China Biologics Market Study

Independent Market Research Report

Confidential For

Frost & Sullivan
March 2024

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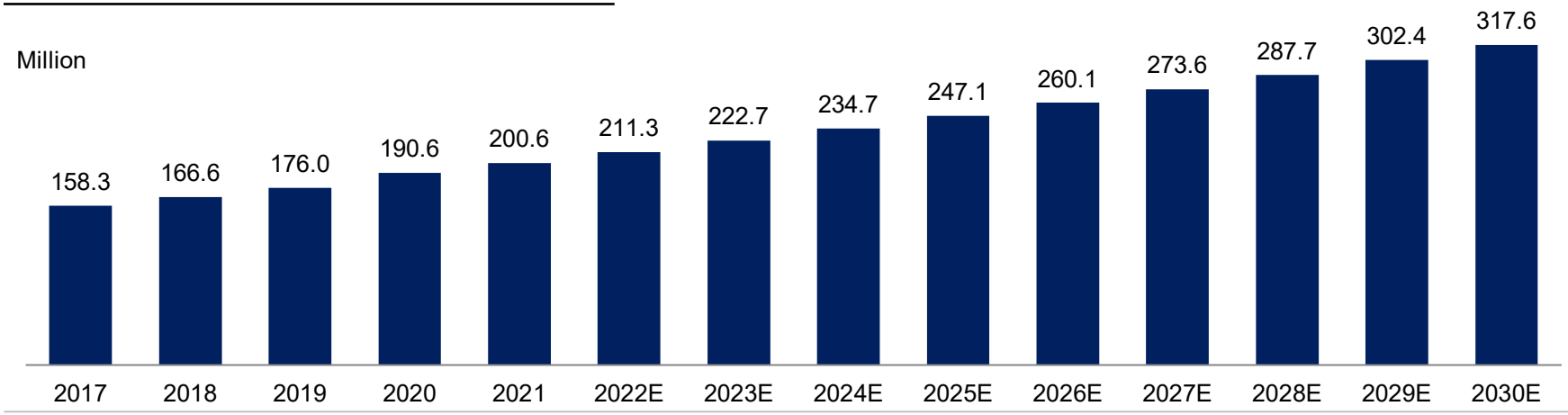
China Aging Population Trend, 2017-2030E

- With the implementation of the "One Child Policy" and increasing life expectancy, China has entered an aging society. From 2017 to 2021, population is aging rapidly in China with people aged above 65 grew at a CAGR of 6.1% over the period. According to the NBSC, individuals aged above 65 years old reached 200.6 million in 2021. The number of individuals aged above 65 years old is growing at a fairly fast pace and is expected to continue its growth momentum into the future. This number of people is expected to reach 247.1 million and 317.6 million by 2025 and 2030, respectively, representing a CAGR of 5.4% from 2021 to 2025 and 5.2% from 2021 to 2030.
- China's demographic shift offers immense opportunities for the pharmaceutical market, as elder people generally have a greater need for medications to fight diseases.

China Aging Population Trend, 2017-2030E

Period	CAGR
2017-2021	6.1%
2021-2025E	5.4%
2025E-2030E	5.1%



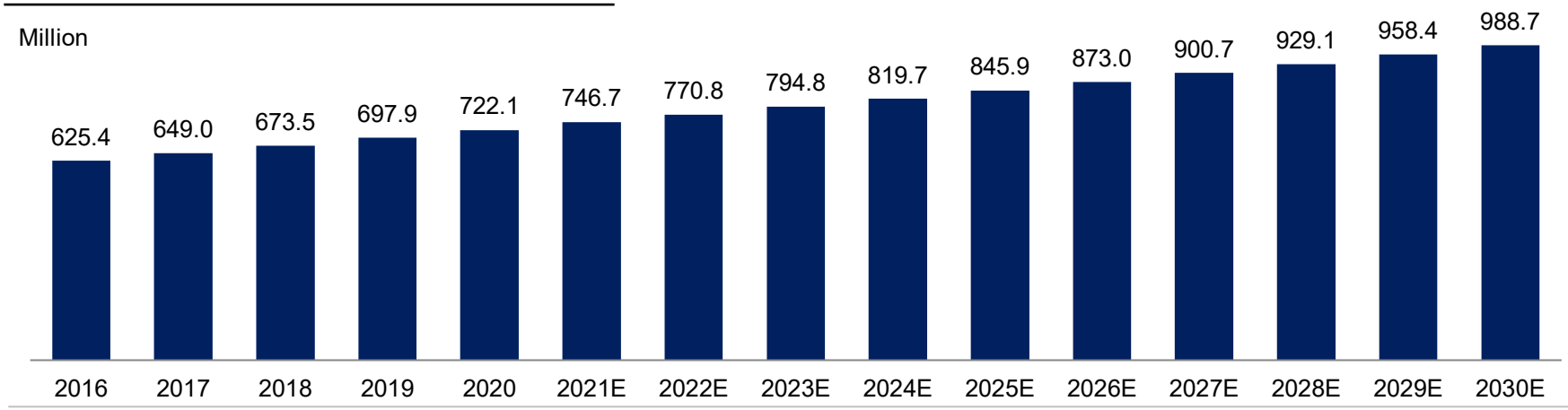
Source: NBSC, Frost & Sullivan analysis

Global Aging Population Trend, 2016-2030E

- The world's aging population is experiencing growth in terms of both number and proportion. In 2020, It is estimated that there are 722.1 million people aged 65 years old and above in the world. The population aged 65 years old and above grew at a CAGR of 3.7% from 2016 to 2020.
- Declining fertility and increasing longevity are the key drivers of population aging globally. It is estimated that the number of people aged 65 and above in the world would reach 845.9 million in 2025, with a CAGR of 3.2% from 2020 to 2025. The size of the aging population will keep the upward tendency, it is anticipated to reach 988.7 million by 2030.

Global Aging Population Trend, 2016-2030E

Period	CAGR
2016-2020	3.7%
2020-2025E	3.2%
2025E-2030E	3.2%



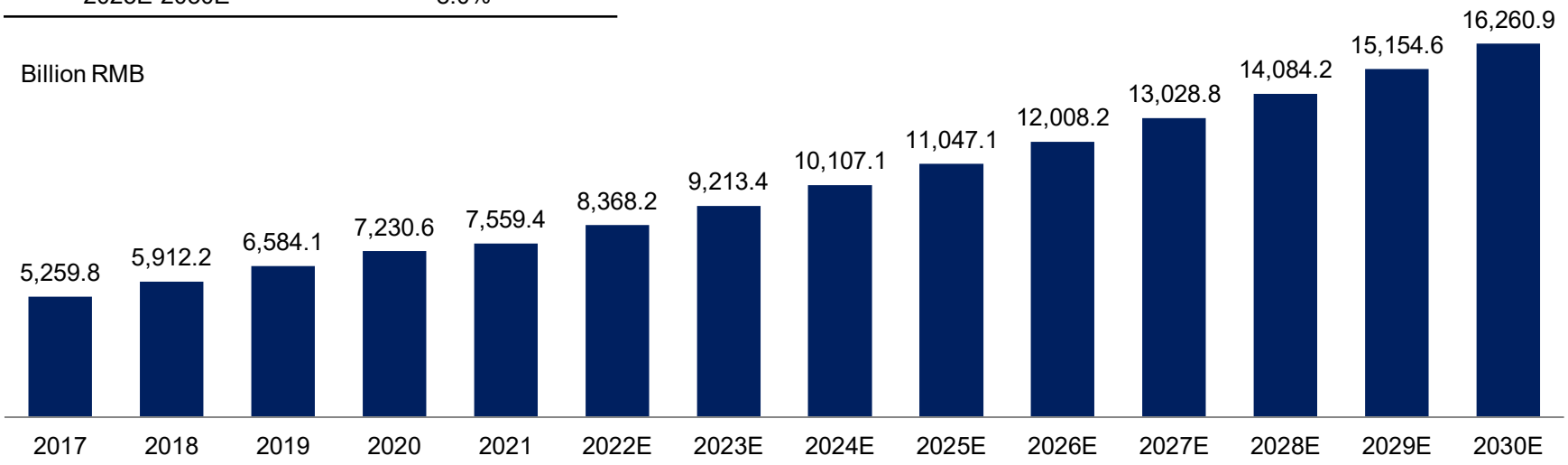
Source: WorldBank, Frost & Sullivan analysis

China Healthcare Expenditure, 2017-2030E

- The total healthcare expenditure of China has experienced steady growth. From 2017 to 2021, the total healthcare expenditure of China has increased from RMB5,259.8 billion to RMB7,559.4 billion, representing a CAGR of 9.5%. Furthermore, the rapid increase in China's healthcare expenditures will continue in the future. The total healthcare expenditure of China is forecasted to reach RMB11,047.1 billion by 2025, representing a CAGR of 9.9% from 2021 to 2025.

China Total Healthcare Expenditure, 2017-2030E

Period	CAGR
2017-2021	9.5%
2021-2025E	9.9%
2025E-2030E	8.0%



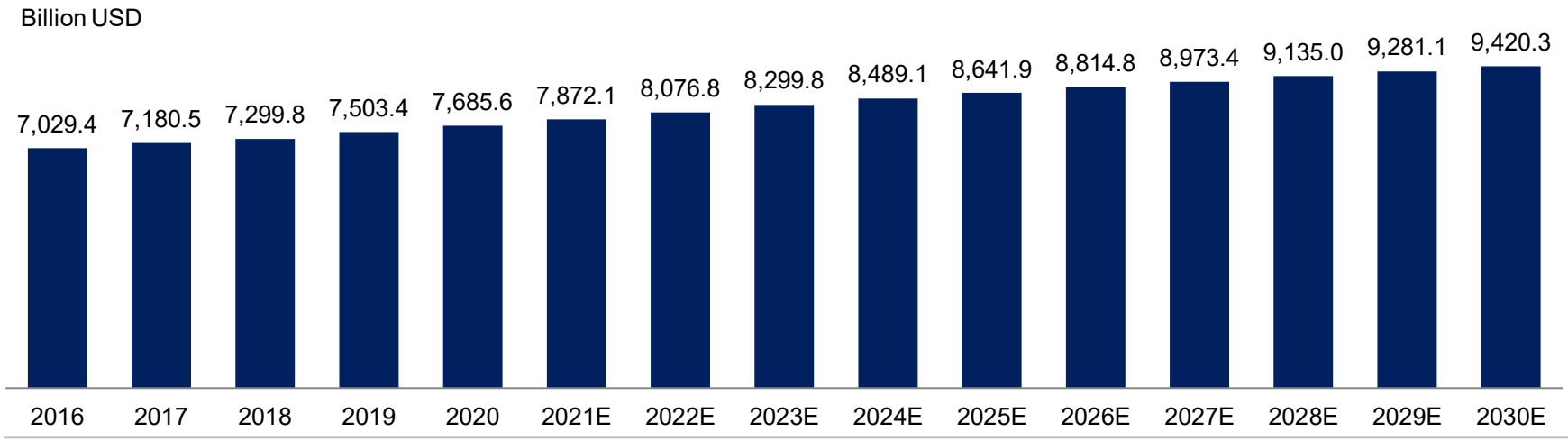
Source: NHFPC, WHO, Frost & Sullivan analysis

Global Healthcare Expenditure, 2016-2030E

- The aim of healthcare expenditure is to achieve social equity and protect the health of residents. Generally speaking, global healthcare expenditure is growing steadily. Total global healthcare expenditure reached USD7,685.6 billion in 2020 and grew at a CAGR of 2.3% from 2016 to 2020.
- Global healthcare expenditure is inevitably increased with the expansion of the aging population. Total healthcare expenditure is expected to be USD9,420.3 billion in 2030 with a CAGR of 1.7% from 2025 to 2030.

Global Total Healthcare Expenditure, 2016-2030E

Period	CAGR
2016-2020	2.3%
2020-2025E	2.4%
2025E-2030E	1.7%



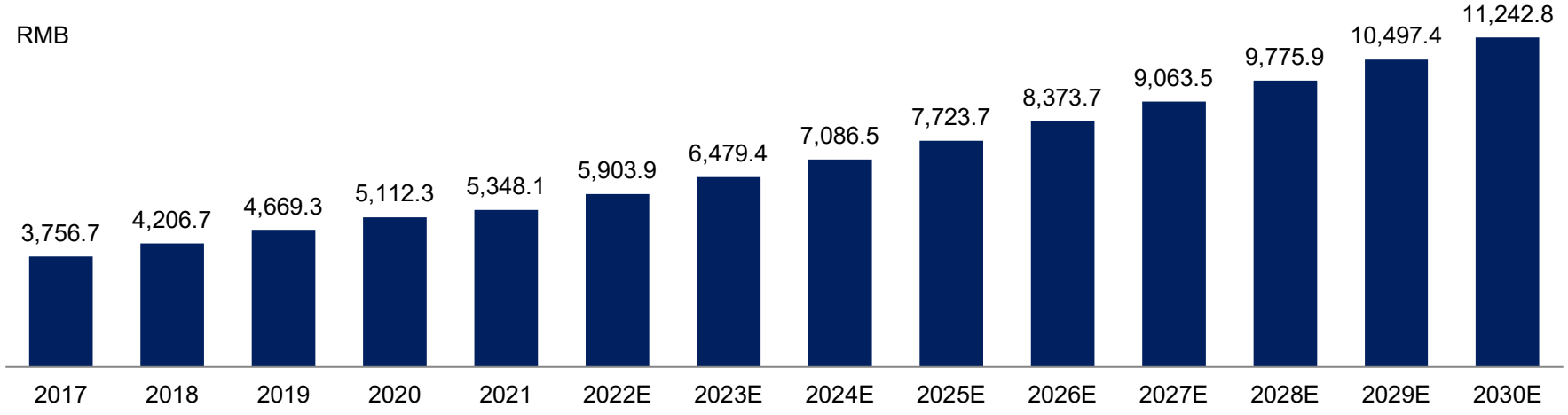
Source: NHFPC, WHO, Frost & Sullivan analysis

Per Capita Healthcare Expenditure in China

- The per capita healthcare expenditure in China has grown rapidly in recent years.
- According to information from the National Bureau of Statistics and EIU, from 2017 to 2021, the per capita healthcare expenditure has grown from RMB 3,756.7 to RMB5,348.1, representing a CAGR of 9.2% in this period. And the per capita healthcare expenditure is expected to reach RMB 7,723.7 and 11,242.8 in 2025 and 2030 respectively, representing a CAGR of 9.6% from 2020 to 2025 and 7.8% from 2025 to 2030.

Per Capita Healthcare Expenditure in China, 2017-2030E

Period	CAGR
2017-2021	9.2%
2021-2025E	9.6%
2025E-2030E	7.8%



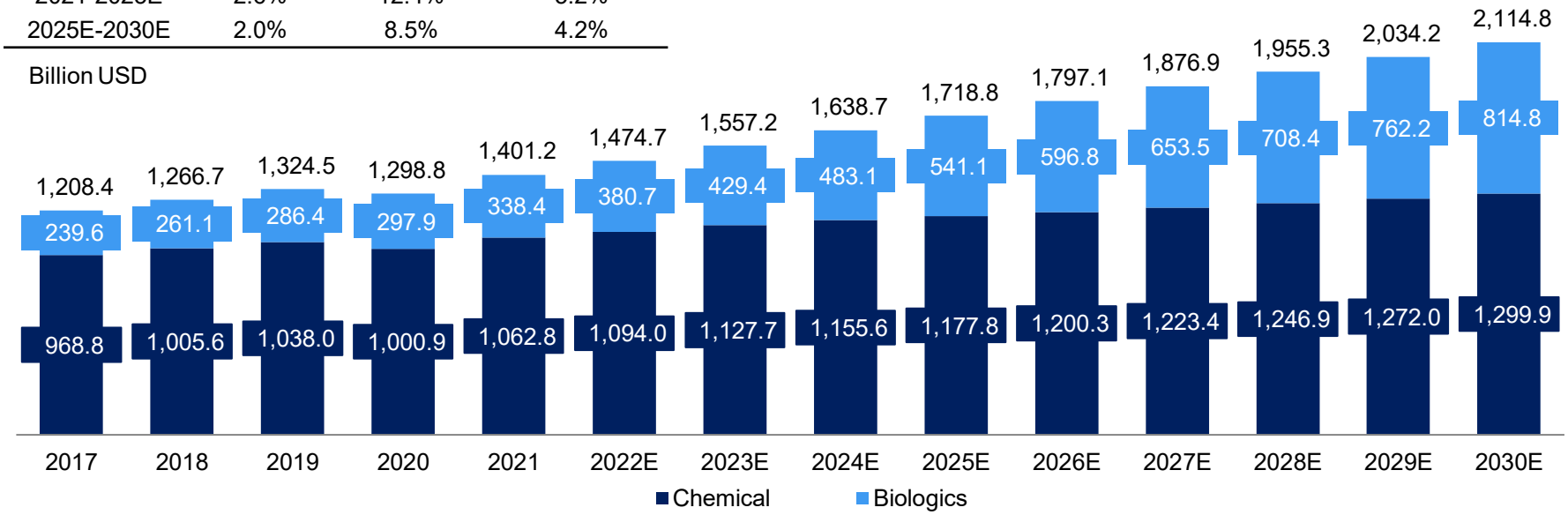
Source: NHFPC, WHO, Frost & Sullivan analysis

Historical and Forecasting Global Pharmaceutical Market Size

- Global total pharmaceutical market reached USD1,401.2 billion in 2021 and is expected to expand to USD1,711.4 billion in 2025, representing a CAGR of 3.8% during this period. Stable growth is projected for the global pharmaceutical market. From 2025 to 2030, the pharmaceutical market would rise at a CAGR of 5.2% and reach USD2,114.8 billion.
- Due to the high efficacy in treating a wide range of diseases, increasing R&D investment, significant biotechnology development and increasing affordability, the global biologics segment has and is expected to continue to grow at a rapid pace. Both global and China biologics industries are highly competitive, with a large number of competitors with significant resources and brand awareness, and maybe deeply entrenched in certain market segments, whether by geographic region or by drug type. The global biologics market increase with a CAGR of 8.5% from 2025 to 2030.

Global Pharmaceutical Market, 2017-2030E

Period	CAGR		
	Chemical	Biologics	Total
2017-2021	2.3%	9.0%	3.8%
2021-2025E	2.6%	12.4%	5.2%
2025E-2030E	2.0%	8.5%	4.2%



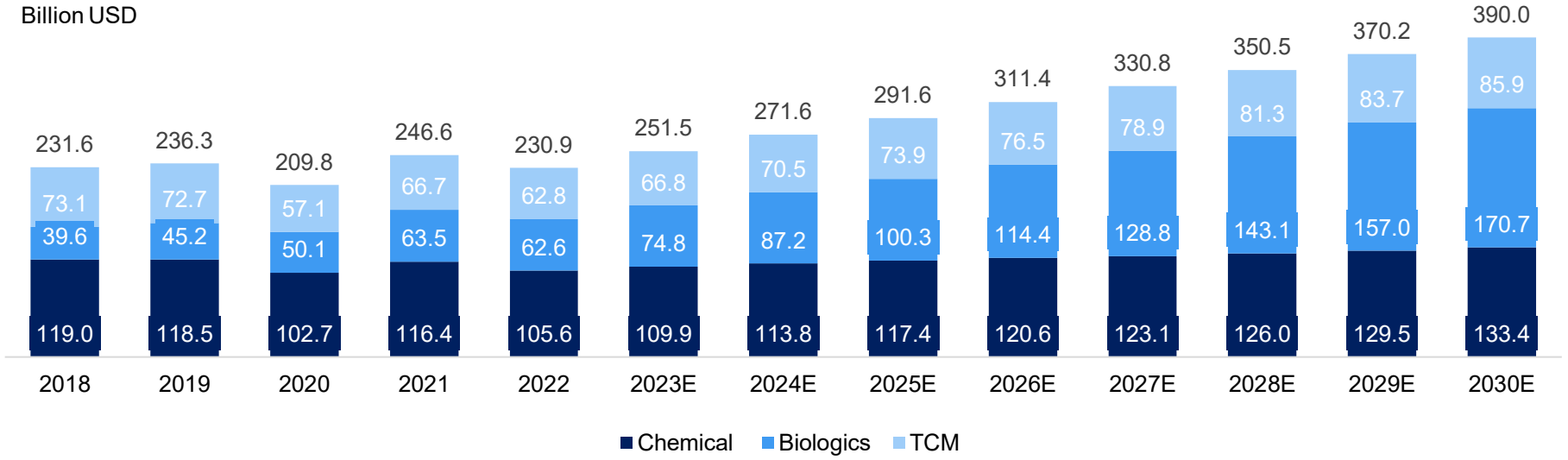
Source: Frost & Sullivan analysis

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

- China pharmaceutical market is composed by three segments, namely chemical drug, biologics and TCMs. The size of China pharmaceutical market was USD 230.9 billion in 2022, and is expected to reach USD 291.6 billion and USD 390.0 billion in 2025 and 2030 respectively, representing a CAGR of 8.1% from 2022 to 2025 and 6.0% from 2025 to 2030.
- In the next decade, the biopharmaceutical market is expected to be the fastest-growing market.
- Biologics accounted for approximately 17.1% and 27.1% of China's overall pharmaceuticals market in 2018 and 2022, respectively, and the market share is expected to rise further to 43.8% in 2030.

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

CAGR	Chemical Drugs	Biologics	TCMs	Total
2018-2022	-2.5%	12.6%	-3.3%	0.3%
2022-2025E	3.6%	17.0%	5.6%	8.1%
2025E-2030E	2.6%	11.2%	3.0%	6.0%

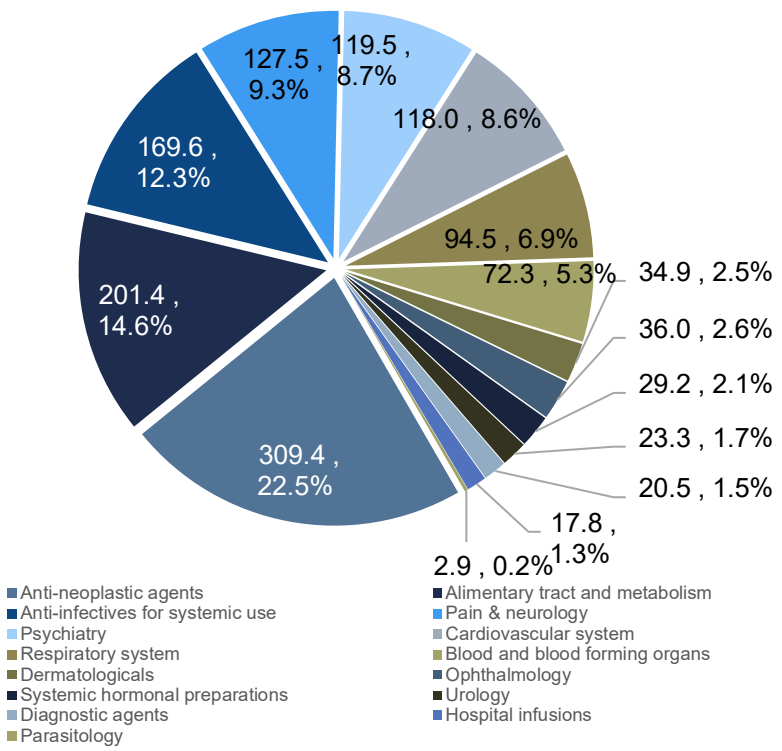


Source: Frost & Sullivan analysis

Breakdown of Global and China Pharmaceutical Market by Therapeutic Area, 2021

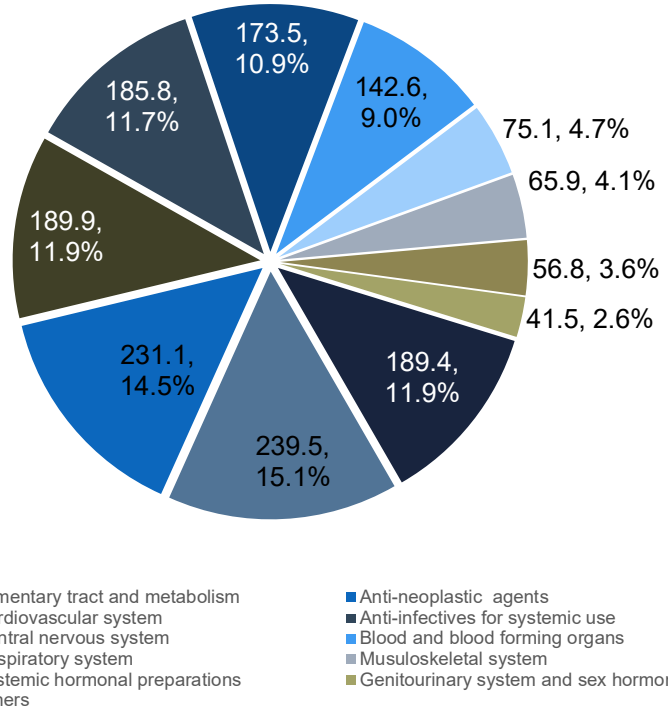
Breakdown of Global Pharmaceutical Market by Therapeutic Area, 2021

Billion USD



Breakdown of China Pharmaceutical Market by Therapeutic Area, 2021

Billion RMB



Source: Frost & Sullivan analysis

Growth Drivers of China Pharmaceutical Market

Increasing Disposable Income	• China resident annual disposable income has experienced fast growth in the past few years, increasing from RMB25,974.0 in 2017 to RMB35,128.0 in 2021 at a CAGR of 7.8% during this period. With the economic development, the per capita annual disposable income is expected to further grow to RMB47,262.0 in 2025. The growth of per capita annual income of Chinese residents has a positive effect on the purchasing power and the level of health awareness among the Chinese population.
Aging Population	• As the overall metabolic and immune capacities of elder people gradually decline, they are more likely to suffer from chronic diseases, and therefore incur high costs on long-term medication and scientific disease management. The aging population reached 200.6 million in 2021, accounting for 14.2% of the total population. The proportion is projected to further increase to 17.3%, representing a population 247.1 million in 2025.
Favorable Policies	• Chinese government promulgated a series of policies to encourage R&D, as well as strengthen the regulation on the pharmaceutical market. • For example, shortening the review and approval time span for innovative drugs IND and BLA applications will accelerate the process of drugs with the potential to address the urgent clinical needs to get into the market. Patent protection is greatly enhanced as well. All these reforms will attract MNC pharmas to launch more innovative drugs to China market. Furthermore, the government has issued favorable policies in terms of tax reduction, talents incentive programs and special public R&D funds to support R&D activities of domestic companies in particular. • A series of strengthening regulations, such as new GMP and two-invoice implementation, will lead to a more efficient and disciplined pharmaceutical market with healthy competition and sustainable development.
Improve Public Medical Insurance	• Public medical insurance is the largest single-payer for pharmaceuticals in China. The latest version of NRDL not only expand to include more drugs to be reimbursable but also adopt dynamic adjustment via price negotiation to include more advanced drugs in the List with a more economical price. Currently, there are 2,860 drugs in the NRDL.

Source: Frost & Sullivan analysis

Future Trends of China Pharmaceutical Market

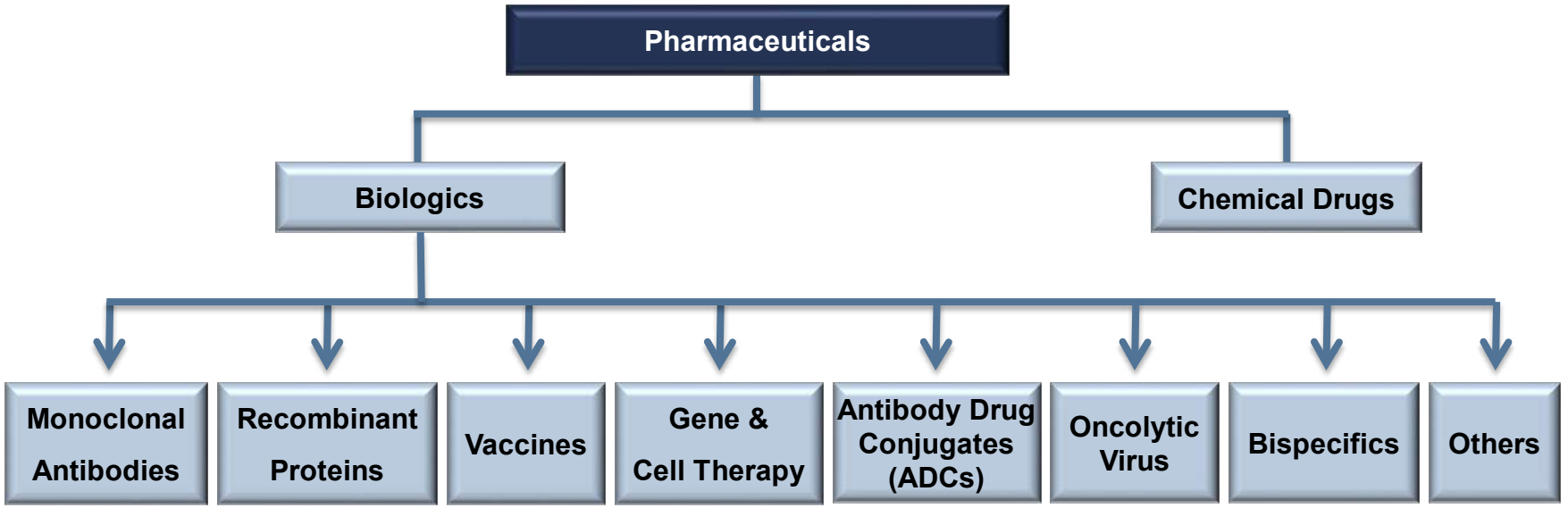
Expansion of Innovative Drug Market	• With the pilot scheme of centralized procurement of generics and inclusion of innovative drugs into NRDL, it is believed that China pharmaceutical market is shifting towards the innovation-driven market. Also, the government promulgated a series of policies to encourage R&D, such as accelerated drug review and approval, patent protection, tax reduction, etc. The development of innovative drugs is therefore encouraged and will lead to innovative drug market expansion in the future.
More Biotech Companies to Get Involved	• Due to the strong support from the government, capital investment and talent reserve, biotech companies are expected to play a more important role in the pharmaceutical market with their innovative drugs under clinical development and to be launched in the near future. For example, China market has launched 12 PD-1/PD-L1 drugs so far, with their sales revenue reaching tens of millions in a few months, showing the huge potential of innovative drugs in China pharmaceutical market. This will attract more biotech companies to get involved.
Alignment with International Standard	• In recent years, China has joined the ICH as the 8th number, which emblems the onset of alignment of the pharmaceutical industry practices with international standards, indicating an effort to realize a gradual transformation of drug application and registration process toward the higher and unified standard. It is expected that the drug review and approval system will be gradually improved.
Novel Therapies Available to Patients Sooner	• Historically, novel therapies usually have a gap of a few years in approval time between China and other major markets due to a less efficient approval process. The gap is narrowed through reform on the review and approval process as well as the ICH alignment. The approval process is further accelerated through enabling priority review and listing the drugs of clinically urgent, potentially bringing more novel drugs to China market in a more timely manner. In this way, effective novel therapies will benefit patients sooner.

Source: Frost & Sullivan analysis

Biologics Market Segmentation

- Segmentation is based on existing and emerging biologics products, which may vary across regions.

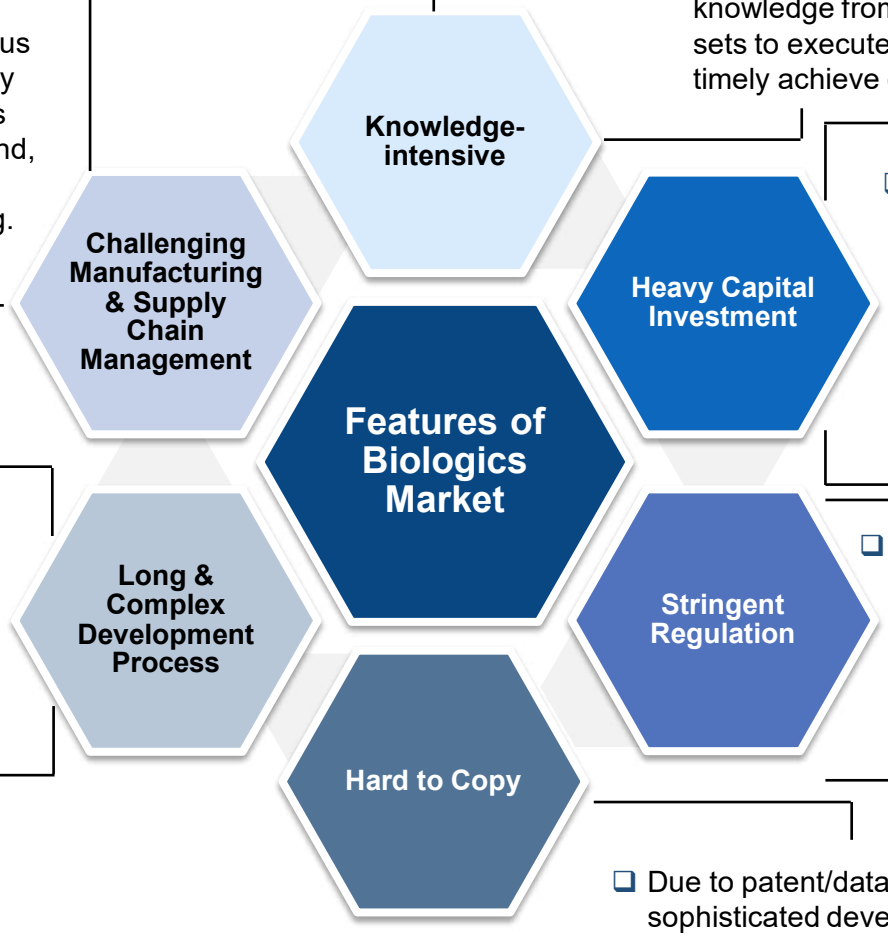
Total Biologics Market: Market Segmentation, Global



- **Definition:** The FDA is defining Biologics as products that include a wide range of products such as vaccines, blood and blood components, allergenic, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins. Biologics are isolated from a variety of natural sources - human, animal, or microorganism - and may be produced by biotechnology methods and other cutting-edge technologies. In addition, gene-based and cellular biologics often are at the forefront of biomedical research and emerging category such as ADCs and oncolytic virus have also been put in the spotlight.

Source: FDA, Frost & Sullivan analysis

Features of Biologics Market

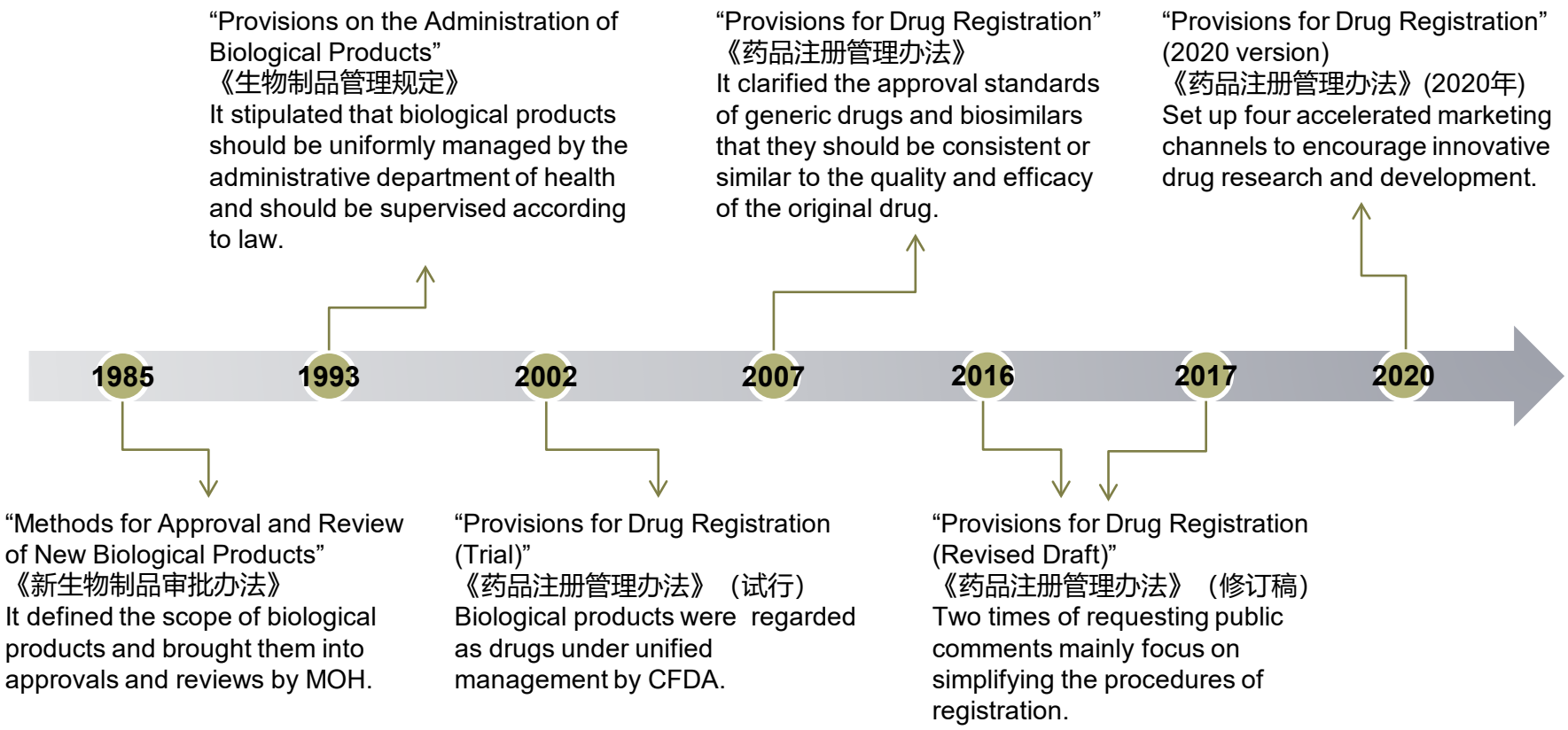


- As new technologies are introduced, such as continuous manufacturing, the complexity of the biologic supply chain is increasing. With rising demand, producing sufficient products on time becomes challenging.
- Development and marketing of biologics is a very complex process and requires the integration of knowledge from multiple disciplines and special skill sets to execute the company's business strategy and timely achieve objectives.
- The sophistication of the biological market comes at a great cost. Large-scale biotech-manufacturing facilities require $200 million to $700 million or more to build, compared with similar-scale small-molecule facilities that may cost just $30-100 million. Later-on marketing activities are costly, too.
- The development of new biologics is a long, complex and costly endeavor. It usually takes about 10-15 years, on average, to bring a medicine through the discovery and clinical trial phases to patients.
- Because biologics are sensitive to minor environmental changes, regulators have imposed stricter regulations on biologics approval, including requiring comprehensive clinical data, complex registration process and continuing post-market surveillance.
- Due to patent/data protection and sophisticated development of biologics, it is difficult to simply copy successful biologics.

Source: Frost & Sullivan analysis

China Regulatory Regime of Biologics

- In 1985, the first regulation on the biological product was published, and in 2002, the “Provisions for Drug Registration (Trial)” first regulated biologics and chemical drugs with the same policy. In 2017, the fourth version of “Provisions for Drug Registration (Revised Draft) ”, of which the regulations standard of biological products are adjusted to simplify the registration procedures was issued and the 2007 version was no longer effective after then.



Source: NMPA, Frost & Sullivan analysis

Characteristics of Biologics Compared with Small Molecule Drugs

- Biologics are large and complex, often consisting of heterogeneous mixtures. They have high efficacy and few side effects. They are generally made in genetically engineered cells that impose their own variabilities – in post-translation modifications such as glycosylation – on the processes used to make such drugs.
- A comparison of small-molecule and biological drugs makes it clear as to why there are so many challenges with the production of biologics than that of traditional small molecule drugs.

	Small Molecule Drugs	Biologics
Size	• Small (single molecule) • Low molecular weight	• Large (mixture of related molecules) • High molecular weight
Structure	• Simple, well defined, independent of manufacturing process	• Complex (heterogeneous), defined by the exact manufacturing process
Manufacturing	• Produced by chemical synthesis • Predictable chemical process • Identical copy can be made	• Produced in living cell culture, having species specificity • Difficult to control from starting material to final product • Impossible to ensure identical copy
Stability	• Stable	• Unstable, sensitive to external conditions
Immunogenicity	• Mostly non-immunogenic	• Immunogenic
Efficacy	• Generally less selective • Less potent	• High selectivity (affinity/potency) • Better efficacy
Safety	• On-and off-target related toxicity	• React highly specific against one target • Less side effects and toxicity

Source: Frost & Sullivan analysis

Comparison of Manufacturing in Biologics and Small Molecule Drugs

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

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

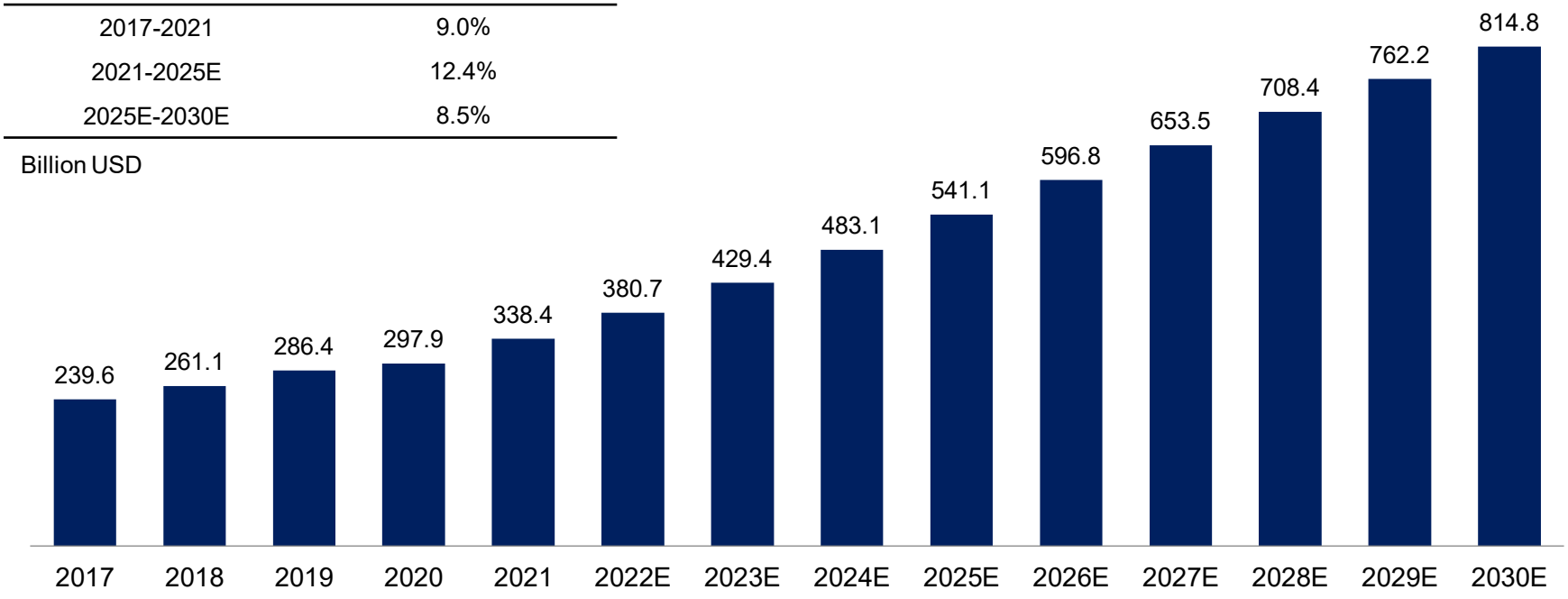
Source: Frost & Sullivan analysis

Global Biologics Market Size and Forecast, 2017-2030E

- Global biologics market valued USD 239.6 billion in 2017 and reached USD 338.4 billion in 2021, representing a CAGR of 9.0 % during this period.
- Driven by a combination of favorable factors, including patent expiry of blockbuster original biologics, increasing medical demand and more well evolvement of the regulatory system, global biologics market size is expected to significantly boom in the near future, growing from USD 338.4 billion in 2021 to USD 541.1 billion in 2025 with a CAGR of 12.4%, further to reach USD 814.8 billion in 2030E.

Global Biologics Market Size and Forecast, 2017-2030E

Period	CAGR
2017-2021	9.0%
2021-2025E	12.4%
2025E-2030E	8.5%



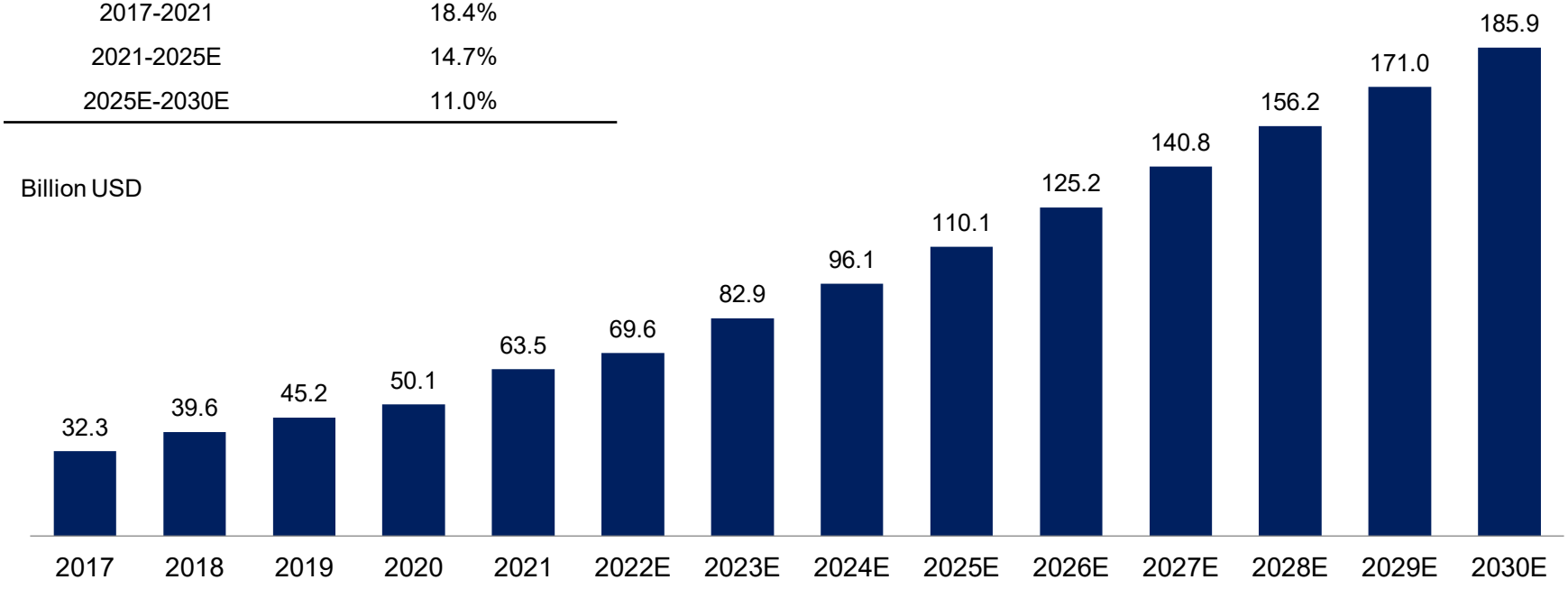
Source: Frost & Sullivan analysis

China Biologics Market Size and Forecast, 2017-2030E

- Driven by the improving affordability, as well as the enlarging patient pool, the biologics market size in China is expected to further grow to USD 110.1 billion in 2025 and USD 185.9 billion in 2030, representing a CAGR of 14.7% from 2021 to 2025, 11.0% from 2025 to 2030.
- Compared with the global biologics market, the growth rate of the China biologics market is much higher than that of the global level during the same periods.The CAGR from 2021 to 2030 is 12.7%.

China Biologics Market Size and Forecast, 2017-2030E

Period	CAGR
2017-2021	18.4%
2021-2025E	14.7%
2025E-2030E	11.0%



Source: Frost & Sullivan analysis

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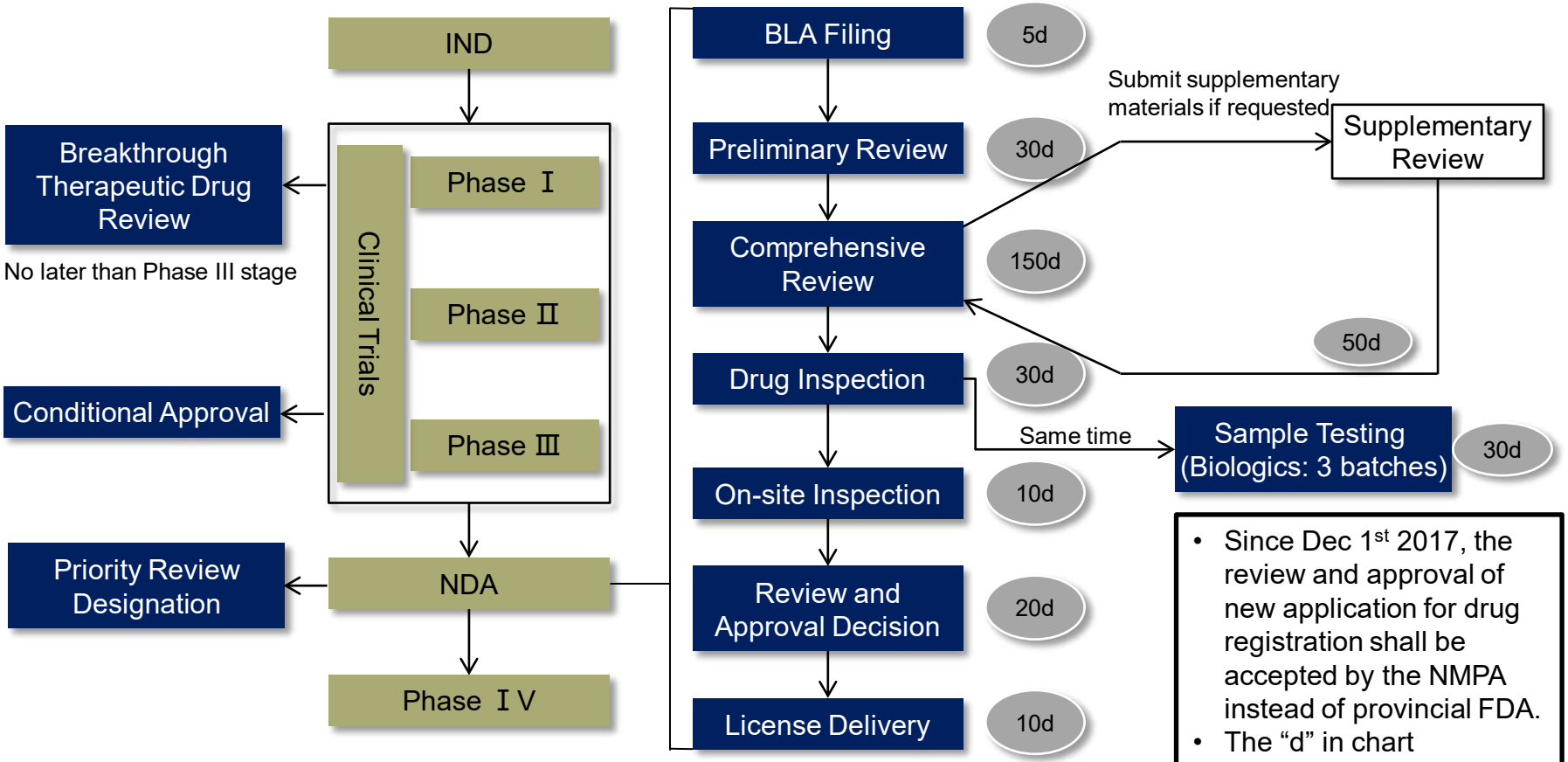
Drug Registration Procedure in China

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.

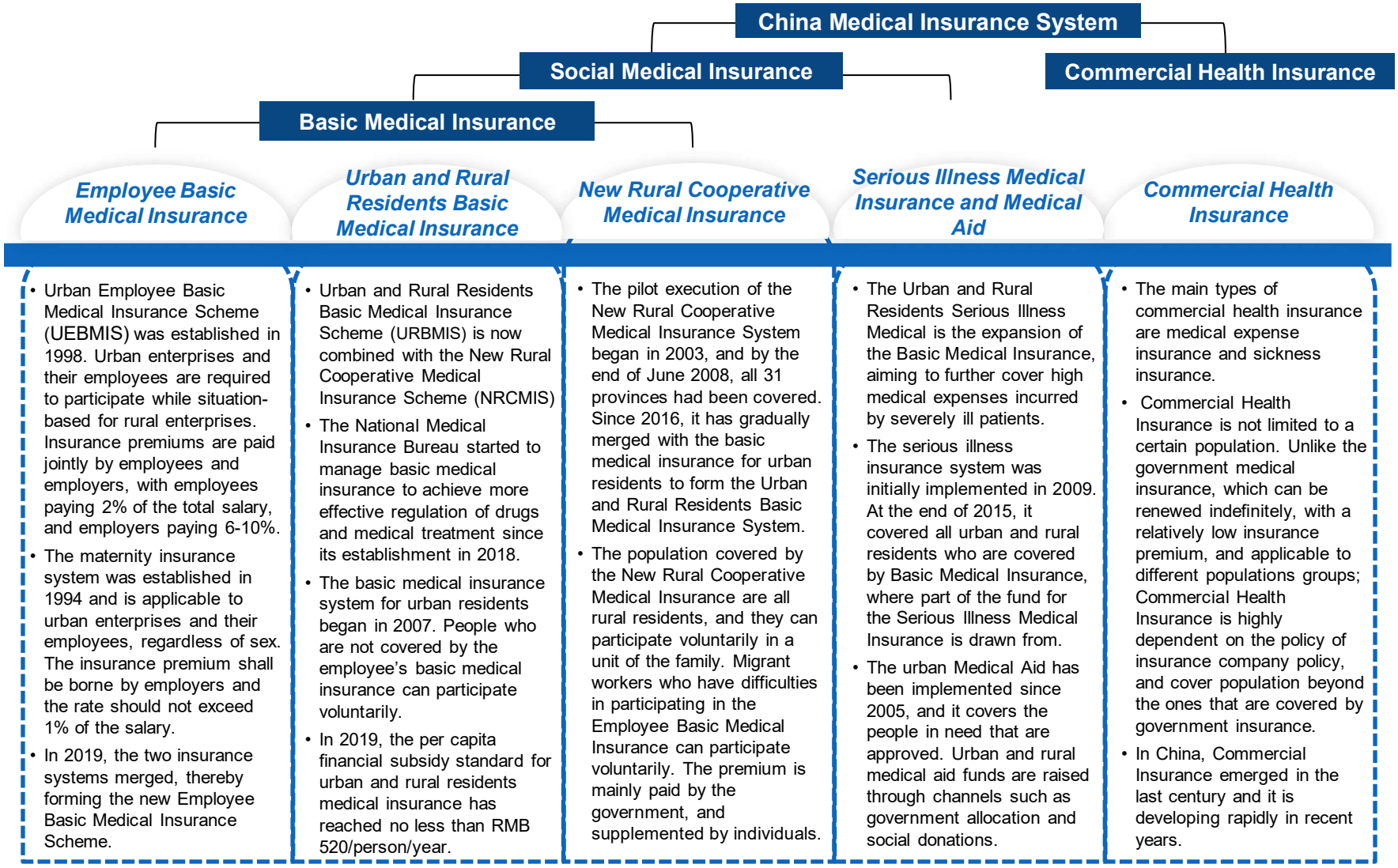


- Since Dec 1st 2017, the review and approval of new application for drug registration shall be accepted by the NMPA instead of provincial FDA.
- The “d” in chart represents “workdays”.

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

Source: NMPA, Frost & Sullivan analysis

Overview of Medical Insurance System in China



Source: NMPA, 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	94.2%	96.4%	96.7%	96.4%	96.6%

*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

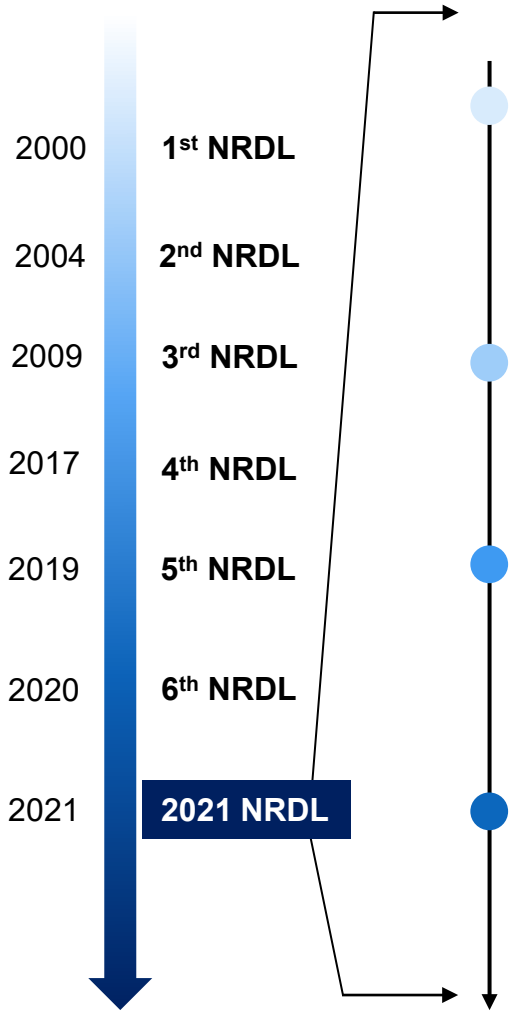
Note: URBMIS = Urban and Rural Residents Basic Medical Insurance Scheme; UEBMIS = Urban Employee Basic Medical Insurance Scheme; NRCMIS = New Rural Cooperative Medical Insurance Scheme

Source: MORHSS, Frost & Sullivan analysis

Analysis of Healthcare Reimbursement System in China

Recent Progress and Impact of the 2021 NRDL

Progression of NRDL



Recent Progression of 2021 NRDL

- In Dec 2021, NHSA and MOHRSS released the official work plan for the adjustment of the 2021 NRDL, enforced from January 1st, 2022. The latest NRDL negotiation aims to eliminate medications with unreasonably high prices, optimize clinical use of medications, and further lower prices of current drugs by inducing virtuous competition

- 117 kinds of drugs were involved in price negotiation, and 94 of them were smoothly negotiated. 74 kinds of drugs have been newly included in NRDL for the first time, leading to a 61.71% decline in prices.

- Affected by fair competition in the market, the drug list and payment standard should also be adjusted accordingly. Some drugs in previous NRDL occupied too many funds with a relatively high price. 11 previously included drugs were removed from the list due to substitutability, low clinical value and low utilization rate. This allows newer drugs and drugs with higher efficacies to be included in NRDL in the coming future.

- 20 drugs for chronic diseases such as hypertension, diabetes, and hyperlipidaemia have been newly included. Besides, 18 oncology drugs, 15 drugs for infectious diseases, 7 drugs for rare diseases, 2 drugs for covid-19 and 12 drugs for other indications have been newly included.

Implication for Innovation

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

2021 NRDL restricts the price of drugs strictly by introducing economic competition among different drugs with the same indication. The substitutability of drugs is now an important indicator, and only the most cost-effective drugs are expected to enter NRDL.

Numerous domestic innovative drugs were included by 2021 NRDL, marking the initiation of a rapid increase of sales and the rapid transformation of the Chinese pharmaceutical industry towards innovation.

Since the implementation of the self-declaration system of pharma, only drugs that meet the conditions of 2021 NRDL plans can be included in the adjustment scope.

Source: MORHSS, Frost & Sullivan analysis

Opinions on Deepening the Reform of the Evaluation and Approval Systems and Encouraging Innovation on Drugs and Medical Devices - I

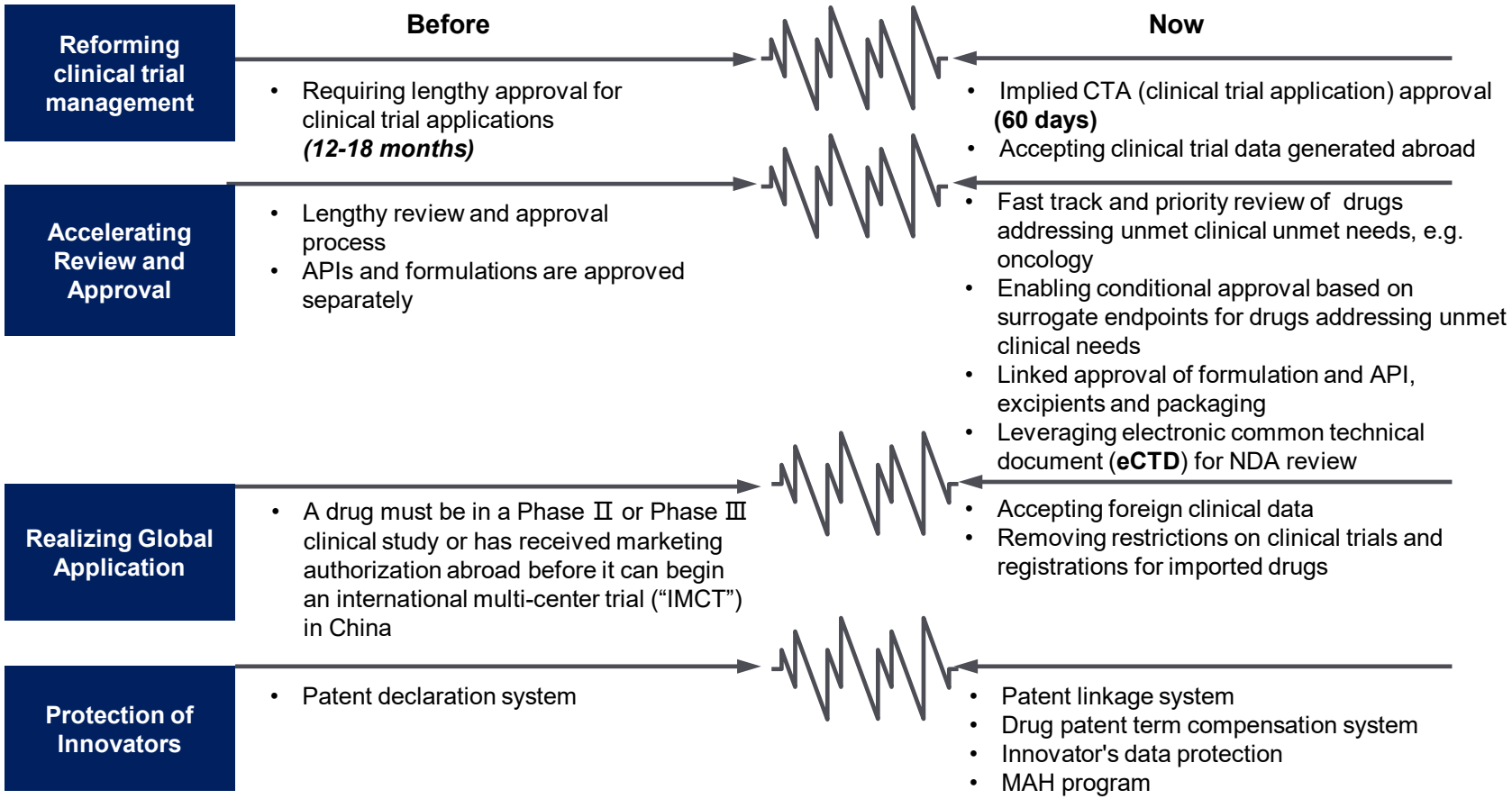
- In Oct 2017, the General Office of the CPC Central Committee and the General Office of the State Council issued the Opinions on Deepening the Reform of the Evaluation and Approval Systems and Encouraging Innovation on Drugs and Medical Devices (《关于深化审评审批制度改革鼓励药品医疗器械创新的意见》).
- As the review process of innovative drugs has been reformed recently, more advanced and more effective treatments are expected to enter the China market at an expedited pace.

	Content	Potential Benefits
Reforming clinical trial management	• Implementing record-filling system instead of qualification for clinical trial sites • Accepting clinical trial data generated abroad • Improving the efficiency of ethic review, optimizing the approval procedure for clinical trials	➢ Increasing availability of clinical trial sites ➢ Making simultaneous marketing in domestic and overseas markets possible ➢ Shortening the approval time of IND applications
Accelerating review and approval	• Accelerating the review and approval of drugs with urgent clinical needs	➢ Shortening the approval time of NDA applications
Encouraging innovation	• Enhancing the protection of patents and clinical trial data • Developing pilot pharmaceutical patent term compensation system • Making dynamic adjustments to the National Drug Reimbursement List (NRDL)	➢ Extending the patent term of innovative drugs ➢ Raising the affordability and availability of innovative drugs
Life-cycle management	• Implementing the Marketing Authorization Holder (MAH) system	➢ In favor of innovative SMEs and start-ups who can benefit from a wider range of R&D and manufacturing options

Source: NMPA, Frost & Sullivan analysis

Opinions on Deepening the Reform of the Evaluation and Approval Systems and Encouraging Innovation on Drugs and Medical Devices - II

- Opinions on Reform of the Drug and Medical Device Review and Approval (“关于深化审评审批制度改革鼓励药品医疗器械创新的意见”) shifts the regulatory system and environment of China pharmaceutical market. It promotes the acceleration of drug approval and encouraged the innovation of drug and medical devices.



Source: NMPA, Frost & Sullivan analysis

Favorable Government Policy of Pharmaceutical Industry

Review of Clinical Trial and New Drug Application

Release Date	Issuing Authority	Policies	Comments
Aug, 2015	State Council	*Opinions of the State Council on Reform of the System of Evaluation, Review and Approval of Drugs and Medical Devices* 《国务院关于改革药品医疗器械审评审批制度的意见》	• Accelerating the review and approval of innovative drug trials. • Implementing specific review, evaluation and approval system to accelerate the review and approval process for innovative drugs that are in use of prevention and treatment of AIDS, malignant tumors, major infectious diseases, rare diseases, as well as drugs listed in national science and technology projects and national key R&D programs.
Mar, 2016	State Council	*Guiding Opinions of the General Office of the State Council on Promoting the Sound Development of the Medical Industry* 《国务院办公厅关于促进医药产业健康发展的指导意见》	• Deepening review and approval system reforms. Establishing a more scientific and efficient review and approval system for drug and medical devices. • Strengthening the construction of review teams, and recruiting experts and scholars with international review and approval experience.
Oct, 2016	State Council	*Healthy China 2030* 《“健康中国2030”规划纲要》	• Strengthening drug safety supervision. • Deepening the reform of the review and approval system for pharmaceuticals (medical devices), establishing a review and approval system based on clinical curative effects. • Improving the approval standards for drugs (medical devices).
May, 2017	CFDA	*Policies of Encouraging Drug Medical Equipment Innovation to Reform the Clinical Trial Management* 《关于鼓励药品医疗器械创新改革临床试验管理的相关政策（征求意见稿）》	• Changing the approach to achieve qualification of clinical trial institutions to recordation. • Supporting researchers and clinical trial institutions to conduct clinical trials.
May, 2018	CFDA	*Notice for Optimizing the Examination, Assessment and Approval of Drug Registration* 《关于优化药品注册审评审批有关事宜的公告》	In order to improve the efficiency of review and approval of innovative drugs as well as simplify the procedure: • The review and approval for rare diseases that seriously endanger life with no effective treatment could be sped up through a communication system between CDE and applicants. • The clinical data obtained overseas with no ethnic difference could directly apply for drug launch registration.

Source: Government Website, Frost & Sullivan analysis

Favorable Government Policy of Pharmaceutical Industry

Review of Clinical Trial and New Drug Application

Release Date	Issuing Authority	Policies	Comments
Jul, 2018	CFDA	*Technical Guidelines for Accepting Data from Overseas Clinical Trials of Drugs* 《接受药品境外临床试验数据的技术指导原则》	• In order to encourage synchronous drug R&D both domestic and abroad, the acceptable overseas clinical trials data are clarified. • The overseas R&D of generic drugs with complete and assessable bioequivalence data can also be used for registration applications.
Jul, 2018	CFDA	*Announcement on Adjusting the Examination and Approval Procedure of Drug Clinical Trials* 《关于调整药物临床试验审评审批程序的公告》	• Drug clinical trial filing system: The drug clinical trial can be carried out according to the submitted scheme if the applicant fails to receive the negative or doubtful opinions from the CDE within 60 days from the accepted and payment date of the application.
Oct, 2018	CFDA	*Announcement on the urgent clinical need for approval of new drugs abroad* 《关于临床急需境外新药审评审批相关事宜的公告（2018年第79号）》	Establish a special channel for review and approval of overseas innovative drugs that are urgently needed, which has launched in the United States, the EU or Japan in the past 10 years but not in China, meeting one of the following circumstances: • Drugs for the treatment of rare diseases • Drugs for serious life-threatening diseases without effective treatment • Drugs have obvious clinical advantages for serious life-threatening diseases. The innovative drugs from abroad can be declared for manufacturing directly without domestic clinical data after demonstration of no ethnic difference.
Sep, 2019	NHC, NHSA, NMPA	*Notice for the Publication of the Health China_ Implementation Plan for Cancer Prevention (2019-2022 edition)* 《关于印发健康中国行动——癌症防治实施方案（2019—2022年）的通知》	• Establish a comprehensive clinical evaluation system for anticancer drugs. • Speed up the approval of new anticancer drugs at home and abroad.

Source: Government Website, Frost & Sullivan analysis

Favorable Government Policy of Pharmaceutical Industry

Review of Clinical Trial and New Drug Application

Release Date	Issuing Authority	Policies	Comments
July, 2020	NMPA	*Breakthrough Therapeutic Drug Review Working Procedures (for trial implementation)* 《突破性治疗药物审评工作程序（试行）》	During the clinical trial of the drug, the application shall meet the following conditions at the same time: • For the prevention and treatment of diseases that seriously endanger life or seriously affect the quality of life; • For diseases that do not yet have effective prevention and treatment, the drug can provide effective prevention and treatment; or compared with existing treatment methods, the drug has obvious clinical advantages
July, 2020	NMPA	Procedures for the Review and Approval of Drug Conditional Approval for Marketing Application (for trial implementation) 《药品附条件批准上市申请审评审批工作程序（试行）》	Accelerate the marketing approval of the following drugs • Drugs urgently needed in public health proposed by the national health authorities and other relevant departments. • Vaccines urgently needed for major public health emergencies should be vaccines for the prevention of major public health emergencies (Level II) or diseases related to special major public health emergencies (Level I)
July, 2020	NMPA	*Procedures for Priority Review and Approval of Drug Marketing Authorization (for trial implementation)* 《药品上市许可优先审评审批工作程序（试行）》	Expedite the marketing authorization of the following drugs: • Urgently needed shortage drugs, innovative drugs and improved new drugs for the prevention and treatment of major infectious diseases and rare diseases; • New varieties, dosage forms and specifications of medicines for children that meet the physiological characteristics of children; • Vaccines and innovative vaccines urgently needed for disease prevention and control; • Drugs included in the procedures for breakthrough therapeutic drugs; • Drugs that meet the conditional approval

Source: Government Website, Frost & Sullivan analysis

Favorable Government Policy of Pharmaceutical Industry

Review of Innovation Encouragement

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

Source: Government Website, Frost & Sullivan analysis

Favorable Government Policy of Pharmaceutical Industry

Review of Innovation Encouragement

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

Source: Government Website, Frost & Sullivan analysis

Favorable Government Policy of Pharmaceutical Industry

Review of Innovation Encouragement

Release Date	Issuing Authority	Policies	Comments
Feb, 2019	MoF	*Notice on VAT policy for rare disease drugs* 《关于罕见病药品增值税政策的通知》	• To encourage the development of the rare disease pharmaceutical industry and reduce the cost of medication for patients. VAT general taxpayers who produce, wholesale and retail rare disease drugs can pay VAT at a 3% levy rate according to the simple method, starting from March 1, 2019.
Aug, 2019	NMPA	*Pharmaceutical Administration Law of the People's Republic of China* 《中华人民共和国药品管理法》	• It is the second major systematic and structural amendment to the Pharmaceutical Administration Law since its first promulgation in 1984. • Focus on supporting clinical value-oriented drug innovations which have significant effects on human disease. Encourage the development of new medicines with new treatment mechanism on severely life-threatening diseases, rare diseases and children's diseases. • Establish related laws of clinical trial acquiescence system, clinical trial institution filing management system, priority review and approval system, conditional approval system, etc. • Established a listing authorization system to encourage innovation.
Jan, 2020	NMPA	*Measures for Drug Registration Management (2020)* 《药品注册管理办法》	• Construct drug categories such as innovative drugs, improved new drugs, and generic drugs. • Establish four accelerated channels for breakthrough therapeutic drug approval, conditional approval, priority review and approval and special approval to promote the development of innovative drugs.
Mar, 2021	State Council	*14th Five-Year Plan for National Strategic Emerging industry Development* 《"十四五"国家战略性新兴产业发展规划》	• Continuously optimize and accelerate the drug review and approval system. • Intellectual property protection and encouragement of pharmaceutical innovation, multi-party collaboration to promote the high-quality development of drugs.

Source: Government Website, Frost & Sullivan analysis

Favorable Government Policy of Pharmaceutical Industry

Review of Registration Category

Release Date	Issuing Authority	Policies	Comments
Jul, 2016	NDRC	*Notice for the Division of Work for Key Departments Engaged in Prompting Medicine Industry Develop Healthily* 《关于促进医药产业健康发展的指导意见重点工作部门分工方案》	• Accelerate the international registration and certification of branded generic drugs.
Oct, 2017	CFDA	*Decision on Adjusting Events Related to Imported Drug Registration Management* 《关于调整进口药品注册管理有关事项的决定》	• The drugs that conduct global multi-center clinical trials in China are permitted to develop Phase 1 clinical trials at the same time. • The drugs that conduct global multi-center clinical trials can directly apply for market registration in China. • Accelerate past registration applications for global multi-center clinical drugs.
Jan, 2020	NMPA	*Measures for Drug Registration Management (2020)* 《药品注册管理办法》	• Optimize the review and approval process, improve the predictability of registration time, and reduce the burden on enterprises. • Add a chapter on "Accelerating Drug Marketing Registration Procedures" to support clinically value-oriented drug innovation. Establish four accelerated channels for breakthrough therapeutic drug approval, conditional approval, priority review and approval and special approval. • Strengthen the supervision of the whole life cycle of drugs, clarify the processes of clinical trials, listing registration and post-marketing management.

Source: Government Website, Frost & Sullivan analysis

Favorable Government Policy of Pharmaceutical Industry

Review of Medical Reimbursement

Release Date	Issuing Authority	Policies	Comments
Jan, 2016	State Council	*Advices for Integrating Basic Medical Insurance Systems for Urban and Rural Residents* 《关于整合城乡居民基本医疗保险制度的建议》	• Harmonizing the medical insurance product list and medical service items for urban and rural residents; • Clarifying the scope of payment for medicines and medical services.
Mar, 2016	State Council	*Guiding Opinions of the General Office of the State Council on Promoting the Sound Development of the Medical Industry* 《国务院办公厅关于促进医药产业健康发展的指导意见》	• Implementing hospital, medical insurance, and drug coordinated reforms, taking full advantages of the market system and form actual trade prices of drugs mainly by market competitions.
Jun, 2016	MoHRSS	*Guiding Opinions of Actively Prompting Hospital, Medical Insurance and Drug Coordinated Reforms* 《关于积极推动医疗、医保、医药联动改革的指导意见》	• Strengthening medical insurance management mechanism innovations. • Adjusting to the reforms of governance approaches, transforming ideas, innovating management methods, establishing and improving negotiation and risk sharing mechanism, improving agreement management, and strengthening bilateral consultation based on equality.
Jul, 2017	MoHRSS	*Notice of involving 36 varieties of drugs into List B of the Catalog for National Basic Medical Insurance, Work-related Injury Insurance and Maternity Insurance Drugs* 《关于将36种药品纳入国家基本医疗保险、工伤保险和生育保险药品目录乙类范围的通知》	• Among the 44 negotiated varieties, 36 drugs are involved in medical insurance including 31 western drugs and 5 Chinese traditional drugs.

Source: Government Website, Frost & Sullivan analysis

Favorable Government Policy of Pharmaceutical Industry

Review of Medical Reimbursement

Release Date	Issuing Authority	Policies	Comments
Jul, 2018	NHC, MoHRSS, MoF	*Notice for Improving Basic Medical Insurance for Urban and Rural Residents in 2018* 《关于做好2018年城乡居民基本医疗保险工作的通知》	• In 2018, the standard of financial subsidy and individual payment of medical insurance for urban and rural residents was raised simultaneously.
Oct, 2018	NHSA	*Notice for the inclusion of 17 anticancer drugs in List B of the National Basic Medical Insurance, Industrial Injury Insurance and Birth Insurance Catalogue* 《关于将17种抗癌药纳入国家基本医疗保险、工伤保险和生育保险药品目录乙类范围的通知》	• The 17 drugs included in the drug catalogue involve 12 solid tumor drugs and 5 heamatological tumor drugs. • The payment standard of most imported drugs is much lower than the market price of the surrounding countries, which will greatly reduce the burden of drug use for cancer patients in China.
Nov, 2019	MoHRSS	*Notice for the inclusion of 2019-Negotiations-Drugs in List B of the National Basic Medical Insurance, Industrial Injury Insurance and Birth Insurance Catalogue* 《关于将2019年谈判药品纳入国家基本医疗保险、工伤保险和生育保险药品目录乙类范围的通知》	• Included 97 successful negotiations drugs (70 new drugs + 27 renewal drugs).
Dec, 2021	NHSA	*Notice for the Publication of the National Essential Medicine Catalogue (2021 edition)* 《关于印发国家基本药物目录（2021年版）的通知》	• 2,860 drugs are in the NRDL • 74 drugs are newly included into NRDL, with 67 of them are negotiations.

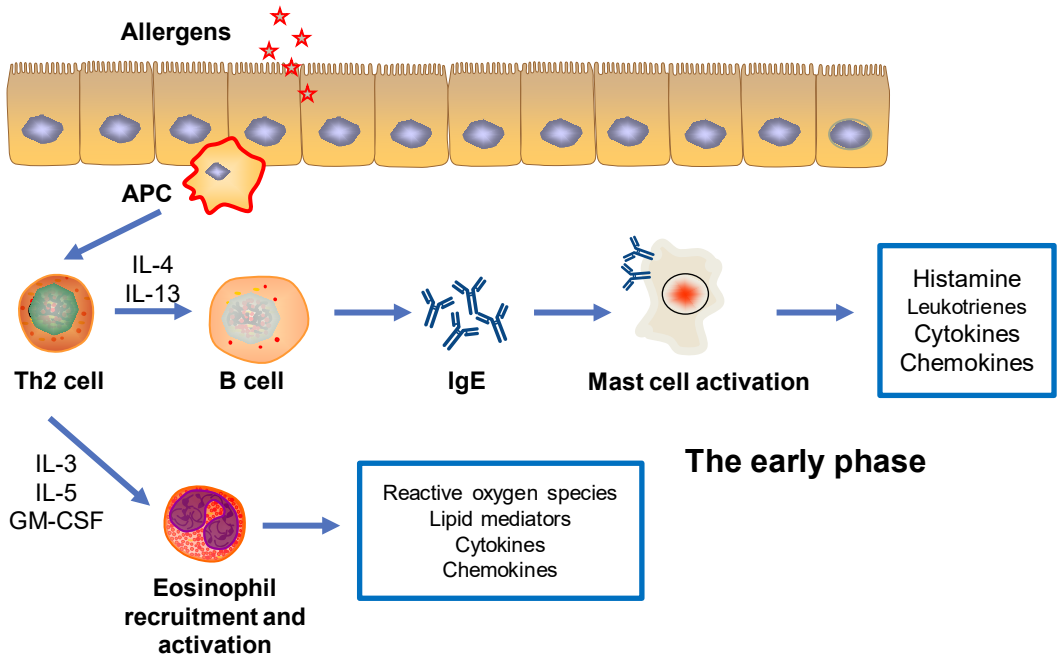
Source: Government Website, Frost & Sullivan analysis

Table of Contents

Overview of Allergic Diseases

- Allergy diseases are a group of conditions caused by hypersensitivity of the immune system due to contact with harmless allergens in the external environment.
- Hay fever, food allergies, atopic dermatitis, allergic rhinitis, uricaria and allergic asthma are common allergic diseases and the most common allergens, which could induce allergy, are pollen, certain foods, medication and insect stings.

Mechanism of Allergic inflammation



Common Symptoms

- Red eyes
- Itchy rash
- Sneezing
- Rhinorrhea
- Dyspnea
- Swelling

Source: Literature Review, Frost & Sullivan analysis

Immune Responses and Inflammatory Markers

- Both allergic and non-allergic diseases can induce immune responses.
- Immune responses can be classified into three inflammatory endotypes (type 1, type 2 and type 3). Each endotype has a unique signature profile composed of specific immune cells, inflammatory mediators, and physiological functions.
- Type II immunity consists of GATA-3+ ILC2S, Tc2 cells, and TH2 cells, and type II cytokines produced by TH2 cells can induce the activation of mast cells, basophil and eosinophil, as well as the production of IgE antibody to protect against helminths and venoms. Several cytokines and pathways, such as IL-4, IL-5, IL-13, TSLP and JAK, were found to be involved in the activation of type II immune response. Aberrant activation of type II immune response can cause allergic diseases.
- Among all type II inflammatory cytokines, IL-4 and its receptor are the most studied, and Dupixent, an IL-4Rα targeted mAb, has been approved for indications including Asthma, AD and CRSwNP. Researches on new indications such as COPD, nasal polyposis, eosinophilic esophagitis, have been processed in their clinical stage because of the extraordinary curative effect and safety.

Immune Responses

Endotype	Type 1	Type 2	Type 3
Effector Cells	Th 1 Cell, CD8+ T Cell, NK Cell, ILC1	Th2 Cell, TSLP, Eosinophil, ILC2	Th17 Cell, Neutrophil, ILC3
Primary Cytokines	• IL-12 is a potent proinflammatory cytokine that enhances the cytotoxic activity of T lymphocytes and resting Natural Killer Cells. • IFNγ is a cytokine that plays an important role in tissue homeostasis, immune response and inflammatory response.	• IL-4 promotes T cell growth and can potentially induce the growth and activity of cytolytic T cells. Also, it induces the differentiation of naive CD4+ T cells into TH2 cells. • TSLP is able to strongly activate dendritic cells and provides evidence at a molecular level that epithelial cells/tissue microenvironments can directly communicate with dendritic cells.	• IL-17 is a proinflammatory cytokine which stimulates the recruitment of neutrophils and monocytes into inflamed areas. • IL-22 is a cytokine primarily associated with the maintenance of barrier function and the induction of innate antimicrobials at mucosal surfaces.

Source: Literature Review, Frost & Sullivan analysis

Development Path of Allergy Treatment

- In the past century, several effective treatments of allergy have been introduced, first extract from natural material, then synthetic glucocorticoid, and to date, the biologics. Since the mechanisms of allergic disease are becoming increasingly well defined, in the future, therapeutic strategies will attempt to harness such mechanisms to optimize clinical efficacy.
- The emergence of biological and targeted therapies has brought profound changes to the treatment paradigm for allergic diseases in recent years. Traditional treatment options, such as glucocorticoids and antihistamines, are generally limited in efficacy and associated with severe adverse events, especially for long-term treatment.
- Since the first biologic drug was approved for the treatment of allergic diseases by the FDA in 2003, biologics that target interleukin (IL) family and inflammatory responses related IgE have been widely used for the treatment of allergic diseases.
- Biologic therapies continue to be extensively studied for treating a wide spectrum of allergic diseases given their high efficacy and excellent safety. In addition, small-molecular targeted therapies, such as janus kinase (JAK) inhibitors, can also be used to treat allergic diseases. However, studies have found that JAK inhibitors are less tolerated in children with and therefore are not recommended as a preferred pediatric treatment option.

Milestones in Allergy Treatment

Desensitization Therapy
1911, first immunotherapy trial for hay fever

- ***Densensitization*** is a medical treatment for environmental allergies, such as insect bites, and asthma.
- By progressively exposing people to larger amount of allergen, desensitization therapy can change the immune response of patients and make it less sensitive.

Antihistamines
1942, first antihistamine used clinically in man

- ***Antihistamines*** are synthetic antagonists that competitively bind at H1 receptor and H2 receptor. Antihistamines targeting H1 receptor can regulate the responses of immune system while antihistamines targeting H2 receptor can suppress the secretion of acid in stomach.
- Antihistamines are used to suppress or alleviate symptoms in various allergic diseases. They are effective in treating seasonal hay fever to relieve sneezing and rhinorrhea.

Glucocorticoids
1972, first successful report of inhaled glucocorticoid for the treatment of asthma

- ***Glucocorticoids*** are a group of corticosteroids produced by adrenal gland.
- Glucocorticoids have been widely used in treating asthma and other allergic diseases for its anti-inflammatory and immunosuppressive effects.
- Glucocorticoids indirectly inhibit the activity of phospholipase A2, an enzyme that plays an essential role in the synthesis of prostaglandins and leukotrienes.

Biologic Therapy
2003, FDA approved the first monoclonal antibody for asthma, omalizumab.
2015, FDA approved the first IL-5 antagonist monoclonal antibody, Mepolizumab.

- ***Biologic therapy*** is a treatment designed to regulate the ability of immune system against infections and diseases.
- Biologics targeting IL-5, IL-4 and IgE are widely used in allergic asthma especially uncontrolled asthma.

Source: Literature Review, Frost & Sullivan analysis

Growth Drivers of Allergic Diseases Market


Increasing Disposable Income	• China residents annual disposable income has experienced fast growth during the past few years, increasing from RMB23,821 in 2016 to RMB32,189 in 2020 at a CAGR of 7.8% during this period. With the economic development, the per capita annual disposable income is expected to further grow to RMB46,902.4 in 2025. The growth of per capita annual income of Chinese residents has a positive effect on the purchasing power and the level of health awareness among the Chinese population.	●	◕
Improve Public Medical Insurance	• Public medical insurance is the largest single payer for pharmaceutical in China. The latest version of NRDL not only expand to include more drugs to be reimbursable but also adopt dynamic adjustment via price negotiation to include more advanced drugs in the List with a more economical price. Currently, there are total 2,860 drugs in the NRDL.	◑	●
Technology Advancement	• Technology advancement brings revolution to the pharmaceutical R&D and manufacturing process, enabling the advent of targeted therapy for allergy treatment. Patients suffering from allergic diseases have benefited a lot from the newly developed monoclonal antibody drugs. With the further R&D investment and efforts, more novel therapies will be launched and further improve the life quality of allergic disease patients.	●	◑

◔ → ● *Influence: Weak to Strong*

Source: Frost & Sullivan analysis

Future Trends of Allergic Diseases Market

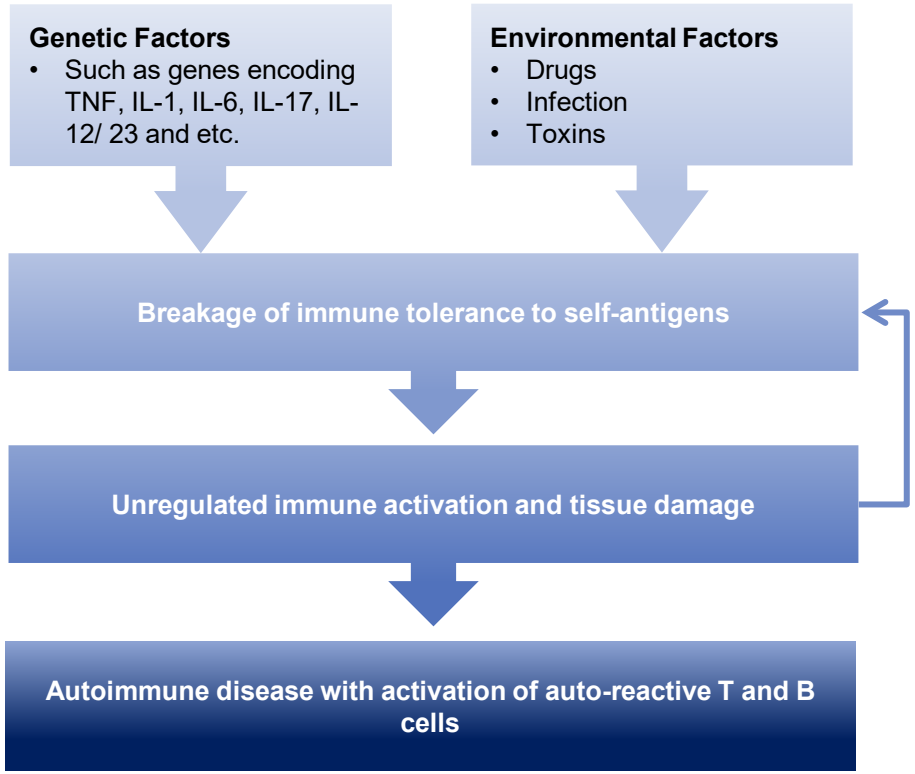
			
Development of biologics	• The current understanding of the human immune system has identified multiple potential therapeutic targets and biologic therapies have been specifically developed them. The use of biologics in allergic disease is a natural progression of this development because allergic disease is characterized by inflammatory responses with multiple pathways and triggers.	●	◕
Targeted therapy rather than tradition method	• Traditional method of treatment for allergic diseases may result in adverse effect like ecchymosis, acne and facial erythema which mainly comes from the off-target effect of drugs. By targeting specific immune pathways, biologics can be very effective while minimizing the side effects.	◑	◔
Higher Penetration and Rapid Market Growth	• The diagnosis rate and treatment rate for allergic diseases are far from that of the developed countries. A large amount of population suffer from lack of concerns and medication, which could be a huge potential market. As the increasing affordability and healthcare awareness, the market and the penetration of drugs for allergic disease will experience a rapid growth for several years in the future.	●	●

◔ → ● *Influence: Weak to Strong*

Source: Frost & Sullivan analysis

Overview of Autoimmune Disease

- An autoimmune disease is a condition in which the body's immune system mistakenly attacks the body, which can be associated with either abnormally low activity or over-activity of the immune system.
- There are more than one hundred different types of autoimmune disorders, which can affect almost any part of the body, including the heart, brain, nerves, muscles, skin, eyes, joints, lungs, kidneys, glands, the digestive tract, and blood vessels.



Mechanisms for Autoimmune Diseases

- Autoimmune diseases can be divided into organ-specific and systemic autoimmune diseases based on the self-antigens targeted by immune cells.
- The exact underlying pathophysiology of these illnesses is still unknown, while autoimmune diseases arise in the context of a break in the immune tolerance to self.
- The mechanisms for the abrogation of immune self-tolerance appear to be multifactorial, including genetic and environmental, which will lead to unregulated immune activation against self-antigens and subsequent tissue destruction.
- B cells and T cells recognize self-antigens and dominate the phenotype of the patient with autoimmunity, although other immune components including antigen-presenting cells and complement are involved in various steps from initiation of the autoimmune response to tissue destruction.

Source: Literature Review, Frost & Sullivan analysis

Treatment Revolution for Auto-immune Disease

Anti-inflammatory Agents

- Treatments were generally effective for alleviating of pain, fever, and inflammatory responses, but were limited to treating the symptoms of the disease.

Salicylates → **NSAIDs**, **Glucocorticoids**, **DMARDs**

- Active components of Willow spp.
- Identified in the mid-19th century

- Due to the chemical advances in the 19th–20th centuries.

Targeted Biologics

- Targeted Biologics target the underlying sources of autoimmune disease, which improves physical functioning and prevents irreversible damage, making disease remission possible.

Anti-TNF Antibodies

- Total five innovative TNF-targeting drugs have been approved.

Interleukin Related Drugs

- Include marketed drugs targeting at IL-1, IL-6,IL-17, IL-23, etc.

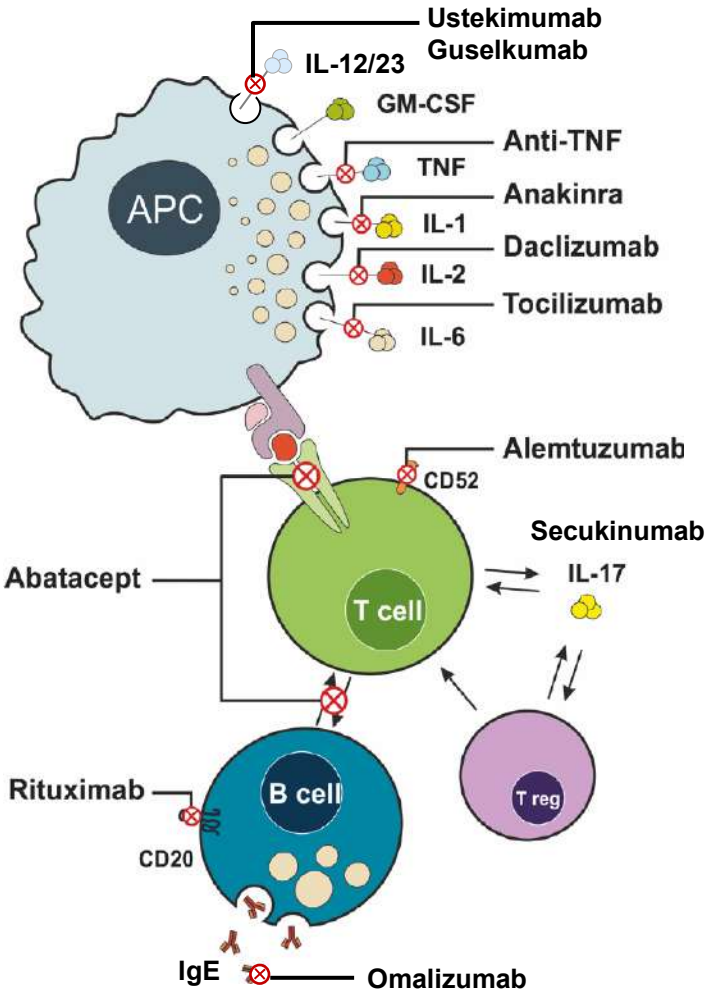
JAK Inhibitors

- Include JAK1, JAK2, TYK2 and JAK3.

Others

- Include other monoclonal antibodies targeting at CD20, CD22, CD28, BLyS, BTK inhibitors etc.

Future: More effective therapies being developed



Note:
NSAIDs: Non-steroidal anti-inflammatory drugs
DMARDs: Disease-modifying anti-rheumatic drugs

Source: Literature Review, Frost & Sullivan analysis

Comparison of Autoimmune Disease Treatment

Treatment Category	Common Types	Common Drugs	Mechanism	Advantages
Biologics	Biologics	• Adalimumab • Etanercept • Golimumab • Infliximab	Target at molecules involved in the activation of the immune system, such as tumor necrosis factor (TNF), interleukin (IL), B-cells and T-cells.	Newly emerging effective biologic drugs are available for patients with severe or resistant diseases.
Small Molecular	Nonsteroid anti-inflammatory drugs (NSAIDs)	• Aspirin • Ibuprofen • Naproxen	Block prostaglandins, which can sensitize the nerves and magnify pain feelings during inflammation.	Work quickly and generally have fewer side effects than corticosteroids.
	Conventional DMARDs	• Methotrexate • Leflunomide	Inhibit the enzymes that affects DNA-synthesis for the proliferation of white blood cells, thus causing immunosuppression.	Long-term medication can effectively control symptoms and achieve stable efficacy.
	Corticosteroids	• Methylprednisolone • Dexamethasone • Prednisone	Stop the release of molecules that cause inflammation and also stop body from having an immune response.	Fast and strong anti-inflammatory effect that can be applied in many situations.
	JAK inhibitors	• Tofacitinib • Baricitinib	Inhibit immune cell function by inhibiting signal transduction of cytokines and growth factors.	Have shown satisfactory efficacy in patients resistant to other medications.
	Other Immuno-suppressants	• Such as mTOR inhibitors (Sirolimus, Everolimus)	Block the mammalian target of rapamycin (mTOR) which regulates cellular metabolism, growth, and proliferation.	Have shown tumor responses in clinical trials against both autoimmune diseases and various tumor types.

Source: Literature Review, Frost & Sullivan analysis

Autoimmune Disease Treatment Diagram

Traditional Anti-inflammatory Agents

Traditional anti-inflammatory agents could alleviate pain, fever and inflammatory responses. However, studies have found that non-steroidal anti-inflammatory drugs (NSAIDs) and disease-modifying antirheumatic drugs (DMARDs) showed limited efficacy as compared to biologic drugs, especially in patients with more advanced autoimmune diseases, and there remain concerns over the potential side effects from long-term use of corticosteroids.
Mainly include:
– NSAIDs
– DMARDs
– Corticosteroids

Biologic Drugs TNF-targeting Antibodies

Antibodies targeting TNF, a type of pro-inflammatory cytokine, are the most widely used biologic drugs for the treatment of various autoimmune diseases, such as ankylosing spondylitis and rheumatoid arthritis.
Mainly include:
– Adalimumab
– Infliximab
– Golimumab
– Certolizumab
– Etanercept

Biologic Drugs Interleukin-targeting Antibodies

IL-targeting antibodies have the potential to be the next-generation biologics for the treatment of autoimmune diseases.
Mainly include:
– IL-17 antibodies
– IL-12 antibodies
– IL-23 antibodies
– IL-4 antibodies

Small-molecule Targeted Drugs

A limited number of small-molecule targeted drugs, such as janus kinase (JAK) inhibitors and PDE-4 inhibitors, have also been explored as potential treatment for various autoimmune diseases such as RA, AS and Ps. However, their potential to become recommended treatment options for autoimmune diseases is still under evaluation due to concerns over their safety profile.

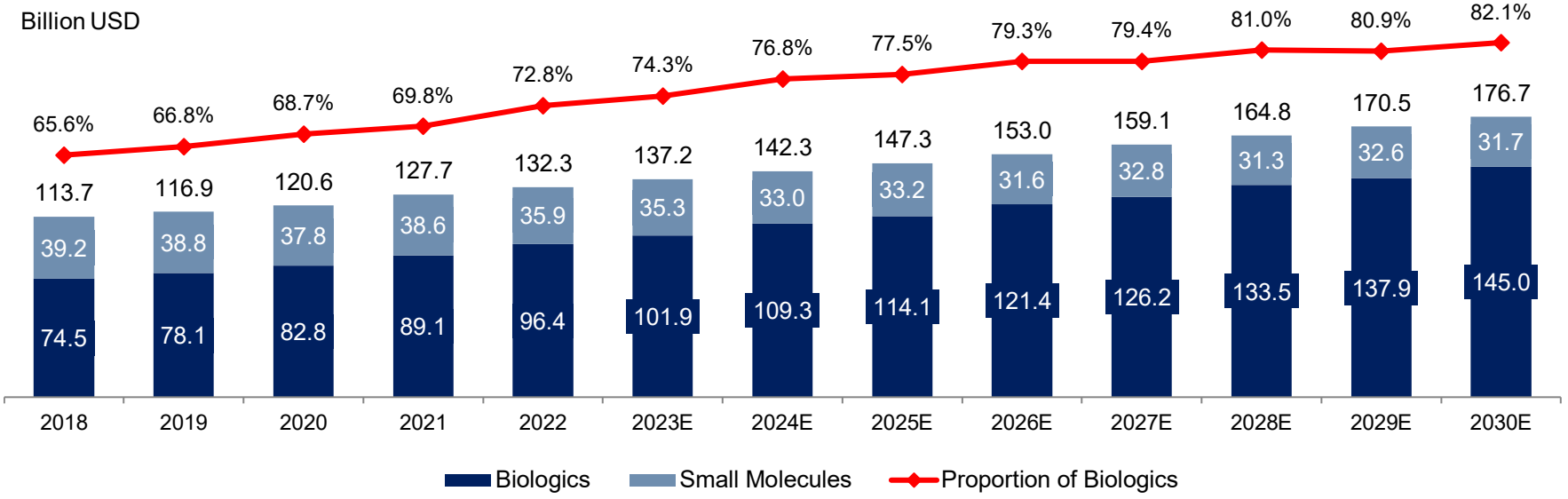
Source: Literature Review, Frost & Sullivan analysis

Global Autoimmune Disease Drug Market, 2018-2030E

- The global autoimmune disease drug market size is expected to grow from USD 132.3 billion in 2022 to USD 147.3 billion in 2025 with a CAGR of 3.6%. The CAGR from 2022 to 2030 is 3.7%.
- Global biologics autoimmune diseases treatment market increased from USD 96.4 billion in 2022 and would reach USD 114.1 billion in 2025 with a CAGR of 5.8%. With the off-patented of many blockbusters in the global autoimmune diseases market, the growth rate of market size would experience a slight decrease in the following years. Nevertheless, targeted biologics have already replaced small molecules as the major treatment of autoimmune diseases.

Global Autoimmune Disease Drug Market, 2018-2030E

Period	Biologics	Small Molecules	Total Market
2018-2022	6.6%	-2.1%	3.9%
2022-2025E	5.8%	-2.6%	3.6%
2025E-2030E	4.9%	-0.9%	3.7%



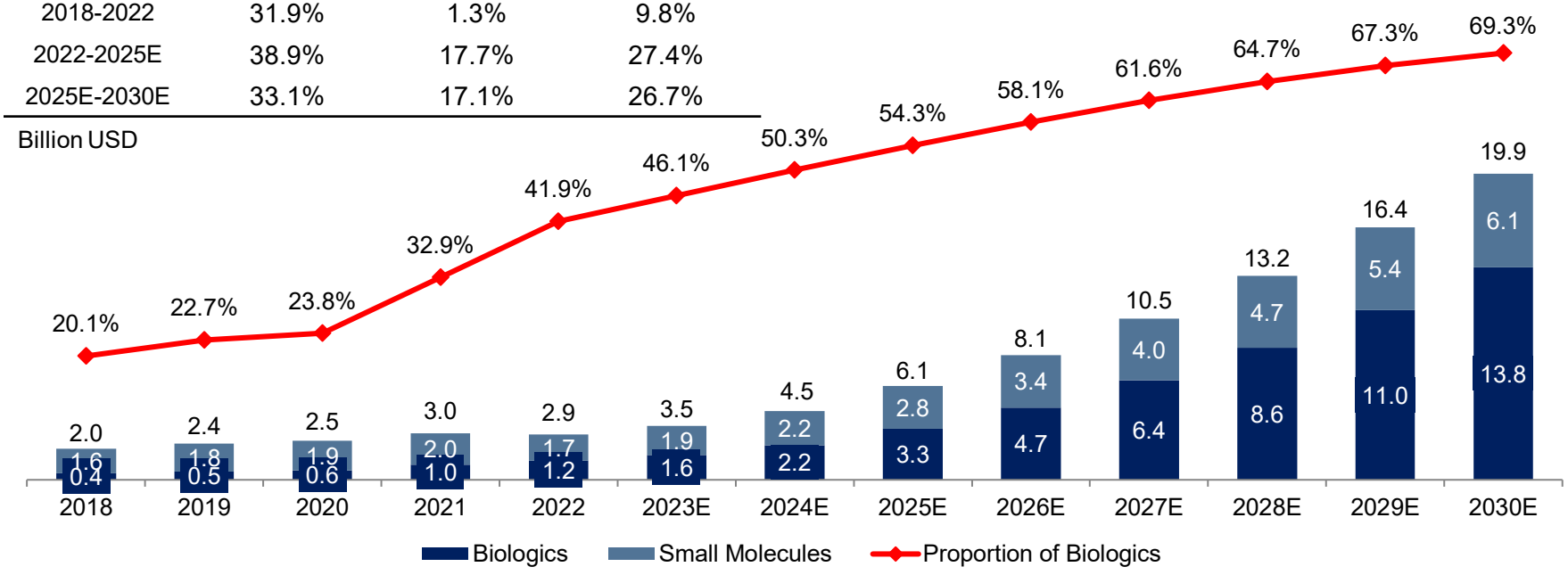
Source: Literature Review, Frost & Sullivan analysis

China Autoimmune Disease Drug Market, 2018-2030E

- Based on China's huge population, there is a large patient pool in the Chinese market. With the development and improvement of diagnostics for autoimmune diseases in China, the market demand for medical services would be spurred in the following years. The overall market is expected to reach USD 6.1 billion in 2025, representing a CAGR of 27.4% from 2022. The CAGR from 2022 to 2030 is 27.0%.
- Given the large patient pool in China, and the development and advancement of innovative therapies for autoimmune diseases, the market of biologics would increase rapidly after 2018 because of the boom of innovative biologics R&D. The market share of biologics would increase from 20.1% in 2018 to 69.3% by 2030 in China autoimmune diseases treatment market.

China Autoimmune Disease Drug Market, 2018-2030E

Period	Biologics	Small Molecules	Total Market
2018-2022	31.9%	1.3%	9.8%
2022-2025E	38.9%	17.7%	27.4%
2025E-2030E	33.1%	17.1%	26.7%



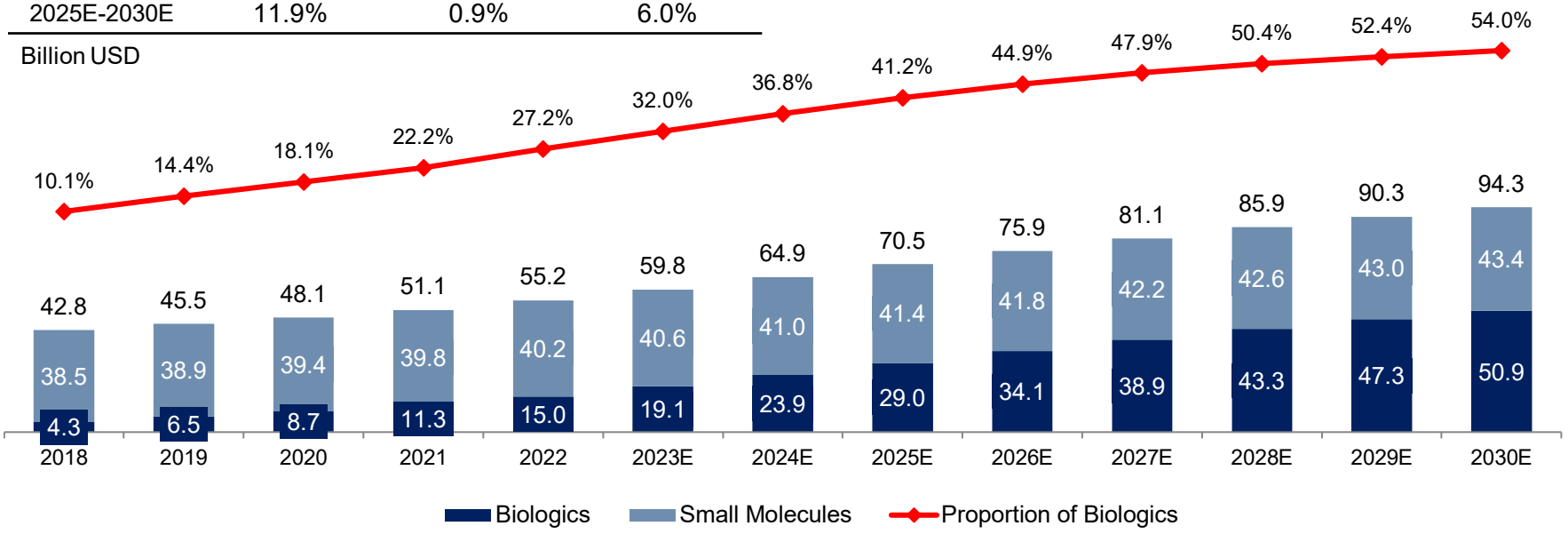
Source: Literature Review, Frost & Sullivan analysis

Global Allergic Disease Drug Market, 2018-2030E

- The global allergic disease Drug market size is expected to grow from USD 55.2 billion in 2022 to USD 70.5 billion in 2025 with a CAGR of 8.5%. The CAGR from 2022 to 2030 is 6.9%.
- Global biologics allergic diseases treatment market increased from USD 15.0 billion in 2022 and would reach USD 29.0 billion in 2025 with a CAGR of 24.6%.

Global Allergic Disease Drug Market, 2018-2030E

Period	Biologics	Small Molecules	Total Market
2018-2022	36.5%	1.1%	6.6%
2022-2025E	24.6%	1.0%	8.5%
2025E-2030E	11.9%	0.9%	6.0%



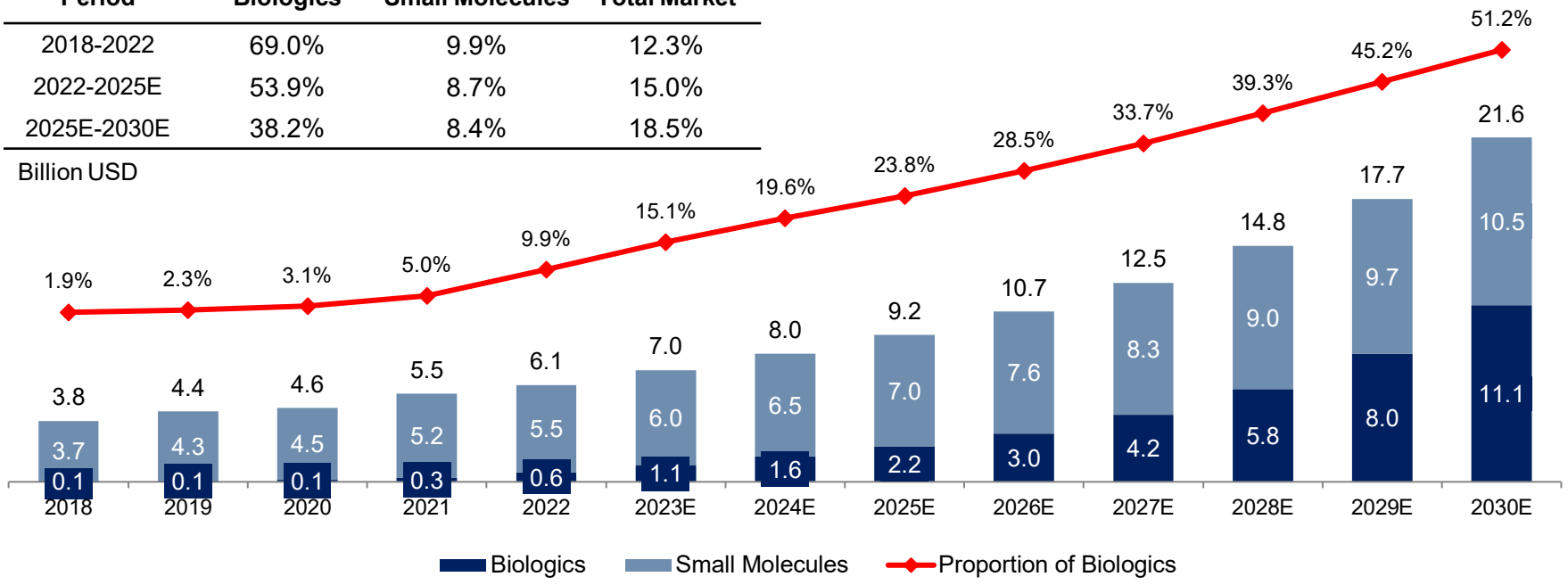
Source: Literature Review, Frost & Sullivan analysis

China Allergic Disease Drug Market, 2018-2030E

- Based on China's huge pool of patients with allergic diseases. The overall market is expected to reach USD 9.2 billion in 2025, representing a CAGR of 15.0% from 2022. The CAGR from 2022 to 2030 is 17.2%.
- The market of biologics is expected to reach USD 2.2 billion in 2025, representing a CAGR of 53.9% from 2022. The market share of biologics would increase from 1.9% in 2018 to 51.2% by 2030 in China allergic diseases treatment market.

China Allergic Disease Drug Market, 2018-2030E

Period	Biologics	Small Molecules	Total Market
2018-2022	69.0%	9.9%	12.3%
2022-2025E	53.9%	8.7%	15.0%
2025E-2030E	38.2%	8.4%	18.5%

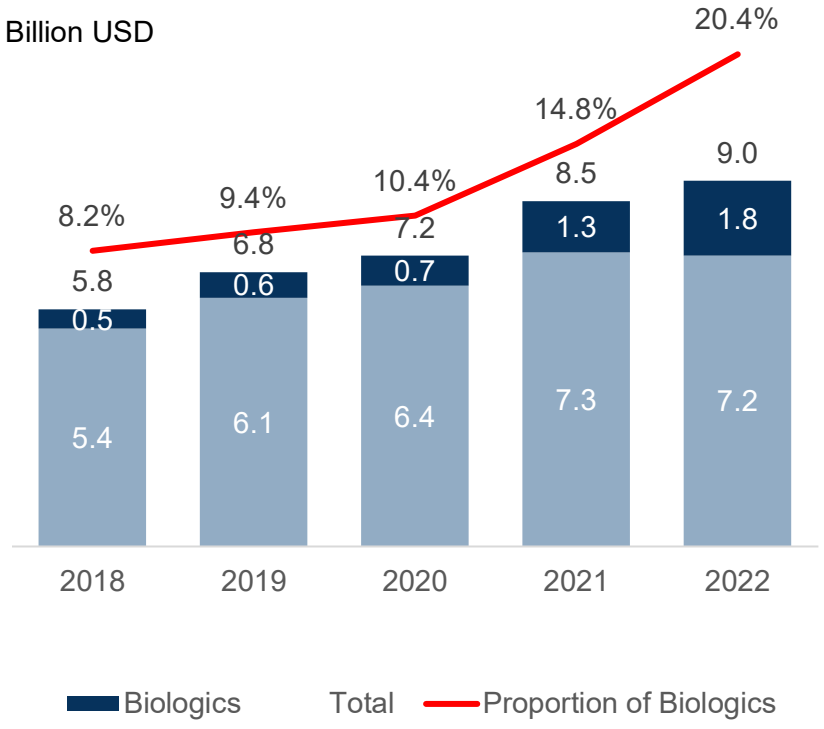


Source: Literature Review, Frost & Sullivan analysis

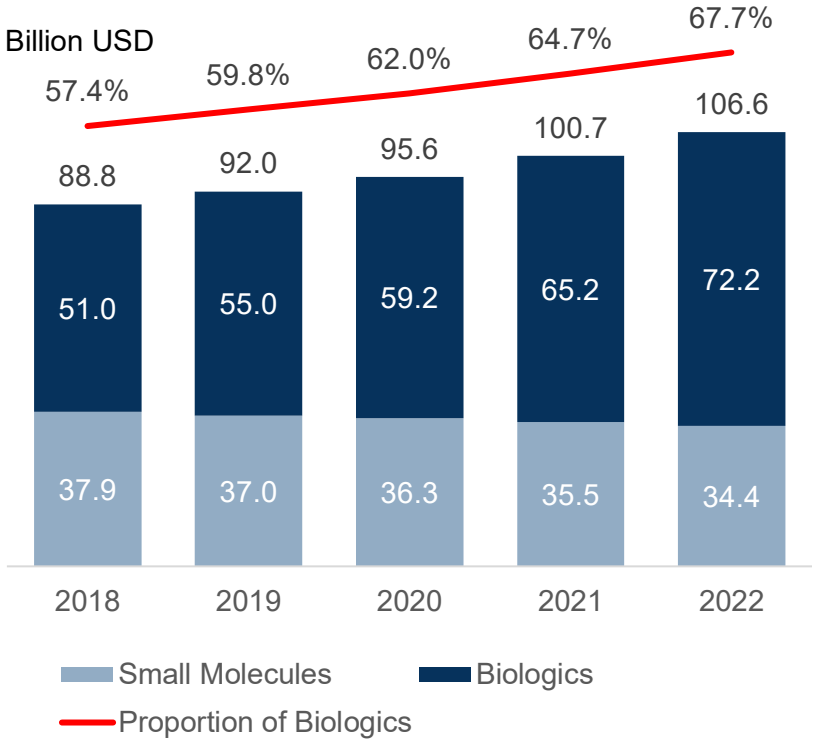
Allergic Disease & Autoimmune Disease Drug Market in China and the U.S., 2018-2021

- China's autoimmune and allergic drug market was US$7.2 billion in 2020, 7.5% of the U.S. market of US$95.6 billion.
- China's autoimmune and allergic drug market was US$8.5 billion in 2021, 8.5% of the U.S. market of US$100.7 billion.
- The autoimmune and allergic disease drug market in China expanded from US$7.2 billion to US$8.5 billion, representing a 18.8% growth year on year.

Allergic Disease & Autoimmune Disease Drug Market in China, 2018-2021



Allergic Disease & Autoimmune Disease Drug Market in the U.S., 2018-2021



Source: Literature Review, Frost & Sullivan analysis

Growth Drivers of Autoimmune Disease Drug Market


Need for Personalized Treatment	• For decades, numerous autoimmune disease patients have suffered from drug-related toxicity and lack of personalized treatments which are responsive to their specific diseases. Such need for personalized treatment, as well as advances in genetics and medicine, provides the impetus for driving the discovery and development of effective personalized medicines for autoimmune diseases.	●	◕
The Increasing Number of Rheumatic Immunity Departments	• Currently, 60% of hospitals in China do not have an independent rheumatology department, and more than 80% of the 7,200 rheumatologists work in tertiary hospitals. In the future, as more treatment institutions set up independent departments of rheumatism and immunity, the medical resources of systemic diseases will be greatly improved, patients can be diagnosed and treated earlier.	◔	◕
Increasing Affordability	• In the 2021 NRDL, 4 in 67 newly included drug are used to treat autoimmune diseases, which significantly improved patients' affordability. With the further NRDL negotiation, the emergence of domestic innovative biologics, as well as increasing per capita disposable income, the affordability of autoimmune diseases drugs will keep increasing, driving the market growth.	●	●

◔ → ● *Influence: Weak to Strong*

Source: Frost & Sullivan analysis, 2018 Chinese guideline for the diagnosis and treatment of rheumatoid arthritis

Future Trends of Autoimmune Disease Drug Market


More indications to be covered with innovative biologics.	• Currently, autoimmune diseases are still cannot be cured. With an increased understanding of the pathophysiology of autoimmune diseases and associated biologic pathways, more innovative biologics such as anti-IL-6 antibodies, anti-IL-17 antibodies and anti-TNF-α antibodies are expected to be developed. These newly developed biologics not only provide more available drugs for patients with autoimmune diseases such as RA and systemic lupus erythematosus but also help address more therapeutic areas.	●	◕
Broad Use as First-Line Medications.	• Current drawbacks of biologic therapies, including the inconvenience of intravenous administration and the associated high costs, prevent wider use of biologics as first-line medications for autoimmune diseases. With the improvement of manufacturing technology and economic conditions, biologics are likely to be used as first-line medications for autoimmune diseases.	◑	●
Higher Penetration	• As the patent of the original drug expires, more and more biosimilars will enter the market, the number of alternative drugs for patients with autoimmune diseases will increase and the penetration of biologics will increase.	●	●

◔ → ● *Influence: Weak to Strong*

Source: Frost & Sullivan analysis

Affordability and Availability of Biologics in Treating Allergic and Autoimmune Diseases

Penetration

USA

- With a leading position in global drug research and development, a first-mover advantage and a sound market operation mechanism, biologics are used earlier in the treatment of allergic and autoimmune diseases in the USA. The high penetration rate of biologics also owns to the higher national economic level.

50.7%

A study of patients with rheumatoid arthritis enrolled in 2010-2012 showed that the penetration rate of biologics in the U.S. rheumatoid arthritis patient population was approximately 50.7%.

China

- Due to the late start of innovative drug research and development and the time-consuming approval process for imported drugs, the variety of biologics in treating allergic and autoimmune diseases is limited in China. At the same time, the limited level of the national economy also makes the penetration rate of biologics low in the Chinese patient .

8.3%

A study conducted by CREDIT of patients with rheumatoid arthritis enrolled in 2016-2017 showed that the penetration rate of biologics in the Chinese rheumatoid arthritis patients was about 8.3%.

Adherence

USA

- Considering that patients often have to afford more than traditional DMARDs when treating with biologics, the level of the national economy greatly affects patient adherence for biologics.
- In a study of drug adherence in patients with psoriasis, adherence was measured by using proportion of days covered (PDC) dichotomized as adherent (≥0.80) or nonadherent (<0.80). In the U.S. psoriasis patients, the adherence for adalimumab, etanercept, and ustekinumab was 72.4%, 68.6%, and 74.2%, respectively.

China

- Chinese patients' adherence for biologics is relatively lower than international, possible reasons are:
  - The price of biologics is higher than that of traditional DMARDs, and due to the impact of economic level, patients in China rarely use biologics regularly for a long time.
  - The level of awareness of the disease is not enough, and some patients will stop or reduce the drug after the condition improves.

Source: Frost & Sullivan analysis

Top 10 Grossing Biologics for Allergic and Autoimmune Diseases

- Humira, a TNF-α inhibitor marketed by Abbvie, is the world's best-selling biologic for allergic and autoimmune diseases in 2020, with a total sales of $19,832 million.

Rank	Brand Name	Generic Name	Company	2020 Sales ($ Million)
1	Humira	Adalimumab	Abbvie	19,832
2	Stelara	Ustekinumab	J&J	7,707
3	Enbrel	Etanercept	Pfizer+Amgen	6,346
4	Ocrevus	Ocrelizumab	Roche	4,614
5	Remicade	Infliximab	J&J+Merck+Mitsubishi Tanabe Pharma	4,512
6	Dupixent	Dupilumab	Sanofi	4,031
7	Cosentyx	secukinumab	Novartis	3,995
8	Entyvio	Vidolizumab	Takeda	3,776
9	Simponi	Golimumab	J&J+Merck+Mitsubishi Tanabe Pharma	3,476
10	Orencia	abatacept	BMS + Ono	3,363

Source: Frost & Sullivan analysis

Top 10 Grossing Biologics for Allergic and Autoimmune Diseases

- Humira, a TNF-α inhibitor marketed by Abbvie, is the world's best-selling biologic for allergic and autoimmune diseases in 2021, with a total sales of $20,694 million.

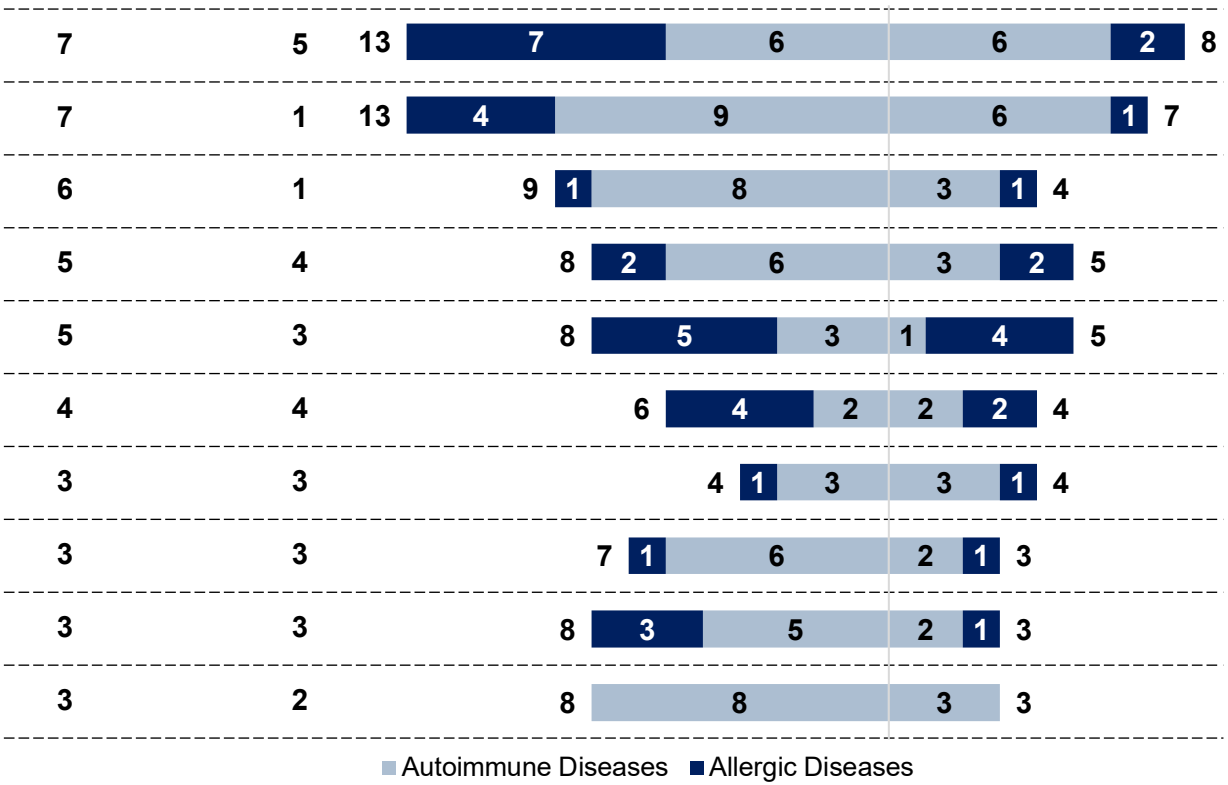
Rank	Brand Name	Generic Name	Company	2021 Sales ($ Million)
1	Humira	Adalimumab	Abbvie+Eisai	20,694
2	Stelara	Ustekinumab	J&J	9,134
3	Dupixent	Dupilumab	Sanofi+Regeneron	6,198
4	Enbrel	Etanercept	Pfizer+Amgen	5,650
5	Ocrevus	Ocrelizumab	Roche	5,530
6	Cosentyx	secukinumab	Novartis	4,718
7	Entyvio	Vidolizumab	Takeda	4,601
8	Actemra/RoActemra	Tocilizumab	Chugai+Roche	3,897
9	Xolair	Omalizumab	Novartis + Roche	3,557
10	Remicade	Infliximab	J&J+Merck+Mitsubishi Tanabe Pharma	3,489

Source: Frost & Sullivan analysis

General Competitive Landscape of Biologics for Autoimmune Diseases and Allergic Diseases in China

- The pipelines of Qyuns and Bio-Thera contain the largest number of biologics for the treatment of autoimmune diseases and allergic diseases, of which Qyuns contains 5 biologics that are registered as Class 1.

Companies	Number of Biologics	Number of Class 1 Biologics*	Number of Indications	Number of Targets*
Qyuns	7	5	13	8
Bio-Thera	7	1	13	7
Hisun	6	1	9	4
Sunshine Guojian	5	4	8	5
Chia Tai-tianqing	5	3	8	5
Keymed Bio	4	4	6	4
Akeso Bio	3	3	4	4
Suncadia	3	3	7	3
Genrix Bio	3	3	8	3
Junshi Pharma	3	2	8	3

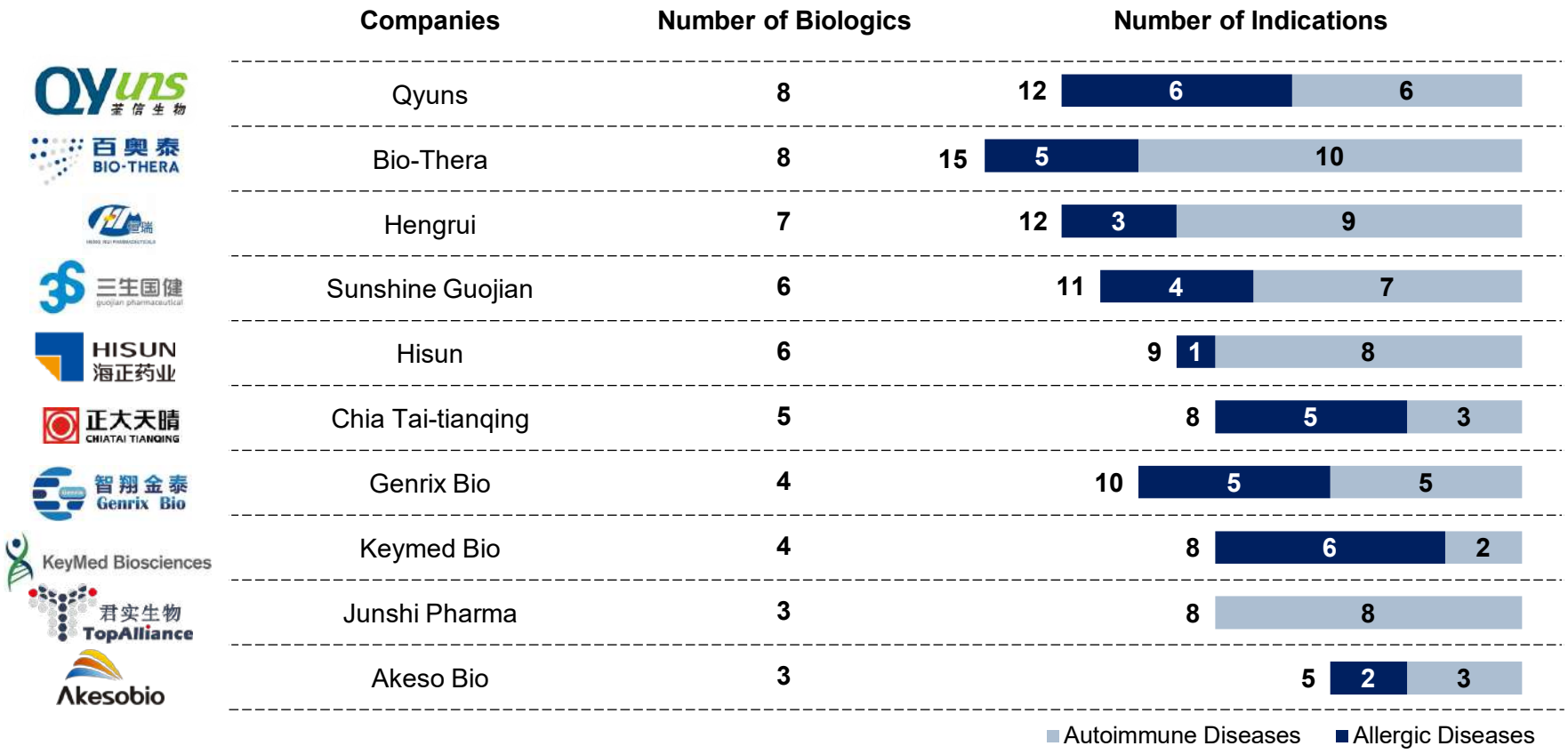


*This table only includes biologics, indications and targets that have been marketed, are in the BLA stage, are in clinical trials, or have got IND approval.
Class 1 biologic indicates innovative biological products that have not been marketed in China or overseas.
Biologics with undisclosed targets are considered to have only one target; IL-23p19 and IL-23p40 are considered different; Multiple undisclosed targets of the same company are considered different.
This table was last updated on Dec 12, 2022

Source: NMPA, CDE, Frost & Sullivan analysis

General Competitive Landscape of Biologics for Autoimmune Diseases and Allergic Diseases in China

- The pipelines of Qyuns and Bio-Thera contain the largest numbers of biologics for the treatment of autoimmune diseases and allergic diseases.



*This table only includes biologics, indications and targets that have been marketed, are in the BLA stage, are in clinical trials, or have got IND approval.
Each company's repeat indications only count once in this table.
This table was last updated on Mar 2nd , 2024

Source: NMPA, CDE, Frost & Sullivan analysis

Growth Driver and Future Trends of Autoimmune Disease and Allergic Disease Drug Market

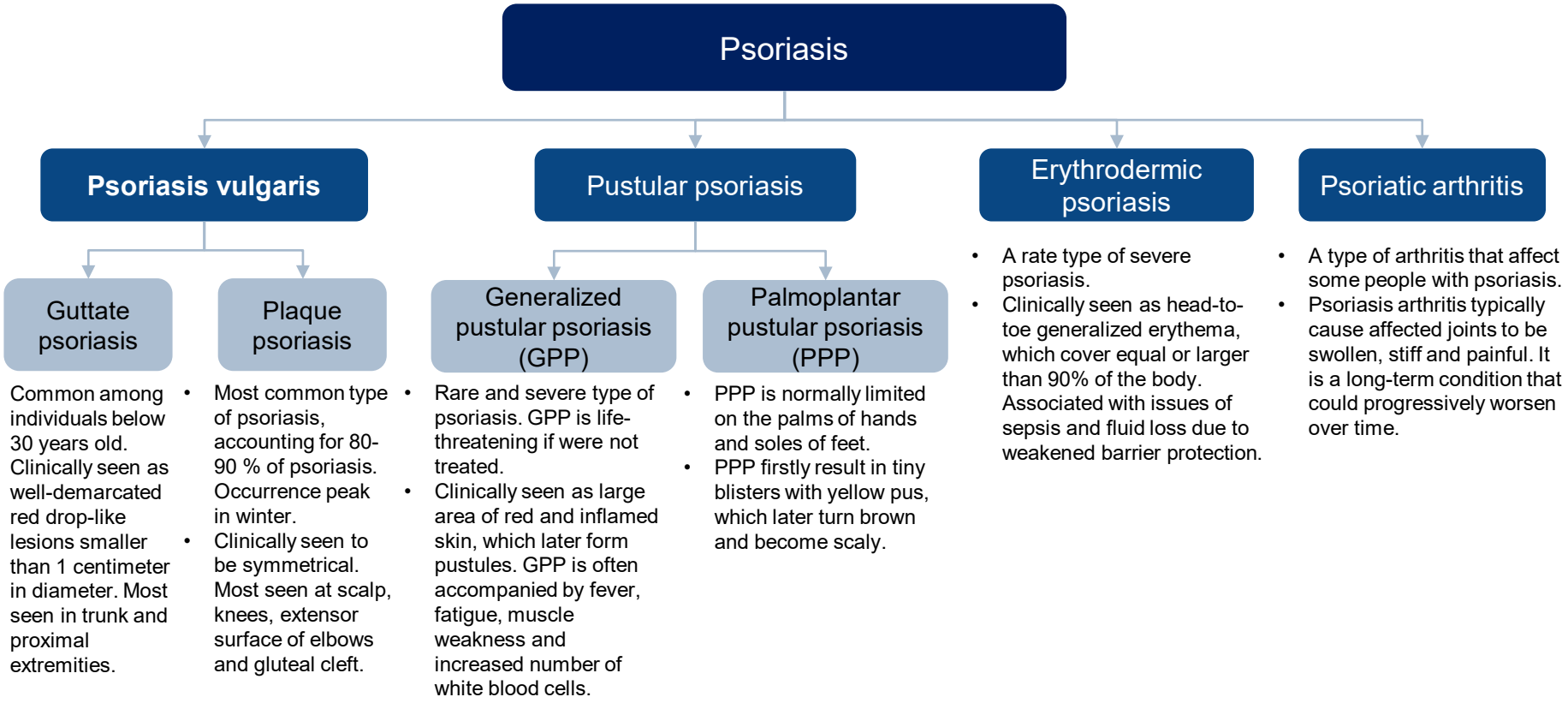
Vast underserved medical needs	• Although the superior efficacy and safety profile of biologics has resulted in growing acceptance among patients and doctors globally, the penetration rate of biologics in China remains low. There is still great potential for biologic drugs to capture more market share in China in competition with other pharmaceutical products for the same indications.
Favorable government policies in China	• China is striving to establish clear regulatory pathways to assure market access for quality biologic drugs. For example, pursuant to the Opinions on Deepening the Reform of the Evaluation and Approval Systems and Encouraging Innovation on Drugs and Medical Devices, which became effective in October 2017, China will further improve its evaluation and approval system through various measures, such as increasing availability of clinical trial sites, shortening the approval time of IND and BLA submissions as well as extending the patent term of innovative drugs, thus raising the affordability and availability of innovative drugs.
Expansion of approved biologic drugs and indications	• In the past, the number of approved biologic drugs and indications in China was relatively limited. Until 2021, there had been only 37 approved mAbs accumulatively in China, compared with 115 in the U.S. Dupilumab, an anti-IL-4R antibody, has been approved by the FDA for five indications since 2017, but only received NMPA approval for one indication since 2020. However, given the market opportunities, there has been increasing R&D investment in biologic drugs from Chinese domestic drug developers, which, in combination with favorable government policies, will help introduce more innovative biologic drugs for a wider spectrum of indications to the China market.
Improved affordability	• The high costs associated with current biologic therapies have imposed significant socioeconomic burden on both the patients and society and discouraged wide application of biologic drugs as first-line treatments for autoimmune and allergic diseases. The inclusion of innovative biologic drugs in the NRDL which led to significant price cuts, advancement in science and improvement of manufacturing technology are expected to reduce the costs associated with biologic drugs in China, which in turn could improve their affordability and increase accessibility

Source: Frost & Sullivan analysis

Table of Contents

Overview of Psoriasis

- Psoriasis is an autoimmune disease triggered by certain environmental exposures that result to chronic inflammatory skin condition, which typically results in growth of extra blood vessels and over-rapid replication of skin cells. Psoriasis is characterized to be well-demarcated, raised erythematous plaque with silver scales. Psoriasis can occur at any stage of life, though has two onset age peaks between 30-39 and 50-69.
- Psoriasis could be classified into psoriasis vulgaris, pustular psoriasis, erythrodermic psoriasis and psoriatic arthritis based on their featured characterizations of clinical manifestations.



Source: Guideline for the diagnosis and treatment of psoriasis in China (2018 version), Frost & Sullivan analysis

Risk Factors and Classification of Psoriasis

- Risk factors of psoriasis include family history of psoriasis, smoking, alcohols, obesity, infections and certain medications.
- Psoriasis could be classified into mild, moderate and severe psoriasis, based on typical evaluation tools including Psoriasis Area and Severity Index (PASI), physician global assessment (PGA) and dermatology life quality index (DLQI).

Risk Factors

Psoriasis severity evaluation tools

PASI (0 ~ 72)	A measurement of the discoloration, thickness, scaling, and coverage of these plaques.	• 1 - 4: mild • 5 - 10: moderate • > 10: severe
PGA (0 ~ 4)	PGA scoring system is based on response to treatment as measured by lesion erythema, induration, and scale, with score assignments that range from clear, almost clear, mild, moderate, to severe.	• 0: Clear • 1: Almost clear • 2: Mild • 3: Moderate • 4: Severe
DLQI (0 ~ 30)	A simple, self-administered and user-friendly validated questionnaire.	• 0-1: no effect at all on patient's life • 2-5: Small effect • 6-10: Moderate effect • 11-20: Very large effect • 21-30: Extremely large effect

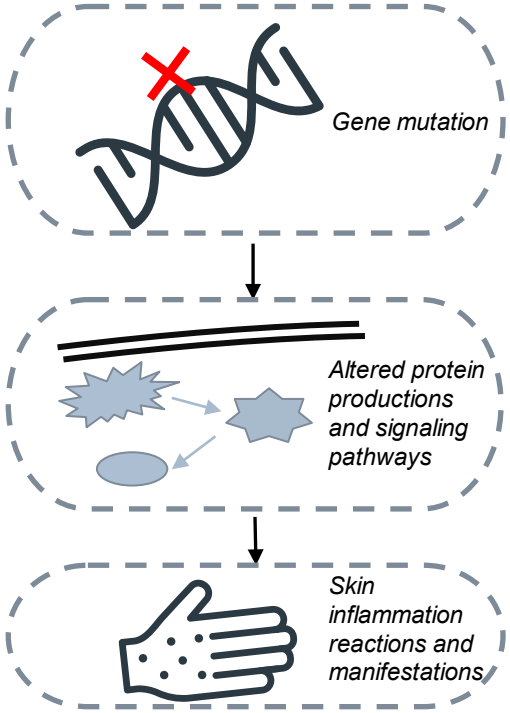
Source: Frost & Sullivan analysis

Overview of Generalized Pustular Psoriasis (GPP)

- GPP is the rarest, though extremely severe type of psoriasis. GPP would be life-threatening if remain untreated. GPP have repeated episodes in patients, where large area of skin become red, inflamed and form small pus-filled blisters upon occurrence. GPP is often accompanied by fever, fatigue, muscle weakness, increased number of white blood cells and systemic inflammation throughout the body. The recurrence could be triggered by infection, medications, menstruation, pregnancy or due to unknown triggers. Current medical treatments of GPP are systemic therapies, such as systemic corticosteroid therapy, though extensive side effects and precipitation of GPP after withdrawal of corticosteroids have been seen.
- Targeted biologics are great candidates to treat GPP. That is because GPP is associated with gene mutations. Mutations in genes such as IL36RN, IL-12/ IL-23 and AP1S3 have been reported to increase the risk of developing GPP, since these genes play roles in making proteins that are responsible for regulating inflammations.

Gene mutations involved in GPP

Mutation in IL36RN	Mutation in IL-12/ IL-23 genes	Mutation in AP1S3
Reduced production of IL-36Ra protein, which block the activity of proteins that trigger signalling pathways to promote skin inflammation.	Abnormal production of IL-12 and IL-23 that play roles in differentiating helper T cell 1 (TH1) and maintain TH17responses, which regulates immune responses.	Abnormal accumulation of p62, which mediates NF-kB activation and upregulation of IL-36Ra proteins
Overactivated signalling pathways to promote skin inflammation	Overactivated signalling pathways to promote skin inflammation	Overactivated signalling pathways to promote skin inflammation

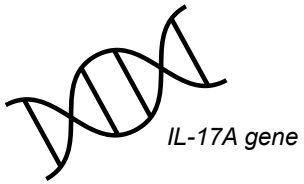


Source: Literature Review, Frost & Sullivan analysis

Overview of Psoriatic Arthritis (PsA)

- PsA occurs in some patients with psoriasis. If affected, joints of these patients would become swollen, stiff and painful. It is a long-term condition that could progressively worsen, that could eventually lead to permanently damaged or deformed joints where surgeries might be needed. Therefore, early diagnosis and treatment of psoriatic arthritis are demanded, which could effectively prevent or minimize permanent damage to the joints.
- Proinflammatory cytokines are associated with occurrence of psoriatic arthritis. That is, elevated level of proinflammatory cytokines are found in joints of patients with PsA. That makes proinflammatory cytokines potential targets of biologics for the treatment of PsA.

Pathogenesis of psoriatic arthritis



Upregulation of IL-17A gene

Promote production of IL-17A

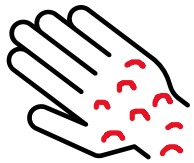
IL-17A IL-17A IL-17A

IL-17A acts on cellular targets within skin, such as neutrophils, to stimulate production of proinflammatory cytokines.

TNF-α TNF-α TNF-α

Excess production of TNF-alpha in the skin or joints

Rapid growth of skin cells and/or damage to joint tissue



Promote skin and joint inflammation

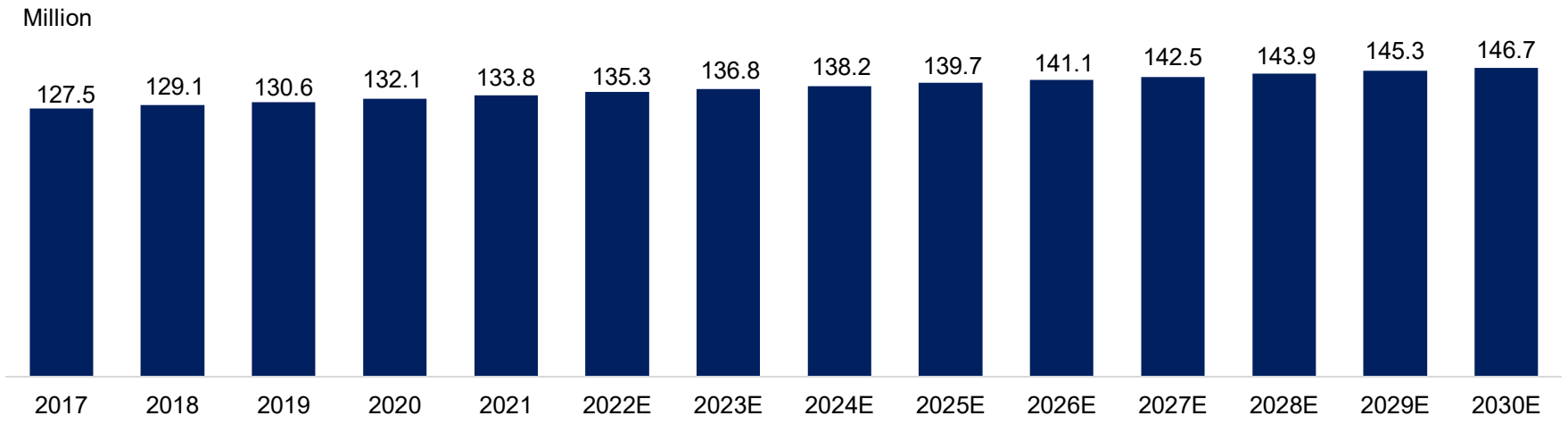
Source: Frost & Sullivan analysis

Global Prevalence of Psoriasis, 2017-2030E

- The number of patients with Psoriasis was 133.8 million in 2021, with a CAGR of 1.2% during 2017 and 2021. This number is expected to rise and approach 139.7 million in 2025 and 146.7 million in 2030, respectively.

Global Prevalence of Psoriasis, 2017-2030E

Period	CAGR
2017-2021	1.2%
2021-2025E	1.1%
2025E-2030E	1.0%



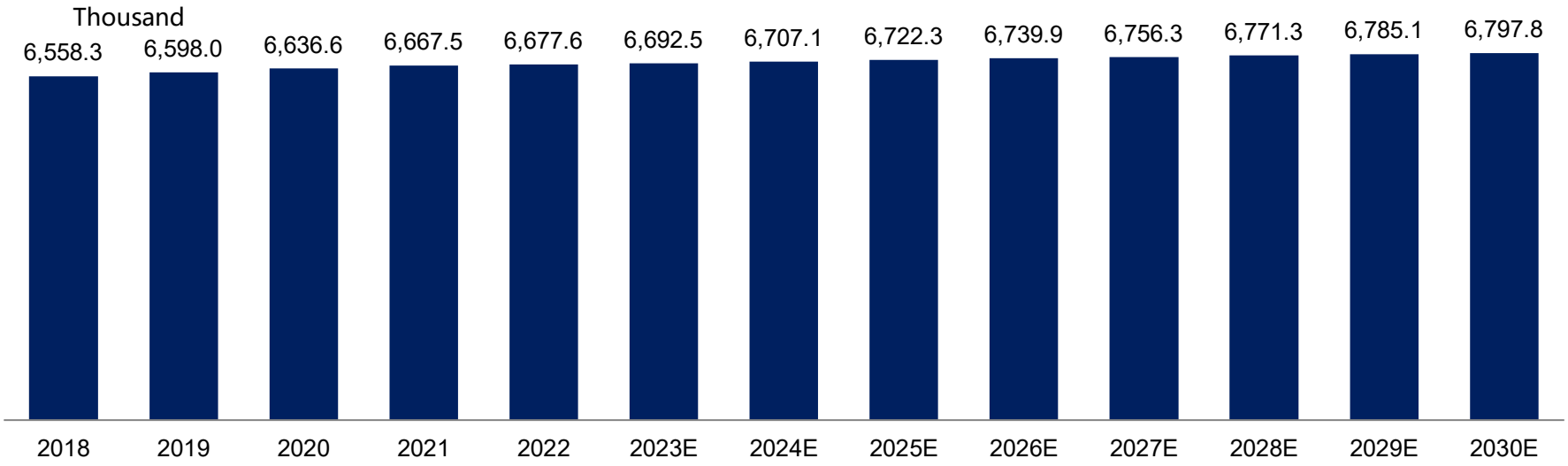
Source: Literature review, Frost & Sullivan analysis

Prevalence of Psoriasis in China，2018-2030E

- According to epidemiology studies, the prevalence of Psoriasis in China had reached 6,677.6 thousand in 2022, with a CAGR of 0.5% from 2018 to 2022. The number of patients is expected to reach 6,797.8 thousand in 2030. 20% to 30% of patients have moderate-to-severe disease.

Prevalence of Psoriasis in China，2018-2030E

Period	CAGR
2018-2022	0.5%
2022-2025E	0.2%
2025E-2030E	0.2%



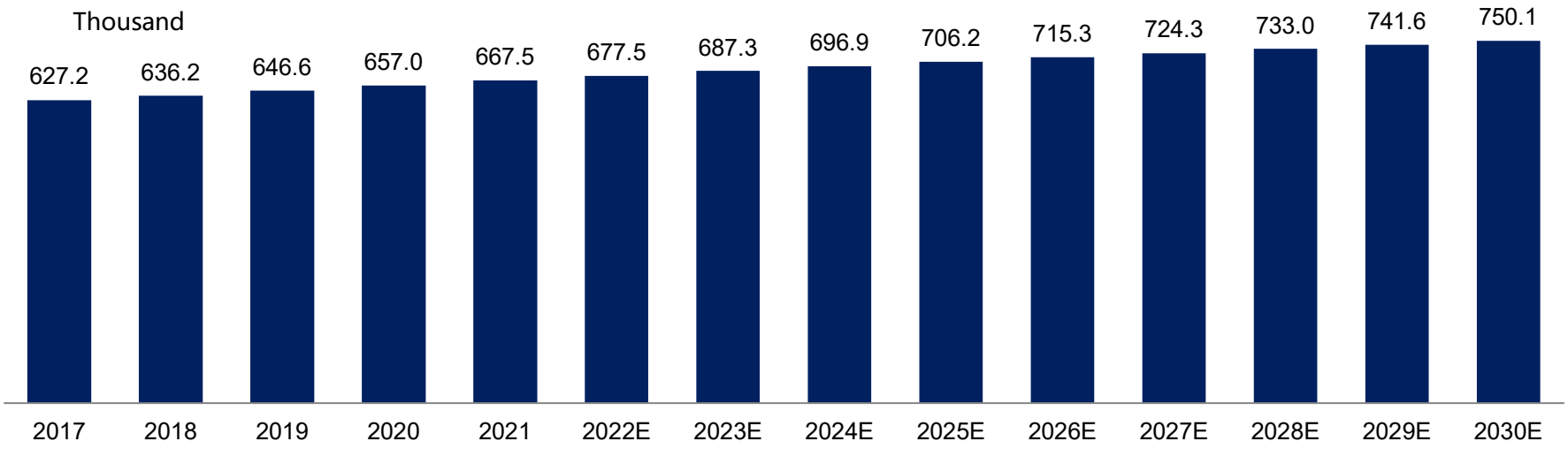
Source: Frost & Sullivan analysis

Prevalence of PsA in China，2017-2030E

- According to epidemiology studies, the prevalence of PsA in China had reached 667.5 thousand in 2021, with a CAGR of 1.6% from 2017 to 2021. The number of patients is expected to reach 750.1 thousand in 2030.

Prevalence of PsA in China，2017-2030E

Period	CAGR
2017-2021	1.6%
2021-2025E	1.4%
2025E-2030E	1.2%



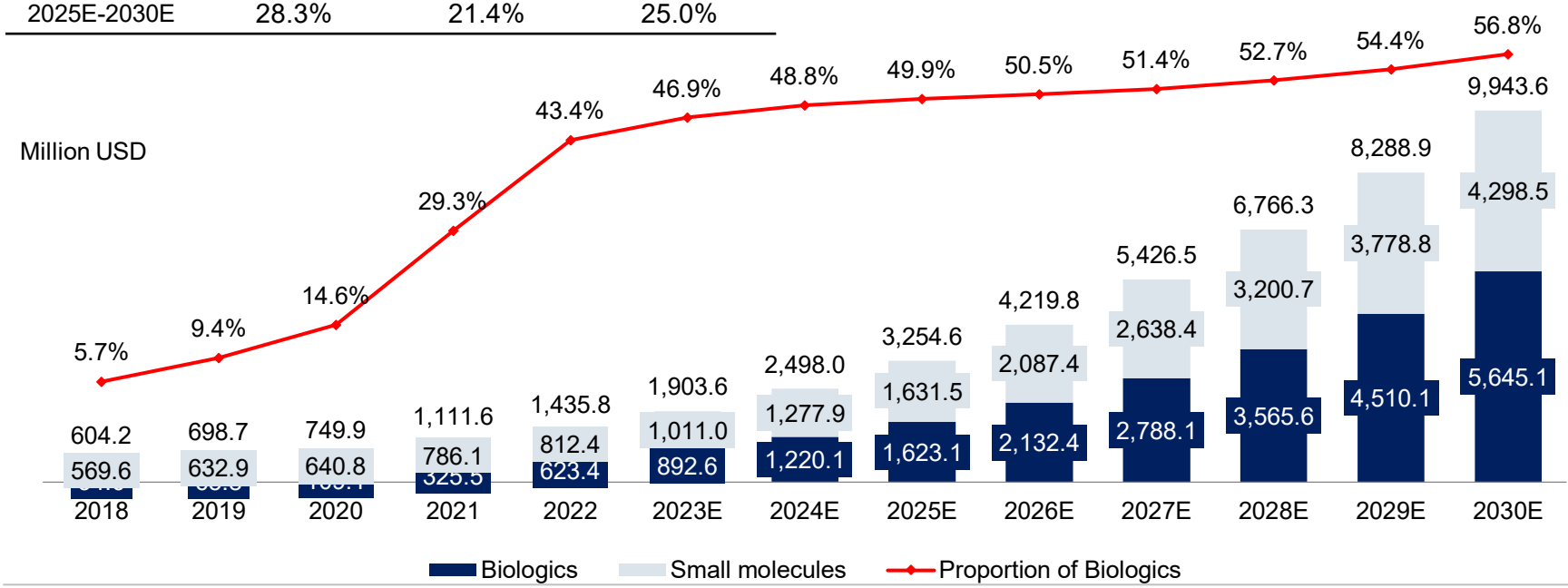
Source: Frost & Sullivan analysis

Psoriasis Drugs Market in China, 2018-2030E

- In China, Psoriasis Drugs Market reached USD 1,435.8 million in 2022 and is expected to increase to USD 1,631.5 million by 2025 at a CAGR of 31.4%. Psoriasis Drugs Market is projected to reach USD 9,943.6 billion by 2030 at a CAGR of 25.0% after 2025. Psoriasis biologics market is projected to reach USD 1,623.1 million in 2025 with a CAGR of 37.6% from 2022 to 2025.

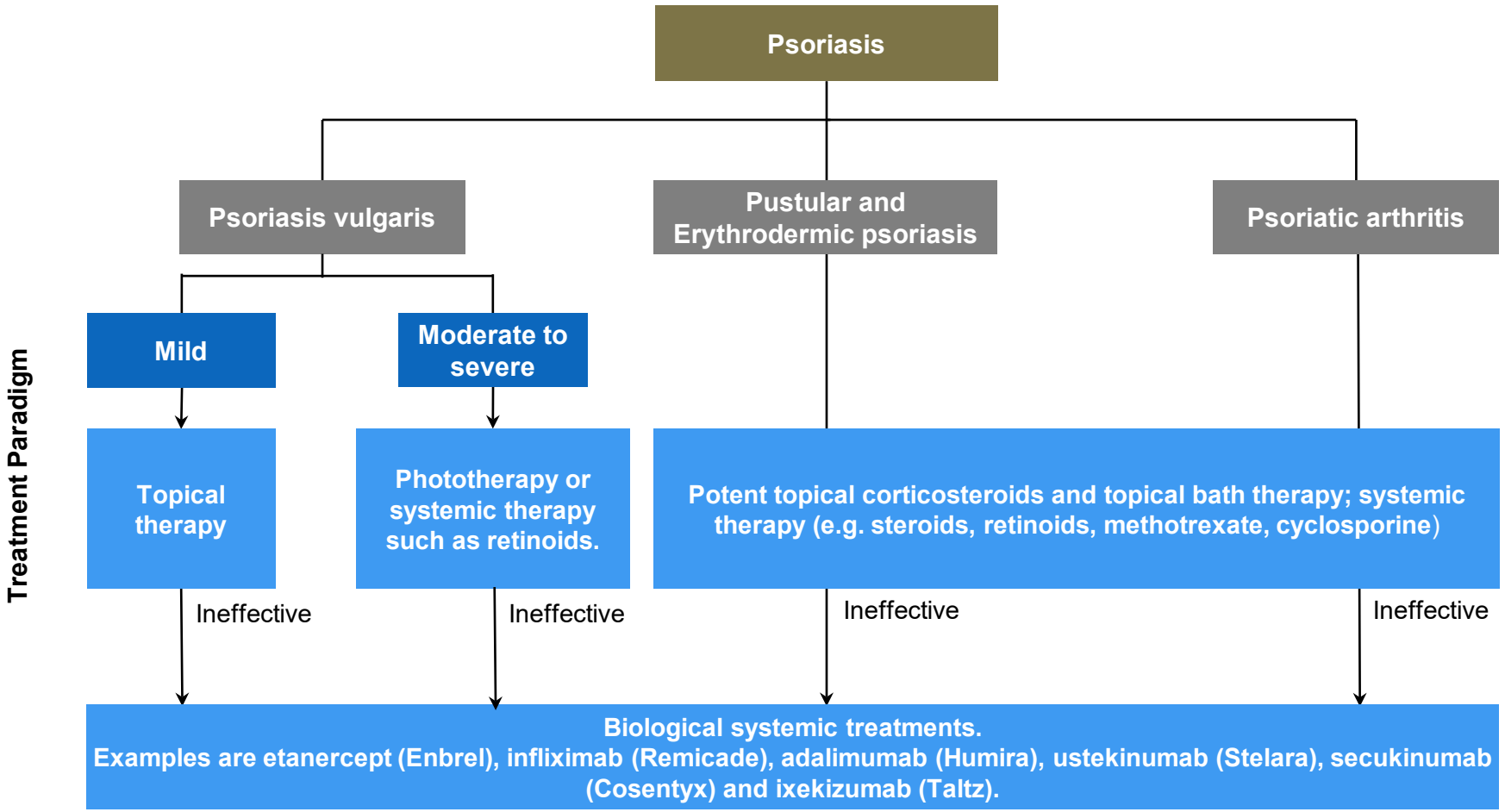
Psoriasis Drugs Market in China, 2018-2030E

Period	Biologics	Small Molecules	Total Market
2018-2022	106.0%	9.3%	24.2%
2022-2025E	37.6%	26.2%	31.4%
2025E-2030E	28.3%	21.4%	25.0%



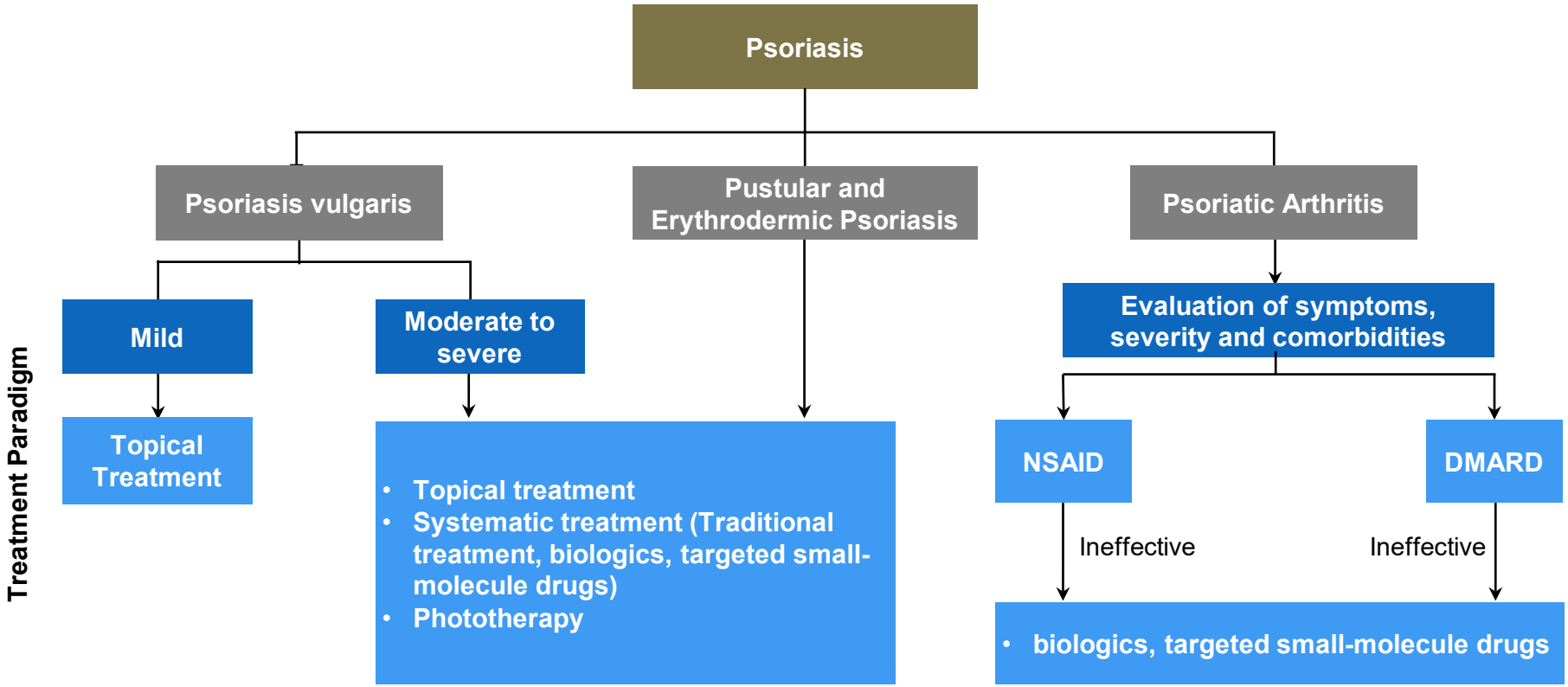
Source: Frost & Sullivan analysis

Treatment Paradigm of Psoriasis in the USA



Source: Mayoclinic Psoriasis, Frost & Sullivan analysis

Treatment Paradigm of Psoriasis in China



NSAID: nonsteroidal anti-inflammatory drug
DMARD: Disease-modifying antirheumatic drugs
Targeted small-molecule drugs: JAK inhibitors, PDE4 inhibitors

Source: Guideline for the diagnosis and treatment of psoriasis in China, Frost & Sullivan analysis

Unmet Medication Demands of Psoriasis

Psoriasis medications are not equally accessible	• Accessibility to skin specialists and psoriasis medications are unequal world-wide. According to the WHO, many patients suffer unnecessary, uncontrolled and irreversible deformities of their body due to lack of early diagnosis and appropriate treatments of psoriasis. This is mainly due to the unequal accessibility to health care, especially in low- to middle-income countries. Therefore, health care and medications that are more affordable and accessible to lower-income countries should be developed.
Available medicine are only to control symptoms	• Medications that are commercially available on the market for clinical use are only to control the symptoms of psoriasis, yet no cure of psoriasis is available. The current benchmark of most clinical trials of medications for psoriasis show a 75% reduction in the PASI score (PASI 75), and PASI 75 is the FDA-approved criterion for efficacy of new psoriasis treatments. Therefore, a psoriasis medication that would result in a complete cure of psoriasis is still to be sought.
Side effects are resulted by currently available medications	• Many side effects are likely to be resulted upon ingestion of currently available medications for psoriasis. That are, hepatotoxicity and nephrotoxicity could be resulted by ingesting methotrexate or cyclosporine, teratogenicity could be resulted upon consumption of oral retinoids. Therefore, a new medication that could result in potent effect on treating psoriasis without causing undesired side effects is at demand.

Source: Frost & Sullivan analysis

Competitive Landscape of Biologics in Psoriasis Treatment in China - I

Marketed Targeted Biologics for Psoriasis in China

Target	Brand Name	INN	Company	Indication	NMPA Approval Time
IL-23	Tremfya®	Guselkumab	Janssen (JNJ)	Plaque psoriasis	2019-12-31
	益路取®	Tildrakizumab-asmn	Sun Pharma; Kangzhe Biotech	Plaque psoriasis	2023-05-26
IL-17A	Cosentyx®	Secukinumab	Novartis	Plaque psoriasis	2019-03-28
	TALTZ®	Ixekizumab	Eli Lilly	Plaque psoriasis	2019-09-03
IL-17RA	LUMICEF®	Brodalumab	Kyowa Kirin	Plaque psoriasis, psoriatic arthritis	2020-06-17
IL-12, IL-23	Stelara®	Ustekinumab	Janssen (JNJ)	Plaque psoriasis	2017-11-07
IL-8	恩博克®	Anti interleukin-8 humanized monoclonal antibody	ASIA SPACE	Psoriasis	2003-12-15
IL-36R	Spevigo®	Spesolimab	Boehringer Ingelheim	Generalized pustular psoriasis	2022-12-13
TNF-α, TNF-β	YISAIPU®	Recombinant Human Tumor Necrosis Factor-α ReceptorⅡ:IgG Fc Fusion Protein	Sunshine Guojian	Plaque psoriasis	2005-01-01
	安佰诺®	Recombinant Human Tumor Necrosis Factor-α ReceptorⅡ:IgG Fc Fusion Protein	Hisun	Plaque psoriasis	2015-04-09
TNF-α	HUMIRA®	Adalimumab	Abbvie	Plaque psoriasis	2017-05-19
	Remicade®	Infliximab	Janssen (JNJ)	Plaque psoriasis	2018-12-04
	QLETLI®	Adalimumab-BAT1406	BIO-THERA	Psoriasis	2019-11-13
	安健宁®	Adalimumab-HS016	Hisun	Plaque psoriasis	2019-12-11
	苏立信®	Adalimumab-IBI303	INNOVENT	Psoriasis	2020-09-02
	汉达远®	Adalimumab-HLX03	Henlius	Psoriasis	2020-12-02
	类停®	Infliximab-CMAB008	MABTECH	Plaque psoriasis	2021-07-12
	安佰特®	Infliximab-HS626	Hisun	Psoriasis	2021-09-24
	泰博维®	Adalimumab-TQZ2301	Chia Tai-tianqing	Psoriasis	2022-01-18
	佳佑健®	Infliximab-GB242	Yuxi Genor Biotechnology	Psoriasis	2022-02-23
	君迈康®	Adalimumab-UBP1211	Junshi Pharma	Psoriasis	2022-03-01

*This table was last updated on Mar 2nd, 2024

Source: NMPA, Frost & Sullivan analysis

Competitive Landscape of Biologics in Psoriasis Treatment in China - II

Clinical trial status

Biologic Pipeline for Psoriasis Treatment in China

Target	Drug Code	Company	Indication	Status	First Posted Date
IL-23	IBI112	INNOVENT	Plaque psoriasis	Phase Ⅲ	2022-12-26
	QX004N	Qyuns	Psoriasis	Phase Ⅱ	2023-01-06
	Risankizumab	Boehringer Ingelheim	Plaque psoriasis, psoriatic arthritis	Phase Ⅰ	2019-07-18
	NBL-012	NovaRock	Psoriasis	Phase Ⅰ	2021-06-03
IL-17A	GR1501	Genrix Bio	Plaque psoriasis	BLA	2023-03-25
	SHR-1314	Henrui	Plaque psoriasis	BLA	2023-04-27
	JS005	Junshi	Plaque psoriasis	Phase Ⅲ	2023-07-12
	Secukinumab-BAT2306	Bio-Thera	Plaque psoriasis	Phase Ⅲ	2022-07-25
	SSGJ-608	Sunshine Guojian	Plaque psoriasis	Phase Ⅲ	2022-11-10
	AK111	Akeso	Plaque psoriasis	Phase Ⅲ	2023-02-15
	HB0017	Huaota Biopharm; Huabo Bio	Plaque psoriasis	Phase Ⅲ	2024-02-26
	SYS6012	CSPC	Plaque psoriasis	Phase Ⅰ	2023-12-05
	BR201	BioRay	Plaque psoriasis	Phase Ⅰ	2023-11-16
	Netakimab	BIOCAD	Plaque psoriasis	Phase Ⅰ	2022-10-19
	Secukinumab-CMAB015	Mabpharm	Plaque psoriasis	Phase Ⅰ	2023-01-18
	NVS451	National Vaccine & Serum Institute	Plaque psoriasis	Phase Ⅰ	2023-05-08
	FTC001/CNTO6785	Shandong Fontacea	Plaque psoriasis	Phase Ⅰ	2023-06-26
IL-17A, IL-17F	Bimekizumab	UCB Pharma	Plaque psoriasis	BLA	2023-07-20
	LZM012	LIVZON	Plaque psoriasis	Phase Ⅲ	2023-06-27
IL-17	SCT650C	SinoCelltech	Plaque psoriasis	Phase Ⅰ/Ⅱ	2024-02-22

*This table was last updated on Mar 2nd, 2024

Source: CDE, Frost & Sullivan analysis

Competitive Landscape of Biologics in Psoriasis Treatment in China - III

Clinical trial status

Biologic Pipeline for Psoriasis Treatment in China

Target	Drug Code	Company	Indication	Status	First Posted Date
IL-12, IL-23	Ustekinumab-QX001S	Qyuns	Plaque psoriasis	BLA	2023-08-12
	Ustekinumab-BAT2206	Baiaotai	Plaque psoriasis, psoriatic arthritis	Phase Ⅲ	2021-06-25
	AK101	Akeso	Plaque psoriasis	BLA	2023-08-23
	Ustekinumab-SYSA1902	CSCP	Plaque psoriasis	Phase Ⅲ	2023-01-29
IL-36R	Imsidolimab	AnaptysBio	Generalized pustular psoriasis	Phase Ⅲ	2023-03-09
	TQH2929	Chiatai Tianqing	Psoriasis	Phase Ⅰ	2023-11-02
	HB0034	Huaota Biopharm; Huabo Bio	Generalized pustular psoriasis	Phase Ⅱ	2024-02-18
TNF-α	Adalimumab-SCT630	SinoCelltech	Plaque psoriasis	BLA	2021-12-16
	Adalimumab-DB101	Tong Hua Dong Bao Group	Plaque psoriasis	Phase Ⅲ	2019-02-26
	Adalimumab-HL01	Hualan Genetic Engineering	Psoriasis	Phase Ⅲ	2020-02-07
	Adalimumab-WHSW	Wuhan Biological Products Research	Plaque psoriasis	Phase Ⅲ*	2020-11-03
	Golimumab-BAT2506	Bio-Thera	Psoriatic arthritis	Phase Ⅲ	2021-02-18
	Adalimumab-HOT-3010	Huaota Biopharm	Plaque psoriasis	Phase Ⅲ	2021-07-30
	Adalimumab-K3	Lvzhu	Plaque psoriasis	Phase Ⅰ	2018-11-13
	Adalimumab-MG011	NCPC Genetech Biology	Psoriasis	Phase Ⅰ	2020-01-15

*This table was last updated on Mar 2nd , 2024

Wuhan Biologics has submitted BLA application for Adalimumab-WHSW on 2023-12-19, but detailed indication for this application was not disclosed

Source: CDE, Frost & Sullivan analysis

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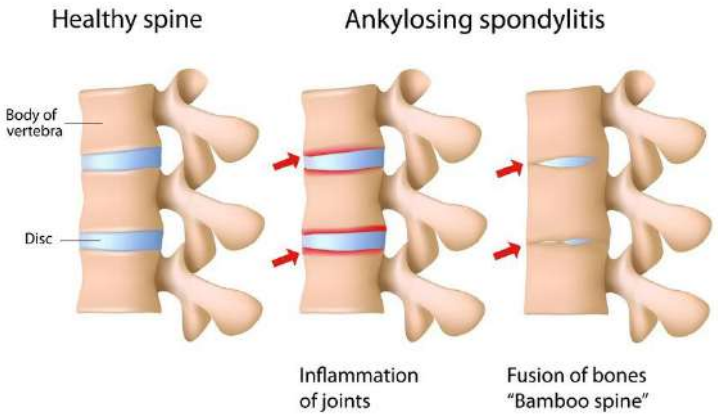
Overview of Ankylosing Spondylitis (AS)

- Ankylosing spondylitis is a type of arthritis that causes inflammation in certain parts of the spine. Inflammatory responses that happen in the joints and tissues of the spine can cause stiffness over time, leading to a rigid spine that is difficult to bend.
- Although the cause of ankylosing spondylitis is unclear, it is speculated to be a combination of genetic and environmental factors. More than 90% of patients have a specific human leukocyte antigen called HLA-B27 antigen.

Ankylosing Spondylitis



Risk Factors

- **Genetic** (HLA-B27 gene)
- **Age and Sex** (Affects more men, occurs in early adulthood)
- **Environmental** (Smoking, Stress, etc)
- **Inflammation & Ossification**

Signs and Symptoms

- **Joints:** back joint dysfunction or stiffness
- **Eyes:** inflammation of the eye's middle layer or redness
- **Visual:** blurred vision or sensitivity to light
- **Other affected areas:** bone tissue formation, fatigue, hunched back, inflamed tendons, inflammatory bowel disease, physical deformity,

Complication

- **Restricted lung capacity and function**
- **Reduced flexibility**
- **Eye inflammation:** rapid-onset eye pain, sensitivity to light, and blurred vision
- **Osteoporosis**
- **Gastrointestinal disorders:** stomach ulcers, diarrhea, and problems digesting
- **Heart disease:** aortitis, aortic valve disease, and conduction problems

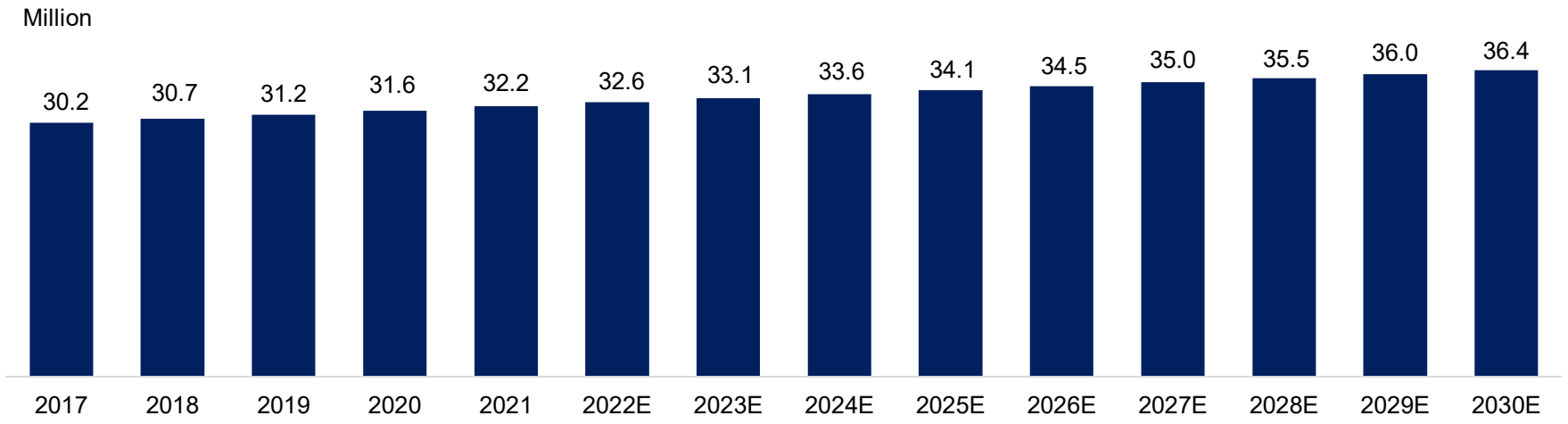
Source: Literature Review, Frost & Sullivan analysis

Global Prevalence of Ankylosing Spondylitis , 2017-2030E

- The number of patients with AS was 32.2 million in 2021, with a CAGR of 1.6% during 2017 and 2021. This number is expected to rise and approach 34.1 million in 2025 and 36.4 million in 2030, respectively.

Global Prevalence of Ankylosing Spondylitis , 2017-2030E

Period	CAGR
2017-2021	1.6%
2021-2025E	1.5%
2025E-2030E	1.3%



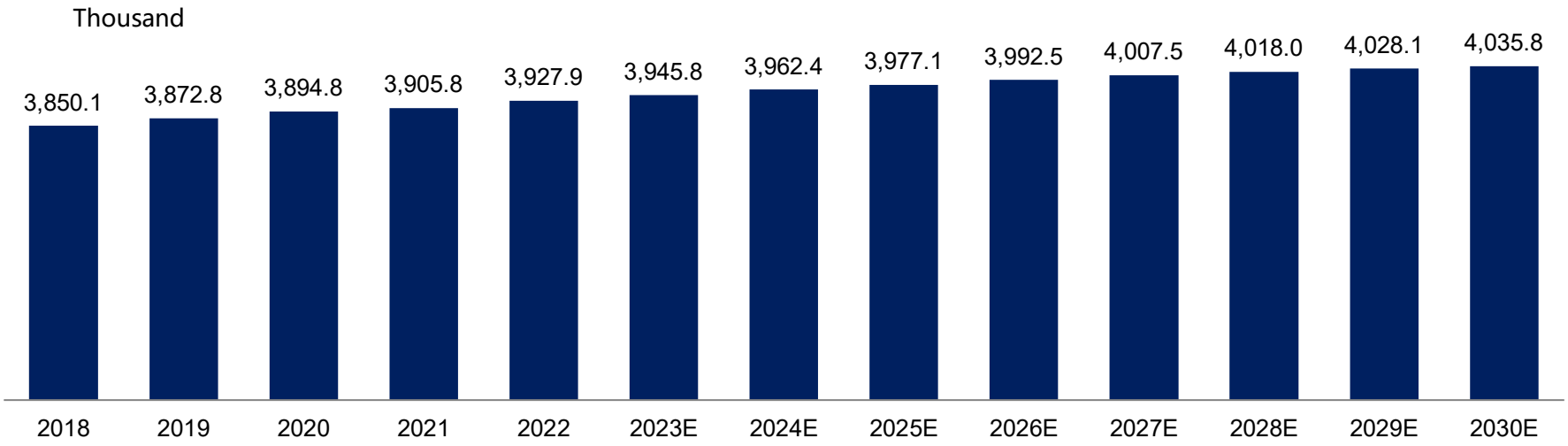
Source: Literature review, Frost & Sullivan analysis

Prevalence of Ankylosing Spondylitis in China，2018-2030E

- According to epidemiology studies, the prevalence of Ankylosing spondylitis in China had reached 3,927.9 thousand in 2022, with a CAGR of 0.5% from 2018 to 2021. The number of patients is expected to reach 4,035.8 thousand in 2030.

Prevalence of Ankylosing Spondylitis in China，2018-2030E

Period	CAGR
2018-2022	0.5%
2022-2025E	0.4%
2025E-2030E	0.3%



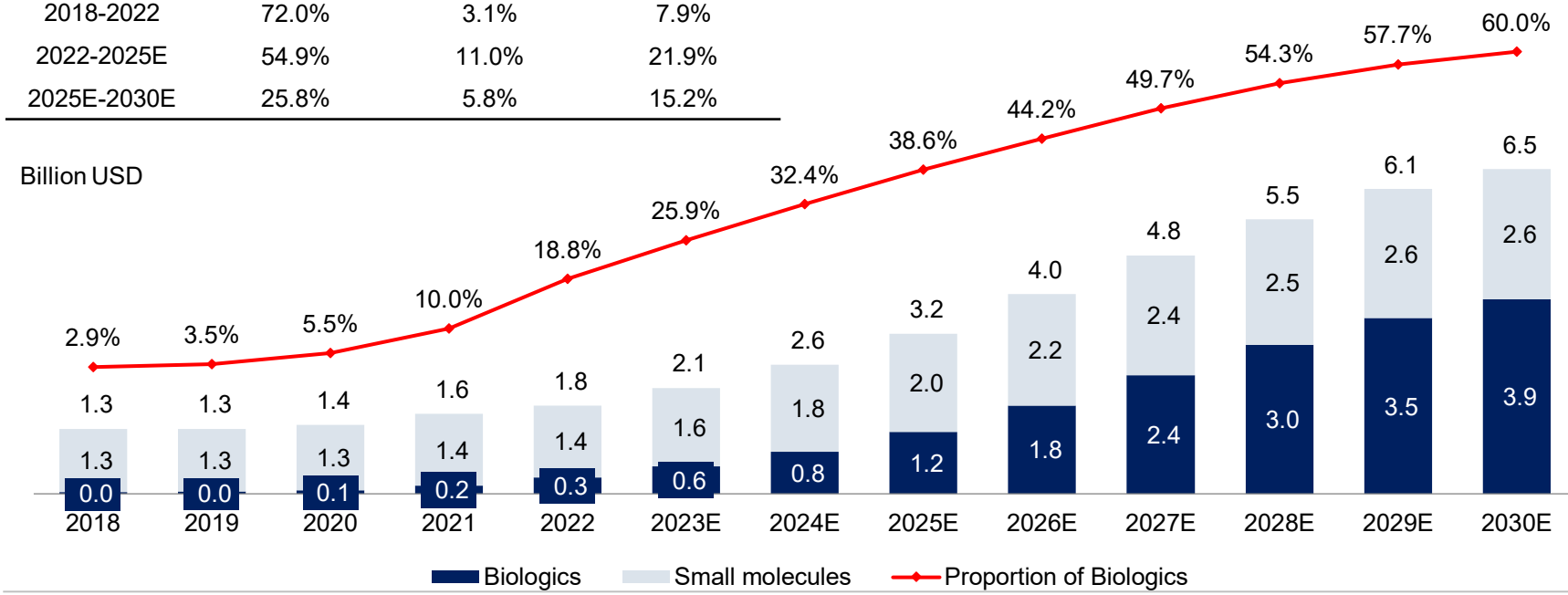
Source: Frost & Sullivan analysis

AS Drugs Market in China, 2018-2030E

- In China, AS Drugs Market reached USD 1.8 billion in 2022 and is expected to increase to USD 3.2 billion by 2025 at a CAGR of 23.6%. AS Drugs Market is projected to reach USD 6.5 billion by 2030 at a CAGR of 15.2% after 2025. AS biologics market is projected to reach USD 1.2 billion in 2025 with a CAGR of 54.9% from 2022 to 2025. AS biologics market reached USD 0.3 billion in 2022. The growth is partially driven by the increasing number of available drugs, especially biologic drugs, indicated for AS in China.

AS Drugs Market in China, 2018-2030E

Period	Biologics	Small Molecules	Total Market
2018-2022	72.0%	3.1%	7.9%
2022-2025E	54.9%	11.0%	21.9%
2025E-2030E	25.8%	5.8%	15.2%



Source: Frost & Sullivan analysis

Treatment Diagram of Ankylosing Spondylitis in China

- The goal of most treatments is to relieve pain and stiffness, control or reduce inflammation, prevent complications, prevent further joint damage, maintenance of function, and improve the quality of life.
- Non-steroidal anti-inflammatory drugs (NSAID) are recommended as the first-line treatment and TNF inhibitors are the second-line treatment. NSAID therapy can quickly improve patients' lower back pain and stiffness, as well as reduce joint swelling and pain. However, NSAID therapy may lead to side effects such as nausea, allergy, and high blood pressure. TNF-α inhibitors can rapidly reduce disease activity and are shown in randomized trials to provide substantial improvements in function. The long-term benefit of TNF-α inhibitor therapy appears to be durable.

	NSAIDs Therapy	Traditional DMARDs Therapy	Glucocorticoid Therapy	Biologics Therapy
Drugs	Traditional NSAIDs	Sulfasalazine	Glucocorticoid	TFNi: Etanercept; Infliximab; Adalimumab
Pharmaco-logy	Quickly improve patients' lower back pain and stiffness, reduce joint swelling and pain	Relief joint pain, swelling and stiffness; Reduce serum IgA levels; Relief peripheral arthritis symptoms	Anti-inflammatory; Anti-allergic and immunosuppressive; Inhibit inflammatory mediators, like TNF-α	Support the immune system to block TNF and reduce inflammation caused by too much TNF
Dosage	The same NSAIDs should be used for at least 2 weeks; change to another NSAIDs if ineffective after 2-4 weeks	This medicine takes effect slowly; increase 0.25g per week from 2.0g and use for 4-6 weeks, or even 1-3 years	Internal injection in the joint cavity; oral and intravenous application are not recommended; apply less than 2-3 times a year	The TNF-α inhibitor treatment is recommended for 6-12 weeks, or even 2 years. Change to another inhibitor if ineffective
Side Effects	Stomach pain; heartburn; nausea; allergy; high blood pressure, etc.	Digestive symptoms; rash; blood Cell reduction; headache; dizziness, etc.	Long-term large-dose use can cause osteoporosis and muscular atrophy, etc.	Nausea; headache; itchiness; dizziness; difficulty breathing; chest pain, etc.

Note: DMARDs (disease-modifying anti-rheumatic drugs) include methotrexate, leflunomide, sulfasalazine, hydroxychloroquine, azathioprine, cyclophosphamide and so on. NSAIDs (Nonsteroidal Antiinflammatory Drugs) include aspirin, acetaminophen, indomethacin, naproxen, etc.

Source: Diagnosis and treatment of ankylosing Spondylitis in China (2020 ver.)Frost & Sullivan analysis

Unmet Medication Demands of AS

First-line treatment with limited effectiveness

- There is currently no cure for AS. At present, nonsteroidal anti-inflammatory drugs are still used clinically as a first-line treatment plan for ankylosing spondylitis, which relieves symptoms by eliminating inflammation, which can only achieve the purpose of anti-inflammatory and analgesic, and cannot completely block the erosion and destruction of bone. At the same time, nonsteroidal anti-inflammatory drugs are only suitable for early patients, and long-term use of drugs will also cause harm to the gastrointestinal tract, liver and kidney function, and induce a series of complications.

Lack of IL-17A targeted drugs

- Most of the monoclonal antibodies that have been listed so far are drugs that target TNF-α and IL-17A, and the FDA approves two and NMPA approves only one. However, compared to TNF-α, IL-17A is at the end of the cytokine network, and targeting IL-17A can play a more direct role. Moreover, targeting IL-17A may have a low effect on the normal immune response compared to more upstream targets, preserving the immune function associated with normal cytokines while ensuring precise regulation of the pathological process.

No special treatment for juvenile ankylosing spondylitis

- Ankylosing spondylitis can also occur in children under 16 years old, called juvenile-onset AS. Different characteristics were found in JoAS and adult-onset AS (AoAS). Patients with JoAS appear to have more peripheral joint involvement (especially knees and ankles) and more root joint involvement (hips and shoulders); they are more likely to proceed to hip arthroplasty and often initially present with peripheral rather than axial symptoms, while patients with AoAS appear to have more axial symptoms and radiographic disease, particularly in the lumbar spine, and worse axial metrology. Currently, there is no obvious difference in medication between JoAS and AoAS. However, given that the symptoms are different, special treatment for JoAS is needed.

Source: Frost & Sullivan analysis

Global Competitive Landscape of Biologics in AS Treatment - I

FDA Approved Targeted Biologics for AS

Brand Name	INN	Company	Target	FDA Approval Time
Enbrel®	Etanercept	Amgen	TNF-α, TNF-β	2003-07-24
Remicade®	Infliximab	Janssen (JNJ)	TNF-α	2004-12-17
Humira®	Adalimumab	AbbVie	TNF-α	2006-07-31
Simponi®	Golimumab	Centocor	TNF-α	2009-04-24
Cimzia®	Certlizumab pegol	UCB	TNF-α	2013-10-18
Cosentyx®	Secukinumab	Novartis	IL-17A	2016-01-15
Inflectra®	infliximab-dyyb	Celltrion	TNF-α	2016-04-05
Erelzi®	Etanercept-szzs	Sandoz	TNF-α, TNF-β	2016-08-31
Amjevita®	Adalimumab-atto	Amgen	TNF-α	2016-09-23
Renflexis®	Infliximab-abda	Samsung Bioepis	TNF-α	2017-04-24
Cyltezo®	Adalimumab-adbm	Boehringer Ingelheim	TNF-α	2017-08-29
Ixifi®	Infliximab-qbtx	Pfizer	TNF-α	2017-12-12
Hyrimoz®	Adalimumab-adaz	Sandoz	TNF-α	2018-10-31
Eticovo®	Etanercept-ykro	Samsung Bioepis	TNF-α, TNF-β	2019-04-27
Hadlima®	Adalimumab-bwwd	Samsung Bioepis	TNF-α	2019-07-23
Taltz®	Ixekizumab	Eli Lilly	IL-17A	2019-08-26
Abrilada®	Adalimumab-afzb	Pfizer	TNF-α	2019-11-18
Avsola®	Infliximab-axxq	Amgen	TNF-α	2019-12-06
Hulio®	Adalimumab-fkjp	Mylan	TNF-α	2020-07-09
Yusimry®	Adalimumab-aqvh	Coherus	TNF-α	2021-12-21
Simlandi®	adalimumab-ryvk	Alvotech/Teva	TNF-α	2024-02-23

*This table was last updated on Mar 2nd ,2024

Source: FDA, Frost & Sullivan analysis

Competitive Landscape of Biologics in AS Treatment in China - I

Marketed Targeted Biologics for AS in China

Target	Brand Name	INN	Company	NMPA Approval Time
IL-17A	Cosentyx®	Secukinumab	Novartis	2020-04-28
	Taltz®	Ixekizumab	Eli Lilly	2022-07-29
TNF-α	YISAIPU® (Injection)	Recombinant Human Tumor Necrosis Factor-α ReceptorⅡ:IgG Fc Fusion Protein	Sunshine Guojian	2005-01-01
	Enbrel®	Etanercept	Pfizer	2010-02-26
	强克®	Recombinant Human Tumor Necrosis Factor-α ReceptorⅡ:IgG Fc Fusion Protein	Celgen	2011-04-11
	HUMIRA®	Adalimumab	AbbVie	2013-04-11
	安佰诺®	Recombinant Human Tumor Necrosis Factor-α ReceptorⅡ:IgG Fc Fusion Protein	Hisun	2015-04-09
	Simponi®	Golimumab	Janssen (JNJ)	2018-01-04
	Remicade®	Infliximab	Janssen (JNJ)	2018-12-04
	QLETLI®	Adalimumab-BAT1406	Bio-Thera	2019-11-13
	安健宁®	Adalimumab-HS016	Hisun	2019-12-11
	苏立信®	Adalimumab-IB303	INNOVENT	2020-09-02
	汉达远®	Adalimumab-HLX03	Henlius	2020-12-02
	类停®	Infliximab-CMAB008	Hisun	2021-07-12
	安佰特®	Infliximab-HS626	Mabpharm	2021-09-24
	泰博维®	Adalimumab-TQZ2301	Chia Tai-tianqing	2022-01-18
	佳佑健®	Infliximab-GB242	Yuxi Genor Biotechnology	2022-02-23
	君迈康®	Adalimumab-UBP1211	Junshi Pharma	2022-03-01
	安佳润®	Adalimumab-SCT630	SinoCelltech	2023-06-07
	安美诗®	Etanercept-QL0902	QILU	2023-12-19

*This table was last updated on Mar 2nd , 2024

Source: NMPA, Frost & Sullivan analysis

Competitive Landscape of Biologics in AS Treatment in China - II

Clinical trial status

Biologic Pipeline for AS Treatment in China

Target	Drug Code	Company	Status	First Posted Date
IL-17A	QX002N	Qyuns	Phase Ⅲ	2023-08-31
	GR1501（xeligekimab）	GenrixBio	BLA	2024-01-04
	Netakimab	Biocad	Phase Ⅲ	2022-09-30
	AK111	Akeso	Phase Ⅲ	2023-10-08
	SHR-1314（vunakizumab）	Hengrui	BLA	2024-02-08
	JS005	Junshi	Phase Ⅱ	2021-09-30
	HB0017	Huabo	Phase Ⅱ	2023-04-12
	SSGJ-608	SunShine Guojian	Phase Ⅱ	2024-01-29
	Secukinumab-CMAB015	MabPharm	Phase Ⅰ	2023-01-18
IL17A, IL17F	Bimekizumab	UCB	BLA	2023-07-20
	LZM012	LIVZON	Phase Ⅲ	2023-07-28
TNF-α	Adalimumab-HL01	Hualan Genetic Engineering	Phase Ⅲ	2020-02-07
	Adalimumab-BC002	Danhong	Phase Ⅲ	2020-08-10
	Etanercept-BF02	Genekey Biotech	Phase Ⅰ	2016-04-27
	Etanercept-SCB-808	Clover Biopharmaceuticals	Phase Ⅰ	2021-04-19
	Adalimumab-HOT-3010	Huaota Biopharm	Phase Ⅰ	2018-09-21
	Adalimumab-K3	Lvzhu	Phase Ⅰ	2018-11-13
	Adalimumab-WHSW	WIBP	Phase Ⅰ	2019-05-24
	Golimumab-BAT2506	Bio-Thera	Phase Ⅰ	2019-05-29
	Adalimumab-JY026	Eastern Biotech;	Phase Ⅰ	2019-10-29
	Adalimumab-MG011	NCPC Genetech Biology	Phase Ⅰ	2020-01-15
	Adalimumab-CMAB815	Anhui Weiming Damu Biomedical Company	PK study	2021-07-05

*This table was last updated on Mar 2nd , 2024

Wuhan Biologics has submitted BLA application for Adalimumab-WHSW on 2023-12-19, but detailed indication for this application was not disclosed

Source: CDE, Frost & Sullivan analysis

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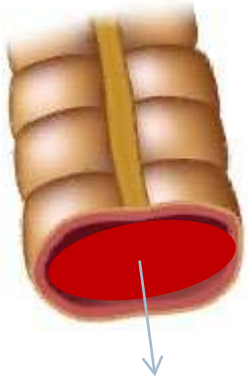
Overview of Ulcerative Colitis (UC)

- Ulcerative colitis (UC), a form of inflammatory bowel disease, is an immune-mediated disorder characterized by chronic mucosal inflammation of the colon and alternating periods of active disease and remission.
- While UC is more common in Western countries, the incidence and prevalence of UC have been steadily rising in China.

Healthy

Ulcerative Colitis



Ulceration within the mucosa

Causes

- Exact cause of UC remains unknown.
- Possible cause: immune system malfunction

Symptoms

- Diarrhea, often with blood or pus
- Abdominal pain and cramping
- Rectal pain
- Rectal bleeding — passing small amount of blood with stool
- Urgency to defecate
- Inability to defecate despite urgency
- Weight loss
- Fatigue
- Fever
- In children, failure to grow

Risk Factors

Diet, Stress;
Heredity;
Age;
Race or ethnicity;
Family history.

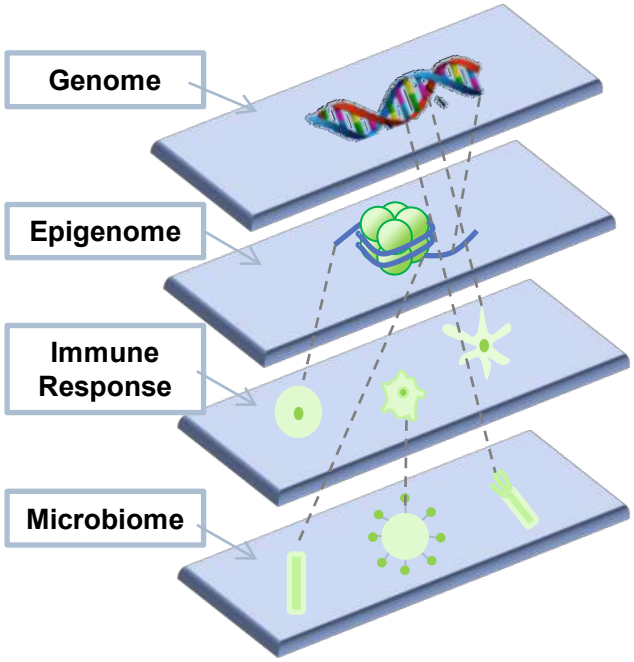
Diagnosis Method

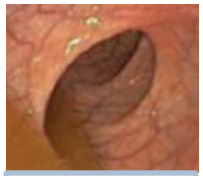
- Direct visualization (sigmoidoscopy or colonoscopy) ;
- Barium enema.

Source: Literature Review, Frost & Sullivan analysis

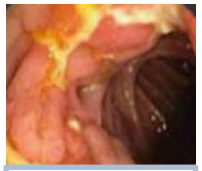
Overview of Crohn's Disease (CD)

- Crohn's disease(CD) is a debilitating and incurable chronic inflammatory bowel disease (IBD). It is characterized by mucosal ulceration and inflammation, which may occur anywhere along the gastrointestinal tract but most commonly affect the distal small intestine.
- Crohn's disease is more common in the western world and has an increasing incidence in the developing world.





Normal



CD

Causes

- Exact causes remain unknown.

Symptoms

- Abdominal;
- Pain;
- Diarrhe;
- Fatigue;
- Weight loss;
- Fever;
- Rectal bleeding and anal fissures;
- Ulcers in the gut;
- Mouth ulcers;
- Altered appetite, etc.

Risk Factors

- Cigarette smoking;
- Age (commonly develops between the ages of 15 and 35);
- Family history (appears to be inherited in many cases).

Diagnosis Method

- Stool and blood tests;
- Biopsy;
- Sigmoidoscopy;
- Colonoscopy;
- Endoscopy;
- CT scan or barium enema X-ray.

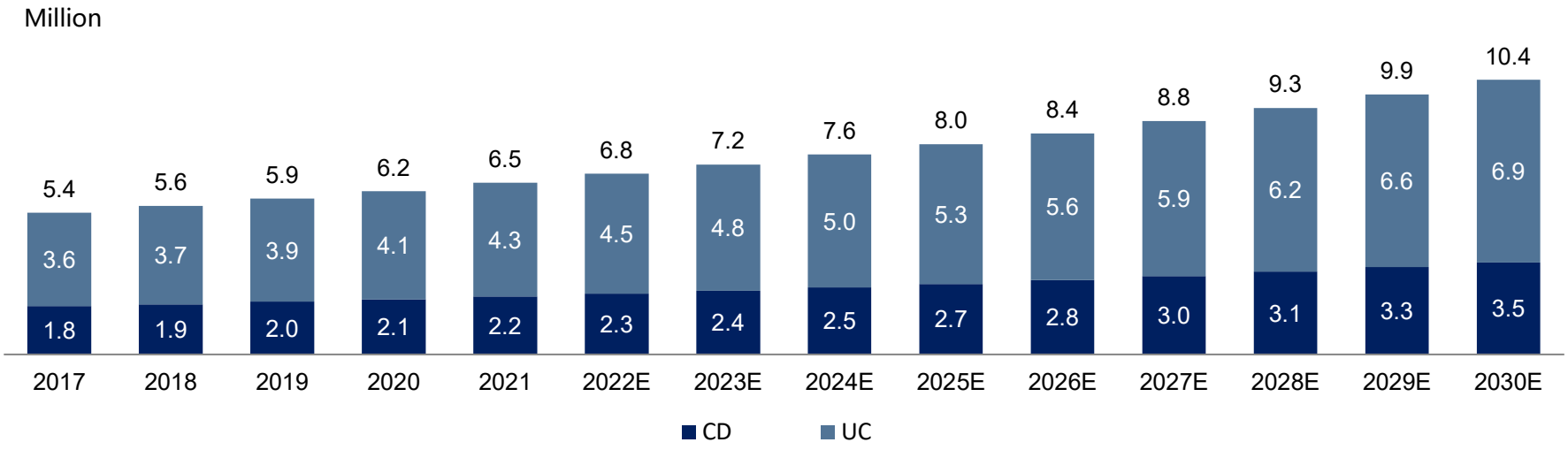
Source: Literature Review, Frost & Sullivan analysis

Global Prevalence of IBD，2017-2030E

- According to epidemiology studies, the global prevalence of IBD had reached 6.5 million in 2021, with a CAGR of 4.9% from 2017 to 2021. The number of patients is expected to reach 10.4 million in 2030.

Global Prevalence of IBD，2017-2030E

Period	CAGR
2017-2021	4.9%
2021-2025E	5.2%
2025E-2030E	5.5%



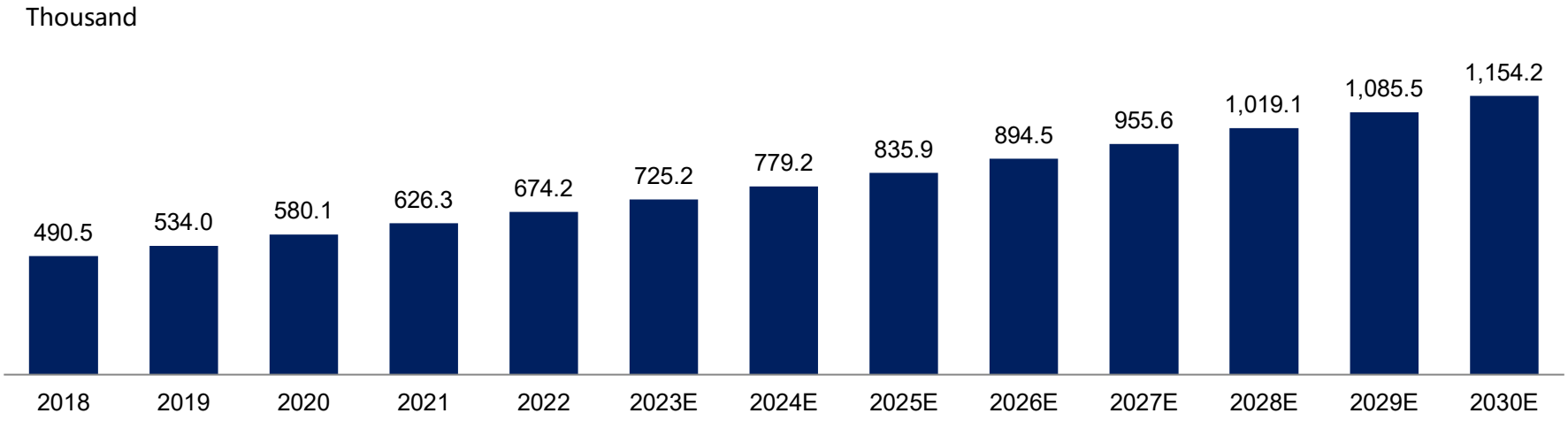
Source: Frost & Sullivan analysis

Prevalence of IBD in China，2018-2030E

- According to epidemiology studies, the prevalence of IBD in China had reached 674.2 thousand in 2022, with a CAGR of 8.3% from 2018 to 2022. The number of patients is expected to reach 1154.2 thousand in 2030, representing a CAGR of 7.0% from 2022 to 2030.

Prevalence of IBD in China，2018-2030E

Period	CAGR
2018-2022	8.3%
2022-2025E	7.4%
2025E-2030E	6.7%



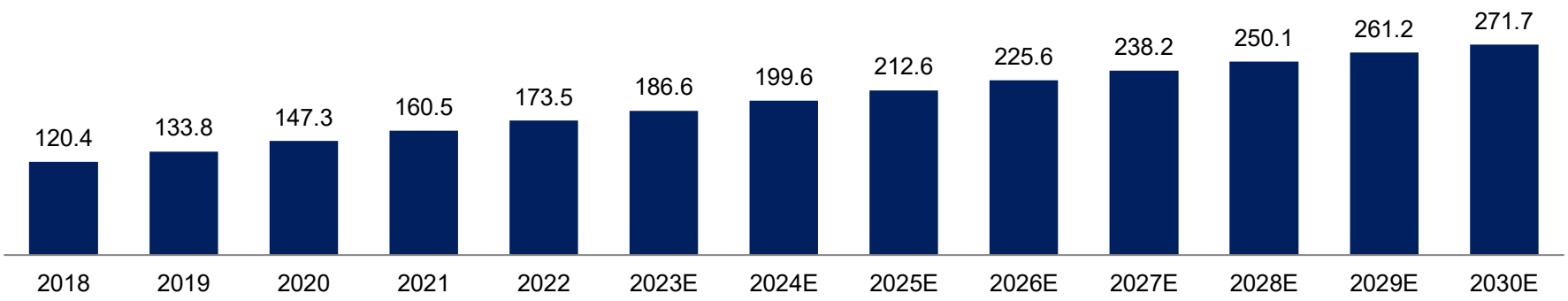
Source: Frost & Sullivan analysis

Prevalence of CD in China，2018-2030E

- According to epidemiology studies, the prevalence of CD in China had reached 173.5 thousand in 2022, with a CAGR of 9.6% from 2018 to 2022. The number of patients is expected to reach 271.7 thousand in 2030, representing a CAGR of 5.8% from 2022 to 2030.

Prevalence of CD in China，2018-2030E

Period	CAGR
2018-2022	9.6%
2022-2025E	7.0%
2025E-2030E	5.0%



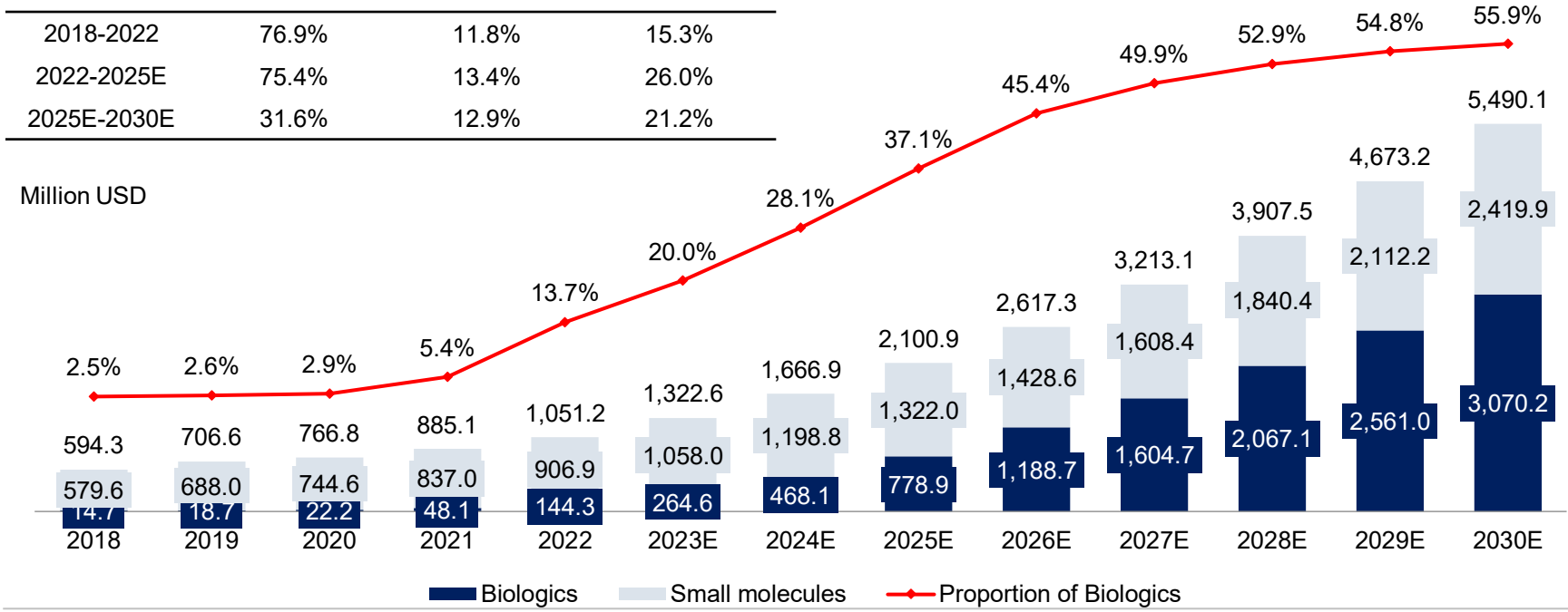
Source: Frost & Sullivan analysis

IBD Drugs Market in China, 2018-2030E

- In China, IBD Drugs Market reached USD 1,051.2 million in 2022 and is expected to increase to USD 2,100.9 million by 2025 at a CAGR of 26.0%. IBD Drugs Market is projected to reach USD 5,490.1 million by 2030 at a CAGR of 21.2% after 2025. IBD biologics market is projected to reach USD 778.9 million in 2025 with a CAGR of 75.4% from 2022 to 2025. IBD biologics market reached USD 144.3 million in 2022. The IBD Drugs market is difficult to split into UC and CD regarding the significantly overlapped therapies. CAGR of the total market from 2022 to 2030 is 23.0%.

IBD Drugs Market in China, 2018-2030E

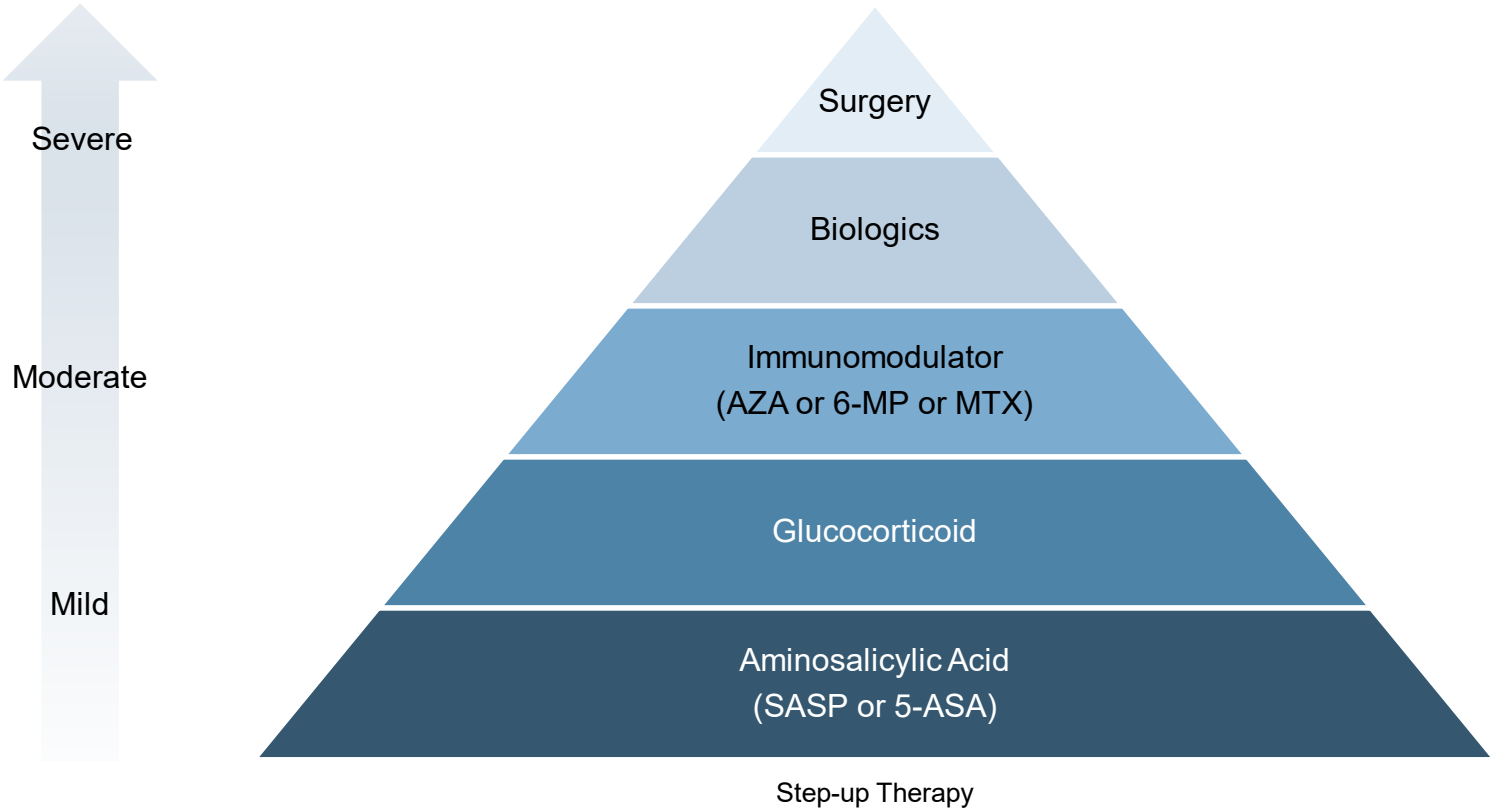
Period	Biologics	Small Molecules	Total Market
2018-2022	76.9%	11.8%	15.3%
2022-2025E	75.4%	13.4%	26.0%
2025E-2030E	31.6%	12.9%	21.2%



Source: Frost & Sullivan analysis

Treatment Diagram of IBD in China

- The goal of inflammatory bowel disease treatment is to reduce the inflammation that triggers signs and symptoms. IBD treatment usually involves either drug therapy or surgery.
- Anti-inflammatory drugs are often the first step in the treatment of inflammatory bowel disease. Immunomodulators such as azathioprine can suppress the immune response to release inflammation-inducing chemicals in the intestinal lining. Biologics works by neutralizing proteins produced by the immune system.



Source:《炎症性肠病诊断与治疗的共识意见(2018·北京)》, Frost & Sullivan analysis

Unmet Medication Demands of IBD

Lack of new treatment options

- The advent of anti-TNF-α agents has dramatically changed the treatment algorithms for IBD, but primarily and more importantly secondary loss of response is often observed. Moreover, TNF-α inhibitors are usually associated with higher risk of serious infections. Currently, TNF-α inhibitor occupies a large proportion of IBD treatment market. Biologics target IL-12/IL-23 and ITGA4/ITGB7 should be paid more attention for their higher efficacy and safety.

Low remission rate of existing drugs

- Despite the current array of treatment options in UC and CD, remission rates in induction trials are still less than 50%, revealing a therapeutic ceiling in the management of both diseases and potential challenges that need to be addressed. Therefore, developing new and more precise drugs is needed.

Lack of drugs for special patient population

- Despite current advances in surgical and medical treatment, currently existing medications do not meet the needs of some special patients. For example, the long-term healing rate of perianal fistulas remains disappointing, with significant recurrence rates, particularly in complex fistulas. Moreover, UC patients with ulcerative proctitis are found to be refractory to standard medical therapies. The elderly patient also needs special medical therapies for the presence of comorbidities, increased and the risk of development of more significant adverse events. Therefore, developing drugs for special patient population is needed.

Source: Frost & Sullivan analysis

Competitive Landscape of biologics in IBD Treatment in China - I

Marketed Targeted Biologics for IBD in China

Target	Brand Name	INN	Company	Indications	NMPA Approval Time
IL-23, IL-12	Stelara®	Ustekinumab	Janssen (JNJ)	CD	2020-03-12
TNF-α	Remicade®	Infliximab	Janssen (JNJ)	CD	2006-05-03
				UC	2018-12-24
	QLETLI®	Adalimumab-BAT1406	Bio-Thera	CD	2020-07-09
	安健宁®	Adalimumab-HS016	Hisun	CD	2020-05-06
	Humira®	Adalimumab	AbbVie	CD	2020-01-13
	苏立信®	Adalimumab-IBI303	Innovent	CD	2020-09-02
	类停®	Infliximab-CMAB008	MabPharm	CD	2021-07-12
				UC	2021-07-12
	安佰特®	Infliximab-HS626	Hisun	CD	2021-09-24
				UC	2021-09-24
	佳佑健®	Infliximab-GB242	Yuxi Genor Biotechnology	CD	2022-02-23
				UC	2022-02-23
	君迈康®	Adalimumab-UBP1211	Junshi Pharma	CD	2022-03-01
	安佳润®	Adalimumab-SCT630	SinoCelltech	CD	2023-06-07
Integrin α4/ Integrin β7	Entyvio®	Vedolizumab	Takeda	CD	2020-03-12
				UC	2020-03-12

*This table was last updated on Mar 2nd , 2024

Source: NMPA, Frost & Sullivan analysis

Competitive Landscape of biologics in IBD Treatment in China - II

Clinical trial status

Biologic Pipeline for IBD Treatment in China

Target	Drug Code	Company	Indications	Status	First Posted Date
IL-23, IL-12	Ustekinumab-BAT2206	Bio-Thera	CD	Phase Ⅰ	2020-05-06
			UC	Phase Ⅰ	2020-05-06
	AK101	Akeso	UC	Phase Ⅰ	2020-08-13
IL-23	Risankizumab	AbbVie	IBD*	BLA	2023-07-06
	LY3074828	Eli Lilly	CD	Phase Ⅲ	2020-04-24
			UC	Phase Ⅲ	2020-01-15
	Guselkumab	Janssen (JNJ)	CD	Phase Ⅲ	2020-06-08
			UC	Phase Ⅲ	2022-12-23
	IBI112	INNOVENT	UC	Phase Ⅱ	2022-04-28
	QX004N	Qyuns	CD	Phase Ⅰ	2022-12-28
TNF-α	Adalimumab-TQZ2301	Chia Tai-tianqing	CD	Phase Ⅰ	2018-11-13
			UC	Phase Ⅰ	2018-11-13
	Adalimumab-HLX03	Henlius	CD	BLA	2024-02-29
TNFSF15	PF-06480605	Pfizer	UC	Phase Ⅱ	2021-03-11
			CD	Phase Ⅰ	2021-11-17
IL6ST	TJ301	IMAB	UC	Phase Ⅱ	2018-08-03
Undisclosed	HZBio2	Grand pharma	CD	Phase Ⅰ	2022-05-16
			UC	Phase Ⅰ	2022-05-16
NA (MSC, mesenchymal stem cells)	TH-SC01	Tuohong Kangheng Pharma	CD	Phase Ⅰ	2024-02-07

*This table was last updated on Mar 2nd , 2024

* AbbVie's Risankizumab has not declared its specific indication for the drugs BLA application

Source: CDE, Frost & Sullivan analysis

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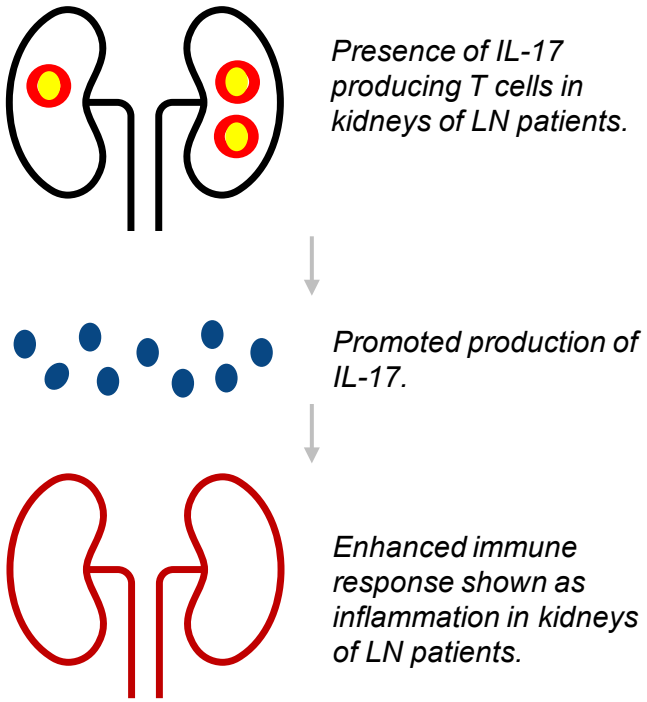
Overview and Classification of Lupus Nephritis (LN)

- LN is a complication of systemic lupus erythematosus, that is, when inflammation occurs specifically in the kidney. LN is a result of autoantibodies affecting and altering structures in the kidney. The clinical manifestations of LN include proteinuria, hematuria, hypertension, swollen body parts, impaired kidney functions, and eventually kidney failure. The occurrence of LN is more common among men than among women.
- Similar to other autoimmune inflammatory diseases, LN is associated with the mutation of genes and the overproduction of proinflammatory substances. IL-17 cytokines produced by Th17 cells are promising targets to treat LN, since these cytokines have receptors expressed in most renal cells, and are involved in inflammatory pathways.
- LN can be classified into six classes based on the pathologies.

Classification of LN

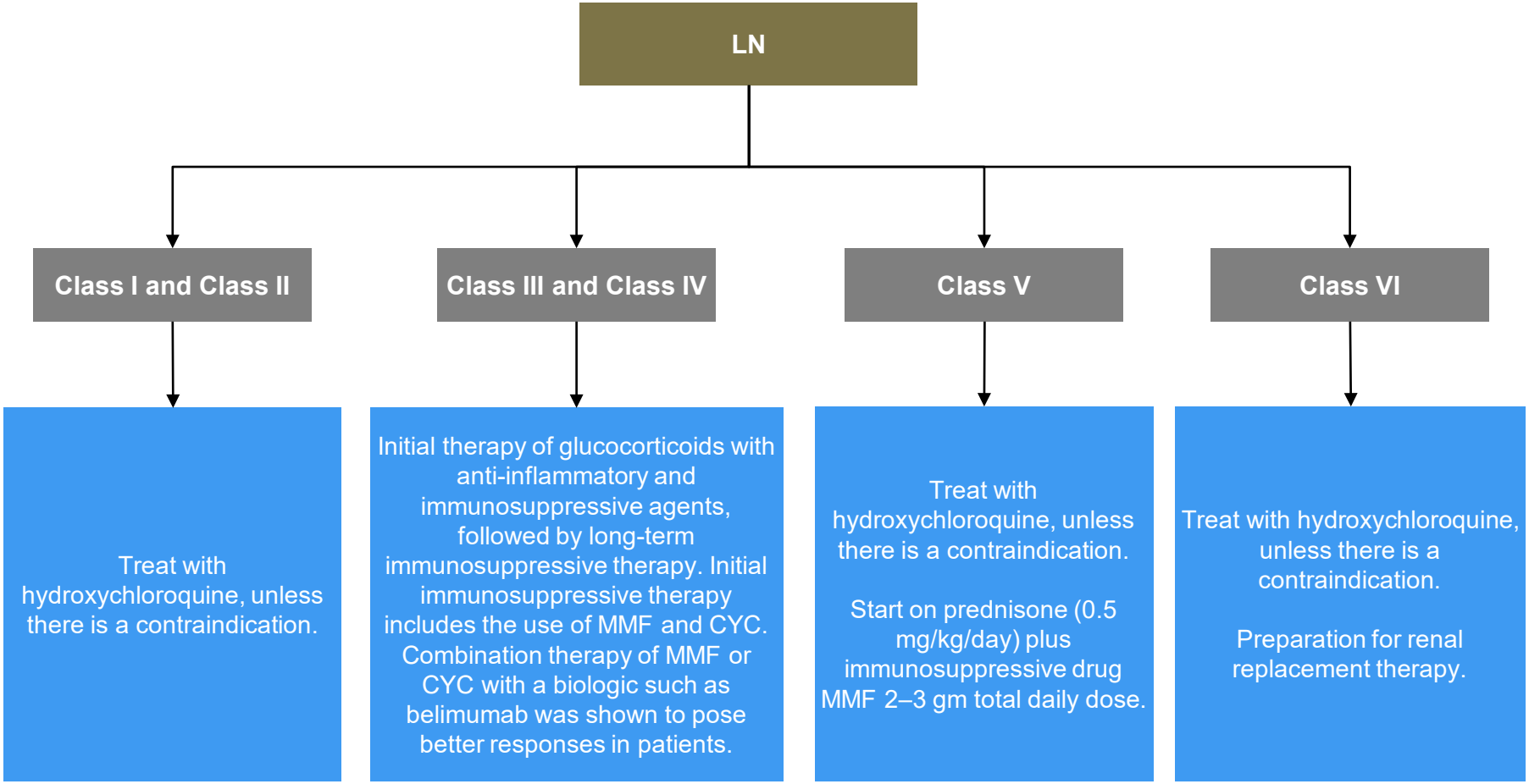
Class	Pathological classification
Class I	Minimal mesangial LN
Class II	Mesangial proliferative LN
Class III	Focal LN
Class IV	Diffuse LN
Class V	Membranous LN
Class VI	Advanced sclerosing LN

Potential pathogenesis of LN associated with IL-17



Source: Literature Review, Frost & Sullivan analysis

Treatment Diagram of LN in the USA



MMF: Mycophenolate mofetil
CYC: cyclophosphamide

Source: Literature Review, Frost & Sullivan analysis

Treatment Diagram of LN in China

Treatment options

Initial treatment

Glucocorticoid

- Usage and dosage depend on LN class, activity and severity.
- Common dosage is 0.5~1.0 mg· kg-1·d-1, and the dosage will be reduced gradually.

Hydroxychloroquine

- Usage and dosage depend on LN class, activity and severity.
- Common dosage is kept below 5 mg·kg-1·d-1

Maintenance treatment

- Class I and Class II:
  - Urinary protein < 0.5 g/24h: exclusive use of glucocorticoids or combination of glucocorticoids and immunosuppressive drugs
- Class III ± Class V and Class IV ± Class V :
  - Glucocorticoids combined with mycophenolate mofetil or glucocorticoids combined with cyclophosphamide
- Class V:
  - Angiotensin-converting enzyme (ACE) inhibitors or Angiotensin receptor blockers (ARB).
- Podocyte injury in LN:
  - Exclusive use of glucocorticoids, use of calcineurin inhibitors could be considered when necessary.
- Thrombotic microangiopathy in LN:
  - Intravenous cyclophosphamide, use of glucocorticoids and immunosuppressive drugs could be considered if needed.

Source:《狼疮肾炎诊疗规范, 2021》, Frost & Sullivan analysis

Unmet Medication Demands of LN

Limited medications are available	• Only belimumab and voclosporin are approved by the FDA for the treatment of LN. Other medications are only able to lessen symptoms and prevent the worsening of LN. More new medications that can treat LN are still in demand.
Lack of consideration for prescription differences	• Patients with different features, such as ethnicity, will show different responses to different medications given at the same dosage. For instance, black and Hispanic patients respond more frequently to MMF than CYC, while these two medications are considered by the American College of Rheumatology and European League Against Rheumatism to have the same selectivity. Besides, patients with different drug metabolisms will require different dosages of the same medication.
Limited efficient medications without side effects	• Current medications for treating LN are mainly based on combinations of non-selective immunosuppressive drugs such as steroids plus CYC or MMF. These treatments often trigger profound side effects such as short-term and long-term toxicities due to their non-specific, anti-proliferative or anti-metabolic features. Therefore, it is necessary to develop new treatments of LN that are more specific and selective with fewer side effects.

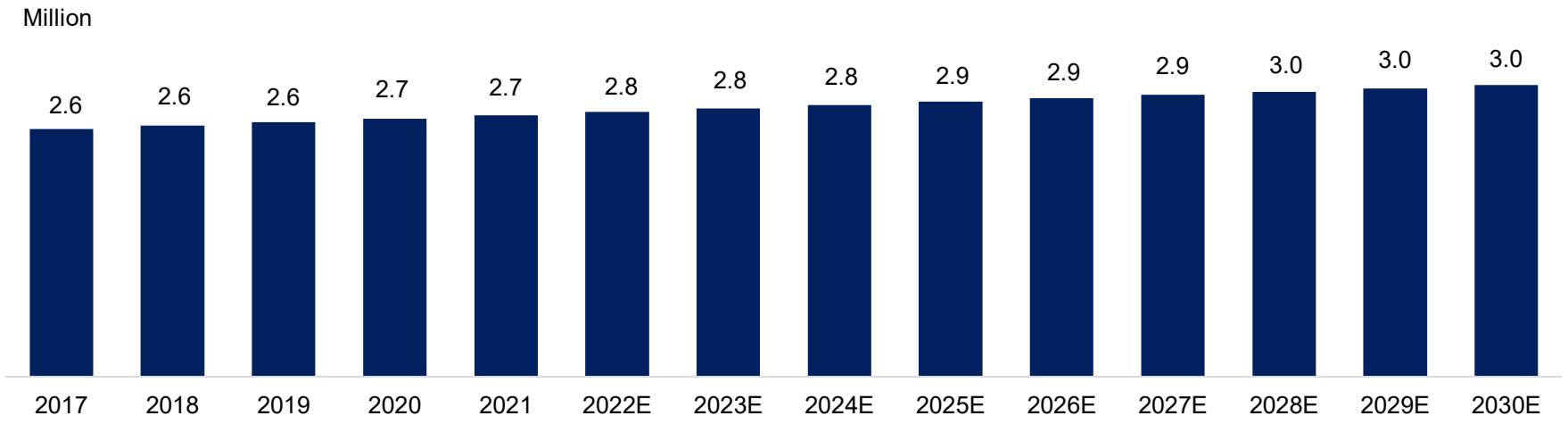
Source: Frost & Sullivan analysis

Global Prevalence of LN, 2017-2030E

- The number of patients with LN was 2.7 million in 2021, with a CAGR of 1.4% during 2017 and 2021. This number is expected to rise and approach 2.9 million in 2025 and 3.0 million in 2030, respectively.

Global Prevalence of LN, 2017-2030E

Period	CAGR
2017-2021	1.4%
2021-2025E	1.3%
2025E-2030E	1.2%



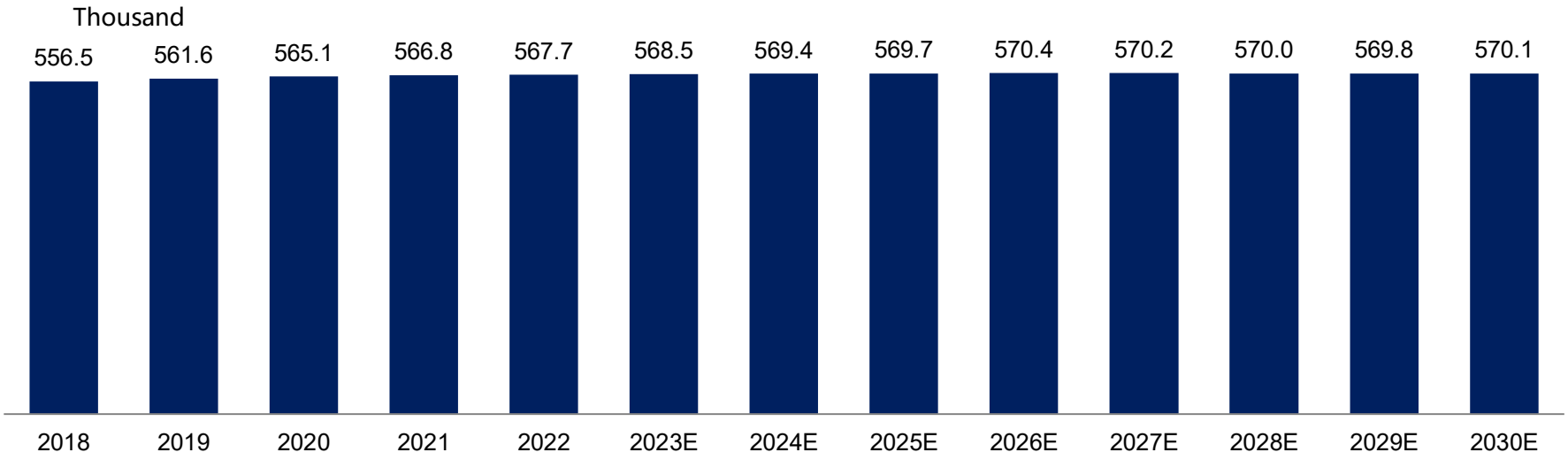
Source: Literature review, Frost & Sullivan analysis

Prevalence of LN in China，2018-2030E

- According to epidemiology studies, the prevalence of LN in China had reached 567.7 thousand in 2022, with a CAGR of 0.5% from 2018 to 2022. The number of patients is expected to reach 570.1 thousand in 2030, with a CAGR of 0.0% from 2022 to 2030.

Prevalence of LN in China，2018-2030E

Period	CAGR
2018-2022	0.5%
2022-2025E	0.1%
2025E-2030E	0.0%



Source: Frost & Sullivan analysis

Global Competitive Landscape of Biologics in LN Treatment

Clinical trial status

FDA Approved Targeted Biologics for LN

Brand Name	INN	Company	Target	FDA Approval Time
Benlysta®	Belimumab	GSK	BAFF	2020-12-17

* First table was last updated on Mar 2nd ,2024

Source: FDA, ClinicalTrials, Frost & Sullivan analysis

Competitive Landscape of Biologics in LN Treatment in China

Clinical trial status

Marketed Targeted Biologics for LN in China

Target	Brand Name	INN	Company	NMPA Approval Time
BAFF	Benlysta®	Belimumab	GSK	2022-02-09

Clinical trials of biologics Pipeline in LN Treatment in China

Target	Drug Code	Company	Status	First Posted Date
BAFF/APRIL	Telitacicept	Remegen	Phase Ⅱ	2022-12-30
IL-17A	Secukinumab	Novartis	Phase Ⅲ	2020-12-08
	SHR-1314	Suncadia Biopharma	Phase Ⅱ	2021-06-08
	GR1501	Genrix Bio	Phase Ⅱ	2023-02-08
IFNAR1	Anifrolumab	AstraZeneca	Phase Ⅲ	2022-06-20
CD80,CD86	BMS-188667	Bristol-Myers	Phase Ⅲ	2015-01-26
CD20	Obinutuzumab	Roche	Phase Ⅲ	2022-01-07
	MIL-62	Mabworks Biotech	Phase Ⅰ/Ⅱ	2021-07-13
BAFFR	VAY736	Novartis	Phase Ⅲ	2022-04-29
CD40	CFZ533	Novartis	Phase Ⅱ	2019-06-13
FcRn	Efgartigimod	Vetter Pharma-Fertigung; Zailab; argenx BV	Phase Ⅱ	2022-12-07

*This table was last updated on Mar 2nd , 2024

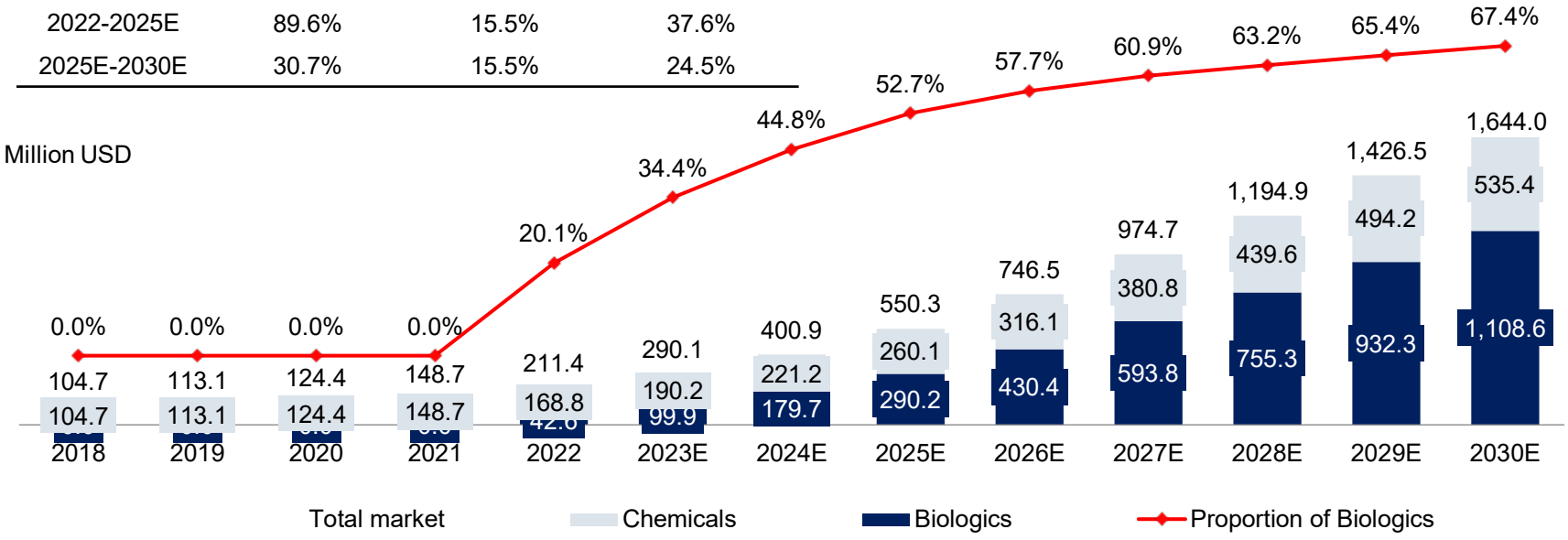
Source: NMPA, CDE, Frost & Sullivan analysis

LN Drugs Market in China, 2018-2030E

- In China, LN Drugs Market reached USD 211.4 million in 2022 and is expected to increase to USD 550.3 million by 2025 at a CAGR of 37.6%. LN Drugs Market is projected to reach USD 1,644.0 million by 2030 at a CAGR of 24.5% after 2025. LN biologics market is projected to reach USD 290.2 million in 2025. LN biologics market is projected to reach USD 1,108.6 million in 2030 with a CAGR of 30.7% from 2025 to 2030.

LN Drugs Market in China, 2018-2030E

Period	Biologics	Chemical	Total Market
2018-2022	-	12.7%	19.2%
2022-2025E	89.6%	15.5%	37.6%
2025E-2030E	30.7%	15.5%	24.5%



Source: Frost & Sullivan analysis

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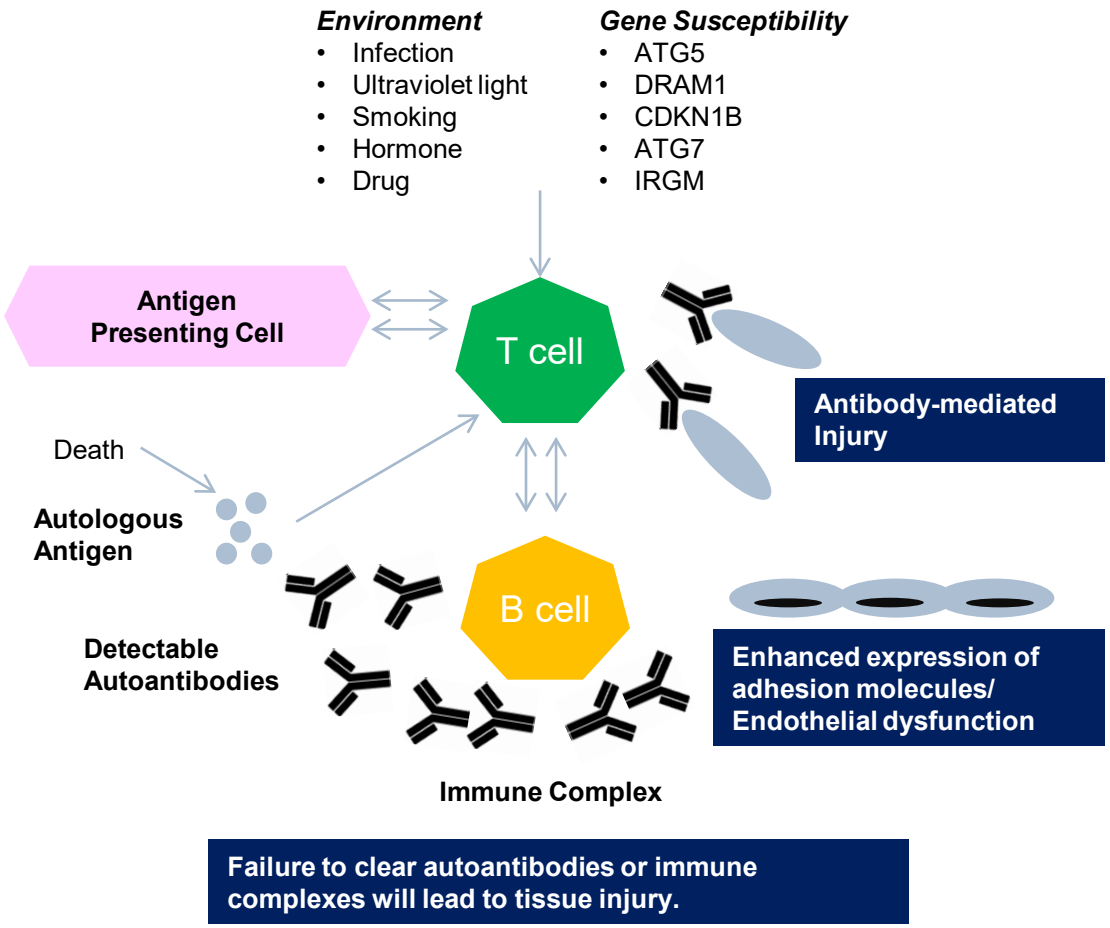
Overview of Systemic Lupus Erythematosus (SLE)

Disease Overview

- Systemic lupus erythematosus (SLE) is an autoimmune disease associated with substantial morbidity and mortality. It is the most common type of lupus, causing widespread inflammation and tissue damage in the affected organs. An autoimmune disease occurs when the body's tissues are attacked by its immune system. Patients with lupus have unusual antibodies in their blood that are targeted against their body tissues. This is a multisystem autoimmune disease that can potentially lead to serious organ complications and even death. Common symptoms of SLE include painful and swollen joints, fever, chest pain, hair loss, mouth ulcers, swollen lymph nodes, feeling tired, and a red rash which is most commonly on the face.
- The cause of SLE is still not clear. It is thought to involve genetics together with environmental factors.
- Common initial symptoms include fever, malaise, joint pains, muscle pains, and fatigue, and the symptoms vary widely and come and go unpredictably with disease development.

Pathogenesis of Systemic Lupus Erythematosus



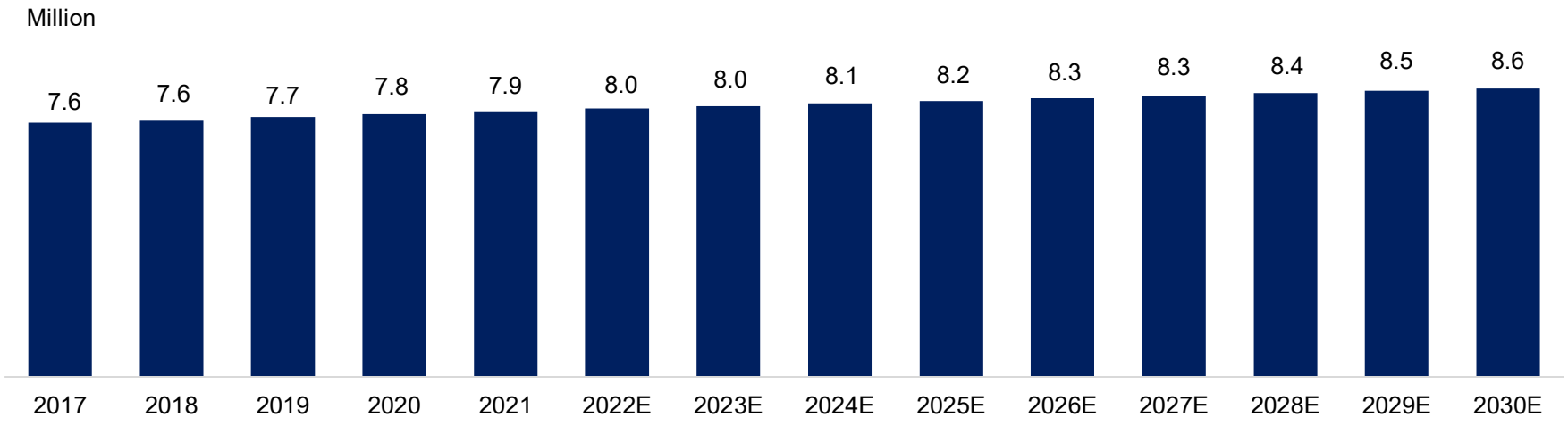
Source: Literature Review, Frost & Sullivan analysis

Global Prevalence of SLE, 2017-2030E

- The number of patients with SLE was 7.9 million in 2021, with a CAGR of 1.1% during 2017 and 2021. This number is expected to rise and approach 8.2 million in 2025 and 8.6 million in 2030, respectively.

Global Prevalence of SLE, 2017-2030E

Period	CAGR
2017-2021	1.1%
2021-2025E	1.0%
2025E-2030E	0.9%



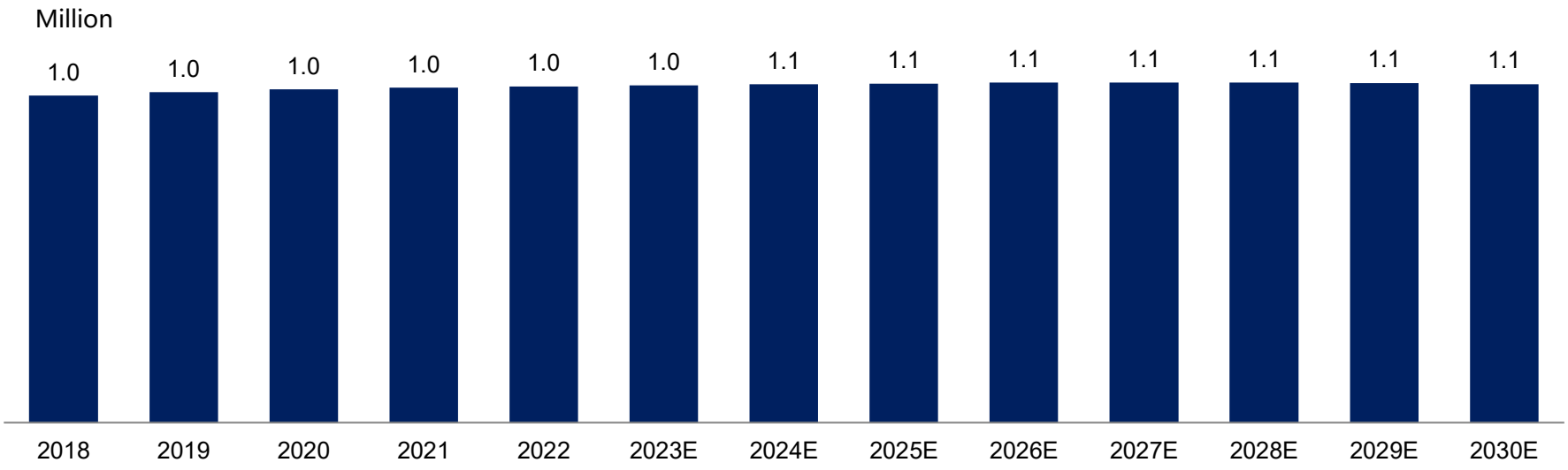
Source: Literature review, Frost & Sullivan analysis

Prevalence of SLE in China，2018-2030E

- According to epidemiology studies, the prevalence of SLE in China had reached 1.0 million in 2022, with a CAGR of 0.7% from 2018 to 2022. The number of patients is expected to reach 1.1 million in 2030, with a CAGR of 0.1% from 2022 to 2030.

Prevalence of SLE in China，2018-2030E

Period	CAGR
2018-2022	0.7%
2022-2025E	0.3%
2025E-2030E	0.0%



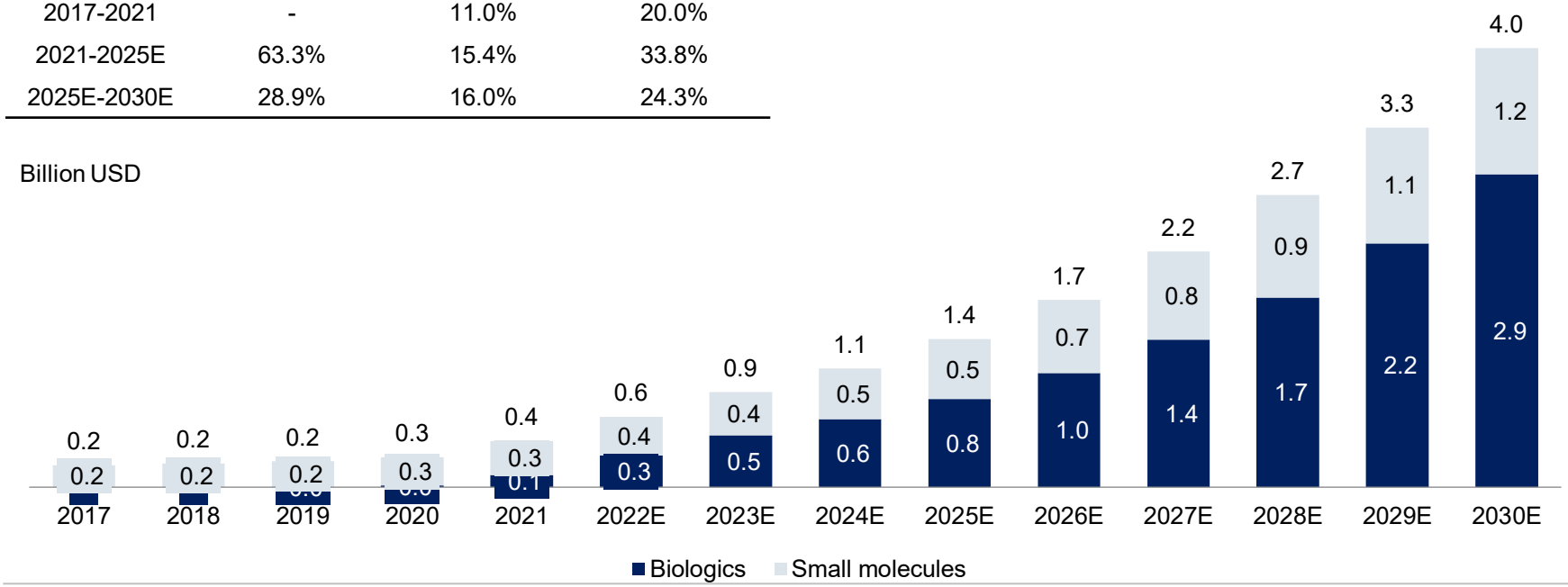
Source: Frost & Sullivan analysis

SLE Drugs Market in China, 2017-2030E

- In China, SLE Drugs Market reached USD 0.4 billion in 2021 and is expected to increase to USD 1.4 billion by 2025 at a CAGR of 33.8%. SLE Drugs Market is projected to reach USD 4.0 billion by 2030 at a CAGR of 24.3% after 2025. SLE biologics market is projected to reach USD 0.8 billion in 2025 with a CAGR of 63.3% from 2021 to 2025.

SLE Drugs Market in China, 2017-2030E

Period	Biologics	Small Molecules	Total Market
2017-2021	-	11.0%	20.0%
2021-2025E	63.3%	15.4%	33.8%
2025E-2030E	28.9%	16.0%	24.3%



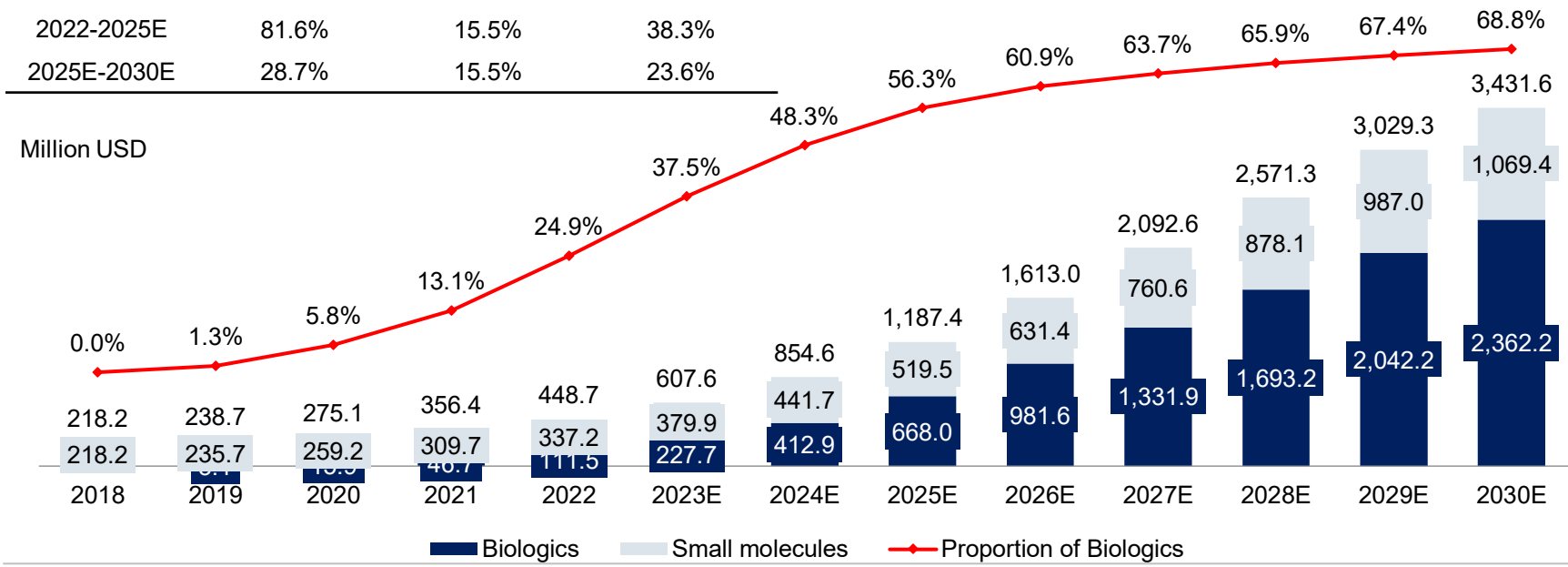
Source: Frost & Sullivan analysis

SLE Drugs Market in China, 2018-2030E

- In China, SLE Drugs Market reached USD 448.7 million in 2022 and is expected to increase to USD 1,187.4 million by 2025 at a CAGR of 15.5%. SLE Drugs Market is projected to reach USD 3,431.6 million by 2030 at a CAGR of 15.5% after 2025. SLE biologics market reached USD 111.5 million in 2022 and is projected to reach USD 2,362.2 million in 2030 with a CAGR of 46.5% from 2022 to 2030.

SLE Drugs Market in China, 2018-2030E

Period	Biologics	Small Molecules	Total Market
2018-2022	-	11.5%	19.7%
2022-2025E	81.6%	15.5%	38.3%
2025E-2030E	28.7%	15.5%	23.6%



Source: Frost & Sullivan analysis

Treatment Diagram of System Lupus Erythematous in China

- Due to the high heterogeneity of SLE, treatment of SLE should focus on early-stage diagnostics and treatment to avoid or delay lesions for organizations. In China Treatment Diagram for Systemic Lupus Erythematous, SLE can be classified into three periods, early stage, middle stage, and late stage. Different treatments are applied for different stages.

Early Stage

- 1L NSAIDS/antimalarial
- 2L Thalidomide/ local hormone use
- If need, Methotrexate/Azathioprine

Moderate Stage

- glucocorticoid combined with
  - Methotrexate
  - Azathioprine

Late Stage

- Rituximab*
- Glucocorticoid combined with cyclophosphamide
- Cyclophosphamide/ciclosporin
- Mycophenolate mofetil

*:off-label

Source:《系统性红斑狼疮诊断及指南》, Frost & Sullivan analysis

Overview of Systemic Lupus Erythematosus Therapies

- Systemic lupus erythematosus (SLE) is a chronic disease. Currently, the treatment objective is to induce remission. Practical treatment depends on the type of symptoms you have and how serious they are. A few combination medications can also be used to control SLE and prevent tissue damage.

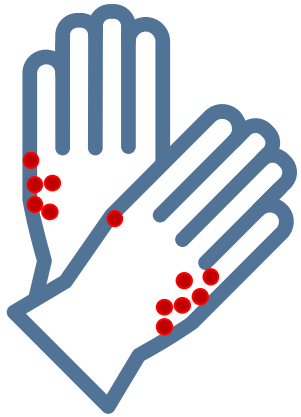
Therapy Categories	Common Drugs	MOA
NSAIDS	• Ibuprofen • Naproxen	• Help to decrease joint swelling, joint pain, fever, and inflammation of the heart and lung linings.
Corticosteroids	• Prednisone • Cyclophosphamide • Cyclosporine	• Regulate the immune system to control inflammation in the body
Antimalarial drugs	• Hydroxychloroquine	• Effective for SLE related arthritis, fatigue, rashes, and mouth sores.
Biological therapy	• Belimumab	• Belimumab is a BAFF inhibitor, which showed statistically significant, albeit modest, efficacy for the treatment of SLE. It represents a step forward in advance against SLE.

Source: Frost & Sullivan analysis

Unmet Medication Demands of SLE

Limited medications are available

- Currently, only one monoclonal antibody was approved by NMPA to treat Systemic Lupus Erythematosus. According to 2020 Chinese guidelines for the diagnosis and treatment of systemic lupus erythematosus, first-line medications for treating SLE are mainly NSAIDs, corticosteroids, and antimalarial drugs which are noted to have short-term and long-term side effects and are thought to be major issues in SLE management. Potential risks include fatigue, infections, malignancy, infertility, cardiovascular side effects, retinal side effects, and gastrointestinal side effects. These medications are known to only have the ability to help relieve many of the symptoms and reduce the chances of organ damage.



Results of several clinical trials focusing on other targets are not optimistic

- Recent advances in our understanding of SLE pathogenesis have pointed out new targets for treatment but the results of several clinical trials focusing on other targets are not optimistic. For example, rituximab against B lymphocytes CD20 antigen, two double-blind placebo-controlled trials (EXPLORER and LUNAR) subsequently failed to meet the primary endpoints in systemic and renal SLE, respectively.

Source: Frost & Sullivan analysis

Global Competitive Landscape of Biologics in SLE Treatment - I

Clinical trial status

FDA Approved Targeted Biologics for SLE

Brand Name	INN	Company	Target	FDA Approval Time
Benlysta®	Belimumab	GSK	BAFF	2011-03-09
Saphnelo®	Anifrolumab	AZN	IFNAR1	2021-08-02

*First table updated on Mar 2nd 2024

Source: FDA, Clinicaltrials, Frost & Sullivan analysis

Competitive Landscape of Biologics in SLE Treatment in China

Clinical trial status

Marketed Targeted Biologics for SLE in China

Target	Brand Name	INN	Company	NMPA Approval Time
BAFF	Benlysta®	Belimumab	GSK	2019-07-16
BAFF/APRIL	泰爱®	Telitacicept for Injection	Remegen	2021-03-09

Biologic Pipeline for SLE Treatment in China

Target	Drug Code	Company	Status	First Posted Date
IFNAR1	Anifrolumab	AZN	Phase Ⅲ	2021-08-09
	GR1603	Genrix Bio	Phase Ⅰ/Ⅱ	2021-12-03
	QX006N	Qyuns	Phase Ⅰ	2021-11-23
BAFF	UBP1213sc	Junshi Biosciences	Phase Ⅰ	2022-02-18
BAFFR	VAY736	Novartis	Phase Ⅲ	2023-01-09
CLEC4C	BIIB059	Biogen; Vetter Pharma-Fertigung	Phase Ⅲ	2022-06-07
CD20	Obinutuzumab	Roche	Phase Ⅲ	2022-10-27
	MIL62	Mabworks	Phase Ⅱ/Ⅲ	2023-02-08
CD40L	IBI355	Innovent Bio	Phase Ⅰ	2023-10-19
	Dapirolizumab Pegol	UCB	Phase Ⅲ	2022-11-07
CD38	SG301	Shangjian Biotech	Phase Ⅰ	2023-11-06
	CM313	Keymed	Phase Ⅰ/Ⅱ	2022-07-08
CD22	SM03	Longrui	Phase Ⅰ	2015-01-07
CD79B, FCGR2B	PRV-3279	Zhongmei Huadong	Phase Ⅱ	2023-08-02
Undisclosed	SHR-2001	Hengrui	Phase Ⅰ	2023-07-10
APRIL,BAFF	ALPN-303	Ajinomoto Bio-Pharma	Phase Ⅰ	2023-12-22
CD19	relma-cel，JWCAR029	JW (Cayman) Therapeutics	Phase Ⅰ/Ⅱ	2023-12-25

*This table was last updated on Mar 2nd , 2024

Source: NMPA, CDE, Frost & Sullivan analysis

Table of Contents

Overview of Asthma

- Asthma is a condition in which patients' airways narrow and swell and may produce extra mucus. This can make breathing difficult and trigger coughing and wheezing. For a significant number of asthma patients, this disease can be a major problem that interferes with daily activities and may potentially lead to life-threatening asthma attacks.
- Among all the subtypes, severe asthma is the most serious and life-threatening form of asthma. It is characterized as someone diagnosed with asthma requiring medium or high-dose inhaled corticosteroids combined with other longer-acting medications. It accounts for 5-10% of the overall asthma population.
- There is an inherited tendency towards the development of asthma which is related to a hypersensitivity reaction of the immune response.

Introduction

- Asthma is a chronic inflammatory lung disease that can cause repeated episodes of cough, wheezing and breathing difficulty. During the acute episodes, the airway lining in the lungs becomes inflamed and swollen. Mucus production occurs in the airway and muscles surrounding the airway spasm. Combined, these cause a reduction in air flow.

Symptoms

Common signs and symptoms of an acute asthma episode include:

- Coughing
- wheezing——may be absent
- Breathlessness —— while walking or while at rest
- Respiratory rate increased
- Chest tightness
- Chest or abdominal pain
- Fatigue, feeling out of breath
- Increased pulse rate
- Inability to participate in sports

Risk Factors

- Genetics and Family History
- Viral Respiratory Infection
- Occupational Exposure
- Maternal Age
- Smoking

Disease Burden

- The physical and socio-economic burden is significant, with 5-10% of patients with severe cases accounting for 50% of asthma-related costs

Severity Classification

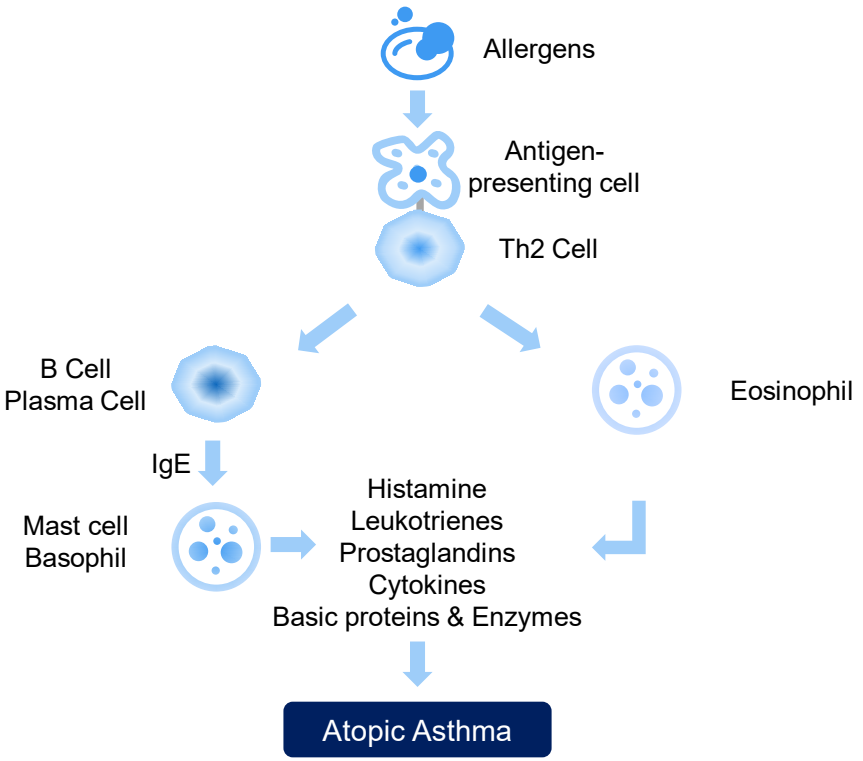
Mild Intermittent Asthma → Mild Persistent Asthma → Moderate Persistent Asthma → Severe Persistent Asthma

Source: Literature Review, Frost & Sullivan analysis

Overview of Atopic Asthma

- Atopic Asthma is due to an allergy to allergens which are usually suspended in the air in the form of pollen, dust, smoke, automobile exhaust or animal dander.
- There is an inherited tendency towards the development of atopic asthma which is related to a hypersensitivity reaction of the immune response.
- Atopic Asthma is characterized by infiltration of the bronchial mucosa with eosinophils and Th2-type cells, circulating specific immunoglobulin E (IgE) antibodies and positive skin test to common aeroallergens, and airway-hyper responsiveness.

Pathogenesis



Uptake and processing of inhaled allergens by dendritic cells situated in the airway epithelium and submucosa

Secondary effector cells such as macrophages, basophils and eosinophils are recruited by Th2 cells into the inflammatory zone and become primed.

Controlled by T lymphocytes, mucosal-type mass cells (tryptase positive, chymase negative) are highly responsible to inhaled allergens in causing bronchoconstriction

Eosinophils are a rich source of granule basic proteins, generating eicosanoids and release potentially tissue-damaging superoxide and a rage of cytokines and chemokines

Activation of mediator secretion

Source: Literature Review, Frost & Sullivan analysis

Treatment Paradigm for Adults and Adolescents of Asthma in China

- The long-term goals of asthma management are to control symptoms and reduce the risk of exacerbations, airway damage and side-effects of medication with identification of patients' own goals. Asthma treatment is modified in a continuous cycle of assessment, treatment, adjustment and review response.
- Medication for asthma includes controllers and relievers, the fundamental treatment is the oral corticosteroids with different dosages and combination with other medications, biologics such as IgE antibodies, and anti-IL-5 drugs might be added as the severity of asthma increases. Although recommended to be used under severe conditions by GINA 2020, some innovative biologics (Dupilumab and Omalizumab) are as well approved for moderate-to-severe asthma treatment, which provides more options for patients and physicians.
- For asthma patients, the controller is a preferred treatment option based on the patient's assessment of disease progression and symptoms. The alternative controller is a treatment strategy in clinical treatment where the best treatment option is not determined.
- Once a patient is diagnosed with asthma, physicians prescribe medicine depending on the severity of the disease, in an attempt to enhance the patient's lung function and increase the probability of recovery.

Treatment Paradigm for Asthma Patients*

	Mild Asthma		***Moderate Asthma***		***Severe Asthma***
Preferred Controller	**No medication recommended**	**Low-dose ICS****	**Low-dose ICS/LABA**	**Medium-dose and high-dose ICS/LABA**	**Add-on therapy, including tiotropium, oral corticosteroid, Anti-IgE, anti-IL-4Rα and anti-IL-5 medications**
Alternative Controller	Low-dose ICS	LTRA and Low-dose theophylline	Medium-dose and high-dose ICS; Low-dose ICS/LTRA(or theophylline)	Add-on tiotropium bromide; Medium-dose and high-dose ICS/LTRA(or theophylline)	——

Anti-IL-4Rα (Dupilumab) and anti-IgE (omalizumab) are both approved for the treatment of moderate to severe asthma aged 12 years and older.

Reliever Options: As-needed short-acting beta-agonist (SABA) or low-dose ICS-formoterol

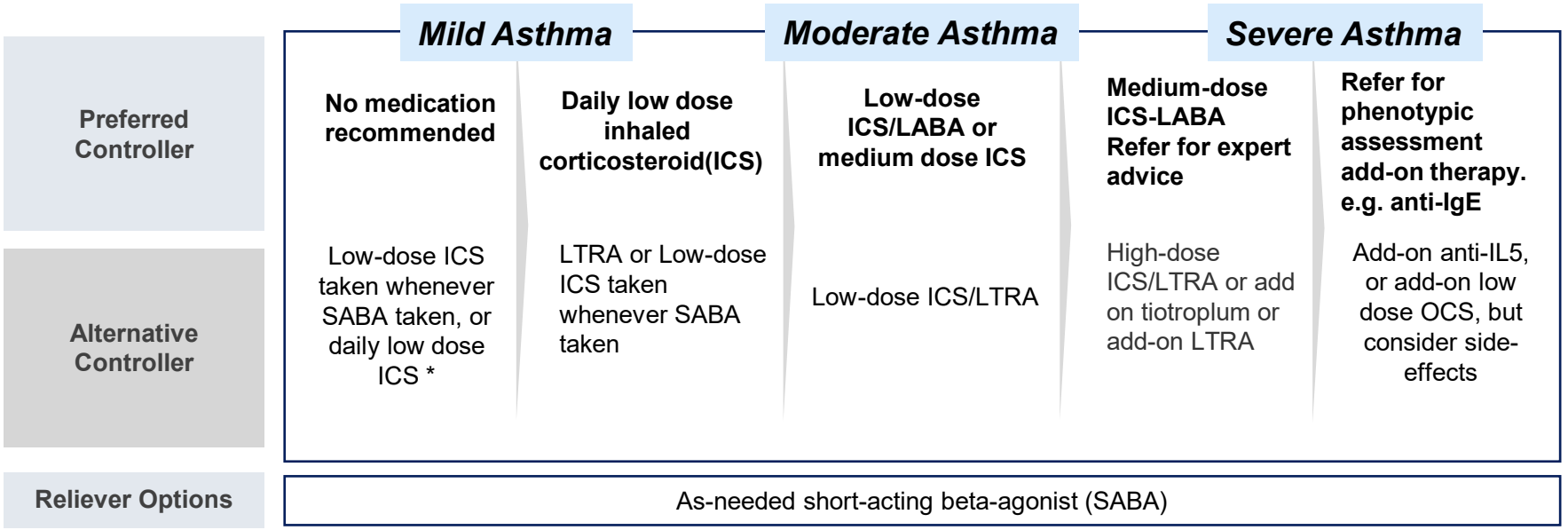
*The treatment options can be applied to adults, adolescents, and children ≥ 6 years old; theophylline is not recommended for children ≤ 12 years old;
**ICS: Inhaled corticosteroids; LTRA: Leukotriene receptor antagonist; LABA: Long-acting beta2-agonist; SABA: Short-acting beta2-agonist
Several biologics have been approved for the treatment in moderate to severe asthma.

Source: Asthma Group of Chinese Thoracic Society, Literature Review, Frost & Sullivan analysis

Treatment Paradigm for Children Aged 6-11 Years of Asthma in China

- Medications for asthma include controllers and relievers, and differences exist between adults and children according to the 2020 Global initiative for asthma. The following paradigm shows the treatment for children aged 6-11 years with asthma. The fundamental treatment is corticosteroids with different dosages and combination with other medications, biologics such as IgE antibodies and anti-IL5 drugs might be added with increasing severity. Compared the treatment for adults with that for children aged 6-11 years, they mainly differ in the dosage of medications and alternative controllers.

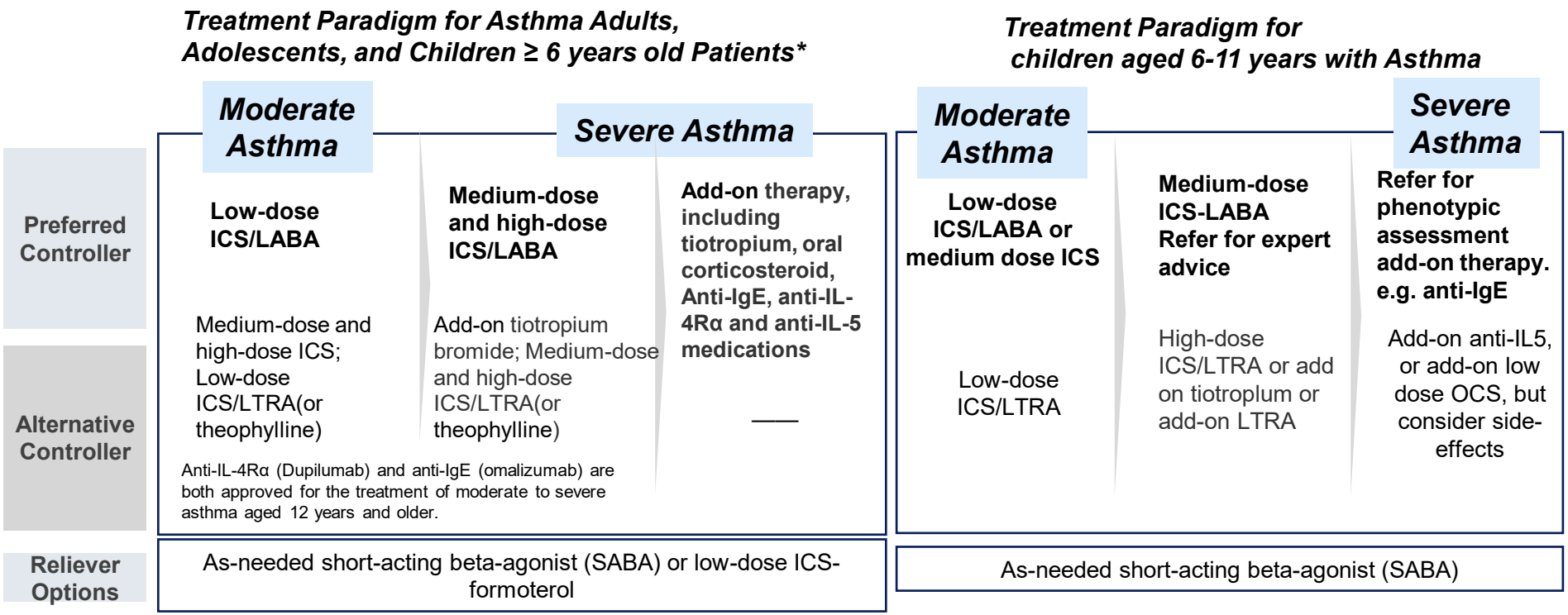
Treatment Paradigm for children aged 6-11 years with Asthma



*ICS: Inhaled corticosteroids; LTRA: Leukotriene receptor antagonist; LABA: Long-acting beta2-agonist; SABA: Short-acting beta2-agonist
Several biologics have been approved for clinical trails in moderate to severe asthma.

Source: Asthma Group of Chinese Thoracic Society, Literature Review, Frost & Sullivan analysis

Treatment Paradigm for moderate-to-severe asthma patients



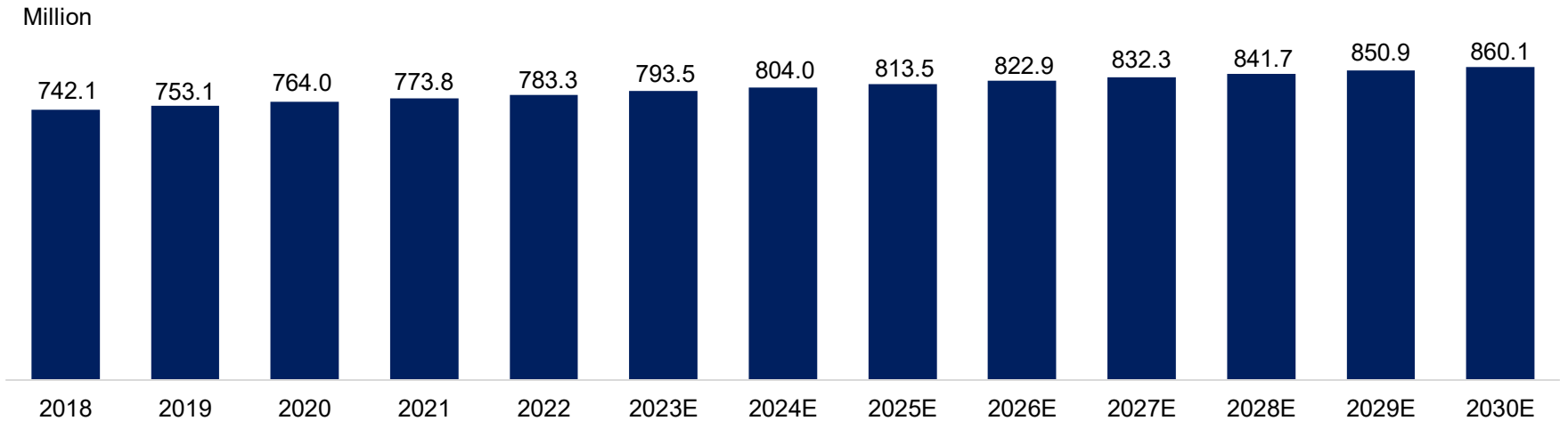
*The treatment options can be applied to adults, adolescents, and children ≥ 6 years old; theophylline is not recommended for children ≤ 12 years old;
**ICS: Inhaled corticosteroids; LTRA: Leukotriene receptor antagonist; LABA: Long-acting beta2-agonist; SABA: Short-acting beta2-agonist
Several biologics have been approved for the treatment in moderate to severe asthma.

Global Prevalence of Asthma, 2018-2030E

- Asthma is a globally significant long-term disease of the lungs with major public health consequences including high morbidity, and mortality in severe cases. The number of patients with asthma was 783.3 million in 2022, with a CAGR of 1.4% during 2018 and 2022. This number is expected to rise and approach 813.5 million in 2025 and 860.1 million in 2030, respectively.

Global Prevalence of Asthma, 2018-2030E

CAGR	Total
2018-2022	1.4%
2022-2025E	1.3%
2025E-2030E	1.1%



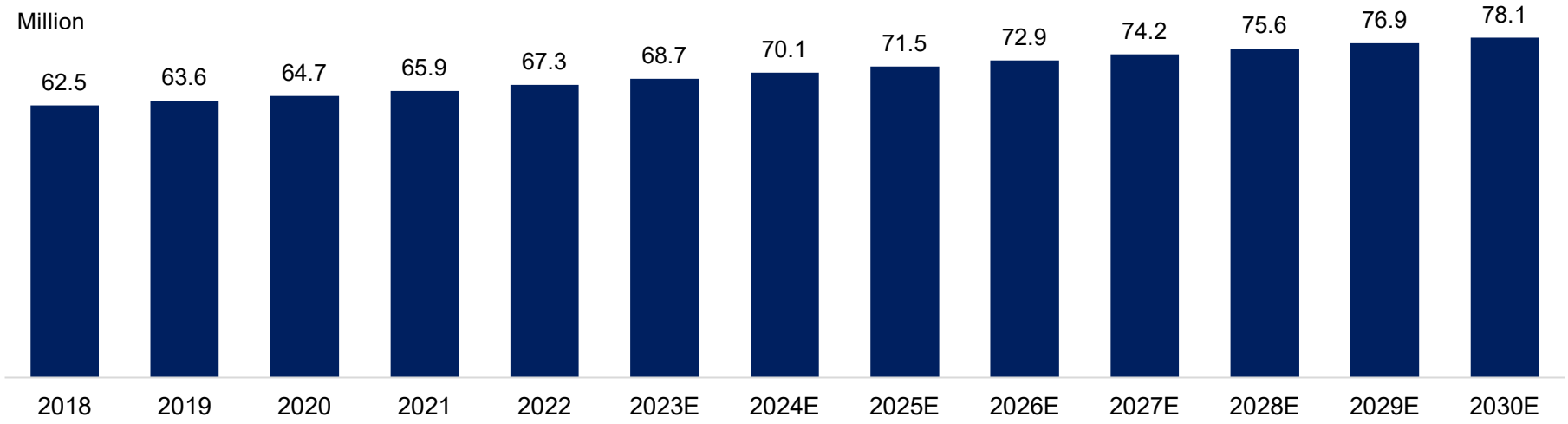
Source: Literature review, Frost & Sullivan analysis

Prevalence of Asthma in China, 2018-2030E

- The total number of patients affected by asthma in China had reached 67.3 million in 2022, with a CAGR of 1.8% from 2018 to 2022. This number is expected to continue to climb and eventually reach 78.1 million in 2030. 11% of patients have severe disease

Prevalence of Asthma in China, 2018-2030E

CAGR	Asthma patients
2018-2022	1.8%
2022-2025E	2.0%
2025E-2030E	1.8%



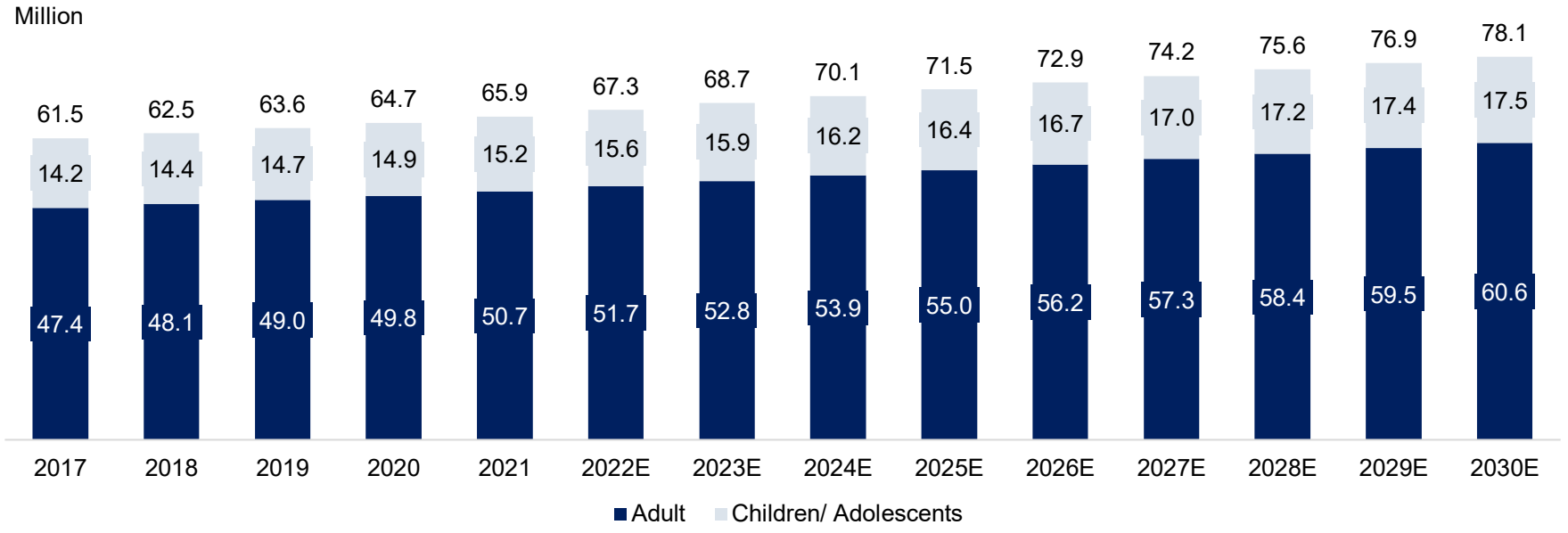
Source: Literature review, Frost & Sullivan analysis

Prevalence of Asthma in China Breakdown by Age, 2017-2030E

- In China, the number of adult patients affected by asthma reached 50.7 million in 2021, with a CAGR of 1.7% from 2017 to 2021, and this number is forecasting to reach 60.6 million in 2030; the number of children/adolescents patients affected by asthma reached 15.2 million in 2021, with a CARG of 1.8% from 2017 to 2021 and this number is forecasting to reach 17.5 million in 2030.

Prevalence of Asthma in China Breakdown by Age, 2017-2030E

CAGR	Adult	Children/ Adolescents	Total
2017-2021	1.7%	1.8%	1.7%
2021-2025E	2.1%	2.0%	2.1%
2025E-2030E	1.9%	1.3%	1.8%



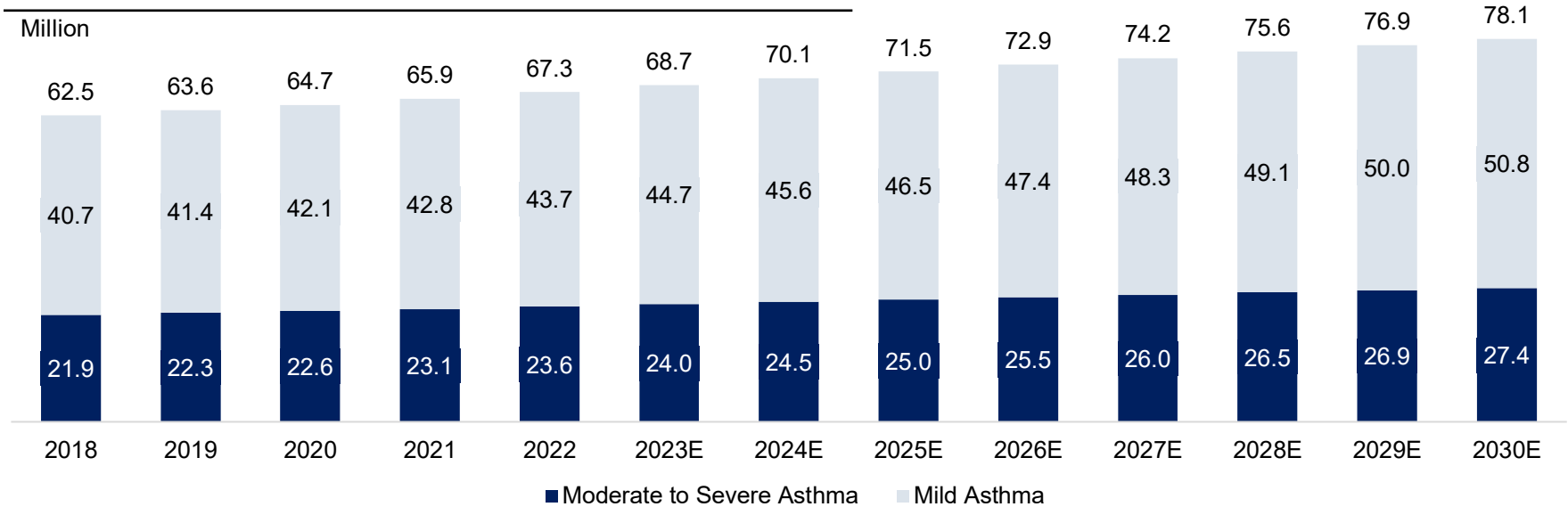
Source: Literature review, Frost & Sullivan analysis

Prevalence of Asthma in China Breakdown by Severity, 2018-2030E

- In China, the number of patients affected by mild asthma reached 43.7 million in 2022, with a CAGR of 1.8% from 2018 to 2022, and this number is forecasting to reach 50.8 million in 2030; the number of patients affected by moderate to severe asthma reached 23.6 million in 2022, with a CARG of 1.8% from 2018 to 2022 and this number is forecasting to reach 27.4 million in 2030.

Prevalence of Asthma in China Breakdown by Severity, 2018-2030E

CAGR	Moderate to Severe Asthma	Mild Asthma	Total
2018-2022	1.8%	1.8%	1.8%
2022-2025E	2.0%	2.0%	2.0%
2025E-2030E	1.8%	1.8%	1.8%



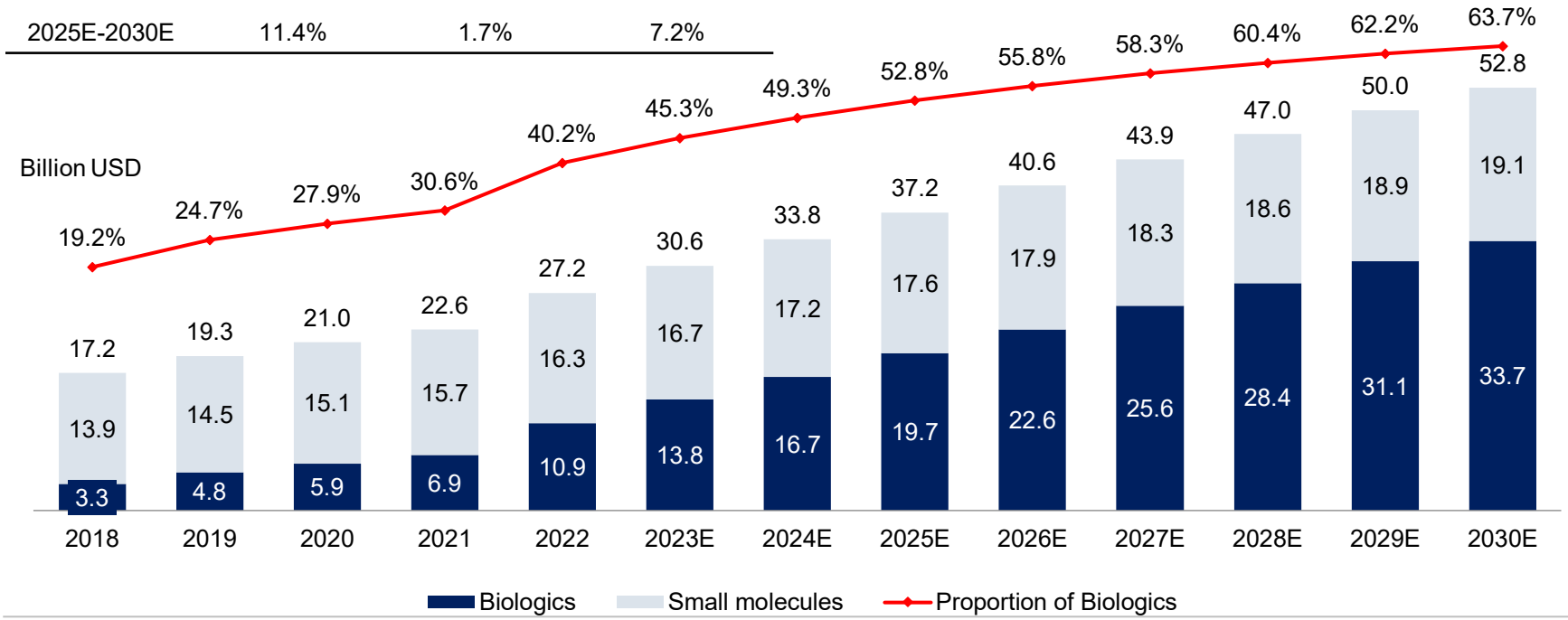
Source: Literature review, Frost & Sullivan analysis

Global Asthma Drugs Market, 2018-2030E

- Global Asthma Drugs Market reached USD 27.2 billion in 2022 and is expected to increase to USD 37.2 billion by 2025 at a CAGR of 11.0%. Asthma Drugs Market is projected to reach USD 52.8 billion by 2030 at a CAGR of 7.2% after 2025. The CAGR of total market from 2022 to 2030 is 8.7%. Asthma biologics market is projected to reach USD 19.7 billion in 2025 with a CAGR of 21.6% from 2022 to 2025.

Global Asthma Drugs Market, 2018-2030E

Period	Biologics	Small Molecules	Total Market
2018-2022	34.8%	4.0%	12.1%
2022-2025E	21.6%	2.6%	11.0%
2025E-2030E	11.4%	1.7%	7.2%



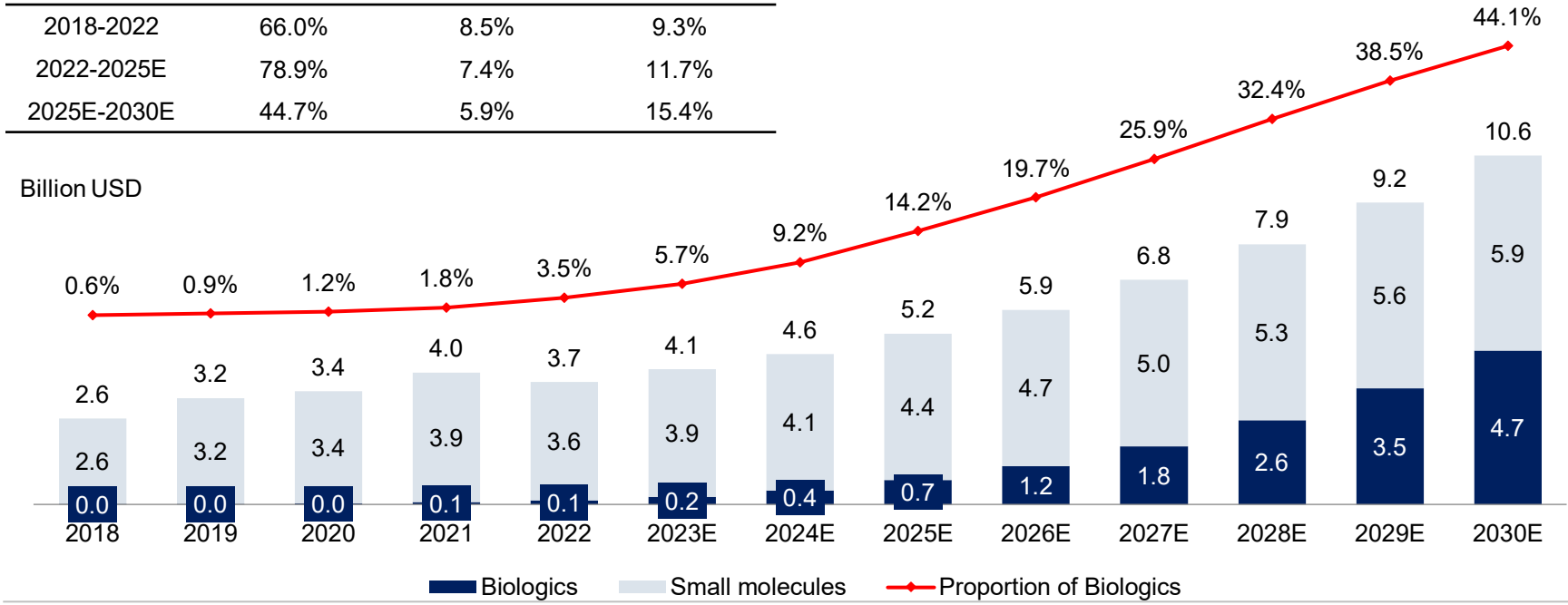
Source: Frost & Sullivan analysis

Asthma Drugs Market in China, 2018-2030E

- In China, Asthma Drugs Market reached USD 3.7 billion in 2022 and is expected to increase to USD 5.2 billion by 2025 at a CAGR of 11.7%. Asthma Drugs Market is projected to reach USD 10.6 billion by 2030 at a CAGR of 15.4% after 2025. The CAGR of total market from 2022 to 2030 is 14.0%. Asthma biologics market is projected to reach USD 0.7 billion in 2025 with a CAGR of 78.9% from 2022 to 2025. Asthma biologics market reached USD 0.1 million in 2022.

Asthma Drugs Market in China, 2018-2030E

Period	Biologics	Small Molecules	Total Market
2018-2022	66.0%	8.5%	9.3%
2022-2025E	78.9%	7.4%	11.7%
2025E-2030E	44.7%	5.9%	15.4%



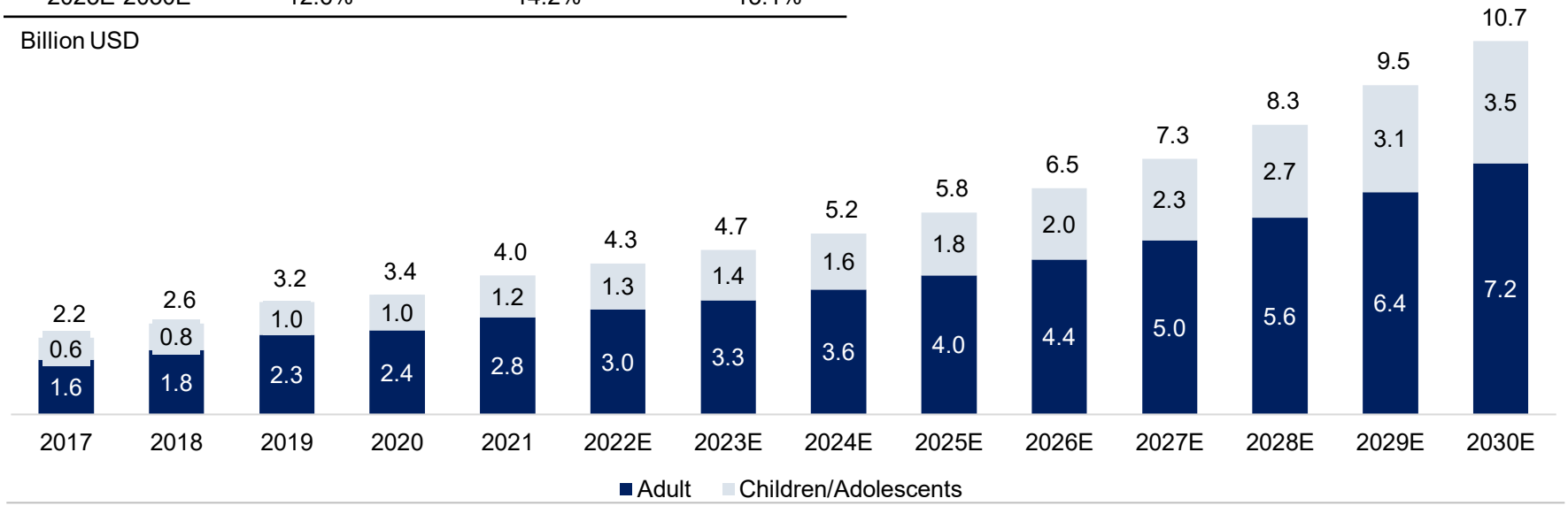
Source: Frost & Sullivan analysis

Asthma Drugs Market in China Breakdown by Age, 2017-2030E

- In China, asthma drugs market for adult patients reached USD 2.8 billion in 2021 and with a CAGR of 15.6% from 2017 to 2021, and this number is forecasting to reach 7.2 billion in 2030. Asthma drugs market for children/adolescents patients reached USD 1.2 billion in 2021 and with a CAGR of 17.1% from 2017 to 2021, and this number is forecasting to reach 3.5 billion in 2030.

Asthma Drugs Market in China Breakdown by Age, 2017-2030E

CAGR	Adult	Children/ Adolescents	Total
2017-2021	15.6%	17.1%	16.0%
2021-2025E	9.3%	10.8%	9.8%
2025E-2030E	12.6%	14.2%	13.1%



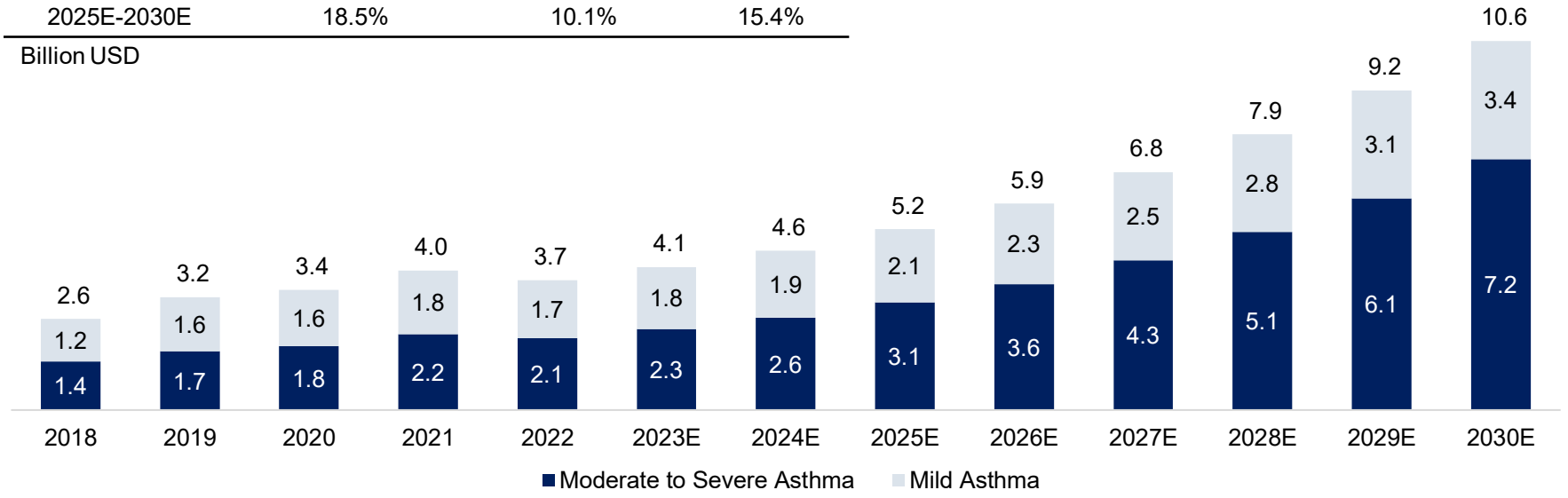
Source: Literature Review, Frost & Sullivan analysis

Asthma Drugs Market in China Breakdown by Severity, 2018-2030E

- In China, asthma drugs market for moderate to severe patients reached USD 2.1 billion in 2022 and with a CAGR of 10.3% from 2018 to 2022, and this number is forecasting to reach 7.2 billion in 2030. Asthma drugs market for mild patients reached USD 1.7 billion in 2022 and with a CAGR of 8.0% from 2018 to 2022, and this number is forecasting to reach 3.4 billion in 2030.

Asthma Drugs Market in China Breakdown by Severity, 2018-2030E

CAGR	Moderate to Severe Asthma	Mild Asthma	Total
2018-2022	10.3%	8.0%	9.3%
2022-2025E	14.4%	8.3%	11.7%
2025E-2030E	18.5%	10.1%	15.4%



Source: Literature Review, Frost & Sullivan analysis

Unmet Medication Demands of Asthma

Underuse and resistance of first-line ICS

- Despite the high agreement among physicians that ICS represents the cornerstone for asthma treatment, the results show underuse in first-line ICS for asthma patients. Conventional treatment options, such as inhaled and oral corticosteroids, are lack effectiveness in controlling moderate and severe asthma conditions. Moreover, the maintenance treatment of systemic corticosteroids can cause dose-dependent growth suppression and a series of severe adverse effects in children and adolescents, which leaves them with even more limited treatment options.
- Some patients are completely resistant to the effects of steroids regardless of the dose. Therefore, user-friendly design of inhaler devices and specialized medication development for steroid-insensitive patients are of paramount significance to enhance asthma management in clinical practice.

Lack of individualized therapies

- Asthma has complex and heterogeneous nature which needs target treatment to the individual patient. Therefore, it may be beneficial to adopt the precision medicine approach, particularly given that the use of targeted biological therapy in patients with severe eosinophilic asthma is indeed progressing rapidly. Nevertheless, for many patients with unique phenotyping such as neutrophilic asthma, efficacious therapy in addition to surgical measures has not been established yet. Therefore, treatment options with efficacy over the range of asthma severities and subtypes are needed to improve the health outcomes of various asthma patients.

Source: Frost & Sullivan analysis

Global Competitive Landscape of Biologics in Asthma Treatment - I

Clinical trial status

FDA Approved Targeted Biologics for Asthma

Target	Brand Name	INN	Company	FDA Approval Time
IgE	Xolair®	Omalizumab	Genentech	2003-06-20
IL-5	Nucala®	Mepolizumab	GSK	2015/11/4
	Cinqair®	Reslizumab	Teva Pharmaceutical	2016-05-23
	Fasenra®	Benralizumab	AstraZeneca	2017-11-14
IL-4Rα	Dupixent®	Dupilumab	Sanofi/ Regeneron	2018-10-19
TSLP	Tezspire®	Tezepelumab	Amgen/AstraZeneca	2021-12-17

Global Biologic Pipeline in Asthma Treatment

Target	Drug Code	Company	Status	First Posted Date
TSLP	SHR-1905	Atridia	Phase Ⅰ	2021-03-16
	AZD8630	AstraZeneca	Phase Ⅰ	2021-11-08
IL-4Rα	CBP-201	Connect Biopharmaceuticals	Phase Ⅱ	2021-02-26
IL-5	Depemokimab	GSK	Phase Ⅲ	2021-01-22
IgE	FB825	Oneness Biotech	Phase Ⅱ	2021-08-17
IL-33	SAR440340(Itepekimab)	Sanofi/ Regeneron	Phase Ⅱ	2018-01-02
	Tozorakimab	AstraZeneca	Phase Ⅱ	2020-09-30
IL-17A	CJM112	Novartis	Phase Ⅱ	2017-10-03
Tryptase	MTPS9579A	Genentech	Phase Ⅱ	2019-09-17
PSGL-1	SelK2	Tetherex Pharmaceuticals	Phase Ⅱ	2020-09-07
CD4	Tregalizumab	T-Balance Therapeutics	Phase Ⅱ	2020-12-17

*This table was last updated on Mar 2nd , 2024

Source: FDA, Frost & Sullivan analysis

Global Competitive Landscape of Biologics in Asthma Treatment - II

Clinical trial status

Global Biologic Pipeline in Asthma Treatment

Target	Drug Code	Company	Status	First Posted Date
IL-6	FB704A	Oneness Biotech	Phase Ⅱ	2021-08-24
LIGHT	AVTX-002	Avalo Therapeutics	Phase Ⅱ	2022-03-21
OX40L	Amlitelimab	Sanofi	Phase Ⅱ	2022-06-16
CD6	Itolizumab	Equillium	Phase Ⅰ	2019-07-05
ST2	Melrilimab	GSK	Phase Ⅰ	2020-04-28
IL-17RB	SM17	SinoMab	Phase Ⅰ	2022-04-18
IL-13	SAR443765	Sanofi	Phase Ⅱ	2023-10-20
	Lebrikizumab	Roche	Phase Ⅲ	2023-11-16
TLSPR	UPB-101	Upstream Bio	Phase Ⅰ	2022-07-07
IFNG	ETH47	Ethris	Phase Ⅰ	2023-12-18
IL-4Rα/TSLP	IBI3002	Innovent	Phase Ⅰ	2024-01-19

*This table was last updated on Mar 2nd , 2024

Source: FDA, Frost & Sullivan analysis

Competitive Landscape of Biologics in Asthma Treatment in China- I

Clinical trial status

Marketed Targeted Biologics for Asthma in China

Target	Brand Name	INN	Company	NMPA Approval Time
IgE	Xolair®	Omalizumab	Novartis	2017-08-28
IgE	Aomaishu(奥迈舒)	Omalizumab alfa	Mabpharm	2023-05-19
IL-4R	Dupixent	Dupilumab	Sanofi	2023-09-26

Biologic Pipeline in Asthma Treatment in China

Target	Drug Code	Company	Status	First Posted Date
TSLP	Tezepelumab	AstraZeneca	Phase Ⅲ	2019-07-15
	TQC2731	Chia Tai-tianqing	Phase Ⅱ	2022-06-21
	SHR-1905	Hengrui	Phase Ⅱ	2022-09-29
	CM326	Keymed Bioscience	Phase Ⅱ	2023-03-17
	QX008N	Qyuns	Phase Ⅰ	2022-07-08
	HBM9378	Harbour biomed; Kelun-Biotech	Phase Ⅰ	2022-08-29
	LQ043	Novamab	Phase Ⅰ	2023-01-13
	GR2002	Genrixbio	Phase Ⅰ	2023-05-25
	STSA-1201	Staidson Biopharmaceuticals	Phase Ⅰ	2023-08-01
	MG-ZG122	Mabgeek	Phase Ⅰ	2022-12-12
IL-4R	CM310	Keymed Bioscience	Phase Ⅱ/Ⅲ	2023-03-08
	CBP-201	Connect Biopharmaceuticals	Phase Ⅱ	2021-08-18
	GR1802	Genrix bio	Phase Ⅱ	2022-05-12
	MG-K10	Mabgeek	Phase Ⅰ/Ⅱ	2022-04-29
	SHR-1819	Hengrui	Phase Ⅰ	2021-02-01
	LQ036	Novamab	Phase Ⅱ	2024-02-04
IL-5	Mepolizumab	GSK	BLA	2023-03-14
	GSK3511294(Depemokimab)	GSK	Phase Ⅲ	2021-09-18
	SSGJ-610	Sunshine Guojian	Phase Ⅱ	2022-08-22
	SHR-1703	Suncadia bio; Hengrui	Phase Ⅱ	2022-09-05

*This table was last updated on Mar 2nd , 2024

Source: NMPA, CDE, Frost & Sullivan analysis

Competitive Landscape of Biologics in Asthma Treatment in China -II

Clinical trial status

Biologic Pipeline in Asthma Treatment in China

Target	Drug Code	Company	Status	First Posted Date
IL-4Rα, IL-5	RC1416	Regenecore	Phase Ⅰ	2023-06-20
IL-5Rα	Benralizumab	AstraZeneca	BLA	2023-06-29
IgE	Omalizumab-HS632	Hisun	Phase Ⅰ	2020-04-29
	Omalizumab-SYN008	CSPC Baike	Phase Ⅰ	2020-11-03
	Omalizumab-SYB507	Yuanda Shuyang	Phase Ⅰ	2020-11-09
	JYB1904	Jiye Biotechnology	Phase Ⅰ	2022-04-28
IL-25	XKH001	kanova biopharma	Phase Ⅰ	2022-03-07
ST2	9MW1911	Mabwell	Phase Ⅰ	2021-10-13
	TQC2938	Chiatai Tianqing	Phase Ⅰ	2023-03-31
Undisclosed	Recombinant ε and γ Human Immunoglobulin Fc Fusion Protein	Kexin Biotech	Phase Ⅰ	2018-11-16
	ZHB107-108	ZonHon Biopharma	Phase Ⅰ	2023-11-17

*This table was last updated on Mar 2nd , 2024

Source: NMPA, CDE, Frost & Sullivan analysis

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Overview of Atopic Dermatitis (AD)

- Atopic dermatitis offers a wide clinical spectrum ranging from minor forms such as pityriasis alba (dry depigmented patches) or hand eczema to major forms with an erythrodermic rash. Pruritus and chronic or relapsing eczematous lesions with typical shape and distribution are essential for diagnosis.
- AD can have a detrimental effect on the lives of patients and their families throughout their lifespan. This includes impacts on quality of life (QoL) and social, academic, and occupational impacts. AD places a tremendous financial burden on patients, their families, and society as a whole through direct medical costs and decreased productivity.

Pathophysiology

- A multiplicity of factors, including skin barrier abnormalities, defects in innate immunity response, Th2-skewed adaptive immune response, and altered skin resident microbial flora are involved in the pathogenesis of atopic dermatitis. Whether skin inflammation is initiated by skin barrier dysfunction ("outside-in" hypothesis) or by immune dysregulation ("inside-out" hypothesis) is still in debate.

Major Risk Factors

- **Family history of atopy**
- **Loss of function mutations in the FLG gene**

Symptoms

- Itching, which may be severe, especially at night
- Red to brownish-gray patches, especially on the hands, feet, ankles, wrists, inside the bend of the elbows and knees, and in infants, the face and scalp
- Small, raised bumps, which may leak fluid and crust over when scratched
- Thickened, cracked, scaly, and dry skin

Negative Impact

Based on public survey, AD was commonly linked to limited lifestyle (51.3%), avoidance of social interaction (39.1%), and impacted activities (43.3%)

Source: Literature Review, Frost & Sullivan analysis

Classification of Atopic Dermatitis by Th2 type

- Atopic Dermatitis can be divided into Type2-High and Type2-Low/ Non Type2 phenotypes based on the degree of Type2 inflammation.
- 54.5% of oral corticosteroids patients present high eosinophilic levels and 67.4% have high FeNO levels. Making Type2-high asthma the predominant phenotype.
- Evidence has proved that levels of IL-4, IL-5, IL-13 and IL-10 were elevated in the skin of patients with AD, IL-5 and IL-3 levels were further increased in patients with elevated IgE levels.

IL-4

- Key Th2 cytokine, critical for Th2 cell differentiation, IgE production and eosinophil recruitment.
- Capable of increasing the expression of CCL26 which is a key chemokine for eosinophil recruitment.
- Changes to IL-4 expression can result in a defective barrier with increased permeability to allergens.

IL-13

- Critical mediator of allergic inflammation, expressed in both acute and chronic lesions of AD.
- Functional overlap of IL-4 and IL-13, the effects of IL-4 on attenuating expression of the EDC genes filaggrin and on collagen synthesis in dermal fibroblast also apply to IL-13.
- Increased IL-13 signaling via STAT6 contributes to the pathogenesis of allergic inflammation and loss of skin barrier function.

IL-5

- Critical cytokine for eosinophil development, survival and proliferation, elevated levels detected in the skin of AD patients, which are also correlated with IgE levels.
- Plays a role in recruiting eosinophils to the site of allergen exposure.

IL-10

- Critical anti-inflammatory cytokine, expression induced after the pro-inflammatory mediators.
- IL-10 down-regulated expression of the anti-microbial peptides necessary for host defense.
- Treatment of keratinocytes with low doses of IL-4 induced expression of the IL-10R1, whereas, at higher doses, the expression decreases in a dose-dependent manner.

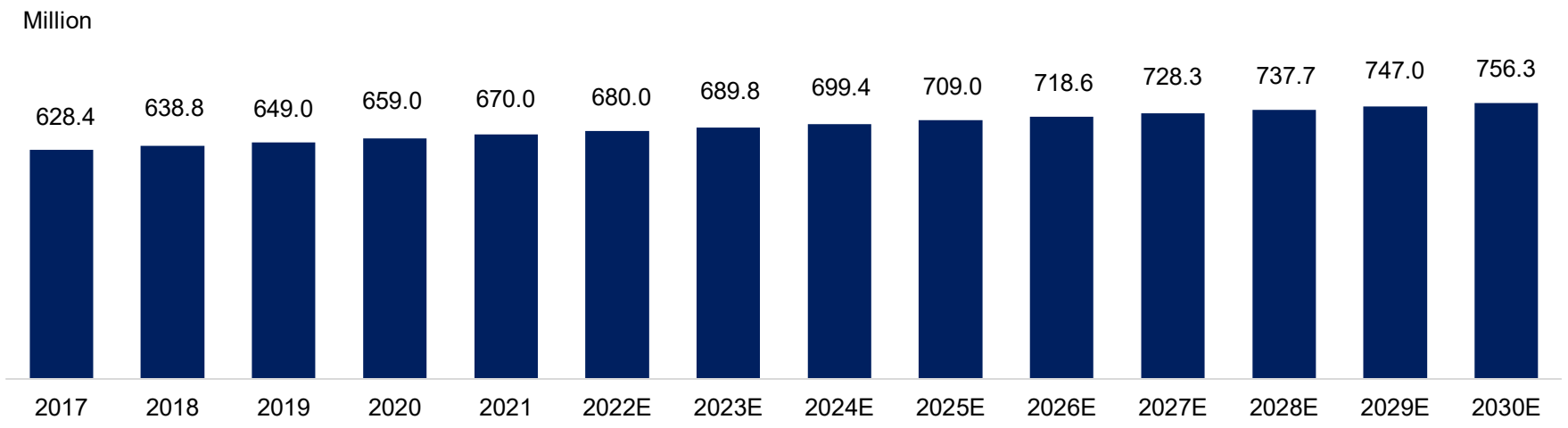
Source: Literature Review, Frost & Sullivan analysis

Global Prevalence of Atopic Dermatitis, 2017-2030E

- The number of patients with atopic dermatitis was 670.0 million in 2021, with a CAGR of 1.6% during 2017 and 2021. This number is expected to rise and approach 709.0 million in 2025 and 756.3 million in 2030, respectively.

Global Prevalence of Atopic Dermatitis, 2017-2030E

Period	CAGR
2017-2021	1.6%
2021-2025E	1.4%
2025E-2030E	1.3%



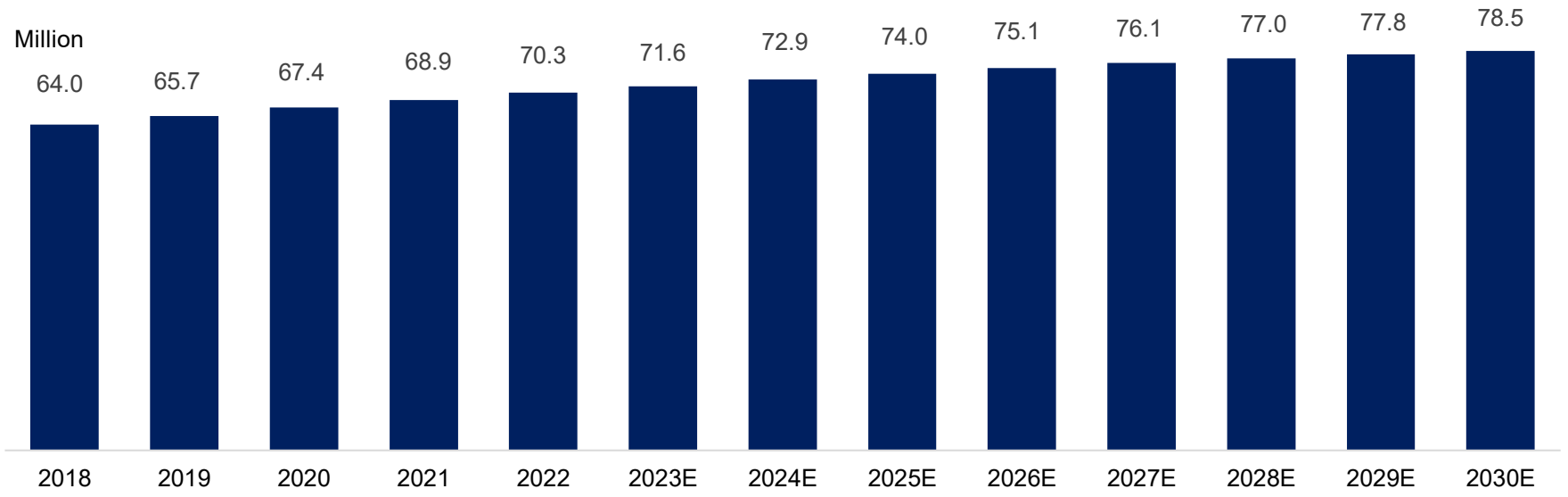
Source: Literature review, Frost & Sullivan analysis

Prevalence of Atopic Dermatitis in China, 2018-2030E

- The prevalence of atopic dermatitis in China had reached 70.3 million in 2022, with a CAGR of 2.3% from 2018 to 2022. It is estimated to reach 78.5 million patients in 2030. 30% of patients have moderate-to-severe disease

Prevalence of Atopic Dermatitis in China, 2018-2030E

Period	CAGR
2018-2022	2.3%
2022-2025E	1.8%
2025E-2030E	1.2%



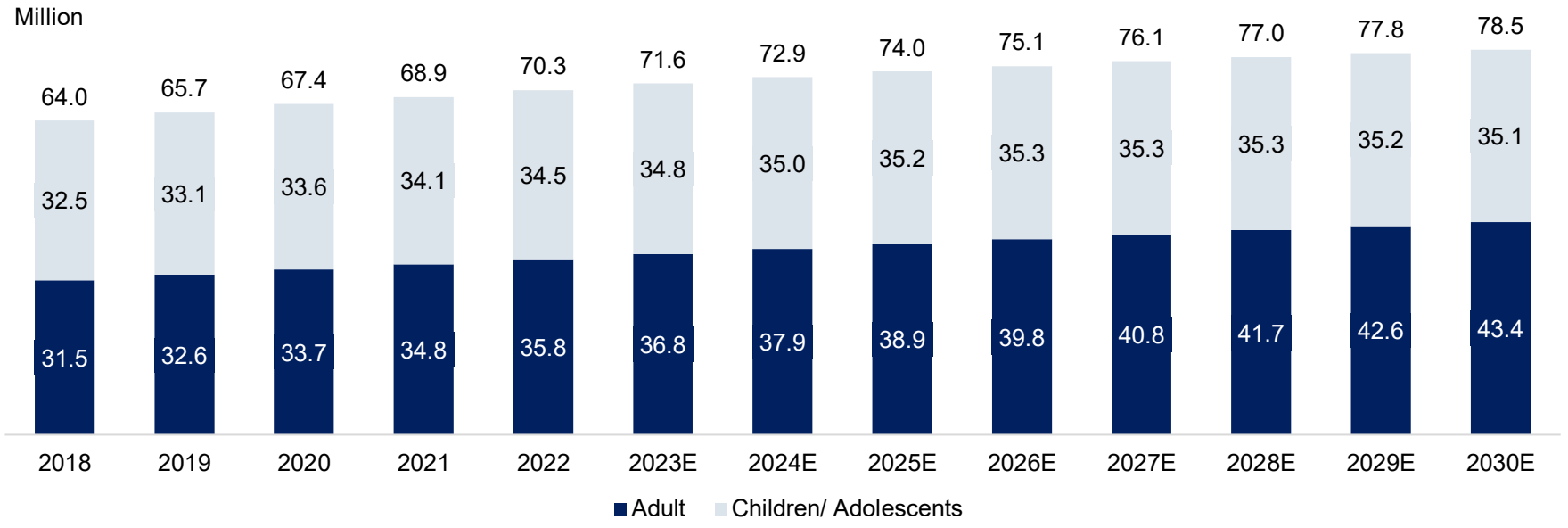
Source: Frost & Sullivan analysis

Prevalence of Atopic Dermatitis in China Breakdown by Age, 2018-2030E

- In China, the number of adult patients affected by atopic dermatitis reached 35.8 million in 2022, with a CAGR of 3.2% from 2018 to 2022, and this number is forecasting to reach 43.4 million in 2030; the number of children/adolescents patients affected by atopic dermatitis reached 34.5 million in 2022, with a CARG of 1.5% from 2018 to 2022 and this number is forecasting to reach 35.1 million in 2030.

Prevalence of Atopic Dermatitis in China Breakdown by Age, 2018-2030E

CAGR	Adult	Children/ Adolescents	Total
2018-2022	3.2%	1.5%	2.3%
2022-2025E	2.8%	0.7%	1.8%
2025E-2030E	2.2%	-0.1%	1.2%



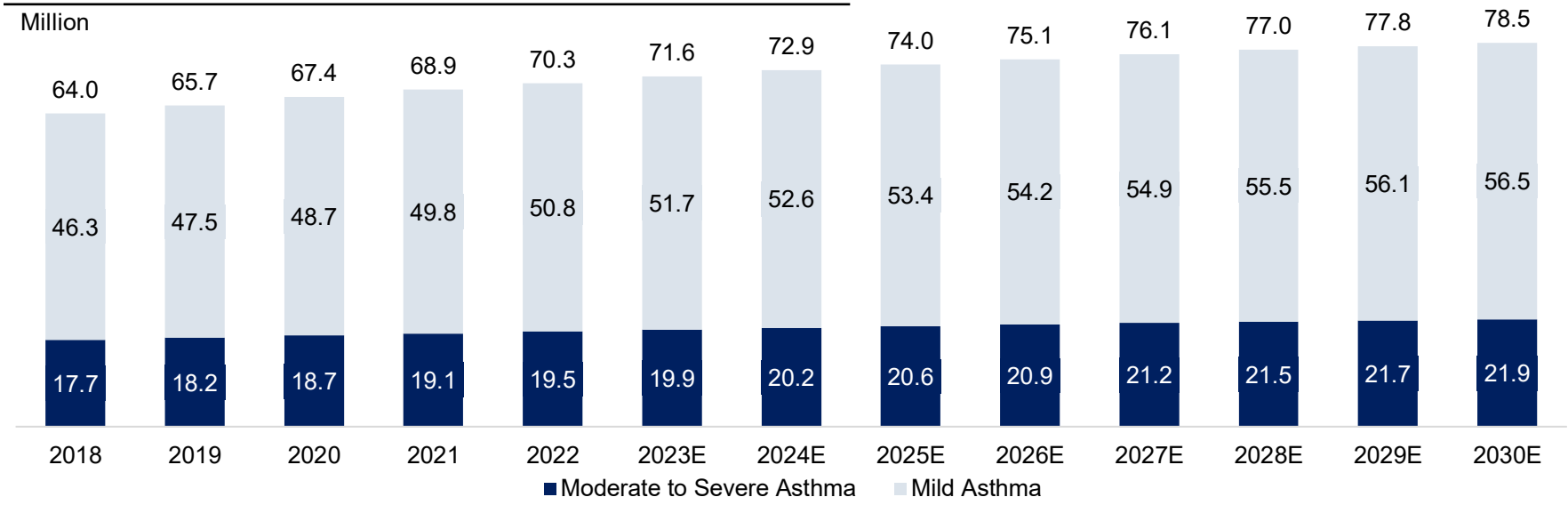
Source: Literature Review, Frost & Sullivan analysis

Prevalence of Atopic Dermatitis in China Breakdown by Severity, 2018-2030E

- In China, the number of patients affected by mild atopic dermatitis reached 34.5 million in 2022, with a CAGR of -7.1% from 2018 to 2022, and this number is forecasting to reach 35.1 million in 2030; the number of patients affected by moderate to severe atopic dermatitis reached 35.8 million in 2021, with a CARG of 19.2% from 2018 to 2022 and this number is forecasting to reach 43.4 million in 2030.

Prevalence of Atopic Dermatitis in China Breakdown by Severity, 2018-2030E

CAGR	Moderate to Severe Asthma	Mild Asthma	Total
2018-2022	2.4%	2.3%	2.3%
2022-2025E	1.9%	1.7%	1.8%
2025E-2030E	1.3%	1.1%	1.2%



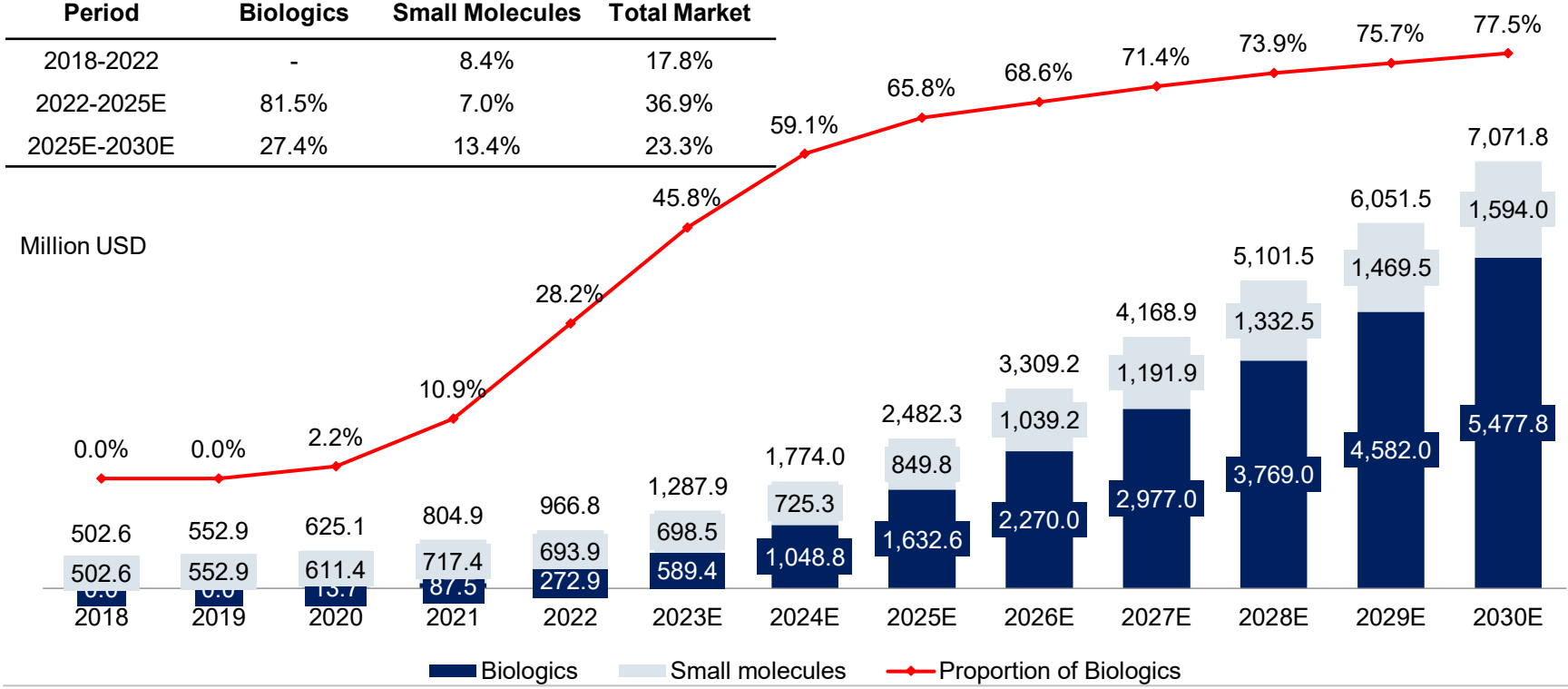
Source: Literature review, Frost & Sullivan analysis

Atopic Dermatitis Drugs Market in China, 2018-2030E

- In China, AD Drugs Market reached USD 966.8 million in 2022 and is expected to increase to USD 2,482.3 million by 2025 at a CAGR of 36.9%. AD Drugs Market is projected to reach USD 7,071.8 million by 2030 at a CAGR of 23.3% after 2025. The CAGR of total market from 2022 to 2030 is 28.2%. AD biologics market is projected to reach USD 1,632.6 billion in 2025 with a CAGR of 81.5% from 2022 to 2025. AD biologics market reached USD 271.9 million in 2022.

Atopic Dermatitis Drugs Market in China, 2018-2030E

Period	Biologics	Small Molecules	Total Market
2018-2022	-	8.4%	17.8%
2022-2025E	81.5%	7.0%	36.9%
2025E-2030E	27.4%	13.4%	23.3%



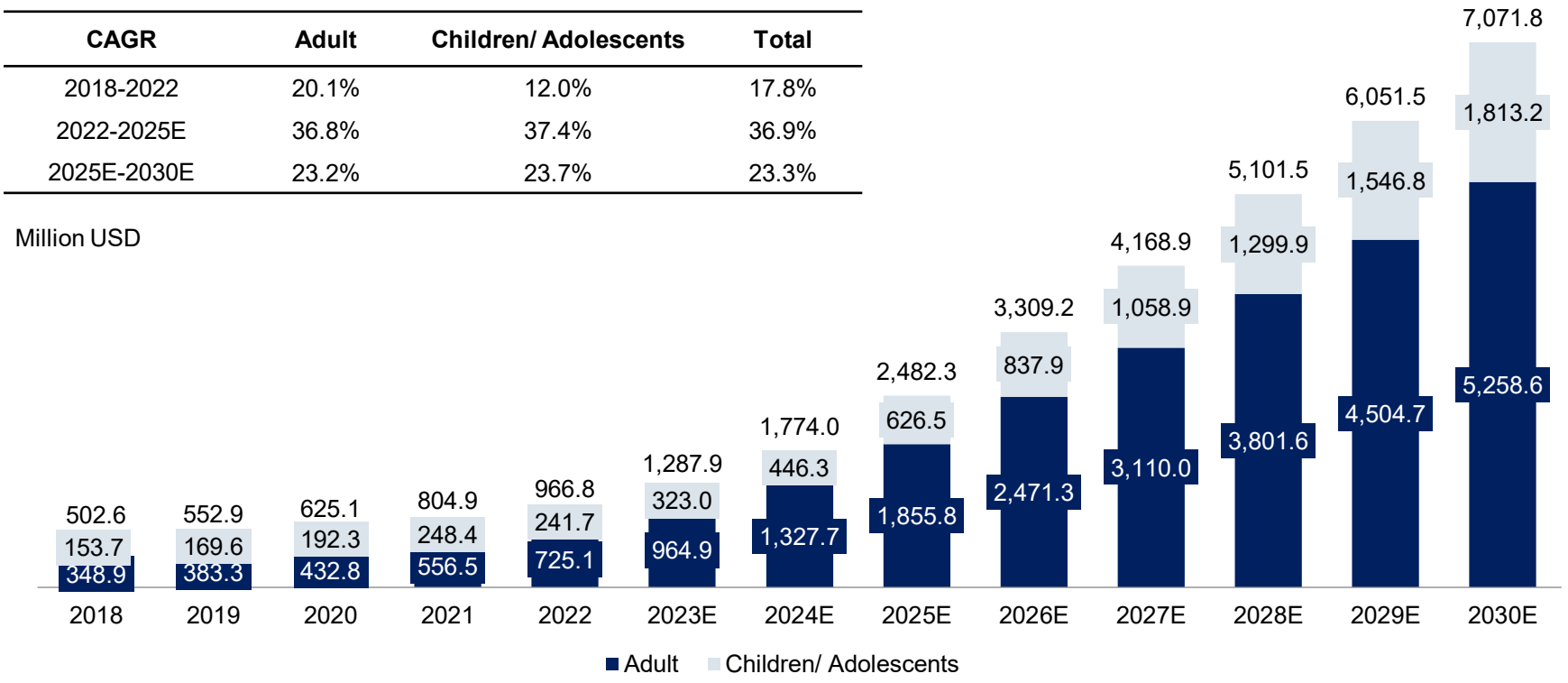
Source: Frost & Sullivan analysis

Atopic Dermatitis Drugs Market in China Breakdown by Age, 2018-2030E

- In China, atopic dermatitis drugs market for adult patients reached USD 725.1 million in 2022 and with a CAGR of 20.1% from 2018 to 2022, and this number is forecasting to reach 5258.6 million in 2030. Atopic dermatitis drugs market for children/adolescents patients reached USD 241.7 million in 2022 and with a CAGR of 12.0% from 2018 to 2022, and this number is forecasting to reach 1831.2 million in 2030.

Atopic Dermatitis Drugs Market in China Breakdown by Age, 2018-2030E

CAGR	Adult	Children/ Adolescents	Total
2018-2022	20.1%	12.0%	17.8%
2022-2025E	36.8%	37.4%	36.9%
2025E-2030E	23.2%	23.7%	23.3%



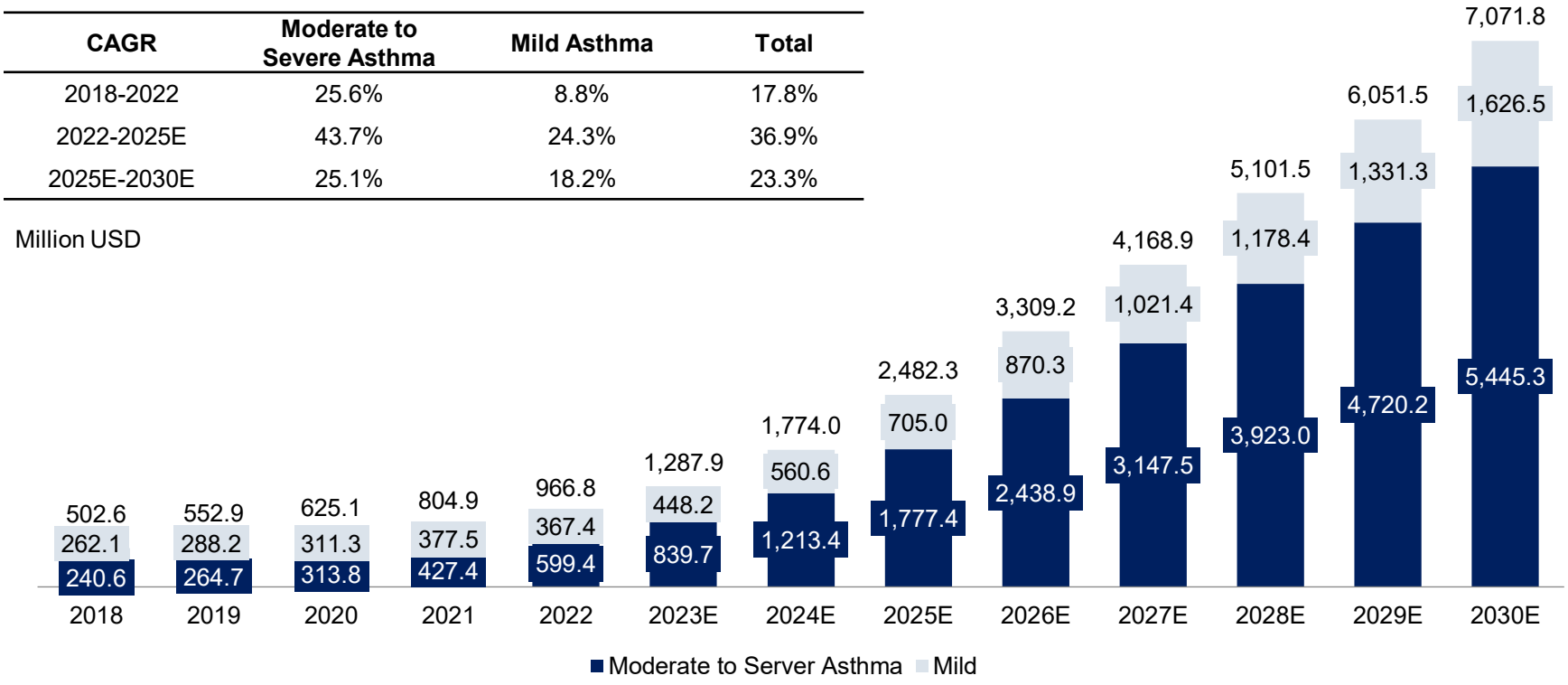
Source: Literature Review, Frost & Sullivan analysis

Atopic Dermatitis Drugs Market in China Breakdown by Severity, 2018-2030E

- In China, atopic dermatitis drugs market for moderate to severe patients reached USD 599.4million in 2022 and with a CAGR of 25.6% from 2018 to 2022, and this number is forecasting to reach 5445.3 million in 2030. Atopic dermatitis drugs market for mild patients reached USD 367.4 million in 2022 and with a CAGR of 8.8% from 2018 to 2022, and this number is forecasting to reach 1626.5 million in 2030.

Atopic Dermatitis Drugs Market in China Breakdown by Severity, 2018-2030E

CAGR	Moderate to Severe Asthma	Mild Asthma	Total
2018-2022	25.6%	8.8%	17.8%
2022-2025E	43.7%	24.3%	36.9%
2025E-2030E	25.1%	18.2%	23.3%



Source: Literature Review, Frost & Sullivan analysis

Atopic Dermatitis Treatment Options in China

- The basic treatment options of atopic dermatitis in China mainly include topical corticosteroids and calcineurin inhibitors. Antiseptics may be added in cases of superinfection. In addition, systemic immunosuppressants are critical therapy choices once atopic dermatitis becomes severe, traditional immunosuppressants and biological immunosuppressants are proven effective in this scenario.

Stepwise Treatment Paradigm for Atopic Dermatitis Patients

Severe Atopic Dermatitis

- Hospitalization
- Systemic application of immunosuppressants，options include CsA, MTX, AZA, and MMF
- Short-term application of systemic corticosteroids
- Biological immunosuppressant: Dupilumab
- NB-UVB or UVA1 phototherapy

+Fundamental treatment

Moderate Atopic Dermatitis

- Applying TCS or TCI based on affected location
- Using wet-wrap therapy when acute attack occurs
- TCS/TCI as active maintenance therapy
- NB-UVB or UVA1 phototherapy

+Fundamental treatment

Mild Atopic Dermatitis

- Applying TCS or TCI based on affected location
- Using oral antihistamine to treat comorbidities(eg, Urticaria and allergic rhinitis) or constant itch
- Anti-infectives

+Fundamental treatment

Fundamental Treatment

- Patient education, bathing, daily moisturizers, avoidance of environmental stimulators and allergens, and necessary food intervention

* Note: PDE-4 inhibitors are recommended in Guideline for Basic Diagnosis and Treatment of AD in China (2022) as other tropical drugs: topical phosphodiesterase-4 (PDE4) Inhibitors (Ciborol Ointment) can be used to treat Mild-to-Moderate patients that are 2-years and older.
Guideline for Diagnosis and Treatment of Moderate-to-severe AD (2023) recommends JAK inhibitors as systemic therapeutic agents: two JAK inhibitors are currently approved in China for the treatment of AD: abcixitinib and upatinib. Prior to the use of JAK inhibitors, a number of screenings are required, including tuberculosis and hepatitis viral infection.

CsA: cyclosporine A; MTX: methotrexate; AZA: azathioprine; MMF: mycophenolate mofetil; TCS: topical corticosteroids; TCI: topical calcineurin inhibitors

Source: Chinese Society of Dermatology, Frost & Sullivan analysis

Unmet Medication Demands of AD

Ineffective existing treatment regimens

- At present, the treatment of atopic dermatitis is based on external drugs such as topical glucocorticoids, oral glucocorticoids and immunosuppressants, due to the lack of pertinence, often the symptoms are not cured, the patient's condition is prone to recurrence, rebound, long-term medication may also bring about obvious side effects such as reduced immunity. According to the "Investigation Report on the Survival Status of Patients with Atopic Dermatitis in China", more than 75% of doctors believe that the existing treatment plan has defects such as poor treatment effect and many side effects

Lack of biologics for the treatment of AD

- Currently, biological agents for the treatment of atopic dermatitis on the market can precisely target the inflammatory pathways related to the pathogenesis of atopic dermatitis, and have been proved to have higher safety and efficacy. However, the number of biologics approved for the treatment of AD is currently very limited, with only one drug approved by the NMPA. It is necessary to develop more effective biologics to meet patients' needs.

Lack of pediatric medication

- Atopic dermatitis is one of the most common diseases in dermatology, most patients develop AD at an early age. However, only Dupixent is currently approved by the FDA to treat patients under 6 years old with uncontrolled moderate-to-severe atopic dermatitis. More biologics for the treatment of atopic dermatitis that are on the market or are in the clinical stage need to be validated for their safety and efficacy in pediatric patients.

Source: Frost & Sullivan analysis

Competitive Landscape of Biologic Treatment in AD in China

Clinical trial status

Marketed Targeted Biologics for AD in China

Target	Brand Name	INN	Company	NMPA Approval Time
IL-4Rα	Dupixent®	Dupilumab	Sanofi / Regeneron	2020-06-17

Biologic Pipeline in AD Treatment in China

Target	Drug Code	Company	Status	First Posted Date
IL-4Rα	CM310(Stapokibart)	Keymed Bioscience	BLA	2023-12-07
	CBP-201	Connect Biopharmaceuticals	Phase Ⅱ	2020-11-20
	TQH2722	Chia Tai-tianqing	Phase Ⅱ	2023-03-27
	QX005N	Qyuns	Phase Ⅱ	2022-07-14
	MG-K10	Mabgeek	Phase Ⅲ	2023-11-29
	SSGJ-611	Sunshine Guojian	Phase Ⅲ	2023-12-18
	SHR-1819	Hengrui	Phase Ⅱ	2022-09-27
	GR1802	Genrix Bio	Phase Ⅲ	2023-12-14
	AK120	Akeso	Phase Ⅰ/Ⅱ	2021-08-20
	BA2101	Boan Bio	Phase Ⅰ	2023-01-16
IL-13	Lebrikizumab	Vetter Pharma	Phase Ⅰ	2024/02/18
	Cendakimab	BMS	Phase Ⅰ	2022-11-17
TSLP	CM326	Keymed Bioscience	Phase Ⅱ	2022-08-25
	GR2002	Genrix Bio	Phase Ⅰ	2023-11-27
IL-33	MEDI3506	AstraZeneca	Phase Ⅰ	2021-09-22
ST2	9MW1911	Mabwell	Phase Ⅰ	2021-10-13
CD200R	LY3454738	Lilly	Phase Ⅱ	2023-08-23
OX40	AMG 451	Amgen	Phase Ⅲ	2023-07-11
	Amlitelimab	Genzyme	Phase Ⅱ	2024/02/20
	IBI356	Innovent Bio	Phase Ⅰ	2023-12-25
	BAT6026	Biothera Biopharmaceutical	Phase Ⅰ/Ⅱ	2023-06-12
IL-2R	SIM0278	Simcere	Phase Ⅰ	2023-08-15
IL-17RB	SM17	Sinolink Pharma	Phase Ⅰ	2023-10-07

*This table was last updated on Mar 2nd , 2024

Source: NMPA, CDE, Frost & Sullivan analysis

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Overview of CRS

- Rhinosinusitis (RS) refers to the presence of inflammation in the paranasal sinuses mucosa (i.e., the lining of the sinuses) and the contiguous mucosa of the nasal passages.
- If the inflammation is present for more than 12 weeks, then chronic rhinosinusitis (CRS) is present.
- CRS is classified into 2 phenotypes, CRS with nasal polyps (CRSwNP) and CRS without nasal polyps (CRSsNP).

Symptoms

- Nasal blockage / obstruction / congestion
- Nasal discharge (anterior / posterior nasal drip)
- Facial pain/pressure
- Reduction or loss of smell;

Risk Factors

- Allergy
- Bacterial Infection
- Biofilms
- Fungal Infection
- Genetic Disorders
- Osteitis
- Mucociliary Dysfunction
- OMC Compromise
- Staphylococcal Superantigen
- Miscellaneous

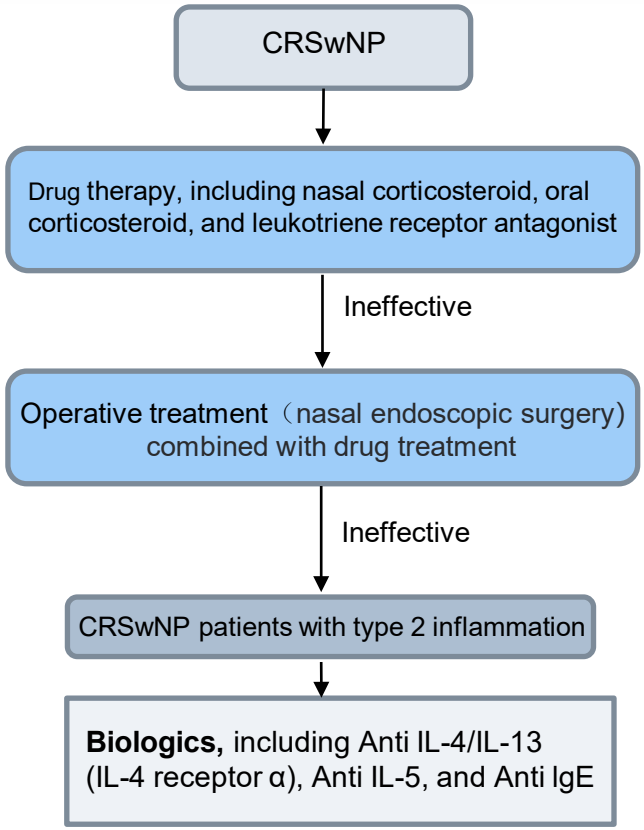
Inflammatory mechanisms

- **Type 1 cytokines:**
  - *Include IFN-gamma (**IFN-g**) and **IL-12** with the response geared towards addressing **viral** pathogens*
- **Type 2 cytokines:**
  - ***IL-4, IL-5, and IL-13**, which promote anti-helminth **immunity** and regulate tissue regeneration following injury*
- **Type 3 cytokines**:
  - *Include **IL-17A and IL-22** with immunologic effects directed against **extracellular bacteria and fungi***

Source: TEXAS SINUS INSTITUTE, EPOS2020, Frost & Sullivan analysis

Treatment paradigm of CRSwNP in China

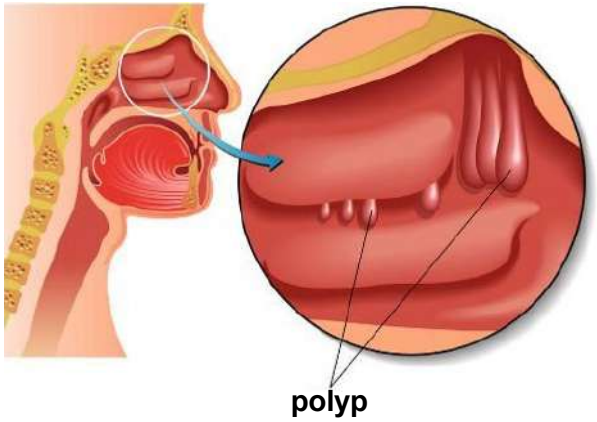
- Currently the standard of care for CRSwNP contains drug treatment, including corticosteroid as well as leukotriene receptor antagonist, and operation. Biologics are used in patients with type 2 inflammation who do not respond well to surgery and medical treatment.
- The diagram below illustrates the recommended treatment paradigm for CRSwNP in China.

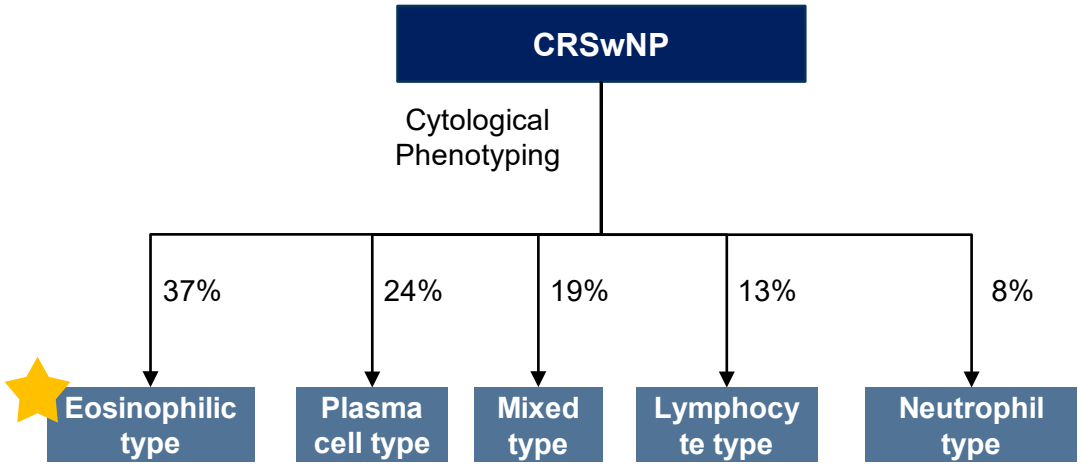


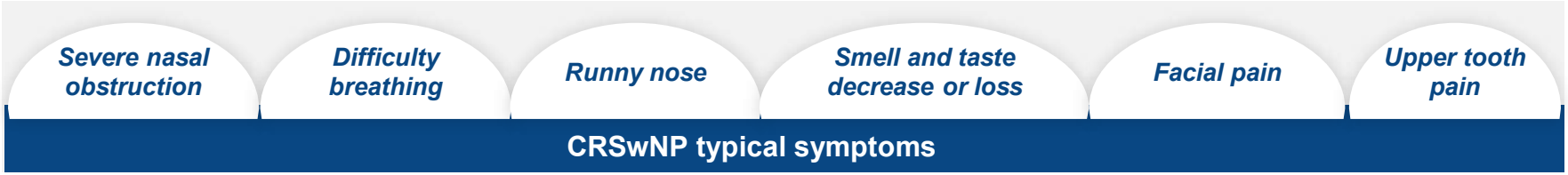
Source: Chinese guidelines for diagnosis and treatment of chronic rhinosinusitis (2018), Chinese Expert Consensus on the Use of Biologics in Patients with Chronic Rhinosinusitis (2022), Frost & Sullivan analysis

Overview of CRSwNP

- Chronic rhinosinusitis with nasal polyps (CRSwNP) is defined as a subgroup of chronic rhinosinusitis (CRS) that is characterized by the presence of fleshy swellings (nasal polyps) that develop in the lining of the nose and paranasal sinuses.
- CRSwNP is mostly characterized by a moderate to severe T helper type 2 (T2)-mediated inflammation with hypereosinophilia and increased IgE concentrations.
- Patients with CRSwNP generally account for 15-25% of all CRS patients.







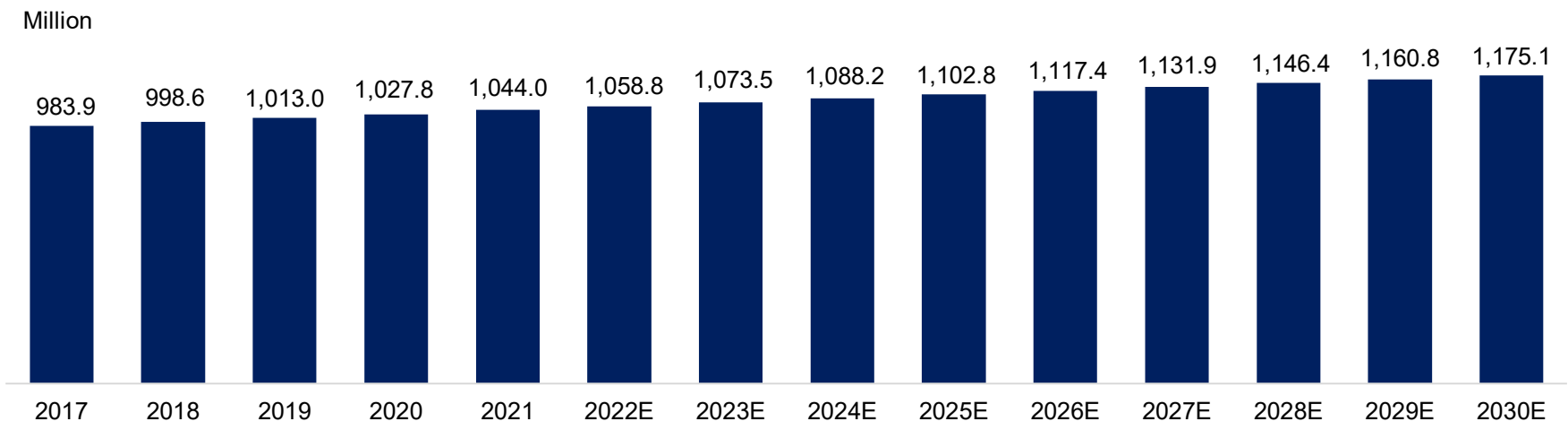
Source: Literature Review, Frost & Sullivan analysis

Global Prevalence of CRS, 2017-2030E

- The number of patients with CRS was 1,044.0 million in 2021, with a CAGR of 1.5% during 2017 and 2021. This number is expected to rise and approach 1,102.8 million in 2025 and 1,175.1 million in 2030, respectively.

Global Prevalence of CRS, 2017-2030E

Period	CAGR
2017-2021	1.5%
2021-2025E	1.4%
2025E-2030E	1.3%



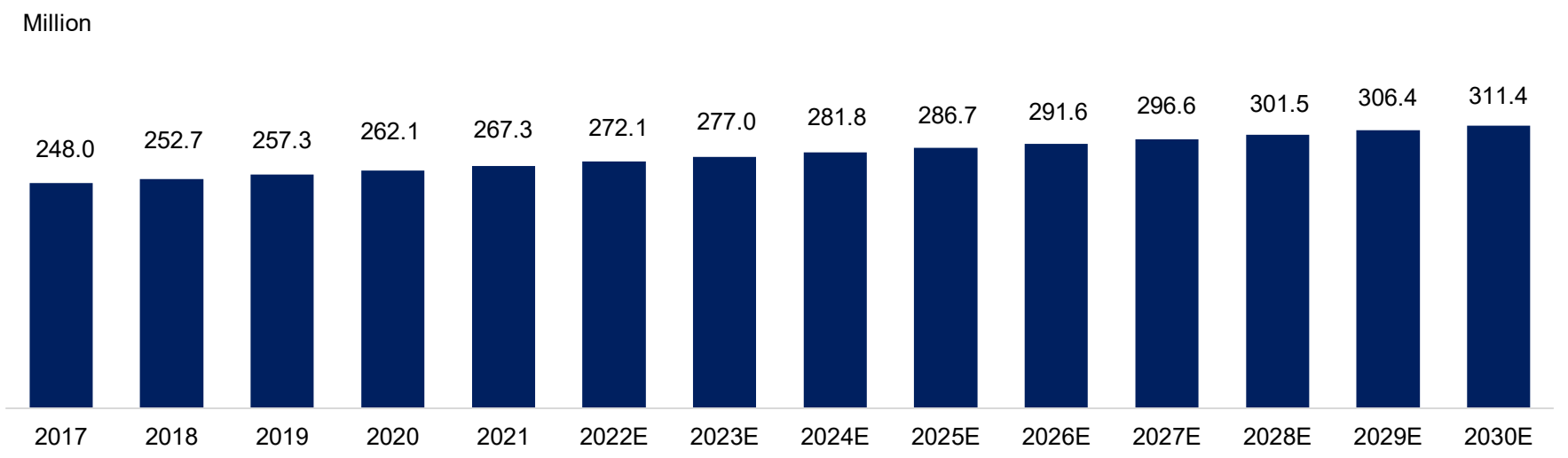
Source: Literature review, Frost & Sullivan analysis

Global Prevalence of CRSwNP, 2017-2030E

- The number of patients with CRSwNP was 267.3 million in 2021, with a CAGR of 1.9% during 2017 and 2021. This number is expected to rise and approach 286.7 million in 2025 and 311.4 million in 2030, respectively.

Global Prevalence of CRSwNP, 2017-2030E

Period	CAGR
2017-2021	1.9%
2021-2025E	1.8%
2025E-2030E	1.7%



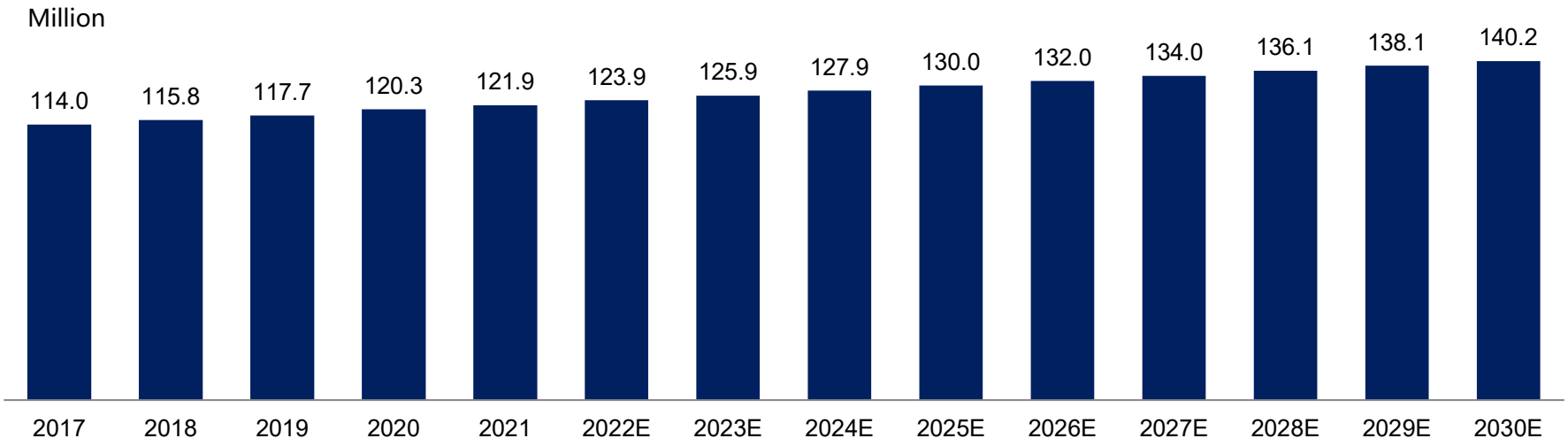
Source: Literature review, Frost & Sullivan analysis

Prevalence of CRS in China，2017-2030E

- According to epidemiology studies, the prevalence of CRS in China had reached 121.9 million in 2021, with a CAGR of 1.7% from 2017 to 2021. The number of patients is expected to reach 140.2 million in 2030.

Prevalence of CRS in China，2017-2030E

Period	CAGR
2017-2021	1.7%
2021-2025E	1.6%
2025E-2030E	1.5%



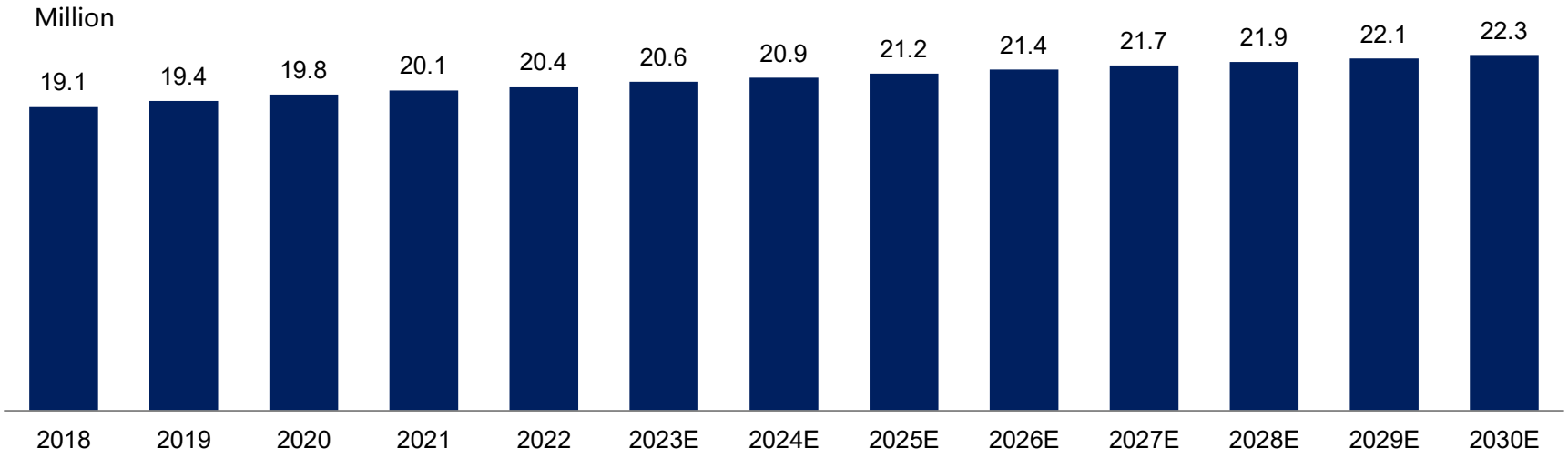
Source: Frost & Sullivan analysis

Prevalence of CRSwNP in China，2018-2030E

- According to epidemiology studies, the prevalence of CRSwNP in China had reached 20.4 million in 2022, with a CAGR of 1.6% from 2018 to 2022. The number of patients is expected to reach 22.3 million in 2030.

Prevalence of CRSwNP in China，2018-2030E

Period	CAGR
2018-2022	1.6%
2022-2025E	1.3%
2025E-2030E	1.1%



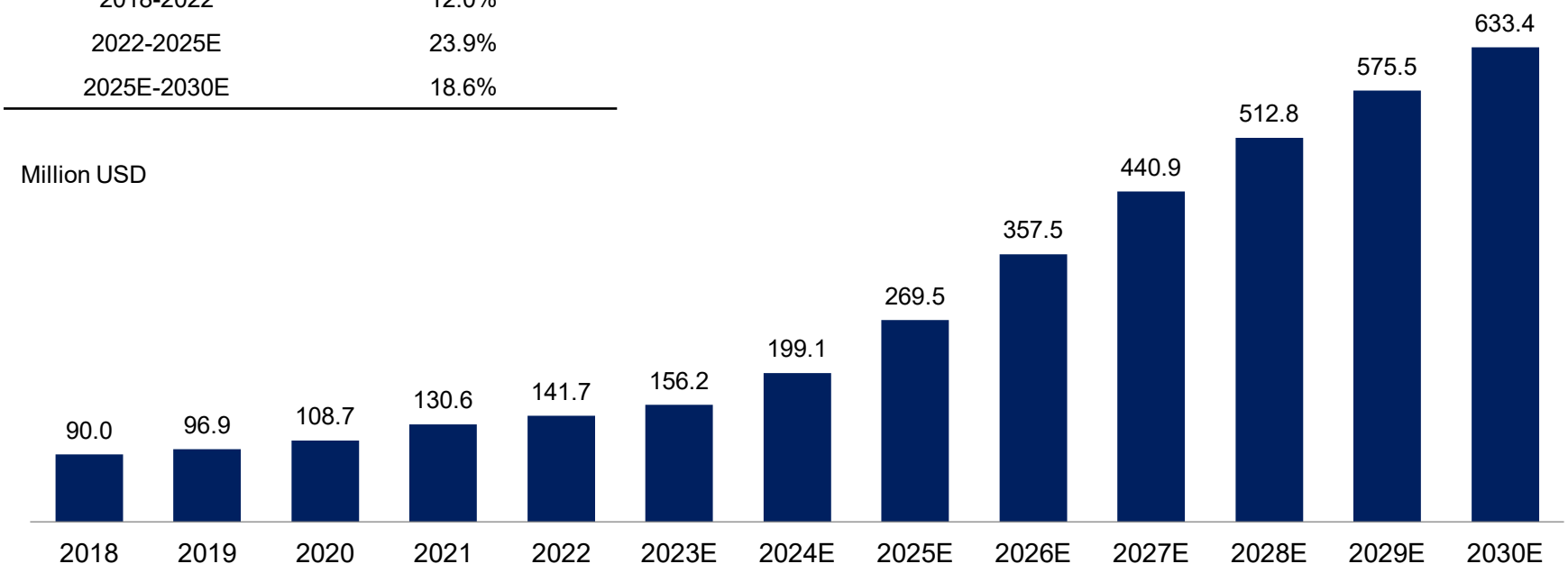
Source: Frost & Sullivan analysis

CRSwNP Drugs Market in China, 2018-2030E

- In China, CRSwNP Drugs Market reached USD 141.7 million in 2022 and is expected to increase to USD 269.5 million by 2025 at a CAGR of 23.9%. CRSwNP Drugs Market is projected to reach USD 633.4 million by 2030 at a CAGR of 18.6% after 2025. The CAGR from 2022 to 2030 is projected to reach 20.6%.

CRSwNP Drugs Market in China, 2018-2030E

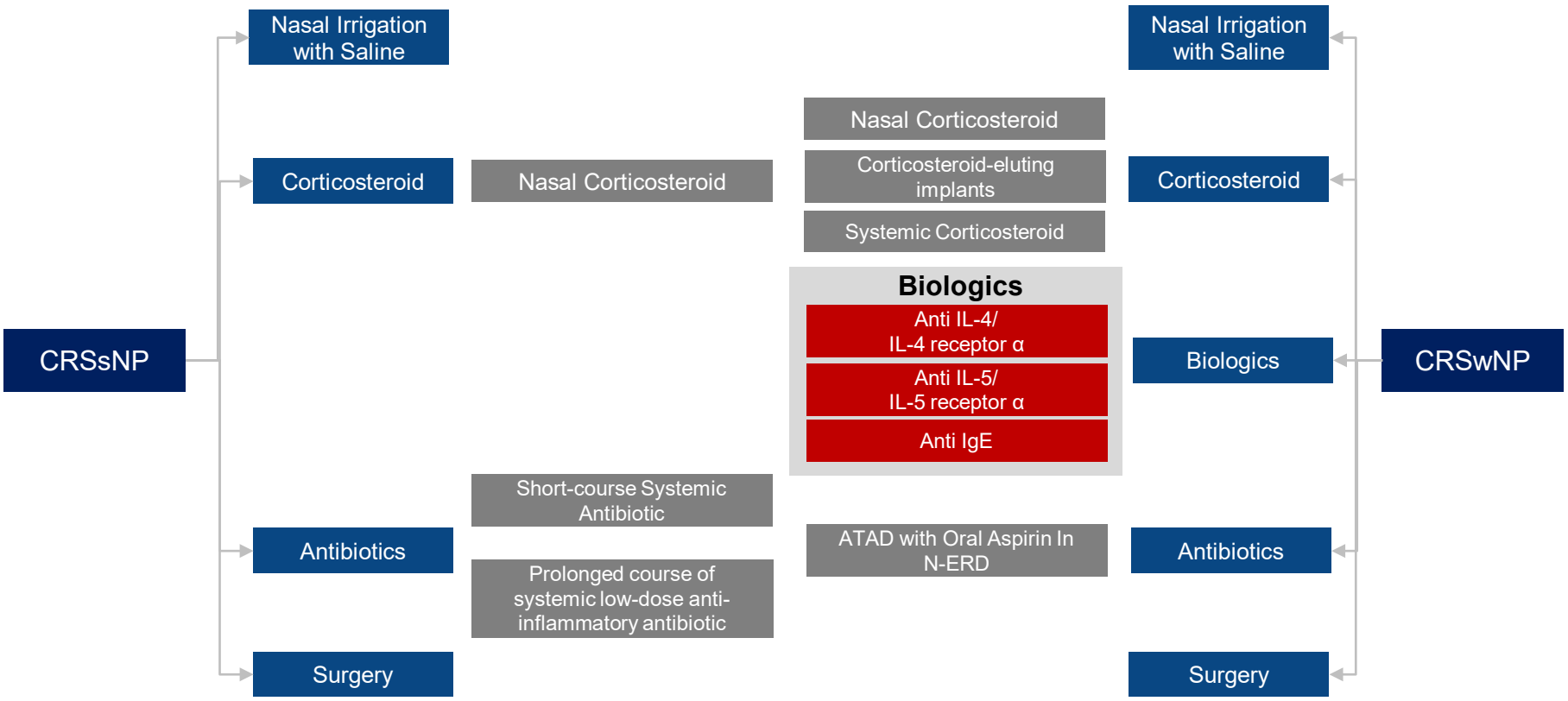
Period	CAGR
2018-2022	12.0%
2022-2025E	23.9%
2025E-2030E	18.6%



Source: Frost & Sullivan analysis

Treatment Paradigm of CRS

- CRS is a challenging condition to cure, and the patients usually need appropriate long-term treatment plans to manage symptoms. Biologics can be used for the treatment of CRSwNP, especially refractory CRSwNP, which can achieve good results. Dupixent is the first and so far the only biologics for the treatment of CRSwNP. EMA and FDA accepted GSK's fling of Nucala for use in CRSwNP in 2020, once approved, it will become the first anti-IL-5 biologic for CRSwNP.
- When glucocorticoids couldn't prove efficiency, biological treatment can reduce polyps and improve the patient's nasal ventilation function.
- Surgical treatment will only be applied to CRSwNP refractory CRSsNP.



ATAD: Aspirin Treatment After Desensitization; N-ERD: NSAID-exacerbated respiratory disease

Source: EPOS2020, Frost & Sullivan analysis

Unmet Medication Demands of CRSwNP

Ineffective drugs and side effects

- Evidence-based recommendations for the management of CRSwNP call for the use of intranasal and oral corticosteroids/systemic corticosteroid(SCS). There is good evidence that both intranasal corticosteroids and SCS are effective to some extent in the management of CRSwNP. However, there are also limitations with these treatments, and their short-lived benefits need to be balanced with the need for long-term control and safety. Existing data support the infrequent use of SCS in the immediate- and short-term periods for patients with CRSwNP; however, their long-term benefits are limited. SCS treatment can lead to serious treatment-related adverse effects, and even short-term corticosteroid use is associated with an increased risk of acute complications such as sepsis, venous thromboembolism, and fracture.

Lack of biologics for the treatment of CRSwNP

- Biologics are proved to be more effective and safer in the treatment of CRSwNP both experimentally and clinically. As of now, only Dupilumab, Omalizumab and Mepolizumab are approved in the EU and US as add-on therapy in adult patients with severe CRSwNP who are inadequately controlled with intranasal corticosteroids. The availability of these targeted therapies could significantly improve the management of patients with CRSwNP, but needs remain unmet. It is noting that no biologics have been approved in China to treat CRSwNP, and the number of drugs in the clinical stage is very small.

Source: Frost & Sullivan analysis

Global Competitive Landscape of Biologics in CRSwNP Treatment

Clinical trial status

FDA Approved Targeted Biologics for CRSwNP

Brand Name	INN	Company	Target	FDA Approval Time
Dupixent®	Dupilumab	Sanofi/ Regeneron	IL-4Rα	2019-06-26
Xolair	Omalizumab	Roche	IgE	2020-12-01
Nucala®	Mepolizumab	GSK	IL-5	2021-07-29

Global Biologic Pipeline in CRSwNP Treatment

Drug Code	Company	Target	Status	First Posted Date
Benralizumab	AstraZeneca	IL-5Rα	Phase Ⅲ	2019-11-08
Tezepelumab	AstraZeneca/Amgen	TSLP	Phase Ⅲ	2021-04-21
GSK3511294(Depemokimab)	GSK	IL-5	Phase Ⅲ	2022-03-10
CBP-201	Connect Biopharmaceuticals	IL-4Rα	Phase Ⅱ	2021-03-05

*This table was last updated on May 5, 2022, first table update to Mar 2nd , 2024

Source: FDA, Frost & Sullivan analysis

Competitive Landscape of Biologics in CRSwNP Treatment in China

Clinical trial status

Marketed Targeted Biologics for CRSwNP in China

There are currently no biologics approved by NMPA for the treatment of CRSwNP.

Biologic Pipeline in CRSwNP Treatment in China

Target	Drug Code	Company	Status	First posted Date
IL-4Rα	CM310	Keymed Bioscience	Phase Ⅲ	2022-06-20
	GR1802	Genrix Bio	Phase Ⅱ	2023-01-03
	QX005N	Qyuns	Phase Ⅱ	2023-01-06
	Dupilumab	Sanofi	Phase Ⅲ	2023-03-24
	SSGJ-611	Sunshine Guojian	Phase Ⅱ	2023-04-27
IL-5	Mepolizumab	GSK	Phase Ⅲ*	2021-04-12
	Depemokimab	GSK	Phase Ⅲ	2022-05-20
	Mepolizumab-BAT2606	Bio-Thera	Phase Ⅰ	2022-07-27
TSLP	Tezepelumab	Amgen/AstraZeneca	Phase Ⅲ	2021-03-25
	SHR-1905	Hengrui	Phase Ⅱ	2023-05-29
	TQC2731	Chia Tai-tianqing	Phase Ⅱ	2023-08-01
	CM326	Keymed Bioscience	Phase Ⅰ/Ⅱ	2022-03-14
IL-5Rα	Benralizumab	AstraZeneca	Phase Ⅲ	2020-06-02

*This table was last updated on Mar 2nd , 2024

GSK has submitted BLA application again for Mepolizumab in China on 2024-02-06, but detailed indication for this submission was not disclosed officially

Source: NMPA, CDE, Frost & Sullivan analysis

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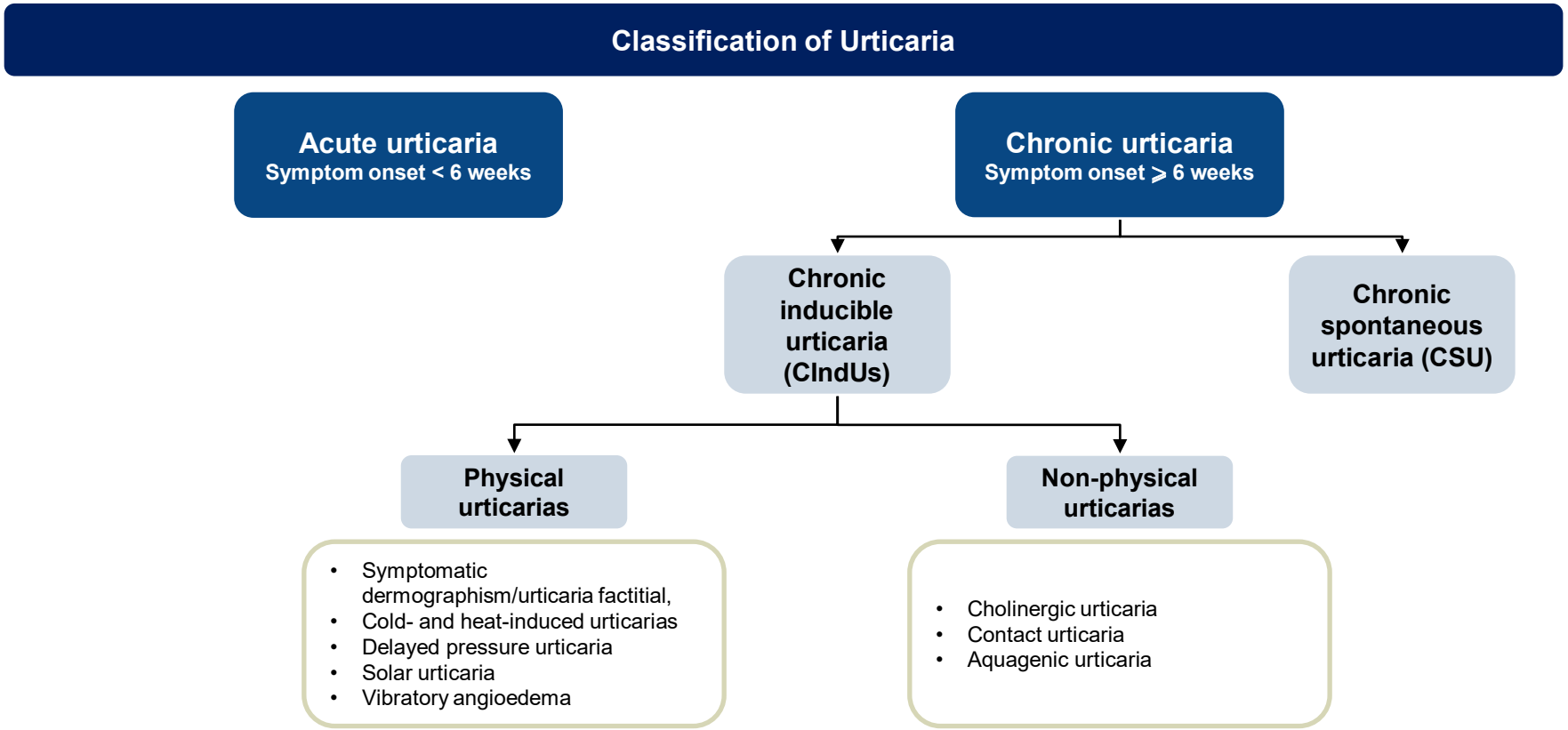
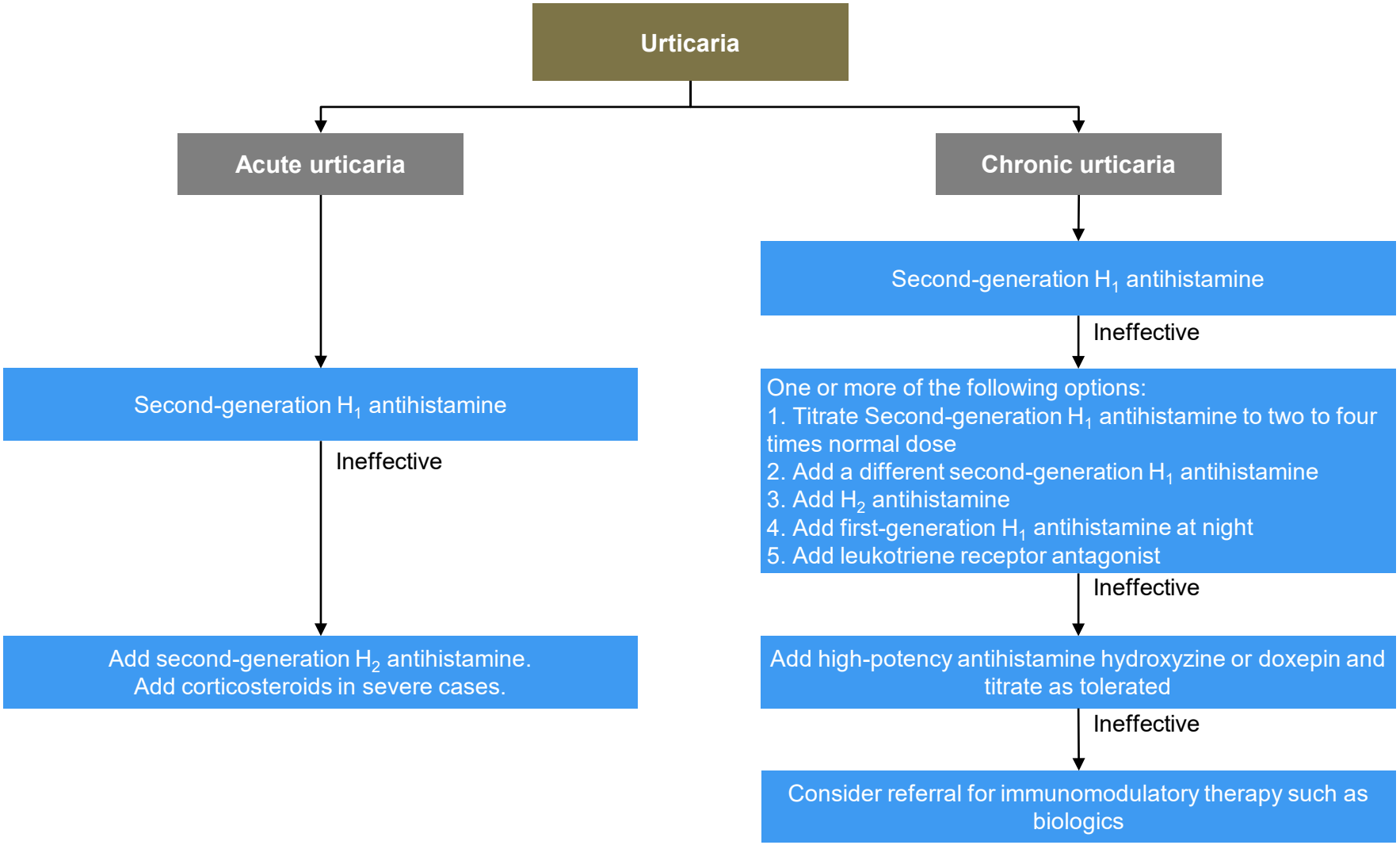
Overview and Classification of Urticaria

- Urticarial is an allergic disease that causes classic Type I hypersensitivity reaction, which can be triggered by diverse causes.
- Urticarial is characterized to be profoundly itchy, slightly raised skin lesions ranging from 1 mm to 10 cm in size, that are stimulated by skin contact. Interestingly, urticarial can 'come and go' in a short time.
- Occurrence of urticarial is often acute and short, which often lasts for several days to a week. Nevertheless, there is a chance that urticarial will become a chronic disease, which lasts for longer than 6 weeks.



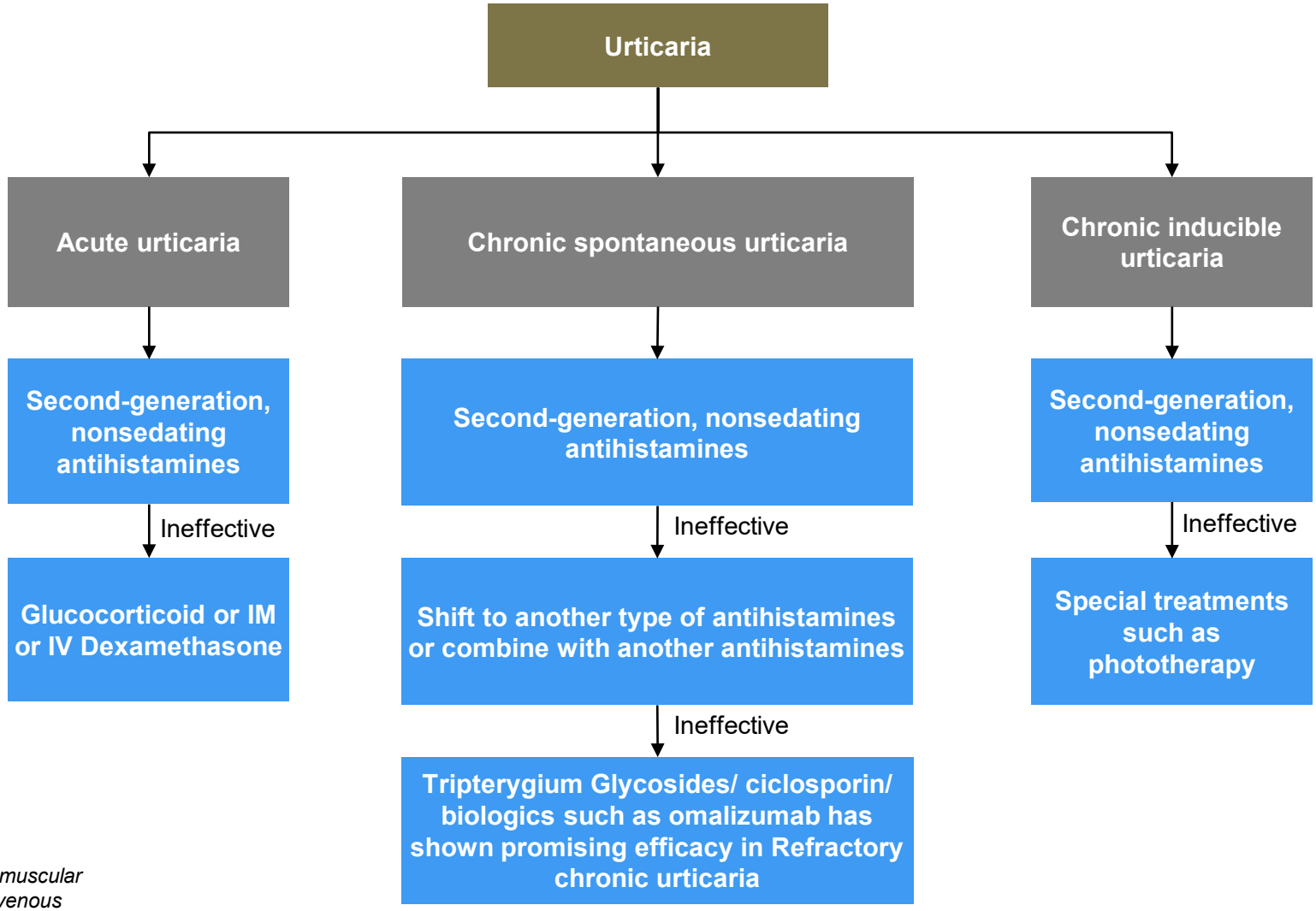
Source: Literature Review, Frost & Sullivan analysis

Treatment Paradigm of Urticaria in the USA



Source: Acute and Chronic Urticaria: Evaluation and Treatment, Frost & Sullivan analysis

Treatment Paradigm of Urticaria in China



IM: Intramuscular
IV: Intravenous

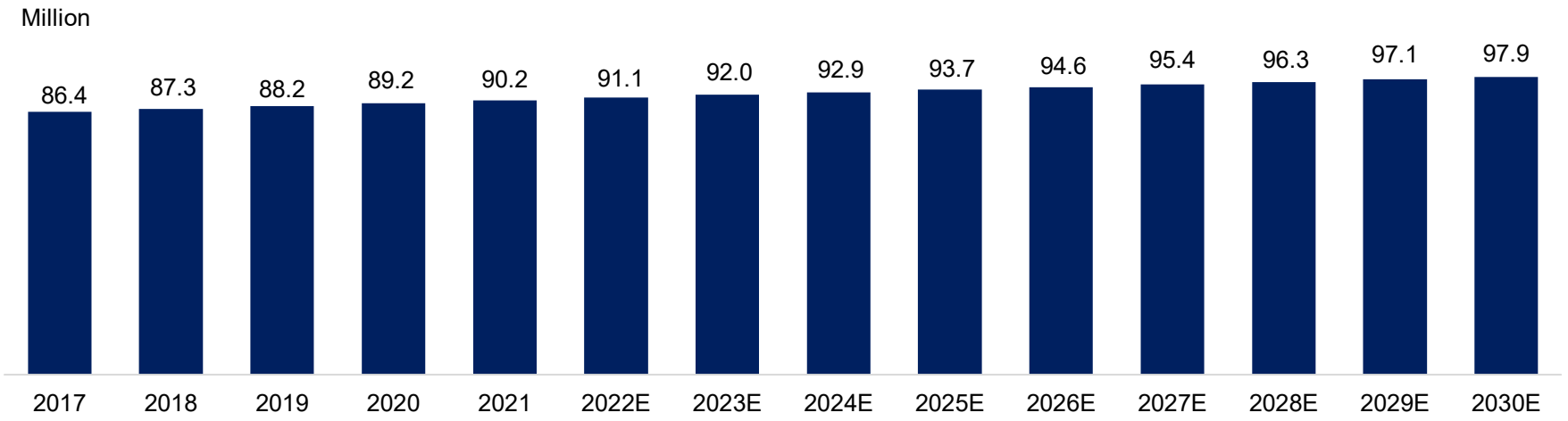
Source: Diagnosis and treatment of urticaria in China (2018 ver.), Frost & Sullivan analysis

Global Prevalence of Chronic Urticaria, 2017-2030E

- The number of patients with Chronic urticaria was 90.2 million in 2021, with a CAGR of 1.1% during 2017 and 2021. This number is expected to rise and approach 93.7 million in 2025 and 97.9 million in 2030, respectively.

Global Prevalence of Chronic Urticaria, 2017-2030E

Period	CAGR
2017-2021	1.1%
2021-2025E	1.0%
2025E-2030E	0.9%



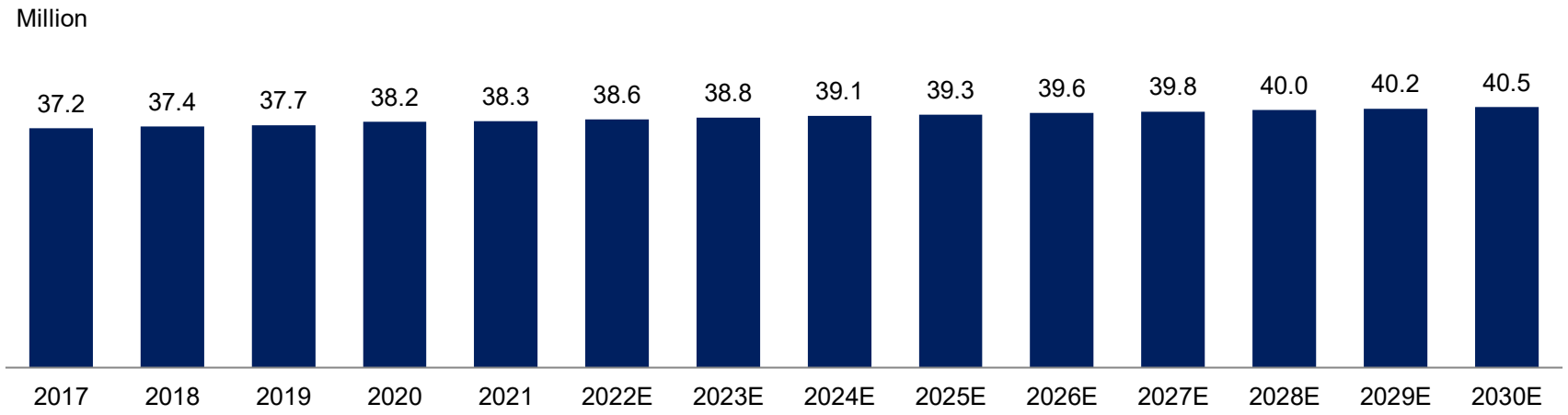
Source: Literature review, Frost & Sullivan analysis

Prevalence of Chronic Urticaria in China, 2017-2030E

- In 2021, the number of chronic urticaria patients in China is 38.3 million and the prevalence of chronic urticaria is expected to increase slightly in the next few decades. The number of chronic urticaria patients in China is expected to reach 40.5 million by 2030.

Prevalence of Chronic Urticaria in China, 2017-2030E

Period	GAGR
2017-2021	0.8%
2021-2025E	0.7%
2025E-2030E	0.6%



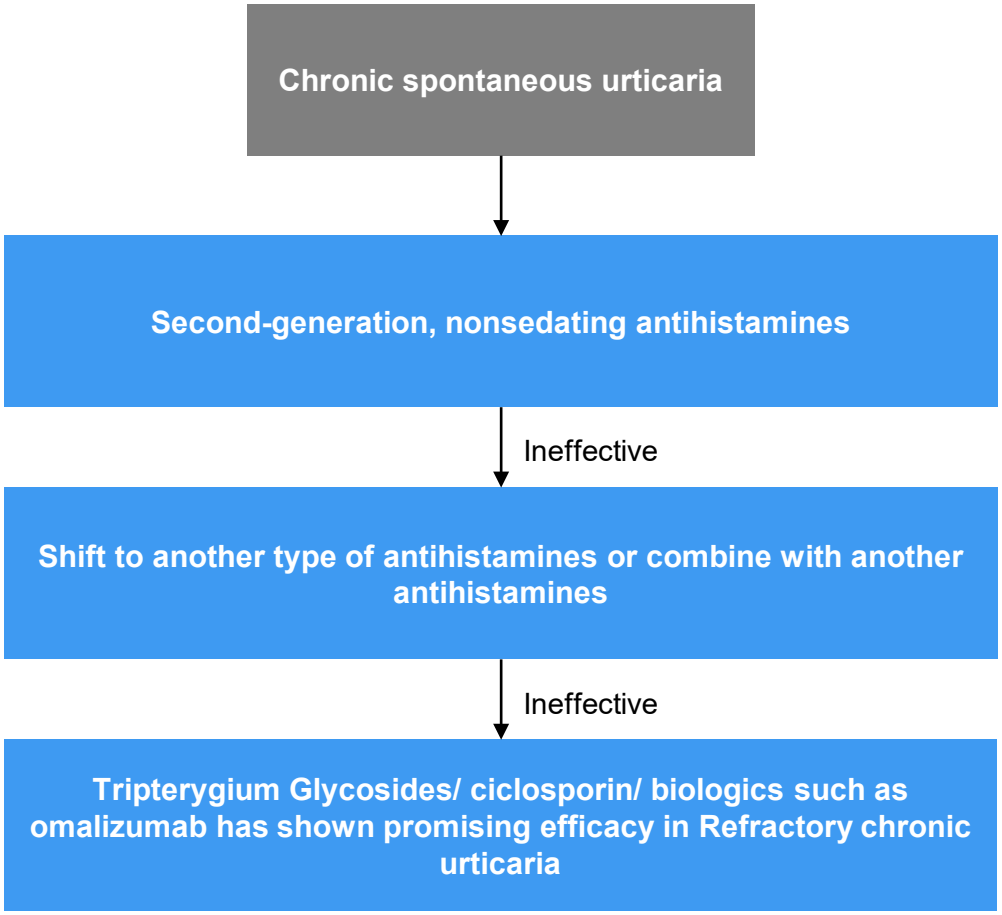
Source: Literature Review, Frost & Sullivan analysis

Unmet Medication Demands of Urticaria

Ineffective controlling of urticaria among all patients	• The most common first-line treatment of urticaria is H_1 antihistamines. However, up to 50% of patients do not fully respond to H_1 antihistamines. More effective treatments for a wider range of urticaria patients are needed.
Frequent side effects	• Due to the low efficacy of first-line treatment among up to half of urticaria patients, it is necessary to titrate the antihistamine dosage up for higher potency and efficacy, which will subsequently result in more severe side effects among patients. Therefore, a potent and effective treatment option with limited side effects is to be sought.
Uncontrollable of long urticaria duration	• Urticaria, especially CSU, has a long duration among some patients. The duration generally lasts for 1-5 years and could be longer in more severe cases. The long duration of CSU not only poses negative effects on patient's health condition, but also other aspects such as financial and psychological conditions of patients. Therefore, new effective therapeutic strategies that can effectively cure the disease and shorten the disease duration are urgently demanded.

Source: Frost & Sullivan analysis

Treatment Paradigm of Chronic Spontaneous Urticaria in China



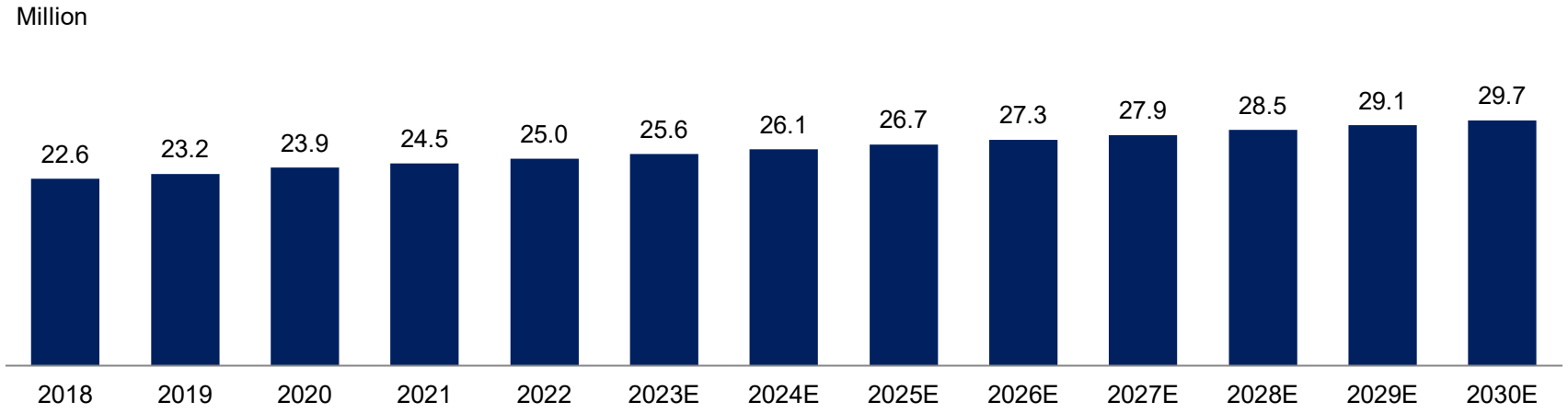
Source: Diagnosis and treatment of urticaria in China (2018 ver.), Frost & Sullivan analysis

Prevalence of Chronic Spontaneous Urticaria in China, 2018-2030E

- In 2022, the number of chronic spontaneous urticaria patients in China is 25.0 million, with a CAGR of 2.5% during 2018 and 2022. The number of chronic spontaneous urticaria patients in China is expected to reach 29.7 million by 2030.

Prevalence of Chronic Spontaneous Urticaria, 2018-2030E

Period	GAGR
2018-2022	2.5%
2022-2025E	2.3%
2025E-2030E	2.1%



Source: Literature Review, Frost & Sullivan analysis

Competitive Landscape of Biologics in Chronic Spontaneous Urticaria Treatment in China

Clinical trial status

Marketed Targeted Biologics for Chronic Spontaneous Urticaria in China

Brand Name	INN	Company	Target	First Posted Date
Xolair	Omalizumab	Novartis	IgE	2022-04-13

Biologic Pipeline for for Chronic Spontaneous Urticaria Treatment in China

Target	Drug Code	Company	Status	First Posted Date
IgE	Omalizumab-SYN008	BKSW	BLA	2023-06-21
	UB-221	United Biopharma	Phase Ⅱ	2023-11-14
	LP-003	LongBio Pharma	Phase Ⅱ	2023-10-27
IL-4Rα	Dupilumab	Sanofi	Phase Ⅲ	2020-04-24
	GR1802	Genrixbio	Phase Ⅱ	2023-03-03
	BA2101	Boan Biotech	Phase Ⅰ	2023-01-16

*This table was last updated on Mar 2nd , 2024

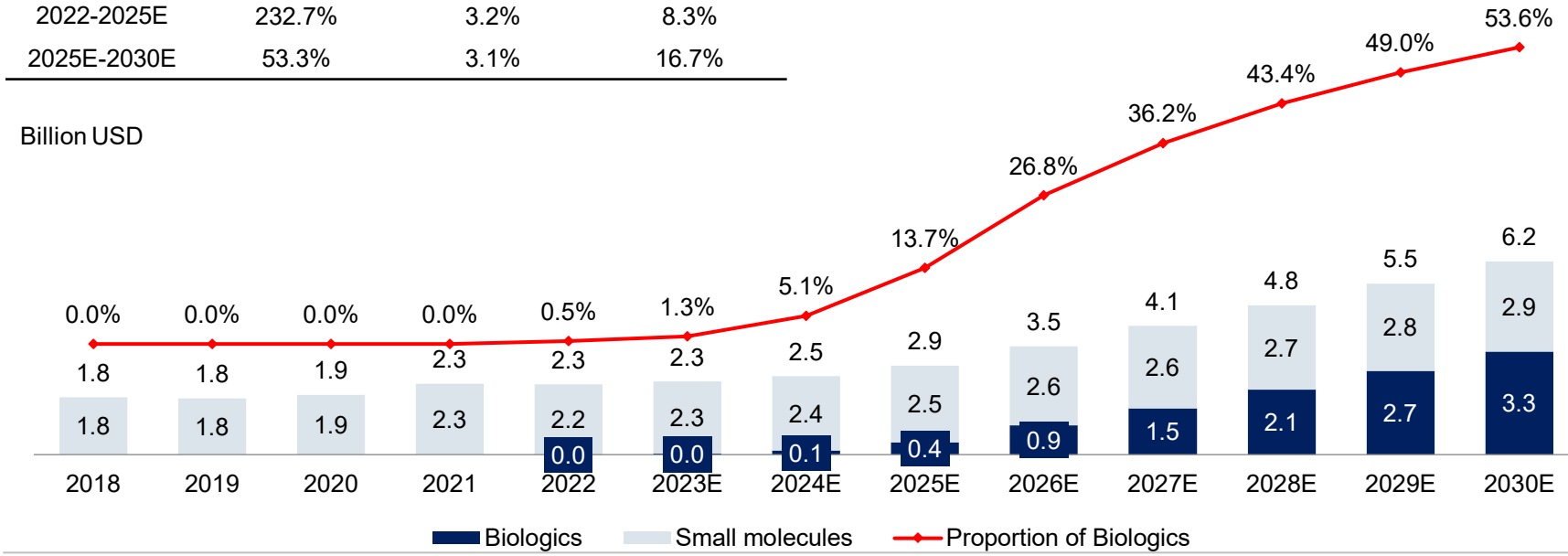
Source: MNPA, Clinical Trials, Frost & Sullivan analysis

CSU Drugs Market in China, 2018-2030E

- In China, CSU Drugs Market reached USD 2.3 billion in 2022 and is expected to increase to USD 2.9 billion by 2025 at a CAGR of 8.3%. CSU Drugs Market is projected to reach USD 6.2 billion by 2030 at a CAGR of 16.7% after 2025. CSU biologics market is projected to reach USD 0.4 billion in 2025. CSU biologics market is projected to reach USD 3.3 billion in 2030 with a CAGR of 53.3% from 2025 to 2030.

CSU Drugs Market in China, 2018-2030E

Period	Biologics	Chemical	Total Market
2018-2022	-	5.0%	5.1%
2022-2025E	232.7%	3.2%	8.3%
2025E-2030E	53.3%	3.1%	16.7%



Source: Frost & Sullivan analysis

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Overview of COPD

- COPD is recognized as a disease with a heavy medical burden globally and there remain large unmet needs for the evaluation and treatment of patients with COPD, especially in the aspects of misdiagnosis.
- COPD will cause de destruction of barriers between alveoli inside lungs, causing airways to get swollen and clogged with mucus. Stale air then gets stuck inside the lung and it becomes harder for the lung to get enough fresh oxygen with each breath. In most cases, COPD develops very slowly, symptoms may come over years before being diagnosed.
- According to public information and literature review, it is being increasingly recognized that approximately 20 percent to 40 percent of patients with COPD have a predominant type 2 inflammation, this is commonly detected by elevated blood eosinophil counts.

Key Symptoms:

- Breathing difficulty
- Cough
- Mucus (Sputum) production and wheezing

Cause of disease:

- Long-term exposure to irritating gases like chemical fumes or toxic substances at work
- Particular matter (most frequently cigarette smoke and secondhand smoke)
- Genetic reasons, defect in DNA called “alpha-1 antitrypsin deficiency”
- Untreated asthma

Stage One	Mild COPD
GOLD Standard	FEV_1 about 80% or more of normal
Clinical Features	Slight limitations to breathing, some patients would experience cough and phlegm
Stage Two	**Moderate COPD**
GOLD Standard	FEV_1 between 50% and 80% of normal
Clinical Features	More coughing and mucus production, medical care needed for breathing limitation treatment
Stage Three	**Severe COPD**
GOLD Standard	FEV_1 between 30% and 50% of normal
Clinical Features	Large impact on patient’s quality of life, easy to feel fatigue and have difficulty exercising
Stage Four	**End-Stage COPD**
GOLD Standard	Lower FEV_1 than stage 3 or low blood oxygen levels
Clinical Features	Affects patient’s life profoundly, life-threatening flare-ups and breathing issues, having trouble with oxygen receiving and develop hypoxia or hypoxemia, cyanosis and other symptoms

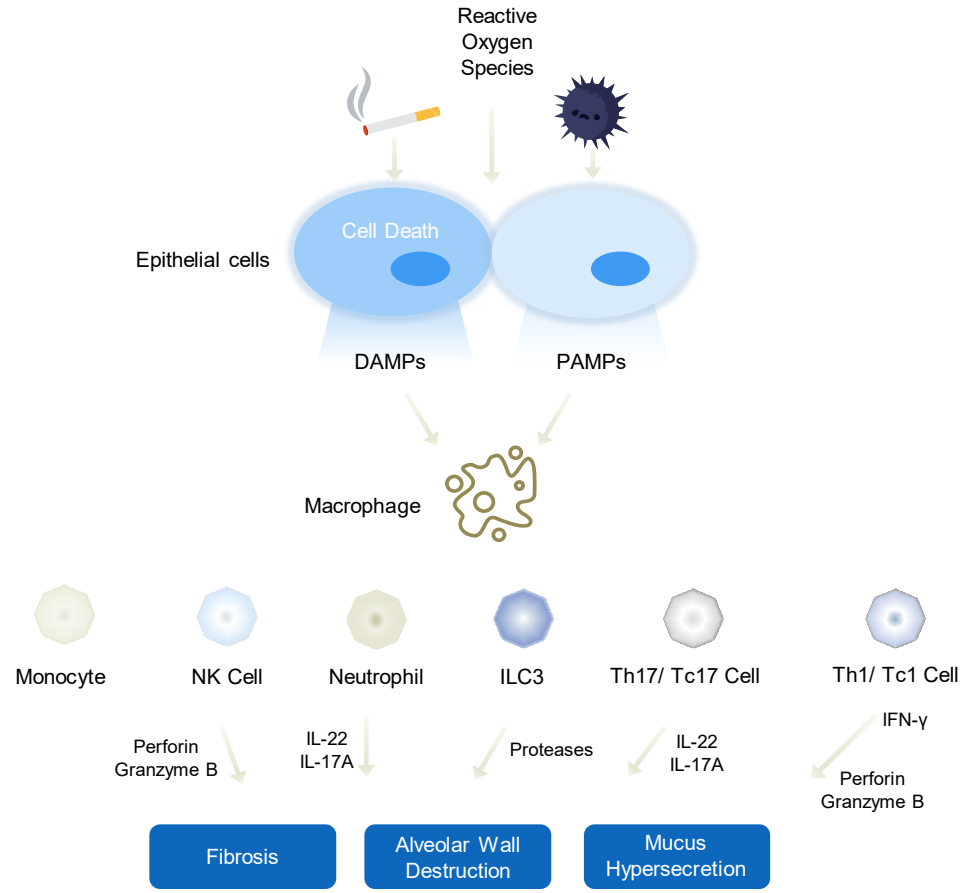
Prevention and Treatment

- COPD is a disease that can be prevented and treated with airflow limitation. The airflow limitation is not completely reversible and shows a progressive development. It is related to the abnormal inflammatory response of the lungs to harmful gases such as cigarette smoke or harmful particles.
- The main treatment method is to prevent and control chronic inflammation mainly by drug treatment, reduce the clinical symptoms of patients, and improve their life. At the same time, COPD patients can also be treated by rehabilitation, oxygen therapy and surgery.

Note: FEV_1: Forced Expiratory Volume in 1 second

Source: Literature Review, Frost & Sullivan analysis

Pathogenesis of COPD



Airway inflammation could be induced by toxic particles of inhaled cigarette smoke which contains numerous toxic chemicals

Excessive accumulation of Reactive Oxygen Species will lead to harmful modifications in proteins, lipids and DNA

Pattern Recognition Receptors are activated by DAMPs, producing inflammatory cytokines and nucleotide-binding oligomerization domain like receptor (NLR)P3 inflammasome.

(NLR)P3 inflammasome leads to the secretion of interleukins which will then lead to the activation of neutrophils, Th17 cells, Th1 cells and result in inflammation

Alveolar wall destruction is caused by elastin degradation resulted from alveolar macrophage released proteases

Chemokines and cytokines secreted by alveolar macrophage promote expression of adhesion molecules on endothelial cells, which facilitates the migration of a variety of inflammatory cells

Note: DAMP: Damage-Associated Molecular Patterns; PAMP: Pathogen-Associated Molecular Patterns; NK Cells: Natural Killer Cells; ILC3:Innate Lymphoid Cell 3; Th: Helper T Lymphocyte; Tc: Cytotoxic T Lymphocyte;

Source: Literature Review, Frost & Sullivan analysis

Classification of COPD by Airflow Obstruction

- Chronic Airflow Obstruction (CAO) is a physiological state that could be assessed using FEV_1/FVC ratio. FEV1 is a good marker of severity because of its high correlation with the Forced Vital Capacity (FVC) and the Total Lung Capacity (TLC).
- There are two main benefits of quantification using FEV_1/FVC ratio. On one hand, it provides clearer differentiation between the severity of COPD assessed using FEV_1 and the severity of CAO assessed using the FEV1/FVC ratio. On the other hand, unlike either FEV_1 or the FVC, the FEV_1/FVC ratio is independent of ethnicity, making it valid across ethnic groups.

Stages	GOLD Standard	CAO
Stage One (Mild COPD)	FEV_1 about 80% or more of normal	FEV_1/FVC ratio < 5th percentile
Stage Two (Moderate COPD)	FEV_1 between 50% and 80% of normal	FEV_1/FVC ratio < 1.78th percentile
Stage Three (Severe COPD)	FEV_1 between 30% and 50% of normal	FEV_1/FVC ratio < 0.0027th percentile
Stage Four (End-Stage COPD)	Lower FEV_1 than stage 3 or low blood oxygen levels	FEV_1/FVC ratio < $3.0^{th} \times 10^{-10}$ percentile

Classification Build-up Method:

- "FEV_1 -based staging" is the COPD severity grading method recommended by GOLD
- The FEV_1/FVC ratio cut-points were calculated using the upper limit of the proportion of participants in each FEV1-based staging category divided by FVCs illustrated in the Burden of Obstructive Lung Disease (BOLD) study.
- The FEV_1/FVC percentile is calculated by the following equation:

$$(b_0 + A) + b_1 \times age$$

Where the coefficients are decided by age and gender

Cross Tabulation between FEV$_1$/FVC-Based Staging & GOLD Staging

		FEV$_1$/FVC-Based Staging			
		Mild	Moderate	Severe	Very Severe
GOLD Staging	Mild	54%	28%	2%	0%
	Moderate	42%	60%	44%	3%
	Severe	4%	12%	47%	49%
	Very Severe	0%	0%	8%	49%

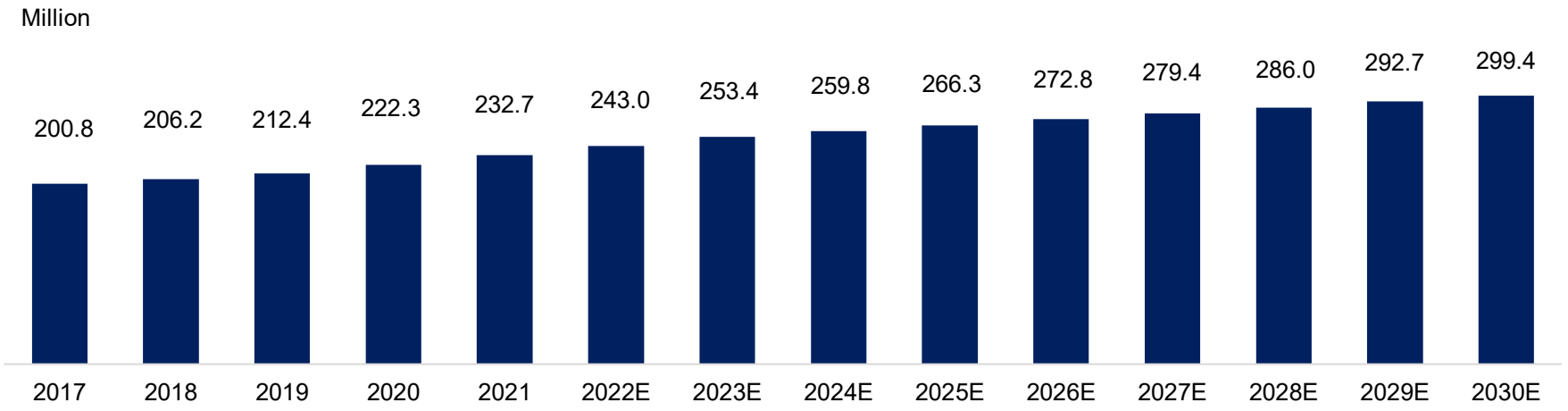
Source: Literature Review, Frost & Sullivan analysis

Global Prevalence of COPD, 2017-2030E

- The number of patients with COPD was 232.7 million in 2021, with a CAGR of 3.8% from 2017 and 2021. This number is expected to rise and approach 266.3 million in 2025 and 299.4 million in 2030, respectively.

Global Prevalence of COPD, 2017-2030E

CAGR	Total
2016-2020	3.8%
2020-2025E	3.4%
2025E-2030E	2.4%



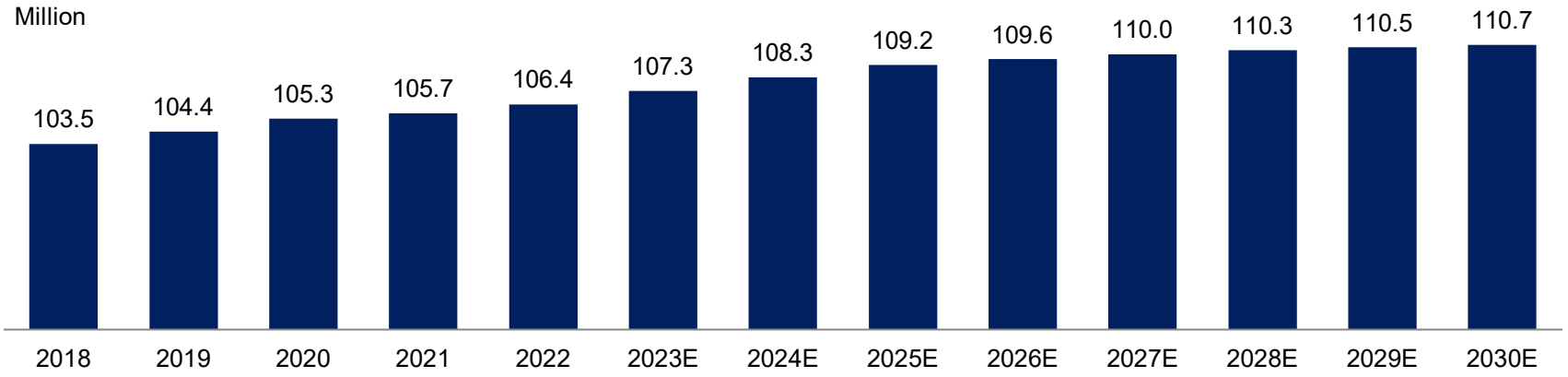
Source: Literature review, Frost & Sullivan analysis

Prevalence of COPD in China, 2018-2030E

- In 2022, the number of COPD patients in China is as high as 106.4 million. Driven by the exposure of risk factors and the aging of the population, the prevalence of COPD is expected to increase in the next few decades, and the prevalence rate is expected to reach 110.7 million by 2030, which will bring a great burden to the global economy and society.

Prevalence of COPD in China, 2018-2030E

Period	GAGR
2018-2022	0.7%
2022-2025E	0.9%
2025E-2030E	0.3%



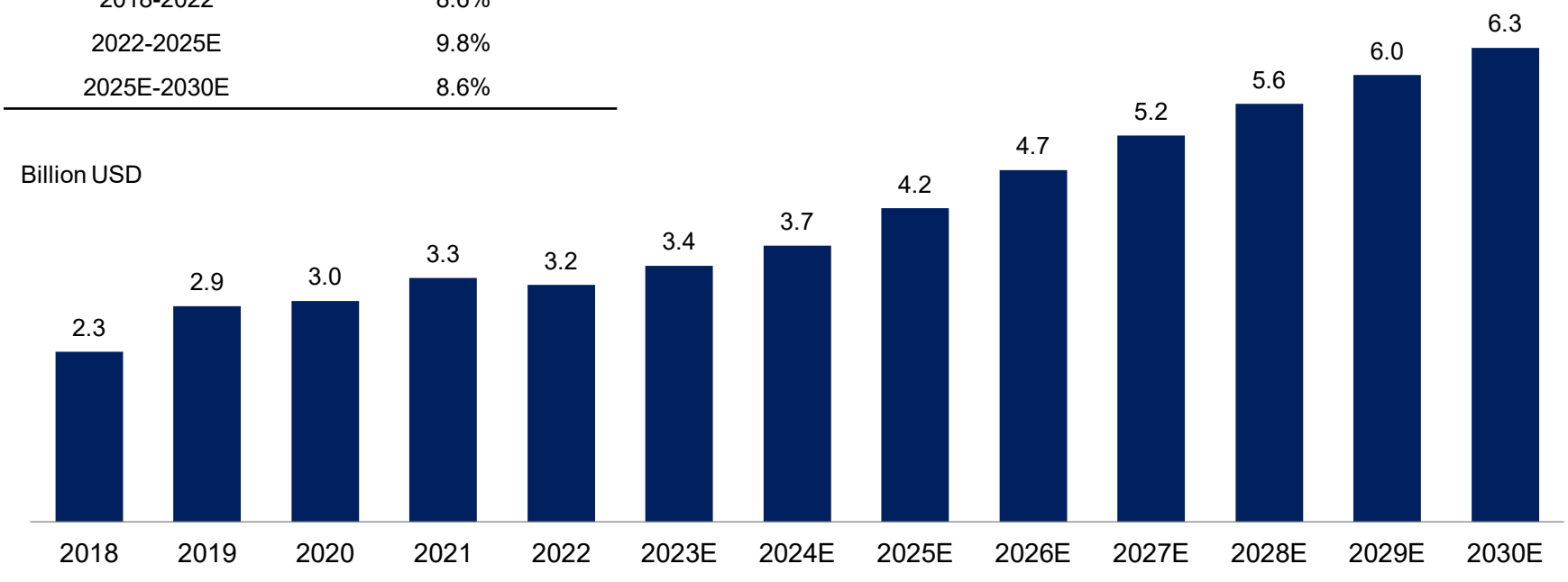
Source: GBD, Literature Review, Frost & Sullivan analysis

COPD Drugs Market in China, 2018-2030E

- In China, COPD Drugs Market reached USD 3.2 billion in 2022 and is expected to increase to USD 4.2 billion by 2025 at a CAGR of 9.8%. COPD Drugs Market is projected to reach USD 6.3 billion by 2030 at a CAGR of 8.6% after 2025. The CAGR from 2022 to 2030 is 9.1%.

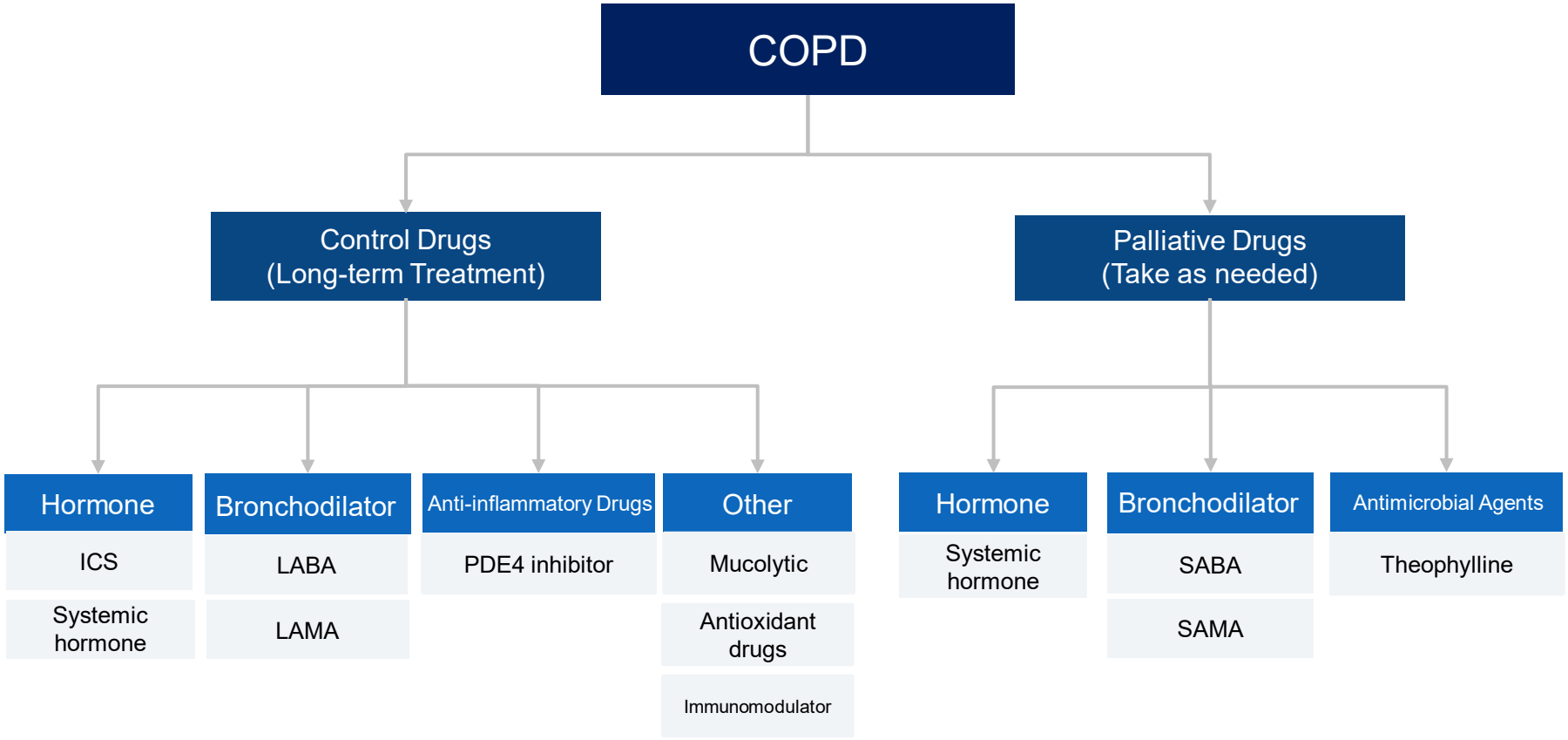
COPD Drugs Market in China, 2018-2030E

Period	CAGR
2018-2022	8.6%
2022-2025E	9.8%
2025E-2030E	8.6%



Source: Frost & Sullivan analysis

Treatment Diagram of COPD



- ICS: Inhaled corticosteroids LABA: Long-acting β_2 receptor agonist LAMA: Long-acting anticholinergic drugs
- SABA: Short-acting β_2 receptor agonist SAMA: Short-acting anticholinergic drugs

Source: Diagnosis and treatment of COPD (2021 ver.), Frost & Sullivan analysis

Unmet Medication Demands of COPD

- COPD is recognized as a disease with a heavy medical burden in the world, which has an important impact on both developed and developing countries. There are still many unmet needs in the evaluation and treatment of patients with chronic obstructive pulmonary disease, especially in the aspects of misdiagnosis.

Unmet medical needs of COPD

High incidence and low diagnosis rate

- The incidence of COPD in China ranges from 1.2% to 8.87%, with an average incidence of 5.87%. The prevalence rate of COPD in males (7.76%) was higher than that in females (4.07%), and the prevalence rate in rural areas (7.62%) was higher than that in urban areas (6.09%).
- The diagnosis rate of COPD in China is only 23.61%.

Lack of standardized diagnosis and treatment

- The routine treatment rate of COPD patients in China is only 7.9%, and the health service needs of patients have not been met. Prevention and COPD management still need to be strengthened.
- Although there is already a standardized diagnosis and treatment plan, there are few doctors who strictly follow the diagnosis and treatment plan to guide decision-making.

The risk factors of the disease are difficult to control

- Smoking and air pollution are the two main risk factors of chronic obstructive pulmonary disease in China. In 2018, the smoking rate of people aged 15 and over in China was 26.6%, of which 50.5% for men and 2.1% for women.
- China has high indoor bituminous coal emissions and a high incidence of COPD.

Disease Management of patients with COPD

COPD Management Objective:

① Prevention of disease progression
② Relief of symptoms
③ Improve sports endurance
④ Improve health
⑤ Prevention and treatment of complications
⑥ Prevention and treatment of deterioration
⑦ Reduce mortality

- So far, drug treatment alone is not enough to completely control the symptoms of COPD or significantly change the progression of the disease.
- In the treatment of most patients, additional bronchodilators or non-drug therapy are usually required to help control symptoms as the disease progresses.
- The promotion of a healthy lifestyle and non-drug intervention in the treatment of COPD have achieved great results. The lifestyle of patients with chronic obstructive pulmonary disease should increase physical activity, quit smoking, limit alcohol consumption and balance calorie intake.

Source: Frost & Sullivan analysis

Competitive Landscape of Biologics in COPD Treatment in China

Clinical trial status

Marketed Targeted Biologics for COPD in China

There are currently no biologics approved by NMPA for the treatment of COPD.

Biologic Pipeline in COPD Treatment in China

Target	Drug Code	Company	Status	First Posted Date
IL-4Rα	Dupilumab	Sanofi	Phase Ⅲ*	2019-10-08*
	SSGJ-611	Sansheng Guojian	Phase Ⅱ	2023-10-12
IL-5	Mepolizumab	GSK	Phase Ⅲ	2021-02-02
IL-33	Itepekimab	Sanofi	Phase Ⅲ	2021-04-28
	MEDI3506	AstraZeneca	Phase Ⅲ	2022-06-02
IL-5Rα	Benralizumab	AstraZeneca	Phase Ⅲ	2021-05-27
ST2	9MW1911	Mabwell Bioscience	Phase Ⅰ/Ⅱ	2023-02-14

*This table was last updated on Mar 2nd , 2024

* 2024-01-25 is the date CDE disclosed Dupixent's BLA application submission, no detailed indication was disclosed.

Source: NMPA, CDE, Frost & Sullivan analysis

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Overview and Classification of Pruritus

- Pruritus, is an uncomfortable and irritating sensation that makes patients want to scratch. Pruritus is often caused by dry skin, which more often affects older adults. The affected skin becomes abnormal, red, rough, or bumped, depending on the cause of the itchiness. Pruritus can be classified into acute and chronic phenotypes, depending on the duration of onset. Pruritus lasts for over 6 weeks in duration is defined as chronic pruritus.
- The causes of pruritus range from intrinsic to extrinsic factors. Intrinsic factors may be relevant to chronic infection, such as the block of blood circulation, change of endocrine and metabolism, the hereditary tendency to allergies, etc. Extrinsic factors consist of food, inhaled substances, chemical materials, animal hair, fur skin, etc.
- Prurigo Nodularis (PN) is a chronic skin disorder characterized by the presence of hard and extremely itchy bumps known as nodules, which tend to be found in easy-to-scratch areas, such as the arms, legs, the upper back and abdomen.

Classification of Pruritus based on pathologies

Skin-derived pruritus	Neuropathic pruritus	Neurogenic pruritus	Psychogenic pruritus	Mixed pruritus
• Originate from the skin. Caused by inflammation, dryness, or damaged skin. Produced by the conduction of C nerve fiber. • Example: urticaria, scabies, etc.	• Coverage is limited to a certain point. Associated with pathological alterations in the affected pathway of sensory nerve fibers. • Example: Postherpetic neuralgia	• Derived form the central nervous system. Itchiness produced by the induction and transmission of medicators such as interleukin-31 (IL-31) and receptors without nerve damage. • Example: Bile stasis itching	• Caused by psychologic factors, such as skin dryness and irritating factors, and psychiatric abnormalities. • Example: Parasitic phobia	• Caused by multiple factors and mediated by two or more mechanisms. • Example: atopic dermatitis

Source: Literature Review, Frost & Sullivan analysis

Overview of Prurigo Nodularis

- Prurigo nodularis (PN) is a chronic inflammatory skin disease and can be symptomized by extreme itchiness, where rashes appear in a symmetrical shape, and most commonly appear on the arms, legs, upper back, and abdomen. PN is usually severe and chronic, it occurs either in episodes or continuously. PN can affect people at any age, but it occurs more often in elderlies.
- Although the exact pathogenesis of PN remains unknown, its occurrence is widely understood, which is due to the abnormal function of the immune system and nerves in the skin. Elevated Interleukin-31 (IL-31) is often observed on the skin of PN patients, thus IL-31 and IL-31R have become new potential targets of biological treatments.
- PN is associated with many comorbidities, which result in a great burden on patients and affect their quality of life.

Overview of PN comorbidities

Skin diseases	• PN is often found in patients with other pruritic diseases, including atopic dermatitis, cutaneous T-cell lymphoma, lichen planus, xerosis cutis, keratoacanthomas and bullous pemphigoid.
Infections	• PN-associated infections include bacterial, viral, and parasitic infections. Bacterial infections with Tuberculosis, Mucogenicum and H. pylori, viral infections with Herpes zoster and Hepatitis C and parasitic infections with Ascaris and Strongyloides are often seen in PN patients.
Systemic diseases	• Systemic diseases such as HIV, kidney disease, liver disease and various cancers are frequently seen in PN patients.
Neurological and psychogenic diseases	• Neurological damages to organs or tissues like the brain and spinal cord are often associated with PN. Psychogenic diseases such as depression, anxiety, and especially dissociative disorders that lead to excessive scratching are seen in PN patients.

Source: Literature Review, Frost & Sullivan analysis

Treatment Diagram of Prurigo Nodularis in China

Medical treatment options

Topical treatment

- Topical antihistamine: treat local or generalized pruritus.
- Topical steroids: critical treatment for inflammatory skin irritations, also used in non-inflammatory and systemic cases.
- Topical anaesthetics: used to effectively control local itchiness
- Topical capsaicin: used externally to control local and limited itchiness.
- Topical calcineurin inhibitors: used to control itchiness caused by inflammatory skin diseases
- Others: include mint, zinc oxide, camphor to reduce itchiness

Systemic treatment

- Antihistamine: effective control of histamine-based pruritus.
- Steroids: systemic steroids to rapidly and effectively control inflammatory skin disease condition.
- Opioid receptor agonists or antagonist: effective treatment of pruritus subtypes.
- Antiepileptic drugs: effectively treat pruritus subtypes.
- Antidepressant: act on 5-hydroxytryptamine (serotonin) and histamine to control itchiness.
- Serotonin receptor inhibitor: inhibit serotonin receptor to control itchiness.
- Thalidomide: commonly used to control prurigo nodularis and persistent pruritus that is not responsive to other treatments
- Immunosuppressant: used to control inflammatory skin disease itchiness
- Biologic targeted therapy: monoclonal antibody against interleukin-31 receptor that is associated with prurigo nodularis.

Source:《慢性瘙痒管理指南(2018)》Mayoclinic, Frost & Sullivan analysis

Unmet Medication Demands of Prurigo Nodularis

Less effective in elderlies	• The management of prurigo nodularis in elder patients is difficult, due to their limited physical and cognitive abilities. Besides, the frequent occurrence of comorbid conditions and polypharmacy may increase the risk of adverse drug interactions. Therefore, suitable and effective treatments that take elderlies' health conditions into account are needed to be developed.
Lack of long-term treatment with limited side effects	• Some current prurigo nodularis treatments such as topical steroids and topical anesthetics are recommended to be used for a limited time duration. Because advanced side effects and irritations may be caused. Therefore, effective treatments with fewer side effects over a long time of application are in demand.
Insufficient clinically available drugs	• Currently, there is no biologic approved by the FDA or NMPA for the treatment of prurigo nodularis, only some medications can be applied to relieve symptoms and prevent degradation. Nevertheless, the number of biologics that have advanced to their clinical stages is limited. More attention should be paid to finding novel targets and developing new therapies.

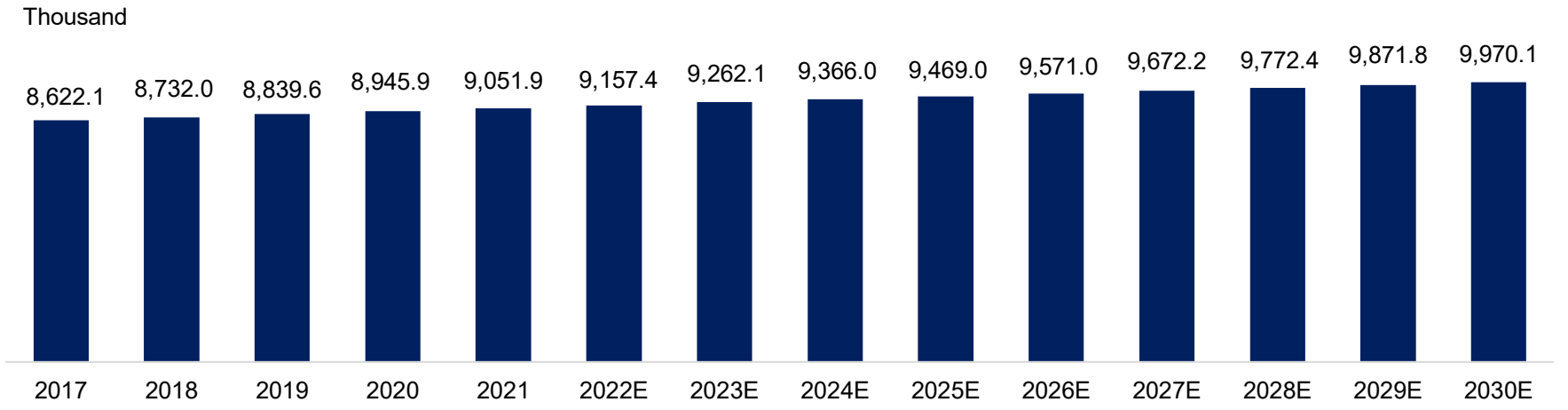
Source: Frost & Sullivan analysis

Global Prevalence of PN, 2017-2030E

- The number of patients with PN worldwide was 9,051.9 thousand in 2021, with a CAGR of 1.2% from 2017 and 2021. This number is expected to rise and approach 9,469.0 thousand in 2025 and 9,970.1 thousand in 2030, respectively.

Global Prevalence of PN, 2017-2030E

CAGR	Total
2017-2021	1.2%
2021-2025E	1.1%
2025E-2030E	1.0%



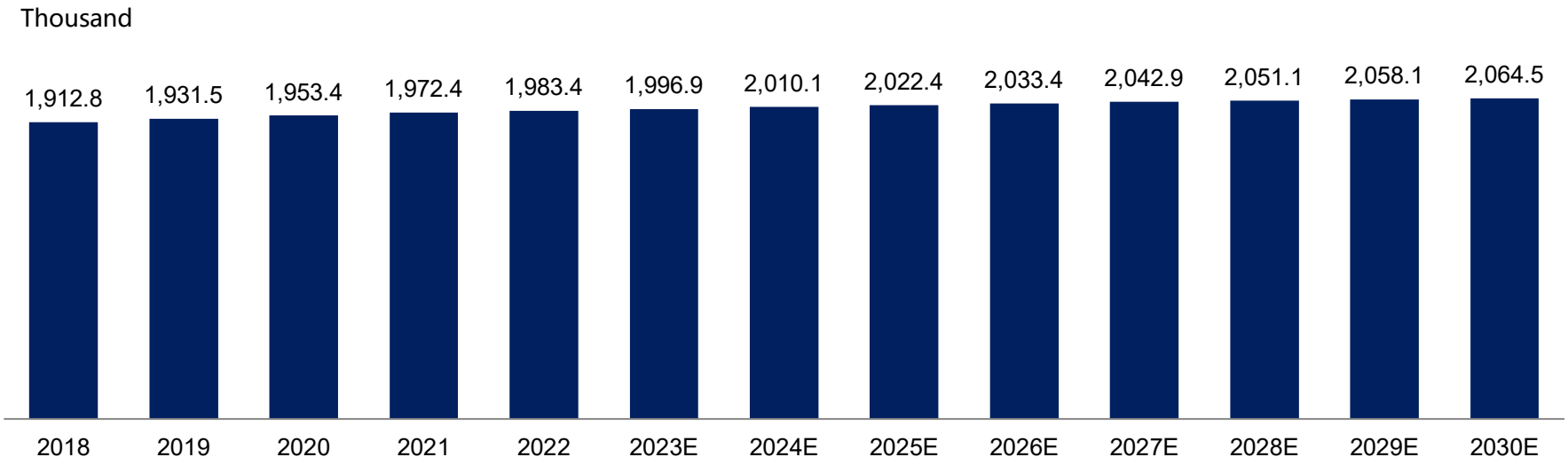
Source: Frost & Sullivan analysis

Prevalence of PN in China，2018-2030E

- According to epidemiology studies, the prevalence of PN in China had reached 1,983.4 thousand in 2022, with a CAGR of 0.9% from 2018 to 2022. The number of patients is expected to reach 2,064.5 thousand in 2030.

Prevalence of PN in China，2018-2030E

Period	CAGR
2018-2022	1.0%
2022-2025E	1.0%
2025E-2030E	0.9%



Source: Frost & Sullivan analysis

Global Competitive Landscape of Biologics in PN Treatment

Clinical trial status

FDA Approved Targeted Biologics for PN

Brand Name	INN	Company	Target	FDA Approval Time
Dupixent	Dupilumab	Sanofi	IL-4Rα	2022-09-28

*The first table was updated on Mar 2nd ,2024

Source: FDA, Frost & Sullivan analysis

Competitive Landscape of Biologics in PN Treatment in China

Clinical trial status

Marketed Targeted Biologics for PN in China

Brand Name	INN	Company	Target	NMPA Approval Time
Dupixent	Dupilumab	Sanofi	IL-4Rα	2023-09-22

Biologic Pipeline in PN Treatment in China

Target	Drug Code	Company	Status	First posted Date
IL-4Rα	QX005N	Qyuns	Phase Ⅱ	2022-12-16
	BA2101	Boan Biotech	Phase Ⅰ	2023-01-16

*This table was last updated on Mar 2nd , 2024

Source: NMPA, Frost & Sullivan analysis

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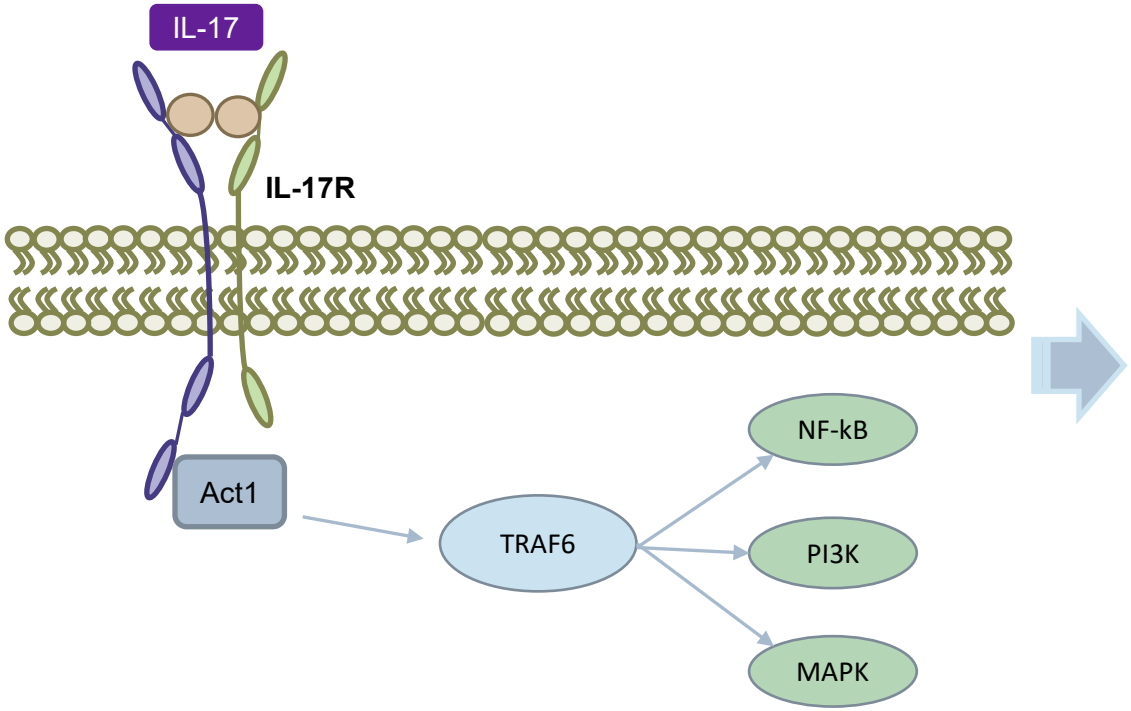
Overview of IL-17A

- There are in total six types of Interleukin 17 (IL-17), IL-17 A to IL-17 F. IL-17 cytokines produced by Th17 cells is involved in the immune responses to fungal and bacterial infection and autoimmune diseases, which mediate diverse signaling cascades through a pathway that depends on ACT1, that ultimately mediate the activation of pro-inflammatory mediators being associated with innate immune signaling. IL-17A and IL-17F are very well characterized, due to their prominent activities in psoriasis, psoriatic arthritic, inflammatory bowel diseases and other autoimmune diseases.



- Upon binding of IL-17 to IL-17R, heterodimerization of IL-17R will be initiated, and ACT1 proteins that enhance proinflammatory cytokine expressions will be recruited. The subsequent recruitment of the tumor necrosis factor (TNF) receptor-associated factors (TRAFs) family, typically TRAF6 promotes activation of downstream signaling pathways. The subsequent pathways include NF-kB, PI3K, MAPK cascades and production of proinflammatory cytokines.
- Blocking of IL-17A could effectively inhibit the IL-17 pathway being involved in defense mechanisms against various microbial pathogens and tissue inflammations, This subsequently prevents the occurrence of signaling cascades that result in undesired diseases.

Source: Literature Review, Frost & Sullivan analysis

Global Marketed IL-17A Antibody

➢ Marketed Drugs

Drug Code	Company	Brand name	Target
Secukinumab	Novartis	Cosentyx	IL-17A
Ixekizumab	Eli Lilly	Taltz	IL-17A
Bimekizumab-bkzx	UCB Pharma	Bimzelx	IL-17A,1L-17F

*Number of marketed drugs was last updated on Mar 2nd , 2024
Bimzelx is not counted as IL-17A antibody

Source: FDA, NMPA, Frost & Sullivan analysis

China Competitive Landscape of IL-17A Antibody - I

- Clinical trial

Drug Code	Company	Target
China		
QX002N	Qyuns	IL-17A
AIN457 (Secukinumab)	Novartis	IL-17A
LZM012	Livzon/ Kanova Biopharm	IL-17A, IL-17F
JS005	Junshi Biosciences	IL-17A
608	Sunshine Guojian Pharmaceutical	IL-17A
ABY-035	Affibody	IL-17A, Albumin
Bimekizumab	UCB Biopharma	IL-17A, IL-17F
GR1501	Genrix Bio	IL-17A
Ixekizumab	Eli Lilly	IL-17A

*Number of drug candidates was last updated on Mar 2nd , 2024

Source: CDE, Frost & Sullivan analysis

China Competitive Landscape of IL-17A Antibody - II

➢ Clinical trial

Drug Code	Company	Target
China		
AK111	Akeso	IL-17A
SHR-1314	Suncadia biopharm/ Hengrui	IL-17A
HB0017	Huabo	IL-17A
BAT2306	Bio-thera	IL-17A
SYS6012	SCPC	IL-17A
BR201	BioRay	IL-17A
SM17	Sinolink	IL-17RB
SCT650C	Sinocelltech	IL-17

*This table was last updated on Mar 2nd, 2024

Source: CDE, Frost & Sullivan analysis

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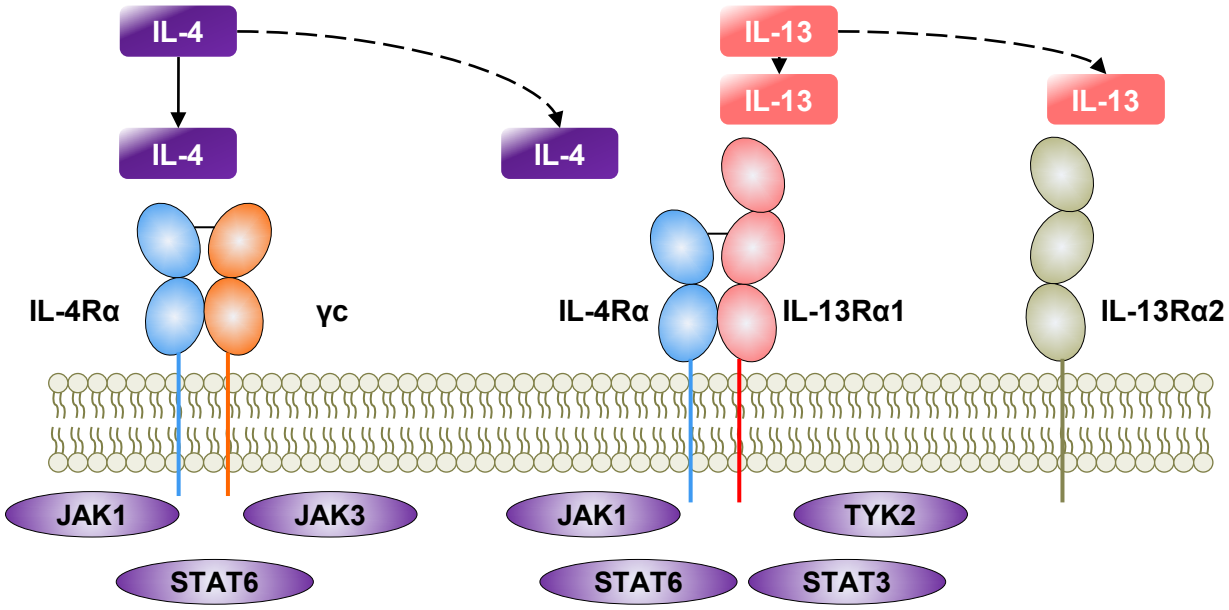
Overview of IL-4Rα

- Interleukin 4 Receptor (IL-4R) also known as CD124, IL-4Rα and BSF receptor, is a type I cytokine receptor produced by activated Th2 cells and mast cells and plays an important role in Th2-biased immune responses, alternative macrophage activation, mucosal immunity, allergic inflammation, tumor progression, and atherogenesis.



- B cells
- T cells
- Monocytes
- Eosinophils
- Fibroblasts

- Epithelial cells
- Smooth muscle cells
- Fibroblasts
- Monocytes
- Activated B cells

- **IL-4Rα is a key component of type I receptors and type II receptors** in type 2 inflammatory pathway.
- Blocking IL-4Rα can simultaneously block two powerful regulators of type 2 immune responses—IL-4 and IL-13 acts through type I and type II receptors to block the central pathway of Th2 inflammation.

Source: Literature Review, Frost & Sullivan analysis

Global Competitive Landscape of IL-4Rα Antibody - II

- Clinical trial

Drug Code	Company
Global	
Dupilumab	Sanofi/ Regeneron
AZD1402	AstraZeneca
AK120	Akeso
CBP-201	Connect Biopharm
AUP-16	Aurealis Therapeutics
Comekibart	Mabgeek
NM26	Numab Therapeutics

*This table was last updated on Mar 2nd , 2024

Source: FDA, NMPA, Frost & Sullivan analysis

China Competitive Landscape of IL-4Rα Antibody – I

➢ Clinical trial

Drug Code	Company
China	
Dupilumab	Sanofi/ Regeneron
611	Sunshine Guojian Pharmaceutical
AK120	Akeso
CM310 (Stapokibart)	Keymed Biosciences
CBP-201	Connect Biopharm
QX005N	Qyuns Therapeutics
MG-K10	Mabgeek
SHR-1819	Hengrui

*This table was last updated on Mar 2nd , 2024

Source: FDA, NMPA, Frost & Sullivan analysis

China Competitive Landscape of IL-4Rα Antibody – II

- Clinical trial

Drug Code	Company
RC1614	Sunshine Guojian Pharmaceutical
GR1802	Genrix bio
THQ2722	Chiatai Tianqing
MK-K10	Mabgeek Biotech
LQ036	Novamab Biopharma
BA2101	BoAn Biotech

*This table was last updated on Mar 2nd , 2024

Source: FDA, NMPA, Frost & Sullivan analysis

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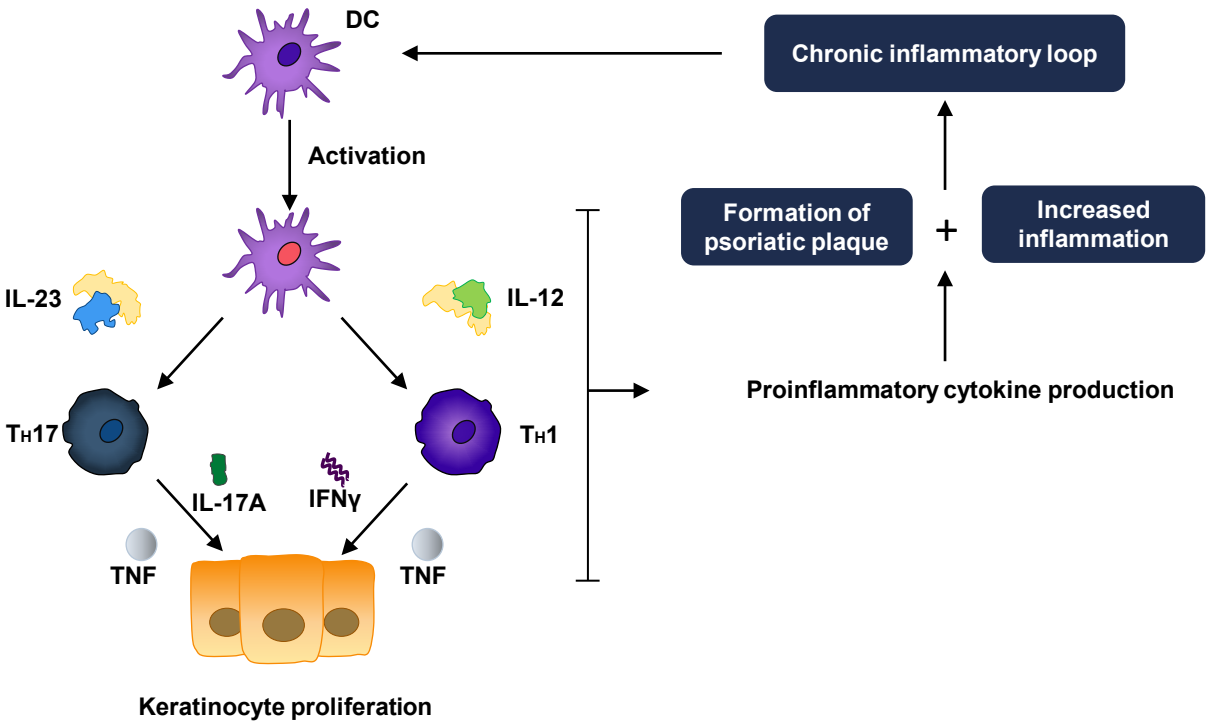
Overview of IL-12 and IL-23

- IL-12 and IL-23 are produced by inflammatory myeloid cells and influence the development of T_H1 cell and IL-17–producing T helper (T_H17) cell responses, respectively. IL-12 is composed of the IL-12p40 subunit linked to the IL-12p35 subunit while IL-23 is composed of the IL-23p19 subunit and the IL-12p40 subunit. Compounds/antibodies that target IL-12p40 can act on both IL-12 and IL-23.

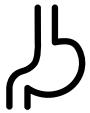


Clinical Applications

Targeting IL-12/IL-23 can be applied to treat inflammatory diseases, such as psoriasis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, multiple sclerosis.

Psoriasis

Ankylosing arthritis



Crohn's disease

Multiple sclerosis

Source: Literature review, Frost & Sullivan analysis

Global/ China Competitive Landscape of IL-12/IL-23 Antibody

➢ Marketed Drugs

Drug Code	Company	Brand name	Target
Ustekinumab	Janssen	Stelara	IL-12/IL-23
ustekinumab-auub	Amgen	Wezlana	IL-12/IL-23
Mirikizumab-mrkz	Lily	Omvoh	IL-23
Guselkumab	Janssen	Tremfya	IL-23
Tildrakizumab-asmn	Sun Pharmaceutical	Ilumya	IL-23A
Risankizumab-rzaa	AbbVie	Skyrizi	IL-23

*This table was last updated on Mar 2nd , 2024

Source: FDA, NMPA, Frost & Sullivan analysis

Global Competitive Landscape of IL-12/23 Antibody - I

- Clinical trial

Drug Code	Company	Target
Global		
Ustekinumab	Janssen	IL-12、IL-23
Risankizumab	AbbVie	IL-23
Guselkumab	Janssen	IL-23

*This table was last updated on May 5, 2022

Source: ClinicalTrials, Frost & Sullivan analysis

China Competitive Landscape of IL-12/23 Antibody

- Clinical trial

Drug Code	Company	Target
China		
Risankizumab	Boehringer Ingelheim	IL-23
Guselkumab	Janssen	IL-23
QX001S	Qyuns	IL-12、IL-23
Tildrakizumab	Sun Pharmaceutical	IL-23
BAT2206	Bio-thera	IL-12、IL-23
AK101	Akeso	IL-12、IL-23、IL-12R
IBI112	INNOVENT	IL-23
NBL-012	Xinshi	IL-23
QX004N	Qyuns	IL-23A

*number of drug candidates is updated to Mar 2nd , 2024

Source: CDE, Frost & Sullivan analysis

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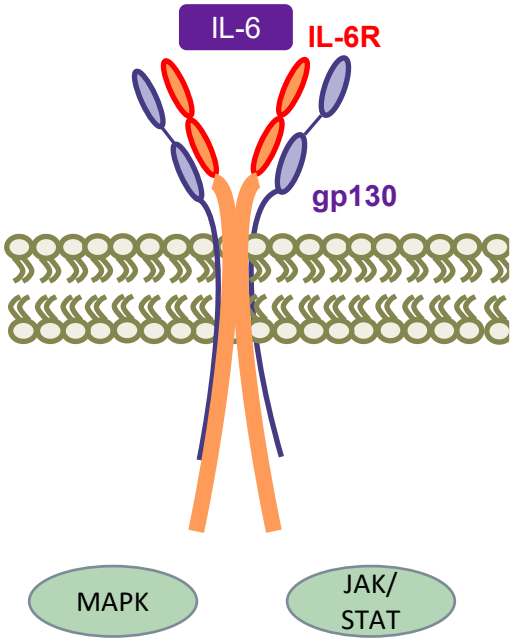
Overview of IL-6R

- Interleukin-6 (IL-6) receptor, which exists as membrane-bound and soluble forms, plays critical roles in the immune response. It requires co-receptors gp130 to trigger further signaling. IL-6 are pro-inflammatory cytokines and mediators of acute-phase responses. As a result of binding between IL-6 and IL-16R, subsequent intracellular inflammation-causing cascades are initiated via JAK/ STAT or MAPK pathways.



IL-6 can induce various inflammatory responses due to its wide presence in diverse organ cells such as livers, bones, osteoblasts and inflamed joints while increasing B-cell and T-cell activities.

Therefore, blocking IL-6R could effectively prevent the cascading inflammatory responses, hence avoiding the occurrence of diverse undesirable diseases such as autoimmune diseases and pain in organs.

Source: Literature Review, Frost & Sullivan analysis

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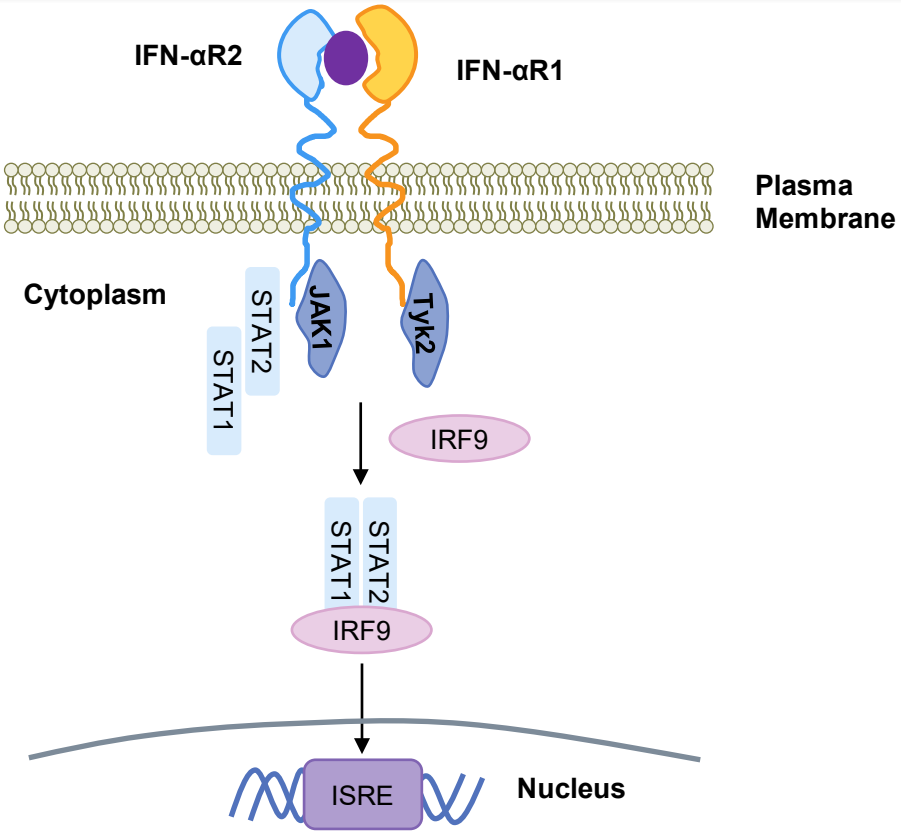
Overview of IFN-αR1

- Interferon-α/β receptors are transmembrane proteins made of two chains, IFN-αR1 and IFN-αR2. IFN-αR1 has an extracellular ligand-binding domain that is made of four subunits. Type I IFNs are cytokines being produced by leukocytes, monocytes and fibroblasts in response to pathogens, bacteria, parasites or tumor cells, so to activate the immune system, mainly the innate immune system. Type I IFNs bind to the Interferon-α/β receptor to activate the JAK-STAT signaling pathway.



- Binding of type I IFNs to Interferon-α/β receptor follows a JAK-STAT signaling pathway. IFN-αR1 plays an important role in initiating the JAK-STAT signaling pathway upon the interaction between the IFN-αR1 tail and Tyk2 (first member of the JAK family).
- Blocking the IFN-αR1 can prevent the occurrence of JAK-STAT signaling pathway resulting by binding between type I IFNs and Interferon-α/β receptor.

Source: Literature Review, Frost & Sullivan analysis

Global/ China Competitive Landscape of IFN-αR1 Antibody

- Clinical trial

Drug Code	Company	Target
China		
Anifrolumab	AstraZeneca	IFNAR1
QX006N	Qyuns	IFNAR1
GR1603	Genrixbio	IFNAR1

*China Competitive Landscape table was last updated on Mar 2nd ,2024

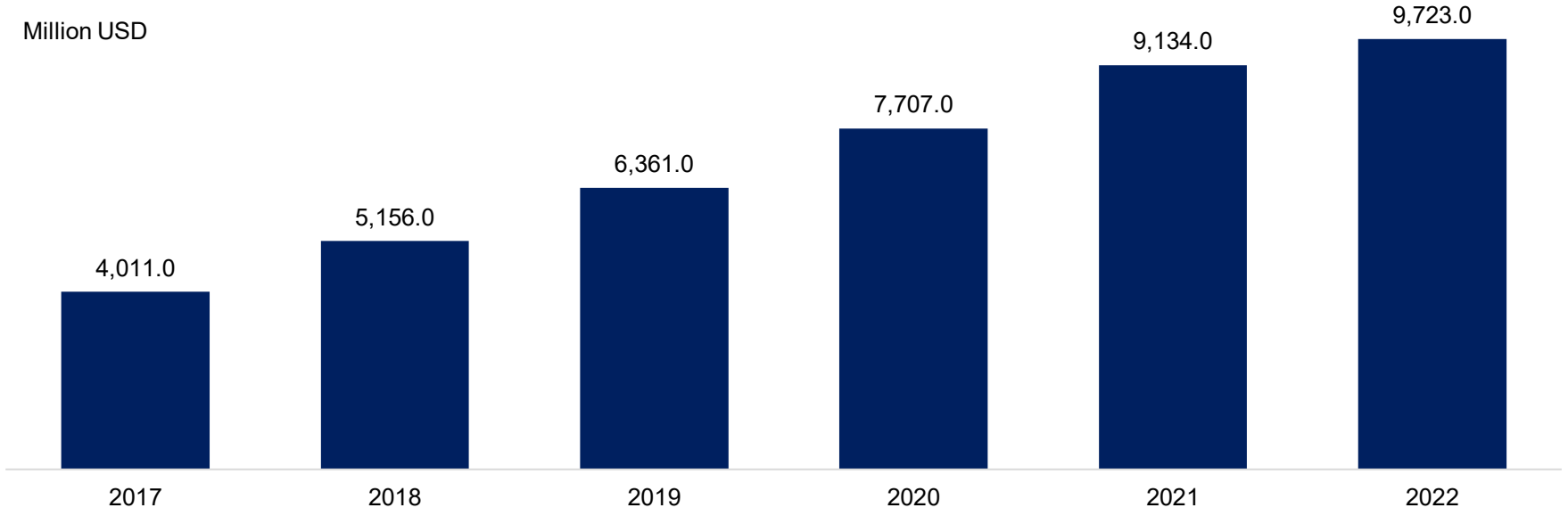
Source: FDA, NMPA, ClinicalTrials, CDE, Frost & Sullivan analysis

Global Sales of Ustekinumab (Stelara®), 2017-2022

- The global sales of Ustekinumab with the brand name Stelara® recorded by JNJ has increased from USD 4,011.0 million in 2017 to USD 9,723.0 million in 2022, representing a CAGR of 19.4%.

Global Sales of Ustekinumab (Stelara®), 2017-2022

Period	CAGR
2017-2022	19.4%



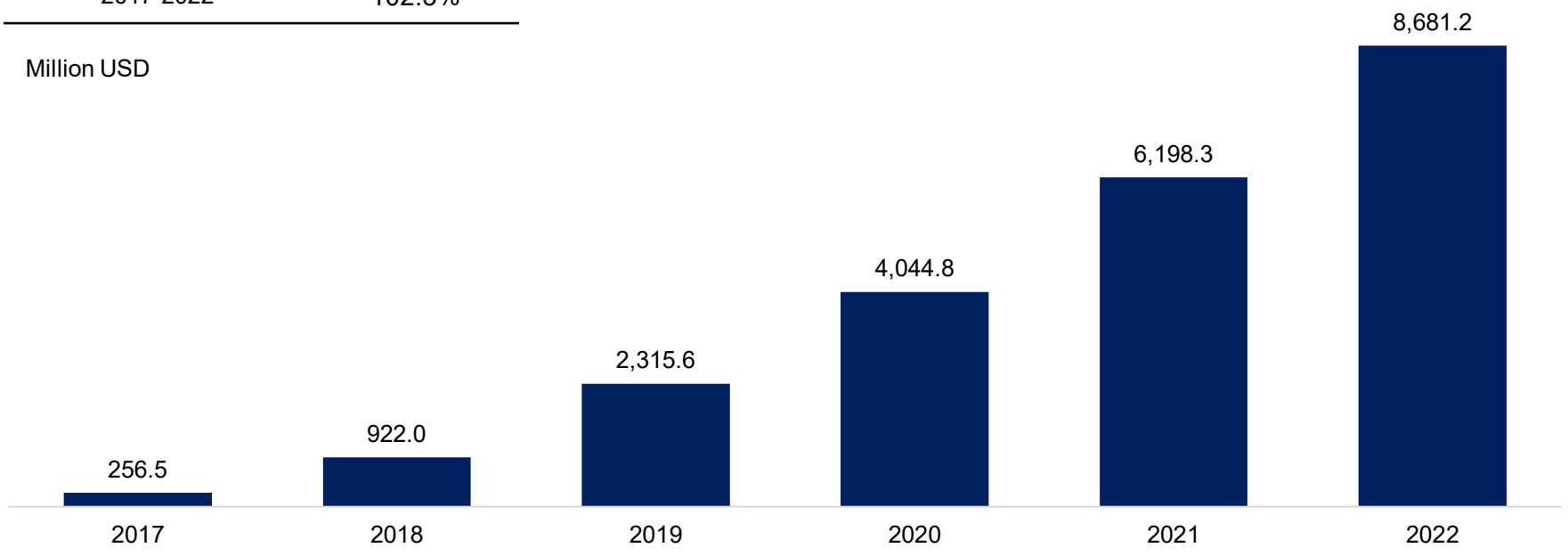
Source: JNJ annual report, Frost & Sullivan analysis

Global Sales of Dupilumab (Dupixent®), 2017-2022

- The global sales of Dupilumab with the brand name Dupixent® recorded by Regeneron&Sanofi has increased from USD 256.5 million in 2017 to USD 8,681.2 million in 2022, representing a CAGR of 102.3%.

Global Sales of Dupilumab (Dupixent®), 2017-2022

Period	CAGR
2017-2022	102.3%



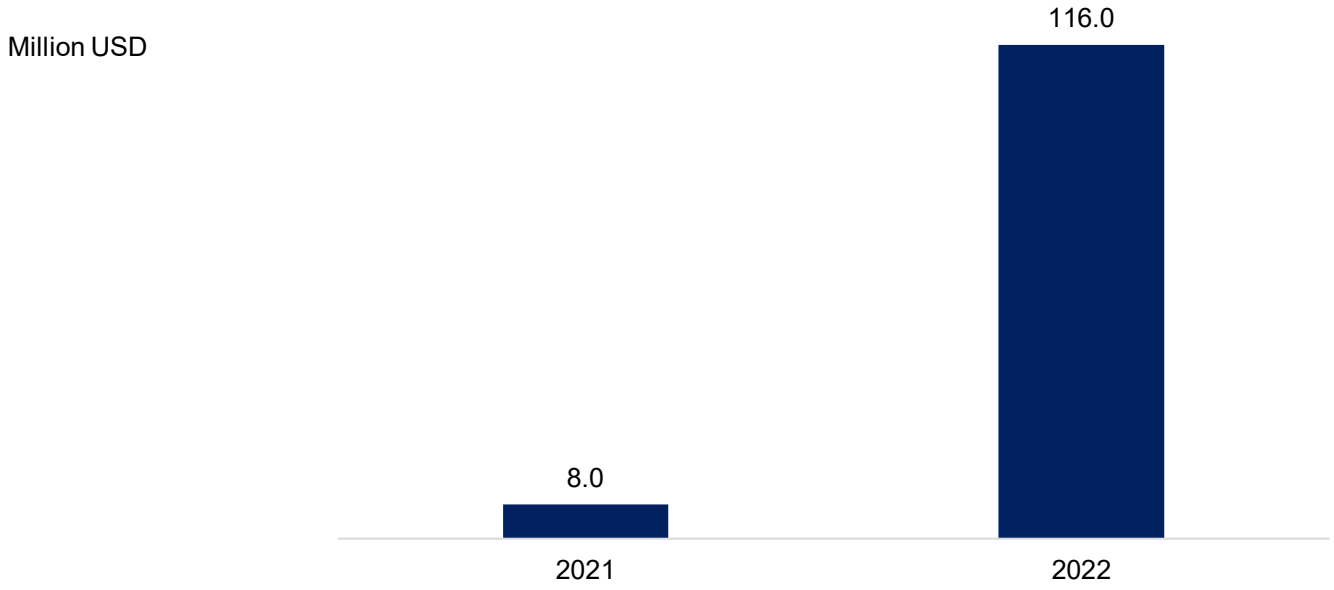
Source: Regeneron annual report, Frost & Sullivan analysis

Global Sales of Anifrolumab (Saphnelo®), 2021-2022

- Anifrolumab was first approved by FDA in 2021 for treating SLE and the global sales of Anifrolumab with the brand name Saphnelo® recorded by AstraZeneca has increased from USD 8.0 million in 2021 to USD 116.0 million in 2022.

Global Sales of Anifrolumab (Saphnelo®), 2021-2022

Period	% Change
2021-2022	1350.0%



Source: AstraZeneca annual report, Frost & Sullivan analysis

Annual Cost of Biologics for Autoimmune and Allergic Diseases in China-I

INN (Brand Name)	Indication	Dosage and Administration	Latest Price	Annual cost
Ustekinumab (Stelara®)	Psoriasis	The recommended dosage for patients less than or equal to 100 kg is 45 mg administered subcutaneously initially and 4 weeks later, followed by 45 mg administered subcutaneously every 12 weeks.	RMB 4,318 for 0.5ml:45mg	• First year: RMB 21,590 (5 doses) • Second year and thereafter: RMB 17,272 (4 doses per year)
Dupilumab (Dupixent ®)	Atopic Dermatitis	The recommended dose is an initial dose of 600 mg (two 300 mg injections in different injection sites), followed by 300 mg given every other week.	RMB 3,160 for 2ml:300mg	• First year: RMB 85,320 (27 doses) • Second year and thereafter: RMB 82,160 (26 doses per year)
Secukinumab (Cosentyx ®)	Ankylosing Spondylitis	The recommended dosages are: • With a loading dosage: 150 mg at Weeks 0, 1, 2, 3, and 4 and every 4 weeks thereafter. • Without a loading dosage: 150 mg every 4 weeks.	RMB 1,188 for 1ml:150mg	• With a loading dosage: RMB 19,008 (16 doses) • Without a loading dosage: RMB 15,444 (13 doses)

Source: FDA drug label, Frost & Sullivan analysis

Annual Cost of Biologics for Autoimmune and Allergic Diseases in China-II

INN (Brand Name)	Indication	Dosage and Administration	Latest Price	Annual cost
Ixekizumab (Taltz ®)	Ankylosing Spondylitis	The recommended dosage is 160 mg by subcutaneous injection (two 80 mg injections) at Week 0, followed by 80 mg every 4 weeks.	RMB 1,218 for 1ml:80mg	• First year: RMB 17,052 (14 doses) • Second year and thereafter: RMB 15,834 (13 doses per year)
Belimumab (Benlysta ®)	Systemic Lupus Erythematosus	The recommended dosages are: • Intravenous dosage: 10 mg/kg at 2-week intervals for the first 3 doses and at 4-week intervals thereafter. • Subcutaneous dosage: 200 mg once weekly. (Not approved in China)	RMB 755 for 0.12g / single-dose vial	For patients weighing 60 kg using intravenous dosage: • First year: RMB 52,850 (70 vials) • Second year and thereafter: RMB 49,075 (65 vials per year)
Telitacicept (Tai'ai ®)	Systemic Lupus Erythematosus	The recommended dosage is 160 mg weekly.	RMB 818.8 for 80mg/single-dose vial	• RMB 85,155.2 (104 vials per year)

Source: FDA drug label, Frost & Sullivan analysis

Annual Cost of Biologics for Autoimmune and Allergic Diseases in China-III

INN (Brand Name)	Indication*	Dosage and Administration	Latest Price	Annual cost
Dupilumab (Dupixent ®)	CRSwNP	The recommended dosage for adult patients is 300 mg given every other week.	RMB 3,160 for 2ml:300mg	• RMB 82,160 (26 doses per year)
Dupilumab (Dupixent ®)	Asthma	The Recommended dosage is an initial dose of 400/600 mg followed by 200/300 mg given every other week.	RMB 3,160 for 2ml:300mg	For patients using 600mg & 300mg: • First year: RMB 85,320 (27 doses) • Second year and thereafter: RMB 82,160 (26 doses per year)

* All the indications listed in the table have not been approved in China,

Source: FDA drug label, Frost & Sullivan analysis

Dosing regime of Biologics for Autoimmune and Allergic Diseases in China

INN (Brand Name)	Indication*	Dosage and Administration
Etanercept (Enbrel®)	AS	The recommended dosage is 25mg administered twice weekly, or 50 mg administered once weekly.
Adalimumab (Humira®)	AS	The recommended dosage is 40mg every week.
Infliximab (Remicade®)	AS	The recommended dosage is 3 mg/kg given as an intravenous induction regimen at 0, 2 and 6 weeks followed by a maintenance regimen of 3 mg/kg every 8 weeks thereafter.

* All the indications listed in the table have not been approved in China,

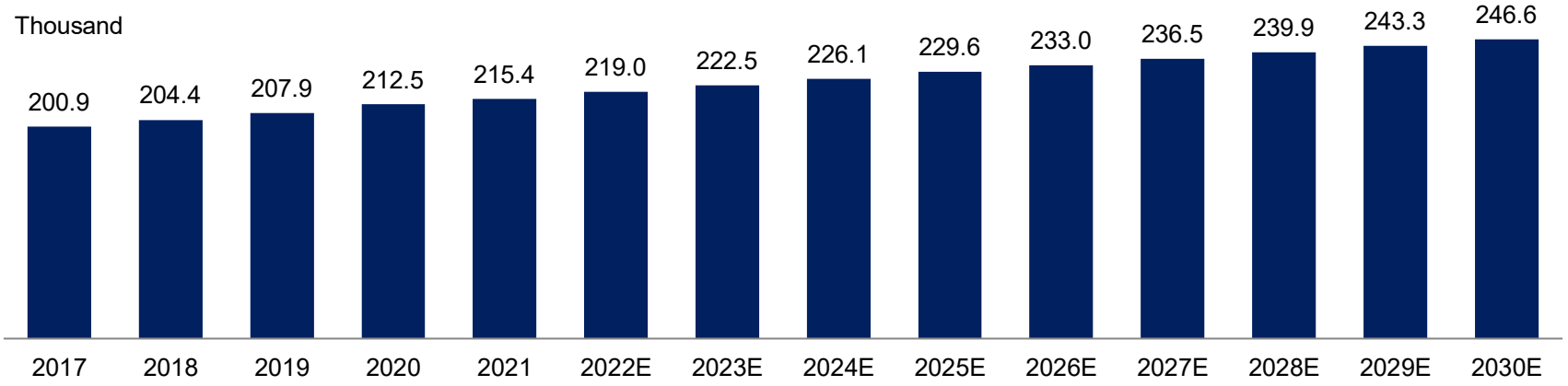
Source: FDA drug label, Frost & Sullivan analysis

Prevalence of EoE in China, 2017-2030E

- In 2021, the number of EoE patients in China is 215.4 thousand. The prevalence of EoE is expected to increase in the next few decades, and the number of EoE patients is expected to reach 246.6 thousand by 2030, representing a CAGR of 1.4% from 2025 to 2030.

Prevalence of EoE in China, 2017-2030E

Period	GAGR
2017-2021	1.8%
2021-2025E	1.6%
2025E-2030E	1.4%



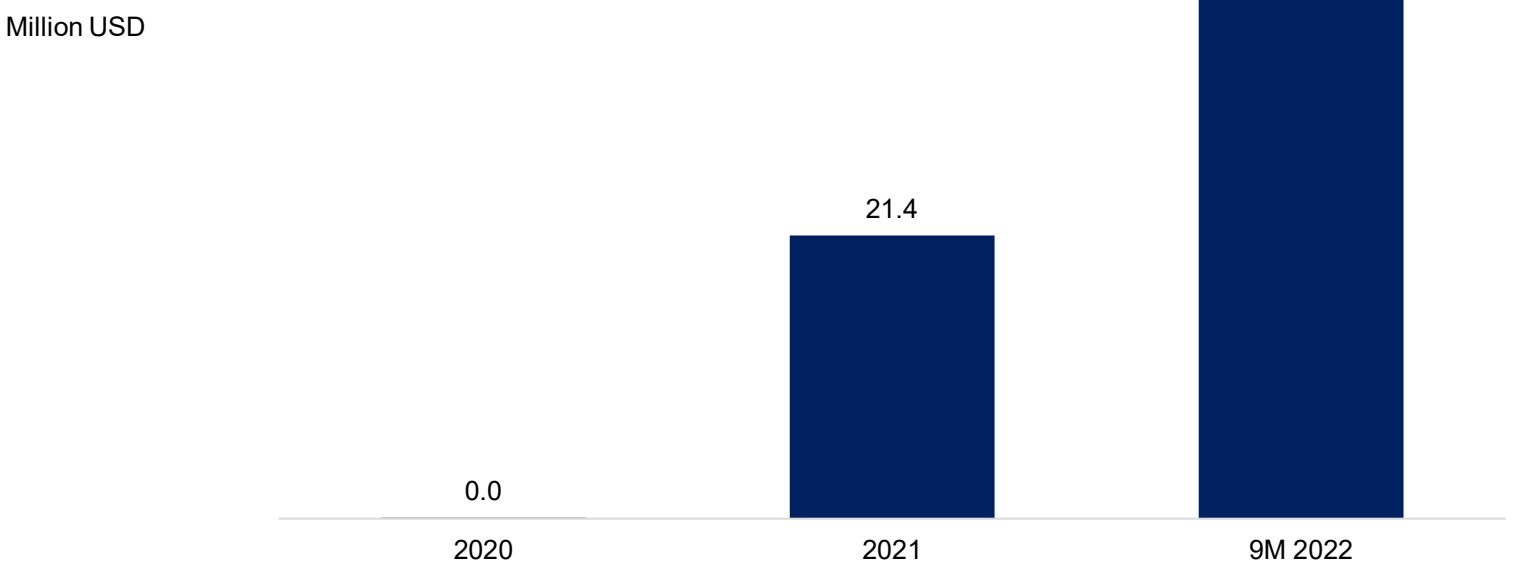
Source: Literature Review, Frost & Sullivan analysis

Sample Hospital Sales of Dupilumab (Dupixent®) in China, 2020-9M 2022

- The sales of Dupilumab with the brand name Dupixent® recorded by sample hospitals in China has increased from USD 42.5 thousand in 2020 to USD 21.4 Million in 2021, the % change has reached 50,159.5%. The sample hospital sales of Dupilumab in China were USD 40.0 million in the first nine months of 2022.

Sample Hospital Sales of Dupilumab (Dupixent®) in China, 2020-9M 2022

Period	% Change
2020-2021	50159.5%



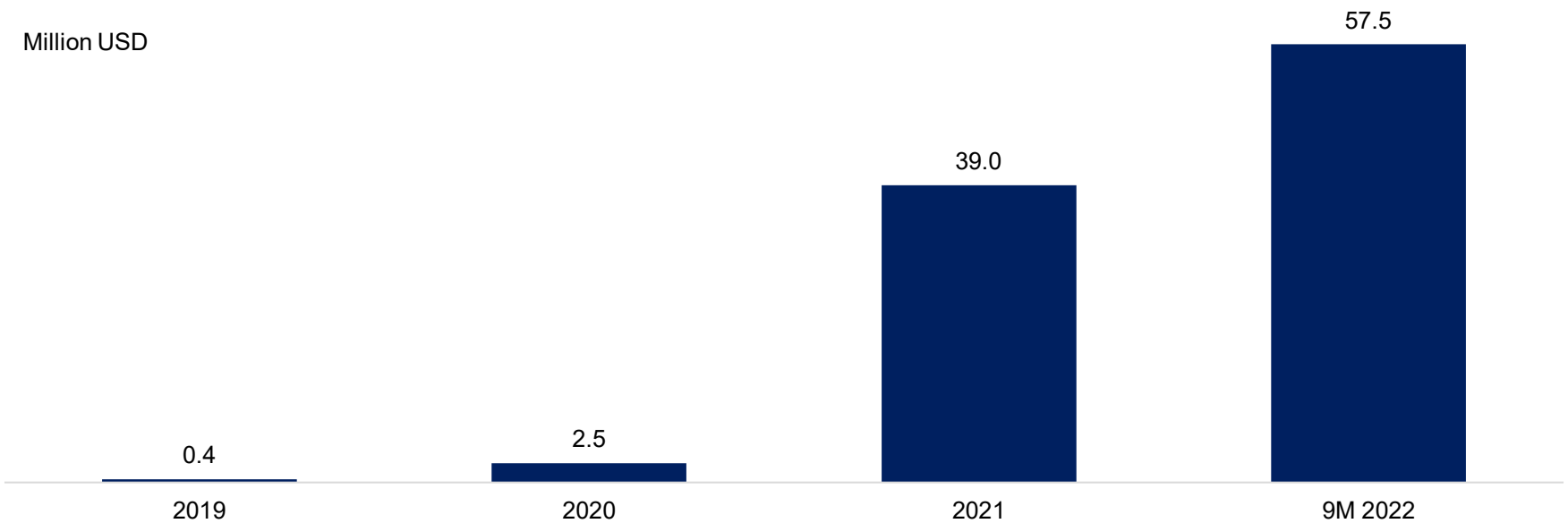
Source: PDB database, Frost & Sullivan analysis

Sample Hospital Sales of Secukinumab (Cosentyx®) in China, 2019-9M 2022

- The sales of Secukinumab with the brand name Cosentyx® recorded by sample hospitals in China has increased from USD 0.4 million in 2019 to USD 39.0 million in 2021, representing a CAGR of 876.0%. The sample hospital sales of Secukinumab in China were USD 57.5 million in the first nine months of 2022.

Sample Hospital Sales of Secukinumab (Cosentyx®) in China, 2019-9M 2022

Period	CAGR
2019-2021	876.0%



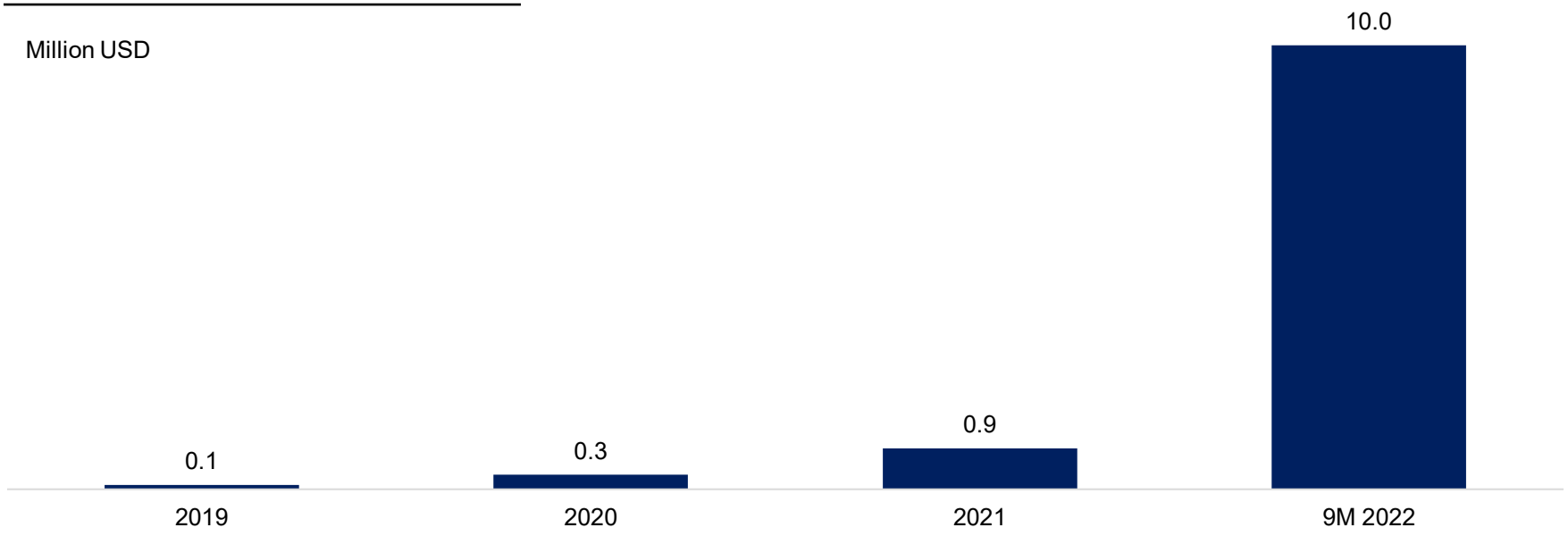
Source: PDB database, Frost & Sullivan analysis

Sample Hospital Sales of Ustekinumab (Stelara®) in China, 2019-9M 2022

- The sales of Ustekinumab with the brand name Stelara® recorded by sample hospitals in China has increased from USD 0.1 million in 2019 to USD 0.9 million in 2021, representing a CAGR of 255.8%. The sample hospital sales of Ustekinumab in China were USD 10.0 million in the first nine months of 2022.

Sample Hospital Sales of Ustekinumab (Stelara®) in China, 2019-9M 2022

Period	CAGR
2019-2021	255.8%



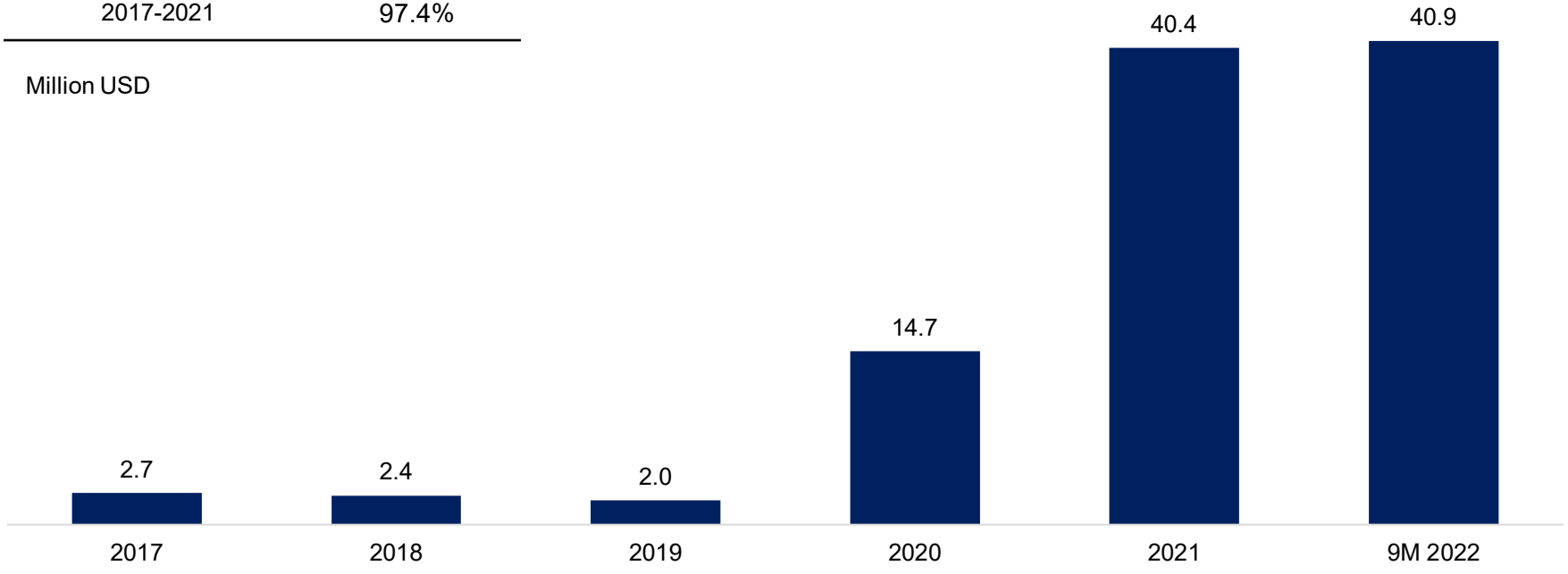
Source: PDB database, Frost & Sullivan analysis

Sample Hospital Sales of Adalimumab in China, 2017-9M 2022

- The sales of Adalimumab, including generic and biosimilars, recorded by sample hospitals in China has increased from USD 2.7 million in 2017 to USD 40.4 million in 2021, representing a CAGR of 97.4%. The sample hospital sales of Adalimumab in China were USD 40.9 million in the first nine months of 2022.

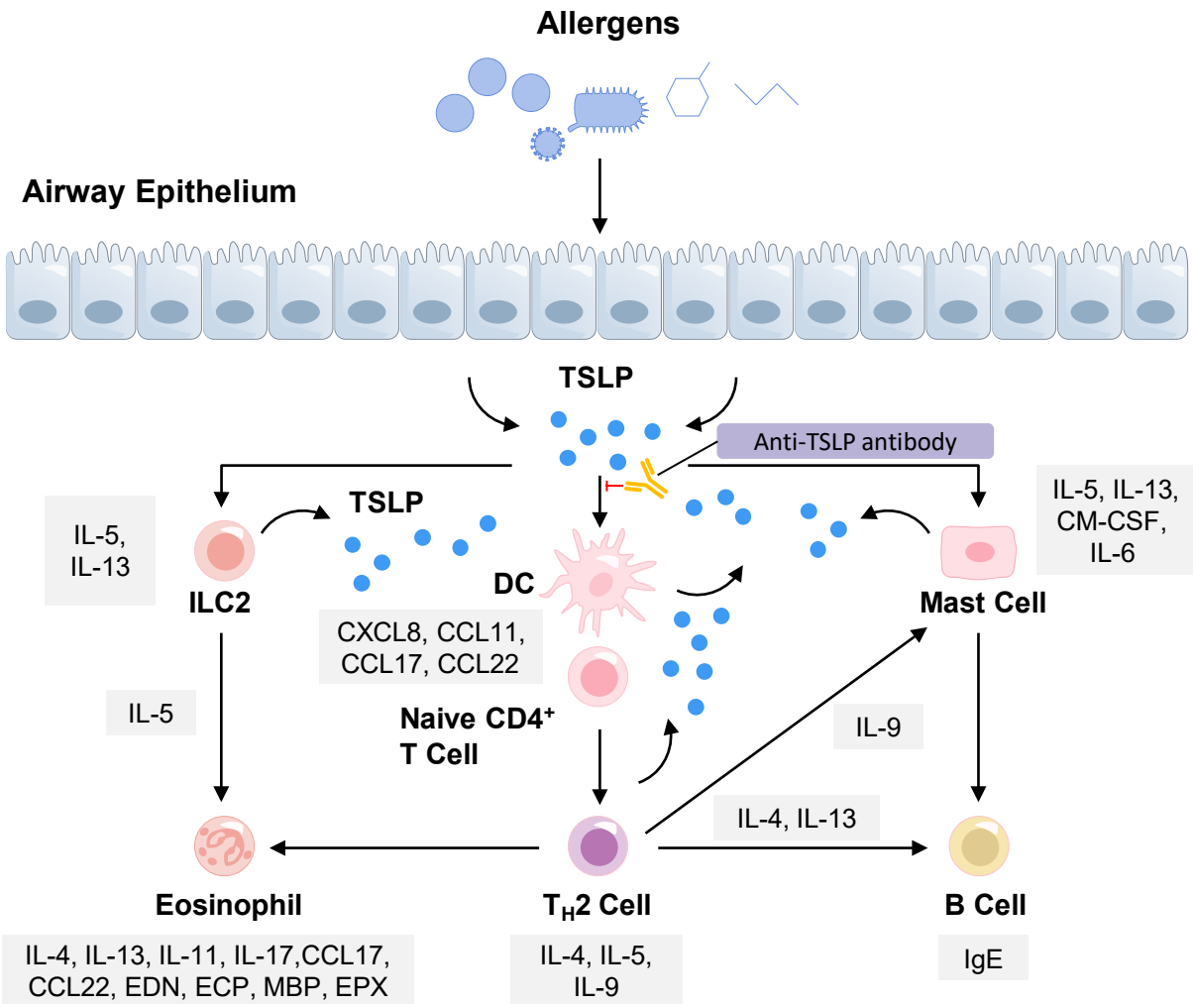
Sample Hospital Sales of Adalimumab in China, 2017-9M 2022

Period	CAGR
2017-2021	97.4%



Source: PDB database, Frost & Sullivan analysis

TSLP in Allergic Diseases and MOA of Anti-TSLP Antibodies



MOA of Anti-TSLP Antibodies:

TSLP plays a pivotal role in the development of allergic diseases. TSLP was initially shown to promote allergic responses by acting on DCs and inducing their expression of OX40L, CD80 and CD86, thereby promoting the differentiation of naive $CD4^+$ T cells into pro-inflammatory T_H2 cells that produce IL-4, IL-5, IL-13 and TNF. Subsequently, it was shown that TSLP-activated DCs also stimulate naive CD4+ T cells to differentiate into T follicular helper cells, which can induce IgG and IgE secretion by memory B cells, linking TSLP to IgE production in allergy. TSLP also promotes the release of TH2 cytokines and chemokines by eosinophils, mast cells and macrophages.

Biological functions of TSLP require heterodimer formation between the TSLP receptor (TSLPR) and IL-7 receptor-α, which polarize dendritic cells to induce type 2 inflammation and directly expand and/or activate Th2 cells, group 2 innate lymphoid cells, basophils, and other immune cells. Anti-TSLP antibodies could prevent TSLP-TSLPR interactions.

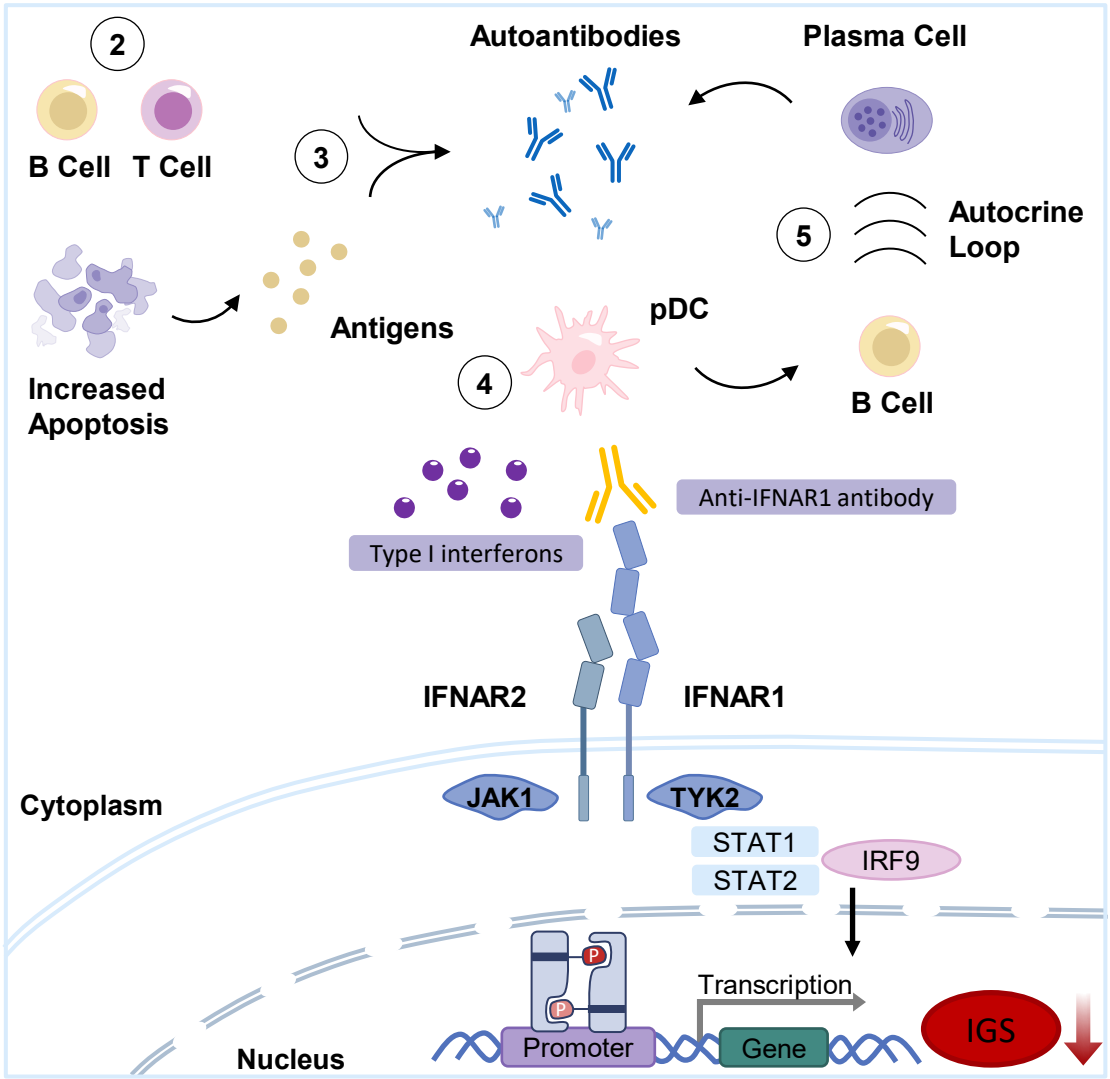
* TSLP, thymic stromal lymphopoietin; DC, dendritic cell; CCL, CC-chemokine ligand; ECP, eosinophil cationic protein; EDN, eosinophil-derived neurotoxin; EPX, eosinophil peroxidase; GM-CSF, granulocyte-macrophage colony-stimulating factor; MBP, major basic protein

Source: Literature Review, Frost & Sullivan analysis

MOA of Anti-IFNAR1 Antibodies in SLE Pathogenesis

Genetic, epigenetic, environmental, and hormonal factors

1



MOA of Anti-IFNAR1 Antibodies:

Genetic, epigenetic, environmental, and hormonal factors lead to an increased rate of apoptosis. Autoreactive B and T cells specific for self-nuclear antigens recognize and process these antigens, which, in turn, leads to autoantibody and immune complex generation. Toll-like receptor signaling in B cells and pDCs (not shown) results in increased levels of type 1 interferons mainly produced by pDCs. Type 1 interferons further stimulate B cells in an autocrine loop, and B cells exhibit class switching, which leads to a persistent production of autoantibodies.

Anti-IFNAR1 antibody binds to IFNAR1, thus inhibiting dimerization and subsequent intracellular signaling mechanisms mediated by STAT1/2 and IRF9. The net result is a decreased transcription of proinflammatory genes in cells of both the innate and adaptive immune systems.

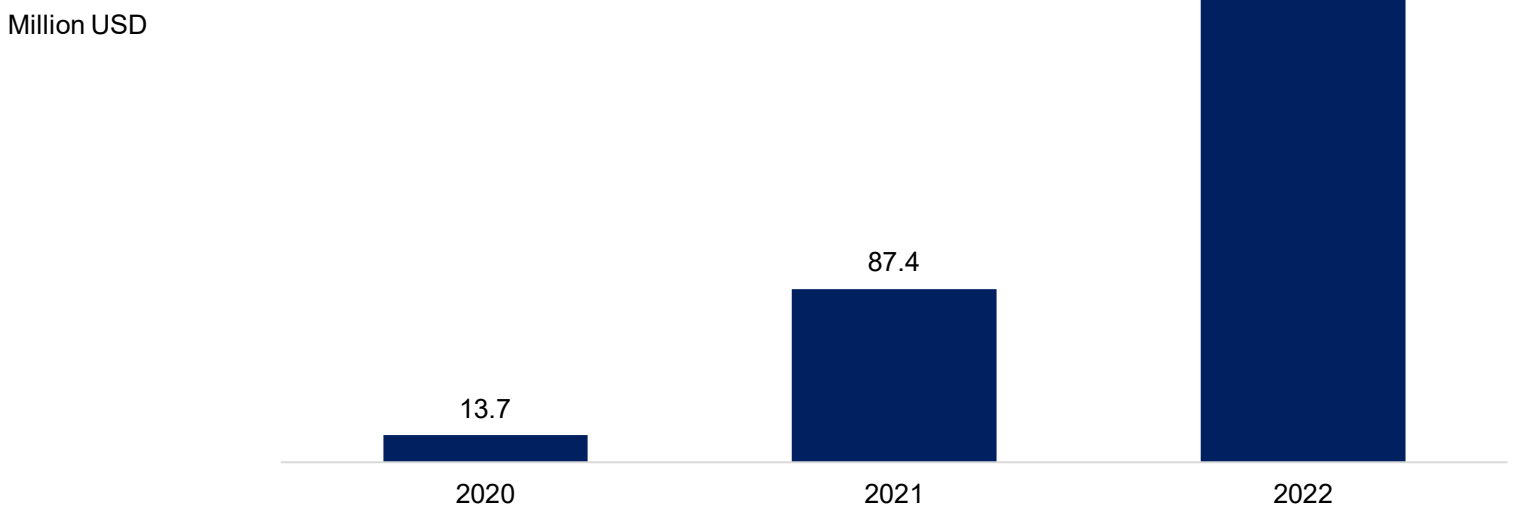
Source: Literature Review, Frost & Sullivan analysis

Sales of Dupilumab (Dupixent®) in China, 2020-2022

- The sales of Dupilumab in China with the brand name Dupixent® disclosed by Sanofi has increased from USD 13.7 million in 2020 to USD 248.1 Million in 2022, with a CAGR of 325.0% from 2020 to 2022.

Sales of Dupilumab (Dupixent®) in China, 2020-2022

Period	CAGR
2020-2022	325.0%



* Note: Sales of Dupixent are both recorded by Sanofi (in EUR) and Regeneron (in USD), but only Sanofi disclosed its sales in China. The exchange rates in each year are calculated by the global sales recorded by Sanofi and Regeneron.

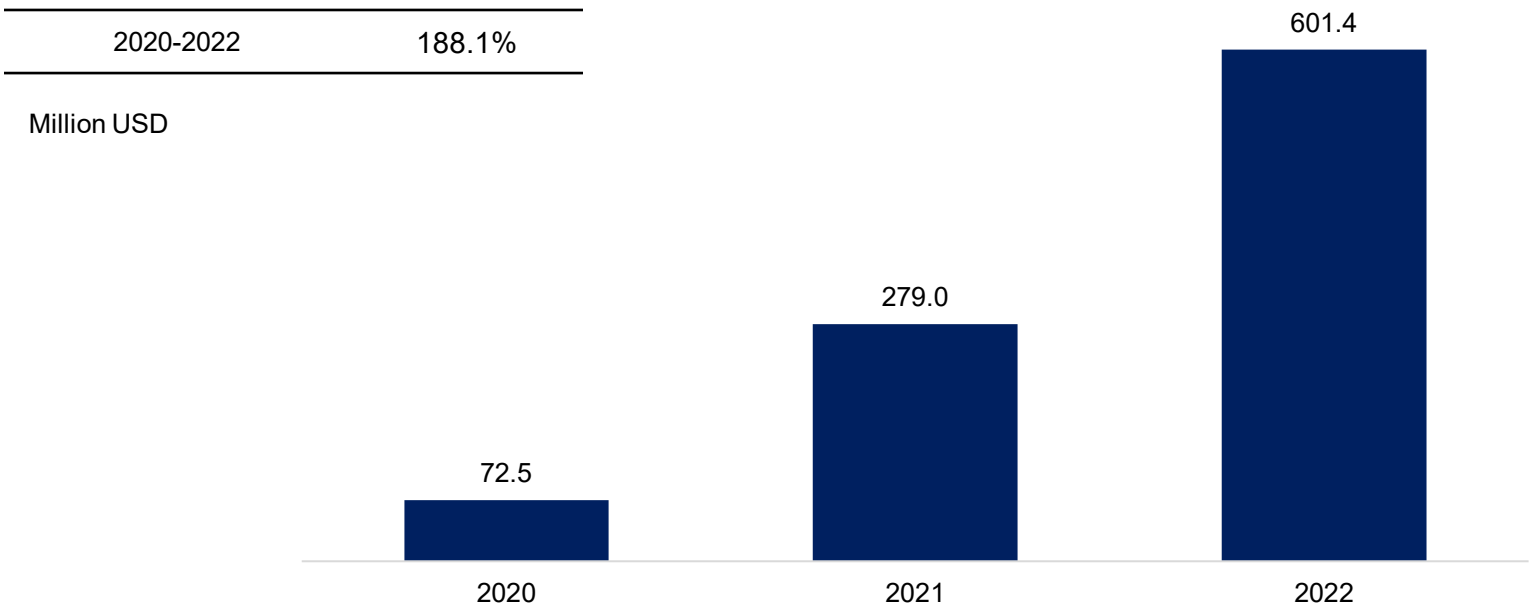
Source: Sanofi Annual Report, Frost & Sullivan analysis

Sales of Secukinumab (Cosentyx®) in China, 2020-2022

- The sales of Secukinumab in China with the brand name Cosentyx® has increased from USD 72.5 million in 2020 to USD 601.4 Million in 2022, with a CAGR of 188.1% from 2020 to 2022.

Sales of Secukinumab (Cosentyx®) in China, 2020-2022

Period	CAGR
2020-2022	188.1%



Source: KOL interview, Frost & Sullivan analysis

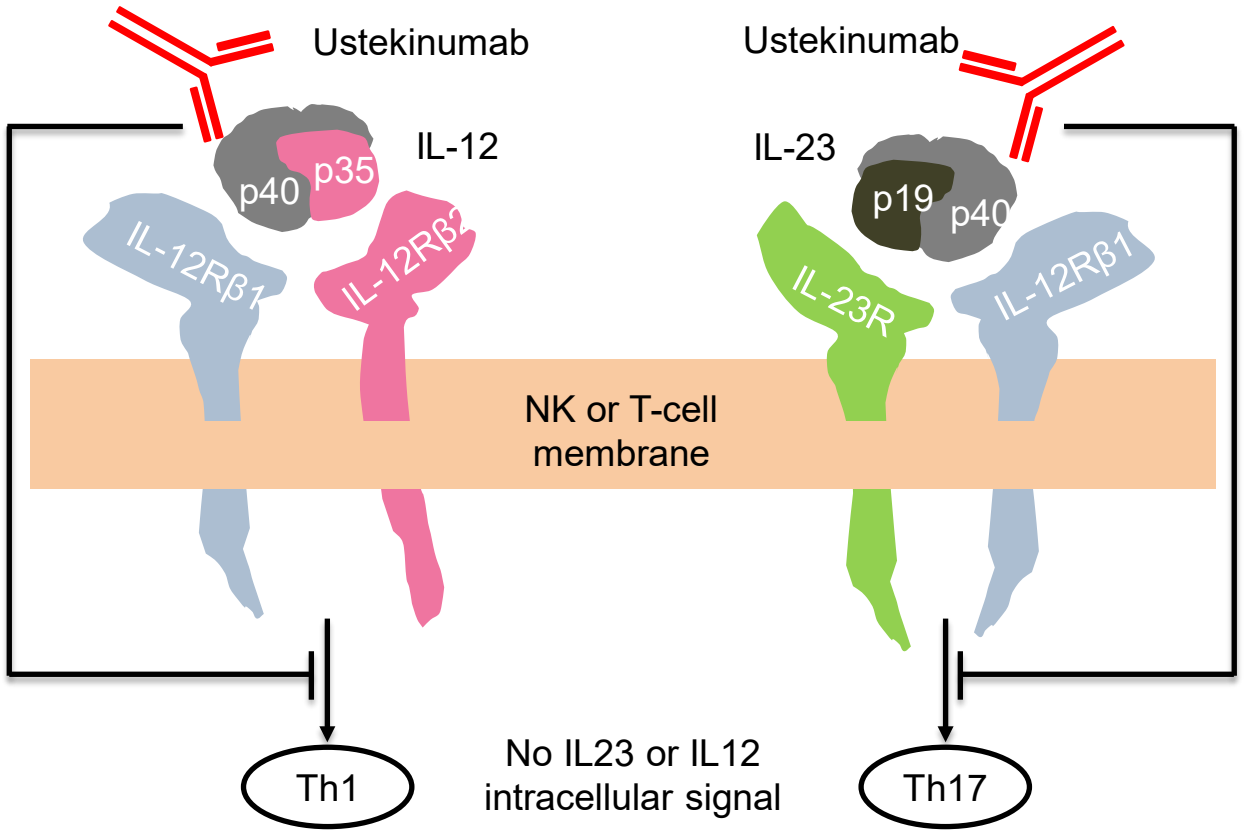
Potential Market Size, 2021

Indication	Potential Market Size (Billion USD)
Psoriasis	7.8
PN	25.1
AS	12.1
SLE	10.8
CD	0.7
AD	263.1
Asthma	66.7
CRSwNP	256.1

Source: Frost & Sullivan analysis

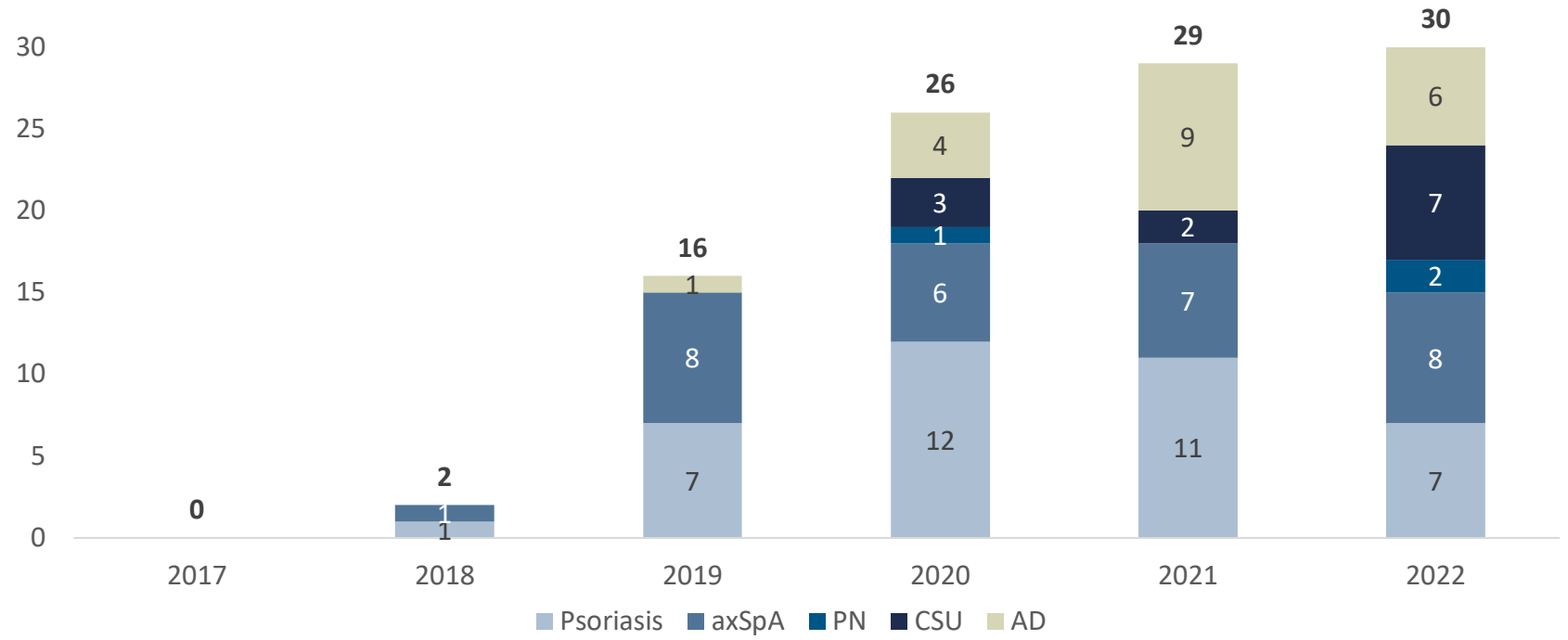
MOA Diagram of Ustekinumab

Ustekinumab binds to the p40 subunit of IL-12 and IL-23 preventing their interaction with the natural killer (NK) or T-cell surface IL-12 receptor β1 (IL-12Rβ1) and inhibiting IL-12 and IL-23 signaling, activation and cytokine production



Source: Frost & Sullivan analysis

IND Approval for Psoriasis, axSpA, PN, CSU, AD, 2017-2022



*axSpA includes nr-axSpA and AS
Only biologics included.

Source: CDE, Frost & Sullivan analysis

IL-4Rα Antibody and Indications Under Development Globally

IL-4R is well-validated, broad-acting target and controls the signaling of both IL-4 and IL-13, which is critical in the initiation of type 2 inflammation (a pattern of immune response that underpins the pathophysiology of several chronic allergic diseases). IL-4R inhibitors are under development for 20 indications globally, including 5 approved indications and 15 in the clinical stage

No.	Indications	Status
1	Atopic Dermatitis	Approved
2	Prurigo Nodularis	Approved
3	Chronic Rhinosinusitis With Nasal Polyps	Approved
4	Asthma	Approved
5	Eosinophilic Esophagitis	Approved
6	CRSsNP	Clinical stage
7	Allergic Fungal Rhinosinusitis	Clinical stage
8	Peanut Allergy	Clinical stage
9	Cold Urticaria	Clinical stage
10	Bullous Pemphigoid	Clinical stage
11	Atopic Keratoconjunctivitis	Clinical stage
12	Allergic Bronchopulmonary Aspergillosis	Clinical stage
13	Chronic Spontaneous Urticaria	Clinical stage
14	Neurodermatitis	Clinical stage
15	Chronic Obstructive Pulmonary Disease	Clinical stage
16	Alopecia Areata	Clinical stage
17	Conjunctivitis	Clinical stage
18	Keloid	Clinical stage
19	Eosinophilic Gastritis	Clinical stage
20	Allergies Food Milk	Clinical stage

Source: Frost & Sullivan analysis

Overall Sales Data for Listed Drug

Type	Brand Name	Generic Name	Company	Global Sales (USD Million)
Branded Drug	Humira	Adalimumab	AbbVie	21,237
	Stelara	Ustekinumab	J&J	9,723
	Skyrizi	Risankizumab-rzaa	AbbVie	5,165
	Enbrel	Etanercept	Amgen+Pfizer	5,120
	Cosentyx	Secukinumab	Novartis	4,788
	Orencia	Abatacept	BMS+Ono	3,686
	Tremfya	Guselkumab	J&J	2,668
	Remicade	Infliximab	J&J+Merck+Mitsubishi Tanabe Pharma	2,557
	Taltz	Ixekizumab	Lily	2,482
	Simponi	Golimumab	J&J+Merck+Mitsubishi Tanabe Pharma	2,397
	Cimzia	Certolizumab pegol	UCB+Astellas	2,197
	Benlysta	Belimumab	GSK	1146
	Ilumya	Tildrakizumab-asmn	Sun Pharma	315
	Siliq	Brodalumab	Valeant	/
Biosimilar	Inflectra	Infliximab-dyyb	Pfizer	532
	Amjevita	Adalimumab-atto	Amgen	439
	Yusimry	Adalimumab-aqvh	Coherus BioSciences	26
	Erelzi	Etanercept-szzs	Novartis	/
	Renflexis	Infliximab-abda	Merck	/
	Cyltezo	Adalimumab-adbm	Boehringer-Ingelheim	/
	Ixifi	Infliximab-qbtx	Pfizer	/
	Hyrimoz	Adalimumab-adaz	Novartis	/
	Eticovo	Etanercept-ykro	Samsung Bioepis	/
	Hadlima	Adalimumab-bwwd	Samsung Bioepis	/
	Abrilada	Adalimumab-afzb	Pfizer	/
	Avsola	Infliximab-axxq	Amgen	/
	Hulio	Adalimumab-fkjp	Kyowa Kirin	/

Source: Official website, Annual report, Frost & Sullivan analysis

Expiry Date of Patents for Marketed Drugs- I

Brand Name	Generic Name	Region	Expiry Date of Patent
Tezspire	Tezepelumab	U.S.	Methods of treatment 2038-08-23, Polypeptides 2029-02-03
		EU	Polypeptides 2028-09-09
Enbrel	Etanercept	U.S.	Formulations and methods of preparing formulations 2037-10-19, DNA encoding fusion protein and methods of making fusion protein 2029-04-24, Fusion protein and pharmaceutical compositions 2028-11-22, Methods of treatment using aqueous formulations 2023-06-08
Saphnelo	Anifrolumab	U.S.	2025-2029, 2033-2036
		EU	2025-2029, 2036
		Japan	2025-2029, 2033-2036
		China	2025-2029
Dupixent	Dupilumab	U.S.	Methods of Treatment 2034-07-10, Methods of Treatment 2033-12-22, Formulation 2032-10-17, Methods of Treatment 2028-04-17, Methods of Treatment 2027-10-02, Composition of Matter 2027-10-02
		EU	Supplementary Protection Certificate 2032-09-28, Composition of Matter 2029-10-27
		Japan	2026, 2029
Skyrizi	Risankizumab-rzaa	U.S.	2034-02-04
		Canada	2031-11-02
Fasenra	Benralizumab	U.S.	2024, 2028-2034
		Europe	2025, 2028-2034
		Japan	2025, 2034
		China	China 2021, 2028
Siliq	Brodalumab	Canada	2031-01-12
Taltz	Ixekizumab	U.S.	2028, 2030
		Europe	2027, 2031
		Japan	2023, 2029
Cosentyx	Secukinumab	U.S.	Active ingredient 2028
		Europe	Active ingredient 2030
		Japan	Active ingredient 2029
Ilumya	Tildrakizumab-asmn	Canada	2028-02-21

Source: Official website, Annual report, Frost & Sullivan analysis

Expiry Date of Patents for Marketed Drugs- II

Brand Name	Generic Name	Region	Expiry Date of Patent
Tysabri	Natalizumab	U.S	Methods of treatment 2027, Methods of treatment 2023, Humanized recombinant antibodies, Nucleic acids and host cells, Processes for production, Therapeutic compositions, Methods of use 2020
		Europe	Methods of use 2023, humanized immunoglobulins, Nucleic acids, Pharmaceutical compositions, Medical uses 2020
Tremfya	Guselkumab	Canada	2026-12-28
Benlysta	Belimumab	U.S.	2025
		Europe	2026
Stelara	Ustekinumab	U.S.	Composition of Matter 2023-09
		Europe	Composition of Matter 2024-01
Simponi	Golimumab	U.S.	2024
		Europe	2024
Cimzia	Certolizumab pegol	U.S.	2024
		Europe	2021
Humira	Adalimumab	U.S.	2023
Entyvio	Vedolizumab	U.S.	2021-09
		Europe	2017-08 (in some certain countries 2022-08)
Orencia	Abatacept	U.S.	2019-10
		Europe	2017-12
Remicade	Infliximab	U.S.	2018-09
		Europe	2015-02
Xolair	Omalizumab	U.S.	2017-06-20
		Europe	2017-08
Cinqair	Reslizumab	U.S.	2017

Source: Official website, Annual report, Frost & Sullivan analysis

Remicade Influences for Biologics Drug Candidates

- From our perspective, the approval of Remicade in China will not result in high entry barriers for the biologics drug candidates which are still at early stage clinical trials.
- According to public information, Remicade's global sales have declined significantly from 9 billion in 2014 to 2 billion in 2021, and the impact of biosimilars is one of the essential factors .
- The infliximab biosimilars marketed in China are recognized as being almost consistent with the Remicade in terms of efficacy, safety, pharmaceutical characteristics and quality, and the price is lower than Remicade. So, the approval of Remicade in China will not result in high entry barriers for the biologics drugs candidates.

Source: Public Information, Annual report, Frost & Sullivan analysis

Appendix

- As of March 22, 2023, there were 2 anti-IL-17A antibodies approved globally, secukinumab and ixekizumab, both of which were also approved in China, and there were 11 IL-17A antibodies in clinical development in China.
- As of March 22, 2023, anifrolumab was the only IFN receptor inhibitor approved by the FDA for SLE treatment and no drug of the same target was approved for SLE by the NMPA.
- As of March 22, 2023, there were 12 IL-4R-targeting biologic candidates in the clinical stage in China, including QX005N.
- As of March 22, 2023, only 3 biologics had been approved by FDA for the treatment of CRSwNP, namely dupilumab targeting IL-4R, omalizumab targeting IgE and mepolizumab targeting IL-5, and none had been approved in China.
- As of March 22, 2023, there were four IL-23 and/or IL-12 antibodies approved globally, namely, ustekinumab, guselkumab, tildrakizumab and risankizumab. There were ten antibody candidates targeting IL-23 and/or IL-12 in the clinical stage in China.
- The global sales of Cosentyx reached USD 4,788 million in 2022.
- As of March 22, 2023, there was only one FDA-approved biologic drugs belimumab for the treatment of LN.
- In 2022, the total global sales of IL-17A targeted antibodies, including secukinumab and ixekizumab, reached USD 7,270 million. The global sales (tildrakizumab excluded with undisclosed data) of IL-23 targeted antibodies, including ustekinumab, guselkumab, and risankizumab, reached USD 17,556 million

Target	Drug	Global sales 2022 (million USD)	SUM - Global sales 2022 (million USD)
IL-17A	Secukinumab	4788	7270
	Ixekizumab	2482	
IL-23	Ustekinumab	9723	17556
	Guselkumab	2668	
	Tildrakizumab-asmn	undisclosed	
	Risankizumab-rzaa	5165	

Source: Frost & Sullivan analysis

Appendix

- Recently, tyrosine kinase 2 (TYK2) inhibitors, a newer family of small-molecule targeted drugs, have demonstrated in clinical studies promising efficacy profiles for treating Ps, including improvements on traditional limitations of JAK-related toxicities.
- A considerable proportion of AS patients first develop symptoms in their early adulthood or adolescence, and require long-term treatment to control disease progression.
- In addition to traditional treatments and targeted biologics, tofacitinib by Pfizer, a small molecule Janus kinase (JAK) inhibitor, has been approved for AS treatment by the FDA and the NMPA. However, tofacitinib is recommended by the FDA only for AS patients who are intolerant or non-responsive to one or more TNF inhibitors as there still remain serious concerns over the safety profile of JAK inhibitors.
- In contrast, IL-23 and IL-12 inhibitors, such as ustekinumab, have exhibited strong safety profile while maintaining satisfactory efficacy. However, all such types of biologics are likely to result in drug-resistance. Therefore, CD patients will likely need to switch between such types of biologics.
- Dupilumab had also been admitted to the NRDL.
- Biologic drugs are large-molecule drugs, which include monoclonal antibodies (mAbs), recombinant proteins, vaccines and other emerging categories.
- Allergic diseases are conditions caused by hypersensitivity of the immune system due to contact with allergens in the external environment,such as pollen, certain food, medication and insect stings, which can also affect multiple organs. Autoimmune and allergic diseases can trigger serious symptoms such as acute pain, persistent itchiness and disfigurement and, in some cases, may even lead to life-threatening complications and be fatal. In addition, despite their non-contagious nature, the social stigma often associated with these diseases due to the visibility of the lesions and inadequate understanding in the general public may further affect patients' mental well-being and reduce their quality of life, posing a significant socioeconomic burden on both the patients and society. Most autoimmune and allergic diseases are chronic diseases and require long-term care at high costs. It has been challenging to develop effective treatments of these diseases for long-term use because their pathogeneses are yet to be fully understood. In recent years, the emergence of biologic and targeted therapies has brought profound changes to the treatment paradigm for these diseases with improved efficacy and safety profiles.

Source: Frost & Sullivan analysis

Appendix

- Autoimmune and allergic diseases represent the second-largest therapeutic area globally, market development in China has lagged significantly behind. While the total patient population of autoimmune and allergic diseases in China exceeded 420 million in 2021, as compared to 100 million in the United States.
- A number of blockbuster drugs developed by MNCs were approved in China and admitted to the NRDL.
- As traditional anti-inflammatory agents are noted with limited efficacy in patients with more severe symptoms and there remain concerns over the potential side effects from long-term use of some of these agents, biologic drugs have emerged as promising innovative therapies for many autoimmune diseases over the past decades. Biologic drugs have revolutionized autoimmune disease treatment by targeting specific factors driving disease progression, instead of suppressing the immune system undiscriminatingly, thereby reducing the serious side effects that can result. Antibodies targeting TNF, a type of pro-inflammatory cytokine, are the most widely used biologic drugs for the treatment of various autoimmune diseases, such as ankylosing spondylitis (AS) and rheumatoid arthritis (RA). However, there remain substantial limitations associated with TNF inhibitors. Studies have shown that up to 40% of patients become intolerant or fail to achieve adequate disease control with anti-TNF therapies.
- In recent years, studies have demonstrated that interleukins, a type of cytokines, play essential roles in modulating the growth, differentiation and activation of various immune cells, including T cells, during inflammatory and immune responses. Therefore, IL inhibitors have been developed as the next-generation biologic drugs for autoimmune diseases. The IL family include a variety of cytokines, among which those related to T helper cells 17 and T helper cells 2 (Th17 and Th2), such as IL-17, IL-12 and IL-23, are the most studied.
- Secukinumab is currently approved in over 90 countries worldwide, including the U.S., the EU, Japan and China.
- In 2021, secukinumab recorded sales of US$4.7 billion and US$279.0 million globally and in China, respectively. IL-17A antibodies are expected to experience rapid increase in their market shares, primarily driven by improving drug affordability and fast expansion of approved indications.
- Ustekinumab, the first marketed anti-IL-12/IL-23 antibody in the world, is approved by the FDA for the treatment of moderate-to-severe plaque psoriasis, active psoriatic arthritis (PsA), moderately to severely active Crohn's disease and moderately to severely active ulcerative colitis. Since its launch in 2009, it has been widely regarded as one of the major treatments for Ps worldwide. In 2021, it recorded sales of US$9.1 billion globally and ranked the ninth best-selling drug worldwide in the same year. Despite increasing competition (including potential biosimilar competition), the sales of ustekinumab are expected to remain stable considering itscontinuous expansion of approved indications.

Source: Frost & Sullivan analysis

Appendix

- Other promising innovative biologic treatments for autoimmune diseases include interferon (IFN) inhibitors and B cell–related therapies. IFNs are a family of cytokines that help enhance antiviral responses and immune activation, and have been found to play important roles in antoimmune and chronic inflammatory responses. B cell–related therapies aim to inhibit autoreactive B cell activation and autoantibody production. Popular B cell–related targets include, among others, B lymphocyte stimulator (BLyS or BAFF), a member of the TNF cytokine family and a key factor in the differentiation and survival of B cells, a proliferation inducing ligand (APRIL), and various membrane protein present on B cells, such as CD20, CD40 and CD80. IFN inhibitors and B cell–related therapies have been approved as treatment for SLE and are under investigation as potential treatment options for other autoimmune diseases such as RA and lupus nephritis (LN).
- In addition, small-molecule targeted therapies, such as janus kinase (JAK) inhibitors, have also been explored as potential treatment for autoimmune diseases such as RA and AS. JAK is a family of signaling molecules involved in the intracellular transduction of immune signaling of various cytokine receptor cells. JAK inhibitors have shown clear clinical benefit in patients with certain autoimmune diseases in terms of symptom relief and reduction of inflammation. However, the FDA required warning for several first-generation JAK inhibitors with respect to the increased risks of major cardiovascular events and malignancies in patients and the long-term safety profile of later-generation candidates is still under evaluation.
- Because Ps is incurable, the goal of treatment is to control disease progression and maintain long-term efficacy. Treatment paradigms are based on the patients' conditions, including the type of Ps, the severity of the conditions and any co-morbidities. Topical drugs are usually used to treat patients with mild Ps but can cause local adverse reactions if used long term. It may be inconvenient for patients with extensive rashes and there is significant variation in patient compliance. Non-steroidal anti-inflammatory drugs (NSAIDs) and diseasemodifying anti-rheumatic drugs (DMARDs) are also commonly used to control Ps and alleviate symptoms such as pain, stiffness and swelling. However, studies have found that NSAIDs and DMARDs showed limited efficacy as compared to targeted biologic drugs. Small molecule targeted drugs are a relatively new class of medications as a potentially promising treatment option for Ps patients. For example, JAK inhibitors have shown promising clinical results but may lead to more severe side effects and higher toxicity, causing the FDA to advise that they should be used with caution for patients with certain risk factors. PDE-4 inhibitors, another family of small molecule drugs, have shown good safety profile but with limited efficacy. As a result, their use as a recommended long-term treatment option for a broad section of Ps patients remains under evaluation.

Source: Frost & Sullivan analysis

Appendix

- However, drug accessibility and treatment compliance for biologic drugs in the treatment of autoimmune diseases have historically been relatively low in China, primarily due to limited number of approved biologic drugs, high treatment cost associated with the MNC-developed blockbuster drugs and lack of awareness and education regarding autoimmune diseases.
- TNF inhibitors and IL inhibitors are considered first-generation and second-generation drugs. As TNF inhibitors have significant limitations, including multiple adverse effects and a high rate of non-responsiveness, IL inhibitors present a promising treatment for Ps. Common IL targets under investigation include IL-12, IL-23 and IL-17.
- Medications indicated for AS mainly include NSAIDs, conventional DMARDs and corticosteroids.However, they are noted with limited efficacy in patients with more severe disease and their effectiveness in suppressing bone erosion and remodeling associated with AS remains unclear. In addition, there are grave safety risks associated with long-term systemic use of such therapies, especially corticosteroids. Maintenance treatment with systemic use of corticosteroids can cause a series of severe adverse effects, such as osteoporosis, adrenal suppression and hyperglycemia (high blood sugar), and dose-dependent growth suppression in children and adolescents. In the past decades, biologic drugs have emerged as promising innovative therapies for AS.
- There are two types of approved biologic drugs in China for the treatment of AS, namely, TNF inhibitors and IL-17 inhibitors. TNF, most prominently TNF-, is a type of proinflammatory cytokine produced by certain types of white blood cells during acute inflammation and plays a role in the regulation of the immune system. Dysregulation of TNF may lead to excessive inflammation, which in turn may cause various autoimmune and immune-mediated disorders. TNF inhibitors block the binding of TNF to TNF receptors, thereby suppressing their biological effects. TNF inhibitors are currently the most commonly used biologic drugs for AS in China. However, studies have shown that up to 40% of patients with AS become intolerant or fail to achieve adequate disease control with anti-TNF therapies, indicating significant heterogeneity in treatment response. Thus, there remains an unmet medical need for novel treatments with a different mechanism of action. With recent scientific advancements demonstrating the role of IL-17A in AS pathogenesis, IL-17A antibodies have emerged as a new class of biologic drugs for AS and, together with TNF inhibitors, have been recommended by prevailing clinical guidelines as second-line treatment for AS patients with high disease activity after undertaking first-line traditional treatments.

Source: Frost & Sullivan analysis

Appendix

- In addition to traditional treatments and targeted biologics, tofacitinib by Pfizer, a small molecule Janus kinase (JAK) inhibitor, has been approved for AS treatment by the FDA and the NMPA. However, tofacitinib is recommended by the FDA only for AS patients who are intolerant or non-responsive to one or more TNF inhibitors as there still remain serious concerns over the safety profile of JAK inhibitors.
- The types of drugs that have been used to treat SLE mainly include corticosteroids, DMARDs, antimalarial drugs (such as hydroxychloroquine) and biologic drugs. High doses of corticosteroids can be helpful in severe cases of SLE, but the patients face considerable risk of disease progression, relapse over time and serious side effects, including osteoporosis (weak bones), high blood pressure and diabetes. In addition, treatment with DMARDs may result in an increased risk of serious infections and certain types of cancer. Hydroxychloroquine may offer relief for SLE-related symptoms, such as arthritis, fatigue and rashes, but is associated with increased risk of retinopathy. There remain significant unmet needs for new therapeutics for SLE that effectively control disease activity, have a favorable safety profile and improve the patients' quality of life. Over the past decades, there has been growing interest in the development of biologic drugs indicated for SLE, including, most importantly, interferon (IFN) receptor inhibitors and B cell depletion therapies aiming to inhibit autoreactive B cell activation and autoantibody production.
- Belimumab is a human monoclonal antibody that inhibits BLyS or BAFF, a member of the TNF cytokine family produced by myeloid lineage cells, such as dendritic cells and macrophages, and a key factor in the differentiation and survival of B cells. Telitacicept targets two cell-signaling molecules critical for B cell development: BLyS and a proliferation inducing ligand (APRIL). Belimumab was also approved by the FDA in 2011
- Several types of medications may be used to treat UC/CD, including anti-inflammatory drugs, glucocorticoids, immunosuppressants and biologic drugs. Anti-inflammatory drugs mainly include aminosalicylic acids (5-ASA), which can reduce inflammation but studies have shown that they are not effective at inducing remission in active CD or preventing relapse in inactive CD. While patients can initially respond to glucocorticoids therapy, a large portion of them develop a dependency on glucocorticoids or have a relapse within 1 year. In addition, use of glucocorticoids is often limited by a relatively high risk of serious adverse effects including bone loss, metabolic complications, increased intraocular pressure and glaucoma and potentially lethal infections. Immunosuppressants may also trigger profound side effects such as short-term and long-term toxicities due to their non-specific, anti-proliferative or antimetabolic features. In the past five years, the introduction of biologic drugs has heralded a new era of evolving biologically targeted treatments for UC/CD.

Source: Frost & Sullivan analysis

Appendix

- NSAIDs are recommended as the first-line treatment for AS in China.
- There are three types of approved biologic drugs in China for the treatment of UC/CD, namely, TNF-α inhibitors, integrin α4 (ITGA4)/integrin β7 (ITGB7) inhibitors and IL-12/IL-23 inhibitors. TNF-α inhibitors block the binding of TNF to TNF receptors, thereby suppressing their biological effects. Integrin α4/integrin β7 inhibitors bind to the surface of white blood cells so they cannot pass through tissue layers and exacerbate inflammation. However, use of certain integrin α4/integrin β7 inhibitors carries an increased risk of progressive multifocal leukoencephalopathy, a severe brain condition. In contrast, IL-23 and IL-12 inhibitors, such as ustekinumab, have exhibited strong safety profile while maintaining satisfactory efficacy. However, all such types of biologics are likely to result in drug-resistance. Therefore, CD patients will likely need to switch between such types of biologics.
- Allergy desensitization is a therapy that aims to weaken a patient's allergic reactions by exposing them to gradually increasing doses of allergens. Allergy desensitization is widely used for treatment of allergies of pollen, mites, animal dander and certain medications, but it is barely effective for systemic allergic diseases without a specific allergen, such as AD, PN, CRSwNP, asthma and COPD. Antihistamines and glucocorticoids are then introduced into the treatment of allergic diseases to suppress or alleviate symptoms in various allergic diseases. However, such traditional treatment options are generally limited in efficacy and associated with severe adverse events, especially for long-term treatment. Since the first biologic drug, an IgE inhibitor, was approved for the treatment of allergic diseases by the FDA in 2003, biologic drugs have been widely used globally for the treatment of allergic diseases. Several cytokines and pathways, such as IL-4, IL-5, IL-13, TSLP and JAK, were found to be involved in the activation of type 2 immune response. Among all type 2 inflammatory cytokines, IL-4 and its receptor are the most studied.
- Due to the relative late start of development, biologic antibodies were firstly approved for the treatment of allergic diseases in China in 2017. To date, market penetration and treatment compliance with biological therapies for allergic diseases remain relatively low in China as a result of the high costs associated with current biologic therapies.
- Small-molecule targeted therapies, such as JAK inhibitors, can also be used to treat allergic diseases. However, the FDA and the EMA has required warning for several JAK inhibitors with respect to their safety concerns.
- AD is one of the most common skin disorders globally and in China.
- Mild cases of AD can be treated with moisturizing agents and topical treatments, such as topical corticosteroids and calcineurin inhibitors. However, overuse of these drugs may cause side effects, including thinning skin or impaired immune system

Source: Frost & Sullivan analysis

Appendix

- NSAIDs are recommended as the first-line treatment for AS in China.
- In recent years, biologic drugs with better safety and efficacy profiles have become an emerging treatment for severe AD. In particular, as IL-4, IL-13, IL-5 and IL-10 are important cytokines involved in the pathogenesis of AD, they present potential targets suitable for biologic development. IL-4R is the mainstream target under investigation for AD treatment due to its role in controlling the signaling of both IL-4 and IL-13, and research on other targets, such as IL-31, IL-33 and OX40, is also ongoing. In addition, small-molecule treatments, including PDE-4 inhibitors and JAK inhibitors, have been explored as potential treatment options for AD patients. In particular, PDE-4 inhibitors have shown a good safety profile but limited efficacy, while JAK inhibitors are approved for patients who have had an inadequate response or intolerance to one or more TNF inhibitors.
- Because of the discovery of new therapeutic targets in recent years, there has been increasing research on biologic drugs for treating PN as a potentially promising treatment option.
- As of the Latest Practicable Date, dupilumab was the only treatment approved by the FDA for PN.
- The efficacy of nasal saline irrigation and surgery is limited, with a high nasal polyps recurrence rate of up to 60%. Corticosteroids, biologics and antibiotics subsequently emerged as treatment options for CRSwNP patients. Antibiotics therapy after desensitization, are primarily used for NSAID-exacerbated respiratory disease, a chronic eosinophilic, inflammatory disorder of the respiratory tract occurring in patients with asthma and/or CRSwNP. Corticosteroids for CRSwNP include intranasal corticosteroids, systemic corticosteroids and corticosteroid-eluting implants, which are primarily used following endoscopic sinus surgery. While intranasal and systemic corticosteroids are effective to some extent in the management of CRSwNP, their long-term benefits are limited. According to the Guidelines for the Diagnosis and Treatment of CRS in China (2018) (中國慢性鼻竇炎診斷和治療指南(2018)), it is difficult to maintain the clinical efficacy of systemic corticosteroids in the treatment of CRSwNP, which may lead to recurrence of nasal polyps.
- Since IL-4 and IL-13, the key Th2 cytokines, are overexpressed in CRSwNP, IL-4R is a promising target for CRSwNP as IL-4R antibody can block at least two immune signaling pathways. While IL-5 is a key signaling factor for eosinophil activation by Th2 cells and is highly expressed in eosinophilic diseases, IL-5 inhibitors can be particularly effective for treatment of eosinophilic CRSwNP. In contrast, as TSLP is an upstream regulator of type 2 inflammation, TSLP inhibitors can be a treatment for patients with low-level or no expression of type 2 biomarkers.
- Asthma, a condition that affects the lungs and respiratory functions, is one of the world's most common diseases.

Source: Frost & Sullivan analysis

Appendix

- The primary treatment for asthma is often long-term medications for the control and management of asthma symptoms because it is considered to be a chronic disease. Such long-term medications mainly include inhaled corticosteroids (ICSs) and bronchodilators.
- Omalizumab, an IgE inhibitor, was the first targeted biologic therapy developed and approved for severe asthma. IgE inhibitors can limit the degree of release of mediators of the allergic response by inhibiting the interaction between IgE and the IgE receptors. As IL-5 is a key signaling factor for eosinophil activation by Th2 cells and is highly expressed in eosinophilic diseases, IL-5 inhibitors have also been developed for treatment of asthma and are the most common type of biologics for treatment of asthma in the United States. IL-4R inhibitor, which blocks both the IL-4 and IL-13 signaling pathways, and TSLP inhibitor, which can be effective for patients with low-level or no expression of type 2 biomarkers, subsequently obtained FDA approval for treatment of asthma.
- Chronic obstructive pulmonary disease is a chronic inflammatory lung disease which obstructs air flow from the lungs.
- COPD is mainly treated with drugs to prevent and control chronic inflammation and reduce clinical symptoms. Meanwhile, COPD patients can also be treated by rehabilitation, oxygen therapy and surgery. Control drugs for long-term treatment of COPD primarily include corticosteroids, including inhaled corticosteroids (ICSs) and systemic corticosteroids, longacting bronchodilators (LABA and LAMA) and anti-inflammatory drugs, such as PDE4 inhibitors. Other drug treatments such as mucolytic, antioxidant drugs and immunomodulators can also be used to control inflammation. In the initial treatment of COPD, patients are recommended to use one bronchodilator. For patients with higher moderate exacerbations and more severe dyspnea, combination therapy of LABA and LAMA are recommended. For patients with higher eosinophil count, combined therapy of ICS with LABA and LAMA are recommended to improve lung function and reduce exacerbations. However, approximately 40% of moderate-to-severe COPD patients on triple therapy of ICS with LABA and LAMA still remain uncontrolled and continue to experience exacerbations. Therefore, there are significant unmet clinical needs from COPD patients.
- As asthma and COPD share common pathophysiological mechanisms, IL-4R and IL-5, two of the most common developed targets for treatment of asthma, are also being developed as targets for treatment of COPD. Since IL-33 can induce Th2 cytokine production and promote the pathogenesis of COPD, IL-33 and its receptor, ST2, can be promising targets for treatment of COPD as well.

Source: Frost & Sullivan analysis

Appendix

- Among the 100 top-selling drugs in 2022, around one fifth were autoimmune or allergic drugs, including two—Humira (adalimumab) (No. 2; US$21.2 billion) and Stelara (ustekinumab) (No. 9; US$9.7 billion)—in the top 10. Humira, in particular, was the world's best-selling drug for eight years in the last ten (2013-2022). In contrast, market development in China has lagged significantly behind.
- Cosentyx (secukinumab) was approved in China for moderate-to-severe plaque Ps in March 2019 and admitted to the NRDL in March 2021. While its unit price (150 mg) decreased from RMB2,998 to RMB1,188. Dupixent (dupilumab) was approved for moderate-to-severe AD in June 2020 and admitted to the NRDL in January 2021. It took seven years for Humira (adalimumab) to achieve annual sales of US$100.0 million in China since its approval in the country in 2010, whereas it took Cosentyx only two years to reach the same milestone.
- Globally, biologic drugs with superior efficacy and safety have been increasingly accepted by physicians and patients. The evolution of treatment paradigm from traditional anti-inflammatory agents to biologics is also accompanied by continuous upgrades in classes of biologic drugs. For example, compared to first-generation inhibitors targeting TNF-, which have relatively high risk of serious infections, novel biologics targeting interleukins (e.g., IL-17 and IL-23)have demonstrated better efficacy and/or safety for certain indications and are under extensive investigation with more drugs potentially to be approved. The same trendies also found and followed in China, and drives an increasing demand for novel biologic drugs.
- There are expected to be 6.9 million Ps patients in China by 2030, 20% to 30% of whom having moderate-to-severe disease.
- TNF-alpha inhibitors (currently the most prevalent biologic drugs for AS in China), are recommended by prevailing clinical guidelines as second-line treatment for AS patients with high disease activity after undertaking first-line traditional treatments. IL-17A inhibitors have shown clear clinical benefit in patients who are intolerant to or fail to achieve adequate disease control with TNF- inhibitors.
- As of the Latest Practicable Date, we had obtained IND approval for QX005N for five indications (namely, AD, PN, CRSwNP, CSU and asthma), one of the most among IL-4R-targeting drug candidates in China.
- QX005N was the first biologic drug candidate developed by a Chinese domestic company to start a clinical trial for PN in China.

Source: Frost & Sullivan analysis

Appendix

- QX001S is potentially China's first approved ustekinumab biosimilar. Initially approved by the FDA in 2009, ustekinumab was the first biologic treatment to selectively inhibit the IL-23 and IL-12 pathways and has been widely regarded as one of the major treatments for Ps worldwide
- ustekinumab ranked the ninth best-selling drug worldwide in 2021
- IL-23p19 has emerged as a key target associated with superior efficacy for Ps patients with more severe symptoms or inadequate response to existing treatments
- Risankizumab, an FDA-approved IL-23 inhibitor for moderate-to-severe plaque Ps
- IFNAR1 inhibitors are the only class of biologic drugs approved by the FDA for SLE over the past 50 years, except for B lymphocyte stimulator (BLyS) inhibitors
- Anifrolumab, the FDA-approved IFNAR1 inhibitor, had demonstrated clear clinical benefit in patients with moderate-to-severe SLE in a Phase III study (TULIP-2) and a Phase IIb study (MUSE). As of the Latest Practicable Date, there were no approved IFNAR1 inhibitors in China for the treatment of SLE, leaving a huge underserved market. As of the same date, QX006N was one of the only two IFNAR1 inhibitors developed by Chinese domestic companies that had entered clinical stage for SLE in China.
- TSLP-targeting therapy is the only class of biologic drugs globally approved for asthma that can slow disease progression for asthma patients with low-level or no expression of type 2 biomarkers
- IL-23p19 has emerged as a key target associated with superior efficacy for Ps patients with more severe symptoms or inadequate response to existing treatments.
- IL-4R, a well-validated, broad-acting target for a wide range of indications.
- IL-17A inhibitors have demonstrated clear clinical benefit in AS patients who are intolerant to or fail to achieve effective disease control with traditional therapies
- IL-17A inhibitors, together with TNF-alpha inhibitors (currently the most prevalent biologic drugs for AS in China), are recommended by prevailing clinical guidelines as second-line treatment for AS patients with high disease activity after undertaking first-line traditional treatments. IL-17A inhibitors have shown clear clinical benefit in patients who are intolerant to or fail to achieve adequate disease control with TNF- inhibitors.
- QX005N was the first biologic drug candidate developed by a Chinese domestic company to start a clinical trial for PN in China

Source: Frost & Sullivan analysis

Appendix

- Due to its chronic nature, long-term disease management for Ps has been essential to the development of new Ps treatment options.
- IL-23p19 has emerged as a key target associated with superior efficacy for Ps patients with more severe symptoms or inadequate response to existing treatments. In particular, drugs targeting IL-23p19 are expected to show an improved efficacy profile with higher potency than those targeting IL-12/IL-23p40. Additionally, it has been reported to be a target with favorable safety profile that is suitable for long-term use
- There has been significant unmet clinical needs from PN patients due to limited understanding of the pathogenesis of PN and a lack of effective PN treatments
- Dupilumab was the only treatment approved by the FDA for PN and there was no approved biologic drug for the treatment of PN in China
- Only one IFN receptor inhibitor, anifrolumab, had been approved by the FDA for SLE and no drug of the same target had been approved for SLE by the NMPA.
- Approximately 50% of patients with severe asthma are estimated to have low-level or no expression of type 2 biomarkers and classified as having type 2-low or non-type 2 allergic diseases. For patients without the elevation of those biomarkers, there continue to be important and unmet medical needs. As TSLP is an upstream regulator of type 2 inflammation, TSLP inhibitors can be a treatment for patients with low-level or no expression of type 2 biomarkers. Based on published clinical data, asthma patients receiving anti-TSLP antibody treatment of experienced significantly fewer exacerbations irrespective of their type 2 biomarker status. Thus, the development of TSLP-targeting biologic treatment may be a promising strategy for addressing the clinical needs of patients with type 2-low allergic diseases.
- As of the Latest Practicable Date, tezepelumab was the only FDA-approved TSLP-targeting biologic and no TSLP-targeting biologics had been approved in China. The high costs of tezepelumab as well as other biologics may in turn limit patients' access.
- However, in recent decades, there have been growing interest in the industry toward the development of rabbit mAbs as many studies have shown that the unique features of B-cell ontogeny and antibody repertoire make rabbits a valuable source for antibodies that have high affinity and specificity, which could potentially translate into strong bioactivity, and are easier to humanize, leading to lower risk of immunogenicity.
- A significant proportion of autoimmune and allergic disease patients (e.g., Ps patients) in China initially receive treatment in local hospitals, so an extensive sales network providing robust coverage of local sales channels is essential.

Source: Frost & Sullivan analysis

Appendix

- Competition within China's biologic drug market for autoimmune and allergic diseases is expected to continue to intensify in the following years, primarily due to growing efforts among pharmaceutical companies to address the vast underserved medical needs in the field, favorable government policies and expansion of approved biologic drugs and indications
- Ustekinumab, one of the major biologic treatments and best-selling drugs for the treatment of Ps worldwide.
- TNF- inhibitors and IL-17A inhibitors which are or will be approved by the NMPA for the treatment of Ps in China. In addition, traditional non-biologic medications are still regarded as important treatments for autoimmune and allergic disease in China and widely prescribed
- Biologic therapies have relatively limited track record in the treatment of autoimmune and allergic diseases in China, and therefore market education is needed before marketing our future approved drugs.
- The number of innovative drugs included in the NRDL is expected to increase in the future.
- The underdevelopment of the China market has historical reasons. Due to an innovation gap, most of the innovative biologic drugs available in China have been expensive blockbuster drugs developed by multinational corporations, or MNCs, and typically not covered by public medical insurance. This has had two effects. On the one hand, because autoimmune and allergic diseases are often not fatal, Chinese patients, when they have limited ability to pay and are price-sensitive, are less inclined to address them with significant economic resources as committedly as they might with fatal diseases such as cancer, leading to discontinued treatment, ineffective traditional treatment or no treatment at all. On the other hand, due to limited returns, the MNCs have not invested extensively in physician and patient education in China, which has perpetuated poor awareness. As a result, diagnosis and treatment rates for many diseases in this field have been low. The status quo indicates a deep structural misalignment with the unmet medical need. Autoimmune and allergic diseases are serious diseases. They can severely affect patients' quality of life in various manifestations, including great pain, persistent itchiness, disfigurement, disability, severe psychological pressure and social exclusion. They create profound disease burden for patients and society and require safe and effective treatment.
- Drugs developed by Chinese domestic companies are expected to have a price advantage. Domestic companies may also leverage their in-depth understanding and extensive coverage of local patients and hospitals to, together with MNCs, improve awareness of autoimmune and allergic diseases and biologic therapies through more precise and effective marketing activities and patient education

Source: Frost & Sullivan analysis

Appendix

- L-17A, a key player in the pathogenesis of various autoimmune diseases, including Ps and AS.
- Benefiting from its strong efficacy and safety profile, ustekinumab can be administered with a lower dose frequency (typically one dose every three months after the loading doses) than IL-17 inhibitors (usually one dose every month after the loading doses).
- In particular, drugs targeting IL-23p19 are expected to show an improved efficacy profile with higher potency than those targeting IL-12/IL-23p40. Additionally, it has been reported to be a target with favorable safety profile that is suitable for long-term use.
- Conjunctivitis, which is one of the most common AEs observed in patients using dupilumab.
- As of March 22, 2023, dupilumab was the only treatment approved by the FDA for PN and there was no approved biologic drug for the treatment of PN in China.
- IL-17A is a member of the IL-17 superfamily of cytokines, which perform regulatory functions in the host immune system by inducing and working in synergy with various other pro-inflammatory cytokines, enhancing chronic inflammation. In addition, IL-17A is also involved in the regulatory mechanism of bone remodeling, by inducing the expression of receptor activator of nuclear factor-B ligand (RANKL), which activates osteoclast, a type of bone cells responsible for bone erosion and remodeling. Elevated levels of IL-17A have been detected in the serum and synovial joint fluid of AS patients and identified as a major factor in AS pathogenesis IL-17A inhibition has been shown to have significant clinical efficacy in treating AS.
- TNF inhibitors are currently the most commonly used biologic drugs for AS in China. However, studies have shown that up to 40% of patients with AS become intolerant to or fail to achieve adequate disease control with anti-TNF therapies, indicating significant heterogeneity in treatment response.
- IL-17A inhibitors are recommended by prevailing clinical guidelines as second-line treatment (the same as TNF inhibitors) for AS patients with high disease activity after receiving first-line traditional treatments.
- IL-17A inhibitors are recommended by prevailing clinical guidelines as second-line treatment (the same as TNF inhibitors) for AS patients with high disease activity after receiving first-line traditional treatments.
- Topical drugs, NSAIDs and DMARDs are commonly used to control Ps but with limited efficacy as compared to biologic drugs with specific targeting, which as a relatively new class of drugs, have not yet been recommended as a main line of treatment for Ps by prevailing clinical guidelines.

Source: Frost & Sullivan analysis

Appendix

- In recent years, biologic drugs with better safety and efficacy profiles have become an emerging treatment for severe AD. However, as a relatively new class of drugs, they have not yet been recommended as a main line of treatment for AD by prevailing clinical guidelines.
- While our Phase Ia trial was labeled as Ia, this trial is essentially a Phase I trial as it was conducted in healthy subjects and with safety and tolerability of the drug candidate as the primary endpoints, and equivalent to a conventional Phase I trial designed to evaluate similar drug candidates for similar indications, according to Frost & Sullivan. Additionally, the commencement of the Phase Ib/II trial was based on the trial results from such Phase Ia trial, indicating the same effect as the completion of a Phase I trial.
- According to Frost & Sullivan, the prevalence of PN in China remained stable at approximately 1.9 million from 2017 to 2021 and is anticipated to reach approximately 2.1 million in 2030. There has been a lack of effective treatments for PN and development of the PN drug market in China is still at an early stage.
- Because of the discovery of new therapeutic targets in recent years, there has been increasing research on biologic drugs for treating PN as a potentially promising treatment option. However, as a relatively new class of drugs, they have not yet been recommended as a main line of treatment for PN by prevailing clinical guidelines.
- Biologics (including IgE inhibitors) are recommended by prevailing clinical guidelines as third-line treatment for CSU patients. As a result, the development of new therapies with improved efficacy and safety is underway.
- Biologic drugs are a relatively new class of drugs under investigation for treating pruritus, which have not yet been recommended as a main line of treatment by prevailing clinical guideline.
- In the updated guidelines published by ASAS and European Alliance of Associations for Rheumatology (EULAR) for the management of AS, IL-17A inhibitors are recommended as seond-line treatment (the same as TNF inhibitors) for AS patients with persistently high disease activity after receiving first-line traditional treatments.
- Corticosteroids are recommended as initial treatment for SLE patients. Low-dose corticosteroids, hydroxychloroquine or NSAIDs are recommended for patients with mild symptoms. For SLE patients with more severe conditions, combined therapies of corticosteroids, biologic drugs and DMARDs are recommended.
- Similar to treatment options for SLE, the types of drugs that have been used to treat LN mainly include corticosteroids, DMARDs (such as hydroxychloroquine) and biologic drugs, with corticosteroids and hydroxychloroquine recommended as basic treatment options. As the investigation of biologic drugs for the treatment of LN is still at an early stage, there was noclear designation of line of treatment for biologic drugs for this indication. Compared to SLE,biologic drugs and drug candidates indicated for LN are even more limited.

Source: Frost & Sullivan analysis

Appendix

- In contrast, biologics are proved to be more effective and safer in the treatment of CRSwNP in both clinical and animal studies. However, as a relatively new class of drugs, they have not been recommended as a main line of treatment for CRSwNP by prevailing clinical guidelines.
- We are developing QX005N, a humanized IgG4 monoclonal antibody directed against IL-4R, for the treatment of moderate-to-severe asthma. IL-4R is a promising therapeutic target for allergic diseases driven by the type 2 immune response.
- The prevalence of asthma in China increased from 61.5 million in 2017 to 65.9 million in 2021 and is estimated to reach 78.1 million in 2030. The market for biologic drugs targeting asthma in China is estimated to increase from US$0.1 billion in 2021 to US$4.4 billion in 2030, at a CAGR of 52.3%. Biologic drugs accounted for 1.8% of the drug market for asthma in China in 2021, which is estimated to increase to 41.1% in 2030.
- The long-term goals of asthma management are to control symptoms and reduce the risk of exacerbations, airway damage and side-effects of medication. Medications for asthma primarily include inhaled corticosteroids (ICSs) and bronchodilators. ICSs are widely used for long-term treatment of asthma in people of all ages who require daily management. Bronchodilators for the treatment of asthma include long-acting 2 receptor agonist (LABA), long-acting muscarinic antagonist (LAMA), short-acting 2 receptor agonist (SABA), and short-acting muscarinic antagonist (SAMA). However, for patients with moderate-to-severe asthma, treatment with ICS and bronchodilators alone may not be effective enough to control the disease due to a variety of factors including intolerance after long-term administrations and side effects. In addition, research has shown that SABA overuse and subsequent ICS underuse are responsible for safety concerns and poor outcomes, including hospitalization and possibly death. Therefore, the Global Initiative for Asthma (“GINA”), a medical organization that works with public health officials and healthcare professionals globally and publishes guidelines for the treatment of asthma, made a fundamental change to its recommendations for the pharmacological treatment of asthma in 2019, which no longer recommended regular use of SABAs for asthma patients who should all be prescribed ICSs, either regularly or as needed for respiratory symptoms. Moreover, the maintenance treatment of systemic corticosteroids can cause dose-dependent growth suppression and a series of severe adverse effects in children and adolescents, which leaves them with even more limited treatment options. In contrast, biologics that specifically target cytokine signaling pathways have shown to be a well-tolerated and effective option for patients with moderate-to-severe asthma. Therefore, for patients with moderate-to-severe asthma, biologics have a more important role in disease management and can work as an add-on treatment with LABA, LAMA, SABA, SAMA and/or ICS. However, as a relatively new class of drugs, they have not yet been recommended as a main line of treatment for asthma by prevailing clinical guidelines.

Source: Frost & Sullivan analysis

Appendix

- As of the Latest Practicable Date, the only approved biologic drug for treatment of asthma in China was omalizumab, an Ig E inhibitor. As of the Latest Practicable Date, no IL-4R- targeting biologics had been approved in China and there were seven IL-4R inhibitor candidates in the clinical stage in China.
- asthma has a complex and heterogeneous nature which each patient needs targeted treatment. Therefore, the demand for targeted biologic treatment is increasing. As of the Latest Practicable Date, dupilumab was the only FDA-approved IL-4R inhibitor for asthma. While dupilumab can cost over RMB82,000 a year based on its pricing in China for the treatment of AD in 2021, according to Frost & Sullivan, we aim to make QX005N more accessible to patients in China.
- Biologic drugs and candidates for asthma in China primarily include IgE inhibitors, IL-5 inhibitors, IL-4R inhibitors and TSLP inhibitors. While current antibodies targeting IL-5/IL-5R, IL-4R and IgE are shown to reduce exacerbations and improve symptoms and quality of life in patients with asthma, the efficacy of these biologic treatment has shown to be correlated to the levels of certain type 2 biomarkers, such as blood eosinophil counts and IgE. According to Frost & Sullivan, approximately 50% of patients with severe asthma are estimated to have low-level or no expression of type 2 biomarkers and classified as having type 2-low or non-type 2 allergic diseases. For patients without the elevation of those biomarkers, there continue to be important and unmet medical needs. As TSLP is an upstream regulator of type 2 inflammation, TSLP inhibitors can be a treatment for patients with low-level or no expression of type 2 biomarkers. Based on published clinical data, asthma patients receiving anti-TSLP antibody treatment of experienced significantly fewer exacerbations irrespective of their type 2 biomarker status. Thus, the development of TSLP-targeting biologic treatment may be a promising strategy for addressing the clinical needs of patients with type 2-low allergic diseases. As of the Latest Practicable Date, no TSLP-targeting biologics had been approved in China and there were seven anti-TSLP candidates in the clinical stage in China.
- Since IL-33 can induce Th2 cytokine production and promote the pathogenesis of COPD, IL-33 and its receptor, ST2, can be promising targets for the treatment of COPD as well. However, as a relatively new class of drugs, biologics have not yet been recommended as a main line of treatment for COPD by prevailing clinical guidelines.
- While both biologics and immunosuppressants are particularly useful when patients are not responsive to corticosteroid for induction or relapse prevention, biologics have been demonstrated in studies to achieve higher response rate with less flare up and side effect rates compared to immunosuppressants. However, biologics have not yet been recommended as a main line of treatment for UC/CD by prevailing clinical guidelines.

Source: Frost & Sullivan analysis

Appendix

- It is market practice in the pharmaceutical industry for similar collaboration agreements to be entered into for a long term, primarily due to the substantial amount of capital and contributions committed by the collaboration partners and the risks involved.
- According to published literatures and other public information, approximately 20-40% of patients with COPD have predominant type 2 inflammation.
- According to published literatures and other public information, approximately 50-70% of patients with asthma have predominant type 2 inflammation.
- Huadong Medicine and ZhongmeiHuadong do not have marketed biologics for treating the autoimmune and allergic diseases. Huadong Medicine and ZhongmeiHuadong only have marketed small-molecule drugs in the autoimmune and allergic diseases, they have more than 30 small-molecule drugs in treating autoimmune and allergic diseases, most of the small-molecule drugs are launched around 2020. Huadong Medicine and ZhongmeiHuadong only have one biologics for treating SLE in the pipeline, the published information show that this HDM3002（PRV-3279）pipeline product is current approved for IIa clinical trail. They also have more than 7 small-molecule drugs in pipeline for autoimmune and allergic diseases. Specific sales revenue/ marketing network of each marketed drugs for autoimmune and allergic diseases are not disclosed in Huadong Medicine and ZhongmeiHuadong's annual report, thus we cannot attain the information publicly. We also think as Huadong Medicine and ZhongmeiHuadong only have small-molecule drugs for autoimmune and allergic diseases, which differs from The Company's product profile in biologics, the sales revenue/ marketing network of these small-molecule drugs cannot be compared to The Company's product.
- The CDE issued the Guidelines for Biosimilar Similarity Evaluation and Indication Extrapolation Techniques (《生物類似藥相似性評價和適應症外推技術指導原則》) in 2021, which is designed to further regulate and guide the development as well as evaluation of biosimilar drugs and to promote the development of the biomedical industry. Later in 2022, the CDE also issued the Technical Guidelines for Clinical Pharmacological Studies of Biosimilars (《生物類似藥臨床藥理學研究技術指導原則》) and provided technical guidance on the clinical pharmacological research of biosimilars to further promote R&D of biosimilars in China.
- No biosimilar or generic of secukinumab or ixekizumab had been approved for the treatment of AS in China as of the Latest Practicable Date.
- DMARDs showed limited efficacy as compared to targeted biologic drugs, which has becomea main treatment option for moderate-to-severe plaque Ps in China

Source: Frost & Sullivan analysis

Appendix

- No biosimilar or generic of belimumab or telitacicept had been approved for the treatment of SLE in China as of the Latest Practicable Date
- The growth of China's LN drug market is mainly driven by the expected sales growth of recently approved in the near future based on the progress of their clinical trials, especially biologic drugs that generally have higher prices than traditional treatment options. Additionally, the improving ability and propensity of the patients in China to pay for long-term advanced therapies also contribute to the expected expansion of the LN drug market.
- corticosteroids and hydroxychloroquine recommended as initial treatment options and standard of care for LN.
- No biosimilar or generic of ustekinumab or vedolizumab had been approved for the treatment of UC/CD in China as of the Latest Practicable Date
- The expected rapid growth from 2021 to 2023 is primarily because (i) the sales of dupilumab (the only biologic drug approved in China for AD and included in the NRDL as of the Latest Practicable Date) in China since its approval for AD in 2020 has experienced substantial global revenue growth from US $13.7 million in 2020 to US$248.1 million in 2022, at a CAGR of 325.0%, indicating a high demand for AD biologics in China and further growth of the China AD drug market; (ii) there has been increasing R&D of AD biologics by domestic companies and several domestically developed AD biologic drug candidates have entered the clinical trial stage, which, once approved for commercialization, are expected to further drive the growth of the China AD drug market; and (iii) the diagnosis and treatment rates of AD are expected to increase due to improving affordability and health awareness of Chinese AD patients, which is also expected to contribute to the rapid growth of the China AD drug market.
- Treatment of AD usually involves a step-up approach, i.e., depending on the severity and extent of a patient's symptoms, different medication and treatment options may be recommended. The standard of care for AD in China mainly includes bathing, improvement of the living environment and food intervention. In addition, topical corticosteroids and calcineurin inhibitors are the first line of treatment and important drugs for AD.
- In severe cases of AD, phototherapy and systemic immunosuppressants are recommended by the Guideline for Diagnosis and Treatment of AD in China (2020) (《中國特應性皮炎診療指南(2020版)》)
- According to the Guideline for Diagnosis and Treatment of AD in China (2020), biologics, as a main treatment option for AD patients, are recommended to be combined with topical drugs and moisturizers for long-term use
- Biologics have become a guideline treatment option but as a relatively new class ofdrugs, they have not yet been recommended as a main treatment option for PN by prevailing clinical guidelines.

Appendix

- However, as a relatively new class of drugs, they have not yet been recommended as a main treatment option for CRSwNP by prevailing clinical guidelines. Currently, the standard of care for CRSwNP include corticosteroid, LTRA and surgery. The diagram below illustrates the recommended treatment pathway for CRSwNP in China
- Such long-term medications mainly include inhaled corticosteroids (ICSs) and bronchodilators, including long-acting 2-agonist (LABA), long-acting muscarinic antagonist (LAMA), short-acting 2-agonist (SABA), and short-acting muscarinic antagonist (SAMA)
- However, as a relatively new class of drugs, they have not yet been recommended as a main treatment option for asthma by prevailing clinical guidelines. Currently, the standard of care for moderate-to-severe asthma includes ICS and LABA. The diagram below illustrates the recommended treatment pathway for adults and adolescents with moderate-to-severe asthma in China
- As of the Latest Practicable Date, no biosimilar or generic of omalizumab had been approved for the treatment of asthma in China
- According to Frost & Sullivan, among Chinese domestic companies, we had one of the most numbers of IND-approved drug candidates in autoimmune and allergic diseases as of the Latest Practicable Date
- In particular, our pipeline featured QX001S, an IL-12/IL-23p40 inhibitor for psoriasis (Ps), the first domestically developed ustekinumab biosimilar for BLA submission in China and potentially one of the first ustekinumab biosimilars to be approved in China
- The first domestically developed ustekinumab biosimilar for BLA submission in China and potentially one of the first ustekinumab biosimilars to be approved in China
- Inflammatory digestive diseases, particularly inflammatory bowel disease (IBD), are conditions characterized by chronic inflammation of the digestive system
- Research has shown that IL-17A plays an important role in the pathogenesis of AS and is also involved in autoantibody production and organ damage in SLE patients, which could lead to LN development
- Studies have shown that elevated expression of Th17-related cytokines (such as IL-17) in the urinary system is also associated with enhanced recruitment of immune cells to the kidney and thereby leading to LN development in SLE patients
- Similar to treatment options for SLE, the types of drugs that have been used to treat LN mainly include corticosteroids, DMARDs (such as hydroxychloroquine) and biologic drugs, with corticosteroids and hydroxychloroquine recommended as initial treatment options and standard of care

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- According to the Guideline for Diagnosis and Treatment of AD in China (2020), biologics, as a main treatment option for AD patients, are recommended to be combined with topical drugs and moisturizers for long-term use
- the EASI and IGA scales are the most authoritative evaluation methods to determine the severity of an AD patient's symptoms
- Urticaria is considered a disease driven mainly by mast cell degranulation, followed by the release of various mediators, including inflammatory cytokines such as IL-4.
- TSLP is at the top of multiple inflammatory cascades and involved in over-reactive immune response in multiple allergic disorders
- Studies have shown that smoking promotes an amplified IL-33 cytokine response and progression of COPD
- c-kit, which activates the SCF/c-kit signal transduction pathway and causes the differentiation, maturation, survival, proliferation and degranulation of mast cells that lead to the release of histamine and other mediators. As urticaria is considered a disease driven mainly by mast cell degranulation
- Biologic drugs are a relatively new class of drugs under investigation for treating pruritus, which have not yet been recommended as a first or second line of treatment by prevailing clinical guidelines
- Early development of therapeutic antibodies normally includes three stages: (i) antibody screening to get mAbs with high affinity and specificity to a specific target human antigen, (ii) antibody engineering of the screened antibodies to get humanized antibody leads with strong bioactivity and good physical/chemical and PK/PD properties, and (iii) pre-clinical in vivo studies including pharmacodynamic, toxicology, etc., to determine an antibody molecule for further CMC development and clinical studies
- While Huadong Medicine and Zhongmei Huadong are large comprehensive pharmaceutical companies with a focus on the autoimmune and allergic disease field, we do not consider them to be our competitors primarily because (i) for the same indications, such as Ps and AD, their focus is primarily on developing systematic topical drugs that are more commonly used for mild diseases, which would not directly compete with our biologic drug candidates that are intended for more severe cases and instead are complementary to our business; and (ii) while Zhongmei Huadong had a biologic drug candidate for SLE in the clinical trial stage as of the Latest Practicable Date, we do not consider it to be a direct competitor to QX006N as these two drug candidates have different mechanisms of action and both are still in early clinical trial stage with considerable time before their commercialization

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- In addition, Huadong Medicine obtained the commercialization right of etanercept (a TNF inhibitor) and tofacitinib (a JAK inhibitor), both developed by Pfizer, for the treatment of AS in China in 2022.
- Inmagene has four pipeline products at the clinical stage targeting IL-17A, OX40, Bruton tyrosine kinase and IL-36R. In for the treatment of autoimmune and inflammatory diseases including psoriatic arthritis, psoriasis and atopic dermatitis, which will compete with the business of the Group.

Appendix: NRDL price for marketed drugs

Marketed IL-17A Inhibitors for AS in China

Brand Name	INN	Company	Branded or Biosimilar	Availability of biosimilar	Correpondin g Original	NRDL covered	NRDL Median price in CNY 2022
Cosentyx	Secukinumab	Novartis	Branded	/	/	Yes	1,188.0
Taltz	Ixekizumab	Eli Lilly	Branded	/	/	Yes	1,218.0

NRDL median price in CNY 2022 for this drug's minimum formulation unit is the price for other included in NRDL

Source: Frost & Sullivan analysis

Appendix: NRDL price for marketed drugs

Marketed IL Inhibitors for Psoriasis in China

Brand Name	INN	Company	Branded or Biosimilar	Availability of biosimilar	Correpondin g Original	2022 NRDL covered	NRDL Median price in CNY 2022
Tremfya	Guselkumab	Janssen (J&J)	Branded	/	/	No	/
Stelara	Ustekinumab	Janssen (J&J)	Branded	/	/	Yes	4318.0
Cosentyx	Secukinumab	Novartis	Branded	/	/	Yes	1,188.0
TALTZ	Ixekizumab	Eli Lilly	Branded	/	/	Yes	1,218.0
LUMICEF	Brodalumab	Kyowa Kirin	Branded	/	/	No	/
Enboke (恩博克)	/	ASIA SPACE	Branded	/	/	Yes	270.0
Spevigo	Spesolimab	Boehringer, Ingelheim	Branded	/	/	No	/

NRDL median price in CNY 2022 for this drug's minimum formulation unit is the price for other included in NRDL

Source: Frost & Sullivan analysis

Appendix: NRDL price for marketed drugs

Marketed Targeted Biologics for SLE in China

Brand Name	INN	Company	Branded or Biosimilar	Availability of biosimilar	Correpondin g Original	NRDL covered	NRDL Median price in CNY 2022
Benlysta	Belimumab	GSK	Branded	/	/	Yes	727.5
Tai'ai (泰愛)	Telitacicept	Remegen	Branded	/	/	Yes	818.8

NRDL median price in CNY 2022 for this drug's minimum formulation unit is the price for other included in NRDL

Source: Frost & Sullivan analysis

Appendix: NRDL price for marketed drugs

Marketed Targeted Biologics for UC/CD in China

Brand Name	INN	Company	Branded or Biosimilar	Availability of biosimilar	Correponding Original	NRDL covered	NRDL Median price in CNY 2022
Stelara	Ustekinumab	Janssen (J&J)	Branded	/	/	Yes	4318.0
Remicade	Infliximab	Janssen (J&J)	Branded	MabPharm: Leiting (类停) Hisun: Anbaite (安佰特) Yuxi Genor: Jiayoujian (佳佑健) Celltrion: Remsima	/	Yes	2,006.8
Qletli (格乐立)	Adalimumab	Bio-Thera	Biosimilar	/	AbbVie: Humira	Yes	1,080.0
Anjianning(安健宁)	Adalimumab	Hisun	Biosimilar	/	AbbVie: Humira	Yes	1148.0
Humira	Adalimumab	AbbVie	Branded	Hisun: Anjianning(安健宁) Innovent: Sulinno(苏立信) Henlius: Handayuan(汉达远) Bio-Thera: Qletli(格乐立) Chia Tai Tianqing: Taibowei(泰博维) Junshi: Junmaikang(君迈康) SinoCellTech: Anjiarun(安佳润)	/	Yes	1,290.0
Sulinno (苏立信)	Adalimumab	Innovent	Biosimilar	/	AbbVie: Humira	Yes	1,088.0
Leiting(类停)	Infliximab	MabPharm	Biosimilar	/	Janssen (J&J): Remicade	Yes	1,268.0
Anbaite(安佰特)	Infliximab	Hisun	Biosimilar	/	Janssen (J&J): Remicade	Yes	1,268.0
Jiayoujian(佳佑健)	Infliximab	Yuxi Genor	Biosimilar	/	Janssen (J&J): Remicade	Yes	1,280.0
Junmaikang(君迈康)	Adalimumab	Junshi Pharma	Biosimilar	/	AbbVie: Humira	Yes	998.0
Entyvio	Vedolizumab	Takeda	Branded	/	/	Yes	4,980.0

NRDL median price in CNY 2022 for this drug's minimum formulation unit is the price for other included in NRDL

Source: Frost & Sullivan analysis

Appendix: NRDL price for marketed drugs

Marketed Anti-IL-4Rα Biologics for AD in China

Brand Name	INN	Company	Branded or Biosimilar	Availability of biosimilar	Correpondin g Original	NRDL covered	NRDL Median price in CNY 2022
Dupixent	Dupilumab	Sanofi / Regeneron	Branded	/	/	Yes	3,160.0

NRDL median price in CNY 2022 for this drug's minimum formulation unit is the price for other included in NRDL

Source: Frost & Sullivan analysis

Appendix: NRDL price for marketed drugs

Marketed Targeted Biologics for Chronic Spontaneous Urticaria in China

Brand Name	INN	Company	Branded or Biosimilar	Availability of biosimilar	Correpondin g Original	NRDL covered	NRDL Median price in CNY 2022
Xolair	Omalizumab	Novartis/Genentech	Branded	/	/	Yes	1,406.0

NRDL median price in CNY 2022 for this drug's minimum formulation unit is the price for other included in NRDL

Source: Frost & Sullivan analysis

Appendix: NRDL price for marketed drugs

Marketed Targeted Biologics for Asthma in China

Brand Name	INN	Company	Branded or Biosimilar	Availability of biosimilar	Correpondin g Original	NRDL covered	NRDL Median price in CNY 2022
Xolair	Omalizumab	Novartis/Genentech	Branded	/	/	Yes	1,406.0

NRDL median price in CNY 2022 for this drug's minimum formulation unit is the price for other included in NRDL

Source: Frost & Sullivan analysis

Appendix: NRDL price for marketed drugs

FDA Approved Targeted Biologics for Asthma

Brand Name	INN	Company	Branded or Biosimilar	Availability of biosimilar	Correponding Original	NRDL covered	NRDL Median price in CNY 2022
Xolair	Omalizumab	Novartis/Genentech	Biosimilar	/	/	Yes	1,406.0
Nucala	Mepolizumab	GSK	Branded	/	/	No	/
Cinqair	Reslizumab	Teva Pharmaceutical	Branded	/	/	No	/
Fasenra	Benralizumab	AstraZeneca	Branded	/	/	No	/
Dupixent	Dupilumab	Sanofi/Regeneron	Branded	/	/	No*	3,160.0
Tezspire	Tezepelumab	Amgen/AstraZeneca	Branded	/	/	No	/

Note*: Dupixent were covered in 2022 NRDL but not for the indication asthma

NRDL median price in CNY 2022 for the above drug's minimum formulation unit are the price for other indication included in NRDL

Source: Frost & Sullivan analysis

Appendix：government policies specific to the R&D and commercialization for biologics and biosimilar

Date	Issuing Authority	Policies	Comments
2015.02	The former State Food and Drug Administration	Technical Guidelines for the Development and Evaluation of Biosimilar Drugs (Trial) 《生物类似药研发与评价技术指导原则（试行）》	• Guide and regulate the research and development and evaluation of biosimilar drugs, promote the healthy development of the biomedical industry. • Propose regulatory requirements for the definition, development as well as evaluation of biosimilars, pharmaceutical research and evaluation, non-clinical research and evaluation, clinical research and evaluation, etc.
2017.03	National Pharmacopoeia Committee	Notice of soliciting opinions on the Principles and Procedures for Naming Common Names of Biological Products 《生物制品通用名命名原则规程》征求意见的通知	• Further improve and standardize the management of the common name of biological products in China, so that the naming principle of the common name of biological products in China can meet the development needs of biological products as well as promote the internationalization process of biological products in China.
2017.10	General Office of the CPC Central Committee, etc	Opinions on Deepening the Reform of the Review and Approval System to Encourage Innovation of Pharmaceutical Medical Devices 《关于深化审评审批制度改革鼓励药品医疗器械创新的意见》	• Pay equal attention to encouraging innovation as well as promoting the production of generic drugs, also reducing the burden of drug use. Regularly publish a list of drugs whose patent rights have expired, terminated, or are invalid and have not yet been applied for generic drugs. Guide the research, development and production of generic drugs. Improve the accessibility of drugs to the public. Improve the relevant research and evaluation technical guidelines to support the imitation of biosimilar drugs as well as combination products of drug and device with clinical value. Accelerate the consistent evaluation of the quality and efficacy of generic drugs.
2021.02	Drug Evaluation Center, State Drug Administration	Guidelines for Biosimilar Similarity Evaluation and Indication Extrapolation Techniques 《生物类似药相似性评价和适应症外推技术指导原则》	• To further regulate and guide the development as well as evaluation of biosimilar drugs, promote the healthy development of the biomedical industry. Further supplement the pharmaceutical recommendations of biosimilar drug similarity evaluation and indication extrapolation, so as to provide technical reference for the industry, developers and regulators.
2021.12	State Drug Administration, etc	"14th Five-Year Plan" National Drug Safety and promotion of high-quality development plan 《“十四五”国家药品安全及促进高质量发展规划》	• Continue to promote consistent evaluation of the quality and efficacy of generic drugs. Improve consistency evaluation policies as well as technical standards. Update and improve the list of reference preparations, also promote the quality improvement of generic drugs. Continue to monitor the quality of generic drugs after passing the conformance evaluation. Strengthen the construction of biosimilar drug review regulations and technical standards system, also promote the high-quality development of biosimilar drugs.
2022.02	Drug Evaluation Center, State Drug Administration	Technical Guidelines for Clinical Pharmacological Studies of Biosimilars 《生物类似药临床药理学研究技术指导原则》	• Under the framework of the Technical Guidelines for the R&D and Evaluation of Biosimilars as well as the Technical Guidelines for Similarity Evaluation and Indication Extrapolation of biosimilars, guiding suggestions for clinical pharmacological research of biosimilars were further proposed to provide technical reference for the research and development of biosimilars.

Source: government documentations，Frost & Sullivan analysis

Appendix: Patents for Cosentyx

Patents for Cosentyx

Patent	Expire Year	Country
Composition of matter	2026	U.S.
Patent term extension (PTE)	2029	U.S.
Psoriatic arthritis use	2031	U.S.
Psoriasis use	2032	U.S.
Ankylosing spondylitis use	2033	U.S.
Regulatory data protection (RDP)	2027	U.S.
Composition of matter	2025	Europe
Supplementary protection certificate (SPC)	2030	Europe
Pediatric exclusivity (PE)	2030	Europe
Psoriasis use	2031	Europe
Ankylosing spondylitis use	2026	Europe
Composition of matter	2025	Japan
Three PTEs	2026, 2028, 2029	Japan
Psoriasis use	2031	Japan
Three PTEs	2032, 2032, 2033	Japan
Psoriatic arthritis use	2031	Japan
Regulatory data protection (RDP)	2022	Japan

In the EU, the patent on ankylosing spondylitis use is being opposed in the European Patent Office (EPO)

Source: Novartis Annual Report, Frost & Sullivan analysis

Appendix: Patents for Taltz

Patents for Taltz

Patent	Expire Year	Country
Compound patent	2030	U.S.
Biologics data protection	2028	U.S.
Compound patent	2031	Europe
Data protection	2027	Europe
Compound patent	2030	Japan
Data protection	2024	Japan

Source: Lilly Annual Report, Frost & Sullivan analysis

Appendix: Patents for Dupixent

Patents for Dupixent

Patent	Expire Year	Country
Compound patent	2027 (2031 with PTE)	U.S.
Later filed patents	2041 (pending)	U.S.
Regulatory exclusivity	2029	U.S.
Compound patent	2029 (2032 with SPC)	Europe
Later filed patents	2040 (pending)	Europe
Regulatory exclusivity	2027	Europe
Compound patent	2029 (2034 with PTE)	Japan
Later filed patents	2040 (pending)	Japan
Regulatory exclusivity	2026	Japan

PTE: Patent Term Extension, SPC: Supplementary Protection Certificate

Source: Sanofi Annual Report, Frost & Sullivan analysis

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- As of the Latest Practicable Date, there were three IL-23 antibodies approved globally, namely, guselkumab, tildrakizumab and risankizumab. Among them, guselkumab and tildrakizumab had been approved in China. As of the Latest Practicable Date, there were seven antibody candidates targeting IL-23 in the clinical stage in China.
- As of the Latest Practicable Date, there was two biologic drugs for asthma approved in China, including omalizumab and one new biologic drug. As of the Latest Practicable Date, no generic of omalizumab had been approved for the treatment of asthma in China.
- While its unit price (300 mg) decreased from RMB6,666 in 2020 to RMB3,160 in 2022.
- As indicated in the 2022 Drug Evaluation Report released by the NMPA, among 769 IND approvals granted in 2022, fewer than 140 were in the autoimmune and allergic field, compared with more than 430 in oncology.
- According to Frost & Sullivan, the total patient population of autoimmune and allergic diseases in China exceeds 426 million, as compared to 101 million in the United States in 2022.
- The China's autoimmune and allergic disease drug market is estimated to grow to US$41.5 billion in 2030, at a CAGR of 21.1% from 2022, and with the proportion of biologic drugs increased to about 60%.
- As of the Latest Practicable Date, there were two anti-IL-17A antibodies approved globally, namely, secukinumab and ixekizumab, both of which were also approved in China. Secukinumab is currently approved in over 90 countries worldwide, including the U.S., the EU, Japan and China. In China, secukinumab is approved for the treatment of AS in adults and moderate-to-severe plaque psoriasis in people 6 years of age and older.
- As of the Latest Practicable Date, there were 14 IL-17A antibodies in clinical development in China.
- According to Frost & Sullivan, the market size of autoimmune and allergic disease drugs amounted to US$187.5 billion in 2022, which was 12.5% for all drugs combined.
- As indicated in the 2022 Drug Evaluation Report released by the NMPA, among 769 IND approvals granted in 2022, fewer than 140 were in the autoimmune and allergic field, compared with more than 430 in oncology.
- According to Frost & Sullivan, dupilumab can cost over RMB82,000 a year, based on its pricing in China for the treatment of AD in 2022.
- Until 2022, there has been only 51 approved mAbs cumulatively in China, compared with 126 in the U.S. Particularly, among the approved innovative mAbs in China, only nine biosimilars were developed by Chinese domestic companies

Source: Frost & Sullivan analysis