improve patient compliance. In addition, in the field of drug treatment, it is also expanding from anti-tumor and anti-autoimmune fields to anti-infection and other fields. Antibiotics that previously required intravenous injection (such as β-lactams) are expected to achieve subcutaneous delivery.
Deepening Cooperation with Pharmaceutical Companies	• Although there are not many biological drugs based on recombinant human hyaluronidase that have been approved worldwide for subcutaneous delivery, and Halozyme's current cooperation model has target exclusivity, with the continuous development of the global biological drug market, patients' quality of life has become more and more important, and the demand for switching from intravenous injection to subcutaneous injection has been gradually released. Therefore, emerging recombinant human hyaluronidase companies such as China's Bao Pharma are expected to reach cooperation with biopharmaceutical companies in the early clinical stages to achieve earlier commercialization of subcutaneous administration for more innovative biological drugs with new targets and a large number of biosimilars in the future. At the same time, there is also broad room for cooperation for biosimilars of approved products.

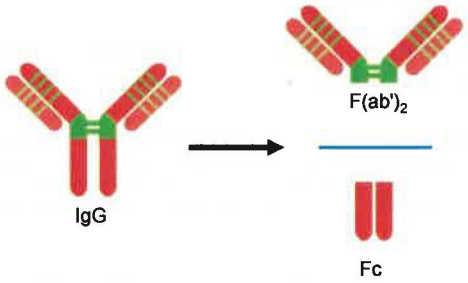
Source: Frost & Sullivan analysis

IgG-Degrading Enzymes Overview

- IdeS and IdeZ Proteases are immunoglobulin G (IgG)-degrading enzymes that are valuable tools for the characterization of therapeutic antibodies, Fc fusion proteins and antibody-drug conjugates.
- IdeS (immunoglobulin G [IgG]-degrading enzyme of *Streptococcus pyogenes)* is a cysteine proteinase that can cleave all four human IgG subclasses with a unique degree of specificity below the disulfide bridge in the hinge region. IdeS sequentially cleaves the two heavy chains of IgG with different kinetics, thus releasing the $F(ab')_2$ fragment from the Fc fragment. IdeS is also being studied for its therapeutic potential in several autoimmune diseases as well as in oncology and gene therapy.
- IdeZ Protease is derived from *Streptococcus equi subspecies zooepidemicus.* Both IdeS and IdeZ Proteases effectively cleave human IgG1, IgG2, IgG3 and IgG4, monkey, sheep, rabbit, humanized and chimeric IgGs as well as Fc-fusion proteins. However, only IdeZ Protease cleaves mouse IgG2a and IgG3.
- A recombinant IdeS is commercially available (Imlifidase, Ideferix®) and is the only desensitization treatment European Medicines Agency-approved for kidney transplant patients with donor-specific antibodies.

Mechanism

Immunoglobulin G-degrading enzyme cleaves IgG antibodies into $F(ab')_2$ and Fc fragments.



Advantages of IgG-Degrading Enzymes (IdeS)

- **High Specificity**: IdeS exhibits high specificity by cleaving the hinge region of the IgG heavy chain.
- **Rapid Action**: After binding to IgG, IdeS can quickly cleave the hinge region of the IgG molecule. This process typically occurs **within a few hours** and significantly reduces the IgG levels in the blood.
- **Reduced Immune Side Effects**: By cleaving the Fc region, IdeS effectively reduces inflammatory reactions and side effects associated with immune responses.
- **Wide Application Range**: IdeS is not only effective in autoimmune diseases but also has potential applications in transplant medicine and antibody-based therapies.

Source: Literature Review, Frost & Sullivan analysis

Applications of IgG-Degrading Enzyme (IdeS)

Autoimmune Diseases

- **Application**: IdeS is particularly useful in treating **autoimmune diseases** where IgG antibodies are involved in pathogenesis. It helps to alleviate symptoms in conditions such as **Immune Thrombocytopenic Purpura (ITP), ANCA-associated vasculitis, and Myasthenia Gravis.**
- **Mechanism**: By cleaving the hinge region of IgG, IdeS reduces the immunopathology caused by antibody-mediated tissue damage.

Anti-glomerular basement membrane disease (GBM)

- **Application**: GBM is an autoimmune condition where the body's immune system attacks the glomerular basement membrane in the kidneys and the alveolar basement membrane in the lungs. This is mediated by anti-GBM antibodies, which are IgG antibodies that bind to collagen in the basement membranes.
- **Mechanism of Action**: By cleaving IgG at the hinge region, IdeS would effectively lower the levels of pathogenic antibodies, potentially reducing the severity of the disease.

Guillain-Barré Syndrome (GBS)

- **Application**: Guillain-Barré Syndrome (GBS) is an acute autoimmune disorder that affects the peripheral nervous system, often triggered by an infection. In GBS, IgG antibodies can attack the myelin sheath of nerves, leading to muscle weakness and paralysis.
- **Mechanism of Action**: IdeS could be used to rapidly degrade these pathogenic IgG antibodies, which might reduce the autoimmune attack on the peripheral nerves.

Transplant Medicine

- **Application**: In **transplantation**, especially kidney and heart transplants, donor-specific antibodies (DSA) often lead to acute rejection of the transplanted organ. IdeS can rapidly degrade these antibodies, reducing the risk of antibody-mediated rejection (AMR) and improving transplant outcomes.
- **Mechanism**: IdeS effectively reduces the levels of harmful DSAs, decreasing the likelihood of rejection and improving graft survival rates.

Rare Diseases

- **Application**: Rare immunoglobulin-related diseases such as **hypergammaglobulinemia** and **IgG-mediated infections** may benefit from IgG depletion strategies. IdeS has shown potential for treating conditions where IgG antibodies play a central role in pathogenesis.
- **Mechanism**: By rapidly degrading IgG, IdeS can help manage high IgG levels that contribute to disease, providing a novel approach for treating these rare conditions.

Other Potential Applications

- **Application**: Besides autoimmune diseases and transplantation, IdeS is being explored for treating **IgE-mediated allergic reactions** and other immune disorders where IgG antibodies contribute to pathological responses.
- **Mechanism**: Its ability to specifically target and degrade IgG could be extended to other antibody-driven diseases, such as chronic allergic conditions, by potentially reducing the allergic immune response.

Competitive Landscape of IgG Degrading Enzyme in China

There is only one IgG Degrading Enzyme products in clinical trials in China. As of the LPD, no IgG Degrading Enzyme drug has approved in China.

IgG Degrading Enzyme Pipeline

Drug Name	Company	Target	Indications	Stage	Area	Clinical Regulatory Authorities	First Posted Date
KJ103	**Bao Pharma**	IgG	Desensitization treatment of highly sensitized adult kidney transplant patients	III	China	NMPA	2025/07/30
			Anti Glomerular Basement Membrane (GBM)	II	China	NMPA	2024/09/23
			Acute severe autoimmune diseases mediated by pathogenic IgG autoantibodies	I	New Zealand	Medsafe	2022/05/19

Note: As of 2025.11.22

Source: CDE, NMPA, Frost & Sullivan Analysis

The Overview of IgG-Mediated Autoimmune Diseases

- In the process of IgG antibodies taking effect, the immune system may mediate the attack of the disease itself through a variety of immune mechanisms, including complement system activation, Fc receptor mediation, immune complex formation and deposition, etc. These mechanisms can occur independently, or they may be superimposed or synergistic, depending on the specific case mechanism of the disease and the immune response triggered by the environment.

➢ In IgG-mediated autoimmune diseases, IgG, as the main type of autoantibody, mediates the immune system's attack on its own tissues through a variety of immune mechanisms. These mechanisms include:

Complement System Activation

IgG binds to C1q in the complement system through its Fc segment, activating the classical complement pathway.

- It may form a membrane attack complex (MAC), which directly leads to cell lysis.
- It may release inflammatory mediators, attracting neutrophils and macrophages, triggering inflammatory responses and tissue damage.

Fc Receptor-Mediated Effects

The Fc segment of IgG antibodies binds to Fcγ receptors on the surface of immune cells, inducing different types of immune responses:

- NK cells: Kill target cells through antibody-dependent cell-mediated cytotoxicity.
- Dendritic cells and monocytes: Promote the release of inflammatory factors and aggravate tissue destruction.

Formation and Deposition of Immune Complexes

Antigen-antibody complexes may form in the blood circulation and then deposit in tissues (such as glomeruli, blood vessel walls).

- It may activate local inflammatory responses and attract immune cell infiltration.
- Leading to chronic inflammation and tissue damage, such as glomerulonephritis in systemic lupus erythematosus.

Inducing the Release of Inflammatory Factors

IgG antibodies bind to target antigens or activate immune cells through the FcγR signaling pathway, leading to the release of a large number of inflammatory factors (such as IL-6, TNF-α), thereby inducing systemic or local inflammation.

Main Disease Name	Mechanism
Rheumatoid Arthritis	Antibodies first bind to antigens (such as CCP) to form immune complexes, activate complement, and induce inflammatory responses. They then recruit macrophages and neutrophils through FcγR, further exacerbating joint damage.
Myasthenia Gravis	Antibodies block acetylcholine receptor function and rely primarily on FcγR signaling rather than complement action.
Systemic Lupus Erythematosus	In the early stage, circulating immune complex deposition is the main symptom, leading to local inflammation. As the inflammation expands, complement activation and FcγR-mediated cytotoxicity may overlap.
Primary Biliary Cholangitis	Initially, anti-mitochondrial antibodies (AMA, IgG subtype) recognize bile duct epithelial cell antigens; as the disease progresses, local inflammatory factors are released, exacerbating bile duct fibrosis.

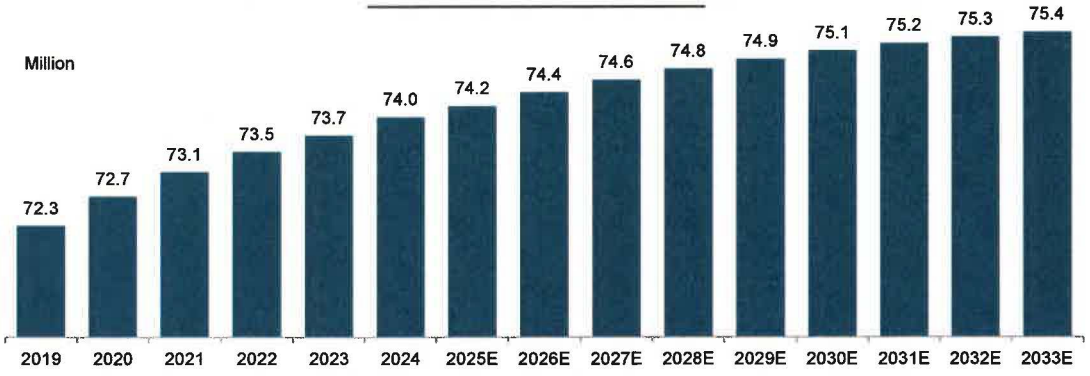
Source: Literature review, Frost & Sullivan analysis

Prevalence of IgG-Mediated Autoimmune Diseases in China, 2019-2033E

- From 2019-2033, the prevalence of IgG-mediated autoimmune diseases in China is expected to show a slow but steady increase. In 2019, the total number of patients was 72.3 million, with a CAGR of 0.5% over the next five years to reach 74.0 million in 2024. From 2024-2029, the growth rate is expected to slow down, with a CAGR of 0.2%, bringing the patient population to 74.9 million by 2029. This trend is projected to continue from 2029 to 2033, with a CAGR of 0.1%, with the number of patients reaching 75.4 million by 2033.

Prevalence of IgG-Mediated Autoimmune Diseases in China, 2019-2033E

Period	CAGR
2019-2024	0.5%
2025-2029E	0.2%
2029E-2033E	0.1%



Source: Annual Reports, NMPA, CDE, Literature review, Frost & Sullivan analysis

Current Limitations of IgG-Mediated Autoimmune Diseases

Insufficient Research on the Functions of IgG Subtypes	• IgG comprises four major subclasses (IgG1, IgG2, IgG3, and IgG4), each with distinct functional and pathological roles. Current research on the specific roles of each subclass in various autoimmune diseases is limited. This knowledge gap restricts our comprehensive understanding of disease mechanisms. Moreover, the development of precise therapies requires deeper subclass analysis, but current technological methods still need improvement.
Insufficient Specificity and Sensitivity of Diagnosis	• Although IgG autoantibodies are critical markers for diagnosing many autoimmune diseases, their specificity and sensitivity are limited. Some IgG antibodies may also be present in healthy individuals, leading to false-positive results. Furthermore, the dynamic changes in IgG antibody levels in different diseases are not fully understood, which can compromise diagnostic accuracy. Hence, relying solely on IgG antibody detection may not be sufficient to distinguish disease subtypes or assess disease activity.
Complexity and Heterogeneity of Disease Mechanisms	• IgG-mediated autoimmune diseases often involve multiple mechanisms, such as complement activation, immune complex deposition, and Fc receptor-mediated responses. These mechanisms can vary significantly between different diseases or even among patients with the same disease. Additionally, the interplay between genetic and environmental factors further contributes to disease heterogeneity. This complexity makes it challenging to develop universal diagnostic or therapeutic approaches.
Nonspecificity of Therapeutic Targets	• Treatments for IgG-mediated diseases often rely on broad immunosuppression or generalized antibody clearance. These approaches may cause non-specific immune suppression, increasing the risk of infections and other side effects. Furthermore, these therapies often fail to selectively target pathogenic IgG antibodies and may affect normal IgG functions. Developing more specific treatment strategies remains a significant challenge.

Source: Frost & Sullivan Analysis

Unmet Needs and Market Prospects of IgG-Mediated Autoimmune Diseases

Development of Precision Diagnostic Technologies	• Currently, the diagnosis of IgG-mediated diseases primarily relies on antibody detection, which falls short in accurately distinguishing disease subtypes or predicting progression. There is a critical need for advanced diagnostic tools that can monitor IgG subclasses and dynamic changes with high sensitivity, such as mass spectrometry-based methods. These precision diagnostic technologies can assist clinicians in refining personalized treatment strategies while substantially reducing the rates of misdiagnosis and missed diagnoses. The market potential is immense, especially with the growing demand for early detection of complex diseases like SLE and RA.
Breakthroughs in Targeted Therapies	• Existing therapies largely rely on broad immunosuppression, lacking the ability to specifically target pathogenic IgG antibodies. Future research should focus on developing subclass-specific IgG blockers or Fc receptor antagonists to reduce side effects and enhance efficacy. Advances in biologics and antibody engineering present new opportunities in this field. The global market has a strong demand for precision therapies, particularly for high-prevalence diseases such as rheumatoid arthritis and multiple sclerosis.
Development of Innovative Immunomodulatory Drugs	• Innovative drugs targeting IgG-mediated autoimmune diseases are advancing rapidly, offering more precise treatment options. FcRn antagonists (e.g., Efgartigimod and Rozanolixizumab) have reached late-stage clinical trials and demonstrated significant efficacy, with some already approved for conditions like myasthenia gravis. Bispecific antibodies and small-molecule immunomodulators are also under clinical development, aiming to enhance efficacy while reducing side effects. Additionally, the exploration of combination therapies has emerged as a key focus, promising more comprehensive treatment solutions. The commercialization of these innovative drugs is set to drive market growth and bring new hope to patients.
Improving Global Treatment Accessibility	• While novel therapies for IgG-mediated diseases are emerging, their high cost and complexity limit accessibility in developing countries. Thus, there is a need to develop cost-effective treatments that are easier to store and transport, along with increased government and institutional support to reduce the financial burden on patients. Market prospects are particularly significant in emerging economies, where large patient populations and substantial unmet needs offer critical growth opportunities for pharmaceutical companies.

Source: Frost & Sullivan Analysis

Global Competitive Landscape of IgG Degrading Enzyme

There are currently one IgG Degrading Enzyme product marketed globally. Idefirix® received a conditional marketing authorization valid throughout the EU on 25 August 2020.

Marketed IgG Degrading Globally

Drug Name	Generic name	Company	Target	Indications	Approved region	Approved Date
Idefirix®	Imlifidase	Hansa Biopharma	IgG	Desensitization treatment of highly sensitized adult kidney transplant patients	EMA	2020/08/25

IgG Degrading Enzyme Pipeline

Drug Name	Company	Target	Indications	Stage	Area	Clinical Regulatory Authorities	First Posted Date
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			Anti Glomerular Basement Membrane (GBM)	II	China	NMPA	2024/09/23
			Acute severe autoimmune diseases mediated by pathogenic IgG autoantibodies	I	New Zealand	Medsafe	2022/05/19
Idefirix®	Hansa Biopharma	IgG	Anti Glomerular Basement Membrane (GBM)	III	EU/US/UK	EMA/FDA/MHRA	2023/01/11
			Guillain-Barré syndrome (GBS)	II	EU/UK	EMA/MHRA	2018/12/19
			Crigler–Najjar syndrome	II	EU	EMA	2024/07/24
			Muscular dystrophy	I	EU	EMA	2023/01/31
HNSA-5487	Hansa Biopharma	IgG	Autoimmune diseases	I	EU	EMA	2023/04/20
VTX-PID	Vivet Therapeutics	IgG	Adeno-associated virus infection	I	EU	EMA	2023/09/28
S-1117	Seismic Therapeutic	IgG	Chronic inflammatory demyelinating polyneuropathy, Myasthenia gravis, Immune thrombocytopenia	I	Australia	TGA	2025/02/14

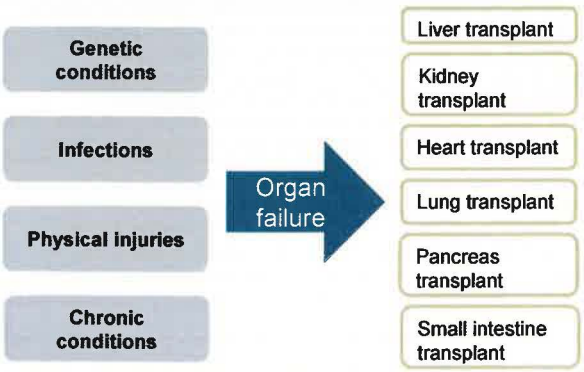
Source: Clinicaltrials.gov, EMA, FDA, MHRA, TGA, Frost & Sullivan Analysis

Note: 1. As of 2025.11.22; 2. FDA: Food and Drug Administration (US); 3. EMA: European Medicines Agency (EU); 4. MHRA: Medicines and Healthcare products Regulatory Agency (UK); 5. TGA: Therapeutic Goods Administration (Australia); 6. NMPA: National Medical Products Administration (China); 6. Medsafe: New Zealand Medicines and Mec
Area = Clinical trial locations per official records. Each area maps to its clinical regulatory authorities

Overview of Organ Transplantation in China

- Organ transplantation is where failing or damaged organ of patient is to be removed and replaced with a well-functioning one. The source of replacing organ could be a deceased donor, a living donor, or an animal. Organ transplantation is required when a patient's organ is working very poorly or failing. Most common organ transplantations are liver, kidney, heart, lung, pancreas and small intestine transplantation. The causes of organ failure could be genetic conditions, infections, physical injuries to organs or organ damage due to chronic conditions.
- Though organ transplantation technologies are available in China, expansion of organ transplant market is limited due to organ availabilities. Since September 2013, distribution of donated organs will be regulated by nationally unified system, where organs are assigned to patients based on a comprehensive evaluation of patients' demanding on organs. This enables transparent and fair assignment of highly limited and valuable donated organs in China.
- In China, only medical institutions with practicing qualifications for human organ transplantation are allowed to perform organ transplant surgeries. In 2019, there were 170 medical institutions being qualified to perform organ transplant, this number increased to 180 by 2021 at a CAGR of 2.90%.

Common causes and types of organ transplantation



Distribution of qualified hospitals for transplantation in China

Source: NHC, List of medical institutions with practicing qualification for human organ transplantation

Transplant Rejection Classification

Transplant rejection can be classified as hyperacute, acute, or chronic:

- Hyperacute rejection is typically caused by specific antibodies against the graft and occurs within minutes or hours after grafting.
- Acute rejection develops days or weeks after transplantation and can be caused by specific lymphocytes in the recipient that recognize human leukocyte antigen (HLA) antigens in the grafted tissue or organ.
- Chronic transplant rejection, on the other hand, usually manifests months or years after organ or tissue transplantation and involves various mechanisms, including chronic inflammation and humoral and cellular immune reactions, which play crucial roles in its immunopathogenesis.

	Type	Onset	Mechanism	Type of Hypersensitivity
Host against Graft	Hyperacute	Immediate	**Preformed antibodies** against the donated tissue. Caused by accidental ABO **Blood type mismatching** of the donor and recipient which is very rare. Results in **thrombosis and occlusion of the graft vessel.**	II
	Acute	Weeks to months	T-Cell mediated immune response directly against foreign MHC (Major Histocompatibility Complex) in the donated organ. Results in **leukocyte infiltration of the graft vessel**. Most common type.	IV
	Chronic	Months to years	T-Cell directed against the foreign MHC (Major Histocompatibility Complex) molecules which look like self-MHC presenting a foreign antigen. Results in **intimal thickening and fibrosis of graft vessels** as well as organ atrophy.	III & IV
Graft against Host		Months to years	Donor T-Cells in the graft proliferate and attack the recipient's tissue. Most commonly seen in **Bone Marrow Transplants**. Symptoms commonly include **diarrhea, rash and jaundice.**	IV

Source: Literature Review, Frost & Sullivan analysis

Symptoms and Treatment of Transplant Rejection

Symptoms of Organ Rejection

Kidney Transplant
- Reduced Urine Output
- Pain over the Transplant Site
- Fever
- High Blood Pressure
- Swelling

Heart Transplant
- Shortness of Breath
- Fatigue
- Swelling
- Fever

Liver Transplant
- Jaundice
- Fever
- Abdominal Pain
- Elevated Liver Enzymes

Lung Transplant
- Cough
- Fever
- Shortness of Breath
- Low Oxygen Levels

Treatment Strategies

Immunosuppressive Drugs
- **Calcineurin Inhibitors**: Tacrolimus and Cyclosporine
- **Corticosteroids** : Prednisone
- **Antiproliferative Agents**: Mycophenolate Mofetil (MMF) and Azathioprine

Plasmapheresis
- **Plasmapheresis** is a procedure used in **antibody-mediated rejection (AMR)** to remove harmful antibodies from the blood.

Intravenous Immunoglobulin (IVIg)
- **IVIg** is used in conjunction with plasmapheresis in cases of antibody-mediated rejection. IVIg contains pooled human antibodies that can neutralize the harmful donor-specific antibodies (DSAs) and suppress the immune response, helping to stabilize the transplant.

IgG-Degrading Enzyme (IdeS)
- **IdeS** is an emerging treatment for **antibody-mediated rejection (AMR)**. By specifically degrading IgG antibodies, including **donor-specific antibodies**, it can reduce the immune attack on the transplanted organ. This enzyme may complement existing treatments, such as plasma exchange and IVIg, and provide a more targeted approach to treating antibody-mediated rejection.

Risk Factors for Rejection

- Mismatch Between Donor and Recipient: HLA Mismatch & Blood Group Compatibility
- Pre-existing Antibodies : Donor-Specific Antibodies (DSA)
- Delayed Graft Function
- Non-adherence to Immunosuppressive Medications

Source: Literature Review, Frost & Sullivan analysis

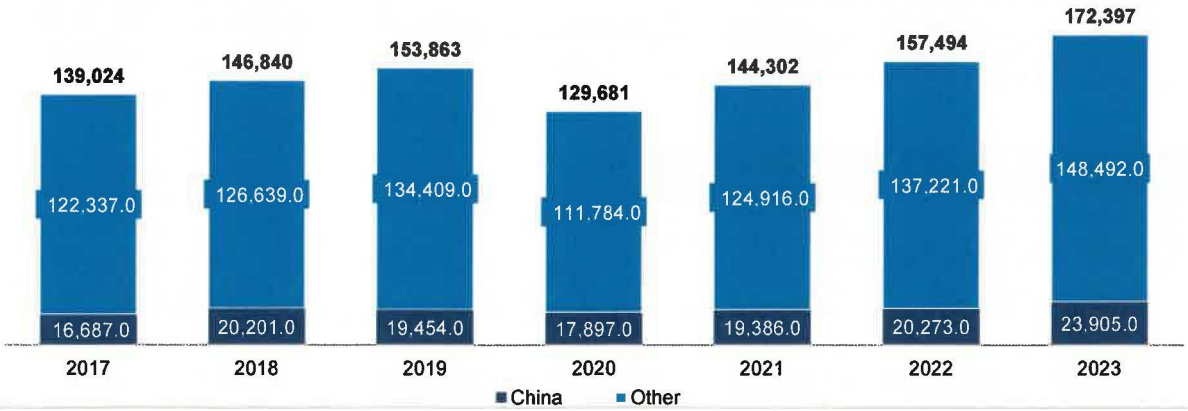
Organ Transplantation Operations in China and Globally, 2017-2023

- The number of organ transplantation operations globally has grown from 139,024 in 2017 to 172,397 in 2023. With the development of organ transplantation, the improvement of transplantation efficacy and the widening of transplantation indications, more and more patients gradually accept organ transplantation as a routine treatment.
- The number of organ transplantation operations in China has grown from 16,687 in 2017 to 23,905 in 2023. With the development of organ transplantation, the improvement of transplantation efficacy and the widening of transplantation indications, more and more patients gradually accept organ transplantation as a routine treatment.

Organ Transplantation Operations in China and Globally, 2017-2022

Period	CAGR	
	China	Global
2017-2022	6.2%	3.7%

Unit



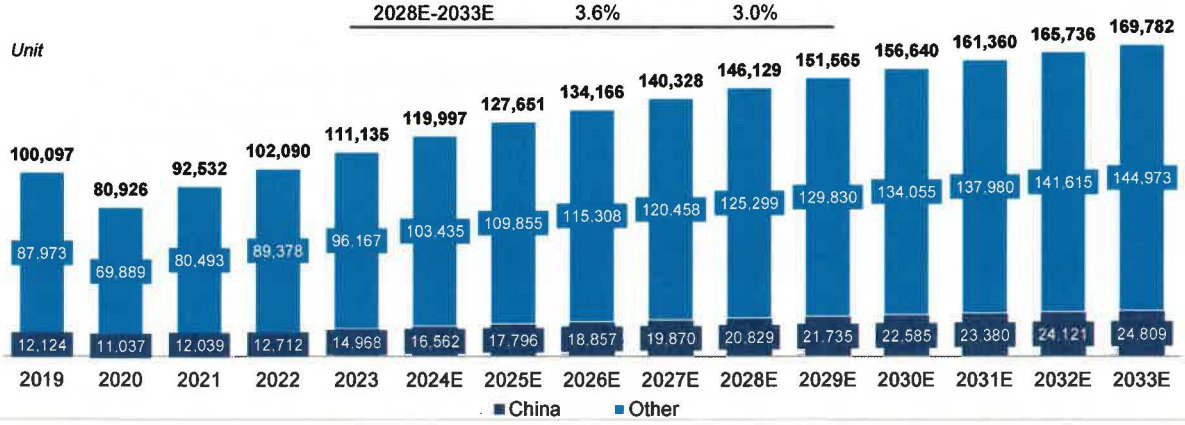
Source: Global Observatory on Donation and Transplantation, 2023 National Report on the Service, Quality and Safety in Medical Care System, Frost & Sullivan Analysis

Kidney Transplantation Operations in China and Globally, 2019-2033E

- In 2019, the number of kidney transplants in China was 12,124, while the global figure stood at 100,097. By 2023, China's transplant volume had increased to 14,968, with a CAGR of 5.4%. During the same period, the global transplant volume reached 111,135, with a CAGR of 2.6%. By 2028, the number of kidney transplants in China is expected to rise to 20,829, corresponding to a CAGR of 6.8%, while the global figure is projected to reach 146,129, with a CAGR of 5.6%. Looking ahead to 2033, the kidney transplant volume in China is anticipated to reach 24,809, with a CAGR of 3.6%, while the global number is estimated to grow to 169,782, with a CAGR of 3.0%.

Kidney Transplantation Operations in China and Globally, 2019-2033E

Period	CAGR	
	China	Global
2019-2023	5.4%	2.6%
2023-2028E	6.8%	5.6%
2028E-2033E	3.6%	3.0%



Source: Global Observatory on Donation and Transplantation, 2023 National Report on the Service, Quality and Safety in Medical Care System, Frost & Sullivan Analysis

Kidney Transplantation Rejection Treatment Paradigm in China

In the preoperative period for kidney transplantation, recommended therapies include **plasma exchange/immunoadsorption**, **high-dose IVIG**, and **B cell depletion regimens**. Among these, IVIG is more commonly used due to its convenience of administration and fewer side effects.

Preoperative Prevention

For highly sensitized kidney transplant recipients:

- Plasma exchange / Immunoadsorption
- High-dose intravenous immunoglobulin (IVIG)
- B cell depletion regimen (rituximab or combination regimen)

Perioperative Period of Kidney Transplantation

Immunosuppressive induction therapy refers to the short-term use of monoclonal or polyclonal antibody-based immunosuppressive drugs in kidney transplant recipients during the perioperative period. Based on the immune risk stratification of kidney transplant recipients, the following drugs are recommended for the prevention of acute rejection:

- Interleukin-2 receptor alpha (IL-2RA) or lymphocyte-depleting antibodies (ATG, ALG) (A, 1a).
- Rabbit anti-humanthymocyte globulin (rATG) (B, 2c).
- Anti-human T lymphocyte porcine immunoglobulin (p-ATG) (D,5)

Maintenance Period of Kidney Transplantation

There are a variety of combined treatment options for immunosuppressive therapy during the postoperative maintenance period, which are classified according to the strength of recommendation and level of evidence as follows:

- CNI (Tac/CsA) + MPA + glucocorticoids (A, 1a)
- CNI (Tac/CsA) + MZR + glucocorticoids, CNI (Tac/CsA) + mTORi + glucocorticoids (A, 1b)

Strength of Recommendations	Evidence Quality	Description
A	1a	Systematic review of RCTs
	1b	RCTs with small confidence intervals
	1c	Any evidence of "all or no effect" in RCTs
B	2a	Systematic review of cohort studies
	2b	Single cohort studies
	2c	Patient outcomes-based studies
	3a	Systematic review of case-control studies
	3b	Single case-control studies
C	4	Case series reports, low-quality cohort studies, and low-quality case-control studies
D	5	Expert opinion

Note: Interleukin-2 receptor alpha, IL-2RA; Anti-thymocyte globulin, ATG; Anti-human T lymphocyte immunoglobulin, ALG; Calcineurin inhibitor, CNI; Cyclosporin A, CsA; Tacrolimus, Tac; Mycophenolic acid, MPA; Mizoribine, MZR; Mammalian target of rapamycin inhibitors, mTORi

Source: 《肾移植排斥反应临床诊疗技术规范（2019版）》, 《中国肾脏移植受者免疫抑制治疗指南（2023版）》, Frost & Sullivan analysis

Competitive Landscape of IgG Degrading Enzyme for Kidney Transplant Rejection in China

There is only one IgG Degrading Enzyme products in clinical trials in China. As of the LPD, no IgG Degrading Enzyme drug has been approved in China.

Pipeline in Anti-GBM Treatment

Drug Name	Company	Target	Indications	Stage	Approved Date
KJ103	**Bao Pharma**	IgG	Desensitization treatment of highly sensitized adult kidney transplant patients	II/III	2023/12/25
			Anti Glomerular Basement Membrane (GBM)	II	2024/09/23
			Acute severe autoimmune diseases mediated by pathogenic IgG autoantibodies	I	2022/05/19

Note: As of 2025.03.12

Source: CDE, NMPA, Frost & Sullivan Analysis

Global Competitive Landscape of IgG Degrading Enzyme for Kidney Transplant Rejection

There are currently one IgG Degrading Enzyme product marketed for kidney transplant rejection. Idefirix® received a conditional marketing authorization valid throughout the EU on 25 August 2020.

Marketed IgG Degrading Enzyme for Kidney Transplant Rejection Treatment

Drug Name	Generic name	Company	Target	Indications	Approved region	Approved Date
Idefirix®	Imlifidase	Hansa Biopharma	IgG	Desensitization treatment of highly sensitized adult kidney transplant patients	EMA	2020/08/25

Pipeline in Kidney Transplant Rejection Treatment

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Note: As of 2025.03.12

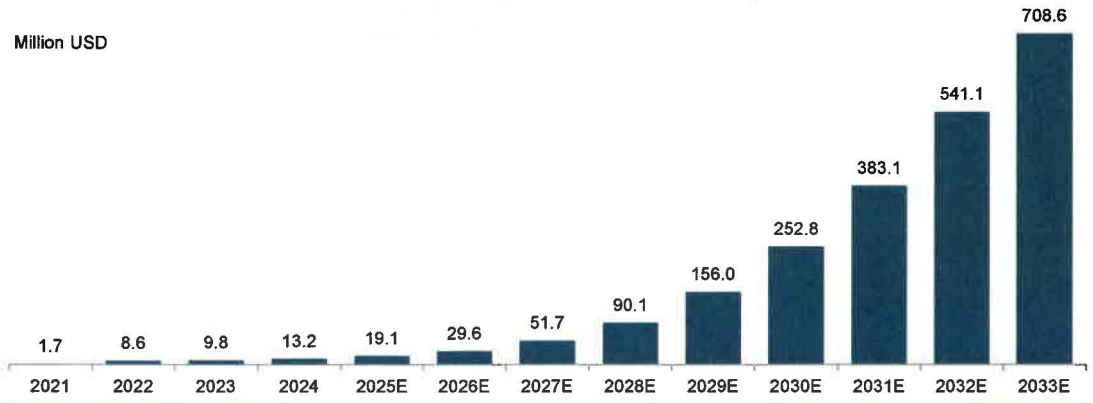
Source: Clinicaltrials.gov, CDE, NMPA, Frost & Sullivan Analysis

IgG Degrading Enzyme Kidney Transplant Market Globally, 2021-2033E

- The global IgG degrading enzyme kidney transplant market is projected to achieve a CAGR of 69.1% between 2025 and 2029, with market size increasing from USD 19.1 million in 2025 to USD 156.0 million in 2029. Between 2029 and 2033, the CAGR slows to 46.0%.
- In China, there is no IgG degrading enzyme products for kidney transplant. However, the Chinese market is expected to show great growth, with a CAGR of 28.5% from 2029 to 2033, expanding from RMB 408.3 million to RMB 1,113.6 million.

IgG Degrading Enzyme Kidney Transplant Market Globally, 2021-2033E

Period	CAGR
2025E-2029E	69.1%
2029E-2033E	46.0%



Source: Frost & Sullivan analysis

Unmet Needs in the Treatment of Transplant Rejection

Early Diagnosis and Monitoring of Rejection	• Rejection reactions after organ transplantation often begin subtly, and early symptoms may not be obvious. Current diagnostic methods, such as biopsies, are invasive, time-consuming, and cannot comprehensively and continuously monitor immune responses. Effective early diagnostic methods are still lacking, especially for antibody-mediated rejection (AMR). There is a need to develop non-invasive, sensitive blood biomarkers that can detect rejection early, particularly tests for donor-specific antibodies (DSA), to provide real-time monitoring and enable early intervention.
Treatment of Antibody-Mediated Rejection (AMR)	• Antibody-mediated rejection (AMR) occurs when the antibodies of the immune system attack the transplanted organ. This leads to severe organ damage and significantly reduces transplant success rates. Immunosuppressants play a crucial role in the treatment or prevention of chronic active AMR. The risk of early AMR is especially high if the transplantation is performed in an HLA-incompatible constellation. To improve the access of sensitized patients to transplantation, current treatments for AMR are limited, and new targeted therapies,such as IgG-degrading enzyme, are urgently needed.
Long-Term Graft Survival and Induction of Transplant Tolerance	• While current treatments can control rejection in the short term, long-term survival of the transplanted organ is still affected by chronic rejection, immune system attack, and other complications. Long-term dependence on immunosuppressive drugs increases the risk of side effects and associated health problems. There is a need for strategies to induce transplant tolerance, allowing the immune system to naturally accept the transplanted organ without lifelong immunosuppressive therapy. New therapies such as immune modulation and IgG-degrading enzymes could help improve long-term survival and reduce drug dependency.

Source: Literature review, Frost & Sullivan analysis

The Overview of Xenotransplantation

1 Introduction

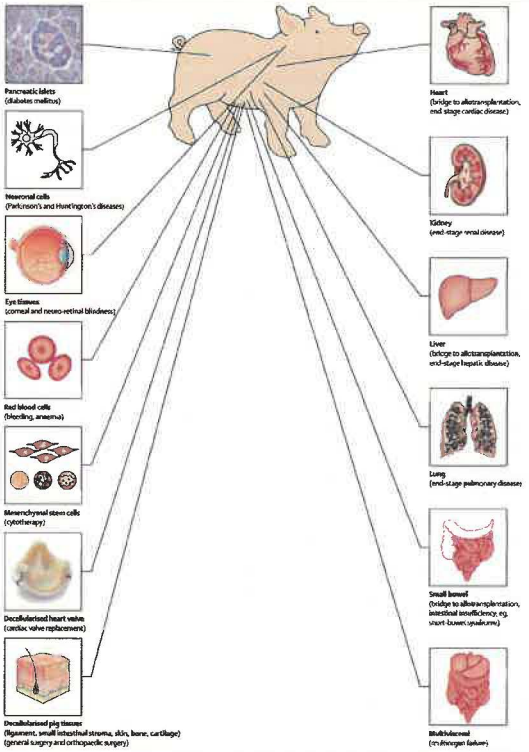
Xenotransplantation involves the transplantation of organs, tissues, or cells from a non-human species into a human recipient. It is a promising area of research aimed to overcome the limitations of human organ availability and provide timely treatment for patients with end-stage organ failure or other critical conditions.

2 Source Species

- **Pigs as the Primary Source:** Pigs are the most commonly used species due to their anatomical and physiological similarities to humans, rapid breeding, and ease of genetic modification.
- **Non-Human Primates:** Rarely considered due to ethical issues and higher risk of zoonotic disease transmission.

3 Types

- **Solid Organs:** Transplantation of organs like kidneys, hearts, and livers.
- **Tissues:** Examples include pig skin for burn victims and pancreatic islets for diabetes treatment.
- **Cells:** Use of porcine islets for insulin production in diabetes patients or other regenerative purposes.



4 Key Challenges

- **Immune Rejection:** The human immune system often rapidly attacks animal-derived transplants, leading to hyperacute, acute, or chronic rejection. .
- **Zoonotic Disease Risks:** There is a potential for cross-species transmission of pathogens, raising significant safety concerns.
- **Ethical and Social Issues:** The use of animals for transplantation raises ethical debates about animal welfare, the morality of genetic modification, and acceptance within different cultures.

5 Current Status

- **Gene Editing:** Techniques like CRISPR-Cas9 have been used to produce genetically modified pigs that lack certain antigens (e.g., α-Gal) and to enhance compatibility with the human immune system..
- **Clinical Trials:** Recent advancements include successful transplantation of pig kidneys and hearts into brain-dead human recipients, demonstrating proof of concept for short-term organ function.
- **Immunosuppressive Strategies:** Research is focusing on developing advanced immunosuppressive therapies to prevent rejection and prolong graft survival.

Source: Literature review, Frost & Sullivan analysis

Current Limitations of Xenotransplantation

Immune Rejection	• One of the main issues with xenotransplantation is immune rejection. The human immune system mounts a strong rejection response against animal organs and cells, including hyperacute rejection, acute vascular rejection, and cellular rejection, which can lead to rapid failure of the transplanted organ. Although some immunosuppressive drugs can mitigate this rejection, their long-term efficacy is limited, and suppressing the immune system can lead to infections and other side effects. Developing novel immunosuppressants that can effectively prevent xenograft rejection remains a challenge.
Organ Function and Longevity	• Even with successful transplantation, the long-term function and survival of xenografts remain uncertain. Animal organs may not fully adapt to the human physiological environment, leading to unstable organ function or early failure. Furthermore, xenograft organs face ongoing immune attacks and potential genetic mismatches, which can affect their long-term functionality. For example, the mismatch of the coagulation system, which can lead to microvascular thrombosis and dysfunction after transplantation New strategies are needed to optimize organ preservation techniques, enhance organ tolerance, and extend the longevity of organ function.
Risk of Zoonotic Infections	• The animal organs used in xenotransplantation may carry potential zoonotic pathogens, increasing the risk of human infection with novel viruses or bacteria. For example, pig organs may introduce swine coronaviruses, parvoviruses, and other pathogens, potentially triggering new human diseases. While gene editing has reduced the risk of pathogen transmission, completely eliminating this risk remains difficult. Developing technologies to comprehensively control and monitor potential pathogens is crucial for achieving safe xenotransplantation.
Ethical and Public Acceptance Issues	• Another significant challenge of xenotransplantation is ethical issues and public acceptance. Using animal organs for human transplantation raises ethical concerns regarding animal welfare, species boundaries, and human gene editing. Public acceptance of animal genetic editing technologies and interspecies organ transplantation varies, which affects the adoption and clinical application of these technologies. Therefore, establishing clear ethical frameworks and legal regulations to ensure the ethical legitimacy of xenotransplantation remains one of the barriers to advancing this field.

Source: Frost & Sullivan Analysis

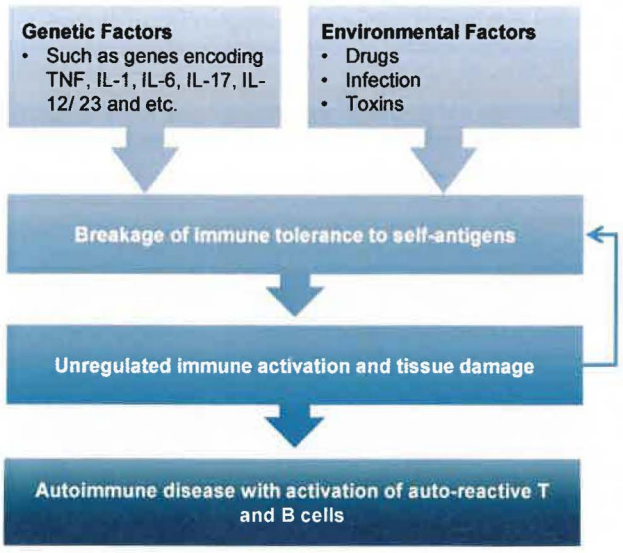
Unmet Needs and Market Prospects of Xenotransplantation

Gene Editing for Organ Compatibility	• While gene editing technology has made progress in reducing immune rejection, current gene-editing methods have not fully eliminated organ-host immunological mismatches. Future developments will need more innovative gene-editing strategies to further optimize the animal organ genome, enhancing its compatibility with human recipients. This will not only help reduce the risk of immune rejection but also improve the function and long-term survival rate of xenografts.
Improved Organ Harvesting and Preservation Techniques	• One of the challenges facing xenotransplantation is how to efficiently harvest and preserve organs from animals. Current organ preservation techniques typically only maintain short-term organ function, limiting the clinical application of xenografts. To enable broader use, there is a need to develop techniques that extend organ preservation time while maintaining organ function after transplantation. Innovative organ preservation methods will provide more opportunities for xenotransplantation, especially in the context of organ donor shortages.
Regulatory Framework and Standardization	• Xenotransplantation's clinical application faces strict regulatory requirements, but there is currently a lack of unified international standards and regulatory frameworks, leading to differences in how xenotransplantation technologies are approved and applied in various countries. To promote the global adoption of xenotransplantation, there is an urgent need for international legal and ethical frameworks that ensure the safety and compliance of these technologies. This would not only accelerate research and clinical applications but also bridge the technological gaps between countries.
Public Awareness and Education	• The promotion of xenotransplantation relies not only on scientific and technological advancements but also on public understanding and support. Currently, public awareness of xenotransplantation is limited, and there are fears and doubts among some groups. To facilitate the widespread application of xenotransplantation, efforts must be made to educate the public about its scientific basis, safety, and potential, dispelling misconceptions about the technology. Increasing public acceptance will directly influence the development and market adoption of xenotransplantation.

Source: Frost & Sullivan Analysis

Overview of Autoimmune Disease

- An autoimmune disease is a condition in which the body's immune system mistakenly attacks the body, which can be associated with either abnormally low activity or over-activity of the immune system.
- There are more than one hundred different types of autoimmune disorders, which can affect almost any part of the body, including the heart, brain, nerves, muscles, skin, eyes, joints, lungs, kidneys, glands, the digestive tract, and blood vessels.



Mechanisms for Autoimmune Diseases

- Autoimmune diseases can be divided into organ-specific and systemic autoimmune diseases based on the self-antigens targeted by immune cells.
- The exact underlying pathophysiology of these illnesses is still unknown, while autoimmune diseases arise in the context of a break in the immune tolerance to self.
- The mechanisms for the abrogation of immune self-tolerance appear to be multifactorial, including genetic and environmental, which will lead to unregulated immune activation against self-antigens and subsequent tissue destruction.
- B cells and T cells recognize self-antigens and dominate the phenotype of the patient with autoimmunity, although other immune components including antigen-presenting cells and complement are involved in various steps from initiation of the autoimmune response to tissue destruction.

Source: Literature Review, Frost & Sullivan analysis

Treatment Revolution for Auto-immune Disease

Anti-inflammatory Agents

- Treatments were generally effective for alleviating of pain, fever, and inflammatory responses, but were limited to treating the symptoms of the disease.

Salicylates → **NSAIDs**, **Glucocorticoids**, **DMARDs**

- Active components of Willow spp.
- Identified in the mid-19th century
- Due to the chemical advances in the 19th–20th centuries.

Targeted Biologics

- Targeted Biologics target the underlying sources of autoimmune disease, which improves physical functioning and prevents irreversible damage, making disease remission possible.

Anti-TNF Antibodies

- Total five innovative TNF-targeting drugs have been approved.

Interleukin Related Drugs

- Include marketed drugs targeting at IL-1, IL-6,IL-17, IL-23, etc.

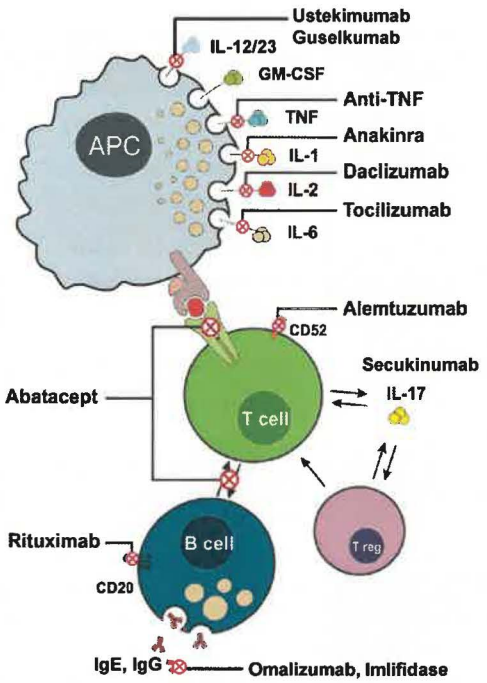
JAK Inhibitors

- Include JAK1, JAK2, TYK2 and JAK3.

Others

- Include IgG-degrading enzymes and other monoclonal antibodies targeting at CD20, CD22, CD28, BLyS, BTK inhibitors etc.

Future: More effective therapies being developed



Note:
NSAIDs: Non-steroidal anti-inflammatory drugs
DMARDs: Disease-modifying anti-rheumatic drugs

Source: Literature Review, Frost & Sullivan analysis

Comparison of Autoimmune Disease Treatment

Treatment Category	Common Types	Common Drugs	Mechanism	Advantages
Biologics	Biologics	• Adalimumab • Etanercept • Golimumab • Infliximab	Target at molecules involved in the activation of the immune system, such as tumor necrosis factor (TNF), interleukin (IL), B-cells and T-cells.	Newly emerging effective biologic drugs are available for patients with severe or resistant diseases.
	IgG-Degrading Enzymes	• Imlifidase	IdeS specifically recognizes and cuts IgG antibodies, reducing the number and effect of IgG antibodies.	Work quickly, directly target and remove IgG antibodies efficiently.
Small Molecular	Nonsteroid anti-inflammatory drugs (NSAIDs)	• Aspirin • Ibuprofen • Naproxen	Block prostaglandins, which can sensitize the nerves and magnify pain feelings during inflammation.	Work quickly and generally have fewer side effects than corticosteroids.
	Conventional DMARDs	• Methotrexate • Leflunomide	Inhibit the enzymes that affects DNA-synthesis for the proliferation of white blood cells, thus causing immunosuppression.	Long-term medication can effectively control symptoms and achieve stable efficacy.
	Corticosteroids	• Methylprednisolone • Dexamethasone • Prednisone	Stop the release of molecules that cause inflammation and also stop body from having an immune response.	Fast and strong anti-inflammatory effect that can be applied in many situations.
	JAK inhibitors	• Tofacitinib • Baricitinib	Inhibit immune cell function by inhibiting signal transduction of cytokines and growth factors.	Have shown satisfactory efficacy in patients resistant to other medications.
	Other Immuno-suppressants	• Such as mTOR inhibitors (Sirolimus, Everolimus)	Block the mammalian target of rapamycin (mTOR) which regulates cellular metabolism, growth, and proliferation.	Have shown tumor responses in clinical trials against both autoimmune diseases and various tumor types.

Source: Literature Review, Frost & Sullivan analysis

Comparison of Small Molecular Treatment, Antibody-Based Therapies and IgG-Degrading Enzymes

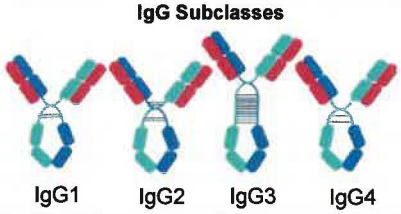
Treatment Category	Small Molecular Treatment	Antibody-Based Therapies	IgG-Degrading Enzymes
Advantages	Easy to penetrate biological membranes and reach intracellular targets.	Highly specifically recognize antigens, precisely bind to targets.	Work quickly, directly target and remove IgG antibodies efficiently.
	They can modulate various pathways, making them versatile for different diseases.	Newly emerging effective biologic drugs are available for patients with severe or resistant diseases.	Immediate effect in acute settings: These treatments are effective in critical conditions needing rapid response.
	Small molecules are often chemically stable and less sensitive to storage conditions.	The research and development is relatively mature, with many successful marketed drug cases.	IgG-degrading enzymes could specifically degrade IgG without compromising other immune components.
	Can often be taken orally, making them easier for patients to use daily.	Customizable to target specific antigens.	They are expected to be combined with existing therapies for better outcomes.
Disadvantages	The efficacy may not be so powerful, and the initial control of the disease may be insufficient for severe patients.	Patients often need professional healthcare settings for administration (injection or infusion).	The stability and in vivo half-life of the enzyme need to be optimized to ensure continuous drug efficacy.
	They may interact with unintended targets, leading to side effects.	Antibody molecules are relatively large, and the tissue penetration is relatively poor, the effect on some deep tissue lesions is limited.	The research and development is in the early stage, with relatively insufficient clinical experience and long-term safety to be verified.
	They may not match the precision of biologics like antibodies.	Expensive to produce and administer.	Narrow range of application in single clinical use: These are mainly suitable for acute cases or specific autoimmune diseases.

Source: Literature Review, Frost & Sullivan analysis

Overview of IgG Pathological Abnormal Autoimmune Diseases

- IgG is the most important antibody in the human body, with antibacterial, antiviral, toxin neutralizing and immune regulation functions. It is also the only type that can pass through the placenta and play an important role in neonatal anti-infection.
- According to the different heavy chain antigenicity and the number of disulfide bonds, IgG can be divided into four subclasses: IgG1, IgG2, IgG3, and IgG4. The overall structure of different IgG subtypes is similar, but the important structural differences in their binding to auxiliary molecules and receptors can play different biological functions. Given the different amino acid sequences of the hinge region of the heavy chain of each IgG subclass, the four IgG subclass antibodies play different functions in the progression of different clinical diseases. IgG subclasses have important clinical application value in autoimmune diseases, infectious diseases, allergic diseases and other diseases.

Structure of different IgG Subclasses



- IgG1 deficiency is positively correlated with hypoglobulinemia. IgG1 deficiency also increases the risk of infection in patients, the most common of which is respiratory tract infection.
- The IgG2 subclass plays a key role in the response to bacterial polysaccharide antigens. Therefore, individuals with IgG2 deficiency are particularly susceptible to invasion by Haemophilus influenzae, Neisseria meningitidis, and Streptococcus pneumoniae.
- IgG3 subclass is a class of antibodies with pro-inflammatory effects. Generally, the process of viral infection is characterized by an increase in IgG3.
- IgG4 is associated with a variety of autoimmune diseases, such as pemphigus, myasthenia gravis, TTP, and chronic inflammatory demyelinating polyneuropathy.

IgG Pathological Abnormal Autoimmune Diseases

- Pemphigus
- Myasthenia gravis (MG)
- Rheumatoid arthritis (RA)
- Thrombotic thrombocytopenic purpura (TTP)
- Chronic inflammatory demyelinating polyneuropathy (CIDP)
- Systemic lupus erythematosus (SLE)
- Limbic encephalitis
- Neuromyotonia
- Thyroiditis
- Morvan syndrome, etc.

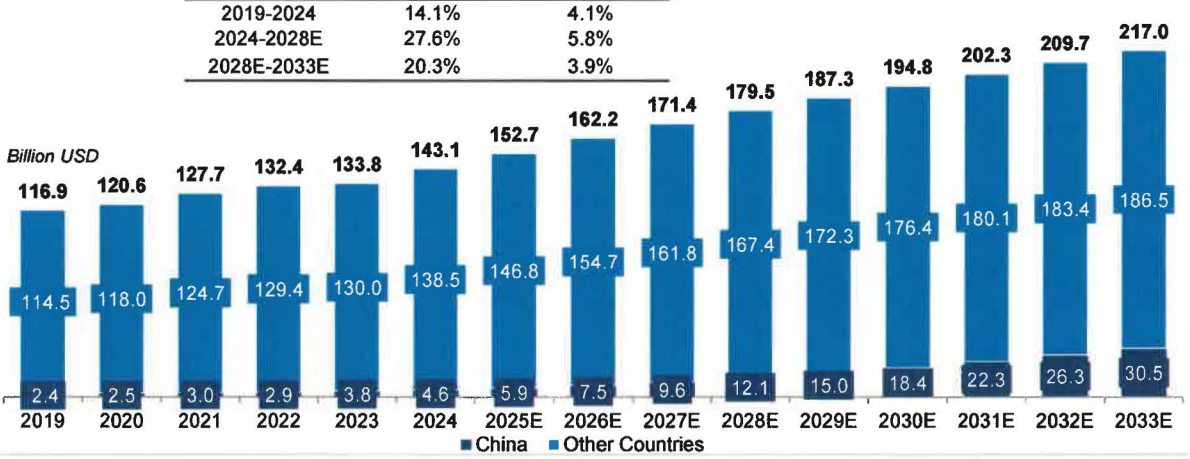
Source: Literature Review, Frost & Sullivan analysis

Autoimmune Disease Drug Market Size in China and Globally, 2019-2033E

- Based on China's huge population and the development and improvement of diagnostics for autoimmune diseases in China, the market demand for medical services will be spurred in the coming years. The overall autoimmune disease drug market in China is expected to reach USD 12.1 billion in 2028, with a CAGR of 27.6% from 2024 to 2028, and a CAGR of 20.3% from 2028 to 2033. Meanwhile, the global autoimmune disease drug market size increased from USD 116.9 billion in 2019 to USD 143.1 billion in 2024 with a CAGR of 4.1%, is expected to continue to increase to USD 179.5 billion in 2028 with a CAGR of 5.8% from 2024 to 2028, and is expected to continue to increase to USD 217.0 billion in 2033 with a CAGR of 3.9% from 2028 to 2033.

Autoimmune Disease Drug Market Size in China and Globally, 2019-2033E

Period	CAGR	
	China	Global
2019-2024	14.1%	4.1%
2024-2028E	27.6%	5.8%
2028E-2033E	20.3%	3.9%



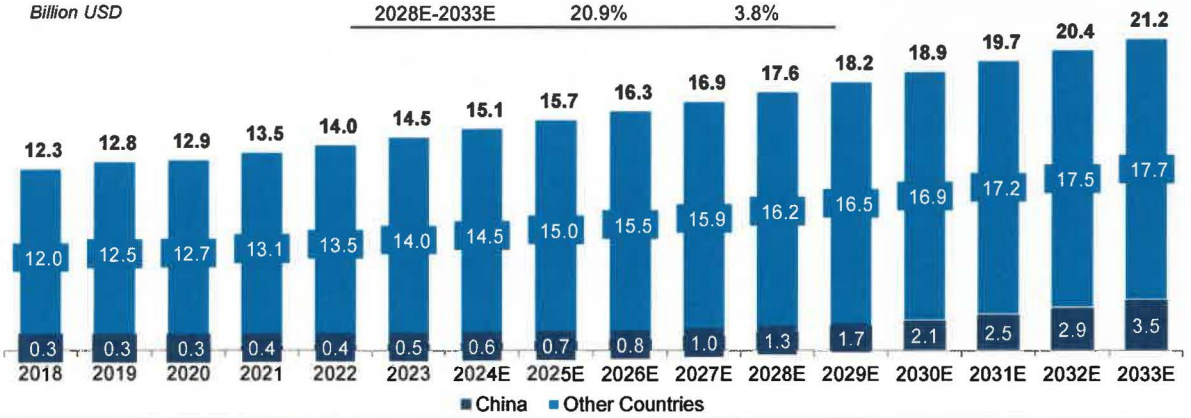
Source: Frost & Sullivan Analysis

IgG-Mediated Autoimmune Diseases Market Size in China and Globally, 2018-2033E

- The global IgG-mediated autoimmune diseases market grew steadily from USD 12.3 billion in 2018 to USD 14.5 billion in 2023, with a compound annual growth rate (CAGR) of 3.3%. It is expected to continue expanding at a CAGR of 3.9% between 2023 and 2028, reaching USD 17.6 billion by 2028, and further at 3.8% CAGR to USD 21.2 billion by 2033.
- In contrast, the Chinese market experienced rapid growth, rising from USD 0.3 billion in 2018 to USD 0.5 billion in 2023 (CAGR 12.8%). Future growth in China is forecasted at a much faster pace, with a CAGR of 23.0% from 2023 to 2028 and 20.9% from 2028 to 2033, reaching USD 3.5 billion by 2033.

IgG-Mediated Autoimmune Disease Market Size in China and Globally, 2018-2033E

Period	CAGR	
	China	Global
2018-2023	12.8%	3.3%
2023-2028E	23.0%	3.9%
2028E-2033E	20.9%	3.8%



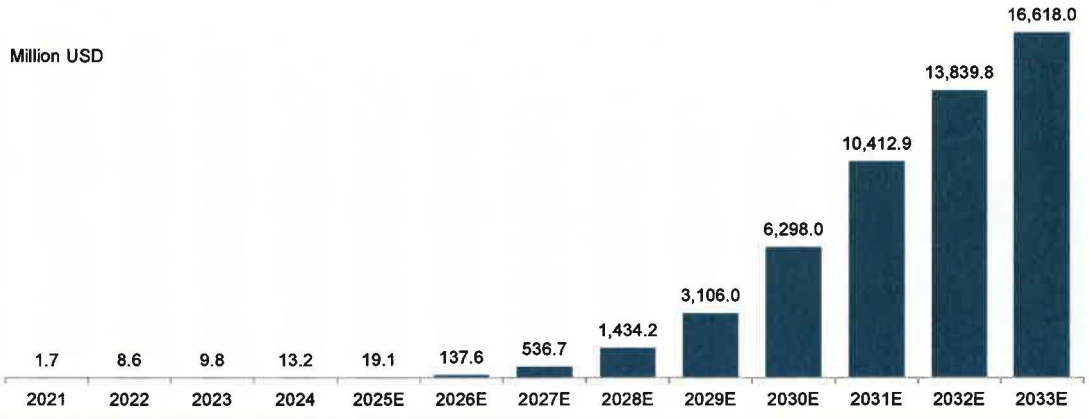
Source: Frost & Sullivan Analysis

Global IgG Degrading Enzyme Market Size, 2021-2033E

- The global IgG degrading enzyme market is projected to achieve a CAGR of 257.3.0% between 2025 and 2029, with market size increasing to USD 3,106.0 million in 2029. Between 2029 and 2033, the CAGR slows to 52.1%.

Global IgG Degrading Enzyme Market Size, 2021-2033E

Period	CAGR
2025E-2029E	257.3%
2029E-2033E	52.1%



Source: Frost & Sullivan analysis

Growth Drivers of Autoimmune Disease Drug Market

Need for Personalized Treatment

- For decades, numerous autoimmune disease patients have suffered from drug-related toxicity and lack of personalized treatments which are responsive to their specific diseases. Such need for personalized treatment, as well as advances in genetics and medicine, provides the impetus for driving the discovery and development of effective personalized medicines for autoimmune diseases.

The Increasing Number of Rheumatic Immunity Departments

- Currently, 60% of hospitals in China do not have an independent rheumatology department, and more than 80% of the 7,200 rheumatologists work in tertiary hospitals. In the future, as more treatment institutions set up independent departments of rheumatism and immunity, the medical resources of systemic diseases will be greatly improved, patients can be diagnosed and treated earlier.

Increasing Affordability

- In the 2021 NRDL, 4 in 67 newly included drug are used to treat autoimmune diseases, which significantly improved patients' affordability. With the further NRDL negotiation, the emergence of domestic innovative biologics, as well as increasing per capita disposable income, the affordability of autoimmune diseases drugs will keep increasing, driving the market growth.

Source: Frost & Sullivan analysis, 2018 Chinese guideline for the diagnosis and treatment of rheumatoid arthritis

Future Trends of Autoimmune Disease Drug Market

More indications to be covered with innovative biologics	• Currently, autoimmune diseases are still cannot be cured. With an increased understanding of the pathophysiology of autoimmune diseases and associated biologic pathways, more innovative biologics such as IgG-degrading enzyme, anti-IL-6 antibodies, anti-IL-17 antibodies and anti-TNF-α antibodies are expected to be developed. These newly developed biologics not only provide more available drugs for patients with autoimmune diseases such as RA and systemic lupus erythematosus but also help address more therapeutic areas.
Increased Focus on Rare Autoimmune Diseases	• Many rare autoimmune diseases, such as Systemic Lupus Erythematosus (SLE), anti-GBM, TTP, etc., lack effective treatments or are inadequately addressed by existing therapies. Traditional treatments often offer symptomatic relief but fail to target the underlying causes of the diseases. This creates an urgent need for novel drugs that can specifically target the autoimmune processes involved in these conditions. As drug development in autoimmune disorders continues, more attention is being given to rare and neglected autoimmune diseases, expanding the scope of market opportunities.
Higher Penetration	• As the patent of the original drug expires, more and more biosimilars will enter the market, the number of alternative drugs for patients with autoimmune diseases will increase and the penetration of biologics will increase.

Source: Frost & Sullivan analysis

Anti-Glomerular Basement Membrane Disease Overview

- Anti–glomerular basement membrane (anti-GBM) disease is an organ-specific autoimmune disorder characterized by autoantibodies against the glomerular and alveolar basement membranes, leading to rapidly progressive glomerulonephritis and severe alveolar hemorrhage. These antibodies, primarily directed against the non-collagenous domain of the α-3 chain of type IV collagen, trigger inflammatory responses involving local complement activation and recruitment of polymorphonuclear leukocytes.
- Environmental factors, particularly smoking and exposure to hydrocarbon solvents, can precipitate the onset of GBM in genetically susceptible individuals.

Pathophysiology

- Anti-GBM is due to circulating autoantibodies directed at the glomerular basement membrane. This binding of autoantibodies can be seen as a linear deposition of **immunoglobulins (IgG, and very rarely IgA)** along the basement membrane. The **inflammatory response** in that area results in the typical picture of glomerulonephritis.
- **Type IV collagen** is a main constituent of all basement membranes, which are a specialized form of extracellular matrix, supporting tissue integrity and performing numerous key functions including cell signaling and tissue regeneration. Type IV collagen also contains non-collagenous domains. **The non-collagenous domain of α-3 (α3NC1)** is thought to be the antigen activating the anti-GBM autoantibody.
- Although anti-GBM is regarded as an autoantibody-mediated disease, a vital role is played by **T-cells** in the initiation and progression of the disease. T-cells cause B-cells to increase antibody production and play a direct role in renal and pulmonary injury.

Causative factors

Genetic Factors

- Anti-GBM disease shows a strong association with HLA-DR2.
- Association of anti-GBM nephritis is with HLA-DRB1 alleles (HLA-DRB1 1501 and 1502 alleles), HLA-DQA1 01 alleles, and HLA-DQB1 06 alleles.
- HLA-DRB1*1501 and 1502 alleles increase the susceptibility, while HLA-DR1 and HLA-DR7 are protective.

Environmental Factors

- Smoking
- Exposure to metal dust, organic solvents, or hydrocarbons
- Bacteremia
- Endotoxemia
- Infections, such as influenza A
- Drugs that cause regulatory T-cell depletion
- Inhalation of cocaine
- Higher inspired oxygen

Source: Literature Review, Frost & Sullivan analysis

Anti-Glomerular Basement Membrane Disease Treatment

- Treatment aims to rapidly remove pathogenic autoantibody, typically with the use of plasma exchange, along with steroids and cytotoxic therapy to prevent ongoing autoantibody production and tissue inflammation. Initiating treatment as early as possible is crucial for preventing progressive renal failure and pulmonary damage.
- Currently, the recommended treatment for anti-GBM antibody disease is **plasma exchange combined with glucocorticoids and immunosuppressants**. Some patients can also receive hormone pulse therapy according to their condition. When patients progress to ESRD, renal replacement therapy is required.
- The IgG-degrading enzyme of Streptococcus pyogenes (IdeS) is a novel therapeutic proteinase that cleaves human IgG preventing subsequent complement and neutrophil- induced injury. It works with dramatic efficacy and efficiency, decreasing the anti-GBM antibody titer to an undetectable/ non-toxic level within hours.

Treatment	Illustration
Plasmapheresis	• Plasmapheresis is generally instituted after the diagnosis of anti-GBM disease is established either by kidney biopsy or by detection of anti-GBM antibodies. • 4-liter plasma exchanges daily or every other day is usually performed. Plasmapheresis is continued for 2-3 weeks or until the patient's clinical course has improved and serum anti-GBM antibodies are not detected.
Immunosuppressive Therapy	• Immunosuppressive therapy is required to inhibit antibody production and rebound hyper synthesis, which may occur following discontinuation of plasma exchange. • Cyclophosphamide, Corticosteroids, Azathioprine and Rituximab(a chimeric monoclonal antibody) can be applied to the immunosuppressive treatment of anti-GBM disease.
Kidney Transplantation	• Kidney transplantation has been used for end-stage renal disease secondary to anti-GBM disease. It is optimal to delay kidney transplantation until anti-GBM antibodies are undetectable in the serum for 12 months and the disease has been in remission for at least 6 months without the use of cytotoxic agents.

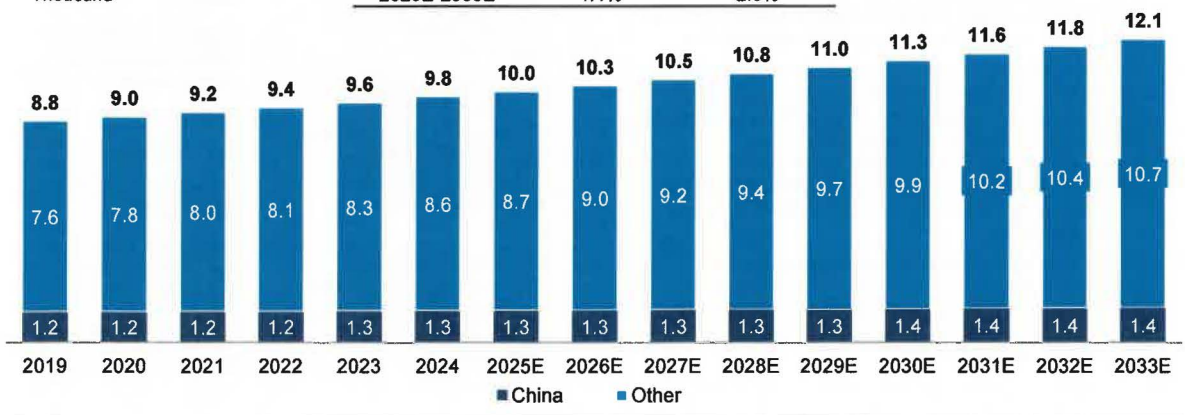
Source: Literature Review, Frost & Sullivan analysis

Incidence of anti-GBM in China and Globally, 2019-2033E

- From 2019 to 2024, the number of new cases of GBM globally rose from 8.8 thousand to 9.8 thousand, with a CAGR of 2.2%. It is expected to continue increasing to 11.0 thousand by 2029, reflecting a CAGR of 2.3% from 2024 to 2029. Projections indicate that by 2033, the incidence is anticipated to reach 12.1 thousand.
- From 2019 to 2024, the number of new cases of GBM in China rose from 1.2 thousand to 1.3 thousand, with a CAGR of 1.1%. It is expected to continue increasing to 1.3 thousand by 2029, reflecting a CAGR of 1.0% from 2024 to 2029. Projections indicate that by 2033, the incidence is anticipated to reach 1.4 thousand.

Incidence of anti-GBM in China and Globally, 2019-2033E

Period	CAGR	
	China	Global
2019-2024	1.1%	2.2%
2024-2029E	1.0%	2.3%
2029E-2033E	1.1%	2.5%



Source: Frost & Sullivan Analysis

Global and China Competitive Landscape of Anti-GBM

As of the LPD, no drug has been approved in China or globally.

Pipeline in Anti-GBM Treatment

Drug Name	Company	Target	Indications	Stage	Approved Date	Area
Imlifidase	Hansa Biopharma	IgG	Anti Glomerular Basement Membrane (GBM)	III	2023/01/11	US, EU
KJ103	Bao Pharmaceuticals (宝济药业)	IgG	Desensitization treatment of highly sensitized adult kidney transplant patients	II/III	2023/12/25	China
			Anti Glomerular Basement Membrane (GBM)	II	2024/09/23	China
			Acute severe autoimmune diseases mediated by pathogenic IgG autoantibodies	I	2022/05/19	China

Note: As of 2025.03.12

Source: Clinicaltrials.gov, CDE, NMPA, Frost & Sullivan Analysis

Unmet Needs in the Treatment of Anti-GBM

Challenges in Early Diagnosis	• Anti-GBM disease often presents with non-specific symptoms like hematuria, proteinuria, and rapidly progressing renal failure, which can mimic other conditions, such as ANCA-associated vasculitis or systemic lupus erythematosus. Due to this overlap, early diagnosis can be challenging. Detecting anti-GBM antibodies through serological testing is crucial, but not all patients test positive, and the sensitivity of these tests can vary. Improved diagnostic tools, including more sensitive antibody tests and biomarkers, are needed to diagnose the disease early, which is essential for initiating timely treatment and preventing irreversible kidney damage.
Limited and Variable Treatment Response	• The standard treatment for anti-GBM disease includes plasmapheresis, corticosteroids, and immunosuppressive drugs. However, these treatments do not guarantee success in all patients. Some patients respond poorly, and renal function may continue to decline despite aggressive treatment. Furthermore, there is a lack of targeted therapies that specifically address the underlying autoimmune mechanisms of anti-GBM disease. More effective and personalized treatment options are needed to improve outcomes, especially for those who are unresponsive to conventional therapies
Recurrence After Kidney Transplantation	• Patients who experience anti-GBM disease and require kidney transplantation face a significant risk of disease recurrence in the transplanted kidney. This recurrence can lead to graft loss and potentially fatal outcomes. Current immunosuppressive strategies, though used to prevent recurrence, have not been completely successful. Understanding the mechanisms behind disease recurrence and developing preventive measures, such as targeted therapies to prevent the formation of anti-GBM antibodies post-transplant, are critical to improving long-term transplant success and patient survival.

Source: Literature review, Frost & Sullivan analysis

Overview of Thrombocytopenia (TP)

- Thrombocytopenia is a condition in which you have a low blood platelet count (< 100000/μL). Platelets (thrombocytes) are colorless blood cells that help blood clot. Platelets stop bleeding by clumping and forming plugs in blood vessel injuries. Thrombocytopenia might occur as a result of a bone marrow disorder such as leukemia or an immune system problem. Or it can be a side effect of taking certain medications. Thrombocytopenia can be mild and cause few signs or symptoms. In rare cases, the number of platelets can be so low that dangerous internal bleeding occurs.

Etiology

Trapped platelets → Enlarged spleen	Normally, spleen works to fight infection and filter unwanted material from blood, while an **enlarged spleen**, caused by a number of disorders can harbor many platelets, which decreases the number of platelets in circulation.
Decreased production of platelets → Leukemia and other cancers	Cancer cells inhibits the growth and development of megakaryocytes and the production of platelets.
Decreased production of platelets → Types of anemia	Anemia influences the production of platelets
Decreased production of platelets → Viral infection	Viral infections, such as hepatitis C or chronic liver disease and some rare bacterial infection may lead to thrombocytopenia.
Decreased production of platelets → Chemo-therapy induced	Thrombocytopenia is one of the most common adverse effects that chemotherapy and radiation therapy cause.
Increased breakdown of platelets → ITP*	Autoimmune diseases, such as lupus and rheumatoid arthritis, cause this type. The body's immune system mistakenly attacks and destroys platelets.

Note: ITP (Immune Thrombocytopenia)

Signs and Symptoms

- Bruising
- Superficial bleeding
- Prolonged bleeding
- Fatigue
- Bleeding (gums or nose)
- Blood in urine or stools
- heavy menstrual flows
- Enlarged spleen

Risk Factors

- Drug
- Infection
- Bleeding

Source: Frost & Sullivan Analysis

Overview of Thrombocytopenia (TP)

- Thrombocytopenia is a condition characterized by a platelet count that is lower than normal. Platelets are small blood cells produced in the bone marrow from larger cells. They play a crucial role in clotting by sticking together to form a plug, known as a blood clot, to seal wounds. These cells are also referred to as thrombocytes, as a blood clot is also called a thrombus.
- In adults, a normal platelet count ranges from 150,000 to 450,000 platelets per microliter of blood. A count below 150,000 platelets per microliter indicates thrombocytopenia. With a low platelet count, there can be difficulty in stopping bleeding, which might occur internally, beneath the skin, or on the skin's surface. Severe bleeding generally occurs only when the platelet count is very low.

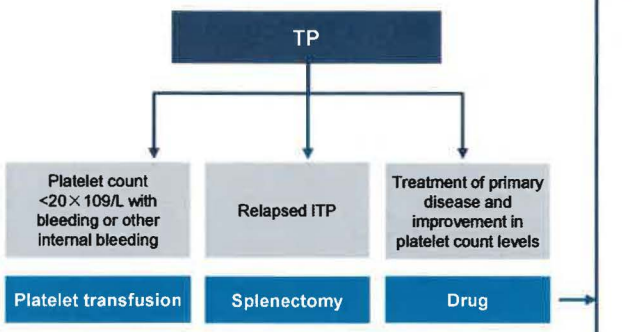
Classification	
1.Artificial thrombocytopenia	pseudothrombocytopenia
	Platelet satellism
	Giant platelets
2.Decreased product thrombocyte	Megakaryocyte hypoplasia or suppression
	Ineffective thrombopoiesis
	Defeat in mechanism which are controlling thrombopoiesis
	Herediter trombositopenia
3.Increased platelet destruction	Immunologic
	Nonimmunologic
4.Abnormal platelet distribution	The disease that capture spleen (neoplasia,congestive, infiltration)
	Hypothermyia

Pathogenesis

- **Decreased Platelet Production**
- **Increased Platelet Consumption And Destruction**
- **Abnormal Platelet Distribution**
- **Blood Dilution**

Source: Literature Review, Frost & Sullivan Analysis

Treatment Paradigm of TP in China



Drug Categories	Drug
Drugs to Promote Platelet Production	Recombinant Human Thrombopoietin
	Eltrombopag
	Romiplostim
Glucocorticoids	Prednisone
	Dexamethasone
	Methylprednisolone
Immunoglobulins	Intravenous Immunoglobulin
Immunosuppressants	Cyclosporine
Monoclonal Antibody Immunosuppressants	Rituximab
Other Immunosuppressive Drugs	Azathioprine
	Cyclophosphamide
	Mycophenolate Mofetil
	Danazol
	Thalidomide
	Tacrolimus
	Long-term Acting Immunoglobulin

Source: 中国成人血小板减少症诊疗专家共识, Frost & Sullivan Analysis

Global Competitive Landscape of TTP

As of the LPD, There are 3 marketed drugs for TTP worldwide, and only one in the clinical trials.

Marketed drugs of TTP Treatment

Generic Name	Drug name	Company	Target	Indications	Approved Date	Area
Apadamtase alfa	ADZYNMA	Takeda	VWF	TTP	2023-11-09	US, EU, Japan
Caplacizumab	CABLIVI	Sanofi	VWF	TTP	2018-08-30	US, EU, Japan
Rituximab	RITUXAN	Roche	VWF	TTP	1997-11-26	US, EU, Japan, China

Pipeline in TTP Treatment

Drug Name	Company	Target	Indications	Stage	Approved Date
Egaptivon Pegol	Archemix	VWF	TTP	II	2007-07-25

Note: As of Nov 30, 2024

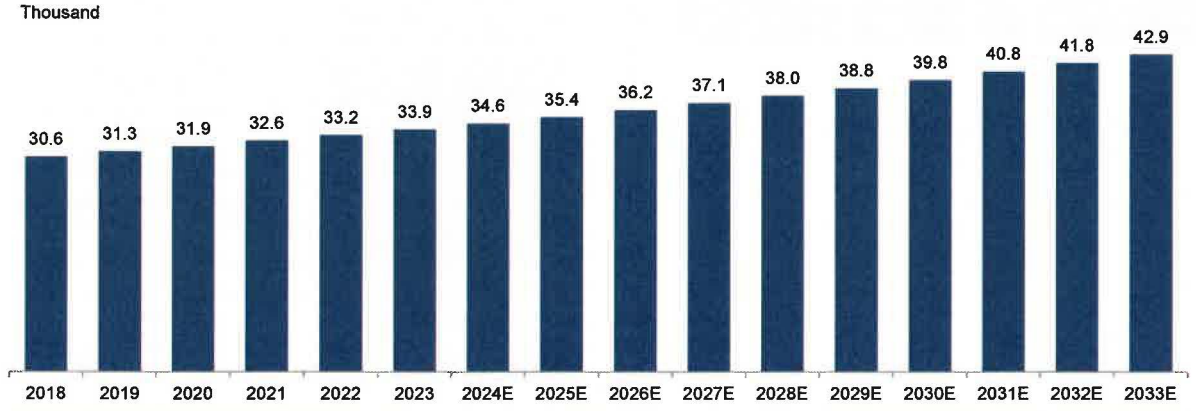
Source: Clinicaltrials.gov, CDE, NMPA, Frost & Sullivan Analysis

Global Prevalence of TTP, 2018-2033E

- From 2018 to 2023, the prevalence of TTP globally rose from 30.6 thousand to 33.9 thousand, with a CAGR of 2.1%. It is expected to continue increasing to 38.0 thousand by 2028, reflecting a CAGR of 2.3% from 2023 to 2028. Projections indicate that by 2033, the incidence is anticipated to reach 42.9 thousand.

Global Prevalence of TTP, 2018-2033E

Period	CAGR
2018-2023	2.1%
2023-2028E	2.3%
2028E-2033E	2.5%



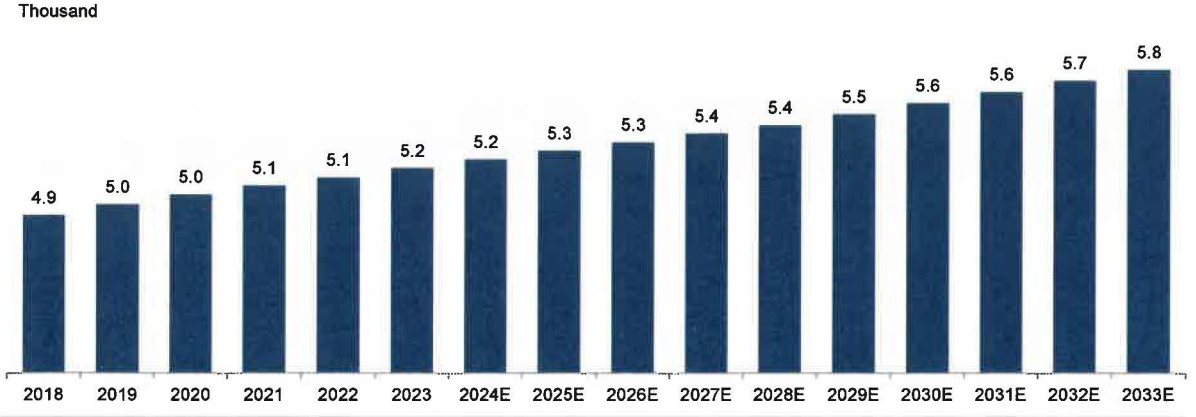
Source: Frost & Sullivan analysis

Prevalence of TTP in China, 2018-2033E

- From 2018 to 2023, the prevalence of TTP in China rose from 4.9 thousand to 5.2 thousand, with a CAGR of 1.4%. It is expected to continue increasing to 5.4 thousand by 2028, reflecting a CAGR of 0.9% from 2023 to 2028. Projections indicate that by 2033, the incidence is anticipated to reach 5.8 thousand.

Prevalence of TTP in China, 2018-2033E

Period	CAGR
2018-2023	1.4%
2023-2028E	0.9%
2028E-2033E	1.2%



Source: Frost & Sullivan Analysis

Competitive Landscape of TTP in China

As of the LPD, There is only one drugs in Clinical trial for TTP, and there is no drug marketed in China for TTP.

Pipeline in TTP Treatment

Generic Name	Company	Target	Indications	Stage	Approved Date
Apadamtase alfa	Takeda	VWF	TTP	II	2023-11-09

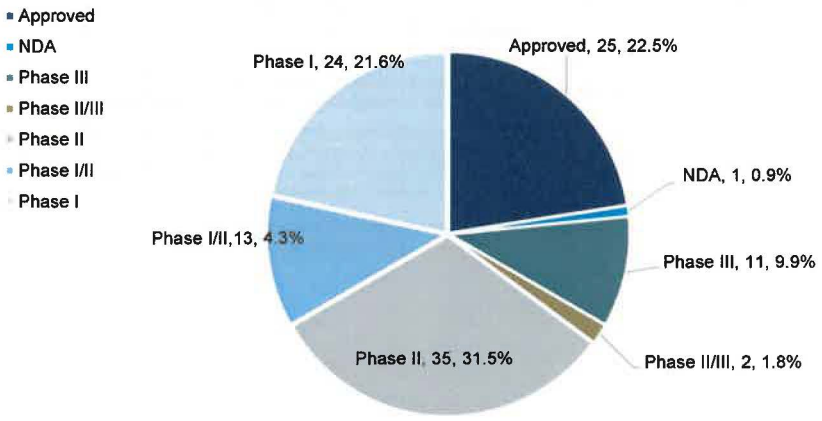
Note: As of Nov 30, 2024

Source: CDE, NMPA, Frost & Sullivan Analysis

Global TP Treatment Pipelines

- As of Nov 30, 2024, there are 86 active pipelines in clinical trials for treating TP in the world. Among them, 1 was in NDA state and 11 were in clinical phase III, most of them were in clinical phase II and clinical phase I.

Global TP Treatment Pipelines



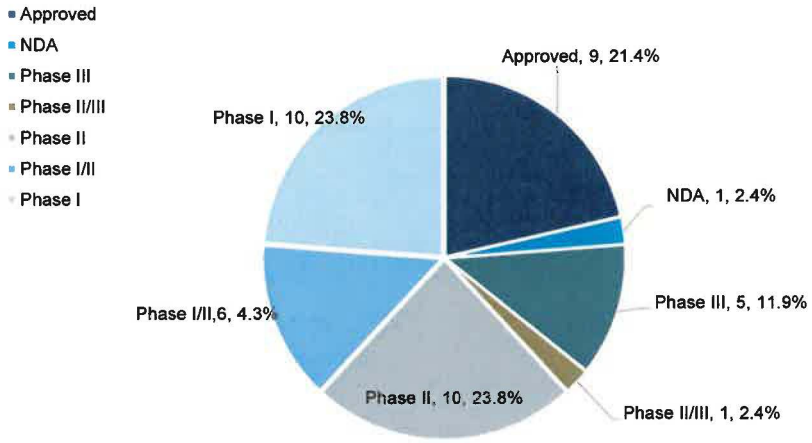
Note: As of Nov 30, 2024

Source: Clinicaltrials.gov, CDE, NMPA, Frost & Sullivan Analysis

TP Treatment Pipelines in China

- As of Nov 30, 2024, there are 33 active pipelines in clinical trials for treating TP in China. Among them, 1 was in NDA state and 5 were in clinical phase III, most of them were in clinical phase II and clinical phase I.

TP Treatment Pipelines in China



Note: As of Nov 30, 2024

Source: CDE, NMPA, Frost & Sullivan Analysis

Competitive Landscape of TP in China

Marketed drugs of TP Treatment

Generic Name	Company	Target	Indications	Approved Date
Hetrombopag olamine	Hengrui	TPOR	Aplastic Anemia (AA), Immune Thrombocytopenia (ITP)	2021-06-16
Avatrombopag	Astellas Pharma	TPOR	Thrombocytopenia, Immune Thrombocytopenia (ITP)	2020-04-14
Iusutrombopag	Shionogi Pharmaceutical	TPOR	Thrombocytopenia	2023-06-27
Eltrombopag	GSK	TPOR	Immune Thrombocytopenia (ITP), Aplastic Anemia (AA)	2017-12-28
Romiplostim	Amgen	TPOR	Immune Thrombocytopenia (ITP)	2022-01-07
Recombinant human thrombopoietin-TPIAO	3SBio	TPOR	Immune Thrombocytopenia (ITP), Chemotherapy-induced Thrombocytopenia	2005-05-20
desmopressin	Ferring Pharma	AVPR2	Central Diabetes Insipidus, Thrombocytopenia, Enuresis, Hemophilia A, von Willebrand Disease, Central Diabetes Insipidus	1995-06-01
Azathioprine	GSK	Rac1b	Hepatitis, Rheumatoid Arthritis (RA), Dermatomyositis (DM), Organ Transplant Rejection, Systemic Lupus Erythematosus (SLE), Immune Thrombocytopenic Purpura (ITP), Nodular Polyarteritis, Autoimmune Hemolytic Anemia	1996-01-30
Meprednisone	Pfizer	GR	Leukemia, Enteritis, Immune Thrombocytopenia (ITP), Renal Failure, etc.	1999-01-01

Note: As of Nov 30, 2024

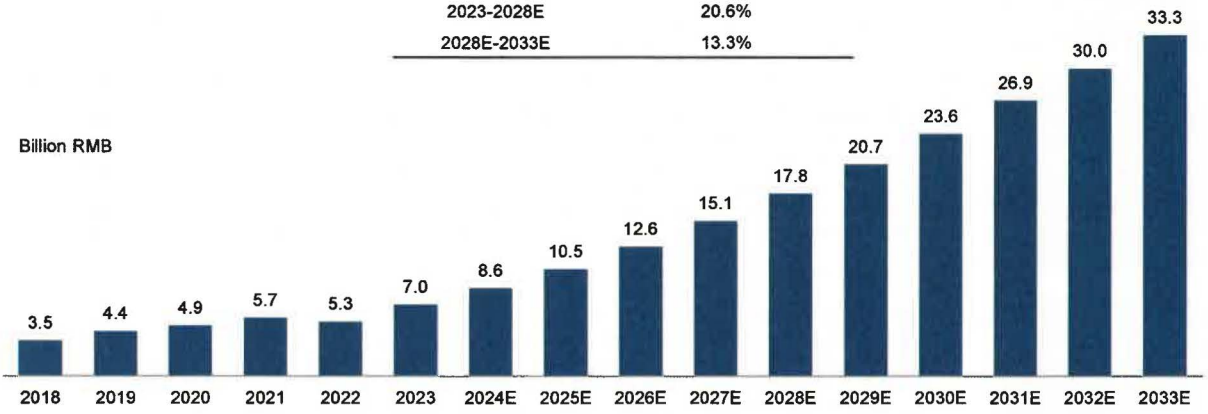
Source: CDE, NMPA, Frost & Sullivan Analysis

China Thrombocytopenia Treatment Market, 2018-2033E

- The China thrombocytopenia treatment increased from 3.5 billion RMB to 7.0 billion RMB at a CAGR of 15.0% from 2018 to 2023. The number is projected to reach 17.8 billion RMB in 2028 and 33.3 billion RMB in 2033 at a CAGR of 20.6% and 13.3% from 2023 to 2028 and from 2028 to 2033 respectively.

China Thrombocytopenia Treatment Market, 2018-2033E

Period	CAGR
2018-2023	15.0%
2023-2028E	20.6%
2028E-2033E	13.3%



Source: Frost & Sullivan Analysis

Unmet Needs in the Treatment of Thrombocytopenia

Prevention of Thrombocytopenia	• In CIT cases, the platelet count remains a relative high level in two or three days after recieving chemotherapy, and the TPO level remains relatively low due to the negative feedback loop between them. When the platelet count has not yet decreased and the TPO level is relatively low, supplementing exogenous TPO to improve the lowest platelet count level and shorten the duration at lowest level is the basis for preventing thrombocytopenia.
Challenges in the Treatment of ITP	• Firstly, as the first-line therapy in the treatment of ITP, glucocorticoids have undesirable long-term therapeutic effects and may cause many treatment-related adverse reactions, such as diabetes, osteoporosis, femoral head necrosis, infection and thrombosis, all of which can not be ignored. Secondly, High recurrence rate is another tricky issue. Patients with ITP nowadays only have 15% of five-year survival rate. Thirdly, rhTPOs require daily injection, having adverse impact on the adherence. Patients usually have undesirable response rate to rhTPOs, meaning it, as monotherapy, can not maintain long-term therapeutic effects.
Challenges in the Treatment of CLD with Thrombocytopenia	• Firstly, China has a large chronic liver disease patient pool, and thrombocytopenia is quite common in CLD patients. Thrombocytopenia greatly increases the bleeding risk. Patients with chronic liver disease and liver cirrhosis are not easy to stop the bleeding once they bleed, and severe bleeding such as gastrointestinal bleeding, fundus hemorrhage, and cerebral hemorrhage may occur. Secondly, patients with chronic liver disease combined with thrombocytopenia may have difficulty in receiving invasive examinations and treatments such as liver biopsy and liver interventional therapy for liver cancer.

Source: Literature review, Frost & Sullivan analysis

Specific Current Treatment Limitations of Thrombotic Thrombocytopenic Purpura (TTP)

Limited Efficacy in Severe Cases	• Current treatments like plasma exchange and immunosuppression show limited efficacy in severe TTP cases, particularly in patients with significant organ damage. These therapies cannot fully prevent the formation of microvascular thrombi, potentially resulting in long-term damage to the heart, kidneys, or nervous system. Additionally, the time to therapeutic response is slow, making it less effective for life-threatening conditions. Innovative therapies are needed to achieve more rapid and targeted effects to reduce acute complications and chronic sequelae.
High Risk of Relapse	• TTP patients, particularly those with acquired TTP, often face a high risk of relapse even after treatment. This is attributed to insufficient recovery of ADAMTS13 activity or persistent antibodies. Current therapies lack long-term preventive measures against relapse, necessitating frequent monitoring and repeated treatments. Developing durable treatments, such as immunomodulators that suppress antibody production, represents a critical unmet need in this area.
Side Effects of Current Therapies	• Therapies for TTP, such as plasma exchange and immunosuppressants, are often associated with a range of side effects that impact patient quality of life and treatment safety. For instance, plasma exchange can cause allergic reactions (e.g., urticaria and breathing difficulties), hypotension, and increased risk of thrombosis. Moreover, prolonged use of immunosuppressants (e.g., corticosteroids or rituximab) elevates infection risks and may lead to metabolic complications such as osteoporosis, diabetes, and kidney damage. These side effects are particularly severe in immunocompromised or physically frail patients. Addressing treatment-related adverse effects and developing safer therapeutic options have become urgent priorities in this field.
Limited Accessibility in Resource-Limited Settings	• Plasma exchange therapy and costly biologics, such as Caplacizumab, are often inaccessible in resource-limited settings. This lack of access leads to delayed or inadequate treatment for many patients, increasing mortality and the risk of long-term complications. Moreover, the complexity and high cost of treatment place a significant burden on healthcare systems. Developing cost-effective therapies suitable for diverse healthcare environments is essential to improving global accessibility.

Source: Frost & Sullivan Analysis

Unmet Needs of Thrombotic Thrombocytopenic Purpura (TTP)

Rapid and Accurate Diagnosis	• Diagnosis of TTP still relies on clinical symptoms and laboratory tests, particularly the measurement of ADAMTS13 activity. However, changes in ADAMTS13 activity can be influenced by other factors, leading to misdiagnosis or delayed diagnosis. There is a need for faster and more accurate diagnostic tools to identify and treat TTP early, especially during the initial stages, to avoid treatment delays and reduce the risk of complications.
Individualized Treatment and Management of Refractory TTP	• Current treatment approaches for TTP are largely standardized, but there is significant variability among patients, particularly in immune response, ADAMTS13 activity, and antibody levels. There is a need for personalized treatment plans that can be adjusted based on the specific conditions of the patient to optimize treatment outcomes. Furthermore, for refractory TTP patients, existing therapies like plasma exchange and immunosuppressants are often ineffective, and new treatment options, such as targeted therapies or novel immunomodulatory drugs, are urgently needed.
Long-term Survival and Complication Management	• Although acute TTP episodes can be relieved with existing treatments, patients often face reduced long-term quality of life and risk of complications. The long-term survival of TTP patients depends on comorbidities such as renal failure and cancer. The 10-year survival rate of patients with significant comorbidities is less than 50%. Additionally, there is evidence that TTP may predispose patients to autoimmune diseases such as Sjögren's disease or SLE. Therefore, there is a need to develop treatment options that can reduce relapse rates and improve long-term quality of life, as well as provide safer management strategies for side effects caused by immunosuppressive therapy.
Special Needs for TTP During Pregnancy	• Pregnancy is a known trigger for the initial onset or recurrence of TTP, and pregnancy outcomes have historically been poor, with high rates of recurrent TTP, fetal loss, preeclampsia, and HELLP syndrome. Studies have shown that normalizing ADAMTS13 levels with immunosuppressive therapy before pregnancy, as well as monitoring ADAMTS13 and prophylactic use of hormones or plasma exchange during pregnancy can improve maternal and fetal outcomes. However, it is unclear whether women with TTP are routinely counseled on these options.

Source: Frost & Sullivan Analysis

Guillain-Barré Syndrome Disease Overview

- Guillain-Barré Syndrome (GBS) is an immune-mediated peripheral neuropathy of acute onset characterized by symmetrical weakness and decreased or absent reflexes.is described by a wide range of motor impairment, flaccidity, hyporeflexia, and progressive and ascending flaccid paralysis. Sensory disturbances and cranial nerve deficits occur in some patients
- It is a rare condition, and while it is more common in adults and in males, people of all ages can be affected.

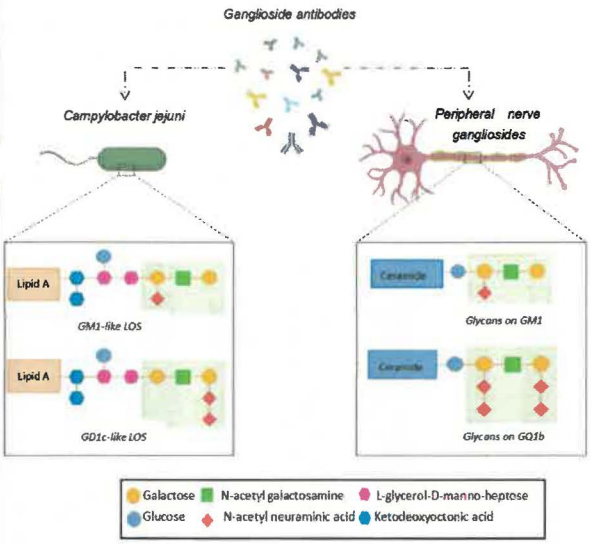
Mechanism

- Lipo-oligosaccharide (LOS) on the outer membrane of Campylobacter jejuni induces cross-reactive antibodies which, through molecular mimicry, bind to the structurally identical glycans (areas in green) present on peripheral nerve gangliosides (GM1 and GQ1b in the example above), resulting in damage to axons and Schwann cells.

Causes

The three factors that most affect GBS are prodromal infections, vaccines, and related surgery:

- Most cases follow an infection with a virus or bacteria. This leads the immune system to attack the body itself. Infection with the bacteria Campylobacter jejuni, which causes gastroenteritis (including symptoms of nausea, vomiting and diarrhoea), is one of the most common risk factors for GBS. People can also develop GBS after having the flu or other viral infections including cytomegalovirus, Epstein-Barr virus, and the Zika virus.
- In rare instances, vaccinations may increase the risk of people getting GBS, but the chance of this occurring is extremely low. Studies show that people are much more likely to get GBS from infections such as the flu than from the vaccine given to prevent the infection, in this case the flu vaccine.
- Occasionally, surgery can trigger GBS.



Source: Literature review, Frost & Sullivan analysis

Treatment Options of Guillain-Barré Syndrome Disease

- According to WHO, there is no known cure for GBS, but treatments can help improve symptoms of GBS and shorten its duration. Given the autoimmune nature of the disease, its acute phase is typically treated with immunotherapy, such as **intravenous immunoglobulin (IVIG)** or **plasma exchange** to remove antibodies from the blood. Among them, IVIG is a more convenient treatment and can be considered the first-line option in clinical practice.
- In cases where muscle weakness persists after the acute phase of the illness, patients may require rehabilitation services to strengthen their muscles and restore movement.
- Immunoglobulin G-degrading enzyme of Streptococcus pyogenes (IdeS) splits IgG antibodies, can be effectively blocked without side effects. It is a new **potential treatment** for GBS.

Treatment Options

Intravenous Immunoglobulin (IVIG)

- Inhibit Fc-mediated activation of immune cells.
- Inhibit bind of antiganglioside antibodies to their neural targets
- Inhibit local complement activation

Lower serum inflammatory factors, reduce the long-term incidence of GBS and reduce the risk of disability in patients

Plasma Exchange

- Remove neurotoxic antibodies
- Remove complement factors
- Remove other humoral mediators of inflammation

Reduces inflammation and immune-mediated damage of nerve roots and peripheral nerves

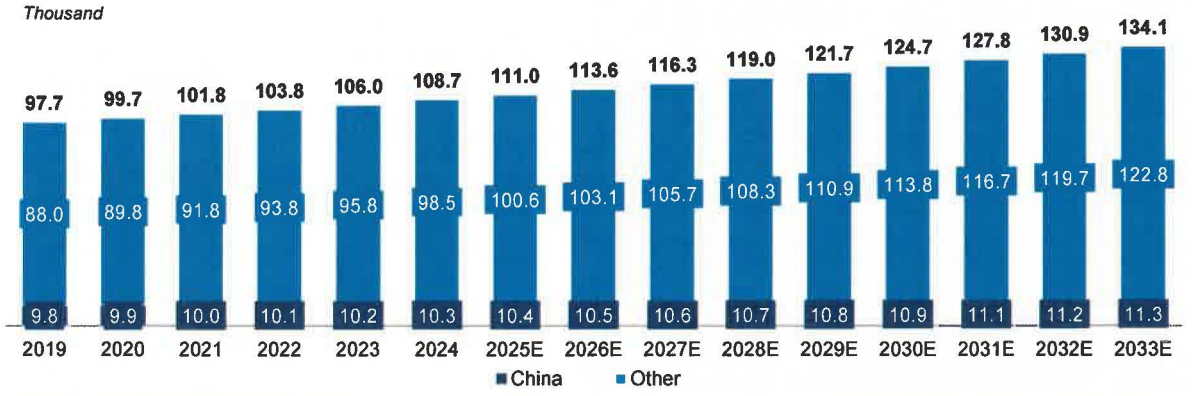
Source: 《中国吉兰-巴雷综合征诊治指南2024》, Literature review, WHO, Frost & Sullivan analysis

Incidence of GBS in China and Globally, 2019-2033E

- From 2019 to 2024, the number of new cases of GBS globally rose from 97.7 thousand to 108.7 thousand, with a CAGR of 2.2%. It is expected to continue increasing to 121.7 thousand by 2029, reflecting a CAGR of 2.3% from 2024 to 2029. Projections indicate that by 2033, the incidence is anticipated to reach 134.1 thousand.
- From 2019 to 2024, the number of new cases of GBS in China rose from 9.8 thousand to 10.3 thousand, with a CAGR of 1.1%. It is expected to continue increasing to 10.8 thousand by 2029, reflecting a CAGR of 1.0% from 2024 to 2029. Projections indicate that by 2033, the incidence is anticipated to reach 11.3 thousand.

Incidence of GBS in China and Globally, 2019-2033E

Period	CAGR	
	China	Global
2019-2024	1.1%	2.2%
2024-2029E	1.0%	2.3%
2029E-2033E	1.1%	2.5%



Source: Frost & Sullivan Analysis

Global Competitive Landscape of GBS

Marketed drugs of GBS Treatment

Generic Name	Drug name	Company	Target	Indications	Approved Date
Human immunoglobulin	YIMMUGO	Biotest	Immunoglobulin	Secondary Immunodeficiency, Primary Immunodeficiency, Immune Thrombocytopenia (ITP), Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), Multifocal Motor Neuropathy (MMN), GBS, Kawasaki Disease	2022-11-14
Human immunoglobulin	IQYMUNE	LFB Group	Immunoglobulin	Primary Immunodeficiency, Immune Thrombocytopenia (ITP), GBS, Kawasaki Disease, Secondary Immunodeficiency	2015-09-04
Human immunoglobulin	N/A	Otsuka Pharma	Immunoglobulin	Infectious Diseases, Kawasaki Disease, GBS, Pemphigus, Immune Thrombocytopenia (ITP), Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), etc.	1992-01-01
Human immunoglobulin	PRIVIGEN	CSL Behring	Immunoglobulin	Primary Immunodeficiency, Immune Thrombocytopenia (ITP), Secondary Immunodeficiency, Kawasaki Disease, GBS, Multifocal Motor Neuropathy (MMN), etc.	1985-11-01
Human immunoglobulin	HYQVIA	Baxter	Immunoglobulin	Primary Immunodeficiency, X-linked Agammaglobulinemia (XLA), Immune Thrombocytopenia (ITP), GBS, Kawasaki Disease, Multifocal Motor Neuropathy (MMN), Pemphigus, etc.	1956-05-01
Human immunoglobulin	LIV-GAMMA SN	SK Plasma	Immunoglobulin	X-linked Agammaglobulinemia (XLA), Immune Thrombocytopenia (ITP), GBS, Kawasaki Disease, Infectious Diseases	/

Pipeline in GBS Treatment

Drug Name	Company	Target	Indications	Stage	Approved Date
Eculizumab	AZ	C5	GBS	III	2021-02-12
ANX 005	Annexon Biosciences	C1q	GBS	III	2021-01-08
Efgartigimod	Argenx	FcRn	GBS	II	2023-01-27
Imlifidase	Hansa Biopharma	IgG	GBS	II	2018-12-19
EGF1-48	Bioasis Technologies	/	GBS	I	2022-06-16

Note: As of 2025.03.12

Source: Clinicaltrials.gov , CDE, NMPA, Frost & Sullivan Analysis

Competitive Landscape of GBS in China

No drug has been approved for GBS indications or entered clinical stage in China.

Note: As of 2025.03.12

Source: CDE, NMPA, Frost & Sullivan Analysis

Unmet Needs in the Treatment of GBS

Challenges in Early Diagnosis	• The diagnosis of GBS is often delayed due to its diverse clinical presentations and the lack of definitive diagnostic tools in its early stages. GBS is currently diagnosed based on clinical symptoms, such as progressive weakness and areflexia, supported by tests like lumbar puncture and electrodiagnostic studies. However, these methods are not foolproof and may fail to identify atypical or early cases. This diagnostic complexity is particularly problematic because timely treatment is crucial to prevent severe complications, such as respiratory failure requiring mechanical ventilation. Efforts are being made to identify biomarkers that can facilitate early and accurate diagnosis. This would not only improve patient outcomes but also enable better stratification of patients for clinical trials, potentially leading to more targeted therapies.
Inadequate Treatment Accessibility and Efficacy	• While treatments like intravenous immunoglobulins (IVIG) and plasmapheresis are the standard of care, they are not universally effective across all patient subtypes or regions. These therapies are expensive and require specialized infrastructure, making them inaccessible in many low-resource settings. Furthermore, some patients do not respond adequately to these treatments, leaving them at risk for prolonged paralysis or complications. Recent research has highlighted the potential of novel therapies, such as IgG. The drugs have shown promise in clinical trials, but they are not yet widely available. The development and approval process for such treatments remain lengthy, leaving patients with limited immediate options.
Long-term Disability and Recovery	• Even with optimal treatment, many GBS patients experience a protracted recovery period, often spanning months to years. During this time, residual symptoms such as muscle weakness, chronic pain, and fatigue can significantly impair quality of life. Additionally, understanding the long-term impact of GBS on diverse populations remains limited. Subtypes of GBS, influenced by genetic, environmental, and demographic factors, may require distinct therapeutic approaches. Ongoing research into disease heterogeneity and the mechanisms underlying nerve repair is critical to addressing these gaps

Source: Literature review, Frost & Sullivan analysis

IgG degrading enzymes in AAV gene therapy

Major Barrier of AAV gene therapy

NAbs present a significant barrier to the broad application of AAV in the clinic:

- NAbs can mitigate AAV infection through binding to AAV capsids and blocking critical steps in transduction such as cell surface attachment and uptake, endosomal escape, productive trafficking to the nucleus, or uncoating.
- NAbs can mitigate AAV infection by promoting AAV opsonization by phagocytic cells, thereby mediating their rapid clearance from the circulation.
- Vector immunogenicity represents a major challenge in readministration of AAV vectors. High-titer NAbs are produced following AAV vector administration, thereby preventing prospective AAV redosing.

Challenges of Approaches to clear NAbs

- Preexisting humoral immunity to recombinant adeno-associated virus (AAV) vectors restricts the treatable patient population and efficacy of human gene therapies. Approaches to clear neutralizing antibodies (NAbs), such as plasmapheresis and immunosuppression, are either ineffective or cause undesirable side effects.

Application and Advantage of IgG degrading enzyme

- An antibody clearance strategy to rapidly and transiently degrade neutralizing antibodies using an IgG degrading enzyme prior to AAV administration could potentially improve the efficacy of AAV gene therapy.

Source: Literature review, Frost & Sullivan analysis

Growth Drivers of IgG-Degrading Enzymes

Increasing Awareness of Autoimmune Disease	• With the growing global awareness of health, more patients are becoming better informed about managing autoimmune diseases (such as rheumatoid arthritis, lupus, and Guillain-Barré Syndrome). Patients are increasingly seeking more effective treatment options, especially novel therapies that can regulate the immune system and reduce long-term side effects. IgG-degrading enzymes, as biologics that specifically degrade harmful immunoglobulins (such as IgG), can play a critical role in treating autoimmune diseases. With increasing patient demand and a shift in treatment philosophy, the development and application of IgG-degrading enzymes will have a broader market in the future
Rising Disposable Income of the General Population	• With economic growth, especially in developing countries, the disposable income of residents is steadily increasing. This provides financial support for the widespread use of new treatments, particularly innovative biologics. IgG-degrading enzymes, as a high-end biopharmaceutical, may see increased demand driven by economic factors, especially when patients can afford higher treatment costs. The rise in disposable income enables more people to access such advanced immune therapies, thus promoting the development and adoption of this technology.
Technology Development and Government Support	• Advances in biopharmaceutical technologies, particularly in genetic engineering and enzyme production, provide strong technical support for the production and optimization of IgG-degrading enzymes. At the same time, with the growing demand for treatments for autoimmune diseases, governments are increasingly supporting the research and development of new drugs. Policies like Orphan Drug Designation help reduce R&D costs and accelerate the clinical trials and approval processes for IgG-degrading enzymes, speeding up their market introduction.

Source: Literature review, Frost & Sullivan analysis

Future Trends of IgG-Degrading Enzymes

Expanding Indications Beyond Autoimmune Diseases	• IgG-degrading enzymes are primarily being researched for autoimmune diseases, but their potential applications are expanding. Beyond conditions like rheumatoid arthritis, lupus, and Guillain-Barré syndrome, these enzymes may be applied to other disorders driven by IgG antibodies, such as chronic inflammatory diseases. The ability to specifically target and degrade pathogenic IgG antibodies could open new therapeutic pathways for conditions with an underlying autoimmune or immune-mediated component.
Combination Therapies with Other Immunomodulators	• Another trend is the exploration of IgG-degrading enzymes in combination with other immunomodulatory therapies, such as monoclonal antibodies, or gene therapies. By combining these therapies, it may be possible to enhance the efficacy of treatment and reduce side effects. For example, using IgG-degrading enzymes to modulate the immune response while simultaneously using other agents to target specific disease pathways could lead to more personalized and effective treatment options for autoimmune diseases and cancer.
Improved Safety and Specificity	• The future of IgG-degrading enzymes lies in improving their safety and specificity. Researchers are focusing on engineering these enzymes to target only pathogenic antibodies while minimizing the impact on normal immune function. This precision could lead to fewer side effects and broader applications. Additionally, advancements in protein engineering, such as optimizing enzyme stability and activity, could improve the efficacy and make them suitable for a wider range of diseases, including rare or complex autoimmune disorders.

Source: Literature review, Frost & Sullivan analysis

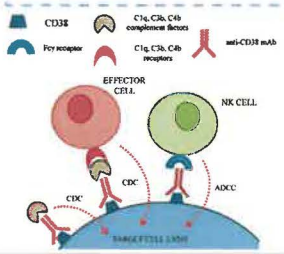
Antibodies Resistant to Enzyme Degradation in Combination Use with Protein-Degrading Enzyme

- The combination of antibodies resistant to enzyme degradation and protein-degrading enzymes represents a novel therapeutic strategy. The IgG degrading enzyme KJ103 + anti-enzyme cleavage CD20/38 antibody combination therapy is expected to stand out with its unique advantages such as enhanced treatment efficacy by reducing immunoglobulin interference and potential to lower antibody dosage, showing great promise in expanding clinical applications for tumor treatment and possessing significant market potential due to its ability to attract a wide range of patients and provide a more cost-effective solution.

KJ103

The IgG degrading enzyme KJ103 has unique enzymatic activity, which can specifically act on the hinge region of immunoglobulin molecules and effectively degrade excess IgG in the blood. Its function include:

- Reduce blood immunoglobulin levels to the original level or lower.
- Reduce a series of pathological effects caused by hyperglobulinemia.
- Create favorable conditions for subsequent combined treatment.



Combination Use with Antibodies

When KJ103 is used in combination with anti-enzyme cleavage antibodies, the degradation of IgG by KJ103 can reduce the adverse effects of hyperglobulinemia on the tumor microenvironment, reduce the interference of immunoglobulins on antibody activity, and enable the antibodies to more efficiently exert their function of targeting tumor cells.

Combination use may also reduce the clinical dosage of antibodies, reduce immune-related adverse reactions that may be caused by high-dose antibodies, such as reducing the risk of side effects such as cytokine release syndrome, and reduce the economic burden of medication for patients, providing patients with safer, more economical and effective treatment options.

➢ Anti-enzyme cleavage CD20/CD38 antibodies have highly specific targeting capabilities and can accurately identify and bind to CD20/CD38 antigens on the surface of tumor cells. Particularly, the anti-enzymatic property gives these antibodies the function of being difficult to be degraded by enzymes in the body, thereby playing a key targeted attack role in tumor treatment more stably and safely.

CD20 Antibody

It mainly targets B cell-related tumors.

- Chronic lymphocytic leukemia: Degrading immunoglobulins can optimize the CD20 antibody-mediated cell killing process and improve the efficiency of tumor cell clearance.
- Follicular lymphoma: Reduce the obstruction of globulin, enhance the binding of the antibody to tumor cells and subsequent immune responses, effectively inhibiting tumor growth and spread.

CD38 Antibody

It shows significant efficacy in CD38-targeted hematological tumors.

- Multiple myeloma: Promote the CD38 antibody to inhibit tumor cell proliferation and survival.
- Waldenström macroglobulinemia: Improve the treatment obstruction caused by hyperglobulinemia and enhances the effect of the antibody on tumor cells.
- Mantle cell lymphoma: Assist the CD38 antibody to enhance the immune attack and delay disease progression.

Source: Literature Review, Frost & Sullivan analysis

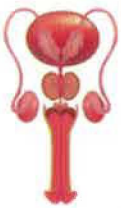
Infertility – overview and causative factors

Disease overview

- Infertility is a disease of the male or female reproductive system, which refers to a person who has not taken any contraceptive measures for more than one year and has a normal sexual life without successful pregnancy.
- Infertility can be due to male factors, female factors, or other unexplained factors. For patients with infertility caused by complex or multiple causes, it is difficult to find the cause and difficult to treat the symptoms.

Causative factors

Male factor



Abnormal semen transport leading to infertility

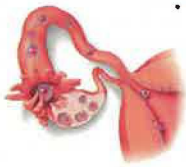
- **Structural diseases:** such as Klinefelter syndrome, Cryptorchidism, blocked and damaged testicles, etc., can hinder semen transportation.
- **Sexual dysfunction:** Diseases such as premature ejaculation and Retrograde ejaculation can cause semen to be unable to be ejected into the vagina normally.

Abnormal sperm production or function infertility

- **Endocrine disorders:** Endocrine diseases such as Kallmann syndrome affect the synthesis of gonadotropins, leading to spermatogenic dysfunction.
- **Infectious factors:** Viruses such as mumps virus and Treponema pallidum can cause orchitis, leading to destruction and atrophy of the seminiferous tubules; gonorrhea, tuberculosis, and filariasis can cause obstruction of the vas deferens; infection can destroy the spermatogenic environment, ultimately leading to reduced sperm production. Reduced functionality.

Female factor

fallopian tube infertility



- Diseases such as pelvic infection, endometriosis, and fallopian tube tuberculosis can damage the fallopian tube mucosa, cause fallopian tube obstruction, produce cicatricose, cause fallopian tube wall stiffness and adhesion, and affect the fallopian tube's egg pickup and transport functions.

Ovulation disorder infertility

- **Endocrine Disorders:** such as hormonal disorders, polycystic ovary syndrome, etc., can affect the menstrual cycle, leading to amenorrhea or chronic ovulation disorders, affecting the release of eggs from the ovaries.
- **Uterine or cervical abnormalities:** including cervical abnormalities, uterine polyps, or abnormal uterine shape. Noncancerous tumors or polyps in the endometrium may block the fallopian tubes or prevent a fertilized egg from implanting in the uterus, causing infertility.

Other factors

immune factors

- Anti-sperm autoimmune antibodies produced by men and anti-sperm alloimmune antibodies produced by women can render sperm inactive, agglutinated or dead.

life factors

- Aging, smoking, drinking, being overweight or underweight are all risk factors for infertility.

environmental factors

- Heat, radiation and toxic substances can cause the spermatogenic epithelium to fall off and affect the male spermatogenesis process.

Medical and surgical history

- Opioids, anti-cancer drugs, chemotherapy drugs, etc. can affect sperm production and damage female fertility.

Source: Literature review, Frost & Sullivan analysis

Infertility – Treatment Options

- Infertility can be treated with medications, surgery, and assisted reproductive technology (ART).
- ART include all fertility treatments that work with eggs and embryos, often requiring a combination of assisted reproductive medications.

Treatment	Illustrate
 **Medications**	• Medication is the conventional treatment for infertility conditions. Women are the main audience for drug treatment, and drug treatment is used to solve female ovulation problems and thereby relieve infertility symptoms. • Assisted reproductive drugs mainly include down-regulating drugs, ovulation-stimulating drugs, ovulation-inducing drugs, luteal support drugs and conditioning Chinese medicines.
 **Surgery**	• Abnormalities of the female reproductive system, such as endometriosis and Tubal Occlusion, can be treated with surgery. Laparoscopic surgery is a common type of surgery. • In male patients, surgical treatments include varicocelectomy, vasectomy reversal, and epididymal vasostomy.
 **Assisted Reproductive Technology (ART).**	• Assisted reproductive technology treatments include artificial insemination, in vitro fertilization and embryo transfer. • In vitro fertilization and embryo transfer involve surgically removing eggs from a woman's ovaries, combining the eggs with sperm in the laboratory, and then transplanting the fertilized eggs into the uterus of the woman to be pregnant for the purpose of assisted reproduction.

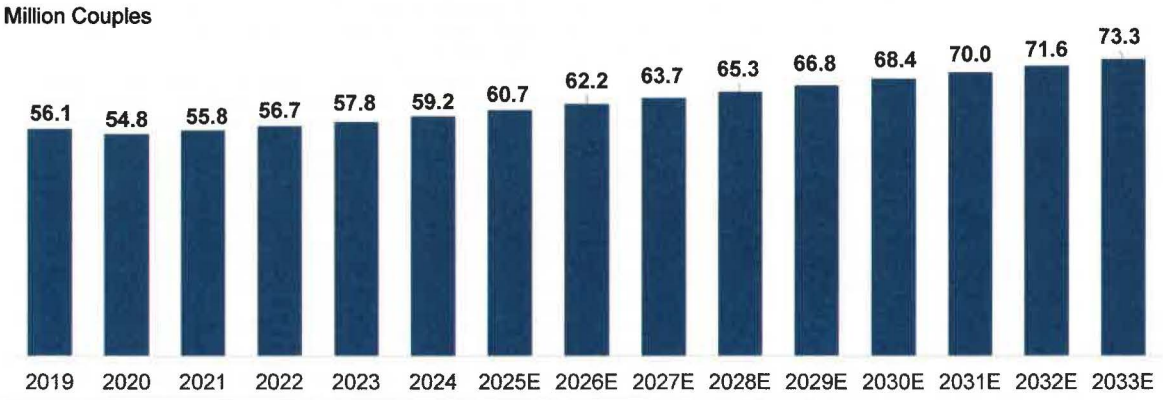
Source: Literature review, Frost & Sullivan analysis

The Number of Infertile Couple in China, 2018-2033E

- In 2024, There are 59.2 million infertile couples in China, with a CAGR of 1.1% from 2019 to 2024. It is estimated that there will be 73.3 million couples of childbearing age in China suffering from infertility in 2033, with a CAGR of 2.3% from 2029 to 2033.

The Number of Infertile Couple in China, 2018-2033E

Period	CAGR
2019-2024	1.1%
2025E-2029E	2.4%
2029E-2033E	2.3%



Source: Literature review, Frost & Sullivan analysis

Classification and mechanism of assisted reproductive drugs – I

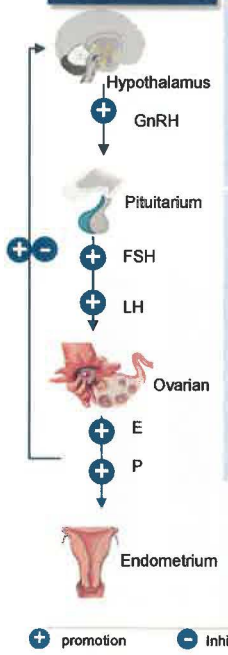
- Assisted reproductive drugs mainly treat infertility by solving ovulation problems in infertile women.
- The female hormonal cycle of normal ovulation consists of three phases: follicular phase, ovulation phase and luteal phase. Assisted reproductive drugs correspond to the female reproductive hormone cycle and are mainly divided into: down-regulation, ovulation induction, and luteal support drugs. Among them, ovulation induction drugs have the mechanism of inducing ovulation and controlling ovarian stimulation, and are one of the most commonly used assisted reproductive drugs in clinical practice.

Female ovulation hormone cycle	Drug classification and mechanism of action	
Follicular phase: Hypothalamus → Gonadotropin-releasing hormone (GnRH)	***Down-regulatory drugs***	• By regulating the level of GnRH hormone and reduces the secretion of FSH and LH hormones in the subsequent process, the development of follicular slows down, thereby playing a down-regulating effect.
Ovulation period: Pituitarium → Follicle-stimulating hormone (FSH) / Luteinizing hormone (LH) → Ovarian → Estrogen (E) / Progestogens (P)	***Ovulation induction drugs***	Ovulation induction drugs have two main mechanisms of action: • **Ovulation induction (OI):** For women with little or no ovulation, induce the development of a single follicle or a few follicles to help patients form a normal ovulation cycle. • **Controlled ovarian stimulation (COS):** For patients with normal ovarian ovulation function, the ovaries are stimulated to produce multiple follicles in each cycle, leading to the release of multiple eggs to increase the chance of pregnancy.
Luteal phase: Endometrium	***Luteal support drugs***	• By increasing the levels of estrogen and progesterone in the patient's body, it promotes endometrial hyperplasia and increases the chance of embryo implantation and pregnancy.

Source: Literature review, Frost & Sullivan analysis

Classification and mechanism of assisted reproductive drugs – II

- Down-regulation, ovulation induction, and luteal support drugs mainly fall into the following common categories:



	Drug	Mechanism
Down regulation	Gonadotropin-releasing hormone (GnRH)	• If the patient's GnRH release is abnormal, GnRH can be continuously delivered to the patient's body through a subcutaneous or vascular connection light pump to stimulate the pituitary gland to release FSH and LH.
	GnRH analogs (GnRHa)	• GnRH analogs are synthetic hormones similar to natural GnRH, including GnRH-a promoters and GnRH-A antagonists • When GnRH analogues are injected, the pituitary gland is continuously (rather than periodically) exposed to synthetic GnRH, resulting in continued production of FSH and LH • In infertility treatment, GnRH promotors are used in combination with antagonists to regulate the patient's ovulation cycle.
ovulation induction	Clomifene (CC)	• The anti-estrogen drug Clomifene is the most common prescription drug for ovulation induction. It mainly competes to occupy the hypothalamic estrogen receptor, interferes with the negative feedback of estrogen on the hypothalamic-pituitary-gonadal axis, promotes the increase of FSH and LH secretion, and stimulates follicle growth
	Aromatase inhibitors (LE)	• The mechanism of LE to induce ovulation is not very clear. Research speculates that LE can block the production of estrogen and reduce the body's estrogen level. It never relieves the negative feedback effect of estrogen, promotes the increase of Gn secretion and stimulates follicular development.
	Gonadotropins (Gn)	• There are various types of Gn drugs, which are divided into natural Gn and genetically recombinant Gn. • Natural Gn includes human menopausal gonadotropin (hMG), urinary follicle-stimulating hormone (uFSH), and human chorionic gonadotropin (uhCG) • Gene recombinant Gn includes recombinant FSH (rhFSH), recombinant luteinizing hormone (rhLH) and recombinant HCG (rhHCG) • Gonadotropins can be used to stimulate the simultaneous growth and maturation of multiple follicles
Luteal support	Progesterone	• Progesterone is a natural progesterone secreted by the corpus luteum of the ovary and the placenta; drugs are divided into natural progestins and synthetic progestins • Progesterone can 1) promote thickening of the endometrium; 2) reduce uterine contractions to ensure that fertilized eggs grow safely in the uterine cavity; 3) prevent embryo rejection
	estrogen	• Estrogen can increase the blood supply to the myometrium, promote the proliferation of Myometrial Smooth Muscle Cells, and thicken the myometrium.

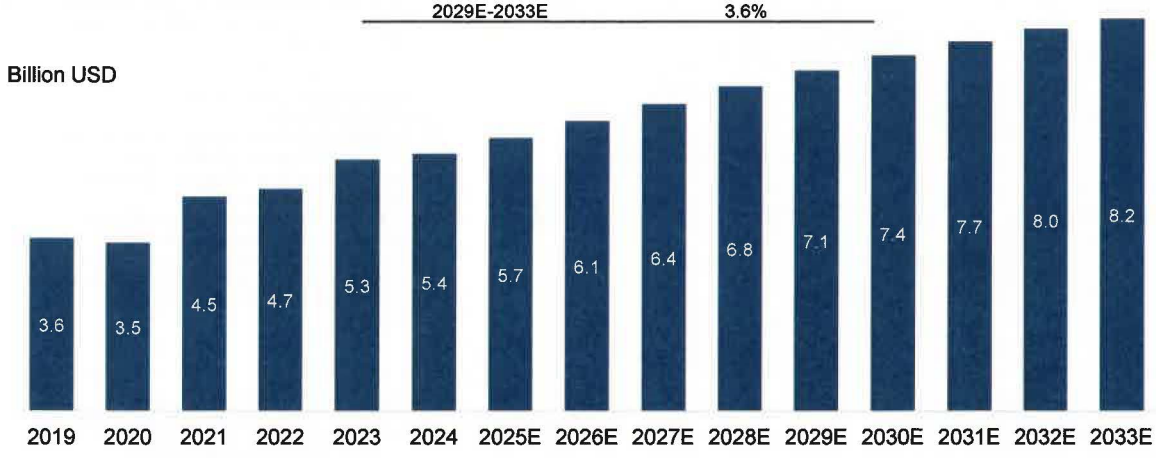
Source: Literature review, Frost & Sullivan analysis

Global Market Size and Forecast of Assisted Reproductive Drug, 2019-2033E

- The size of Assisted Reproductive Drugs market globally was USD 5.4 billion market size in 2024, with a CAGR of 8.3% from 2019 to 2024. It is expected to reach to USD 8.2 billion in 2033, with a CAGR of 3.6% from 2029 to 2033.

Global Market size and forecast of Assisted Reproductive Drugs, 2019-2033E

Period	CAGR
2019-2024	8.3%
2025E-2029E	5.7%
2029E-2033E	3.6%



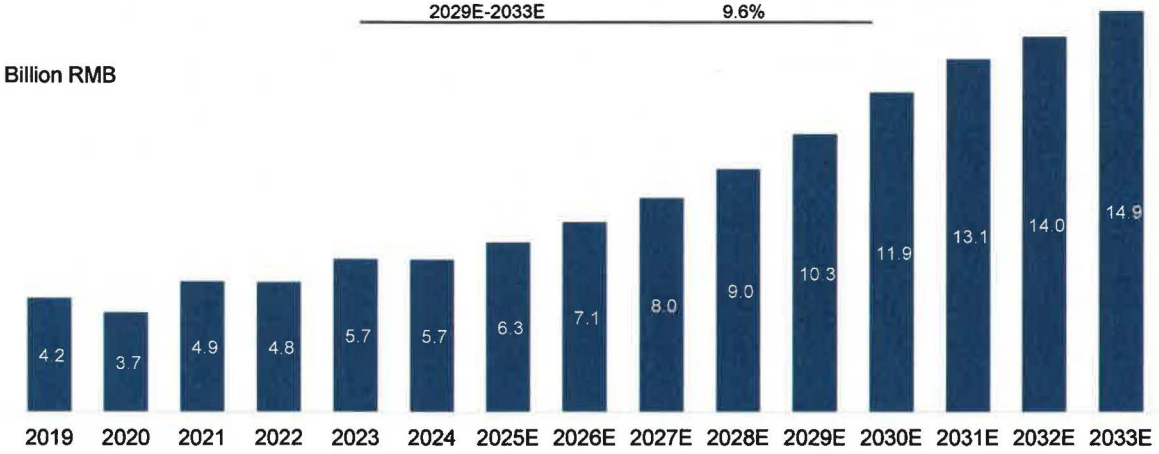
Source: Literature review, Frost & Sullivan analysis

Market Size and Forecast of Assisted Reproductive Drugs in China, 2019-2033E

- The size of Assisted Reproductive Drugs market in China was RMB 5.7 billion market size in 2024, with a CAGR of 6.3% from 2019 to 2024. It is expected to reach to RMB 17.0 billion in 2033, with a CAGR of 9.6% from 2029 to 2033.

Market size and forecast of Assisted Reproductive Drugs in China, 2019-2033E

Period	CAGR
2019-2024	6.0%
2025E-2029E	13.1%
2029E-2033E	9.6%



Source: Literature review, Frost & Sullivan analysis

Classification and comparative analysis of follicle stimulating hormone drugs

- Follicle stimulating hormone (FSH) is one of the important assisted reproductive drugs. FSH is a gonadotropin synthesized and secreted by the pituitarium. It promotes the development and maturation of follicles in women and promotes the maturation and spermatogenesis of testicular seminiferous tubules in men.
- Follicle stimulating hormone is divided into urinary follicle-stimulating hormone uFSH and recombinant human follicle-stimulating hormone rhFSH. rhFSH is produced through genetic recombination and has higher purity.

Classification and comparative analysis of follicle stimulating hormone

	Urinary follicle stimulating hormone (uFSH)	Recombinant human follicle stimulating hormone (rhFSH)
Source	• Extracted from gonadotropin hormones (hMG, including follicle-stimulating hormone FSH and luteinizing hormone LH) in the urine of menopausal women	• Produced by introducing the genes of human FSH alfa and beta subunits into Syrian Hamster ovary cells through genetic engineering technology
Preparation	• Use protein purification technology to remove LH and urine protein, and extract FSH. However, very small amounts of LH and urine protein will still be collected and lyophilized • According to the degree of purification, it is divided into FSH-P and FSH-HP preparations	• There are currently 6 rhFSH preparations with slightly different compositions on the market. • human FSH alfa and beta are both obtained from cell culture supernatants through ultrafiltration, but are prepared through different chromatographic purification.
Purity	• FSH-P preparation>95%, FSH-HP>99%	• >99%
Acceptance	• Low, injection is painful; sources are different, batch quality varies greatly; urine donor safety risk is high	• Higher, less pain in injection, high drug purity
Effect	**Data show that rhFSH is more clinically effective than uFSH:** • rhFSH has high biological activity, which can improve embryo quality, gather more follicles, and increase pregnancy rate. • In a shorter treatment time, rhFSH can collect oocytes and obtain embryos at a lower total dose. • During the frozen-thawed embryo transfer treatment cycle, the clinical pregnancy rate of rhFSH cycle treatment is higher than that of uFSH cycle treatment.	

Source: Literature review, Frost & Sullivan analysis

Recombinant human follicle stimulating hormone – comparison and analysis of main dosage forms

- Currently, there are three main types of recombinant human follicle stimulating hormone dosage forms on the market: rhFSH freeze-dried powder, water injection and FSH-CTP long-acting injectable. The three types of dosage forms have similar therapeutic effectiveness and safety, but there are differences in clinical use, price, duration of efficacy, etc. Therefore, doctors can prescribe different dosage forms of recombinant human follicle stimulating hormone based on factors such as disease progression and financial ability of different patients. To meet the medication needs of different patient groups.

Comparative analysis of the main dosage forms of recombinant human follicle stimulating hormone

	Freeze-dried powder	Water injection	FSH-CTP long-acting injectable
Dosage form introduction	• Recombinant human follicle stimulating hormone sterile freeze-dried preparation, an earlier traditional preparation developed	• Recombinant human follicle stimulating hormone multi-dose liquid preparation, generally used with prefilled pens	• Recombinant human follicle stimulating hormone introducing CTP (carboxyl terminal peptide) sequence • Compared with other dosage forms, the absorption rate is slowed down and the half-life can be extended by about 2~3 times.
Clinical use	• The freeze-dried powder drug needs to be dissolved into a solution and then injected for administration. It must be used under the supervision of medical staff.	• Patients can inject themselves using recombinant human follicle stimulating hormone injection pen	• Injection frequency can be reduced to once a week, resulting in higher patient compliance
Effectiveness	• Literature shows that the serum concentration-time curve values after administration of the freeze-dried powder dosage form and the water injection dosage form are similar, so these two preparations have **relatively consistent clinical effectiveness**.		• Literature shows that FSH-CTP long-acting injection treatment is similar to the daily injection of rhFSH preparations in terms of main clinical endpoint data such as the average number of eggs retrieved, and therefore has similar clinical treatment effects.
Security	• Literature shows that patients have good systemic and local tolerance to both freeze-dried powder and water injection preparations. The incidence and severity of adverse events of the two preparations are similar, and there is **no significant difference in tolerability**.		• Literature shows that the patient tolerance and incidence of adverse events of FSH-CTP long-acting injections are similar to those of daily injections of rhFSH preparations.

Source: Literature review, Frost & Sullivan analysis

Recombinant human follicle stimulating hormone – analysis of main mechanisms of action

- Recombinant human follicle stimulating hormone (rhFSH) acts on FSH receptors on target cells. rhFSH binds to the G-protein-coupled transmembrane FSHR expressed on target cells, activating different signaling pathways and triggering different mechanisms of action based on specific physiological sex, development and environment.
- rhFSH has different mechanisms in male and female groups. In women, the main role of rhFSH is to regulate ovarian folliculogenesis and steroid hormone production; in men, rhFSH plays a role in regulating the maturation of testicular Sertoli cells and sperm production.

The mechanism of action of recombinant human follicle stimulating hormone

Female

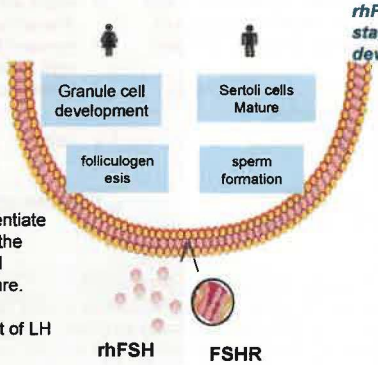
- In women, rhFSH acts on receptors (FSHR) on ovarian target cells – granulosa cells. Granulosa cells are one of the ovarian cells that produce the two steroid hormones estrogen and progesterone.

rhFSH has different mechanisms at different stages of the female ovulation hormone cycle:

End of luteal phase
- FSH acts on FSH receptors on granulosa cells to promote the recruitment and growth of early preantral follicles.

Follicular phase
- Increased FSH levels in the body can promote the growth and development of granulosa cells, differentiate intimal cells, form follicular fluid, and then expand the follicular cavity, thereby stimulating the growth and development of follicles and allowing them to mature.

Pre-ovulation stage
- Acts on FSH receptors, promotes the development of LH receptor cells in granulosa cells, and prepares for ovulation



Male

- In men, rhFSH exerts its effects through a receptor (FSHR) located on the Sertoli cells of the testicles.
- Circulating levels of FSH in adult men are directly related to their Sertoli cell number and testicular volume.

rhFSH has different mechanisms at different stages of the male physiological development cycle:

Sertoli cell maturation
- FSH regulates proliferation and maturation of prepubertal Sertoli cells

Sperm formation
- Sperm production occurs in the seminiferous tubules of the testes and is controlled by the action of FSH and LH
- FSH drives Sertoli cells to produce regulatory molecules and nutrients needed for spermatogenesis, guiding spermatogonia to proliferate and mature by activating gene transcription related to metabolic balance and cell survival.

Source: Literature review, Frost & Sullivan analysis

Recombinant Human Follicle Stimulating Hormone – Analysis Of Main Indications

- China's NMPA approved recombinant follicle stimulating hormone for the treatment of patients with three types of infertility symptoms: 1) female patients who do not ovulate and do not respond to clomiphene treatment; 2) patients who receive ovulation induction treatment through assisted reproductive technology; 3) Patients with severe LH and FSH deficiency. Internationally, the FDA and EMA has also approved recombinant follicle-stimulating hormone for use in male patients with hypogonadism.
- Clinical experiments have proven that recombinant human follicle-stimulating hormone is 84% effective in treating female infertility symptoms and 63% effective in treating male infertility symptoms.

	Indications and treatment options	Approval authority
Adult women	• Induction of ovulation and pregnancy in anovulatory infertile women in whom the cause of infertility is functional and not due to primary ovarian failure • Recombinant human follicle-stimulating hormone is used alone to stimulate the ovaries to produce multiple eggs at once.	FDA & EMA & MPA
	• Development of multiple follicles in ovulatory infertile women as part of Assisted Reproductive Technology (ART) cycles. • Recombinant human follicle stimulating hormone is used alone to stimulate the ovaries to produce multiple eggs at once.	FDA & EMA & MPA
	• Severe lack of luteinizing hormone (LH) and follicle stimulating hormone (FSH) • Recombinant human follicle-stimulating hormone is used with the drug LH to stimulate egg maturation in the ovaries	EMA & NMPA
Adult male	• Induction of spermatogenesis in infertile men with primary and secondary hypogonadotropic hypogonadism for whom the cause of infertility is not due to primary testicular failure. • Combined treatment with recombinant human follicle stimulating hormone and human chorionic gonadotropin (hCG) can effectively stimulate sperm production	EMA & FDA

Effectiveness of rhFSH in treating infertile women

- Data show that 84% of adult women who did not produce eggs and did not respond to clomiphene treatment successfully produced eggs after receiving recombinant human follicle-stimulating hormone treatment.
- Recombinant human follicle stimulating hormone has a more consistent efficacy with human FSH in stimulating ovaries

Effectiveness of rhFSH in treating infertile men

- Data show that after receiving recombinant human follicle-stimulating hormone combined with hCG treatment, 63% of men with hypogonadism began to produce sperm.

Source: Literature review, Frost & Sullivan analysis

Recombinant Human Follicle Stimulating Hormone – Analysis of Clinical Studies in Male Infertile Patients

- Follicle stimulating hormone plays an important role in sperm production, but the mechanism of recombinant human follicle stimulating hormone in the treatment of male infertility is currently unclear. Therefore, a number of clinical trials at home and abroad are actively promoted to explore the role of recombinant human follicle stimulating hormone in the treatment of male infertility. Its main role and related mechanisms in patients with male infertility and oligospermia patients.
- In the future, with the acceleration of clinical trials of recombinant human follicle stimulating hormone, its treatment field will be further expanded to male infertility patients in China, helping to solve problems such as hypogonadism in male patients, promoting the growth of demand for recombinant human follicle stimulating hormone patients, and accelerating the industry further development.

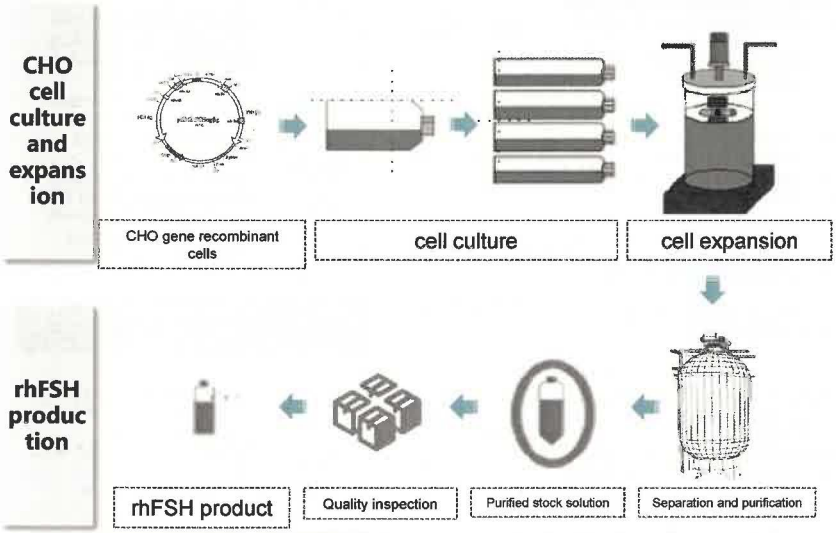
Examples of Clinical Studies	Main Conclusions
Treatment of idiopathic oligozoospermia with recombinant human follicle-stimulating hormone: a prospective, randomized, double-blind, placebo-controlled clinical study in Chinese population	• Three months after treatment with a dose of rhFSH exceeding 200IU, the patient's sperm count increased significantly; starting from the fifth month of treatment, sperm morphology and motility improved significantly. • The natural pregnancy rate and artificial insemination rate of patients who received 300IU rhFSH for 5 consecutive months were significantly improved. • Semen parameters (total sperm count, sperm concentration, forward motility and morphology) were significantly improved in patients with normal and low levels of inhibin B
Recombinant human follicle stimulating hormone for treatment of male idiopathic infertility: a randomized, double-blind, placebo-controlled, clinical trial	• In patients treated with 150 IU rhFSH for 12 weeks, rhFSH did not lead to improvements in sperm parameters or increase in pregnancy rates. However, testicular volume and sperm DNA coagulation rate were significantly increased in the treatment group.
Use of recombinant human follicle-stimulating hormone in the treatment of male factor infertility	• rhFSH at a dose of 100 IU IM on alternate days for 3 months increases the spermatogonial population and sperm production in idiopathic patients with oligozoospermia with normal FSH and inhibin B plasma levels and a cytological picture of hypospermatogenesis.

Source: Literature review, Frost & Sullivan analysis

Recombinant human follicle stimulating hormone – production process analysis

- Recombinant human follicle stimulating hormone (rhFSH) uses gene recombination technology to clone the human follicle stimulating hormone gene into the genome of Chinese hamster ovary cells (CHO) and express it. After a series of cell expansion, separation and purification, canning quality inspection and other processes, the finished product of recombinant human follicle stimulating hormone is produced.
- Compared with urine-derived follicle stimulating hormone, the production technical barriers of recombinant human follicle stimulating hormone are high, the production process is stable, and the products are of higher purity and uniform quality.

Production process



Key production processes

- **Gene recombination and cell culture:** Select appropriate and optimal target genes, vectors, cell lines and cell cultures to obtain rhFSH with high biological activity and purity.
- **Purification process:** An efficient and stable protein purification process can improve the rhFSH recovery rate and filter out high-purity and highly active raw solutions.
- **Quality inspection:** Quality inspection tests include biological activity, purity, exogenous DNA residues, bacterial endotoxin monitoring, etc. Comprehensive quality inspection can ensure the quality of rhFSH stock solution and the same quality between batches

The importance of production technology

- The recombinant human follicle stimulating hormone produced by stable cell culture and purification processes has **higher purity**.
- The comprehensive quality inspection process can ensure uniform product quality, reduce contamination of LH and other metabolites, thereby reducing drug side effects and ensuring **high safety** of finished drug products.

Source: Literature, Frost & Sullivan analysis

Marketed Recombinant Human Follicle Stimulating Hormone (rhFSH) in China (1/2)

- There are currently 9 rhFSH injection marketed in China. Merck's GONAL-F®, LG Chem's Follitrope®, Organon's PUREGON®, and Ferring Pharmaceuticals' Rekovelle® are imported drugs, while Shengji Pharm's 晟诺娃®, GenSci's Jinsaiheng® 金赛佳®,Qilu Pharmaceutical's Anxinbao® and Jingze's 泽盼喜® are Chinese domestic drugs.

Drug name	Generic name	Company	First approval date	Strength	Indications	Formulation
泽盼喜®	Recombinant Human Follitropin for Injection	景泽生物 Jingze	2025/05/09	75IU(5.5μg)	• Women who do not ovulate and do not respond to clomiphene treatment; • For patients undergoing superovulation or Assisted Reproductive Technology(ART); • For patients with severe LH and FSH deficiency	Powder form
Rekovelle®	Human Follitropin delta injection	Ferring FERRING PHARMACEUTICALS	2024/05/09	12μg (0.36ml) 36μg (1.08ml) 72μg (2.16ml)	• Controlled ovarian stimulation for the development of multiple follicles in women undergoing assisted reproductive technologies (ART)	Liquid form
Anxinbao®	Recombinant Human Follitropin for Injection	齐鲁制药 齐鲁制药 QILU PHARMACEUTICAL	2021/12/14	75IU(5.5μg)	• Women who do not ovulate and do not respond to clomiphene treatment; • For patients undergoing superovulation or Assisted Reproductive Technology(ART); • For patients with severe LH and FSH deficiency	Powder form
Follitrope®	Recombinant Human Follitropin Prefilled Syringe	LG Chem LG化学	2021/04/07	75IU(0.15ml) 150IU(0.3ml) 225IU(0.45ml) 300IU(0.6ml)	• For patients undergoing superovulation or Assisted Reproductive Technology(ART);	Liquid form
Jinsaiheng®	Recombinant Human Follitropin for Injection	长春金赛 GenSci 金赛药业	2015/05/27	75IU(5.5μg)	• Women who do not ovulate and do not respond to clomiphene treatment; • For patients undergoing superovulation or Assisted Reproductive Technology(ART);	Powder form
PUREGON®	Recombinant Follitropin Beta Injection	欧加隆 ORGANON	2005/10/28	300IU(0.36ml) 600IU(0.72ml)	• Women who do not ovulate and do not respond to clomiphene treatment; • For patients undergoing superovulation or Assisted Reproductive Technology(ART);	Liquid form
GONAL-f®	Recombinant Human Follitropin Injection	默克 MERCK	2000/04/26	150IU(11ug) 300IU(22ug) 450IU(33ug) 900IU(66ug)	• Women who do not ovulate and do not respond to clomiphene treatment; • For patients undergoing superovulation or Assisted Reproductive Technology(ART); • For patients with severe LH and FSH deficiency.	Powder form/ Liquid form

Note: As of 2025.11.22
Source:NMPA, Frost & Sullivan analysis

Marketed Recombinant Human Follicle Stimulating Hormone (rhFSH) in China (2/2)

- There are currently 9 rhFSH injection marketed in China. Merck's GONAL-F®, LG Chem's Follitrope®, Organon's PUREGON®, and Ferring Pharmaceuticals' Rekovelle® are imported drugs, while Shengji Pharm's 晟诺娃®, GenSci's Jinsaiheng® 金赛佳®,Qilu Pharmaceutical's Anxinbao® and Jingze's 泽盼喜® are Chinese domestic drugs.

	Drug name	Generic name	Company	First approval date	Strength	Indications	Formulation
	晟诺娃®	Corifollitropin alfa N01 injection	宝济药业 金诺药业 BAO PHARMA	2025/08/19	100μg (0.5ml)	• Used in combination with gonadotropin-releasing hormone antagonists for controlled ovarian stimulation to promote the development of multiple follicles	Liquid form
	金赛佳®	Corifollitropin alfa N02 injection	长春金赛 GenSci 金赛药业	2025/09/23	100μg (0.5ml)	• Used in combination with gonadotropin-releasing hormone antagonists for controlled ovarian stimulation to promote the development of multiple follicles	Liquid form

Note: As of 2025.11.22
Source:NMPA, Frost & Sullivan analysis

Marketed Recombinant Human Follicle Stimulating Hormone (rhFSH) in China (1/2)

- There are currently 9 rhFSH injection marketed in China. Merck's GONAL-F®, LG Chem's Follitrope®, Organon's PUREGON®, and Ferring Pharmaceuticals' Rekovelle® are imported drugs, while Shengji Pharm's 晟诺娃®, GenSci's Jinsaiheng® 金赛佳®,Qilu Pharmaceutical's Anxinbao® and Jingze's 泽盼喜® are Chinese domestic drugs.

	Drug name	Generic name	Company	First approval date	Sales of 2023 (million RMB)/market share	Sales of 2024 (million RMB)/market share	Cost of one treatment cycle for ART (RMB)	National Reimbursement Drug List
	GONAL-f®	Recombinant Human Follitropin Injection	MERCK	2000/04/26	1,234.2/ 55.91%	1,209.5/ 51.5%	5,544	/
	PUREGON®	Recombinant Follitropin Beta Injection	ORGANON	2005/10/28	588.0/ 26.64%	582.8/ 24.8%	9,402	/
	Jinsaiheng®	Recombinant Human Follitropin for Injection	GenSci 金赛药业	2015/05/27	363.5/ 16.47%	485.2/ 20.6%	5,424	/
	Follitrope®	Recombinant Human Follitropin Prefilled Syringe	LG化学	2021/04/07	0.9/ 0.04%	23.4/ 1.0%	5,387	/
	Anxinbao®	Recombinant Human Follitropin for Injection	齐鲁制药 QILU PHARMACEUTICAL	2021/12/14	21.0/ 0.95%	30.2/ 1.3%	5,424	/
	Rekovelle®	Human Follitropin delta injection	FERRING PHARMACEUTICALS	2024/05/09	/	18.8/0.8%	/	/
	泽盼喜®	Recombinant Human Follitropin for Injection	Jingze	2025/05/09	/	/	/	/

Note: 1. As of 2025.11.22; 2. 泽盼喜®, 晟诺娃®,金赛佳® has recently been launched and has not yet been priced; thus treatment cost cannot be calculated.
Source:NMPA, Frost & Sullivan analysis

Marketed Recombinant Human Follicle Stimulating Hormone (rhFSH) in China (2/2)

- There are currently 9 rhFSH injection marketed in China. Merck's GONAL-F®, LG Chem's Follitrope®, Organon's PUREGON®, and Ferring Pharmaceuticals' Rekovelle® are imported drugs, while Shengji Pharm's 晟诺娃®, GenSci's Jinsaiheng® 金赛佳® ,Qilu Pharmaceutical's Anxinbao® and Jingze's 泽盼喜® are Chinese domestic drugs.

	Drug name	Generic name	Company	First approval date	Sales of 2023 (million RMB)/market share	Sales of 2024 (million RMB)/market share	Cost of one treatment cycle for ART (RMB)	National Reimbursement Drug List
	晟诺娃®	Corifollitropin alfa N01 injection	宝济药业	2025/08/19	/	/	/	/
	金赛佳®	Corifollitropin alfa N02 injection	长春金赛	2025/09/23	/	/	/	/

Note: 1. As of 2025.11.22; 2. 泽盼喜®, 晟诺娃®, 金赛佳® has recently been launched and has not yet been priced; thus treatment cost cannot be calculated.
Source:NMPA, Frost & Sullivan analysis

Competitive Landscape of recombinant human follicle-stimulating hormone(rhFSH) products in clinical trials in China

Short-acting

		Drug Name	Drug Category	Original Drug	Generic Name	Company	Indication	Stage	First Posted date
rhFSH	1	JZB33	Biosimilars	Follitropin alfa	rhFSH injection	Jingze	• Women who do not ovulate and do not respond to clomiphene treatment; • For patients undergoing superovulation or Assisted Reproductive Technology(ART); • For patients with severe LH and FSH deficiency	NDA	2025/06/27
	2	Follitropin alfa	Biosimilars	Follitropin alfa	rhFSH injection	Livzon	• Women who do not ovulate and do not respond to clomiphene treatment; • For patients undergoing superovulation or Assisted Reproductive Technology(ART); • For patients with severe LH and FSH deficiency	NDA	2025/01/25
	3	LM001	Biosimilars	Follitropin alfa	rhFSH injection	Alphamab	• For patients undergoing superovulation or Assisted Reproductive Technology(ART);	NDA	2021/12/23
	4	QL-1012D	Biosimilars	Follitropin alfa	rhFSH injection	Qilu	• Women who do not ovulate and do not respond to clomiphene treatment; • For patients undergoing superovulation or Assisted Reproductive Technology(ART); • For patients with severe LH and FSH deficiency	I	2025/02/05

Long-acting

FSH-CTP	1	Follitropin	New Drug	/	FSH-CTP fusion protein injection	SL Pharm	• For patients undergoing superovulation or Assisted Reproductive Technology(ART);	NDA	2025/01/24
rhFSH Fc fusion protein	1	UN008	New Drug	/	rhFSH Fc fusion protein injection	Youhuikang	• For patients undergoing superovulation or Assisted Reproductive Technology(ART);	I/II	2021/06/03

Note: As of 2025/11/22. SL Pharm's Follitropin alfa was withdrawn by company itself. TWP-201 of Therawisdom and KN015 of Alphamab were inactive for over 3 years in clinical phase I; According to the NMPA, 3 FSH-CTP pipelines are classified as Category 3.2 biological products. Since the original innovator drug has not been approved for marketing in China, they are categorized as new drugs in China.
Source: CDE, Frost & Sullivan analysis

Marketed Recombinant Human Follicle Stimulating Hormone (rhFSH) Overseas (1/2)

- There are 7 shorting-acting rhFSH injection marketed overseas. Merck's GONAL-f®, Organon's FOLLISTIM®, Theramex's Overleap®, Gedeon Richter's Bemfola®, Ferring Pharma's Rekovelle®, CinnaGen's Cinnal-f® and Reliance Life Science's FostiRel®.

Marketed short-acting rhFSH

Drug name	Generic name	Company	First approval date	Approval Area	Target	Indications
GONAL-f®	Recombinant Human Follitropin Injection	Merck	1995/10/20	US, EU	FSHR	• Ovulation induction • Polycystic ovary syndrome • Hypogonadotropic hypogonadism • Follicle stimulating hormone deficiency • Luteinizing hormone deficiency • Oligospermia
FOLLISTIM®	follitropin beta	Organon	1996/05/02	US, EU	FSHR	• Ovulation induction • Polycystic ovary syndrome • Male infertility • Hypogonadotropic hypogonadism • Infertility
Overleap®	Recombinant Follitropin alfa	Theramex	2013/09/27	EU	FSHR	• Ovulation induction • Hypogonadotropic hypogonadism • Luteinizing hormone deficiency • Follicle stimulating hormone deficiency • Polycystic ovary syndrome
Bemfola®	Recombinant Human Follitropin alfa	Gedeon Richter	2014/03/26	EU	FSHR	• Ovulation induction • Hypogonadotropic hypogonadism • Luteinizing hormone deficiency • Follicle stimulating hormone deficiency • Polycystic ovary syndrome
Rekovelle®	Human Follitropin delta injection	Ferring Pharma	2016/12/12	EU, Japan	FSHR	• Ovulation induction
Cinnal-f®	Recombinant Human Follitropin alfa	CinnaGen	2013/12/31	Iran	FSHR	• Ovulation induction
FostiRel®	Recombinant Human Follitropin beta	Reliance Life Science	2021/01/01	India	FSHR	• Ovulation induction • Polycystic ovary syndrome • Hypogonadism • Male sexual dysfunction

Note: As of 2025.11.22

Source: FDA, EMA, PDMA, CDSCO, Frost & Sullivan analysis

Marketed Recombinant Human Follicle Stimulating Hormone (rhFSH) Overseas (2/2)

Marketed long-acting rhFSH

Drug name	Generic name	Company	First approval date	Area	Target	Indications
Elonva®	Corifollitropin alfa	Organon	2010/01/25	EU	FSHR	• Hypogonadotropic hypogonadism • Ovulation induction

Note: As of 2025.11.22

Source: EMA, Frost & Sullivan analysis

Global Marketed Recombinant Human Follicle Stimulating Hormone (rhFSH)

Marketed short-acting rhFSH

Drug name	Generic name	Company	First approval date	Approval Area	Target
GONAL-f®	Recombinant Human Follitropin Injection	Merck	1995/10/20	US, EU, CN, JP	FSHR
PUREGON®/ FOLLISTIM AQ®	follitropin beta	Organon	1996/05/02	US, EU, CN	FSHR
Overleap®	Recombinant Follitropin alfa	Theramex	2013/09/27	EU	FSHR
Cinnal-f®	Recombinant Human Follitropin alfa	CinnaGen	2013/12/31	Iran	FSHR
Bemfola®	Recombinant Human Follitropin alfa	Gedeon Richter	2014/03/26	EU	FSHR
Jinsaiheng®	Recombinant Human Follitropin for Injection	GeneScience Pharmaceutical	2015/05/27	CN	FSHR
Rekovelle®	Human Follitropin delta injection	Ferring Pharma	2016/12/12	EU, JP, CN	FSHR
FostiRel®	Recombinant Human Follitropin beta	Reliance Life Science	2021/01/01	India	FSHR
Follitrope®	Recombinant Human Follitropin Prefilled Syringe	LG Chem	2021/04/07	CN	FSHR
Anxinbao®	Recombinant Human Follitropin for Injection	Qilu Pharmaceuticals	2021/12/14	CN	FSHR
泽盼喜®	Recombinant Human Follitropin for Injection	Jingze Pharmaceuticals	2025/05/09	CN	FSHR

Marketed long-acting rhFSH

Drug name	Generic name	Company	First approval date	Area	Target
Elonva®	Corifollitropin alfa	Organon	2010/01/25	EU	FSHR
晟诺娃®	Corifollitropin alfa N01 injection	Bao Pharma	2025/08/19	CN	FSHR
金赛佳®	Corifollitropin alfa N02 injection	GenSci	2025/09/23	CN	FSHR

Note: As of 2025.11.22; 2. Puregon®" (Europe/China) and "Follistim AQ®" (US) are brand names for the same product.

Source: FDA,EMA,PDMA, NMPA, Frost & Sullivan analysis

Competitive Landscape of recombinant human follicle-stimulating hormone(rhFSH) products in clinical trials Overseas

Short-acting rhFSH Pipeline

	Drug Name	Drug Category	Original Drug	Generic Name	Company	Indication	Stage	Area	Clinical Regulatory Authorities	First Posted Date
1	DA-3801	Biosimilars	rhFSH	rhFSH injection	Dong-A ST	• Ovulation induction	III	Korea	MFDS	2013/03/29
2	Primapur	Biosimilars	Follitropin alfa	rhFSH injection	IVFarma	• Ovulation induction	III	Russia	Ministry of Health of the Russian Federation	2017/03/22
3	FSH-GEX	New drug	Follitropin episilon	rhFSH injection	Biosilu Healthcare Glycotope GmbH	• Infertility	II	EU	EMA	2012/11/28

Long-acting rhFSH Pipeline

	Drug Name	Drug Category	Original Drug	Generic Name	Company	Indication	Stage	Area	Clinical Regulatory Authorities	First Posted Date
1	AS900672	New drug	Hyperglycosylated rhFSH	rhFSH injection	Merck	• Ovulation induction	II	US	FDA	2007/07/23

*Note: As of 2025.11.22; **All these products have not made any progress in 3-5 years.***

Area = Clinical trial locations per official records. Each area maps to its clinical regulatory authorities

Source: Clinicaltrials, Frost & Sullivan analysis

Global Competitive Landscape of FSH-CTP Drugs

Marketed FSH-CTP Drugs

Generic Name	Drug Name	Company	Target	Indications	Area	Approved Date
Corifollitropin alfa	Elonva	MSD	FSHR	Hypogonadotropic hypogonadism, ovulation induction	EU	2010-01-25

Pipeline of FSH-CTP Drugs in Clinical Stage

Drug Name	Company	Target	Indications	Stage	Area	Clinical Regulatory Authorities	First Posted Date
Follitropin	SL Pharm	FSHR	For patients undergoing superovulation or assisted reproductive technology (ART)	NDA	China	NMPA	2025-01-24

Note: As of 2025.11.22; The pipeline includes only Phase I clinical trials and above.
Area = Clinical trial locations per official records. Each area maps to its clinical regulatory authorities

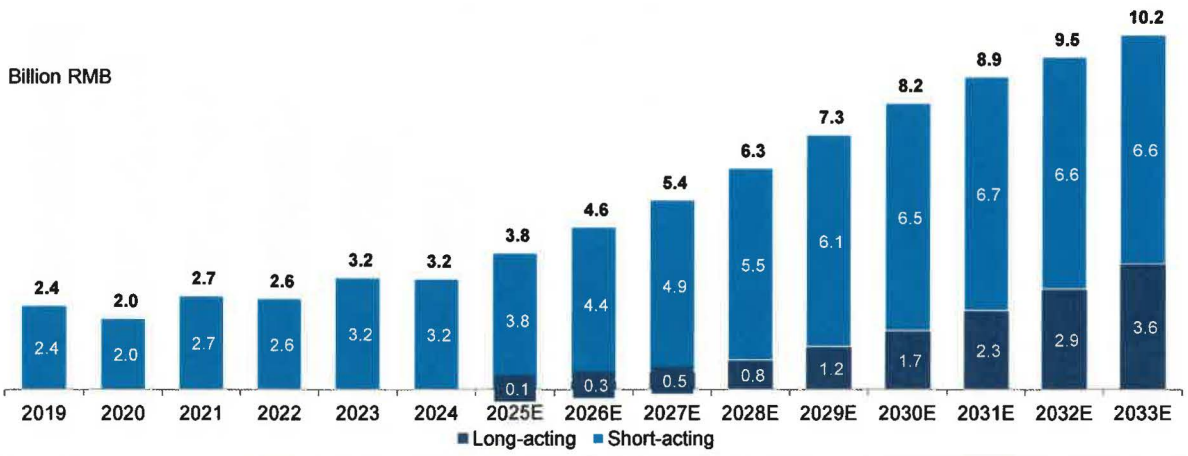
Source: CDE, NMPA, Frost & Sullivan Analysis

Market size and forecast of FSH in China, 2019-2033E

- The long-acting FSH is expected to reach to RMB 1.2 billion in 2029, and it is expected to reach to RMB 3.6 billion in 2033, with a CAGR of 30.8% from 2029 to 2033.

Market size and forecast of FSH in China, 2019-2033E

Period	CAGR		
	Long-acting	Short-acting	Total
2019-2024	-	5.7%	5.7%
2025E-2029E	-	12.0%	17.3%
2029E-2033E	30.8%	2.0%	10.2%



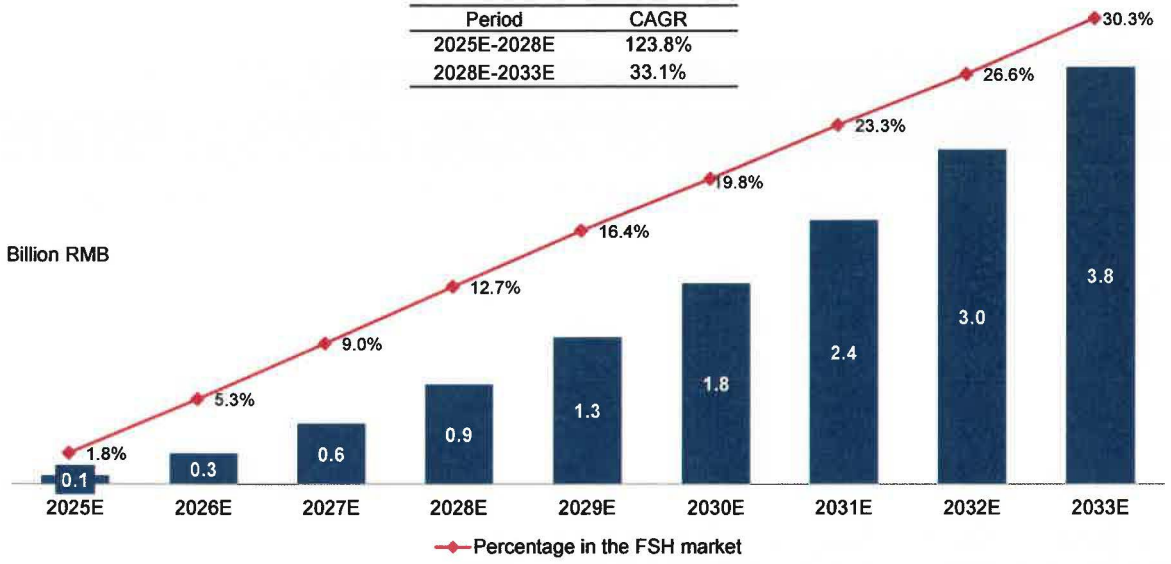
Source: Literature review, Frost & Sullivan analysis

Market size and forecast of Long-acting FSH in China, 2018-2033E

- The long-acting FSH market size increased from RMB 0.1 billion in 2025 to RMB 0.9 billion in 2028, with a CAGR of 123.8% from 2025 to 2028. It is expected to reach to RMB 3.8 billion in 2033, with a CAGR of 33.1% from 2028 to 2033.

Market size and forecast of long-acting FSH in China, 2025-2033E

Period	CAGR
2025E-2028E	123.8%
2028E-2033E	33.1%



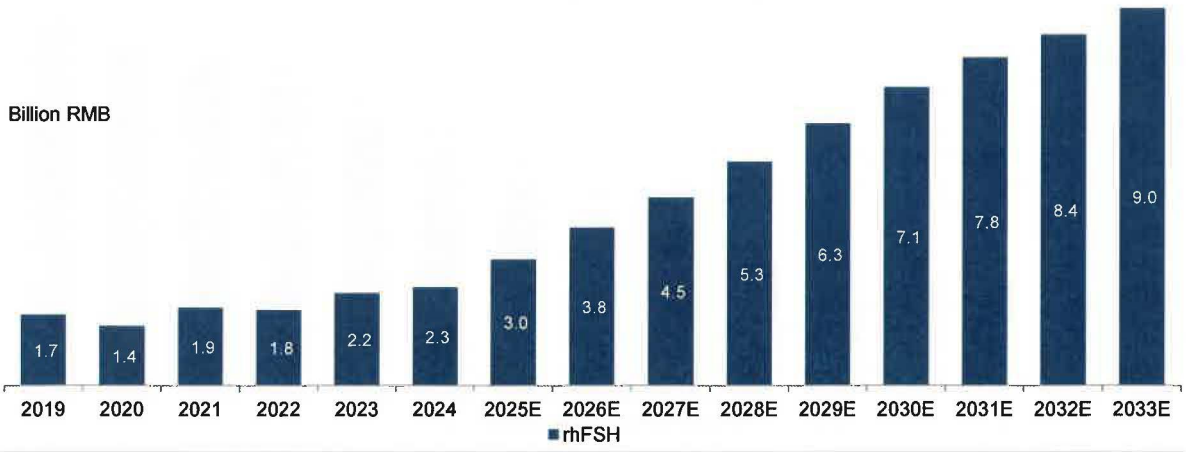
Source: Frost & Sullivan analysis

Market size and forecast of rhFSH in China, 2018-2033E

- The rhFSH market size increased from RMB 1.7 billion in 2019 to RMB 2.3 billion in 2024, with a CAGR of 6.8% from 2019 to 2024. It is expected to reach to RMB 9.0 billion in 2033 with a CAGR of 9.5% from 2029 to 2033.

Market size and forecast of rhFSH in China, 2018-2033E

Period	CAGR
2019-2024	6.8%
2025E-2029E	20.1%
2029E-2033E	9.5%



Source: Literature review, Frost & Sullivan analysis

Analysis of market drivers for recombinant human follicle stimulating hormone drugs in China – I

The number of infertility patients increase

- In recent years, the prevalence of infertility has continued to rise in China and globally. The number of infertile couples in China is increasing year by year and is expected to reach 55.9 million in 2025. As the childbearing age of women is pushed back and the number of "older" women planning to have children increases after China's "two-child policy" is implemented, the quality of eggs decreases with age, and babies born to older mothers are more likely to have genetic defects, chromosomal abnormalities and other genetic diseases. The number of patients and the demand for "Well-Bear and Well-Rear" continue to rise, which will promote the steady development of the assisted reproductive drug treatment market. Recombinant human follicle stimulating hormone drugs, as a commonly used assisted reproductive drug in clinical practice, will also witness significant demand growth.

Increased acceptance of assisted reproduction

- In May 2015, the National Health Commission issued the "Notice on Guiding Principles for Human Assisted Reproductive Technology Allocation Planning" to clarify the regulatory requirements for assisted reproductive services. Driven by supervision, the assisted reproductive service industry has gradually become standardized and developed healthily. Policy promotion has increased consumers' recognition and trust in assisted reproductive services, thereby increasing demand for assisted reproductive drugs such as recombinant human follicle-stimulating hormone. In addition, the popularity of overall reproductive treatment education in China has increased, and more families of childbearing age have increased awareness of assisted reproductive services. When facing fertility difficulties, they actively seek professional, scientific, and standardized assisted reproductive services, driving the use of recombinant human follicle-stimulating hormone reproductive auxiliary drugs.

Increased affordability of assisted reproductive services

- In March 2022, Beijing included 16 assisted reproductive technology projects such as in vitro fertilization embryo culture, blastocyst culture, and frozen embryo recovery into the reimbursement scope of Beijing's Class A medical insurance. Although Urofollitropin and recombinant follitropin drug products have not yet been included in medical insurance, this move will open a green light for the infertility assisted reproductive drug market. At the same time, China's per capita disposable income is growing and the willingness to consume medical care is increasing. The affordability of ovulation induction drugs will further increase in the future.

Source: Literature review, government documents, Frost & Sullivan analysis

Analysis of market drivers for recombinant human follicle stimulating hormone drugs in China – II

Assisted reproductive institution licenses continue to be issued

- The "Notice on Issuing the Guiding Principles for the Application Planning of Human Assisted Reproductive Technology (2021 Edition)" issued by the General Office of the National Health Commission in 2021 proposed that my country's assisted reproductive institutions can calculate and plan based on the permanent population of each province (region, city) , one institution can be set up for every 2.3 million to 3 million people. In addition, Shanghai, Hebei, Henan, Tianjin, Guizhou, Anhui, Shaanxi, Shanxi and other provinces and cities have promulgated local-level assisted reproductive technology application plans based on the national assisted reproductive technology application planning guidelines and combined with the actual application and development of local assisted reproductive technology, adding assisted reproductive institutions and approving the issuance of licenses for new institutions. As the number of assisted reproductive institutions in various places increases and the coverage of assisted reproductive technology continues to expand, residents' growing needs for assisted reproduction will be further met, promoting the application of assisted reproductive treatments and drugs. Assisted reproductive drugs with significant clinical effects such as recombinant human follicle stimulating drugs The market demand for hormones will increase significantly.

Increase in male infertility symptoms

- With the rapid social development in various countries, people's life pressure and social pressure continue to increase, and the quality of male sperm has continued to decline in recent years. A meta-study shows that the sperm count of men in North America, Europe, Asia and other places dropped significantly between 1973 and 2018, and the sperm count has continued to decline more significantly since 2000. The decline in sperm quantity and quality is one of the main reasons for reduced male fertility. The incidence of male infertility and other diseases has increased significantly, and male patients' demand for assisted reproduction has also increased. In the future, as the efficacy of recombinant human follicle-stimulating hormone drugs in male patients is verified, its market demand will further increase.

Improvement of technology of recombinant human follicle stimulating hormone

- Recombinant human follicle stimulating hormone drugs have higher biological activity and purity, higher product quality and yield, and significant clinical advantages. Therefore, its preparation and production processes also face extremely high technical barriers. As the industry's leading domestic drug manufacturers continue to research the production process and technology of recombinant human follicle stimulating hormone, the preparation technology of recombinant human follicle stimulating hormone with high purity and high specific activity continues to be developed. The improvement of process and production technology will promote recombinant human follicle stimulating hormone. The purity and stability of human follicle stimulating hormone are improved. Improvements in the production process and technology of recombinant human follicle stimulating hormone will promote the improvement of its product quality, increase the demand for treatment of infertility patients, and accelerate the development of the recombinant human follicle stimulating hormone drug market.

Source: Literature review, government documents, Frost & Sullivan analysis

Analysis of market development trends of recombinant human follicle stimulating hormone drugs in China – I

Recombinant follicle stimulating hormone replaces Urofollitropin	• Urofollitropin has low purity, but it still occupies some market share in China due to its price advantage. In the international follicle stimulating hormone market, recombinant human follicle stimulating hormone has already replaced Urofollitropin as the mainstream ovulation induction drug. Compared with Urofollitropin, recombinant human follicle stimulating hormone has higher purity, higher biological activity, higher psychological acceptance by patients, and lower risk of contamination. In the future, as the production technology of recombinant human follicle stimulating hormone continues to be optimized and production enterprises form economies of scale, the preparation cost of recombinant human follicle stimulating hormone will be further reduced, breaking the price advantage of Urofollitropin, becoming the mainstream drug in China's follicle stimulating hormone drug market, and gradually replacing Urofollitropin's market share.
Domestic recombinant follicle stimulating hormone forms an import substitution	• China's follicle stimulating hormone drug industry has developed relatively late. At present, the recombinant human follicle stimulating hormone market is still dominated by foreign capital. There are only two recombinant human follitropin stimulating hormone products produced by Kinsey Pharmaceuticals and Qilu Pharmaceuticals in China. As Chinese manufacturers' R&D and production technologies gradually mature, the clinical progress of recombinant human follicle stimulating hormone research companies such as Jingze Biopharmaceutical (Hefei) Co., Ltd will continue to advance, and the process of domestic substitution of recombinant human follicle stimulating hormone in China's recombinant human follicle stimulating hormone market will accelerate.
Development and application of long-acting recombinant human follicle stimulating hormone	• Currently, follicle stimulating hormone, which is mainly used clinically, has a short half-life in the human body, and patients need to continue subcutaneous injections 1 to 2 times a day. Frequent injections bring inconvenience to patients and lead to poor patient compliance. The development of long-acting follicle stimulating hormone will solve the short half-life of existing drugs. At the same time, the industry-leading Chinese recombinant human follicle stimulating hormone drug manufacturer is also actively developing domestic long-acting recombinant human follicle stimulating hormone drugs that are more suitable for Asian patients and have better efficacy based on the basic characteristics of Asian patients such as height and weight. In the future, in the case of a single medication, based on clinical diagnosis and treatment needs, patient follow-up frequency, basic patient characteristics and other factors, the development of long-acting recombinant human follicle stimulating hormone drugs that can maintain the patient's blood concentration for a longer period of time is one of the important directions for industry development.

Source: Literature review, Frost & Sullivan analysis

Analysis of market development trends of recombinant human follicle stimulating hormone drugs in China – II

Development of dosage optimization plan for recombinant human follicle stimulating hormone drug	• During the clinical treatment of recombinant human follicle stimulating hormone drugs, medical staff need to prepare the injection dose of the drug based on the patient's height, weight, age and other basic conditions, disease severity, treatment progress and other factors, and adjust it according to the course of treatment. The recombinant human follicle stimulating hormone products currently on the market have relatively single specifications. It is difficult for patients to use the entire drug at a time, which may cause problems such as drug storage, contamination, and inaccurate dosage. Therefore, recombinant human follicle stimulating hormone drug R&D companies will develop multi-specification recombinant human follicle stimulating hormone preparations that are more in line with clinical usage habits and suitable for different patient groups to improve their clinical use. The convenience of use further promotes the market penetration of recombinant human follicle stimulating hormone drugs.
Expansion of indications for recombinant human follicle stimulating hormone drugs	• Clinical trials of recombinant human follicle stimulating hormone in infertility patients are continuing to be carried out. In particular, multiple clinical trials in the treatment of male infertility are actively promoted at home and abroad, and we continue to explore the role of recombinant human follicle stimulating hormone in the treatment of male infertility, its role and related mechanisms in patients with infertility and oligozoospermia. In the future, with the acceleration of clinical trials of recombinant human follicle stimulating hormone, its treatment areas will further expand to more male and female infertility patients, helping to solve the problem of hypogonadism in male patients and too little or no ovulation and other issues in women, which will promote the further growth of patient demand for recombinant human follicle stimulating hormone and promote the rapid development of the recombinant human follicle stimulating hormone drug market.
Recombinant human follicle stimulating hormone drugs used in combination with other assisted reproductive drugs	• During the process of assisted reproductive treatments such as in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI), female infertility patients need to use down-regulating drugs and stimulating drugs according to the patient's treatment needs. Different medications such as ovulation drugs, luteal support drugs, etc. In the future, assisted reproductive treatment drugs with significant clinical advantages such as recombinant human follicle stimulating hormone and progesterone sustained-release gel will be used in combination with a wide range of patient groups such as female patients undergoing assisted reproduction to improve the quality of patients' eggs or embryos, increase egg retrieval, improve its clinical pregnancy rate, increase the clinical penetration rate of recombinant human follicle stimulating hormone and other drugs, and promote the further development of the assisted reproductive drug market.

Source: Literature review, Frost & Sullivan analysis

Overview of Human Chymotrypsin

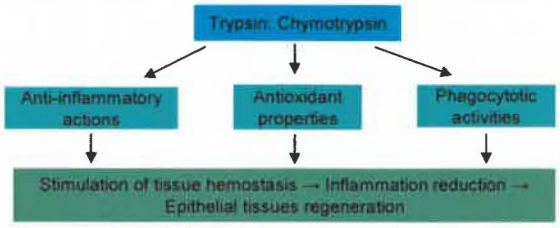
- Human chymotrypsin is a digestive enzyme that works in the duodenum. In medical treatment, it mainly plays the role of removing blood clots, anti-inflammatory, and anti-bacterial infection. In addition, SARS-COV-2 and tumor treatment represented by pancreatic cancer have also been shown to be related to chymotrypsin.

1 Structure, localization and mechanism

- Chymotrypsin (EC 3.4.21.1) is a pancreatic serine protease, a digestive enzyme that functions in the duodenum, where it breaks down protein and polypeptides (proteolysis). Chymotrypsin cleaves at the N-terminal of aromatic amino acid residues (tyrosine, tryptophan and phenylalanine) of peptides.

2 Role in inflammation

- Wound healing and tissue repair:
  - ➢ Chymotrypsin is widely used to help speed up the repair of traumatic, surgical, and orthopedic injuries. Its anti-inflammatory, antioxidant, and anti-infective properties help resolve inflammation caused by injury and help facilitate the healing process. It works by inhibiting chronic fibrin formation and this in turn helps to prevent the reabsorption of hematoma and the formation of edema.



- Arthritis:
  - ➢ Abnormality in the chymotrypsin levels causes different diseases such as inflammatory arthritis, diabetes, pharyngitis and pancreatic cancer. Chymotrypsin and cathepsin catalyze the cleavage of Interleukin 1-β (IL -1β) precursor into active IL -1β leading to arthritis.

3 Role in antibacterial activity

- Antibiotics are used to treat bacterial infection and the rise of drug-resistant bacteria has limited their usage. Some serine proteases have been found to be part of new antimicrobial agents. For instance, an ovary-specific trypsin-like protease, Ovochymase in *amphioxus Branchiostoma belcheri* with antibacterial activity has been reported.

4 Role in diseases

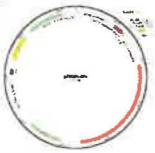
- The chymotrypsin-like protease (3CLPro), is essential for the cleavage of the viral polyprotein into functional nonstructural proteins that are critical for the replication of SARS-CoV-2 and other coronaviruses. Thus, 3CLPro has been recognized as a promising therapeutic target in the development of antiviral drugs aimed at controlling SARS-CoV-2 infections.
- Radiotherapy and chemotherapy are the known methods for pancreatic cancer management, but because of the undesirable side effects, new less invasive treatments are being sought for. The anti-inflammatory effects of pancreatic enzymes, and also the reduction of phagocytic and microbial activity on the immune system through the interaction of proteases with α 1-antitrypsin and α 2-macroglobulin, may reinforce their anti-tumor effect.

Source: Literature review, Frost & Sullivan Analysis

Human Chymotrypsin Extraction Processes

Construction of recombinant human chymotrypsinogen expression strain

Optimize the amino acid sequence of natural human chymotrypsinogen and obtain the nucleotide sequence → Recombine nucleotide sequences into expression vectors → Transform the recombinant expression vector into bacteria (mostly *E.coli* or *Pichia pastoris*)



Expanded fermentation of recombinant human chymotrypsinogen

Scale up recombinant expression strains from shake flask culture to fermenter-scale batch production → Add inducer to induce the culture strain to express the target protein product → Centrifugation, cell disruption, product purification → Final product preparation (after activity detection)

Activity detection of recombinant human chymotrypsin

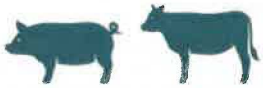
- The activity of human chymotrypsin products should be tested according to the chymotrypsin titer determination method stipulated by relevant institutions (such as the Chinese Pharmacopoeia stipulates that the titer per mg must not be less than 800U).
- The products should also be tested for endotoxins and bacterial protein residues.

Source: Frost & Sullivan analysis

Development and Advantages of Recombinant Human Chymotrypsin

Animal-free and humanized biological products are the current development trend of the biopharmaceutical industry. Compared with traditional chymotrypsin products, the advantages of recombinant human chymotrypsin are its high purity production, improved expression levels, simplified extraction process, reduced safety risks and aligns with biopharmaceutical development trends. However, there are currently no recombinant human chymotrypsin pharmaceutical products on the medicine market in China and abroad.

Development History of Chymotrypsin



19th Century German scientist Wilhelm Friedrich Kühne successfully isolated an enzyme from "pancreatic juice" called trypsin, which can degrade other biological substances.

1950s Medical circles in various countries have begun to study the use of chymotrypsin (α-Chymotrypsinum), this proteolytic enzyme, to treat various inflammations, ulcers, suppuration, hematoma, empyema, skin diseases, and digestive tissue cells.

Late 20th Century Scientists successfully cloned and expressed recombinant human chymotrypsin through genetic engineering technology, which was an important milestone in the development of chymotrypsin products.

- **High Purity Production**: Recombinant engineering bacteria can produce high-purity human chymotrypsinogen, which, after activation, yields human chymotrypsin with higher purity. This increase in purity helps reduce potential impurities and contaminants, enhancing the safety and efficacy of the product.
- **Improved Expression Levels**: Compared to traditional expression systems, recombinant engineering bacteria can express human chymotrypsin more efficiently, avoiding the low expression levels caused by the digestion of host cell life-sustaining proteins in other systems.
- **Simplified Extraction Process**: The production process of recombinant human chymotrypsin simplifies the traditional extraction steps, such as gradient salting out, trypsin activation, and recrystallization refinement with ammonium sulfate and ethanol, which are characterized by long operation times, poor extraction specificity, and low yields.
- **Reduced Safety Risks**: Using recombinant human chymotrypsin to replace chymotrypsin extracted from animal pancreases reduces the risk of introducing animal-derived viruses and minimizes the potential immune reactions after heterologous proteins enter the human body, thereby significantly increasing the safety of medication.
- **Aligns with Biopharmaceutical Development Trends**: The production of recombinant human chymotrypsin aligns with the trend of biopharmaceuticals moving towards animal-free components and higher safety standards, which is crucial for the large-scale production of human chymotrypsin in the field of biopharmaceuticals.

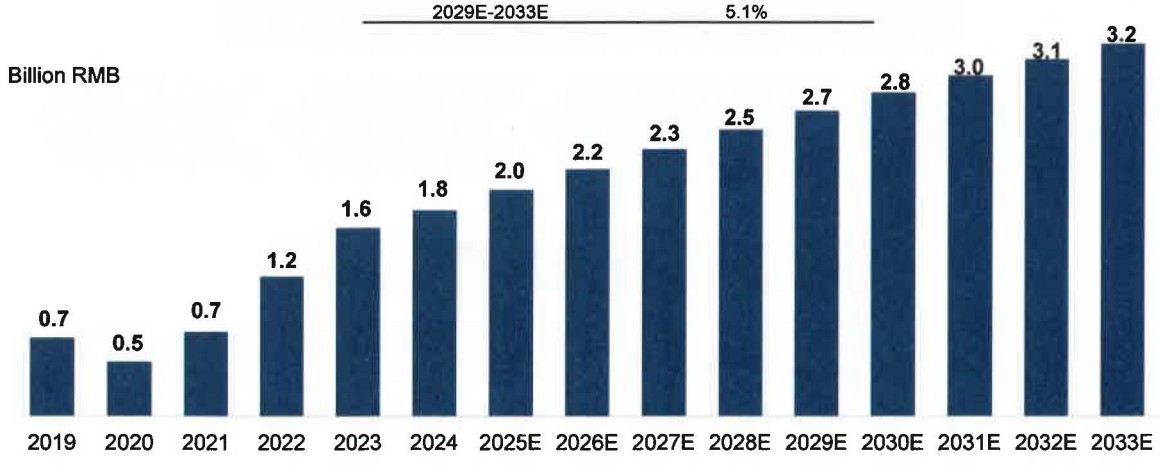
Source: Frost & Sullivan analysis

Chymotrypsin Market in China, 2019-2033E

- From 2019-2024, the chymotrypsin market in China grew from RMB 0.7 billion to RMB 1.8 billion, with a CAGR of 21.3% during this period. Affected by the epidemic, sales in 2020 have dropped significantly. It is expected that by 2029, the market size will grow to RMB 2.7 billion, and by 2033, to RMB 3.2 billion.

Chymotrypsin Market in China, 2019-2033E

Period	CAGR
2019-2024	21.3%
2024-2029E	8.2%
2029E-2033E	5.1%



Source: Literature review, Frost & Sullivan analysis

Competitive Landscape of the Recombinant Human Chymotrypsin in China

- Currently, there are no recombinant human chymotrypsin pharmaceutical products on the medicine market in China and abroad.
- 3 recombinant human chymotrypsin drugs are in clinical trials, 2 of them is in the phase II stage, and the other one is in the phase I stage.

Pipeline of Recombinant Chymotrypsin

Drug Code	Company	Status	First Posted Date
KJ101	Shanghai Bao Pharmaceutical	Phase II	2025-06-17
HY1005-Oral	Wuhan Healthgen Biotechnology	Phase II	2024-12-12
HY1005-Injection		Phase I	2024-05-29

Note: As of 2025.11.22

Source: CDE, Frost & Sullivan analysis

Drivers of the Recombinant Human Chymotrypsin Market in China

Technological Progress and Innovation	• With the rapid development of biotechnology, the production technology of recombinant human chymotrypsin has been continuously improved, which has improved the purity and stability of the product. Compared with animal-derived chymotrypsin, the production process of recombinant human chymotrypsin is simplified and conducive to large-scale production, which not only enhances the market competitiveness of the product, but also provides patients with a safer and more effective treatment plan.
Indications Increase for Advanced Enzymatic Therapies	• With the aging of the population and changes in the disease spectrum, the demand for chymotrypsin continues to grow. Chymotrypsin has been proven to be effective in resolving inflammation caused by injury, promoting wound healing and tissue repair, and treating bacterial infections. In addition, studies have shown that it may also become a therapeutic target for SARS-COV-2 and may be used in anti-tumor combination therapies represented by pancreatic cancer. Chymotrypsin has broad application prospects and is expected to promote the expansion of the market.
Favorable Government Policies and Healthcare Reforms	• China's supportive policies for the biopharmaceutical industry, including incentives such as tax breaks, financial support, and fast-track approval of recombinant products, have encouraged local production and innovation, providing a favorable policy environment for the development of the chymotrypsin industry. In addition, the emphasis on the biopharmaceutical industry in the 14th Five-Year Plan also provides guidance and impetus for the development of the chymotrypsin market. The government's emphasis on self-sufficiency in biopharmaceuticals is consistent with the growing popularity of recombinant human chymotrypsin, and this regulatory support ensures a favorable environment for market expansion.
Growing Investment in Biopharmaceutical Research	• China's robust investment in biopharmaceutical R&D has accelerated the development of novel therapeutic enzymes, including recombinant human chymotrypsin. Collaboration between academic institutions, biotech firms, and pharmaceutical companies fosters innovation in drug development. This has not only improved the therapeutic potential of chymotrypsin but also widened its application in various medical fields. Increased funding ensures sustained progress in both product development and commercialization.

Source: Frost & Sullivan Analysis

Development Trends of the Recombinant Human Chymotrypsin Market in China

Shift from Biochemical Extraction to Recombinant Technology	• Recombinant human chymotrypsin is rapidly replacing traditional biochemical extraction methods due to its higher purity and consistency. Unlike animal-derived enzymes, recombinant technology eliminates the risks of contamination and batch-to-batch variation. This shift is driven by stricter regulatory requirements and the growing demand for safer pharmaceutical products. The transition also addresses ethical concerns surrounding animal-derived materials, enhancing its acceptance in the market. As a result, recombinant chymotrypsin is emerging as a preferred choice for healthcare providers and patients.
Cost Reduction through Synthetic Biology Innovations	• Synthetic biology advancements are significantly reducing the production costs of recombinant human chymotrypsin. Techniques such as optimized gene editing, high-efficiency expression systems, and precision fermentation have improved yields and streamlined manufacturing. Lower production costs make the therapy more affordable and accessible, particularly in price-sensitive markets. These innovations also enable scalability, ensuring that manufacturers can meet growing demand without compromising quality. As production becomes more cost-efficient, competitive pricing will further drive market adoption.
Increased Investment in Synthetic Biology Research	• China's robust investment in synthetic biology is accelerating the development of more efficient and cost-effective recombinant technologies. Collaboration between biotech firms, research institutes, and government initiatives fosters innovation in enzyme production. This focus on R&D enables breakthroughs in strain engineering, metabolic optimization, and downstream processing. The growing research ecosystem ensures continuous improvements in production methods and product quality. Such advancements position China as a global leader in the recombinant enzyme industry.
Stricter Regulations Encouraging Technological Adoption	• Stricter regulations on enzyme safety and quality are pushing manufacturers to adopt recombinant and synthetic biology technologies. Regulatory bodies are phasing out biochemical extraction methods due to their limitations in purity and safety. Recombinant production, by contrast, aligns with international standards for pharmaceutical manufacturing, ensuring compliance and market access. This regulatory shift is accelerating the adoption of advanced technologies across the industry. By meeting these standards, Chinese manufacturers can enhance their competitiveness both domestically and internationally..

Source: Frost & Sullivan Analysis

Overview of Human Trypsin Inhibitors

- Human trypsin inhibitors are a class of proteins or peptides with significant biological functions. They work by binding to the active sites of trypsin, inhibiting its enzymatic activity and protecting the body's tissues from excessive proteolytic damage. These inhibitors have broad medical applications, particularly in treating inflammatory conditions such as pancreatitis and sepsis.

➢ Human trypsin inhibitors can be categorized from the following perspectives:

Based on Source

Natural Extracted Inhibitors
These are derived from human fluids or tissues, such as ulinastatin, extracted from human urine.
They are naturally occurring proteins isolated through specific extraction techniques.

Recombinant Inhibitors
Produced through genetic engineering, using systems like E. coli, yeast, or mammalian cells.
Recombinant inhibitors offer high purity, controlled production, and are becoming the mainstream method for manufacturing such drugs.

Based on Chemical Structure

Serine Protease Inhibitors
These inhibitors bind to the active sites of serine proteases, such as trypsin, to block their activity.

Metalloprotease Inhibitors
These inhibit metalloproteases by removing or disrupting essential metal ions in their structure.

Peptide Inhibitors
These are smaller molecules with rapid metabolism and potent inhibitory effects.

Based on Biological Function

Anti-inflammatory Inhibitors
These inhibit trypsin activity and reduce tissue inflammation.
Commonly used in the treatment of acute pancreatitis, septic shock, and inflammatory diseases.

Anti-fibrotic Inhibitors
These prevent organ fibrosis, such as in the liver or lungs, by blocking excessive enzyme activity.

Digestive System Protectors
Regulate pancreatic enzyme secretion to protect the gastrointestinal mucosa and assist in treating pancreatic diseases.

Source: Literature review, Frost & Sullivan Analysis

Human Trypsin Inhibitors Extraction Processes

1. Biochemical Extraction Process

Material Preparation
Source selection: fresh or frozen human plasma, serum or urine.
Buffer: such as Tris-HCl buffer, adjust the pH appropriately.

Preliminary Treatment
Impurity removal: remove cell debris and insoluble matter by centrifugation.
Salting out: Precipitate protein. Collect the precipitate after centrifugation.

Protein Enrichment
Purify the target protein by dialysis, ion exchange chromatography, hydrophobic chromatography,etc.

Specific Separation
Affinity chromatography: Immobilize trypsin in the affinity chromatography column, load the sample and elute the target protein.
Gel filtration chromatography: Separate proteins according and remove small molecule impurities.

Detection and Collection
SDS-PAGE: Perform electrophoresis analysis on the purified product to confirm the molecular weight and purity.
Activity detection: Verify its inhibitory activity on trypsin through enzyme inhibition experiment.

Final Purification and Storage
Concentration: Use ultrafiltration equipment to concentrate the target protein.
Freeze drying: Freeze drying before long-term storage and store at -80° C.

2. Recombinant Extraction Process

The extraction process of recombinant human trypsin inhibitor is similar to that of recombinant human chymotrypsin, both of which require large-scale production through genetic engineering.

Gene Cloning:
- Insert the target gene into the expression vector to ensure correct expression in the host.

Expression Optimization:
- Optimize protein expression conditions using appropriate inducers, temperature, and expression time.

Cell Lysis and Protein Recovery:
- Lyse the cells using physical or chemical methods to recover the soluble or inclusion body proteins.

Protein Purification:
- Purify the target protein using affinity chromatography or size-exclusion chromatography.

Tag Removal (Optional):
- Remove tags from the expression vector using enzymatic cleavage to obtain pure protein.

Detection and Functional Validation:
- Verify the protein purity and activity using SDS-PAGE, Western Blotting and functional assays.

Storage:
- Store the purified protein at low temperatures to ensure long-term stability.

Source: Frost & Sullivan analysis

Development and Advantages of Recombinant Human Trypsin Inhibitors

Recombinant human trypsin inhibitors have the advantages of high purity, high efficacy, low cost, controllable conditions and large-scale production, and can meet the needs of production, medicine and scientific research. However, there are currently no recombinant human trypsin inhibitors pharmaceutical products on the medicine market in China and abroad.

Development History of Recombinant Human Trypsin Inhibitors

Early 1980s The development of gene cloning and expression vectors enabled scientists to express trypsin inhibitors in hosts like E.coli.

1985 Scientists successfully cloned and expressed the human trypsin inhibitor gene, producing biologically active recombinant proteins for the first time.

1990s With improvements in protein purification and expression techniques, recombinant human trypsin inhibitors entered clinical trials for diseases like pancreatitis.

2000s to Present Recombinant trypsin inhibitors have been increasingly applied in various medical fields, including chronic inflammation and surgical organ protection.

Advantages of Recombinant Human Trypsin Inhibitors

- **High Yield and High Purity**
Genetic engineering enables efficient expression of recombinant proteins in host cells, making them easy to isolate and purify.

- **Lower Cost**
Recombinant technology is more cost-effective than extraction from natural sources, especially for industrial-scale production.

- **Consistent Quality**
By controlling production conditions (e.g., temperature and inducers), consistent high-quality proteins can be obtained.

- **Ethical Considerations**
Recombinant methods avoid extracting proteins from human tissues or animal fluids, eliminating ethical concerns.

- **Customizable Features**
Recombinant technology allows customization of protein features, such as adding tags or modifying activity.

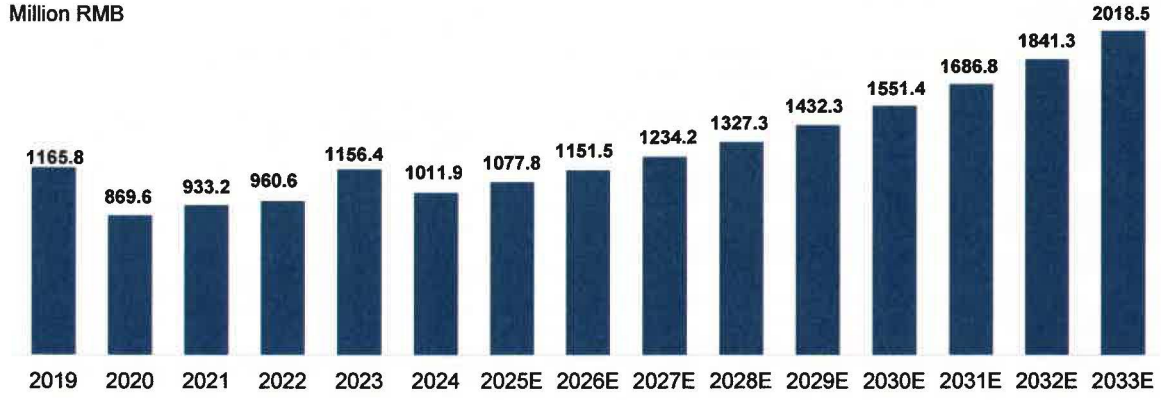
Source: Frost & Sullivan analysis

Ulinastatin Market in China, 2019-2033E

- The Chinese Ulinastatin market saw a decline from RMB 1,165.8 million in 2019 to RMB 1,011,9 million in 2024, with a negative CAGR of -2.8%. However, the market is expected to recover and grow at a CAGR of 7.2% from 2024 to 2029, reaching RMB 1,432.3 million by 2029. Growth is projected to accelerate further, with a CAGR of 9.0% from 2029 to 2033, reaching RMB 2,018.5 million by 2033.

Ulinastatin Market in China, 2019-2033E

Period	CAGR
2019-2024	-2.8%
2024-2029E	7.2%
2029E-2033E	9.0%



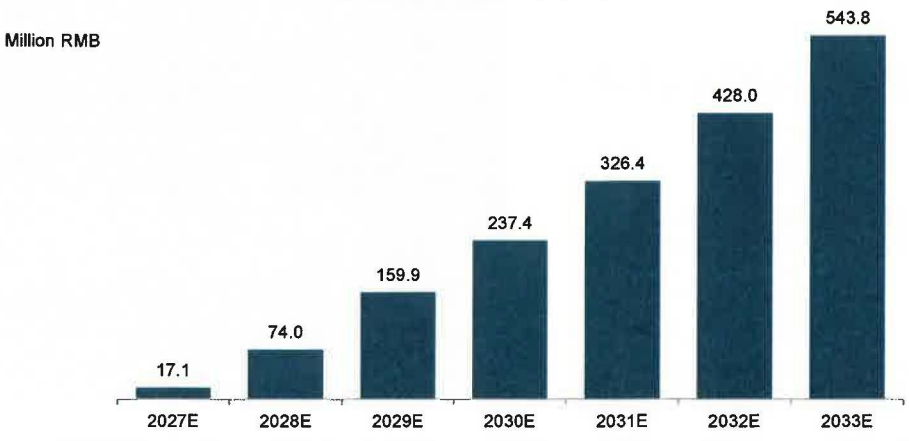
Source: Literature review, Frost & Sullivan analysis

Recombinant Ulinastatin Market in China, 2027E-2033E

- The recombinant ulinastatin market in China is expected to achieve a compound annual growth rate (CAGR) of 49.0% between 2028 and 2033. The market size is projected to grow rapidly from RMB 74.0 million in 2028 to RMB 543.8 million in 2033, demonstrating robust market expansion.

Recombinant Ulinastatin Market in China, 2027E-2033E

Period	CAGR
2028E-2033E	49.0%



Source: Frost & Sullivan analysis

Drivers of the Recombinant Human Trypsin Inhibitors Market in China

Growing Medical Demand	• With an aging population and rising prevalence of chronic diseases, China is experiencing increased demand for treatments for pancreatitis and chronic inflammation. This has significantly boosted the need for recombinant human trypsin inhibitors, which offer high safety and minimal side effects. Furthermore, the expansion of the pharmaceutical market and improved health awareness are driving growth in this sector.
Policy Support and Increased R&D Investment	• The Chinese government has strongly supported biopharmaceutical development, including recombinant protein drugs, through industry policies. Moreover, national and local research funds have provided financial support for the R&D of recombinant human trypsin inhibitors. This has enhanced the competitiveness of domestic companies and attracted international collaboration and investment.
Advancements of Recombinant Technology and Industrial Upgrading	• China has made significant progress in genetic engineering and biomanufacturing in recent years. These technological innovations have improved production efficiency and product quality while reducing costs. Additionally, domestic companies have gradually mastered core technologies, enabling localization of the supply chain.
Expanding Clinical Applications	• The application of recombinant human trypsin inhibitors is expanding from traditional treatments like pancreatitis to areas such as organ transplant protection and cancer adjunct therapies. With more indications being clinically validated and approved, the market potential for these drugs continues to grow. This diversification in clinical demand is further driving market development.

Source: Frost & Sullivan Analysis

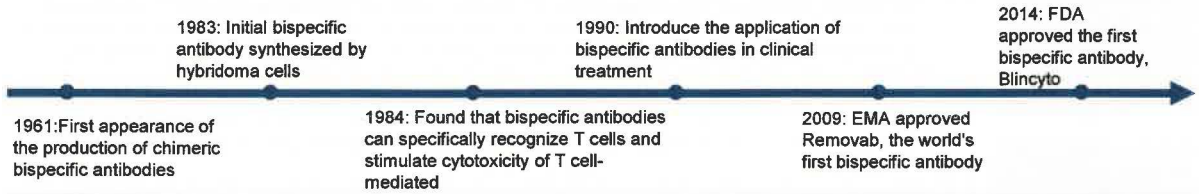
Development Trends of the Recombinant Human Trypsin Inhibitors Market in China

Recombinant Technology Gradually Replacing Biochemical Extraction	• Recombinant human trypsin inhibitors, with their high purity and controllable production, are becoming the mainstream alternative to traditional biochemical extraction methods. Biochemical extraction suffers from limited raw material sources, complex production processes, and high costs, whereas recombinant technology overcomes these bottlenecks. Moreover, recombinant methods eliminate the risk of viral or pathogen contamination associated with biological sources. This trend is driving the market toward greater efficiency and safety.
Cost Reduction through Synthetic Biology Innovations	• The rapid advancement of synthetic biology is significantly reducing the production costs of recombinant human trypsin inhibitors. By optimizing host cells and metabolic pathways, researchers can greatly enhance protein expression levels and simplify purification processes. Additionally, high-throughput screening and gene editing tools further improve production efficiency. As production costs decline, these products will become increasingly competitive in the Chinese market.
Expansion of Clinical Indications Driving Market Growth	• The indications for recombinant human trypsin inhibitors are expanding beyond pancreatitis to broader areas such as organ protection, cancer adjunct therapies, and other chronic inflammatory diseases. Increasing clinical trials have validated their efficacy and safety across various treatments, creating new growth opportunities. Particularly in cancer treatment, their potential role as tumor microenvironment modulators is being gradually explored. In the future, the expansion of indications will be a key driver of market growth.
Technological Breakthroughs by Domestic Companies Enhancing Global Competitiveness	• Chinese companies are making continuous progress in genetic engineering and protein expression technologies, narrowing the gap with international leaders. By independently developing efficient expression systems and optimizing fermentation processes, domestic manufacturers have achieved significant cost reductions and quality improvements. Moreover, an increasing number of Chinese companies are entering global markets through technology exports and strategic partnerships, enhancing their international influence. This not only strengthens their leadership in the domestic market but also opens a window for global development in the recombinant human trypsin inhibitor industry.

Source: Frost & Sullivan Analysis

Analysis of the Development Process and Mechanism of Bispecific Antibody Drugs

- Bispecific antibodies can recognize and specifically bind to two antigens or epitopes of antigens. Theoretically, it can block the biological functions mediated by two antigens/epitopes at the same time or draw the two antigen cells closer, thereby enhancing their interaction.
- In recent years, with the in-depth understanding of the pathogenesis of various diseases and the development and progress of monoclonal antibodies, the development and progress of bispecific antibodies have been promoted. With the development of antibody construction, expression and purification technology, dozens of structures of bispecific antibodies have appeared. At present, tumor is one of the hot areas of double antibody research.



	Killing mediated immune cell	Blocking the proliferation signaling pathway	Dual target inhibition	Receptor co-stimulation or inhibition
Mechanism	It uses bridging effector T cells and tumor cells, and individually bridging NK cells. The antibody activates and relocates immune cells to promote the immune cells to kill the cancer cells.	Blocking the signal transduction pathways of growth factor receptors of tumor cells nad their downstream.	Acting on two different targets on cancer cells in order to inhibit compensatory or synergistic effects	Target two different receptors on immune cells, promote the activation of immune cells or block the suppression of immune cells
Example	• CD19+CD3 • EpCAM+CD3	• HER2+HER3 • IGF-1R+HER3	• VEGF+Ang-2 BsAb • EGFR+C-met	• PD-1 + CTLA-4 • PD-1 + LAG3

Source: Frost & Sullivan Analysis

Structural Classification of Bispecific Antibodies

- Currently, bispecific antibodies are generally divided into two categories according to their structure: IgG-type structure and non-IgG-type structure. Among them, the IgG structure can be divided into two types: symmetric and asymmetric, where the asymmetric structure has obvious advantages.
- T-cell-engaging bispecific antibodies have been widely developed for cancer treatment. Representative drugs targeting CD3/CD20, CD3/BCMA and CD3/CD19 have shown promising efficacy in hematological cancers due to their enhanced cytotoxicity, targeting specificity, as well as unique mechanism of action focusing on direct engagement with surface antigens, T-cell response modulation and interactions with other signaling pathways.

	Non-IgG	Symmetric IgG	Asymmetric IgG
Advantage	• 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 limits of Knob-into-hole 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
Disadvantage	• 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
Marketed Examples	• Blinatumomab applies Tandem scFV and BiTE technology platform.Amgen is marketed in 2014, acute lymphocytic leukemia	PD-1 and CTLA-4 bispecific antibody Cadonilimab which listed in 2022	• Emicizumab applies KIH technology platform, marketed by Roche in 2017, hemophilia A • Catumaxomab applies Triomab asyme 1+1 (Rat-mouse hybrid IgG) platform, developed by TRION Pharma GmbH and Neovii Biotech GmbH in 2009 (withdrawn from the market in 2017), malignant pleural effusion

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

Clinical Advantage of Bispecific Antibody

Compared with Mono Therapy

- **Mediate Immune Cell Killing towards Tumors:** BsAbs have two antigen-binding arms, one of which binds to the target antigen and the other binds to the labeled antigen on the effector T cell, which activates the effector T cell to kill tumor cells.
- **Stronger Specificity and Reduced Off-target Toxicity:** In contrast to mAbs, BsAbs interact with two different surface antigens respectively, which can effectively enhance the binding specificity and reduce side effects such as off-target.
- **Lower Drug Resistance:** 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 of two different growth-promoting receptors on a single tumor cell may increase the antiproliferative effect and help to avoid the development of resistance.

Compared with Combo Therapy

- **Reduce the Cost of Treatment:** In terms of dosage, since the therapeutic effect of BsAbs can reach 100-1000 folds of the common antibody, the lowest dose can be 1/2000 of the original, which significantly reduces the cost of drug treatment. The use of BsAbs compared to combination therapy with two monospecific drugs makes it possible to optimize expenses by reducing the cost of development and clinical trials.
- **Better Clinical-Doability:** Bispecific antibodies require only single administration compared to combo therapies that require multiple injections of two or more antibodies, simplifying the frequency and practice of administration, it shows great advantages in clinical trial development, clinical application as well as patient compliance.
- **Improved Safety:** In some clinical trials, the incidence of SAE of combo therapy of Nivolumab and Ipilimumab is higher than mon therapy, such as CheckMate 067. However, currently the early clinical trials have shown that PD-1/PD-L1 x CTLA-4 BsAbs has improved safety.

Source: Literature Review, Frost & Sullivan Analysis

Growth Drivers and Future Trends of BsAb Drugs Market

Growth Drivers	More Durable Efficacy	• BiAb could block two signal pathways simultaneously which enhances the synergistic effects of the two. As for superior cytotoxic effects, there is a lower rate of resistance to BsAb due to the targeting of two different antigens. This mechanism can reduce tumor cell escape, diminish the side-effects that might be caused by mAb, and then improve therapeutic efficacy. • Cancer and other diseases are multifactorial, with many signaling pathways implicated in pathogenesis, so single-target immunotherapy is not sufficient to eliminate tumor cells. However, BsAbs can potentially increase binding specificity by interacting with two different cell-surface antigens instead of one, which brings higher safety and efficacy
	Higher Potential for Multiple Usage	• 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 multi-potential feature enables BsAb to serve as the new solution for incurable diseases.
Future Trends	Development of BsAb Manufacturing Technologies	• The development of BsAbs has long been hampered by manufacturing problems such as product instability, low expression yields, and immunogenicity. The optimism of BsAbs generating process enables newer formats of BsAbs that are more stable, easier to produce, and less immunogenic have been made available. • Large-scale production and purity are long-term pursuits. Thus, the ideal platform should encompass the entire development process from discovery and preclinical studies to clinical material production. Simplifying the structure and production procedure are the keys when designing a BsAb format.
	More Investigations in Curing Solid Tumors	• Contrary to the success BsAbs in hematological malignancies, the effect of these antibodies in solid tumors is still rather limited. The essential hurdles are critical on-target off-tumor binding, sparse T-cell infiltration, and quality of tumor-infiltrating lymphocyte (TIL) effector cells due to the presence of an immunosuppressive tumor microenvironment (TME). Due to continuous research efforts, more tumor-specific TAAs would become available, and combined with constantly evolving technologies allowing conditional masking of BsAbs, and on-target off-tumor effects should be manageable in the near future.
	Expended Indications	• Beyond the treatment of tumors, bispecific antibody therapies also serve as an important therapeutic modality for the treatment of other disease types such as inflammatory diseases. They also have multiple other modes of action such as helping macromolecules cross the blood-brain barrier and acting as cofactors to activate signaling cascade pathways. With more new targets uncovered, this innovative therapeutic modality is expected to benefit many more patients in the future.

Source: Frost & Sullivan Analysis

Overview of HER2 Antibody

- Human Epidermal growth factor Receptor 2 (HER2) is a transmembrane tyrosine kinase receptor that belongs to the epidermal growth factor receptor (EGFR/ErbB) family. Overexpression or amplification of the HER-2 gene is common in a variety of cancers, especially breast and gastric cancers, and is often associated with aggressive tumor properties and poor prognosis. Antibody drugs targeting HER-2 have significantly improved the treatment of related cancers.

➢ Currently, clinical antibodies targeting HER2 are mainly divided into the following categories:

Monoclonal Antibodies

Trastuzumab
Trastuzumab is the first approved HER2 monoclonal antibody. It mainly blocks downstream signal transduction by binding to the extracellular domain of HER2 and kills tumor cells through antibody-dependent cell-mediated cytotoxicity (ADCC) effect.

Pertuzumab
Pertuzumab is a monoclonal antibody that binds to different epitopes of HER2. It can inhibit the heterodimerization of HER2 and HER3, thereby enhancing the signal blocking effect. It has obvious synergistic effect when used in combination with trastuzumab.

Antibody-Drug Conjugate (ADC)

Trastuzumab emtansine (T-DM1)
Trastuzumab emtansine is a HER2 monoclonal antibody combined with the cytotoxic chemotherapy drug DM1. It delivers the drug to HER2 overexpressing tumor cells through antibodies, thereby improving the efficacy and reducing the toxicity of non-targeted tissues.

T-DXd (DS-8201)
A novel ADC drug with a higher drug-antibody ratio (DAR) and penetration ability for the treatment of patients with tumors resistant to other HER2 therapies.

Bispecific Antibodies

This type of antibody simultaneously targets HER2 and other molecules (e.g. CD3 or HER3), enhancing anti-tumor activity through a dual-target mechanism. For example, ZW25 (targeting two different epitopes of HER2) has shown good promise in clinical trials.

Source: Literature review, Frost & Sullivan Analysis

Development and Advantages of HER2 Antibody

HER2 antibodies revolutionized cancer treatment by precisely targeting HER2-overexpressing tumor cells, reducing damage to normal tissues, and significantly improving patient survival rates. Since the discovery of HER2's role in aggressive cancers in the 1980s, therapies like trastuzumab, pertuzumab, and ADCs have continuously advanced, expanding treatment options to various cancers. With diverse mechanisms of action, good tolerability, and ongoing innovations like bispecific antibodies and HER2-low therapies, HER2 antibodies remain a cornerstone of precision oncology and a beacon of hope for improving cancer outcomes.

Development History of HER2 Antibody

1987 Studies first revealed the association between HER2 gene amplification and aggressive breast cancer with poor prognosis.

1998 Trastuzumab, the first monoclonal antibody targeting HER2, was approved by the FDA for HER2 positive metastatic breast cancer.

Early 2000s Pertuzumab, approved in 2012, combined with trastuzumab and chemotherapy; T-DM1, approved in 2013, further enhanced the therapeutic efficacy for HER2-positive breast cancer.

2015 to Present Recent advancement include bispecific antibodies and therapies for HER2-low-expression cancers. The application of HER2 antibody has expanded to various cancers.

Precise Targeting: HER2 antibodies can specifically recognize and bind to HER2 receptors, targeting cancer cells that overexpress HER2. This specificity reduces damage to normal cells and enhances therapeutic selectivity.

Multiple Mechanisms of Action: HER2 antibodies work through a combination of signaling blockade and immune-mediated mechanisms. They can induce ADCC, recruiting immune cells to eliminate cancer cells. ADCs enable direct delivery of chemotherapeutic agents to tumor sites, increasing efficacy. Additionally, new-generation bispecific antibodies enhance therapeutic diversity by targeting both HER2 and other molecules, such as HER3.

Good Tolerability: HER2 antibodies generally have a wide therapeutic window and are well-tolerated by patients. Clinical data show that adverse effects from HER2 therapies are manageable, improving patient adherence.

Continuous Innovation Potential: HER2 antibodies offer room for continuous improvements and innovations in molecular design. Antibody engineering has optimized their affinity and pharmacokinetics. Technologies like bispecific and nanobodies expand therapeutic applications.
New antibody therapies for HER2-low expression and HER2-mutated cancers are advancing through clinical trials.

Source: Frost & Sullivan analysis

Competitive Landscape of Marketed HER2 Antibody in China

	Brand name	Generic name	Company	Target	NMPA Approval	Region*	NRDL Status
Monoclonal Antibody	Herceptin	Trastuzumab	Roche	HER2	2002-01-01	United States	List B
	Perjeta	Pertuzumab	Roche	HER2	2018-12-17	United States	List B
	Cipterbin	Inetetamab	3s Guojian Pharmaceutical	HER2	2020-06-17	China	List B
	Margenza	Margetuximab	MacroGenics	HER2	2023-08-29	United States	Not Included
ADC	Kadcyla	Trastuzumab Emtansine	Roche	HER2	2020-01-21	United States	List B
	Enhertu	Trastuzumab Deruxtecan	AstraZeneca	HER2	2023-02-21	United States	Not Included
	爱地希	Disitamab Vedotin	RemeGen	HER2	2021-06-08	China	List B

Note: *Region stands for the country / region where the product first gain approval.
As of 2025.03.12

Source: NMPA, FDA, Frost & Sullivan analysis

Competitive Landscape of HER2 Antibody Pipeline in China

- The following table shows the HER2 antibody pipeline currently under development in China that has reached Phase II and above. The remaining 27 drugs are in Phase I/II and Phase I.

	Drug Code	Company	Target	Status	First Posted Date
Monoclonal Antibody	HLX22	Henlius Biotech	HER2	Phase III	2024-08-01
	IAH0968	Sunho BioPharmaceutical	HER2	Phase II/III	2023-01-03
	SHRA1811	Hengrui Pharmaceutical	HER2	NDA	2024-09-14
	A166	Kelun Pharmaceutical	HER2	NDA	2023-05-11
	IBI354	Innovent Biologics	HER2	Phase III	2025-02-06
	GQ1005	Qide Medical Technology	HER2	Phase III	2024-12-24
	TQB2102	Chia Tai-tianqing Pharmaceutical	HER2	Phase III	2024-08-19
	BL-M07D1	Biokin Pharmaceutical	HER2	Phase III	2024-03-14
ADC	JSKN-003	Alphamab Oncology	HER2	Phase III	2023-10-07
	DB-1303	Duality Biologics Pharmaceutical	HER2	Phase III	2023-08-30
	DP303C	CSPC Pharmaceutical	HER2	Phase III	2023-06-12
	FS-1502	Fosun Pharmaceutical	HER2	Phase III	2023-02-27
	MRG002	MiracoGen	HER2	Phase III	2021-05-31
	ARX788	Amtrx Biopharma	HER2	Phase II/III	2020-06-30
	SHR-4602	Hengrui Pharmaceutical	HER2	Phase II	2024-07-09
	FDA022	Fudan-Zhangjiang Bio-Pharmaceutical	HER2	Phase II	2024-04-23
	BB1701	Bliss Biopharmaceutical	HER2	Phase II	2022-08-10
	DX126-262	DAC Biotech	HER2	Phase II	2022-04-26
Bispecific Antibody	ZW25	BeOne	HER2	NDA	2024-06-07
	KN026	Alphamab Oncology	HER2	Phase III	2022-01-17

Note: As of 2025.03.12
Source: NMPA, FDA, Frost & Sullivan analysis

Drivers of the HER2 Antibody Market in China

High Incidence and Unmet Clinical Needs	• In China, HER2-positive breast and gastric cancers have relatively high incidence rates. Unmet clinical needs include: • 1. More effective and tolerable drugs for early-stage HER2-positive breast cancer adjuvant therapy. • 2. Limited treatment options for HER2-positive gastric cancer, with current therapies (e.g., trastuzumab combined with chemotherapy) showing suboptimal efficacy and resistance issues. • 3. A lack of therapeutic options for HER2-low expression and HER2-mutated patients, highlighting the urgent need for innovation.
Policy Support and Enhanced Local Innovation Capacity	• Regulatory reforms in China, such as the "priority review" policy, have accelerated the approval process for innovative drugs. Domestic biopharmaceutical companies, such as Innovent Biologics and Hengrui Medicine, have significantly enhanced their R&D capabilities for HER2-targeted drugs, with continuous progress in clinical trials and new drug launches.
Improved Drug Affordability and Accessibility	• The high cost of HER2 antibody drugs (e.g., trastuzumab and pertuzumab) previously limited their widespread use. However, the introduction of domestic alternatives has significantly reduced treatment costs, with biosimilars priced much lower than imported products. Additionally, the inclusion of trastuzumab and similar drugs in the national healthcare insurance scheme has further increased patient accessibility and market penetration.
Advancements in Precision Medicine and Combination Therapies	• The widespread adoption of genetic testing has improved the precision of HER2 detection (e.g., FISH and IHC), enabling early access to targeted therapy for HER2-positive patients. HER2 antibodies are also demonstrating superior efficacy in combination therapies, such as trastuzumab with pertuzumab and docetaxel, which are becoming standard practice. These advancements are driving further expansion of HER2 antibody applications.

Source: Frost & Sullivan Analysis

Development Trends of the HER2 Antibody Market in China

From Monoclonal Antibodies, ADC to Bispecific Antibodies	• HER2 antibody development is evolving from traditional monoclonal antibodies to ADCs. Domestic ADCs, such as RemeGen's disitamab vedotin, have shown excellent efficacy and safety profiles, offering new treatment options for HER2-positive breast and gastric cancers. Additionally, numerous Chinese companies (e.g., Hutchmed and Akeso) are accelerating clinical trials of HER2 ADCs, with more domestic ADCs expected to enter the market soon. In addition, pharmaceutical companies are also committed to the development of bispecific antibodies. The HER2 bispecific antibody drug Zanidatamab, which is being developed by BeOne, has entered the stage of applying for listing.
Breakthroughs in HER2-Low Expression Patient Treatments	• The success of DS-8201 (Enhertu) has opened up new treatment options for HER2-low expression patients, a population that accounts for approximately half of breast cancer cases. Chinese companies are also actively developing therapies for this group, such as Hengrui Medicine's ADCs targeting HER2-low expression. The future expansion of HER2 antibody indications is expected to benefit a broader patient population.
Regional Market Expansion and Internationalization	• Previously, the HER2 antibody market was concentrated in major cities and large hospitals. With the reduced prices of domestic drugs and improved healthcare services in lower-tier cities, the use of HER2 antibodies is expanding to grassroots medical institutions. At the same time, Chinese companies are exploring international markets through global clinical trials and regulatory submissions. For example, RemeGen's disitamab vedotin has received FDA breakthrough therapy designation, accelerating the internationalization of Chinese HER2 antibodies.
Cost Optimization and Widespread Application	• Improvements in manufacturing processes and increased production scales are reducing the costs of HER2 antibody drugs. For instance, the development of biosimilars has significantly shortened development cycles and reduced costs. Additionally, government policies promoting generics and biosimilars will further lower costs, making HER2 antibody treatments accessible to more patients.

Source: Frost & Sullivan Analysis

Appendix for Verification - I

- The antibody market in China has demonstrated consistent growth, with market size reaching RMB 640.1 billion in 2033 with the rapid adoption of SC formulations exemplified by daratumumab SC,