Innovative Drug Market Study
Independent Market Research Report

Date : 5 December 2025

For and on behalf of
Frost & Sullivan (Beijing) Inc., Shanghai Branch Co.

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Confidential For

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Frost & Sullivan
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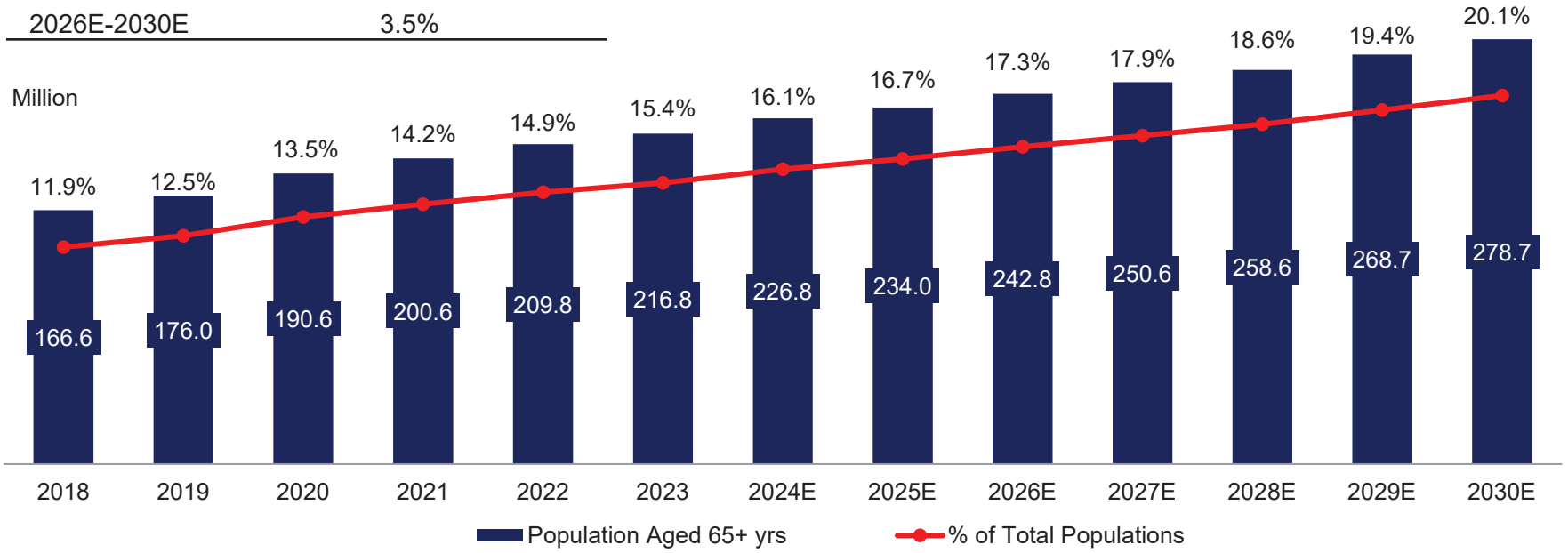
China Aging Population Trend, 2018-2030E

- With the implementation of the 'One Child Policy' and increasing life expectancy, China has entered an aging society. From 2018 to 2023, the population is aging rapidly in China with people aged above 65 growing at a CAGR of 5.4%. According to the National Bureau of Statistics of China (NBSC), the number of individuals aged above 65 years old is estimated to be 216.8 million in 2023. 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 is expected to reach 278.7 million by 2030, representing a CAGR of 3.5% from 2026 to 2030.

China Aging Population Trend, 2018-2030E

Period	CAGR
2018-2023	5.4%
2023-2026E	3.9%
2026E-2030E	3.5%



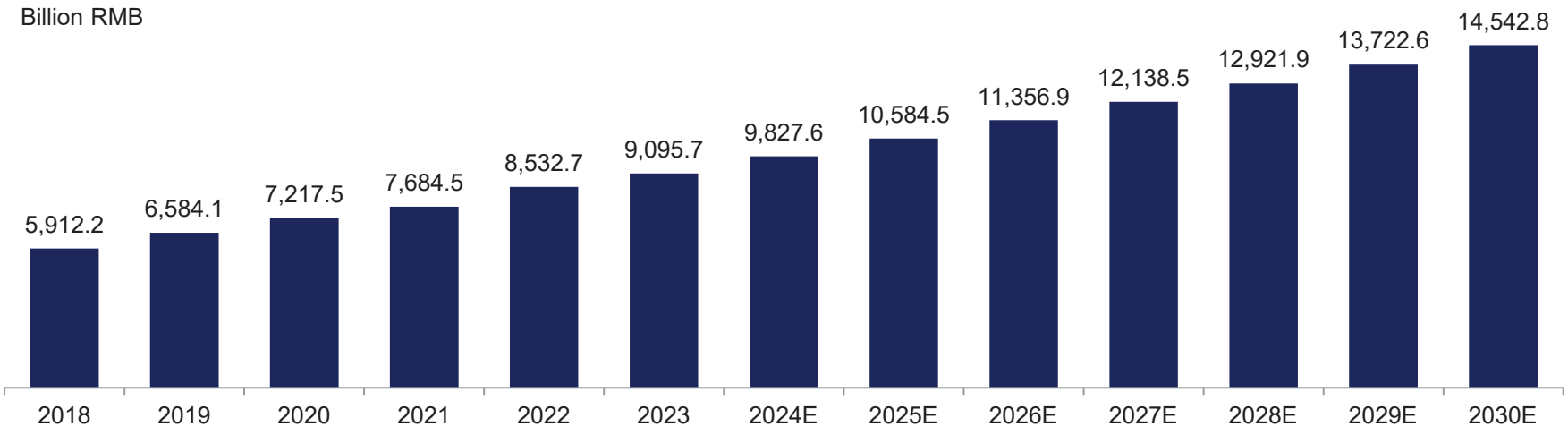
Source: NBSC, Frost & Sullivan Analysis

Total Healthcare Expenditure in China, 2018-2030E

- In China, the total healthcare expenditure reached RMB 9,095.7 billion in 2023 at a CAGR of 9.0% from 2018. It is projected to further increase to RMB 11,356.9 billion in 2026, representing a CAGR of 7.7% from 2023. It is estimated that the number would achieve RMB 14,542.8 billion in 2030, representing a CAGR of 6.4% from 2026 to 2030.

Total Healthcare Expenditure in China, 2018-2030E

Period	CAGR
2018-2023	9.0%
2023-2026E	7.7%
2026E-2030E	6.4%



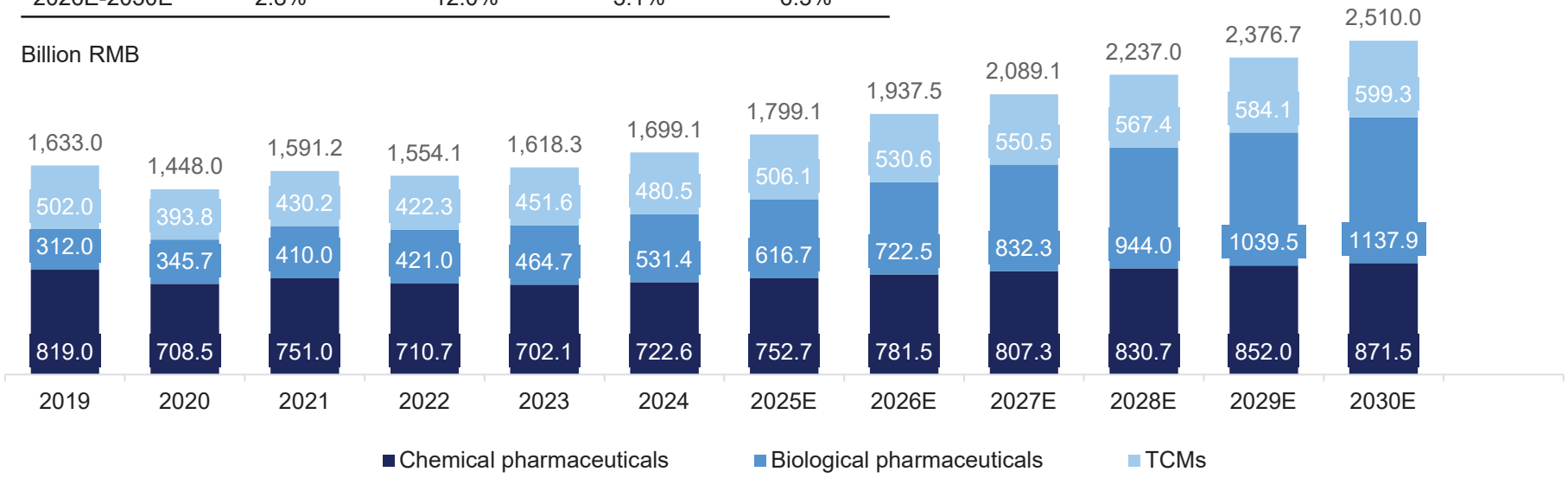
Source: National Health Commission, Frost & Sullivan Analysis

Breakdown of China Pharmaceutical Market by Chemical Drugs, Biologics and TCMs, 2019-2030E

- China pharmaceutical market is composed by three segments, namely chemical pharmaceuticals, biological pharmaceuticals and traditional Chinese medicines (TCMs), among which chemical pharmaceuticals account for the largest market share. The size of China pharmaceutical market was RMB 1699.1 billion in 2024, and is expected to reach RMB 2089.1 billion and RMB 2510.0 billion in 2027 and 2030 respectively, representing a CAGR of 7.1% from 2023 to 2026 and 6.3% from 2027 to 2030.

Breakdown of China Pharmaceutical Market by Chemical Drugs, Biologics and TCMs, 2019-2030E

CAGR	Chemical pharmaceuticals	Biological pharmaceuticals	TCMs	Total
2018-2023	-2.3%	12.1%	-1.4%	0.8%
2023-2026E	3.6%	15.8%	5.5%	7.1%
2026E-2030E	2.8%	12.0%	3.1%	6.3%

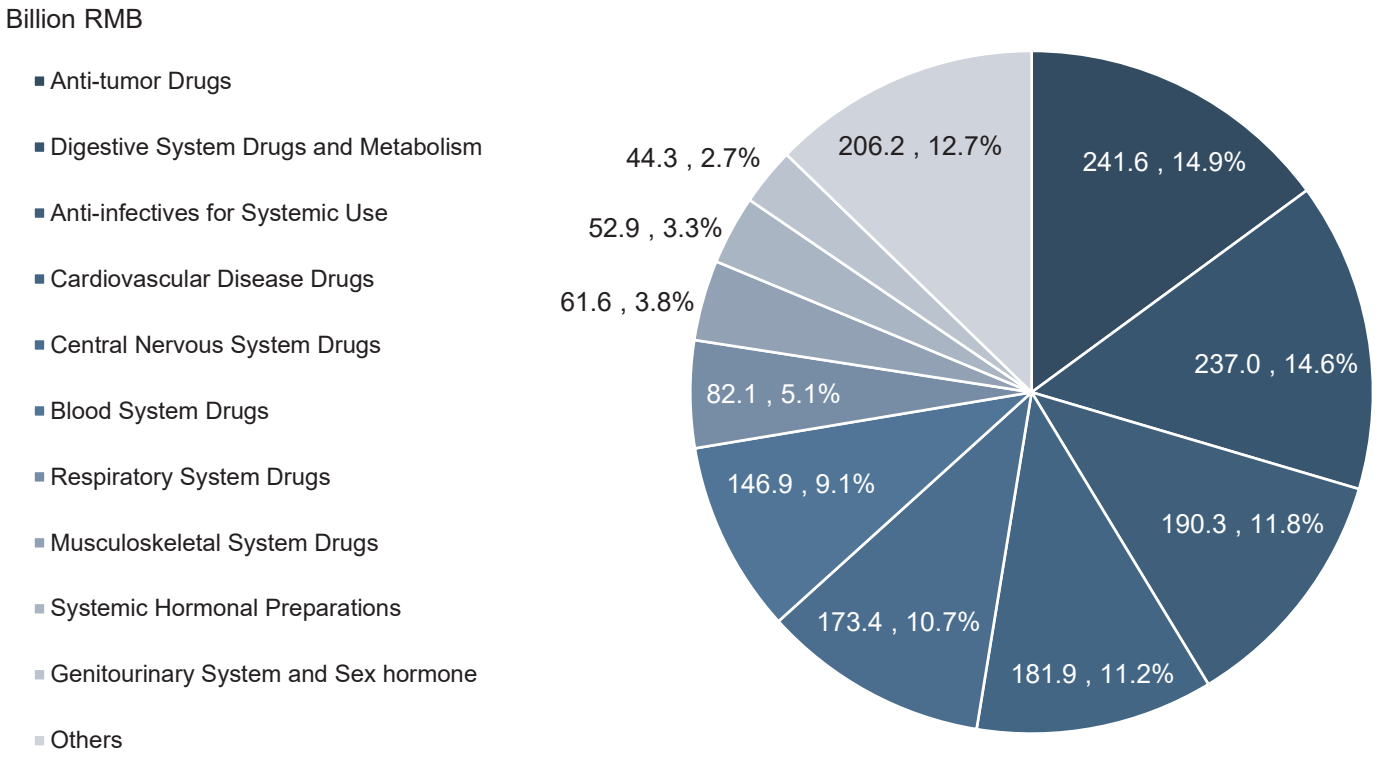


Source: Frost & Sullivan Analysis

Breakdown of China Pharmaceutical Market by Therapeutic Area, 2023

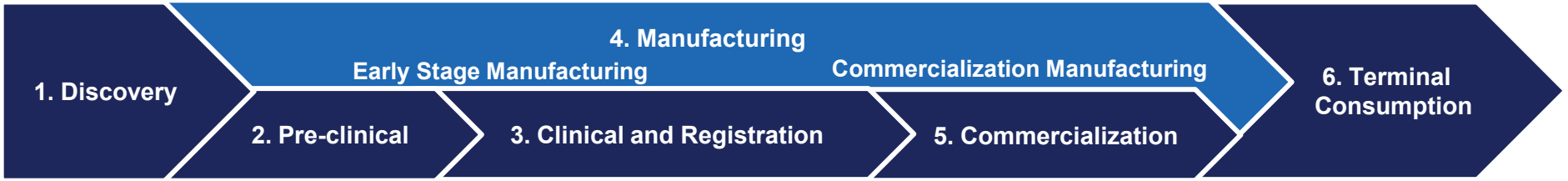
- In terms of market size, anti-tumor, digestive tract and metabolism and anti-infectives for systemic use are three major therapeutic areas in China, respectively accounting for 14.9%, 14.6% and 11.8%.

Breakdown of China Pharmaceutical Market by Therapeutic Area, 2023



Source: Frost & Sullivan Analysis

Processes in New Drug Research and Development



1. Discovery

Target Identification
- The process of identifying the direct molecular target of a small molecule.

Target Validation
- The process by which the predicted molecular target of a small molecule is verified.

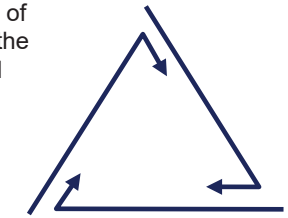
Lead Generation
- The process by which the targeted small molecule is evaluated and undergo limited optimization to identify promising compounds.

Lead Optimization
- The process by which a drug candidate is designed after an initial lead compound is identified.

2. Pre-clinical

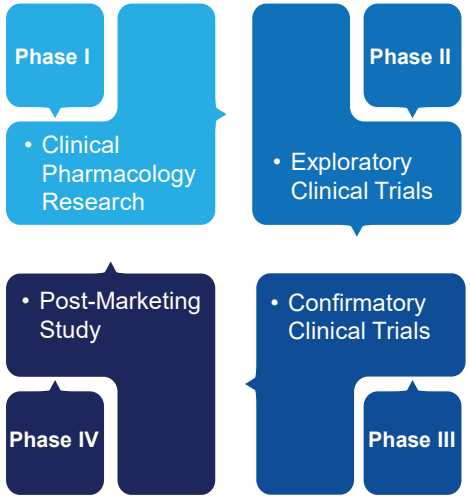
Safety Assessment:
- A comprehensive and systematic investigation and analysis of all aspects of risks to health and safety associated with major incidents that may potentially occur in the course of operation of the major hazard facility.

Pharmacokinetic and Pharmacology Research:
- The study of the disposition of a drug after its delivery to an organism, mainly refer to the ADME(absorption, distribution, metabolism, and excretion) research.



Pharmacodynamics Research:
- The quantitative study of the relationship between drug exposure (concentrations or dose) and pharmacologic or toxicologic responses.

3. Clinical and Registration



4. Manufacturing

Early Stage Manufacturing (From Pre-clinical to Clinical)

Commercialization Manufacturing

Source: Frost & Sullivan Analysis

Processes in New Drug Research and Development

5. Commercialization

Factors involved in a new drug commercialization process:

Commercial plan establishment

- To orchestrate the cross-functional activities required to execute the launch

New drug launch plan implementation

- Execute market access strategies;
- Establish pricing and reimbursement programs;
- Conduct prescription fulfillment.

Confirmation of launch project's scope:

- Set up goals, objectives, and life cycle characteristics of the new drug;
- Control and monitor the launch scope and schedule

Risk management:

- Changes and developments in the regulatory approval process;
- Increased competition from branded and generic drugs;
- The level of acceptance from patients, KOLs, and payers to the new drug.

6. Terminal Consumption

Hospital terminal

- The primary drug sales channel. Its selling drugs contain in-patient drugs, out-patient RX drugs, injection and non-injection, and out-patient OTC drugs.

Retail terminal

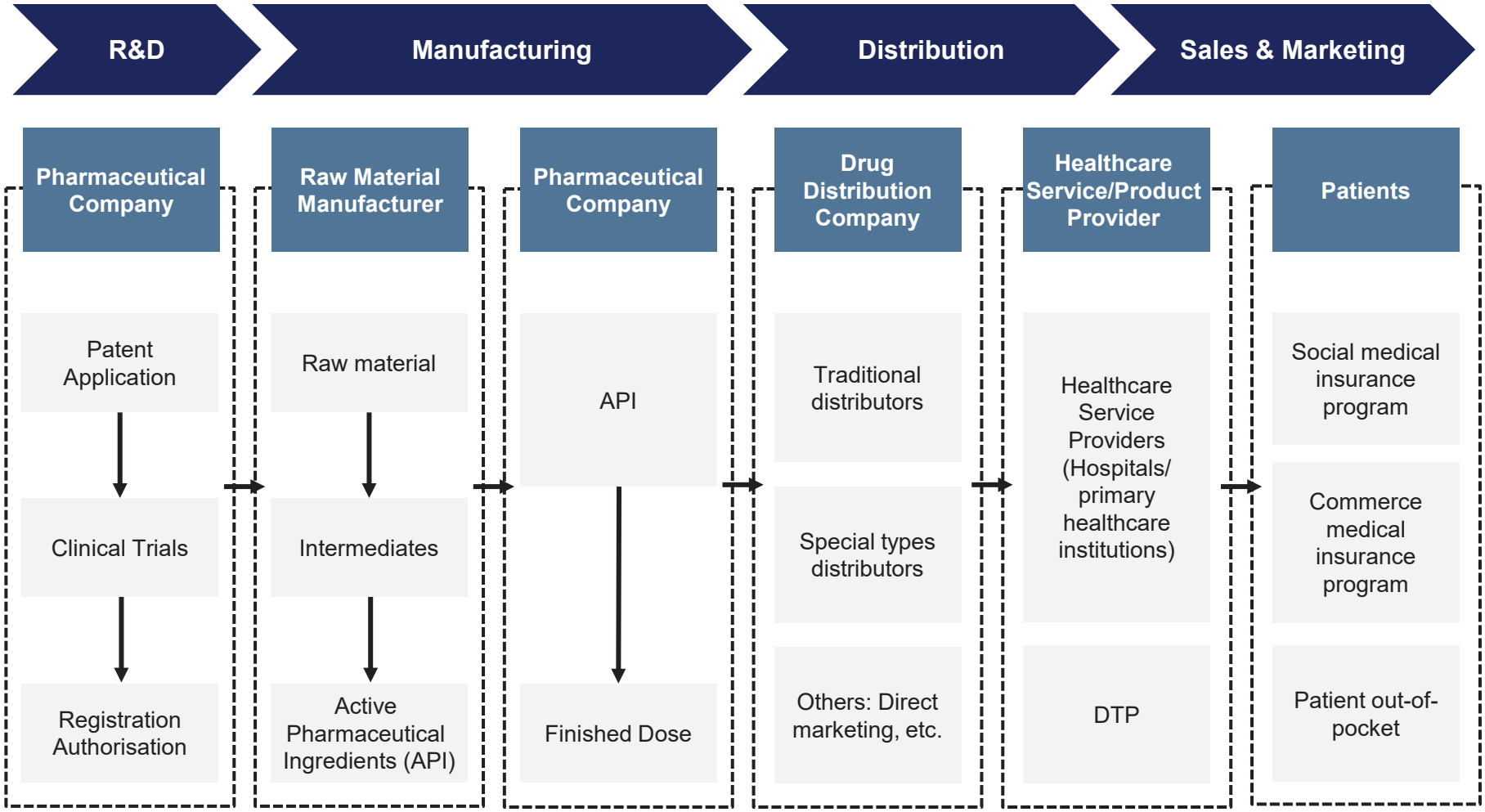
- The second largest drug sales channel. Its selling drugs contain RX drugs and OTC drugs.

Network terminal

- A promising drug sales channel. Its selling drugs contain RX drugs and OTC drugs.

Source: Frost & Sullivan Analysis

Overview of Value Chain in Pharmaceutical Industry

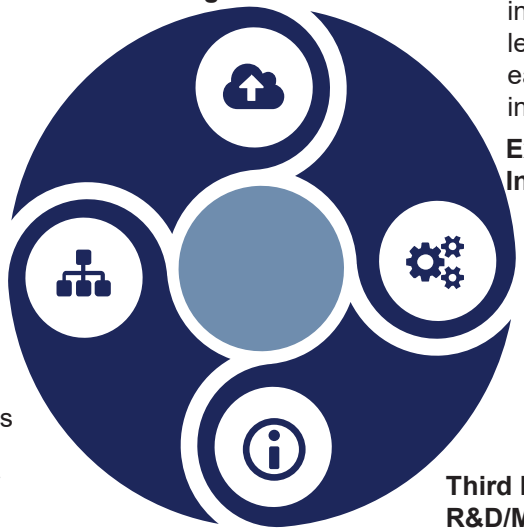


Source: Frost & Sullivan Analysis

Representative Business Strategies in Pharmaceutical Industry

Integrating Upstream R&D/ Licensing-in Innovative Drug

- Pharmaceutical company can enlarge its pipeline coverage, existing marketed product, Tas by expanding R&D business or licensing in innovative drugs.



Expansion to International Market

- With NMPA regulation, cGMP and other regulation in China getting more consistent with international level, Chinese pharmaceutical companies are easier and faster to obtain approval from international agency.

Pharmaceutical Company Integrating Downstream Sales Channel

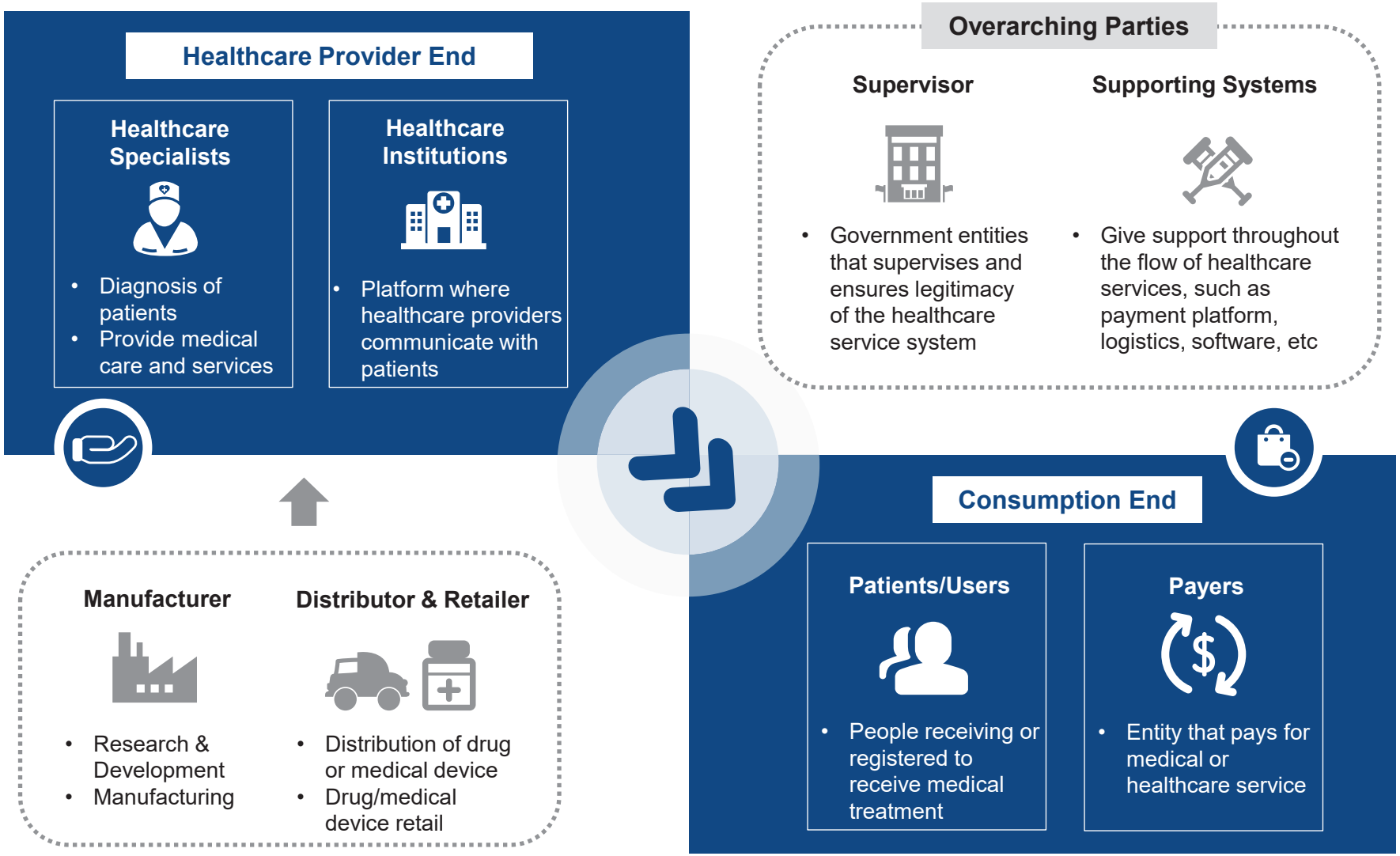
- Pharmaceutical company with mature products and manufacture process can also seek downstream help on sales channel, especially with the carrying out of two invoice policy and other healthcare system reform regulations.

Third Party R&D/Manufacturer

- The whole chain in pharmaceutical industry requires professional knowledge and experience, making third party company more critical, especially for medium and small company, such as innovative R&D company.

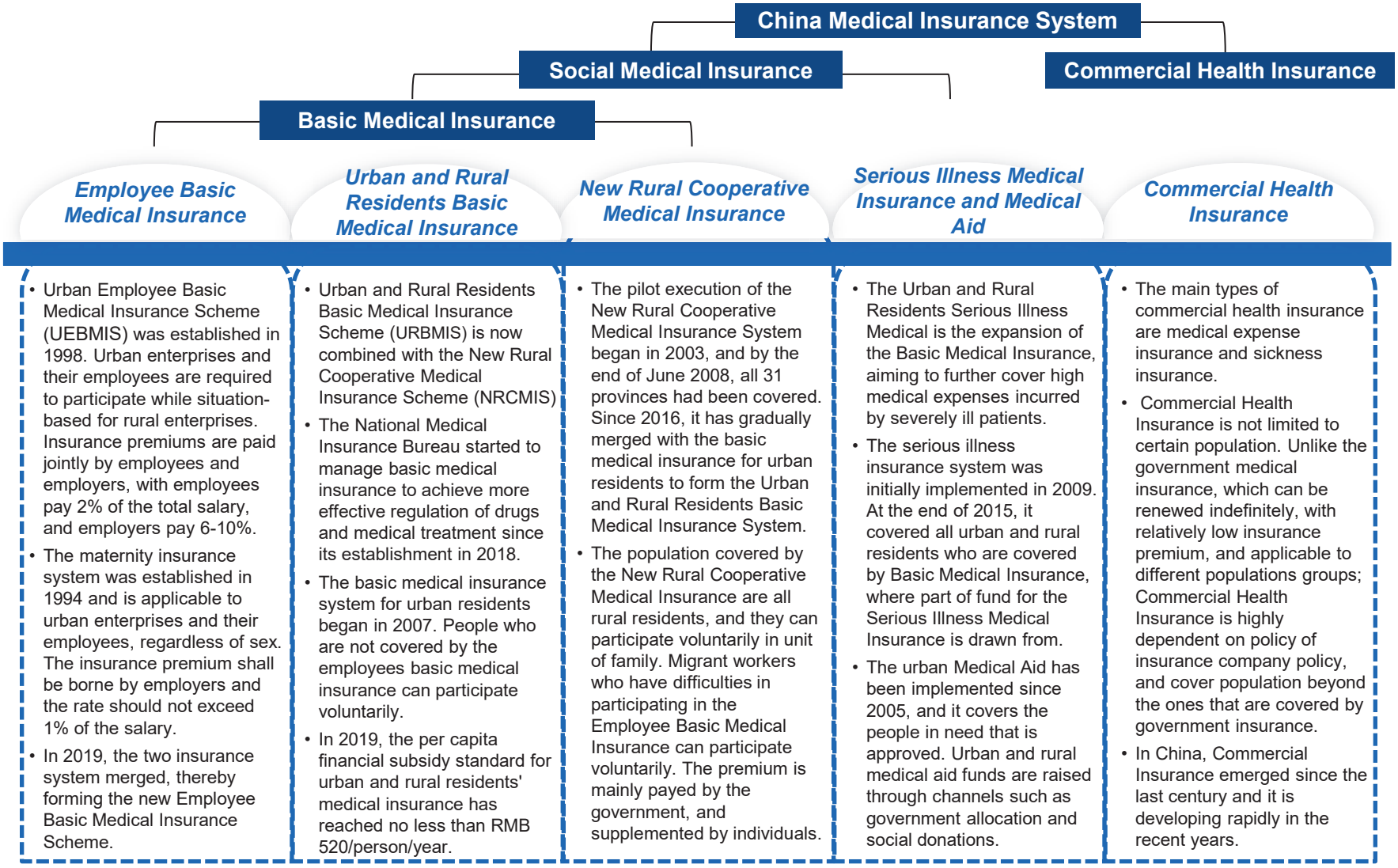
Source: Frost & Sullivan Analysis

Value Chain of Healthcare Service Market



Source: Frost & Sullivan Analysis

Overview of Medical Insurance System in China



Source: Frost & Sullivan Analysis

Overview of Pharmaceutical Marketing, Promotion and Channel Management Services (MPCMS) Market in China

MPCMS Market in China

- China's pharmaceutical marketing, promotion and channel management services industry is highly specialized. The players in this market generally collaborate with pharmaceutical manufacturers to implement or support promotion and marketing activities for their pharmaceutical products to targeted physicians in China. They generally adopt a physician oriented academic promotion approach, which includes educating physicians on the proven clinical data, usage, side effects and other clinical aspects of the pharmaceutical products, organizing clinical seminars, sponsoring medical conferences and providing other value-added promotion-related services.

Professionals and Specialization Play an important role in Pharmaceutical Marketing

- Accompanied with professional teams and experience, marketing, promotion and channel management service providers in China usually secure marketing, promotion and sales rights to pharmaceutical products in China from suppliers, and generate their revenue from the sale of the products to distributors, who then on-sell the products to hospitals. This approach stands in contrast with the approach that prevails in more developed markets, where service providers typically operate a fee-for-service model, under which they are remunerated based on a pre-determined percentage of total sales generated.

Specialized Team Performs Better than Regular In-house Sales Force

- While some of the pharmaceutical manufacturers struggle to solve the rising cost associated with maintaining an in-house sales force and the complexity and difficulty of gaining market access and conducting promotion activities independently, the and specialized MPCMS team and professionals with proven capabilities and consistent track record to offer a wide range of services, or the one-stop solutions, is better positioned to attract suppliers.

Source: Frost & Sullivan Analysis

Components of Pharmaceutical MPCMS in China

Registration Services	• Including both handling registration for new imported pharmaceutical products and renewal of expiring imported pharmaceutical products registrations.
Customs Clearance and Logistics	• Coordinating inspection by public health bureaus of imported pharmaceutical products and providing warehousing, logistics and other managerial aspects for sales of the pharmaceutical products.
Tendering and Bidding Services	• Participating in tendering and bidding processes that are a requirement for selling pharmaceutical products to public hospitals and medical institutions.
Appointing and Managing Distributors	• Distributors are usually responsible for processing purchase orders, delivering products and collecting payments etc.
Managing and Optimizing Inventory Levels	• Managing and optimizing inventory levels at distributors and hospitals to improve the operation efficiency.
Collecting, Integrating and Analyzing Sales Data	• Services of collecting, integrating and analyzing sales data can help to provide clients with comprehensive information for market analysis and performance evaluation as well as gain greater insight into market trends and boost sales by quicker response time.
Marketing & Promotion Services	• Marketing & Promotion services refer to formulating marketing and promotion strategies, educating individual physicians on the clinical uses and benefits of pharmaceutical products as well as providing professional academic support like organizing academic conferences, seminars and symposiums and other promotional activities.

Source: Frost & Sullivan Analysis

Competitive Advantages of MPCMS Team

Help large pharmaceutical companies sink to the grassroots market.

Typical large pharmaceutical companies possess various product lines; the resources for internal sales teams, however, are rather limited, making it difficult to allocate enough manpower to each product. Whereas professional MPCMS teams are capable to customize marketing plan for each product and thus can achieve broader market coverage.

This is even truer in the hierarchical diagnosis and treatment context, MPCMS teams can help the pharmaceutical companies that otherwise would only target on major hospitals of class II and III sink to the county-level hospitals or primary healthcare institutions.

Help small and medium-sized pharmaceutical companies open up the market efficiently.

Small and medium-sized pharmaceutical companies, especially foreign ones, typically have strong R&D capabilities, yet lack experienced sales teams and local experience. MPCMS teams can help such enterprises with their unique resources and experience to open up market efficiently.

Cut Costs

In an increasingly competitive pharmaceutical market, effective cost control is a critical practice for pharmaceutical companies.

Having huge sales teams in-house not only drives up cost, but also makes the company sluggish while facing the fast changing market.

Meanwhile, the high turnover rate of medical representative disturbs the conventional recruitment and training in pharmaceutical companies. Fortunately, MPCMS teams can help with the workforce reduction, fixed expenses cut down and efficiency improvement with the flexible business models.

Avoid Risks

With the strengthening supervision in the pharmaceutical market, sales that used to skirt in the margin of laws had subjected to the strict restrictions. Now professional MPCMS teams develop customized sales strategies according to the characteristics of the product, and can effectively help pharmaceutical manufacturers avoid risks.

Source: Frost & Sullivan Analysis

Growth Drivers of MPCMS Market in China

Strong growth in China's prescription drug market due to gigantic medical needs from over 1.3 billion population.

Driven by the global headcount and cost-reduction pressures, global pharmaceutical giants have constricted their investment on sales teams in China. Some of them tend to prioritize their product portfolios and seek for third party promotion service providers. As a result, they will consider outsourcing low priority product or divest some out-of-date developed products and non-core portfolio sales and marketing to third party service providers and also leveraging them to help cover key product sales in remote areas. This would help them capture more revenue without incurring additional costs.

For small- and medium-sized overseas pharmaceutical companies, common challenges to accessing this market include the difficulties of navigating China's complex system of tender process participation, hospital procurement and CFDA registrations and renewals, the high costs associated with establishing in-house marketing and promotion teams and a sales network with wide geographic reach, as well as the particularities of selling in local markets. Consequently, small- and medium-sized overseas pharmaceutical companies can benefit greatly from using a domestic marketing, promotion and channel management service team to assist in marketing and selling their products in China.

Many domestic pharmaceutical companies have historically focused on manufacturing and have not established in-house sales and marketing capabilities. As the promotion practices in China become more sophisticated and clinical-based, these companies have also looked to grow sales of their products by outsourcing to capable promotion services teams.

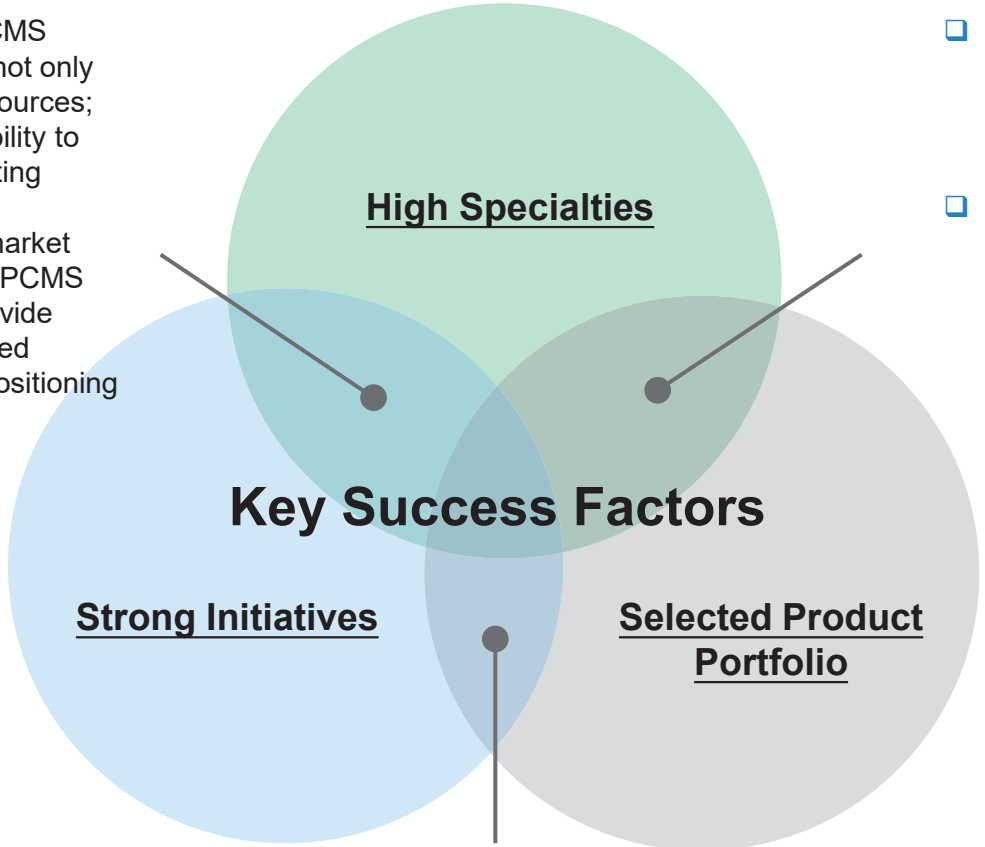
As MPCMS grow, their enhanced marketing and sales capabilities could help provide more values and therefore will attract more pharmaceutical companies to leverage their services in expanding their sales.

MPCMS is expected to be a future trend in China

Source: Frost & Sullivan Analysis

Key Success Factors in MPCMS Market in China

- In order to excel in the MPCMS market, services providers not only need abundant channel resources; more importantly, the capability to provide professional marketing solutions.
- To assist enterprises with market exploitation, a successful MPCMS company is expected to provide services including customized marketing plans, product positioning and sales staff training etc.



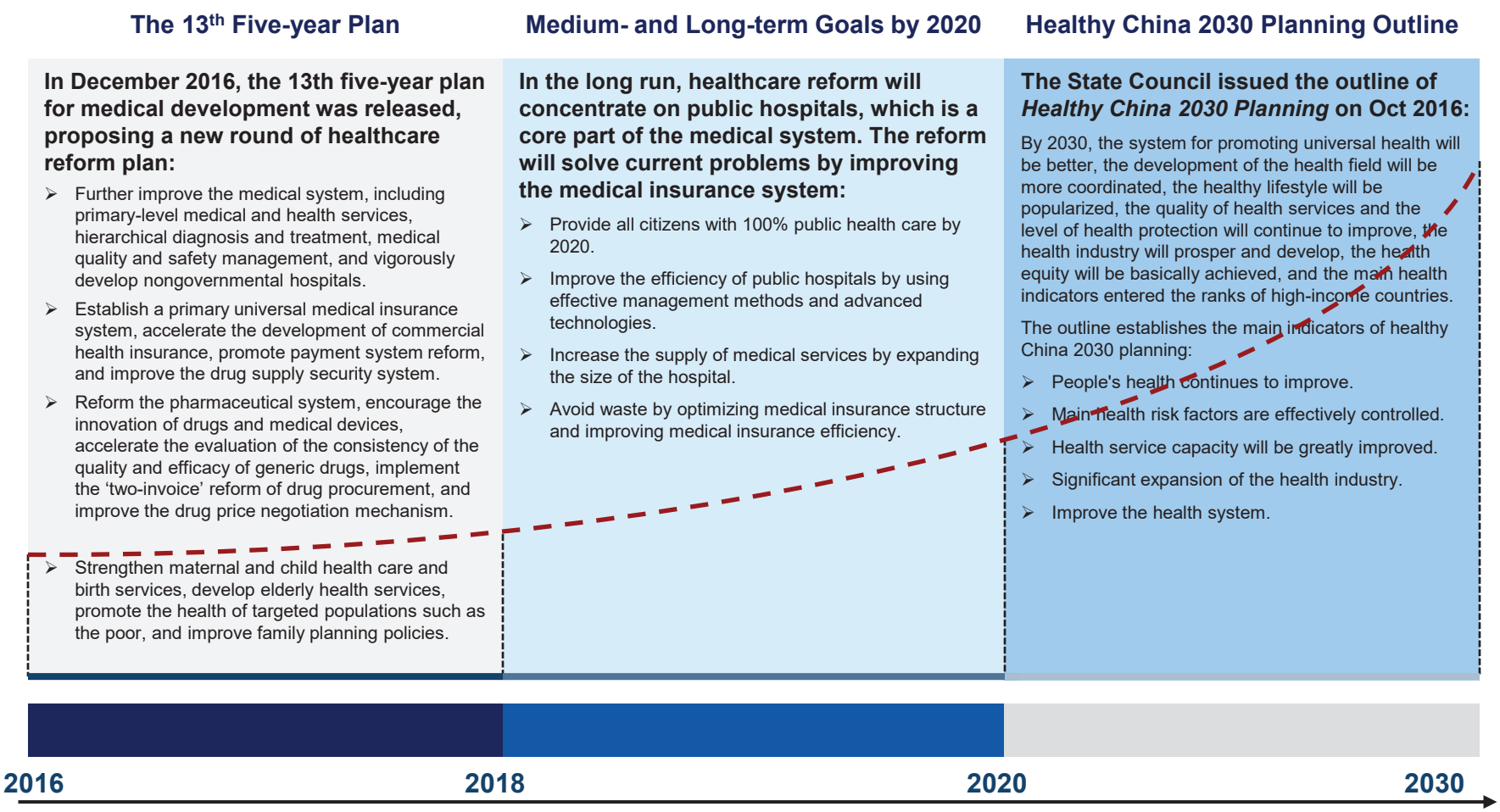
- Whether a MPCMS company in the pharmaceutical industry can quickly occupy the market is determined by the rationality of its product portfolio.
- It is significant for companies to possess not only the market sensitivity, but also the rigorous screening process selecting promising products and partners. It is certain that a company's competitiveness can be greatly enhanced by a rational product portfolio.

- Though local pharmaceutical MPCMS providers hold the initiative in the business with small and medium-sized foreign suppliers, their bargaining power is greatly restricted when facing the pharma giants.
- Common practices to enhance the product mastery include equity participation, buying out the assets of the imported products in China, and signing long-term exclusive agreement(more than 20 years) with the supplier.

Source: Frost & Sullivan Analysis

Overview of Healthcare Reform in China-I

The ultimate goal of healthcare reform: everyone can have access to and afford basic healthcare services



Source: Government Notice, Frost & Sullivan Analysis

Overview of Healthcare Reform in China - II

Key Content	2009-2011	2012-2014	2015-2020
Establish a universal healthcare scheme to meet the essential medical needs of 95% of the population	• Expanding the coverage of UEBMIP, URBMIP, NRCMP	• Aiming to integrate urban and rural resident insurance programs	• Continuously increasing the amount of funding and expanding healthcare coverage
Create and implement national Essential Drug List (EDL) system	• Implementing EDL system at primary healthcare service level • Achieving zero margin on EDL drugs • Procurement through public bidding	• Increasing pharmaceuticals covered under EDL from 307 to 520 • Increasing EDL adoption by various healthcare institutions	• Continuously optimizing EDL
Improve professional medical expertise, especially at the primary healthcare service level	• Establishing urban community healthcare centers and rural medical institutions, including county hospitals and township clinics	• Focusing on strengthening professional expertise of the professionals at various primary healthcare service level	• Further upgrading medical facilities • Focusing on prevention and early detection of diseases
Public hospital reform	• Separating sponsorship and operations of public hospitals • Reducing revenue dependency on pharmaceutical sales	• Encouraging private capital to invest in healthcare services industry	• Large scale privatization or public-private partnership

Source: Government Document, Frost & Sullivan Analysis

Preferential Policies for the Pharmaceutical Industry in China

Policies	Issued Authorities	Issued Dates	Topics	Comments
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》	THE STATE COUNCIL	2016.03	Innovation Encouragement	Focusing on the R&D of innovative drugs with novel targets, high selectivity or new mechanism of action in the fields of tumors, cardiovascular diseases, diabetes, neurodegenerative diseases, mental diseases, immune system diseases, infectious diseases, and rare diseases.
Drug Marketing Authorization Holder System 《药品上市持有人制度试点方案》	NMPA	2016.03	Manufacture Management	The MAH system adopts a management model in which marketing authorization and production authorization are separated, and the marketing authorization holder can entrust the production of products to different manufacturers, and the safety, effectiveness and quality control of the drug are all responsible to the public by the marketing authorization holder.
Policies of Encouraging Drug Medical Equipment Innovation to Reform the Clinical Trial Management 《关于鼓励药品医疗器械创新改革临床试验管理的相关政策（征求意见稿）》	NMPA	2017.05	Review and Approval	If the clinical trial data obtained by the applicant abroad meets the relevant requirements for drug registration in China, it can be used to apply for registration in China after on-site inspection. International multi-center drug clinical trials conducted by foreign companies in China, which meet the relevant requirements for drug registration in China, can directly submit marketing applications after completing the international multi-center clinical trials.
Opinions on Deepening the Reform of Review and Approval System and Encouraging Innovation in Drugs and Medical Devices	THE STATE COUNCIL	2017.10	Review and Approval	To encourage the R&D of innovative drugs and medical devices and give priority to the review and approval system for urgently needed drugs and medical devices, including those that can be used to treat severe life-threatening diseases lacking effective treatment or are urgently needed.
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》	NMPA	2017.12	Review and Approval	Clarifying the scope, procedure, and content of priority review and approval. For example, new drug clinical trial applications that have been simultaneously obtained in the United States and the European Union can enter the priority review.

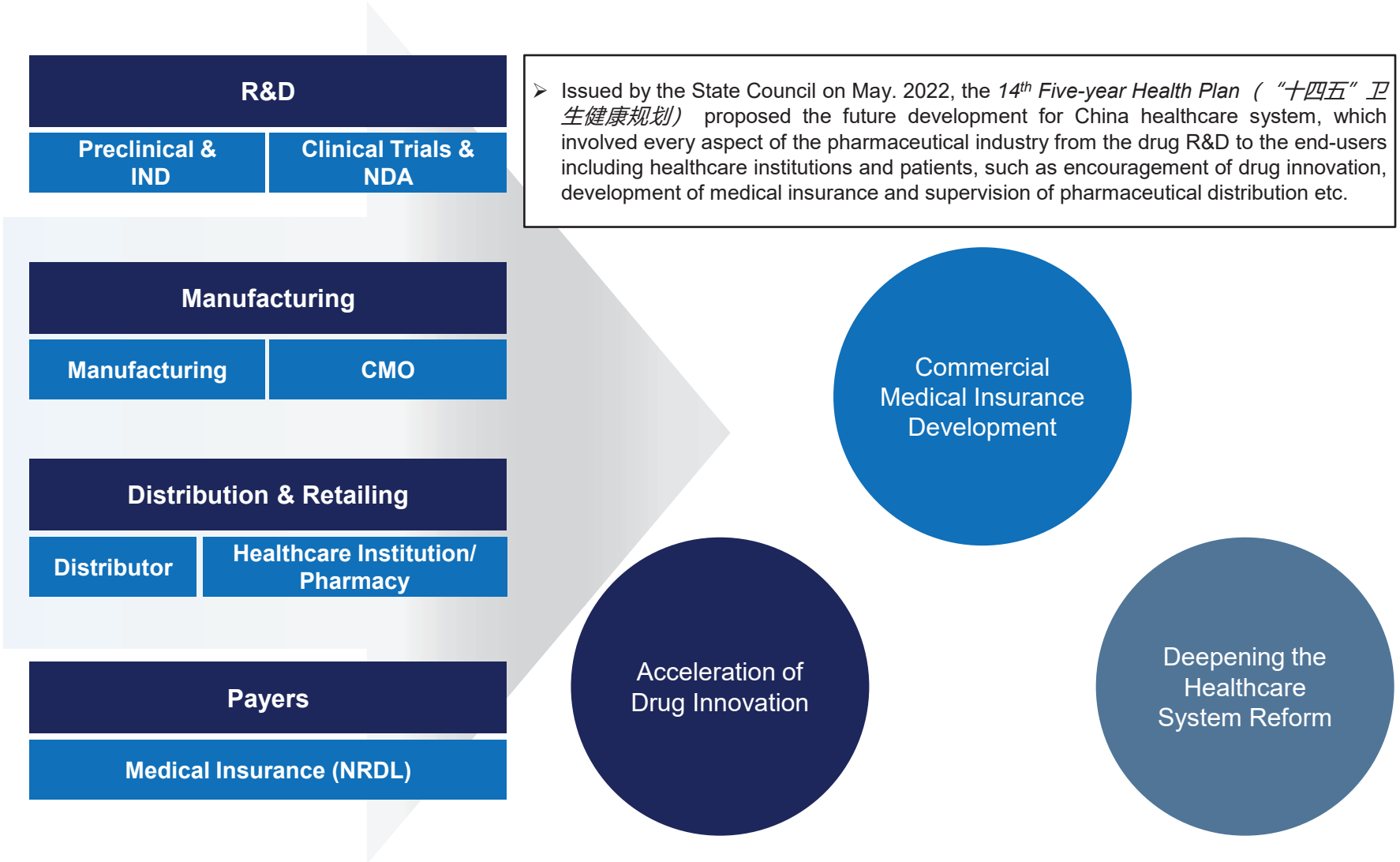
Source: FDA, NMPA, Frost & Sullivan Analysis

Preferential Policies for the Pharmaceutical Industry in China

Policies	Issued Authorities	Issued Dates	Topics	Comments
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》	NMPA	2018.07	Review and Approval	Encourage the simultaneous R&D of drugs at home and abroad, and accelerate the marketing of drugs that are urgently needed, that have definite curative effects, and that have controllable safety risks.
Announcement on the urgent clinical need for approval of new drugs abroad 《临床急需境外新药审评审批工作程序》	NMPA	2018.10	Review and Approval	Establish a special channel to review and approve overseas new drugs that are urgently needed and have been marketed overseas like the USA, the Europe, Japan, etc., but not available at home.
Provisions of Drug Registration 《药品注册管理办法》	NMPA	2020.07	Drug Registration	Clarifying the change path of drug clinical trials will help to standardize and optimize the drug development process and ensure that the risk of new drug R&D can be minimized.
《药品附条件批准上市技术指导原则（试行）》	NMPA	2020.11	Review and Approval	Conditional approval refers to the situation that the existing clinical research data has not met all the requirements of conventional new drug registration, but it shows curative effects and clinical values can be predicted based on surrogate endpoints, intermediate clinical endpoints or early clinical trials.
National Reimbursement Drug List (Version 2023) 《国家医保目录（2023）》	NMPA	2023.12	Medical Insurance	Some of innovative drugs entered the national basic medical insurance list on the same year when it was launched.

Source: FDA, NMPA, Frost & Sullivan Analysis

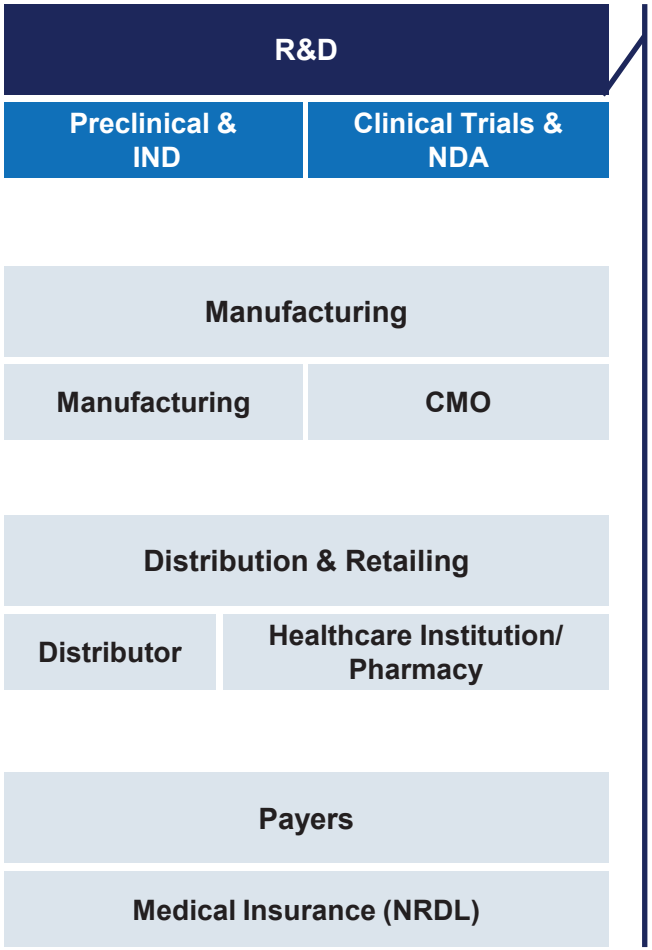
China Systematic Reform on Pharmaceutical Industry



Source: Government Website, Frost & Sullivan Analysis

China Systematic Reform on Pharmaceutical Industry

Quality Consistency Evaluation of Generic Drugs



Quality Consistency Evaluation of Generic Drugs

Main Contents

Consistency evaluation of generics drugs regulate:

- Scope and timeline
- Selection of comparative finished dose。
- Bioequivalence method to evaluate consistency. In vitro disSolution method may be used with a waiver of bioequivalence.
- Pharmaceutical products that have passed consistency evaluation can receive market privileges in medical insurance reimbursement, centralized procurement, and etc.

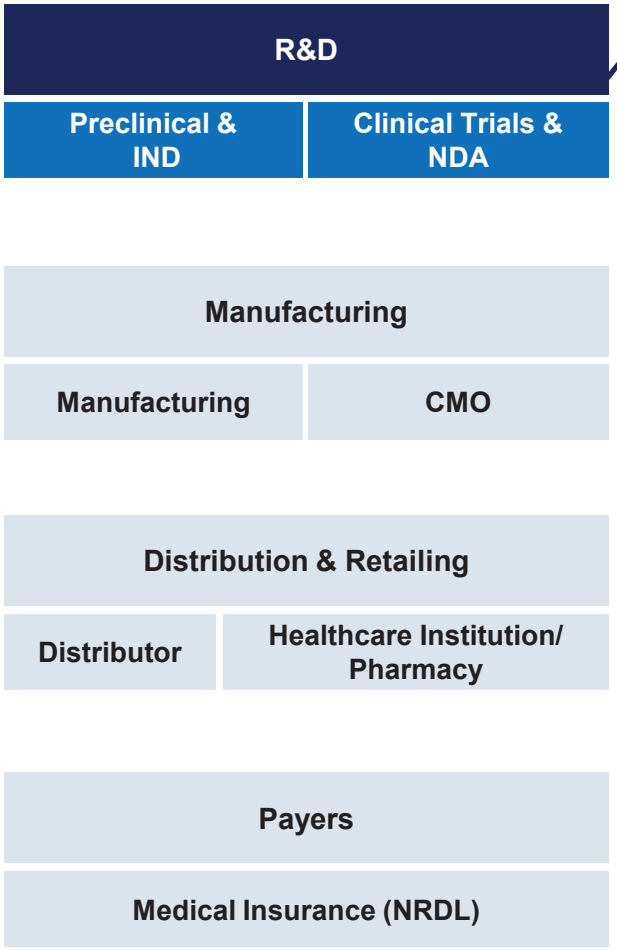
Influences

- Past poor regulations on generics hinder the market development and patients' medication safety.
- Manufacturers (normally large ones) first pass the consistency evaluation will enjoy privileges over competitors.
- Policy aims to eliminate the small and mid-sized manufacturers with backward production capability.
- Improve the overall quality of generic drugs in China and improve the market concentration.

Source: Government Website, Frost & Sullivan Analysis

China Systematic Reform on Pharmaceutical Industry

Self-inspection of Clinical Trial Data



Self-inspection of Clinical Trial Data

《国家食品药品监督管理总局关于开展药物临床试验数据自查核查工作的公告》

Main Contents

- NMPA required compulsory self-inspection of clinical trial data for a total of 1,622 existing drug applications, which initiated the first round of self-inspection of clinical trial data in China.
- Upon self-inspection, applicants are allowed to voluntarily withdraw the applications. If the applicants do not withdraw the applications and later are found to use inauthentic clinical data during NMPA inspection, their applications will not be accepted in the next three years, and the related institutions and CRO will be blacklisted.

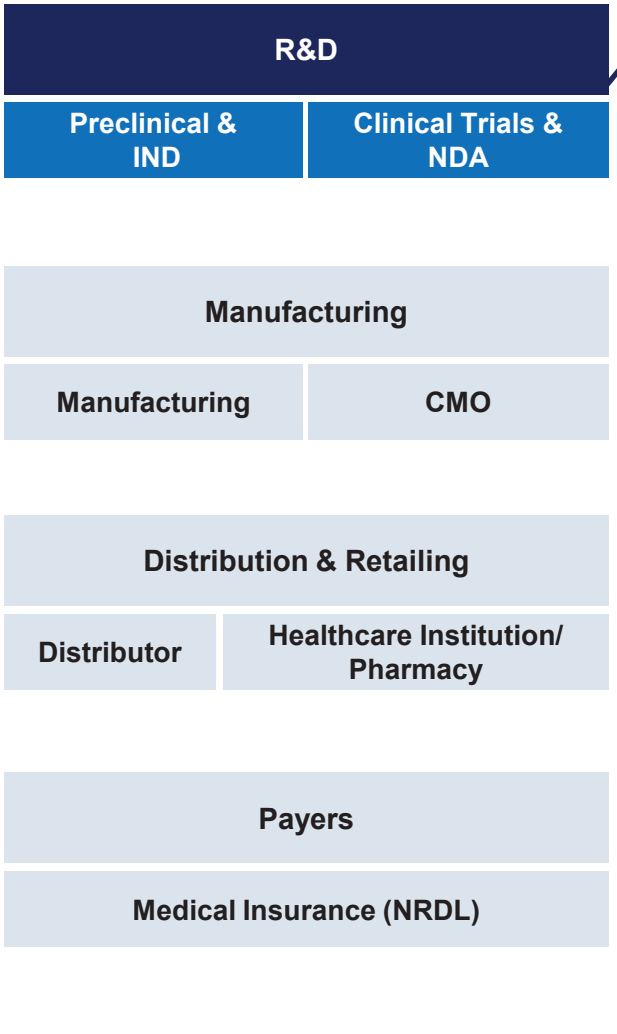
Influences

- The enforcement of self-inspection and inspection of clinical trial data indicates that the government has sped up its campaign to improve the quality of domestic pharmaceutical R&D, encourage innovation and promote fair competition.
- In addition, this measure will also shrink the backlog of drug applications and accelerate drug application review.

Source: Government Website, Frost & Sullivan Analysis

China Systematic Reform on Pharmaceutical Industry

Reform of the Drug and Medical Device Review and Approval



Reform of the Drug and Medical Device Review and Approval

《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》

	Before	Now
Reforming clinical trial management	• Requiring lengthy approval for clinical trial applications ***(12-18 months)***	• Implied CTA approval**(60 days)** • Accepting clinical trial data generated abroad
Accelerating Review and Approval	• Lengthy review and approval process • APIs and formulations are approved separately	• Priority review • Enabling conditional approval • Linked approval of formulation and API, excipients and packaging • Leveraging electronic common technical document (**eCTD**) for NDA review
Realizing Global Application	• A drug must be in a Phase II or Phase III clinical study or has received marketing authorization abroad before it can begin an international multi-center trial ("IMCT") in China	• Accepting foreign clinical data • Removing restrictions on clinical trials and registrations for imported drugs
Protection of Innovators	• Patent declaration system	• Patent linkage system • Drug patent term compensation system • Innovator's data protection • MAH program

Source: Government Website, Frost & Sullivan Analysis

China Systematic Reform on Pharmaceutical Industry

Marketing Authorization Holder (MAH)

R&D

Preclinical & IND	Clinical Trials & NDA

Manufacturing

Manufacturing	CMO

Distribution & Retailing

Distributor	Healthcare Institution/ Pharmacy

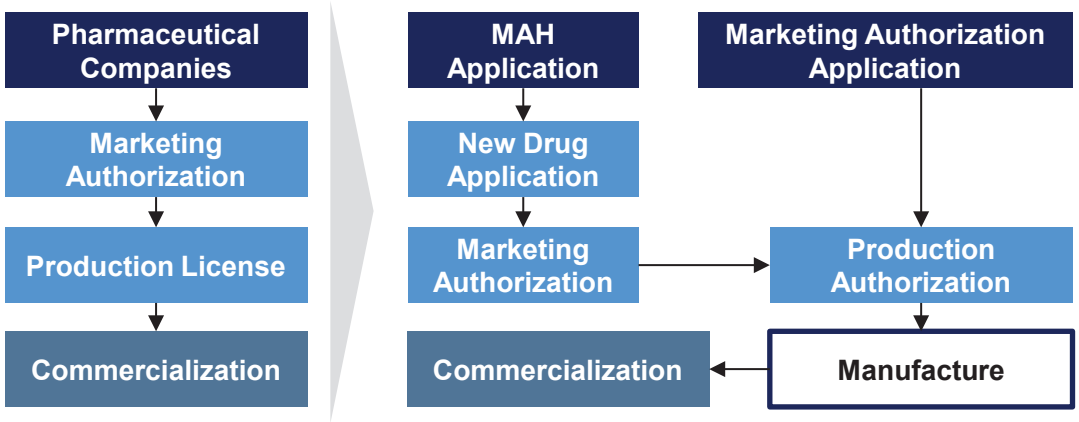
Payers

Medical Insurance (NRDL)

Marketing Authorization Holder (MAH)

《国务院办公厅关于印发药品上市许可持有人制度试点方案的通知》

Evolution of MAH System in China



- MAH system enables the R&D organizations or personnel to apply and obtain drug marketing authorizations and drug approval license, and the MAHs can entrust the CMOs to manufacture drugs instead of obtaining production license themselves, so that they can focus on R&D rather than allocate the manpower and investment on manufacturing.
- MAH system helps promoting R&D innovation, accelerating industrial restructuring and optimizing resource allocation.

Source: Government Website, Frost & Sullivan Analysis

China Systematic Reform on Pharmaceutical Industry

Good Manufacture Practice of Medical Products

R&D

Preclinical & IND	Clinical Trials & NDA

Manufacturing

Manufacturing	CMO

Distribution & Retailing

Distributor	Healthcare Institution/ Pharmacy

Payers

Medical Insurance (NRDL)

Good Manufacture Practice of Medical Products
《药品生产质量管理规范》

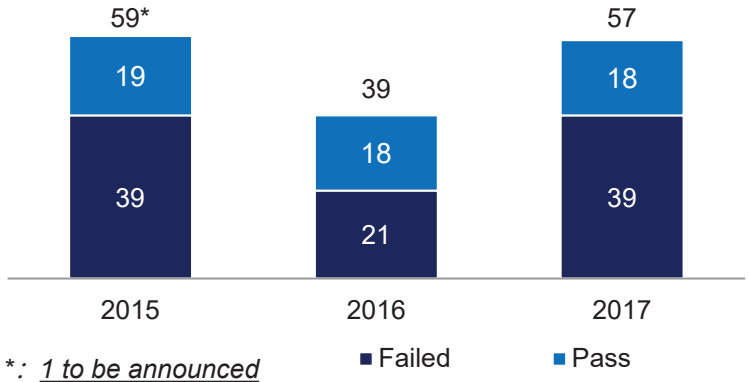
Features of New GMP

Introduction of Quality Risk Management	Enhancing Qualifications of Key Personnel
Fortifying Management of Marketed Drugs	Consistency of Drug Manufacturing and Registration

Unannounced Inspection
《药品医疗器械飞行检查办法》

- Unannounced inspection covers the whole value chain of pharmaceutical industry value chain. It aims to find any non-compliance activities of GLP, GMP, GSP etc.

Unannounced Inspection Status, 2015-2017



Pass Rate	
2015	32.2%
2016	46.2%
2017	31.6%

*: *1 to be announced*

Source: Government Website, Frost & Sullivan Analysis

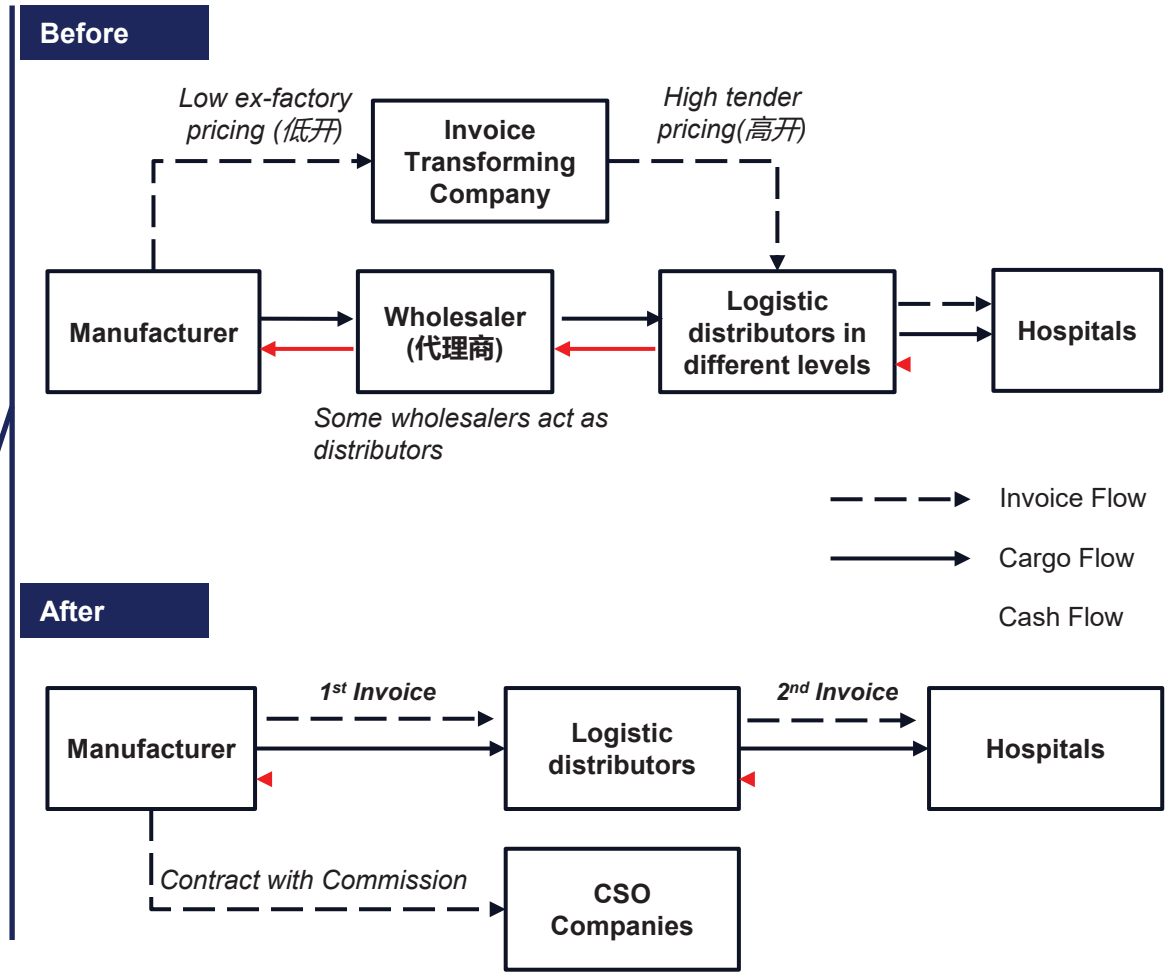
China Systematic Reform on Pharmaceutical Industry

Two-Invoice System

R&D
Preclinical & IND / **Clinical Trials & NDA**
Manufacturing
Manufacturing / **CMO**
Distribution & Retailing
Distributor / **Healthcare Institution/ Pharmacy**
Payers
Medical Insurance (NRDL)

Two-Invoice System

《关于在公立医疗机构药品采购中推行“两票制”的实施意见（试行）的通知》



Source: Government Website, Frost & Sullivan Analysis

China Systematic Reform on Pharmaceutical Industry

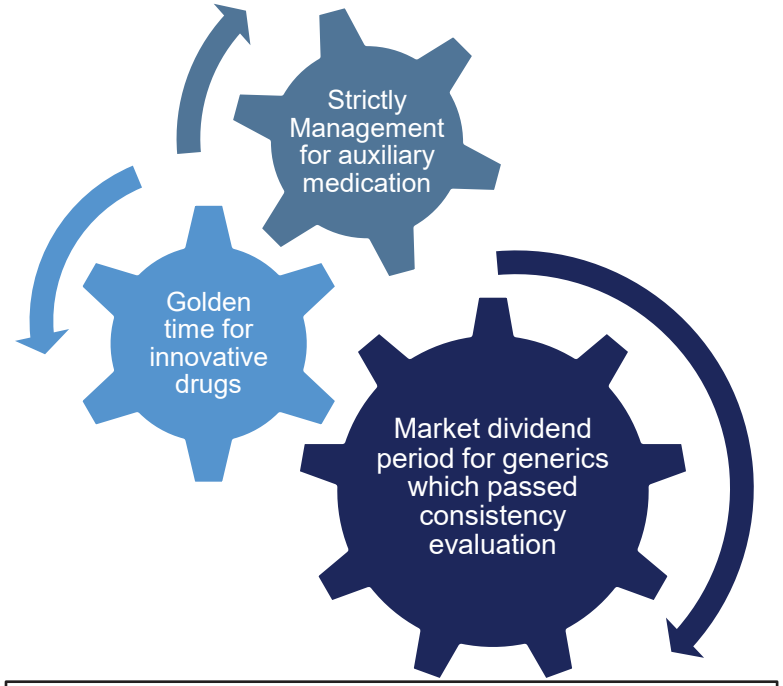
Centralized Procurement of Drugs

R&D	
Preclinical & IND	**Clinical Trials & NDA**
Manufacturing	
Manufacturing	**CMO**
Distribution & Retailing	
Distributor	**Healthcare Institution/ Pharmacy**
Payers	
Medical Insurance (NRDL)	

Centralized Procurement of Drugs

《国务院办公厅关于印发国家组织药品集中采购和使用试点方案的通知》

Centralized Procurement of Drugs Benefits



- Through price for quantity, pharmaceutical companies can obtain as high as 60%~70% of total annual drug deals of the public healthcare institutions in pilot cities.

Pilot City	
Beijing	4
Shanghai	
Tianjin	
Chongqing	
Guangzhou	7
Shenzhen	
Shenyang	
Dalian	
Xi'an	
Chengdu	
Xiamen	

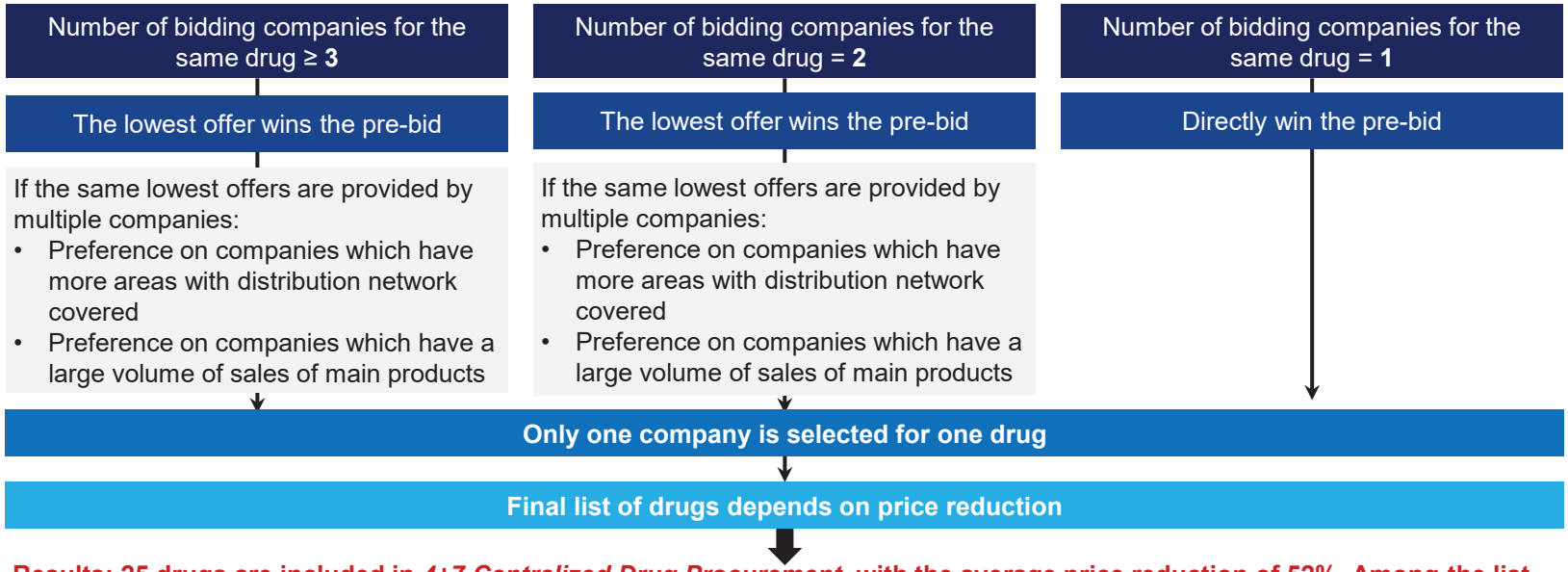
Source: Government Website, Frost & Sullivan Analysis

Centralized Drug Procurement in China

Phase 1 of 4+7 centralized drug procurement

- In China, *Centralized Drug Procurement* (《药品集中采购》) is a pilot scheme issued by the government. Public health institutions are required to determine the drug procurement quantity and procurement cycle, and purchase the drug with the same price by open tendering. In Dec 2018, 11 cities in China were included in the *4+7 Centralized Drug Procurement* (《4+7城市药品集中采购文件》), which had a significant influence on Chinese pharmaceutical market.

Illustration on Determination of Drugs for *4+7 Centralized Drug Procurement*



Results: 25 drugs are included in *4+7 Centralized Drug Procurement* with the average price reduction of 52%. Among the list, 23 are generic drugs, 2 are post-LOE originators.

Implication for the market:

- **High quality drug preference**: In this round of bidding, only generics passing GCE and post-LOE originals can participate.
- **Potential elimination of small to mid-sized pharmas:** companies able to survive in the long run could be those with extensive drug portfolio, cost-saving capability, brand recognition and track record for good quality.
- **Incentive of price for volume**: total 25 out of 31 drug win the biddings with the average price reduction by over 50%.

Source: Official government website, Frost & Sullivan Analysis

Expanding Centralized Drug Procurement in China

Phase 2 of 4+7 centralized drug procurement

- In Sept. 2019, Shanghai published *Document of centralized drug procurement in alliance area (《联盟地区药品集中采购文件》)*. It was reported that 25 provinces will be included in *Centralized Drug Procurement* with 25 kinds of drugs, which representing *Centralized Drug Procurement* will be significantly enlarged in 2020.
- In November 2019, China has made clear 24 goals in medical reform, according to a circular *(《国务院深化医药卫生体制改革领导小组关于进一步推广福建省和三明市深化医药卫生体制改革经验的通知国医改发〔2019〕2号》)* recently issued by the State Council's health reform leading group.

Immediate Impact

- Because of the intended quantity commitment for each bid-winning drug, the healthcare institutions will procure the bid-winning drugs with the priority and doctors will prescribe the drugs to meet the quantity commitment. As a result, the sales volume of the drug will sharply increase, consequently gaining the market share of total volume despite of the average selling price erosion.

Medium-term Impact

- Typically, Chinese pharmaceutical manufacturers have a sales and marketing expense of 20%~50%, but can be up to 75% in some particular cases. With the implementation of *Expanding Centralized Drug Procurement* causing the price reduction of drugs, pharmaceutical companies must dramatically reduce the sales and marketing expense in order to stay profitable.

Key implication:

- Recent policies called for promoting the experience of medical reform in eastern China's Fujian Province and its city of Sanming, which coordinates medical service, medical insurance and pharmaceutical reforms.
- These regulations are stepping up reform on procurement of medicine and medical consumables and revising the price of medical service dynamically and in a timely manner.
- The centralized drug procurement is favorable to pharmaceutical companies with large production capacity and mature technology for high quality drugs.

Source: Official government website, Frost & Sullivan Analysis

National Centralized Drug Procurement in China

Round 8

- The 1st round (phase 1&2) national centralized drug procurement is progressing smoothly. The purchase execution exceeded expectations and the agreed purchase volume was completed in advance. By the end of December 2019, the average procurement progress among the 25 selected drugs had reached 183%, accounting for 78% of the total procurement volume of drugs with same generic names.
- The burden on patients has been significantly reduced and the quality of drug use has been improved, with positive results achieved. In order to further benefit more patients, the 8th round of national centralized drug procurement began on March 29th, 2023. This slide will elaborate the possible impact it has.

Therapeutic areas covered

- It is reported that the 8th round of centralized procurement covers various fields of drugs such as anti-infective, heparin, anti-thrombotic, cardiovascular drugs, anti-allergy drugs and mental health drugs. The current round of national centralized procurement involves the largest number of antibiotic varieties, with 14 systemic antibiotics being included, accounting for 35% of the total types of drugs. In this round, 252 products were qualified, approximately 40% of which were antibacterial drugs.

Timetable

- The eighth round of national procurement involves a total of 39 major categories of products, and the bidding took place in Hainan on March 29th.

Achievements obtained

- Since 2018 to the 8th round of centralized procurement, the National Healthcare Security Administration has organized and carried out seven rounds of centralized procurement, involving 333 types of drugs with an average price reduction of over 50%.
- In the 8th round of centralized procurement, more than 200 enterprises participated in the bidding, and 148 were successful.

Influences

- The 8th round of centralized procurement includes the largest number of antibacterial drugs, most of which are injections. This is expected to effectively curb the problem of antibiotic abuse in hospitals. Besides, two major varieties of heparin drugs, including nadroparin calcium injection and enoxaparin sodium injection, with a total of 20 specifications. The current round of national centralized procurement involves 252 specializations, and the average price reduction reaches 56%, estimated to be able to cut down 16.7 billion RMB per year.

Source: Frost & Sullivan Analysis

National Centralized Drug Procurement in China

Round 9

- The 1st round (phase 1&2) national centralized drug procurement is progressing smoothly. The purchase execution exceeded expectations and the agreed purchase volume was completed in advance. By the end of December 2019, the average procurement progress among the 25 selected drugs had reached 183%, accounting for 78% of the total procurement volume of drugs with same generic names.
- The burden on patients has been significantly reduced and the quality of drug use has been improved, with positive results achieved. The 9th round of national centralized drug procurement began on August 28th, 2023. Two anti-bacterial drugs have been involved in, which are Cefotiam hydrochloride for injection and Azithromycin suspension. This slide will elaborate the possible impact the 9th round has. The latest round (10th) of national centralized drug procurement has begun, which is Insulin renewal.

Therapeutic areas covered

- It is reported that the 9th round of centralized procurement covers various fields of drugs such as cardiovascular disease drugs, anti-tumor drugs, anti-infective, drugs, digestive system drugs, mental health medications, etc..

Achievements obtained

- Since 2018 to the 9th round of centralized procurement, the National Healthcare Security Administration has organized and carried out seven rounds of centralized procurement, involving 374 types of drugs with an average price reduction of over 50%.
- In the 9th round of centralized procurement, more than 260 enterprises participated in the bidding, and 205 were successful.

Timetable

- The 9th round of national procurement involves a total of 41 major categories of products.
- Patients were able to use the drugs involved in 9th round of national procurement in March 2024.

Influences

- The 9th round of national centralized procurement involves 270 specializations, and the average price reduction reaches 58%, estimated to be able to cut down 18.2 billion RMB per year.

Source: Frost & Sullivan Analysis

Zero-markup Drug Policy

Policy Evolvement	Execution Outcome
1954 Establishment of drug markup policy • Hospitals were allowed to add 15% drug markup to make up for the lack of financial subsidies.	• Hospitals prescribed high price drugs to obtain revenue, increasing the economic burden of patients.
2009 NDRC Implementation opinions on the establishment of basic pharmaceutical system 《关于建立国家基本药物制度的实施意见》 • Zero markup drug policy began to be implemented in primary medical and health institutions.	• Due to the lack of government subsidies and the shortage of basic drugs, the implementation effect is not ideal.
2012 NDRC Notice on promoting pharmaceutical price reform in county level public hospitals 《关于推进县级公立医院医药价格改革工作的通知》 • Zero markup drug policy began to be implemented in county level institutions.	• Drugs changed from the source of income to the source of cost. Therefore, hospitals had to purchase drugs independently, so their bargaining power became stronger.
2017 NDRC Notice on promoting the comprehensive reform of public hospitals 《关于全面推开公立医院综合改革工作的通知》 • Zero markup drug policy began to be implemented in all institutions.	• All public hospitals at all levels in China had ended the drug markup before the end of September, 2017.

Policy Impact for Stakeholders

Patients

- Reduce medical expenditure, soothing the nervous relationship between patients and doctors

Hospitals

- Reduce revenue and increase funding gap
- Lead to the transition of “depending on the drug as main revenue source ”to “depending on the medical skill as main revenue source

Medical Insurance System

- Reduce medical insurance expenditure and expand coverage

Healthcare System

- Conducive to the return of public welfare of public medical institutions

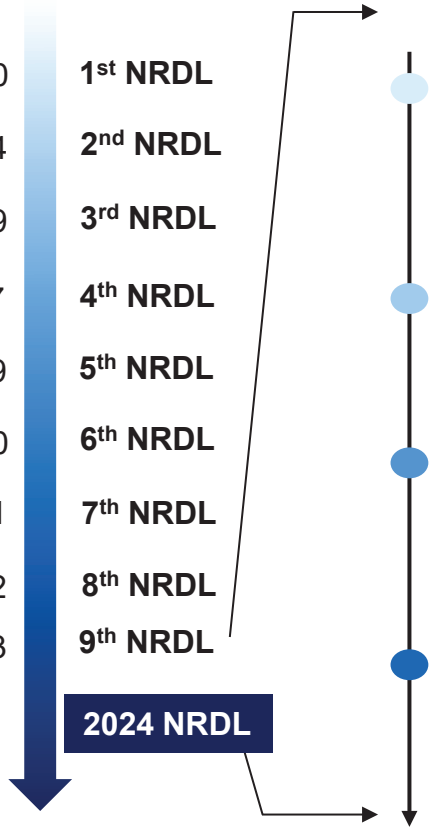
Source: NDRC, Frost & Sullivan Analysis

Analysis of Healthcare Reimbursement System in China

Recent Progress and Impact of the 2024 NRDL

- In the 2024 NRDL, 91 drugs were newly included in the list, with a price reduction of 63%. The inclusion of numerous domestic innovative drugs has significantly promoted the sales of innovative drugs and the transformation of Chinese pharmaceutical industry to innovation.

Progression of NRDL



Recent Progression of 2024 NRDL

- In Dec 2024, NHSA and MOHRSS finished the work for the adjustment of the 2024 NRDL, and the 2024 NRDL will implement from Jan 1st 2024. The 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 89 of them were smoothly negotiated. 91 kinds of drugs have been newly included in NRDL for the first time, leading to a 63% decline in prices.
- 1 previously included drugs were removed from the list, all of which are the varieties that have been cancelled by the NMPA.
- indicating the government Anti-tumor drugs, rare disease drugs and anti-virus drugs have been newly included, such as Ivonescimab and Livtencity, is speeding up the review and approval of innovative drugs, urgently clinically needed drugs and rare disease treatment drugs.

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.

2024 NRDL restricts the price of drugs strictly by adding rules for non-exclusive drug bidding. If a drug is included in the list through bidding, the lowest price quoted by each enterprise shall be taken as the payment standard for the generic name drug.

Numerous domestic innovative drugs were included by 2024 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 2024 NRDL plans can be included in the adjustment scope.

Source: MORHSS, Frost & Sullivan Analysis

Growth Driver and Future Trend of China Pharmaceutical Market

Growth Drivers of China Pharmaceutical Market

Increasing Disposable Income

- With the economic development, the 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

- Due to declining metabolism and immune capacities of elder people, they are more likely to suffer from chronic diseases. Aging population reached 200.6 million in 2021, accounting for 14.2% of the total population.

Favorable Policies

- Chinese government has promulgated a series of policies to encourage R&D, as well as strengthened the regulation on pharmaceutical market, which will lead to a more efficient and disciplined pharmaceutical market with healthy competition and sustainable development.

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, China pharmaceutical market is shifting towards an innovative-driving market. Also, the government promulgated a series of policies to encourage R&D.

More Biotech Companies to Get Involved

- Due to strong support from government, capital investment and talent reserve, biotech companies are expected to play a more important role in pharmaceutical market with their innovative drugs under clinical development and to be launched in the near future.

Alignment with International Standard

- China has joined the ICH as the 8th member, which suggests the onset of alignment of the pharmaceutical industry practices with international standards, indicating an effort to realize higher and unified standard drug application and registration process.

Source: Frost & Sullivan Analysis

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5	Hematology Drug Market in China
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7	Breast Cancer Drug Market in China

Introduction of Infectious Disease

Definition	• Infection is the invasion of an organism's body tissues by disease-causing agents, their multiplication, and the reaction of host tissues to these organisms and the toxins they produce. Infectious disease, also known as transmissible disease or communicable disease, is illness resulting from an infection.

Classification	• Infections are caused by microorganisms. According to the infectious disease pathogens in nature, infectious disease can be classified as
	  • Bacteria: cholera, plague, dysentery, staphylococcal and streptococcal infections, salmonella, meningitis;
	  • Viruses: measles, influenza, parainfluenza, HIV, viral hepatitis, meningitis, cytomegalovirus infection;
	  • Mycosis (fungal infection): athlete, aspergillosis, candidiasis, mucormycosis, cryptococcosis;
	  • Others: Prions and Protozoal.

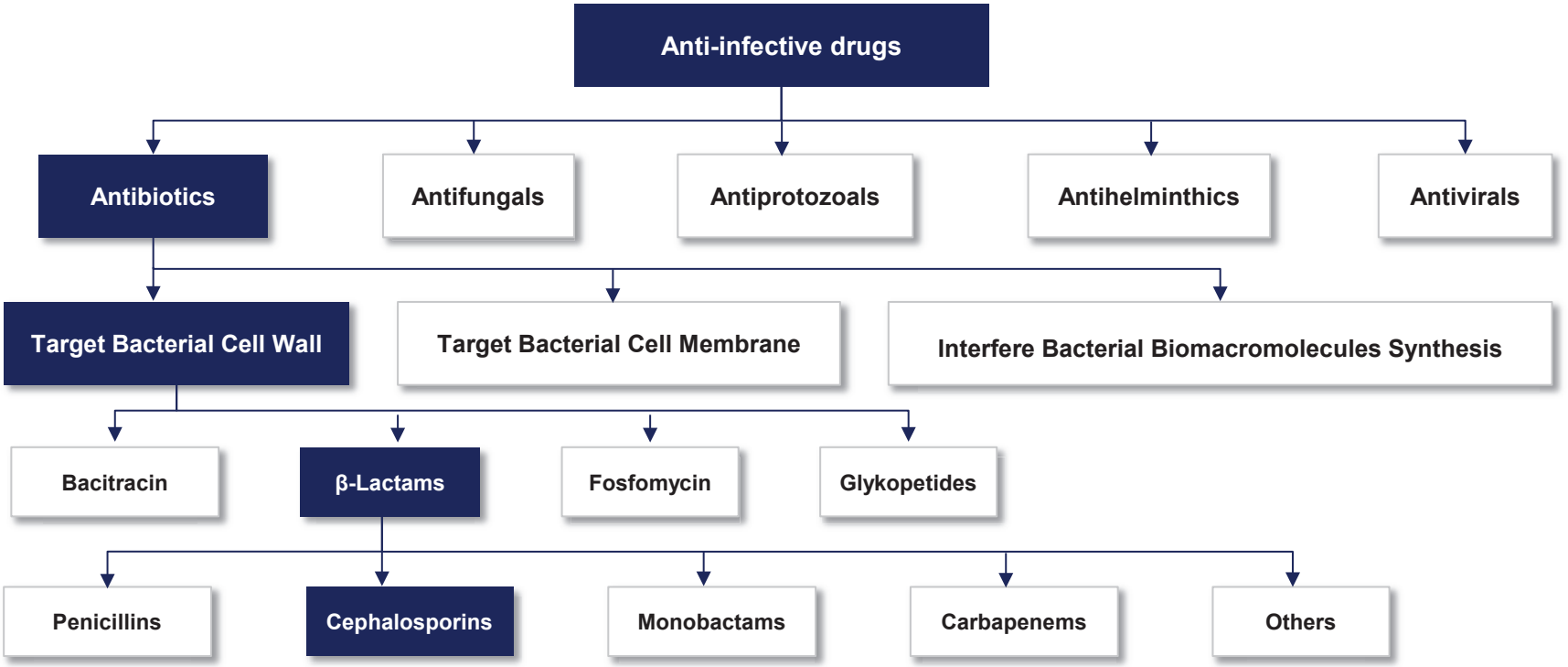
Mechanism	• Microorganisms cause disease in the course of stealing space, nutrients, and/or living tissue from their symbiotic hosts. To do this, microbes do most of the following:
	  • Gain access to the host (contamination)
	  • Adhere to the host (adherence)
	  • Replicate on the host (colonization)
	  • Invade tissues (invasion)
	  • Produce toxins or other agents that cause host harm (damage)

Clinical Response	• Inapparent infection – no clinical symptoms generated • Carrier state – usually no clinical symptoms but host can transmit infection for long periods • Clinical symptoms: mild disease, severe disease, residual impairment and death
Transmission Modes	• Infectious disease can be spread via direct transmission including aerosol, skin-to-skin contact and/or indirect transmission like fomites (clothes, door handles etc.), vectors (e.g. mosquitoes) and intermediate hosts (e.g. snails) etc.

Source: Frost & Sullivan Analysis

Introduction of Infectious Disease

- Anti-infectives is a group of drug to kill or inhibit different kinds of pathogenic microbes though oral, intramuscular injection intravenous injection or topical use. Anti-infectives are widely used in all kinds of infection disease and complication triggered by other disease. As one of the most popular categories of clinical drug, there are a variety of anti-infectives. It can be classified into following general categories:



Source: Frost & Sullivan Analysis

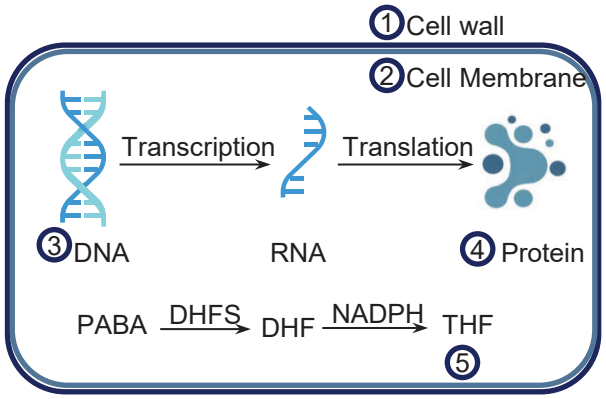
Introduction of Anti-infective Drugs

Antifungal	• Antifungal can be classified into three categories: targeting synthesis of sterols like Imidazole; targeting cell wall synthesis like echimocandin and targeting nucleic acid synthesis like 5-fluorocytosine.
Antibacterial	• Antibacterial may either kill or inhibit the growth of bacteria. A limited number of antibiotics also possess antiprotozoal activity. Antibacterials are commonly classified based on their mechanism of action. Those that target the bacterial cell wall like penicillins or the cell membrane like polymyxins or interfere with essential bacterial enzymes like rifamycins have bactericidal activates. • Antibiotics revolutionized medicine in the 20th century. However, their effectiveness and easy access have also led to their overuse, prompting bacteria to develop resistance. This has led to widespread problems.
Antiviral	• Antiviral drugs are a class of medication used specifically for treating viral infections. Most antivirals are used for specific viral infections, while a broad-spectrum antiviral is effective against a wide range of viruses. Unlike most antibiotics, antiviral drugs do not destroy their target pathogen; instead they inhibit their development.
Other types	• Other types of anti-infectives like targeting chlamydia, mycoplasma, worm or rickettsia. Those factor can trigger infection as well.

Source: Frost & Sullivan Analysis

Overview of Antibacterial Drugs

- Bacteria are a type of biological cell. Typically a few micrometres in length, bacteria have a number of shapes, ranging from spheres to rods and spirals. Bacteria have basic structures such as cell wall, cell membrane, cytoplasm and nucleoplasm, and some bacteria also have special structures such as capsule, flagella, fimbria and spores. Bacteria are the causative agent of many diseases, and can spread diseases among normal human body through various methods, such as contact, digestive tract, respiratory tract, insect bites, etc., with strong infectivity and great harm to society.
- Antibiotics are a type of antimicrobial substance active against bacteria. It is the most important type of antibacterial agent for fighting bacterial infections, and antibiotic medications are widely used in the treatment and prevention of such infections.



The basic structure of Bacterial

Target and Action	Representative Drugs
1. Cell Wall Construction	
Inhibit synthesis of cell wall by inhibiting formation of the peptidoglycan layer, dephosphorylation of C55-ip or inactivating the MurA	β-lactams, Glykopetides, Bacitracin, Fosfomycin
2. Structure and Function of Cell Membrane	
Disrupt both the outer and inner membranes	Colistin, Polymyxin B
3. Structure and Function of DNA	
Prevent DNA from unwinding and duplicating	Quinolones, Nitrofurantoin
4. Protein Synthesis	
Truncate the biosynthesis of proteins by disturbs peptide elongation at the ribosomal subunit, giving rise to inaccurate mRNA translation	Aminoglykosides, Lincosamide, Makrolides, Oxazolidone, Tetracyclines
5. Folic Acid Synthesis	
Inhibit synthesis of folic acid by inhibiting interfering with the enzyme DHPS	Sufonamides, Trimethoprim

Source: Frost & Sullivan Analysis

Introduction of Antibacterial Drugs - I

MOA	Classification	Introduction	Main Target	Drugs
Cell wall synthesis blockade	Penicillin	Penicillin is used to treat gram positive cocci infection like hemolytic streptococcus, streptococcus pneumoniae. It can also treat for streptococcus viridians and enterococcus endocarditis.	G+/G-	Amoxicillin，Methicillin, Piperacillin
	Cephalosporin	Mainly applied to methicillin sensitive staphylococcus aureus. Upper and lower respiratory tract infection, urinary tract infection, bloodstream infections, endocarditis, bone/joint infection and skin/soft tissue infection caused by streptococcus pneumoniae. Can be used for serious infections caused by gram negative bacilli like lower respiratory tract infection, blood stream infection, abdominal cavity infection, pyelonephritis and complicated urinary tract infection, pelvic inflammatory disease, joint infection, etc. The fourth generation cephalosporin have good effect to both gram negative and positive bacteria. Cephalosporins are perceived as the most established mechanism of action in the anti-bacterial drug.	G+; G+/G-	Cefaclor, Cefpirome, Cefalexin, Ceftazidime
	Carbapenem	Last resort of medicine for Infection caused by aerobic gram negative multiple resistant bacteria, include klebsiella pneumonia, escherichia coli, enterobacter cloacae, citrobacter, serratia marcescens, etc.	G+/G-	Imipenem, Ertapenem, Meropenem
	Lipopeptides	There are several sub-classes of lipopetides include Glycopeptide, Lipoglycopepide and other lipopeptide. A lipopeptide is a molecule consisting of a lipid connected to a peptide. Bacteria express these molecules. They are able to self-assemble into different structures. Lipopeptides are used as antibiotics. Certain lipopeptides can have strong antifungal and hemolytic activities. It has been demonstrated that their activity is generally linked to interactions with the plasma membrane, and sterol components of the plasma membrane could play a major role in this interaction.	G+	Vancomycin, Dalbavancin, Oritivancin, Daptomycin
Target folate metabolism	Sulfonamide	It inhibits bacterial growth by interfering with the folate metabolism of bacteria. Sulfonamide have similar structure with PABA (precursor of folate), and block PABA involved into next metabolism step, which will impact nucleic acids synthesis.	G+/G-	Sulfamethoxazole

Source: IDSA, Frost & Sullivan Analysis

Introduction of Antibacterial Drugs - II

MOA	Classification	Introduction	Main Target	Drugs
Ribosomal protein synthesis inhibitors	Macrolide	The macrocyclic esters can be irreversibly incorporated into the bacterial ribosomal 50 subunit, which selectively inhibit protein synthesis by blocking the effect of transpepsin and mRNA migration. It can be used for legionellosis	G+	Erythromycin, azithromycin
	Lincosamide	The Lincosamide antibiotics are able to bind to the 50S ribosomal subunit of the ribosome to prevent the prokaryotic translation, thus killing the bacteria. These drugs have good antimicrobial activity against gram-positive bacteria and anaerobic bacteria. Currently, streptococcus pneumoniae have high resistance to Lincosamide	G+	Lincomycin, Clindamycin
	Oxazolidinone	Oxazolidinone has demonstrated highly activity against antibiotic-susceptible and antibiotic resistat aerobic gram-positive pathogens. Oxazolidinone can stop the growth and reproduction of bacteria by disrupting translation of mRNA into proteins in the ribosome. It appears to work on the first step of protein synthesis, initiation, unlike most other protein synthesis inhibitors, which inhibit elongation. With high bioavailability in oral formulation and virtually no resistance, Oxazolidinone is considered as a reliable therapy to severe gram-positive pathogens especially MRSA and VRE.	G+	Linezolid Tedizolid
	Tetracyclines	In combination with the 30S ribosome, it block amino acid get into ribosome, thereby preventing the amino acid residues formatting peptide chains. Glycylcycline is a structural variant name of tetracycline with stronger affinity.	G+	Minocycline, Doxyccline, Tigecycline
	Streptogramin	Streptogramins are effective in the treatment of vancomycin-resistant Staphylococcus aureus (VRSA) and vancomycin-resistant Enterococcus (VRE), two of the most rapidly growing strains of multidrug-resistant bacteria.	G+	quinupristin-dalfopristin
	Aminoglycoside	It is used to treat medium to serious gram negative bacillus infection. Combine therapy for serious staphylococcus aureus (not first choice)	G-	Kanamycin, Tobramycin, Gentamycin
DNA topoiso-merase	Quinolone	Treat genitourinary infection caused by Pseudomonas aeruginosa; respiratory tract infection caused by gram negative bacillus like klebsiella pneumoniae. Methoxicillin sensitive staphylococcus aureus (MSSA).	G-	Gemifloxacin Moxifloxacin

Source: IDSA, Frost & Sullivan Analysis

4 Generations of Cephalosporin

1st generation

- **Nephrotoxicity:** More severe than other generation cephalosporins
- **β-Lactamase Stability:** Poor than other generation cephalosporins
- **Drug Resistance:** easy
- **Activity against G(-) Bacteria:** Worse antibacterial activity of most Gram-negative bacteria
- **Activity against G(+) Bacteria:** Greater than the second and third generation
- **Clinical Use:** Mainly used for Gram-positive bacteria such as penicillin-resistant Staphylococcus aureus

2nd generation

- **Nephrotoxicity:** Less than the the first generation cephalosporins
- **β-Lactamase Stability:** Better than first-generation cephalosporins
- **Activity against G(+) Bacteria:** Less than first-generation cephalosporins
- **Activity against G(-) Bacteria:** Greater than the first generation
- **Clinical Use:** enteritis, biliary tract infections, bacteremia and urinary tract infections caused by some sensitive bacteria

3rd generation

- **Nephrotoxicity:** Almost no nephrotoxicity
- **β-lactamase stability:** Very high stability
- **Activity against G(+) Bacteria:** Less than the first and second generation
- **Activity against G(-) Bacteria:** Broad spectrum of activity and further increased activity against gram-negative organisms
- **Pseudomonas aeruginosa:** Significant antibacterial activity
- **Clinical Use:** Severe urinary tract infection, drug-resistant G-bacterium infection, sepsis and meningitis

4th generation

- **β-lactamase stability:** Very high stability
- **Third-line antibacterial drugs:** Stringent regulations of use
- **Antibacterial spectrum:** extended-spectrum and activity against G(+) and G(-) Bacteria better than third-generation cephalosporins
- **Clinical Use:** Serious life-threatening infections of Gram-negative bacteria; many can cross the blood–brain barrier and are effective in meningitis

• First-generation cephalosporins are more effective against G(+) bacteria, though they also work against some G(-) bacteria.	• Second-generation cephalosporins target both G(+) e and G(-) bacteria. But they're a little less effective against G (+) bacteria compared to first-generation cephalosporins.	• Third-generation cephalosporins are effective against many G(-) bacteria and bacteria that haven't responded to first- or second-generation cephalosporins.	• Fourth-generation cephalosporins work against both G(+) and G(-) bacteria. They're generally used for more severe infections or for those with weakened immune systems.

Antibacterial spectrum of cephalosporins

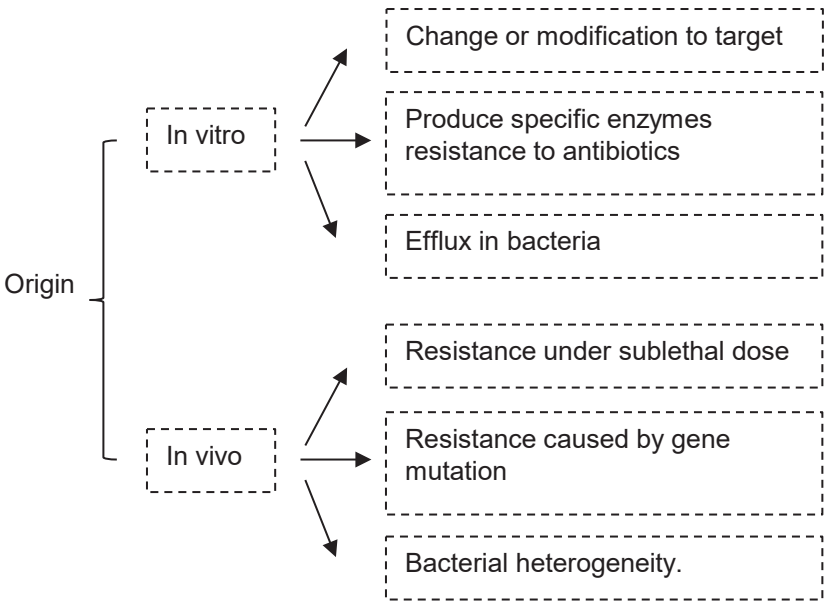
Source: Frost & Sullivan Analysis

Overview and Multi-drug Resistance (MDR)

Definition of MDR

- To survive and reproduce against new antibacterial drugs, bacteria constantly evolve and develop cross-resistance, resulting in the emergence of multidrug-resistant bacteria. Multidrug-resistant bacteria refer to the resistance of three or more types of antibacterial drugs, which is caused by repeated use of broad-spectrum antibacterial drugs to treat bacteria in the body and therefore, develop strong resistance.

Mechanisms of Resistance



Source: Frost & Sullivan Analysis

Main Types of MDR

- Vancomycin-resistant enterococci (VRE)
- Methicillin-resistant staphylococcus aureus (MRSA)
- Methicillin-resistant coagulase negative staphylococci (MRCNS)

What's MRSA?

- Staphylococcus aureus is an important pathogenic gram-positive bacterium in clinical practice. It can cause severe infections such as endocarditis, meningitis, sepsis, as well as common infections such as wounds, respiratory tract, and urinary tract infections. Methicillin-resistant Staphylococcus aureus (MRSA) is a strain of Staphylococcus aureus that has developed resistance to some antibiotics used to treat infections caused by Staphylococcus aureus. The spread of MRSA infection is a serious public health issue.

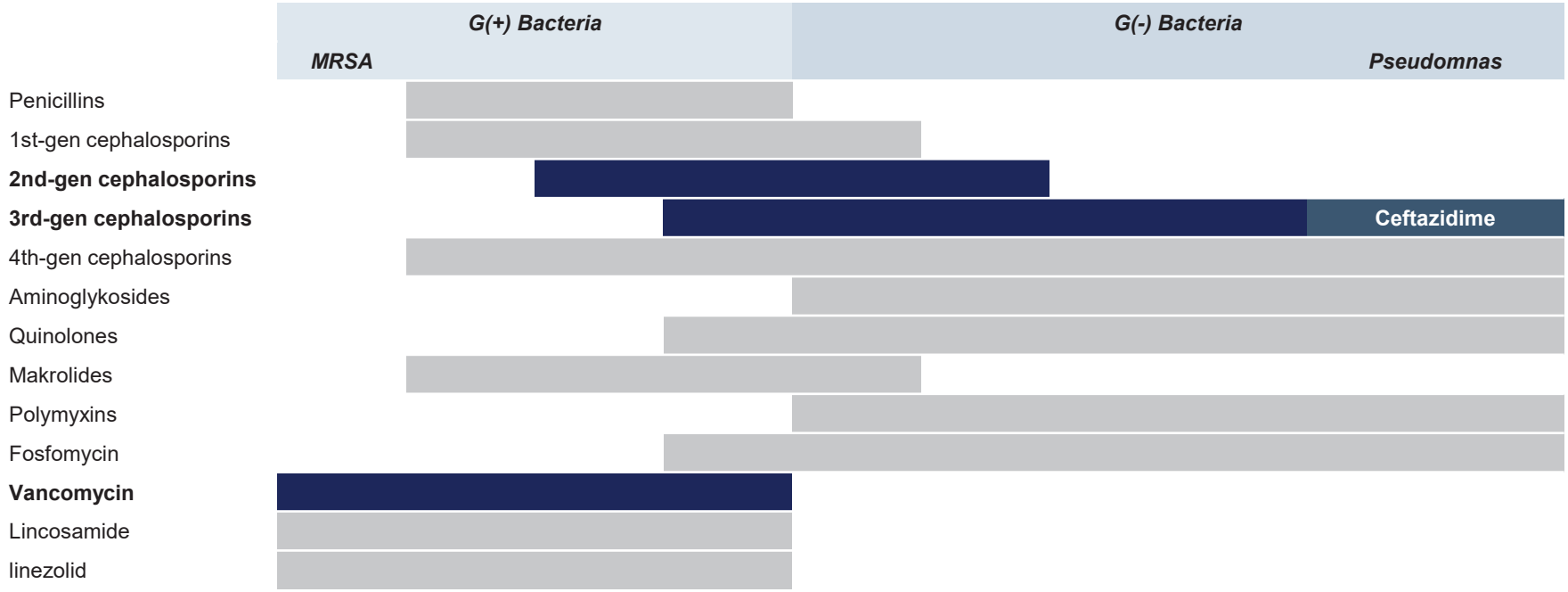
Mechanisms of MRSA Resistance

1. The decreased affinity with antibiotics reduces the ability of antibiotics to inhibit the synthesis of cell wall peptidoglycan. MRSA can produce a large amount of beta-lactamase, which can hydrolyze beta-lactam antibiotics. 2. Blocking the binding of vancomycin to the target sites on the peptidoglycan precursor, thus leading to vancomycin resistance. 3. Multi-drug resistant possibility.

Spectrum of Representative Antibacterial Drugs

- The 1st generation and 2nd generation cephalosporins, classified as unrestricted-use antibacterial drugs, not only are applicable to most tissue infections, endocarditis caused by MSSA, group A hemolytic streptococcus and pneumococcus, but also are widely used in perioperative prevention.
- Ceftazidime is the only drug in 3rd–generation Cephalosporins which is effective in *Pseudomnas* infection.
- Vancomycin is considered as the last defense against severe infections that are ineffective against all antibiotics, such as “superbugs”-methicillin-resistant Staphylococcusaureus infections(MRSA).

Spectrum of Representative Antibacterial Drugs



Guidelines for Clinical Use of Antibacterial Drugs.v2015

Only part of the representative drugs are listed.

Source: Frost & Sullivan Analysis

National Regulations of China Antibacterial Drug Market - I

- Due to increasing anti-infectives abuse and severer bacterial resistance, China government has been consistently introducing laws, regulations and policies to guide rational anti-infectives clinical use and restrict clinical abuse since 2004. The following table sets forth primary related regulations and policies which were issued since 2004:

2004

Guiding principles for the clinical use of antibacterial drugs
《抗菌药物应用指导原则》

- Correct and reasonable clinical application of antibacterial drugs should base on the following two aspects: 1) the presence of indications of antimicrobial drugs; 2) correct and reasonable drug categories and dosage regimen.

2005

Establishment of surveillance networks on the clinical use of antibacterial drugs and bacterial resistance
建立抗菌药物临床应用及细菌耐药监测网

- The NHFPC firstly announces on establishing a national surveillance network for the clinical use of antibacterial drugs and bacterial resistance. And 109 hospitals are engaged in the pilot program.

2006

Notice on further improving the surveillance networks on clinical use of antibacterial drugs and bacterial resistance from the General Office of the Ministry of Health*
卫生部办公厅关于进一步做好抗菌药物临床应用和细菌耐药监测工作的通知

- All hospitals managed or affiliated by the Ministry of Health shall be listed in the pilot long-list of the two surveillance networks.

2008

Notice on further strengthening the administration of the clinical use of antibacterial drugs from the General Office of the Ministry of Health*
卫生部办公厅关于进一步加强抗菌药物临床应用管理的通知

- Strengthen the management of perioperative preventive use of antibacterial drugs, fluoroquinolone drugs. Strengthen the guidance and supervision of the clinical use of antibacterial drugs according to the regulations from antibacterial drug classification management system.

2009

Notice on related issues about further strengthening the administration of the clinical use of antibacterial drugs from the General Office of the Ministry of Health
卫生部办公厅关于抗菌药物临床应用管理有关问题的通知

- Emphasize the importance of administration of the clinical use of antibacterial drugs.

** Ministry of Health is renamed into National Health and Family Planning Commission, namely NHFPC.*

Source: Government Documents, Frost & Sullivan Analysis

National Regulations of China Antibacterial Drug Market - II

2012

Administrative measures for the clinical use of antibacterial drugs
《抗菌药物临床应用管理办法》

- The regulation is issued by the NHFPC to standardize administration of the clinical use of antibacterial drugs, which expressly illustrate the three-level antibacterial drug classification management system. Provincial antibacterial drug lists should be formulated and drugs can be prescribed by qualified doctors. Medical institutions shall strictly control the types and amount of antibacterial drugs in supply.

Notice on strengthening the surveillance of clinical use of antibacterial drugs and bacterial resistance
关于加强抗菌药物临床应用和细菌耐药监测工作的通知

- Expand the surveillance network of clinical use of antibacterial drugs and bacterial resistance to 1,349 class II and Class III hospitals.

2013

Notice on further conducting the special campaign of the clinical use of antibacterial drugs
关于进一步开展全国抗菌药物临床应用专项整治活动的通知

- Consolidate and expand the management of clinical use of antibacterial drugs.

2014

Notice on further efforts on implementing the administration of the clinical use of antibacterial drugs in 2014, from the NHFPC General Office
国家卫生计生委办公厅关于做好2014年抗菌药物临床应用管理工作的通知

- Improve management of clinical use of antibacterial drugs in class II hospitals and primary medical institutions.

2015

Notice on releasing a special plan to further improve the medical services
关于印发进一步改善医疗服务行动计划的通知

- The antibacterial drug utilization rate of inpatients shall not be more than 60% and total antibacterial drug dosage in 100 patients per day shall be under 40 DDDs (Defined Daily Doses) in general hospitals by 2017. The indicators in other hospitals shall meet the standard of clinical application of antibacterial drugs.

Guiding principles for the clinical use of antibacterial drugs, 2015 version
《抗菌药物应用指导原则（2015年版）》

- The Principles give the detailed instructions on the clinical use of antibacterial drugs for the therapeutic and preventive purpose. The indications and precautions of various antibacterial drugs are summarized accordingly as well. The Principle requires all medical institutions to establish the management system of the clinical use of antibacterial drugs.

** Ministry of Health is renamed into National Health and Family Planning Commission, namely NHFPC.*

Source: Government Documents, Frost & Sullivan Analysis

National Regulations of China Antibacterial Drug Market - III

2016

Notice for the National Action Plan for Curbing Bacterial Resistance (2016-2020)
关于印发遏制细菌耐药国家行动计划（2016-2020年）的通知

- Encourage the research and development of antimicrobial drugs and new anti-infective drugs, equipment and vaccines.
- Strengthen the supervision and control over the development, production, distribution, application and environmental protection of antimicrobial drugs.
- Standardize the clinical use management of antibiotics.

2017

Notice for Further Strengthening the Management of Antibacterial Drugs to Curb Bacterial Resistance, from the NHFPC General Office
国家卫计委办公厅关于关于进一步加强抗菌药物临床应用管理遏制细菌耐药的通知

- Strengthen the relevant requirements, according to the weakness in the implement of antibacterial drug clinical use.

2018

Notice for Continually Improving the Management of Antibacterial Drugs Clinical Use
关于持续做好抗菌药物临床应用管理有关工作的通知

- Continue to strengthen the management and conventions of key clinical use of antibacterial drugs, especially the usage on children and elderly people.
- Further strengthen the clinical application management of antibiotics.
- Reduce unreasonable preventative use and intravenous infusion of antibiotics.

2022

Notice for the National Action Plan for Curbing Bacterial Resistance (2022-2025)
关于印发遏制细菌耐药国家行动计划（2022-2025年）的通知

Aims as follows：

- The incidence of both drug-resistant infections within healthcare facilities and community-acquired drug-resistant infections continues to decline.
- The drug resistance rates of major human and animal pathogens continuously decrease or the rate of drug resistance growth slows down.
- The awareness of urban and rural residents regarding the issue of anti-bacterial drug resistance and the accuracy of knowledge regarding infection prevention and regarding rational use of antimicrobial drugs reach 80%, while the accuracy of their use behavior reaches 60%.
- The appropriate prescription rate of antimicrobial drugs for outpatient and inpatient treatment in secondary and above healthcare institutions nationwide reaches over 75%.
- The proportion of retails selling antimicrobial drugs based on prescriptions reaches 100%.

Source: Government Documents, Frost & Sullivan Analysis

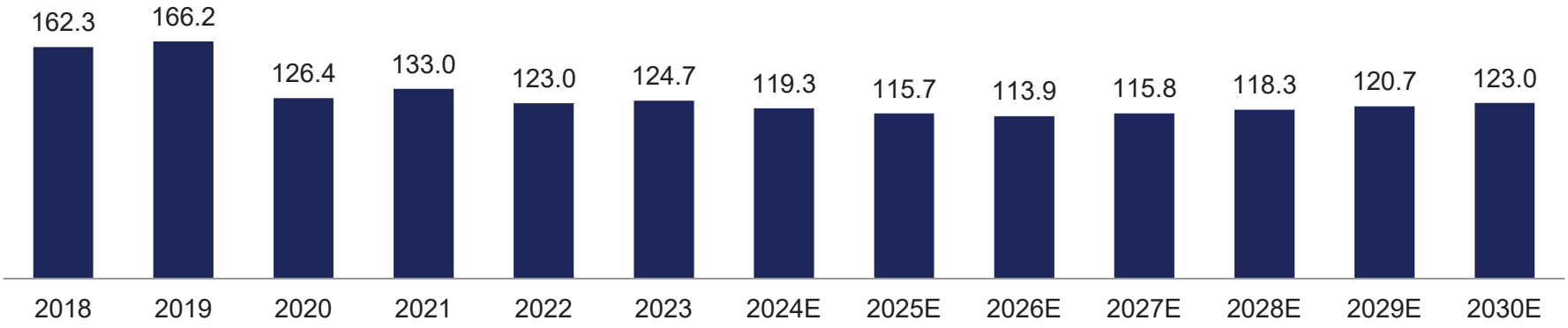
China Anti-bacterial Drug Market, 2018-2030E

- China anti-bacterial market size dropped to 126.4 billion RMB in 2020 for two main reasons. For one thing, it is because of a sharp decrease in the number of in-patient and out-patient visits caused by Covid-19. When Covid-19 pandemic ends, the number of outpatient visits is estimated to increase, and China's anti-bacterial drug market will recover in few years. For another, several anti-bacterial drugs had been involved the national centralized drug procurement in 2020, leading to substantial price cuts and lowered profit margins for generic drugs, thus influencing the whole market size.
- In order to address increasing anti-bacterial drug abuse and evolving bacterial resistance, the PRC government implemented a series of clinical use regulations and policies to promote the prudent use of such drugs. The number of anti-bacterial drugs allowed to be on the hospital formulary list have been substantially lowered. Therefore, China anti-bacterial drug might shrink in the future.

China Anti-bacterial Drug Market Size, 2018-2030E

Billion RMB

Period	CAGR
2018-2023	-5.1%
2023-2026E	-3.0%
2026E-2030E	-1.9%



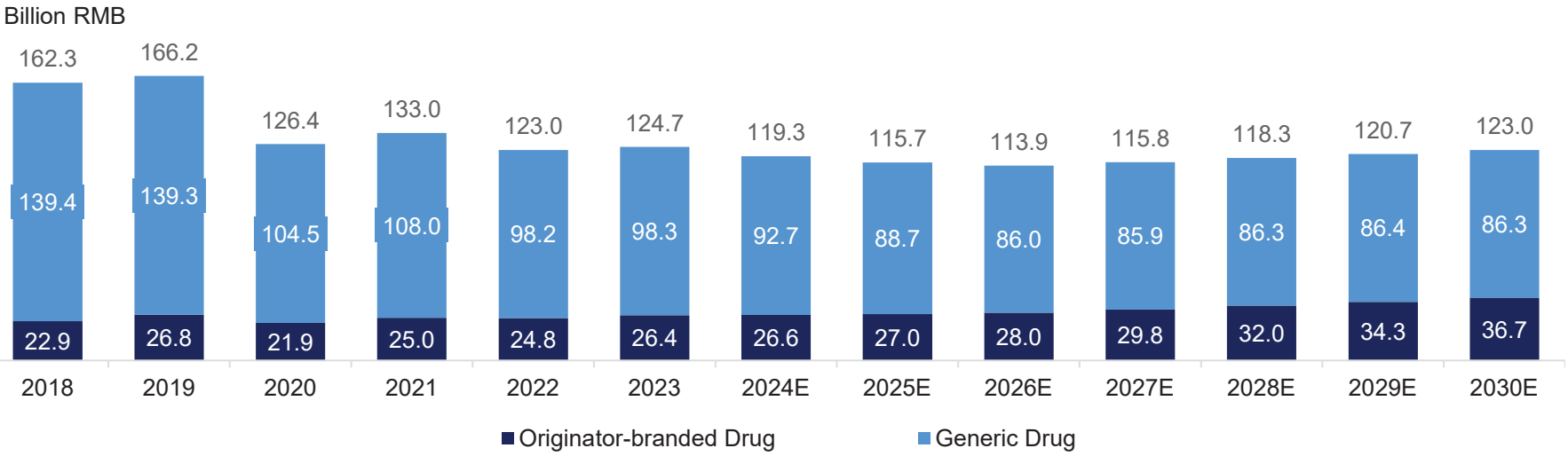
Source: Frost & Sullivan Analysis

Breakdown of China Anti-bacterial Drug Market, By Originator-branded Drug and Generic Drug, 2018-2030E

- Originator-branded anti-bacterial drugs with high manufacturing quality standards have captured stable growth momentum in recent years in China, mainly driven by the established trust of healthcare professionals and patients for their proven safety and efficacy profiles.
- Influenced by the Covid-19 pandemic, the number of in-patient and out-patient visits sharply decreased in 2020 (a fluctuation in hospital traffic), thus China anti-bacterial market including originator-branded anti-bacterial drug market shrinking in 2020. Expecting that more novel anti-bacterial drugs will be launched, the market share of originator-branded drugs will keep rising. On the other hand, in light of the policies promoting more appropriate and accurate usage of anti-bacterial drugs, high-quality originator-branded drugs have demonstrated the potential to further capture significant market share.

Breakdown of China Anti-bacterial Drug Market, By Originator-branded Drug and Generic Drug, 2018-2030E

CAGR	Originator-branded Drug	Generic Drug	Total
2018-2023	2.9%	-6.7%	-5.1%
2023-2026E	1.9%	-4.4%	-3.0%
2026E-2030E	7.0%	0.1%	1.9%

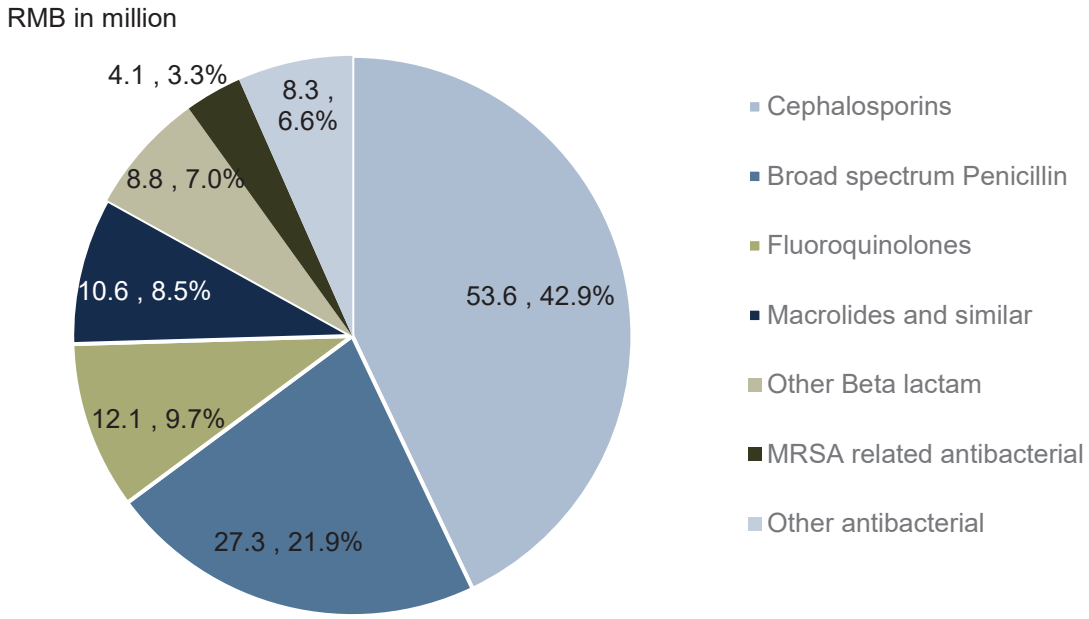


Source: Frost & Sullivan Analysis

Breakdown of China Anti-bacterial Drug Market, 2023 (Pie chart)

- Cephalosporin, Penicillin and Quinolone are three major classes of anti-bacterial drugs in China, and they dominated the whole market with a share of around 75% collectively in 2023.

Breakdown of China Anti-bacterial Drug Market, 2023



As of April 7th, 2025

Source: Frost & Sullivan Analysis

Competitive Landscape on Anti-MRSA Injections

Generic Name	Brand Name	Dosage form	Manufacturer
Vancomycin Hydrochloride	稳可信 Vancocin	Injection	Edding
Vancomycin Hydrochloride	方刻林 Vancorin	Injection	Cheil Jedang Corporation（Imported generic, no sales in 2022）
Vancomycin Hydrochloride	万君雅 Vanconal	Injection	Alpharma（Imported generic, no sales in 2022）
Vancomycin Hydrochloride	--	Injection	Livzon Pharm
Vancomycin Hydrochloride	--	Injection	Zhejiang Hisun Pharmaceutical Co.Ltd.
Vancomycin Hydrochloride	--	Injection	Gental Pharma CO., LTD
Vancomycin Hydrochloride	--	Injection	Zhejiang Medicine
Vancomycin Hydrochloride	--	Injection	Lukang Pharmaceutical Group Co., Ltd.
Vancomycin Hydrochloride	--	Injection	Nanjing H&D Pharmaceutical Technology CO.,LTD
Vancomycin Hydrochloride	--	Injection	Hainan Poly Pharm Co., Ltd.
Norvancomycin Hydrochloride	--	Injection	Shineway
Norvancomycin Hydrochloride	--	Injection	North China Pharmaceutical Company Ltd.
Norvancomycin Hydrochloride	--	Injection	Zhebei Pharmaceutical
Linezolid Glucose	斯沃 Zyvox	Injection	Pfizer
Linezolid Glucose	--	Injection	Shijiazhuang No.4 Pharm
Linezolid Glucose	--	Injection	Chifengyuansheng
Linezolid Glucose	--	Injection	Sichuan Kelun Pharmaceutical Co.,Ltd.
Linezolid Glucose	--	Injection	Southwest Pharmaceutical Co., Ltd.
Linezolid Glucose	--	Injection	Sichuan Meida Kangjiale Pharmaceutical Co.,Ltd.
Linezolid Glucose	--	Injection	Zhejiang Medicine Co.,Ltd.
Linezolid Glucose	--	Injection	Jiangsu Chia Tai Fenghai Pharmaceutical Co.Ltd
Linezolid Glucose	--	Injection	Hansoh Pharmaceutical Group Company Limited
Linezolid Glucose	--	Injection	Broadwell
Linezolid Glucose	--	Injection	Suzhou Pharmaceutical
Linezolid Glucose	--	Injection	Jiangsu Chia Tai-tianqing Pharmaceutical Co., Ltd.
Linezolid Glucose	--	Injection	Huapont Pharm
Linezolid Glucose	--	Injection	Huaxia Sheng Sheng Pharmaceutical (Beijing) Co., Ltd.
Teicoplanin	他格适 Targocid	Injection	Sanofi S.p.A
Teicoplanin	--	Injection	Zhejiang Medicine
Teicoplanin	--	Injection	Zhejiang Hisun Pharmaceutical Co.Ltd.
Teicoplanin	--	Injection	Cheil Jedang Corporation
Teicoplanin	--	Injection	North China Pharmaceutical Company Ltd.

As of April 7th, 2025, 2025Original drug is highlighted in red. Only listing major manufacturers.

Source: Frost & Sullivan Analysis

Competitive Landscape on Anti-MRSA Injections (To be continued)

Generic Name	Brand Name	Dosage form	Manufacturer
Daptomycin	克必信 CUBICIN	Injection	Patheon Italia S.P.A.
Daptomycin	--	Injection	Hainan Poly Pharm.Co.,Ltd.
Daptomycin	--	Injection	Jiangsu Hengrui Medicine Co.,Ltd.
Daptomycin	--	Injection	Qilu Pharmaceutical Co.,Ltd.
Daptomycin	--	Injection	North China Pharmaceutical Company Ltd.
Daptomycin	--	Injection	Aosaikang Pharmaceutical Co. Ltd.
Daptomycin	--	Injection	Anshi Pharmaceutical Inc.
Daptomycin	--	Injection	Zhejiang Hisun Pharmaceutical Co.Ltd.
Daptomycin	--	Injection	Hangzhou Zhongmei Huadong Pharmaceutical Co.,Ltd.
Omadacycline	--	Tablet	Haimen Pharma INC.
Omadacycline	--	Injection	Zhejiang Hisun Pharmaceutical Co.Ltd.
Contezolid	--	Tablet	Huahai Pharmaceutical Co.,Ltd.

As of April 7th, 2025

Original drug is highlighted in red. Only listing major manufacturers.

Source: Frost & Sullivan analysis

Growth Drivers of Anti-MRSA Drug Market

Developing novel anti-MRSA drugs	• To deal with the threat from MRSA, scientists have developed several types of anti-bacterial drugs, such as Vancomycin, Linezolid, Teicoplanin and Daptomycin which also have shown great anti-bacterial effects. However, bacteria have generally developed resistance to these drugs mentioned above. Therefore, continuing to develop novel anti-bacterial drugs would be the main method to combat MRSA. Extraction from organism, chemical synthesis and structural modification to existing bacterial drugs are three major to obtain novel compounds.
More likely occurred in hospitalized patients	• MRSA infections are caused by a type of Gram-positive bacteria that have become resistant to many of the anti-bacterial drugs used to treat ordinary staph infections, as a result of decades of often unnecessary usage of anti-bacterial drugs in China. Most cases of MRSA infections in China occurred in hospitalized patients who have received different types of anti-bacterial drugs.
In-hospital infection control matters	• Medical institutions tend to be exposed to complex pathogenic environment, and that is why operation rooms, ICU and pathology laboratories should follow high-level disinfection standards. Failure to properly disinfect or sterilize equipment carries not only risk associated with breach of host barriers but also risk for person-to-person transmission and transmission of environmental pathogens. The outbreak of pathogen spread may result in the occurrence of super virus or super bacteria. Many MRSA infection cases are typically are associated with invasive procedures or device, such as surgeries, intravenous tubing or artificial joints.
Difficult to treat and can lead to serious consequences	• MRSA infections have a strong prevalence around the globe, and is difficult to treat and can lead to serious consequences. For example, MRSA pneumonia patients generally have increased mortality rates, extended hospitalizations, and higher healthcare expenses compared to non-MRSA pneumonia patients.

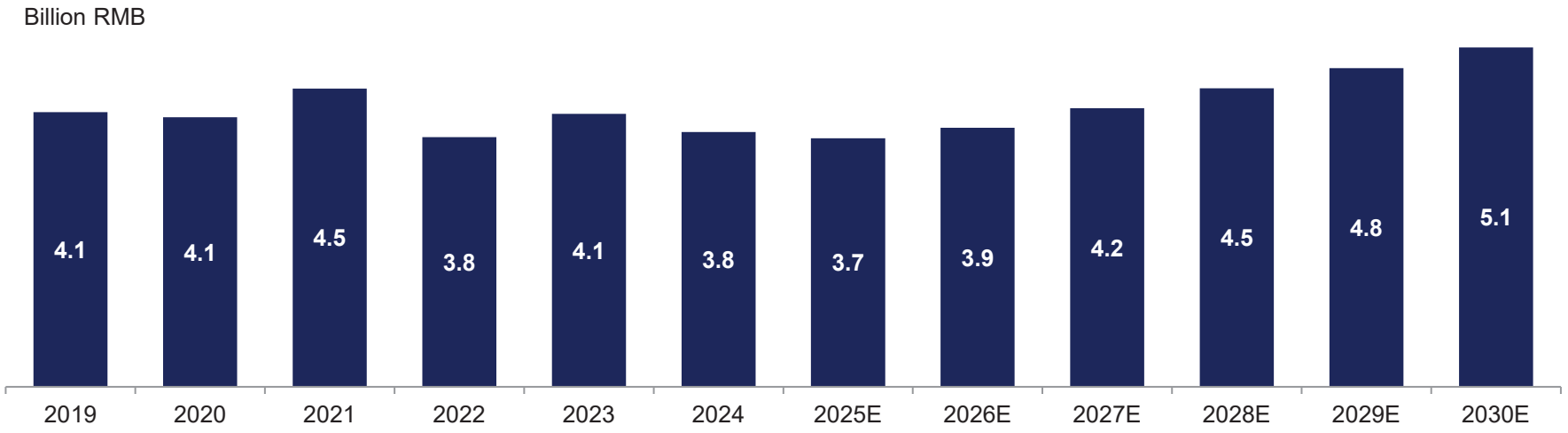
Source: Frost & Sullivan Analysis

China Anti-MRSA Drug Market, 2019-2030E

- Most cases of MRSA infections occurred in hospitalized patients in China. Driven by increases in hospitalization and the diagnosis rate for MRSA infections, the MRSA infections treatment market in China is expected to increase to RMB 4.2billion in 2027 at a CAGR of 3.0% from 2024 to 2027 and to RMB 5.1 billion in 2030 at a CAGR of 6.8% from 2027 to 2030.
- There was a sudden drop in the anti-MRSA drug market in 2022 since Linezolid injection had been included in the fifth round of national centralized drug procurement in 2021. The price of Linezolid infection reduced by 70%-85% after being involved in national centralized drug procurement list. The launch of novel anti-MRSA such as Omadacycline and Contezolid would serve as a new growth driver of the market. Besides, the estimated increase in the incidence of drug-resistance bacterial infection at hospital might result in an improved frequency of using anti-MRSA drugs.

China Anti-MRSA Drug Market, 2019-2030E

Period	CAGR
2019-2024	-1.5%
2024-2027E	3.0%
2027E-2030E	6.8%



Source: Frost & Sullivan analysis

Competitive Landscape on Vancomycin Approved by NMPA

- As of the Latest Practicable Date, six generic versions of Vancocin Injection have been approved by NMPA. These Six domestic generic versions of Vancocin injection have passed the GQCE in June 2021, November 2021, April 2023, May 2024, Sept 2024, Sept 2024, respectively. Currently, there are six domestic generic versions of Vancocin injections applying the the GQCE.

Generic Name	Brand Name	Dosage form	Manufacturer
Vancomycin Hydrochloride	稳可信 Vancocin	Injection	Edding
Vancomycin Hydrochloride	方刻林 Vancorin	Injection	Cheil Jedang Corporation（Imported generic, no sales in 2023）
Vancomycin Hydrochloride	万君雅 Vanconal	Injection	Alpharma（Imported generic, no sales in 2023）
Vancomycin Hydrochloride	--	Injection	Livzon Pharm
Vancomycin Hydrochloride	--	Injection	Zhejiang Hisun Pharmaceutical Co.Ltd.
Vancomycin Hydrochloride	--	Injection	Gentle Pharma Co., LTD (Imported generic)
Vancomycin Hydrochloride	--	Injection	Zhejiang Medicine
Vancomycin Hydrochloride	--	Injection	Lukang Pharmaceutical Group Co., Ltd.
Vancomycin Hydrochloride	--	Injection	Nanjing H&D Pharmaceutical Technology CO.,LTD
Vancomycin Hydrochloride	--	Injection	Hainan Poly Pharm Co., Ltd.
Vancomycin Hydrochloride	--	Capsule	Sshpharm

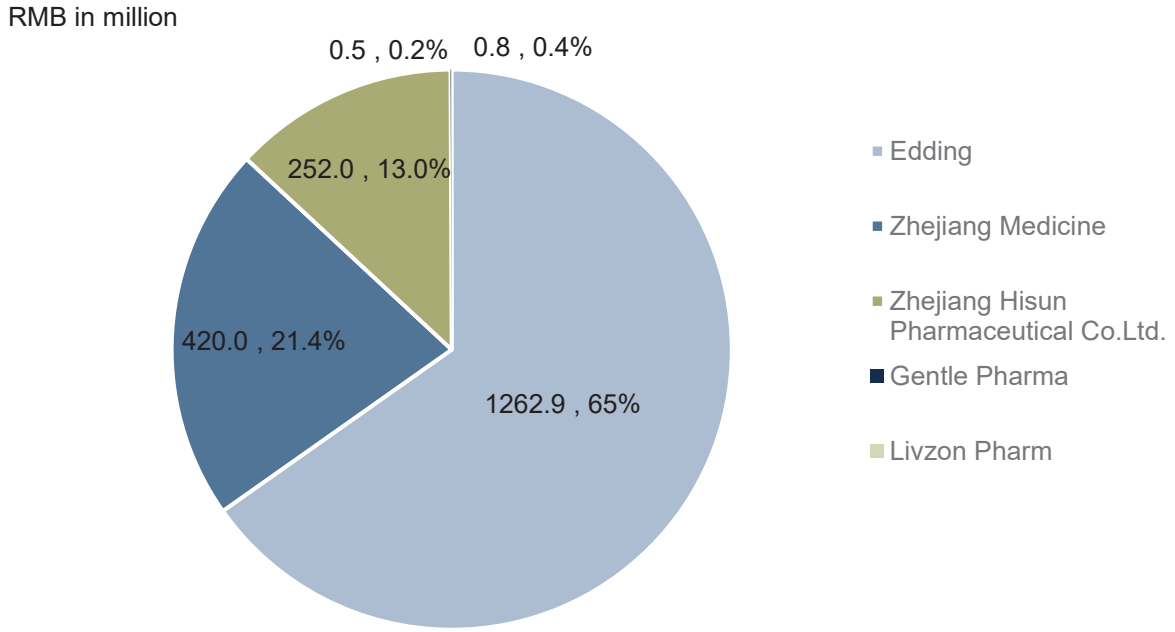
As of April 7th, 2025, 2025Original drug is highlighted in red

Source: Frost & Sullivan analysis

Market Share of Vancomycin in China, 2024 Pie chart)

- Vancomycin captured a significant market share of 42.2% in term of in the MRSA infection treatment market. Edding's originator-branded vancomycin product, Vancocin, is the market leader in the Vancomycin category, dominating a market share of 65% in 2024. Zhejiang Medicine, as the second largest manufacturer, had a market share of 23.0%, followed by the other players who collectively controlled around 15.5% of the market.

Market Share of Vancomycin in China, 2024



As of April 7th, 2025

Source: Frost & Sullivan analysis

Core Strengths of Vancocin (Original Vancomycin Hydrochloride for Injection)

- Vancomycin is the "gold standard" for the treatment of MRSA infections and is the only first-line drug among major therapies included in the NRDL for the treatment of MRSA infections. Launched in China in 1988, vancomycin has been recommended by a number of major clinical practice guidelines in China and globally. Vancocin is the market leader for the treatment of MRSA infections in China, and it remains a strong market demand.

Gold standard	• Vancomycin is the well-recognized "gold standard" treatment for MRSA infections in China and globally. It has been recommended by a number of clinical practical guidelines for the treatment of MRSA infections both in China and globally.
The only first-line treatment on the NDRL	• Vancomycin is the only first-line drug among major therapies for the treatment of MRSA infections on the NRDL. Two major competing molecules for vancomycin, namely linezolid and teicoplanin, are second-line treatments for MRSA infections on the NRDL, and a second line treatment for MRSA infections is generally only entitled to reimbursement under the NRDL when administrated to a patient who has demonstrated intolerance to vancomycin.
Rare resistance	• vancomycin has very rare reported resistance among MRSA patients in China, demonstrating its strong efficacy.
High-quality manufacturing	• Vancocin is manufactured in accordance with EU cGMP standards, ensuring a high level of quality consistency that has been difficult to achieve for generic competitors in China. Vancocin is the reference drug for the GQCE, demonstrating its proven high quality.

Source: Frost & Sullivan Analysis

Competitive Landscape on Cefaclor in China

- As of the Latest Practicable Date, there were thirteen, one, and fifteen generic versions of Ceclor Sachet, Cefaclor Sustained Release Tablets (II) and Cefaclor Capsules that have passed the GQCE, respectively. One generic version of Ceclor Sachet are in the process of applying for the GQCE qualification. No generic version of Cefaclor Sustained Release Tablets (II) and no Cefaclor Capsules are in the process of applying for the GQCE qualification.

Dosage form	Typical Manufacturer	Insurance reimbursement	Centralized procurement
Capsule	Edding (希刻劳，1998）	Yes	No
	Suzhou Chung-hwa Chemical & Pharmaceutical Industrial Co.,Ltd	Yes	Yes
	Nucien Pharmaceutical	Yes	Yes
	Lijian Pharma	Yes	Yes
	Yangtze River Pharmaceutical Group Co.,Ltd.	Yes	No
	Baiyunshan Pharmaceutical Holdings Co.,Ltd.	Yes	No
	Livzon Pharm	Yes	No
	……		
Suspension	Edding (希刻劳，1998）	Yes	No
	Sino Pharma Zhijun	Yes	Yes
	Kinhoo Pharmaceutical	Yes	Yes
	Jida Pharmaceutical Co.,Ltd	Yes	Yes
	Shijiazhuang No.4 Pharmaceutical	Yes	Yes
	……		
Sustained Release Tablets	Edding (希刻劳，2002）	Yes	Not mentioned
	Hansoh Pharmaceutical Group Company Limited	Yes	
	Yangtze River Pharmaceutical Group Co.,Ltd.	Yes	
	Yabang Pharmaceutical Co.,Ltd.	Yes	
	Anglikang Pharmaceutical Co.,Ltd.	Yes	
	……		
Granules	Haikou Pharmaceutical Factory Co.,Ltd.	Yes	Not mentioned
	Sino Pharma	Yes	
	Tiandi Pharmaceutical Co.,Ltd.	Yes	
	Lijian Pharmaceutical Co.,Ltd.	Yes	
	……		

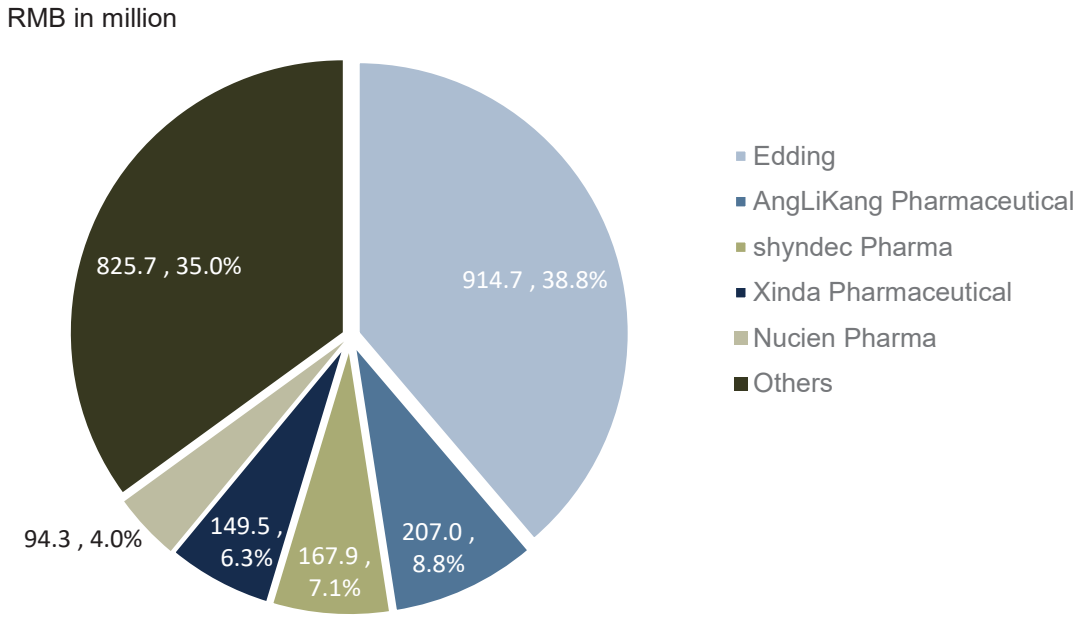
As of April 7th, 2025Original drug is highlighted in red. Only listing major manufacturers.

Source: Frost & Sullivan analysis

Market Share of Cefaclor in China, 2024 (Pie chart)

- Ceclor is the market leader with a 38.8% market share in China's cefaclor drug market in terms of sales revenue in China in 2023.
- Ceclor Sachet held a dominant and growing market share of 72%, 77% and 79% in retail channel sales of cefaclor in China in 2022, 2023 and 2024, respectively. Cefaclor captured a significant share of 16.1% in China's pediatric anti-bacterial drug market in terms of 2023 sales revenue in China

Market Share of Cefaclor in China, 2024



As of April 7th, 2025

Source: Frost & Sullivan analysis

Core Strengths of Ceclor (Original Cefaclor)

- Ceclor, the original cefaclor, has three dosage forms, including cefaclor suspension, cefaclor capsules and cefaclor sustained release tablets. Ceclor is the leading brand in the cefaclor category. Ceclor has established its market leadership due to the following core strengths.

Proven safety and efficacy profile	• Having been marketed in China for more than 30 years, cefaclor has proven safety and efficacy profiles, which are critical for pediatric use. Compared to azithromycin cefaclor has a better safety profile with lower incidence rates for both gastrointestinal and cardiac side effects. In addition, compared to azithromycin, cefaclor has a superior efficacy profile with higher adsorption rate, shorter time to peak serum concentration and higher sensitivity to, and lower resistance for, the bacterium that is responsible for a majority of community-acquired pneumonia.
Major guidelines recommendation	• Cefaclor is one of the leading oral molecules among cephalosporins, which have been recommended for the treatment of respiratory infections in pediatric patients by a number of clinical practice guidelines both in China and globally.
Strong brand	• Ceclor Sachet, (Cefaclor for suspension), as an originator-branded product, enjoys a strong brand reputation among physicians, pediatric patients and their parents. Ceclor Sachet is especially known for its “small strawberry” logo and pleasant strawberry taste.
High-quality manufacturing	• Ceclor is manufactured in advanced manufacturing facilities. Leveraging the extensive know-how and state-of-the-art manufacturing facility, Ceclor is produced with effective quality control and assurance, especially on controlling impurity levels and ensuring product quality consistency. All three dosage forms of Ceclor are the reference drugs of the GQCE in China, reflecting their high quality.

Source: Frost & Sullivan Analysis

Competitive Landscape on Pediatric Anti-bacterial Drugs

- There are only five originator-branded anti-bacterial drugs for pediatric use currently marketed in China, namely Ceclor Sachet and the originator-branded version of cefixime, azithromycin, cefprozil, and cefpodoxime proxetil, all of which are highlighted in red in the table below.

Generic Name	Brand Name	Dosage form	Manufacturer
Cefaclor	希刻劳	Suspension	Edding
Cefaclor	-	Suspension	Hainan Sanye
Cefaclor	-	Suspension	Shijiazhuang No.4 Pharm
Cefaclor	-	Suspension	Shijiazhuang Huaxin
Cefaclor	-	Suspension	Guangzhou Baiyunshan
Cefaclor	-	Suspension	Shandong Yikang
Cefaclor	-	Granules	Tianjing Ertong
Cefaclor	-	Granules	Sunflower
Cefaclor	-	Granules	Hainan Jindao
Cefaclor	-	Granules	Shandong Lukang
Cefixime	-	Granules	Sinopharm Zhijun
Cefixime	-	Granules	Zhejiang Shapuaisi
Cefixime	世福素	Granules	Astellas Pharma Inc / Guangzhou Baiyunshan
Cefixime	-	Granules	Guangdong Hengjian
Cephalexin	-	Granules	Huabei Qinghuangdao
Cefadroxil	-	Granules	Sunflower
Cefdinir	-	Tablets (dispersible tablets)	Sinopharm Zhijun
Amoxicillin	-	Granules	Hainan Sanye
Amoxicillin	-	Granules	Shanghai Huayuan
Amoxicillin	-	Granules	Simcere
Amoxicillin	-	Granules	Sunflower
Amoxicillin	-	Granules	Sichuan Yike
Amoxicillin and Clavulanate Potassium	-	Granules	Sunflower
Amoxicillin and Clavulanate Potassium	-	Granules	Simcere
Amoxicillin and Clavulanate Potassium	-	Granules	CSPC Zhongnuo
Amoxicillin and Clavulanate Potassium	-	Suspension	Guangzhou Baiyunshan
Amoxicillin and Clavulanate Potassium	-	Suspension	Bright Future
Amoxicillin and Clavulanate Potassium	-	Suspension	Furen

As of April 7th, 2025; Original drug is highlighted in red. Only listing major manufacturers.

Source: Frost & Sullivan analysis

Competitive Landscape on Pediatric Anti-bacterial Drugs (To be continued)

Generic Name	Brand Name	Dosage form	Manufacturer
Azithromycin	希舒美	Suspension	Pfizer
Azithromycin	-	Suspension	CSPC Ouyi
Azithromycin	-	Suspension	Sichuan Pharm
Azithromycin	-	Suspension	Shandong Lvyin
Azithromycin	-	Suspension	Shijiazhuang Huaxin
Azithromycin	-	Suspension	Sunflower
Cefprozil	施复捷	Suspension	BMS
Cefprozil	-	Suspension	Hainan Rizhongtian
Cefprozil	-	Suspension	Sino Pharma
Cefprozil	-	Suspension	Nanjing Yihua
Cefprozil	-	Granules	Guangzhou Baiyunshan
Cefprozil	-	Granules	Simcere
Cefprozil	-	Granules	Haerbin Kaicheng
Cefprozil	-	Granules	Qilu Pharmaceutical
Cefuroxime Axetil	-	Suspension	Shandong Lukang
Cefuroxime Axetil	-	Suspension	Brilliant Pharmaceutical
Cefuroxime Axetil	-	Granules	Lijian Pharma
Cefuroxime Axetil	-	Granules	Sina Pharma
Cefuroxime Axetil	-	Granules	Shijiazhuang No.4 Pharma
Cefpodoxime Proxetil	博拿	Suspension	Daiichi Sankyo / Sichuan Hexin
Cefpodoxime Proxetil	-	Suspension	WahSun Pharmaceutical
Cefpodoxime Proxetil	-	Suspension	Nucien Pharmaceutical
Cefpodoxime Proxetil	-	Suspension	Guangzhou Baiyunshan
Cefpodoxime Proxetil	-	Suspension	Chongqing Kerui
Cefpodoxime Proxetil	-	Suspension	Hainan Sanye
Cefpodoxime Proxetil		Granules	Shanghai Pharma
Cefpodoxime Proxetil	-	Granules	Tianjin Jinkang

As of April 7th, 2025; Original drug is highlighted in red. Only listing major manufacturers.

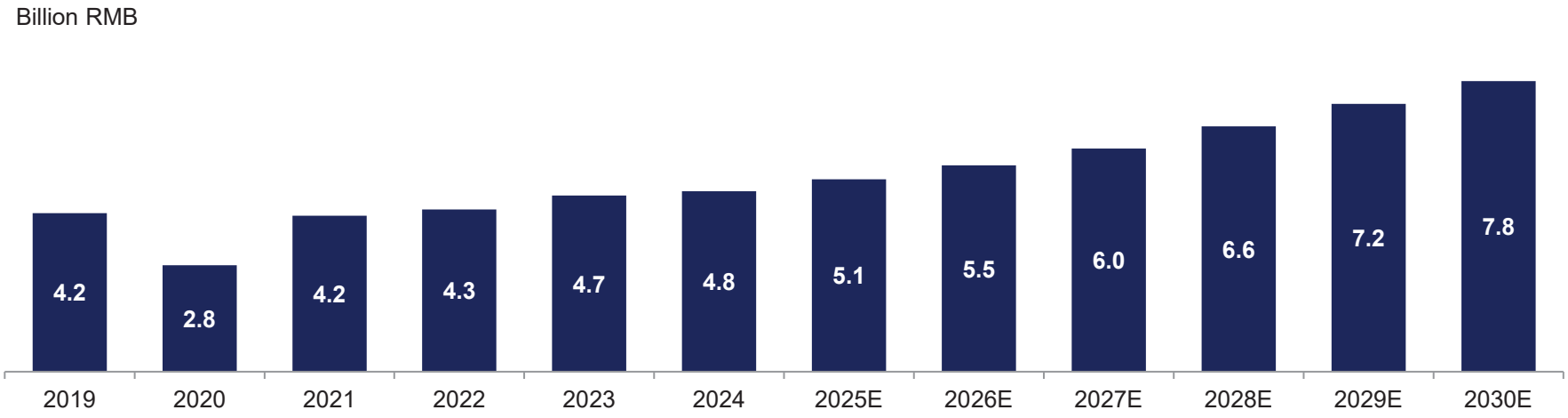
Source: Frost & Sullivan analysis

China Pediatric Anti-bacterial Drug Market Size, 2019-2030E

- The China pediatric anti-bacterial drug market increased from 4.2 billion RMB to 4.8 billion RMB at a CAGR of 2.6% from 2019 to 2024 with a temporary drop in 2020 due to the impact of Covid-19. The number is projected to reach 6.0 billion RMB in 2027 and 7.8 billion RMB in 2030 at a CAGR of 7.4% and 9.2% from 2024 to 2027 and from 2027 to 2030 respectively.
- Commonly used pediatric anti-bacterial drugs include cefaclor, azithromycin, amoxicillin, cefixime, cefprozil, cefuroxime, cefpodoxime, and others. Among these, the most frequently utilized pediatric anti-bacterial drugs are amoxicillin, azithromycin, cefixime, and cefaclor, collectively accounting for approximately 80% of the pediatric anti-bacterial drug market in terms of revenue in 2024, respectively.

China Pediatric Anti-bacterial Drug Market Size, 2019-2030E

Period	CAGR
2019-2024	2.6%
2024-2027E	7.4%
2027E-2030E	9.2%



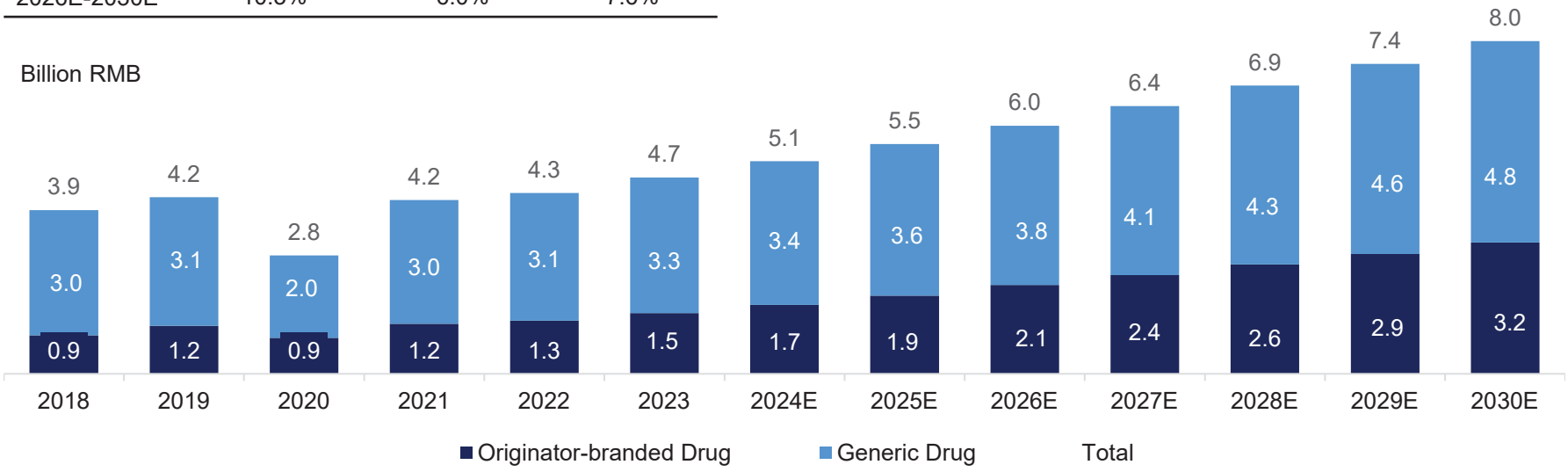
Source: Frost & Sullivan analysis

Breakdown of China Pediatric Anti-bacterial Drug Market, By Originator-branded Drug and Generic Drug, 2018-2030E

- Due to the stringent requirements for drug safety, originator-branded drugs have captured a significant market share of 30.9% in China's pediatric anti-bacterial drug market in terms of 2023 sales revenue. Sales of originator-branded anti-bacterial drugs for pediatric use grew rapidly from RMB 0.9 billion in 2018 to RMB 1.5 billion in 2023 at a CAGR of 9.5% and are expected to grow to RMB 2.1 billion in 2026 at a CAGR of 13.6% from 2023 and RMB 3.2 billion in 2030 at a CAGR of 10.3% from 2026.

Breakdown of China Pediatric Anti-bacterial Drug Market, By Originator-branded Drug and Generic Drug, 2018-2030E

CAGR	Originator-branded Drug	Generic Drug	Total
2018-2023	9.5%	1.6%	3.7%
2023-2026E	13.6%	5.5%	8.2%
2026E-2030E	10.3%	6.0%	7.6%



Source: Frost & Sullivan Analysis

Growth Drivers of Pediatric Anti-bacterial Drug Market

More clinical trials in children will be conducted	• Based on current clinical applications, there are issues with the use of pediatric antibiotics, such as off-label use, using adult dosages in children, and limited formulations. When the pediatric market size is estimated, only anti-bacterial drug with pediatric formulations will be calculated. However, the fact is there are cases of off-label, using reduced dosages in children, but this part of market can not be accounted in. As more clinical trials for pediatric indication are conducted and more drugs with pediatric formulations get approved, the entire pediatric market will enlarge. Therefore, the future growth in China's pediatric anti-bacterial market is mainly driven by the launch of new pediatric drugs.
Strengthen support for laws and regulations related to pediatric drug use	• The government can introduce policies to encourage pharmaceutical companies to conduct clinical trials for pediatric drugs and provide financial or policy support to companies developing pediatric drugs. This can promote the development and production of drug dosage forms suitable for children's use. The monitoring and reporting of adverse drug reactions can accumulate more comprehensive information and data on pediatric drug use. Therefore, the future growth in China's pediatric anti-bacterial market is mainly driven by the launch of new pediatric drugs.

Source: Frost & Sullivan Analysis

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2	Anti-infection Drug Market in China
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7	Breast Cancer Drug Market in China

Overview of Respiratory Disease

- Respiratory disease is a type of disease that affects the lungs and other parts of the respiratory system. Respiratory disease may be caused by infection, smoking tobacco, or breathing in secondhand tobacco smoke, radon, asbestos, or other forms of air pollution.
- Respiratory disease can be classified into three different types: immunological respiratory disease, infectious respiratory disease and lung cancer.
- Asthma is a common long-term inflammatory disease of the airways of the lungs. COPD is a common obstructive lung disease characterized by long-term breathing problems and poor airflow. Both asthma and COPD have high prevalence in China and have been significantly underdiagnosed and undertreated.

	Description	Treatment
Immunological Respiratory Disease	• Immunological lung diseases are a group of diseases mediated by immune mechanism, which occurs in bronchi, alveoli or pulmonary stroma.	• Immunological respiratory diseases include asthma, the obstructive lung disease, including COPD, restrictive lung diseases, chronic respiratory disease (CRD) and others. • **Inhaled medicine is the first-line therapeutic drug for most immunological respiratory diseases, such as bronchodilators for COPD, ICS for asthma, and others.**
Infectious Respiratory Disease	• Infections can affect any part of the respiratory system. They are traditionally divided into upper respiratory tract infections and lower respiratory tract infections.	• The most common upper respiratory tract infection is the common cold, while the lower respiratory tract infection is pneumonia. Bacteria, virus and fungi can all cause the infection, like tuberculosis, SASS, covid-19 and others. • Global and Chinese guidelines have recommended **that aerosol inhalation of antibiotics as an important adjunctive treatment for HAP (hospital-acquired pneumonia) / VAP (ventilator-associated pneumonia).**
Lung Cancer	• Oncological respiratory diseases refer to lung disease caused by tumor.	• The major histological types of respiratory system cancer include small cell lung cancer, non-small cell lung cancer (NSCLC), denocarcinoma of the lung, squamous cell carcinoma of the lung and other lung cancers (carcinoid, Kaposi's sarcoma, melanoma, etc.) • Chemotherapy, surgery, targeted drugs and immunotherapy are the main treatment for lung cancer.

Source: Frost & Sullivan analysis

Classification of Asthma According to Severity

Key Message

- The degree of asthma can be divided into four grades, such as mild, moderate, severe and critical. The classification depends on daytime and nocturnal symptoms, seizure frequency, activity limitation, pulmonary function test and PEF mutation rate.
- Mild patients can inhale β_2 agonists and take oral theophylline controlled release drugs. Moderate patients can use dry powder inhalation of β_2 agonists, intravenous drip of theophylline, and oral glucocorticoid drugs. Severe patients need to use oxygen jet atomization inhalation, intravenous injection of β_2 agonists, oxygen therapy, intravenous injection of hormone drugs and so on.

Severity classification of asthma

	Intermittent state (Level 1)	Mild persistent (Level 2)	Moderate persistent (Level 3)	Severe persistent (Level 4)
Symptom frequency	<once a week	≥once a week, but<once a day	Have symptoms every day	Have symptoms every day
Occurrence frequency	Appear briefly	May affect activity and sleep	Affect activity and sleep	Appear frequently
Nocturnal asthma	≤2 times per month	Twice a month, but<once a week	≥once a week	Appear frequently
FEV_1Share of expected value	≥80%	≥80% or PEF≥80%	60%~70% or PEF=60%~79%	<60% or PEF< 60%
PEF Mutation rate	<20%	20%～30%	>30%	>30%

FEV_1 is the volume of maximum expiratory volume after maximum deep inhale and maximum expiratory volume in the first second. FEV_1% measurement is a common index to determine asthma and COPD PEF: Peak Expiratory Flow

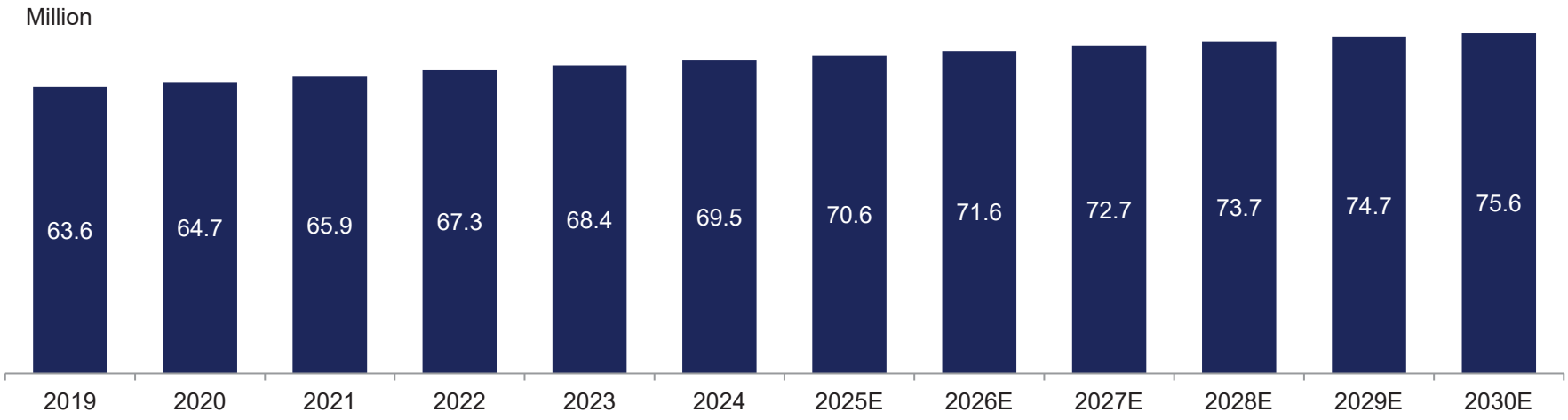
Source: 2017 GINE, Frost & Sullivan Analysis

Prevalence of Asthma in China, 2019-2030E

- In China, asthma has a large patient pool, reaching 69.5 million in 2023. It is projected to increase to 72.7 thousand in 2027 and 75.6 million in 2030, representing a CAGR of 1.5% from 2024 to 2027 and 1.4% from 2026 to 2030. The total number of asthma patients in China was 69.5 million in 2024, including 56.1 million adult and 13.4 million pediatric asthma patients.

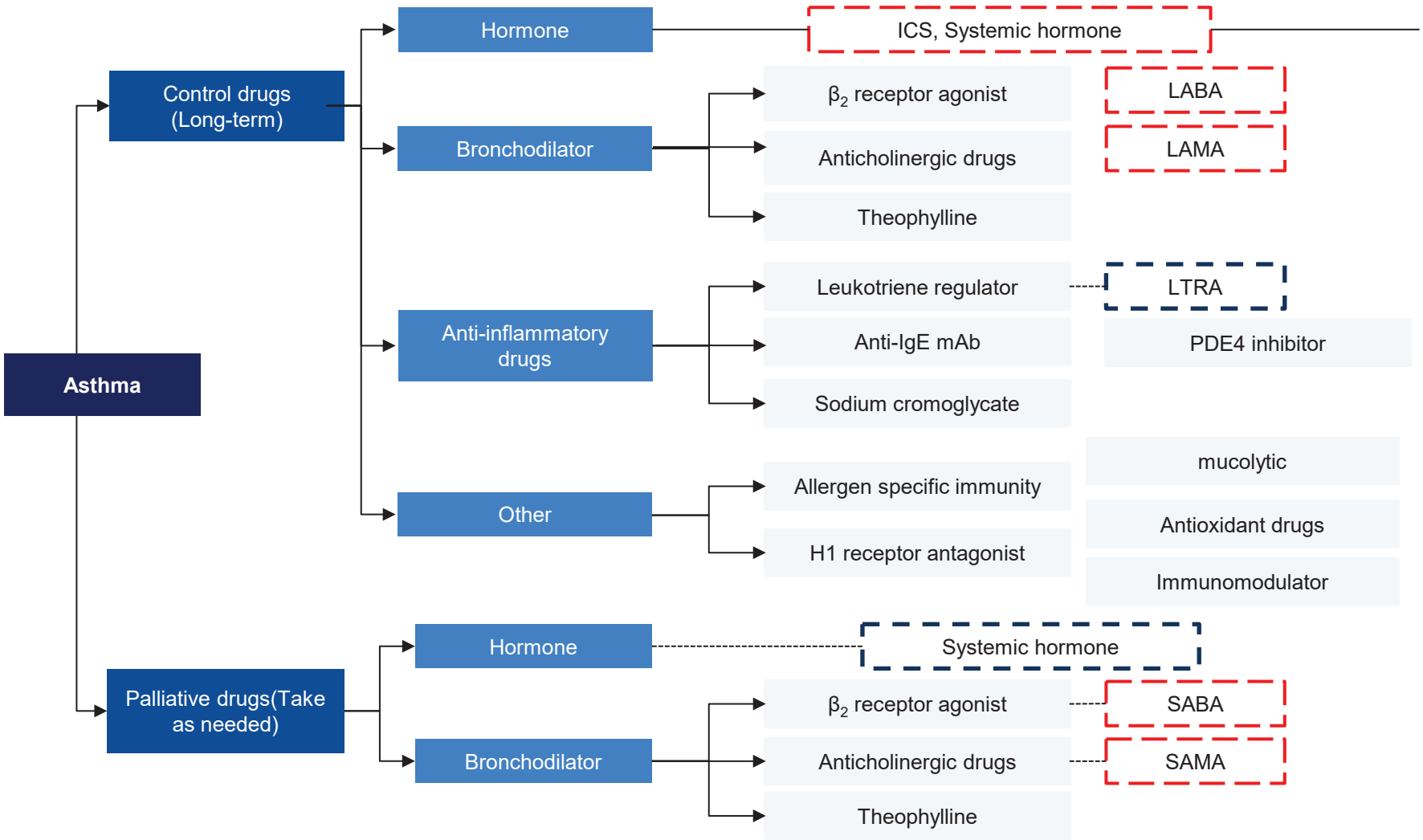
Prevalence of Asthma in China, 2019-2030E

Period	CAGR
2019-2024	1.8%
2024-2027E	1.5%
2027E-2030E	1.3%



Source: Frost & Sullivan analysis

Treatment Paradigm of Asthma



ICS: Inhaled corticosteroids LABA: Long-acting β2 receptor agonist LAMA: Long-acting anticholinergic drugs LTRA: Leukotriene receptor antagonists
mAb: Monoclonal antibody SABA: Short-acting β2 receptor agonist SAMA: Short-acting anticholinergic drugs

Source: Literature Review, Frost & Sullivan Analysis

Long-term Treatment for Patients with Asthma

Key Message

- Asthma control is usually achieved and maintained for at least 3 months, and downgrade treatment can be tried to achieve the minimum use of drugs to maintain symptom control.
- One of the drugs for the treatment of asthma is control drugs, that is, drugs that need to be used daily and maintained for a long time, including ICS, ICS/LABA, etc.; the other is palliative drugs, which are used in acute attacks, mainly by rapidly relieving bronchospasm to relieve asthma symptoms, mainly bronchodilation drugs, including SABA, ICS/ Formoterol, short-acting Theophylline and so on.

Therapeutic regimen	Level 1	Level 2	Level 3	Level 4	Level 5
Recommended choice of control drugs	ICS (Use on demand)	Low dose ICS or ICS + Formoterol	Low dose ICS/LABA	Medium dose ICS/LABA	Targeted biologics, such as anti-IgE mAb, anti-IL-5 mAb
Other choice of control drugs	SABA + Low dose ICS (Use on demand)	LTRA + Low dose Theophylline	Medium dose ICS or Low dose ICS + LTRA	High dose ICS/LAMA or High dose ICS + LTRA	High dose ICS/LAMA or High dose ICS + LTRA
Palliative drug	ICS + Formoterol (Use on demand) or SABA (Use on demand)	ICS + Formoterol (Use on demand) or SABA (Use on demand)	ICS + Formoterol (Use on demand) or SABA (Use on demand)	ICS + Formoterol (Use on demand) or SABA (Use on demand)	ICS + Formoterol (Use on demand) or SABA (Use on demand)

Source: 2020支气管哮喘防治指南, Frost & Sullivan Analysis

Unmet Medical Needs for Asthma

- It is estimated that about 300 million people worldwide suffer from asthma, and that number is expected to rise to 400 million by 2025. The high incidence of asthma leads to a heavy burden on health and economy. About 20% of patients have severe persistent asthma, and there are still many unmet medical needs.

Unmet medical needs for Asthma

Low patient compliance

- Observational studies of mild asthma patients in China show that doctors believe that 75% of the patients' condition is well or completely controlled, but according to the global asthma initialization standard, only 14.2% of the patients' condition is well controlled. Low treatment compliance leads to nocturnal symptoms, deterioration, work and activity disorders in many patients.

Lack of patient education

- Doctors have less education for patients, and patients have lower awareness of the condition and treatment plan.
- At the same time, patients lack confidence in the effectiveness of the treatment. Research shows that 49.1% of patients in China believe that there is no effective treatment for asthma.

The patient is seriously affected by nocturnal symptoms

- More than 90.0% of asthma patients in China are affected by nocturnal symptoms, which is higher than that observed in the United States and the European Union. The treatment required for these symptoms is acute treatment with cough as the secondary symptom, rather than routine maintenance drug use.

Disease Management of Asthma Patients

Management status:

- At present, there are a series of drug choices and state-of-the-art guidelines for the treatment of asthma to help diagnose and manage this chronic disease. In spite of this, the morbidity and mortality of asthma are still on the rise.

Increased demand for health education:

- Disease management and control of patients with asthma urgently need to guide educational programs and health resources. A large number of asthma patients do not fully understand the real control methods and available treatments of asthma. They usually underestimated the authenticity of the disease and overestimated the degree of control of asthma.
- More treatment options provide more patients with better opportunities for asthma control. However, more choices also mean an increased demand for education, and patient communication must be strengthened to address patient culture and lifestyle practices.

Strengthen the management of asthma:

- Patient organizations can monitor each other's drug compliance and increase their awareness of the disease through communication with each other.

Source: Literature Review, Frost & Sullivan Analysis

Classification and Analysis of Inhalant by Inhaler

- Inhalation is a standard and powerful therapy for the treatment of asthma and COPD with its advantages include rapid onset of action, superior efficacy and safety profiles and minor side effects over traditional therapies.
- Inhalation preparations require the combined use of drugs and Inhaler. According to Inhaler, they can be generally divided into: DPI, MDI, Nebulizer, SMI, Nasal sprays; which DPI, MDI and Nebulizer are three major types.
- There is no special technique needed to use nebulizer, which means nebulizer use requires very little in-clinic coaching. The characteristics of nebulizers make them especially suitable for pediatric use in China.

Inhalant	Introduction	Pros	Cons	Inhaler
DPI	One or more drugs are administered through inhaler to enter the respiratory tract in the form of dry powder to achieve the purpose of treatment.	• No propellant • High dosage, convenient • Low cost	• Difficult to imitate • Inhaler's flowed friction may affect drug delivery and distribution	
MDI	Drugs are packed together with a suitable propellant in a pressure-resistant container with a special valve system, and the sprayed Drugs are used for lung absorption.	• Quick, positioning effect • Clean and sterile • Quantitative and accurate	• Potential environmental protection and toxic side effects of propellants • Low dosage(System limitations) • Need patient coordination	
Nebulizer	Using high-speed oxygen gas flow, the liquid is formed into a mist, and then inhaled by the respiratory tract to achieve the purpose of treatment.	• Continuous or multiple large doses • Low coordination requirements • No propellant that may damage the atmosphere	• Expensive • Long single use time	
SMI	The drug is delivered in a slow mist, which does not depend on the inhalation speed of the drug.	• The drug stays in the upper respiratory tract less • Less side effects • High efficacy	• Expensive • Difficult to imitate	
Nasal sprays	Glucocorticoid drugs and antihistamines used to treat allergic rhinitis.	• Sustained release • Large particle size and high viscosity	• Dry nose (side effects) • Drug dependence	

DPI: Dry-powder inhaler *MDI: Metered-dose inhaler* *SMI: Soft-mist inhaler*

Source: Literature Review, Frost & Sullivan Analysis

Analysis of Quality Standards for Inhalant

Key Message

- Inhalant have their special concerns in formulation prescription, drug delivery device, preparation process, quality research, stability study, etc., which can have a crucial impact on the quality controllability, safety and effectiveness of inhalation preparations. Therefore, the quality control research part is one of the key points of pre-clinical and even clinical research of Inhalant.

1 Quality research and quality standards

Minimum loading	• Check the minimum loading of the product to verify the content uniformity and drug particle size after spraying
leakage rate	• Control the content of basic remedy per actuation, the uniformity of the content, and the particle size of the sprayed drug
Basic remedy per actuation (pre press)	• The determination of the content of basic remedy per actuation ensures the consistency of clinical administration
Content uniformity	• Ensure the consistency of the drug content in the initial and later stages of the container
Number of actuations per bottle	• Inspection method: ensure that the number of actuations per bottle is not less than the total marked times
Particle size determination	• The percentage of tiny drug particles in aerosol should not be less than 15% of the labeled amount of the basic remedy content per actuation, and 10% for powder aerosol
Drug residues in Inhaler	• Check and determine in prescription screening and preparation process
Dispersion test	• Avoid aggregation of drug particles
Spray mode	• Ensure the consistency and uniformity of the spray state
Low temperature research	• Ensure the tightness of the valve system and its impact on key product inspection items
Microbial Limit	• Microbiological limit check according to non-sterile products
Delivery rate and total	• Measuring device: composed of breathing simulator and filter system, the dead volume of the filter paper cover does not exceed 10% of the tidal volume of the breathing simulator

per actuation: per press

Source: Literature Review, Frost & Sullivan Analysis

High R&D Barriers for Inhalant

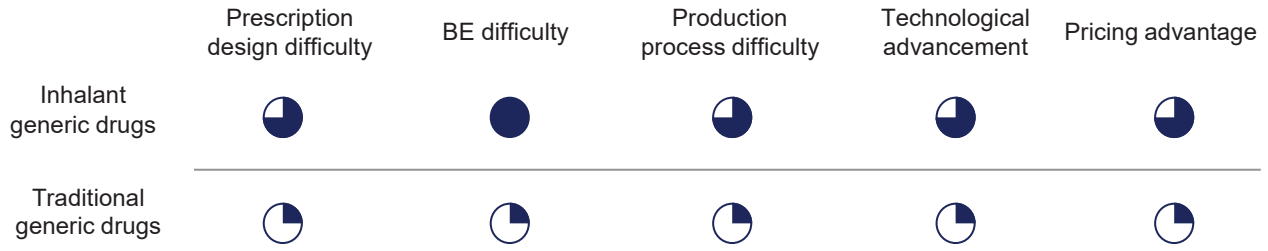
Key Message

- For inhalant, prescription design and process production are difficult, need to have advanced technical level to ensure continuous quantitative administration of accuracy and stability.
- Inhalant as high-end generic drugs, are more difficult than traditional generic drugs in terms of formulation prescription, drug delivery device, formulation process, quality research, and stability research, so the pricing advantage is more obvious. For example, the generic price of Budenofalk® is only 9.8% lower than the original drug price.

1 R&D standards for Inhalant

APIs and excipients	• Refer to pH, pKa, density, etc. Investigate propellants, cosolvents, surfactants
Safety evaluation	• Use a suitable cell model to observe the morphological changes, integrity and vitality of cells to judge the safety of the test substance
Drug particles	• The particle size of the drug is usually below 7 μm. The particle size is too large (>10μm) or too small (<0.5μm) may reduce the efficacy
Micronization	• Systematic study on micronization process (feed speed, air pressure, air flow rate, etc.)
Control of moisture	• Strictly control the moisture content of APIs and excipients to avoid the introduction of moisture in the production environment
Propellant ratio	• If a single propellant cannot meet the clinical use requirements, it is necessary to mix propellants with different vapor pressures
Canning process	• Each canning process should be considered and selected in conjunction with specific prescriptions
Other	• Control the difference of loading, content, moisture, impurities, osmotic pressure, valve system measurement, tightness, etc. Focus on drug aggregation and microcrystalline growth

2 Comparison of Inhalant generic drugs and Traditional generic drugs



API: Active Pharmaceutical Ingredients BE: Bioequivalence

Source: Literature Review, Frost & Sullivan Analysis

Analysis of Quality Consistency Evaluation of Inhalant

- In August 2019, CDE released the *"经口吸入制剂仿制药药学和人体生物等效性研究指导原则 (征求意见稿) "*. Under the premise that the test preparation and the reference preparation have the same in vitro pharmacological quality, the bioequivalence of human body is generally verified through in vitro pharmacokinetic (PK-BE), pharmacodynamics (PD-BE), and clinical endpoint studies. For inhalant, it is very difficult to achieve both in vitro and in vivo consistency.

Evaluation method	Specific details	Main content
Pharmaceutical research	Nebulizer	Using the same prescription, sterile production process and packaging materials as the reference preparation, the key quality attributes are consistent
	Inhalation aerosol	Consistent with the prescription of the reference preparation, the key quality attributes such as the existence form of the APIs, spray characteristics and inhalation characteristics
	Inhalation powder	Consistent with the formulation of the reference preparation, the key quality attributes such as inhalation characteristics are consistent. Special attention should be paid to the existing form of the APIs and excipients (such as the crystal form, particle size, etc. of the APIs)
Human bioequivalence research	PK-BE studies	Refer *to "以药动学参数为终点评价指标的化学药物仿制药人体生物等效性研究技术指导原则",* and pay attention to the evaluation indexes and acceptance criteria of bioequivalence
	PD-BE studies	The equivalent endpoint is set in advance, and the sensitive dose on the steep part of the dose response curve is selected to evaluate the effectiveness of the drug in terms of equivalence
	Clinical endpoint studies	For ICS, it is recommended to conduct a randomized, double-blind, and parallel controlled trial design to monitor the effect of hormones on the lower HPA axis. Generally proves the equivalence of asthma treatment, which can be analogized to COPD
	Study on fixed dose compound preparation	The PK-BE of each active ingredient in the compound should be demonstrated separately in the PK-BE study, and the effectiveness of all active ingredients should be considered in the PD-BE or clinical endpoint study
	Study on preparations with multiple specifications	For generic inhalant that require human bioequivalence studies, (1) PK-BE studies are generally recommended for each specification; (2) PD-BE or clinical endpoint studies should consider all declared specifications for clinical the study

API: Active Pharmaceutical Ingredients BE: Bioequivalence ICS: Inhaled corticosteroids

Source: CDE , Frost & Sullivan Analysis

Analysis and Future Trends of Entry Barriers for Inhalant Drug

Analysis of entry barriers for inhalant

R&D barriers

- Compared with ordinary preparations, inhalant have special requirements on drug particle size and inhaler, so the R&D barriers are higher.
- Developing and/or manufacturing drugs with fewer side effects and fast-acting effect, given that patients with respiratory diseases usually have severe symptoms and rapid disease progression
- Lack of innovative drug development given the lack of innovative compounds being discovered in recent years.

Competition barriers

- Given that most respiratory disease patients need long-term drug treatment, many such patients have developed drug compliance for currently administered therapies, which sets entry barriers for new market players.

Production barriers

- Mass production is easy to be unstable: due to the administration of inhalation preparations at the microgram level, the tolerance for errors is small. Therefore, instability of the inhalation preparations in the mass production process is prone to instability phenomenon.
- Technical barriers in manufacturing generics, especially for administration tools such as inhaler.

Future trends of entry barriers for inhalant

Domestic substitution

- The domestic inhalant market has grown rapidly, but it has been dominated by foreign companies. With the continuous expiration of product patents such as 舒利迭® and 普米克®, domestic companies with certain R&D capabilities can develop high-end generic drugs for inhalants, and have price advantages. In the future, the inhalant market may quickly realize domestic substitution.

Direction of innovation

- The innovation direction of inhalant mainly includes compound products, dosage form improvement and new indication expansion. Compound preparations have become one of the mainstream strategies. Due to the high technical barriers of inhalants, the improvement of dosage forms is a strategy for generic drugs to enter the market. The application of inhalants in other fields, such as the central nervous system, is also one of the current research directions.

Increased supervision

- In August 2019, CDE released *the "经口吸入制剂仿制药药学和人体生物等效性研究指导原则（征求意见稿）"*, drawing on the relevant evaluation guidelines of the FDA, based on in vitro and in vivo studies, and consistent The evaluation criteria are in line with international mature markets. This opinion will accelerate the introduction of generic standards for inhaled preparations and improve the quality standards for inhaled preparations.

Source: Frost & Sullivan Analysis

Clinical Advantages of Inhalant in the Treatment of Asthma

Key Message

- Inhalant have the advantage that traditional ways cannot be substituted in the prevention and treatment of respiratory diseases, and are the main method and powerful therapy for the treatment of asthma .
- In recent years, it has been used in the treatment of lung infections, pulmonary cystic fibrosis, and respiratory tract tumors. It has also been used in systemic diseases such as diabetes, and has been widely used.

1 Overview of Inhalant

- Inhalation preparations refer to preparations that deliver drugs to the respiratory tract and/or lungs in a mist form by a specific device to exert local or systemic effects.
- The physiological characteristics of the lungs determine the advantages of inhalant: the alveolar wall is thin so the drugs are easily absorbed; large absorption surface area; biological metabolic enzymes are concentrated in distribution, have low biological activity, and are not easy to degrade protein polypeptide drugs; rich blood volume, which is beneficial to drug absorption; avoid the first-pass effect of drugs in the liver.

2 Comparison between inhalant and traditional ways

	Inhalation	Oral administration	Intravenous administration
Convenience	+	+	-
Effective speed	++	+	+++
Bioavailability	++	+	+++
Drug dose	+	++	++
Adverse reactions	+	+++	+++

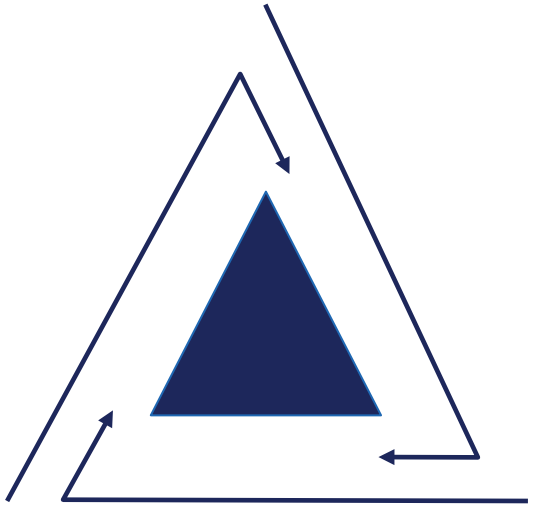
- Compared with ordinary oral preparations, the inhaled preparations can directly reach the absorption or action site, and the absorption effect is fast, which can avoid the first pass effect of hepar, reduce the dosage of medication, and improve the bioavailability;
- Compared with the injection preparation, it can reduce the mechanical damage of local tissues, reduce or avoid some adverse drug reactions, and improve patient compliance.

Source: Literature Review, Frost & Sullivan Analysis

Growth Driver of China Inhalant Market

National policy promotion

- In recent years, China has actively promoted drug consistency evaluation to improve the quality and accessibility of generic drugs for the benefit of the majority of patients. At present, the consistency evaluation standard of oral solid preparation and injection has been issued, and the consistency evaluation standard in the field of inhalation disease is expected to be released and implemented in the near future, which will further promote the development of inhalant market.



Increased affordability of patients

- With the continuous growth of per capita disposable income and the increasing total expenditure on health care in various countries, patients' ability to pay for inhaled drugs is increasing. At the same time, under the implementation of the 4+7 volume procurement policy, the financial burden of patients has been greatly improved.

Increased clinical needs

- The problem of aging in China is becoming more and more serious, and patients' compliance with inhalers is a key issue. MDI is powered by high-pressure gas, while DPI requires external force. MDI can help patients with limited use and improve drug compliance.
- Air pollution brings many respiratory diseases. Atmospheric particulate exposure can increase the morbidity and mortality of respiratory diseases such as asthma. Inhaled drugs have excellent clinical effects on a series of serious chronic diseases led by asthma, COPD and allergic rhinitis, and a large number of patients will further drive market growth.

Source: Literature Review, Frost & Sullivan Analysis

China Originator-branded ICS Nebulizer Suspensions Approved by NMPA

Drug Name	Brand Name	Company	Target	Indications	Insurance reimbursement	Centralized procurement	Manufacturer for Marketed Generics	Number of Ongoing Clinical Trials for Generics	Approved Date
Fluticasone Propionate Nebuliser Suspension	Flixotide Nebules	Edding (Licensing in from GlaxoSmithKline Australia Pty Ltd)	GR	Indicated for the treatment of Acute Exacerbation of Asthma in Children aged 4 to 16 years	Yes	No	**TWO** Chenpon Pharmaceutical (launched 2024); Joincare Pharmaceutical Group Industry Co., Ltd. (launched 2024)	6	2017/9/20
Budesonide Suspension for Inhalation	Pulmicort Respules（普米克令舒）	AstraZeneca	GR	Indicated for maintenance treatment of asthma and as prophylactic therapy in children 12 months to 8 years of age	Yes	Yes	**Seven** Chitai Tianqing (launched 2020); Joincare (launched 2020); Purity Pharmaceutical (launched 2021); CF PharmTech (launched 2021); Licheng Pharmaceutical (Launched 2024); Renhe Yikang Group Co., Ltd. (Launched 2024); Fresh Pharmaceutical Co., Ltd (Launched 2024)	17	2001/11/22
Beclometasone Dipropionate Suspension for Inhalation	Clenil 宝丽亚	Chiesi Farmaceutici SpA	GR	Indicated for asthma and allergic rhinitis	Yes	No	**None**	3	2013/1/1

Note: As of April 7th, 2025; Combined ICS Nebulizers are not included in this table

Source: NMPA, Frost & Sullivan Analysis

Core Strengths of Flixotide Nebules

- Flixotide Nebules, the original fluticasone, will be positioned well to capture the significant market opportunity once approved due to the following core strengths.

Better efficacy	• Fluticasone propionate is a new generation of inhaled corticosteroid (ICS) medication. Its molecular structure is unique, with stronger lipophilicity and receptor affinity, thus less hormonal dosage can achieve the same anti-inflammatory effect as other ICS drugs, such as Budesonide (BUD) and Beclometasone Dipropionate (BDP). A meta-analysis published in May 2022 in Pediatric Research showed that, in terms of forced expiratory volume in one second (FEV1), FPN increased 18.8% (16.4%,20.0%) and 18.8% (17.1%, 20.3%) from baseline at 8 weeks and 12 weeks respectively comparing with BUD increasing 12.7% (11.2%, 14.7%) and 13.9% (12.7%, 15.4%) from baseline, showing that the efficacy of FPN was better than that of BUD. In terms of percentage of symptom-free days in 1 to 12 weeks, FPN (81.9%) was higher than that of BDP (50.5%), showing that the efficacy of FPN was better than that of BDP.
Off-label use	• In some provinces of China, FPN has been approved for the treatment of adult asthma beyond its approved indications. Firstly, this has been supported by clinical practice internationally, with countries such as the UK (originator), Australia, and Singapore approving it for the treatment of adult asthma. Secondly, China's clinical guidelines also recommend its use for the treatment of adult asthma. The off-label use of drugs can sometimes solve the problem of certain diseases without available treatments, and can also explore more indications and more precise clinical applications for drugs already on the market.

Note: Zhu H, et al. Quantitative comparison of different inhaled corticosteroids in the treatment of asthma in children. Pediatr Res. 2023 Jan;93(1):31-38.

Source: Frost & Sullivan Analysis

Fluticasone Propionate Nebulizer Suspension Approved by NMPA

- There are two generic versions of FPN launched in China currently.

Drug Name	Brand Name	Company	Target	Indications	Insurance reimbursement	Centralized procurement	Approved Date
Fluticasone	Flixotide Nebules	Edding (Licensing in from GlaxoSmithKline Australia Pty Ltd)	GR	Indicated for the treatment of Acute Exacerbation of Asthma in Children aged 4 to 16 years	Yes	No	2017/9/20
Fluticasone	/	Chenpon Pharmaceutical	GR	Indicated for the treatment of Acute Exacerbation of Asthma in Children aged 4 to 16 years	Yes	No	2024/06/04
Fluticasone	/	Joincare Pharmaceutical Group Industry Co., Ltd.	GR	Indicated for the treatment of Acute Exacerbation of Asthma in Children aged 4 to 16 years	Yes	No	2024/05/21

Note: As of April 7th, 2025

Source: NMPA, Frost & Sullivan Analysis

Competitive Landscape of China Fluticasone Propionate Nebulizer Suspension Pipeline

- There are eight generic versions of fluticasone propionate nebulizer suspension in pipeline in the nation.

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
Fluticasone Propionate Nebulizer Suspension	GR	Furou Pharmaceutical	BE	Indicated for the treatment of Acute Exacerbation of Asthma in Children aged 4 to 16 years	2024-09-24
Fluticasone Propionate Nebulizer Suspension	GR	Zhixing Pharmaceutical	BE	Indicated for the treatment of Acute Exacerbation of Asthma in Children aged 4 to 16 years	2024-07-23
Fluticasone Propionate Nebulizer Suspension	GR	Hunan Xianshi Pharmaceutical Co., Ltd	BE	Indicated for the treatment of Acute Exacerbation of Asthma in Children aged 4 to 16 years	2024-06-18
Fluticasone Propionate Nebulizer Suspension	GR	Gaozhi Pharmaceutical	BE	Indicated for the treatment of Acute Exacerbation of Asthma in Children aged 4 to 16 years	2024-04-19
Fluticasone Propionate Nebulizer Suspension	GR	Daphne Pharmaceutical Co.,Ltd.	BE	Indicated for the treatment of Acute Exacerbation of Asthma in Children aged 4 to 16 years	2024-04-09
Fluticasone Propionate Nebulizer Suspension	GR	Purity Pharmaceutical Co., Ltd	BE	Indicated for the treatment of Acute Exacerbation of Asthma in Children aged 4 to 16 years	2024-03-11

Note: As of April 7th, 2025

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of China Fluticasone Propionate Nebulizer Suspension Pipeline

- There are eight generic versions of fluticasone propionate nebulizer suspension in pipeline in the nation.

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
Fluticasone Propionate Nebulizer Suspension	GR	Jewim Pharmaceutical(Shandong)Co.,Ltd.	BE	Indicated for the treatment of Acute Exacerbation of Asthma in Children aged 4 to 16 years	2025-03-07
Fluticasone Propionate Nebulizer Suspension	GR	Sichuan Purity Pharmaceutical Co., Ltd	BE	Indicated for the treatment of Acute Exacerbation of Asthma in Children aged 4 to 16 years	2025-02-13

Note: As of April 7th, 2025

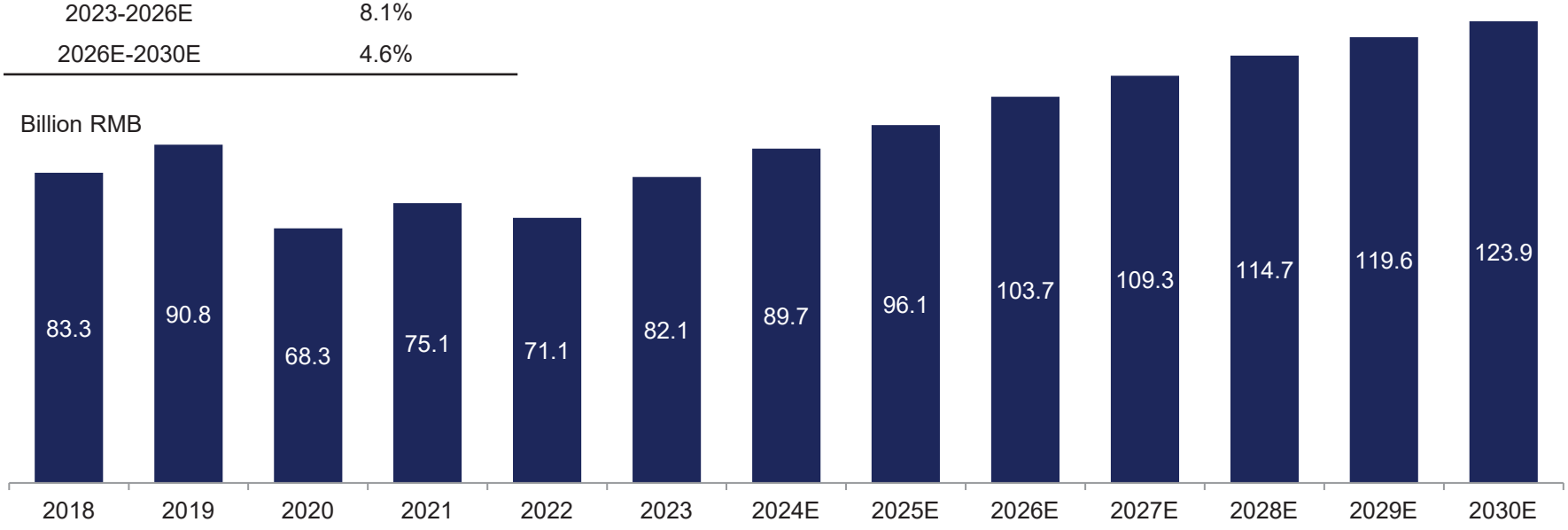
Source: CDE, Frost & Sullivan Analysis

China Respiratory Drug Market, 2018-2030E

- China respiratory drug market decreased from RMB 83.3 billion in 2018 to RMB 82.1 billion in 2023, primarily due to the impact of covid-19 pandemic. The market is expected to increase to RMB 103.7 billion in 2026 at a CAGR of 8.1% from 2023 and RMB 123.9 billion in 2030 at a CAGR of 4.6% from 2026. The growth of China's respiratory market is mainly driven by favorable government policies, increasing diagnosis and treatment and increasing healthcare affordability in China

China Respiratory Drug Market, 2018-2030E

Period	CAGR
2018-2023	-0.3%
2023-2026E	8.1%
2026E-2030E	4.6%



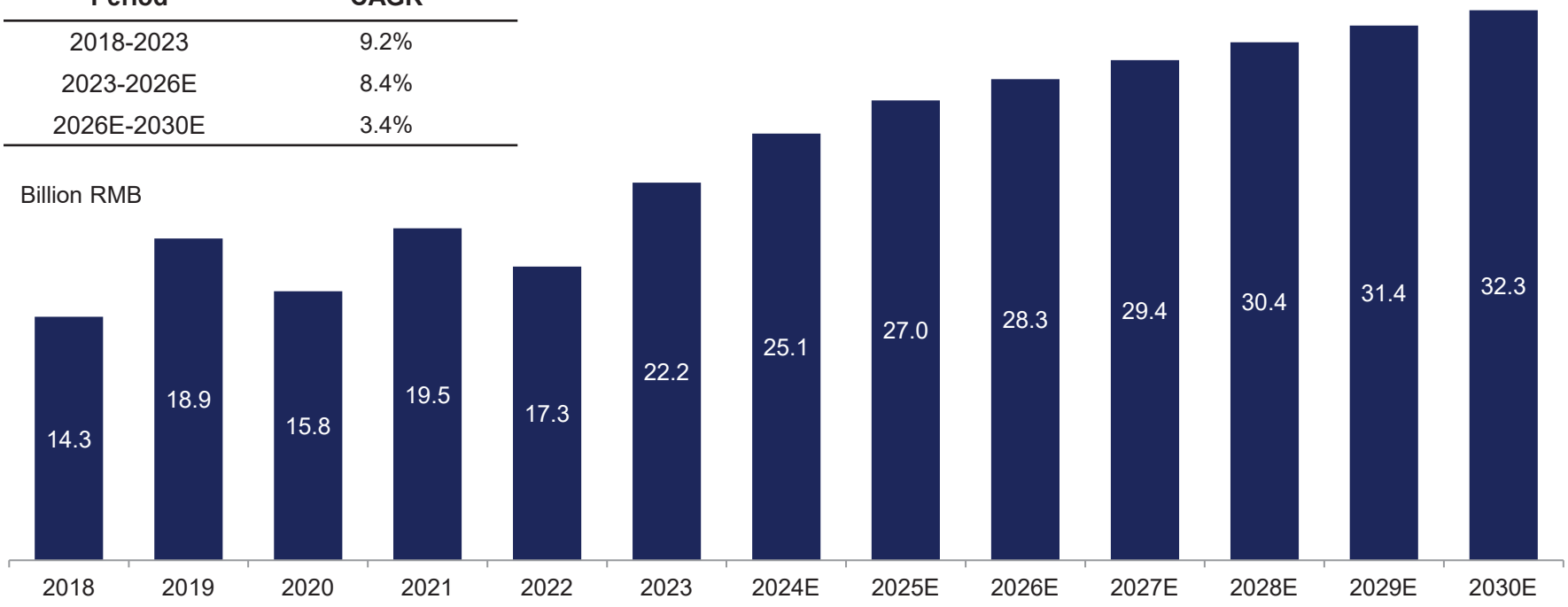
Source: Frost & Sullivan analysis

China Respiratory Inhalant Market, 2018-2030E

- China respiratory inhalant market reached RMB 22.2 billion in 2023 from RMB 14.3 billion in 2018 at a CAGR of 9.2%, and it is expected to increase to RMB 28.3 billion in 2026 and RMB 32.3 billion in 2030 at a CAGR of 8.4% and 3.4% respectively. ICS-related inhalants occupied the respiratory inhalant market with a share of over 50%, and Budesonide, Budesonide-Formoterol, Fluticasone Propionate-Salmeterol Xinafoate are three major ICS-related inhalants.

China Respiratory Inhalant Market, 2018-2030E

Period	CAGR
2018-2023	9.2%
2023-2026E	8.4%
2026E-2030E	3.4%



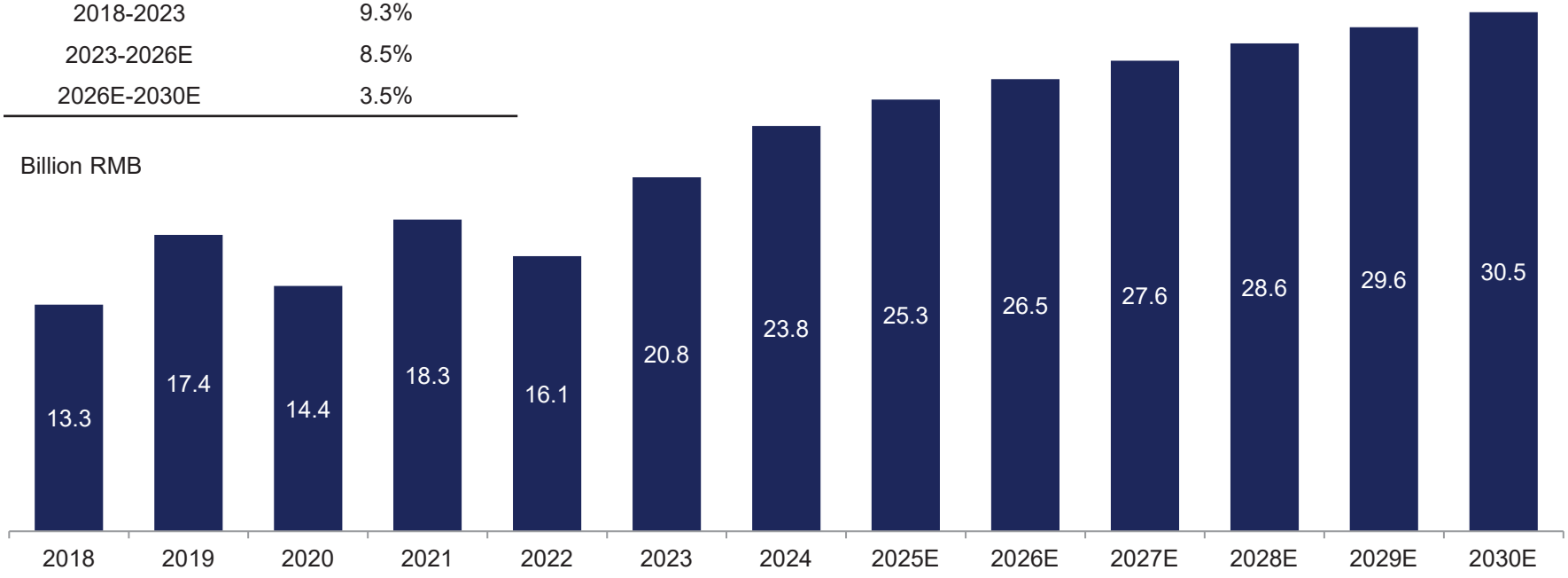
Source: Frost & Sullivan analysis

China Asthma and COPD Inhalant Market, 2018-2030E

- China asthma and COPD inhalant market reached RMB 20.8 billion in 2023 from RMB 13.3 billion in 2018 at a CAGR of 9.3%, and it is expected to increase to RMB 26.5 billion in 2026 and RMB 30.5 billion in 2030 at a CAGR of 8.5% and 3.5% respectively

China Asthma and COPD Inhalant Market, 2018-2030E

Period	CAGR
2018-2023	9.3%
2023-2026E	8.5%
2026E-2030E	3.5%



Source: Frost & Sullivan analysis

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7	Breast Cancer Drug Market in China

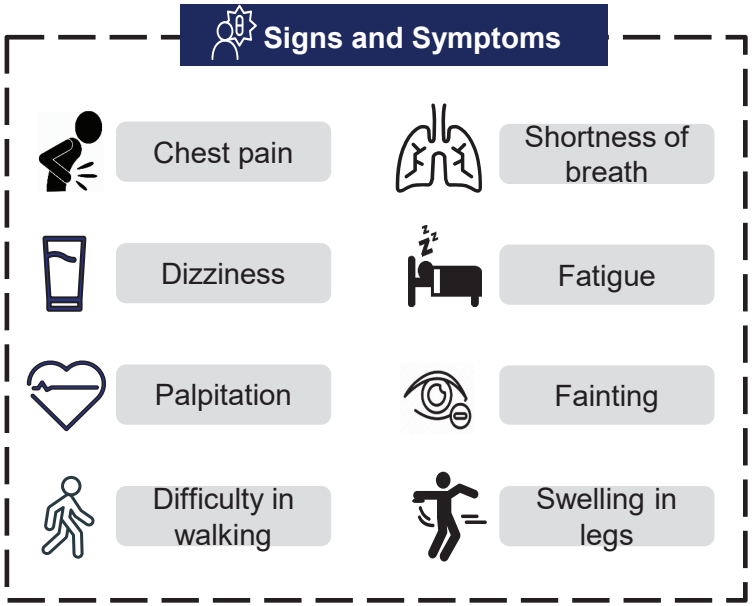
Overview and Cardiovascular Diseases

- Cardiovascular disease is a group of diseases affecting your heart and blood vessels. These diseases can affect one or many parts of your heart and/or blood vessels. A person may be symptomatic (physically experiencing the disease) or asymptomatic (not feeling anything at all).
- Cardiovascular disease can be roughly divided into heart issues and vessel issues, including narrowing of the blood vessels in your heart, other organs or throughout your body, heart and blood vessel problems present at birth, disfunction of heart valves and irregular heart rhythms. According to global burden of disease database, CVDs have the heaviest disease burden among all therapeutic areas.

Indications of Cardiovascular Diseases

Arrhythmia	• Problem with one's heart's electrical conduction system, leading to abnormal heart rhythms
Coronary artery disease	• Problem with one's heart's blood vessels
Heart failure	• Problem with one's heart pumping/relaxing functions
Peripheral artery disease	• Issue with the blood vessels of your arms, legs or abdominal organs, such as narrowing or blockages
Congenital heart disease	• Heart issue that born with, which can affect different parts of your heart
Deep vein thrombosis	• Blockage in one's veins, vessels that bring blood back from your brain/body to your heart

Signs and Symptoms



Risk Factors

Source: Frost & Sullivan Analysis

Overview and Hypertriglyceridaemia (HTG)

- Dyslipidemia is a common metabolic disease. There were more than 518.9 million dyslipidemia patients in China in 2023, representing a high prevalence rate of 36.8% among the total population. Hypertriglyceridaemia is a common indicator of cardiometabolic risk factors and is closely associated with atherosclerotic cardiovascular diseases. Moderately elevated plasma triglyceride concentrations (150-500 mg/dL) reflect the accumulation of triglyceride-rich lipoprotein (TRL) remnants and small dense LDL particles that are highly atherogenic. Severe hypertriglyceridaemia is normally defined as TG levels ≥ 500 mg/dL. Treatment of hypertriglyceridaemia involves lifestyle modification and medication intervention. pharmacotherapy is indicated for patients with established CVD or those at moderate-to-high risk of CVD. Statin therapy is the cornerstone of pharmacological treatment for hypertriglyceridaemia, followed by fibrates and omega-3 fatty acids.

Definition of HTG

- Triglycerides are a type of fat (lipid) found in your blood. When you eat, your body converts any calories it doesn't need to use right away into triglycerides. The triglycerides are stored in your fat cells. If one regularly eats more calories than he burns, particularly from high-carbohydrate foods, he may have high triglycerides (hypertriglyceridemia).

Health Range

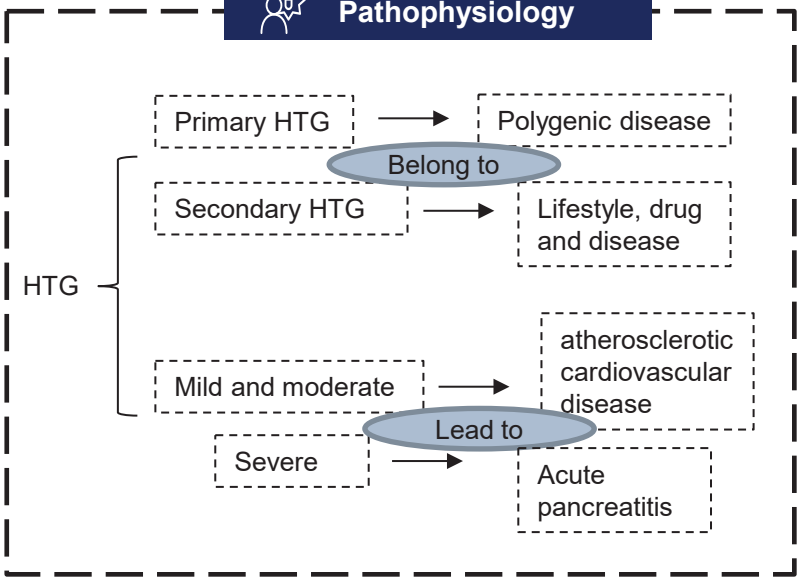
Normal < 150 mg/dL	Borderline high 150-200 mg/dL	High 200-500 mg/dL	Very high > 500 mg/dL

Why do high triglycerides matter?

High triglycerides may contribute to hardening of the arteries or thickening of the artery walls (arteriosclerosis) — which increases the risk of stroke, heart attack and heart disease

Source: Frost & Sullivan Analysis

Pathophysiology



Evidence Associated with Cardiovascular Risk

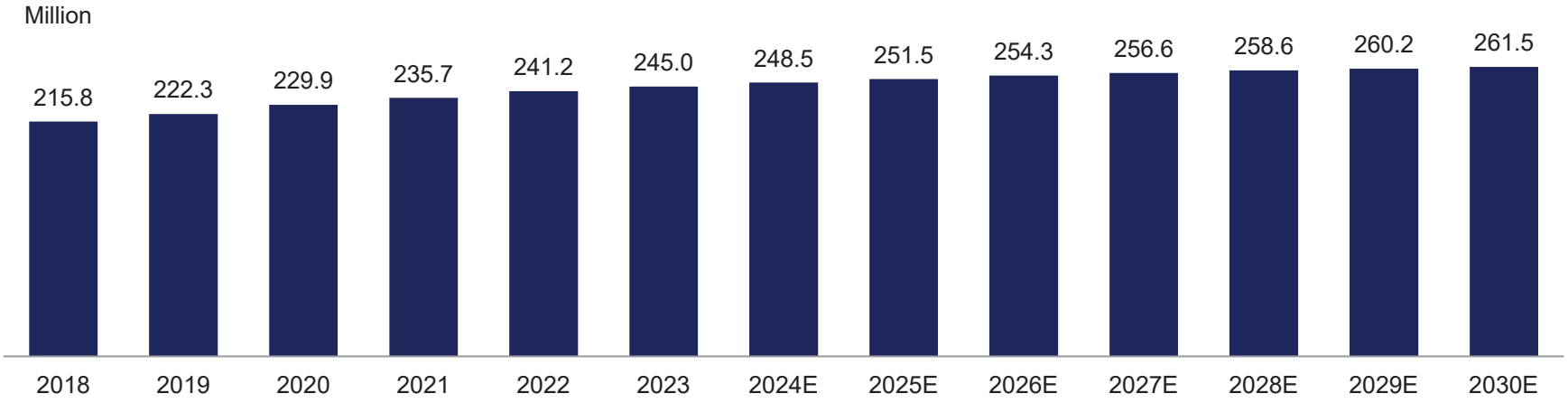
71% up	27% up	1.8% up
TG ≥ 2.3 mmol/L plus HDL-C ≤ 0.9 mmol/L	TG ≥ 2.3 mmol/L plus LDL-C < 1.8 mmol/L ACS patients with the treatment of Statins	The level of TG increases by per 0.113 mmol/L

Prevalence of Hypertriglyceridemia (HTG) in China, 2018-2030E

- HTG has high prevalence in China. There were approximately 245.0 million HTG patients in China in 2023. In 2023, there were approximately 49.0 million statin-treated adult patients (20% of statin-treated patients) in China with elevated TG levels (≥150 mg/dL). 5% of HTG patients are severe HTG patients. Since Vascepa is indicated as an adjunct to maximally tolerated statin therapy to reduce the risk of myocardial infarction, stroke, coronary revascularization, and unstable angina requiring hospitalization in adult patients with elevated triglyceride (TG) levels(≥ 150 mg/dL). Addressable patients for the CRR indication must have either established CVD or diabetes and two or more additional risk factors for CVD. Besides, Vascepa is also indicated as adjunct to diet to reduce TG levels in adult patients with severe hypertriglyceridemia. Both of populations above are addressable patients for Vascepa.
- The prevalence of HTG in the US is higher than that in China. According to ***Triglycerides and cardiovascular disease: a scientific statement from the American Heart Association***, about 31% of American adults have TG levels ≥ 150 mg/dl, and the proportion of patients with TG ≥ 200 mg/dl and TG ≥ 500 mg/dl achieved 16.2% and 1.1% respectively. Excessive fat and sugar intake on the daily basis is main reason why the USA present a higher prevalence of HTG than China.

Prevalence of Hypertriglyceridemia in China, 2018-2030E

Period	CAGR
2018-2023	2.6%
2023-2026E	1.2%
2026E-2030E	0.7%



Source: Frost & Sullivan analysis

Treatment Paradigm of Hypertriglyceridemia

- Statin therapy is the current mainstay for CV risk reduction, including for dyslipidemia patients. Statin therapy may reduce the risk of major CV events by approximately 25% to 35% primarily through lowering low-density lipoprotein cholesterol ("LDL-C") levels, leaving significant persistent CV risk of approximately 65% to 75%. High triglyceride ("TG") levels remain important markers of risk for CV events, independent of LDL-C level. Older generation TG-lowing therapies failed to demonstrate incremental CV benefit among statin-treated patients with well-controlled LDL-C. Many of HTG patients are taking statin therapy directed at lowering the risk of CVD primarily by lowering their LDL-C levels.

Hypercholesterolemia Treatment

Life style changes including diet control and exercise

Medication

Drug Class	Drug
HMG-CoA reductase inhibitors	Lovastatin and Pravastatin etc.
Cholesterol absorption inhibitors	Ezetimibe
PCSK9	Alirocumab, Evolocumab
Fibric acid derivatives	Gemfibrozil and Fenofibrate etc.
Niacin	Nicotinic acid
Bile acid sequestrants	Cholestyramine
MTP inhibitor	Lomitapide
Antisense apolipoprotein	Mipomersen
Omega-3 fatty acids	Icosapent ethyl

Source: AACE 2017, Frost & Sullivan analysis

Overview of Lipid-Regulating Drugs

- Statin therapy is the current mainstay for CV risk reduction, including for dyslipidemia patients. The market size of statin therapy increased rapidly from RMB 20.7 billion in 2017 to RMB 16.3 billion in 2022 at a CAGR of -4.7%. The originator-branded version of atorvastatin calcium, a leading statin product, was one of the best-selling drugs in China in 2021, and its sales revenue in China reached approximately RMB 5.4 billion in 2021.

Mechanism of Action ("MoA")	Primary MoA Target	Generic/Patented	Representative Brand	Manufacture for the Representative Band	China Launch Time
Niacin	Lowing TG Levels	Generic	N/A	N/A	1981
Fibrates	Lowing TG Levels	Generic	N/A	N/A	1988
Statin	Lowing LDL-C Levels	Generic	Lipitor	Pfizer	1999
Cholesterol absorption inhibitors	Lowing LDL-C Levels	Generic	Zetia	MSD	2007
PCSK-9 inhibitors	Lowing LDL-C Levels	Patented	Repatha	Amgen	2018
			Praluent	Sanofi	2019

Source: Frost & Sullivan Analysis

Unmet Needs in the Treatment of Hypertriglyceridemia

Statin Intolerance	• In general, HTG patients have good tolerance with Statins, the proportion of those are not able to tolerate the severe adverse effects is varying from 5% to 30%. Statin intolerance includes complete intolerance (5%) and partial intolerance (25%). Patients who are completely statin intolerance are not applicable to statin therapy or combo-therapy with statins. Partial statin intolerance refers to being unable to tolerate a certain therapeutic dose of statins. For most of statin intolerance patients, switching statin types and doses should be taken into account. For those receiving statin therapy failure, non-statin drugs are highly recommended, such as fibrates, omega-3 fatty acids and PCSK-9 inhibitors.
Adding IPE on statin therapy is able to lower TG lever and reduce cardiovascular risk	• The incidence of high triglycerides (HTG) is high in China, and even after statin treatment, there are still a large number of patients with elevated triglycerides (TG) who do not meet the treatment goal. The tolerance of high-dose statins in our population is poorer than that in western countries, and in clinical practice, it is usually recommended to start with moderate-dose or moderate-intensity statins. The ***Chinese guideline on the primary prevention of cardiovascular diseases*** recommends that if patients still fail to get their TG-level controlled after treatment with moderate-dose statins, consideration should be given to using high-dose IPE in combination therapy to further lower TG levels. Even after controlling LDL-C with statin therapy, high TG levels still increase the risk of cardiovascular disease, and IPE is also recommended by multiple guidelines for use in combination with statins to reduce cardiovascular risk.
Drug Intervention and Lifestyle Modification Go Hand in Hand	• Apart from drug intervention, adopting a healthy lifestyle matters too. Healthy lifestyle choices include exercising regularly, avoiding sugar and refined carbohydrates, losing weight, choosing healthier fats and limiting alcohol intake. Regular exercise can lower triglycerides and boost "good" cholesterol. Extra calories are converted to triglycerides and stored as fat, so reducing your calories will reduce triglycerides. Besides, avoiding trans fats or foods with hydrogenated oils or fats can lower triglycerides. Alcohol is high in calories and sugar and has a particularly potent effect on triglycerides, so controlling alcohol is also important.

Source: Literature review, Frost & Sullivan analysis

Overview of Omega-3 Fatty Acid

- Cardiovascular disease is a group of diseases affecting your heart and blood vessels. These diseases can affect one or many parts of your heart and/or blood vessels. A person may be symptomatic (physically experiencing the disease) or asymptomatic (not feeling anything at all).
- Cardiovascular disease can be roughly divided into heart issues and vessel issues, including narrowing of the blood vessels in your heart, other organs or throughout your body, heart and blood vessel problems present at birth, disfunction of heart valves and irregular heart rhythms.

Classification of Omega-3 Fatty Acid

ALA

- Rich in vegetables, fruits and soy products. Alpha-linolenic acid (ALA) is an omega 3 fatty acid essential for human health and serves as a precursor in the human body to the formation of DHA and EPA.

EPA

- Polyunsaturated fatty acid, containing a 20-C structure. Rich in marine animals (especially in marine fishes). EPA is not able to be self-synthesized by human bodies and it usually comes from food. IPE, standing for icosapent ethyl, is purely EPA ethyl ester.

DHA

- Polyunsaturated fatty acid, containing a 22-C structure. Rich in marine animals (especially in marine fishes). EPA is not able to be self-synthesized by human bodies and it usually comes from food.

How Does it Work

Anti-inflammatory

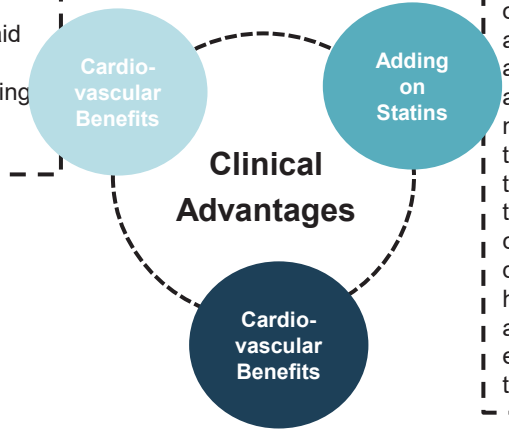
Lower triglycerides

Inhibit lipid oxidation & cholesterol synthesis

Clinical Advantages

IPE

A qualified health claim from FDA said EPA and DHA are beneficial in reducing coronary heart disease.



IPE is the first and only omega-3 fatty acid drug, approved by FDA as an adjunct to maximally tolerated statin therapy to reduce the risk of cardiovascular diseases requiring hospitalization in adult patients with elevated triglyceride.

IPE

Guideline from American Diabetes Association (2022) **recommends to add IPE to statins to reduce one's cardiovascular risk** especially for patients whose LDL-C under control but TG staying high level after statin therapy.

Source: Frost & Sullivan Analysis

Main Prescription Omega-3 Fatty Acid Drugs Clinical Research Results

Median Difference of Lipid parameter From Placebo in Studies of Patients With Severe Hypertriglyceridemia (triglyceridemia levels ≥ 500 mg/dL) Who Have Received Prescription Omega-3 Fatty Acid Products

The result has shown that Vascepa produces significant reduction in all six lipid parameters, TGs, Non-HDL-C, TC, LDL-C, VLDL-C and Apo-B, while Lovaza and Epanova probably lead to a considerable increase in LDL-C levels. Compared to Lovaza and Epanova, Vascepa can effectively avoid the risk of LDL-C levels rise when reducing TG levels, showing its uniqueness among omega-3 fatty acid drugs. Vascepa has incredible clinical effects in reducing all six lipid parameters compared to placebo.

Brand Name	Lovaza			Epanova			Vascepa		
Active Ingredient	EPA ethyl ester plus DHA ethyl ester			EPA free fatty acid plus DHA free fatty acid			Icosapent ethyl (IPE)		
Parameter (mg/dL)	Baseline in drug group	Change in drug group (%)	Difference from placebo (%)	Baseline in drug group	Change in drug group (%)	Difference from placebo (%)	Baseline in drug group	Change in drug group (%)	Difference from placebo (%)
TGs	816	-44.9	-51.6	655	-31	-21	680	-27	-33
Non-HDL-C	271	-13.8	-10.2	225	-8	-10	225	-8	-18
TC	296	-9.7	-8.0	254	-6	-9	254	-7	-16
LDL-C	89	+44.5	+49.3	90	+26	+15	91	-5	-2
VLDL-C	175	-41.7	-40.8	126	-35	-21	123	-20	-29
Apo B	/	/	/	118	+6	+2	121	-4	-9

To be noted, Vascepa is the only omega-3 fatty acid drug that obtained FDA approval for cardiovascular risk reduction. However, the effects of Lovaza and Epanova on cardiovascular mortality and morbidity have not been determined.
Since the release of the clinical trial results of REDUCE-IT, several guidelines have been updated accordingly. Vascepa has been recommended by the American Diabetes Association, the National Lipid Association, the European Society of Cardiology, and the European Atherosclerosis Society.

Difference= Median of [Drug % Change – Placebo % Change]

Source: Frost & Sullivan Analysis

Vascepa Clinical Research Results

Effect of Vascepa on Time to First Occurrence of Cardiovascular Events in Patients with Elevated Triglyceride Levels and Other Risk Factors for Cardiovascular Disease in REDUCE-IT

	Vascepa	Placebo	Vascepa vs. Placebo
	Incidence Rate (per 100 patient years)		Hazard Ratio (95% CI)
Primary composite endpoint			
Cardiovascular death, myocardial infarction, stroke, coronary revascularization, hospitalization for unstable angina (5-point MACE)	4.3	5.7	0.75 (0.68, 0.83)
Key secondary composite endpoint			
Cardiovascular death, myocardial infarction, stroke (3-point MACE)	2.7	3.7	0.74 (0.65, 0.83)
Other secondary endpoints			
Fatal or non-fatal myocardial infarction	1.5	2.1	0.69 (0.58, 0.81)
Emergent or urgent coronary revascularization	1.3	1.9	0.65 (0.55, 0.78)
Cardiovascular death	1.0	1.2	0.80 (0.66, 0.98)
Hospitalization for unstable angina	0.6	0.9	0.68 (0.53, 0.87)
Fatal or non-fatal stroke	0.6	0.8	0.72 (0.55, 0.93)

VASCEPA significantly reduced the risk for the primary composite endpoint (time to first occurrence of cardiovascular death, myocardial infarction, stroke, coronary revascularization, or hospitalization for unstable angina; p<0.0001) and the key secondary composite endpoint (time to first occurrence of cardiovascular death, myocardial infarction, or stroke; p<0.0001).

Source: Frost & Sullivan Analysis

Icosapent Ethyl (IPE) Approved by NMPA

- 立瑞欣 developed by Guowell Pharma and 唯思沛 developed by Edding Pharm are the only two IPE in the Chinese market.唯思沛 has got approved in the indication of CRR, but 立瑞欣 has not yet.

Drug Name	Brand Name	Company	Drug Type	Indications	Approved Date
Icosapent ethyl	立瑞欣	Guowell Pharma	Generic	Indicated to lower the level of TG in adult patients with severe HTG	2023/1/31
Icosapent ethyl	Vascepa 唯思沛	Amarin Pharmaceuticals/ Edding Pharm	Original	Indicated to lower the level of TG in adult patients with severe HTG	2023/5/29
			Original	As an adjunct statin therapy to reduce the risk of myocardial infarction, stroke, coronary revascularization, and unstable angina requiring hospitalization in adult patients with elevated triglyceride (TG) levels (≥ 150 mg/dL) and established cardiovascular disease or diabetes mellitus and 2 or more additional risk factors for cardiovascular disease*	2024/6/28

Note: CRR*
As of April 7th, 2025

Source: NMPA, Frost & Sullivan Analysis

Competitive Landscape of Icosapent Ethyl (IPE) Pipeline in China

Drug Name	Target	Company	Clinical Stage	Indications	NDA Acceptance Date
Icosapent ethyl	/	Mochida Pharmaceutical Co.,Ltd. Catalent Japan K.K. Kakegawa Plant Sumitomo Dainippon Pharma Co., Ltd.	NDA	Indicated to lower the level of TG in adult patients with severe HTG	2024-07-02
Icosapent ethyl	/	Guowell Pharma	NDA	As an adjunct statin therapy to reduce the risk of myocardial infarction, stroke, coronary revascularization, and unstable angina requiring hospitalization in adult patients with elevated triglyceride (TG) levels (≥ 150 mg/dL) and established cardiovascular disease or diabetes mellitus and 2 or more additional risk factors for cardiovascular disease*	2024-09-12

Note: Icosapent ethyl fromGuowei is generic drug, its lowering HTG indication has approved, so we list its NDA of a new indication. Other *generics are not included.*
**:CRR*
As of April 7th, 2025

Source: CDE, Frost & Sullivan Analysis

Growth Driver of China IPE Market

Lowering Patient Costing and NRDL Inclusion

- Since prescription Omega-3 fatty acid drugs are under prescription, the hypertriglyceridemia is chronic disease which requires long-term treating process, the annual cost is a major consideration and factor for patients' options.
- The establishment of National Healthcare Security Administration promotes the rapid progress of medical insurance, including the NRDL revision by price negotiation and dynamic adjustment to include more drugs in the reimbursement list in a more flexible manner, lowering total costs, increasing the compliance and drug accessibility.

Combo-therapy for Higher Efficacy than Mono-therapy

- Vascepa is recommended to taken with statin drugs for higher efficacy. For most cases, the underlying basis of CVD is complicated, which leads to limited treating response for mono-therapy.
- Combo-therapy with proved clinical result ensures the recommended drugs are acting separated, or together, other than conflicted, contributing better treating performance and benefit on the long run.

Lowering SAEs, Easing Usage Approach

- Since hypertriglyceridemia and CVD are highly related to aging process, the aged population would be a larger part in the future.
- For aged patients, the SAEs and usage approach, namely frequency, dosage form, are another major consideration. Oral drug with lower SAE rate is better for mass usage for safety reason, which can be ensured by drug purification.

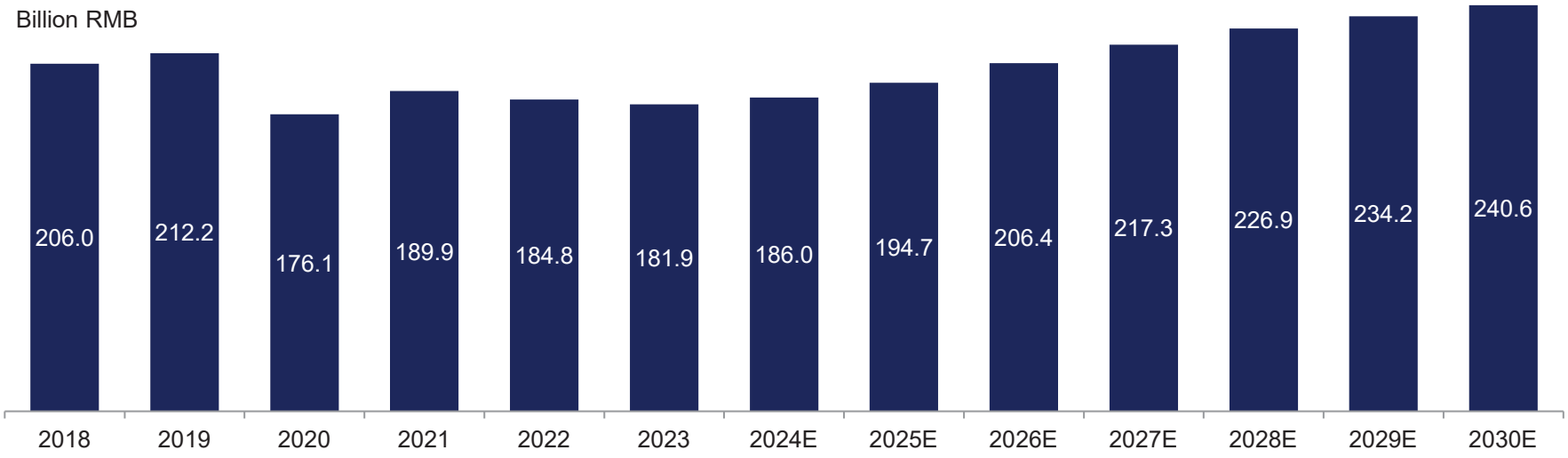
Source: Frost & Sullivan Analysis

China Cardiovascular Drug Market, 2018-2030E

- China cardiovascular drug market decreased from RMB 206.0 billion in 2018 to RMB 181.9 billion in 2023. The market is expected to increase to RMB 206.4 billion in 2026 at a CAGR of 4.3% from 2023 and RMB 240.6 billion in 2030 at a CAGR of 3.9% from 2026, largely driven by an aging population, urban lifestyle and continuous research and development for CVD drugs.

China Cardiovascular Drug Market, 2018-2030E

Period	CAGR
2018-2023	-2.5%
2023-2026E	4.3%
2026E-2030E	3.9%



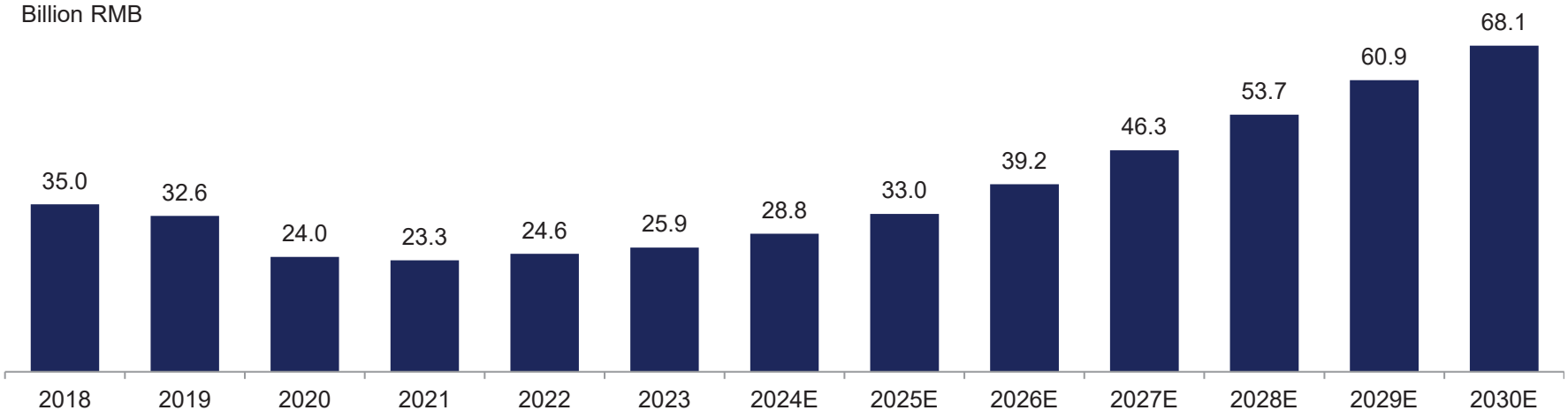
Source: Frost & Sullivan analysis

Lipid-regulation Drug Market in China, 2018-2030E

- China lipid-lowering drug market size reached 35.0 billion RMB in 2018, went down to 25.9 billion RMB in 2023 influenced by the national centralized drug procurement. Atorvastatin and rosuvastatin were involved in the first round of national centralized drug procurement, simvastatin and pravastatin in the second and third round respectively. However, the market size is estimated to rise to 68.1 billion by 2030 due to the launch of various lipid-lowering drugs with different mechanisms of action, such as omega-3 fatty acid, PCSK9 inhibitors and MTP inhibitors, etc.

Lipid-regulation Drug Market in China, 2018-2030E

Period	CAGR
2018-2023	-5.8%
2023-2026E	14.7%
2026E-2030E	14.8%



Source: Frost & Sullivan Analysis

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7	Breast Cancer Drug Market in China

Overview of Thrombocytopenia

- 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.
	Types of anemia	Anemia influences the production of platelets
	Viral infection	Viral infections, such as hepatitis C or chronic liver disease and some rare bacterial infection may lead to thrombocytopenia.
	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

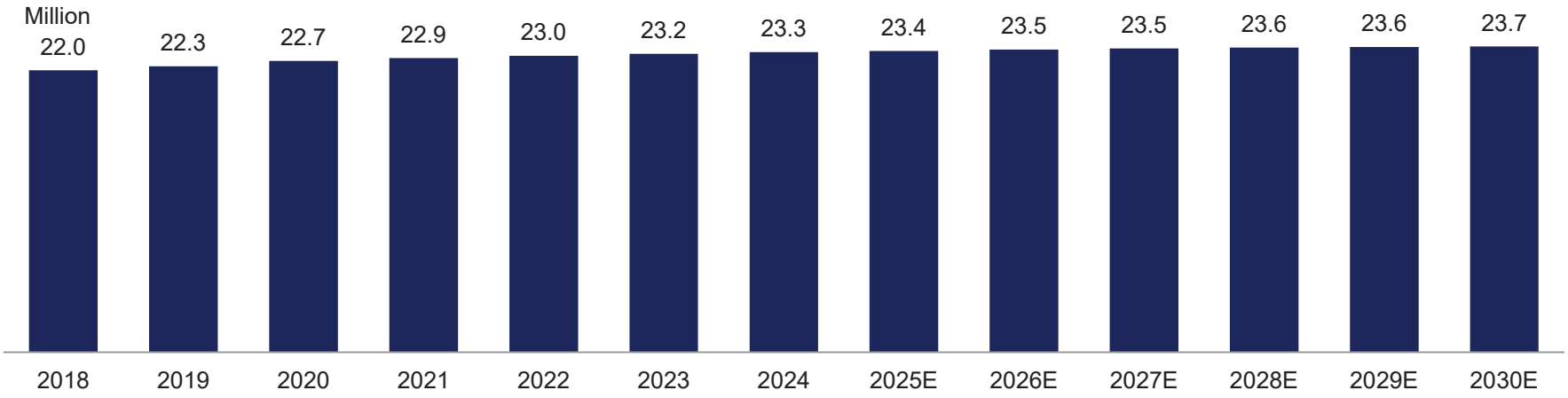
Source: Frost & Sullivan Analysis

Prevalence of Thrombocytopenia in CLD Patients in China, 2019-2030E

- Thrombocytopenia is the most common hematological abnormality encountered in patients with chronic liver disease (CLD), occurring in 78% of patients with cirrhosis or fibrosis.
- The number of CLD patients with thrombocytopenia went up from 22.0 million in 2018 to 23.2 million in 2023 at a CAGR of 1.0%, and it is estimated to increase to 23.5 million in 2026 and 23.7 million in 2030.

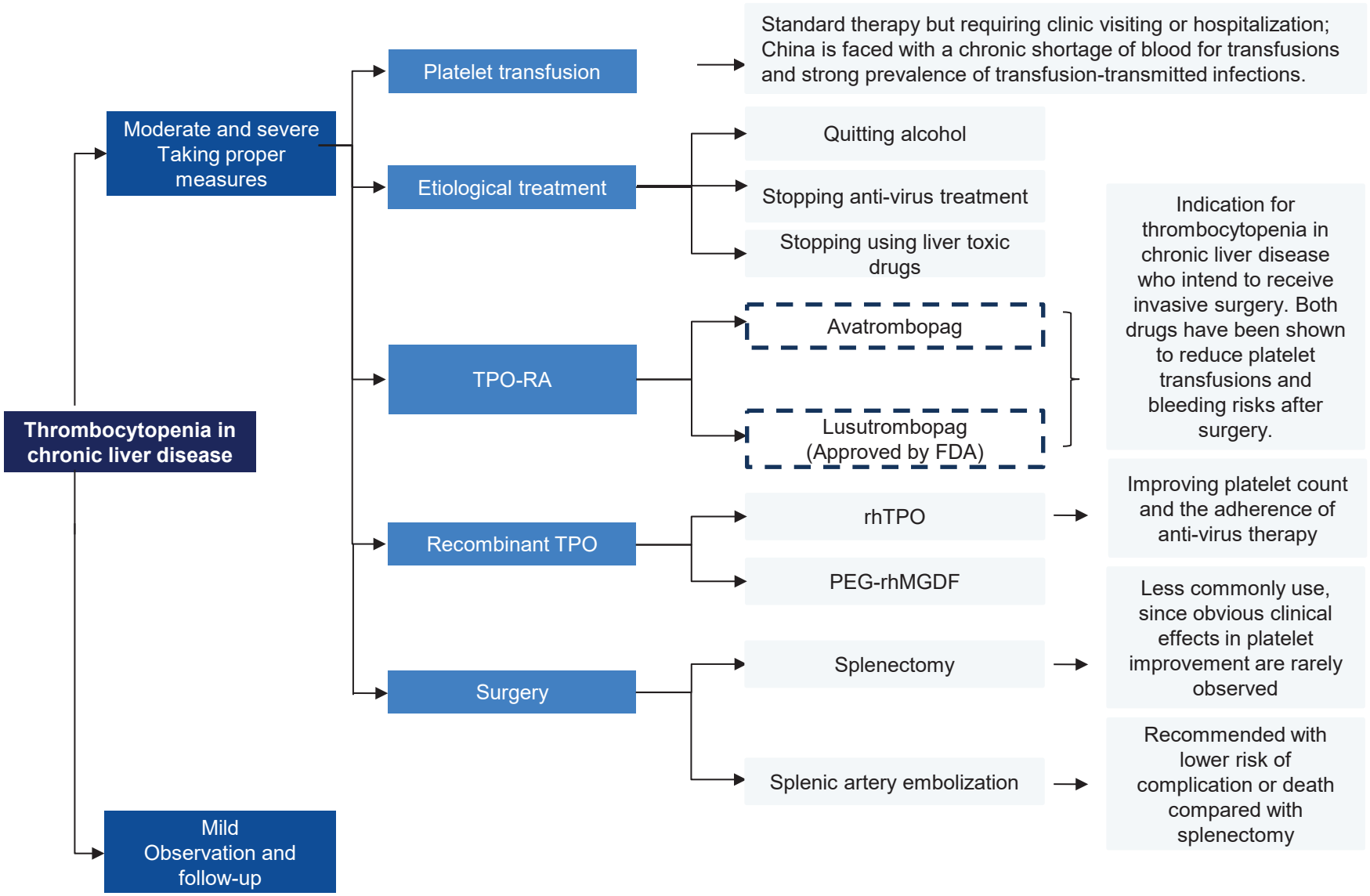
Prevalence of Thrombocytopenia in CLD Patients in China, 2019-2030E

Period	CAGR
2019-2024	0.9%
2024-2027E	0.4%
2027E-2030E	0.2%



Source: Frost & Sullivan Analysis

Treatment Paradigm of Thrombocytopenia in CLD



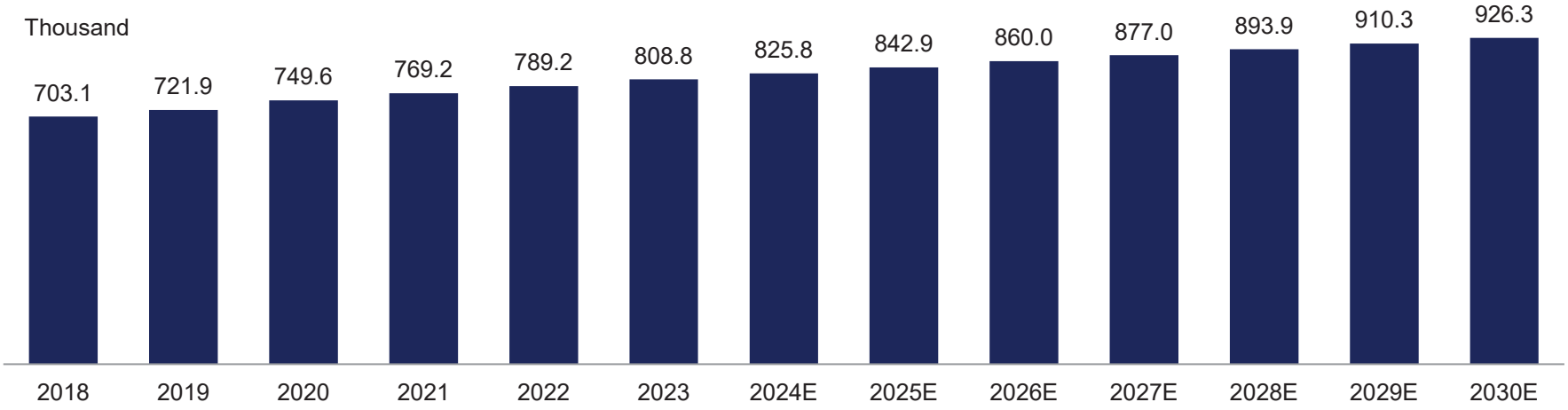
Source: Literature Review, Frost & Sullivan Analysis

Prevalence of Thrombocytopenia in CIT Patients in China, 2018-2030E

- Thrombocytopenia is the most common hematological abnormality encountered in cancer patients who received chemotherapy. The number of CIT patients with thrombocytopenia went up from 703.1 thousand in 2018 to 808.8 thousand in 2023 at a CAGR of 2.8%, and it is estimated to increase to 860.0 thousand in 2026 and 926.3 thousand in 2030. Around 80% of cancer patients have received chemotherapy, 20.5% of which may occur CIT.

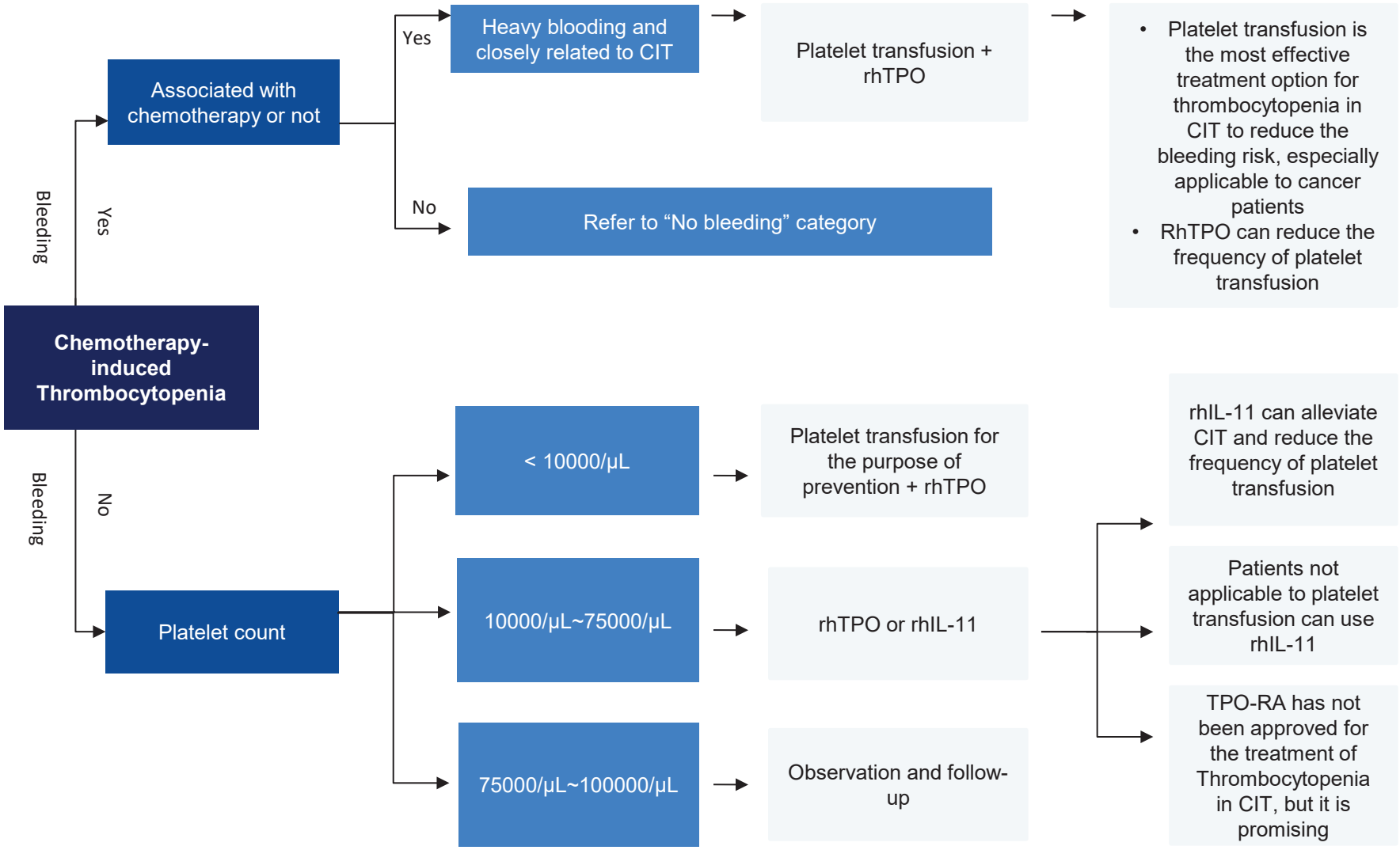
Prevalence of Thrombocytopenia in CIT Patients in China, 2018-2030E

Period	CAGR
2018-2023	2.8%
2023-2026E	2.1%
2026E-2030E	1.9%



Source: Frost & Sullivan Analysis

Treatment Paradigm of CIT



Source: Literature Review, Frost & Sullivan Analysis

Unmet Needs in the Treatment of Thrombocytopenia

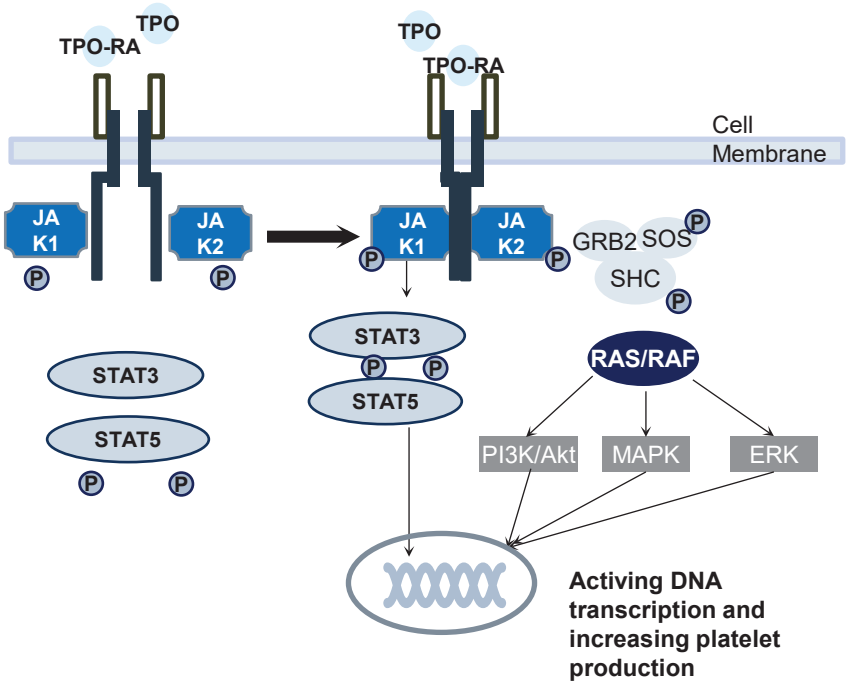
Prevention of Thrombocytopenia	• In CIT cases, the platelet count remains a relative high level in two or three days after recieving chemotherapy, and the TPO level remains relatively low due to the negative feedback loop between them. When the platelet count has not yet decreased and the TPO level is 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

Overview of TPO-RA

- Thrombopoietin (Tpo) is cytokine that has been reported to play an important role in proliferation and differentiation of megakaryocyte progenitors. It also stimulates the growth of other blood cells including granulocytes, erythrocytes and monocytes. Thrombopoietin receptor agonists (Tpo-RAs) can bind to the thrombopoietin (Tpo) receptor, causing conformational change in the Tpo receptor, activation of the JAK2/STAT5 pathway, and a resulting increased megakaryocyte progenitor proliferation and increased platelet production.
- Compared to traditional platelet transfusion and rhTPO, TPO-RA therapy is perceived to be an efficient drug treatment for CLD-associated TCP and CIT patients.

Mechanism of Action

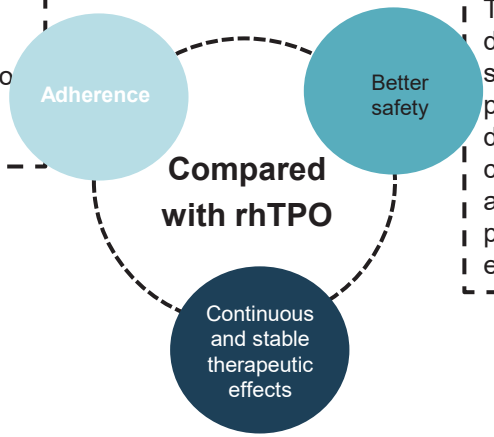


Indications

ITP | CIT | CLD combined with thrombocytopenia

Clinical Advantages

Compared with injection, tablet enables patients to have higher adherence



TPO-RAs have demonstrated a superior safety profile with less drug complication and minor potential side effects

For one thing, patients usually have a higher response rate to TPO-RA than to rhTPO. For another, compared with rhTPO, TPO-RA dose not compete with endogenous TPO, does not induce TPO antibodies and can achieve a stable and predictable increase in platelet count.

Source: Literature review, Frost & Sullivan analysis

TPO-RA Approved by NMPA (Only Originator-branded Drugs Included)

Drug Name	Brand Name	Company	Target	Indications	Approved Date	Included in NRDL or not	Treatment Cost per Cycle (RMB)
Lusutrombopag	芦曲泊帕 Mulpleta	Edding Pharm	TPOR	Thrombocytopenia in chronic liver disease	2023/6/27	Yes (in NRDL 2023)	4053
Romiplostim	惠尔凝 Nplate	Kyowa Kirin Co., Ltd.	TPOR	Immune thrombocytopenia	2022/1/7	Yes (in NRDL 2022)	/
Hetrombopag olamine	恒曲	Jiangsu Hengrui Medicine Co.,Ltd.	TPOR	Primary immune thrombocytopenia; Severe aplastic anemia	2021/6/16	Yes (in NRDL 2021)	/
Avatrombopag maleate	苏可欣 Doptelet	Dova Pharmaceuticals, Inc / Fosun Pharma	TPOR	Thrombocytopenia in chronic liver disease	2020/4/14	Yes (in NRDL 2020)	5820
				Immune thrombocytopenia	2024/6/18	No	/
Eltrombopag diolamine	瑞弗兰 Promacta/Revolade	Novartis	TPOR	Severe aplastic anemia	2023/2/21	Yes (in NRDL 2023)	/
				Immune thrombocytopenia	2017/12/28	Yes (in NRDL 2021)	/

Note: As of April 7th, 2025; Generics are not included.

Source: NMPA, Frost & Sullivan Analysis

Competitive Landscape of China TPO-RA Pipeline

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
None					

Note: As of April 7th, 2025; Generics are not included.

Source: NMPA, Frost & Sullivan Analysis

Core Strengths of Mulpleta (Original Lusutrombopag)

Better safety	• Lusutrombopag has demonstrated a superior safety profile with less significant drug-drug interactions and signature adverse events, compared to IL-11 and rhTPO[1]. Lusutrombopag do not have contraindications stated in their FDA-approved labels.[1] The most common or important side effects of IL-11 include allergic reaction, nausea and vomiting, fluid retention and fever.
Strong Efficacy	• Patients usually have a higher response rate to TPO-RA than to rhTPO, accompanying with fast drug response with observable platelet increase within 3-5 days post treatment. Procedures should be completed 5 to 8 days after the completion of TPO-RA.[1] Platelet values increase because of these thrombopoietin receptor agonists but return to baseline levels 30 days after the first dose. Additionally, compared with rhTPO, TPO-RA dose not compete with endogenous TPO, does not induce anti-platelet antibodies and can achieve a stable and predictable increase in platelet count.[2,3] • Mulpleta was effective quickly in 3-5 days, with a response rate of 81.8% at any time during the study period.[4]
Convenience	• Mulpleta is orally administrated, which is more convenient for patients compared to IL-11 and rhTPO products, which are only available for intravenous administration. Compared with intravenous administration, oral administration enables patients to have higher adherence.
No drug interaction concern and taken on an empty stomach or with a meal	• Mulpleta is metabolized primarily by the enzyme CYP4A11 and is not subject to conventional drug interactions.[6] Compared to Doptelet, Mulpleta is the only approved oral small-molecule non-peptide TPO-RA that can be taken on an empty stomach or with a meal.[7]

Note:1. ***Current Treatment of Thrombocytopenia inChronic Liver Disease*** *2.* ***Thrombopoietin Receptor Agonists (TPO-RAs): Drug Class Considerations for Pharmacists*** *3.* ***Thrombopoietin receptor agonist (TPO-RA) treatment raises platelet counts and reduces anti-platelet antibody levels in mice with immune thrombocytopenia. 4. Hidaka H, Kurosaki M, Tanaka H, et al.Lusutrombopag Reduces Need for Platelet Transfusion in Patients With Thrombocytopenia Undergoing Invasive Procedures[J]. Clin Gastroenterol Hepatol, 2019, 17(6): 1192-1200. 5. Ding Z, Wu H, Zeng YY, et al. Lusutrombopag for thrombocytopenia in Chinese patients with chronic liver disease undergoing invasive procedures. Hepatol Int. 2023 Feb;17(1):180-189. doi: 10.1007/s12072-022-10421-9. 6. Drug label 7. Randomized Controlled Trial Clin Ther. 2019 Sep;41(9):1747-1754.e2.***

Source: Frost & Sullivan Analysis

Growth Driver of Tpo-RA Drugs

Lowering Patient Costing and NRDL Inclusion

- Most of chronic liver diseases are marching to cirrhosis in late stage, leading to liver cancer finally. Since the whole span takes years, drug price and total cost are important factors in drug selection.
- The establishment of National Healthcare Security Administration promotes the rapid progress of medical insurance, including the NRDL revision by price negotiation and dynamic adjustment to include more drugs in the reimbursement list in a more flexible manner, lowering total costs, increasing the compliance and drug accessibility.

Indication Expansion

- Thrombocytopenia occurs in most CLD patients, however, there are still more common causative factors to trigger thrombocytopenia, namely chemotherapy, immune system disorder, infections.
- In clinical usage, Tpo-RAs have already been mainly applied on ITP and CLD-thrombocytopenia; in future, Tpo-RA could also be applied for different causes induced thrombocytopenia.

Lowering SAEs, Easing Usage Approach

- Since thrombocytopenia is highly related to aging process, the aged population would be a larger part in the future.
- For aged patients, the SAEs and usage approach, namely frequency, dosage form, are another major consideration. Oral drug with lower SAE rate is better for mass usage, especially for long-acting, controlled releasing dosage form.

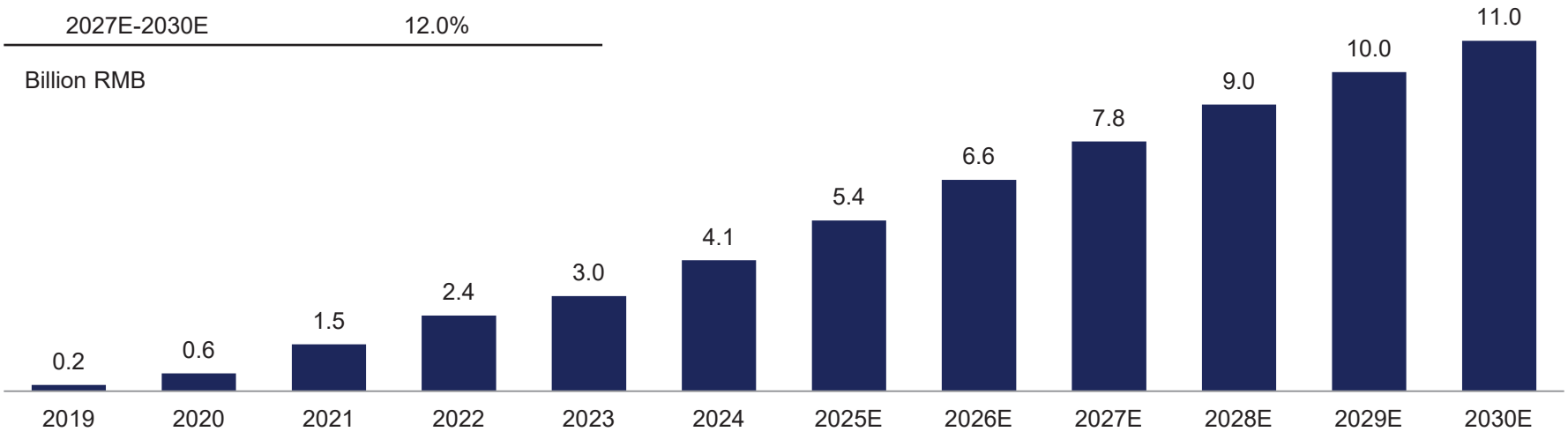
Source: Frost & Sullivan Analysis

China TPO-RA Market, 2019-2030E

- The China TPO-RA market increased from 0.2 billion RMB to 4.1 billion RMB at a incredible CAGR of 84.5% from 2019 to 2024. The number is projected to reach 7.8 billion RMB in 2027 and 11.0 billion RMB in 2030 at a CAGR of 24.0% and 12.0% from 2024 to 2027 and from 2027 to 2030 respectively.

China TPO-RA Market, 2019-2030E

Period	CAGR
2019-2024	84.50%
2024-2027E	24.0%
2027E-2030E	12.0%



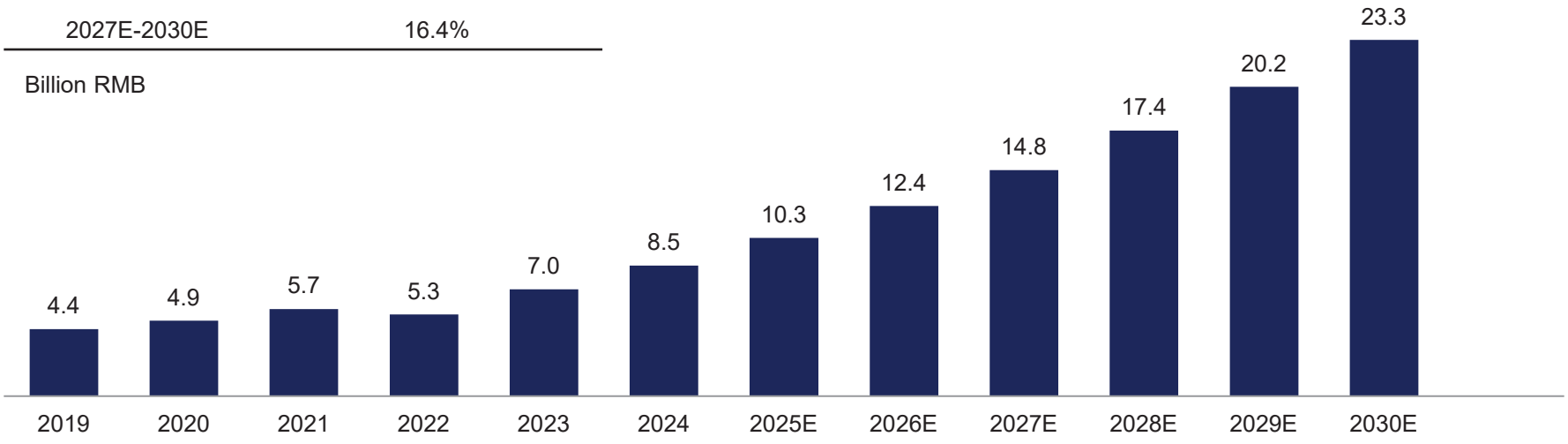
Source: Frost & Sullivan Analysis

China Thrombocytopenia Treatment Market, 2018-2030E

- The China thrombocytopenia treatment increased from 4.4 billion RMB to 8.5 billion RMB at a CAGR of 14.2% from 2019 to 2024. The number is projected to reach 14.8 billion RMB in 2027 and 23.3 billion RMB in 2030 at a CAGR of 20.1% and 16.4% from 2024 to 2026 and from 2027 to 2030 respectively.

China Thrombocytopenia Treatment Market, 2019-2030E

Period	CAGR
2019-2024	14.2%
2024-2027E	20.1%
2027E-2030E	16.4%



Source: Frost & Sullivan Analysis

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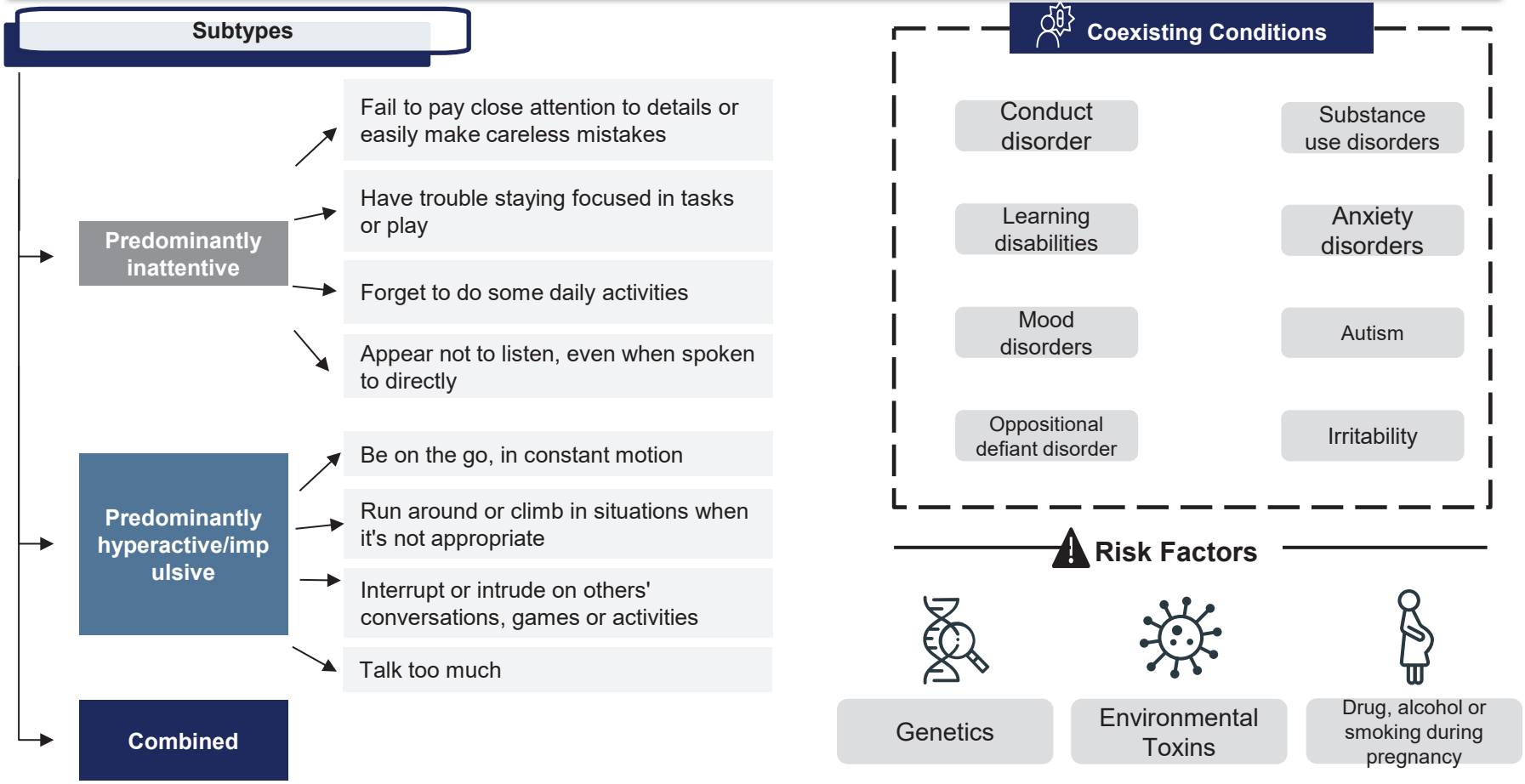
6	**Attention Deficit/Hyperactivity Disorder Drug Market in China**
7	Breast Cancer Drug Market in China

Overview of Attention Deficit/Hyperactivity Disorder (ADHD)

- Attention-deficit/hyperactivity disorder (ADHD) is a chronic condition that affects millions of children and adolescents and often continues into adulthood. ADHD includes a combination of persistent problems, such as difficulty sustaining attention, hyperactivity and impulsive behavior. Children and adolescents with ADHD may also struggle with low self-esteem, troubled relationships and poor performance in school. Symptoms sometimes lessen with age. While treatment won't cure ADHD, it can help a great deal with symptoms. Treatment typically involves medications and behavioral interventions. Early diagnosis and treatment can make a big difference in outcome.



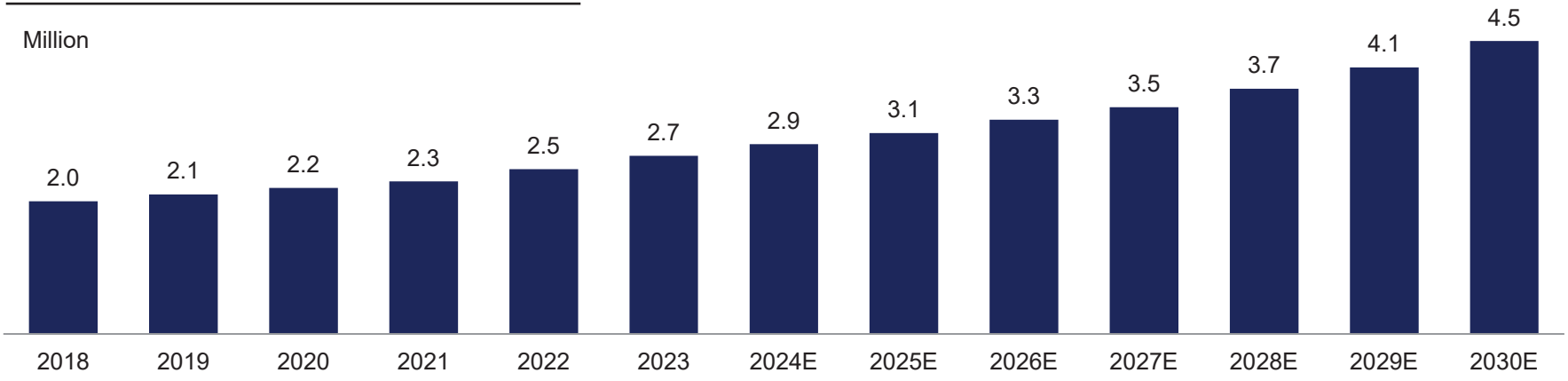
Source: Literature review, Frost & Sullivan analysis

Number of Diagnosed ADHD Children and Adolescents in China, 2018-2030E

- ADHD is one of the most common neurodevelopmental disorders of childhood. It is usually first diagnosed in childhood and often lasts into adulthood. Children with ADHD may have trouble paying attention, controlling impulsive behaviors (may act without thinking about what the result will be), or be overly active. Currently, ADHD diagnosis rate in China is relatively low, contributed by complexity of diagnosis, lack of patient education, and social factors. The average diagnosis rate is expected to increase in future.
- ADHD has been significantly underdiagnosed and undertreated in China. The diagnosed ADHD children and adolescents in China was approximately 2.7 million in 2023, and it is expected to reach 3.3 million by 2026, growing at a CAGR of 6.3% from 2023 to 2026, driven by the improved disease awareness and the rising diagnosis rate for ADHD.

Number of Diagnosed ADHD Children and Adolescents in China, 2018-2030E

Period	CAGR
2018-2023	6.1%
2023-2026E	6.3%
2026E-2030E	8.1%



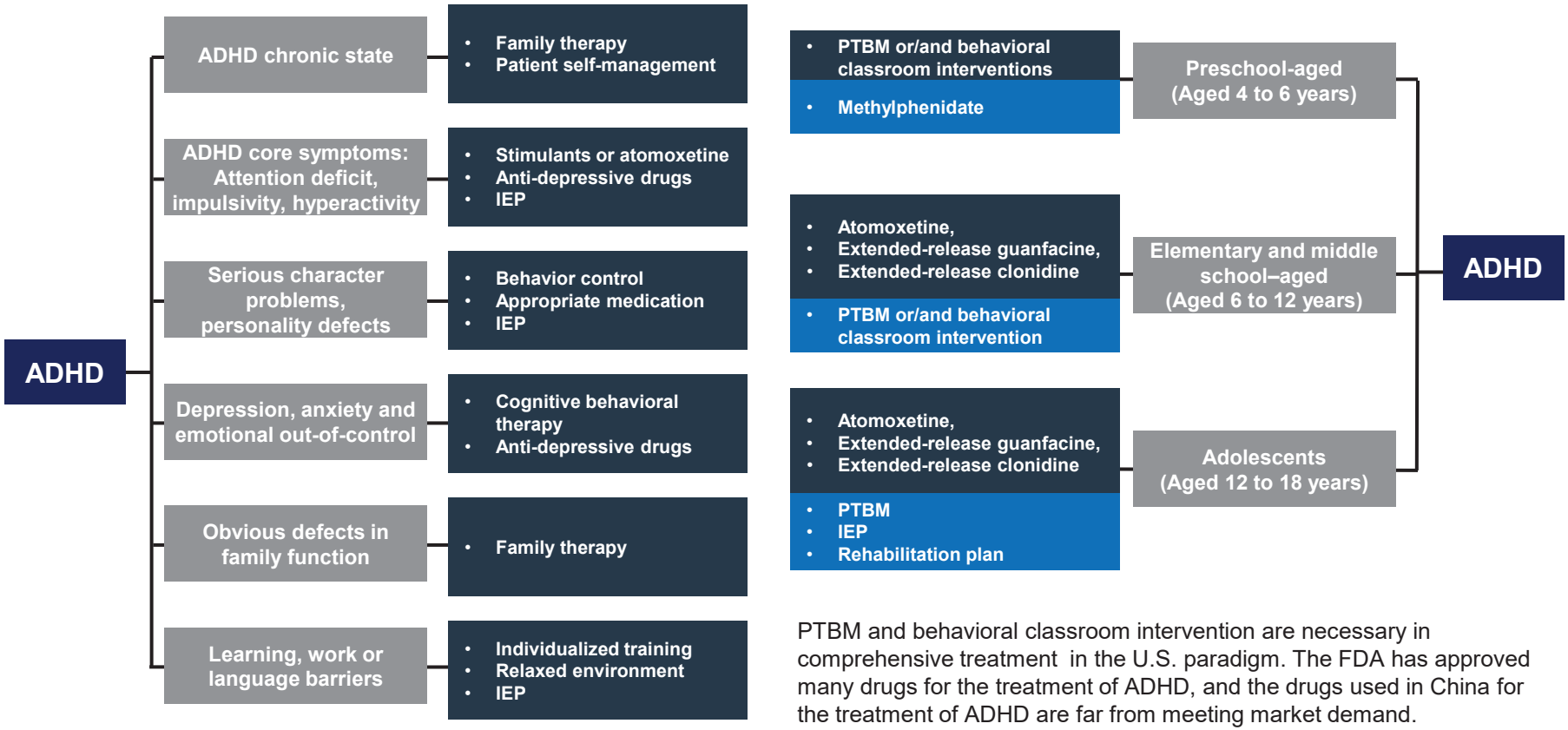
Source: Frost & Sullivan analysis

Estimated addressable ADHD patient population in China

	Population under Age of 18	ADHD Prevalence Rate in Population under Age of 18	Diagnosis Rate	Number of Diagnosed ADHD Children and Adolescents	Drug Treatment Rate	Estimated Addressable ADHD Population
China (2023)	289 million	6.7%	14%	2.7 million	31%	840 thousand
China (2026E)	270 million	7.1%	17%	3.3 million	35%	1,155 thousand
China (2030E)	240 million	8.1%	23%	4.5 million	45%	2,025 thousand
The U.S.	74 million	9.5%	85.3%	6.0 million	80%	4800 thousand

Source: CDC, Frost & Sullivan analysis

Treatment Paradigm of ADHD, China vs. U.S.



PTBM and behavioral classroom intervention are necessary in comprehensive treatment in the U.S. paradigm. The FDA has approved many drugs for the treatment of ADHD, and the drugs used in China for the treatment of ADHD are far from meeting market demand.

IEP: Individualized education plan PTBM: Parent-child interaction therapy

Stimulants: Methylphenidate Anti-depressive drugs: Bupropion

Source: American Academy of Pediatrics, 中国注意缺陷多动障碍防治指南, Frost & Sullivan analysis

Unmet Needs in the Treatment of ADHD

- "Diagnosis and treatment rates need to be improved", “A lack of professionals in psychologists and pediatricians“, "ADHD in adults is difficult to identify or tends to be misdiagnosed, and “a lack of clinical research for adult ADHD." They are reasons for the unmet needs in the treatment of ADHD. Ways to improve the diagnosis and treatment rates include Expanding the workforce of specialized medical professionals in psychiatry and pediatrics and improving their medical expertise, Promoting ADHD drugs in the market, and Refining the diagnosis and treatment process.

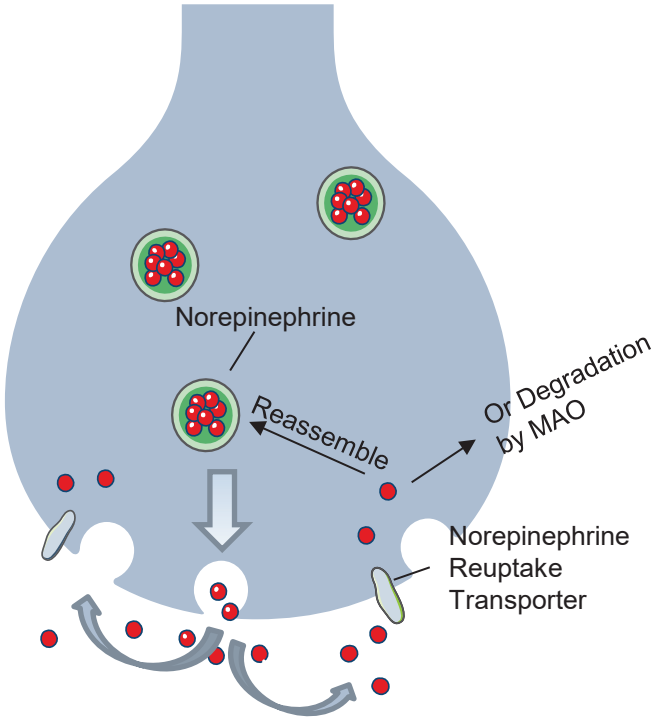
Diagnosis and treatment rate need to be improved	• The prevalence estimates of ADHD children and adolescents in China was 6.5%, and only 10-11% of them get diagnosed. ADHD in China has been significantly underdiagnosed and undertreated. As disease awareness, diagnosis and treatment rate improve, increasing number of ADHD patients will get medical treatment and emotional support.
Lack of psychologists and pediatricians with medical expertise	• ADHD is a complex disease, and its pathogenesis has not been figured out. Apart from medication intervention, emotion management, support and love from school and family and regular mental health monitoring are all essential. Psychologists and pediatricians need to equip themselves with more medical expertise, more importantly with good communication skills with children and adolescents.
Lack of treatment options for adult patients	• ADHD is not limited to children -- 30% to 70% of kids with ADHD continue to have symptoms when they grow up. In addition, people who were never diagnosed as kids may develop more obvious symptoms in adulthood, causing trouble on the job or in relationships. However, the fact is that about 4.5% will show ADHD symptoms, while many adults do not realize they have ADHD, or they are misdiagnosed as bipolar disorder. Therefore, the unmet need of adult ADHD is underestimated. The low diagnosis rate and treatment of ADHD in adult patients also results in that fewer studies of ADHD drugs and treatment options in adults than in children and adolescents.

Source: Literature review, Frost & Sullivan analysis

Overview of Selective Norepinephrine Reuptake Inhibitor (SNRI)

- Selective norepinephrine reuptake inhibitors (SNRI) are medications prescribed to manage symptoms of attention deficit hyperactivity disorder (ADHD). SNRIs work by increasing the level of norepinephrine in the brain. Norepinephrine is one of the chemicals (neurotransmitters) in the brain that plays a role in regulating attention and mood. An increase in norepinephrine levels is found to improve ADHD symptoms in children and adolescents.

Mechanism of Action



Clinical Advantages

Patients using CNS stimulants are more likely to face drug addiction issues than using SNRIs.

Less possibility of drug abuse

Longer duration of action

SNRIs have a longer duration of action than stimulants

Compared with stimulants

Avoiding adverse effects that stimulants lead to

Twitch, weight loss and decreased appetite are the most common adverse effects, which can be improved by switching to use SNRIs.

Indications

ADHD

Depression

Source: Literature review, Frost & Sullivan analysis

Drugs indicated for ADHD Approved by NMPA (Only Originator-branded Drugs Included)

Drug Name	Brand Name	Company	Target	Drug Type	Indications	Approved Date
Atomoxetine Hydrochloride Capsules	Strattera（择思达）	Eli Lilly	NRI	SNRI	ADHD	2006/05/12
Atomoxetine Hydrochloride Oral Solution	/	Eli Lilly	NRI	SNRI	ADHD	2018/09/11
Methylphenidate Hydrochloride Prolonged-Release Tablets	CONCERTA（专注达）	Johnson & Johnson	SLC6A2, 5-HT1 receptor	Stimulator	ADHD	2005/1/24
Methylphenidate Hydrochloride Extended-release Chewable Tablets	/	NextWave Pharmaceuticals	SLC6A2, 5-HT1 receptor	Stimulator	ADHD	2023/12/13
Methylphenidate Hydrochloride for Sustained-release Suspension	/	NextWave Pharmaceuticals	SLC6A2, 5-HT1 receptor	Stimulator	ADHD	2023/12/29
extended-release Clonidine	/	Xiamen LP Pharmaceutical Co.,Ltd.	Alpha-2 adrenoceptor	Alpha-2 adrenergic agonists	ADHD	2022/6/30

Note: As of April 7th, 2025

Source: NMPA, Frost & Sullivan Analysis

Competitive Landscape of China ADHD Treatment Drug Pipeline

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
EDP-125	SNRI	Ceclor Pharmaceutical Co., Ltd. (Subsidiary of Edding)	Phase 3	ADHD	2021//8/24
AK0901	SLC6A3, SLC6A2	Commave Therapeutics SA / Ark Biopharmaceutical Co., Ltd.	Phase 3	ADHD	2024/2/23

Note: As of April 7th, 2025

Source: CDE, Frost & Sullivan Analysis

Growth Driver of ADHD Drug Market in China

Innovative medicine is needed	• At present, only methylphenidate and atomoxetine were used to treat ADHD in China. Some drugs with novel mechanisms of action are under research, some of which have shown good safety and efficacy. New launched drugs are expected to the growth driver of ADHD drug market.
Large potential market demand	• In recent years, due to the improvement in the diagnosis rate, treatment rate, and the disease awareness in ADHD, the expected addressable patient population is rising, and the market size is considerable. Besides, the latest research showed that 30% to 70% of ADHD children and adolescents will continue to have symptoms in adulthood. However, adults do not realize they have ADHD, or they are often misdiagnosed as bipolar disorder. Therefore, the unmet need of adult ADHD is likely to be the growth driver of ADHD drug market.
National policy promotion	• China is paying more and more attention to ADHD and has issued policies *《关于进一步加强精神卫生工作的指导意见》* and *《中国注意缺陷多动障碍防治指南》*. Under the guideline of these policies, the country has made great efforts to develop new drugs, and major hospitals have also developed ADHD consulting services, which will further promote the development of ADHD market.

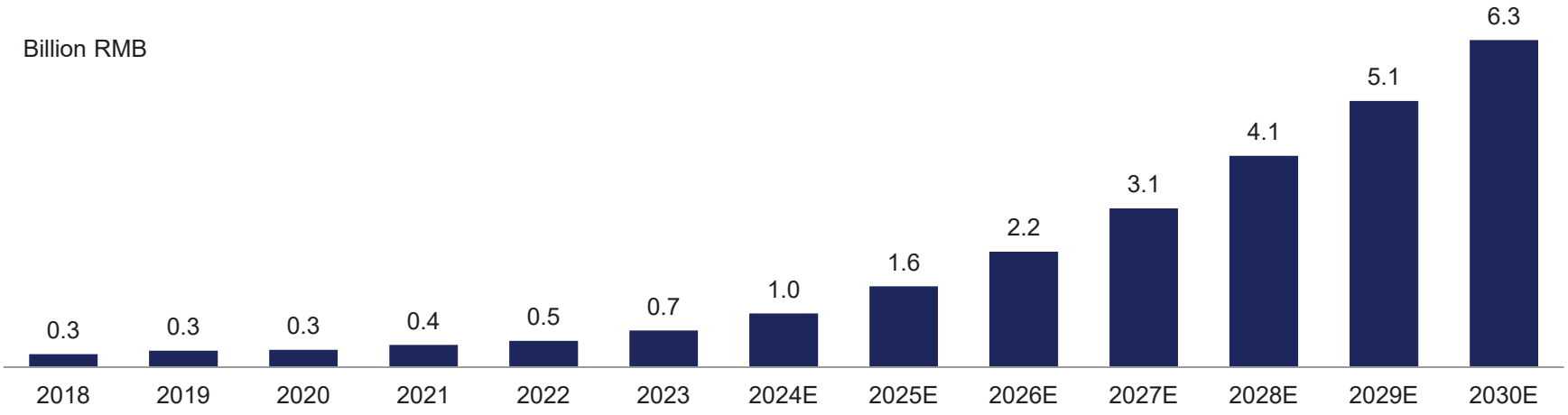
Source: 中国注意缺陷多动障碍防治指南, Frost & Sullivan Analysis

Market Size of ADHD Treatment in China, 2018-2030E

- Firstly, as the diagnosis rate, treatment rate, and the disease awareness in ADHD improve, the expected addressable patient population is rising, and the market size is considerable. Secondly, the current main medications used to treat ADHD in China are methylphenidate and atomoxetine as well as extended-release clonidine which was lunched last year. As novel drugs with new mechanism of action are developed in the future and enter the market, such as targeting Nrf2, the ADHD treatment market is expected to expand. Guanfacine has been approved for the treatment of ADHD in the USA, and it can be expected to be launched in China with approval for the treatment of ADHD, which might contribute to the whole market size. Thirdly, from the perspective of dosage form, more oral liquid preparations were launched, which improves the drug compliance for children. Fourthly, adult ADHD patients tend to be undiagnosed or misdiagnosed as bipolar disorder.

Market Size of ADHD Treatment in China, 2018-2030E

Period	CAGR
2018-2023	23.0%
2023-2026E	46.5%
2026E-2030E	29.7%



Source: Frost & Sullivan Analysis

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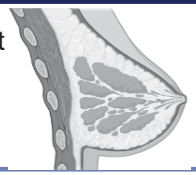
7	**Breast Cancer Drug Market in China**

Overview of Breast Cancer

- Breast cancer is a malignant tumor that occurs in the epithelial tissue of the breast. It is the most common malignant tumor in women and occasionally in men. Developing from breast tissue, breast cancer may present as a lump in the breast, a change in breast shape, dimpling of the skin, fluid coming from the nipple, a newly inverted nipple, or a red or scaly patch of skin. The incidence of breast cancer is related to high endogenous estrogen levels in patients, endometriosis, menstrual fertility factors, genetic factors, environmental and lifestyle factors, etc., and the incidence peaks around the age of 45-49. Treatment measures should be based on histological classification, TNM staging and molecular classification of breast cancer. About 24% of HR+/HER2- breast cancer patients are diagnosed with advanced disease.

Definition

- Breast cancer is cancer that develops from breast tissue. Worldwide, breast cancer is the leading type of cancer in women, but is occasionally occurring in men.



Molecular classification

		ER	PR	HER2-	Ki-67
Luminal	Luminal A	+	+ (High expression)	-	Low
	Luminal B (HER2-)	+	- Or low expression	-	High
	Luminal B (HER2+)	+	any	+	any
Erb-B2 expression		-	-	+	/
Basal-like		-	-	-	/

Histological classification

non-invasive carcinoma	Carcinoma in situ means that the lesion is limited to the primary site without metastasis, including ductal carcinoma in situ and lobular carcinoma in situ
invasive carcinoma	Cancer cells infiltrate and invade surrounding tissues extensively, occurring metastasis
Others	Rare and accounting for a small proportion

Risk Factors

- Genetic predisposition (BRCA1 or BRCA2 mutations)
- Estrogen and progesterone exposure
- Oral contraceptives or birth control drugs
- Atypical hyperplasia of the breast
- Lobular carcinoma in situ
- Lifestyle factors (weight, food, alcohol, physical activity)
- Breast density (dense breast tissue)
- Family history of breast cancer

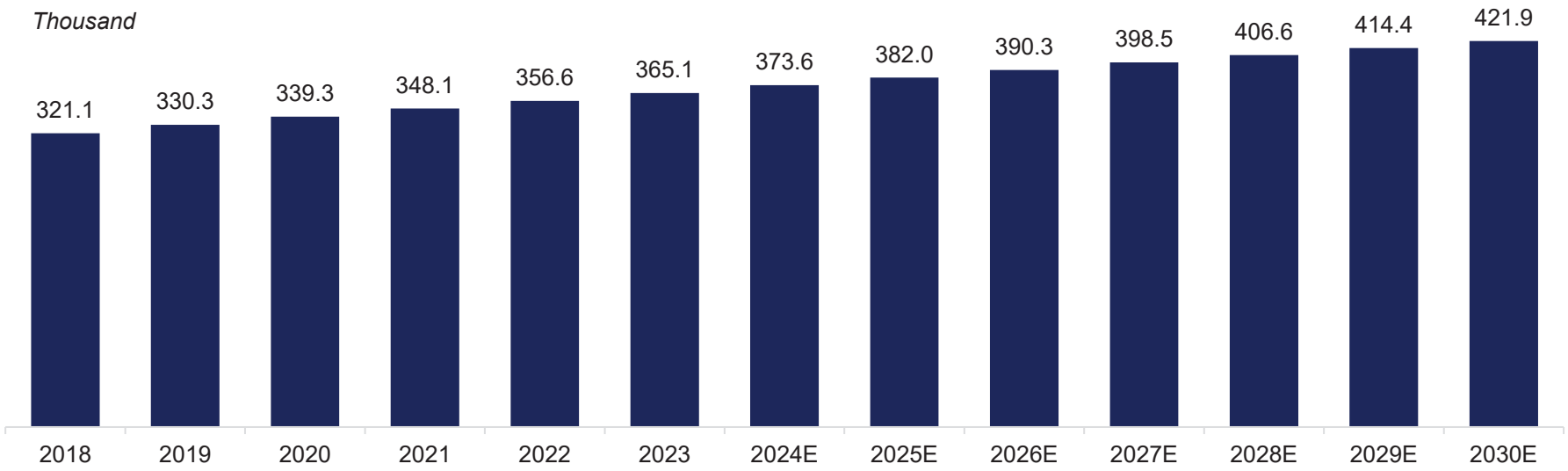
Source: Literature review, Frost & Sullivan analysis

Incidence of Breast Cancer in China, 2018-2030E

- Incidence number of breast cancer in China increased from 321.1 thousand to 365.1 thousand in 2018 and 2023. The number is expected to grow to 390.3 thousand in 2026 at a CAGR of 2.2% from 2023 to 2026. The number is expected to grow to 421.9 thousand in 2030, at a CAGR of 2.0%.

Incidence of Breast Cancer in China, 2018-2030E

Period	CAGR
2018-2023	2.6%
2023-2026E	2.2%
2026E-2030E	2.0%



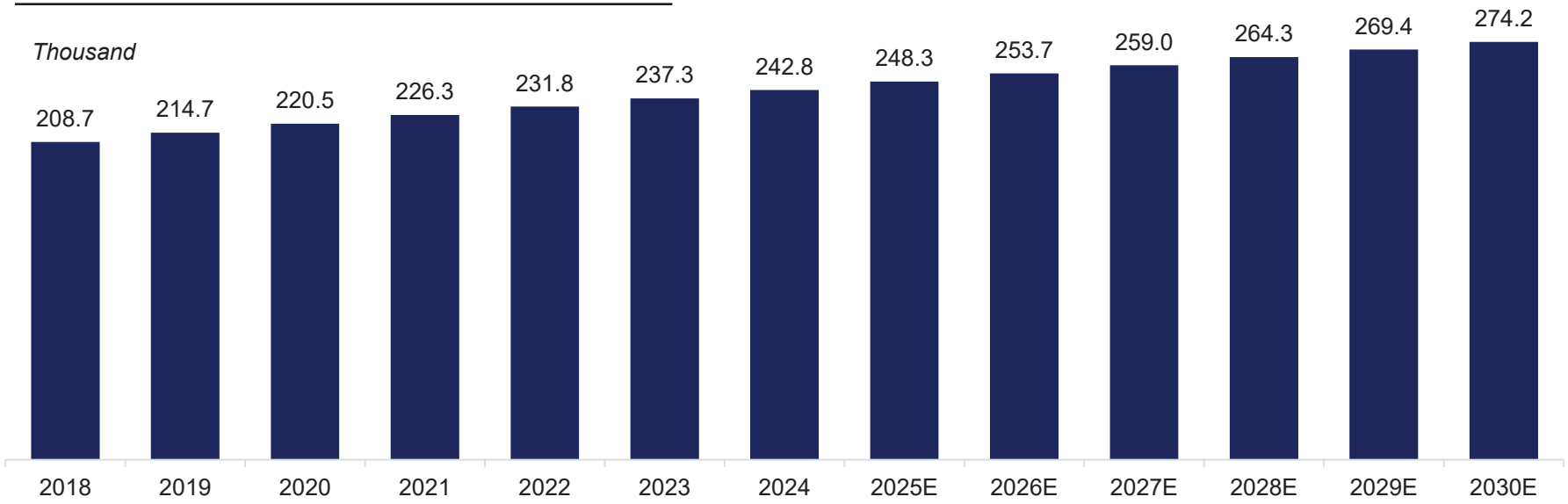
Source: NCCR, Frost & Sullivan Analysis

Incidence of HR+, HER2- Breast Cancer in China, 2019-2030E

- Incidence number of HR+, HER2- breast cancer in China increased from 208.7 thousand to 237.3 thousand in 2018 and 2023. The number is expected to grow to 253.7 thousand in 2026 at a CAGR of 2.2% from 2023 to 2026. The number is expected to grow to 274.2 thousand in 2030, at a CAGR of 2.0%.

Incidence of HR+, HER2- Breast Cancer in China, 2019-2030E

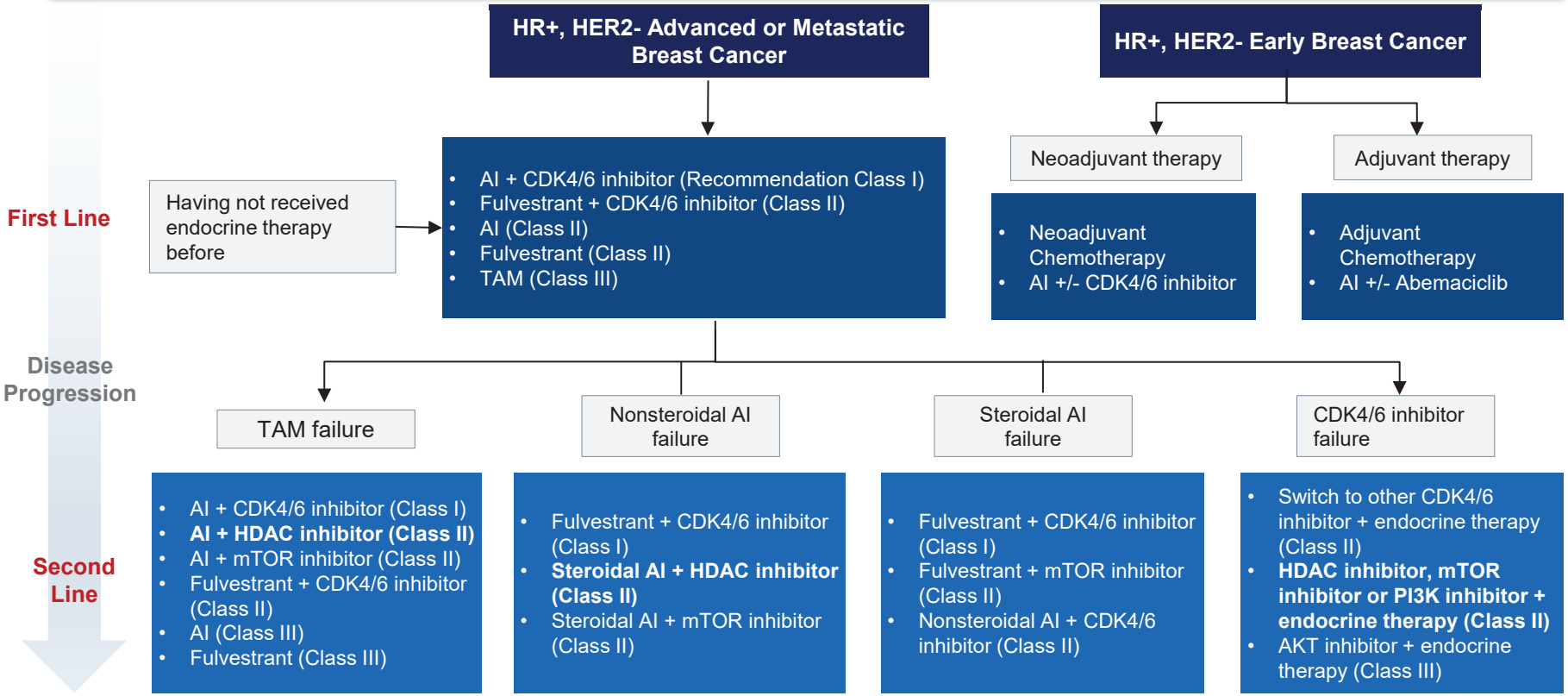
Period	CAGR
2019-2024	2.5%
2024-2027E	2.2%
2027E-2030E	1.9%



Source: NCCR, Frost & Sullivan Analysis

Treatment Paradigm of HR+, HER2- Breast Cancer in China

- CDK4/6 inhibitors combination with aromatase inhibitors is currently the preferred first-line treatment of HR+, HER2- advanced or metastatic breast cancer. Around 65% of HR+, HER2- breast cancer patients received the second-line treatment. In the second-line treatment, fulvestrant plus CDK4/6 inhibitors is preferred. Besides, other small molecular targeted therapy, such as HDAC inhibitors, mTOR inhibitors and PI3K inhibitors, combination with endocrine therapy are also recommended in the second treatment.
- Abemaciclib, one CDK4/6 inhibitor, has been approved in combination with endocrine therapy for the adjuvant treatment of adult patients with HR-positive, HER2-negative early breast cancer at high risk of recurrence.



Source: CSCO2024, Frost & Sullivan Analysis

Unmet Needs in the Treatment of HR+, HER2- Breast Cancer

Hormone Resistance after Endocrine Therapy	• Since endocrine therapy may lead to hormone resistance in patients, apart from CDK4/6 inhibitors, there are currently few targeted drug options for hormone resistance after endocrine therapy in China. Only Chidamide, an HDAC inhibitor and Everolimus, an mTOR inhibitor are available. Therefore, there is a huge unmet clinical need in patients with HR+ advanced breast cancer who are resistant to endocrine therapy.
CDK4/6 Inhibitor Resistance	• CDK4/6 inhibitors are able to work on overactivated CDK4/6 to restore normal cell cycle, trigger immune response and changing tumor microenvironment. CDK4/6 inhibitors successfully improve the prognosis of advanced breast cancer patients and prolong patients' PFS. However, CDK 4/6 inhibitor resistance and disease progress might happen, and they are the biggest issues that patients have to be faced with. Chemotherapy and other alternative targeted therapy, such as mTOR inhibitors and HDAC inhibitors, are appliable to patients with CDK4/6 resistance.
Recurrent and Metastatic Breast Cancer	• In the treatment of recurrent and metastatic breast cancer, chemotherapy and targeted drugs are important treatment options. Targeted drugs mainly work on HR, CDK signaling pathway, mTOR signaling pathway and HDAC signaling pathway to inhibit the proliferation of tumor cells. Combination chemotherapy regimens are frequently favored over single agents for the treatment of metastatic breast cancer, in an attempt to achieve superior tumor response rates. It is not known however whether giving more intensive chemotherapy regimens results in better health outcomes, when both survival and toxicity are considered, and whether better response rates and rates of progression free survival actually translate to better overall survival.

Source: Literature review, Frost & Sullivan analysis

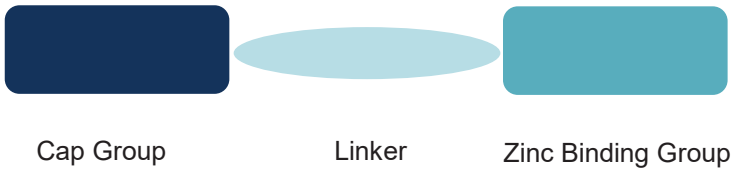
Overview of Histone Deacetylase (HDAC) Inhibitors

- HDAC is an epigenetic regulator that plays a key role in the structural modification of chromosomes and the regulation of gene expression. If the level of acetylation in the human body is unbalanced (especially the level is reduced), it may lead to the occurrence of tumors. HDAC1 is highly expressed in prostate, gastric, lung, esophageal, colon and breast cancers. High levels of HDAC2 were found in colorectal, cervical and gastric cancers. In addition, HDAC3 is overexpressed in colon and breast tumors, whereas HDAC6 is highly expressed in mammary tumors, HDAC8 is overexpressed in neuroblastoma cells and HDAC11 mainly in rhabdomyosarcoma. HDACs can be divided into four different types, including I (HDAC 1/2/3/8 subtypes), II (HDAC4/5/6/7/9/10 subtypes), III (sirtuins) and IV (HDAC11 subtype). HDAC inhibitors usually present selectivity to the certain type or subtype of HDAC.

Definition of HDAC

- HDAC is an epigenetic regulator that plays a key role in the structural modification of chromosomes and the regulation of gene expression. It has become one of the key targets of anti-tumor therapy. In the human body, histone acetyltransferase (HAT) and HDAC jointly regulate the level of histone acetylation. If the level of acetylation in the human body is unbalanced (especially the level is reduced), it may lead to the occurrence of tumors.

Structure of HDACi



Indications of HDACi

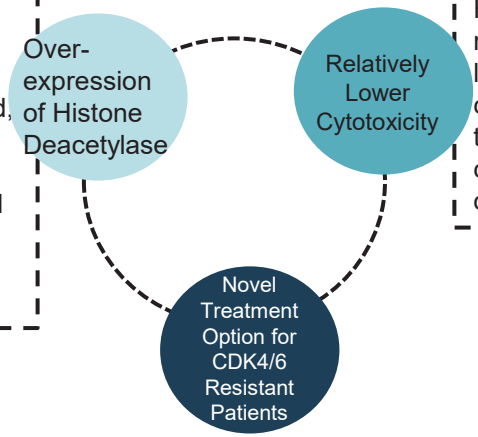
Approved	Breast cancer	Peripheral T-cell lymphoma
In Pipeline	Multiple myeloma	B-cell lymphoma	Renal cell cancer

How Do inhibitors Work

- Induce cell-cycle arrest and apoptosis
- Inhibit migration, invasion
- Inhibit angiogenesis

Clinical Advantages

In many cancer tissues, HDAC over-expression has been observed, therefore, HDAC inhibitors are potential to a novel target therapy option to many types of cancer.



HDAC has relatively lower cytotoxicity than chemotherapy drugs.

Endocrine therapy combined with CDK4/6 inhibitors has proven to be the first-line therapy for HR+, HER2- breast cancer. HDAC inhibitors provide a new treatment option for those resistant to CDK4/6 inhibitors, and it is recommended as second-line therapy.

Source: Literature review, Frost & Sullivan analysis

HDAC Inhibitors Approved by NMPA in Anti-tumor Therapeutic Areas

Drug Name	Brand Name	Company	Target	Indications	Approved Date
Chidamide	Epidaza（爱谱沙）	Chipscreen	HDAC	Patients with relapsed or refractory peripheral T-cell lymphoma who have received at least one prior systemic chemotherapy	2014/12
				Combination of aromatase inhibitors in the treatment of locally advanced or metastatic HR+/HER2- breast cancer patients who have relapsed or progressed after endocrine therapy	2019/11
Entinostat	景助达	Taizhou EOC Pharma Co., Ltd	HDAC	Combination of aromatase inhibitors in the treatment of locally advanced or metastatic HR+/HER2- breast cancer patients who have relapsed or progressed after endocrine therapy	2024/4

Note: As of April 7th, 2025

Source: NMPA, Frost & Sullivan Analysis

Competitive Landscape of China HDAC Pipeline in Anti-tumor Therapeutic Areas

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
Abexinostat (艾贝司他)	HDAC	Xynomic Pharma	Phase 3	Advanced or metastatic renal cell cancer	2019/07/05
			Phase 3	Relapsed or refractory follicular lymphoma	2024/03/19
LBH589 (帕比司他)	HDAC	Novartis	Phase 3	Multiple Myeloma	2015/02/13
HG146	HDAC	HitGen Inc	Phase 2	Relapsed or metastatic adenoid cystic carcinoma	2024/12/12
BEBT-908	HDAC	BeBetter Med Inc.	Phase 1/2	Recurrent or metastatic breast cancer	2021/12/27
			Phase 1/2	Advanced non-small cell lung cancer	2021/12/29
			Phase 2	Relapsed or refractory lymphoma	2021/02/03
NL-101	HDAC	Minsheng Pharma	Phase 2	Relapsed or refractory MCL or FL	2021/06/25
伏立诺他	HDAC	Sino Pharma Group	Phase 2	Cutaneous T cell lymphoma	2014/04/30
Purinostat (普依司他)	HDAC	Bailing Group Pharmaceutical Co., Ltd.	Phase 1/2	Advanced Solid Tumor	2024/05/22
JS125	HDAC	Junshi Biosciences	Phase 1	Advanced Solid Tumor	2024-10-11
ricolinostat	HDAC	Penn Pharmaceutical Services Limited / Parexel China Co.,Ltd.	Phase 1	Chemotherapy-induced peripheral neuropathy	2022/01/17
贝林司他	HDAC	CGeneTech	Phase 1	Relapsed or refractory peripheral T-cell lymphoma	2020/04/15
Bisthianostat (倍赛诺他)	HDAC	Shanghai Institute of Materia Medica, Chinese Academy of Sciences	Phase 1	Relapsed or refractory multiple myeloma	2018/04/11
Heptyphemide (海博非明)	HDAC	Hisun Pharmaceutical Co.Ltd.	Phase 1	Lymphoma	2017/12/11

Note: As of April 7th, 2025; Generics are excluded

Source: CDE, Frost & Sullivan Analysis

Core Strengths of Entinostat compared with Chidamide

Better safety and longer overall survival	• Entinostat has lower incidence of hematologic toxicity and gastrointestinal reactions. • Entinostat in combination with aromatase inhibitors has longer overall survival compared with Chidamide in combination with aromatase inhibitors (38.4 months VS 30.3 months).
Better patient compliance	• Entinostat (once a week) has a longer dosing interval than Chidamide (twice a week), which leads to better patient compliance.

Source: Frost & Sullivan Analysis

Growth Driver of HR+, HER2- Therapeutic Drug Market in China

Resistance to endocrine therapy	• Endocrine therapy has a long history in the treatment of HR+, HER2- breast cancer, from estrogen receptor inhibitors, estrogen receptor modulators to aromatase inhibitors. It is true that numerous patients benefit from endocrine therapy, but they are faced with primary or secondary resistance. In order to extend the duration of response, targeted therapy combination with endocrine therapy has gradually become the mainstream in the treatment of HR+, HER2- breast cancer.
Great patient pool	• Breast cancer is a big threat to women all over the world due its high incidence and mortality. HR+, HER2- breast cancer accounts for nearly 60% to 70%, meaning there are great clinical needs to these patients. Market demand drives research and development. Increasing number of novel targeted drugs will be developed in the future.
Emerging targeted therapy	• PI3K-AKT-mTOR inhibitors, CDK4/6 inhibitors and HDAC inhibitors are all common targeted therapies in the combination with endocrine therapy. When patients do not response well to one type of targeted drugs, they have alternatives. Therefore, patients will benefit more when more targets are studied to develop into drugs.
Increasing incidence in breast cancer	• The latest cancer burden data released by the International Agency for Research on Cancer shows an increase in breast cancer incidence. One of the fundamental reasons is the constant changes in breast cancer risk factors. First, delayed childbirth, decreased number of pregnancies, and shortened breastfeeding period in modern times are important triggering factors for breast cancer. Second, modern young women also have the habit of taking health supplements, many of which contain estrogen. Excessive intake can cause high estrogen levels, leading to breast hyperplasia and even breast cancer. Finally, long-term staying up late, sustained mental stress, irregular schedules, unhealthy diets, and other problems in modern life can also increase cancer incidence.

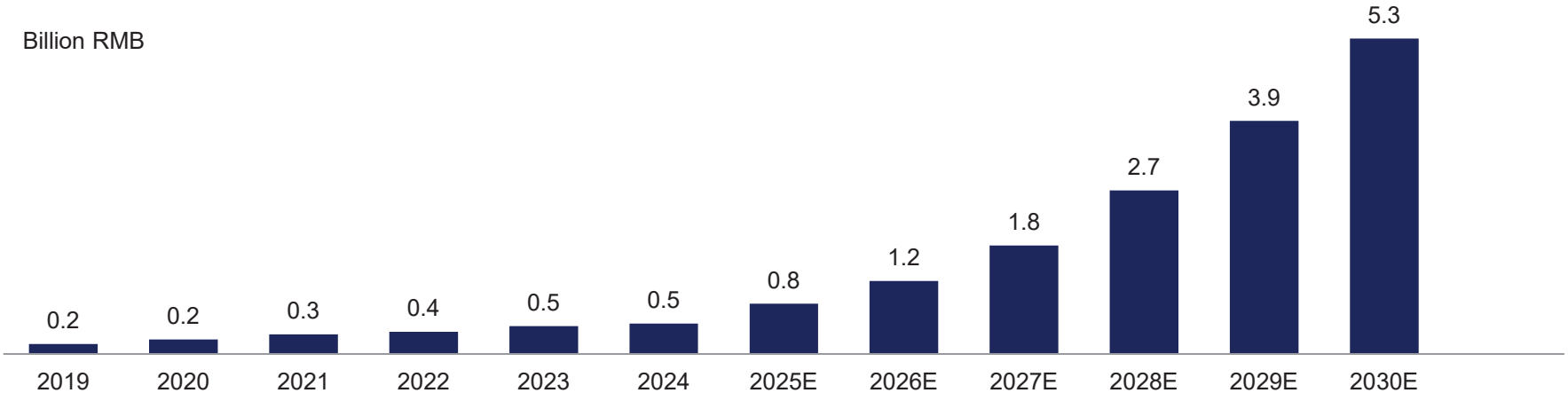
Source: Frost & Sullivan Analysis

Market Size of HDAC Inhibitor in China, 2019-2030E

- China HDAC inhibitor market increased from 0.2 billion RMB in 2019 to 0.5 billion RMB in 2024. It is estimated to grow to 1.8 billion RMB in 2027 and 5.3 billion in 2030 at a CAGR of 52.7% and 42.8% from 2024 to 2027 and 2027 to 2030 respectively.

Market Size of HDAC Inhibitor in China, 2018-2030E

Period	CAGR
2019-2024	25.4%
2024-2027E	52.7%
2027E-2030E	42.8%



Source: Frost & Sullivan Analysis

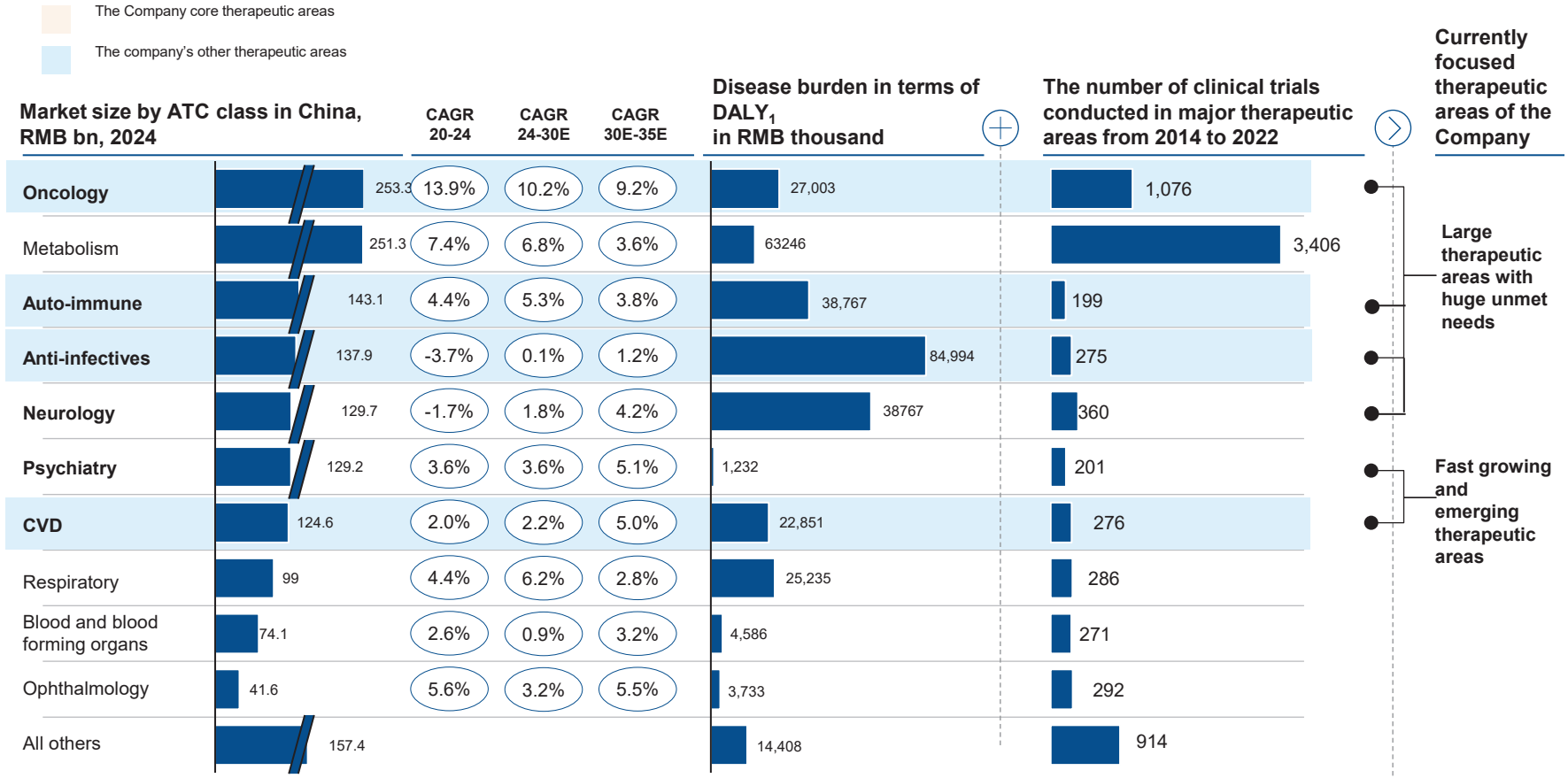
Growth Driver of HDAC Inhibitor Market in China

Indication expansion	• Indication expansion is one of drivers for the future market of HDAC inhibitors. Although only breast cancer and peripheral T-cell lymphoma were approved in China, clinical trials for multiple myeloma, renal cell carcinoma, B-cell lymphoma, mantle cell lymphoma, and follicular lymphoma are being conducted domestically, and more indications are expected to be expanded in the future.
Clinical promotion	• After more drugs from the same class (HDAC Inhibitors) are launched in the future, it will contribute to the clinical promotion of the entire class of drugs, which will expand the overall market. At the same time, after the drugs enter clinical use, more post-market clinical data can be obtained for retrospective research, which will improve the recommendation level of this class of drugs in the guidelines.
Sales revenue surges when HDAC inhibitors are included in NRDL	• Chidamide was the only HDAC inhibitor approved by NMPA so far, and its indication of PTCL has been covered by insurance reimbursement while the indication of breast cancer has not been covered. Before the indication of PTCL was covered by insurance reimbursement, its penetration was around 5.8% in 2016 and 9.3% in 2017, while it surged to 21.5 in the year when the indication of PTCL was covered by insurance reimbursement. From 2018 on, its sales revenue keeps a strong growth.(around 20%-30%). The case from Chidamide demonstrates that being covered by insurance reimbursement would be a significant growth driver of HDAC inhibitor market.

Source: Frost & Sullivan Analysis

The Market Size, Disease Burden and the Number of Clinical Trials Conducted in Major Therapeutic Areas in China

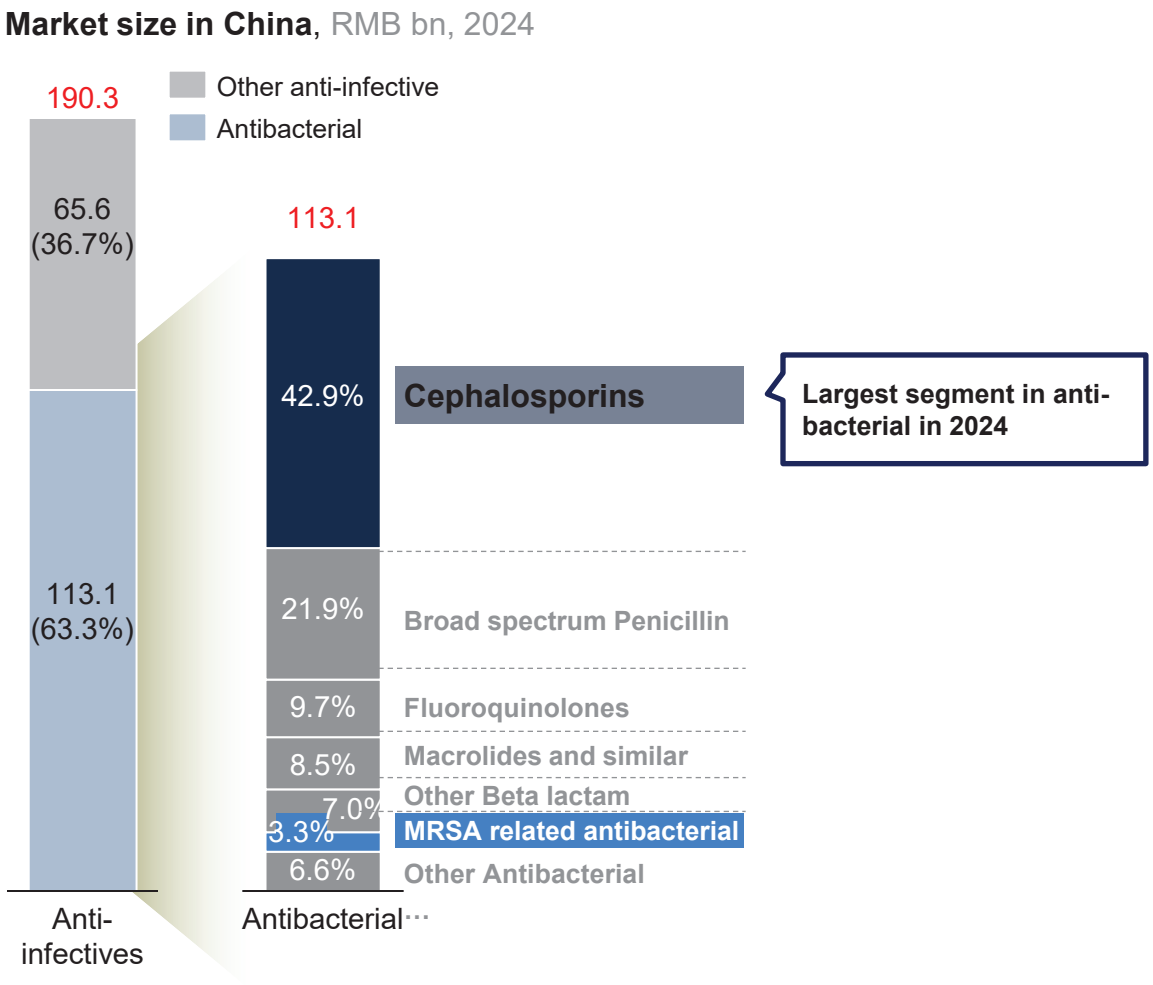
- CV and Anti-infectives are two large therapeutic areas with huge unmet needs, and hematology and hematopoietic system and respiratory are two fast-growing and emerging therapeutic areas. Compared with oncology, CVD, anti-infectives, respiratory are less competitive therapeutic areas.



Note: 1. Disability-Adjusted Life Years; The Therapeutic Areas Edding's products in.

Source: Frost & Sullivan Analysis

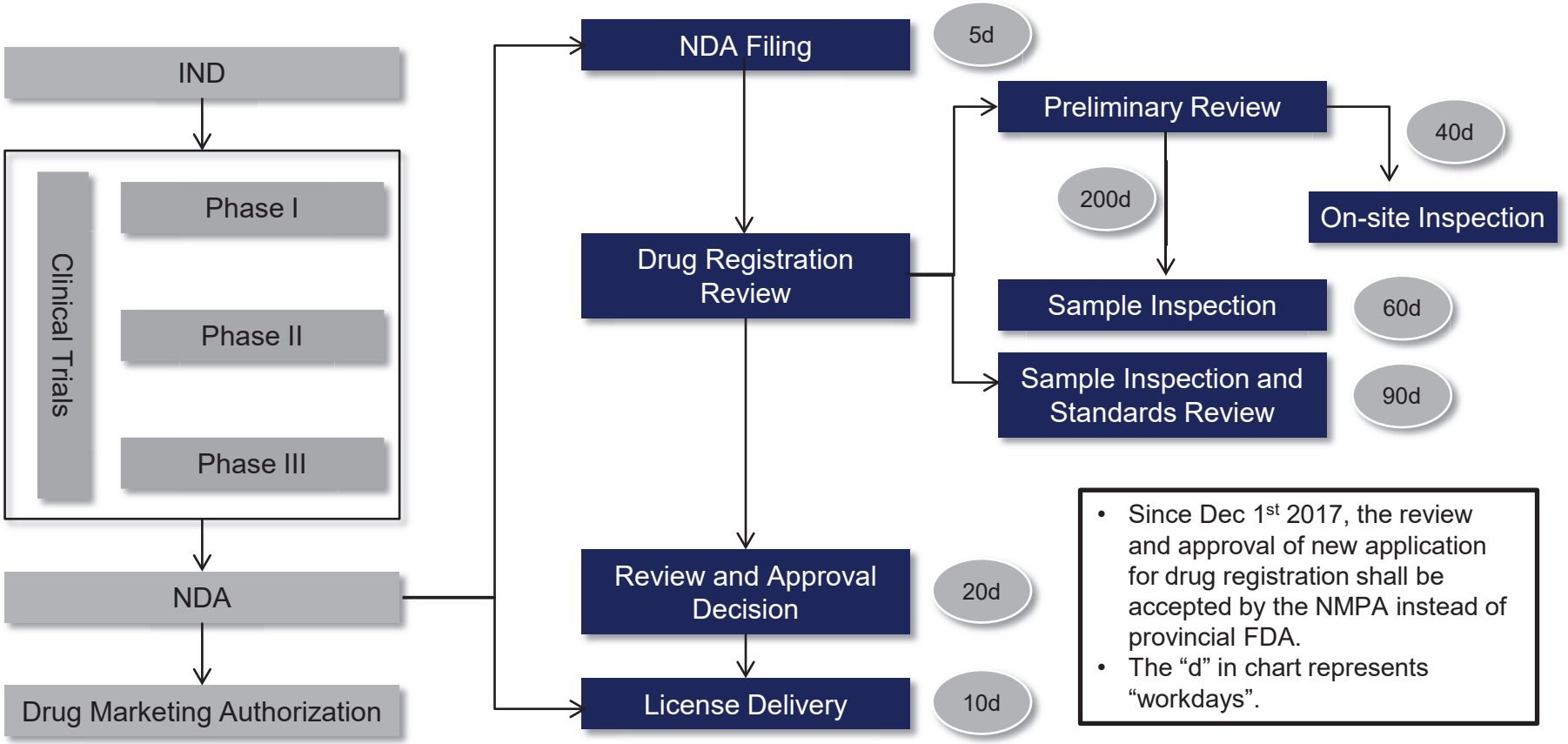
Subgroups of Anti-bacteria, 2024



Source: Frost & Sullivan Analysis

Drug Registration Procedure in China

- According to Provision for Drug Registration（药物注册管理办法）and Notice of Adjustment of Drug Registration Acceptance （关于调整药品注册受理工作的公告）in 2017, the drug registration has changed in processing time limitation and authorities supervising NMPA reviews to accelerate the NDA review and approval.



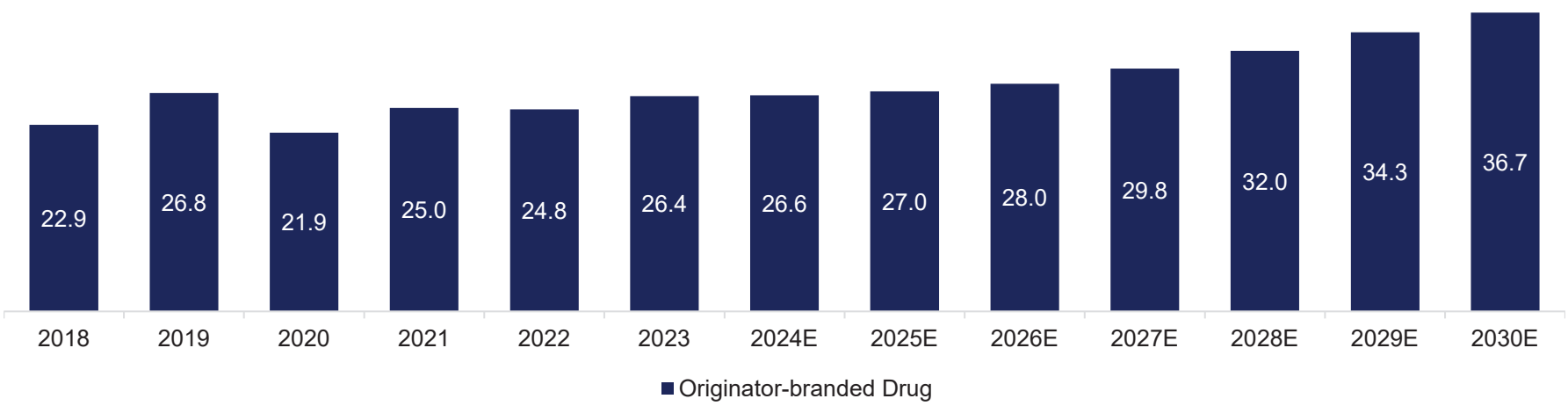
Note: The Procedure is a general approval pathway. In reality, approval pathway may vary case by case.

Source: CMA, Frost & Sullivan analysis

China Originator-Branded Anti-bacterial Drug Market Size, 2018-2030E

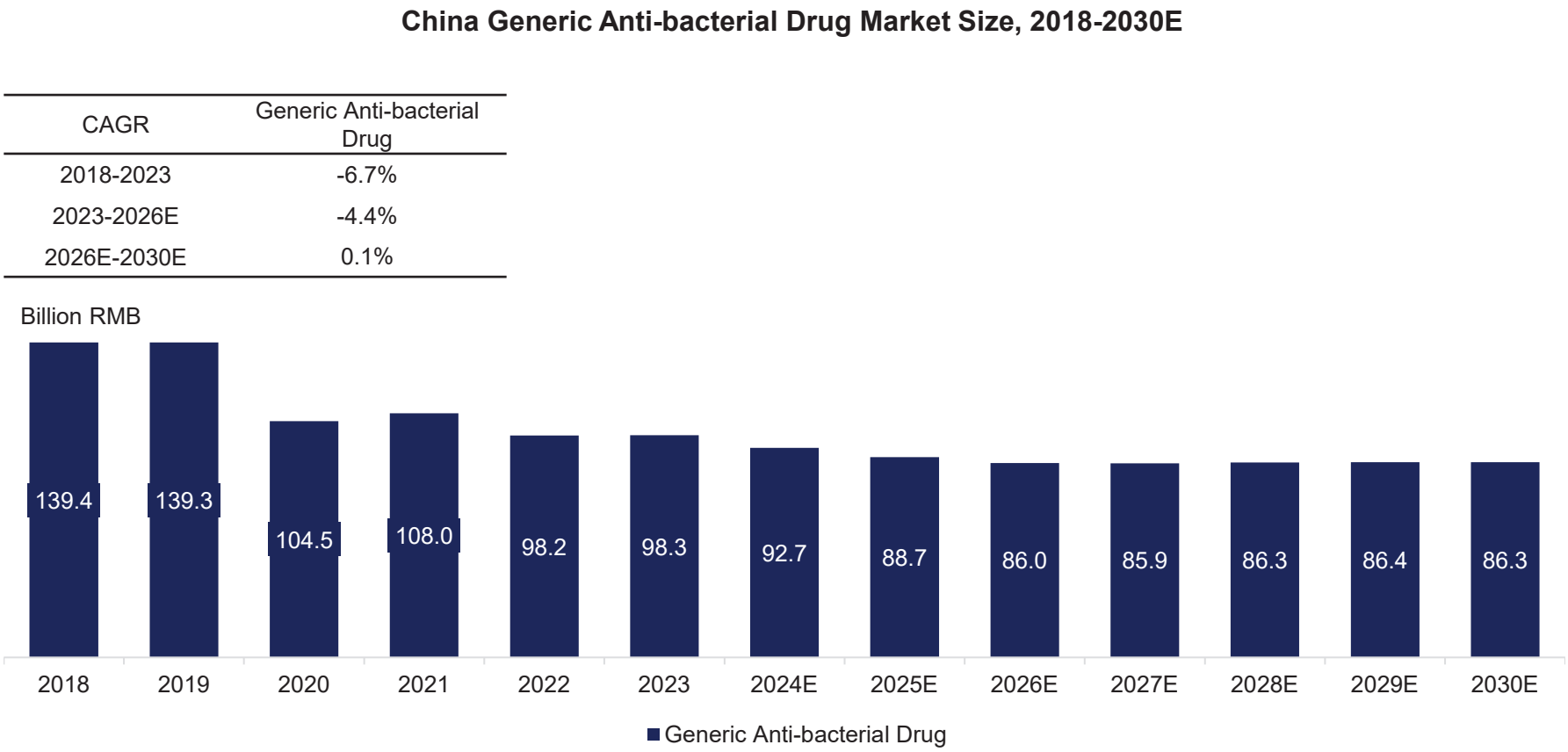
China Originator-Branded Anti-bacterial Drug Market Size, 2018-2030E

CAGR	Originator-branded Drug
2018-2023	2.9%
2023-2026E	1.9%
2026E-2030E	7.0%



Source: Frost & Sullivan Analysis

China Generic Anti-bacterial Drug Market Size, 2018-2030E



CAGR	Generic Anti-bacterial Drug
2018-2023	-6.7%
2023-2026E	-4.4%
2026E-2030E	0.1%

Source: Frost & Sullivan Analysis

Comparison Table of MAH and Exclusive Marketing and Distribution Right Holder

	MAH	Marketing and Distribution Right Holder
Rights	Full product rights, including research and development, manufacturing and/or supply chain management, and sales and marketing	Sales and marketing rights, which is authorized by the MAH
Revenue Structure	Sales revenue. MAH can either sell products by itself, or entrust CSOs to sell.	Sales revenue, or promotion service fee
Research and Development	Responsible for product research and development, including clinical trials	Not responsible for product research and development
Manufacturing	MAH can either manufacture products by itself, or entrust CMOs to manufacture.	Not responsible for manufacturing, can only purchase finished products or providing promotion services for finished products
Gross Profit Margin	Primarily determined by selling price and cost of manufacturing and/or supply chain functions	Primarily determined by negotiation with the MAH
Quality Management	Responsible for the product quality in the whole life cycle of a drug, including post-marketing research, monitoring, reporting and handling of adverse reactions of the drug	Not responsible for product quality management pharmacovigilance (PV) functions

Source: Frost & Sullivan analysis

Comparison Table of MAH and Exclusive Marketing and In-licensing Right

Dimension	MAH (Marketing Authorisation Holder)	In-licensing Right
Core Definition	The legal entity holding the drug approval, serving as the sole point of responsibility for regulatory authorities.	Limited rights granted via a commercial agreement from the MAH or IP owner.
Legal & Regulatory Responsibility	Bears full, ultimate legal and regulatory responsibility for the product's entire life cycle, including PV, quality, and traceability.	Bears contractually agreed responsibilities; ultimate regulatory liability remains with the licensor (MAH).
Scope of Rights	Holds comprehensive rights to the product, including R&D, manufacturing, sales, pricing, and management of all IP.	Rights are strictly limited to the scope defined in the agreement (e.g., specific region, indication, or time period).
Financial Model	Asset-Owner Model: Entitled to all product sales revenue and bears all associated costs. Profit margin depends on manufacturing and supply chain efficiency.	Service/Distributor Model: Revenue typically comes from sales royalties or promotion service fees. Profit margin depends on negotiation leverage with the licensor.
Risk Profile	High Risk: Bears all core risks, including R&D failure, production quality, post-market safety, and market fluctuations.	Controlled Risk: Primarily bears risks related to upfront payments and local market launch success, avoiding core R&D and regulatory risks.

Source: Frost & Sullivan analysis

Market Size of Major Subgroups in the CVD and Respiratory System Therapeutic Area in China, 2023

Market Size of Major Subgroups in the CVD Therapeutic Area in China, RMB bn, 2023		CAGR 18-23	CAGR 23-30E
Lipid-regulating	25.9	-5.8%	14.8%
Vasotherapeutics	21.4	0.5%	2.9%
Renin-angiotensin System	23.8	-3.0%	1.0%
Cardiac Therapy	24.2	-6.3%	3.4%
Calcium Antagonists	27.2	-2.4%	2.2%
Diuretics	2.9	2.8%	2.5%

The Company's Targeted Sub-therapeutic Area

Market Size of Major Subgroups in the Respiratory System Therapeutic Area in China, RMB bn, 2023		CAGR 18-23	CAGR 23-30E
Anti-asthma and COPD	53.7	-1.0%	3.8%
Cough and Cold	15.9	-1.1%	6.8%
Systemic Antihistamines	5.5	1.2%	1.8%
Nasal	2.5	6.4%	7.8%
Throat	0.1	21.9%	9.1%
Others	4.4	8.9%	16.0%

The Company's Targeted Sub-therapeutic Area

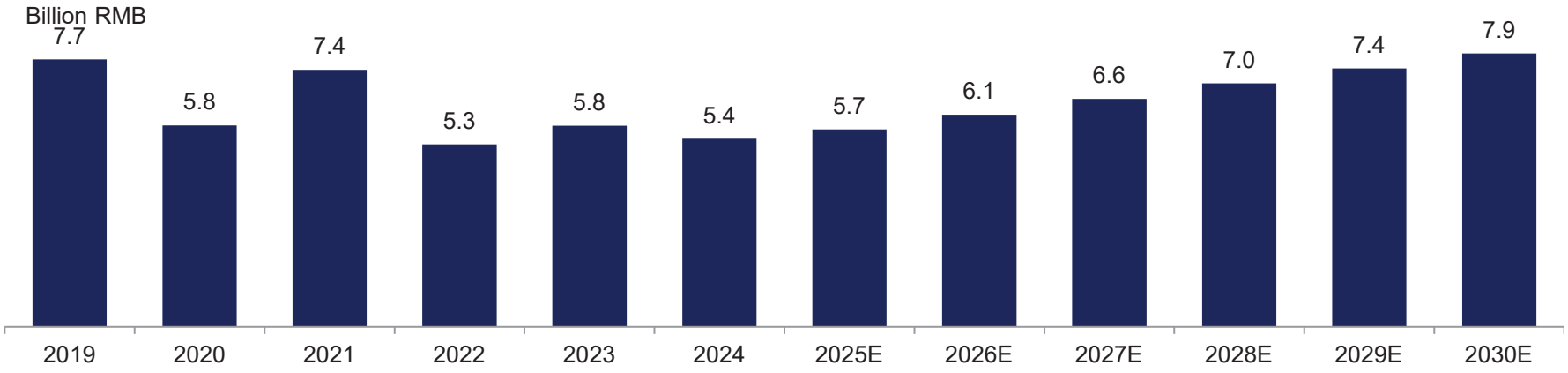
Source: Frost & Sullivan Analysis

China ICS Nebulizer Drug Market, 2019-2030E

- The China ICS nebulizer drug market slightly decreased from 7.7 billion RMB to 5.4 billion from 2019 to 2030 due to the VBP. The number is projected to reach 6.6 billion RMB in 2027 and 7.9 billion RMB in 2030 at a CAGR of 6.6% and 6.3% from 2024 to 2027 and from 2027 to 2030 respectively.
- Affected by volume-based procurement, the market for Budesonide Suspension will drop by around 1.9% in 2024 compared with 2022, but sales volume increased by over 80%, Sales volume of budesonide nebulizer suspension continued to rise by 80% from 2022 to 2024; the sale revenue and volume for FPN and Beclometasone Dipropionate Suspension are growing steadily, the sales volume of FPN continued to rise by 40% from 2022 to 2024, showing that the clinical demand for ICS nebulizers remain strong in the future.

China ICS Nebulizer Drug Market, 2019-2030E

Period	CAGR
2019-2024	-6.8%
2024-2027E	6.6%
2027E-2030E	6.3%



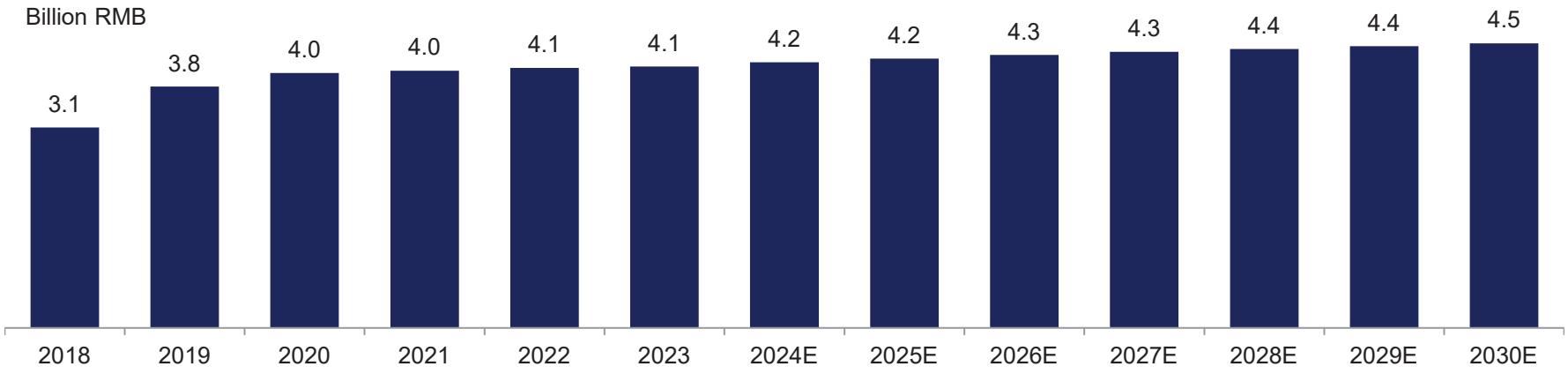
Source: Frost & Sullivan Analysis

China ICS/LABA Combination DPI Drug Market, 2018-2030E

- The China ICS/LABA combination DPI drug market increased from 3.1 billion RMB to 4.1 billion from 2018 to 2023. The number is projected to reach 4.3 billion RMB in 2026 and 4.5 billion RMB in 2030 at a CAGR of 1.4% and 1.0% from 2023 to 2026 and from 2026 to 2030 respectively.

China ICS/LABA Combination DPI Drug Market, 2018-2030E

Period	CAGR
2018-2023	5.5%
2023-2026E	1.4%
2026E-2030E	1.0%



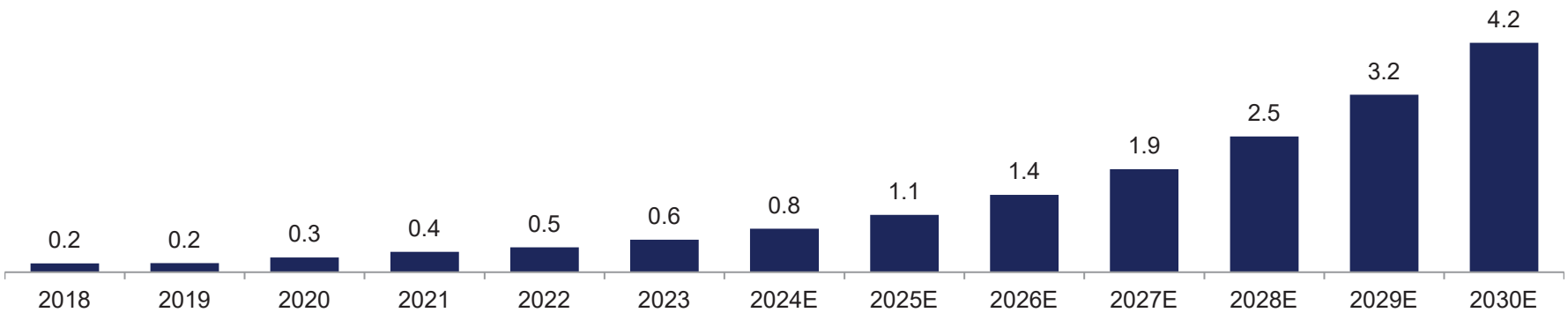
Source: Frost & Sullivan Analysis

China CLD-associated TCP Treatment Market, 2018-2030E

- The China CLD-associated TCP Treatment Market increased from 0.2 billion RMB to 0.6 billion from 2018 to 2023. The number is projected to reach 1.4 billion RMB in 2026 and 4.2 billion RMB in 2030 at a CAGR of 33.6% and 31.3% from 2023 to 2026 and from 2026 to 2030 respectively.

China CLD-associated TCP Treatment Market, 2018-2030E

Period	CAGR
2018-2023	29.7%
2023-2026E	33.6%
2026E-2030E	31.3%



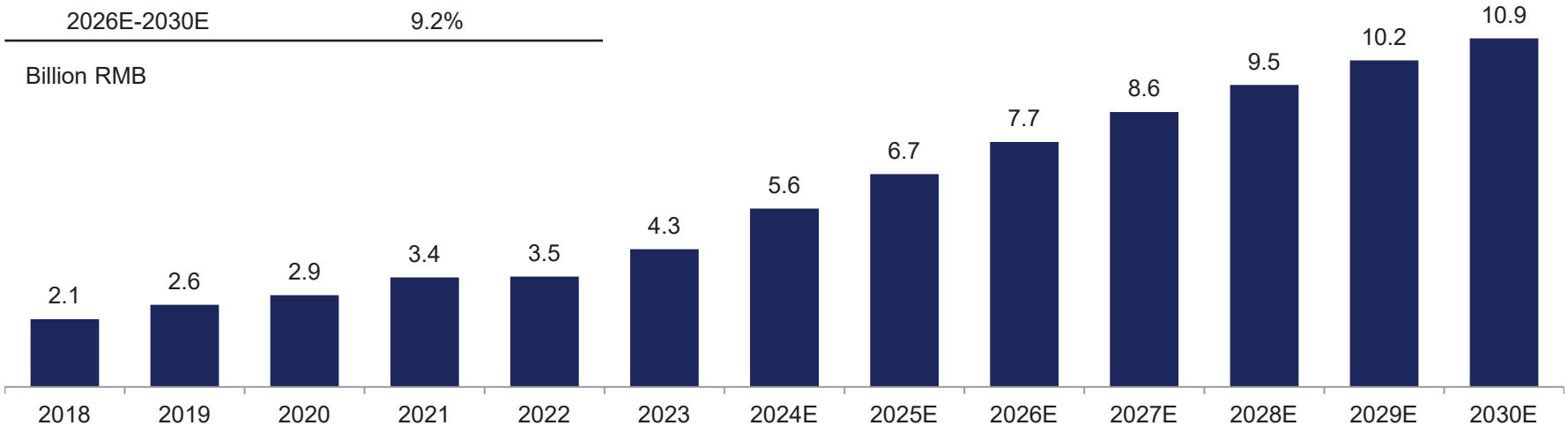
Source: Frost & Sullivan Analysis

China CIT Treatment Drug Market, 2018-2030E

- The China CIT Treatment Drug Market increased from 2.1 billion RMB to 4.3 billion from 2018 to 2023. The number is projected to reach 7.7 billion RMB in 2026 and 10.9 billion RMB in 2030 at a CAGR of 21.2% and 9.2% from 2023 to 2026 and from 2026 to 2030 respectively.

China CIT Treatment Drug Market, 2018-2030E

Period	CAGR
2018-2023	15.2%
2023-2026E	21.2%
2026E-2030E	9.2%



Source: Frost & Sullivan Analysis

ICS/LABA Combination DPI Approved by NMPA

Drug Name	Brand Name	Company	Target	Indications
Budesonide and Formoterol Fumarate Powder for Inhalation	信必可都保 Symbicort Turbuhaler	AstraZeneca	GR, ADRB2	Asthma, COPD
Indacaterol Acetate and Mometasone Furoate Powder for Inhalation	恩明润 Atectura	Grand Medical Pty Ltd	GR, ADRB2	Asthma
Salmeterol Xinafoate and Fluticasone Propionate Powder for Inhalation	舒利迭 Seretide	GSK	GR, ADRB2	Asthma, COPD
Fluticasone Furoate and Vilanterol Trifenatate Powder for Inhalation	万瑞舒 Relvar	GSK	GR, ADRB2	Asthma, COPD

Note: As of April 7th, 2025

Source: NMPA, Frost & Sullivan Analysis

Verification

- As of Dec 31, 2024, the Target Group had around 1,000 sales representatives across 30 provinces in China and covering over 17,000 hospitals, 19,000 pharmacies and 260 business corporations. This highly effective commercialization team achieved an average sales per sales representative of RMB 2.5 million, positioning it as one of the most productive in the industry, significantly higher than market peers.
- Edding pharma is a leading integrated pharmaceutical company with a diversified product portfolio in some of the largest and fast-growing therapeutic areas in China, including anti-infectives, CVD and respiratory system.
- In China, per capita annual disposable income increased from RMB28,228 in 2018 to RMB 39,218 in 2023, representing a CAGR of 6.8%. With increasing disposable income, an aging population, rising health awareness and life expectancy and implementation of healthcare reform plans, China's total healthcare expenditure has experienced significant growth, and is expected to further grow in the future.
- Heavy investment and a long return period have become the main barriers to entering China's pharmaceutical market. The development cycle of a new pharmaceutical product may last more than 15 years, and the development cost may exceed several hundreds of millions of Renminbi. Moreover, significant investments are required for production facilities, quality systems and technical teams. In addition, new entrants to the PRC pharmaceutical market must also navigate a stringent regulatory landscape. The strengthening of China's supervision of the pharmaceutical market, the GQCE requirement for generic pharmaceuticals, and registration system for clinical trials of pharmaceuticals in China may increase compliance and other costs and create a high entry barrier for new entrants.
- Innovative drugs have higher technical barriers and enjoy marketing exclusivity and significant pricing power. Innovative drugs refer to API and its preparation that contain new compounds with clearly defined structure and pharmacological effects, and indicate clinical value in China. In particular, the invention patents and protection periods over innovative drugs exclude others from manufacturing and marketing of products with the same chemical structure, dosage form or indication in China or other countries for an extended period of time. In addition, innovative drugs are perceived to have potentially greater efficacy and/or safety than generic drugs and are therefore generally subject to less competition and relatively lower pricing pressure.
- In China, physicians and patients generally attach more importance to the brand and credibility of pharmaceuticals in part due to their concerns about safety, efficacy and quality of drugs. As a result, originator-branded drugs with long-established usage history, well-recognized brands and proven safety and efficacy profiles often command significant market share in China, even though they are typically priced at a premium to competing domestic generics. Originator-branded drugs marketed in China are preferred reference drugs for the GQCE, which are generally perceived to have high manufacturing quality standards with a superior safety and efficacy profile. In many provinces in China, originator-branded drugs are classified into a higher quality class than competing domestic generics in the price bidding of the centralized tender processes, and therefore do not compete directly with domestic generics on price.
- In China, domestically manufactured drugs are primarily distributed to regional distributors directly from manufacturing facilities. Imported drugs in China are distributed either by companies appointing an importer primarily for customs clearance and delivery of drugs to regional distributors, or companies clearing customs and deliver the products to regional distributors directly. Regional distributors are primarily responsible for operating local distribution centers and warehouses, maintaining a sufficient level of inventory, and providing end-to-end delivery of drugs to hospitals and pharmacies. In the drug distribution process in China, regional distributors play a much more important role than importers. They are responsible for management of drug procurement, sales and inventory management for hospitals and pharmacies and maintain market access for drugs. Importers for imported drugs, on the other hand, primarily provide support services, including customs clearance and logistic services for the delivery of drugs to regional distributors.

Source: Frost & Sullivan analysis

Verification

- A marketing authorization holder, or MAH, is the holder of drug authorization certificate, including the IDL license for imported drugs. A MAH is entitled to the product rights for a relevant drug, including for research and development, manufacturing and/or supply chain management and sales and marketing. Accordingly, a MAH shall assume the responsibility for the product quality in the whole life cycle of a drug, including for pre-clinical research, clinical trials, production and marketing, post-marketing research, monitoring, reporting and handling of adverse reactions of the drug. Importantly, a MAH may manufacture and sell the drug by itself, or entrust third-party CMOs and CSOs for the relevant functions. Under the MAH system, a MAH can flexibly choose business partners for research and development, manufacturing, and sales and marketing, while maintaining its position as the product right holder. For example, a MAH in China can entrust overseas CMOs for the manufacturing of a drug. As such, the MAH system in China lays the foundation for the acquisition and in-licensing of innovative drugs from global pharmaceutical companies to China. However, given that the MAH system was recently adopted in China, there are very few commercialized products that are manufactured and supplied by CMOs in China. The following table illustrates the differences between an MAH and exclusive marketing and distribution right holder.
- The GQCE is vital to the pharmaceutical industry in China because the sales revenue of generic pharmaceuticals accounts for a significant proportion of the total healthcare expenditure. Since implementation of GQCE requirements, generic drugs failing to pass the GQCE are expected to be gradually eliminated and less competitive pharmaceutical companies will be driven out of the market, while competitive ones will further increase their market share by leveraging their product advantages.
- The officially-listed reference drugs for the GQCE are typically the originator-branded version of a generic drug. To pass the GQCE, domestic generics must demonstrate the same quality as, and be biopharmaceutically equivalent to, the reference drug. A reference drug for the GQCE is generally perceived to have high manufacturing quality standards with a superior safety and efficacy profile. We expect that the demand for high-quality originator-branded drugs will continue to grow in China.
- Pharmaceutical companies with a high-quality product portfolio, scalable production capacity and secure supply chain will benefit from the centralized procurement scheme while other less competitive pharmaceutical companies will be driven out of the market, translating to an increasing degree of market concentration.
- In November 2018, the PRC government launched a centralized drug procurement pilot scheme for tendering a limited number of drugs with target procurement quantities in 11 cities in China, and subsequently the drug and geographic coverage under the scheme in 2019 and 2020.
- As of the Latest Practicable Date, according to recent market observations, a type of drug will generally be eligible for inclusion in the centralized drug procurement scheme if there are four or more generic drugs that have passed the GQCE, under the same generic name.
- For example, there were more than 2.5 billion annual incidences of respiratory infections and 23 million annual incidences of urinary tract infection in China in 2024.

Source: Frost & Sullivan analysis

Verification

- China's anti-infective drug market is relatively mature and the market players mainly are domestic pharmaceutical companies. Each type of drugs (categorized by generic names) typically has multiple existing market players. Because the anti-infective drug market is relatively mature, it is unlikely that there will be a significant new market player emerging in China in the near future.
- The barriers for pharmaceutical companies to enter into the anti-infectives therapeutic area in China include: (i) extensive supervision and control in China for the use of anti-infective drugs in order to prevent antibiotics resistance; and (ii) high technical barriers associated with manufacturing anti-infective drugs due to multi-drug resistance. The challenges for pharmaceutical companies to enter into the anti-infective therapeutic area in China include: (i) developing and/or manufacturing effective anti-infective drugs to combat multi-drug-resistant bacteria and viruses; and (ii) developing and/or manufacturing anti-infective drugs with sound and tested safety profile.
- As of the Latest Practicable Date, nine generic versions of Vancocin Injection have been approved, including three imported generics and six domestic generics. Six domestic generic versions of Vancocin injection have passed the GQCE in June 2021, November 2021, April 2023, May 2024, Sept 2024, Sept 2024, respectively. Currently, there are six domestic generic versions of Vancocin injections applying the the GQCE.
- Cefaclor captured a significant share of 15.8% in China's pediatric anti-bacterial drug market in terms of 2022 sales revenue in China. Ceclor Sachet had an established market leadership in the sachet specification within the cefaclor class with a market share of approximately 75.9% and captured a significant market share of 72.7% in China's pediatric cefaclor drug market in terms of sales revenue in 2022.
- Cefaclor captured over 3.9% market share within the cephalosporins market in China in 2023.
- As of the Latest Practicable Date, there were nine, one, and eleven generic versions of Ceclor Sachet, Cefaclor Sustained Release Tablets (II) and Cefaclor Capsules that have passed the GQCE, respectively. One generic version of Ceclor Sachet are in the process of applying for the GQCE qualification, respectively. No generic version of Cefaclor Sustained Release Tablets (II) and no Cefaclor Capsules are in the process of applying for the GQCE qualification.
- Historical concerns about CV risks associated with certain glucose-lowering medications gave rise to the introduction of CV outcomes trials, which were used as evidence to rule out increased risk of a major adverse CV event for glucose-lowering therapies.
- CVD is one of the most prevalent diseases in China. In 2024, there were approximately 330 million CVD patients in China, including more than 13 million cerebral stroke patients and more than 11.4 million coronary heart disease patients. More than 5.15 million patients died due to CVD in China in 2024, translating to a higher mortality rate of 3.65‰ compared to the mortality rate of 2.04‰ for cancer in China and the mortality rate of 2.17‰ for CVD in the U.S.
- Prevention and treatment of CVD is one of the major initiatives promoted by Health China 2030, which set ambitious targets to significantly optimize diagnosis, treatment and death rates of CV patients by 2030, including a target to lower the mortality rate of CVD to 1.9‰ to 2030.
- There are approximately 1.3 million patients in China that undergo percutaneous coronary intervention ("PCI") each year.
- In China, there are 11.39 million cases of coronary heart disease and 13 million cases of stroke.

Source: Frost & Sullivan analysis

Verification

- China's CVD drug market is relatively mature, where major market players include MNCs, domestic leading pharmaceutical companies and domestic local pharmaceutical companies. The overall CVD market is relatively competitive. However, innovative CVD drugs, such as innovative lipid-regulating drugs and oral anticoagulants, face relatively limited competition.
- The barriers for pharmaceutical companies to enter into the CVD therapeutic area in China include: (i) high technical barriers for developing innovative CVD drugs due to the complicated pathology in CVD; (ii) the time-consuming clinical trial process, given that surrogate endpoint is not applicable to evaluate the clinical benefit in the CVD field; and (iii) heavy capital investment for developing CVD drugs due to long research and development cycle and low clinical conversion efficiency. The challenges for pharmaceutical companies face in capturing such opportunities in the CVD therapeutic area include: (i) due to the relatively high diagnosis and mature existing therapeutics for CVD, new CVD drugs need to achieve breakthrough results in terms of efficacy or safety in order to capture the market opportunities; and (ii) the necessity of NRDL listing in China, which is usually very important for CVD drugs because a large amount of CVD patients have relatively low affordability for CVD drugs.
- Approximately 121 million adults in the United States live with one or more types of CVD with an estimated one million new or recurrent coronary events and 795,000 new or recurrent strokes occur each year. Combining the rates of cardiovascular death, stroke and heart attack, one major adverse cardiovascular event occurs in the U.S. roughly every 13 seconds.
- Sales of Vascepa in the U.S. increased significantly from US$179.8 million in 2017 to US$577.9 million in 2022, representing a CAGR of 33.9% from 2017 to 2022.
- There were 107.1 million COPD patients in China in 2023.
- Due to high barriers for research and development of the inhaler, China's inhalation drug market is highly concentrated, dominated by originator-branded drugs manufactured by MNCs.
- More than 70% of asthma patients in China have not been diagnosed, and the control rate in China was only 28.3% in 2022, which was significantly lower than the same indicator of 40.0% in the U.S. Similarly, less than 30% of COPD patients in China have been diagnosed, and the control rate in China was only 20.2% in 2022, which was significantly lower than the same indicator of 58.3% in the United States.
- The Health China 2030 plan recommended yearly lung function tests for populations over 40 years old and those with chronic respiratory disease, with a target to significantly increase diagnosis and treatment rates and lower mortality rate for asthma and COPD. Specifically, it targets to increase the diagnosis rate of COPD from 10% in 2015 to 30% by 2030 and lower the mortality rate of COPD from 0.1‰ in 2015 to 0.08‰ by 2030.
- The sales revenue of FPN in China increased from RMB91.8 million in 2020 to RMB99.9 million in 2021 and further to RMB195.3 million in 2022.
- As of the Latest Practicable Date, FPN was the only marketed fluticasone propionate nebulizer suspension in China, and there were no other generics approved. Additionally, there were only three generics of FPN under clinical development in China.

Source: Frost & Sullivan analysis

Verification

- IL-11 has slow drug response. Platelet increase generally starts after seven days after the administration of IL-11 drugs. In addition, IL-11 may induce adverse effects such as CV events. rhTPO has faster response than IL-11. However, it has a high potential to induce critical adverse events, including portal vein thrombosis and paradoxical thrombocytopenia. Compared to IL-11 products, rhTPO products are perceived to be less affordable. Both IL-11 and rhTPO products are only available for intravenous administration. Due to the historical lack of approved drugs, the drug treatment rate for CIT patients is still extremely low in China, representing large unmet medical needs.
- Mulpleta (lusutrombopag) has been approved in Japan, the U.S. and the EU for the treatment of CLD-associated TCP, and Mulpleta has sustained customer demand in the markets where it has been approved.
- there are approximately 5.0 million CLD patients in the U.S., and approximately 57.3 thousand patients died in 2022 as a result of liver diseases in the U.S. TCP is commonly associated with CLD, which was observed in approximately 76% of patients in the U.S.
- Methylphenidate is a type of stimulant, which is clinically perceived to have stronger efficacy compared to non-stimulant drugs, such as atomoxetine. Despite relatively shorter effective time, methylphenidate has a faster on-set time compared to atomoxetine, ensuring its higher efficacy. However, methylphenidate has more adverse events reported, including certain severe adverse events such as CV risk. Methylphenidate, as a stimulant drug, is a controlled drug that can only be prescribed in hospitals by selected healthcare professionals. In contrast, atomoxetine has fewer and milder adverse events reported, although it has the potential of increasing suicide risk. As a non-controlled drug, atomoxetine generally has no usage restrictions and can be prescribed to patients with other neurological comorbidity.
- EDP 125 is the only SNRI candidate in Phase III clinical trial or later stages in China.
- Furthermore, the PRC government introduced and implemented the Guiding Opinions of the General Office of the State Council on Promoting the Sound Development of the Medical Industry (《國務院辦公廳關於促進醫藥產業健康發展的指導意見》) in 2016 to encourage drug innovation. This initiative focuses on the research and development of innovative drugs with new targets, high selectivity, or novel mechanisms of action in various therapeutic areas such as anti-tumor, cardiovascular diseases, diabetes, neurodegenerative diseases, mental diseases, immune system diseases, infectious diseases, and rare diseases.
- In terms of drug registration, the Chinese government released and implemented the Opinions of the State Council on Reform of the System of Evaluation, Review and Approval of Drugs and Medical Devices (《國務院關於改革藥品醫療器械審評審批制度的意見》) in 2015. This policy encourages the innovation of drugs that prioritize clinical value. It also aims to improve the procedures for the review, evaluation, and approval of innovative drugs, with a focus on expediting the review and evaluation of innovative drugs with urgent clinical needs. Regarding drug manufacturing management, the Chinese government introduced Notice of the General Office of the State Council on Issuing the Plan for the Pilot Program of the System of the Holders of Drug Marketing Licenses (《國務院辦公廳關於印發藥品上市許可持有人制度試點方案的通知》) in 2016. This program allows marketing authorization holders to entrust the production of their products to various manufacturers, providing flexibility in the manufacturing process.

Source: Frost & Sullivan analysis

Verification

- TPO is a type of protein in human body that helps in the growth and development of certain cells involved in blood production. It specifically plays a role in the growth of cells responsible for producing platelets. TPO-RAs are medications that can bind to the TPO receptor, causing changes in its structure. This activation of the TPO receptor triggers a pathway which ultimately results in more platelet production. In addition to its effects on platelets, TPO also stimulates the growth of other types of blood cells. Compared to the traditional method of receiving platelet transfusions, using TPO-RAs as a therapy is considered an effective drug treatment for conditions associated with low platelet counts, such as CLD associated TCP and CIT.
- Medical evidence suggests that the combination of exemestane with HDAC inhibitors, with fewer drug-related severe adverse events, shows a better safety profile compared to the combination of exemestane with mTOR inhibitors.
- According to a study conducted by the Chinese Pediatric Society of Chinese Medical Association in 2020, only less than 10% of children with ADHD received treatment.
- The inclusion of Zinacef in the centralized drug procurement scheme resulted in higher market concentration, which could increase competition among the leading pharmaceutical companies in the market.
- In 2019, atorvastatin, one of the major lipid-regulating drugs, was included in the centralized drug procurement scheme. Consequently, the selling price of atorvastatin experienced a substantial reduction, ranging from 82.6% to 94.9%. Despite this price decrease, the total sales revenue of atorvastatin in China only declined by about 35% between 2019 and 2020. The implementation of the centralized drug procurement scheme has played a crucial role in improving the affordability of atorvastatin in China.
- The decline in market size from 2019 to 2020 can be attributed partially to the expansion of the centralized drug procurement scheme, as well as to governmental policies aimed at limiting the use of anti-bacterial drugs in clinical settings. In 2017, the Chinese government issued the Notice for Further Strengthening the Management of Antibacterial Drugs to Curb Bacterial Resistance. This notice mandates medical institutions to create their own catalog of anti-bacterial drugs and define prescription privileges for healthcare professionals across all levels regarding the use of such medications.
- LABAs are inhaler medications that are used to treat asthma and COPD. These medications work by helping to relax the muscles in the airways, making it easier to breathe. They can also prevent the growth of certain cells in the airways that can contribute to breathing difficulties. Additionally, LABAs can help to reduce inflammation and protect the cells that line the respiratory tract, which can be irritated in conditions like asthma and COPD.
- As of the Latest Practicable Date, only two TPO-RA drug indicated for the treatment of CLD-associated TCP, Mulpleta and Doptelet, received new drug approval in China.

Source: Frost & Sullivan analysis

Verification

- Methylphenidate is a short-acting stimulant with a duration of action of one to four hours and a pharmacokinetic half-life of two to three hours, while single-dose atomoxetine can provide 24-hour efficacy, despite a 5-hour plasma half-life. Unlike CNS stimulants, SNRIs do not increase the level of dopamine in the striatum and nucleus accumbens.
- It is estimated that for drugs included in the centralized drug procurement scheme, the drug procurement quota typically amounts to approximately 50% to 80% of the annual procurement volume of public medical institutions in China.
- As of the Latest Practicable Date, cefaclor sachet, cefaclor capsule, cefuroxime sodium for injection, cefuroxime axetil tablets, ceftazidime for injection were included in the centralized drug procurement scheme.
- Cefaclor capsule was included in the centralized drug procurement scheme in November 2020, followed by cefaclor sachet in November 2022. Cefuroxime axetil tablets were included in the scheme in March 2019, while cefuroxime sodium for injection, ceftazidime for injection and medium and long chain fat emulsion injection (C8-24Ve) were included in October 2021. (execution time)
- Histone deacetylase (HDAC) is a special protein that helps control how genes work by making changes to the structure of chromosomes. It works together with histone acetyltransferase (HAT) to control the level of histone acetylation in human body. Histone acetylation affects how tightly the DNA is packaged and can determine whether genes are turned on or off. As a result, HDAC and HAT are important regulators that help with the regulation of gene expression and play a role in how the body functions at a genetic level.
- Current evidence suggests that lowering serum LDL-C levels, regardless of the method used, results in cardiovascular benefits. Therefore, LDL-C is the primary intervention target for ASCVD prevention and control with statin therapy as the cornerstone for LDL-C lowering treatment. After VBP inclusion, lowered statin prices led to an even more widely adoption among Chinese ASCVD patients. With the increasing aging population, Chinese lipid-regulating market is expected to further grow.
- The introduction of statins to inhibit cholesterol synthesis, ezetimibe to reduce cholesterol absorption, and Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors to increase cholesterol clearance has led to an unprecedented improvement in the ability to manage LDL-C and a major advance in the prevention and treatment of ASCVD. However, the observations presented through various randomized controlled trials show that an ideal level of LDL-C post statin therapy, in combination with ezetimibe and/or PCSK9 inhibitors has only resulted in **1/3rd** reduction of cardiovascular events. The remaining **2/3rd** cases which still occur after treating LDL-C are called residual cardiovascular (CV) risk. Elevated TG or TRL-C (triglyceride rich lipoprotein cholesterol) is an important factor contributing to the increased residual cardiovascular risk. HTG (TG>150 mg/dL) is also one of the most common dyslipidemia phenotypes in Chinese population.
- Vascepa is the only triglyceride lowering drug approved by FDA and NMPA as an adjunct statin therapy (maximally tolerated in US) to reduce the risk of myocardial infarction, stroke, coronary revascularization, and unstable angina requiring hospitalization in adult patients with elevated triglyceride (TG) levels (≥ 150 mg/dL) and established cardiovascular disease or diabetes mellitus and 2 or more additional risk factors for cardiovascular disease. It provides an unique and powerful weapon for clinical physicians to tackle cardiovascular residual risks, especially for ASCVD EHR(extreme high risk) and VHR(very high risk) patients.

Source: Frost & Sullivan analysis

Verification

- According to the Frost & Sullivan Report, the distribution of imported drugs in China primarily takes two forms: in the first, companies appoint an importer primarily for customs clearance as well as distribution and delivery of drugs to regional distributors; or in the second, companies clear customs as well as distribute and deliver the products to regional distributors directly. Regional distributors are primarily responsible for operating local distribution centers and warehouses, maintaining a sufficient level of inventory, and providing end-to-end delivery of drugs to hospitals and pharmacies. In the first form, distribution cost attributable to importers typically amounts to low-single digit percentage of product sales of a company in China. In the second form, companies can eliminate such distribution cost, but companies need to devote resources to build their own distribution network of regional distributors and develop their capabilities for product delivery to such regional distributors, according to the same source. On the other hand, domestically manufactured drugs are primarily distributed to regional distributors directly from manufacturing facilities.
- In the distribution process for imported drugs in China, regional distributors play a much more important role than importers. They are responsible for management of drug procurement, sales and inventory management for hospitals and pharmacies and maintaining market access for drugs. Importers for imported drugs, on the other hand, primarily provide supportive services, including customs clearance and logistic services for the delivery of drugs to regional distributors. Companies may choose to appoint an importer due to various commercial reasons, including but not limited to (i) historical distribution pattern (i.e. the drugs are historically distributed to importers and in order to maintain stability of the distribution network, companies may keep their importers in the distribution network); (ii) cost-effectiveness analysis (i.e. the time and resources needed for developing own regional distributor network and product delivery functions outweigh the distribution cost attributable to importers); and (iii) other commercial reasons, including existing long-term cooperation arrangements, favourable payment terms, etc.
- Importers in China generally maintain a safety product inventory level ranging from three to nine months to avoid potential supply shortage.
- DDI system the Target Group utilizes to monitor inventory accumulation and ultimate sales to end-customers is also used by many MNCs and biotechnology companies in China.
- In addition, the DDI system is a market intelligence and analytics tool and is widely used by pharmaceutical companies in China to assess and evaluate the trend of in-market sales.
- The Target Group's insurance coverage is considered to be in line with the market practice taking into account that the Target Group insurance covers all the applicable insurance required by Chinese laws and regulations; the Target Group property insurance coverage is in accordance with customary industry practice; and (iii) not all companies in the Target Group's industry maintain product liability insurance.
- According to Frost & Sullivan and based on their analysis of publicly available information, the Target Group's ESG performance is comparable to the Target Group's industry peers, taking into account the Target Group's implementation of measures (i) effectively preventing and reducing hazards and risks associated with the Target Group's operations while ensuring the health and safety of the Target Group's employees and surrounding communities, (ii) implementing pollution controls for wastewater, waste gas, and solid waste, and (iii) promoting equal opportunities for all employees irrespective of gender, age, race, religion, or any other social or personal characteristics.
- According to a market research conducted by F&S, the upfront and milestone payment of oncology drugs in the previous license-in cases between 2017 and 2023 could range from USD3.7 million to USD1,330 million and the royalty. rate could range from 8% to 20%.

Source: Frost & Sullivan analysis

Development Path of Cancer Treatment

- Cancer treatment has gone through a long process of development in history, and it will continue to evolve over time with the innovative and hard work of scientists around the world.
- Today, major treatments include surgery, radiotherapy, chemotherapy, targeted therapy, and immunotherapy.

Milestones in Cancer Treatment

Surgery
1881, first successful surgery performed for stomach cancer

- ***Surgery*** is a procedure in which a surgeon removes cancer from patient's body.
- Surgery works best for solid tumors that are contained in one area. It is not used for leukemia or for cancers that have spread. Surgery may be performed before or after other forms of treatment.
- In addition to removal of the primary tumor, surgery is often necessary for staging.

Radiotherapy
1903, first successful use of radiation to cure skin cancer

- ***Radiotherapy*** is a cancer treatment that uses high doses of radiation to kill cancer cells and shrink tumors.
- Radiotherapy can be used to treat many types of cancer including solid tumors and leukemia. And in many cases, patients receive radiotherapy with other cancer treatments, such as surgery and chemotherapy.
- Radiation not only kills or slows the growth of cancer cells, it can also affect nearby healthy cells, which will cause side effects.

Chemotherapy
1949, FDA approved first chemotherapy drug - nitrogen mustard - for the treatment of Hodgkin lymphoma

- ***Chemotherapy*** is a cancer treatment that uses chemical substances, especially one or more anti-cancer drugs to stop or slow the growth of cancer cells.
- Chemotherapy can be used to treat many types of cancer alone or in combination with other treatments.
- Chemotherapy also causes side effects such as mouth sores, nausea, and hair loss.
- Typical chemotherapeutic drugs include alkylating agents, antimetabolites, anti-tumor antibiotics and etc..

Targeted Therapy, Immunotherapy
2014, FDA approves the first bi-specific antibody drug, Blinatumomab

- ***Targeted therapies*** act on specific targets that are associated with cancer growth, thus they do less harm to normal cells. Most targeted therapies are either small-molecule drugs or monoclonal antibodies.
- ***Immunotherapy*** Immunotherapy includes cellular Immunotherapy, cytokines, antibody-like drug, oncolytic virus, fusion proteins.
- Antibody-like drugs include monoclonal antibody, bispecific antibody, antibody conjugate drug (ADC) and multi-specific antibodies.

Source: Literature Review, Frost & Sullivan Analysis

Oncology Treatment Evolvement

Primary Treatment

1. Surgery

- Cancer surgery removes the tumor and nearby tissue during an operation. Best for early stage tumors that are contained in one area but is limited for cancers that have metastasized.

2. Radiotherapy

- High doses of radiation to kill cancer cells and shrink tumors including solid tumors and leukemia.
- Affects nearby healthy cells, causing side effects such as fatigue, hair loss and skin changes.

3. Chemotherapy

- Uses one or more anti-cancer drugs to stop or slow the growth of cancer cells.
- Targets all fast growing cells, causing side effects such fatigue, hair loss, easy bruising and bleeding, and infection.

4. Targeted Therapy

- Act on specific targets that are associated with cancer growth
- Less harmful to normal cells than traditional therapies
- Include both small molecule drugs and monoclonal antibodies

Treatment Evolution

5. Immuno-Oncology Therapy

Immunotherapy includes cellular Immunotherapy, cytokines, antibody-like drug, oncolytic virus, fusion proteins.
Antibody-like drugs include monoclonal antibody, bispecific antibody, antibody conjugate drug (ADC) and multi-specific antibodies.

Significant Evolution

- The use of chemotherapy to treat cancer began in the early 20th century. in the 1960s and early 1970s, combination chemotherapy showed efficacy in curing acute leukemia in children and advanced Hodgkin's disease, overcoming the pessimism that prevailed at the time about the ability of drugs to cure advanced cancer and promoting research in adjuvant chemotherapy. Today, important molecular mutations are often used to screen for potential new drugs as well as targeted therapies, and remain the cornerstone of anticancer drug therapy for many cancer patients.
- While monoclonal antibodies have become the backbone of cancer therapy, bispecific antibodies in immunotherapy are emerging as an important and promising component of the next generation of therapeutic antibodies due to their ability to simultaneously target two epitopes in the tumor cell or tumor microenvironment.

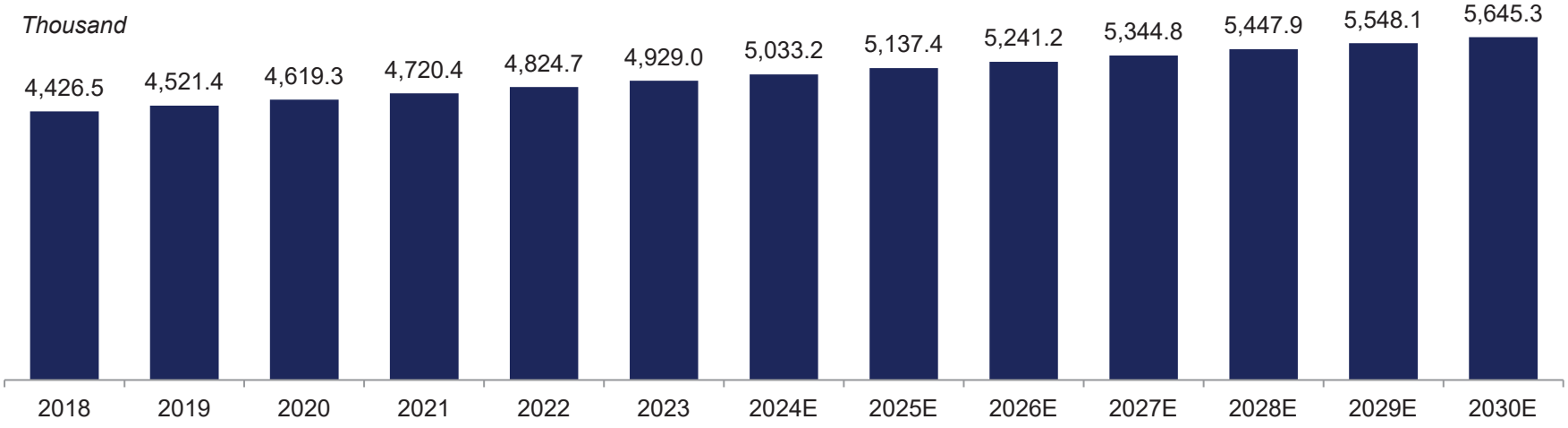
Source: Literature Review, Frost & Sullivan Analysis

China Cancer Incidence, 2018-2030E

- In China, cancer incidence number reached 4929.0 thousand in 2023 at a CAGR of 2.2% from 2018. It is projected to further increase to 5241.2 thousand in 2026, representing a CAGR of 2.1% from 2023. It is estimated that the number would achieve 5645.3 thousand in 2030, representing a CAGR of 1.9% from 2026 to 2030.

China Cancer Incidence, 2018-2030E

Period	CAGR
2018-2023	2.2%
2023-2026E	2.1%
2026E-2030E	1.9%



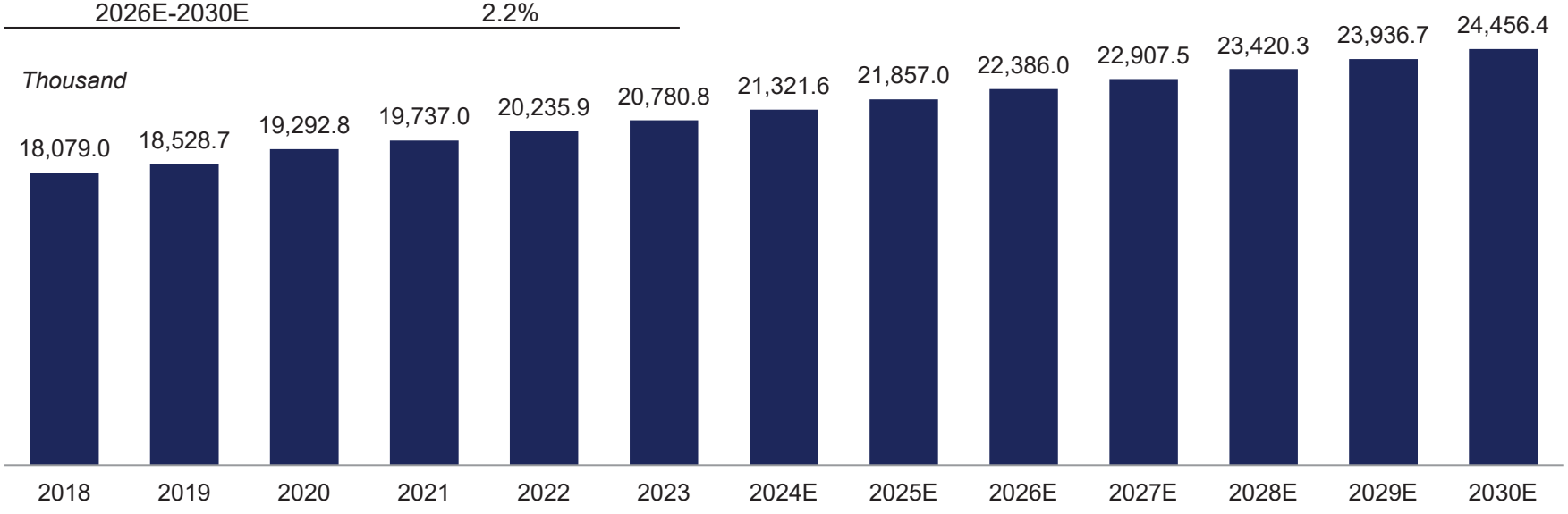
Source: NCCR, Frost & Sullivan Analysis

Global Cancer Incidence, 2018-2030E

- In global, cancer incidence number reached 20,780.8 thousand in 2023 at a CAGR of 2.8% from 2019. It is projected to further increase to 22,386.0 thousand in 2026, representing a CAGR of 3.4% from 2023. It is estimated that the number would achieve 24,456.4 thousand in 2030, representing a CAGR of 2.2% from 2026 to 2030.

Global Cancer Incidence, 2018-2030E

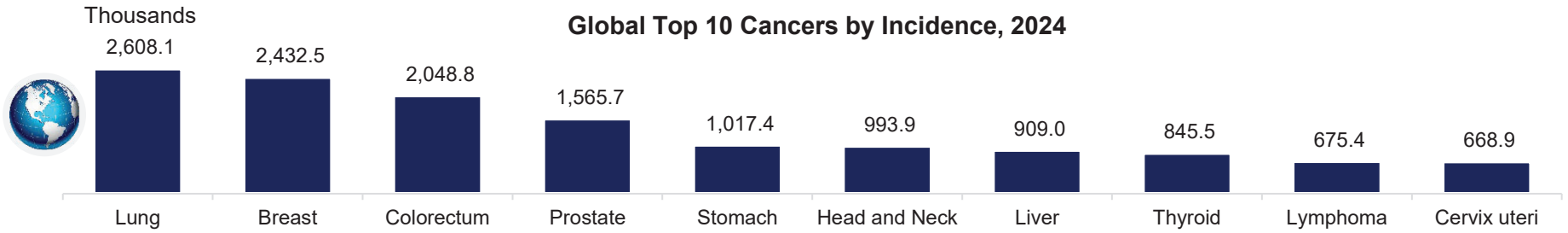
Period	CAGR
2018-2023	2.8%
2023-2026E	3.4%
2026E-2030E	2.2%

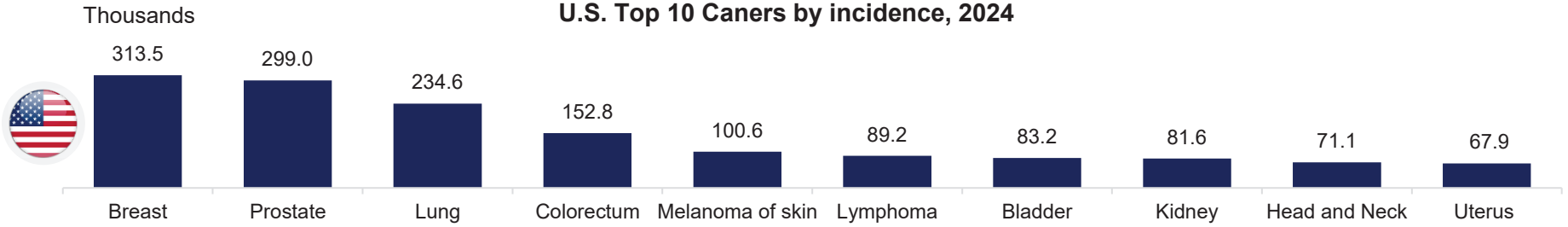


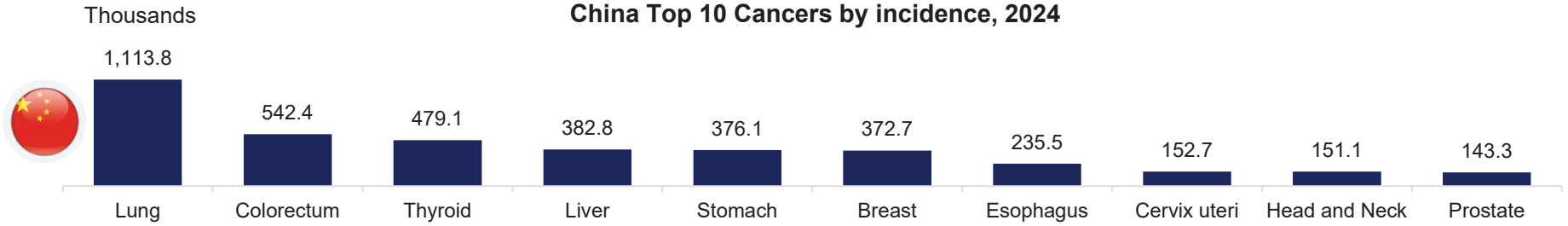
Source: IARC, Frost & Sullivan Analysis

Top 10 Cancers by Incidence, 2024

- The top 5 cancers by incidence globally in 2024 are lung cancer, breast cancer, colorectal cancer, prostate cancer and stomach cancer.
- The increasing smoking population are the risk factors of lung cancer in China. And the higher incidence of stomach and colorectal cancer are associated with unhealthy diet, eating habits and manner in China.



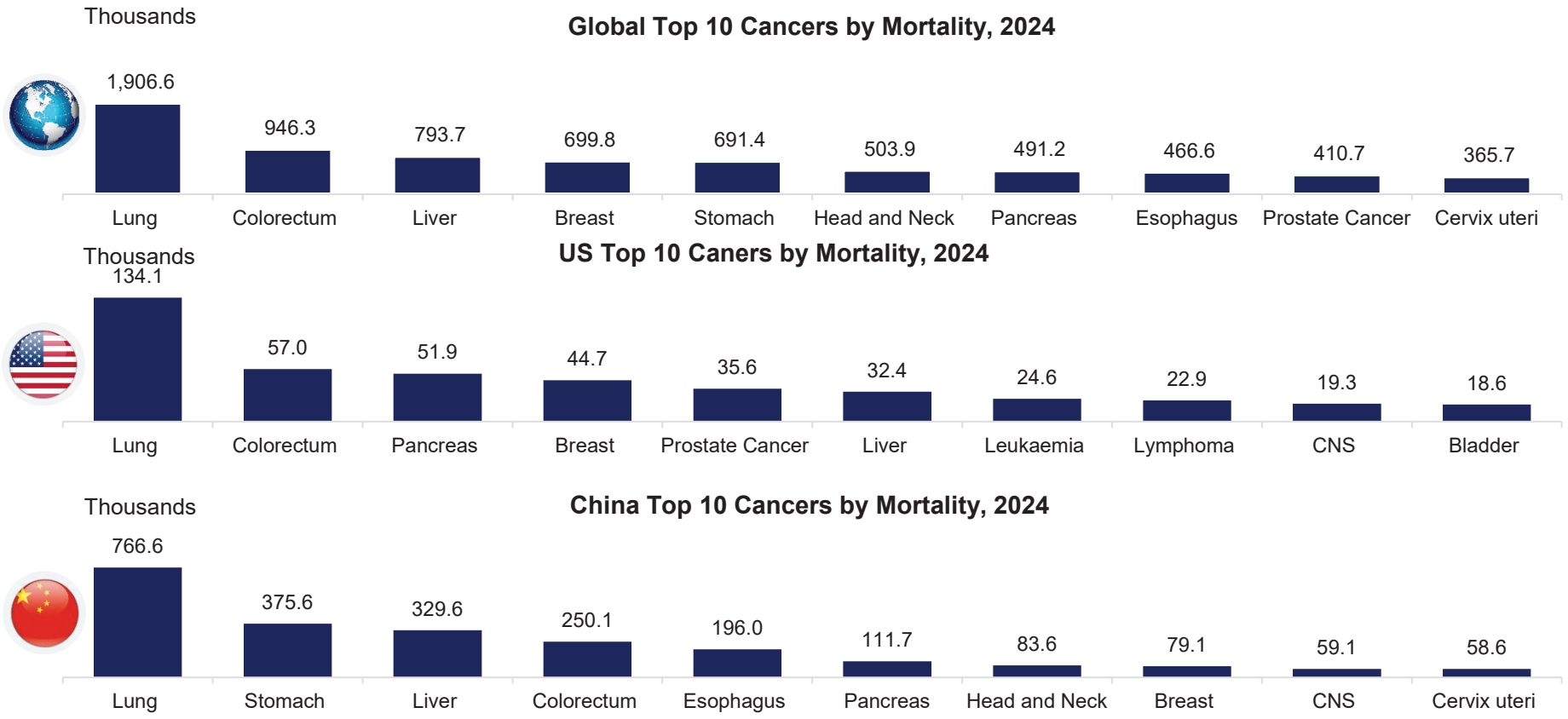




Source: Globocan, IARC, NCCR, Frost & Sullivan analysis

Top 10 Cancers by Mortality, 2024

- The top 5 cancers by mortality globally in 2024 are lung cancer, colorectum cancer, Liver cancer, breast cancer and stomach cancer.

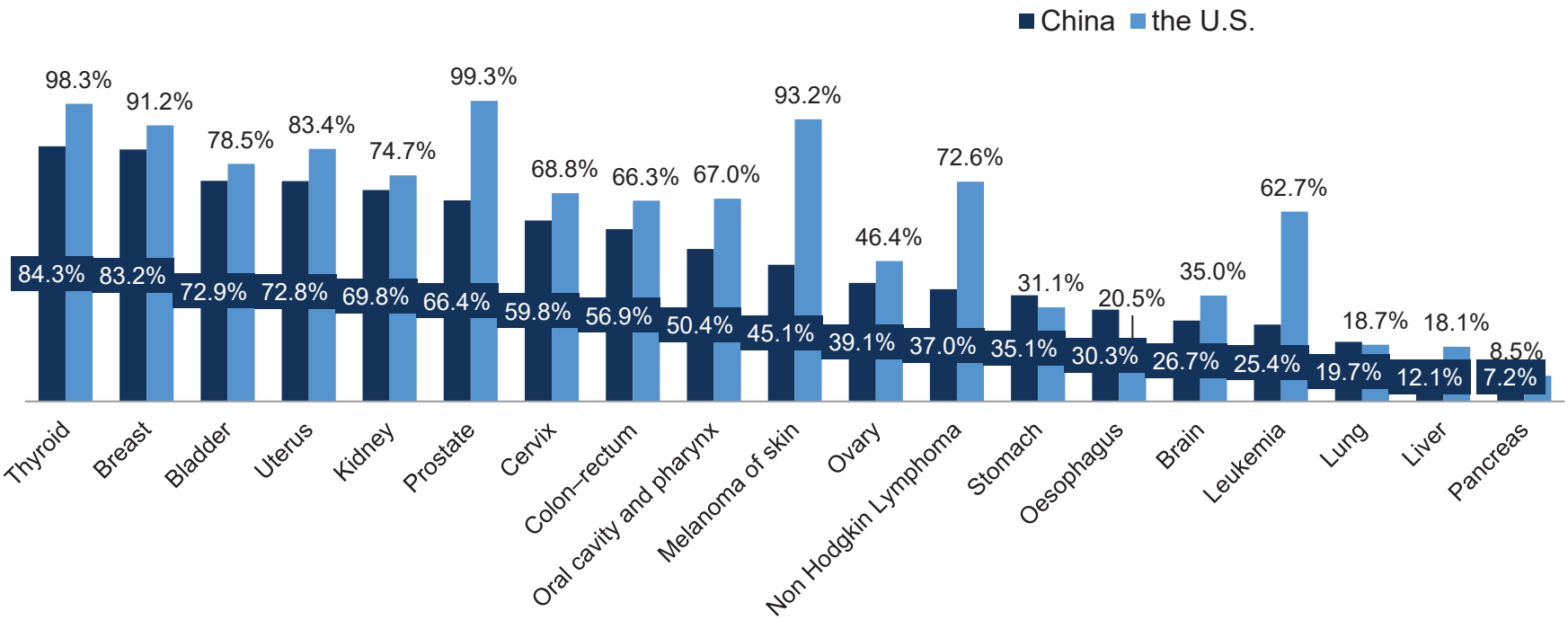


Source: Globocan, IARC, NCCR, Frost & Sullivan analysis

Comparison of 5-year Survival Rate of Cancers in China and the U.S.

- China's 5-year survival rate lags far behind the U.S. in prostate cancer, melanoma of skin, non Hodgkin lymphoma and leukemia.
- Cholangiocarcinoma has a high degree of malignancy, strong invasiveness, rapid cancer progression, and its mortality rate is actually at the forefront of all cancer types. An epidemiological study on the incidence and mortality of 16,189 cholangiocarcinoma patients in the United States from 2000 to 2015 showed that the annual incidence and mortality of cholangiocarcinoma in the United States during the study period were 11.977/100000 person-year and 10.295/ For 100,000 person-years, the fatality rate can reach 86.0%.

5-year Survival Rate of Cancers in China and the U.S.



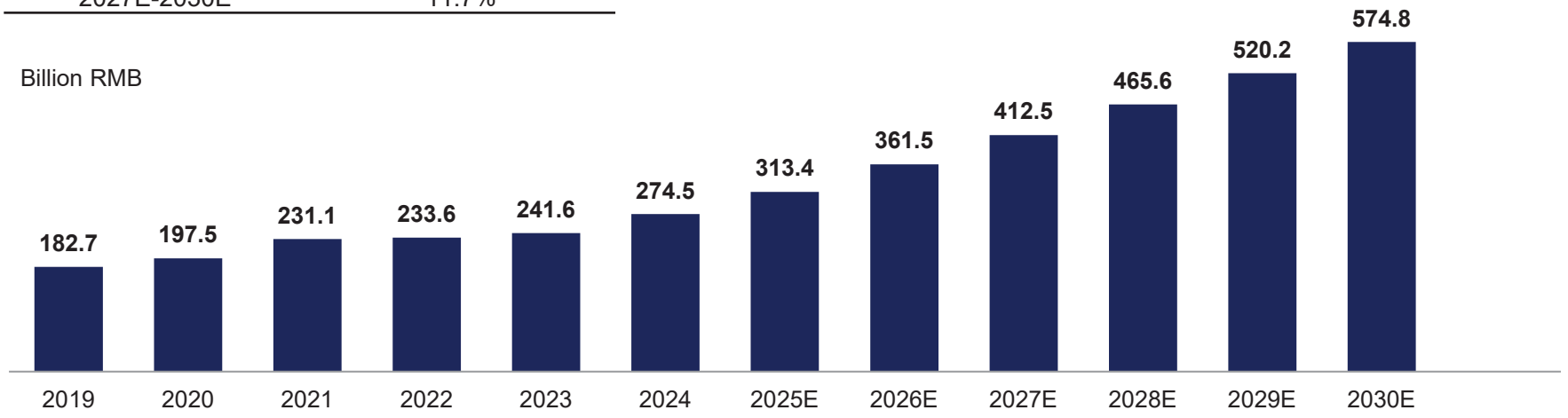
Source: NCCR, IARC, Frost & Sullivan Analysis

China Oncology Drug Market, 2019-2030E

- In Chinese drug market, sales of oncology products has risen steadily in the recent years. Chinese oncology market, generating RMB274.5 billion in 2024, experienced a CAGR of 8.5% over the past 5 years.
- The ever-changing of successful innovative oncology treatments have promised a high return of pharmaceutical manufacturers. Chinese oncology market is expected to uptrend in the following years. From 2024 to 2027, Chinese oncology market is going to reach RMB412.5 billion at wholesale price level with CAGR of 14.5%. Forecasted data shows that global oncology market would be RMB574.8 billion in 2030, representing a CAGR of 11.7% from 2027 to 2030.
- While competition in China's oncology drug market is fierce, companies with in-house capabilities throughout the entire value chain of oncology drug development, including drug discovery, process development, clinical development, quality control and assurance and commercialization, are better positioned to capture the growth potential of this market.

China Oncology Drug Market, 2019-2030E

Period	CAGR
2019-2024	8.5%
2024-2027E	14.5%
2027E-2030E	11.7%



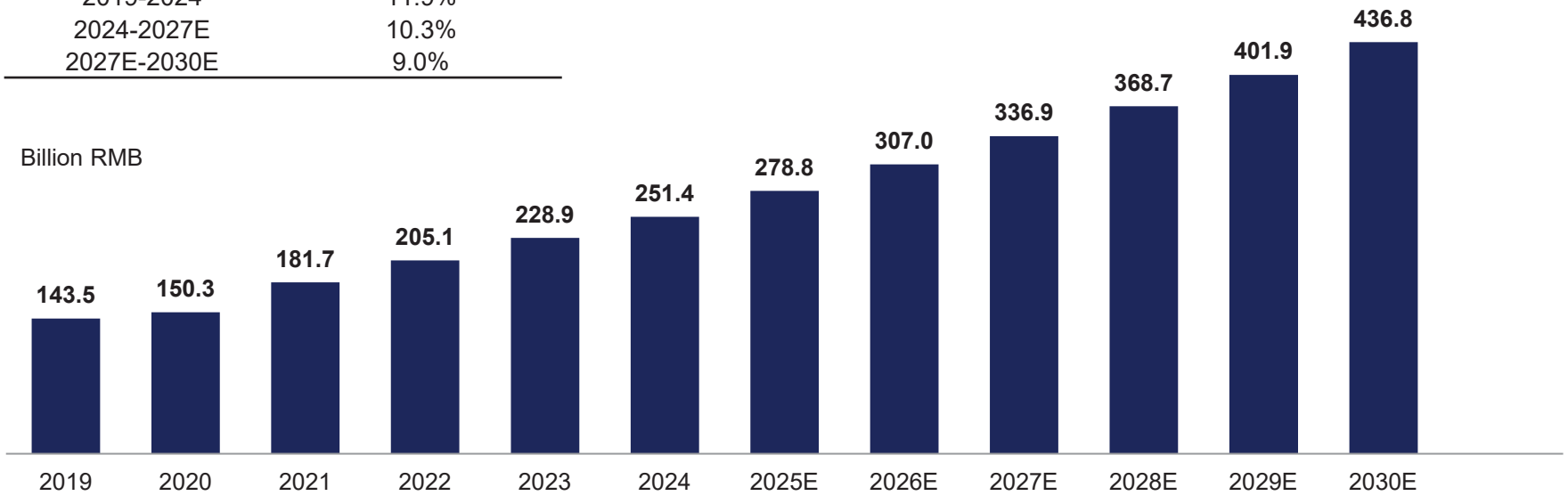
Source: Annual Reports of Listed Medical Companies, NMPA, CDE, NRDL, MOHRSS, NCCR, Frost & Sullivan Analysis

Global Oncology Drug Market, 2019-2030E

- From 2019 to 2023, Global market of cancer drugs expanded from USD143.5 billion to USD251.4 billion, representing a CAGR of 11.9% during this period. The steadily growing market results from the expanding patient pool and increasing affordability of healthcare service.
- Global oncology market is expected to garner USD336.9 billion by 2027, with a CAGR of 10.3% during the forecasted period from 2024 to 2027. Immunotherapies/ biologics are emerging as potential therapies to get the permanent cure for various cancer types. Amongst various biologics, drugs based on monoclonal antibodies (mAbs) have gained significant attention in recent years and would further propel the growth of oncology/cancer drugs market due to their high efficacy.
- Global oncology market is expected to generate USD436.8 billion revenue by 2030, with an annual growth rate of 9.0% from 2027 to 2030.

Global Oncology Drug Market, 2019-2030E

Period	CAGR
2019-2024	11.9%
2024-2027E	10.3%
2027E-2030E	9.0%



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

Growth Drivers of Oncology Drug Market

Increasing Cancer Incidence	• Global cancer incidence grew over past years, and it is expected that it to grow in the future. The total cancer incidence has reached 20.7 million globally in 2023, and is expected to further increase to 22.3 million in 2026. The increase of cancer incidence can be attribute to increasing lifespan, more aging population, and obesity. The high incidence create a demand for oncology drugs that will drive the growth of oncology drug market.
Improving Affordability	• According to WHO, nearly 1 in 6 death worldwide is due to cancer, and approximately 70% of those deaths occur in low- and middle-income countries. Managing cancer is complicated by increasing prices and insufficient benefits for patients and public health of new medicine coming to market. Thus, an improved affordability of patient is a key in pushing oncology drug market forward by alleviating the burden of cancer treatment. In many countries, the cancer reimbursement system is getting more mature, for example. Medicare Program in US and NRDL dynamic reimbursement list in China have both made efforts in realizing cancer patient reimbursement.
Investigation on Innovative Targeted Drugs	• With a deeper understanding on cancer, it is revealed that even patients with the same type of cancer exhibit different genotype or different expression level of certain proteins that are key in tumor formation pathway. These proteins can potentially serve as tumor prognostic biomarkers. Intensive researches have been done in some of the previously oriented tumor related targets, which reveals a potential of treating a wide patient population with different tumor features. Such investigations has demonstrated the importance of potential new targets that have in fulfilling unmet need of patient subgroups. Thus, the more innovative targets identified and applied in drug development, the more clinical need will be addressed, and the further the oncology market expansion.
Technology Advancement	• Technology advancement brings revolution to the pharmaceutical R&D and manufacturing process, enabling the advent of targeted therapy, immuno-oncology therapy etc. to address the unmet clinical needs. Patients suffering from cancers have benefited from improving 5-year survival rate. The demand of oncology drugs has significantly been driven up. With the further R&D investment and efforts, more novel therapies will be launched and further prolong the survival of cancer patients. Market is expected to further go up with increasing clinical demand.
Rising Small and Mid-sized Pharmas	• Small and mid-sized pharmas which can offer potentially more promising career opportunities are attractive for sales and R&D talents trained at MNCs. With engagement by talents attrition from MNCs, R&D activities are no longer dominated by MNCs. Small and mid-sized pharmas concentrate more on specialty drugs like oncology and are more flexible in operation, injecting vitality to the oncology drug industry.

Source: Frost & Sullivan Analysis

Future Trends of Oncology Drug Market

Precision Cancer Treatment	• Oncology market is promoting precision treatment. In order to provide precision treatment to different subtypes of patients, targeted cancer therapy emerges and develops rapidly, which involves drugs or other substances to block the growth and spread of cancer by interfering with those specific molecular targets. With the continuous exploration on innovative targeted drugs, precision treatment of cancer will be applied to a wider tumor-related targets, making it a future trend. For example, in China, besides a previous hot fad of exploring targets such as EGFR, VEGFR and CD20, oncology drugs targeting CD47, NKG2A, HLA, CSF-1R, etc. are being investigated more recently, urging the precision treatment of related cancer.
Inclusion of more Oncology Drugs in NRDL	• The establishment of National Healthcare Security Administration promotes the rapid progress of medical insurance, including the NRDL revision by price negotiation and dynamic adjustment, through which oncology drugs can be included in the reimbursement list in a more flexible manner, benefiting the potential patients by expanding the anti tumor drugs on the list. For example, since the dynamic implementation, 17, 18, 23, 21 oncology drugs (including chemical and biological drugs) were included in the 2020-to-2023 NRDL.
Development of Innovative Immunotherapies	• In the past few decades, immunotherapy has revolutionized cancer treatment and rejuvenated the field of tumor immunology. However, Most of the immunomodulatory approaches currently being developed engage the adaptive immune system and there are still some deficiencies with current immunotherapies, such as respond rate issues associated with PD-1/PD-L1 therapy. With the increasing significant progress in understanding the molecular basis of the immune response to cancer as well as the basic mechanisms of cellular immunology, innovative immunotherapies such as immunocytokines and innate immunotherapies will gradually emerge, thereby offering an alternative immunotherapeutic option.
Managing Cancer as a Chronic Disease	• Newer treatments extend survival and active treatment time frames. Furthermore, patients unable to take current cancer therapies or who have developed resistance to initial therapies may be able to take advantage of new options and lines of therapy, resulting longer lifespan. • With the availability of oncology drugs and awareness of health management, cancer is expected to have longer 5-year survival rate, becoming a kind of chronic disease like diabetes and hypertension and making cancer requires more than treatment but also follow-up and rehabilitation after treatment, which develops an increasing demand for more advanced screening methods, such as gene sequencing and imaging detection, and rehabilitation solutions, such as special nutritional support, cachexia treatment and comorbidity treatment.

Source: Frost & Sullivan Analysis

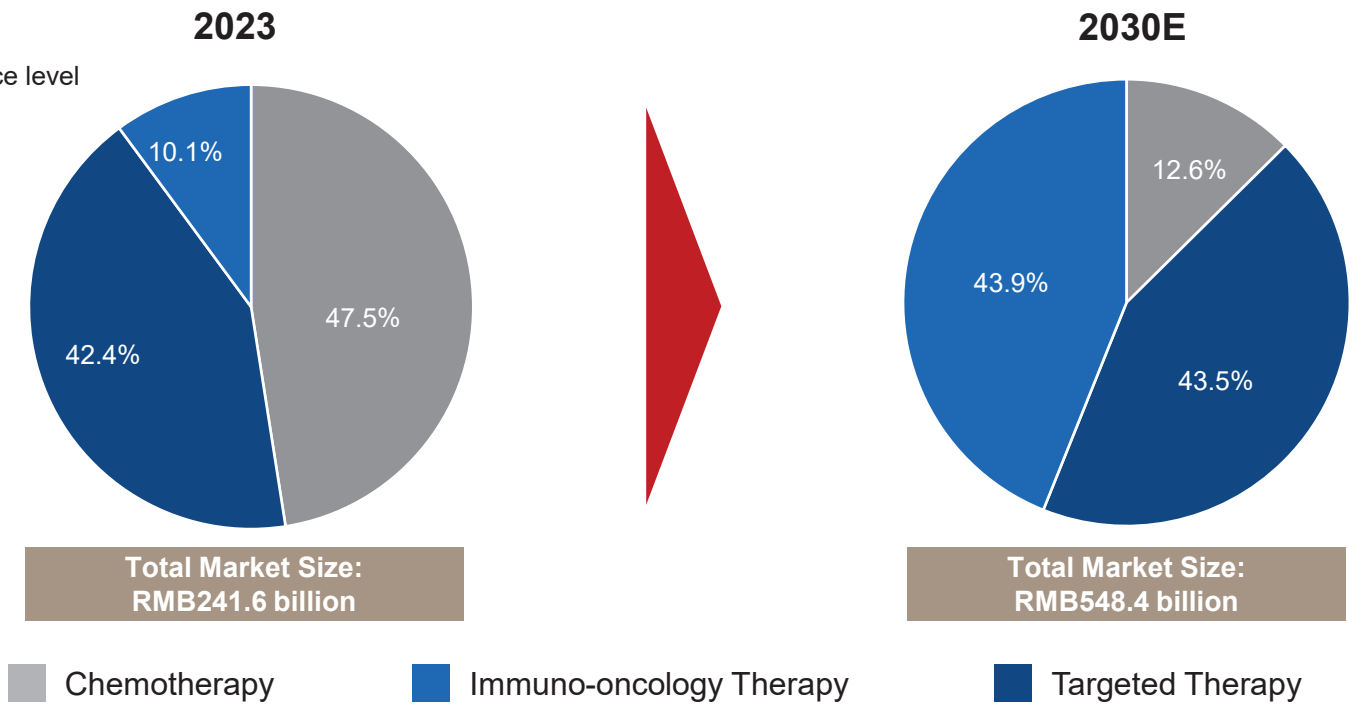
Breakdown of China Oncology Market by Therapy, 2023 and 2030E

- Currently, China oncology market is dominant by chemotherapy drugs which takes up to 47.5% of total. Targeted drugs including small-molecularly targeted drugs and biologics, which take a proportion of 42.4%, leaving 10.1% for immuno-oncology therapy in 2023.
- With reimbursement policies, new drug development and patients' increasing affordability, the targeted therapy and immuno-oncology therapy would occupy most of the market by 2030. It is expected that the share of immuno-oncology therapy approaches 43.9% while targeted drugs share would reach 43.5%.

Breakdown of China Oncology Market by Therapy, 2023 and 2030E

Billion RMB

At wholesale price level



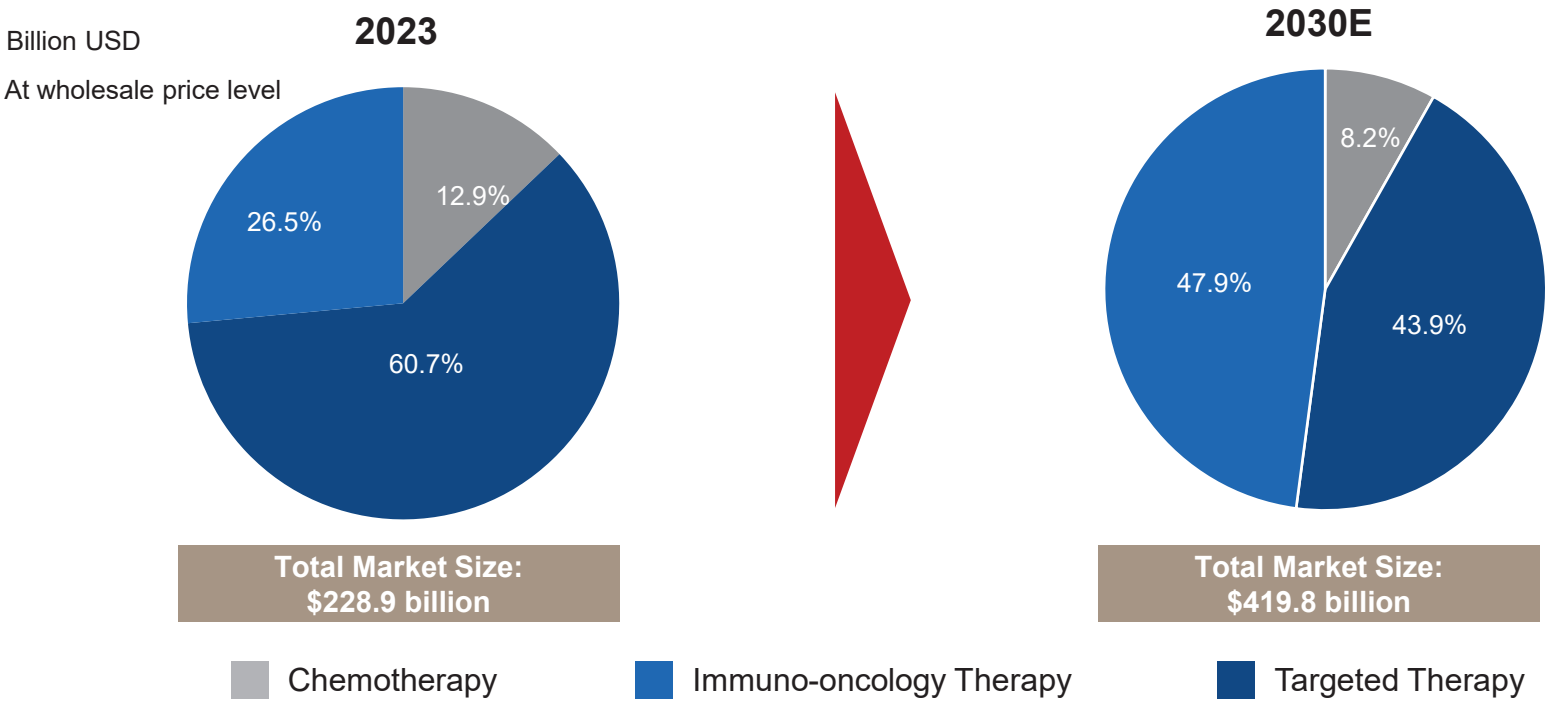
Chemotherapy includes chemical drugs, traditional Chinese medicine injections and adjuvant anti-tumor drugs.

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

Breakdown of Global Oncology Market by Therapy, 2023 and 2030E

- Currently, global oncology market is dominant by targeted therapy, which takes up to 60.7% of total market share. Chemotherapy is taking a proportion of 12.9%, the remaining 26.5% corresponds to immuno-oncology therapy in 2023.
- It is expected that the share of immuno-oncology therapy approaches 47.9% while targeted drugs share would reach 43.9%.

Breakdown of the Oncology Market by Therapy in Global, 2023 and 2030E



Chemotherapy includes chemical drugs and adjuvant anti-tumor drugs.

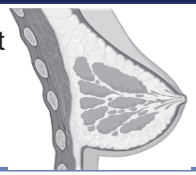
Source: Annual Reports of Listed Medical Companies, NMPA, CDE, NRDL, MOHRSS, FDA, IARC, GLOBOCAN, Frost & Sullivan Analysis

Overview of Breast Cancer

- Breast cancer is a malignant tumor that occurs in the epithelial tissue of the breast. It is the most common malignant tumor in women and occasionally in men. Developing from breast tissue, breast cancer may present as a lump in the breast, a change in breast shape, dimpling of the skin, fluid coming from the nipple, a newly inverted nipple, or a red or scaly patch of skin. The incidence of breast cancer is related to high endogenous estrogen levels in patients, endometriosis, menstrual fertility factors, genetic factors, environmental and lifestyle factors, etc., and the incidence peaks around the age of 45-49. Treatment measures should be based on histological classification, TNM staging and molecular classification of breast cancer. About 24% of HR+/HER2- breast cancer patients are diagnosed with advanced disease.

Definition

- Breast cancer is cancer that develops from breast tissue. Worldwide, breast cancer is the leading type of cancer in women, but is occasionally occurring in men.



Molecular classification

		ER	PR	HER2-	Ki-67
Luminal	Luminal A	+	+ (High expression)	-	Low
	Luminal B (HER2-)	+	- Or low expression	-	High
	Luminal B (HER2+)	+	any	+	any
Erb-B2 expression		-	-	+	/
Basal-like		-	-	-	/

Histological classification

- **non-invasive carcinoma**: Carcinoma in situ means that the lesion is limited to the primary site without metastasis, including ductal carcinoma in situ and lobular carcinoma in situ
- **invasive carcinoma**: Cancer cells infiltrate and invade surrounding tissues extensively, occurring metastasis
- **Others**: Rare and accounting for a small proportion

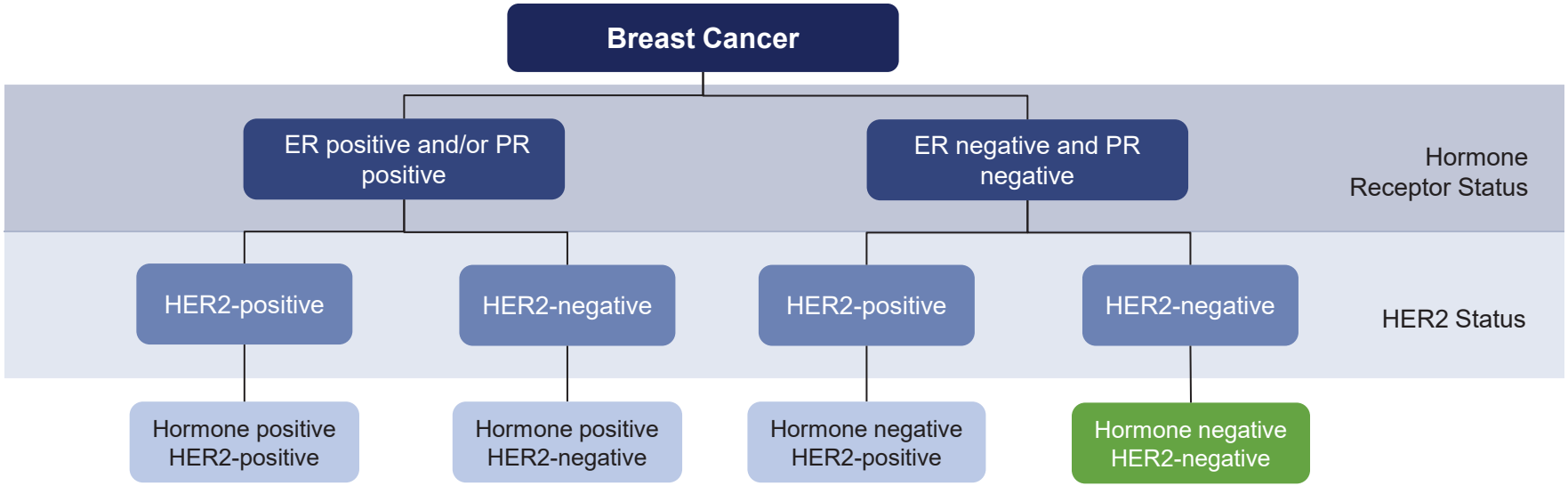
Risk Factors

- Genetic predisposition (BRCA1 or BRCA2 mutations)
- Estrogen and progesterone exposure
- Oral contraceptives or birth control drugs
- Atypical hyperplasia of the breast
- Lobular carcinoma in situ
- Lifestyle factors (weight, food, alcohol, physical activity)
- Breast density (dense breast tissue)
- Family history of breast cancer

Source: Literature Review, Frost & Sullivan analysis

Classification of Breast Cancer

- Breast cancer classification divides breast cancer into categories according to different gene expression and receptor status.
- Among all different kinds of receptors in breast cancer cells, three most important classification being: estrogen receptor (ER), progesterone receptor (PR), and HER2.
- Either a test called an immunohistochemistry (IHC) test or fluorescence in situ hybridization (FISH) test is used to find out if cancer cells have a high level of the HER2 protein. About 20% of breast tumors have higher levels of a protein known as HER2. These cancers are called HER2-positive breast cancers, otherwise called HER2-negative breast cancer (HER2-negative breast cancer includes HER2 low expression).



- It is not clear if one test is more accurate than the other, but FISH is more expensive and takes longer to get the results. Often the IHC test is done first.
- If the IHC result is 0, the cancer is considered HER2-negative. These cancers do not respond to treatment with drugs that target HER2.
- If the IHC result is 1+, the cancer is considered HER2-negative. If the IHC result is 2+, the HER2 status of the tumor is not clear and is called "equivocal." This means that the HER2 status needs to be tested with FISH to clarify the result. Some breast cancers that have an IHC result of 1+ or an IHC result of 2+ along with a negative FISH test might be called HER2-low cancers.
- If the IHC result is 3+, the cancer is HER2-positive. These cancers are usually treated with drugs that target HER2.

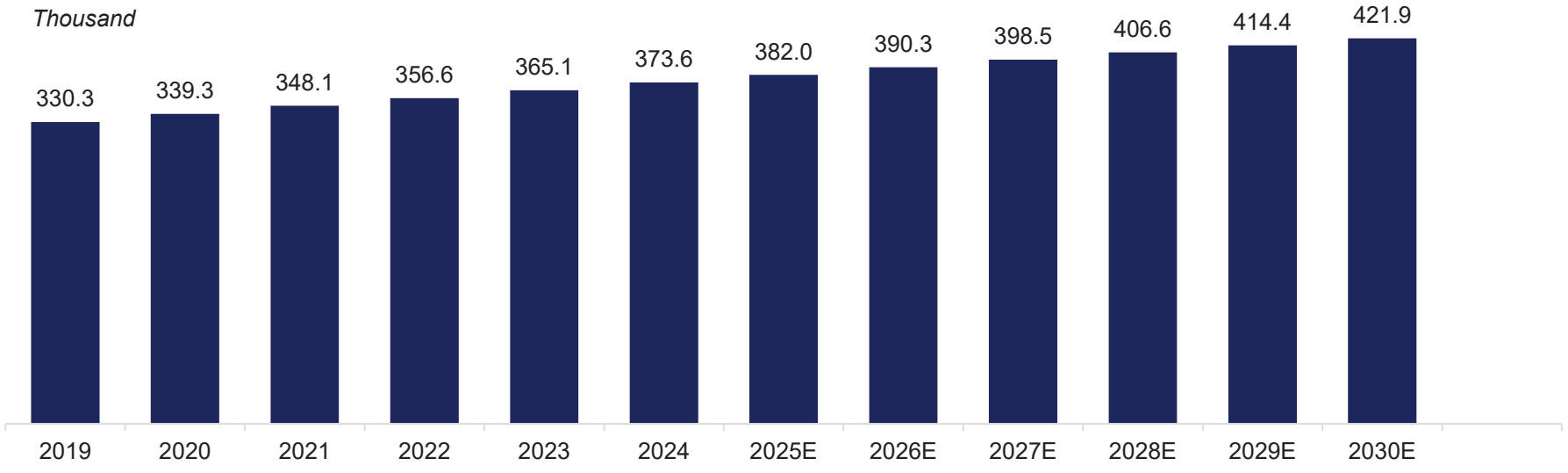
Source: Literature Review, Frost & Sullivan analysis

Incidence of Breast Cancer in China, 2019-2030E

- Incidence number of breast cancer in China increased from 330.3 thousand to 373.6 thousand in 2019 and 2024. The number is expected to grow to 398.5 thousand in 2027 at a CAGR of 2.5% from 2024 to 2027. The number is expected to grow to 421.9 thousand in 2030, at a CAGR of 1.9%.

Incidence of Breast Cancer in China, 2018-2030E

Period	CAGR
2019-2024	2.5%
2024-2027E	2.2%
2027E-2030E	1.9%



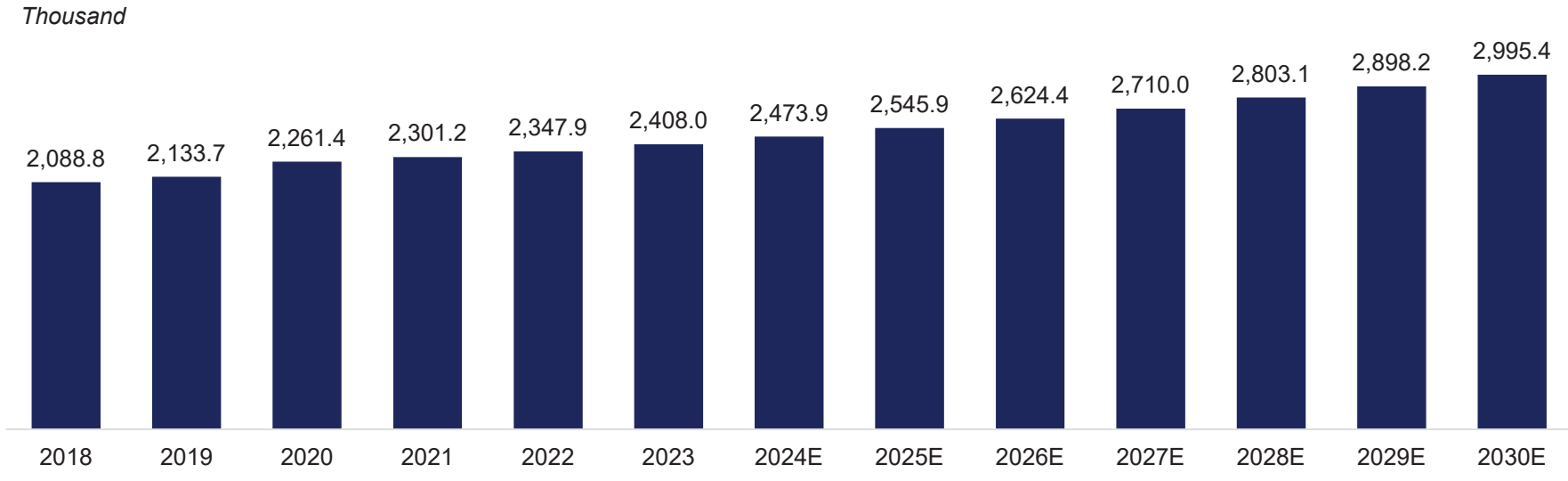
Source: NCCR, Frost & Sullivan Analysis

Global Incidence of Breast Cancer, 2018-2030E

- Incidence number of breast cancer around the world increased from 2,088.8 thousand to 2,408.0 thousand in 2018 and 2023. The number is expected to grow to 2,624.4 thousand in 2026 at a CAGR of 2.9% from 2023 to 2026. The number is expected to grow to 2,995.4 thousand in 2030, at a CAGR of 3.4%.

Global Incidence of Breast Cancer, 2018-2030E

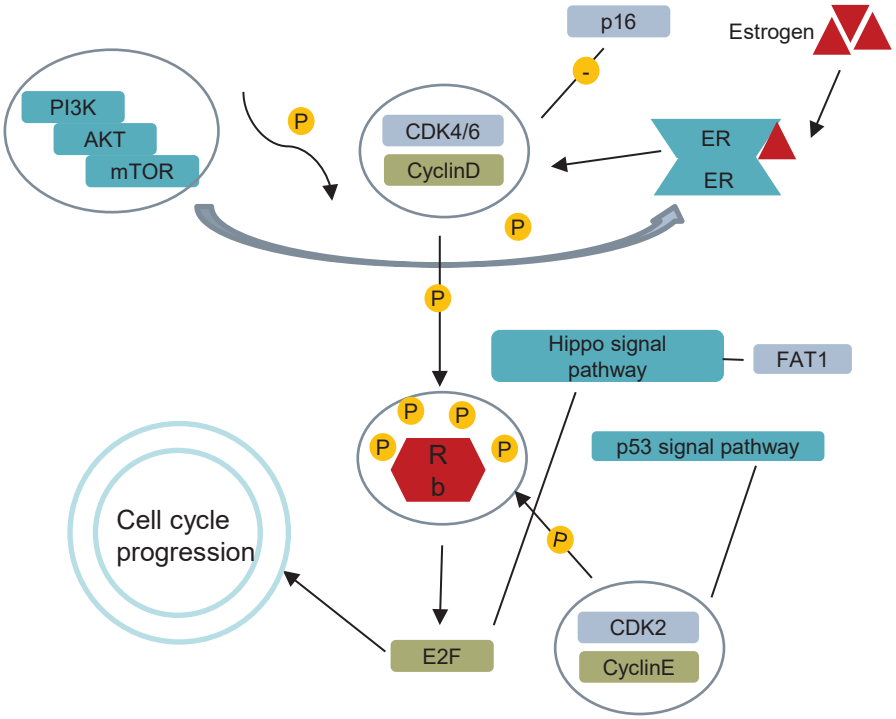
Period	CAGR
2018-2023	2.9%
2023-2026E	2.9%
2026E-2030E	3.4%



Source: IARC, Frost & Sullivan Analysis

Overview of CDK4/6 Inhibitors and CDK4/6 Inhibitor Resistance

- CDK4/6 stands for cyclin-dependent kinase 4/6. CDK4/6 inhibitors are able to inhibit the proliferation of tumor cells by blocking the cell division cycle. CDK4/6 inhibitors have been shown to have good efficacy in treating HR+, HER2- breast cancer. Currently, their combination with endocrine therapy has become the first-line therapy.



How Do inhibitors Work

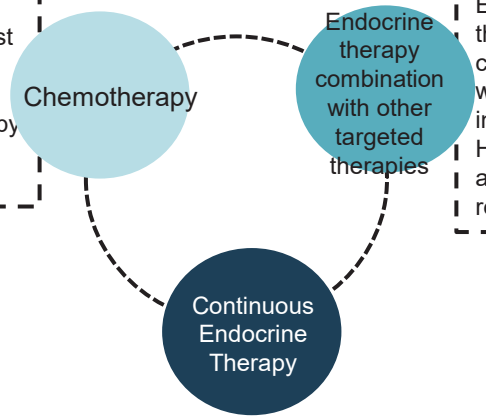
Restore normal cell cycle	Trigger immune response	Change tumor microenvironment

Drug Resistance Mechanism

- The loss of retinoblastoma protein
- Over-expression of CyclinD and dysfunction of p16
- PIK3CA mutation
- The loss of FAT1 modulates up the expression of CDK6 via hippo signal pathway, leading to CDK4/6 inhibitor resistance

Treatment Strategy after CDK4/6 Resistance

Some of recurrent and metastatic breast cancer who have received CDK4/6, choose chemotherapy as the second-line treatment option.



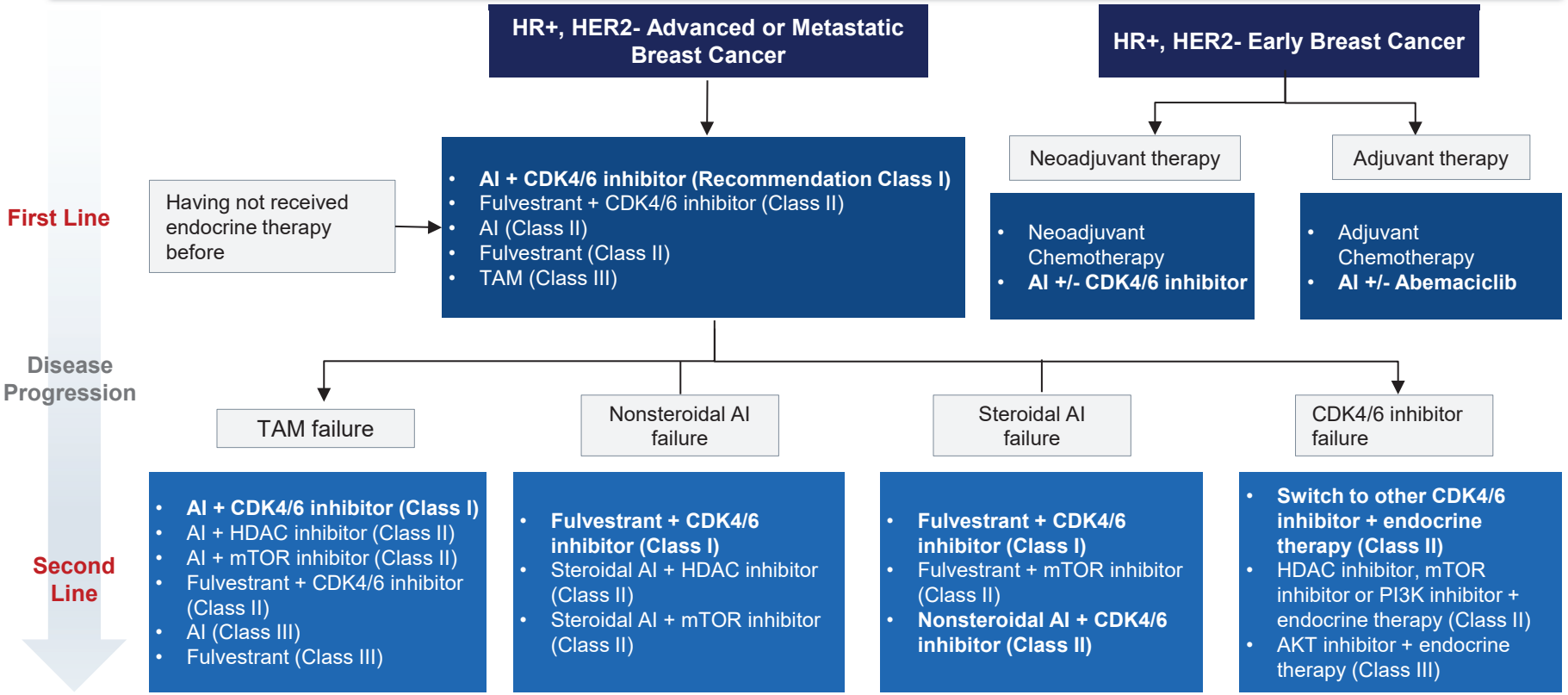
Endocrine therapy combination with mTOR inhibitors or with HDAC inhibitors are recommended.

Endocrine therapy is a commonly used treatment strategy after resistance to CDK4/6 inhibitors. Although preclinical studies have shown that resistance to CDK4/6 inhibitors may alter ER biology and induce a decrease in ER protein expression or mRNA levels in ER+ BC cell lines, thereby leading to endocrine drug resistance. However, identifying patients with residual endocrine sensitivity can help to better treat the disease after progression.

Source: Literature review, Frost & Sullivan analysis

Treatment Paradigm of HR+, HER2- Breast Cancer in China

- CDK4/6 inhibitors combination with aromatase inhibitors is currently the preferred first-line treatment of HR+, HER2- advanced or metastatic breast cancer. Around 65% of HR+, HER2- breast cancer patients received the second-line treatment. In the second-line treatment, fulvestrant plus CDK4/6 inhibitors is preferred. Besides, other small molecular targeted therapy, such as HDAC inhibitors, mTOR inhibitors and PI3K inhibitors, combination with endocrine therapy are also recommended in the second treatment.
- Abemaciclib, one CDK4/6 inhibitor, has been approved in combination with endocrine therapy for the adjuvant treatment of adult patients with HR-positive, HER2-negative early breast cancer at high risk of recurrence.



Source: CSCO2024, Frost & Sullivan Analysis

CDK4/6 Inhibitors on HR+, HER2- Breast Cancer Approved by NMPA (First-line advanced or metastatic breast cancer)

Drug Name	Brand Name	Target	Company	Indications	Approval Date
Dalpiciclib	艾瑞康®	CDK4/6	Hengrui Medicine Co.,Ltd.	In combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer (First line)	2023/06
Ribociclib	Kisqali®	CDK4/6	Novartis	In combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer (First line)	2023/05
Abemaciclib	Verzenios®	CDK4/6	Eli Lilly	In combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer (First line)	2020/12
Palbociclib	Ibrance®	CDK4/6	Pfizer	In combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer (First line)	2018/07

Note: Generics are not included.
As of April 7th, 2025

Source: NMPA, Frost & Sullivan Analysis

CDK4/6 Inhibitors on HR+, HER2- Breast Cancer Approved by NMPA (Second-line advanced or metastatic breast cancer)

Drug Name	Brand Name	Target	Company	Indications	Approval Date
Dalpiciclib	艾瑞康®	CDK4/6	Hengrui Medicine Co.,Ltd.	In combination with fulvestrant for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer (Second line)	2022/01
Abemaciclib	Verzenios®	CDK4/6	Eli Lilly	In combination with fulvestrant for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer (Second line)	2020/12

Note: Generics are not included.
As of April 7th, 2025

Source: NMPA, Frost & Sullivan Analysis

CDK4/6 Inhibitors on HR+, HER2- Breast Cancer Approved by NMPA (HR-positive, HER2-negative Early Breast Cancer)

Drug Name	Brand Name	Target	Company	Indications	Approval Date
Abemaciclib	Verzenios®	CDK4/6	Eli Lilly	In combination with endocrine therapy (tamoxifen or an aromatase inhibitor) for the adjuvant treatment of adult patients with HR-positive, HER2-negative early breast cancer at high risk of recurrence (Early Adjuvant treatment)	2021/12

Note: Generics are not included.
As of April 7th, 2025

Source: NMPA, Frost & Sullivan Analysis

CDK4/6 Inhibitors on HR+, HER2- Breast Cancer Approved by NMPA

Drug Name	Brand Name	Target	Company	Indications	Treatment Line	Approval Date
Dalpiciclib	艾瑞康®	CDK4/6	Hengrui Medicine Co.,Ltd.	In combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer	First line	2023/06
				In combination with fulvestrant for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer	Second line	2022/01
Ribociclib	Kisqali®	CDK4/6	Novartis	In combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer	First line	2023/05
Abemaciclib	Verzenios®	CDK4/6	Eli Lilly	In combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer	First line	2020/12
				In combination with fulvestrant for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer	Second line	2020/12
				In combination with endocrine therapy (tamoxifen or an aromatase inhibitor) for the adjuvant treatment of adult patients with HR-positive, HER2-negative early breast cancer at high risk of recurrence	Early adjuvant therapy	2021/12
Palbociclib	Ibrance®	CDK4/6	Pfizer	In combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer	First line	2018/07

Note: Generics are not included.
As of April 7th, 2025

Source: NMPA, Frost & Sullivan Analysis

Competitive Landscape of China CDK4/6 Inhibitors on HR+, HER2- Breast Cancer in Pipeline (First-line advanced or metastatic breast cancer)

Drug Name	Target	Company	Clinical Stage	Indications	NDA Acceptance date
GB491	CDK4/6	G1 Therapeutics / Genor Biopharma Co.,Ltd.	NDA	In combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer (First line)	2024-03-13

As of April 7th, 2025

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of China CDK4/6 Inhibitors on HR+, HER2- Breast Cancer in Pipeline (Second-line advanced or metastatic breast cancer)

Drug Name	Target	Company	Clinical Stage	Indications	NDA Acceptance date
GB491	CDK4/6	G1 Therapeutics / Genor Biopharma Co.,Ltd.	NDA	In combination with fulvestrant for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer (Second line)	2023-03-28
Birociclib	CDK4/6	Xuanzhu Biopharmaceutical Co., Ltd.	NDA	In combination with fulvestrant for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer (Second line)	2023-08-30
FCN-437c	CDK4/6	Fosun Pharma	NDA	In combination with fulvestrant for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer (Second line)	2023-11-21
BPI-16350	CDK4/6	Betta Pharmaceuticals Co.Ltd	NDA	In combination with fulvestrant for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer (Second line)	2024-05-01

As of April 7th, 2025

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of China CDK4/6 Inhibitors on HR+, HER2- Breast Cancer in Pipeline (HR-positive, HER2-negative Early Breast Cancer)

Drug Name	Target	Company	Clinical Stage	Indications	NDA Acceptance date
Ribociclib	CDK4/6	Novartis	NDA	In combination with endocrine therapy (tamoxifen or an aromatase inhibitor) for the adjuvant treatment of adult patients with HR-positive, HER2-negative early breast cancer at high risk of recurrence (early adjuvant treatment)	2023-12-19

As of April 7th, 2025

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of China CDK4/6 Inhibitors on HR+, HER2- Breast Cancer in Pipeline (Third- or later-line advanced or metastatic breast cancer)

Drug Name	Target	Company	Clinical Stage	Indications	NDA Acceptance date
Birociclib	CDK4/6	Xuanzhu Biopharmaceutical Co., Ltd.	NDA	Monotherapy for HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression after two or more endocrine therapies and one or more chemotherapy (Third- or later-line)	2023-10-11

As of April 7th, 2025

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of China CDK4/6 Inhibitors on HR+, HER2- Breast Cancer in Pipeline

Drug Name	Target	Company	Clinical Stage	Indications	Treatment Line	NDA Acceptance Date
GB491	CDK4/6	G1 Therapeutics / Genor Biopharma Co.,Ltd.	NDA	In combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer	First line	2024-03-13
				In combination with fulvestrant for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer	Second line	2023-03-28
Birociclib	CDK4/6	Xuanzhu Biopharmaceutical Co., Ltd.	NDA	In combination with fulvestrant for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer	Second line	2023-08-30
				Monotherapy for HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression after two or more endocrine therapies and one or more chemotherapy	Third- or later-line	2023-10-11
FCN-437c	CDK4/6	Fosun Pharma	NDA	In combination with fulvestrant for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer	Second line	2023-11-21
Ribociclib	CDK4/6	Novartis	NDA	In combination with endocrine therapy (tamoxifen or an aromatase inhibitor) for the adjuvant treatment of adult patients with HR-positive, HER2-negative early breast cancer at high risk of recurrence	Early adjuvant therapy	2023-12-19
BPI-16350	CDK4/6	Betta Pharmaceuticals Co.Ltd	NDA	In combination with fulvestrant for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer	Second line	2024-05-01

As of April 2nd, 2025

Source: CDE, Frost & Sullivan Analysis

Core Strengths of GB491

Better safety, better tolerance to patients, higher patient compliance	• Hematologic toxicity: The incidence of grade 3/4 neutrophil count reduction in GB491 was 48.9%, significantly lower than Dalpiciclib (85.8%), and also lower than Palbociclib (66.0%) and Ribociclib (62%); the incidence of grade 4 neutrophil count reduction in GB491 was only 4.9%, significantly lower than Dalpiciclib (22.1%), and also lower than Palbociclib (10%) and Ribociclib (6.8%). The overall incidence of anemia and thrombocytopenia was 34.3% and 19.7%, respectively, which was significantly lower than that of Abemaciclib (anemia 70.2%, thrombocytopenia 41.3%). **GB491 allows continuous medication without treatment holidays.** • Gastrointestinal reactions: The overall incidence of diarrhea with GB491 was much lower than that with Abemaciclib, and there was no grade ≥ 3 diarrhea with GB491. GB491 is able to **improve patient compliance** compared with its competitors. • Hepatotoxicity: GB491 presents a low incidence of adverse reactions on liver and does not increase the risk of additional hepatotoxicity. • Other adverse effects: GB491 has no VTE events, no risk of QT prolongation and only rare incidence of skin rash.
Significantly improved clinical benefits for patients with poor prognosis	• For patients with liver metastasis, primary drug resistance, metastatic organ number ≥ 4, and those who have received prior chemotherapy, the PFS was greatly improved and the risk of disease progression and death was significantly reduced compared with placebo group. The clinical benefits of GB491 are significantly improved for patients with poor prognosis. Due to the great safety profile of GB491, GB491 presents distinguish advantages on patients with poor prognosis.
Able to improve the quality of life	• The average age of breast cancer onset in China is 45 to 49 years old currently, and patients usually have high requirements for quality of life. Better safety and tolerability is able to improve the quality of life.
Excellent efficacy profile	• mPFS, the primary study endpoint and ORR and CBR, the secondary endpoints have been reached, showing excellent efficacy profile.
Development and commercialization right	• Genor was granted an exclusive license agreement for the development and commercialization of GB491 in the Asia-Pacific region (excluding Japan).

Source: Frost & Sullivan Analysis

Efficacy Profile of GB491 Compared with Its Launched Competitor Products on the first-line treatment of HR-positive, HER2-negative advanced or metastatic breast cancer

- Lerociclib demonstrated an excellent safety and tolerability profile; and compared favorably with other CDK4/6 inhibitors although cross-trial comparisons may cause bias.

Drug name	mPFS, Study group VS Ccontrol group (month)	ORR (%)	mOS (month)
GB491/Lerociclib	Not reached vs 16.56 HR 0.464 (0.293, 0.733) P=0.0004	59.1% vs 45.8%	Not reached
Dalpiciclib	30.6 vs 18.2 HR 0.51 (0.38, 0.69) P<0.0001	57.4% (51.6%, 63.1%) vs 47.7% (39.6%, 55.9%)	Not reached
Ribociclib	25.3 vs 16.0 HR 0.568 （0.457, 0.704） P<0.000001	42.5% (37.2%, 47.8%) vs 28.7% (23.9%, 33.6%)	63.9 (52.4, 71.0) vs 51.4 (47.2, 59.7) Statistically significant difference
Abemaciclib	28.18 vs14.76 HR 0.540 (0.418, 0.698) P=0.000002	49.7% (44.3%, 55.1%) vs 37.0% (29.6%, 44.3%)	67.1 vs 54.5 No statistically significant difference
Palbociclib	27.6 vs14.5 HR 0.563 (0.461, 0.687) P<0.000001	47.5% (42.8%, 52.3%) vs 38.7% (32.3%, 45.5%)	53.9 (49.8, 60.8) vs 51.2 (43.7, 58.9) No statistically significant difference

Note: HR: hazard ratio, In cancer research, hazard ratios are often used in clinical trials to measure survival at any point in time in a group of patients who have been given a specific treatment compared to a control group given another treatment or a placebo.

Source: Frost & Sullivan Analysis, Drug labels

Efficacy Profile of GB491 Compared with Its Launched Competitor Products on the second-line treatment of HR-positive, HER2-negative advanced or metastatic breast cancer

- In cancer research, hazard ratios are often used in clinical trials to measure survival at any point in time in a group of patients who have been given a specific treatment compared to a control group given another treatment or a placebo. GB491 has a lower HR, showing its outstanding safety advantages over its competitor products, especially in patients with poor prognosis, such as liver metastasis, primary drug resistance, metastatic organ number ≥ 4, and those who have received prior chemotherapy.

Drug name	mPFS, Study group VS Ccontrol group	HR* in patients with liver metastasis (months)	HR in patients with primary drug resistance (months)	HR in patients with metastatic organ number ≥ 4 (months)	HR in patients having received prior chemotherapy (months)
GB491/Lerociclib	11.07 vs 5.49 HR 0.451 (0.311-0.656) P<0.0001	0.487 (0.297, 0.796)	0.374 (0.182, 0.769)	0.326 (0.160, 0.665)	0.286 (0.138, 0.593)
Abemaciclib	11.41 vs 5.59 HR 0.48 (0.32–0.72) P=0.002	0.513 (0.270, 0.974)	Not reported	Not included	0.348 (0.165, 0.734)
Dalpiciclib	15.7 vs 7.2 HR 0.42 (0.309, 0.581) P<0.0001	Not reported	0.57 (0.28, 1.13)	0.68 (0.42, 1.09)	Not included

Note: HR: hazard ratio, In cancer research, hazard ratios are often used in clinical trials to measure survival at any point in time in a group of patients who have been given a specific treatment compared to a control group given another treatment or a placebo.

Source: Frost & Sullivan Analysis, Drug labels

Safety Profile of GB491 Compared with Its Launched Competitor Products

- GB491 presents a lower incidence of hematologic toxicity, gastrointestinal reactions and adverse reactions on liver compared with its competitors, and it also does not increase the risk of additional hepatotoxicity. GB491 has no VTE events, no risk of QT prolongation and only rare incidence of skin rash, too. Therefore, GB491 allows continuous medication without treatment holidays and is able to improve patient compliance. Its better safety and tolerability is able to improve the quality of life.

Drug name	continuous medication without treatment holidays	Grade 3/4 Neutropenia (%)	Grade 4 Neutropenia (%)	Diarrhea	Skin rash	VTE events	QT prolongation	Hepatotoxicity
GB491/Lerociclib	Yes	48.9%	4.9%	25.4%	4.9%	Not reported	Not reported	No needed
Abemaciclib	Yes	29.8%	1.0%	81%	14%	Attention	Not reported	Liver function monitoring
Dalpiciclib	No	85.8%	22.1%	10%	24.1%	Not reported	Not reported	No needed
Palbociclib	No	66%	10%	26%	18%	Attention	Not reported	No needed
Ribociclib	No	62%	6.8%	35%	17%	Attention	Warning	Liver function monitoring

Source: Frost & Sullivan Analysis, Drug labels

Pain point analysis of Breast Cancer Treatment in China

Low diagnostic rate	• In China, the early detection rate of breast cancer is relatively low, and the proportion identified through screening is even lower, far away from western countries. Traditional breast cancer diagnosis and treatment are often integrated into general surgery, making it challenging to achieve comprehensive management for breast cancer patients, including diagnosis, full-cycle treatment, and post-treatment rehabilitation. This approach also falls short of meeting patients' needs for precise and individualized diagnosis and treatment, which is essential for improving the survival rates of breast cancer patients.
Systemic damage from chemotherapy	• Unlike targeted drugs, chemotherapy lacks high selectivity. Chemo drugs can kill rapidly dividing cells, including both cancer cells and normal cells, causing side effects such as hair loss, nail changes, mouth sores, etc., and affecting the blood-forming cells of the bone marrow, which may lead to increased chance of infections (from low white blood cell counts).
Pain and aesthetical damage from surgery	• Breast surgery still carries the risk of postoperative pain syndrome and may result in suboptimal outcomes. After breast cancer surgery, 52.6% of patients experience intercostobrachial nerve pain, 1.3% suffer from neuroma pain, and 3.2% of patients experience phantom breast pain. Additionally, other neuropathic pains in areas such as the shoulder, chest, and scapular regions are observed in 27.2% of patients. Opting for breast reconstruction, which often requires multiple surgeries to achieve desired results, can further extend the treatment period.
Local recurrence and distant metastasis	• Recurrence and metastasis are major challenges in the treatment of breast cancer. Breast cancer recurrence can be divided into two types: local recurrence and distant metastasis. Local recurrence is when cancer cells reinvade the breast lymph nodes and can usually be managed with treatment. However, distant metastasis is more serious, with cancer cells spreading through the blood to internal organs such as the liver, bones, and brain, which can have fatal consequences.

Source: Frost & Sullivan Analysis

Future Trends for Breast Cancer Treatment Market

Increasing Incidence in Breast Cancer	• The latest cancer burden data released by the International Agency for Research on Cancer shows an increase in breast cancer incidence. One of the fundamental reasons is the constant changes in breast cancer risk factors. First, delayed childbirth, decreased number of pregnancies, and shortened breastfeeding period in modern times are important triggering factors for breast cancer. Second, modern young women also have the habit of taking health supplements, many of which contain estrogen. Excessive intake can cause high estrogen levels, leading to breast hyperplasia and even breast cancer. Finally, long-term staying up late, sustained mental stress, irregular schedules, unhealthy diets, and other problems in modern life can also increase cancer incidence.
Emerging Targeted Therapy	• CDK4/6 combination with AI therapy is currently the first-line treatment of HR+, HER2- breast cancer. Additionally, PI3K-AKT-mTOR inhibitors and HDAC inhibitors are common targeted therapies in the combination with hormone therapy. When patients do not response well to one type of targeted drugs, they have alternatives. Therefore, patients will benefit more when more targets are studied to develop into drugs.
New Antibody-drug Conjugates to Possibly Change Treatment Landscape	• Novel antibody-drug conjugates may transform the treatment landscape for HER2-low expressing breast cancers. HER2-positive breast cancers, constituting about 20% of all breast cancers, are characterized by high invasiveness and poor prognosis. The advent of anti-HER2 targeted therapies, such as trastuzumab, pertuzumab, pyrotinib, and trastuzumab emtansine (T-DM1), has significantly improved the prognosis for HER2-positive breast cancer. HER2-low expressing breast cancers, which account for approximately 45%-55% of breast cancer patients, do not benefit from traditional anti-HER2 targeted treatments. Studies have shown that the novel antibody-drug conjugate Trastuzumab deruxtecan (T-DXd) can reduce the risk of disease progression or death by 50% in patients with metastatic breast cancer expressing low levels of HER2 compared to chemotherapy. In August 2022, T-DXd was approved by the FDA for the treatment of adults with unresectable or metastatic HER2-low expressing breast cancer, altering the therapeutic outlook for this subset of breast cancer.

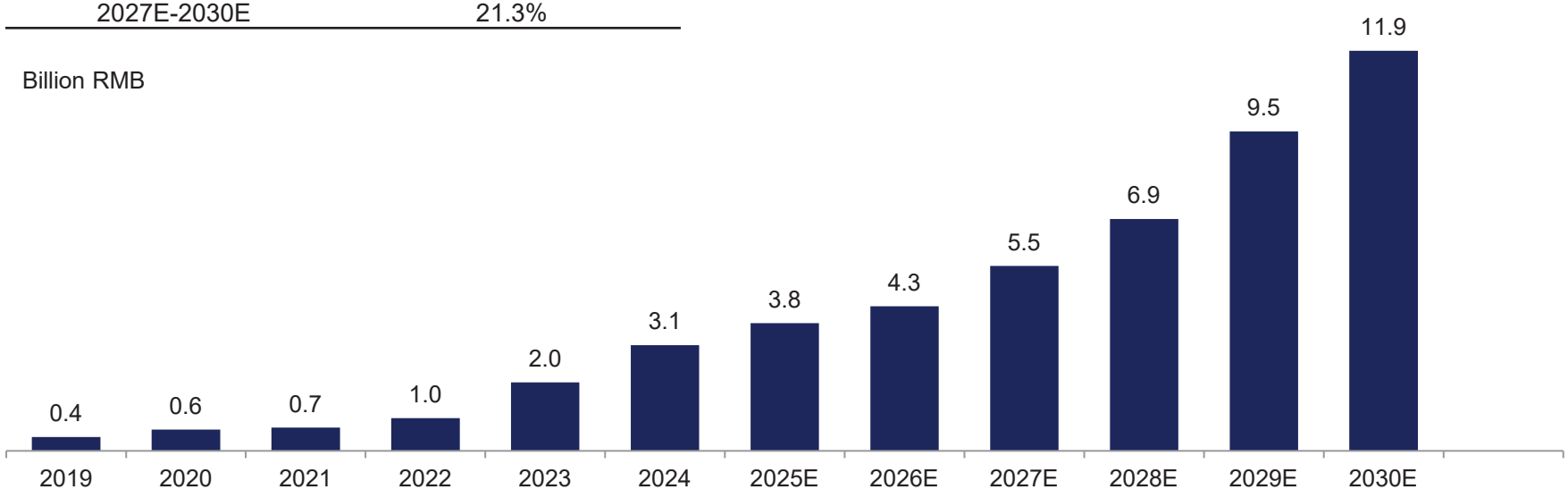
Source: Frost & Sullivan Analysis

Market Size of CDK4/6 Inhibitors in China, 2019-2030E

- In China, the CDK4/6 inhibitor market reached RMB 3.1 billion in 2024 at a CAGR of 50.3% from 2019. It is projected to further increase to RMB 5.5 billion in 2027, representing a CAGR of 20.5% from 2024. It is estimated that the number would achieve RMB 11.9 billion in 2030, representing a CAGR of 21.3% from 2027 to 2030.

Market Size of CDK4/6 Inhibitors in China, 2019-2030E

Period	CAGR
2019-2024	50.3%
2024-2027E	20.5%
2027E-2030E	21.3%



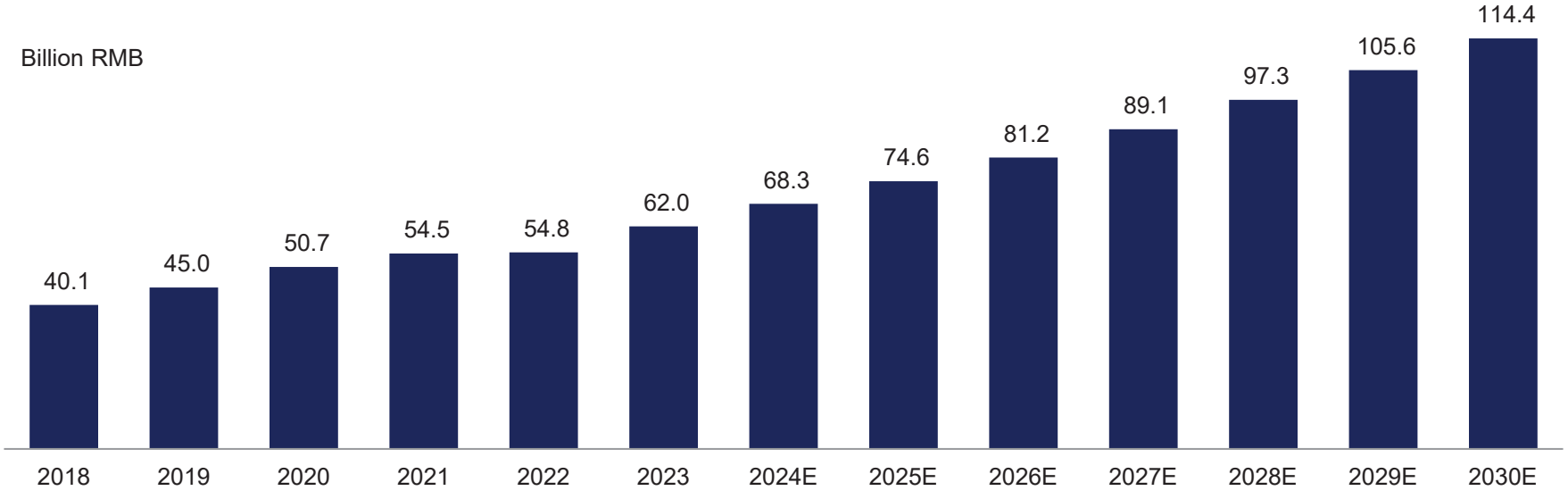
Source: National Health Commission, Frost & Sullivan Analysis

Historical and Forecasted of China Breast Cancer Drug Market Size, 2018-2030E

- China's breast cancer drug market size reached RMB62.0 billion in 2023, with a CAGR of 9.1% from 2018 to 2023. The market size will climb to RMB81.2 billion and RMB114.4 billion in 2026 and 2030 respectively.

Historical and Forecasted of China Breast Cancer Drug Market Size, 2018-2030E

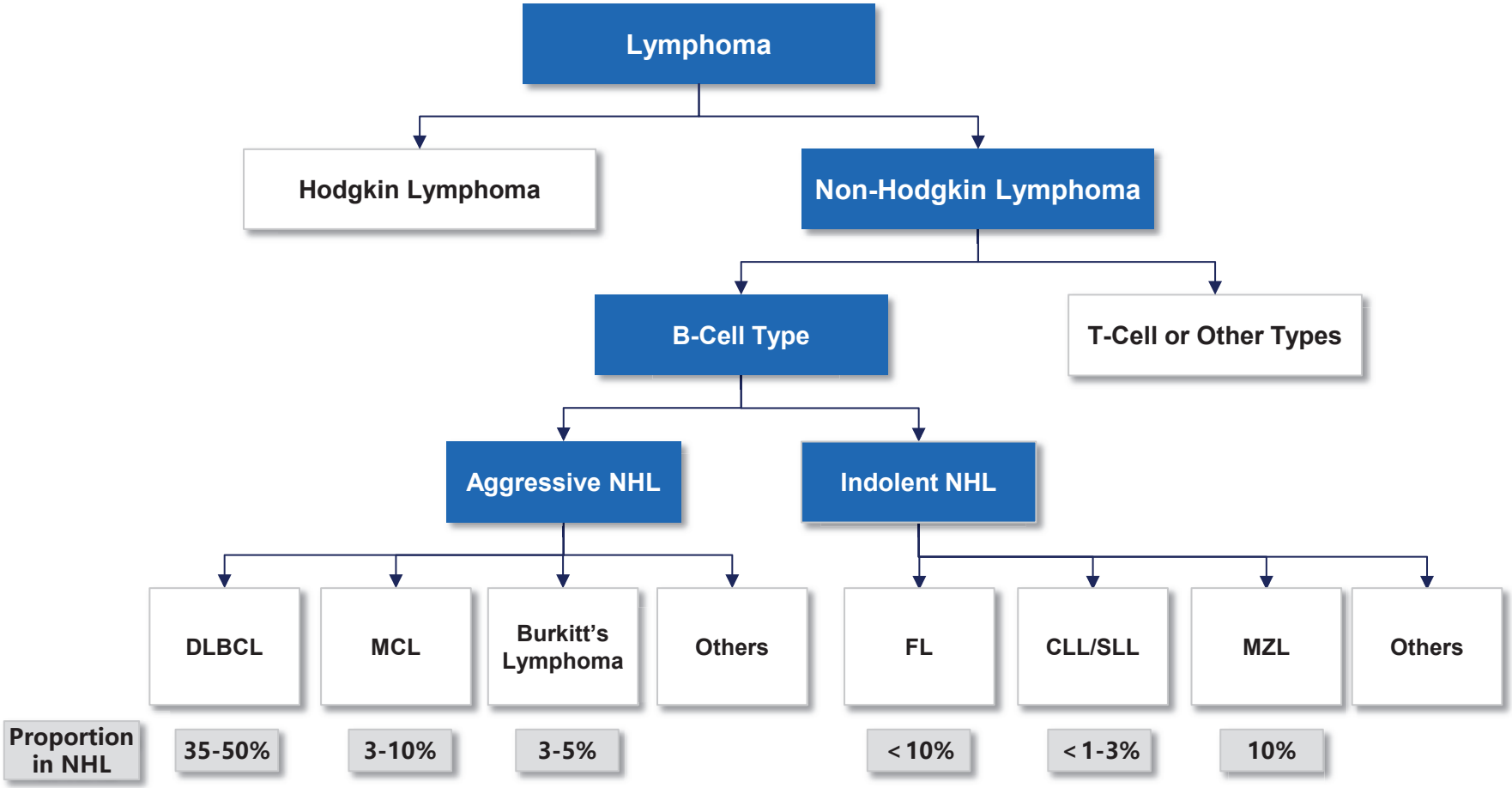
Period	CAGR
2018-2023	9.1%
2023-2026E	9.4%
2026E-2030E	8.9%



Source: Frost & Sullivan Analysis

Overview of Lymphoma

- The two main categories of Lymphoma are Hodgkin's lymphomas (HL) and the non-Hodgkin lymphomas (NHL), the latter accounts for around 90% of lymphoma with various subtypes globally.
- NHL subtypes are categorized by the characteristics of the lymphoma cells, including their appearance, the presence of proteins on the surface of the cells and their genetic features.



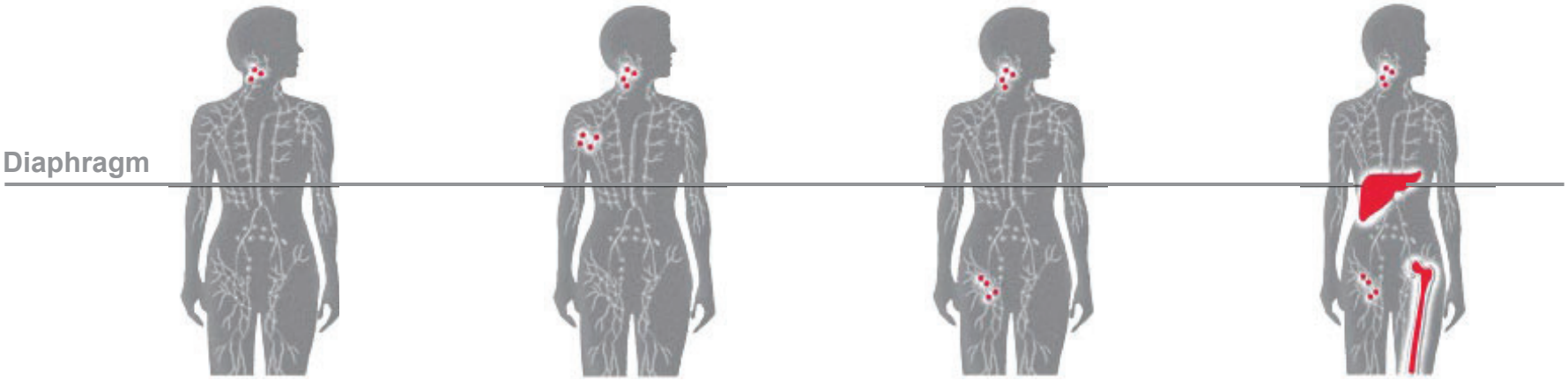
Note: DLBCL=Diffuse Large B Cell Lymphoma; MCL= Mantle Cell Lymphoma; FL=Follicular Lymphoma; CLL=Chronic Lymphocytic Leukemia; SLL=Small Lymphocytic Lymphoma; MZL=Marginal Zone Lymphoma

Source: Literature Review, Frost & Sullivan Analysis

Ann Arbor Staging Classification for Lymphoma

- Ann Arbor staging is the staging system for lymphoma, applicable for both Hodgkin's lymphoma and non-Hodgkin lymphoma. The principal stage is determined by location of the tumor:
  - Stage I indicates that the cancer is located in a single region, usually one lymph node and its surrounding area. Few or no outward symptoms perform in this stage.
  - Stage II indicates that the cancer is located in two or more regions, including an affected lymph node or lymphatic organ and a second affected area. Both affected areas are confined to the same side of the diaphragm, which means both above or below the diaphragm.
  - Stage III indicates that the cancer has spread to both sides of the diaphragm, including one organ or area near the lymph nodes or the spleen.
  - Stage IV indicates diffusion or disseminated involvement of one or multiple extra lymphatic organs, including any involvement of the liver, bone marrow, or nodular involvement of the lungs.

Ann Arbor Staging Classification for non-Hodgkin Lymphoma



Stage I
- Localized disease
- single lymph node region or single organ

Stage II
- Two or more lymph node regions on the same side of the diaphragm

Stage III
- Two or more lymph node regions above and below the diaphragm

Stage IV
- Widespread disease
- Multiple organs, with or without lymph node involvement

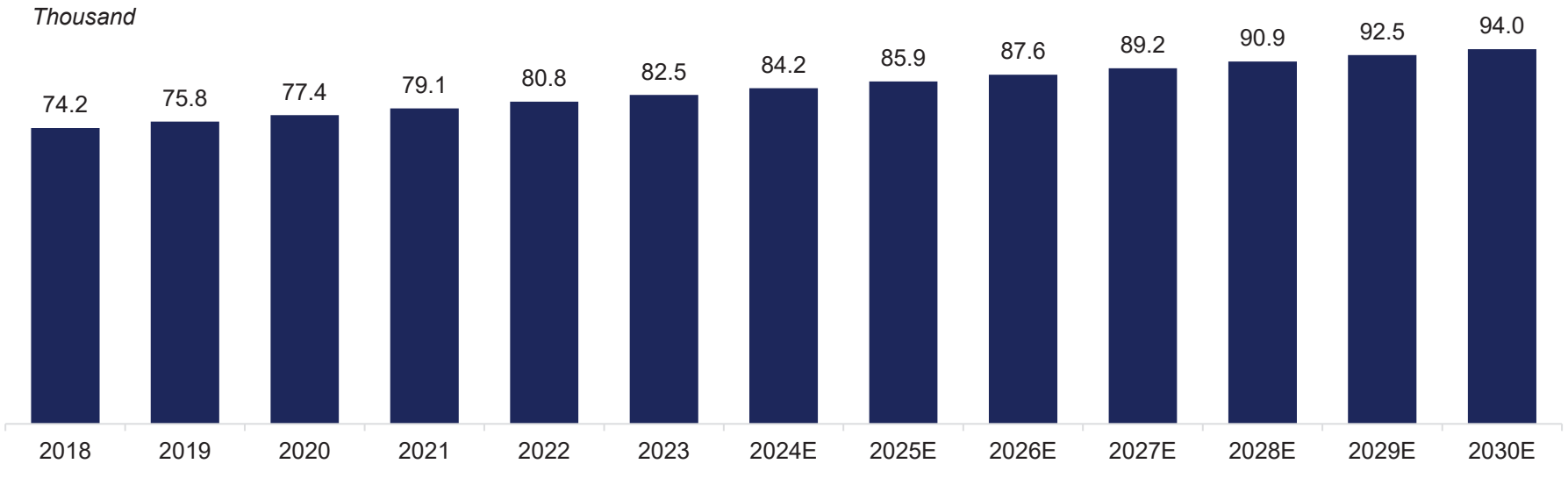
Source: Literature Review, Frost & Sullivan Analysis

Incidence of NHL in China, 2018-2030E

- Incidence number of NHL in China increased from 74.2 thousand to 82.5 thousand in 2018 and 2023. The number is expected to grow to 87.6 thousand in 2026 at a CAGR of 2.0% from 2023 to 2026. The number is expected to grow to 94.0 thousand in 2030, at a CAGR of 1.8%.

Incidence of NHL in China, 2018-2030E

Period	CAGR
2018-2023	2.1%
2023-2026E	2.0%
2026E-2030E	1.8%



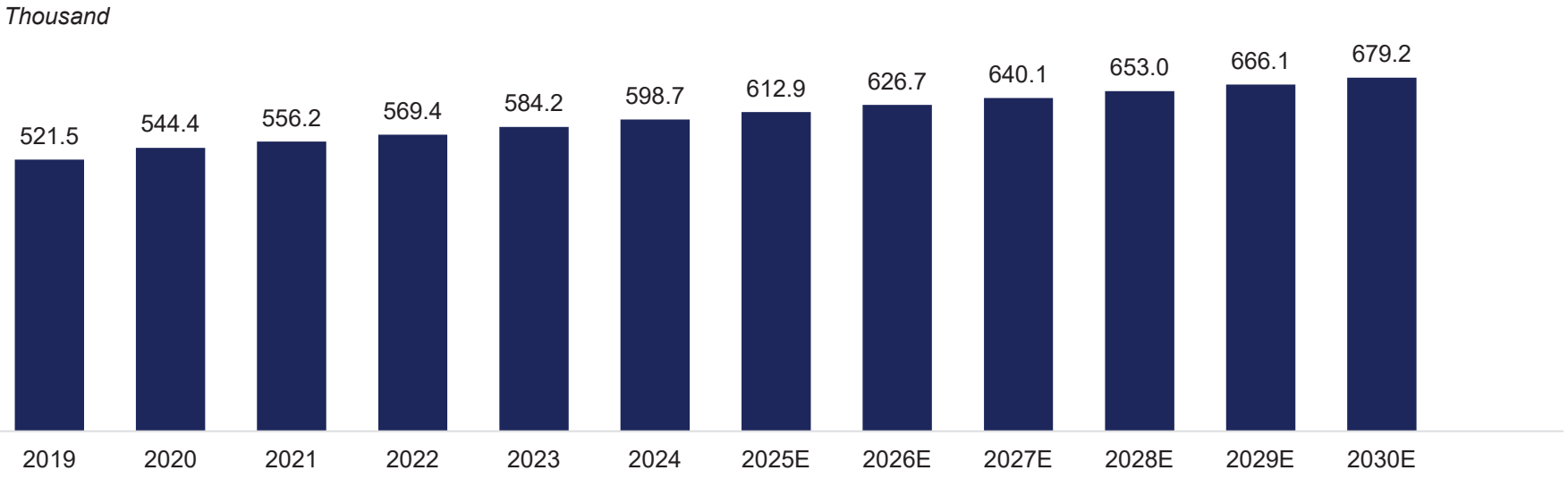
Source: NCCR, Frost & Sullivan Analysis

Global Incidence of NHL, 2018-2030E

- Incidence number of NHL around the world increased from 509.6 thousand to 584.2 thousand in 2018 and 2023. The number is expected to grow to 626.7 thousand in 2026 at a CAGR of 2.4% from 2022 to 2026. The number is expected to grow to 679.2 thousand in 2030, at a CAGR of 2.0%.

Global Incidence of NHL, 2019-2030E

Period	CAGR
2019-2024	2.8%
2024-2027E	2.3%
2027E-2030E	2.0%



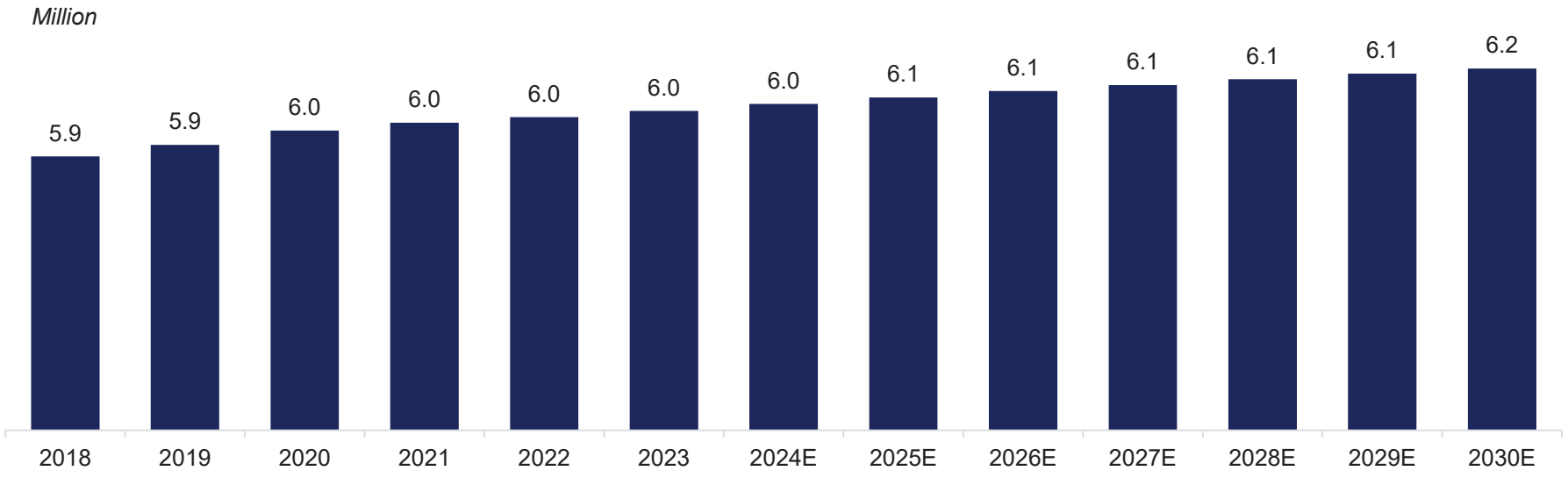
Source: IARC, Frost & Sullivan Analysis

Prevalence of RA in China, 2018-2030E

- Prevalence number of RA in China increased from 5.9 million in 2018 to 6.0 million in 2023. The number is expected to grow to 6.1 million in 2026 at a CAGR of 0.3% from 2023 to 2026. The number is expected to grow to 6.2 million in 2030, at a CAGR of 0.3%.

Prevalence of RA in China, 2018-2030E

Period	CAGR
2018-2023	0.5%
2023-2026E	0.3%
2026E-2030E	0.3%



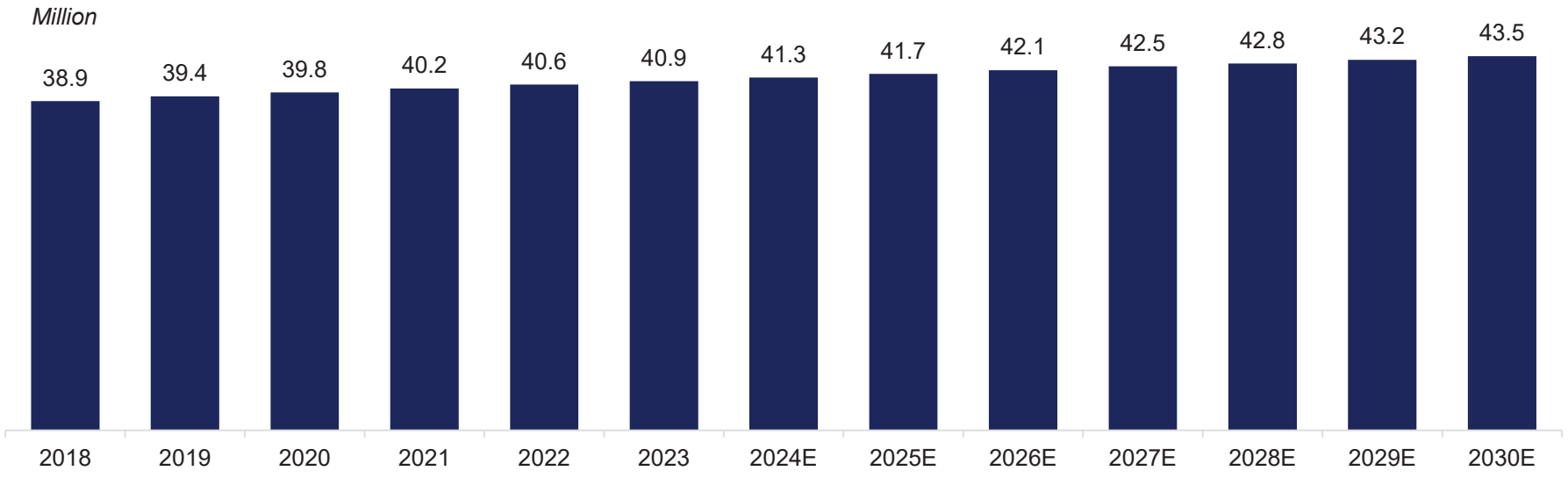
Source: NCCR, Frost & Sullivan Analysis

Global Prevalence of RA, 2018-2030E

- Global prevalence number of RA increased from 38.9 million in 2018 to 40.9 million in 2023. The number is expected to grow to 42.1 million in 2026 at a CAGR of 0.9% from 2023 to 2026. The number is expected to grow to 43.5 million in 2030, at a CAGR of 0.8%.

Global Prevalence of RA, 2018-2030E

Period	CAGR
2018-2023	1.0%
2023-2026E	0.9%
2026E-2030E	0.8%



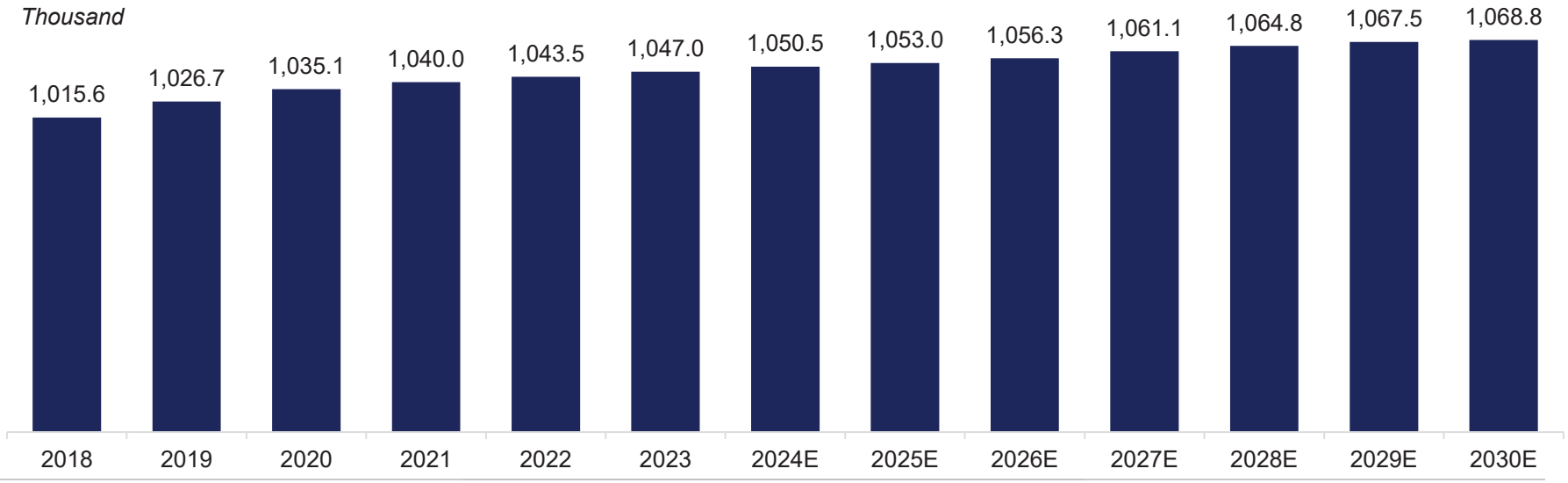
Source: NCCR, Frost & Sullivan Analysis

Prevalence of SLE in China, 2018-2030E

- Prevalence number of SLE in China increased from 1,015.6 thousand in 2018 to 1,047.0 thousand in 2023. The number is expected to grow to 1,056.3 thousand in 2026 at a CAGR of 0.3% from 2023 to 2026. The number is expected to grow to 1,068.8 thousand in 2030, at a CAGR of 0.3%.

Prevalence of SLE in China, 2018-2030E

Period	CAGR
2018-2023	0.6%
2023-2026E	0.3%
2026E-2030E	0.3%



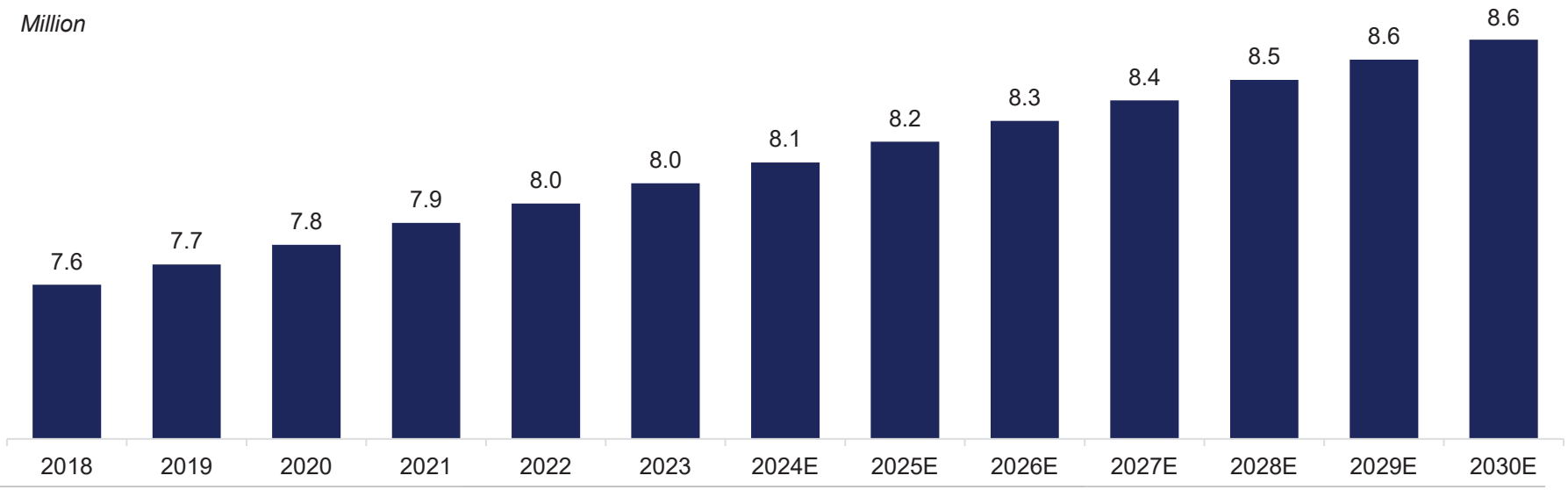
Source: NCCR, Frost & Sullivan Analysis

Global Prevalence of SLE, 2018-2030E

- Global prevalence number of SLE increased from 7.6 million in 2018 to 8.0 million in 2023. The number is expected to grow to 8.3 million in 2026 at a CAGR of 1.1% from 2023 to 2026. The number is expected to grow to 8.6 million in 2030, at a CAGR of 1.0%.

Global Prevalence of SLE, 2018-2030E

Period	CAGR
2018-2023	1.1%
2023-2026E	1.1%
2026E-2030E	1.0%



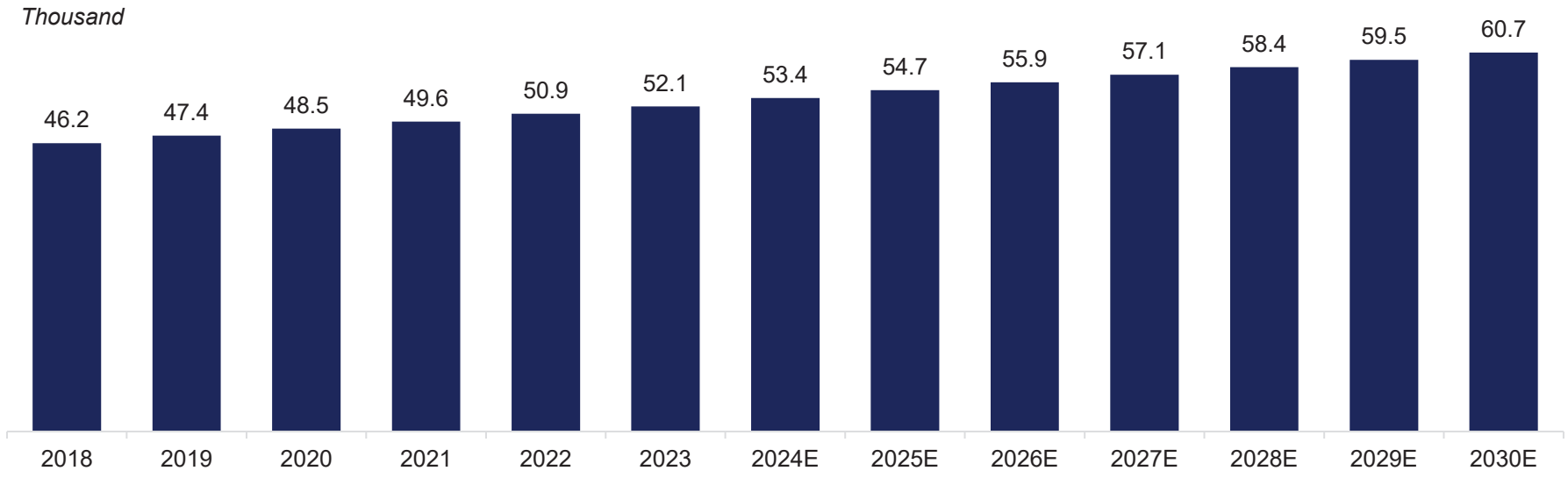
Source: NCCR, Frost & Sullivan Analysis

Prevalence of MS in China, 2018-2030E

- Prevalence number of MS in China increased from 46.2 thousand in 2018 to 52.1 thousand in 2023. The number is expected to grow to 55.9 thousand in 2026 at a CAGR of 2.4% from 2023 to 2026. The number is expected to grow to 60.7 thousand in 2030, at a CAGR of 2.1%.

Prevalence of MS in China, 2018-2030E

Period	CAGR
2018-2023	2.4%
2023-2026E	2.4%
2026E-2030E	2.1%



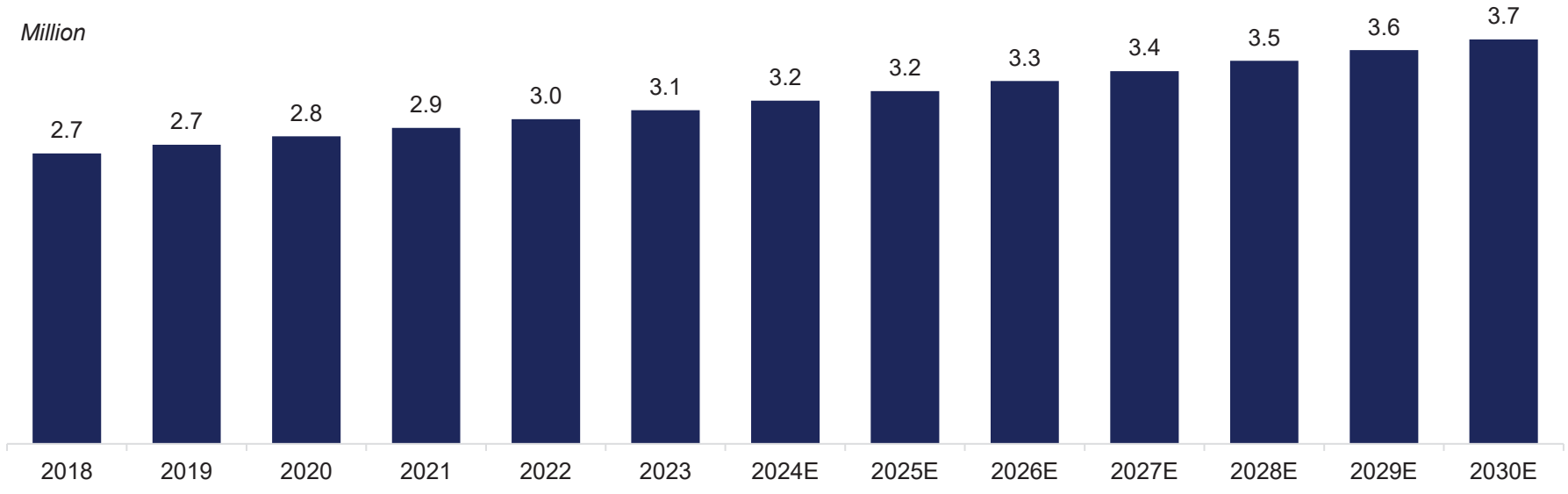
Source: NCCR, Frost & Sullivan Analysis

Global Prevalence of MS, 2018-2030E

- Global prevalence number of MS increased from 2.7 million in 2018 to 3.1 million in 2023. The number is expected to grow to 3.3 million in 2026 at a CAGR of 2.8% from 2023 to 2026. The number is expected to grow to 3.7 million in 2030, at a CAGR of 2.8%.

Global Prevalence of MS, 2018-2030E

Period	CAGR
2018-2023	2.8%
2023-2026E	2.8%
2026E-2030E	2.8%



Source: NCCR, Frost & Sullivan Analysis

CD3/CD20 Bispecific Antibodies Approved by NMPA

Drug Name	Brand Name	Target	Company	Indications	Approval Date
Mosunetuzumab	Lunsumio	CD3, CD20	Roche	Indicated for the treatment of adult patients with relapsed or refractory follicular lymphoma who have received at least two prior lines of systemic therapy.	2024/12/23
Glofitamab-gxbm	Columvi	CD3, CD20	Roche	Indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma who received two or more lines of systemic therapy	2023/11/07

As of April 7th, 2025

Source: NMPA, Frost & Sullivan Analysis

CD3/CD20 Bispecific Antibodies Approved by FDA

Drug Name	Brand Name	Target	Company	Indications	Approval Date
Glofitamab-gxbm	COLUMVI	CD3, CD20	Roche	Indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma who received two or more lines of systemic therapy	2023-06-15
Epcoritamab-bysp	EPKINLY	CD3, CD20	Genmab/Abbvie	Indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma who received two or more lines of systemic therapy	2023-05-19
Mosunetuzumab-axgb	LUNSUMIO	CD3, CD20	Roche	Indicated for the treatment of adult patients with relapsed or refractory follicular lymphoma after two or more lines of systemic therapy	2022-12-22

As of April 7th, 2025

Source: FDA, Frost & Sullivan Analysis

Competitive Landscape of China CD3/CD20 Bispecific Antibodies in Pipeline

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
Epcoritamab-bysp	CD3, CD20	Genmab/Abbvie	NDA	Diffuse Large B Cell Lymphoma	2024-11-06
			Phase 3	Follicular Lymphoma	2023-03-28
Mosunetuzumab-axgb	CD3, CD20	Roche	Phase 3	Follicular Lymphoma	2021-09-02
TQB2825	CD3, CD20	Nanjing Shunxin Pharmaceutical of Chiatai Tianqing Pharmaceutical Group	Phase 2	B-cell non-Hodgkin Lymphoma	2025-01-24
Odronextamab	CD3, CD20	Regeneron Pharmaceuticals/ ZAI Lab (Shanghai) Co.,Ltd.	Phase 2	B-cell non-Hodgkin Lymphoma	2020-10-10
CM355	CD3, CD20	Keymed Biosciences/ Innocare Pharma	Phase 1/2	B-cell non-Hodgkin Lymphoma	2021-10-27
GB261	CD3, CD20	Genor Biopharma	Phase 1/2	B-cell non-Hodgkin Lymphoma, Chronic Lymphocytic Leukemia, Small Lymphocytic Lymphoma	2022-07-22
MBS303	CD3, CD20	Mabworks Biotechnology Co.,Ltd	Phase 1/2	B-cell non-Hodgkin Lymphoma	2023-02-14
SCTB35	CD3, CD20	SinoCelltech Ltd.	Phase 1/2	Systemic Lupus Erythematosus	2024-11-07
			Phase 1	B-cell non-Hodgkin Lymphoma	2024-03-25
EX103	CD3, CD20	Excelmab	Phase 1	B-cell non-Hodgkin Lymphoma	2021-08-20
JS203	CD3, CD20	Junshi Biosciences	Phase 1	B-cell non-Hodgkin Lymphoma	2022-09-19

As of April 7th, 2025

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of Global CD3/CD20 Bispecific Antibodies in Pipeline

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
Odronextamab	CD3, CD20	Regeneron Pharmaceuticals	Phase 3	Follicular Lymphoma	2023-10-19
			Phase 3	Diffuse Large B Cell Lymphoma	2023-10-19
			Phase 3	Marginal Zone Lymphoma	2023-11-28
GB261	CD3, CD20	Genor Biopharma	Phase 1/Phase 2	B-cell non-Hodgkin Lymphoma, Chronic Lymphocytic Leukemia	2021-06-11
CM355	CD3, CD20	InnoCare Pharma	Phase 1/Phase 2	B-cell Non-Hodgkin Lymphoma	2022-01-27
MBS303	CD3, CD20	Mabworks Biotech Co., Ltd.	Phase 1/Phase 2	Non-Hodgkin Lymphoma	2023-04-10
EX103	CD3, CD20	Excelmab	Phase 1/Phase 2	Non-Hodgkin Lymphoma	2023-09-01
JNJ-87801493	CD3, CD20	Janssen	Phase 1	Non-Hodgkin Lymphoma	2023-11-18
SCTB35	CD3, CD20	Sinocelltech Ltd.	Phase 1	Non-Hodgkin Lymphoma	2024-03-19
Imvotamab	CD3, CD20	IGM Biosciences, Inc.	Phase 1	Idiopathic Inflammatory Myopathies, Inflammatory Myopathies	2024-07-29

As of April 7th, 2025

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Overview of T-cell Engagers

Mechanism of Action	• Engineered to harness the human body's immune response against cancer, T-cell engagers has represented a promising frontier in innovative cancer therapies. These specialized antibodies are designed to redirect the immune system's T cells, guiding them to recognize and eliminate cancer cells effectively. T-cell engagers achieve this by simultaneously binding to a specific antigen on the surface of a cancer cell and to a critical activation molecule on T cells, such as CD3. This dual-binding mechanism effectively brings T cells into close proximity with cancer cells, facilitating targeted cell destruction and offering a potent approach to cancer treatment.
Potential in Oncology and Autoimmune Disease	• Additionally, T-cell engagers are increasingly being explored for applications beyond oncology, including the treatment of autoimmune disorders. These molecules work by simultaneously binding to T cells and a specific antigen present on the surface of cells involved in the autoimmune response. The engagement directs the T cells to target and potentially destroy the antigen-presenting cells, which helps in modulating the immune response and reducing the autoimmune attack on the body's own tissues.
CD3 T-cell Engagers	• CD3 is an integral membrane protein within the T-cell receptor (TCR) complex, prominently expressed on the surface of T cells. This protein plays a pivotal role in the activation of both cytotoxic and helper T cells, which are essential for orchestrating targeted immune responses. As an essential component of the immune response, CD3 serves as an important target for T-cell engagers to fight cancer through linking T cells to cancer cells. One of the key mechanisms of CD3 bispecific antibodies is to redirect T cells, facilitating their infiltration into the TME. This is particularly significant in addressing the challenge of "cold tumors", which are characterized by low immunogenicity and poor response to first-generation immuno-oncology therapies. By redirecting T cells and promoting their penetration into the TME, CD3-targeted therapies can potentially transform these cold tumors into more immunologically active sites. There are three CD3 TCE being approved by FDA.
Widespread Attention in the R&D of TCE	• The research and development of T-cell engagers has received widespread attention. Recently, a number of blockbuster license deals regarding T-cell engager have been made. EpimAb Biotherapeutics and Vignette Bio announced strategic collaboration to develop EMB-06, a BCMA×CD3 bispecific antibody in Sept 2024; EpimAb will receive total upfront considerations of $60 million in cash and equity of Vignette, and will be eligible to receive up to $575 million development, regulatory and commercial milestones, plus royalties on net sales. WuXi Bio signed $1.5bn TCE antibody pact with GSK in Jan 2023; under the agreement, WuXi Biologics will receive $40 million upfront and up to $1.46 billion in milestones for the four TCE antibodies, plus royalties.

Source: Frost & Sullivan Analysis

Pain Points and Challenges of T-cell Engagers

Concern on high toxicities and on-target effects on healthy cells	• The success of Bi-TCE therapy in solid-tumor malignancies will likely rely on one of additional factors, which is mitigation of severe toxicity and on-target effects on healthy cells. Bi-TCE therapy toxicity, namely cytokine release syndrome (CRS), is highly predictable and some form of systemic inflammatory response is expected in nearly all patients. Early identification of toxicity and intervention with corticosteroids has certainly proven efficacious in preventing severe toxicity leading to end-organ dysfunction.
Identification and selection of patients	• Another key success factor of Bi-TCE therapy in solid-tumor malignancies is ideal identification and selection of patients who may benefit most from immunologic response. Ideal patient selection represents yet another challenge which may be an area of focus for future research. We now have identified a plethora of tumor-associated antigens (TAAs) that demonstrate high specificity for target antigen-expressing tumor, yet TAA as a biomarker has been insufficient in patient selection to identify exceptional responders.

Source: Frost & Sullivan Analysis

Core Strengths of GB261

Good efficacy better safety, better tolerance to patients	• GB261 is a novel differentiated CD20/CD3 bi-specific T-Cell Engager with **ultra-low affinity to bind CD3 and has Fc-enabled functions (ADCC and CDC)**. Its completed Phase Ph1/2 multi-center study of B-NHL (DLBCL and FL) in China and Australia demonstrated **promising efficacy and a favorable safety profile**. Specially, GB261 has been shown to significantly reduce **cytokine release (CRS) compared with bi-specifics in the same class**. Its outstanding safety profile allows its potential indications **beyond oncology and is possibly applicable to various autoimmune diseases** where there is a large unmet medical need in patients.
Global cooperation	• **Genor Biopharma has entered into an exclusive global licensing agreement with TRC 2004, INC. on August 5th, 2024.** Genor Biopharma has agreed, among others, to grant the licensee an exclusive worldwide license to develop, use, manufacture, commercialize and otherwise exploit GB261 excluding mainland China, Hong Kong, Macau and Taiwan. Genor Biopharma shall receive a significant equity participation in the licensee; a double digit million US dollars upfront payment; up to 443 million US dollars in milestone payments; tiered single to double digits royalty payments on net sales. **The license-out deal on GB261 demonstrates it has got international recognition.**
Incredible potential in autoimmune disease	• **CD20 monoclonal antibodies have approved and marketed for the treatment of many autoimmune diseases, such as rheumatoid arthritis (RA), multiple sclerosis (MS), granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and pemphigus vulgaris (PV), which brings imagination of CD20/CD3 bispecific in autoimmune diseases.** • **Oositive phase III results for Roche's Gazyva/Gazyvaro, a CD20 monoclonal antibody, shows superiority to standard therapy alone in people with lupus nephritis.** In the study, a higher proportion of people treated with Gazyva/Gazyvaro plus standard therapy (mycophenolate mofetil and glucocorticoids) achieved a complete renal response (CRR) at 76 weeks compared to those treated with standard therapy alone. Safety was in line with the well-characterized profile of Gazyva/Gazyvaro. No new safety signals were identified. **The success of Gazyva/Gazyvaro in lupus nephritis has brought more imagination** to **CD20/CD3 bispecific antibodies in the treatment of autoimmune disorders**.

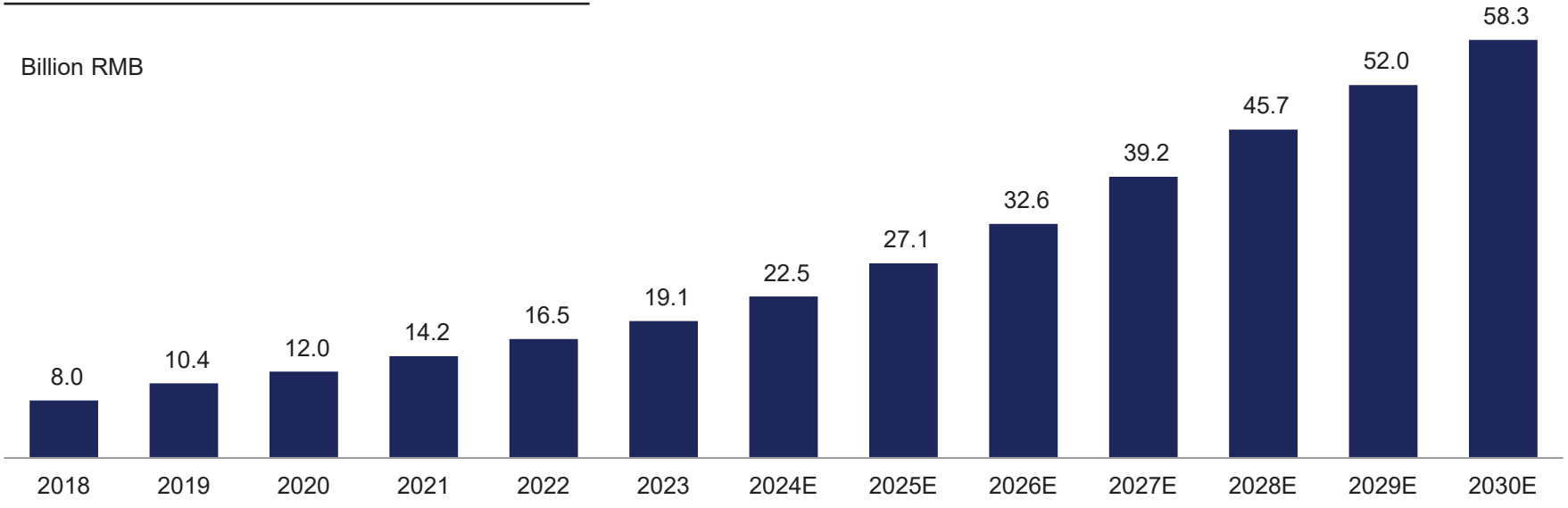
Source: Frost & Sullivan Analysis

Historical and Forecasted of China Lymphoma Drug Market Size, 2018-2030E

- China's lymphoma drug market size reached RMB19.1 billion in 2023, with a CAGR of 19.0% from 2018 to 2023. The market size will climb to RMB32.6 billion and RMB58.3 billion in 2026 and 2030 respectively.

Historical and Forecasted of China Lymphoma Drug Market Size, 2018-2030E

Period	CAGR
2018-2023	19.0%
2023-2026E	19.6%
2026E-2030E	15.6%



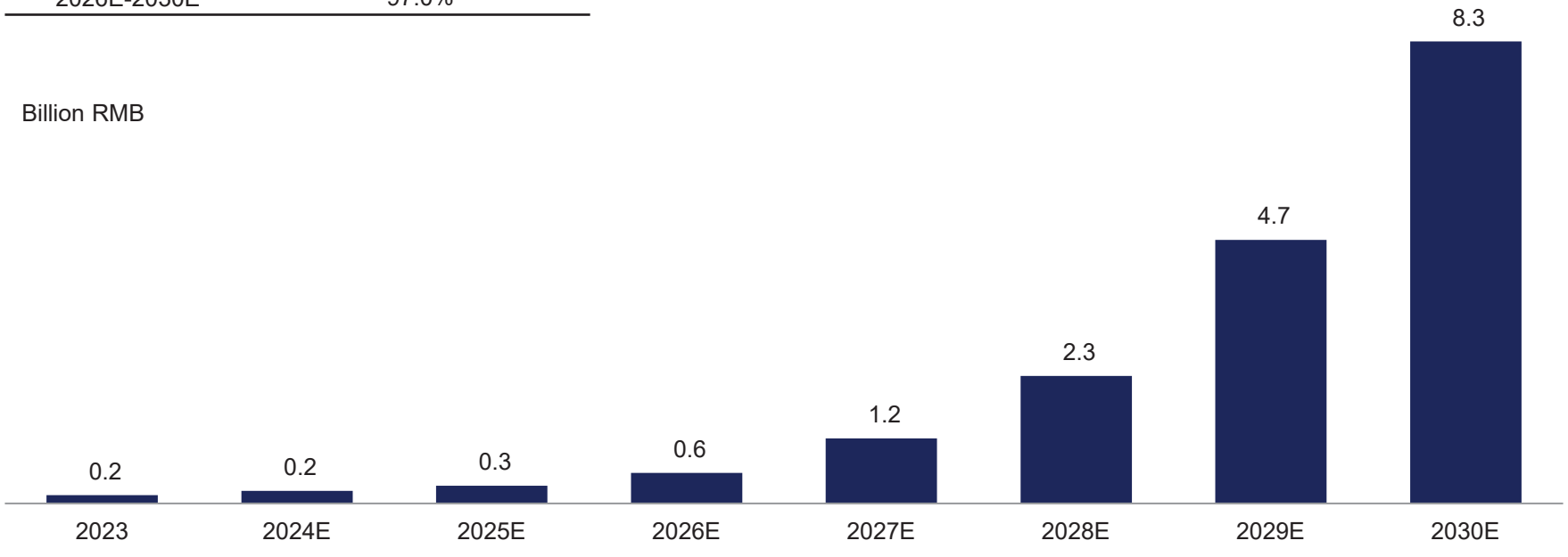
Source: Frost & Sullivan Analysis

Historical and Forecasted of China T-cell Engager Market Size, 2018-2030E

- China's T-cell engager market size reached RMB0.2 billion in 2023. The market size will climb to RMB0.6 billion and RMB8.3 billion in 2026 and 2030 respectively.

Historical and Forecasted of China T-cell Engagers Market Size, 2018-2030E

Period	CAGR
2023-2026E	54.2%
2026E-2030E	97.0%



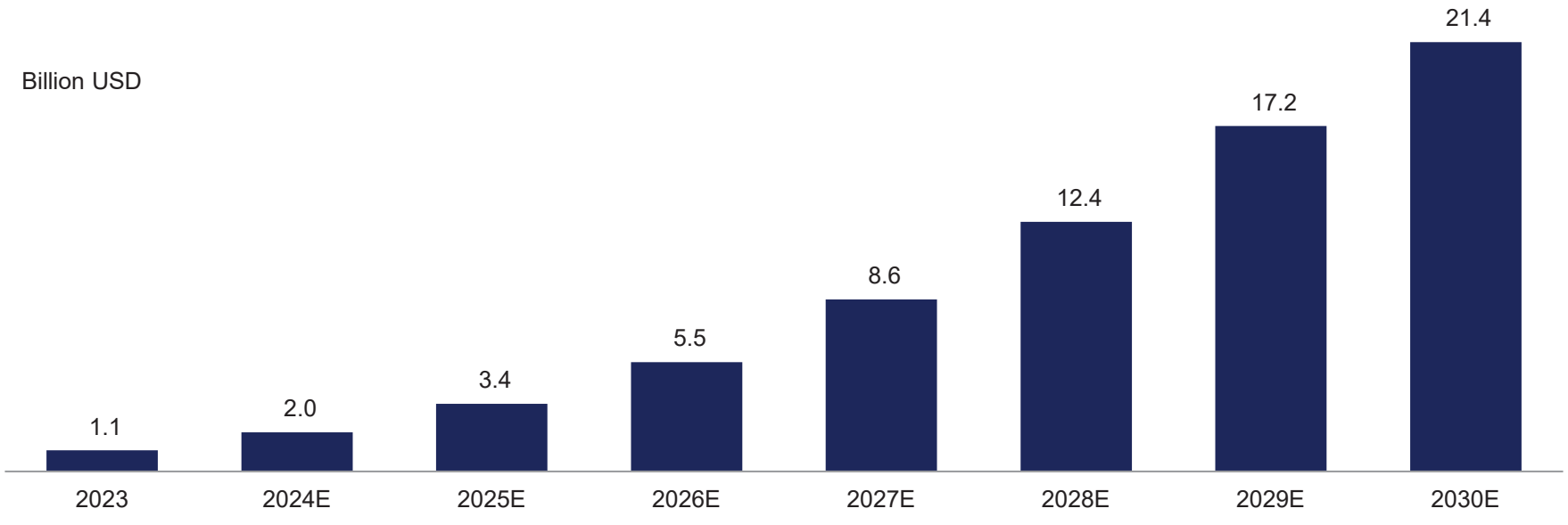
Source: Frost & Sullivan Analysis

Historical and Forecasted of Global T-cell Engager Market Size, 2018-2030E

- Global T-cell engager market size reached USD1.1 billion in 2023. The market size will climb to USD5.5 billion and USD21.4 billion in 2026 and 2030 respectively.

Historical and Forecasted of Global T-cell Engagers Market Size, 2018-2030E

Period	CAGR
2023-2026E	73.2%
2026E-2030E	40.7%



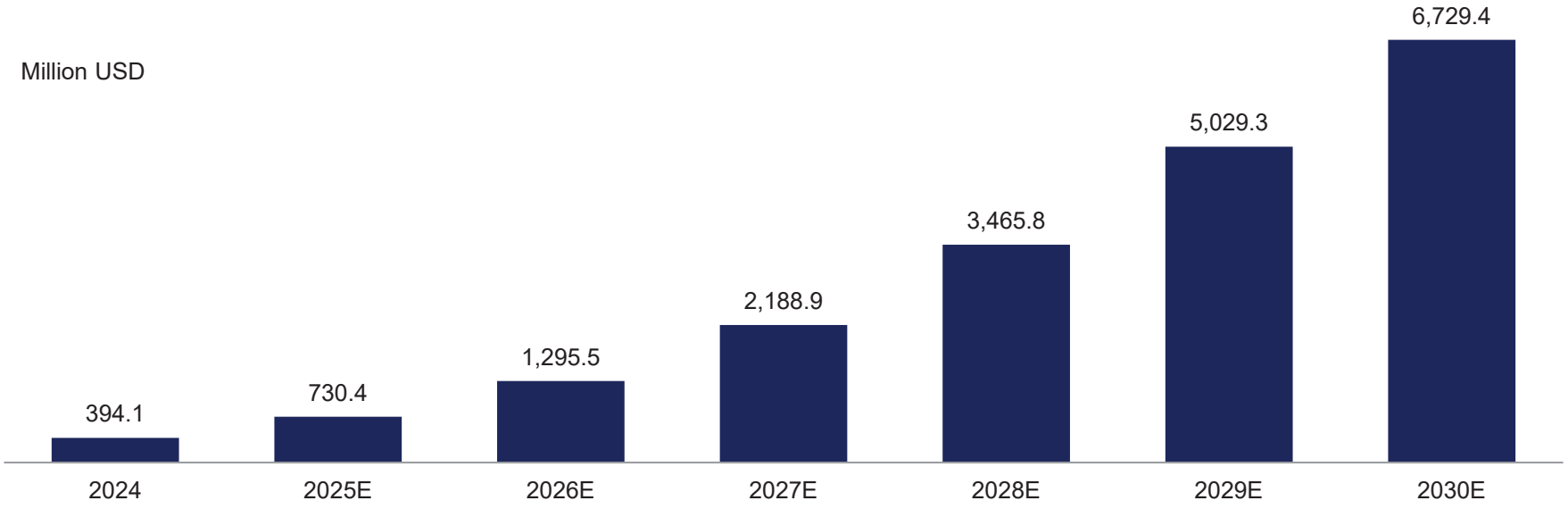
Source: Frost & Sullivan Analysis

Historical and Forecasted of Global CD20/CD3 T-cell Engager Market Size, 2024-2030E

- Global CD20/CD3 T-cell engager market size reached USD146.0 million in 2023. The market size will climb to USD1.3 billion and USD6.0 billion in 2026 and 2030 respectively.

Historical and Forecasted of Global CD20/CD3 T-cell Engagers Market Size, 2024-2030E

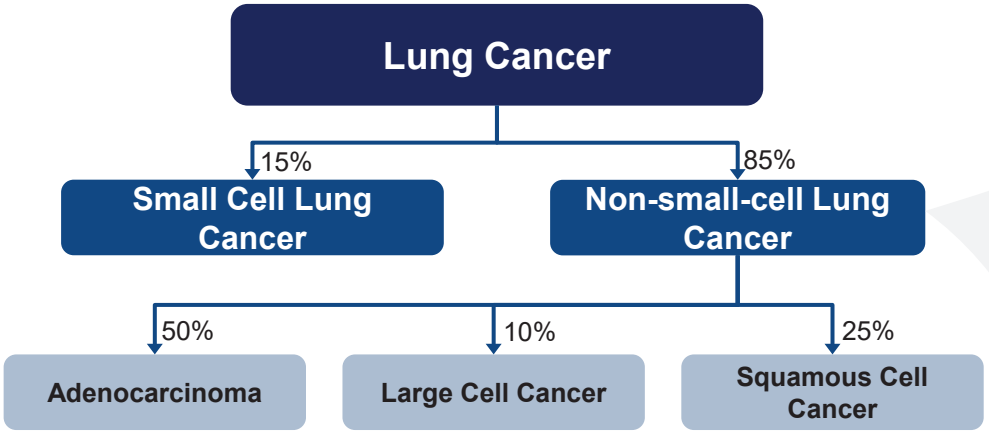
Period	CAGR
2024-2027E	77.1%
2027E-2030E	45.4%



Source: Frost & Sullivan Analysis

Overview of Non-small-cell Lung Cancer (NSCLC)

- Non-small-cell lung cancer (NSCLC) is any type of epithelial lung cancer other than small cell lung cancer (SCLC). NSCLC accounts for over 85% of LC, which is the most common cancer and the leading cause of cancer death globally. The most common types of NSCLC are squamous cell carcinoma, large cell carcinoma, and adenocarcinoma. All types can occur in unusual histologic variants and developed as mixed cell-type combinations.
- Symptoms of more advanced NSCLC cases include bone pain, headache, weakness and vomiting.



- Most common subtype.
- Adenocarcinoma is usually found in outer parts of the lung, it tends to grow slower than other types of lung cancer.

- It can appear in any part of the lung. It tends to grow and spread quickly, which can make it harder to treat.

- These cancers start in early versions of squamous cells, which are flat cells that line the inside of the airways in the lungs.

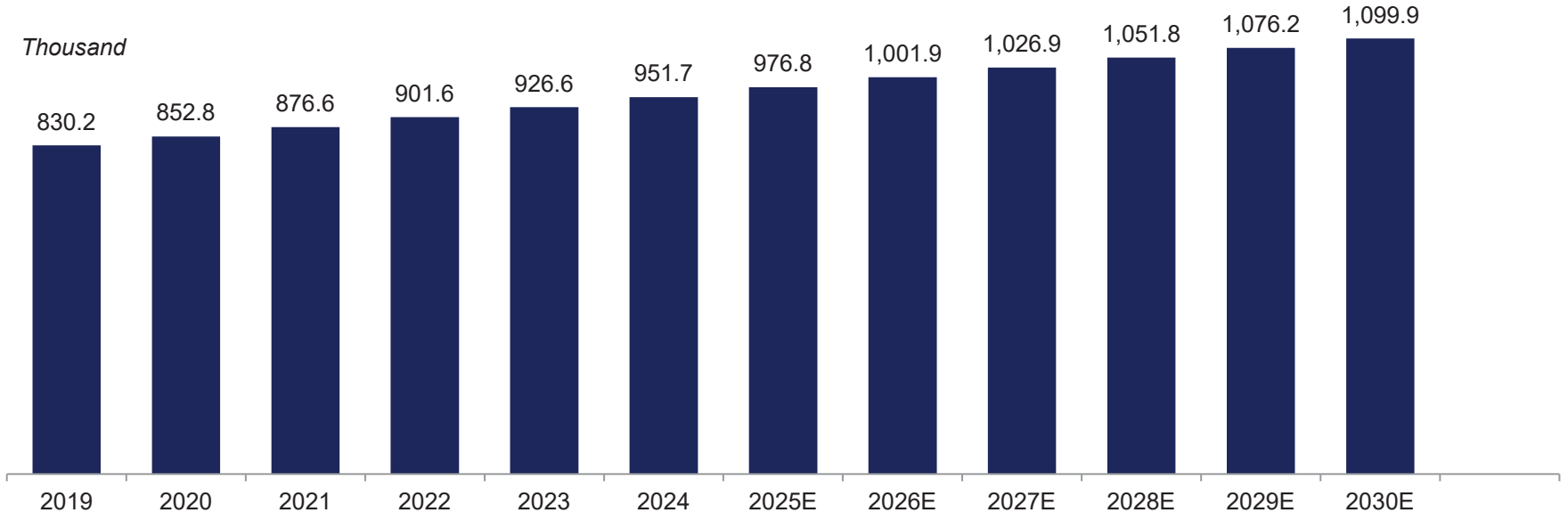
Source: Literature Review, Frost & Sullivan Analysis

Incidence of Non-Small Cell Lung Cancer in China, 2018-2030E

- In China, the number of new cases of non-small cell lung cancer rose to 926.6 thousand in 2023, with a CAGR of 2.8% from 2018. It is expected to continue increasing to 1,001.9 thousand by 2026, reflecting a CAGR of 2.6% from 2023. Projections indicate that by 2030, the incidence is anticipated to reach 1,100.0 thousand, at a CAGR of 2.4% from 2026 to 2030.

Incidence of Non-Small Cell Lung Cancer in China, 2018-2030E

Period	CAGR
2019-2023	2.8%
2024-2027E	2.6%
2027E-2030E	2.3%



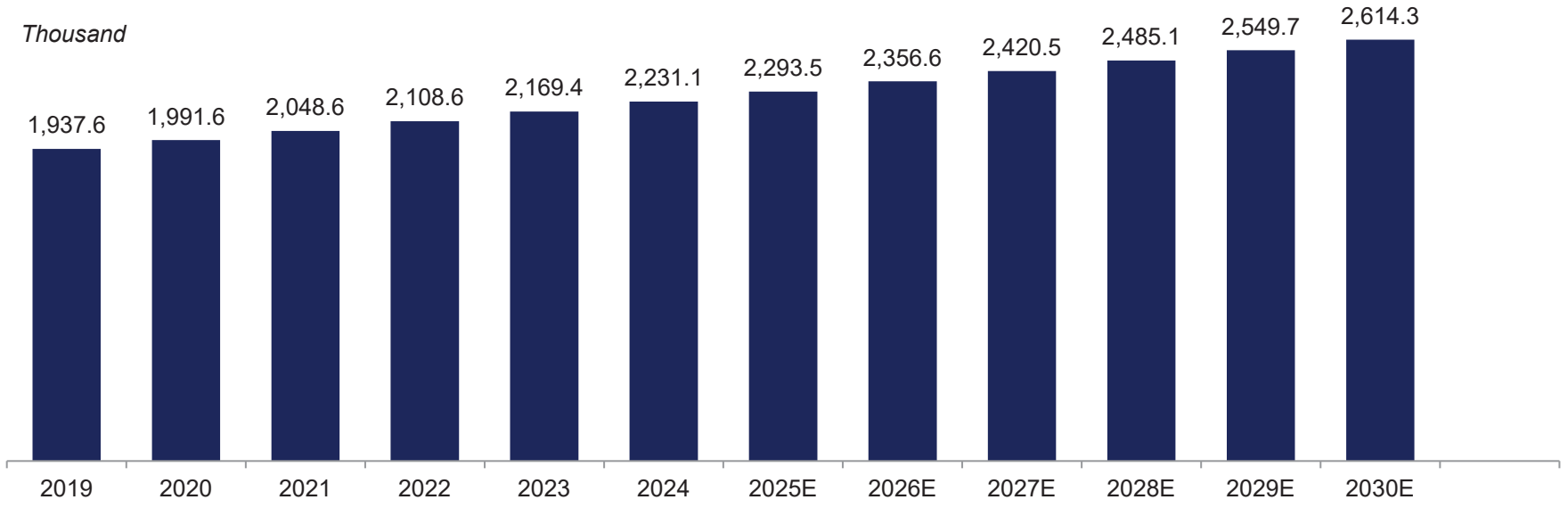
Source: NCCR, Frost & Sullivan Analysis

Global Incidence of Non-Small Cell Lung Cancer, 2018-2030E

- The worldwide number of new cases of non-small cell lung cancer rose to 2,169.4 thousand in 2023, with a CAGR of 2.8% from 2018. It is expected to continue increasing to 2,356.6 thousand by 2026, reflecting a CAGR of 2.8% from 2023. Projections indicate that by 2030, the incidence is anticipated to reach 2,614.3 thousand, at a CAGR of 2.6% from 2026 to 2030.

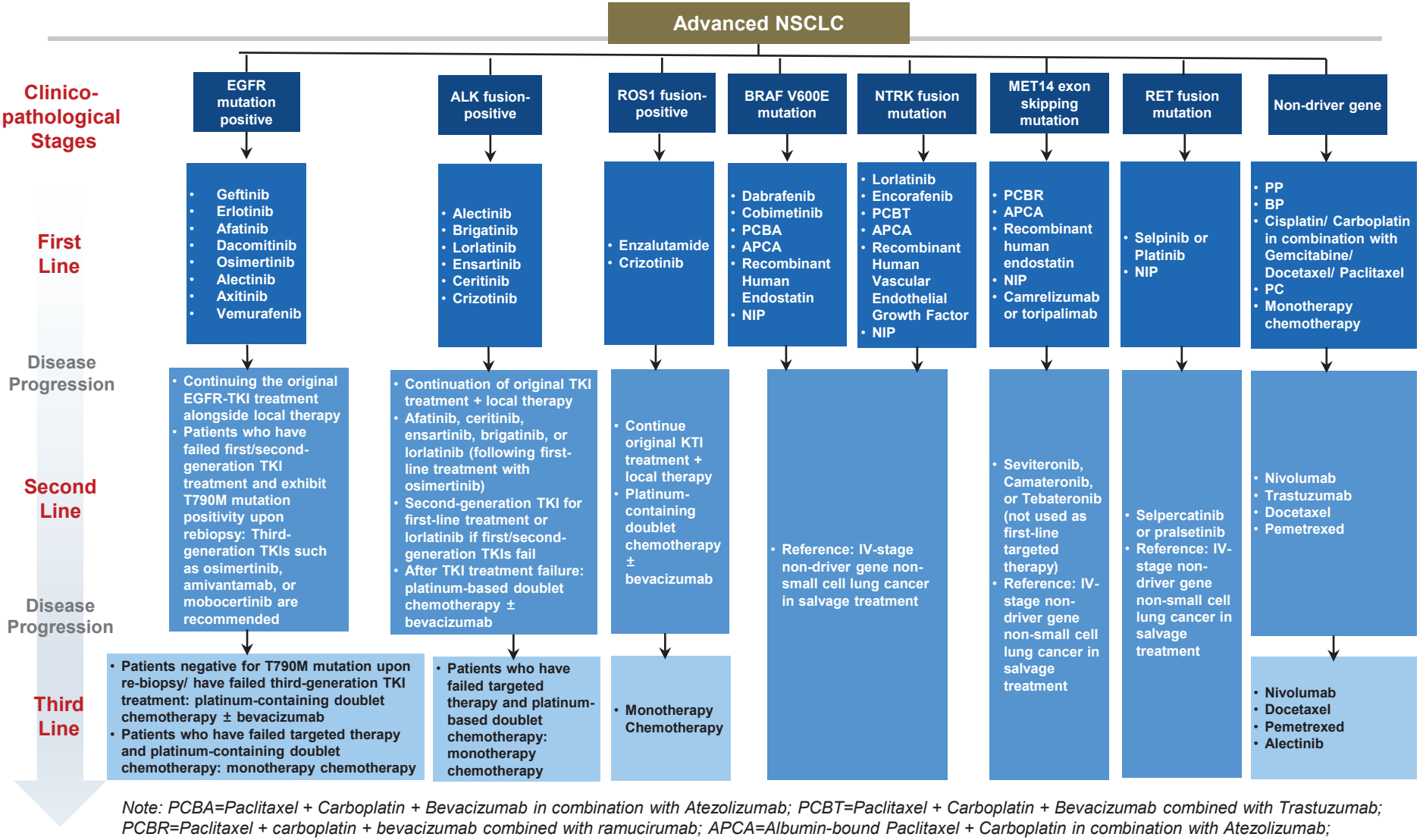
Global Incidence of Non-Small Cell Lung Cancer, 2019-2030E

Period	CAGR
2019-2024	2.9%
2024-2027E	2.8%
2027E-2030E	2.6%



Source: NCCR, Frost & Sullivan Analysis

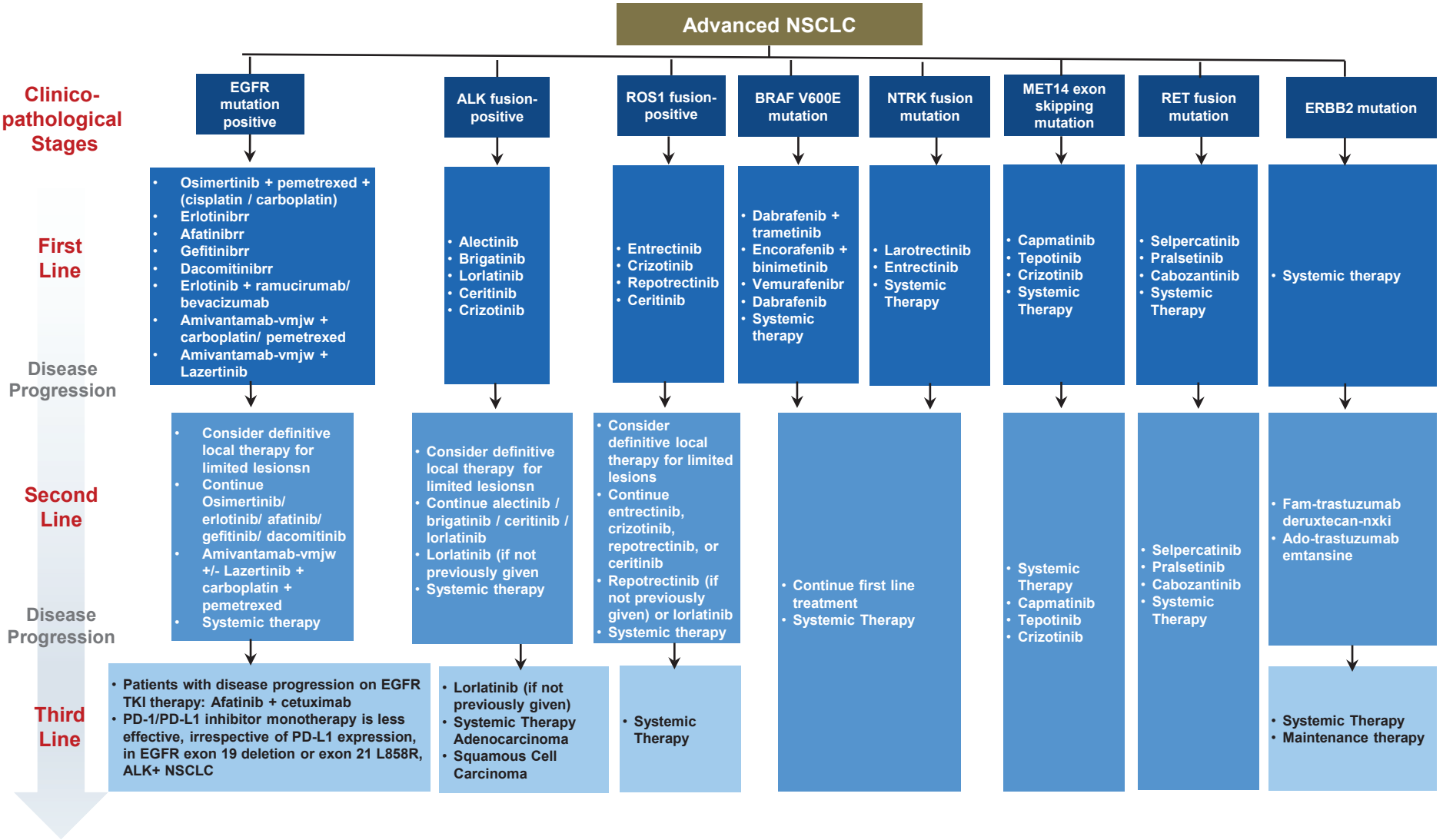
Treatment Paradigm of NSCLC in China



Note: PCBA=Paclitaxel + Carboplatin + Bevacizumab in combination with Atezolizumab; PCBT=Paclitaxel + Carboplatin + Bevacizumab combined with Trastuzumab; PCBR=Paclitaxel + carboplatin + bevacizumab combined with ramucirumab; APCA=Albumin-bound Paclitaxel + Carboplatin in combination with Atezolizumab; NIP=Nivolumab and Ipilimumab in combination with Pembrolizumab; PP=Pemetrexed in combination with platinum agents; BP=Bevacizumab in combination with platinum-based doublet chemotherapy; PC=PD-L1 inhibitors as monotherapy or in combination with chemotherapy

Source: CSCO2023, Frost & Sullivan Analysis

Treatment Paradigm of NSCLC in the US



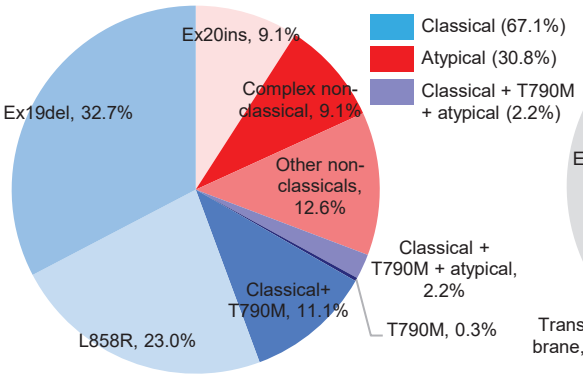
Source: NCCN2024, Frost & Sullivan Analysis

Distribution and Frequency of EGFR Mutations in NSCLC

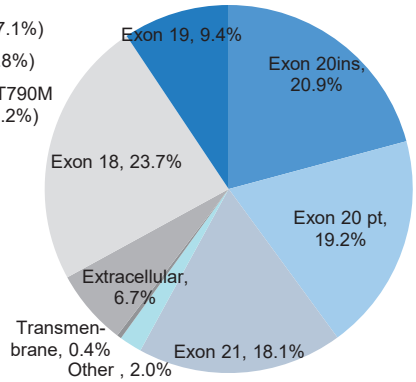
- Approximately 23.9% of patients with NSCLC in the United States and 39.8% of patients in China have EGFR mutations. These mutations enhance the kinase activity of EGFR, leading to overactivation of downstream signaling pathways involved in promoting cell survival.

Distribution and Frequency of EGFR Mutations in NSCLC

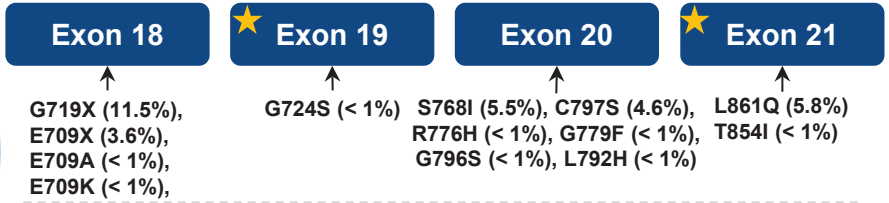
(A) EGFR-mutant NSCLC Patients



(B) Atypical EGFR Mutations



(C) Non-classic EGFR TKI Mutation sites



Note of Charts:
(A) *Percentage of patients with NSCLC containing classical and atypical EGFR mutations (n = 11,619 patients). Classical EGFR mutations are L858R, T790M and various Exl9dels (Methods)*
(B) *Percentage of atypical EGFR mutations observed in patients with NSCLC (n =7,199 mutations). Atypical EGFR mutations are defined as non-classical, non-synonymous mutations.*
(C) *Lollipop plot of atypical EGFR mutations in patients with NSCLC (n =7,199 mutations).*

- In EGFR-mutant NSCLC, 67.1% of EGFR mutations in NSCLC are exon 19 deletion and exon 21 (L858R) replacement, often referred to as EGFR common mutations or classic mutations, and other EGFR mutations are called uncommon mutations or non-classic mutations because of the low mutation rate, such as G719X, L861Q, S768I, etc., and uncommon mutations account for more than 30% of the total.
- In non-classic EGFR mutations, mutations carried by advanced or metastatic NSCLC include E709A, E709K, R776H, G724S, G779F. Each of them is lower than 1%. E709K mutations account for about 3.6%.
- Among non-classic mutations potentially developed by locally advanced or metastatic NSCLC resistant to 3rd generation EGFR inhibitors, C797S occupies 4.6% while each of G796S, L792H, T854I lower than 1%.

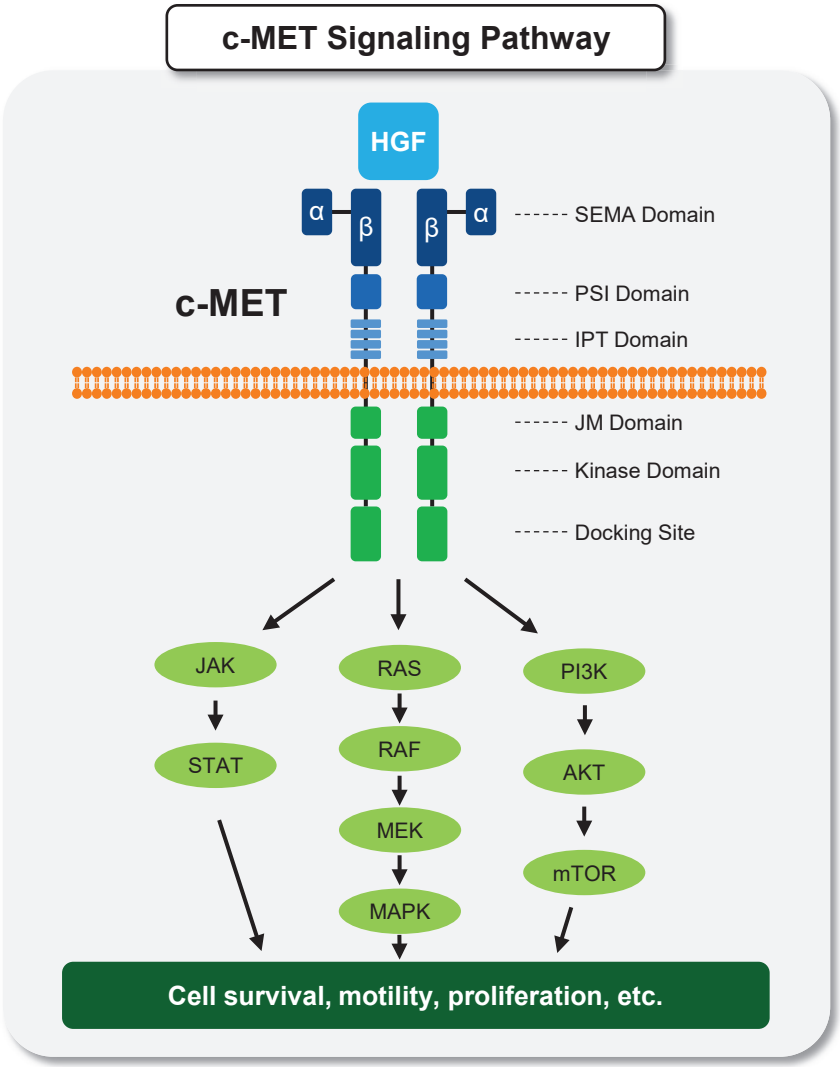
Proportion of mutations in NSCLC, US vs. China

23.9%

39.8%

Source: Literature Review, NIH, Frost & Sullivan Analysis

Overview of c-MET Signaling Pathway



Overview of c-MET

c-MET (mesenchymal-epithelial transition factor) is a receptor tyrosine kinase (RTK) expressed on the surfaces of various cells.

- As a proto-oncogene located on human chromosome 7 (7q21-q31), aberrant activations of c-MET had been detected in many cancers including lung, liver, colorectal, breast, pancreatic, ovarian, prostate, and gastric cancers.

Signaling Pathway of c-MET

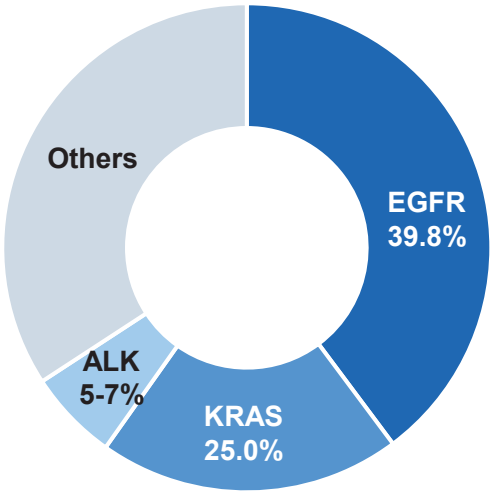
- MET alterations in NSCLC mainly include MET gene exon 14 skipping mutation, MET gene amplification, MET gene fusion and MET protein overexpression. One of the causes of EGFR-TKI resistance involves c-MET gene amplification, and approximately 20% to 30% of EGFR-TKI resistance are attributed to c-MET gene amplification.
- Activated by its cognate ligand HGF, c-MET promotes tumor development and progression by stimulating downstream signaling pathways including **PI3K/AKT, Ras/MAPK, JAK/STAT**, SRC, Wnt/β-catenin, etc.
- Signal transduction between the c-MET and EGFR pathways has also been found in many cancers. Studies have shown that c-MET might be an effective therapeutic target to **overcome EGFR inhibitor resistance** in lung cancer.

Source: Literature Review, Frost & Sullivan Analysis

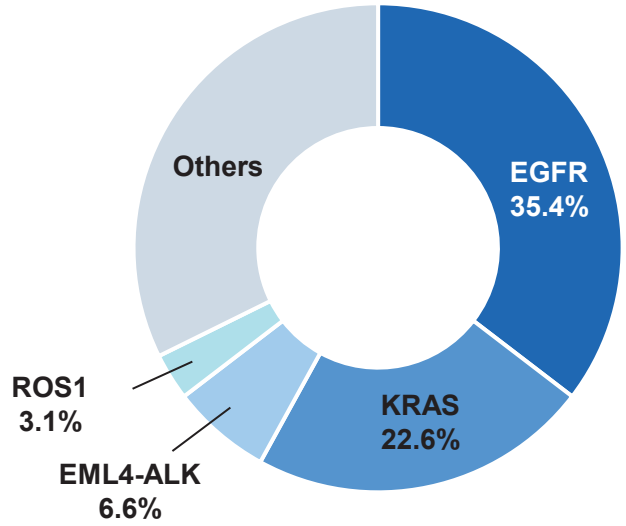
Frequency of Driver Gene Mutation in NSCLC

- In China, EGFR mutations are the most common type of driver gene variants in NSCLC, occurring in 39.8% of NSCLC patients, while KRAS mutations and ALK rearrangements are the other two types of NSCLC driver gene variants, accounting for 25% and 5-7% of NSCLC patients in China, respectively.
- According to Dang, AT.H., et al, EGFR mutations are the most common type of NSCLC driver variants globally, occurring in 35.4% of NSCLC patients.

Major driver gene variants in NSCLC in China



Major driver gene variants in NSCLC globally



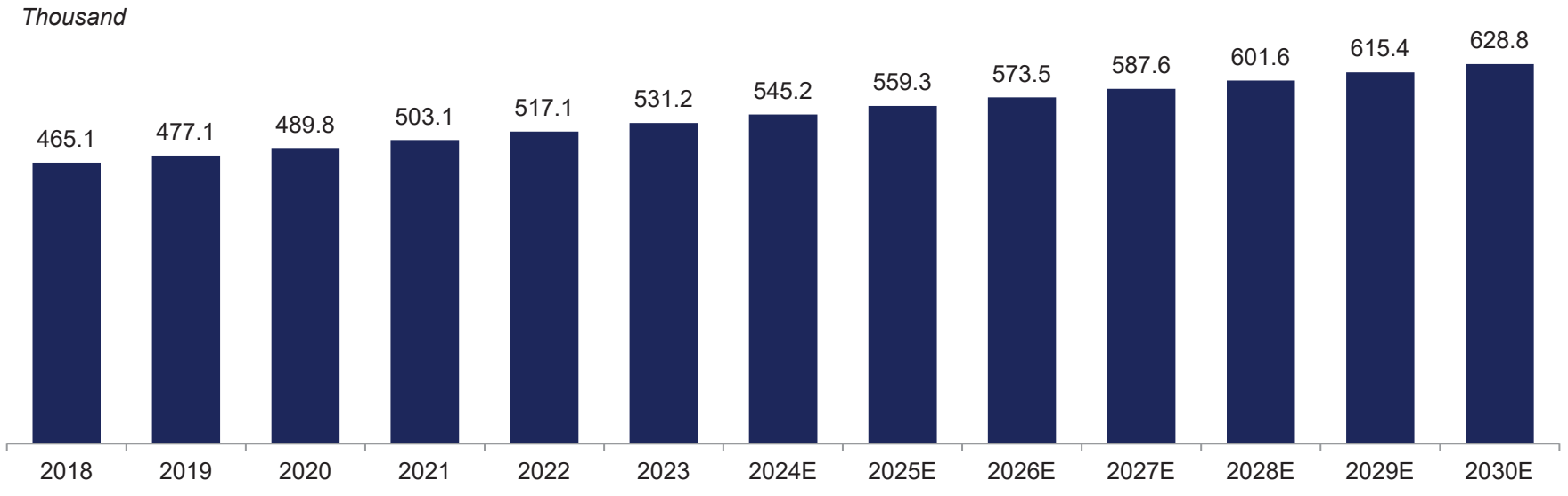
Source: Literature Review, Frost & Sullivan Analysis

Incidence of Colorectal Cancer in China, 2018-2030E

- In China, the number of new cases of colorectal cancer rose to 531.2 thousand in 2023, with a CAGR of 2.7% from 2018. It is expected to continue increasing to 573.5 thousand by 2026, reflecting a CAGR of 2.6% from 2023. Projections indicate that by 2030, the incidence is anticipated to reach 628.8 thousand, at a CAGR of 2.3% from 2026 to 2030.

Incidence of Colorectal Cancer in China, 2018-2030E

Period	CAGR
2018-2023	2.7%
2023-2026E	2.6%
2026E-2030E	2.3%



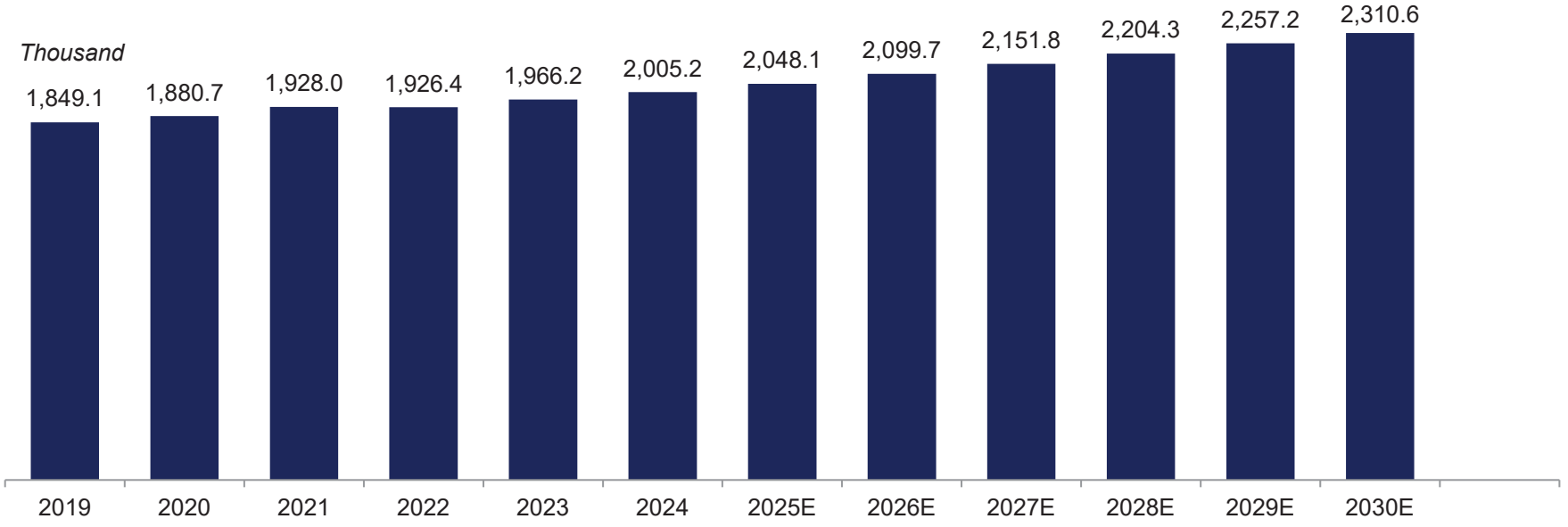
Source: NCCR, Frost & Sullivan Analysis

Global Incidence of Colorectal Cancer, 2018-2030E

- The worldwide number of new cases of colorectal cancer rose to 2,031.5 thousand in 2023, with a CAGR of 2.4% from 2018. It is expected to continue increasing to 2,186.9 thousand by 2026, reflecting a CAGR of 2.5% from 2023. Projections indicate that by 2030, the incidence is anticipated to reach 2,402.4 thousand, at a CAGR of 2.4% from 2026 to 2030.

Global Incidence of Colorectal Cancer, 2019-2030E

Period	CAGR
2019-2024	1.6%
2024-2027E	2.4%
2027E-2030E	2.4%



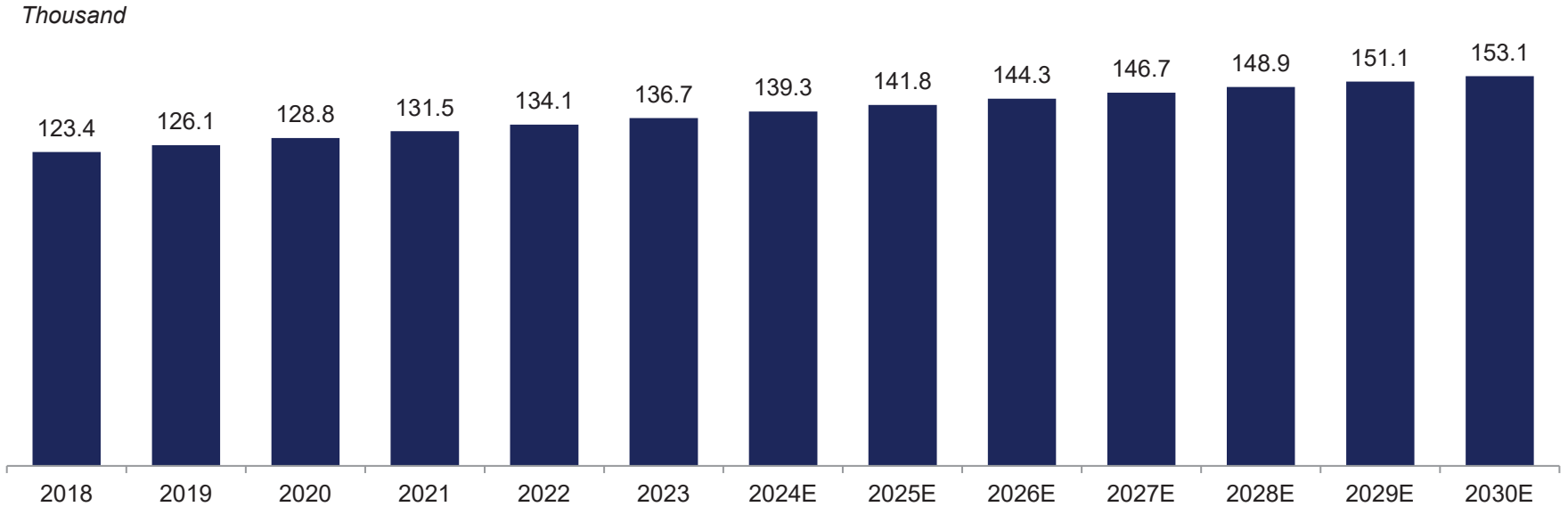
Source: NCCR, Frost & Sullivan Analysis

Incidence of Head and Neck Squamous Cell Carcinoma in China, 2018-2030E

- In China, the number of new cases of head and heck squamous cell carcinoma rose to 136.7 thousand in 2023, with a CAGR of 2.1% from 2018. It is expected to continue increasing to 144.3 thousand by 2026, reflecting a CAGR of 1.8% from 2023. Projections indicate that by 2030, the incidence is anticipated to reach 153.1 thousand, at a CAGR of 1.5% from 2026 to 2030.

Incidence of Head and Neck Squamous Cell Carcinoma in China, 2018-2030E

Period	CAGR
2018-2023	2.1%
2023-2026E	1.8%
2026E-2030E	1.5%



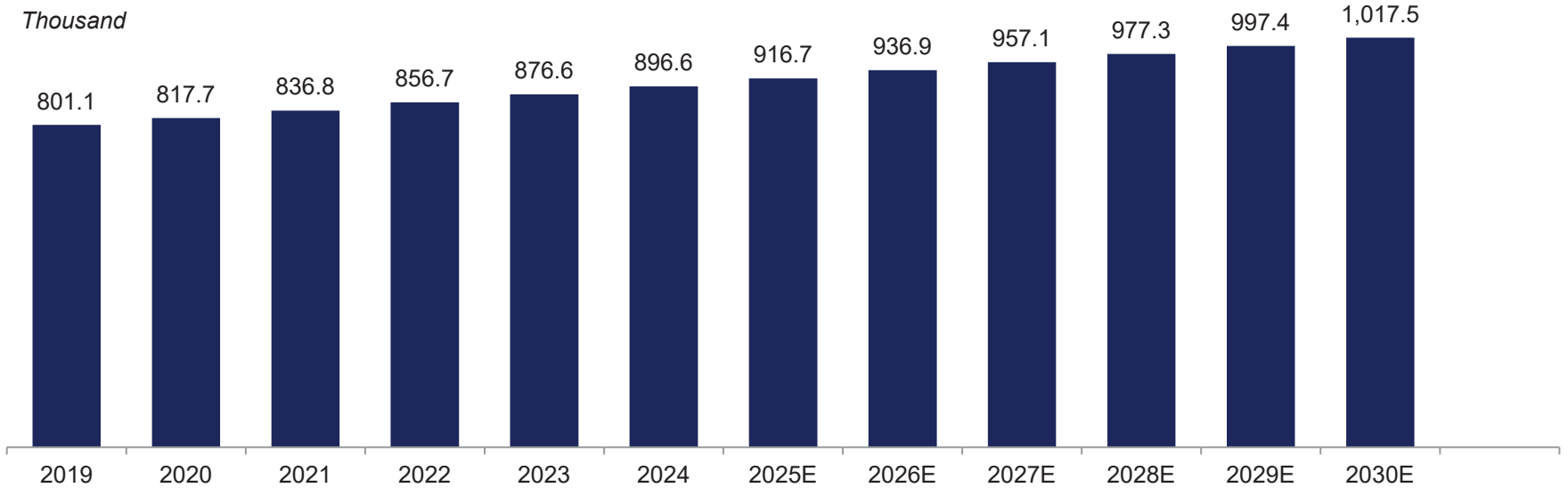
Source: NCCR, Frost & Sullivan Analysis

Global Incidence of Head and Neck Squamous Cell Carcinoma , 2019-2030E

- The worldwide number of new cases of head and neck squamous cell carcinoma rose to 876.6 thousand in 2023, with a CAGR of 2.3% from 2018. It is expected to continue increasing to 936.9 thousand by 2026, reflecting a CAGR of 2.2% from 2023. Projections indicate that by 2030, the incidence is anticipated to reach 1,017.5 thousand, at a CAGR of 2.1% from 2026 to 2030.

Global Incidence of Head and Neck Squamous Cell Carcinoma , 2019-2030E

Period	CAGR
2019-2024	2.3%
2024-2027E	2.2%
2027E-2030E	2.1%



Source: NCCR, Frost & Sullivan Analysis

EGFR/c-MET Bispecific Antibodies Approved by NMPA

Drug Name	Brand Name	Target	Company	Indications	Approval Date
Amivantamab	RYBREVANT	EGFR, c-MET	Johnson & Johnson	NSCLC	2025-02-08

As of April 7th, 2025

Source: FDA, Frost & Sullivan Analysis

EGFR/c-MET Bispecific Antibodies Approved by FDA

Drug Name	Brand Name	Target	Company	Indications	Approval Date
Amivantamab	RYBREVANT	EGFR, c-MET	Johnson & Johnson	Previously Treated NSCLC with EGFR Exon 20 Insertion Mutations	2021-05-21
				First-Line Treatment of NSCLC with EGFR Exon 20 Insertion Mutations	2024-03-01
				First-Line Treatment of NSCLC with EGFR Exon 19 Deletions or Exon 21 L858R Substitution Mutations	2024-08-19
				Previously Treated NSCLC with EGFR Exon 19 Deletions or Exon 21 L858R Substitution Mutations	2024-09-19

As of April 7th, 2025

Source: FDA, Frost & Sullivan Analysis

Competitive Landscape of China EGFR/c-MET Bispecific/Trispecific Antibodies in Pipeline

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
Amivantamab	EGFR/c-MET	Johnson & Johnson	NDA	In combination with Lazertinib for the first-line treatment of advanced and metastatic NSCLC with Exon 19 Deletions or Exon 21 L858R Substitution Mutations (estimated)	NMPA NDA Acceptance (2024-01-26)
			NDA	In combination with Carboplatin and Pemetrexed for the first-line treatment of advanced and metastatic NSCLC with EGFR Exon 20 insertion mutations (estimated)	NMPA NDA Acceptance (2023-12-08)
			NDA	In combination with Carboplatin and Pemetrexed for the second-line treatment of advanced and metastatic NSCLC with EGFR Exon 20 insertion mutations (estimated)	NMPA NDA Acceptance (2023-10-26)
HS-20117	EGFR/c-MET	Hansoh BioMedical Co.,Ltd.	Phase 3	NSCLC	2024-05-27
MCLA-129	EGFR/c-MET	Betta Pharmaceuticals Co.Ltd	Phase 2	NSCLC	2025-03-20
EMB-01	EGFR/c-MET	EpimAb Biotherapeutics	Phase 1/2	NSCLC	2022-01-30
			Phase 1/2	GC, HCC, CCA, CRC and Other Solid Tumor	2022-09-26
GB263T	EGFR/c-MET/c-MET	Genor Biopharma	Phase 1/2	NSCLC and Other Advanced Solid Tumor	2022-07-14
SHR-9839	EGFR/c-MET	Hengrui Medical Company	Phase 1/2	Advanced Solid Tumor	2024-06-05
PRO1286	EGFR/c-MET	ProfoundBio (Suzhou) CO., Ltd	Phase 1/2	Advanced Solid Tumor	2025-02-08
BG-T187	EGFR/c-MET/c-MET	BeiGene	Phase 1	Advanced Solid Tumor	2024-12-18
TAVO412	c-Met，EGFR，VEGF	Tavotek Biotherapeutics	Phase 1	Solid tumor，Non-Small Cell Lung Cancer，Liver cancer，Gastric cancer	2024-12-30
ALK202	EGFR/c-MET	Shanghai Anlingke Biopharmaceutical Co., Ltd	Phase 1	Advanced Solid Tumor	2025-03-26
HS-20122	EGFR/c-MET	Shanghai Hansoh BioMedical Co.,Ltd.	Phase 1	Advanced Solid Tumor	2025-04-02

As of April 7th, 2025

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of Global EGFR/c-MET Bispecific/Trispecific Antibodies in Pipeline

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
amivantamab	EGFR/c-MET	Johnson & Johnson	Phase 3	Unresectable or Metastatic Left-sided Colorectal Cancer	2024-10-29
HS-20117	EGFR/c-MET	Hansoh BioMedical	Phase 2/3	Non-Squamous NSCLC	2024/5/16
MCLA-129	EGFR/c-MET	Merus N.V.	Phase 2	Advanced Non-Small Cell Lung Cancer with Actionable Gene Alterations and MET Amplification.	2025-03-14
EMB-01	EGFR/c-MET	EpimAb Biotherapeutics Co., Ltd.	Phase 1/2	NSCLC and Other Advanced Solid Tumor	2019/1/9
GB263T	EGFR/c-MET/c-MET	Genor Biopharma	Phase 1/2	NSCLC and Other Advanced Solid Tumor	2022/4/18
SHR-9839	EGFR/c-MET	Hengrui Pharmaceutical Co., Ltd.	Phase 1/2	Advanced Solid Tumor	2024/6/25
BG-T187	EGFR/c-MET/c-MET	BeiGene	Phase 1	Advanced Solid Tumor	2024/9/19

As of April 7th, 2025

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Overview of EGFR/c-MET Bispecific or Trispecific Antibodies

Mechanism of Action	• Bispecific/Trispecific antibodies targeting dual or triple tumor-associated antigens have the advantages of invoking the synergistic effect between two or three signaling pathways, increasing target tissue specificity and reducing systemic toxicity.
Multi-line treatment and wide range of patients	• Amivantamab-vmjw, one EGFR/c-MET Bispecific antibody has been approved in first-line and second-line treatment of advanced and metastatic NSCLC and been recommended in the latest NCNC guideline 2024. • On August 19, 2024, the FDA approved Lazertinib in combination with Amivantamab-vmjw for the first-line treatment of advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations. In the first-line treatment, Amivantamab-vmjw is able to target chemotherapy-naïve patients. • On September 19, 2024, the the FDA approved Amivantamab-vmjw in combination with carboplatin and pemetrexed for the treatment of advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations, whose disease has progressed on or after treatment with an EFGR tyrosine kinase inhibitor. In the first-line treatment, Amivantamab-vmjw is able to target patients after failure of first-line EFGR tyrosine kinase inhibitors.

Source: Frost & Sullivan Analysis

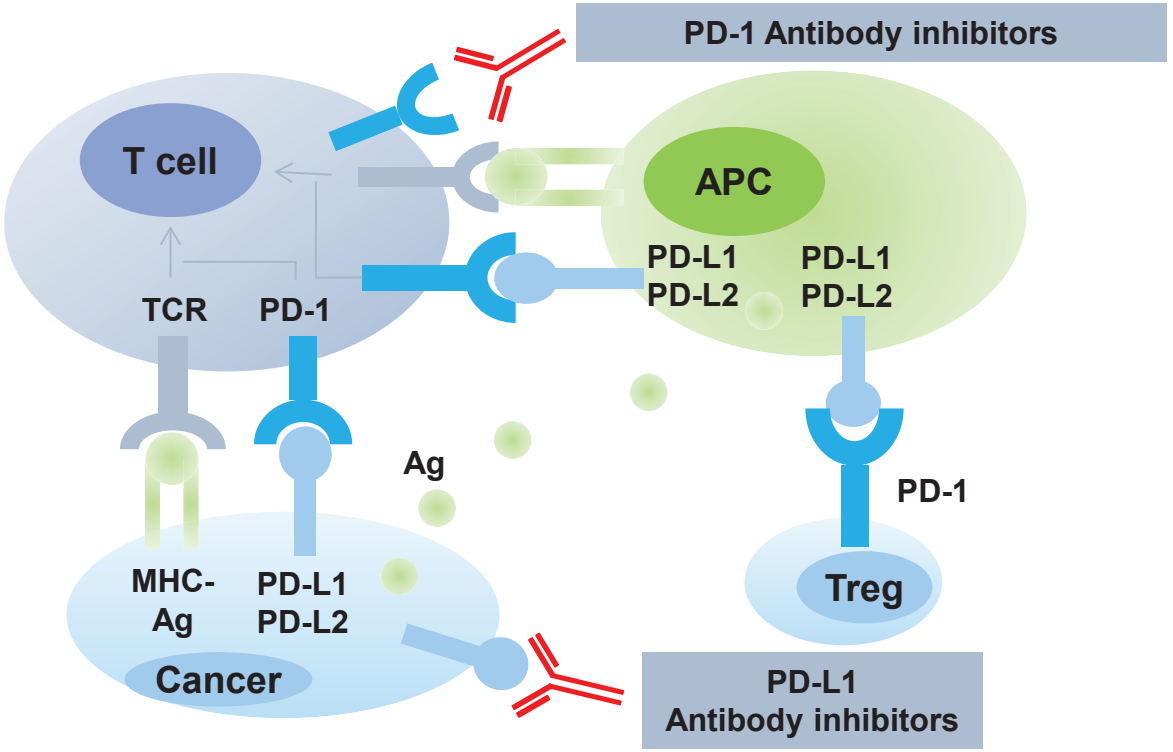
Core Strengths of GB263T

Huge potient market on NSCLC	• To date, Amivantamab has been approved by FDA in the first-line and second-line treatment of NSCLC with EGFR Exon 20 insertion mutations or Exon 19 deletions or Exon 21 L858R substitution mutations. Johnson & Johnson gave a USD 5 billion peak sales forecast on its investor conference. • The Phase I result of GB263T in NSCLC patients demonstrates similar efficacy profile but better safety profile compared with its competitors Amivantamab from Johnson & Johnson and MCLA-129 from Merus N.V., especially a lower incidence of IRR (infusion related reactions). EGFR/c-MET bispecific antibodies been proven to be effective in treating NSCLC, showing huge future market.
Larger oncology indications apart from NSCLC	• EGFR mutations and c-Met over-expression can be detected in many types of cancer, such as lung cancer, colorectal cancer, head and neck cancer, gastric cancer, etc. Based on the fact that Erbitux (one EGFR inhibitor) has been approved for colorectal cancer, head and neck cancer, the efficacy of EGFR/c-MET bispecific or tri-specific antibodies can be partially verified. Additionally, both of Amivantamab and MCLA-129, two EGFR/c-MET bispecific antibodies have demonstrated their promising efficacy profile on CRC and HNC based on its previous clinical results. According to J&J, the safety and efficacy of the Amivantamab combined with either FOLFOX or FOLFIRI was evaluated. The OrigAMI-1 phase Ib/II study involved 43 patients with RAS/RAF wild-type mCRC who were EGFR inhibitor-naïve. After a median follow-up of 7.3 months, the ORR was 49%, (95% CI 33–65), DCR was 88% (95% CI 75–96) and median PFS was 7.5 months (95% CI 7.4–not estimable). It is also encouraging that there were no unexpected or unmanageable side effects with these drug combinations. Therefore, EGFR/c-MET bispecific antibodies are promising to extend its indications to CRC, HNC and other cancers.

Source: Frost & Sullivan Analysis

Mechanism of Anti-PD-1/PD-L1 Therapy

- Programmed death protein 1 (PD1) is a common immunosuppressive member on the surface of T cells and plays an imperative part in downregulating the immune system and advancing self-tolerance. Its ligand programmed cell death ligand 1 (PDL1) is overexpressed on the surface of malignant tumor cells, where it binds to PD1, inhibits the proliferation of PD1-positive cells, and participates in the immune evasion of tumors leading to treatment failure. The PD1/PDL1-based pathway is of great value in immunotherapy of cancer and has become an important immune checkpoint in recent years.
- Antigen(Ag) is capable of stimulating an immune response. Antigen-presenting cells (APCs) can bind to Ag to activate T-cell receptor (TCR) and major histocompatibility complex(MHC) binding. Regulatory T cells (Treg) create a highly immunosuppressive tumor environment by maintaining the expression of PD-1 on its surface. When PD-1 binds PD-L1/L2, the T cell receives an inhibitory signal. The inhibition via PD-1 and its ligands lead to T-cell anergy and blockade of a productive antitumor immune response. Anti-PD-1 mAb is designed to prevent PD-1 binding PD-L1/L2. By this means, the function of T cell recovers.



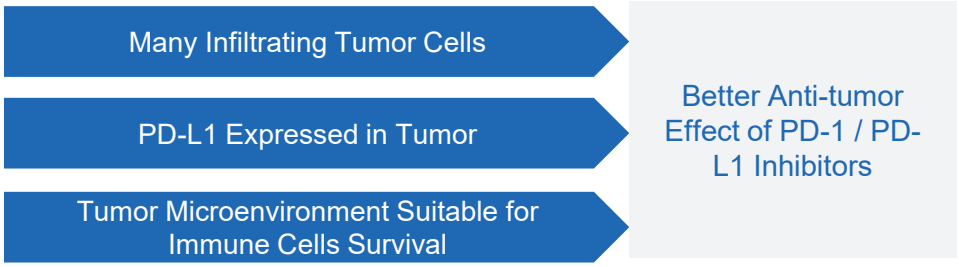
Source: Literature Review, Frost & Sullivan analysis

Clinical Limitations of PD-1/PD-L1 Treatment

- Although the emergence of PD-1 / PD-L1 inhibitors has brought new treatment for many cancer patients, the tumor cells and tumor microenvironment can limit the effect of PD-1/L1 inhibitors, and the number of patients who can benefit from these drugs is limited. In addition, the time period of PD-1/L1 inhibitors activating immune cells is limited, which brings new challenges to patients who fail to achieve therapeutic effect in the treatment period.

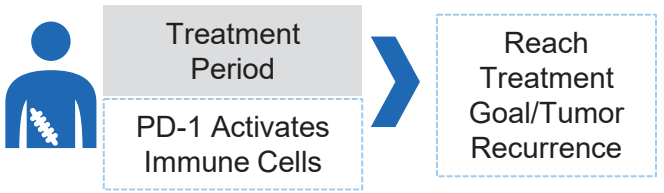
Limited Number of Benefited Patients

- Immune regulation targeting PD-1 and PD-L1 is affected by a variety of immune signaling pathways. Although significant and lasting effects have been achieved in some patients, the response rate is low in patients who receiving treatment. The mono-therapy response rate of PD-1/PD-L1 is rarely more than 29%, which means that about 71% of patients with PD-1 reactive cancer need to seek other treatments.
- The therapeutic effect of PD-1 / PD-L1 inhibitors is usually related to tumor immune microenvironment (infiltration of CD8+ T lymphocytes in tumor tissue, expression of PD-L1), tumor immunogenicity (tumor mutation load, clonal neoantigen load, microsatellite status) and tumor gene mutation. These factors are often different among patients, and the therapeutic effect is also different.



Limited Immune Cells Activation

- Although PD-1/PD-L1 inhibitors can activate the function of failing immune cells in a short time, these drugs can not prevent the final decline of immune cells. Specifically, PD-1/PD-L1 inhibitors can activate immune cells for a period of time, but this effect is not lasting.
- Therefore, the therapeutic effect of PD-1/PD-L1 inhibitors is often considered to have a certain period. Even if patients whose tumor can not be completely removed during that period continue to use PD-1/PD-L1 inhibitors, often will not have sustained effects, or even face worse effects after complete T cell failure.



Source: Frost & Sullivan analysis

Entry Barriers of PD-1/PD-L1 Antibody Drug Market

Gradually Saturated and Shaped Market	• The market is increasingly crowded with multiple PD-1/PD-L1 inhibitors, making it difficult for new entrants to compete. This is exacerbated by the fact that the market is maturing, with several agents approved across various cancer indications, leading to a complex landscape that is challenging to navigate. Besides, the dynamics of the PD-1/PD-L1 market are shaped by brand-level dynamics, where leading brands like Keytruda have established a dominant position, making it challenging for new entrants to capture significant market share.
Regulatory Scrutiny	• There is growing regulatory pressure, with demands for local data and head-to-head comparisons against the latest standard of care. This raises the evidence bar for new entrants and increases development risk. FDA's comments on current PD-1/PD-L1 development trends and its position in recent reviews indicate that relevant regulatory reviews will become increasingly stringent. FDA's requirements for local data and direct comparison with the latest treatment standards have raised the threshold for evidence, increasing both innovation costs and development risks. Meanwhile, NMPA has also strengthened its supervision of innovative drug approvals, with stricter approval requirements and more cautious approval of homogeneous studies and pseudo-innovative drugs.
Payer Pressure	• Facing the complex landscape of the PD-1/PD-L1 market, payers are increasingly challenged to assess the incremental benefits of new PD-1/PD-L1 therapies, especially combination therapies. Consequently, payers will push for head-to-head trials related to therapeutic standards and may even compare them with competitive new PD-1/PD-L1 therapies to measure different values. In addition, the need to compare real-world evidence for safety and efficacy will increase. Overall, due to the continuous increase in budget pressures, payers' scrutiny of value will also intensify.

Source: Frost & Sullivan Analysis

Growth Drivers of PD-1/PD-L1 Antibody Drug Market

Indication Development	• Approved indications have covered a wide range of cancers from uncommon cancers such as Hodgkin's lymphoma to gastric and liver cancer that have huge patient groups. Each year companies are running clinical trials to include more cancer types as indications, driving the market forward.
Favorable Policy	• Massive policies has been promulgated to support and standardize the development of the anti-tumor drug industry, including accelerating approval for marketing, prioritizing review and approval, and strengthening the clinical application management of anti-tumor drugs. In March 2023, the Center for Drug Evaluation issued a notice on the *Center for Drug Evaluation to Accelerate the Review of Innovative Drug Marketing License Applications (Trial)* to further speed up the review and approval of innovative drug. In January 2024, the Center for Drug Evaluation released *the Technical Guiding Principles to Support Optional Dosing Schemes of Anti-PD-1/PD-L1 Antibodies for Tumor Treatment Based on Pharmacokinetic Methods* to guide companies to optimize anti-PD -1/PD-L1 antibody clinical dosage to improve patient compliance and overall quality of life. Besides, from June 2018, various PD-1 / PD-L1 monoclonal antibodies have been approved for listing in China. The favorable drug review policy and medical insurance policy will continue to expand the capacity of China's PD-1 / PD-L1 antibody market.
Address Unmet Clinical Needs of Benefited Patients	• PD-1 normalizes anti-tumor immunity by reversing T cells or effector T cells (Teff) exhaustion within TME. Although significant and lasting effects have been achieved in some patients, the response rate is low in patients who receiving treatment. Until 2018, the response rate of PD-1 / PD-L1 is rarely more than 40%. This means that about 60% of patients with PD-1 reactive cancer need to seek other treatments. Drug resistance is another drawback after using PD-1/PD-L1 inhibitors for a long term (Possible MOA includes disappearance of tumor antigens, exhaustion of T cells, and increase in immunosuppressive cells.) • Compared with PD-1/PD-L1 monotherapy, PD-1/CTLA-4 bispecific antibodies are able to simultaneously exerting the synergistic anti-tumor effects of two immune checkpoints and further improve tumor response to monotherapy. In the meanwhile, PD-1/CTLA-4 bispecific antibodies show better safety profile with less side effects compared with the combination of two immune checkpoint inhibitors. • PD-1/VEGF bispecific antibodies target and block VEGF in the tumor microenvironment not only to inhibit the formation of tumor blood vessels, tumor growth and tumor metastasis, but also activate some immune cells and allow more immune cells to infiltrate into tumor tissues. Compared with the combination of PD-1 inhibitors and VEGF inhibitors, PD-1/VEGF bispecific antibodies can be more specifically enriched in tumor tissues, targeted to block VEGF in the tumor, relieve the immunosuppressive microenvironment, create a microenvironment that is conducive to the function of PD-1, synergistically inhibit the function of PD-1, relieve the inhibition of tumor cells on T cell immune response, and further exert anti-tumor effect.

Source: Frost & Sullivan Analysis

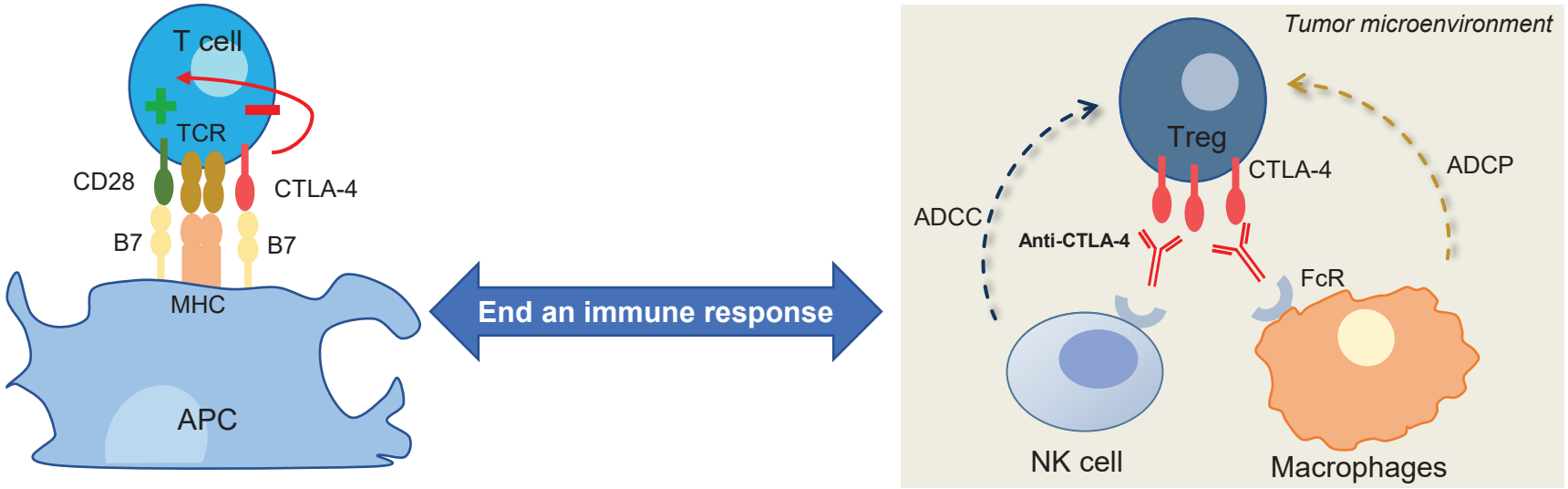
Future Trends of PD-1/PD-L1 Antibody Drug Market

Combination Therapy and Expanding to First-Line Treatment	• The number of clinical trials for combination therapies has surged, with a focus on targets like VEGF and CTLA-4, showing better results than single treatments. FDA has approved multiple PD-1/PD-L1 combination therapies, for example, Nivolumab and ipilimumab combination as first-line treatment for adult patients with pleural mesothelioma who are not candidates for surgery, and more are anticipated, enhancing the efficacy of cancer treatment. • At present, numbers of clinical trials of PD-1/L1 mAbs are conducted for the first-line treatment of cancer. Companies are making efforts to advance from third-line or second-line to first-line therapy and continue to expand to consolidation therapy for locally advanced cancer and neoadjuvant therapy for early or mid-stage cancer. Hence, more PD-1/L1 mAbs will be approved for first-line treatment of cancer in the near future.
New MOA Exploration through the Emerging Bi-specific antibody	• Dual targeting of both innate and adaptive checkpoints is theoretically attractive. Dual targeting of discrete checkpoints, e.g. PD1/PD-L1 or CTLA4, can be synergistic with regard to their anti-tumor effects. BsAbs further differentiate from mono-specific approaches by engaging surface targets across two different cell types (trans-binding), on the same cell surface (cis-binding), or soluble proteins at/near the cell surface. In terms of cis-binding, relative cell surface expression levels can be exploited to enhance cell binding selectivity through the adjustment of binding arm affinities. • Compared with PD-1/PD-L1 monotherapy, PD-1/CTLA-4 bispecific antibodies are able to simultaneously exerting the synergistic anti-tumor effects of two immune checkpoints and further improve tumor response to monotherapy. In the meanwhile, PD-1/CTLA-4 bispecific antibodies show better safety profile with less side effects compared with the combination of two immune checkpoint inhibitors. • PD-1/VEGF bispecific antibodies target and block VEGF in the tumor microenvironment not only to inhibit the formation of tumor blood vessels, tumor growth and tumor metastasis, but also activate some immune cells and allow more immune cells to infiltrate into tumor tissues. Compared with the combination of PD-1 inhibitors and VEGF inhibitors, PD-1/VEGF bispecific antibodies can be more specifically enriched in tumor tissues, targeted to block VEGF in the tumor, relieve the immunosuppressive microenvironment, create a microenvironment that is conducive to the function of PD-1, synergistically inhibit the function of PD-1, relieve the inhibition of tumor cells on T cell immune response, and further exert anti-tumor effect.
Better Affordability and Accessibility	• Up to 2024 Oct, in the field of cancer treatment,14 PD-1 and 9 PD-L1 mAbs have been approved, and 2 PD-1 bispecific antibody drugs has been launched. Due to continued NRDL negotiations and access to new products, the prices of PD-1/L1 antibody will be declined, for example, the prices of antitumor Drugs has been decreased about 65% in 2023 negotiations NRDL, which makes PD-1/L1 mAbs popularized and more affordable for patients.

Source: Frost & Sullivan analysis

Mechanism of Action of CTLA-4

- CTLA-4 (Cytotoxic T Lymphocyte Associated Protein 4), also known as CD152 (Cluster of Differentiation 152), is a protein receptor expressed constitutively on T cells that functions as an immune checkpoint and downregulates immune responses. It can down-regulates the immune response and prevent autoimmune diseases.
- The key to the immune regulation function of CTLA-4 is to control CD4+FoxP3-, CD8+T cells and Tregs. CTLA-4 can discontinue activated T cell response and mediate the inhibitory function of Tregs.
- Current studies have shown that CTLA-4 inhibits T cell responses mainly through two pathways. One is to reduce TCR (T cell receptor) and CD28 signal by binding to B7 (CD80 or CD86) competitively with CD28 or recruiting phosphatases to the intracellular domain of CTLA-4. The other is to reduce the expression level of CD80 and CD86 in antigen presenting cells (APC) or remove them from APC by transendocytosis, then reduce the involvement of CD28 in T cell activation.
- Selective depletion of Tregs in the tumor microenvironment results in tumor immunity. Higher levels of CTLA-4 on intratumoral Tregs allow their selective depletion by anti-CTLA-4 antibodies, perhaps through antibody-dependent cellular phagocytosis (ADCP) by macrophages and/or antibody-dependent cellular cytotoxicity (ADCC) by NK cells.
- The anti-tumor effect induced by the binding of the Fc terminus of anti-CTLA-4 antibodies to Fc receptors (FcγRs) has been a research hotspot in recent years. Anti-CTLA-4 antibodies with strong FcγR binding ability can inhibit tumor growth and drive immune remodeling, which is not only caused by Treg depletion and CTLA-4 blockade, but also by FcγR binding and type I interferon.
- MOAs of IgG1 type anti-CTLA4 mAb described thus far include blockade of CTLA4 binding to its ligands of CD80/CD86 on APCs, ADCC-/macrophage mediated depletion of tumor-infiltrate regulatory T cell (Treg) via its Fc function and the remodeling of innate immunity in TME through Fcγ receptor (FcγR)-engagement.



Notes: APC: antigen presenting cell; CTLA-4: cytotoxic T-lymphocyte associated protein 4; FcR: Fc receptor; MHC: major histocompatibility complex; NK: natural killer; TCR: T cell receptor; Treg: regulatory T cells; ADCC: antibody-dependent cellular cytotoxicity; ADCP: antibody-dependent cellular phagocytosis.

Source: Literature Research, Frost & Sullivan Analysis

Entry Barriers of CTLA-4 Antibody Drugs Market

Toxicity and Safety Concerns	• CTLA-4 antibody inhibitors, such as ipilimumab, are known to cause significant immune-related adverse events (irAEs), which can be associated with substantial morbidity and mortality. These side effects limit the therapy's applicability and require careful management, posing a barrier to the development and adoption of new CTLA-4 antibody drugs.
Limited Efficacy	• The value of anti-CTLA-4 antibodies in cancer therapy is well established. However, the broad application of currently available anti-CTLA-4 therapeutic antibodies is hampered by their narrow therapeutic index. It is therefore challenging to develop the next generation of anti-CTLA-4 therapeutics with improved safety and efficacy. • Response rates to CTLA-4 therapies are generally lower compared to other immunotherapies, such as PD-1/PD-L1 inhibitors. This lower efficacy can make it challenging for new CTLA-4 drugs to demonstrate superior or non-inferior outcomes in clinical trials, particularly when compared to established treatments
Competition from Established Therapies	• The market for cancer immunotherapies is already saturated with established PD-1/PD-L1 inhibitors, which have proven efficacy and a more favorable safety profile for some patient populations. This competition makes it difficult for new CTLA-4 targeting therapies to gain a foothold.

Source: Frost & Sullivan Analysis

Growth Drivers of CTLA-4 Antibody Drugs Market

Unmet Clinical Needs and Expansion of Indications	• The number of cancer patients, including those with NSCLC, melanoma, renal cell cancer, and GI cancer, is expected to rise due to aging and environmental pollution. Currently, few CTLA-4 antibody drugs are approved globally with limited indications, covering hepatocellular carcinoma, non-small cell lung cancer, melanoma, renal cell carcinoma, malignant pleural mesothelioma, colorectal, esophageal, and cervical cancers. Many cancer patients lack access to these drugs, creating significant unmet needs. As indications expand, more patients will benefit, driving growth in the CTLA-4 antibody drug market.
Enhancement of Drug Efficacy	• CTLA-4 antibody drugs have achieved an objective response rate of 93% in cervical cancer treatments, reflecting their superior anti-tumor efficacy. Continued advancements in antibody technology and therapeutic strategies are expected to further improve objective response rates. This exceptional efficacy not only enhances clinical outcomes but also increases physicians' confidence in prescribing these drugs, thus fueling the market's expansion.
Rising Industry Competition	• In recent years, the development of CTLA-4 antibody drugs has attracted increasing participation from biotech company. At present, large pharmaceutical companies lead the market, but smaller biotech are achieving rapid breakthroughs. This dynamic, healthy competition is expected to catalyze significant innovation and advancement in the CTLA-4 antibody drug landscape.
Supportive Regulatory Policies	• Malignant tumors, such as lung cancer and melanoma, remain critical global healthcare challenges due to rising incidence and mortality rates. CTLA-4-targeted therapies have demonstrated significant anti-tumor efficacy, driving continued focus and investment. Over the past decade, China has enacted favorable policies to promote the development of innovative treatments, including streamlined clinical trial approvals. These measures have accelerated the growth of CTLA-4 antibody drugs and contributed to market expansion.

Source: Frost & Sullivan analysis

Future Trends of the CTLA-4 Antibody Drug Market

Continuous Expansion of Indications	• The approved indications for CTLA-4 antibody drugs have broadened from the initial treatments for hepatocellular cancer and non-small cell lung cancer to include melanoma, cervical cancer. In addition, multiple clinical trials are currently investigating its efficacy in diseases such as lymphoma and esophageal cancer. Looking ahead, the focus of CTLA-4 drug development will continue to be on expanding indications to address unmet clinical needs, providing broader patient access to these therapies.
Dual-Target CTLA-4 as a Development Trend	• CTLA-4 is a pivotal target in immune checkpoint inhibition, playing a crucial role in tumor immunotherapy. With a deepening understanding of the tumor microenvironment (TME), dual-target CTLA-4 drugs have emerged as a promising development trend. These drugs simultaneously target CTLA-4 and additional pathways, such as PD-1, PD-L1, and CD47, aiming to enhance therapeutic efficacy while minimizing side effects. The approval of Akeso's Cadonilimab, the first global dual-target CTLA-4 drug, represents a significant breakthrough, heralding a new era of innovation and opportunity in dual-target drug development.
Enhanced Safety Profile and Excellent Efficacy Profile	• While CTLA-4 antibody drugs have proven effective, they can trigger immune-related side effects, such as rashes and colitis, which may lead to treatment discontinuation or compromise patient outcomes. Moving forward, the industry's focus will shift towards minimizing these immune-related adverse events by optimizing the pH sensitivity of CTLA-4 antibodies and utilizing dual-target therapies. These strategies are expected to reduce antibody-mediated cytotoxicity, enhancing both the safety and efficacy of CTLA-4 therapies. • PD-1/CTLA-4 bispecific antibodies may be able to improve efficacy and lower antibody-dependent cellular cytotoxicity (ADCC), antibody-dependent cellular phagocytosis (ADCP), complement-dependent cytotoxicity (CDC), and cytokine release compared with CTLA-4 mAb in the meanwhile through antibody structure design.
Improved Accessibility	• Currently, the combination of CTLA-4 and PD-1 antibody therapies is endorsed by the American Society of Clinical Oncology (ASCO) as a first-line treatment for non-small cell lung cancer and hepatocellular carcinoma. Additionally, the Chinese Society of Clinical Oncology (CSCO) recommends these therapies as a second-line treatment for cervical cancer. As more CTLA-4 drugs are integrated into first- and second-line cancer treatments, patient access to these life-saving therapies is expected to increase significantly, further improving treatment accessibility and availability across broader patient populations.

Source: Frost & Sullivan analysis

Core Strengths of GB268

Huge potient market	• The efficacy of PD-1 inhibitor, anti-EGFR antibody, CTLA-4 inhibitors have been verified in various types of cancers and many products have been launched so far. And it is encouraging that Ivonescimab, one PD-1/VEGF bispecific antibody demonstrates better safety and efficacy profile compared with Pembrolizumab in first-line PD-L1 positive advanced and metastatic NSCLC. PD-1/CTLA-4/VEGF tri-specific antibodies may have advantages in improving tumor response to immunotherapy, and could be promising to extend its indications many types of cancer.
Specific structure degisn	• The specific design enables GB268 to just patially block CTLA-4 signal pathway, rendering a better safety as well as anti-tumor activity observed in preclinical in vivo studies. Such design may offer better anti tumor response and better safety in human which will be verified in the upcoming first in human study.

Source: Frost & Sullivan Analysis

PD-1/CTLA-4 Bispecific Antibodies Approved by NMPA

Drug Name	Brand Name	Target	Company	Indications	Approval Date
Cadonilimab	开坦尼	PD-1/CTLA-4	Akeso Pharmaceuticals, Inc.	First-line treatment of patients with locally advanced unresectable or metastatic gastric or gastroesophageal junction adenocarcinoma	2024-09-30
				Indicated for patients with recurrent or metastatic cervical cancer who have failed previous platinum-based chemotherapy	2022-06-28

As of April 7th, 2025

Source: NMPA, Frost & Sullivan Analysis

PD-1/CTLA-4 Bispecific Antibodies Approved by FDA

Drug Name	Brand Name	Target	Company	Indications	Approval Date
None					

As of April 7th, 2025

Source: NMPA, Frost & Sullivan Analysis

Competitive Landscape of China PD-1/CTLA-4 Bispecific Antibodies in Pipeline

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
Cadonilimab	PD-1/CTLA-4	Akeso Pharmaceuticals, Inc.	NDA	First-line treatment of persistent, recurrent or metastatic cervical cancer with platinum-based chemotherapy with or without bevacizumab	2024-04-24
QL1706	PD-1/CTLA-4	QILU PHARMACEUTICAL CO.,LTD	Phase 3	Esophageal squamous cell carcinoma	2025-02-19
			Phase 3	small cell lung cancer	2025-02-11
MEDI5752	PD-1/CTLA-4	AstraZeneca	Phase 3	Unresectable pleural mesothelioma	2024-12-27
			Phase 2	Advanced hepatocellular carcinoma and biliary tract cancer	2023-03-24
			Phase 3	Relapsed and metastatic cervical cancer	2025-01-24
			Phase 3	Non-squamous non-small cell lung cancer	2025-01-24
			Phase 3	Head and Neck Squamous Cell Carcinoma	2025-01-14
SI-B003	PD-1/CTLA-4	Baili Pharmaceutical Co., Ltd.	Phase 1	Relapsed and metastatic colorectal cancer, melanoma, non-small cell lung cancer, urothelial carcinoma, triple-negative breast cancer, cervical cancer, gastric cancer, and renal cell carcinoma	2020-08-05

As of April 7th, 2025

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of Global PD-1/CTLA-4 Bispecific Antibodies in Pipeline (1)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
Cadonilimab	PD-1/CTLA-4	Akeso Pharmaceuticals, Inc.	Phase 3	Cervical cancer	2021-07-29
			Phase 3	Gastric and gastroesophageal junction adenocarcinoma	2021-08-17
			Phase 3	Hepatocellular carcinoma	2022-08-05
			Phase 3	Nasopharyngeal cancer	2022-10-20
			Phase 3	Ovarian cancer	2024-08-07
			Phase 3	Colorectal cancer	2024-08-22
			Phase 3	Non-small cell lung cancer	2024-09-27

As of April 2nd, 2025

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of Global PD-1/CTLA-4 Bispecific Antibodies in Pipeline (2)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
MEDI5752	PD-1/CTLA-4	AstraZeneca	Phase 3	Non-small cell lung cancer	2023-08-09
			Phase 3	Cervical cancer	2023-10-12
			Phase 3	Pleural mesothelioma	2023-10-24
			Phase 3	Head and neck squamous cell carcinoma	2023-11-13
Vudalimab	PD-1/CTLA-4	Xencor, Inc.	Phase 2	Metastatic castration-resistant prostate cancer	2021-08-13
			Phase 2	Ovarian cancer, Endometrial cancer, Cervical carcinoma, Metastatic castration-resistant prostate cancer	2021-09-02
			Phase 2	Non-squamous non-small cell lung cancer	2023-12-15

As of April 7th, 2025

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of Global PD-1/CTLA-4 Bispecific Antibodies in Pipeline (3)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
SI-B003	PD-1/CTLA-4	Baili Pharmaceutical Co., Ltd.	Phase 2	Small cell lung cancer	2023-06-29
			Phase 2	Non-small cell lung cancer, Nasopharyngeal carcinoma	2023-07-21
			Phase 2	Urothelial carcinoma and other solid tumor	2023-07-28
			Phase 2	Cervical cancer	2023-08-14
			Phase 2	Head and neck squamous cell carcinoma	2023-08-23
			Phase 2	Esophageal cancer, gastric cancer, colorectal Cancer	2023-08-23
			Phase 2	Breast cancer	2023-09-21
MGD019	PD-1/CTLA-4	MacroGenics	Phase 2	Metastatic castration-resistant prostate cancer	2023-05-08
			Phase 2	Platinum-resistant ovarian cancer or clear cell gynecologic cancer	2024-12-12
Botensilimab	PD-1/CTLA-4	Agenus	Phase 2	Pancreatic cancer	2025-02-20

As of April 7th, 2025

Source: CDE, Frost & Sullivan Analysis

PD-1/VEGF Bispecific Antibodies Approved by NMPA

Drug Name	Brand Name	Target	Company	Indications	Approval Date
Ivonescimab	依达方	PD-1/VEGF	Akeso Pharmaceuticals, Inc.	In combination with chemotherapy for the treatment of locally advanced or metastatic non-squamous non-small cell lung cancer with EGFR mutations that have progressed after treatment with an EGFR-TKI	2024-05-24

As of April 7th, 2025

Source: NMPA, Frost & Sullivan Analysis

PD-1/VEGF Bispecific Antibodies Approved by FDA

Drug Name	Brand Name	Target	Company	Indications	Approval Date
None					

As of April 7th, 2025

Source: NMPA, Frost & Sullivan Analysis

Competitive Landscape of China PD-1/VEGF Bispecific Antibodies in Pipeline

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
SCTB14	PD-1/VEGF	SinoCelltech Ltd.	Phase 3	Driver gene-negative locally advanced or metastatic NSCLC	2025-04-03
			Phase 2/3	EGFR-TKI treatment failed EGFR mutation locally advanced or metastatic NSCLC	2025-03-15
SSGJ-707	PD-1/VEGF	Sunshine Guojian Pharmaceutical Co., Ltd.	Phase 2	Advanced gynecologic cancer	2024-08-06
MHB039A	PD-1/VEGF	Minghui Pharmaceutical (Hangzhou) Co., Ltd	Phase 1/2	Advanced solid tumor	2024-03-01
LM-299	PD-1/VEGF	LaNova Pharmaceutical	Phase 1/2	Advanced solid tumor	2024-09-14
RC148	PD-1/VEGF	Remegen Co.,Ltd.	Phase 1	Advanced solid tumor	2023-08-10
JS207	PD-1/VEGF	Junshi Biosciences	Phase 2	mCRC	2025-03-10
		Junshi Biosciences	Phase 2	NSCLC	2025-03-07
RC148	PD-1/VEGF	Remegen Co.,Ltd.	Phase 1	Advanced solid tumor	2025-02-19

As of April 7th, 2025

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of Global PD-1/VEGF Bispecific Antibodies in Pipeline

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
Ivonescimab	PD-1/VEGF	Akeso Pharmaceuticals, Inc.	Phase 3	Non-squamous non-small cell lung cancer	2022-01-11
			Phase 3	Head and neck squamous cell carcinoma	2024-09-19
			Phase 3	Hepatocellular carcinoma	2024-09-19
SSGJ-707	PD-1/VEGF	Sunshine Guojian Pharmaceutical Co., Ltd.	Phase 2	Non-small cell lung cancer	2024-04-12
			Phase 2	Metastatic colorectal cancer	2024-07-10
			Phase 2	Advanced or recurrent endometrial cancer, Platinum-resistant ovarian cancer	2024-07-26
RC148	PD-1/VEGF	RemeGen Co., Ltd.	Phase 2	HR-negative, HER2-low Expressing unresectable locally advanced or metastatic breast cancer	2024-10-15
SCTB14	PD-1/VEGF	SinoCelltech Ltd.	Phase 1/2	Advanced solid tumor	2024-03-12
MHB039A	PD-1/VEGF	Minghui Pharmaceutical (Hangzhou) Co., Ltd	Phase 1/2	Advanced solid tumor	2024-04-03
AI-081	PD-1/VEGF	OncoC4, Inc.	Phase 1/2	Advanced solid tumor	2024-10-10
LM-299	PD-1/VEGF	LaNova Pharmaceutical	Phase 1/2	Advanced solid tumor	2024-10-21
JS207	PD-1/VEGF	Junshi Biosciences	Phase 1	Advanced solid tumor	2023-09-01

As of April 7th, 2025

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of China PD-1/CTLA-4/VEGF Trispecific Antibodies in Pipeline

- There is no PD-1/CTLA-4/VEGF trispecific antibodies launched in China.

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
HC010	PD-1, CTLA-4, VEGF	Hongcheng Biopharma	Phase 1	Advanced Solid Tumor	2024-02-20

As of April 2nd, 2025

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of Global PD-1/CTLA-4/VEGF Trispecific Antibodies in Pipeline

- There is 2 PD-1/CTLA-4/VEGF trispecific antibodies launched globally.

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
CS2009	PD-1, CTLA-4, VEGF	CStone Pharmaceuticals	Phase 1	Advanced Solid Tumors	2024-12-19
HC010	PD-1, CTLA-4, VEGF	Hongcheng Biopharma	Phase 1	Advanced Solid Tumor	2024-03-13

As of April 2nd, 2025

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Verification

- EGFR over-expression can be detected in 40% to 70% of colorectal cancer cells, and it is significantly associated with increased tumor metastatic potential and decreased survival rate of colorectal cancer. Cetuximab, one anti-EGFR monoclonal antibody, has been approved by FDA and NMPA for the first and second treatment of mCRC in combination with chemotherapy.
- Almost all HNSCC have over-expression of EGFR. Anti-EGFR monoclonal antibodies competitively block endogenous EGFR natural ligands by binding to EGFR, hinder the formation of EGFR dimers, and inhibit tumor cell growth; in addition, anti-EGFR monoclonal antibodies can improve radiotherapy effects by affecting tumor cell cycle, DNA damage repair and angiogenesis. Cetuximab has been approved by FDA and NMPA for the first treatment of relapsed or metastatic HNSCC in combination with chemotherapy and approved for the locally advanced HNSCC in combination with radiotherapy.
- EGFR-KTI and c-MET inhibitors have been approved for treatment of advanced and metastatic NSCLC. amivantamab, one EGFR/c-MET bi-specific antibody has been approved by FDA for the first-line and second-line treatment of advanced and metastatic NSCLC.
- As 20241120, eleven anti--PD-1 monoclonal antibodies have been approved by NMPA, seven approved by FDA.
- As 20241120, one anti-CTLA-4 monoclonal antibody has been approved by NMPA, two approved by FDA.
- As 20241120, five anti-VEGF monoclonal antibody has been approved by NMPA, four approved by FDA.
- The number of cancer deaths in China in 2022 is 2574.2 thousand; the number of cancer deaths worldwide in 2022 is 9743.8 thousand.

Source: Frost & Sullivan analysis