Innovative Small Molecule Targeting Drug Market Study

Confidential For

TransThera 药捷安康

Date : _____

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

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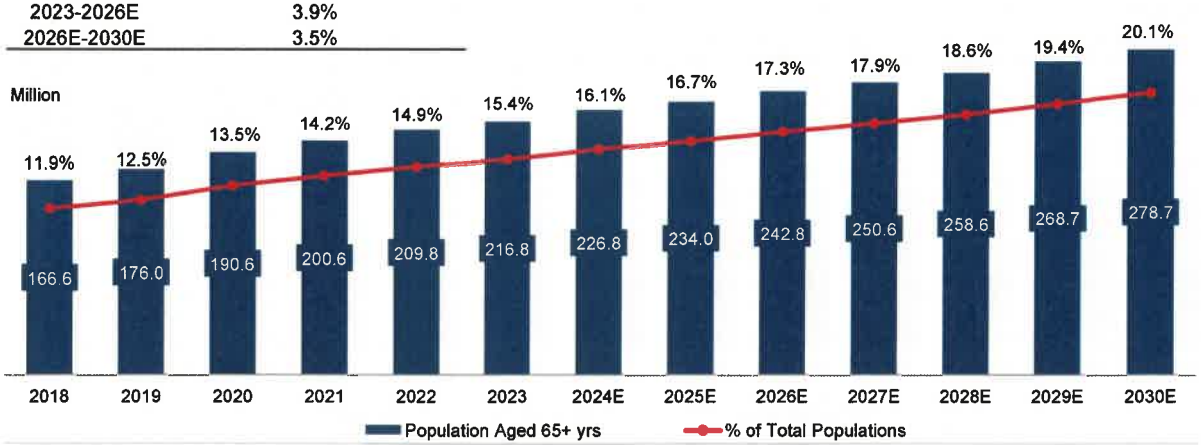
China Aging Population Trend, 2018-2030E

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

China Aging Population Trend, 2018-2030E

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



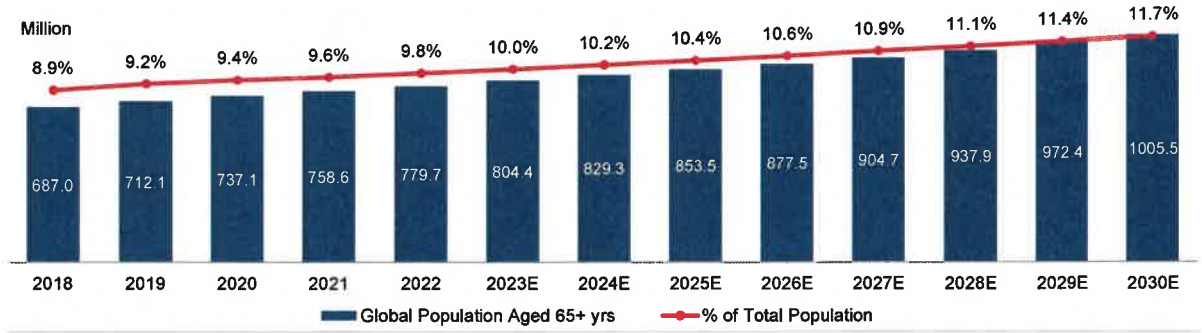
Source: NBSC, Frost & Sullivan Analysis

Global Aging Population Trend, 2018-2030E

- The world's aging population is experiencing growth in terms of both number and proportion. In 2022, there were 779.7 million people aged over 65 years old in the world, accounting for 9.8% of the world's population. The population over 65 years old grows at a CAGR of 3.2% during the period of 2018 to 2022.
- Declining fertility and increasing longevity are the key drivers of population aging globally. It is estimated that the number of people aged over 65 in the world would reach 877.5 million in 2026, accounting for 10.6% of the total population, with a CAGR of 3.0% from 2022 to 2026. Size of aging population will keep the upward trend, anticipating to reach 1005.5 million by 2030.

Global Aging Population Trend, 2018-2030E

Period	CAGR
2018-2022	3.2%
2022-2026E	3.0%
2026E-2030E	3.5%



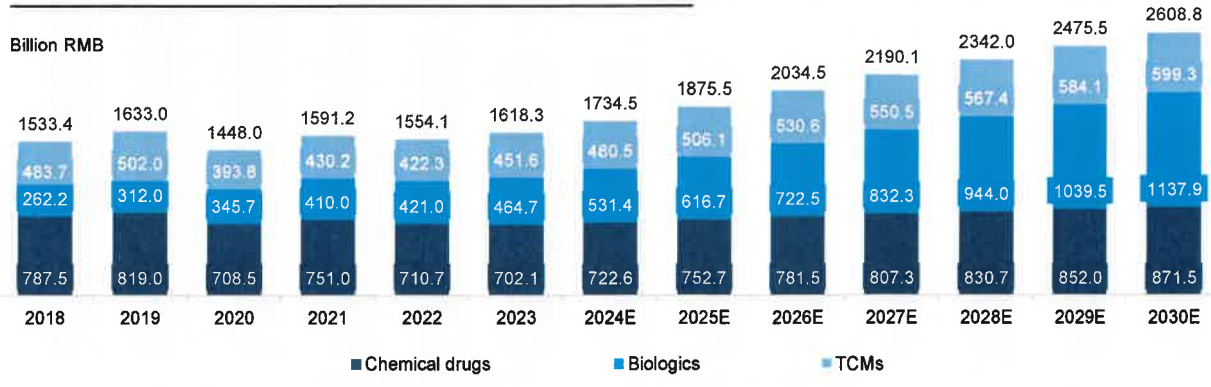
Source: World Bank, Frost & Sullivan Analysis

Breakdown of China Pharmaceutical Market by Chemical Drugs, Biologics and TCMs, 2018-2030E

- China pharmaceutical market is composed by three segments, namely chemical drugs, biologics and Chinese medicines (TCMs), among which chemical drugs account for the largest market share. The size of China pharmaceutical market was RMB 1,618.3 billion in 2023, and is expected to reach RMB 2,034.5 billion and RMB 2,608.8 billion in 2026 and 2030 respectively, representing a CAGR of 7.9% from 2023 to 2026 and 6.4% from 2026 to 2030.

Breakdown of China Pharmaceutical Market by Chemical Drugs, Biologics and TCMs, 2018-2030E

CAGR	Chemical Drugs	Biologics	TCMs	Total
2018-2023	-2.3%	12.1%	-1.4%	1.1%
2023-2026E	3.6%	15.8%	5.5%	7.9%
2026E-2030E	2.8%	12.0%	3.1%	6.4%



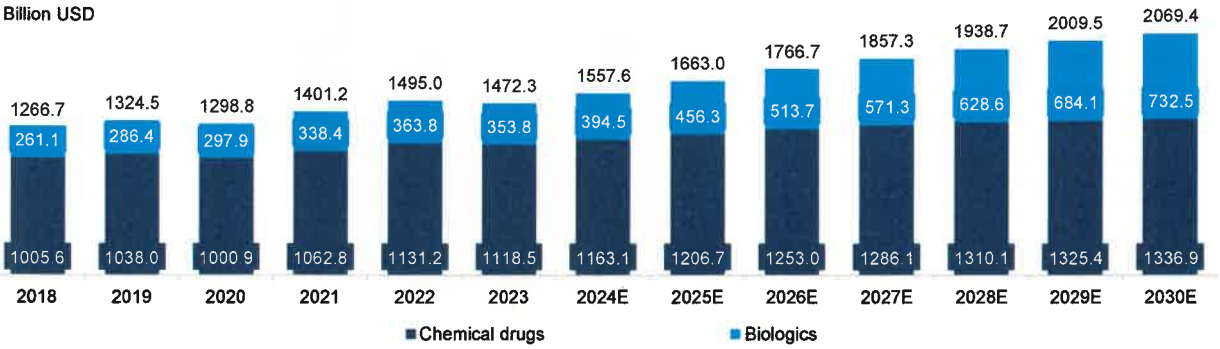
Source: Frost & Sullivan Analysis

Breakdown of Global Pharmaceutical Market by Chemical Drugs and Biologics, 2018-2030E

- Global pharmaceutical market is composed by two segments, namely chemical drugs, biologics, among which chemical drugs account for the largest market share. The size of Global pharmaceutical market was USD 1,472.3 billion in 2023, and is expected to reach USD 1,766.7 billion and USD 2,069.4 billion in 2026 and 2030 respectively, representing a CAGR of 6.3% from 2023 to 2026 and 4.0% from 2026 to 2030.

Breakdown of Global Pharmaceutical Market by Chemical Drugs and Biologics, 2018-2030E

CAGR	Chemical Drugs	Biologics	Total
2018-2023	2.2%	6.3%	3.1%
2023-2026E	3.9%	13.2%	6.3%
2026E-2030E	1.6%	9.3%	4.0%

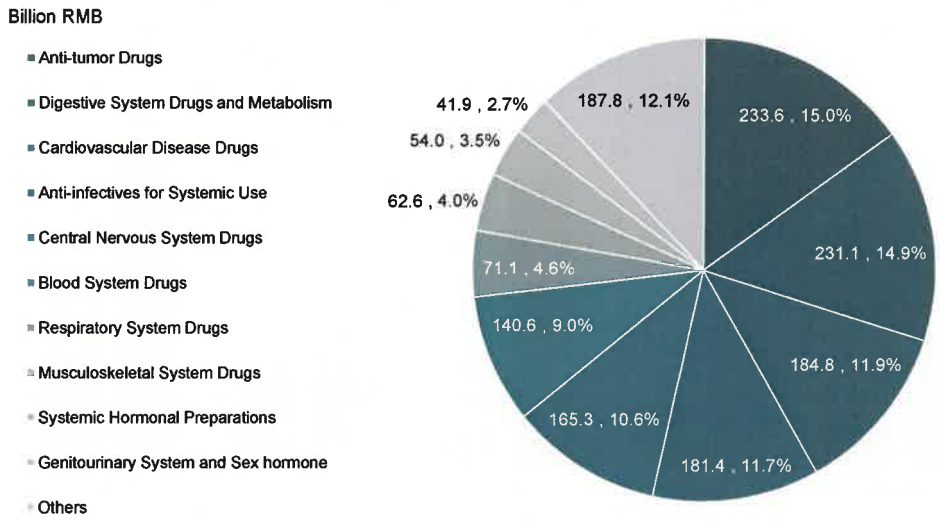


Source: Frost & Sullivan Analysis

Breakdown of China Pharmaceutical Market by Therapeutic Area, 2022

- In terms of market size, anti-tumor, digestive tract and metabolism and cardiovascular disease are three major therapeutic areas in China, respectively accounting for 15.0%, 14.9% and 11.9%.

Breakdown of China Pharmaceutical Market by Therapeutic Area, 2022

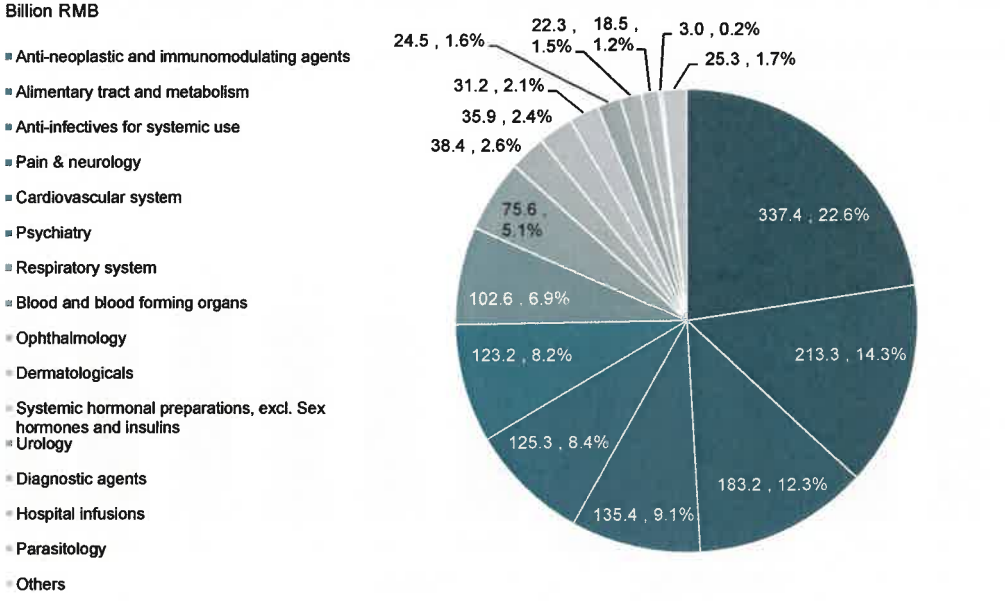


Source: Frost & Sullivan Analysis

Breakdown of Global Pharmaceutical Market by Therapeutic Area, 2022

- In terms of market size, anti-neoplastic and immunomodulating agents, alimentary tract and metabolism and anti-infectives for systemic use are three major therapeutic areas globally, respectively accounting for 22.6%, 14.3% and 12.3%.

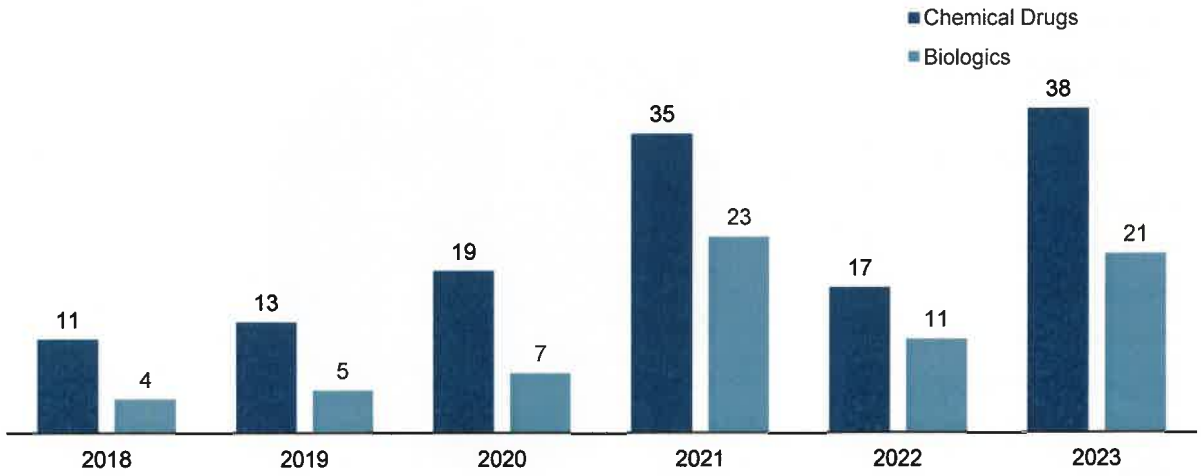
Breakdown of Global Pharmaceutical Market by Therapeutic Area, 2022



Source: Frost & Sullivan Analysis

Innovative Drugs Approved by NMPA, 2018-2023

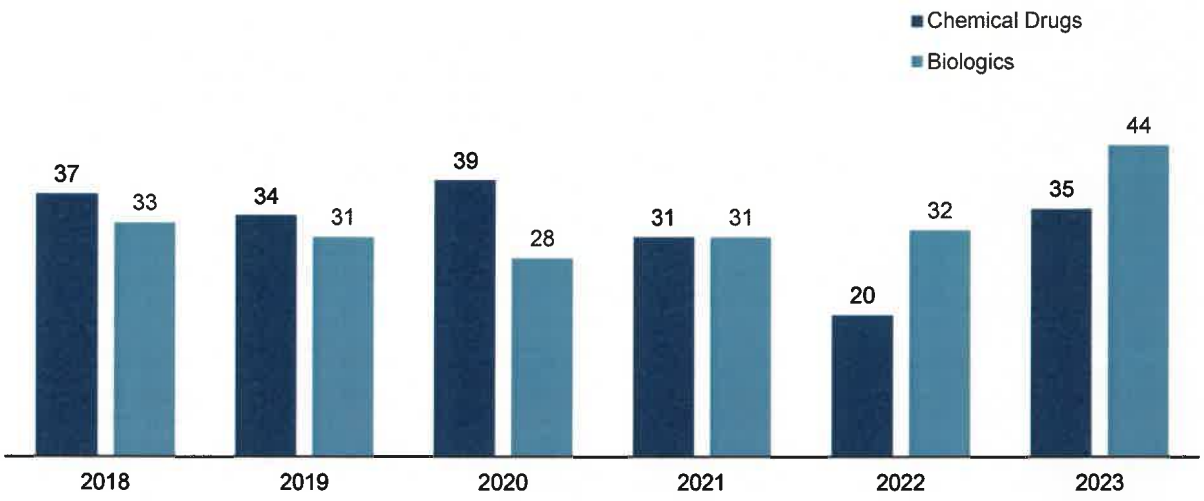
- The following bar chart set forth the number of small molecule drugs approved by NMPA from 2018 to 2023. The number of chemical drugs is relatively more than approved biologics.



Source: NMPA, Frost & Sullivan Analysis

Innovative Drugs Approved by FDA, 2018-2023

- The following bar presents the number of small molecule drugs approved by FDA from 2018 to 2023.



Source: FDA, Frost & Sullivan Analysis

Growth Drivers for China Pharmaceutical Market

Increasing Disposable Income	• In China, per capita annual disposable income increased from RMB28,228 in 2018 to RMB 36,883 in 2022, representing a CAGR of 6.9%. This growth in disposable income has greatly increased the purchasing power as well as the health awareness of the PRC population, increasing their willingness to pay for healthcare, including pharmaceuticals.
Aging population	• In China, population aged 65 years or above increased from 158.3 million, or 11.4% of the entire population, in 2017, to 209.8 million, or 14.9% of the entire population, in 2022. The accelerating aging trend, prolonged life expectancy and prevalence of chronic diseases will further drive up the demand for relevant pharmaceuticals in China.
Favorable Policies	• China government issued a series of policies to encourage the R&D, as well as strengthen the regulation on pharmaceutical market. • For example, shortening the review and approval time span for innovative drugs IND and NDA applications, which will accelerate the new drug review and approval process to address the urgently clinical needs. Patent protection is greatly enhanced as well. All these reforms will attract MNC pharma to launch more global innovative drugs in China market. Furthermore, government has issued favorable policies in terms of tax reduction, talents incentive program and special public R&D fund to support R&D activities of domestic companies in particular. Consequently, that available novel oncology therapies will become increasingly diverse will boost consumption in the future. • A series of strengthening regulations, such as new GMP and two-invoice implementation, will gear the market towards a more market-oriented and consolidated market as well as healthy competition and sustainable development.
Improve Public Medical Insurance	• Public medical insurance is the largest single payer for pharmaceutical in China. The latest version of NRDL not only expand to include more drugs to be reimbursable but also adopt dynamic adjustment via price negotiation to include more advanced drugs in the List with a more economical price. In the 2023 NRDL, 126 drugs were newly included in the list, with a price reduction of 61.7%. The inclusion of numerous domestic innovative drugs has significantly promoted the sales of innovative drugs and the transformation of Chinese pharmaceutical industry to innovation.

Source: Frost & Sullivan Analysis

Future Trends of China Pharmaceutical Market

Expansion of Innovative Drug Market	• With the pilot scheme of centralized procurement of generics and inclusion of innovative drugs into NRDL, it is believed that China pharmaceutical market is shifting towards the innovative driven market. Also, the government promulgated a series of policies to encourage R&D, such as the accelerated drug review and approval, patent protection, tax reduction, and etc. Development of innovative drugs is therefore encouraged and will lead to innovative drug market expansion in the future.
More Biotech Companies to Get Involved	• Due to the strong support from government, capital investment and talent reserve, the biotech companies is expected to play a more important role in pharmaceutical market with their innovative drugs under clinical development and to be launched in the near future. For example, China market has launched 7 PD-1/PD-L1 drugs so far, with their sales revenue reaching tens of millions in a few months, showing a huge potential of innovative drugs in China pharmaceutical market. This will attract more biotech companies to get involved.
Alignment with International Standard	• In recent years, China has joined the ICH as the 8th number, which emblems the onset of alignment of the pharmaceutical industry practices with international standards, indicating an effort to realize a gradual transformation of drug application and registration process toward higher and unified standard. It is expected that the drug review and approval system will be gradually improved.
Novel Therapies Available to Patients Sooner	• Historically, novel therapies usually have a gap of few years in approval time between China and other major markets due to less efficient approval process. The gap is narrowed through reform on review and approval process as well as the ICH alignment. The approval process is further accelerated through enabling priority review and listing the drugs of clinically urgent, potentially bringing more novel drugs to China market in a more timely manner. In this way, effective novel therapies will benefit patients sooner.

Source: Frost & Sullivan Analysis

Favorable Government Policy of Pharmaceutical Industry

Review of Clinical Trial and New Drug Application

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

Source: Government Website, Frost & Sullivan Analysis

Favorable Government Policy of Pharmaceutical Industry

Review of Clinical Trial and New Drug Application

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

Source: Government Website, Frost & Sullivan Analysis

Favorable Government Policy of Pharmaceutical Industry

Review of Clinical Trial and New Drug Application

Release Date	Issuing Authority	Policies	Comments
Sep, 2019	NHC, NHSA, NMPA	*Notice for the Publication of the Health China_ Implementation Plan for Cancer Prevention (2019-2022 edition)* 《关于印发健康中国行动——癌症防治实施方案（2019—2022年）的通知》	• Establish a comprehensive clinical evaluation system for anticancer drugs. • Speed up the approval of new anticancer drugs at home and abroad.
Nov, 2019	NMPA	*Notice on Soliciting Opinions on the Working Procedures of Breakthrough Therapeutics and the Priority Review and Approval Process* 《关于突破性治疗药物工作程序和优先审评审批工作程序征求意见的通知》	• For innovative drugs or improved new drugs that are used to prevent or treat severely life-threatening diseases, and that have no effective prevention measures or have sufficient evidence to show obvious clinical advantages compared with existing therapies, they can apply for Breakthrough Treatment Drugs. • Breakthrough Treatment Drugs can be reviewed and approved first.
Mar, 2020	NMPA, NHC	*Announcement on the Release of Administrative Regulations on Extended Clinical Trials of Medical Devices (Trial)* 《关于发布医疗器械拓展性临床试验管理规定（试行）的公告》	• Meet the public clinical needs and support clinical experimental on medical instruments as soon as possible. • Standardize the development of extended clinical trials and the collection of safety data for medical devices. • Safeguard the rights and interests of subjects.
Apr, 2020	NMPA, NHC	*Announcement on the Release of Quality Management Practices for Drug Clinical Trials* 《关于发布药物临床试验质量管理规范的公告》	• Deepen the reform of drug evaluation and approval system and encourage innovation. • Further promote standardized research and improve the quality of drug clinical trials in China.
Dec, 2020	NMPA	*Guidelines for Statistical Design of Antitumor Drug Clinical Trials (Trial)* 《抗肿瘤药物临床试验统计学设计指导原则（试行）》	• The statistical methods for the commonly used efficacy endpoints are proposed in the guidelines, and the statistical design requirements are putted forward from the perspectives of exploratory and confirmatory trials.
Nov, 2023	NMPA	*the Measures for the Supervision and Inspection of Drug Clinical Trial Institutions (Trial)* 《药物临床试验机构监督检查办法（试行）》	• According to the nature and purpose of the inspection, inspections carried out on testing institutions are divided into daily supervision inspections, reasoned inspections and other inspections. Different types of inspections can be combined.

Source: Government Website, Frost & Sullivan Analysis

Favorable Government Policy of Pharmaceutical Industry

Review of Innovation Encouragement

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

Source: Government Website, Frost & Sullivan Analysis

Favorable Government Policy of Pharmaceutical Industry

Review of Innovation Encouragement

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

Source: Government Website, Frost & Sullivan Analysis

Favorable Government Policy of Pharmaceutical Industry

Review of Innovation Encouragement

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

Source: Government Website, Frost & Sullivan Analysis

Favorable Government Policy of Pharmaceutical Industry

Review of Innovation Encouragement

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

Source: Government Website, Frost & Sullivan Analysis

Favorable Government Policy of Pharmaceutical Industry

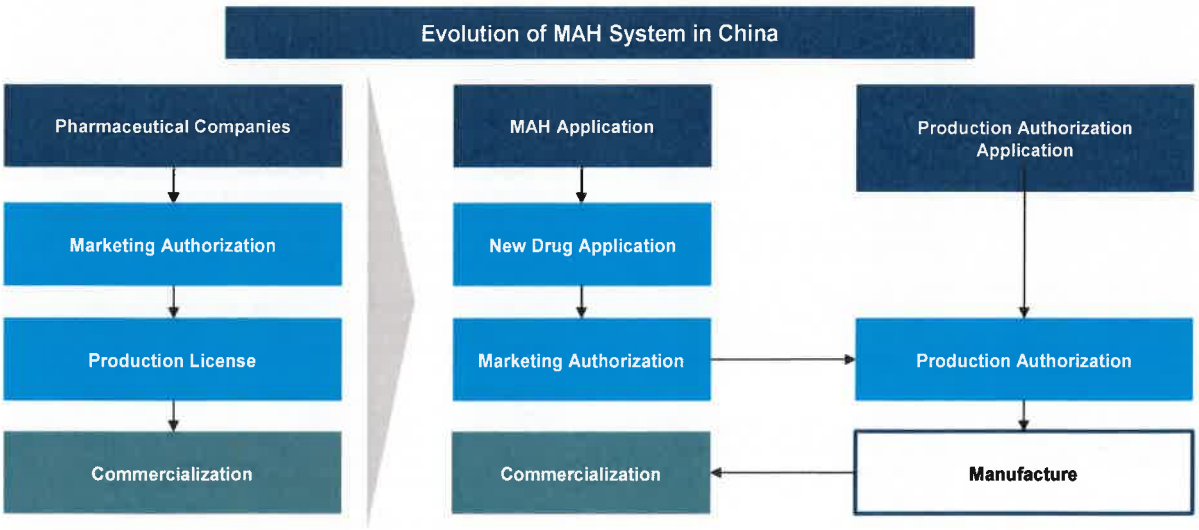
Review of Innovation Encouragement

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

Source: Government Website, Frost & Sullivan Analysis

Policy Analysis of Marketing Authorization Holder (MAH)

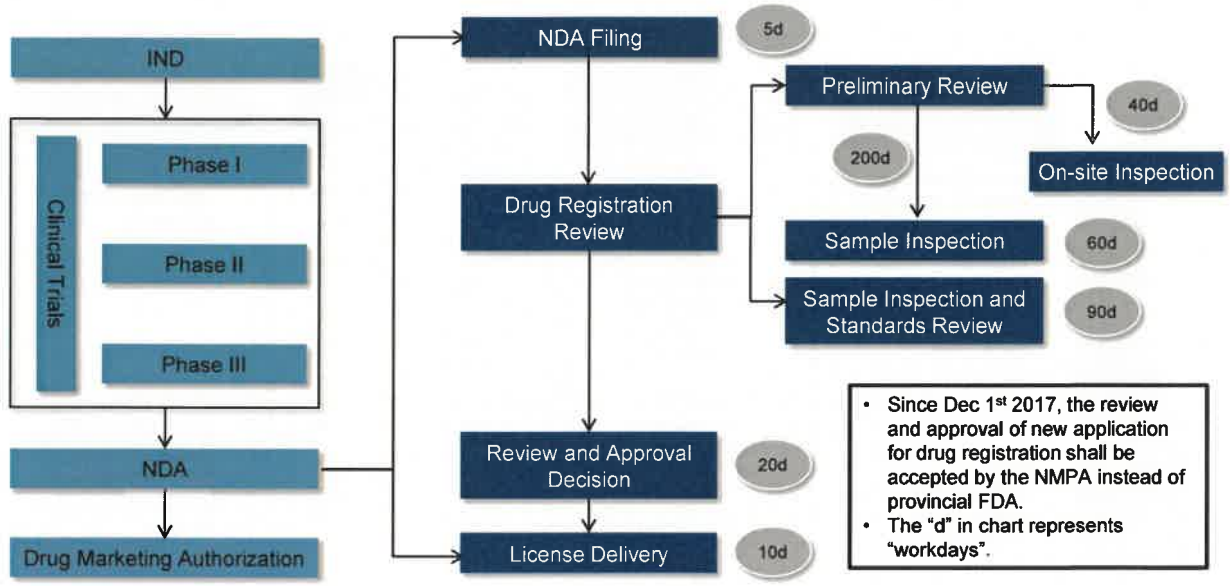
- MAH system enables the R&D organizations or personnel to apply for and obtain drug marketing authorizations and drug approval license, and the MAHs can entrust the CMOs to manufacture drugs instead of obtaining production license themselves, so that they can focus on R&D rather than allocate the manpower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



Source: Government Website, Frost & Sullivan Analysis

Drug Registration Procedure in China

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

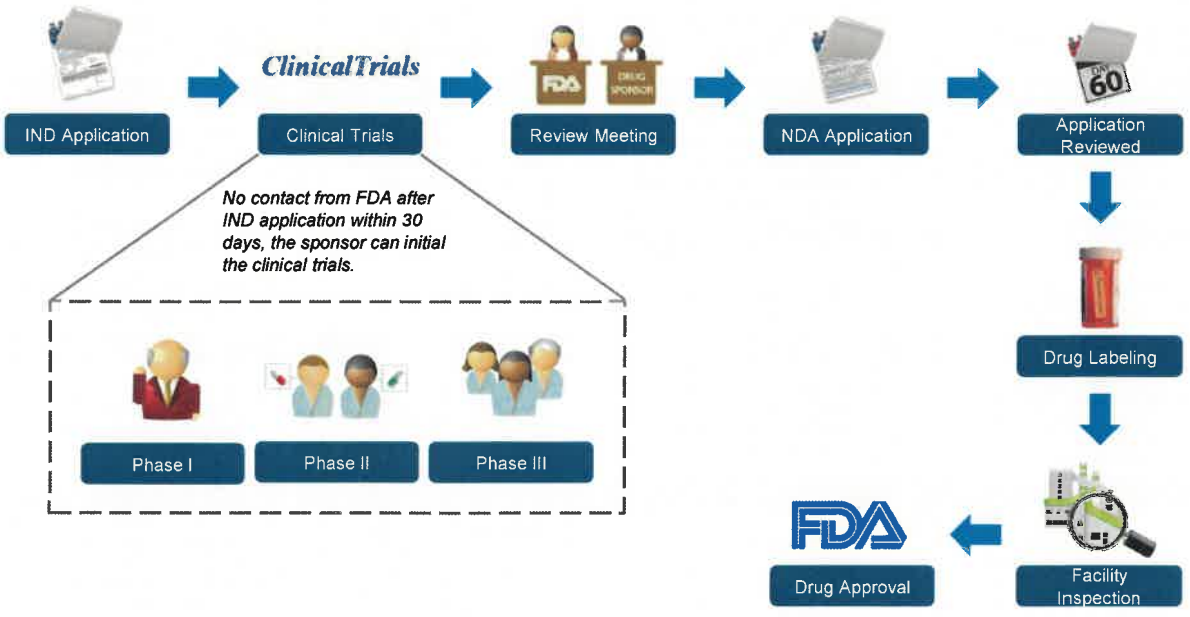


Note: The Procedure is a general approval pathway. In reality, approval pathway may vary case by case.

Source: CMA, Frost & Sullivan analysis

Drug Registration Procedure in the US

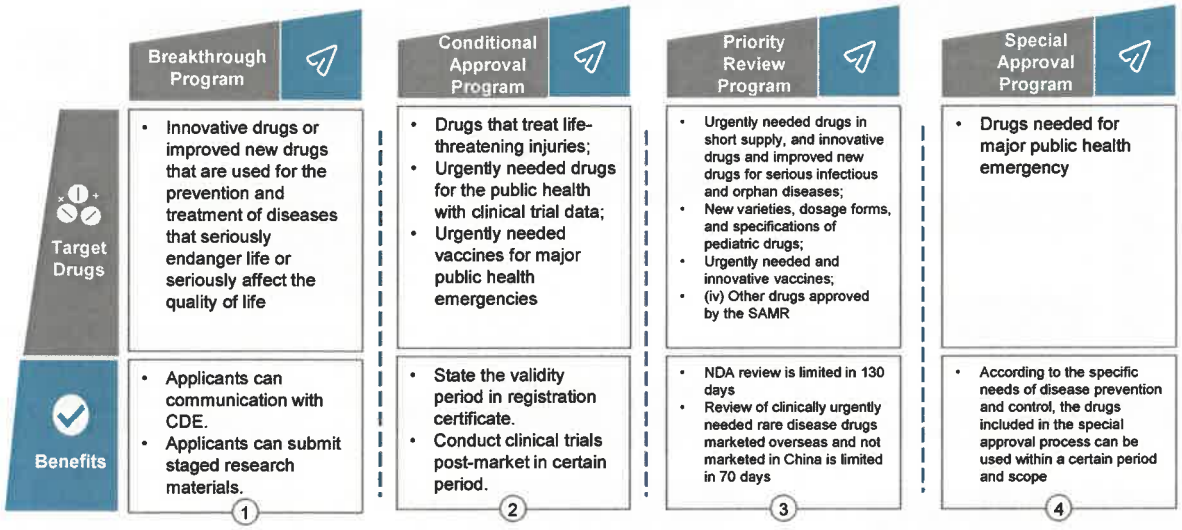
- Drug registration in the US needs to comply with Federal Food, Drug and Cosmetic Act (FD&C Act), which stipulates the application filling and clinical trial requirements from IND application to drug approval.



Source: FDA, Frost & Sullivan analysis

Grants Programs to Innovative Drugs in China

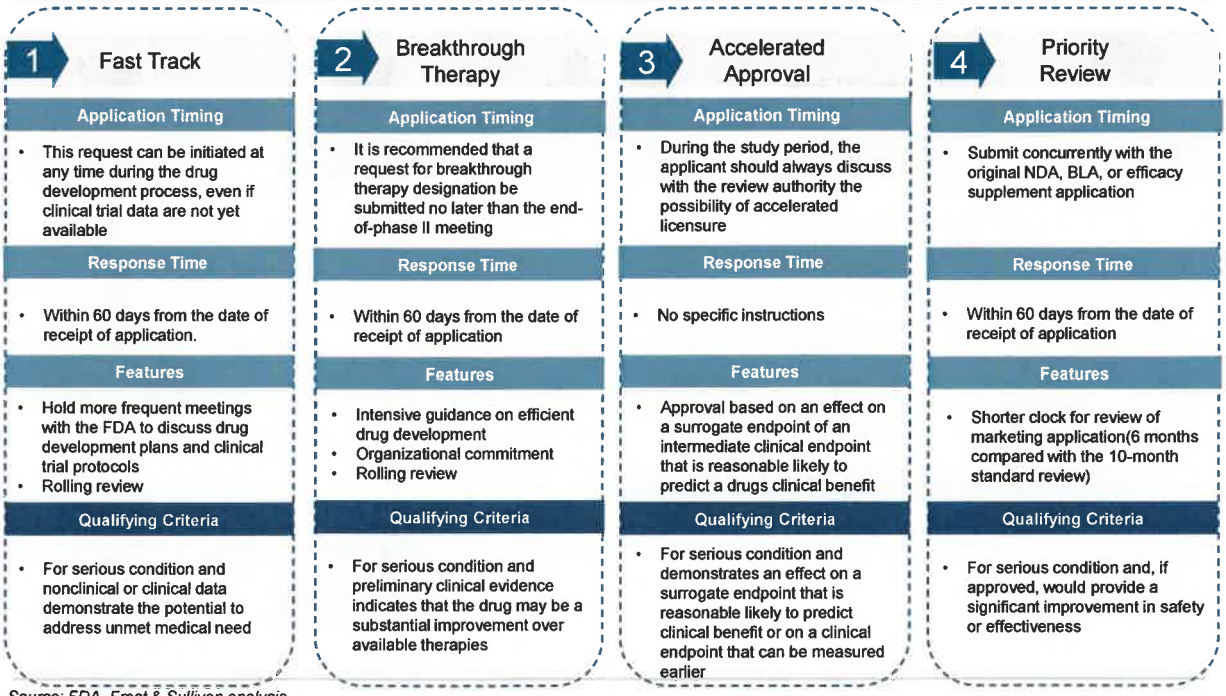
- On March 30, 2020, the State Administration for Market Regulation (SAMR), released a revised Drug Registration Regulation (Revised DRR) as part of its efforts to strengthen and streamline its regulation of the pharmaceutical industry, which went into effect on July 1, 2020. There are four programs included in the regulation, target drugs and benefit of each program are illustrated as follows:



Source: Frost & Sullivan Analysis

FDA Expedited Programs for New Drug Approval

- FDA has developed four distinct and successful approaches to make innovative drugs or those with advantages over existing treatments as soon as possible. FDA expedited programs aims to help spur the development of new therapies for serious conditions.



Source: FDA, Frost & Sullivan analysis

Overview of Orphan Drugs

- According to the FDA, an orphan drug is defined as one intended for the treatment, prevention or diagnosis of a rare disease or condition.
- Pharmaceutical companies tended not to develop treatments for rare diseases due to poor economic potential. To address the problem, the Orphan Drug Act of 1983 was passed in the United States to facilitate development of orphan drugs by including a number of incentives such as market exclusivity and funding for clinical research.

Rare Diseases

Definition	Rare diseases are defined by FDA as a disease or condition affecting < 200,000 people in the States.
Epidemiology	Rare diseases affect approximately 30 million people in the US, of whom an estimated 50% are children. Worldwide, up to 350 million people are estimated to suffer from a rare disease.
Constitution	Presently, there are estimated to be 7000 diseases considered rare in the US, with more diseases being defined each year.

	Before 1983 No Policy Regarding Orphan Drug	After 1983 The Introduction of Orphan Drug Act (ODA)
Number of Orphan Drugs Approved	• In the decade before 1983, only 10 products had been developed by the pharmaceutical industry to treat rare diseases.	• As of 2016, there had been 449 approved orphan therapies for 549 orphan indications.
Patients Treated	• Adequate drugs or biologicals were not available for many rare diseases and conditions. • For example, people with cystic fibrosis rarely lived beyond their early teens in the 1980s.	• More drugs are available for people with rare diseases. • As of 2010, 200 of the roughly 7,000 officially designated orphan diseases have become treatable.
Pharma Company R&D Status	• Pharmaceutical companies are less likely to study orphan drugs possibly due to the small populations, high development costs, and limited commercial value.	• Pharma companies are more likely to invest in orphan drug R&D because ODA provides financial incentives for the development of new drugs for rare diseases, such as market exclusivity and funding for clinical research.

Source: Literature Review, FDA, Frost & Sullivan analysis

Orphan Drug Development in the U.S.

- Orphan Drug Designation (ODD) is granted to drug products that are used to treat a rare disease by Office of Orphan Products Development (OOPD), defined by the Orphan Drug Act of 1983.
- A well-defined ODD submission criteria together with a standardized procedure set a basis for qualified candidate to benefit from ODD incentives including favorable policy and expedited review.

- The criteria for ODD application is listed clearly with the qualification of the drug and its targeted indication well-defined. This helps the sponsors to navigate through the process and obtain the ODD smoothly. As a result, qualified sponsors could benefit from corresponding favorable policies of ODD with less uncertainty.

Well-defined ODD Criteria/Procedure

- Given the severe nature of the diseases targeted by orphan drugs, drugs with ODD tend to be eligible for the expedited review process of FDA (fast track, breakthrough therapy, accelerated approval and priority review).
- As a result, orphan drugs could benefit from the flexibility of FDA review, and thereby significantly shorter development time. An analysis has shown that it takes 3.9 years for orphan drugs from Phase II to launch, as opposed to 5.4 years for non-orphan drugs.

Eligible for Expedited Review

Favorable Policy

Incentives for ODD

ODD incentives mainly include cost reduction, market exclusivity and clinical research subsidies.

Cost Reduction
- Waiver of the user fee (application fee) upon filing a marketing application
- Tax credits for clinical research undertaken by the sponsor to generate required data for market approval

Market Exclusivity
- Marketing exclusivity for an approved drug for 7 years after product approval (compared to the normal 5-year period)

Clinical Research Subsidies
- Protocol assistance from either Center for Drug Evaluation and Research (CDER) or Center for Biologics Evaluation and Research (CBER)
- Financial assistance from the Office of Orphan Products Development (OOPD)

Source: Literature Review, FDA, Frost & Sullivan analysis

Overview of Healthcare Insurance System in China

Public Medical Insurance	UEBMIS	**Urban Employee Basic Medical Insurance Scheme (UEBMIS)** • The scheme for urban employees, which is jointly funded by employers and employees, was established in 1998 to provide reimbursement for medical services and drugs. • Under UEBMIS, employees including retirees are entitled to the healthcare insurance benefits. Generally, it is funded by (i) monthly payments from the beneficiary, such as the employee, and (ii) co-payments made by the employer of the beneficiary, both of which are subject to a ratio set forth by the local Labor and Social Security Authority. The ratio is calculated based on the monthly salary of the employee.
	URBMIS & NRCMIS	**Urban Resident Basic Medical Insurance Scheme (URBMIS)** • The scheme for urban residents, financed by governments and individuals, was set up in 2007, and is now administered by the MOHRSS to provide coverage for major illnesses for urban residents not covered under UEBMIS. • Most of its participants are urban residents who are currently unemployed or retired. Participants of the URBMIS are required to contribute to the payment of insurance premiums on a monthly basis. **New Rural Cooperative Medical Insurance Scheme (NRCMIS)** • The NRCMIS piloted in 2003 given the government's dedication to establish the rural cooperative medical care system so as to improve access to medical services and drug supply in rural areas. The NRCMIS is funded by allocations from the central government, subsidies from local governments and fees paid by rural Chinese who participate the system voluntarily. **Consolidation of URBMIS and NRCMIS** • In 2016, a few provinces in China have piloted consolidation of NRCMIS and URBMIS because of their similarities in funding Source and levels, which paves the way towards a nationwide, consolidated, medical insurance system. Opinions of Consolidation of URBMIS and NRCMIS (《国务院关于整合城乡居民基本医疗保险制度的意见》) required all provinces must put forward implementation plans of such consolidation by the end of 2016.
	Medical Aid Scheme	Medical aid schemes are subsidized by local and central government funds and private donations and vary according to the local financial situation, to benefit low income patients with non-reimbursement expenses for inpatient and outpatient services.
Commercial Medical Insurance		Private medical institutions are pressing for patient reimbursement through the social insurance schemes for services provided at private hospitals. Any difference in the reimbursed amount and the fee for service would be paid out-of-pocket or through Appendix commercial insurance. Such a move would encourage greater use of private facilities and also boost demand for private insurance.

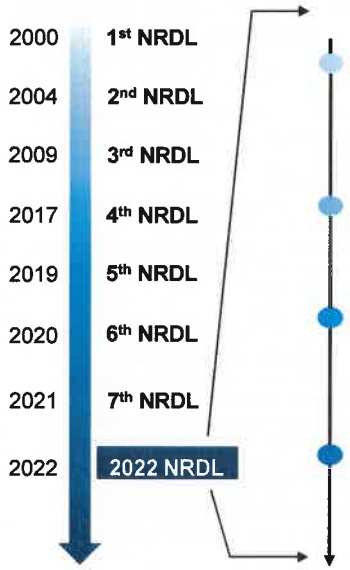
Source: NHFPC, Frost & Sullivan Analysis

Analysis of Healthcare Reimbursement System in China

Recent Progress and Impact of the 2022 NRDL

- In the 2022 NRDL, 111 drugs were newly included in the list, with a price reduction of 60.1%. The inclusion of numerous domestic innovative drugs has significantly promoted the sales of innovative drugs and the transformation of Chinese pharmaceutical industry to innovation.

Progression of NRDL



Recent Progression of 2022 NRDL

- In Jan 2023, NHSA and MOHRSS released the official work plan for the adjustment of the 2022 NRDL, enforced from March 1st, 2022. The latest NRDL negotiation aims to eliminate medications with unreasonably high prices, optimize clinical use of medications, and further lower prices of current drugs by inducing virtuous competition.
- 147 kinds of drugs were involved in price negotiation, and 121 of them were smoothly negotiated. 111 kinds of drugs have been newly included in NRDL for the first time, leading to a 60.1% decline in prices.
- 3 previously included drugs were removed from the list, all of which are the varieties that have been cancelled by the NMPA.
- 56 drugs for chronic diseases such as hypertension, diabetes, and hyperlipidaemia have been newly included. Besides, 23 oncology drugs, 17 anti-infective drugs, 7 drugs for rare diseases, 22 children's drugs, 2 drugs for covid-19 and 2 national essential drugs have been newly included.

Implication for Innovation

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

2022 NRDL restricts the price of drugs strictly by adding rules for non-exclusive drug bidding. If a drug is included in the list through bidding, the lowest price quoted by each enterprise shall be taken as the payment standard for the generic name drug.

Numerous domestic innovative drugs were included by 2022 NRDL, marking the initiation of a rapid increase of sales and the rapid transformation of the Chinese pharmaceutical industry towards innovation.

Since the implementation of the self-declaration system of pharma, only drugs that meet the conditions of 2022 NRDL plans can be included in the adjustment scope.

Source: MORHSS, Frost & Sullivan Analysis

Overview of Healthcare Insurance System in the US

Public Medical Insurance	Medicaid	• Medicaid is a medical and healthcare program for low-income groups. • Targeted at low-income parents, the elderly, children, and people with disabilities. • Jointly funded by the U.S. federal government and the state governments. • The CMS center supervises the implementation of the projects in each state.
	Medicare	• Established in accordance with the Social Security Amendment in 1965, which is operated by the US federal government. • It serves the elderly over the age of 65 or persons with disability or end-stage renal disease who meet certain conditions and are under the age of 65.
	CHIP(Children 's Health Insurance Program)	• Determined by the Balanced Budget Act of 1997, which provided health insurance for children from low- and middle-income families in the United States in the form of federal funding provided by the federal government. • The targets are those children whose family income is less than twice the federal poverty line and who have not participated in other private insurance.
Commercial Medical Insurance		• Commercial insurance providers are private insurance companies that contract with businesses or individuals to help cover healthcare costs according to criteria set forth in a formal health plan. Private health insurance plans typically require that the company or the individual receiving coverage pay a predetermined deductible or a monthly premium before benefits take effect. • Unlike heavy reliance on public medical insurance in China, commercial medical insurance contributes the majority of the healthcare services payment in US. Types of commercial medical insurance includes: 1. **Preferred provider organizations (PPOs):** PPOs operate off a list of preferred healthcare providers that patients can choose from for their coverage. Patients save the most money on their healthcare plans by selecting the preferred providers affiliated with a PPO. 2. **Health maintenance organizations (HMOs):** HMOs are groups of physicians, medical facilities, and healthcare services that work to keep patients under the care of providers within their network. Healthcare providers in HMOs coordinate a patient's healthcare decisions and suggest a suitable hospital for urgent care. 3. **Point-of-service Plans:** Point-of-service plans form a hybrid between PPOs and HMOs. As with HMOs, point-of-service plans allow you to select physicians and services from within a dedicated network of providers.

Source: Frost & Sullivan Analysis

Growth Drivers of Innovative Drugs Market

Enlarging Patient Pool	• In China, disease spectrum is transforming from infectious diseases to chronic diseases among which include oncology are getting increasingly prevalent. China cancer incidence almost reached 4.81 million in 2022, and it is estimated to further increase to 5.79 million in 2030 The cancer treatment features high cost and long-term medication demand. This is particularly true for cancers with limited treatment options, where novel targets such as FGFR, KRAS, and c-MET have garnered significant development focus in recent years.
Technology Advancement	• The development of technology promotes the development of biologics. Biotechnology can create substances that cannot be found in nature, integrate two substances into one molecule to exploit benefits from both of them, and even utilize viruses for their unique features. • Multidisciplinary such as genome technology and information technology has promoted the development of precision medicine, so it is necessary to develop small molecule drugs with better targeting, which will increase the need for innovative chemical medicine.
Promotion of Commercial Healthcare Insurance	• In addition to national medical insurance, lots of pharmaceutical companies are exploring new ways to solve the accessibility of innovative drugs through cooperation with commercial healthcare insurance platform. In addition to national medical insurance, many pharmaceutical companies are exploring new ways to solve the accessibility of innovative drugs through cooperation with commercial insurance companies or third-party insurance platforms. As the national medical insurance is characterized by "low guarantee and wide coverage", and the connection between pharmaceutical companies and commercial healthcare insurance undoubtedly provides a new payment method to increase the possibility of drug accessibility. • In recent years, the participation rate of commercial medical insurance is increasing year by year, such as Huihu Bao (惠沪保), Huirong Bao (惠蓉保), and Lecheng global special drug insurance (乐城全球特药险). In 2022, "Huhui Bao" expanded the number of domestic specific high-value drugs to 25, including car-t treatment drugs, PD-1 antibody products, ADCs and overseas special drugs, with the maximum total insured amount increasing to 3.1 million. In 2022, Huirong Bao expanded the list of special drugs to 58 as well.
Favorable Policy	• China government promulgated a series of policies to shorten the review and approval interval for innovative drugs. Also, priority review is implemented, which will accelerated getting to the market process for drugs with potential to address the urgently clinical need. Patent protection is greatly enhanced as well. All these reforms will attract MNC to market more global innovative drugs in China market and stimulate domestic players to invest more on research & development. Consequently, that available innovative drugs become increasingly diverse will boost consumption in the future.

Source: Frost & Sullivan Analysis

Future Trends of Innovative Drugs Market

Focusing on Chronic Diseases	• In China, disease spectrum is transforming from infectious diseases to chronic diseases, including cardiovascular diseases, cancer and chronic respiratory diseases. According to *China's Mid - and Long-term Plan for Chronic Diseases (2017-2025)*《中国防治慢性病中长期规划（2017-2025年）》issued by the State Council, Chronic diseases account for 86.6% of total deaths, and the disease burden has accounted for more than 70% of the total disease burden. Therefore, from the perspective of clinical demand, China's innovative drug research and development in the future will mainly focus on cancer, cardiovascular diseases, diabetes and other chronic diseases, while anti-infective drugs will still maintain a certain proportion.
Multi-disciplinary Integration	• After the two revolutions in life science caused by the development of molecular biology and genomics, the third revolution is characterized by the integration of multiple disciplines. It will be triggered by the convergence of disciplines such as life science, physics, engineering and information technology. The cross-fusion of gene editing technology, tumor immunotherapy, big data, artificial intelligence, 3D printing technology and other fields will promote the research and development of new drugs.
Cooperative Innovation	• Pharmaceutical enterprises can obtain resources from other entities to shorten the research and development time, reduce the research and production costs, and accelerate the entry of innovative drugs into the market. Pharmaceutical enterprises can entrust manufacturing enterprises with the production of innovative drugs, thus saving the capital and time of self-built factories and production lines. And pharmaceutical enterprises can cooperate with universities, research institutes CROs to do innovative drug research, which can reduce the cost and share the risk.
Improving Affordability	• The average disposable income of the Chinese population is expected to continue growing rapidly, increasing the willingness and ability of patients to pay for medications. As more Chinese households increase their spending power, they can afford more expensive medical treatments, particularly for life-threatening diseases.

Source: Frost & Sullivan Analysis

Entry Barriers of Small Molecular Targeted Drug Market

Overcoming Drug Resistance Issues	• The first entry barrier for small molecule targeted drugs is overcoming their drug resistance issues. Almost all small molecule targeted drugs will encounter resistance problems after a period of clinical use. Drug resistance mechanisms include increased drug efflux and reduced cellular uptake, target cell gene mutations, changes in target cell signaling pathways, target cell phenotype remodeling, and reactivation of DNA damage repair systems, etc.. Solving the problem of resistance to targeted drugs determines its future clinical application space.
Not Broad Spectrum and Genetic Testing is Required	• Small molecule targeted drugs are usually only effective for patients with specific genetic mutations and do not have broad-spectrum properties. For example, in the selection of targeted anti-tumor drugs, it is usually necessary to first identify the type of gene mutations carried by patients, which highlights the importance of genetic testing for the use of targeted drugs.
In-depth understanding of disease mechanisms and key pathogenic factors	• An in-depth understanding of disease mechanisms and elucidation of key pathogenic factors are the core of achieving precise molecular targeting of different key targets. Effectively entering cells and reaching the target are the focus of the research and development of small molecule targeted drugs.
Target Discovery, Compound Screening and Optimization	• Target discovery, compound screening and optimization are key factors that determine the success of small molecular targeted drug development. Serious homogeneous competition and congestion in popular targets, as well as the lack of original targets and original technical routes, are important challenges for the research and development of small molecular targeted drugs. Achieving target innovation and compound design innovation are potential entry barriers.

Source: Frost & Sullivan Analysis

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Development Path of Cancer Treatment

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

Milestones in Cancer Treatment

Surgery
1881, first successful surgery performed for stomach cancer

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

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

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

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

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

Targeted Therapy and Immunotherapy
1997, FDA approves the first molecularly targeted cancer drug, rituximab

- ***Targeted therapies*** act on specific targets that are associated with cancer growth, thus they do less harm to normal cells. Most targeted therapies are either small-molecule drugs or monoclonal antibodies.
- ***Immunotherapy*** induces the patient's own immune system to fight cancer. Immunotherapy includes cytokines, monoclonal antibodies, checkpoint inhibitors (checkpoint monoclonal antibodies), cellular immunotherapies and cancer vaccines.

Source: Literature Review, Frost & Sullivan Analysis

Oncology Treatment Evolvement

Primary Treatment

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

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

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

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

Treatment Evolution

5. Immuno-Oncology Therapy
- Induce the patient's own immune system to fight cancer
- Include cytokines, monoclonal antibodies, checkpoint inhibitors, cellular immunotherapies and cancer vaccines.

Significant Evolution

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

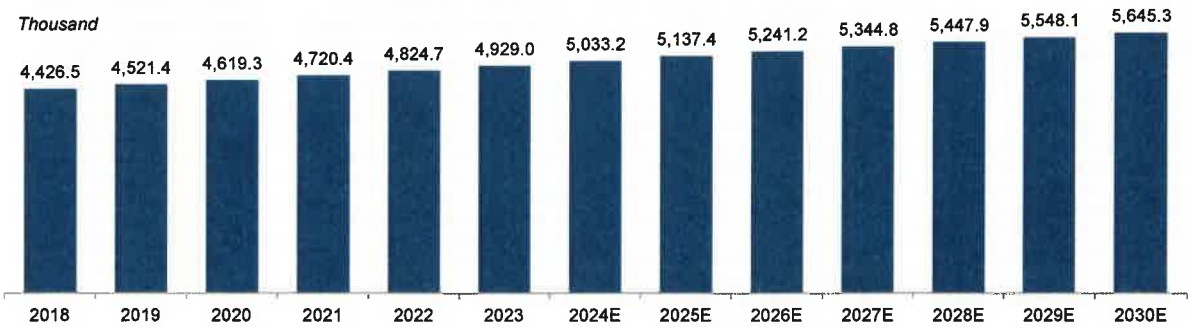
Source: Literature Review, Frost & Sullivan Analysis

China Cancer Incidence, 2018-2030E

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

China Cancer Incidence, 2018-2030E

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



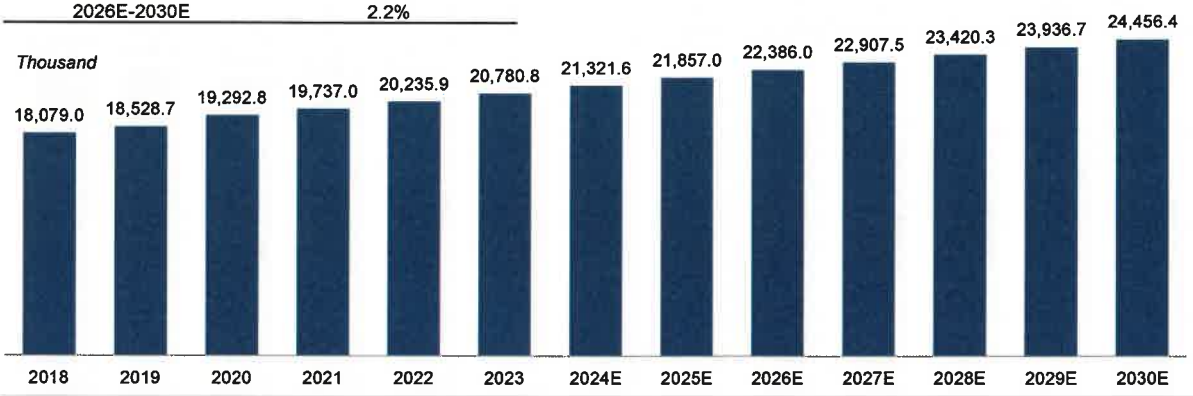
Source: NCCR, Frost & Sullivan Analysis

Global Cancer Incidence, 2018-2030E

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

Global Cancer Incidence, 2018-2030E

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



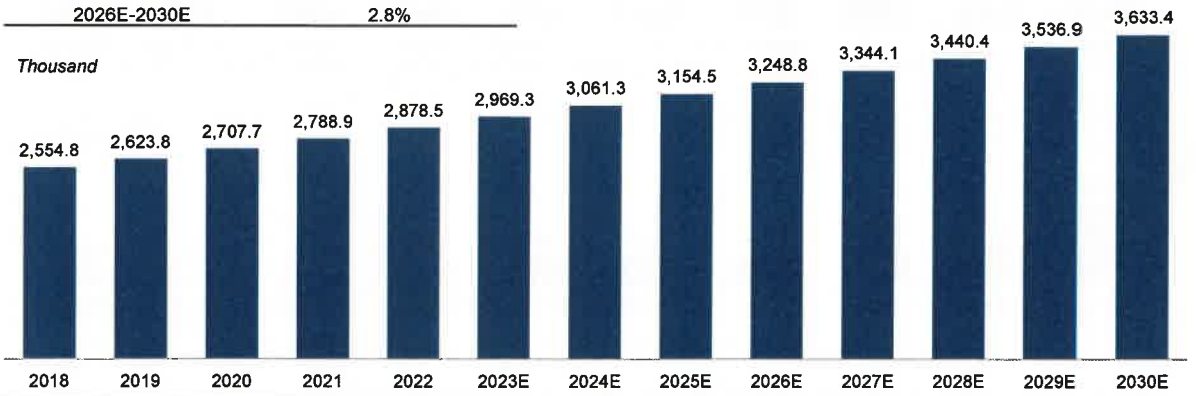
Source: IARC, Frost & Sullivan Analysis

China Cancer Mortality, 2018-2030E

- In China, cancer mortality reached 2878.5 thousand in 2022 at a CAGR of 3.0% from 2018. It is projected to further increase to 3248.8 thousand in 2026, representing a CAGR of 3.1% from 2022. It is estimated that the mortality would achieve 3633.4 thousand in 2030, representing a CAGR of 2.8% from 2026 to 2030.

Cancer Mortality in China, 2018-2030E

Period	CAGR
2018-2022	3.0%
2022-2026E	3.1%
2026E-2030E	2.8%



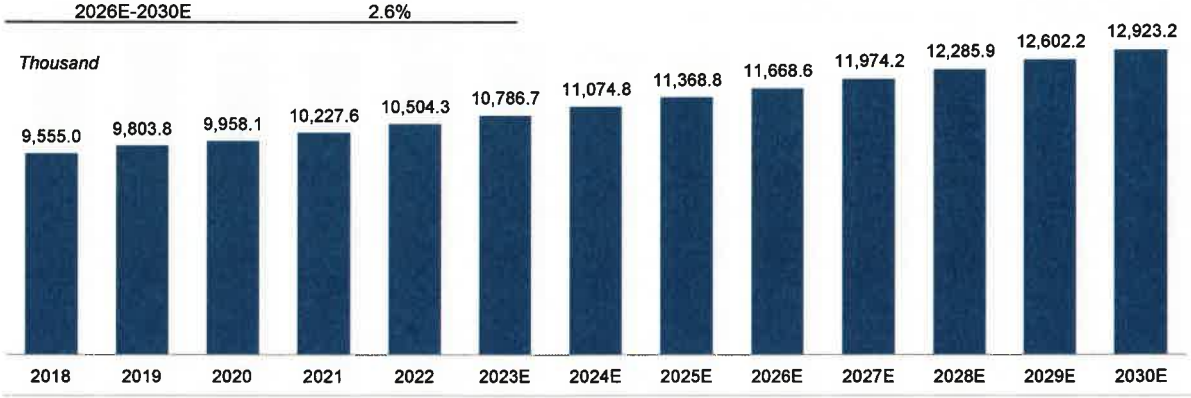
Source: NCCR, Frost & Sullivan Analysis

Global Cancer Mortality, 2018-2030E

- In global, cancer mortality reached 10504.3 thousand in 2022 at a CAGR of 2.4% from 2018. It is projected to further increase to 11668.6 thousand in 2026, representing a CAGR of 2.7% from 2022. It is estimated that the incidence would achieve 12923.2 thousand in 2030, representing a CAGR of 2.6% from 2026 to 2030.

Global Cancer Mortality, 2018-2030E

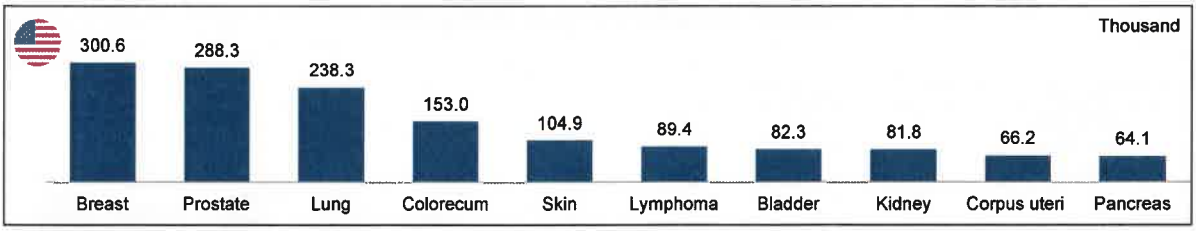
Period	CAGR
2018-2022	2.4%
2022-2026E	2.7%
2026E-2030E	2.6%

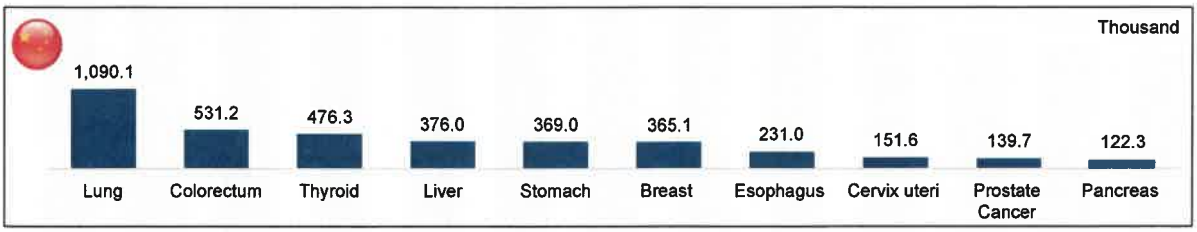


Source: IARC, Frost & Sullivan Analysis

Top 10 Cancers by Incidence in 2023, US VS China

- The USA and China have demonstrated different structures of Top 10 cancers in terms of new cases in 2023.
- Breast cancer has the largest number of patients in the USA, while lung cancer threatened the lives of the most cancers patients in the China.

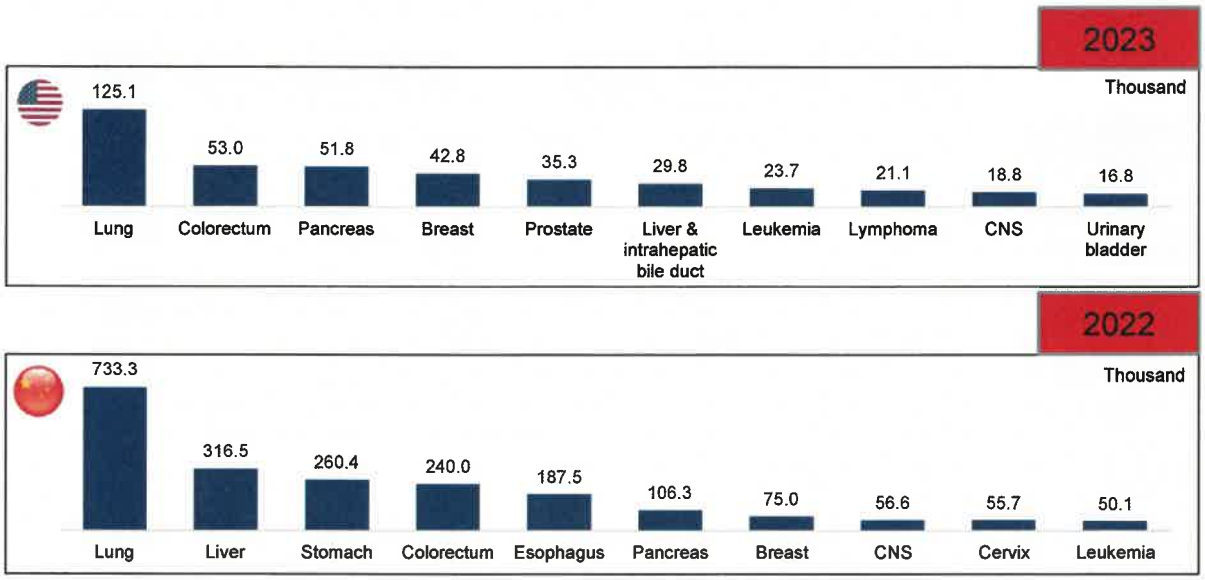




Source: NCCR, IARC, Frost & Sullivan Analysis

Top 10 Cancers by Mortality, US 2023 VS China 2022

- The mortality of lung cancer ranks the highest in the USA. Colorectum is the second most fatal in the global., whereas it ranks the fifth in China. Liver cancer is the second most mortal cancer in China.

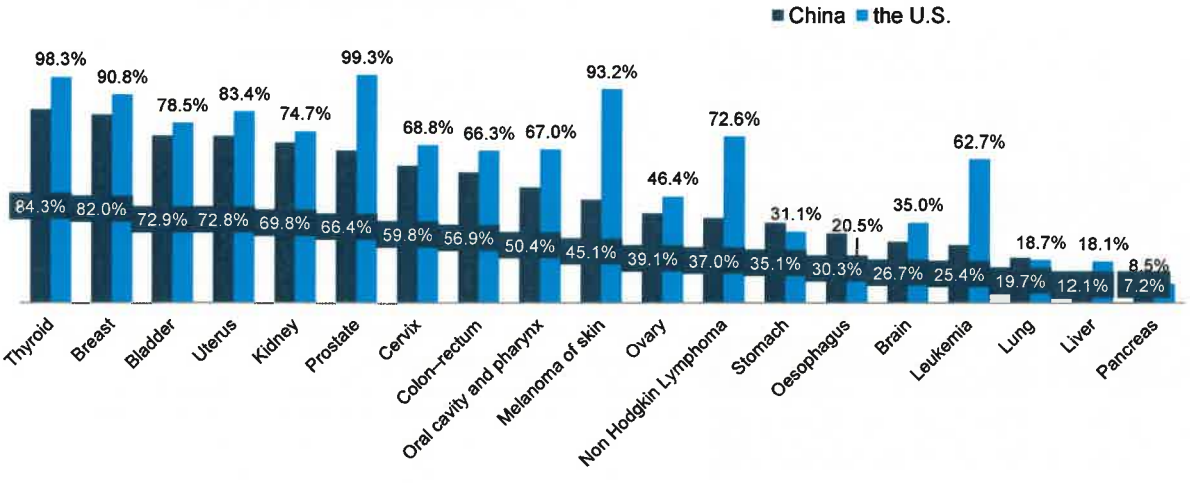


Source: NCCR, IARC, Frost & Sullivan Analysis

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

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

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



Source: NCCR, IARC, Frost & Sullivan Analysis

Comparison of Manufacturing in Biologics and Small Molecule Drugs

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

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

Source: Frost & Sullivan Analysis

Overview of Combination Therapies

- Combination therapy, a treatment modality that combines two or more therapeutic agents, is a cornerstone of cancer therapy. The amalgamation of anti-cancer drugs enhances efficacy compared to the mono-therapy approach because it targets key pathways in a characteristically synergistic or an additive manner.
- Studies have shown significant improvements in the overall outcome of certain cancer patients when a targeted therapy is used in combination with chemotherapy
- The use of two precision oncology that affect different cancer pathways can slow disease progression and address, delay or prevent acquired resistance to a greater extent than using just one precision oncology. Highly selective tyrosine kinase inhibitors are ideal candidates for combination therapies because, due to their high selectivity, each drug can be used at its maximum dose without intolerable side effects.

		Combination Therapy Examples
Primary	Surgery + Adjuvant Therapy	• Mastectomy + Docetaxel + Herceptin for breast cancer
Secondary	Molecularly targeted therapy + Chemotherapy	• Bevacizumab + 5-fluorouracil-based chemotherapy for metastatic colorectal cancer
	Immuno-oncology therapy + Chemotherapy	• Pembrolizumab + Pemetrexed and platinum chemotherapy for NSCLC
	Immuno-oncology therapy + Immuno-oncology therapy	• Nivolumab + Ipilimumab for melanoma, renal cell carcinoma and colorectal cancer
	Molecularly targeted therapy + Immuno-oncology therapy	• Avelumab + Axitinib for late stage RCC
Emerging	Cell and gene therapy	• Chemotherapy and CAR-T therapy for B cell lymphoma

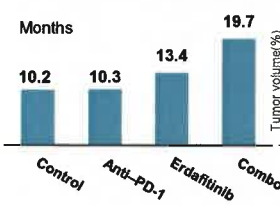
Source: Literature Review, Frost & Sullivan Analysis

Case Study: Combination Therapies of FGFR Inhibitor and PD-1 Monoclonal Antibody

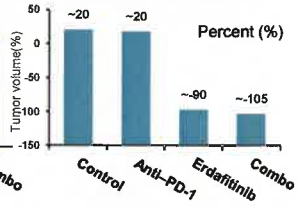
- Cancer immunotherapies, such as those targeting the immune checkpoint PD-1, have revolutionized cancer treatment across a variety of tumor types. The success of targeted or immune therapies is often hampered by the emergence of drug resistance.
- For this study, mice used were hemizygous for FGFR2K660N with the p53 inactivation mutation. Mice with lung tumors confirmed by MRI were randomized into four treatment groups: control, anti–PD-1, erdafitinib, and combination of erdafitinib and anti–PD-1 (combo).

Erdafitinib and anti–PD-1 combination induced tumor regression and improved survival

Improvement of mPFS



Change of Tumor Volume

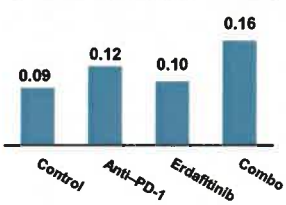


- Erdafitinib monotherapy treatment resulted in substantial tumor control but no significant survival benefit. Although anti–PD-1 alone was ineffective, the erdafitinib and anti–PD-1 combination induced significant tumor regression and improved survival.

Combo with anti–PD-1 increase TCR clonality and antitumor T-cell response

- Both T-cell fraction and clonality were increased after anti–PD-1 treatment compared with the control group.
- The combination of erdafitinib and anti–PD-1 led to an increase in T-cell clonality relative to erdafitinib monotherapy, suggestive of expansion of tumor-specific T-cell clones induced by erdafitinib.
- The increment of T-cell fraction leads to higher response rate of treatment, namely enhance the capability of immune response. And the cells titer reflect the activation of target immune cells as well.

Mean T-Cell Fraction in Lung



In following immune cells:
- T cells
- Proliferative T cells
- CD8+ cytotoxic T cells
- CD4+ helper T cells,
- CD8+ effectors & central memory cells

the titer of cells are obviously higher in combo treatment group compared with other 3 groups.

Palakurthi S, et al (2019). The Combined Effect of FGFR Inhibition and PD-1 Blockade Promotes Tumor-Intrinsic Induction of Antitumor Immunity. *Cancer Immunol Res.* 2019 Sep;7(9):1457-1471

Source: Literature Review, Frost & Sullivan Analysis

China Top 10 Best-selling Oncology Drugs by Sales Revenue, 2022

- In China, the top 10 oncology drugs includes 5 biologics and 5 chemotherapy drugs.
- All the top 10 selling drugs in China are included in the NRDL.
- As of February 19th 2025, 95 types of novel small molecule oncology targeted drugs have been approved by NMPA.
- During 2018 and 2023, around one of third anti-tumor drugs approved by NMPA are small molecule oncology targeted drugs.

Rank	Product	Revenue (Million RMB)	Category
1	Bevacizumab	8,879.0	Biologics
2	Osimertinib	7,731.0	Chemical Drug
3	Trastuzumab	7,173.0	Biologics
4	Nab-paclitaxe	5,341.0	Chemical Drug
5	Anlotinib	4,504.0	Chemical Drug
6	Pertuzumab	4,272.0	Biologics
7	Rituximab	4,065.0	Biologics
8	Doxorubicin	4,013.0	Chemical Drug
9	Goserelin Acetate	3,752.1	Chemical Drug
10	Leuprorelin	3,379.4	Biologics

Source: Annual Report, Frost & Sullivan Analysis

Global Top 10 Best-selling Oncology Drugs by Sales Revenue, 2022

- Globally, the top 10 oncology drugs includes 5 biologics and 5 chemical drugs.
- As of February 19th 2025, 102 types of novel small molecule oncology targeted drugs have been approved by FDA.
- During 2018 and 2023, around one of third anti-tumor drugs approved by FDA are small molecule oncology targeted drugs.

Rank	Product	Revenue (Million RMB)	Category
1	Pembrolizumab	20,937.0	Biologics
2	Lenalidomide	9,978.0	Chemical Drug
3	Nivolumab	9,492.0	Biologics
4	Daratumumab	7,977.0	Biologics
5	Denosumab	6,101.4	Biologics
6	Ibrutinib	5,820.0	Chemical Drug
7	Osimertinib	5,444.0	Chemical Drug
8	Palbociclib	5,120.0	Chemical Drug
9	Enzalutamide	4,827.5	Chemical Drug
10	Pertuzumab	4,280.0	Biologics

Source: Annual Report, Frost & Sullivan Analysis

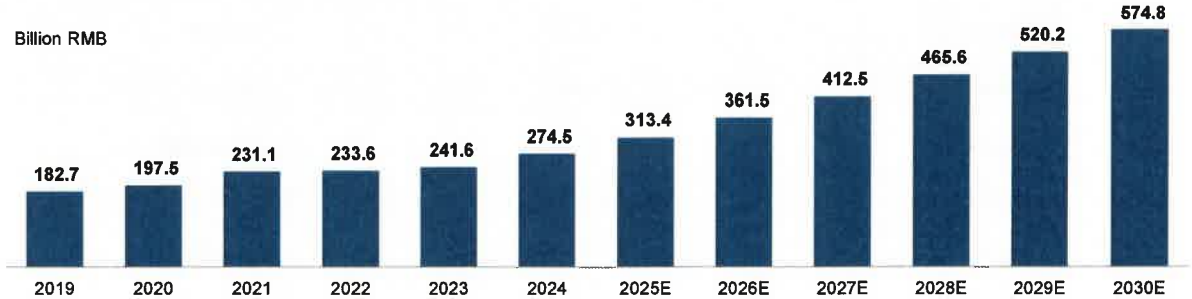
Updated

China Oncology Drug Market, 2019-2030E

- In Chinese drug market, sales of oncology products has risen steadily in the recent years. China oncology market, generating RMB274.5 billion in 2024, experienced a CAGR of 8.5% over the past 6 years.
- The ever-changing of successful innovative oncology treatments have promised a high return of pharmaceutical manufacturers. China oncology market is expected to uptrend in the following years. From 2024 to 2027, China oncology market is going to reach RMB412.5 billion at wholesale price level with CAGR of 14.5%. Forecasted data shows that China oncology market would be RMB574.8 billion in 2030, representing a CAGR of 11.7% from 2027 to 2030.
- While competition in China's oncology drug market is fierce, companies with in-house capabilities throughout the entire value chain of oncology drug development, including drug discovery, process development, clinical development, quality control and assurance and commercialization, are better positioned to capture the growth potential of this market.

China Oncology Drug Market, 2019-2030E

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



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

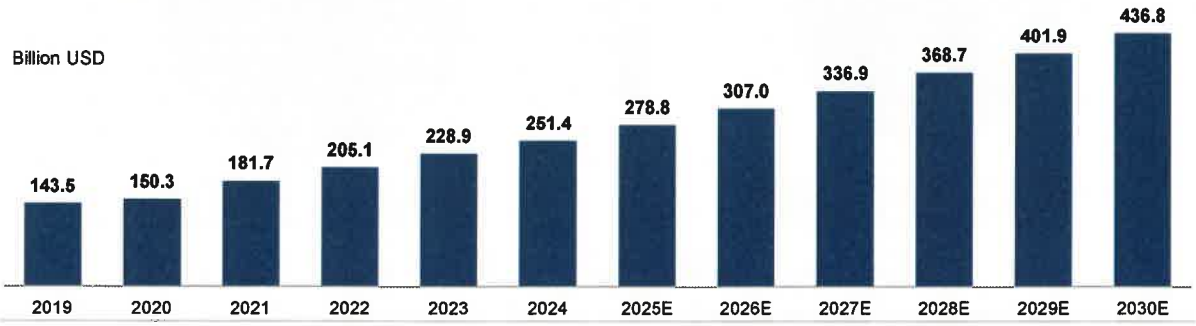
Updated

Global Oncology Drug Market, 2019-2030E

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

Global Oncology Drug Market, 2019-2030E

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

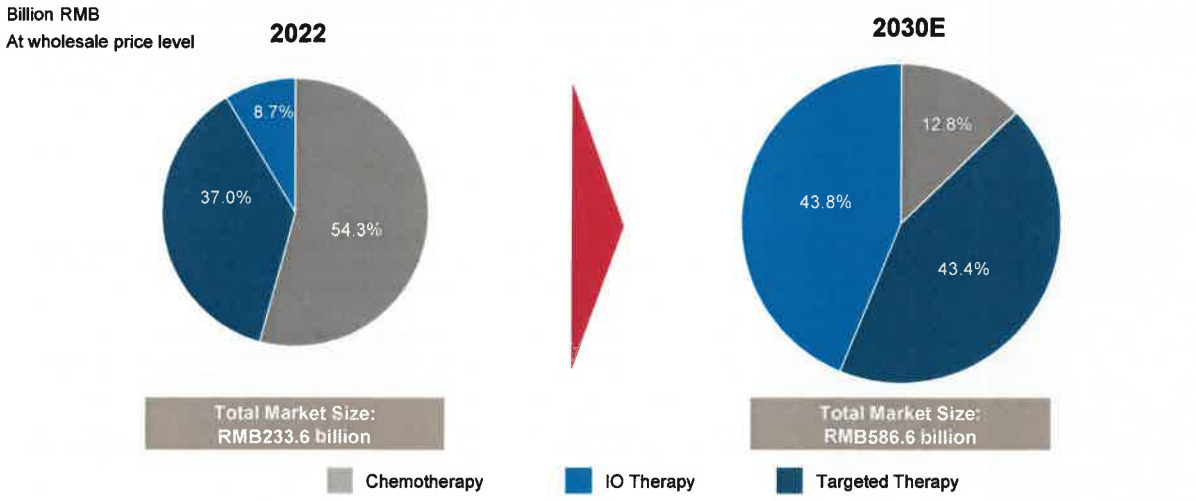


Source: Annual Reports of Listed Medical Companies, NMPA, CDE, NRDL, MOHRSS, FDA, IARC, GLOBOCAN, Frost & Sullivan Analysis

Breakdown of China Oncology Market by Therapy, 2022 and 2030E

- Currently, China oncology market is dominant by chemotherapy drugs which takes up to 54.3% of total. Targeted drugs including small-molecularly targeted drugs, biologics, are taking a proportion of 37.0%, leaving 8.7% for IO therapy in 2022.
- With reimbursement policies, new drug development and patients' increasing affordability, the targeted therapy and IO therapy would occupy most of the market by 2030. It is expected that the share of IO therapy approaches 43.8% while targeted drugs share would reach 43.4%.

Breakdown of China Oncology Market by Therapy, 2022 and 2030E



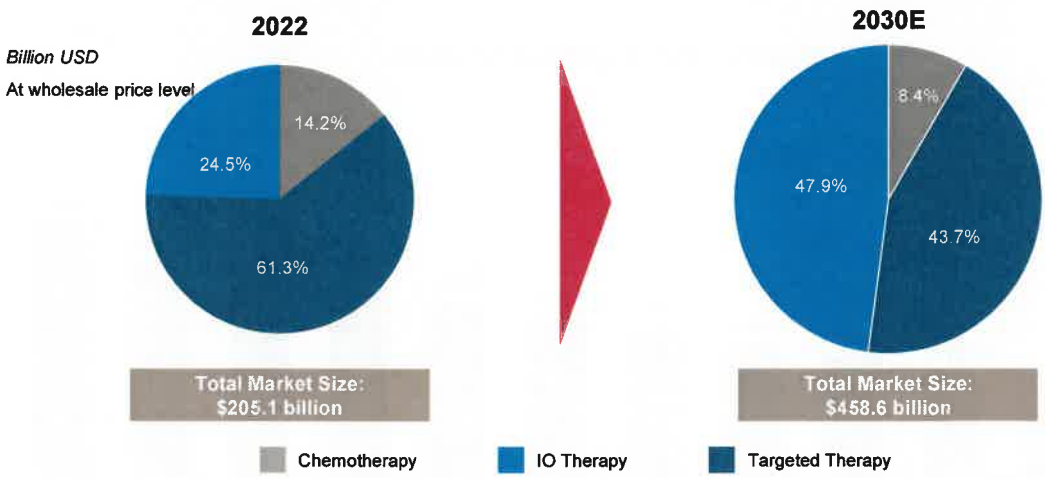
Chemotherapy includes chemical drugs, traditional Chinese medicine injections and adjuvant anti-tumor drugs.

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

Breakdown of Global Oncology Market by Therapy, 2022 and 2030E

- Currently, global oncology market is dominant by targeted therapy, which takes up to 61.3% of total market share. Chemotherapy is taking a proportion of 14.2%, the left 24.5% corresponds to IO therapy in 2022.
- In 2022, the global market for targeted therapies and immunotherapies reached a combined USD205.1 billion. The targeted therapy drug market is expected to grow to USD200.4 billion by 2030; Currently, targeted therapies and immunotherapies comprise 85.8% of the global market and are expected to comprise 91.6% by 2030.

Breakdown of Global Oncology Market by Therapy, 2022 and 2030E



Chemotherapy includes chemical drugs and adjuvant anti-tumor drugs.

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

Future Trends of China Oncology Drug Market

Increasing needs for targeted drugs	• Compared with chemotherapy, targeted drugs can provide better targeting of cancer cells and reduce damage to normal cells. In developed countries, targeted drugs have become the first-line drugs for cancer treatment. It is expected that in the future, with the improvement of medical standards and medical payment capabilities, and the discovery of more biomarkers and targets, more targeted drugs will emerge.
Inclusion of more Oncology Drugs in NRDL	• The establishment of National Healthcare Security Administration promotes the rapid progress of medical insurance, including the NRDL revision by price negotiation and dynamic adjustment, through which oncology drugs can be included in the reimbursement list in a more flexible manner, benefiting the potential patients by expanding the anti tumor drugs on the list. A total of 126 new drugs were added in 2023 NRDL, including 21 oncology drugs. It is expected that in the future, the national medical insurance directory will be dynamically adjusted to include more innovative oncology drugs every year, which will also greatly improve the paying ability of Chinese cancer patients.
Genetic and molecular testing accelerates precision medicine	• With the continuous progress of precision medicine in the field of cancer diagnosis and treatment, the definition of patient populations has gradually evolved from the original histological classification to molecular classification. Therefore, the number of patients with some specific molecular classifications is significantly smaller than those previously defined by histological classification. • On the other hand, drug research and development abilities continue to improve, and an increasing number of new drugs are designed for specific targets based on the molecular pathological mechanisms of the disease, and their effectiveness is higher than chemotherapy. With the continued approval of PCR diagnostic kits and NGS-based companion diagnostic kits, molecular testing can detect not only common mutations, but also rare mutations. • Taking the treatment of cholangiocarcinoma as an example, the molecular subtyping of cholangiocarcinoma plays an increasingly important role in selecting therapeutic drugs, establishing clinical treatment plans, and establishing individualized treatment models based on molecular subtypes.

Source: Frost & Sullivan Analysis

Future Trends of Global Oncology Drug Market

Increasing Cancer Incidence	• Global cancer incidence grew over past years, and it is expected that it to grow in the future. The total cancer incidence has reached 20.2 million globally in 2022, and is expected to further increase to 24.5 million in 2030. The increase of cancer incidence can be attribute to increasing lifespan, more aging population, and obesity. The high incidence create a demand for oncology drugs that will drive the growth of oncology drug market.
Improving Affordability	• According to WHO, nearly 1 in 6 death worldwide is due to cancer, and approximately 70% of those deaths occur in low- and middle-income countries. Managing cancer is complicated by increasing prices and insufficient benefits for patients and public health of new medicine coming to market. Thus, an improved affordability of patient is a key in pushing oncology drug market forward by alleviating the burden of cancer treatment. In many countries, the cancer reimbursement system is getting more mature, for example. Medicare Program in US and NRDL dynamic reimbursement list in China have both made efforts in realizing cancer patient reimbursement.
Investigation on Innovative Targeted Drugs	• With a deeper understanding on cancer, it is revealed that even patients with the same type of cancer exhibit different genotype or different expression level of certain proteins that are key in tumor formation pathway. These proteins can potentially serve as tumor prognostic biomarkers. Intensive researches have been done in some of the previously oriented tumor related targets, which reveals a potential of treating a wide patient population with different tumor features. Such investigations has demonstrated the importance of potential new targets that have in fulfilling unmet need of patient subgroups. Thus, the more innovative targets identified and applied in drug development, the more clinical need will be addressed, and the further the oncology market expansion.
Longer Survival of Cancer Patients	• With expanding treatment options offered to cancer patients, and especially the ones who suffer from drug resistance, the overall survival of those patients is being improved. It indicates a trend that in the future, cancer patients will live longer, revealing the need of developing oncology drugs that will potentially treat patients in later lines. Driven by this, it is expected that the oncology drug market will expand continuously.

Source: Frost & Sullivan Analysis

Overview of Cholangiocarcinoma

Symptoms, Risk Factors, Pathogenesis and Survival Rate

- Cholangiocarcinoma (CCA), also known as bile duct cancer, is a rare disease in which malignant cells form in the bile ducts, the branched tubes that connect the liver and gallbladder to the small intestine.
- Common signs of bile duct cancer include jaundice , fatigue and pain in the abdomen, and the risk factors of CCA usually point to a common role chronic biliary inflammation in CCA development.
- iCCA is sometimes misdiagnosed as Hepatocellular carcinoma (HCC). Considering this typical vascular pattern for HCC, contrast-enhanced ultrasound (CEUS) misdiagnosed as HCC a significantly higher number of ICC than CT (52% vs. 4.2%, P = 0.004) and MRI (52% vs. 9.1%, P = 0.02).

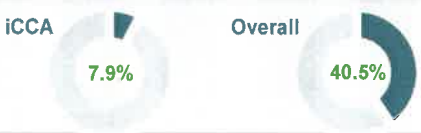
Symptoms

- Pruritus
- Painless obstructive jaundice
- Vague abdominal pain
- Anorexia
- Distended gallbladder
- Fatigue

Cholangiocarcinoma do not usually cause any symptoms in the early stage, but often result when bile ducts become blocked by the tumor.

Survival Rate

Currently, there is no direct assay for early detection of CCA. Hence, the CCA patients are normally found at the late stage of cancer with low survival rate. In the China, the five-year survival rate for iCCA is 7.9%, which is lower than the five-year survival rate of all cancer types combined at 43.7%. In the USA, the five-year survival rate for iCCA and eCCA are 9% and 11% respectively, which are lower than the five-year survival rate of all cancer types combined at 69%.



Molecular and genetic pathogenesis

- With the research goes deeper, it reveals the involvement of molecular pathways in development of CCA. In specific, the pathways include genetic mutations, chromosomal changes, aberrant epigenetic landscapes, microRNAs dysregulation, etc.
- For example, gene fusions (e.g. ROS or FGFR) resulting from chromosomal rearrangement are one of the most common events considered contributing to cancer development of CCA.

Gene alterations distribution in intrahepatic CCA

- The most commonly altered genes in intrahepatic cholangiocarcinoma (iCCA) were IDH1 (30%), ARID1A (23%) BAP1 (20%), TP53 (20%) and FGFR2 gene fusions (14%).
- FGFR Alterations (including fusion and rearrangement, point mutation, gene amplification) are observed in 25.2% of CCA patients, and FGFR fusions and rearrangements are observed in 7.4% of CCA patients.

Source: Literature Review, Frost & Sullivan Analysis

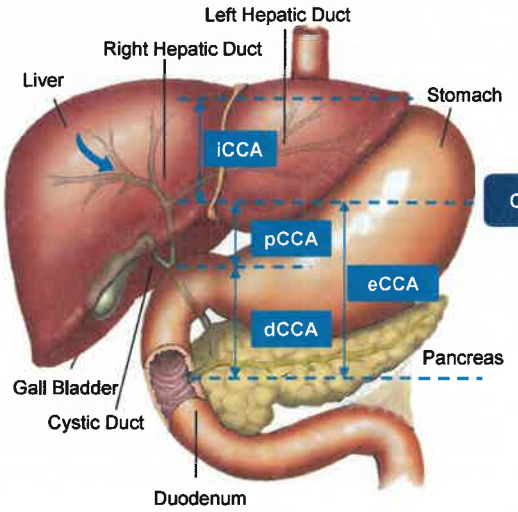
Overview of Cholangiocarcinoma (CCA)

Classification

- Cholangiocarcinomas (CCAs) are tumors that develop along the bile duct. Depending on their sites of origin, CCA can be categorized into intrahepatic (iCCA) and extrahepatic cholangiocarcinoma (eCCA), with the later further divided into perihilar and distal CCA, abbreviated as pCCA and dCCA, respectively.
- Biliary tract cancers (BTC) represent the second most common type of hepatobiliary cancer worldwide, and are typically consist of CCAs and gallbladder carcinoma (GBC).

Bile Duct Anatomy

- Liver cells make bile. Bile flows into small channels (bile canaliculi) that converge into thin tubes called ducts.
- These ducts form larger channels that flow into **left and right hepatic ducts**.
- The duct connected to the gallbladder is called **cystic duct**.
- They join to carry the bile to the first part of the small intestine called the **duodenum**.



Classification of Cholangiocarcinoma

CCA

- **Intrahepatic CCA (20%)**: Intrahepatic CCA (iCCA) occurs in the parts of the bile ducts within the liver.
- **Extrahepatic CCA (80%)**: Extrahepatic CCA (eCCA) is found outside the liver.
  - **pCCA (50%)**: Perihilar CCA (pCCA) occurs in the bile ducts just outside of the liver, from the joint of left and right hepatic duct to the site above cystic origin.
  - **dCCA (30%)**: Distal CCA (dCCA) occurs in the portion of the bile duct nearest the small intestine.

Source: Literature Review, Frost & Sullivan Analysis

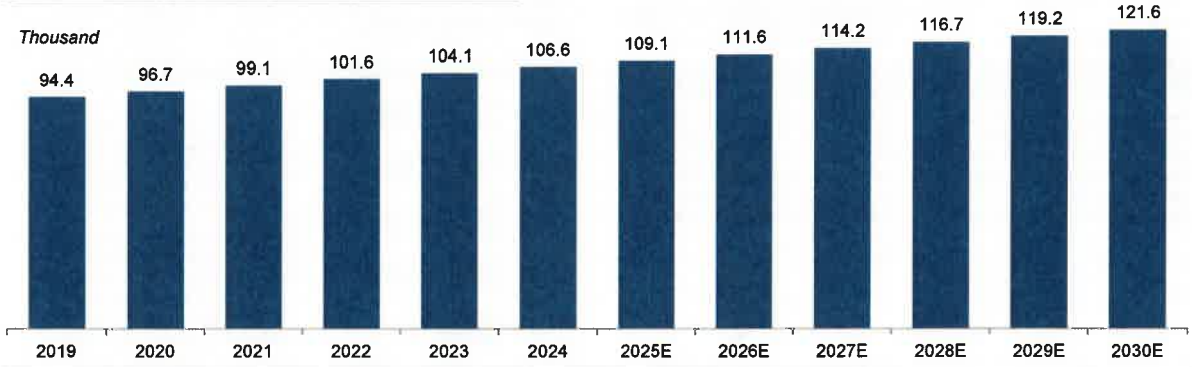
Updated

Incidence of Cholangiocarcinoma in China, 2019-2030E

- In China, new case of cholangiocarcinoma reached 106.6 thousand in 2024 at a CAGR of 2.5% from 2019. It is projected to further increase to 114.2 thousand in 2027, representing a CAGR of 2.4% from 2024. It is estimated that the incidence would achieve 121.6 thousand in 2030, representing a CAGR of 2.2% from 2026 to 2030.

Incidence of Cholangiocarcinoma in China, 2019-2030E

Period	CAGR
2019-2024	2.5%
2024-2027E	2.4%
2027E-2030E	2.2%



Source: NCCR, Frost & Sullivan Analysis

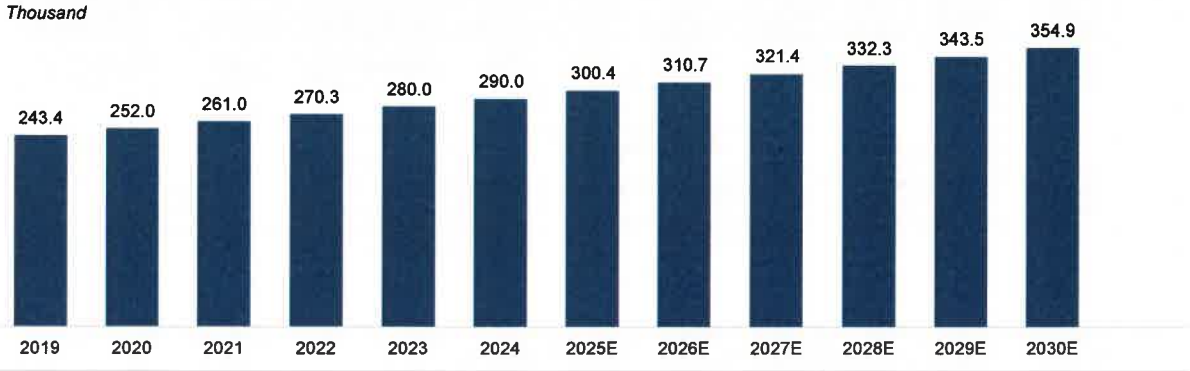
Updated

Global Incidence of Cholangiocarcinoma, 2018-2030E

- Incidence number of CCA around the world increased from 243.4 thousand to 290.0 thousand in 2019 and 2024. The number is expected to grow to 321.4 thousand in 2027 at a CAGR of 3.5% from 2024 to 2027. The number is expected to grow to 354.9 thousand in 2030, at a CAGR of 3.4%.

Global Incidence of Cholangiocarcinoma, 2018-2030E

Period	CAGR
2019-2024	3.6%
2024-2027E	3.5%
2027E-2030E	3.4%



Source: IARC, Frost & Sullivan Analysis

Diagnosis Paradigm of CCA in China

- There are four main types of examination method for the diagnosis of cholangiocarcinoma, including medical examination, laboratory test, medical and pathology test, among which pathology test is considered the golden standard for diagnosing CCA.
- For ICC, genetic tests including FISH testing the positivity of FGFR2 rearrangement and IDH1/2 gene sequencing are recommended to see whether patients are qualified for targeted therapy, revealing an need to develop companion diagnostic for promising targeted therapies.

	Medical Examination	Laboratory Tests	Medical Imaging	Pathology Test
Overview	• Examines one's body by looking, feeling and listening any abnormalities with regard to the disease of interest • A routine test done as one of the first approaches to detect cancer.	• Measures levels of certain substances in blood, urine and other body fluids. • Done to help identify abnormalities that can be caused by cancer.	• Utilizes imaging techniques to create pictures of the interior of the body. • It allows doctor to examine one's bones and internal organs to detect the presence of tumor.	• The test process of biopsy or cytology specimen under microscope or through other procedure. • Crucial to getting a precise diagnosis

Inclusion (CCA specific)	• Medical history inquiry
	• Physical examination (inspection; palpation; percussion; auscultation)
		• Blood Test:
		  • Liver function test
		  • Tumor marker test
			Imaging test can be classified into invasive and non-invasive approaches.
			• Non-invasive: CT, MRI, PET-CT, ultrasound, and MRCP*.
			• Invasive: ERCP, PTC and laparoscopy
				• Microscopic examination
				• Immunohistochemistry (IHC)
				• Molecular testing
				  • DNA sequencing
				  • FISH*

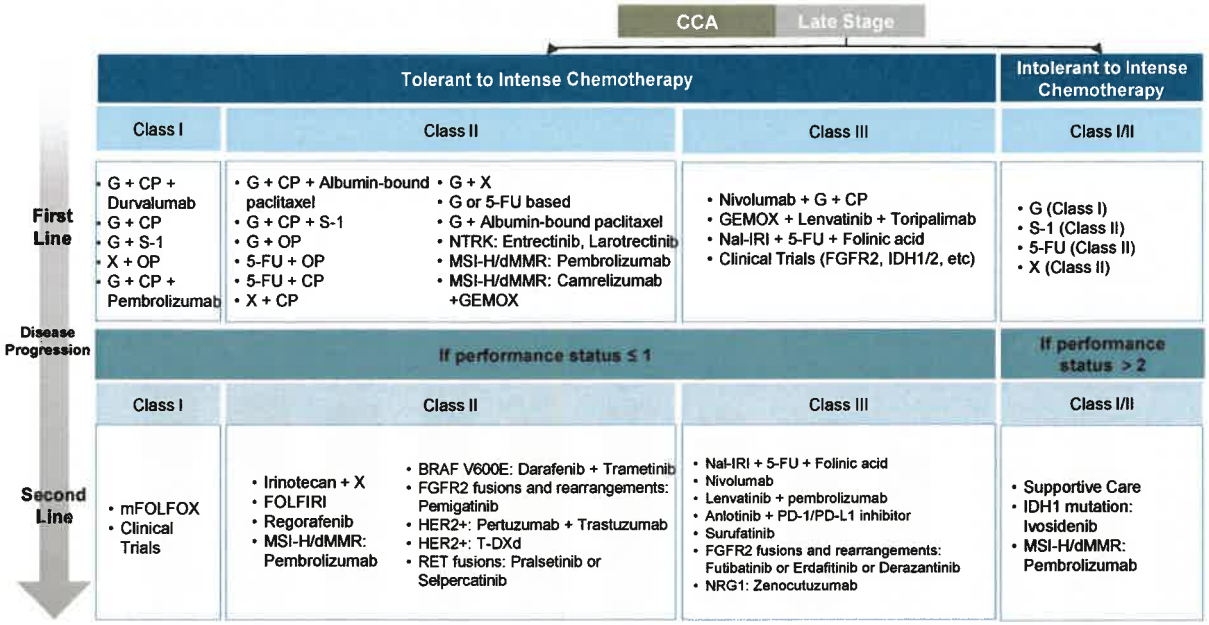
Specific Items	• Review of overall health • Signs of jaundice (skin / eyes) • Tenderness, existence of lumps / endema at abdominal region	• Liver function indicators: bilirubin, albumin and liver enzymes (alkaline phosphatase, AST, ALT and GGT) • CCA tumor markers: CEA, CA 19-9.	• CT, MRI and MRCP (to detect the presence of a bile duct blockage or tumor) • ERCP (to take image while obtaining tissue or fluid samples for later pathological evaluation)	• Microscopic examination: samples of tissues and cells obtained from the bile duct are evaluated with microscope to assess tumor burden • IHC and molecular testing: further confirm or supplement the diagnostic result
Clinical Implications	• Symptoms are not usually apparent in the early stages. • Jaundice and abdominal pain developed during later stage of CCA are common in many cancers.	• Biomarkers including CEA and CA19-9 can be used as initial screening approach for high-risk group, but their specificity and sensitivity await improvement.	• Ultrasound is used as initial screening approach for the high-risk. • CT, MRI and MRCP are recommended for determining the CCA staging. • ERCP is the primary option to collect sample for pathology tests.	• IHC is recommended when pathological differentiation is difficult. IHC and molecular testing can serve as CDx for targeted cancer therapy. • For ICC especially, FISH testing for FGFR2 rearrangement positivity and IDH1/2 gene sequencing are recommended.

**Note: CT - computerized tomography, MRI - magnetic resonance imaging, PET - positron emission tomography, ERCP - endoscopic retrograde cholangiopancreatography, MRCP - Magnetic resonance cholangiopancreatography, PTC - Percutaneous transhepatic cholangiography, IHC – Immunohistochemistry, FISH - Fluorescent in situ hybridization, CDx = Companion Diagnostic*

Source: CSCO, Frost & Sullivan Analysis

Treatment Paradigm of CCA in China

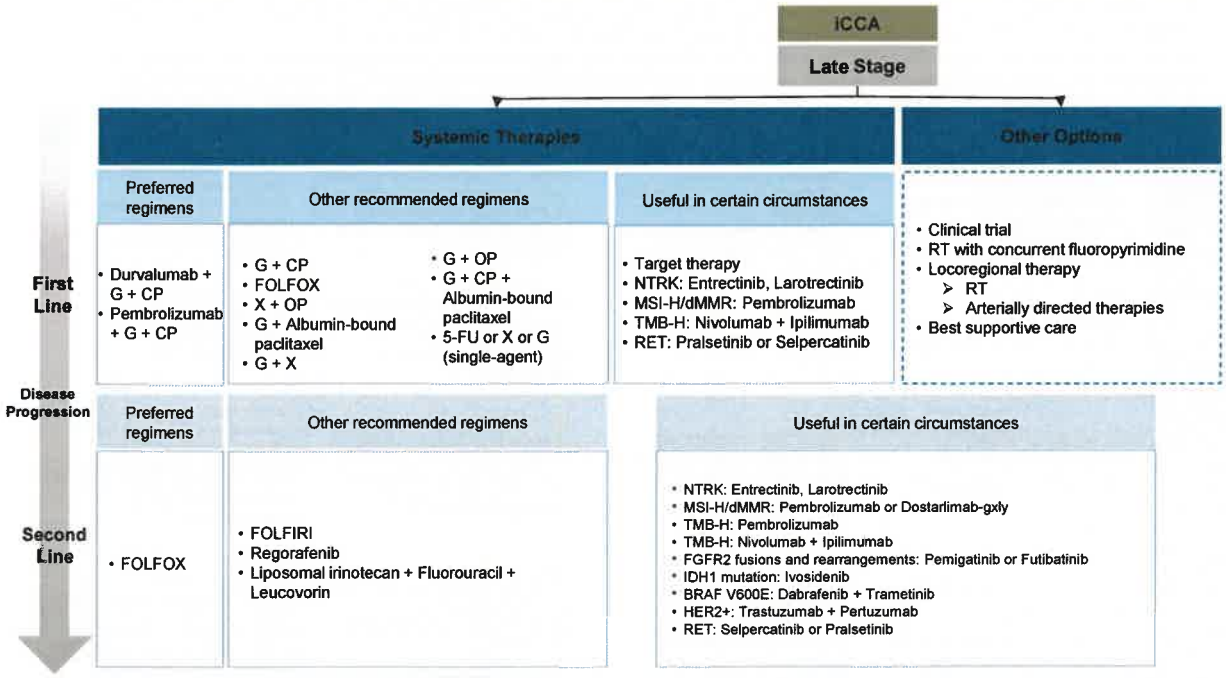
Surgery and liver transplantation are the primary treatment options for eligible CCA patients



Note: G = Gemcitabine; CP = Cisplatin; S-1 = Tegafur/Gimeracil/Oteracil; OP = Oxaliplatin, X = Capecitabine; 5-FU = 5-Fluorouracil; mFOLFOX = Oxaliplatin + 5-Fluorouracil; FOLFIRI = Folinic acid, Fluorouracil and Irinotecan; T-DXd = Trastuzumab Deruxtecan

Source: CSCO2023, Frost & Sullivan Analysis

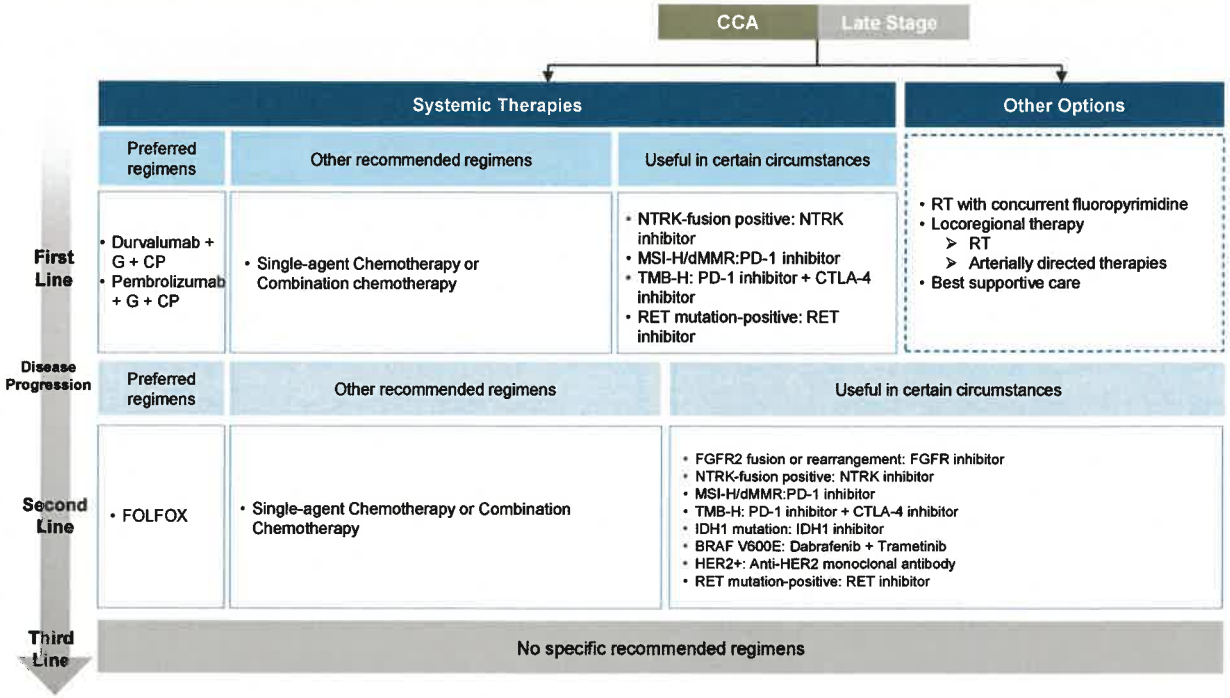
Treatment Paradigm of iCCA in the US



Note: G = Gemcitabine; CP = Cisplatin; OP = Oxaliplatin, X = Capecitabine; 5-FU = 5-Fluorouracil; FOLFOX = Oxaliplatin + 5-Fluorouracil; FOLFIRI = Folinic acid, Fluorouracil and Irinotecan; T-DXd = Trastuzumab Deruxtecan

Source: NCCN2023 V3, Frost & Sullivan Analysis

Treatment Paradigm of iCCA in the US and China



Note: G = Gemcitabine; CP = Cisplatin; FOLFOX = Oxaliplatin + 5-Fluorouracil
Note: Around 62% of patients with advanced unresectable or metastatic CCA proceed to second-line treatment, and 32% receive at least third-line therapy.

Source: NCCN2023 V3, CSCO2023, Frost & Sullivan Analysis

Pain Points of the Treatment of CCA

Related to Disease:

Delay and Difficulty in Diagnosis

- There are no obvious clinical symptoms in early stage of CCA, and CCA is relatively aggressive with high tendency of invasion and metastasis to other tissue. Therefore, most patients with iCCA have lost the opportunity for surgical treatment such as radical resection, as they are not diagnosed before late stage of disease.
- Moreover, there are currently not yet any precise biomarkers for diagnosis of early stage of CCA, which limit the early treatments and does harm to patient prognosis.

High Disease Heterogeneity

- The molecular and cellular mechanism of CCA are diverse (heterogeneity), as the origin of cancer cell are various, thereby lead to different symptoms and disease stages of CCA.
- In addition, gene alteration among different subtypes of CCA are various. For instance, IDH1 mutation and FGFR2 fusion/ rearrangement positive CCA patients subject to different conditions and therefore should not be treated uniformly. Such disease heterogeneity poses a challenge for developing treatment of drug diseases.

Related to Treatment:

Recurrence Rate

- High recurrence rate is one of major reason of the failure of CCA treatment, affect quality of patients' lives.
- For early stage patients of CCA, the current early treatment is mainly surgery combined with chemotherapy and radiotherapy, however, the postoperative recurrence rate is high, with poor survival rate. Additionally, if patient is not able to obtain adequate treatment in time, CCA will be highly possible to progress soon, leading to heavy disease burden. Therefore, there is an increasing demand for targeted therapy against FGFR and other oncogenic pathways that offer improved therapeutic efficacy.

Limited Treatment Options

- For patients with advanced CCA, surgical treatments are not available due to cancer invasion. In placement, as the first-line recommended treatment for advanced CCA, Gemcitabine+cisplatin lead to heavy systemic adverse effects and limited efficacy. Highly specific treatments are required urgently due to the limited options of CCA treatment.
- Although there is already a FGFR inhibitor (Pemigatinib) targeting on FGFR2 fusion/ rearrangement inhibitor approved by FDA, the problem of drug resistance is unavoidable. According to a research paper published on Cancer Treat Reviews in 2023, approximately 95% of CCA patients may eventually develop acquired drug resistance after receiving treatment of an FGFR inhibitor.Thus, more CCA treatments are required.

Source: Frost & Sullivan Analysis

Competitive Landscape of Small Molecular Targeted Drug on Cholangiocarcinoma Approved by NMPA

Drug Name	Brand Name	Target	Company	Indications	Cost	Approval Date
Pemigatinib	Pemazyre®	FGFR 1/2/3	Innovent/Incyte Corporation	Previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement	RMB 66547 per 21-day treatment cycle	2022/3/29

As of Feb 19th, 2025

Source: NMPA, Frost & Sullivan Analysis

Competitive Landscape of Small Molecular Targeted Drug on Cholangiocarcinoma Approved by FDA

Drug Name	Brand Name	Target	Company	Indications	Cost	Approval Date
Futibatinib	Lytgobi®	FGFR1/2/3/4	Taiho Pharmaceutical	Previously treated, unresectable, locally advanced or metastatic intrahepatic cholangiocarcinoma harboring fibroblast growth factor receptor 2 (FGFR2) gene fusions or other rearrangements	USD $27,492 per month	2022/9/30
Infigratinib	Truseltiq®	FGFR 1/2/3	BridgeBio Pharma / Helsinn Group	Previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement	/	2021/5/28
Pemigatinib	Pemazyre®	FGFR 1/2/3	Incyte Corporation	Previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement	USD $19,759 per 21-day treatment cycle	2020/4/20
Ivosidenib	Tibsovo®	IDH1	Servier Pharmaceuticals	Locally advanced or metastatic cholangiocarcinoma who have been previously treated	/	2018/7/20 (2021/8/25 approved for the indication of CCA)

Note: Approval date: First approval date
Based on business plan considerations, Helsinn Group announced the withdrawal of its application for marketing Infigratinib in the United States.
As of Feb 19th, 2025

Source: FDA, Frost & Sullivan Analysis

Competitive Landscape of China Small Molecular Targeted Drug on Cholangiocarcinoma in Pipeline (1/2)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
TQB3454	IDH1	Tai-tianqing Pharmaceutical Co., Ltd	Phase 3	Advanced CCA	2023/8/2
Brigimadlin (BI 907828)	MDM2	Boehringer Ingelheim	Phase 2	CCA, Pancreatic cancer, Bladder cancer, Lung cancer	2023/11/9
Tinengotinib	**FGFR, VEGFR, JAK2, Aurora A/B**	**TransThera**	**Phase 2***	**Advanced or metastatic CCA**	**2023/9/22**
HTMC0435	PARP1/2	Huilun Life Technology Co., Ltd	Phase 2	Advanced BTC	2023/3/6
HMPL-453	FGFR1/2/3	Hutchison Medipharma Ltd	Phase 2	Advanced iCCA	2020/5/22
ICP-192	FGFR2	Tiancheng Pharmaceutical Technology Co., Ltd	Phase 2	Previously treated, unresectable, locally advanced or metastatic iCCA	2022/8/18
Pyrotinib	EGFR, HER2, HER4	Hengrui Medicine Co.,Ltd.	Phase 2	Advanced BTC	2021/4/29
E7090	FGFR1/2/3	Eisai Inc.	Phase 2	advanced or metastatic CCA	2020/8/14
Anlotinib	VEGFR1/2/3, FGFR1/2/3, KIT, PDGFR	Chia Tai Tianqing Pharmaceutical Group Co., Ltd.	Phase 2	iCCA; eCCA; GBC; GEJ adenocarcinoma; GEP-NENs; UC	2020/3/20
Erdafitinib	FGFR1/2/3/4, CSF1R, KIT, RET, VEGFR, PDGFR	Janssen Biotech	Phase 2	NSCLC, UC, CCA	2017/7/5

Note: First posted date: 首次公示日期;
*Note: According to CDE, it still shows Tinengotinib for CCA is in phase 2, we refer to that.
HCC= Hepatocellular carcinoma; iCCA= intrahepatic cholangiocarcinoma; eCCA=extrahepatic cholangiocarcinoma; GBC=gallbladder cancer; GEJ adenocarcinoma=Gastroesophageal Junction Adenocarcinoma; GEP-NENs=gastroentero-pancreatic neuroendocrine neoplasms; CRC= Colorectal cancer; CRPC= Castrate-resistant prostate cancer; UC=urothelial carcinoma; TNBC= Triple-negative breast cancer;
As of Feb 19th, 2025

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of China Small Molecular Targeted Drug on Cholangiocarcinoma in Pipeline (2/2)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
SPH5030	HER2	Shanghai Pharmaceuticals Holding Co., Ltd.	Phase 2	Advanced or metastatic BTC	2024/4/26
GFH018	TGFBR1	GenFleet Therapeutics Co., Ltd	Phase 1/2	HCC, CCA, GBC and other solid tumor	2022/7/1
KBP-2205	PARP	Keythera Biopharmaceutical Co., Ltd	Phase 1	Advanced CCA and other solid tumor	2024/4/24
AB-218	IDH1	Baoyuan Biopharmaceutical Technology	Phase 1	Advanced CCA and other solid tumor	2023/3/2
AL8326	AURKB, VEGFR, FGFR	Edcheng	Phase 1	Advanced CCA and other solid tumor	2022/6/1
ZSP1241	FGFR4	Zhongsheng Pharmaceutical Co.,Ltd.	Phase 1	CCA, liver cancer, gastric cancer, esophageal cancer, colorectal cancer and other advanced solid tumor	2018/11/09
EOC317	VEGFR2, FGFR	Taizhou EOC Pharma Co., Ltd.	Phase 1	CCA, bladder cancer, gastric cancer, breast cancer and other solid tumor	2018/04/09
AST2169	KRAS G12D	Allist Pharmaceuticals Co.,Ltd.	Phase 1	Advanced CCA and other solid tumor	2024/4/2
CG-7321	Not disclosure	Cynogen Pharmaceutical Technology Co., Ltd	Phase 1	Advanced CCA and other solid tumor	2024/3/5
ABSK121-NX	FGFR1/2/3	Abbisko Therapeutics Co, Ltd	Phase 1	Urothelial Carcinoma, Intrahepatic Cholangiocarcinoma and Other Solid Tumor	2023/4/19
FH-2001	VEGFR, FGFR	Fosun Pharmaceutical Development Co.,Ltd.	Phase 1	Advanced CCA and other solid tumor	2022/2/22
JSI-1187	MAPK1, MAPK3	JS InnoPharm Limited	Phase 1	Advanced CCA and other solid tumor	2022/2/8

As of Feb 19th, 2025

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of China FGFR Inhibitor on Cholangiocarcinoma in Pipeline

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
ICP-192	FGFR2	Tiancheng Pharmaceutical Technology Co., Ltd	Phase 2	Previously treated, unresectable, locally advanced or metastatic iCCA	2022-08-18
E7090	FGFR1/2/3	Eisai Inc.	Phase 2	advanced or metastatic CCA	2020-08-14
HMPL-453	FGFR1/2/3	Hutchison Medipharma Ltd	Phase 2	Advanced iCCA	2020-05-22
ABSK121-NX	FGFR1/2/3	Abbisko Therapeutics Co, Ltd	Phase 1	Urothelial Carcinoma, Intrahepatic Cholangiocarcinoma and Other Solid Tumor	2023-04-19
ZSP1241	FGFR4	Guangdong Zhongsheng Pharmaceutical Co.,Ltd.	Phase 1	Solid Tumor	2018-11-09

As of Feb 19th, 2025

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of China FGFR Inhibitors on Cholangiocarcinoma with Prior FGFR Inhibitor Treatment in Pipeline

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
Tinengotinib	**FGFR, VEGFR, JAK2, Aurora A/B**	**TransThera**	**Phase 2***	**FGFR-altered Advanced or Metastatic CCA with Prior Chemotherapy or FGFR Inhibitor Treatment**	**2023-09-22**
ABSK121-NX	FGFR1/2/3	Abbisko Therapeutics Co, Ltd	Phase 1	Urothelial Carcinoma, Intrahepatic Cholangiocarcinoma and Other Solid Tumor	2023-04-19

***Note: According to CDE, it still shows Tinengotinib for CCA is in phase 2, we refer to that.**
As of Feb 19th, 2025

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of Global Small Molecular Targeted Drug on Cholangiocarcinoma in Pipeline (1/3)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
Tinengotinib	**FGFR, VEGFR, JAK2, Aurora A/B**	**TransThera**	**Phase 3**	**Cholangiocarcinoma**	**2023/7/17**
TQB3454	IDH1	Chia Tai Tianqing Pharmaceutical Group Co., Ltd.	Phase 3	Biliary Carcinoma	2023/8/14
Anlotinib	PDGFR, KIT, VEGFR, FGFR, RET	Chia Tai Tianqing Pharmaceutical Group Co., Ltd.	Phase 3	Advanced Biliary Cancer	2021/3/22
Varlitinib	HER2/4, EGFR	Aslan Pharmaceuticals	Phase 2/3	Biliary Tract Cancer	2017/3/28
Neratinib	HER2/4, EGFR	Convalife Co., Ltd.	Phase 2	Biliary Tract Cancer	2024-07-25
Olaparib	PARP1/2/3	AstraZeneca	Phase 2	Cholangiocarcinoma	2024-06-04
SPH5030	HER2	Shanghai Pharmaceuticals Holding Co., Ltd	Phase 2	Biliary Tract Cancer	2024-05-30
3D185	FGFR1/2/3	3D Medicines (Beijing) Co., Ltd.	Phase 2	Cholangiocarcinoma	2021/9/10
ABC294640	SPHK2	RedHill Biopharma Limited	Phase 2	Cholangiocarcinoma	2017/12/19
Apatinib	VEGFR2	HengRui Medicine Co., Ltd.	Phase 2	Intrahepatic Cholangiocarcinoma	2018/5/11
BI 907828	MDM2	Boehringer Ingelheim	Phase 2	Pancreatic Neoplasms, Solid Tumors, Biliary Tract Cancer, Lung Neoplasms, Bladder Cancer	2022/8/23

Only clinical stage above phase 2 are include.
As of Feb 19th, 2025

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Competitive Landscape of Global Small Molecular Targeted Drug on Cholangiocarcinoma in Pipeline (2/3)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
Derazantinib	CSF1R, VEGFR2, FGFR1/2/3	Basilea Pharmaceutical	Phase 2	Intrahepatic Cholangiocarcinoma	2017/7/26
E7090	FGFR1/2/3	Eisai Co., Ltd.	Phase 2	Cholangiocarcinoma	2020/1/23
Entinostat	HDAC	Syndax Pharmaceuticals / Edding Pharma	Phase 2	Cholangiocarcinoma	2017/8/15
GSK1120212	MAP2K1/2	GlaxoSmithKline	Phase 2	Cholangiocarcinoma	2013/9/17
ICP-192	FGFR	InnoCare Pharma Tech Co., Ltd.	Phase 2	Intrahepatic Cholangiocarcinoma	2023/1/10
HMPL-453	FGFR1/2/3	Hutchmed	Phase 2	Intrahepatic Cholangiocarcinoma	2020/4/20
Lenvatinib	PDGFA, KIT, RET, VEGFR, FGFR	Eisai Co., Ltd.	Phase 2	Biliary Tract Cancer	2015/10/19
Merestinib	MET, NTRK, RON, AXL, ROS1, PDGFRA, FLT3, TEK, DDR, MERTK, TYRO3, MNK	Eli Lilly	Phase 2	Biliary Tract Cancer	2016/3/17
Niraparib	PARP1/2	GlaxoSmithKline	Phase 2	Mesothelioma, Uveal Melanoma, Renal Cell Carcinoma, Cholangiocarcinoma	2017/7/2
Erdafitinib	FGFR1/2/3/4	Janssen Biotech	Phase 2	CCA; UC; Non-Hodgkin Lymphoma	2016-03-04
Regorafenib	BRAF, DDR2, MAPK11, RET, NTRK1, FRK, ABL1, TEK, PDGFR, RAF1, KIT, VEGFR, EPHA2, FGFR	Bayer	Phase 2	Biliary Tract Cancer	2014/4/16

Only clinical stage above phase 2 are include.
As of Feb 19th, 2025

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Competitive Landscape of Global Small Molecular Targeted Drug on Cholangiocarcinoma in Pipeline (3/3)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
SHR1258	HER2/4, EGFR	HengRui Medicine Co., Ltd.	Phase 2	Biliary Tract Cancer	2020/10/1
Sitravatinib	TYRO3, AXL, MERTK, VEGFR2, KIT, RET, PDGFR, MET	Seoul National University Hospital, BeiGene	Phase 2	Biliary Tract Cancer	2021/1/27
Surufatinib	FGFR1, CSF1R, VEGFR1/2/3	Hutchison Medipharma Limited	Phase 2	Biliary Tract Cancer	2016/11/17
Quemliclustat	CD73	Arcus Biosciences	Phase 2	Biliary Tract Cancer	2023/9/21
CX-4945	CK2	Senhwa Biosciences, Inc.	Phase 1/2	Cholangiocarcinoma	2014/5/1
Fadraciclib	CDK2/9	Cyclacel Pharmaceuticals, Inc.	Phase 1/2	Biliary Tract Cancer	2021/7/30
FT 2102	IDH1	Novo Nordisk	Phase 1/2	Cholangiocarcinoma	2018/9/26
MEK162	MAP2K1, MAP2K2	Array BioPharma	Phase 1/2	Biliary Tract Cancer	2013/4/10
RLY-4008	FGFR2	Relay Therapeutics, Inc.	Phase 1/2	Cholangiocarcinoma	2020/8/25
TNG462	PRMT5	Tango Therapeutics, Inc.	Phase 1/2	Cholangiocarcinoma	2023/2/17
Tucatinib	HER2	Seagen	Phase 1/2	Cholangiocarcinoma	2020/6/12

Only clinical stage above phase 2 are include.
As of Feb 19th, 2025

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Competitive Landscape of Global FGFR Inhibitor on Cholangiocarcinoma in Pipeline

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
E7090	FGFR1/2/3	Eisai Co., Ltd.	Phase 2	Cholangiocarcinoma	2020/1/23
ICP-192	FGFR1/2/3/4	InnoCare Pharma Tech Co., Ltd.	Phase 2	Intrahepatic Cholangiocarcinoma	2023/1/10
HMPL-453	FGFR1/2/3	Hutchison Medipharma Limited	Phase 2	Intrahepatic Cholangiocarcinoma	2020/4/20
RLY-4008	FGFR2	Relay Therapeutics, Inc.	Phase 1/2	Unresectable or Metastatic iCCA and Other Advanced Solid Tumors	2020/8/25
TYRA-200	FGFR1/2/3	Tyra Biosciences, Inc.	Phase 1	Unresectable Locally Advanced or Metastatic iCCA and Other Advanced Solid Tumors with Activating FGFR2 Gene Alterations	2023/12/7
KIN3248	FGFR1/2/3/4	Kinnate Biopharma	Phase 1	Urothelial Carcinoma, Intrahepatic Cholangiocarcinoma and Other Solid Tumor	2022/2/16
ABSK121-NX	FGFR1/2/3	Abbisko Therapeutics Co, Ltd	Phase 1	Urothelial Carcinoma, Intrahepatic Cholangiocarcinoma and Other Solid Tumor	2022/11/25

As of Feb 19th, 2025

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Competitive Landscape of Global FGFR Inhibitors on Cholangiocarcinoma with Prior FGFR Inhibitor Treatment in Pipeline

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
Tinengotinib	**FGFR, VEGFR, JAK2, Aurora A/B**	**TransThera**	**Phase 3**	**FGFR-altered Advanced or Metastatic CCA with Prior Chemotherapy or FGFR Inhibitor Treatment**	**2023-07-17**
RLY-4008	FGFR2	Relay Therapeutics, Inc.	Phase1/2	Unresectable or Metastatic iCCA and Other Advanced Solid Tumors	2020-08-25
TYRA-200	FGFR1/2/3	Tyra Biosciences, Inc.	Phase 1	Unresectable Locally Advanced or Metastatic iCCA and Other Advanced Solid Tumors with Activating FGFR2 Gene Alterations	2023-12-07
ABSK121-NX	FGFR1/2/3	Abbisko Therapeutics Co, Ltd	Phase 1	Urothelial Carcinoma, Intrahepatic Cholangiocarcinoma and Other Solid Tumor	2022-11-25

As of Feb 19th, 2025

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Competitive Landscape of China/Global FGFR Inhibitors on Cholangiocarcinoma with Prior FGFR Inhibitor Treatment in Pipeline

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date	Study Location
Tinengotinib	**FGFR, VEGFR, JAK2, Aurora A/B**	**TransThera**	**Phase 3**	**FGFR-altered Advanced or Metastatic CCA with Prior Chemotherapy or FGFR Inhibitor Treatment**	**2023-07-17**	**The U.S., South Korea, Taiwan, United Kingdom and eight countries in EU**
			Phase 2*	**FGFR-altered Advanced or Metastatic CCA with Prior Chemotherapy or FGFR Inhibitor Treatment**	**2023/9/22**	**China**
RLY-4008	FGFR2	Relay Therapeutics, Inc.	Phase1/2	Unresectable or Metastatic iCCA and Other Advanced Solid Tumors	2020-08-25	the US Australia France Germany and other countries and regions
TYRA-200	FGFR1/2/3	Tyra Biosciences, Inc.	Phase 1	Unresectable Locally Advanced or Metastatic iCCA and Other Advanced Solid Tumors with Activating FGFR2 Gene Alterations	2023-12-07	the US
ABSK121-NX	FGFR1/2/3	Abbisko Therapeutics Co, Ltd	Phase 1	Urothelial Carcinoma, Intrahepatic Cholangiocarcinoma and Other Solid Tumor	2022-11-25	the US
				Urothelial Carcinoma, Intrahepatic Cholangiocarcinoma and Other Solid Tumor	2023-04-19	China

Note: According to CDE, it still shows Tinengotinib for CCA is in phase 2, we refer to that.
As of Feb 19th, 2025

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

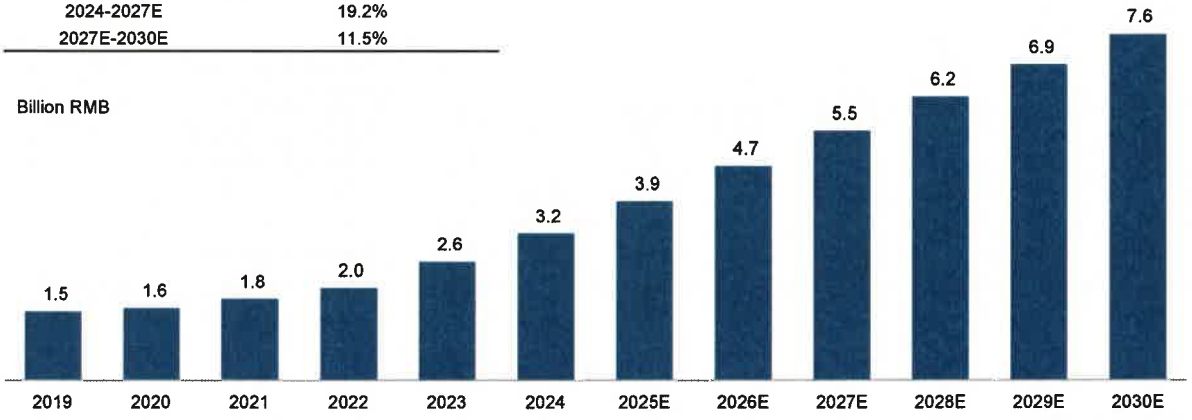
Updated

Historical and Forecasted of China CCA Drug Market Size, 2019-2030E

- China's CCA drug market has grown from RMB1.5 billion in 2019 to RMB3.2 billion in 2024 at a CAGR of 16.4%, and expected to increase to RMB5.5 billion in 2027 at a CAGR of 19.2% from 2024 and RMB7.6 billion in 2030 at a CAGR of 11.5% from 2027.

Historical and Forecasted of China CCA Drug Market Size, 2019-2030E

Period	CAGR
2019-2024	16.4%
2024-2027E	19.2%
2027E-2030E	11.5%



Source: Frost & Sullivan Analysis

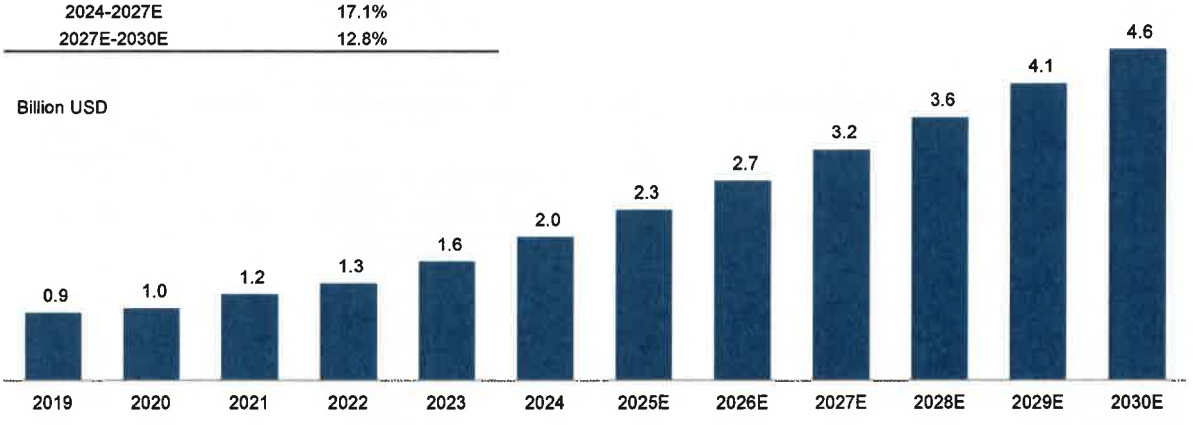
Updated

Historical and Forecasted of Global CCA Drug Market Size, 2019-2030E

Global CCA drug market has grown from USD0.9 billion in 2019 to USD2.0 billion in 2024 at a CAGR of 16.2%, and expected to increase to USD3.2 billion in 2027 at a CAGR of 17.1% from 2024 and USD4.6 billion in 2030 at a CAGR of 12.8% from 2027.

Historical and Forecasted of Global CCA Drug Market Size, 2019-2030E

Period	CAGR
2019-2024	16.2%
2024-2027E	17.1%
2027E-2030E	12.8%



Source: Frost & Sullivan Analysis

Future Trends for CCA Treatment Market

Technologies to overcome drug resistance challenges	• CCA is characterized by low incidence, low early diagnosis rates, a median survival period of less than 1 year, limited treatment options, and extremely poor prognosis, presenting significant challenges in the medical field. Although most patients with FGFR mutation-positive CCA benefit from novel FGFR inhibitors, the majority eventually develop resistance, leading to disease progression and ultimately mortality. With advancing research on FGFR inhibitor treatments for CCA and a deeper understanding of resistance mechanisms, new therapeutic strategies are emerging to address drug resistance. For instance, efforts are underway to combine FGFR inhibitors with drugs of different mechanisms of action to overcome resistance issues.
Advancement in the line of therapy for small molecule targeted drugs	• The primary treatment for CCA mainly includes chemotherapy and immune checkpoint inhibitors, with targeted drugs like FGFR, IDH, and BRAF V600 inhibitors used in later stages. These small molecule targeted drugs, known for their specificity, safety, and compliance, are becoming more common, especially with drugs like pemigatinib. Their effectiveness and ability to meet unmet needs may push them to earlier treatment lines, as seen with osimertinib in NSCLC. FGFR inhibitors, in particular, are expected to see increased demand and a similar shift towards earlier use.
Precision diagnosis and targeted therapy	• The deep anatomical location of CCA, along with its strong tumoral infiltration and invasive nature, makes surgical resection alone insufficient for satisfactory outcomes. Increasingly, researchers recognize the importance of considering the biological characteristics of tumors in CCA treatment. With the development of genetic testing technologies, there is a deeper understanding of the molecular and biological characteristics of different subtypes of cholangiocarcinoma, bringing hope to its treatment with an increasing number of molecularly targeted drugs. Precision medicine, utilizing cutting-edge medical technologies and omics approaches such as proteomics and genomics, offers precise diagnoses at the molecular level, potentially providing new treatment paradigms for intrahepatic cholangiocarcinoma. For example, the "Expert Consensus on the Pathological Diagnosis of Intrahepatic CCA (2022)" includes IDH1 inhibitor ivosidenib and RET inhibitor pralsetinib as targeted therapies corresponding to specific immunotherapeutic biomarkers in its treatment recommendations, also advising genetic testing for IDH1, RET, and other genes in patients with intrahepatic cholangiocarcinoma. Precision diagnosis and targeted therapy are poised to become significant trends in the treatment of cholangiocarcinoma.

Source: Frost & Sullivan Analysis

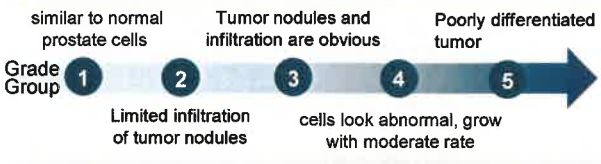
Overview of Prostate Cancers

- Prostate cancer is an epithelial malignant tumor occurs in the prostate. It is the most common malignant tumor of the male genitourinary system, and it mostly occurs in people over 65 years of age.
- Prostate cancer progresses slowly and is usually asymptomatic in the early stages. Once metastasis or migration, the condition becomes more serious, which brings heavy disease burden to the patient's life.

Risk Factors of PC

- The peak age of prostate cancer mostly onset is 65-80 years old.
- If 2 or more immediate family members suffer from prostate cancer, the risk of developing prostate cancer will increase by 5-11 times

Pathology Stages and Grades



- Pathologists grade prostate cancers using numbers from 1 to 5 based on how much the cells in the cancerous tissue look like normal prostate tissue under the microscope. This is called the Gleason system.

Symptom:

- Early prostate cancer usually has no clear symptoms, often similar to those of benign prostatic hyperplasia.
- Metastatic prostate cancer (especially bone metastasis) can cause symptoms, such as:

Difficulty maintaining stream of urine	Frequent urination
Bone pain	Dysuria (painful urination)
Hematuria	Difficulty erection

Diagnostic criteria

Metastatic castrate-resistant prostrate cancer (mCRPC) is diagnosed by:

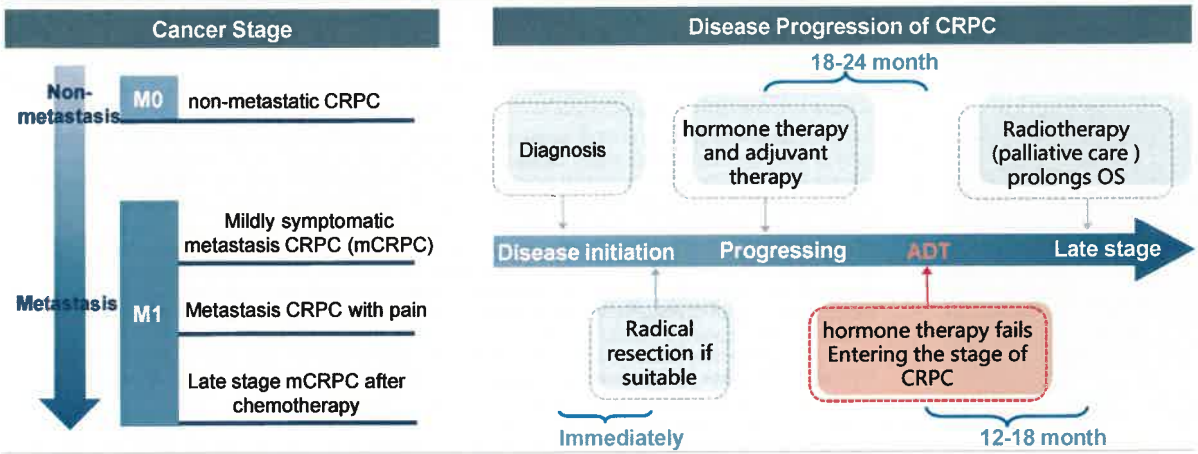
Source: Frost & Sullivan analysis

Overview of Castration-Resistant Prostate Cancers (CRPC)

- Prostate cancer that is resistant to surgery and medical endocrine castration treatment progresses to castration-resistant prostate cancer (CRPC). In CRPC, tumor progresses quickly, and is likely to metastasis, the median survival time is relatively short, and the treatment options are limited.
- At present, there is no verified treatment that can cure CRPC, thereby can merely prolong the survival time. The 5yr-survival rate of patients with chemotherapy-naïve mCRPC is less than 30% globally.
- Approximately 77% of mCRPC patients receive first-line therapy, of whom around 49% proceed to second-line therapy.

Definition

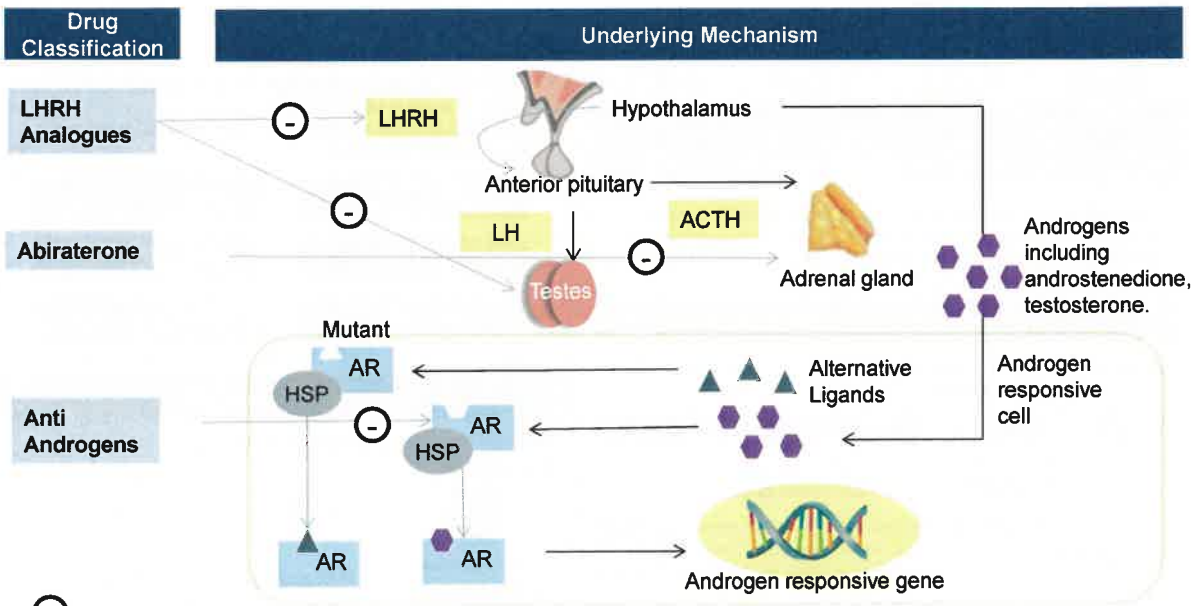
- Castrate-resistant prostate cancer (CRPC) is defined by disease progression despite androgen depletion therapy (ADT), and/or the appearance of new metastases.
- A combination of endocrine treatments can slow the progression of prostate cancer, while after 1.5-2 years, patient are expected to generate castration resistance.
- CRPC is burdened with poor prognosis and impaired quality of life. Historically, the estimated mean survival of patients with CRPC was 12-18 months, according to the extent of metastatic disease and presence of symptoms.



Source: Frost & Sullivan analysis

Androgen Receptor Signaling Pathway

- The prostate is an androgen-dependent organ; the androgen receptor (AR), which execute androgen hormones are the key regulator and driver of PCa and CRPC development.



Note: ⊖ refers to inhibition.

Source: Frost & Sullivan analysis

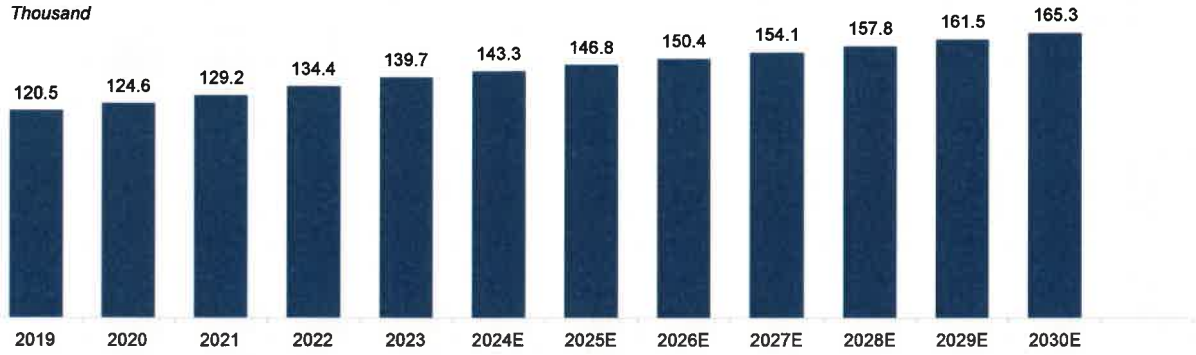
Updated

Incidence of Prostate Cancer in China, 2018-2030E

- Incidence number of prostate cancer in China increased from 120.5 thousand to 143.3 thousand in 2019 and 2024. The number is expected to grow to 154.1 thousand in 2027 at a CAGR of 3.8% from 2023 to 2026. The number is expected to grow to 179.8 thousand in 2030, at a CAGR of 3.6%.

Incidence of Prostate Cancer in China, 2019-2030E

Period	CAGR
2019-2024	3.6%
2024-2027E	3.8%
2027E-2030E	3.6%



Source: NCCN, Frost & Sullivan Analysis

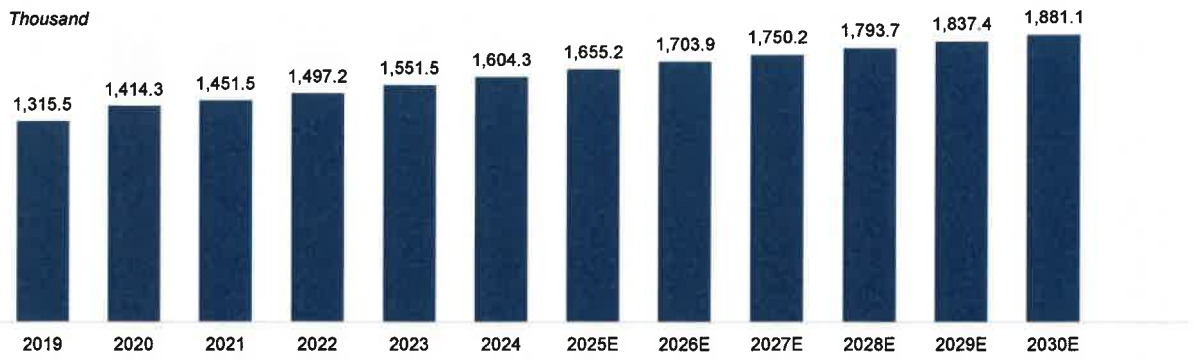
Updated

Global Incidence of Prostate Cancer, 2018-2030E

- Incidence number of prostate cancer around the world increased from 1,315.5 thousand to 1,604.3 thousand in 2019 and 2024. The number is expected to grow to 1,750.2 thousand in 2027 at a CAGR of 3.2% from 2023 to 2026. The number is expected to grow to 1,881.1 thousand in 2030, at a CAGR of 2.5%.

Global Incidence of Prostate Cancer, 2019-2030E

Period	CAGR
2019-2024	4.0%
2024-2027E	3.2%
2027E-2030E	2.5%



Source: IARC, Frost & Sullivan Analysis

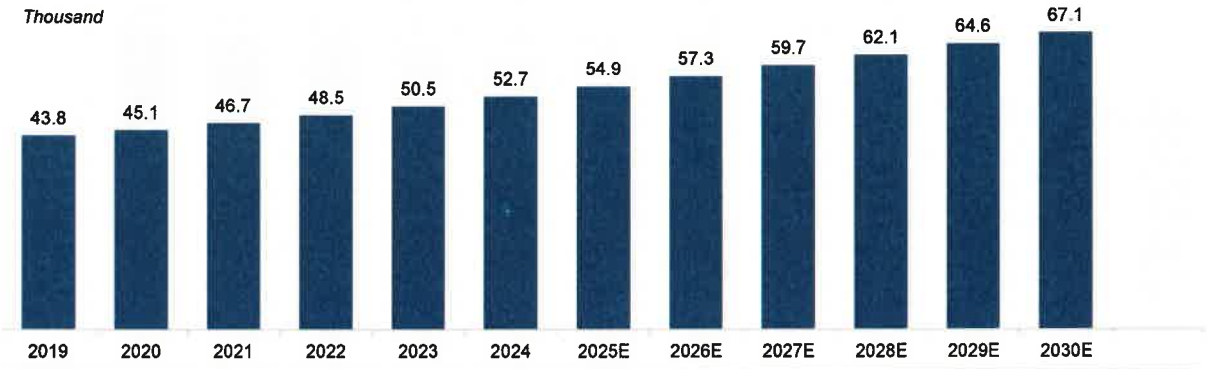
Updated

Incidence of mCRPC in China, 2019-2030E

- Incidence number of mCRPC in China increased from 43.8 thousand to 52.7 thousand in 2019 and 2024. The number is expected to grow to 59.7 thousand in 2027 at a CAGR of 4.3% from 2024 to 2027. The number is expected to grow to 67.1 thousand in 2030, at a CAGR of 4.1%.

Incidence of mCRPC in China, 2019-2030E

Period	CAGR
2019-2024	3.4%
2024-2027E	4.3%
2027E-2030E	4.1%



Source: NCCN, Frost & Sullivan Analysis

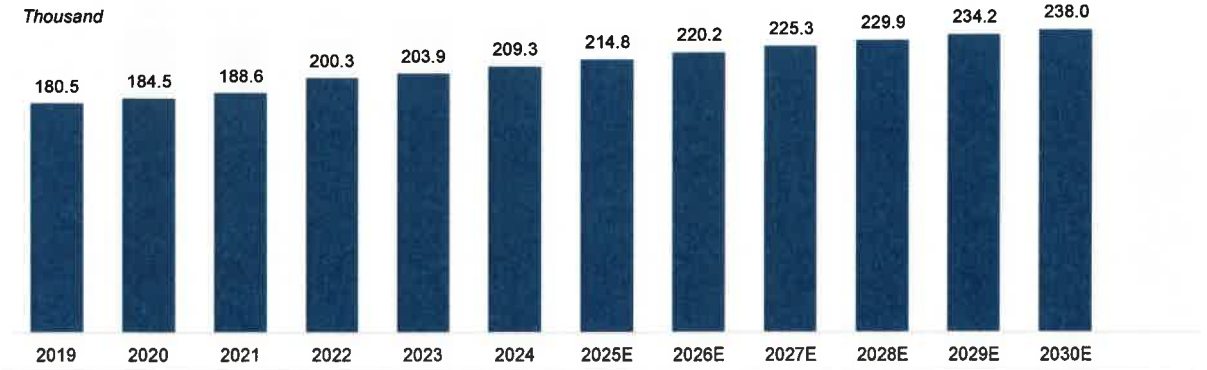
Updated

Global Incidence of mCRPC, 2018-2030E

- Incidence number of mCRPC around the world increased from 180.5 thousand to 209.3 thousand in 2019 and 2024. The number is expected to grow to 225.3 thousand in 2027 at a CAGR of 2.6% from 2024 to 2027. The number is expected to grow to 238.0 thousand in 2030, at a CAGR of 2.0%.

Global Incidence of mCRPC, 2019-2030E

Period	CAGR
2019-2024	2.9%
2024-2027E	2.6%
2027E-2030E	2.0%



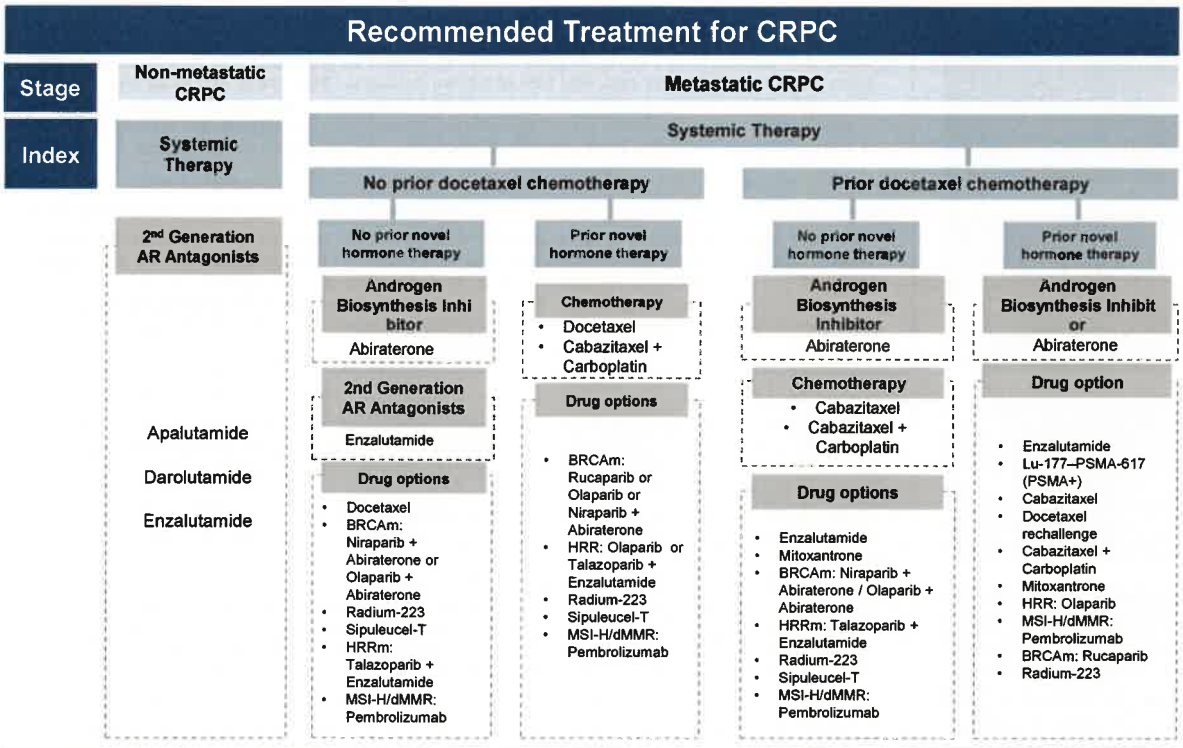
Source: IARC, Frost & Sullivan Analysis

Treatment Paradigm of CRPC in China

Stage	Classification	Recommendation Class I	Recommendation Class II	Recommendation Class III
Non-metastatic CRPC	PSADT ≤ 10 months	• Apalutamide • Darolutamide • Enzalutamide	• Abiraterone • Other second-line hormone therapies	• Radiation therapy • Follow-up
	PSADT > 10 months	• Monitoring	• Other second-line hormone therapies	
Metastatic CRPC	No prior novel hormone therapy and no prior chemotherapy	• Abiraterone or Prednisone • Enzalutamide • Docetaxel • Radium-223 (with bone metastasis)	• Olaparib + Abiraterone • Rezvilutamide • Sipuleucel-T	• Other second-line hormone therapies
	Prior novel hormone therapy and no prior chemotherapy	• Docetaxel • Olaparib • Radium-223 (with bone metastasis)	• Enzalutamide or Abiraterone or Prednisone • Sipuleucel-T • Cabazitaxel • Enzalutamide + Docetaxel	• Abiraterone or Dexamethasone
	Prior docetaxel chemotherapy and no prior novel hormone therapy	• Abiraterone or Prednisone • Enzalutamide • Olaparib • Radium-223 (with bone metastasis)	• Olaparib + Abiraterone • Cabazitaxel • Rezvilutamide	
	Prior novel hormone therapy and prior docetaxel chemotherapy	• Olaparib	• Radium-223 (with bone metastasis) • Docetaxel rechallenge • Lu-177–PSMA-617	• Clinical Trials • Pembrolizumab • Mitoxantrone • Platinum-based chemotherapy • Etoposide

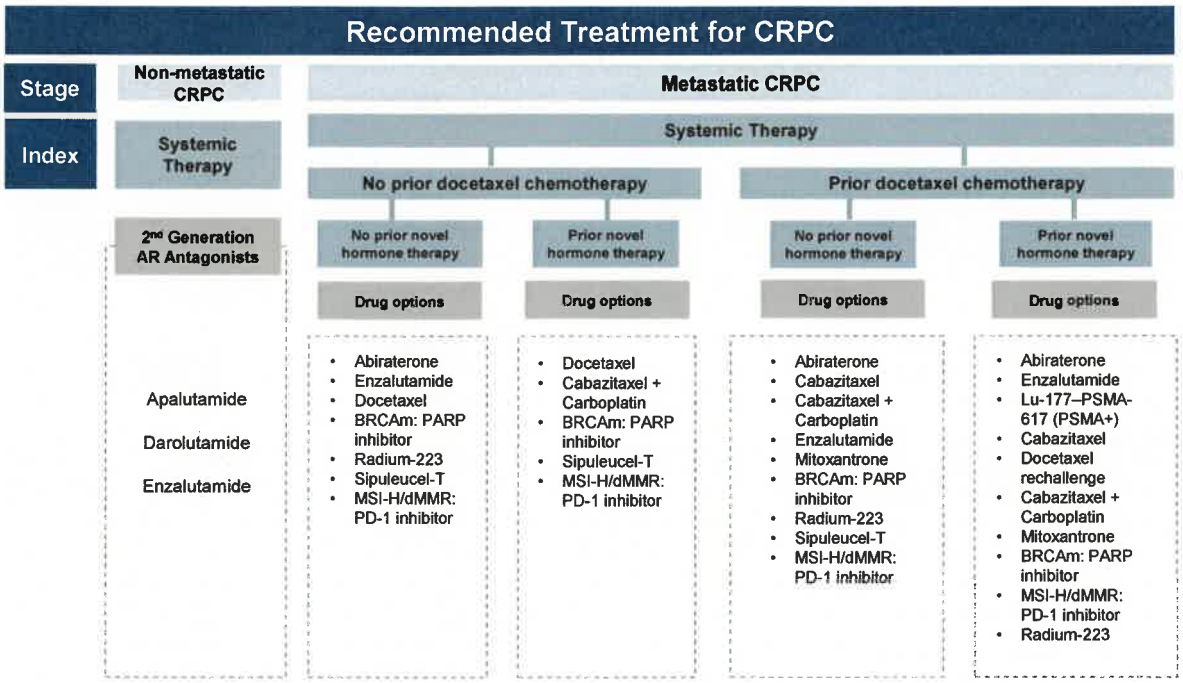
Source: CSCO2023, Frost & Sullivan Analysis

Treatment Paradigm of CRPC in the US



Source: NCCN2024 V3, Frost & Sullivan analysis

Treatment Paradigm of CRPC in the US and China



Source: CSCO2023, NCCN2024 V3, Frost & Sullivan analysis

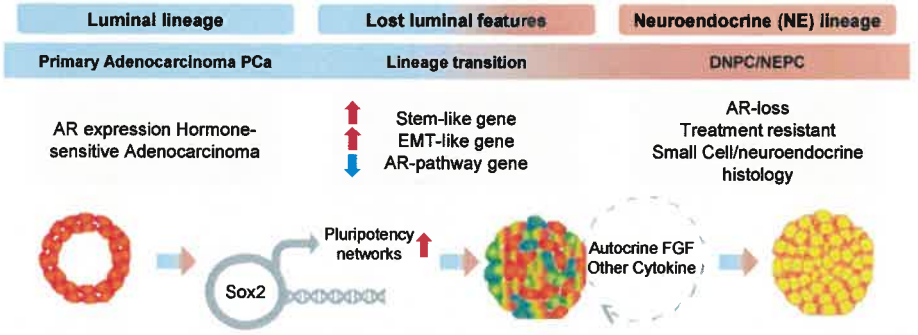
Pain points of the Treatment of CRPC in China

Screening and detection of prostate cancer need to be improved	• Due to poor awareness and limited diagnostic methods, most of the prostate cancer patients in China are in late stage once diagnosed. Also, only 30% of the new incident in China are in early stage once diagnosed, and the rest are patients are unable to receive local radical treatment, with the poor prognosis. • In addition, the number of prostate cancer incidence will increase exponentially with the dramatic increment of aging population. Therefore, timely and effective screening and detection is more important.
Tumor progress rapidly and lack of approved targeted therapy	• ADT is the important treatment for prostate cancer, and it is also the basis of current therapies. However, patients with CRPC have generate resistant to ADT, thus losing core treatment methods. Due to the rapid progression of prostate cancer, the median survival time of patients is only 1-2 years. • As research of CRPC develops in depth, the disease progressing mechanism are gradually figured out, such as VEGFR is developed to be novel target of CRPC treatments. Thus, more specific therapies with better efficacy and safety profile are expected to be developed.
Burden of QoL and mental health of patient	• Prostate cancer and ADT therapy will bring a series of treatment-related pains to patients. Bone metastasis is one of the most common complications of advanced prostate cancer. Patients will experience persistent pain in chest and back, and possibly fractures. Secondly, the tumor compresses the urinary system, leading to dysuria, hematuria, and lumps. • Severe illness will cause inconvenience to patients' mobility, and affect the quality of life. At the same time, castration therapy can damage the sexual function and cause negative psychological effects.
Lack of molecular testing will increase continuously and facilitates the precision medicine.	• The diagnosis of lung cancer has moved from early pathological classification to molecular classification. With the continuous approval of PCR diagnostic kits and NGS-based companion diagnostic kits, molecular detection of lung cancer has been able to detect not only common mutations but also rare mutations. • With the continuous approval of products for molecular testing, along with the continuous improvement of detection performance, and the continuous improvement of market application, the precision treatment of non-small cell lung cancer will continue to thrive in the future.

Source: Frost & Sullivan Analysis

Mechanism of Action of Tinengotinib in the Treatment of mCRPC

- Howard Hughes Medical Institute investigator; Chairman of the Human Oncology and Pathogenesis Program at the Memorial Sloan-Kettering Cancer Center.
- Recipient of the 2005 ASCO Karnofsky Memorial Award, in recognition of his pioneering contributions to the molecular targeted therapy of Chronic Myelogenous Leukemia (CML) and prostate cancer.
- Developer of the revolutionary CML treatment drugs imatinib (first-generation Gleevec) and dasatinib (second-generation Gleevec); CRPC treatment drugs enzalutamide and apalutamide.



Tinengotinib kinase profile

Kinase	IC50/nM
FGFR1	2
FGFR2	1.5
FGFR3	5
JAK1	15
JAK2	0.75
KDR	2.5
Aurora	1.2

- The Charles Sawyer Laboratory at MSKCC discovered that neuroendocrine transdifferentiation (lineage plasticity) of hormone-sensitive prostate cancer cells is one of the key resistance mechanisms to enzalutamide/abiraterone. The occurrence of lineage reprogramming is highly associated with the upregulation of the FGFR/JAK pathway.
- Simultaneous inhibition of the FGFR and JAK pathways can reverse neuroendocrine cells back to their original hormone-sensitive state.
- Tinengotinib is the world's first and only investigational drug capable of simultaneously and effectively inhibiting the FGFR/JAK pathway.

Source: Literature Review, Frost & Sullivan analysis

Competitive Landscape of Small Molecule Targeted Drugs on mCRPC Approved by NMPA

Drug Name	Brand Name	Category	Company	Indications	Approval Date
Olaparib	Lynparza®	PARP inhibitor	AstraZeneca / MSD	Previous treated metastatic castration-resistant prostate cancer (mCRPC) with BRCA mutation	2018/08/22 (2020/01/20 for mCRPC)
Enzalutamide	Xtandi®	Androgen receptor antagonist	Astellas	Metastatic castration-resistant prostate cancer (mCRPC) after failure in ADT therapy	2019/11/18
Abiraterone	Zytiga®	Androgen receptor antagonist	Janssen	Metastatic castration-resistant prostate cancer (mCRPC)	2015/8/18
TALZENNA	talazoparib®	PARP inhibitor	Pfizer	Metastatic castration-resistant prostate cancer (mCRPC)	2024/10/29
Apalutamide	Erleada®	AR inhibitor	Janssen-Cilag International NV	Metastatic castration-resistant prostate cancer (mCRPC)	2024/6/18

Note: Approval date: First approval date
As of Feb 19th, 2025

Source: NMPA, Frost & Sullivan Analysis

Competitive Landscape of Small Molecule Targeted Drugs on mCRPC Approved by FDA

Drug Name	Brand Name	Category	Company	Indications	Approval Date
Abiraterone	Zytiga®	Androgen receptor antagonist	Janssen	Metastatic castration-resistant prostate cancer (mCRPC)	2011/4/28
Enzalutamide	Xtandi®	Androgen receptor antagonist	Astellas	Metastatic castration-resistant prostate cancer (mCRPC)	2012/8/31
Olaparib Tablet	Lynparza®	PARP inhibitor	AstraZeneca / MSD	For the treatment of adult patients with deleterious or suspected deleterious germline or somatic homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC)	2017/8/17 (2020/5/19 for mCRPC)
Rucaparib	Rubraca®	PARP inhibitor	Clovis Oncology	mCRPC patients with a deleterious BRCA mutation	2016/12/19 (2020/5/15 for mCRPC)
Talazoparib	Talzenna®	PARP inhibitor	Pfizer	In combination with enzalutamide for the treatment of adult patients with HRR gene-mutated metastatic castration-resistant prostate cancer (mCRPC)	2018-10-16 (2023/6/20 for mCRPC)

Note: Approval date: First approval date
As of Feb 19th, 2025

Source: FDA, Frost & Sullivan Analysis

Competitive Landscape of China Small Molecular Targeted Drug on mCRPC in Pipeline (1/2)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
Talazoparib	PARP1,PARP2	Pfizer	NDA	mCRPC	2023-04-01
MK-5684	CYP11A1	Orion Corporation/MSD	Phase 3	mCRPC	2024-02-26
Capivasertib	AKT	AstraZeneca	Phase 3	mCRPC	2022-12-16
Fluzoparib	PARP1	Hengrui Medicine Co.,Ltd.	Phase 3	mCRPC	2021-01-12
Ipatasertib	AKT	Roche	Phase 3	mCRPC	2018-04-10
Abemaciclib	CDK4,CDK6	Eli Lilly	Phase 2/3	mCRPC	2021-09-17
HWH340	PARP1,PARP2	Humanwell Healthcare (group) Co.,Ltd.	Phase 2	mCRPC	2022-12-22
ZEN-3694	BET	Newsoara Biopharma	Phase 2	mCRPC	2021-07-30
Mefuparib	PARP1,PARP2	Cisen Pharmaceutical CO.,LTD.	Phase 2	mCRPC	2021-06-21
SC10914	PARP1,PARP2	De Novo Pharmatech Co., Ltd / Qingfeng pharmaceutical industry Co., Ltd.	Phase 2	mCRPC	2020-06-15
IMP1734	PARP1	Impact Therapeutics	Phase 1/2	Breast cancer, mCRPC, Ovarian cancer, Fallopian tube cancer, Peritoneal cancer	2024-02-26
HP518	AR	Hinava Pharma Co., Ltd	Phase 1/2	mCRPC	2023-11-28
XNW5004	EZH2	Xinnuowei Pharmaceutical Technology	Phase 1/2	mCRPC	2023-09-06

As of Feb 19th, 2025

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of China Small Molecular Targeted Drug on mCRPC in Pipeline (2/2)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
Tinengotinib	**FGFR, VEGFR, JAK2, Aurora A/B**	**TransThera**	**Phase 1/2**	**mCRPC**	**2021-11-08**
MAK683	EED	Novartis	Phase 1/2	Diffuse large B-cell lymphoma, follicular lymphoma, T-cell lymphoma, nasopharyngeal cancer, gastric cancer, ovarian clear cell carcinoma, sarcoma	2020-08-31
SHR2554	EZH2	Hengrui Medical Company Limited Company	Phase 1/2	mCRPC	2018-10-23
CG-7321	/	Cynogen Pharmaceutical Technology Co., Ltd	Phase 1	mCRPC	2024-03-05
QLH12016	/	QILU PHARMACEUTICAL CO.,LTD	Phase 1	mCRPC	2023-08-29
HRS-5041	AR	Hengrui Medicine Co.,Ltd.	Phase 1	mCRPC	2023-07-07
PF 06821497	EZH2	Pfizer	Phase 1	r/r small cell lung cancer, follicular lymphoma, mCRPC	2023-06-01
HSK38008	AR-V7	Haisco Pharmaceutical Group	Phase 1	mCRPC	2023-04-06
DG01	SRD5A3,GSPT 1	Suzhou Degen Biopharmaceutical Co., Ltd	Phase 1	mCRPC	2024-09-14
Rezvilutamide	AR	Hengrui Medical Company Limited Company	Phase 1	mCRPC and nmCRPC	2022-10-25
Enzalutamide deuterated	AR	Hinava Pharma Co., Ltd	Phase 1	mCRPC	2021-09-30
TQB3720	AR	Chiatai Tianqing Pharmaceutical Group	Phase 1	mCRPC	2021-01-26

Note: Highlight in yellow are MTKi
As of Feb 19th, 2025

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of Global Small Molecular Targeted Drug on mCRPC in Pipeline (1/5)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
Capivasertib	AKT	AstraZeneca	Phase 3	mCRPC	2022/4/27
HC-1119	AR	Hinova Pharmaceuticals Inc.	Phase 3	mCRPC	2019/2/22
Masitinib	KIT, FYN, LYN, PDGFR, CSF1R, 3CLpro	AB Science	Phase 3	mCRPC	2018/12/3
Niraparib	PARP, CYP17A1	Janssen Research & Development, LLC	Phase 3	mCRPC	2018/11/21
ODM-208	CYP11A1	Merck Sharp & Dohme LLC	Phase 3	mCRPC	2023/11/18
Darxicilib	CDK4/6	HengRui Medicine Co., Ltd.	Phase 2	mCRPC	2024/7/15
131I-MIP-1095	PSMA	Progenics Pharmaceuticals, Inc.	Phase 2	mCRPC	2019/5/7
Abemaciclib	CDK4/6	Eli Lilly and Company	Phase 2	mCRPC	2021/2/12

Highlight in yellow are MTKi
As of Feb 19th, 2025
Only clinical stage above phase 2 are included.

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Competitive Landscape of Global Small Molecular Targeted Drug on mCRPC in Pipeline (2/5)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
AZD4635	A2AR	AstraZeneca / Parexel	Phase 2	mCRPC	2020/7/31
Cabozantinib	MET, AXL, RET, ROS1, TYRO3, MERTK, KIT, NTRK2, FLT3, TEK, VEGFR	Exelixis	Phase 2	mCRPC	2020/11/17
GT0918	AR	Suzhou Kintor Pharmaceutical Inc.	Phase 2	mCRPC	2019/4/2
GTx-758	ER-α	GTx	Phase 2	mCRPC	2012/6/8
Irofulven	PTGR1	Allarity Therapeutics / Lantern Pharma Inc.	Phase 2	mCRPC	2018/8/22
LY3023414	mTOR, PI3K	Eli Lilly and Company	Phase 2	mCRPC	2015/4/2
MLN0128	TORC1/2	Millennium Pharmaceuticals, Inc.	Phase 2	mCRPC	2014-03-19
MLN8237	AURKA	Millennium Pharmaceuticals, Inc.	Phase 2	mCRPC	2013/2/26
Navarixin	CXCR2	Merck Sharp & Dohme Corp.	Phase 2	Non-small Cell Lung Cancer, mCRPC, Microsatellite Stable Colorectal Cancer	2018/3/22

As of Feb 19th, 2025
Highlight in yellow are MTKi
Only clinical stage above phase 2 are included.

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Competitive Landscape of Global Small Molecular Targeted Drug on mCRPC in Pipeline (3/5)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
Onvansertib	PLK1	Cardiff Oncology	Phase 2	mCRPC	2018/1/29
Palbociclib	CDK4/6	Pfizer	Phase 2	mCRPC	2016/9/19
Senaparib	PARP1/2	Impact Therapeutics, Inc.	Phase 2	mCRPC	2021/3/30
SHR3680	AR	Jiangsu HengRui Medicine Co., Ltd.	Phase 2	mCRPC	2020/10/27
SX-682	CXCR1/2	Syntrix Biosystems, Inc.	Phase 2	mCRPC	2024/1/29
Trametinib	MAP2K1/2	Novartis	Phase 2	mCRPC	2016/8/26
ZEN-3694	BET	Astellas Pharma Inc / Newsoara Biopharma Co., Ltd.	Phase 2	mCRPC	2021/8/2

As of Feb 19th, 2025
Only clinical stage above phase 2 are included.

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Competitive Landscape of Global Small Molecular Targeted Drug on mCRPC in Pipeline (4/5)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
INV-9956	CYP11A1	Shenzhen Ionova Life Sciences Co., Ltd.	Phase 1	mCRPC	2024/9/23
Tinengotinib	**FGFR, VEGFR, JAK2, Aurora A/B**	**TransThera**	**Phase 1/2**	**mCRPC**	**2024-06-13**
Gedatolisib	mTOR, PI3K	Celcuity Inc	Phase 1/2	mCRPC	2024/1/5
XNW5004	EZH2	Evopoint Biosciences Inc./Merck Sharp & Dohme LLC	Phase 1/2	mCRPC	2023/9/5
ONCT-534	AR	Oncternal Therapeutics, Inc	Phase 1/2	mCRPC	2023/6/23
HST-1011	CBLB	HotSpot Therapeutics, Inc	Phase 1/2	mCRPC	2022/12/22
NUV-868	BRD4	Nuvation Bio Inc.	Phase 1/2	mCRPC	2022/2/23
EPI-7386	AR	ESSA Pharmaceuticals	Phase 1/2	mCRPC	2021/10/13
TT-10	ADORA2A	Portage Biotech/Tarus Therapeutics, Inc.	Phase 1/2	mCRPC	2021/7/20
SC10914	PARP1/2	Qingfeng Pharmaceutical Co. Ltd.	Phase 1/2	mCRPC	2020/7/27
Etrumadenant	ADORA2A, ADORA2B	Arcus Biosciences, Inc./Gilead Sciences	Phase 1/2	mCRPC	2020/5/11
Copanlisib	PI3Kα, δ	Bayer	Phase 1/2	mCRPC	2020/2/5
Tazemetostat	EZH2	Epizyme, Inc.	Phase 1/2	mCRPC	2019/11/27

As of Feb 19th, 2025
Highlight in yellow are MTKi
Only clinical stage above phase 2 are included.

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Competitive Landscape of Global Small Molecular Targeted Drug on mCRPC in Pipeline (5/5)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
Afuresertib	AKT	Laekna Limited	Phase 1/2	mCRPC	2019/8/19
CCS1477	P300, CBP	CellCentric Ltd.	Phase 1/2	mCRPC	2018/6/26
CPI-1205	EZH2	Constellation Pharmaceuticals	Phase 1/2	mCRPC	2018/3/29
TRC253	AR	Tracon Pharmaceuticals Inc./Janssen Pharmaceutica N.V., Belgium	Phase 1/2	mCRPC	2016/12/9
KPT-8602	XPO1	Karyopharm Therapeutics Inc	Phase 1/2	mCRPC	2016/1/7
Ribociclib	CDK4/6	Novartis	Phase 1/2	mCRPC	2015/7/10
VT-464	CYP17A1	Innocrin Pharmaceutical	Phase 1/2	mCRPC	2015/2/11
AZD5363	AKT	AstraZeneca	Phase 1/2	mCRPC	2014-04-23
Onalespib	HSP90	Astex Pharmaceuticals, Inc.	Phase 1/2	mCRPC	2012/9/14
ACE-232	CYP11A1	Acerand Therapeutics (Hong Kong) Limited	Phase 1	Prostate Cancer, MCRPC	2025-01-30
OP-3136	KAT6A、KAT6B	Olema Pharmaceuticals, Inc.	Phase 1	mBC, NSCLC, mCRPC	2025-01-20

As of Feb 19th, 2025
Only clinical stage above phase 2 are included.

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Global Competitive Landscape of MTK inhibitors for mCRPC At Clinical Stage

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date	Study Location
Masitinib	KIT, FYN, LYN, PDGFR, CSF1R, 3CLpro	AB Science	Phase 3	mCRPC	2018/12/3	Canada, France, India, Italy, Malaysia, Russian Federation
Cabozantinib	MET, AXL, RET, ROS1, TYRO3, MERTK, KIT, NTRK2, FLT3, TEK, VEGFR	Exelixis	Phase 2	mCRPC	2020/11/17	The US
Tinengotinib	**FGFR, VEGFR, JAK, Aurora**	**TransThera**	**Phase 1/2**	**mCRPC**	**2024-06-13**	The US
		TransThera	**Phase 1/2**	**mCRPC**	**2021-11-08**	China

Note: Only clinical stage above phase 2 are include.
As of Feb 19th, 2025

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

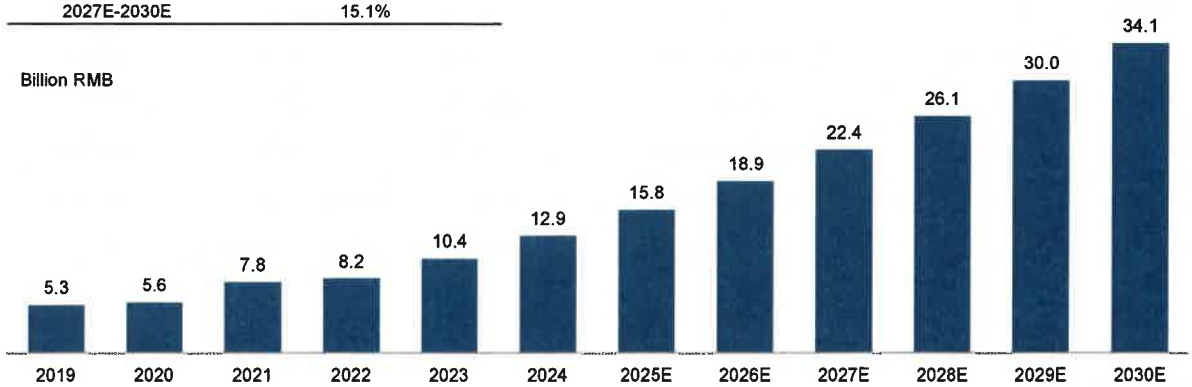
Updated

Historical and Forecasted of China Prostate Cancer Drug Market Size, 2019-2030E

- China's Prostate Cancer drug market has grown from RMB5.3 billion in 2019 to RMB12.9 billion in 2024 at a CAGR of 19.6%, and expected to increase to RMB22.4 billion in 2027 at a CAGR of 20.1% from 2024 and RMB34.1 billion in 2030 at a CAGR of 15.1% from 2027.

Historical and Forecasted of China Prostate Cancer Drug Market Size, 2019-2030E

Period	CAGR
2019-2024	19.6%
2024-2027E	20.1%
2027E-2030E	15.1%



Source: Frost & Sullivan Analysis

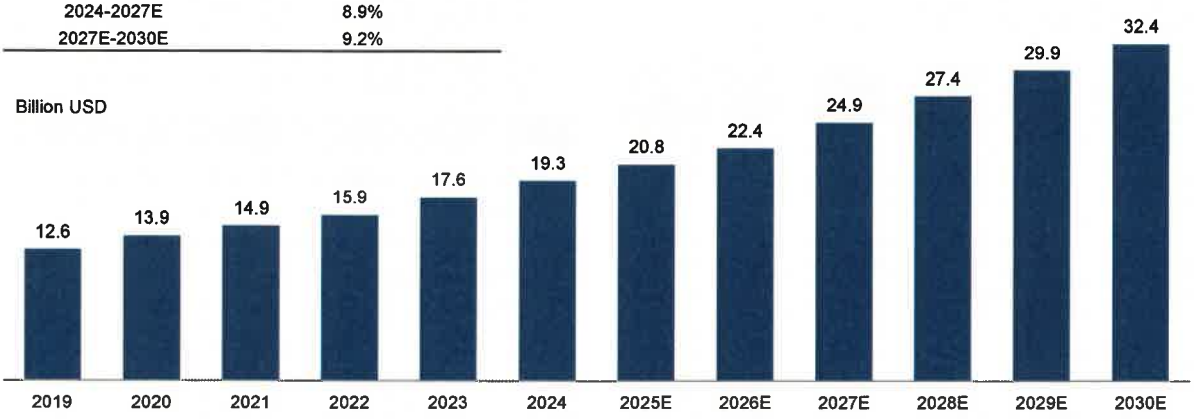
Updated

Historical and Forecasted of Global Prostate Cancer Drug Market Size, 2019-2030E

- Global Prostate Cancer drug market has grown from USD12.6 billion in 2019 to USD19.3 billion in 2024 at a CAGR of 8.8%, and expected to increase to USD24.9 billion in 2027 at a CAGR of 8.9% from 2024 and USD32.4 billion in 2030 at a CAGR of 9.2% from 2027.

Historical and Forecasted of Global Prostate Cancer Drug Market Size, 2019-2030E

Period	CAGR
2019-2024	8.8%
2024-2027E	8.9%
2027E-2030E	9.2%



Source: Frost & Sullivan Analysis

Future Trends for mCRPC Treatment Market

Steadily Increasing New Case Numbers	• The number of new prostate cancer cases in China grew from 97,000 in 2017 to 121,000 in 2021. It is expected that the incidence of prostate cancer will continue to rise, reaching 161,000 by 2026 and 199,000 by 2030. With the increase in new cases of prostate cancer in China and the advancement of early diagnosis and screening, the market demand for related drugs is also growing, indicating a positive development trend in the Chinese prostate cancer treatment drug market.
Significant progress in clinical research	• Currently, the frontline treatment for CCA predominantly involves various chemotherapy regimens and some combinations with immune checkpoint inhibitors, with small molecule targeted drugs like FGFR inhibitors, IDH inhibitors, and BRAF V600 inhibitors recommended for later lines of therapy. However, small molecule targeted drugs offer several advantages over current therapies, such as higher specificity, better safety profiles, and improved patient compliance. With the gradual approval and commercialization of targeted drugs for cholangiocarcinoma, such as pemigatinib, the use of small molecule targeted drugs is expected to become more widespread in this field. Considering factors such as improved efficacy and unmet clinical needs, there is a trend for these therapies to move to earlier lines of treatment, similar to the trajectory observed with osimertinib in the NSCLC domain, which evolved from a second-line to a frontline recommendation due to its clinical success and ability to meet unmet needs. FGFR small molecule inhibitors also face a significant unmet clinical demand and are likely to follow a similar trend in the future.
Targeted therapies to be the potential mainstream	• The primary treatment regimens for patients with CRPC still predominantly involve androgen receptor inhibitors or hormone therapy under corticosteroids. As the disease progresses to the mCRPC stage, novel hormone therapies and chemotherapy become the first-line treatment options. Considering the different mutation genotypes that may exist in mCRPC patients, the NCCN Guidelines Version 4.2022 for Prostate Cancer recommend corresponding targeted therapies for those whose first-line treatments become resistant or fail. For instance, olaparib is used for treating mCRPC with HRR mutations, and rucaparib is used for treating mCRPC with BRCA mutations. The expansion of genetic mutation testing in the future could lay the foundation for precise treatment of patients, and the development of new targeted therapies for more mutation genotypes is expected to bring more clinical benefits to mCRPC patients.

Source: Frost & Sullivan Analysis

Overview of Breast Cancer

- Breast cancer is a malignant tumor that occurs in the epithelial tissue of the breast. It is the most common malignant tumor in women and occasionally in men. Developing from breast tissue, breast cancer may present as a lump in the breast, a change in breast shape, dimpling of the skin, fluid coming from the nipple, a newly inverted nipple, or a red or scaly patch of skin. The incidence of breast cancer is related to high endogenous estrogen levels in patients, endometriosis, menstrual fertility factors, genetic factors, environmental and lifestyle factors, etc., and the incidence peaks around the age of 50. Treatment measures should be based on histological classification, TNM staging and molecular classification of breast cancer.

Definition

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

Histological classification

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

Molecular classification

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

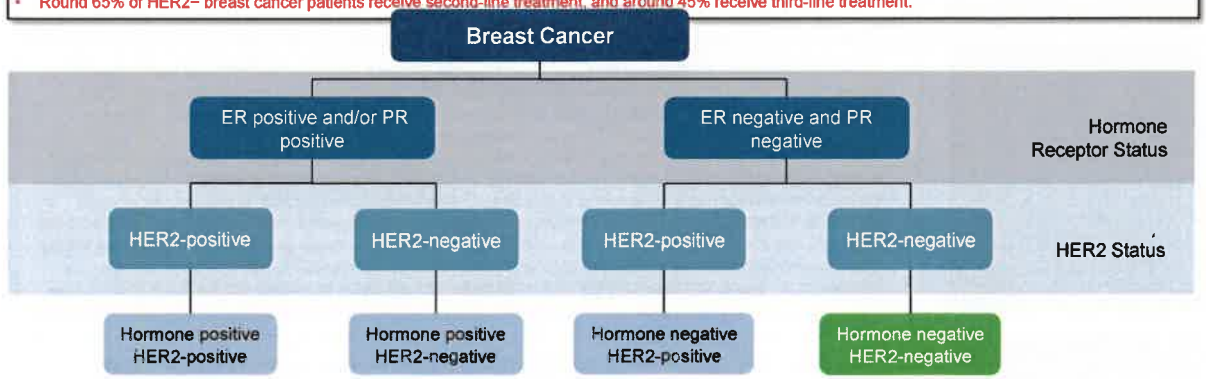
Risk Factors

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

Source: Literature Review, Frost & Sullivan analysis

Classification of Breast Cancer

- Breast cancer classification divides breast cancer into categories according to different gene expression and receptor status.
- Among all different kinds of receptors in breast cancer cells, three most important classification being: estrogen receptor (ER), progesterone receptor (PR), and HER2.
- Either a test called an immunohistochemistry (IHC) test or fluorescence in situ hybridization (FISH) test is used to find out if cancer cells have a high level of the HER2 protein. About 20% of breast tumors have higher levels of a protein known as HER2. These cancers are called HER2-positive breast cancers, otherwise called HER2-negative breast cancer (HER2-negative breast cancer includes HER2 low expression).
- Loss of hormone receptor in metastasis was more common than acquisition. The loss of ER and PR in metastasis was observed in 14.8% and 27.7% of patients, respectively, while the acquisition of ER and PR in metastasis was observed in 6.3% and 5.5% of patients, respectively.
- More breast cancer cases in low socioeconomic status areas (25.5%) were diagnosed at later stages (stages III & IV) than those in high (20.4%) or highest (14.8%) in China. More than 90% of breast cancers are not metastatic at the time of diagnosis in the USA.
- Round 65% of HER2− breast cancer patients receive second-line treatment, and around 45% receive third-line treatment.



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

Source: Literature Review, Frost & Sullivan analysis

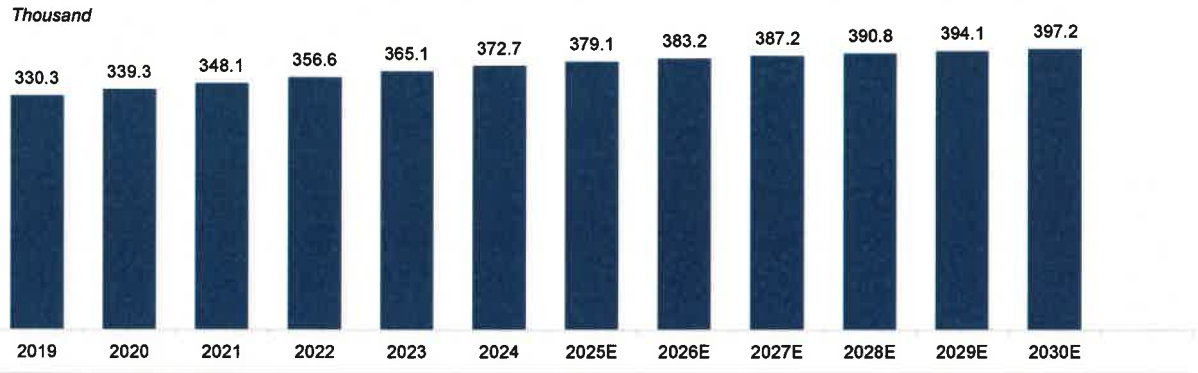
updated

Incidence of Breast Cancer in China, 2019-2030E

- Incidence number of breast cancer in China increased from 330.3 thousand to 372.7 thousand in 2019 and 2024. The number is expected to grow to 387.2 thousand in 2027 at a CAGR of 1.3% from 2024 to 2027. The number is expected to grow to 397.2 thousand in 2030, at a CAGR of 0.9%.

Incidence of Breast Cancer in China, 2019-2030E

Period	CAGR
2019-2024	2.4%
2024-2027E	1.3%
2027E-2030E	0.9%



Source: NCCR, Frost & Sullivan Analysis

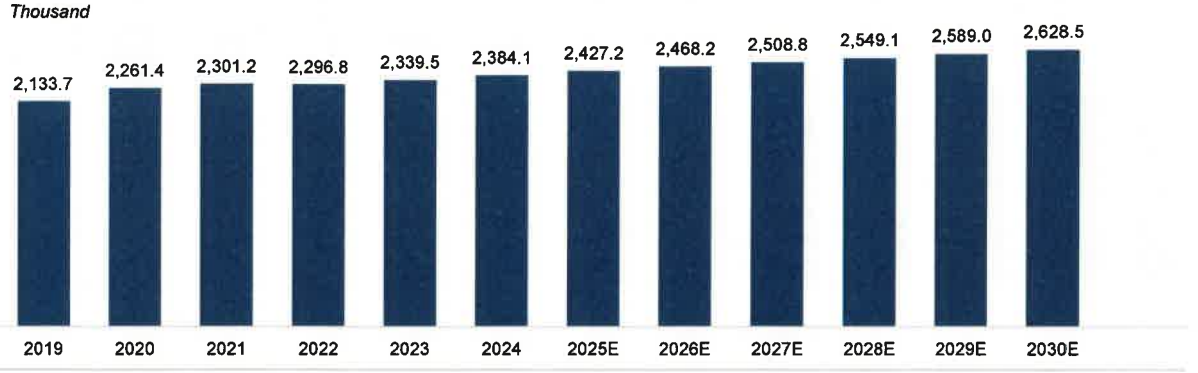
updated

Global Incidence of Breast Cancer, 2019-2030E

- Incidence number of breast cancer around the world increased from 2,133.7 thousand to 2,384.1 thousand in 2019 and 2024. The number is expected to grow to 2,508.8 thousand in 2027 at a CAGR of 1.7% from 2024 to 2027. The number is expected to grow to 2,628.5 thousand in 2030, at a CAGR of 1.6%.

Global Incidence of Breast Cancer, 2019-2030E

Period	CAGR
2019-2024	2.7%
2024-2027E	1.7%
2027E-2030E	1.6%



Source: IARC, Frost & Sullivan Analysis

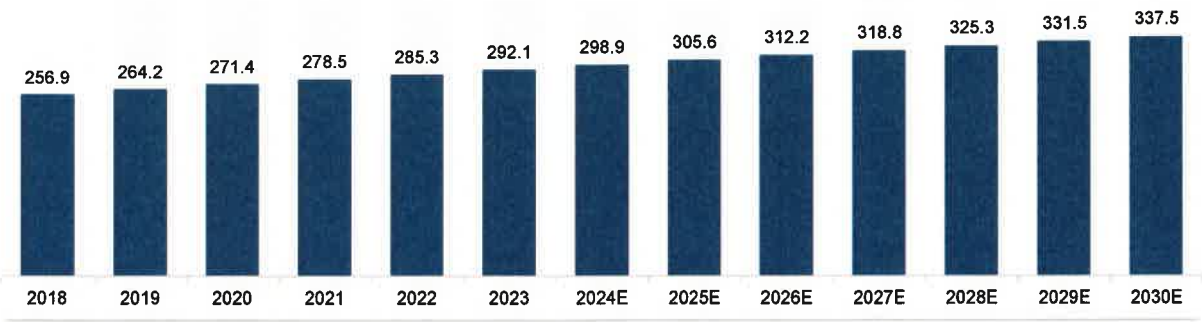
Incidence of HER2- Breast Cancer in China, 2018-2030E

- HER2-negative breast cancer accounts for approximately 80% of the total breast cancer population.
- Incidence number of HER2- breast cancer in China increased from 256.9 thousand to 292.1 thousand in 2018 and 2023. The number is expected to grow to 312.2 thousand in 2026 at a CAGR of 2.2% from 2023 to 2026. The number is expected to grow to 337.5 thousand in 2030, at a CAGR of 2.0%.

Incidence of HER2- Breast Cancer in China, 2018-2030E

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

Thousand



Source: NCCR, Frost & Sullivan Analysis

updated

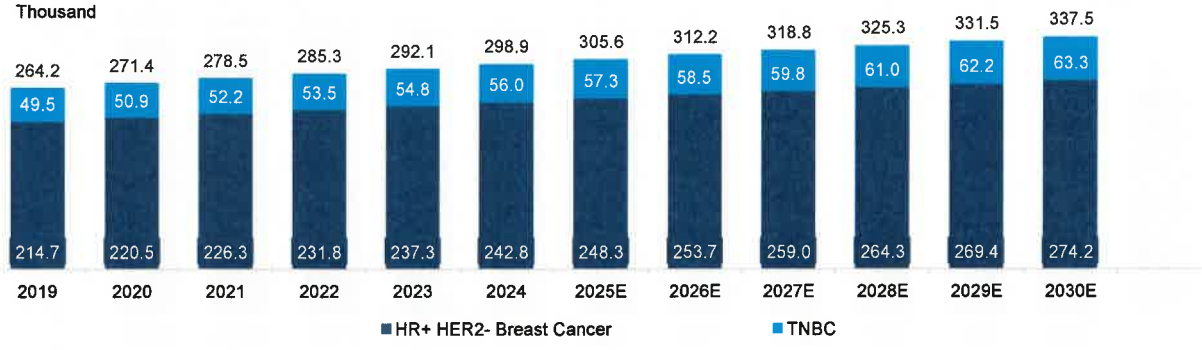
Incidence of HER2- Breast Cancer in China, 2019-2030E

- HER2-negative breast cancer accounts for approximately 80% of the total breast cancer population.
- Incidence number of HER2- breast cancer in China increased from 262.2 thousand to 298.9 thousand in 2019 and 2024. The number is expected to grow to 318.8 thousand in 2027 at a CAGR of 2.2% from 2024 to 2027. The number is expected to grow to 337.5 thousand in 2030, at a CAGR of 2.0%.

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

CAGR	HR+ HER2- Breast Cancer	TNBC	HER2- Breast Cancer
2019-2024	2.6%	2.6%	2.6%
2024-2027E	2.2%	2.2%	2.2%
2027E-2030E	2.0%	2.0%	2.0%

Thousand



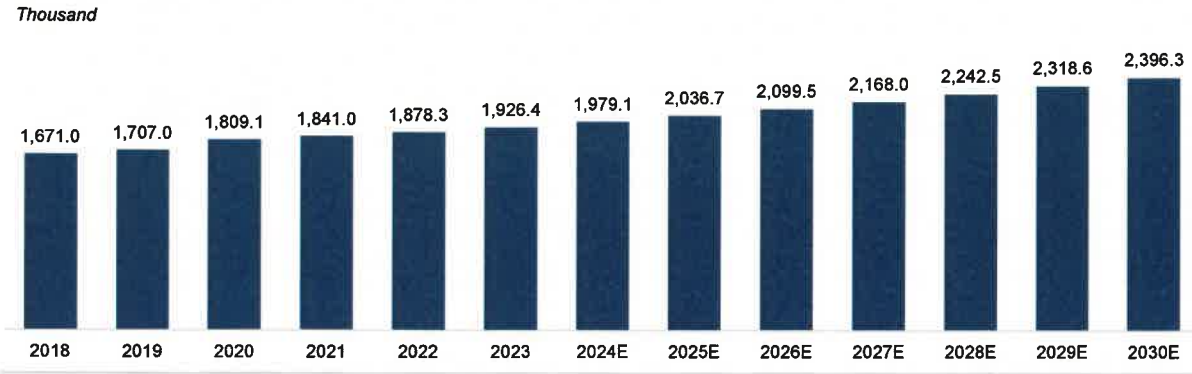
Source: NCCR, Frost & Sullivan Analysis

Global Incidence of HER2- Breast Cancer, 2018-2030E

- HER2-negative breast cancer accounts for approximately 80% of the total breast cancer population.
- Incidence number of HER2- breast cancer around the world increased from 1,671.0 thousand to 1,926.4 thousand in 2018 and 2023. The number is expected to grow to 2,099.5 thousand in 2026 at a CAGR of 2.9% from 2023 to 2026. The number is expected to grow to 2,396.3 thousand in 2030, at a CAGR of 3.4%.

Global Incidence of HER2- Breast Cancer, 2018-2030E

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



Source: IARC, Frost & Sullivan Analysis

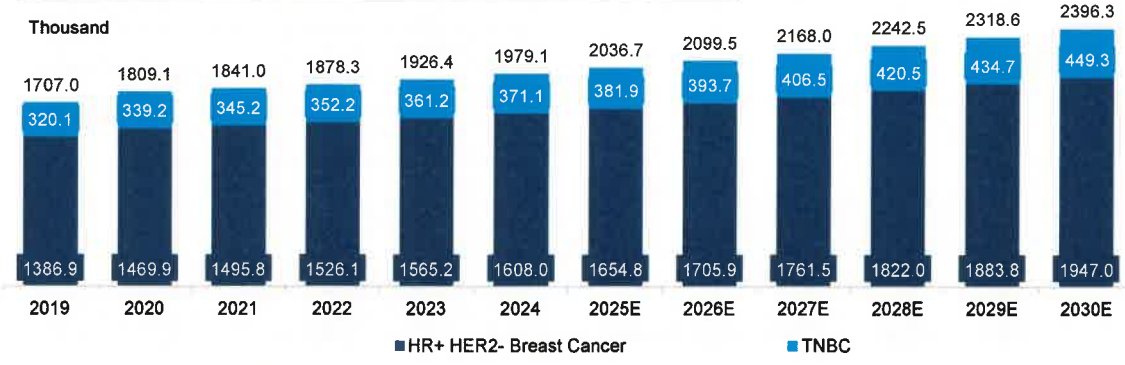
updated

Global Incidence of HER2- Breast Cancer, 2019-2030E

- HER2-negative breast cancer accounts for approximately 80% of the total breast cancer population.
- Incidence number of HER2- breast cancer around the world increased from 1,707.0 thousand to 1,979.1 thousand in 2019 and 2024. The number is expected to grow to 2,168.0 thousand in 2027 at a CAGR of 2.9% from 2024 to 2027. The number is expected to grow to 2,396.3 thousand in 2030, at a CAGR of 3.4%.

Global Incidence of HER2- Breast Cancer, 2018-2030E

CAGR	HR+ HER2- Breast Cancer	TNBC	HER2- Breast Cancer
2019-2024	2.9%	2.9%	2.9%
2024-2027E	2.9%	2.9%	2.9%
2027E-2030E	3.4%	3.4%	3.4%



Source: NCCR, Frost & Sullivan Analysis

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

Classification	Recommendation Class I	Recommendation Class II	Recommendation Class III
Having not received hormone therapy	• AI+CDK4/6 inhibitor (Palbociclib or Abemaciclib)	• AI+Ribociclib • Fulvestrant + CDK4/6 inhibitor • AI • Fulvestrant	• TAM
TAM failure	• AI+CDK4/6 inhibitor (Palbociclib or Abemaciclib)	• AI+HDACi (Chidamide) • AI+Ribociclib • AI+Dalpiciclib • AI+Everolimus	• AI • Fulvestrant
Nonsteroidal AI failure	• Fulvestrant + CDK4/6 inhibitor (Palbociclib or Abemaciclib or Dalpiciclib) • Steroidal AI + HDAC inhibitor	• Steroidal AI + Chidamide • Fulvestrant + Ribociclib • Steroidal AI + Everolimus	• Fulvestrant • Steroidal AI • TAM or Toremifene • Progesterone
Steroidal AI failure	• Fulvestrant + CDK4/6 inhibitor (Palbociclib or Abemaciclib or Dalpiciclib)	• Fulvestrant + Ribociclib • Fulvestrant + Everolimus • Nonsteroidal AI + CDK4/6 inhibitor	• Fulvestrant • Nonsteroidal AI • TAM or Toremifene • Progesterone
CDK4/6 inhibitor failure		• Other CDK4/6 inhibitor + hormone therapy • Other Targeted Drugs, such as Everolimus or Chidamide or Alpelisib+hormone therapy	• Progesterone • Toremifene

Note: AI: Aromatase inhibitor

Source: CSCO2023, Frost & Sullivan Analysis

Treatment Paradigm of Advanced HR+, HER2- Breast Cancer in the US

	Chemotherapy options: HER2- with visceral crisis or endocrine refractory	Systemic therapy options: HR+ with HER2- and no visceral crisis

Preferred options	• Anthracyclines such as doxorubicin or liposomal doxorubicin
	• Taxanes such as paclitaxel
	• Anti-metabolites such as capecitabine or gemcitabine
	• Microtubule inhibitors such as vinorelbine or eribulin
		• First-line options:
		  • Aromatase inhibitor with CDK4/6 inhibitor (Ribociclib, Abemaciclib, or Palbociclib)
		  • Fulvestrant with CDK4/6 inhibitor
		• Second-line and next-line options:
		  • Fulvestrant with CDK4/6 inhibitor (Abemaciclib, Palbociclib, or Ribociclib) if CKD4/6 inhibitor not used before
		  • For PIK3CA tumor mutation, Alpelisib with Fulvestrant
		  • Everolimus with hormone therapy (Exemestane, Fulvestrant, or Tamoxifen)

Other recommended	• Cyclophosphamide • Docetaxel • Albumin-bound paclitaxel • Epirubicin • Ixabepilone	• Selective ER down-regulator (Fulvestrant). For an ESR1 mutation, Elacestrant. • Selective ER down-regulator with a non-steroidal aromatase inhibitor • Non-steroidal aromatase inhibitor (Anastrozole or Letrozole) • Selective estrogen receptors modulator (Tamoxifen) • Steroidal aromatase inactivator (Exemestane)
Used in some cases	• Doxorubicin and cyclophosphamide (AC) • Epirubicin and cyclophosphamide (EC) • Cyclophosphamide, methotrexate, and fluorouracil (CMF) • Docetaxel and capecitabine • Gemcitabine and paclitaxel (GT) • Gemcitabine and carboplatin • Carboplatin and paclitaxel or albumin-bound paclitaxel	• Megestrol acetate • Ethinyl estradiol • Abemaciclib • For NTRK fusion, Larotrectinib or Entrectinib • For MSI-H/dMMR, Pembrolizumab or Dostarlimab-gxly • For TMB-H, Pembrolizumab • For RET-fusion, Selpercatinib

Source: NCCN2023, Frost & Sullivan Analysis

Treatment Paradigm of Advanced HR+, HER2- Breast Cancer in the US and China

	Chemotherapy options: HER2- with visceral crisis or endocrine refractory	Systemic therapy options: HR+ with HER2- and no visceral crisis

Preferred options	• Anthracyclines
	• Taxanes
	• Anti-metabolites
	• Microtubule inhibitors
		• First-line options:
		  • Aromatase inhibitor with CDK4/6 inhibitor
		  • Fulvestrant with CDK4/6 inhibitor
		• Second-line and next-line options:
		  • Fulvestrant with CDK4/6 inhibitor if CKD4/6 inhibitor not used before
		  • PIK3CA inhibitor with Fulvestrant
		  • Aromatase inhibitor with mTOR inhibitor
		  • Aromatase inhibitor with HDAC inhibitor (CSCO recommends)

Other recommended	• Chemotherapy options	• Aromatase inhibitor • Selective estrogen receptor down-regulator • Selective estrogen receptor modulator
Used in some cases	• Combination chemotherapy options	• Progestogens • Estrogen • NTRK fusion-positive: NTRK inhibitor • MSI-H/dMMR: PD-1 inhibitor • TMB-H: PD-1 inhibitor • RET fusion-positive: RET inhibitor

Source: NCCN2023, CSCO2023, Frost & Sullivan Analysis

Treatment Paradigm of Advanced TNBC in China

Classification	Recommendation Class I	Recommendation Class II	Recommendation Class III

Paclitaxel treatment sensitive	• 1. Single-agent Taxanes
	  • Albumin-bound Paclitaxel
	  • Docetaxel
	  • Paclitaxel
	• 2. Combined Treatment
	  • TX regimen
	  • GT regimen
	  • TP regimen
		• 1. Single-agent Treatment
		  • Capecitabine
		  • Vinorelbine
		  • Gemcitabine
		  • Etoposide
		• 2. Combined Treatment
		  • Albumin-bound Paclitaxel + PD-1 inhibitor
		  • Taxane + Bevacizumab
			• Olaparib
			• Liposomal Paclitaxel
			• Liposomal Doxorubicin
			• Chemotherapy + PD-1 inhibitor

Paclitaxel treatment failure	• 1. Single-agent Treatment
	  • Eribulin
	  • Vinorelbine
	  • Gemcitabine
	  • Capecitabine
	• 2. Combined Therapy
	  • NP
	  • GP
	  • Utidelone + Capecitabine
	  • NX
		• 1.Single-agent Treatment
		  • Albumin-bound Paclitaxel
		  • Sacituzumab Govitecan-hziy
		  • Etoposide
		• 2. Combined Treatment
		  • Capecitabine + Bevacizumab
		  • Albumin-bound Paclitaxel + other chemotherapy
			• Olaparib
			• Liposomal Doxorubicin
			• Liposomal Paclitaxel
			• Chemotherapy + PD-1 inhibitor

Note: T: Taxanes, including Albumin-bound Paclitaxel, Docetaxel, Paclitaxel; X: Capecitabine; G: Gemcitabine; N: Vinorelbine; P: Platinum agents, including Carboplatin, Cisplatin

Source: CSCO2023, Frost & Sullivan Analysis

Treatment Paradigm of Advanced TNBC in the US

	Systemic therapy options: HR- with HER2- (TNBC)
Preferred options	• Anthracyclines such as Doxorubicin or Liposomal Doxorubicin • Taxanes, such as Paclitaxel • Anti-metabolites such as Capecitabine or Gemcitabine • Microtubule inhibitors such as Vinorelbine or Eribulin • For PD-L1-positive, Pembrolizumab with chemotherapy • For germline BRVA1 or BRCA2 mutations, Olaparib, Talazoparib, Cisplatin, or Carboplatin • Sacituzumab govitecan-hziy • Fam-trastuzumab deruxtecan-nxki (T-DXd)
Other recommended	• Cyclophosphamide • Docetaxel • Albumin-bound Paclitaxel • Epirubicin • Ixabepilone
Used in some cases	• Doxorubicin and Cyclophosphamide • Epirubicin and Cyclophosphamide • Cyclophosphamide, Methotrexate, and Fluorouracil • Docetaxel and Capecitabine • Gemcitabine and Paclitaxel • Gemcitabine and Carboplatin • Carboplatin and Paclitaxel or Albumin-bound paclitaxel

Source: NCCN2023, Frost & Sullivan Analysis

Treatment Paradigm of Advanced TNBC in the US and China

	Systemic therapy options: HR- with HER2- (TNBC)
Preferred options	• Anthracyclines • Taxanes • Anti-metabolites • Microtubule inhibitors • PD-1 inhibitor • BRVA1/2 mutations: PARP inhibitor • Sacituzumab govitecan-hziy • T-DXd
Other recommended	• Chemotherapy options
Used in some cases	• Combination chemotherapy options

Source: NCCN2023, CSCO2023, Frost & Sullivan Analysis

Pain point analysis of Breast Cancer Treatment in China

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

Source: Frost & Sullivan Analysis

Competitive Landscape of China Small Molecular Targeted Drug on TNBC in Pipeline (1/2)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
Trilaciclib	CDK4,CDK6	G1 Therapeutics	Phase 3	Locally advanced or metastatic TNBC	2021-09-28
Alpelisib	PI3Kα	Novartis	Phase 3	Locally advanced or metastatic TNBC	2020-12-03
Capivasertib	AKT	AstraZeneca	Phase 3	TNBC	2020-10-09
orbit azine	PC3	Zhenxing Medical Technology Co., Ltd	Phase 2	Advanced TNBC	2023-04-21
BEBT-209	CDK4,CDK6	BeBetter Med Co., Ltd	Phase 2	Advanced TNBC	2022-12-09
ZEN-3694	BET	Newsoara Biopharma Co., Ltd	Phase 2	TNBC	2022-09-14
Chiauranib	AURKB, CSF1R, KIT, VEGFR, PDGFR	Chipscreen Biosciences Co., Ltd.	Phase 2	TNBC	2022-02-23
VB15010	PRAP1	Vybio	Phase 1/2	TNBC and other advanced or metastatic solid tumor	2024-09-13
KBP-2205	PARP	Keythera (Suzhou) Biopharmaceutical Co., Ltd	Phase 1/2	三阴性乳腺癌	2024-04-24
JS105	PI3Kα	Junshi Biosciences Co., Ltd.	Phase 1/2	TNBC	2023-11-27
C019199	CSF1R	Haixi Pharmaceuticals	Phase 1/2	TNBC and other advanced or metastatic solid tumor	2023-06-30
Tinengotinib	**FGFR, VEGFR, JAK2, Aurora A/B**	**TransThera**	**Phase 1/2**	TNBC and other advanced or metastatic solid tumor	**2021-11-08**
Mavorixafor	CXCR4	Abbisko Therapeutics Co., Ltd	Phase 1/2	TNBC	2021-04-07
Afuresertib	AKT	Cambrex Corporation / Laekna LLC	Phase 1/2	TNBC	2021-03-15

As of Feb 19th, 2025
Highlight in yellow are MTKi

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of China Small Molecular Targeted Drug on TNBC in Pipeline (2/2)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
MB0151	SSTR2	Mainline Biosciences|	Phase 1/2	TNBC	2025-02-07
ATX-295	KIF18A	Accent Therapeutics	Phase 1	TNBC	2025-01-29
HS-10502	PARP1	Jiangsu Hansoh Pharmaceutical Co., Ltd.	Phase 1	TNBC	2025-01-10
GH2616	KIF18A	Suzhou Genhouse Pharmaceutical	Phase 1	TNBC	2025-01-03
TY-0540	CDK2, CDK4, CDK6	TYK Medicines Co., Ltd	Phase 1	TNBC and other solid tumor	2023-11-13
FNX006	RAF1, SRC, VEGFR2, FRA1	Chengdu FANXI Biopharma Co., Ltd	Phase 1	TNBC and other solid tumor	2021-02-08
Fluzoparib	PARP1	Hengrui Medicine Co.,Ltd.	Phase 1	Recurrent and metastatic TNBC	2019-05-16
HW060015	/	Humanwell Healthcare (Group) Co., Ltd.	Phase 1	TNBC and other solid tumor	2024-05-17

As of Feb 19th, 2025
Highlight in yellow are MTKi

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of Global Small Molecular Targeted Drug on TNBC in Pipeline (1/5)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
Capivasertib	AKT	AstraZeneca	Phase 3	Locally Advanced or Metastatic TNBC	2019/6/25
Ipatasertib	AKT	Hoffmann-La Roche	Phase 3	Locally Advanced or Metastatic TNBC	2017/11/9
Alpelisib	PI3Kα	Novartis Pharmaceuticals	Phase 3	Advanced TNBC Who Carry Either a PIK3CA Mutation or Have PTEN Loss	2017-01-06
Anlotinib	PDGFR、KIT、VEGFR、FGFR、RET	Chia Tai Tianqing Pharmaceutical Group Co., Ltd.	Phase 3	TNBC	2020-05-28
Olaparib	PARP1、PARP2、PARP3	AstraZeneca	Phase 2/3	Neoadjuvant Treatment of TNBC	2017/5/12
Adavosertib	WEE1	AstraZeneca	Phase 2	Metastatic TNBC	2017-01-06
Apatinib	VEGFR2	HengRui Medicine Co., Ltd.	Phase 2	Metastatic TNBC	2010/8/6
AZD5363	AKT	AstraZeneca	Phase 2	Combination With Paclitaxel in Advanced or Metastatic TNBC	2015/4/22

Note: Only clinical stage above phase 2 are include.
Highlight in yellow are MTKi
As of Feb 19th, 2025

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Competitive Landscape of Global Small Molecular Targeted Drug on TNBC in Pipeline (2/5)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
Buparlisib	PI3K	Novartis	Phase 2	Metastatic TNBC	2012/6/27
CFI-400945	PLK4	AstraZeneca	Phase 2	Advanced or Metastatic TNBC	2022/4/20
Chiauranib	AURKB、VEGFR、CSF1R、PDGFR、KIT	Chipscreen Biosciences, Ltd.	Phase 2	Advanced TNBC	2022/4/20
Enzalutamide	AR	Astellas Pharma Inc	Phase 2	Early Stage AR (+) TNBC	2016/4/25
Fluzoparib	PARP1	HengRui Medicine Co., Ltd.	Phase 2	Neoadjuvant Treatment of TNBC	2023/4/28
IPI-549	PI3Kγ	Roche Pharma AG	Phase 2	TNBC	2019/5/23
LY3023414	mTOR、PI3K	Eli Lilly and Company	Phase 2	Metastatic TNBC	2019/7/25
PF-06873600	CDK2/4/6	Pfizer	Phase 2	TNBC and other solid tumor	2018/5/8
RP-6306	PKMYT1	Canadian Cancer Trials Group，Repare Therapeutics	Phase 2	TNBC other advanced solid tumor	2022/11/4
Rucaparib	PARP1/2/3	Clovis Oncology, Inc.	Phase 2	TNBC	2010/2/24

Note: Only clinical stage above phase 2 are include.
Highlight in yellow are MTKi
As of Feb 19th, 2025

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Competitive Landscape of Global Small Molecular Targeted Drug on TNBC in Pipeline (3/5)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
Selumetinib	MEK1/2	AstraZeneca	Phase 2	Metastatic TNBC	2019/1/11
TAK-228	mTORC1、mTORC2	Takeda	Phase 2	Metastatic TNBC	2017/6/21
TAK-117	PI3Kα	Takeda	Phase 2	Metastatic TNBC	2017/6/21
Tenalisib	PI3Kδ、PI3Kγ	Rhizen Pharmaceuticals	Phase 2	Metastatic TNBC	2024/1/3
Trilaciclib	CDK4、CDK6	G1 Therapeutics, Inc.	Phase 2	Early-stage TNBC	2021/11/9
Uprosertib	AKT	GlaxoSmithKline	Phase 2	Advanced TNBC	2013/10/17
ZEN-3694	BET	Pfizer / Newsoara Biopharma Co., Ltd.	Phase 2	TNBC	2019/4/3

Note: Only clinical stage above phase 2 are include.
As of Feb 19th, 2025

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Competitive Landscape of Global Small Molecular Targeted Drug on TNBC in Pipeline (4/5)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
Tinengotinib	**FGFR, VEGFR, JAK2, Aurora A/B**	**TransThera**	**Phase 1/2**	**TNBC**	**2021-02-08**
AK-01	AURKA	Eli Lilly and Company	Phase1/2	TNBC, SCLC, Head and neck cancer	2017/3/28
AT-1965	CMTR2	Alyssum Therapeutics	Phase1/2	TNBC and other solid tumor	2024/1/31
Ceralasertib	ATR	AstraZeneca	Phase1/2	TNBC and other solid tumor	2014/10/15
E7449	PARP1/2	Eisai Limited	Phase1/2	TNBC, B-cell Malignancies, Melanoma, Ovarian Cancer	2012/6/13
Fruquintinib	VEGFR1、VEGFR2、VEGFR3	Hutchison Medipharma Limited / BeiGene	Phase1/2	TNBC, Endometrial Cancer, Colorectal Cancer	2020/10/8
Gedatolisib	mTOR、PI3K	Kari Wisinski，Pfizer，Celcuity, Inc.，Celcuity Inc	Phase1/2	TNBC	2019/4/11
JS105	PI3Kα	Risen Pharma Tech Co., Ltd.	Phase1/2	TNBC and other solid tumor	2024/1/17
Mavorixafor	CXCR4	Abbisko Therapeutics Co, Ltd	Phase1/2	TNBC	2021/11/2
Niraparib	PARP1、PARP2	Tesaro, Inc.，Merck Sharp & Dohme Corp.，Merck Sharp & Dohme LLC	Phase1/2	TNBC, Ovarian Cancer	2016/1/18
NUV-868	BRD4	Nuvation Bio Inc.	Phase1/2	TNBC and other solid tumor	2022/2/23
Onvansertib	PLK1	Cardiff Oncology	Phase1/2	TNBC	2022/5/20

Note: Only clinical stage above phase 2 are include.
Highlight in yellow are MTKi
As of Feb 19th, 2025

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Competitive Landscape of Global Small Molecular Targeted Drug on TNBC in Pipeline (5/5)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
Pamiparib	PARP1、PARP2	BeiGene	Phase1/2	TNBC, Ovarian Cancer	2017/11/7
PF-07104091	CDK2	Pfizer	Phase1/2	TNBC, Small Cell Lung Cancer, Ovarian Cancer, Non-Small Cell Lung Cancer	2020/9/17
PQR309	PI3K、mTOR	PIQUR Therapeutics AG	Phase1/2	Locally Advanced or Metastatic TNBC	2016/3/31
Ruxolitinib	JAK1、JAK2	Incyte Corporation	Phase1/2	TNBC	2014/1/22
Talazoparib	PARP1、PARP2	Pfizer	Phase1/2	Metastatic TNBC	2019/7/31
Neratinib	HER2、HER4、EGFR	Puma Biotechnology, Inc.	Phase1/2	Metastatic TNBC	2010/4/28
Romidepsin	HDAC	Bristol-Myers Squibb	Phase1/2	Locally Recurrent or Metastatic TNBC	2015/3/19
Azenosertib	WEE1	Zentalis Pharmaceuticals	Phase1/2	TNBC	2024/4/8
SMP3124LP	CHEK1	Sumitomo Pharma America, Inc.	Phase1/2	TNBC and other solid tumor	2024/7/30
VIO-01	PARP1	Valerio Therapeutics	Phase1/2	TNBC and other solid tumor	2024/2/14

Note: Only clinical stage above phase 2 are include.
As of Feb 19th, 2025

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Global Competitive Landscape of MTK Inhibitors for TNBC At Clinical Stage

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date	Study Location
Anlotinib	PDGFR、KIT、VEGFR、FGFR、RET	Chia Tai Tianqing Pharmaceutical Group Co., Ltd.	Phase 3	TNBC	2020-06-01	China
Chiauranib	AURKB、VEGFR、CSF1R、PDGFR、KIT	Chipscreen Biosciences, Ltd.	Phase 2	Advanced TNBC	2022-02-23	China
Tinengotinib	FGFR, VEGFR, JAK, Aurora	TransThera	Phase 1/2	TNBC and other solid tumor	2021-02-08	The US, China
FNX006	RAF1, SRC, VEGFR2, FRA1	Chengdu FANXI Biopharma Co., Ltd	Phase 1	TNBC and other solid tumor	2021-02-08	China

Note: Only clinical stage above phase 2 are include.
As of Feb 19th, 2025

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Competitive Landscape of Small Molecule Targeted Drug on HR+, HER2- Breast Cancer Approved by NMPA

Drug Name	Brand Name	Target	Company	Indications	Approval Date
Entinostat	景助达®	HDAC	Taizhou EOC Pharma Co., Ltd	In combination with an aromatase inhibitor for the treatment of HR+, HER2-, advanced or metastatic breast cancer	2024/04/24
Ribociclib	Kisqali®	CDK4/6	Novartis	In combination with an aromatase inhibitor for the treatment of HR+, HER2-, advanced or metastatic breast cancer	2023/01/19
Dalpiciclib	艾瑞康®	CDK4/6	Hengrui Medicine Co.,Ltd.	In combination with an aromatase inhibitor or fulvestrant for the treatment of HR+, HER2-, advanced or metastatic breast cancer	2021/12/31
Abemaciclib	Verzenios®	CDK4/6	Eli Lilly	HR+, HER2-, early stage or advanced or metastatic breast cancer	2020/12/29
Palbociclib	Ibrance®	CDK4/6	Pfizer	HR+, HER2-, advanced or metastatic breast cancer	2018/07/31 (Capsule) 2022/08/10 (Tablet)
Chidamide	Epidaza®	HDAC1/2/3/10	Chipscreen Biosciences Co.,Ltd.	In combination with an aromatase inhibitor for the treatment of HR+, HER2-, advanced or metastatic breast cancer	2014/12/23 (2019/10/15 Approved for HR+, HER2- breast cancer)
Everolimus	Afinitor®	mTOR	Novartis	In combination with exemestane for the treatment of HR+, HER2-, advanced breast cancer	2013-01-22 (2022/03/30 Approved for HR+, HER2- breast cancer)

Note: Approval date: First approval date. Indication refers to the latest indication; None of these products were MTK inhibitors.
As of Feb 19th, 2025

Source: NMPA, Frost & Sullivan Analysis

Competitive Landscape of Small Molecule Targeted Drug on HR+, HER2- Breast Cancer Approved by FDA

Drug Name	Brand Name	Target	Company	Indications	Approval Date
Capivasertib	TRUQAP®	AKT	AstraZeneca	In combination with fulvestrant for the treatment of HR+, HER2-, locally advanced or metastatic breast cancer with one or more PIK3CA/AKT1/PTEN-alteration	2023-11-16
Alpelisib	PIQRAY®	PI3Kα	Novartis	HR+, HER2-, PIK3CA-mutated, advanced or metastatic breast cancer	2019-05-24
Abemaciclib	VERZENIO®	CDK4/6	Eli Lilly	In combination with an aromatase inhibitor or fulvestrant or as monotherapy for the treatment of HR+, HER2- advanced or metastatic breast cancer	2017-09-28
Ribociclib	KISQALI®	CDK4/6	Novartis	HR+, HER2- advanced or metastatic breast cancer	2017-03-13
Palbociclib capsule	IBRANCE®	CDK4/6	Pfizer	for the treatment of HR+, HER2- advanced or metastatic breast cancer in combination with an aromatase inhibitor or fulvestrant	2015-02-03

Note: Approval date: First approval date; Indication refers to latest indication.
As of Feb 19th, 2025

Source: FDA, Frost & Sullivan Analysis

Competitive Landscape of China Small Molecular Targeted Drug on HR+, HER2- Breast Cancer in Pipeline (1/3)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
Capivasertib	AKT	AstraZeneca	NDA	HR+ and HER2- Local Advanced, Recurrent or Metastatic Breast Cancer	2023-10-10
FCN-437c	CDK4,CDK6	Avanc Pharma	NDA	HR+ and HER2- Advanced Breast Cancer	2023-11-21
GB491	CDK4,CDK6	G1 Therapeutics / Genor Biopharma Co.,Ltd.	NDA	HR+ and HER2- Local Advanced or Metastatic Breast Cancer	2024-03-13
Birociclib	CDK4,CDK6	Xuanzhu Biopharmaceutical Co., Ltd.	NDA	HR+ and HER2- Advanced Breast Cancer	2023-09-05
BPI-16350	CDK4,CDK6	Betta Pharmaceuticals Co.Ltd	NDA	HR+ and HER2- Local Advanced, Recurrent or Metastatic Breast Cancer	2024-05-01
Inavolisib	PI3Kα	Roche	NDA	HR+, HER2-, PIK3CA-mutated, Advanced or Metastatic Breast Cancer	2024-06-03
TQB3616	CDK4,CDK6	Chiatai Tianqing Pharmaceutical Group	NDA	HR+ and HER2- Advanced Breast Cancer	2024-08-13
Afuresertib	AKT	Laekna LLC	Phase 3	HR+ and HER2- Local Advanced or Metastatic Breast Cancer	2024-05-14
Atirmociclib	CDK4	Pfizer	Phase 3	HR+ and HER2- Advanced or Metastatic Breast Cancer	2024-04-26
BEBT-209	CDK4,CDK6	BeBetter Med Co., Ltd	Phase 3	HR+ and HER2- Advanced Breast Cancer	2022-02-28
BKM120	PI3K	Novartis	Phase 3	HR+ and HER2- Advanced Breast Cancer	2015-01-21
Taselisib	PI3Kα	Roche	Phase 3	HR+ and HER2- Local Advanced, Recurrent or Metastatic Breast Cancer	2016-12-22

Note: Only clinical stage above phase 2 are include.
As of Feb 19th, 2025

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of China Small Molecular Targeted Drug on HR+, HER2- Breast Cancer in Pipeline (2/3)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
SPH4336	CDK4,CDK6	Shanghai Pharmaceuticals Holding Co.,Ltd.	Phase 2/3	HR+ and HER2- Local Advanced, Recurrent or Metastatic Breast Cancer	2023-04-26
Alpelisib	PI3Kα	Novartis	Phase 2	HR+, HER2-, PIK3CA-mutated Advanced Breast Cancer	2020-08-13
HRS-6209	CDK4	Hengrui Medicine	Phase 1/2	HR+ and HER2- Breast Cancer	2024-08-05
Tinengotinib	**FGFR, VEGFR, JAK2, Aurora A/B**	**TransThera**	**Phase 1/2**	**HR+ and HER2- Breast Cancer and Other Solid Tumor**	**2021/11/8**
APG-2575	BCL2	Ascentage Pharma Co.,Ltd.	Phase 1/2	HR+ and HER2- Breast Cancer and Other Solid Tumor	2021-11-09
BPI-1178	CDK4,CDK6	Beierda Pharmaceutical (Suzhou) Co., Ltd	Phase 1/2	HR+ and HER2- Breast Cancer and Other Solid Tumor	2020-02-18
JS105	PI3Kα	Risen (Suzhou) Pharma Tech Co., Ltd.	Phase 1/2	HR+ and HER2- Local Advanced, Recurrent or Metastatic Breast Cancer and Other Solid Tumor	2023-11-27
TQB3909	BCL2	Chiatai Tianqing Pharmaceutical Group	Phase 1/2	HR+ and HER2- Local Advanced or Metastatic Breast Cancer	2023-02-07
BEBT-908	HDAC,PI3K	BeBetter Med Co., Ltd	Phase 1/2	HR+ and HER2- Local Advanced, Recurrent or Metastatic Breast Cancer and Other Solid Tumor	2021-12-27
Purinostat	HDAC1,HDAC2	Zenitar Biomedical Technology Co., Ltd	Phase 1/2	HR+ and HER2- Breast Cancer and Other Solid Tumor	2024-05-22
KBP-2205	PARP	Keythera (Suzhou) Biopharmaceutical Co., Ltd	Phase 1/2	HR+ and HER2- Breast Cancer and Other Solid Tumor	2024-04-24

Note: Only clinical stage above phase 2 are include.
Highlight in yellow are MTKi
As of Feb 19th, 2025

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of China Small Molecular Targeted Drug on HR+, HER2- Breast Cancer in Pipeline (3/3)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
BL0175	ER	Shanghai bestlink Biotechnology Co., Ltd	Phase 1	HR+ and HER2- Breast Cancer	2025-1-24
HP568	ER	Hinova Pharmaceuticals Inc.	Phase 1/2	HR+ and HER2- Breast Cancer	2025-1-3
BGB-21447	BCL2, CDK4	BeiGene	Phase 1	HR+ and HER2- Breast Cancer	2025-1-3
HS-10502	PARP1	Shanghai Hansoh BioMedical Co.,Ltd.|Hansoh Pharmaceutical Group Company Limited	Phase 1	HR+ and HER2- Breast Cancer	2024-12-16
TQB3912	AKT	Chia Tai-tianqing Pharmaceutical	Phase 1/2	HR+ and HER2- Breast Cancer	2024-12-06

Note: Only clinical stage above phase 2 are include.
Highlight in yellow are MTKi
As of Feb 19th, 2025

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of Global Small Molecular Targeted Drug on HR+, HER2- Breast Cancer in Pipeline (1/4)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
BPI-16350	CDK4、CDK6	Betta Pharmaceuticals Co., Ltd.	Phase 3	HR+ and HER2- Locally Advanced, Recurrent or Metastatic Breast Cancer	2022/6/27
Buparlisib	PI3K	Novartis	Phase 3	HR+ and HER2- Locally Advanced or Metastatic Breast Cancer	2012/6/4
Inavolisib	PI3Kα	Roche	NDA	HR+ and HER2- Breast Cancer	2024/10/10
Ipatasertib	AKT	Roche	Phase 3	HR+ and HER2- Locally Advanced Unresectable or Metastatic Breast Cancer	2019/8/19
Lerociclib	CDK4、CDK6	Genor Biopharma Co., Ltd.	Phase 3	HR+ and HER2- Locally Advanced or Metastatic Breast Cancer	2021/9/23
PF-07220060	CDK4	Pfizer	Phase 3	HR+ and HER2- Breast Cancer	2023/10/27
TQB3616	CDK4、CDK6	Chia Tai Tianqing Pharmaceutical Group Co., Ltd.	Phase 3	HR+ and HER2- Breast Cancer	2022/5/9
XZP-3287	CDK4、CDK6	Xuanzhu Biopharmaceutical Co., Ltd.	Phase 3	HR+ and HER2- Recurrent/Metastatic Breast Cancer	2021/10/14
Gedatolisib	mTOR、PI3K	Celcuity, Inc.	Phase 3	HR+ and HER2- Breast Cancer	2022/8/16
Niraparib	PARP1、PARP2	GSK	Phase 3	HR+ and HER2- Breast Cancer, TNBC	2021/6/7
AZD5305	PARP1	AstraZeneca	Phase 3	HR+ and HER2- Locally Advanced or Metastatic Breast Cancer	2024/4/24

Note: Only clinical stage above phase 2 are include.
As of Feb 19th, 2025

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Competitive Landscape of Global Small Molecular Targeted Drug on HR+, HER2- Breast Cancer in Pipeline (2/4)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
GSK3326595	PRMT5	GSK	Phase 2	HR+ and HER2- Breast Cancer	2020/12/21
HS-10342	CDK4、CDK6	Hansoh Pharmaceutical Co., Ltd.	Phase 2	HR+ and HER2- Advanced and/or Metastatic Breast Cancer	2021/9/16
MLN0128	mTORC1、mTORC2	Calithera Biosciences, Inc, Millennium Pharmaceuticals, Inc.	Phase 2	HR+ and HER2- Advanced or Metastatic Breast Cancer That Has Progressed During or After Aromatase Inhibitor Therapy	2016/4/29
PF-06873600	CDK2、CDK4、CDK6	Pfizer	Phase 2	HR+ HER2- Metastatic Breast Cancer, Ovarian Cancer, Fallopian Tube Cancer, Primary Peritoneal Cancer, TNBC	2018/5/8
Samuraciclib	CDK7	Carrick Therapeutics Limited, Pfizer	Phase 2	HR+ and HER2- Breast Cancer	2023/7/27
SFX-01	SHP2	Evgen Pharma	Phase 2	HR+ and HER2- Metastatic Breast Cancer	2016/11/22
SPH4336	CDK4、CDK6	Shanghai Pharmaceuticals Holding Co., Ltd	Phase 2	HR+ and HER2- Breast Cancer	2023/5/24
Famitinib	FLT3、KIT、PDGFR、VEGFR、SRC、RET、FGFR	HengRui Medicine Co., Ltd.	Phase 2	HR+ and HER2- Breast Cancer	2021/2/2
Cabozantinib	MET、AXL、RET、ROS1、TYRO3、MERTK、KIT、NTRK2、FLT3、TEK、VEGFR	Exelixis	Phase 2	HR+ and HER2- Breast Cancer	2011/9/28

Note: Only clinical stage above phase 2 are include.
Highlight in yellow are MTKI
As of Feb 19th, 2025

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Competitive Landscape of Global Small Molecular Targeted Drug on HR+, HER2- Breast Cancer in Pipeline (3/4)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
Rucaparib	PARP1、PARP2、PARP3	Clovis Oncology, Inc.	Phase 2	HR+ and HER2- Breast Cancer, TNBC	2010/2/24
MK-6482	HIF2A	MSD	Phase 2	HR+ and HER2- Metastatic Breast Cancer	2024/5/24
PF-07220060	CDK4	Pfizer	Phase 2	HR+ and HER2- Breast Cancer	2024/6/18
RYZ101	SSTR2	RayzeBio, Inc.	Phase 1/2	HR+ and HER2- Breast Cancer	2024-09-19
Tinengotinib	**FGFR, VEGFR, JAK2, Aurora A/B**	**TransThera**	**Phase 1/2**	**HER2-negative Breast Cancer, TNBC and Other Solid Tumor**	2021/02/08
APG-2575	BCL2	Ascentage Pharma Group Inc.	Phase 1/2	HR+ and HER2- Metastatic Breast Cancer and Other Solid Tumor	2021/7/1
Avutometinib	RAF、MEK	Verastem Oncology / Eli Lilly and Company	Phase 1/2	HR+ and HER2- Breast Cancer	2022/11/8
AZD8421	CDK2	AstraZeneca	Phase 1/2	HR+ and HER2- Breast Cancer	2024/1/3
BPI-1178	CDK4、CDK6	Beta Pharma (Suzhou) Co., Ltd.	Phase 1/2	Advanced HR+/HER2- Breast Cancer	2020/2/24
Debio 1347	FGFR1、FGFR2、FGFR3	Debiopharm International SA	Phase 1/2	FGFR-Amplified Endocrine Receptor Positive Metastatic Breast Cancer	2017/11/17
JS105	PI3Kα	Risen (Suzhou) Pharma Tech Co., Ltd.	Phase 1/2	HR+ and HER2- Breast Cancer and Other Solid tumor	2024/1/17
PF-07104091	CDK2	Pfizer	Phase 1/2	TNBC，Small Cell Lung Cancer，Ovarian Cancer，HR-positive HER2-negative advanced or metastatic breast cancer，NSCLC	2020/9/17
TQ-B3525	PI3Kα、PI3Kδ	Chia Tai Tianqing Pharmaceutical Group Co., Ltd.	Phase 1/2	HR-positive, HER2-negative and PIK3CA Mutation Advanced Breast Cancer	2020/4/21

Note: Only clinical stage above phase 2 are include.
Highlight in yellow are MTKi
As of Aug 1st, 2024

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Competitive Landscape of Global Small Molecular Targeted Drug on HR+, HER2- Breast Cancer in Pipeline (4/4)

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date
TQB3909	BCL2	Chia Tai Tianqing Pharmaceutical Group Co., Ltd.	Phase 1/2	HR+ and HER2- Advanced Breast Cancer	2023/3/20
Tuvusertib	ATR	MSD	Phase 1/2	HR+ and HER2- Breast Cancer	2023/8/14
XL765	PI3K、mTOR	Sanofi	Phase 1/2	HR+ and HER2- Breast Cancer	2010/3/8
XZP-3287	CDK4、CDK6	Sihuan Pharmaceutical Holdings Group Ltd.	Phase 1/2	HR+ and HER2- Advanced Breast Cancer and Other Solid Tumor	2020/9/7
Purinostat	HDAC1、HDAC2	Zenitar Biomedical Technology Co., Ltd	Phase 1/2	HR+ and HER2- Breast Cancer and Other Solid Tumor	2024/5/28
VIO-01	PARP1	Valerio Therapeutics	Phase 1/2	HR+ and HER2- Breast Cancer and Other Solid Tumor	2024/2/14

Note: Only clinical stage above phase 2 are include.
As of Feb 19th, 2025

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Global Competitive Landscape of MTK Inhibitors for HR+/HER2− Breast Cancer At Clinical Stage

Drug Name	Target	Company	Clinical Stage	Indications	First Posted Date	Study Location
Famitinib	FLT3、KIT、PDGFR、VEGFR、SRC、RET、FGFR	HengRui Medicine Co., Ltd.	Phase 2	HR+ and HER2- Breast Cancer	2021/2/2	China
Cabozantinib	MET、AXL、RET、ROS1、TYRO3、MERTK、KIT、NTRK2、FLT3、TEK、VEGFR	Exelixis	Phase 2	HR+ and HER2- Breast Cancer	2011/9/28	The US
Tinengotinib	FGFR, VEGFR, JAK, Aurora	TransThera	Phase 1/2	HR+ and HER2- Breast Cancer and Other Solid Tumor	2021/2/8	The US, China

Note: Only clinical stage above phase 2 are include.
As of Feb 19th, 2025

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

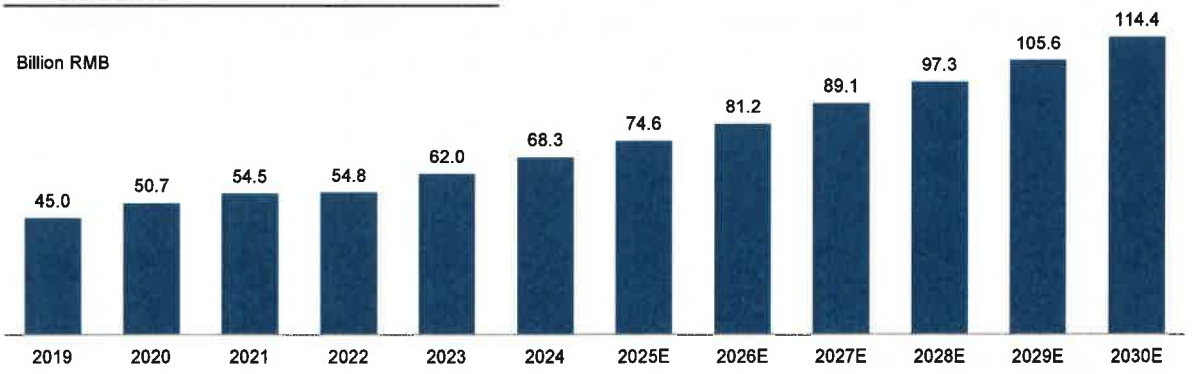
Historical and Forecasted of China Breast Cancer Drug Market [illegible], 2019-2030E

updated

- China's Breast Cancer drug market has grown from RMB45.0 billion in 2019 to RMB68.3 billion in 2024 at a CAGR of 8.7%, and expected to increase to RMB89.1 billion in 2027 at a CAGR of 9.3% from 2024 and RMB114.4 billion in 2030 at a CAGR of 8.7% from 2027.

Historical and Forecasted of China Breast Cancer Drug Market Size, 2019-2030E

Period	CAGR
2019-2024	8.7%
2024-2027E	9.3%
2027E-2030E	8.7%



Source: Frost & Sullivan Analysis

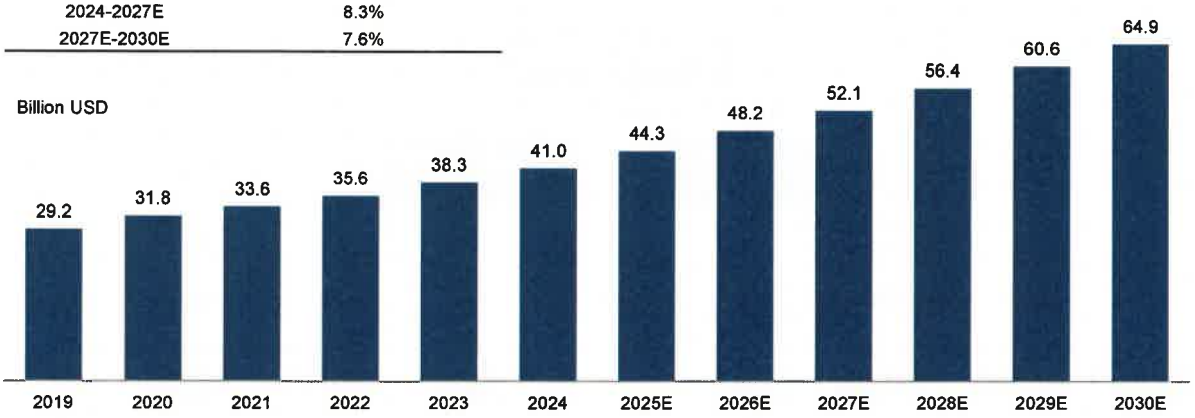
Historical and Forecasted of Global Breast Cancer Drug Market Size, 2019-2030E

updated

- Global Breast Cancer drug market has grown from USD29.2 billion in 2019 to USD41.0 billion in 2024 at a CAGR of 7.0%, and expected to increase to USD52.1 billion in 2027 at a CAGR of 8.3% from 2024 and USD64.9 billion in 2030 at a CAGR of 7.6% from 2027.

Historical and Forecasted of Global Breast Cancer Drug Market Size, 2019-2030E

Period	CAGR
2019-2024	7.0%
2024-2027E	8.3%
2027E-2030E	7.6%



Source: Frost & Sullivan Analysis

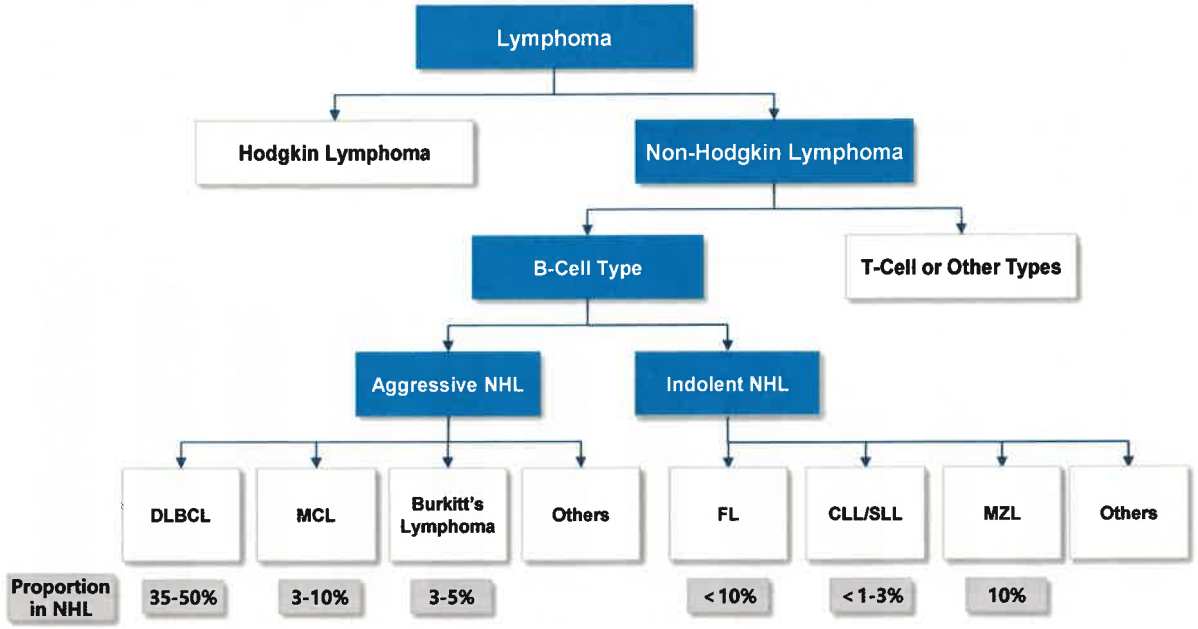
Future Trends for Breast Cancer Treatment Market

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

Source: Frost & Sullivan Analysis

Overview of Lymphoma

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

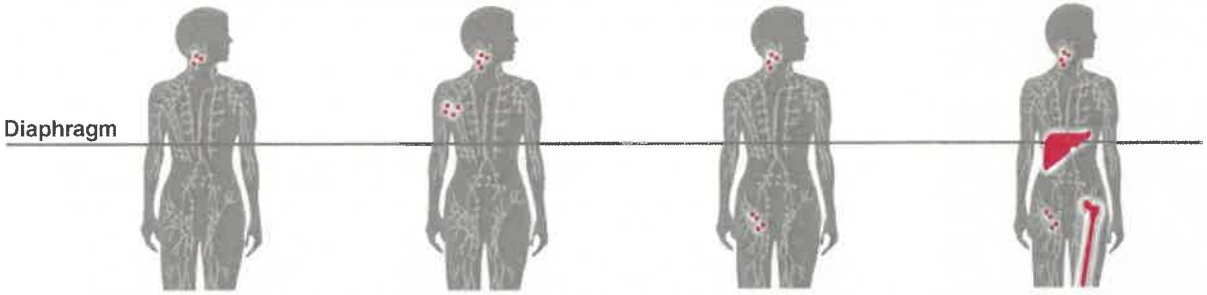


Note: DLBCL=Diffuse Large B Cell Lymphoma; MCL= Mantle Cell Lymphoma; FL=Follicular Lymphoma; CLL=Chronic Lymphocytic Leukemia; SLL=Small Lymphocytic Lymphoma; MZL=Marginal Zone Lymphoma
Source: Literature Review, Frost & Sullivan Analysis

Ann Arbor Staging Classification for Lymphoma

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

Ann Arbor Staging Classification for non-Hodgkin Lymphoma



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

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

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

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

Source: Literature Review, Frost & Sullivan Analysis

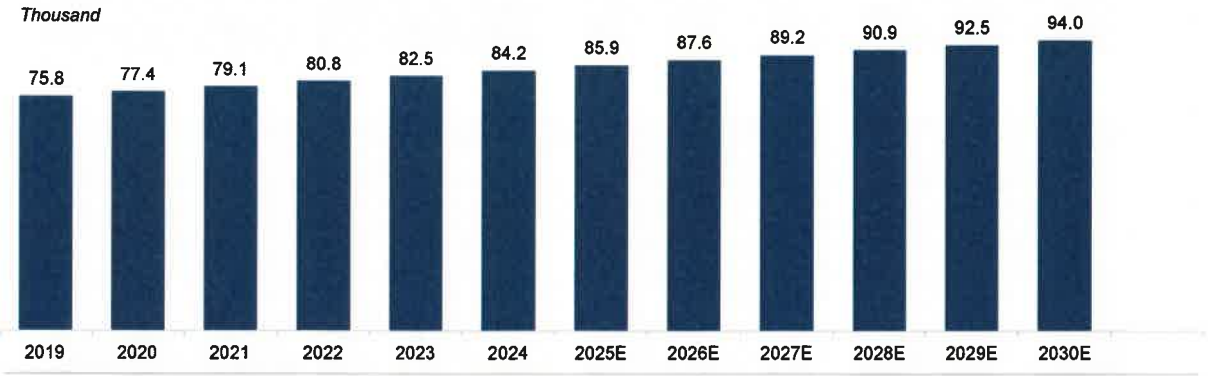
updated

Incidence of NHL in China, 2019-2030E

- Incidence number of NHL in China increased from 75.8 thousand to 84.2 thousand in 2019 and 2024. The number is expected to grow to 89.2 thousand in 2027 at a CAGR of 2.0% from 2024 to 2027. The number is expected to grow to 94.0 thousand in 2030, at a CAGR of 1.8%.

Incidence of NHL in China, 2019-2030E

Period	CAGR
2019-2024	2.1%
2024-2027E	2.0%
2027E-2030E	1.8%



Source: NCCR, Frost & Sullivan Analysis

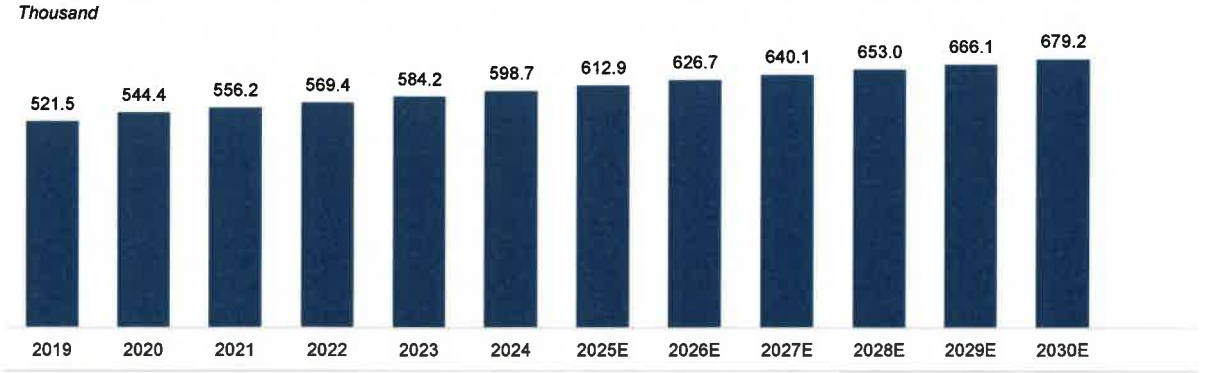
updated

Global Incidence of NHL, 2018-2030E

- Incidence number of NHL around the world increased from 509.6 thousand to 598.7 thousand in 2019 and 2024. The number is expected to grow to 640.1 thousand in 2027 at a CAGR of 2.4% from 2024 to 2027. The number is expected to grow to 679.2 thousand in 2030, at a CAGR of 2.0%.

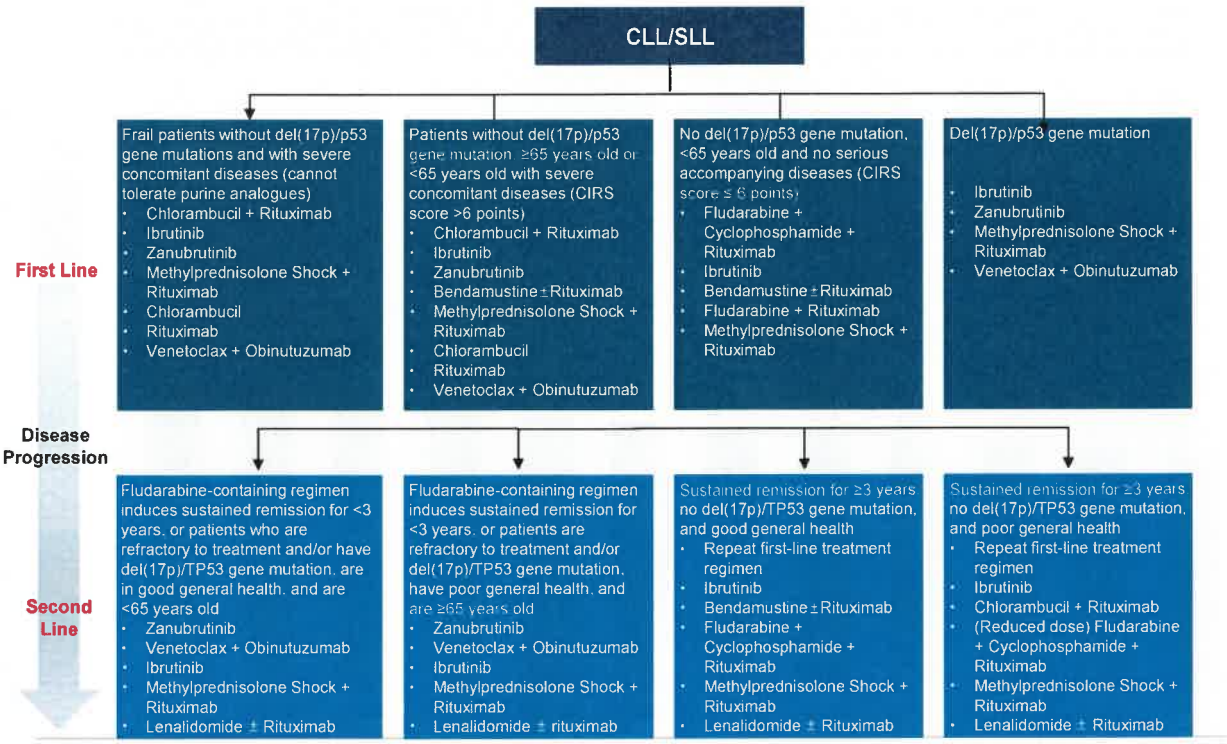
Global Incidence of NHL, 2019-2030E

Period	CAGR
2019-2024	2.8%
2024-2027E	2.4%
2027E-2030E	2.0%



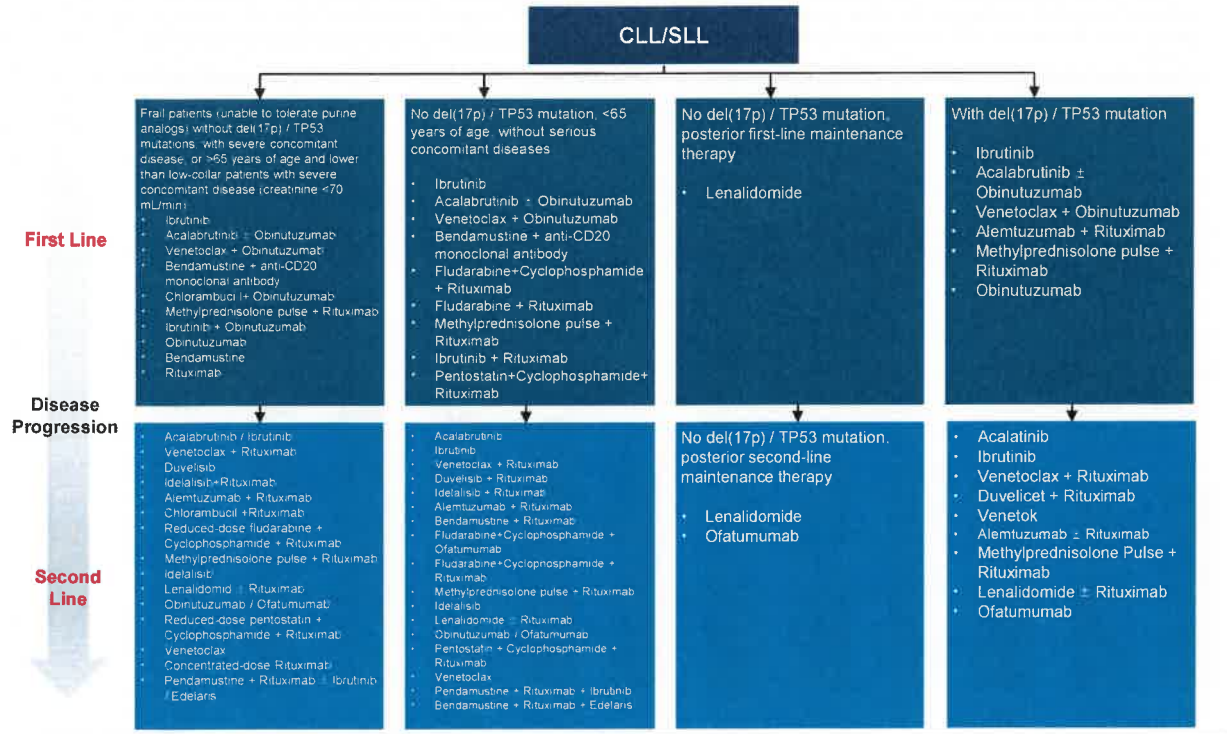
Source: IARC, Frost & Sullivan Analysis

Treatment Paradigm of CLL/SLL in China



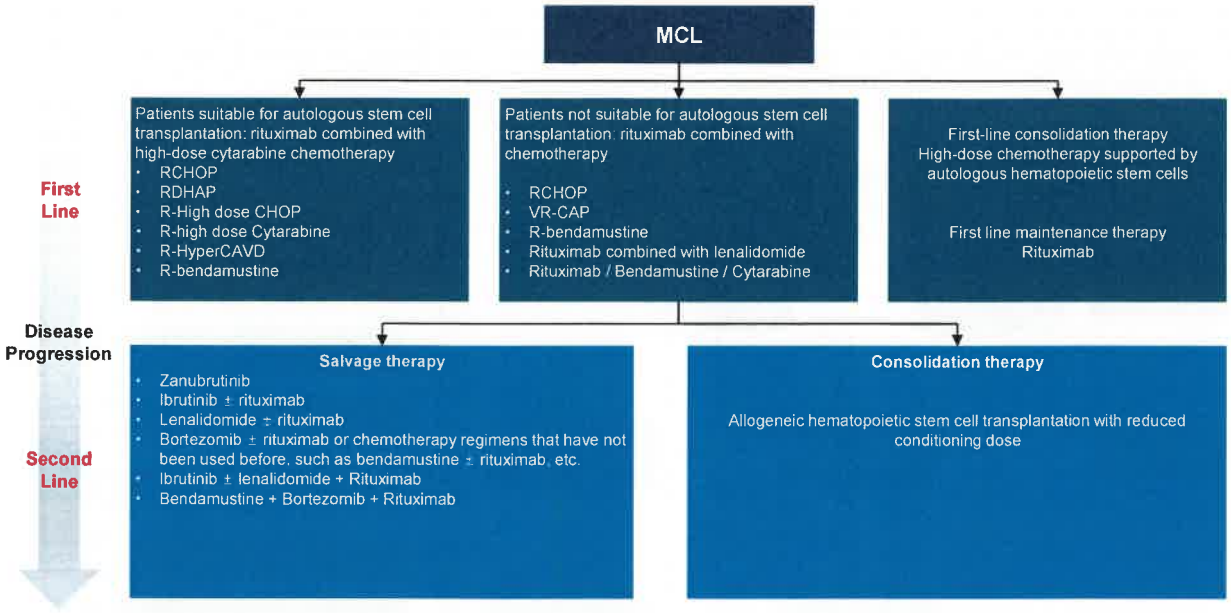
Source: CSCO, Frost & Sullivan Analysis

Treatment Paradigm of CLL/SLL in the US



Source: NCCN, Frost & Sullivan Analysis

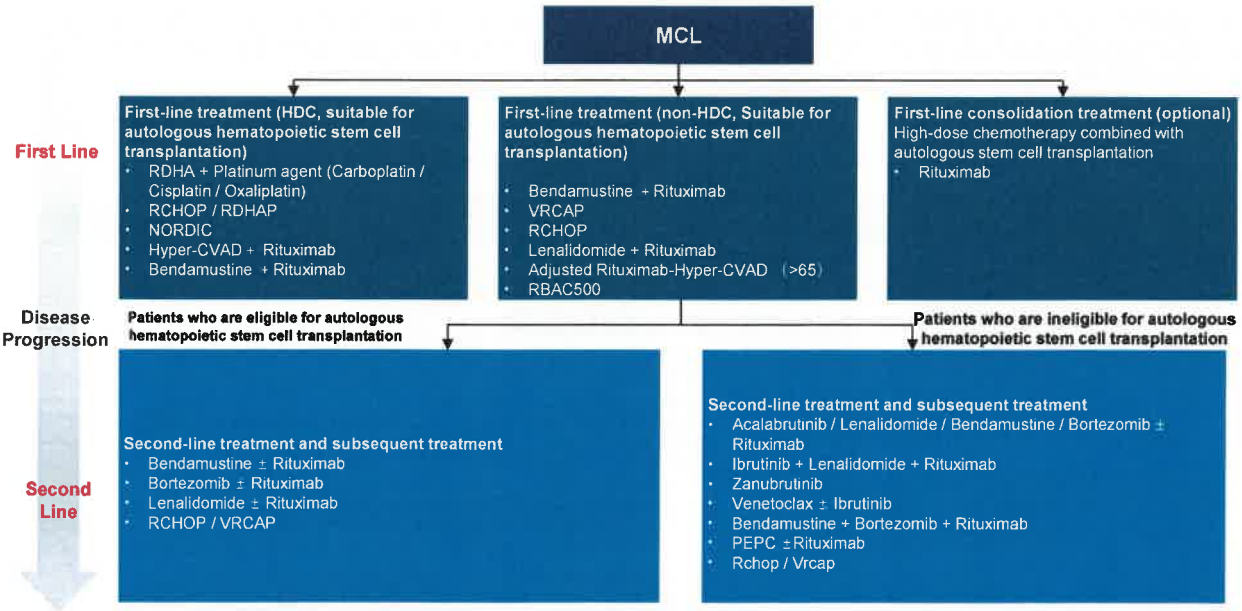
Treatment Paradigm of MCL in China



RCHOP(Rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) ;
RDHAP(Rituximab, dexamethasone, cisplatin, cytarabine);
R-High-dose CHOP(Rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone);
R-High-dose cytarabine (rituximab, cytarabine)
VRCAP (rituximab, cyclophosphamide, doxorubicin, bortezomib, prednisone)

Source: CSCO, Frost & Sullivan Analysis

Treatment Paradigm of MCL in the US



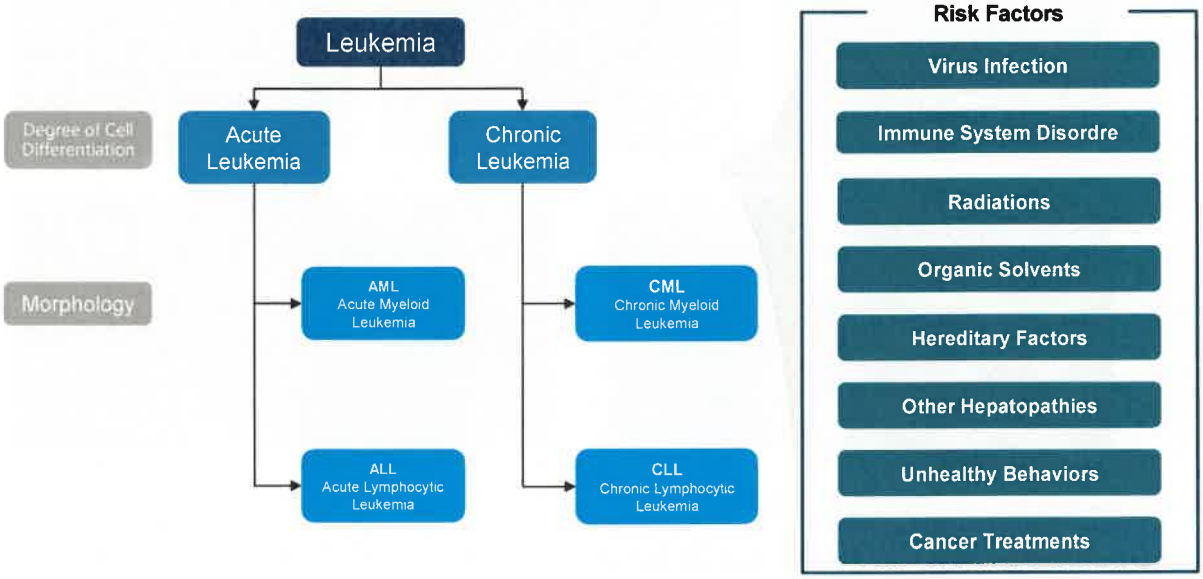
RCHOP (Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, Prednisone);
RDHAP (Rituximab, Dexamethasone, Cisplatin, Cytarabine);
CVP (Cyclophosphamide, Vincristine, Prednisone);
NORDIC: Rituximab, Cyclophosphamide, Vincristine, Doxorubicin, and Prednisone combined alternately with Rituximab, Dose-intensified induction immunochemotherapy with high-dose Cytarabine ;

RDHA (Rituximab, Dexamethasone, Cytarabine);
Hyper-CVAD (Cyclophosphamide, Vincristine, Doxorubicin, and Dexamethasone alternating with high-dose Methotrexate and Cytarabine), combined with Rituximab ;
VRCAP (Rituximab, Cyclophosphamide, Doxorubicin, Bortezomib, Prednisone);
RBAC500 (Rituximab, Bendamustine, Cytarabine);
PEPC (Prednisone, Etoposide, Promazine, Cyclophosphamide)

Source: NCCN, Frost & Sullivan Analysis

Overview of Leukemia

- Leukemia is a type of cancer which affects the production and function of blood cells, which could be caused by hereditary and environmental factors. Leukemia is rare disease(fewer than 200,000 cases per year in the U.S.), but is the most common cancer in children and teens. Most children leukemias are ALL and AML, chronic leukemias are rare in Children.
- Symptoms of leukemia vary a lot depending on its type, the common ones shares by all types include infections, blood clots or bleeding/bruising.



Source: Literature Review, Frost & Sullivan Analysis

Overview of Acute Myeloid Leukemia (AML)

- According to French-American-British (FAB) classification standard, AML can be divided into 7 subtypes, M0 through M7 on the basis of cell types from which the leukemia develops and their level of maturity. All microscopic cell observations used for FAB classification were realized after routine staining.
- AML is initially treated with chemotherapy tumor cell remission purpose. Long-term post-remission therapy is required to prevent relapse.

The French-American-British (FAB) classification for AML

FAB subtype	Name	Main Characteristics
M0	Undifferentiated acute myeloblastic	• Characterized by undifferentiated progenitor cells
M1	Acute myeloblastic leukemia with minimal maturation	• Evidence of granulocytic differentiation • No further maturation observed
M2	Acute myeloblastic leukemia with maturation	• Presence of maturation at or beyond the promyelocyte stage
M3	Acute promyelocytic leukemia (APL)	• Abnormal promyelocytes, heavy granulation • Nucleus varies greatly in size and shape, cytoplasm completely occupied by closely packed or coalescent large granules • High proportion of the hyper granular promyelocytes and fagot cells disrupted
M4	Acute myelomonocytic leukemia	• Both granulocytic and monocytic differentiation are present in varying proportions • Percentage of myeloblasts and promyelocytes always exceeds 20%
M4 eos	Acute myelomonocytic leukemia with eosinophilia	
M5	Acute monocytic leukemia	• Two subtypes occur: Poorly Differentiated, characterized by large blasts in the bone-marrow and peripheral blood, Differentiated, characterized by larger nucleus with cerebriform appearance • Both subtypes present almost total replacement of the marrow by leukemic cells
M6	Acute erythroid leukemia	• Erythropoietic component usually exceeds 50% of all the nucleated cells in the bone marrow • Presence of erythroblasts in the peripheral blood.
M7	Acute megakaryoblast leukemia	• Rapid myelofibrosis due to release of Platelet Derived Growth Factor • Resistant to treatment

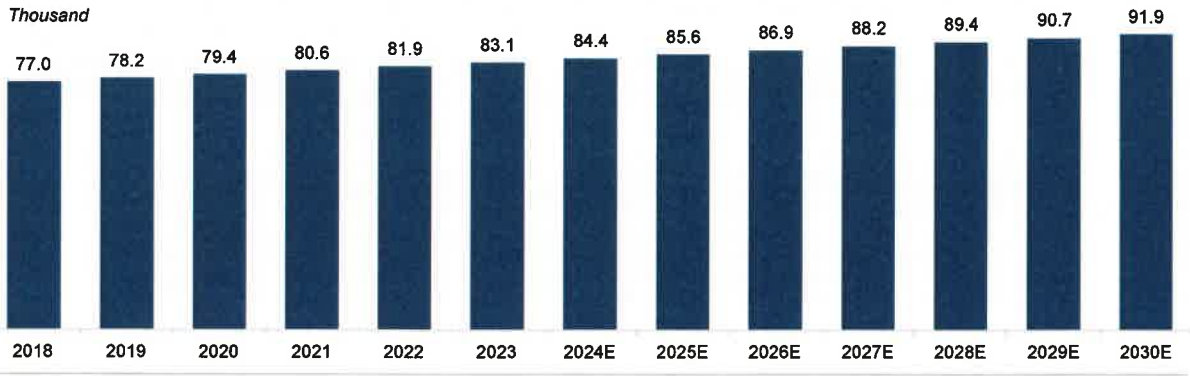
Source: Proposals for the Classification of the Acute Leukemias FAB, Frost & Sullivan Analysis

Incidence of Leukaemia in China, 2018-2030E

- Incidence number of leukaemia in China increased from 77.0 thousand to 83.1 thousand in 2018 and 2023. The number is expected to grow to 86.9 thousand in 2026 at a CAGR of 1.5% from 2023 to 2026. The number is expected to grow to 91.9 thousand in 2030, at a CAGR of 1.4%.

Incidence of Leukaemia in China, 2018-2030E

Period	CAGR
2018-2023	1.5%
2023-2026E	1.5%
2026E-2030E	1.4%



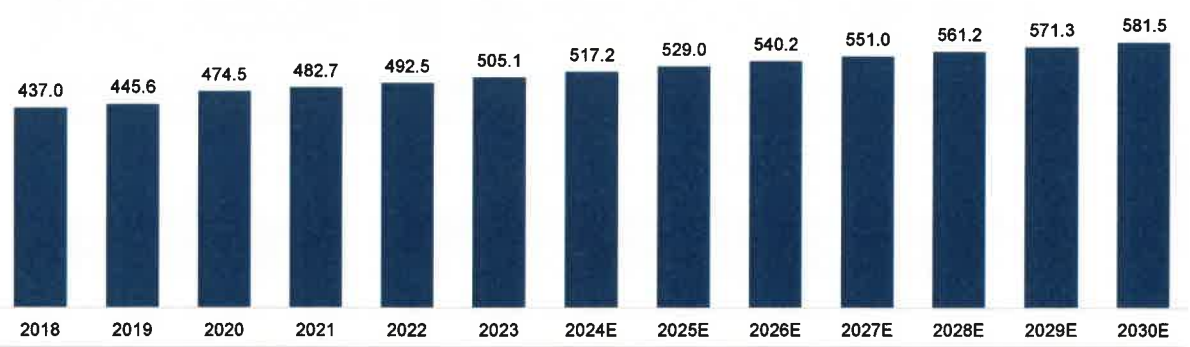
Source: NCCR, Frost & Sullivan Analysis

Global Incidence of Leukaemia, 2018-2030E

- Incidence number of leukaemia around the world increased from 437.0 thousand to 505.1 thousand in 2018 and 2023. The number is expected to grow to 540.2 thousand in 2026 at a CAGR of 2.3% from 2023 to 2026. The number is expected to grow to 581.5 thousand in 2030, at a CAGR of 1.9%.

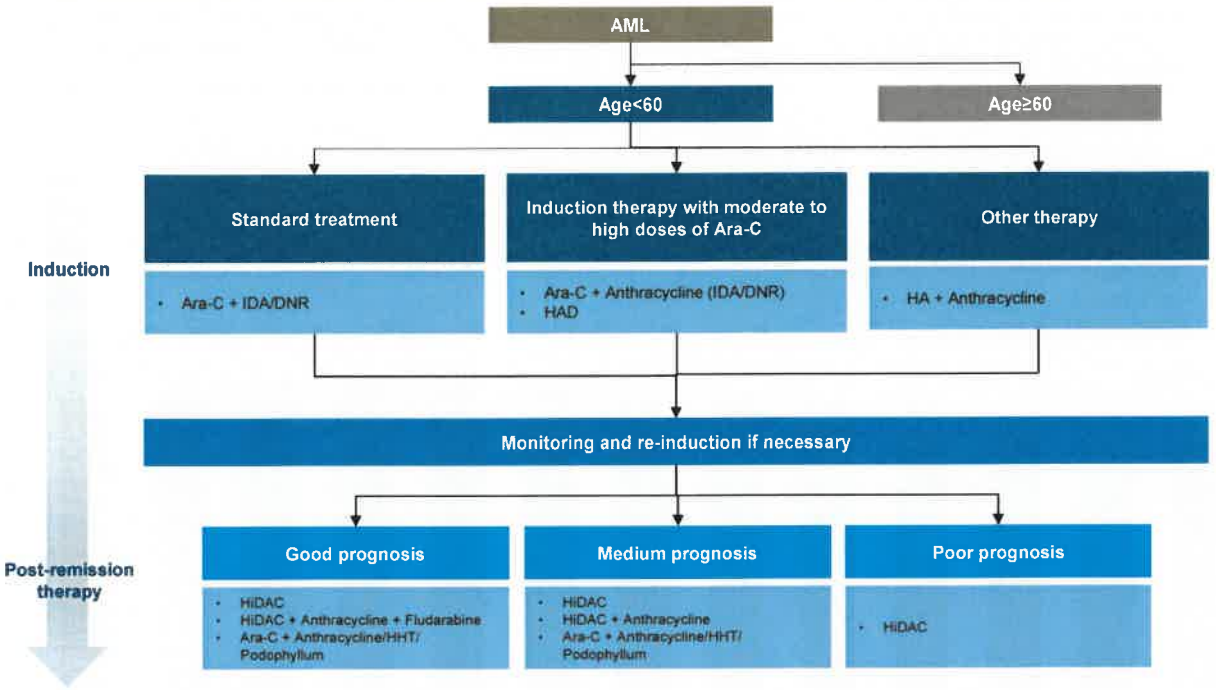
Global Incidence of Leukaemia, 2018-2030E

Period	CAGR
2018-2023	2.9%
2023-2026E	2.3%
2026E-2030E	1.9%



Source: IARC, Frost & Sullivan Analysis

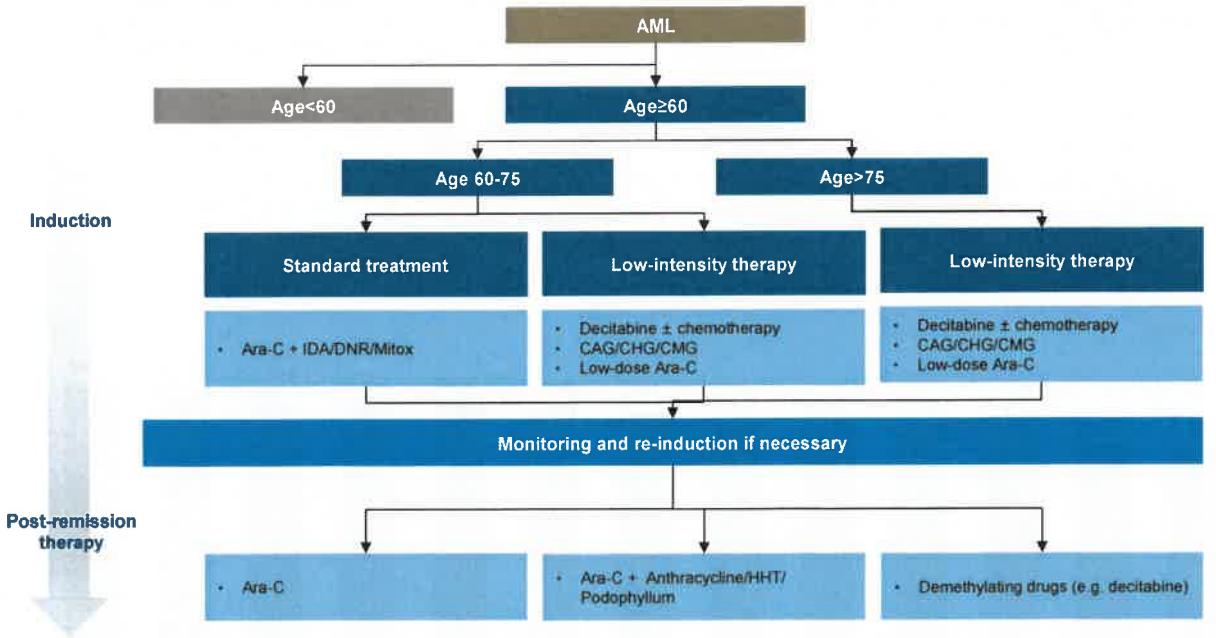
Treatment Paradigm of Acute Myeloid Leukemia (AML) in China - 1



HAD: HHT+Ara-C+DNR; HA: HHT+Ara-C; HiDAC: High dose Ara-C

Source: CSCO, Frost & Sullivan Analysis

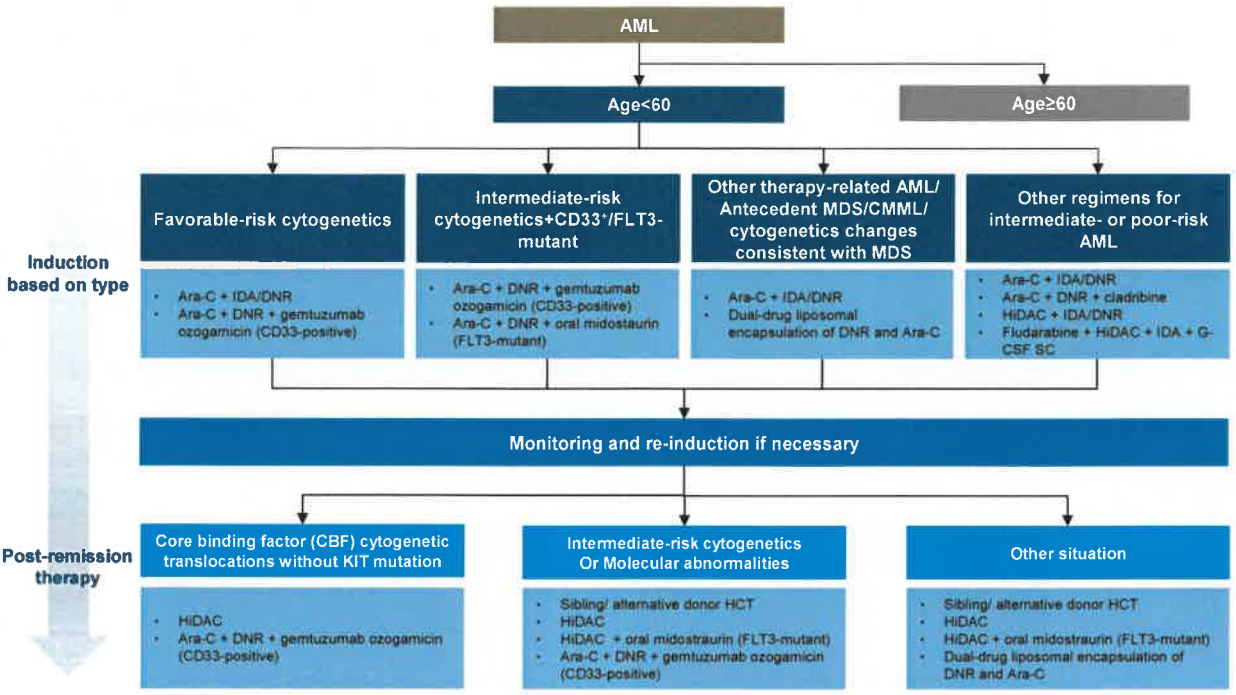
Treatment Paradigm of Acute Myeloid Leukemia (AML) in China - 2



C: Ara-C; A: Acla; H: HHT; M: Mitox; G: G-CSF

Source: CSCO, Frost & Sullivan Analysis

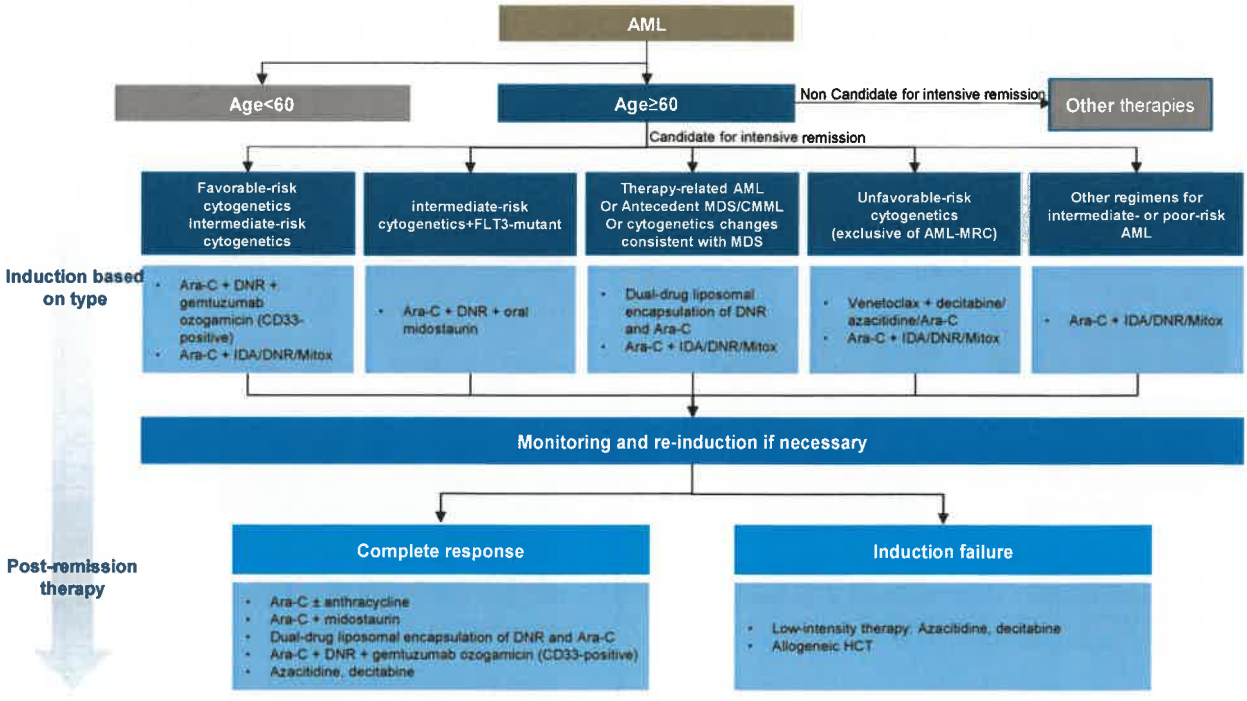
Treatment Paradigm of Acute Myeloid Leukemia (AML) in the U.S. - 1



HiDAC: High-dose cytarabine

Source: NCCN, Frost & Sullivan Analysis

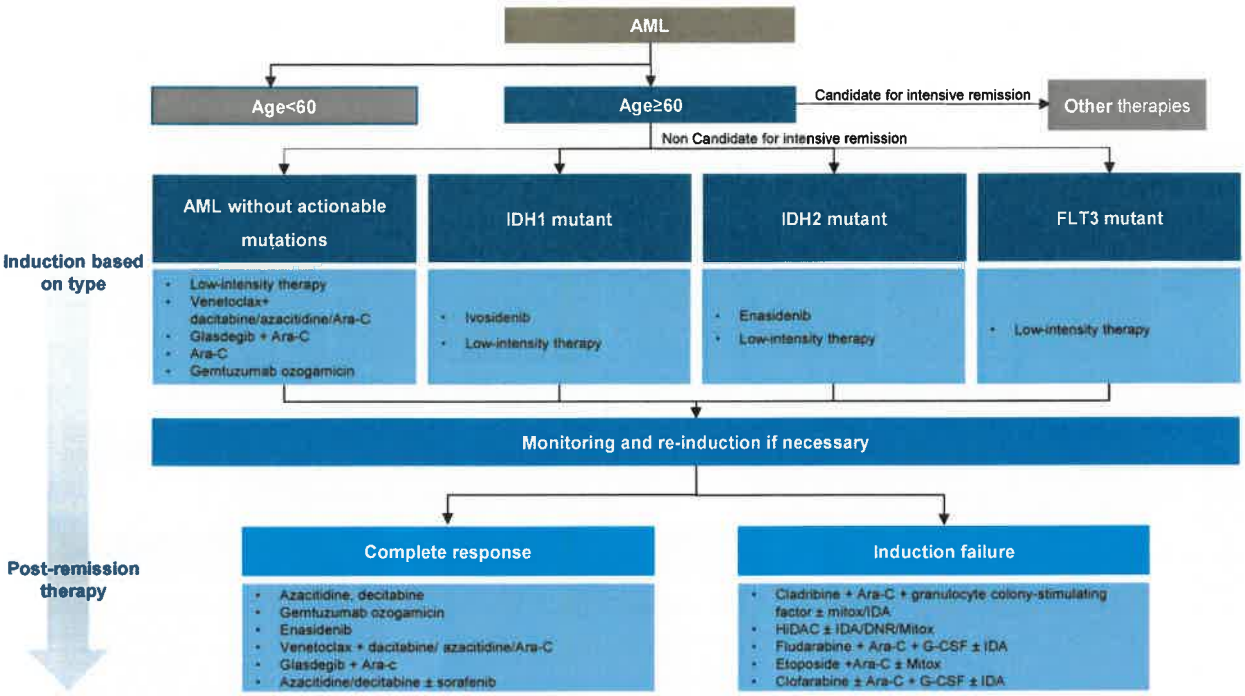
Treatment Paradigm of Acute Myeloid Leukemia (AML) in the U.S. - 2



HiDAC: High-dose cytarabine

Source: NCCN, Frost & Sullivan Analysis

Treatment Paradigm of Acute Myeloid Leukemia (AML) in the U.S. - 3

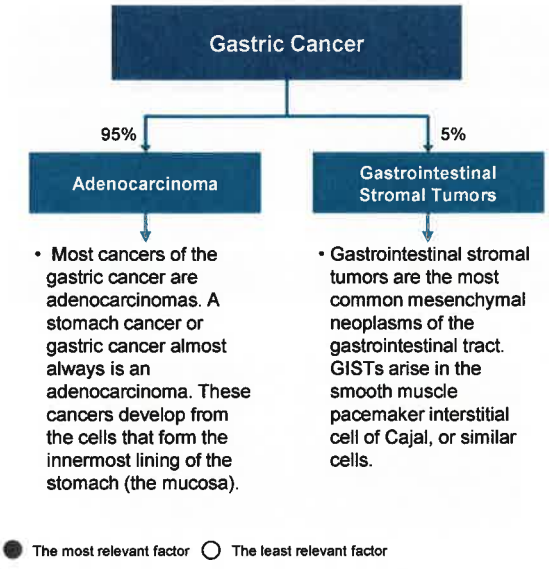


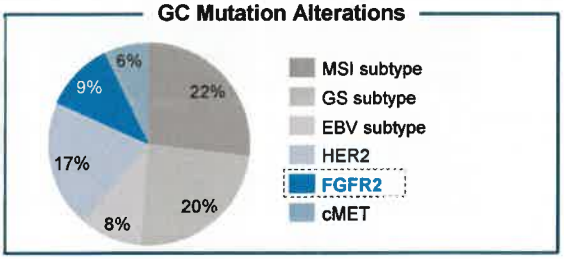
HiDAC: High-dose cytarabine; Low-intensity therapy: Azacitidine/decitabine

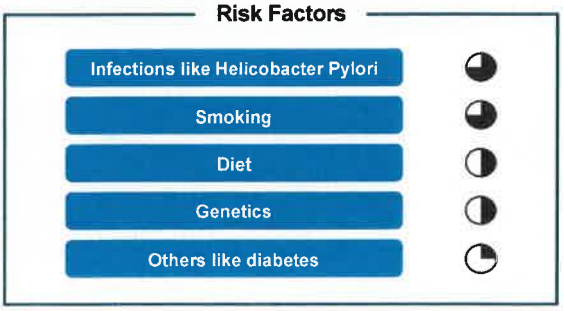
Source: NCCN, Frost & Sullivan Analysis

Overview of Gastric Cancer

- Gastric cancer is a type of tumor developing from the lining of the stomach. The cancer may spread from the stomach to other parts of the body, particularly the liver, lungs, bones, lining of the abdomen and lymph nodes. Most of the time, stomach cancer develops in stages over years.
- Early symptoms may include heartburn, upper abdominal pain, nausea and loss of appetite. Later signs and symptoms may include weight loss, yellowing of the skin, etc.







● The most relevant factor ○ The least relevant factor

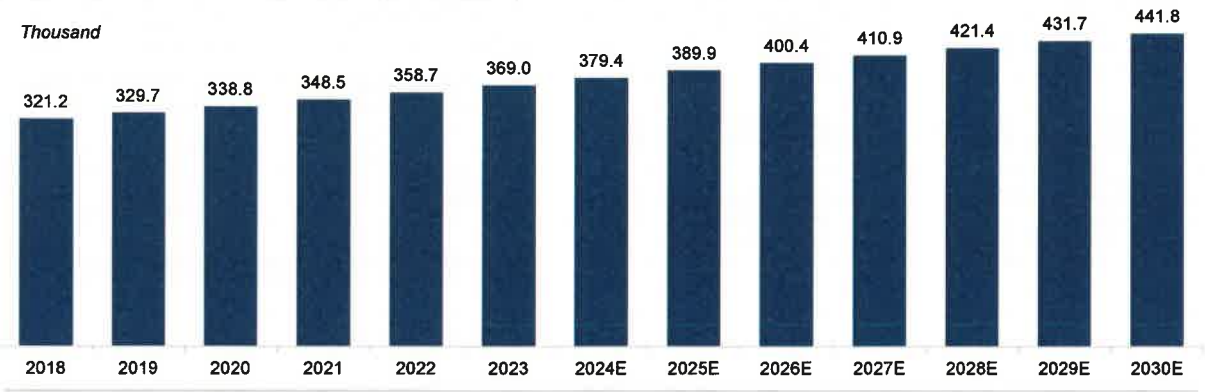
Source: Literature Review, Frost & Sullivan Analysis

Incidence of Gastric Cancer in China, 2018-2030E

- Incidence number of gastric cancer in China increased from 321.2 thousand to 369.0 thousand in 2018 and 2023. The number is expected to grow to 400.4 thousand in 2026 at a CAGR of 2.8% from 2023 to 2026. The number is expected to grow to 441.8 thousand in 2030, at a CAGR of 2.5%.

Incidence of Gastric Cancer in China, 2018-2030E

Period	CAGR
2018-2023	2.8%
2023-2026E	2.8%
2026E-2030E	2.5%



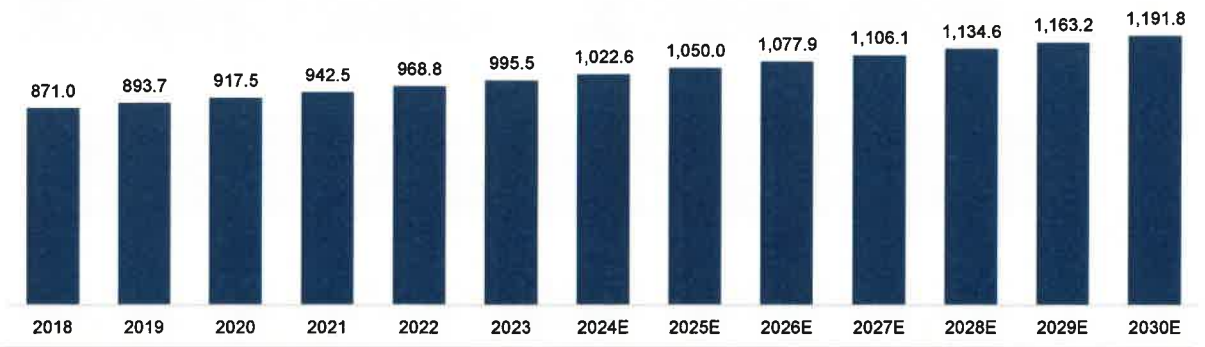
Source: NCCR, Frost & Sullivan Analysis

Global Incidence of Gastric Cancer, 2018-2030E

- Incidence number of gastric cancer around the world increased from 871.0 thousand to 995.5 thousand in 2018 and 2023. The number is expected to grow to 1,077.9 thousand in 2026 at a CAGR of 2.7% from 2023 to 2026. The number is expected to grow to 1,191.8 thousand in 2030, at a CAGR of 2.5%.

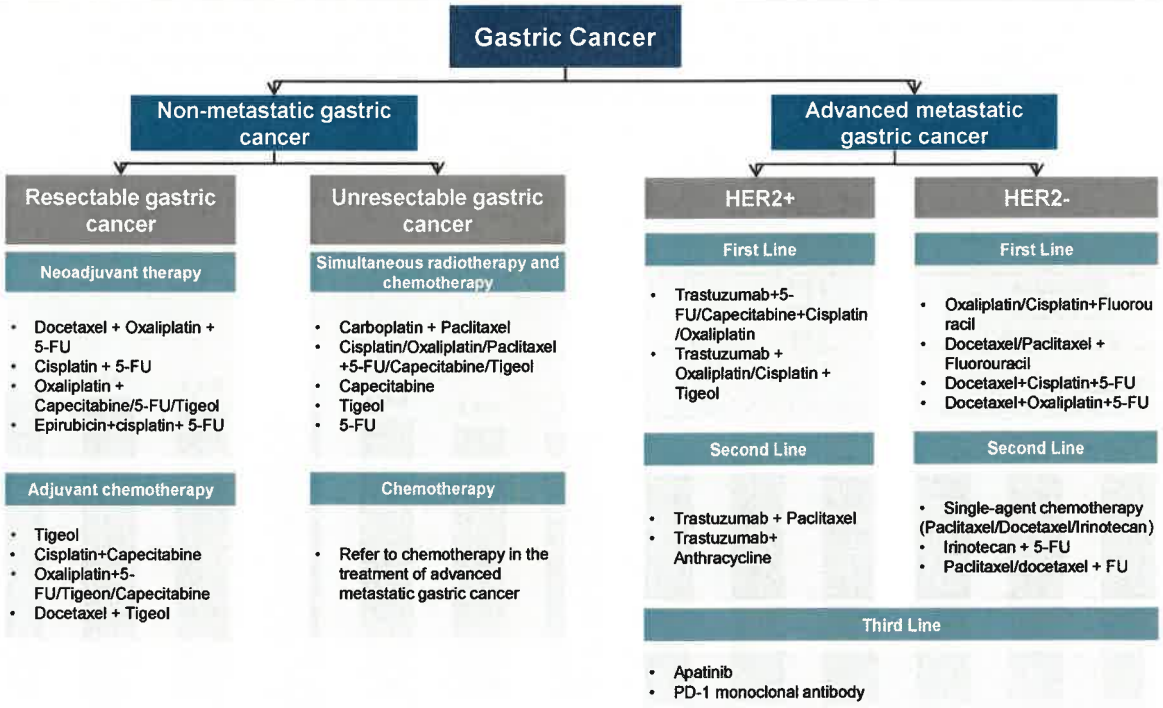
Global Incidence of Gastric Cancer, 2018-2030E

Period	CAGR
2018-2023	2.7%
2023-2026E	2.7%
2026E-2030E	2.5%



Source: IARC, Frost & Sullivan Analysis

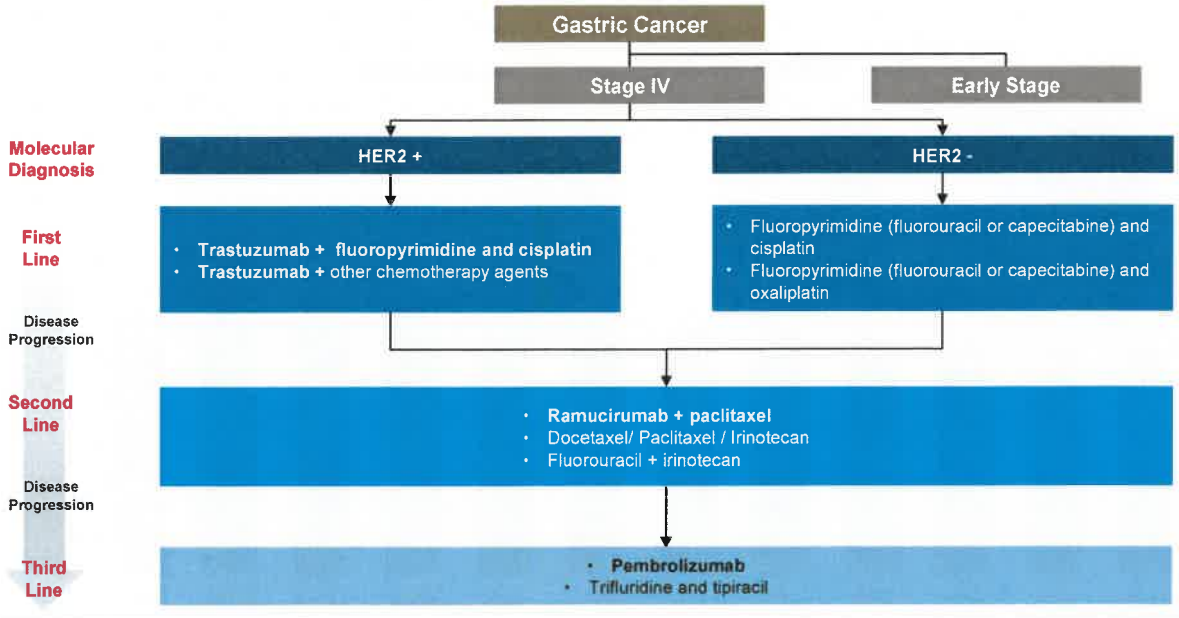
Treatment Paradigm for Gastric Cancer in China



Source: CSCO, Frost & Sullivan Analysis

Treatment Paradigm for Gastric Cancer in the U.S.

- Surgery is the main method in treating gastric cancer of stage I-III. However, if the cancer deteriorates to stage IV, the treatment switches to precision oncology therapies in combination with chemotherapies to alleviate symptoms and improve the patients' life quality. Therapies for HER2 negative patients' treatment are still limited.



Source: NCCN, Frost & Sullivan Analysis

Pain Points of Gastric Cancer Treatment

Lack of Biomarkers for Diagnosis	• The lack of specific symptoms may lead to a delayed GI cancer diagnosis as the early stages of GI cancer are usually asymptomatic or associated with nonspecific symptoms. In gastric cancer, for example, if the tumor is detected and treated before it invades the muscular layer of the stomach, the 5-year survival rate can reach 90%, it is important to establish early detection system. • In diagnosis of GI cancer, such as HCC, the lack of precise biomarkers lead to the misdiagnosis. Based on these unmet clinical needs, there will be potentially more biomarkers for HCC diagnosis, for instance, TGF-β1 is a primary signal of HCC disease progression, and can be a biomarker for diagnosis of early stage HCC. The diagnosis of gastric cancer is based on detection of gastroscopy, which brings huge discomfort for patients. Thus, chemical biomarkers of gastric cancer is required for both early diagnosis and follow up assessment for patients.
Lack of Sufficient Specific Therapies to Overcome Drug Resistance	• Currently, according to the treatment paradigm of GI cancers, insufficient quantity of specific therapy has lead to poor treatment options of advanced or metastasis GI cancers. For instance, for patients with advanced or metastasis gastric cancer, beside HER2 inhibitors and the combination of PD-1 monoclonal antibodies and VEGFR inhibitor, there is not yet any other treatment option. Unfortunately, in most of patients, cancer progress after previous targeted therapy due to drug resistance. • Compared with GI cancer, the treatment paradigm of NSCLC is now well-developed, whose disease may still be controlled well using other treatment options after the failure of 1st-line treatment. This indicates a trend that in the future, cancer patients will live longer, revealing the need of developing oncology drugs that will potentially treat patients in later lines.

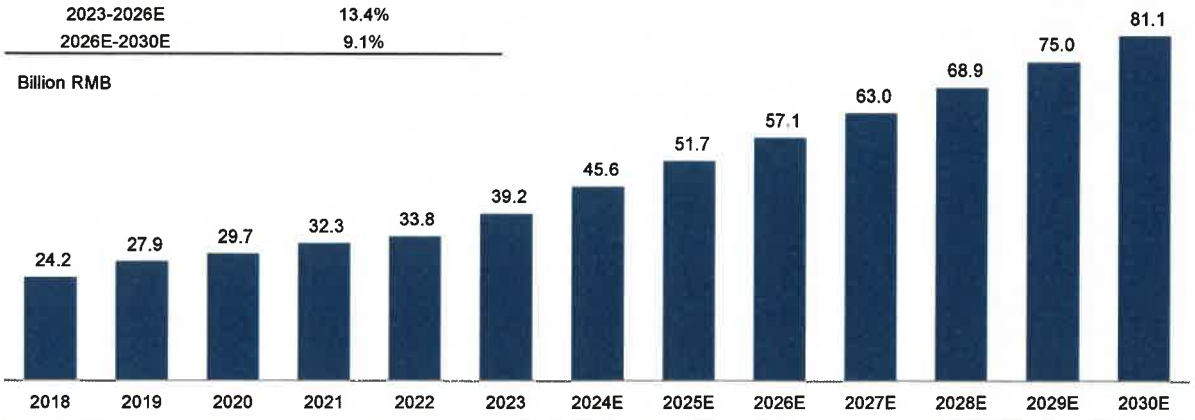
Source: Frost & Sullivan Analysis

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

- China's gastric cancer drug market size reached RMB39.2 billion in 2023, with a CAGR of 10.1% from 2018 to 2023. The market size will climb to RMB57.1 billion and RMB81.1 billion in 2026 and 2030 respectively.

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

Period	CAGR
2018-2023	10.1%
2023-2026E	13.4%
2026E-2030E	9.1%



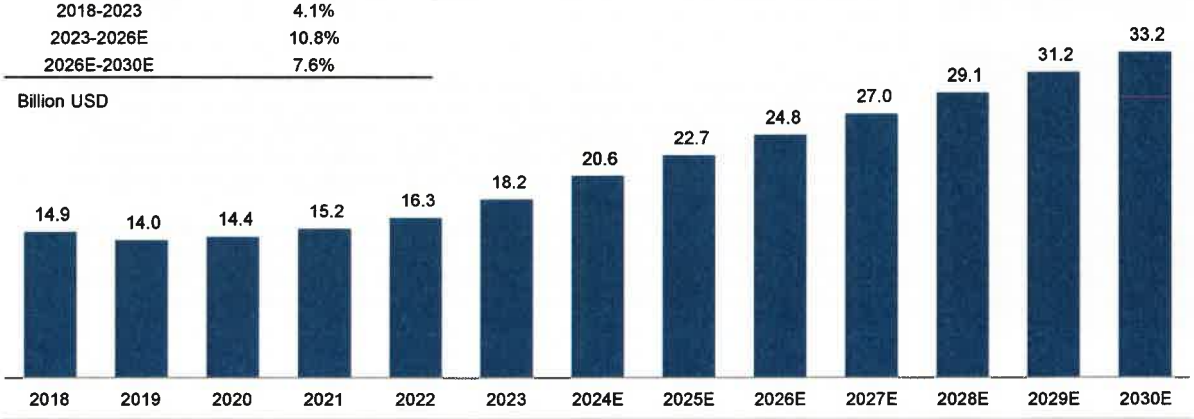
Source: Frost & Sullivan Analysis

Historical and Forecasted of Global Gastric Cancer Drug Market Size, 2018-2030E

- The global gastric cancer drug market size reached USD18.2 billion in 2023, with a CAGR of 4.1% from 2018 to 2023. The market size is expected to reach USD24.8 billion in 2026, with a CAGR of 10.8% from 2023 to 2026. The market will further grow to USD33.2 billion in 2030, with a CAGR of 7.6% from 2026 to 2030.

Historical and Forecasted of Global Gastric Cancer Drug Market Size, 2018-2030E

Period	CAGR
2018-2023	4.1%
2023-2026E	10.8%
2026E-2030E	7.6%



Source: Frost & Sullivan Analysis

Future Trends of Gastric Cancer Treatment Market

Increasing Patient Pool

- Gastrointestinal cancer include a series of cancer types in digestion system, the total capacity of GI cancer incidence is relatively huge. Influenced by the deteriorating environment, obesity and inadequate life style (excess sugar and fat), the risk of gastrointestinal cancer developing is increasing. Also, in some area in the world, the incidence of colorectal increase obviously, due to the CRC oncology screening programs launched in population.

Early Diagnosis and Prompt Treatment

- Gastrointestinal cancer usually lacks typical symptoms at disease onset, therefore increases the difficulty to detect at early stages. Patients are usually diagnosed incidentally at physical examinations or by atypical symptoms. Moreover, treatment options become significantly limited at late stages, resulting in low survival. With advancement in screening techniques and the increasing awareness of the disease, it is expected that in the future, GI cancer will be diagnosed at the early stage, and even if not, are given more treatment options when they progress to later stage.

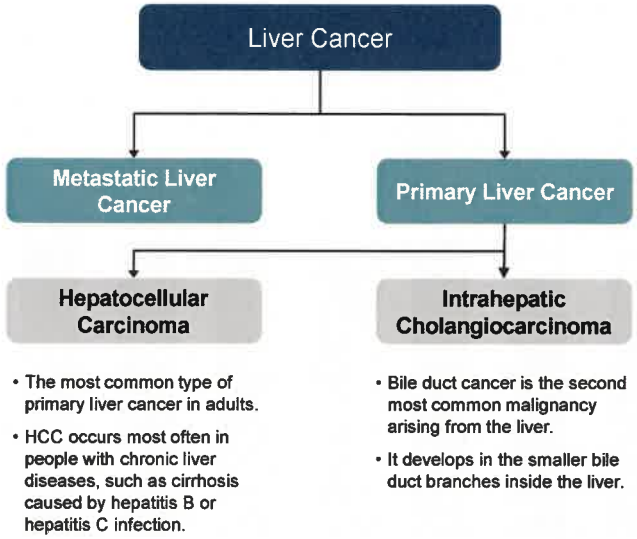
Emerging Innovative Specific Therapies

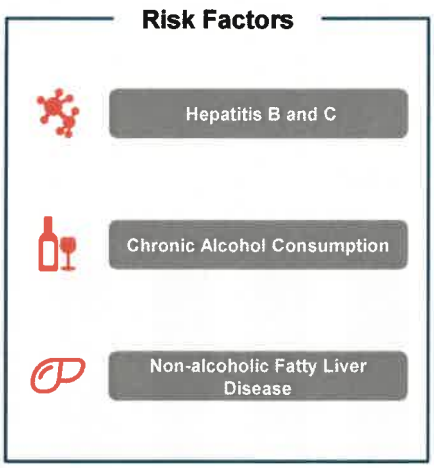
- Existing chemotherapy treatments demonstrate limited efficacy in treating relapsed or refractor patients with GI cancer due to issues such as drug resistance, metastasis, and uncontrolled disease progression. To address the conundrum, specific therapies including large molecular therapies (such as biologicals) and small molecular therapies (such as targeted drugs) are on the rise.
- For instance, there is not yet any specific therapy for pancreatic cancer, which lead to low survival rate of patients. Recently, a series of KRAS inhibitors (such as AMG-510) are in global developing pipeline, as the alteration of KRAS is a major factor in the cancer progression of pancreatic cancer.

Source: Frost & Sullivan Analysis

Overview of Liver Cancer

- Liver Cancer is the growth and spread of unhealthy cells in the liver. Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer (~90%), and is the most common cause of death in people with cirrhosis.
- The major symptoms of HCC include yellow skin, abdominal swelling due to fluid in the abdominal cavity, easy bruising from blood clotting abnormalities, loss of appetite, unintentional weight loss, abdominal pain, nausea, vomiting, etc.





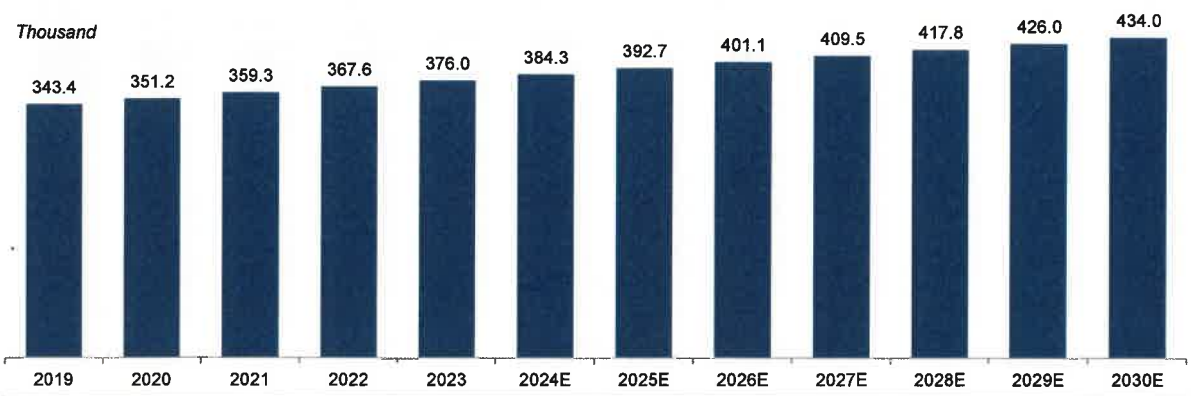
Source: Frost & Sullivan Analysis

Incidence of Liver Cancer in China, 2019-2030E

- In China, new case of liver cancer reached 376.0 thousand in 2023 at a CAGR of 2.3% from 2019. It is projected to further increase to 401.1 thousand in 2026, representing a CAGR of 2.2% from 2023. It is estimated that the incidence would achieve 434.0 thousand in 2030, representing a CAGR of 2.0% from 2026 to 2030.

Incidence of Liver Cancer in China, 2019-2030E

Period	CAGR
2019-2023	2.3%
2023-2026E	2.2%
2026E-2030E	2.0%



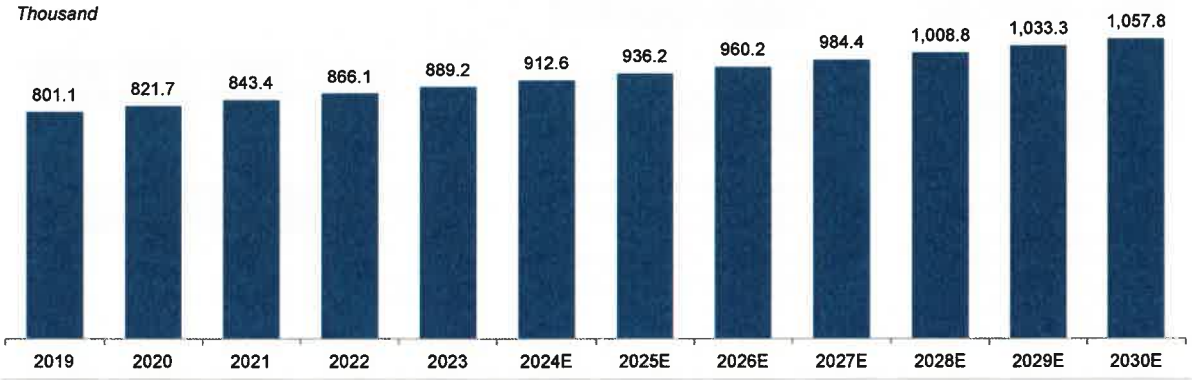
Source: NCCR, Frost & Sullivan Analysis

Global Incidence of Liver Cancer, 2019-2030E

- Between 2019 and 2023, there was an increase in the global incidence of liver cancer from 801.1 thousand to 889.2 thousand, representing a CAGR of 2.6%. It is projected that this number will continue to rise to 960.2 thousand by 2026, at a CAGR of 2.6% from 2023 to 2026. By 2030, it is expected to reach 1,057.8 thousand, growing at a CAGR of 2.4%.

Global Incidence of Liver Cancer, 2019-2030E

Period	CAGR
2019-2023	2.6%
2023-2026E	2.6%
2026E-2030E	2.4%

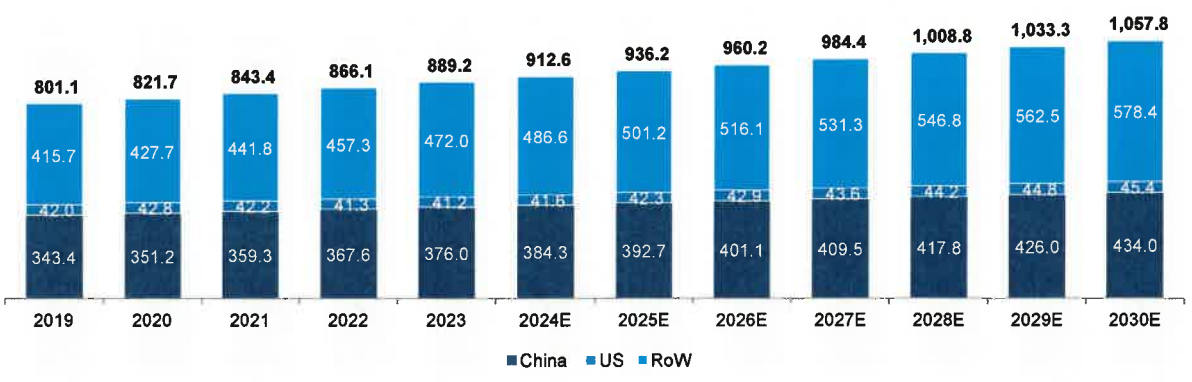


Source: IARC, Frost & Sullivan Analysis

Global Incidence of Liver Cancer by Region, 2019-2030E

Global Incidence of Liver Cancer by Region, 2019-2030E

Period	CAGR			
	China	US	RoW	Total
2019-2023	2.3%	-0.5%	3.2%	2.6%
2023-2026E	2.2%	1.4%	3.0%	2.6%
2026E-2030E	2.0%	1.4%	2.9%	2.4%



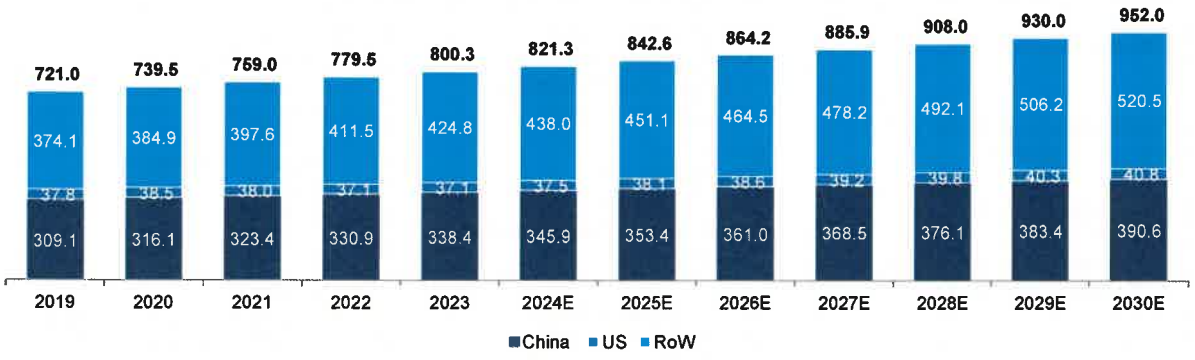
Source: IARC, Frost & Sullivan Analysis

Global Incidence of Hepatocellular Carcinoma by Region, 2019-2030E

Global Incidence of Hepatocellular Carcinoma by Region, 2019-2030E

Period	CAGR			
	China	US	RoW	Total
2019-2023	2.3%	-0.5%	3.2%	2.6%
2023-2026E	2.2%	1.4%	3.0%	2.6%
2026E-2030E	2.0%	1.4%	2.9%	2.4%

Thousand



Source: IARC, Frost & Sullivan Analysis

Treatment Paradigm of HCC in China

- According to CSCO Guidelines, HCC treatment options are different depend on the stage of the disease. For early stage HCC patients, locoregional therapies are mostly adopted while for late stage patients, the recommended treatment options are majorly systemic therapies.

Disease Stage	Recommended Therapies	Summary
Early Stage	**Liver Resection**; **Tumor Ablation**; **Radiation Therapy**; **Radio-immuno-therapy**; **Liver Transplant-ation** + TACE; Immuno-modulators; Chemotherapy; Targeted Therapy (e.g. sorafenib)	Early stage HCC treatment options are majorly locoregional ones such as liver resection, ablation, radiation therapy, radioimmunotherapy, which can be used in combination with TACE, immunomodulators, chemotherapy or targeted therapies to achieve a better treatment outcome.
Late Stage	**Small molecule targeted therapy**: **1st Line:** Sorafenib, Lenvatinib, Donafenib; Sintilimab + Bevacizumab Apatinib + Camrelizumab, Immobilizumab + temselimumab, akradine; **2nd Line:** Regorafeni b, Apatinib) **Checkpoint inhibitors + (Monoclonal antibody)** (**1st Line:** Atelizumab + Bevacivumab; **2nd Line**: PD-1) **Chemotherapy** (Oxaliplatin-based, etc)	Late stage HCC treatment options are majorly systemic treatments, including small molecular targeted therapy, checkpoint inhibitor alone or with anti-angiogenic monoclonal antibodies (such as bevacivumab) as well as chemotherapy.

Source: CSCO 2022, Frost & Sullivan Analysis

Treatment Paradigm of HCC in the U.S.

- All patients with hepatocellular carcinoma (HCC) should be evaluated for potential curative treatments, including surgical resection, liver transplantation, and ablative strategies for smaller lesions.
- Locoregional therapy for HCC includes ablation techniques like microwave or radiofrequency ablation, effective for small tumors up to 3 cm, and arterially directed therapies such as TAE and TACE targeting the tumor's arterial supply. Radiotherapy is used for inaccessible tumors or when other treatments are unsuitable due to patient health conditions.

Hepatocellular Carcinoma

Resectable or transplantable HCC	Liver-confined unresectable HCC	Extrahepatic/metastatic HCC
Resections (preferred) **Transplant** (preferred) (if met transplant criteria) **Locoregional therapy** • Ablation,(preferred) • Arterially directed therapies • Radiation therapy (RT)	**Locoregional therapy** • Ablation,(preferred) • Arterially directed therapies • Radiation therapy (RT) **Clinical Trial** **Systmatic therapy** • **1st Line:** Atezolizumab + bevacizumab; Tremelimumab-actl + durvalumab • **2nd Line:** Cabozantinib / Regorafenib/ Lenvatinib / Sorafenib	**Clinical Trial** **Systmatic therapy** • **1st Line:** Atezolizumab + bevacizumab; Tremelimumab-actl + durvalumab • **2nd Line:** Cabozantinib / Regorafenib/ Lenvatinib / Sorafenib **Palliative Care:** • Radiation therapy, Stereotactic Body Radiotherapy (SBRT)

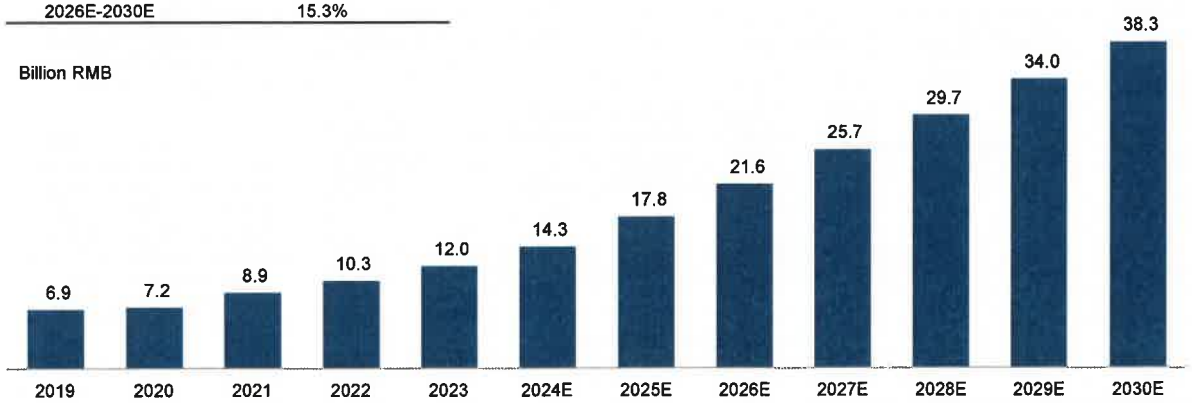
Source: NCCN 2024, Frost & Sullivan Analysis

Historical and Forecasted of China HCC Drug Market Size, 2019-2030E

- China's HCC drug market size reached RMB12.0 billion in 2023, with a CAGR of 14.7% from 2019 to 2023. The market size will climb to RMB21.6 billion and RMB38.3 billion in 2026 and 2030 respectively.

Historical and Forecasted of China HCC Drug Market Size, 2019-2030E

Period	CAGR
2019-2023	14.7%
2023-2026E	21.7%
2026E-2030E	15.3%



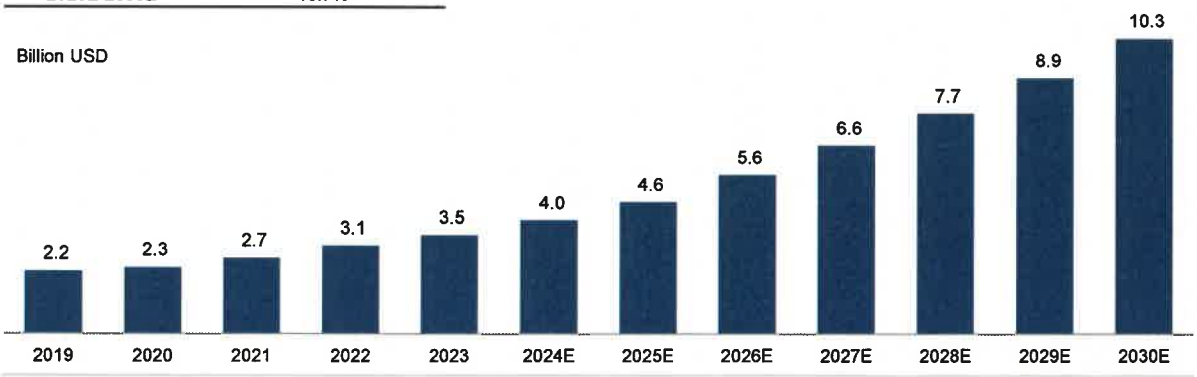
Source: Frost & Sullivan Analysis

Historical and Forecasted of Global HCC Drug Market Size, 2019-2030E

- The global HCC drug market size reached USD3.5 billion in 2023, with a CAGR of 11.9% from 2019 to 2023. The market size is expected to reach USD5.6 billion in 2026, with a CAGR of 21.7% from 2023 to 2026. The market will further grow to USD10.3 billion in 2030, with a CAGR of 16.7% from 2026 to 2030.

Historical and Forecasted of Global HCC Drug Market Size, 2019-2030E

Period	CAGR
2019-2023	11.9%
2023-2026E	17.2%
2026E-2030E	16.7%



Source: Frost & Sullivan Analysis

Competitive Landscape of Small Molecule Targeted Drug on HCC Approved by NMPA

Drug Name	Brand Name	Target	Company	Indication	Approval Date
Donafenib	泽普生Zepsun	FLT3 , BRAF , KIT , RAF1 , BRAF V600E , VEGFR2 , VEGFR3 , PDGFRB	Zelgen	HCC	2021-06-08
Apatinib	艾坦Aitan	VEGFR2	Jiangsu Hengrui Pharmaceuticals Co., Ltd.	HCC	2020-12-29
Lenvatinib	乐卫玛 LENVIMA	PDGFA , KIT , RET , VEGFR , FGFR	Eisai Co., Ltd.	HCC	2018-09-04
Regorafenib	拜万戈 Stivarga	BRAF , DDR2 , MAPK11 , RET , NTRK1 , FRK , ABL1 , TEK , PDGFR , RAF1 , KIT , VEGFR , EPHA2 , FGFR	Bayer AG	HCC	2017-03-22
Sorafenib	多吉美 Nexavar	FLT3 , BRAF , KIT , RAF1 , BRAF V600E , VEGFR2 , VEGFR3 , PDGFRB	Bayer AG	HCC	2006-09-12

Note: Approval date: First approval date
As of Feb 19th 2025

Source: NMPA, Frost & Sullivan Analysis

Competitive Landscape of Small Molecule Targeted Drug on HCC Approved by FDA

Drug Name	Brand Name	Target	Company	Indications	Approval Date
Cabozantinib	CABOMETYX	c-Met,AXL,RET,ROS1,TYRO3,MERTK,KIT,NTRK2,FLT3,TEK,VEGFR	EXELIXIS INC	HCC	2016-4-25
Lenvatinib	LENVIMA	PDGFA,KIT,RET,VEGFR,FGFR	EISAI INC	HCC	2015-2-13
Regorafenib	STIVARGA	FLT3 , BRAF , KIT , RAF1 , BRAF V600E , VEGFR2 , VEGFR3 , PDGFRB	BAYER HLTHCARE	HCC	2012-09-27
Sorafenib	Nexavar	FLT3 , BRAF , KIT , RAF1 , BRAF V600E , VEGFR2 , VEGFR3 , PDGFRB	Bayer AG	HCC	2006-9-12

Note: Approval date: First approval date
As of Feb 19th 2025

Source: FDA, Frost & Sullivan Analysis

Pain Points of Treatment on hepatocellular carcinoma

Therapeutic Limitations in HCC	• Sorafenib and lenvatinib, two small molecule targeted drugs, are first-line treatment options for late-stage cases. However, fewer than one-third of patients benefit from sorafenib, and drug resistance typically develops within six months of the initial regimen. • Current immuno-oncology therapies still do not provide significant benefits in terms of progression-free and overall survival. The limited efficacy of these treatments highlights theurgent need for more effective strategies, such as innovative bispecific antibodies
The Biomarker Gap in HCC Targeted and Immune Therapies	• Currently, there is a lack of reliable molecular biomarkers to predict adverse reactions to targeted and immunotherapies. Consequently, severe treatment-related adverse events (TRAEs) cannot be avoided during therapy, leading to dose reduction or treatment discontinuation due to intolerance. This ultimately compromises the maintenance of therapeutic efficacy

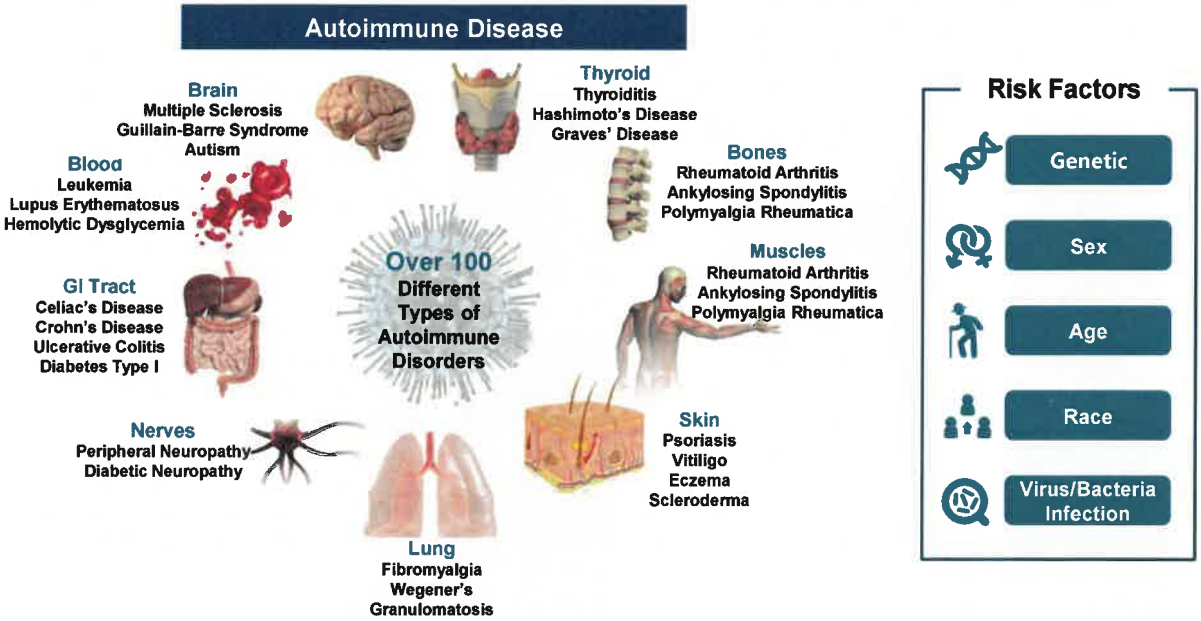
Source: Frost & Sullivan Analysis

Table of Contents

Overview of Autoimmune Disease

Major Type and Risk Factor

- An autoimmune disease is a condition in which the body's immune system mistakenly attacks body, which can be associated with over-activity of the immune system. Autoimmune diseases are hard to diagnose, and many different types of autoimmune disease share similar symptoms.
- There are roughly 100 different types of autoimmune disorders, which can affect almost any part of the body, including the heart, brain, nerves, muscles, skin, eyes, joints, lungs, kidneys, glands, the digestive tract, and blood vessels.



Source: Literature Review, Frost & Sullivan Analysis

Classification and Characteristics of Autoimmune Disease

Classification of Autoimmune Disease

Systemic Autoimmune Disease:	Organ-specific Autoimmune Disease:
• In systemic diseases the immune system attacks self antigens in several organs.	• Immune response is directed toward antigens in a single organ.
• Systemic Lupus Erythematosus (SLE) • Rheumatoid Arthritis (RA) • Atopic Dermatitis (AD) • Sjögren's Syndrome (SS) • Ankylosing Spondylitis (AS) • Psoriasis (PS), and etc.	• Chronic Lymphocytic Thyroiditis • Chronic Ulcerative Colitis • Primary Biliary Cirrhosis (PBC) • Idiopathic Thrombocytopenic Purpura (ITP) • Multiple Sclerosis • Acute Idiopathic Polyneuritis, and etc

Characteristics of Autoimmune Disease

Hard-to-treat

- Autoimmune disease exhibit complicated mechanism, multiple clinical manifestation and associated with genetic factors.
- There is no specified antigen found so far for autoimmune disease, and therefore not able to give targeted treatment clinically.
- Up to this point, as the only clinically available option, immunosuppressive therapy brings no cure while often leads to severe infections.

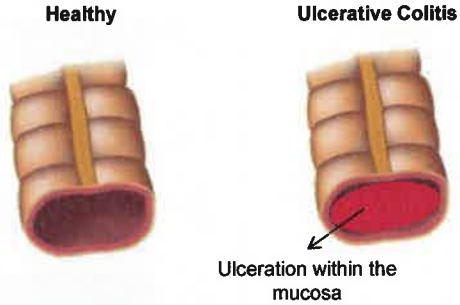
Substantial socio-economic burden

- The prevalence of autoimmune disease continuously increases in both developing and developed countries.
- Patients suffer from compromised body function, quality of life, productivity and social participation, which together increase burden of the family and society.
- Autoimmune diseases usually requires meticulous care as well as continuous and expensive drug treatment, exerting high spending pressure on patients and the society.

Source: Frost & Sullivan Analysis

Overview of Ulcerative Colitis (UC)

- UC is a chronic immune-mediated inflammatory condition of the large intestine that is frequently associated with inflammation of the rectum but often extends proximally to involve additional areas of the colon.
- Several risk factors including environmental factors, diet, intestinal infectious agents, hygiene, stress, and lifestyle have been reported to be associated with the increased incidence of UC.



Risk Factors	• Diet, Stress • Heredity • Age • Race or ethnicity • Family history

Causes	• Exact cause of UC remains unknown. • Possible cause: immune system malfunction
Symptoms	• Diarrhea, often with blood or pus • Abdominal pain and cramping • Rectal pain • Rectal bleeding — passing small amount of blood with stool • Urgency to defecate • Inability to defecate despite urgency • Weight loss • Fatigue • Fever
Diagnosis Method	• Direct visualization (sigmoidoscopy or colonoscopy) • Barium enema.

Source: Literature review, Frost & Sullivan Analysis

Overview of Ulcerative Colitis (UC)

Disease Burdens and Epidemiology

- As a progressive disease with chronic nature, Ulcerative Colitis (UC) inflicts not only physical, but also psychological, economic and social burdens on patients.
- Ulcerative Colitis (UC) is more common in western countries than in China. The patient population is higher in UC male than in female, and the median age of disease onset is around 40.
- Approximately 70% of Chinese UC patients have a moderate or severe disease course.

Disease Burdens

Physical Burden
- Lack of control over bodily functions
- Impaired activity

Psychological Burden
- Fear of disease progression and life quality change; anxiety

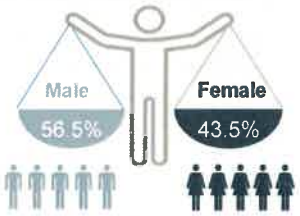
Economic Burden
- Long-term medical costs will exert financial burden on patients

Social Burden
- Employment opportunities and social activities are hampered

Potential Risks if left uncontrolled

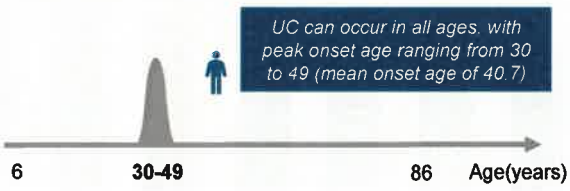
- Progression to Colorectal Cancer (CRC)
- Severe psychological disorders
- Impact on employment opportunities and social activities

Disease Epidemiology



According to a retrospective study on UC epidemiology in China, there is a higher incidence of UC in male compared to female, with the male to female ratio of ~1.3:1.

Age profile of UC patients



Source: Literature review, Frost & Sullivan Analysis

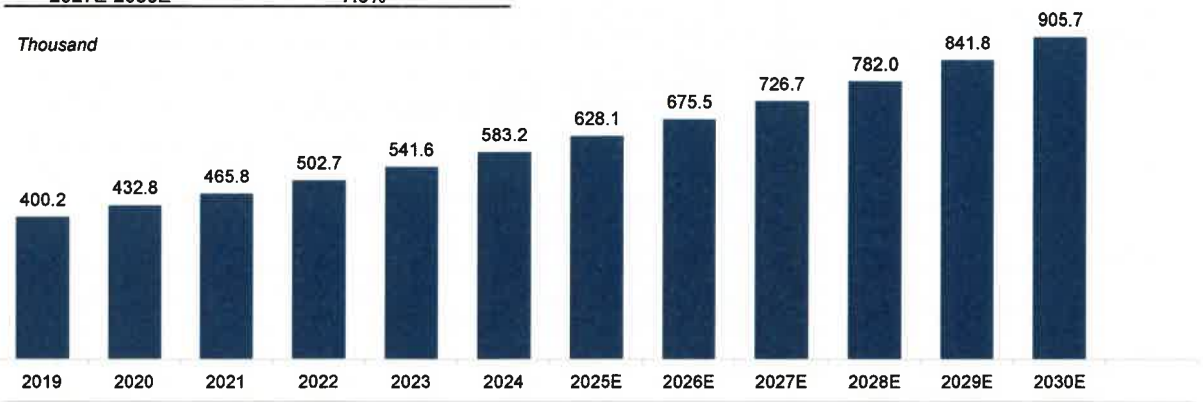
Updated

Prevalence of Ulcerative Colitis in China, 2018-2030E

- Prevalence number of ulcerative colitis in China increased from 370.1 thousand to 541.6 thousand in 2018 and 2023. The number is expected to grow to 675.5 thousand in 2026 at a CAGR of 7.6% from 2023 to 2026. The number is expected to grow to 905.7 thousand in 2030, at a CAGR of 7.6%.

Prevalence of Ulcerative Colitis in China, 2019-2030E

Period	CAGR
2019-2024	7.9%
2024-2027E	7.6%
2027E-2030E	7.6%



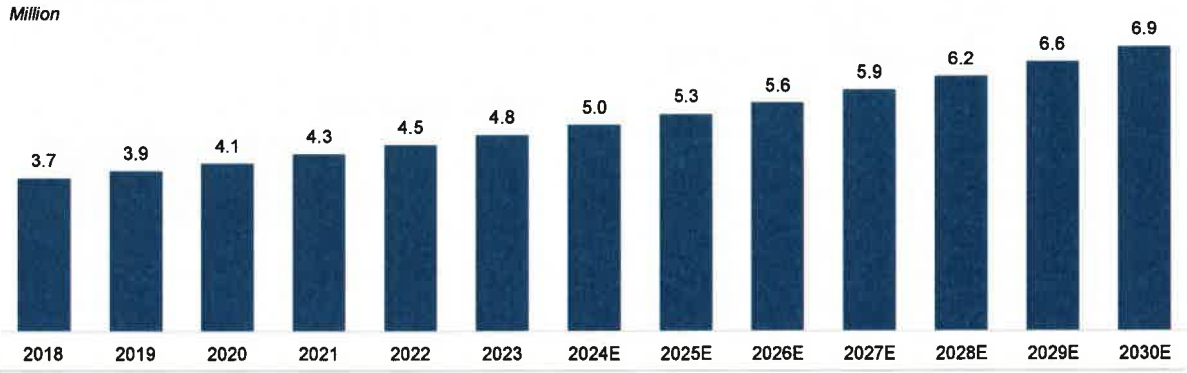
Source: Literature Review, Frost & Sullivan Analysis

Global Prevalence of Ulcerative Colitis, 2018-2030E

- Prevalence number of ulcerative colitis around the world increased from 3.7 million to 4.8 thousand in 2018 and 2023. The number is expected to grow to 5.6 million in 2026 at a CAGR of 5.2% from 2023 to 2026. The number is expected to grow to 6.9 million in 2030, at a CAGR of 5.6%.

Global Prevalence of Ulcerative Colitis, 2018-2030E

Period	CAGR
2018-2023	5.1%
2023-2026E	5.2%
2026E-2030E	5.6%



Source: Literature Review, Frost & Sullivan Analysis

Treatment Paradigm of Ulcerative Colitis in China

- The treatment paradigm of UC can be divided into active treatment and maintenance treatment.
- Mesalazine is the first-line treatment for mild to moderate active UC. If the treatment with sufficient Mesalazine is ineffective, it is recommended to replace it with oral systemic glucocorticoids or biologics to induce remission.
- For patients with moderate to severe active UC, orally or intravenously Glucocorticoid is recommended, while for those poor response to or intolerant to Mesalazine, immunosuppressive drugs as well as Glucocorticoid, biologics and small molecule inhibitors are recommended.
- For maintenance treatment of mild to moderate UC, Mesalazine is the first drug option. Immunosuppressive drugs, biologics and small molecule inhibitors are applicable to patients failure to prior glucocorticoid therapy.
- For maintenance treatment of moderate to severe UC, biologics and small molecule inhibitors are highly recommended.

	Disease Stage	Major Treatments
Active	Mild to Moderate	• Mesalazine** • Glucocorticoid • Biologics (Infliximab/Adalimumab/Vedolizumab/Ustekinumab) • Selective leukoadsorption therapy • Traditional Chinese Medicine (TCM)
	Moderate to Severe	• Glucocorticoid • Biologics (Infliximab/Vedolizumab) • Immunosuppressive drugs (6-Mercaptopurine/Azathioprine) • JAK inhibitor (Upadacitinib)
Maintenance	Mild to Moderate	• Mesalazine • Immunosuppressive drugs (6-Mercaptopurine/Azathioprine/Thalidomide) • Biologics (Infliximab/Vedolizumab) • JAK inhibitor (Upadacitinib/Tofacitinib*)
	Moderate to Severe	• Biologics (Infliximab/Vedolizumab) • JAK inhibitor (Upadacitinib/Tofacitinib*)

*Note: Tofacitinib has not approved for the indication of UC in China.
**Note: Mesalazine is a type of aminosalicylate

Source: Guidelines for diagnosis and treatment of ulcerative colitis in China 2023, Frost & Sullivan Analysis

Competitive Landscape of Small Molecule Targeted Drug on Ulcerative Colitis Approved by NMPA

Drug Name/Code	Brand Name	Target	Company	Indications	Approval Date
Upadacitinib	Rinvoq®	JAK1	AbbVie	Atopic Dermatitis; Rheumatoid Arthritis; Psoriatic Arthritis; Ulcerative Colitis; Crohn's Disease	2022-02-18 (2023-02 approved for the indication of Ulcerative Colitis)

*Note: Approval date: First approval date
As of Feb 3rd, 2024

Source: NMPA, Frost & Sullivan Analysis

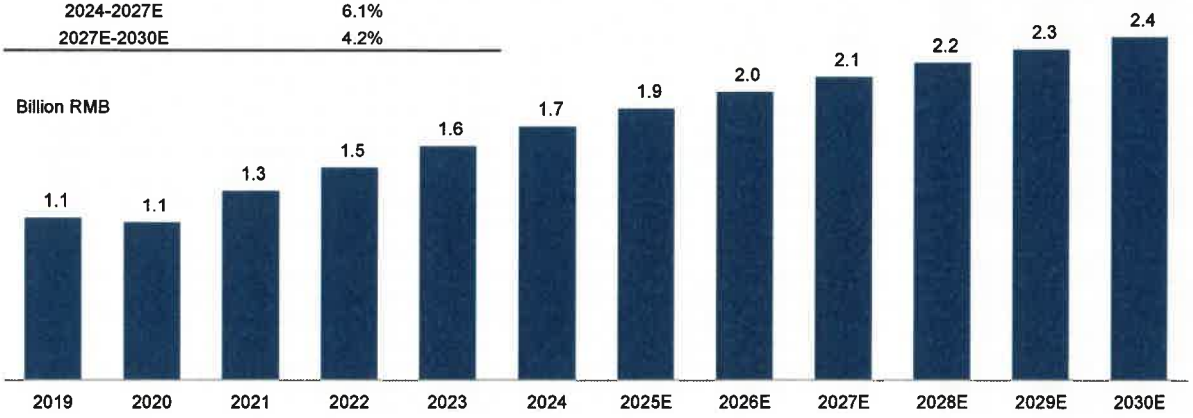
Updated

Historical and Forecasted of China Ulcerative Colitis Drug Market Size, 2019-2030E

- China's ulcerative colitis drug market has grown from RMB1.1 billion in 2019 to RMB1.7 billion in 2024 at a CAGR of 9.4%, and expected to increase to RMB2.1 billion in 2027 at a CAGR of 6.1% from 2024 and RMB2.4 billion in 2030 at a CAGR of 4.2% from 2027.

Historical and Forecasted of China Ulcerative Colitis Drug Market Size, 2019-2030E

Period	CAGR
2019-2024	9.4%
2024-2027E	6.1%
2027E-2030E	4.2%



Source: Frost & Sullivan Analysis

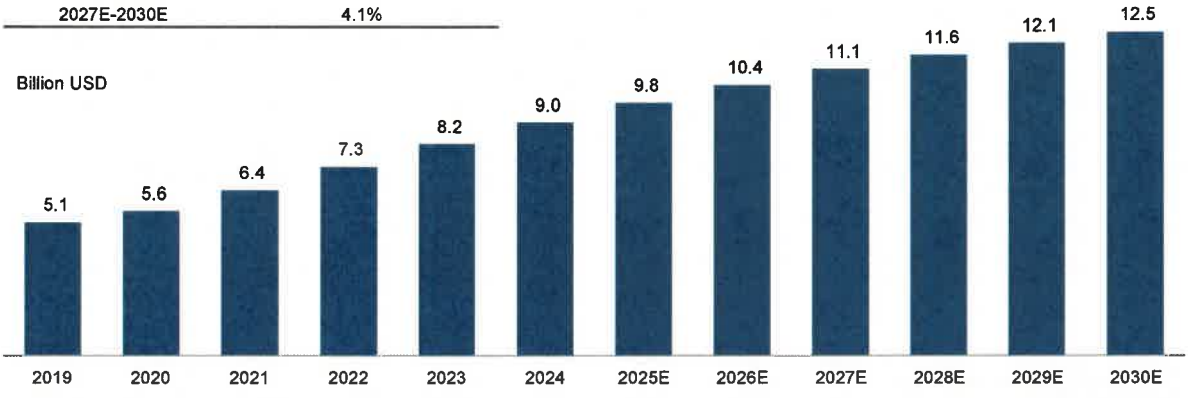
Updated

Historical and Forecasted of Global Ulcerative Colitis Drug Market Size, 2019-2030E

- Global ulcerative colitis drug market has grown from USD5.1 billion in 2019 to USD9.0 billion in 2024 at a CAGR of 11.9%, and expected to increase to USD11.1 billion in 2027 at a CAGR of 7.1% from 2024 and USD12.5 billion in 2030 at a CAGR of 4.1% from 2027.

Historical and Forecasted of Global Ulcerative Colitis Drug Market Size, 2019-2030E

Period	CAGR
2019-2024	11.9%
2024-2027E	7.1%
2027E-2030E	4.1%



Source: Frost & Sullivan Analysis

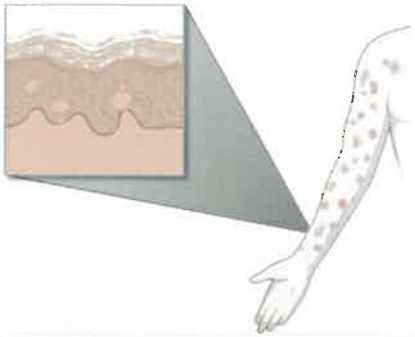
Future Trends of Inflammatory Bowel Disease Treatment Market

Expanded Patient Pool of Inflammatory Bowel Disease	• In recent years, the prevalence of IBD in China has rapidly increased, driving more basic clinical researches and helping accumulate clinical experience dealing with Chinese patients. In the globe, total prevalence of IBD has reached to 6.2 million in 2020 and is expected to grow to above 8.0 million in 2030. Similar in China, the prevalence of IBD are expected to grow from 0.6 million to 0.9 million from 2020 to 2025. Due to the increase of diagnosis rate and treatment rate, the market size of IBD treatment is supposed to expand constantly.
Precision Diagnosis	• The current diagnostic methods of Inflammatory Bowel Disease (IBD) involve a combination of physical, biochemical, imaging, endoscopic and histopathological tests. Recently, novel diagnosis method arise, such as calprotectin and myeloperoxidase (MPO) can reflect the progression of IBD, according to previous researches. With the advance of pathogenetic research enabling the development of a diagnostic golden standard, the accuracy and precision of IBD diagnosis is expected to be improved, accordingly. Thus, the capacity of IBD market will sustain rapid growth.
Multidisciplinary Collaboration	• The extraintestinal symptoms of UC include joint damage, skin and mucosal manifestations, ocular lesions, hepatobiliary diseases, thromboembolic diseases, etc., while the symptoms of CD include not only intestinal disorder, but also osteoporosis and anemia. The symptoms of IBD involve multiple organs, systems and clinical disciplines. Collaborations between different clinical departments will continue to produce timely, adequate and effective diagnosis and treatment for patients with IBD.
Development of Novel Specific Therapies	• According to treatment paradigms of UC and CD, non-specific therapies still take the lead of clinical treatment. For instance, aminosalicylic acid is the basic treatment of UC in China, while corticosteroids plays an important role in CD treatment. In depth studies on pathogenesis of UC and CD has produced novel specific therapeutic agents, which potentially have better efficacy and safety profile. Benefited from the development of novel specific therapies, the treatment rate of IBD increase obviously, which promote the market growth of IBD treatment.

Source: Frost & Sullivan Analysis

Overview of Atopic Dermatitis (AD)

- AD is a chronic, inflammatory skin disorder characterized by dry skin, intense itches and relapsing lesions.
- The pathogenesis of AD is complex, involving genetic susceptibility, a combination of impaired skin epithelial barriers, altered microbiota on the skin surface, as well as the aberrant inflammation driven by activated immune cells, including skin-infiltrating T cells.



Risk Factors	• Family history of atopy • Loss of function mutations in the FLG gene • Depression or anxiety • Sleep loss • Asthma and allergies • Skin diseases (e.g. ichthyosis)

Causes	• Genetic factors
	• Epidermal barrier dysfunction
	• Immunologic mechanisms
	• Environmental triggers
	  • Excessive bathing or washing
	  • Harsh soaps
	  • Sweating
	  • Rough fabrics and wool

Symptoms	• Intense pruritus • Scaly, dry skin • Rash that bubbles up, then weeps clear fluid • Secondary bacterial infections (superinfections)

Diagnosis Method	• Clinical evaluation
	  • Personal and family history
	  • Physical exam
	  • Skin patch allergy test

Source: Literature review, Frost & Sullivan Analysis

Overview of Atopic Dermatitis (AD)

Disease Burdens and Epidemiology

- While not a life-threatening illness, Atopic Dermatitis (AD) still imposes not only physical and psychological burden on the individual, but also heavy economic and social burden on the whole society.
- Beginning in early childhood and often persisting into adulthood (though frequently resolves or lessens significantly by adulthood), Atopic Dermatitis (AD) can have a detrimental effect on the lives of patients and their families through out the lifespan.
- Approximately 25-30% of AD patients have a moderate or severe disease course in China.

Disease Burdens

Physical Burden
- Unbearable pruritus
- Impaired physical functioning via clothing restrictions
- Sleep deprivation

Psychological Burden
- Behavioral problems on children (e.g. irritability, crying)
- Cosmetic concerns affecting self-esteem

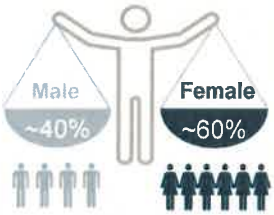
Economic Burden
- Direct medical costs
- Indirect costs (decreased productivity, absenteeism)

Social Burden
- Hindered academic and career progression due to social isolation

Potential Complications if Left Uncontrolled

- Secondary bacterial infections (superinfections)
- Erythroderma (erythema that covers more than 70% of the body surface area) is rare but can result when atopic dermatitis is severe.

Disease Epidemiology



The reason for the gender differences is unclear, and a possible one can be that androgens appear to have immuno-suppressive effect while estrogens are proinflammatory and might increase the susceptibility to atopy.

Age Profile of AD Patients

Atopic dermatitis in children often abates by age of 5 although exacerbations are common throughout adolescence and into adulthood

Source: Literature review, Frost & Sullivan Analysis

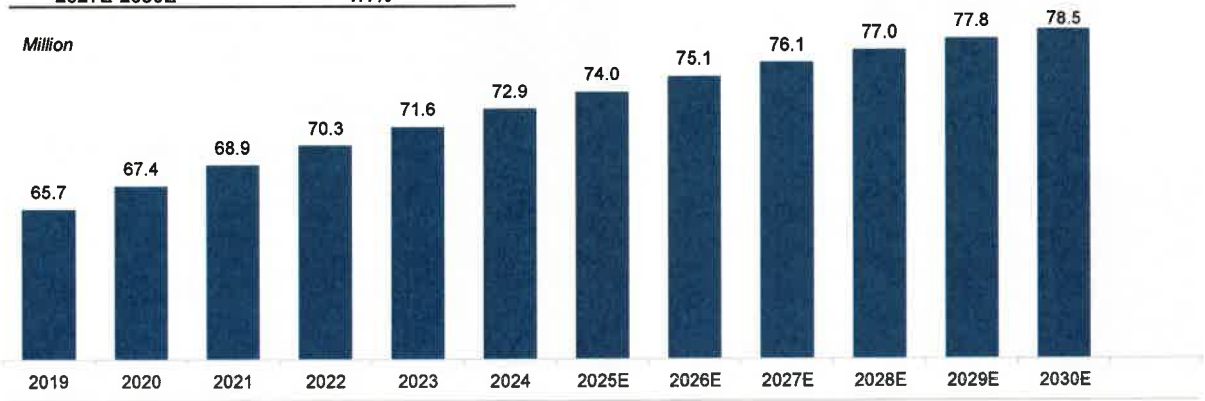
Updated

Prevalence of Atopic Dermatitis in China, 2018-2030E

- Prevalence number of atopic dermatitis in China increased from 65.7 million to 72.9 million in 2019 and 2024. The number is expected to grow to 76.1 million in 2027 at a CAGR of 1.6% from 2024 to 2027. The number is expected to grow to 78.5 million in 2030, at a CAGR of 1.1%.

Prevalence of Atopic Dermatitis in China, 2019-2030E

Period	CAGR
2019-2024	2.3%
2024-2027E	1.6%
2027E-2030E	1.1%



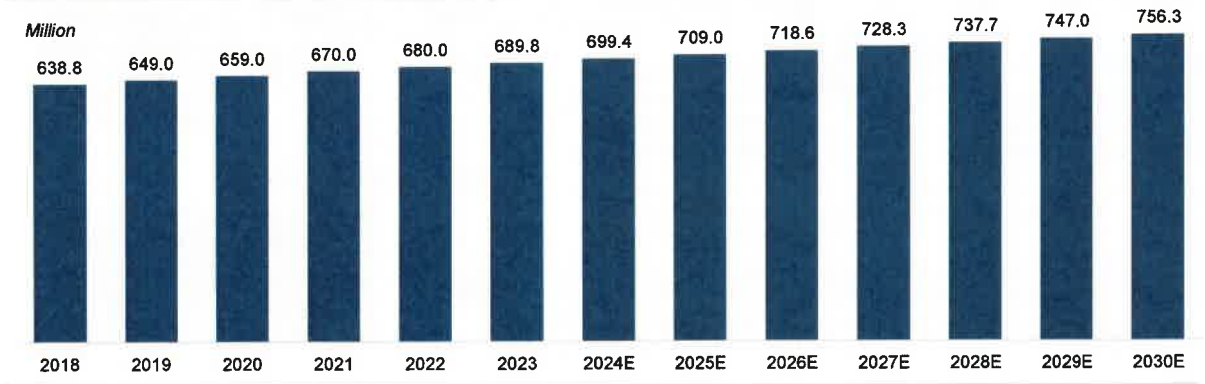
Source: Literature Review, Frost & Sullivan Analysis

Global Prevalence of Atopic Dermatitis, 2018-2030E

- Incidence number of atopic dermatitis around the world increased from 638.8 million to 689.8 million in 2018 and 2023. The number is expected to grow to 718.6 million in 2026 at a CAGR of 1.4% from 2023 to 2026. The number is expected to grow to 756.3 million in 2030, at a CAGR of 1.3%.

Global Prevalence of Atopic Dermatitis, 2018-2030E

Period	CAGR
2018-2023	1.5%
2023-2026E	1.4%
2026E-2030E	1.3%



Source: Literature Review, Frost & Sullivan Analysis

Treatment Paradigm of Atopic Dermatitis in China

- The treatment of AD is mainly implemented according to disease stage, and the main therapies include topical therapy, systematic therapy, UV therapy, etc. The main purpose of treatment is to relieve or eliminate clinical symptoms, restore homeostasis of skin, eliminate triggers, prevent recurrence and complications, so as to improve the quality of life of patients.
- Topical therapy includes corticosteroids and calcineurin inhibitors.
- Systemic therapy includes antihistamines, immunosuppressive drugs, Glucocorticoid and IL-4Rα Inhibitors.

Treatment Methods	Major Treatment options
Fundamental	• Bath and skin care • Emollients (moisturize your skin) • Avoiding allergens
Drug Treatment	• Topical Medication, including topical corticosteroid (TCS), Topical calcineurin inhibitor (TCI, such as Tacrolimus and Pimecrolimus), Phosphodiesterase-4 inhibitor (PDE-4 inhibitor) • Systematic therapy, including antihistamines (Loratadine and Cetirizine), immunosuppressive drugs (Cyclosporine and Methotrexate), Glucocorticoid and IL-4Rα Inhibitor (Dupilumab)
UV Therapy	• UV
Traditional Chinese Medicine (TCM)	• Glycyrrhizic acid agent
Antimicrobial therapy	• Anti-bacterial medicines (erythromycin family and tetracycline family) • Anti-virus medicines • Anti-fungal medicines

Treatment Improvement Potential

- **Drug Resistance**: Currently, topical corticosteroid (TCS) is the first-line treatment option for AD. For moderate and severe patients, immunosuppressive drugs are recommended. Considering the side effects, using immunosuppressive drugs may cause serious infections, and liver and kidney function should be monitored. IL-4Rα Inhibitors such as dupilumab, have been proved effective to adult and children, and recommended in maintenance treatment of AD.
- **Safety profile:** Safety concerns limit the long-term use of the current treatment options (antihistamines, immunosuppressive drugs, Glucocorticoid), particularly for children, due to the increased body surface area to mass ratio in children, which results in increased absorption and systemic exposure. In addition, the current treatment options have been reported to be associated with side effects, including application site burning and stinging.

Source: Guidelines for Primary Diagnosis and Treatment of Atopic Dermatitis (2022), Frost & Sullivan Analysis

Pain point analysis of Atopic Dermatitis Treatment in China

High side effects of Immunosuppressants

- Immunosuppressants and corticosteroids are the main clinical treatments for mid- and late-stage AD patients.
- Immunosuppressants often require long-term use and can affect the body's normal immune function, with relatively significant side effects. Additionally, cessation of these drugs may lead to severe secondary infections, making it difficult for patients to recover quickly. Therefore, there is an urgent need to develop therapeutic drugs with low side effects and high clinical efficacy.

Safety hazards of corticosteroids

- The use of systemic corticosteroids requires careful attention to dosing and frequency, as well as close monitoring of adverse reactions post-administration. Moreover, systemic corticosteroids, besides having high requirements for applicable conditions, cannot be administered over a long term. Furthermore, an extensive randomized safety clinical trial review by the FDA published in 2021 mandated the inclusion of a black box warning in the prescribing information for JAK inhibitors (tofacitinib, upadacitinib, baricitinib), which are approved for the treatment of rheumatoid arthritis and ulcerative colitis, indicating an increased risk of serious heart-related events, cancer, blood clots, and death.
- Therefore, there is need to develop drugs with low side effects, low dosing frequency and high safety.

Source: Frost & Sullivan Analysis

Competitive Landscape of Small Molecule Targeted Drug on Atopic Dermatitis Approved by NMPA

Drug Name/Code	Brand Name	Target	Company	Indications	Approval Date
Abrocitinib	CIBINQO®	JAK1	Pfizer	Atopic Dermatitis	2022-04-08
Upadacitinib	RINVOQ®	JAK1	AbbVie	Atopic Dermatitis; Rheumatoid Arthritis; Psoriatic Arthritis; Ulcerative Colitis; Crohn's Disease	2022-02-18 (Approved for the indication of Atopic Dermatitis)

*Note: Approval date: First approval date
As of Feb 19th, 2025

Source: NMPA, Frost & Sullivan Analysis

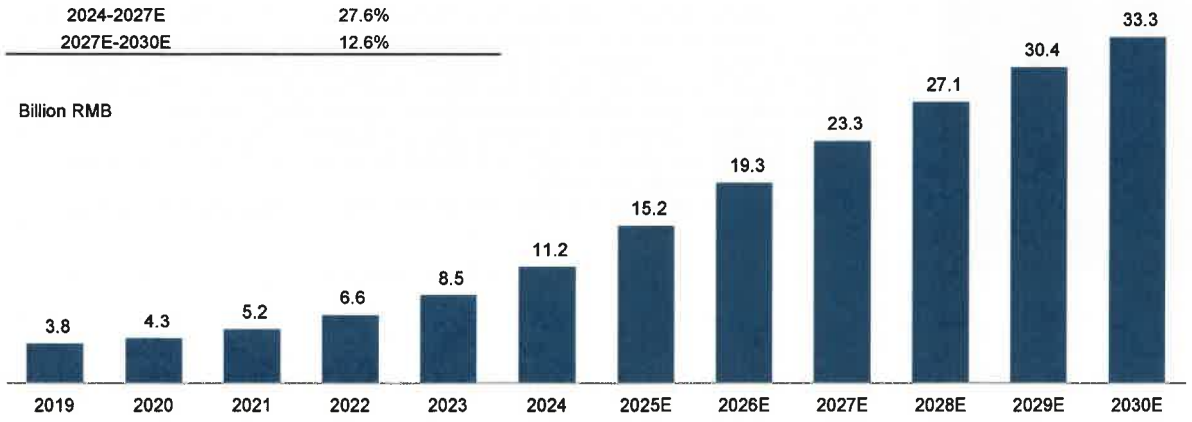
Updated

Historical and Forecasted of China Atopic Dermatitis Drug Market Size, 2019-2030E

- China's atopic dermatitis drug market has grown from RMB3.8 billion in 2019 to RMB11.2 billion in 2024 at a CAGR of 24.0%, and expected to increase to RMB23.3 billion in 2027 at a CAGR of 27.6% from 2024 and RMB33.3 billion in 2030 at a CAGR of 12.6% from 2027.

Historical and Forecasted of China Atopic Dermatitis Drug Market Size, 2019-2030E

Period	CAGR
2019-2024	24.0%
2024-2027E	27.6%
2027E-2030E	12.6%



Source: Frost & Sullivan Analysis

Future Trends for Atopic Dermatitis Treatment Market

Steadily Increasing New Case Numbers	• In recent years, as people's stress levels have increased and the social environment has deteriorated, the prevalence of atopic dermatitis in China has shown an upward trend, currently estimated at 12.94%. Its occurrence is mainly related to factors such as living environment, psychological stress, abnormal skin barrier function, genetics, infections, and immunity. Under the socio-economic environment still affected by the pandemic in the short term, the prevalence may further increase.
Discovery of New Genetic Loci	• Currently, genetic factors are considered one of the main risk factors for atopic dermatitis. In recent years, FLG-related loci and several new loci, such as 20q13.33 and IL-18RAP, have been identified as potentially related to atopic dermatitis. In 2013, Ellinghaus and others identified susceptibility gene loci for AD, including 4q27 (IL2/IL21), 11p13 (PRR5L), 16p13.13 (CLEC16A/DEXI), and 17q21.32 (ZNF652). In 2015, Schaarschmidt and colleagues discovered two new loci, 2q24.3 and 9p21.3, in AD patients in Germany. This provides possibilities for future targeted therapies.

Source: Frost & Sullivan Analysis

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Overview of Heart Failure

- Heart failure is a complex of clinical syndromes caused by the changes in structure and function of myocardial, leading to low ventricular ejection.
- Heart failure is a common final stage of many heart diseases, and is also a disease with high prevalence and mortality. Although the treatment of heart failure has made continuous progress in recent years, the disease is still a fatal clinical disease.

Definition

- Heart failure (HF), also as known as congestive heart failure (CHF), is a complex clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood.

Risk factors

- Hypertension
- Diabetes
- Metabolic syndrome
- Atherosclerosis
- Current smoking history
- Previous myocardial infarction

Pathogeny

- **Symptoms of HF**

Heart failure symptoms are traditionally divided into left- and right-sided.

Failure of left ventricle causes congestion of the lungs' blood vessels, so the symptoms are predominantly respiratory.
- Dyspnea (shortness of breath)
- Cardiac asthma
- Dizziness & confusion

Right-sided heart failure is caused by pulmonary heart disease, so the symptoms are predominantly in pulmonary circulation,
- Swelling under the skin
- Nocturia
- Ascites and liver enlargement

- **Inducing factors**

- ✓ Respiratory tract infection, rheumatism, etc
- ✓ Severe arrhythmia
- ✓ Increased cardiac load
- ✓ Drug effect
- ✓ Inappropriate activities
- ✓ Excessive physical activity

Pathophysiological mechanism:
- **Continuously activated neurohumoral factors** can directly produce toxic effects on the heart and aggravate heart failure.
- **Myocardial remodeling** is a dynamic pathological process in which the biological characteristics of cardiomyocytes are abnormal and the interaction between cardiomyocytes and non cardiomyocytes is unbalanced under stress.

Source: Literature Review, Frost & Sullivan Analysis

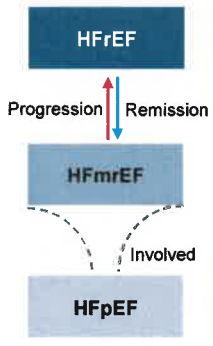
Classification of Heart Failure

- Ejection fraction (EF) is considered important in classification of patients with HF because of differing patient demographics, comorbid conditions, prognosis, and response to therapies and because most clinical trials selected patients based on EF.
- Patients with heart failure are classified into two groups according to their left ventricular ejection fraction: heart failure with reduced ejection fraction (HFrEF) and heart failure with preserved ejection fraction (HFpEF), (HFpEF including HFmrEF). Each has its own distinct pathophysiology.

Overview of ejection fraction (EF):

- EF is a measurement, expressed as a percentage, of how much blood the left ventricle pumps out with each contraction. A normal ejection fraction should be between 50-70 percent.
- If the heart muscle has become so thick and stiff that the ventricle holds a smaller than usual volume of blood, the ejection fraction seems insufficient for physical activities.

Subgroups of heart failure:



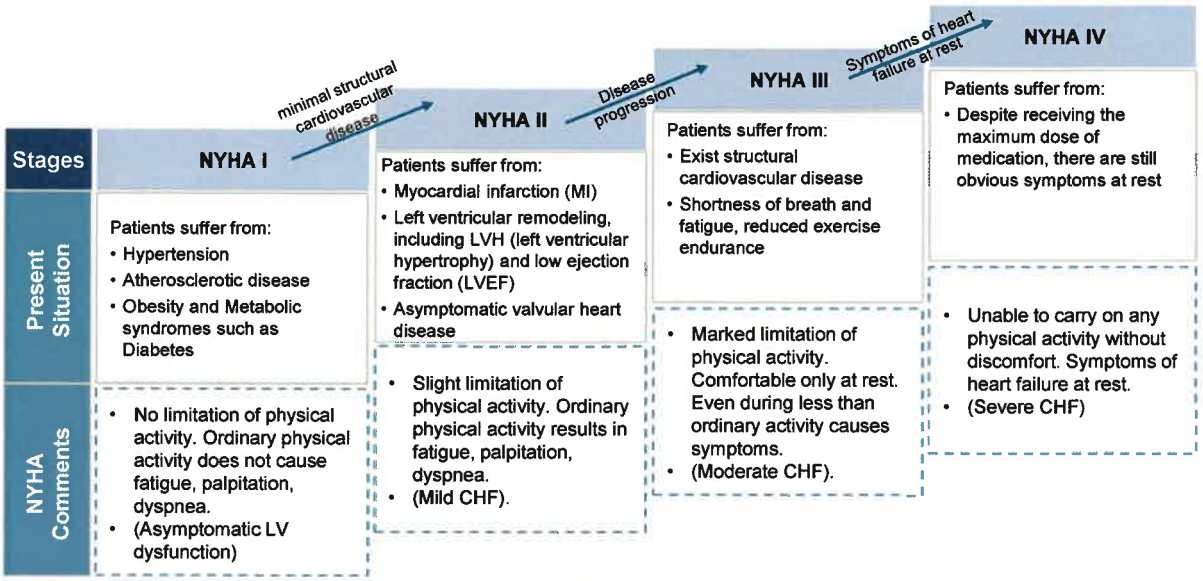
Classification	EF (%)	Description
Heart failure with reduced ejection fraction (HFrEF)	≤ 40	Also referred to as systolic HF. Randomized controlled trials have mainly enrolled patients with HFrEF.
Heart failure with mid-range ejection fraction (HFmrEF)	41~49	These patients fall into a borderline or intermediate group. Their characteristics, treatment patterns, and outcomes appear similar to those of patients with HFpEF.
Heart failure with preserved ejection fraction (HFpEF)	≥ 50	Also referred to as diastolic HF. Several different criteria have been used to further define HFpEF. The diagnosis of HFpEF is challenging because it is largely one of excluding other potential noncardiac causes of symptoms suggestive of HF.

Notes: According to ACCF/AHA guideline of HF, HFmrEF is involved in HFpEF, thereby the diagnosis and treatment of HFmrEF same with HFpEF

Source: Literature Review, Frost & Sullivan Analysis

Four Progression Stages of Heart Failure from NYHA

- New York Heart Association (NYHA) functional classification provide useful and complementary information about the presence and severity of HF by focusing on exercise capacity and the symptomatic status of the disease. It is widely used in clinical practice and research and for determining the eligibility of patients for certain healthcare services.
- The stages are progressive and inviolate; once a patient moves to a higher stage, regression to an earlier stage of HF is not observed.



Source: Literature Review, Frost & Sullivan Analysis

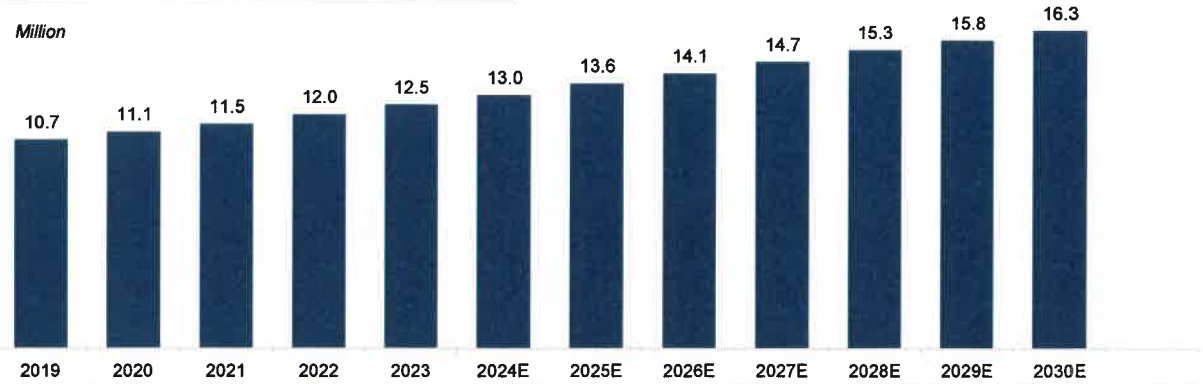
Updated

Prevalence of Heart Failure in China, 2019-2030E

- Prevalence number of heart failure in China increased from 10.7 million to 13.0 million in 2019 and 2024. The number is expected to grow to 14.7 million in 2027 at a CAGR of 4.1% from 2024 to 2027. The number is expected to grow to 16.3 million in 2030, at a CAGR of 3.7%.

Prevalence of Heart Failure in China, 2019-2030E

Period	CAGR
2019-2024	4.2%
2024-2027E	4.1%
2027E-2030E	3.7%



Source: Literature Review, Frost & Sullivan Analysis

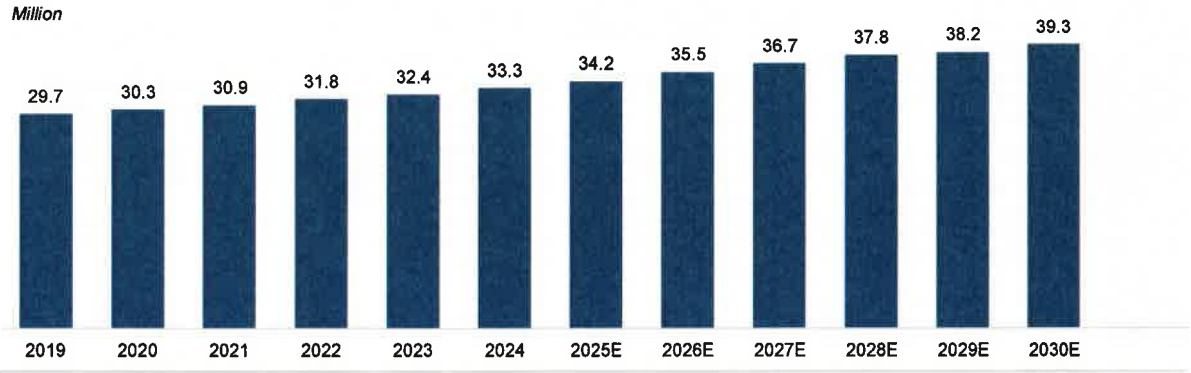
Updated

Global Prevalence of Heart Failure, 2019-2030E

- Prevalence number of heart failure around the world increased from 29.7 million to 33.3 million in 2019 and 2024. The number is expected to grow to 36.7 million in 2027 at a CAGR of 3.1% from 2024 to 2027. The number is expected to grow to 39.3 million in 2030, at a CAGR of 2.6%.

Global Prevalence of Heart Failure, 2019-2030E

Period	CAGR
2019-2024	2.2%
2024-2027E	3.1%
2027E-2030E	2.6%



Source: Literature Review, Frost & Sullivan Analysis

Treatment Paradigm of Heart Failure in the US and China

- The treatment paradigm for heart failure in the United States and China is similar.
- Most of the drugs currently approved for heart failure are neurohormonal modulators, and few directly target cardiomyocytes to improve primary cardiac pathology.
- Currently, there is a gap in the treatment of HFpEF, and most approved drugs for HFrEF are ineffective for HFpEF. A number of clinical trials addressing the effects of drugs on HFpEF are underway, providing possible medical evidence for the future treatment of HFpEF.

Treatment paradigm of HFrEF:

Disease progression and drug intolerant

Primary Treatment

1st Line

- ACEI (If ARNI intolerance)/ ARBs (ARNI and ACEI intolerance) / ARNI
- Diuretics are recommended in patients with HFrEF with fluid retention

2nd Line

NYHA class II ~ IV; LVEF≤35%

- Beta Blockers are recommended to reduce mortality and hospitalizations
- SGLT2i are recommended to reduce the composite of cardiovascular death or HF hospitalization
- MRAs are recommended to reduce morbidity and mortality

OR

NYHA class II ~ III; LVEF≤35%

- Implantable cardioverter defibrillators (ICDs)
- Cardiac resynchronization therapy (CRTs)
- Anti-arrhythmic drugs, such as Ivabradine

Treatment paradigm of HFpEF:

- Blood pressure control remains the currently most important recommendation in patients with HFpEF. In hypertensive patients with HFpEF, aggressive treatment (often with several drugs with complementary mechanisms of action) is recommended. Similar with HFrEF, ACEI and/or ARBs are often considered as the first-line agents.
- Diuretics are recommended in patients with HFpEF with fluid retention and volume overload.
- Beta blockers are often prescribed to these patients for management of comorbidities.
- Sacubitril-valsartan reduces HF hospitalizations.
- The sodium-glucose cotransport-2 inhibitors (SGLT2i) have emerged as promising therapies for HFpEF.

LVEF=left ventricular ejection fraction; ACEI= Angiotensin-converting-enzyme inhibitors; ARB= Angiotensin II receptor antagonist; ARNI=Angiotensin Receptor-Neprilysin Inhibitor

Source: 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure; National Heart Failure Guideline 2023; Frost & Sullivan Analysis

Heart Failure Drugs Pain Points

Category	Classification	Mechanism	Typic
Osmoregulation	Diuretics	Diuretics are agents that can adequately control the fluid retention associated with HFrEF. Diuretic is initiated at low doses and is titrated up as needed and as tolerated.	• Bumetanide • Furosemide • Chlorothiazide
Endocrine regulation	ACEI	ACE inhibitors decrease peripheral resistance and reduce the load on the failing myocardium, thus preventing vasoconstriction.	• Captopril • Enalapril • Lisinopril
	ARB	ARBs block the binding of angiotensin II to its receptor, which in turn leads to vasoconstriction and prevents the release of aldosterone.	• Candesartan • Losartan • Valsartan
	Beta-Blocker	By blocking β_1 receptors, beta blockers prevent ventricular remodeling promoted by the stimulated RAAS and sympathetic system	• Bisoprolol • Carvedilol
	Vasodilators	Vasodilators bind to receptors on endothelial cells of the blood vessel, which stimulate calcium release, and prevent constriction of the blood vessels.	• Benazepril • Captopril
Nervous regulation	Aldosterone receptor antagonists	Aldosterone is an endogenous steroid hormone that increases sodium retention and facilitates magnesium/potassium loss.	• Spironolactone • Eplerenone
	Ivabradine	It can specifically inhibiting the cardiac pacemaker current (If), which controls the spontaneous diastolic depolarization in sinoatrial (SA) node and hence regulates the heart rate.	N/A

Treatment Improvement Potential

- To date, there are mainly three categories of drugs, namely osmoregulation, endocrine registration and nervous regulation drugs. However, there are not yet agents targeting on cardiomyocytes to improve the ejection in the treatment of HFrEF.
- Trials using comparable and efficacious agents for HFrEF have generally been disappointing when used in patients with HFpEF / HFmrEF. Thus, most of the recommended therapies for HFpEF / HFmrEF are directed at symptoms, especially comorbidities, and risk factors that may worsen cardiovascular disease.

Source: Frost & Sullivan Analysis

Analysis of Drug Treatment of Heart Failure

- The drug intervention of HF primarily relies on ACEI/ARB, β-Blocker and aldosterone antagonist, which have been proven effective on HFrEF while poor efficacy on HFpEF. In particular, there are currently no drugs can target on cardiomyocytes and eliminate inflammation.

HF therapy:

ACEI/ARB is used as a cornerstone medicine, combined with β-blocker to regulate the nervous system, and supplemented with aldosterone antagonists.

Mechanism: Inhibit angiotensin converting enzyme II, thereby delaying ventricular remodeling (enlargement) and lowering blood pressure.
- Enalapril
- Candesartan

1 ACE Inhibitors (ACEI) & Angiotensin II Receptor Blockers(ARB)

2 β-Blocker

Mechanism: Inhibit over-activated sympathetic nerve activity, thereby inhibiting myocardial contraction, lowering heart rate and blood pressure.
- Bisoprolol

3 Aldosterone Antagonists

Mechanism: Blocks aldosterone in renin-angiotensin-aldosterone system (RAAS), thereby lowering blood pressure, reducing the risk of cardio-death and risk of hospitalization
- Eplerenone

1 *Unmet clinical need in drug intervention of HFpEF*

- There is no effective clinical treatment for HFpEF due to uncertain disease mechanism.
- In HFpEF, the myocardium becomes too stiff to pump blood effectively. Most patients with HFpEF suffer from diabetes and other metabolic syndromes.

- Cardiac inflammation, leading to endothelial dysfunction, has been identified as one of independent causes of cardiovascular event in HFpEF.
- Anti-inflammation agents, targeting on cardiac inflammation, may address the unmet clinical needs of eliminating inflammation of HFpEF.

2 *Need novel agents that directly target on cardiomyocytes*

- Currently, primary therapies and other treatment paradigm recommending drugs focus more on RAAS endocrine system or symptoms of HF rather than improve the myocardial cell necrosis.

- Traditional HF treatment cannot improve clinical outcome of HF, but only delay the time before complete failure by regulating endocrine. The prognosis of HF can be improved only if the remodeling of cardiac muscle can be controlled. This requires agents to target directly on cardiomyocytes.

Source: Literature Review, Frost & Sullivan Analysis

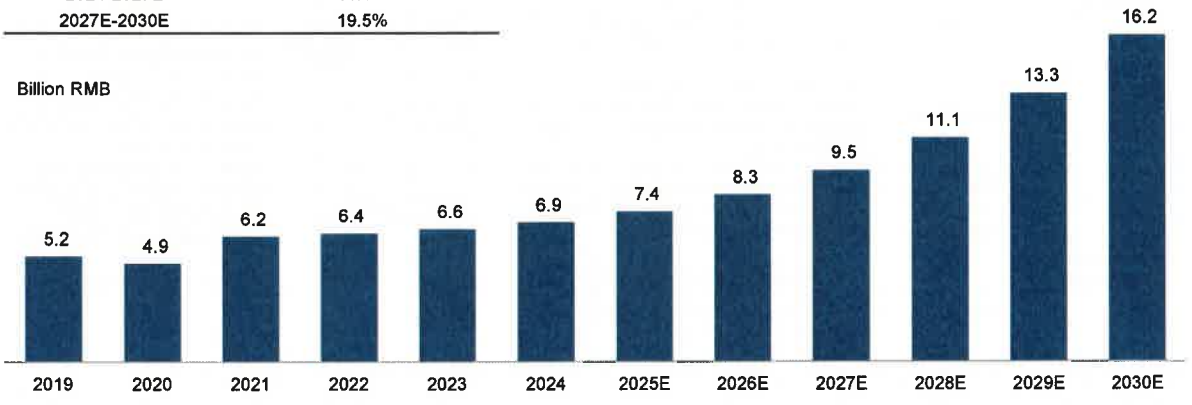
Updated

Historical and Forecasted of China Heart Failure Drug Market Size, 2019-2030E

- China's heart failure drug market has grown from RMB5.2 billion in 2019 to RMB6.9 billion in 2024 at a CAGR of 5.7%, and expected to increase to RMB9.5 billion in 2027 at a CAGR of 11.1% from 2024 and RMB16.2 billion in 2030 at a CAGR of 19.5% from 2027.

Historical and Forecasted of China Heart Failure Drug Market Size, 2019-2030E

Period	CAGR
2019-2024	5.7%
2024-2027E	11.1%
2027E-2030E	19.5%



Source: Frost & Sullivan Analysis

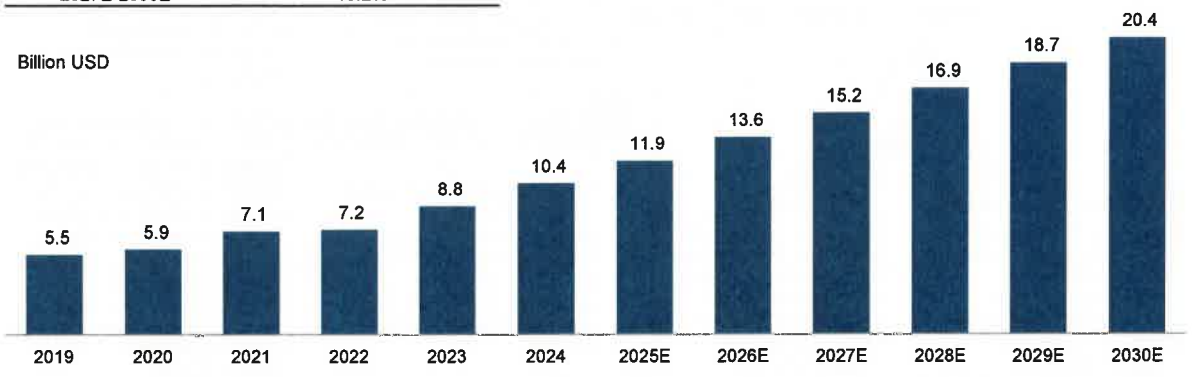
Updated

Historical and Forecasted of Global Heart Failure Drug Market Size, 2019-2030E

- Global heart failure drug market has grown from USD5.5 billion in 2019 to USD10.4 billion in 2024 at a CAGR of 13.6%, and expected to increase to USD15.2 billion in 2027 at a CAGR of 13.6% from 2024 and USD20.4 billion in 2030 at a CAGR of 10.2% from 2027.

Historical and Forecasted of Global Heart Failure Drug Market Size, 2019-2030E

Period	CAGR
2019-2024	13.6%
2024-2027E	13.6%
2027E-2030E	10.2%



Source: Frost & Sullivan Analysis

Future Trends of Heart Failure Treatment Drug Market

Increasing Aging Population and Heart Failure Prevalence	• Because the overall metabolic and immune capacities of elder people gradually decline, they are more likely to suffer from chronic diseases. Therefore, aging has become a common risk factor for a number of chronic diseases including heart failure, which is related to variety of cardiovascular diseases. Global aging population has reached 779.7million in 2022, and is expected to further increase to 877.5 million in 2026. Global heart failure patient pool will sustain rapid growth in the future due to the increasing aging population, which will drive the market expansion of heart failure treatment.
Advancement of Diagnosis Method	• For a long time, diagnosis of HF relies more on historical and physical test, functional test, imaging test and limited biochemical test, which is not sufficient as the cause and complication of HF are too complicated. Recently, the development of novel Biomarkers of Myocardial Injury (Cardiac Troponin T/I) and multiple other biomarkers including those reflecting inflammation, oxidative stress, neurohormonal disarray, and myocardial and matrix remodeling, have been widely examined for their diagnosis value in HF. Also, some novel non-invasive imaging methods are used as diagnostic support for HF, such as Ultrasonic Cardiogram (UCG) is able to detect abnormal cardiac structure and function. • Along with the improvement of HF diagnosis methods, the treatment market of heart failure is hopefully expand in the future.
Investigation on Innovative Drugs with Novel Mechanism	• According to diverse guidelines of heart failure, there are mainly three types of drugs directed to HF, namely osmoregulation, endocrine registration and nervous regulation drugs. However, none of those three categories of agents focus directly on cardiomyocytes to improve the ejection in the treatment of HFrEF, but targeting on other external factors. • At present, the prognosis of HFrEF is relatively poor, and there is not yet any agents show promising efficacy to HFpEF. Also, exist drugs on HF are facing problems of drug resistance. For instance, some patients tolerate to ACEI and ARBs, thereby have to use ARNI as replacement. • Thus, there is an obvious gap of innovative drugs with novel mechanism, which target directly on cardiomyocytes and potentially have good efficacy and safety profile on the indication of HFpEF.

Source: Frost & Sullivan Analysis

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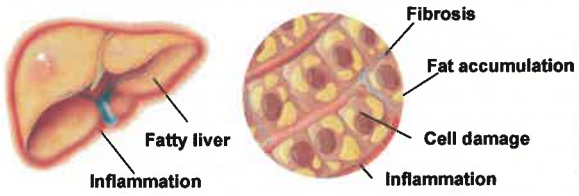
Overview of Nonalcoholic Steatohepatitis (NASH)

Symptoms, Causes and Risk Factors

- Nonalcoholic steatohepatitis (NASH) is liver inflammation and damage caused by a buildup of fat in the liver. It is the more severe form of nonalcoholic fatty liver disease (NAFLD), an umbrella term for a range of liver conditions affecting people who drink little to no alcohol. If left untreated, NASH can cause scarring of the liver, which leads to permanent scarring (cirrhosis) and liver cancer.
- As NASH progresses, symptoms including fatigue, weight loss, an ache in the upper right part of the belly, and more may appear, though it may take many years for NASH to become severe enough to cause symptoms.



Risk Factors

1. Obesity
2. Diabetes
3. High Cholesterol
4. High Blood Sugar (Hyperglycemia)
5. High Level of Fats (Triglycerides)
6. Underactive Thyroid

Symptoms

- Fatigue
- Pain in the upper right abdomen
- Bleeding and bruising easily
- Jaundice
- Fluid accumulation in abdomen
- Weight loss
- Nausea
- Confusion
- Drowsiness
- Slurred speech

Causes

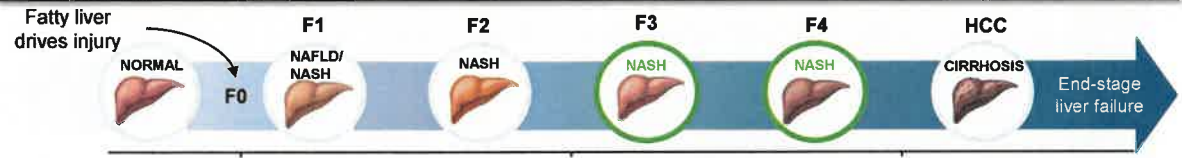
- Exact cause for why fat accumulates in the liver of certain individuals and fatty liver inflammation that progresses to cirrhosis is unknown
- NASH is often linked to insulin resistance, oxidative stress, hepatocyte apoptosis, and pro-inflammatory cytokine activation.
- These combined health problems appear to promote the deposit of fat in the liver

Source: Literature Review, Frost & Sullivan Analysis

Overview of Nonalcoholic Steatohepatitis (NASH)

NAFLD Activity Score (NAS)

- The NAFLD activity score' (NAS) is the most widely used histological grading and staging system for NAFLD. Total NAS score represents the sum of scores for steatosis, lobular inflammation, ballooning, and fibrosis, and ranges from 0-8.
- A score of ≥5 with steatosis and hepatocyte ballooning is generally considered diagnostic of non-alcoholic steatohepatitis (NASH), but patients can still have NASH with lower NAS scores if steatosis and hepatocyte ballooning are present.
- NASH is characterized by ballooning degeneration and lobular inflammation with or without hepatic fibrosis, in addition to steatosis in the liver. Patients with NASH can progress to cirrhosis and are at increased risk of liver cancer and even death resulting from liver disease.



	Not NAFLD	Steatosis / Steatohepatitis	Fibrosis / Ballooning / Cirrhosis	Cirrhosis
Steatosis	None to minimal (<5%)	Any degree >5%, often in zone 3 or panacinar	Any degree, often in zone 3 or panacinar when fibrosis is mild	None to minimal
Inflammation	Usually mild	Any degree, usually mainly lobular	Any degree, usually more lobular when fibrosis is mild	Any degree, portal inflammation prominent
Fibrosis Stage	None or stage 1-2	None or stage 1-2	Sometimes none, often perisinusoidal in zone 3	More than stage 2 fibrosis
NAS score	0 -1	1-5	3–8 (definite) or 2–6 (borderline)	0–3

Non-alcoholic Fatty Liver (NAFL):
- Fat builds-up in the liver (steatosis) in individuals with no excessive alcohol use

Non-alcoholic Steatohepatitis (NASH):
- Steatosis is accompanied with inflammation
- Three lesions define NASH histologically: steatosis, inflammation and ballooning

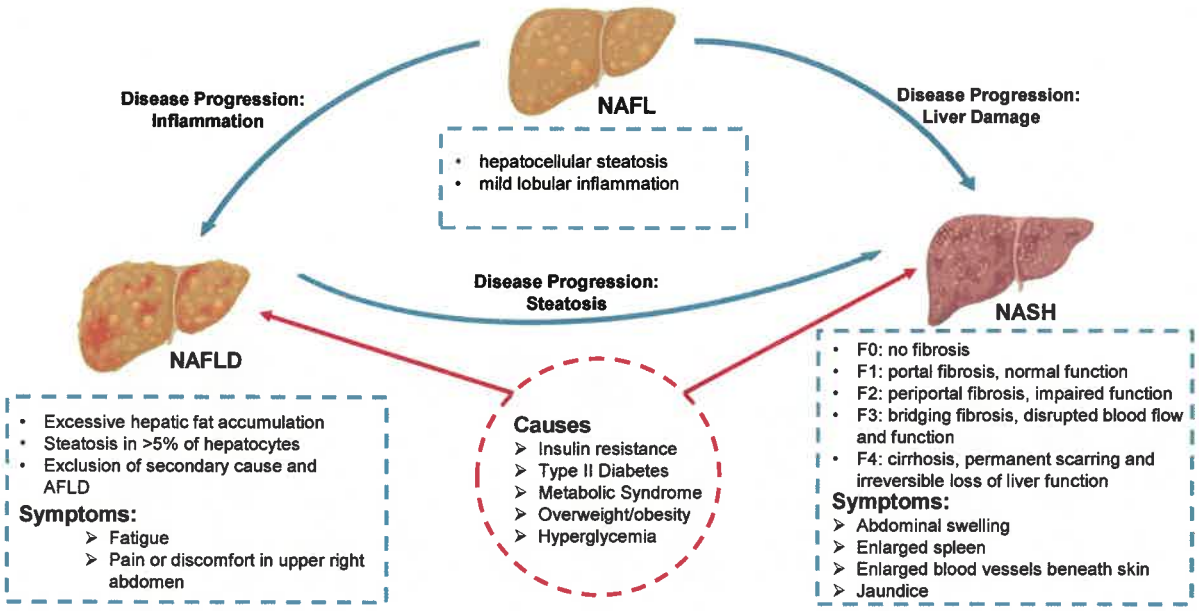
NASH with Fibrosis and Ballooning:
- Hepatocyte suffering apoptosis and inflammation lead to the release of collagen fibers that form scar tissue, resulting in hepatic fibrosis

Severe Progression to Cirrhosis and HCC:
- Evolve to cirrhosis or hepatocellular carcinoma
- NAFLD-cirrhosis or NAFLD-hepatocellular carcinoma are now 2nd major cause of liver transplantation in the US

Source: Literature Review, Frost & Sullivan Analysis

Diseases Progression and Relation of NAFLD/NASH

- Along with the accumulation of fat and the process of steatosis, NAFL can convent into NAFLD or NASH which is even more severe.
- The causes of NAFLD and NASH is almost similar, as NAFLD is likely to progress to NASH with more serious symptoms.



Source: Literature Review, Frost & Sullivan Analysis

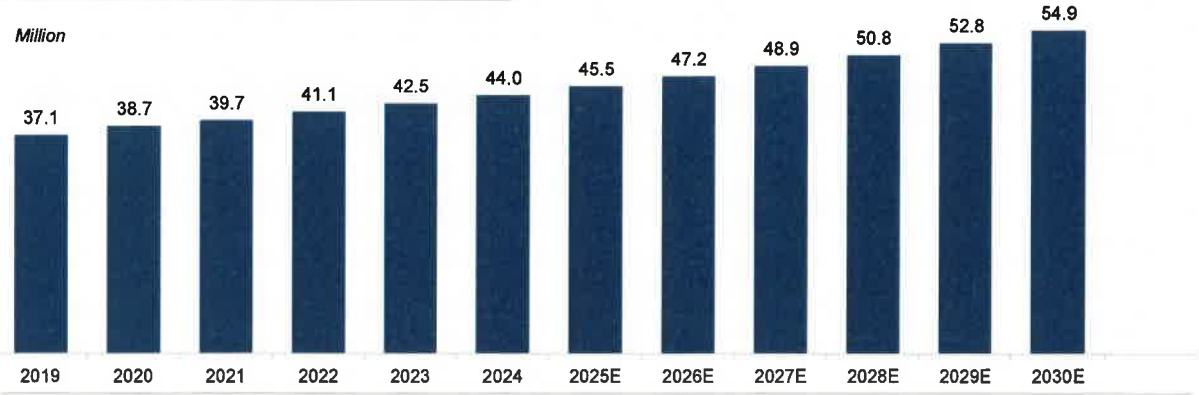
Updated

Prevalence of NASH in China, 2019-2030E

- Prevalence number of NASH in China increased from 37.1 million to 44.0 million in 2019 and 2024. The number is expected to grow to 48.9 million in 2027 at a CAGR of 3.5% from 2024 to 2027. The number is expected to grow to 54.9 million in 2030, at a CAGR of 3.9%.

Prevalence of NASH in China, 2019-2030E

Period	CAGR
2019-2024	3.3%
2024-2026E	3.5%
2027E-2030E	3.9%



Source: Literature Review, Frost & Sullivan Analysis

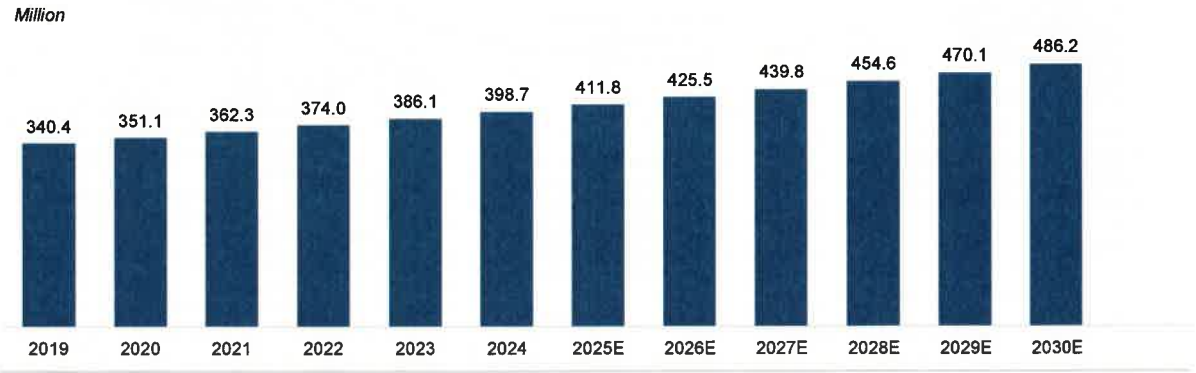
Updated

Global Prevalence of NASH, 2018-2030E

- Prevalence number ofNASH around the world increased from 340.4 million to 389.7 million in 2019 and 20234 The number is expected to grow to 439.8 million in 2027 at a CAGR of 3.3% from 2024 to 2027. The number is expected to grow to 486.2 million in 2030, at a CAGR of 3.4%.

Global Prevalence of NASH, 2019-2030E

Period	CAGR
2019-2024	3.2%
2024-2027E	3.3%
2027E-2030E	3.4%



Source: Literature Review, Frost & Sullivan Analysis

Treatment Paradigm of NASH

- In March 14th, FDA approved Rezdiffra (resmetirom) for the treatment of adults with noncirrhotic non-alcoholic steatohepatitis (NASH) with moderate to advanced liver scarring (fibrosis), to be used along with diet and exercise. Previously, patients with NASH who also have notable liver scarring did not have a medication that could directly address their liver damage. Rezdiffra's approval will, for the first time, provide a treatment option for these patients, in addition to diet and exercise.
- In both US and China, treatment of NASH can be divided into lifestyle intervention, drug intervention and surgical intervention. and the prevention and treatment of metabolic syndrome, type two diabetes mellitus and other comorbidities are important. Despite of the newly approved drug resmetirom, the NASH treatment is still focusing on multi-mechanistic strategy of combination therapy, given the complexity in pathophysiology and heterogeneity nature of the disease.

US guidance of NASH:

Category	Classification	Target	Mechanism of Action
Behavior Intervention	Lifestyle Intervention	N/A	Lifestyle modification consisting of diet, exercise, and weight loss has been advocated to treat patients with NAFLD/NASH.
Drug Intervention	Pioglitazone	(PPAR)-γ	Pioglitazone improves glycaemic control in people with Type 2 diabetes by improving insulin sensitivity through its action at PPAR gamma 1 and PPAR gamma 2, and affects lipid metabolism through action at PPAR alpha
	Semaglutide / Liraglutide	GLP-1R	GLP-1 RAs: augmentation of hyperglycemia-induced insulin secretion, suppression of glucagon secretion at hyper- or euglycemia
Surgical Intervention	Bariatric surgery	N/A	Weight loss is effective in improving all disease features of NAFLD, including fibrosis. Bariatric surgery improves or eliminates comorbid disease in most patients and improves long-term survival of NASH.

China guideline of NASH:

Category	Classification	Target	Mechanism of Action
Behavior Intervention	Lifestyle Intervention	N/A	In order to achieve weight loss and reduce BMI value, diet and adequate exercises has been used to treat patients with NAFLD/NASH.
Drug Intervention	Liraglutide / Pioglitazone	GLP-1R/ (PPAR)-γ	For patients with metabolic syndrome (MetS), such as diabetes, hypertension and obesity, metformin and other precision drugs are recommended to regulate the metabolism of patients, thereby improve NAFLD indices and delay the progression of NAFLD/NASH.
	Hepatoprotective drugs	N/A	A category of drugs improve liver function, promote regeneration of damaged liver cells, and enhance liver detoxification functions.
Surgical Intervention	Bariatric surgery	N/A	For patients with severe (BMI>40kg/m^2) or moderate obesity (35 kg/m^2≤BMI≤39.9 kg/m^2), bariatric surgery are recommended to efficiently reduce the weight of patients.

Notes: MetS= Metabolic Syndrome

Source: American Association of Clinical Endocrinology Clinical Practice Guideline for the Diagnosis and Management of Nonalcoholic Fatty Liver Disease in Primary Care and Endocrinology Clinical Settings; Guidelines for the Prevention and Treatment of NAFLD 2018; Frost & Sullivan

Analysis of Drug Treatment of NASH

- Current drug intervention can only slow the accumulation of fat in liver tissue, which hardly resolve NASH and have no consistently reliable effect on fibrosis. Given the high prevalence of NASH, the associated morbidity, the growing burden of end-stage liver disease, and limited availability of livers for organ transplantation, it is believed that identifying therapies that will slow the progress of, halt, or reverse NASH will address an unmet medical need.

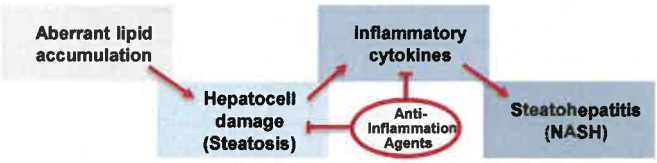
1 ***Current drug intervention of NASH are mainly focus on metabolism regulations***

U.S.
- (PPAR)-γ agonists: Thiazolidinediones / Pioglitazone
- Vitamin K

China
- (PPAR)-γ agonists: Pioglitazone
- GLP-1 agonists: Liraglutide

- Current drug intervention can only slow the accumulation of fat in liver tissue, while hardly resolve NASH and have no consistently reliable effect on fibrosis.
- Metabolism regulation includes glucose metabolism (Insulin resistance), lipid metabolism, and bile acid metabolism

2 ***MetS will lead to Steatosis, which can be targeted by anti-inflammation agents***



- Along with disease progression, aberrant lipid accumulation lead to hepatocellular damage and release inflammatory cytokines, and further lead to fibrosis.
- Targeting on cell damage and immune response, anti-inflammation agents may address the unmet clinical needs of eliminating inflammation and reversing NASH.

3 ***Future outlook: The combination of Anti-fibrotic and anti-inflammation interventions is expected to synergistically treat NASH.***

In addition to anti-inflammation agents, anti-fibrotic via cell apoptosis & liver fibrosis agents has been studied as well so that the combination of anti-fibrotic and anti-inflammation interventions potentially become a novel topic of drug development.

Source: Literature Review, Frost & Sullivan Analysis

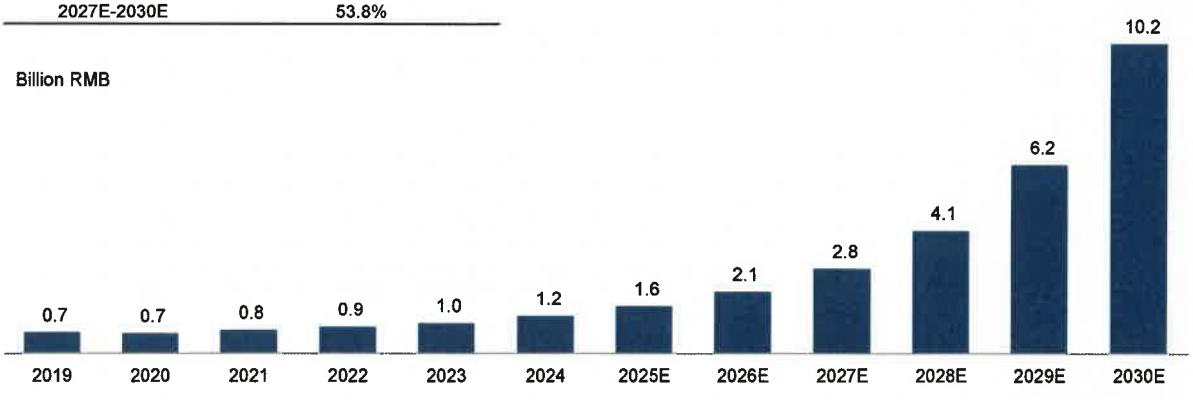
Updated

Historical and Forecasted of China NASH Drug Market Size, 2019-2030E

- China's NASH drug market has grown from RMB0.7 billion in 2019 to RMB1.2 billion in 2024 at a CAGR of 12.0%, and expected to increase to RMB2.8 billion in 2027 at a CAGR of 31.2% from 2024 and RMB10.2 billion in 2030 at a CAGR of 53.8% from 2027.

Historical and Forecasted of China NASH Drug Market Size, 2019-2030E

Period	CAGR
2019-2024	12.0%
2024-2027E	31.2%
2027E-2030E	53.8%



Source: Frost & Sullivan Analysis

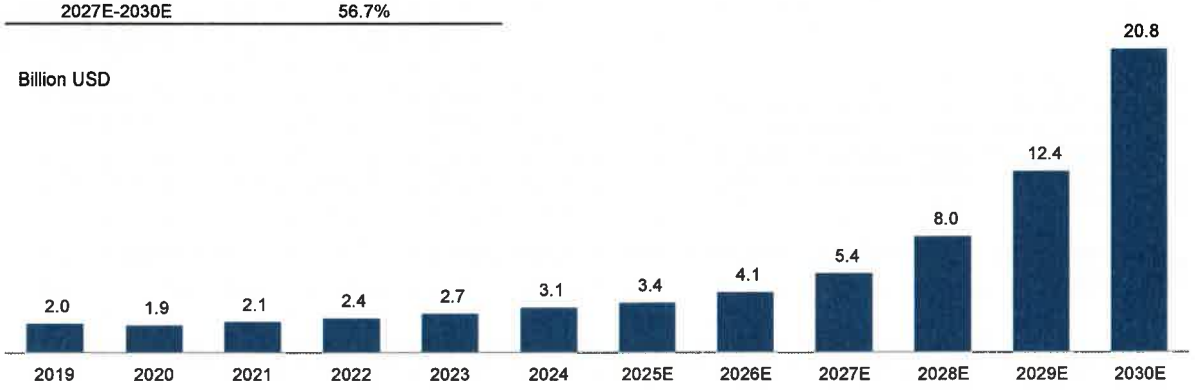
Updated

Historical and Forecasted of Global NASH Drug Market Size, 2019-2030E

- Global NASH drug market has grown from USD2.0 billion in 2019 to USD3.1 billion in 2024 at a CAGR of 9.1%, and expected to increase to USD5.4 billion in 2027 at a CAGR of 20.5% from 2024 and USD20.8 billion in 2030 at a CAGR of 56.7% from 2027.

Historical and Forecasted of Global NASH Drug Market Size, 2019-2030E

Period	CAGR
2019-2024	9.1%
2024-2027E	20.5%
2027E-2030E	56.7%



Source: Frost & Sullivan Analysis

Future Trend of NASH Treatment Drug Market

Increasing Prevalence of NAFLD/NASH	• In the globe, total prevalence of NASH has reached to 374.0 million in 2020 and is expected to grow to 486.2 million in 2030. Driven by aging population, high obesity rate, unhealthy lifestyle, as well as the more NAFLD patients are progress to NASH in the future, the patient pool for NASH sustains constant growth, which will drive the market expansion of NASH treatment.
Increment of Diagnosis rate and Consultation Rate	• For a long time, diagnosis of NASH lack of standard measurement and relies on the subjective perception of the disease of doctor. Such as blood test of liver enzymatic function and imaging have been used as an accessory method to confirm liver fat content and impairment of function, but could not conclusively confirm the presence of NASH. Local doctors, with the traditional view of fatty liver, even with liver enzyme abnormality , hepatitis rather than NASH would most likely be the diagnosis results. Benefit from the development of non-invasive diagnosis methods, such as FiberTouch and novel biomarkers (e.g. CK-18), the diagnosis rate of NASH will increase in the future. • Also, there are large quantity of patients in early stage of NASH, however due to less severe symptom, patients are less willing to obtain medical services until reaches later stages, where fibrosis and cirrhosis are harder to reverse. As NASH was recently brought to attention to the public, and diagnosis method has improved a lot, the willingness of consultation among NASH/NAFLD patients will expand in the future.
Innovative Drugs with Novel Mechanism Lead to Better Efficacy and Higher Treatment Rate	• Currently there is no approved drug to specifically targeting several aspects of the manifestation of NASH such as fibrosis or more severely, cirrhosis. Most applicable suggestions from doctors to alleviate NASH symptoms are simply through a healthier diet and life style to reduce fat in liver, which though has been shown to prevent the progression of NASH and ameliorate fibrosis, however, the effect is to a limited extent. • Along with the development of highly specific innovative drugs, such as THR-β agonists and VAP-1 inhibitors, the prognosis of patients have been obviously improved. Novel highly specific therapies target on MetS, inflammation and fibrosis rather than non-specifical liver protection (vitamin E or Hepatoprotective drugs), thereby obtain better efficacy and safety profile correspondingly. Hopefully, the disease progression of NASH can be slow down and even reversed. • Continuous attempts are being made to involve new mechanisms, which will further encourage and expediate potential effective agents to be applied in clinical practices more extensively, thereby improve the market size of NASH treatment.

Source: Frost & Sullivan Analysis

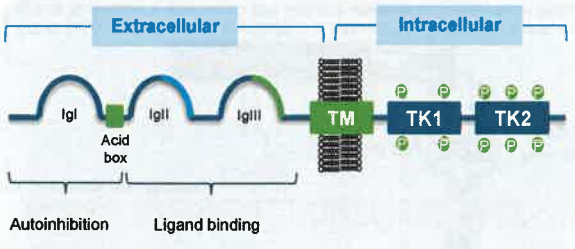
Table of Contents

Overview of FGFR

FGFR Structure and FGFR Family

- The fibroblast growth factor receptors (FGFRs) are a subfamily of receptor tyrosine kinases (RTK) that transduce biochemical signals induced by fibroblast growth factors (FGFs).

FGFR Structure



TM: Trans-membrane

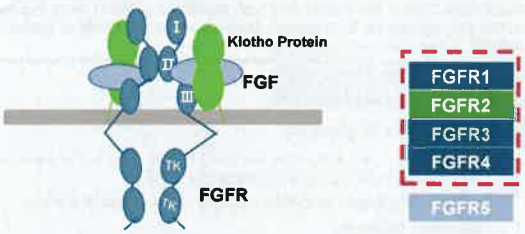
FGFR typically composed of three parts:

Extracellular domain:
- contains three immunoglobulin-like domains (Ig Ⅰ~IgⅢ)
- the ligand binding site is usually located at IgII and IgIII

Transmembrane domain:
- consisted of single-pass hydrophobic alpha helix
- facilitates signal transduction from extracellular region into the cytoplasmic domain

Intracellular domain:
- encompasses a tyrosine kinase domain
- transduce the signal to initiate downstream signal transduction

FGFR Family



TK: Tyrosine kinase domain; **FGF:** fibroblast growth factor

Members

FGFRs consist of five members (namely FGFR1, FGFR2, FGFR3, FGFR4) that share remarkable sequence homology.

Ligands

FGFR signaling is primarily triggered by the binding of the receptors to FGF ligands, with members of FGFR family exhibit ligand specificity.

Function

The FGFRs regulate important biological processes including cell proliferation and differentiation during development and tissue repair.

Notes: The Klotho proteins, αKlotho and βKlotho, are essential components of endocrine fibroblast growth factor (FGF) receptor complexes for their high-affinity binding.

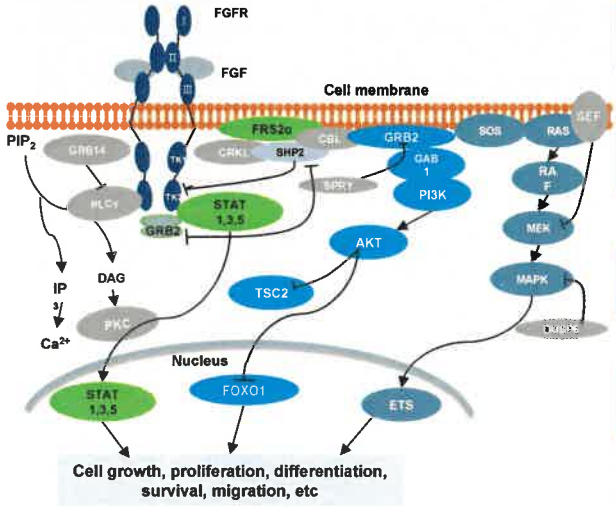
Source: Literature Review, Frost & Sullivan Analysis

Overview of FGFR

FGF/FGFR Pathway

- FGFRs are expressed on the cell membrane and can be stimulated and activated by extracellular signals. The native ligand of FGFRs is fibroblast growth factors (FGFs).
- The binding of FGF drives the dimerization of FGFR; subsequently, trans-autophosphorylation of the intracellular kinase domain is induced, followed by the activation of downstream transduction pathways, and participate in various vital physiological processes to maintain normal cell growth. However, dysfunction of these receptors lead to abnormal cell signaling, whose constitutive activity via ligand-independent activity resulting in oncogenetic activity.

FGF/FGFR Pathway



FGF/FGFR Signal Transduction

Ligand (FGF) binding

FGFRs dimerization

Phosphorylation of kinase domain

Downstream pathway activation

Normal Signal

In normal cell signaling, FGF/FGFR pathway mediates cell development processes, especially embryogenesis, angiogenesis, and tissue regeneration

Abnormal Signal

FGFR alteration including genetic substitutions, insertions, deletions, duplications or fusion lead to constitutive abnormal cell signaling, and thereby tumor growth.

FGFR alterations are observed in different types of cancers such as urothelial carcinoma, cholangial carcinoma, ovarian cancer, breast cancer, lung cancer, gastrointestinal cancers, etc.

Source: Literature Review, Frost & Sullivan Analysis

Overview of FGFR Target

FGFR Inhibitors

- Due to the frequent observation of FGFR signaling deregulation in many types of cancer, numerous targeted therapies, including small-molecule tyrosine kinase inhibitors (TKIs), FGFR specific antibody-based therapies and ligand traps, have been investigated in preclinical or clinical studies to attenuate FGFR signaling in cancer, suppressing tumor growth.
- Polyclonal secondary FGFR2 mutations drive acquired resistance to FGFR inhibition in patients with FGFR2-alteration cholangiocarcinoma.
- Existing co-mutations have also been implicated to confer primary resistance to FGFR inhibitors in CCA. In a comprehensive genomic profiling study of FGFR2 rearranged CCA in the FIGHT-202 trial, mutations in BAP1 were the most frequently encountered co-mutation and was associated with a somewhat shorter mPFS (6.9 months vs. 9.1 months). Patients with CDKN2A/B or PBRM1 mutations had a significantly shorter mPFS (CDKN2A/B, 6.4 months vs. 9.0 months; PBRM1, 4.7 months vs. 7.0 months.

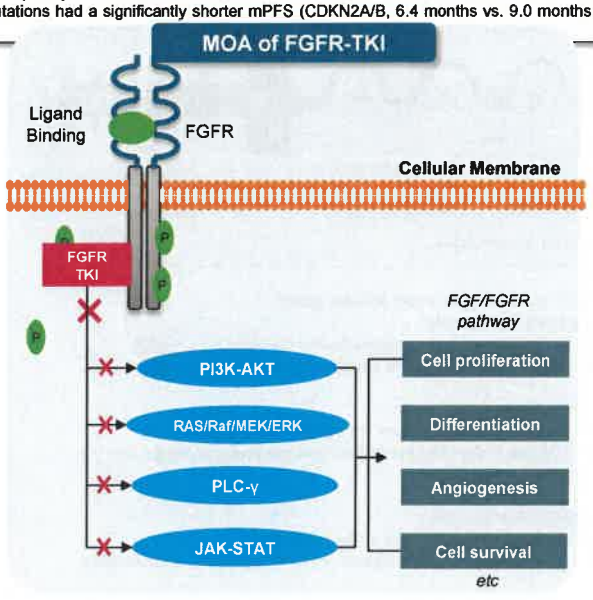
Overview of FGFR-TKIs

2 Mechanism of Action.

- FGFR-TKI works by inhibiting the FGFR phosphorylation and thereby the downstream tumor-genesis pathway.
- Studies demonstrated that nearly all patients treated with existing FGFR inhibitors ultimately experienced disease progression due to acquired resistance to FGFR inhibitors.

2 Acquired resistance to FGFR inhibitor

- Most acquired resistance to FGFR inhibitors can be attributed to polyclonal mutations in the FGFR2 kinase domain, such as the gate keeper mutation V564F, the molecular brake mutation N549K, the irreversible inhibitor specific mutation C491S, and a various of other mutations.
- Tinengotinib is the world's first and the only investigational drug that has entered registrational stage to treat FGFR inhibitor relapsed or refractory CCA patients.



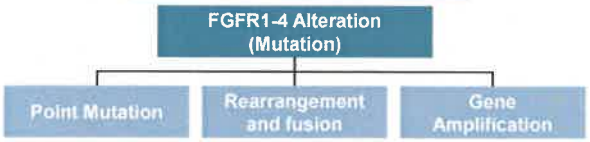
Source: Literature Review, Frost & Sullivan Analysis

Alterations of FGFR

Overview

- Numerous human pathological conditions are associated with the deregulation of FGFR signaling, which is largely attributed to several underlying mechanism of FGFR alteration, including point mutation, rearrangement and fusion, as well as gene amplification. FGFR mutation was observed in multiple cancers including urothelial cancer, cholangiocarcinoma, endometrial cancer, breast cancer, etc. FGFR alteration is prevalent in solid tumor patients, accounting for approximately 7.1% of all solid tumor patients. There is a greater demand for targeted therapies against FGFR and other oncogenic pathways, as well as higher therapeutic efficacy.

Overview of FGFR mutations



Point Mutation:

- Refers to a change in single nucleotide of DNA. For FGFR, oncogenic point mutations of FGFRs are observed both within and beyond kinase domain, and the majority of site mutation in FGFR have been reported to occur in FGFR2.

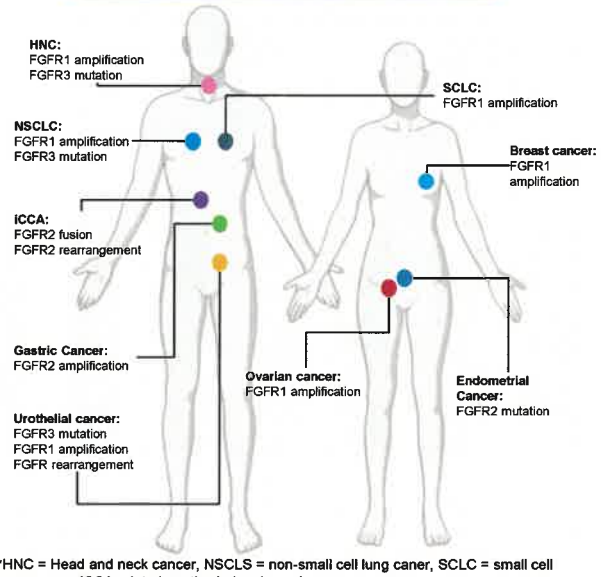
Gene Fusion and Rearrangement:

- Chromosomal rearrangement could result in gene fusions that hybrid two genes. For FGFR, it will lead to increased receptor dimerization and activation, as well as the dysregulated expression of FGFR or its fusion partner gene, leading to tumor growth.

Gene Amplification:

- Gene amplification refers to an increase in the number of copies of a gene without proportional increase in other genes. For FGFR, such alteration results in enhanced FGFR expression, which drives tumorigenesis.

Cancers with FGFR Alterations



*HNC = Head and neck cancer, NSCLS = non-small cell lung caner, SCLC = small cell lung cancer, iCCA = intrahepatic cholangiocarcinoma

Source: Literature Review, Frost & Sullivan Analysis

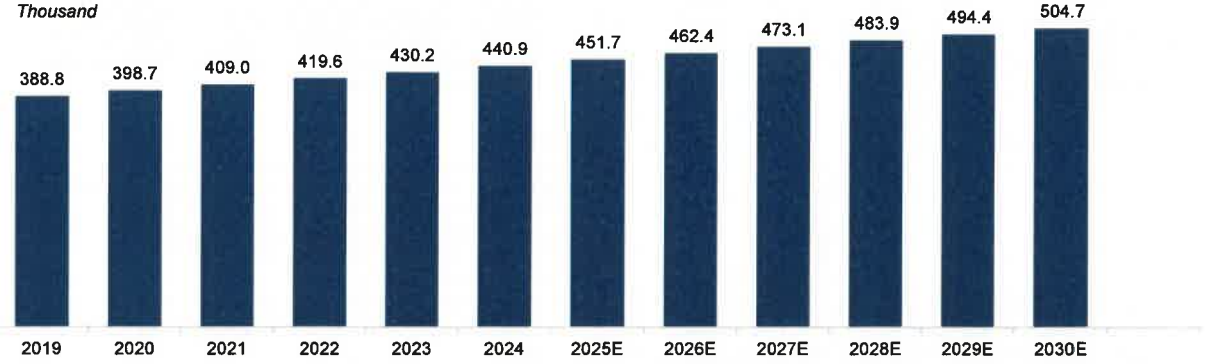
updated

Incidence of Major Tumor Types with FGFR Alteration in China, 2019-2030E

- Incidence number of major tumor types with FGFR alteration in China increased from 388.8 thousand to 440.9 thousand in 2019 and 2024. The number is expected to grow to 473.1 thousand in 2027 at a CAGR of 2.4% from 2024 to 2027. The number is expected to grow to 504.7 thousand in 2030, at a CAGR of 2.2%.

Incidence of Major Tumor Types with FGFR Alteration in China, 2019-2030E

Period	CAGR
2019-2024	2.6%
2024-2027E	2.4%
2027E-2030E	2.2%



Note: The article, Landscape of FGF/FGFR Alterations in 12,372 Chinese Cancer Patients, analyzed frequencies of FGFR aberrations in 12,372 solid tumors, including 20 types of cancer, such as urinary tract cancer (30.5%), endometrium cancer (16.9%), gastric cancer (13.3%), breast cancer (13.2%), colorectal cancer (10.2%), etc.. Another article, Cholangiocarcinoma With FGFR Genetic Aberrations: A Unique Clinical Phenotype mentioned around 25.2% of CCA patients are identified with FGFR aberrations. Based on the analysis, we estimate the China incidence of major tumor types with FGFR alteration.

Source: NCCR, Frost & Sullivan Analysis

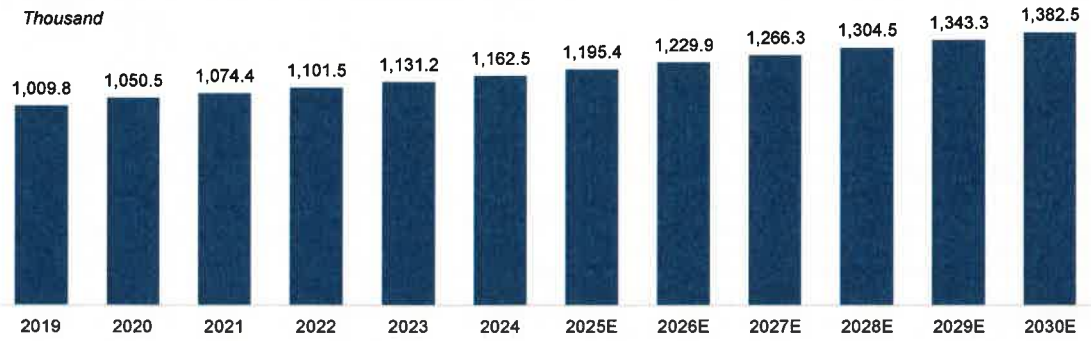
updated

Global Incidence of Major Tumor Types with FGFR Alteration, 2019-2030E

- Incidence number of major tumor types with FGFR alteration around the world increased from 1009.8 thousand to 1,162.5 thousand in 2019 and 2024. The number is expected to grow to 1,266.3 thousand in 2027 at a CAGR of 2.8% from 2024 to 2027. The number is expected to grow to 1,382.5 thousand in 2030, at a CAGR of 3.0%.

Global Incidence of Major Tumor Types with FGFR Alteration, 2019-2030E

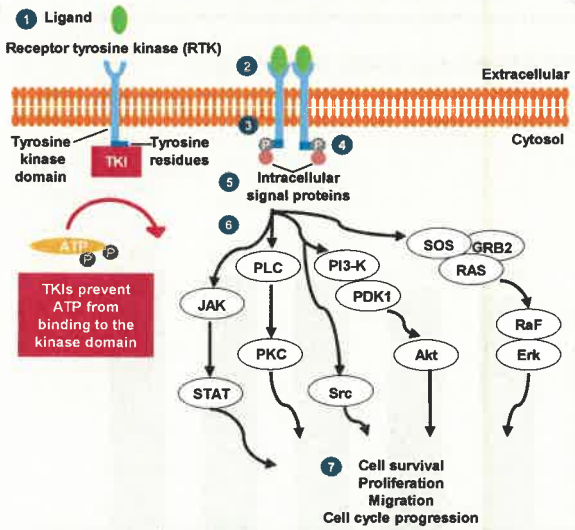
Period	CAGR
2019-2024	2.8%
2024-2027E	2.8%
2027E-2030E	3.0%



Note: The article, The FGFR Landscape in Cancer: Analysis of 4,853 Tumors by Next-Generation Sequencing, analyzed frequencies of FGFR aberrations in 4,853 solid tumors, including more than 15 types of cancer, such as urothelial cancer (32%), breast cancer (18%), endometrial cancer (13%), gastric cancer (7%), colorectal cancer (4.4%), etc.. Another article, Cholangiocarcinoma With FGFR Genetic Aberrations: A Unique Clinical Phenotype mentioned around 25.2% of CCA patients are identified with FGFR aberrations. Based on the analysis, we estimate the global incidence of major tumor types with FGFR alteration.
Source: IARC, Frost & Sullivan Analysis

Tyrosine Kinase Inhibitors

MoA of a tyrosine kinase inhibitor (TKI)



Schematic view of the MoA of RTKs. 1. Ligands bind the receptor. 2. Receptors join and dimerize. 3. Dimerization causes tyrosine kinase domains to become activated. 4. Receptor phosphorylates the opposite tyrosine residue. 5. The phosphorylated tyrosine residues activate the intracellular signal proteins. 6. Activated intracellular signal proteins trigger intracellular signaling pathways. 7. The integration of the activation of these intracellular cascades leads to outputs at the cellular level, including cell survival, proliferation, migration, cell cycle progression.

Overview

- A tyrosine kinase is an enzyme that can transfer a phosphate group from ATP to the tyrosine residues of specific proteins inside a cell to produce cell signal transduction resulting in a range of cellular processes. The family of tyrosine kinases encompasses the receptor tyrosine kinase proteins which contain a transmembrane (TM) domain and the non-receptor tyrosine kinases which do not possess transmembrane domains.
- The TM domain plays an important role in the dimerization process necessary for signal transduction, making receptor tyrosine kinases (RTKs) key regulatory signaling proteins governing cancer cell growth and metastasis. The discovery of RTK overexpression in various cancers has led to the development of several tyrosine kinase inhibitors (TKIs) for the treatment of malignancies.

MoA

TKIs do not prevent ligand binding or dimerization, but by preventing ATP from binding to the kinase domain, they block cross-phosphorylation of receptors and phosphorylation of substrates, and in consequence, signal transduction and cancer cell proliferation. TKIs can block substrate phosphorylation in 3 ways:

- Competing with ATP for binding to activated kinases
- Binding to ATP pocket and an adjacent region on inactive kinases
- Binding to sites on kinases remote from the ATP pocket, such as the substrate recognition region

Source: Literature Review, Frost & Sullivan Analysis

Comparison of Multi-targeted and Highly-selective Kinase Inhibitors

	Multi-targeted Kinase Inhibitor	***Highly Selective Kinase Inhibitor***
Diagnosis	• Based on histological diagnosis without the need for additional personalized patient selection	• The diagnosis is based on specific biomarkers detected from tumor or blood samples
Target Number	• Multi-target kinase inhibitor, which exert its anti-cancer activity by simultaneously targeting a wide range of kinases, target multiple signaling molecules in multiple signaling pathways	• Target on mono-signaling molecule in a single process
Limitation	• Having potential clinical efficacy for patients with unknown mutation types • The side effect of off target is more likely to occur, and there is greater safety risk in clinical use • Multi-target kinase inhibitor can extensively inhibit a variety of kinase targets. With extensive toxic effects, the R&D process requires considerable experience in drug development • Both desired targets and toxic targets must be considered in the design process • Disables exact titration of inhibition of the separate targets • Optimal inhibition of several targets might not be feasible at a dose with acceptable toxicity • May have hidden potential to other targets	• Tumors can become less responsive over time and ultimately progress due to acquired resistance mutations. • Need to consider drug-drug interaction when combining multiple drugs. • Less convenient to the patient and can result in more dosing mistakes. • The toxicities will be the sum of the toxicities of either agent alone when combination with other inhibitors. • Ineffective in the treatment of complex disease and highly heterogeneous cancers.
Advantages	• Helpful to overcome drug-resistance mechanisms such as bypass effects caused by single-target drugs, and has advantages in rescue treatment after failure of single-target treatment • Efficient for patients with several tumour types • Able to cut off multiple pathways for tumour growth and survival • Able to stop cross-talk among other receptors • Avoids possible drug-drug interactions • Convenient and less complex for patients	• Conducive to potentially develop novel combo therapies. • Able to titrate the dose of either agent to optimize target inhibition.

Source: Literature review, Frost & Sullivan Analysis

Competitive Landscape of FGFR inhibitors Approved by NMPA

Drug Name/Code	Brand Name	Target	Company	Indications	Approval Date
Pemigatinib	Pemazyre®	FGFR 1/2/3	Innovent / Incyte Corporation	Cholangiocarcinoma	2022/3/29

As of Dec 23rd ,2024

Source: NMPA, Frost & Sullivan Analysis

Competitive Landscape of FGFR inhibitors Approved by FDA

Drug Name/Code	Brand Name	Target	Company	Indications	Approval Date
Futibatinib	Lytgobi®	FGFR1/2/3/4	Taiho Pharmaceutical	Previously treated, unresectable, locally advanced or metastatic intrahepatic cholangiocarcinoma harboring fibroblast growth factor receptor 2 (FGFR2) gene fusions or other rearrangements	2022/9/30
Infigratinib	Truseltiq®	FGFR 1/2/3	BridgeBio Pharma / Helsinn Group	Previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement	2021/5/28
Pemigatinib	Pemazyre®	FGFR 1/2/3	Incyte Corporation	Previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement	2020/4/20
Erdafitinib	BALVERSA®	CSF1R, KIT, RET, VEGFR2/3, PDGFR, FGFR1/2/3/4	Janssen Biotech	Locally advanced or metastatic urothelial carcinoma (mUC) with susceptible FGFR3 genetic alterations whose disease has progressed on or after at least one line of prior systemic therapy	2019/04/12

Based on business plan considerations, Helsinn Group announced the withdrawal of its application for marketing infigratinib in the United States.
As of Feb 19th 2025

Source: FDA, Frost & Sullivan Analysis

Competitive Landscape of China FGFR inhibitors in Pipeline (1/2)

Drug Name	Target	Company	Clinical Stage	Indication	First Posted Date
TNP-2198 Capsule	TenNor Therapeutics	DdrP	Phase II	Helicobacter pylori infection	2023-02-28
Tegoprazan	Luoxin Pharmaceutical Co.,Ltd.	H+/K+ ATPase	Phase II	Helicobacter pylori infection	2022-06-17
盐酸柯诺拉赞片 (Hydrochloride Konularz Tablet)	Nanjing Shenzhou Jiamei Pharmaceutical Co.,Ltd.	H+/K+ ATPase	Phase II	Helicobacter pylori infection	2022-03-25
沃诺拉赞 (TAK-438) 20mg O/E Tablet	Takeda	H+/K+ ATPase	Phase II	Helicobacter pylori infection	2019-12-25
[14C] LX-15028	Luoxin Pharmaceutical Co.,Ltd.	H+/K+ ATPase	Phase III	Duodenal ulcer, Helicobacter pylori infection, Non-erosive gastroesophageal reflux disease, Reflux esophagitis	2022-06-13
	Jiangsu Simorda			Duodenal ulcer, Gastric ulcer,	

As of Feb 19th 2025
Note: TT-00434 is not listed on CDE.

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of China FGFR inhibitors in Pipeline (2/2)

Drug Name	Target	Company	Clinical Stage	Indication	First Posted Date
BB102	FGFR4	Broaden Biotechnology Co., Ltd	Phase 1	Advanced solid tumor	2022-09-23
BPI-17509	FGFR1/2/3	Betta Pharmaceuticals Co.Ltd	Phase 1	Advanced solid tumor	2019-10-23
BPI-43487	FGFR4	Betta Pharmaceuticals Co.Ltd	Phase 1	Advanced solid tumor	2021-03-25
HS-10340	FGFR4	Hansoh BioMedical Co.,Ltd.	Phase 1	Advanced solid tumor	2020-03-10
HS236	FGFR4	Hisun Pharmaceutical Co.Ltd.	Phase 1	Advanced solid tumor	2020-08-21
ICP-105	FGFR4	Tiancheng Pharmaceutical Technology Co., Ltd	Phase 1	Solid tumor	2018-08-24
JK0564	pan-FGFR	Jikun Pharmaceutical Technology Co., Ltd	Phase 1	Advanced solid tumor	2023-09-20
RG002	pan-FGFR	Lingda Biopharmaceutical Co., Ltd	Phase 1	Advanced solid tumor	2023-01-03
SC0011	pan-FGFR	Shijiazhuang Sagacity New Drug Development	Phase 1	Advanced solid tumor	2021-02-18
SY-4798	FGFR4	Shouyao Holdings (Beijing) Co., Ltd.	Phase 1	Advanced solid tumor	2021-04-14
SYHX2005	FGFR4	CSPC Ouyi Pharmaceutical Co.,Ltd.	Phase 1	Advanced solid tumor	2022-11-04
ZSP1241	FGFR4	Guangdong Zhongsheng Pharmaceutical Co.,Ltd.	Phase 1	Liver cancer, gastric cancer, cholangiocarcinoma, esophageal cancer, colorectal cancer and other advanced solid tumors	2018-11-09

As of Feb 19th 2025

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of Global FGFR inhibitors in Pipeline (1/3)

Drug Name	Target	Company	Clinical Stage	Indication	First Posted Date
Aldafermin	FGFR1、FGFR2、FGFR3	NGM Biopharmaceuticals	Phase 2/3	Primary Sclerosing Cholangitis (ALPINE-PSC)	2024-10-24
Fisogatinib	FGFR4	CStone Pharmaceuticals，Blueprint Medicines Corporation	Phase 2/3	Hepatocellular Carcinoma	2024-7-18
Rogaratinib	pan-FGFR	Bayer	Phase 2/3	Urothelial carcinoma	2018-01-25
AZD4547/ ABSK091	FGFR1/2/3	AstraZeneca/ Abbisko Therapeutics Co, Ltd	Phase 2/3	Squamous Cell Lung Cancer	2016-11-16
E7090	FGFR1/2/3	Eisai Co., Ltd.	Phase 2	Cholangiocarcinoma	2020-01-23
			Phase 2	Advanced or Recurrent Solid Tumor	2021-07-15
HMPL-453	FGFR1/2/3	Hutchmed	Phase 2	Advanced Intrahepatic Cholangiocarcinoma	2020-04-20
			Phase 1/2	Combination With Chemotherapy or Anti-PD-1 Antibody in the Treatment of Advanced Solid Tumor	2021-12-29
ICP-192	pan-FGFR	InnoCare Pharma Tech Co., Ltd.	Phase 2	Bladder Urothelial Cancer	2020-07-30
			Phase 2	Unresectable or Metastatic iCCA	2023-01-10
			Phase 2	Advanced Solid Tumor	2022-05-12
ABSK011	FGFR4	Abbisko Therapeutics Co, Ltd	Phase 2	Hepatocellular Carcinoma	2022-07-01
ABSK061	FGFR2/3	Abbisko Therapeutics Co, Ltd	Phase 2	Advanced Solid Tumor	2024-11-09
3HP-2827	FGFR2	3H (Suzhou) Pharmaceuticals Co., Ltd.	Phase 1/2	Solid Tumor	2024-04-22
EVER4010001	FGFR4	EverNov Medicines (Zhuhai Hengqin) Co., Ltd，Medidata Solutions	Phase 1/2	Advanced Solid Tumors	2021-01-07
RLY-4008	FGFR2	Relay Therapeutics, Inc.	Phase 1/2	Intrahepatic Cholangiocarcinoma，Cholangiocarcinoma and Other Solid Tumor	2020-08-25

As of Feb 19th 2025

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Competitive Landscape of Global FGFR inhibitors in Pipeline (2/3)

Drug Name	Target	Company	Clinical Stage	Indication	First Posted Date
FGF-401	FGFR4	Novartis Pharmaceuticals	Phase 1/2	Hepatocellular Carcinoma (HCC) and Other Solid Tumor	2014-12-25
TYRA-300	FGFR3	Tyra Biosciences, Inc	Phase 1/2	Locally Advanced or Metastatic Urothelial Carcinoma and Other Solid Tumor	2022-09-16
TransCon CNP	FGFR	Ascendis Pharma	Phase 1	Achondroplasia	2024-12-13
TT-00434	**FGFR1/2/3**	**Transthera**	**Phase 1**	**Advanced Solid Tumor**	**2021-04-05**
ABSK121	FGFR1/2/3	Abbisko Therapeutics Co, Ltd	Phase 1	Advanced Solid Tumor	2022-11-25
Alofanib	FGFR2	Russian Pharmaceutical Technologies	Phase 1	Metastatic Gastric Cancer	2019-08-28
ASP5878	pan-FGFR	Astellas Pharma Inc	Phase 1	Solid Tumor	2014-01-16
CPL304110	FGFR1/2/3	Celon Pharma SA	Phase 1	Gastric Cancer, Bladder Cancer, Squamous Non-small Cell Lung Cancer, Cholangiocarcinoma, Sarcoma, Endometrial Cancer, Other Solid Tumor	2019-11-04
H3B-6527	FGFR4	H3 Biomedicine Inc. / Eisai Inc.	Phase 1	Advanced Hepatocellular Carcinoma	2016-07-15

As of Feb 19th 2025

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Competitive Landscape of Global FGFR inhibitors in Pipeline (3/3)

Drug Name	Target	Company	Clinical Stage	Indication	First Posted Date
ICP-105	FGFR4	InnoCare Pharma Tech Co., Ltd.	Phase 1	Solid Tumor	2018-08-22
KIN3248	FGFR2/3	Kinnate Biopharma	Phase 1	Intrahepatic Cholangiocarcinoma, Urothelial Carcinoma and Other Solid Tumor	2022-02-16
LOXO-435	FGFR3	Eli Lilly and Company	Phase 1	Metastatic Bladder Cancer and Ureteral Cancer	2022-11-14
LY2874455	pan-FGFR	Eli Lilly and Company	Phase 1	Relapsed and Refractory Adult Acute Myeloid Leukemia	2017-04-24
LY3084077	FGFR1	Eli Lilly and Company	Phase 1	Healthy Volunteers	2013-05-03
TYRA-200	FGFR1/2/3	Tyra Biosciences, Inc	Phase 1	Locally Advanced Cholangiocarcinoma, Intrahepatic Cholangiocarcinoma and Other Solid Tumor	2023-12-07
ZSP1241	FGFR4	Zhongsheng Pharmaceutical Co., Ltd.	Phase 1	Hepatocellular Carcinoma, Cholangiocarcinoma, Gastric Cancer, Esophageal Cancer, Colorectal Cancer	2018-11-08
BB102	FGFR4	BrodenBio Co., Ltd.	Phase 1	Solid Tumor	2024-02-14

As of Feb 19th 2025

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Competitive Landscape of China MTK inhibitors targeting on FGFR/VEGFR & Aurora or JAK in Pipeline

Drug Name	Target	Company	Clinical Stage	Indication	First Posted Date
Tinengotinib	**FGFR, VEGFR, JAK2, Aurora A/B**	**TransThera**	**Phase 2**	**FGFR-altered Advanced or Metastatic CCA with Prior Chemotherapy or FGFR Inhibitor Treatment**	**2023-09-22**
			Phase 2	**HER2- Breast Cancer, Metastatic Castration Resistant Prostate Cancer, Gastric Cancer and Other Solid Tumor**	**2021-11-08**
AL8326	AURKB, VEGFR, FGFR	Advenchen	Phase 3	Small Cell Lung Cancer	2023-10-20
TQB2868	PDGFR、KIT、VEGFR、FGFR、RET、PD-1、TGFB	Chia Tai Tianqing Pharmaceutical Group Nanjing Shunxin Pharmaceutical Co., Ltd.	Phase 2	Pancreatic Neoplasms	2025-1-10
MAX-40279-01	FGFR, HPK1, FLT3, VEGF, PDGF, JAK	MaxiNovel Technology Co., Ltd	Phase 2	Advanced Colorectal Cancer	2021-11-29
			Phase 2	Advanced Gastric Cancer and Gastroesophageal Junctional Carcinoma	2022-02-16
			Phase 1/2	Combination with KN-046 in the Treatment of Advanced and Metastatic Solid Tumor	2022-04-11
			Phase 1/2	Myelodysplastic Syndrome, Relapsed/Refractory Acute Myeloid Leukemia	2021-06-02

As of Feb 19th 2025
***Note: According to CDE, it still shows Tinengotinib for CCA is in phase 2, we refer to that.**

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of Global MTK inhibitors targeting on FGFR/VEGFR & Aurora or JAK in Pipeline

Drug Name	Target	Company	Clinical Stage	Indication	First Posted Date
Tinengotinib	**FGFR, VEGFR, JAK2, Aurora A/B**	**TransThera**	**Phase 3**	**FGFR-altered Advanced or Metastatic CCA with Prior Chemotherapy or FGFR Inhibitor Treatment**	**2023-07-17**
			Phase 1/2	**Metastatic Castration Resistant Prostate Cancer**	**2024-06-13**
			Phase 1/2	**HER2- Breast Cancer, Metastatic Castration Resistant Prostate Cancer, Gastric Cancer and Other Solid Tumor**	**2021-02-08**
			Phase 1/2	**Combination with Atezolizumab in the Treatment of Cholangiocarcinoma, Biliary Tract Cancer, HER2- Breast Cancer, Triple Negative Breast Cancer, Small-cell Lung Cancer, Bladder Cancer, Prostate Cancer and Other Solid Tumor**	**2022-02-23**
AL8326	AURKB, VEGFR, FGFR	Advenchen	Phase 3	Small Cell Lung Cancer	2024-02-08
AUR-109	PDGFR、KIT、VEGFR、FGFR、RET、PD-1、TGFB	Aurigene	Phase 2	Pancreatic Neoplasms	2025-01-10
Max-40279-01	FGFR, HPK1, FLT3, VEGF, PDGF, JAK	MaxiNovel Technology Co., Ltd	Phase 2	Advanced Colorectal Cancer	2021-11-22
			Phase 2	Advanced Gastric Cancer and Gastroesophageal Junctional Carcinoma	2022-05-27
			Phase 1/2	Myelodysplastic Syndrome, Relapsed/Refractory Acute Myeloid Leukemia	2021-09-29
			Phase 1/2	Advanced and Metastatic Solid Tumor	2022-06-21

As of Dec 23rd 2024

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Competitive Landscape of China/Global MTK inhibitors targeting on FGFR/VEGFR & Aurora or JAK in Pipeline

Drug Name	Target	Company	Clinical Stage	Indication	First Posted Date*	Study Locations
Tinengotinib	FGFR, VEGFR, JAK2, Aurora A/B	TransThera	Phase 3	FGFR-altered Advanced or Metastatic CCA with Prior Chemotherapy or FGFR Inhibitor Treatment	2023-07-17	The U.S., South Korea, Taiwan, United Kingdom and eight countries in EU
			Phase 2	FGFR-altered Advanced or Metastatic CCA with Prior Chemotherapy or FGFR Inhibitor Treatment	2023-09-22	China
			Phase 1/2	Metastatic Castration Resistant Prostate Cancer	2024-06-13	the US
			Phase 1/2	HER2- Breast Cancer, Metastatic Castration Resistant Prostate Cancer, Gastric Cancer and Other Solid Tumor	2021-02-08	the US
			Phase 2	HER2- Breast Cancer, Metastatic Castration Resistant Prostate Cancer, Gastric Cancer and Other Solid Tumor	2021-11-08	China
			Phase 1/2	Combination with Atezolizumab in the Treatment of Cholangiocarcinoma, Biliary Tract Cancer, HER2- Breast Cancer, Triple Negative Breast Cancer, Small-cell Lung Cancer, Bladder Cancer, Prostate Cancer and Other Solid Tumor	2022-02-23	China
AL8326*	AURKB, VEGFR, FGFR	Advenchen	Phase 3	Small cell lung cancer	2024-02-08	China
			Phase 2	Small cell lung cancer	2022-05-05	the US
			Phase 2	Advanced colorectal cancer	2021-11-29	China
MAX-40279-01	FGFR, HPK1, FLT3, VEGF, PDGF, JAK	MaxiNovel Technology Co., Ltd	Phase 2	Advanced gastric cancer and gastroesophageal junctional carcinoma	2022-02-16	China
			Phase 2	Combination with KN-046 in the Treatment of Advanced and Metastatic Solid Tumor	2022-04-11	China
			Phase 1/2	Myelodysplastic Syndrome, Relapsed/Refractory Acute Myeloid Leukemia	2021-06-02	China

As of Feb 19th, 2025

*Note:Tinengotinib is currently under development as an alternative and add-on options for the patients

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

Competitive Landscape of China/Global MTK inhibitors targeting on FGFR/VEGFR & Aurora or JAK in Pipeline

Drug Name	Target	Company	Clinical Stage	Indication	First Posted Date*	Study Locations
TQB2868	PDGFR、KIT、VEGFR、FGFR、RET、PD-1、TGFB	Chia Tai Tianqing Pharmaceutical Group Nanjing Shunxin Pharmaceutical Co., Ltd.	Phase 2	Pancreatic Neoplasms	2025-1-10	CHINA
AUR-109	PDGFR、KIT、VEGFR、FGFR、RET、PD-1、TGFB	Aurigene	Phase 2	Pancreatic Neoplasms	2025-01-07	INDIA

As of Feb 19th, 2025

*Note:Tinengotinib is currently under development as an alternative and add-on options for the patients

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

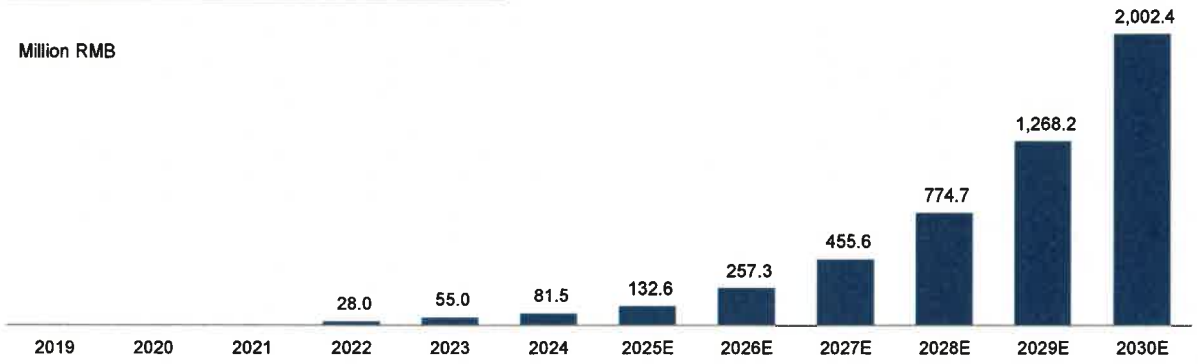
updated

Historical and Forecasted of China FGFR Inhibitor Market Size, 2019-2030E

- China's FGFR inhibitor market has grown from RMB28.0 million in 2022 to RMB81.5 million in 2024, and expected to increase to RMB455.6 million in 2027 at a CAGR of 77.5% from 2024 and RMB2,002.4 million in 2030 at a CAGR of 63.8% from 2027.

Historical and Forecasted of China FGFR Inhibitor Market Size, 2019-2030E

Period	CAGR
2019-2024	NA
2024-2027E	77.5%
2027E-2030E	63.8%



Source: Frost & Sullivan Analysis

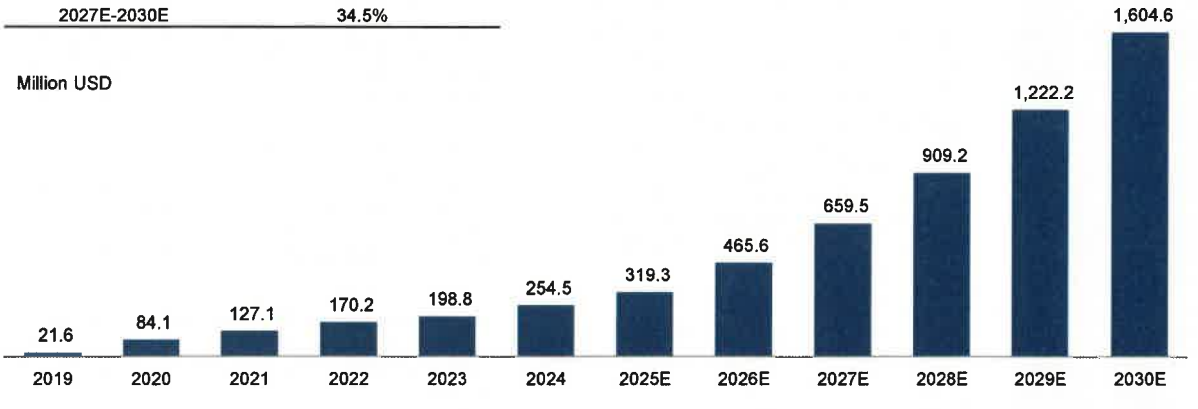
updated

Historical and Forecasted of Global FGFR Inhibitor Market Size, 2019-2030E

- Global FGFR inhibitor market has grown from USD21.6 million in 2019 to USD254.5 million in 2024 at a CAGR of 63.8%, and expected to increase to USD659.5 million in 2027 at a CAGR of 37.4% from 2024 and USD1,604.6 million in 2030 at a CAGR of 34.5% from 2027.

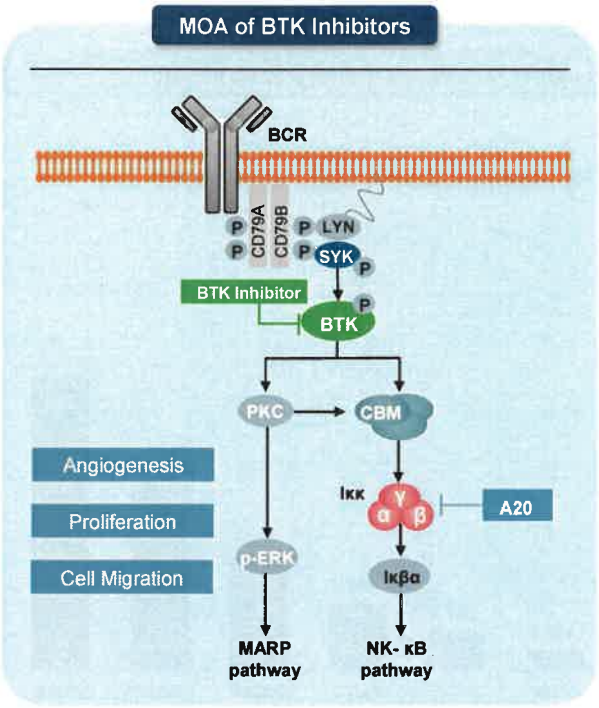
Historical and Forecasted of Global FGFR Inhibitor Market Size, 2019-2030E

Period	CAGR
2019-2024	63.8%
2024-2027E	37.4%
2027E-2030E	34.5%



Source: Frost & Sullivan Analysis

Overview of Bruton's Tyrosine Kinase (BTK) Inhibitors



Drug Properties

1 Drug Target

- BTK is a cytoplasmic, non-receptor tyrosine kinase (PTK) that belongs to the Tec (tyrosine kinase expressed in hepatocellular carcinoma) kinase family, and plays a central role in signaling of various cell surface receptors, most prominently of the B-cell antigen receptor (BCR).

2 Mechanism

- BCR signaling in normal B cells ultimately results in activation of a transcriptional program that fosters proliferation, differentiation and survival of selected B cells, which is the basis for specific antibody and production and response.
- BTK plays a central role in the pathogenesis of B-cell lymphomas by continuously activating downstream signals of the B-cell receptor.

3 Approved Drug

- Ibrutinib (PCI-32765, brand name: Imbruvica) is the first-in-class, highly potent small molecule inhibitor that selectively binds to cysteine 481 residue in the allosteric inhibitory segment of BTK kinase domain. It demonstrated high clinical activity in B-cell malignancies, especially in patients with chronic lymphocytic leukemia (CLL), mantle cell lymphoma (MCL), and Waldenstrom's macroglobulinemia (WM). Despite their efficacy, treatment failure often occurs through the development of resistance or intolerance, with over 36-months follow-up showing the overall discontinuation rate of ibrutinib treatment in patients with 0, 1 to 2, and ≥3 prior treatments was 36%. Acalabrutinib and zanubrutinib are second generation BTK inhibitors, which are more potent and selective than ibrutinib with reduced off-target side effects.

4 Side Effect

- Untoward effects, such as bleeding, dermatitis, diarrhea and atrial fibrillation have been observed and attributed in part to its off-target effects on the epidermal growth factor receptor and the Tec family proteins other than BTK.
- In addition, resistance to ibrutinib has been observed.

Source: Literature Review, Frost & Sullivan Analysis

Comparison Between Covalent and Non-covalent BTK Inhibitors

- Non-covalent reversible BTK inhibitors have shown great potentials in current studies, as they are able to address the drug resistance by alternative binding site, and have good safety profiles compared with covalent irreversible BTK inhibitors as well.
- Current research results show that non-covalent reversible BTK inhibitors have potential efficacy in patients who are resistant to previous covalent BTK inhibitors, prolonging the life of leukemia patients.

	Covalent	Non-covalent
Definition	• BTK inhibitors that form covalent bond to BTK protein. • Irreversible due to the feature of covalent bond.	• BTK inhibitors that bind BTK protein with other molecular interactions such as hydrogen bond. • Reversible
Drug Resistance	• Covalent BTK inhibitors can form a covalent bond with the C481 site of BTK, however it was found that when C481S mutation occurs, the BTK inhibitor cannot maintain the covalent bond, leading to drug resistance.	• Non-covalent BTK inhibitors do not bind with C481 residue, thereby can inhibit BTK even in the presence of C481S mutation.
Efficacy	• Due to the feature of covalent bonds, the stability of covalent bond is much higher than non-covalent molecular interaction. Therefore, covalent BTK inhibitors take rapid effect with lower IC_{50} value.	• By inhibiting B-cell activation and downstream survival signaling pathways, non-covalent agents inhibit the proliferation of B-cell tumors with high expression of BTK. Thus, these agents have respectable efficacy.
Adverse Effect	• As covalent binding are too stable that hardly to break, irreversible inhibition of multiple pathway lead to adverse effect.	• Non-covalent BTK inhibitors have higher selectivity, and does not interfere with the activity of ITK. Thus, it has better safety profiles compared with covalent agents.

Source: Frost & Sullivan Analysis

Competitive Landscape of BTK Inhibitor Approved by NMPA

Drug Name	Brand Name	Target	Company	Molecular feature	Indications	Approval Date
Jaypirca	Pirtobrutinib	BTK	Lilly del Caribe, Inc.	Non-covalent; reversible	Mantle cell lymphoma	2024-10-22
Acalabrutinib	CALQUENCE®	BTK	AstraZeneca	Covalent; Irreversible	MCL; CLL/SLL	2023-03-21
Orelabrutinib	Yi Kainuo®	BTK	InnoCare	Covalent; Irreversible	MCL; CLL/SLL; MZL	2020-12-25
Zanubrutinib	BRUKINSA®	BTK	BeiGene	Covalent; Irreversible	MCL; CLL/SLL; Fahrenheit giant globulinemia	2020-06-02
Ibrutinib	IMBRUVICA®	BTK	Janssen	Covalent; Irreversible	MCL; CLL/SLL; Fahrenheit giant globulinemia	2017-08-24

Note: Approval date: First approval date
CLL/SLL= Chronic Lymphoblastic Leukemia / Small lymphocyte lymphoma; MCL= Mantle Cell Lymphoma; MZL=Marginal Zone Lymphoma
As of Feb 19th 2025

Source: NMPA, Frost Sullivan Analysis

Competitive Landscape of BTK Inhibitor Approved by FDA

Drug Name	Brand Name	Target	Company	Molecular feature	Indications	Approval Date
Pirtobrutinib	JAYPIRCA®	BTK	Loxo Oncology	Noncovalent; Reversible	MCL	2023-01-27
Zanubrutinib	BRUKINSA®	BTK	BeiGene	Covalent; Irreversible	MCL; CLL/SLL; Fahrenheit giant globulinemia; MZL	2019-11-14
Acalabrutinib	CALQUENCE®	BTK	AstraZeneca / Innate Pharma	Covalent; Irreversible	MCL; CLL/SLL	2017-10-31
Ibrutinib	IMBRUVICA®	BTK	Janssen / AbbVie	Covalent; Irreversible	MCL; CLL/SLL; Fahrenheit giant globulinemia; cGVHD; MZL	2013-11-13

Note: Approval date: First approval date;
CLL/SLL= Chronic Lymphoblastic Leukemia / Small lymphocyte lymphoma, MZL= Marginal Zone Lymphoma, MCL= Mantle Cell Lymphoma, cGVHD= Chronic Transplantation Anti-Host Disease
As of Feb 19th 2025

Source: FDA, Frost Sullivan Analysis

Competitive Landscape of China BTK Inhibitor in Pipeline (1/3)

Drug Name	Target	Molecular feature	Company	Clinical Stage	Indications	First Posted Date
LOXO-305	BTK	Noncovalent; Reversible	LOXO ONCOLOGY	NDA	MCL	2023-10-16
				Phase 3	CLL, SLL	2022-08-08
Fenebrutinib	BTK	Noncovalent; Reversible	Roche	Phase 3	Multiple Sclerosis	2021-09-13
LOU064	BTK	Covalent; Irreversible	Novartis	Phase 3	Chronic Inducible Urticaria	2024-01-29
ARQ-531	BTK	Noncovalent; Reversible	MSD	Phase 3	CLL, SLL	2023-03-28
Rilzabrutinib	BTK	Covalent; Reversible	Sanofi(China)Investment Co.,Ltd.	Phase 3	Primary Immune Thrombocytopenia	2022-03-15
SAR442168	BTK	Covalent; Irreversible	Sanofi	Phase 3	Multiple Sclerosis	2021-01-26
SHR1459	BTK	Covalent; Irreversible	Hengrui Pharmaceuticals Co., Ltd.	Phase 2	Idiopathic Membranous Nephropathy	2018-10-19
				Phase 1/2	B-cell NHL	2021-07-09
CT-1530	BTK	Covalent; Irreversible	Centaurus BioPharma Co.,Ltd.	Phase 2	MCL	2020-07-29
HWH486	BTK	Not disclosure	Humanwell Healthcare (group) Co.,Ltd.	Phase 2	Chronic Spontaneous Urticaria	2023-11-20
MH048	BTK	Noncovalent; Reversible	Minghui Pharmaceutical Co., Ltd	Phase 2	B-cell Lymphoma	2022-04-14
LP-168	BTK	(Covalent; Irreversible) and (Noncovalent; Reversible)	Lupeng Pharmaceutical Company Limited	Phase 2	MCL	2023-01-12

Note: CLL/SLL= Chronic Lymphoblastic Leukemia / Small lymphocyte lymphoma, WM= F giant globulinemia, MZL= limbic lymphoma, MCL= Mantle Cell Lymphoma; NHL=Non-Hodgkin lymphoma; DLBLC= Diffuse Large B Cell Lymphoma; PCNSL = Primary Central Nervous System Lymphoma; FL=Follicular Lymphoma
As of Dec 23rd 2024

Source: CDE, Frost & Sullivan Analysis

updated

Competitive Landscape of China BTK Inhibitor in Pipeline (2/3)

Drug Name	Target	Molecular feature	Company	Clinical Stage	Indications	First Posted Date
HS-10561	BTK	Not disclosure	Hansoh Pharmaceutical	Phase 1/2	Chronic spontaneous urticaria (CSU)	2025-03-12
CX1440	BTK	Not disclosure	Bangshun Pharmaceutical Co., Ltd	Phase 1/2	Primary Immune Thrombocytopenia	2022-09-07
HBW-3210	BTK	Noncovalent; Reversible	Hyperway Pharmaceuticals	Phase 1/2	B-cell Lymphoma	2023-10-09
HBW-3220	BTK	Noncovalent; Reversible	Hyperway Pharmaceuticals	Phase 1/2	B-cell Lymphoma	2022-05-20
HZ-A-018	BTK	Covalent	HealZen	Phase 1/2	Primary Central Nervous System Lymphoma	2021-02-01
TM471-1	BTK	Covalent	HENAN ZHIWEI BIOMEDICINEO.LTD	Phase 1/2	B-cell NHL	2024-12-23
TQB3019	BTK	Not Disclosure	Chia Tai Tianqing Pharmaceutical Group Co., Ltd.	Phase 1	Advanced Malignant Cancer	2025-04-22
TT-01488	BTK	**Noncovalent; Reversible**	**TransThera**	**Phase 1**	**B-cell Lymphoma**	**2023-01-04**
BT-1053	BTK	Not Disclosure	Brilliant Co., Ltd|ScinnoHub Pharmaceutical Co., Ltd	Phase 1	B-cell NHL	2019-10-16
DTRMWXHS-12	BTK	Covalent; Irreversible	DTRM Biopharma	Phase 1	MCL	2019-06-14
PRT1419	BTK	Noncovalent; Reversible	PIU PHARMED	Phase 1	B-cell NHL	2021-12-15
DB-175	BTK	Covalent; Irreversible	Shanghai Jiabao Yaoyin Pharmaceutical Technology Co., Ltd	Phase 1	DLBLC	2023-07-07

Note: CLL/SLL= Chronic Lymphoblastic Leukemia / Small lymphocyte lymphoma, WM= F giant globulinemia, MZL= limbic lymphoma, MCL= Mantle Cell Lymphoma; NHL=Non-Hodgkin lymphoma; DLBLC= Diffuse Large B Cell Lymphoma; PCNSL = Primary Central Nervous System Lymphoma; FL=Follicular Lymphoma
As of Dec 23rd 2024

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of China BTK Inhibitor in Pipeline (3/3)

Drug Name	Target	Molecular feature	Company	Clinical Stage	Indications	First Posted Date
SN1011/EVER001	BTK	Covalent; Reversible	SinoMab BioScience	Phase 1	Systemic Lupus Erythematosus	2020-12-30
			SinoMab BioScience/Everest Medicines	Phase 1	Glomerular Disease	2023-02-28
SS-001	BTK	Not Disclosure	淄博百极常生制药 (No Official English Name)	Phase 1	B-cell Lymphoma	2021-11-01
TQB3702	BTK	Not Disclosure	Chia Tai-tianqing Pharmaceutical Co., Ltd.	Phase 2 Phase 1 Phase 1	B-cell Lymphoma LSE Hematological Cancer	2024-08-21 2024-06-14 2024-01-12
WXSH0057	BTK	Reversible	BESTAND MEDICAL TECHNOLOGY CO., LTD.	Phase 1	B-Cell Lymphoma	2022-08-26
XNW 1011	BTK	Covalent; Reversible	Suzhou Xinnuowei Pharmaceutical Technology	Phase 1	B-cell Lymphoma	2019-09-16
YZJ-3058	BTK	Not Disclosure	Haiyan Pharma	Phase 1	Rheumatoid Arthritis	2021-08-09
ZXBT-1158	BTK	Not Disclosure	BeBetter Med Co., Ltd	Phase 1	B-Cell Lymphoma	2021-01-18

Note: CLL/SLL= Chronic Lymphoblastic Leukemia / Small lymphocyte lymphoma, WM= F giant globulinemia, MZL= limbic lymphoma, MCL= Mantle Cell Lymphoma; NHL=Non-Hodgkin lymphoma; DLBLC= Diffuse Large B Cell Lymphoma; PCNSL = Primary Central Nervous System Lymphoma; FL=Follicular Lymphoma
As of Feb 19th 2025

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of Global BTK Inhibitor in Pipeline (1/3)

Drug Name	Target	Molecular feature	Company	Clinical Stage	Indications	First Posted Date
Evobrutinib	BTK	Covalent	Merck	Phase 3	Relapsing Multiple Sclerosis	2020-04-08
Fenebrutinib*	BTK	Noncovalent; Reversible	Roche	Phase 3	Relapsing Multiple Sclerosis	2020-10-14
LOU064	BTK	Covalent; Irreversible	Novartis	Phase 3	Chronic Spontaneous Urticaria	2021-09-01
				Phase 3	Relapsing Multiple Sclerosis	2021-12-07
ARQ-531	BTK	Noncovalent; Reversible	MSD	Phase 3	CLL, SLL	2022-11-22
Rilzabrutinib	BTK	Covalent; Reversible	Sanofi	Phase 3	Immune Thrombocytopenia	2020-09-24
SAR442168	BTK	Covalent; Irreversible	Sanofi	Phase 3	Relapsing Multiple Sclerosis	2020-06-01
TL-925	BTK	Not Disclosure	Telios Pharma	Phase 2	Allergic Conjunctivitis	2024-03-05
				Phase 2	Dry Eye Disease	2024-01-26
BIIB091	BTK	Noncovalent; Reversible	Biogen	Phase 2	Relapsing Multiple Sclerosis	2023-04-04
BMS-986142	BTK	Reversible	Bristol-Myers Squibb	Phase 2	Rheumatoid Arthritis	2015-12-23
				Phase 2	Atopic Dermatitis	2021-07-29
Branebrutinib / BMS-986195	BTK	Covalent; Irreversible	Bristol-Myers Squibb	Phase 2	Autoimmune Disorder, Rheumatoid Arthritis, Systemic Lupus Erythematosus, Primary Sjogren's Syndrome	2019-12-05
CC-292	BTK	Covalent; Irreversible	Celgene	Phase 2	Rheumatoid Arthritis	2013-11-03

Note: CLL/SLL= Chronic Lymphoblastic Leukemia / Small lymphocyte lymphoma, WM= F giant globulinemia, MZL= limbic lymphoma, MCL= Mantle Cell Lymphoma; NHL=Non-Hodgkin lymphoma; DLBLC= Diffuse Large B Cell Lymphoma; PCNSL = Primary Central Nervous System Lymphoma; FL=Follicular Lymphoma
*: FDA Places Clinical Hold on Roche's BTK Inhibitor Fenebrutinib for Multiple Sclerosis. As a result of the hold, new enrollment for the FENhance 1 trial (NCT04586023) in the US will be paused, while enrollment in countries outside of the US will continue.
As of Feb 19th 2025

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Competitive Landscape of Global BTK Inhibitor in Pipeline (2/3)

Drug Name	Target	Molecular feature	Company	Clinical Stage	Indications	First Posted Date
DTRMWXHS-12	BTK	Covalent; Irreversible	DTRM Biopharma	Phase 2	CLL, SLL, DLBLC, FL, Richter's Transformation	2020-03-12
LP-168	BTK	(Covalent; Irreversible) and (Noncovalent; Reversible)	Lupeng Pharmaceutical Company LTD.	Phase 2	MCL	2023-02-08
PRN473	BTK	Covalent; Reversible	Sanofi	Phase 2	Atopic Dermatitis	2021-08-05
SHR1459 /Edralbrutinib	BTK	Covalent; Irreversible	Reistone Biopharma	Phase 2	Primary Membranous Nephropathy	2021-11-29
				Phase 2	Neuromyelitis Optica Spectrum Disorders	2020-12-17
TAS5315	BTK	Covalent; Irreversible	Taiho Pharmaceutical Co., Ltd.	Phase 2	Chronic Spontaneous Urticaria	2022-04-19
				Phase 2	Rheumatoid Arthritis	2018-07-30
Tirabrutinib	BTK	Covalent; Irreversible	Ono Pharmaceutical Co. Ltd / Gilead Sciences	Phase 2	Primary Central Nervous System Lymphoma	2021-07-01
				Phase 2	Chronic Lymphocytic Leukemia	2016-12-06
				Phase 2	Sjogren's Syndrome	2017-04-04
TL-895	BTK	Covalent; Irreversible	Telios Pharma, Inc.	Phase 2	Myelofibrosis	2020-11-24
				Phase 1/2	MCL, DLBCL, CLL, SLL	2016-07-07
CT-1530	BTK	Covalent; Irreversible	Centaurus Biopharma Co., Ltd.	Phase 1/2	CLL, WM, MZL, DLBLC	2016-12-05

Note: CLL/SLL= Chronic Lymphoblastic Leukemia / Small lymphocyte lymphoma, WM= F giant globulinemia, MZL= limbic lymphoma, MCL= Mantle Cell Lymphoma; NHL=Non-Hodgkin lymphoma; DLBLC= Diffuse Large B Cell Lymphoma; PCNSL = Primary Central Nervous System Lymphoma; FL=Follicular Lymphoma
As of Feb 19th 2025

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Competitive Landscape of Global BTK Inhibitor in Pipeline (3/3)

Drug Name	Target	Molecular feature	Company	Clinical Stage	Indications	First Posted Date
TT-01488	**BTK**	**Noncovalent; Reversible**	**TransThera**	**Phase 1**	**B-Cell Lymphoma**	**2023-01-13**
ABBV-101	BTK	Not Disclosure	AbbVie	Phase 1	B-cell Lymphoma	2023/3/3
AC0058	BTK	Covalent; Irreversible	ACEA Therapeutics, Inc	Phase 1	Systemic Lupus Erythematosus	2019/3/18
AVL-292/Spebrutinib	BTK	Covalent; Irreversible	Celgene	Phase 1	B-cell NHL, CLL, WM	2011/5/11
BIIB068	BTK	Reversible	Biogen	Phase 1	Systemic Lupos Erythematosus	2016/7/12
EVER001/ SN1011	BTK	Covalent; Reversible	Everest Medicines/ SinoMab BioScience	Phase 1	Primary Membranous Nephropathy	2023/4/6
			SinoMab BioScience	Phase 1	Autoimmune Diseases	2019/8/1
HM71224/ LY3337641	BTK	Covalent; Irreversible	Hanmi Pharmaceutical Company Limited	Phase 1	Rheumatoid Arthritis	2013/1/10
HMPL-760	BTK	Noncovalent; Reversible	HUTCHMED	Phase 1	B-Cell NHL	2022/1/13
IMG-004	BTK	Noncovalent; Reversible	Inmagene LLC	Phase 1	Healthy Participants	2022/4/27
JNJ-64264681	BTK	Covalent; Irreversible	Johnson & Johnson	Phase 1	NHL, CLL	2019/12/24
MH048	BTK	Noncovalent; Reversible	Minghui Pharmaceutical Co., Ltd	Phase 1	B-Cell Lymphoma	2020/12/30
TAK-020	BTK	Covalent; Irreversible	Takeda	Phase 1	Healthy Volunteers	2015/4/9
TQB3702	BTK	Not Disclosure	Chia Tai Tianqing Pharmaceutical Group Co., Ltd.	Phase 1	Hematologic Tumor	2022/11/9

Note: CLL/SLL= Chronic Lymphoblastic Leukemia / Small lymphocyte lymphoma, WM= F giant globulinemia, MZL= limbic lymphoma, MCL= Mantle Cell Lymphoma; NHL=Non-Hodgkin lymphoma; DLBLC= Diffuse Large B Cell Lymphoma; PCNSL = Primary Central Nervous System Lymphoma; FL=Follicular Lymphoma
As of Feb 19th 2025

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Global Competitive Landscape of Noncovalent Reversible BTK Inhibitors for Cancer Treatment at Clinical Stage

Drug Name	Target	Molecular feature	Company	Clinical Stage	Indications	First Posted Date	Study Location
				NDA	MCL	2023-10-16 (NMPA accepts NDA)	NDA from NMPA
LOXO-305	BTK	Noncovalent; Reversible	LOXO ONCOLOGY	Phase 3	CLL, SLL	2020-12-14	The US, Australia, Austria, Belgium, Canada, China, Croatia, Czechia, France, Germany, Hungary, Ireland, Israel, Italy, Japan, Korea, Poland, Russian Federation, Singapore, Spain, Switzerland, Taiwan (China), Turkey, the UK
ARQ-531	BTK	Noncovalent; Reversible	MSD	Phase 3	CLL, SLL	2022-11-22	The US, Australia, Brazil, Bulgaria, Chile, China, Colombia, Denmark, Guatemala, Hong Kong (China), Hungary, Lithuania, Malaysia, Mexico, Poland, Romania, Singapore, South Africa, Turkey, Ukraine
MH048	BTK	Noncovalent; Reversible	Minghui Pharmaceutical Co., Ltd	Phase 2	B-cell Lymphoma	2022-04-14	China
LP-168	BTK	(Covalent; Irreversible) and (Noncovalent; Reversible)	Lupeng Pharmaceutical Company Limited	Phase 2	MCL	2023-01-12	China
HBW-3210	BTK	Noncovalent; Reversible	Hyperway Pharmaceuticals	Phase 1/2	B-cell Lymphoma	2023-10-09	China
HBW-3220	BTK	Noncovalent; Reversible	Hyperway Pharmaceuticals	Phase 1/2	B-cell Lymphoma	2022-05-20	China
TT-01488	BTK	Noncovalent; Reversible	TransThera	Phase 1	B-cell Lymphoma	2023-01-04	China
HMPL-760	BTK	Noncovalent; Reversible	HUTCHMED	Phase 1	B-cell NHL	2021-12-15	China

Note: CLL/SLL= Chronic Lymphoblastic Leukemia / Small lymphocyte lymphoma, WM= F giant globulinemia, MZL= limbic lymphoma, MCL= Mantle Cell Lymphoma; NHL=Non-Hodgkin lymphoma; DLBLC= Diffuse Large B Cell Lymphoma; PCNSL = Primary Central Nervous System Lymphoma; FL=Follicular Lymphoma

As of Feb 19th 2025

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

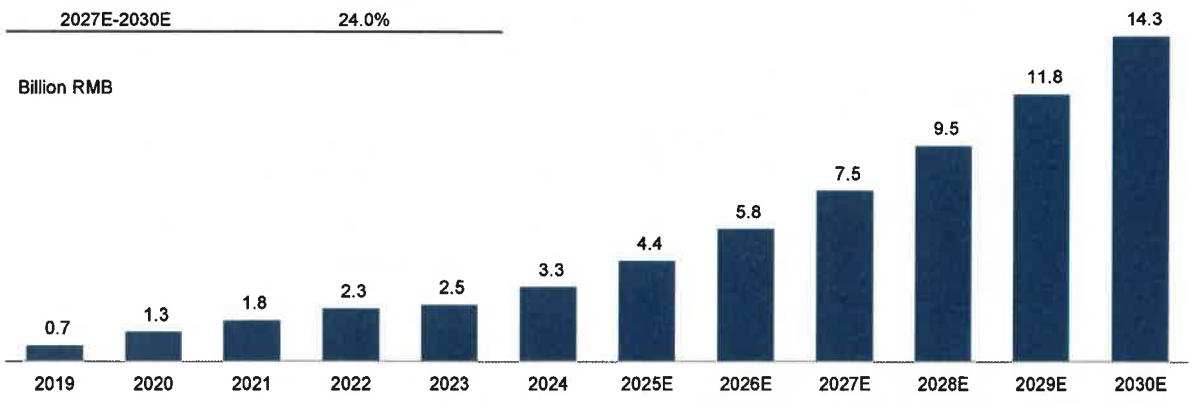
updated

Historical and Forecasted of China BTK Inhibitor Market Size, 2019-2030E

- China's BTK inhibitor market has grown from RMB0.7 billion in 2019 to RMB3.3 billion in 2024 at a CAGR of 36.2%, and expected to increase to RMB7.5 billion in 2027 at a CAGR of 31.9% from 2024 and RMB14.3 billion in 2030 at a CAGR of 24.0% from 2027.

Historical and Forecasted of China BTK Inhibitor Market Size, 2019-2030E

Period	CAGR
2019-2024	36.2%
2024-2027E	31.9%
2027E-2030E	24.0%



Source: Frost & Sullivan Analysis

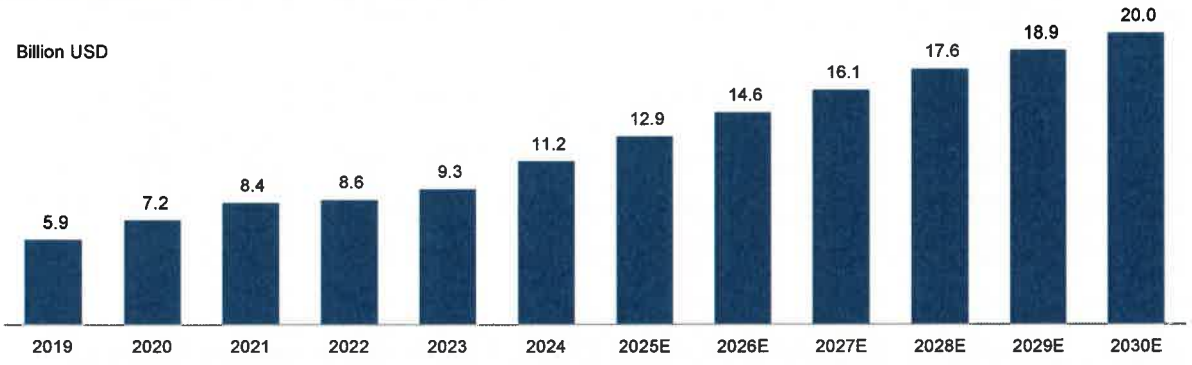
updated

Historical and Forecasted of Global BTK Inhibitor Market Size, 2019-2030E

- Global BTK inhibitor market has grown from USD5.9 billion in 2019 to USD11.2 billion in 2024 at a CAGR of 13.9%, and expected to increase to USD16.1 billion in 2027 at a CAGR of 12.9% from 2024 and USD20.0 billion in 2030 at a CAGR of 7.4% from 2027.

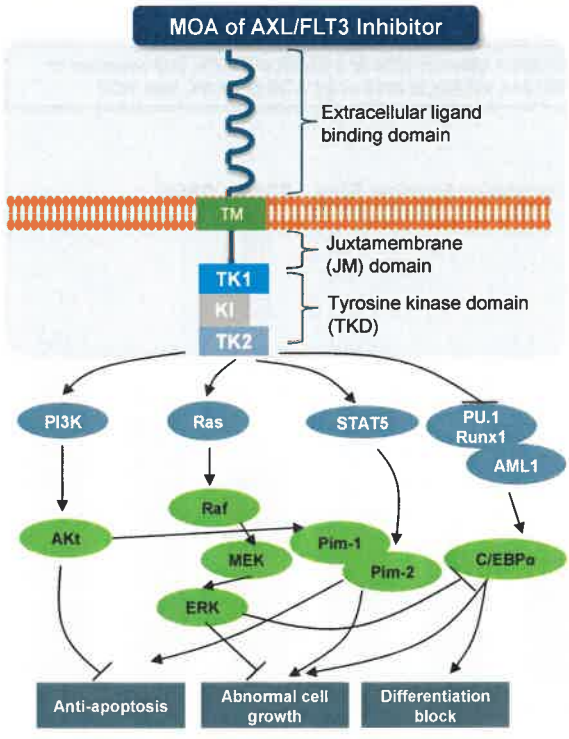
Historical and Forecasted of Global BTK Inhibitor Market Size, 2019-2030E

Period	CAGR
2019-2024	13.9%
2024-2027E	12.9%
2027E-2030E	7.4%



Source: Frost & Sullivan Analysis

Overview of FLT3 Inhibitor and AXL Inhibition



1 *Overview of FLT3 receptor*

- Currently, 25-30% of AML patients harbor a constitutively active FLT3 (Fms-like tyrosine kinase 3) receptor, which is encoded by the self-activating FLT3 allele (located on chromosome 13q12) with the internal tandem duplication (FLT3-ITD).
- In normal bone marrow, FLT3 is selectively expressed on CD34+ hematopoietic stem cells and immature hematopoietic progenitors. The binding of its ligand (FL or FLT3 ligand) promotes the phosphorylation of the tyrosine kinase domain, activating the receptor and consequently the downstream effectors.
- In acute myeloid leukemias, FLT3 stimulation by its ligand promotes the proliferation of leukemic blasts which express the receptor.

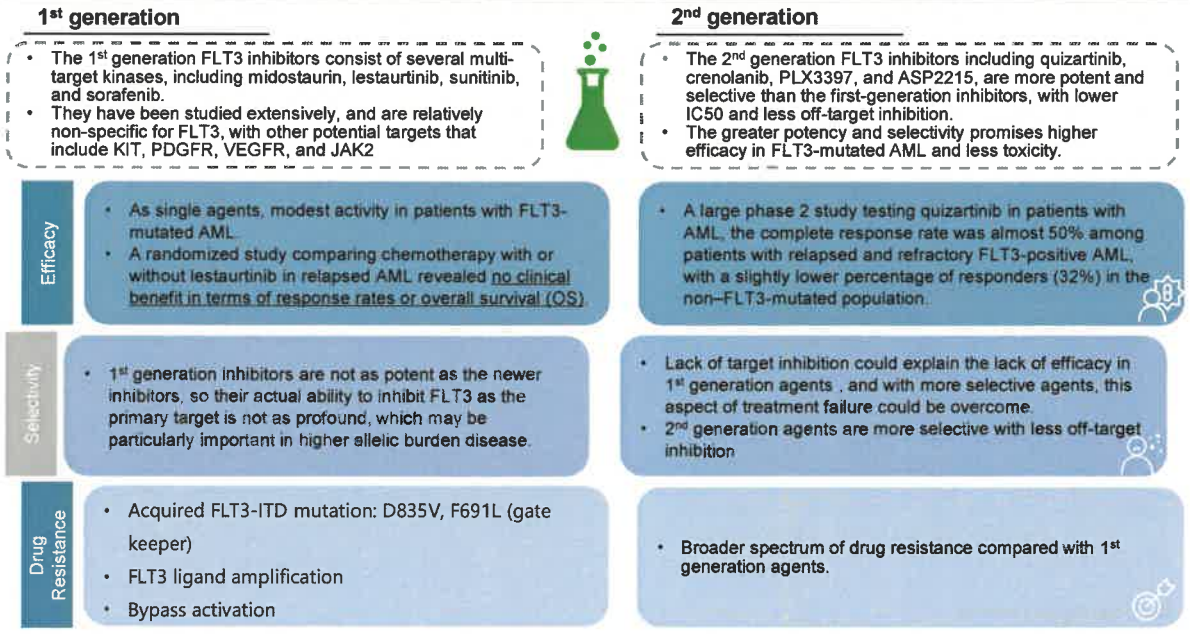
2 *Overview of AXL tyrosine kinase receptor*

- AXL is a member of the TAM (TYRO3, AXL, and MER) family activated by the high-affinity ligand Gas6.
- High levels of AXL expression has been associated with poor prognosis in various cancers, including ovarian, urothelial, lung cancer and acute myeloid leukemia.
- Overactivation AXL signaling is associated with drug resistance, tumor cell growth, metastasis, invasion, epithelial-mesenchymal transition, angiogenesis, immune regulation, and stem cell maintenance, implicating AXL as a promising drug target in cancer treatment.

Source: Literature Review, Frost & Sullivan Analysis

Comparison Between 1st and 2nd Generations of FLT3 Inhibitors

- The 1st generation FLT3 inhibitors are mostly multi-target kinase, targeting on multiple targets including FLT3; however 2nd generation FLT3 inhibitors tend to improve the selectivity. To date, there are not yet any 2nd generation FLT3 inhibitors gains approval.
- The 2nd generation FLT3 inhibitors are more potent and selective than the first-generation inhibitors, with less off-target inhibition., which promises higher efficacy in FLT3-mutated AML and less toxicity.



Source: Literature Review, Frost & Sullivan Analysis

Competitive Landscape of AXL/FLT3 Inhibitor Approved by NMPA

Drug Name	Brand Name	Target	Company	Indications	Approval Date
Gilteritinib	XOSPATA®	AXL/FLT3	Astellas Pharma	AML	2021/1/30

AML=Acute Myeloid Leukemia
As of Feb 19th 2025

Source: NMPA, Frost & Sullivan Analysis

Competitive Landscape of AXL/FLT3 Target Inhibitor Approved by FDA

Drug Name	Brand Name	Target	Company	Indications	Approval Date
Gilteritinib	XOSPATA®	AXL/FLT3	Astellas Pharma	AML	2018/11/28

AML=Acute Myeloid Leukemia
As of Dec 23rd 2024

Source: FDA, Frost & Sullivan Analysis

Competitive Landscape of China AXL/FLT3 Inhibitor in Pipeline

Drug Name	Target	Company	Clinical Stage	Indication	First Posted Date
FC084CSA	AXL	FindCure Biosciences (ZhongShan) Co., Ltd.	Phase 1/2	Advanced Malignant Solid Tumors	2024-10-16
TT-00973	**AXL/FLT3**	**TransThera**	**Phase 1**	**Solid Tumor**	**2022-11-10**
XZB-0004	AXL	Xuanzhu Biopharmaceutical Co., Ltd. / SignalChem Lifesciences Corporation	Phase 1	Solid Tumor	2023-02-24
FC084	AXL	FindCure Biosciences Co., Ltd.	Phase 1	Solid Tumor	2023-02-23

The list only includes clinical trials that indicated to solid tumors.
As of of Dec 23rd 2024

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of Global AXL/FLT3 Inhibitor in Pipeline

Drug Name	Target	Company	Clinical Stage	Indication	First Posted Date
BGB324	AXL	BerGenBio ASA / Merck Sharp & Dohme LLC	Phase 2	Advanced Adenocarcinoma of the Lung	2017-06-12
XZB-0004 / SLC-391	AXL	SignalChem Lifesciences Corporation / Xuanzhu Biopharmaceutical Co., Ltd.	Phase 1/2	Advanced or Metastatic Non-Small Cell Lung Cancer	2023-05-16
TT-00973	**AXL/FLT3**	**TransThera**	**Phase 1**	**Advanced Solid Tumor**	**2023-01-06**
AB801	AXL	Arcus Biosciences, Inc.	Phase 1	Advanced Solid Tumor	2023-11-07
FC084	AXL	FindCure Biosciences Co., Ltd.	Phase 1	Advanced Solid Tumor	2024-01-30
TP-0903	AXL	Sumitomo Pharma Oncology, Inc.	Phase 1	Advanced Solid Tumor	2016-04-06

The list only includes clinical trials that indicated to solid tumors.
As of of Dec 23rd 2024

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Global Competitive Landscape of AXL Inhibitors Indicated for Solid Tumor at Clinical Stage

Drug Name	Target	Company	Clinical Stage	Indication	First Posted Date	Study Location
BGB324	AXL	BerGenBio ASA / Merck Sharp & Dohme LLC	Phase 2	Advanced Adenocarcinoma of the Lung	2017-06-12	The US, Norway, Spain, the UK
XZB-0004 / SLC-391	AXL	SignalChem Lifesciences Corporation / Xuanzhu Biopharmaceutical Co., Ltd.	Phase 1/2	Advanced or Metastatic Non-Small Cell Lung Cancer	2023-05-16	The US, Canada
			Phase 1	Advanced Solid Tumor	2023-02-24	China
TT-00973	AXL/FLT3	TransThera	Phase 1	Advanced Solid Tumor	2022-11-10	China
AB801	AXL	Arcus Biosciences, Inc.	Phase 1	Advanced Solid Tumor	2023-11-07	The US
FC084	AXL	FindCure Biosciences Co., Ltd.	Phase 1	Advanced Solid Tumor	2023-02-23	China
TP-0903	AXL	Sumitomo Pharma Oncology, Inc.	Phase 1	Advanced Solid Tumor	2016-04-06	The US

The list only includes clinical trials that indicated to solid tumors.
As of Dec 23rd 2024

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

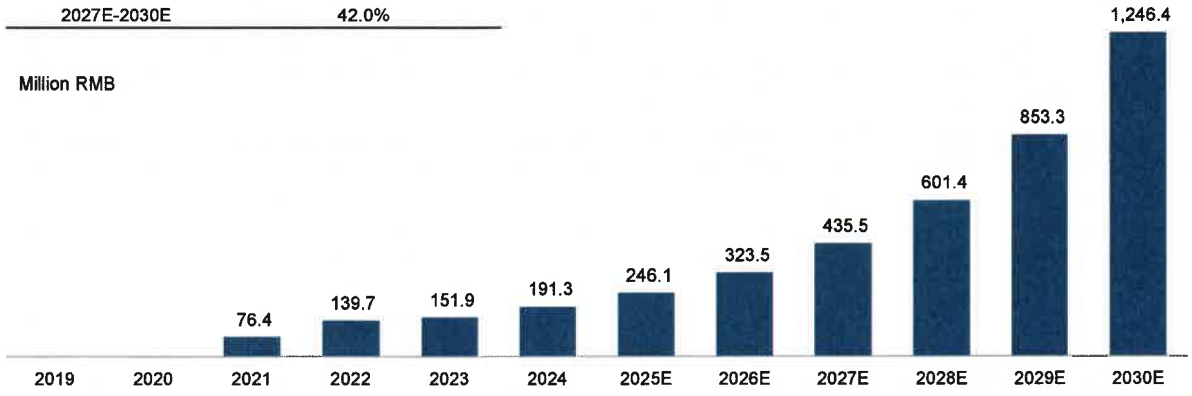
updated

Historical and Forecasted of China AXL/FLT3 Inhibitor Market Size, 2019-2030E

- China's AXL/FLT3 inhibitor market has grown from RMB76.4 million in 2021 to RMB191.3 million in 2024, and expected to increase to RMB435.5 million in 2027 at a CAGR of 31.5% from 2024 and RMB1,246.4 million in 2030 at a CAGR of 42.0% from 2027.

Historical and Forecasted of China AXL/FLT3 Inhibitor Market Size, 2019-2030E

Period	CAGR
2019-2024	NA
2024-2027E	31.5%
2027E-2030E	42.0%



Source: Frost & Sullivan Analysis

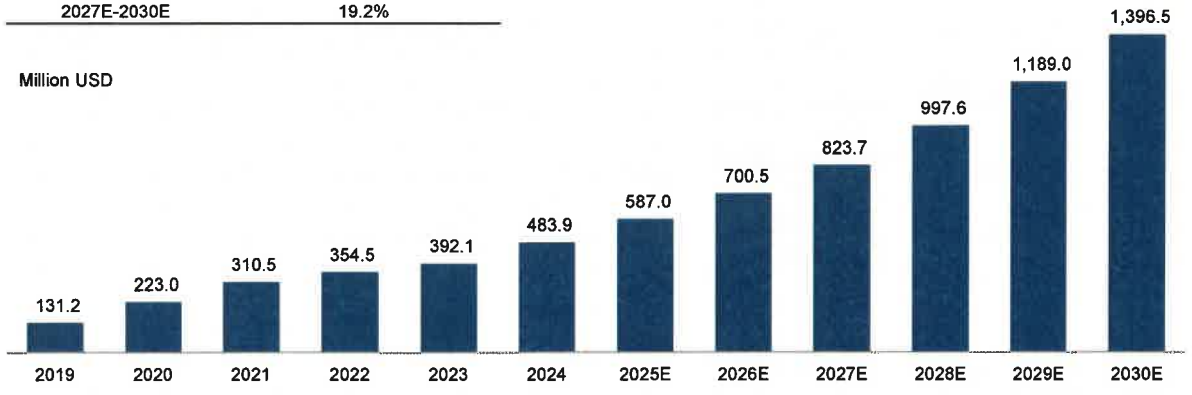
updated

Historical and Forecasted of Global AXL/FLT3 Inhibitor Market Size, 2019-2030E

- Global AXL/FLT3 inhibitor market has grown from USD131.2 million in 2019 to USD483.9 million in 2024 at a CAGR of 29.8%, and expected to increase to USD823.7 million in 2027 at a CAGR of 19.4% from 2024 and USD1,396.5 million in 2030 at a CAGR of 19.2% from 2027.

Historical and Forecasted of Global AXL/FLT3 Inhibitor Market Size, 2019-2030E

Period	CAGR
2019-2024	29.8%
2024-2027E	19.4%
2027E-2030E	19.2%



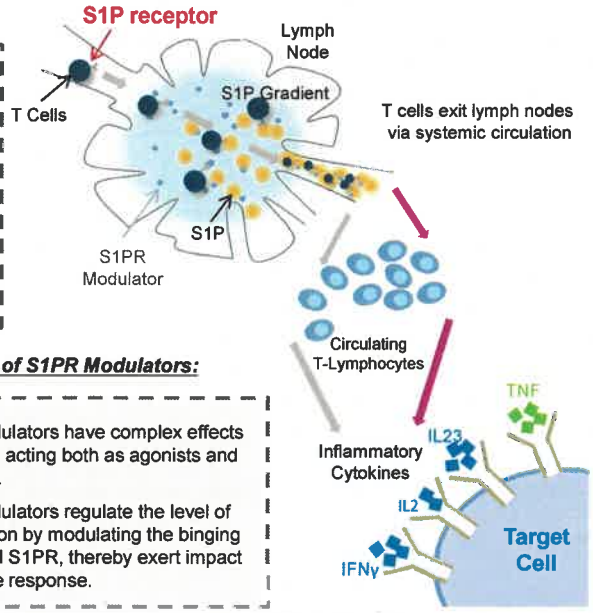
Source: Frost & Sullivan Analysis

Overview of S1P1 Receptor

- Sphingosine-1-phosphate (S1P) is a signaling lipid that regulates many cellular processes in mammals. One well-studied role of S1P signaling is to modulate T- cell trafficking, which has a major impact on adaptive immunity.

1 *Overview of S1PRs:*

- Sphingosine-1-phosphate (S1P) is a lysophospholipid with a polar head-group and lipophilic tail, produced intracellularly via phosphorylation of sphingosine. S1P is a signaling lipid which is an important regulator in inflammation, angiogenesis, and vascular permeability.
- S1P is able to affect many processes by signaling extracellularly through S1P receptors (S1PRs).
- Usually, the major role of S1P is a ligand which binds S1P receptor to regulate cellapoptosis, cytoskeleton remodeling, and inflammation. It also works as a regulator of a rangeof inflammatory cytokines, including but not limited to IL-2, IL-23, and TNF.



2 *Overview of S1PR1:*

- S1PR1 is one of the most widely studied receptors of S1P.
- S1PR1 plays a role in immune responses by affecting recruitment and trafficking of innate immune cells, macrophage polarization, and plasmacytoid dendritic cell functions.

3 *Function of S1PR Modulators:*

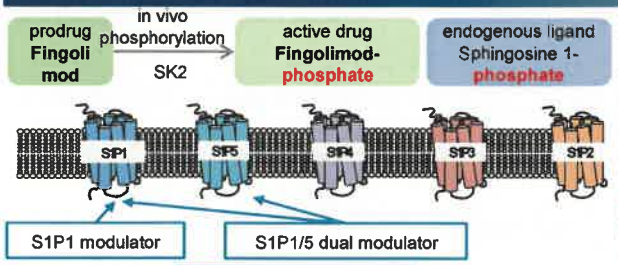
- S1PR modulators have complex effects on S1PRs, acting both as agonists and antagonist.
- S1PR modulators regulate the level of inflammation by modulating the binging of S1P and S1PR, thereby exert impact on immune response.

Source: Literature Review, Frost & Sullivan Analysis

Overview of S1P1 Receptor Modulator

- The S1P1 expresses on lymphocytes and plays a crucial role in the trafficking of lymphocytes from lymphoid organs. Besides, S1P1 is a promising target for inflammatory diseases with a favorable safety profile. S1P1 modulators reduce the number of circulating lymphocytes in the blood and prevent reactive lymphocytes from migrating to inflammatory sites.
- Non-selective S1P1 Receptor Modulator's intended action is through binding of the S1P1 receptor on lymphocyte surfaces. However, its non-selective modulation of S1P3, S1P4, and S1P5 may lead to unwanted cardiovascular adverse effects, including bradycardia, atrioventricular block and hypertension, etc.

MOA of S1P receptor modulator



Action mode on S1P1

S1P1 agonist
S1P1 activation (agonism)
→ Phosphorylation
→ Internalization
→ Recycling
→ Resensitization

→ Absence of in the S1P1 cell surface
→ Blockage of lymphocytes egress
→ **Temporal lymphopenia (hours)**

S1P1 modulator
S1P1 activation (agonism)
→ Phosphorylation
→ Internalization
→ Degradation
→ Functional antagonism

→ Long time absence of S1P1
→ Blockage of lymphocytes egress
→ **Sustained lymphopenia (days)**

- Reducing the peripheral absolute lymphocyte count (ALC) is a promising therapeutic approach in treating autoimmune diseases. S1P1 receptor modulator is known to decrease the peripheral ALC.

- S1P1 receptor surface expression is required for S1P gradient-mediated lymphocyte migration out of lymphoid tissue into the circulation. Binding and internalization of the S1P1, 4, and 5 receptor results in retention of certain lymphocyte populations within lymph nodes and other lymphoid tissues, with subsequent reduction in peripheral blood lymphocyte count and lymphocyte availability for recruitment to sites of inflammation.

- Selectivity is important for S1P molecules, as binding to S1P2 and 3 receptors leads to off-target toxicities and increased risk for cardiac, pulmonary, and tumor-related even.

Source: Literature Review, Frost & Sullivan Analysis

Competitive Landscape of S1P Receptor Modulator Approved by NMPA

Drug Name	Brand Name	Target	Company	Molecular feature	Indications	Approval Date
Ozanimod	ZEPOSIA®	S1P1/5	Bristol Myers Squibb	Selective	multiple sclerosis	2023-01-31
Siponimod	MAYZENT®	S1P1/5	Novartis	Selective	multiple sclerosis	2020-05-07
Fingolimod	GILENYA®	S1P1/3/4/5	Novartis	Non-selective	multiple sclerosis	2019-07-12

As of Feb 19th 2025

Source: NMPA, Frost & Sullivan Analysis

Competitive Landscape of S1P Receptor Modulator Approved by FDA

Drug Name	Brand Name	Target	Company	Molecular feature	Indications	Approval Date
Etrasimod	VELSIPITY®	S1P1/4/5	Pfizer	Selective	ulcerative colitis	2023/10/12
Ponesimod	PONVORY®	S1P1	Actelion pharmaceutical Ltd.; Janssen	Selective	multiple sclerosis	2021/3/18
Ozanimod	ZEPOSIA®	S1P1/5	Bristol-Myers Squibb	Selective	multiple sclerosis; ulcerative colitis	2020/3/25 (2021/05/27 for UC)
Siponimod	MAYZENT®	S1P1/5	Novartis	Selective	multiple sclerosis	2019/3/26
Fingolimod	GILENYA®	S1P1/3/4/5	Novartis	Non-selective	multiple sclerosis	2010/9/21

Note: Approval date: First approval date
As of Feb 19th 2025

Source: FDA, Frost & Sullivan Analysis

Competitive Landscape of China S1P Receptor Modulator in Pipeline

Drug Name	Target	Company	Clinical Stage	Indication	First Posted Date
Etrasimod	S1PR1/4/5	Everstar Therapeutics	Phase 3	Ulcerative Colitis	2019-12-02
TT-01688	**S1P1**	**TransThera**	**Phase 2**	**Atopic Dermatitis**	**2022-06-23**
			Phase 1	**Moderate and Severe Ulcerative Colitis**	**2022-03-14**
CBP-307	S1P1	Connect Biopharmaceutical Co., Ltd	Phase 2	Ulcerative Colitis	2018-08-16
HE009	S1P1	Helioeast Pharmaceutical Co.,Ltd	Phase 1	Systemic Lupus Erythematosus	2022-12-22
Ethoximod	S1P1	Institue of Materia Medica Chinese Academy of Medical Science	Phase 1	Psoriasis	2022-09-13
Proximod	S1P1	Institue of Materia Medica Chinese Academy of Medical Science	Phase 1	Rheumatoid Arthritis	2022-01-20

As of Feb 19th 2025

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of Global S1P Receptor Modulator in Pipeline (1/2)

Drug Name	Target	Company	Clinical Stage	Indication	First Posted Date
Cenerimod	S1P1	Idorsia Pharmaceuticals Ltd.	Phase 3	Systemic Lupus Erythematosus	2023-01-05
Mocravimod	S1P1	Priothera	Phase 3	Acute Myeloid Leukemia	2022-06-23
NXC736	S1P1/4	NEXTGEN Bioscience	Phase 2	Alopecia Areata	2023-10-27
ONO-2808	S1P5	Ono Pharmaceutical Co. Ltd	Phase 2	Multiple System Atrophy (MSA)	2023-06-28
ABX-101	S1P	Abalonex, LLC	Phase 2	Traumatic Brain Injury, Cerebral Edema	2023-10-23
OPL-0301	S1P1	Valo Health, Inc.	Phase 2	Myocardial Infarction	2022-04-14
VTX002/ OPL-002	S1P1	Oppilan Pharma Ltd	Phase 2	Ulcerative Colitis	2021-12-14
BMS-986166	S1P1	Bristol-Myers Squibb	Phase 2	Atopic Dermatitis	2021-08-20
Amiselimod	S1P1	Bausch Health Americas, Inc. / Mitsubishi Tanabe Pharma	Phase 2	Ulcerative Colitis	2021-04-23
			Phase 2	Relapsing-remitting Multiple Sclerosis	2013-07-02
			Phase 2	Crohn's Disease	2015-03-17
			Phase 2	Plaque Psoriasis	2013-11-19

As of Dec 23rd 2024

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Competitive Landscape of Global S1P Receptor Modulator in Pipeline (2/2)

Drug Name	Target	Company	Clinical Stage	Indication	First Posted Date
SCD-044	S1P1	Sun Pharmaceutical Industries Limited	Phase 2	Atopic Dermatitis	2020-12-21
			Phase 2	Dermatitis, Atopic	2020-12-24
CBP-307	S1P1	Connect Biopharmaceutical Co., Ltd	Phase 2	Moderate to Severe Ulcerative Colitis	2021-01-07
Ethoximod	S1P1	Institue of Materia Medica Chinese Academy of Medical Science	Phase 1	Psoriasis	2024-04-11
Proximod	S1P1	Institue of Materia Medica Chinese Academy of Medical Science	Phase 1	Rheumatoid Arthritis	2024-04-11
LC51-0255 (TT-01688)	**S1P1**	**LG Chem / TransThera**	**Phase 1**	**Ulcerative Colitis**	**2020-04-24**
SAR247799	S1P	Sanofi	Phase 1	Microvascular Coronary Artery Disease	2018-03-12
CP1050	S1P	Curadim Pharma Co., Ltd.	Phase 1	Healthy Subjects	2018-03-16
BMS-986104	S1P1	Bristol-Myers Squibb	Phase 1	Rheumatoid Arthritis	2014-08-07
ASP4058	S1P1/5	Astellas Pharma	Phase 1	Healthy Subjects	2013-12-02
GSK2018682	S1P1	GlaxoSmithKline	Phase 1	Multiple Sclerosis, Relapsing-Remitting	2011-11-06
CS-0777	S1P1	Daiichi Sankyo, Inc.	Phase 1	Multiple Sclerosis	2008-02-15

As of Feb 19th 2025

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

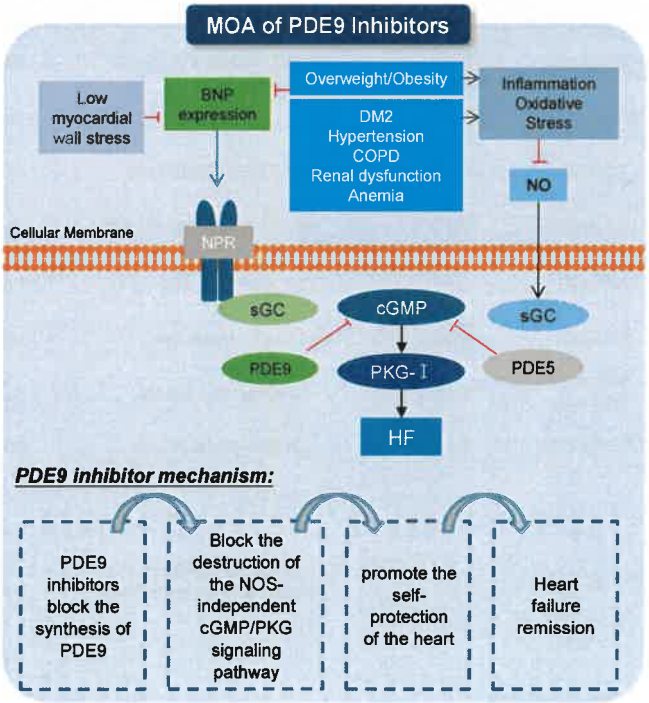
Overview of PDE9 Inhibitors

1 *Overview of PDE Family*

- A phosphodiesterase (PDE) is an enzyme that breaks a phosphodiester bond. Usually, phosphodiesterase refers to cyclic nucleotide phosphodiesterases, comprising a group of enzymes that degrade the phosphodiester bond in the second messenger molecules cAMP and cGMP.

2 *PDE9 Function in Heart Failure*

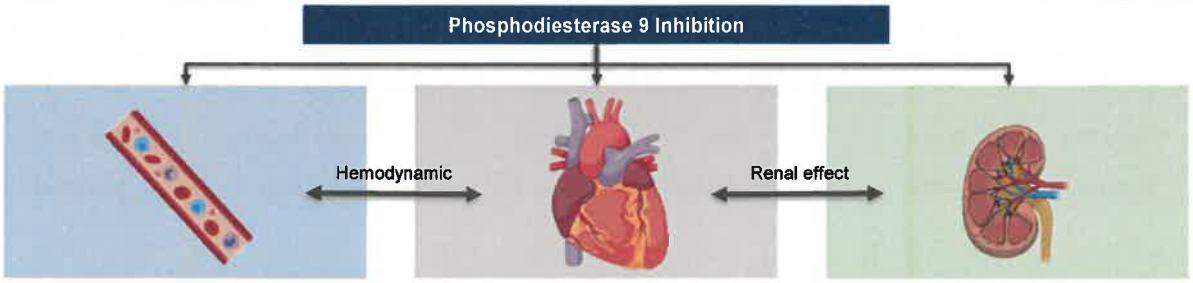
- NP/cGMP signaling regulates cardiomyocyte growth, survival, and stress response, and its activation is cardioprotective. PDE9 catalyzes the hydrolysis of cGMP and negatively modulates cardiac NP/cGMP signaling. In re-established human heart failure, particularly in HFpEF, PDE9 expression and activity are strongly enhanced in cardiomyocytes, blunting NP/cGMP signaling and making the heart more susceptible to failure, suggesting that PDE9 may play a critical role in NP/cGMP signaling in failing hearts. In addition, PDE9 levels are associated with left ventricular filling pressure, left ventricle size as a marker of diastolic burden and right ventricular function in heart failure.
- PDE9 expresses in cardiomyocytes, the protein level of which is markedly elevated in heart failure patients, associated with ventricular dysfunction. PDE9 negatively modulates the intrinsic cardioprotective natriuretic peptide (NP)-coupled cGMP signaling pathway.



Source: Literature Review, Frost & Sullivan Analysis

Overview of PDE9 Inhibitors

- According to the research on animal models1 ,PDE9 inhibitor shows both renal effect as well as hemodynamic effect to HF. PDE9 inhibitors not only restore the NP activity and protect cardiomyocytes, but also improve renal function including diuresis and natriuresis, which is similar to Diuretics in HF recommended treatments.



Potential therapeutic effect of PDE9 inhibitors:

Hemodynamic Effect

- PDE9 suppress the pathway of NP signal, and contribute to worsening of HF. **PDE9 inhibitors restore the NP activity and protect cardiomyocytes.**
- PDE9 inhibitors show positive effects on hemodynamics such as improve peripheral resistance.

Heart Effect

- Influenced by PDE9 inhibitors in animal models, the cardiac output and preload volume are restored, and promote the self-protection of the heart. Thus, PDE9 inhibitor can potentially improve the prognosis of heart failure or even reversing heart failure.

Renal Effect

- Inhibition of PDE9 increased urinary cGMP concentrations, which in HF, occurred in conjunction with marked **improvements in renal function** including a significant diuresis, natriuresis, and increase in creatinine clearance.

Notes: ANP=atrial natriuretic peptide; cGMP=cyclic guanosine monophosphate; NP=natriuretic peptide

Source: Literature Review, Frost & Sullivan Analysis

Competitive Landscape of China PDE-9 Inhibitor in Pipeline

Drug Name	Target	Company	Clinical Stage	Indication	First Posted Date
BI 409306	PDE9	Boehringer Ingelheim	Phase 2	Mild Psychotic Syndrome	2019/11/26
TT-00920	**PDE9**	**TransThera**	**Phase 1**	**Heart Failure**	**2021/7/9**

As of Feb 19th 2025

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of Global PDE-9 Inhibitor in Pipeline

Drug Name	Target	Company	Clinical Stage	Indication	First Posted Date
Tovinontrine	PDE9	Cardurion Pharmaceuticals, Inc.	Phase 2	Heart Failure	2024-01-22
E2027	PDE9	Eisai Inc.	Phase 2	Dementia With Lewy Bodies, Parkinson Disease	2021-02-21
ASP4901	PDE9A	Astellas Pharma Inc.	Phase 2	Benign Prostate Hyperplasia	2014-01-17
PF-04447943	PDE9A	Pfizer	Phase 2	Alzheimer Disease	2009-06-30
TT-00920	**PDE9**	**TransThera**	**Phase 1**	**Heart Failure**	**2021-09-14**

As of Feb 19th 2025

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Global Competitive Landscape of PDE9 Inhibitors at Clinical Stage for the Treatment of Heart Failure

PDE9 inhibitor acted directly on cardiomyocytes to mechanistically synergize with current therapeutic approaches to form a novel and promising treatment regimen for both HFrEF and HFpEF

Drug Name	Target	Company	Clinical Stage	Indication	First Posted Date	Study Location
Tovinontrine	PDE9	Cardurion Pharmaceuticals, Inc.	Phase 2	Heart Failure	2024-01-22	The US, Bulgaria, Canada, Czech Republic, Germany, Hungary, Poland
TT-00920	PDE9	TransThera	Phase 1	Heart Failure	2021-09-14	The US
			Phase 1	Heart Failure	2021-07-09	China

As of Feb 19th 2025

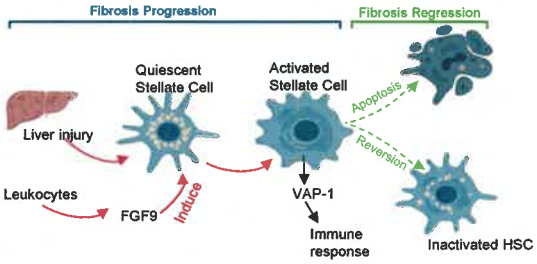
Source: ClinicalTrials.gov, CDE, Frost & Sullivan Analysis

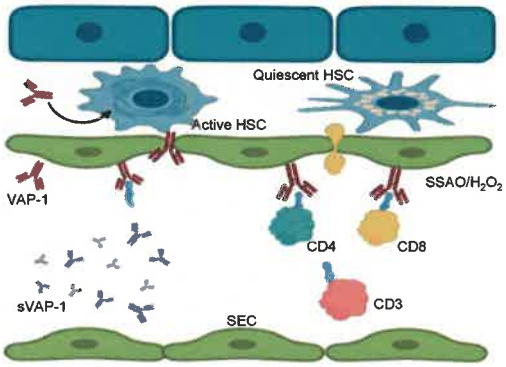
Overview of VAP-1 Signaling Pathway

- Vascular adhesion protein 1 (VAP-1) is an endothelial surface glycoprotein expressed on the hepatic endothelium, plays a integral role in leukocyte migration into sites of inflammation in vivo.
- VAP-1 inhibitors block the extravasation of leukocyte and further suppress immune response.

1 *Overview of VAP-1:*

- Vascular adhesion protein 1 (VAP-1) is an endothelial surface glycoprotein, which plays a integral role in leukocyte trafficking into sites of inflammation in vivo.
- VAP-1 is expressed on the hepatic endothelium and recruits leukocytes to the liver, active hepatic stellate cells (HSC) to enhance fibroblasts and thereby induce immune response.
- VAP-1 is also produced as a soluble form (sVAP-1) that work as a monoamine oxidase, and can be used as a novel biomarker of inflammation.





2 *Mechanism of VAP-1 inhibitor:*

- Due to role of VAP-1 in leukocyte extravasation, targeting VAP-1 has potential as a therapeutic strategy for limiting hepatic inflammation and fibrosis.
- Aberrant leukocyte migration is a key pathogenic event in autoimmune disorders, which results in fibrosis.
- VAP-1 inhibitors block the extravasation of leukocyte and further suppress immune response.
- By inhibiting adhesive function with monoclonal-antibodies and small molecular VAP-1 inhibitors, production of interleukin (IL)-4, IL-5, and IL-13 are reduced, thereby chronic inflammations are alleviated.

Source: Literature Review, Frost & Sullivan Analysis

Competitive Landscape of China VAP-1 inhibitors in Pipeline

Drug Name	Target	Company	Clinical Stage	Indication	First Posted Date
TT-01025	**TransThera**	**Phase 1**	**Phase**	**NASH**	**2021/6/25**

As of Dec 23rd 2024

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of Global VAP-1 inhibitors in Pipeline

Drug Name	Target	Company	Clinical Stage	Indication	First Posted Date
VX-01	VAP-1	Vantage Biosciences Ltd, Vantage Biosciences Australia Pty Ltd	Phase 2	Diabetic Retinopathy, NPDR - Non Proliferative Diabetic Retinopathy	2025-01-13
PXS-4728/ BI-1467335*	VAP-1	Pharmaxis	Phase 2	REM Sleep Behavior Disorder	2023-06-15
ASP8232	VAP-1	Astellas Pharma Europe B.V.	Phase 2	Chronic Kidney Disease, Type 2 Diabetes	2015-02-06
			Phase 2	Diabetic Macular Edema	2014-11-26
PRX167700	VAP-1	Proximagen Limited	Phase 2	Knee osteoarthritis	2013-09-18
NNC0560-0004	VAP-1	Novo Nordisk A/S	Phase 1	Liver Diseases	2023-11-15
Ecc0509	VAP-1	Eccanga Pty Ltd	Phase 1	NASH, Osteoarthritis	2021-08-19
TERN-201	VAP-1	Terns Pharmaceuticals Inc	Phase 1	NASH	2021-05-21
TT-01025	**VAP-1**	**TransThera**	**Phase 1**	**NASH**	**2021-01-29**

As of Dec 23rd 2024
Boehringer Ingelheim has discontinued BI 1467335 development for non-alcoholic steatohepatitis (NASH) treatment after reviewing results from a Phase I clinical trial, which indicated a risk of drug interactions.

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

Global Competitive Landscape of VAP-1 Inhibitors at Clinical Stage for the Treatment of NASH

Drug Name	Target	Company	Clinical Stage	Indication	First Posted Date	Study Location
Ecc0509	VAP-1	Eccanga Pty Ltd	Phase 1	NASH	2021-08-19	Australia
TERN-201	VAP-1	Terns Pharmaceuticals Inc	Phase 1	NASH	2021-05-21	the US
TT-01025	VAP-1	TransThera	Phase 1	NASH	2021-01-29	the US
			Phase 1	NASH	2021-06-25	China

As of Feb 19th 2025
Boehringer Ingelheim has discontinued BI 1467335 development for non-alcoholic steatohepatitis (NASH) treatment after reviewing results from a Phase I clinical trial, which indicated a risk of drug interactions.

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

Verification

Hormone therapy and chemotherapy are the main treatments for advanced HR+HER2- breast cancer. AI combined with CDK4/6 inhibitors is the first-line standard treatment for HR+, HER2- advanced breast cancer. When CDK4/6 inhibitors are not available, single-agent hormone therapy is also feasible, such as fulvestrant, AI, and estrogen receptor modulators. For patients with HR+HER2-endocrine therapy resistance, consider single-agent chemotherapy or combined chemotherapy. The main chemotherapy drugs used include anthracyclines (doxorubicin or liposomal doxorubicin), taxanes (paclitaxel), anti-metabolites (capecitabine or gemcitabine), microtubule inhibitors (vinorelbine or eribulin).

For patients with triple-negative breast cancer, chemotherapy is the current primary treatment option. In addition, for PD-L1-positive TNBC patients, the NCCN guideline recommends chemotherapy combined with PD-L1; Besides, the ADC drugs Sacituzumab govitecan-hziy and T-DXd are also recommended for the treatment of triple-negative breast cancer. T-DXd approved in the US as the first HER2- directed therapy for patients with HER2-low metastatic breast cancer.

Olaparib, PARP inhibitor is indicated for previous treated metastatic castration-resistant prostate cancer (mCRPC) with BRCA mutation, not indicated for universal mCRPC patients.

PLUVICTO is a radioligand therapeutic agent indicated for the treatment of adult patients with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor (AR) pathway inhibition and taxane-based chemotherapy.

The sales revenues of two blockbuster original MTK inhibitors, Cabozantinib (traded by CABOMETYX & COMETRIQ) and Lenvatinib (traded by Lenvima) were USD 1.40 billion and 1.84 billion respectively in 2022.

VAP-1, also known as semicarbazide sensitive amine oxidase, catalyzes the oxidative conversion of endogenous primary amines to the corresponding cytotoxic aldehydes and hydrogen peroxide. VAP-1 is expressed in the human hepatic endothelium acting as a cell adhesion molecule and plays an important role in leukocyte adhesion and transmigration in the liver. This function is dependent on the amine oxidase enzyme activity of VAP-1. The level of its circulating soluble form (sVAP-1) increases during liver inflammation and is known to correlates with disease severity and the presence of fibrosis in NASH. Genetic or pharmacological inhibition of VAP-1 enzyme activity has shown reduction of oxidative stress and recruitment of inflammatory cells to the liver and also attenuation of fibrosis in multiple preclinical NASH models.

There is a lack of an effective small molecular targeted therapy that universally addresses mCRPC patients in the second-line setting.

The mPFS of Futibatinib in patients with advanced and metastatic iCCA with FGFR2 fusion and rearrangement and progressive disease (PD) after ≥1 prior treatment was 8.9 months

Verification

The mPFS of Pemigatinib in patients with advanced and metastatic CCA with FGFR2 fusion and rearrangement after ≥1 prior treatment was 6.9 months.

For patients receiving biologics, over 40% fail to achieve relief, and over 60% fail to achieve complete remission. Although JAK inhibitors have been approved in the U.S. for UC, an IBD that causes inflammation and ulcers (sores) in one digestive tract, and AD treatment, they have been plagued by safety concerns and received black box warnings from the FDA regarding increased risks of severe infections, malignancies, and thrombosis, limiting their long-term use.

Approximately 30%-35% of moderate and severe patients fail to response to anti-TNF-α agents, and approximately 30%-40% of moderate and severe UC patients using anti-TNF-α agents are able to achieve one-year clinical remission.

For moderate and severe AD patients receiving biologics, approximately 40% to 60% are able to get 4-point improvement in Worst Pruritus.

The standard first-line treatment is systemic chemotherapy, with a low median OS (approximately 12 months) and a low ORR of approximately 19%. If genetic testing reveals FGFR2 alterations, targeted therapies represented by FGFR inhibitors become the recommended choice for second-line treatment. However, drug-related adverse reactions pose challenges to medication compliance. Additionally, despite initial responses, almost all patients still experience disease progression after six to nine months of treatment. Currently, there is no recommended therapy for the third-line treatment of CCA. Patients are left to choose chemotherapy with unclear clinical benefits. Literature data indicated a low ORR of not exceeding 8-10%, a median PFS of approximately 3 months, and a median OS of approximately 6 months, with poor tolerability.

The five-year survival rate of chemotherapy-naïve mCRPC is approximately 30% globally.

The actual five-year survival rate after liver transplantation is approximately 30%.

Nearly 60% of prostate cancer is in the late stage or occur metastasis at the first diagnosis in China, severely affect its prognosis.

BI-1467335 is an irreversible VAP-1 inhibitor and had been evaluated in Phase II clinical trials for NASH. The Phase II NASH study outcomes demonstrated positive effectiveness, validating the potential of VAP-1 inhibition for NASH indication. However, its clinical development was discontinued following the discovery of substantial drug interactions of the compound in clinical studies.

Verification

The NLRP3 inflammasome is a critical component of the innate immune response, activated by various stimuli such as PAMPs, DAMPs, and tissue damage signals. When sensing intracellular damage signal, it triggers the organization of inflammasome complex. This inflammasome complex leads to maturation of IL-1 , IL-18, and Gasdermin D (GSDMD) to promote a downstream inflammatory response as well as pyroptosis. Inappropriate activation of NLRP3 has been implicated in a variety of inflammatory diseases, including inflammatory bowel diseases, metabolic diseases and neurodegenerative diseases. Notably, numerous preclinical and clinical studies have identified the NLRP3 inflammasome as a key therapeutic target in obesity.

In the U.S. and China, surgery is the preferred choice for eligible patients in all types of CCA, facilitated by neo-adjuvant therapy or other pre-operative procedures to achieve surgical eligibility. Liver transplantation was also considered an ideal treatment option for CCA. However, due to difficulty in finding well-matched organs, the treatment was no longer a preferred treatment. For late stage CCA with advanced/metastatic disease, immune checkpoint inhibitor in combination with chemotherapy of gemcitabine and cisplatin is currently the preferred treatment in the first-line setting. For the second-line treatment, FOLFOX regimen is recommended for all types of late stage CCA. Targeted therapies are useful when patients qualify for genetic testing of FGFR2, NTRK, MSI-H/dMMR, and IDH1, providing more precise treatment options. The safety and efficacy of FGFR inhibitors (pemigatinib and futibatinib) approved for the second-line treatment of advanced/metastatic CCA have been validated in early studies.