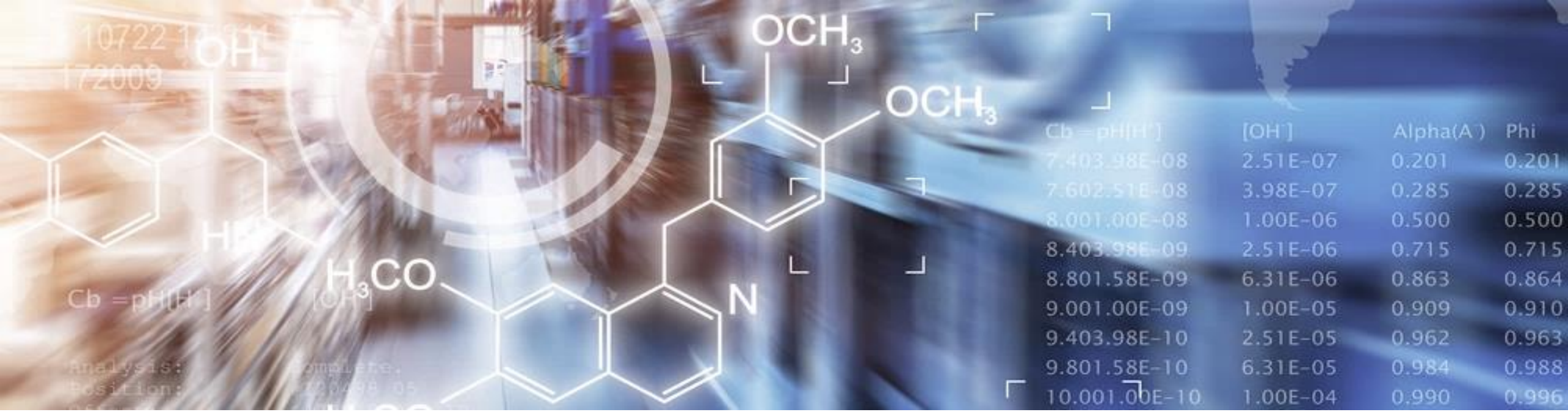


Industry report on Global and China small molecule drug market

China Insights Consultancy

October 2025

旺山旺水 VIGONVITA

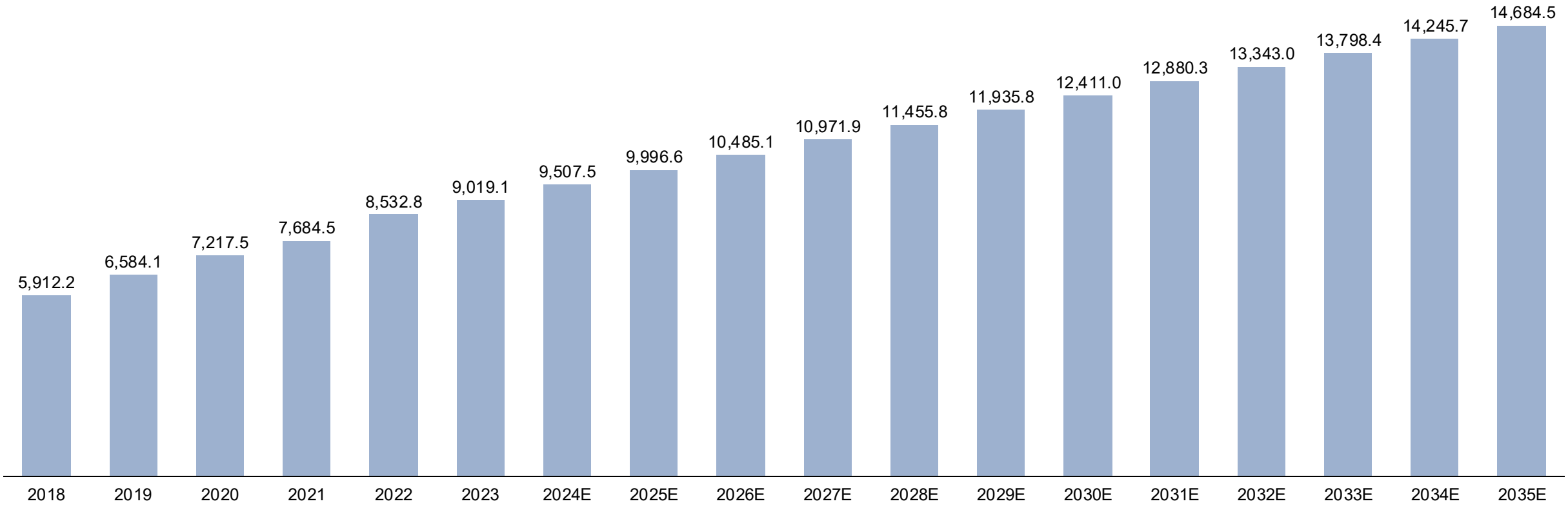
Table of contents

China total healthcare expenditure

China total healthcare expenditure, 2018-2035E

CAGR	2018-23	2023-35E
China healthcare expenditure	8.8%	4.1%

RMB billion



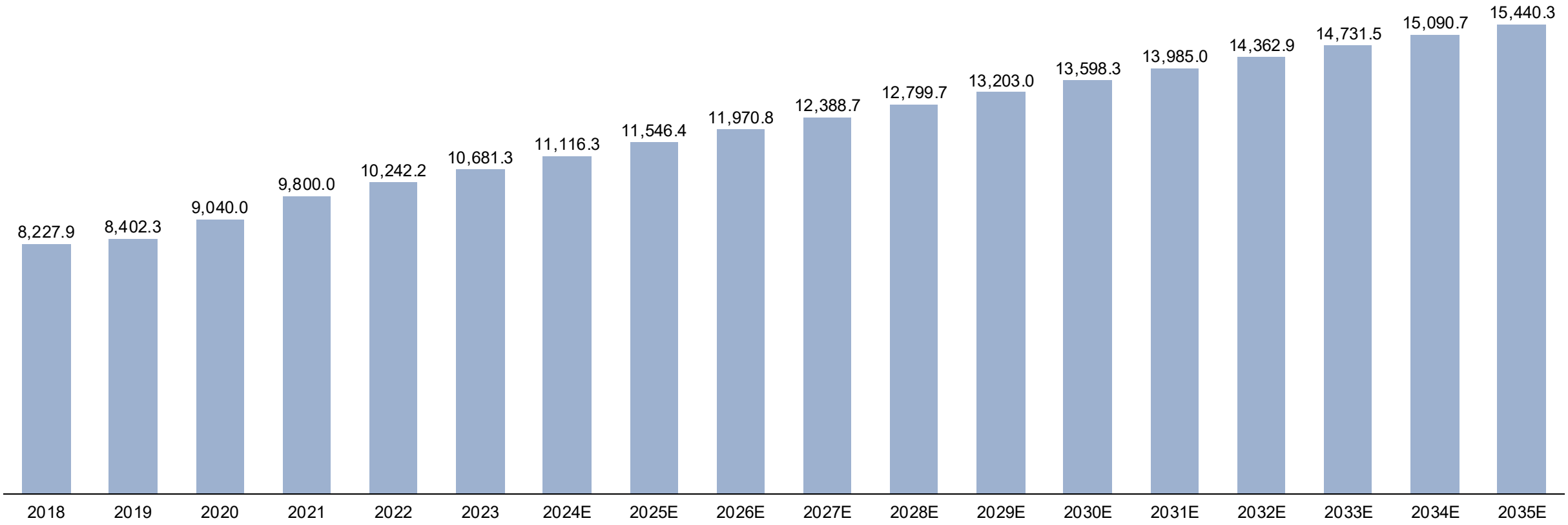
Source: National Bureau of Statistics, China Insights Consultancy

Global total healthcare expenditure

Global total healthcare expenditure, 2018-2035E

CAGR	2018-23	2023-35E
Global total healthcare expenditure	5.4%	3.1%

USD billion



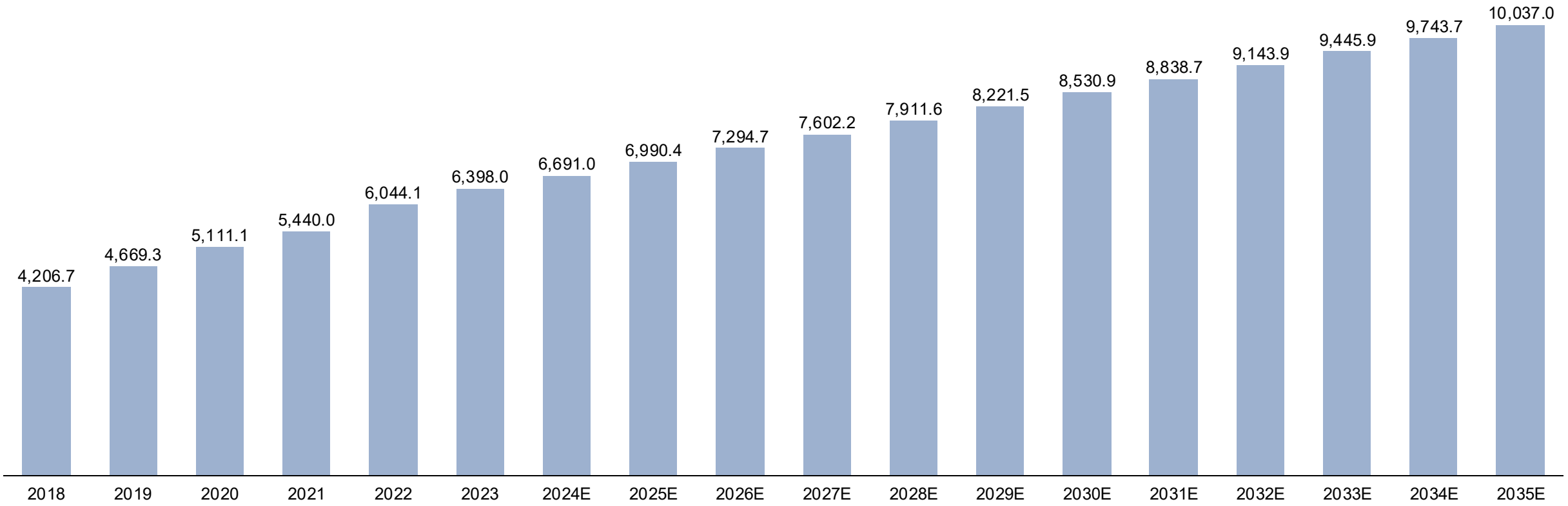
Source: WHO, UN, China Insights Consultancy

China healthcare expenditure per capita

China healthcare expenditure per capita, 2018-2035E

CAGR	2018-23	2023-35E
China healthcare expenditure per capital	8.7%	3.8%

RMB



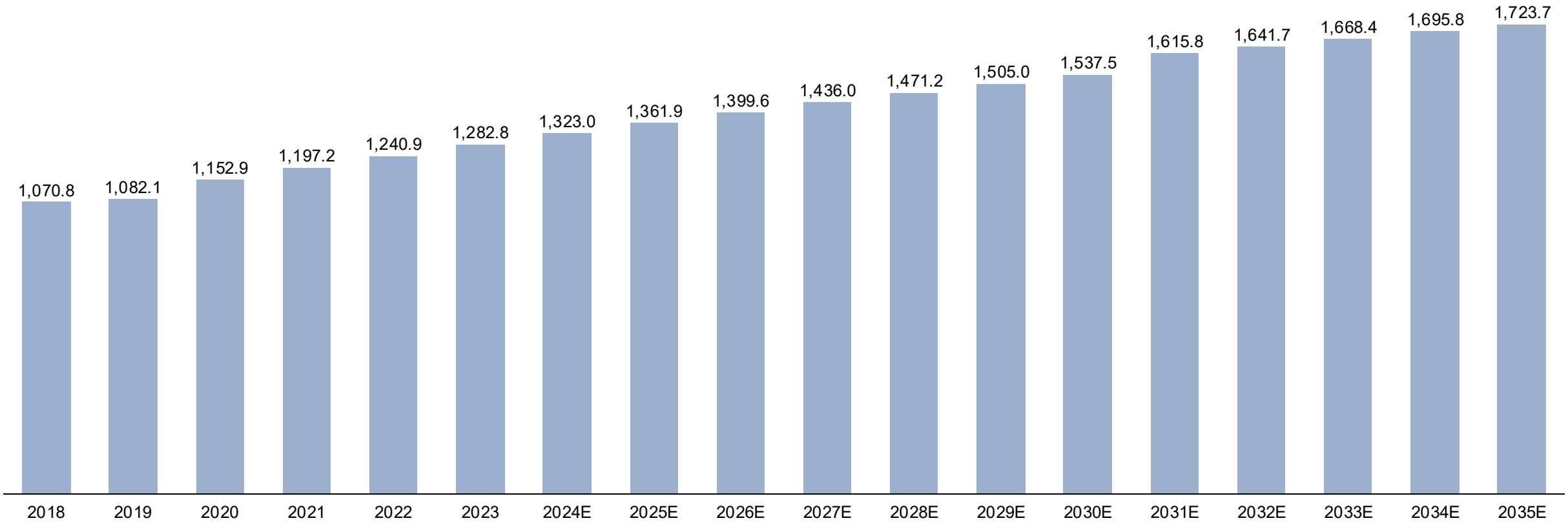
Source: National Bureau of Statistics, China Insights Consultancy

Global healthcare expenditure per capita

Global healthcare expenditure per capita, 2018-2035E

CAGR	2018-23	2023-35E
Global healthcare expenditure per capita	3.7%	2.5%

USD



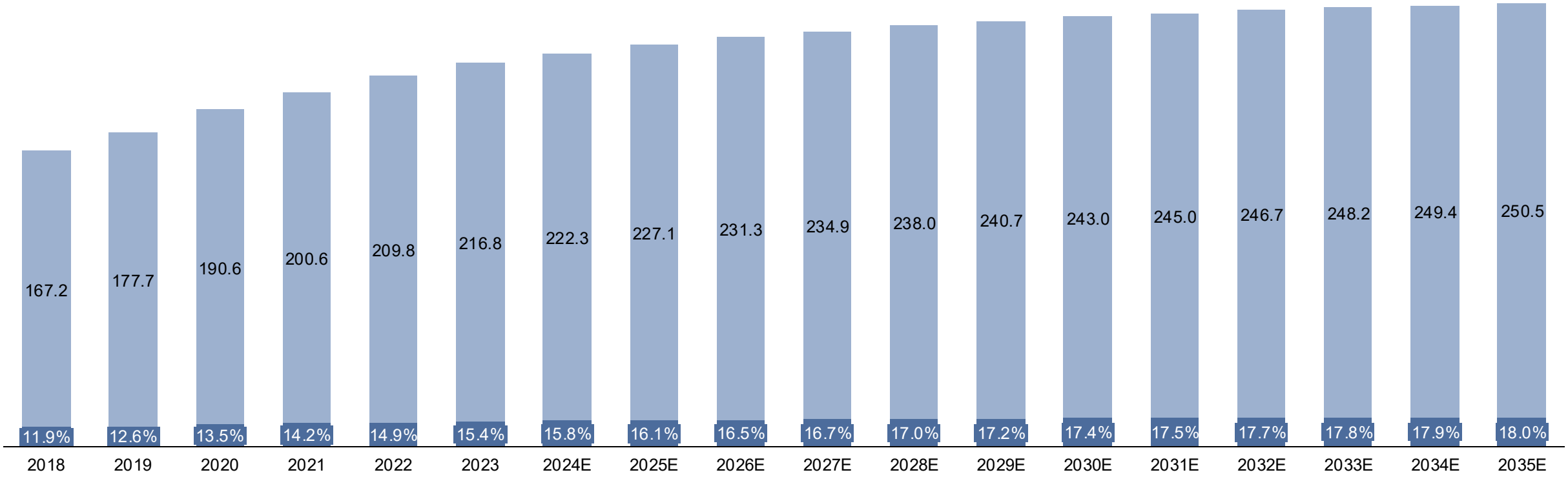
Source: WHO, UN, China Insights Consultancy

China population aging tendency

China population aging tendency, 2018-2035E

CAGR	2018-23	2023-35E
Population of 65+	5.3%	1.2%
Proportion of total population		

ppl million



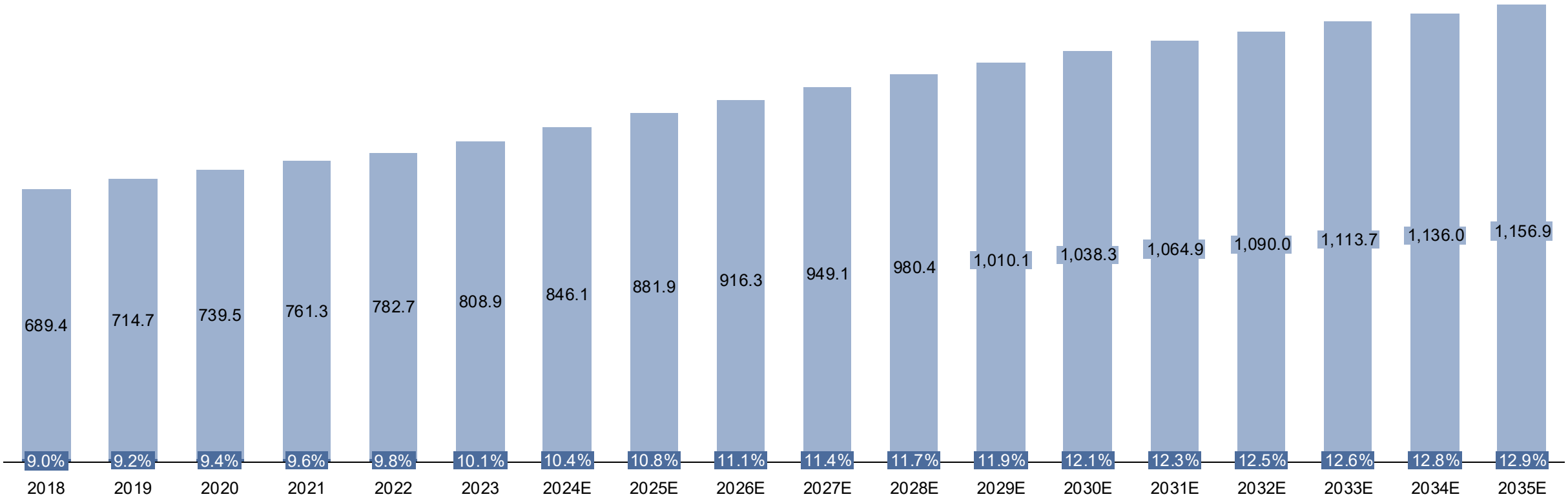
Source: National Bureau of Statistics, China Insights Consultancy

Global population aging tendency

Global population aging tendency, 2018-2035E

CAGR	2018-23	2023-35E
Population of 65+	3.2%	3.0%
Proportion of total population		

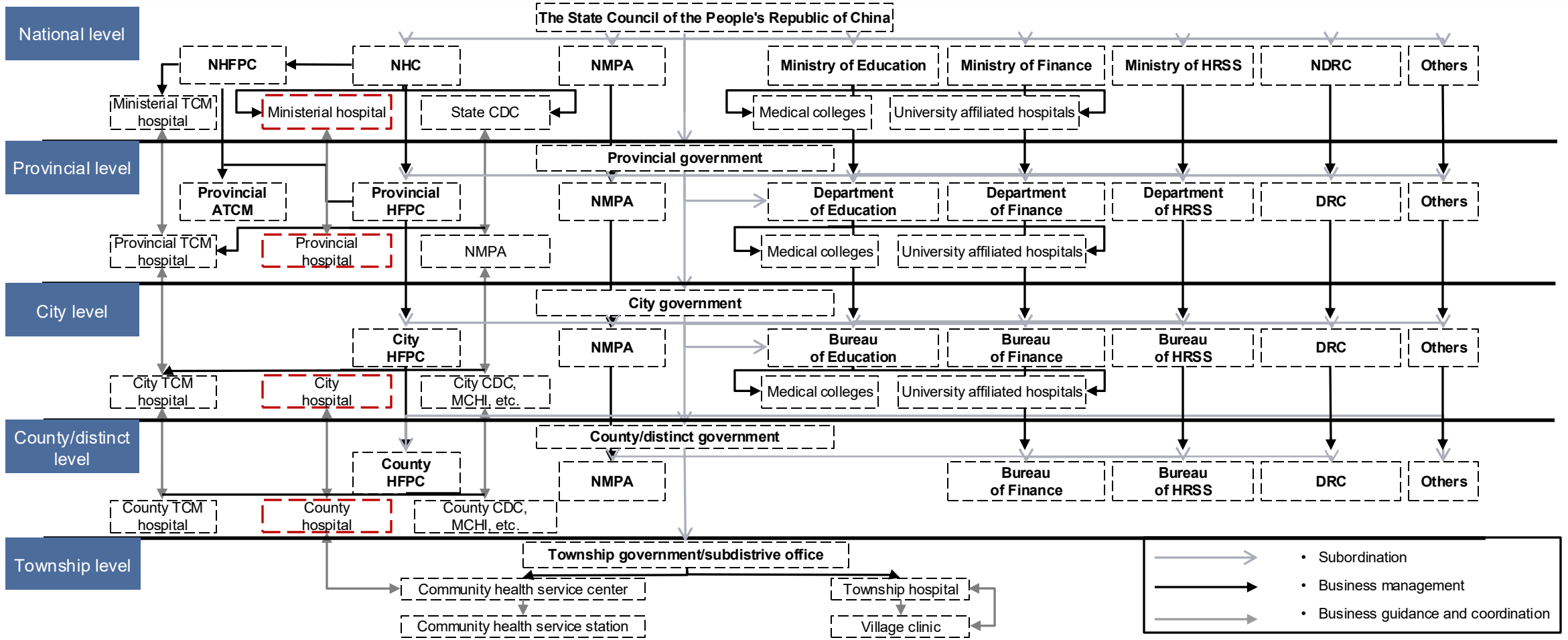
ppl million



Source: WHO, UN, China Insights Consultancy

Introduction to the Chinese healthcare system

Introduction to the Chinese healthcare system

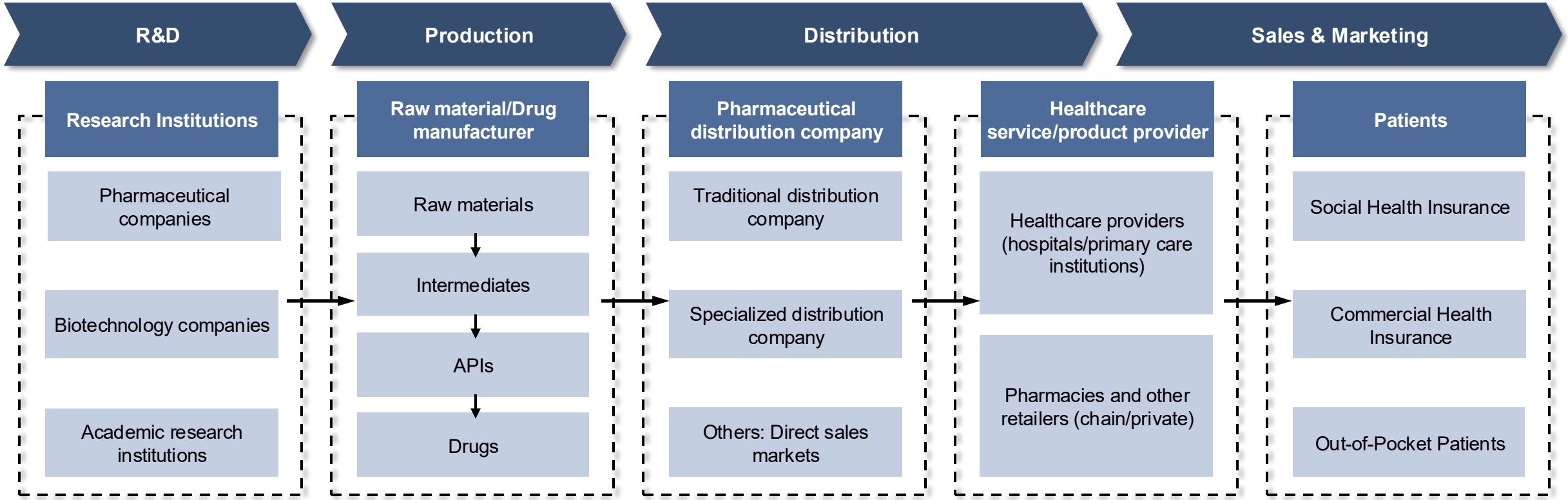


Source: WHO, China Insights Consultancy

The pharmaceutical industry value chain spans from upstream raw material producers and drug manufacturers to downstream sales terminals like hospitals, pharmacies, and patients

Pharmaceutical market value chain analysis

- The pharmaceutical industry is a crucial component of the national economy.
- Within the pharmaceutical industry, **raw material producers and drug manufacturers** are positioned at the upstream end of the value chain, providing production services. **Commercial companies** offer distribution and logistics services for the pharmaceutical industry. The downstream end of the value chain includes sales terminals such as **hospitals, pharmacies, and patients**.



Source: China Insights Consultancy

The differences between innovative drugs and generic drugs mainly include drugs registration and approval process, clinical trial requirements, R&D period, R&D cost, etc.

Introduction and analysis of the difference in innovative drug and generic drug

Innovative drug

- In the United States, the FDA's approval of new drugs is mainly for **new drug applications (NDA)**.
- In China, according to the " Requirements for Registration Classification and Application Dossiers of Chemical Drugs" (《化学药品注册分类及申报资料要求》), chemical drugs can be further divided into innovative drugs, modified new drugs, generic drugs, etc. **Class 1: Innovative drugs** never sold in domestic and overseas market. Refer to those containing new chemical compound with clear structure and pharmacological effect and with clinical value. **Class 2: Improved new drugs** never sold in domestic and overseas market. Refer to those with their structure, dosage form, formulation and technology, administration route and indications optimized based on known active ingredients, and with significant clinical advantages.

Generic drug

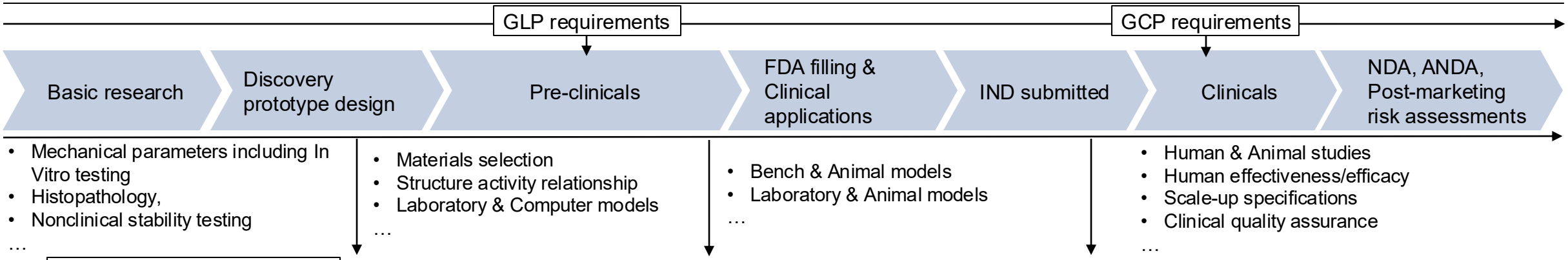
- In the United States, the application for marketing of generic drugs is subject to the **abbreviated new drug application (ANDA)**.
- In China, generic drugs belong to **Class 3 and 4 chemical drugs**. **Class 3:** Generic drugs of domestic applicants produced based on originators sold in overseas market but not yet in domestic market. The quality and efficacy of such drugs shall be consistent with that of originators. **Class 4:** Generic drugs of domestic applicants produced based on originators sold in domestic market. The quality and efficacy of such drugs shall be consistent with that of originators. Generic drugs in both China and the United States must have the same active ingredients, dosage forms, specifications, indications, routes of administration, and dosage as the reference original preparations, and must be proven to be as safe and effective as the reference preparations.

Item	Innovative drug		Generic drug
Application process	More strict		Easier
R&D cost	Higher		Lower
R&D period	Longer	**VS**	Shorter
Product price	Higher		Lower
Clinical trial (Not included bioequivalence trail)	Required		Not required (FDA)

Source: NMPA, FDA, China Insights Consultancy

The FDA new drug application process is a formal submission wherein drug sponsors propose that the FDA grants approval for a new pharmaceutical to be sold and marketed in the United States

Overview of FDA new drug application process



The FDA approval process

- The FDA's Center for Drug Evaluation and Research (CDER) in charge of overseeing the drug approval process before a drug is marketed. CDER review each drug closely using an independent team of clinicians and scientists who evaluate safety, efficacy and labeling of the drug product. After approval, FDA follow-up continues to make sure new drugs continue to be safe and effective.
- Generally, there are four phases of a drug approval process: 1.Pre-clinical, IND; 2.Clinical; 3.NDA Review; 4.Post-marketing risk assessments. The full research, development and approval process can last from 12 to 15 years. However, In order to incentivize the development of therapies to fill unmet needs for serious conditions, the FDA has developed various programs to expedite drug development and review. These four programs are: **fast track**, breakthrough therapy, accelerated approval, and priority review.
- In addition, supporting the development and evaluation of new treatments for rare diseases is also a key priority for the FDA The FDA has authority to grant **orphan drug designation** to a drug or biological product to prevent, diagnose or treat a rare disease or condition.

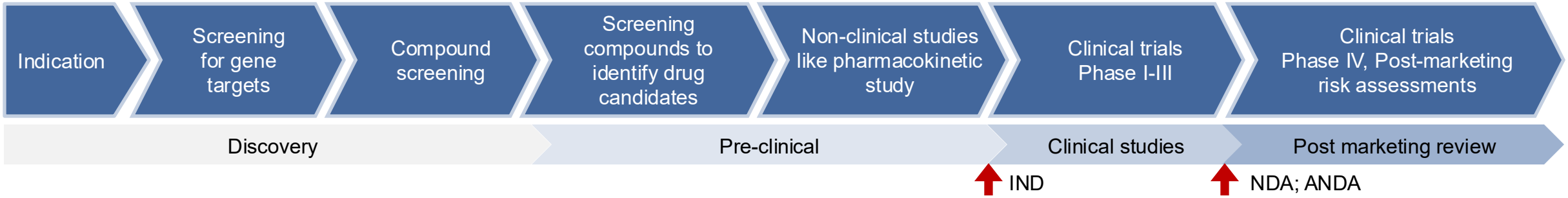
The FDA's Fast Track program is designed to facilitate the development and expedite the review of drugs to treat serious conditions and fill an unmet medical need. The purpose is to get important new drugs to the patient earlier. The Fast Track program is intended to help patients with serious conditions receive new drugs more quickly.

The Orphan Drug Act (ODA) was passed in 1983 to encourage the development of drugs for rare diseases. The FDA's Orphan Drug Designation program provides orphan status to drugs and biologics that are intended for the safe and effective treatment, diagnosis or prevention of rare diseases or disorders that affect fewer than 200,000 people in the US. The program provides incentives for sponsors to develop products for rare diseases.

Source: FDA; China Insights Consultancy

The CDE of NMPA is responsible for evaluating drug clinical trial applications, drug marketing authorizations, supplementary applications, registration renewal applications of drugs manufactured overseas

Overview of NMPA and CDE new drug application process



Non-clinical research refers to various toxicity tests conducted in laboratory conditions using experimental systems to evaluate drug safety, including single-dose toxicity tests, repeated-dose toxicity tests, reproductive toxicity tests, mutagenicity tests, carcinogenicity tests, various irritancy tests, dependence tests and other toxicity tests related to drug safety evaluation.

Animal experiments are widely used in medical, biomedical and veterinary research, and are essential means of drug development and preclinical testing, including toxicology and safety studies. They help us advance our scientific understanding, serve as models to study disease, help us develop and test potential new medicines and therapies. Animal experiments eliminate some potential drugs as either ineffective or too dangerous to use on human beings.

Good clinical practice (GCP) is an international ethical and scientific quality standard for designing, recording and reporting trials that involve the participation of human subjects. The GCP guidelines detail the requirements for trial documentation, protocol amendments, requirements such as indemnity, reporting lines for adverse events and provision of medical care for trial participants. Compliance with this standard provides public assurance that the rights, safety and wellbeing of trial subjects are protected and that clinical-trial data are reliable.

Clinical trials of biomedical interventions typically proceed through four phases:

- Phase I evaluates the tolerability and pharmacokinetics of a drug in human body.
- Phase II conducts a preliminary assessment of the efficacy and safety of a drug in a specific population with defined indication.
- Phase III evaluates overall efficacy and safety profile with an adequate sample size and robust control measures, to provide confirmatory evidence.
- Phase IV is the post-marketing research conducted after the approval, to investigate the efficacy and AEs under widespread use conditions.

Source: NMPA; China Insights Consultancy

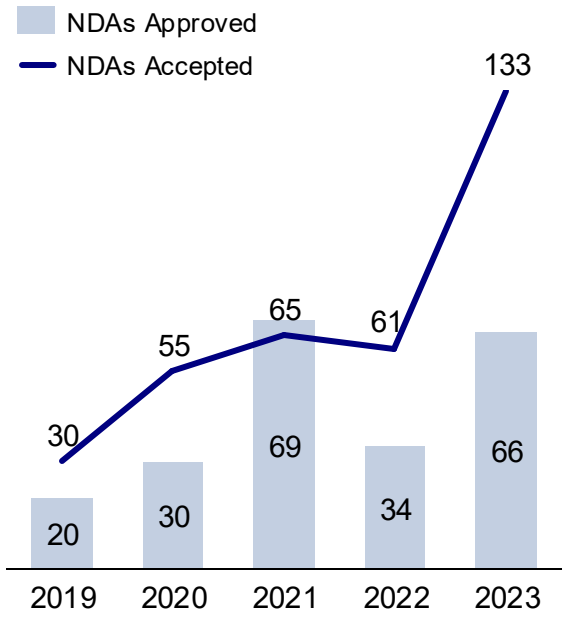
With the optimization of the evaluation and approval process for innovative drugs, the number of accepted and approved innovative drug NDAs has increased in recent years

Introduction to the evaluation and approval pathway for innovative drugs in China

- "The Opinion on Deepening the Reform of the Evaluation and Approval System to Encourage Innovation in Drugs and Medical Devices" (*《关于深化审评审批制度改革鼓励药品医疗器械创新的意见》*) and similar encouraging/supportive policy changes have transformed the regulatory system and environment of the pharmaceutical market in China. It promotes the acceleration of drug approval and encourages innovation in drugs and medical devices.

	Previously	Currently
Reform clinical trial management	• Clinical trial applications require a lengthy approval process **(12-18 months)**	• CTA approval **(60 days)** • Acceptance of clinical trial data generated abroad
Accelerate approval	• Lengthy review and approval processes • Separate approvals for active pharmaceutical ingredients and formulations	• **Rapid tracking and prioritized review** for drugs meeting medical needs (such as cancer) • **Support for conditional approval** based on surrogate endpoints to meet medical needs • **Associated approval** for formulation and active pharmaceutical ingredients, excipients, and packaging
Achieve global application	• Before a drug can participate in International Multicenter Clinical Trials (IMCT) in China, it **must be in Phase II or Phase III clinical research or have obtained marketing approval overseas**	• **Acceptance of overseas clinical data** • Removal of restrictions on imported drugs and clinical trial registration
Protect innovators	• Patent Application System	• Patent Linkage System • Drug Patent Term Extension System • Data Protection for Innovators • Marketing Authorization Holder (MAH) System

Number of Innovative Drug NDAs Accepted and Approved, 2019-2023



Source: NMPA; China Insights Consultancy

An abbreviated new drug application (ANDA) contains data which is submitted to FDA for the review and potential approval of a generic drug product

Overview of FDA generic drug application process

- Drug companies must submit an **abbreviated new drug application (ANDA)** to FDA for approval to market a generic drug that is the same as (or bioequivalent to) the brand product. FDA reviews the application to ensure drug companies have demonstrated that the generic medicine can be substituted for the brand-name medicine that it copies.
- Within 60 days after receiving the application, the FDA will conduct a preliminary integrity check on the materials and decide whether the generic drug can be registered and further reviewed. Applicants who pass the preliminary review will receive a written notice. The subsequent FDA review mainly includes four aspects of review, **namely chemical and microbiological review, label review, bioequivalence review and production site inspection**. After all of them are passed, the generic drug applied for marketing will be approved by ANDA.

Materials for ANDA

1	ANDA application form
2	Contents of application materials
3	The basis for the ANDA application must include the name, dosage form and strength of the referenced drug, and a statement as to whether the referenced drug is still in the market exclusivity period
4	The conditions of use of the generic drug include the conditions of use of the referenced brand-name drug/innovator drug.
5	The active ingredient is the same as that of the brand-name drug/innovator drug
6	The route of administration, dosage form and strength should be consistent with the reference brand-name drug/innovator drug
7	The results of the bioequivalence (BE) study to show that the generic drug is equivalent to the reference the brand-name drug/innovator drug and provide the analysis and statistical methods used
8	The label is the same as the brand-name medicine's label
9	All Common Technical Document (CTD) information for Chemistry, Manufacturing and Controls (CMC), production records, description of production equipment and information related to excipients
10	Generic drug samples
11	Other information required by FDA
12	Relevant patents or exclusivities are addressed
13	Financial certifications

Source: FDA, China Insights Consultancy

In China, for generic drugs, when submitting a registration application after completing clinical trials, the applicant must submit the corresponding materials and trial data

Overview of NMPA generic drug application process

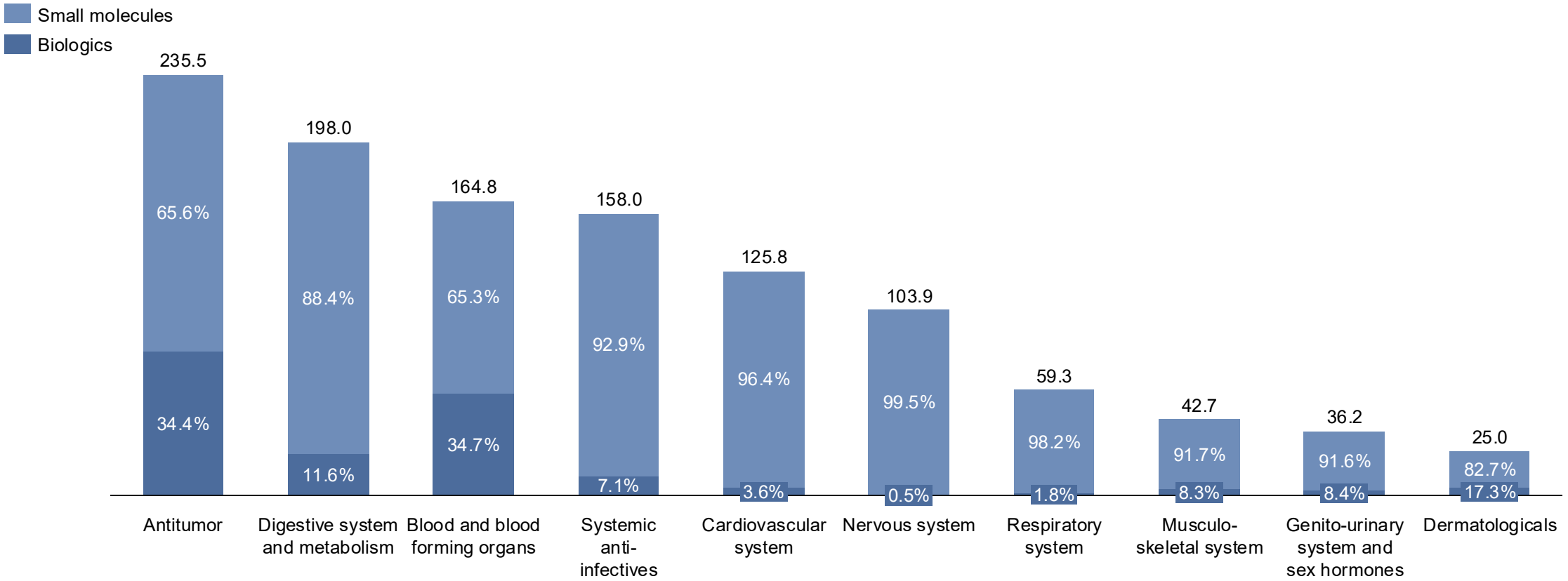
- For generic drugs in China, when applying for marketing registration **after completing clinical trials**, the materials submitted to NMPA should include a **clinical trial database** and a **submission document** prepared in accordance with "M4: Common Technical Documents (CTD) for the Registration of Pharmaceuticals for Human Use" 《M4：人用药物注册申请通用技术文档（CTD）》, which includes five modules.

	Organization	Content
Module 1	**Administrative Information and Prescribing Information**	• This module should contain documents specific to each region; for example, application forms or the proposed label for use in the region.
Module 2	**Common Technical Document Summaries**	• This module should begin with a general introduction to the pharmaceutical, including its pharmacologic class, mode of action, and proposed clinical use
Module 3	**Quality**	• Mainly includes basic information of API, CMC (chemistry, production and quality control), property identification, quality control, reference drugs, packaging system, stability, dosage form, product composition, excipients and literature references, etc.
Module 4	**Nonclinical Study Reports**	• Mainly includes pharmacology, pharmacokinetics, toxicology and literature references
Module 5	**Clinical Study Reports**	• A bioequivalence test report is required, including the selection of reference preparations and test drugs, test design and evaluation, etc.

- The applicant for the registration of generic drugs is required to fill out the drug registration application form and submit the registration application materials to the CDE of NMPA. The CDE will first conduct a formal review of the submitted materials, and if they meet the requirements, the application will be accepted. An acceptance notice will be sent to the applicant, and the evaluation process will be initiated. During the evaluation process, based on the risk situation of the applicant and the drug variety, a decision will be made **within 40 days** on whether to initiate a site inspection or sample registration testing.
- The CDE will conduct a comprehensive evaluation of the drug's **safety, efficacy, and quality control based on the drug registration application materials, inspection results, and test results**. If necessary, the CDE may request the applicant to provide additional materials. After forming a comprehensive opinion, the **CDE will submit it along with other relevant documents to the NMPA**, which will make the final approval decision based on the comprehensive opinion.

Source: NMPA, China Insights Consultancy

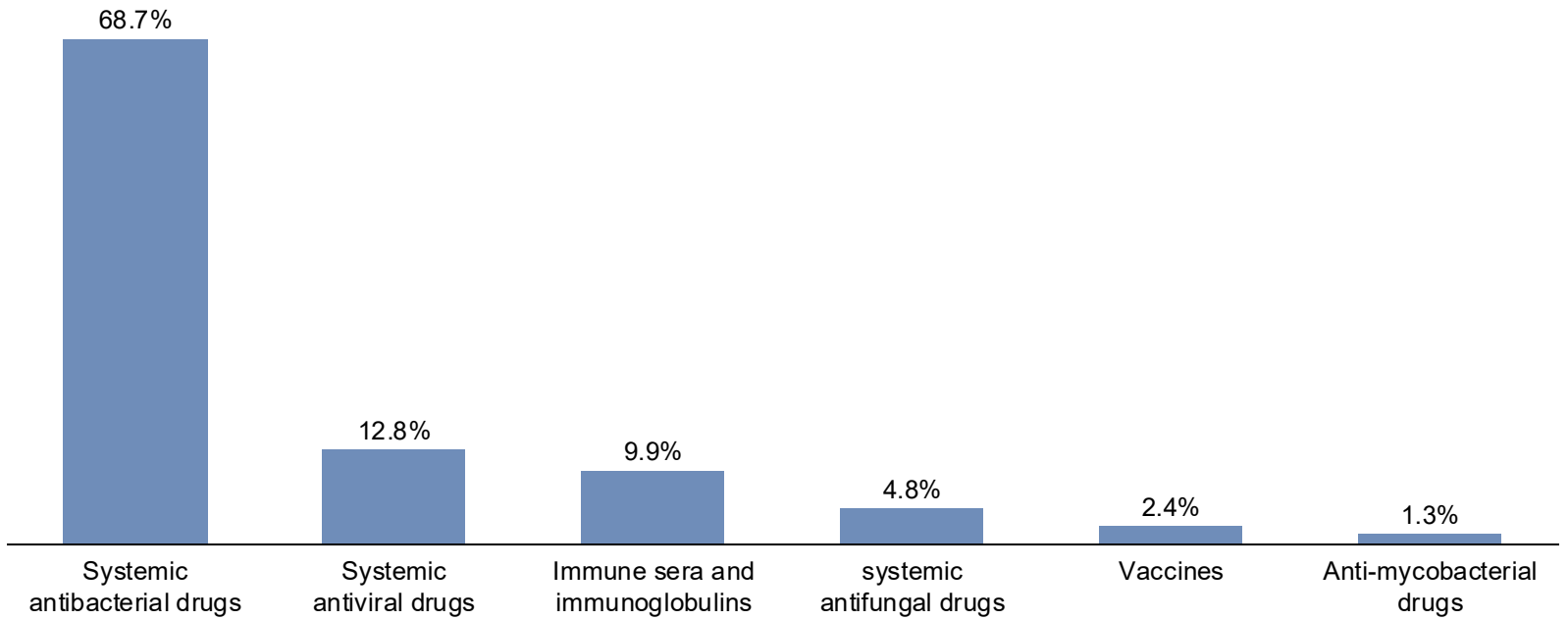
Top 10 Therapeutic fields in terms of Revenue in China, 2024



- Innovative small molecules are at the forefront of drug development due to their versatility and effectiveness in treating a wide range of conditions, from infectious diseases and cancer to neuropsychiatric and reproductive disorders. They represent the most widely approved drug class, with 32 approved small molecule drugs in the U.S. in 2024, accounting for 64% of all approved drugs, and 42 approved drugs in China in 2024, accounting for 45% of all approved drugs.

Source: National Bureau of Statistics, NHC, China Insights Consultancy

Breakdown of systemic anti-infectives, in terms of sales value, 2024



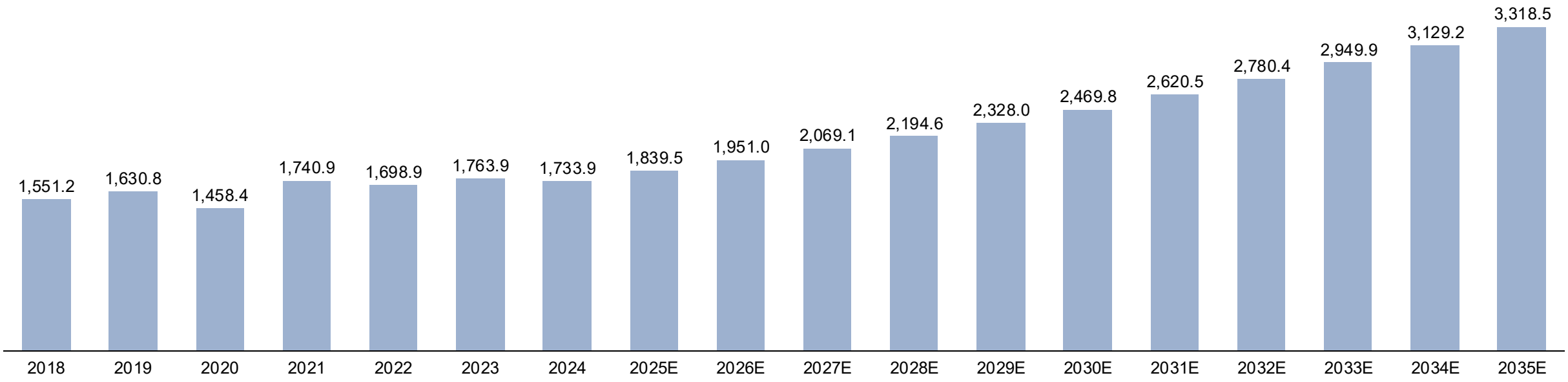
Source: National Bureau of Statistics, NHC, China Insights Consultancy

Market size of pharmaceutical market in China, by drug type, 2018-2035E

Market size of pharmaceutical market in China

CAGR	2018-24	2024-35E
China pharmaceutical market	1.9%	6.1%

RMB billion



In 2024, China's pharmaceutical market saw a modest decline in overall sales, attributed to stringent healthcare cost control policies, the expanded implementation of volume-based procurement driving steep price cuts, tighter regulatory oversight on commercialization practices, and broader macroeconomic pressures dampening healthcare expenditure. These factors collectively contributed to a contraction in market value amid the industry's ongoing adaptation to policy-driven structural reforms. The contraction in 2024 represents a transitory adjustment post-pandemic, attributable to demand normalization and market recalibration. Sustained recovery is expected as structural stability accelerates, and R&D pipelines underpin long-term growth.

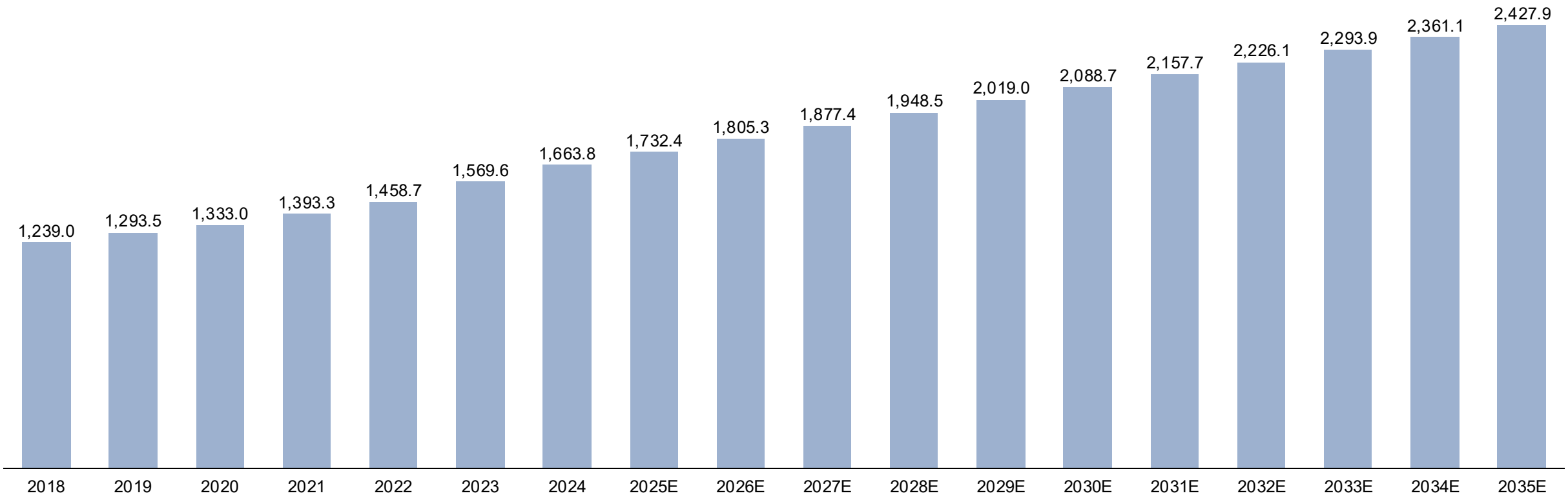
Source: National Bureau of Statistics, NHC, China Insights Consultancy

Market size of pharmaceutical market in global, by drug type, 2018-2035E

Market size of pharmaceutical market in global, by drug type

CAGR	2018-24	2024-35E
Global pharmaceutical market	5.0%	3.5%

USD billion



Source: WHO, China Insights Consultancy

The differences between small molecule drugs and biologics include structure, administration, penetrability, etc.

Comparison of small molecule drugs and biologics

- Small molecule drugs, especially oral small molecule drugs, have some advantages. First, small molecule drugs can act on both cell surface targets and intracellular targets, enriching the selection of innovative drug targets. Second, from the perspective of patient use, oral small molecule drugs can improve drug accessibility and patient compliance. From the perspective of overall social medical costs, oral small molecule drugs can save patients from frequent medical treatment and injections, saving a lot of medical resources and costs.

Analysis of the advantages and disadvantages of small molecule drugs and biologics

Item	Small molecule drugs	Biologics
Relative molecular mass (Da)	<1,000	150,000
Structure	Simple and stable structure	The structure is complex, usually showing a certain degree of heterogeneity, and is greatly affected by the production process
Scope	Intracellular, extracellular	Cell surface
Route of administration	Oral, intravenous injection, etc.	Intravenous or subcutaneous injection
Penetrability	Easily penetrates cell membranes and partially penetrates the blood-brain barrier	Can hardly cross blood-brain barrier
Storage and transport	Relatively low sensitivity to storage conditions and easy to transport	More stringent storage and transportation conditions
Absorption	Some small molecules have high bioavailability	Low bioavailability, absorbed by the lymphatic system

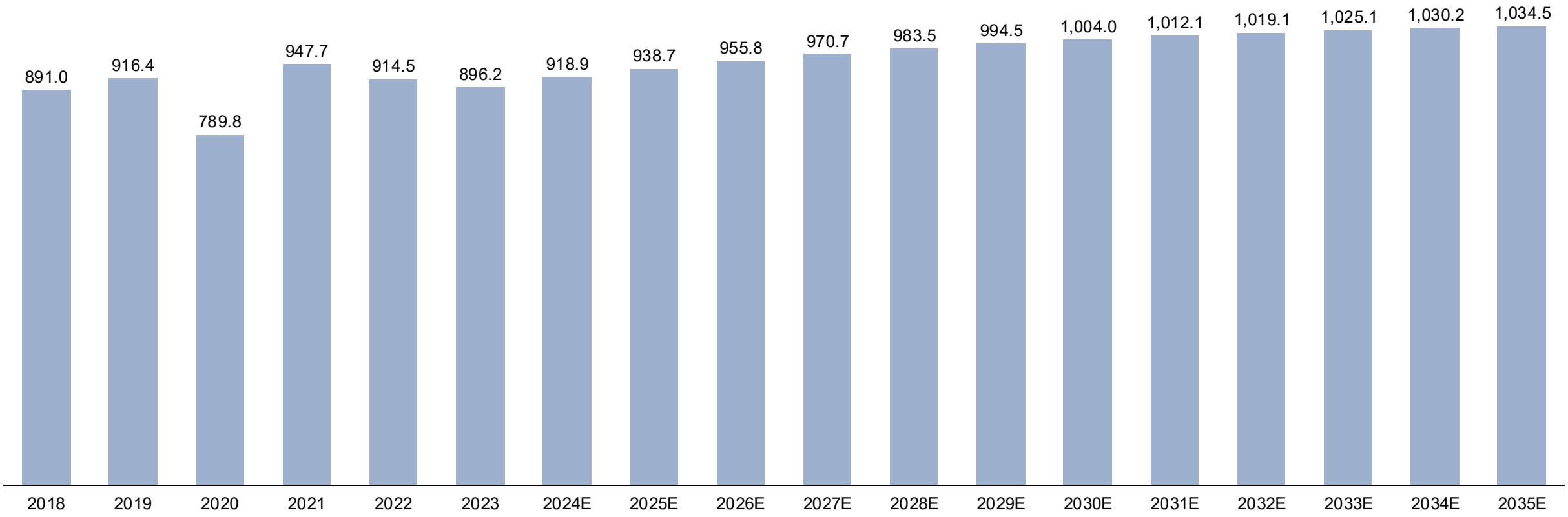
Source: China Insights Consultancy

Market size of small molecule drug in China, 2018-2035E

Market size of small molecule drug in China

CAGR	2018-23	2023-35E
Small molecule drugs	0.1%	1.2%

RMB billion



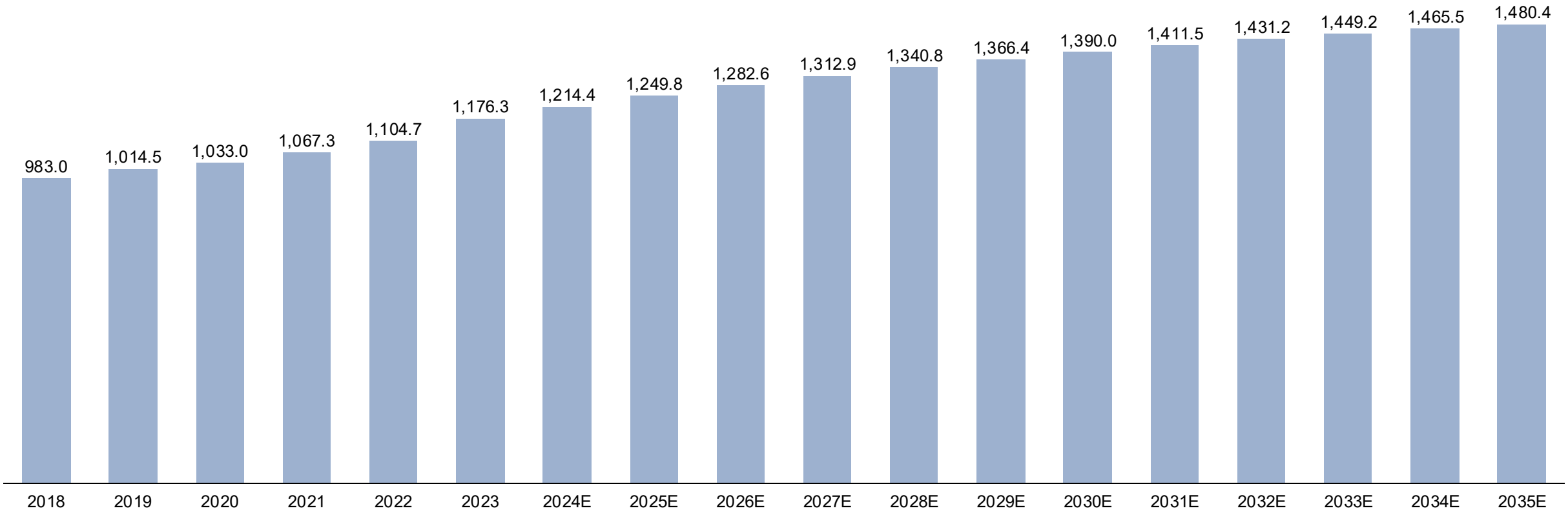
Source: National Bureau of Statistics, NHC, China Insights Consultancy

Market size of small molecule drug in global, 2018-2035E

Market size of small molecule drug in global, 2018-2035E

CAGR	2018-23	2023-35E
Small molecule drugs	3.7%	1.9%

USD billion



Source: WHO, China Insights Consultancy

Table of contents

Innovative drugs (Class 1) refer to the drugs containing new chemical compound with clear structure and pharmacological effect and with clinical value

Overview of innovative drugs

Definition:

- In China, according to the "Provisions for Drug Registration" (《药品注册管理办法》), drugs are classified and registered for management based on categories such as traditional Chinese medicine, chemicals, and biologics. Among them, chemical drugs are those produced using techniques such as chemical synthesis, with relatively small molecular weights, and are also referred to as **chemical small molecule drugs**.
- According to the "Requirements for Registration Classification and Application Dossiers of Chemical Drugs" (《化学药品注册分类及申报资料要求》), chemical drugs can be further divided into innovative drugs, modified new drugs, generic drugs, etc. **Class 1: Innovative drugs** never sold in domestic and overseas market. Refer to those containing new chemical compound with clear structure and pharmacological effect and with clinical value. **Class 2: Improved new drugs** never sold in domestic and overseas market. Refer to those with their structure, dosage form, formulation and technology, administration route and indications optimized based on known active ingredients, and with significant clinical advantages.

Characteristics of innovative small molecule drugs

✓ Small molecule drugs typically have a molecular weight of less than 1000Da. Currently marketed small molecule targeted drugs can be classified based on the target and mechanisms of action, mainly into kinase inhibitors, epigenetic inhibitors, and proteasome inhibitors. The diverse mechanisms of action of these drugs allow small molecule drugs to be used in a wide range of therapeutic areas, with the main indications being oncology, neurology, antivirals, cardiovascular diseases, and gastrointestinal disorders.

Drug Type	Mechanism & Application
Kinase inhibitor	Protein kinases influence protein activity and function levels through phosphorylation. Inhibitors that can block the action of protein kinases are commonly used in the treatment of cancer and immune diseases
Epigenetic inhibitor	Epigenetics primarily studies heritable phenomena that alter phenotype without changes to the DNA sequence. It is widely applied in the treatment of cancers, immune diseases and rare diseases
Proteasome inhibitor	By binding to the functional groups at the active site of proteases, these inhibitors reduce protease activity and suppress viral replication, mainly used in cancer treatment

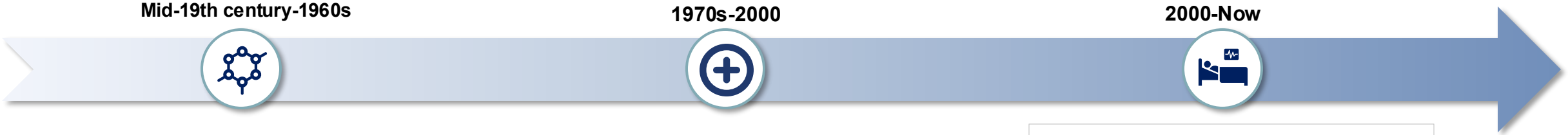
Importance of innovative drugs

- ✓ Improve the development of novel molecular structures
- ✓ Meet the **growing and vastly unmet demands** for disease treatment
- ✓ Providing **safer and more effective treatment options** for a wide range of patients

Sources: Signal Transduction and Targeted Therapy, NMPA, China Insights Consultancy

The development history of innovative small molecule drugs includes three main stages, compound-based stage, target-based stage and patient-based stage

Development history of innovative small molecule drugs



01

Compound-based stage

- The first stage is the compound-based stage. Drug development mainly relied on extracting compounds from nature or synthesizing them through chemical methods, with the aim of identifying bioactivity in these compounds for disease treatment. **Penicillin** is a typical example of this stage. It was discovered and named by British bacteriologist Alexander Fleming in 1928, and after decades of isolation and purification, it was officially approved for market use in 1943.

02

Target-based stage

- The second stage is the target-based stage, which began with the rise of molecular biology, high-throughput screening, and combinatorial chemistry in the 1970s. With a deeper understanding of the nature and mechanisms of diseases, drug development shifted towards identifying specific genetic mutations (targets) carried by patient populations based on clear molecular biological mechanisms. Compounds that could regulate these targets were then screened and optimized for drug-like properties, with the final step being clinical validation. In 2001, **imatinib (Gleevec)**, developed by Novartis, was approved by the FDA for the treatment of cancers caused by cell division. It became the world's **first approved small molecule targeted therapy drug.**

03

Patient-based stage

- The third stage of small molecule drug development is the patient-based era, which began with the completion of the **human genome project** in 2000. The core concept of this stage is to develop drugs based on the patient's specific disease etiology, moving beyond reliance on a single target. Instead, treatments are tailored to the genetic characteristics of different patients, leading to personalized medicine. A representative example of this stage is **gefitinib**, the world's **first EGFR tyrosine kinase inhibitor**. It pioneered the use of biomarker-based companion diagnostics and marked the official beginning of the era of precision medicine.

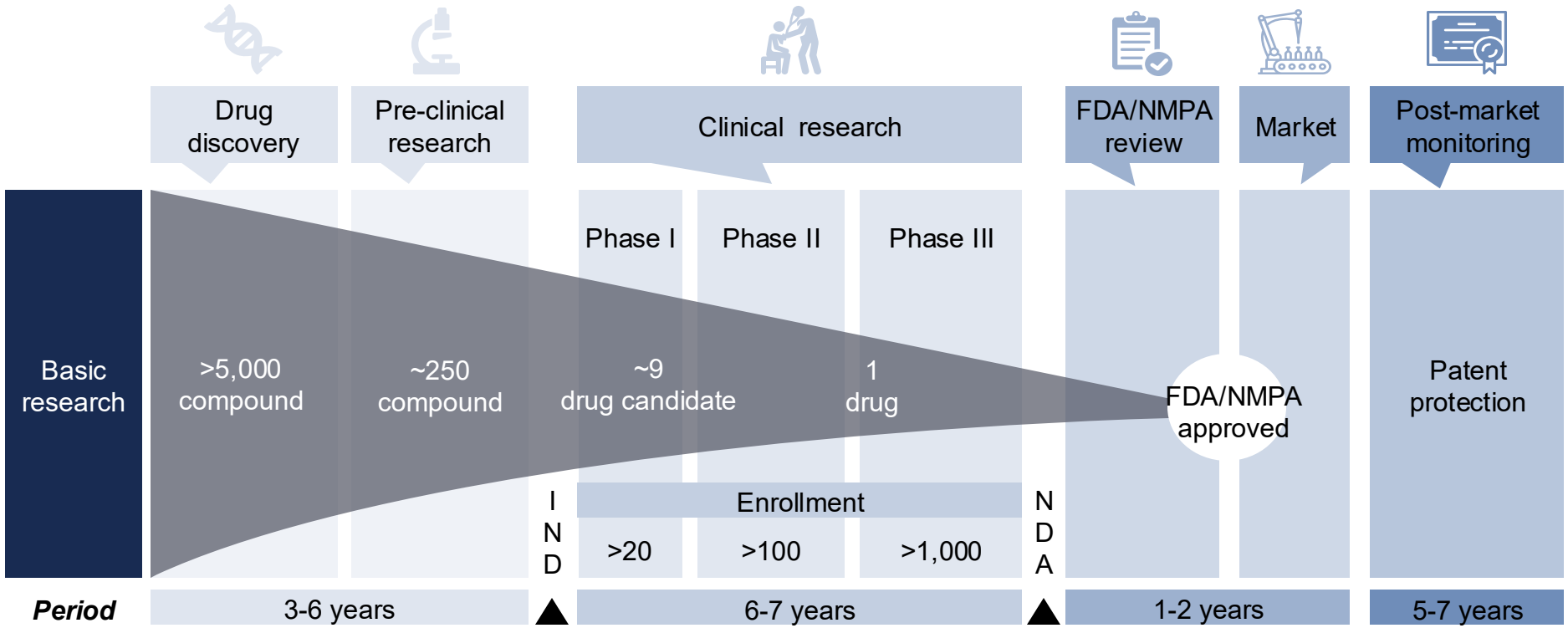
Sources: China Insights Consultancy

The R&D of innovative small molecule drugs is a long-duration process, target and molecule structure discovery are the main challenges in the drugs design

Introduction of drug discovery and development process

- The R&D cycle of innovative small molecule drugs, from target identification to regulatory approval and market launch, typically takes several decades. Due to uncertainties related to factors such as compound properties, dosage form, and stability, it is a **high-risk, high-investment, and long-duration** process.

Innovative small molecule drugs discovery and development process



- In the entire R&D process of innovative small molecule drugs, **target discovery and molecule structure discovery** are key challenges in small molecule drug design. The human body contains more than 20,000 types of proteins, however, drugs with well-defined target mechanisms are focused on only 600-700 proteins. This is because proteins have a wide variety of structural and functional differences, and the characteristics of **different proteins** can lead to varying biological effects of drugs.
- Additionally, the **binding affinity** between the target and the drug is another critical factor influencing the drug's action. Appropriate drug structural modifications are necessary to effectively regulate and optimize the drug's properties.

Sources: China Insights Consultancy

The current innovative drug R&D models are mainly divided into three types: independent R&D, license-in and cooperative development

Introduction of R&D model of innovative drug companies

- The patent protection period for new drugs is 20 years. When a new drug is approved for sale, the actual effective patent protection period usually remains 6-10 years. If many generic drugs appear after the patent expires, the sales price and sales of patented drugs will drop rapidly. This is the **"patent cliff"** problem that pharmaceutical companies must face. The only way to solve this problem is to continuously develop new drugs and continuously enrich the pipeline of products under development.
- The current innovative drug development models are mainly divided into the following three types:

R&D model	Independent R&D	License-in	Cooperative development
Introduction	Refers to pharmaceutical companies that primarily adopt independent R&D as their main development model, with the **market (clinical needs) as the primary driver**. These companies need to establish strong drug discovery and clinical development teams, possess substantial technical expertise, and have a rich pipeline of independent research products	The strategy of focusing on license-in, compared to independent R&D, is **more cost-effective**, has a **higher success rate**, and **shorter development cycles**. It is suitable for pharmaceutical companies with strong product screening capabilities and clinical development expertise	Sign a **cooperative development contract** to jointly undertake the clinical development and industrialization of drugs in the cooperation
Income distribution	The drug R&D results obtained are owned by the enterprise, and all subsequent operating income from successful listing belongs to the company	The company pays the cost of introducing the drug in advance and carries out subsequent research and development. The profit after the drug is successfully developed and launched on the market is determined according to the contract	Income distribution is carried out according to the contract. The actual ratio may depend on the cost or resource input depending on the specific situation
Cost allocation	All by the companies	The in-licensing companies do not need to afford the costs of drug discovery	Cost allocation is carried out according to the contract
Risk-taking	All by the companies	The in-licensing companies assume the clinical development risks	The risks are shared jointly by both parties in the collaboration

Sources: China Insights Consultancy

Innovative drugs accelerate approval pathways in China and the US

Innovative drugs policy in China and the US

✓ The FDA currently has four accelerate approval pathways, including Priority Review, Accelerate Approval, Fast Track, and Breakthrough Therapy Designation:

	Start year	Objective and measure
Priority Review	1992	To shorten the review process from 10 months to 6 months
Accelerate Approval	1992	If the drug shows significant clinical efficacy, it may be approved based on evidence provided by a surrogate endpoint or a single-arm clinical trial, subject to verification by further confirmatory trials
Fast Track	1997	Accelerate the development process and provide rolling review and approval of applications
Breakthrough Therapy Designation	2012	More regular guidance from the FDA in the early stages

✓ China's pharmaceutical reforms in recent years have also introduced a series of accelerate drug review and approval pathways to speed up drug development and review:

	Start year	Objective and measure
Priority Review	2015	The standard review period is shortened from 200 days to 130 days
Conditional Approval	2017	It may be approved based on evidence provided by a surrogate endpoint or a single-arm clinical trial, subject to verification by further confirmatory trials
Overseas New Drugs Catering to Clinical Urgent Needs	2018	Completed within 3 months after acceptance for orphan diseases treatment drugs; and 6 months after acceptance for other overseas new drugs
Breakthrough Therapy Designation	2020	Accelerate the development process and provide rolling review and approval of applications. More regular guidance from the NMPA in the early stages

Sources: FDA, NMPA, China Insights Consultancy

China continues to deepen reforms in pharmaceutical review and approval, gradually transitioning the drug market towards a landscape led by innovative drugs (1/2)

Overview of China's policy encouraging innovation in innovative drugs

Department	Policy Name	Key Contents	Issuance Time
National Health Commission	《深化医药卫生体制改革 2023年下半年重点工作任务》	Promoting medical and pharmaceutical reform and innovation. Supporting drug R&D innovation, standardizing centralized procurement to ensure quality and availability of medications	2023-07
CDE	《药审中心加快创新药上市许可申请审评工作规范(试行)》	This accelerated review and approval process targets three categories of innovative drugs: breakthrough therapy drugs, innovative drugs for children, and innovative drugs for rare diseases, expediting their market entry to meet the medication needs of relevant patients	2023-04
The State Council	《"十四五"市场监管现代化规划》	Steadily enhance the safety, efficacy, and accessibility of drugs. Optimize management methods to accelerate the market entry of new and high-quality drugs. Improve rapid review and approval mechanisms for innovative drugs and vaccines, speeding up access to urgently needed drugs for clinical use and rare disease treatments. Strengthen guidance for the development of major innovative drugs. Encourage simultaneous domestic and international research and application for new drugs	2023-04
The State Council	《"十四五"国民健康规划》	Deepen the reform of the drug and medical device review and approval system. Accelerate the review and approval of qualifying innovative drugs, urgently needed drugs in short supply, medical devices, and treatments for rare diseases	2022-05
NMPA	《中华人民共和国药品管理法实施条例(修订草案征求意见稿)》	In the event of a patent dispute during a drug registration application, the parties may file a lawsuit in the people's court or apply for an administrative ruling from the State Council's patent administration department. During this period, the technical review of the drug will not be suspended	2022-05
CDE	《单臂临床试验用于支持抗肿瘤药上市申请的适用性技术指导原则》	The development strategy of single-arm clinical trials has significantly shortened the time to market for new drugs. In recent years, many new drugs have demonstrated highly promising efficacy data in the early stages of clinical research. As a result, an increasing number of development companies are opting to use single-arm clinical trials to support the marketing applications for anti-tumor drugs	2022-03
CDE	《药审中心加快创新药上市申请审评工作程序(试行)(征求意见稿)》	The main focus is to encourage the research and development of new drugs to meet clinical needs, promptly summarize and apply experiences from emergency reviews during the pandemic, and accelerate the review process for innovative drugs	2022-02

Source: CDE; NMPA; China Insights Consultancy

China continues to deepen reforms in pharmaceutical review and approval, gradually transitioning the drug market towards a landscape led by innovative drugs (2/2)

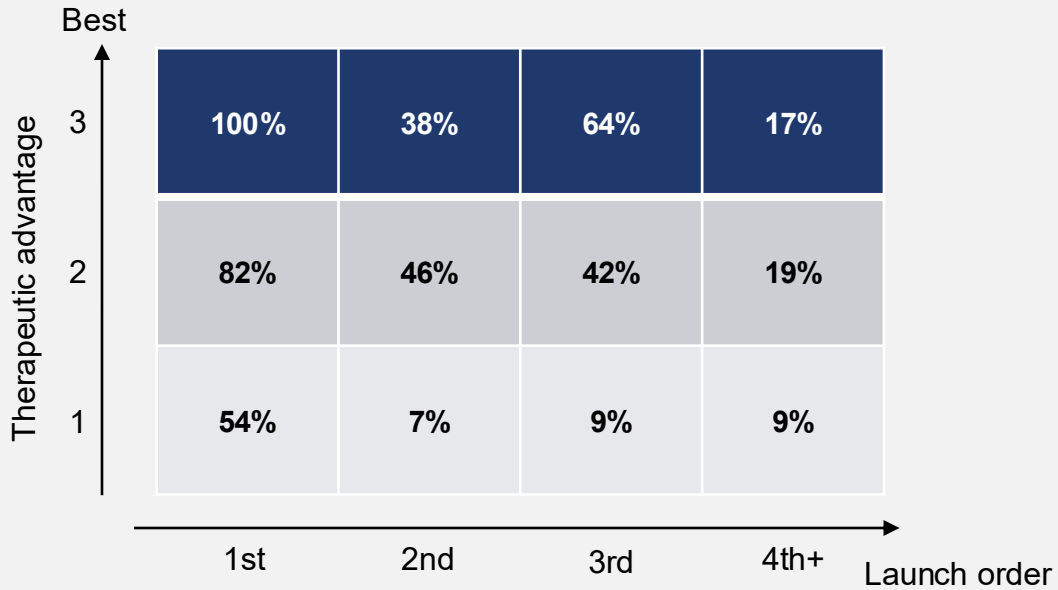
Overview of China's policy encouraging innovation in innovative drugs

Department	Policy Name	Key Contents	Issuance Time
MIIT and others	《"十四五"医药工业发展规划》	Promoting the industrialization and application of innovative drugs and high-end medical devices, and improving the support system for pharmaceutical innovation	2022-01
The State Council	《"十四五"市场监管现代化规划》	Improving the rapid review and approval mechanisms for innovative drugs, vaccines, and medical devices to accelerate the review and approval process for urgently needed drugs for clinical use, treatments for rare diseases, and medical devices	2022-01
NDRC	《"十四五"生物经济发展规划》	Developing synthetic biology technologies and promoting innovation in synthetic biology. Systematically advancing applications in areas such as new drug development, disease treatment, agricultural production material synthesis, environmental protection, energy supply, and new material development	2021-12
NMPA	《"十四五"国家药品安全及促进高质量发展规划》	The regulatory environment supporting high-quality industrial development is further optimized. The reform of the review and approval system continues to deepen, approving a batch of urgently needed innovative drugs for clinical use, accelerating the market entry of innovative drugs with clinical value to promote public health. The evaluation capability of innovative products has significantly improved, enabling globally innovative drugs and medical devices applied for in China to be quickly launched in the domestic market	2021-12
The State Council	《"十四五"全民医疗保障规划》	Improving the evaluation mechanism for drugs covered by medical insurance, strengthening the monitoring of the implementation of the medical insurance drug list and the evaluation of innovative drugs, supporting pharmaceutical innovation, and enhancing the accessibility of negotiated drugs	2021-09
NPC	《中华人民共和国国民经济和社会发展第十四个五年规划和2035年远景目标纲要》	Improving the rapid review and approval mechanisms for innovative drugs, vaccines, and medical devices, accelerating the review and approval of urgently needed drugs and medical devices for clinical use and rare disease treatments, and facilitating the prompt domestic launch of urgently needed new drugs and medical devices already approved abroad	2021-03
NDRC and others	《关于扩大战略性新兴产业投资培育壮大新增长点增长极的指导意见》	Implement a biotechnology benefit project to create a market for domestically innovated drugs and other products	2020-09
NMPA	《突破性治疗药物申评工作程序(试行)》	During clinical trials, applicants can apply for the breakthrough therapy designation for innovative or improved new drugs that treat life-threatening diseases or significantly improve quality of life, typically no later than the start of phase I trials	2020-07

Source: CDE; NMPA; China Insights Consultancy

Comparison of first-in-class and best-in-class innovative drugs

Comparison of first-in-class and best-in-class innovative drugs

	First-in-class (FIC)	Best-in-class (BIC)
Definition	• The FDA defines a first-in-class drug as one that uses a novel and unique mechanism of action to treat a medical condition. FIC drugs target molecules that have not been targeted by preceding drugs and provide a novel mechanism of action, adding to new therapeutic options for patients	• A best-in-class drug strategy may involve demonstrating therapeutic superiority without compromising safety or quality of life to become the first choice of treatment
Comparison		

Key insights

- ✓ The oncology market prefers first-in-class (FIC) products. For example, Johnson & Johnson/AbbVie ibrutinib (Imbruvica) is launched 4 years earlier than its competitors, establishing its dominance in the market; and pembrolizumab (Keytruda) and nivolumab (Opdivo), which pioneered the immunosuppressant industry, have been proven to have excellent therapeutic effects after long-term use.
- ✓ In the non-oncology market, the preference for fast followers is even more obvious. In migraine, psoriasis and some other inflammatory diseases, it is more difficult to develop products with obvious differentiation, so it is difficult for a single drug to dominate the market.

Sources: Nature Reviews Drug Discovery, China Insights Consultancy

Entry barriers to innovative drug industry

Entry barriers to innovative drug industry

Technology and expertise barrier	➢ Developing innovative drugs requires cutting-edge technologies and expertise in molecular biology, chemistry, and clinical development. Companies with limited resources or technical capabilities may struggle to compete with more established players who possess the necessary infrastructure and skilled personnel. Besides, it's difficult to develop the new molecular.
Capital barrier	➢ Developing innovative drugs, especially new molecular entities, requires significant financial investment. The costs involved in drug discovery, preclinical testing, clinical trials, and regulatory approval are substantial, often running into lots of money. These high costs create a barrier for smaller companies to enter the market.
Clinical trials barrier	➢ Innovative drug development often involves large-scale, multi-phase clinical trials, which can be difficult and expensive to execute. Recruiting patients for clinical trials, particularly for rare diseases or specific patient populations, presents additional challenges and delays.
Intellectual property barrier	➢ Patent laws create a legal barrier to entry by protecting the intellectual property (IP) rights of innovative drug developers. Other forms of IP protection, such as data exclusivity and trade secrets, play a critical role in maintaining a competitive edge in the innovative drug market. Legal challenges to patents, such as patent infringements or disputes, can also serve as barriers to market entry.

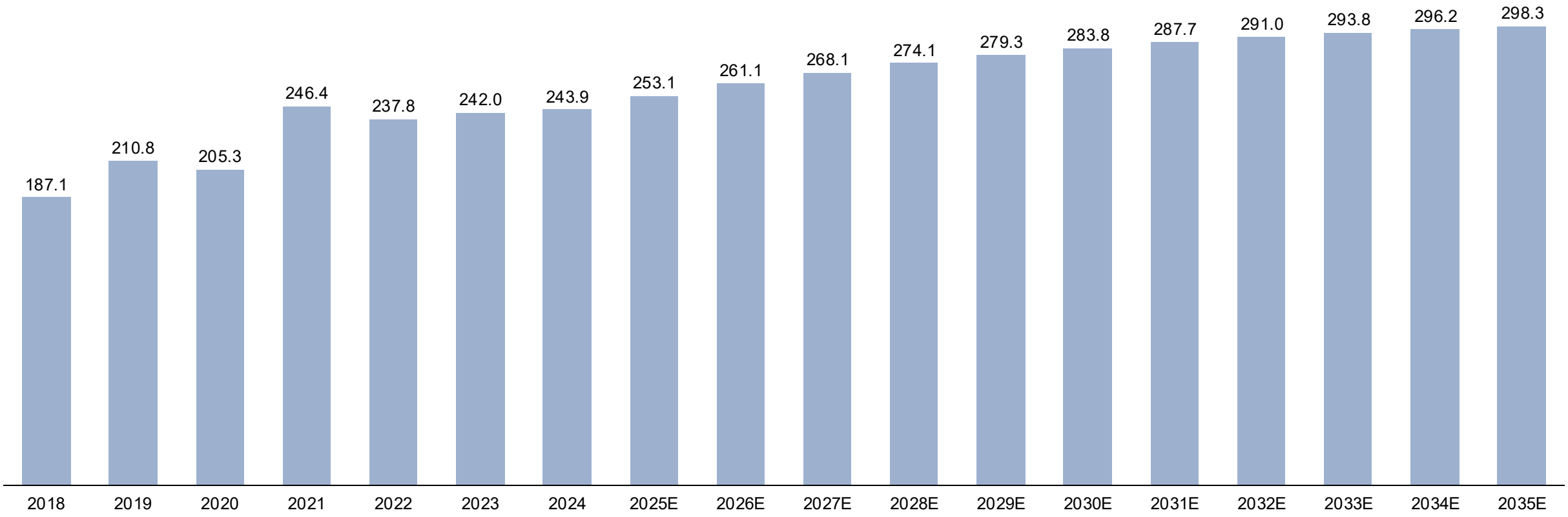
Sources: China Insights Consultancy

Market size of innovative small molecule drug in China, 2018-2035E

Market size of innovative small molecule drug in China

CAGR	2018-24	2024-35E
Innovative small molecule drugs	4.5%	1.8%

RMB billion



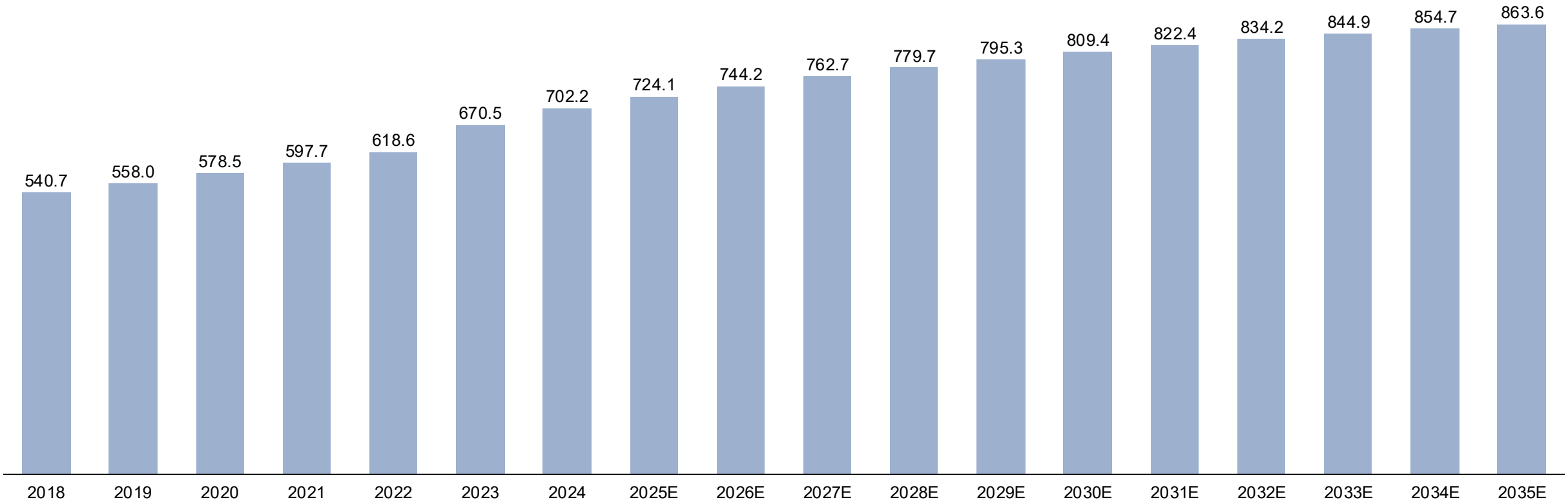
Source: National Bureau of Statistics, NHC, China Insights Consultancy

Market size of innovative small molecule drug in global, 2018-2035E

Market size of innovative small molecule drug in global

CAGR	2018-24	2024-35E
Innovative small molecule drugs	4.5%	1.9%

USD billion



Source: WHO, China Insights Consultancy

Growth drivers for innovative drug industry

Growth drivers for innovative drug industry

Demand for healthcare: unmet clinical needs

- Diseases with limited treatment options, such as certain cancers, rare genetic disorders, or autoimmune diseases, create a strong demand for new, effective therapies. The need to address **unmet medical needs** is a major driver for innovation in drug development.
- The **emergence of new diseases** (e.g., COVID-19, antibiotic-resistant infections) and the growing prevalence of chronic diseases (e.g., diabetes, heart disease) also drive the demand for novel treatments.

Technological advancement

- Breakthroughs in biotechnology, genomics, and molecular biology are enabling the development of more targeted, precise, and personalized therapies. **Innovations** such as gene editing personalized medicine, and biologics are expanding the possibilities for novel drug development.
- Advances in high-throughput screening, such as **artificial intelligence for drug discovery**, making the drug development process more efficient.

Favorable government policies

- Both FDA and NMPA have **encouraged approval policies** for innovative drugs such as priority review, accelerate approval, fast track, and breakthrough therapy designation and so on.
- Incentives such as extended patent protection, data exclusivity, and orphan drug incentives create a favorable environment for innovative drug development by providing companies with **market exclusivity** for a set period.

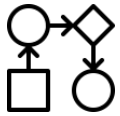
Growing R&D investment

- The investments target new therapeutic targets and improve existing therapies, promoting the development of breakthrough medicines. Pharmaceutical companies and academics cooperation between technical institutions is also very important. The cooperation in expertise and resource will accelerate the drug discovery and development process, ultimately supporting the development of innovative drugs industry.

Sources: China Insights Consultancy

Future trends for innovative drug industry

Future trends for innovative drug industry

 **Personalized drugs**	• The move towards personalized medicine will continue to grow, with therapies increasingly being designed based on individual genetic profiles, biomarkers, and other molecular characteristics. This approach allows for more effective treatments with fewer side effects, as drugs are specifically targeted to the patient‘s unique disease biology. Innovative drugs are an important way to meet personalized drug treatment
 **Multi-targeted drugs**	• The key to innovative drugs R&D is new targets, new mechanisms, and new structures, which require multidisciplinary collaboration, especially for targets in unknown areas. In the future, with the continuous development of technology, such as the use of AI drug discovery technology, innovative drugs will continue to develop towards multi-target trends, and multi-targeted innovative drugs are expected to achieve multiple functions
 **Targeted drug delivery**	• Advances in drug delivery technologies, such as controlled release formulations, nanoparticles, and targeted delivery methods, are opening new possibilities for improving the effectiveness and safety of innovative drugs • The next wave of innovative drugs will target previously unexplored or under-explored biological pathways. Advances in understanding disease mechanisms at the molecular level will enable the development of drugs that target new proteins, enzymes, and cell receptors
 **Improved patient compliance**	• National Medical Insurance Bureau negotiations and centralized volume-based procurement are two major initiatives in medical reform implemented by the National Medical Insurance Administration. the time from the launch of innovative drugs to the inclusion in medical insurance has been greatly shortened. Besides, incentive policies such as volume-based procurement have effectively reduced the burden on patients and improved the accessibility of drugs for patients

Sources: China Insights Consultancy

Table of contents

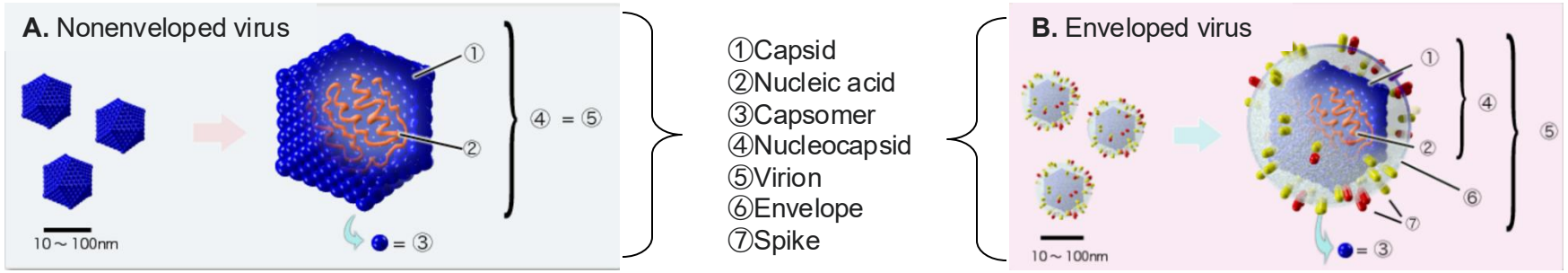
A virus is a pathogen that must parasitize and replicate inside living cells; virus infectious diseases are one of the main diseases that directly endanger human health

Definition and impact of viral infections

Definition:

- A virus is a pathogen that must **parasitize and replicate inside living cells**. It cannot exhibit life phenomena on its own without a cellular form. It invades an organism through an infection mechanism and uses the host cell system to replicate itself. It is usually composed of a genetic material nucleic acid (DNA/RNA) and a protective shell (protein).
- A complete virus particle, known as a virion, consists of **nucleic acid** surrounded by a protective coat of protein called a **capsid**. These are formed from protein subunits called capsomeres. Viruses can have a lipid "envelope" derived from the host cell membrane.

Basic structure of viruses



- From the time a virus attaches to a host cell until it completes replication and releases new virus particles, it goes through 8 stages: **Attachment, Penetration, Uncoating, Expression, Replication, Assembly, Maturation, and Release**, which is called the virus replication cycle.
- Viruses can be divided into DNA viruses and RNA viruses according to the different genetic materials. The replication of DNA viruses occurs in the cell nucleus; the replication of RNA viruses is more special; it often occurs in the cytoplasm. DNA viruses are usually double-stranded viruses and RNA viruses are single-stranded viruses. The error rate when replicating RNA is relatively high, so **RNA viruses have higher variability than DNA viruses**, and are more likely to cause infection and disease.

Impact of viral infections

- Viral infection manifests itself as invading the tissues of organisms and then multiplying, and the host tissues react to these viruses; infectious diseases are diseases caused by infection that harm or damage the host and affect its normal physiological functions.
- Infectious diseases are one of the main diseases that directly **endanger human health** today and are also one of the important reasons **that restrict social and economic development**. Especially since the outbreak of the COVID-19 pandemic, viral infections have posed a huge threat to human survival and development and are an issue that governments and medical systems in various countries urgently need to address.

Sources: The Journal of Biological Chemistry, China Insights Consultancy

DNA viruses major include HBV, varicella-zoster virus, monkeypox virus and so on, RNA viruses major include SARS, RSV, COVID-19 and so on

Major types and characteristics of viral infections

- **DNA viruses** are widely present in humans, vertebrates, insects, and various cell lines. Common types include **HBV, varicella-zoster virus, monkeypox virus, and variola virus**. The genetic structure of DNA viruses is relatively complex, with larger genomes, and their stability is higher than that of RNA viruses. **RNA viruses** are more diverse, with common examples including **COVID-19, SARS, MERS, RSV, and HIV-1**. Due to the strong mutation capabilities, RNA viruses are more prone to producing variant strains, making the prevention and control of infectious diseases caused by RNA viruses more challenging compared to DNA viruses.
- This Law of the People's Republic of China on the Prevention and Treatment of Infectious Diseases (《中华人民共和国传染病防治法》) is enacted to prevent, control and put an end to the outbreak and spread of infectious diseases and to ensure the health of the people and public sanitation. The infectious diseases governed by the Law are divided into Classes A, B and C:
  - **Class A** are plague and cholera.
  - **Class B** are infectious SARS, AIDS, viral hepatitis, poliomyelitis, highly pathogenic avian influenza, measles, epidemic hemorrhagic fever, rabies, epidemic encephalitis B, dengue fever, anthrax, bacillary and amebic dysentery, pulmonary tuberculosis, typhoid and paratyphoid, epidemic cerebrospinal meningitis, pertussis, diphtheria, tetanus infantum, scarlet fever, brucellosis, gonorrhoea, syphilis, leptospirosis, schistosomiasis and malaria.
  - **Class C** are influenza, epidemic parotitis, rubella, acute hemorrhagic conjunctivitis, leprosy, epidemic and endemic typhus, kala-azar, echinococcosis, filariasis, and infectious diarrhea other than cholera, bacillary and amebic dysentery, typhoid and paratyphoid.

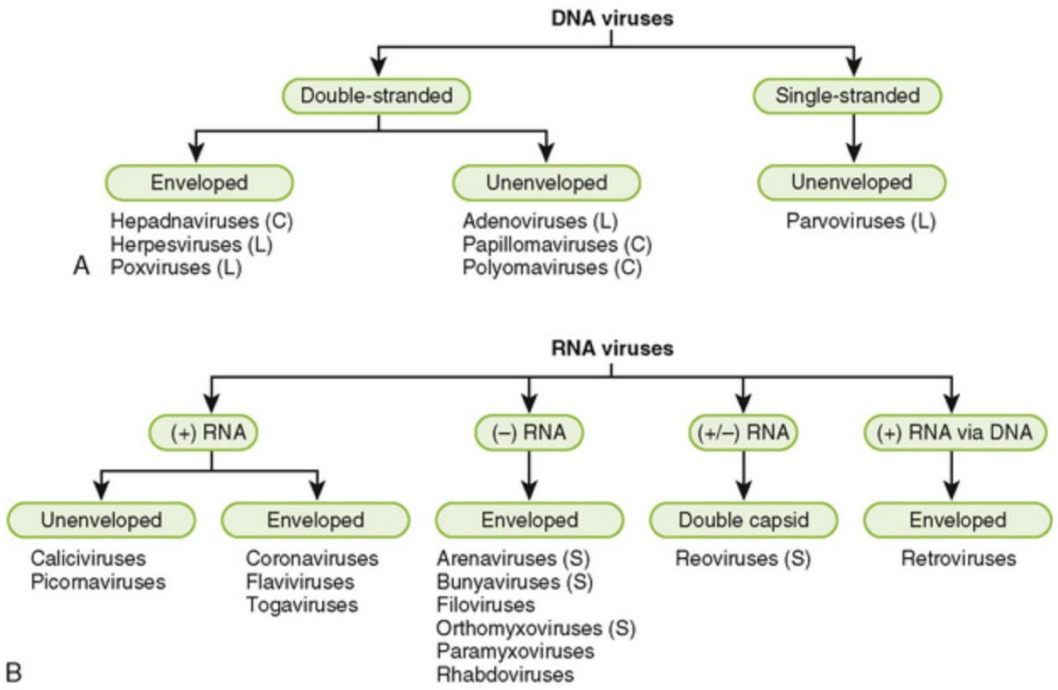
Common viral infectious diseases

Infectious diseases	Virus	Channels of transmission	Pathogenesis
COVID-19	COVID-19	Close-range droplet transmission or contact with the patient's respiratory secretions, inhalation of aerosols	Attack respiratory system cells
SARS	SARS	Close-range droplet transmission or contact with the patient's respiratory secretions	Attack respiratory system cells
AIDS	HIV-1	Sexual, blood, mother-to-child transmission	Attack lymphocytes, damaging the immune system
Viral hepatitis	HAV, HBV, HCV	Fecal-oral, blood, mother-to-child transmission	Attack liver cells
Poliomyelitis	Poliovirus	Fecal-oral, mouth-to-mouth, droplet transmission	Attack motor neuron in central nervous system

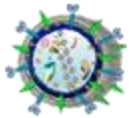
Sources: Law of the People's Republic of China on the Prevention and Treatment of Infectious Diseases, China Insights Consultancy

The types of RNA viruses are more diverse, with higher variability, making them more complex than DNA viruses

Comparison of DNA and RNA viruses



- The studies show that the mutation rates range from 10^{-8} to10^{-6} s/n/c for DNA viruses and from 10^{-6} to 10^{-4} s/n/c for RNA viruses. The high mutation rate is one of the factors contributing to the rapid evolution of RNA viruses, making them more variable to the environments.

Classification of viruses		
	DNA virus	• dsDNA virus • ssDNA virus
	RNA virus	• dsRNA virus • negative sense ssRNA virus • positive sense ssRNA virus • naked RNA virus

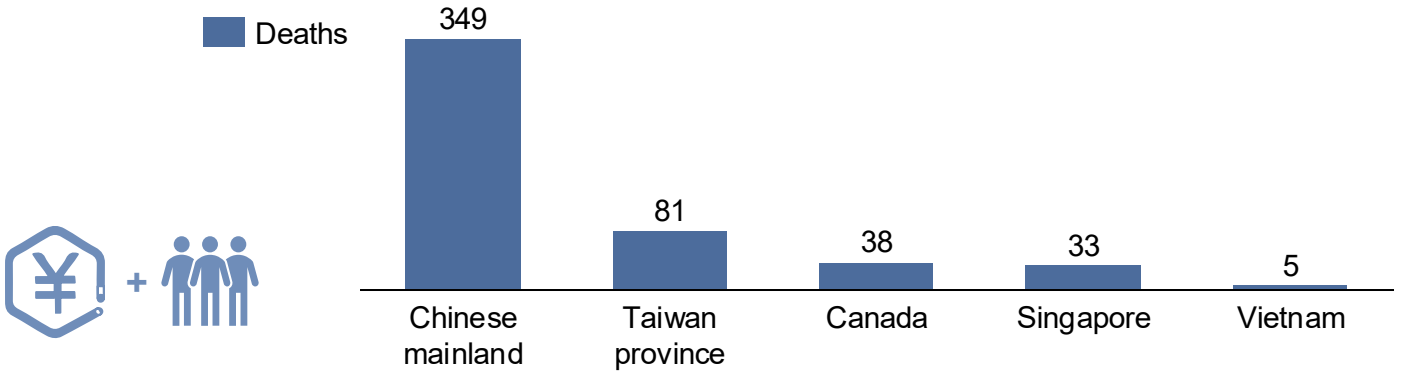
Representative viruses		
Group	**Virus**	**Antiviral drugs**
DNA virus	HBV	Nucleoside analogues, IFN-α
	VZV	Acyclovir analogues, Acyclic nucleoside analogues, Pyrophosphate analogues
	HSV	Acyclovir analogues, Acyclic nucleoside analogues, Pyrophosphate analogues
RNA virus	HCV	DAAs
	RSV	Nucleoside analogues, Corticosteroids
	Influenza	Neuraminidase inhibitors, Hemagglutinin inhibitors, M2 ion channel blockers

Sources: Journal of virology, Scientific reports, Oncohema key, China Insights Consultancy

Infectious diseases caused by viruses have caused a huge disease burden on human life

Disease burden caused by viral infections

- Epidemic infectious diseases caused by viruses have caused a huge disease burden on human life and a serious economic blow to social development. The threats and challenges to human society have long existed. Just like the SARS in history, according to statistics from the WHO, from November 1, 2002 to July 31, 2003, **8,096** people were infected with SARS worldwide, **782** people died, and the mortality rate reached **9.56%**. The following shows the five countries or regions with the highest mortality rates in the world during the statistical period and the corresponding deaths:



	Chinese mainland	Taiwan province	Canada	Singapore	Vietnam
Infected number	5,327	346	250	238	63
Mortality rate	6.6%	23.4%	15.2%	13.9%	7.9%

- The series of travel bans, consumption bans, and import and export controls triggered by SARS worldwide greatly affected economic development and caused a certain degree of social panic. The economic losses caused by SARS to ASEAN countries such as Vietnam, Singapore, and Brunei amounted to about **USD$30 billion**, which had a huge impact on economic development.

- Other epidemic infectious diseases caused by viruses have always been harmful to humans. For example, the deaths caused by HIV has exceeded 600,000 each year in recent years. As of the end of 2021, there were **38.4 million HIV-infected people** in the world. The average cost of AIDS treatment is very expensive. Global patients need to spend about **USD$50,000** each year for treatment. As of December 21, 2022, the latest data released by the WHO shows that the **COVID-19 infected people worldwide has reached 650,332,889**, and the number of **deaths has reached 6,649,874.**

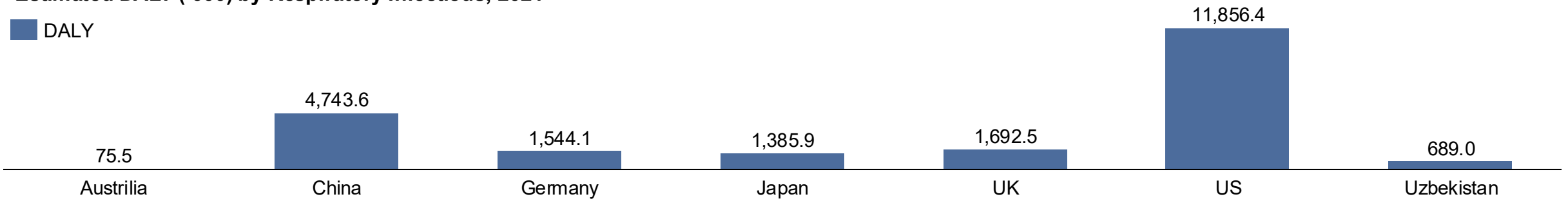
- Epidemics caused by viruses have long become a global public health issue that cannot be ignored. Today's climate change and globalization have accelerated the spread of viruses. The prevention and control of viral infectious diseases is the focus of the development of medical and health care in various countries. Among them, antiviral drugs, as a means of specifically treating viral infections, carry a considerable part of the responsibility and mission.

Sources: WHO, China Insights Consultancy

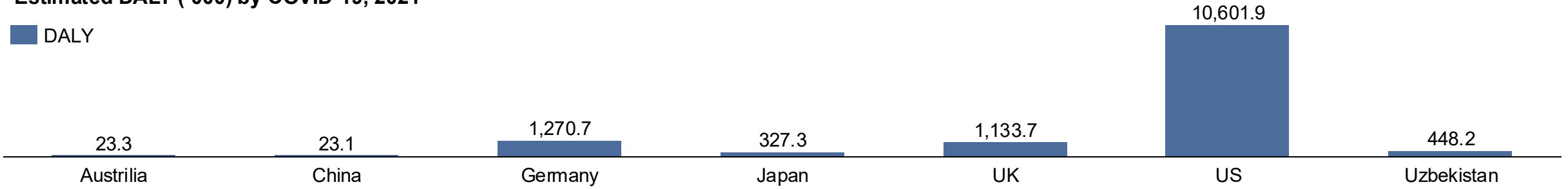
One DALY represents the loss of the equivalent of one year of full health

Disease burden using DALY

Estimated DALY ('000) by Respiratory Infectious, 2021



Estimated DALY ('000) by COVID-19, 2021



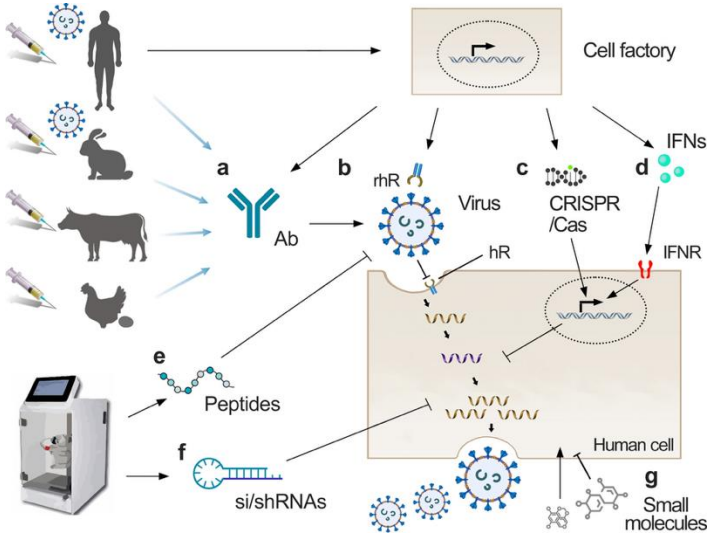
- The overall burden of disease is assessed using the disability-adjusted life year (DALY), a time-based measure that combines years of life lost due to premature mortality (YLLs) and years of life lost due to time lived in states of less than full health, or years of healthy life lost due to disability (YLDs). One DALY represents the loss of the equivalent of one year of full health. Using DALYs, the burden of diseases that cause premature death but little disability (such as drowning or measles) can be compared to that of diseases that do not cause death but do cause disability (such as cataract causing blindness).

Sources: WHO, China Insights Consultancy

Antiviral drugs can be divided into 7 categories according to the molecular forms; Oligonucleotide drugs are an emerging type of drug that is expected to be used for antiviral

Main categories and applications of antiviral drugs

➢ The mechanism of antiviral drugs is mainly to resist further infection of the virus in the host by affecting a certain link of the virus replication cycle. According to an article published in "Cellular and Molecular Life Sciences" in 2022, antiviral drugs can be further divided into the following 7 categories according to the molecular forms:



a. **Neutralizing antibodies (nAbs)** stick to the viral surface proteins and stop virus from getting inside our cells. nAbs also signal to immune cells to come and help destroy the virus.

b. **Neutralizing recombinant soluble human receptors:** It was shown that recombinant soluble human angiotensin-converting enzyme 2 (ACE2) receptor can block SARS-CoV-2 infection.

c. **CRISPR/Cas systems** are the adaptive immune systems that protect against invading bacteriophages and foreign nucleic acids. However, such systems should be exploited more for chronic and latent viral infections.

d. **Interferons (IFNs)** are a group of signaling proteins made and released by human cells in response to infection with several viruses causing degradation of viral nucleic acids in infected cells and triggering antiviral responses in nearby non-infected cells. Recombinant human IFNs (rhIFNs) have been approved for treatment of hepatitis C virus (HCV) and hepatitis B virus (HBV) infections.

e. **Antiviral peptides (AVP)** are polymers that have been experimentally verified to interfere with virus replication.

f. **Antiviral nucleic acid polymers (NAPs)** can directly inhibit viral entry or replication by binding to the virus particle, its building blocks, or RNA/DNA replication intermediates. Several NAPs are under development for treatment of hepatitis C, influenzas virus, norovirus, HSV, and HIV infections.

g. **Small-molecule** or small molecular-weight antivirals attenuate viral replication. Some small molecules affect critical functions of viral factors, whereas others interfere with host factors and pathways necessary for virus replication.

Oligonucleotide drugs are an emerging type of drug that is expected to be used in the antiviral field in recent years. In terms of molecular structure, oligonucleotide drugs can be mainly divided into two categories: antisense oligonucleotides (ASOs) and small interfering RNA (siRNA). Oligonucleotide drugs usually target mRNA for drug intervention, which **broadens the range of targets** available for treatment, covers special targets that are difficult to be effective with protein targets, and develops targets related to genetic diseases caused by genetic defects. In addition, oligonucleotide drugs can assemble sequences for viral genes and then screen effective sequences, **shortening the new drug development cycle.**

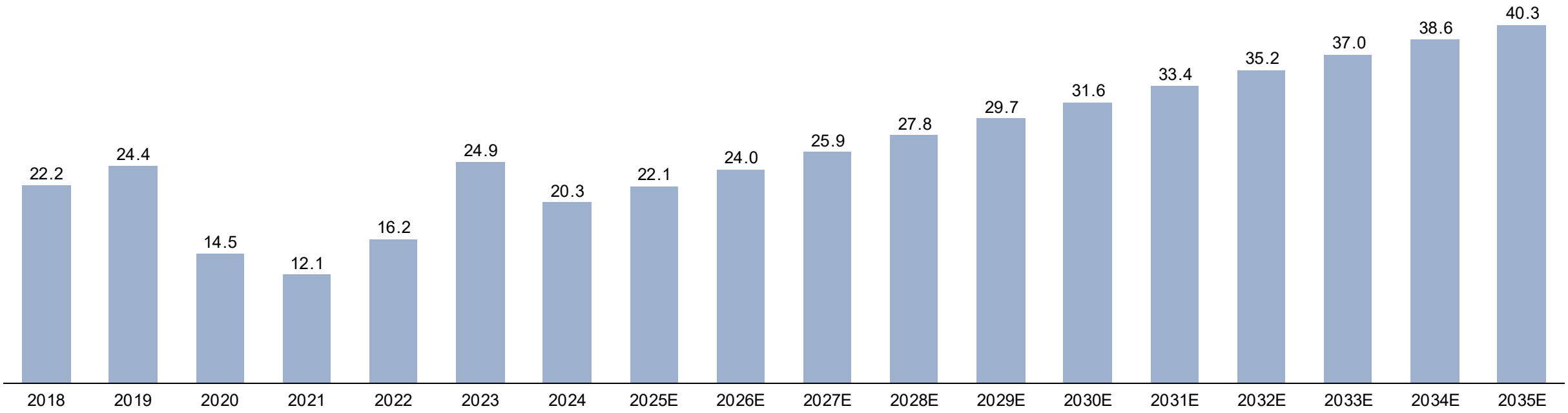
Sources: Cellular and Molecular Life Sciences, China Insights Consultancy

Market size of antiviral drugs in China, 2018-2035E

Market size of antiviral drugs in China

CAGR	2018-24	2024-35E
China antiviral drugs	-1.5%	6.4%

RMB billion



The decrease of China's antiviral drug market in 2024 primarily due to weakened pandemic-driven demand and sustained pressure from VBP and healthcare cost containment policies, collectively compressing market size. The market is projected to recover, driven by accelerated launches of novel antivirals and stabilized post-VBP pricing, fostering structural demand growth.

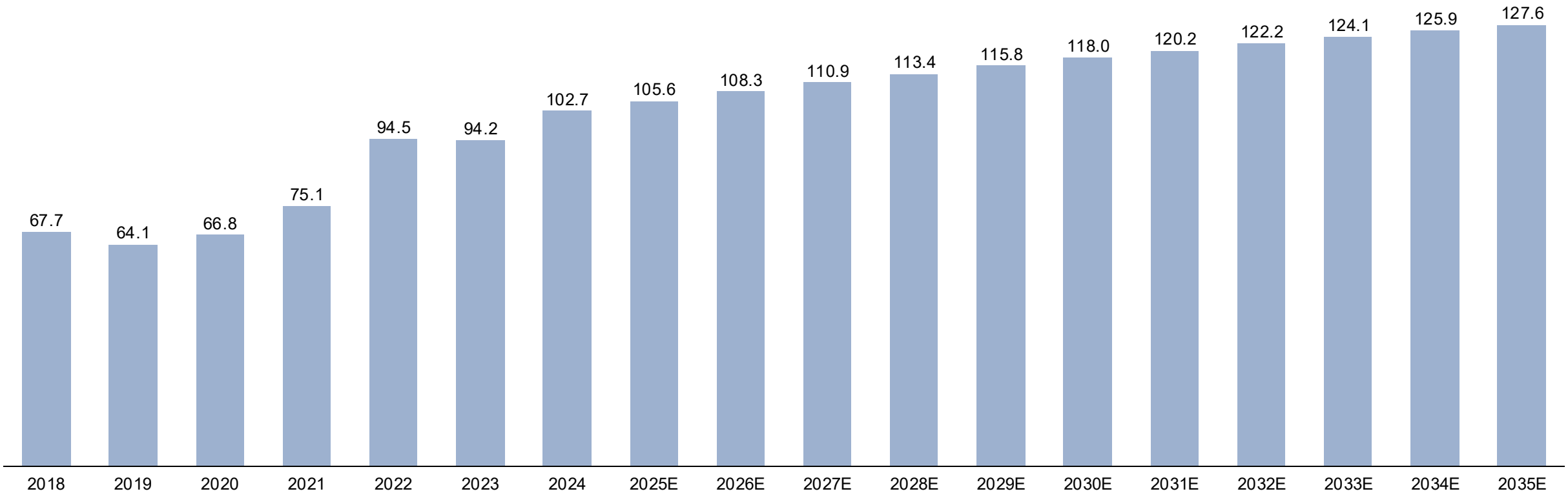
Sources: China Insights Consultancy

Market size of antiviral drugs in global, 2018-2035E

Market size of antiviral drugs in global

CAGR	2018-24	2024-35E
Global antiviral drugs	7.2%	2.0%

USD billion



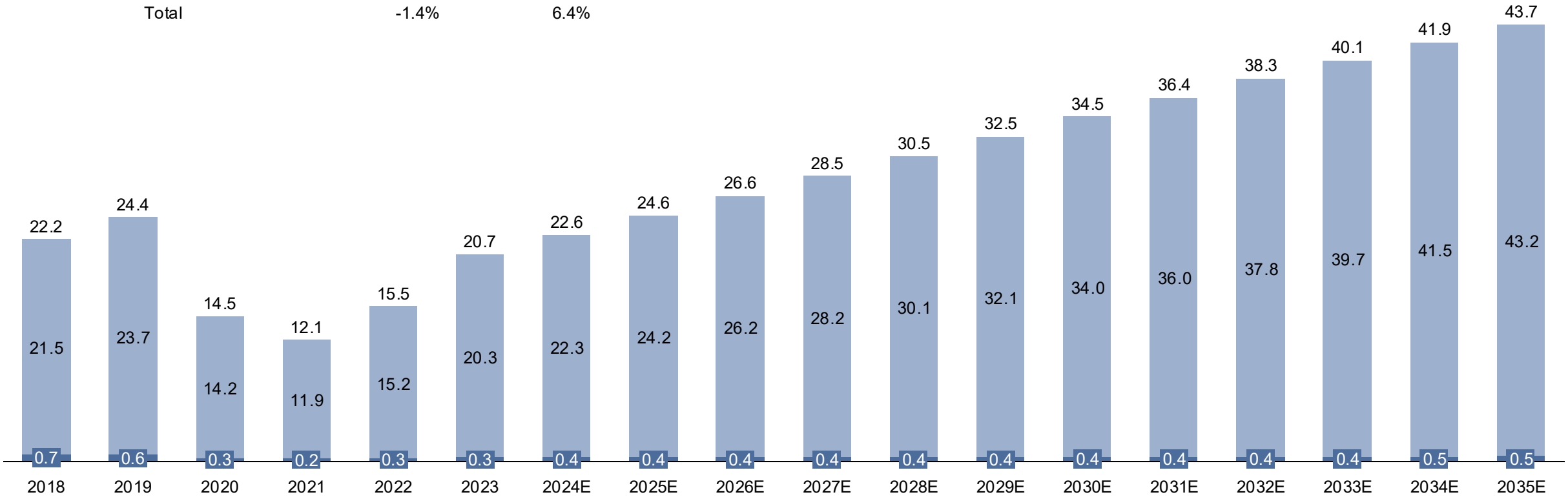
Sources: China Insights Consultancy

Market size of antiviral drugs in China, 2018-2035E

Market size of antiviral drugs in China (not include COVID-19)

CAGR	2018-23	2023-35E
Small molucule antiviral drugs	-1.4%	6.4%
Other antiviral drugs	-12.1%	2.6%
Total	-1.4%	6.4%

RMB billion



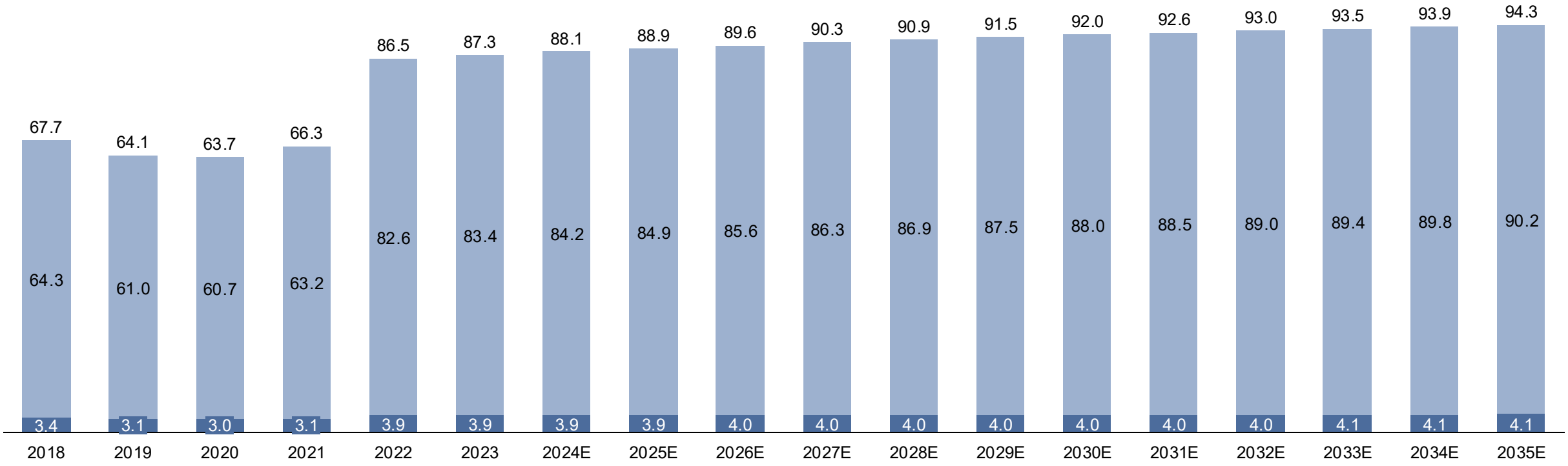
Sources: China Insights Consultancy

Market size of antiviral drugs in global, 2018-2035E

Market size of antiviral drugs in global (not include COVID-19)

CAGR	2018-23	2023-35E
Small molucule antiviral drugs	5.3%	0.7%
Other antiviral drugs	3.1%	0.3%
Total	5.2%	0.6%

USD billion



Sources: China Insights Consultancy

Market drivers and development trends of global antiviral drugs

Market drivers and development trends of global antiviral drugs

 **Advances and diversification of disease diagnosis methods**	• Viral infectious diseases have always been one of the major threats to human health. With the continuous advancement of disease detection technologies, diagnostic methods have become more diversified, the cost of immune testing for antibodies and antigens has decreased, and accessibility for populations has improved. As a result, the diagnostic rate for viral infectious diseases has steadily increased, allowing more people to receive appropriate treatment. The expanding population using antiviral medications has driven the stable growth of the global antiviral drug market, as well as the antiviral drug markets in China and the US
 **Drug innovation to address viral resistance and mutation**	• The resistance of viruses has been continuously rising, affecting the ability of drugs to block viral replication. At the same time, due to the high mutation rate of certain viruses, viral mutations have rendered many older drugs ineffective against the virus. However, new molecular diagnostic technologies, such as high-throughput sequencing, have accelerated the discovery of viral mutations, enabling more timely and targeted drug development for viral variants. This has continued to drive research and development in the antiviral field and foster the growth of the industry
 **Increased risk of viral infection**	• Since the COVID-19, with extensive public education and awareness campaigns, the general public's awareness of antiviral measures has gradually increased. The proportion of people purchasing medications to treat or prevent severe illness has steadily risen, leading to a corresponding increase in the demand for antiviral drugs
 **Policy support**	• The Chinese government has implemented a series of favorable policies regarding the treatment of viral infectious diseases, including encouraging the development of innovative antiviral drugs, such as shortening approval times and accelerating the market launch of promising drugs to address demand. At the same time, domestic pharmaceutical companies benefit from supportive factors like tax incentives, talent incentive programs, and specialized public research funding for R&D. Similarly, other countries, such as the US, have introduced similar favorable policies. The FDA granted emergency use authorization for Paxlovid and Molnupiravir to combat the COVID-19 pandemic
 **Technology advanced**	• The development of new antiviral drugs requires the integration of various technologies, including target discovery, molecular structure modification, drug screening, and virus detection and characterization. In recent years, the rapid advancement of technologies such as artificial intelligence has become a fundamental driving force in the development of new antiviral drugs. For example, digital technologies and machine learning assist in the further study and data analysis of potential target proteins, while also helping scientists better understand the biological characteristics of viruses and their transmission patterns, providing more references for drug development. In addition, the rapid development of nucleic acid-based drugs has shifted the focus of drug targets from proteins to upstream mRNA, which offers new avenues for drug intervention. This expansion in target selection provides more options for the development of new antiviral drugs and the exploration of new application areas.

Sources: China Insights Consultancy

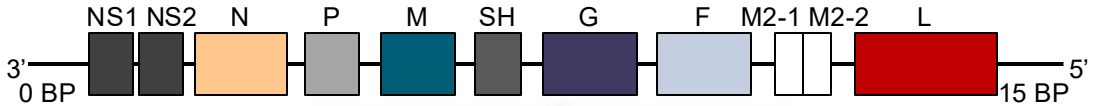
RSV is an enveloped RNA virus that could cause seasonal epidemic, especially in children, the elderly, and immunocompromised patients

Definition and impact of RSV infections

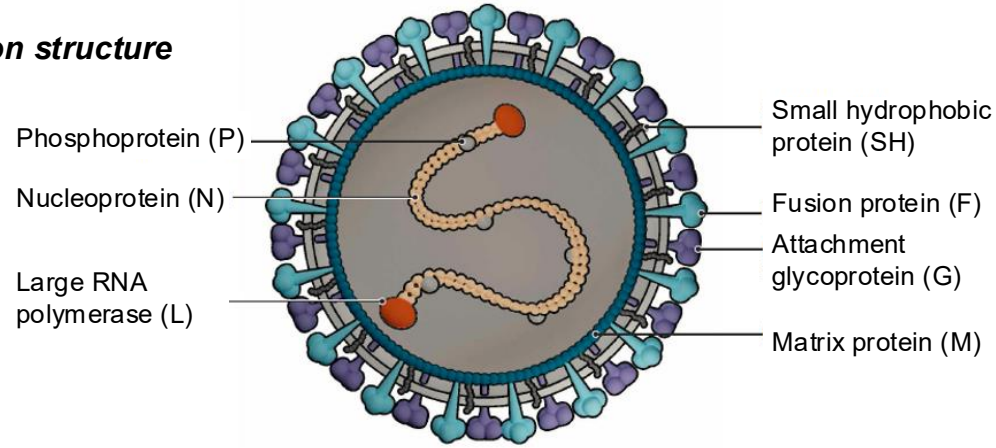
Introduction

- RSV is a non-segmented negative-sense single-stranded enveloped RNA virus that belongs to Pneumoviridae family, Orthopneumovirus genus.
- The virus was first isolated from chimpanzees in 1956 and was subsequently recovered from infants with severe lower respiratory tract disease.
- The virus is a human restricted pathogen that typically spreads via hands, fomites and the aerosol route. Infection with RSV does not grant permanent or long-term immunity, with reinfections common through life.

RSV RNA genome



RSV virion structure



Transmission and seasonality of RSV

- The basic reproduction number R_0 is estimated to be 1.2 to 3.0, **similar to that of influenza.**
- The incubation period can be 2-8 days and could easily lead to reinfection.
- Epidemic caused by RSV is seasonal, which mainly **circulates in winter and early spring in the Northern Hemisphere**, while tends to occur more often during rainy seasons in tropical and subtropical areas.

Pathogenesis and risk factors

Pathogenesis

- Current mainstream opinion on RSV infection mechanism holds that nucleocapsid enters the host cell under endocytosis **mediated by F protein.**
- RSV itself is not cytopathic, but it replicates in and causes damage to human airways, thus predisposing the patient to secondary bacterial infections, and providing RSV with a mechanism to evade systematic immunity.

Susceptible population

- **Children**, **the elderly**, and **immunocompromised patients** are more inclined to be infected.
- Risk factors of disease progression include premature birth, children with congenital heart disease or chronic lung disease, weakened immune systems, and aging, especially over 65 years old.

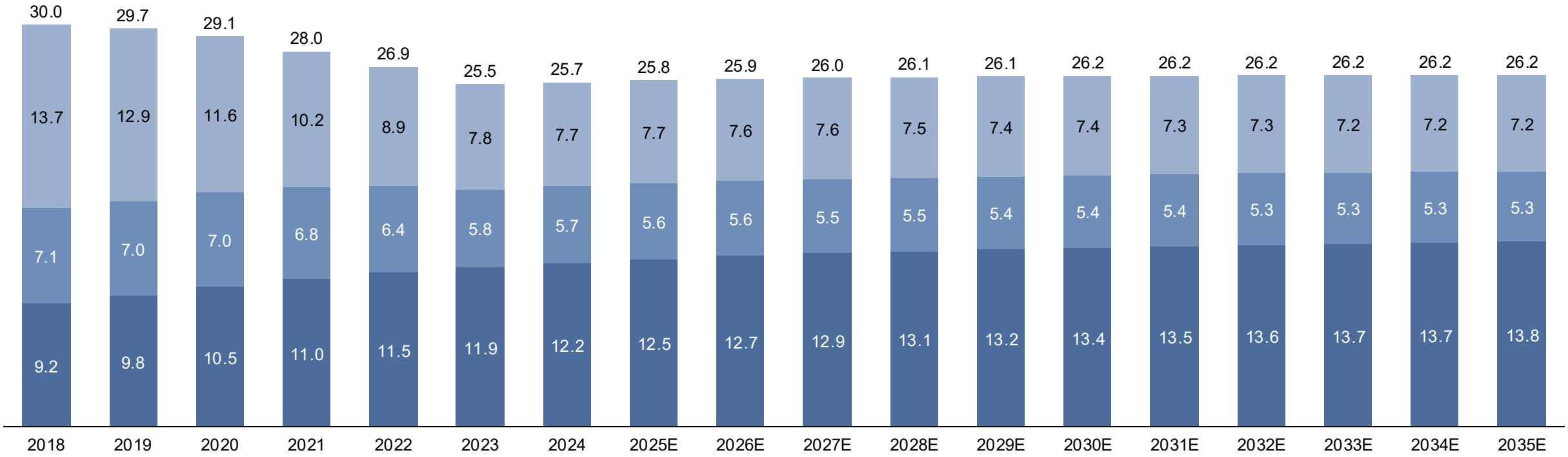
Sources: AAP, BMJ, Science Translational Medicine, China Insights Consultancy

Epidemiology of RSV in China, 2018-2035E

Epidemiology of RSV in China

CAGR	2018-24	2024-35E
<2 years old	-9.0%	-0.7%
2-5 years old	-3.6%	-0.8%
>65 years old	4.9%	1.1%

ppl million



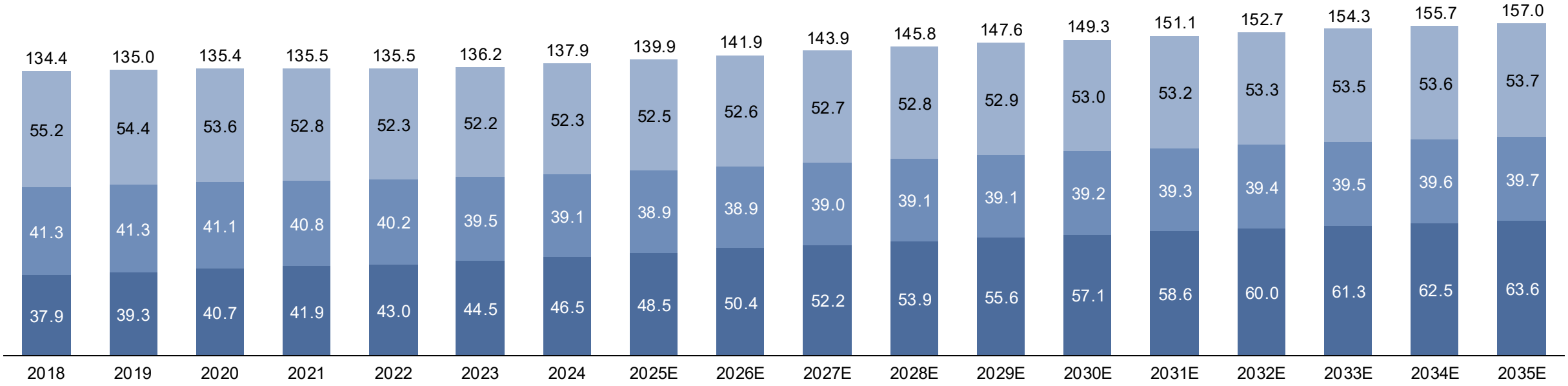
Sources: The Journal of Infectious Diseases, Journal of Clinical Pediatrics, China Insights Consultancy

Epidemiology of RSV in global, 2018-2035E

Epidemiology of RSV in global

CAGR	2018-24	2024-35E
<2 years old	-0.9%	0.2%
2-5 years old	-0.9%	0.1%
>65 years old	3.5%	2.9%

ppl million



- The global prevalence of RSV is expected to increase from 136.2 million in 2023 to 157.0 million in 2035, with a CAGR of 1.2%. In China, the prevalence is forecasted to rise from 25.6 million in 2023 to 26.2 million in 2035, with a CAGR of 0.2%.Infants and young children are the primary victims of RSV infection, with 50-70% being infected in their first year of life and 90% in their second year. In China, infants and young children aged 1-24 months account for approximately 30.6% of the RSV patient population.

Sources: The Journal of Infectious Diseases, UN, The Lancet, China Insights Consultancy

RSV antiviral inhibitors are designed to achieve antiviral effect interacting with a certain step in the replication cycle

Introduction of potential targets of RSV treatment drugs

Comparison of RSV antiviral inhibitors

Target	Step	Mechanism	Action site
G protein	Attachment	• Inhibit virus attaching host cells	Extracellular
F protein	Entry	• Inhibit membrane fusion through the inhibition of either protein-protein interactions or protein-lipid interactions	Extracellular
N protein	Replication	• Inhibit nucleoprotein binding RSV genome RNA to form RNP	Intracellular
L protein	Transcription	• Inhibit RNA polymerase activity possessed by L protein, thus interacting virus genome replication and mRNA transcription	Intracellular

- ✓ The life cycle of virus infection consists of many stages, and the dysfunction of any stage could influence the whole replication cycle, thus achieving the purpose of preventing the virus from infection
- ✓ In the process of RSV entering host cell, The attachment glycoprotein binds to the chemokine receptor on the apical surface of ciliated epithelial cells, and the F protein mediates entry of the nucleocapsid into the cytoplasm. RSV-N is tightly bound to viral genomic RNA, forming The N-RNA complex serves as a template for the RSV polymerase complex, consisting of the L and P proteins to synthesize mRNAs and progeny genomes

- In recent years, direct antiviral drugs are being developed as new candidate drugs for the treatment of RSV, mainly targeting various proteins involved in the viral replication cycle, including **fusion protein (F protein), nucleoprotein (N protein), adhesion protein (G protein) and RNA polymerase (L protein).**
- The **L protein** encoded by RSV is an RNA-dependent RNA polymerase (**RdRp**) that uses the RNP complex as a template for transcription and replication. It catalyzes the synthesis of viral mRNA, which is essential for viral protein production. Together with the P protein, the L protein forms a heterodimer that determines the active form of the RSV polymerase.

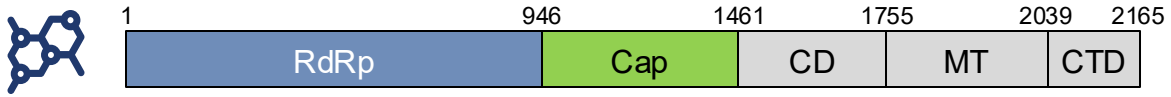
Sources: Antiviral Research, Molecules, China Insights Consultancy

RSV RNA-dependent RNA polymerase (RdRp) is composed of a multifunctional large (L) polymerase protein and a cofactor phosphoprotein (P)

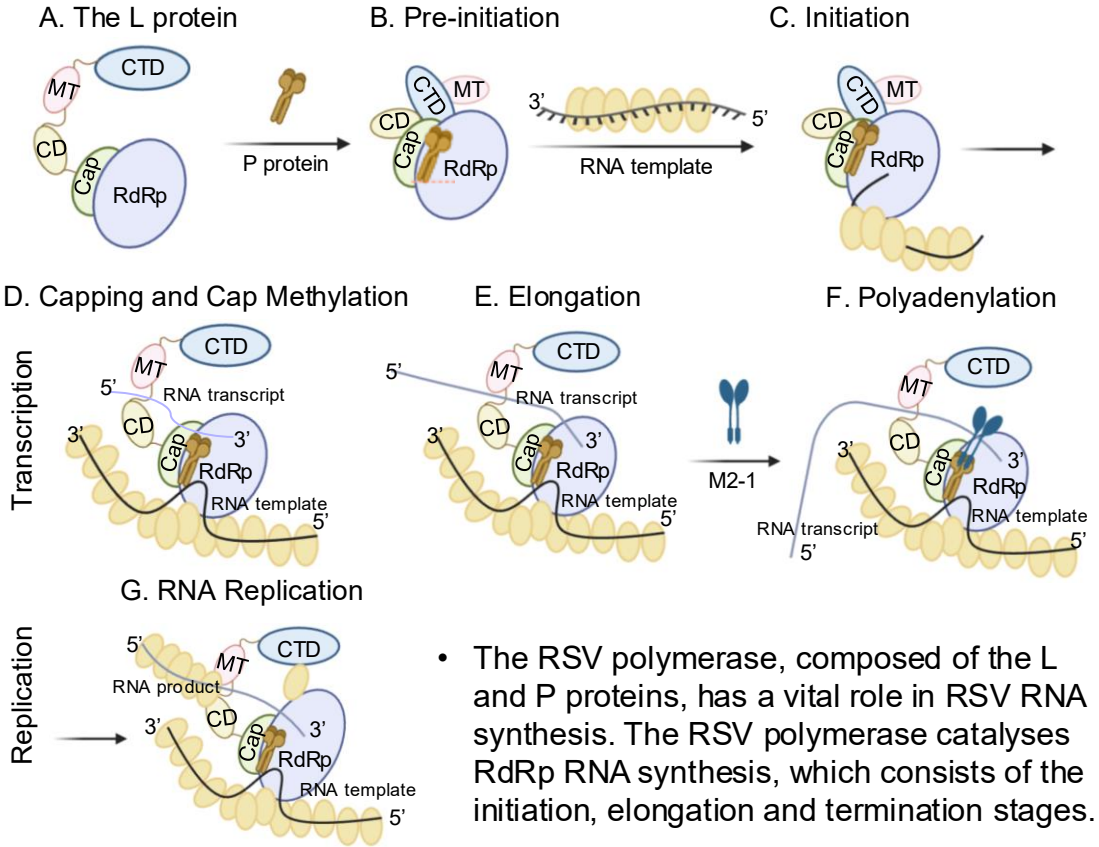
Mechanism of RdRp for RSV

- The RSV RNA genome consists of a single-strand negative-sense RNA encapsidated by the nucleoprotein (N) to form a ribonucleoprotein particle. The **ribonucleoprotein particle is transcribed and replicated** by the RSV RNA-dependent RNA polymerase (**RdRp**), which is composed of a **multifunctional large (L) polymerase protein and a cofactor phosphoprotein (P)**. It transcribes the RNA genome into ten viral mRNAs and replicates full-length viral genomic and antigenomic RNAs. The RSV polymerase initiates RNA synthesis by binding to the conserved 3'-terminal RNA promoters of the genome or antigenome.
- The RSV L protein is a polypeptide that executes the synthesis of viral genomic or antigenomic RNAs and mRNAs and catalyzes three distinct enzymatic activities: ribonucleotide polymerization, mRNA 5' cap addition, and cap methylation.
- The **RSV L protein** consists of five domains: the **RdRp domain**, the capping domain (Cap), the connector domain (CD), the methyltransferase domain (MT) and the carboxy-terminal domain (CTD). Of these, three domains—RdRp, Cap and MT—**possess enzymatic activity and are responsible for RNA synthesis.**

The structure of RSV L protein



RSV RNA synthesis process

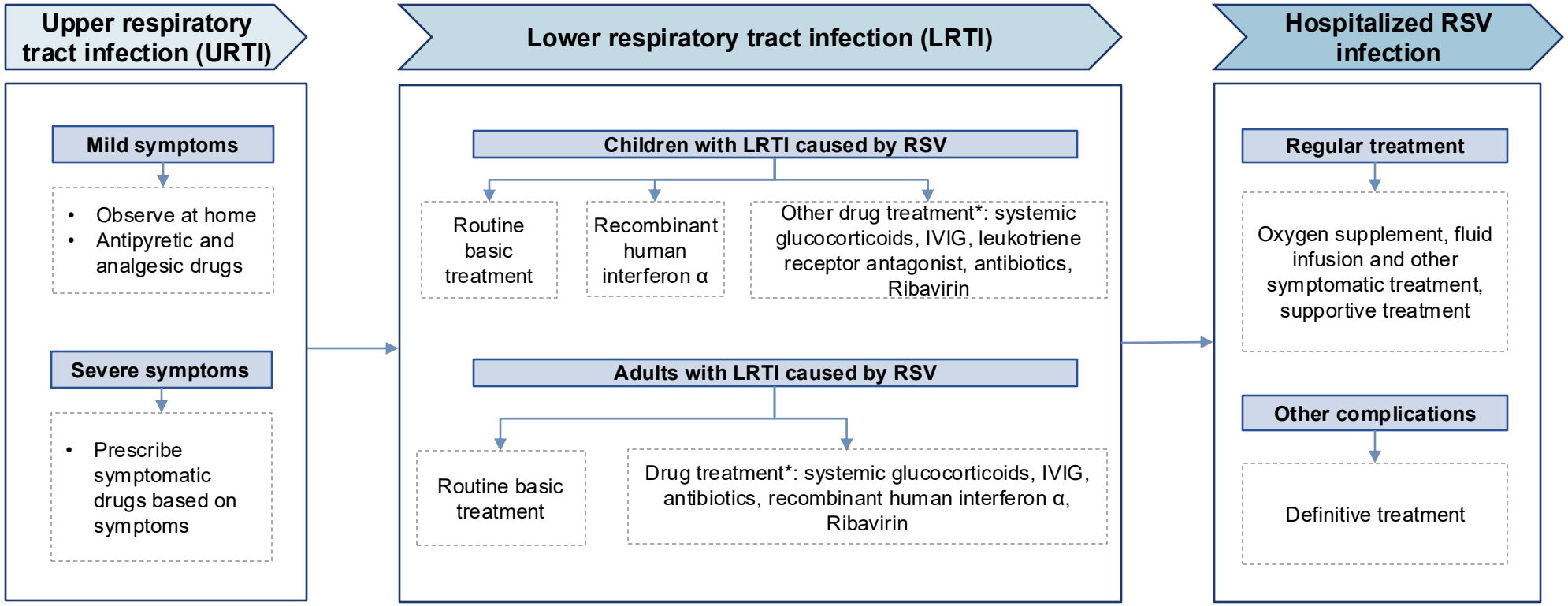


- The RSV polymerase, composed of the L and P proteins, has a vital role in RSV RNA synthesis. The RSV polymerase catalyses RdRp RNA synthesis, which consists of the initiation, elongation and termination stages.

Sources: Viruses, Nature, ACS Omega, China Insights Consultancy

The clinical manifestations of RSV infection in children vary greatly; Besides, the elderly are also the main infected population

Treatment pathways of different susceptible population of RSV



*Note: all drug treatments for adults are not recommended; except recombinant human interferon α, all other drug treatments are not recommended for children

- Studies show that the hospitalization rate of RSV-related disease in children aged 5 years and younger is around 1.7%, and the in-hospital mortality rate is around 0.5% in the world. Among older adults (≥65 years old) the hospitalization rate is about 15%-25%, and the in-hospital mortality rate is about 6%-8% worldwide. According to the Chinese pediatric guideline for diagnosis, treatment, and prevention of respiratory syncytial virus infection, the hospitalization rate of RSV-related disease in children aged 5 years and younger is 0.7%-1.0%.

Sources: Influenza Other Respir Viruses, Clin Infect Dis, medRxiv AAP,《儿童呼吸道合胞病毒感染诊断、治疗和预防专家共识（2023版）》,《人呼吸道合胞病毒下呼吸道感染治疗及预防指南（2024版）》, China Insights Consultancy

The standard treatment for both children and adults is limited to supportive care, and the only two approved drugs, Palivizumab and Ribavirin, are only indicated for limited patient groups under specific circumstances

Treatment pathways of different susceptible population of RSV

Treatment	Mechanism	Target population	Clinical efficacy & safety	NMPA	FDA
Prophylaxis					
Palivizumab	Binding RSV fusion protein on the surface of the virus and blocking a critical step in the membrane fusion process	• Approved only for certain high-risk infants and young children[1] • Limited off-label use for high-risk immuno-comprised adult patients	• Reveals certain level of prophylaxis effect • Very limited prevention duration and patient coverage	○	√
Therapeutics					
Ribavirin	Inhibiting activity of inosine phosphate dehydrogenase to interfere with early viral transcription and increasing mutation accumulation in viral genome	• Approved only for hospitalized high-risk infants and young children • Off-label use for immuno-compromised adult patients with high risks of severe infection	• Broad-spectrum drug with no clinically significant effect • Limited patient coverage and complicated administration • Associated with multiple frequently occurred serious adverse events	×	×
Interferon	A broad-spectrum drug that realize antiviral effect through regulating the immunity's antiviral capacity	• Children with RSV bronchiolitis and pneumonia	• No direct antiviral effect • Adverse effects such as flu-like symptoms	○	N/A[2]

✓ Currently, the standard treatment for RSV is limited to **supportive care**, such as **oxygen supplement, nasal decongestants, nutrition and hydration, and the use of bronchodilators, epinephrine, and steroids.**

✓ Clinical treatment drugs for RSV infection in **children** include interferon, Ribavirin, bronchodilators, etc. Among them, since there is currently insufficient evidence to prove the effectiveness of Ribavirin in the treatment of RSV infection, its routine use is not recommended.

✓ The treatment standards for the management of RSV infection in **adults** are mainly limited to supportive treatments such as bronchodilators, supplemental oxygen, intravenous infusions, and antipyretics.

√ Recommend × Not recommend as routine treatment ○ No approved drug

Note: 1. Only accounts for <5% children under 24 months, which could be translated to only <2% among all children under 5 years old; 2. Currently IFN only has been proposed by Chinese experts' consensus as tentative use in RSV

Sources: AAP, BMJ, Therapeutic Advances in Infectious Disease, China Insights Consultancy

Global competitive landscape of small molecule antiviral drug for RSV treatment

Updated 1011

Pipelines of RSV treatment drugs in China, as of LPD

Trial number	Candidate	Formulation	MoA	Company	Clinical phase	Location	First posted date	Indication
CTR20240557	AK0529	Enteric capsules	F protein	Ark Biopharmaceutical	III	China	2024/03/12	RSV for children
CTR20234163	VV116	Dry Suspension	RdRp	Vigonvita Life Sciences	II/III	China	2024/01/23	RSV for children
NCT05568706	EDP-938	Tablets	N protein	Enanta	IIb	U.S.	2022/10/06	RSV for adults
CTR20181808	AK0529	Enteric capsules	F protein	Ark Biopharmaceutical	II	China	2018/12/13	RSV for adults
NCT04816721	EDP-938	Tablets	N protein	Enanta	II	U.S.	2021/03/25	RSV for children
NCT06585150	GS-5245	Oral administration	RdRp	Gilead Sciences	II	U.S.	2024/09/05	RSV for adults
NCT07214571	S-337395	Oral administration	RdRp (L protein)	Shionogi/UBE Corporation	II	UK	2025/10/09	RSV for adults
NCT06170242	EDP-323	Oral administration	RdRp (L protein)	Enanta	IIa	U.S.	2023/12/14	RSV for adults
CTR20240957	VV116	Dry Suspension	RdRp	Vigonvita Life Sciences	I	China	2024/03/22	RSV for adults
CTR20253751	SYH2066	Oral administration	N/A	CSPC	I	China	2025/09/19	RSV for adults

➢ Only one product around the China targeted RdRp on the pipelines of RSV treatment drugs.

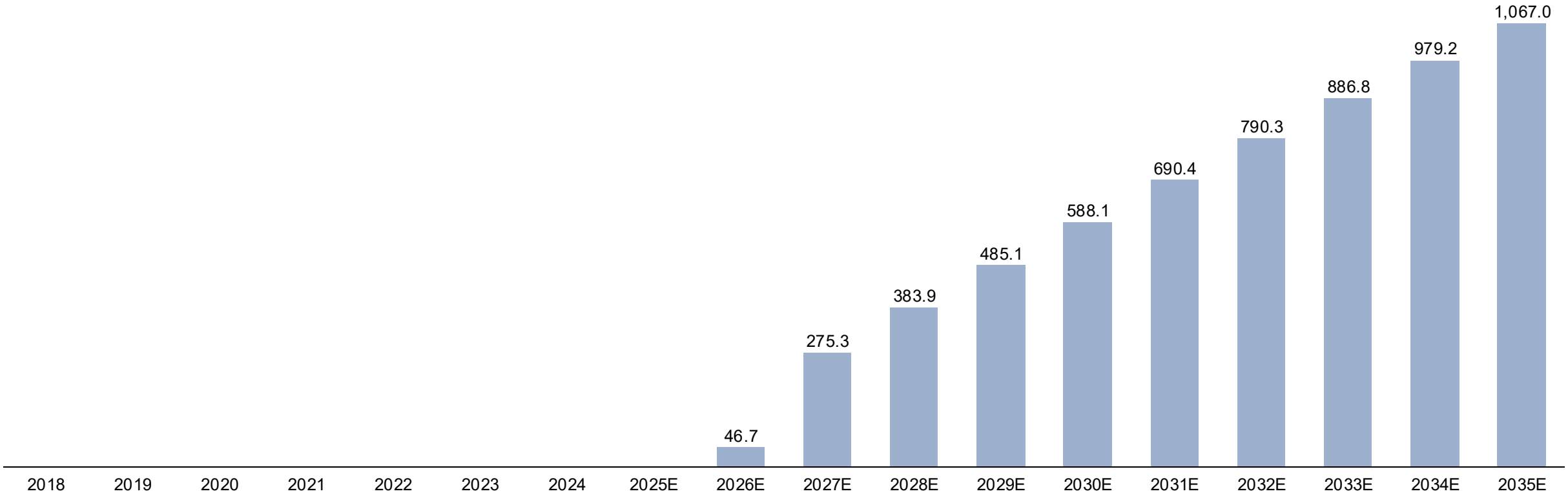
Sources: CDE, China Insights Consultancy

Market size of RSV treatment drugs in China, 2018-2035E

Market size of RSV treatment drugs in China*

CAGR	2018-23	2026-35E
China RSV treatment drugs	-	41.6%

RMB million



* Only includes the RSV target drugs, excluding interferon and Ribavirin.

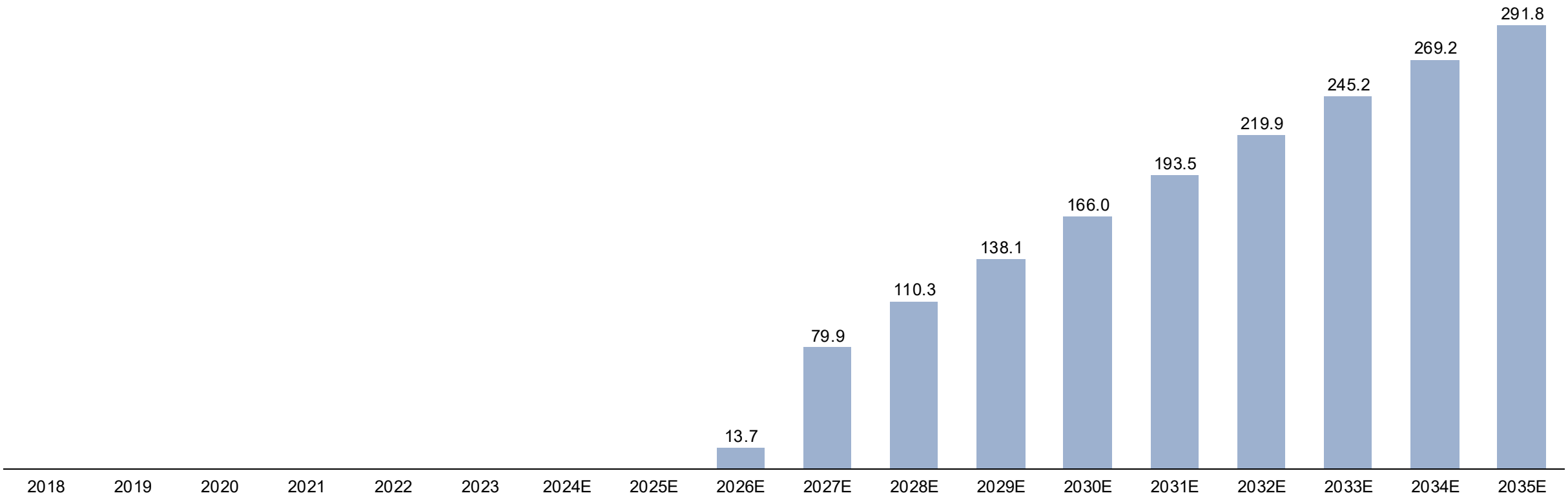
Sources: China Insights Consultancy

Market size of RSV treatment drugs for <2 yrs old young children in China, 2018-2035E

Market size of RSV treatment drugs for <2 yrs old young children in China*

CAGR	2018-23	2026-35E
China RSV treatment drugs for infants	-	40.5%

RMB million



* Only includes the RSV target drugs, excluding interferon and Ribavirin.

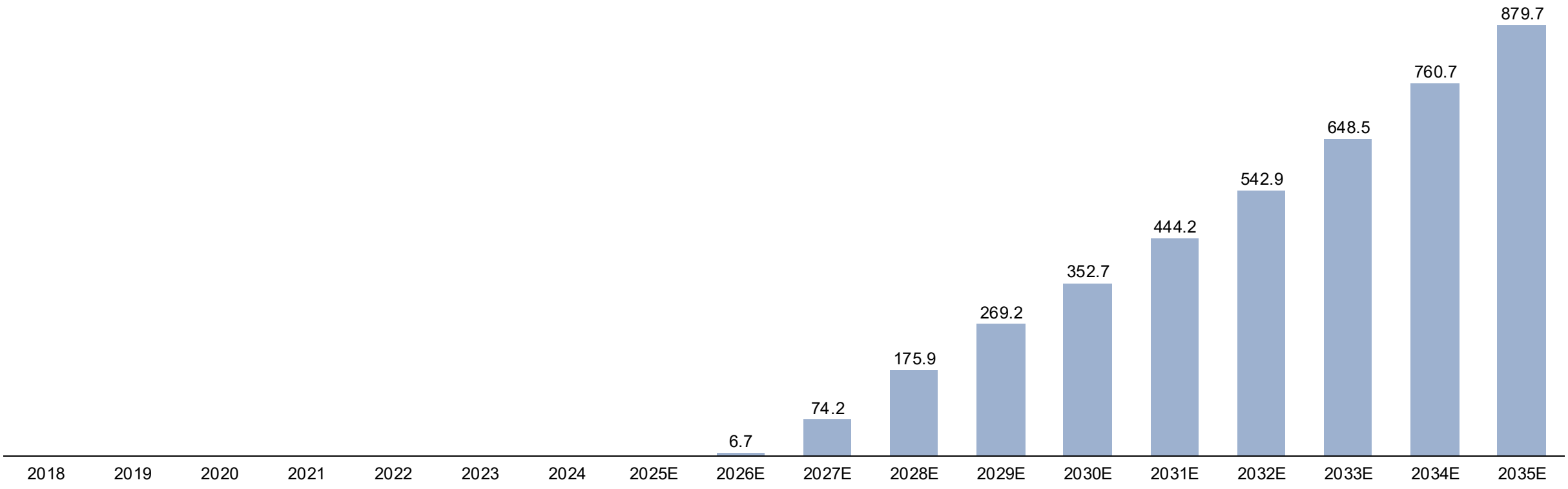
Sources: China Insights Consultancy

Market size of RSV treatment drugs in global, 2018-2035E

Market size of RSV treatment drugs in global*

CAGR	2018-23	2026-35E
Global RSV treatment drugs	-	72.0%

USD million



* Only includes the RSV target drugs, excluding interferon and Ribavirin.

Sources: China Insights Consultancy

Market drivers and development trends for RSV treatment drugs in China

Drivers & Trends	Description
1 **Expansion of population vulnerable to RSV infection**	• As the virus is highly contagious, reinfected and cannot generate post-infection immunity, and vaccines are still at least a few years away even after over 60 years of development, there has long been large demand in the market for effective and targeted RSV antiviral drugs • With the continuous delay of women's marriage and childbearing age, the aging of the population, and the worsening of living environment, susceptible population, such as premature infants, newborns with underlying diseases increases, and elderly adults, is expected to further expand, thus promoting the potential market
2 **Development of RSV-targeted antiviral drugs**	• Currently, only aerosolized Ribavirin, a broad-spectrum antiviral drug, and Palivizumab, an RSV specific monoclonal antibody, have been approved under multiple special conditions for the treatment and prevention of RSV infection. Whereas, due to the huge limitations in clinical applications, efficacy, medication safety and treatment cost, the practical medication value of Ribavirin and Palivizumab is very low • At present, there are a number of RSV-targeted antiviral drugs in different clinical phases in China and around the world, and some of them have shown positive clinical trial results and entered later phases. It is expected that more economical antiviral drugs with better specificity, safety and efficacy will largely contribute to the growth of RSV drug market
3 **Improving recognition of the diagnosis, treatment and prognosis of RSV infection**	• Since the symptoms manifested after RSV infection are very similar to common flu and the illness is to some extent self-limited, parents of child patients or patients themselves are usually unable to distinguish and estimate the disease severity, and the public lacks appropriate knowledge in relevant disease treatment and prognosis • However, along with the subsequent influence from COVID-19, the diagnosis and treatment capabilities have been enormously enhanced both in China and around the world. Following the deeper understanding of RSV infection mechanism and pathogenesis, continuous improvement in clinical treatment paradigm, and increase in per capita health expenditure, RSV infection patients' understanding about the disease and willingness to accept professional treatment will further improve
4 **Increasing requirement for clinical management quality and medical burden reduction**	• RSV infection will not only seriously affect health conditions, but also incur asthma, chronic obstructive pneumonia, cardiovascular disease and other diseases in the future, if without proper treatment and prognosis. Innovative RSV-targeted antiviral drugs could help improve treatment efficiency, and at the same time guarantee long-term health and life quality, reducing the potential economic and mental burden for patients' families. • Moreover, for the society as a whole, effective RSV antiviral drugs will in the longer term help stabilize and reduce the burden of national medical resources, improve national health level, and promote the sustainable development environment. Under the multiple positive significance brought by effective RSV antiviral drugs, the corresponding market will also achieve rapid and good development.

Sources: China Insights Consultancy

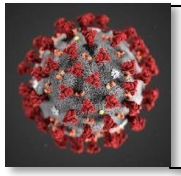
Entry barriers to RSV treatment drugs market

Entry barriers	Description
R&D of antiviral drugs	• New drug research and development is a long and systematic project, especially for field such as the RSV antiviral drug, which has long been stuck around the globe. One of the reasons is that the history of human research and development of antiviral drugs is relatively short. Another is that different from bacteria with independent metabolic system, antiviral drugs can only inhibit virus replication by interfering with the infection link, and many organelles used in virus replication are from the human body itself, so it is very difficult to develop effective antiviral drugs with small side effects. In addition, the design of dosage form and administration mode of RSV antiviral drugs will also affect the beneficiary population.
Unclear mechanism and pathogenesis of RSV infection and enhanced disease	• Though RSV was first discovered over 60 years ago, the specific mechanism of how the viruses infect, including how they interact with receptors on the epithelial cells they target and how they further replicate, has not been fully understood • Without clear understanding of the infection mechanism and pathogenesis, it would be difficult to develop targeted drugs that could function the most efficiently
Difficulties in clinical design for pediatric drugs	• Since RSV influences vulnerable population the most, especially infants and toddlers, clinical design of anti-RSV drugs is also one of the critical issues. Young children are a special group for drug use, whose body systems and function of organs have not developed completely, thus could lead to young children's lower drug metabolism and being more inclined to adverse reactions. Therefore, beside administration compliance, clinical design of pediatric drugs requires much higher in drug safety and formulation stability.

Sources: China Insights Consultancy

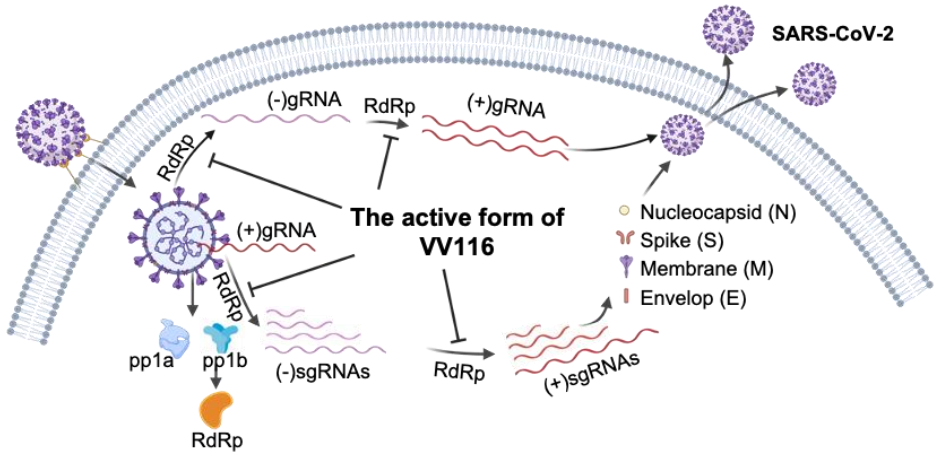
SARS-CoV-2 is a strain of coronavirus that causes COVID-19, the main targets for COVID-19 drugs are concentrated on RdRp and 3CL

Definition and and key targets of coronavirus



- Severe acute respiratory syndrome coronavirus 2 (**SARS-CoV-2**) is a single-stranded RNA enveloped virus with spike proteins on the outer membrane. It primarily infects the respiratory system, leading to flu-like symptoms, which typically include cough, fever, muscle pain, and difficulty breathing. The virus can spread through close-range droplets, contact with respiratory secretions from infected individuals, or inhalation of aerosolized particles. The incubation period for COVID-19 is generally 2 to 14 days. Currently, the main targets for coronavirus drugs are concentrated on **RdRp and 3CL**.

Mechanism of RdRp (VV116)

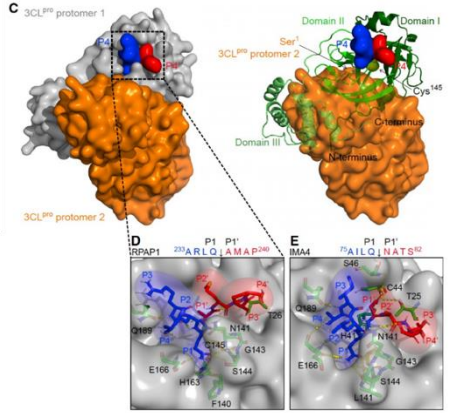


- **RNA-dependent RNA polymerase (RdRp)** is a crucial component of the coronavirus RTC. During the replication process, the coronavirus relies on its own encoded RdRp, which is responsible for two key stages: chain initiation and chain elongation. RdRp is a major target for antiviral therapies against COVID-19.

- The sequence of coronavirus RdRp is **highly conserved**, meaning that drugs targeting the enzyme could potentially have **broader activity**, providing similar therapeutic effects against different types of coronaviruses.
- Nucleoside analogs, such as **VV116**, inhibit viral replication by incorporating into the RNA replication process, adding nucleotides that induce a roadblock in RdRp, causing **chain termination**. This effectively inhibits viral replication. After entering the cell, the parent nucleoside of VV116 undergoes three phosphorylation steps to be converted into its active triphosphate form. This active form is incorporated into the RNA chain of the coronavirus under the catalysis of RdRp.

The mechanism of 3CLpro

- The 3CL protease (3CLpro) is responsible for cleaving the viral genome translation products, generating **non-structural proteins (NSPs)** that are essential for **assembling the RTC**. COVID-19 drugs inhibit 3CL protease activity by covalently binding to the enzyme or through hydrogen bonding, thereby reducing the frequency of viral replication and demonstrating antiviral activity.

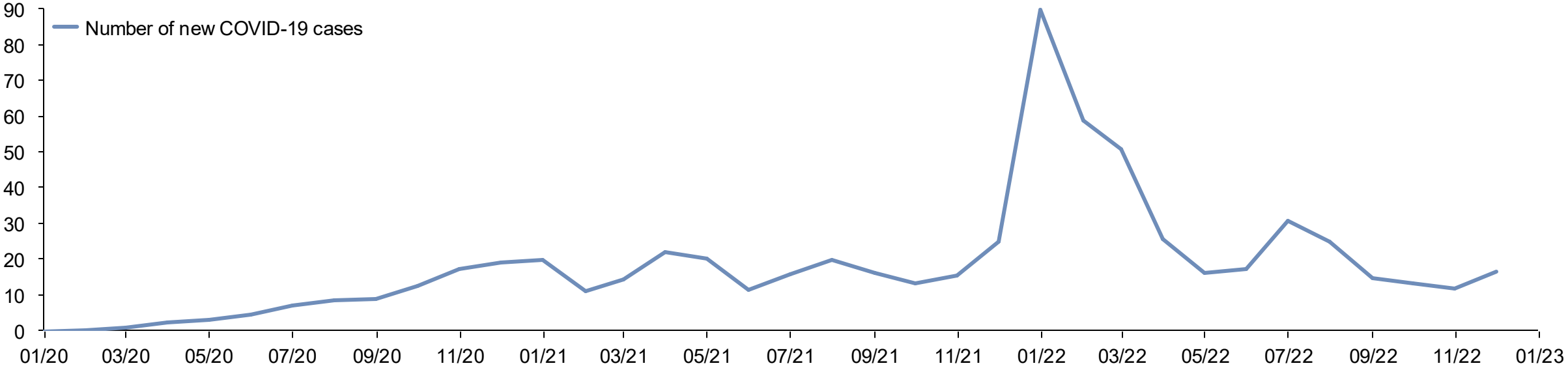


Sources: Nature structural&molecular biology, Phytotherapy Research, China Insights Consultancy

In recent decades, global health emergencies have occurred frequently

Introduction to the pandemic trends

Historical information on the number of new COVID-19 cases worldwide

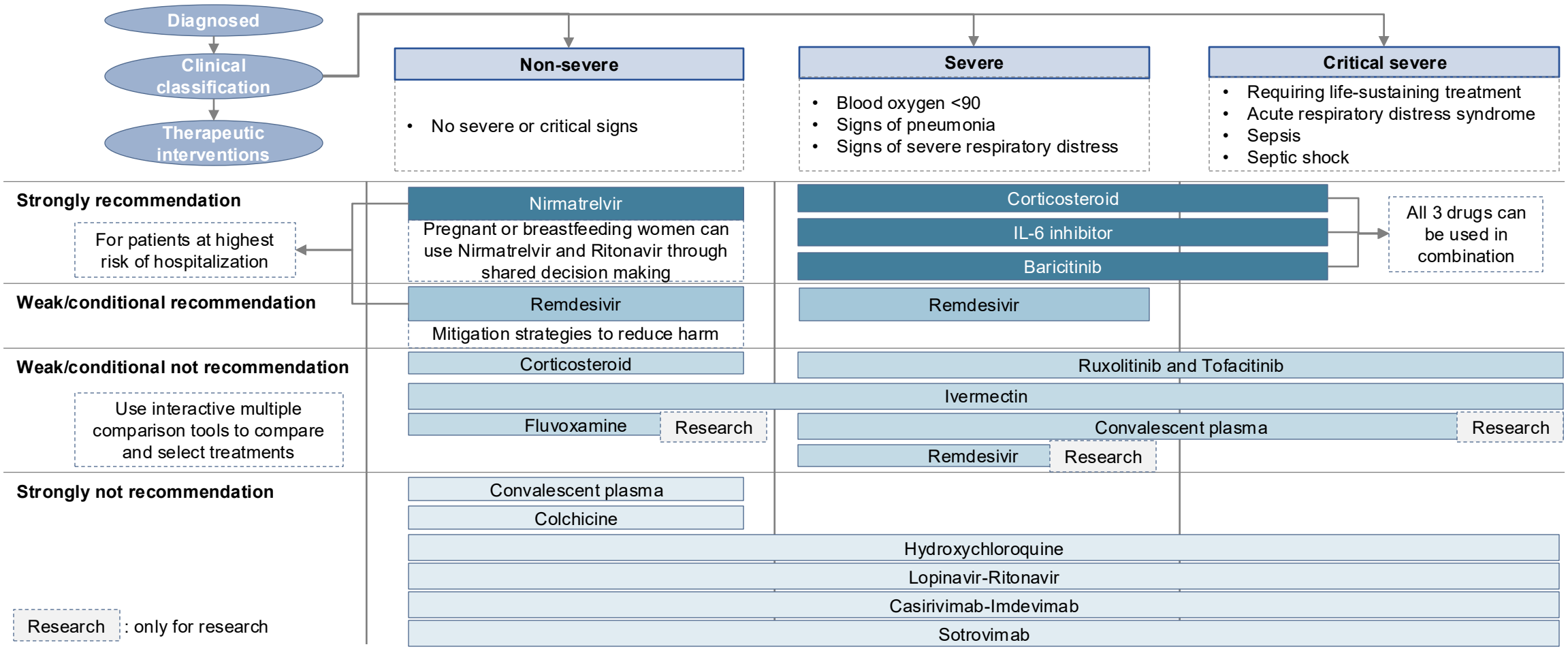


- Some researches shows that influenza pandemics have been reported for at least 500 years, with inter-pandemic intervals averaging approximately 40-50 years. While in recent decades, with the deepening of globalization, large-scale public health emergencies have become increasingly frequent, such as SARS, Ebola, H1N1, MERS, and the COVID-19 outbreak in 2020, as well as recent outbreaks of Dengue fever and Monkeypox. These large-scale emergencies have a significant impact on the global economy and society, especially in the early stages of the pandemic when many countries' healthcare systems were unable to cope with the surge in cases, leading to shortages of medical resources and delays in timely treatment for patients. Additionally, during the short period after the outbreak, effective vaccines and medications could not be quickly developed and produced for prevention and response.

Sources: WHO, The Science of Influenza, China Insights Consultancy

Post-infection treatment pathways of coronavirus by WHO

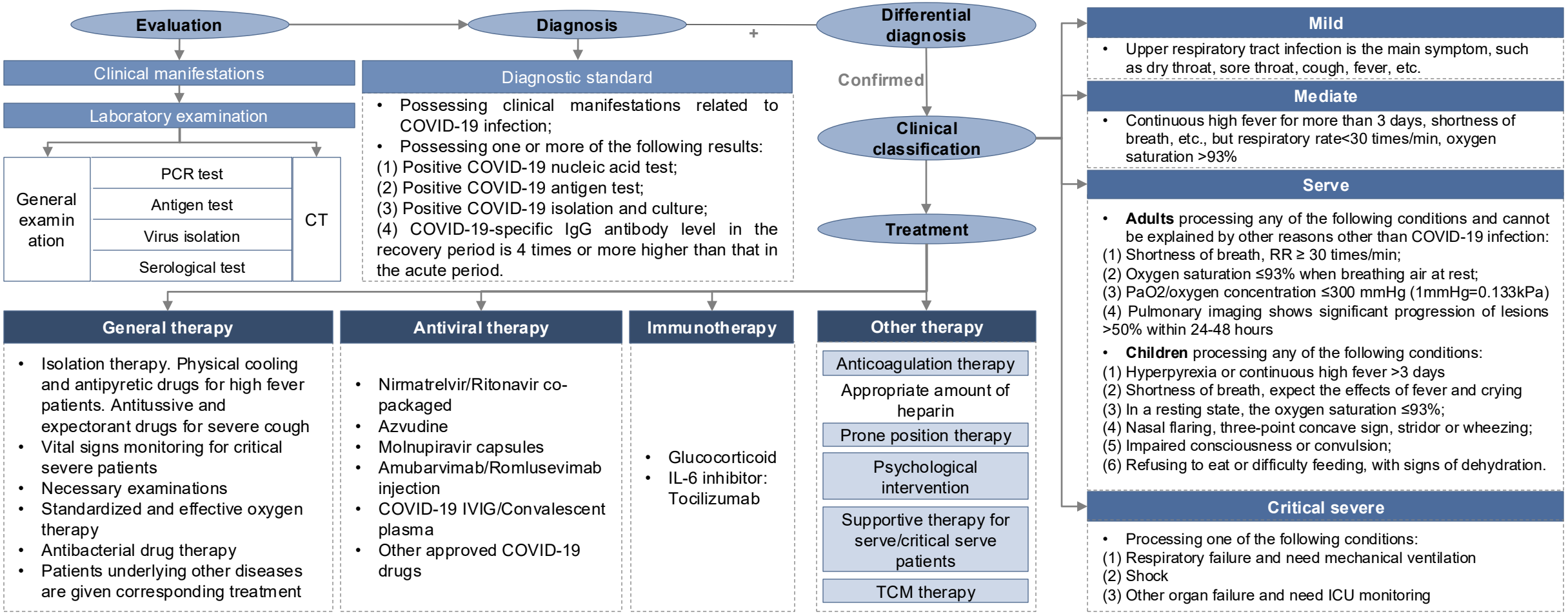
Post-infection treatment pathways of coronavirus by WHO



Sources: WHO, China Insights Consultancy

Post-infection treatment pathways of coronavirus in China

Post-infection treatment pathways of coronavirus in China



Sources: NHC, China Insights Consultancy

Small molecule COVID-19 drugs have clear advantages over neutralizing antibodies in terms of patient compliance, production costs, and clinical efficacy

Advantages of small molecule COVID-19 drugs

➢ Currently, COVID-19 drugs that have been approved for marketing or are in the clinical research stage can be divided into two categories worldwide: one is **large molecule neutralizing antibodies (NAb)** targeting the S protein, and the other is **small molecule** drugs that interfere with viral replication.

Neutralizing antibody

- Neutralizing antibodies block viral infection during the stage when the virus binds to human cells, thus achieving antiviral effects. The SARS-CoV-2 attaches to host cells by binding its S protein receptor-binding domain (RBD) with the host cell's angiotensin-converting enzyme 2 (ACE2). Targeting the S protein of the virus, monoclonal neutralizing antibodies **block the interaction between the virus RBD and ACE2**, effectively preventing the virus from infecting human cells and achieving therapeutic goals.
- For example, the combination of **Amubarvimab and Romlusevimab**, the only monoclonal antibody combination approved in China, works as follows: Amubarvimab binds to the RBD, prevents the virus from entering the host cell. Romlusevimab inhibits the necessary rearrangement of the spike protein required for viral membrane fusion with the host cell.

VS

Small molecule

- Small molecule COVID-19 drugs target another crucial step in the viral life cycle—**replication**. The drugs currently available or under development mainly fall into two categories: **RNA polymerase inhibitors and protease inhibitors**. One important part involved in viral genome replication is RNA-dependent RNA polymerase (RdRp). With the help of **RdRp**, the coronavirus can replicate its genome.
- Small molecule COVID-19 drugs mimic ATP and enter the replication machinery of RdRp, getting trapped between RdRp and the template RNA. This causes RNA synthesis to stop, effectively **inhibiting viral replication**. Additionally, human RNA polymerases do not have RNA-dependent RNA polymerase activity, which means that small molecules targeting viral RdRp **do not interfere with the normal physiological functions** of host cells. This makes RdRp an ideal target for antiviral drugs.

✓ Neutralizing antibodies have **high production costs** and are typically administered via injection, which leads **to poor compliance and unsuitable** for large-scale distribution. The NAb are generally limited to specific scenarios and particular populations. More critically, most neutralizing antibody drugs are **not effective** against the Omicron variant, making it difficult to show strong clinical efficacy.

✓ In contrast, small molecule COVID-19 drugs have better clinical results against the Omicron variant. The drugs can be taken orally, which are more convenient for patients and improving patient compliance compared to injection. Small molecule drugs are also less expensive to produce, offering a price advantage, and can more effectively target intracellular sites. Overall, in the field of COVID-19 treatment, small molecule drugs have clear advantages over neutralizing antibodies in terms of **patient compliance**, **production costs**, and **clinical efficacy**.

Sources: China Insights Consultancy

Pipelines of small molecule COVID-19 drugs in global, (registered in ClinicalTrials.gov)

Pipelines of small molecule COVID-19 drugs in global target RdRp, as of LPD

Trial number	Candidate	MoA	Company	Clinical phase	First posted date	Indication
NCT04818320	Favipiravir	RdRp	Promomed, LLC	III	2022/01/11	Hospitalized Patients With COVID-19
NCT05033145	Azvudine	RdRp	HRH Pharmaceuticals	III	2021/09/02	Mild Stage Patients Infected With the SARS-CoV-2 Virus
NCT04939428	Molnupiravir	RdRp	Merck	III	2021/06/25	Prevention of COVID-19 in Adults Residing With a Person With COVID-19
NCT04292730	Remdesivir	RdRp	Gilead Sciences	III	2020/03/03	Moderate COVID-19
NCT04431453	Remdesivir	RdRp	Gilead Sciences	II/III	2020/06/16	<18 Years of Age With COVID-19

Sources: ClinicalTrials, China Insights Consultancy

Pipelines of small molecule COVID-19 drugs in China, (registered in CDE)

Pipelines of small molecule COVID-19 drugs in China target RdRp, as of LPD

Trial number	Candidate	MoA	Company	Clinical phase	First posted date	Indication
NCT05908071	SHEN26	RdRp	Sinovac Biotech	III	2023/06/18	Mild to Moderate COVID-19
ChiCTR2200063762	ASC10	RdRp	Ascletis Pharma	I	2022/09/16	COVID-19 Patients

Sources: CDE, China Insights Consultancy

Approvals of small molecule COVID-19 drugs in global

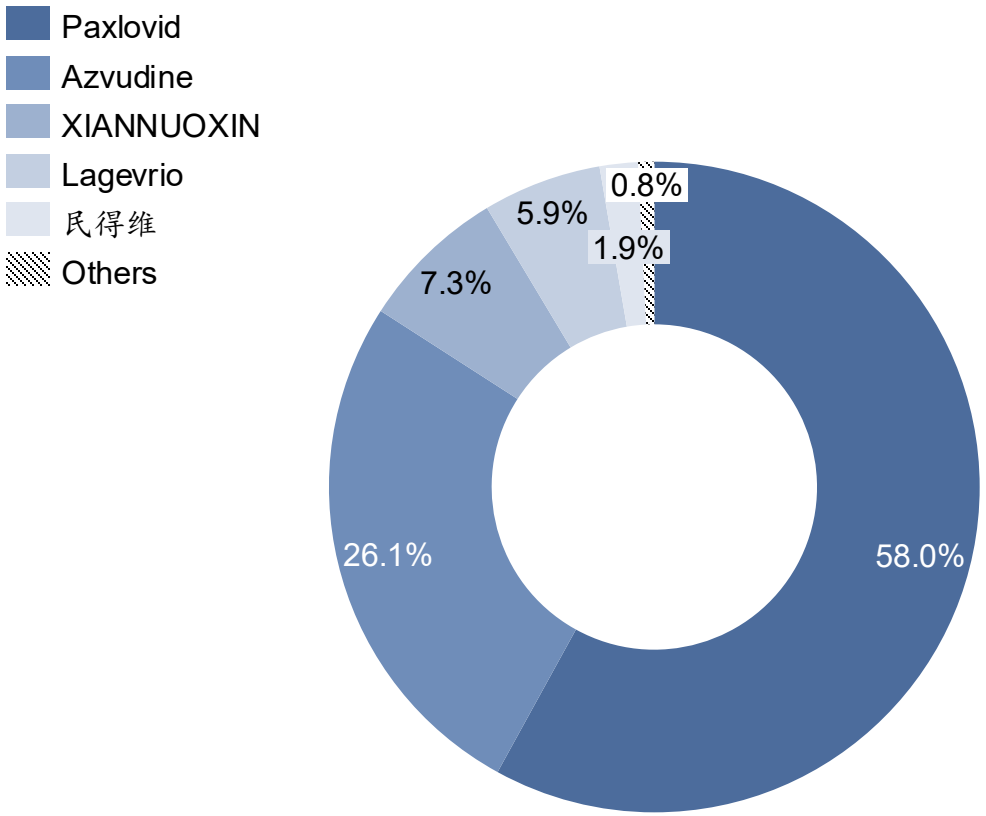
Approvals of COVID-19 small molecule drugs in global, as of LPD

Drug name	Product name	MoA	Company	Approval
Favipiravir	Avigan®	RdRp	Fujifilm/Hisun Pharmaceutical	EUA: 2020/2/15 China 2020/5/30 Russia
Proxalutamide	/	AR antagonist	Kintor Pharmaceutical	EUA: 2021/7/16 Brazil
Nirmatrelvir/Ritonavir	Paxlovid®	3CL	Pfizer	EUA: 2021/12/22 US 2022/2/10 Japan
				Conditional Approval: 2021/12/31 UK 2022/1/28 EU 2022/2/11 China
Molnupiravir	Lagevrio®	RdRp	Merk	EAU: 2021/11/4 UK 2021/12/23 US 2021/12/24 Japan
				Conditional Approval: 2022/12/30 China
Remdesivir	Veklury®	RdRp	Gilead Sciences	EUA: 2020/5/7 Japan
				Conditional Approval: 2020/10/22 US
				Conditional Approval: 2020/7/3 EU
VV116	民得维®	RdRp	Junshi Biosciences/Vigonvita Life Sciences	EUA: 2021/12/28 Uzbekistan
				Approval: 2025/1/10 China
Azvudine	捷倍安®	RdRp	Genuine Biotech	Conditional Approval: 2022/7/25 China
Simnotrelvir/Ritonavir	先诺欣®	3CL	Simcere Pharmaceutical	Approval: 2024/7/8 China
S-217622	Xocova®	3CL	Shionogi	EUA: 2022/11/22 Japan
Leritrelvir	乐睿灵®	3CL	Zhongsheng Pharmaceutical	Conditional Approval: 2023/03/23 China
Atilotrelvir/Ritonavir	Tazovid®	3CL	Akeylink Biotechnology	Conditional Approval: 2023/11/23 China

Sources: NMPA, FDA, EMA, China Insights Consultancy

Competitive landscape of COVID-19 drugs in China, 2023

Competitive landscape of COVID-19 drugs in China, by sales, 2023



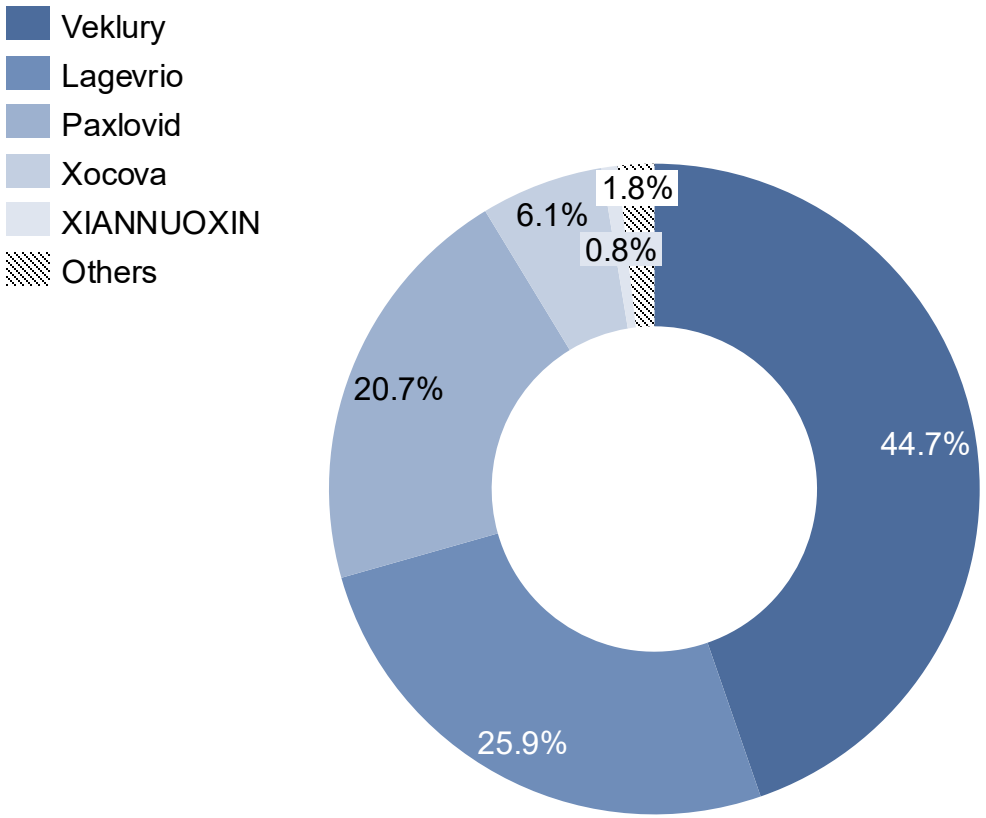
Ranking	Drug name	Market share
1	Paxlovid	58.0%
2	Azvudine	26.1%
3	XIANNUOXIN	7.3%
4	Lagevrio	5.9%
5	民得维	1.9%
Others		**0.8%**
Total		**100%**

In 2024, Paxlovid led the global market, and Paxlovid dominated the Chinese market with a 46% share.

Sources: China Insights Consultancy

Competitive landscape of COVID-19 drugs in global, 2023

Competitive landscape of COVID-19 drugs in global, by sales, 2023

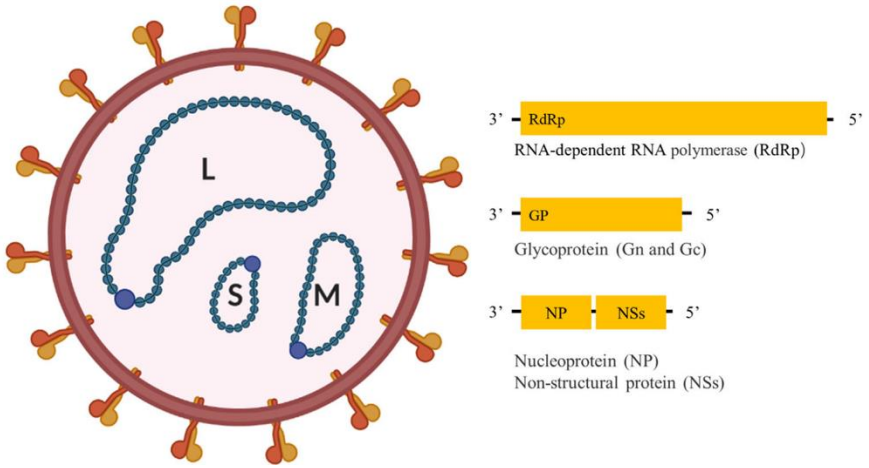


Ranking	Drug name	Market share
1	Veklury	44.7%
2	Lagevrio	25.9%
3	Paxlovid	20.7%
4	Xocova	6.1%
5	XIANNUOXIN	0.8%
Others		**1.8%**
Total		**100%**

Sources: China Insights Consultancy

Overview of Severe Fever with Thrombocytopenia Syndrome Virus (SFTSV)

Overview of SFTSV



- The severe fever with thrombocytopenia-causing phlebovirus has been officially named Dabie bandavirus, which belongs to the genus bandavirus in the family Phenuiviridae, order Bunyavirales . Synonymously this virus is known as Severe Fever with Thrombocytopenia Syndrome Virus (SFTSV) or Huaiyangshan Banyangvirus. Dabie bandavirus causes the clinical condition known as severe fever with thrombocytopenia syndrome (SFTS) which was **first discovered in China in 2009**.
- SFTSV comprises a segmented, negative-strand RNA that **includes large (L), medium (M), and small (S) segments** . The L segment encodes the RNA-dependent RNA polymerase (RdRp), which functions as the viral transcriptase/replicase. The M segment encodes a membrane protein precursor that matures into two glycoproteins, Gn and Gc, which constitute the envelope. The S segment is an ambisense RNA that encodes two proteins; the antisense RNA encodes Np and the sense RNA encodes NSs. Np functions in viral RNA encapsidation/ formation of the RNP complex and NSs interfere with host interferon production.

Characteristic:

(1) Source of infection: Infected animals are the main source of infection, which may be cattle, sheep, cats, dogs and rodents. Patients can also be the source of infection, and the virus can be isolated from the blood within 7 to 10 days after the onset of the disease.

(2) Transmission route: SFTSV is mainly transmitted through the bites of vectors such as infected long-horned ticks and can also cause infection through unprotected contact with the blood, secretions, excretions and contaminants of infected animals or patients.

(3) Susceptible population: The general population is susceptible.

Mechanism:

- The pathogenesis of the disease has **not yet been fully elucidated**. SFTSV directly acts on multiple cells in the human body, causing tissue and organ damage. The virus attacks the human lymph nodes, causing lymphadenopathy and necrotizing lymphadenitis. After rapid replication in the lymph nodes and spleen, it enters the systemic circulation, forming viremia and attacking multiple tissues and organs at the same time. SFTSV infection leads to immune dysfunction. In severe cases, it can induce cytokine storms and endothelial damage, and patients may die from bleeding or multiple organ failure.

Sources: Frontiers in Immunology, Experimental & Molecular Medicine, NHC, China Insights Consultancy

Treatment pathways of SFTSV

Treatment pathways of SFTSV in China

➢ There is **no specific treatment for SFTSV**, and it is mainly symptomatic supportive treatment and treatment for complications.

General treatment

1. **Nutritional support therapy**. Rest in bed, give easily digestible, nutritious semi-liquid or soft food, ensure calorie supply and maintain water, electrolyte and acid-base balance.
2. **Physical cooling** is given to patients with fever, and drugs can be used to reduce fever when the fever is high.
3. **Plasma and platelets** can be transfused for patients with obvious bleeding or significantly reduced platelet count (such as less than 20×10^9 /L).
4. For severe and critical patients with progressive deterioration of the condition and over-activation of the body's inflammatory response, **glucocorticoids** should be used early and short-term as appropriate.
5. Severe and critical cases should be transferred to the **ICU** for treatment.
6. **Antiviral treatment**: Ribavirin (use with caution), Favipiravir (patients with low viral load), calcium channel blockers (Benidipine Hydrochloride and Nifedipine have a certain inhibitory effect)
7. **Glucocorticoids** are not recommended as a routine treatment for SFTS

Complications treatment

1. **Viral myocarditis**. Rest in bed and strengthen monitoring; control the intake and output, and avoid excessive fluid load; give coenzyme Q10, vitamin C and other nutritional myocardial treatments.
2. **Encephalitis**. Give symptomatic comprehensive treatment such as mannitol to reduce intracranial pressure; pay attention to airway protection and give mechanical ventilation when necessary.
3. **Secondary bacterial and fungal infections**. For those who are considered to have secondary bacterial and fungal infections, antibacterial or fungal drugs can be given empirically, and the treatment plan can be adjusted according to the drug sensitivity results.

Traditional Chinese Medicine treatment

1. **Mild**. Recommended prescription: Yin Qiao San (银翘散).
2. **Severe**. Recommended Chinese patent medicine: Xue Bi Jing Injection (血必净注射液).
3. **Recovery period**. Recommended prescription: Zhu Ye Shi Gao Tang (连翘竹叶石膏汤).

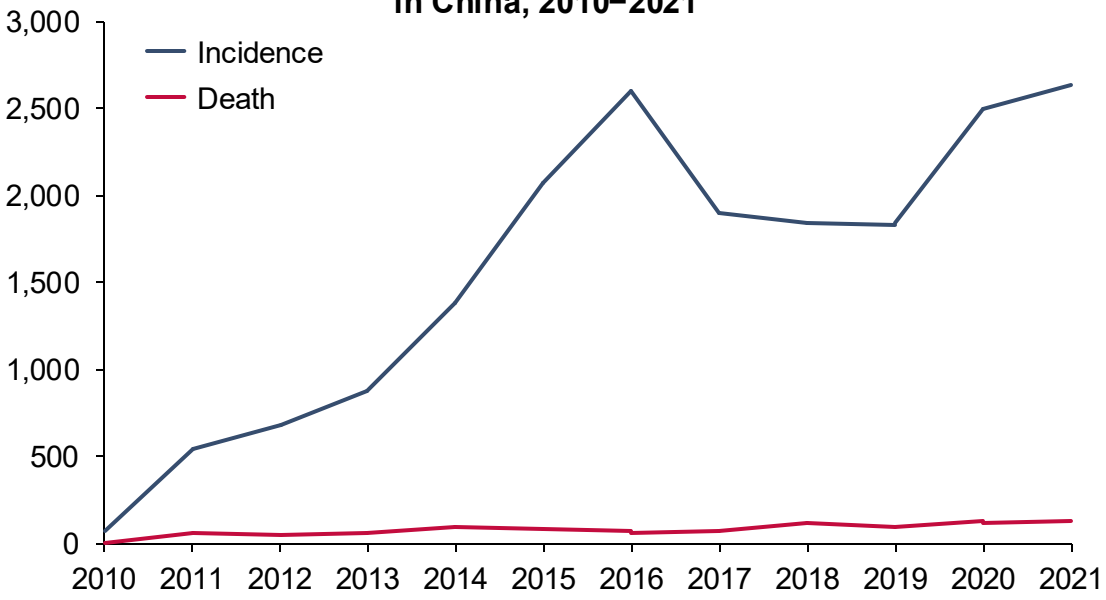
Sources: 发热伴血小板减少综合征诊疗方案（2023版），重症发热伴血小板减少综合征诊治专家共识（2022），China Insights Consultancy

Epidemiological characteristics and unmet needs for SFTSV drugs

Epidemiological characteristics and unmet needs for SFTSV drugs

✓ The incidence rate of SFTS in China showed an upward trend and the case fatality rate showed a downward trend. From 2010 to 2021, a total of **18,968 cases** of SFTS were reported in **27 provinces**, with an average annual incidence rate of 0.11/100,000, and a total of **973 SFTS deaths** were reported in **11 provinces**, with a case **fatality rate of 5.13%.** The annual incidence of SFTS showed seasonality with only one peak from May to August. The incidence of SFTS in China is concentrated in summer and autumn, with the number of cases from April to October accounting for 96.63% of the whole year. The annual incidence rate in people over 50 years old was higher, and the cases in farmers accounted for 86.02%. The cases and deaths of SFTS in areas with high incidences, such as Shandong, Henan, Anhui, Hubei and Liaoning provinces, accounted for 92.97% and 89.21%, respectively, and the disease also expanded to southwestern, northeastern, eastern and western China.

Reported severe fever with thrombocytopenia syndrome cases in China, 2010−2021



Unmet needs and social significances

a) There was a significant expansion of SFTSV infections from 2010 to 2021. In the future, as the activity range of ticks, the vectors of SFTSV, and the natural hosts such as cattle, sheep, and birds continue to expand, and **large-scale animal transportation** continues to form new epidemic areas, the number of people infected with SFTSV will continue to increase, and the demand for treatment will continue to expand.

b) SFTSV is accompanied by many complications, and severe patients may die from bleeding or multiple organ failure. The mortality rate of severe patients is high, and the mortality rate of SFTS patients with multiple organ failure and central nervous system involvement is as high as 44.7%. Countries such as Japan and South Korea have reported that the mortality rate of local SFTS is also over 20%. At the same time, the pathogenesis of SFTSV is still unclear, and there is currently **no specific treatment drug or vaccine for its infection around the world.**

c) The outbreak of SFTSV may trigger public panic, especially in the early stages of the epidemic. Due to information asymmetry and the public's lack of understanding about how the virus is transmitted, excessive anxiety and panic may arise, which can have a certain impact on the social economy.

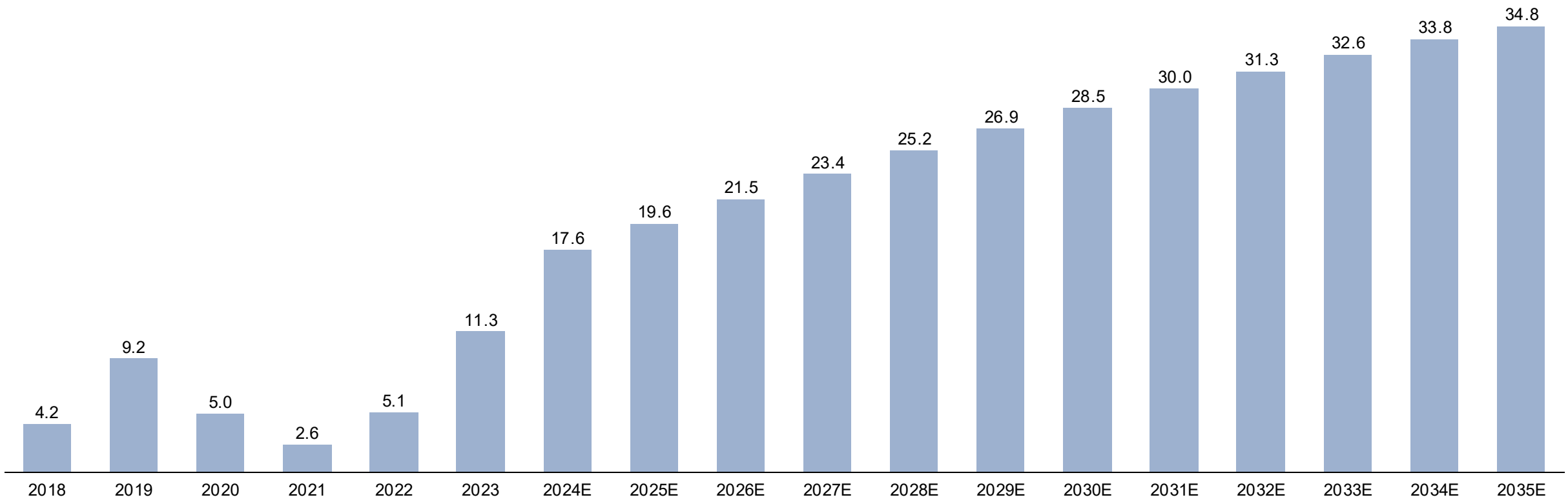
Sources: Disease Surveillance, Chinese Journal of Clinical Infectious Diseases, China Insights Consultancy

Market size of flu drugs in China, 2018-2035E

Market size flu drugs in China

CAGR	2018-23	2023-35E
China flu drugs	21.9%	9.8%

RMB billion



Sources: China Insights Consultancy

Pipelines of SFTSV drugs in China, (registered in CDE)

Pipelines of SFTSV drugs in China, as of LPD

Trial number	Candidate	MoA	Company	Clinical phase	First posted date	Indication
CXHL2400602 CXHL2400603 CXHL2400604	VV261	RdRp	Vigonvita Life Sciences	I	2024/08/27	SFTSV

Sources: China Insights Consultancy

Table of contents

Definition and main indications of neuropsychiatric disorders

Definition and main indications of neuropsychiatric disorders

- Neuropsychiatry encompasses affective, cognitive, and behavioral disorders arising from overt brain dysfunction or indirect effects of extracranial diseases, fundamentally addressing psychiatric issues related to neurology.
- In neuropsychiatry, cognition is considered an "emergent property" of the brain, whereas other behavioral and neurological disciplines may view thought and brain as separate entities. Throughout the chronicles of neuroscience, the term neuropsychiatry has held varying connotations in different epochs, contingent upon prevailing social, cultural, and political factors.

Distinct etiology of neuropsychiatric disorder

Intrinsic factors	**Genetic susceptibility**	**Early trauma**	**Brain injury**	**Aging**
Extrinsic factors	**Life stressors**	**Bereavement**	**Abuse**	**Substance use disorder**

Main treatment pathways of neuropsychiatric disorders	Physical therapy	• Drug treatment
		• Transcranial Magnetic Stimulation
		• Electric shock treatment
	Psychotherapy	• Individual/group/family therapy, behavioral therapy

Major indications

Bipolar disorder	Depressive disorder	Schizophrenia
Epilepsy	Parkinson's disease	Alzheimer's disease

Principal clinical manifestations

1. Cognitive impairment
2. Early manifestation of cerebral pathology
3. Concurrent occurrence of various psychiatric symptoms
4. Occasional presentations mimicking endogenous psychiatric disorders

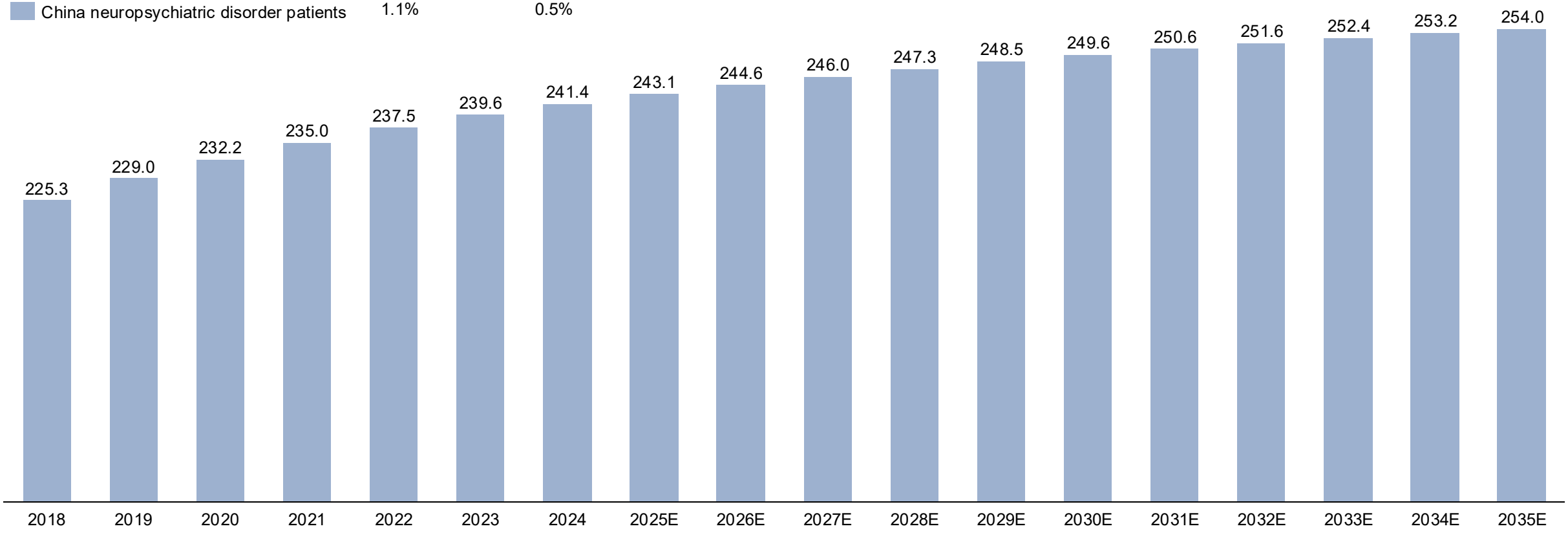
Sources: WHO, China Insights Consultancy

Epidemiology of neuropsychiatric disorders, 2018-2035E

Epidemiology of neuropsychiatric disorders, China

CAGR	2018-24	2024-35E
China neuropsychiatric disorder patients	1.1%	0.5%

ppl million



*Note: including anxiety disorders, depression, schizophrenia, sleep disorders, stress-related disorders, drug dependence and other addictive disorders, neurodevelopmental disorders and psychiatric disorders

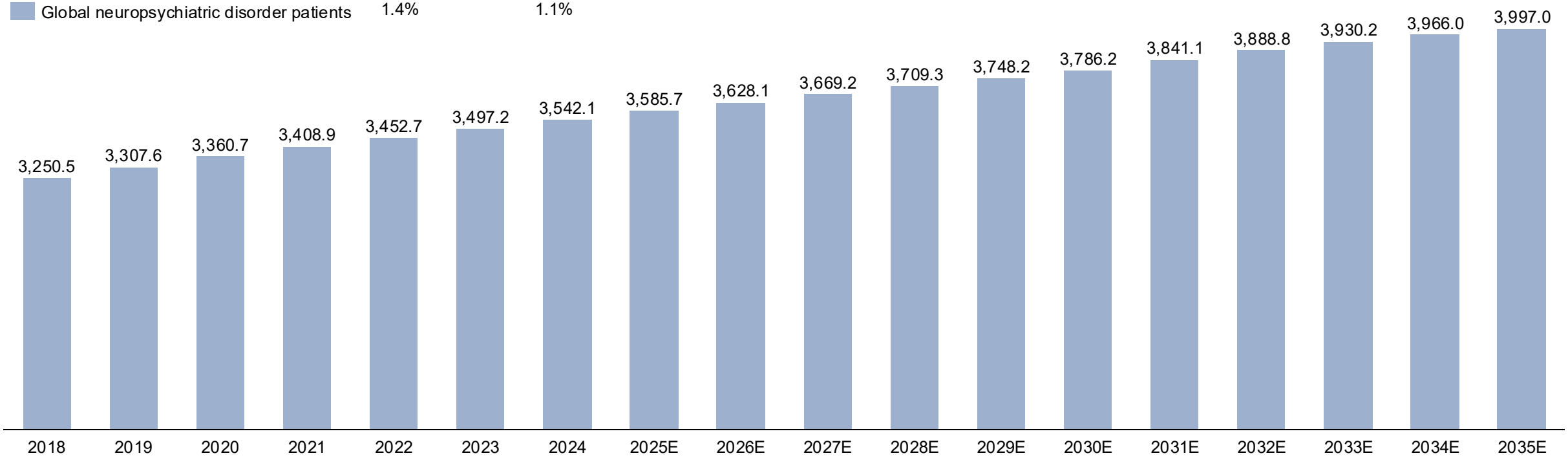
Sources: 中华精神科杂志, China Insights Consultancy

Epidemiology of neuropsychiatric disorders, 2018-2035E

Epidemiology of neuropsychiatric disorders, global

CAGR	2018-24	2024-35E
Global neuropsychiatric disorder patients	1.4%	1.1%

ppl million



*Note: including anxiety disorders, depression, schizophrenia, sleep disorders, stress-related disorders, drug dependence and other addictive disorders, neurodevelopmental disorders and psychiatric disorders

- According to WHO, worldwide, the number of individuals affected by these disorders was 3,542.1 million in 2024 and is projected to reach 3,997.0 million by 2035.

Sources: 中华精神科杂志, China Insights Consultancy

Difficulties and limitations of current drug treatment in neuropsychiatric disorders

Difficulties and limitations of current drug treatment in neuropsychiatric disorders

1 Patient compliance

- Many neurological and psychiatric disorders are chronic or lifelong conditions. Therefore, medication non-adherence is highly prevalent among psychiatric patients, manifesting as underdosing, missed doses, or premature discontinuation of pharmacotherapy, collectively termed poor medication compliance, which significantly impacts therapeutic outcomes.
- Poor medication adherence and further affect prognosis and functional recovery, leading to symptom recurrence and increased disease burden.

2 Limitation of efficacy

- Neurological and psychiatric disorders involve complex pathophysiological mechanisms. This complexity and heterogeneity make identifying effective therapeutic targets challenging.
- Current pharmacological treatments primarily focus on symptom relief, such as improving mood in depression, without addressing underlying causes. This highlights the urgent need for innovative therapies that can target the root causes of these complex disorders.

3 Delayed onset of efficacy

- Current antidepressants' limitations, including delayed onset of action, unreliability, and high recurrence rates, fail to meet some patients' therapeutic requirements. Suboptimal symptom control and insufficient cognitive improvement lead to reduced patient confidence in medication, slower quality-of-life improvements, poor self-care capabilities, inefficient recovery in daily activities, academic performance, and occupational functioning, ultimately impacting social reintegration.

4 Side effects

- Common adverse effects of neuropsychiatric medications include central nervous system effects (sedation, somnolence, dizziness, ataxia, cognitive deficits, memory impairment), systemic effects (hematological, gastrointestinal, weight changes, skeletal health), and idiosyncratic reactions, significantly impacting patients' work and daily life, resulting in poor medication experience and further reducing treatment adherence. Medication safety concerns further complicate clinical implementation.

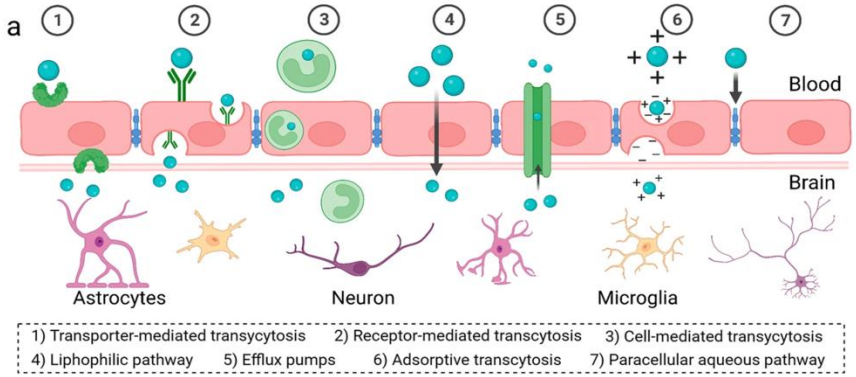
Sources: China Insights Consultancy

Challenges and technical breakthroughs of blood-brain barrier in neuropsychiatric drugs

Challenges and technical breakthroughs of blood-brain barrier in neuropsychiatric drugs

- Blood-brain barrier (BBB) is a highly selective barrier system composed of specialized endothelial cells, tight junctions, basement membrane, and astrocytic end-feet. This unique structure plays a crucial role in maintaining central nervous system homeostasis while presenting significant challenges for drug delivery.
- The ability of drug molecules to cross the BBB primarily depends on their molecular weight (optimally <400-500 Da), lipophilicity (appropriate octanol/water partition coefficient), and molecular properties.

➢ The blood-brain barrier, as a crucial barrier between the central nervous system and peripheral circulation, presents multiple challenges for neuropsychiatric drug delivery due to its unique structural and functional characteristics. These barriers work in combination to significantly impact therapeutic effectiveness:



Transport routes of the drug molecules across the BBB occurs via the pathways including paracellular and transcellular diffusion, receptor-mediated transcytosis, cell-mediated transcytosis, transporter-mediated transcytosis, and adsorptive mediated transcytosis

- ☐ The P-glycoprotein (P-gp) mediated efflux mechanism, an active transport system that pumps many therapeutic drugs out of the central nervous system, for instance, antiepileptic drugs like carbamazepine are frequently affected by P-gp efflux, resulting in insufficient brain drug concentrations
- ☐ Limited paracellular transport pathway, where tight junctions between cells restrict drug passage, as exemplified by many antidepressants with large molecular weight and high hydrophilicity that struggle to enter the brain via paracellular routes
- ☐ Complex protein binding interactions affecting drug free concentrations, a typical example being antipsychotics drugs like clozapine with high plasma protein binding rates, which reduces the proportion of free drug available to cross the blood-brain barrier
- ☐ Significant variations in drug penetration rates, leading to considerable individual differences in therapeutic effects among different compounds within the same drug class. These factors collectively create challenges for drug delivery.

- The BBB composes of tightly connected brain endothelial cells, efflux transporters (such as P-gp and BCRP), and metabolic enzymes, effectively prevents most large and hydrophilic drugs from entering brain tissue. Metabolic enzymes within the BBB degrade drugs before they reach the brain, further reducing their activity and efficacy. Even if a drug successfully crosses the BBB, targeted delivery within the brain remains a significant challenge, making it difficult to precisely act on specific lesion areas.
- To overcome these barriers, substantial financial and technological investments are required to advance strategies such as nano-delivery systems, carrier-mediated transport, and temporary BBB disruption. However, these high R&D costs and elevated failure rates contribute to rising drug prices, increasing the economic burden on CNS patients.

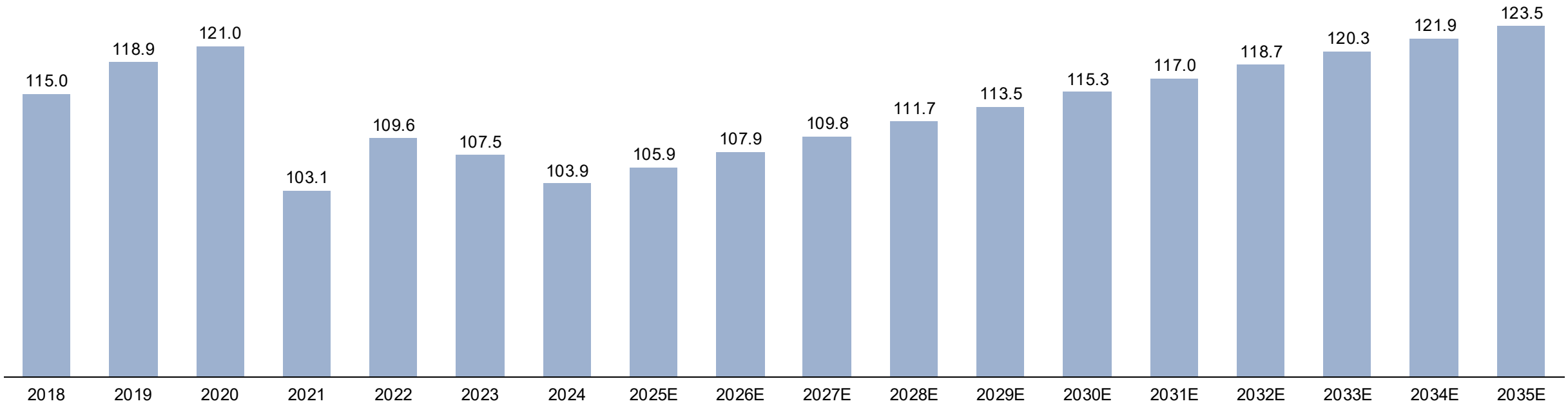
Sources: The blood–brain barrier: Structure, regulation and drug delivery, China Insights Consultancy

Market size of neuropsychiatric drugs, China, 2018-2035E

Market size of neuropsychiatric drugs, China

CAGR	2018-24	2024-35E
China neuropsychiatric drug market	-1.7%	1.6%

RMB billion



The neuropsychiatric drug market declined in 2024 due to VBP-driven price reductions, healthcare cost controls, and reduced demand for deferrable treatments amid economic headwinds. Future recovery is anticipated as structural demand growing from pricing stabilizes and aging populations.

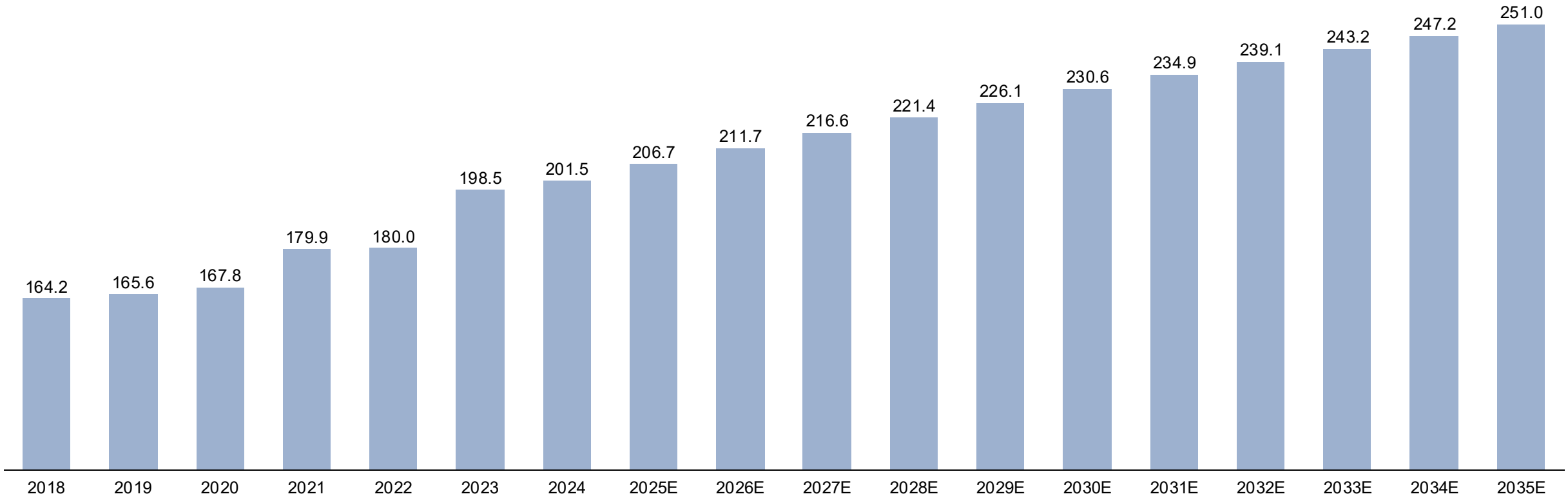
Sources: China Insights Consultancy

Market size of neuropsychiatric drugs, global, 2018-2035E

Market size of neuropsychiatric drugs, global

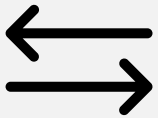
CAGR	2018-24	2024-35E
Global neuropsychiatric drug market	3.5%	2.0%

USD billion



Sources: China Insights Consultancy

Market drivers and development trends of neuropsychiatric drugs in China

Market drivers and future trends	
 **Accelerating innovative drug development to meet unmet clinical needs**	• With increased support for innovative drug development in China, neurological and psychiatric disorders such as epilepsy, depression, and schizophrenia are receiving focused attention. Traditional treatments often have limited efficacy and significant side effects, particularly in complex indications like drug-resistant epilepsy and treatment-resistant depression, creating an urgent need for novel therapies. By introducing drugs targeting new mechanisms (e.g., selective neurotransmitter modulators) and disease-modifying therapies, innovative drugs will offer more precise and effective treatment options for patients.
 **Advanced technologies drive drug delivery and precision treatment**	• Small-molecule innovative drugs, known for their compact structure, ability to cross BBB, and high oral bioavailability, have become a critical focus in neuropsychiatric drug development. These drugs can precisely target specific molecular pathways, such as sodium channel modulators for epilepsy or fast-acting NMDA receptor antagonists for depression, significantly enhancing treatment specificity and efficacy. Additionally, small molecules are easier to produce and store on a large scale, reducing treatment costs and improving accessibility for patients. These advancements pave the way for disease-modifying therapies, particularly for complex conditions like epilepsy and schizophrenia.
 **Local innovation and international cooperation**	• The Chinese government is continuously optimizing drug regulatory policies, including priority reviews and expedited approvals, creating a favorable environment for the launch of innovative drugs. Moreover, China is gradually emerging as a significant player in the global pharmaceutical market. Domestic pharmaceutical companies are increasing R&D investments in areas such as epilepsy and schizophrenia, while attracting strategic partnerships with multinational pharmaceutical companies. This dual-driven model of local innovation and international collaboration not only meets domestic market demands but also supports the globalization of locally developed drugs.
 **Social demand and economic growth drive market expansion**	• As public awareness of neurological and psychiatric health issues rises, the diagnosis rates of disorders like depression and schizophrenia are increasing significantly. Combined with the expansion of health insurance policies and improved coverage, patient acceptance of innovative drugs continues to grow. The rapid expansion of China's pharmaceutical market is also attracting increased capital and corporate investment, particularly in the fields of anti-epileptic and antidepressant drugs. This is expected to drive larger-scale market development and foster the widespread clinical application of next-generation drug technologies.

Sources: China Insights Consultancy

Definition, etiology, and clinical manifestation of depressive disorder

Definition of depressive disorder

- **Depressive disorder** refers to a group of mental disorder characterized by **a dysphoric mood and a loss of interest and pleasure**, with or without illusion, delusion, and agitation symptoms. According to the clinical features, the disease can be categorized into **major depressive disorder, seasonal mood disorders, perinatal depression, persistent depressive disorder, and depression with psychotic symptoms**.

Etiology of depressive disorder

- **Genetic factors** The onset of depression shows a familial clustering tendency, indicating the correlation between it and genetic factors. According to genomic researches, mutations in 5-HT transporters, MAO-A, and BDNF may play important roles in the etiology of depression.
- **Biochemical disorders** The disruption of the balances among neurotransmitters and the abnormal neuroendocrine hormone levels can be observed in depression patients. These biochemical disorders are considered to be directly related to the onset of depression.
- **Abnormality in neural electrophysiology** The abnormalities in neural electrophysiology are observed in depression patients by EEG and BEP, which showed strong connection to the onset and severity of depression.
- **Social psychological stressor** It has long been recognized that strong social psychological stressors can be a trigger to the onset of depression.

Clinical manifestations of depressive disorder

Core symptoms

- Core symptoms refer to the typical clinical manifestations of depressive disorder, which can be regarded as important diagnostic criteria of depressive disorder
- Main core symptoms include depressive mood, loss of interest and pleasure.

Psychological symptoms

- Psychological symptoms refer to the mental disorders of depression patients, which may be various from patient to patient, making it complicated to treat for the doctors
- Common psychological symptoms include disorders in emotion and cognition, anxiety, suicidal tendency, etc.

Somatic symptoms

- Somatic symptoms refer to the behavioral disorders of depression patients
- Main somatic symptoms include insomnia, anorexia, sexual dysfunction, etc.

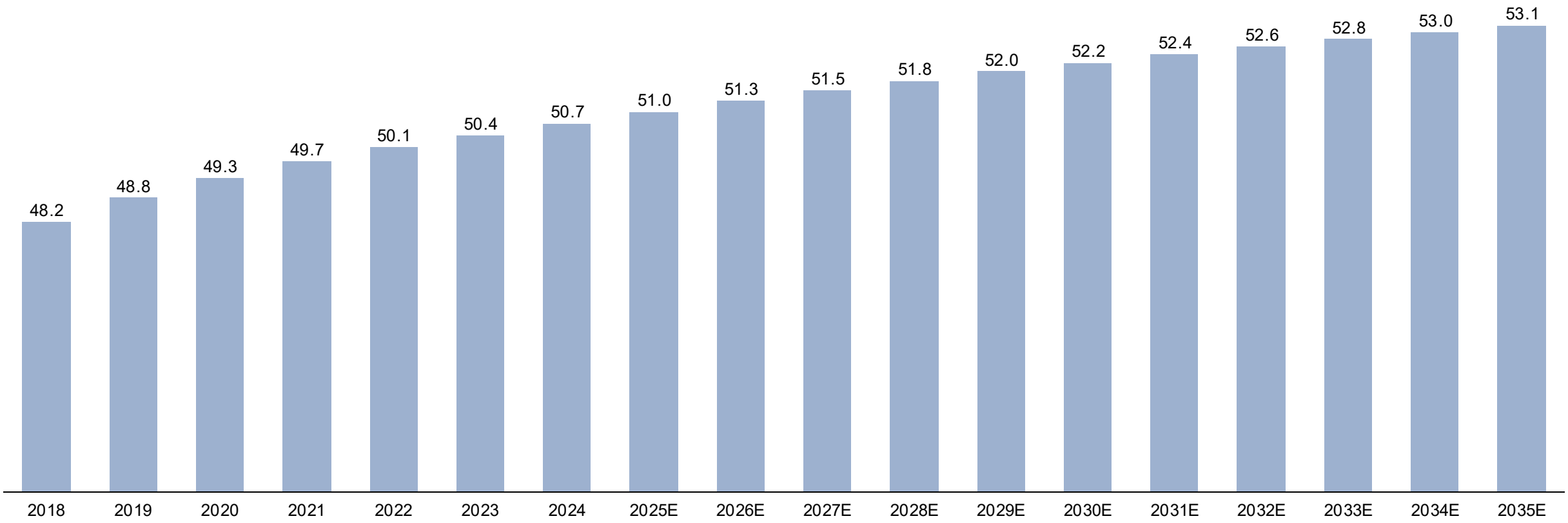
Sources: J Pediatr Health Care., Psychiatry, China Insights Consultancy

Prevalence of depression in China, 2018-2035E

Prevalence of depression in China

CAGR	2018-2024	2024-2035E
Depression patients in China	0.8%	0.4%

ppl million



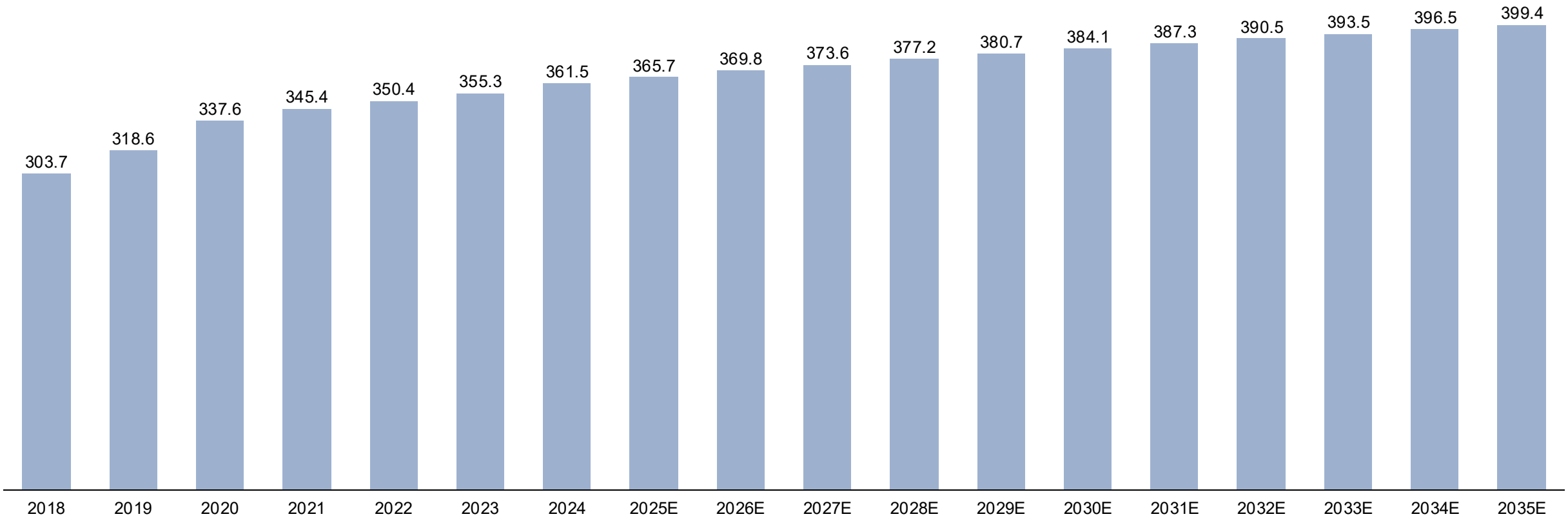
Sources: China Insights Consultancy

Prevalence of depression, global, 2018-2035E

Prevalence of depression, global

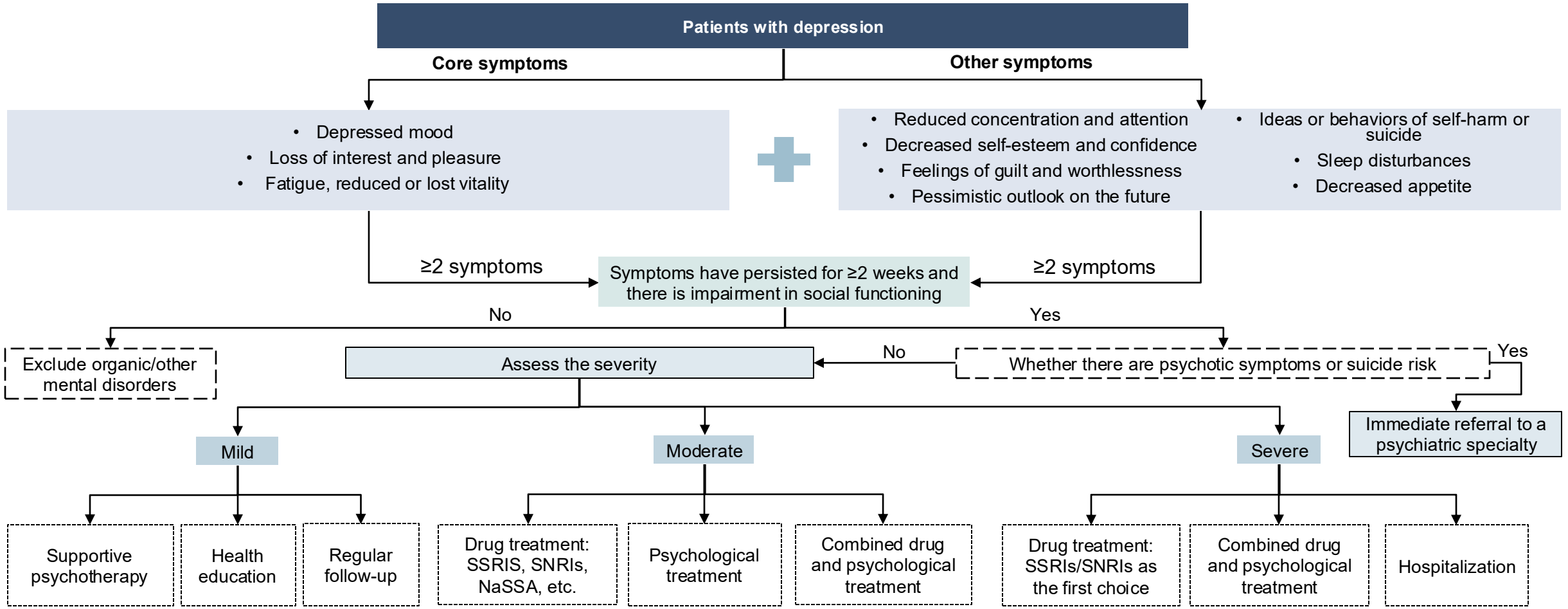
CAGR	2018-24	2024-35E
Global depression patients	2.9%	0.9%

ppl million



Sources: China Insights Consultancy

Treatment pathway of depression



Source: 抑郁症基层诊疗指南(2021年), China Insights Consultancy

Summary of common antidepressants

Summary of common antidepressants

Medication category	Representative drugs	Mechanism	$T_{1/2}$ (h)	T_{max} (h)	Common ADR
Selective serotonin reuptake inhibitor (SSRI)	Fluoxetine; Paroxetine	Selectively inhibits the reuptake of 5-HT, enhancing the transduction among 5-HTergic neurons	24-72	4-8	Gastrointestinal symptoms, insomnia, sexual dysfunction, obesity, etc.
Selective serotonin-norepinephrine reuptake inhibitor (SNRI)	Venlafaxine; Duloxetine	Blocks the reuptake of serotonin and norepinephrine to modulate their level in brain	3-12	2-6	Similar to SSRI
Noradrenergic and specific serotonergic antidepressant (NaSSA)	Mirtazapine	Blocks the α_2 adrenergic receptors to activate noradrenergic neurons, promoting the secretion of 5-HT	20-40	~2	Sedation and obesity
Norepinephrine-dopamine reuptake inhibitor (NDRI)	Bupropion	Inhibits the reuptake of dopamine and norepinephrine, activating related neurons	~11	~5	Headache, tremor, convulsion, agitation, insomnia, and gastrointestinal symptoms
Serotonin antagonist/reuptake inhibitor (SARI)	Trazodone	Inhibits 5-HT receptors, the reuptake of 5-HT and norepinephrine	4-8	~1	Sedation, cardiovascular adverse reactions, and sexual dysfunction
Noradrenaline reuptake inhibitor (NaRI)	Reboxetine	Inhibits the reuptake of norepinephrine, activating related neurons	~13	~2	Anticholinergic reactions and cardiovascular adverse reactions
Tricyclic antidepressants (TCAs) and tetracyclic antidepressant (TeCAs)	Amitriptyline; clomipramine	Inhibits the reuptake of norepinephrine and 5-HT and blocks the receptors of multiple neurotransmitters, enhancing the transduction among neurons	9-36	1-6	Anticholinergic reactions, cardiovascular adverse reactions, sexual dysfunction, obesity, etc.
Monoamine oxidase inhibitor (MAOI)	Moclobemide	Selectively inhibits the activity of monoamine oxidase	1-2	1-2	Anticholinergic and allergic reactions

- As of the Latest Practicable Date, there were 24* innovative small molecule antidepressants approved for marketing in China.

Source: Lancet, WHO, Psychiatry, Drug instructions, China Insights Consultancy

Unmet clinical needs of depression

➢ The poor compliance of depression patients and high recurrence rate of depression

- Though accepted standard treatment, more than 50% of the depression patients are not able to be cured, leading to the recurrence of the depressive symptoms. Moreover, the cure of depression relies on long-term systematic therapy, which can be a huge challenge to the compliances of the patients. The interruption of standard treatment is estimated as a main reason for the recurrence of depression.

➢ Severe side effect of antidepressants

- The antidepressants may lead to severe side effects, including gastrointestinal symptoms, migraine, hypertension, sexual dysfunction, etc. According to former surveys, 86% of the patients reported at least one side effect, 55% of which were described as 'bothersome'. These side effects may be a psychological burden to depression patients and reduce their compliance, which may eventually lead to a poor prognosis.

➢ Slow onset of the antidepressants

- It usually takes the depression patients a few days to recognize the therapeutical responses to the antidepressants, while the side effect of the drugs occurs in a shorter period. The extra psychological burden would be added to the patients when they are with the most severe symptoms, making the gap period the most dangerous one for the patients, which may cause suicidal intensions.

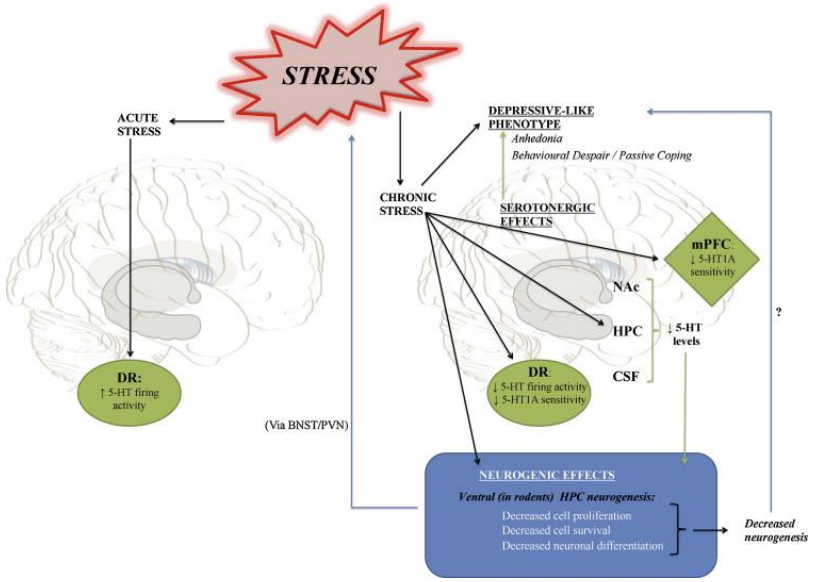
- According to the Lancet, global productivity losses due to depression amount to approximately $1 trillion annually. Additionally, the high suicide rate among individuals with depression further burdens society. In China, about 280,000 people die by suicide each year.

Source: CCDRFS, Dialogues Clin Neurosci., JAMA, Psychiatry, China Insights Consultancy

Introduction to rapid-onset antidepressants

Definition of rapid-onset antidepressant

- The onset of traditional antidepressants relies on the low sensitivity of 5-HT receptors, which requires a consistent medication intake for a few days, largely slowing down the antidepressant effect to act. **The slow-onset of antidepressant effect and relatively rapid-onset side effect may temporally aggravate the symptoms, bringing extra physical and psychological burdens to the patients.**
- **Rapid-onset antidepressants refer to the antidepressant whose antidepressant effect would take place within a shorter period.** By targeting novel and/or multiple **5-HT receptors**, these drugs are able to modulate neuron's sensitivity to neurotransmitters rapidly.



5-HT's role in the onset of depression

5-HT receptors and transporters as targets of rapid-onset antidepressants

- 5-HT is one of the main neurotransmitters in the central nervous system. With most of 5-HTergic neurons locate in dorsal raphe (DR) and affect depression-related areas like prefrontal cortex (PFC) and hippocampus, **its receptors are considered as the most promising target for the treatment of depression**.
- According to former researches, the reduced 5-HT level in the synaptic clefts is related to the onset of depression. **Novel antidepressants can block certain 5-HT receptors and inhibit the reuptake of 5-HT, promoting the level of 5-HT in the synaptic clefts, relieving depression-related symptoms.**
- The onset of the therapeutical effect of traditional antidepressants, targeting single 5-HT receptor, takes a few days, bringing extra burden to the patients. **Novel antidepressants which target multiple 5-HT receptors and the transporters of 5-HT, can modify the biochemical environment in a short period, enabling rapid onsets of their therapeutical effect.**

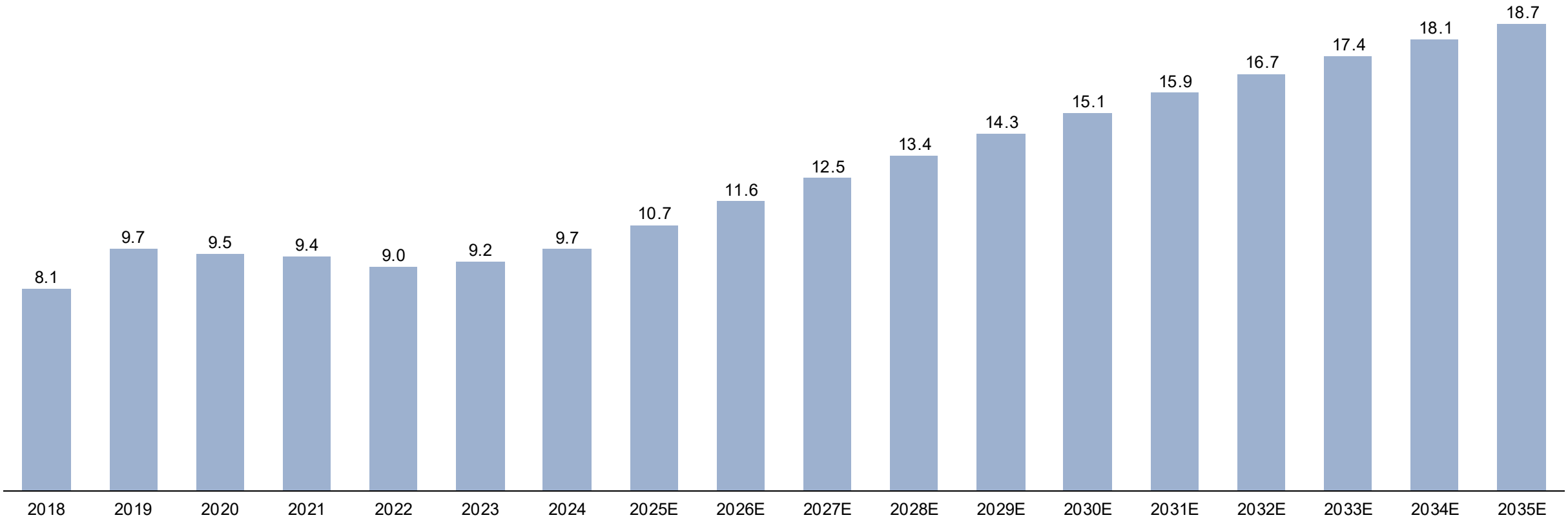
Source: Neurosci Biobehav Rev, CNKI, Psychiatry, China Insights Consultancy

Market size of antidepressants in China, 2018-2035E

Market size of antidepressants in China

CAGR	2019-24	2024-29E	2029E-2034E
Market size of antidepressants in China	0.0%	8.1%	4.8%

RMB billion



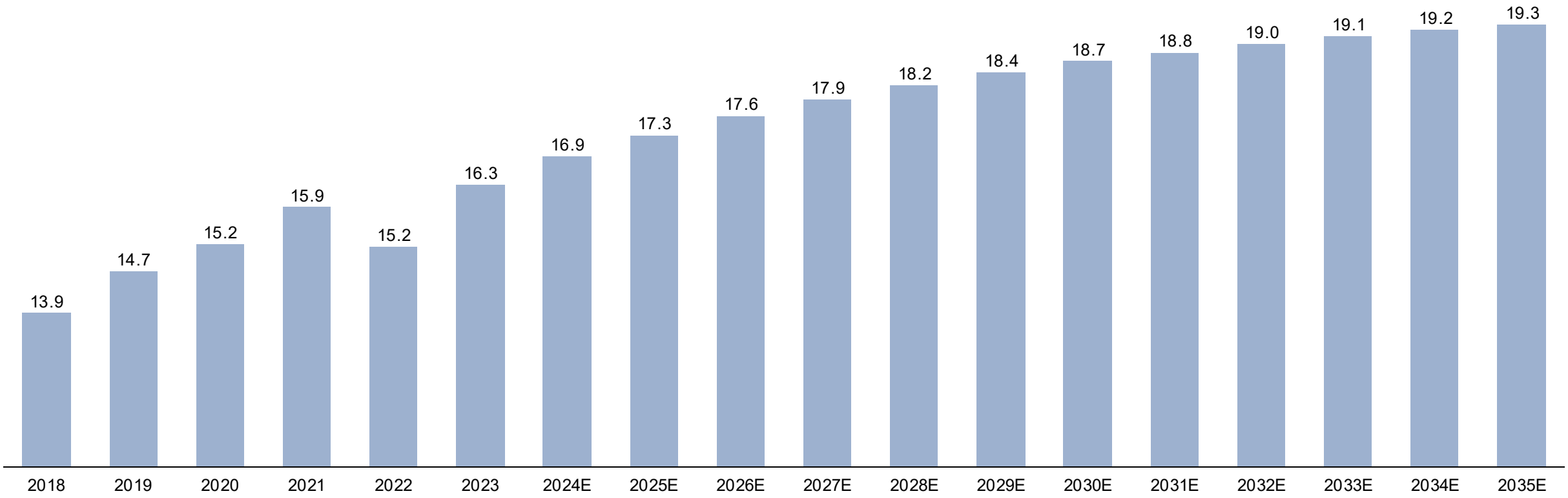
Sources: China Insights Consultancy

Global market size of antidepressants, 2018-2035E

Global market size of antidepressants

CAGR	2018-23	2023-35E
Global market size of antidepressants	3.3%	1.4%

USD billion



Sources: China Insights Consultancy

Pipelines of innovative antidepressants in China (registered in CDE) (1/2)

Pipelines of innovative antidepressants in China, as of LPD

Trial number	Candidate	Target	Company	Clinical phase	First posted date	Indication
CTR20241229	JJH201501	DAT, NET, 5-HTT	Jebel Pharmaceutical	Ⅲ	2024/04/09	Depression
CTR20244865	Ammoxetine	NET, 5-HTT	CSPC Pharmaceutical	Ⅲ	2025/01/14	Depression
CTR20211474	Mitizodone Phosphate	5-HT receptor, 5-HT_{1A} receptor	Sunshine Lake Pharma	II/III	2021/07/12	Depression
CTR20221222	GW117	5-HT_{2C} receptor, MT_1/MT_2 receptor	Guangwei Pharmaceutical	Ⅱ	2022/05/27	Depression
CTR20221896	Liafensine	DAT, NET, 5-HTT	Denovo Biopharmaceutical	Ⅱ	2022/07/29	Refractory depression
CTR20231966	HS-10353	GABAA receptor	Hansoh Pharmaceutical	Ⅱ	2023/07/03	Perinatal depression
CTR20231965				Ⅱ	2023/07/05	Depression
CTR20233894	JS1-1-01	DAT, NET, 5-HTT	Tasly Pharmaceutical	Ⅱ	2023/12/04	Depression
CTR20242132	MI078	GABAA receptor	Minova Pharmaceutical	Ⅱ	2024/07/01	Perinatal depression
CTR20242430	BI1569912	GluN2B, NMDA receptor	Boehringer Ingelheim GmbH	Ⅱ	2024/07/12	Depression
CTR20243913	NH102	5-HT_{2A} receptor, DAT, NET, 5-HTT	Nhwa Pharmaceutical	Ⅱ	2024/11/01	Depression
CTR20250124	ZG-001	BDNF-TrkB	Zhigen Pharmaceutical	Ⅱ	2025/01/14	Adult depression with suicidal intention
CTR20250116	LV232	5-HTT, 5-HT_3 receptor	Vigonvita Life Sciences	Ⅱ	2025/01/16	Depression
CTR20250210	KH607	GABAA receptor	Kanghong Pharmaceutical	Ⅱ	2025/01/26	Depression
CTR20251117	SIPI6398	HTR1A,HTR2A,DRD2,DRD3	Zhongze Therapeutics	Ⅱ	2025/03/28	Depression
CTR20252210	TJ0113	MCL1	Hangzhou PhecdaMed	Ⅱ	2025/06/05	Depression

Sources: CDE, China Insights Consultancy

Pipelines of innovative antidepressants in China (registered in CDE) (2/2)

Updated 1011

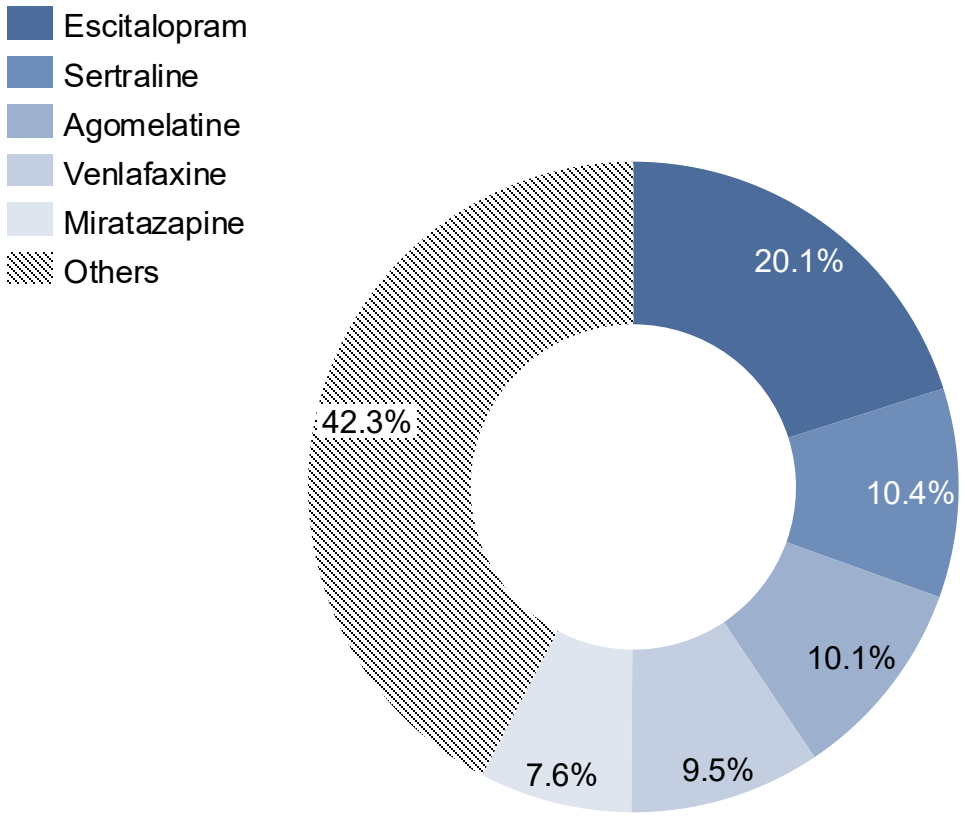
Pipelines of innovative antidepressants in China, as of LPD

Trial number	Candidate	Target	Company	Clinical phase	First posted date	Indication
CTR20240090	SAL0114	NMDA receptor	Salubris Pharmaceutical	Ⅰ/Ⅱ	2024/01/15	Depression
CTR20190930	HEC113995PA·H_2O	N/A	HEC Group	Ⅰ	2019/06/03	Depression
CTR20191556	FZ016	5-HT_{1A} receptor	Pkucare Pharmaceutical	Ⅰ	2019/08/02	Depression
CTR20233134	NORA520	GABAA receptor	Gerbera Therpeutics	Ⅰ	2023/10/13	Perinatal depression
CTR20240549	GW201	NMDA receptor	Guangwei Pharmaceutical	Ⅰ	2024/02/23	Depression
CTR20243899	HS-10506	Highly-selective OXR2	Hansoh Pharmaceutical	Ⅰ	2024/10/16	Insomnia; depression with insomnia
CTR20252238	NH104	N/A	Jiangsu Nhwa Pharmaceutical	Ⅰ	2025/07/01	Insomnia; depression with insomnia
CTR20253463	SP-101	NMDAR GluN2A	Spirovant Sciences	Ⅰ	2025/09/04	Depression with acute suicidal ideation or behavior

Sources: CDE, China Insights Consultancy

Competitive landscape of antidepressants in China, by molecule, 2023

Competitive landscape of antidepressants in China



Ranking	Drug name	Market share
1	Escitalopram	20.1%
2	Sertraline	10.4%
3	Agomelatine	10.1%
4	Venlafaxine	9.5%
5	Miratazapine	7.6%
Others		**42.3%**
Total		**100%**

Sources: China Insights Consultancy

Competitive landscape of antidepressants in China, by molecule, 2024

Competitive landscape of antidepressants in China

Ranking	Drug name	MoA	Indication	Administration	Line of therapy*	Top 2 company	Market share
1	Escitalopram	SSRI	MAD, GAD	Oral	First-line	SHANDONG JINGWEI PHARMACEUTICAL	8.1%
						LUNDBECK	7.1%
2	Sertraline	SSRI	MDD, OCD, SAD, panic disorder, PTSD	Oral	First-line	VIATRIS	6.3%
						HUAHAI PHARMACEUTICAL	3.0%
3	Venlafaxine	SNRI	MDD, GAD	Oral	First-line	PFIZER	3.2%
						KANGHONG PHARMCEUTICAL	1.6%

*Not differentiated by specific treatment line; guidelines recommended that providers consider side effects (to avoid or to harness for the benefit of the patient), cost, and patient preference in selecting a first-line antidepressant

Sources: Medical clinics of North America, China Insights Consultancy

Competitive landscape of antidepressants in China, by molecule, 2024

Competitive landscape of antidepressants in China

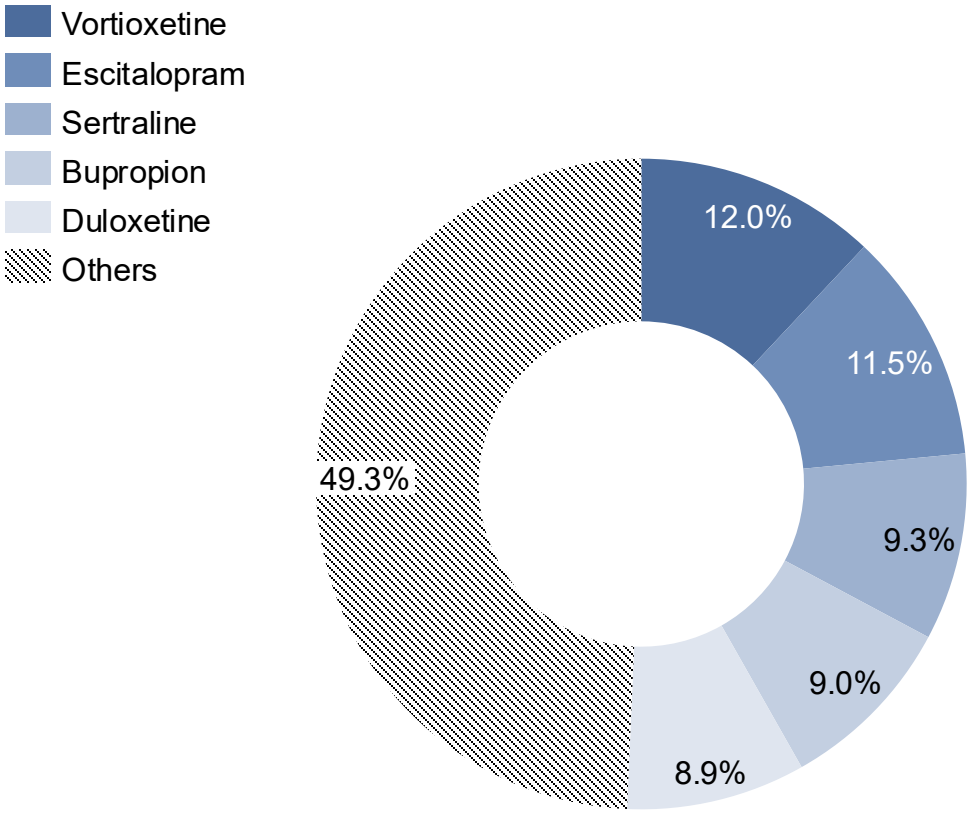
Ranking	Drug name	MoA	Indication	Administration	Line of therapy*	Top 2 company	Scope of Business	Market share
1	Escitalopram	SSRI	MAD, GAD	Oral	First-line	Company A	A company based in Shandong, specializing in the R&D, production, and sales of high-quality pharmaceutical products.	8.1%
						Company B	A Denmark-based global pharmaceutical company focused on treatments and drug development for central nervous system (CNS) disorder.	7.1%
2	Sertraline	SSRI	MDD, OCD, SAD, panic disorder, PTSD	Oral	First-line	Company C	A company headquartered in the U.S., it is a global healthcare company committed to delivering high-quality medicines and medical solutions, operating over multiple countries and regions.	6.3%
						Company D	A company headquartered in Zhejiang, specializing in APIs and pharmaceutical preparation, covering multiple therapeutic areas.	3.0%
3	Venlafaxine	SNRI	MDD, GAD	Oral	First-line	Company E	A U.S.-headquartered global biopharmaceutical leader that played a vital role in developing COVID-19 vaccines and rare disease treatments.	3.2%
						Company F	A company headquartered in Sichuan, focusing on innovative drug research and development, known for ophthalmology, neurology, and immunology drugs, with a growing presence in biologics and international markets.	1.6%

*Not differentiated by specific treatment line; guidelines recommended that providers consider side effects (to avoid or to harness for the benefit of the patient), cost, and patient preference in selecting a first-line antidepressant

Sources: Medical clinics of North America, China Insights Consultancy

Competitive landscape of antidepressants in global, by molecule, 2023

Competitive landscape of antidepressants in global



Ranking	Drug name	Market share
1	Vortioxetine	12.0%
2	Escitalopram	11.5%
3	Sertraline	9.3%
4	Bupropion	9.0%
5	Duloxetine	8.9%
Others		**49.3%**
Total		**100%**

Sources: China Insights Consultancy

Competitive landscape of antidepressants in global, by molecule, 2023

Competitive landscape of antidepressants in global

Ranking	Drug name	MoA	Indication	Administration	Line of therapy*	Top 2 company	Market share
1	Vortioxetine	Not fully understood (SMS)	MDD (adult), anxiety disorder	Oral	First-line	TAKEDA PHARM USA LUNDBECK	7.7% 4.1%
2	Escitalopram	SSRI	MDD, GAD	Oral	First-line	LUNDBECK EUROFARMA	2.0% 0.5%
3	Sertraline	SSRI	MDD, OCD, SAD, panic disorder, PTSD	Oral	First-line	VIATRIS EUROFARMA	1.4% 0.6%
4	Bupropion	NDRI and nicotinic receptor antagonist	MDD, seasonal affective SAD	Oral	First-line	BAUSCH HEALTH AXSOME THERAPEUT	2.8% 1.3%
5	Duloxetine	SNRI	MDD, GAD	Oral	First-line	LILLY LIBBS	1.4% 0.6%
6	Venlafaxine	SNRI	MDD, GAD, SAD, panic disorder	Oral	First-line	VIATRIS TORRENT	1.7% 0.4%
7	Mirtazapine	NaSSA	MDD, OCD, anxiety	Oral	First-line	AUROBINDO PHARM ORGANON	0.3% 0.3%
8	Paroxetine	SSRI	MDD, OCD, SAD, panic disorder	Oral	First-line	GLAXOSMITHKLINE EUROFARMA	0.9% 0.4%
9	Fluoxetine	SSRI	MDD, OCD, panic disorder, bulimia nervosa	Oral	First-line	LILLY TEUTO BRASILEIRO	0.6% 0.3%
10	Desvenlafaxine	Unknown	MDD (adult)	Oral	First-line	PFIZER EUROFARMA	1.4% 0.4%

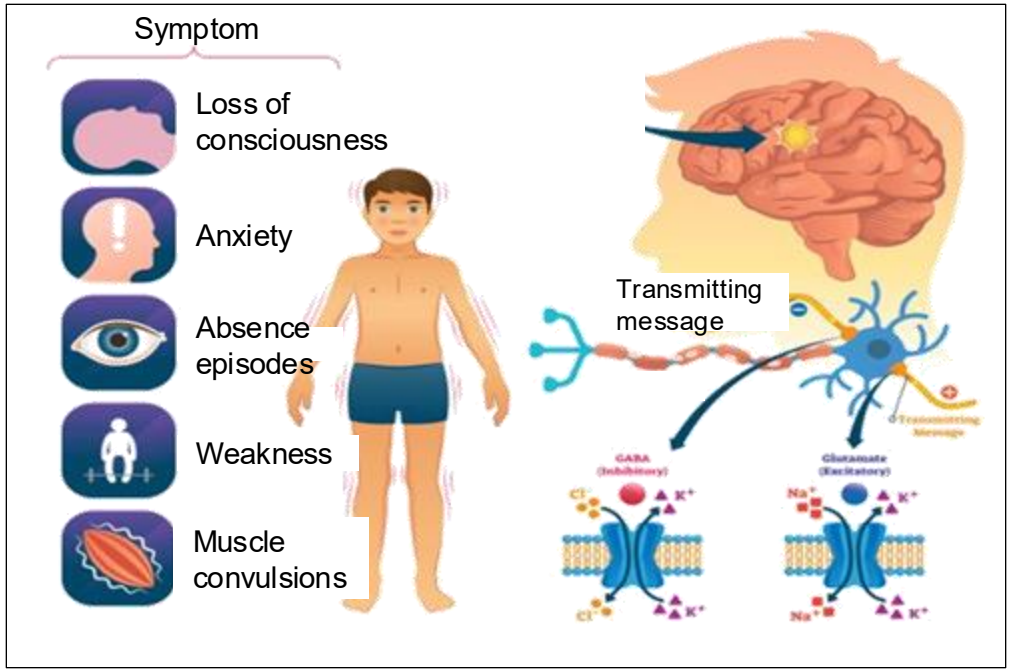
*Not differentiated by specific treatment line; guidelines recommended that providers consider side effects (to avoid or to harness for the benefit of the patient), cost, and patient preference in selecting a first-line antidepressant

Sources: Medical clinics of North America, China Insights Consultancy

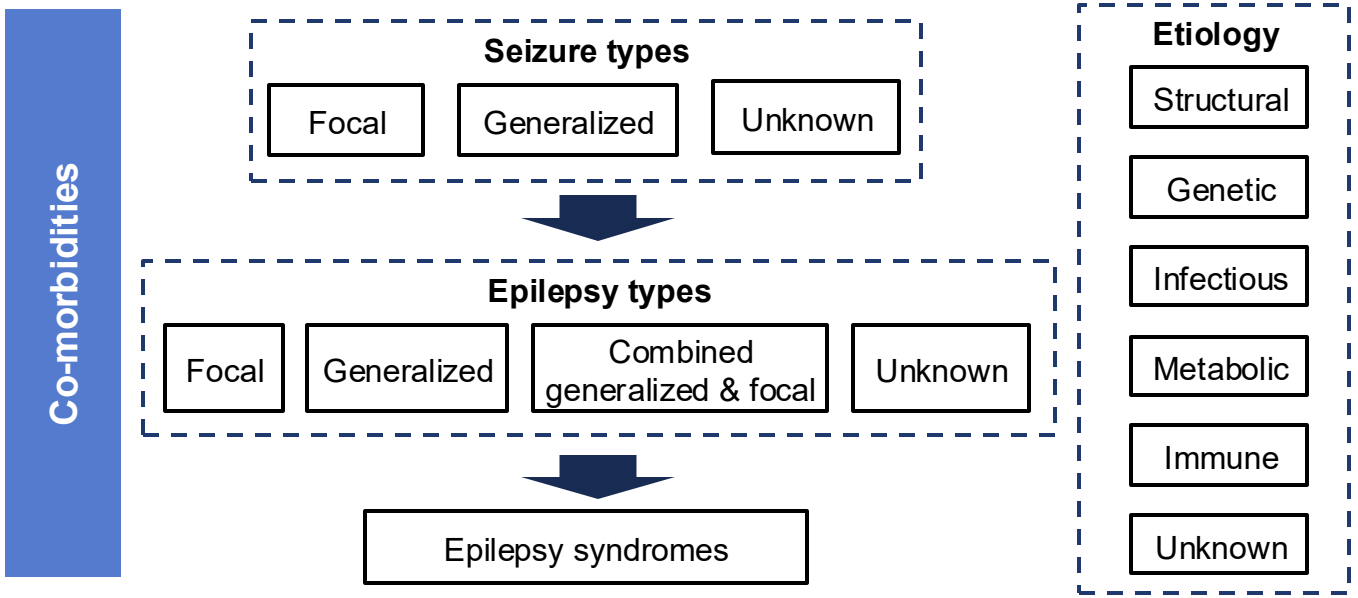
Definition and introduction of epilepsy

Definition and introduction of epilepsy

- Epilepsy is a chronic neurological disorder that affects populations worldwide. It is characterized by recurrent seizures. During an epileptic seizure, there may be brief involuntary convulsions in a specific part of the body or the entire body (referred to as focal or generalized seizures), sometimes accompanied by loss of consciousness and urinary or fecal incontinence.
- Epileptic seizure refers to a transient, one-time clinical manifestation caused by abnormal, excessive, and synchronized neuronal discharges in the brain. Seizures are characterized by three key elements: clinical presentation, the form of onset and termination, and underlying brain abnormalities.



Classification of epileptic seizure



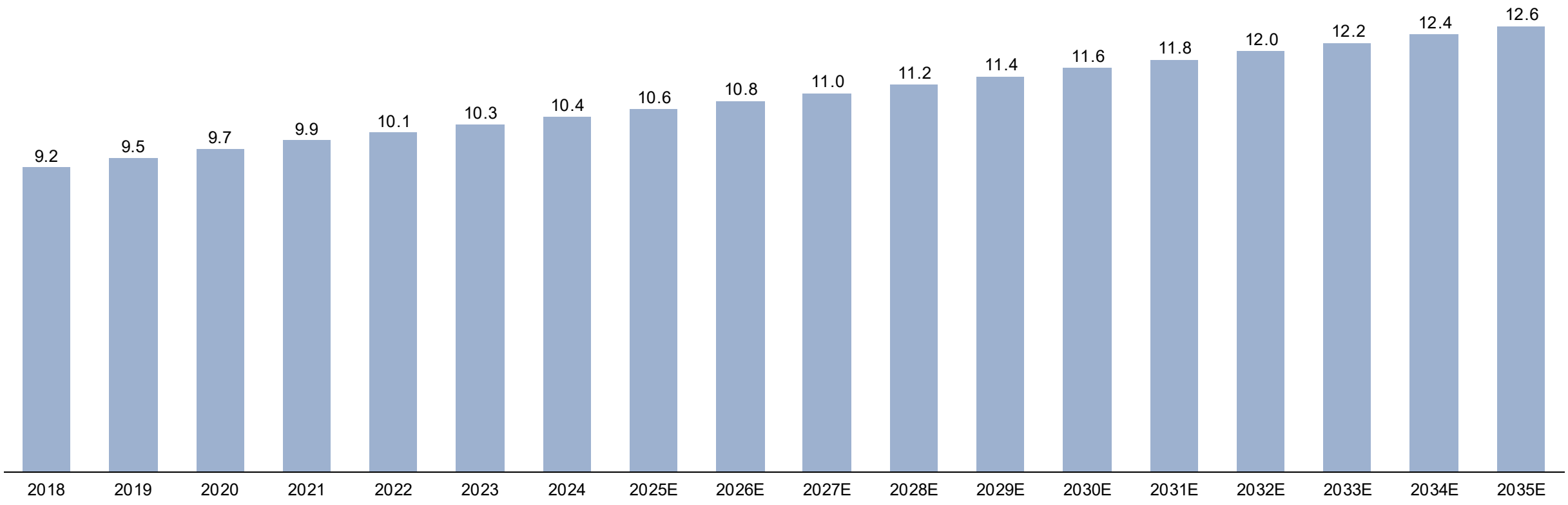
Sources: 临床诊疗指南癫痫病分册（2023修订版）, International league against epilepsy, China Insights Consultancy

Epidemiology of epilepsy, China, 2018-2035E

Epidemiology of epilepsy, China

CAGR	2018-24	2024-35E
China epilepsy patient	2.1%	1.7%

ppl million



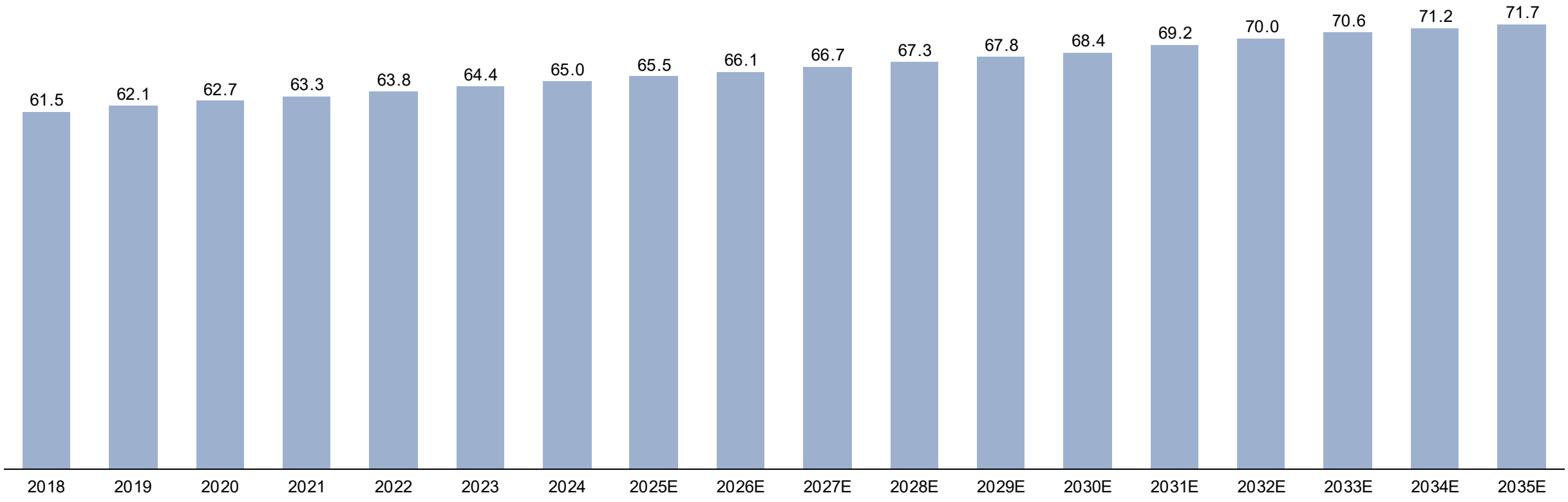
Sources: 临床诊疗指南癫痫病分册（2023修订版）, China Insights Consultancy

Epidemiology of epilepsy, global, 2018-2035E

Epidemiology of epilepsy, global

CAGR	2018-24	2024-35E
Global epilepsy patient	0.9%	0.9%

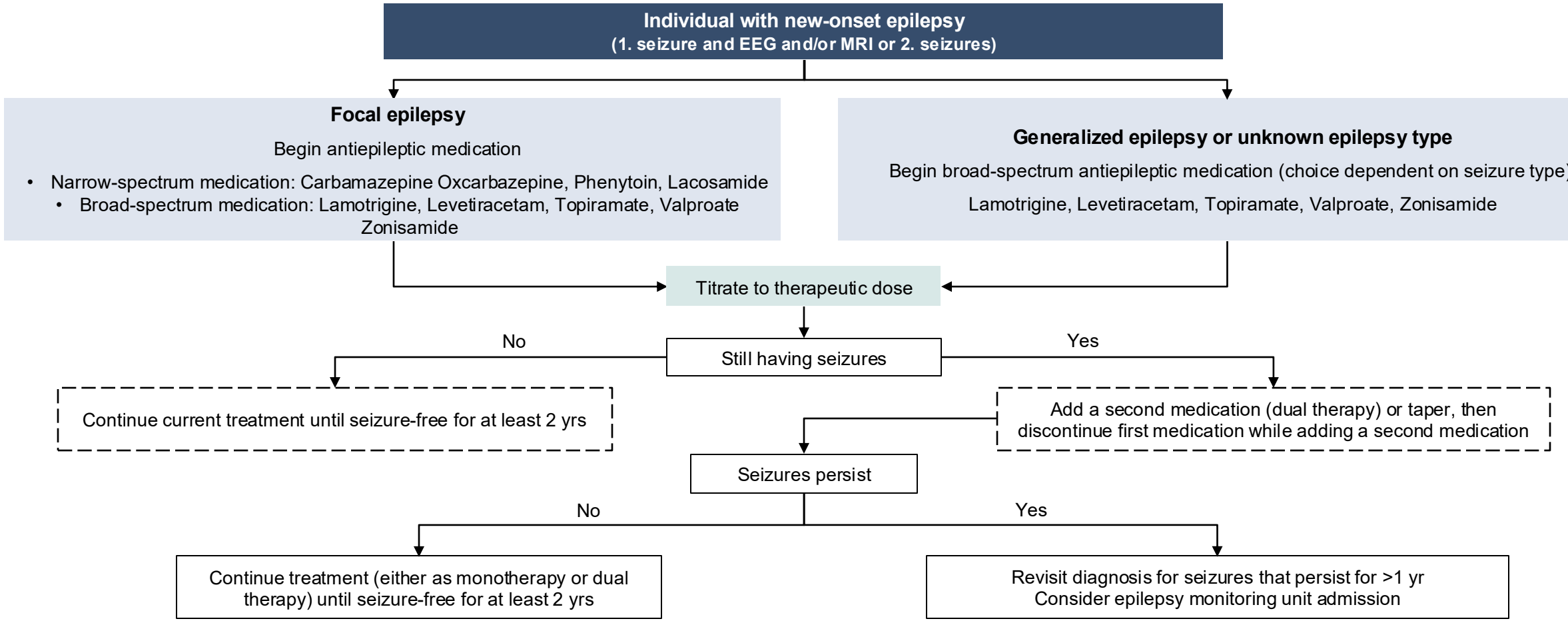
ppl million



Sources: WHO, Lancet, China Insights Consultancy

Treatment pathway of epilepsy

Treatment pathway of patients with new-onset epilepsy



Sources: New-onset seizure in adults and adolescents,临床诊疗指南癫痫病分册（2023修订版）, China Insights Consultancy

Drug treatment regimens for epilepsy

Drug treatment for epilepsy

- Among all epilepsy patients, 40% are non-convulsive (primarily manifesting as absence seizures), while 60% exhibit convulsive symptoms. Of these, one-third (20% of the total) have generalized seizures, and two-thirds (40% of the total) have focal seizures. According to clinical practice guidelines for epilepsy, 70% of newly diagnosed epilepsy patients can achieve seizure control with a single antiepileptic drug (AED). Therefore, selecting the appropriate initial treatment is crucial for improving the success rate of epilepsy management.
- Antidepressant medications typically begin to take effect within 10–14 days and reach full therapeutic efficacy within 4–6 weeks.

Drug treatment recommendation of epileptic seizures

Symptoms	Clinical manifestation	First-line treatment	Add-on treatment	Other reference treatment
Generalized seizures: 20%	Generalized Tonic-Clonic Seizures	Valproate, Lamotrigine, Carbamazepine, Oxcarbazepine, Levetiracetam	Levetiracetam, Topiramate, Valproate, Lamotrigine, Perampanel, Lacosamide, Clobazam*	-
	Tonic or Atonic Seizures	Valproate	Lamotrigine, Rufinamide*	Topiramate
	Absence Seizures	Valproate, Ethosuximide*, Lamotrigine	Valproate, Ethosuximide*, Lamotrigine	Clonazepam, Clobazam*, Levetiracetam, Topiramate, Zonisamide, Perampanel
	Myoclonic Seizures	Valproate, Levetiracetam, Topiramate	Levetiracetam, Valproate, Topiramate	Clonazepam, Clobazam*, Zonisamide, Perampanel
Focal seizures: 40%	Paroxysmal Seizures, Automatisms	Carbamazepine, Lamotrigine, Oxcarbazepine, Levetiracetam, Valproate, Perampanel, Lacosamide	Carbamazepine, Levetiracetam, Lamotrigine, Oxcarbazepine, Gabapentin, Valproate, Topiramate, Zonisamide, Perampanel, Lacosamide, Clobazam*	Phenobarbital, Phenytoin sodium

Sources:临床诊疗指南癫痫病分册（2023修订版），China Insights Consultancy

Common adverse reactions of first-line antiepileptic drugs

Common adverse reactions of first-line antiepileptic drugs

Drug	Dose-Related Side Effects	Long-Term Treatment Side Effects	Idiosyncratic Side Effects	Effects on Pregnancy
Carbamazepine	Diplopia, dizziness, blurred vision, nausea, drowsiness, neutropenia, hyponatremia	Hyponatremia	Rash, aplastic anemia, Stevens-Johnson syndrome, liver damage	FDA Pregnancy Safety Category D. Crosses the placental barrier, potentially causing neural tube defects.
Valproate	Tremor, anorexia, nausea, vomiting, drowsiness	Weight gain, hair loss, menstrual irregularities or amenorrhea, polycystic ovary syndrome	Hepatotoxicity (especially in children under 2 years old), thrombocytopenia, acute pancreatitis (rare), valproate-induced encephalopathy	FDA Pregnancy Safety Category D. Crosses the placental barrier, potentially causing neural tube defects and neonatal bleeding.
Phenobarbital	Fatigue, drowsiness, depression, attention disturbance, hyperactivity, irritability (in children), aggressive behavior, memory impairment	Rare: rough skin, reduced libido; sudden withdrawal may cause withdrawal symptoms such as anxiety and insomnia	Rash, toxic epidermal necrolysis, hepatitis	FDA Pregnancy Safety Category D. Crosses the placental barrier, may cause neonatal bleeding.
Lamotrigine	Diplopia, dizziness, headache, nausea, vomiting, drowsiness, ataxia, somnolence	Aggressive behavior, irritability	Rash, aplastic anemia, Stevens-Johnson syndrome, toxic epidermal necrolysis, liver damage, aplastic anemia	FDA Pregnancy Safety Category C.
Oxcarbazepine	Fatigue, drowsiness, diplopia, dizziness, ataxia, nausea	Hyponatremia	Rash	FDA Pregnancy Safety Category C.
Levetiracetam	Headache, drowsiness, irritability, infection, flu-like syndrome	Rare	No reported	FDA Pregnancy Safety Category C.
Topiramate	Anorexia, attention, speech, and memory impairment, paresthesia, anhidrosis	Kidney stones, weight loss	Acute angle-closure glaucoma (rare)	FDA Pregnancy Safety Category C.

Sources:临床诊疗指南癫痫病分册（2023修订版），China Insights Consultancy

Unmet clinical needs of epilepsy treatment

Unmet clinical needs of epilepsy treatment

1 Side effects of existing drugs

- Over the past few decades, more than 20 types of antiepileptic drugs have been developed. However, limited efficacy and significant side effects still affect the treatment outcomes for epilepsy patients. For example, first-generation ASMs mainly include phenobarbital, PHT, carbamazepine and clonazepam. These drugs are associated with prominent side effects, such as drowsiness, dizziness, and nausea. Additionally, they often have multiple drug interactions, requiring strict dosage control and monitoring of adverse reactions. Second-generation ASMs, such as gabapentin, lamotrigine, levetiracetam and pregabalin, have reduced side effects compared to first-generation drugs. However, despite the widespread use of second-generation drugs over the past years, it seems that these drugs have not significantly improved the overall efficacy and tolerability of epilepsy treatment.

2 Refractory epilepsy

- Although the WHO points out that 70% of epilepsy patients can achieve seizure control with antiepileptic drugs, around 30% of patients are resistant to existing drugs, and the seizures cannot be effectively controlled, a condition known as refractory epilepsy. These patients face a limited choice of medications due to heterogeneity and drug resistance. For example, developmental and epileptic encephalopathy (DEE) encompass over 25 different syndromes. In terms of treatment, most DEE patients undergo polytherapy, using a combination of medications, and often change drugs over time. However, nearly all patients experience multiple seizures and side effects related to the treatment.

3 Treatment gap

- Epilepsy patients in impoverished countries often do not receive effective treatment due to a lack of knowledge, scarcity of resources, and shortages of medication. 80% of epilepsy patients have not sought medical care or received effective treatment around the world. Inadequate treatment facilities and a lack of appropriate medications result in high disability and mortality rates for many epilepsy patients. In China, about 50% of epilepsy patients have not yet to receive standardized medication treatment in rural areas. Additionally, there is widespread misunderstanding of epilepsy in some areas, causing most patients to delay seeking medical care after onset, which creates a significant treatment gap.

Sources: Lancet, WHO, China Insights Consultancy

Main mechanisms and comparison of anti-seizure medications

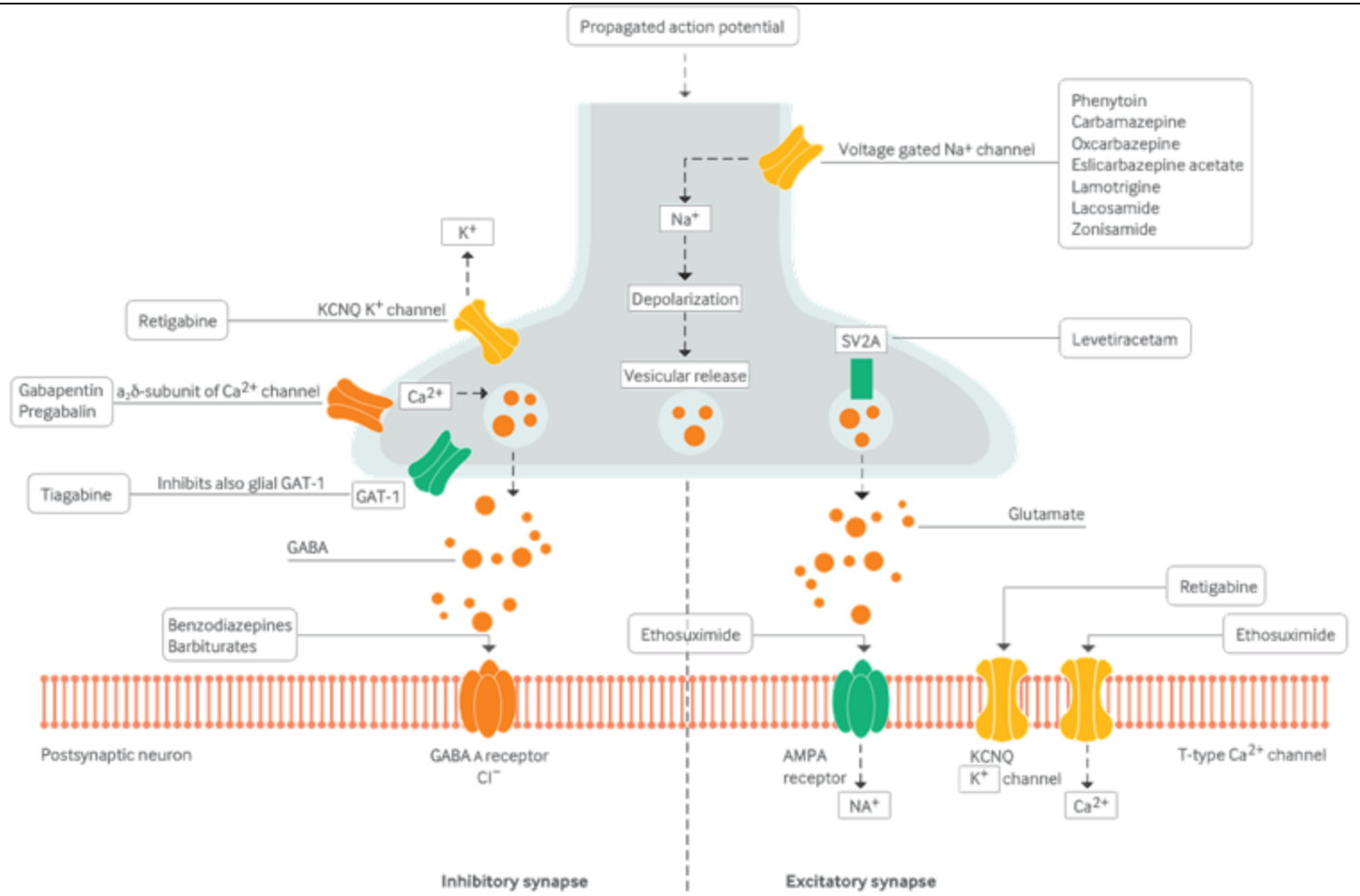
Main mechanisms and comparison of anti-seizure medications

Drug Name	Bioavailability (%)	First-Order Kinetics	Protein Binding Rate (%)	Half-Life (h)	Time to Peak Plasma Concentration (h)	Active Metabolites	Effect on Liver Enzymes
Carbamazepine	75-85	Yes	65-80	25-34 (initial use), 8-20 (after 4 weeks)	4-8	Yes	Inducer (auto-induction)
Clonazepam	>80	Yes	85	20-60	1-4	Yes	/
Phenobarbital	80-90	No	45-50	40-90	1-6	No	Inducer
Lamotrigine	98	Yes	55	15-30	2-3	No	None
Oxcarbazepine	<95	Yes	40	8-25	4.5-8	Yes	Weak inducer
Valproate	70-100	Yes	90-95	8-15	1-4	Yes	Inhibitor
Levetiracetam	<100	Yes	0	6-8	0.6-1.3	No	None
Topiramate	≥80	Yes	13	20-30	2-4	No	Inhibitor
Zonisamide	≥50	Yes	50	50-70	2-6	No	None
Gabapentin	<60	No	0	5-7	2-3	No	None
Lacosamide	≈100	Yes	95	105	0.5-2.0	No	Weak inhibitor, weak inducer

Sources: 临床诊疗指南癫痫病分册（2023修订版）, China Insights Consultancy

MOA of antiepileptic drugs, act by diverse mechanisms, involving modulation of volt age activated ion channels, potentiation of GABA , and inhibition of glutamate

Main mechanisms and comparison of antiepileptic drugs



Mechanisms of action of antiepileptic drugs

- Mechanisms of action of antiepileptic drugs, which act by diverse mechanisms, mainly involving modulation of voltage activated ion channels, potentiation of GABA, and inhibition of glutamate. Approved antiepileptic drugs have effects on inhibitory (left hand side) and excitatory (right hand side) nerve terminals.
- The antiepileptic efficacy in trials of most of these drugs as initial addon does not differ greatly, indicating that seemingly similar antiseizure activity can be obtained by mechanisms aimed at diverse targets.

- Note: AMPA, α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid; GABA, γ-aminobutyric acid; GAT-1, sodium dependent and chloride dependent GABA transporter 1; SV2A, synaptic vesicle glycoprotein 2A

Sources: BMJ, China Insights Consultancy

Main mechanisms and comparison of antiepileptic drugs

Main mechanisms and comparison of antiepileptic drugs

- As of the Latest Practicable Date, there were 23* innovative small molecule antiepileptic drugs approved for marketing in China.
- The mechanisms of action of antiepileptic drugs can be categorized into single mechanisms and multiple mechanisms. The exact mechanisms of antiepileptic drugs are not yet fully understood. Known mechanisms include voltage-dependent sodium channel blockers, increasing levels of gamma-aminobutyric acid (GABA) in the brain or synapses, selectively enhancing GABAA-mediated effects, directly promoting chloride ion influx, and calcium channel blockers. The mechanisms of action of antiepileptic drugs are shown in the following table:

AEDs type	Voltage-dependent Sodium Channel Blockers	Increase Brain or Synaptic GABA Levels	Selectively Enhance $GABA_A$-mediated Effects	Directly Promote Chloride Ion Influx	Calcium Channel Blockers	Others
Carbamazepine	++	?			+ (L-type)	+
Valproate	?	+	?		+ (T-type)	++
Phenobarbital		+	+	++	?	
Lamotrigine	++	+			++(N, P/Q, R, T-type)	+
Gabapentin	?	?			++(N-type, P/Q-type)	?
Zonisamide	++	?			++(N, P, T-type)	
Oxcarbazepine	++	?			+(N, P-type)	+
Levetiracetam		?	+		+ (N-type)	++
Topiramate	++	+	+		+ (L-type)	+
Lacosamide	++					
Perampanel						++ (AMPA receptor)

*Note: in terms of molecule

Sources: 临床诊疗指南癫痫病分册（2023修订版）, China Insights Consultancy

Annual cost calculation of major antiepileptic drugs

Annual cost calculation of major antiepileptic drugs

Annual cost = Price range (Min price ~ Max price) x Daily dosage x 365 x Patient compliance

Patient compliance (also adherence) describes the degree to which a patient correctly follows medical advice.

- Some drugs need to be considered in case of relapse.
- The final annual treatment cost is a range.

Example

Sodium valproate annual cost = 0.18 ~ 2 RMB/200mg x 6 (1200mg/day) x 365 x 37%

Item	Levetiracetam	Lamotrigine	Sodium Valproate
Drug name	Levetiracetam	Lamotrigine tablets	Sodium valproate sustained-release tablets
Original company	UCB	GSK	Sanofi
Specification	250mg*30 tablets	25mg*30 tablets	500mg*30 tablets
Recommend dosage	500mg/time 2 time/day	25mg/time/day	600-1,200mg/day given in 2-3 divided doses
Annual cost before medical insurance	2,511.9 RMB	287.7 RMB	596.9 RMB
Annual cost after medical insurance	2,387.7 RMB	255.2 RMB	556.4 RMB

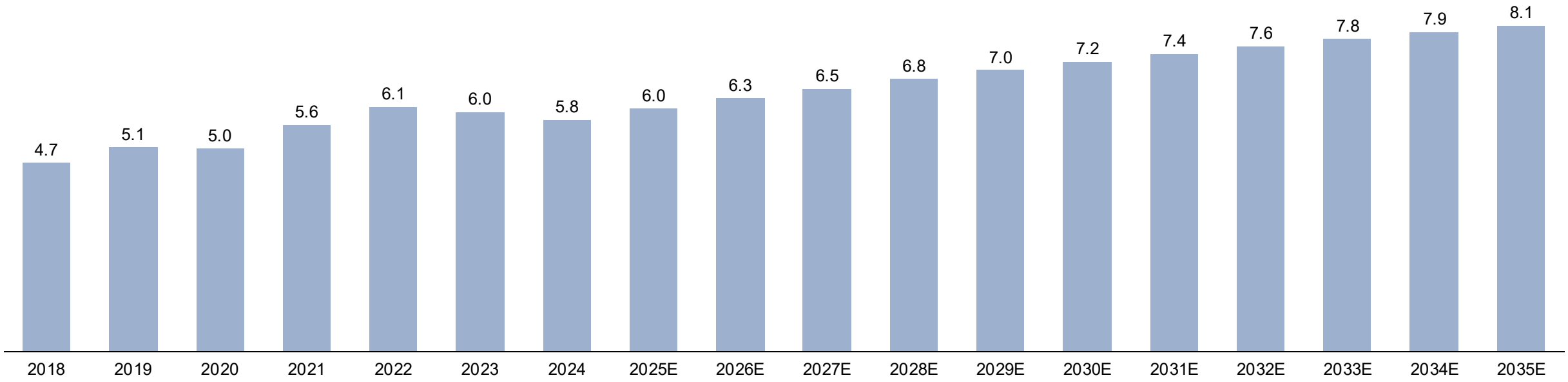
Sources: China Insights Consultancy

Market size of antiepileptic drugs, China, 2018-2035E

Market size of antiepileptic drugs, China

CAGR	2019-24	2024-29E	2029E-2034E
China antiepileptic drugs market	2.6%	3.9%	2.6%

RMB billion



China's antiepileptic drug market contracted in 2024, driven by VBP price reductions and healthcare cost containment policies, alongside reduced demand for non-urgent treatments amid economic headwinds. A significant portion of anti-epileptic drugs serve as symptom controllers (e.g., maintenance therapies), which are more susceptible to deferral or dosage reduction under financial constraints compared to life-saving interventions. Long-term growth is underpinned by R&D intensification driven by disease complexity (diverse etiology/symptom subtypes), precision medicine enhancing treatment efficacy, and indication expansion into pediatric/geriatric populations. Aging demographics and improved healthcare accessibility will sustain demand.

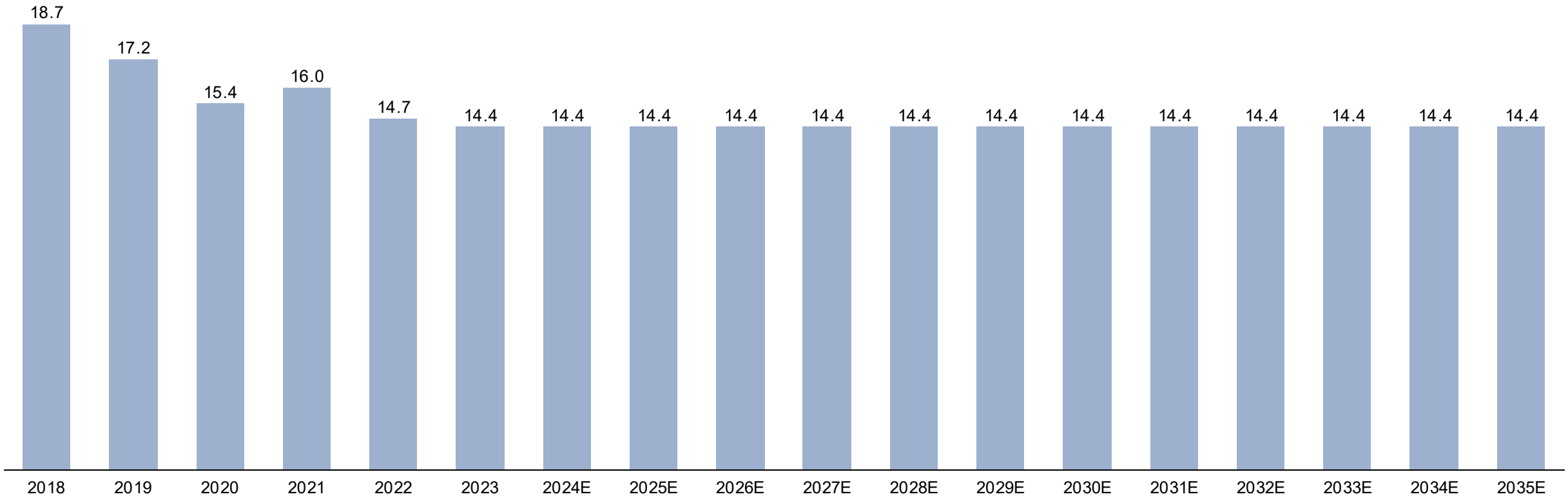
Sources: China Insights Consultancy

Market size of antiepileptic drugs, global, 2018-2035E

Market size of antiepileptic drugs, global

CAGR	2018-23	2023-35E
Global antiepileptic drug market	-5.1	0.0%

USD billion



Sources: China Insights Consultancy

Pipelines of antiepileptic drugs in China (registered in CDE)

Updated 1011

Pipelines of innovative small molecule antiepileptic drugs, as of LPD

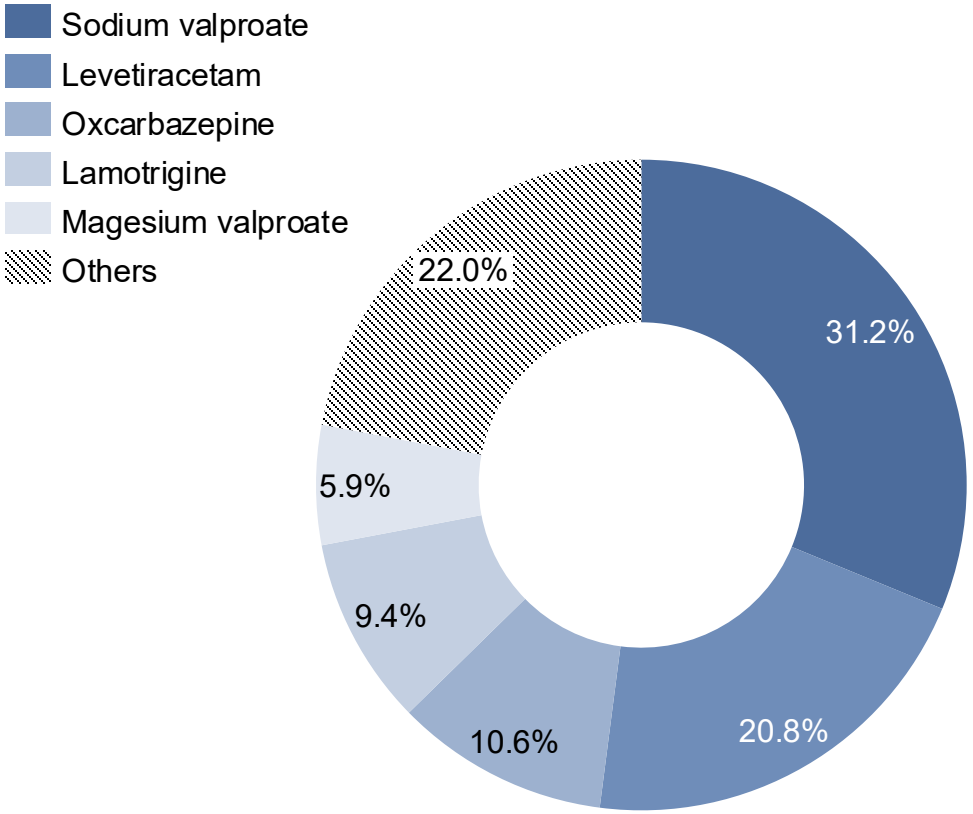
Trial number	Candidate	Company	Clinical phase	First posted date	Indication	Single/Combo
CTR20252345	Bexicaserin	Longboard Pharmaceuticals	III	2025/06/20	Seizures associated with developmental epileptic encephalopathy (DEE)	Single
CTR20241138	派恩加滨片 (Pynegabine)	Hainan Haiyao	II	2024/04/23	Focal epilepsy in patients who are refractory to or intolerant of other antiepileptic medications	Single
CTR20251874	NS-041	Neushen Therapeutics	II	2025/05/21	Epilepsy	Single
CTR20200373	TPN102	Vigonvita Life Sciences	I	2020/03/17	Epilepsy	Single
CTR20200915	WX0005	Harbin Pharmaceutical Group	I	2020/05/25	Intended for the treatment of epilepsy	Single
CTR20210823	Phenzolzine capsule	Jilin Yinglian shangde	I	2021/04/19	Tonic-clonic seizures, absence seizures, and temporal lobe epilepsy	Single

*Note: TAK-935 Phase III failed

Sources: China Insights Consultancy

Competitive landscape of antiepileptic drugs in China, by molecule, 2023

Competitive landscape of antiepileptic drugs



Ranking	Drug name	Market share
1	Sodium valproate	31.2%
2	Levetiracetam	20.8%
3	Oxcarbazepine	10.6%
4	Lamotrigine	9.4%
5	Magnesium valproate	5.9%
Others		**22.0%**
Total		**100%**

Sources: China Insights Consultancy

Definition, risk factors, and clinical manifestation of schizophrenia

Definition of schizophrenia

- **Schizophrenia** refers to a group of mental illness characterized by **disorders in perception, emotion, cognition, and behavior**, which may result in various clinical manifestations. Most schizophrenias onset during young adulthood, **bringing almost life-long suffering to the patients**.
- Being a common severe mental disorder, the basic features of schizophrenia have not been elucidated yet. Due to the lack of objective indicators, **the diagnosis of schizophrenia mainly relies on medical history and mental examinations**.

Risk factors of schizophrenia

- **Genetic factors** The onset of schizophrenia shows a familial clustering tendency. Recent researches also revealed serval candidate gene whose mutation may play important roles in the onset of schizophrenia, indicating genetic factors may serve as risk factors of schizophrenia.
- **Neurodevelopmental factors** According to neuroanatomic and neuropathologic findings, schizophrenia patients' brains show unique structure from the normal ones, which may be caused by the abnormalities during neurodevelopment.
- **Neurobiochemical factors** Researchers believe that abnormal neurotransmitter level may contribute to the onset of schizophrenia. Dopamine, 5-HT, and acetylcholine are considered as the candidate factors.
- **Social psychological factors** Though with few academic researches on the correlation between social psychological factors and the onset of schizophrenia, multiple cases of schizophrenia caused by psychological stressors have been reported, implying the possible relationship.

Clinical manifestations of schizophrenia

Prodromal phase

- Changes in emotion, cognition, behavior, and senses, usually unobvious and may be ignored.

Symptomatic phase

- **Positive symptoms** Patients may suffer from emerging abnormal mental states, including illusion, delusion, and formal thought disorders.
- **Negative symptoms** Patients may lose normal psychological function, leading to avolition, anhedonia, affective blunting, social withdrawal, and alogia.
- **Anxiety and depression** About 80% of schizophrenia patients suffer from anxiety and depression, which may lead to drug abuses and committing suicides.
- **Agitation symptoms** It is estimated that schizophrenia patients are 4 times more likely to commit violence than normal people.
- **Other symptoms** Including disorders in memory and self-awareness.

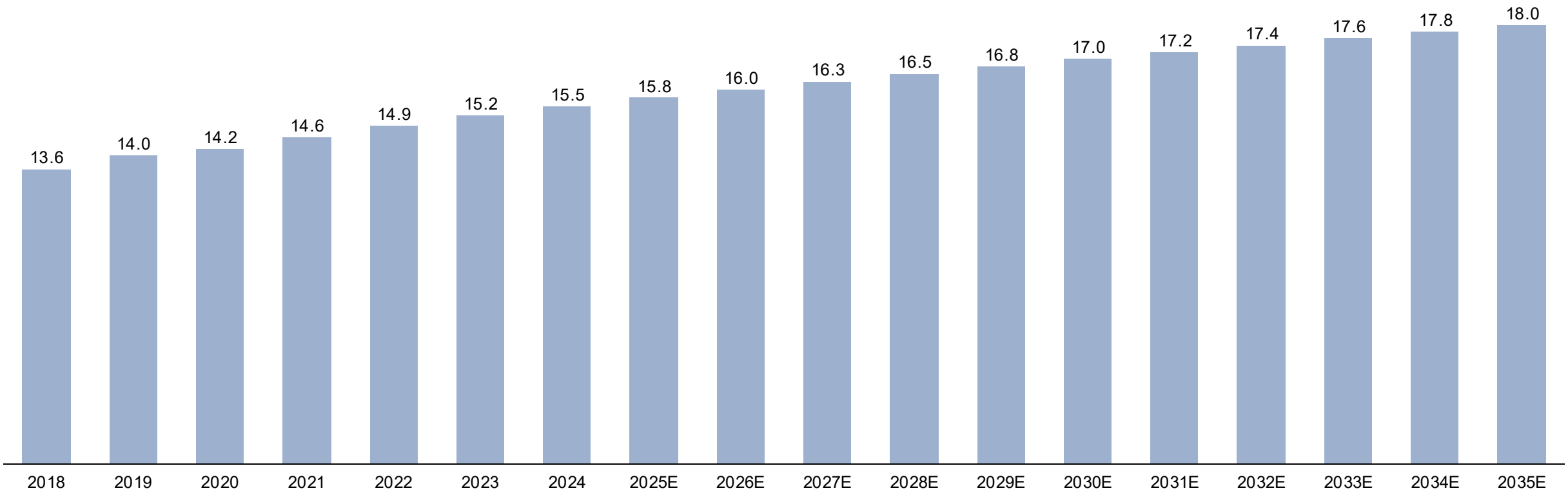
Sources: Psychiatry, China Insights Consultancy

Prevalence of schizophrenia in China, 2018-2035E

Prevalence of schizophrenia in China

CAGR	2018-24	2024-35E
Schizophrenia patients in China	2.2%	1.4%

ppl million



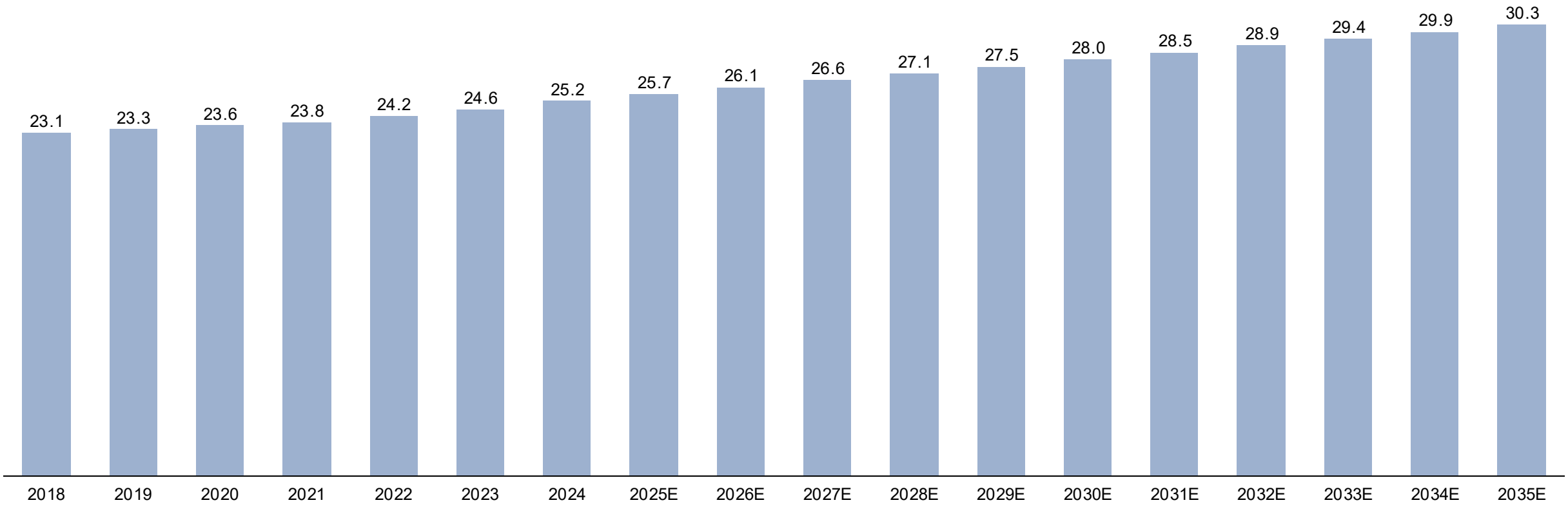
Sources: CAS, China Insights Consultancy

Global prevalence of schizophrenia, 2018-2035E

Global prevalence of schizophrenia

CAGR	2018-24	2024-35E
Global prevalence of schizophrenia	1.5%	1.7%

ppl million



Sources: China Insights Consultancy

Treatments of schizophrenia

Medication Therapy

- **antipsychotics are the preferred treatment of schizophrenia.** As the course of schizophrenia can be roughly divided into acute phase, stable phase, and recovery phase with different clinical manifestation and treatment target, the medication therapy for schizophrenia should be performed and watched by professional medical expertise in order to reach the best therapeutical effect.

Physiotherapy

- **Electroconvulsive therapy (ECT) and modified electroconvulsive therapy (MECT) have been proved to be effective to schizophrenia patients, especially those who are at an acute phase.** Some clinical evidence also suggested that transcranial magnetic simulation (TMS) and deep brain stimulation (DBS) may be an effective therapeutical method, which requires further clinical trials to validate.

Psychological and Social Intervention

- Though the mental symptoms of schizophrenia may be relieved through medication therapies and physiotherapies, it is also important to reestablish the patients' social abilities. **Psychological and social interventions are considered as an effective way for the patients to return to normal social life.**

Sources: Psychiatry, China Insights Consultancy

Summary of main antipsychotics

Summary of main antipsychotics

	Drug name	Initial approval	Original manufacture	Mechanism	Dose
Conventional antipsychotics	Perphenazine	1957	Merck & Co., Inc.	Dopamine receptor and α-adrencoeptors antagonist	For treatment: Starting from 6-10mg a day, gradually increased to 20-60mg a day For maintenance: 10-20mg a day
	Haloperidol	1967	Janssen Pharmaceutical NV	Dopamine, 5-HT receptor, and α-adrencoeptors antagonist	For treatment: Starting from 6-10mg a day, gradually increased to 10-40mg a day For maintenance: 4-20mg a day
	Sulpiride	1979	Sanofi S.A	Dopamine and 5-HT receptor antagonist	For treatment: Starting from 0.2-0.3g a day, gradually increased to 0.6-1.2g a day For maintenance: 0.2-0.6g a day
Atypical antipsychotics	Clozapine	1973	Novartis AG	5-HT, dopamine receptors, and α-adrencoeptors antagonist	For treatment: Starting from 50-75mg a day, gradually increased to 200-400mg a day For maintenance: 100-200mg a day
	Risperidone	1992	Janssen Pharmaceutical NV	5-HT, dopamine, histamine receptors and α-adrencoeptors antagonist	Starting from 1-2mg a day, gradually increased to 4-6mg a day
	Olanzapine	1996	Eli Lilly and Company	5-HT, dopamine, acetylcholine, histamine receptors and α-adrencoeptors antagonist	Starting from 10mg a day and can be adjusted to 5-20mg a day
	Aripiprazole	2002	Otsuka Pharmaceutical	Dopamine and 5-HT receptor modulator	Starting from 10mg a day and can be adjusted to no more than 30mg a day
	Lurasidone	2010	Sumitomo Dainippon Pharma	Dopamine receptor agonism and 5-HT receptor modulator	Starting from 40mg a day and can be adjusted to no more than 80mg a day

- As of the Latest Practicable Date, 22* innovative small molecule antipsychotics have been approved for marketing in China.

*Note: in terms of molecule

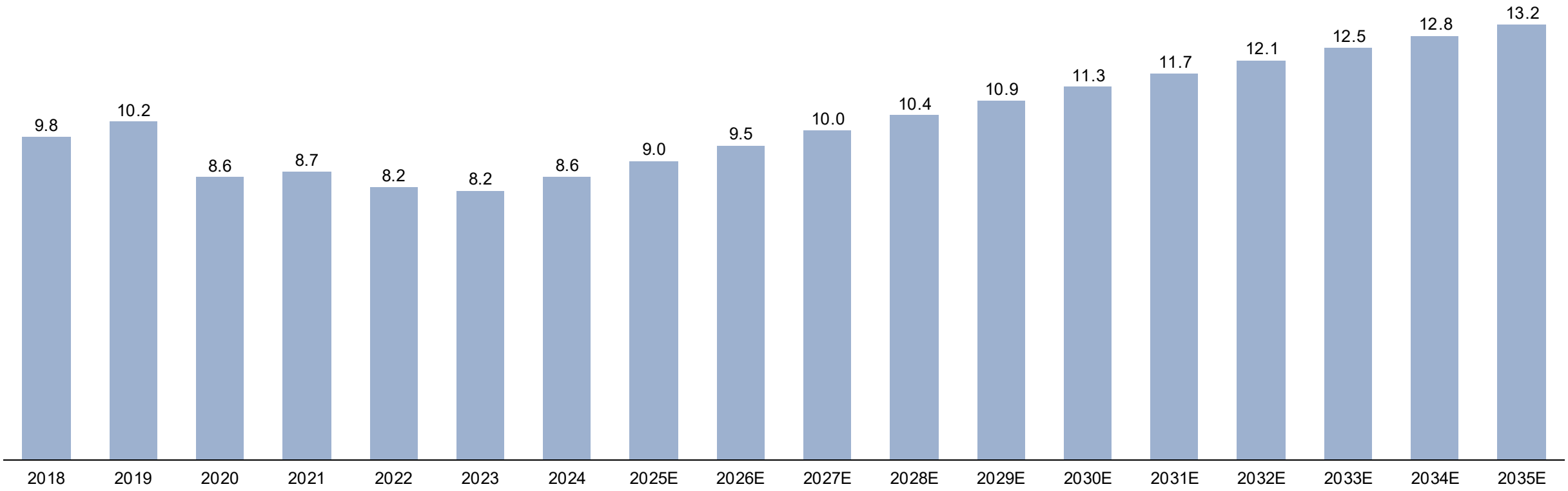
Source: Drug Instructions, China Insights Consultancy

Market size of antipsychotics in China, 2018-2035E

Market size of antipsychotics in China

CAGR	2019-24	2024-29E	2029E-2034E
Market size of atypical antischizophrenic drugs in China	-3.5%	4.9%	3.4%

RMB billion



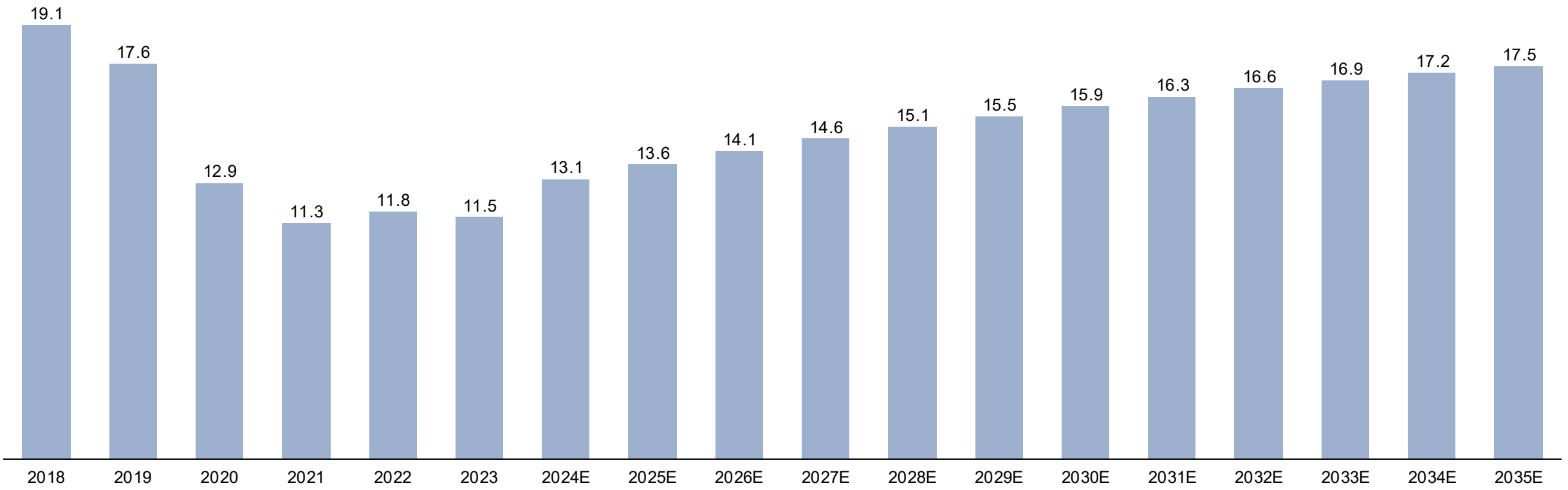
Sources: China Insights Consultancy

Global market size of antipsychotics, 2018-2035E

Global market size of antipsychotics

CAGR	2018-23	2023-35E
Global market size of antischizophrenic drugs	-9.6%	1.8%

USD billion



Sources: China Insights Consultancy

Pipelines of innovative small molecule antipsychotics in China (registered in CDE)

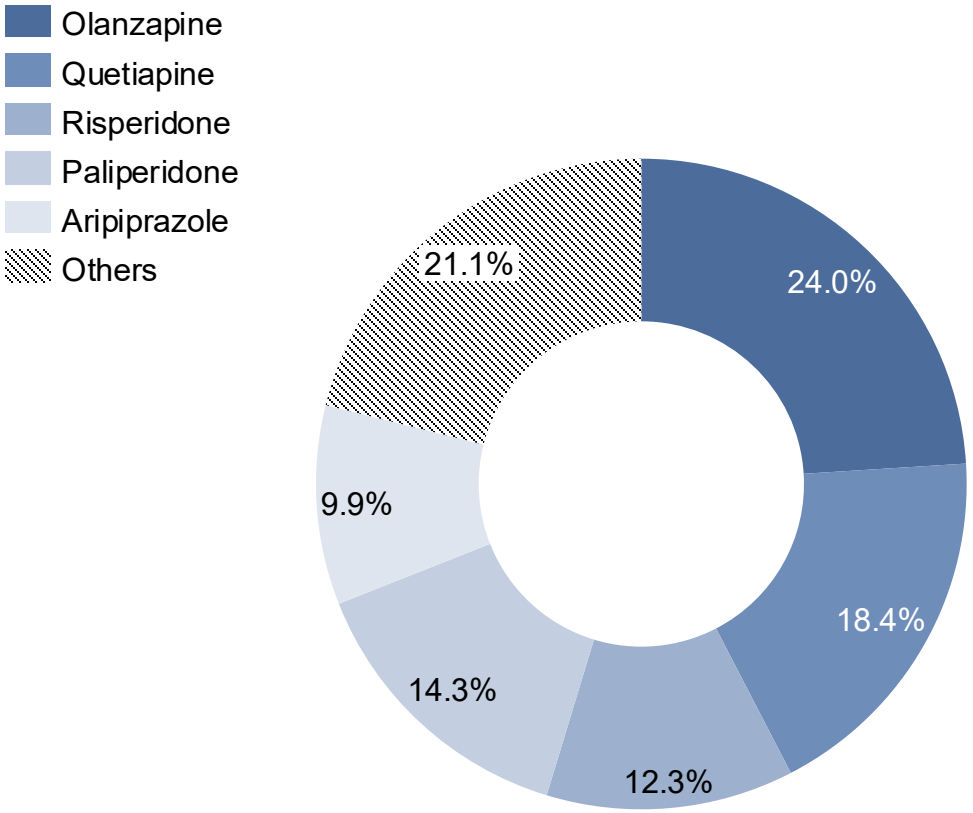
Updated 1011

Pipelines of innovative small molecule antipsychotics in China, as of LPD

Trial number	Candidate	Target	Company	Clinical phase	First posted date	Indication
CTR20231088	KarXT	M_1/M_4 receptor, mACh receptor	Zai Lab/ Karuna Therapeutics	NDA	2023/04/23	Schizophrenia
CTR20210675	BI 425809	GlyT1	Boehringer Ingelheim International	III	2021/04/01	Schizophrenia
CTR20253241	SIPI6398	5-HT_{1A} receptor, 5-HT_{2A} receptor, D_2 receptor	Zhongze Therapeutics	IIb	2025/08/18	Schizophrenia
CTR20241250	HS-10380	5-HT_{1A} receptor, D_2 receptor, D_3 receptor	Hansoh Pharmaceutical	II	2024/04/19	Schizophrenia at acute phase
CTR20241006	NHL35700	PDE10A	Nhwa Pharmaceutical	II	2024/04/02	Schizophrenia
CTR20241704	JX11502MA	5-HT_{1A} receptor, 5-HT_{2A} receptor, D_2 receptor	Jingxin Pharmaceutical	II	2024/05/13	Adult schizophrenia
CTR20253838	NS-136	M_4 receptor	Neushen Therapeutics	II	2025/09/22	Schizophrenia
CTR20220076	CY150112	DRD3	Nhwa Pharmaceutical	Ib	2022/01/18	Schizophrenia
CTR20192086	Pomaglumetad methionil	mGluR2 and mGluR3	Denovo Biopharma	I	2019/10/18	Schizophrenia
CTR20212631	MK-8189	PDE10A	MSD International	I	2021/10/19	Schizophrenia
CTR20221720	TPN672	5-HT_{1A} receptor, 5-HT_{2A} receptor, D_2/D_3 receptor	Kanion Pharmaceutical	I	2022/07/11	Schizophrenia
CTR20233319	VV119	D_2 receptor, D_3 receptor, 5-HT_{1A} receptor, 5-HT_{2A} receptor, 5-HTT	Vigonvita Life Sciences	I	2023/10/18	Schizophrenia
CTR20234241	NH300231	5-HT_{2A} receptor, DRDs	Nhwa Pharmaceutical	I	2024/01/02	Schizophrenia
CTR20240654	HS-10509	N/A	Hansoh Pharmaceutical	I	2024/02/27	Schizophrenia
CTR20241353	LPM526000133	N/A	Luye Pharma Group	I	2024/05/06	Schizophrenia with negative symptoms
CTR20242970	LPM787000048	5-HT_{2C} receptor, TAAR1	Luye Pharma Group	I	2024/08/13	Schizophrenia
CTR20250202	SPH9788	N/A	Shanghai Pharmaceuticals	I	2025/02/13	Schizophrenia
CTR20251193	NH140068	HTR,DRD,TAAR	Shanghai Shujing Biotechnology	I	2025/04/07	Schizophrenia

Competitive landscape of antipsychotics in China, by molecule, 2023

Competitive landscape of antipsychotics in China

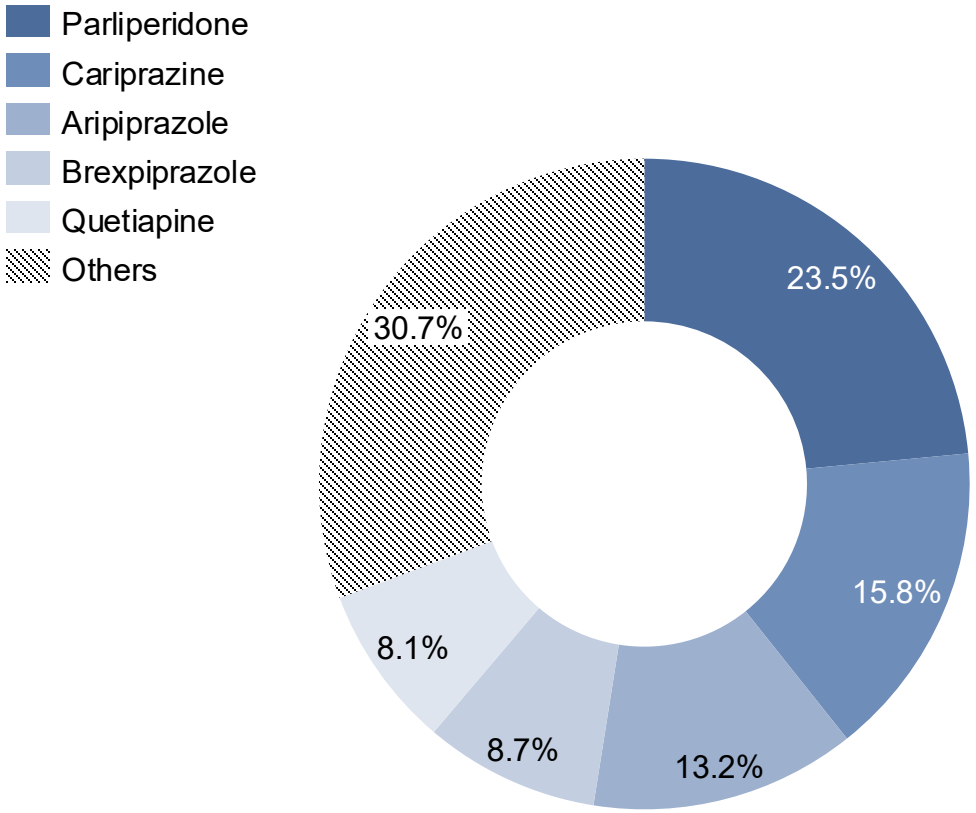


Ranking	Drug name	Market share
1	Olanzapine	24.0%
2	Quetiapine	18.40%
3	Risperidone	12.3%
4	Paliperidone	14.3%
5	Aripiprazole	9.9%
Others		**21.1%**
Total		**100%**

Sources: China Insights Consultancy

Competitive landscape of antipsychotics in global, by molecule, 2023

Competitive landscape of antipsychotics in global



Ranking	Drug name	Market share
1	Parliperidone	23.5%
2	Cariprazine	15.80%
3	Aripiprazole	13.2%
4	Brexpiprazole	8.7%
5	Quetiapine	8.1%
Others		**30.7%**
Total		**100%**

Sources: China Insights Consultancy

Table of contents

Definition and introduction of reproductive disease in China

Definition and introduction of reproductive disease in China

- Reproductive health diseases include a variety of conditions that affect the male and female reproductive systems and their functions. Common female conditions include polycystic ovary syndrome (PCOS), endometriosis, infertility, cervicitis, and sexually transmitted infections (STIs). Male reproductive health issues primarily involve andrology-related diseases, such as erectile dysfunction (ED), premature ejaculation (PE), benign prostatic hyperplasia (BPH), oligospermia, and azoospermia.

Reproductive disease

ED
- Psychological distress and reduced self-esteem
- Relationship difficulties
- Potential indicator of underlying cardiovascular disease and metabolic disorders

PCOS
- Infertility from irregular menstruation and ovulation disorders
- Metabolic disorders with increased diabetes risk
- Psychological distress from appearance changes (acne, hirsutism)

PE
- Significant reduction in sexual satisfaction
- Psychological burden leading to anxiety and avoidance behavior
- Relationship difficulties affecting overall quality of life and self-esteem

Endometriosis
- Chronic pelvic pain affecting daily activities
- Fertility complications and pregnancy difficulties
- Multiple surgeries leading to financial burden

Male reproductive disease | Female reproductive disease

BPH
- Chronic urinary symptoms disrupting daily activities and sleep patterns
- Progressive bladder dysfunction leading to urinary retention risk
- Quality of life reduction

Uterine Fibroids
- Anemia from abnormal uterine bleeding
- Urinary and bowel complications from compression
- Increased pregnancy complications and miscarriage risk

Common conditions of reproductive disease

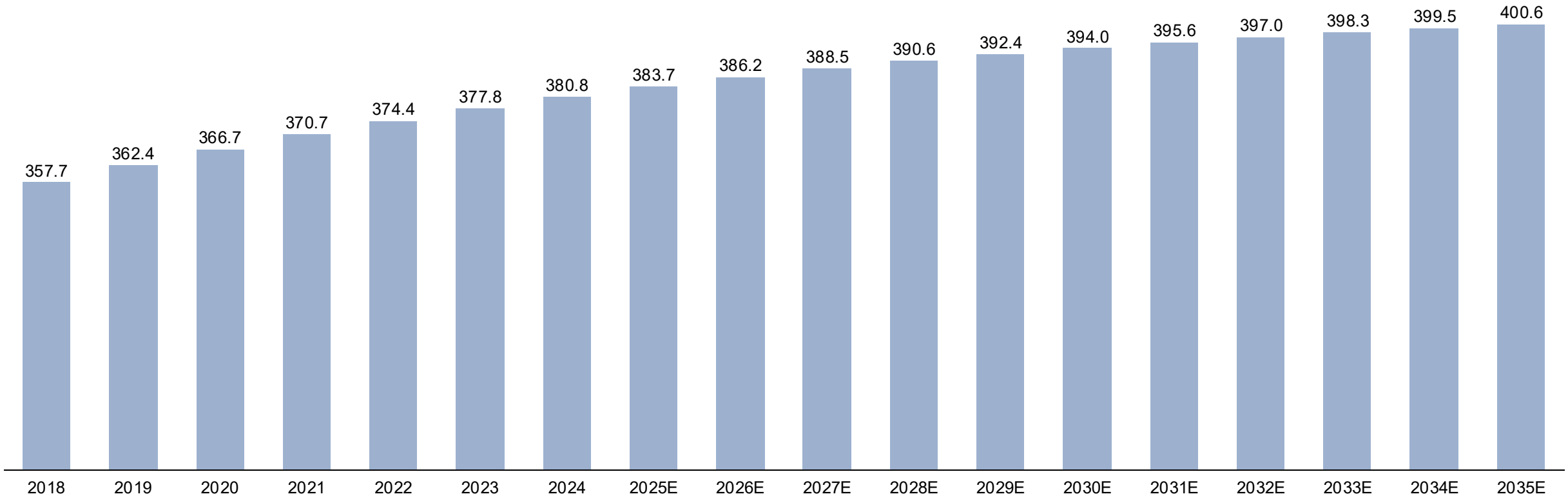
Sources: China Insights Consultancy

Epidemiology of male reproductive disease in China, include ED, PE, BPH and others, 2018-2035E

Epidemiology of male reproductive disease, China

CAGR	2018-24	2024-35E
China male reproductive disease patients	1.1%	0.5%

ppl million



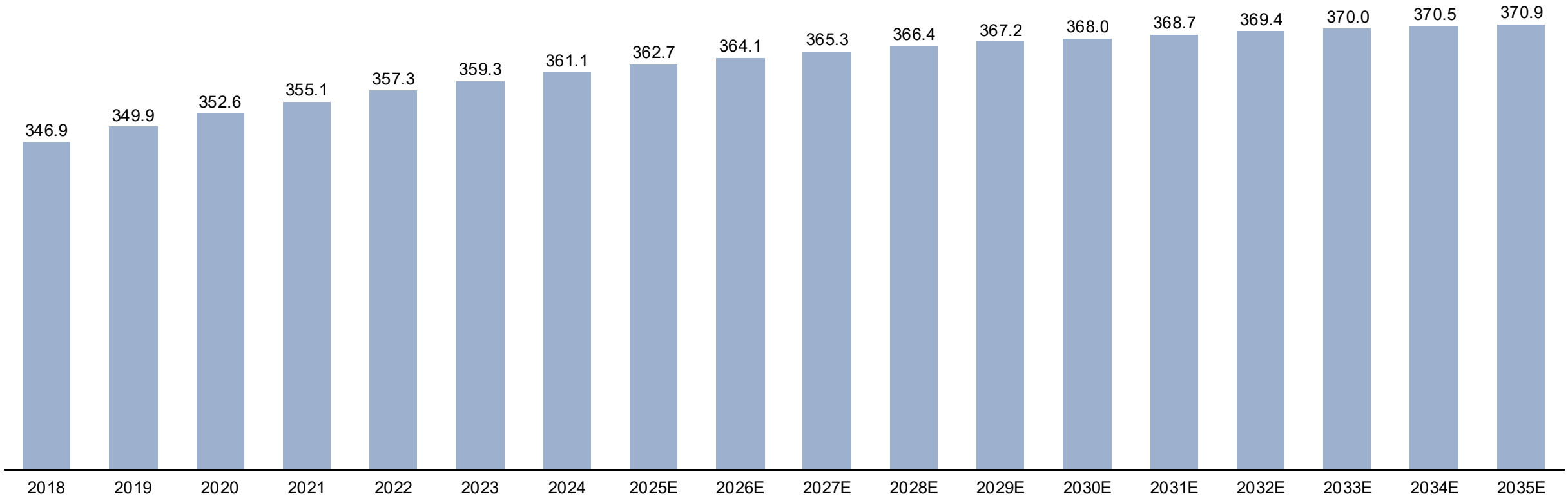
Sources: WHO, China Insights Consultancy

Epidemiology of erectile dysfunction in China, 2018-2035E

Epidemiology of ED, China

CAGR	2018-24	2024-35E
China ED patients	0.7%	0.2%

ppl million



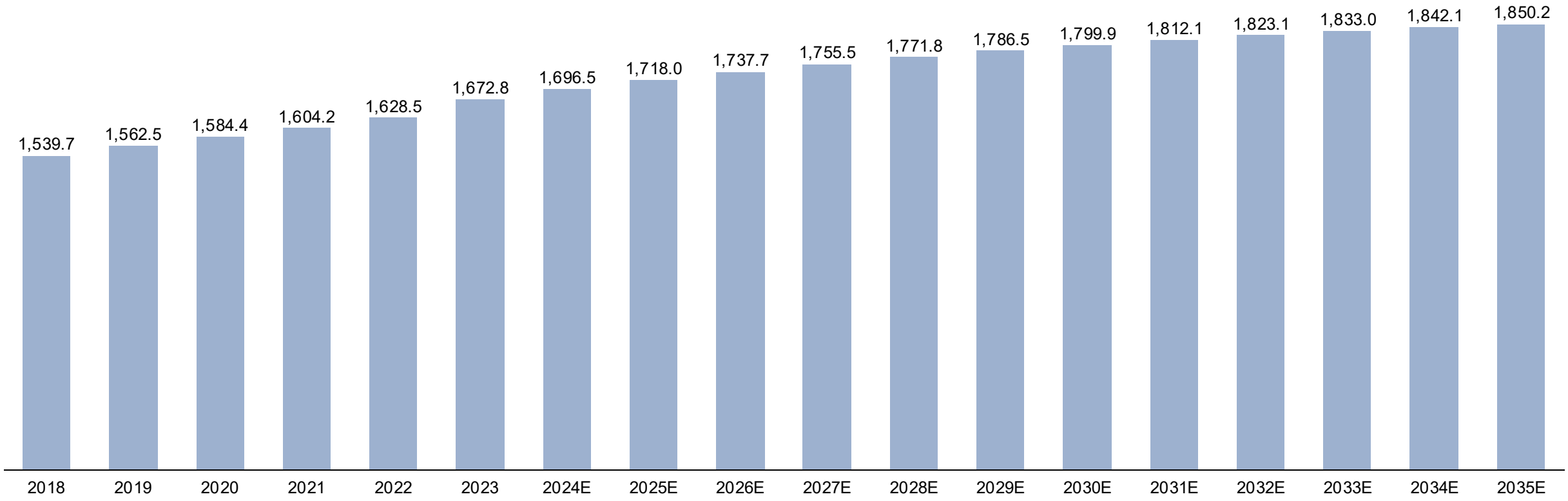
Sources: Meta-Analysis of Prevalence of Erectile Dysfunction in Mainland China: Evidence Based on Epidemiological Surveys, China Insights Consultancy

Epidemiology of male reproductive disease, global, include ED, PE, BPH and others, 2018-2035E

Epidemiology of male reproductive disease, global

CAGR	2018-23	2023-35E
Global reproductive disease patient	1.7%	0.8%

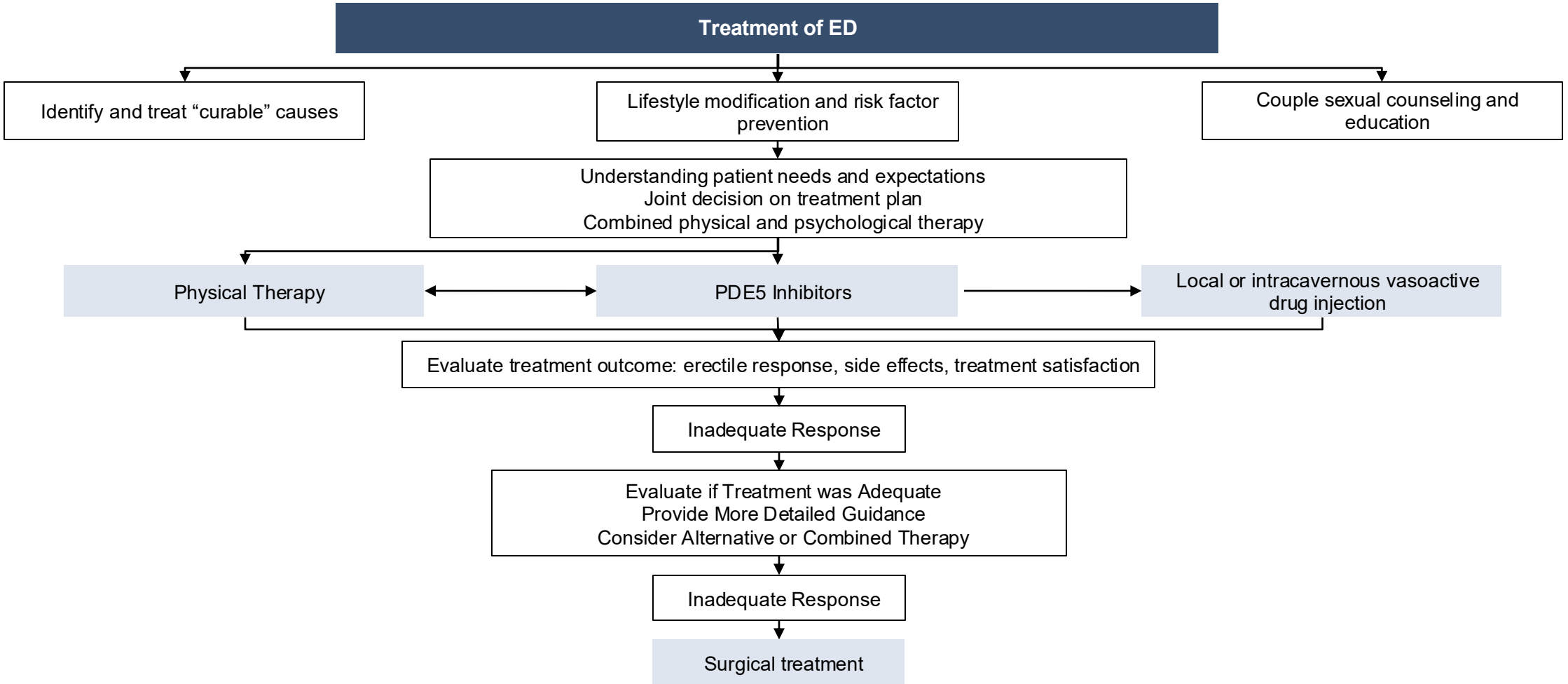
ppl million



Sources: WHO, China Insights Consultancy

Treatment pathways of ED

Treatment pathways of ED



Sources: 中华男科学会ED诊治指南, China Insights Consultancy

Treatment pathways of ED

Treatment pathways of ED

Evidence for ED Treatment	Level of Evidence (LE)	Grade of Recommendation (GR)
Principles of individualized treatment for ED	1	A
Treating both partners of ED patients	1	A
If an ED-related cause is identified, target it for treatment	1	B
Treatment or counseling for lifestyle factors and risk factor intervention for ED	1	A
Treatment or counseling for psychological guidance for ED	2	B
PDE5 inhibitors are the first-line treatment for ED	1	A
Select a suitable PDE5 inhibitor treatment for ED patients	1	B
For non-responsive patients, assess if proper use and dosage of PDE5 inhibitors were followed	3	B
Testosterone supplementation improves erectile function in patients with low testosterone	3	C
Use of oral or injectable testosterone improves erectile function	3	C
Surgical treatments (vascular surgery, venous surgery, penile prosthesis) improve erectile function	4	C
Penile prosthesis implantation improves erectile function	4	C
Low-intensity extracorporeal shockwave therapy improves erectile function	4	C
Intracavernosal injections improve erectile function	1	B
Use of intraurethral or topical medications improves erectile function	3	B
Rehabilitation therapy following trauma or surgery helps improve erectile function	2	A
Testosterone supplementation improves hypogonadism-related erectile dysfunction	1	A
Treatment for hyperprolactinemia helps improve erectile dysfunction caused by elevated prolactin	1	A
Psychological therapy improves erectile dysfunction caused by psychological factors	2	B

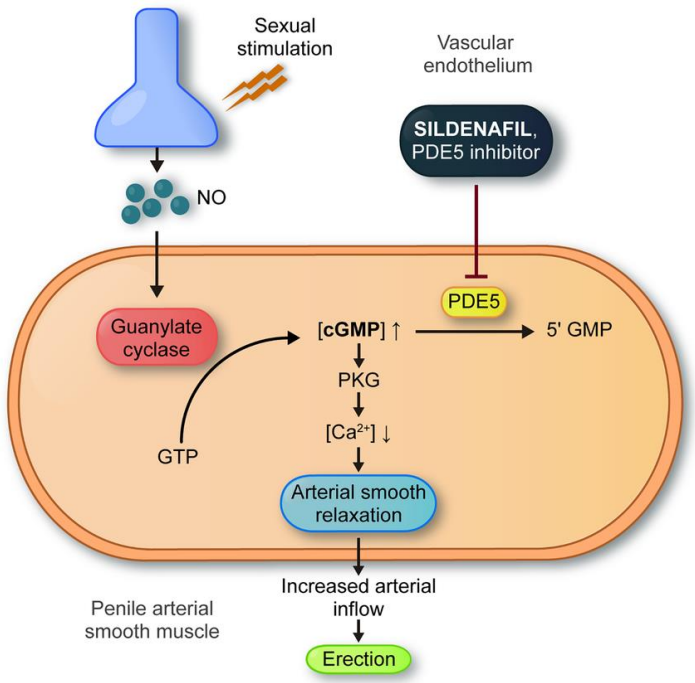
Key takeaway

- PDE5i are the first-line medication for ED treatment with a Grade A recommendation (Level 1 evidence). PDE5i work by inhibiting phosphodiesterase type 5, increasing cyclic guanosine monophosphate (cGMP) levels in cavernosal smooth muscle, enhancing nitric oxide-mediated vasodilation, thereby improving erectile function.
- The guidelines suggest selecting appropriate PDE5i based on individual patient circumstances, expectations, and drug characteristics, while paying attention to contraindications, particularly the interaction with nitrates.

Sources: 中华男科学会ED诊治指南, China Insights Consultancy

Main mechanisms and comparison of different PDE5i

Main mechanisms and comparison of different PDE5i



General mechanism of action of sildenafil in erectile dysfunction

Parameters	TPN171H, 20mg	Sildenafil, 100mg	Tadalafil, 20mg	Vardenafil, 20mg	Avanafil, 100mg	Aildenafil, 30mg
C_{max}	145.8 μg/L	560 μg/L	378 μg/L	18.7 μg/L	1,250 μg/L	247.3 μg/L
T_{max}(Median)	0.5-1.3 h	0.8-1 h	2 h	0.9 h	0.25 h	1 h
T1/2	8.02-10.88 h	2.6-3.7 h	17.5 h	3.9 h	3-5 h	~4 h
AUC	1,069.1 μg.h/L	1,685 μg.h/L	8,066 μg.h/L	56.8 μg.h/L	/	1,368.3 μg.h/L
Plasma Protein Binding	N/A	96%	94%	94%	99%	96%
Bioavailability	N/A	41%	N/A	15%	15%	/
Selectivity for PDE5/PDE6 (fold difference)	32	10	700	>15	>100	/
Selectivity for PDE5/PDE11 (fold difference)	1,610	>700	1LA1:10 1LA4:40	300	>10,000	/

Sources: Drug Design, Development and Therapy 2021, China Insights Consultancy

Adverse reaction of different PDE5i

Adverse reaction of different PDE5i

Adverse Reactions	Sildenafil	Tadalafil	Vardenafil	Aildenafil	Avanafil
Dose	50mg	20mg	5mg/20mg	60mg	100mg
Headache	21%	15%	15%	4%	8%
Dizziness	4%	/	2%	5%	1%
Dyspepsia	9%	10%	4%	/	/
Flushing	19%	3%	11%	7%	5%
Visual Abnormalities	2%	/	/	1%	/
Back Pain	4%	6%	2%	/	3%
Myalgia	2%	3%	/	/	/
Limb Pain	/	3%	/	/	/

- PDE5 inhibitors represent a major first-line oral therapy option for men with ED. Marketed drugs exhibit higher inhibitory activity on PDE6 and PDE11, leading to significant adverse effects in patients. There is a huge clinical need for safer and longer-acting targeted therapies.

Sources: 爱力士, Viagra, Cialis label, China Insights Consultancy

Drug instruction and comparison of different PDE5i

Drug instruction and comparison of different PDE5i

Characteristics	Sildenafil (Viagra)	Vardenafil (Levitra)	Vardenafil ODT (Staxyn)	Tadalafil (Cialis)	Avanafil (Stendra)	Aildenafil (爱力士)
Manufacturer	Pfizer	Bayer/GlaxoSmithKline	Bayer/GlaxoSmithKline	Eli Lilly	Vivus	Youcare Pharmaceutical
Year Approved	1998	2003	2010	2003	2012	2021
Dosage	25-100 mg/day	5-20 mg/day	10 mg/day	5-20 mg/day (as needed); 2.5-5 mg/day once daily	50-200 mg/day	60 mg/day
Timing	1 hour before sexual activity	1 hour before sexual activity	1 hour before sexual activity	At least 0.5 hours before sexual activity	0.5 hours before sexual activity	1 hour before sexual activity
Duration	3.5-4 hours post dose	-	-	Up to 36 hours post dose	Up to 4 hours post dose	
Special Considerations	Renal: CrCl < 30 mL/minute: starting dose 25 mg; Hepatic impairment: starting dose 25 mg	Renal: Do not use in patients receiving hemodialysis; Hepatic: Moderate impairment: starting dose 5 mg; maximum 10 mg	Renal: Do not use in patients receiving hemodialysis; Hepatic: Moderate/severe impairment: do not use; Drug Interactions: Moderate/potent CYP3A4 inhibitors: do not use	As-needed use: Renal: • CrCl 30-50 mL/minute: starting dose 5 mg/day; maximum 10 mg/48 hours • CrCl < 30 mL/minute	Renal: Do not use if CrCl < 30 mL/minute in patients receiving hemodialysis; Hepatic: Severe impairment	Maximun 60 mg/24 hours

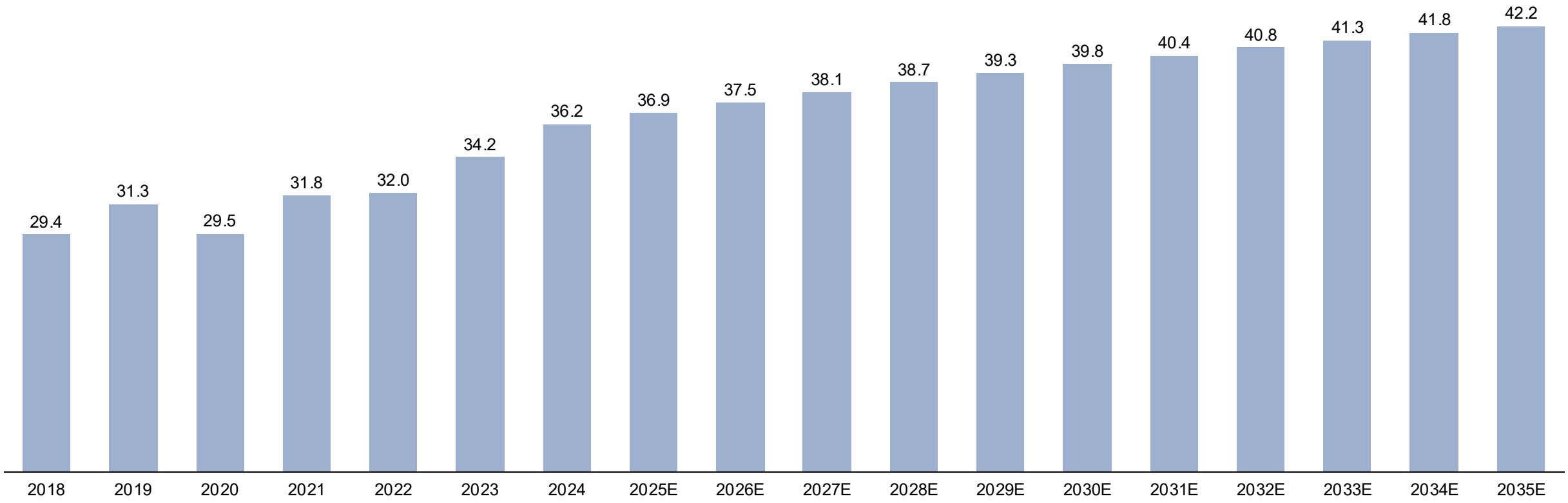
Sources: Drug instructions, China Insights Consultancy

Market size of reproductive disease drug market, China, 2018-2035E

Market size of reproductive disease drug market, China

CAGR	2018-24	2024-35E
China reproductive disease drug market	3.5%	1.4%

RMB billion



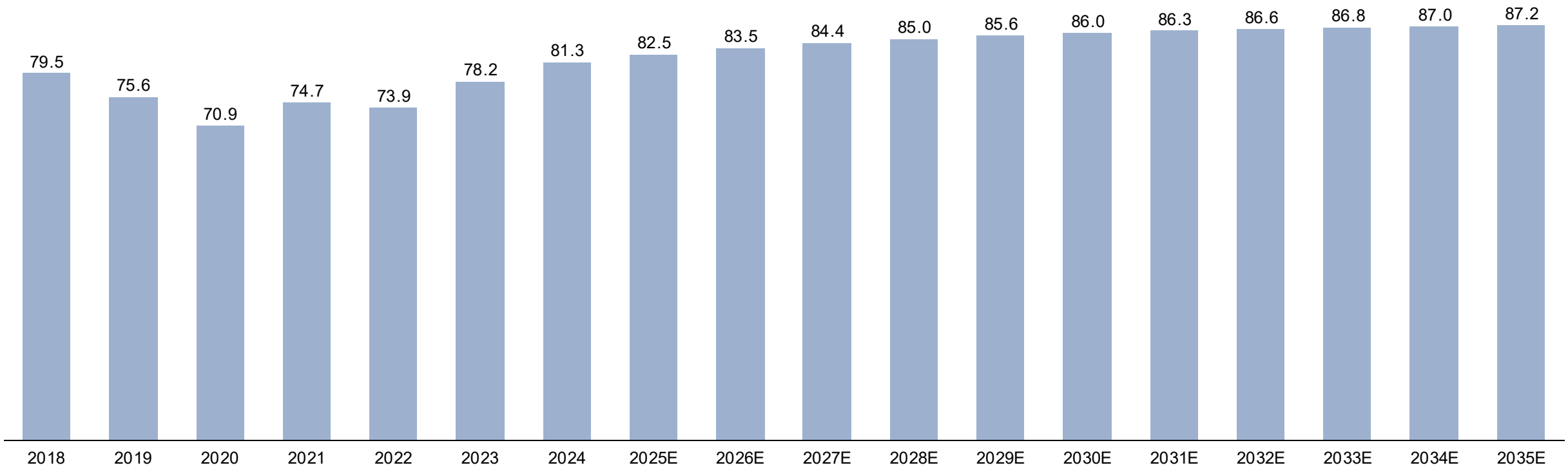
Sources: China Insights Consultancy

Market size of reproductive disease drug market, global, 2018-2035E

Market size of reproductive disease drug market, global

CAGR	2018-24	2024-35E
Global reproductive disease drug market	0.4%	0.6%

USD billion



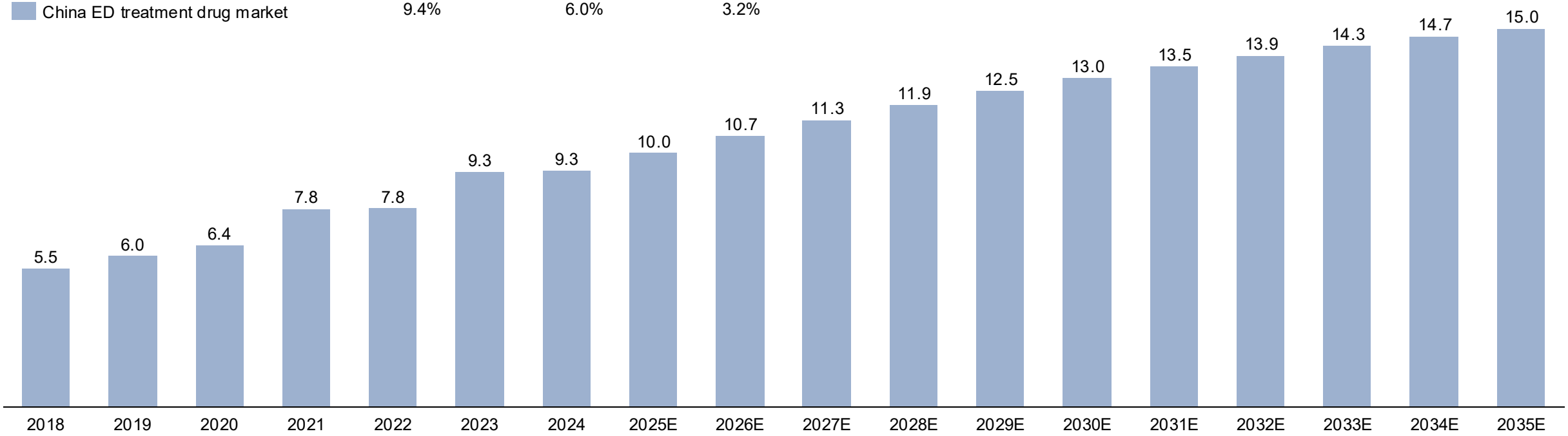
Sources: China Insights Consultancy

Market size of ED treatment drugs, China, 2018-2035E

Market size of ED treatment drugs, China

CAGR	2019-24	2024-29E	2029E-2034E
China ED treatment drug market	9.4%	6.0%	3.2%

RMB billion



- The medical consultation rate for ED in China significantly lower than the 40-50% in developed countries, indicating substantial growth potential as public health awareness improves and medical education expands; Meanwhile, rising disposable income in China is driving pharmaceutical consumption upgrade, while expanded medical insurance coverage and improved healthcare channels have enhanced drug accessibility; Furthermore, China's market is still in a development phase with considerable room for market cultivation and education, coupled with an accelerating aging population and increasing prevalence of ED-related conditions such as diabetes and cardiovascular diseases, which expand the potential patient pool. In contrast, developed markets have reached maturity, with stable consultation rates and drug accessibility, minimal demographic changes, and limited growth drivers.

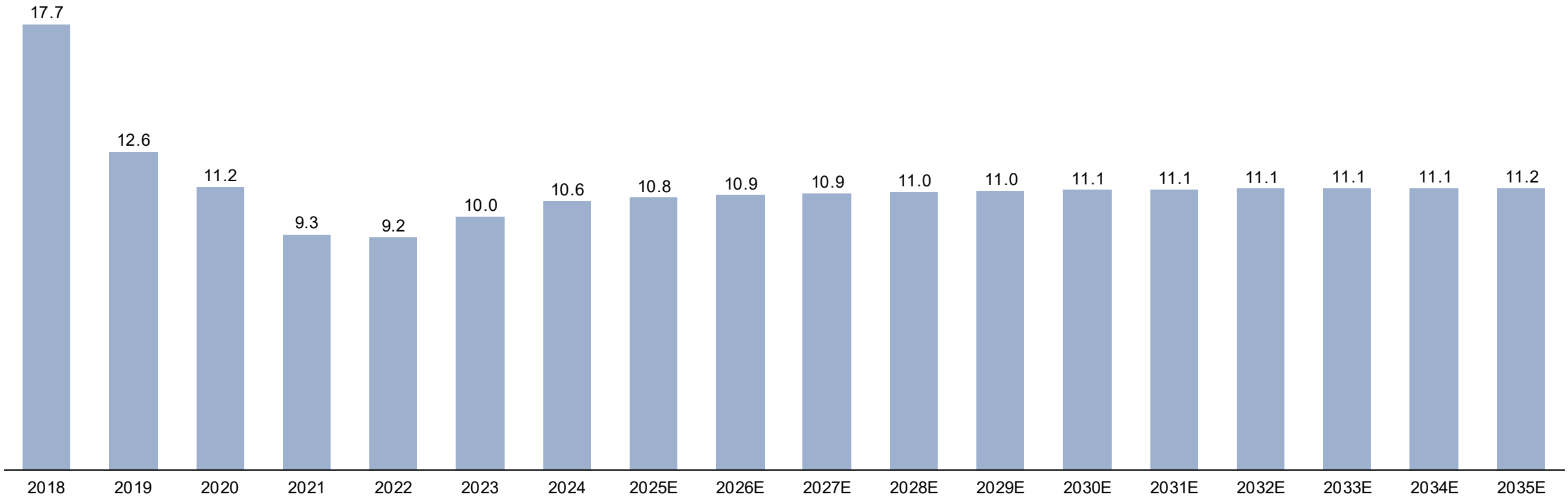
Sources: China Insights Consultancy

Market size of ED treatment drugs, global, 2018-2035E

Market size of ED treatment drugs, global

CAGR	2018-24	2024-35E
Global ED treatment drug market	-8.1%	0.4%

USD billion



Sources: China Insights Consultancy

Pipelines of PDE5i in China (registered in CDE)

Updated 1011

Pipelines of PDE5i, as of LPD

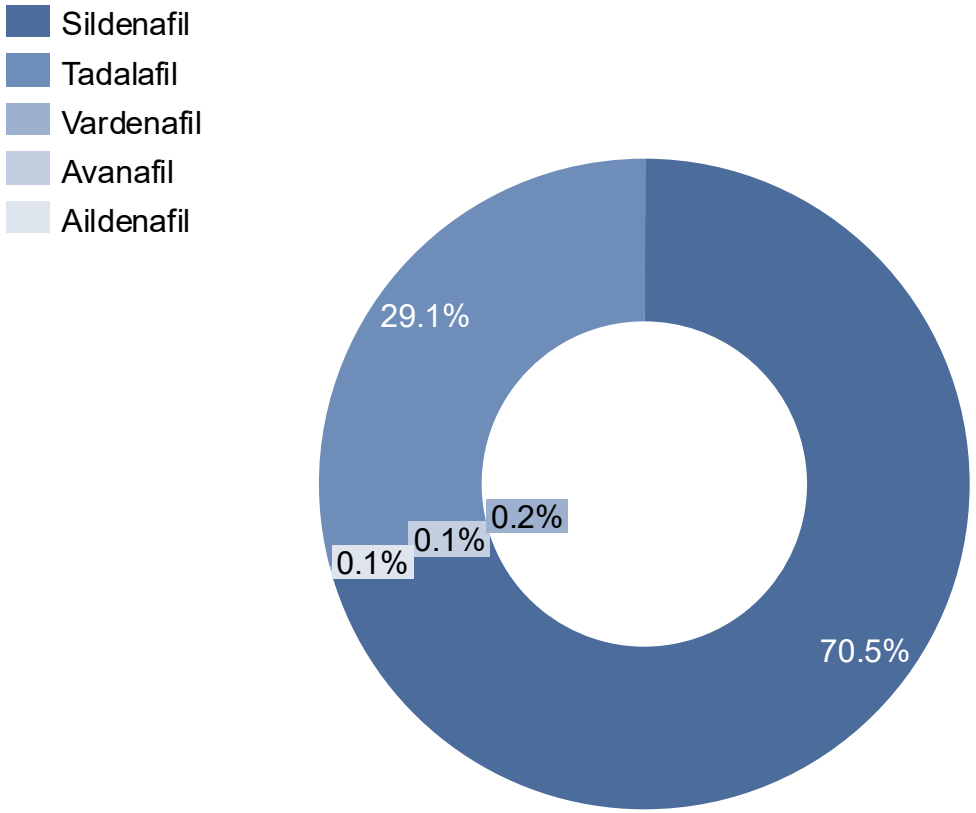
Trial number	Candidate	MoA	Company	Clinical phase	First posted date	Indication	Single/Combo
CTR20240721	TPN171	PDE5i	Vigonvita Life Sciences	NDA approval	2025/07/08	ED	Single
CTR20240170	Youkenafil Hydrochloride	PDE5i	Yangtze River Pharmaceutical	NDA approval	2025/07/22	ED	Single
CTR20222332	TPN729MA	PDE5i	Topfond Pharmaceutical	III	2022/10/09	ED	Single
CTR20253583	CMS203	PDE5i	Shandong Lukang Pharmaceutical	IIb	2025/09/04	ED	Single
CTR20211982	Fadanafil	PDE5i	Xuanzhu Bio	II	2021/08/10	ED	Single
CTR20233686	DDCI-01	PDE5i	Chongqing Dikangerle Pharmaceutical	II	2023/11/21	LUTS secondary to BPH with ED	Single
CTR20191491	Xiongdinafil Citrate	PDE5i	Suzhou Maidixian Pharmaceutical	I	2019/07/30	ED	Single

*Note: Only include PDE5i pipelines with ED indication

Sources: CDE, China Insights Consultancy

Competitive landscape of PDE5i, China, 2023, by molecule

Competitive landscape of PDE5i, China



Ranking	Drug name	Market share
1	Sildenafil	70.5%
2	Tadalafil	29.1%
3	Vardenafil	0.2%
4	Avanafil	0.1%
5	Aildenafil	0.1%
Total		**100%**

Sources: China Insights Consultancy

Competitive landscape of PDE5i, China, 2024, by molecule

Competitive landscape of PDE5i, China

Ranking	Drug name	MoA	Indication	Administration	Line of therapy	Top 2 company	Market share
1	Sildenafil	PDE5i	ED and PAH	Oral	First-line	Pfizer	23.6%
						Guangzhou Baiyunshan Pharmaceutical	20.8%
2	Tadalafil	PDE5i	ED	Oral	First-line	Menarini	10.6%
						Tasly	4.6%
3	Vardenafil	PDE5i	ED	Oral	First-line	Sichuan Kelun Pharmaceutical	0.5%
						Shenyang Hongqi Pharmaceutical	0.1%

Sources: China Insights Consultancy

Competitive landscape of PDE5i, China, 2024, by molecule

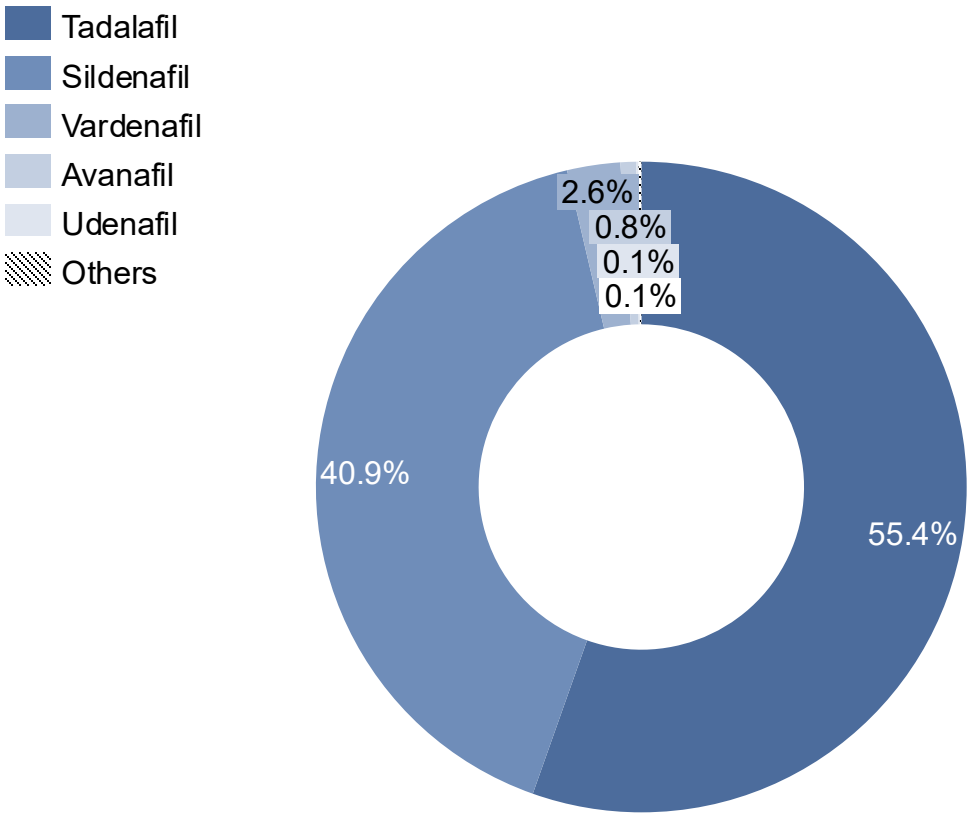
Competitive landscape of PDE5i, China

Ranking	Drug name	MoA	Indication	Administration	Line of therapy	Top 2 company	Scope of Business	Market share
1	Sildenafil	PDE5i	ED and PAH	Oral	First-line	Company A	A U.S.-headquartered global biopharmaceutical leader that played a vital role in developing COVID-19 vaccines and rare disease treatments	23.6%
						Company B	A company headquartered in Guangdong, specializing in respiratory drugs, anti-inflammatory medicines, and over-the-counter healthcare products.	20.8%
						Company C	An Italy-based international pharmaceutical group focuses on cardiology, gastroenterology, anti-infectives, and pain management.	10.6%
2	Tadalafil	PDE5i	ED	Oral	First-line	Company D	A company headquartered in Tianjin, integrating traditional Chinese medicine (TCM) with modern drug development, specializing in cardiovascular, oncology, and metabolic disease treatments.	4.6%
						Company E	A company headquartered in Sichuan, one of the largest infusion therapy providers in China, known for intravenous (IV) fluids, antibiotics, and oncology drugs.	0.5%
3	Vardenafil	PDE5i	ED	Oral	First-line	Company F	A company headquartered in Shenyang, specializing in anti-tuberculosis drugs including rifampicin, isoniazid, and other WHO-prequalified products. It is expanding into men's health and reproductive medicine with integrated API and formulation capabilities.	0.1%

Sources: China Insights Consultancy

Competitive landscape of PDE5i, global, 2023, by molecule

Competitive landscape of PDE5i, global



Ranking	Drug name	Market share
1	Tadalafil	55.4%
2	Sildenafil	40.9%
3	Vardenafil	2.6%
4	Avanafil	0.8%
5	Udenafil	0.1%
Others		**0.2%**
Total		**100%**

Sources: China Insights Consultancy

Market drivers and development trends of PDE5i in China

Future trends	
 **Aging Population and Lifestyle Changes**	• China is experiencing rapid population aging, with the population aged 60 and above expected to exceed 300 million by 2025. Meanwhile, modern lifestyle factors such as increased urban stress, sedentary behavior, and dietary changes have led to rising ED incidence rates. These demographic and lifestyle changes directly drive the growing market demand for PDE5i medications. The elderly's pursuit of better quality of life, coupled with the increasing number of young and middle-aged ED patients, forms the demographic foundation for market growth.
 **Enhanced Disease Awareness and Healthcare Accessibility**	• In recent years, with the popularization of public health education and the development of internet healthcare, people's understanding of ED has deepened, and their willingness to seek medical treatment has significantly increased. The rise of online consultation platforms has broken traditional medical barriers, providing patients with more private and convenient diagnosis and treatment channels. The expansion of medical insurance coverage and the improvement of hierarchical diagnosis and treatment systems have also enabled more patients to receive standardized treatment. These factors collectively drive market expansion and improve treatment penetration rates.
 **Innovation and Market Competition Optimization**	• Domestic pharmaceutical companies are increasing their R&D investment in the PDE5i field, with new drugs and dosage forms constantly emerging. Innovative formulations such as orally disintegrating tablets and quick-dissolving tablets have improved medication convenience, meeting the needs of different patient groups. With the improved quality and price advantages of domestic generic drugs, market competition has become more rational, promoting healthy overall market development. More new PDE5i products with independent intellectual property rights are expected to emerge in the future, further enriching treatment options.
 **Policy Support and Standardized Management**	• National drug regulatory authorities have strengthened the supervision of ED treatment medications, promoting standardized management of prescription drugs, curbing illegal sales, and purifying the market environment. Meanwhile, the establishment of a dynamic adjustment mechanism for medical insurance catalogs has created conditions for more innovative drugs to be included in medical insurance coverage. These policy measures ensure patient medication safety while providing a favorable institutional environment for industry development, conducive to long-term healthy market growth.

Sources: China Insights Consultancy

Table of contents

Definition and historical development of modern generic drugs

Definition and historical development of modern generic drugs

Definition:

- According to the definition by the U.S. FDA, the purpose of generic drugs is to enhance competition and increase drug accessibility. Generic drugs must demonstrate the same clinical efficacy as the reference branded drugs in clinical practice. Reference formulations can include the original branded drug or internationally recognized equivalent drugs. These reference formulations are officially designated as products with reasonable prescription processes, stable quality, and proven efficacy
- To effectively replace branded drugs, generic drugs must be as safe and effective as the original, achieving both pharmaceutical equivalence and clinical equivalence. Pharmaceutical equivalence means that the active ingredients, dosage form, strength, route of administration, and labeling of the generic drug must match those of the branded drug. For oral formulations, clinical equivalence is typically demonstrated through bioavailability studies. This requires that the rate and extent of drug absorption in the body (as measured by Cmax and AUC) for the generic fall strictly within the range of 80% to 125% of the reference drug

Historical development

Early 20th century

- The regulatory history of the U.S. generic drug industry began in the early 20th century. The **Federal Pure Food and Drugs Act** of 1906 brought drugs under federal regulation. In 1937, Massengill Company's use of toxic diethylene glycol as a solvent in a sulfanilamide elixir caused 107 deaths, leading to the **Federal Food, Drug, and Cosmetic Act** of 1938, which required safety testing before drug approval. In the 1960s, the thalidomide disaster caused over 10,000 birth defects globally, prompting the **Kefauver-Harris Amendment** in 1962. This law mandated that both new and generic drugs prove safety and efficacy before FDA approval
- The complex approval process raised new drug development costs, while generic manufacturers faced the dual burden of meeting rigorous data requirements and waiting for branded drug patents to expire

1980s

- In 1983, Bolar Pharmaceuticals imported Roche's patented flurazepam hydrochloride and conducted bioequivalence testing before the patent expired. Roche sued for patent infringement and won. This highlighted the conflict between branded drug companies extending patents and generics aiming for early market entry
- This led to the **Hatch-Waxman Act** of 1984, which required **NDAs** to include patent information, with exclusivity and patent extensions for approved drugs. Generic companies only needed to conduct bioequivalence studies and submit an **Abbreviated New Drug Application (ANDA)**, reducing development costs. This established the foundation for the modern U.S. generic drug industry

Early 21st century

- China's generic drug regulatory history has developed rapidly in the past two decades. Following the reform and opening-up, the rise of private and foreign companies led to a surge in low-cost generics. However, market regulation was weak, and there was no patent protection for drugs until 2005, when the **Compulsory Licensing of Patents for Public Health** regulations were introduced
- In 2007, the **SFDA** formally introduced the concept of "generic drugs" and established quality control across the entire drug development process. The **State Council** in 2015 emphasized the consistency evaluation of generics and branded drugs, improving the approval system. In 2016, the **NMPA** launched the full implementation of this evaluation. By 2018, further reforms accelerated the review process, leading to significant growth in China's generic drug market

Sources: FDA, CDE, China Insights Consultancy

Overview of the classification of generic drugs in China

Overview of the classification of generic drugs in China

- Pharmaceuticals are typically classified into **chemical generics** and **biosimilars** based on their characteristics and synthesis methods. The former refers to low molecular weight drugs synthesized chemically, while the latter encompasses high molecular weight drugs or biologics produced through biological processes. Given the distinct differences in their manufacturing processes and composition, the regulatory policies for these two categories of drugs vary accordingly

Chemical generics

- In the United States, generic drugs are submitted for approval through the Abbreviated New Drug Application (ANDA). While in China, chemical generics fall under Categories 3 and 4 of chemical drugs: Category 3 applies to domestically developed generics of originator drugs that are approved overseas but not yet in China, while Category 4 applies to generics of originator drugs already approved in China
- Both in the U.S. and China, generics must match the reference listed drug (RLD) in active ingredient, dosage form, strength, indication, route of administration, and usage. They must also demonstrate equivalent safety and efficacy to the RLD. Consistency evaluation is generally based on bioequivalence (BE) studies, which confirm that under the same dosage and cross-over study conditions in the same subjects, the test and reference drugs show no statistically significant differences in the rate and extent of absorption of the active ingredient into the bloodstream
- High-end originator drugs are often protected by formulation and manufacturing process patents, such as those for oral controlled-release formulations. Some RLDs also have BE-related patent protections. Overcoming these patent barriers is essential for generics to gain approval before the originator's patent expiry. Furthermore, the lack of universally applicable in vitro-in vivo correlation (IVIVC) technology adds challenges, making in vivo BE testing for high-end generics particularly difficult. Complex manufacturing processes may also hinder commercialization

Biosimilars

- Biosimilars have significantly higher molecular weights and more complex structures compared to chemical generics, making perfect replication during manufacturing nearly impossible—even originator manufacturers experience batch-to-batch variability. As a result, biosimilars cannot replicate all characteristics of the reference biologic. Due to these complexities, the approval requirements for biosimilars differ from those of chemical generics. Rather than demonstrating exact equivalence, biosimilars must prove similarity, typically through **Phase I-III clinical trials** to validate safety and efficacy, with **Phase IV post-marketing surveillance** required for safety monitoring
- Furthermore, biosimilars may not always be interchangeable with the reference biologic in clinical practice, depending on the submitted data and regulatory approval. In the U.S., biosimilars are not eligible for an **Abbreviated New Drug Application (ANDA)** but require a full **Biologics License Application (BLA)** with comprehensive clinical trial data
- While in China, biosimilars fall under the **biologics registration categories** and are divided into therapeutic and preventive biologics. **Therapeutic biosimilars** belong to Category 3 therapeutic biologics, further classified into biosimilars and biologics approved overseas but not yet in China. **Preventive biosimilars** fall under Category 3 preventive biologics, including domestically approved vaccines and vaccines approved overseas but not yet in China

Sources: FDA, CDE, China Insights Consultancy

Overview of regulatory policies for generic drugs in China

Overview of regulatory policies for generic drugs in China

- In China, when applying for market registration of a generic drug after completing clinical trials, the submission to the National Medical Products Administration (NMPA) must include a clinical trial database and a dossier prepared in accordance with the **M4: Common Technical Document (CTD) for the Registration of Pharmaceuticals for Human Use**. This dossier is divided into five modules:

Administrative documents	Summaries of CTD content	Quality information	Non-clinical study reports	Clinical study reports
• Includes a cover letter, content index, application form, product information, and manufacturer certifications	• Includes the CTD table of contents, quality overview, non-clinical overview, clinical overview, non-clinical written summaries and tabulated summaries, and clinical summary	• Includes active pharmaceutical ingredient (API) details, CMC (chemistry, manufacturing, and controls), characterization, quality control, reference products, packaging systems, stability, dosage form, composition, excipients, and references	• Includes pharmacology, pharmacokinetics, toxicology, and references	• Includes bioequivalence (BE) study reports detailing the selection of the reference formulation and test drug, study design, and evaluation

- Applicants must complete a **Drug Registration Application Form** and submit the dossier to the **Center for Drug Evaluation (CDE)** of NMPA. The CDE conducts an initial formal review, and if the submission meets requirements, it is accepted, and the applicant receives a notification of acceptance. The CDE then initiates the review process, and within 40 days, based on the risk profile of the applicant and the drug, decides whether to conduct on-site inspections and sample testing for registration
- The CDE evaluates the safety, efficacy, and quality controllability of the drug based on the submitted documents, inspection results, and testing outcomes. Applicants may be required to provide supplemental information as necessary. Once a comprehensive opinion is formed, it is submitted to the **NMPA** along with supporting materials. The NMPA makes the final approval decision based on the overall review

Sources: FDA, CDE, China Insights Consultancy

Impact of centralized procurement policies on the generic drug industry

Impact of centralized procurement policies on the generic drug industry

- Centralized volume-based procurement (VBP) in China is a national initiative where the government organizes bulk purchasing of drugs that have passed consistency evaluation, reducing reliance on medical representatives for sales. Procurement volumes are disclosed in tenders, enabling companies to balance pricing with production capacity. VBP aims to cut inflated drug prices, lower patient costs, and foster a healthier pharmaceutical and medical practice environment, guiding the industry toward high-quality development
- As of December 2024, China has conducted 9 batchs of national-level drug centralized VBP across 10 cycles. The number of selected drugs and participating companies has shown a steady growth trend and the enthusiasm of companies to participate in the initiative has also risen accordingly. Each round of national centralized procurement has achieved an average price reduction of approximately 50-60%

Date	Batch	Number of products	Winning Companies	Price Reduction
Dec 2018	Pilot Batch	25	25	52%
Sep 2019	First Expansion	25	45	59%
Jan 2020	Second Batch	32	77	53%
Aug 2020	Third Batch	55	125	53%
Feb 2021	Fourth Batch	45	118	52%
Jun 2021	Fifth Batch	61	148	56%
Nov 2021	Sixth Batch	16 (Insulin)	10	53%
Jul 2022	Seventh Batch	60	217	48%
Apr 2023	Eighth Batch	39	174	56%
Nov 2023	Ninth Batch	41	205	58%

Key Analysis

- The benefits of centralized VBP for winning companies are evident, with the most direct being increased market penetration of selected products. For instance, after Pfizer's atorvastatin calcium and amlodipine besylate failed to secure bids in the initial "4+7" procurement, their Q2 2019 sales dropped by 20%, with much of the market share captured by winning companies
- For companies on the VBP list, drug sales volumes are guaranteed by national and provincial governments, enabling cost reductions through economies of scale. This minimizes marketing and sales expenses, allowing generic drug manufacturers to save costs and maintain profit margins. However, risks arise if a company fails to renew its bid or secure future VBP contracts, disrupting production and marketing plans and potentially increasing costs

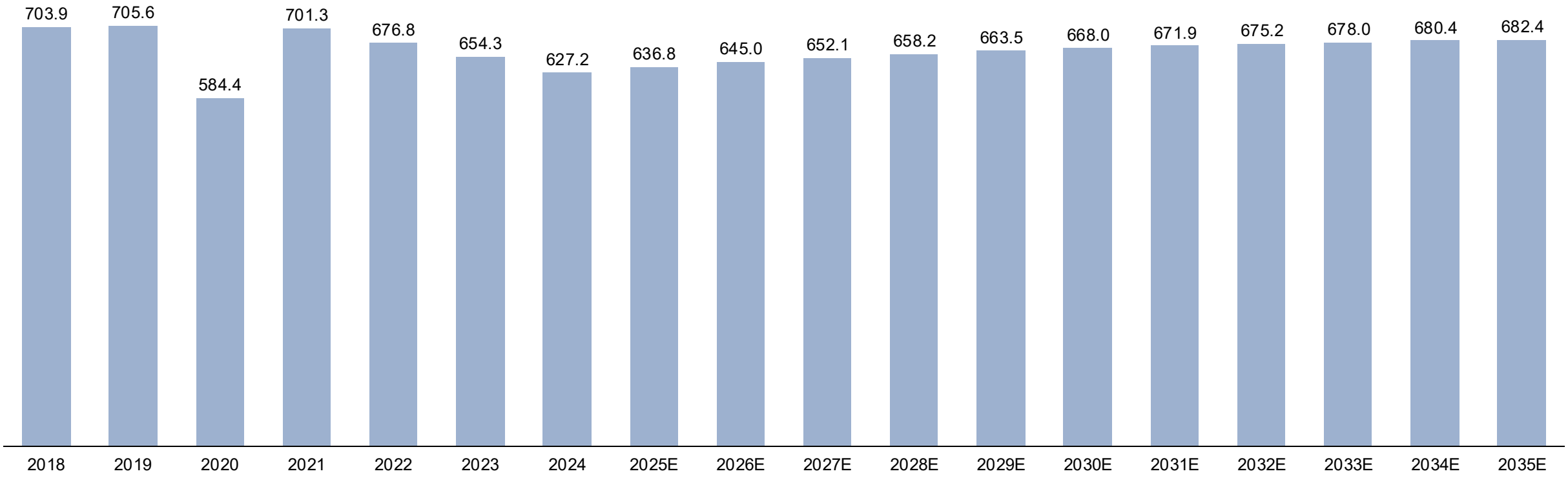
Sources: the State Council, China Insights Consultancy

Market size of generic drug market, China, 2018-2035E

Market size of generic drug market, China, 2018-2035E

CAGR	2018-24	2024-35E
Generic drugs	-1.9%	0.8%

RMB billion



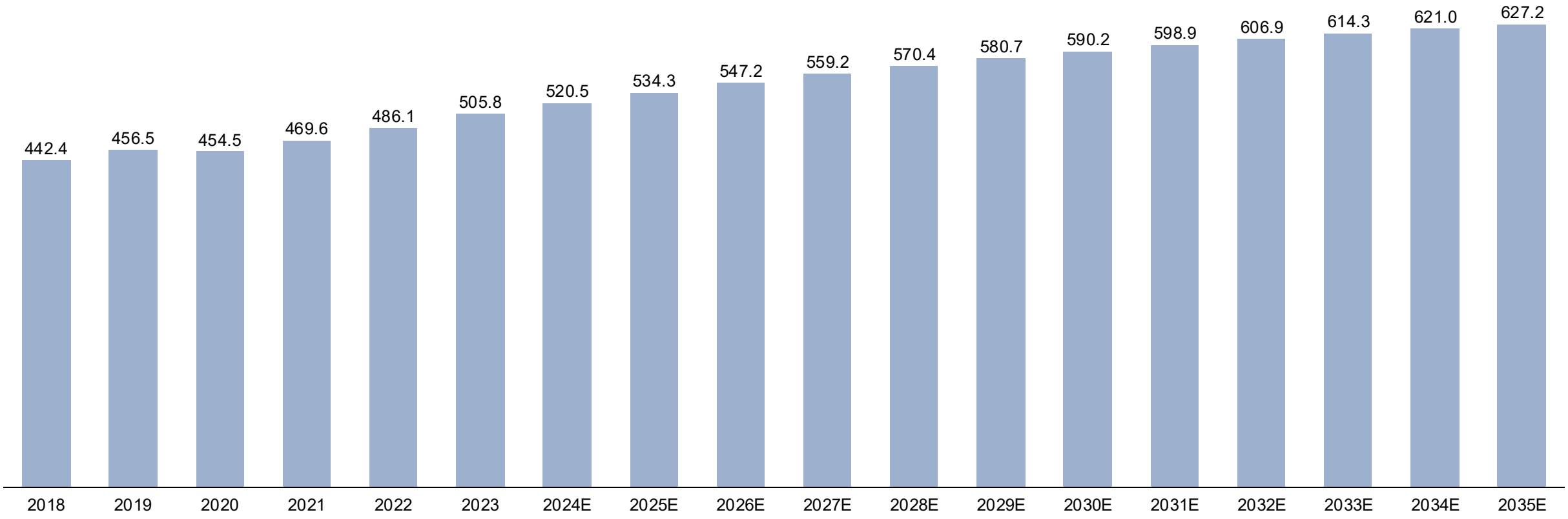
Sources: National Bureau of Statistics, NHC, China Insights Consultancy

Market size of generic drug in global, 2018-2035E

Market size of generic drug in global

CAGR	2018-23	2023-35E
Generic drugs	2.7%	1.8%

USD billion

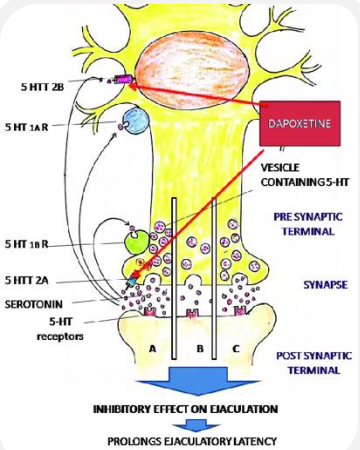


Source: WHO, China Insights Consultancy

Table of contents

Mechanism of dapoxetine hydrochloride

Mechanism of dapoxetine hydrochloride



- Dapoxetine hydrochloride is a selective serotonin reuptake inhibitor (SSRI) that inhibits the serotonin transporter (SERT), effectively reducing presynaptic reuptake of serotonin (5-hydroxytryptamine, 5-HT). This pharmacological action increases the concentration of 5-HT in the synaptic cleft, facilitating the activation of 5-HT2C and 5-HT1A receptors on the postsynaptic membrane. Consequently, it prolongs the latency of pudendal motor neuron reflexes and increases intravaginal ejaculatory latency time (IELT)
- Male ejaculation is a reflexive activity orchestrated by an intricate interaction between the central nervous system (CNS) and spinal networks. This process integrates sensory receptors, central motor pathways, and spinal reflex arcs. Among the neurotransmitters involved, 5-HT and dopamine, along with their respective receptor subtypes, play pivotal roles in the modulation of ejaculatory control
- Dapoxetine hydrochloride, as a member of the SSRI class, predominantly exists in its ionic form under physiological conditions, which supports its rapid systemic distribution. Compared to other SSRIs, dapoxetine exhibits distinctive pharmacokinetic advantages, including high safety and tolerability, a rapid time to peak plasma concentration, and a notably short elimination half-life. These attributes make it particularly suitable for on-demand use in the management of premature ejaculation

Efficacy and safety

- Dapoxetine has a rapid time to peak concentration (Tmax of 1–2 hours) and a short half-life (95% eliminated within 24 hours), making it suitable for on-demand treatment of premature ejaculation (PE). As a short-acting SSRI with quick onset, acceptable safety, and tolerability, dapoxetine has been approved for the on-demand treatment of PE in multiple countries and regions worldwide. It is the first and currently the only oral medication approved in China for the treatment of PE
- The efficacy and safety of dapoxetine have been demonstrated in Phase III clinical trials involving 6,081 participants. The studies showed that dapoxetine doses of 30 mg and 60 mg extended intravaginal ejaculatory latency time (IELT) by 2.5- and 3.0-fold, respectively, with significant improvements in PE symptoms and related parameters. In patients with a baseline IELT of less than 0.5 minutes, IELT increased by 3.5–4.3 times. The incidence rates of adverse events for dapoxetine at doses of 30 mg or 60 mg were as follows: nausea (17.3%), dizziness (9.4%), headache (7.9%), diarrhea (5.9%), drowsiness (3.9%), fatigue (3.9%), and insomnia (3.8%)

Sources: International Journal of Reproductive BioMedicine, China Insights Consultancy

Indication of dapoxetine hydrochloride and epidemiology of PE

Indication of dapoxetine hydrochloride and epidemiology of PE

- Dapoxetine hydrochloride is indicated for the treatment of PE symptoms in men aged 18 to 64 years. PE is a common male sexual dysfunction characterized clinically by factors such as IELT, control over ejaculation, sexual satisfaction, and partner relationship issues. However, due to a lack of evidence-based definitions, consensus among academic institutions remains difficult to achieve. According to the *2022 Guidelines for the Diagnosis and Treatment of Premature Ejaculation* by the Chinese Urological Association, PE is defined by three key elements:
    1. A short intravaginal ejaculatory latency time (IELT)
    2. A lack of control over ejaculation
    3. Distress and interpersonal difficulties caused by the above factors for the patient and/or their sexual partner

Category	Primary PE	Secondary PE	Natural Variable PE	Subjective PE
IELT	Around 1 minute	Short (<3 minutes)	Short to normal	Normal to extended
Symptoms	Persistent	Newly developed, associated with specific known diseases; previously normal IELT	Inconsistent	Subjective feeling of short IELT despite normal time
Etiology	Biogenic and genetic factors	Medical or psychological factors	Psychological	Psychological
Treatment	Pharmacological and psychological	Pharmacological and psychological	Psychological education	Psychological consultation or no medication needed
Prevalence	Low	Low	High	High

Epidemiology

- **The prevalence of PE in the general population is approximately 20%-30%.** Variability in definitions and standards across studies, as well as cultural differences and the sensitivity of the condition due to personal privacy concerns, contribute to inconsistencies in reported prevalence. Research on primary and secondary PE in the general population is limited, and prevalence estimates fluctuate significantly across epidemiological studies. Based on data from two studies on IELT in general male populations in five countries (the United States, the United Kingdom, Turkey, the Netherlands, and Spain) and the ISSM definition of PE, the prevalence of primary PE, characterized by an IELT of approximately one minute, is estimated to be no more than 4% of the general population

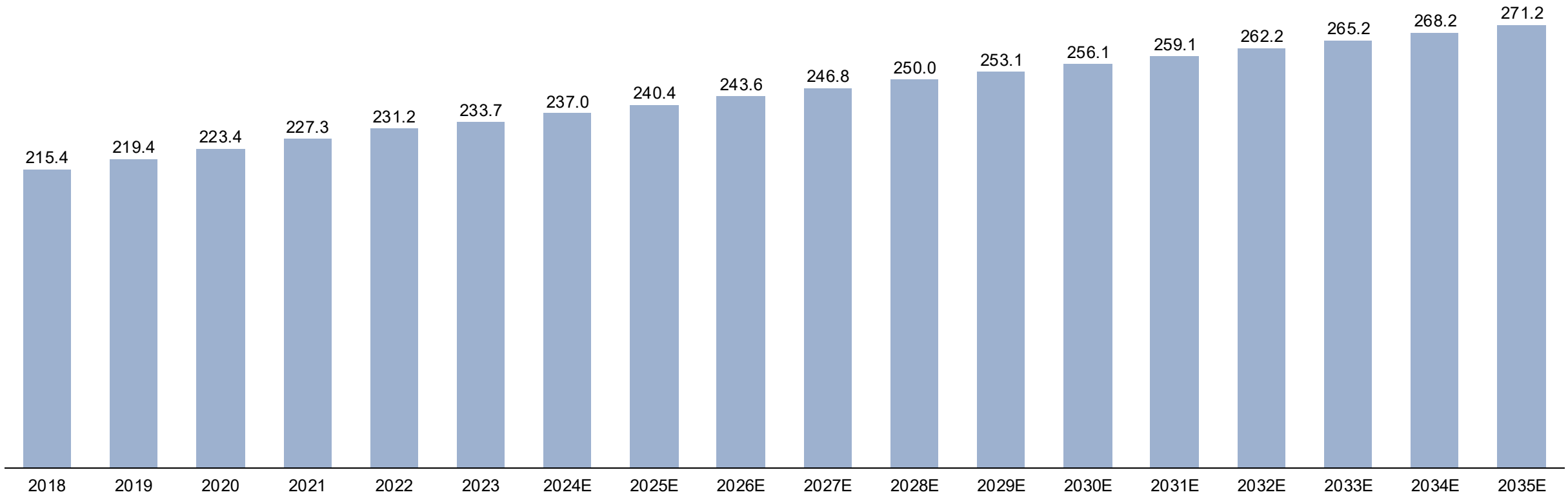
Sources: National Journal of Andrology, China Insights Consultancy

Prevalence of PE in China, 2018-2035E

Prevalence of PE in China

CAGR	2018-23	2023-35E
PE	1.6%	1.2%

ppl million



Sources: National Journal of Andrology, China Insights Consultancy

Treatment pathway of PE

Treatment pathway of PE

- The treatment of PE is categorized into three main approaches: pharmacological therapy, behavioral therapy, and sexological psychological interventions. Due to the complexity of PE's etiology and symptoms, pharmacological therapy often requires combination with psychological and behavioral interventions for comprehensive improvement. For patients with PE, it is recommended to prioritize or simultaneously address erectile dysfunction (ED), other sexual dysfunctions, or urogenital infections (such as prostatitis). **Dapoxetine and local anesthetics are considered first-line treatment options**

Treatment Method	Medications/Methods	Mechanism of Action
Pharmacological Therapy	• Dapoxetine • Phosphodiesterase type 5 inhibitors (PDE5i) • α1-adrenergic receptor blockers • Tramadol	• Regulate receptor activity, inhibit neural impulses, and reduce sensitivity
	• Local anesthetics	• Provide local anesthesia to decrease penile sensitivity and delay climax time
Behavioral Therapy	• "Start-stop" method • "Squeeze" method	• Use physical methods to reduce PE severity and prolong IELT
Psychological Interventions	• Proper education, encouraging communication, reducing anxiety, and psychological counseling	• Address psychological issues, promote a correct attitude, and alleviate anxiety
Traditional Chinese Medicine	• Jin Suo Gu Jing Wan (金锁固精丸) • Tian Wang Bu Xin Dan (天王补心丹) • Acupuncture • Topical herbal applications	• Focus on nourishing yin, tonifying deficiencies (滋阴补虚), and regulating body functions
Surgical Therapy	• Selective dorsal penile nerve denervation surgery	• Permanently reduces penile sensitivity. Irreversible and lacks robust evidence from clinical studies

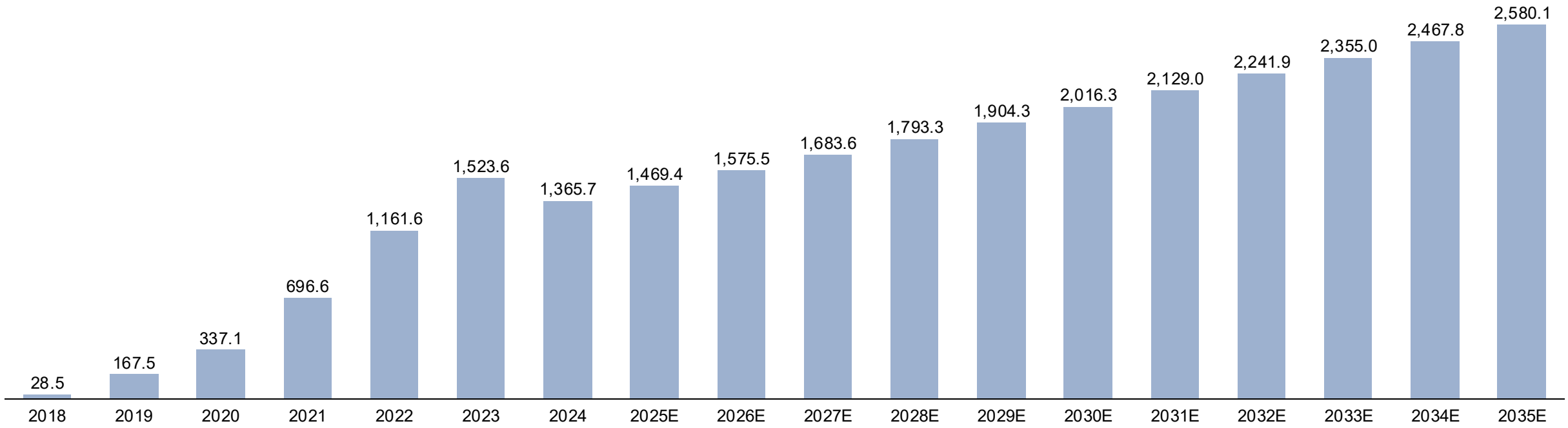
Sources: National Journal of Andrology, China Insights Consultancy

Market size of dapoxetine hydrochloride in China, 2018-2035E

Market size of dapoxetine hydrochloride in China

CAGR	2018-24	2024-35E
Dapoxetine hydrochloride	90.5%	6.0%

RMB million

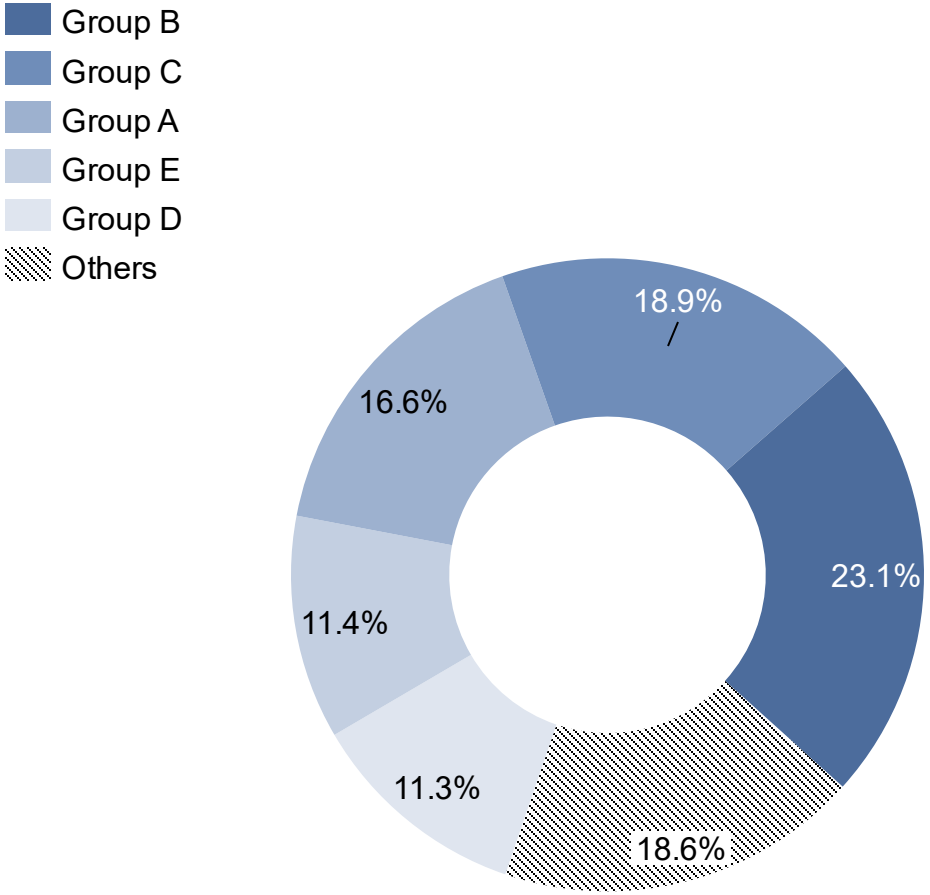


The sales declined primarily due to the implementation of national volume-based procurement, which led to steep price cuts and intensified competition from domestic generics, compressing end-market volume and profit margins. As patient awareness and treatment rates for premature ejaculation improve, combination therapies and telehealth channels expand, heightened health consciousness, and broader insurance coverage, demand for Dapoxetine hydrochloride is expected to rebound.

Sources: China Insights Consultancy

Competitive landscape of dapoxetine hydrochloride in China, by sales, 2024

Competitive landscape of dapoxetine hydrochloride in China



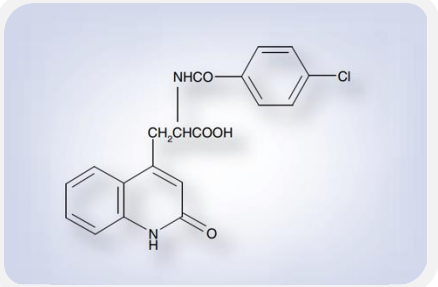
Ranking	Company	Market share
1	Group B	23.1%
2	Group C	18.9%
3	Group A	16.6%
4	Group E	11.4%
5	Group D	11.3%
Others		**18.7%**
Total		**100%**

Sources: China Insights Consultancy

Table of contents

Mechanism of rebamipide

Mechanism of rebamipide



- Rebamipide, a gastroprotective drug, was developed in Japan and was proven to be superior to cetraxate, the former most prescribed drug of the same category, in 1989 in the treatment for gastric ulcers. The initially discovered basic mechanisms of action of rebamipide included its action as a prostaglandin inducer and oxygen free-radical scavenger
- Several basic and clinical studies have been performed for functional dyspepsia, chronic gastritis, NSAID-induced gastrointestinal injuries, gastric ulcer following eradication therapy for Helicobacter pylori, gastric ulcer after endoscopic surgery and ulcerative colitis. In addition, several molecules have been identified as therapeutic targets of rebamipide to explain its pleiotropic pharmacological actions.

Mechanisms of action

- The precise mechanism of rebamipide for the prevention of gastropathy and the acceleration of gastric ulcer healing is still unknown. However, rebamipide has been shown to increase gastric mucosal prostaglandins, inhibit the production of the superoxide anion radical and scavenge the hydroxyl radical, suppress the production of inflammatory cytokines and reduce gastric mucosal inflammatory cell infiltration
- Recent animal studies suggest that rebamipide has pleiotropic actions, such as promoting restoration of Sonic hedgehog expression, normalizing MAPK signaling, counteracting the downregulation of bFGF and keeping the epithelial tight junction complex in the gastric mucosa

Pharmacokinetic properties

- Rebamipide is rapidly absorbed with a peak plasma level of 216 ng/ml in 2.4 h and eliminated with half-life of 1.9 h
- Gastrointestinal distribution is much higher than distribution to the other organs. The majority of rebamipide is excreted in an unchanged form. Approximately 10% of the administered dose is excreted in urine and the remainder is found in feces
- High concentrations of rebamipide (0.5 mM) do not affect various cytochrome P450 subtype-mediated drug metabolism. Little or no drug–drug interaction is observed

Clinical efficacy

- Rebamipide promotes gastric ulcer healing following 1 week of eradication therapy
- The combination of proton pump inhibitors plus rebamipide is more effective than the proton pump inhibitor alone for treating ulcers larger than 20 mm with 4 weeks after endoscopic submucosal dissection
- Further clinical studies are required to prove the beneficial effect on the treatment of functional dyspepsia
- Additional indication of rebamipide enema for the treatment of ulcerative colitis is expected

Sources: Expert Rev., China Insights Consultancy

Indication of rebamipide and epidemiology of gastrointestinal diseases

Indication of rebamipide and epidemiology of gastrointestinal diseases

- Rebamipide is clinically used to treat various gastrointestinal diseases such as peptic ulcer disease (PUD) , gastritis, and H. pylori infection

Peptic ulcer disease:

- PUD is defined as a localized defect in the gastric or duodenal mucosa that extends through the muscularis mucosae, typically caused by an imbalance between mucosal defensive factors and aggressive factors such as gastric acid and pepsin. It is commonly associated with Helicobacter pylori infection and the use of nonsteroidal anti-inflammatory drugs (NSAIDs)

Epidemiology

- In 2019, the global prevalence of PUD was approximately 8.09 million, representing a 25.82% increase from 1990
- In a questionnaire survey conducted in Shanghai in 2021, a total of 1,108 participants were enrolled. Endoscopic diagnosis revealed a peptic ulcer prevalence of 9.1%, including 5.8% with duodenal ulcers, 2.5% with gastric ulcers, and 0.8% with combined ulcers

Gastritis:

- Gastritis refers to inflammation of the gastric mucosa caused by various etiologies, characterized histologically by tissue-level inflammation. Gastritis can be classified into acute gastritis and chronic gastritis. Chronic gastritis is a common clinical condition involving chronic inflammation of the gastric mucosa caused by multiple factors, with H. pylori infection being the primary etiology

Epidemiology

- The incidence of gastritis and chronic gastritis in China is approximately 85% and 30%, respectively
- Among these, chronic atrophic gastritis (CAG) is the most common form of chronic gastric mucosal inflammation. CAG is often defined as a precancerous condition, and research generally considers gastritis to be the starting point for gastric cancer development. A nationwide multicenter study in China showed that CAG accounts for 25.8% of gastritis cases

- The occurrence of gastritis and PUD is closely associated with H. pylori infection, which is particularly recognized as the primary cause of CAG. H. pylori has been classified as a Group I carcinogen for its role in promoting the progression from CAG to gastric cancer. In China, the prevalence of H. pylori infection is as high as 50%, and approximately 42% of the cancer burden attributable to infections is linked to H. pylori

Sources: Chin J Gen Pract, Chin J Dig, Global Cancer Burden Data, China Insights Consultancy

Treatment pathway of PUD and gastritis

Treatment pathway of PUD and gastritis

- **The primary treatment approach is pharmacotherapy.** Dietary and lifestyle adjustments are also essential components of PUD and chronic gastritis treatment
  - **For PUD,** The treatment goals are to remove the underlying cause (eradicate H. pylori, discontinue aspirin or other NSAIDs if possible, quit smoking, etc.), eliminate symptoms, heal the ulcer, prevent ulcer recurrence, and avoid complications
  - **For chronic gastritis**, the treatment goals are to eliminate the underlying cause, alleviate symptoms, improve gastric mucosal histology, enhance quality of life, and prevent relapse and complications

Primary treatment for PUD

Treatment Type	Method	
Pharmacotherapy	• Inhibition of gastric acid secretion	• The main gastric acid secretion inhibitors are PPIs and H2-RAs. PPIs are more potent and longer-lasting, making them the first-choice treatment for peptic ulcers
	• Mucosal protective treatment	• Gastric mucosal protectants, including weak antacids and bismuth agents, can quickly relieve symptoms and improve ulcer healing when added to acid secretion inhibitors
Eradication of H. pylori	• Bismuth quadruple therapy: Proton pump inhibitor (PPI) + bismuth agent + two antimicrobial agents	
NSAID-induced ulcers Treatment	• If use is necessary, NSAIDs that are less damaging to the gastrointestinal mucosa should be chosen, or highly selective COX-2 inhibitors should be used to reduce adverse effects	

Primary treatment for chronic gastritis

Treatment Type	Method	
Etiological Treatment	• H. pylori-positive chronic gastritis	• Bismuth quadruple therapy: Proton pump inhibitor (PPI) + bismuth agent + two antimicrobial agents
	• Chronic gastritis with bile reflux	• Prokinetic drugs: Domperidone, mosapride, etc. • Aluminum magnesium carbonate combined with bile acids • Ursodeoxycholic acid
	• Drug-induced chronic gastritis	• First-line PPI: Omeprazole, lansoprazole, pantoprazole, etc. • H2 receptor antagonists (H2RA) • Mucosal protectants
Symptomatic Treatment	• Depending on the condition and severity of symptoms, PPI or H2RA, antacids, and gastric mucosal protectants are used	
Chinese Medicine Treatments	• Moxibustion combined with acupuncture to alleviate symptoms in patients with spleen and stomach deficiency-cold syndrome	

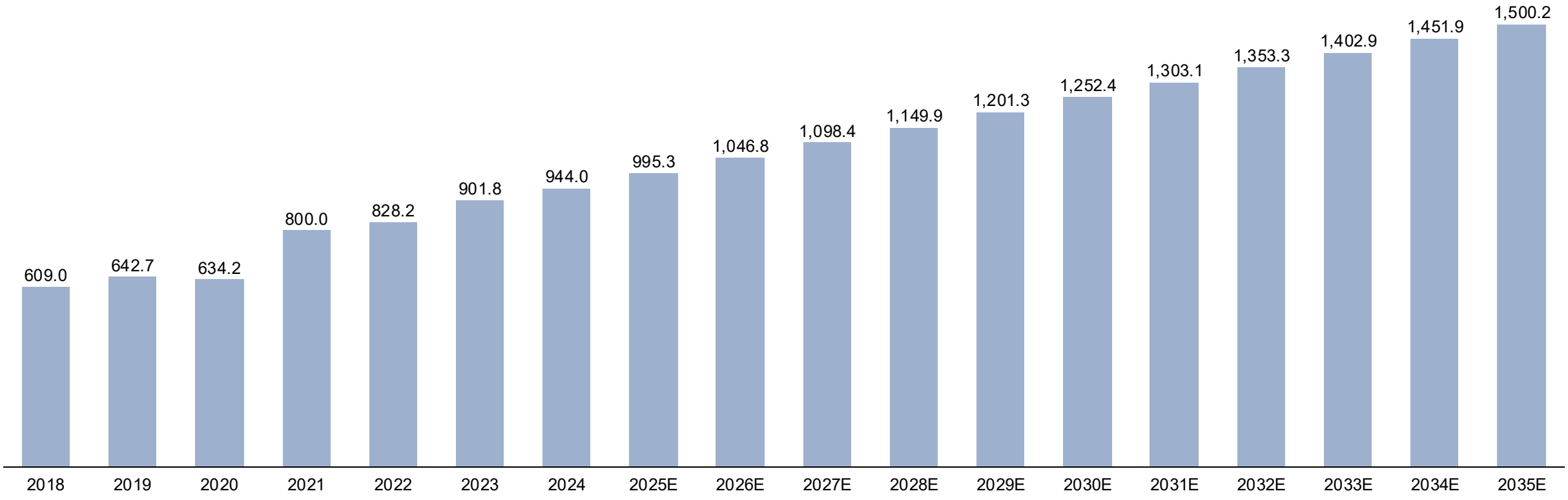
Sources: Chinese Journal of General Practitioners, Chin J Gen Pract, Chin J Dig, China Insights Consultancy

Market size of rebamipide in China, 2018-2035E

Market size of rebamipide in China

CAGR	2018-24	2024-35E
Rebamipide	7.6%	4.3%

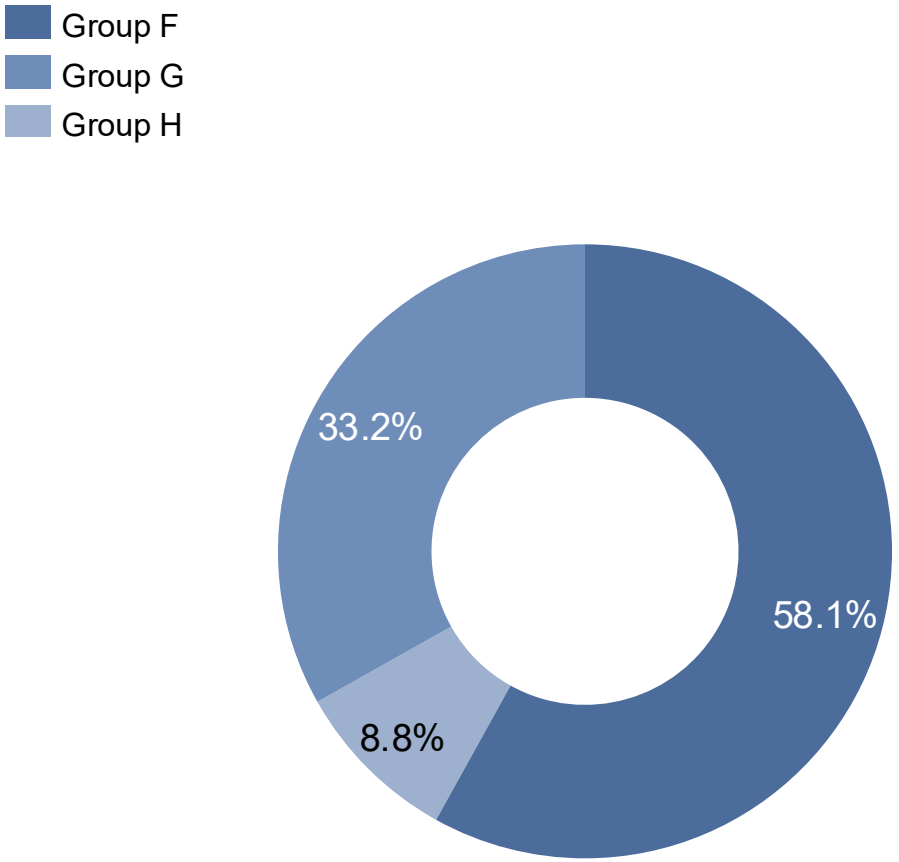
RMB million



Sources: China Insights Consultancy

Competitive landscape of rebamipide in China, by sales, 2024

Competitive landscape of rebamipide in China



Ranking	Company	Market share
1	Group F	58.1%
2	Group G	33.2%
3	Group H	8.7%
Others		
Total		**100%**

Sources: China Insights Consultancy

Industry Overview section – Competitive landscape and portfolio coverage

Company/Competitors	Redacted name	Scope of business
Shandong Hubble Kisen Biological Technology Co., Ltd.	Group A	the research and development, production and sales of anti-tumor drugs, cardiovascular and cerebrovascular drugs, diabetes drugs, dermatology drugs, gynecological disease drugs, and biological drugs
BERLIN-CHEMIE AG	Group B	the production and sale of high-quality pharmaceutical products, mainly in the fields of gastroenterology, pain management, cardiovascular diseases, biologics and oncology
Sichuan Kelun Pharmaceutical Co., Ltd.	Group C	the research and development, production and sales of products, mainly in anesthesia and analgesia, central nervous system, anti-infection, parenteral nutrition and other fields
Jiangsu Lianhuan Pharmaceutical Group Co., Ltd.	Group D	the production and sale of tablets, hard capsules, granules, suppositories, and APIs, mainly in the fields of urinary system, antihistamines, cardiovascular, steroid hormones and antibiotics
Henan Tianfang Pharmaceuticals Group Co.	Group E	the production, sales and pharmaceutical operation of finished preparations, chemical synthesis APIs and biological fermentation APIs, mainly in antibiotics, cardiovascular and cerebrovascular diseases, diabetes and other fields
Zhejiang Yuanlijian Pharmaceutical Co., Ltd.	Group F	the R&D, production and sale of drugs in digestion field
Otsuka Holdings Co., Ltd.	Group G	the R&D, production and sale of nutraceuticals (nutrition and pharmaceuticals) and cosmedics (cosmetics and medicine)
Chongqing Shenghuaxi Pharmaceutical Co. Ltd.	Group H	the R&D, production and sale of APIs and pharmaceutical preparations, mainly in cardiovascular, nervous system, anti-infection and other categories

Sources: China Insights Consultancy

- Antiviral. Viral diseases are one of the major threats to human health and have imposed a substantial burden on the global economy. In recent years, climate change and globalization have accelerated the spread of viruses. Since the establishment of the “Public Health Emergency of International Concern” pursuant to the “International Health Regulations” in 2005, the World Health Organization has declared seven virus outbreak-related international public health emergencies and issued warnings about the potential for more severe global pandemics caused by viral infections in the future. The prevention and control of viral diseases has become a key focus in the global healthcare industry. However, for many viral diseases with significant public health burdens, there are a limited number of, and in some cases, no available vaccines or antiviral drugs, resulting in significant unmet need. Meanwhile, the ongoing emergence of new viruses and variants has underscored urgent needs for more adaptable broad-spectrum therapies.

Industry Regulatory Authorities, Regulatory Framework, Industry Development Trends, and Major Legal and Policy Impacts on Business Development

Industry Classification and Basis for Determination

The company is primarily engaged in the research, development, production, and sales of pharmaceuticals. According to the "National Economic Industry Classification (GB/T4754-2017)" issued by the National Bureau of Statistics, the company falls under the pharmaceutical manufacturing industry, specifically "Chemical Pharmaceutical Preparation Manufacturing" (C2720). Furthermore, based on the "Strategic Emerging Industry Classification (2018)" (Order No. 23 of the National Bureau of Statistics), the company's industry segment is classified under 4.1 Biopharmaceutical Industry, specifically 4.1.2 "Chemical Pharmaceutical and Active Pharmaceutical Ingredient Manufacturing."

Regulatory Authorities Governing the Pharmaceutical Industry

Administration	Authorities
National Medical Products Administration (NMPA)	Responsible for the safety supervision and management of pharmaceuticals (including traditional Chinese medicine and ethnic medicine), medical devices, and cosmetics; management of pharmaceutical, medical device, and cosmetic standards; registration and quality control of pharmaceuticals; post-market risk management; professional qualification management of licensed pharmacists; organization and supervision of inspections; international cooperation and participation in global regulatory standards; and guidance to provincial, autonomous region, and municipal regulatory departments. The agency also implements directives from the central government.
National Healthcare Security Administration (NHSA)	Formulates legal drafts, policies, and standards related to medical insurance, maternity insurance, and medical assistance; oversees the implementation of healthcare security funds supervision mechanisms; reforms healthcare payment methods; formulates policies related to medical financing and benefits; establishes drug, consumables, and medical service payment standards; supervises and regulates medical service prices and procurement policies; manages contracted medical institutions and ensures compliance with insurance-covered services.
National Health Commission (NHC)	Responsible for drafting health-related policies, laws, and development plans; overseeing public health and disease prevention strategies; establishing national essential medicine policies and shortage warnings; supervising medical institutions and healthcare services; managing national immunization programs; guiding elderly healthcare services; and collaborating with traditional Chinese medicine management.

Sources: China Insights Consultancy

序号	监管制度	主要内容
新药相关法律法规与监管体制		
1	非临床研究	根据《药品注册管理办法（2020）》，药物非临床安全性评价研究应当在经过药物非临床研究质量管理规范（GLP）认证的机构开展，并遵守药物非临床研究质量管理规范。
2	临床试验申请	根据《药品注册管理办法（2020）》规定，药物临床试验应当经批准。申请人完成支持药物临床试验的药学、药理毒理学等临床前研究后，提出药物临床试验申请的，应当按照申报资料要求提交相关研究资料。国家药品监督管理局药品审评中心应当组织药学、医学和其他技术人员对已受理的药物临床试验申请进行审评。对药物临床试验申请应当自受理之日起六十日内决定是否同意开展，并通过国家药品审评中心网站通知申请人审批结果；逾期未通知的，视为同意，申请人可以按照提交的方案开展药物临床试验。
3	临床试验	药物临床试验是指以药品上市注册为目的，为确定药物安全性与有效性在人体开展的药物研究。药物临床试验分为Ⅰ期临床试验、Ⅱ期临床试验、Ⅲ期临床试验、Ⅳ期临床试验以及生物等效性试验等。根据药物特点和研究目的，研究内容包括临床药理学研究、探索性临床试验、确证性临床试验和上市后研究。
4	药物临床试验质量管理	《药物临床试验质量管理规范（2020修订）》（GCP）旨在保证药物临床试验过程规范，数据和结果的科学、真实、可靠，以及保护受试者的权益和安全。GCP是药物临床全过程的质量标准，包括方案设计、组织实施、监查、稽查、记录、分析、总结和报告。
5	药品审评审批制度	根据《药品注册管理办法（2020）》规定，药品注册申请人在完成支持药品上市注册的药学、药理毒理学和药物临床试验等研究，确定质量标准，完成商业规模生产工艺验证，并做好接受药品注册核查检验的准备后，提出药品上市许可申请，按照申报资料要求提交相关研究资料。药品审评中心应当组织药学、医学和其他技术人员，按要求对已受理的药品上市许可申请进行审评。《药品注册管理办法（2020）》支持以临床价值为导向的药物创新，设立突破性治疗药物、附条件批准、优先审评审批、特别审批四个加快上市注册程序，明确审评时限，提高药品注册效率和注册时限的预期性。
6	上市许可持有人制度	《中华人民共和国药品管理法（2019修订）》规定国家对药品管理实行药品上市许可持有人制度。药品上市许可持有人依法对药品研制、生产、经营、使用全过程中药品的安全性、有效性和质量可控性负责。药品上市许可持有人是指取得药品注册证书的企业或者药品研制机构等。药品上市许可持有人应当依照法律规定，对药品的非临床研究、临床试验、生产经营、上市后研究、不良反应监测及报告与处理等承担责任。
7	临床指导原则	国家药品监督管理局药品审评中心下发的《以临床价值为导向的抗肿瘤药物临床研发指导原则》（下称“指导原则”），指导原则从患者需求的角度出发，对抗肿瘤药物的临床研发提出建议，以期指导申请人在研发过程中，落实以临床价值为导向，以患者为核心的研发理念。
基本医疗保险相关法律法规与监管体制		
8	基本医疗保险制度	国务院于2016年1月3日颁布并施行《关于整合城乡居民基本医疗保险制度的意见》，目的在于推进整合城镇居民基本医疗保险和新型农村合作医疗，逐步在全国范围内建立起统一的城乡居民医保制度。城乡居民医保制度覆盖范围包括现有城镇居民基本医疗保险和新型农村合作医疗所有应参保（合）人员，即覆盖除职工基本医疗保险应参保人员以外的其他所有城乡居民。
9	基本医疗保险药品目录	2018年3月，十三届全国人大一次会议表决通过了关于国务院机构改革方案的决定，组建国家医保局。2020年7月30日，国家医保局颁布并于2020年9月1日起施行《基本医疗保险用药管理暂行办法》，根据该暂行办法规定基本医疗保险用药范围通过制定《基本医疗保险药品目录》进行管理，符合《基本医疗保险药品目录》的药品费用，按照国家规定由基本医疗保险基金支付。
药品生产企业相关法律及监管体制		
10	药品生产许可制度	《中华人民共和国药品管理法（2019修订）》规定，国内对药品生产企业实行行业准入许可制度，在国内开办药品生产企业，从事药品生产活动，应当经所在地省、自治区、直辖市人民政府药品监督管理部门批准，取得药品生产许可证。无药品生产许可证的，不得生产药品。药品生产许可证应当标明有效期和生产范围，到期重新审查发证。
11	药品生产质量管理规范	根据现行有效的《中华人民共和国药品管理法（2019修订）》，从事药品生产活动，应当遵守药品生产质量管理规范，建立健全药品生产质量管理体系，保证药品生产全过程持续符合法定要求。《药品生产监督管理办法（2020）》不再要求药品生产企业取得GMP认证，但省、自治区、直辖市药品监督管理部门根据监管需要，对持有药品生产许可证的药品上市许可申请人及其受托生产企业，按法定要求进行上市前的药品生产质量管理规范符合性检查。
12	药品委托生产制度	《中华人民共和国药品管理法（2019修订）》明确了药品上市许可持有人自行生产药品的，应当依法取得药品生产许可证；委托生产药品，应当委托符合条件的药品生产企业。此外，《药品生产监督管理办法（2020）》进一步明确受托生产企业不得将接受委托生产的药品再次委托第三方生产以及经批准或者通过关联审评审批的原料药不得再行委托生产。
药品知识产权保护相关法律及监管体制		
13	药品知识产权保护制度	根据《中华人民共和国专利法（2020修订）》，发明专利权的期限为二十年，实用新型专利权的期限为十年，外观设计专利权的期限为十五年，均自申请日起计算。发明专利权的期限为二十年，为补偿新药上市审评审批占用的时间，对在中国获得上市许可的新药相关发明专利，国务院专利行政部门应专利权人的请求给予专利权期限补偿，补偿期限不超过五年，新药批准上市后总有效专利权期限不超过十四年。

Sources: China Insights Consultancy

领域	主要法律法规内容	
新药研制相关环节	基本指导原则	根据《中华人民共和国药品管理法》规定，国家支持以临床价值为导向、对人的疾病具有明确或者特殊疗效的药物创新，鼓励具有新的治疗机理、治疗严重危及生命的疾病或者罕见病、对人体具有多靶向系统性调节干预功能等的新药研制，推动药品技术进步。根据《药品注册管理办法》规定，国家药品监督管理局建立药品加快上市注册制度，支持以临床价值为导向的药物创新。
	非临床研究及其质量管理	根据《中华人民共和国药品管理法》规定，开展药物非临床研究，应当符合国家有关规定，有与研究项目相适应的人员、场地、设备、仪器和管理制度，保证有关数据、资料和样品的真实性。根据《药品注册管理办法》规定，药物非临床安全性评价研究应当在经过药物非临床研究质量管理规范认证的机构开展，并遵守药物非临床研究质量管理规范。
	临床试验申请	根据《中华人民共和国药品管理法》规定，开展药物临床试验，应当经国务院药品监督管理部门批准。国务院药品监督管理部门应当自受理临床试验申请之日起六十个工作日内决定是否同意并通知临床试验申办者，逾期未通知的，视为同意。
	临床试验及其质量管理	根据《中华人民共和国药品管理法》规定，从事药品研制活动，应当遵守药物临床试验质量管理规范。开展药物临床试验，应当在经备案的且具备相应条件的临床试验机构进行。
仿制药研发	一致性评价	根据《关于开展仿制药质量和疗效一致性评价的意见》等规定，化学药品新注册分类实施前批准上市的仿制药，凡未按照与原研药品质量和疗效一致原则审批的，均须开展一致性评价。 化学药品新注册分类实施前批准上市的含基本药物品种在内的仿制药，自首家品种通过一致性评价后，其他药品生产企业的相同品种原则上应在3年内完成一致性评价。逾期未完成的，企业经评估认为属于临床必需、市场短缺品种的，可向所在地省级药品监管部门提出延期评价申请，经省级药品监管部门会同卫生行政部门组织研究认定后，可予适当延期。逾期再未完成的，不予再注册。
药品注册	药品审评审批制度	根据《中华人民共和国药品管理法》规定，对申请注册的药品，国务院药品监督管理部门应当组织药学、医学和其他技术人员进行审评，对药品的安全性、有效性和质量可控性以及申请人的质量管理、风险防控和责任赔偿等能力进行审查；符合条件的，颁发药品注册证书。根据《药品注册管理办法》规定，对药品上市许可申请审评的工作由药品审评中心组织药学、医学和其他技术人员开展。国家药品监督管理局持续推进审评审批制度改革，优化审评审批程序，提高审评审批效率。支持以临床价值为导向的药物创新，设立突破性治疗药物、附条件批准、优先审评审批、特别审批四个加快上市注册程序，明确审评时限，提高药品注册效率和注册时限的预期性。
	上市许可持有人制度	根据《中华人民共和国药品管理法》规定，国家对药品管理实行药品上市许可持有人制度。药品上市许可持有人依法对药品研制、生产、经营、使用全过程中药品的安全性、有效性和质量可控性负责。药品上市许可持有人是指取得药品注册证书的企业或者药品研制机构等。药品上市许可持有人应当依照法律规定，对药品的非临床研究、临床试验、生产经营、上市后研究、不良反应监测及报告与处理等承担责任。
药品生产相关环节	药品生产许可制度	根据《中华人民共和国药品管理法》规定，从事药品生产活动应当经所在地省、自治区、直辖市人民政府药品监督管理部门批准，取得药品生产许可证。无药品生产许可证的，不得生产药品。药品生产许可证应当标明有效期和生产范围，到期重新审查发证。
	药品生产及质量管理制度	根据《中华人民共和国药品管理法》，从事药品生产活动，应当遵守药品生产质量管理规范，建立健全药品生产质量管理体系，保证药品生产全过程持续符合法定要求。《中华人民共和国药品管理法》、《药品生产监督管理办法》和《药品生产质量管理规范》对企业从事药品生产活动应当具备的条件及满足的标准提出了明确要求。
	药品生产监督管理办法	根据《药品生产监督管理办法》规定，省、自治区、直辖市药品监督管理部门根据监管需要，对持有药品生产许可证的药品上市许可申请人及其受托生产企业，按法定要求进行上市前的药品生产质量管理规范符合性检查。省、自治区、直辖市药品监督管理部门应当坚持风险管理、全程管控原则，根据风险研判情况，制定年度检查计划并开展监督检查。
药品知识产权保护	药品知识产权保护制度	根据《中华人民共和国专利法》，发明专利权的期限为二十年，为补偿新药上市审评审批占用的时间，对在中国获得上市许可的新药相关发明专利，国务院专利行政部门应专利权人的请求给予专利权期限补偿，补偿期限不超过五年，新药批准上市后总有效专利权期限不超过十四年。
基本医疗保险	基本医疗保险药品目录	2020年7月30日，国家医疗保障局颁布并于2020年9月1日起施行《基本医疗保险用药管理暂行办法》，根据该暂行办法规定基本医疗保险用药范围通过制定《基本医疗保险药品目录》进行管理，符合《基本医疗保险药品目录》的药品费用，按照国家规定由基本医疗保险基金支付。

Sources: China Insights Consultancy

序号	产业政策名称	发布单位	发布时间	主要政策内容
1	《关于深化医药卫生体制改革的意见》	国务院	2009.03	建立全国普及的医疗保健体制，为居民提供安全、有效、便利和负担得起的医疗保健服务。到2020年，覆盖城乡居民的基本医疗卫生制度。
2	《关于加快医药行业结构调整的指导意见》	工业和信息化部、原卫生部、原国家食品药品监督管理局	2010.10	鼓励医药企业技术创新，加大对医药研发的投入，鼓励开展基础性研究和开发共性、关键性以及前沿性重大医药研发课题。支持企业加强技术中心建设，通过产学研整合技术资源，推动企业成为技术创新的主体。
3	《国务院关于加快培育和发展战略性新兴产业的决定》	国务院	2010.10	大力发展用于重大疾病防治的生物技术药物、新型疫苗和诊断试剂、化学药物、现代中药等创新药物大品种，提升生物医药产业水平。
4	《关于深化药品审评审批改革进一步鼓励药物创新的意见》	原国家食品药品监督管理局	2013.02	提出进一步加快创新药物审评，对重大疾病具有更好治疗作用、具有自主知识产权的创新药物注册申请等，给予加快审评；调整创新药物临床试验申请的审评策略、优化创新药物审评流程、配置优质审评资源；对实行加快审评的创新药物注册申请，采取早期介入、分阶段指导等措施，加强指导和沟通交流。
5	《医药工业发展规划指南》	工业和信息化部、国家发展和改革委员会等六部委	2016.10	紧跟国际医药技术发展趋势，开展重大疾病新药的研发，重点发展针对恶性肿瘤、心脑血管疾病、糖尿病等疾病的创新药物；加快临床急需、新专利到期药物的仿制药开发，提高患者用药可及性。提高仿制药质量水平，重点结合仿制药质量和疗效一致性评价提高固体制剂生产技术和质量控制水平。
6	《关于进一步改革完善药品生产流通使用政策的若干意见》	国务院办公厅	2017.01	进一步改革完善药品生产流通使用有关政策提出如下意见：提高药品质量疗效，促进医药产业结构调整；整顿药品流通秩序，推进药品流通体制改革；规范医疗和用药行为，改革调整利益驱动机制。
7	《关于改革完善仿制药供应保障及使用政策的意见》	国务院办公厅	2018.03	促进仿制药研发，提升仿制药质量疗效，提高药品供应保障能力，更好地满足临床用药及公共卫生安全需求，加快我国由制药大国向制药强国跨越。
8	《国家组织药品集中采购和使用试点方案》	国务院办公厅	2019.01	选择北京、天津、上海、重庆和沈阳、大连、厦门、广州、深圳、成都、西安11个城市，从通过质量和疗效一致性评价的仿制药对应的通用名药品中遴选试点品种，国家组织药品集中采购和使用试点，进行带量采购，量价挂钩、以量换价，形成药品集中采购价格，试点城市公立医疗机构或其代表根据上述采购价格与生产企业签订带量购销合同。
9	《深化医药卫生体制改革2019年重点工作任务》	国务院办公厅	2019.05	完善医保药品目录动态调整机制，将基本药物目录内符合条件的治疗性药品按程序优先纳入医保目录范围。把高血压、糖尿病等门诊用药纳入医保报销。
10	《中华人民共和国国民经济和社会发展第十四个五年规划和2035年远景目标纲要》	全国人民代表大会	2021.03	推进国家组织药品和耗材集中带量采购使用改革，发展高端医疗设备。完善创新药物、疫苗、医疗器械等快速审评审批机制，加快临床急需和罕见病治疗药品、医疗器械审评审批，促进临床急需境外已上市新药和医疗器械尽快在境内上市。
11	《“十四五”医药工业发展规划》	工业和信息化部、国家发展改革委等九部委	2021.12	①加强临床急需品种开发引进。以临床需求为导向，持续更新《鼓励仿制药品目录》并完善相关配套政策，促进临床急需、专利到期药物的仿制开发。②增强易短缺药供应保障能力。以基本药物、儿童药品、急抢救药品等为重点，完善易短缺药采购支付政策，对符合条件的品种及时纳入挂网采购，调动企业生产积极性。③巩固原料药制造优势，加快发展一批市场潜力大、技术门槛高的特色原料药新品种以及核酸、多肽等新产品类型。依托原料药基础，打造“原料药+制剂”一体化优势。

Sources: China Insights Consultancy

On June 1, 2020, the newly revised Patent Law of the People's Republic of China came into effect. Article 42 of Chapter V of the new patent law introduced, for the first time at the legislative level, a patent term compensation system for new drugs. The original text states:

"If an invention patent is granted after four years from the date of application and three years from the date of the substantive examination request, the administrative department for patents under the State Council shall, at the request of the patent holder, compensate for the unreasonable delays in the patent authorization process, except for delays caused by the applicant. To compensate for the time taken for the review and approval process of new drugs, the administrative department for patents under the State Council shall, at the request of the patent holder, provide patent term compensation for invention patents related to new drugs approved for marketing in China. The compensation period shall not exceed five years, and the total effective patent term after the new drug's approval for marketing shall not exceed fourteen years."

New drug development is a challenging and lengthy process. Often, even after a patent is granted, the drug may still be in clinical trials, and a marketing application may not be submitted until ten or even twenty years later. Given that the standard patent protection period is 20 years, this situation often results in a post-market patent protection period of less than ten years. With the implementation of the revised patent law, patent holders can now apply for patent term compensation, which extends the actual protection period of drug patents, allowing pharmaceutical companies to generate more revenue and recoup their substantial R&D investments. This policy serves as a significant incentive for pharmaceutical companies to invest in new drug development, driving technological innovation in the pharmaceutical sector. For issuers in the innovative drug sector, this is a highly favorable policy that protects their rights and ensures post-market returns.

The advancement of the national regulatory framework and the improvement of the approval system have also contributed to the rapid development of the innovative drug sector in which the issuer operates. The full implementation of the "60-day implied approval system" for clinical trials shortens the review period by one-third compared to the previous 90-day review timeline. Moreover, the establishment of an accelerated drug registration process optimizes the evaluation and approval workflow. This prioritizes the review of drugs urgently needed for clinical use, such as orphan drugs, pediatric medicines, cancer treatments, major infectious disease drugs, and innovative high-end medical devices, significantly reducing review times.

Among the numerous reform measures, the Marketing Authorization Holder (MAH) system is particularly noteworthy. Previously, only pharmaceutical manufacturing companies were allowed to apply for drug registrations. Researchers and research institutions that wanted to register a drug had to invest in building their own manufacturing facilities, which tied product registration with production approval and hindered drug innovation. In 2015, China launched pilot programs for the MAH system in ten provinces and cities, allowing pharmaceutical research institutions and researchers to apply for drug registrations. This reform has reduced the financial and time burdens on drug developers, enabling new drugs to reach the market 3-5 years earlier.

In 2019, the MAH system was incorporated into the newly revised Drug Administration Law and was fully implemented nationwide. This reform greatly facilitates drug research and innovation by separating marketing authorization from production licensing. It enables drug developers to focus their resources, technology, and manpower on continuous research and development. It also clarifies and strengthens the legal responsibilities of developers throughout the entire lifecycle of drug R&D, production, distribution, and use, encouraging continuous improvement and technical advancement to ensure drug safety and quality. Furthermore, the MAH system helps address issues such as unauthorized product ownership transfers and ensures that drug developers can leverage technical transfers, contract manufacturing, and other cooperative models to improve production efficiency and foster specialization within the pharmaceutical industry.

Overall, these regulatory and review reforms serve to standardize and support the issuer’s business operations, fostering sustainable growth and innovation in the pharmaceutical sector.

Sources: China Insights Consultancy