Global Inhalation Formulation Market Study

Independent Market Research

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Frost & Sullivan
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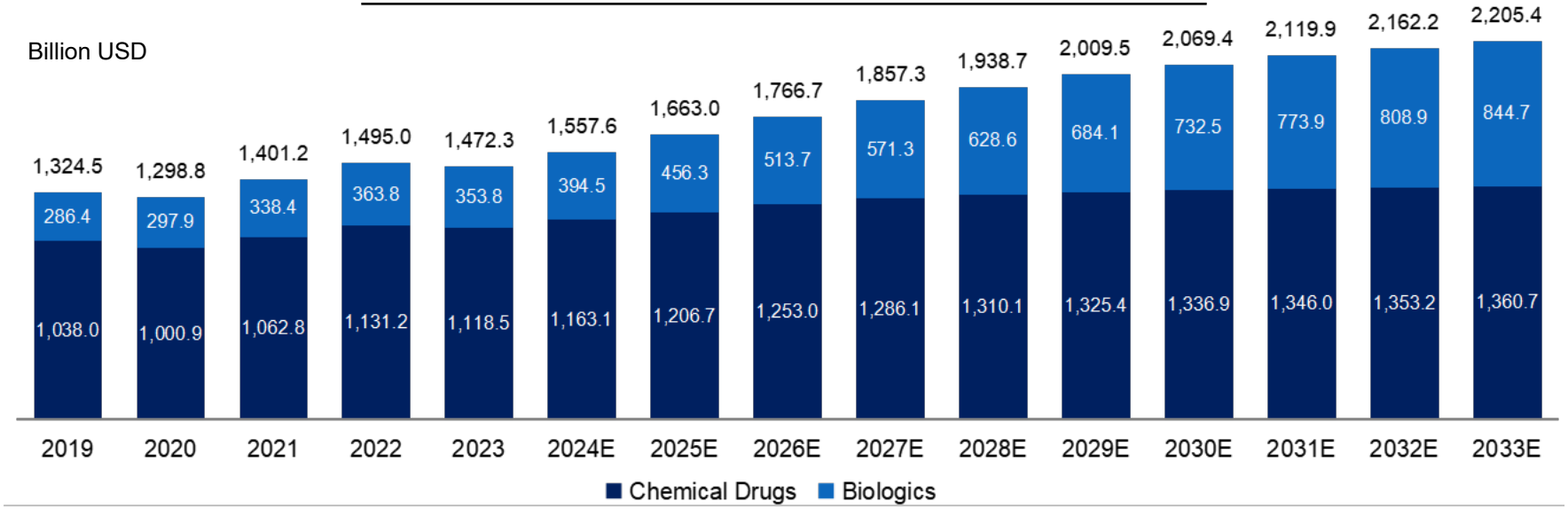
Content

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

- Global pharmaceutical market is composed of two segments, namely chemical drugs and biologics. The size of global pharmaceutical market was USD1,472.3 billion in 2023, and is expected to reach to USD1,938.7 billion and USD2,205.4 billion in 2028 and 2033, representing a CAGR of 2.7% from 2019 to 2023, 5.7% from 2023 to 2028, and 2.6% from 2028 to 2033.
- The chemical drugs took USD1,118.5 billion market size in 2023, and is expected to reach to USD1,360.7 billion in 2033. Chemical drugs are drugs produced by chemical synthesis, and the molecular weight is generally below 1000Da, which can also be regarded as small molecular drugs.

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

Period	CAGR		
	Chemical Drugs	Biologics	Total
2019-2023	1.9%	5.4%	2.7%
2023-2028E	3.2%	12.2%	5.7%
2028E-2033E	0.8%	6.1%	2.6%



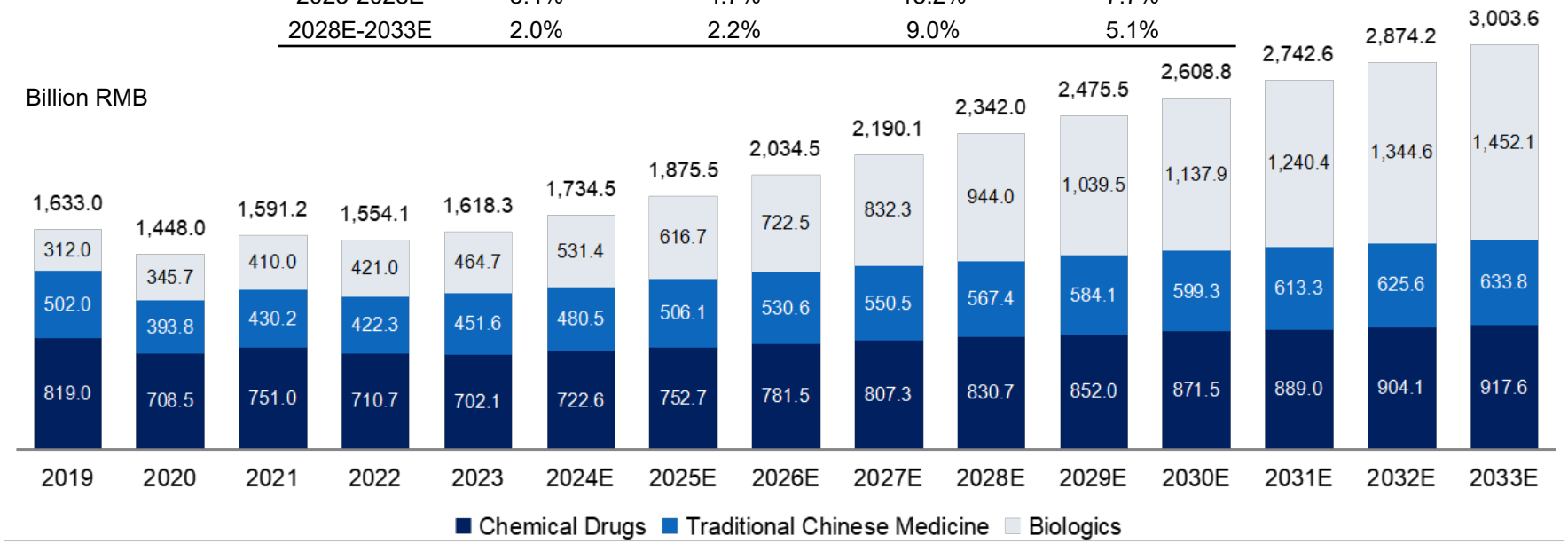
Source: Annual Reports of Listed Medical Companies, NMPA, CDE, NRDL, MOHRSS, FDA, Frost & Sullivan Analysis

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

- China pharmaceutical market is composed of there segments, namely chemical drugs, traditional chinese medicine and biologics. The size of China pharmaceutical market was RMB1,618.3 in 2023, and is expected to reach to RMB2,342.0 billion and RMB3,003.6 billion in 2028 and 2033, representing a CAGR of -0.2% from 2019 to 2023, 7.7% from 2023 to 2028, and 5.1% from 2028 to 2033.
- Chemical drugs took RMB702.1 billion market size in 2023, and is expected to reach to and RMB830.7 billion and RMB917.6 billion in 2028 and 2033.

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

Period	CAGR			
	Chemical Drugs	TCM	Biologics	Total
2019-2023	-3.8%	-2.6%	10.5%	-0.2%
2023-2028E	3.4%	4.7%	15.2%	7.7%
2028E-2033E	2.0%	2.2%	9.0%	5.1%



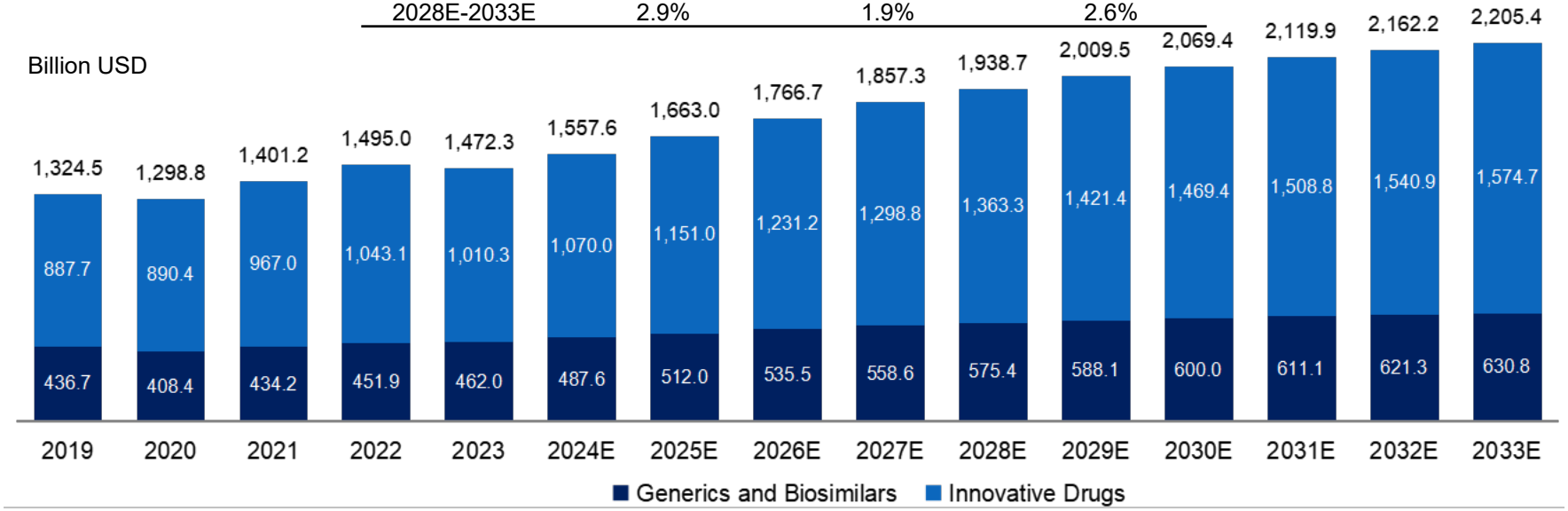
Source: Annual Reports of Listed Medical Companies, NMPA, CDE, NRDL, MOHRSS, Frost & Sullivan Analysis

Breakdown of Global Pharmaceutical Market by Innovative Drugs, Generics and Biosimilar, 2019-2033E

- In 2023, the global innovative drugs market reaches USD1,043.1 billion, accounting for 68.6% of the whole pharmaceutical market. With the continuous development and breakthroughs in the field of biotechnology and the emergence of biotechnology companies in recent years, more breakthrough innovative drugs are expected to be successfully developed and enter the market in the future, further driving the growth of innovative drug market.
- Due to the concentrated innovative expiration of innovative drugs, growth in emerging pharmaceutical markets, and a series of incentive policies for generic drug, the global generic drug market is expected to grow from USD436.7 billion in 2019 to USD462.0 billion by 2023, which represents a CAGR of 1.4%. The global health care burden continues to grow, and drug cost control has gradually become a new norm in all countries. And there is still huge room for the growth of generic drug as the number of chronic diseases cases continues to increase. The market is expected to grow to USD575.4 billion by 2028 and to USD630.8 billion by 2033.

Breakdown of Global Pharmaceutical Market by Innovative Drugs, Generics and Biosimilars, 2019-2033E

Period	CAGR		
	Innovative Drugs	Generics and Biosimilars	Total
2019-2023	3.3%	1.4%	2.7%
2023-2028E	6.2%	4.5%	5.7%
2028E-2033E	2.9%	1.9%	2.6%



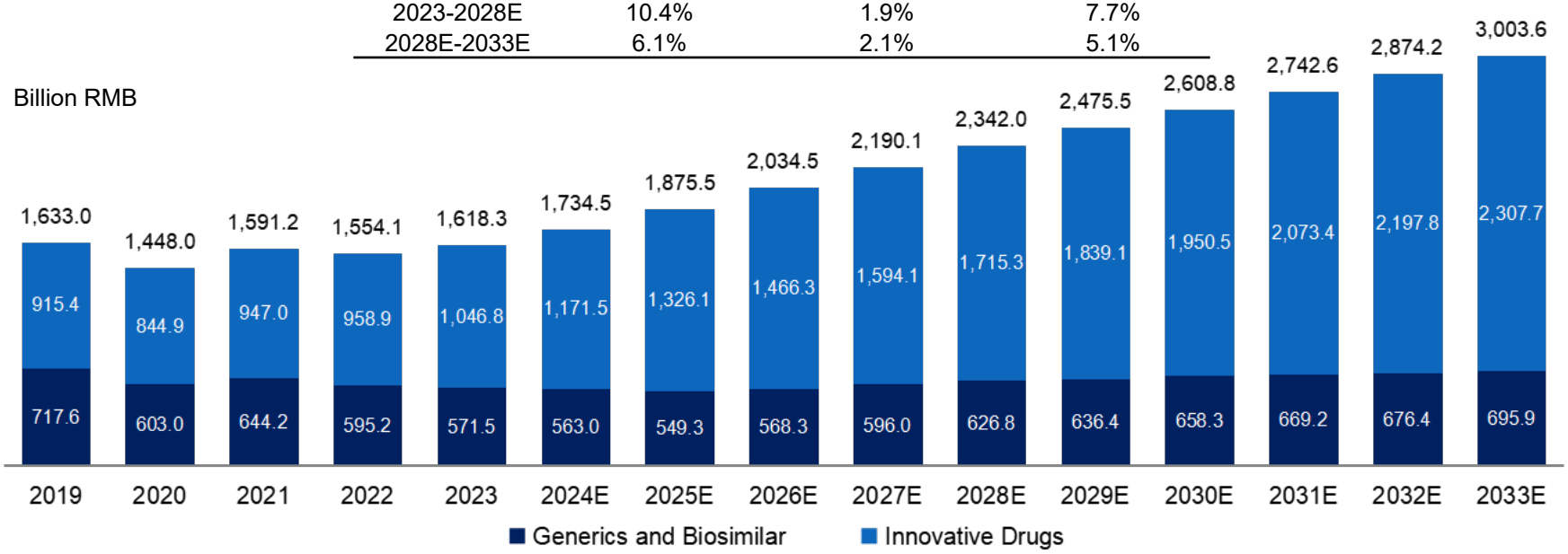
Source: Annual Reports of Listed Medical Companies, NMPA, CDE, NRDL, MOHRSS, FDA, Frost & Sullivan Analysis

Breakdown of China Pharmaceutical Market by Innovative Drugs, Generics and Biosimilar, 2019-2033E

- In 2023, the China innovative drugs market reaches RMB1,046.8 billion, accounting for 64.7% of the whole pharmaceutical market. Due to favorable policies related to innovative drugs, health insurance adjustments, and increased R&D spending, the innovative drug market is growing fast.
- As a major country producing generic drugs, China's generic drug market share in the overall pharmaceutical market is higher than the global level, and reaching RMB571.5 billion in 2023. With the continuous promotion of the consistency evaluation of generic drugs and the implementation of volume-based procurement, China's generic drug market pattern is gradually reshaping. A large number of inferior generic drugs will be eliminated, which is expected to slow down the growth of generic drug market in the future. However, at the same time, the overall competitiveness of China's generic drugs will be improved and the market will be further concentrated. Under the overall medical insurance cost control condition, high-quality generic drugs are expected to become the new growth driver of the generic drug market. By 2033, China's generic drug market is forecasted to reach RMB695.9 billion.

Breakdown of China Pharmaceutical Market by Innovative Drugs, Generics and Biosimilar, 2019-2033E

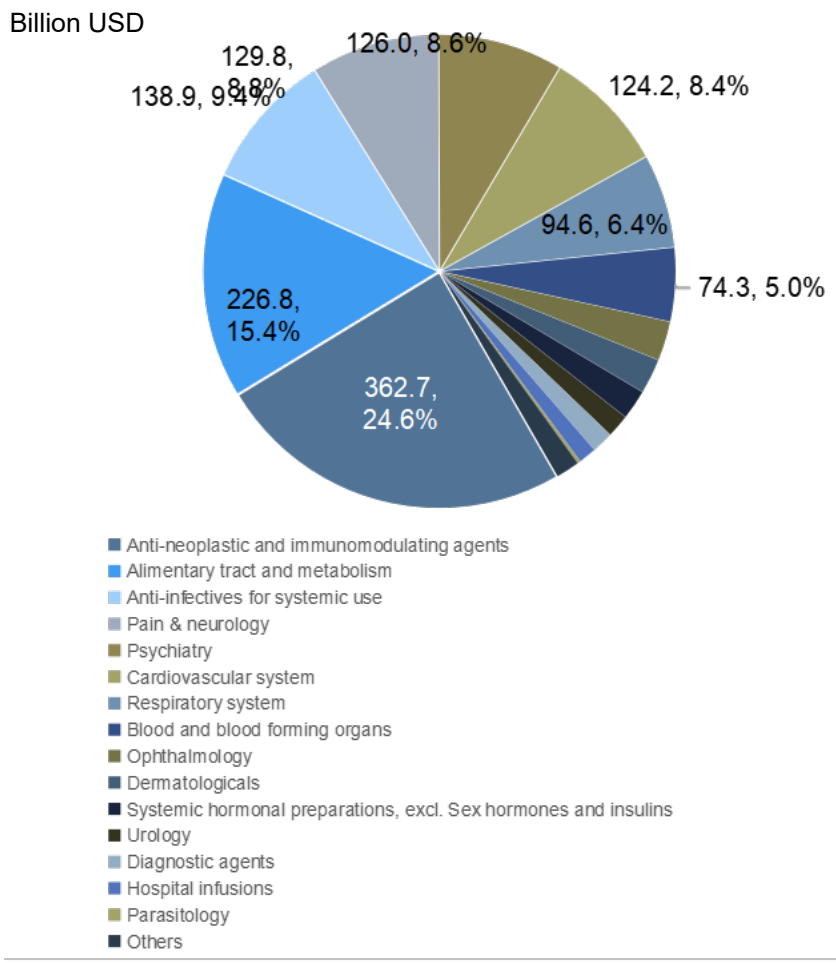
Period	CAGR		
	Innovative Drugs	Generics and Biosimilars	Total
2019-2023	3.4%	-5.5%	-0.2%
2023-2028E	10.4%	1.9%	7.7%
2028E-2033E	6.1%	2.1%	5.1%



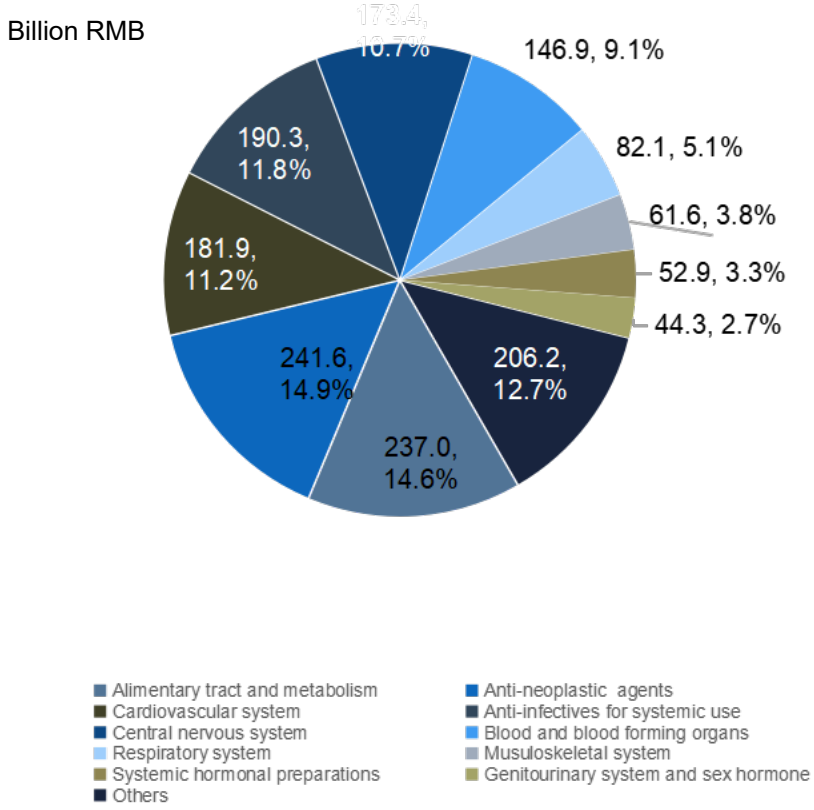
Source: Annual Reports of Listed Medical Companies, NMPA, CDE, NRDL, MOHRSS, Frost & Sullivan Analysis

Breakdown of Global and China Pharmaceutical Market by Therapeutic Area, 2023

Breakdown of Global Pharmaceutical Market by Therapeutic Area, 2023



Breakdown of China Pharmaceutical Market by Therapeutic Area, 2023

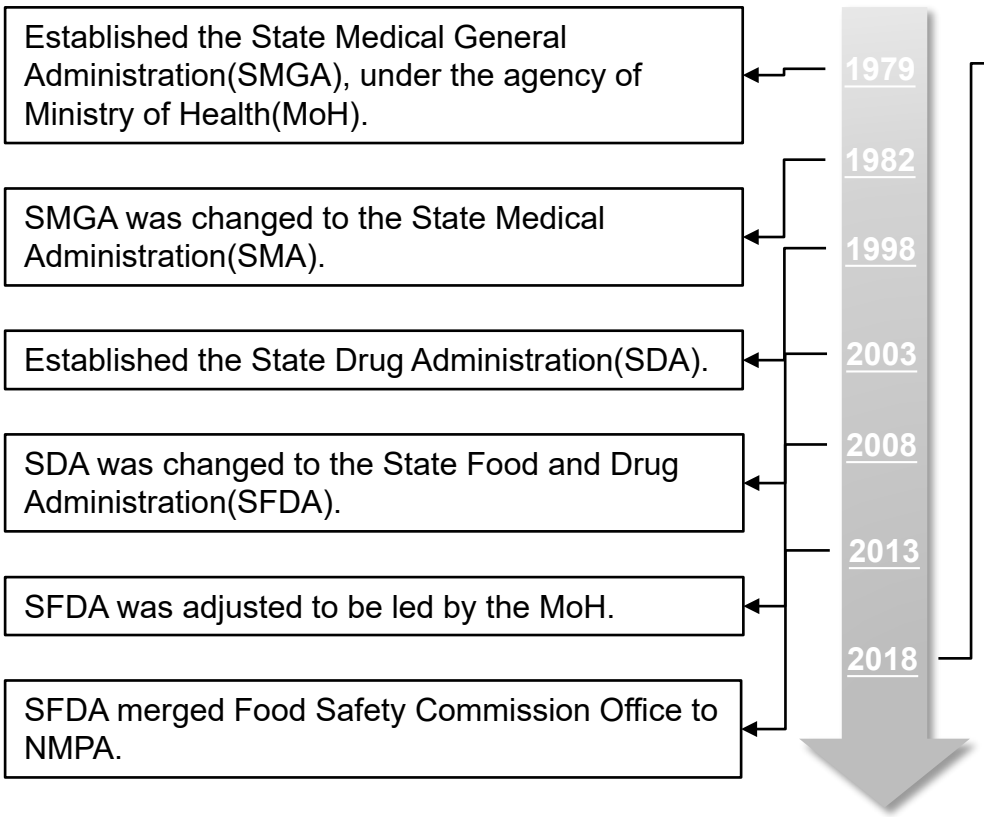


Source: Frost & Sullivan analysis

National Medical Products Administration (NMPA) Introduction

- The first meeting of the 13th National People's Congress on March 17, 2018 adopted the "First Decision of the 13th National People's Congress on the Decision of the State Council's Institutional Reform Plan", approved the "Organizational Reform Plan of the State Council", and acknowledged the establishment of the NMPA, which is managed by the State Administration for Market Regulation.
- This reform separated food and drug, implemented hierarchical management of market supervision.

Development History of NMPA



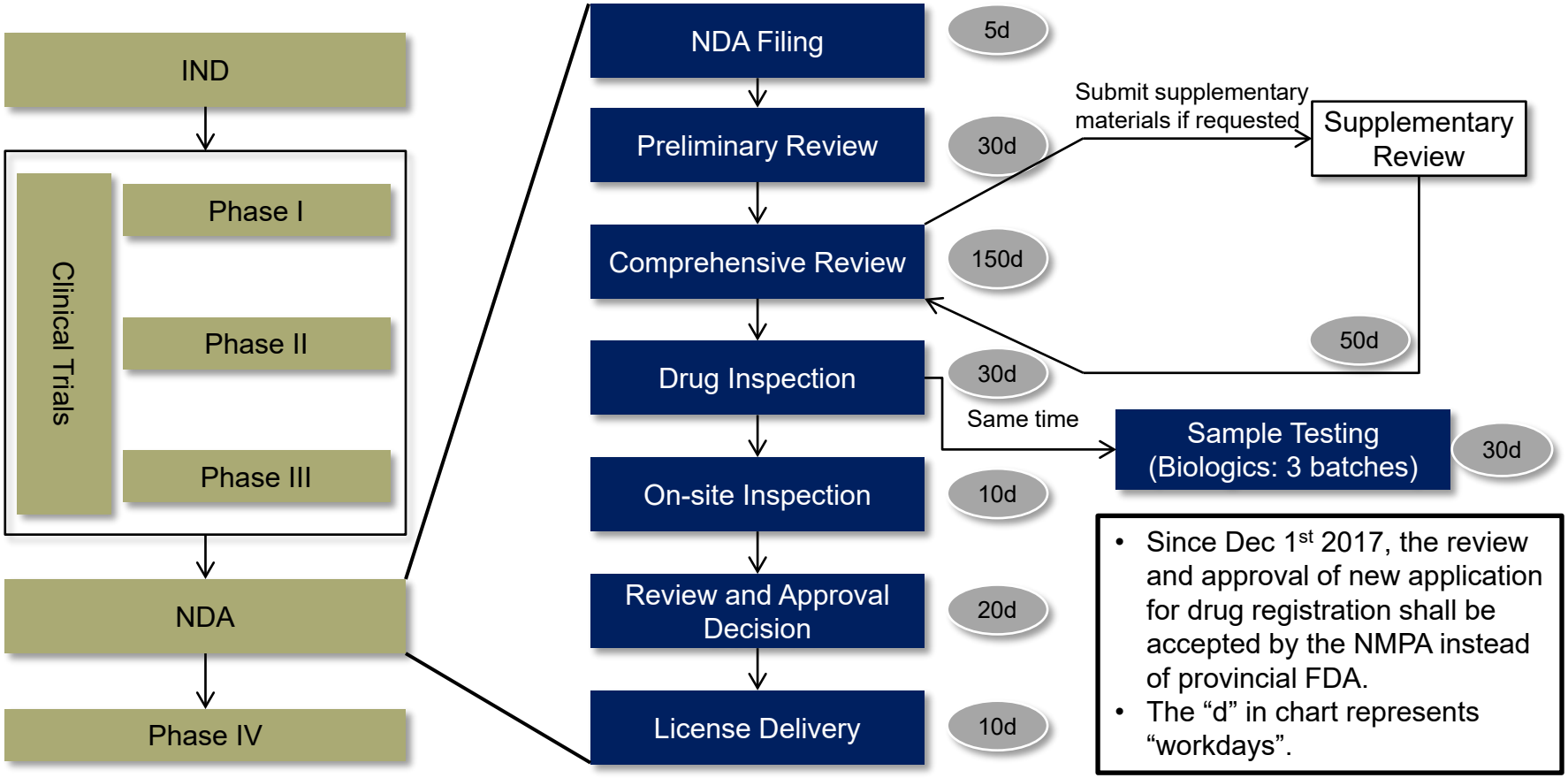
At the first session of the 13th National People's Congress, the NMPA was approved to be established and administered by the State Administration for Market Regulation.

- To supervise the safety of drugs (including traditional Chinese medicines (TCMs) and ethno-medicines, the same below), medical devices and cosmetics.
- To undertake standards management for drugs, medical devices and cosmetics.
- To regulate the registration of drugs, medical devices and cosmetics.
- To undertake quality management for drugs, medical devices and cosmetics.
- To undertake post-market risk management for drugs, medical devices and cosmetics.
- To undertake management of qualifications for licensed pharmacists.
- To organize and guide the supervision and inspection of drugs, medical devices and cosmetics.
- To engage in international exchange and cooperation in the regulation of drugs, medical devices and cosmetics, and participate in developing relevant international regulatory rules and standards.
- To guide the work of drug regulatory departments of all provinces, autonomous regions, and municipalities directly under the Central Government.
- To complete other tasks assigned by the CPC Central Committee and the State Council.

Source: NMPA, Frost & Sullivan analysis

Drug Registration Procedure in China

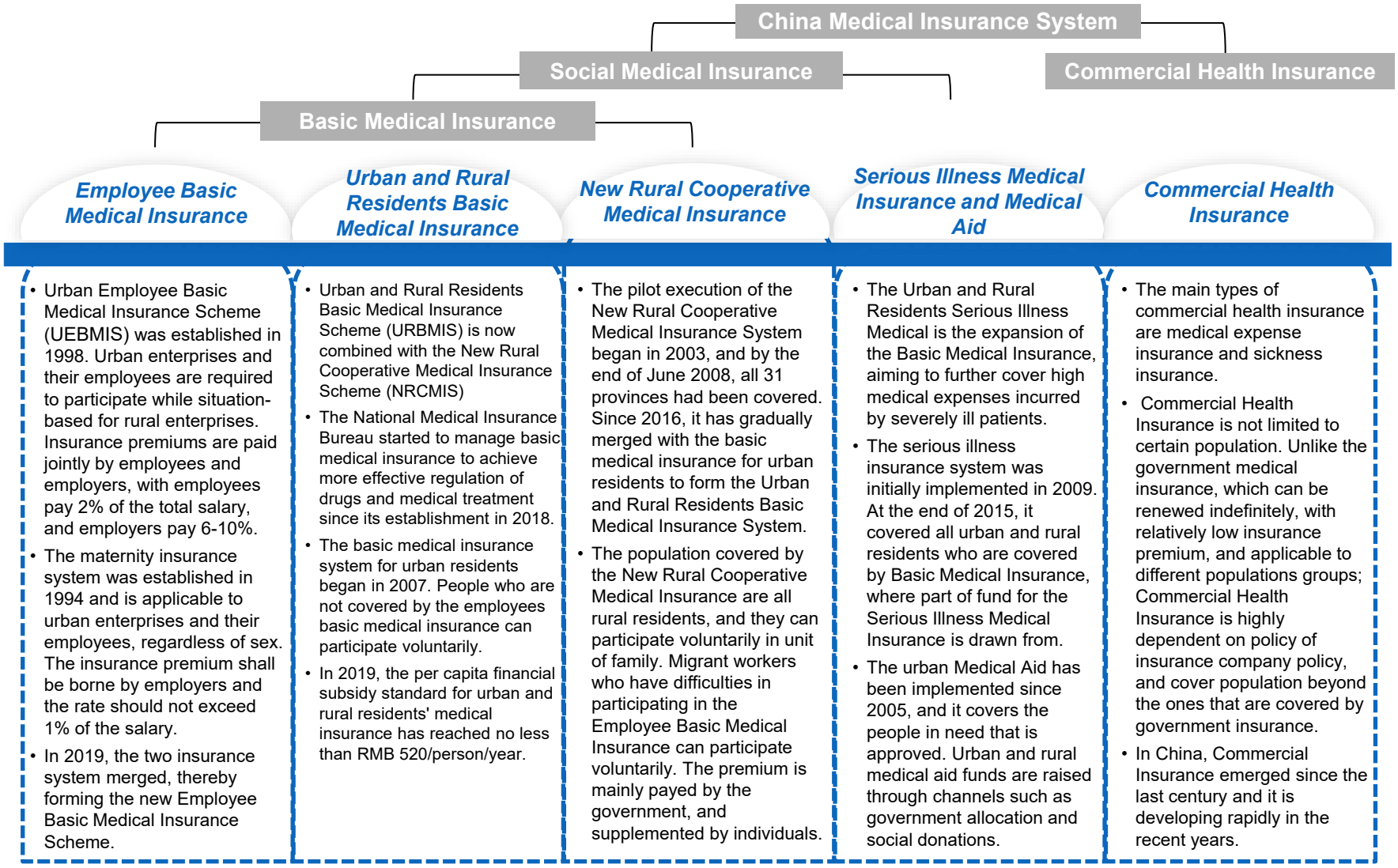
- According to Provision for Drug Registration（药物注册管理办法）and Notice of Adjustment of Drug Registration Acceptance （关于调整药品注册受理工作的公告）in 2017, the drug registration has changes on processing time limitation and authorities supervising NMPA reviews to accelerate the NDA review and approval.
- The time required to obtain approval by the NMPA and other comparable regulatory authorities is unpredictable but can take up to 5-10 years following the commencement of clinical trials and depends on numerous factors, including the substantial discretion of the regulatory authorities.



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

Source: CMA, Frost & Sullivan analysis

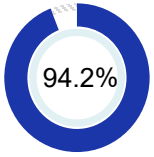
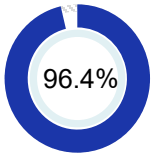
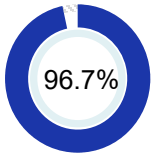
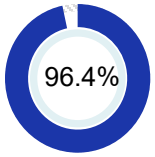
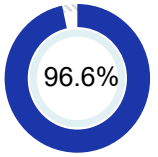
Overview of Medical Insurance System in China



Source: MOHRSS, Frost & Sullivan analysis

Historical Coverage of Basic Social Medical Insurance Scheme

- Chinese government has dedicated strong effort to increasing the accessibility and affordability of healthcare services through the healthcare reform. Huge investment has been made to construct and upgrade healthcare infrastructure, and expand medical insurance coverage. A medical insurance system encompassing URBMIS and UEBMIS has been established to cover nearly all the population of 96.6% in 2021.

Unit: Million People	2017	2018	2019	2020	2021
URBMIS	873.6	897.4	1025.1	1016.8	1010.0
UEBMIS	303.2	316.8	329.3	344.6	354.2
NRCMIS*	133.0	130.0	\	\	\
Total Population Covered by 3 Schemes	1309.8	1344.6	1354.4	1361.3	1364.2
Population in China	1390.0	1395.4	1400.1	1411.8	1412.6
Coverage Rate					

*2017 data only includes five provinces in Mainland China (Liaoning, Jilin, Anhui, Guizhou and Shaanxi).
2018 data only includes seven provinces in Mainland China (Liaoning, Jilin, Anhui, Hainan, Guizhou and Shaanxi, Tibet)
In 2019, NRCMIS has been fully consolidated with URBMIS

Note: URBMIS = Urban and Rural Residents Basic Medical Insurance Scheme; UEBMIS = Urban Employee Basic Medical Insurance Scheme; NRCMIS = New Rural Cooperative Medical Insurance Scheme

Source: MORHSS, Frost & Sullivan analysis

The Importance of Formulation Development in Drug R&D and Production

Key Information

- Preparation development is an important part of drug R&D. Early preparation researches do not require to develop a full prescription; all studies revolve around toxicology studies and ease of administration during Phase I clinical trail, with the goal of bringing the drug to clinical application as soon as possible. As the programs progress, drug delivery methods and prescription studies become more and more comprehensive.

Drug discovery stage

- The main task of preparation study is in the area of physicochemical and ADME-related properties of compounds, such as solubility, permeability, chemical stability, metabolic stability, P450 inhibition and substrates, developability assessment, selection of salts and crystal forms.
- The difficulties in the preparation work are the limited API, the setting of the drug developability criteria (stability and bioavailability in the best dissolved state).

Preclinical research stage

- The main tasks of preparation study are the formulation development for toxicology research, screening and selection of salt and crystal forms, pre-formulation studies, and preparation development for Phase I clinical trails.
- Difficulties in preparation study include limited API, low solubility, low bioavailability, inability to meet in vivo detection limits in animals, and limited R&D time.

Clinical development Stage

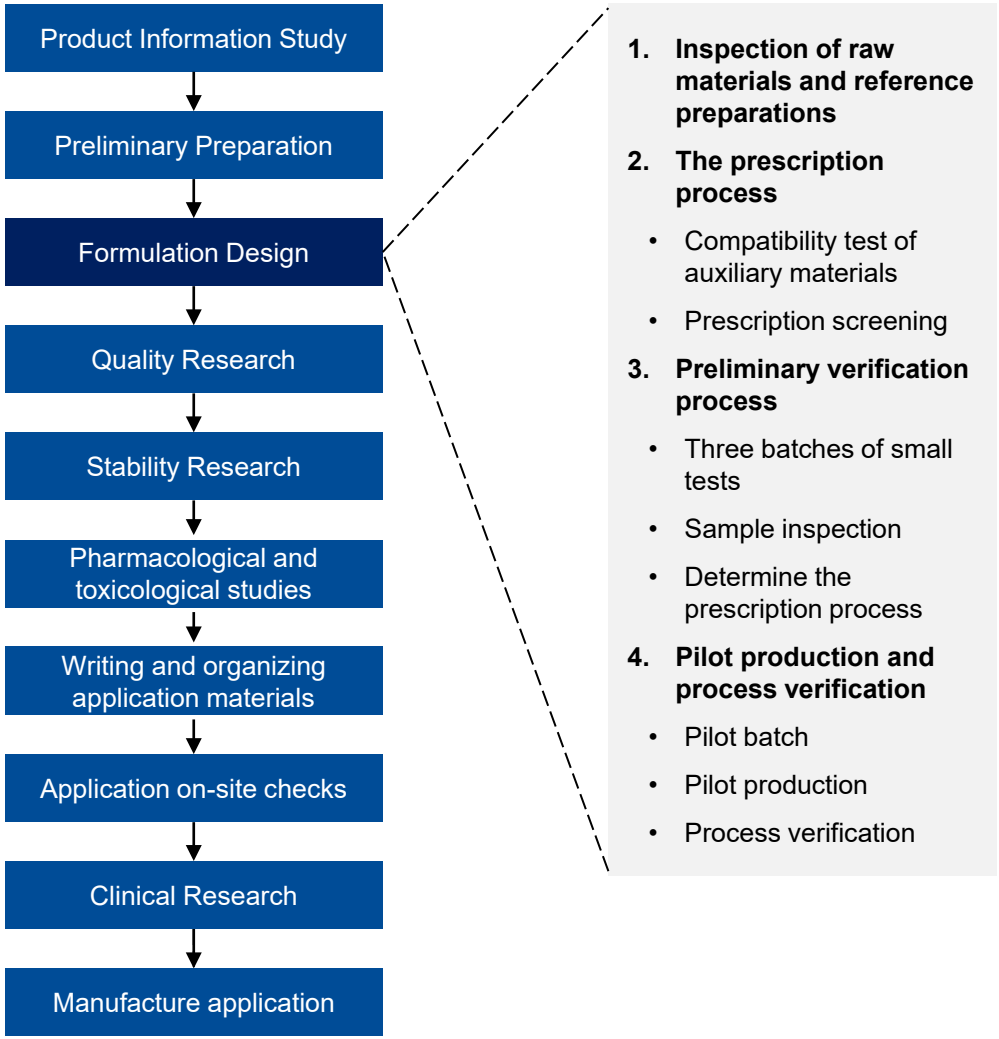
- The main task of preparation study is the R&D of the commercially available preparations for Phase IIb and/or Phase III studies; preparation development, validation and technology transfer to production.
- The difficulties in preparation study are technology scale-up and robustness, stability prediction and preparation shelf-life estimation, as well as the communication between R&D and production.

Source: Frost & Sullivan analysis

Formulation design is an important step in generic preparation R&D

Key Information

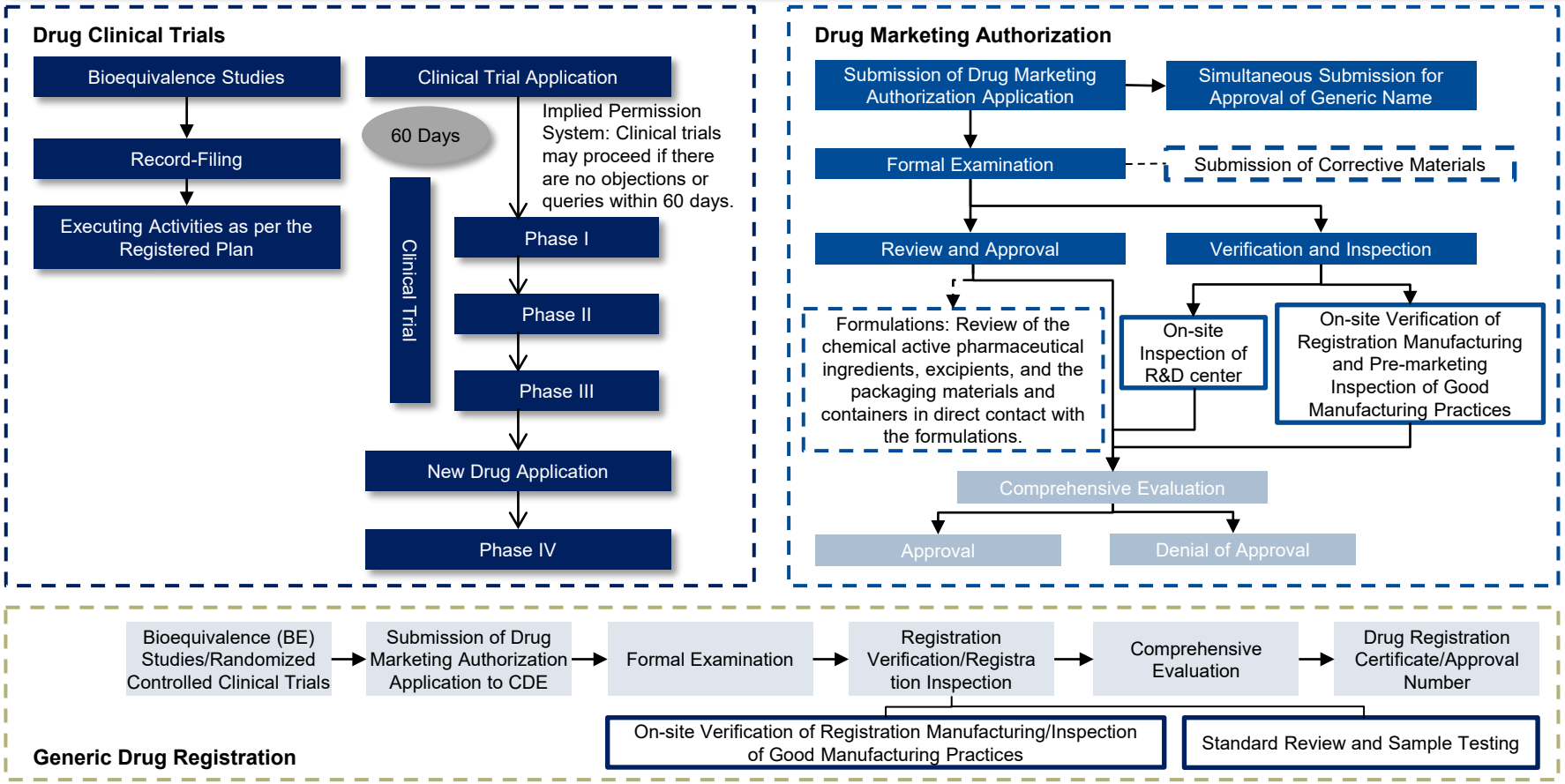
- In order for generic drugs to achieve the same performance as the innovative drugs, it is necessary to maintain the consistency of prescription and manufacture R&D. However, the prescription is difficult to be consistent, as the type, model and source of excipients used may differ, and the physical and chemical properties of the raw materials themselves may also be different. All of these factors may affect the product performance. There will also be difference in the manufacture process, such as the mixing sequence and granulation binder addition method. Performance and parameter control of equipment may also differ, affecting the preparation performance.
- Therefore, whether the production process can be industrialized and reproduced stably plays a key role in the development of preparations.



Source: Frost & Sullivan analysis

Overview of Drug Registration Application

- Before applying for registration with the Center for Drug Evaluation, generic drugs usually need to demonstrate bioequivalence tests (pharmacokinetic studies/pharmacodynamic studies) or randomized controlled clinical trials to prove the human bioequivalence of generic drugs and reference formulation. Compared to randomized controlled clinical trials, pharmacokinetic and pharmacodynamic studies generally have lower design requirements and clinical costs. However, whether each generic drug needs to undergo a randomized controlled clinical trial depends on the type of the generic drug.



Source: Measures for the Administration of Drug Registration (2020), Frost & Sullivan Analysis

Growth Drivers for Global and China Pharmaceutical Market

Aging population	• As the global population continues to age, the demand for pharmaceutical products and services is on the rise. This trend is particularly evident in China, where the aging population is driving significant growth in the pharmaceutical market. In China, population aged above 65 reached 216.8 million in 2023, accounting for 15.4% of the total population. The proportion is projected to further increase to 17.3%, representing a population 242.8 million in 2026, which will bring continuous growth of population with chronic diseases. The pharmaceutical industry is responding to this demographic shift by developing innovative products and investing in research and development to meet the evolving healthcare needs of older adults, especially for whom with chronic diseases.
Increasing Disposable Income	• One of the major drivers of the robust growth of global and China pharmaceutical market is the rising disposable income of patients from both developed and developing countries. For instance, China residents average annual disposable income is experience fast growth during the past few years, increasing from RMB28,228 in 2018 to RMB39,218 in 2023 at a CAGR of 6.8% during this period. The growth of per capita annual income has a positive effect on the purchasing power and the level of health awareness which could promote the pharmaceutical market, especially with chronic diseases, such as asthma and COPD.
Favorable Policies	• China government promulgated a series of policies to encourage the R&D, enhance the drug affordability, as well as strengthen the regulation on pharmaceutical market. 1) Regulatory reform that shorten the review and approval time span for innovative drugs IND and NDA applications, which will accelerate getting to the market process for drugs with potential to address the urgently clinical needs. 2) In addition to R&D incentives, policies that ensure accessibility of essential drugs particularly for diseases that disproportionately affect low-income populations. This can help improve healthcare outcomes and reduce the burden of disease in these regions. In 2021, “14th Five-Year Plan for the Development of the Pharmaceutical Industry” 《“十四五”医药工业发展规划》 emphasized the need to continuously update the "Catalogue of Encouraged Generic Drugs"《鼓励仿制药品目录》and improve relevant supporting policies to promote the generic development of drugs that are urgently needed in clinical practice and whose patents have expired. This initiative also emphasized the need to increase the registration of generic drugs and raise the proportion of high-value-added products, such as first generic drugs in developed countries. Also, the continuous implement of NRDL and NCDP has significantly alleviated the financial burden on patients. 3) Moreover, policies aimed at strengthening China's healthcare infrastructure and expanding insurance coverage can also drive growth in the pharmaceutical market. Improved access to healthcare services can lead to increased demand for pharmaceutical products, particularly for chronic disease management and preventive care.
Technical Advancement and Innovation	• The growth of the global pharmaceutical market is also being fueled by technological advancements. For instance, the preparation development in the pharmaceutical industry has been playing a crucial role in driving market growth. Pharmaceutical preparations are the final products that are administered to patients, and their development is essential for ensuring the safety, efficacy, and quality. Advances in preparation development, including novel drug delivery systems, improved formulations, and enhanced manufacturing processes, are contributing to the development of more effective and patient-friendly pharmaceutical products. As new technologies continue to emerge and preparations become more advanced, the industry will be well-positioned to meet the growing demand for pharmaceutical products and improve healthcare outcomes for patients around the world.

Source: Frost & Sullivan analysis

Future Trends of China Pharmaceutical Market

Innovation in Formulation Design	• Formulation innovation is poised to become a significant trend in the global and China pharmaceutical market. With global and China's aging population, the prevalence of chronic diseases like chronic respiratory diseases and cardiovascular conditions increasing, long-term relieving or controlling medication is essential, yet often leads to poor adherence among chronic disease patients, and drug safety issues affect clinical application. Innovation in formulation can improve drug delivery by controlling release timing (long-acting and sustained release), which reduces medication frequency and enhances patient compliance. They also allow precise targeting, increasing drug utilization and reducing harm to healthy tissues. By embracing innovative formulation design, pharmaceutical companies can meet the evolving needs of patients and healthcare providers. With continued investment in formulation innovation, the pharmaceutical industry is poised to drive significant advancements in drug development and patient care.
Improving Treatment Accessibility and Affordability	• In recent years, there has been a growing recognition of the need to improve treatment accessibility and affordability, and both the global and China pharmaceutical markets have been working towards addressing these challenges. Original drugs are often more expensive than their generic counterparts due to a variety of factors such as research and development expenses, patent protection, and marketing efforts that contribute to the overall cost of pharmaceuticals. In this context, high-end generic drugs, which are bioequivalent to original drugs but typically sold at a lower cost, have been instrumental in expanding access to essential medications and reducing healthcare expenditures, making them the first choice for payers. As a result, with the increasing demand for affordable healthcare and the expiration of patents on many blockbuster drugs, the generic pharmaceutical market is poised for expansion.
Rise of R&D-oriented Small and Medium-sized Pharmaceutical Companies	• In the past, the top 20 pharmaceutical companies dominated the global pharmaceutical market, but in the future they will face huge challenges from small and medium-sized innovative pharmaceutical companies. Small and medium-sized pharmaceutical companies that are innovative and R&D-oriented usually have strong R&D capabilities and more flexible R&D models in a certain therapeutic area. They have expanded from internal R&D to internal R&D, collaborative R&D, patent licensing and R&D outsourcing and other combination forms. A diversified R&D model allows R&D resources to be shared and improves R&D efficiency; and focusing on developing blockbuster drugs in this field has a higher chance.

Source: Frost & Sullivan analysis

Content

Overview of Respiratory Disease

- Respiratory disease is a type of disease that affects the lungs and other parts of the respiratory system. Respiratory disease may be caused by infection, smoking tobacco, or breathing in secondhand tobacco smoke, radon, asbestos, or other forms of air pollution.
- Respiratory disease can be classified into three different types: immunological respiratory disease, infectious respiratory disease and lung cancer.

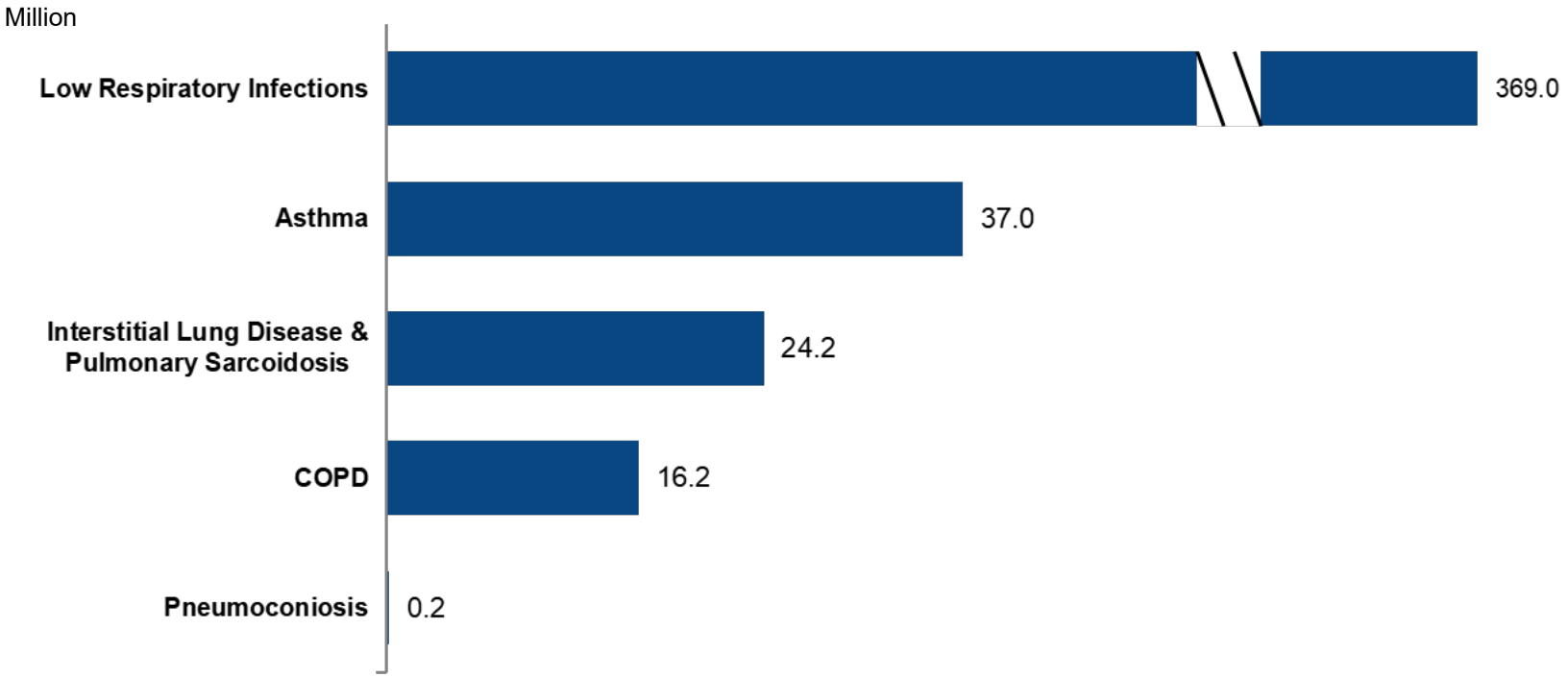
	Description	Treatment
Immunological Respiratory Disease	• Immunological lung diseases are a group of diseases mediated by immune mechanism, which occurs in bronchi, alveoli or pulmonary stroma. • According to their symptomatology and anatomic involvement, infectious respiratory disease are traditionally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

Source: Frost & Sullivan Analysis, Literature Review

Global Top Respiratory Diseases by Incidence, 2021

The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) provides the most comprehensive measurement of epidemiological features of non-communicable diseases (NCDs) to date. Among NCDs, respiratory diseases account for a substantial burden and premature mortality worldwide. In Recent years, over 50 million new cases of chronic respiratory disease, involving asthma, COPD, interstitial lung diseases and pulmonary sarcoidosis, were estimated globally.

Global Top Respiratory Diseases by Incidence – GBD study



Note: Causative agents of lower respiratory infections are viral or bacterial (including streptococcus pneumoniae and mycobacterium avium complex).

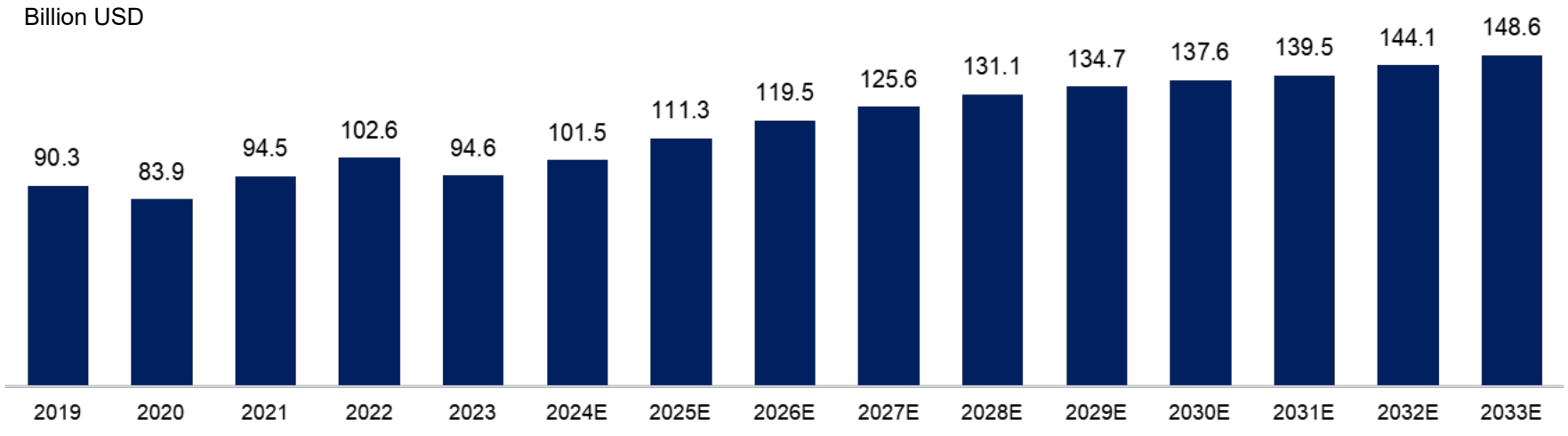
Source: Global Disease Burden, Frost & Sullivan analysis

Global Respiratory System Pharmaceutical Market, 2019-2033E

- From 2019 to 2023, global market of respiratory system drugs expanded from USD90.3 billion to USD94.6 billion, representing a CAGR of 1.2%, and is expected to reach USD131.1 billion in 2028 and USD148.6 billion by 2033, with a CAGR of 6.8% and 2.5% from 2023 to 2028 and from 2028 to 2033 respectively.

Global Respiratory System Pharmaceutical Market, 2019-2033E

Period	CAGR
2019-2023	1.2%
2023-2028E	6.8%
2028E-2033E	2.5%



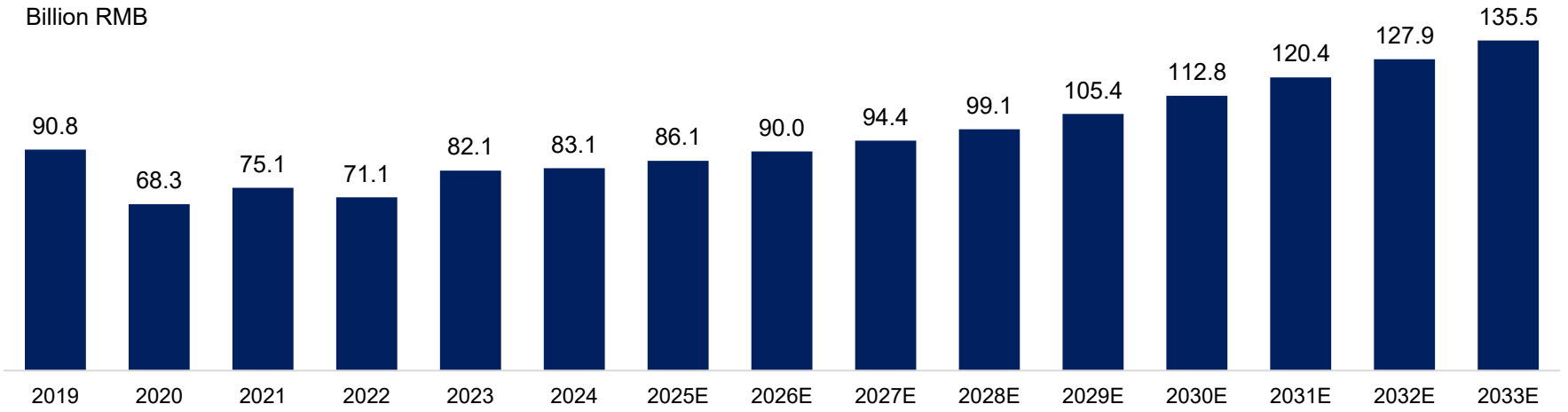
Source: Frost & Sullivan Analysis

China Respiratory System Pharmaceutical Market, 2019-2033E

- From 2019 to 2024, China market of respiratory system drugs decreased from RMB90.8 billion to RMB83.1 billion, representing a CAGR of -1.8%, and is expected to reach RMB99.1 billion and RMB135.5 billion by 2033, with a CAGR of 4.5% and 6.5% from 2024 to 2028 and from 2028 to 2033 respectively.

China Respiratory System Pharmaceutical Market, 2019-2033E

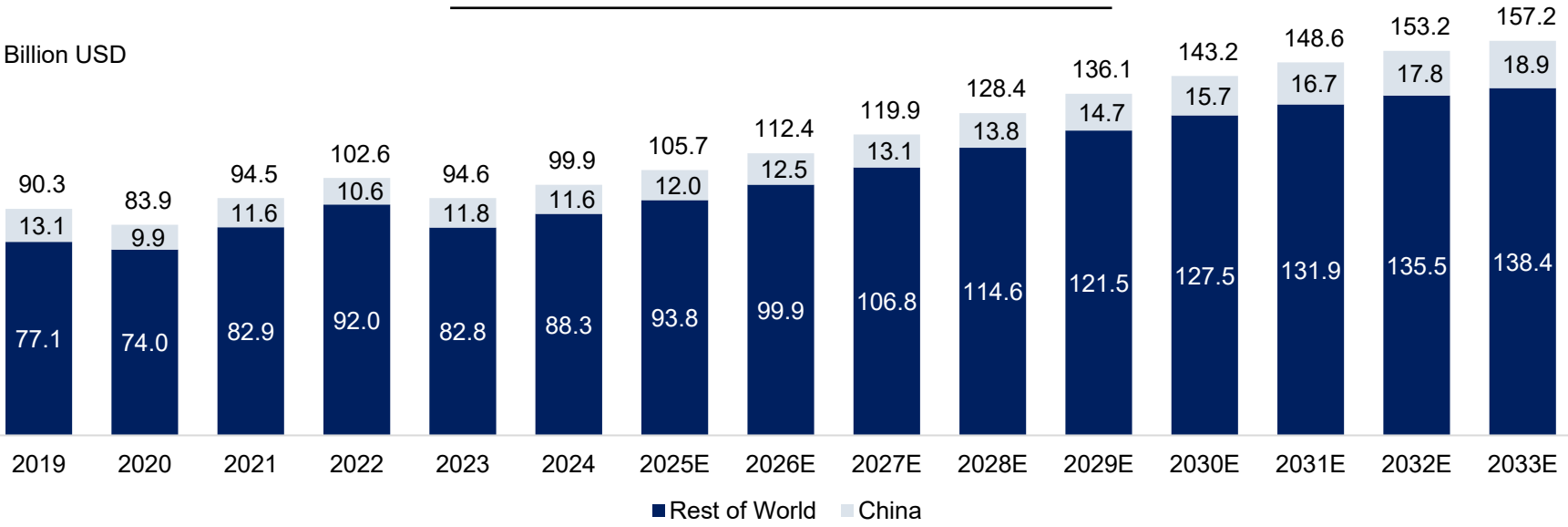
Period	CAGR
2019-2024	-1.8%
2024-2028E	4.5%
2028E-2033E	6.5%



Source: Frost & Sullivan Analysis

Global and China Respiratory System Pharmaceutical Market, 2019-2033E

Period	Global	China
2019-2024	2.0%	-2.5%
2024-2033E	5.2%	5.6%



Inhalation Formulation Therapeutic Areas Mainly Include Asthma, COPD and Rhinitis

Asthma

- Bronchial asthma is a common and prevalent disease. Asthma is an important disease that affects people's physical and mental health. Risk factors for the development of asthma include host factors and environmental factors. The pathogenesis includes airway neuromodulation disorder, genetic mechanism, neural signal transduction mechanism, airway remodeling, and their interaction.
- Untimely and unregulated treatment of asthma can be fatal. Inhalation can effectively control and relieve patient's asthma symptoms, making work and life mostly unaffected.

Chronic Obstructive Pulmonary Disease (COPD)

- It is a preventable and treatable disease characterized by airflow limitation that is not fully reversible, progresses progressively, and is associated with an abnormal inflammatory response of the lungs to harmful gases or particles such as cigarette smoke.
- The pathogenesis of COPD is not fully understood. The main treatment is based on medication to stop and control chronic inflammation, relieve clinical symptoms and improve patients' life. At the same time, COPD patients can be treated by rehabilitation, oxygen therapy and surgical methods.

Rhinitis

- It is an inflammation of nasal mucosa caused by viruses, bacteria, allergens, various physicochemical factors, and certain systemic diseases. The main pathological changes of rhinitis are congestion, swelling, exudation, hyperplasia, atrophy or necrosis of nasal mucosa.
- The pathogenesis of rhinitis is mainly caused by viral infections, genetic factors, nasal mucosal susceptibility and antigenic substances. Nasal sprays are the first choice of medication for chronic rhinitis and have good anti-inflammatory effects.

Source: Frost & Sullivan analysis

Overview of Asthma Types and Prevalence

Key Information

- Asthma is a chronic lung disease that affects the airways in the lungs. It is caused by inflammation and muscle tightening around the airways, which makes it harder to breathe. Symptoms can include coughing, wheezing, shortness of breath and chest tightness. These symptoms can be mild or severe and can come and go over time.
- Asthma is often under-diagnosed and under-treated, particularly in low- and middle-income countries. People with under-treated asthma can suffer sleep disturbance, tiredness during the day, and poor concentration. If symptoms are severe, people with asthma may need to receive emergency health care and they may be admitted to hospital for treatment and monitoring. In the most severe cases, asthma can lead to death.

1 Asthma Types

Allergic Asthma	• It is common in children, people with a family history or have previous history of allergic diseases such as eczema, allergic rhinitis, or food and drug allergies.
Nonallergic Asthma	• For some adult asthma occurs unrelated to allergies. The patient's sputum may have neutrophils, eosinophils, or just some inflammatory cells.
Late-onset asthma	• Some adults, especially women, experience asthma attack for the first time in adulthood. Patients tend to be non-allergic and often require high doses of ICS or are insensitive to cortisol hormones.
Asthma combined with mixed airflow limitation	• Some patients with long-term asthma develop to mixed airflow limitation, which is thought to be caused by airway remodeling.
Asthma combined with obesity	• Some obese patients with asthma have significant respiratory symptoms and a few airway inflammation with eosinophil infiltration.

2 Risk Factor

- Active smoking: It has been shown that it is more difficult to maintain asthma control in smokers with asthma than in nonsmokers with asthma. Altered airway inflammation and corticosteroid insensitivity are thought to be the mechanisms behind the adverse effects of smoking in asthma patients.

- Pollution: Exposure to outdoor and indoor air pollution remains a significant risk factor for both the development of asthma and the triggering of asthma symptoms.

- Genetics of asthma: Several genetic and environmental factors are also known to modulate the clinical expression of the disease and its associated phenotypes. In addition to environmental exposures, genetic factors have an important effect on the inception, severity, and treatment of asthma.

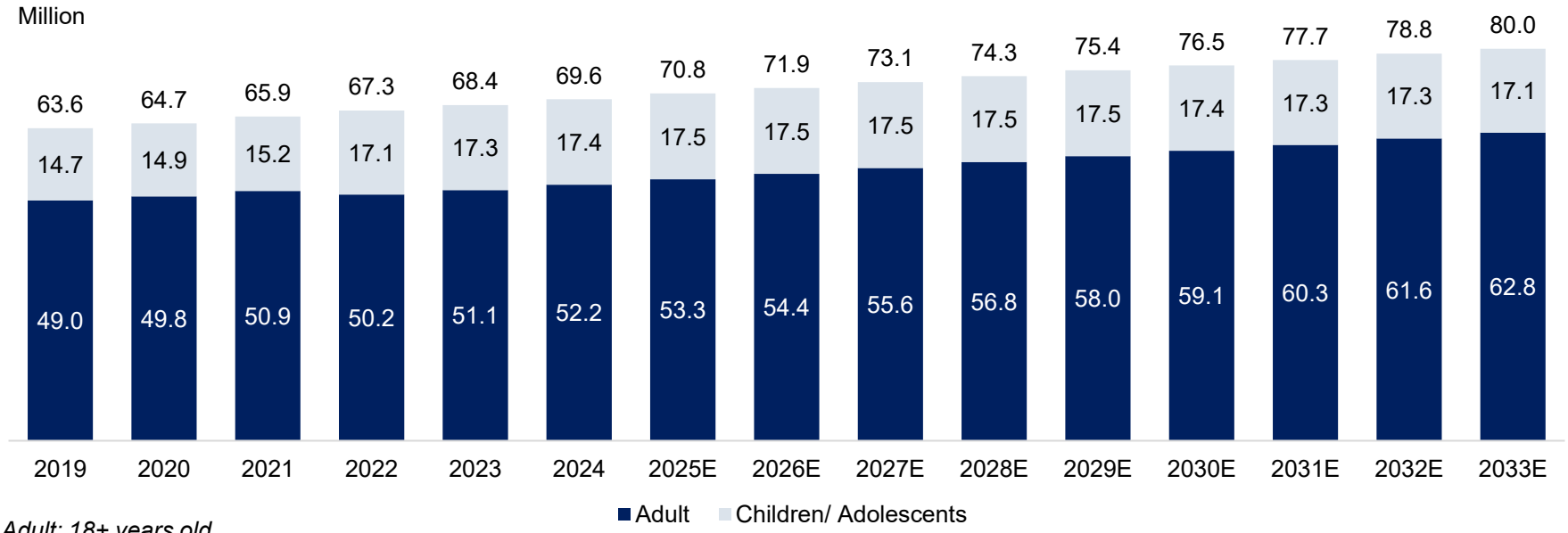
Source: Literature Review, Frost & Sullivan analysis

Prevalence of Asthma in China Breakdown by Age, 2019-2033E

- In China, the number of adult patients affected by asthma reached 52.2 million in 2024, with a CAGR of 1.3% from 2019 to 2024, and this number is forecasting to reach 62.8 million in 2033; the number of children/adolescents patients affected by asthma reached 17.4 million in 2024, with a CARG of 3.5% from 2019 to 2024 and this number is forecasting to reach 17.1 million in 2033.

Prevalence of Asthma in China Breakdown by Age, 2019-2033E

CAGR	Adult	Children/ Adolescents	Total
2019-2024	1.3%	3.5%	1.8%
2024-2028E	2.2%	0.2%	1.7%
2028E-2033E	2.0%	-0.4%	1.5%



Adult: 18+ years old

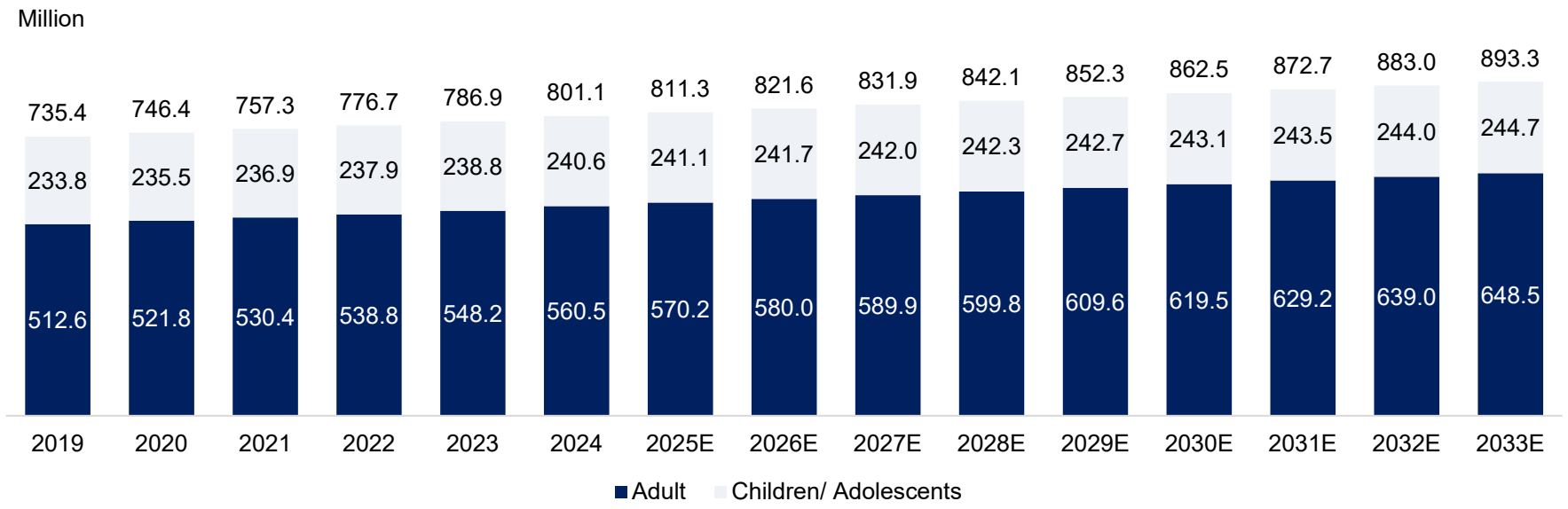
Source: Literature review, Frost & Sullivan analysis

Prevalence of Asthma in Global Breakdown by Age, 2019-2033E

- Globally, the number of adult patients affected by asthma reached 560.5 million in 2024, with a CAGR of 1.8% from 2019 to 2024, and this number is forecasting to reach 648.5 million in 2033; the number of children/adolescents patients affected by asthma reached 240.6 million in 2024, with a CARG of 0.6% from 2019 to 2024 and this number is forecasting to reach 244.7 million in 2033.

Prevalence of Asthma in Global Breakdown by Age, 2019-2033E

CAGR	Adult	Children/ Adolescents	Total
2019-2024	1.8%	0.6%	1.7%
2024-2028E	1.7%	0.2%	1.3%
2028E-2033E	1.6%	0.2%	1.2%



Adult: 18+ years old

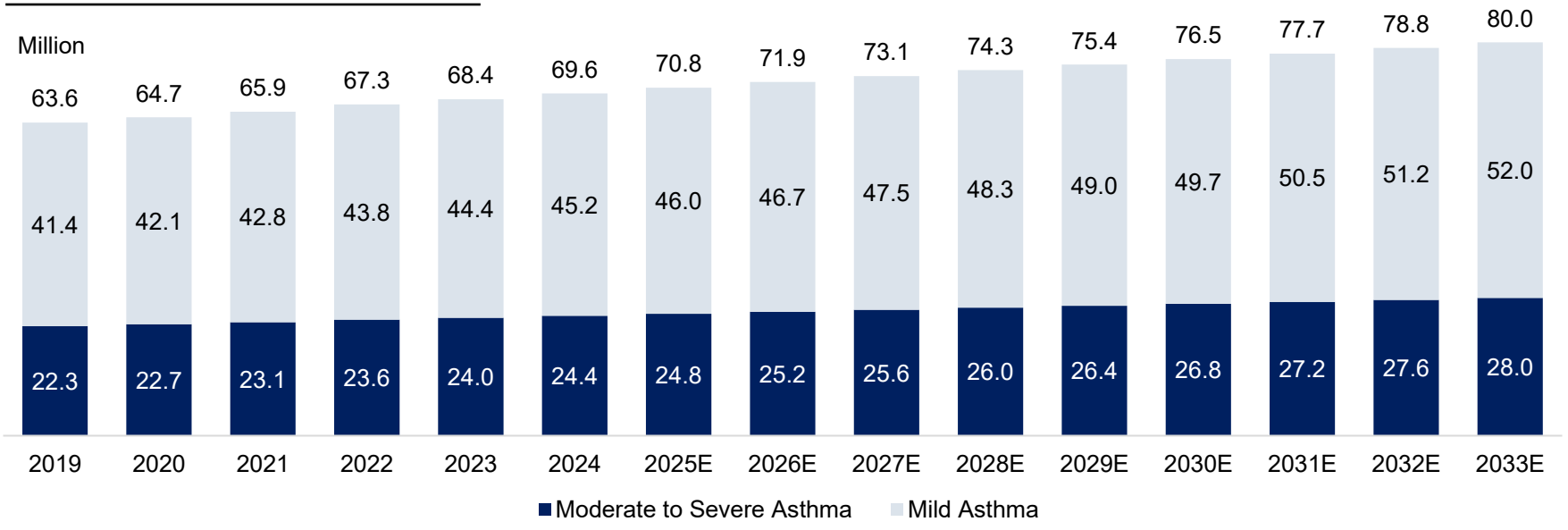
Source: Literature review, Frost & Sullivan analysis

Prevalence of Asthma in China Breakdown by Severity, 2019-2033E

- The epidemic of asthma that has been observed in both children and adult is still continuing in China. The total number of patients affected by asthma in China had reached 63.6 million in 2019, with a CAGR of 1.8% from 2019 to 2024. This number is expected to continue to climb and eventually reach 80.0 million in 2033.

Prevalence of Asthma in China Breakdown by Severity, 2019-2033E

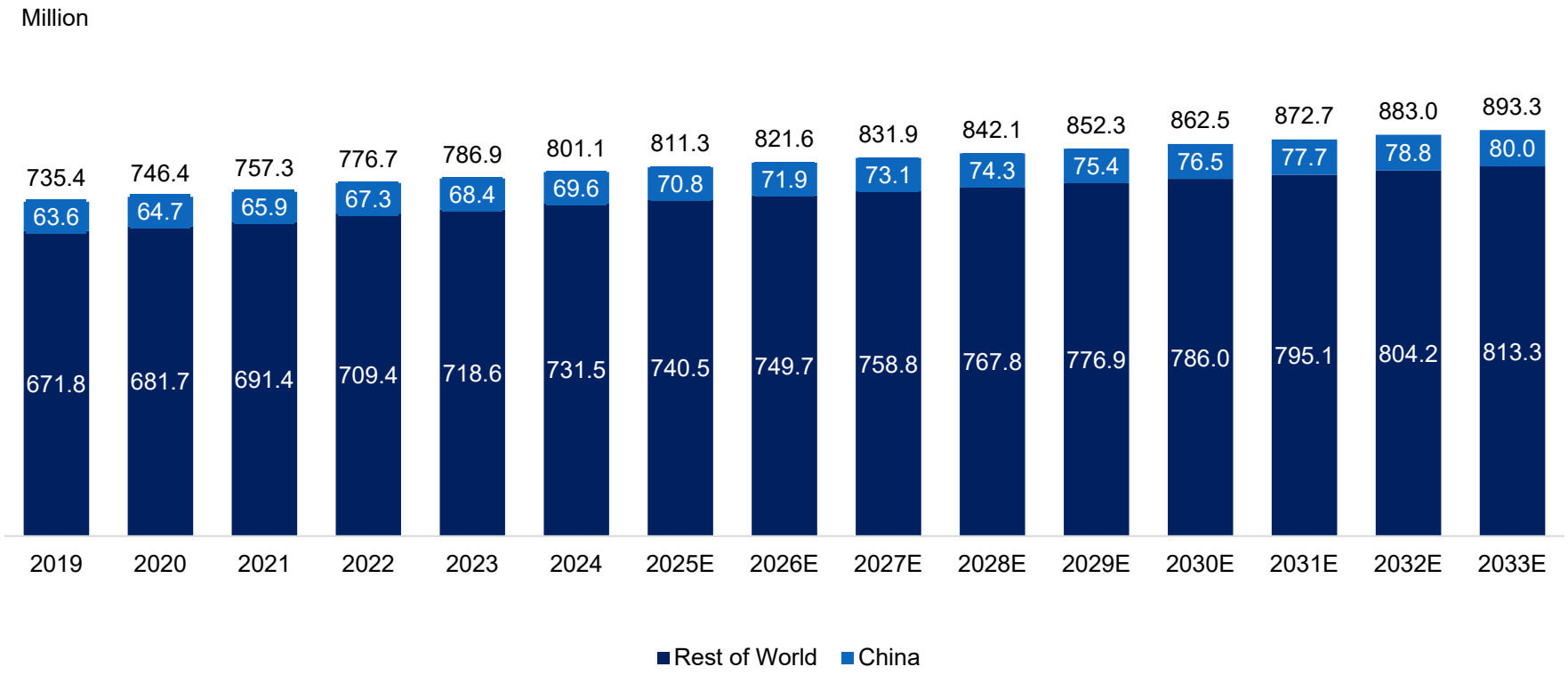
CAGR	Total
2019-2024	1.8%
2024-2030E	1.6%



Source: Literature review, Frost & Sullivan analysis

Prevalence of Asthma in Global and China, 2019-2033E

Period	Global	China
2019-2024	1.7%	1.8%
2024-2033E	1.2%	1.6%



Asthma Severity Classification

Key Information

- The degree of asthma can be classified into four grades - intermitted, mild, moderate, and severe. The classification relies on grading daytime and nighttime symptoms, frequency of attacks, activity limitations, pulmonary function tests, and PEF Variation rate.
- Asthma is to be treated in a graded manner, and generally level 2 or above will affect daily life. Mild patients mainly have shortness of breath and chest distress during exercise, with a slight increase in respiratory rate. They may inhale β2 adrenoceptor agonists and take theophylline controlled-release drugs orally to relieve symptoms. Moderate patients, with marked increase in respiratory rate, loud croup and emotional anxiety, can use dry powder inhaler (DPI) for β2 adrenoceptor agonists, intravenous theophylline drips, and oral glucocorticoid medications.
- Patients with severe and critical conditions require oxygen jet Nebulization inhalation, intravenous β2 adrenoceptor agonists, oxygen therapy, and intravenous hormonal drugs, etc.

1 Severity classification of asthma

	Intermittent (Grade 1)	Mild Persistent (Grade 2)	Moderate Persistent (Grade 3)	Severe Persistent (Grade 4)
Frequency of Symptoms	<1 time per week	≥1 time per week, but <1 time per day	Symptoms occur daily	Symptoms occur throughout the day
Frequency of Occurrence	brief attacks	attacks may interfere with daily activities and sleep	attacks interfere with daily activities and sleep	attacks occur frequently
Nocturnal asthma symptoms	≤ 2 times per month	>2 times per month, but <1 time per week	≥1 time per week	occur frequently
FEV_1 as % of expected value	≥80% or PEF≥80% personal best	≥80% or PEF≥80% personal best	60%~79% or PEF=60%~ 79% personal best	<60% or PEF< 60% personal best
PEF Variation rate	<20%	20%～30%	>30%	>30%

Note: FEV_1 : forced expiratory volume in one second; PEF: Peak expiratory flow; FVC: forced vital capacity

Source: Guidelines for Bronchial Asthma Prevent and Management (2020 edition), Frost & Sullivan analysis

The Goal of Asthma Treatment is to Achieve Overall Control

Key Information

- The goal of asthma management is to achieve and maintain symptom control. Control means to minimize disease symptoms, damage and risk after treatment. Control is an important evaluation indicator when patients receive treatment. Regardless of disease severity, achieving good control is the goal of asthma treatment. The level of asthma control is classified as totally controlled, partially controlled, and uncontrolled.
- The guidelines emphasize that most patients with asthma can achieve the therapeutic goal of asthma control with pharmacological treatment, especially with the implementation of effective management. Poorly controlled asthma seriously affects patients' daily life, work, and school, leading to recurrent acute attacks, emergency medical treatment and hospitalization. It will also lead to impairment of lung function, and increased treatment costs, resulting in reduced social productivity and severe socioeconomic burden.

	Total control	Partial control	Uncontrolled
Symptoms	All ages, excluding 5-11 years old children: ≤2 days/week 5-11 years old children: ≤2 days/week, but not >1 time/day	All ages (excluding 5-11 years old children): >2 days/week 5-11 years old children: >2 days/week, or ≤2 days/week occur multiple attacks	All ages: everyday
Wake up at night	Adults and children≥12 years old: ≤2/month 5-11 years old children: ≤1/month; 0-4 years old children: ≤1/month	Adults and children≥12 years old: 1-3/week 5-11 years old children: ≥2/month; 0-4 years old children: >1/month	Adults and children≥12 years: ≥4/week 5-11 years old children: ≥2/week; 0-4 years old children: >1/week
Normal activity disruption adrenoceptor agonists	None ≤2days/week	Limited >2days/week	Very limited Several times/day
FEV_1 or peak flow rate	>80% expected value or personal best value	60～80% expected value or personal best value	<60% expected value or personal best value
FEV_1/FVC (5-11 years old children)	>80%	75～80%	<75%
Oral glucocorticoids are required for aggravate	0～1/year	Adults and children≥5 years old: ≥2/year 0-4 years old children: 2 to 3/year	Adults and children ≥5 years old: ≥2/year 0-4 years old children: >3/year
Recommended treatment	Maintain the current stage of treatment; Follow-up every 1 to 6 months; Consider step-down therapy if disease is stable and controlled for ≥3 months	Up 1 step treatment Reassess in 2 to 6 weeks Consider other treatment if adverse drug reactions occur	Consider short-term use of systemic ICS, rising 1 to 2 steps of treatment; Reassess in 2 weeks and consider other treatments if adverse effects occur

Source: Chinese expert consensus on the control of bronchial asthma, Frost & Sullivan analysis

Long-term Treatment Options for Asthma Patients

- Asthma treatment should base on the severity of the patient's condition, and the selection of therapeutic drugs should base on a stepwise treatment principle according to changes in disease control (escalating or downgrading). Usually asthma control is achieved and maintained for at least 3 months, and step-down therapy can be tried to eventually achieve maintenance of symptom control with minimal medication. One kind of medications for asthma treatment is maintenance medications, i.e. medications that need to be used daily for a long time, which include inhaled glucocorticoids (ICS), ICS/long-acting β2 adrenoceptor agonists (ICS/LABA), etc. The other kind is reliever medication, when are used in acute attacks and mainly serve to relieve asthma symptoms by rapidly relieving bronchospasm. Reliever medications are mainly bronchodilators, including fast-acting and short-acting oral β2 adrenoceptor agonists (SABA), and ICS/formoterol. ICS/LABA can deliver both anti-inflammatory and bronchodilator effects, resulting in enhanced symptom control and improved lung function. In addition to pharmacological treatments, other strategies should be considered where relevant, to assist in improving symptom control and/or reducing future risk. In clinical practice, the severity of asthma can be classified into four grades -intermitted, mild, moderate, and severe. Severity of asthma is classified by the level of treatment used for asthma control.

Severity Classification	Mild		Moderate	Severe	
Treatment Options	**Level 1**	**Level 2**	**Level 3**	**Level 4**	**Level 5**
Recommended Maintenance Medication	As-needed ICS/formoterol	Low-dose ICS or as-needed ICS/formoterol	Low-dose ICS/LABA	Medium ICS/LABA	Add other treatments, such as anti-IgE, anti-IL5/5R, anti-IL4R
Other Maintenance Medication	As-needed SABA plus low-dose ICS	Leukotriene receptor antagonists(LTRA) Low-dose theophylline	Medium/low-dose ICS plus LTRA (or add theophylline)	High-dose ICS/LAMA (or add LTRA or add theophylline)	High-dose ICS/LABA(or add LAMA, or add theophylline, or add low-dose oral hormone)
Recommended Reliever Medication	As-needed ICS/formoterol (recommended)				
Other Reliever Medication	As-needed SABA				
Non-pharmacological Treatment	• Cessation of smoking, environmental tobacco exposure and vaping • Physical Activity • Pulmonary rehabilitation programs • Avoidance of occupational or domestic exposures to allergens or irritants, and so on				

Note:
LAMA inhalation is only used in adults aged 18 years and older.
SABA: short-acting β2-agonist; LAMA: long-acting anticholinergic drug; ICS: inhaled glucocorticosteroid
Intermittent asthma typically doesn't require daily controller medication. Instead, a quick-relief bronchodilator, as a rescue inhaler is often recommended.

Source: Guidelines for Bronchial Asthma Prevent and Management (2020 edition), Global Initiative for Asthma (2024 edition), Frost & Sullivan analysis

Inhaled Glucocorticosteroids are the Mainstay for Asthma Patients

Key Information

- Asthma management needs long-term treatment and medication according to the patient's condition, sometimes it needs to continue until the end of the patient's life.
- Inhaled glucocorticosteroids (ICS) are the most effective and safe class of controller medication available for the treatment of asthma. ICS can effectively control airway inflammation, reduce airway hyper reactivity, reduce asthma symptoms, improve lung function and quality of life, reduce the frequency of asthma attacks, and reduce the severity of attacks. Common ICS mainly include beclomethasone, budesonide, and fluticasone propionate, etc.

1 Doses of inhaled glucocorticosteroids (ICS) commonly used in clinical practice [adults and adolescents over 12 years of age]

Drug	low dose	medium dose	High dose
Beclomethasone dipropionate (HFA)	200-500	>500-1,000	>1,000
Beclomethasone dipropionate (HFA)	100-200	>200-400	>400
Budesonide (DPI)	200-400	>400-800	>800
Ciclesonide (HFA)	80-160	>160-320	>320
Fluticasone propionate (DPI)	100-250	>250-500	>500
Fluticasone propionate (HFA)	100-250	>250-500	>500
Mometasone furoate (DPI)		200	400
Mometasone furoate (HFA)		200-400	>400
Fluticasone furoate (DPI)		100	200

2 Difficulties in long-term treatment of asthma patients

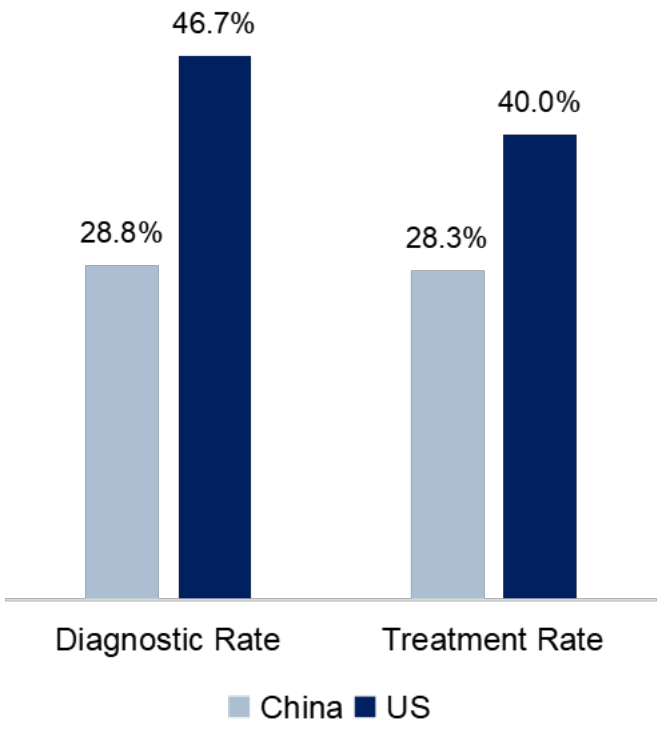
- Patients' drug compliance is low, and thus difficult to adhere to treatment
- Poor technique uses for medication devices, especially the inhalational drugs
- Lack of advance identification of high-risk patients and understanding of their lung function
- Individual circumstances vary greatly and require individualized treatment
- Symptoms are easily ignored and patients have low awareness of long-term asthma treatment

Note: CFC: chlorofluorocarbon projectile; DPI: dry powder inhaler; HFA: hydrofluoroalkane projectile

Source: Guidelines for Bronchial Asthma Prevent and Management (2020 edition), Frost & Sullivan analysis

Asthma Unmet Medical Needs

Current Status of Asthma Diagnosis and Treatment in China and US



Unmet medical needs for Asthma

High Incidence Rate but Low Diagnosis rate

- The prevalence of asthma has reached near 70 million in China, while the diagnosis rate of asthma in China is only 28.8% in 2016, which is much lower than 46.7% in the U.S. The low diagnosis rate of asthma in China has significant implications for public health, as it can lead to underestimation of the true prevalence of asthma and result in inadequate management of the condition.

Low Adherence of Long-term Treatment

- Although there exists standardized treatment guideline, a few patients can consistently follow their prescribed medication regimens and management plans. This can result in poor asthma control, increased risk of exacerbations, and reduced quality of life. Studies[1] have shown that the total control rate of asthma in China is only 28.5%, indicating a widespread problem that requires attention.

Lack of Targeted Therapies for Severe Asthma

- While many patients with asthma are able to control their symptoms with standard treatments such as inhaled corticosteroids and bronchodilators, there is a subset of patients who continue to experience frequent exacerbations and poor disease control despite high-dose standard therapy. These patients are often referred to as having severe asthma, and they represent a significant unmet need in the field of asthma management.

Low Penetration Rate of Lifelong Disease Management

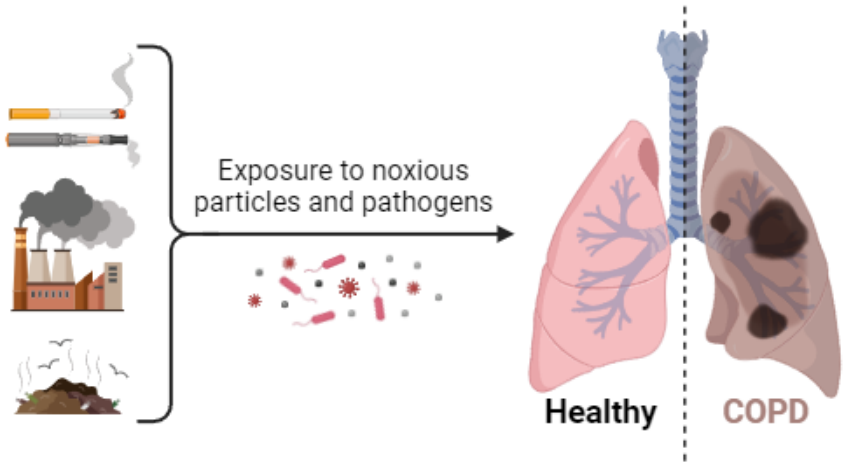
- One of the primary challenges in achieving a high penetration rate of lifelong disease management programs is the limited awareness and education among individuals with chronic conditions. Many individuals may not be aware of the existence of these programs or may lack understanding of their potential benefits. Additionally, healthcare providers may not always prioritize or emphasize the importance of these programs to their patients, further contributing to the lack of awareness.

Note：《The level of asthma control in China from a national asthma control survey》

Source: the GBD study, Literature Review，Frost & Sullivan Analysis

Overview of COPD

- Chronic obstructive pulmonary disease (COPD) is a common disease that can be prevented and treated. It is characterized by persistent respiratory symptoms and airflow restrictions, including chronic cough, sputum production, progressive dyspnea, and risk factors for COPD History of exposure (even if there are no symptoms of dyspnea). Severe comorbidities may have an impact on morbidity and mortality.



Classification

GOLD I level (mild)	• FEV_1≥80% Predicted Value
GOLD II level (moderate)	• 50%≤FEV_1<80% Predicted Value
GOLD III level (severe)	• 30%≤FEV_1<50% Predicted Value
GOLD IV (extremely severe)	• FEV1<30%Predicted Value or FEV_1<50% Predicted Value with respiratory failure

Risk Factors

- **Genetic predisposition:** The uncommon genetic disorder alpha-1-antitrypsin deficiency is the cause of some cases of COPD. Other genetic factors likely make certain smokers more susceptible to the disease.
- **Environmental exposure：** Environmental factors such as increased air pollution, tobacco smoke, occupational exposure to dusts and chemicals are frequently quoted as adjuvant factors for COPD and possible causes of the increased prevalence

- COPD mostly occurs in people more than 40 years of age. GOLD divided COPD into four stages according to severity. According to the research more than a half of the patients are in stage 1, about one-third are in stage 2 and less than 1% are in stage 4.

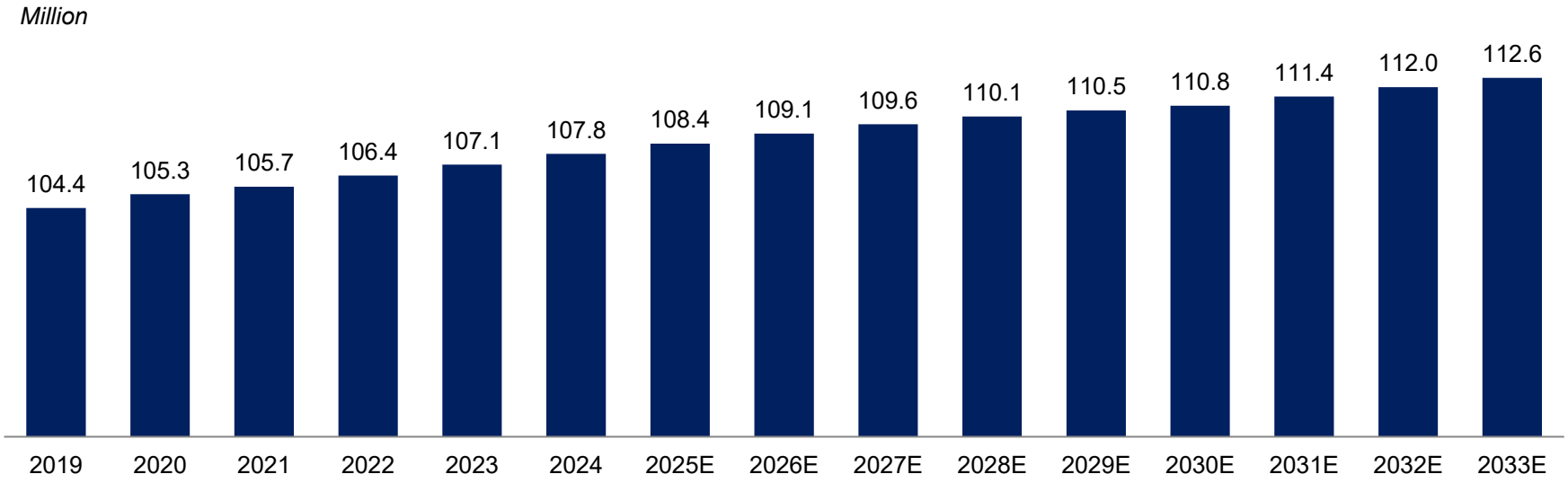
Source: Literature Review, Chinese guideline for diagnosis and treatment of allergic rhinitis (2022, revision), Frost & Sullivan Analysis

Prevalence of COPD in China, 2019-2033E

- In 2024, the number of COPD patients in China is 107.8 million. The prevalence of COPD is expected to increase in the next few years, and the number of COPD patients is expected to reach 110.1 million and 112.6 million by 2028 and 2033, representing a CAGR of 0.5% and 0.4% from 2024 to 2028 and from 2028 to 2033.

Prevalence of COPD in China, 2019-2033E

Period	CAGR
2019-2024	0.6%
2024-2028E	0.5%
2028E-2033E	0.4%

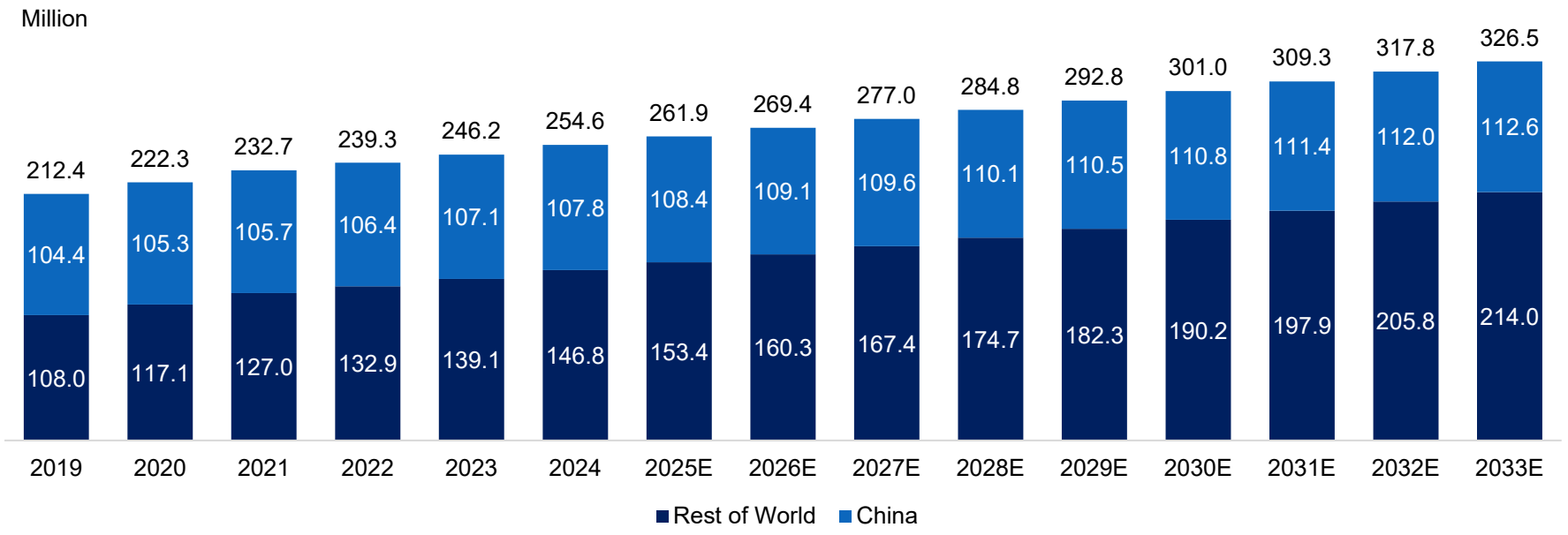


Global Prevalence of COPD, 2019-2033E

- Globally, the number of patients affected by COPD reached 254.6 million in 2024, with a CAGR of 3.7% from 2019 to 2024, and this number is forecasting to reach 326.5 million in 2033; the number of patients affected by COPD in China reached 107.8 million in 2024, with a CARG of 0.6% from 2019 to 2024 and this number is forecasting to reach 112.6 million in 2033.

Global Prevalence of COPD, 2019-2033E

CAGR	Global	China
2019-2024	3.7%	0.6%
2024-2033E	2.8%	0.5%



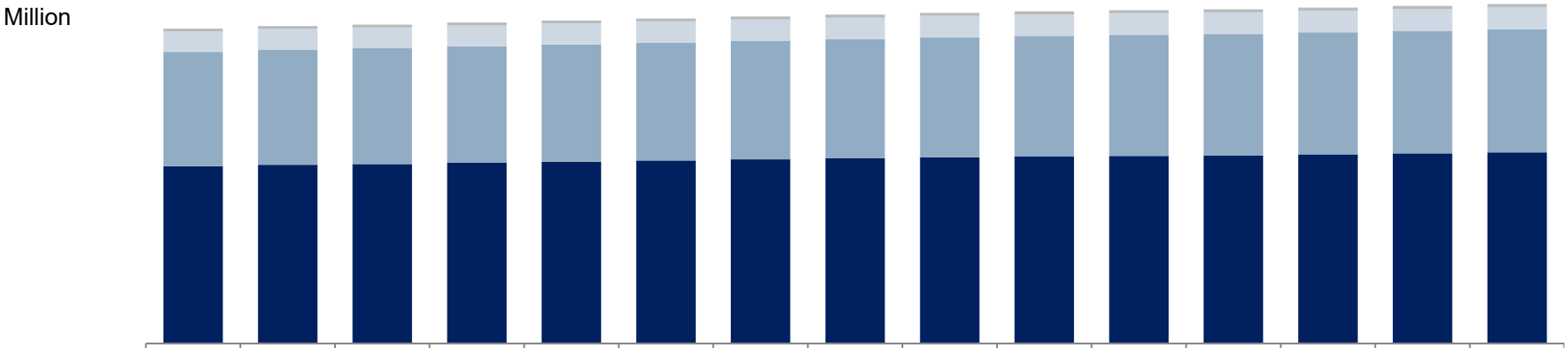
Source: Literature review, Frost & Sullivan analysis

China Prevalence of COPD Breakdown by Severity, 2019-2033E

- In 2024, the number of COPD patients in China is 107.8 million. The prevalence of COPD is expected to increase in the next few years, and the number of COPD patients is expected to reach 110.1 million and 112.6 million by 2028 and 2033, representing a CAGR of 0.6% and 0.5% from 2024 to 2028 and from 2028 to 2033.
- In 2024, prevalence distribution of COPD patients presented 60.7 million, 39.1 million, 7.0 million and 1.0 million, with GOLD stage I, II, III, IV, respectively.

China Prevalence of COPD Breakdown by Severity, 2019-2033E

CAGR	China
2019-2024	0.6%
2024-2033E	0.5%



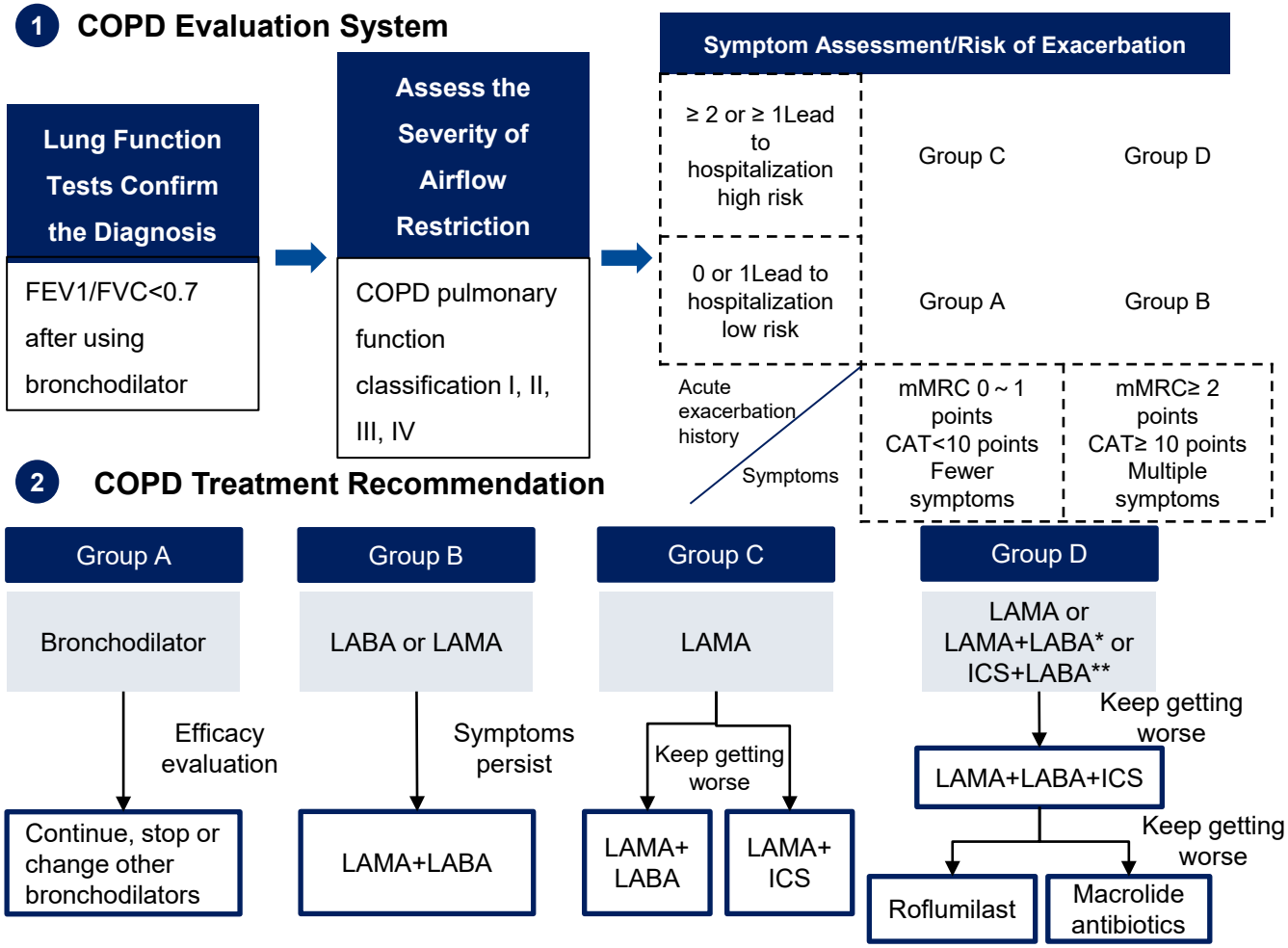
	2019	2020	2021	2022	2023	2024	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E
Total	104.4	105.3	105.7	106.4	107.1	107.8	108.4	109.1	109.6	110.1	110.5	110.8	111.4	112.0	112.6
GOLD IV	0.9	0.9	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
GOLD III	6.8	6.8	6.9	6.9	7.0	7.0	7.0	7.1	7.1	7.2	7.2	7.2	7.2	7.3	7.3
GOLD II	37.9	38.2	38.4	38.6	38.9	39.1	39.4	39.6	39.8	40.0	40.1	40.2	40.4	40.6	40.9
GOLD I	58.8	59.3	59.5	59.9	60.3	60.7	61.0	61.4	61.7	62.0	62.2	62.4	62.7	63.0	63.4

Source: Literature review, Frost & Sullivan analysis

COPD ABCD Diagnostic System and Treatment Recommendation

Key Information

- According to different symptoms and degree of exacerbation history, COPD drug treatment can be divided into 4 categories. COPD treatment is based on bronchodilators. Bronchodilators cause airway dilation by changing the tension of airway smooth muscles. Regular use can effectively prevent or reduce the symptoms of COPD. They mainly include β2 receptor agonists and anticholinergic antagonists.
- The initial treatment of COPD is usually LABA and LAMA. For patients with moderate to very severe COPD, ICS combined with LABA can improve lung function and health and reduce acute exacerbations more effectively than a single agent. Triple therapy improves symptoms and reduces risk better than single medication.



Note: * The clinical symptoms are obvious, CAT score> 20 points; ** If EOS ≥300μiLAMA: long-acting cholinergic drug; LABA: long-acting β2 receptor agonist; ICS: inhaled glucocorticoid; CAT: COPD assessment test; EOS: eosinophils; mMRC: modified version of British Medical Research Council Breathing Questionnaire
GLOBAL STRATEGY FOR PREVENTION, DIAGNOSIS AND MANAGEMENT OF COPD: 2024 Report merged C and D group into a single group termed E to highlight the clinical relevance of exacerbations.

Source: Guidelines for the diagnosis and management of chronic obstructive pulmonary disease(revised version 2021), Frost & Sullivan Analysis

COPD ABE Diagnostic System and Treatment Recommendation

- The main treatment goals are to reduce symptoms and future risk of exacerbations. The management strategy of stable COPD should be predominantly based on the assessment of symptoms and the history of exacerbations. Pharmacotherapy can reduce COPD symptoms, reduce the frequency and severity of exacerbations, and improve health status and exercise tolerance. Data suggest beneficial effects onrates of lung function decline and mortality.

Diagnostic System

Spirometrically Confirmed Diagnosis

Post-bronchodilator FEV1/FVC<0.7

Assessment of Airflow Obstruction

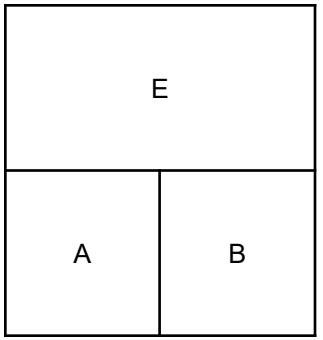
GRADE	FEV1 (% predicted)
GOLD 1	≥80
GOLD 2	50-79
GOLD 3	30-49
GOLD 4	<30

Assessment of Symptoms/risk of Exacerbations

Exacerbation History (per year)

> 2 moderate exacerbations or >1 leading to hospitalization

0 or 1 moderate exacerbations (not leading to hospitalization)



Pharmacological Treatment

Group	Initial Pharmacological Treatment	Follow-up Pharmacological Treatment
A	A bronchodilator	Dyspnea: LABA or LAMA or LABA+LAMA Exacerbations: LABA or LAMA or LABA+LAMA or LABA+LAMA+ICS
B	LABA+LAMA	
E	LABA+LAMA Consider LABA+LAMA+ICS if blood eos ≥ 300	

Non-Pharmacological Treatment

Group	Essential	Recommended	Depending on Local Guidelines
A	Smoking cessation	Physical Activity	Vaccinations such as influenza, COVID-19, RSV and so on
B and E	Smoking cessation Pulmonary rehabilitation		

Source: Guidelines for the diagnosis and management of chronic obstructive pulmonary disease(revised version 2021), Global Initiative for COPD (revised version 2024), Frost & Sullivan Analysis

Commonly Used Maintenance Medications in COPD

Key Information

- The drug treatment of chronic obstructive pulmonary disease (COPD) is mainly used to relieve symptoms, reduce the frequency and severity of disease deterioration, and improve exercise endurance and health. So far, there is no conclusive clinical trial evidence that existing drugs can adjust the long-term decline in lung function.
- There are many types of drugs commonly used to treat chronic obstructive pulmonary disease, and the choice of each type of drug depends on the availability, cost, and side effects of the drug. Because the relationship between the severity of symptoms, airflow limitation, and severity of exacerbation may vary between patients, each treatment plan needs to be individualized.
- There are four common Inhalation Formulations: SABA, LABA, SAMA, and LAMA, and there are different device types for each drug.

Drug Name	Aerosol	Dry Powder Inhaler	Soft Mist Inhaler	Nebulized Inhaler	Side Effect
β − 2 receptor antagonist: short − term medication (SABA)					
Fenoterol	√			√	• Induces a patient's heart rate disturbance • Induced hypokalemia • Withdrawal syndrome: anxiety, gastrointestinal reactions, etc.; • severely can lead to increased blood pressure, tachycardia, angina pectoris
Levalbuterol	√			√	
Salbutamol	√	√		√	
Terbutaline		√			
β − 2 receptor antagonist: long − term medication (LABA)					
Formoterol Tartrate				√	
Formoterol		√		√	
Indacaterol		√			
Odatro			√		
Salmeterol					
ts: short-term medication (SAMA)					
Anticholinergic agents: short-term medication (SAMA)					
Ipratropium Bromide	√			√	
Oxitropium Bromide	√				
ıg-term medicati					
Anticholinergics: Long-term medication (LAMA)					• Inhaled anticholinergic drugs are poorly absorbed, which limits the effects of drugs • Dry mouth and urinary system symptoms • Wearing a mask and inhaling causes the solution to come into contact with the eyes and induce glaucoma
Aclidinium Bromide	√	√			
Glycopyrrolate		√			
Tiotropium Bromide	√	√	√		
Umeclidinium Bromide		√			
Refennasine				√	

Source: Guidelines for the diagnosis and management of chronic obstructive pulmonary disease(revised version 2021), Frost & Sullivan Analysis

Commonly-used Maintenance Drugs for COPD

Key Information

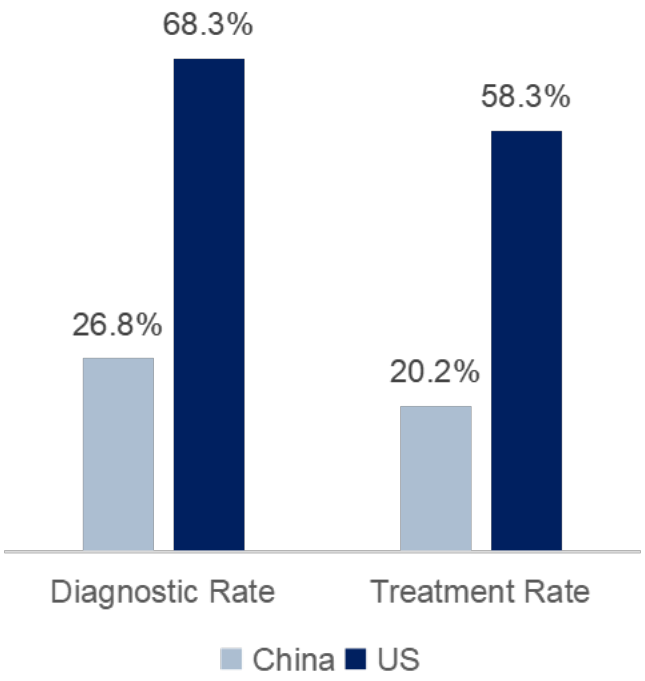
- According to the type of Inhalation Formulation, the combination medication can be divided into four categories: SABA/SAMA, LABA/LAMA, LABA/LAMA/ICS, LABA/ICS
- Combination therapy in inhalation therapy can be achieved by various methods, which can improve lung function, increase the degree of bronchodilators, and reduce the risk of side effects. At the same time, it will also improve FEV1, and improve the symptoms and health of COPD patients.

Drug Name	Aerosol	Dry Powder Inhaler	Soft Mist Inhaler	Nebulized Inhaler	Side Effect
Short-acting β-2 receptor antagonist combined with anticholinergic agent (SABA/SAMA)					• Short maintenance time, causing symptoms such as dry mouth
Fenoterol/Ipratropium Bromide			√	√	
Salbutamol/Ipratropium Bromide	√		√	√	
Long-acting β-2 receptor antagonist combined with anticholinergics (LABA/LAMA)					• Slow onset, cannot be used as an acute drug • Anticholinergic agents can cause symptoms such as dry mouth
Formoterol/Aclidinium Bromide					
Formoterol/Glycopyrrolate	√				
Indacaterol/Glycopyrrolate		√			
Vilanterol/Umeclidinium bromide		√			
Odaterol/Tiotropium Bromide			√		
Triple combination (LABA/LAMA/ICS)					• Not obvious for patients with worsening condition
Fluticasone/Umetium Bromide/ Veranterol		√			
Beclomethasone/Formoterol/ Glycopyrrolate	√				
Long-acting β-2 receptor antagonist combined with corticosteroids (LABA/ICS)					• ICS has a withdrawal effect, FEV1 decreases • Corticosteroids can cause muscle weakness and decreased muscle function
Formoterol/beclomethasone					
Formoterol/Budesonide	√	√			
Formoterol/Mometasone	√				
Salmeterol/Fluticasone	√				
Vilanterol/Fluticasone Furoate	√	√			
		√			

Source: Guidelines for the diagnosis and management of chronic obstructive pulmonary disease(revised version 2021), Frost & Sullivan Analysis

COPD Unmet Medical Needs

Current Status of COPD Diagnosis and Treatment in China and US



Unmet medical needs for COPD

Vast disease burden but low diagnosis rate

- Globally, the COPD-related age-standardized incidence rate decreased from 216.48/100,000 in 1990 to 200.49/100,000 in 2019. But the number of new cases increased from 8,722,966 in 1990 to 16,214,828 in 2019. The number of deaths increased from 2,520,219 in 1990 to 3,280,636 in 2019, and the number of DALYs increased from 59,241,939 in 1990 to 74,432,367 in 2019. However, the diagnosis rate of COPD in China is only 26.8%, which refers to vast unmet medical need in China.

Low adherence of long-term treatment

- Individuals suffering from COPD necessitate ongoing management, with standardized long-term inhalation therapy forming a crucial component of treatment for those with stable COPD. Nevertheless, a notable number of patients struggle with adhering to their medication regimen, as evidenced by self-adjusting dosage, interrupting medication, or experiencing adverse outcomes due to non-standardized inhalation techniques. The ability to take medication appropriately is important. Easy to use, low resistance devices may help patients take their medication and achieve good drug deposition.

Risk factors are difficult to control

- Smoking and air pollution are the two main risk factors for the development of COPD in China. In 2018, the smoking rate of people aged 15 years old and above in China was 26.6%, of which is 50.5% for men and 2.1% for women.

Low Penetration Rate of Lifelong Disease Management

- The management of patient disease encompasses seven objectives: to halt disease advancement, to relieve symptoms, to enhance patient capacity for exercise, to enhance overall health, to prevent and address complications, to manage exacerbations provoked by treatment, and to diminish mortality. Thus far, drug therapy alone has been inadequate in fully managing COPD symptoms or significantly impacting disease progression. Moreover, individuals with COPD should adopt a lifestyle involving heightened physical activity, cessation of smoking, limited alcohol intake, and a balanced calorie consumption.

Source: the GBD study, Frost & Sullivan Analysis

Overview of Allergic Rhinitis (AR)

- Allergic rhinitis is an IgE-mediated inflammatory disease of the nasal mucosa triggered by exposure to allergens and is a disease of the upper respiratory tract (i.e., above the larynx).

Symptoms

- The **typical symptoms** of AR are paroxysmal sneezing, watery nasal discharge, nasal itching, and nasal congestion; it may be accompanied by **ocular symptoms**, including eye itching, tearing, red eyes, and burning sensation, which are more common in patients with hay fever allergies.
- Patients with AR may be **complicated with bronchial asthma**. In addition to nasal symptoms, they may also be accompanied by **pulmonary symptoms** such as wheezing, coughing, shortness of breath, and chest tightness.

Classification

- Allergic rhinitis was previously subdivided, based on time of exposure, into **seasonal, perennial, and occupational.**
- The recent classification of allergic rhinitis as suggested by ARIA (Allergic Rhinitis and its Impact on Asthma) guidelines is based on：
  - **Duration**: “intermittent” or “persistent” disease
  - **Severity of symptoms and Quality of life**: “mild” or “moderate-severe”

Complications

- The Allergic rhinitis is a **major airway disease**, which causes **morbidity** and significantly **impairs** a patient’s ability to function and their quality of life. It is also associated with other conditions:
  - Asthma
  - Anosmia
  - nasal polyps
  - Sinusitis
  - dental malocclusion
  - Otitis media
  - Lower airway infection

Risk Factors

- **Genetic predisposition:** A genetic background in terms of a family history of atopic disease has been the strongest risk factor for the development of allergic symptoms.
- **Environmental exposure：** Environmental factors such as increased air pollution, changed lifestyle, and decrease in bacterial/viral infection are frequently quoted as adjuvant factors for allergic sensitization and possible causes of the increased prevalence

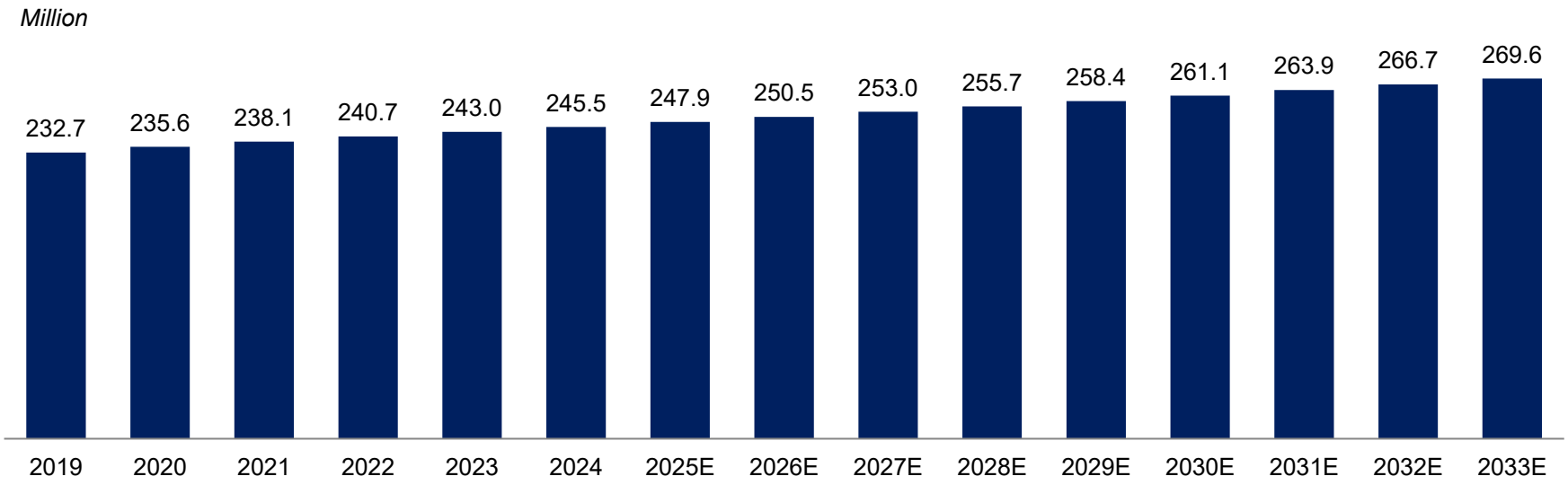
Source: Literature Review, Chinese guideline for diagnosis and treatment of allergic rhinitis (2022, revision), Frost & Sullivan Analysis

Prevalence of AR in China, 2019-2033E

- In 2024, the number of AR patients in China is 245.5 million. The prevalence of AR is expected to increase in the next few years, and the number of AR patients is expected to reach 255.7 million and 269.6 million by 2028 and 2033, representing a CAGR of 1.0% and 1.1% from 2024 to 2028 and from 2028 to 2033.

Prevalence of AR in China, 2019-2033E

Period	CAGR
2019-2024	1.1%
2024-2028E	1.0%
2028E-2033E	1.1%

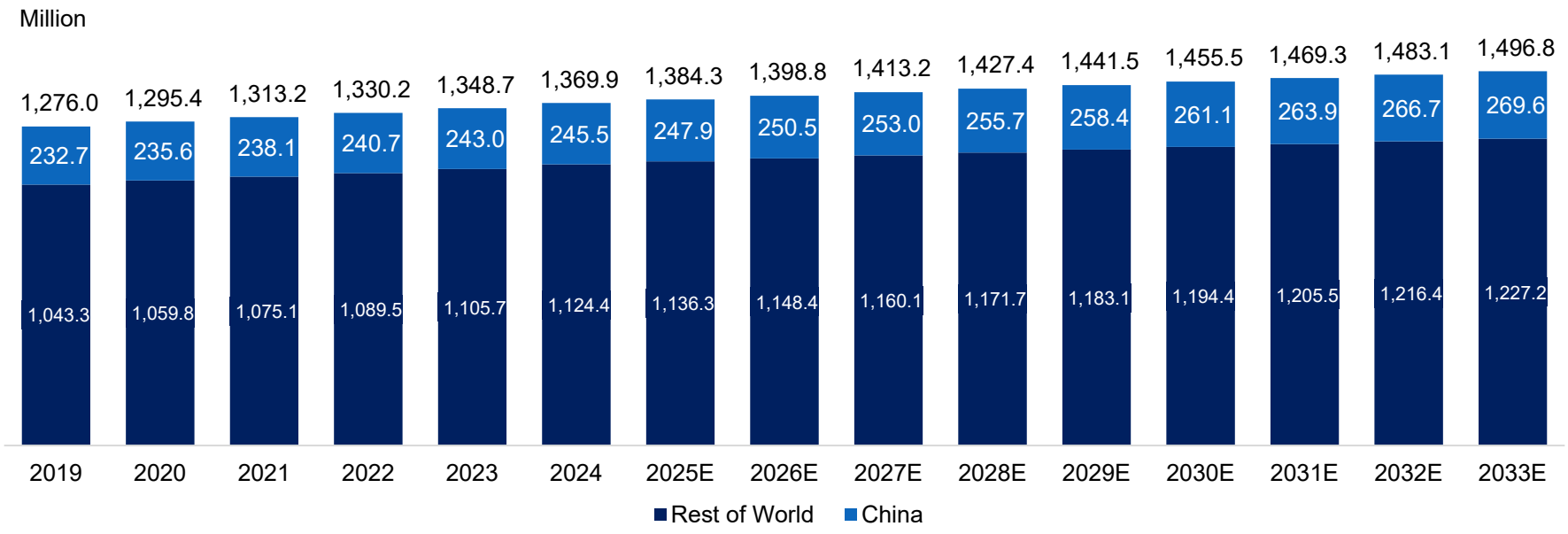


Global Prevalence of Allergic Rhinitis, 2019-2033E

- Globally, the number of patients affected by allergic rhinitis reached 1,369.9 million in 2024, with a CAGR of 1.4% from 2019 to 2024, and this number is forecasting to reach 1,496.8 million in 2033.

Global Prevalence of Allergic Rhinitis, 2019-2033E

CAGR	Global	China
2019-2024	1.4%	1.1%
2024-2033E	1.0%	1.0%



Source: Literature review, Frost & Sullivan analysis

Overview of Allergic Rhinitis

Key Information

- Allergic rhinitis, is an IgE-mediated inflammation of the nasal mucosa that is dominated by eosinophils after nasal mucosa ‘s exposure to the inhaled allergens, and is a type I hypersensitivity. Clinical symptoms include nasal congestion, clear nasal drip, paroxysmal sneezing, nasal itching, etc. It may be accompanied by symptoms on eyes such as itchy eyes and lacrimation, etc. The main signs are pale and swollen nasal mucosa, edema of the inferior nasal concha, and watery nasal discharge. Some allergic rhinitis is combined with asthma, chronic cough, and other lower airway diseases.
- The current global incidence of allergic rhinitis is increasing every year, and the influence of topography, climate as well as the rapid urbanization has all accelerated the prevalence of allergic rhinitis in China. Allergic rhinitis has increased the health economics burden in China and has had a significant negative impact on patients' sleep, social life, school and work, increasing anxiety and depression.

1 Allergic rhinitis classification

Classification by allergen	• Seasonal: airborne allergens (pollen and fungi) are the most common allergens • Perennial: symptoms can occur throughout the year and allergens include dust mites, animal dander, etc
Classification by frequency of symptoms	• Intermittent (<4 days/week or <4 weeks/year) • Persistent (≥4 days/week and ≥4 weeks/year)
Classification by severity	• Mild: Symptoms do not affect patient's daily life, work and study • Moderately to severe: symptoms seriously affect patient's daily life

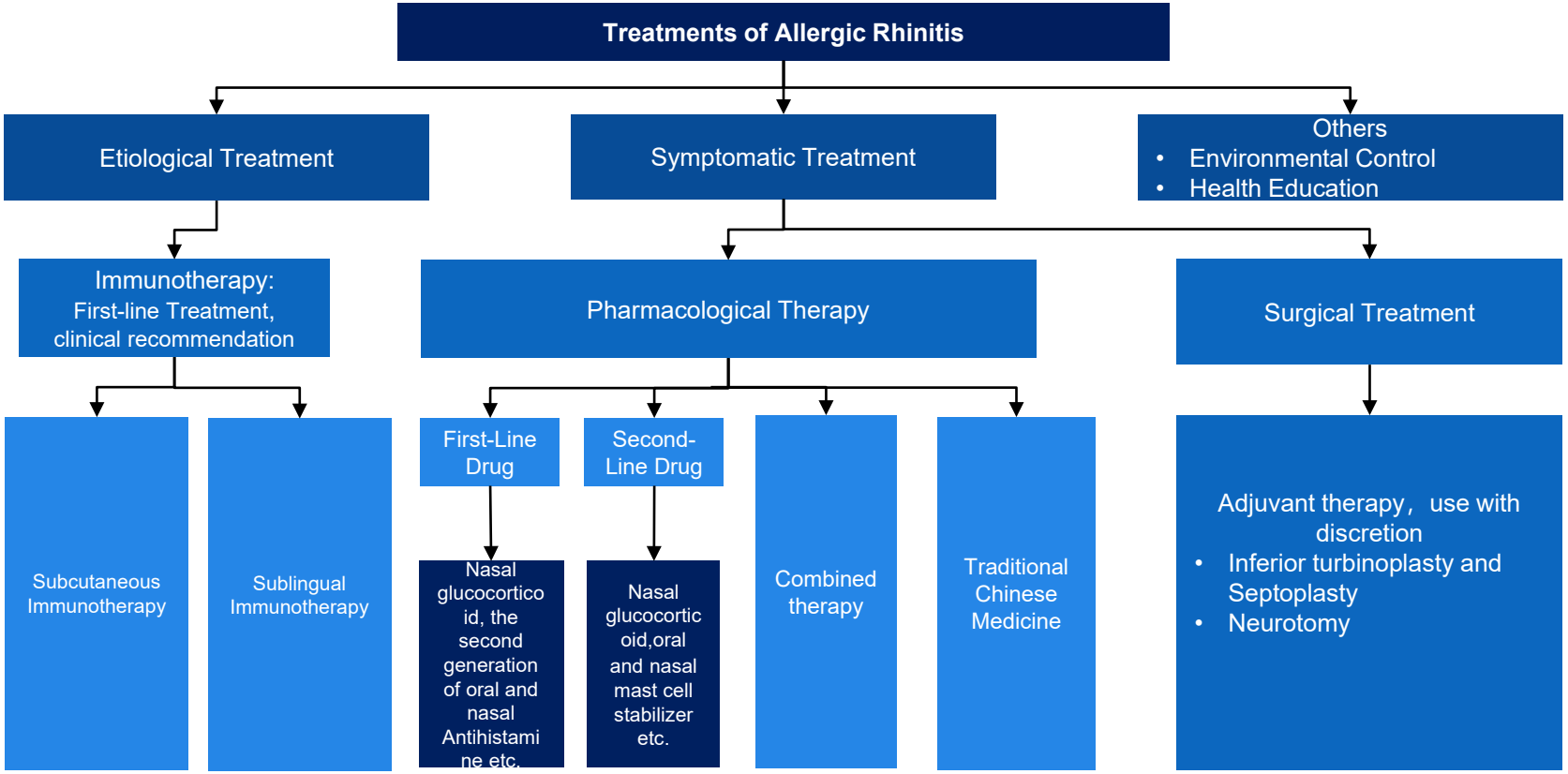
2 Allergic rhinitis diagnosis

Symptom observation	• Symptoms: runny nose, nasal obstruction, nasal itching, sneezing, with or without eye symptoms • Disease persistence: persistent/intermittent
Clinical Tests	• Laboratory tests: positive for SPT and/or serum sIgE antibodies Airborne allergens nasal irritation test: positive

Source: Literature Review, Frost & Sullivan analysis

Treatment Paradigm of Allergic Rhinitis

- The treatment principle of allergic rhinitis include the environmental control, pharmacological therapy, immunotherapy and health education. Besides, the treatments of AR can be identified with etiological treatment and symptomatic treatment. The former one includes immunotherapy, and the latter one includes pharmacological therapy and surgical treatment. Common adverse effects of current main treatments are nasal dryness and tingling caused by pharmacological therapy, and redness and swelling at the injection site caused by immunotherapy.
- Nasal sprays are recommended as first-line therapy for allergic rhinitis (AR) by providing direct delivery of medication to the nasal mucosa, reducing the potential for systemic adverse effects, decreasing burden of disease, and improving quality of life.



Note: Bentrio is a thixotropic gel emulsion that is sprayed into the nostrils via a standard nasal spray applicator, which create a barrier between allergens/viruses and the nasal mucosa. creates a controlled environment for allergens/viruses exposure.

Source: Chinese Guideline for Diagnosis and Treatment of Allergic Rhinitis (2022, revision), Frost & Sullivan Analysis

Medication Treatment Diagram of Allergic Rhinitis in China

- Intranasal corticosteroids are the gold standard in the pharmacological therapy of AR.

Pharmacotherapy	MOA	Medication Options	Routine of Administration	Recommended Level
Corticosteroids	Significantly inhibit recruitment of basophils, eosinophils, neutrophils and mononuclear cells to nasal secretions in nasal allergen challenge models.	Mometasone, Fluticasone, Budesonide	Nasal	First-line
			Oral	Second-line
Antihistamines	Inhibit histamine-induced inflammation.	Oral Antihistamine: Loratadine, Desloratadine, Cetirizine, Mizolastine, etc. Intranasal spray antihistamines: Azelastine, Levocabastin	Nasal	First-line
			Oral	First-line
Leukotriene receptor antagonists	Act by attracting eosinophils, increasing microvascular leakage and elevating mucous gland secretion.	Montelukast	Oral	First-line
Mast cell stabilizers	Stabilize the membrane of mast cells and basophils to prevent degranulation, thereby inhibiting the release of a variety of proinflammatory mediators.	Sodium cromoglicate, Tranilast	Nasal	Second-line
			Oral	Second-line
Anticholinergics	Inhibit both watery secretion of nasal glands and vasodilatation of airway blood vessels.	Ipratropium Bromide	Nasal	Second-line
Decongestants	Constrict blood vessels in the nasal mucosa and improve nasal patency, thus relieving the symptom of nasal obstruction in patients with AR.	Pseudoephedrine, Naphazoline	Nasal	Second-line

Source: Literature Review, Frost & Sullivan analysis

Medication Recommendation for Allergic Rhinitis

Key Information

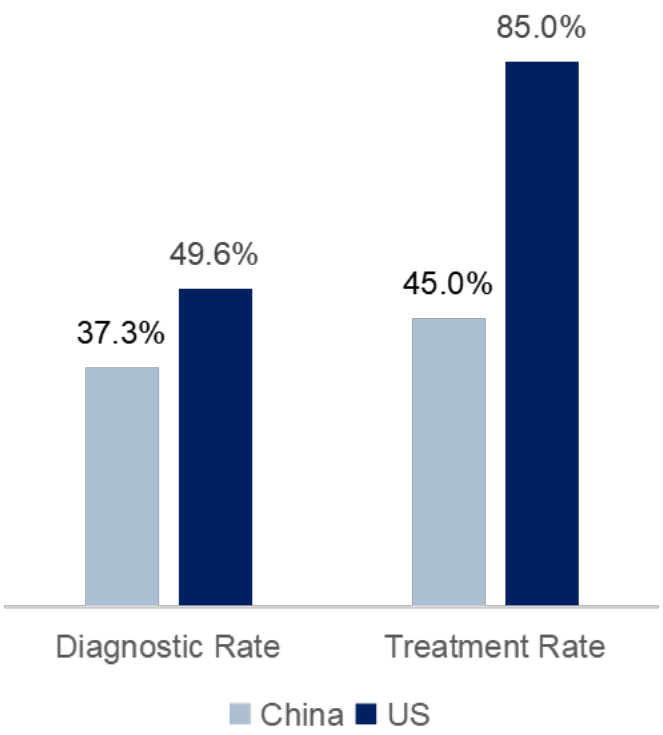
- Principles of drug therapy for allergic rhinitis, such as inhaled glucocorticoids (ICS) + nasal glucocorticoids (INCS) or combined ICS/long-acting β2 adrenoceptor agonists (LABA) + INCS interventions, or options for upper-lower airway co-interventions such as leukotriene receptor antagonists, anti-IgE monoclonal antibodies, etc.
- H1-Antihistamines are characterized by their rapid onset of action. The duration of action is long and could significantly relieve rhinitis symptoms. Nasal antihistamines + nasal glucocorticosteroids improve the patient's nasal symptoms better than single drug therapy.
- Nasal glucocorticosteroids are safe and well tolerated, with strong anti-inflammatory effects and significant improvement in nasal symptoms. It is the top choice of drug especially for mild and moderate-to-severe patients.

	Medication classification	Representative Medication
First-line medication	H1-Antihistamine	Oral Antihistamine: Loratadine, Desloratadine, Cetirizine, Mizolastine, etc. Intranasal spray antihistamines: Azelastine, Levocabastin
	Leukotriene receptor antagonists	Montelukast
	Nasal glucocorticoid	Mometasone, Fluticasone, Budesonide
Second-line medication	Mast cell stabilizer	Sodium cromoglicate, Tranilast
	Nasal decongestant	Pseudoephedrine, Naphazoline
	Nasal anticholinergic drugs	Ipratropium Bromide
	Nasal irrigation	Helps to remove thick nasal secretions and moisturize the nasal mucosa
Other treatment	Desensitization	Immunotherapy specifically targeting IgE-mediated diseases with specific allergen-induced allergic reactions
	Surgical treatment and avoidance of exposure to allergens	Surgery contains neurotomy and endoscopic nasocular surgery

Source: Literature Review, Frost & Sullivan analysis

Allergic Rhinitis Unmet Medical Needs

Current Status of Allergic Rhinitis Diagnosis and Treatment in China and US



Source: the GBD study, Frost & Sullivan Analysis

Unmet medical needs for Allergic Rhinitis

Urbanization leads to an increase in allergic rhinitis cases

- Research evidence demonstrates that genetic and environmental factors play an important role in the etiology of allergic rhinitis. Even a slight increase in daily concentrations of air pollutants can cause adverse health effects.
- China is undergoing rapid urbanization and the number of motor vehicles are rising, posing a great threat to the disease management of patients with allergic rhinitis.

Symptoms are difficult to cure, with the majority of patients are children

- Allergic rhinitis is a chronic disease. Current treatment options are mainly symptomatic and no fully cure treatment available.
- According to numerous studies, allergic rhinitis patient group is predominantly child, which poses a long-lasting difficulty for the management of patient's condition.

Patients with mild symptoms do not actively seek medical care

- Due to the low awareness of allergic rhinitis and the fact that allergic rhinitis often occurs in the presence of allergens, many patients only seek medical treatment when complications occur, such as asthma or colds.
- Some patients mistake allergic rhinitis for cold and take medication themselves at home.

Low Penetration Rate of Lifelong Disease Management

Surveys indicate that a significant number of patients do not receive medical care for their condition and/or are not diagnosed with the disease. This includes patients often stopping medication on their own, and the most common reason why patients stop treatment is the lack of lasting symptom relief. Asthma, sinusitis, nasal polyposis, and sleep apnea are common comorbidities that are often unrecognized components of the total disease burden. Therefore, necessary and adequate disease awareness education and patient self-management are still needed. At the same time, disease management needs to determine the control and severity of the disease and guide corresponding drug control or immunotherapy according to its type and severity.

Overview of Idiopathic Pulmonary Fibrosis

- Interstitial lung diseases (ILDs) refer to a heterogeneous and complex group of conditions characterized by inflammation, fibrosis, or both, in the interstitium of the lungs. Increasing fibrosis, worsening respiratory symptoms, and decline in pulmonary function are each signs of progression that, alone or in combination, can indicate progressive pulmonary fibrosis (PPF), formerly progressive fibrosing interstitial lung disease (ILD).
- Idiopathic pulmonary fibrosis (IPF) is a chronic condition in which scar tissue build up in lungs from unknown causes. This makes breathing increasingly difficult as lungs lose elasticity. IPF typically affects elder people, most commonly occurring in people above 65 years of age and extremely rarely occur in people under 50.
- IPF is a very deadly disease, with an average overall survival of approximately only 4 years upon initial diagnosis. Various treatments can help reduce the rate of progression of IPS, however there's currently no treatment that can stop or reverse the late stage scarring of the lungs. The five-year survival rate estimated at a range from 20% to 40%, even lower than those observed in certain types of cancer. IPF is one of the most common rare diseases.

Risk Factors of IPF	Symptoms of IPF	Treatment of IPF
Exposure to metal and wood dust	Shortness of breath	Lung Transplant
Smoking	Persistent dry cough	Medication to slow fibrosis
Gastro-esophageal reflux disease (GERD)	Tiredness	Medication to improve symptoms
Viral infections	Loss of appetite and weight loss	Oxygen therapy
Family history of IPF	Rounded and swollen fingertips (clubbed fingers)	Pulmonary rehabilitation

Source: Literature Review, Frost & Sullivan Analysis

Treatment Paradigm of IPF

- Treatment considerations should include both pharmacological (nintedanib and pirfenidone) and nonpharmacological (oxygen supplementation and/or pulmonary rehabilitation) therapies. Patients should also be evaluated and treated for existing comorbidities, including pulmonary hypertension, gastroesophageal reflux, obstructive sleep apnea, and lung cancer.
- While pirfenidone and nintedanib represent significant advancements in slowing disease progression, there is an urgent need for more effective therapies that address the underlying mechanisms of fibrosis.

Treatment of IPF

Pharmacological
- Nintedanib
- Pirfenidone

Non-Pharmacological
- Smoking cessation
- Oxygen supplementation
- Pulmonary rehabilitation
- Mechanical ventilation
- Lung transplantation if increased risk of mortality

Monitor for Disease Progression

- Consider pulmonary function testing and the 6-minute-walk test every 4-6 months or sooner if clinically indicated
- Consider annual HRCT if there is clinical suspicion of worsening or risk of lung cancer
- Consider an HRCT if there is concern for an acute exacerbation
- Consider a CT pulmonary angiogram if there is a clinical concern for pulmonary embolism

Acute Exacerbation

- Corticosteroids

Evaluate and list for lung transplantation

Clinical trial for possible enrollment is recommended for patients at all stages.

Note: HRCT: High-Resolution Computed Tomography

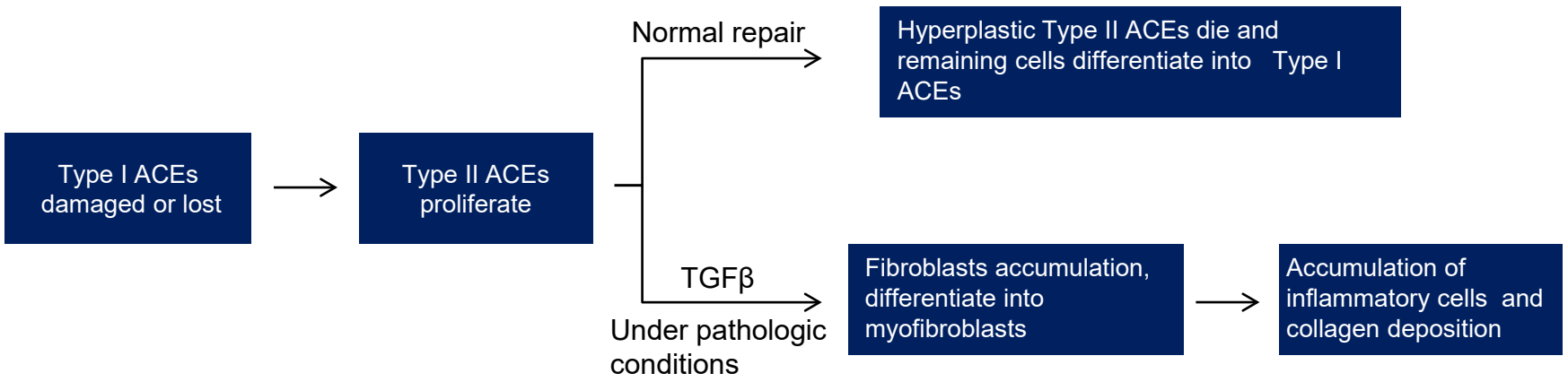
Pathogenesis of Idiopathic Pulmonary Fibrosis

- Idiopathic pulmonary fibrosis(IPF) is defined as a specific form of chronic, progressive fibrosing interstitial pneumonia of unknown cause, occurring primarily in older adults, limited to the lungs, and associated with the histopathologic and radiologic pattern of usual interstitial pneumonia(UIP).

Pathogenesis

Despite decades of intense research and exploration of numerous potential causes, the etiology and precise pathobiology of IPF remains unknown. IPF is believed to be the result of an aberrant wound healing process involving abnormal and excessive deposition of collagen(fibrosis) in the pulmonary interstitium with minimal associated inflammation.

Hypothesized pathogenetic model for IPF



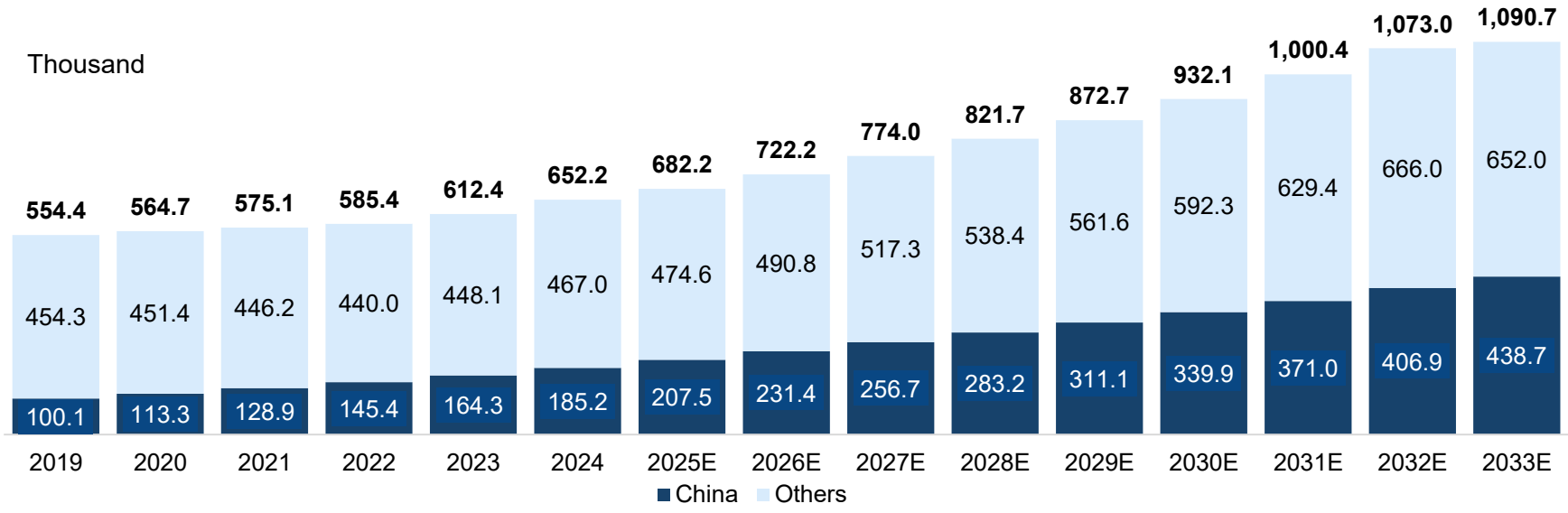
Source: Literature Review, Frost & Sullivan Analysis

Global and China Incidence of IPF, 2019-2033E

- The incidence of IPF in China increased from 100.1 thousand in 2019 to 185.2 thousand in 2024, with a CAGR of 13.1%, It is predicted that the number will continue to increase, reaching 283.2 thousand in 2028, with a CAGR of 11.2% from 2024 to 2028, 438.7 thousand in 2033 with a CAGR of 9.1% from 2028 to 2033.
- The global incidence of IPF increased from 554.4 thousand in 2019 to 652.2 thousand in 2024, with a CAGR of 3.3%. It is predicted that the number will continue to increase, reaching 821.7 thousand in 2028, with a CAGR of 5.9% from 2024 to 2028, 1,090.7 thousand in 2033 with a CAGR of 5.8% from 2028 to 2033.

Incidence of IPF, 2019-2033E

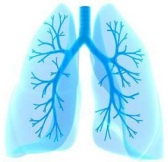
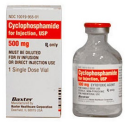
Period	Global	China
2019-2024	3.3%	13.1%
2024-2028E	5.9%	11.2%
2028E-2033E	5.8%	9.1%



Source: Frost & Sullivan Analysis

Treatment of Idiopathic Pulmonary Fibrosis

Idiopathic pulmonary fibrosis (IPF) is a chronic and progressive lung disease characterized by the scarring of lung tissue. The exact cause of IPF is unknown, which makes it difficult to treat. the treatment of idiopathic pulmonary fibrosis involves a multidisciplinary approach that addresses the various aspects of the disease, including symptom management, physical rehabilitation, and medical interventions. While there is currently no cure for IPF, these treatment options can help improve the prognosis and quality of life for patients living with this challenging condition. Ongoing research into new therapies and interventions offers hope for further advancements in the management of IPF in the future.

Lung Transplant	Lung transplantation is an established therapeutic option for chronic lung diseases. Lung transplantation has been shown to be very effective for patients with IPF, the 5 year survival rate of IPF patients who received lung transplants is 50% – 55%, compared to 20% in general. However, lung transplantation is a major operation and is only recommended for younger patients, donor lungs are also quite rare and patients may have to stay of the waiting list for a long time.	
Medication to Slow Fibrosis	Currently only two drugs are approved globally for treatment of IPF, Esbriet (Pirfenidone) and Ofev (Nintedanib). Both have been clinically shown to slow down the development of scar tissue in lungs of IPF patients. However, unfortunately, both of them have not been shown sufficient antifibrotic activity to reverse the fibrotic progression, and side effects, such as GI intolerance, phototoxicity and liver toxicity, which could leas to discontinuation of the treatment	
Medication to Improve Symptoms	In addition to medication that slow scar tissue formation, doctors also prescribe medicine that treat symptoms and risk factors of IPF: • Corticosteroids (e.g. Cortisone, Prednisone) and other immunosuppressants (e.g. Cyclophosphamide, azathioprine) to reduce inflammation. • Proton pump inhibitors to treat gastrointestinal reflux disease (GERD) , which effects 90% of IPF patients.	
Oxygen Therapy	To compensate for the increasing difficulty of breathing, IPF patients can maintain blood oxygen levels by breathing concentrated oxygen. IPF patient qualifies for oxygen therapy if the oxygen saturation falls below 88% at rest.	
Pulmonary Rehabilitation	People with idiopathic pulmonary fibrosis (IPF) and other types of PF can experience increasing shortness of breath and cough. These symptoms may lead to a progressive decline in physical activities and social isolation, and worsening breathlessness, fatigue, and mood disorders including depression and anxiety. Pulmonary rehabilitation has been found to improve physical function, breathlessness (dyspnea), mood, and quality of life in people with IPF and other types of PF.	

Source: Literature Review, Frost & Sullivan Analysis

Global Competitive Landscape of IPF inhalation formulation

- Across the globe and in China, there is no approved IPF inhalation drug.

Global IPF Inhalants at Clincal Stage

Dosage Form	Generic Name	Drug Name	Manufacturer	Clinical Stage	Indications	First Posted Date
Nebulization	Treprostinil	RIN-PF-303	United Therapeutics	Phase III	IPF	2021-1-14
	Treprostinil	RIN-PF-301	United Therapeutics	Phase III		2022-2-25
	/	ARO-MMP7	Arrowhead Pharmaceuticals	Phase I/II		2022-9-13
	/	TRK-250	Toray Industries	Phase I		2018-11-1
	/	PRS-220	Pieris Australia	Phase I		2022-7-26
	/	AGMB-447	Agomab Spain	Phase I		2023-12-26
DPI	/	GB0139	Galecto Biotech	Phase II		2019-2-6
	/	LTI-03	Lung Therapeutics	Phase I		2020-1-18
	/	RSN0402	Shenzhen Resproly Biopharmaceutical	Phase I		2024-7-1

*This table was last updated on Sep 16th , 2025

Source：FDA, EMA, ClinicalTrials, EU CTR, Annual Report, Frost & Sullivan Analysis

China Competitive Landscape of IPF inhalation formulation

IPF Inhalation Formulation at Clinical Stage in China

Dosage Form	Manufacturer	Clinical Stage	Indication	First Posted Date/Clinical Trial Approval Date
Nebulization	Joincare Haibin Pharmaceutical	Phase I	IPF	2022-11-15
	Chengdu Huitai Biopharmaceutical	Phase I		2024-06-11
	Chengdu Beite Xinqi Biomedical	Phase I		2024-06-27
	Zhejiang Jinhua Conba BioPharm	Clinical Approval		2024-05-15
Aerosol	Shanghai Synvida Biotechnology	Phase II		2025-07-16

*This table was last updated on Sep 16th , 2025

Source：FDA, EMA, ClinicalTrials, EU CTR, Annual Report, Frost & Sullivan Analysis

Overview of Pulmonary Hypertension

- Pulmonary hypertension (PH) is a pathophysiological disorder that may involve multiple clinical conditions and may be associated with a variety of cardiovascular and respiratory diseases. The complexity of managing PH requires a multifaceted, holistic, and multidisciplinary approach, with active involvement of patients with PH in partnership with clinicians. Pulmonary hypertension is defined by a mean pulmonary arterial pressure > 20 mmHg. PH-ILD stands for pulmonary hypertension associated with ILD.
- Pulmonary hypertension is a major global health issue. All age groups are affected. Due to the presence of cardiac and pulmonary cases of PH, prevalence is higher in individuals aged > 65 years. Significant unmet needs in PAH treatments remain due to variable patient responses, side effects, and lack of a cure.

Early → **Late**

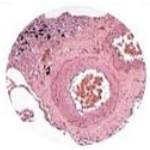
- Dyspnoea on exertion
- Fatigue and rapid exhaustion
- Dyspnoea when bending forward
- Palpitations
- Haemoptysis
- Exercise-induced abdominal distension and nausea
- Weight gain due to fluid retention
- Syncope (during or shortly after physical exertion)

- Rare symptoms due to pulmonary artery dilation
- Exertional chest pain
- Hoarseness
- Shortness of breath, wheezing, cough, lower respiratory tract infection, atelectasis

- In PAH patients, a large proportion of the blood vessels are obstructed by pathological lesions, which force the right ventricle to increase the effort to pump blood across the lesions until it can no longer do so, at which point the signs and symptoms of right heart failure becomes evident.
- Currently, there is no cure for PAH, and treatments focus on managing symptoms and improving outcomes through vasodilators, prostacyclin analogs, and combination therapies. PAH treatments do not specifically target pulmonary vascular remodeling and inflammation, there is an urgent need to better identify the pathobiological mechanisms in order to support therapeutic innovation aimed at reversing these features and regenerating normal pulmonary vessels.

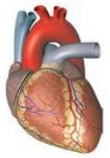
Clinical Classification

Pulmonary Arterial Hypertension (PAH)



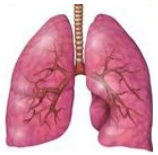
- Idiopathic/heritable
- Associatedconditions

PH Associated with Left Heart Disease



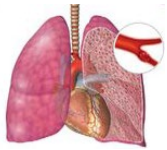
- IpcPH
- CpcPH

PH Associated with Lung Disease



- Non-severe PH
- Severe PH

PH Associated with Pulmonary Artery Obstructions



- CTEPH
- Other pulmonary obstructions

PH with Unclear and/or Multifactorial Mechanisms

- Haematologic disorders
- Systemic disorders

Global Prevalence of PAH, 2019-2033E

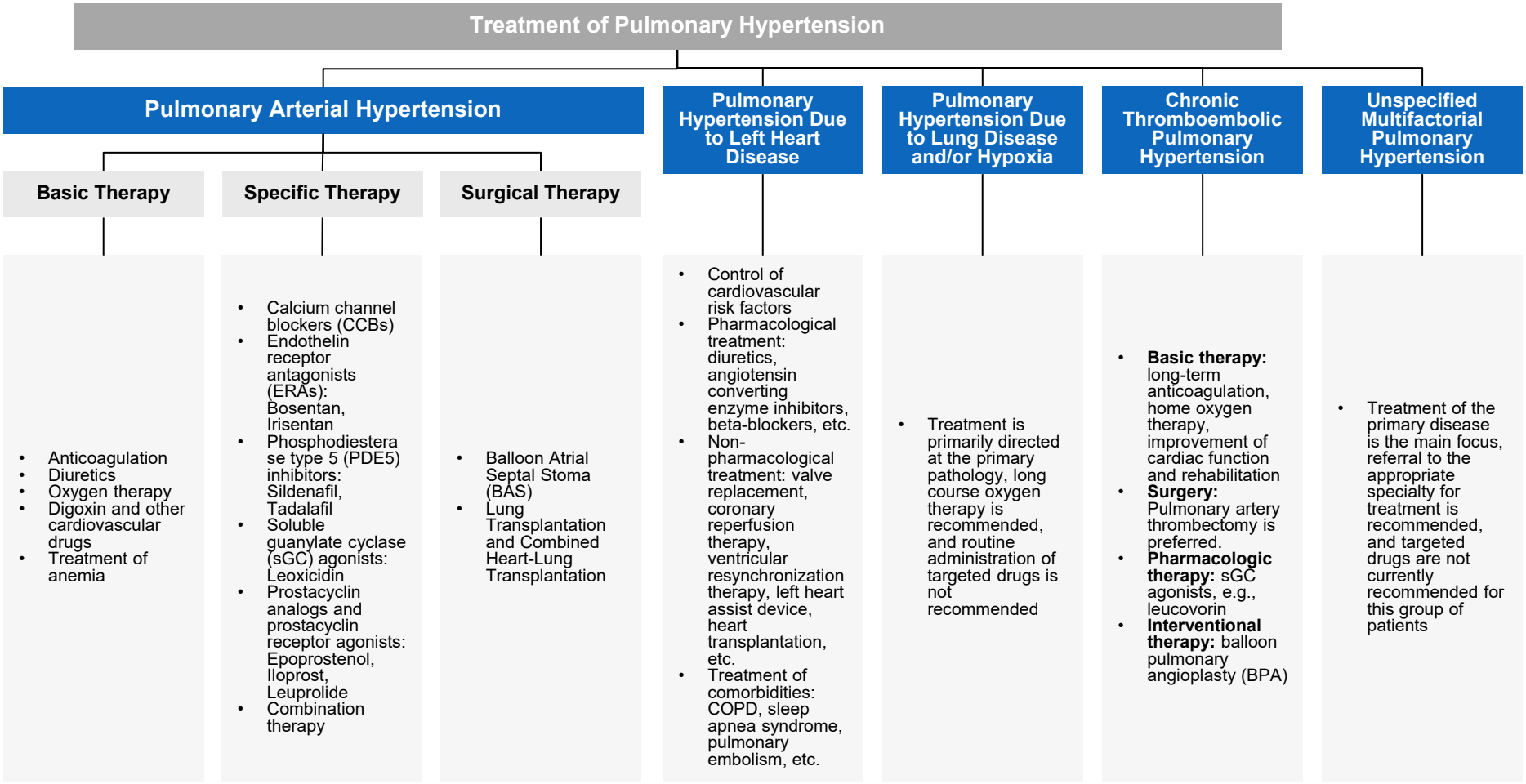
- Globally, the number of patients affected by PAH reached 370.8 thousand in 2024, with a CAGR of 1.0% from 2019 to 2024, and this number is forecasting to reach 404.1 million in 2033; the number of patients affected by PAH in China reached 86.6 thousand in 2024, with a CARG of 2.2% from 2019 to 2024 and this number is forecasting to reach 99.9 thousand in 2033.

Global Prevalence of PAH, 2019-2033E

CAGR	Global	China
2019-2024	1.0%	2.2%
2024-2028E	1.1%	1.4%
2028E-2033E	0.9%	1.8%

Source: Literature review, Frost & Sullivan analysis

Therapeutic Paradigms of Pulmonary Hypertension



Source: Guideline on Diagnosis and Treatment of Pulmonary Hypertension, Frost & Sullivan Analysis

Therapeutic Paradigms of Pulmonary Arterial Hypertension

- Therapy with PAH-approved drugs needs to be initiated in PAH patients who are not vasoreactive or are vasoreactive but not responding appropriately to CCBs. For the initial therapy, drugs are classified according to the grade of recommendation and the level of evidence on the basis of published RCTs. In addition, initial drug therapies are also stratified according to WHO-FC. One of the primary limitations of current PAH therapies is their focus on symptom management rather than halting or reversing disease progression. Most approved treatments, including endothelin receptor antagonists (ERAs), phosphodiesterase type 5 inhibitors (PDE-5is), soluble guanylate cyclase (sGC) stimulators, and prostacyclin analogs, aim to improve pulmonary vasodilation and alleviate symptoms such as shortness of breath and fatigue. While these therapies improve functional capacity and quality of life, they do not address the underlying vascular remodeling and inflammation that drive disease progression. As a result, PAH remains incurable, and patients often experience worsening of their condition over time.

- Supervised exercise training
- Psycho-social support
- Avoid strenuous physical activity
- Avoid pregnancy
- Influenza and pneumococcal immunization

General measures and supportive therapy

- Oral anticoagulants: IPAH, heritable PAH and PAH due to anorexigens, APAH
- Diuretics
- Oxygen
- Digoxin

Expert Referral

Acute vasoreactivity test

Vasoreactive

Yes

CCB

Sustained response

No

Non-vasoreactive

Initial Therapy with PAH approved drugs

Recommendation	Evidence	WHO-FC II	WHO-FC III	WHO-FC-IV
I	A or B	Ambrisentan, Bosentan, Macitentant +-, Riociguatt, Sildenafil, Tadalafil	Ambrisentan, Bosentan, Epoprostenol i.v., **Iloprost inhaled,** Macitentanti +-, Riociguatt, Sildenafil, Tadalafil **Treprostinil s.c., inhaled +**	Epoprostenol i.v.
IIa	C		Iloprost i.v. + Treprostinil i.v.	Ambrisentan, Bosentan, **Iloprost inhaled and i.v. +,** Macitentanti +-, Riociguatt +, Sildenafil, Tadalafil **Treprostinil s.c.,i.v. inhaled +**
IIb	B		Beraprostt +	
	C		Initial Combination Therapy	Initial Combination Therapy
Inadequate Clinical Response		Sequential Combination Therapy (ERAs+/Prostanoids+/PDE-5i or sGCS) Lung Transplantation Balloon Atrial Septostomy		

Note: APAH: associated pulmonary arterial hypertension; CCB: calcium channel blockers; ERA: endothelin receptor antagonist; sGCS: soluble guanylate cyclase stimulators; IPAH: idiopathic pulmonary arterial hypertension; i.v.: intravenous; PDE-5i: phosphodiesterase type-5 inhibitor; s.c.: subcutaneous; WHO-FC: World Health Organization functional class.
Level of evidence is based on the WHO-FC of the majority of the patients of studies. "+" approved only by the FDA (macitentan, riociguat, Treprostinil inhaled); in New Zealand (iloprost i.v); in Japan and S.Korea (beraprost). "-" positive opinion for approval of the CHMP of EMA

Source: Literature reviews, Frost & Sullivan Analysis

Global Competitive Landscape of PAH Inhalation Formulation

- There were 4 approved PAH inhalation drugs globally. Peak sales revenue of Tyvaso DPI was recorded USD731.1 million in 2023. Peak sales revenue of Tyvaso was recorded USD714.7 million in 2022.

Global Approved PAH Inhalation Formulation

Dosage Form	Manufacturer	Generic Name	Brand Name	Market Authority	First Approval Date	Indications	2023 Sales Revenue, USD Million
DPI	United Therapeutics	Treprostinil	Tyvaso	FDA	2009-07-30	PAH	731.1
	Liquidia Technologies	Treprostinil	Yutrepia	FDA	2024-08-16		NA
Nebulization	Bayer	iloprost	Ventavis	EMA/NMPA	2003-09-13 (EMA) 2005-05-25 (NMPA)		NA
	United Therapeutics	Treprostinil	Tyvaso DPI	FDA	2022-05-23		502.6

Global PAH Inhalation Formulation at Clincal Stage

Dosage Form	Drug Name	Manufacturer	Clinical Stage	Indications	First Posted Date
DPI	Seralutinib	GB002, Inc.	Phase III	PAH	2023-7-7
	MK-5475	Merck Sharp & Dohme LLC	Phase II/III		2021-2-1
	RT-234	Respira Therapeutics, Inc.	Phase II		2020-2-12
	LAM-001	OrphAI Therapeutics	Phase II		2023-4-5
	Mosliciguat	Pulmovant, Inc.	Phase II		2024-10-10
	Treprostinil Inhalation Powder	Mannkind Corporation	Phase I		2018-3-14
	BAY1237592	Bayer	Phase I		2018-11-27
Nebulization	L606	Pharmosa Biopharm Inc.	Phase I		2019-8-1
	AER-901	Aerami Therapeutics	Phase I		2021-5-26

*This table was last updated on Sep 16th , 2025

Source：FDA, EMA, ClinicalTrials, EU CTR, Annual Report, Frost & Sullivan Analysis

China Competitive Landscape of PAH Inhalation Formulation

PAH Inhalation Formulation at Clincal Stage in China

Dosage Form	Drug Name	Manufacturer	Clinical Stage	Indications	First Posted Date
DPI	AV-101	Aerovate Therapeutics	Phase III	PAH	2023-10-16
DPI	MK-5475	Merck	Phase I		2021-09-13

*This table was last updated on Sep 16th, 2025

Source：FDA, EMA, ClinicalTrials, EU CTR, Annual Report, Frost & Sullivan Analysis

Overview of Mycobacterium avium complex (MAC) Lung Disease

- Nontuberculous mycobacteria (NTM) are ubiquitous organisms that can be isolated from the environment, including water and soil, and they cause pulmonary and extrapulmonary disease. Pulmonary disease (PD) is the most common clinical presentation of NTM infection, and although the cause of NTM-PD development is not clearly understood, it may be associated with both host and bacterial factors. MAC is the most common cause of NTM-PD worldwide.
- MAC lung disease is an infection caused a group of bacteria called mycobacterium avium complex. MAC organisms are common in soil and water and are easily inhaled during daily activities. MAC lung disease, can be associated with progressive and chronic lung damage and increase mortality, reported a five-year mortality greater than 25%, especially for immunocompromised populations. Patients with MAC lung disease have substantial disease burden and limited treatment options. For patients with treatment-refractory MAC lung disease (persistent MAC-positive sputum despite ≥6 months of guideline-based therapy (GBT)), international guidelines recommend the addition of amikacin liposome inhalation suspension to GBT regimens.

Indications	Regimen	Duration of therapy
Non-cavitary nodular bronchiectatic form	• Azithromycin 500 mg tiw • clarithromycin 1,000 mg tiw • rifampin 600 mg tiw • ethambutol 25 mg/kg tiw	12 Months beyond sputum culture conversion to negative
Fibrocavitary form or cavitary nodular bronchiectatic form	• Azithromycin 250–500 mg daily • clarithromycin 1000 mg daily and rifampin 450–600 mg daily and ethambutol 15 mg/kg daily • and/or amikacin 15 mg/kg IV or IM tiw	
Macrolide-resistant	• Rifampin 450–600 mg daily and ethambutol 15 mg/kg daily • and/or moxifloxacin 400 mg daily • and/or clofazimine 100 mg daily • **and/or inhaled amikacin** • and/or bedaquiline	

- Antibiotics are the first-line treatment for MAC, they commonly require prolonged use of over 12 months and therefore can lead to resistance and low treatment compliance. Moreover, Injectable aminoglycosides, including amikacin and streptomycin, have been recommended for MAC-PD if the disease is associated with cavitary disease or macrolide resistance. However, serious systemic side effects, including auditory, vestibular, and renal toxicity could limit the long-term systemic administration of these drugs.
- Administering amikacin by a liposome may be an effective alternative for significantly reduce off-target effects, maintain therapeutic levels more effectively, and potentially allow for lower doses of the drug, thereby minimizing systemic toxicity and enhancing its safety and efficacy profiles.

*tiw: three times weekly

Source: Literature review, Frost & Sullivan analysis

Global and China Competitive Landscape of MAC Lung Disease Inhalation Formulation

- Arikayce is an aminoglycoside antibacterial indicated in adults who have limited or no alternative treatment options, for the treatment of mycobacterium avium complex (MAC) lung disease as part of a combination antibacterial drug regimen in patients who do not achieve negative sputum cultures after a minimum of 6 consecutive months of a multidrug background regimen therapy. Arikayce is designated an orphan medicine from EMA and FDA.
- In China, there is no inhalation drug for MAC lung disease inhalation that have been approved or entered clinical stage.

Global Approved MAC Lung Disease Inhalation Formulation

Dosage Form	Manufacturer	Generic Name	Brand Name	Market Authority	First Approval Date	Indications	2023 Sales Revenue, USD Million
(liposomal) Nebulization	Insmed	AMIKACIN SULFATE	Arikayce	FDA, EMA	2018-09-28 (FDA) 2020-10-27 (EMA)	MAC Lung Disease	305.2

Global MAC Lung Disease Inhalation Formulation at Clincal Stage

Dosage Form	Generic Name	Drug Name	Manufacturer	Clinical Stage	Indications	First Posted Date
Nebulization	Clofazimine	Icon-1	Mannkind Corporation	Phase III	MAC Lung Disease	2024-5-17

*This table was last updated on Sep 16th, 2025

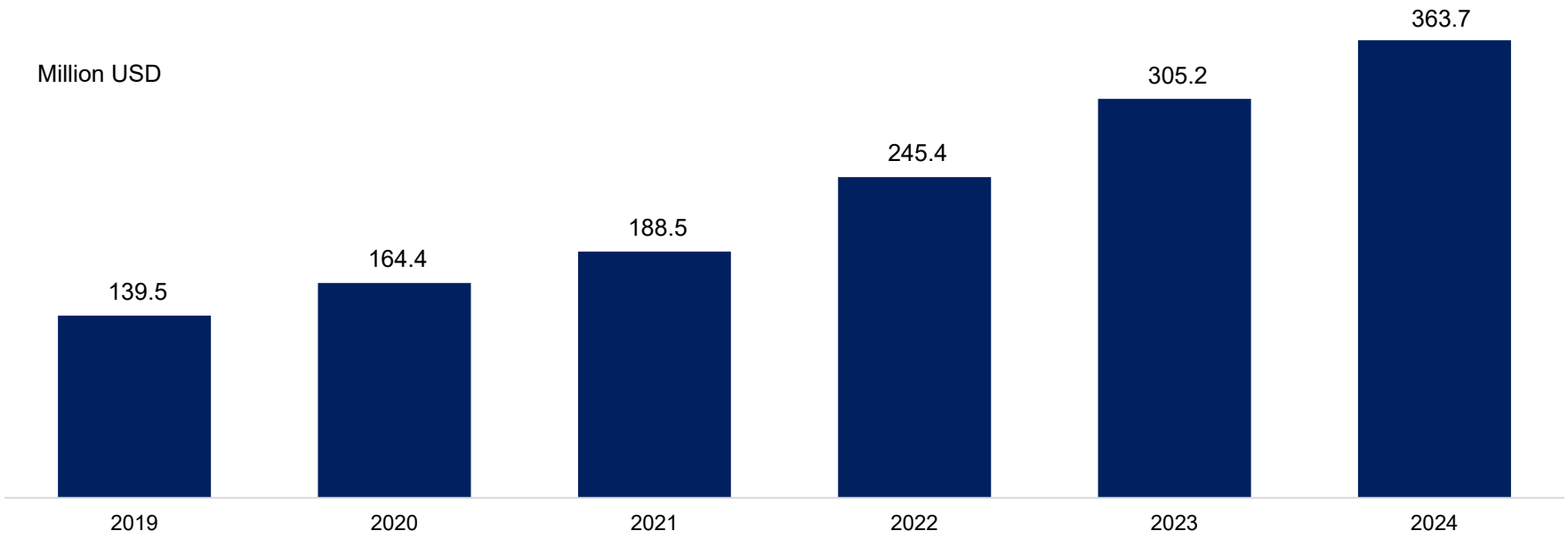
Source：FDA, EMA, ClinicalTrials, EU CTR, Annual Report, Frost & Sullivan Analysis

Historical Global Sales Revenue of Arikayce, 2019-2024

- In 2024, global sales revenue of Arikayce reached USD363.7 million, increase from USD139.5 million in 2019, with a CAGR of 21.1% from 2019 to 2024.

Global Sales Revenue of Arikayce, 2019-2024

Period	CAGR
2019-2024	21.1%



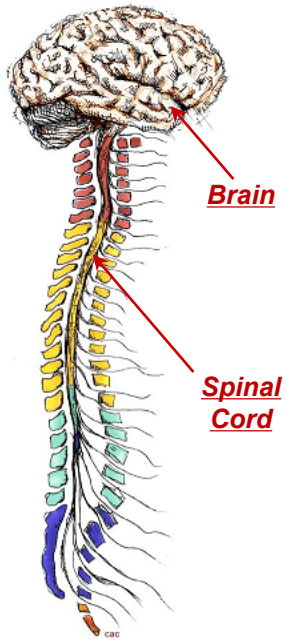
Source：Insmed Annual Report, Frost & Sullivan Analysis

Content

Overview of Central Nervous System (CNS) Disease

- The central nervous system (CNS) is the part of the nervous system consisting of the brain and spinal cord. The central nervous system controls thought processes, guides movement, and registers sensations throughout the body.
- CNS diseases are a group of neurological disorders that affect the structure or function of either the spinal cord or brain, which collectively form the central nervous system. A CNS disease may be an inherited metabolic disorder; the result of damage from an infection, a degenerative condition, stroke, a brain tumor or other problem; or arise from unknown or multiple factors.
- According to 2021 Global Burden of Disease study, billions of people worldwide have been affected by CNS disorders, where an estimated 12 million people suffer from Pakinson's disease and 57 million from Alzheimer's and other dementias

Illustration of CNS



CNS Disease

Neuro-degeneration	Functional Disorders	Structural Disorders	Infections	Demyelinating Disease
Neurodegenerative disease is an umbrella term for a range of conditions which primarily affect the neurons by progressive loss of structure or function of neurons, including death of neurons. Neurodegenerative diseases include Parkinson disease, multiple sclerosis, amyotrophic lateral sclerosis, Huntington chorea, and Alzheimer disease.	Functional disorders are dissociative seizures or functional movement disorders. These are identified as being internally inconsistent recognized disease processes. **Functional disorders include migraine, epilepsy, dizziness, and neuralgia.**	Structural disorders refers to a group of neurological disorders that affect the structure of the brain or spinal cord. Structural disorders include brain or spinal cord injury, Bell's palsy, cervical spondylosis, carpal tunnel syndrome, brain or spinal cord tumors, peripheral neuropathy, and Guillain-Barré syndrome.	Central nervous system infections include bacterial and aseptic (typically viral) meningitis, viral and autoimmune encephalitis and myelitis, which targets the spinal cord. Symptoms usually start with fever and can progress to irritability, refusal to eat, headache, neck pain, and sometimes seizures.	A demyelinating disease can result in damage to the myelin sheath that surrounds nerve fibers in the brain, optic nerves and spinal cord. When the myelin sheath is damaged, nerve impulses slow or even stop, causing neurological problems. Multiple sclerosis is the most common demyelinating disease of CNS.

Source: GBD, Literature Review, Frost & Sullivan Analysis

Epidemiology of Major Central Nervous System Diseases

Major CNS Diseases	Definition	Prevalence Rate in China
Attention deficit/hyperactivity disorder (ADHD)	ADHD is an organic disorder of the nervous system. ADHD, which in severe cases can be debilitating, has symptoms thought to be caused by structural as well as biochemical imbalances in the brain; in particular, low levels of the neurotransmitters dopamine and norepinephrine, which are responsible for controlling and maintaining attention and movement.	6.26% (children and adolescents)
Parkinson's Disease	Parkinson's disease is a long-term degenerative disorder of the central nervous system that mainly affects the motor system. It happens when nerve cells in the brain don't produce enough of a brain chemical called dopamine.	1.37% (60+)
Migraine	Migraine is a type of headache characterized by recurrent attacks of moderate to severe throbbing and pulsating pain on one side of the head. The pain is caused by the activation of nerve fibers within the wall of brain blood vessels traveling inside the meninges (three layers of membranes protecting the brain and spinal cord).	1.68‰
Epilepsy	Epilepsy is an unpredictable, serious, and potentially fatal disorder of the nervous system, thought to be the result of faulty electrical activity in the brain. Epileptic seizures result from abnormal, excessive, or hypersynchronous neuronal activity in the brain. About 50 million people worldwide have epilepsy, and nearly 80% of epilepsy occurs in developing countries. Epilepsy becomes more common as people age.	2.2‰

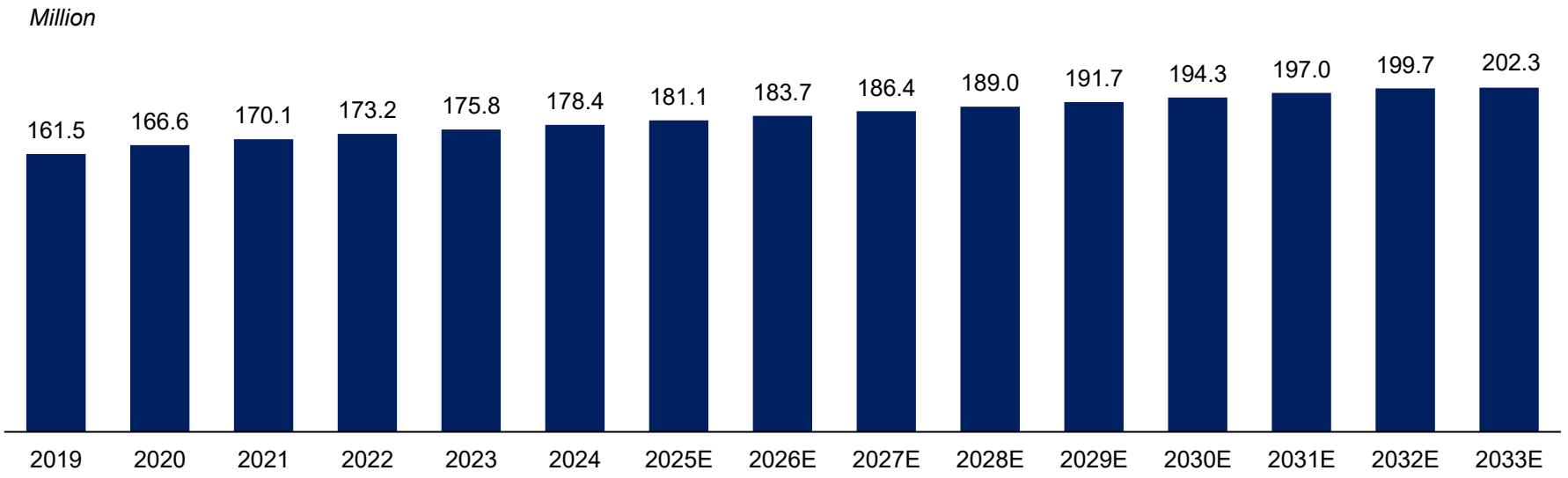
Source: Literature Review, Frost & Sullivan Analysis

Prevalence of Migraine in China, 2019-2033E

- In 2024, the prevalence of migraine in China has reached 178.4 million. The prevalence of migraine is expected to increase in the next few years, and the number of migraine patients is expected to reach 202.3 million by 2033, representing a CAGR of 1.5% and 1.4% from 2024 to 2028 and from 2028 to 2033.

Prevalence of Migraine in China, 2019-2033E

Period	CAGR
2019-2024	2.0%
2024-2028E	1.5%
2028E-2033E	1.4%

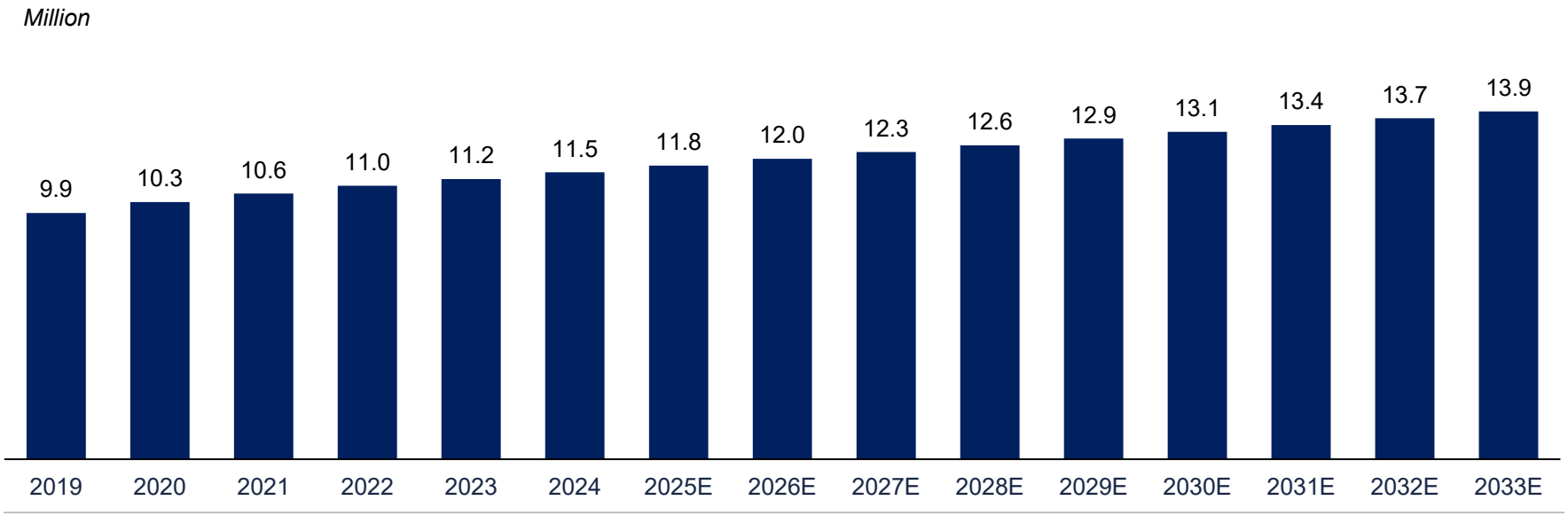


Prevalence of Epilepsy in China, 2019-2033E

- In 2024, the prevalence of epilepsy in China has reached 11.5 million. The prevalence of epilepsy is expected to increase in the next few years, and the number of epilepsy patients is expected to reach 13.9 million by 2033, representing a CAGR of 2.3% and 2.1% from 2024 to 2028 and from 2028 to 2033.

Prevalence of Epilepsy in China, 2019-2033E

Period	CAGR
2019-2024	3.1%
2024-2028E	2.3%
2028E-2033E	2.1%

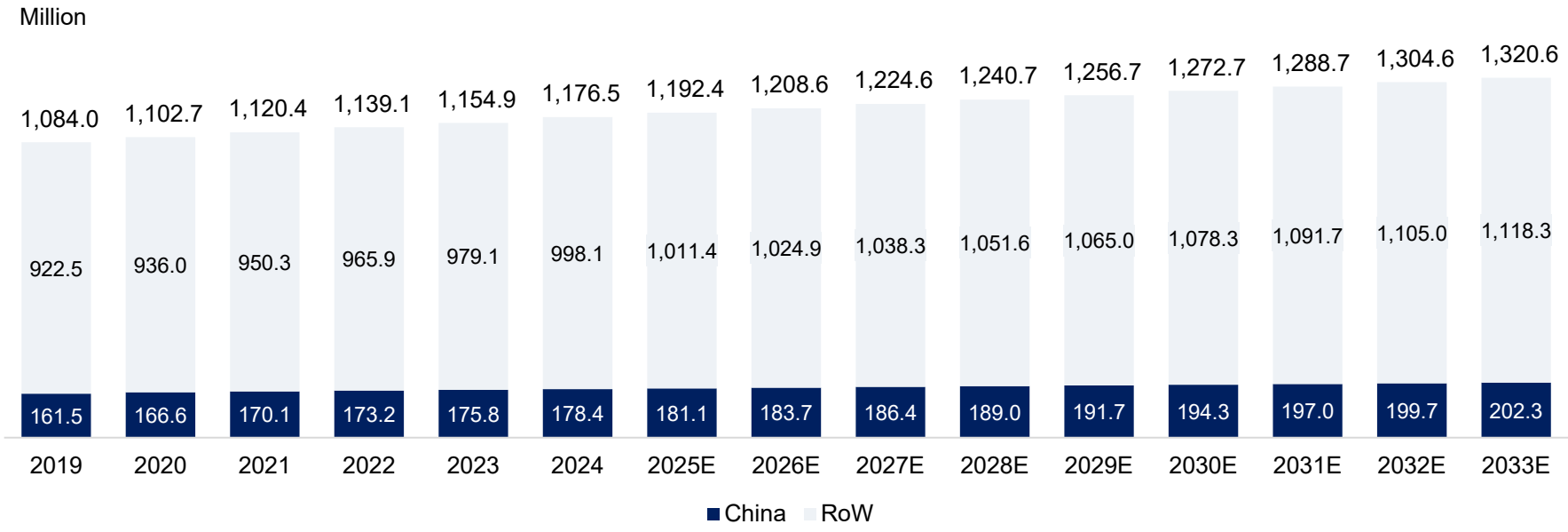


Global Prevalence of Migraine, 2019-2033E

- Globally, the number of patients affected by migraine reached 1,176.5 million in 2024, with a CAGR of 1.7% from 2019 to 2024, and this number is forecasting to reach 1,320.6 million in 2033; the number of patients affected by migraine in China reached 178.4 million in 2024, with a CARG of 2.0% from 2019 to 2024 and this number is forecasting to reach 202.3 million in 2033.

Global Prevalence of Migraine, 2019-2033E

CAGR	Global	China
2019-2024	1.7%	2.0%
2024-2028E	1.3%	1.5%
2028E-2033E	1.3%	1.4%



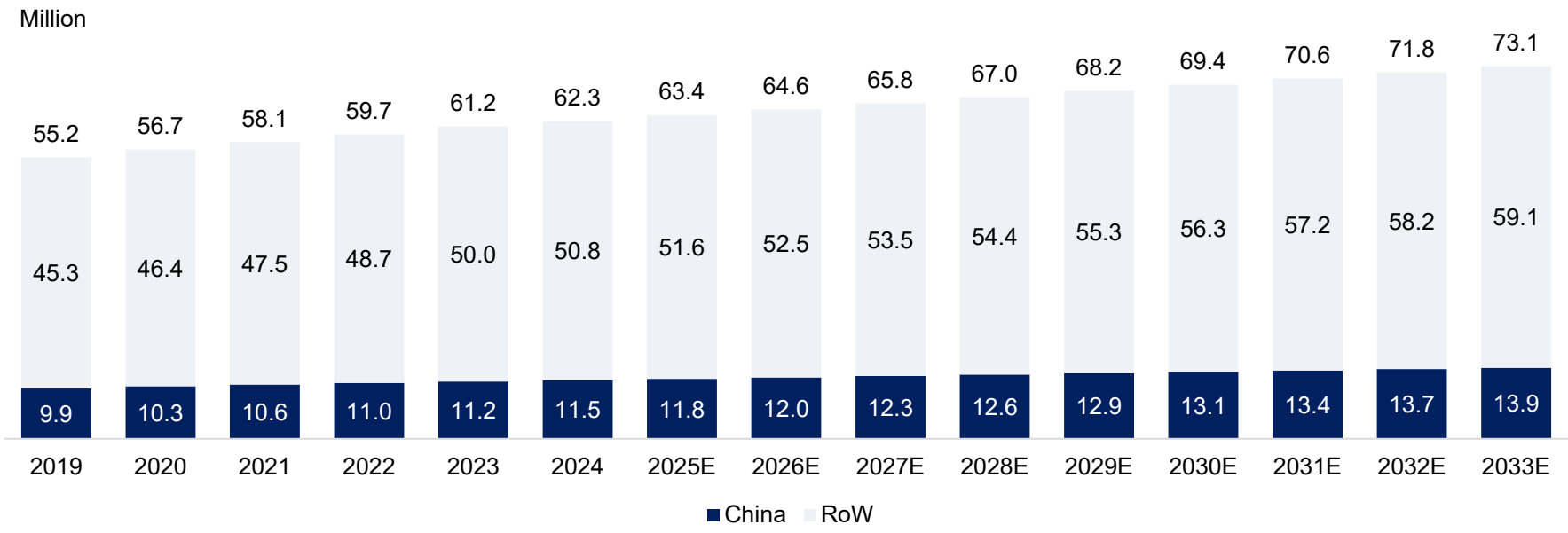
Source: Literature review, Frost & Sullivan analysis

Global Prevalence of Epilepsy, 2019-2033E

- Globally, the number of patients affected by epilepsy reached 62.3 million in 2024, with a CAGR of 2.4% from 2019 to 2024, and this number is forecasting to reach 73.1 million in 2033; the number of patients affected by epilepsy in China reached 11.5 million in 2024, with a CARG of 3.1% from 2019 to 2024 and this number is forecasting to reach 13.9 million in 2033.

Global Prevalence of Epilepsy, 2019-2033E

CAGR	Global	China
2019-2024	2.4%	3.1%
2024-2028E	1.8%	2.3%
2028E-2033E	1.8%	2.1%



Source: Literature review, Frost & Sullivan analysis

Representative Drugs for CNS Disease

Category	Mechanism of action	Representative drugs
Anesthetics	Anesthetics are used to reduce or prevent pain during a surgery. There are three main types: local (numbs one small area of the body), regional (blocks pain in an area of the body, such an arm or leg) and general (causes a reversible loss of consciousness).	Propofol, Sevoflurane, Atracurium
Psychoanaleptics	A psychoanaleptic drug is a medication that produces an arousing effect. Psychooanaleptic drugs include antidepressant drugs and psychostimulants.	Escitalopram, Venlafaxine, Setraline
Psycholeptics	A psycholeptic drug is a medication which produces a calming effect upon a person. Psycholeptic drugs include antipsychotic drugs, anxiolytic drugs, hypnotics and sedatives.	Olanzapine, Quetiapine, Midazolam,
Antiepileptics	Antiepileptic drugs are used in the treatment of epileptic seizures. Anticonvulsants suppress the rapid and excessive firing of neurons during seizures. Anticonvulsants also prevent the spread of the seizure within the brain.	Sodium Valproate, Levetiracetam, Oxcarbazepine, **Diazepine**
Anti-Parkinson	An anti-Parkinson medication is a type of drug which is intended to treat and relieve the symptoms of Parkinson's disease. Most of these agents act by either increasing dopamine activity or reducing acetylcholine activity in the central nervous system.	Pramipexole, Levodopa+Benserazide, Entacapone
Anti-Alzheimer	Five medications are currently used to treat the cognitive problems of Alzheimer's disease: four are acetylcholinesterase inhibitors (tacrine, rivastigmine, galantamine and donepezil) and the other (memantine) is an NMDA receptor antagonist.	Donepezil, Rivastigmine, Galantamine, Memantine
Other	Include parasympathomimetics, drugs used in addictive disorders, antivertigo preparations, and other nervous system drugs	Neostigmine, Nicotine, Betahistine, Edaravone

Source: Frost & Sullivan Analysis

Global and China Competitive Landscape of Migraine Inhalants

Global and China Approved Migraine Inhalants

Dosage Form	Manufacturer	Generic Name	Brand Name	Market Authority	First Approval Date	Indications	2023 Sales Revenue, USD Million
Nasal Spray	GSK	Sumatriptan	Imitrex	FDA	1997-08-26	Migraine	NA
	Bausch Health	Dihydroergotamine mesylate	Migranal	FDA	1997-12-08		NA
	Amneal Pharmaceuticals	Zolmitriptan	Zomig	FDA	2003-09-30		NA
	Currax Pharmaceuticals	Sumatriptan Succinate	Onzetra Xsail	FDA	2016-01-27		NA
	Tonix Pharmaceuticals	Sumatriptan	Tosymra	FDA	2019-01-25		1.5
	Pfizer	Zavegepant	Zavzpret	FDA	2023-03-09		NA
	Jewim Pharmaceutical	Zolmitriptan	/	NMPA	2013-10-09		NA

China Migraine Inhalants at Clinical Stage

Dosage Form	Generic Name	Drug Name	Manufacturer	Clinical Stage	Indications	First Posted Date
Nasal Spray	Zavegepant	Zavegepant	Pfizer	Phase III	Migraine	2023-08-10
	/	PRT-064040	Sichuan Purity	Phase I	Migraine	2025-05-30

*This table was last updated on Sep 16th, 2025

Source：FDA, EMA, ClinicalTrials, EU CTR, Annual Report, Frost & Sullivan Analysis

Global and China Competitive Landscape of Epilepsy Inhalants

Global and China Approved Epilepsy Inhalants

Dosage Form	Manufacturer	Generic Name	Brand Name	Market Authority	First Approval Date	Indications	2023 Sales Revenue, USD Million
Nasal Spray	UCB	Midazolam	Nayzilam	FDA	2019-05-17	Epilepsy	101.7
	Neurelis	Diazepam	Valtoco	FDA NMPA	2020-01-10 (FDA) 2023-06-07 (NMPA)		NA

Global Epilepsy Inhalants at Clincal Stage

Dosage Form	Generic Name	Drug Name	Manufacturer	Clinical Stage	Indications	First Posted Date
Nasal Spray	Alprazolam	STAP001	UCB	Phase III	Epilepsy	2021/10/14

China Epilepsy Inhalants at Clinical Stage

Dosage Form	Generic Name	Drug Name	Manufacturer	Clinical Stage	Indications	First Posted Date
Nasal Spray	Midazolam	NA	Sichuan Purity Pharmaceutical	BE	Epilepsy	2023-08-28
	Alprazolam	STAP001	Alexza/UCB	Phase III		2022-02-25
	diazepam	NRL-1	China Medical Systems	Phase I		2020-07-24
	Midazolam	NA	Yichang Humanwell	Phase I		2020-03-24

*This table was last updated on Sep 16th, 2025

Note: 2023 Sales revenue of Nayzilam reached EUR94 million. 2023 sales revenue of Valtoco is not publicly disclosed.

Source: FDA, EMA, ClinicalTrials, EU CTR, Annual Report, Frost & Sullivan Analysis

Content

Overview and Clinical Advantages of Inhalation

Key Information

- Inhalation have advantages that cannot be replaced by traditional delivery methods in the treatment of respiratory diseases. It is the main and gold therapy for the treatment of asthma and chronic obstructive pulmonary disease (COPD).
- In recent years, it has also been used to treat pulmonary infection, cystic pulmonary fibrosis and respiratory tract neoplasm, as well as systemic diseases such as diabetes mellitus. Overall, it is widely used.

1 Overview of Inhalation

- Inhalation are preparations in which the drug is delivered to the respiratory tract and/or lungs in a mist form by a specific device to reach local or systemic effects.
- The physiological characteristics of lung determine the advantages of inhaled preparations for drug delivery: the alveolar wall is thin, thus drug is very easy to be absorbed; lung has a large absorption surface area; biological metabolic enzymes' distribution is concentrated, their biological activity is low, and they are not easy to degrade protein peptide drugs; the blood volume is rich which facilitate drug absorption; the drug liver first-pass effect could be avoided.

2 Comparison of Inhalation with traditional drug delivery methods

Comparison of inhaled drug delivery with oral and intravenous drug delivery

Characteristics	Inhalation drug delivery	Oral administration	Intravenous injection
Convenience of use	Convenient	Convenient	Convenient
Speed of onset	fast	slow	fast
Bioavailability	high	low	high
drug dosage	low	high	high
Adverse Reaction	rare, mostly	more common than inhalation	more common than inhalation

- Compared with ordinary oral preparations, the drugs of Inhalation Formulations can directly reach the absorption or action site, bypass the slower gastrointestinal absorption of the oral drugs, provide rapid relief and are easier and more convenient to administer.
- Compared with injectable preparations, it can reduce the mechanical injury to local tissues, can reduce or avoid some of the adverse drug reactions, and improve patient compliance. Therefore, in recent years, it won increasing attention from the pharmaceutical industry.

Source: Literature Review, Frost & Sullivan analysis

Classification of Inhalation Formulation

Inhalation	Description	Advantage	Disadvantage	Typical Patient Groups	Picture
Dry Powder Inhaler (DPI)	Dry Powder Inhaler is a drug delivery system in which one or more dry powder form drugs are administered into the respiratory tract via a special inhalation device to exert systemic or local effects. DPIs are breath-activated, meaning that the patient's inhalation triggers the release of the medication.	Without propellant and breath activated, which eliminates need for coordination Environmentally friendly Generally compact and portable, which improves patient adherence. Good compatibility and low production cost	Requires strong inhalation effort, which may not be suitable for children, elderly or severely ill patients. Can be affected by humidity, which may potentially clog the powder.	Suitable for patients who can inhale quickly and deeply to activate the device. Not ideal for very young children or individuals with severe respiratory distress who cannot generate the necessary inspiratory flow. Often used by adolescents and adults with conditions like asthma and COPD.	
Inhalation Aerosol/Metered Does Inhaler (MDI)	For MDI, drug is put and sealed together with a suitable propellant housed within a plastic container which has a special valve system. The contents are sprayed out as mist form by the pressure of the propellant for pulmonary inhalation.	Has fast effect and positioning power Compact and portable, which improves patient adherence. Widespread availability of different medications in MDI form. Easier to maintain cleanliness compared to DPI	Propellant has environmental and toxic side effects Coordination required, which can be challenging for children and certain other patient groups Potential incomplete or suboptimal delivery of medication in the event of improper technique	Used across various age groups, including children, adolescents, and adults. Requires coordination of actuation and inhalation, so may be challenging for some young children or elderly patients with coordination difficulties.	
Nebulization Inhaler	Nebulized inhalers, normally in the form of suspension and solution, use high-speed oxygen airflow to nebulize medicine, which is then inhaled by the respiratory tract to achieve the purpose of treatment. The suspension consists of small liquid droplets or particles of the medication that are aerosolized by the nebulizer, allowing for easy inhalation and absorption into the lungs.	Easy to use, making it beneficial for those who may have difficulty using inhalers due to coordination issues. Versatile and can be used for a wide range of medications. Flexibility allowing for continuous or multiple high doses depending on patient needs.	Time of single usage is long Most of them are restricted to in-hospital use	Suitable for infants, young children, the elderly and individuals who are unable to use MDIs or DPIs effectively, such as those with severe asthma or COPD exacerbations. Ideal for delivering medication over an extended period, allowing for normal inhalation and exhalation.	
Soft Mist Inhaler (SMI)	Soft Mist Inhaler is a relatively new form of inhaler, which can deliver drugs in a slow mist and does not depend on the inhalation speed of drugs.	Higher lung deposition and better medication absorption due to use of slow-moving mist. Easier coordination between actuation and inhalation compared to traditional MDIs.	Generally more costly than MDIs. Availability of medications may be more limited compared to MDIs and DPIs.	Appropriate for various patient groups, including those who may have difficulty with the coordination required for MDIs. Produce a slow-moving mist that allows for easier inhalation, suitable for older patients or those with compromised hand strength and coordination.	
Nasal sprays	Nasal sprays are glucocorticoid drugs and antihistamines that are used in the treatment of allergic rhinitis.	Gel increase deposition and slow elimination at the nose area Provides systemic effects with high Bioavailability through the nasal mucosa. Large particle size and high viscosity	Dry nose side effects, irritation or dryness in nasal passages Long-term usage of decongestant sprays can lead to rebound congestion dependence	Typically used for patients with conditions affecting the nasal passages, such as allergic rhinitis. Easy to use for most age groups	

Source: Literature Review, Frost & Sullivan analysis

Classification of Inhalation Formulation (Continue)

Key Findings:

- Inhalation require the combined use of drugs and inhalation devices. Each device offers distinct advantages necessary to address the complex interplay of patient physiology and disease characteristics. Base on inhalation devices, inhalation can usually be categorized as: Dry Powder Inhaler (DPI), Metered Does Inhaler (MDI), Nebulization Inhaler (Nebulization), Soft Mist Inhaler (SMI), and Nasal sprays. Among these, MDI is currently the most widely used one, and DPI is considered to be the main direction of future inhalation development.
- Inhalation Formulation devices are complex, and thus difficult to make generic one. Take MDI as an example, it generally consists of main drug, excipient (propellant agent), pressure-resistant container, dosing valve system and injection device.
- DPI is portable and easier to use than MDI. It requires strong inhalation effort and is recommended for patients ≥5 years old who has both adequate inspiratory flow and cognitive ability. In most cases, it is not recommended for acuity diseases.
- MDI is restricted in children: For young children under 4 years old, they need to use chamber with face masks and elaborative instruction, which may be a problem in a busy clinical practice. For acute asthma, it is usually not recommended for its complicated operation.
- Nebulization, easier to use with a power source, can be used at any age and any disease severity or acuity, who may struggle with DPIs. Another benefit of Nebulization with diseases other that COPD and asthma is the ability to use very high drug doses, such as inhalable tobramycin for Pseudomonas endobronchial infections in cystic fibrosis.
- The SMI, a modern inhalation device that produces a slow, long-lasting aerosol that reduces drug deposition in the oropharynx when inhaled by the patient is a small, portable, handheld device requiring no power source. Its power primarily relies on the mechanical power of the spring, and no liquid gas propellant is required. In contrast to MDI, SMI helps to harmonize drive and inhalation and does not require patients to exceed the inspiratory flow threshold for DPI. Therefore, SMI can overcome the difficulties patients may experience with MDI and DPI.

Source: Literature Review, Frost & Sullivan analysis

Analysis of Inhaled Medication Classification

Types	Products	Indication	Advantages & Disadvantages
Muscarinic Antagonists (long-acting LAMA)	Fenoterol, Terbutaline, Salbutamol, Ipratropium Tiotropium, Umeclidinium, Glycopyrronium	COPD, Asthma	Prevent bronchoconstriction by blocking acetylcholine receptors in the airways; Acts slight slower than β2 adrenoceptor agonists, but lasts for a longer time, has fewer adverse effects, and can be inhaled for a long periods of time.
Glucocorticoid ICS	Budesonide, Fluticasone, and Mometasone	Asthma, Allergic rhinitis	Corticosteroids work by reducing airway inflammation, thereby improving respiratory function, offering both immediate relief and long-term respiratory health maintenance to patients with varying degrees of respiratory disease severity. The most effective anti-inflammatory drug currently available for the treatment of bronchial asthma. It may lead to mild adverse effects, the more common are hoarseness and throat discomfort.
β2 adrenoceptor agonists (short-acting SABA/long-acting LABA)	SABA：Abuterol, salbutamol, levalbuterol LABA：Salbutamol, formoterol,	COPD, Asthma	Beta-agonists manage respiratory conditions by relaxing the muscles of the airways, leading to their widening and making it easier to breathe. They achieve this by stimulating beta-adrenergic receptors in the smooth muscle of the airways. There are many different types , including short-acting (action lasts 4-6 hours) and long-acting (lasts 12 hours); fast-acting (onset of action in minutes) and slow-acting (onset of action in half an hour). The increase of dosage may lead to metabolic disorder.
β2 adrenoceptor agonists+ Glucocorticoid	Fluticasone+Salbutamol, Budesonide+Eformoterol, Mometasone +Eformoterol	COPD, Asthma	Increase patient compliance and reduce the adverse effects of high doses of hormones.
Anticholinergic drugs+ β2 adrenoceptor agonists	Atrovent+Salbutamol, Glycopyrrolate Bromide+Indacaterol, Atrovent+Eformoterol, Aclidinium bromide+Eformoterol, Umeclidinium Bromide+Vilanterol	COPD, Asthma	More potent and easier to control than single agents.
Others	Acetylcysteine, Zanamivir, Iloprost, Sumatriptan, Sevoflurane, and Ambroxol	Asthma, COPD, Influenza, Anesthesia, Hypertension, etc.	NA

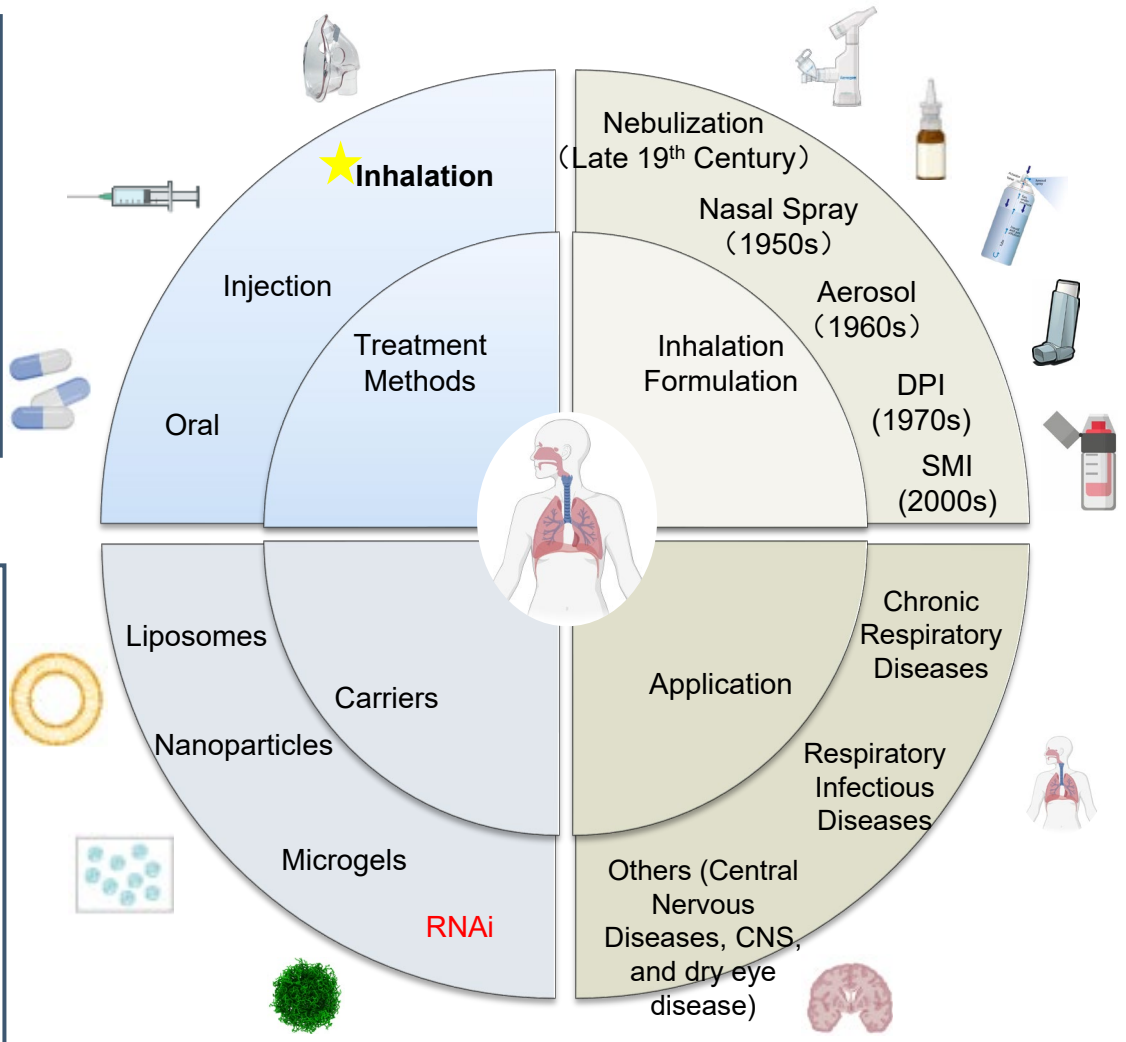
Key Findings：

- The current inhaled preparations mainly include glucocorticoids, β2 adrenoceptor agonists, anticholinergic receptors, and compounded preparations. Drug combination has become a trend in COPD treatment, thus the development of compounded preparations is sought after and the current commonly used compound is double drug. On September 18, 2017, the FDA approved GSK/Innoviva's new triple combination (ICS/LAMA/LABA) drug Trelegy Ellipta for marketing. It is the world's first triple Inhalation Formulation for stable COPD treatment and is officially approved in China in November 2019.

Source: Literature Review, Frost & Sullivan analysis

Development Path of Treatment Methods of Respiratory Diseases

- The physiological characteristics of the lungs determine the advantages of inhalation formulations.
- **Inhaled medicine is the first-line therapeutic drug and also the mainstay therapeutic option for most respiratory diseases, such as bronchodilators for COPD, ICS for asthma, and others.**



Inhalation formulations require the combined use of the drug and an inhalation device. Based on the type of inhalation device, they can generally be classified into: Dry Powder Inhalers (DPI), Metered Dose Inhalers (MDI), Nebulizations, Soft Mist Inhalers (SMI), and Nasal Sprays. Among these, MDIs are currently the most widely used, while DPIs and SMIs are considered the main direction for the future development of inhalation formulations.

Carriers play a pivotal role in pulmonary drug delivery. Liposomes, particularly highlighted, offer extended drug half-life, good biocompatibility, and versatility. They encapsulate drugs, enhancing drug efficacy and reducing side effects. Liposomes' unique ability to reduce irritation and damage to lungs during inhalation therapy underscores their importance in pulmonary drug delivery.

- COPD and asthma are effectively managed with inhaled bronchodilators and steroids. Also, in respiratory infections, inhaled antibiotics offer direct targeting of pathogens in the lungs.
- Additionally, pulmonary delivery of insulin and antidepressants highlights its potential in treating systemic conditions.

Development Path of Treatment Methods of Respiratory Diseases (Continue)

➢ Key findings:

- Other than respiratory diseases, intranasal administration (nasal spray), have been investigated its use in CNS and dry eye disease.
- The nose-to-brain drug-delivery system has emerged as a promising strategy to overcome the challenges associated with conventional drug administration for central nervous system disorders. This emerging field is driven by the anatomical advantages of the nasal route, enabling the direct transport of drugs from the nasal cavity to the brain, thereby circumventing the blood–brain barrier. Compared to oral administration or intracerebroventricular injection, intranasal administration, especially to the upper portion of the nasal cavity, has been shown to achieve direct CNS delivery of a variety of compounds without invasiveness or major complications. Additionally, it causes rapid increases in CNS levels of these compounds, and for some—such as insulin—avoids any significant peripheral uptake. Mechanisms involved in intranasal delivery of drugs to the brain are still being elucidated, some of the pathways involved are known. For example, intranasal drugs have been shown to rapidly travel extracellularly along the olfactory nerve pathways leading from the upper part of the nasal cavity directly to the brain. This pathway is likely one of the largest contributors to intranasal drug delivery, as drug concentrations in the olfactory bulbs following intranasal delivery are among the highest in the CNS.
- By stimulating the trigeminal nerve in the nasal cavity, nasal sprays can enhance natural tear production, providing relief without the need for topical eye drops. This method not only improves patient compliance but also targets the underlying causes of tear film instability, offering a promising alternative for those suffering from dry eye symptoms.
- RNAi technology can potentially redefine the treatment landscape for respiratory diseases, with the ability to target genes or pathways that underlie the disease, in contrast to most existing treatments that only treat the symptoms. By addressing disease causing mechanisms, siRNA therapy could modify the course of disease and achieve more sustained disease control. To date, there are no approved siRNA inhalation drugs globally.

Source: Literature Review, Frost & Sullivan analysis

Inhalation Formulation's R&D Entry Barrier (1/2)

Key Information

- For Inhalation Formulations, prescription design and manufacturing process are both difficulties in R&D. Advanced techniques are required to ensure the integration of medicine and medical devices, as well as the continuity, accuracy, and stability of continuous dosing.
- As high-quality generic drug, inhalant preparations are more difficult to develop than traditional generic drugs in the aspects of reparation prescription, drug delivery device, preparation process, quality research, stability research, etc. Thus, Inhalation Formulation has obvious pricing advantage.

1 Research and development standard of inhalation formulation technology

API and excipients Excipients' safety evaluation	• Reference pH, pKa value, density, particle size distribution, powder surface characteristics, powder shape, crystalline form, moisture, solubility, solvation/ or hydrated state. Propellants agent, solubilizing agents, surfactant, etc. • Use a suitable cell model to observe the cell morphological changes, integrity and viability to determine the safety of the tested substance
Partical of drug	• The particle size of the drug is usually in a range of 3-5 um. Particle sizes that are too large (>10μm) or too small (<0.5μm) may prevent drug deposition and reduce treatment efficacy
Micronization process	• Systematic study of the micronization process(speed of feed, air pressure, air flow rate, particle crushing cycle time, dispersion patterns, particle size of the powder, high temperature degradation of the main drug and possible microbial contamination, etc.)
Moisture and environmental humidity control	• Strictly control the moisture of APIs and excipients, avoid the introduction of moisture in the production environment and production utensils and containers, avoiding the impact of moisture to the maximum extent possible
Propellants ratio	• If a single propellant agent cannot meet the needs of clinical use, a mix of propellant agents with different vapor pressures is required
Canning technique	• Each canning process should be considered and selected in conjunction with the specific prescription
Others	• Control of loading variation, content, moisture, impurities, osmotic pressure, test of valve system, sealing, etc. Pay attention to drug aggregation and microcrystal growth.

2 Comparison of generic inhalation drug with traditional generic drug

	Prescription design difficulty	BE Difficulty	Production Technique Difficulty	Advanced (Technology)	Pricing Advantages
Generic inhalation drug	◕	●	◕	◕	◕
Traditional inhalation drug	◔	◔	◔	◔	◔

Source: Frost & Sullivan analysis

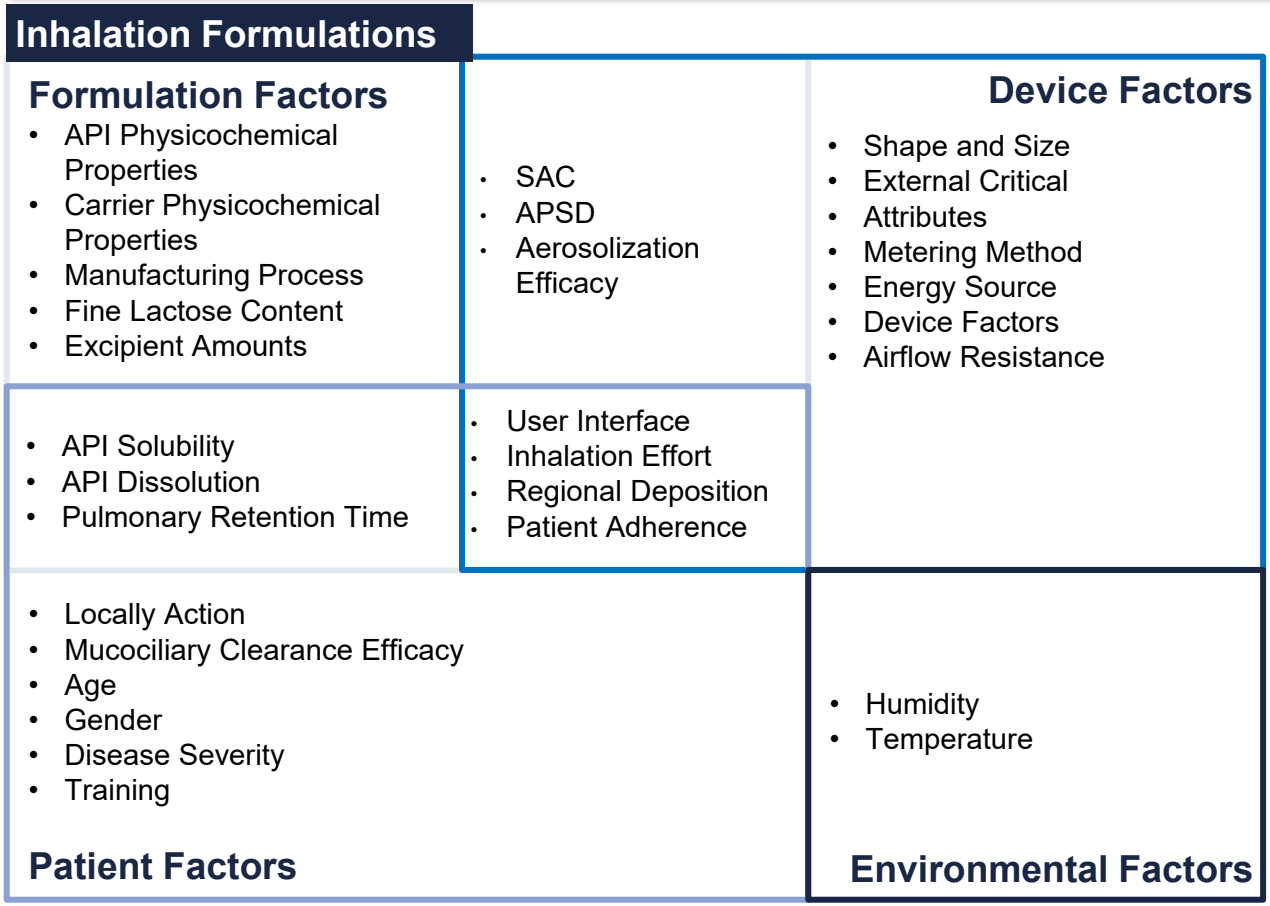
Inhalation Formulation's R&D Entry Barrier (2/2)

Particle Engineering and Device Design	• Particle engineering is the cornerstone of successful inhalation formulations. Compared to other routes of administration, drug delivery via the lungs demands heightened control of the drug particle. Every attribute, from particle size, shape, density, and surface characteristics, can critically impact drug effectiveness, thus adding layers of complexity to the formulation development process. These properties must be precisely engineered on a micron scale and maintain uniformity and stability across time and varied environments. • Device design is a crucial and complex component that requires a rare combination of scientific expertise, engineering skills, and patient-centric design. The intricacy of delivery systems extends to their materials and formulation stability, necessitating the use of biocompatible components to prevent reactions with the medication. Within these compact devices, a sophisticated network of air passages, valves, and nozzles is engineered to consistently deliver drug particles with micron-level precision to the deepest areas of the lungs, while remaining portable, affordable, and intuitive for patients of all ages and abilities. • Also, Overcoming these technical hurdles demands significant investments in research, testing, and innovation, as exemplified by the extensive R&D efforts required to develop consistent and stable formulations like those needed for MDIs and DPIs.
Product Performance Evaluation	• Product performance evaluation is crucial in bridging the gap between laboratory testing and the clinical performance of inhalation formulations. Unlike oral or injectable formulations, inhalation products navigate the complex anatomy and physiology of the respiratory tract while accounting for various patient and environmental factors.
Process Engineering	• Process engineering to translate a lab-scale inhalation formulation into a commercially viable, industrial-scale manufacturing process presents a formidable challenge. Small attributes, such as particle size distribution, powder flow, and dose uniformity, these formulations often requires precise ratios of active pharmaceutical ingredients (APIs) and excipients, which can vary in compatibility and behavior at scale.
Clinical Development	• Clinical development for inhalation formulations is far more complex and stringent compared to other formulation types. Large-scale human clinical trials, often involving over 500 patients, are required to demonstrate bioequivalence due to the inherent variability in patient factors and device use. Inhalation formulations also demand additional studies, such as local and systemic safety assessments, device usability tests, intricate PK/PD studies, and long-term safety and efficacy evaluations. In addition, local delivery in inhalation formulations also presents unique challenges. For example, variability in patient inhalation techniques can affect drug deposition, making it challenging to control dosage consistency. The potential for irritation or adverse reactions in the delicate lung tissues necessitates meticulous monitoring and control measures during trials. These complexities demand stringent protocols, and close supervision, all of which contribute to the intricacy of clinical trials for inhalation formulations.

Source: Frost & Sullivan Analysis

Regulatory and Scientific Challenges in the Development of Inhalation Formulations and Oral Formulations

- Compared to other oral formulation types, inhalation formulations are highly challenging to develop and manufacture, where the interplay of numerous factors affect the ability of the product to achieve an optimal therapeutic outcome. These factors originate from 4 major aspects of the drug product, namely, the drug formulation, the delivery device, the patient and the environment.



The development of inhalation formulations are significantly more complex compared to traditional oral formulations.

Inhalation Formulations' efficacy and safety relies on contributions from numerous factors that originate from 4 aspects of the drug product: the formulation, the drug delivery device, the patient population and the environment, while traditional oral formulations only contributes from 2 aspects, namely formulation and patient factors.

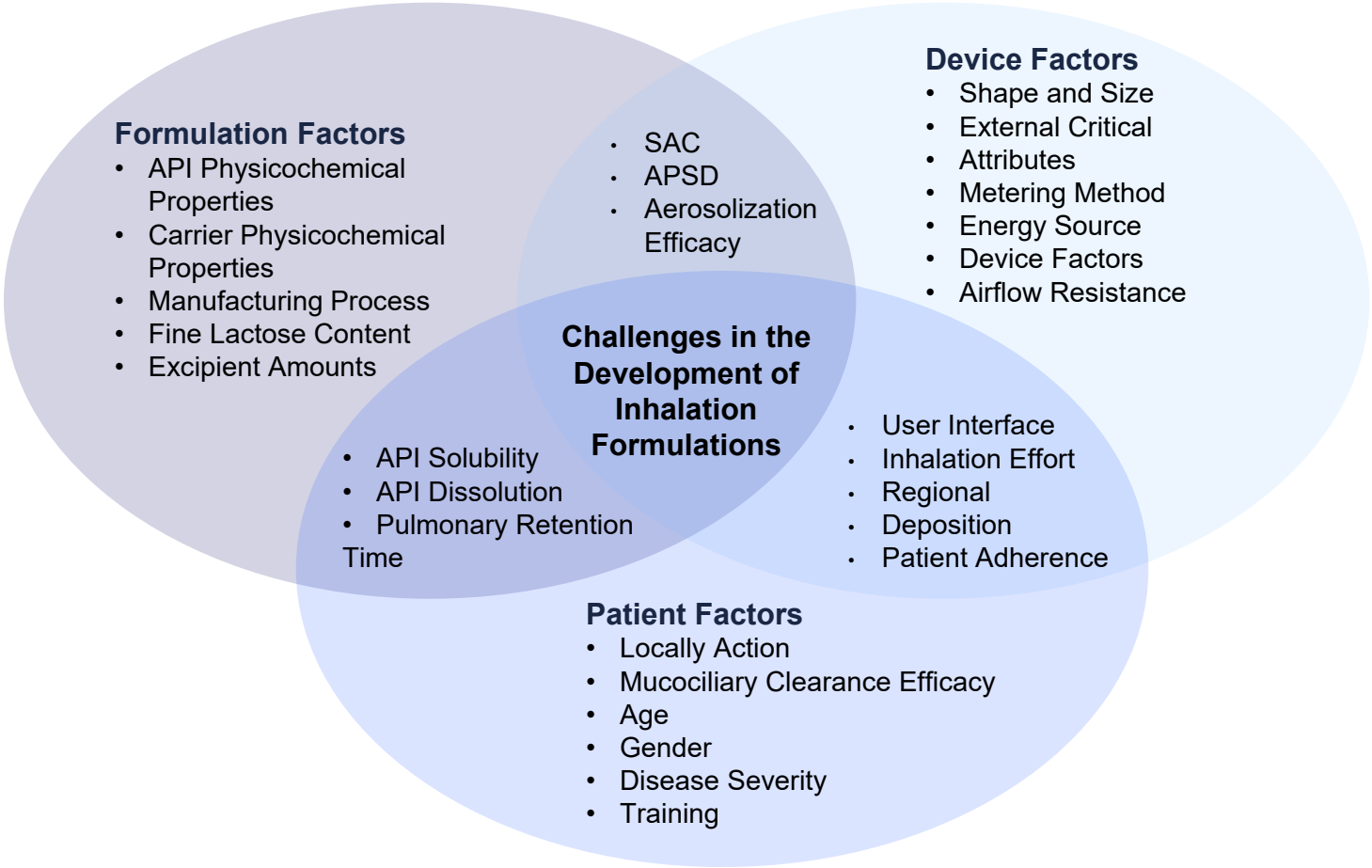
Some factors are inherent to one aspect of the drug product while others arise from the interaction between different aspects. For instance, regional deposition is impacted by both the drug delivery device as well as the patient.

SAC: single actuation content; APSD: aerodynamic particle size distribution

Source: Literature Review, Frost & Sullivan analysis

Regulatory and Scientific Challenges in the Development of Inhalation Formulations and Oral Formulations

- Compared to other oral formulation types, inhalation formulations are highly challenging to develop and manufacture, where the interplay of numerous factors affect the ability of the product to achieve an optimal therapeutic outcome. These factors originate from 3 major aspects of the drug product, namely, the drug formulation, the delivery device, and the patient.



Source: Literature Review, Frost & Sullivan analysis

Chemical Drug Application Category in China

- In 2020, NMPA launched a new classification system for chemical drugs, with the release of the Requirements for Registration Classification and Application Dossiers of Chemical Drugs (“化学药品注册分类及申报资料要求”).
- Under the new classification, 'new drug' now refers only to new chemical entities or improved new forms of known chemical entities that have never been marketed anywhere in the world, namely Class 1, 2 and 5.1.

Category	Classification	Definition / Scope
New drugs	Class 1 Innovative new drugs which have never been marketed within or outside China	Active ingredients and their formulations which have clinical value and contain compounds with new structure and pharmacological effects.
	Class 2 Improved new drugs which have never been marketed within or outside China	2.1-Drug substances and preparations which contain optical isomers of the known active ingredients by using the splitting or the synthesis method; turn known active ingredients into ester or salt(including salt containing hydrogen bonds or coordination bonds); change the acid radical, alkali base or metal element of the known active ingredients of salts; or turn into other non-covalent bond derivatives (such as complex chelate or inclusion compound), which also have an obvious clinical advantage.
		2.2-New drug preparations using the new dosage form(including the new drug delivery system); the new prescription process or the administration route of known active ingredients, and which also have an obvious clinical advantage.
		2.3- New compound preparations of known active ingredients, which also have an obvious clinical advantage.
		2.4-New preparations of known active ingredients with new indications
Generic	Class 3 Domestic drugs which imitate innovative drugs that have not been marketed within China but have been marketed outside of China	Drug substances or preparations that have the same active ingredients, dosage form, strengths, indication, administration route, usage and dosage as innovative drugs
	Class 4 Domestic drugs which imitate innovative drugs that have been marketed within China	Drug substances or preparations that have the same active ingredients, dosage form, strengths, indication, administration route, usage and dosage as innovative drugs
Imported Drugs	Class 5 Imported drugs which have been marketed outside China, apply China domestic market approval.	5.1-Innovative drugs (including drug substances and preparations) that have approved outside China
		5.2-Non-innovative drugs (including drug substances and preparations) that have approved outside China

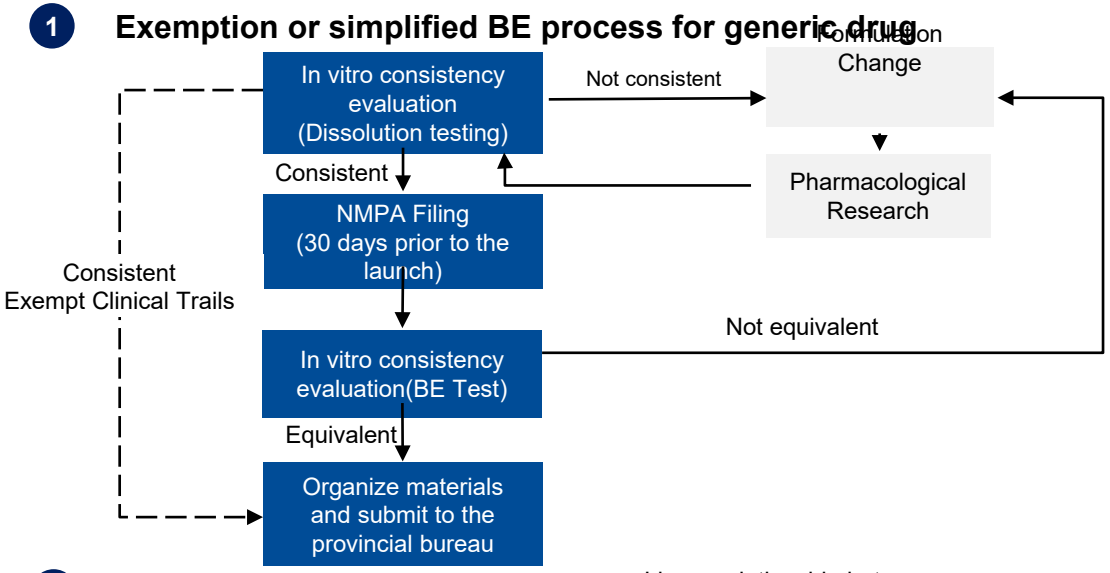
Source: NMPA, Frost & Sullivan Analysis

Comparison of BE process for generic drug and inhalations

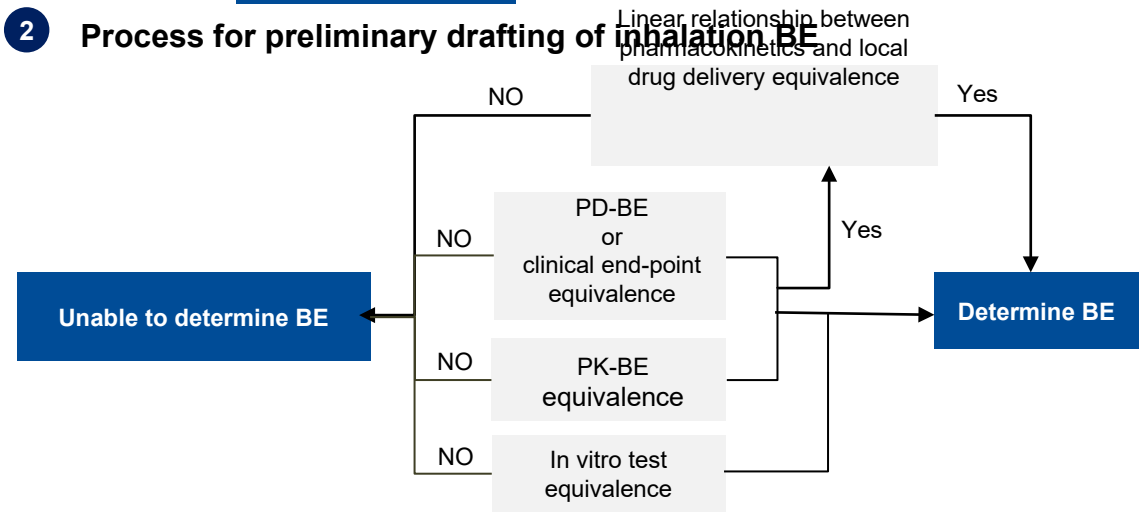
Key Information

- In 2018, the State Drug Administration (SDA) released the Drug Varieties Subject to Exempted or Simplified Human Bioequivalence (BE) Test, which identified a list of 48 varieties in the 289 catalog that can exempt or simplify BE testing based on the BCS classification principles. Most of the products are widely used in clinical practice, with large demand, but low price and small profit margin.
- Inhalations, unlike traditional dosage forms, are designed to act locally on the lung and their drug delivery is not solely dependent on systemic circulation. Finding clinically relevant biomarkers that can detect potential differences in local drug delivery is challenging. Therefore, the combination of inhalation formulation and device increases the complexity of BE establishment.

1 Exemption or simplified BE process for generic drug



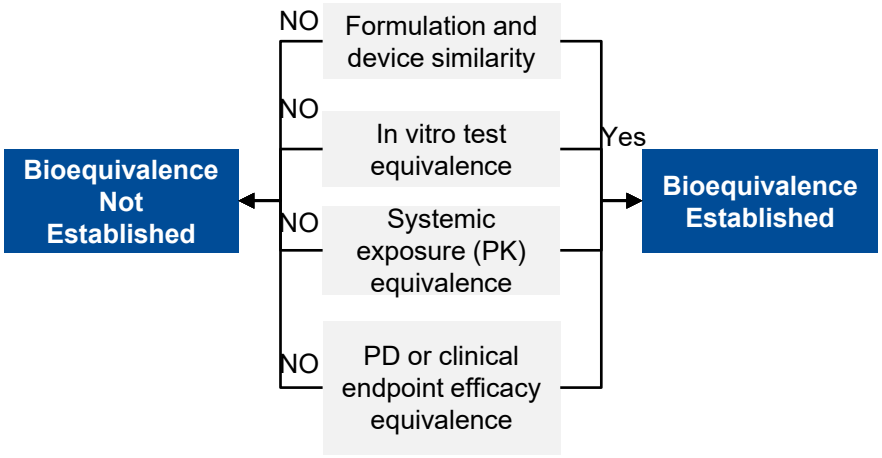
2 Process for preliminary drafting of inhalation BE



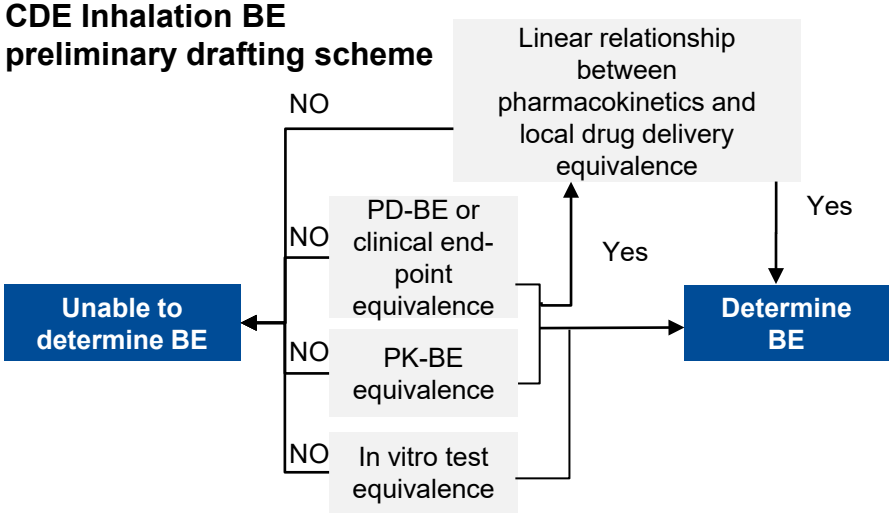
Source: CDE, & Sullivan analysis

Comparison of BE for Inhalation in China with FDA and EMA

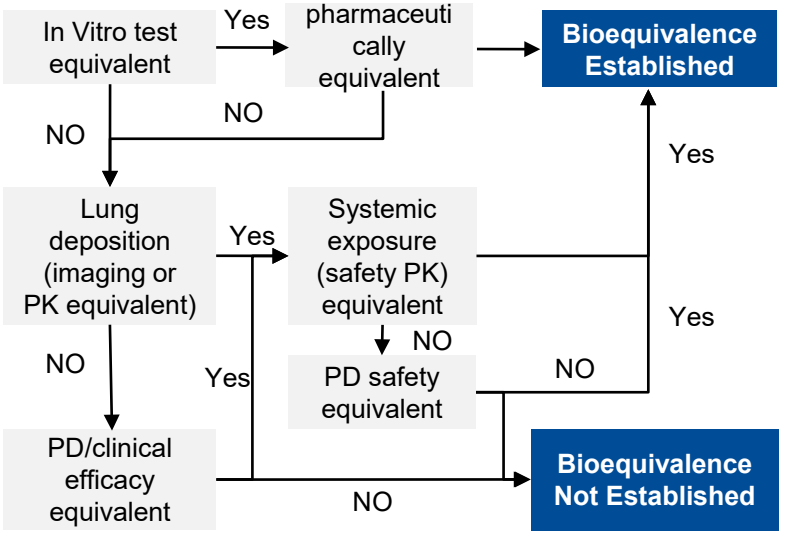
FDA: weight-of-evidence approach



CDE Inhalation BE preliminary drafting scheme



EMA：step-wise approach



Key Findings：

- The concentrations in target tissues after administration of locally acting Inhalation Formulations are asynchronous with blood concentrations, and there is a lack of correlation between their pharmacokinetics and effect/toxicity organ exposure; classical pharmacokinetic studies have limitations for Inhalation Formulations.
- The FDA uses the weight-of-evidence approach, which is the most stringent. All four BE requirements for generic inhalation drug should be met before the final bioequivalence can be determined. The EMA requirements are relatively loose, and there are more bioequivalence BE pass conditions. The CDE as a whole is similar to the FDA's BE criteria for inhalation, and multiple conditions need to be met at the same time to determine BE. The evaluation system is gradually becoming more complete.

Source: FDA, EMA, CDE, Frost & Sullivan analysis

Analysis of Consistency Evaluation of Inhalation Formulation (1/2)

Evaluation Methodology	Specific details	Main content
Evaluation methods for pharmaceutical research	Liquid preparation for Nebulization	For inhalation solutions, generic preparations should usually use the same prescriptions, non-invasive production processes and packaging materials as the reference preparations, with the same key quality attributes
	Metered dose inhaler	Consistent with the prescription of the reference preparation, and with the API presence form (dissolved state, crystal form, shape/crystal habit, particle size, etc.), spray characteristics spray pattern, spray geometry, etc.) and inhalation characteristics (delivery dose, micro-particle aerodynamic characteristics, etc.) as well as other key quality attribute
	Dry powder inhaler	Consistent with reference preparation's key quality attributes such as the prescriptions and inhalation characteristics(e.g. delivery dose, aerodynamic characteristics of fine particles). Special attention should be paid to the presence of generic preparations and reference preparations in the form of raw materials and excipients (such as the crystal form of API, shape/crystal habit, particle size, etc., the shape of excipients, surface morphology, particle size, the combination of raw materials and excipients, etc.)

Source: CDE, Frost & Sullivan analysis

Analysis of Consistency Evaluation of Inhalation Formulation (2/2)

Evaluation Methodology	Specific details	Main content
Evaluation methods for human bioequivalence studies	PK-BE Research	The general requirements and experimental design can be referred to *the Technical Guidelines for Human Bioequivalence Studies of Generic Chemical Drugs with Pharmacokinetic Parameters as Endpoint Evaluation Indicators*, focusing on bioequivalence evaluation indicators and acceptance criteria
	PD-BE Research	It is suggested that the equivalence endpoint should be set in advance, and the sensitive dose of the steep part of the 136 dose response curve should be selected to evaluate the equivalence of drug effectiveness. If PK data cannot be obtained, a PD study with the maximum recommended dose should be conducted to evaluate the safety
	Research of Clinical endpoints	For ICS, a randomized, double-blind, positive drug-parallel controlled trial design is recommended to demonstrate non-inferiority. The effect of hormones on the lower HPA axis is also monitored. For products with indications that include both asthma and COPD, equivalence of treatment for asthma can generally be analogous to COPD, obtaining two indications simultaneously.
	Study of fixed-dose compound preparation	For fixed-dose compounded preparations with known active ingredients, the PK-BE of each active ingredient in the compound should be demonstrated separately in PK-BE studies, and the effectiveness of all active ingredients should be considered together in PD-BE or clinical endpoint studies
	Studies on the presence of multiple specification preparations	For generic Orally Inhaled Drug Products requiring BE studies, (1) PK-BE studies are usually recommended for each specification; (2) PD-BE or clinical endpoint studies should be considered for all declared specifications

Key Findings:

- In December 2020 the CDE released the Guidelines for Pharmacological and Human Bioequivalence Studies of Generic Orally Inhaled Drug Products which clarify that in order to adequately evaluate the consistency of generic orally Inhalation Formulation with reference preparation, under the premise of consistent in vitro pharmacological quality between the tested preparation and the reference preparation, PK-BE, PD-BE, and clinical Endpoint studies could demonstrate BE. For inhaled preparations, it is very difficult to achieve both in vitro and in vivo consistency.

Source: CDE, Frost & Sullivan analysis

International and Domestic Guidelines on Bioequivalence of Human PK Studies

Comparison Items	FDA	EMA	CDE
Method	Single-dose double crossover study design under fasted conditions	Single dose in patient population to study pulmonary deposition and systemic exposure (optional use of imaging to study pulmonary deposition equivalence)	Randomized, single-dose, crossover design study design under fasted conditions
Dosage	Minimum inhalation volume sufficient to characterize the PK curve	Minimum inhalation volume detectable by current technology	Select the minimum inhalation amount sufficient to characterize the PK properties and detectable by current technology
Time	Sampling time should cover the expected pulmonary absorption and gastrointestinal absorption time		
Population	Healthy Subjects	Target Patients	Healthy Subjects
Measured Object	Usually the active ingredient of the drug in the plasma		
Grade Standard	The 90% confidence interval (CI) for the geometric mean T/R ratio of AUC is within 80.00% ~ 125.00%; the 90% CI for the C_{max} ratio (T/R) is within 80.00% ~ 125.00%	90% CI for T_{max}, C_{max} ratio (T/R) between 80.00% and 125.00%; 90% confidence interval for the geometric mean T/R ratio of AUC between 80.00% and 125.00% (when using imaging studies: 90% confidence interval for radioactivity in each region between 80.00% and 125.00% using 2D scintigraphy)	The 90% confidence interval for the geometric mean T/R ratio of C_{max}, $AUC_{0-\infty}$ and AUC_{0-1} was within 80.00% ~ 125.00%

Source：Frost & Sullivan Analysis

Guidance on Vitro Testing in Bioequivalence Studies

Comparison Items	FDA	EMA	CDE
Active Ingredients	The polymorphism and crystallization of APIs exist in the same form	Same form of active substance	Same form as the reference formulation
Inactive Ingredients	Qualitative same, quantitative basically the same (same ±5% or less)	Any qualitative or quantitative differences in excipients should not affect the performance of the product	Same form as the reference formulation
Drug Delivery Device	Similar shape, size and intrinsic resistance of the equipment, same basic operation, functional mechanism and metering principle	The operation of releasing a sufficient amount of actives should be similar, with the same intrinsic resistance	Principle, structure, delivery method, packaging form, and intrinsic resistance approximation of drug delivery devices
Delivered Dosage	Average delivered dose or single actuation content test with population bioequivalence as the equivalence criterion	Target delivery dose should be similar (±15% difference)	Same delivery rate and delivery dosage
Aerodynamic Particle Size Distribution	The particle size distribution of the drug particles should be similar when measured using a validated particle size measurement method (e.g., laser diffraction)	At least 3 batches of test and reference preparations should be used to compare each Phase of the cascade impinger (limit of variation ± 15%)	Consistent aerodynamic properties and particle size of fine particles

Source：Frost & Sullivan Analysis

International and Domestic Guidelines on Bioequivalence of Human PD and Clinical Endpoint Studies

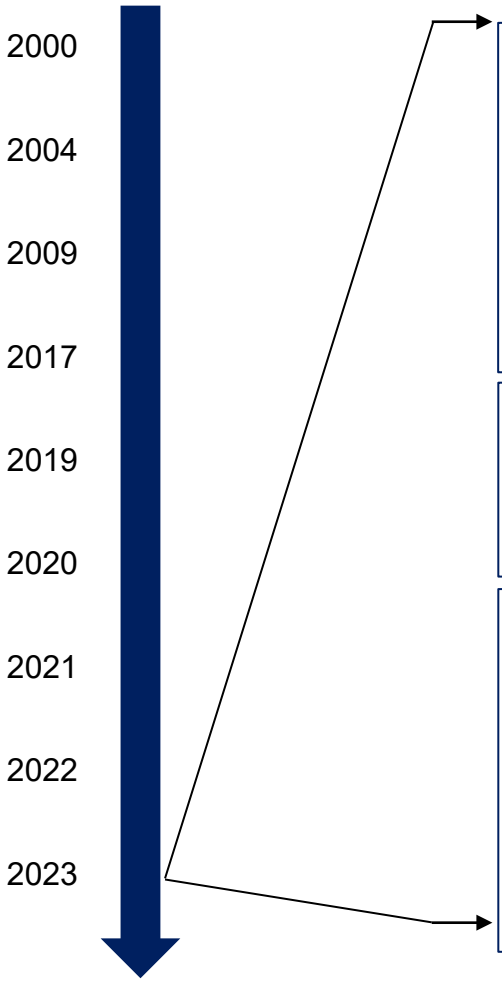
Comparison Items	FDA	EMA	CDE
Method	Randomized, double-blind, multi-dose, cross-reference study	Research on bronchodilation, improvement of airway function and broncho-protection	Single-word administration of bronchodilator or bronchial provocation test; randomized, double-blind, positive drug-parallel controlled trial design
Indicators	FeV_1, FeNO	FEV_1, PEF	Lung function indicators

FeNO: Exhale nitric oxide; PEF; Peak expiratory flow

Source：Frost & Sullivan Analysis

Adjustment of Inhalation by Dynamic Adjustment Mechanism of NRDL

NRDL Progress



The latest progress of the 2023 edition of NRDL

In December 2023, China's National Healthcare Security Administration (NHSA) published the 2023 National Reimbursement Drug List (2023 NRDL), implementing a comparable level of pricing discounts to those seen in 2021.
The simple renewal mechanism was refined in 2023, and the price adjustment mechanism was also introduced to cover the entire drug lifecycle, leading to a further slowdown in the rate of price cuts and providing a more predictable market access environment to pharmaceutical companies.

A total of 126 drugs were added to the 2023 NRDL, and one drug was removed. Out of 143 negotiated drugs/drugs participating in bidding, 121 drugs were successfully included in the final NRDL. The success rate was 84.6%, and the average price cut of the 121 drugs was 61.7%, close to 2022's 60.1%.

Since establishment of National Healthcare Security Administration , the NHSA has carried out the adjustment of the NRDL for six years, **newly adding 744 drugs** to the NRDL in total, and removing a number of drugs with uncertain efficacy, clinical abuse or elimination, leading to profound changes in the use of drugs.
Since 2018, the proportion of medical insurance drugs used in medical institutions has increased year by year, and the dominant position has been further consolidated, and the rationality of clinical drug use has been improved.

Inhalation Area Adjustment

Due to the large price reduction of generic drugs by volume-based procurement and the fact that innovative drugs are time-consuming and costly, recently, there has been an upsurge in the R&D of improved preparations in China. The food and drug administration has also issued relevant regulations. For this time, 6 new inhalants have passed the review, and many negotiations are expected to succeed.

Among them, 3 inhalations for respiratory diseases has been involved in the NRDL 2023: 1) Procaterol Hydrochloride DPI (short-acting β agonist inhalers) entered medical insurance catalogue 2020, and its solution for inhalation entered NRDL 2023; 2) Azelastine Hydrochloride and Fluticasone Propionate Nasal Spray first entered medical insurance catalog, which provided 2 types of first-line therapies for the treatment of allergic rhinitis; 3) Ambroxol Hydrochloride Solution For Inhalation first entered NRDL, which is indicated for the treatment of allergic rhinitis secretion disorders in acute and chronic bronchopulmonary affections.

One of the highlights is that the new 2023 edition of the NRDL relaxes restrictions on some inhalation products, including removal of the previous “moderate to severe” restriction of Umeclidinium Bromide and Vilanterol Trifenatate Powder for Inhalation.

Source: Ministry of Human Resources and Social Security of the PRC, Frost & Sullivan analysis

NRDL Dynamic Adjustment Relax Restrictions for Inhalation (1/2)

Category	Name	2009 NRDL	2017 NRDL	2019 NRDL	2020 NRDL	2021 NRDL	2022 NRDL	2023 NRDL
Aerosol	Glycopyrronium Bromide and Formoterol Fumarate	N/A	N/A	N/A	List B	List B	List B	List B
Aerosol, Nebuliaztion, Nasal spray	Fluticasone Furoate	N/A	N/A	N/A	List B	List B	List B	List B
Aerosol, DPI, Nebuliaztion, Nasal spray	Beclometasone Dipropionate	List B	List A	List A	List A	List A	List A	List A
Aerosol	Beclometasone Dipropionate and Formoterol	N/A	List B limited to second-line therapy	List B	List B	List B	List B	List B
Aerosol, DPI, Nebuliaztion, Nasal spray	**Budesonide**	**List B**	**List B limited to second-line therapy**	**List B**	**List B**	**List B**	**List B**	**List B**
Aerosol, Nebuliaztion, Nasal spray	Fluticasone	List B	List B	List B	List B	List B	List B	List B
Nasal spray	**Mometasone Furoate**	**N/A**	**List B**	**List B**	**List B**	**List B**	**List B**	**List B**
Nasal spray	Triamcinolone Acetonide	List C	List B	List B	List B	List B	List B	List B
Aerosol, DPI, Nebuliaztion	**Salbutamol**	**List B**	**List A**	**List A**	**List A**	**List A**	**List A**	**List A**
Nebulization	Levosalbutamol	N/A	N/A	N/A	List B	List B	List B	List B
DPI, Nebulization	Procaterol	N/A	N/A	N/A	List B	List B	List B	List B
DPI	Budesonide and Formoterol	List B limited to second-line therapy	List B limited to second-line therapy	List B	List B	List B	List B	List B

Note: ⇕ Relaxation of restrictions
Restrictions increase

Source: National Healthcare Security Administration, Ministry of Human Resources and Social Security of the PRC, Frost & Sullivan analysis

NRDL Dynamic Adjustment Relax Restrictions for Inhalation (2/2)

Category	Name	2009 NRDL	2017 NRDL	2019 NRDL	2020 NRDL	2021 NRDL	2022 NRDL	2023 NRDL
Nebuliaztion, DPI	Formoterol	List B limited to second-line therapy	List B limited to second-line therapy	List B	List B	List B	List B	List B
Aerosol, DPI	Salmeterol	List B limited to second-line therapy	List B limited to second-line therapy	List B	List B	List B	List B	List B
Aerosol, DPI	**Fluticasone and Salmeterol**	**List B limited to second-line therapy**	**List B limited to second-line therapy**	**List B**	**List B**	**List B**	**List B**	**List B**
Aerosol, DPI, Nebuliaztion	**Terbutaline**	List B	List B	List B	List B	List B	List B	List B
Nebulization	Ambroxol Hydrochloride	N/A	N/A	N/A	N/A	N/A	N/A	List B
Aerosol, Nebuliaztion	Ipratropium Bromide	List B	List A	List A	List A	List A	List A	List A
Aerosol, Nebuliaztion	Ipratropine Bromide and Salbutamol	List B limited to second-line therapy	List B	List B	List B	List B	List B	List B
Aerosol, DPI	**Tiotropium Bromide**	**List B**	**List B**	**List B**	**List B**	**List B**	**List B**	**List B**
Aerosol	Sodium Cromoglicate	List B	List B	List B	List B	List B	List B	List B
DPI	Umeclidinium Bromide and Vilanterol Trifenatate	N/A	N/A	Limited to moderate to severe COPD	Limited to moderate to severe COPD	Limited to moderate to severe COPD	Limited to moderate to severe COPD	COPD

Note：↘ Relaxation of restrictions
↗ Restrictions increase

Key Findings: The new 2023 edition of the NRDL relaxes restrictions on some inhalation products, including four products into the scope of **List** B. The latest adjustment to expand the scope of inhalations in the health reimbursement has a positive effect on the R&D, production, and commercialization of inhalations.

Source: National Healthcare Security Administration, Ministry of Human Resources and Social Security of the PRC, Frost & Sullivan analysis

Inhalation R&D Favorable Policies

Healthy China Initiative (2019-2030)

Objective: By 2022 and 2030, the mortality rate of chronic respiratory diseases for people aged 70 and below will decrease to 90,000/100,000 and below and 81,000/100,000 and below, respectively;
The rate of awareness for COPD among people aged 40 and above will reach 15% and above and 30% and above, respectively.

Action Plan for the Prevention and Treatment of Chronic Respiratory Diseases 2024-2030

Background: To implement the decisions and deployments of the Central Committee of the Communist Party of China regarding the Health China Strategy, and to fulfill the requirements of the “State Council‘s Opinions on Implementing the Healthy China Action” and the “Healthy China Action (2019-2030)“ (健康中国行动2019-2030年), this implementation plan is formulated to deepen the prevention and control of chronic respiratory diseases and to improve the respiratory health levels of residents in our country.

Government Policy

- Incorporate pulmonary function tests into routine medical examinations for people aged 40 and above. Promote the measurement of lung function for high-risk groups, and provide timely referral services for patients who are suspected to have COPD. Promote local community health service centers and township health centers to equip with lung function examine equipment, etc., and improve the training for professional workers. (National Health Commission takes the lead, and the National Development and Reform Commission and Ministry of Finance divide the labor according to each responsibilities)
- Study includes the health management of patients with COPD into the national basic public health service items, makes sure the implementation of the hierarchical diagnosis and treatment system, provides screening intervention, diagnosis, treatment, follow-up management, functional rehabilitation and other full prevention and management services for COPD patients and people at risk , and improves the rate of early diagnosis and treatment of COPD and standardized management rate at the early stage. (National Health Commission takes the lead, and the Ministry of Finance takes its responsibility)
- Focus on improving the prevention and treatment level of chronic respiratory diseases at local level, and strengthen the allocation of relevant diagnosis and treatment equipment (inhalators, oxygen therapy equipment, non-invasive ventilator, etc.) and long-term treatment management drugs in local medical institutions(National Health Commission takes the lead, and the National Development and Reform Commission and Ministry of Finance divide the labor according to each responsibilities)
- Enhance primary healthcare service capacity for the prevention and treatment of chronic respiratory diseases. Strengthen standardized training for primary medical staff on the screening and diagnosis of common chronic respiratory diseases, and improve the ability of primary healthcare institutions to screen high-risk populations, make preliminary diagnoses, and manage health for chronic respiratory diseases. Enhance the availability of diagnostic and treatment equipment and medications for long-term control of COPD in primary healthcare institutions

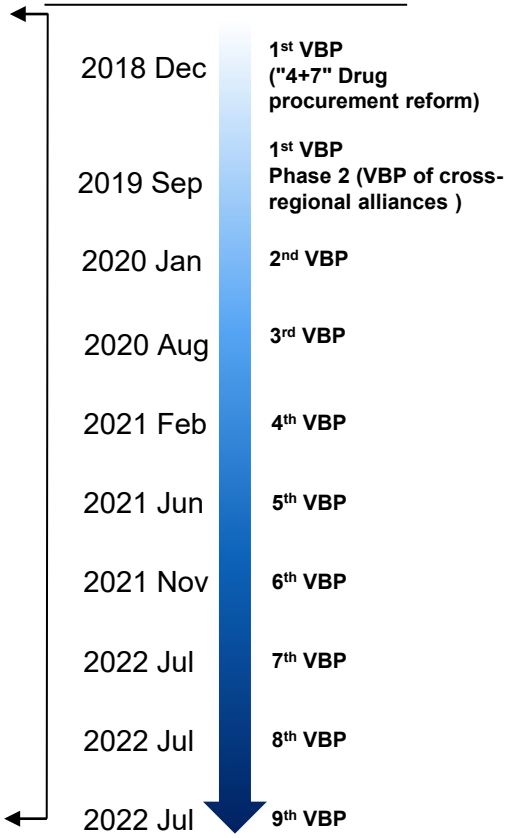
Source: Healthy China initiative, Frost & Sullivan analysis

National Centralized Drug Procurement in China

- Led and organized by the National Healthcare Security Administration (NHSA), the NCDP policy is implemented through a comprehensive service platform. NHSA selects drugs with sufficient market competition and large market scale, negotiates prices with enterprises (no distinction between brand-name drug and generic drug) based on their quoted prices, supply capacity, market recognition and other comprehensive conditions. The bid-winning enterprise reduces its price drastically, and in order to guarantee its benefits, NHSA promises 50%—70% of the total annual drug utilization volume of all public medical institutions in the alliance regions (different proportions are set according to the characteristics of drugs).

- The latest and ninth round of China's centralized drug procurement program has resulted in an average price cut of 58% on 41 types of medicine.
- Drugs involved in the bulk-buy tackle diseases including high blood pressure, diabetes, cancer, infection, and gastrointestinal and cardiovascular conditions, and around half of them are injectable medications.
- The price reduction is expected to save RMB18.2 billion annually. Patients can access drugs at the discounted prices in March, it added. The bidding involved 382 medical products from 262 enterprises, and around 78 percent of participating companies ended up winning bids.

Progression of VBP



Inclusion of Inhalation Formulation

No. Round	Generic Name	No. Manufacturers
4th	Salbutamol	4
5th	Budesonide	4
	Ipratropium Bromide	4
	Ipratropium Bromide Compound	4
7th	Terbutaline	5
9th	Levosalbutamol	8

Source: Frost & Sullivan analysis

National Centralized Drug Procurement in China

Impact on The Inhalation Formulation

1

Domestic Inhalation Replacing Imported

- The NCDP policy promoted the substitution of domestic drugs for imported drugs. Since the first inhaler involved in the 4th VBP, all bid-winning enterprises are domestic. The NCDP policy altered the medication behavior of medical institutions through the substitution of bid-winning brands for bid-non-winning brands. Prices of bid-winning brands significantly decrease. Therefore, it is evident that bid-winning enterprises would enjoy a significant pricing advantage.
- On the other hand, bid-winning enterprises occupy 50%-70% market share of policy-related drugs in the next procurement cycle. Policy-related drugs also have direct access to medical institutions, which means that after policy intervention, bid-winning enterprises would dominate the market compared to bid-non-winning enterprises.

2

Significant Increase of Substitution of Generic Drugs for Innovative Drugs

- There was a significant increase of substitution of generic drugs for original drugs. Originators will be gradually replaced by generic drugs in the centralized drug procurement.
- Originators have higher R&D expenditures and have limited room for price reduction and lack of motivation to participated in the national centralized drug procurement. Since the first inhaler involved in the 4th VBP, no original inhalation drugs were included.

3

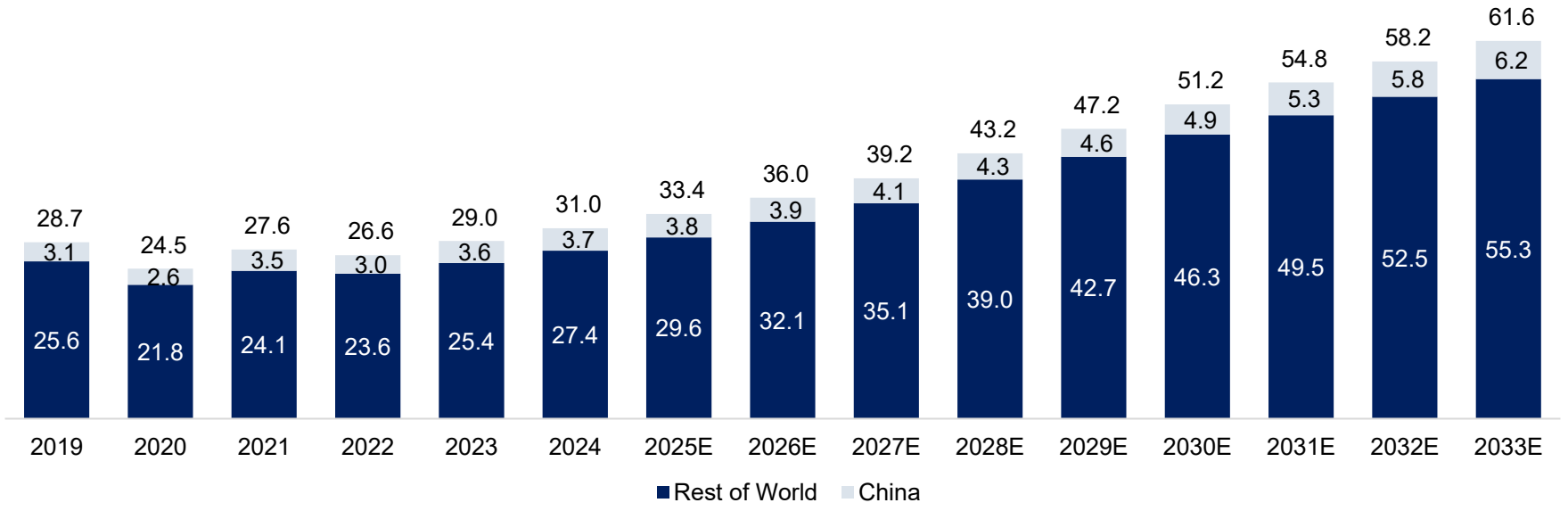
Improving the Utilization Volume

- Domestic inhaler manufacturers that are able to survive in the long run of drug procurement could be those with extensive drug portfolio, cost-saving capability, brand recognition. To cope with this challenge also opportunity, domestic companies are expected to reduce the production and sales & marketing expenditures, expand their product line, invest more in R&D.
- By contrast, with the promotion of NCDP Program, large-scale pharmaceutical companies are faced with more challenges such as the “Patent Cliff”. Meanwhile, because of smaller profit margins, innovative pharmaceutical companies with better cost control will stand out from fierce competition.

Global and China Market Size of Inhalation Formulations, 2019-2033E

Period	China	Global
2019-2024	3.3%	1.6%
2024-2033E	6.1%	7.9%

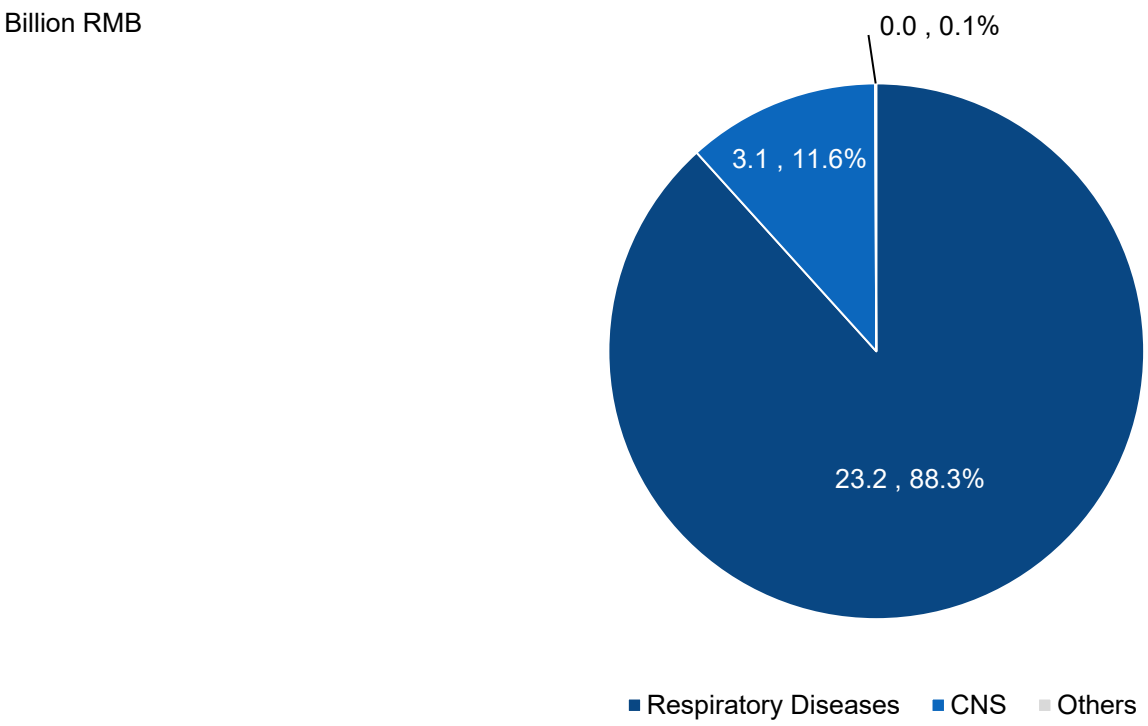
Billion USD



Breakdown of Inhalation Formulations Market in China by Indication, 2024

- In 2024, respiratory disease have the largest inhalation formulation market in China, accounting for 88.3% of the total with a market size of RMB23.2 billion in 2024.

Breakdown of Inhalation Formulations Market in China by Indication, 2024

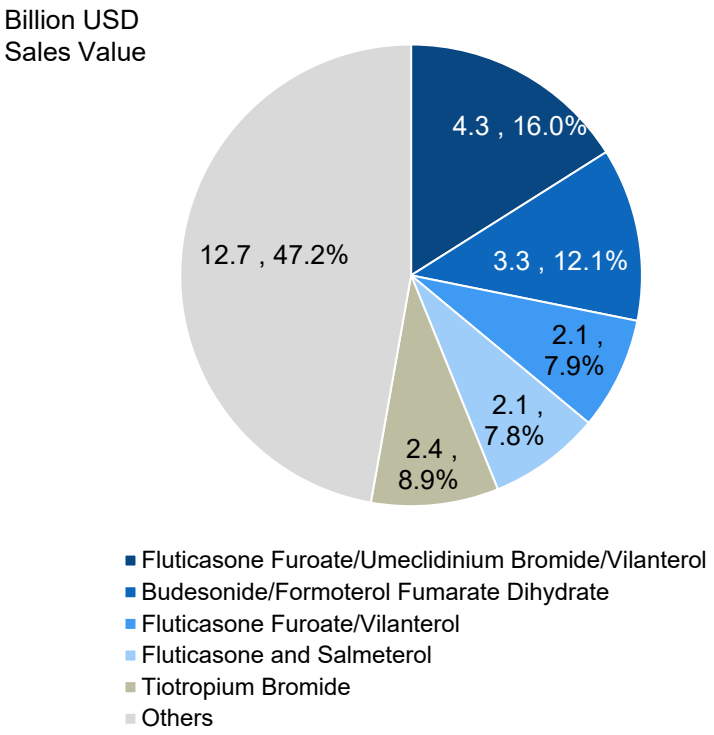


Source: Frost & Sullivan analysis

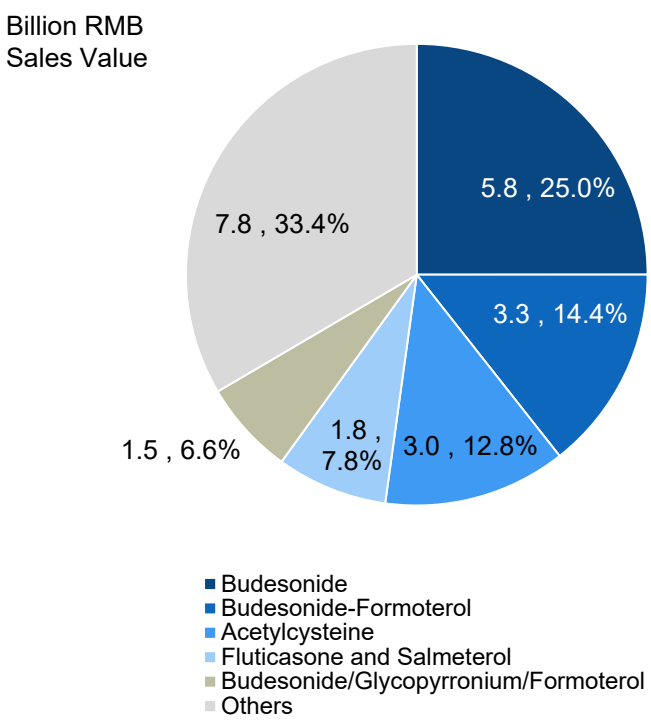
Breakdown of Global and China Respiratory Disease Inhalation Formulations Market by Generic Name, 2024

- In 2024, Budesonide have the largest inhalation preparation market in China, accounting for 25.0% of the total with a market size of RMB5.8 billion in 2024. Budesonide Formoterol is the second largest inhalation preparation market after Budesonide, accounting for 14.4% of the total Chinese market.

Breakdown of Global Respiratory Disease Inhalation Formulations Market by Generic Name, 2024



Breakdown of China Respiratory Disease Inhalation Formulations Market by Generic Name, 2024



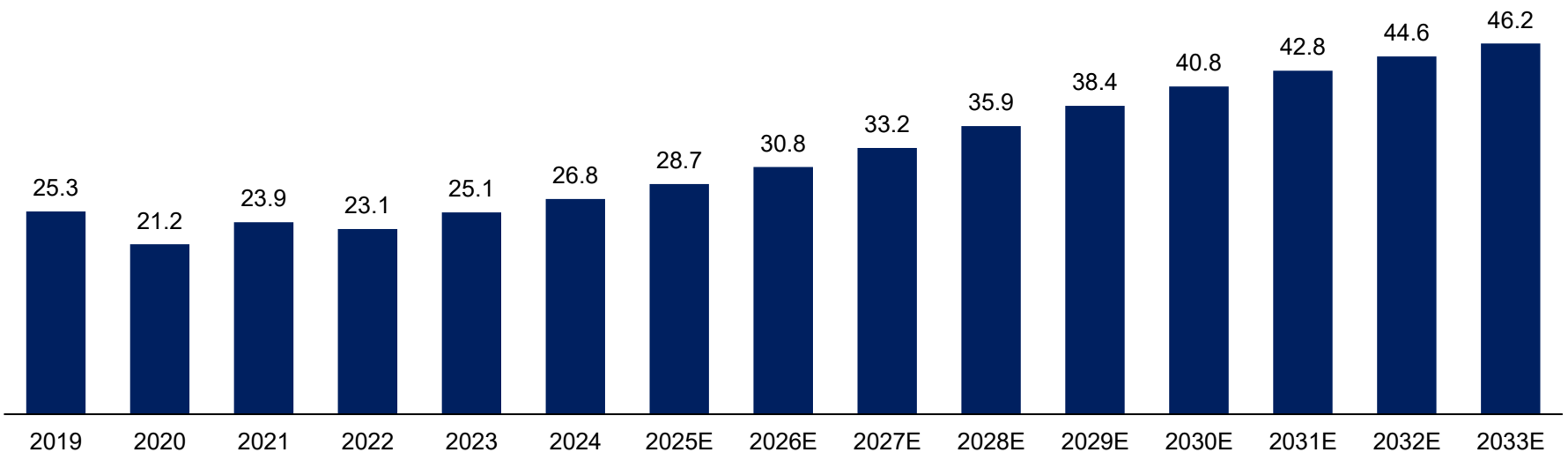
Source: Frost & Sullivan analysis

Global Market Size of Inhalation Formulations for Respiratory Diseases, 2019-2033E

- From 2019 to 2024, global market of inhalation formulations for respiratory diseases in decreased from USD25.3 billion to USD26.8 billion, representing a CAGR of 1.2%, and is expected to reach USD35.9 billion and USD46.2 billion by 2028 and 2033, with a CAGR of 6.2% from 2024 to 2033.

Breakdown of Global Market Size of Inhalation Formulations for Respiratory Diseases, 2019-2033E

Period	CAGR
2019-2024	1.2%
2024-2033E	6.2%



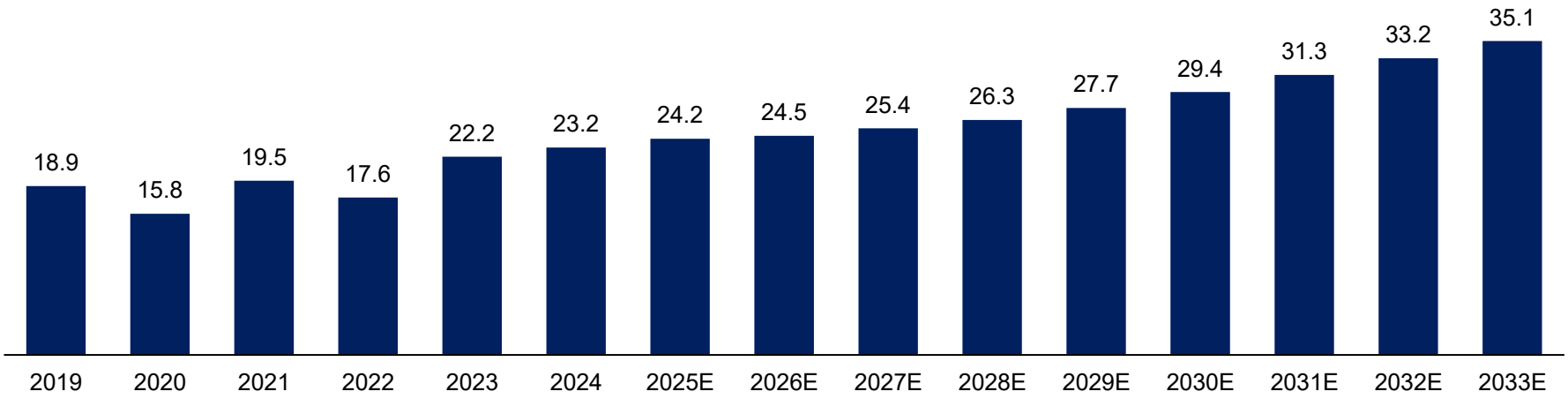
Source: Frost & Sullivan analysis

Market Size of Inhalation Formulations for Respiratory Diseases in China, 2019-2033E

- From 2019 to 2024, China market of inhalation formulations for respiratory diseases in China increased from RMB18.9 billion to RMB23.2 billion, representing a CAGR of 4.2%, and is expected to reach RMB26.3 billion and RMB35.1 billion by 2028 and 2033, with a CAGR of 3.2% and 6.0% from 2024 to 2028 and from 2028 to 2033 respectively.

Breakdown of Market Size of Inhalation Formulations for Respiratory Diseases in China, 2019-2033E

Period	CAGR
2019-2024	4.2%
2024-2033E	4.7%

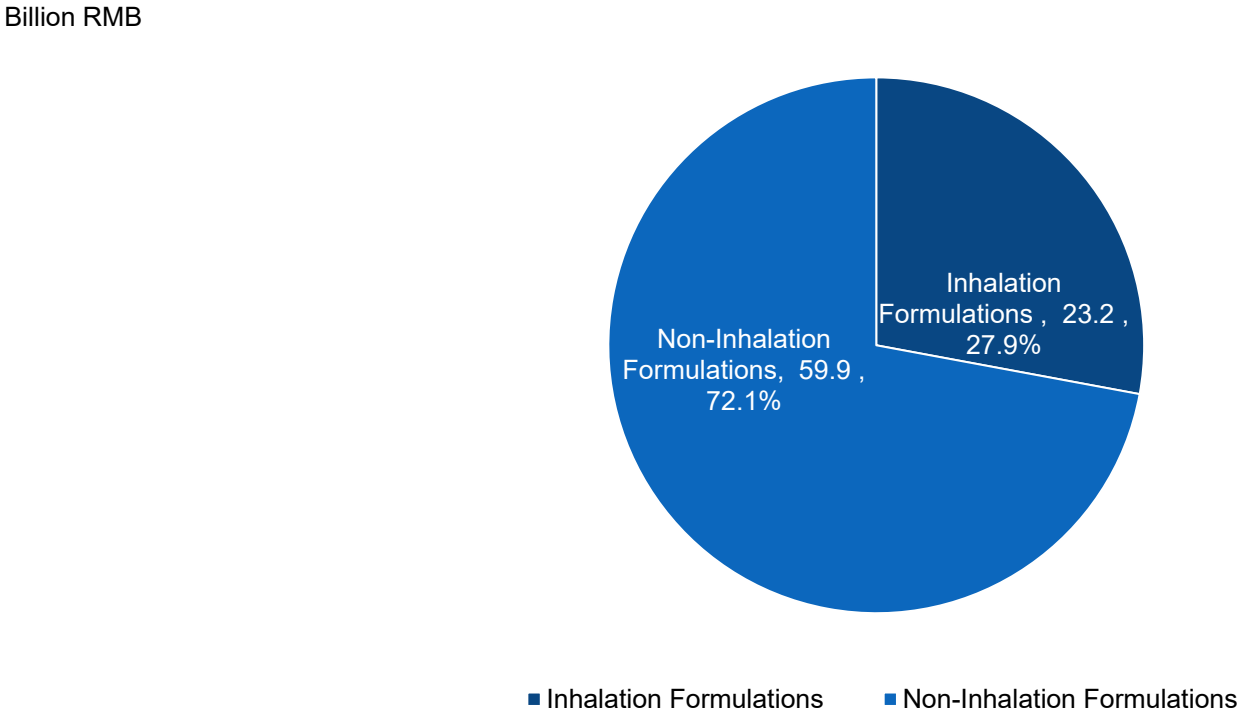


Source: Frost & Sullivan analysis

Breakdown of China Respiratory System Pharmaceutical Market, 2024

- In 2024, China market of inhalation formulations for respiratory diseases reached RMB23.2 billion, accounting for 27.9% of the total respiratory system pharmaceutical market which reached RMB 83.1 billion in 2024.

Breakdown of China Respiratory System Pharmaceutical Market, 2024



Source: Frost & Sullivan analysis

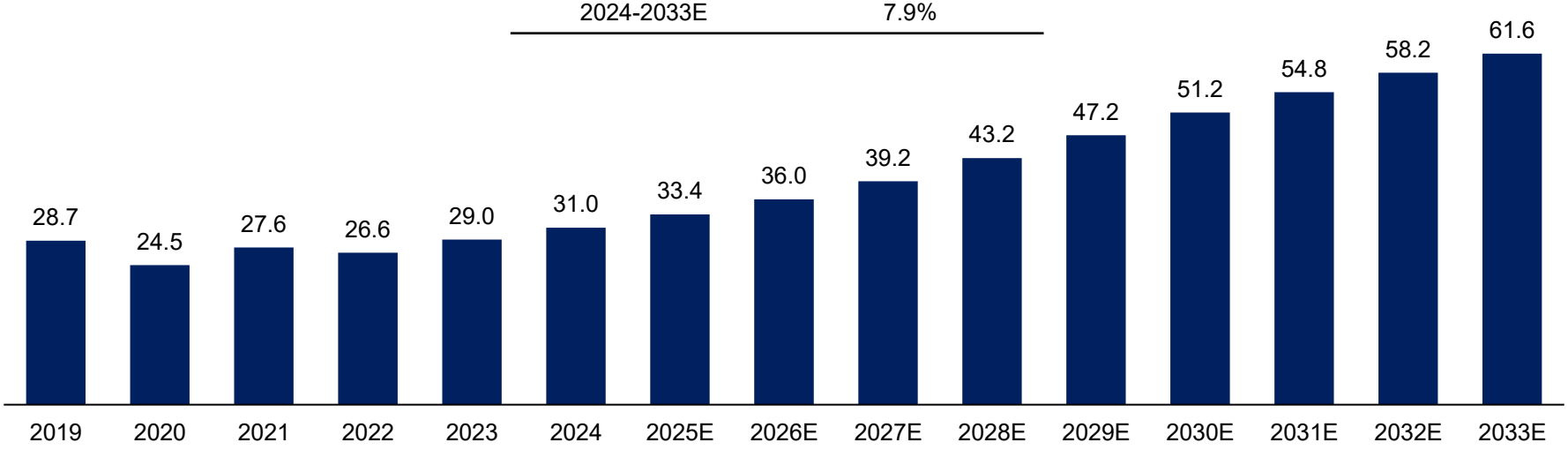
Global Market Size of Inhalation Formulations, 2019-2033E

- From 2019 to 2024, global market of inhalation formulations increased from USD28.7 billion to USD31.0 billion, representing a CAGR of 1.6%, and is expected to reach RMB43.2 billion and RMB61.6 billion by 2028 and 2033, with a CAGR of 8.6% and 7.3% from 2024 to 2028 and from 2028 to 2033 respectively.

Breakdown of Global Market Size of Inhalation Formulations, 2019-2033E

Billion USD

Period	CAGR
2019-2024	1.6%
2024-2033E	7.9%



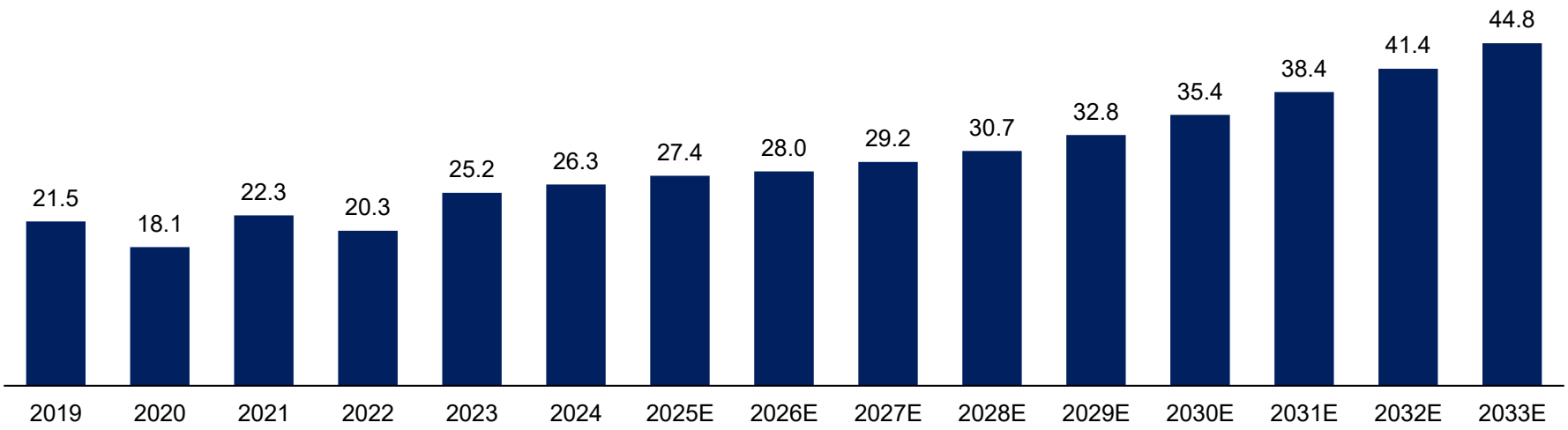
Source: Frost & Sullivan analysis

Breakdown of Market Size of Inhalation Formulations in China, 2019-2033E

- From 2019 to 2024, China market of inhalation formulations increased from RMB21.5 billion to RMB26.3 billion, representing a CAGR of 4.1%, and is expected to reach RMB30.7 billion and RMB44.8 billion by 2028 and 2033, with a CAGR of 3.9% and 7.8% from 2024 to 2028 and from 2028 to 2033 respectively.

Breakdown of Market Size of Inhalation Formulations in China, 2019-2033E

Period	CAGR
2019-2024	4.1%
2024-2033E	6.1%



Source: Frost & Sullivan analysis

Global Top10 Inhalation Formulation in Respiratory Diseases by Sales Revenue, 2024

Rank	Brand Name	Generic Name	Manufacturer Name	Device Type	2024 Sales Revenue, USD Billion
1	Trelegy/Ellipta	Fluticasone Furoate/ Umeclidinium Bromide/Vilanterol	GSK	DPI	3.5
2	Symbicort	Budesonide/ Formoterol Fumarate Dihydrate	AZ	MDI/DPI	2.9
3	BreoEllipta	Fluticasone Furoate/Vilanterol	GSK	DPI	1.4
4	**Seretide/Advair**	**Fluticasone/Salmeterol**	**GSK**	**MDI/DPI**	**1.4**
5	**Spiriva**	**Tiotropium Bromide**	**BI**	**DPI**	**1.1**
6	Breztri/Trixeo	Budesonide/Glycopyrrolate/ Formoterol	AZ	MDI	1.0
7	**Ventolin**	**Salbutamol**	**GSK**	**MDI**	0.9
8	Anoro/Ellipta	Umeclidinium Bromide/Vilanterol	GSK	DPI	0.7
9	**Pulmicort**	**Budesonide**	**AZ**	**Nebulization (Suspension)/DPI**	**0.7**
10	Flixotide/Flovent	Fluticasone Propionate	GSK	MDI/DPI	0.7

Source: Annual Report, Frost & Sullivan analysis

Global and China Competitive Landscape of Inhaler Manufacturers

- In addition to the rising prevalence of respiratory diseases, the increasing product developmental activities is also expected to drive the demand for respiratory inhalations. For instance, BI developed a novel inhalation formulation - the Respimat® Soft Mist™ Inhaler (SMI) in response to the need for a pocket-sized device that can generate a single-breath, inhalable aerosol from a drug solution using a patient-independent, reproducible, and environmentally friendly energy supply.
- The key respiratory inhalers companies operating in the global market include AZ, BI, GSK and Chiesi. The domestic market for inhalation formulation is growing rapidly. The domestic manufacturers, such as Joincare, Chia Tai-tianqing Pharmaceutical and Sichuan Purity, with research and development capabilities, have leveraged their price and production advantage, and accelerated the domestic substitution of China inhalation formulation market.

Company Name	Dry Powder Inhaler	Inhalation Aerosol/Metered Does Inhaler	Nebulization Inhaler	Soft Mist Inhaler	Nasal sprays
AZ	✓	✓	✓		✓
BI	✓	✓	✓	✓	△
GSK	✓	✓	✓		✓
Cipla	△	✓	△		✓
Chiesi	✓	✓	✓		△
Viatris/Pfizer	△	△	✓		✓

JoinCare	○	○	○		○
Chia Tai-tianqing Pharmaceutical	○	X	○		
Sichuan Purity	X	○	○		○
CF PharmTech	X	○	✓	X	○

Note: "✓" means approved in and outside of China; "△" means approved outside of China; "○" means approved only in China; "X" means at Pre-Clinical/Clinical Stage

Source: Annual Report, Frost & Sullivan analysis

CF PharmTech Product Porfolio

	ICS	ICS/H1	LABA	LAMA	LABA/LAMA	ICS/ LABA	ICS/ LAMA	ICS/ SABA	ICS/ LABA/ LAMA	SABA	SABA/SAMA
Nebulization			✓	X		X				✓✓	
Suspension	✓										
Nasal Spray	XX	✓									
Dry Powder Inhaler											
Inhalation Aerosol/Metered Does Inhaler				X	X	XXX					
DPI				XX	X						
MDI											

Note: “✓” means approved; “X” means at Clinical Stage

Growth Drivers for Inhalation Formulation Market

Changes in Disease Patterns, Safety, and Medication Adherence Issues Increase the Demand for Inhalation Formulations	• With China's aging population, the prevalence of chronic respiratory conditions, involving asthma and COPD is increasing. Long-term medication often leads to poor adherence among chronic respiratory disease patients, and drug safety issues affect clinical application. Inhalation Formulation have advantages that cannot be replaced by traditional delivery methods in the treatment of respiratory diseases. Inhalation formulation can directly reach the absorption or action site, with rapid absorption, avoiding the first-pass effect of the liver, reducing drugs doses and improving bioavailability, reducing the mechanical injury to local tissues and improving patient compliance. The higher safety and unique clinical benefits of inhalation formulation are driving growing demand and industry focus on inhalation formulations.
Enhanced Patient Empowerment	• With the continuous increase in per capita disposable income and the rising total expenditure on healthcare in various countries, patients' ability to afford inhaled medication has improved. Additionally, the continuous involvement of inhalation formulations by NRDL and NCDP has significantly alleviated the financial burden on patients.
Breakthroughs in Formulation Technology, Enhanced Product Quality	• In recent years, there have been significant breakthroughs in inhalation formulation technology, leading to enhanced product quality and improved patient outcomes. For instance, development of more efficient delivery systems have led to the creation of devices that are not only more user-friendly, but also more effective at delivering medication to the lungs. Furthermore, advancements in particle engineering have allowed for the creation of inhalable medications with improved properties, such as increased stability and enhanced dispersibility. These advancements have the potential to revolutionize the way in which respiratory medications are delivered, offering new hope to individuals suffering from conditions such as asthma, chronic obstructive pulmonary disease (COPD), and allergic rhinitis. As research and development in this field continues to progress, it is likely that we will see even more innovative solutions emerge, further improving the lives of patients with respiratory conditions.
Favorable Policies	• China government promulgated a series of policies to encourage the R&D, as well as strengthen the regulation on inhalation formulation market. • In 2021, the national “14th Five-Year Plan for the Development of the Pharmaceutical Industry” (“十四五”医药工业发展规划) emphasized the need to enhance high-end formulation production technologies. The focus is on developing complex formulation technologies with high selectivity and long-acting controlled release characteristics. The plan also aims to increase the registration of generic drugs in developed countries and raise the proportion of high-value-added products, such as first generic drugs and complex formulations. Furthermore, “Consultation guidance on generic orally inhaled drug products pharmaceuticals and bioequivalence research” (经口吸入制剂仿制药生物等效性研究指导原则) issued by NMPA explicitly stated the guidance of accelerating the consistency evaluation of generic drugs. High-quality enterprises with technical and R&D advantages will be able to pass evaluations more quickly and steadily, while many low-quality, non-compliant small enterprises will be Phased out faster. • In conclusion, favorable regulatory and policy environment have been actively promoting the development and approval of inhalation formulations. This has created a conducive environment for pharmaceutical companies to invest in research and development of novel inhalation products.

Source: Frost & Sullivan analysis

Future Trends of Inhalation Formulation Industry

Domestic Products Replacing Imports in China	• The domestic market for inhalation formulation is growing rapidly but faces challenges such as high production costs, quality control issues, and drug instability. These core technologies have been monopolized by pharmaceutical manufacturers in developed countries, leading to slower industry development in China and a significant gap compared to foreign countries. Till now, several inhalation formulations, manufactured by domestic companies have been successfully approved for marketing. China's medical insurance is shifting from "proportional payment" to "equal payment for the same generic name," discouraging the prescription of expensive original drugs. This policy change favors domestic generic inhalation formulations due to their price advantage. With patents for drugs like Pulmicort expiring, domestic manufacturers like CF PharmTech with research and development capabilities have produced high-end generic versions. These companies can gain market share by leveraging their price advantage, and the trend of bulk procurement may accelerate domestic substitution in the inhalation formulation market.
Formulation Upgrade and Iteration	• By improving the formulation of inhalation, products are continuously upgraded to achieve longer-lasting effects and reduced dosing frequency. The formulation upgrades not only enhance the clinical advantages of the products but also allow the developing companies to continuously capture market share and extend the product's market lifecycle. Furthermore, the same active pharmaceutical ingredient will likely see the emergence of more new combined formulations using different technologies, which could potentially change the market landscape for inhalation formulation in the future.
Innovative Direction	• The main directions for innovation in inhalation formulations include combination products, dosage form improvements, and the expansion of new indications. Combination formulations have become one of the mainstream strategies, as they can enhance therapeutic effects and increase the difficulty of generic drug replication. Due to the high technical barriers of inhalation formulations, improving dosage forms is a development strategy for generic drug manufacturers to enter the market. Another current research direction for inhalation formulations is their application in other fields, such as the central nervous system.
Enhanced Regulation	• In December 2020, the NMPA/CDE issued the “Consultation guidance on generic orally inhaled drug products pharmaceuticals and bioequivalence research” (经口吸入制剂仿制药生物等效性研究指导原则) which draws on the relevant evaluation guidelines of the FDA. These guidelines are based on a combination of in vitro and in vivo studies, aligning the consistency evaluation standards with those of mature international markets. This opinion will accelerate the establishment of standards for generic inhalation formulations and improve the quality standards of inhalation drugs.

Source: Frost & Sullivan Analysis

Entry Barriers of Inhalation Formulation Industry

Drug Research and Development Barrier	• Inhalation formulations are a combination of pharmacology, inhalation kinetics, particle dynamics, fluid mechanics, surface science and inhaler design and processing. For example, inhalation formulations have special requirements for drug particle, size, shape, density and surface characteristics, and inhalation device, according to the physiological structure of the respiratory tract, the drug particle size is less than 7 μm to make the drug effectively distributed in the treatment site, and the particles that are too large (more than 10 μm) or too small (less than 0.5 μm) may make the drug unable to be effectively deposited and reduce the efficacy. On the other hand, inhalation devices need to meet the reproducibility and particle size distribution of doses, so the R&D barriers are high, and there are few domestic companies that do a complete inhalation formulation platform layout. • The integration of the inhalation formulation drug and the drug delivery device imposes high demands on patient operation. The proficiency of the operation directly impacts individual absorption effectiveness, and improper handling can lead to issues such as nozzle misalignment, incomplete inhalation, nasal inhalation, excessive inhalation speed, and drug deposition in the oral cavity, thus affecting bioequivalence outcomes. Additionally, regulatory agencies like the FDA, EMA and NMPA enforce strict requirements for bioequivalence clinical trials with stringent approval procedures. The domestic evaluation system is continually evolving and is expected to become more rigorous. In comparison to developed regions such as Europe and the United States, the field of inhalation formulations in our country is still in its early stages. Aside from requiring medical staff training, the selection of devices should consider the evaluation of drug, device, and patient factors influencing inhalation therapy, thereby further complicating the clinical development process.
Large-scale Production Barrier	• To maintain cGMP compliance and ensure consistent product quality, pharmaceutical production involves intricate process pathways, stringent cleanliness criteria for the production area, rigorous equipment validation, and strict quality assurance. It necessitates a high level of expertise, adherence to regulations, and professional experience among personnel. The complexity of manufacturing processes for inhalation products, including precise control over environmental conditions and advanced packaging solutions, makes large-scale production challenging. The administration of Inhalation Formulations at the microgram level leaves little room for error, thus imposing production and quality control g strict requirements on drug particles and devices. As a result, the mass production of Inhalation Formulations is susceptible to instability. Furthermore, industrialized equipment is currently expensive, and the primary packaging equipment for domestic DPI largely relies on imports.
Talent Barrier	• Talent barrier in the inhalation formulation industry presents a significant challenge to the development and production of effective inhalation products. Successful development of inhalation products requires collaboration across multiple disciplines, including material science, engineering, pharmacology, and medicine. Each discipline brings crucial insights into the formulation and delivery process, from designing compounds that are stable and efficient to ensuring their safe delivery to patients. Assembling and managing a multidisciplinary team capable of handling such varied aspects can be difficult, often necessitating strategic partnerships and comprehensive project management.
High Capital Investment	• The inhalation formulation industry presents a significant entry barrier in the form of high capital investment requirements. This industry demands substantial financial resources to establish manufacturing facilities, conduct research and development activities, and navigate the complex regulatory landscape. The need for specialized equipment and technology further adds to the capital-intensive nature of entering this sector. Moreover, stringent quality control standards and the requirement for extensive clinical trials contribute to the high cost of entry. As a result, potential entrants face considerable financial challenges in establishing a foothold in the inhalation formulation industry. This entry barrier underscores the importance of strategic planning and robust financial backing for any entity seeking to venture into this specialized sector.

Source: Frost & Sullivan Analysis

Content

Budesonide Overview

Key Information

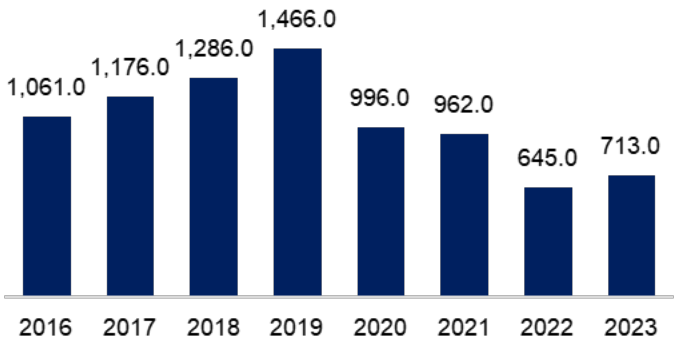
- Budesonide Suspension was first approved by the FDA under the brand name Pulmicort Respules in 2000 developed by Astra Zeneca.
- Global sales of Pulmicort (originator manufactured by AZ) have continued to grow in recent years until 2019. In 2023, global sales has decreased to 713.0 million dollars, due to the drastic growth of generic drug sales.
- Budesonide suspensions are the main/front-line drugs used in hospitals for the treatment of symptoms of asthma.
- Budesonide Suspension is the only inhalable corticosteroid included in the WHO Model List of Essential Medicines for Children and has been recognized as a Category B drug under the PDA Pregnancy Category, indicating that it can be used routinely and safely during pregnancy in light of its good safety profile.
- Market size of budesonide mainly contributed by suspension formulation other than aerosols and dry powder inhalers.
- In China, there are 6 Budesonide suspension approved till June 2024. Among them, 4 domestic manufacturers have been selected by the fifth batch of National Centralized Drug Procurement, while the originator has not been chosen.

1 Budesonide Overview

- **Original:** AstraZeneca Pulmicort (First Approved in 1997)
- **Type:** ICS
- **Indication:** 1, Budesonide suspension (Nebulization) is used for is indicated for the maintenance treatment of asthma and as prophylactic therapy in children 12 months to 8 years of age. 2, Budesonide DPI is indicated for the maintenance treatment of asthma as prophylactic therapy in adult and pediatric patients six years of age or older. It is also indicated for patients requiring oral corticosteroid therapy for asthma. 3, Budesonide Nasal Spray is a corticosteroid indicated for treatment of seasonal or perennial allergic rhinitis in adults and children ≥ 6 years. 4, Budesonide Aerosol is indicated for severe asthma and asthmatic bronchitis in adults and children ≥2 years.
- **Mechanism of Action:** It works in the airways and lung tissues to constrict the dilated mucosal vessels through the combined effect of various links. It will improve the sensitivity of bronchial smooth muscle and inflammatory cells to β2 agonists, etc., to generate a good therapeutic effects on asthma.

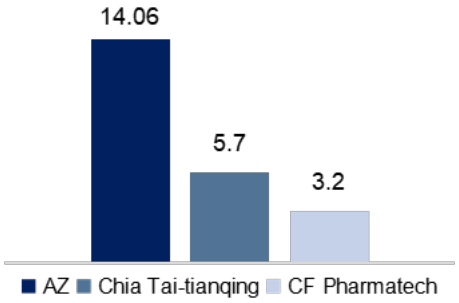
2 Global Pulmicort Sales Revenue

USD Million



3 Comparison of Bid Price of Budesonide Between Original and bid-winning drug in China

Single dose/RMB



Source: CDE, Annual Report, Frost & Sullivan Analysis

Clinical Advantages Analysis of Budesonide Suspension (1/2)

- According to Guidelines for Bronchial Asthma Prevent and Management in China (2020 edition), all adult, adolescent and child asthma patients are recommended to receive maintenance therapy containing ICS to reduce the risk of severe acute exacerbations. In addition, ICSs, typically budesonide suspension, offer benefit in the acute setting and in pediatric populations because their improved efficacy and adherence.
- Budesonide suspension for nebulization is the only China VBP scheme involved ICSs inhalation preparations, which also indicates its established market presence.

Suitability for Pediatric Populations	• Inhaled glucocorticoid therapy has been shown to be effective in pediatric populations with all levels of persistent asthma, from mild to severe. A placebo-controlled study compared the effectiveness of the LABA salmeterol with that of the ICS budesonide in a large cohort of asthmatic pediatric populations over a 12-month period. This study found budesonide to be more effective than either salmeterol or placebo in the management of persistent childhood asthma. • In addition, budesonide suspension for nebulization is the only ICS preparation currently approved and recommended by clinical guideline for use in children as young as 1 year old.
Effective Management of Severe Asthma	• Nowadays, asthmatic patients are imposed on substantial socioeconomic burden worldwide. Although management of asthma by ICSs can reduce the risk of hospitalization due to severe asthma exacerbation, some patients still have to be admitted to hospital because of poor knowledge for asthma self-management and its severity. • Budesonide suspension for nebulization may assist in reducing asthma-related symptoms in severe asthma exacerbation, which may contribute to shorten length of hospital stay and to reduce symptoms and medical expenditure irrespective of the presence or absence of respiratory infection.
Improved Adherence and Convenience	• Clinical studies have consistently demonstrated that budesonide suspension for nebulization showed a comparable tolerability and efficiency to other ICSs adopting DPIs and MDIs in patients with moderate to severe asthma, as a maintenance medication. • By delivering the medication directly to the lungs in a fine mist, nebulization ensures optimal deposition of the drug in the airways, leading to significant improvements in lung function and symptom control. This mode of delivery is particularly advantageous for patients who may struggle with the coordination required for using DPIs or MDIs, such as young children, elderly individuals, or those with severe respiratory impairment.

Source: Literature review, Frost & Sullivan analysis

Clinical Advantages Analysis of Budesonide Suspension (2/2)

- Differences in dose–response relationships for efficacy and systemic exposure were unique for each ICS regimen and reflected in their therapeutic indices. ICS dose regimens were categorized as follows for duration of action: short, 4–6 h (flunisolide hydrofluoroalkane); medium, 14–16 h (budesonide); long, 25–40 h (fluticasone propionate); and ultra-long, greater than 80 h (fluticasone furoate).
- Since the other two similar inhaled glucocorticoid drugs have not been included in the national VBP catalog, the prices of fluticasone propionate and beclomethasone propionate are several times the price of budesonide suspension for inhalation selected.

Pharmacological Basis of Differences in Dose Response, Dose Equivalence, and Duration of Action of ICS

	Budesonide	Fluticasone Propionate	Beclomethasone Propionate
Relative Receptor Affinity	935	1775	1345
Glucocorticoid Receptor Dissociation Constant ,nmol/L	0.431	0.246	0.324
Lung Absorption Rate Constant, h^{-1}	0.248	0.096	0.257
Lung Bioavailability, %	26	28	20
Oral Bioavailability, %	11	1	41
Plasma Clearance, L/h	84	69	120

ICS dose regimens were categorized as follows for duration of action: short, 4–6 h (flunisolide hydrofluoroalkane); medium, 14–16 h (budesonide); long, 25–40 h (fluticasone propionate); and ultra-long, greater than 80 h (fluticasone furoate).

Price of China Approved ICS for Asthma

	VBP Inclusion	Manufacturer	Package	Price/unit, RMB
Budesonide Suspension for Nebulization	✓	Jiangsu Chia Tai-tianqing Pharmaceutical	2ml: 1mg	5.65
		ShenZhen Taitai/JoinCare		3.39
		Sichuan Purity		2.79
		CF PharmTech		3.19
Fluticasone Propionate Suspension for Nebulization	/	GSK	2ml: 0.5mg	11.96
Beclomethasone Dipropionate Suspension for Nebulization	/	Chiesi	2ml: 0.8mg	9.49

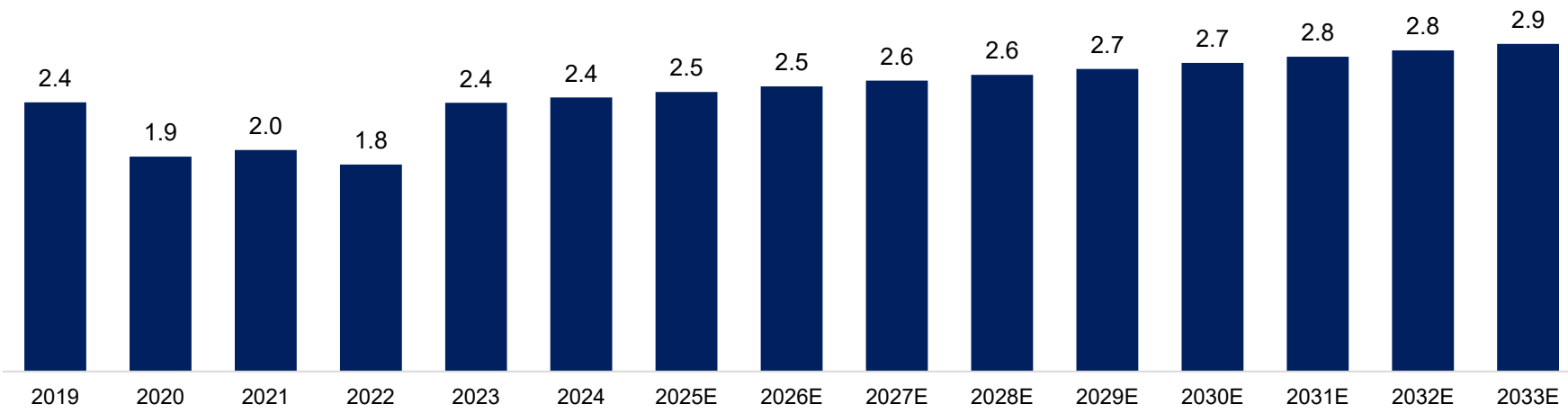
Source: Literature review, Frost & Sullivan analysis

Global Budesonide Inhaler Market, 2019-2033E

- In 2024, global market of budesonide inhaler reached USD2.4 billion and is expected to reach USD2.6 billion and USD2.9 billion by 2028 and2033, with a CAGR of 2.0% and 2.0% from 2024 to 2028 and from 2028 to 2033 respectively.

Global Budesonide Inhaler Market, 2019-2033E

Period	CAGR
2019-2024	0.4%
2024-2028E	2.0%
2028E-2033E	2.0%



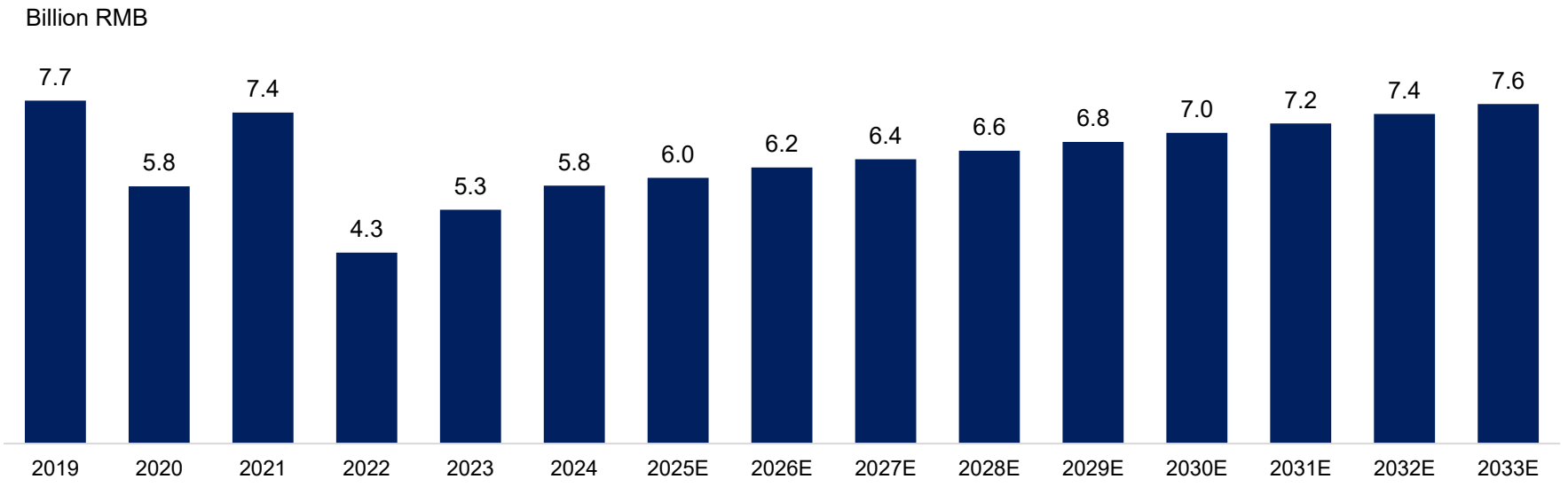
Source: Frost & Sullivan Analysis

China Budesonide Inhaler Market, 2019-2033E

- From 2019 to 2024, China market of budesonide inhaler decreased from RMB7.7 billion to RMB5.8 billion, representing a CAGR of -5.5%, and is expected to reach RMB6.6 billion and RMB7.6 billion by 2028 and2033, with a CAGR of 3.2% and 3.0% from 2024 to 2028 and from 2028 to 2033 respectively. In 2024, China market of budesonide suspension for inhalation reached RMB5.7 billion.

China Budesonide Inhaler Market, 2019-2033E

Period	CAGR
2019-2024	-5.5%
2024-2033E	3.1%



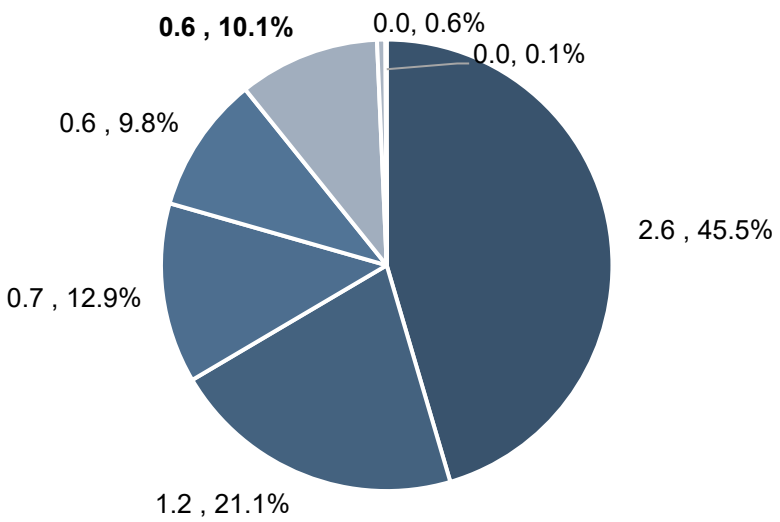
Source: Frost & Sullivan Analysis

Competitive Landscape of Budesonide Manufacturer in China, 2024

- As of 2024, the main budesonide market is suspension market, the overall budesonide market is dominated by the original company AstraZeneca, which has total annual sales of RMB 2.6 billion, accounting for 45.5% of all manufacturers in China. CF PharmTech had sales of RMB 0.6 billion, accounting for 9.8% of the total annual sales.

Sales Revenue Segmented Budesonide Manufacturer in China, 2024

Billion RMB



Source: Frost & Sullivan analysis

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Sales Revenue Segmented Budesonide Manufacturer in China, 2024

	Sales Revenue/million RMB	%
Astra Zeneca	2,588.0	45.5%
Jiangsu Chia Tai-tianqing	1,199.7	21.1%
Sichuan Purity	735.0	12.9%
Joincare	557.5	9.8%
CF PharmTech	574.5	10.1%
Nanjing Licheng	34.2	0.6%
Hebei Chuangjian Pharmaceutical	5.1	0.1%
Total	5694.0	100.0%

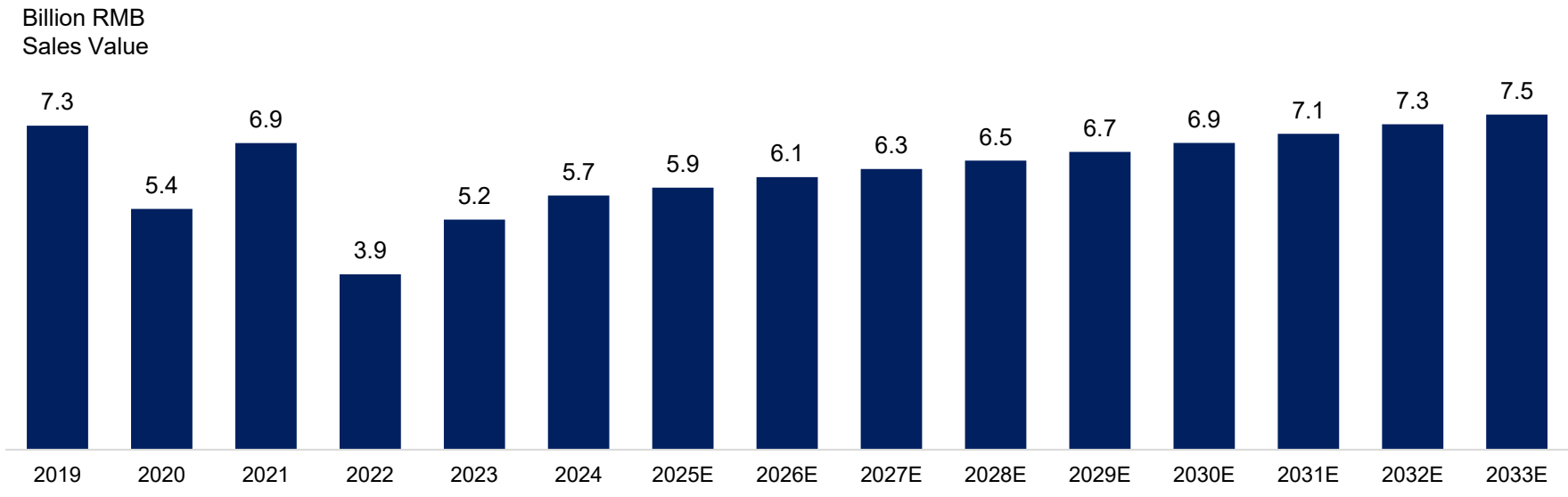
Source: Frost & Sullivan analysis

China Budesonide Suspension for Nebulization Market, 2019-2033E

- From 2019 to 2024, China market of budesonide suspension for nebulization decreased from RMB7.3 billion to RMB5.7 billion, representing a CAGR of -4.7%, and is expected to reach RMB7.5 billion by 2033, with a CAGR of 3.1% from 2024 to 2033.

China Budesonide Suspension for Nebulization Market, 2019-2033E

Period	CAGR
2019-2024	-4.7%
2024-2033E	3.1%



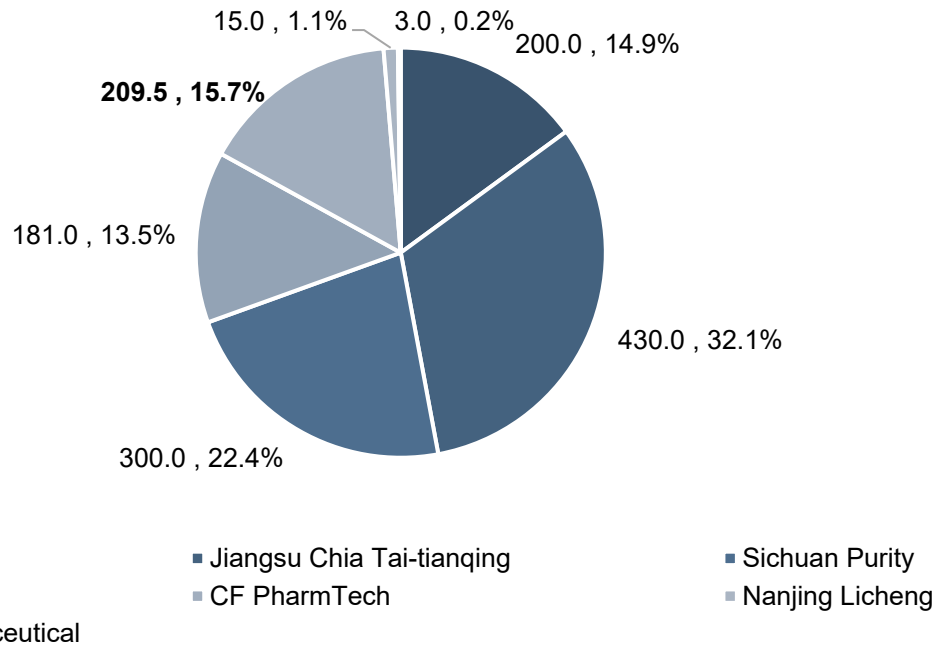
Source: Frost & Sullivan Analysis

Competitive Landscape of Budesonide Suspension for Nebulization Manufacturer in China, 2024

- CF PharmTech had sales volume of 209.0 million, accounting for 15.7% of the total.

Sales Volume Segmented Budesonide Nebulization Manufacturer in China, 2024

Million Unit



Source: Frost & Sullivan analysis

Competitive Landscape of Budesonide Suspension for Nebulization Manufacturer in China, 2024

- CF PharmTech had sales volume of 209.0 million, accounting for 15.7% of the total.

Sales Volume Segmented Budesonide Nebulization Manufacturer in China, 2024

	Sales Volume/Million Unit	%
Astra Zeneca	200.0	14.9%
Jiangsu Chia Tai-tianqing	430.0	32.1%
Sichuan Purity	300.0	22.4%
Joincare	181.0	13.5%
CF PharmTech	209.5	15.7%
Nanjing Licheng	15.0	1.1%
Hebei Chuangjian Pharmaceutical	3.0	0.2%
Total	1320.0	100.0%

Source: Frost & Sullivan analysis

Competitive Landscape of Budesonide Suspension for Nebulization Manufacturer in China, 2022-2024

	2022			2023			2024		
Manufacturer	Market Share of Sales Revenue, %	Market Share of Sales Volume, %	Unit Proce, RMB	Market Share of Sales Revenue, %	Market Share of Sales Volume, %	Unit Proce, RMB	Market Share of Sales Revenue, %	Market Share of Sales Volume, %	Unit Proce, RMB
AstraZeneca	41.5%	16.8%	12.94	43.2%	17.9%	12.94	45.5%	14.9%	12.94
Jiangsu Chia Tai-tianqing Pharmaceutical	21.4%	19.9%	5.65	19.1%	20.4%	5.65	21.1%	32.1%	2.79
Sichuan Purity	14.5%	27.3%	2.79	14.7%	23.2%	2.79	12.9%	22.4%	2.45
ShenZhen Taitai/JoinCare	14.0%	21.7%	3.39	12.0%	18.9%	3.39	9.8%	13.5%	3.08
CF PharmTech	**8.7%**	**14.3%**	**3.19**	**11.0%**	**19.6%**	**3.19**	**10.1%**	**15.7%**	**2.95**
Nanjing Licheng							0.6%	1.1%	2.28
Hebei Chuangjian Pharmaceutical							0.1%	0.2%	1.70
Total	100.0%	100.0%		100.0%	100%		100.0%	100.0%	

Source: Frost & Sullivan Analysis

Competitive Landscape of Budesonide in China

Marketed Budesonide in China

Dosage Form	Manufacturer	First Approval Date	Indications	2023 Medical Insurance Status	VBP
Aerosol (MDI)	IG Spruhtechnik	1999-10-29	Asthma, Chronic bronchitis	/	/
	Boehringer Ingelheim	2002-07-19			
	AstraZeneca	2004-11-1			
	SPH Sine Pharmaceutical	2020-06-03			
	Chiesi Farmaceutici	2020-02-13			
	Lunan Better Pharmaceutical	2020-05-20			
DPI	AstraZeneca	2000-06-16	Asthma	List B since 2017	
	Sandoz	2000-06-16			
	Shanghai Sine	2008-01-01			
	Orion Corporation	2009-07-14			
Nasal Spray	AstraZeneca	2001-03-14	Allergic rhinitis	/	
	Synmosa Pharmaceutical	2008-11-04			
	Nanchang Baiji Medicine Technology	2023-11-21			
	Sichuan Purity	2024-01-05			

*This table was last updated on Sep 16th, 2025
Note: 1, "/" means not listed or not involved

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of Budesonide in China

Marketed Budesonide in China

Dosage Form	Manufacturer	First Approval Date	Indications	2023 Medical Insurance Status	VBP
Nebulization	AstraZeneca	2001-11-22	Asthma	List B since 2009	/
	Jiangsu Chia Tai-tianqing Pharmaceutical	2020-02-25			√
	ShenZhen Taitai/JoinCare	2020-07-21			√
	Sichuan Purity	2021-04-13			√
	CF PharmTech	**2021-05-11**			√
	Nanjing Licheng	2024-06-18			√
	Hebei Chuangjian Pharmaceutical	2024-09-19			√
	Zhejiang Fresh Pharmaceutical	2024-09-26			/
	Cipla (Jiangsu) Pharmaceutical	2025-06-17			/

Budesonide at Clinical Stage in China

Dosage Form	Manufacturer	Clinical Stage	Indications	First Posted Date
Aerosol (MDI)	Jiangsu Chia Tai-tianqing Pharmaceutical	Phase I	Asthma	2024-11-15
	Lunan Better Pharmaceutical Co., Ltd	BE		2024-12-06
Nasal Spray	Shanghai Baian Pharmaceutical Co., Ltd	BE	Allergic rhinitis	2018-01-02
Nebulization	Tianjin Jin Yao Pharmaceutical	NDA	Asthma	/
	Zhejiang Fresh Pharmaceutical	NDA	Asthma	/
	Renhe Yikang Group	NDA	Asthma	/
	Aitme (Suzhou) Medical Technology	NDA	Asthma	/
	Ningbo Meishu Medical	NDA	Asthma	/
	Shandong Heqi Pharmaceutical	NDA	Asthma	/

Source: CDE, Frost & Sullivan Analysis

*This table was last updated on Sep 16th, 2025

Competitive Landscape of Budesonide in China

Budesonide at Clinical Stage in China

Dosage Form	Manufacturer	Clinical Stage	Indications	First Posted Date
Nebulization	Lexen Pharmaceutical (Suzhou)	NDA	Asthma	/
	IVAX-Teva Pharmaceutical	BE		2020-11-16
	Superior Inhalation Pharmaceutical	BE		2021-06-17
	Sichuan Kelun	BE		2021-10-22
	Dr Reddy's (Beijing) Pharmaceutical Co.	BE		2022-02-10
	Furou Pharmaceutical Technology	BE		2023-01-31
	Haimen Omni Pharmaceutical	BE		2023-07-19
	Jewim Pharmaceutical	BE		2023-08-10
	Zhejiang Hengyan Pharmaceutical	BE		2023-11-02
	Hunan Sterol pharmaceutical	BE		2024-04-23
	Sichuan HMZS Biopharmaceutical	BE		2024-09-04
	Hunan Xianshi Pharmaceutical	BE		2024-10-08
	Hainan Star Pharmaceutical	BE		2024-10-09
	Shijiazhuang No.4 Pharmaceutical Co.,Ltd.	BE		2025-05-12
	Beijing Kangchuanglian Biopharmaceutical	BE		2025-08-26

*This table was last updated on Sep 16th, 2025

Note: First posted date refers to the date on which the trial record or the clinical application record was first available publicly.

Source: CDE, Frost & Sullivan Analysis

Competitive Landscape of Budesonide in China

Marketed Budesonide in China

Dosage Form	Manufacturer	Brand Name	First Approval Date	Indications	2023 Medical Insurance Status	VBP	Consistency Evaluation
Nebulization/ Suspension	AstraZeneca	Pulmicort Respules	2001-11-22	For the maintenance treatment of asthma in adults and prophylactic therapy for children aged 12 months to 8 years	List B since 2009	/	NA
	Jiangsu Chia Tai-tianqing Pharmaceutical	Tian Qing Su Chang (天晴速畅)	2020-02-25			√	√
	ShenZhen Taitai/JoinCare	Wu Shu (雾舒)	2020-07-21			√	√
	Sichuan Purity	Pu Chang Shu (普畅舒)	2021-04-13			√	√
	CF PharmTech	Chang Qi (长风畅起)	**2021-05-11**			√	√
	Nanjing Licheng	Bai Chang Zhi Shu (佰畅致舒)	2024-06-18			√	√
	Hebei Chuangjian Pharmaceutical	/	2024-09-19			√	√
	Zhejiang Fresh Pharmaceutical	Fu Nai De (福奈德)	2024-09-26			/	√
	Cipla (Jiangsu) Pharmaceutical	/	2025-06-17			/	√

*This table was last updated on Sep 16th, 2025

Source: CDE, Frost & Sullivan Analysis

Azelastine Hydrochloride and Fluticasone Propionate Overview

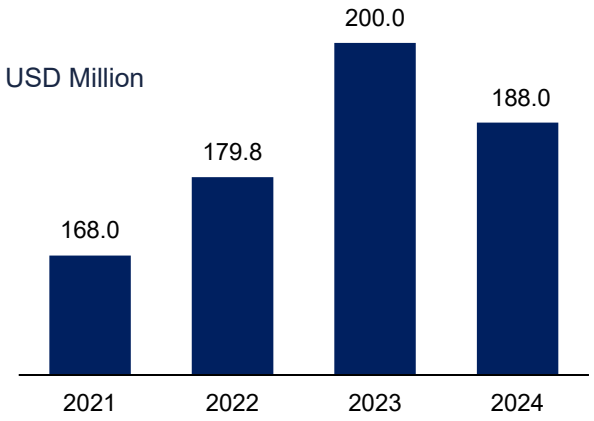
Key Information

- There are 2 azelastine hydrochloride and fluticasone propionate nasal spray product available in China. The original drug, Dymista, was initially launched in the U.S. in 2012 and had sales of $188 million in 2024.
- Clinical evidence: DYMISTA (Azelastine Hydrochloride and Fluticasone Propionate) demonstrated statistically significant greater decreases in rTNSS (reflective total nasal symptom score) and (instantaneous total nasal symptom score) iTNSS as compared to azelastine hydrochloride and to fluticasone propionate monotherapy.
- Till 2023, only CF PharmTech has acquired sales revenue of azelastine hydrochloride and fluticasone propionate nasal spray in China.

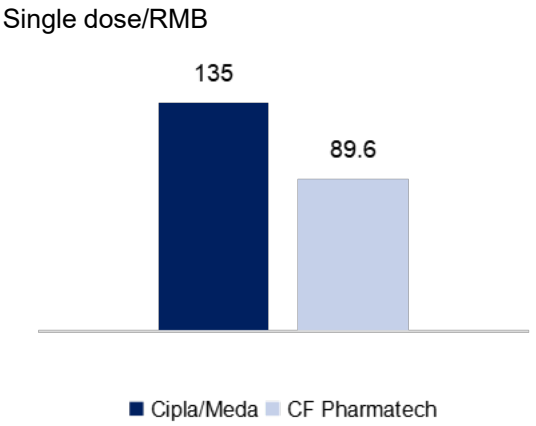
1 Azelastine Hydrochloride and Fluticasone Propionate Overview

- **Original:** Meda Dymista（Approved in 2012）
- **Type:** Antihistamine + ICS
- **Indication:** Azelastine and fluticasone combination nasal spray is used to treat an itchy or runny nose, sneezing, or other symptoms caused by allergic rhinitis in adults and children ≥6 years who are refractory to intranasal antihistamine or corticosteroid monotherapy.
- **Mechanism of Action:** Azelastine hydrochloride and fluticasone propionate is a compound preparation of antihistamine and glucocorticoid, which has inhibited vasodilation and swelling and has strong anti-inflammatory properties. Azelastine blocks histamine receptors in the body, thereby reducing the effects of histamine, a substance produced by the immune system during an allergic reaction.
- **Acquisition**: Mylan has acquired Meda in July 2016 including Dymista.

2 Global Dymista Sales Revenue



3 Comparison of Bid Price of Between Original and Generic in China



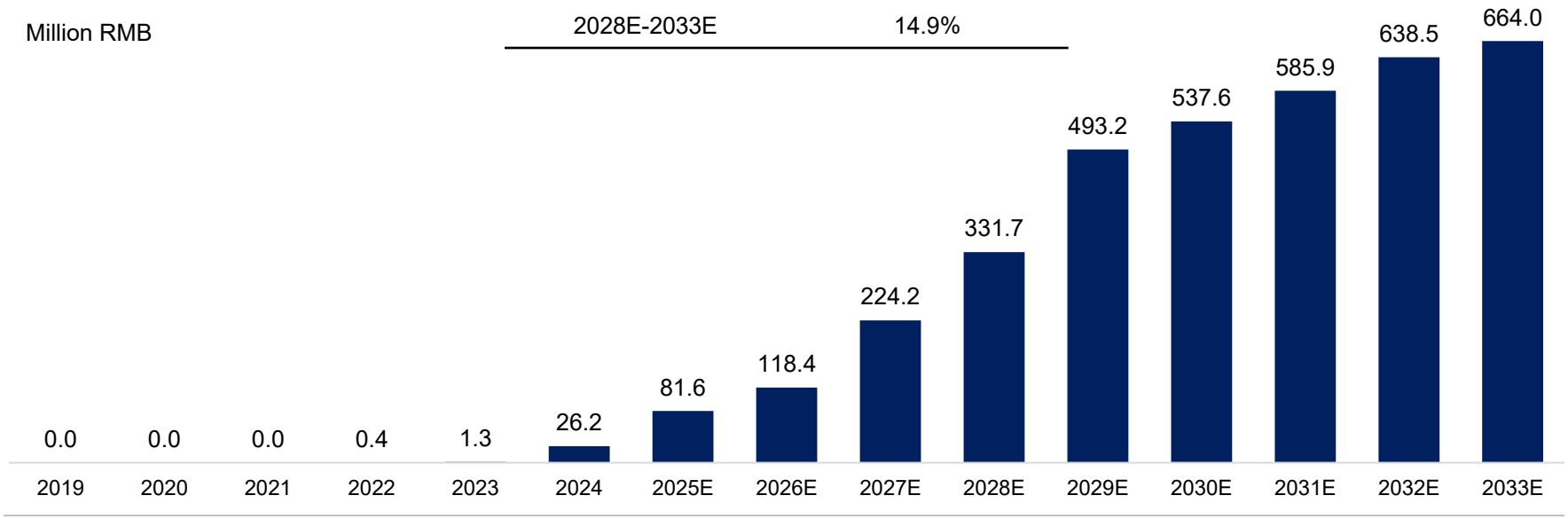
Source：Annual Report, Frost & Sullivan Analysis

China Azelastine Hydrochloride and Fluticasone Propionate Inhaler Market, 2019-2033E

- In 2024, China market of azelastine hydrochloride and fluticasone propionate inhaler reached RMB26.2 million and is expected to reach RMB331.7 million and RMB664.0 million by 2028 and2033, with a CAGR of 88.7% and 14.9% from 2024 to 2028 and from 2028 to 2033 respectively. In China, the size of the azelastine/fluticasone propionate inhaler market reached RMB26.2 million in 2024 and is expected to reach RMB664.0million by 2033, at a CAGR of 43.2%.

China Azelastine Hydrochloride and Fluticasone Propionate Inhaler Market, 2019-2033E

Period	CAGR
2019-2024	/
2024-2028E	88.7%
2028E-2033E	14.9%

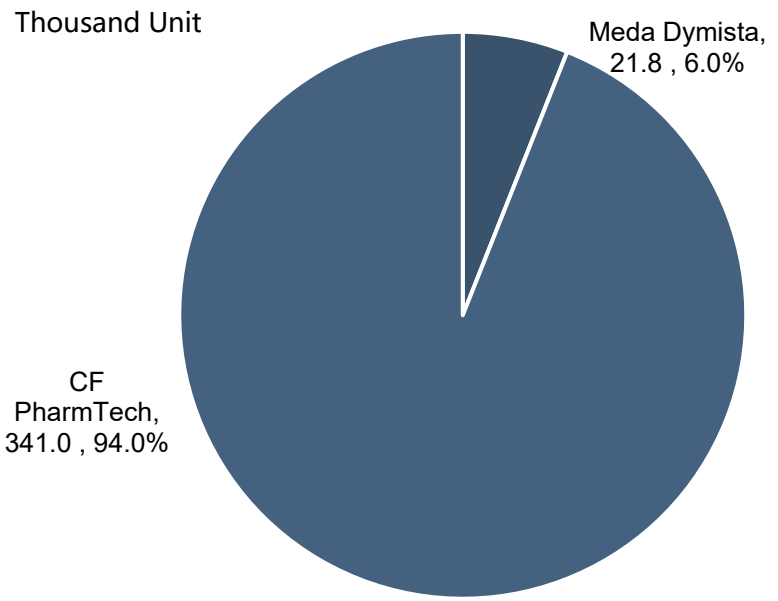


Source: Frost & Sullivan Analysis

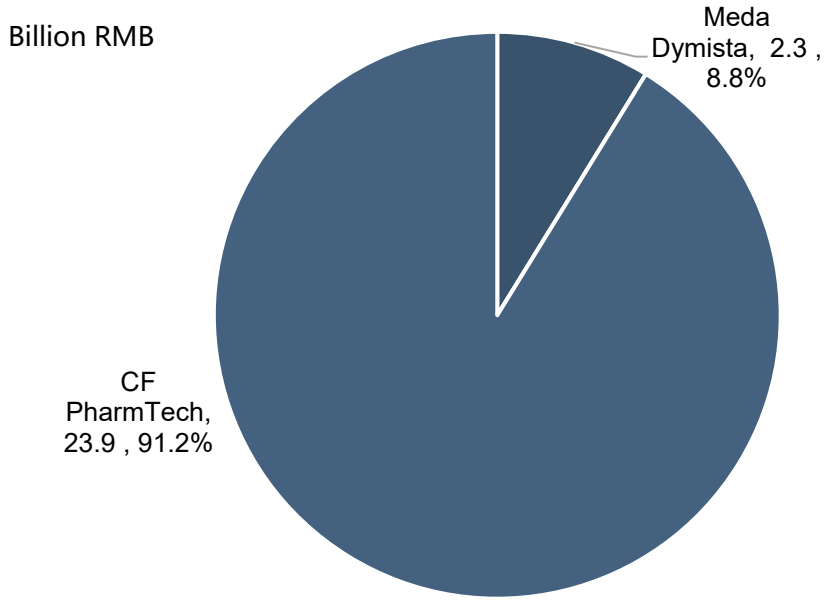
Competitive Landscape of Azelastine Hydrochloride and Fluticasone Propionate Manufacturer in China, 2024

- CF PharmTech had sales volume of 341.0 thousand, accounting for 94.0% of the total. CF PharmTech had sales revenue of RMB 23.9 million, accounting for 91.2% of the total.

Sales Volume Segmented Azelastine Hydrochloride and Fluticasone Propionate Manufacturer in China, 2024



Sales Revenue Segmented Azelastine Hydrochloride and Fluticasone Propionate Manufacturer in China, 2024



Source: Frost & Sullivan analysis

Global Competitive Landscape of Azelastine Hydrochloride and Fluticasone Propionate

Global Marketed Azelastine Hydrochloride and Fluticasone Propionate

Dosage Form	Manufacturer	Brand Name	Market Authority	Indication	First Posted Date
Nasal Spray	Meda/Viatris	Dymista	FDA, EMA, NMPA	Allergic Rhinitis	2012-05-01 (FDA), 2014-10-07 (EMA)
	Apotex	/	FDA		2017-04-28
	Teva	Rowex	FDA		2017-10-06
	Padagis Israel	/	FDA		2021-02-18

Global Azelastine Hydrochloride and Fluticasone Propionate at Clinical Stage

Dosage Form	Manufacturer	Clinical Stage	Indications	First Posted Date
Nasal Spray	EMS	Phase III	Allergic Rhinitis	2023-1-13

*This table was last updated on Sep 16th, 2025

Source: FDA, EMA, ClinicalTrials, Frost & Sullivan Analysis

Competitive Landscape of Azelastine Hydrochloride and Fluticasone Propionate in China

- CDE received clinical trial registration from CF PharmTech and Viatris on April 21st, 2015 and April 8th 2014, respectively, while the clinical trial of them were approved on November 22nd 2016 and February 7th 2017.
- A multi-center, randomized, double-blind, original drug-controlled, and parallel-group clinical trial evaluated the efficacy and safety of Shu Fei Min compared with Dymista. There is no significant differences observed in nasal symptom relieve and safety evaluation between Shu Fei Min and Dymista. In a result, Shu Fei Min showed effects equivalent to those of Dymista in this clinical trial and may benefit Chinese patients with allergic rhinitis.

Marketed Azelastine Hydrochloride and Fluticasone Propionate in China

Dosage Form	Manufacturer	Brand Name	First Approval Date	Indications	2023 Medical Insurance Status	VBP
Nasal Spray	**CF PharmTech**	**Shu Fei Min (舒霏敏)**	**2022-11-01**	the relief of symptoms of seasonal allergic rhinitis in adult and pediatric patients 6 years of age and older.	List B since 2023	/
	Viatris/Meda	Dymista	2023-06-30			

Azelastine Hydrochloride and Fluticasone Propionate at Clinical Stage in China

Dosage Form	Manufacturer	Clinical Stage	Indications	First Posted Date/Clinical Trial Approval Date
Nasal Spray	Jewim	BE	Allergic rhinitis	2024-07-23
	Sichuan Haisike	Clinical Approval		2016-12-19

*This table was last updated on Sep 16th, 2025

Source: NMPA, CDE, Frost & Sullivan Analysis

Salmeterol and Fluticasone Overview

Key Information

Fluticasone and salmeterol is a combination of two medicines that are used to help control the symptoms of asthma and improve breathing, which has become the current front-line therapy for bronchial asthma and COPD. It is recommended by Global Strategy for Asthma Management and Prevention 2024, when a patient's asthma has not been controlled sufficiently on other asthma medicines, or when a patient's condition is so severe that more than one medicine is needed every day. This medicine is also used to treat air flow blockage and reduce the worsening of chronic obstructive pulmonary disease (COPD). This includes chronic bronchitis and emphysema.

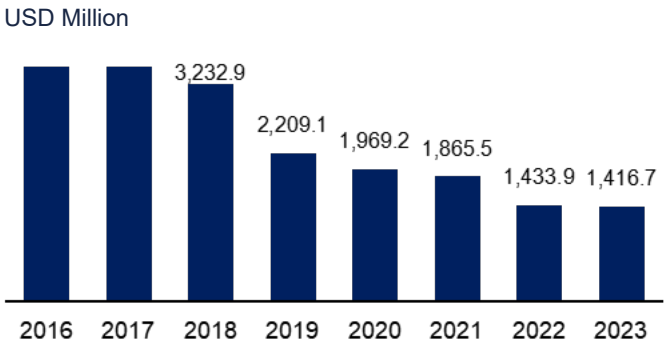
Seretide, the original drug, is one the world's top sales of inhalation formulations. However, sales revenue have been declined recent years mainly due to the patent expiration and GSK's new triple compounded preparation; In 2010 and 2011, it recorded a peak global sales of EUR5,139 million (USD6,821.4 million) and EUR5,061 million (USD7,048.5 million)

In 2019, FDA approved Mylan's generic salmeterol and fluticasone, which lead a head-to-head competition with GSK's Seretide.

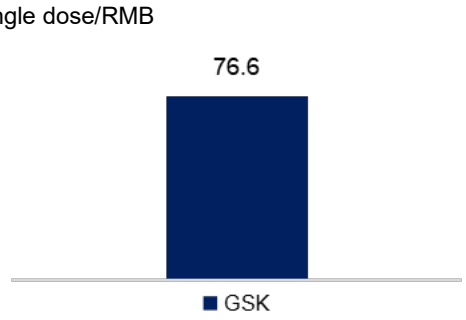
1 Salmeterol and Fluticasone Introduction

- **Original:** GSK Seretide (Approved in 1999)
- **Target:** LABA+ICS compounded preparation
- **Indication:** DPI and aerosol are both indicated for Asthma patients not adequately controlled with inhaled corticosteroids and 'as needed' inhaled short-acting β2 agonist or patients already adequately controlled on both inhaled corticosteroid and long-acting β2 agonist and the symptomatic treatment of patients with COPD, with a FEV1 <60% predicted normal (pre-bronchodilator) and a history of repeated exacerbations, who have significant symptoms despite regular bronchodilator therapy.
- **Mechanism of Action:** Salmeterol is a selective long-acting β2-adrenoceptor agonist that dilates the bronchi and relax the muscles in the airways; fluticasone propionate is a ICS with a high affinity for glucocorticoid receptors and has a strong local anti-inflammatory effect, helping to decrease symptoms such as wheezing, shortness of breath and coughing. Addition of the long-acting beta2-agonist salmeterol to an inhaled corticosteroid in patients with persistent asthma symptoms provides greater clinical benefit than doubling the dosage of the inhaled corticosteroid.

2 Global Seretide Sales Revenue



3 Bid Price of Salmeterol and Fluticasone Aerosols in China



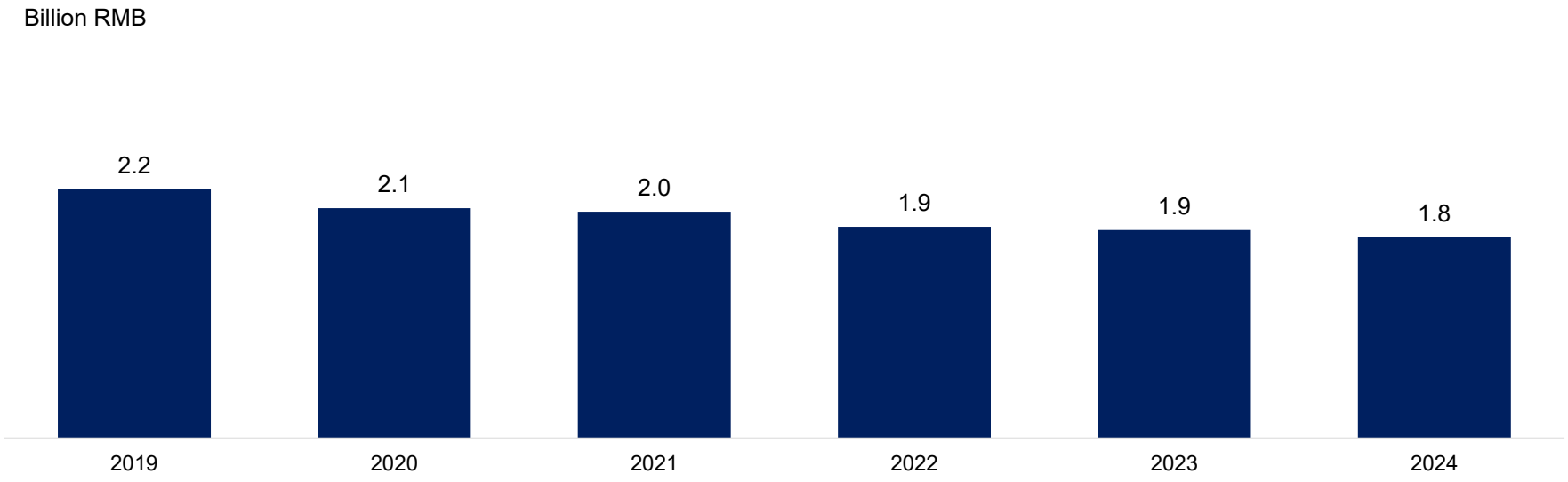
Source: CDE, Annual Report, Frost & Sullivan Analysis

Historical China Salmeterol and Fluticasone Inhaler Market, 2019-2024

- In 2024, China market of salmeterol and fluticasone inhaler reached RMB1.8 billion, decrease from RMB2.2 billion in 2019, with a CAGR of -4.2% from 2019 to 2024.

China Salmeterol and Fluticasone Inhaler Market, 2019-2024

Period	CAGR
2019-2024	-4.2%



Source: Frost & Sullivan Analysis

Competitive Landscape of Salmeterol and Fluticasone in China

Marketed Salmeterol and Fluticasone in China

Dosage Form	Manufacturer	Brand Name	First Approval Date	Indications	2023 Medical Insurance Status	VBP
DPI	GSK	Seretide	2001-11-07	• Twice-daily treatment of asthma in patients aged 4 years and older. • Maintenance treatment of airflow obstruction and reducing exacerbations in patients with COPD	List B since 2017	/
	Joincare	Jian Ke Chang(健可畅)	2024-06-04			
	Sichuan Purity	/	2025-03-04			
	M/s. Cipla Limited	/	2025-06-24			
	Suzhou Oumini Medicine	/	2025-08-26			
MDI	GSK	Seretide Evohaler	2004-04-15	• Asthma in adult and adolescent patients aged 12 years and older		

Salmeterol and Fluticasone at Clinical Stage in China

Dosage FormA	Manufacturer	Clinical Stage	Indications	First Posted Date
Aerosol (MDI)	**CF PharmTech, Inc.**	**BE**	Asthma, COPD	2021-03-14
DPI	Jiangsu Chia Tai-tianqing.	BE		2024-12-23
	Suzhou Oumini	NDA		/
	Hangzhou Jingrui	NDA		
	Jiangsu Simcere	NDA		2024-10-30
	Respirent	NDA		2024-09-27
	EOC Pharma	Phase III		2021-06-25
	Aitme (Suzhou)	Phase III		2024-08-09
	Hangzhou Zhixing Pharmaceutical	Phase III		2025-08-11
	Respirent Pharmaceuticals Co., Ltd	BE		2024-12-23

*This table was last updated on Sep 16th, 2025

Source: NMPA, CDE, Frost & Sullivan Analysis

Tiotropium Bromide Overview

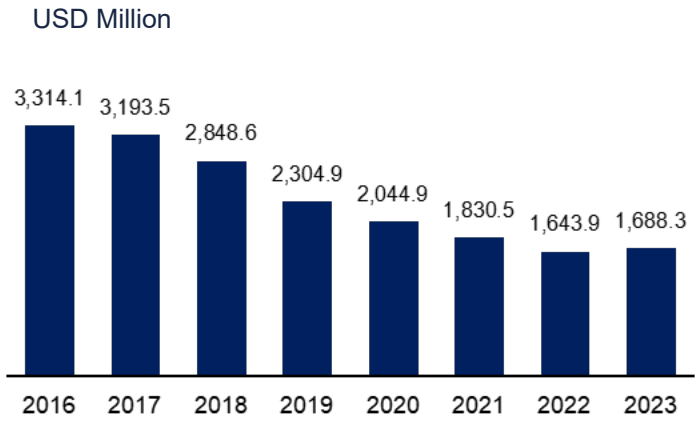
Key Information

- Boehringer Ingelheim was the first to develop Spiriva for the treatment of COPD. In 2012, it recorded a peak global sales of EUR3,562 million (USD4,580.7 million). Since its approval, it has been the first-line drug for the treatment of COPD. Both domestically and internationally, the original tiotropium bromide powder Nebulization is more expensive than the generic drugs. The generic drugs of tiotropium bromide are currently available in Europe, including Teva and Tecnifa.
- Three companies (Chiatai Tianqing, Zhejiang Xianju and Helioeast) have successfully developed the generic drug in China.

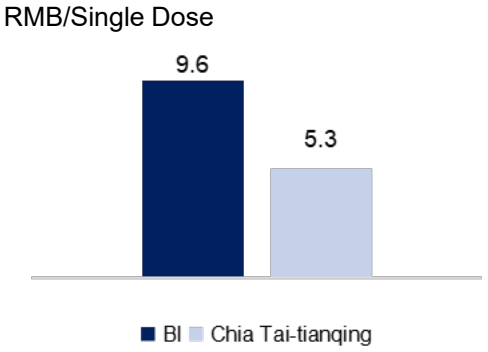
1 Tiotropium Bromide Overview

- **Original:** Boehringer-Ingelheim (Approved in 2004)
- **Type:** LAMA
- **Indication:** COPD, chronic bronchitis and emphysema
- **Mechanism of Action:** Tiotropium Bromide Acts as a bronchodilator by inhibiting M receptors at smooth muscle and thereby easing breathing difficulties. After inhalation, it competitively and reversibly antagonizes M3 receptors, causing airway diastole.

2 Global Spiriva Sales Revenue



3 Comparison of Bid Price of Tiotropium Bromide DPI Between Original and Generic in China



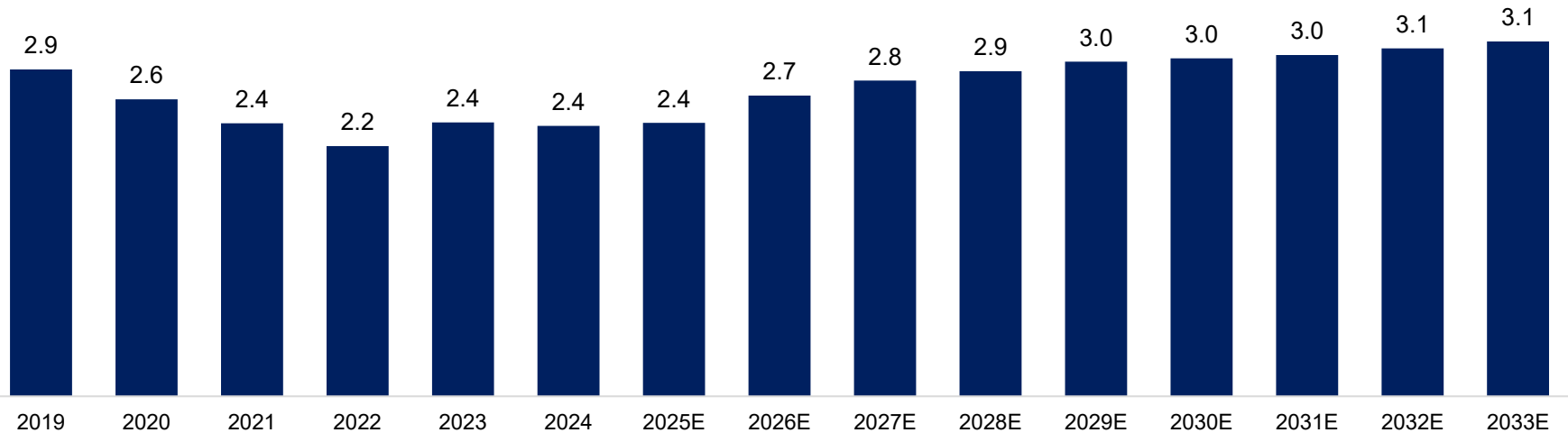
Source: CDE, Annual Report, Frost & Sullivan Analysis

Global Tiotropium Bromide Inhaler Market, 2019-2033E

- From 2019 to 2024, China market of tiotropium bromide inhaler decreased from USD2.9 billion to USD2.4 billion, representing a CAGR of -3.7%, and is expected to reach USD2.9 billion and USD3.1 billion by 2028 and2033, with a CAGR of 4.7% and 1.8% from 2024 to 2028 and from 2028 to 2033 respectively.

Global Tiotropium Bromide Inhaler Market, 2019-2033E

Period	CAGR
2019-2024	-3.7%
2024-2028E	4.7%
2028E-2033E	1.8%



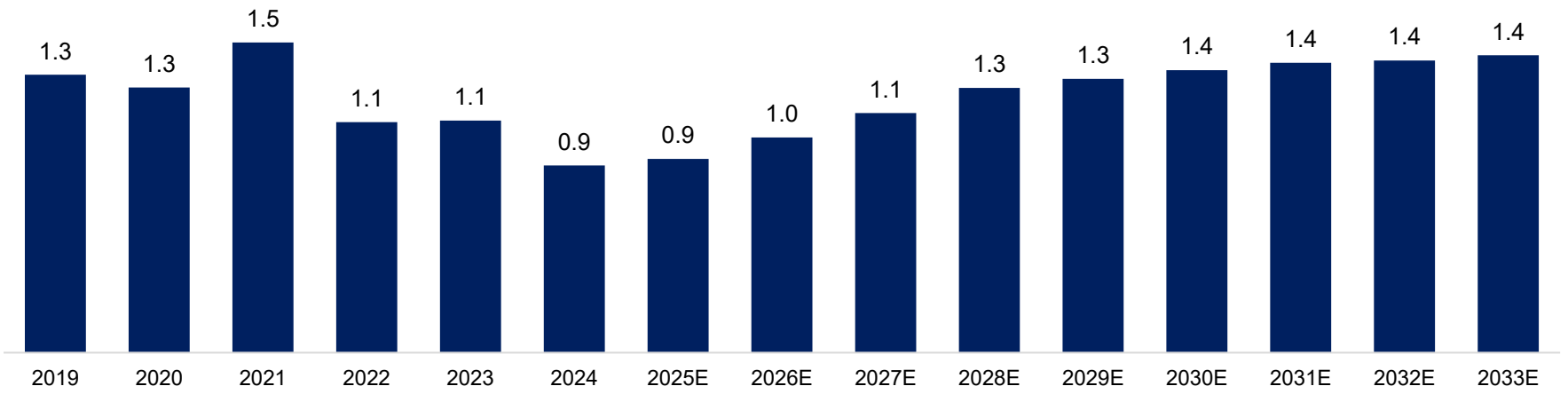
Source: Frost & Sullivan Analysis

China Tiotropium Bromide Inhaler Market, 2019-2033E

- From 2019 to 2024, China market of tiotropium bromide inhaler decreased from RMB1.3 billion to RMB0.9 billion, representing a CAGR of -7.6%, and is expected to reach RMB1.3 billion and RMB1.4 billion by 2028 and2033, with a CAGR of 9.1% and 2.4% from 2024 to 2028 and from 2028 to 2033 respectively.

China Tiotropium Bromide Inhaler Market, 2019-2033E

Period	CAGR
2019-2024	-7.6%
2024-2028E	9.1%
2028E-2033E	2.4%



Source: Frost & Sullivan Analysis

Global Competitive Landscape of Tiotropium Bromide

Global Marketed Tiotropium Bromide

Dosage Form	Manufacturer	Brand Name	Market Authority	First Approval Date	Indications
DPI	BI	Spiriva Handihaler	FDA/EMA	2004-01-30 (FDA) 2002-02-04 (EMA)	Long-term, once daily, maintenance treatment of bronchospasm associated with COPD, and for reducing COPD exacerbations
	Lupin	/	FDA	2023-06-20	
	Teva B.V.	Mivient	EMA	2016-05-26	
	Viatris Limited, Ireland	Sirkava	EMA	2018-09-27	
	Glenmark Arzneimittel	/	EMA	2020-12-17	
	Zentiva k.s.	Dilochob	EMA	2021-01-08	
	Elpen Pharmaceutical	/	EMA	2021-09-08	
	Laboratoires SMB SA	/	EMA	2024-01-11	
	Stada Arzneimittel	/	EMA	2024-05-22	
SMI	BI	Spiriva Respimat	FDA/EMA	2014-09-24 (FDA) 2007-07-24 (EMA)	

Global Tiotropium Bromide at Clinical Stage

Dosage Form	Manufacturer	Clinical Stage	Indications	First Posted Date
DPI	Phargentis SA	Phase III	Asthma, COPD	2022-03-24
	Orion Pharma	Phase I		2018-02-19
SMI	Nephron Pharmaceuticals	Phase II		2020-11-01

*This table was last updated on Sep 16th, 2025

Source: FDA, EMA, ClinicalTrials, Frost & Sullivan Analysis

Competitive Landscape of Tiotropium Bromide in China

In the China market, apart from the originator drug, there are three approved generic tiotropium bromide DPI in China, none of which have completed a bioequivalence.

Marketed Tiotropium Bromide in China

Dosage Form	Manufacturer	Brand Name	First Approval Date	Indications	2023 Medical Insurance Status	VBP
DPI	BI	Spiriva	2005-05-10	Long-term, once daily, maintenance treatment of bronchospasm associated with COPD, and for reducing COPD exacerbations	List B since 2009	/
	Jiangsu Chia Tai-tianqing	Tian Qing Su Le (天晴速乐)	2006-01-01			
	Xianju Zhejiang	Bi Duo Yi (彼多益)	2009-01-01			
	NanChang Helioeast	Hong Ming Rui (弘明瑞)	2013-01-01			
SMI	BI	Spiriva Respimat	2012-05-15			

Tiotropium Bromide at Clinical Stage in China

Dosage Form	Manufacturer	Clinical Stage	Indications	First Posted Date
DPI	Anovent Pharmaceuticals	NDA	COPD	/
	Hangzhou Changxi	NDA		/
	Jewim	NDA		/
	Suzhou Oumini	NDA		/
	Joincare Pharmaceutical	BE		2020-11-27
	Sichuan Purity	BE		2022-03-07
	Tianjin Jin Yao	BE		2022-10-24
	Nanjing Licheng	BE		2023-04-06
	Aiteshenbo (Suzhou) Pharmaceutical	BE		2023-11-28
	Sunshine Lake Pharma Co.,Ltd.	BE		2024-01-16
	Qilu Antibiotics Pharmaceutical	BE		2025-02-23
	BrightGene Pharmaceutical, Aitemei Pharmaceutical	BE		2025-07-23
	CF PharmTech	**Clinical Approval**		2024-07-05

Source: NMPA, CDE, Frost & Sullivan Analysis

*This table was last updated on Sep 16th , 2025

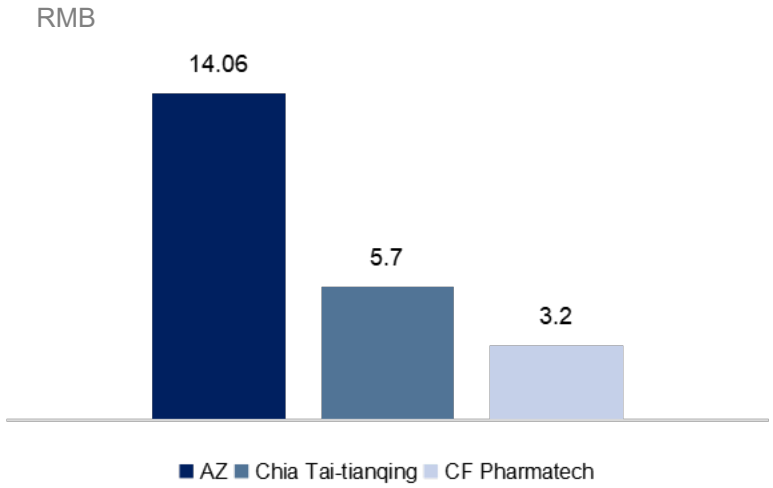
Terbutaline Overview

- In China, there are over 20 terbutaline approved till June 2024. Among them, 5 domestic manufacturers have been selected by the seventh batch of National Centralized Drug Procurement, while the originator has not been chosen. Terbutaline sulfate solution Nebulization is widely used to relieve bronchospasm associated with asthma, chronic bronchitis, emphysema and other pulmonary diseases.

1 Terbutaline Overview

- **Original:** AZ Bricanyl (Approved in 1985)
- **Type:** SABA
- **Indication:** Bronchospasm
- **Mechanism of Action:** Terbutaline is a kind of selective adrenergic β2 receptor agonist, which can relax bronchial smooth muscles, inhibit the release of endogenous spasmogenic substances and endogenous neurotransmitter-induced edema, and improve the clearance ability of bronchial mucosa cilia.

2 Comparison of Bid Price of Terbutaline Between Original and Generic in China



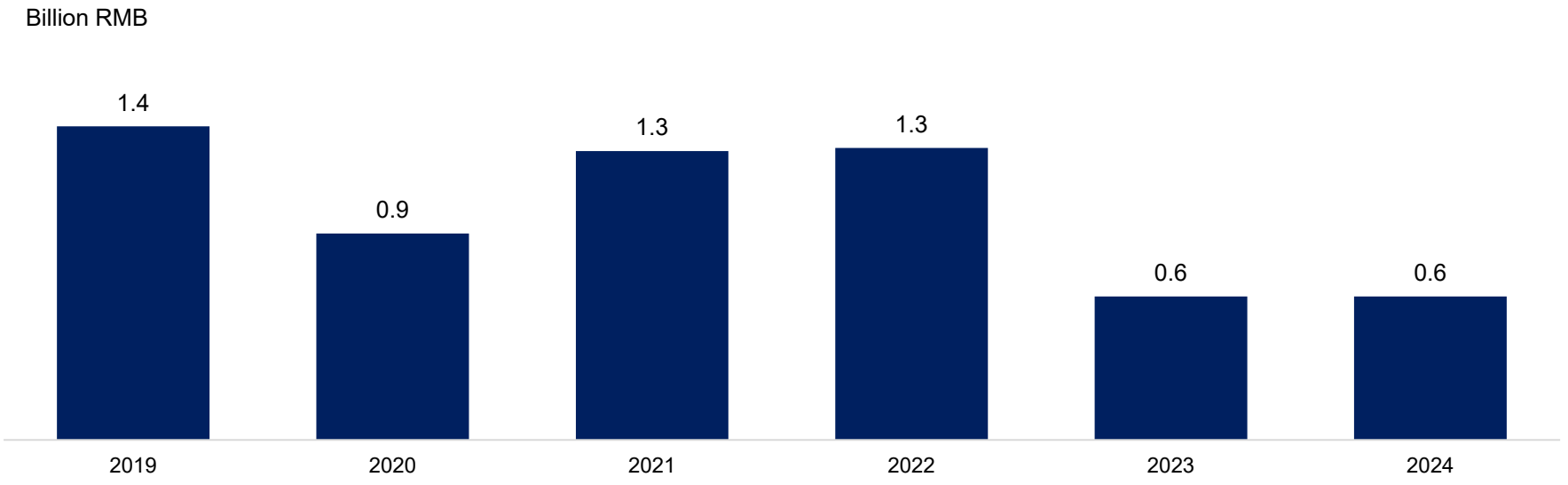
Source: CDE, Annual Report, Frost & Sullivan Analysis

Historical China Terbutaline Inhaler Market, 2019-2024

- In 2024, China market of terbutaline inhaler reached RMB0.6 billion, decreased from RMB1.4 billion in 2019, with a CAGR of -14.5% from 2019 to 2024.

China Terbutaline Inhaler Market, 2019-2024

Period	CAGR
2019-2024	-14.5%



Source: Frost & Sullivan Analysis

Competitive Landscape of Terbutaline in China

Marketed Terbutaline in China

Dosage Form	Manufacturer	Brand Name	First Approval Date	Indications	2023 Medical Insurance Status	VBP
Nebulization	AstraZeneca	Bricanyl	2000-12-15	Bronchospasm	List B since 2009	/
	Deyang Huakang	Hui De Li Kang (汇德立康)	2020-04-09			
	Hebei Renheyikang	Tan Lin Shu (坦林舒)	2020-11-24			√
	Shijiazhuang No.4	Fei Ta Lin (菲他林)	2021-04-07			/
	Suzhou Homesun	Kang Ni (康尼)	2021-06-01			√
	Sichuan Purity	Te Mei Jing (特美净)	2022-02-23			√
	Jiangsu Dahongying Hengshun	Heng Tuo Ni (恒托尼)	2022-06-07			√
	Joincare Haibin	Te Rui Tong (特瑞通)	2022-06-07			√
	Jewim Pharmaceutical	Bei Ke Shu (倍可舒)	2022-11-17			
	Hunan Kelun.	Ke Ai Li (科艾利)	2023-02-07			
	Nanjing Aureole	Ding Xin (丁信)	2023-04-11			
	Shenyang Sinqi	/	2023-04-11			/
	Univision Pharmaceutical	Qing Shuang (庆爽)	2023-05-12			
	Jiangxi Aishite	/	2023-05-19			
	Sichuan HMZS	Yi Kang Xin (亦康欣)	2023-05-19			
	CF PharmTech	Chang Lin (畅霖)	**2023-09-05**			

*This table was last updated on Sep 16th , 2025

Source: NMPA, Frost & Sullivan Analysis

Competitive Landscape of Terbutaline in China

Marketed Terbutaline in China

Dosage Form	Manufacturer	Brand Name	First Approval Date	Indications	2023 Medical Insurance Status	VBP
Nebulization	Chengdu Open	/	2023-12-05	Bronchospasm	List B since 2009	/
	Jiangsu PharmaMax	Li Pu Song (力扑松)	2023-12-13			
	Shandong Hualu	/	2023-12-29			
	Zhejiang CDMO/Jianmin Pharmaceutical	/	2024-04-07			
	Nanjing Aureole	Ding Xin (丁信)	2024-04-11			
	Hainan Huluwa	/	2024-04-17			
	Hainan Star	/	2024-04-24			
	Zhejiang CDMO/Zhejiang Bio-Diamond	/	2024-05-29			
	Kivipharm	/	2024-07-30			
	Hunan Warrant Pharmaceutical	Tai Shi Lin (泰适林)	2024-07-30			
	Zhejiang Jinhua Conba BioPharm.Co.,Ltd.	/	2025-01-08			
	Yangzhou Zhongbao Pharmaceutical Co.,Ltd.	/	2025-05-27			
	An Hui Healstar	/	2025-07-03			
	Jilin Aodong	/	2025-09-02			

Terbutaline at Clinical Stage in China

Dosage Form	Manufacturer	Clinical Stage	Indications	First Posted Date
Nebulization	Zhejiang Shapuaisi	NDA	Bronchospasm	/
	Jilin Aodong	NDA		
	Zhejiang Jinhua Conba	NDA		
	Anhui Jiexi	NDA		
	Yangzhou Zhongbao	NDA		
	Jinan Bairun	NDA		
	Shandong Dayin Jinkong Children's Pharmaceutical	NDA		
	Hebei Jinyihe Biotechnology	NDA		
	Hunan Sterol Pharmaceutical	NDA		

Source: NMPA, Frost & Sullivan Analysis

*This table was last updated on Sep 16th , 2025

Arformoterol Tartrate Overview

- Arformoterol tartrate nebulization (Brovana) was developed by the original manufacturer, Sunovion Pharmaceuticals Inc. Over 10 arformoterol tartrate nebulization have been approved by FDA. Among them, CF PharmTech is the only China developed arformoterol Nebulization products approved by FDA. Domestic manufacturers are rapidly developing this class of drugs in China.

1 Arformoterol Tartrate Overview

- **Original:** Sunovion Pharmaceuticals Inc. (Approved in 2006)
- **Type:** LABA
- **Indication:** chronic obstructive pulmonary disease (COPD), including bronchitis and emphysema
- **Mechanism of Action:** Beta2-receptors are the predominant adrenergic receptors in bronchial smooth muscle. They cause stimulation of intracellular adenyl cyclase, the enzyme that catalyzes the conversion of adenosine triphosphate (ATP) to cyclic-3',5'-adenosine monophosphate (cyclic AMP). Increased intracellular cyclic AMP levels cause relaxation of bronchial smooth muscle and inhibition of release of mediators of immediate hypersensitivity from cells, especially from mast cells. Preclinical studies have suggested that arformoterol is a more potent beta2-agonist than formoterol.

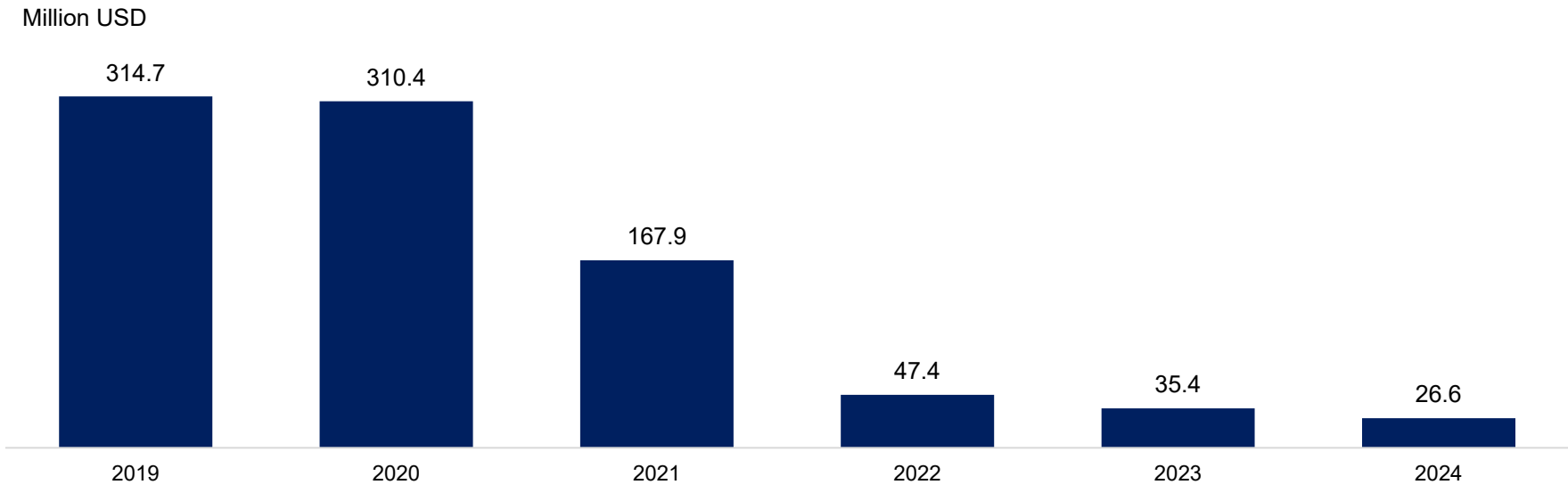
Source: CDE, Annual Report, Frost & Sullivan Analysis

Historical Global Arformoterol Tartrate Inhaler Market, 2019-2024

- In 2024, global market of arformoterol tartrate inhaler reached USD26.6 million, decreased from USD314.7 million in 2019, with a CAGR of -39.0% from 2019 to 2024.

Global Arformoterol Tartrate Inhaler Market, 2019-2024

Period	CAGR
2019-2024	-39.0%



Source: Frost & Sullivan Analysis

Competitive Landscape of Arformoterol Tartrate

Marketed Arformoterol Tartrate in the U.S.

Dosage Form	Manufacturer	Brand Name	First Approval Date	Indications
Nebulization	Lupin/Sunovion Pharmaceuticals	Brovana	2006-10-06	Long-term, twice daily maintenance treatment of bronchoconstriction in patients with COPD, including chronic bronchitis and emphysema
	Slate Run Pharma	/	2021-06-22	
	Cipla	/	2021-06-22	
	Teva	/	2021-11-09	
	Ritedose	/	2022-03-02	
	Alembic	/	2022-05-10	
	Sun Pharm	/	2022-05-26	
	Mannkind Pharma	/	2022-11-15	
	Slayback Pharma	/	2022-11-28	
	Pharmamax	/	2024-04-02	
	CF Pharmtech	**/**	**2024-05-17**	
	Dr Reddys	/	2024-06-03	
	LexenPharm	/	2024-11-18	
	Aucta	/	2025-02-03	
	Micro Labs	/	2025-03-07	
	Saba Ilac Sanayi	/	2025-04-25	

*This table was last updated on Sep 16th, 2025

Source: FDA, CDE, Frost & Sullivan Analysis

Competitive Landscape of Arformoterol Tartrate

Arformoterol Tartrate at Clinical Stage in China

Dosage Form	Manufacturer	Clinical Stage	Indications	First Posted Date/Clinical Approval Date
Nebulization	Jiangsu Chia Tai-tianqing	BE	Long-term, twice daily (morning and evening) maintenance treatment of bronchoconstriction in patients with COPD, including chronic bronchitis and emphysema	2016-12-15
	Jiangsu PharmaMax	Phase III		2022-10-14
	Hunan Warrant	Phase III		2024-04-25
	Jiangsu Hechen	Phase III		2024-08-02
	Hainan Star	Phase III		2024-08-15
	CF PharmTech	**Clinical Approval**		2023-06-25
	Jewim	Clinical Approval		2023-09-16
	Hainan Huluwa	Clinical Approval		2024-07-23
DPI	Guangdong Yili	Phase I		2021-01-22

*This table was last updated on Sep 16th , 2025

Source: FDA, CDE, Frost & Sullivan Analysis

Salbutamol Sulphate Overview

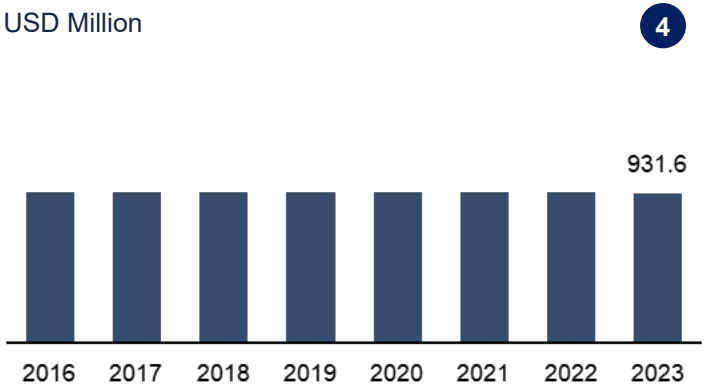
Key Information

- Salbutamol sulfate nebulization was first manufactured by GlaxoSmithKline Pharmaceuticals. From 2016 to 2019, global sales of Ventolin grew from £785 million to £938 million. In 2023, global sales of Ventolin decrease to £749 million.
- In China, there are over 20 salbutamol sulphate nebulization available till June 2024. Among them, 4 domestic manufacturers have been selected by the ninth batch of National Centralized Drug Procurement, while the originator has not been chosen.

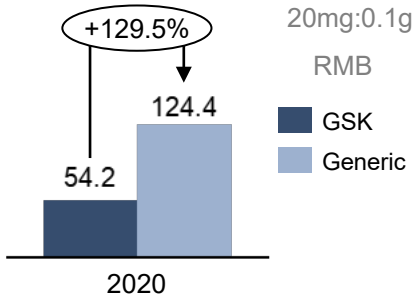
1 Salbutamol Sulphate Overview

- **Original:** GlaxoSmithKline (Approved in 1981)
- **Type:** SABA
- **Indication:** Bronchial asthma and chronic bronchospasm
- **Mechanism of Action:** Stimulates intracellular adenylate cyclase by acting on β-adrenergic receptors, increases cyclic adenosine levels, relaxes bronchial smooth muscle, and inhibits mediator release from tachyphylactic hypersensitive cells (especially mast cells)

2 Global Ventolin Sales Revenue



4 Comparison of Bid Price of Salbutamol Sulphate Between Original and Generic Drug in China



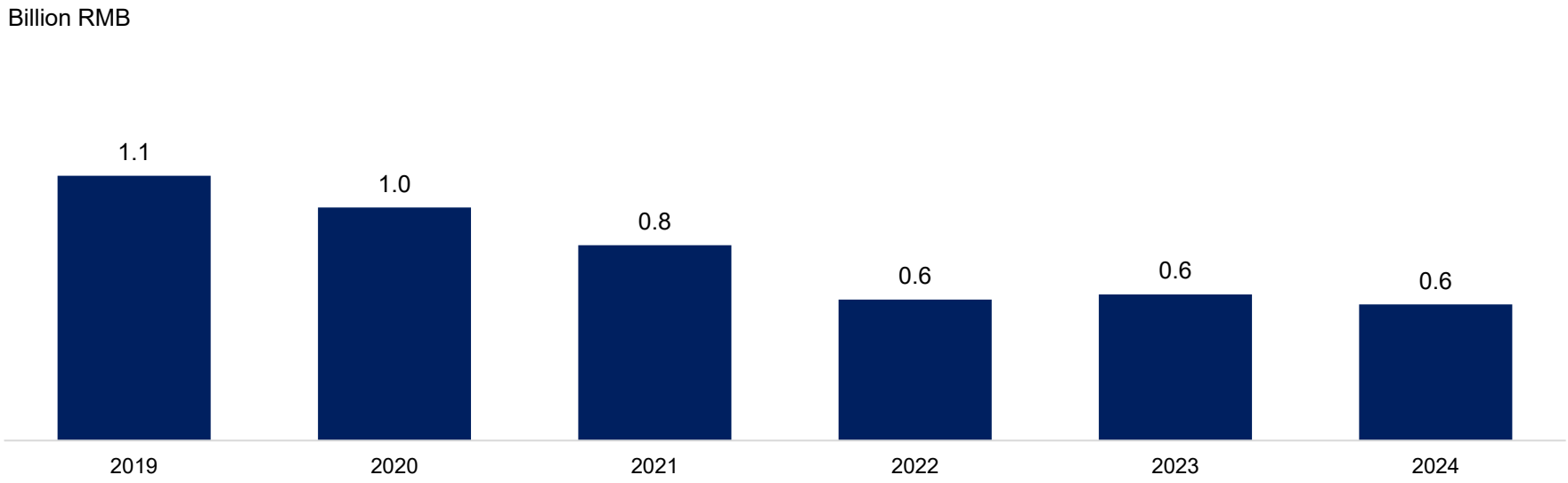
Source: CDE, Annual Report, Frost & Sullivan Analysis

Historical China Salbutamol Sulphate Inhaler Market, 2019-2024

- In 2024, China market of salbutamol sulphate inhaler reached RMB0.6 billion, decreased from RMB1.1 billion in 2019, with a CAGR of -12.5% from 2019 to 2024.

China Salbutamol Sulphate Inhaler Market, 2019-2024

Period	CAGR
2019-2024	-12.5%



Source: Frost & Sullivan Analysis

Competitive Landscape of Salbutamol Sulphate in China

Marketed Salbutamol Sulphate in China

Dosage Form	Manufacturer	First Approval Date	Indications	2023 Medical Insurance Status	VBP
DPI	Shanghai Sine Tianping Pharmaceutical Co.,Ltd.	1995-01-01	Asthma, Bronchospasm	List B since 2017	
	GlaxoSmithKline	2000-08-04			
	GlaxoSmithKline	2000-10-24 (capsule)			
	Orion Corporation	2008-09-02			
Aerosol (MDI)	GlaxoSmithKline	2003-09-19		/	/
	LUNAN BETTER	2006-04-28			
	Jewim	2011-09-23			
	YANGZHOU NO.3	2012-12-11			
	SPH Sine	2015-07-01			
Nebulization	Shanghai Sine-Jinzhu	1999-01-01		List A since 2009	
	Shenzhen Dafo	2000-01-01			/
	GlaxoSmithKline	2001-01-01			
	Hebei Renheyikang	2020-02-05			√
	Suzhou Homesun	2020-07-08			√
	Sichuan Purity/Shandong Hualu	2020-11-02			√
	Zhejiang Fresh	2021-02-02			√

*This table was last updated on Sep 16th , 2025

Source: NMPA, Frost & Sullivan Analysis

Competitive Landscape of Salbutamol Sulphate in China

Marketed Salbutamol Sulphate in China

Dosage Form	Manufacturer	First Approval Date	Indications	2023 Medical Insurance Status	VBP
Nebulization	Jewim	2021-04-07	Asthma, Bronchospasm	List A since 2009	/
	CF PharmTech	**2021-10-26**			
	Weifang Zhongshi	2022-11-15			
	Shanghai Sine	2022-12-09			
	Shanghai ZhaoHui	2022-12-30			
	Hainan Star	2022-12-30			
	Hunan Warrant	2023-03-24			
	Nanjing Aureole	2023-03-24			
	Weifang Zhongshi	2023-04-28			
	Ma'anshan Fengyuan	2023-08-08			
	Lodays	2023-11-07			
	Lexen	2024-03-05			
	Chengdu Huayu	2024-04-24			
	Zhejiang CDMO	2024-06-04			
	Nanjing Aureole	2024-06-18			
	Shandong Hualu	2024-06-18			
	Tianjin Meihua biomedical	2024-09-19			
	Hainan Huluwa	2025-01-02			
	Teva Pharmaceutical	2025-05-27			

*This table was last updated on Sep 16th , 2025

Source: NMPA, Frost & Sullivan Analysis

Glycopyrrolate Bromide Overview

- Glycopyrrolate bromide inhalation powder Nebulization was developed by Novartis and was approved for marketing in China in April 2018. Currently, two pharmaceutical companies (Jiangsu Hengrui and Haisco) have submitted and received approval for clinical trials for glycopyrrolate bromide inhalation powder Nebulization. In Europe only the original company currently markets the product.
- In 2017, the original drug Seebri Breezhaler recorded a peak global sales of USD151 million.

1 Glycopyrrolate Bromide Overview

- **Original:** Novartis (Approved in 2015)
- **Type:** LAMA
- **Indication:** COPD
- **Mechanism of Action:** Glycopyrrolate bromide is a long-acting acetylcholine receptor antagonist (LAMA) that is four times more selective for human acetylcholinergic M3 receptors than M2 receptors, and can specifically bind and inhibit M3-type acetylcholine receptors distributed in bronchial smooth muscle to dilate the airway. Glycopyrrolate bromide can help improve lung function, reduce symptoms such as shortness of breath and cough and enhance the overall quality of life for patients with COPD.

Source: CDE, Annual Report, Frost & Sullivan Analysis

Competitive Landscape of Glycopyrrolate Bromide in China

Marketed Glycopyrrolate Bromide in China

Dosage Form	Manufacturer	Brand Name	First Approval Date	Indications	2023 Medical Insurance Status	VBP
DPI	Novartis	Seebri Neohaler	2018-04-16	long-term, maintenance treatment of airflow obstruction in patients with COPD	/	/

Glycopyrrolate Bromide at Clinical Stage in China

Dosage Form	Manufacturer	Clinical Stage	Indications	First Posted Date/Clinical Trial Approval Date
DPI	Shenzhen Haibin	BE	COPD	2018-10-19
	Sichuan Haisike	BE		2019-12-25
	Reyoung Pharmaceutical	BE		2021-03-25
	Shenzhen Resproly	BE		2022-12-27
	Jewim	Phase I		2024-04-12
	CF PharmTech	**Clinical Approval**		2023-05-08
SMI	Anovent Pharmaceuticals	Phase I		2023-09-11
	Renhe Yikang	Clinical Approval		2023-02-08

*This table was last updated Sep 16th , 2025

Source: NMPA, CDE, Frost & Sullivan Analysis

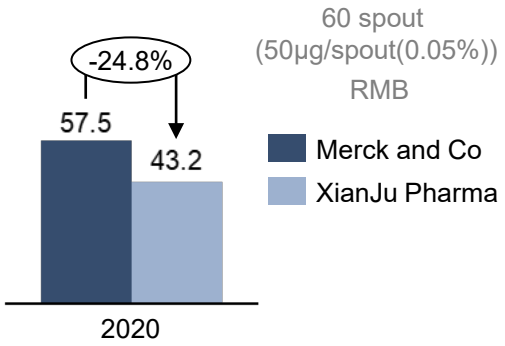
Mometasone Furoate Overview

- Merck Sharp & Dohme first developed Nasonex for the treatment of allergic rhinitis. Generic companies in the U.S. now include Apotex and Amneal, Inc. In 2013, Nasonex recorded a peak global sales of USD1,335 million.
- The price of original mometasone furoate nasal spray are higher than generic drugs.
- Currently, domestic Zhejiang Xianju Pharmaceutical has developed this type of drug and has successfully marketed it in China. 2 pharmaceutical companies, Sichuan Purity and Otsuka Pharmaceutical, are in the NDA stage (inactive).

1 Mometasone Furoate Overview

- **Original:** Merck Sharp & Dohme (Approved in 1997)
- **Type:** ICS
- **Indication:** Allergic Rhinitis
- **Mechanism of Action:** Mometasone furoate nasal spray is a potent anti-inflammatory glucocorticoid with broad inhibitory effects on many cell types (mast cells, eosinophils, neutrophils, macrophages and lymphocytes) and mediators (histamine, leukotrienes and cytokines) involved in the inflammatory response. Mometasone furoate nasal spray can reduce inflammation in the nasal passages, and thereby significantly improves various nasal and ocular symptoms.

2 Comparison of Bid Price of Mometasone Furoate Nasal Spray between Original and Generic Drug in China



Source: CDE, Annual Report, Frost & Sullivan Analysis

Competitive Landscape of Mometasone Furoate in the U.S.

Marketed Mometasone Furoate in the U.S.

Dosage Form	Manufacturer	Brand Name	First Approval Date	Indications
Nasal Spray	APOTEX	Mometasone Furoate	2016-03-22	Allergic rhinitis
	AMNEAL PHARMS	Mometasone Furoate	2017-04-03	
	PERRIGO PHARMA INTL	Nasonex 24HR Allergy	2022-03-17	
	AUROBINDO PHARMA	Mometasone Furoate	2024-03-18	
DPI	Organon/Merck	Asmanex Twisthaler	2005-03-30	Asthma
MDI	Organon/Merck	Asmanex HFA	2014-04-25	Asthma

*This table was last updated on Sep 16th , 2025

Source: FDA, Frost & Sullivan Analysis

Competitive Landscape of Mometasone Furoate in China

Marketed Mometasone Furoate in China

Dosage Form	Manufacturer	Brand Name	First Approval Date	Indications	2023 Medical Insurance Status	VBP
Nasal Spray	Schering-Plough/Organon/Merck	Nasonex	2000-07-14	nasal symptoms of seasonal allergic and perennial allergic rhinitis	List B since 2017	/
	Zhejiang Xianju	Yi Qing (逸青)	2011-12-01			
	Lek Pharmaceuticals	Nasometin	2022-11-15			

Mometasone Furoate at Clinical Stage in China

Dosage Form	Manufacturer	Clinical Stage	Indications	First Posted Date
Nasal Spray	Sichuan Otsuka	NDA	Allergic rhinitis	2019-05-10
	Sichuan Purity	NDA		2020-09-16
	CF PharmTech	**Phase III**		2024-07-12
	Shanghai Baian/Nanchang Baiji	BE		2020-05-06
	Jewim	BE		2022-11-18
	Yangtze River	Clinical Approval		2020-04-26
	Kunming Yuanrui	Clinical Approval		2023-12-12

*This table was last updated on Sep 16th , 2025

Source: NMPA, CDE, Frost & Sullivan Analysis

Formoterol and Beclometasone Overview

- In China, Foster/Fostair MDI, manufactured by Chiesi Farmaceutici is the only formoterol and beclometasone inhalation formulation for long-term treatment of chronic asthma and COPD. In 2017, Foster recorded a peak global sales of USD744.3 million. As of the Latest Practicable Date, there were eight beclomethasone/formoterol MDI products approved globally, including Chiesi Air's Fostair® and its generic drugs.

1 Formoterol and Beclometasone Overview

- **Original:** Chiesi Farmaceutici SPA Foster/Fostair (Approved in 2006)
- **Type:** ICS+LABA
- **Indication:** Long term treatment of chronic asthma and COPD (maintenance and symptomatic treatment)
- **Mechanism of Action:** Formoterol is an inhaled long-acting beta2-adrenergic receptor agonist used as a bronchodilator which acts on bronchial smooth muscle to dilate and relax airways. Beclomethasone dipropionate works by attenuating the inflammatory responses associated with asthma, allergic rhinitis, nasal polyps, and corticosteroid-responsive dermatoses. It suppresses the actions of inflammatory cells, such as mast cells, eosinophils, basophils, lymphocytes, macrophages, and neutrophils.

Source: CDE, Annual Report, Frost & Sullivan Analysis

Competitive Landscape of Formoterol and Beclometasone MDI in Europe

Formoterol and Beclometasone Approved in Europe

Dosage Form	Brand Name	Manufacturer	First Approval Date	Indications
MDI	Foster	Chiesi	2007-02-27	Asthma, COPD
	Aforbe	Mylan	2022-07-13	
	Luforbec	Lupin	2022-07-13	
	/	Zakłady Farmaceutyczne	2022-07-13	
	/	Zentiva Pharma	2022-07-13	
	Befoair	Orion	2023-05-24	
	Bibecfo	Cipla	2023-11-09	
	Airfonsib	Sandoz	2024-01-24	

*This table was last updated on Sep 16th , 2025

Source: NMPA, CDE, HMA, Frost & Sullivan Analysis

Competitive Landscape of Formoterol and Beclometasone in China

Marketed Formoterol and Beclometasone in China

Dosage Form	Manufacturer	First Approval Date	Indications	2023 Medical Insurance Status	VBP
MDI	Chiesi Farmaceutici SpA	2013-02-04	Asthma, COPD	List B since 2017	/
DPI	Chiesi Farmaceutici SpA	2024-12-01		/	/

Formoterol and Beclometasone at Clinical Stage in China

Dosage Form	Manufacturer	Clinical Stage	Indications	First Posted Date/Clinical Trial Approval Date
MDI	REYOUNG PHARMACEUTICAL	BE	Asthma	2021-04-14
	LUNAN BETTER PHARMACEUTICAL	BE		2024-10-14
	Hefei Licheng Pharmaceutical	BE		2025-01-02
	Jewim Pharmaceutical	Phase III		2024-11-05

*This table was last updated on Sep 16th , 2025

Source: NMPA, CDE, Frost & Sullivan Analysis

Competitive Landscape

- Formoterol fumarate Nebulization is used as a long-term (maintenance) treatment to prevent or decrease breathing problems caused by ongoing lung diseases (chronic obstructive pulmonary disease-COPD, including chronic bronchitis and emphysema). Formoterol belongs to the class of drugs known as LABAs. It functions to relax the muscles within the airways, thereby enhancing breathing and alleviating symptoms like wheezing, coughing and breathlessness. A major clinical advantage of formoterol over other inhaled beta-agonists is its rapid onset of action (2-3 minutes), which is at least as fast as salbutamol, combined with a long duration of action (12 hours).
- Revefenacin is a long-term medication used to treat an ongoing lung disease, chronic obstructive pulmonary disease (COPD). Inhaled revefenacin is a LAMA that can stimulate beta-2 adrenergic receptors in the airway smooth muscle, leading to bronchodilation and improved airflow. First developed by Mylan/Theravance, revefenacin was approved by the FDA in 2018 under the brand name Yupelri, its originator drug recorded a global peak sales of US220.8 million in 2023. As of the Latest Practicable Date, there were 3 approved revefenacin nebulization globally. Yupelri is the only officially approved revefenacin inhalants, which is the first FDA approved once-daily, nebulized, maintenance medicine for COPD and potentially to be one of the first NMPA approved once-daily, nebulized, maintenance medicine for COPD. Mankind and Orbicular's revefenacin nebulization were provisional approved by the FDA in 6th Jan 2025 and 19th Nov 2024 respectively.
- Tiotropium bromide monohydrate/olodaterol hydrochloride is a fixed dose combination of LAMA, tiotropium, and LABA, olodaterol, indicated for the long-term, once-daily maintenance bronchodilator treatment of airflow obstruction in patients with COPD, including chronic bronchitis and emphysema. Across the globe, Inspiolto Respimat/Spiolto is the only approved tiotropium bromide and olodaterol hydrochloride SMI. First developed by Boehringer Ingelheim, the tiotropium bromide and olodaterol hydrochloride SMI product was approved by the FDA in 2015 under the brand name Inspiolto Respimat/Spiolto As of the Latest Practicable Date, it remained to be the only approved tiotropium bromide and olodaterol hydrochloride SMI product globally and in China.
- Indacaterol/glycopyrronium bromide, is a fixed-dose combination medication for inhalation consisting of the following two active ingredients an ultra-long-acting beta-adrenoceptor agonist (ultra-LABA) and a muscarinic anticholinergic (LAMA). Indacaterol maleate/glycopyrronium bromide is used as a maintenance bronchodilator treatment to relieve symptoms in adult patients with COPD. Ultibro Breezhaler/Xoterna Breezhaler is the only approved indacaterol maleate and glycopyrronium bromide DPI. First developed by Novartis, the indacaterol maleate and glycopyrronium bromide DPI candidate was approved by the FDA in 2013 under the brand name Ultibro Breezhaler/Xoterna Breezhaler. As of the Latest Practicable date, it remained to be the only approved drug of its kind globally and in China.

Generic Name	Brand Name (Original Drug)	Manufacturer	Marketed Authority	Peak Sales Revenue, USD Million	FDA First Approval Year
Formoterol fumarate Nebulization	Perforomist	Mylan	FDA, NMPA	NA	2007
Revefenacin Nebulization	Yupelri	Mylan/Theravance	FDA	220.8 (2023)	2018
Tiotropium bromide and olodaterol hydrochloride SMI	Inspiolto Respimat/Spiolto	BI	FDA, EMA, NMPA	NA	2015
Indacaterol maleate and glycopyrronium bromide DPI	Ultibro Breezhaler/Xoterna Breezhaler	Novartis	FDA, EMA, NMPA	623.0 (2020)	2013

Source：FDA, EMA, NMPA, Annual Report, Frost & Sullivan Analysis

*This table was last updated on Sep 16th , 2025

Competitive Landscape of Formoterol Fumarate Globally and in China

- First developed by Mylan, formoterol fumarate solution Nebulization was approved by the FDA in 2007 under the brand name Perforomist. As of the Latest Practicable Date, there were 11 and **22** approved formoterol fumarate nebulization globally and in China, respectively. In addition, formoterol fumarate is also marked in other inhalation formats, including DPI.

Global Approved Formoterol Fumarate

Dosage Form	Manufacturer	First Approval Date	Indications
Nebulization	Mylan	2007-05-11	COPD
	Teva	2021-06-22	
	Alemic	2021-11-22	
	Lupin	2022-08-22	
	Ritedose Corp	2022-11-25	
	Wilshire Pharms	2022-12-13	
	Mannkind Pharma	2023-03-22	
	Micro Labs	2024-06-26	
	LEXENPHARM	2024-10-22	
	DR REDDYS	2025-01-30	
	DEVA HOLDING AS	2025-02-11	

China Approved Formoterol Fumarate

Dosage Form	Manufacturer	First Approval Date	Indications	2023 Medical Insurance Status	VBP
DPI	AZ	2000-02-03	COPD	List B	/
Nebulization	Chia Tai-tianqing Pharmaceutical	2020-04-08			
	Weifang Zhongshi Pharmaceutical/Luoxin Aurovitas Pharma(Chengdu)	2022-08-23			
	Mylan	2023-06-30			
	ShenZhen Taitai Pharmaceutical	2023-07-06			
	Jiangsu Dahongying Hengshun	2024-04-24			
	Shandong Hualu Pharmaceutical	2024-05-28			
	Jewim Pharmaceutical	2024-06-28			
	Chengdu Open Pharmaceutical	2024-10-22			
	Sichuan Purity Pharmaceutical	2024-10-22			

Source：FDA, EMA, ClinicalTrials, EU CTR, Annual Report, Frost & Sullivan Analysis

*This table was last updated on Sep 16th , 2025

Competitive Landscape of Formoterol Fumarate Globally and in China

China Approved Formoterol Fumarate

Dosage Form	Manufacturer	First Approval Date	Indications	2023 Medical Insurance Status	VBP
Nebulization	Chiesi Farmaceutici SpA	2024-12-01	COPD	List B	/
	Hebei Renheyikang Pharmaceutical	2024-12-25			
	CF PharmTech	**2025-01-08**			
	Nanjing Licheng Pharmaceutical	2025-01-08			
	Tianjin Tianyao Pharmaceuticals	2025-01-14			
	Lexen Pharmaceutical (Suzhou)	2025-01-14			
	Jiangsu PharmaMax	2025-01-24			
	Hainan Star Pharmaceutical	2025-04-08			
	Hunan Kelun Pharmaceutical Co.,Ltd.	2025-04-22			
	Zhejiang CDMO Pharmaceutical Co., Ltd	2025-04-30			
	Shanghai Sine-Jinzhu Pharmaceutical Co., Ltd	2025-05-27			
	Shijiazhuang No.4 Pharmaceutical Co.,Ltd.	2025-06-24			
	Luo Xin'an Ruoweita Pharmaceutical	2025-07-22			

*This table was last updated on Sep 16th , 2025

Source：FDA, EMA, ClinicalTrials, EU CTR, Annual Report, Frost & Sullivan Analysis

Competitive Landscape of Indacaterol Maleate and Glycopyrronium Bromide Globally and in China

- Clinical evidence proved that treatment with LAMA/LABA combinations has been shown to produce greater improvement in FEV1 and reduction in rescue medication use than ICS/LABA or ICS/LAMA. It can effectively improve lung function, reduce the frequency of acute exacerbations, alleviate dyspnea and other symptoms and significantly enhance the overall quality of life.
- As of the Latest Practicable date, it remained to be the only approved drug of its kind globally and in China. In addition, there were 11 indacaterol maleate and glycopyrronium bromide candidates at clinical stage in China and 1 in Europe as of the same date.

Indacaterol Maleate and Glycopyrronium Bromide at Clinical Stage in Europe

Dosage Form	Manufacturer	Clinical Stage	Indications	First Posted Date/Clinical Trial Approval Date
DPI	Orion Corporation	Phase 1	COPD	2021-4-22

Indacaterol Maleate and Glycopyrronium Bromide at Clinical Stage in China

Dosage Form	Manufacturer	Clinical Stage	Indications	First Posted Date/Clinical Trial Approval Date
DPI	Sichuan Haisike Pharmaceutical	Phase III	COPD	2023-11-30
	Jiangsu Chia Tai-tianqing	BE		2017-11-03
	Shenzhen Haibin Pharmaceutical	BE		2018-11-20
	Jiangxi Aishite Pharmaceutical	BE		2022-07-25
	Sichuan Kelun Pharmaceutical	BE		2025-03-17
	Sichuan Purity	BE		2025-06-17
	JIANGXI GUOYAO	BE		2025-08-20
	Beijing Kangchuanglian	BE		2025-08-21
	Jiangsu Hengrui Medicine	Phase II		2023-09-13
	Jewim Pharmaceutical	Phase I		2024-04-12
	Respirent Pharmaceuticals	Clinical Approval		2023-09-24

Source：FDA, EMA, ClinicalTrials, EU CTR, Annual Report, Frost & Sullivan Analysis

*This table was last updated on Sep 16th , 2025

Competitive Landscape of Revefenacin Nebulization in China

- Till LPD, there is no approved revefenacin Nebulization in China.

China Revefenacin Nebulization at Clinical Stage

Dosage Form	Manufacturer	Clinical Stage	Indications	First Posted Date
Nebulization	Mylan	NDA	COPD	/
	Humanwell Puracap (Likang) Pharmaceuticals	Clinical Approval		2023-09-01
	Yunnan Longhai Natural Phytopharmaceutical	Clinical Approval		2024-02-05
	CF PharmTech	Clinical Approval		2024-08-31

*This table was last updated on Sep 16th , 2025

Source：FDA, EMA, ClinicalTrials, EU CTR, Annual Report, Frost & Sullivan Analysis

Overview of Current and Proposed Surgical and Bronchoscopic Interventions for People with COPD

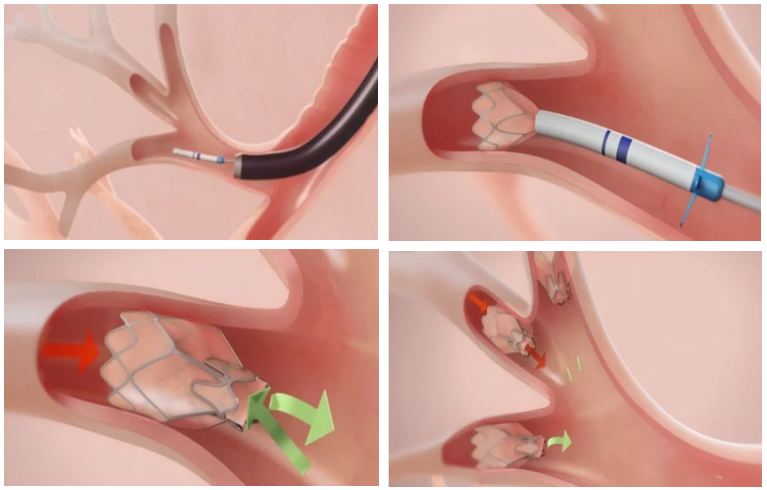
Surgical and Bronchoscopic Interventions for People with COPD

	Chronic Mucus Production	Exacerbations	Dyspnea
Symptoms			
Disorders	• Chronic bronchitis	• Acute and chronic bronchitis • Bulla • **Emphysema** • Tracheobronchomacia	• Bulla • **Emphysema** • Tracheobronchomacia
Surgical and Bronchoscopic Interventions	• Nitrogen Cryospray • Rheoplasty	• Targeted lung denervation	• Giant bullectomy • **Endobronchial valves (EBV)** • Large airway stenting • Lung transplantation

- As an advanced form of COPD, severe emphysema most commonly results from smoking which destroys the alveoli in the lungs, causing reduced lung function, chronic shortness of breath, low blood oxygen levels and progressive lung hyperinflation. Currently, disease management mainly involves bronchodilators and ICS to manage symptoms, pulmonary rehabilitation or oxygen therapy. In 2024, there were around 100 million patients globally suffering from emphysema.
- Due to the morbidity and mortality associated with lung volume reduction (LVRs), less invasive bronchoscopic approaches to lung reduction have been examined. These include a variety of different bronchoscopic procedures to perform lung volume reduction (endoscopic lung volume reduction, ELVR) including airway bypass stents, EBV, self-activating coils, sealants and thermal ablative techniques.
- **EBV are the most well studied therapy of all ELVR techniques.**

Overview of EBV

- EBV is a minimally invasive procedure during which pulmonologists place special one-way valves within airways in the pre-selected lobe of the lungs that are most damaged. During exhalation, the valves open, allowing air and other secretions to escape from the treated lobe. And during inhalation, the valves close, blocking air from entering the treated lobe. Within hours, the treated lobe expectedly collapses, reducing the effects of lung hyperinflation. Once the lung reduces in size, it also reduces pressure on the diaphragm, which helps patient breath better.
- Compared to standard medical treatment, EBV offers significant benefits in terms of survival, lung function, quality of life, and exercise capacity, despite the potential adverse events related to the procedure or the implants.



Source: GLOBAL STRATEGY FOR PREVENTION, DIAGNOSIS AND MANAGEMENT OF COPD: 2024 Report, Frost & Sullivan Analysis

Global Marketed Endobronchial Valves (EBV)

- As of the Latest Practicable Date, there were 2 approved EBV globally and in China.
- Till 2024, around 56,000 patients globally have been treated with Zephyr® Valves for their severe COPD/emphysema.

Brand Name	Manufacturer	Indication	Marketed Authority	2023 Sales Revenue, USD Million	First Approval Year
Zephyr	Pulmonx	Breathing difficulty from severe emphysema	FDA, European Commission	NA	2003 (European Commission) 2015-2-17 (NMPA) 2018-06-29 (FDA)
Spiration	Olympus		FDA, European Commission, NMPA	NA	2008 (European Commission) 2015-08-26 (NMPA) 2018-12-5 (FDA)

*This table was last updated on Sep 16th , 2025

Source：FDA, Euopean Commission, NMPA, ClinicalTrials, Annual Report, Frost & Sullivan Analysis

Competitive Landscape of EBV in China

In China, there were 3 EBV at clinical stage in China.

Manufacturer	Indication	Clinical Stage	First Posted Date
Anhui Feichang Medical Technology	Breathing difficulty from severe emphysema	Confirmatory Trials	2023-09
Jiangsu Sairen Medical Technology		Confirmatory Trials	2024-03
CF PharmTech		Confirmatory Trials	2024-10

*This table was last updated on Sep 16th , 2025

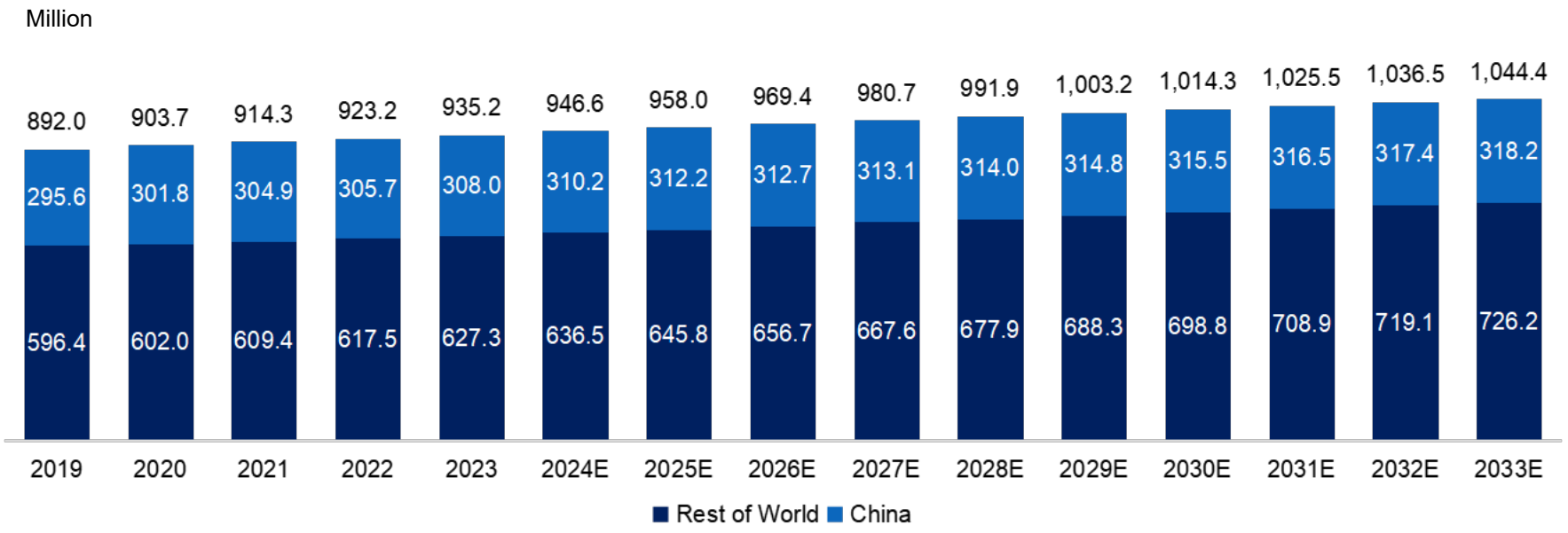
Source：ClinicalTrials, CDE, Frost & Sullivan Analysis

Global Prevalence of DED, 2019-2033E

- Globally, the number of patients affected by DED reached 935.2 million in 2023, with a CAGR of 1.2% from 2019 to 2023, and this number is forecasting to reach 1,044.4 million in 2033; the number of patients affected by DED in China reached 308.0 million in 2023, with a CARG of 1.0% from 2019 to 2023 and this number is forecasting to reach 318.2 million in 2033.

Global Prevalence of DED, 2019-2033E

CAGR	Global	China
2019-2023	1.2%	1.0%
2023-2033E	1.1%	0.3%



Source: Literature review, Frost & Sullivan analysis

Global and China Competitive Landscape of Dry Eye Disease Inhalants

- Dry eye syndrome is a common ocular condition characterized by insufficient tear production or rapid tear evaporation, leading to discomfort, irritation, and potential vision problems. The current treatment paradigm primarily relies on artificial tears, topical anti-inflammatory medications, and in severe cases, tear duct plugs or surgery. However, these approaches often provide only temporary relief and may require frequent application, leading to compliance issues. In recent years, research has explored alternative treatment methods, including inhalation formulations. These formulations aim to stimulate natural tear production by targeting specific nerves.

Global and China Approved Dry Eye Disease Inhalants

Dosage Form	Manufacturer	Generic Name	Brand Name	Market Authority	First Approval Date	Indications	2023 Sales Revenue, USD Million
Nasal Spray	Oyster Point Pharma	Varenicline Tartrate	Tyrvaya	FDA	2021-10-15	Dry eye disease	NA

*This table was last updated on Sep 16th , 2025

Source：FDA, EMA, ClinicalTrials, EU CTR, Annual Report, Frost & Sullivan Analysis

Glossary

“active pharmaceutical ingredient”, or “API”	The biologically active component in a pharmaceutical drug that produces the intended therapeutic effect. APIs are responsible for diagnosing, curing, mitigating, treating, or preventing diseases and are formulated in precise dosages to ensure efficacy and safety. In the context of inhalation therapies, APIs are delivered directly to the respiratory system, enhancing the medication’s effectiveness while minimizing systemic exposure.
“AE”	Adverse effects
“bioavailability”	The proportion of a drug that enters the systemic circulation when introduced into the body and is available for therapeutic action. High bioavailability indicates that a drug is effectively absorbed and utilized by the body, which is crucial for the efficacy of inhalation therapies.
“bioequivalence studies”	Research studies designed to compare the bioavailability of two pharmaceutical substances, typically a generic drug and its brand-name counterpart. BE studies ensure that the generic drug performs in the same manner as the original drug in terms of absorption, distribution, metabolism, and excretion, thereby validating its therapeutic equivalence.
“bronchodilator”	A class of drugs that relaxes the smooth muscles of the airways, thereby alleviating breathing difficulties. Primarily used to treat chronic respiratory diseases such as asthma and COPD.
“central nervous system”, or “CNS”	A system comprises the brain and spinal cord, responsible for processing sensory information and coordinating bodily functions. It serves as the primary target for therapies addressing neurological and psychiatric disorders.
“CFD”	computational fluid dynamics, a method using computer simulations to analyze and predict the behavior of fluids including liquid and gas flows under various conditions
“chronic obstructive pulmonary disease”, or “COPD”	A group of progressive lung diseases, including emphysema and chronic bronchitis, that cause airflow blockage and breathing-related problems. COPD is a primary target indication for many inhalation formulations, aiming to relieve symptoms and improve quality of life.
“chronic respiratory diseases”	A group of persistent or recurring conditions that affect the lungs and airways, including asthma, COPD, and allergic rhinitis. These diseases contribute significantly to the global healthcare burden due to their high prevalence, chronic nature, and significant impact on quality of life.
“CMC”	The comprehensive documentation and processes that define the chemical composition, manufacturing procedures, and quality control measures for pharmaceutical products. CMC encompasses the development, scale-up, and validation of manufacturing methods to ensure consistent product quality and compliance with regulatory standards.

Glossary

“corticosteroids”, or “ICS”	Steroid medications primarily used to reduce inflammation in the airways, controlling and preventing asthma and COPD symptoms. ICS are typically used as long-term maintenance therapy to help patients reduce the frequency and severity of acute exacerbations.
“endobronchial valves”, or “EBV”	Minimally invasive medical devices used to treat emphysema, an advanced form of COPD. EBVs are placed in the airways of the most damaged lung lobes to allow air and secretions to escape during exhalation while blocking air entry during inhalation, promoting the collapse of the treated lobe and reducing lung hyperinflation.
“excipients”	Inactive substances formulated alongside the API in a drug product. Excipients play various roles, including aiding the manufacturing process, enhancing drug stability, and improving the delivery and absorption of the active ingredient in inhalation formulations.
“fixed-dose combination”	Pharmaceutical products that combine two or more active pharmaceutical ingredients (APIs) in a fixed ratio within a single dosage form. Fixed-dose combinations aim to enhance therapeutic efficacy, improve patient adherence, and simplify treatment regimens by providing multiple therapeutic effects through a single administration.
“formulation development”	The process of designing and producing a drug in a specific form to optimize its delivery, stability, efficacy, and patient compliance. For inhalation products, this involves selecting appropriate active and inactive ingredients and determining the delivery mechanism (e.g., DPI, MDI).
“Good Manufacturing Practice”, or “GMP”	A system for ensuring that products are consistently produced and controlled according to quality standards. GMP covers all aspects of production, from raw materials to finished products, ensuring the safety, quality, and efficacy of pharmaceutical products.
“minimally invasive surgery”	A sub-segment of the generalized concept of minimally invasive operation, which is generally for the treatment purpose and performed through small incisions. MIS is widely used in surgical specialties of general surgery, OBGYN, urology, thoracic surgery and orthopedics, among others.
“muscarinic antagonists”	Anticholinergic drugs that block muscarinic receptors in the airways, reducing bronchoconstriction.

Glossary

“mycobacterium avium complex (MAC) lung disease”	A chronic lung infection caused by a group of slow- growing environmental bacteria, primarily affecting immunocompromised populations such as those with HIV/AIDS. MAC lung disease presents significant public health challenges due to its complex treatment regimens and potential for antibiotic resistance.
“nose-to-brain pathway”	An innovative drug delivery method that facilitates the direct transport of medications from the nasal cavity to the brain, bypassing the blood-brain barrier. This pathway is particularly useful for treating central nervous system (CNS) disorders, offering rapid onset of action and improved drug efficacy by targeting brain tissues directly.
“particle size distribution”	The analysis of the range and proportion of particle sizes within an aerosol. For inhalation therapies, maintaining an optimal particle size distribution is essential for ensuring that the medication effectively reaches and deposits in the lower respiratory tract.
“pharmacodynamics”, or “PD”	The study of the biochemical and physiological effects of drugs on the body, including the mechanisms of drug action and the relationship between drug concentration and effect. PD helps in understanding the therapeutic and adverse effects of medications.
“pharmacokinetics”, or “PK”	The branch of pharmacology concerned with the movement of drugs within the body. It involves the study of drug absorption, distribution, metabolism, and excretion (ADME). Understanding PK is essential for determining appropriate dosing regimens and ensuring therapeutic efficacy and safety.
“PI(s)”	The Principal Investigator is the lead researcher responsible for the overall design, conduct, and management of a clinical trial or research study. The PI ensures that the study adheres to the approved protocol, regulatory requirements, and ethical standards.
“siRNA”	small interfering RNA, sometimes known as short interfering RNA or silencing RNA, a class of double stranded noncoding RNA molecules to inhibit gene expression
“volume-based procurement”, or “VBP”	A set of drug procurement regulations implemented in China with the goal of promoting generic substitutes and lowering the price of medications that have outlived their exclusivity periods.

Appendix

- To continually promote the equalization of basic public health services and improve the balance and accessibility of these services, the National Health Commission, Ministry of Finance, National Administration of Traditional Chinese Medicine, and National Disease Control and Prevention Administration have jointly issued the Circular on Basic Public Health Services Work for 2024.
- Program introduces health services specifically for patients with chronic obstructive pulmonary disease (COPD) o continually promote the equalization of basic public health services and improve the balance and accessibility of these services, the National Health Commission, Ministry of Finance, National Administration of Traditional Chinese Medicine, and National Disease Control and Prevention Administration have jointly issued the Circular on Basic Public Health Services Work for 2024.as part of its chronic disease management component. The basic public health service initiative, a universal intervention provided by the state to address major public health concerns and serious health threats, is expanding its coverage to include COPD. As part of the Healthy China Action Plan (2019-2030), the program seeks to implement a tiered diagnosis and treatment system to deliver comprehensive services for high-risk populations and COPD patients. These services span screening, intervention, diagnosis, treatment, follow-up management, and functional rehabilitation, aiming to increase early diagnosis and standardized management of COPD at the community level.
- Efforts to prevent and control respiratory diseases in primary care have progressively strengthened, and including COPD within chronic disease management at the grassroots level marks a significant advancement. This expansion not only supports the prevention and response to common and emerging respiratory infectious diseases but also promotes the integration of epidemic prevention and control measures, reinforcing China’s expertise in managing epidemics.

Supplementary Information for Verification

- Mild average temperatures and improved air quality during 2024 in Jiangsu and Hubei provinces resulted in fewer environmental triggers for respiratory exacerbation in 2024.

Source: Frost & Sullivan Analysis