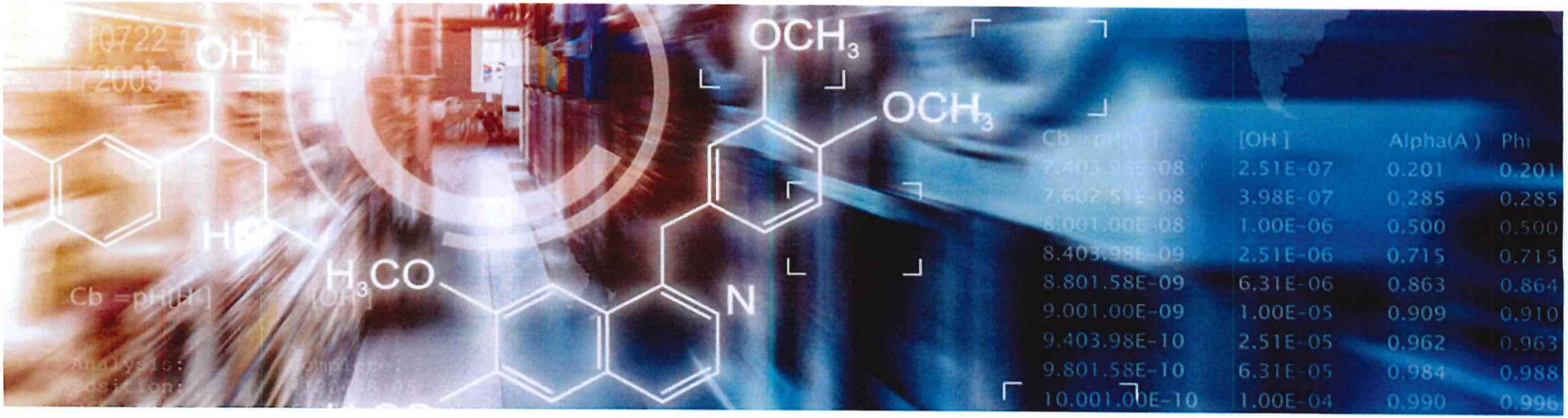

Project Neptune Industry Report on China's Innovative Drug & Generic Drug Market

For and on behalf of
China Insights Industry Consultancy Limited

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Title: Managing Director 董事总经理

Date: October 9, 2025

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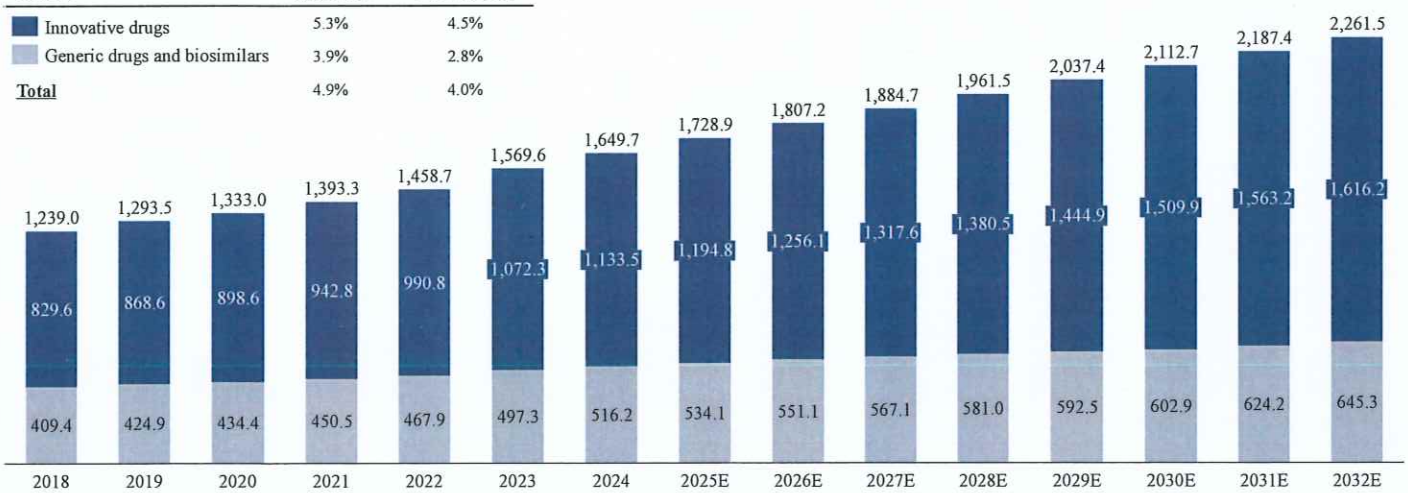
Global pharmaceutical market size, 2018-2032E

Global pharmaceutical market size, 2018-2032E

billion USD

CAGR	2018-2024	2024-2032E
Innovative drugs	5.3%	4.5%
Generic drugs and biosimilars	3.9%	2.8%
Total	4.9%	4.0%



Source: China Insights Consultancy

China's pharmaceutical market size, 2018-2032E

China's pharmaceutical market size, 2018-2032E

billion RMB

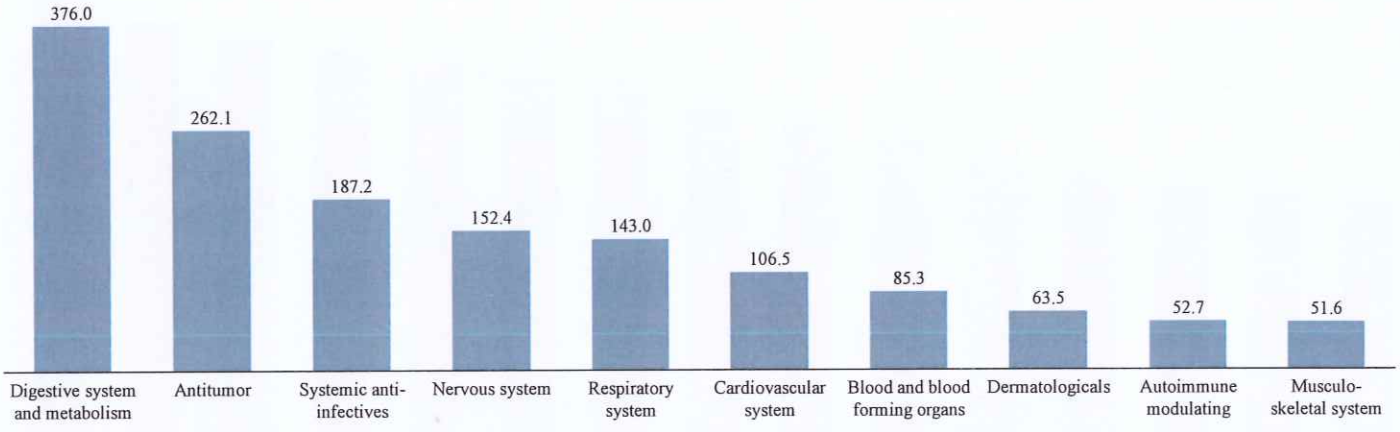
CAGR	2018-2024	2024-2032E
Innovative drugs	3.7%	8.3%
Generic drugs and biosimilars	0.4%	2.7%
Total	2.3%	6.3%

Note: the market size in 2020 and 2022 decreased due to the influence of COVID-19.

Source: China Insights Consultancy

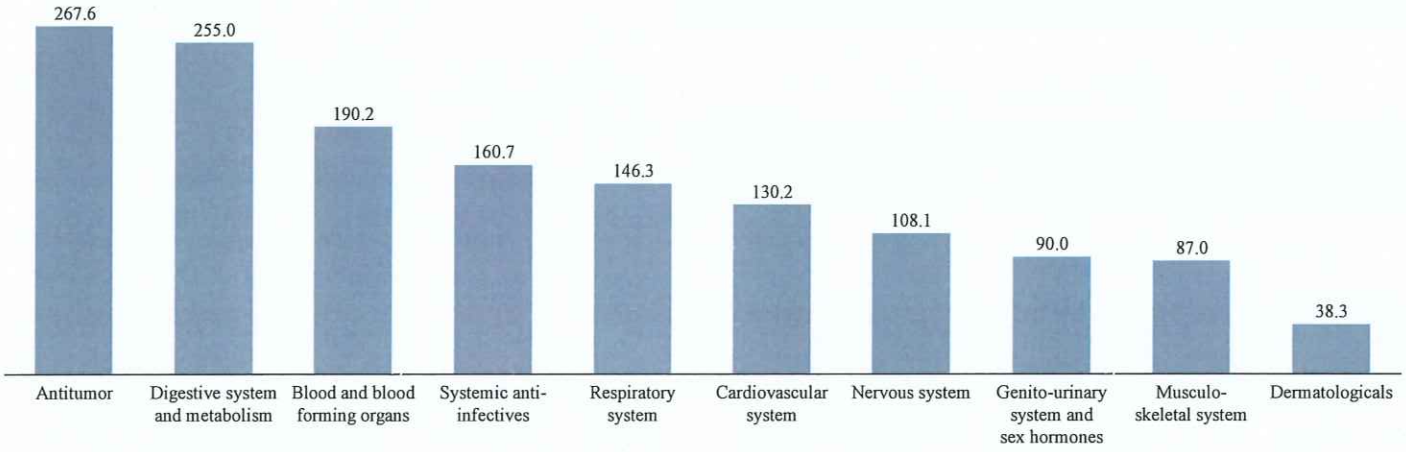
Top 10 therapeutic areas in terms of revenue globally, 2024

billion USD



Source: IMS; China Insights Consultancy

Top 10 therapeutic areas in terms of revenue in China, 2024



Source: China Insights Consultancy

Overview of drug Marketing Authorization Holder(MAH) system

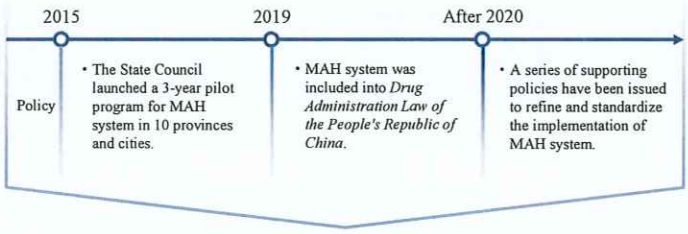
Definition:

- Drug Marketing Authorization Holder(MAH) system, refers to a system whereby entities such as drug R&D institutions, scientific researchers, and CMOs **are responsible for drug quality throughout its life cycle** if they **obtain drug marketing authorization certificates**.(*拥有药品技术的药品研发机构、科研人员、药品生产企业等主体，通过提出药品上市许可申请并获得药品上市许可批件，并对药品质量在其整个生命周期内承担主要责任的制度*)
- Under this system, the marketing authorization holder and the production authorization holder can be the same entity or two independent entities.

According to ***Measures for the Supervision and Administration of Drug Production*** since 2020, there are 4 types of marketing authorization holders:

Types of MAH	Description
A	• The holder fulfills drug production independently.
B	• The holder entrusts other qualified CMOs for drug production.
C	• The holder is entitled to commissions of other pharmaceutical companies to produce drugs.
D	• The holder produces APIs.

Development history of MAH system in China



Analysis of MAH system impact in China

01 ***Further clarifications on responsible entities to ensure drug quality***
- The regulation clarifies that the holder is legally responsible for the safety, effectiveness and quality control of the drug throughout the entire process of drug development, production, operation and use.

02 ***More encouragements on innovations of new drugs***
- The policy encourages pharmaceutical companies and individuals to invest more in new drug development. In order to maintain competitiveness, holders need to continuously upgrade and launch new products, which ensures the sustainable innovation capability.

03 ***Optimization of market resource allocation and efficiency***
- The holders can allocate resources more effectively, including the coordination of R&D, production, and sales, which helps to reduce unnecessary duplication and waste as to improve resource utilization efficiency and create synergy.

Source: gov.cn; China Insights Consultancy

Introduction of small-molecule drug registration classification

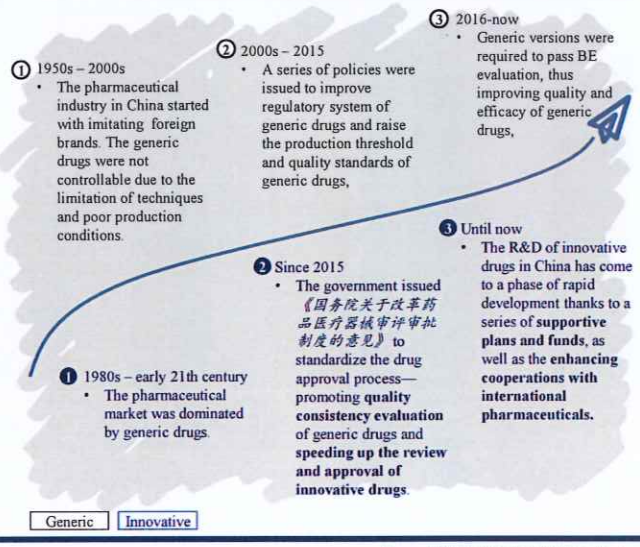
Introduction and classification:

- According to *Drug Registration Management Measure* issued by NMPA in 2020, small-molecule drugs can be classified into 5 categories, including:

Small-molecule drugs (化学药品)	Description
Category I	• Innovative drugs that **have not been marketed in China or abroad**, referring to drugs that contain **NMEs with clear structures, pharmacological effects and clinical value.**
Category II	• Improved new drugs that have been optimized in structure, dosage form, prescription process, route of administration, indications, etc based on known active ingredients.
Category III	• Domestic MAHs have a generic version over the original drug that is marketed abroad but not in China.
Category IV	• Domestic MAHs have a generic version over the original drug that is marketed in China.
Category V	• Drugs that have been marketed abroad apply for a market authorization in China(including original drugs, improved new drugs and generic drugs).

Development history:

- Both the generic drug market and the innovative drugs market in China has gone through a period of exploration, standardization and rapid development.

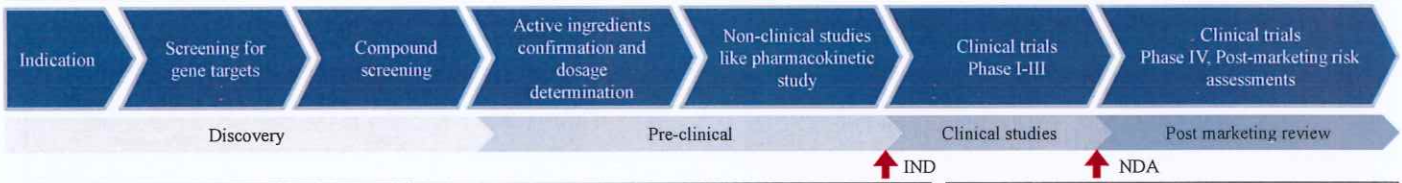


Note: NMEs stand for new molecular entities, referring to active ingredients that contain no active moiety that has been previously approved by the Agency in an application according to FDA.

Source: NMPA; China Insights Consultancy

Overview of NMPA and CDE new drug application process

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

Overview of generic drug application process

Overview of generic drug application process

- Information on original drugs
  - Original CMO, reference preparation(RLD), original specification.
  - Patent information of original drugs.
  - Registration and market status.
  - Original prescription and composition .
  - Other information.
- Procurement of reference preparations, raw materials, chromatographic columns and reference substances, excipients and packaging materials

- Prescription and process
  - Excipient compatibility test
  - Preliminary prescription screening process: three batches of laboratory tests, sample inspection, determination of pilot production and process verification: pilot batch, pilot production and process verification
- Quality
  - Selection of quality research projects and preliminary determination of methods, methodological verification of quality standards, quality comparison studies.
- Stability
  - Influencing factor test, packaging material compatibility test, accelerated test, long-term test, evaluation of stability study results.
- Pharmacology and toxicology
  - Pharmacology and toxicology data collated and summarized.
  - Pharmacology and toxicology tests.

- Application form of drug registration inspection
  - Sample and item
  - Documents of APIs, package verifications, quality standards, inspection reports.
- Site investigation
  - Registration R&D site - pharmaceutical development/pharmacology and toxicology development/drug clinical trials.
  - Production site.

- Clinical
  - The amount of drug absorbed and the diffusion rate in the body
  - Peak blood concentration
- Approval number for market

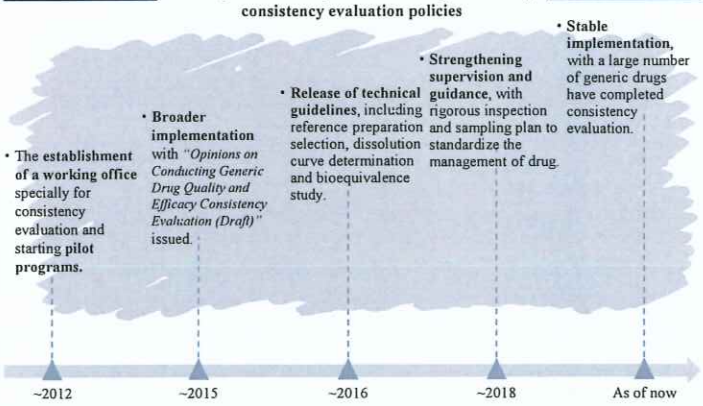
Source: NMPA; China Insights Consultancy

Overview of generic drug consistency evaluation

Introduction of generic drug consistency evaluation:

- The generic drug manufacturers must ***conduct comprehensive and in-depth comparative studies using reference preparations*** as controls, including studies of ***prescriptions, quality standards, crystal forms, particle sizes, and impurities, as well as dissolution curves of solid preparations***, in order to ***improve the success rate of in vivo bioequivalence tests***.
- **Difficult-to-replicate generic drugs** usually refer to the drugs that face significant technical, regulatory or market barriers to "copy". **High-quality generic drugs** refer to drugs that are identical or highly similar to original drugs in terms of active ingredients, dosage form, route of administration, therapeutic effects, etc., and have undergone strict quality control, bioequivalence evaluation and clinical verification to ensure that their efficacy, safety and stability are equivalent to those of original drugs.

Development and implementation of generic drug consistency evaluation policies



Content of generic drug consistency evaluation

Category	Content		Requirement
Pharmaceutical equivalence	Active ingredients	Dosage, route of administration, dosage form	Consistent
	Inactive ingredients	Excipients, e.g. starch, sucrose.	Difference allowed
Bioequivalence	In-vivo	Pharmacokinetic studies Comparative clinical studies	Consistent
Quality control and management	GMP Site investigation		Consistent
Others	Indications, specifications, etc.		Consistent

Source: NMPA; China Insights Consultancy

Analysis and comparisons of R&D models of innovative drugs in China

China's innovative drugs market → R&D models

R&D models	Revenue allocation	Cost allocation	Risk bearing	Resource	Requirement for R&D capability
Independent R&D model • A company **initiates and conducts R&D projects** independently by self-established teams.	• Revenue from successfully marketed products exclusively goes to the company.	• The R&D cost is undertook entirely by the company.	• The company to bear total risks all around the value chain.	• The resources are internally derived.	• The company is required to have robust experience and technical accumulations.
License-in model • A company(licensee) **acquires the rights** to a product, technology, or intellectual property from another organization(licensor).	• The licensee pays royalties, upfront, milestone fees and even sales milestones to the licensor.	• The licensee is not necessarily obliged to take cost of R&D.	• The licensee to bear risks in clinical development.	• The resources are internally derived.	• It depends on the pipeline screening and clinical translation of the licensee.
Co-development model • To develop a new drug together with one or more other organizations.	• The allocation is up to the co-development contract to meet expectations from all parties.	• The cost is shared by all parties according to the contract.	• Risks to be shared.	• Resources are shared among all parties.	• It sets high standards for all parties in terms of personnels, funds, channels.

Source: 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)

China pharmaceutical market → Policy

Overview of China's policy encouraging innovation in innovative drugs

Department	Policy Name	Key Contents	Issuance Time
The State Council	《全链条支持创新药发展实施方案》	Strengthen policy support across the entire chain-coordinating price management, insurance, drug allocation, investment, and optimizing review and assessment mechanisms-to drive breakthroughs in innovative drugs. Mobilize innovation resources and reinforce basic research to lay a solid foundation for China's innovative pharmaceutical development	2024-07
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)

China pharmaceutical market | Policy

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

Following NDA, access to NRDL and bid for regional or centralized VBP are two major events that could potentially impose pressure of price reduction

Global and China pharmaceutical market | China market access

National Drug Reimbursement list application and inclusion process

1. Product launch after regulatory approval
2. Preparation for NRDL listing
3. Pharma companies submit application
4. Expert review and vote for shortlist
5. Price negotiation and tendering
6. NRDL inclusion results

- Preliminary conditions and criteria for eligibility of NRDL released
- Pharmaceutical companies could prepare required qualifications and documents accordingly

- Experts assess clinical value, budget impact and cost-effectiveness of underlying drugs proposed to be included in NRDL

- Drug manufacturers present price quote and bid for NRDL inclusion
- If proposed price exceeds certain threshold, drug manufacturers may lose the bid

- Two drug groups in NRDL with different reimbursement level
- Class A: 100% reimbursed
- Class B: partially reimbursed, varies across municipalities and provinces

- In the new 2024 NRDL, 91 new drugs were added, and their prices were reduced by an average of 63% through negotiations and bidding.
- The catalog now contains a total of 3159 drugs, including 1,765 western medicines and 1,394 traditional Chinese medicines. The new version of the NDRL has added drugs in areas such as anti-tumor, rare diseases, and antivirals. Drugs for chronic diseases such as diabetes have also been included, such as Dorzagliatin for type 2 diabetes patients.

Evolution of centralized VBP program

	2018.11 4+7 pilot	2019.9 4+7 expansion	2019.12 2nd round	2020.7 3rd round	2021.1 4th round	2021.6 5th round	2021.11 6th round	2022.7 7th round	2023.3 8th round	2023.11 9th round	2024.12 10th round
Scale	11 pilot cities	25 provinces	nationwide	nationwide	nationwide	nationwide	Nationwide (for Insulin)	nationwide	nationwide	nationwide	nationwide
# of drugs	25	25	32	55	45	61	16	61	39	42	62
Avg price cut	52%	59%	53%	53%	52%	56%	48%	48%	56%	58%	75%

- China's volume-based procurement (VBP) program encourages generic drug use and reduces costs for off-patent drugs. Initially covering 11 cities in 2018, it quickly expanded nationwide.
- From the second batch, the VBP threshold was set at three companies, adjusted to four or more from the seventh batch.
- Centralized procurement for drugs has yielded cost savings by creating economies of scale and improving purchasing and negotiation power over pricing by pooling procurement process for drugs across multiple buyers. Pharma companies in turn should design market access strategies to cope with expected price cut.

Source: NHSA; frontiers; China Insights Consultancy

Growth drivers and trends in China's pharmaceutical industry

Drivers and trends in China's pharmaceutical industry

Growth drivers & Future trends	
Rising population aging and people's awareness of health	• **China's population is aging increasingly**, which will inevitably rise the prevalence of chronic diseases and drive the need for pharmaceutical treatment options. IARC's 2023 report shows 20 million new cancer cases and 9.7 million deaths globally. Lung cancer and female breast cancer are the most commonly occurring cancers worldwide, accounting respectively for 12.4% and 11.6% of total new cases in 2023 • In addition, the improvement of people's living standards will **increase their awareness of health**. As more patients' diseases are diagnosed at an early stage, more and more patients are willing to choose drugs with better effects and fewer side effects to treat their diseases, which is bound to promote the growth of the pharmaceutical drug market
Ongoing advancements in technology and research	• Ongoing advancements in technology have enabled the design and production of the first, and hard generic drugs as well as innovative drugs with improved efficacy and safety profiles. Novel advancement such as **wider selection of targets, antibody-drug-conjugates** are enhancing the therapeutic potential of targeted anti-cancer drugs. And the small molecule innovative drugs have been **kinase inhibitors, epigenetic inhibitors and proteasome inhibitors and others** • With the technological development, AI and computer-assisted drug development are becoming mainstream, and technological ideas such as PROTAC technology, allosteric modulator, and deuterated drugs are also highly anticipated
Growing investments in research and development activities	• Growing investments in research and development activities by pharmaceutical and biotechnology companies are driving the development of the first, and hard generic drugs and innovative drugs. These investments aim to **explore new therapeutic targets and enhance the efficacy of existing treatments** • Collaborations and partnerships between pharmaceutical companies, and academic institutions are driving the development and commercialization of the first , and hard generic drugs and innovative drugs. These collaborations leverage complementary expertise and resources to accelerate drug discovery and development processes
Policies support new drug development	• In recent years, the government have introduced several policies to support the development of innovative drugs, including **optimizing the review and approval process for new drugs, promoting medical insurance payment, encouraging investment and financing support, price management** and others. For example, 2022.01, MIIT and others released《"十四五"医药工业发展规划》, 2022.03, CDE published《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》and 2023.04, CDE posted《药审中心加快创新药上市许可申请审评工作规范(试行)》,etc. • The implementation of these policies is expected to greatly enhance the innovation capabilities of the pharmaceutical industry, accelerate the research and development and market launch of first, and hard generic drugs and innovative drugs, and increase the commercialization success rate of them, thereby promoting the high-quality development of the entire pharmaceutical industry

Source: China Insights Consultancy

Entry barriers to pharmaceutical industry

Entry barriers to pharmaceutical industry

Entry barriers	
Regulatory Hurdles: Strict Regulations and Lengthy Approval Processes	• The pharmaceutical drug market is highly regulated, with **complex frameworks** imposed by national health authorities in each step of the drug development process. Pharmaceutical/biotech companies must comply with these stringent regulations, which require significantly increased monetary and time input • After a drug is approved, it is subject to **ongoing monitoring** of adverse events and efficacy, which can add to regulatory burden. Companies must also negotiate with healthcare payers to obtain reimbursement and achieve favorable market access
Technological Expertise Required in R&D and Manufacturing	• Early-stage drug development faces challenges in **identifying suitable molecular targets and selecting a lead compound** that effectively modulates the target. Disease-causing cells often lack a uniform target, and a single disease can stem from diverse phenotypic variants. These issues complicate innovative drug discovery • Lead compounds must go through preclinical studies (in cell cultures and animals), formulation development, translation into clinical trials, and commercialization, each of which requires a different skill set
Capital Intensity: Significant Financial Investment for New Drug R&D	• Developing a new drug or first, and hard generic drug requires extensive research, preclinical and clinical trials to ensure safety and efficacy, as well as drug development and manufacturing scale-up, which in total **cost hundreds of millions to billions of dollars**. The high costs and extended development periods deter new entrants, who must gather substantial resources before generating any revenue • The **success rate of drug development is low**, and many candidates fail during clinical trials or regulatory approval, at the end of the drug discovery process. This uncertainty discourages investment, especially in high-risk innovative therapies targeting unmet medical needs
Talent Management: High Recruiting Standards and Extensive Training	• Drug development involves expertise ranging from biochemistry and medicine to business development and marketing. Talents must be adept at **multidisciplinary tasks**. For example, a business development expert should also understand the mechanism and clinical performance of the drug to be promoted, and a medical expert must know regulatory requirements while designing clinical trials • Investing in talent education and training programs can accelerate innovation. However, companies must also manage the resources required for training and the risk of losing trained talent to competitors

Source: China Insights Consultancy

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Introduction to digestive system diseases

Introduction to digestive system

- Digestive system is the most complicated system in human body, charging for the digestive process of foods. Digestive system can be divided into digestive glands and digestive canal.
- **Digestive canal** Digestive canal refers to the canal connected from mouth to anus, including oral cavity, pharynx, esophagus, stomach, small intestine, and large intestine. Covered with different epithelial cells, each part of digestive canal plays a unique role in the digestive process.
- **Digestive gland** Digestive glands refers to a series of organs that secretes digestive enzyme. Salivary gland, liver, pancreas, and those small glands locate in the digestive tracts are defined as digestive glands.

Common digestive system diseases

- **FGID** Functional gastrointestinal disorders (FGIDs) refer to chronic and intermittent discomforts taking place in digestive system without obvious organic changes. As can be caused by unhealthy life style, FIGDs has became one of the troubles for urban citizens.
- **Inflammatory digestive disease** Inflammatory digestive diseases refer to a series of complicated digestive diseases characterized by inflammation. These kind of diseases can be caused by infection, metabolic disorders, or autoimmune factors.
- **PU** Peptic ulcer (PU) refers the inflammatory reaction, necrosis, and shedding of mucosa caused by various pathogenic factors, forming ulcers. PU is a common chronic disease, which can occur in any part of digestive canals, with the stomach and duodenum being the most common.
- **Digestive system tumor** As the most complicated system in human body, tumor can occur in all parts of digestive system, most with poor prognosis.

Diagnostic methods of digestive system diseases

- **Endoscope diagnosis** Endoscope diagnosis is the preferred diagnostic method of digestive system diseases as it can provide clear views of the lesion sites.
- **Imaging diagnosis** As a convenient and reasonably-priced diagnostic method, imaging diagnosis is a vital method for digestive system tumors.
- **Laboratory diagnosis** Laboratory diagnosis can provide information on infection as well as the progression of tumors.

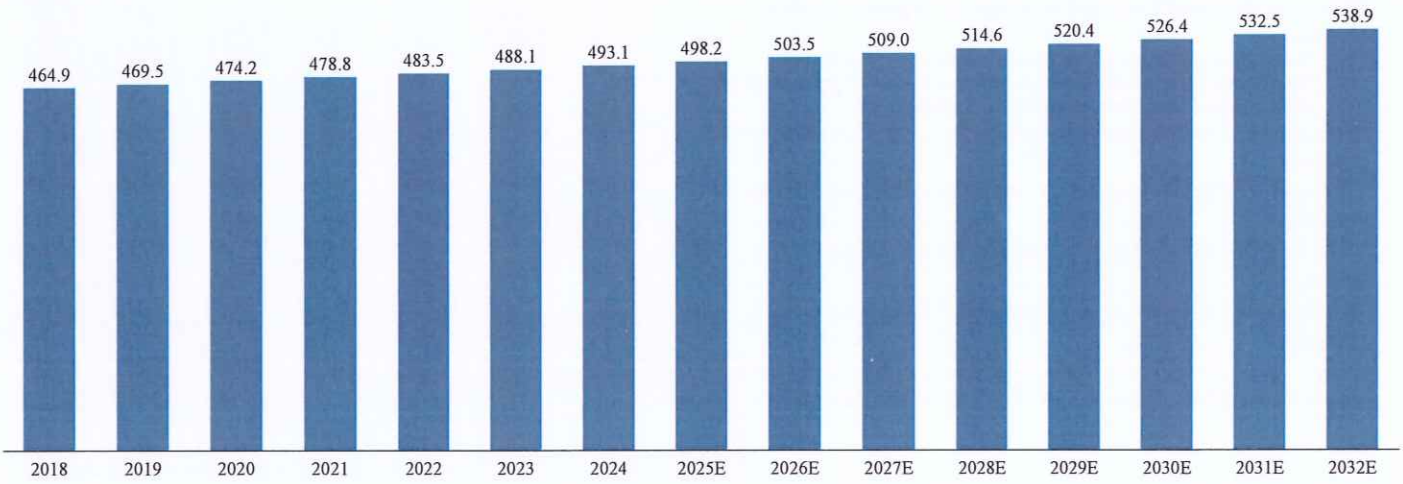
Source: Internal Medicine; Systematic Anatomy; China Insights Consultancy

Prevalence of digestive system diseases in China, 2018-2032E

Prevalence of digestive system diseases in China, 2018-2032E

CAGR	2018-2024	2024-2032E
Digestive system diseases	1.0%	1.1%

million ppl



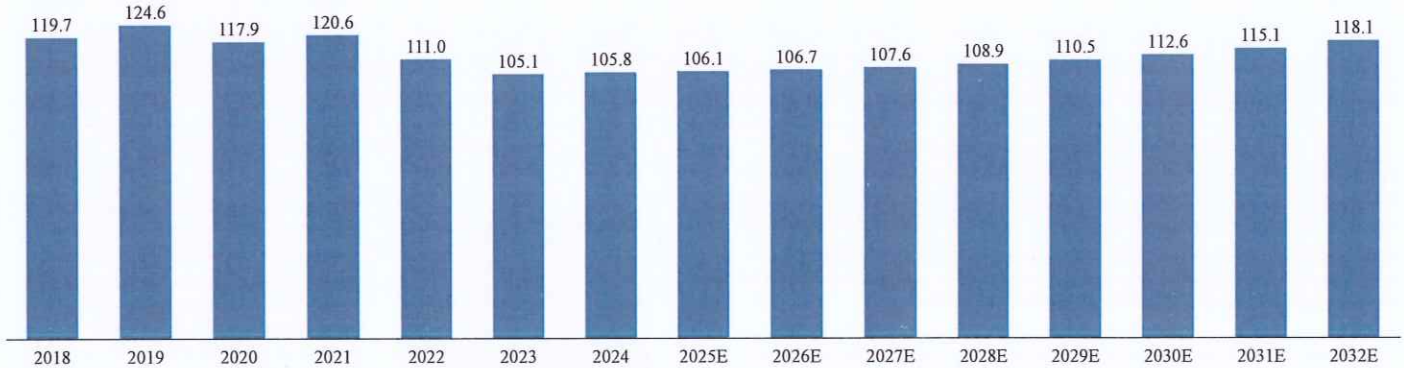
Source: GBD 2021; China Insights Consultancy

Market size of digestive system drugs in China, 2018-2032E

Market size of digestive system drugs in China, 2018-2032E

CAGR	2018-2024	2024-2032E
Digestive drugs	-2.0%	1.4%

billion RMB

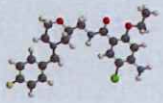


- The implementation of national VBP policy since 2018 has had a significant impact on the digestive system drug market size. For instance, mainly used PPIs(6 out of 7) were included in separate years from 2020 to 2023. the drastic price reduction has caused the market size downregulating, with a CAGR of -2.6% between 2018 and 2023.
- The prevalent rate appeared and was expected to be stable during the predictable period. Accomplished with strengthening disease control, the need of digestive system diseases may gradually stabilize, leading to slight CAGR of the market size.

Source: China Insights Consultancy

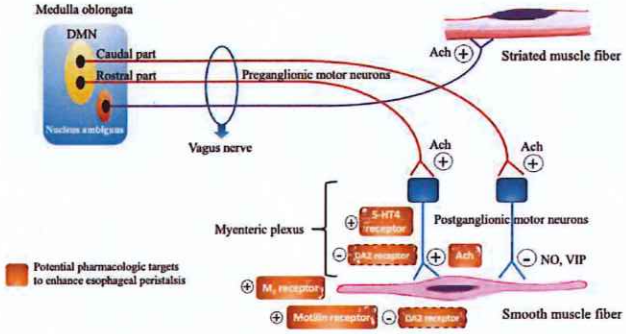
Introduction to gastrointestinal excitomotor

Introduction to gastrointestinal excitomotor



3D structure of mosapride

- **Gastrointestinal excitomotor refers to the drugs that promote the gastrointestinal motility**, which can be applied on patients suffering from different kinds of functional and organic gastrointestinal disorders.
- As the drugs for the most common digestive diseases, **a series of gastrointestinal excitomotor has been approved, including domperidone, mosapride, metoclopramide, itopride, etc.**



Mechanism of small-molecule drugs for digestive system diseases

Introduction to mosapride

- Mosapride is initially developed in 1998 by Sumitomo Pharmaceutical Company and has been **approved for the treatment of FGID and GERD**. As **a powerful gastroprokinetic drug with minor ADRs**, it has now been widely used among patients suffering from the indications.
- Mosapride can act as a **5-HT4 agonist** (with week 5-HT3 antagonistic effect) in human body, promoting the secretion of acetylcholine which is a core neurotransmitter in stimulating gastrointestinal motility.
- After being approved by NMPA in 1999, plenty of pharmaceutical companies has developed the generics of mosapride in China, among which **only four has passed the bioequivalency(BE) trial with Haixi Pharma being the first one**.

Source: CNKI; Frontiers in Pharmacology; China Insights Consultancy

Comparisons of mainly used gastrointestinal excitomotors approved in China

Comparisons of mainly used gastrointestinal excitomotors approved in China, as of LPD

Drug Name	Original Manufacture	Initial Approval by NMPA	Mechanism	Indication	Severe ADRs	Dosage	Annual Expenditure
Metoclopramide	Sanofi Clir SNC	1970	D_2 receptor inhibitor; 5-HT_4 receptor activator	digestive discomfort including nausea, vomiting, belching, etc.; GERD, bile reflux gastritis; gastroparesis caused by different factors	extrapyramidal reaction; prolactin increasing	5-10 mg each time, tid/qid	~¥ 530
Domperidone	Janssen Pharmaceuticals	1989	peripheral D_2 receptor inhibitor	Indigestion, bloating, belching, nausea, vomiting, abdominal pain, etc.	arrhythmia	10 mg each time, tid/qid	~¥ 850
Cisapride	Johnson & Johnson Innovative Medicine	1994	5-HT_4 receptor activator	gastroparesis; GERD; pseudo-intestinal obstruction; chronic constipation	extrapyramidal reaction; reversible hepatic damage	5-10 mg each time, bid/tid/qid	~¥ 470
Mosapride	Sumitomo Dainippon Pharma	1999	5-HT_4 receptor activator	functional dyspepsia with heartburn, belching, nausea, etc.; gastric dysfunction caused by GERD, diabetes, gastrectomy, etc.	-	5 mg each time, tid	~¥ 760
Trimebutine	Jouveinal Inc.	2000	K^+ channel inhibitor; noradrenaline release inhibitor; Ca^+ channel inhibitor; acetylcholine release inhibitor	symptoms caused by gastrointestinal dysmotility; IBS	hepatic damage	0.1-0.2 g each time, tid	~¥ 490
Itopride	Abbott Laboratories	2001	peripheral D_2 receptor inhibitor; acetylcholinesterase inhibitor	symptoms caused by dyspepsia	-	50 mg each time, tid	~¥ 1,000
Cinitapride	Almirall S.A	2018	5-HT_4 receptor activator; peripheral D_2 receptor inhibitor	mild to moderate functional dyspepsia	delayed movement disorders (long-term usage)	1 mg each time, tid	~¥ 3,700

Source: Drug Instructions; NMPA; Pharmcodia; China Insights Consultancy

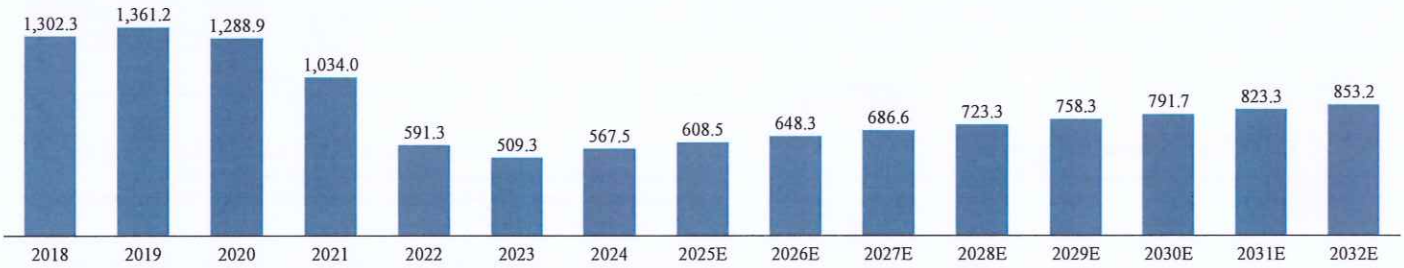
Market size of mosapride in China, 2018-2032E

Mosapride | Market size

Market size of mosapride in China, 2018-2032E

CAGR	2018-2024	2024-2032E
Mosapride	-12.9%	5.2%

million RMB



Key Analysis

- The market size of mosapride experienced a sharp decrease in 2021 since mosapride was included in the 4th round of National VBP scheme, leading to the reduction in unit price.
- With the intense life pace, digestive disorders may become a main trouble of modern citizens. As a powerful gastrointestinal excitomotor, **it is expected that the market size of mosapride would grow steadily at a CAGR of 5.2% in 2023-2032 with the increasing eligible population.**

Note: *the market size is in terms of patient-end revenue.

Source: China Insights Consultancy

Summary of approved mosapride in China

Mosapride | Competition

Summary of approved mosapride in China, as of LPD

Drug name	Company	Specifications (measured by $C_{21}H_{25}ClFN_3O_3 \cdot C_6H_8O_7$)	Initial Approval	Time to pass consistency evaluation*
Mosapride Citrate Tablets	Lunan Pharma	5 mg	1999	2020/07
Mosapride Citrate Tablets	Kanghong Pharma	5 mg	1999	2020/12
Mosapride Citrate Tablets	Hansoh Pharma	5 mg	1999	-
Mosapride Citrate Tablets	Sumitomo Pharma	5 mg	2002	-
Mosapride Citrate Dispersible Tablets	Kanghong Pharma	5 mg	2003	-
Mosapride Citrate Oral Solution	Lunan Pharma	5 mg	2008	-
Mosapride Citrate Tablets	Yabao Pharma	5 mg	2009	2024/04
Mosapride Citrate Capsules	Chenpon Pharma	5 mg	2017/04	-
Mosapride Citrate Tablets	Haixi Pharma	5 mg	2020/06	2020/06 regarded
Mosapride Citrate Granules	Yatai Pharma	5 mg	2021/10	2021/10 regarded
Mosapride Citrate Tablets	Jingxin Pharma	5 mg	2024/09	2024/09 regarded
Mosapride Citrate Tablets	Ningbo Menovo Tiankang	5 mg	2025/08	2025/08 regarded

- ***Haixi Pharma was the 1st in China to be regarded as passing consistency evaluation.***

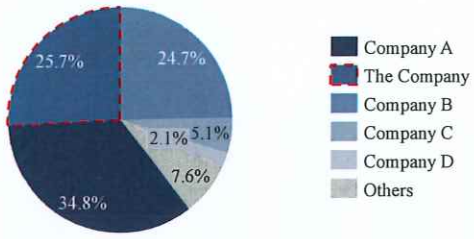
Note: including situations where drugs are regarded as passing consistency evaluation.

Source: NMPA; Pharmcodia; China Insights Consultancy

Competitive landscape of mosapride in China, in terms of sales revenue, 2024

Mosapride | Market share

Market share of mosapride in China, 2024



- Company A, Kanghong Pharma (stock code:002773.SZ), headquartered in Sichuan Province, researches, develops, manufactures, and distributes medicines for ophthalmic, central nervous, digestive and endocrine systems.
- Company B, Lunan Better Pharma, headquartered in Shandong Province, is an integrated pharmaceutical group of producing, researching and selling traditional Chinese medicine, chemical medicine and bio-pharmaceutical medicinal products.
- Company C, Yabao Pharma (stock code:600351.SH), headquartered in Shanxi Province, includes more than 300 kinds of TCM, APIs, patches and pharmaceutical packaging materials.
- Company D, Sumitomo Pharma, founded in 1897 and headquartered in Osaka, Japan, is a multinational pharmaceutical company focusing on oncology, psychiatry, neurology, women's health issues, urological diseases, etc.

CIC 灼识咨询

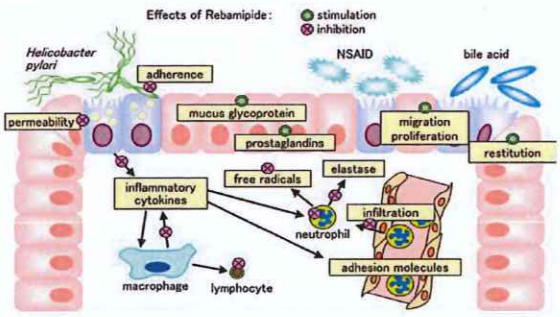
Source: China Insights Consultancy

As a series of relevant products has passed BE trial, the popular digestive drug, rebamipide, is a qualified candidate for VBP scheme

Rebamipide | Introduction

Introduction to gastric mucosal damage

- Gastric mucosa refers to the innermost layer of gastric wall, covered by gastric mucosal barrier, protecting the stomach from being damaged. **Gastric mucosa can be damaged by several factors, mainly related to unhealthy lifestyle.**
- **The most common gastric mucosal damage is gastritis** which can be classified into acute and chronic gastritis according to the course of inflammation. Patients suffering from gastritis may experience inappetence, stomachache, gastrorrhagia, or even gastric perforation. **With the intense pace of life, gastritis has become a common disease for modern citizens.**



Mechanisms of mucosal protective actions of rebamipide

Introduction to rebamipide

- Rebamipide was initially developed by Otsuka Pharmaceutical Company in 1990 and **has been approved for the treatment of acute gastritis and the acute phase of chronic gastritis**.
- As a **ubiquitin associated and SH3 domain containing B (UBASH3B) inhibitor,** rebamipide can relieve the gastric mucosal damage through its mucosal protective, ulcer healing, and anti-inflammatory actions.
- According to the policy, drugs with more than 7 original or generics manufactures passed BE trial can be included in VBP scheme. As a series of products has passed BE trial in 2024, **the popular digestive drug rebamipide is now a qualified candidate for VBP scheme inclusion**.

CIC 灼识咨询

Source: Internal Medicine; Digestive Diseases and Sciences; China Insights Consultancy

Market size of rebamipide in China, 2018-2032E

Market size of rebamipide in China, 2018-2032E

CAGR	2018-2024	2024-2032E
Rebamipide	7.8%	4.8%

million RMB

Source: China Insights Consultancy

Competitive landscape of rebamipide in China

Competitive landscape of rebamipide in China

Drug name	Company	Specifications (Measured by $C_{19}H_{15}ClN_2O_4$)	Initial approval	Time to pass consistency evaluation*
Rebamipide Tablets	Yuanlijian Pharma	0.1 g	2001	2023/11
Rebamipide Tablets **(Original drug)**	Otsuka Pharma	0.1g	2002	-
Rebamipide Capsules	Shenghuaxi Pharma	0.1 g	2011	2024/06
Rebamipide Tablets	Shenghuaxi Pharma	0.1 g	2023/10	2023/10 regarded
Rebamipide Tablets	Haixi Pharma	0.1 g	2024/04	2024/04 regarded
Rebamipide Tablets	Xizhou Pharma	0.1 g	2024/04	2024/04 regarded
Rebamipide Tablets	Brilliant Pharma	0.1 g	2024/06	2024/06 regarded
Rebamipide Tablets	Huanan Pharma	0.1 g	2024/06	2024/06 regarded
Rebamipide Tablets	Meidakang Huakang Pharma	0.1 g	2024/07	2024/07 regarded
Rebamipide Tablets	Muyuan Pharma	0.1 g	2024/08	2024/08 regarded
Rebamipide Tablets	Kirgen Biological Pharma	0.1 g	2024/09	2024/09 regarded
Rebamipide Tablets	Ningbo Tianheng Pharma	0.1 g	2024/10	2024/10 regarded
Rebamipide Tablets	Beijing Jincheng taier Pharma	0.1 g	2024/12	2024/12 regarded
Rebamipide Tablets	Vigonvita Life Sciences	0.1 g	2024/12	2024/12 regarded
Rebamipide Tablets	Cisen Pharma	0.1 g	2025/01	2025/01 regarded
Rebamipide Tablets	Dongyang Xiangsheng Pharma	0.1 g	2025/06	2025/06 regarded
Rebamipide Tablets	Nanyang Tianheng Pharma	0.1 g	2025/09	2025/09 regarded

- ***Haixi Pharma was the 3rd in China to be regarded as passing consistency evaluation.***

Note: including situations where drugs are regarded as passing consistency evaluation.

Source: NMPA; Pharmcodia; China Insights Consultancy

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Introduction to cardiovascular system diseases

Introduction to cardiovascular system

- Cardiovascular system is the most important system in human body, charging for the distribution of nutrients and receiving metabolites from the cells. It is composed of heart and blood vessels.

- **Heart** Heart is the most vital organ in human body, which includes four chambers named as right atrium, right ventricle, left atrium, and left ventricle. The cooperation of four chamber's expansion and contraction provides power to the flow of blood.
- **Blood vessel** Blood vessels can be classified into arteries, veins, and capillaries. The continues blood flow contained in blood vessels plays the core role in the metabolism of human body.

Risk factors of cardiovascular system diseases

- **Genetic factor** Former researches revealed that some cardiovascular system diseases showed family clustering, indicating the genetic factors may play an important role in the onset of cardiovascular system diseases.
- **Environmental factor** It is widely accepted that the onset of cardiovascular system diseases have a close correlation to unhealthy lifestyle. High-salt and high-fat diet, circadian rhythm disruption, alcohol and smoke consumption, infection, and mental stress can be the risk factors of cardiovascular system diseases.

Common cardiovascular system diseases

- **Hypertension** Hypertension refers to the abnormally increased blood pressure, which may lead to the damage of blood vascular epithelial or even cerebral hemorrhage, in some cases. As a common chronic cardiovascular system disease, hypertension has a concealed onset and require long-term lifestyle management to relieve the damage.
- **Cardiac dysfunction** Cardia dysfunction which is characterized by congestion and insufficient perfusion refers to the reduction of heart function caused by all kinds of factors. With the progression of the disease, patients' exercise capacity can be severely damaged, making the disease a heavy burden to the family and whole society.
- **CHD** Coronary atherosclerotic heart disease, also known as coronary heart disease (CHD), refers to the cardiac disease caused by the coronary artery stenosis due to atherosclerosis. With concealed onset and close correlation to unhealthy lifestyle, CHD is now the main cause of death for those died of sudden death.

Source: Internal Medicine; Systematic Anatomy; China Insights Consultancy

Prevalence of cardiovascular system diseases in China, 2018-2032E

Prevalence of cardiovascular system diseases in China, 2018-2032E

CAGR	2018-2024	2024-2032E
Cardiovascular system diseases	3.3%	3.1%

million ppl

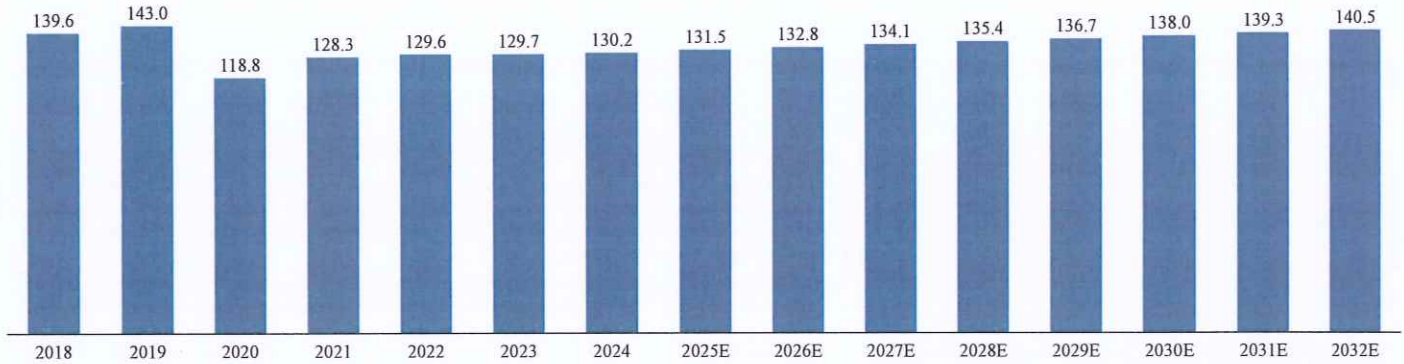
Source: GBD 2021; China Insights Consultancy

Market size of cardiovascular system drugs in China, 2018-2032E

Market size of cardiovascular system drugs in China, 2018-2032E

CAGR	2018-2023	2023-2032E
Cardiovascular drugs	-1.1%	1.0%

billion RMB



- The market size of cardiovascular system drugs in China experienced a sharp decrease during the lockdowns and restrictions of COVID-19, primarily reduced patient visits to healthcare facilities and limited delivery of drugs. It turned out that the market size bounced back in 2021 and had stable growth afterwards. Cardiovascular diseases are generally long-term diseases which require constant medications during the whole life. Driven by the growing aging population and unhealthy diet structure, the prevalence of cardiovascular diseases is expected to increase steadily thus the market size is expected to back to historical level and keep growing.

Source: China Insights Consultancy

Introduction to hypertension

Introduction to hypertension

- **Hypertension refers to the abnormally increased blood pressure**. Most hypertension are categorized as primary hypertension with unknown etiology. Only 5% of hypertension caused by some certain disease are categorized as secondary hypertension.
- **Hypertension is a crucial risk factor for other chronic diseases** as it can damage the vessel epithelial of the whole human body, affecting the function of vital organs, including brain, heart, and kidneys.

Classification of hypertension

Classification	Systolic pressure (mmHg)		Diastolic pressure (mmHg)
Normal	<120	and	<80
High level normal	120-139	and/or	80-89
Hypertension			
Hypertension(Level I)	140-159	and/or	90-99
Hypertension(Level II)	160-179	and/or	100-109
Hypertension(Level III)	≥180	and/or	≥110
Isolated systolic hypertension	≥140	and	≤90
Isolated diastolic hypertension	<140	and	≥90

Common comorbidities of hypertension

- **Cerebrovascular disease** Hypertension may damage the vascular epithelial of vertebral artery and internal carotid artery, leading to cerebral ischemia, as they are the main artery to supply blood to brain tissue. A hypertensive crisis may also cause the rupture in Circulus Willisii, leading to fatal encephalorrhagia.
- **Heart failure** Hypertension will bring extra burden to heart beats, leading to cardiac hypertrophy during the long-term course. The patients would eventually suffer from heart failure as the myocardium can no longer compensate the growing burden.
- **Chronic renal failure** The damage of renal blood vessels caused by hypertension will lead to the dysfunction of kidneys, as the function of the organ relies on its capacity to filter blood.
- **Aortic dissection** Hypertension may damage the epithelial of aorta, forming rupture in arterial media. The dissection may cause extreme pain to the patients and can be fatal upon rupture.

Source: Internal Medicine; CNKI; China Insights Consultancy

Treatment of hypertension relies on lifestyle management, antihypertensive drugs, and renal denervation

Lifestyle management

- As it has been proved that unhealthy lifestyle can be the main risk factor of hypertension, lifestyle management is recommended for all patients suffering from hypertension. **For patients with low risk level hypertension, lifestyle management may be their only necessary therapy**.

Antihypertensive drugs

- **Patients suffering from hypertension with risk level higher than moderate or failed to relieve the disease through lifestyle management shall accept antihypertensive drugs as soon as possible**. According to the clinical guideline, six types of drugs and their single-pill combination (SPC) are recommended for the treatment of hypertension. **The detailed information is summarized as below**.

Drug type	Mechanism	Representative drugs
Ca^{2+} channel blocker (CCB)	Blocking Ca^{2+} channel to relax vascular smooth muscle cells and reduce heart rate	Amlodipine, Verapamil, Diltiazem, etc.
Angiotensin receptor blocker (ARB)	Blocking the interaction between hypertensive hormone, angiotensin II, and its receptor	Valsartan, Irbesartan, Telmisartan, etc.
Angiotensin converting enzyme inhibitor (ACEI)	Blocking the secretion of hypertensive hormone, angiotensin II	Captopril, Enalapril, Benazepril, etc.
Thiazide diuretics	Stimulating urination to reduce effective blood volume	Hydrochlorothiazide, Indapamide, etc.
β-adrernoceptor antagonists	Blocking the interaction between adrenal hormone and myocardium to reduce heart rate	Metoprolol, Bisoprolol, Betaxolol, etc.
Angiotensin receptor-neprilysin inhibitor (ARNI)	Blocking the activity of angiotensin II while stimulating urination	Sacubitril valsartan sodium, etc.

*Patients combined with dyslipidemia are also recommended to accept antilipemic drugs like atorvastatin.

Renal denervation

- For patients with poor compliance, renal denervation can be a possible treatment, which **can reach antihypertensive effect through reducing sympathetic nerve activity**. However, the long-term effect and safety of this procedure still requires further researches.

Source: Internal Medicine; CNKI; Pharmacology; China Insights Consultancy

Summary of approved amlodipine besylate and atorvastatin calcium in China

Summary of approved amlodipine besylate and atorvastatin calcium in China, as of LPD

Drug name	Company	Time to pass the Consistency Evaluation*	Specifications (Measured by amlodipine /atorvastatin calcium)	Initial Approval	VBP Inclusion
Amlodipine Besylate and Atorvastatin Calcium Tablets	Jialin Pharma	2021	5 mg/10 mg; 10 mg/10 mg	2021/06	Since 2023/04 7 provinces (首次，第八批)
Amlodipine Besylate and Atorvastatin Calcium Tablets	Chia-Tai Tianqing	2021	5 mg/10 mg	2021/07	Since 2023/04 7 provinces (首次，第八批)
Amlodipine Besylate and Atorvastatin Calcium Tablets	Han Hui Pharma	2022	5 mg/10 mg; 5 mg/20 mg	2021/07	-
Amlodipine Besylate and Atorvastatin Calcium Tablets	China Resources Holding Sai Ke Pharma	2021	5 mg/10 mg; 5mg/20mg	2021/10	Since 2023/04 8 provinces (首次，第八批)
Amlodipine Besylate and Atorvastatin Calcium Tablets	Haixi Pharma	2022	5 mg/10 mg; 5 mg/20 mg	2022/01	Since 2023/04 9 provinces (首次，第八批)
Amlodipine Besylate and Atorvastatin Calcium Tablets	Garden Pharma	2022	5 mg/10 mg; 5 mg/20 mg; 5 mg/40 mg	2022/03	-
Amlodipine Besylate and Atorvastatin Calcium Tablets	Baiao Pharma	2023	5 mg/10 mg	2023/02	-
Amlodipine Besylate and Atorvastatin Calcium Tablets	Dawnrays Pharma	2023	5 mg/10 mg	2023/04	-
Amlodipine Besylate and Atorvastatin Calcium Tablets	Deshang Pharma	2023	5 mg/10 mg; 5 mg/20 mg	2023/04	-
Amlodipine Besylate and Atorvastatin Calcium Tablets	Chang Dian Pharma	2024	5 mg/10 mg	2023/06	-

Note: including situations where drugs are regarded as passing consistency evaluation.

Source: NMPA; China Insights Consultancy

Summary of approved amlodipine besylate and atorvastatin calcium in China

Amlodipine atorvastatin calcium | Competition

Summary of approved amlodipine besylate and atorvastatin calcium in China, as of LPD

Drug name	Company	Time to pass the Consistency Evaluation*	Specifications (Measured by amlodipine /atorvastatin calcium)	Initial Approval	VBP Inclusion
Amlodipine Besylate and Atorvastatin Calcium Tablets	Chang Dian Pharma	2024	5 mg/10 mg	2023/06	-
Amlodipine Besylate and Atorvastatin Calcium Tablets	Krka Menovo Pharma	2024	5 mg/10 mg	2024/06	-
Amlodipine Besylate and Atorvastatin Calcium Tablets	Rotam Reddy Pharma	2024	5 mg/10 mg; 5 mg/20 mg	2024/06	-
Amlodipine Besylate and Atorvastatin Calcium Tablets	Menovo Pharma	2024	5 mg/10 mg	2024/06	-
Amlodipine Besylate and Atorvastatin Calcium Tablets	Weite Pharma	2025	5 mg/10 mg	2025/07	-
Amlodipine Besylate and Atorvastatin Calcium Tablets	Beijing SL Pharma	2025	5 mg/10 mg	2025/07	-
Amlodipine Besylate and Atorvastatin Calcium Tablets	Anhui Hongye Pharma	2025	5 mg/10 mg; 5 mg/20 mg	2025/08	

Note: including situations where drugs are regarded as passing consistency evaluation.

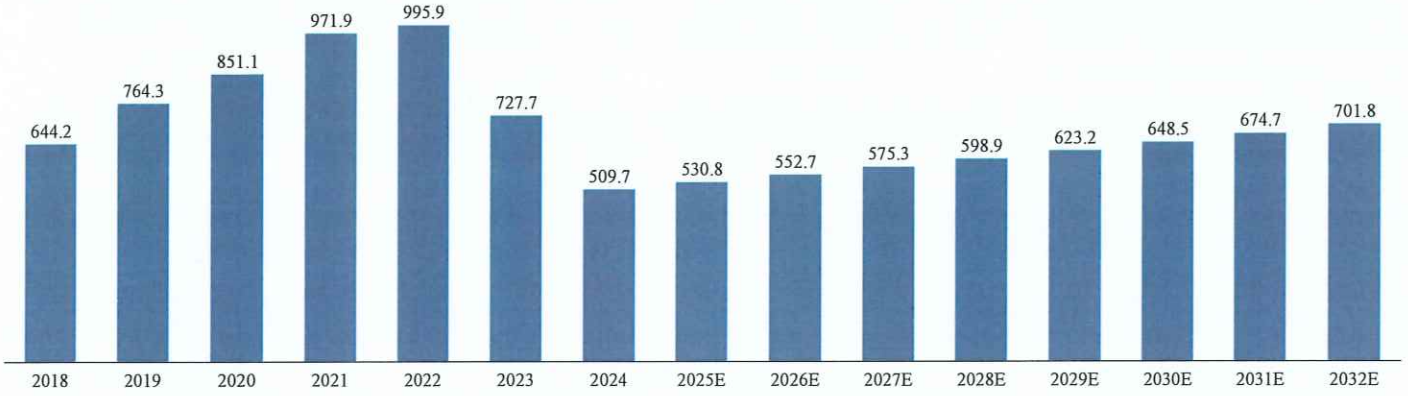
Source: NMPA; China Insights Consultancy

Market size of amlodipine atorvastatin calcium in China, 2018-2032E

Market size of amlodipine atorvastatin calcium in China, 2018-2032E

CAGR	2018-2024	2024-2032E
Amlodipine atorvastatin calcium	-3.8%	3.8%

million RMB



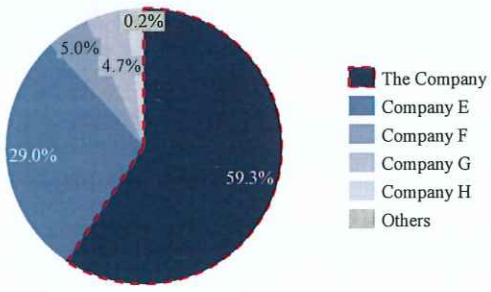
- The market size experienced a sharp decrease in 2023 since amlodipine atorvastatin calcium was included in 8th round of National VBP scheme.

Note: *the market size is in terms of patient-end revenue.

Source: China Insights Consultancy

Market share of amlodipine and atorvastatin calcium (5mg/10mg) in China, 2024

Market share of amlodipine and atorvastatin calcium (5mg/10mg) in China, 2024



- Company E, Hanhui Pharma, founded in 2012 and headquartered in Shanghai, supplies over 60 products to the China's market, covering anti-tumor, anti-infection, cardiovascular, etc.
- Company F, CR Sai Ke Pharma, headquartered in Beijing, a subsidiary of China Resources Group, is an enterprise integrating pharmaceutical production, R&D and marketing.
- Company G, Chia-Tai Tianqing, headquartered in Jiangsu Province, is a multinational pharmaceutical company with integrated R&D, manufacturing, marketing, sales and distribution capabilities. It is a subsidiary of a public listed biopharmaceutical.
- Company H,, Jialin Pharma, founded in 1998 and headquartered in Beijing, is one of the leading players in China's cardiovascular drug market.

Key Analysis

- As the former subsidiary company of the original manufacture of amlodipine besilate and atorvastatin calcium , Hanhui Pharma occupied almost all the market share in China before 2022. **After amlodipine besilate and atorvastatin calcium was included in the VBP scheme, China's domestic generics experienced an extraordinary growth in market share and occupied a large part**.
- With the implementation of VBP policy, **China's generic manufactures are encouraged to participate in the competition with their profits guaranteed.**

Note: *the market shares are in terms of patient-end use.

Source: China Insights Consultancy

Summary of approved valsartan/amlodipine (I) in China (1/3)

Summary of approved valsartan/amlodipine (I) in China, as of LPD (1/3)

Drug Name	Company	Specifications (Measured by valsartan/amlodipine)	Initial Approval	VBP Inclusion
Valsartan and Amlodipine Tablets (I)	Novartis Pharma	80 mg/5 mg	2015/04	-
Valsartan and Amlodipine Tablets (I)	Garden Pharma	80 mg/5 mg	2020/08	Since 2021/02 15 provinces (首次，第四批)
Valsartan and Amlodipine Tablets (I)	Hengrui Pharma	80 mg/5 mg	2020/09	Since 2021/02 16 provinces (首次，第四批)
Valsartan and Amlodipine Tablets (I)	Brilliant Pharma	80 mg/5 mg	2021/03	Since 2023/06 1 province (续采)
Valsartan and Amlodipine Tablets (I)	Huahai Pharma	80 mg/5 mg	2021/04	Since 2022/06 10 provinces (续采)
Valsartan and Amlodipine Tablets (I)	KPC Pharma	80 mg/5 mg	2021/09	Since 2022/11 2 provinces (续采)
Valsartan and Amlodipine Tablets (I)	Shanghai Abbott Pharma	80 mg/5 mg	2021/10	-
Valsartan and Amlodipine Tablets (I)	Apic Hope Pharma	80 mg/5 mg	2021/12	Since 2022/06 6 provinces (续采)
Valsartan and Amlodipine Tablets (I)	Huaxin Pharma	80 mg/5 mg	2021/12	Since 2022/06 5 provinces (续采)
Valsartan and Amlodipine Tablets (I)	Baiao Pharma	80 mg/5 mg	2020/02	Since 2023/06 1 province (续采)

Source: NMPA; Pharmcodia; China Insights Consultancy

Summary of approved valsartan/amlodipine (I) in China (2/3)

Summary of approved valsartan/amlodipine (I) in China, as of LPD (2/3)

Drug Name	Company	Specifications (Measured by valsartan/amlodipine)	Initial Approval	VBP Inclusion
Valsartan and Amlodipine Tablets (I)	Hualon Pharma	80 mg/5 mg	2022/02	Since 2022/06 6 provinces (续采)
Valsartan and Amlodipine Tablets (I)	Lepu Pharma	80 mg/5 mg	2022/02	Since 2022/06 5 provinces (续采)
Valsartan and Amlodipine Tablets (I)	Jiexi Pharma	80 mg/5 mg	2022/02	Since 2023/06 1 province (续采)
Valsartan and Amlodipine Tablets (I)	Haixi Pharma	80 mg/5 mg	2022/04	Since 2022/06 7 provinces (续采)
Valsartan and Amlodipine Tablets (I)	Wangao Pharma	80 mg/5 mg	2022/06	Since 2023/06 3 provinces (续采)
Valsartan and Amlodipine Tablets (I)	Miaoyinchun Pharma	80 mg/5 mg	2022/07	Since 2023/06 1 province (续采)
Valsartan and Amlodipine Tablets (I)	Shijiazhuang No.4 Pharma	80 mg/5 mg	2022/09	Since 2022/12 3 provinces (续采)
Valsartan and Amlodipine Tablets (I)	Cisen Pharma	80 mg/5 mg	2022/11	Since 2023/06 2 provinces (续采)
Valsartan and Amlodipine Tablets (I)	Hualon Pharma	80 mg/5 mg	2022/02	Since 2022/06 6 provinces (续采)

Source: NMPA; Pharmcodia; China Insights Consultancy

Summary of approved valsartan/amlodipine (I) in China (3/3)

Summary of approved valsartan/amlodipine (I) in China, as of LPD (3/3)

Drug Name	Company	Specifications (Measured by valsartan/amlodipine)	Initial Approval	VBP Inclusion
Valsartan and Amlodipine Tablets (I)	Lepu Pharma	80 mg/5 mg	2022/02	Since 2022/06 5 provinces (续采)
Valsartan and Amlodipine Tablets (I)	Lisheng Pharma	80 mg/5 mg	2022/11	Since 2023/01 1 province (续采)
Valsartan and Amlodipine Tablets (I)	China Resources Holding Sai Ke Pharma	80 mg/5 mg	2023/01	-
Valsartan and Amlodipine Tablets (I)	Nuode Pharma	80 mg/5 mg	2023/03	-
Valsartan and Amlodipine Tablets (I)	Xinhua Pharma	80 mg/5 mg	2023/05	-
Valsartan and Amlodipine Tablets (I)	Jianfeng Pharma	80 mg/5 mg	2023/05	-
Valsartan and Amlodipine Tablets (I)	Deyuantang Pharma	80 mg/5 mg	2023/05	-
Valsartan and Amlodipine Tablets (I)	Chase Sun Pharma	80 mg/5 mg	2024/04	-
Valsartan and Amlodipine Tablets (I)	Dawnrays Pharma	80 mg/5 mg	2023/07	-
Valsartan and Amlodipine Tablets (I)	Huluwa Pharma	80 mg/5 mg	2023/11	-
Valsartan and Amlodipine Tablets (I)	Krka Menovo Pharma	80 mg/5 mg	2024/05	-
Valsartan and Amlodipine Tablets (I)	Haiyue Pharma	80 mg/5 mg	2024/06	-

Source: NMPA; Pharmcodia; China Insights Consultancy

Summary of approved valsartan in China (1/3)

Summary of approved valsartan in China, as of LPD (1/3)

Drug Name	Company	Specifications (Measured by valsartan)	Initial Approval	VBP Inclusion
Valsartan Capsules	Livzon Pharma	80 mg	2000	Since 2024/06 2 provinces (续采)
Valsartan Tablets	Siyao Pharma	40 mg	2001	-
Valsartan Capsules	Siyao Pharma	40 mg; 80 mg	2001	Since 2020/08 6 provinces (首次，第三批)
Valsartan Capsules	Enze Jiashi Pharma	80 mg	2001	-
Valsartan Capsules	Tianda Pharma	80 mg	2003	Since 2020/08 7 provinces (首次，第三批)
Valsartan Capsules	TC Pharma	80 mg	2003	Since 2024/06 1 province (续采)
Valsartan Capsules	Novartis Pharma	80 mg; 160 mg	2004	-
Valsartan Dispersible Tablets	Hualon Pharma	80 mg	2005	Since 2023/06 1 province (续采)
Valsartan Dispersible Tablets	Hwasun Pharmaceutics	80 mg	2005/08	Since 2022/12 2 provinces (续采)
Valsartan Dispersible Tablets	Medisan Pharma	80 mg	2006	-
Valsartan Dispersible Tablets	Lunan Pharma	40 mg; 80 mg	2009	-
Valsartan Dispersible Tablets	Renhe Yikang Pharma	80 mg	2009	-

Source: NMPA; Pharmcodia; China Insights Consultancy

Summary of approved valsartan in China (2/3)

Summary of approved valsartan in China, as of LPD (2/3)

Drug Name	Company	Specifications (Measured by valsartan)	Initial Approval	VBP Inclusion
Valsartan Capsules	Lepu Pharma	80 mg	2013	-
Valsartan film-coated tablets	Novartis	160 mg	2017	-
Valsartan Tablets	Huahai Pharma	40 mg; 80 mg; 160mg	2018/05	Since 2020/08 6 provinces (首次，第三批)
Valsartan Capsules	China Resources Holding Sai Ke Pharma	80 mg	2020/02	Since 2020/08 6 provinces (首次，第三批)
Valsartan Capsules	Bright Future Pharma	80 mg; 160 mg	2020/04	-
Valsartan Capsules	Qianjin Pharma	80 mg; 160 mg	2020/07	Since 2020/08 6 provinces (首次，第三批)
Valsartan Tablets	Qianjin Pharma	80 mg	2021/05	-
Valsartan Tablets	Hisun Pharma	80 mg	2021/08	-
Valsartan Capsules	Hwasun Pharmaceutics	80 mg	2022/04	-
Valsartan Tablets	Krka Menovo Pharma	40 mg; 80 mg; 160 mg	2022/06	Since 2024/06 1 province (续采)
Valsartan Tablets	Rundu Pharma	40 mg; 80 mg	2022/06	Since 2023/06 3 provinces (续采)
Valsartan Tablets	Haixi Pharma	40 mg; 80 mg	2022/06	Since 2024/06 1 province (续采)

Source: NMPA; Pharmcodia; China Insights Consultancy

Summary of approved valsartan in China (3/3)

Summary of approved valsartan in China, as of LPD (3/3)

Drug Name	Company	Specifications (Measured by valsartan)	Initial Approval	VBP Inclusion
Valsartan Tablets	Green Cross Pharma	80 mg; 160 mg	2022/11	-
Valsartan Tablets	Nuode Pharma	40 mg; 80 mg; 160 mg	2023/04	Since 2024/06 2 provinces (续采)
Valsartan Tablets	Jiuzhou Fangyuan Pharma	40 mg; 80 mg; 160 mg	2023/06	Since 2024/06 1 province (续采)
Valsartan Tablets	China Resources Holding Sai Ke Pharma	80 mg; 160 mg	2023/07	-
Valsartan Tablets	Lunan Pharma	80 mg	2024/06	-
Valsartan Tablets	SHKB Pharma	160 mg	2024/06	-
Valsartan Tablets	Yike Pharma	80 mg; 160 mg	2024/08	-

Source: NMPA; Pharmcodia; China Insights Consultancy

Introduction to vascular cognitive impairment

Nicergoline | Introduction

Introduction to vascular cognitive impairment

- **Vascular cognitive impairment (VCI) refers to the cognitive impairment caused by different kind of vascular diseases.** Since neurons are sensitive to oxygen supply, the cerebral hypoxia/ischemia damage caused by different factors may lead to irreversible cerebral injuries, causing impairment in cognition.
- To relieve VCI, cholinesterase inhibitors and NMDA receptor inhibitors are applied in clinical practice. **Drugs for microcirculation improvement, neuron protection, and neurotransmitter enhancer are also considered as effective supplementary treatment**.

Classification of VCI

Classification	Related diseases
Risk factor-related VCI	Hypertension, diabetes, hyperlipidemia, etc.
Ischemic VCI	Multiple brain infarction, Cardiac ejection fraction reduction, etc.
Hemorrhagic VCI	Encephalorrhagia, subarachnoid hemorrhage, etc.
Other CVD-related VCI	Cerebral venous sinus thrombosis, cerebral arteriovenous malformation, etc.
AD combined VCI	Alzheimer's disease

Nicergoline' s pharmacological activity in VCI patients

- **Microcirculation improvement** As a selective adrenergic α_1 receptor blocker, nicergoline can induce vasodilation and reduce cerebrovascular resistance, stabilizing cerebral perfusion pressure. Together with its antithrombotic effects, nicergoline can effectively improve cerebral microcirculation.
- **Neurotransmitter enhancement** Nicergoline can act as modulators for a series of neurotransmitters, including acetylcholine and dopamine who are related to the regulation of cognition and emotion. Researches also revealed that nicergoline can enhance neural signal transduction, which promotes neural function.
- **Antioxidation** Nicergoline showed neuroprotective effect in animal models, reducing neural death caused by ischemia damage. Moreover, with its antioxidant effect, nicergoline can inhibit the formation of reactive oxygen species and promote oxygen intake.

Source: CNKI; Neurology; China Insights Consultancy

Summary of approved oral nicergoline in China

Nicergoline | Competition

Summary of approved oral nicergoline in China, as of LPD

Drug Name	Company	Specifications (Measured by $C_{24}H_{26}BrN_3O_3$)	Initial Approval	Time to pass consistency evaluation[a]
Nicergoline Tablets	Zambon Pharma	10 mg	1998	2024/02
Nicergoline Tablets	Rotam Reddy Pharma	5 mg; 10 mg	2000	2023/04
Nicergoline Tablets **(Original drug)**	Viatris Pharma	10 mg; 30 mg	2005	-
Nicergoline Capsules	Fuan Pharma	15 mg; 30 mg	2009	-
Nicergoline Capsules	General Sanyang Pharma	30 mg	2009	-
Nicergoline Tablets	Fangming Pharma	10 mg	2010	2024/06
Nicergoline Tablets	Qidu Pharma	10 mg	2011	-
Nicergoline Tablets	Haixi Pharma	30 mg	2023/11	2023/11
Nicergoline Tablets	Fuan Pharma	30 mg	2024/03	2024/03
Nicergoline Tablets	Thery Pharma	10 mg	2024/06	2024/06
Nicergoline Tablets	Fuyuan Pharma	10 mg	2024/08	2024/08

- ***Haixi Pharma was the 2nd in China to be regarded as passing consistency evaluation.***

Note: including situations where drugs are regarded as passing consistency evaluation.

Source: NMPA; China Insights Consultancy

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Introduction to endocrine system diseases

Introduction to endocrine system

- **Endocrine system consists of a series of endocrine glands and endocrine tissues all over human body**. Common endocrine glands and tissues include hypothalamus, pituitary, thyroid, parathyroid, pancreas, gonads, etc.
- **Different glands or tissues can secrete different hormone into blood, which paly important roles in the maintenance of homeostasis**. Targeted cells with relevant receptors can receive the biological signs from certain hormone and respond to these signs. Both abnormal up-regulation and down-regulation of these hormones will lead to disorders of internal homeostasis.

Common endocrine system diseases

Endocrine gland/tissue	Hormone	Abnormality	Disease
Hypophysis	Human growth hormone	Up-regulation	Gigantism
		Down-regulation	Dwarfism
Hypophysis	Antidiuretic hormone	Up-regulation	SIADH
		Down-regulation	Diabetes insipidus
Thyroid gland	Thyroxine	Up-regulation	Hyperthyroidism
		Down-regulation	Myxedema; cretinism
Parathyroid gland	Parathyroid hormone	Up-regulation	Hyperparathyroidism
Pancreatic islets	Insulin	Down-regulation	T1DM

Treatment of endocrine system diseases

- **Hyperfunction**
  - Remove the hyperactive gland or tissue by surgery
  - Damage the hyperplastic tissue by radiotherapy
  - Endocrine gland/tissue inhibitor
  - Relevant receptor blocker
  - Chemotherapy for endocrine tumor
- **Hypofunction**
  - Hormone replacement therapy
  - Supplement hormone active substances
  - Transplantation of endocrine gland or tissue

Source: Internal Medicine; Systematic Anatomy; China Insights Consultancy

Prevalence of endocrine system diseases in China, 2018-2032E

Prevalence of endocrine system diseases in China, 2018-2032E

CAGR	2018-2024	2024-2032E
Endocrine system diseases	-0.6%	0.9%

million ppl

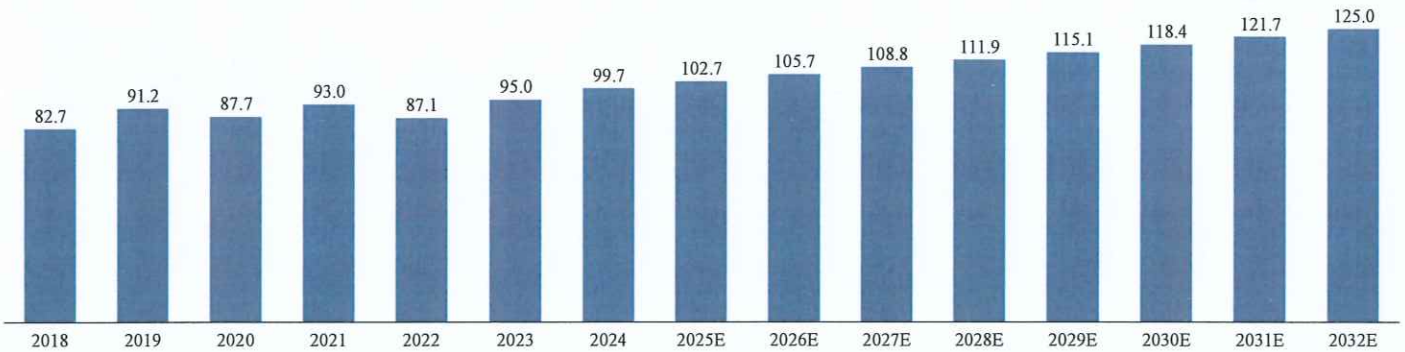
Source: GBD 2021; China Insights Consultancy

Market size of endocrine system drugs in China, 2018-2032E

Market size of endocrine system drugs in China, 2018-2032E

CAGR	2018-2024	2024-2032E
Endocrine drugs	3.2%	2.9%

billion RMB



- Endocrine diseases are disorders that occur when the endocrine system, which is responsible for producing and regulating hormones, does not function properly, including diabetes mellitus, thyroid disorders, etc. **It is expected that endocrine system disease will remain a big problem for the health of modern China citizens in the next few decades**, as the prevalence of common endocrine system diseases can be related to aging and intensifying lifestyle. Moreover, the developing diagnostic methods will also promote the diagnosis rate of chronic endocrine system diseases, driving the market to grow.

Source: China Insights Consultancy

Introduction to hyperparathyroidism

Introduction to parathyroid gland

- **Parathyroid glands are endocrine glands located on both sides of anterolateral trachea, behind thyroid glands**. Parathyroid glands appear in pairs on both sides, with each gland weighs approximately 35-50 mg.
- Parathyroid glands secrete parathyroid hormone which is vital for the balance between calcium and phosphorus *in vivo*. **Patients with parathyroid hormone beyond the normal level may suffer from hypercalcemia, osteoporosis, and renal calculi**.

Classification of hyperparathyroidism

Classification	Etiology
Primary hyperparathyroidism (PHPT)	More than 80% of PHPT are caused by **parathyroid adenoma** with the rest may be caused by parathyroid adenocarcinoma or hyperplasia.
Secondary hyperparathyroidism (SHPT)	SHPT can be the result of **long-term hypocalcemia caused by different factors**. Renal insufficiency, osteomalacia, and intestinal malabsorption are the most common causes.
Tertiary hyperparathyroidism (THPT)	On the basis of SHPT, **part of the hyperplastic tissue may turn into parathyroid adenoma** and start secreting excessive parathyroid hormone, leading to the onset of THPT.

Clinical manifestation of hyperparathyroidism

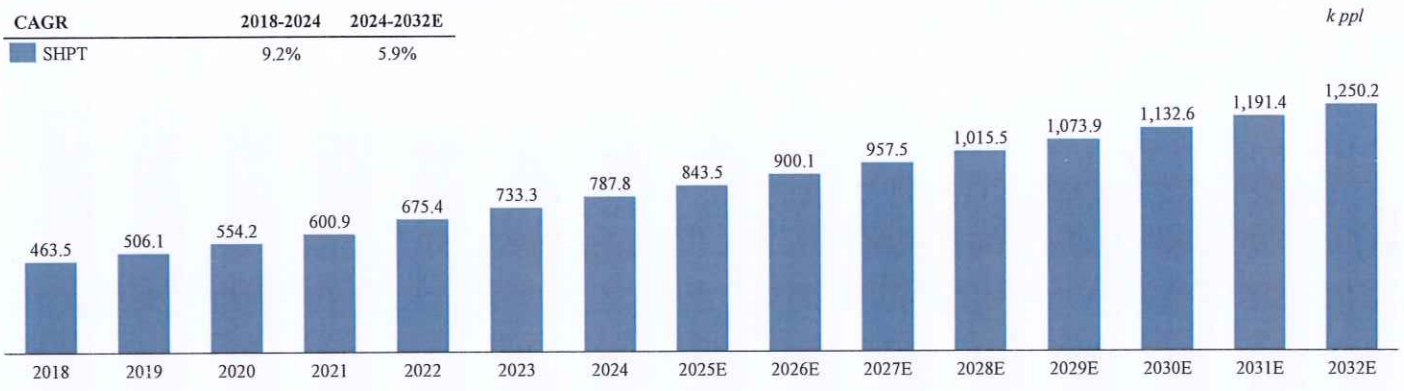
- **Hypercalcemia** Hyperparathyroidism would lead to the up-regulation of serum calcium level, affecting multiple systems. Patients suffering from hypercalcemia may experience central nervous system reaction, myasthenia, gastricism, articular pain, or pruritus. Severe hypercalcemia may lead to fatal crisis.
- **Osteoporosis** Excessive level of parathyroid hormone can damage bones by osteolysis. As the result of bone damage, patients suffering from hyperparathyroidism may experience fractures, skeletal malformations, or osteoporosis.
- **Renal calculi** About 20% of hyperparathyroidism patients suffer from renal calculi as the high serum parathyroid hormone level would lead to concentration dysfunction of renal tubules.

Source: Internal Medicine; Systematic Anatomy; China Insights Consultancy

Prevalence of Maintenance Dialysis-SHPT in China, 2018-2032E

Prevalence of Maintenance Dialysis-SHPT in China, 2018-2032E

CAGR	2018-2024	2024-2032E
SHPT	9.2%	5.9%



Key Note

- As a common comorbidity of long-term hypocalcemia, the prevalence of SHPT is largely related to the prevalence of chronic kidney disease (CKD). **Patients suffering from different phases of CKD have a chance ranging from 16% to 31% to progress to SHPT**. According to former epidemiology researches, **more than 10% of the adults in China are suffering from CKD, with the prevalence rate keep increasing recently, promoting the steady growth of SHPT incidence in China**.

Source: CNKI; GBD 2021; China Insights Consultancy

Treatment of hyperparathyroidism

Medication Therapy

- **For patients with asymptomatic hyperparathyroidism or those who are unable to tolerate surgery, medication therapy is the preferred treatment.** With proper combination of drugs, the serum parathyroid hormone can be kept at normal level for a long period.
- Due to the severe digestive symptoms, interaction between drugs, and other possible ADRs, long-term medication therapy can be a big challenge to the compliance of the patients. Moreover, with the progression of the disease, drug resistance would reduce the therapeutical effect of medication therapy. **With all these factors, medication therapy may not be enough for patients suffering from hyperparathyroidism.**

Surgical Therapy

- **Surgical therapy is the preferred treatment of PHPT and advanced SHPT**. Typical operative methods include total parathyroidectomy (tPTX), subtotal parathyroidectomy (sPTX), and total parathyroidectomy plus auto-transplantation (tPTX-AT), all of which can effectively recover serum parathyroid hormone level and the related symptoms.
- Since PTX may cause severe operative injuries and postoperative complication, **the surgical therapy of hyperparathyroidism is still largely limited**.

Minimally Invasive Treatment

- **Absolute ethanol injection** Ultrasound-guided percutaneous ethanol injection can reduce the volume of damaged parathyroid glands, which is considered as an effective supplementary therapy.
- **Thermal ablation therapy** Thermal ablation therapy, including radiofrequency ablation (RFA), microwave ablation (MWA) and high intensity focused ultrasound (HIFU), is an advanced method to perform parathyroidectomy. But further researches are required to relieve the postoperative complications.
- **Activated Vitamin D injection** Paricalcitol is a Vitamin D_2 mimetics injected to reduce serum parathyroid hormone level.

Source: Internal Medicine; CNKI; Pharmacology; China Insights Consultancy

Comparisons of mainly used drugs for hyperparathyroidism in China

Comparisons of mainly used drugs for hyperparathyroidism in China, as of LPD

Treatment	Representative Drugs	Mechanism	Indication	Severe ADRs	Dosage	Annual Expenditure
Calcimimetic agent	Cinacalcet; Etelcalcetide; Evocalcet	Extracellular calcium-sensing receptor (CaSR) activator	Secondary hyperparathyroidism in chronic kidney diseases caused by dialysis	Cardiac dysfunction caused by hypocalcemia; digestive symptoms	30 – 60 mg each time, bid (cinacalcet); 2.5 – 15 mg each time, tiw (etelcalcetide);	~ ¥ 5,000 (cinacalcet)
Bisphosphonates	Etidronate Disodium; Pamidronate Disodium; Alendronate Sodium	Blocking bone resorption induced by osteoclast	Osteoporosis caused by different causes; heterotopic ossification; hypercalcemia	Osteonecrosis; renal failure; esophageal carcinoma; digestive symptoms	0.2 g each time, bid (etidronate disodium); 30 – 90 mg each time, q3w (pamidronate disodium); 10 mg each time, qd (alendronate sodium)	~ ¥ 1,600 (etidronate disodium)
Vitamin D and its mimetics	Calcitriol; Alfacalcidol	Promoting Ca^{2+} absorption in intestinal tissue	Osteoporosis caused by different causes; secondary hyperparathyroidism in chronic kidney diseases caused by vitamin D deficiency	-	0.25 μg each time, qd (calcitriol); 1 μg each day (alfacalcidol)	~ ¥ 3,300 (alfacalcidol)
Phosphate binder	Sevelamer	Binding to phosphate *in vivo* to inhibit the secretion of parathyroid hormone	Hyperphosphatemia caused by dialysis; SHPT	Digestive symptoms	0.8 – 1.6 g each time, tid	~ ¥ 13,000

Source: Drug Instructions; NMPA; China Insights Consultancy

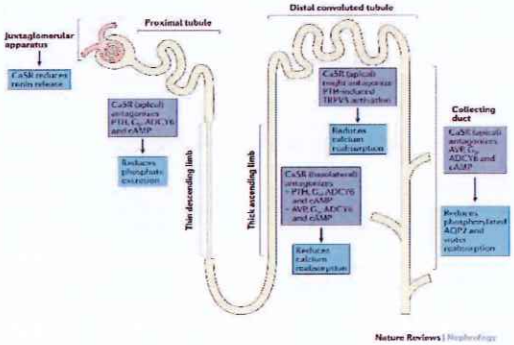
Introduction to calcimimetic agent

Hyperparathyroidism | Calcimimetic agent

Introduction to calcimimetic agent

3D structure of CaSR

- **Calcimimetic agents refer to a series of drugs that can simulate calcium's activation upon extracellular calcium-sensing receptor (CaSR).** For patients suffering from ion metabolism disorder, calcimimetic agent is an effective treatment to prevent from hyperparathyroidism and its comorbidities.
- At present, **3 calcimimetics have been approved by NMPA** for the treatment of hyperparathyroidism in patients suffering from chronic kidney disease (CKD).



CaSR-related pathway

Approved calcimimetic agents in China

Drug name	Original company	Initial approval by NMPA
Cinacalcet	Kyowa Kirin Pharma	2014/08/21
Etelcalcetide	Amgen Europe B.V.	2023/05/06
Evocalcet	Kyowa Kirin Pharma	2024/06/12

- **Secondary hyperparathyroidism is a common comorbidity of CKD** whose patients may suffer from severe calcium metabolic disorder due to the dysfunction of kidney, leading to the parathyroid hyperplasia.
- **Calcimimetic agents is recommended for the treatment of secondary hyperparathyroidism** as they can activate CaSR and block the parathyroid hyperplasia through negative feedback regulation. **Cinacalcet was the first calcimimetic agent approved globally and has bee widely applied among CKD patients.**

Source: Pubmed; NMPA; Uniprot; China Insights Consultancy

Summary of approved cinacalcet in China

Cinacalcet | Competition

Summary of approved cinacalcet in China, as of LPD

Drug name	Company	Time to pass consistency evaluation*	Specifications (Measured by $C_{22}H_{22}F_3N$)	Initial approval	VBP inclusion
Cinacalcet Hydrochloride Tablets **(Original drug)**	Kyowa Kirin Pharma	-	25 mg; 75mg	2014/08	-
Cinacalcet Hydrochloride Tablets	Joy Biophama	2020	25 mg	2020/04	-
Cinacalcet Hydrochloride Tablets	Renhe Yikang Pharma	2020	25 mg; 75 mg	2020/10	Since 2021/06 9 provinces (首次，第五批)
Cinacalcet Hydrochloride Tablets	Hencer Pharma	2020	25 mg	2020/02	Since 2021/06 7 provinces (首次，第五批)
Cinacalcet Hydrochloride Tablets	Haixi Pharma	2021	25 mg	2021/03	Since 2021/06 7 provinces (首次，第五批)
Cinacalcet Hydrochloride Tablets	Baiao Pharma	2020	25 mg	2021/04	Since 2021/06 8 provinces (首次，第五批)
Cinacalcet Hydrochloride Tablets	Shijiazhuang No.4 Pharma	2023	25 mg	2023/05	-
Cinacalcet Hydrochloride Tablets	Yingtai Pharma	2023	25 mg	2023/06	-
Cinacalcet Hydrochloride Tablets	Taifeng Pharma	2023	25 mg	2023/06	-
Cinacalcet Hydrochloride Tablets	Sunshine Mandi Pharma	2023	25 mg	2023/10	-
Cinacalcet Hydrochloride Tablets	Weigao Pharma	2024	25 mg	2024/11	-

Note: including situations where drugs are regarded as passing consistency evaluation.

Source: NMPA; China Insights Consultancy

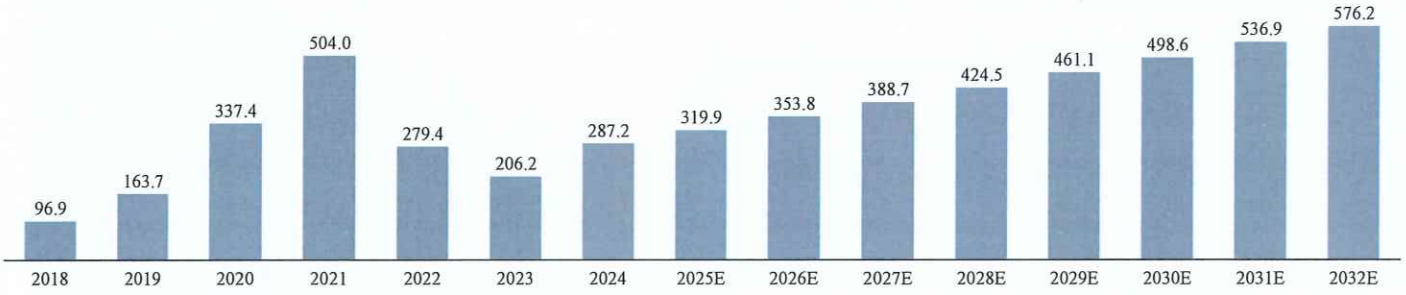
Market size of cinacalcet in China, 2018-2032E

Cinacalcet | Market size

Market size of cinacalcet in China, 2018-2032E

CAGR	2018-2024	2024-2032E
Cinacalcet	19.9%	9.1%

million RMB



Key Analysis

- The market size of cinacalcet experienced a sharp decrease in 2022 since cinacalcet was included in the 5th round of National VBP scheme.
- SHPT is a common comorbidity of renal insufficiency which effects a large proportion of the elderly. With the promotion of people aging, **SHPT can be a big threat to people's health, enabling a steady growth for the market size of cinacalcet**. Moreover, as being included in the National VBP scheme, **the reasonable price can promote the penetration of cinacalcet among SHPT patients.**

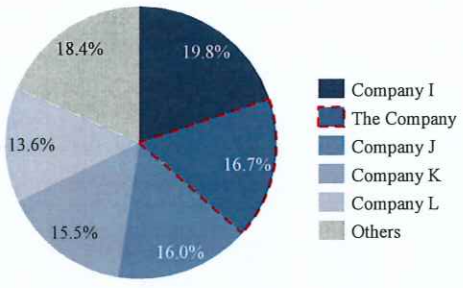
Note: *the market size is in terms of patient-end revenue.

Source: China Insights Consultancy

The VBP policy encourages the development of advanced generics, challenging the dominant position of original manufacture

Cinacalcet | Market share

Market share of cinacalcet in China, 2024



- Company I, Renhe Yikang Pharma, founded in 2018 and headquartered in Hebei Province, is a pharmaceutical group integrating innovative R&D, production and professional marketing.
- Company J, Baiao Pharma, founded in 1995 and headquartered in Beijing, focuses on providing solutions of cardiovascular diseases, rare diseases, liver diseases, etc.
- Company K, Hencer Pharma, founded in 1995 and headquartered in Jiangsu Province, focused on the R&D of nephrology and cardio-cerebrovascular therapeutic areas.
- Company L, Kyowa Kirin Pharma, headquartered in Tokyo, Japan, was founded in 1949. It is dedicated to the R&D, production, and sales of new drugs primarily for the treatment of cancer and kidney diseases.

Key Analysis

- As the original manufacture of cinacalcet, Kyowa Kirin occupied a huge market share in 2021. **After cinacalcet was included in the VBP scheme in 2021.6, China's domestic generics of cinacalcets experienced an extraordinary growth in market share and occupied a large part**.
- With the implementation of VBP policy, **China's pharmaceutical companies are encouraged to develop advanced generics** whose profits would be guaranteed after being included in the VBP scheme.

Note: *the market share is in terms of patient-end revenue.

Source: China Insights Consultancy

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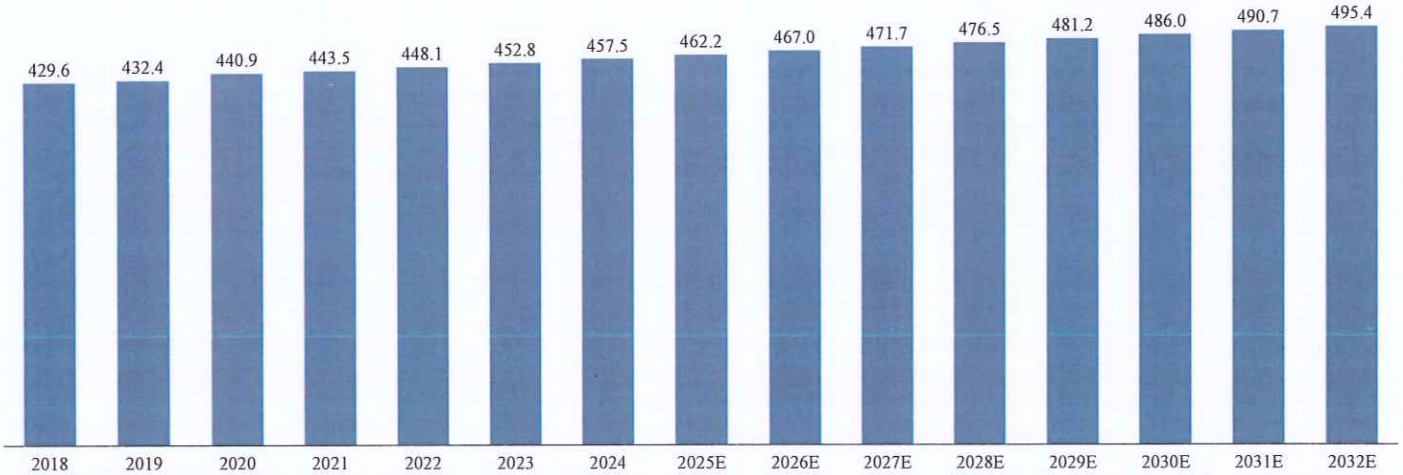
Prevalence of nervous system diseases in China, 2018-2032E

Prevalence of nervous system diseases in China, 2018-2032E

CAGR	2018-2024	2024-2032E
Neurological diseases	1.1%	1.0%

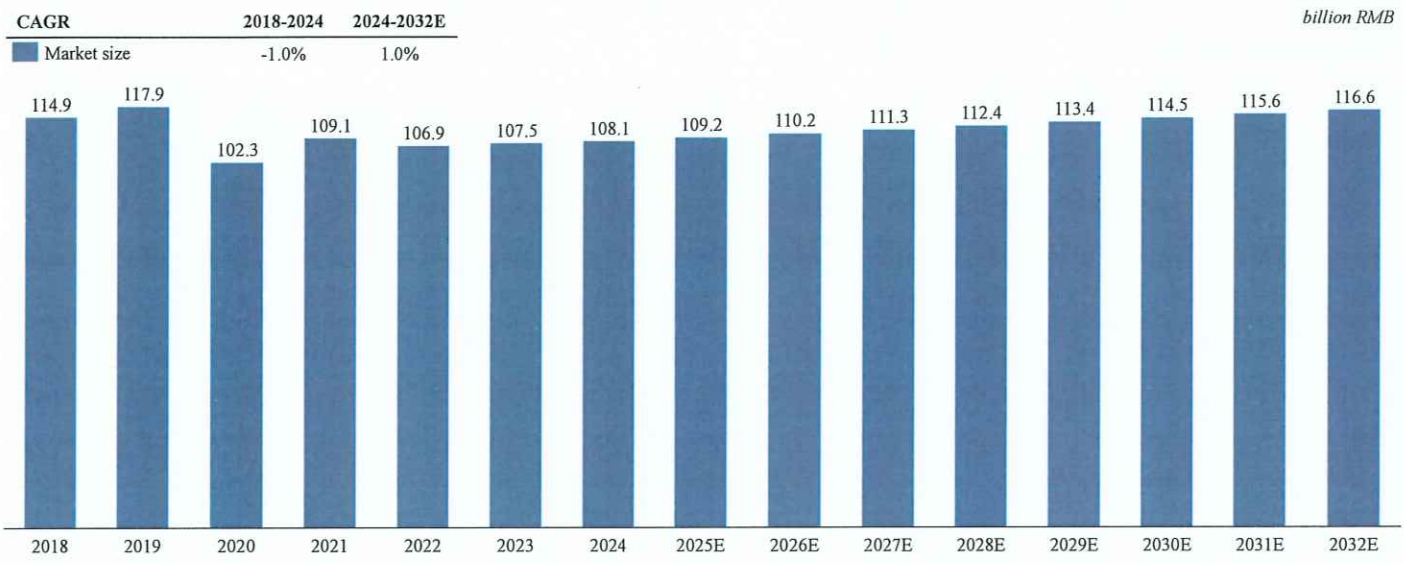
million ppl



Source: GBD 2021; China Insights Consultancy

Market size of nervous system drugs in China

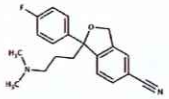
Market size of nervous system drugs in China, 2018-2032E



Source: China Insights Consultancy

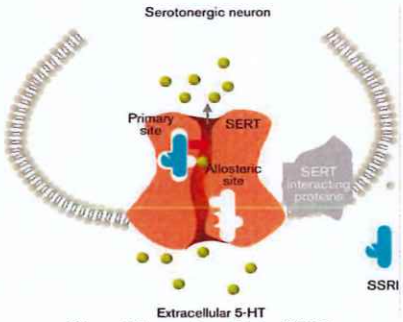
Introduction to escitalopram

Introduction to depressive disorder



Chemical structure of escitalopram

- **Depressive disorder refers to the syndromes characterized by long-term emotional depression,** companied with anxiety, illusions or delusions. As a mental disorder that may lead to commitment of suicide, depressive disorder has become a big threat to the lives of modern citizens.
- The pathogenesis of depressive disorder has not been elucidated yet. **It is widely believed that the dysfunction of neurotransmitter systems plays an important role in the onset of depressive disorder, making relevant drugs preferred therapy for depressive disorder**.
- Escitalopram belongs to selective serotonin reuptake inhibitors (SSRIs), aiming the 5-HT neurotransmitter system, **which is considered as the first choice for depressive disorders among SSRIs**.



The antidepressive effect of SSRIs

Introduction to escitalopram

- 5-HT is a kind of monoamine neurotransmitter, which can be transported into neuron through serotonin transporter (SERT). 5-HT participates in the regulation of behavior, emotion, and memory. It is reported that **up-regulated extracellular 5-HT level can promote the transduction of monoamine neurotransmitter and preform antidepressive effect**.
- SSRIs such as escitalopram can inhibit 5-HT intake through binding to the primary site of SERT, increasing extracellular 5-HT levels. **According to former researches, among all SSRIs drugs, escitalopram and selegiline are with the best balance between therapeutical effect and tolerability**.
- Though with decent therapeutical effect, some patients on SSRIs may suffer from short-term anxiety and suicidal tendency, which requires further trials to explain the underlying mechanism.

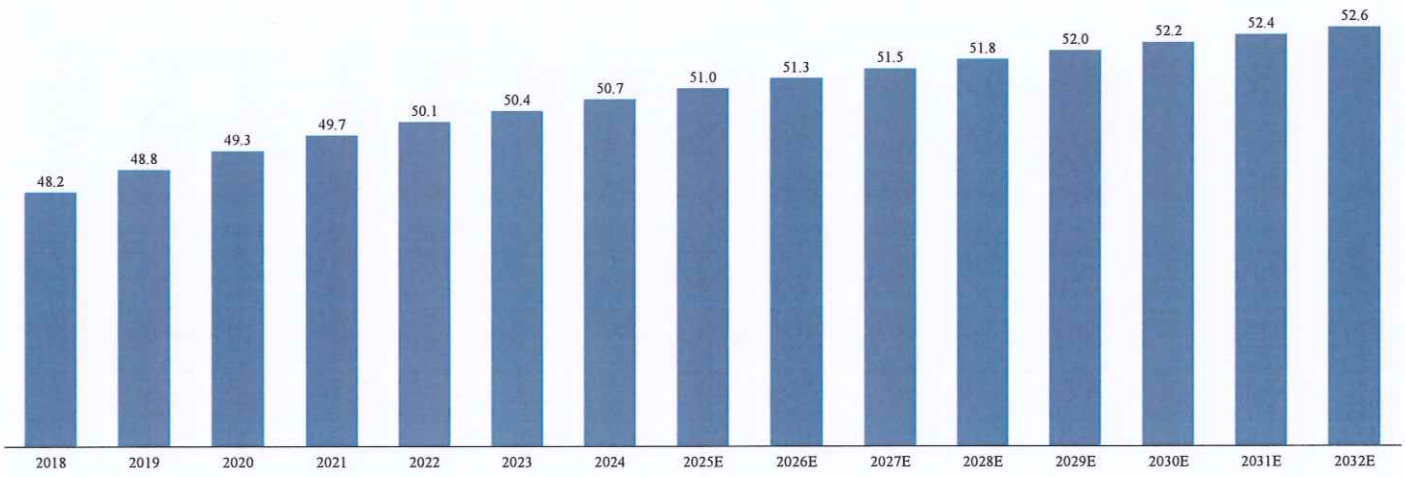
Source: Psychiatry; Pubmed; Drug Instruction; China Insights Consultancy

Prevalence of depressive disorder in China, 2018-2032E

Prevalence of depressive disorder in China

CAGR	2018-2024	2024-2032E
Depressive disorder patients in China	0.8%	0.5%

ppl million



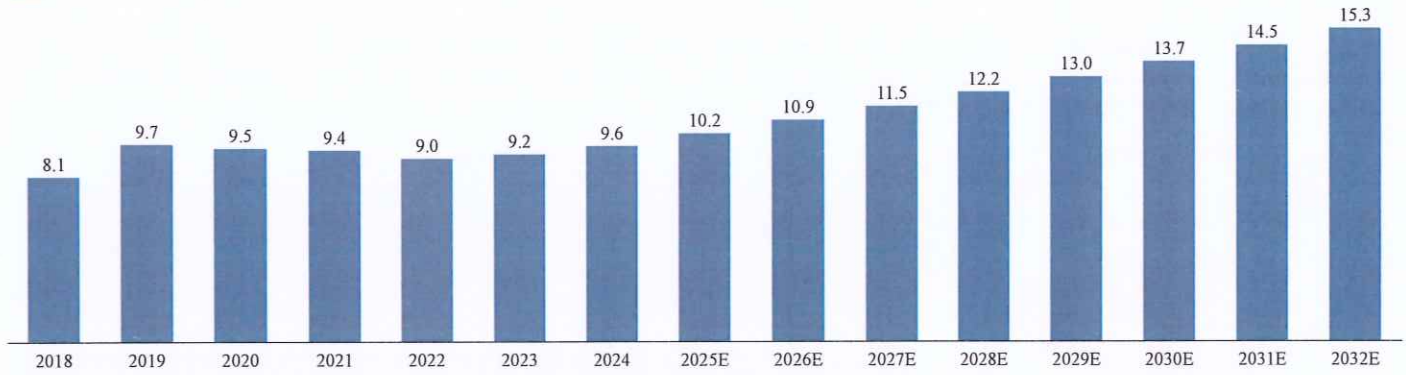
Sources: China Insights Consultancy

Market size of antidepressants in China, 2018-2032E

Market size of antidepressants in China

CAGR	2018-2024	2024-2032E
Market size of antidepressants in China	2.9%	6.0%

RMB billion



- The market size of antidepressants in China remained stable mainly because lagging awareness and underdiagnosis of depression as well as relatively strict policy control over psychotropic drugs. There are signs of potential growth in the coming years. As societal attitudes and healthcare systems evolve, the diagnosis rate and treatment rate of depression are expected to grow, accompanied with introduction of more effective and safer new drugs. The market may see great potential of growth in the future.

Sources: China Insights Consultancy

Summary of approved escitalopram in China (1/2)

Summary of approved escitalopram in China, as of LPD (1/2)

Drug Name	Company	Specifications (Measured by $C_{20}H_{21}FN_2O$)	Initial Approval	VBP Inclusion
Escitalopram Oxalate Tablets	Kelun Pharma	5 mg; 10 mg	2008	Since 2018/12 12 provinces (首次，7+4)
Escitalopram Oxalate Tablets	Jewin Pharma	5 mg; 10 mg; 20 mg	2008	Since 2019/09 8 provinces (首次，第一批)
Escitalopram Oxalate Tablets	Haisen Pharma	5 mg; 10 mg	2013	Since 2023/11 1 province (续采)
Escitalopram Oxalate Tablets	Dongting Pharma	10 mg	2014	Since 2019/09 9 provinces (首次，第一批)
Escitalopram Oxalate Tables	H. Lundbeck A/S	5 mg; 10 mg; 20 mg	2014	-
Escitalopram Oxalate Tablets	Xidian Pharma	5 mg; 10 mg	2014/09	Since 2021/05 7 provinces (续采)
Escitalopram Oxalate Tablets	Huahai Pharma	5 mg; 10 mg	2019/11	Since 2021/05 4 provinces (续采)
Escitalopram Oxalate Tablets	Haixi Pharma	10 mg	2021/03	Since 2022/09 6 provinces (续采)
Escitalopram Oxalate Tablets	HEC Group	5 mg; 10 mg; 15 mg; 20 mg	2021/04	Since 2022/09 6 provinces (续采)
Escitalopram Oxalate Tablets	Garden Pharma	5 mg; 10 mg	2021/06	Since 2022/09 5 provinces (续采)

Source: NMPA; Pharmcodia; China Insights Consultancy

Summary of approved escitalopram in China (2/2)

Summary of approved escitalopram in China, as of LPD (2/2)

Drug Name	Company	Specifications (Measured by $C_{20}H_{21}FN_2O$)	Initial Approval	VBP Inclusion
Escitalopram Oxalate Tables	Bio-diamond Pharma	20 mg	2021/06	-
Escitalopram Oxalate Tablets	Lek Pharma	10 mg	2022/01	-
Escitalopram Oxalate Tablets	Reyoung Pharma	5 mg; 10 mg; 20 mg	2022/08	Since 2021/07 1 province (续采)
Escitalopram Oxalate Oral Solution	Kanghong Pharma	120 mg	2022/12	-
Escitalopram Oxalate Tablets	Jiurui Health	10 mg; 20 mg	2023/03	Since 2024/03 3 provinces (续采)
Escitalopram Oxalate Oral Solution	Guojing Pharma	5 mg; 10 mg	2023/04	-
Escitalopram Oxalate Tablets	Tiandi Hengyi Pharma	5 mg; 10 mg	2023/08	Since 2024/03 3 provinces (续采)
Escitalopram Oxalate Tablets	Kanghong Pharma	5 mg; 10 mg	2023/12	Since 2023/08 4 provinces (续采)
Escitalopram Oxalate Tablets	Xinhua Pharma	10 mg	2024/05	-
Escitalopram Oxalate Tablets	Jiuzhou Fangyuan Pharma	5 mg; 10 mg	2024/07	-
Escitalopram Oxalate Oral Solution	Hetero Labs Limited	240 mg	2024/10	-

Source: NMPA; Pharmcodia; China Insights Consultancy

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Introduction to rheumatism diseases and commonly used anti-inflammatory drugs

- Inflammatory response, or inflammatory reaction, is a protective response involving immune cells, blood vessels, and molecular mediators. It is part of the complex biological response of body tissues to harmful stimuli (such as pathogens, damaged cells, and irritants). When the body is infected or damaged, the inflammatory response is initiated by the host immune response to fight against danger signals. It isolates the infected and damaged parts and attempts to restore the body's balance. It involves the regeneration process of the body's balance, such as wound healing and resistance to pathogens.

Introduction to rheumatic disease

- Rheumatism, also known as rheumatic disease or rheumatic disorder, refers to a class of diseases that invade "joints" or "soft tissues around joints" and cause chronic pain; the damaged tissues include: bones, cartilage, muscles, tendons, ligaments, fascia, and other intrinsic connective tissues. Its symptoms often occur intermittently. Rheumatic diseases mainly include the following types of disease, but not limited to:
  - Rheumatoid arthritis
  - Gouty arthritis
  - Ankylosing spondylitis
  - Psoriatic arthritis
  - Lupus erythematosus
  - Degenerative arthritis
  - Fibromyalgia
  - Scleroderma

……

Commonly used anti-rheumatic drugs include:

- Hydroxychloroquine sulfate, as a traditional antimalarial drug, was first synthesized in 1944. Also, it can **exert anti-inflammatory and immunomodulatory effects** through multiple pathways such as inhibiting the processing and presentation of autoantigens, synovial hyperplasia and lysosomal function so as to reducing the expression of inflammatory cytokines.

- Diclofenac is a **non-steroidal anti-inflammatory analgesic** derived from phenylacetic acid. Its mechanism of action is to inhibit the activity of cyclooxygenase, thereby blocking the conversion of arachidonic acid into prostaglandins. Diclofenac is a stronger non-steroidal anti-inflammatory drug, compared to aspirin and indomethacin.

- Celecoxib is a nonsteroidal anti-inflammatory drug used to **treat mild to moderate pain and help relieve symptoms of arthritis**, such as inflammation, swelling, stiffness, and joint pain. According to *Livia Puljak et al.*, celecoxib is slightly **better** than placebo and some tNSAIDs **in reducing pain and improving physical function**.

Source: 中国风湿病学杂志; NMPA; China Insights Consultancy

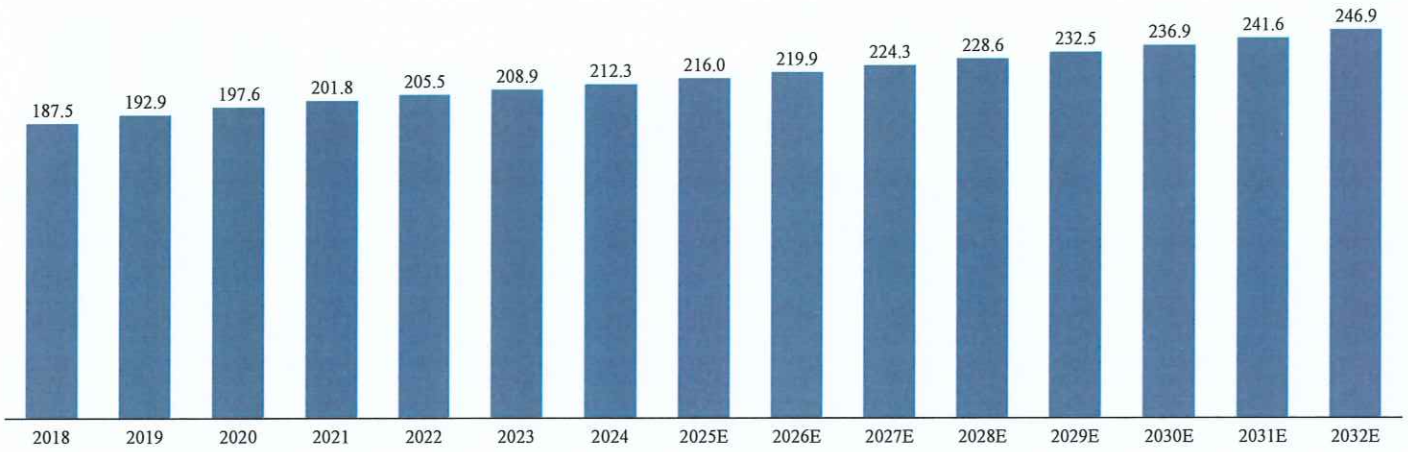
Prevalence of rheumatism in China, 2018-2032E

Rheumatism | Prevalence

Prevalence of rheumatism in China, 2018-2032E

CAGR	2018-2024	2024-2032E
Market size	2.1%	1.9%

million ppl



Source: China Insights Consultancy

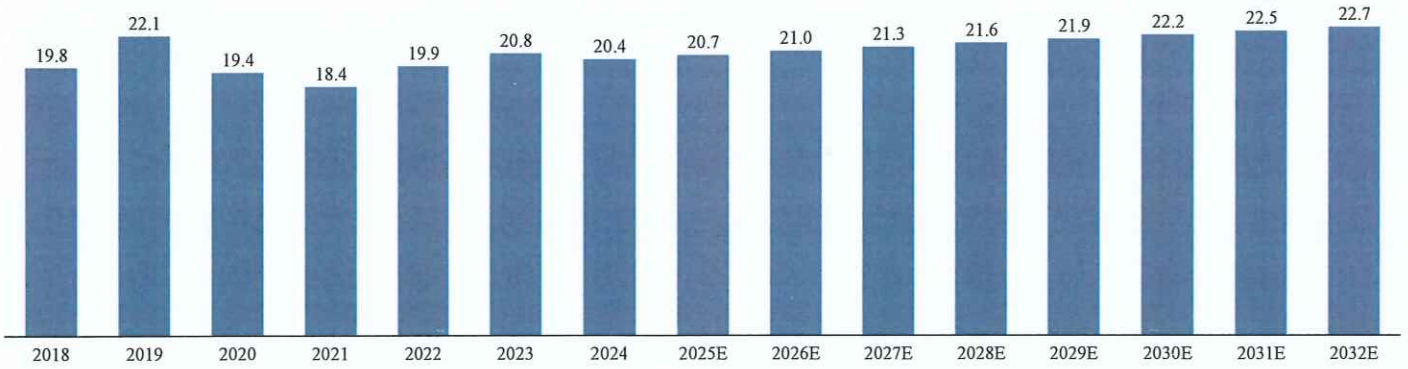
Market size of anti-rheumatic drugs in China

Inflammatory diseases | Market size

Market size of anti-rheumatic drugs in China, 2018-2032E

CAGR	2018-2024	2024-2032E
Market size	0.5%	1.4%

billion RMB



- The market size experienced fluctuations during 2020-2022 because of the pandemic. After that, it grew steadily to 20.4 bn RMB in 2024 and is expected to increase to 23.5 bn by 2032. The prevalence of rheumatic diseases, which are chronic, is estimated to be stable. In the meanwhile, current treatment schemes including traditional chemical drugs and biologics are well-developed and relatively mature. Thus the market size in total is expected to grow stably and slightly.

Source: China Insights Consultancy

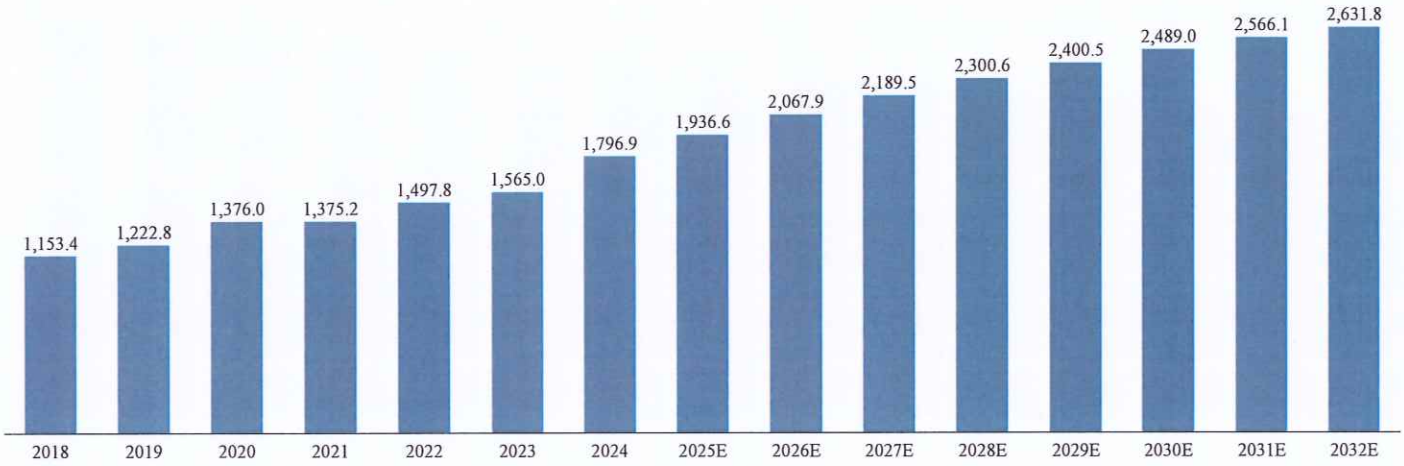
Market size of hydroxychloroquinein China

Inflammatory diseases | Market size

Market size of hydroxychloroquine in China, 2018-2032E

CAGR	2018-2024	2024-2032E
Market size	7.7%	4.9%

million RMB



Source: China Insights Consultancy

Summary of approved hydroxychloroquine in China

Hydroxychloroquine | Competition

Summary of approved hydroxychloroquine in China, as of LPD

Drug name	Company	Specifications (Measured by $C_{20}H_{21}FN_2O$)	Initial approval	Time to pass consistency evaluation*	VBP inclusion
Hydroxychloroquine Sulfate Tablets	Shanghai Pharma	0.1 g; 0.2 g	1999	2022/01	Since 2022/03 5 provinces (省采)
Hydroxychloroquine Sulfate Tablets	Sanofi-aventis Ireland Ltd.	0.2 g	2016	-	Since 2024/04 3 provinces (省采)
Hydroxychloroquine Sulfate Tablets	Haixi Pharma	0.2 g	2023/10	2023/10	Since 2024/06 2 provinces (省采)
Hydroxychloroquine Sulfate Tablets	Sinomune Pharma	0.2 g	2024/04	2024/04	-
Hydroxychloroquine Sulfate Tablets	Xinrui Pharma	0.2 g	2024/04	2024/04	-
Hydroxychloroquine Sulfate Tablets	Grand Pharma	0.2 g	2024/04	2024/04	-
Hydroxychloroquine Sulfate Tablets	Chang Zheng-Cinkate Pharma	0.2 g	2024/05	2024/05	-
Hydroxychloroquine Sulfate Tablets	Hacon Pharma	0.2 g	2024/10	2024/10	-
Hydroxychloroquine Sulfate Tablets	Xi'an Haixin Pharma	0.2 g	2024/12	2024/12	-
Hydroxychloroquine Sulfate Tablets	Fujian Cosunter Pharma	0.2 g	2025/01	2025/01	
Hydroxychloroquine Sulfate Tablets	Porton Pharma	0.1g; 0.2 g	2025/02	2025/02	-

Note: including situations where drugs are regarded as passing consistency evaluation.

Source: NMPA; Pharmcodia; China Insights Consultancy

Summary of approved celecoxib in China (1/2)

Summary of approved celecoxib in China, as of LPD (1/2)

Drug name	Company	Specifications (Measured by $C_{17}H_{14}F_3N_3O_2S$)	Initial approval	Time of passing consistency evaluation*	VBP inclusion
Celecoxib Capsules	Pifzer	0.1 g; 0.2 g	2014	-	-
Celecoxib Capsules	Hengrui Pharma	0.2 g	2019/11	2019/12	-
Celecoxib Capsules	Qingjiang Pharma	0.2 g	2019/12	2020/01	Since 2020/08 7 provinces (首次，第三批)
Celecoxib Capsules	Gowell Pharma	0.1 g; 0.2 g	2020/07	2020/07	Since 2020/08 7 provinces (首次，第三批)
Celecoxib Capsules	CSPC	0.1 g; 0.2 g	2020/07	2020/07	Since 2020/08 9 provinces (首次，第三批)
Celecoxib Capsules	BAHEAL Pharma	0.1 g; 0.2 g	2020/07	2020/07	Since 2020/08 8 provinces (首次，第三批)
Celecoxib Capsules	Qilu Pharma	0.1 g; 0.2 g	2020/09	2020/09	Since 2023/06 1 province (续采)
Celecoxib Capsules	King York Heping Pharma	0.1 g; 0.2 g	2020/12	2020/12	-
Celecoxib Capsules	Simcere Pharma	0.2 g	2021/01	2021/01	-
Celecoxib Capsules	Fuyuan Pharma	0.2 g	2021/01	2021/01	Since 2023/06 3 provinces (续采)
Celecoxib Capsules	Kelun Pharma	0.2 g	2021/05	2021/05	Since 2023/06 1 province (续采)

Note: including situations where drugs are regarded as passing consistency evaluation.

Source: NMPA; China Insights Consultancy

Summary of approved celecoxib in China (2/2)

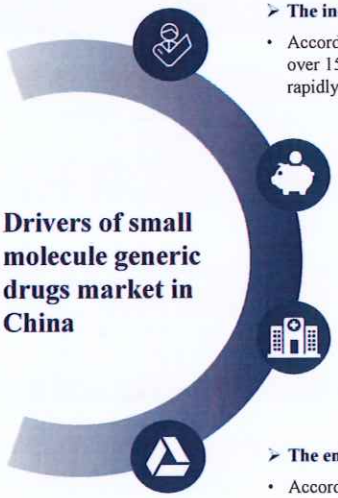
Summary of approved celecoxib in China, as of LPD (2/2)

Drug name	Company	Specifications (Measured by $C_{17}H_{14}F_3N_3O_2S$)	Initial approval	Time to pass consistency evaluation*	VBP inclusion
Celecoxib Capsules	Yangtze River Pharma	0.2 g	2021/07	2021/07	-
Celecoxib Capsules	PKU Healthcare	0.2 g	2021/09	2021/09	-
Celecoxib Capsules	Haixi Pharma	0.2 g	2021/10	2021/10	Since 2023/06 1 province (续采)
Celecoxib Capsules	Yabao Pharma	0.1 g; 0.2 g	2022/01	2022/01	Since 2023/06 4 provinces (续采)
Celecoxib Capsules	Yatai Pharma	0.2 g	2022/11	2022/11	Since 2024/06 1 province (续采)
Celecoxib Capsules	Zitonggong Pharma	0.2 g	2023/04	2023/04	-
Celecoxib Capsules	Yiling Pharma	0.1 g; 0.2 g	2023/04	2023/04	Since 2024/06 2 provinces (续采)
Celecoxib Capsules	Xinsidun Pharma	0.2 g	2023/07	2023/07	-
Celecoxib Capsules	Minhai Pharma	0.2 g	2023/12	2023/12	-
Celecoxib Capsules	Nona Pharma	0.2 g	2024/02	2024/02	Since 2024/06 2 provinces (续采)
Celecoxib Capsules	Coco King Pharma	0.2 g	2024/02	2024/02	-
Celecoxib Capsules	Sciecure Pharma	0.2 g	2024/06	2024/06	-
Celecoxib Capsules	Changzhou Pharma	0.2 g	2024/07	2024/07	-

Note: including situations where drugs are regarded as passing consistency evaluation.

Source: NMPA; Pharmcodia; China Insights Consultancy

Drivers of small molecule generic drugs market in China



➢ **The increased population of patients and variety of diseases promotes the growth of pharmaceutical market**

- According to data from the National Bureau of Statistics, in 2023, China had more than 200 million people aged 65 and above, making up over 15% of the total population. With the promotion of population aging and people's awareness in health, the demand for medication grows rapidly, driving the development of China's generic drugs market, which is an important part of the pharmaceutical market.

➢ **With a lower price compared to original drugs, generic drugs show obvious cost advantages in market competition**

- Due to the high investment in research and development (R&D), original drugs are usually with high price, compared to which generic drugs are more reasonably priced. With the growing demand for medication, generic drugs have obvious cost advantages in the market competition, driving the development of the generic drugs market.

➢ **A series of supporting policies has been issued by China government, providing environment for the development of generic drug market**

- A series of supporting policies have been implemented by China government in the last decade. With the simplified approval process, reduced cost for registration, and the implementation of BE trials, the development of generic drugs are now with a better policy environment, driving the growth of the market.

➢ **The enhancement in pharmaceutical industry enables the development of advanced generic drugs**

- According to China Science and Technology Statistics, China's pharmaceutical R&D expenditure grown at a CAGR of 13.6% from 2016 to 2022. With the enhancement in pharmaceutical researches, China's generic companies are now able to develop more advanced generic drugs, driving the market to grow in a more rapid manner.

Source: National Bureau of Statistics; China Insights Consultancy

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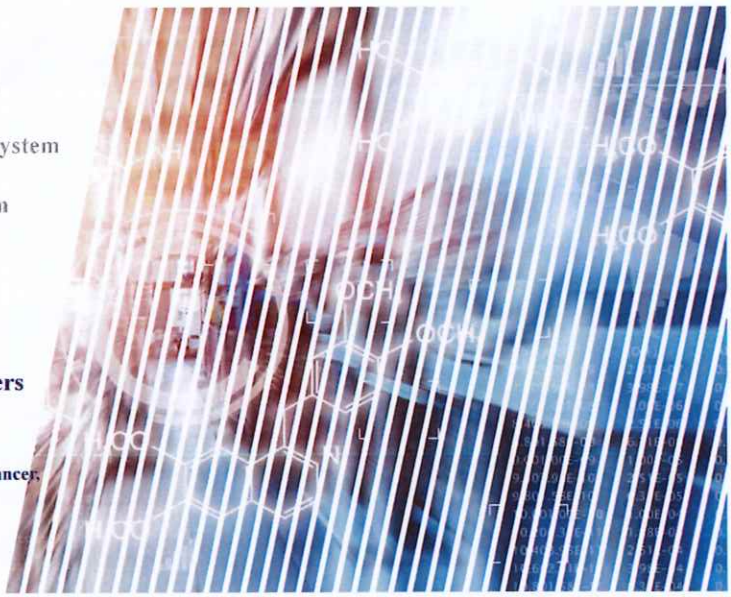


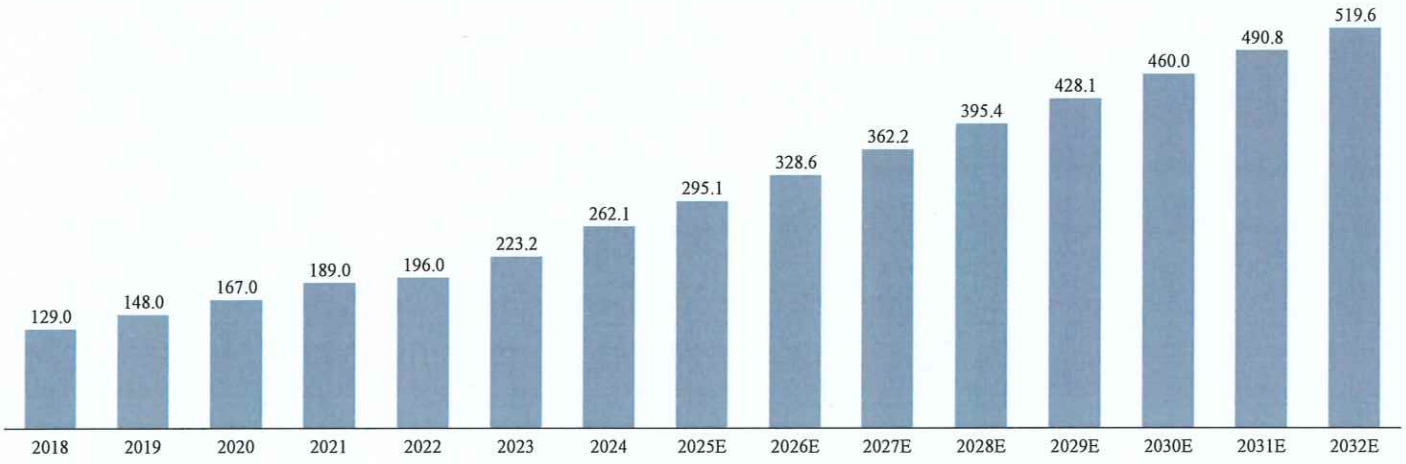
Global oncology drug market size was USD 262.1 billion in 2023 and is expecting to reach about USD 519.6 billion in 2032

Global oncology drug | Market size

Global oncology drug market size, 2018-2032E

CAGR	2018-24	2024-32E
Global	12.5%	8.9%

billion USD



Source: China Insights Consultancy

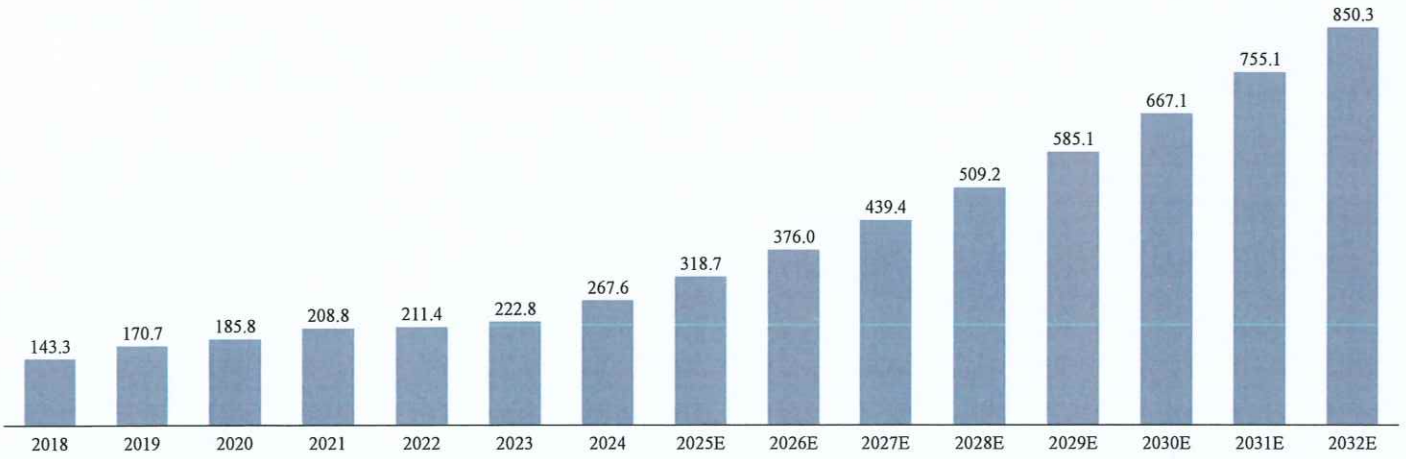
China oncology drug market size was RMB 267.7 billion in 2024 and is expecting to reach about RMB 850.3 billion in 2032

China oncology drug | Market size

China oncology drug market size, 2018-2032E

CAGR	2018-24	2024-32E
China	11.0%	15.5%

billion RMB



Source: Chinese of Society of Clinical Oncology(CSCO);CIC

Current pain points in cancer treatment in China

China oncology drug | Pain points

Current pain points in cancer treatment in China

Uneven Distribution of High-Quality Cancer Treatment Services	Slow Advancement of Treatment Technologies and Personalized Medicine	Heavy Financial and Psychological Burden on Patients and Families	Lack of Standardized Treatment Guidelines Across Regions
☐ Cancer treatment services in China exhibit significant disparities across different regions, reflecting uneven distribution of medical resources and healthcare quality ☐ In economically developed areas like Beijing, Shanghai, and Guangzhou, patients benefit from state-of-the-art cancer treatment technologies, such as precision medicine, targeted therapies, and immunotherapies. Conversely, in less developed regions, limited medical resources result in delayed diagnoses, outdated treatment options, and high treatment costs, contributing to lower survival rates compared to wealthier regions	☐ This is particularly evident in the pace of implementing personalized treatments. The complexity of cancer heterogeneity makes personalized therapy essential. Despite being a future trend, the development and widespread application of such treatments in China have been relatively slow, with most treatments still following standardized guidelines. Challenges include balancing guideline-based care with the need for individualized therapies tailored to each patient's unique cancer profile ☐ Additionally, regulatory frameworks and clinical evidence for off-label use of drugs in personalized care are still evolving	☐ The high cost of treatment is a major factor. Despite the inclusion of more cancer drugs into China's national reimbursement list, the financial strain remains a reality for many families. Even when certain treatments are included in insurance, out-of-pocket expenses and indirect costs like travel for treatment or purchasing drugs from outside hospitals continue to exacerbate financial pressures ☐ In addition to these costs, the psychological burden is equally overwhelming. The constant worry about treatment affordability can lead to reduced medication adherence or even the complete abandonment of necessary therapies, worsening patient outcomes	☐ These variations in medical practices are largely due to disparities in the development and implementation of clinical protocols, particularly between urban and rural areas. Hospitals in major cities often follow more advanced, internationally-aligned guidelines, while smaller, less resourced hospitals may adhere to outdated or locally modified protocols ☐ Furthermore, many of China's clinical guidelines are less rigorous compared to those in developed countries, often lacking comprehensive evidence-based reviews. This inconsistency in guideline quality and application has made it difficult to standardize treatments and accurately assess the efficacy of different approaches

Source: China Insights Consultancy

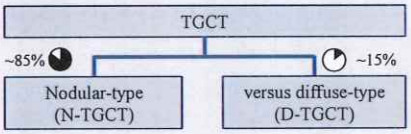
Overview of tenosynovial giant cell tumor (TGCT)

TGCT | Introduction

Overview of tenosynovial giant cell tumor (TGCT)

- Tenosynovial giant cell tumour (TGCT), previously called pigmented villonodular tenosynovitis (PVNS) or giant cell tumour of tendon sheath (GCTTS), is a rare mesenchymal neoplasm arising from the synovium of joints and tendon sheaths. It is molecularly characterized by recurrent genomic aberrations often involving **the colony-stimulating factor 1 gene (CSF1)**
- Most patients affected by TGCT are young and, although usually **not life-threatening**, the disease and its treatment may **impact quality of life (QoL)**
- Effective systemic treatment options are not available in most countries. **In China**, the National Health Commission issued the "Notice on the Publication of the Second Batch of Rare Disease Catalogs" officially **including TGCT in the rare disease catalog** on September 18, 2023

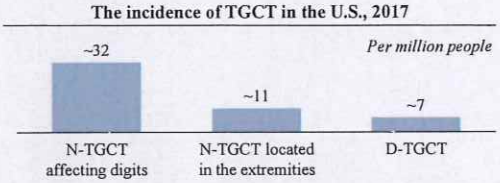
Classification:



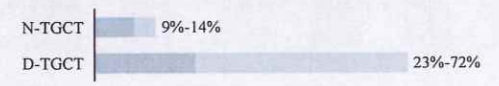
- **N-TGCT:** usually presents as a single lesion and arises in soft tissue, near tendons or interphalangeal joints. Occasionally, N-TGCT can erode bone or involve the overlying skin
- **D-TGCT:** shows extensive and infiltrative involvement of the synovium of the joint and/or tendon sheath and extends into extra-articular structures

Epidemiology:

The incidence of TGCT in the U.S., 2017



Recurrences in TGCT



Diagnosis:

- MRI is the preferred technique for detection and characterization of TGCT
  - The recommended minimal MRI protocol includes T1-weighted, T2-weighted and a fluid-sensitive sequences
  - Gadolinium contrast administration is recommended, and subtraction of pre- and post-contrast T1-weighted images performed
- N-TGCT and D-TGCT share a common pathogenesis, so **detection of CSF1 rearrangement** by cytogenetic or molecular genetic analyses **is neither required for diagnosis nor has predictive value**

Source: TGCT support; Cancer Treatment Reviews; China Insights Consultancy

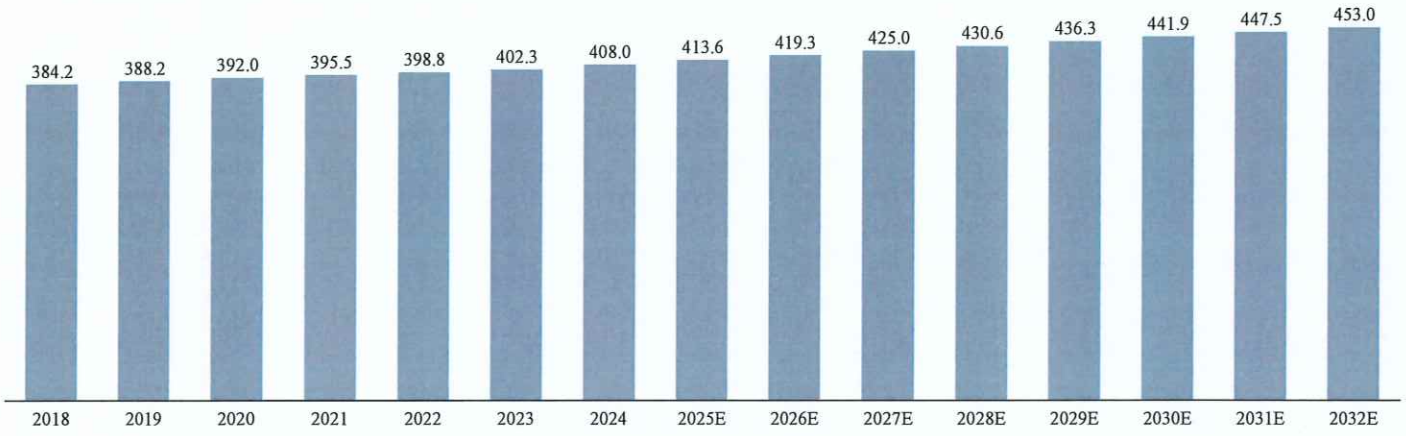
Global incidence of TGCT, 2018-2032E

TGCT | Incidence

Global incidence of TGCT, 2018-2032E

CAGR	2018-2024	2024-2032E
TGCT	1.0%	1.3%

k ppl



Source: China Insights Consultancy

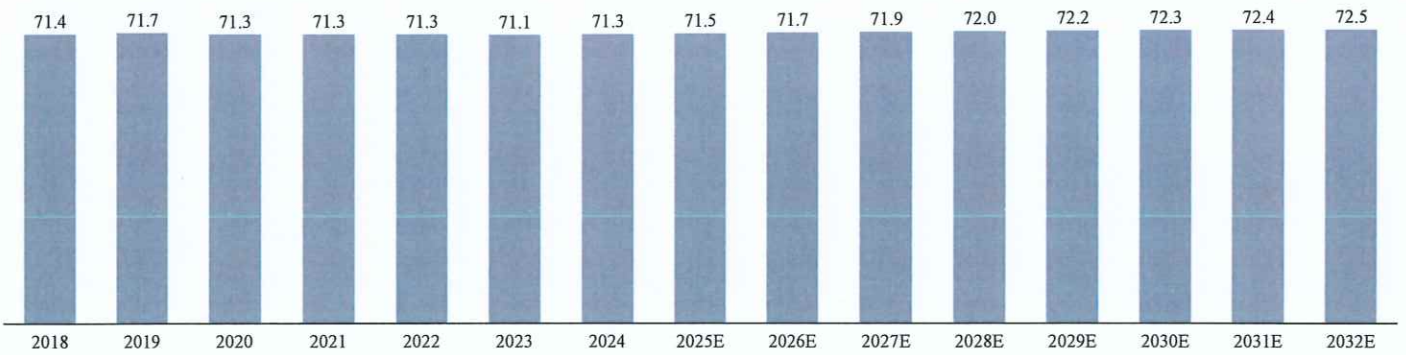
Incidence of TGCT in China, 2018-2032E

TGCT | Incidence

Incidence of TGCT in China, 2018-2032E

CAGR	2018-2024	2024-2032E
TGCT	0.0%	0.2%

k ppl



Source: China Insights Consultancy

Treatment path for TGCT

TGCT › Treatment pathway

Treatment path for TGCT

TGCT

Surgery (common)

- The preferred approach is resection either with **marginal excision in N-TGCT** or with **extensive synovectomy in diffusely involved joints or tendon sheaths for D-TGCT**, preferably when macroscopically complete resection is achievable and it can be accomplished without significant morbidity for durable local control and improved QoL

N-TGCT	D-TGCT
N-TGCT can be managed by complete marginal resection, with low LRR	Surgery for D-TGCT is associated with high LR risk and postoperative complications

Systemic treatment

- In asymptomatic disease, active surveillance (AS) is the initial preferred approach; in symptomatic disease, AS can still be offered particularly if patients perceive the symptoms as manageable
- **Patients with difficult to manage, symptomatic disease, or moderate/severe functional impairment** may be candidates for systemic treatment if surgery would be associated with significant morbidity

CSF1R inhibitors are considered standard agent

- CSF1 is highly expressed in all TGCT providing the basis for targeting the CSF1R pathway. CSF1R pathway inhibitors have shown activity in TGCT with substantial tumour shrinkage, symptomatic and functional improvement, and long-term disease control
- **Pexidartinib (Turalio®) is the only treatment approved by the FDA in 2019.** However, pexidartinib has the potential for severe hepatotoxicity, and the FDA has issued a black box warning for fatal liver injury
- **In China**, since pexidartinib has not yet been launched, it is currently recommended that patients with symptomatic TGCT who are at risk of severe complications or functional limitations, and whose symptoms cannot be improved through surgery, **prioritize participating in clinical trials**

Radiotherapy/Cryotherapy

- **Radiotherapy:** the available literature provides insufficient data to propose reliable recommendations for the use of radiotherapy as a standard treatment for TGCT, including the neoadjuvant, adjuvant, or relapsed setting, even though some retrospective series reported a positive impact
- **Cryotherapy:** it is investigational as available data are insufficient to support the value of this procedure in TGCT

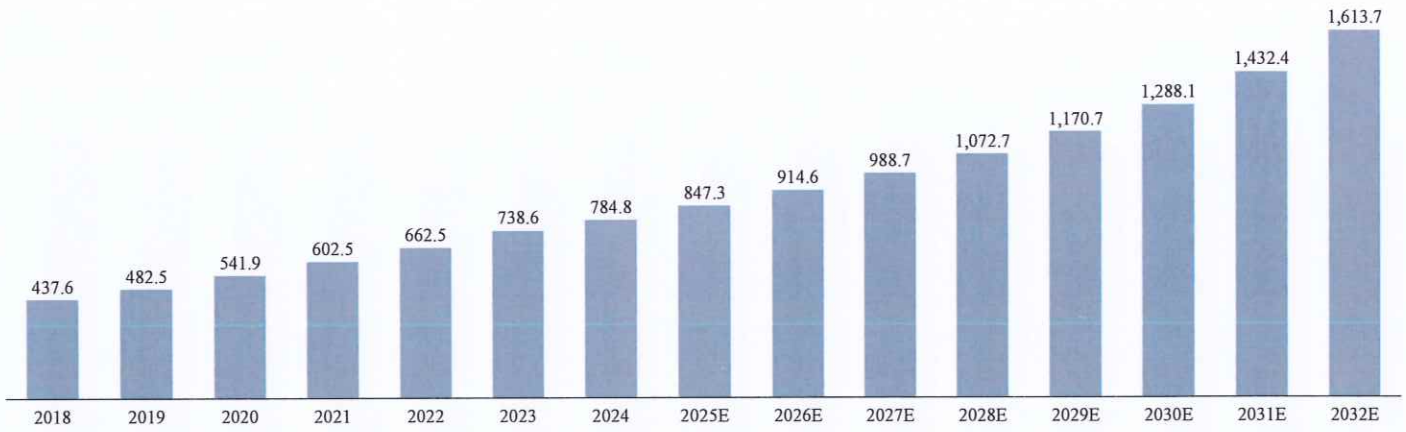
Source: Cancer Treatment Reviews; CSCO2024; China Insights Consultancy

Global market size of TGCT drugs, 2018-2032E

Global TGCT drugs market size, 2018-2032E

CAGR	2018-24	2024-32E
TGCT drugs	10.2%	9.4%

million USD



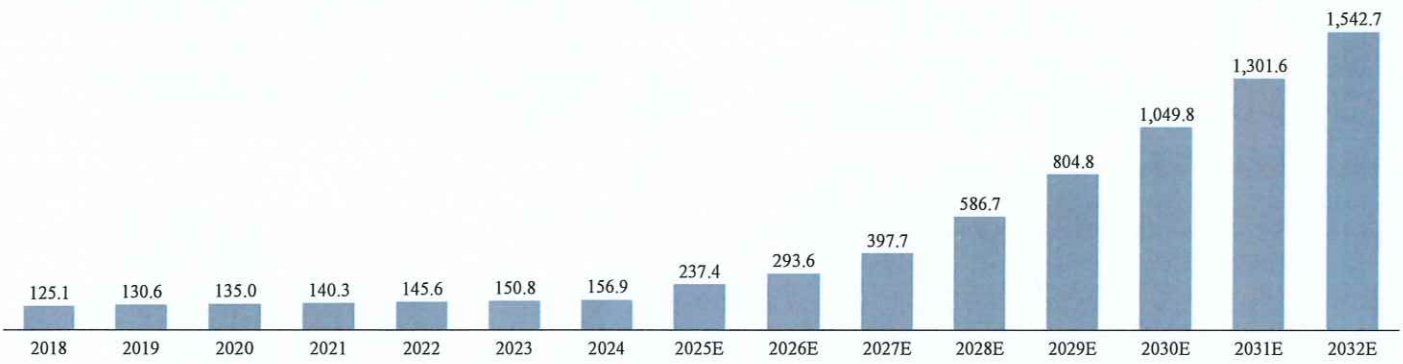
Source: China Insights Consultancy

Market size of TGCT drugs in China, 2018-2032E

China TGCT drugs market size, 2018-2032E

CAGR	2018-24	2024-32E
TGCT drugs	3.8%	33.1%

million RMB



- **The size of TGCT drug market seemed to be stable during the past 5 years due to the fact that there were no highly drugs available except for chemotherapy.** However, a growing number of drug candidates have illustrated significant clinical potential. The new therapies are expected to be approved in 2025, and by then, the market is expected to grow faster and greater.

Source: China Insights Consultancy

Global clinical pipelines of innovative drugs for TGCT, as of LPD

TGCT | Clinical pipeline

Global clinical pipelines of innovative drugs for TGCT, as of LPD

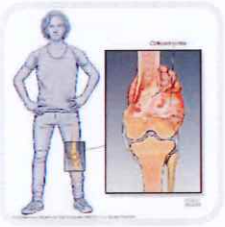
Drug name/code	Target	Company	Phase	Indications	First Posted Date	Trial Number	Location
Pexidartinib[1]	KIT, CSF1R, FLT3	Daiichi Sankyo	NDA	TGCT	2025-01-25	/	China
			II	TGCT	2021-01-11	NCT04703322	Japan
Pimicotinib	CSF1R	Abbisko Therapeutics	NDA	TGCT	2025-06-09	/	China
			I	TGCT	2019-12-10	NCT04192344	Global
Emactuzumab	CSF-1R	SynOx Therapeutics	III	TGCT	2022-06-14	NCT05417789	Global
AMB-05X	CSF1R	AmMax Bio	II	TGCT	2022-04-27	NCT05349643	Global
C019199	CSF1R, DDR1, VEGFR2	Haixi Pharma	I[2]	TGCT	2022-12-09	CTR20223103	China
SYHA-1813	VEGFR, CSF1R	Runshi Pharma	I	TGCT	2021-06-03	CTR20210775	China
BC-006 injection	CSF1R	Dragon Boat Bio	I	Solid tumors including TGCT	2021-07-23	CTR20211792	China
HMPL-653	CSF1R	Hutchison MediPharma	I	TGCT	2022-01-18	CTR20213205	China

Note: 1 Pexidartinib has only been approved in the USA. 2 Haixi Pharma has completed Phase I clinical trial as of the LPD.

Source: CDE; clinicaltrials; China Insights Consultancy

Overview of osteosarcoma

Overview of osteosarcoma



- Osteosarcoma is an osteoid-producing malignancy of mesenchymal origins. This high-grade tumor is the most common primary malignancy of bone and is often fatal in both children and adults
- Similar to other solid tumors, osteosarcoma is highly malignant with a poor prognosis, and it is prone to distant metastasis, particularly to the lungs within a short period. The mortality rate is relatively high

Epidemiology:

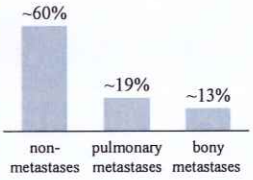
- **Incidence:** the annual incidence of osteosarcoma is **(2~3) per million people**, accounting for 0.2% of all human malignancies and 11.7% of primary bone tumors
- **Age:** osteosarcoma predominantly occurs in adolescents, with **~75%** of cases diagnosed in patients between the ages of 15 and 25
- **Sex:** the male-to-female ratio for this disease is **~14:1**, with this difference being particularly pronounced in individuals under the age of 20
- **Site of onset**: 80%-90% of osteosarcomas occur in long tubular bones, with the most common sites being the distal femur and proximal tibia, followed by the proximal humerus. These three locations account for **~85%** of all limb osteosarcomas

Etiology & Diagnosis

- **Etiology of osteosarcoma:** is complex and not well understood. Increased risk has been associated with multiple germline mutation disorders including hereditary retinoblastoma, Rothmund–Thomson syndrome, Li Fraumeni syndrome, and Bloom syndrome, among others
- **Diagnosis of osteosarcoma:** is best accomplished via a comprehensive multidisciplinary approach. Alkaline phosphatase (ALP) and lactose dehydrogenase (LDH) are useful serum biomarkers

Prognosis

Five-year survival rate



- Metastatic disease is classified by location as either pulmonary or extrapulmonary and is the major cause of osteosarcoma-related death
- While bony metastases are associated with poorer prognoses, the lung is involved in **~80%** of cases and subsequent respiratory compromise is responsible for most of the death toll
- Even in the subset of patients free of primary metastases, **~40%** will go on to eventually develop a secondary metastasis

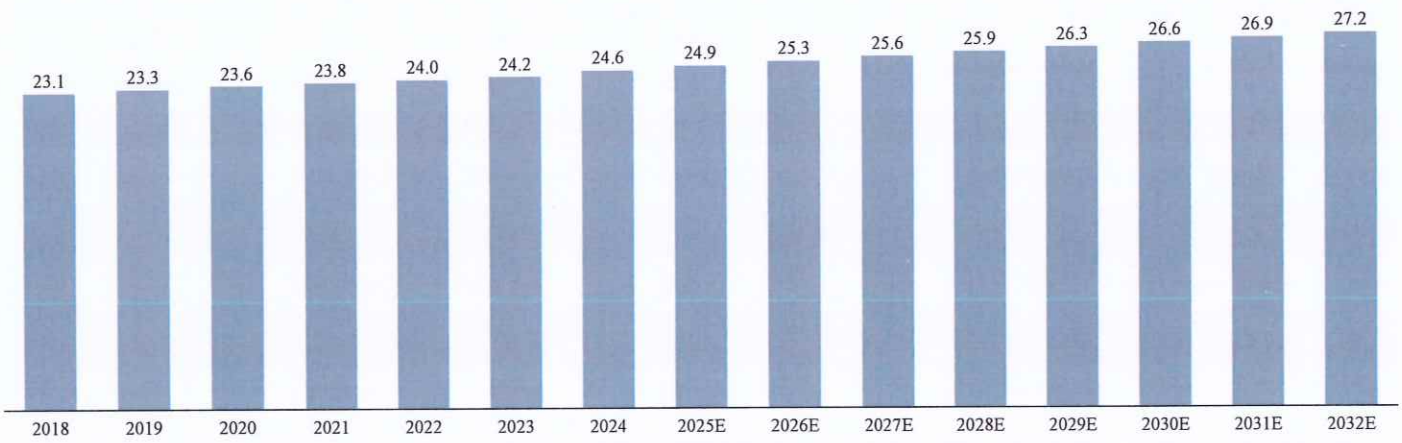
Source: Rheumatol Ther.; CSCO2024; Mayo Clinic; China Insights Consultancy

Global incidence of osteosarcoma, 2018-2032E

Global incidence of osteosarcoma, 2018-2032E

CAGR	2018-2024	2024-2032E
Osteosarcoma	1.1%	1.3%

k ppl



Source: China Insights Consultancy

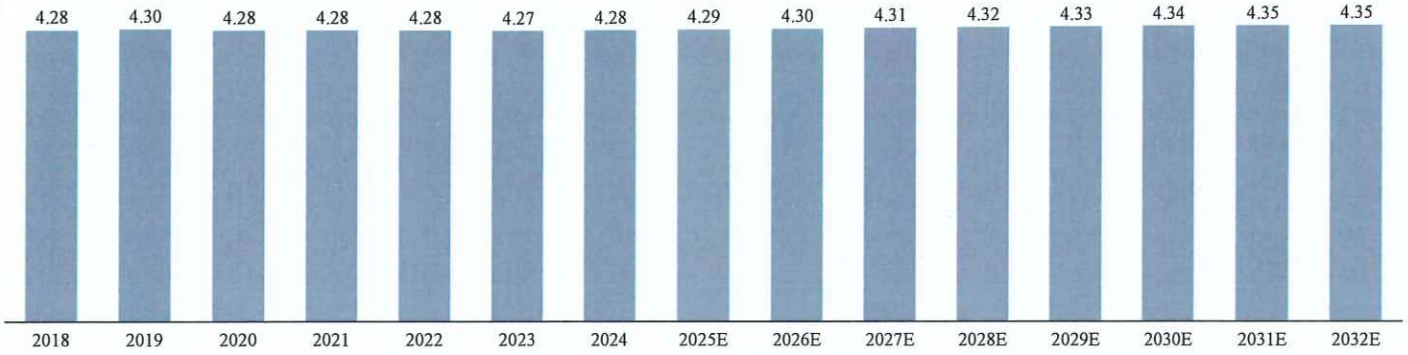
Incidence of osteosarcoma in China, 2018-2032E

Osteosarcoma > Incidence

Incidence of osteosarcoma in China, 2018-2032E

CAGR	2018-2024	2024-2032E
Osteosarcoma	0.0%	0.2%

k ppl



Source: China Insights Consultancy

Treatment path for osteosarcoma

Osteosarcoma > Treatment pathway

Treatment path for osteosarcoma

Osteosarcoma

First-line

➢ **SoC: Neoadjuvant chemotherapy, surgery, and then post-operative adjuvant chemotherapy**

Neoadjuvant chemotherapy → **Surgery** → **Post-operative adjuvant chemotherapy**

a) Neoadjuvant chemotherapy: the goal for a positive treatment with neoadjuvant chemotherapy is to achieve at least 90% necrosis on the surgically resected tumor

- ☐ **Preferred:** MAP (high-dose methotrexate, cisplatin, doxorubicin)
- ☐ MAPI (high-dose methotrexate, cisplatin, doxorubicin, isofosfamide)
- ☐ API (cisplatin, doxorubicin, isofosfamide)
- ☐ AP (cisplatin, doxorubicin)

b) Surgery: usually involves tumor resection with negative margins

- ☐ 4 different types of surgical margins: intralesional, marginal, wide, and radical
- ☐ For high-grade osteosarcoma patients who respond well to neoadjuvant chemotherapy, limb-sparing surgery is the preferred option if a wide resection is possible. Amputation is usually considered only for tumors in difficult locations where limb-sparing surgery cannot ensure clear margins
- ☐ In patients with disseminated disease, the complete resection of pulmonary metastases is vital when possible

c) Post-operative adjuvant chemotherapy: maintaining or adjusting the original chemotherapy regimen depends on the effectiveness of neoadjuvant chemotherapy

➢ **Radiation therapy (not used for a majority of cases) :** may be used to help clear microscopic or minimal residual disease when substantial surgical resection is not possible and should be combined with surgical resection and chemotherapy whenever possible

Second-line

➢ **Preferred: Clinical trials**

➢ **Weak medical evidence support:**

- high-dose ifosfamide + etoposide
- gemcitabine ± docetaxel
- cyclophosphamide + etoposide
- cyclophosphamide + topotecan
- ifosfamide + carboplatin + etoposide
- high-dose methotrexate + etoposide + ifosfamide
- gemcitabine + sirolimus
- lenvatinib + etoposide + ifosfamide
- high-dose ifosfamide
- regorafenib
- sorafenib
- cabozantinib
- sorafenib + everolimus
- immune checkpoint inhibitors (for MSI-H/ dMMR-positive or TMB-H cases)
- radium-223

➢ **Best support care**

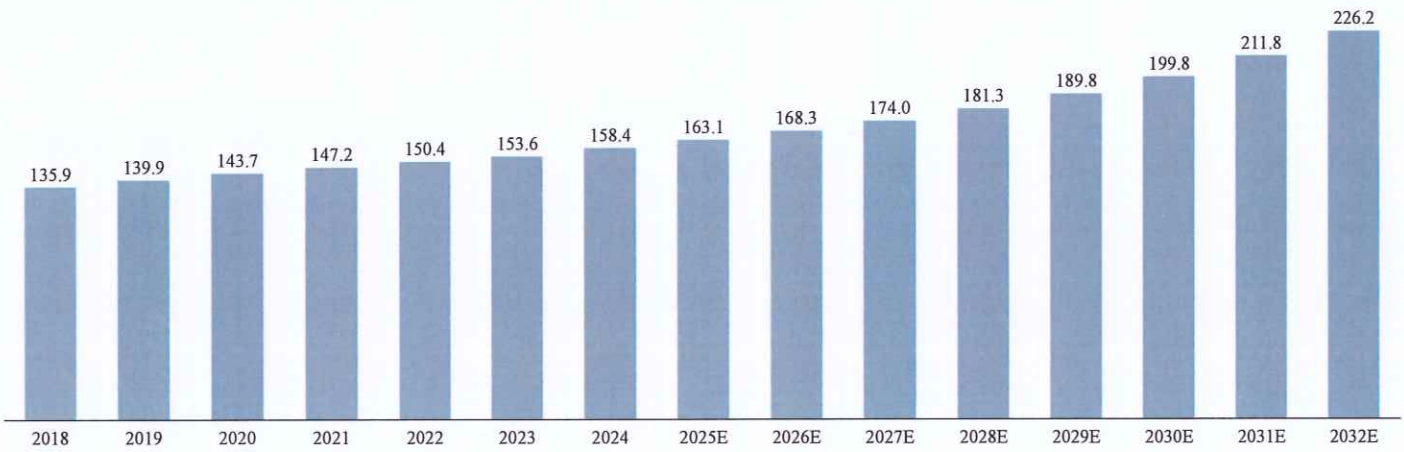
Source: Rheumatol Ther.; CSCO2024; China Insights Consultancy

Global market size of osteosarcoma drugs, 2018-2032E

Global osteosarcoma drugs market size, 2018-2032E

CAGR	2018-24	2024-32E
Osteosarcoma drugs	2.6%	4.6%

million USD



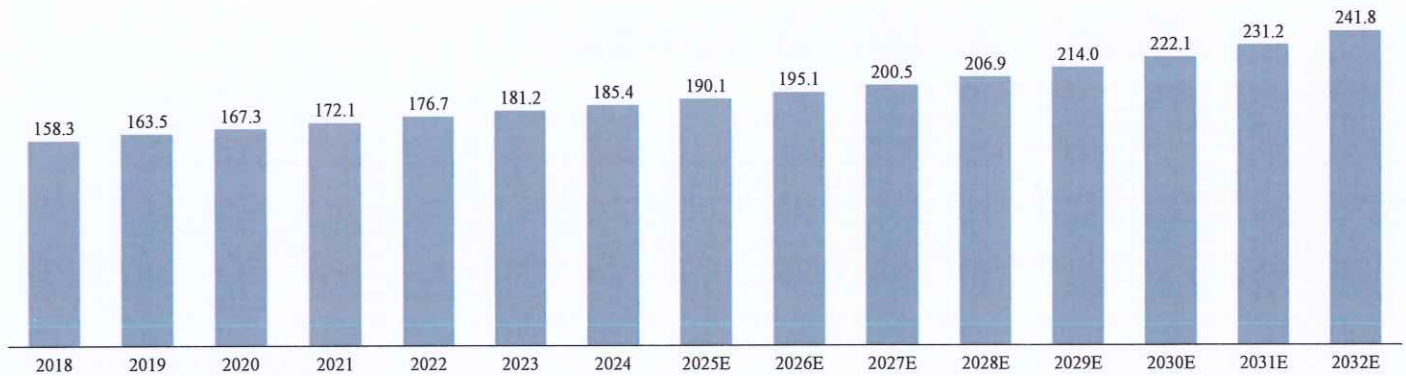
Source: China Insights Consultancy

Market size of osteosarcoma drugs in China, 2018-2032E

China osteosarcoma drugs market size, 2018-2032E

CAGR	2018-24	2024-32E
Osteosarcoma drugs	2.7%	3.4%

million RMB



- **The market stood steady during the past 5 years due to the fact that there lacked efficacious treatments specially for osteosarcoma.** However, with a growing number of clinical trials progressing, some drug candidates emerged and illustrated significant clinical potential. The new therapies are expected to be approved during 2025-2030, at which time the market is expected to embrace much greater growth.

Source: China Insights Consultancy

Global clinical pipelines of innovative drugs for osteosarcoma, as of LPD

Osteosarcoma > Clinical pipeline

Global clinical pipelines of innovative drugs for osteosarcoma, as of LPD

Drug name/code	Target	Company	Phase	Indications	First Posted Date	Trial Number	Location
ZKAB001	PD-L1	Zhaoke (Guangzhou) Oncology Pharm	III	Osteosarcoma maintenance therapy	2019-12-26	CTR20192678	China
HS-20093	VEGF, KIT, TOP2; PD-L1, PDGFR-β, CD276, FGFR,	Hansoh BioMedical	III	3L treatment for Osteosarcoma	2025-04-18	CTR20251474	China
Olaparib With Ceralasertib	PARP, ATR	AstraZeneca	II	Recurrent Osteosarcoma	2020-06-04	NCT04417062	US
ALMB-0168	GJA1	Enlemai Biotechnology	II	Osteosarcoma	2021-09-09	CTR20210451	China
Cabozantinib and BSC[1]	NTRK, c-Met, ROS, VEGFR, RET, AXL, FLT3, KIT	Ipsen	II	Children and AYA[2] With Osteosarcoma	2024-04-02	NCT06341712	Global
ZN-c3	/	K-Group, Beta	I/II	Osteosarcoma	2021-04-06	NCT04833582	Global
Vactosertib	TGF-β1	MedPacto	I/II	Recurrent, Refractory or Progressive Osteosarcoma	2022-10-20	NCT05588648	Global
CD99 CAR-T	CD99	Bio-raid	I/II	Osteosarcoma or soft tissue sarcoma	2024-12-03	CTR20244485	China
C019199	CSF1R, DDR1, VEGFR2	Haixi Pharma	I	Advanced Solid Tumors including Osteosarcoma	2020-10-23	CTR20202045	China
Cabozantinib With Ifosfamide	NTRK, c-Met, ROS, VEGFR, RET, AXL, FLT3, KIT	Exelixis	I	Ewing's Sarcoma and Osteosarcoma	2023-12-05	NCT06156410	US
TQB2928	CD47, SIRPA	Chia Tai Tianqing Pharma	I	Osteosarcoma	2024-01-29	CTR20240257	China
IM-83 (CAR-T)	GPC3	Yimiao Medical Technology	I	Osteosarcoma	2024-05-30	CTR20241991	China

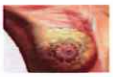
Note: 1 BSC stands for best supportive care. 2 AYA stands for adolescents, and young adults

Source: CDE; clinicaltrials; China Insights Consultancy

Overview of breast cancer

Breast cancer > Introduction

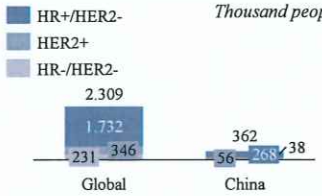
Introduction to breast cancer



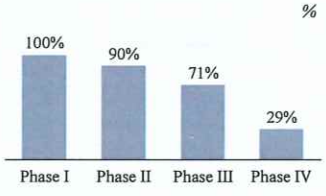
- **Breast cancer (BC)** is a disease that abnormal breast cells grow out of control and form tumors, which the most-commonly diagnosed malignant tumor in women in the world, as well as the first cause of death from malignant tumors
- In 2022, breast cancer caused 670 000 deaths globally. BC is the second most common type of cancer globally and the most prevalent cancer in the U.S.

- Like many other cancers, causes of breast cancer can vary, but genetic predisposition (BRCA1 or BRCA2 mutations), estrogen and progesterone exposure and lifestyle factors and a few factors that have attributed to the heightened risk of breast cancer

The incidence of BC, 2022



Five-year survival rate of BC, 2022



Symptoms

Early stage	Advanced stage
• No apparent symptoms at early stage	• A breast lump or thickening, often without pain • Change in size, shape or appearance of the breast • Dimpling, redness, pitting or other changes in the skin

Stage of BC

Stage	Phase 0	Phase I	Phase II	Phase III	Phase IV
	←	65%	→ ←	27%	→ ← 6 % →
Feature	• CIS	• Early invasive cancer • Tumor size＜2cm	• Tumor size is 2cm-5cm	• Tumor size ＞5cm	• Tumor in any size

Classification of BC*

HR+/HER2-	HER2+	TNBC
• Tumor have ER or PR, which can promote the growth of HR+ tumors, but without HER2	• Tumor have HER2, which has been shown to be associated with aggressive BC	• Tumor tested negative for ER, PR and HER2
• Low grade, slow growing, best prognosis, higher survival rate	• More aggressive and fast-growing than HR+/HER2 type	• Aggressiveness, early relapse, present in advanced stages

- Treatments for breast cancer, therefore, will depend on immunohistochemistry and will include surgery if at **an early stage and chemotherapy, hormonal therapy and immunotherapies based on various factors.**

Note: *ER: estrogen receptor; PR: progesterone receptor; HER2: human epidermal growth factor receptor 2

Source: China Insights Consultancy

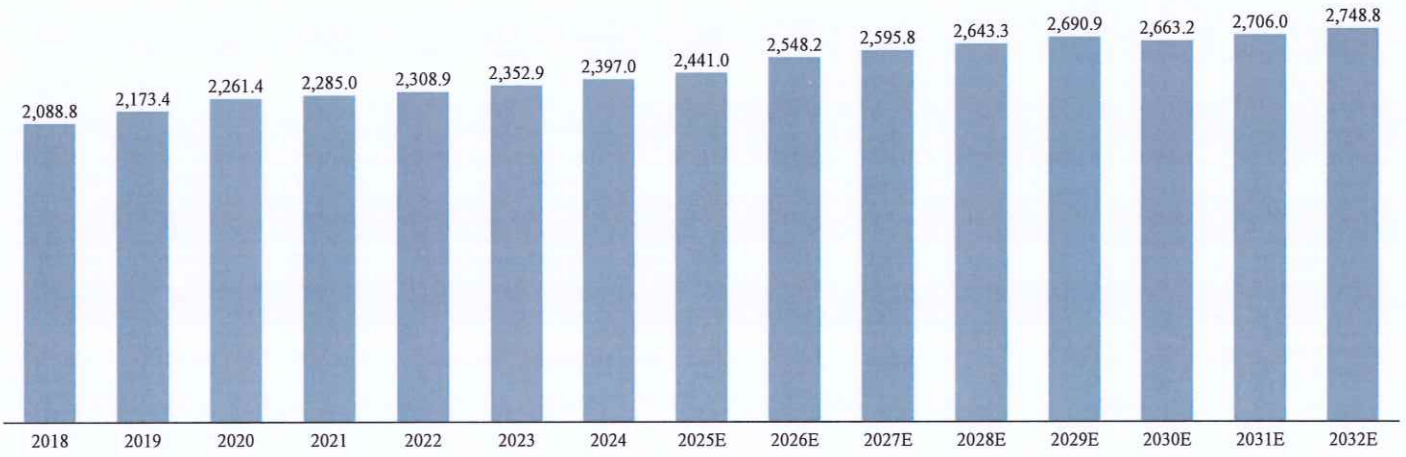
Global incidence of breast cancer, 2018-2032E

Breast cancer | Incidence

Global incidence of BC, 2018-2032E

CAGR	2018-2024	2024-2032E
BC	2.3%	1.7%

k ppl



Source: GLOBOCAN, China Insights Consultancy

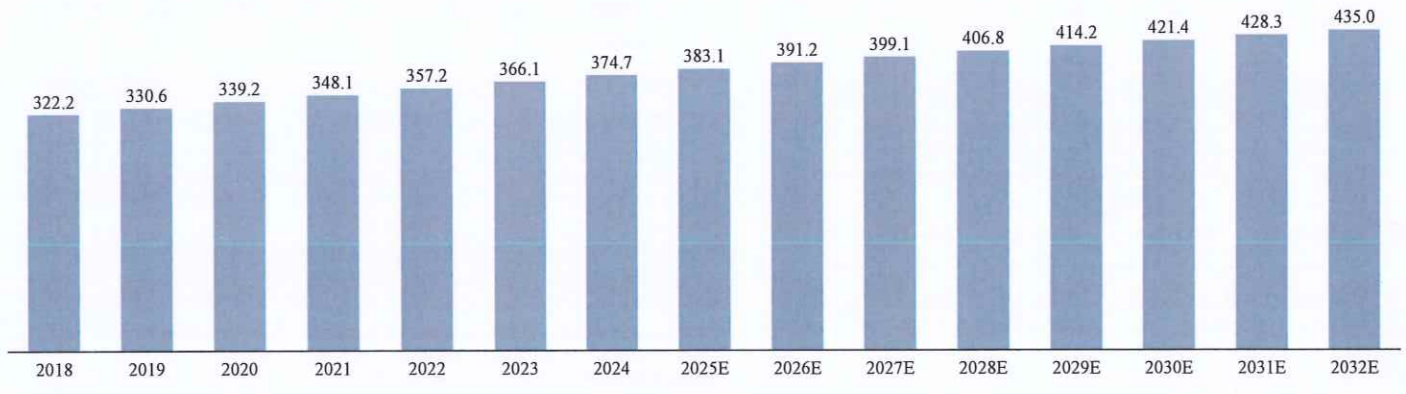
Incidence of breast cancer in China, 2018-2032E

Breast cancer | Incidence

Incidence of BC in China, 2018-2032E

CAGR	2018-2024	2024-2032E
BC	2.5%	1.9%

k ppl



Source: GLOBOCAN, China Insights Consultancy

Treatment path for breast cancer

Breast cancer | Treatment pathway

Treatment path for breast cancer

		First-line	Second-line and beyond	
Breast cancer	Non-metastatic, Her2-, HR+	• Without endocrinotherapy/TAM treatment failure (Grade I): AI + CDK4/6 i (Piperoxili; Abemaciclib)	• Nonsteroidal AI/Steroidal AI treatment failure (Grade I): Fluvestrant + CDK4/6 i (Piperoxili; Abemaciclib; Dalpiciclib)	• CDK4/6 i treatment failure (Grade II): Other CDK4/6 i_+ endocrine therapy; Other targeted drug + endocrine therapy; Rigorously designed clinical trials
	Non-metastatic, Her2+	Trastuzumab sensitive (Grade I): • Taxane + Anti-HER2 McAb + Pertuzumab • Taxane + Anti-HER2 McAb + Pyrotinib	Trastuzumab failure (Grade I): • Pyrotinib + Capecitabine • T-DMI	TKI failure (Grade II): • T-Dxd/T-DMI • Anti-HER2 McAb+Pertuzumab • Rigorously designed clinical trials
	Metastatic, TNBC	Taxanes sensitive (Grade I): • Taxanes monotherapy: Paclitaxel; Albumin-bound paclitaxel; Docetaxel • Combined therapy: Taxanes + Capecitabine/Gemcitabine; Taxanes + Platinum	Taxanes failure (Grade I): • Monotherapy: Eribulin; Vinorelbine; Gemcitabine; Capecitabine • Combined therapy: Vinorelbine + Platinum; Gemcitabine + Platinum; Utidelone + Capecitabine; Vinorelbine + Capecitabine	

Note: TAM: Tamoxifen; AI: Aromatase inhibitors; CDK4/6 i: CDK4/6 inhibitor; McAb: Monoclonal antibody; T-DMI: Trastuzumab emtansine; T-Dxd: Trastuzumab deruxtecan

Source: CSCO2024; China Insights Consultancy

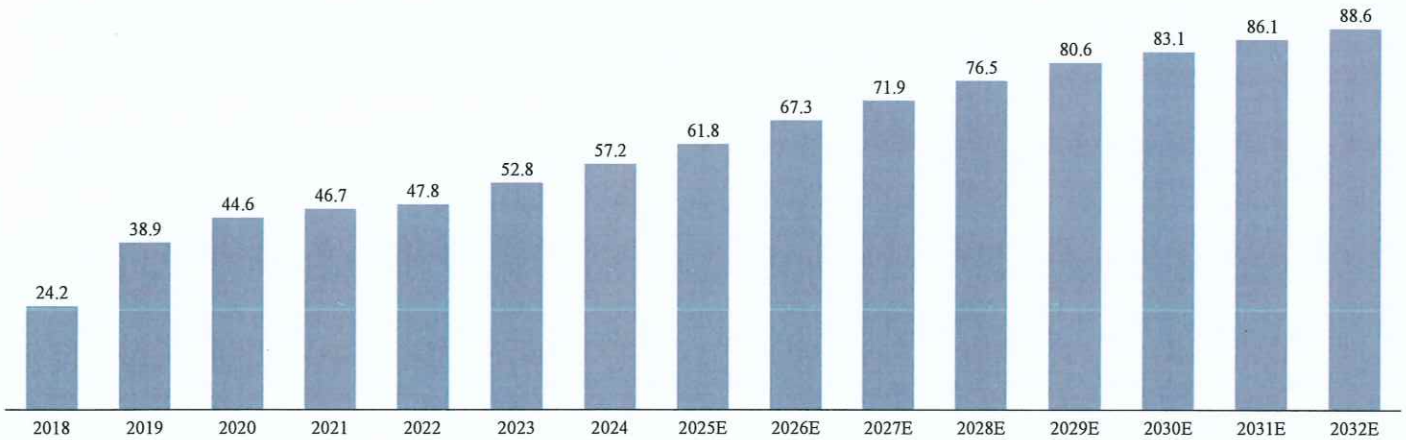
Global Market size of breast cancer drugs, 2018-2032E

Breast cancer | Market size

Global breast cancer drugs market size, 2018-2032E

CAGR	2018-24	2024-32E
Total	15.4%	5.6%

Billion USD

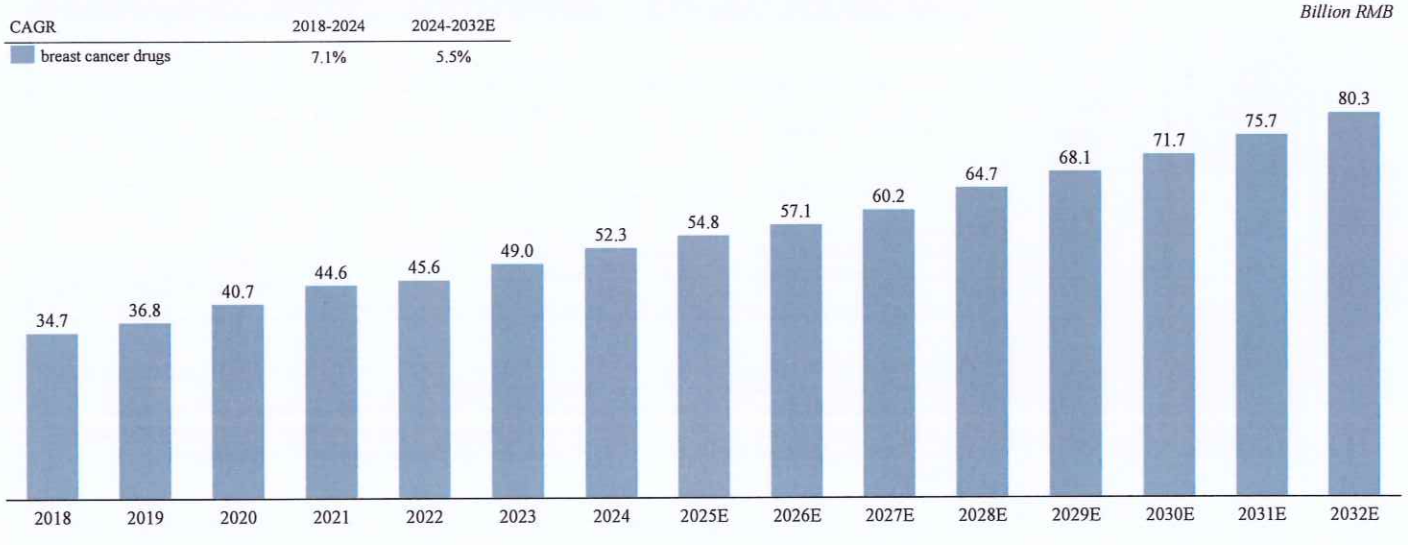


Source: China Insights Consultancy

Market size of breast cancer drugs in China, 2018-2032E

Breast cancer | Market size

Market size of breast cancer drugs in China, 2018-2032E



Source: China Insights Consultancy

Global clinical pipelines of I-O combination therapy for TNBC, phase II and beyond, as of LPD

TNBC | Clinical pipeline

Global clinical pipelines of I-O combination therapy for TNBC, phase II and beyond, as of LPD

Candidate	Target	Modality	Immunotherapy combination	Company	Phase	Indication	First Posted Date	Trial Number	Location[4]
Anlotinib	VEGFR, FGFR, PDGFR, c-kit	TKI	Benmelstobart	Chia Tai Tianqing	III	Locally advanced or metastatic TNBC	2020-06-01	CTR20201065	China
Dato-Dxd	Trop-2	ADC	Durvalimab	Daiichi Sankyo, AstraZeneca	III	Stage I-III TNBC with residual invasive disease after neoadjuvant systemic therapy	2023-03-06	CTR20230608	China
					III	PD-L1+ locally advanced or metastatic TNBC	2023-12-05	CTR20233975	China
MK-2870	Trop-2	ADC	Pembrolizumab	Merck Sharp & Dohme	III	TNBC not achieving pCR at surgery[2]	2024-05-01	NCT06393374	Global
Tavokinogene telseplasmid	IL-12	Plasmid	Pembrolizumab	OncoSec	II	Locally advanced or metastatic TNBC	2018-06-26	NCT03567720	Global
AE-37/GP-2	HER2	Peptide vaccine	Pembrolizumab	Nugenerex Immuno-Oncology	II	Metastatic TNBC	2019-07-18	NCT04024800	US
AK117	CD47	mAb	AK112	Akeso	II	1L unresectable locally advanced or metastatic TNBC	2022-01-30	CTR20220115	China
9MW2821	NECTIN-4	ADC	PD-1 inhibitor[3]	Mabwell	II	Locally advanced or metastatic TNBC	2024-07-02	CTR20242376	China
BL-B01D1	EGFR, HER3	ADC	Toripalimab	Biokin Pharma	II	Locally advanced or metastatic TNBC	2024-07-22	CTR20242251	China

Note:
1. I-O combination therapy refers to at least one immunotherapy combined with other targeted therapies or immunotherapies, or bispecific antibody that targets at least 1 immune checkpoint protein
2. pCR refers to pathological complete response
3. PD-1 inhibitor not specified
4. Trials conducted in more than one country/region denoted as Global, China-only trial and US-only trial denoted as China/US

Source: CDE, clinicaltrials, China Insights Consultancy

Overview of pancreatic cancer

Overview of pancreatic cancer

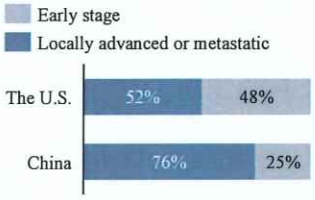
Pathogenesis

- Pancreatic cancer is a cancer in which pancreatic cells become cancerous and have the ability to invade other tissues
- It's mainly adenocarcinoma of pancreas, which originates in the part of the pancreas that makes digestive enzymes. Several other cancers in this area are known as non-adenocarcinomas, and a very small number of tumors originate from neuroendocrine cells

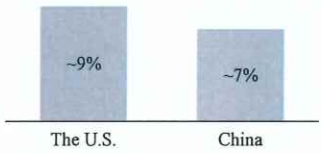
Symptoms

- Early stage
  - Loss of appetite
  - Loss of weight
- Advanced stage
  - Epigastric discomfort
  - Pain in back and loin
  - Dyspepsia
  - Diarrhea

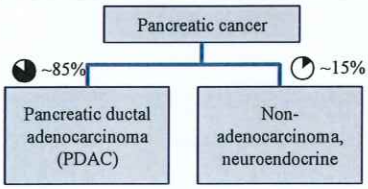
Clinical stages



Five-year survival rate, 2019



Classification



Risk factors

Smoking	High fat diet
Above standard BMI	Intemperance
Family inheritance	Chronic pancreatitis

Analysis

- **Classification:** Pancreatic cancer is mainly divided into two types of pancreatic cancer: pancreatic adenocarcinoma, which is the most common (~85%) arising in exocrine glands of the pancreas, and pancreatic neuroendocrine tumor (PanNET), which is less common (<5%) and occurs in the endocrine tissue of the pancreas
- **Risk factors:** Although the cause of pancreatic cancer is complex and multifactorial, cigarette smoking and family history are dominant
- **Clinical stages:** Pancreatic cancer is mostly diagnosed in an advanced stage, and 80-90% of patients have unresectable tumors at the moment of diagnosis
- **5-year survival rate:** Pancreatic adenocarcinoma has a very poor prognosis, typically after diagnosis, only 24% of people survive 1 year, and 7%-9% live for 5 years

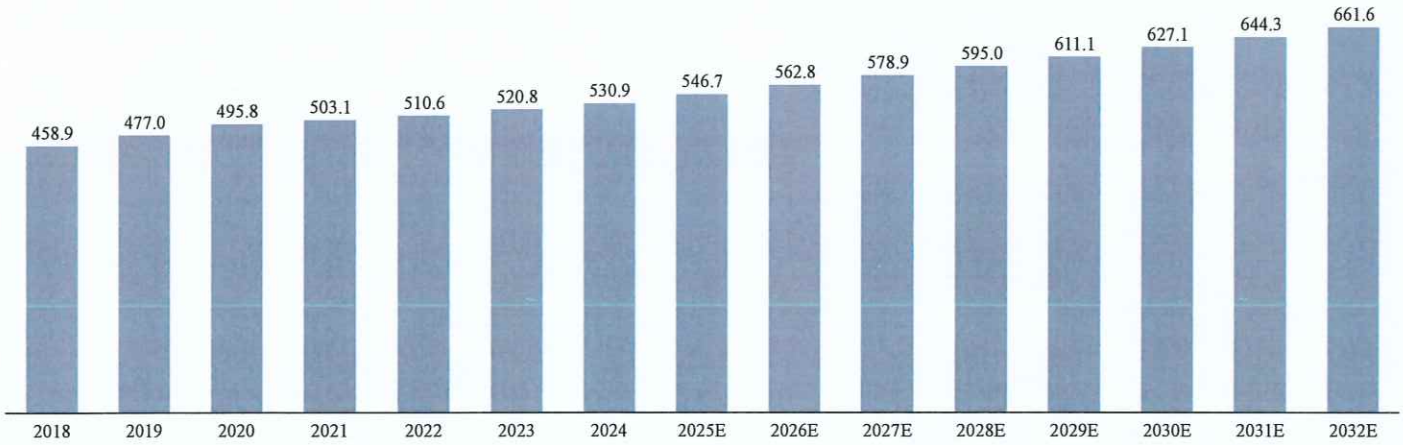
Source: WHO, NCCR, Chin J Cancer Res, China Insights Consultancy

Global incidence of pancreatic cancer, 2018-2032E

Global incidence of pancreatic cancer, 2018-2032E

CAGR	2018-2024	2024-2032E
Pancreatic cancer	2.5%	2.8%

k ppl



Source: GLOBOCAN, China Insights Consultancy

Incidence of pancreatic cancer in China, 2018-2032E

Pancreatic cancer | Incidence

Incidence of pancreatic cancer in China, 2018-2032E

CAGR	2018-2024	2024-2032E
Pancreatic cancer	2.8%	2.0%

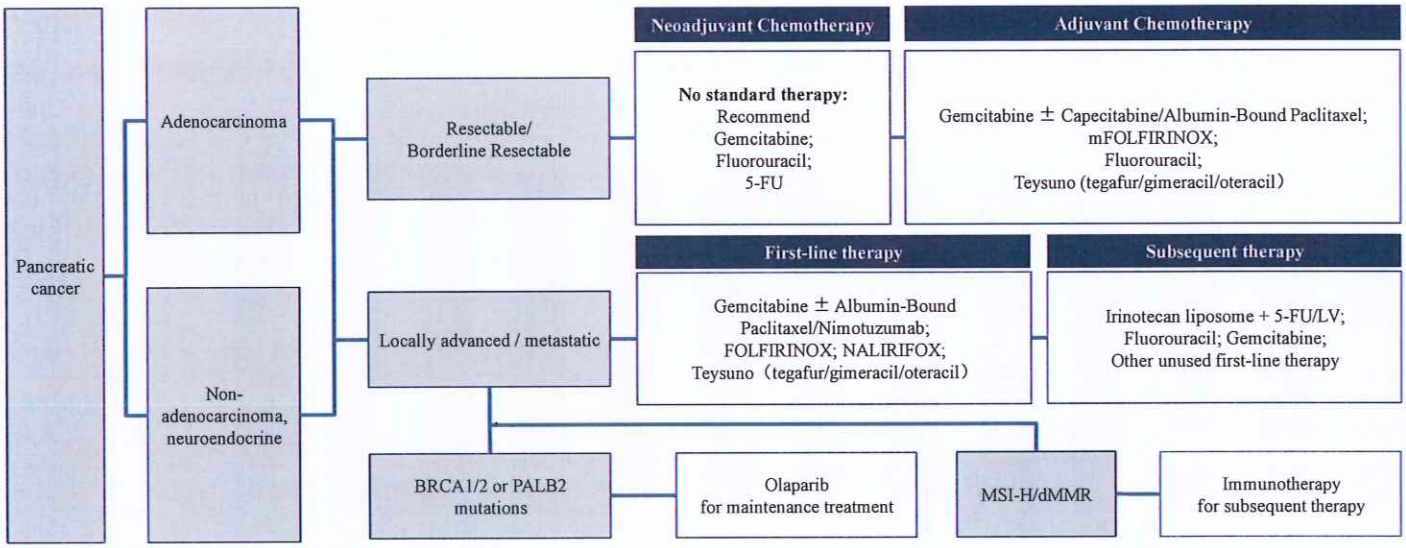
k ppl

Source: GLOBOCAN, China Insights Consultancy

Treatment path for pancreatic cancer

Pancreatic cancer | Treatment pathway

Treatment path for pancreatic cancer



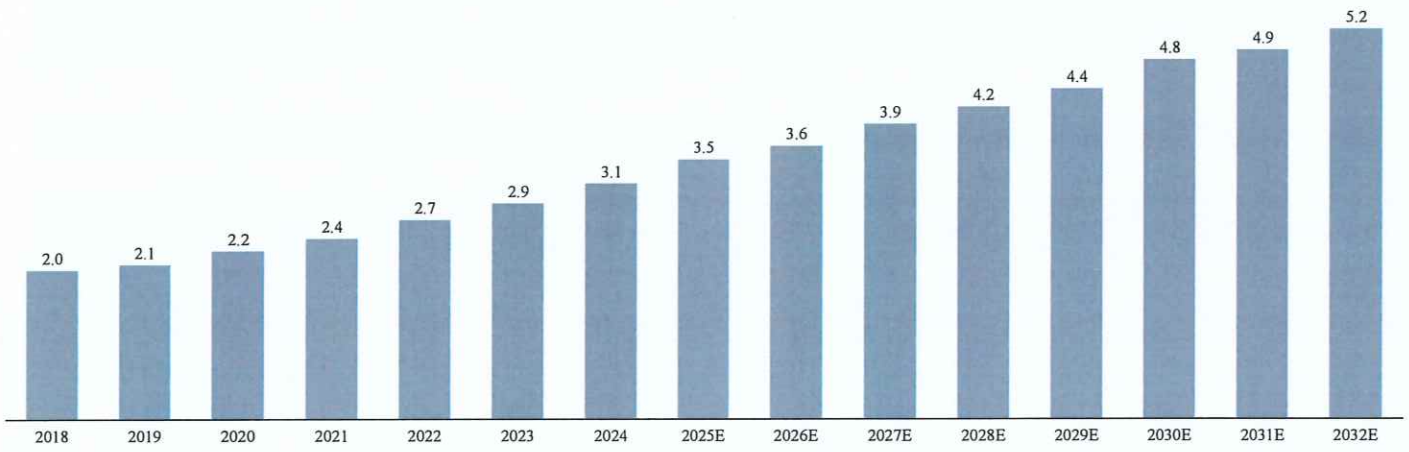
Source: CSCO2024; China Insights Consultancy

Global market size of pancreatic cancer drug, 2018-2032E

Global market size of pancreatic cancer drugs, 2018-2032E

CAGR	2018-2024	2024-2032E
Pancreatic cancer drugs	7.9%	6.5%

billion USD



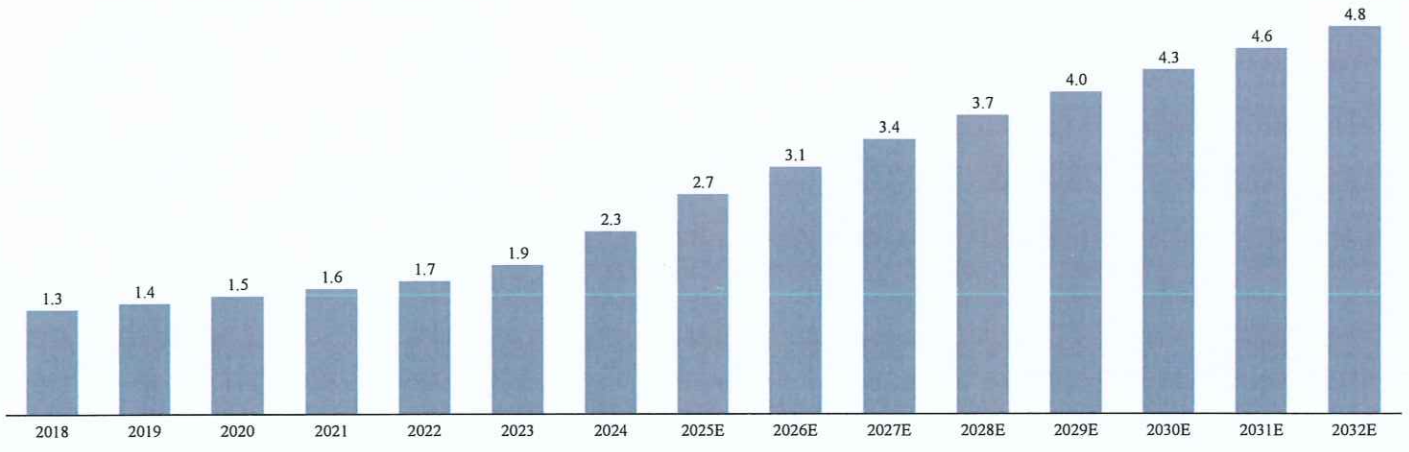
Source: China Insights Consultancy

Market size of pancreatic cancer drugs in China, 2018-2032E

Market size of pancreatic cancer drugs in China, 2018-2032E

CAGR	2018-2024	2024-2032E
Pancreatic cancer drugs	9.7%	9.8%

billion RMB



Source: China Insights Consultancy

Global clinical pipelines of I-O combination therapy for pancreatic cancer, phase II and beyond, as of LPD

Global clinical pipelines of I-O combination therapy for pancreatic cancer, phase II and beyond, as of LPD

Candidate	Target	Modality	Immunotherapy combination	Company	Phase	Indication	First Posted Date	Trial Number	Location[3]
Motixafortide	CXCR4	Peptide antagonist	Cemiplimab	Regeneron Pharma, BioLine Rx	II	Metastatic treatment naive PDAC	2020-09-09	NCT04543071	US
Lenvatinib	KIT, PDGFR-α, VEGFR, FGFR, RET	TKI	Pembrolizumab	Merck Sharp & Dohme	II	PDAC	2021-07-26	NCT04976634	Global
YH003	CD40	mAb	Toripalimab	Eucure Biopharma	II	Unresectable/metastatic PDAC	2021-12-22	CTR20213230	China
Conteltinib	ALK, FAK, IGF1R	TKI	Toripalimab	Centaurus BioPharma	II	Advanced PC	2022-08-11	CTR20222060	China
AGEN1423	TGF-β, CD73	BsAb	Botensilimab	Agenus Inc	II	Advanced PDAC	2022-11-30	NCT05632328	US
Futibatinib	FGFR, TYMS, DNA, PD-1	TKI	Pembrolizumab	Taiho Oncology	II	Locally advanced, unresectable or metastatic PDAC	2023-07-14	NCT05945823	Global
Pimicotinib	CSF-1R	TKI	Toripalimab	Abbisko Therapeutics	II	Advanced PC	2023-10-13	CTR20233124	China
Anlotinib	VEGFR, FGFR, PDGFR, c-kit	TKI	TQB2868	Chia Tai Tianqing	II	metastatic PDAC	2024-03-05	CTR20240527	China

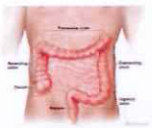
Note:
1. I-O combination therapy refers to at least one immunotherapy combined with other targeted therapies or immunotherapies, or bispecific antibody that targets at least 1 immune checkpoint protein
2. PDAC refers to pancreatic ductal adenocarcinoma
3. Trials conducted in more than one country/region denoted as Global, China-only trial and US-only trial denoted as China/US

Source: CDE, clinicaltrials, China Insights Consultancy

Overview of colorectal cancer

Overview of colorectal cancer

Introduction to colorectal cancer



- As the third most common malignancy and the second most deadly cancer, colorectal cancer (CRC) induces estimated 1.9 million incidence cases and 0.9 million deaths worldwide in 2020. The global number of new CRC cases is predicted to reach 3.2 million in 2040, based on the projection of aging, population growth, and human development. In 2020, CRC accounts for 10% of global cancer incidence and 9.4% of cancer deaths, just lower than lung cancer that comprises 18% of deaths

Symptoms:

- ☐ A change in bowel habits
- ☐ Blood in or on your stool (bowel movement)
- ☐ Diarrhea, constipation, or feeling that the bowel does not empty all the way
- ☐ Abdominal pain, aches, or cramps that don't go away
- ☐ Weight loss and you don't know why

Risk factors:

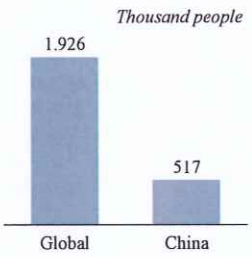
- ☐ Getting older
- ☐ Inflammatory bowel disease such as Crohn's disease or ulcerative colitis
- ☐ A personal or family history of colorectal cancer or colorectal polyps
- ☐ A genetic syndrome such as familial adenomatous polyposis (FAP) or hereditary non-polyposis colorectal cancer (Lynch syndrome)

Lifestyle factors that may contribute to an increased risk of colorectal cancer:

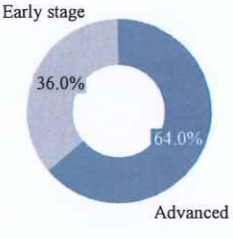
- ☐ Lack of regular physical activity
- ☐ A diet low in fruit and vegetables
- ☐ A low-fiber and high-fat diet, or a diet high in processed meats
- ☐ Overweight and obesity
- ☐ Alcohol consumption
- ☐ Tobacco use

Epidemiology

The incidence of CRC, 2022



Stage of CRC diagnosed



- In China, **CRC patients will usually observe cancer in the advanced stage**. Since the early symptoms of colorectal cancer are not significant, more obvious symptoms such as blood in the stool, abdominal mass, and persistent pain in the pelvis or lower abdomen will appear as the cancer gradually progresses to the advanced stage

Source: NCCN, Transl Oncol., China Insights Consultancy

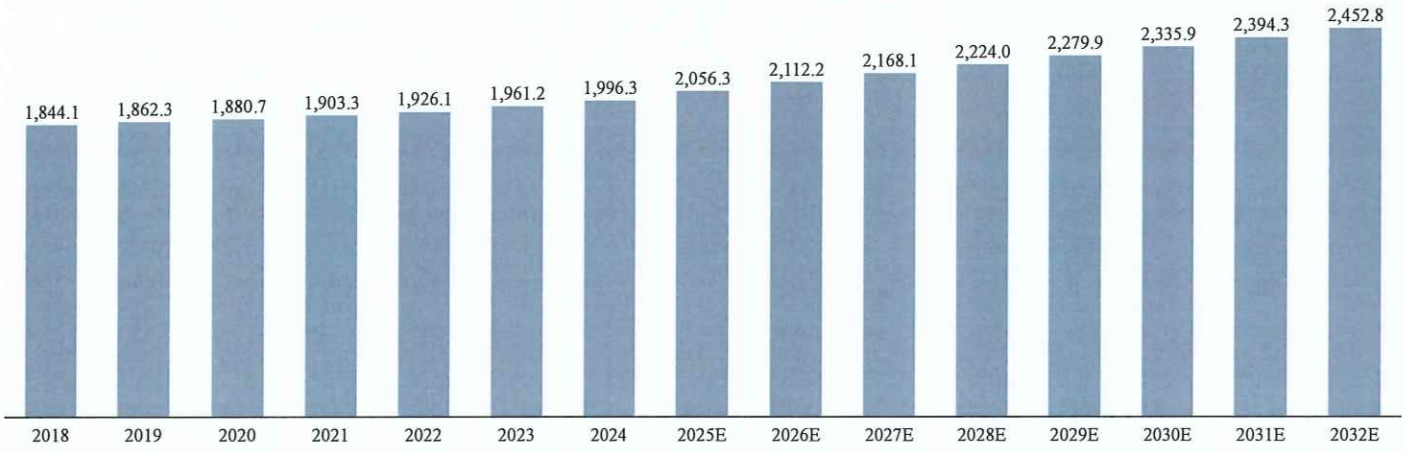
Global incidence of colorectal cancer, 2018-2032E

Colorectal cancer | Incidence

Global incidence of colorectal cancer, 2018-2032E

CAGR	2018-2024	2024-2032E
Colorectal cancer	1.5%	2.5%

k ppl



Source: GLOBOCAN, China Insights Consultancy

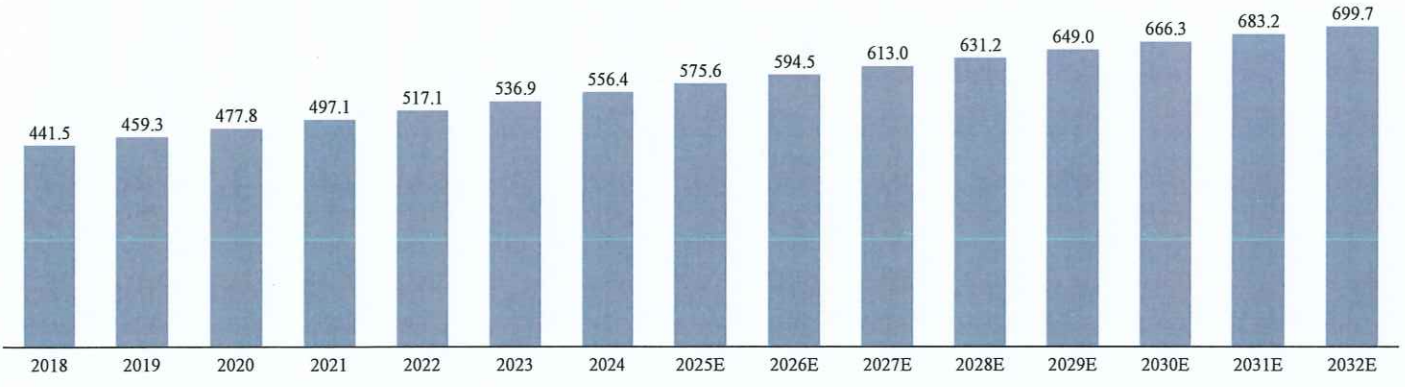
Incidence of colorectal cancer in China, 2018-2032E

Colorectal cancer | Incidence

Incidence of colorectal cancer in China, 2018-2032E

CAGR	2018-2024	2024-2032E
Colorectal cancer	3.9%	2.9%

k ppl



Source: GLOBOCAN, China Insights Consultancy

Treatment path for colorectal cancer

Colorectal cancer | Treatment pathway

Treatment path for colorectal cancer

			First-line	Second-line	Third-line
Colorectal cancer	Colon cancer	Early-stage and non-metastatic	• Surgical Treatment: Colectomy; Local resection; Transanal endoscopic microsurgery (TEM); Abdominoperineal resection (APR); Radical resection of rectal carcinoma • Adjuvant Chemotherapy: 5-FU/Capecitabine monotherapy; Oxaliplatin chemotherapy; Combined chemotherapy		
	Rectal cancer	Advanced/ metastatic	MSI-H/dMMR	*Grade I* • Pembrolizumab	*Grade II* • ICIs	*Grade II* • ICIs
			MSS or MSI-L/pMMR, RAS and BRAF wild type	• (1) Intensive treatment: FOLFOX/FOLFIRI ± Cetuximab; CapivasertibEOX;FOLFOX/CapivasertibEOX/FOLFIRI ± Bevacizumab; (2) Non-intensive treatment: Fluorouracil ± Bevacizumab	*Grade I* • (1) Has treated with oxaliplatin: FOLFIRI ± targeted drug; (2) Has treated with irinotecan: FOLFIRI ± targeted drug/CapivasertibEOX ± Bevacizumab	*Grade I* • Has treated with oxaliplatin and irinotecan: Cetuximab + Irinotecan; Regorafenib; Fruquintinib; Trifluridine and Tipiracil Hydrochloride
			MSS or MSI-L/pMMR, RAS and BRAF mutant type	• (1) Intensive treatment: FOLFOX/CapivasertibEOX/FOLFIRI ± Bevacizumab; (2) Non-intensive treatment: Fluorouracil ± Bevacizumab	• (1)) Has treated with oxaliplatin: FOLFIRI ± Bevacizumab; (2) Has treated with irinotecan: FOLFIRI/CapivasertibEOX ± Bevacizumab	• Has treated with oxaliplatin and irinotecan: Regorafenib; Fruquintinib; Trifluridine and Tipiracil Hydrochloride

Note: * ICIs: Immune checkpoint inhibitors

Source: CSCO2024; China Insights Consultancy

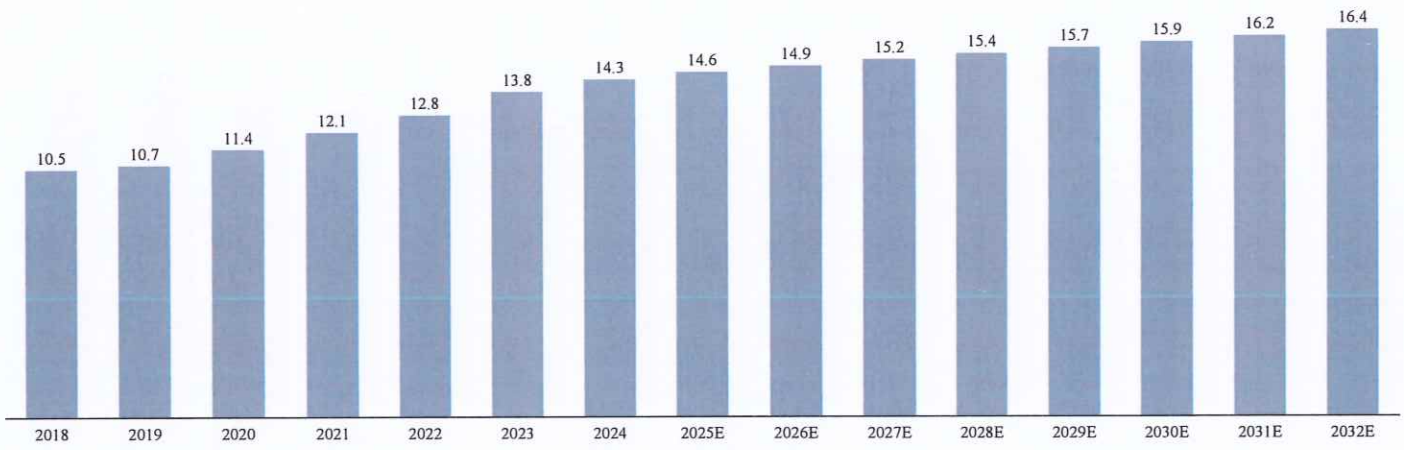
Global market size of colorectal cancer drugs, 2018-2032E

Colorectal cancer | Market size

Global market size of colorectal cancer drugs, 2018-2032E

CAGR	2018-2024	2024-2032E
colorectal cancer drugs	5.3%	1.7%

billion USD



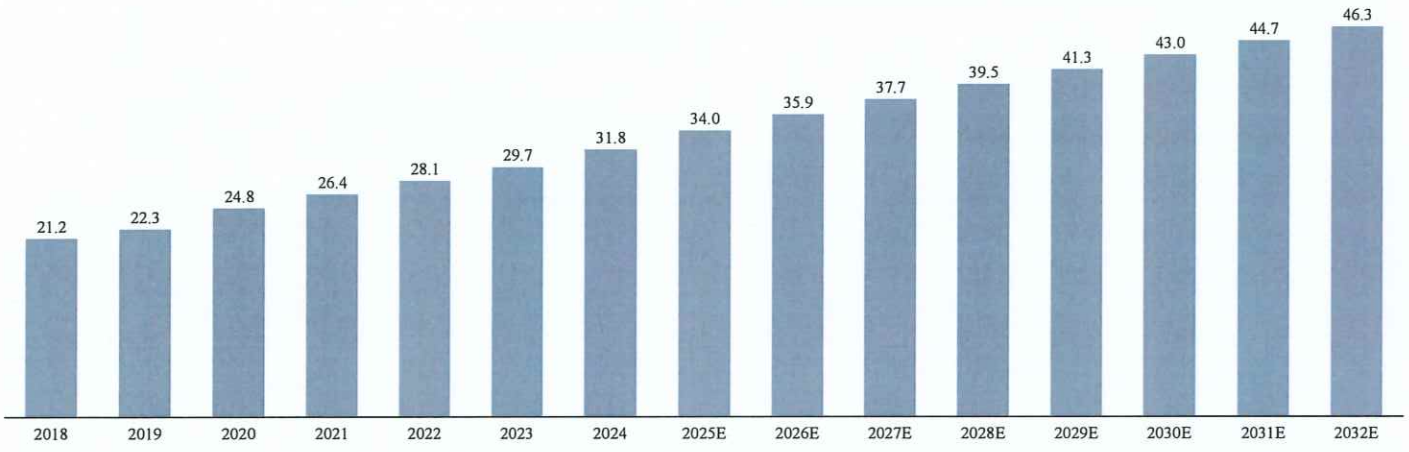
Source: China Insights Consultancy

Market size of colorectal cancer drugs in China, 2018-2032E

Market size of colorectal cancer drugs in China, 2018-2032E

CAGR	2018-2024	2024-2032E
colorectal cancer drugs	6.9%	4.8%

billion RMB



Source: China Insights Consultancy

Global clinical pipelines of I-O combination therapy for colorectal cancer, phase II/III and beyond, as of LPD

Global clinical pipelines of I-O combination therapy for colorectal cancer, phase II/III and beyond, as of LPD

Candidate	Target	Modality	Immunotherapy combination	Company	Phase	Indication	First Posted Date	Trial Number	Location[5]
Nivolumab	PD-1	mAb	Ipilimumab	Bristol-Myers Squibb	III	1L MSI-H/dMMR[2] metastatic CRC	2019-07-05	NCT04008030	Global
HLX04	VEGFR	mAb	Serplulimab	Shanghai Henlius Biotech	III	1L metastatic CRC	2021-03-24	CTR20200692	China
Relatlimab	LAG-3	mAb	Nivolumab	Bristol-Myers Squibb	III	Later line non-MSI-H/dMMR[2] metastatic CRC	2022-04-14	NCT05328908	Global
Chidamid	HDAC	Epigenetic regulator	Sintilimab	Chipscreen Biosciences	III	3L and above advanced MSS/pMMR[3] CRC	2024-08-01	CTR20242806	China
SHR-1701	TGF-β, PD-L1	BsAb	/[4]	Suzhou Suncadia Biopharma	II/III	1L metastatic CRC	2021-04-22	CTR20210880	China

Note:
1. I-O combination therapy refers to at least one immunotherapy combined with other targeted therapies or immunotherapies, or bispecific antibody that targets at least 1 immune checkpoint protein
2. MSI-H/dMMR refers to microsatellite instability high or deficient mismatch repair
3. MSS/pMMR refers to microsatellite stable or proficient mismatch repair
4. SHR-1701 is a TGF-β/PD-L1 bifunctional fusion protein
5. Trials conducted in more than one country/region denoted as Global, China-only trial and US-only trial denoted as China/US

Source: CDE, clinicaltrials, China Insights Consultancy

The trend of combination therapy for cancer is important to explore more efficacious, efficient and safer treatment options.

Cancer therapy | Comparison

Combination cancer therapy:

- The rationale for combination therapy is to use medications that work by different mechanisms, thereby decreasing the likelihood that resistant cancer cells will develop.
- For instance, the optimal treatment to solid tumors is a combination of cancer surgery, radiation therapy, and chemotherapy or other cancer medications(targeted therapy, immunotherapy, etc.).

Principles of drug combination therapy for cancer

- a) Genotype-specific synthetic lethality
- b) Drug-specific synthetic lethality
- c) Collateral lethality
- d) Double blockade of pathway
- e) Multi-node inhibition
- f) Intermittent dosing regimen
- g) Alternating dosing regimen
- h) Overcome non-genetic drug resistance

To overcome the likelihood of resistance, thus achieving long-term control of cancer.

Comparisons of monotherapy and combination therapy for cancer

Dimension	Monotherapy	Combination therapy
Treatment efficacy	◔	◕
Efficiency	◔	◕
Safety	◑	◑
Durability of efficacy	◔	◕

Future drivers and trends of combination therapy

Precision medicine: With the development of gene sequencing and bioinformatics technology, future combination therapy will be more precise in individualizing the patient's gene mutations and tumor characteristics.

Widespread application of immunotherapy: Immunotherapy is becoming more and more important in tumor treatment, and future combination therapy plans may include more immunotherapy drugs.

Research and development of new drugs: With the continuous emergence of new drugs, such as antibody-drug conjugates (ADCs) and CAR-T cell therapy, future combination therapy plans will be more diverse.

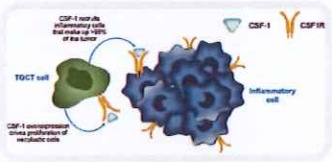
Interdisciplinary cooperation: Tumor treatment requires multidisciplinary cooperation, including oncology, radiology, surgery, pathology, etc. Future combination therapy plans may involve more interdisciplinary cooperation and comprehensive treatment.

Source: China Insights Consultancy

Overview of CSF1R

CSF1R | Introduction

Overview of CSF1R



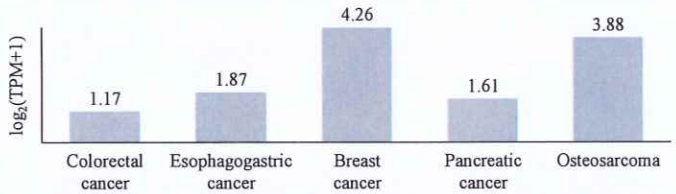
- **Colony-stimulating factor 1 receptor (CSF1R)** is a myeloid receptor with a crucial role in monocyte survival and differentiation. Its overexpression is associated with aggressive tumors characterized by an immunosuppressive microenvironment and poor prognosis
- CSF1R and its ligands, CSF1 and interleukin 34 (IL-34), regulate the function and survival of tumor-associated macrophages, which are involved in tumorigenesis and in the suppression of antitumor immunity

Mechanism of action of CSF1R:

- CSF1R activation requires the binding of ligands like CSF1 or IL-34 and subsequent receptor dimerization. This receptor can be blocked by small molecules that inhibit its tyrosine kinase activity or by human monoclonal antibodies targeting CSF1R, both of which prevent the ligands CSF1 and IL-34 from binding to the receptor
- As a result, tumor-associated macrophages (TAMs) are unable to receive CSF1R signals, which leads to decreased TAM proliferation, differentiation, and survival, ultimately reducing the immunosuppressive effects of TAMs within the tumor microenvironment

CSF1R in Cancer Cells

CSF1R mRNA expression range (CRISPR)

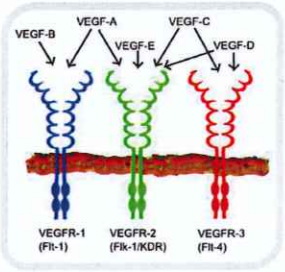


- **CSF1R mRNA is expressed in different cancer cell lines**, and various studies reported that CSF1R mRNA up-regulation correlated with poor prognosis in tumors
- As the intratumoral presence of CSF1R$^+$ macrophages correlates with poor survival in various tumor types, **targeting CSF1R signaling in tumor-promoting TAM represents an attractive strategy to eliminate or repolarize these cells**
- A variety of small molecules and monoclonal antibodies (mAbs) directed at CSF1R or its ligand CSF1 **are in clinical development** both as monotherapy and in combination with standard treatment modalities such as chemotherapy as well as other cancer-immunotherapy approaches

Source: Depmap; Current Oncology Reports; Cancers 2024; China Insights Consultancy

Overview of VEGFR2

Overview of VEGFR2



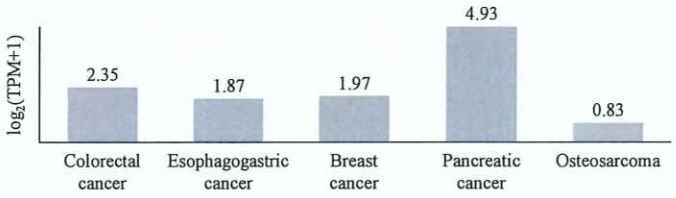
- **Vascular endothelial growth factor receptor 2 (VEGFR2)**, also known as kinase insert domain receptor (KDR), is a VEGF receptor
- The structure of the VEGFR2 is similar to typical tyrosine kinase receptor; VEGFA, VEGFC and VEGFD are bind to VEGFR2. VEGFR2 is the principle VEGF receptor present at the surface of vascular endothelial cell. Vascular permeability and angiogenesis are the ultimate goals for the activation of the receptor

Mechanism of action of VEGFR2:

- The growth and metastasis of tumors directly depend on the process of tumor angiogenesis, which is regulated by both proangiogenic and anti-angiogenic factors produced by host and tumor cells, as well as the activity of regulatory T cells (Tregs). Vascular endothelial growth factors (VEGFs) and their receptor VEGFR2 play a significant role in angiogenesis. Upon activation, VEGFR2 undergoes autophosphorylation, which ultimately leads to the proliferation of endothelial cells, promoting tumor angiogenesis, tumor growth, and metastasis

VEGFR2 in Cancer Cells

VEGFR2 mRNA expression range (CRISPR)

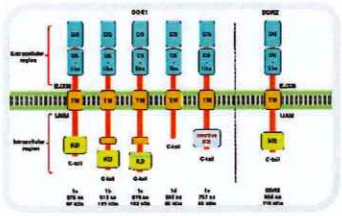


- **VEGFR2 overexpression is observed in different kinds of cancer:** breast cancer, cervical cancer, non-small cell lung cancer, hepatocellular carcinoma, renal carcinoma, and likewise
- **VEGFR2 inhibitors prevent angiogenesis and lymphangiogenesis.** Due to the similarity in the structure among all the VEGF receptors, VEGFR2 inhibitors can target each one of the receptors of the VEGF family. Hence, most of the inhibitors are not specific to VEGFR2 but also inhibit other receptor tyrosine kinases
- **VEGFR2 inhibitors have already matured and shown good efficacy.** They are classified into three types: ATP competitive inhibitors (e.g. Sunitinib), activation of DFG-out conformation of loop (e.g. Sorafenib), and covalent inhibitors (e.g. Vatalanib)

Source: Medicine in Drug Discovery; Depmap; China Insights Consultancy

Overview of DDR1

Overview of DDR1



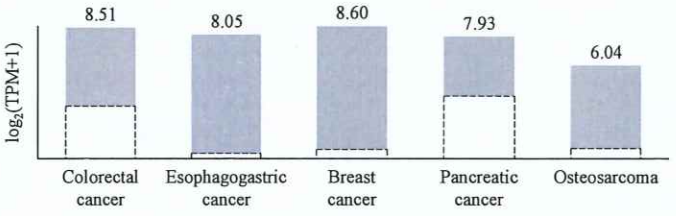
- Discoidin domain receptor 1 (DDR1), a member of the receptor tyrosine kinase (RTK) family, has a closely related counterpart, DDR2, both of which play key roles in cellular signaling and tissue homeostasis
- DDR1 has five isoforms. DDR1a, DDR1b, and DDR1c encode full-length active receptors that participate in signal transduction, whereas DDR1d and DDR1e lack kinase activity because of their incomplete protein structure

Mechanism of action of DDR1:

- DDR1 plays a key role in tumor progression by affecting both tumor cells and microenvironment. In tumor cells, DDR1 promotes proliferation, migration, invasion, and epithelial-mesenchymal transition (EMT) through pathways like mTOR and STAT3. It also stabilizes cell adhesion via interactions with E-cadherin and influences apoptosis and energy metabolism
- In the tumor microenvironment, DDR1 regulates immune cell recruitment, stromal cell remodeling, and angiogenesis. It interacts with collagen to modulate the extracellular matrix (ECM), promoting immune evasion and metastasis. This makes DDR1 a potential target for cancer therapy

DDR1 in Cancer Cells

DDR1 mRNA expression range (CRISPR)



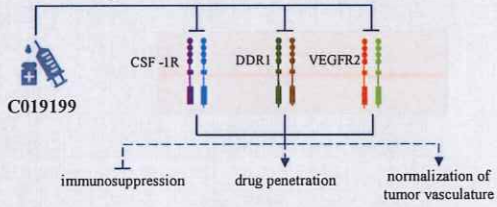
- **Abnormal activation of DDR1 is closely associated with the development of various solid tumors.** DDR1 can prevent immune cells from infiltrating triple-negative breast cancer (TNBC) and eliminating tumor cells. Knocking out DDR1 or inhibiting DDR1 with antibodies can breach the defenses of TNBC, enabling immune cells to successfully penetrate and eliminate tumor cells
- **Various potential candidates have been developed for targeting DDR1**, including kinase inhibitors (both selective and nonselective), proteolysis-targeting chimeras (PROTACs), and antibody drugs, among others. However no drugs targeting DDR1 have yet been approved for clinical use

Source: Drug Discovery Today; BBA - Reviews on Cancer; Depmap; China Insights Consultancy

Introduction to C019199

Introduction to C019199

■ C019199 is an innovative new drug independently developed by Haixi Pharma, targeting the regulation of the tumor immune microenvironment, with global patent protection. C019199 targets **CSF1R, DDR1, and VEGFR2**



- **CSF1R:** C019199 inhibits the CSF1R signaling pathway, suppressing and polarizing tumor-associated macrophages, thus relieving T cell inhibition, promoting T cell infiltration, and enhancing T cell cytotoxicity
- **DDR1:** By inhibiting DDR1, C019199 disrupts the "physical barrier" of the extracellular matrix in tumor tissues, further increasing the infiltration and penetration of immune cells and drugs into the tumor
- **VEGFR2:** Through moderate inhibition of VEGFR2, C019199 induces normalization of tumor vasculature, enabling better penetration of immune cells and drugs into the tumor via blood vessels, while also modulating and reducing Tregs to further relieve tumor-induced immune suppression. Together, these actions synergistically enhance the efficacy of tumor immunotherapy

C019199 has shown good overall safety and tolerability

➢ **Phase I study of C019199 to assess the safety, tolerability, pharmacokinetics, and pharmacodynamics in patients with advanced solid tumors, including TGCT**

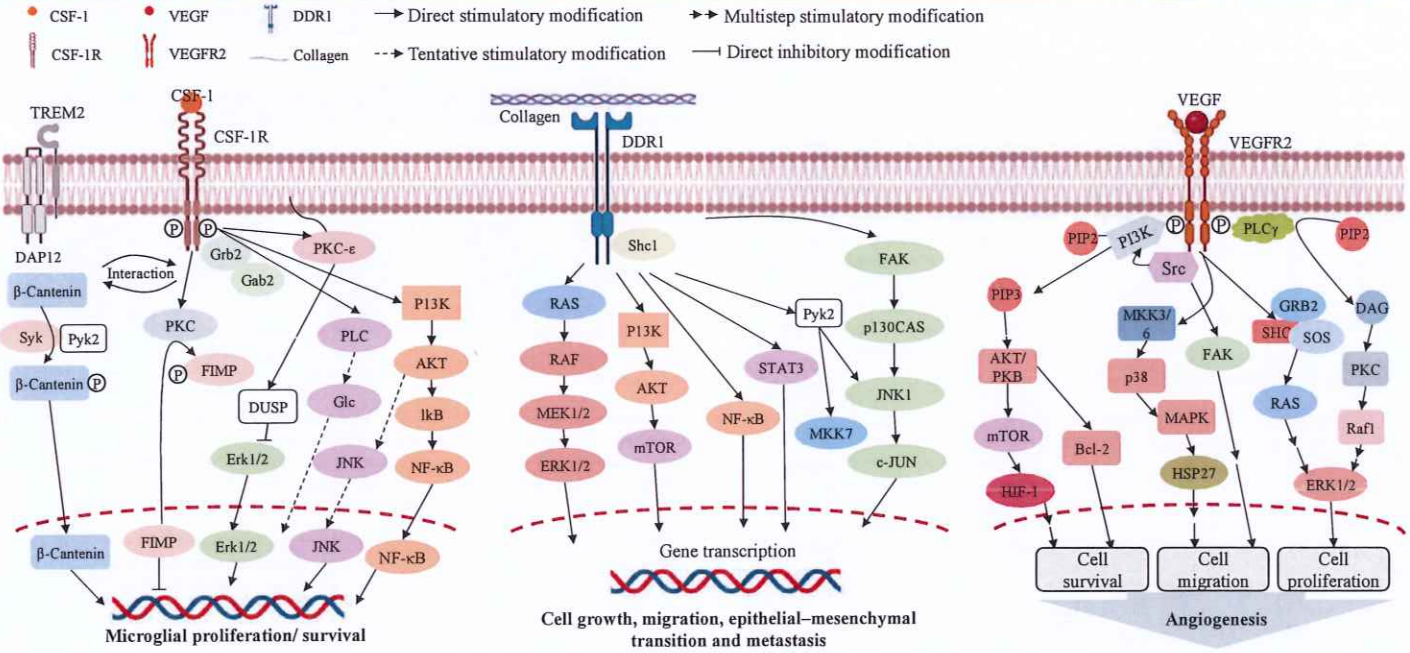
- **Inclusion:** Eligible subjects (age ≥ 18 years and <76 years) with histologically or cytologically confirmed relapsed, refractory, or progressive metastatic solid tumors
- **Efficacy:** In 22 evaluable patients, >50% experienced varying degrees of tumor reduction, although none met the criteria for PR. The overall DCR was 58.6%, with a mPFS of 72 days
- **Safety:** Among the 25 subjects included in the DLT assessment analysis, 2 cases of DLT occurred in the 300mg BID group. There were 10 cases of grade 3 or higher adverse events

➢ **A phase I/II study of C019199 in combination with sintilimab in advanced malignancy *(Still going)***

- **Inclusion:** A total of 10 patients with advanced solid tumors were enrolled in the phase I study, with 6 males and 4 females. Tumor types were colorectal cancer (7 pts), NSCLC(2 pts) and cervical cancer (1 pts), with a median 3 prior systemic therapies
- **Efficacy:** Among 7 colorectal cancer patients, ORR is 14.3% with DCR at 100%. 2 patients with NSCLC and 1 patient with cervical cancer achieved the best response of SD, with a DCR of 100%. Recommended dose is 200 mg QD as the RP2D in selected solid tumors
- **Safety:** No DLT observed in the dose range of 100 mg QD-300 mg QD and the MTD has not been reached

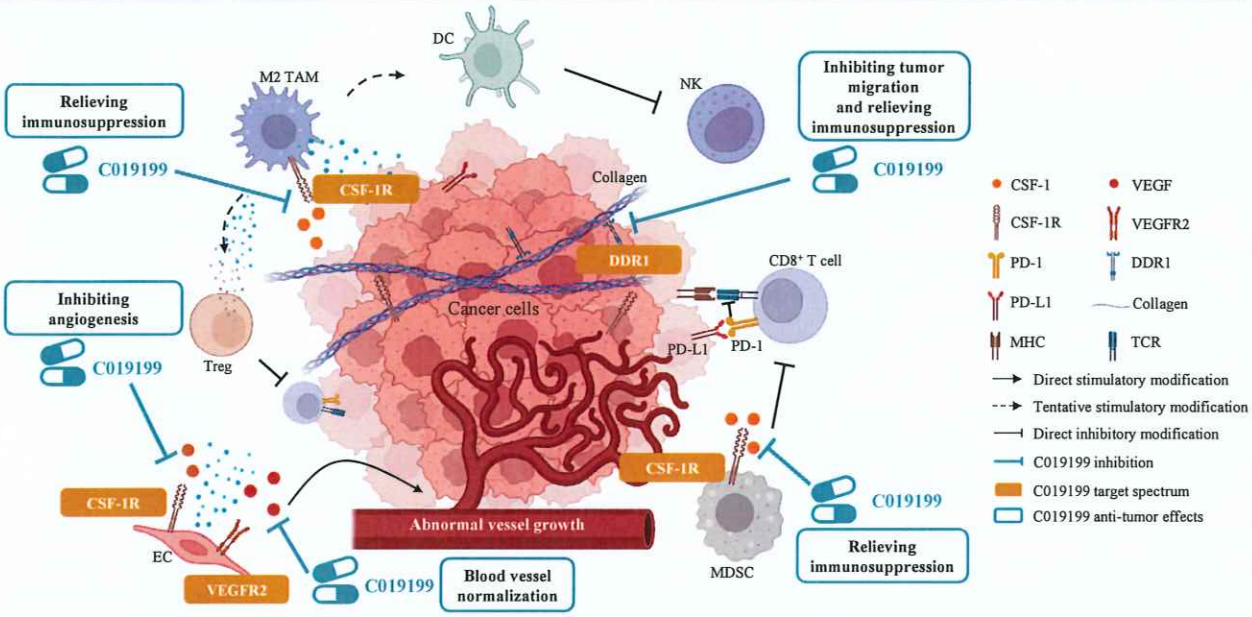
Source: CSCO2022, ASCO2024, China Insights Consultancy

Mechanism of action – CSF-1R/ DDR1/ VEGFR2



Source: Journal of Translational Medicine; Frontiers in Aging Neuroscience; Clinical and Translational Oncology; China Insights Consultancy

C019199 MoA illustration



Note:

CSF1: Colony stimulating factor 1; CSF1-R: Colony stimulating factor 1 receptor; PD-1: Programmed death protein 1; PD-(L)1: Programmed death-ligand 1; MHC: Major histocompatibility complex; VEGF: Vascular endothelial growth factor; VEGFR2: Vascular endothelial growth factor receptor 2; DDR1: Discoidin domain receptor tyrosine kinase 1; TCR: T-cell receptor; DC: Dendritic cell; MDSC: Myeloid-derived suppressor cell; M2 TAM: M2 like tumor-associated macrophage; EC: Endothelial cell; TREG: Regulatory T Cell; NK: Natural killer

Source: Journal for ImmunoTherapy of Cancer; Biomedicines; Journal of Nanobiotechnology; China Insights Consultancy

Comparisons of representative drugs(candidates) with the same target of C019199

C019199 | Comparison

Comparisons of representative drugs(candidates) with the same target of C019199

Drug name	Target	Company	Status	Indication	Trial name	Trial phase	Num. of patient	ORR	AE
Pexidartinib	CSF1R/ FLT3/ c-Kit	Daiichi Sankyo	FDA approval: 2019.8	TGCT not amenable to surgical resection	ENLIVEN	III	N=120	39.3% (vs. 0%, placebo)	13% patients occurred serious adverse events
Vimseltinib	CSF1R	Deciphera	NDA (U.S.)	TGCT not amenable to surgical resection	MOTION	III	N=123	40% (vs. 0%, placebo)	6% of patients discontinued treatment due to TEAEs
ABSK021	CSF1R	Abbisko	Phase III (China & U.S.)	TGCT not amenable to surgical resection	NCT04192344	Ib	N=56	87.5% (50mg QD) 66.7% (25mg QD)	Most of the TEAEs were grade 1/2
Apatinib	VEGFR2	Hengrui	NMPA approval: 2014.10	>2 lines advanced or metastatic gastric cancer	NCT01512745	III	N=267	2.8% (vs. 0%, placebo)	8.5% patients occurred grade 3/4 HFSR adverse events
				Hepatocellular carcinoma after systemic therapy	AHELP	III	N=387	10.7% (vs. 1.5%, placebo)	17.1% patients occurred serious adverse events

- CSF1R has demonstrated effective anti-TCGT tumor activity in clinical studies. Additionally, **high levels of CSF1 are expressed in breast cancer, prostate cancer, pancreatic cancer, kidney cancer, ovarian cancer, and many other types of cancers, suggesting a broad potential for therapeutic application.**
- VEGFR2 inhibitors have also shown effective anti-tumor activity in solid tumors such as gastric cancer and liver cancer. Furthermore, in previous animal studies, the combination of PD-1 inhibitors and VEGFR2 inhibitors was found to reshape the immune microenvironment of patients, thereby helping immunotherapy to more effectively eliminate cancer cells.
- C019199, a tri-target (CSF1R/ VEGFR2 /DDR1) drug, is able to target the regulation of the tumor immune microenvironment. Phase I studies of C019199 as a monotherapy for the treatment of solid tumors demonstrated its safety and anti-tumor activity. When combined with PD-1 immune checkpoint inhibitors, it exhibits synergistic effects, showing good potential for future applications.

Source: ClinicalTrials, NMPA, Hepatology, China Insights Consultancy

As the therapeutical effect of monotherapy of anti-PD-1/PD-L1 drugs is limited, C019199 is expected to have a broad market as a combination with anti-PD-1/PD-L1 drugs

C019199 | Combination

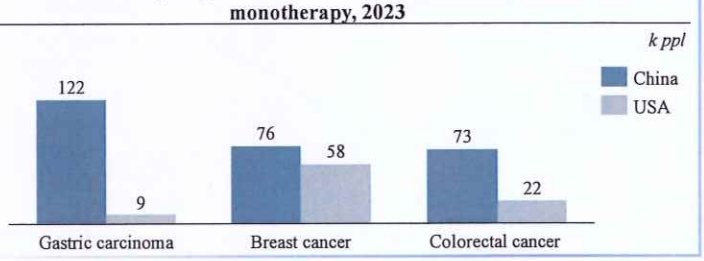
Introduction to PD-1/PD-L1 inhibitors

- As an important pathway for tumor cells to escape from cytotoxicity, some of them may express PD-L1 on cell membrane which can activate PD-1 on the cell membrane of T-lymphocyte, suppressing its immune function.
- PD-1/PD-L1 inhibitor refers to the drugs targeting the signaling pathway of PD-1/PD-L1, blocking its function in immunosuppression, which would induce the anti-oncology effect of immune system.

Disadvantages of anti-PD-1/PD-L1 monotherapy for tumors

- **Limitation of tumor microenvironment:** Anti-PD-1/PD-L1 therapies can eliminate tumor cells by activating the immune system, therefore the therapeutic effect of such drugs largely relies on the function of the immunocytes which can be effected by the tumor microenvironment. Tumor with complicated microenvironment may show poor response to anti-PD-1/PD-L1 monotherapies.
- **Limitation in immunocyte stimulation:** According to former researches, anti-PD-1/PD-L1 therapies can only stimulate the function of immunocytes for a short period. The long-term anti-PD-1/PD-L1 monotherapies can be ineffective if the tumor cells are not totally eliminated during the window of opportunity.

Incidence of eligible patients with no response to anti-PD-1/PD-L1 monotherapy, 2023



Key Analysis

- Though is widely expressed among tumor cells, the therapeutical effect of anti-PD-1/PD-L1 monotherapy may still be limited due to tumor microenvironment or window of opportunity for curing, which makes drug combination a more ideal therapy than monotherapy. **With its unique function in regulating tumor microenvironment, C019199 is expected to have a broad market as a combination with anti-PD-1/PD-L1 drugs, with more than 360,000 patients eligible in China and USA.**

Clinical pipelines of drugs targeting CSF1R, registered on CDE, phase II and III (1/2)

CSF1R | Clinical pipeline

Clinical pipelines of drugs targeting CSF1R, registered on CDE, phase II and III, as of LPD

Drug name/code	Target	Company/institution	Phase	Indications	First Posted Date	Trial Number
Pexidartinib	KIT; CSF1R; FLT3	DAIICHI SANKYO; Catalent CTS	III	TGCT	2020-08-17	CTR20201220
Nintedanib	VEGFR; CSF1R; PDGFR-β; FGFR	Boehringer Ingelheim	III	IPF	2021-07-01	CTR20211487
Surufatinib	CSF1R; FGFR1; VEGFR	Hutchison MediPharma 和记黄埔	III	Advanced neuroendocrine carcinoma	2021-07-09	CTR20211631
Chiauranib	AURKB; VEGFR; PDGFR; KIT; CSF1R	Chipscreen Biosciences 微芯生物	III	Small cell lung carcinoma	2021-11-02	CTR20210658
			III	Ovarian neoplasms	2021-12-20	CTR20211892
			II	Carcinoma, pancreatic ductal	2024-08-20	CTR20242363
			II	TNBC	2023-03-21	CTR20220336
			II	Sarcoma	2022-08-02	CTR20221212
OH2 injection	CSF1R	Binhui Biopharma 武汉滨会生物	III	Melanoma	2023-01-10	CTR20223472
Pimicotinib	CSF1R	Abbisko Therapeutics 和誉生物	III	TGCT	2022-12-30	CTR20223301
			II	Pancreatic neoplasms	2023-10-17	CTR20233124
			II	Graft vs host disease	2023-05-30	CTR20230954
Simmitinib	FGFRs; CSF1R; VEGFR2	Runshi Pharma; Shanghai Institute of Materia Medica Chinese Academy of Sci 润石医药; 中国科学院上海药物研究所	III	Esophageal squamous cell carcinoma	2024-09-13	CTR20243483
			II	Breast neoplasms	2024-08-22	CTR20243138
			II	Solid tumors	2023-12-07	CTR20233821

Source: Pharmacodia; CDE; China Insights Consultancy

Clinical pipelines of drugs targeting CSF1R, registered on CDE, phase II and III (2/2)

Clinical pipelines of drugs targeting CSF1R, registered on CDE, phase II and III, as of LPD

Drug name/code	Target	Company/institution	Phase	Indications	First Posted Date	Trial Number
C-019199	**CSF1R; VEGFR2; DDR1**	**Haixi New Drug Creation 海西新药**	**II**	**Solid tumors**	**2023-06-30**	**CTR20231960**
Tinengotinib	AURKA; AURKB; VEGFR; FGFRs; JAK1; JAK2; CSF1R	TransThera Sciences 药捷安康	II	Solid tumors	2022-04-13	CTR20212760
			II	Biliary tract neoplasms	2022-04-13	CTR20232860

Source: Pharmacodia; CDE; China Insights Consultancy

Clinical pipelines of drugs targeting CSF1R, regulated by FDA, phase II and III (1/2)

Clinical pipelines of drugs targeting CSF1R, regulated by FDA, phase II and III, as of LPD

Drug name/code	Target	Company/institution	Phase	Indications	First Posted Date	Trial Number
Pazopanib	VEGFR;LCK; PDGFR-α; KIT; CSF1R; PDGFR-β; HDAC; FGFR1; FGFR3; ITK	Xynomic Pharma 徐诺药业	III	Locally advanced or metastatic renal cell carcinoma	2018-07-19	NCT03592472
Nivolumab	CSF1R;PDGFR-β;VEGFR;KIT; PDGFR-α;RET;FLT3	Bristol-Myers Squibb	III	Previously untreated advanced or metastatic renal cell carcinoma	2017-05-04	NCT03141177
Pacritinib	CSF1R;FLT3;JAK2;IRAK1;CDK2	Swedish Orphan Biovitrum	III	Primary Myelofibrosis;Post-polycythemia Vera Myelofibrosis;Post-essential Thrombocythemia Myelofibrosis	2017-05-24	NCT03165734
Vimseltinib	CSF1R	Deciphera Pharmaceuticals	III	TGCT; Synovitis, pigmented villonodular	2021-10-14	NCT05059262
			II	Graft vs host disease	2024-09-27	NCT06619561
Bezuclastinib	CSF1R;PDGFR-β;VEGFR;KIT;PDGFR-α;RET;FLT3	Cogent Biosciences	III	Gastrointestinal stromal tumors	2022-01-26	NCT05208047
Nintedanib	VEGFR; CSF1R; PDGFR-β; FGFR	Boehringer Ingelheim	III	Children and adolescents with interstitial lung disease	2022-03-18	NCT05285982
Emactuzumab	CSF1R	SynOx Therapeutics	III	Tenosynovial giant cell tumor	2022-06-14	NCT05417789

Source: Pharmacodia; FDA; China Insights Consultancy

Clinical pipelines of drugs targeting CSF1R, regulated by FDA, phase II and III (2/2)

Clinical pipelines of drugs targeting CSF1R, regulated by FDA, phase II and III, as of LPD

Drug name/code	Target	Company/institution	Phase	Indications	First Posted Date	Trial Number
Pimicotinib	CSF1R	Abbisko Therapeutics 和誉生物	III	Synovitis, Pigmented Villonodular	2023-04-27	NCT05804045
Tinengotinib	AURKA; AURKB; VEGFR; FGFRs; JAK1; JAK2; CSF1R	TransThera Sciences 药捷安康	III	Cholangiocarcinoma	2023-12-20	NCT05948475
			II	Breast neoplasms; TNBC; Thyroid neoplasms; Small cell lung carcinoma; Prostatic neoplasms; Sarcoma; Urinary bladder neoplasms; Gallbladder neoplasms; Stomach neoplasms	2021-03-14	NCT04742959
Seralutinib	PDGFR; CSF1R; KIT; CSF2R; PDGFR-β; PDGFR-α	Gb002	III	Pulmonary arterial hypertension	2023-12-28	NCT05934526
Axatilimab	CSF1R	Incyte Biosciences	III	Recurrent or refractory active chronic graft-versus-host disease	2024-02-16	NCT06263478
Derazantinib	CSF1R; FGFR2; FGFR1; FGFR3; VEGFR2	Basilea Pharmaceutica	II	Cholangiocarcinoma; Biliary tract neoplasms; Carcinoma, hepatocellular;	2017-09-28	NCT03230318
			II	Carcinoma, transitional cell	2019-08-02	NCT04045613
Elzovantinib	CSF1R; c-Met; SRC	Turning Point; Zai Lab 再鼎医药	II	Solid tumors	2019-09-21	NCT03993873
HH185	FGFR1; FGFR3; FGFR2; CSF1R	Keymed Biomedical 康诺亚生物	II	Locally advanced or metastatic cholangiocarcinoma	2021-09-10	NCT05039892
Adrixetinib	AXL; CSF1R; MerTK;	Qurient; Merck	II	Carcinoma, hepatocellular; Esophageal neoplasms; Uterine cervical neoplasms; Stomach neoplasms;	2023-01-12	NCT05438420

Source: Pharmacodia; FDA; China Insights Consultancy

Clinical pipelines of drugs targeting VEGFR2, registered on CDE, phase II and III (1/2)

Clinical pipelines of drugs targeting VEGFR2, registered on CDE, phase II and III , as of LPD

Drug name/code	Target	Company/institution	Phase	Indications	First Posted Date	Trial Number
Anlotinib Dihydrochloride	VEGFR2;KIT;PDGFR-β; FGFR;	Chia-tai Tianqing 正大天晴	III	Advanced non-squamous NSCLC	2019-06-11	CTR20191086
Apatinib Mesylate	VEGFR2	Hengrui Pharmaceuticals 恒瑞医药	III	Recurrent ovarian cancer after failure of platinum-based therapy	2019-07-05	CTR20191305
Famitinib	RPTKs; FLT3; VEGFR	Hengrui Pharmaceuticals 恒瑞医药	II	Lung neoplasms	2021-05-11	CTR20211049
			II	Solid tumors	2020-06-05	CTR20200720
			II	Genital neoplasms, female; Urologic neoplasms	2019-01-23	CTR20191816
Sitravatinib	VEGFR; RET; c-Met; AXL; KIT; MerTK; DDR2; PDGFR	BeiGene 百济神州	III	Carcinoma, hepatocellular	2023-04-21	CTR20231157
			II	Carcinoma, non-small-cell lung	2023-10-27	CTR20233070
			II	Solid tumors	2019-02-28	CTR20182363
Recombinant anti-VEGFR2 mono-antibody	VEGFR2	Buchang Pharma 步长制药	III	Advanced gastric or gastroesophageal junction adenocarcinoma	2023-04-21	CTR20231207
KC1036	AXL; VEGFR2; FLT3	Konruns Pharma 康辰药业	III	Esophageal squamous cell carcinoma	2023-12-26	CTR20234222
			II	Advanced Ewing sarcoma in adolescents 12 years and older	2024-08-05	CTR20242898
			II	Solid tumors	2022-06-08	CTR20220211
AK104	VEGFR; KIT; FGFR4; FGFR; PD-1; CTLA4; PDGFR-α; RET	Akeso 康方生物	III	Incurable, non-metastatic hepatocellular carcinoma	2024-05-10	CTR20241406

Source: Pharmacodia; CDE; China Insights Consultancy

Clinical pipelines of drugs targeting VEGFR2, registered on CDE, phase II and III (2/2)

Clinical pipelines of drugs targeting VEGFR2, registered on CDE, phase II and III , as of LPD

Drug name/code	Target	Company/institution	Phase	Indications	First Posted Date	Trial Number
Simmitinib	FGFRs; CSF1R; VEGFR2	Runshi Pharma 润石医药	III	Esophageal squamous cell carcinoma	2024-09-13	CTR20243483
			II	Breast neoplasms	2024-08-22	CTR20243138
			II	Solid tumors	2023-12-07	CTR20233821
Recombinant anti-VEGFR2 mono-antibody	VEGFR2	Eastern Biotech 北京东方百泰	II	Advanced EGFR mutations NSCLC	2021-06-09	CTR20211128
Recombinant anti-VEGFR2 mono-antibody	VEGFR2	GeneScience 长春金赛	II	Advanced gastric or gastroesophageal junction adenocarcinoma	2022-04-14	CTR20220815
Fruquintinib	VEGFR	Hutchison MediPharma 和记黄埔	II	Locally advanced or metastatic renal cell carcinoma	2022-08-15	CTR20222029
C-019199	**CSF1R; VEGFR2; DDR1**	**Haixi Pharma 海西新药**	**II**	**Solid tumors**	**2023-06-30**	**CTR20231960**
Pulocimab	VEGFR2	KRDF Pharma 康融东方	II	Advanced gastric or gastroesophageal junction adenocarcinoma	2024-04-17	CTR20241225

Source: Pharmacodia; CDE; China Insights Consultancy

Clinical pipelines of drugs targeting VEGFR2, regulated by FDA, phase III(1/3)

Clinical pipelines of drugs targeting VEGFR2, regulated by FDA, phase III, as of LPD

Drug name/code	Target	Company/institution	Phase	Indications	First Posted Date	Trial Number
Pembrolizumab	KIT;PDGFR-α;VEGFR2;FGFR3;FGFR4;FGFR1;FGFR2;RET	Merck Sharp & Dohme	III	Endometrial carcinoma	2019-03-21	NCT03884101
			III	Incurable/non-metastatic hepatocellular carcinoma	2020-01-27	NCT04246177
			III	Esophageal squamous cell carcinoma	2021-07-29	NCT04949256
Nivolumab	KIT; PD-1; RET; DDR2; PDGFR;c-Met;AXL; MerTK; VEGFR2	Mirati Therapeutics Bristol Myers Squibb	III	Non-small-cell lung cancer	2019-04-04	NCT03906071
			III	Renal cell carcinoma	2021-08-03	NCT04987203
			III	Later-lines of metastatic colorectal cancer	2022-05-14	NCT05328908
Atezolizumab	cMet;VEGFR2;ROS;MerTK;TIE2;RET;VEGFR1;KIT;NTRK2;TYRO3;FLT3;AXL	Hoffmann-La Roche	III	Advanced renal cell carcinoma	2019-04-08	NCT04338269
			III	Metastatic non-small cell lung cancer	2020-07-07	NCT04471428
			III	Hepatocellular carcinoma	2021-02-25	NCT04770896
Sitravatinib	VEGFR2; RET; c-Met; AXL; KIT; MerTK; DDR2; PDGFR	Mirati Therapeutics; Bristol Myers Squibb	III	Non-small-cell lung cancer	2019-07-15	NCT03906071
Nofazinlimab	KIT;PDGFR-α;FGFR3;FGFR4;FGFR1;FGFR2;RET;VEGFR2	CStone Pharmaceuticals	III	Advanced hepatocellular carcinoma	2019-12-11	NCT04194775

Source: Pharmacodia; FDA; China Insights Consultancy

Clinical pipelines of drugs targeting VEGFR2, regulated by FDA, phase III(2/3)

Clinical pipelines of drugs targeting VEGFR2, regulated by FDA, phase III, as of LPD

Drug name/code	Target	Company/institution	Phase	Indications	First Posted Date	Trial Number
Panitumumab	EphA2;TRKA;DDR2;FGFR1;VEGFR2;C-Raf;FGFR2;TIE2;CSF1R;ABL1;B-raf V600E;PDGFR-α;PDGFR-β;B-raf;KIT;MAPK11;FRK;RET	Amgen	III	Metastatic colorectal cancer subjects with kirsten rat sarcoma (KRAS) p.G12C mutation	2022-01-20	NCT05198934
Durvalumab and Tremelimumab	KIT; PDGFR-α;CTLA4; FGFR3; FGFR4; FGFR1; FGFR2; RET; VEGFR2;PD-L1	AstraZeneca	III	Locoregional hepatocellular carcinoma	2022-03-28	NCT05301842
Zanzalintinib	VEGFR; c-Met; VEGFR2; AXL; MerTK	Exelixis	III	Squamous cell carcinoma of head and neck	2024-06-07	NCT05678673
			III	Carcinoma, renal cell	2023-01-01	NCT05678673
			III	Colorectal neoplasms	2022-09-07	NCT05425940
Ripretinib	KIT;PDGFR-β;TIE2;PDGFR-α;VEGFR2;B-raf	Deciphera Pharmaceuticals	III	Advanced gastrointestinal stromal tumors with Specific KIT Exon mutations	2023-02-17	NCT05734105
Axitinib intravitreal implant	PDGFR;VEGFR2	Ocular Therapeutix	III	Neovascular age-related macular degeneration	2024-01-25	NCT06223958

Source: Pharmacodia; FDA; China Insights Consultancy

Clinical pipelines of drugs targeting VEGFR2, regulated by FDA, phase III(3/3)

Clinical pipelines of drugs targeting VEGFR2, regulated by FDA, phase III, as of LPD

Drug name/code	Target	Company/institution	Phase	Indications	First Posted Date	Trial Number
Ramucirumab	VEGFR2	AstraZeneca		Second- or Later-line Advanced or Metastatic Gastric or Gastroesophageal Junction Adenocarcinoma Expressing Claudin18.2	2024-04-04	NCT06346392
Vorolanib	VEGFR2; PDGFR; RET; KIT; FLT3	Eyepoint Pharmaceuticals	III	Wet age related macular degeneration	2024-10-31	NCT06668064

Source: Pharmacodia; FDA; China Insights Consultancy

Clinical pipelines of drugs targeting DDR1, registered on CDE

Clinical pipelines of drugs targeting DDR1, registered on CDE, as of LPD

Drug name/code	Target	Company/institution	Phase	Indications	First Posted Date	Trial Number
C-019199	**CSF1R; VEGFR2; DDR1**	**Haixi Pharma海西新药**	**II**	**Solid tumors**	**2023-06-30**	**CTR20231960**
ICP-033	VEGFR; DDR1	InnoCare Pharma Tech 诺诚健华	I	Solid tumors	2022-02-25	CTR20213113
APL-102	MAPKs; CSF1R; VEGFR; PDGFR; B-raf; C-Raf; DDR1	Crownmab Biotech 冠科美博	I	Solid tumors	2021-08-02	CTR20211072

Source: Pharmacodia; CDE; China Insights Consultancy

Clinical pipelines of drugs targeting DDR1, regulated by FDA

Clinical pipelines of drugs targeting DDR1, regulated by FDA, as of LPD

Drug name/code	Target	Company/institution	Phase	Indications	First Posted Date	Trial Number
Merestinib	c-Met; AXL; DDR1; DDR2; MKNK1; MKNK2; ROS; Protein-tyrosine kinases; MST1R; FLT3; MerTK; TIE2; TRKA; NTRK2; NTRK3	Eli Lilly	II	Biliary tract neoplasms	2016-05-19	NCT02711553
			I	Pancreatic neoplasms; Skin melanoma; Breast neoplasms	2016-06-29	NCT02791334
			I	Leukemia, myeloid, acute	2017-08-10	NCT03125239
PRTH-101	DDR1	Incendia Therapeutics	I	Advanced malignancies	2023-03-03	NCT05753722

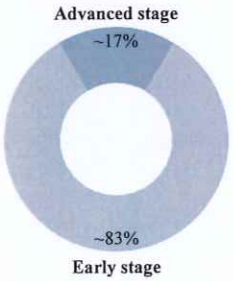
Source: Pharmacodia; FDA; China Insights Consultancy

Overview of renal cell carcinoma

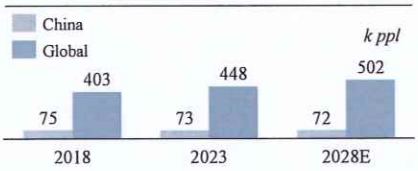
Overview of renal cell carcinoma

- Renal cell carcinoma (RCC) is a malignant tumor originating from the epithelial cells of the renal tubules, accounting for 80%-90% of malignant kidney tumors. The most common histopathological type of renal cell carcinoma is clear cell carcinoma, followed by papillary renal cell carcinoma and chromophobe carcinoma, along with less common types such as collecting duct carcinoma
- With advancements in medical imaging, the detection rate of early-stage renal cell carcinoma has gradually increased. Localized renal cell carcinoma can achieve satisfactory outcomes through nephron-sparing tumor resection or radical nephrectomy (RN). With the ongoing development of targeted therapies and the rise of immunotherapy, the treatment outcomes for advanced renal cell carcinoma have also progressively improved

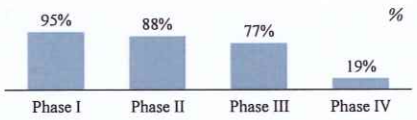
The stage at diagnosis



The incidence of RCC



Five-year survival rate of RCC



Epidemiology:

- **Area:** The highest incidence rates are observed in developed Western countries such as North America and Western Europe, while the lowest rates are found in developing countries in Africa and Asia
- **Sex:** The age-standardized incidence rate of renal cell carcinoma is 6.1 per 100,000 in males and 3.2 per 100,000 in females

Risk factor:

- **Genetics:** Most RCC cases are sporadic, with hereditary cases making up 2% to 4%, typically inherited in an autosomal dominant pattern
- **Smoking:** The relative risk of developing RCC is 1.3 for former smokers and 1.6 for current smokers
- **Obesity:** Obesity may increase the risk of RCC due to higher levels of androgens and estrogens, or through certain cytokines released by fat cells

Source: NHC; The Lancet Global Health; China Insights Consultancy

Drivers of oncology drugs development

Drivers of oncology drugs development

Strong market demand for new and effective anti-cancer treatments

- The incidence and mortality rates of cancer in China remain high, leading to a strong market demand for new and effective anti-cancer drugs. With an aging population and changing lifestyles, the rising prevalence of cancer underscores the importance of innovative drug development

Enhanced research capabilities and improved translation of scientific discoveries

- China's investment in research continues to grow, along with improvements in the translation of research outcomes. These factors are driving technological advancements and innovation in new drug development, particularly in the field of anti-cancer drugs, with an increasing number of research institutions and companies actively participating in drug discovery

Accelerated international collaboration to facilitate market entry and expansion

- Cross-border business development between domestic and foreign pharmaceutical companies is becoming a trend. This collaboration not only accelerates the market entry of innovative anti-cancer drugs but also facilitates market expansion. By leveraging advanced technologies and experiences from abroad, domestic companies can expedite their drug development and market positioning

Government support and strategic guidance to foster innovation in drug development

- The government places a high priority on new drug development, implementing a series of policies to expedite the review and approval processes for new drugs. By establishing guidelines that emphasize "clinical value," the government encourages the research and development of innovative drugs, creating a more favorable environment for enterprises. These policy measures enhance the efficiency of innovative drug development and boost market confidence

Source: China Insights Consultancy

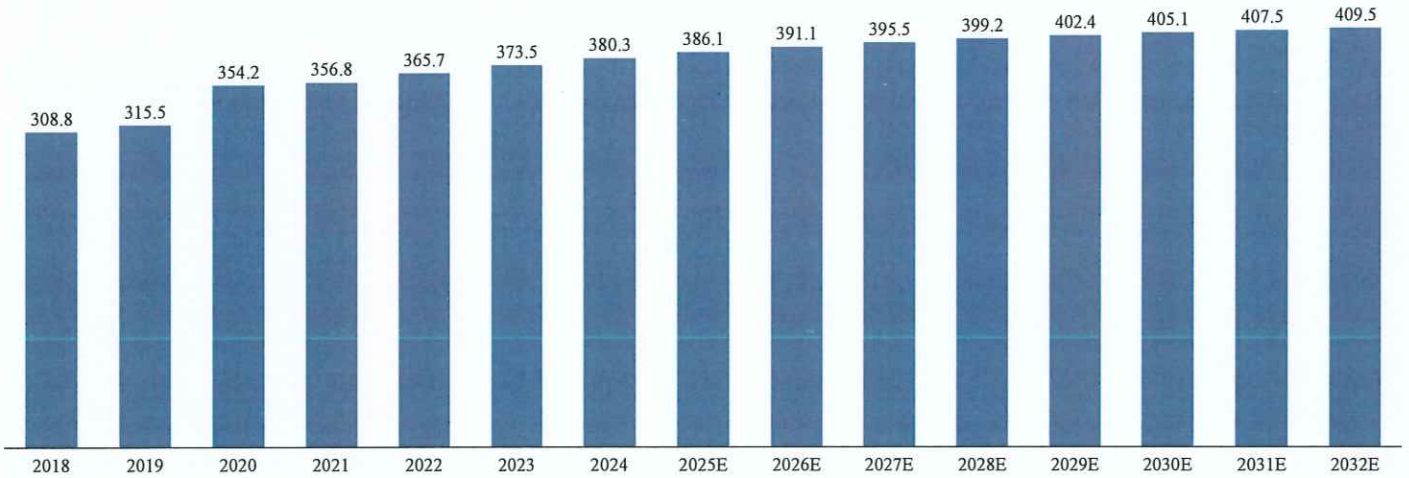
Table of Contents

Prevalence of ophthalmic diseases in China, 2018-2032E

Prevalence of ophthalmic diseases in China, 2018-2032E

CAGR	2018-2024	2024-2032E
Ophthalmic diseases	3.5%	0.9%

million ppl



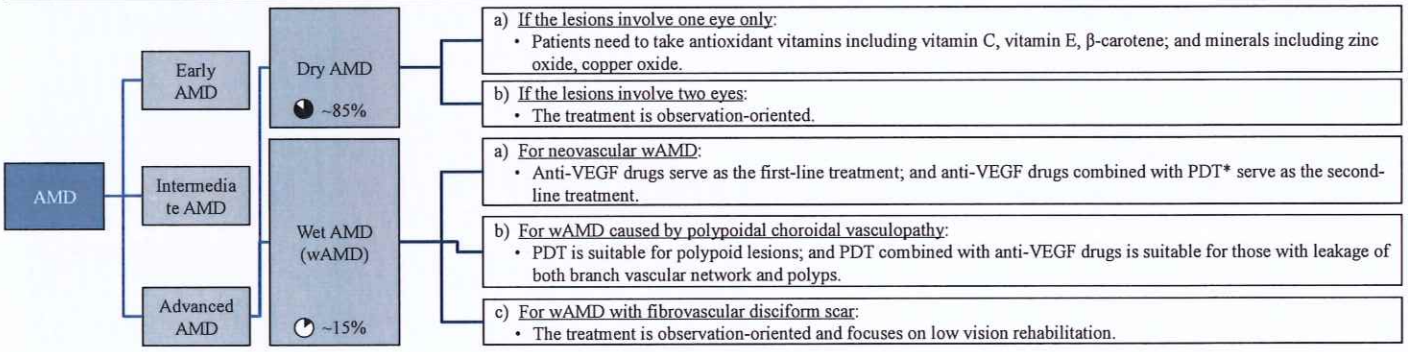
Source: GBD2021; China Insights Consultancy

Introduction to age-related macular degeneration (AMD)

Introduction to AMD

- **Age-related macular degeneration (AMD)** is a disorder of the macula characterized by one or more of the following:
  - 1) Presence of at least intermediate-size drusen;
  - 2) Retinal pigment epithelium (RPE) abnormalities such as hypopigmentation or hyperpigmentation;
  - 3) Presence of any of the following features: geographic atrophy of the RPE, choroidal neovascularization, polypoidal choroidal vasculopathy (PCV), reticular pseudodrusen, or retinal angiomatous proliferation.

Treatment path and options of AMD



Source: CNKI; China Insights Consultancy

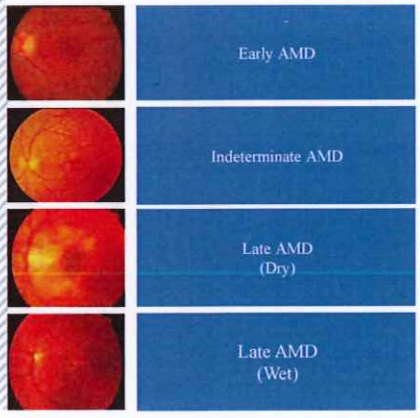
Classification and diagnosis of AMD

Classification of AMD

Early AMD		**Low risk of progression:** • Medium drusen (63 micrometres or more and less than125 micrometres). • Gmentary abnormalities. **Medium risk of progression:** • Large drusen (125 micrometres or more). • Reticular drusen. • Medium drusen with pigmentary abnormalities. **High risk of progression:** • Large drusen (125 micrometres or more) with pigmentary abnormalities. • Reticular drusen with pigmentary abnormalities. • Vitelliform lesion without significant visual loss (best-corrected acuity better than 6/18). • Atrophy smaller than 175 micrometres and not involving the fovea.
Indeterminate AMD		• Retinal pigment epithelial (RPE) degeneration and dysfunction (presence of degenerative AMD changes with subretinal or intraretinal fluid in the absence of neovascularisation). • Serous pigment epithelial detachment (PED) without neovascularisation.
Late AMD	Dry	**Geographic atrophy** (in the absence of neovascular AMD). **Significant visual loss** (6/18 or worse) associated with: • Dense or confluent drusen • Advanced pigmentary changes and/or atrophy • Vitelliform lesion
	Wet	**Wet active:** • Classic choroidal neovascularisation (CNV). • Occult (fibrovascular PED and serous PED with neovascularisation). • Mixed (predominantly or minimally classic CNV with occult CNV). • Retinal angiomatous proliferation (RAP). • Polypoidal choroidal vasculopathy (PCV). **Wet Inactive**: • Fibrous scar. • Sub-foveal atrophy or fibrosis secondary to an RPE tear. • Atrophy (absence or thinning of RPE and/or retina). • Cystic degeneration (persistent intraretinal fluid or tubulations unresponsive to treatment).

Diagnosis of AMD

Main diagnostic methods:
- Fundus fluorescein angiography
- Optical coherence tomography
- Fundus autofluorescence
- Confocal laser fundus imaging.



Source: Allegheny County Medical Society; China Insights Consultancy

Comparison among treatments for wAMD

Comparison among treatments for wAMD

Low ○ ◔ ● High

Treatments		Description	Application scope	Disadvantages	Clinical value
Drug therapy	Intravitreal injection of Anti-VEGF agents	• VEGF is a natural glycoprotein in endothelial cells that plays a dominant role in AMD progression • VEGF inhibitors have demonstrated improved visual and anatomic outcomes compare with other therapies	• Neovascular AMD	• Long-term therapy and direct injection to eyeball lead to poor compliance • Highly-priced (RMB~4,000 per dose)	● • First-line clinical treatment • Most effective and safe medication now
	Antioxidant vitamin and minerals	• Used as supportive therapy for slowing down the progression	• Early AMD	• Only supportive therapy, no help for vision recovery	◔ • Recommended for early AMD
Other therapies	Photodynamic therapy (PDT)	• A two-part process involving systemic administration of a photosensitizing drug followed by nonthermal light application to the macular pathology	• Neovascular AMD with macular neovascularization located outside macula central fovea	• High recurrence rate • Highly-priced (RMB~80,000 per year)	◔ • Second line treatment combined with anti-VEGF
	Laser photocoagulation	• Krypton laser is clinically commonly used to prevent choroid outer layer leakage	• Neovascular AMD	• High recurrence rate • Possible nerve fiber damage	◔ • Supplementary therapy

Source: Chinees Medical Association; China Insights Consultancy

Pain points of current wAMD treatments and future trends

Pain points of current wAMD treatments

1. **Low compliance with intraocular injection**
   - Patients with wAMD often require frequent intraocular injections of anti-VEGF drugs to maintain vision. However, compliance with this treatment modality is low due to high frequency of treatment as well as the discomfort and anxiety that intraocular injections cause.
2. **Drug side effects and safety issues**
   - Although eye injections of anti-VEGF drugs are generally safe, long-term and frequent use may cause systemic side effects, such as high blood pressure. It may also cause ocular complications, such as endophthalmitis, retinal detachment, etc.
3. **High cost of treatment**
   - Anti-VEGF drugs are more expensive and require long-term and frequent use, resulting in high treatment costs. This is a heavy financial burden for patient.
4. **Lack of long-term effective treatment options**
   - Long-term and frequent use of anti-VEGF drugs may cause the sensitivity of eye cells to anti-VEGF drugs to decrease or disappear, resulting in drug resistance and reducing efficacy. It is quite urgent to find a long-term effective treatment option.

Future trends of wAMD treatments

1. **Emerging ophthalmic delivery systems**
   - There is a growing number of innovative delivery systems empowering ophthalmic drugs, for instance, ocular inlay delivery system, nanoparticles, etc. These new delivery systems not only improve the bioavailability and stability of drugs, but also reduce the number of dosing times and the treatment burden of patients.
2. **Innovative therapies on wAMD**
   - Clinical trials of certain gene therapy achieved positive results with long-term follow-up, by enhancing the ability of ocular cells to produce anti-VEGF or reducing the formation of leaky blood vessels. And it potentially works to reduce senescent cells and their metabolin to achieve obvious therapeutic effects.
3. **Enhancing patient compliance**
   - On one hand, it is important to reduce the number of injections and improve patient compliance by developing long-acting drugs or new delivery systems. On the other hand, patient education and support should be strengthened to improve their understanding of the disease and treatment, while providing necessary psychological support regarding their anxiety and fear.

Source: Chinees Medical Association; China Insights Consultancy

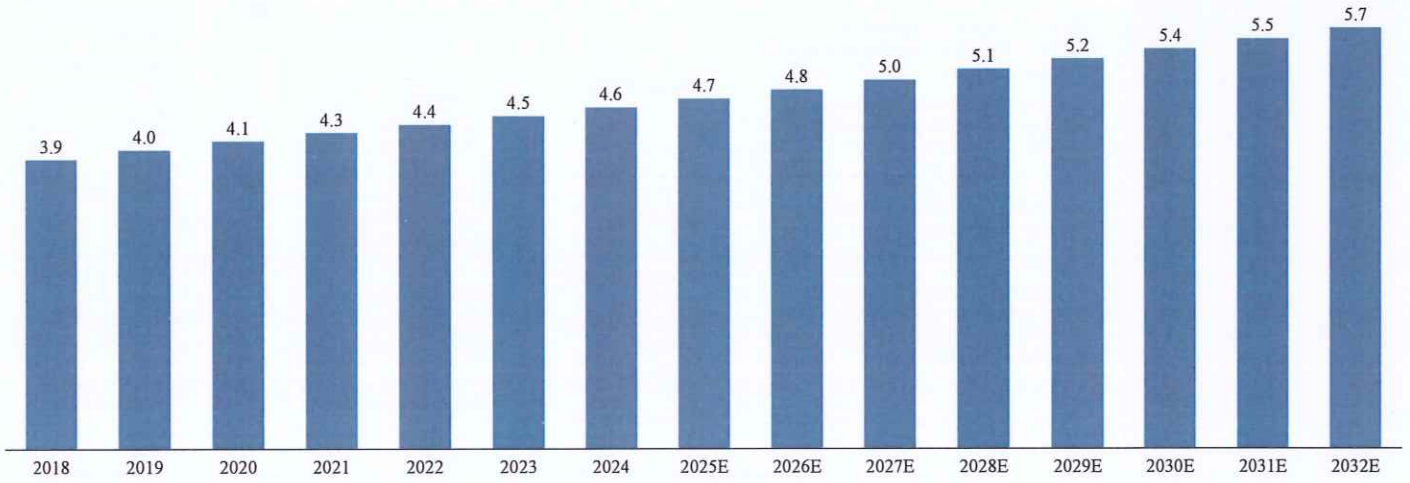
Prevalence of wAMD in China, 2018-2032E

wAMD | Epidemiology

Prevalence of wAMD in China, 2018-2032E

CAGR	2018-2024	2024-2032E
wAMD	2.8%	2.6%

million ppl



Source: Journal of Global Health; China Insights Consultancy

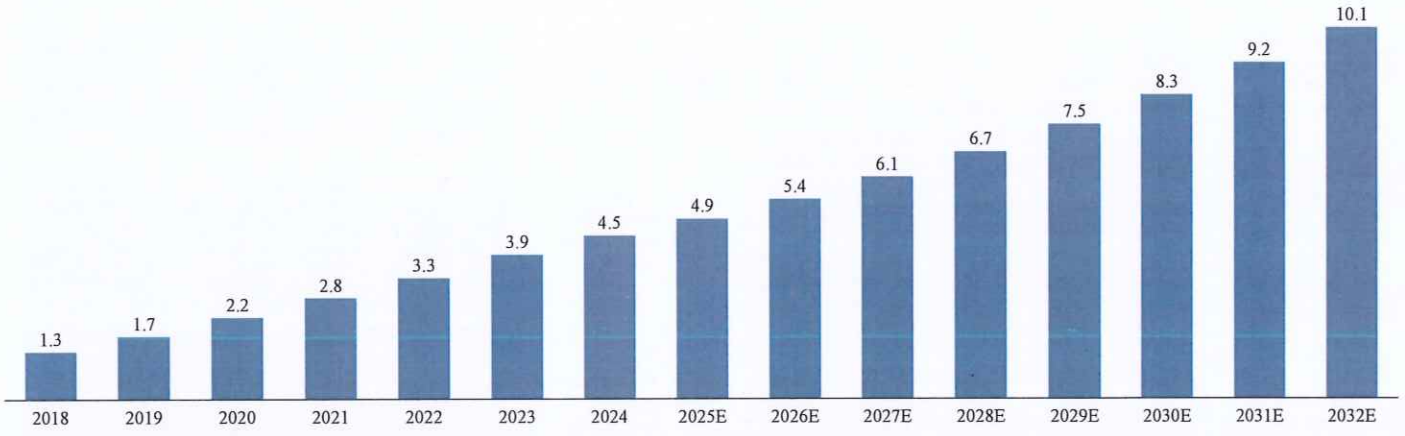
Market size of drugs for wAMD, 2018-2032E

wAMD | Market size

Market size of drugs for wAMD in China, 2018-2032E

CAGR	2018-2024	2024-2032E
Market size	22.8%	11.3%

billion RMB



- Likewise, the global market size of drugs for wAMD is expected to increase from USD5.8 billion in 2023 to USD10.6 billion in 2032, representing a CAGR of 6.9%.

Source: United Union; expert interview; China Insights Consultancy

Introduction to diabetic macular edema (DME)

Introduction to DME

Definition

- **Diabetic retinopathy (DR) is the ocular manifestation of end-organ damage in diabetes mellitus**, the most common early clinically visible manifestations of which include microaneurysm formation and intraretinal hemorrhages. Retinal neurodegeneration is an early event in the pathogenesis of diabetic retinopathy, which could contribute to the development of microvascular abnormalities.
- As DR can lead to a series of microvascular lesions, diabetic macular edema (DME) may occur when macular capillary is damaged, being the consequence of thickening of macular central retinal. **As the main reason of hypopsia, DME can happen at any stage of DR.**

Classification of DR and DME

Disease	Stage	Description
DR	I (Mild nonproliferative)	Capillary hemangioma-like changes
	II (Moderate nonproliferative)	Between mild and severe
	III (Severe nonproliferative)	More than 20 petechia observed in one quadrant; Venous beads-like changes observed in two quadrants; IRMA observed in one quadrant
	IV (Mild proliferative)	NVE or NVD observed
	V (Moderate proliferative)	Fibrous membrane observed with or without preretinal hemorrhage and vitreous hemorrhage
	VI (Severe proliferative)	Retinal detachment observed with fibrous vascular membrane
DME	NCI-DME	Macular retinal damages more than1mm away from fovea
	CI-DME	Macular retinal damages less than 1mm away from fovea

Diagnosis method of DR and DME

- Clinical history
- Ocular examination
- Investigations
  - OCT
  - Fundus fluorescein angiography
  - Systemic

Source: Internal Medicine; CNKI; China Insights Consultancy

Treatment of DME

Chronic diseases management

- Since DME is the complication of diabetes, it is essential to control the damage caused by chronic diseases in order to relieve hypopsia. It has been widely recognized that blood glucose, lipid, and pressure managements are vital parts of the treatment of DME.

Ophthalmic treatment

- **Intravitreal injection of Anti-VEGF agents** According to clinical guidance, Anti-VEGF agents is the first-line therapy for DME, which demonstrated improved visual and anatomic outcomes compare with other therapies. However, due to the poor compliance and high cost, intravitreal injection of Anti-VEGF agents may eventually with poor prognosis.
- **Laser photocoagulation** Laser photocoagulation has been considered as the standard therapy for DME before the invention of Anti-VEGF agents, which can help improve retinal oxygenation, and significantly help recover central vision in the short term. The combination of Anti-VEGF agents and laser photocoagulation can lead to a better therapeutical effect.
- **Hormonal therapy** Since a series of inflammatory factors participate in the progression of DME, intravitreal injection of glucocorticoid is a practical treatment for DME by its anti-inflammatory effects.

Pars plana vitrectomy

- Pars plana vitrectomy (PPV) is an effective therapy for DR and DME patients with poor response to other therapies. However, since the outcome of the surgery may be influenced by plenty of factors, the therapeutical value of PPV in DME and DR still requires further researches to validate.

Source: Internal Medicine; CNKI; Pharmacology; China Insights Consultancy

Clinical pipelines of innovative drugs for DR and DME in China

DR & DME | Clinical pipeline

Clinical pipelines of innovative drugs for DR and DME in China, as of LPD

Drug Name/Code	Drug Type	Target	Company	Phase	Indications	First Posted Date	Trial Number
RC28-E	Biologic	VEGF; FGF	RemeGen Biologics	III	Wet AMD; DME	2023/01/12	CTR20230065
SR1375	Chemical	Unidentified	SIMR Biotechnology	II	Pneumonia; DR; DME; DKD; AD	2024/08/12	CTR20242885
IBI324	Biologic	Ang2; VEGF-A	Innovent Biologics	I	DME	2022/06/17	CTR20221524
ASKG712	Biologic	Ang2; VEGF	Aosaikang Pharma	I	Neovascular AMD; DME	2022/07/29	CTR20221785

Source: Pharmacodia; CDE; China Insights Consultancy

Growth drivers for the ophthalmic drugs market in China

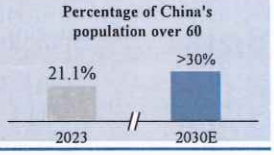
Market overview | Growth driver

Growth drivers for the ophthalmic drugs market in China

- Ophthalmic drugs have become more diverse and user-friendly in terms of dosage forms. Various delivery routes are developed for ophthalmic drugs to ensure the treatment effect and improve patient experience, such as noninvasive gel products, intravitreal injection, subconjunctival injection, etc.
- Domestic drugs also perform well and have large opportunities. For example, Kanghong independently developed Lumitin and broke the monopoly of Lucentis in China's wAMD drugs market.

1 Increasing eye disease patients

- Glaucoma, DME, DR, and many other ophthalmic diseases are highly related to age, whilst an obvious aging trend can be witnessed in China. It is estimated that China's population over 60 will account for more than 30% of the total population by 2035. The deepening of aging will continue to increase the number of eye disease patients and the demand for ophthalmic drugs.



2 Strengthened public awareness

- The awareness of eye care of Chinese residents is constantly being improved, and the consciousness of seeking medical treatment is gradually being strengthened. From 2014 to 2018, the CAGR of the number of eye doctor visits and eye care inpatients in China reached 5.8% and 11.8% respectively. It is expected that the amount of ophthalmic medical treatment will climb to a higher level in the future.
- Besides, national policies such as *The 13th Five-Year National Eye Health Plan (2016-2020)* also promoted the public awareness.

3 Enhanced patient affordability

- With the progress of urbanization, the rapid growth of the income level and the increase of the medical insurance support, residents' affordability for ophthalmic treatment has significantly increased. The potential demands of ophthalmic drugs will continue to be converted to actual demands, and more patients would afford expensive innovative ophthalmic therapies.

4 Enriched drugs and therapies

Source: Ministry of Civil Affairs of China; China Insights Consultancy

Distribution model

Distribution model

	Stock code	Distributor contribution (% of revenue)	Revenue (RMB)	Refund ratio	Distributor inventory ratio
Haixi Pharma	/	100%	309.08 mn (in 2023)	0.1%	[*]
Qingdao Baheal Medical	301015.SZ	68.55%	4,834.79 mn (in 2019)	/	10-18%
XF Pharma	603207.SH	92.28%	401.29 mn (in 2021)	0.42%	12.8%
Yabao Pharma	600351.SH	/	2,558.51 mn (in 2017)	0.35%	/
Buchang Pharma	603858.SH	/	13.66 bn (in 2018)	0.06%	/
Brilliant Pharmaceuticals	/	85.13%	3,236.39 mn (in 2019)	0.70%	5.20%-12.94%
Kingfriend	603707.SH	Main	581.91 mn (in 2016)	0.19%	
Shanghai Yanan Pharma	/	~100.00%	432.22 mn (in 2023)	0.65%	12.79%-19.69%

- According to CIC, the distributor contribution ratio (of revenue), refund ratio [and the distributor inventory ratio] of Haixi Pharma are in line with the industry norm.

Source: prospectus; China Insights Consultancy

Appendix

- The NRDL is a critical component of China's healthcare system, designed to enhance access to essential medications for patients while managing healthcare costs. The NRDL outlines the drugs that are eligible for reimbursement under the national health insurance scheme, significantly influencing the availability and affordability of pharmaceuticals in China..
- To treat cardiovascular diseases, two compounds are commonly used, namely amlodipine and atorvastatin. Amlodipine is a calcium channel blocker that helps relax and widen blood vessels, making it easier for the heart to pump blood, which is primarily used to treat hypertension and angina. Atorvastatin is a statin medication that works by reducing the levels of cholesterol and triglycerides in the blood, which helps lower the risk of heart disease, heart attacks, and strokes by improving cholesterol levels.
- The global oncology drug market is a sector of the biopharmaceutical market focusing on the discovery and commercialization of medicines for the treatment of cancer. The global oncology drug market has expanded significantly in the past, and is projected to further expand at an accelerated pace. Growth in the global oncology drug market is primarily driven by a growing patient pool, development of advanced treatment options such as precision oncology and immuno-oncology as well as combination therapies, improved access to therapies and rise of small- and mid-sized pharmaceutical companies.
- In recent years, the development of innovative drugs for the treatment of TGCT has gained momentum in China, as evidenced by the increasing number of drug candidates registered with the CDE. These emerging therapies are focused on novel targets and aim to address the high unmet medical need in this rare but debilitating disease.
- The development of VEGFR2 inhibitors has matured, with several agents showing robust anti-tumor activity and favorable clinical outcomes in patients with advanced cancers. As the understanding of angiogenesis and tumor microenvironment continues to evolve, VEGFR2 remains a pivotal target in the development of next-generation cancer therapies, particularly in combination with other targeted agents and immunotherapies.

Features of China's Pharmaceutical Market

- Dynamic adjustment of the medical insurance catalog: The National Medical Insurance Administration has been carrying out the adjustment of the drug catalog for many years, and has included more new and beneficial drugs in the medical insurance catalog. For example, the 2024 version of the National Medical Insurance Drug Catalog has added 91 new drugs, bringing the total to 3,159, including innovative drugs and drugs for rare diseases. These adjustments have enabled more patients to enjoy medical insurance reimbursement and reduced the financial burden on patients.
- Improving approval policy: The National Medical Products Administration provides a first-come, first-served service for innovative drugs and products that have been confirmed to be included in the priority review and approval procedures and conditional approval procedures through communication, shortening the time for innovative drugs to be launched on the market. At the same time, The National Health Commission and other departments have promoted the deepening of the reform of the drug review and approval system to improve the effectiveness of review and approval. For example, pilot projects have been carried out in Beijing, Shanghai and other places to shorten the review and approval period for clinical trials of innovative drugs from 60 working days to 30 working days.

Source: prospectus; China Insights Consultancy

Appendix

- Multi-target therapy, or multi-target drug therapy, in oncology refers to a treatment approach that involves the use of drugs that can simultaneously act on multiple molecular targets within a tumor or its microenvironment. This therapeutic strategy is designed to address the complexity and heterogeneity of tumors, which often involve multiple signaling pathways and molecular mechanisms.

Key Points of Multi-target Therapy in Oncology:

- Addressing Tumor Heterogeneity: Tumors are often characterized by genetic and phenotypic heterogeneity, meaning that different cells within the same tumor may have different genetic mutations, signaling pathway activations, and drug sensitivities. Multi-target therapy aims to overcome this heterogeneity by targeting multiple pathways or molecules simultaneously, thereby increasing the likelihood of effective tumor suppression.
- Synergistic Effects: By targeting multiple pathways, multi-target drugs can potentially produce synergistic effects, where the combined action of the drug on different targets results in a greater therapeutic effect than the sum of the individual effects. This can lead to improved efficacy and reduced toxicity compared to single-target therapies.
- Reducing Drug Resistance: Tumors can develop resistance to single-target therapies through various mechanisms, such as mutations in the target molecule or activation of alternative signaling pathways. Multi-target therapy can reduce the risk of drug resistance by targeting multiple pathways simultaneously, making it more difficult for the tumor to evade treatment.
- Improved Patient Outcomes: By targeting multiple aspects of tumor biology, multi-target therapy may lead to improved patient outcomes, including longer survival, better quality of life, and reduced recurrence rates.
- We are also the first pharmaceutical company in Fujian Province and among the first five pharmaceutical companies in China to obtain the MAH license.
- For instance, our generics of diclofenac sodium enteric-coated tablets, nicergoline tablets, rebamipide tablets and agomelatine tablets were the first, second, third and third in their respective product to be approved and regarded as passing the consistency evaluation in China. All these generic drugs have been included in the NRDL, and we have been actively promoting them in the national VBP assessments.
- Our generics of Hydroxychloroquine Sulfate Tablets and Cobamamide Capsules were the second and fifth in their respective product to be approved and regarded as passing the consistency evaluation in China.
- The Global prevalence of ophthalmic diseases increased from 1.7 billion in 2018 to 2.3 billion in 2023, representing a CAGR of 5.9%, and is expected to increase to 2.8 billion at a CAGR of 2.4% by 2032. The overall prevalence in China of ophthalmic diseases increased from 308.8 million in 2018 to 373.5 million in 2023, representing a CAGR of 3.9%, and is expected to increase at a slower pace to 409.5 million by 2032, representing a CAGR of 1.0%.

Source: prospectus; China Insights Consultancy

Appendix

- Nervous system diseases mainly include neurodegenerative diseases, head-and spinal cord-related diseases caused by injury, neurodevelopmental disorders, and neuropsychiatric diseases. The common types include depressive disorder, Huntington's disease, Parkinson's and Alzheimer's, etc. The prevalence of nervous system diseases in China has steadily increased from 429.6 million in 2018 to 452.8 million in 2023, representing a CAGR of 1.1% and is expected to further increase to 495.4 million by 2032 at a CAGR of 1.0%.
- 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. The etiology of depressive disorder involves genetic, biochemical, electrophysiological, and psychosocial factors. The prevalence of depressive disorder in China has steadily increased from 48.2 million in 2018 to 50.4 million in 2023, representing a CAGR of 0.9% and is expected to further increase to 52.6 million by 2032 at a CAGR of 0.5%.
- Medication therapy is the preferred treatment for depressive disorder, targeting biochemical disruptions with various approved options. First-line medications, known for their efficacy and safety, include drugs modulating 5-HT, NE, or dopamine levels, such as escitalopram, mianserine, trazodone, and agomelatine. Second-line treatments, including tricyclic (TCAs) and tetracyclic antidepressants (TeCAs) like amitriptyline and clomipramine, are associated with lower compliance and safety. Third-line options, such as monoamine oxidase inhibitors (MAOIs), are reserved for patients unresponsive to other medications due to their safety concerns, compliance issues, and dietary restrictions. The market size of antidepressants in China increased from RMB8.7 billion to RMB9.2 billion in 2023 at a CAGR of 0.9%, and is expected to grow to RMB16.9 billion by 2032 at a CAGR of 7.1%.
- As of the latest practicable date, drugs for digestive system diseases, cardiovascular system diseases, endocrine system diseases, nervous system diseases, and inflammatory diseases are the main components of the pharmaceutical market. These therapeutic areas accounted for over 25% of the total pharmaceutical sales in China in 2023.
- Haixi Pharmaceutical is the first pharmaceutical company in Fujian Province and among the first five pharmaceutical companies in China to obtain the MAH manufacturing license.
- The generics of Haixi Pharmaceutical, Anbili, Anllitong, Nicergoline tablets, Anbaiyou, Saixifu, Anfeiping, and Yinganke, were the first, third, second, third, second, first, and fifth to be approved and regarded as passing the consistency evaluation in China.
- Single-target drugs, such as monoclone antibodies (mAbs) or highly selective small molecules, which act on single cellular signaling pathway, can only regulate one aspect of a pathological process. However, the most majority of diseases, such as malignant solid tumors and cardiovascular diseases are typically the results of multiple factors acting together, and often involve complex mechanisms, multiple pathological processes and multi-gene correlations. The pathogenesis and progression of such diseases are highly intricate, and single-target drugs' efficacy may be easily offset by negative feedback or compensatory effects thus leading to suboptimal therapeutic outcomes. In contrast, multi-target/multi-mechanism drugs can simultaneously act on multiple pathological processes and related mechanisms of the same disease, which may exert synergistic effect in addition to a greater aggregate effect, thereby enhancing the drugs' efficacy.
- By acting on multiple targets simultaneously, multi-target drugs can reduce the number and dosage of medications a patient needs to take, and small molecule drugs present the opportunity to develop oral administered drugs that can further simplify medication routines, improving patient compliance and quality of life.

Source: prospectus; China Insights Consultancy

Appendix

- As such, C019199 is expected to become the first-in-class therapy for osteosarcoma that fills the treatment gap for second-line and later-stage advanced osteosarcoma, providing tangible survival benefits for this patient population, and a significant improvement in safety, patient compliance and overall quality of life as well.
- HER2- breast cancer accounted for around 80% of the breast cancer patients. The drug resistance of endocrine therapy is the main challenge for the treatment of HR+/HER2- breast cancer. The recurrence rate of HR+/HER2- early breast cancer is over 40% after endocrine therapy combined with CDK4/6 inhibitors, and almost all HR+/HER2- advanced breast cancer patients receiving endocrine therapy combined with CDK4/6 inhibitors would experience disease progression.
- Currently surgical resection remains the most effective treatment for TGCT, but there is a risk of multiple recurrences after surgery, especially for diffuse TGCT. Furthermore, it is often difficult to completely remove the tumor for recurrent, refractory or diffuse TGCT, and surgical treatment may not always alleviate symptoms. In the cases of severe TGCT, multiple surgeries may be required, which can result in significant joint damage, functional impairment and reduced quality of life, with some patients even facing the possibility of amputation.
- Patients with TNBC often develop resistance to chemotherapy within a few months and face a high risk of recurrence within the first two years after treatment. TNBC is considered to be the worst prognosis subtype, with a 5-year survival rate of less than 15%, much lower than other types of breast cancer.
- Unlike chemotherapy, C019199, through its multi-mechanism synergistic effects, modulates TNBC tumor's immunosuppressive microenvironment, transforming TNBC from an immune "cold" tumor into an immune "hot" tumor, making it recognizable by the human body's immune system.
- Currently, there is a lack of effective treatment for most pancreatic cancers. Even for localized, resectable pancreatic cancer, some patients cannot benefit from direct surgery due to its extremely aggressive biological behavior. Commonly recommended first-line chemotherapy drugs, such as gemcitabine and nab-paclitaxel, have limited efficacy, resistance to these treatments is widespread, and median survival rate is low. Clinically single-mechanism immunotherapy is insufficient to address the complexity of pancreatic cancer.
- Digestive system was the sixth largest therapeutic area in China in terms of sales revenue in 2023, accounting for 6.0% of the overall pharmaceutical market.+
- Mosapride, with its advantages in efficacy, safety and patient compliance, is an effective alternative to itopride and domperidone. In terms of sales revenue in China between 2018 and 2022, mosapride citrate tablets had the largest market share among gastrointestinal mobility drugs, surpassing itopride and domperidone, the other two commonly used gastrointestinal mobility drugs.
- Cardiovascular system diseases were the fifth largest therapeutic area in China in terms of sales revenue in 2023, accounting for 7.4% of the overall pharmaceutical market.
- Amlodipine besilate, a long-acting calcium channel blocker, and atorvastatin calcium, a lipid-lowering agent. It can significantly enhance patient adherence to medication and safety. For the middle-aged and elderly populations, it improves compliance with medication and strengthens treatment effectiveness, which are crucial for reducing the high incidence rates of myocardial infarction and stroke in China

Source: prospectus; China Insights Consultancy

Appendix

- Nicergoline tablets used primarily to treat acute or chronic cerebrovascular disease or cerebral metabolic disorders.
- Cinacalcet hydrochloride tablets reduce the levels of parathyroid hormone, calcium, phosphate and the calcium-phosphate product by enhancing the calcium-sensing receptor's sensitivity to the calcium levels in the bloodstream.
- Oncology was the largest therapeutic area in terms of sales revenue in not only China but also the world in 2023, accounting for 12.6% and 14.2% of the Chinese and global pharmaceutical market, respectively.
- The VBP schemes employ a competitive bidding process to set prices for pharmaceutical products and allocate the purchase demand among winning bidders. For pharmaceuticals, the national VBP scheme primarily includes chemical drugs that pass or are regarded as passing the consistency evaluation criteria. Participation by pharmaceutical companies in the national VBP scheme is voluntary. Successful bids under the national VBP scheme are generally valid for two to three years. When there are many winning bidders, the guaranteed purchase amount may be significantly diluted. The provincial VBP schemes are primarily implemented by various alliances formed by government authorities across provinces and cities. Successful bids under provincial VBP schemes are generally valid for one to two years.
- It is common in the pharmaceutical industry in China for suppliers and customers to overlap, given their broad and diverse range of business activities.
- As currently, there is no approved drug therapy specifically for the treatment of osteosarcoma other than chemotherapies, leaving a treatment gap for metastatic or advanced osteosarcoma worldwide.
- As of the end of 2023, there were over 500 CMO/CDMOs in China. In recent years, the trend of "separation of R&D and production" among pharmaceutical companies in China has been on the rise. Contract Manufacturing Organizations (CMOs) / Contract Development and Manufacturing Organizations (CDMOs) have become crucial supports for China's pharmaceutical system. Coupled with the rapid development of the domestic pharmaceutical industry, the supply chain of CMO/CDMO companies has been continually improving.
- For our typical collaboration arrangements, (i) we are the MAH and lead the overall R&D, whereas our partners provide assistance in the process; and (ii) we share the profits derived from the sale of the drug with our partners after it is approved for marketing. The collaboration arrangements of The Company is in line with industry norm.
- For pharmaceuticals, the national VBP scheme primarily includes chemical drugs that have met the consistency evaluation criteria, and that have a certain number of generic alternatives available in the market.
- The reasons for product returns during the Track Record were largely attributable to damage during transportation or handling, or inventory reallocation requests from other sales channels or districts, rather than the inherent quality issue of the drug products. According to CIC, this is in line with the industry norm.

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Source: prospectus; China Insights Consultancy

Appendix

- Successful bids under provincial VBP schemes are generally valid for two to three years.
- Because of the different policy focuses of the national VBP scheme and the provincial VBP schemes, a product's inclusion in the provincial VBP schemes does not necessarily indicate its inclusion in the national VBP scheme. Inclusion in provincial VBP scheme is not a prerequisite for inclusion in national VBP scheme. Participants may directly participate in national VBP schemes if their drugs meet the eligibility criteria (e.g., having passed consistency evaluations). For drugs already included in provincial VBP schemes, they may qualify for national VBP schemes if relevant requirements are met (e.g., successful completion of consistency evaluations, high clinical demand, and sufficient market competition). The bid prices for national VBP schemes are typically required to be no higher than the lowest provincial VBP schemes prices, necessitating c strategic pricing considerations in provincial tenders. Additionally, strong performance in provincial VBP schemes, such as consistent product quality and reliable supply, may improve the likelihood of success when participating in national VBP schemes subsequently.
- Renewal of VBP Schemes. The national VBP scheme itself does not undergo a renewal process. The renewal of expired national VBP schemes is not centrally administered by the national authority but delegated to provincial or inter-provincial procurement alliances. The provinces or alliances implement renewals under the national policy framework, with the authority to determine specific terms. Common approaches include direct contract extensions, re-bidding, or price linkage (adopting prices from other provinces or prior national VBP schemes). Renewal prices are generally required not to exceed the original bid price, though provinces may allow adjustments for cost fluctuations or market conditions. Certain regions streamline the process by referencing renewal outcomes from other provinces or national results. This decentralized model may lead to variations in renewal terms across jurisdictions. If a provincially procured drug is selected in national VBP schemes, the provincial agreement is automatically terminated, and the national price applies. If the bid did not succeed in national VBP schemes, the provincial agreement may continue under its renewal terms.
- In terms of price setting and volume determination, both the national scheme and the provincial schemes employ a competitive bidding process to allocate the demand among winning bidders. As the alliances have the authority to formulate their own provincial VBP schemes, the evaluation, selection and negotiation process of each scheme may differ from each other and from the national VBP scheme to a certain extent.
- The success rate for renewal biddings under both national and provincial VBP schemes is subject to various factors. For national VBP schemes, the success rate is largely affected by factors including whether the manufacturing and sales plan of our products match the timeline of the national renewal biddings process; whether our products meet the requirements or rules under the national VBP scheme; the bid price of our competitors; and our pricing strategies for a certain drug product. For provincial VBP schemes, saved for general affecting factor such as whether our products meet the requirements or rules under each VBP scheme the success rate is also substantially affected by whether the product won the last national bid (as the original winner for a certain province under the national VBP schemes tends to have a strong advantages in that province during subsequent renewal biddings due to its extensive market coverage established during the exclusive validity periods of the national VBP schemes).

Source: prospectus; China Insights Consultancy

Appendix

- This strategic investment aligns with our long-term vision to expand into the field of neural medicine, particularly in the development of treatment options for neurological disorders. The entity's research and development in neural regeneration technology demonstrates growth potential, positioning it as a notable player in the biotech space.
- There are two scenarios involving provincial VBP schemes. First, provincial schemes may target drugs that have not been included in the national VBP schemes. These drugs may include not only recently approved generics that have passed consistency evaluations but also those that have not yet passed consistency evaluations, traditional Chinese medicines, or biologicals. Second, for drugs that have been selected in the national VBP schemes but whose exclusive validity periods have expired, the renewal of the VBP schemes will be implemented at the provincial level.
- Due to the diverse and complex nature of provincial VBP schemes, a product included in a provincial VBP scheme may operate independently of the national VBP scheme, be superseded by the national VBP scheme if the product is later included in the national VBP scheme, or simply serve as a renewal of an expired national VBP scheme. Participants may directly participate in national VBP schemes regardless of whether they are involved in provincial VBP schemes. Drugs qualify for national VBP schemes, as long as they are selected in the catalog during a specific round and have passed consistency evaluations. For drugs that missed the bidding window for national VBP schemes, they must wait until the exclusive validity period expires before they can participate in renewal bidding at the provincial level. However, provincial renewal bidding is subject to various local policies and conditions of relevant alliances, which are constantly evolving and adapting, making the situation relatively complex. Generally, the original winner in a particular province under the national VBP schemes tends to have a strong advantage in that province during subsequent renewal biddings, primarily due to the market coverage established during the exclusive validity periods of the national VBP schemes.
- In addition, the National Health Commission released the Encouragement for Generic Drug Catalog (《鼓勵仿製藥品目錄》) and announced that the catalog would be dynamically adjusted. This demonstrates the government's strong emphasis on the R&D and production of certain generic drugs.
- The Implementation Plan for Full-chain Support for Innovative Drug Development (《全鏈條支持創新藥發展實施方案》) was released to provide support across the entire value chain, including R&D, market approval, production, use, payment, and investment/financing. Against this backdrop, innovative drug companies, including the Company, are expected to benefit from accelerated market access, reduced development costs, and higher returns on investment.
- By 2025, a new Class C National Reimbursement Drug List (《丙類醫保藥品目錄》) is expected to be introduced as a supplement to the basic NRDL (covering Class A and B drugs). This new list will include highly innovative drugs with significant clinical value and patient benefits. As a result, innovative drugs such as C019199 are poised to experience rapid commercialization and expanded patient access.
- In the course of our cooperation with the R&D partners, both parties have full access to R&D data and results solely for project execution, but we as the MAH, are the only party which has the contractual right to use data for regulatory fillings, which is consistent with the standard industry practice for MAH-led generic drug development in China, according to CIC.

Source: prospectus; China Insights Consultancy

Appendix

- According to CIC, it is an industry norm for a pharmaceutical company focusing on R&D and sales of generic drug products like us to provide R&D services to other pharmaceutical companies in the PRC.
- According to CIC, based on the 2023 Statistical Analysis Report on the Operation of the Pharmaceutical Distribution Industry (《2023年藥品流通行業運行統計分析報告》) issued by the Ministry of Commerce of the PRC, the top five drug wholesalers in China accounted for over 45% of the market's drug sales revenue, followed by more than 100 smaller-scale distributors. In 2023, sales amount contributed by state-owned pharmaceutical distributors accounted for approximately 61.8% of the total sales amount in the drug distribution industry in China. According to CIC, state-owned distributors are more frequently selected by public medical institutions to provide drug products under China's VBP schemes, predominately because that a majority of qualified distributors in the market are state-owned enterprises. According to the Chinese Expert Consensus on the Management of Nationally Organized Centralized Procurement Drugs in Medical Institutions (《醫療機構國家組織集中採購藥品管理中國專家共識》), medical institutions should regularly conduct comprehensive evaluations of distributors' supply capabilities and service quality. When selecting distributors, key criteria include supply capacity and distribution service capability, followed by drug quality and corporate management standards, as well as emergency support capacity. Generally, state-owned distributors tend to hold greater advantages in these areas compared to non-state-owned ones, as they often benefit from stronger government support, broader market coverage, tighter channel control, and higher risk resilience. The selection of distributors (whether or not state-owned) by public medical institutions often depends on above-mentioned factors, as well as the level of geographic coverage and channel penetration by distributors, rather than ownership structure alone.
- According to CIC, the ratios adopted by the collaborative R&D agreements are in line with the market norm.
- For listed industry peers, as the relevant drug products are typically disclosed as part of their entire portfolio without separate disclosure on average selling prices or gross margins, the gross profit margin ranges can only be obtained from market research by industry consultant (e.g. the gross profit margins for generic drugs typically range from 72% to 84%, and the data of the Company's products is within this range).

Source: prospectus; China Insights Consultancy

Appendix

- Coronary atherosclerotic heart disease (CAHD), often referred to as coronary artery disease (CAD) or coronary heart disease (CHD), is a condition characterized by the buildup of plaque (a mixture of fat, cholesterol, and other substances) in the coronary arteries.
- Metastatic breast cancer, representing approximately 30% of all breast cancer cases, is a severe and advanced form of breast cancer that poses significant treatment challenges.
- According to CIC, there is currently no approved wAMD drug therapy worldwide that utilizes an oral formulation, and HXP056 has the potential to become one of the first drug therapy to adopt this simple delivery method of oral formulation, improving from the complex administration of existing drug therapies.
- ...given that the adoption of drug products in public medical institutions are primarily determined by the applicable national and provincial centralized procurement policies...
- According to CIC, our inventories turnover days in 2022, 2023, 2024 and the five months ended May 31, 2025 were in line with those of our market peers.
- According to CIC, our trade and bills receivables turnover days in 2022, 2023, 2024 and the five months ended May 31, 2025 were in better position than those of our market peers.
- According to CIC, our trade payables turnover days in 2022, 2023, 2024 and the five months ended May 31, 2025 are in line with those of our market peers.
- HXP056 is an innovative drug candidate that is designed for the treatment of ocular fundus diseases such as wet age-related macular degeneration (wAMD), diabetic macular edema (DME) and retinal vein occlusion (RVO). HXP056 is a novel molecule invented internally and designed as an oral formulation, addressing a significant shortcoming in current therapies that require doctors' visits for vitreous injections which could cause unintended side effects and discomfort for patients, leading to frequent patient non-compliance and resulting in inferior treatment outcome.
- According to CIC, there is currently no approved wAMD drug therapy worldwide that utilizes an oral formulation, and HXP056 has the potential to become one of the first oral drug therapies in this area, improving from the cumbersome administration of current vitreous injections.
- AMD is the most common macular degenerative disease, classified into dry AMD (dAMD) and wet AMD (wAMD). Dry AMD, which accounts for approximately 90% of all AMD cases, is less severe, with only 10% of cases progressing to blindness. Wet AMD, representing about 10% of cases, is more aggressive and, if left untreated, can lead to rapid and severe visual impairment or legal blindness. Among patients with severe vision loss due to AMD, 80% to 90% are attributed to wAMD.
- Currently, the primary treatment options for wAMD in China include intravitreal injections such as ranibizumab, aflibercept, faricimab, and conbercept. However, these monoclonal antibody injections not only impose psychological burden on patients but are also costly. Moreover, some patients do not experience substantial visual improvement, and a subset may exhibit vision decline after 12 months of treatment. There is an urgent need to develop a novel oral drug with greater efficacy. HXP056 is an orally administered small-molecule kinase inhibitor that treats wAMD by inhibiting retinal neovascularization, reducing inflammation, and mitigating pathological changes such as subretinal fibrosis. It holds promise as potentially more effective and convenient treatment for wAMD.

Source: prospectus; China Insights Consultancy

Summary of the therapeutic areas of marketed products (1/4)

Summary of the therapeutic areas of marketed products

Therapeutic area	Product	Disease	Description	Cause of the disease	Symptoms of the disease	Treatment method
Digestive system	Mosapride Citrate Tablets 安必力®	Functional dyspepsia	A kind of dyspepsia without organic lesions	Gastrointestinal motility dysfunction and environmental factors	Mainly gastrointestinal symptoms without specific manifestation	Lifestyle management; antisecretory drugs and gastrointestinal excitomotor
	Rebamipide Tablets 安立定®	Gastric mucosal lesions in acute gastritis or acute exacerbation of chronic gastritis	Pathological changes observed on gastric mucosa	Unhealthy lifestyle, infectious factors, and long-term NSAIDs intakes	Pain in abdominal with or without haematemesis or melena	Symptomatic treatment; hemostasis; medication treatment
Cardiovascular system	Amlodipine Besilate and Atorvastatin Calcium Tablets 海慧通® Valsartan and Amlodipine Tablets (I) 海必平® Valsartan Tablets 海可喜® Bisoprolol Fumarate and Amlodipine Besilate Tablets 海惠宁®	Hypertension	Abnormal elevation of blood pressure	Majority are primary, including genetic factors, unhealthy lifestyle, nental problems, etc. Minority are secondarily caused by other diseases	Mainly headache, fatigue, cardiovascular symptoms, and secondary renal injury	Lifestyle management; antihypertensive drugs; renal denervation
	Amlodipine Besilate and Atorvastatin Calcium Tablets 海慧通®	Coronary heart disease	Heart disease caused by coronary atherosclerosis	Aging, unhealthy lifestyle, hypertension, hyperlipidemia, and diabetes	Mainly fatigue and angina pectoris	Lifestyle management; medication treatment; interventional therapy

Source: Drug instruction; China Insights Consultancy

Summary of the therapeutic areas of marketed products (2/4)

Summary of the therapeutic areas of marketed products

Therapeutic area	Product	Disease	Description	Cause of the disease	Symptoms of the disease	Treatment method
Cardiovascular system	Amlodipine Besilate and Atorvastatin Calcium Tablets 海慧通®	Hypercholesterolemia	Abnormal elevation of serum cholesterol level	Unhealthy lifestyle and endocrine disorder	No specific manifestation at early stage and may lead to vascular diseases at late stage	Lifestyle management; medication treatment; terminal ileum resection
	Nicergoline Tablets	Acute or chronic cerebrovascular disease or cerebral metabolic disorders	Disorders affected cerebrovascular system that may lead to mental or consciousness disorder	Genetic factors, systemic metabolic disorders, infectious factors, and trauma	Mainly headache, mental or cognitive disorder	Symptomatic treatment; medication treatment; interventional therapy
Endocrine system	Cinacalcet Hydrochloride Tablets 瑞安妥®	SHPT	Excessive secretion of parathyroid hormone by the parathyroid glands	Long-term hypocalcemia, hypomagnesemia, or hyperphosphatemia caused by chronic kidney disease, intestinal malabsorption syndrome, Fanconi syndrome, etc.	Mainly bone deformities, pathological fracture, and neurotoxic symptoms	Medication treatment; parathyroidectomy; minimally invasive treatment
Nervous system	Escitalopram Oxalate Tablets 安优凡® Agomelatine Tablets 安百悠®	Depression	A kind of mental disorder characterized by long-term depressive emotion	Has not been elucidated yet	Mainly depressive mood, retardation of thought, and hypobulia	Medication treatment; psychotherapy; physiotherapy
	Escitalopram Oxalate Tablets 安优凡®	Anxiety disorder	A kind of mental disorder characterized by long-term anxious emotion	Disturbance in neurotransmitter level and psychological factors	Persistent or intermittent anxious emotion with or without somatic or behavior symptoms	Medication treatment; psychotherapy

Source: Drug instruction; China Insights Consultancy

Summary of the therapeutic areas of marketed products (3/4)

Marketed product | Summary

Summary of the therapeutic areas of marketed products

Therapeutic area	Product	Disease	Description	Cause of the disease	Symptoms of the disease	Treatment method
Nervous system	Escitalopram Oxalate Tablets 安优凡®	Panic disorder	A kind of mental disorder characterized by intermittent panic attack	Genetic factors, psychological factors, and neuroanatomical factors	Intermittent panic attack, anticipatory anxiety, and behavior disorder	Medication treatment; psychotherapy
Inflammation	Celecoxib Capsules 安妥飞® Hydroxychloroquine Sulfate Tablets 赛西福®	Rheumatoid arthritis	A kind of arthritis with synovitis as the pathological basis	Autoimmune factors, genetic factors, and infectious factors	Mainly systemic arthroncus, articular pain, and deformity	Lifestyle management; medication treatment; surgical treatment
	Celecoxib Capsules 安妥飞®	Osteoarthritis	A kind of degenerative arthropathy	Aging and long-term physical labor	Mainly arthroncus, articular pain, deformity, and limited joint activity	Lifestyle management; reduction in physical labor; medication treatment; surgical treatment
	Celecoxib Capsules 安妥飞®	Ankylosing spondylitis	A kind of chronic arthritis that mainly take place in vertebral column	Autoimmune factors, genetic factors, and infectious factors	Mainly articular pain, deformity, and limited joint activity in vertebral column, some patients may suffer from systemic symptoms	Lifestyle management; medication treatment; surgical treatment; physiotherapy
	Hydroxychloroquine Sulfate Tablets 赛西福®	Juvenile chronic arthritis	A kind of connective tissue disease characterized by chronic arthritis, mainly take place during childhood	Has not been elucidated yet, maybe related to abnormalities in immune system	Mainly fever, skin rashes, hepatosplenomegaly, pleurisy, pericarditis, and arthropathy	Symptomatic treatment; anti-inflammatory agents, immunosuppressant, and adrenocorticotropic hormone treatment; surgical treatment

Source: Drug instruction; China Insights Consultancy

Summary of the therapeutic areas of marketed products (4/4)

Marketed product | Summary

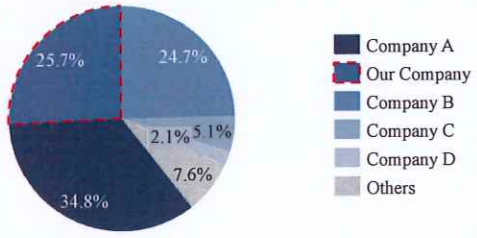
Summary of the therapeutic areas of marketed products

Therapeutic area	Product	Disease	Description	Cause of the disease	Symptoms of the disease	Treatment method
Inflammation	Hydroxychloroquine Sulfate Tablets 赛西福®	Systemic lupus erythematosus	Chronic diffuse connective tissue disease caused by autoimmune factors	Has not been elucidated yet, maybe an autoimmune disease	Characterized by skin rashes, accompanied by several viscera injuries including cardiac damage, pulmonary interstitial fibrosis, pancreatitis, etc.	Symptomatic treatment; avoiding UV light; medication treatment; topical treatment
	Hydroxychloroquine Sulfate Tablets 赛西福®	Discoid lupus erythematosus	A kind of chronic recurrent disease characterized by skin rashes	Genetic factors, drug effects, infectious factors, endocrine factors, exposure to UV light, and disorder in immune system	Chronic and recurrent rashes on skin and mucosa	Avoiding UV light; medication treatment; topical treatment
	Diclofenac Sodium Enteric-coated Tablets 安飞平®	Inflammation	A kind of immune response against noxious stimulus	All kinds of noxious stimulus	Topical or systemic redness, swelling, elevated body temperature, pain, and loss of function	Symptomatic treatment; medication treatment
	Cobamamide Capsules 盈安可®	Anemia	Abnormally reduced red blood cell(RBC) level	Impaired RBC production, hemolytic anemia, blood loss, and hypervolemia	Mainly fatigue, dizziness, headache, shortness of breath, and mental disorder	Etiological treatment; folic acid, vitamin B_{12}, and iron supplements
	Cobamamide Capsules 盈安可®	Neuroinflammation	Inflammations in neuro system	Noxious stimulus affecting neuro system	Topical pain, sensory disturbance, and activity limitation	Etiological treatment; neurotrophic treatment; physiotherapy

Source: Drug instruction; China Insights Consultancy

Competitive landscape of mosapride in China, in terms of sales revenue, 2024

Market share of mosapride in China, 2024



- Company A, Kanghong Pharma (stock code:002773.SZ), headquartered in Sichuan Province, researches, develops, manufactures, and distributes medicines for ophthalmic, central nervous, digestive and endocrine systems.
- Company B, Lunan Better Pharma, headquartered in Shandong Province, is an integrated pharmaceutical group of producing, researching and selling traditional Chinese medicine, chemical medicine and bio-pharmaceutical medicinal products.
- Company C, Yabao Pharma (stock code:600351.SH), headquartered in Shanxi Province, includes more than 300 kinds of TCM, APIs, patches and pharmaceutical packaging materials.
- Company D, Sumitomo Pharma, founded in 1897 and headquartered in Osaka, Japan, is a multinational pharmaceutical company focusing on oncology, psychiatry, neurology, women's health issues, urological diseases, etc.

Source: China Insights Consultancy

Competitive landscape of mosapride in China

Summary of main players of mosapride in China, 2024

Company	Active ingredient	VBP inclusion	Efficacy	Side effect	Unit price trends (CAGR between 18-24)
Company A	Mosapride Citrate (5 mg)	Since 2021/02	The product can serve as gastrointestinal excitomotor, relieving digestive manifestations including belching, nausea, vomiting, etc	Mainly diarrhea, thirst, discomfort, and abnormalities in laboratory tests	-15.7%
The Company		Since 2021/02			-21.5% (2020-2024)
Company B		Since 2021/02			-6.7%
Company C		/			-5.6%
Company D		/			-5.7%

- Company A, Kanghong Pharma (stock code:002773.SZ), headquartered in Sichuan Province, researches, develops, manufactures, and distributes medicines for ophthalmic, central nervous, digestive and endocrine systems.
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Source: NMPA; Drug instructions; China Insights Consultancy

Market drivers and entry barriers of mosapride market in China

Mosapride | Drivers & Barriers

Market driver

- **Population aging** According to data from the National Bureau of Statistics, in 2023, China had more than 200 million people aged 65 and above, making up over 15% of the total population. The increase of aging population will lead to larger demands for medical resources, which may also cause the enlargement of digestive system drug market.
- **Increasing prevalence of digestive system diseases** With accelerated pace of life and changes in diet structure, China's population are facing a bigger threat from digestive system diseases. The growing prevalence of digestive diseases will drive the market of mosapride to grow steadily.
- **Improving health awareness** People now pay more attention to their own health. As the health awareness of patients improving, people are more inclined to reach for professional medical suggestions at the earliest time. Patients who used to ignore mild gastrointestinal discomforts now prefers to seek for drug treatment, driving the digestive drug market to grow.

Entry barrier

- **Strict administration** The manufacturing of medications is under strict administration in China, procedures including GMP certification, drug registration, and consistency evaluation are regulated by multiple laws and regulations. The strict administration of pharmaceutical industry can be one of the main entry barrier to the digestive system drug market.
- **Competition pressure** Mosapride was included in the VBP scheme in 2021, the bid-winning enterprises occupied the majority of the market share. With the continuous implementation of VBP scheme, new players would face more and more intense competition pressure which makes it difficult for them to acquire a considerable market share.
- **R&D capability** The research and development of medication requires excellent R&D capability which can be a main entry barrier to the market.

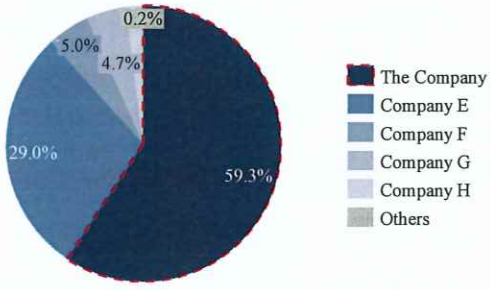
CIC 灼识咨询

Source: China Insights Consultancy

Market share of amlodipine and atorvastatin calcium (5mg/10mg) in China, 2024

Amlodipine atorvastatin calcium | Market share

Market share of amlodipine and atorvastatin calcium (5mg/10mg) in China, 2024



- Company E, Hanhui Pharma, founded in 2012 and headquartered in Shanghai, supplies over 60 products to the China's market, covering anti-tumor, anti-infection, cardiovascular, etc.
- Company F, CR Sai Ke Pharma, headquartered in Beijing, a subsidiary of China Resources Group, is an enterprise integrating pharmaceutical production, R&D and marketing.
- Company G, Chia-Tai Tianqing, headquartered in Jiangsu Province, is a multinational pharmaceutical company with integrated R&D, manufacturing, marketing, sales and distribution capabilities. It is a subsidiary of a public listed biopharmaceutical.
- Company H,, Jialin Pharma, founded in 1998 and headquartered in Beijing, is one of the leading players in China's cardiovascular drug market.

Key Analysis

- As the former subsidiary company of the original manufacture of amlodipine besilate and atorvastatin calcium , Hanhui Pharma occupied almost all the market share in China before 2022. **After amlodipine besilate and atorvastatin calcium was included in the VBP scheme, China's domestic generics experienced an extraordinary growth in market share and occupied a large part**.
- With the implementation of VBP policy, **China's generic manufactures are encouraged to participate in the competition with their profits guaranteed.**

Note: *the market shares are in terms of patient-end use.

CIC 灼识咨询

Source: China Insights Consultancy

Competitive landscape of amlodipine and atorvastatin calcium (5mg/10mg) in China

Summary of main players of amlodipine and atorvastatin calcium (5mg/10mg) in China, 2024

Company	Active ingredient	VBP inclusion	Efficacy	Side effect	Unit price trends (CAGR between 18-24)
The Company	Amlodipine (5 mg) Atorvastatin calcium (10 mg)	Since 2023/04	Being a compound preparation of amlodipine and atorvastatin calcium, the product can be applied as blood pressure and blood lipoid stabilizer	Mainly infection, allergy, and abnormalities in laboratory tests, with on specific side effect observed	-32.6% (2022-2024)
Company E		/			-8.6%
Company F		Since 2023/04			-23.7% (2021-2024)
Company G		Since 2023/04			-22.7% (2021-2024)
Company H		Since 2023/04			-22.2% (2021-2024)

- Company E, Hanhui Pharma, founded in 2012 and headquartered in Shanghai, supplies over 60 products to the China's market, covering anti-tumor, anti-infection, cardiovascular, etc.
- Company F, CR Sai Ke Pharma, headquartered in Beijing, a subsidiary of China Resources Group, is an enterprise integrating pharmaceutical production, R&D and marketing.
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- Company H,, Jialin Pharma, founded in 1998 and headquartered in Beijing, is one of the leading players in China's cardiovascular drug market.

Source: NMPA; Drug instructions; China Insights Consultancy

Market drivers and entry barriers of amlodipine and atorvastatin calcium market in China

Market driver

- **Population aging** As the health situation of cardiovascular system tends to worsen with aging, the prevalence of cardiovascular system diseases(CVD) will grow rapidly due to the deepening population aging, and further leading the growth of cardiovascular system drug market in China.
- **High-fat diet** With the development of economy and agricultural technology, people's diet are turning into a more high-fat manner, which is a main risk factor of multiple cardiovascular system diseases, including coronary heart disease, hypertension, and cardiac dysfunction. The conversion of diet style can increase the incidence of cardiovascular system diseases not only in aging population but also in younger population, driving the market to grow rapidly.
- **The development of early diagnosis of CVD** With the development of innovative diagnostic technology, it is now possible to diagnose cardiovascular system diseases at an earlier stage, encouraging more patients to seek for medication treatment, which drives the development of amlodipine and atorvastatin calcium market in China.

Entry barrier

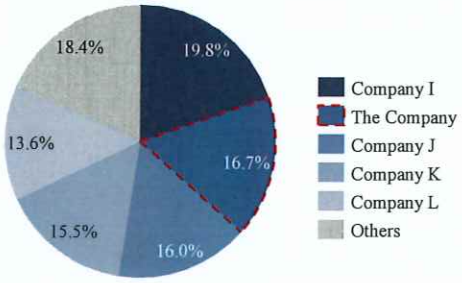
- **Technology barrier** Patients suffering from cardiovascular system diseases are required to take medications for a long period. Due to the situation, amlodipine and atorvastatin calcium products are demanded to maintain a stable efficacy and pharmacological features among different batches. Besides, the plasma concentration of amlodipine and atorvastatin calcium requires to be controlled at a proper level all-day long, which makes drug sustained release technology important in the preparation of the drug. The requirement for mature pharmaceutical technology can be one of the main entry barrier to the amlodipine and atorvastatin calcium market in China.
- **Competition pressure** As a classic drug, many pharmaceutical companies have launched their own amlodipine and atorvastatin calcium products. The market is largely occupied by a large number of generic enterprises, bringing barriers for new entrants to the market.

Source: China Insights Consultancy

The VBP policy encourages the development of advanced generics, challenging the dominant position of original manufacture

Cinacalcet | Market share

Market share of cinacalcet in China, 2024



- Company I, Renhe Yikang Pharma, founded in 2018 and headquartered in Hebei Province, is a pharmaceutical group integrating innovative R&D, production and professional marketing.
- Company J, Baiao Pharma, founded in 1995 and headquartered in Beijing, focuses on providing solutions of cardiovascular diseases, rare diseases, liver diseases, etc.
- Company K, Hencer Pharma, founded in 1995 and headquartered in Jiangsu Province, focused on the R&D of nephrology and cardio-cerebrovascular therapeutic areas.
- Company L, Kyowa Kirin Pharma, headquartered in Tokyo, Japan, was founded in 1949. It is dedicated to the R&D, production, and sales of new drugs primarily for the treatment of cancer and kidney diseases.

Key Analysis

- As the original manufacture of cinacalcet, Kyowa Kirin occupied a huge market share in 2021. **After cinacalcet was included in the VBP scheme in 2021.6, China's domestic generics of cinacalcets experienced an extraordinary growth in market share and occupied a large part**.
- With the implementation of VBP policy, **China's pharmaceutical companies are encouraged to develop advanced generics** whose profits would be guaranteed after being included in the VBP scheme.

Note: *the market share is in terms of patient-end revenue.

Source: China Insights Consultancy

Competitive landscape of cinacalcet in China

Cinacalcet | Competition

Summary of main players of cinacalcet in China, 2024

Company	Active ingredient	VBP inclusion	Efficacy	Side effect	Unit price trends (25 mg) (CAGR between 18-24)
Company I	Cinacalcet Hydrochloride (25/75 mg)	Since 2021/06	The product can be used for the stabilization of iPTH and calcium level in serum	Mainly gastrointestinal symptoms, hypocalcemia, and QT interval prolongation	-43.2% (2020-2023)
The Company		Since 2021/06			0.0% (2021-2024)
Company J		Since 2021/06			0.0% (2021-2024)
Company K		Since 2021/06			0.0% (2021-2024)
Company L		/			-8.7%

- Company I, Renhe Yikang Pharma, founded in 2018 and headquartered in Hebei Province, is a pharmaceutical group integrating innovative R&D, production and professional marketing.
- Company J, Baiao Pharma, founded in 1995 and headquartered in Beijing, focuses on providing solutions of cardiovascular diseases, rare diseases, liver diseases, etc.
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Source: NMPA; Drug instructions; China Insights Consultancy

Market drivers and entry barriers of cinacalcet market in China

Market driver

- **Growing prevalence of SHPT** It is expected that the prevalence of SHPT patients relying on maintenance dialysis in China will be over 1 million by 2032 with a CAGR at 6.1% from 2023. With the stably growing prevalence of SHPT, the need for cinacalcet will accordingly expand.
- **Policy support** Several policies has been released in recent years, encouraging China's pharmaceutical companies to develop advanced generics, for instance, the release of《国务院办公厅关于改革完善仿制药供应保障及使用政策的意见》, and the promotion of VBP Scheme. Under this favorable circumstance, domestic generics of cinacalcets experienced an extraordinary growth in market share. As more generics entered the market, cinacalcet is more accessible to patients, driving the market to grow rapidly.
- 《国务院办公厅关于改革完善仿制药供应保障及使用政策的意见》stated that generic drugs should be clinical-need oriented and encouraged generic version of products that are clinically necessary, but in short supply. Under this circumstance, the market share dominated by the original manufacturer before in cinacalcet market was significantly diluted by domestic ones, including The Company. The Company was among one of the first generic versions of cinacalcet in the market, thus showing a first-mover advantage.
- The VBP scheme is a normalized policy to procure a large amount of medications at lower prices through centralized purchasing. This allows new market entrants, like The Company, to acquire a relatively huge percent of market share within very short time.
- **Expanding indications** With strong effect in stabilizing serum calcium level, cinacalcet can be widely applied in patients with disorders in calcium level. There have been clinical trials showing cinacalcet's therapeutical effect on patients with PHPT who are not suitable for surgery. With the further testimony of clinical trials, the expanding indications are expected to drive the growth of the market.

Entry barrier

- **Technology barrier** Cinacalcet is applied on patients suffering from severe calcium metabolic disorder due to the dysfunction of kidney, who may be on the medication for a long period. Due to the situation, cinacalcets are demanded to maintain a stable efficacy and pharmacological features, which raises technological barriers for new players to the market.
- **Competition pressure** Cinacalcet was included in the VBP scheme in 2021, the bid-winning enterprises occupied the majority of the market share. Besides, more than 10 cinacalcet product has been approved in China. New players will face more and more intense competition pressure which makes it difficult for them to occupy a considerable market share.
- **R&D capability** Compared to classic drugs, the development of cinacalcet requires profound understanding of the physiological mechanisms of calcium sensitive receptors, which brings higher demand to the R&D capability of the enterprise.

Source: China Insights Consultancy