

## INDUSTRY OVERVIEW

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### BROADER DERMATOLOGY TREATMENT AND CARE MARKET

#### Market Composition Overview

The broader dermatology treatment and care market in China could be classified into localized adipose accumulation management medication, scalp diseases and care, skin diseases and care and topical anesthesia, among others as illustrated below.



Source: Frost & Sullivan analysis

The broader dermatology treatment and care market in China has the following features.

- *Mismatch between supply and demand.* The demand for dermatology treatment and care products is increasingly diversified as a result of the growing patient and consumer population, while the variety of supplies is relatively limited. As the population concerned with dermatological problems becomes more widespread, the severity of consumers’ dermatological problems, their age, and their income levels become more diverse, the market demand for dermatological products continues to grow and diversify. Moreover, the development of demands has outpaced that of supply, leaving consumers’ needs not fully met.

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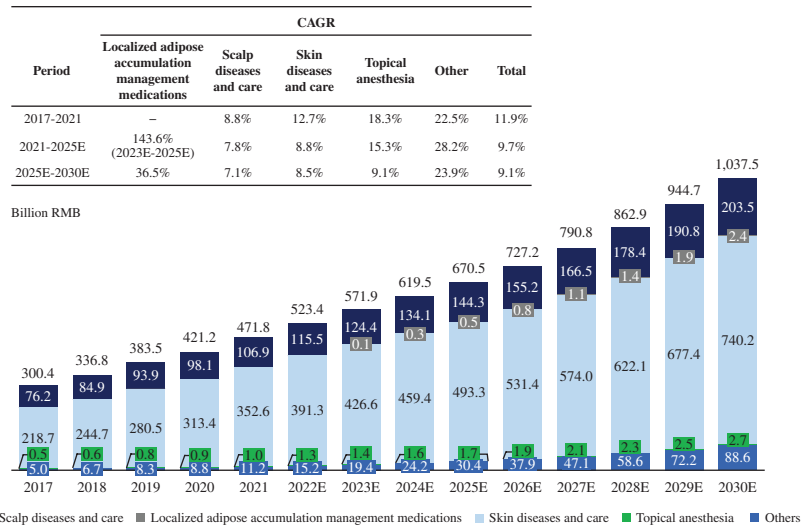
- *The lack of one-stop solution provider with complete product portfolios addressing consumer needs across major treatment fields and treatment and care cycle.* In China’s broader dermatology treatment and care market, few players have extensive product pipelines that cover the major treatment fields and consumers’ diverse demands during their treatment and care cycle. Most companies in the industry specialize in certain field, focusing on developing either dermatology care products or medications for treatment of certain types of diseases. Companies that have diverse product pipelines can benefit from the synergy among their product portfolios to constantly build brand awareness and gain market shares.
- *The demands for dermatologic products are diversified and constantly evolving during consumers’ treatment and care cycle.* The demands for dermatologic products constantly evolve during consumers’ life cycles, such as intense attention among teenagers for skin treatment and care, while high attention in scalp treatment and care among mid-age population. Correspondingly, dermatologic diseases progress such that consumers or patients demand differently with respect to the skin diseases at different stages. For example, mild acne treatment usually suggests monotherapy in topical fashion, and moderate to severe acne treatment usually combines oral and topical drugs treatment.
- *Limited novel therapies in China.* Current topical drugs for dermatologic diseases approved in China are mostly generic drugs. Novel topical therapies for the safe and effective long-term management of dermatologic problems are greatly needed to supplement current treatment regimens.
- *Most companies lack integrated capabilities across the industry value chain.* The whole industry value chain of dermatologic product contains R&D, registration, mass production, marketing and commercialization. In China, a number of brand owners of dermatology products adopt combinations of in-house production, entrusted production, OEM and ODM to control their costs. Biotech companies might rely on CDMO to support their mass production. Companies that have end-to-end operating capabilities across the industry value chain can achieve positive internal synergy and reach operational efficiency.

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### Broader Dermatology Treatment and Care Market Size in China

The following table sets forth the size of the broader dermatology treatment and care market in China:

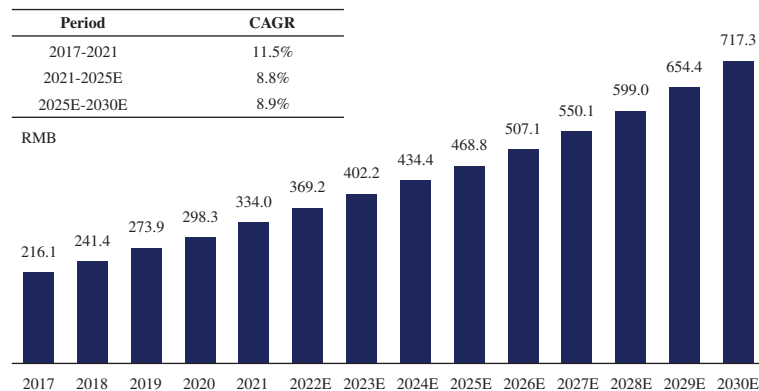
#### Market Size of Broader Dermatology Treatment and Care in China, 2017-2030E



Source: Annual Reports, Expert Interview, Frost & Sullivan analysis

The following table sets forth the historical and expected per capita expenditure on broader dermatology treatment and care in China:

#### Per Capita Expenditure On Broader Dermatology Treatment and Care in China, 2017-2030E

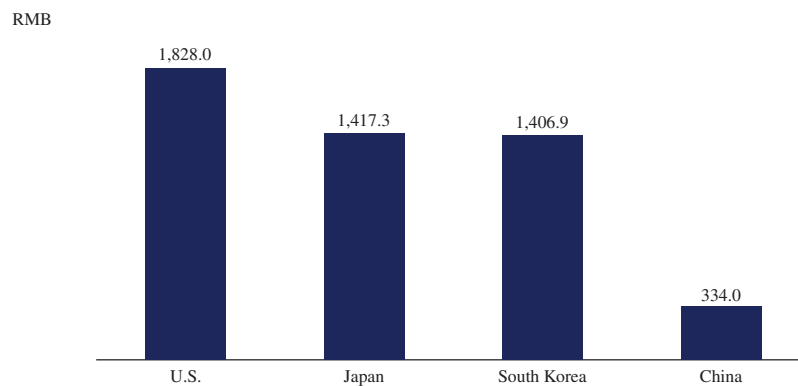


Source: NBSC, Frost & Sullivan analysis

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A gap exists between developed countries and China in terms of per capita expenditure on broader dermatology treatment and care. In 2021, the per capita expenditure on broader dermatology treatment and care in the U.S., Japan and South Korea reached RMB1,828.0, RMB1,417.3 and RMB1,406.9, respectively. By comparison, the per capita expenditure on broader dermatology treatment and care in China in 2021 was RMB334.0, which is still far behind that of developed countries, representing a large market potential.

### Comparison of Per Capita Expenditure on Broader Dermatology Treatment and Care (China, U.S., Japan and South Korea), 2021



Note: Exchange rate: 1 USD=6.4 RMB

Source: World Bank, NBSC, Frost & Sullivan analysis

### Growth Drivers

The following key factors have primarily driven the growth of the broader dermatology treatment and care market in China:

- *Increase in disposable income.* China’s per capita annual disposable income reached RMB35,128.0 in 2021 from RMB25,973.8 in 2017 with CAGR of 7.8%. With the increase in disposable income, an increasing number of Chinese consumers are able to afford the out-of-pocket costs relating to broader dermatology treatment and care products. China is also undergoing a consumption upgrade, making dermatology treatment and care products more appealing to Chinese consumers.
- *The rise of skin disease and care management consciousness and awareness, and willingness to pay.* As the market expands, consumers can receive more information through diverse marketing channels. The ease of access to dermatology treatment and care knowledge has increased consumers’ acceptance of broader dermatology treatment and care products as well as their willingness to pay.

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- *Despite rise of skin and hair management consciousness, the penetration of dermatology products remains low.* Modern sedentary lifestyle, poor dieting, highly-stressful office jobs and other complex factors could induce endocrine and other disorders, which may lead to dermatological complications such as alopecia and skin disease. Despite the rise of skin health and skin disease and care management consciousness, the per capita consumption of broader dermatology treatment and care products in China is still low compared with developed countries.
- *Emergence of safe, effective, and consumers-friendly topical products.* In recent years, a number of novel products with innovative mechanisms of action and dosage forms have been launched or under development in China. The improvement in those new products makes them more effective, safer and more consumer-friendly, which caters to consumers’ diverse demands and drives market growth. Transdermal drug delivery has emerged as one of the most attractive alternative to conventional oral and intravenous administrations because of its direct application at the site of action, consistent and reliable drug concentration over protracted dosing periods, and ease of administration. For dermatologic conditions, local administration helps reduce systemic buildup in drug concentration and the nonspecific action on non-targeted organs by the active ingredients, reducing the risks of side effects brought by the systemic exposure.

### Entry Barriers

Despite the growth drivers discussed above, significant entry barriers remain in the broader dermatology treatment and care market in China:

- *Acute insights into consumer needs.* Dermatologic problems cover a wide range of conditions and target consumers can range from children and teenagers to the elderly. The needs and preference of different consumer groups can be significantly different. For example, alopecia patients are mostly male consumers who mainly focus on effects and safety problems while young consumers also take user experience of products into account. As a result, the acute understanding of consumer needs is critical. It is important for market players to gauge the needs and interests of the target consumer groups in different market segments, to stay abreast and to further guide latest market trends.
- *Scientific understanding of dermatology and pharmacology enabling transdermal drug/substance delivery for precision medicine.* The physicochemical properties of the skin translate to multiple obstacles and restrictions in transdermal delivery. It is important for market players to have a deep understanding of dermatology and pharmacology to conduct investigations and build up effective transdermal drug delivery systems.

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- *Integrated capabilities.* Integrated capabilities, including the capabilities to conduct medical research based on the understanding of the mechanism of action of drugs and the pathophysiology of skin and human bodies, the capabilities to conduct product development based on the characteristics of raw materials and formulation components, the capabilities of registration, mass production as well as commercialization are crucial to developing dermatology treatment and care products. Developing such capabilities requires significant time, resources and expertise, posing a barrier for new market entrants. Mutually beneficial and sustainable collaboration with downstream medical institutions and consumers are indispensable elements for success in this market. It is essential for market players to have solid network, as well as strong capabilities to promote their products in the market.
- *Comprehensive product offerings.* Dermatologic problems cover a wide range of conditions, which are often caused by multiple factors and can rarely be solved by any single treatment. As the dermatologic conditions progress with time, the symptoms and consumers demands vary greatly. Moreover, dermatology treatment usually needs to be accompanied by effective daily care products. To address the diverse dermatological concerns of different consumers, it is crucial for companies in this market to provide a comprehensive portfolio of dermatology products and a one-stop solution tailored to different consumer groups, with ample cross-selling and up-selling opportunities. Developing such a comprehensive portfolio requires significant time and resources.
- *Recognition among consumers, physicians, medical institutions, and other industry stakeholders.* Given that dermatology treatment and care products have a direct effect on consumers, success in this market hinges on strong brand recognition among consumers, physicians, and medical institutions, and other industry stakeholders, who are inclined to adopt well-recognized products with proven efficacy and safety records.

### Pain Points

The following significant pain points remain in the broader dermatology treatment and care market in China:

- *Limitation of the existing treatment.* Due to the low cost, oral antibiotics have been used for dermatologic diseases for a long time, however oral antibiotics treatments have side effects such as growing bacterial resistance and local side effects such as diarrhea and pains. In order to achieve the better treatment effect, gradual increment of drugs dosage over a certain period of time is required. Lower dosage might be unable to give immediate and observable response to skin conditions, resulting longer treatment time.

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- *Lack of alternative solutions.* Alternative treatments of dermatological diseases may improve drug efficiency comparing with the traditional treatment. For example, in atopic dermatitis treatment, the targeted treatment demonstrates improved clinical efficacy. However, such innovation in treatments requires dermatologic companies to constantly invest in R&D and cooperating experienced dermatologists. Currently, the China dermatological treatment and care market for most of the alternative dermatological treatments is still at its nascent stage.
- *Awareness of dermatological issues and low penetration rate.* With lower awareness of dermatologic treatment, only few patients with dermatological diseases seek for professional dermatological assistance. Patients with mild dermatological issues rarely realize the status of their skin health and mild symptoms compromise patients' qualities of life to a small degree. Comparing with developed countries, the per capital consumption of skin diseases and care products is much lower in China, suggesting that the awareness of the importance of skin health and the effects of dermatological product remain low using penetration rate in China market.

### LOCALIZED ADIPOSE ACCUMULATION MANAGEMENT TREATMENT MARKET

An individual has three statuses with respect to body weight from normal weight to obesity, namely normal weight, overweight and obesity. Overweight and obesity are defined as abnormal or excessive fat accumulation that increases the risk of noncommunicable diseases, such as: a) cardiovascular diseases (mainly heart disease and stroke), which were the leading cause of death in recent years; b) diabetes; c) musculoskeletal disorders (especially osteoarthritis - a highly disabling degenerative disease of the joints); and d) some cancers (including endometrial, breast, ovarian, prostate, liver, gallbladder, kidney, and colon cancers). In China, a body mass index between 18.5 kg/m<sup>2</sup> to 23.9 kg/m<sup>2</sup> is considered normal weight, more than or equal to 24 kg/m<sup>2</sup> is considered overweight and more than or equal to 28 kg/m<sup>2</sup> is considered obesity in adults. Subcutaneous adipose accumulation is a typical manifestation of obesity and overweight. There are many causes of obesity or adipose accumulation with lifestyle factors such as a high-calorie diet and lack of exercise being the most important ones. Genetic susceptibility, pathological factors including diabetes, Cushing's syndrome, neuroendocrine tumors and other diseases can lead to clinical signs of obesity or adipose accumulation. Some glucocorticoid drugs' side effects can also lead to obesity or adipose accumulation.

To date, the available anti-obesity treatments on the market include systemic and local treatments. Systemic treatment is the reduction of fat accumulation through the regulation of endocrine or metabolism by drugs such as oral orlistat or subcutaneous administration of GLP-1 receptor agonists, rather than the reduction of localized fat accumulation in specific areas. Local treatment is the reduction of localized fat accumulation through the use of energy-based fat reduction devices, localized fat accumulation management medications and liposuction procedures.

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Localized treatments include two main categories, namely non-surgical fat reduction and surgical fat reduction (liposuction surgery). The non-surgical fat reduction includes localized adipose accumulation management medications and energy-based fat reduction procedures such as cryolipolysis and ultrasonic cavitation. A detailed comparison for these three treatments is set forth below:

	Localized Adipose Accumulation Management Medications	Energy-based Fat Reduction	Liposuction Surgery
Introduction	Functional ingredients mainly include deoxycholic acid and recombinant mutant collagenase.	Energy-based fat reduction is non-surgical procedure that are performed with devices that utilize various forms of energy, such as cold temperature, ultrasound, laser, radiofrequency, etc. for fat reduction and body contouring. Treatments approved in China include cryolipolysis and ultrasonic cavitation.	Liposuction is a surgical procedure that uses a suction technique to remove fat from specific areas of the body, such as the abdomen, hips, thighs, buttocks, arms or neck. It can be performed alone or along with other plastic surgery procedures, such as autologous fat transfer or abdominoplasty. Treatments include suction assisted liposuction (SAL), water-assisted liposuction (WAL), laser liposuction, ultrasound assisted liposuction (UAL), etc.
Mechanisms	The medicine is given to the subcutaneous fat tissue and destroys the membrane of the adipocytes or the extracellular matrix, which induces apoptosis of the adipocytes. Then the body's immune system clears the fatty acid through the lymphatic system and liver.	The device is placed on the area to be treated and brings energy to the subcutaneous layers where fat cells accumulate, which destroys the fat cells or induces apoptosis of the fat cells. Then the body's immune system clears the fatty acid through the lymphatic system and liver.	SAL, WAL, etc. physically crush the localized adipose tissue and suck out the fat through the incision. Laser lipolysis, UAL, etc. rely on energy to induce adipocyte swelling and rupture, and then suck out the lysate through a needle.
Major Equipment	No equipment required	CoolSculpting (Zeltiq), UltraShape V3 (Syneron)	Body-jet (Human Med), VASER (Solta Medical), SP Dynamis (Fotona)
Procedure Duration	15-20 mins	~1 hour	2-4 hours
Invasiveness	Minimally invasive treatment with less postoperative pain	Non-invasive procedures	Invasive surgery with significant postoperative pain
Full Recovery Time <sup>(1)</sup>	2-4 weeks	Within a week	1-3 months
Side Effects	For deoxycholic acid: Swelling (65.8%, median duration: 9-10 days), bruising (54.6%), numbness (49.6%), erythema (38%), induration (22.5%), etc.	Erythema (26.3%), numbness (9.1%), bruising (3.7%), edema/swelling (2.5%), etc.	Swelling (almost every procedure, duration: 4-6 weeks), seromas (3.5%), surface irregularities (8.2%), skin laxity (4.2%), etc.
SAE rates	For deoxycholic acid: 0.1% (recovered mandibular nerve injury) For recombinant mutant collagenase: 0	0.7% (paradoxical adipose hyperplasia)	0.1%. The rates of fatal complications is 1 in 5000.
Treatment Restrictions	Burden on liver to metabolize, several treatments are needed to see the results and long interval between each treatment	High costs, risks of cold injury and erythema, efficacy depending on technical factors including device's applicator	Permanent bumpy and wavy skin due to uneven fat removal, temporary pockets of fluid formed under skin requiring routine drainage operator-dependence, high costs, invasiveness
Efficacy	Percentage of patients who achieved a ≥10% reduction from baseline in submental volume based on MRI is 43.3%.	Average reduction in caliper measurement ranged from 14.7% to 28.5%.	Depending on the volume of adipose tissue aspirated during surgery.

Note:

- Among the three treatment options, localized adipose accumulation management medication is less invasive than liposuction surgery, and energy-based fat reduction is non-invasive. Difference of invasiveness leads to difference of the postoperative discomfort, side effects and the restriction of everyday activities, further resulting in different full recovery time lengths.

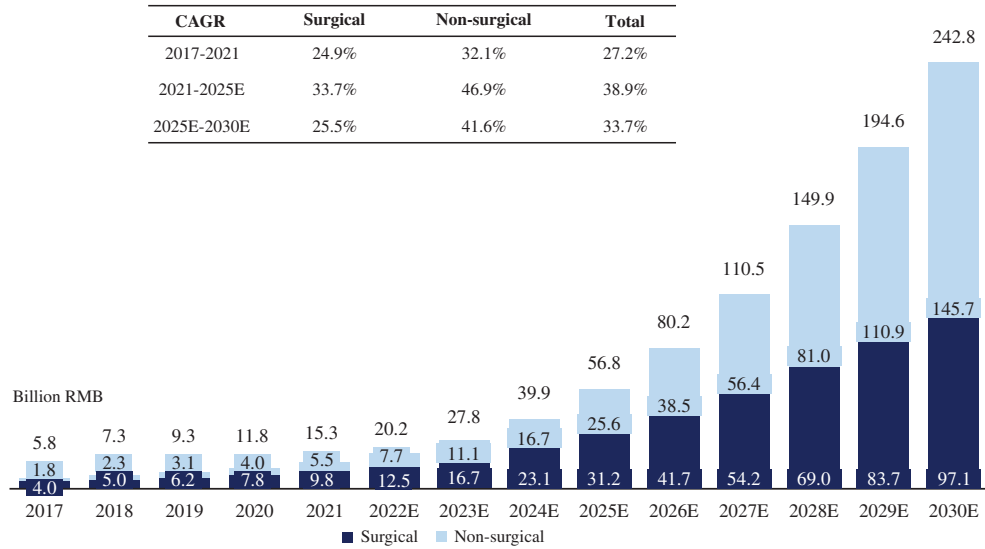
Source: Literature Search, Frost & Sullivan analysis



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The following table sets forth the market size of localized adipose accumulation management treatment in China:

### Localized Adipose Accumulation Management Treatment Market, 2017-2030E



*Note:* The market size data is based on the price at service end, and the non-surgical service data includes localized adipose accumulation management medication.

*Source:* Frost & Sullivan analysis

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### *Localized Adipose Accumulation Management Medication*

Localized adipose accumulation management medication is a dermatology treatment, which is applied in the subcutaneous layer against excessive subcutaneous fat with minimal invasiveness treatment and less postoperative pain in dermatological departments. The medicine is applied to the subcutaneous fat tissue and destroys the membrane of the adipocytes or the extracellular matrix, which induces apoptosis of the adipocytes. Then the body’s immune system clears the fatty acid through the lymphatic system and liver. These treatments can be applied to subcutaneous fat in the body, including but not limited to, the submental area and abdomen. Certain localized adipose accumulation medications can further treat obesity, overweight or other metabolic diseases. The main components of localized adipose accumulation management medication include, among others, collagenase, and phosphatidylcholine. The following table sets forth the characteristics of medication for localized adipose accumulation:

Core Components	Drug Type	Mechanism of Action	Site of Action	Consequence of Adipocytes	Reaction of Surrounding Tissue
<b>Deoxycholic Acid</b>	Small molecule	It can effectively dissolve the adipocyte membrane, leading to the disintegration of adipocytes. It is targeted to adipocytes and has a long-lasting effect.	Cell membrane of adipocytes	Immediate cell lysis and necrosis	Significant inflammation
<b>Recombinant Mutant Collagenase</b>	Biologics	It can degrade the ECM of adipocytes, resulting in the adipocytes losing their support and inducing apoptosis of adipocytes.	Collagen in the extracellular matrix that adipocytes attached to	Subsequent apoptosis	Less inflammation
<b>Phosphatidylcholine</b>	Small molecule	It reacts with sodium deoxycholate to destroy the adipocyte membrane, and the decomposed fat is transformed into water and other fat microspheres to participate in the metabolism of the body.	TNF- $\alpha$ mediated pathway inside adipocytes	Apoptosis	Less inflammation

- Besides the main components that induce reduction of localized subcutaneous fat, localized adipose accumulation management medication products can also contain other additives to promote clinical effects and improve skin conditions.
- Common additive components include L-carnitine, hyaluronic acid, polypeptides, etc.

Main Additives and Their Effects	
⊛ <b>L-carnitine</b>	Promote fatty acid oxidation
⊛ <b>Hyaluronic Acid</b>	Tighten and smooth the look of the skin
⊛ <b>Polypeptides</b>	Stimulate the secretion of more lipolytic enzymes that decompose fat into fatty acids and glycerol, thus promoting fat metabolism

Source: Frost & Sullivan analysis

The Core Product is a localized adipose accumulation management medication. A comprehensive efficacy profile of the Core Product for obesity, overweight or other metabolic diseases should be carried out after pivotal studies. However, based on its Phase I clinical results, it demonstrates its therapeutic potential for localized adipose accumulation to reduce the risks of obesity, overweight or other metabolic diseases. For more information, please see “Business” in this document.

In addition to preliminary clinical results, there is substantial evidence of a positive correlation between localized adipose accumulation and obesity or overweight. A multicenter retrospective cross-sectional study in China showed that both subcutaneous adipose tissue area and subcutaneous adipose tissue index increased gradually in normal weight, overweight and obese people (Kong M. et al. Assessing Visceral Obesity and Abdominal Adipose Tissue Distribution in Healthy Populations Based on Computed Tomography: A Large Multi-center

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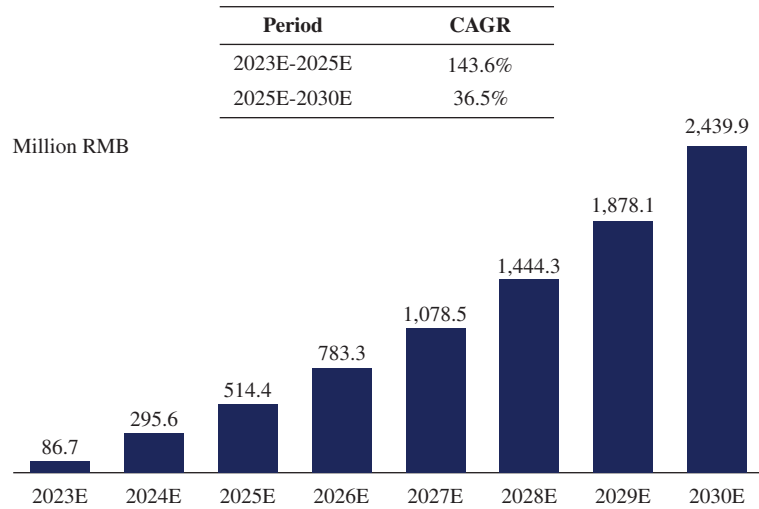
Cross-Sectional Study. *Front Nutr.* 2022;9:871697). Another study showed that increased subcutaneous adipose tissue might increase the risk of diabetes development in men (Matsha TE et al. Visceral and subcutaneous adipose tissue association with metabolic syndrome and its components in a South African population. *Clin Nutr ESPEN.* 2019;32:76-81). In a prospective cohort study, participants with higher waist circumference, an indicator of abdominal adipose accumulation, were more likely to have hypertension and high cholesterol. A high waist circumference (upper decile) was a strong risk factor for type 2 diabetes (RR: 20.4; 95% CI: 12.3, 33.8) (Wang Y, et al. Comparison of abdominal adiposity and overall obesity in predicting risk of type 2 diabetes among men, *Am J Clin Nutr.* 2005;81(3):555-563). Studies on molecular mechanism also supported that adipose tissue lies at the center of obesity and cardiometabolic diseases, representing a major contributor to disease pathogenesis (Sakers A. et al., Adipose-tissue plasticity in health and disease, *Cell* 2022;185(3):419-446). In overweight or obesity patients, white adipose tissue is severely dysfunctional and may not expand properly to store the energy excess, leading to numerous deleterious effects associated with the unhealthy expansion of the white adipose tissue, including inflammation, fibrosis, hypoxia, altered adipokines secretion and mitochondrial dysfunction. Thus, overweight or obesity induces ectopic fat deposition and further leads to systemic insulin resistance and an increased risk of type 2 diabetes (Longo M, et al., Adipose Tissue Dysfunction as Determinant of Obesity-Associated Metabolic Complications, *International Journal of Molecular Sciences*, 2019: 20(9):2358). As the Core Product targets localized adipose accumulation, it can decrease the excessive localized adipose tissue to directly improve the symptoms of obese or overweight and therefore has the potential to reduce risks of metabolic diseases.

### **Market Size of Localized Adipose Accumulation Management Medication**

The following table sets forth the market size of localized adipose accumulation management medication in China. The growth drivers in the market size of localized adipose accumulation management medication in China include: (i) a number of localized adipose accumulation medications are expected to be approved in China in particular, from 2023 to 2025; (ii) the recognition and availability of localized adipose accumulation medications continue to improve due to their safety profiles and ease of treatment; (iii) China's obese population that can receive adipose accumulation management medication is estimated to grow continuously; (iv) customers receiving adipose accumulation management medication generally demonstrate a high re-purchase rate in order to maintain the desired results; (v) from 2023 to 2025, when several localized adipose accumulation management medications are launched in the market, the education and promotion of physicians by each product manufacturer continues to increase the clinical penetration of the products; (vi) the clinical use of the products in hospitals will increase the credibility of the products and the number of users. The addressable market of the Core Product only constitutes a very small subset of the entire broader dermatology treatment and care market in China.

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### Market Size of Localized Adipose Accumulation Management Medications in China, 2023-2030E



*Note:* The assumptions to estimate the significant growth in the market size of localised adipose accumulation management medication during the period from 2023 to 2025 reaching 143.6% are on the following bases: (i) currently, there are no approved drugs for the management of localized fat accumulation in China. However, according to the clinical development pipeline published by the NMPA, two localized adipose accumulation medications are expected to be approved in China from 2023 to 2025. (ii) According to the official literature review “Report on Chinese Residents’ Chronic Diseases and Nutrition” and expert interview, the number of diagnosed patients with obesity or localized adipose accumulation is expected to increase rapidly from 0.3 million to 0.5 million, with a CAGR of 24.1%. (iii) According to expert interview, the recognition and availability of localized adipose accumulation management medication continues to increase due to their improved safety and ease of treatment. As a result, the market penetration of adipose accumulation management medication is expected to increase from 20% to 48%, with a CAGR of 54.9% from 2023 to 2025. The large patient base and rapid growth in sales of approved adipose accumulation management medication will in turn contribute to the rapid growth of the market size at a CAGR of 143.6% during the period from 2023 to 2025.

The assumptions to estimate the significant growth in the market size of localised adipose accumulation management medication during the period from 2025 to 2030 dropping down to 36.5% are on the following bases: (i) according to Frost & Sullivan’s market research and interview with KOLs, the number of patients with obesity or localized adipose accumulation will increase from 0.5 million to 0.8 million with a CAGR of 11.3% during the period from 2025 to 2030. The decrease in the growth rate is due to the large number of patients received localized treatment and improved their lifestyle. (ii) The academic-education and promotion strategies of developers continue to the increasing clinical penetration of the products. The penetration rate of localised adipose accumulation management medications is expected to increase from 48% to 64.2% with a CAGR of 6.0% during the period from 2025 to 2030. From 2025 to 2030, the penetration rate will maintain a more stable growth from 48.0% to 64.2% with a CAGR of 6.0%. With the emergence of localized adipose accumulation medications, expansion of treatment options, and innovation in services, the customer base for localized adipose accumulation medications in China is expected to expand significantly in the first two years, leading to higher growth in penetration rate. After 2025, as a large number of medications and other therapies will be approved, the growth rate of patient numbers become stable, the market has been well-educated, and patients’ treatment preferences will stabilize and thus the penetration of localized adipose accumulation medications will grow at a slower rate than in the previous two years. This trend follows the industry practice of drug market penetration.

*Source: Frost & Sullivan analysis*

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### Competitive Landscape

Currently, there has been no localized adipose accumulation management medication approved in China. Three product candidates are in clinical trial stages in China. CU-20401 is not proposed or intended to be the sole option for addressing obesity, overweight and metabolic diseases. It also may be challenging for us to obtain approval for the use of CU-20401 for abdominal adipose accumulation as no similar drugs have been approved for the same indication.

Drug	Registration Classification <sup>(1)</sup>	Applicant	Indication	Status	First Posted Date <sup>(2)</sup>
Deoxycholic Acid	3	Nanjing Noratech	Improvement in moderate to severe contour bulging/excessive facial fullness due to the accumulation of submental fat in adults	Phase III	2021/09
CU-20401	1	Cutia	Improvement in submental adipose accumulation in adults	Phase I completed	2021/08
			Improvement in abdominal adipose accumulation in adults	Phase I (ongoing)	
Deoxycholic Acid	3	Nanjing Minova	Submental fat	IND Approval	2021/07

*Notes:*

1. Registration Classification:

Class 3: Drugs manufactured by domestic applicants by imitating the original drugs that have been marketed overseas but not yet in China

Class 1: Innovative drugs that have not been marketed in China or overseas

- First posted date denotes the date when the trial is first publicly announced on the CDE website. Information as of November 4, 2022. Phase I trial of CU-20401 in submental adipose accumulation has been completed.
- Deoxycholic acid (Kybella) is an approved localized adipose accumulation management medication globally indicated for improvement in the appearance of moderate to severe convexity or fullness associate with submental fat in adults. A Phase II clinical trial of Sisram’s product candidate RZL-012 has been completed in the U.S. Sisram planned to commence a Phase III clinical trial in China, and such trial has not commenced as of the Latest Practicable Date.
- According to Frost & Sullivan, in the Phase III trials of Kybella, adults with a moderate or severe amount of SMF (as graded by both the clinician using CR-SMFRS and the patient using PR-SMFRS) who were dissatisfied with the appearance of their face/chin based on rating of the SSRS were randomized 1:1 to either Kybella or placebo for up to 6 treatment sessions (every  $28 \pm 5$  days), and efficacy assessments were conducted at 12 weeks after last treatment.

The primary endpoints were percentage of patients who achieved a  $\geq 1$ -grade improvement in SMF from baseline based on both clinician (CR-SMFRS) and patient (PR-SMFRS) assessment (composite CR-1/PR-1 response), and percentage of patients who achieved a  $\geq 2$ -grade improvement in SMF from baseline (composite CR-2/PR-2 response). Secondary endpoints included the percentage of patients who achieved a  $\geq 10\%$  reduction from baseline in submental volume based on MRI and mean change from baseline in the psychological impact of SMF using PR-SMFIS.

Safety was assessed throughout the trials via spontaneous reports of adverse events and findings from clinical laboratory tests, vital sign assessments, and physical examinations.

Source: CDE, Frost & Sullivan analysis

In the U.S. and Europe, deoxycholic acid (Kybella) is an approved localized adipose accumulation management medication in U.S. and Europe indicated for improvement in the appearance of moderate to severe convexity or fullness associate with submental fat in adults. A Phase II clinical trial of Sisram’s product candidate RZL-012 has been completed in the U.S. After administration of RZL-012 into the subcutaneous layer with localized adipose tissue

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accumulation, RZL-012 directly disrupts integrity of adipocyte cell membrane and causes cell necrosis, thereby leading to inflammatory response and formation of fibrotic tissue. The clinical trial has not disclosed safety data. The pre-clinical study demonstrated the treatment limitation of RZL-012 due to the presence of significant liponecrosis induced at the administered areas occurred as early as 24 hours after dosing and inflammation lasted for at least 14 days. Sisram planned to commence a Phase III clinical trial in China, and such trial has not been commenced as of the Latest Practicable Date.

In Asia, Kybella has been approved in Hong Kong and Taiwan and V-OLET, a deoxycholic acid product developed by Daewoong Pharmaceutical, has been approved as localized adipose accumulation management medication to treat moderate to severe contour bulging due to the accumulation of submental fat in adults in South Korea. In Asia, in addition to Kybella, RZL-012 and V-OLET, there are four other competing products, namely MT921, AYP-101, deoxycholic acid (Nanjing Noratech) and deoxycholic acid (Nanjing Minova). MT921, developed by Medytox, is under evaluation in Phase III clinical trials in South Korea.

The table below shows the competitive landscape for CU-20401 and competing products of localized adipose accumulation management medication pipelines in Asia. Other than the below table, no competing candidates will be imported into Asia in the near future according to public information.

Drug	Company	Indication	Highest Development Stage	Region	First Posted Date
V-OLET (Deoxycholic acid)	Daewoong	Moderate to severe contour bulging due to the accumulation of submental fat in adults	Approval	Korea	2021/08
Belkyra/Kybella (Deoxycholic acid)	Allergan	Improvement in the appearance of moderate to severe convexity or fullness associated with submental fat in adults	Approval	Hong Kong	2018/05
				Taiwan	2017/05
MT921 (Cholic acid)	Medytox	Moderate to severe submental fat	Phase III	Korea	2022/01
Deoxycholic Acid	Nanjing Noratech	Improvement in moderate to severe contour bulging/excessive facial fullness due to the accumulation of submental fat in adults	Phase III	China	2021/09
AYP-101 (Polyene phosphatidylcholine)	AMiPharm	Moderate to severe submental fullness	Phase II	Korea	2019/06
CU-20401	Cutia	Improvement in submental adipose accumulation in adults	Phase I completed	China	2021/08
		Improvement in abdominal adipose accumulation in adults	Phase I (ongoing)		2021/08
Deoxycholic Acid	Nanjing Minova	Submental fat	IND Approval	China	2021/07

*Note:* As of November 4, 2022.

Phase I trial of CU-20401 in submental adipose accumulation has completed.

A Phase II clinical trial of Sisram’s product candidate RZL-012 has been completed in the U.S. Sisram planned to commence a Phase III clinical trial in China, and such trial has not been commenced as of March 5, 2023.

*Source:* NMPA, KFDA, Taiwan Food and Drug Administration, Hong Kong Drug Office, CDE, ClinicalTrials.gov, Frost & Sullivan Analysis

The table below shows a detailed comparison between CU-20401 with seven competing products. The data in the table is not based on head-to-head comparison between the relevant drugs. Clinical trials of a drug cannot be directly compared to the clinical trials of another drug and may not be representative of the overall data.

## INDUSTRY OVERVIEW

Core Components	Kybella	CU-20401	RZL-012	V-OLET	MT921	AYP-101	Deoxycholic Acid (Nanjing Noratech)	Deoxycholic Acid (Nanjing Minova)
<b>Drug Type</b>	Deoxycholic acid Chemical drug	Recombinant mutant collagenase Biologics	5-[3,6-dibromo-9H-carbazolo[9-γ]1H-2N,N,N-trimethylpentan-1-ium]methyl chloride Chemical drug	Deoxycholic acid Chemical drug	Cholic acid Chemical drug	Polyene phosphatidylcholine Chemical drug	Deoxycholic acid Chemical drug	Deoxycholic acid Chemical drug
<b>Mechanism of Action</b>	It can dissolve the adipocyte membrane, leading to the disintegration of adipocytes.	It can degrade the ECM of adipocytes, resulting in the adipocytes losing their support and inducing apoptosis of adipocytes.	It can disrupt cell membrane integrity and cause cell necrosis, followed by an inflammatory response and formation of fibrotic tissue.	It can dissolve the adipocyte membrane, leading to the disintegration of adipocytes.	Cholic acid is particularly effective in adipolysis, a process that involves destabilizing and disintegrating the lipid bilayer of adipocytes.	PPC selectively causes apoptosis and lipolysis in fat cells.	It can dissolve the adipocyte membrane, leading to the disintegration of adipocytes.	It can dissolve the adipocyte membrane, leading to the disintegration of adipocytes.
<b>Site of Action</b>	Cell membrane of adipocytes	Collagen in the extracellular matrix that adipocytes attached to	Cell membrane of adipocytes	Cell membrane of adipocytes	Cell membrane of adipocytes	Cell membrane of adipocytes	Cell membrane of adipocytes	Cell membrane of adipocytes
<b>Consequence of Adipocytes</b>	Cell lysis and necrosis	Subsequent apoptosis	Cell lysis and necrosis	Cell lysis and necrosis	Cell lysis and necrosis	Cell lysis and necrosis	Cell lysis and necrosis	Cell lysis and necrosis
<b>Efficacy in Submental Adipose Accumulation</b>	<ul style="list-style-type: none"> <li>52.2% of patients achieved 1-scale decrease in CR-SMFRS after second treatment session and 71.5% after fourth treatment session in phase III trials</li> </ul>	<ul style="list-style-type: none"> <li>37.5% to 75.0% of subjects achieved 1-scale decrease in CR-SMFRS after one treatment session in phase I trial</li> </ul>	<ul style="list-style-type: none"> <li>No reported cases from phase I study</li> </ul>	<ul style="list-style-type: none"> <li>71.5% of patients achieved 1-scale or greater than 1-scale decrease in CR-SMFRS after six treatment session in phase III trials</li> </ul>	<ul style="list-style-type: none"> <li>No reported cases</li> </ul>	<ul style="list-style-type: none"> <li>No reported cases</li> </ul>	<ul style="list-style-type: none"> <li>No reported cases</li> </ul>	<ul style="list-style-type: none"> <li>No reported cases</li> </ul>
<b>Common Side Effects of Injection Sites</b>	<ul style="list-style-type: none"> <li>Hematoma (24.4% in phase I trial, 71.5% in phase III trial)</li> <li>Numbness (4.9% in phase I trial, 66.2% in phase III trial)</li> <li>Erythema (19.5% in phase I trial, 2.66% in phase III trial)</li> <li>Edema (7.3% in phase I trial, 60.4% in phase III trial)</li> <li>Swelling (33.2% in phase III trial, 29.3% in phase I trial, 69.5% in phase III trial)</li> </ul>	<ul style="list-style-type: none"> <li>Hematoma (66.7%)</li> <li>Erythema (16.7%)</li> <li>Pain (81.3%)</li> <li>Edema/swelling (100%)</li> </ul>	<ul style="list-style-type: none"> <li>No reported cases from phase I study</li> </ul>	<ul style="list-style-type: none"> <li>Numbness (11.9%)</li> <li>Edema (14.7%)</li> <li>Hardening (19.3%)</li> <li>Pain (11.0%)</li> </ul>	<ul style="list-style-type: none"> <li>No reported cases</li> </ul>	<ul style="list-style-type: none"> <li>No reported cases</li> </ul>	<ul style="list-style-type: none"> <li>No reported cases</li> </ul>	<ul style="list-style-type: none"> <li>No reported cases</li> </ul>
<b>Serious Adverse Event</b>	Recovered mandibular nerve injury	No serious adverse events from phase I study	No reported cases from phase I study	Injury to the mandibular nerve	No reported cases	No reported cases	No reported cases	No reported cases
<b>Number of Treatments</b>	Up to 6 single treatments	No sufficient data to determine at this stage	No publicly available information	Up to 6 single treatments	No publicly available information	No publicly available information	No publicly available information	No publicly available information
<b>Number of Injections</b>	Depend on treatment area and thickness of subcutaneous fat	Depend on treatment area and thickness of subcutaneous fat	Depend on treatment area and thickness of subcutaneous fat	Depend on treatment area and thickness of subcutaneous fat	Depend on treatment area and thickness of subcutaneous fat	Depend on treatment area and thickness of subcutaneous fat	Depend on treatment area and thickness of subcutaneous fat	Depend on treatment area and thickness of subcutaneous fat
<b>Duration of Treatments</b>	15-20 mins	15-20 mins	15-20 mins	15-20 mins	15-20 mins	15-20 mins	15-20 mins	15-20 mins

Source: Literature search (1. Dayan SH, Schlessinger J, Beer K, et al. Efficacy and Safety of ATX-101 by Treatment Session: Pooled Analysis of Data From the Phase 3 REFINER Trials. *Aesthet Surg J*. 2021;21(1):1-11. 2. Walker P, Lee D. A phase I pharmacokinetic study of ATX-101: serum lipids and adipokines following synthetic deoxycholic acid injections. *J Cosmet Dermatol*. 2021;21(1):1-11. 3. Gueta R, Blaugrund E, Bloomenfeld A, Herbst KL, RZL-012, a New Fat Dissolving Molecule, Tested in Dercum's Disease Patients. *Dermatol Surg*. 2021;47(8):1165-1166. 4. Ryu HJ, Moon HK, Lee J, Yang GH, Yang SY, Yun HY, Chae JW, Kang WH. Evaluation for Potential Drug-Drug Interaction of MT921 Using In Vitro Studies and Physiologically-Based Pharmacokinetic Models. *Pharmaceuticals (Basel)*. 2021 Jul 7;14(7):654. Company Official Website, KFDA Label, FDA Label, Frost & Sullivan analysis



## INDUSTRY OVERVIEW

The table below shows the competitive advantages or disadvantages of CU-20401 compared to other treatment options on the market. Data not based on head-to-head comparison between therapies, clinical trials of a therapy cannot be directly compared to the clinical trials of another therapy and may not be representative of the overall data. Compared to energy-based fat reduction and liposuction surgery, the CU-20401 treatment has the shortest treatment time, lowest SAE rate and lowest treatment cost, which makes it an attractive treatment option for the management of localized adipose accumulation.

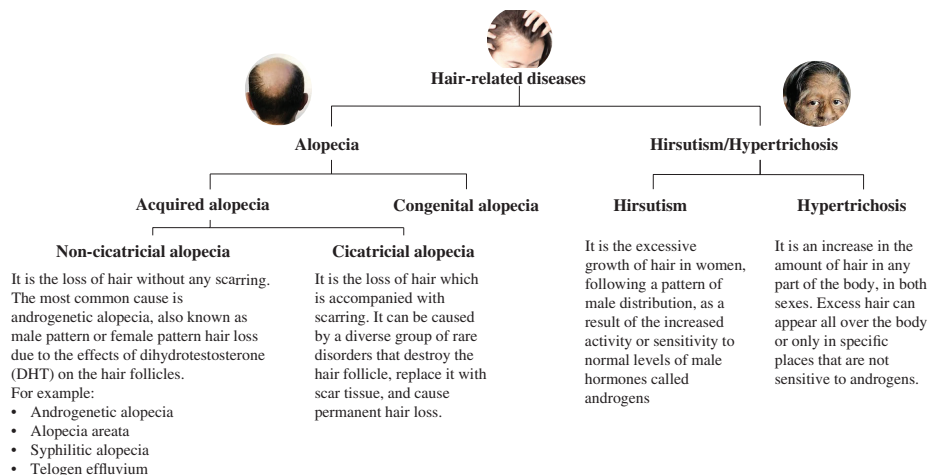
	CU-20401	Energy-based Fat Reduction	Liposuction Surgery
<b>Procedure Duration</b>	15-20 mins	1 hour	2-4 hours
<b>Invasiveness</b>	Minimally invasive treatment with less postoperative pain	Non-invasive procedures	Invasive surgery with significant postoperative pain
<b>Full Recovery Time</b>	2-4 weeks	Within a week	1-3 months
<b>Major Equipment</b>	No equipment required	CoolSculpting (Zeltiq), UltraShape V3 (Syneron)	Body-jet (Human Med), VASER (Solta Medical), SP Dynamis (Fotona)
<b>Common Side Effects</b>	Hematoma (66.7%), erythema (16.7%), pain (81.3%), edema/swelling (100%), etc.	Erythema (26.3%), numbness (9.1%), bruising (3.7%), edema/swelling (2.5%), etc.	Swelling (almost every procedure, duration: 4-6 weeks), seromas (3.5%), surface irregularities (8.2%), skin laxity (4.2%), etc.
<b>SAE rates</b>	Not clear: no reported cases from Phase I clinical trial, Phase II and Phase III clinical results have not been available to date	0.7% (paradoxical adipose hyperplasia)	0.1%. The rates of fatal complications is 1 in 5000.
<b>Effects of Procedures</b>	Multiple treatments may be needed to achieve desired results	Multiple treatments may be needed to achieve desired results	Immediate effects with desired amount of adipose tissue removed after one treatment
<b>Treatment Restrictions</b>	Burden on liver to metabolize, several treatments are needed to see the results and long interval between each treatment	High costs, risks of cold injury and erythema, efficacy depending on technical factors including device's applicator	Permanent bumpy and wavy skin due to uneven fat removal, temporary pockets of fluid formed under skin requiring routine drainage, operator-dependence, high costs, invasiveness

Source: Frost & Sullivan analysis

## SCALP DISEASES AND CARE MARKET

### Scalp Diseases and Care Overview

Alopecia and hirsutism/hypertrichosis are the two major hair-related diseases. Alopecia mainly affects scalp hairs while hirsutism/hypertrichosis mainly affects hairs in multiple body areas such as lips, abdomen, back and limbs. Alopecia is a prevalent and signature scalp condition, and it could be categorized into congenital alopecia and acquired alopecia. Acquired alopecia includes non-cicatricial and cicatricial alopecia, and the latter cause permanent hair loss. Androgenetic alopecia and alopecia areata are the two most prevalent types of alopecia, both of which belong to the non-cicatricial alopecia category. The following figure shows the major categories of hair-related diseases:



Source: Frost & Sullivan analysis

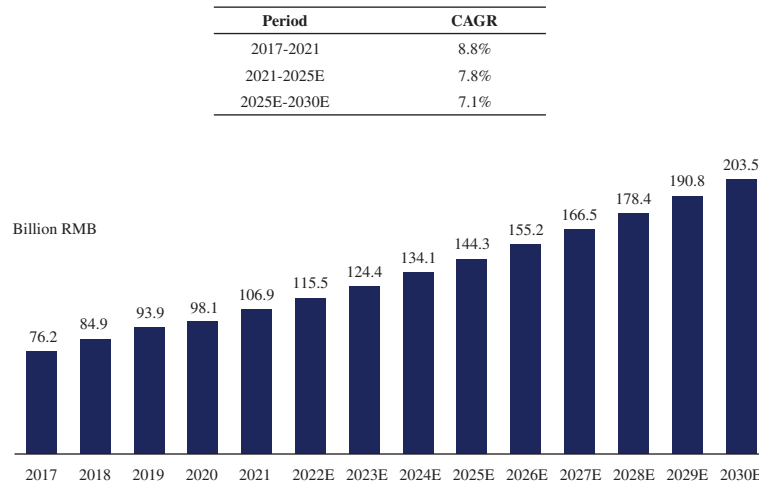


## INDUSTRY OVERVIEW

### Market Size

The following chart shows the historical and projected market size of treatment and care products for alopecia in China:

#### Market Size of Treatment and Care Products for Alopecia in China, 2017-2030E

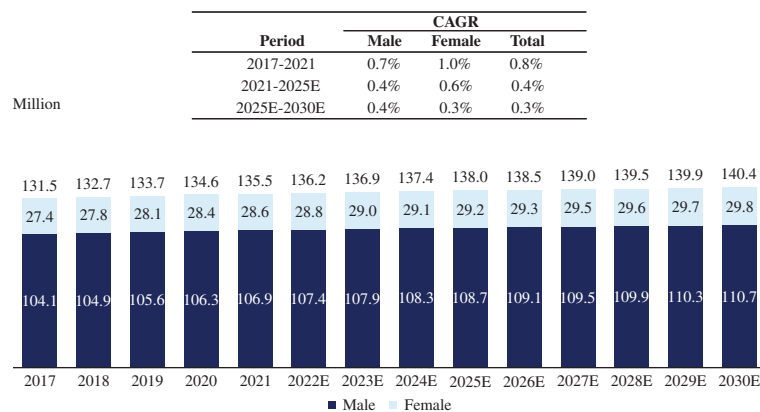


Source: Frost & Sullivan analysis

### Androgenetic Alopecia

Androgenetic alopecia is a common form of scalp hair loss. It is characterized by progressive hair loss, usually in a pattern distribution. The onset may be at any age after puberty and the frequency increases with age. The prevalence of androgenetic alopecia in China reached 135.5 million in 2021, of which 78.9% was male. The prevalence of androgenetic alopecia in female showed a slightly higher growth rate than in male from 2017 to 2021.

#### Prevalence of Androgenetic Alopecia in China, 2017-2030E

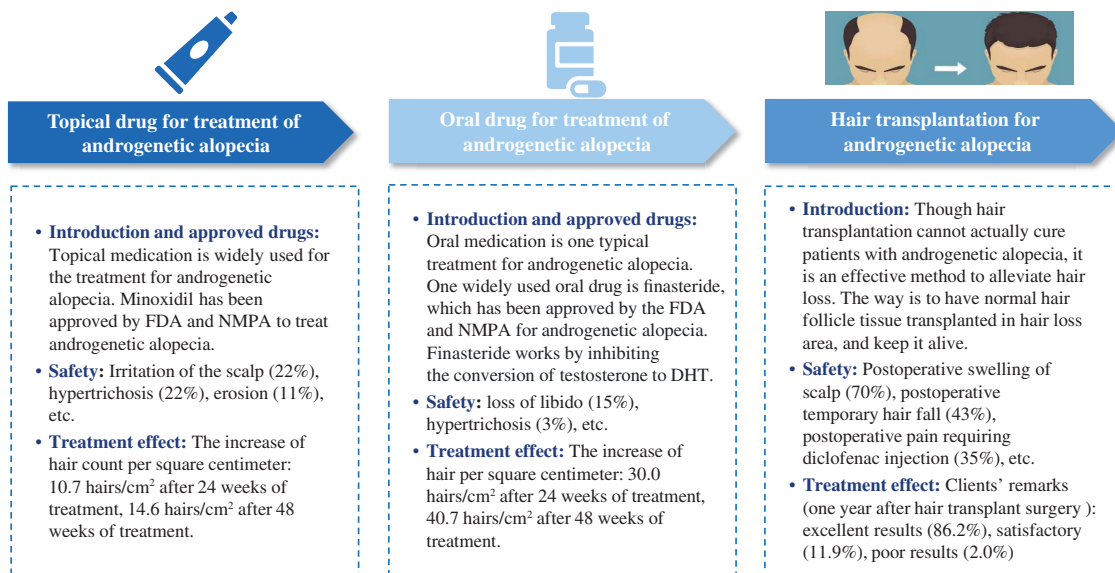


Source: Frost & Sullivan analysis

## INDUSTRY OVERVIEW

### *Current Treatment Paradigm and Unmet Medical Needs*

Typical treatment of androgenetic alopecia includes drug treatment and hair transplant. There are mainly two dosage forms for drug treatments, namely topical dosage form drug and oral dosage form drug. Each dosage form currently has one approved drug to treat male androgenetic alopecia in China, namely finasteride (oral drug) and minoxidil (topical drug). Among the two forms of drugs, topical medications are more acceptable to patients because the risk of causing side effects is relatively lower. The following charts set forth the current treatment paradigm for androgenetic alopecia:



Source: Frost & Sullivan analysis

### *Alternative Solutions*

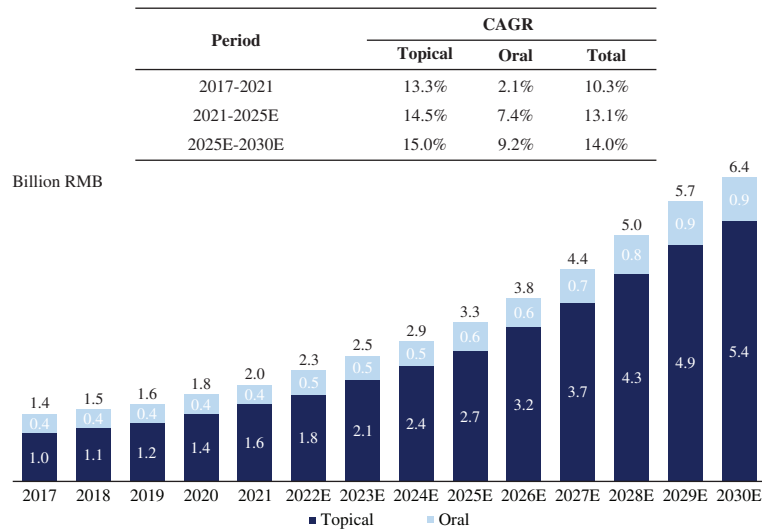
Topical treatments with novel mechanism of action are applied to the affected area of the skin surface, where medications highly concentrate and gradually diffuse through multiple skin layers before reaching circulation system. In contrast, medications are primarily delivered into systemic blood circulation and widely distributed in different organs non-selectively via traditional drug administration routes, including intravenous administration and oral administration. As a result, topical drugs could directly target hair follicles, deliver drug substances more selectively to specific sites with much lower drug concentration in systemic circulation to potentially reduce the risks of complications brought by the systemic drug exposure, such as sexual dysfunction and depression associated with oral finasteride, thus suggesting an potentially alternative solution for androgenetic alopecia.

## INDUSTRY OVERVIEW

### Market Size

The following figure sets forth the historical and projected market size of androgenetic alopecia in China:

#### Market Size of Drugs Approved for Androgenetic Alopecia in China, 2017-2030E



Source: Frost & Sullivan analysis

### Competitive Landscape

The following table shows the competitive landscape of the approved drugs for androgenetic alopecia in China:

Drugs	Dosage Form	Administration Route	RLD Holder/ First Approved Company	Indications	First Approval Date	OTC/Rx	Number of Products (Generics/ Total)	Costs per Treatment Course (RMB)	National Medical Insurance
Minoxidil	Spray	Topical	Jewim Pharmaceutical	Androgenic alopecia	2011/1	Rx	1/1	1,242	No
	Gel	Topical	Bausch+Lomb	Androgenic alopecia	2005/1	OTC	1/1	1,368	No
	Liniment	Topical	Ante Bio-pharmaceutical	Androgenic alopecia	2002/1	OTC	2/2	709	No
	Tincture	Topical	Wansheng Pharmaceutical	Androgenic alopecia	2001/1	OTC and Rx	2/2	680	No
Finasteride	Tablet	Oral	Merck Sharp & Dohme	Male androgenic alopecia	2004/1	Rx	7/8	961	Yes
Cyproterone	Tablet	Oral	Bayer	Severe androgenic alopecia in females	1990/12	Rx	2/2	1,975	Yes

Notes:

- Information as of March 4, 2023. Treatment costs are based on the bidding price.

## INDUSTRY OVERVIEW

- CUP-MNDE, the topical minoxidil spray developed by Bailleul, has not been approved by the NMPA. Cutia distributed CUP-MNDE through third-party cross-border e-commerce platforms as an overseas product. CUP-MNDE is not included in China’s national medical insurance list. Cost per treatment course of CUP-MNDE is around RMB1,080.
- Finasteride for benign prostatic hyperplasia treatment is excluded.
- Cost per treatment course refers to the median price of drugs including all generic drugs and original drugs. It is the sum of medical insurance reimbursement and personal expenditure. The bidding price of drugs is divided by the net content to get the price per unit of drugs. This price is multiplied by the daily dosage guided by the instruction and then multiplied by the number of days of treatment specified in the instruction to get cost per treatment course.

Source: NMPA, Frost & Sullivan analysis

The following table shows the competitive landscape of drugs for androgenetic alopecia under clinical trials in China:

Drugs	Company	Active Ingredients	Indications	Dosage Form	Administration Route	Phase	Date First Posted	Drug Types
Minoxidil topical solution	Jiangsu Chenpai Bond	Minoxidil	Androgenetic alopecia	Topical solution	Topical	ANDA	2022/12	Generic drug
Minoxidil topical solution	Gansu Xifeng	Minoxidil	Androgenetic alopecia	Topical solution	Topical	ANDA	2022/10	Generic drug
Minoxidil topical solution	Zhejiang Dingtai	Minoxidil	Androgenetic alopecia	Topical solution	Topical	ANDA	2022/9	Generic drug
Minoxidil topical solution	Anhui Pioneer	Minoxidil	Androgenetic alopecia	Topical solution	Topical	ANDA	2022/8	Generic drug
Minoxidil topical solution	Zhongshan Wanhan	Minoxidil	Androgenetic alopecia	Topical solution	Topical	ANDA	2022/7	Generic drug
Minoxidil topical solution	Zhejiang Vanguard	Minoxidil	Androgenetic alopecia	Topical solution	Topical	ANDA	2022/6	Generic drug
Minoxidil topical solution	Tianjin Chenguang	Minoxidil	Androgenetic alopecia	Topical solution	Topical	ANDA	2022/6	Generic drug
Minoxidil liniment	Zhejiang Saimo	Minoxidil	Androgenetic alopecia	Liniment	Topical	ANDA	2022/3	Generic drug
Minoxidil tincture	Jiangsu Kanion	Minoxidil	Androgenetic alopecia	Tincture	Topical	ANDA	2021/3	Generic drug
KX-826	Kintor/Koshine	Pyrilutamide (small molecule AR antagonist)	Androgenetic alopecia	Tincture/gel	Topical	III	2021/11	New drug
CU-40102	CUTIA	Finasteride (5- $\alpha$ reductase inhibitors)	Androgenetic alopecia	Spray	Topical	III	2021/10	New drug
CU-40101	CUTIA	Thyroid hormone receptor agonist	Androgenetic alopecia	Liniment	Topical	I	2022/04	New drug
GT20029	Kintor	Topical AR-PROTAC	Androgenetic alopecia Acne vulgaris	Tincture/gel	Topical	I	2021/6	New drug
CU-40104	CUTIA	Dutasteride (5- $\alpha$ reductase inhibitors)	Androgenetic alopecia	Topical agent	Topical	Pre-clinical	N/A	New drug

Note: Information as of January 30, 2023. CU-40103 is under pre-clinical trial stage.

Source: CDE, Frost & Sullivan analysis

## INDUSTRY OVERVIEW

### SKIN DISEASES AND CARE MARKET

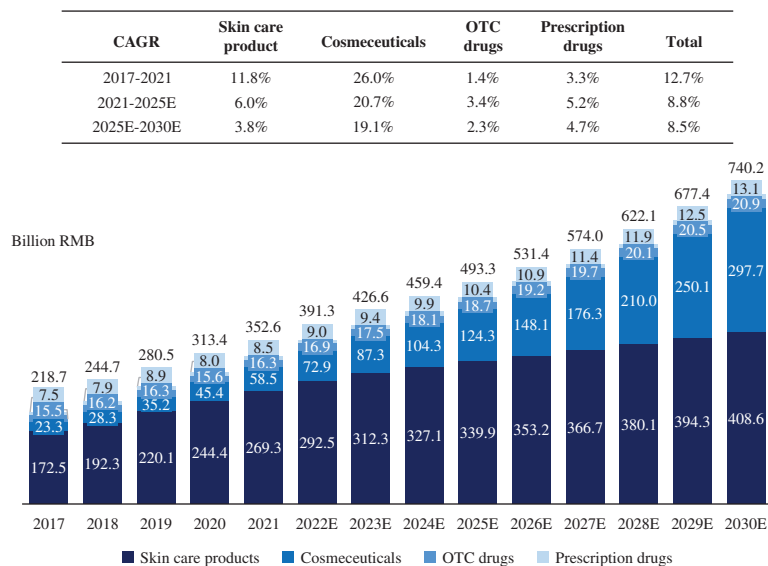
#### Skin Diseases and Care Overview

Skin diseases are mainly originated from malfunction, infection, allergy or genetic aberrations of skin and its appendages, such as acne vulgaris, atopic dermatitis, psoriasis and others. Skin diseases affect patients’ quality of life physically, socially and psychologically.

#### Market Size

The following chart shows the size of skin diseases and care market in China:

**Size of Skin Diseases and Care Market in China, 2017-2030E**



Source: Frost & Sullivan analysis

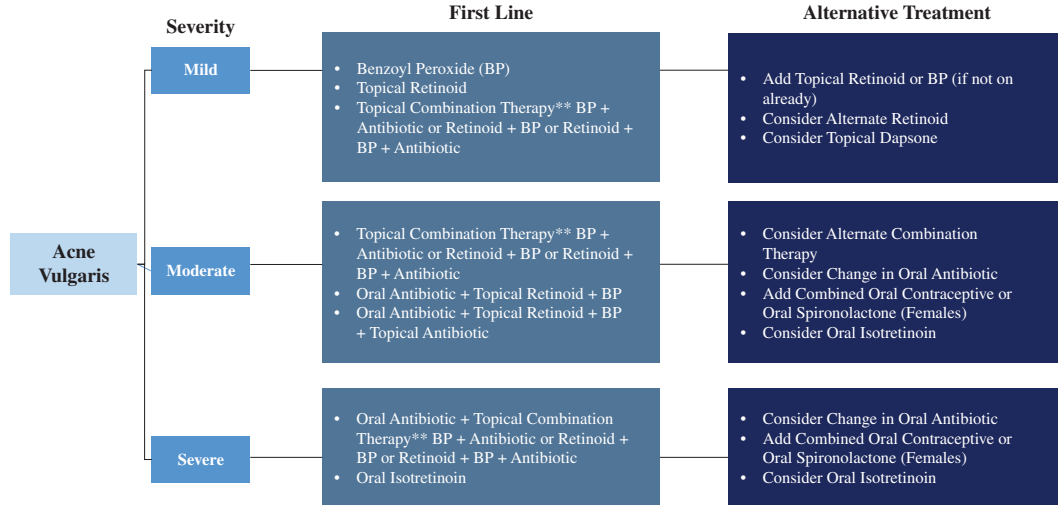
#### Acne Vulgaris

Acne vulgaris is a chronic inflammatory skin condition notable for open or closed comedones and inflammatory lesions, including papules, pustules and nodules. Acne vulgaris is a common disease, especially in adolescents and young adults. It can cause physical and psychological morbidity, such as permanent scarring, poor self-image and depression.

## INDUSTRY OVERVIEW

### Current Treatment Paradigm and Unmet Clinical Needs

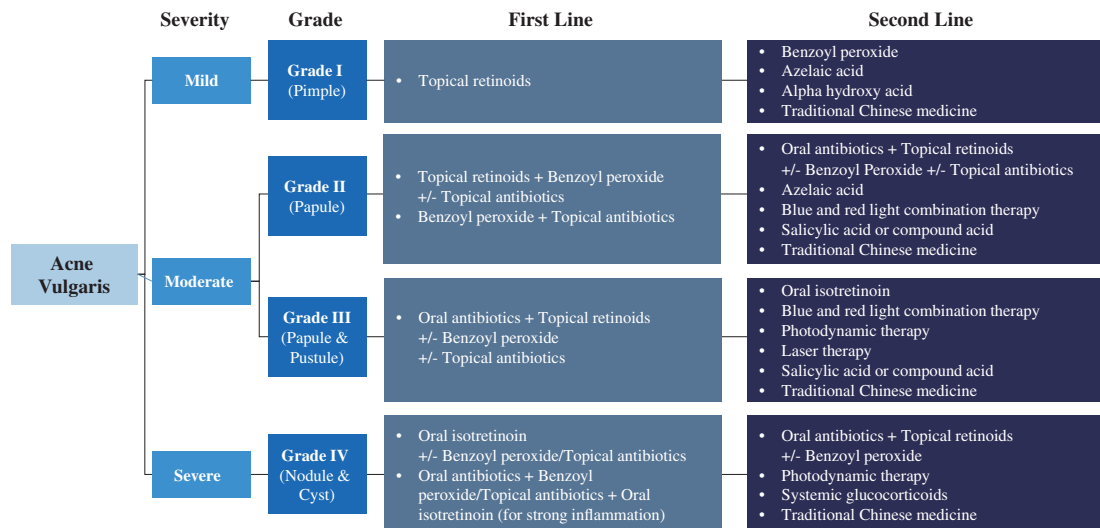
The following sets forth the treatment algorithm of acne vulgaris as recommended by international national guidelines:



Note: \*\* means that the drug is available as a fixed combination product or as a stand-alone ingredient.

Source: *Guidelines of Care for the Management of Acne Vulgaris (J AM ACAD DERMATOL, 2016), Frost & Sullivan analysis*

The following sets forth the treatment algorithm of acne vulgaris as recommended by China’s national guidelines:



Note: For oral antibiotics, tetracyclines including minocycline and doxycycline are recommended by China’s national guidelines. When tetracyclines are contraindicated or cannot be tolerated, macrolides such as erythromycin, roxithromycin and azithromycin, or sulfamethoxazole and trimethoprim combination can be used instead.

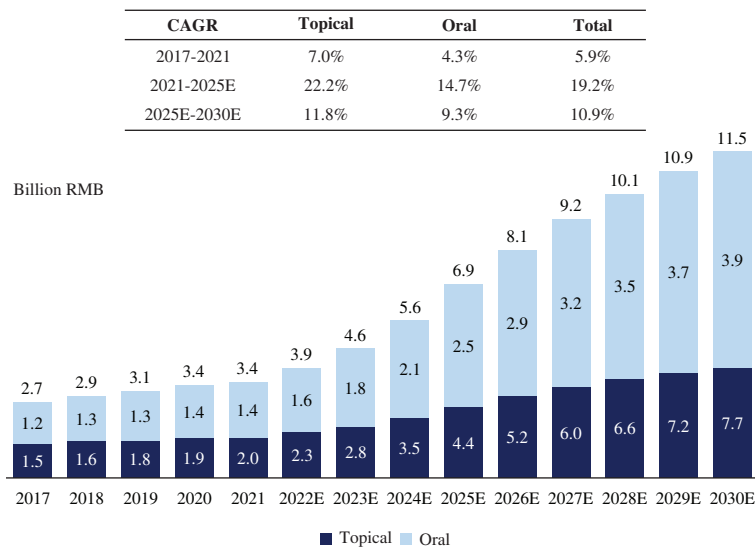
Source: *Chinese Guidelines for the Management of Acne Vulgaris (2019), Frost & Sullivan analysis*

## INDUSTRY OVERVIEW

Acne vulgaris can be classified as mild, moderate or severe depending on its severity. Topical medications can be used as long as acne is present. Mild acne and moderate acne with papules can be treated with a combination of topical medications, such as topical retinoids, benzoyl peroxide and topical antibiotics. When pustules, nodules or cysts are present, moderate acne and severe acne can be treated with systemic and topical medications plus physical and chemical therapies. Supplements are not included in China’s national guidelines for acne treatment. Substantially all patients with acne vulgaris should be treated with drugs such as antibiotics, retinoid and benzoyl peroxide instead of supplements.

The prevalence of acne vulgaris in China has increased from 118.5 million in 2017 to 120.5 million in 2021, and is expected to reach 123.1 million by 2030, showing a gradual upward trend. The market size of acne vulgaris has been increasing with the increase of prevalence rate for many years, and has further increased significantly recent years with the emergence of retinoic acid derivatives such as adapalene. In addition, the demand for less irritating drugs and approval of innovative drugs to treat acne are expected to stimulate the growth of the market in the future. The following chart shows the historical and projected market size of acne vulgaris treatment in China:

**Market Size of Acne Vulgaris Treatment in China, 2017-2030E**



*Note:* The market size of acne vulgaris treatment is estimated to grow as indicated because: (i) a number of acne vulgaris medications are expected to be approved in China, in particular, from 2023 to 2025; (ii) the patients need acne vulgaris treatment are estimated to grow continuously; and (iii) demand for less irritating drugs and approval of innovative drugs to treat acne vulgaris are expected to stimulate the growth of the market.

*Source:* Frost & Sullivan analysis

## INDUSTRY OVERVIEW

The following table sets forth approved topical acne vulgaris drugs in China.

Drugs	Dosage Form	RLD Holder/ First Approved Company	First Approval Date	OTC/Rx	Number of Products (Generics/ Total)	Costs per Treatment Course (RMB)	National Medical Insurance	Administration Route
Clindamycin Phosphate and Benzoyl Peroxide	Gel	GSK	2019/9	Rx	0/1	/	No	Topical
Viaminate and Vitamin E	Gel	China Traditional Chinese Medicine	2019/5	Rx	1/1	/	No	Topical
	Cream	Wu Zhoutong	2006/6	Rx and OTC	14/14	8.8	No	Topical
Erythromycin and Zinc Acetate	Ointment	Tian Cheng	2019/1	Rx	1/1	/	No	Topical
	Gel	Shionogi	2008/9	Rx	1/1	/	No	Topical
Clindamycin Phosphate	Topical Solution	Daphne	2018/11	OTC	5/5	26.8	No	Topical
	Gel	Suzhou No. 4 Pharmaceutical Factory	1997/1	OTC	13/13	25.0	No	Topical
Fusidate	Ointment	Haisco	2017/12	Rx	1/1	38.7	Yes	Topical
	Cream	Leo Pharmaceutical Products	1999/10	Rx	1/2	28.9	Yes	Topical
Isotretinoin Erythromycin	Gel	Sinopharm Wuhan Zhong Lian SiYao	2008/1	Rx	1/1	25.5	No	Topical
Isotretinoin	Gel	Harbin Dazhong	2005/1	Rx	1/1	41.3	Yes	Topical
Nadifloxacin	Cream	Yabang Qiangsheng	2005/1	Rx	3/3	28.5	No	Topical
Clindamycin Hydrochloride	Gel	Golden Sun	2004/1	OTC	1/1	11.9	No	Topical
Azelaic Acid	Cream	Conba	2003/1	Rx	1/1	/	No	Topical
Compound Indometacin	Tincture	Sunflower	2002/1	Rx	1/1	65.0	No	Topical
Tazarotene	Cream	Huapont	2001/1	Rx	1/1	27.1	Yes	Topical
Metronidazole	Gel	Galderma	1998/1	OTC	5/5	48.6	Yes	Topical
Adapalene	Gel	Galderma	1998/1	OTC	9/10	38.6	Yes	Topical
Clindamycin Hydrochloride Metronidazole	Liniment	Dihon	1996/1	Rx and OTC	7/7	25.0	No	Topical
Metronidazole	Cream	Xingao	1996/1	Rx	3/3	4.2	No	Topical
Zinc Oxide and Sulfur Sublimite	Ointment	Zhongzhou	1995/1	OTC	1/1	344.8	No	Topical
Benzoyl Peroxide	Cream	General	1995/1	OTC	4/4	7.6	Yes	Topical
Chlorhexidine Gluconate	Ointment	Hengjian	1994/1	OTC	4/4	18.4	No	Topical
Lincomycin Hydrochloride and Vitamin B6	Cream	Shouxin	1994/1	Rx	7/7	18.4	No	Topical
Benzoyl Peroxide	Gel	Humanwell Chengtian	1994/1	OTC	6/7	22.5	Yes	Topical
Tretinoin	Cream	General	1993/1	Rx	24/24	8.5	Yes	Topical
Compound Sulfur	Cream	Shanghai Zhonghua	1992/1	OTC	5/5	19.6	No	Topical
Vitamin B6	Ointment	King York	1981/1	OTC	6/6	5.4	No	Topical
Erythromycin	Ointment	King York	1981/1	OTC	54/54	4.3	Yes	Topical

*Note:* Information as of January 30, 2023. Treatment costs are based on the bidding price.

*Source:* NMPA, Frost & Sullivan analysis



## INDUSTRY OVERVIEW

The following table sets forth topical acne vulgaris drugs under clinical trials in China.

Drug Name	Company	Indications	Active Ingredients	Phase	Dosage Form	Administration Route	First Posted Date	Drug Types
Fusidic Acid Cream	Gansu Xifeng	Skin infections including acne vulgaris	Fusidic acid (antibiotic)	ANDA	Cream	Topical	2023/1	Generic drug
Clindamycin Phosphate Topical Solution	Sinomune	Acne vulgaris	Clindamycin (antibiotic)	ANDA	Topical solution	Topical	2023/1	Generic drug
Tretinoin and Benzoyl Peroxide Gel	Galderma	Acne vulgaris	Tretinoin and benzoyl peroxide (retinoid and benzoyl peroxide combination)	NDA	Gel	Topical	2023/1	New drug
Fusidic Acid Cream	Foyou	Skin infections including acne vulgaris	Fusidic acid (antibiotic)	ANDA	Cream	Topical	2022/8	Generic drug
Adapalene + Clindamycin Gel	Zhaoke	Moderate acne vulgaris	Adapalene and clindamycin (retinoid and antibiotic combination)	NDA	Gel	Topical	2021/2	New drug
CU-10201	Cutia	Moderate to severe acne vulgaris	Minocycline (antibiotic)	III	Foam	Topical	2021/6	New drug
Aminolevulinic Acid Hydrochloride Topical Powder	Fudan-Zhangjiang	Combined with photodynamic therapy to treat moderate to severe acne vulgaris	Aminolevulinic acid hydrochloride (photosensitizing precursor)	II	Powder	Topical	2021/12	New drug
Tazarotene Clindamycin Phosphate Cream	Sinomune	Moderate acne vulgaris	Tazarotene and clindamycin (retinoid and antibiotic combination)	II	Cream	Topical	2021/1	New drug
KX-826	Kintor/Koshine	Mild to moderate acne vulgaris	Pyrilutamide (small molecule AR antagonist)	I/II	Gel	Topical	2021/3	New drug
GT20029	Kintor	Androgenic alopecia, acne vulgaris	Topical AR-PROTAC	I	Gel/tincture	Topical	2021/6	New drug
Ibuprofen Piconol Cream	Bestcomm	Eczema, contact dermatitis, atopic dermatitis, perioral dermatitis, herpes zoster, acne vulgaris	Ibuprofen piconol (non-steroidal anti-inflammatory drug)	I	Cream	Topical	2018/11	Generic drug

*Note:* Information as of January 30, 2023.

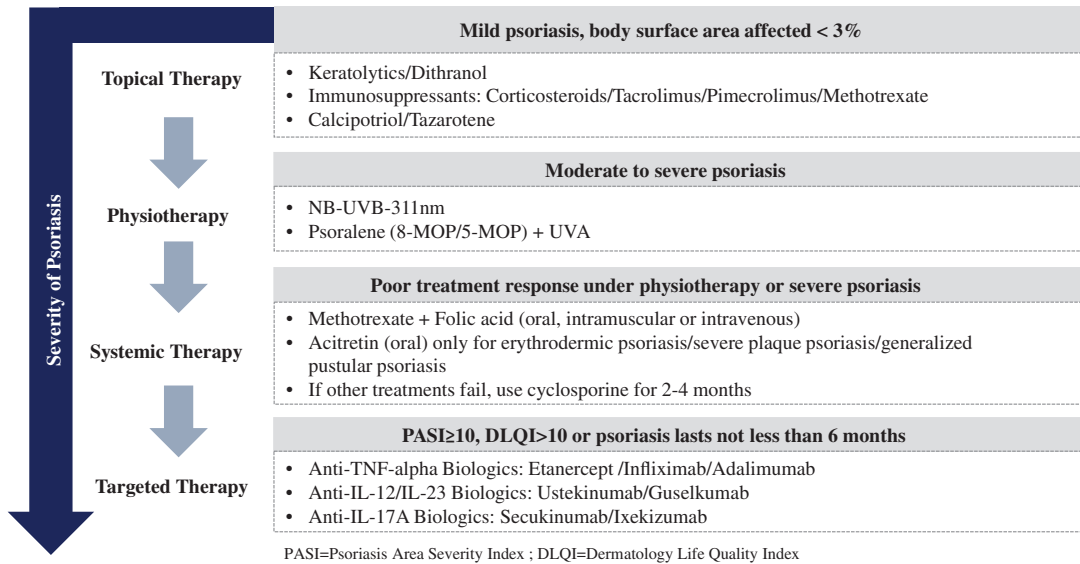
*Source:* CDE, Frost & Sullivan analysis

## INDUSTRY OVERVIEW

### Psoriasis

Psoriasis is a common chronic skin condition that speeds up the life cycle of skin cells. A variety of factors could trigger an episode of psoriasis, such as emotional stress, smoking, heavy alcohol consumption, vitamin D deficiency, injury and streptococcal infection, as well as some abnormality in the immune system.

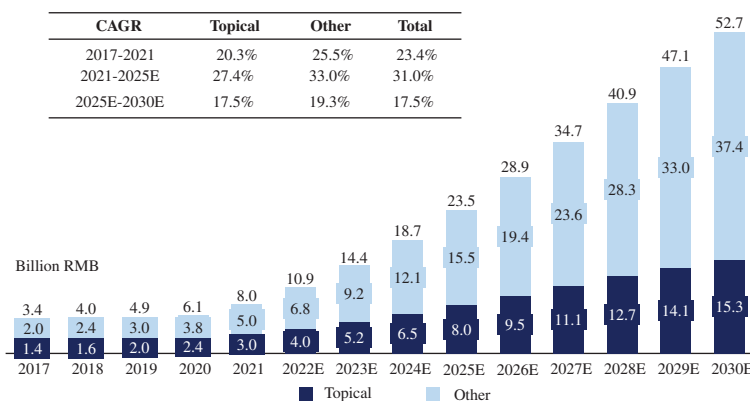
The following chart shows the treatment algorithm of psoriasis in China as recommended by China’s national guidelines:



Source: Literature Review, Frost & Sullivan analysis

The prevalence of psoriasis in China has increased from 6.5 million in 2017 to 6.7 million in 2021, and is expected to reach 6.9 million by 2030, showing a gradual upward trend. The following sets forth the market size of psoriasis treatment in China:

### Market Size of Psoriasis Treatment in China, 2017-2030E



Note: The market size of psoriasis treatment is estimated to grow as indicated because: (i) a number of psoriasis medications are expected to be approved in China; (ii) the patients need psoriasis treatment are estimated to grow continuously; and (iii) demand for less irritating drugs and approval of innovative drugs to treat psoriasis are expected to stimulate the growth of the market.

Source: Frost & Sullivan analysis

## INDUSTRY OVERVIEW

The following table sets forth approved topical medications for the treatment of psoriasis in China:

Drugs	Dosage Form	RLD Holder/First Approved Company	First Approval Date	OTC/Rx	Number of Products (Generics/Total)	Costs per Treatment Course (RMB)	National Medical Insurance	Administration Route
Fluocinonide	Ointment	Nanjing Chang'ao Pharma	2020/6	Rx	1/1	9.5	No	Topical
	Cream	King York	1981/1	Rx	53/53	71.3	No	Topical
Benvitimod	Cream	Zhonghao Pharmaceutical Tianji Pharma	2019/5	Rx	0/1	2318.4	Yes	Topical
Calcipotriol and Betamethasone Dipropionate	Gel	LEO Pharma	2015/6	Rx	0/1	621.5	Yes	Topical
Tazarotene and Betamethasone Dipropionate	Cream	Huapont Pharmaceutical	2015/3	Rx	1/1	536.7	Yes	Topical
Compound Flumetasone	Ointment	Bright Future	2014/12	Rx	0/1	68.3	No	Topical
Calcipotriol	Ointment	Huapont Pharmaceutical	2011/12	Rx	3/4	219.7	Yes	Topical
Dithranol	Wax Stick	Ansheng Fenghuang Pharmaceutical	2007/1	Rx	1/1	347.1	No	Topical
	Ointment	Wuhan Aimin Pharmaceutical	1990/1	Rx	12/12	246.4	Yes	Topical
Tazarotene	Cream	Huapont Pharmaceutical	2004/1	Rx	1/1	50.6	Yes	Topical
Halometasone	Cream	Novartis AG	1999/1	Rx	3/4	102.5	Yes	Topical
Tacalcitol	Ointment	Teijin Pharma	1997/7	Rx	1/2	218.0	Yes	Topical
Borreol Camphor Eucalyptus Oil and Fluocinonide	Paste	Henan Lingrui Pharma	1996/1	Rx	2/2	/	No	Topical
Compound Fluocinonide	Tincture	Hongxing Pharmaceutical	1995/1	Rx	25/25	131.6	No	Topical
Tretinoin	Cream	General Pharmaceutical	1993/1	Rx	24/24	31.7	Yes	Topical
Clobetasol Propionate	Cream	Cr. Shunfeng Pharmaceutical	1988/1	Rx	20/20	25.2	Yes	Topical
Halcinonide	Solution	Tianjiao Pharma	1985/1	Rx	22/22	389.2	Yes	Topical
	Ointment	King York	1985/1	Rx	10/10	5.5	Yes	Topical
	Cream	King York	1985/1	Rx	22/22	47.6	Yes	Topical
Beclometasone Dipropionate	Cream	King York	1982/1	Rx	18/18	17.4	Yes	Topical
Fluocinonide Acetate and Borneol	Cream	King York	1981/1	Rx	10/10	136.9	No	Topical
Triamcinolone Acetonide and Neomycin	Paste	Yangling Biotechnology	1985/1	Rx	20/20	/	No	Topical

*Note:* Information as of January 30, 2023. Treatment costs are based on the bidding price.

*Source:* NMPA, Frost & Sullivan analysis

## INDUSTRY OVERVIEW

The following table sets forth topical psoriasis drugs under clinical trials in China:

Drugs	Category	Company	Indications	Administration Route	Phase	First Posted Date	Drug Types
CKBA Ointment	Th17 Regulator	Botany/Sincere	Plaque Psoriasis	Topical	II	2022/3	New drug
Icotinib Cream	EGFR Inhibitor	Betta Pharmaceutical	Mild to Moderate Psoriasis	Topical	II	2017/7	New drug
MH080 Cream	N/A	Minghui/AustarPharma	Plaque Psoriasis	Topical	I/II	2022/10	New drug
LNK01004 Ointment	JAK Inhibitor	Lynk Pharmaceuticals	Mild to Moderate Plaque Psoriasis	Topical	I	2022/7	New drug
HLK-6002 Ointment	N/A	Shenzhen Yaoxin	Plaque Psoriasis	Topical	I	2022/5	New drug
HY1770 Cream	IL-4R Inhibitor	Pharmavan	Plaque Psoriasis	Topical	I	2021/11	New drug
QY101 Ointment	PDE4 Inhibitor	E-nitiata	Psoriasis	Topical	IND approval	2022/9	New drug
Tazarotene + Clobetasol Ointment	Retinoids + Corticosteroids	Defeng	Plaque Psoriasis	Topical	IND approval	2019/4	New drug

*Note:* Information as of January 30, 2023. CU-10401 is under pre-clinical trial stage.

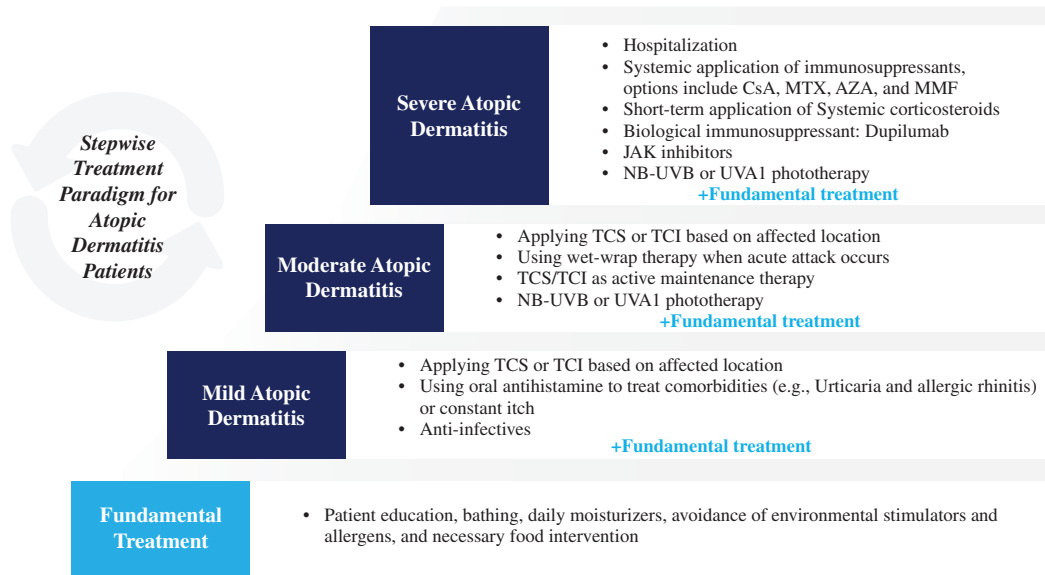
*Source:* CDE, Frost & Sullivan analysis

### Atopic Dermatitis

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 erythrodermic rash. Pruritus and chronic or relapsing eczematous lesions with typical shape and distribution are essential for diagnosis. 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.

## INDUSTRY OVERVIEW

The following chart sets forth the treatment algorithm of atopic dermatitis as recommended by the national guidelines:

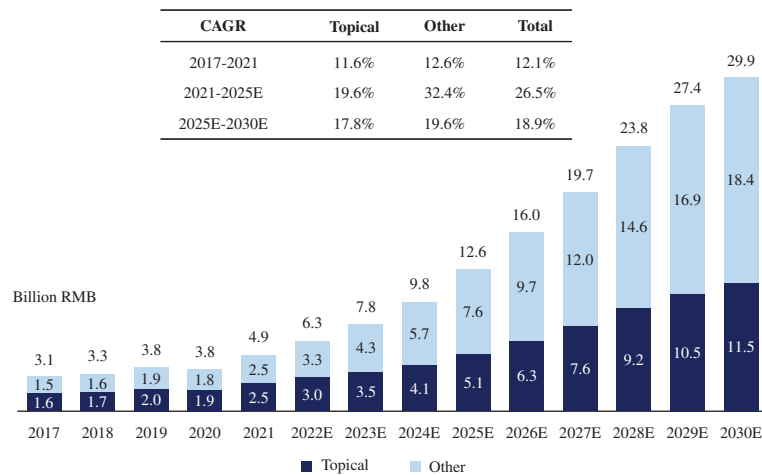


Notes: CsA: cyclosporine A; MTX: methotrexate; AZA: azathioprine; MMF: mycophenolate mofetil; TCS: topical corticosteroids; TCI: topical calcineurin inhibitors

Source: Chinese Society of Dermatology, Frost & Sullivan analysis

The prevalence of atopic dermatitis in China has increased from 62.4 million in 2017 to 69.1 million in 2021 and is expected to reach 81.7 million by 2030, showing a gradual upward trend. The following chart shows the market size of atopic dermatitis treatment by dosage forms in China:

### Market Size of Atopic Dermatitis Treatment in China, 2017-2030E



Note: Other dosage forms include systemic administration and subcutaneous injection.

The market size of atopic dermatitis treatment is estimated to grow as indicated because: (i) a number of atopic dermatitis medications are expected to be approved in China; (ii) the patients need atopic dermatitis treatment are estimated to grow continuously; and (iii) demand for less irritating drugs and approval of innovative drugs to treat atopic dermatitis are expected to stimulate the growth of the market.

Source: Frost & Sullivan analysis

## INDUSTRY OVERVIEW

The following table sets forth approved topical medications for the treatment of atopic dermatitis in China:

Drugs	Dosage Form	R/LD Holder/ First Approved Company	First Approval Date	OTC/Rx	Number of Products (Generics/Total)	Costs per Treatment Course (RMB)	National Medical Insurance	Administration Route
Crisaborole	Ointment	Anacor Pharma/Pfizer/Pharmacia and Upjohn	2020/7/29	Rx	0/1	840.0	Yes	Topical
Clobetasone Butyrate	Cream	GlaxoSmithKline/GSK-China	2011/5/5	Rx	1/2	190.4	No	Topical
Mometasone Furoate	Gel	Zhejiang Xianju Pharma	2008/1/1	Rx	3/3	140.0	Yes	Topical
	Cream	Bayer AG/Shanghai New Asiatic Medicine Industry	1999/1/1	OTC/Rx	9/9	56.0	Yes	Topical
Desonide	Cream	Chongqing Huapont Pharma	2006/1/1	Rx	1/1	117.6	Yes	Topical
Pimecrolimus	Cream	Novartis AG Meda AB	2005/9/29	Rx	1/2	3333.7	Yes	Topical
Compound Flumetasone	Ointment	Bright Future Pharma	2005/4/12	Rx	1/1	67.2	No	Topical
Tacrolimus	Ointment	Astellas Pharma LEO Pharma	2004/11/17	Rx	9/10	3352.2	Yes	Topical
Fluticasone Propionate	Ointment	GlaxoSmithKline	2000/6/16	Rx	5/6	128.8	Yes	Topical
Doxepin Hydrochloride	Cream	Tasly New resources Pharma	2000/1/1	Rx	2/2	12.6	Yes	Topical
Halometasone	Cream	Novartis AG	1999/1/1	Rx	3/4	50.4	Yes	Topical
Boreol Camphor Eucalyptus Oil and Fluocinonide	Patch	Henan Lingrui Pharma	1996/1/1	Rx	2/2	/	No	Topical
Zinc Oxide	Oil	Beijing Twinluck Pharma	1996/1/1	OTC/Rx	1/1	/	Yes	Topical
Halcinonide	Film	King York	1991/1/1	Rx	1/1	22.3	No	Topical
	Cream	King York	1985/1/1	Rx	22/22	47.6	Yes	Topical
	Ointment	King York	1985/1/1	Rx	10/10	5.5	Yes	Topical
	Solution	Tianjiao Pharma	1985/1/1	Rx	22/22	77.8	Yes	Topical
Vitamin B6 and Fluocinonide	Cream	Hunan Tianlong Pharma	1984/1/1	OTC	7/7	58.8	No	Topical
Fluocinonide	Ointment	Nanjing Chang'ao Phar	1982/1/1	Rx	1/1	11.2	No	Topical
	Cream	King York	1981/1/1	Rx	53/53	61.6	No	Topical
Fluocinonide Acetate and Borneol	Cream	King York	1981/1/1	Rx	10/10	136.9	No	Topical
Triamcinolone Acetonide Acetate	Cream	King York	1981/1/1	Rx	22/22	92.4	Yes	Topical

*Note:* Information as of January 30, 2023. Treatment costs are calculated according to bid price.

*Source:* NMPA, Frost & Sullivan analysis

## INDUSTRY OVERVIEW

The following table sets forth topical medications under clinical trial studies for the treatment of atopic dermatitis in China:

Drugs	Category	Company	Indications	Administration Route	Phase	First Posted Date	Drug Types
Diflucortolone Valerate Cream	Corticosteroids	King York	Atopic Dermatitis, Ulcers, Psoriasis, Burns, Dermatitis, Eczema, etc.	Topical	ANDA	2020/12	Generic drug
Difamilast (OPA-15406) Ointment	PDE4 Inhibitor	Otsuka	Atopic Dermatitis	Topical	III	2022/12	New drug
Jaktinib Hydrochloride Cream	JAK Inhibitor	Zelgen	Atopic Dermatitis	Topical	III	2022/6	New drug
Benvitimod Cream	Aryl Hydrocarbon Receptor Agonist	Zhonghao/Shenzhen Tianji	Mild to Moderate Atopic Dermatitis	Topical	III	2022/6	New drug
Ivamacitinib (SHR0302) Ointment	JAK Inhibitor	Reistone/Jiangsu Hengrui	Atopic Dermatitis	Topical	III	2020/12	New drug
Diflucortolone cream	Corticosteroids	Tianjin Pharmaceuticals Research Organization	Atopic Dermatitis, Psoriasis, Lichen Planus, Contact Dermatitis, etc.	Topical	III	2019/3	Generic drug
Fusidic acid-Betamethasone Cream	Antibiotic + Corticosteroids	LEO	Clinical Infectious Atopic Dermatitis, Eczema	Topical	III	2018/7	Generic drug
HY-072808 Ointment	PDE4 Inhibitor	Hefei Pharma Tech	Atopic Dermatitis	Topical	II	2022/8	New drug
PG-011 Gel	JAK Inhibitor	Beijing Puqi Pharma	Atopic Dermatitis	Topical	II	2021/4	New drug
Hemay028 Ointment	PDE4 Inhibitor	Tianjin Hemay	Atopic Dermatitis	Topical	II	2020/3	New drug
MH004 Cream	N/A	Minghui Pharma	Atopic Dermatitis	Topical	I/II	2022/1	New drug
QY101 Ointment	PDE4 Inhibitor	E-nitiate	Atopic Dermatitis	Topical	I	2022/6	New drug
MDI-1228_Mesylyate Gel	JAK Inhibitor	Henan Meiyinnuo	Atopic Dermatitis	Topical	I	2022/5	New drug
Pimeprofen Cream	Nonsteroidal Anti-inflammatory	Shandong Bestcomm/Shantou Special Economic Zone TuobinPharma	Atopic Dermatitis, Acute Eczema, Contact Dermatitis, Rosacea, Acne Vulgaris, etc.	Topical	I	2018/11	Generic drug
HY1770 Cream	IL-4R Inhibitor	Pharmavan	Atopic Dermatitis	Topical	IND approval	2023/1	New drug
QY211 Gel	JAK Inhibitor	E-nitiate	Atopic Dermatitis	Topical	IND approval	2022/11	New drug
TUL01101 Ointment	JAK Inhibitor	Zhuhai United	Atopic Dermatitis	Topical	IND approval	2022/11	New drug
FZJ-003 Gel	JAK Inhibitor	Fudan-Zhangjiang	Atopic Dermatitis	Topical	IND approval	2022/9	New drug
LNK01004 Ointment	Kinase inhibitor	Lynk Pharmaceuticals	Atopic Dermatitis	Topical	IND approval	2022/7	New drug
JK0002 Cream	N/A	Shenzhen Jiake	Atopic Dermatitis	Topical	IND approval	2022/3	New drug

*Note:* Information as of January 30, 2023. CU-10101 is under pre-clinical trial stage.

*Source:* CDE, Frost & Sullivan analysis

## INDUSTRY OVERVIEW

### TOPICAL ANESTHESIA MARKET

#### Topical Anesthesia Overview

Topical anesthetics are highly penetrating local anesthetics which are sprayed or applied to skin or mucous membranes, conjunctive, and other surfaces to cause superficial loss of pain sensation. Topical anesthesia can be applied in consumption and clinical scenarios. In consumption scenarios, topical anesthetics are generally applied before superficial dermatological procedures. In clinical practices, topical anesthetics are applied before puncture procedures and operations concerning superficial tissue. In addition, it can be used as a pretreatment for infiltration anesthesia combined with other anesthetics.

#### Currently Available Topical Anesthetics

The following table sets forth the efficacy, side effects, sites of administration and limitations of topical anesthetics:

Core Components	Efficacy*	Common Side Effects	Site of Administration	Occlusion after Application
<b>Lidocaine and prilocaine</b>	<ul style="list-style-type: none"> <li>67.5% of subjects reported adequate pain relief</li> <li>60.0% of subjects were willing to reuse the product</li> </ul>	<ul style="list-style-type: none"> <li>Paleness (pallor or blanching): 37%</li> <li>Erythema: 30%</li> <li>Alterations in temperature sensations: 7%</li> <li>Edema: 6%</li> <li>Itching: 2%</li> </ul>	Intact skin surface that need dermatological procedures	Needs plastic occlusion
<b>Lidocaine and tetracaine</b>	<ul style="list-style-type: none"> <li>75.0% of subjects reported adequate pain relief</li> <li>82.5% of subjects were willing to reuse the product</li> </ul>	<ul style="list-style-type: none"> <li>Erythema: 47%</li> <li>Skin discoloration (blanching, ecchymosis and purpura):16%</li> <li>Edema: 14%</li> </ul>	Intact skin surface that need dermatological procedures	Forms a self-occlusive film when exposed to air

\* *Note:* For superficial dermatosurgical procedures after 30-minute application. Topical anesthetics with only one core component such as lidocaine gel are not included in the table because they are generally used in endoscopy, endotracheal intubation, mucosa procedures and post herpes neuralgia treatment rather than epidermal anesthesia treatment.

*Source: Literature search, FDA label, Frost & Sullivan analysis*

#### Alternative Solutions

There are two approved topical anesthesia products for puncture and superficial dermatologic procedures in China and none of them is composed of tetracaine which has been tested more effective in pain relief, because subjects with lidocaine/tetracaine treatment reported significantly lesser pain score compared to subjects with lidocaine/prilocaine treatment with statistic significance. The lidocaine/tetracaine compound produces rapid and durable topical anesthesia due to the pharmacokinetics of the two components. The anesthesia produced by lidocaine is faster and more extensive. Tetracaine, a long-acting amino-ester, is more lipophilic than lidocaine, concentrating in the stratum corneum of the epidermis, where it slowly diffuses. The duration of tetracaine is thus prolonged and the systemic uptake is limited. In addition, the application of lidocaine/prilocaine cream needs plastic occlusion while lidocaine/tetracaine cream is self-occluding, which is more convenient for users. The market



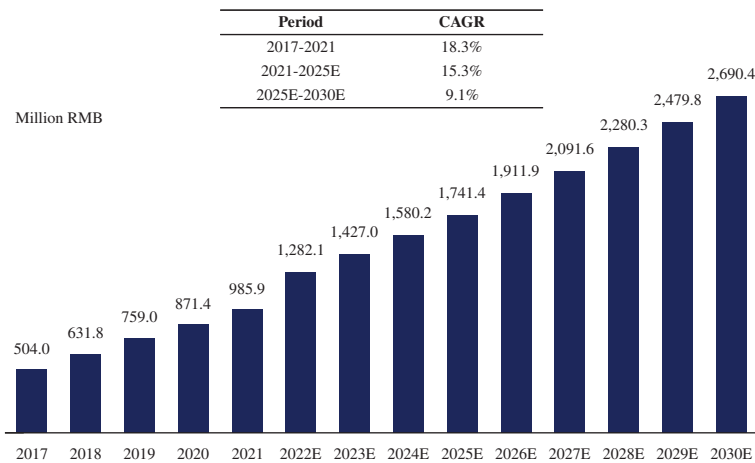
## INDUSTRY OVERVIEW

gives an opportunity for companies that develop products meeting the need for lidocaine/tetracaine topical anesthesia products. Currently, there have been two pipelines of lidocaine/tetracaine products from Liangfu Pharmaceutical and Cutia Therapeutics in ongoing clinical trials in China.

### Market Size of Topical Anesthetics in China

The following chart shows the market size of topical anesthesia products in China:

#### Market Size of Topical Anesthesia Products in China, 2017-2030E




*Note:* The size of topical anesthetics market is estimated to grow as indicated because: (i) a number of topical anesthetics are expected to be approved in China; (ii) the recognition and availability of topical anesthetics continue to improve due to their safety and ease of treatment; (iii) the population that can receive topical anesthetics continue to grow, and (iv) market penetration of topical anesthetics products increases thanks to the approval of generic products in China.

*Source:* Frost & Sullivan analysis

### Competitive Landscape of Topical Anesthetics in China

Currently, there are two topical anesthesia products approved by the NMPA as set forth below.

 <b>NMPA Approved Products For Topical Anesthesia</b>									
Brand Name	Ingredient	Administration Route	Company	Approved Date	OTC/Rx	Indication	Treatment Costs	National Medical Insurance	Drug Types
<b>EMLA</b>	Lidocaine/Prilocaine	Topical	AstraZeneca AB	1998.01	Rx	Topical anesthetic analgesia (for puncture procedure and superficial surgeries)	RMB312.0 (for a skin area of 10 cm <sup>2</sup> )	No	New drug
<b>Compound Lidocaine Cream</b>	Lidocaine/Prilocaine	Topical	Tongfang Pharmaceutical	2006.01	Rx	Topical anesthetic analgesia (for puncture procedure and superficial surgeries)	RMB98.6 (for a skin area of 10 cm <sup>2</sup> )	No	Generic drug

*Note:* Only consider the topical anesthesia products for puncture and superficial dermatological procedures

*Source:* NMPA, Frost & Sullivan analysis

## INDUSTRY OVERVIEW

There are 28 topical anesthesia products under clinical trial development in China, and most of the competing products are compounds of lidocaine and prilocaine. The following table sets forth the topical anesthesia products under clinical trial in China:

Generic Name	Company	Major Indications	Product Development Stage	First Posted Date <sup>(1)</sup>	Drug Types
Lidocaine/Prilocaine	Sihuan/ Yangyankongjian	Topical anesthesia on normal intact skin, genital mucous membranes and ulcer of lower limbs	ANDA	2023/3	Generic drug
Lidocaine/Prilocaine	Hainan Hailing	Topical anesthetic analgesia (for puncture procedure and superficial surgeries)	ANDA	2023/3	Generic drug
Lidocaine/Prilocaine	Suzhou Erye/ Nanjing Haina	Epidermal anesthesia for superficial surgery and puncture procedures Topical anesthesia on genital mucous membranes for superficial minor surgery and as pretreatment for infiltration anesthesia	ANDA	2023/2	Generic drug
Lidocaine/Prilocaine	Hangzhou Solipharma	Epidermal anesthesia for superficial surgery and puncture procedures Topical anesthesia on genital mucous membranes for superficial minor surgery and as pretreatment for infiltration anesthesia	ANDA	2023/2	Generic drug
Lidocaine/Prilocaine	Jiangsu Deyuan	Topical anesthesia on normal intact skin, genital mucous membranes and ulcer of lower limbs	ANDA	2023/1	Generic drug
Lidocaine/Prilocaine	Hunan Jiudian	Topical anesthesia on normal intact skin, genital mucous membranes and ulcer of lower limbs	ANDA	2023/1	Generic drug
Lidocaine/Prilocaine	Hainan Zicheng/ Jiangxi Decheng	Topical anesthesia on normal intact skin, genital mucous membranes and ulcer of lower limbs	ANDA	2022/10	Generic drug
Lidocaine/Prilocaine	Hebei Yadong/ Hebei Xinzhang	Topical anesthesia on normal intact skin, genital mucous membranes and ulcer of lower limbs	ANDA	2022/10	Generic drug
Lidocaine/Prilocaine	Bright Future Pharmaceutical/ Andros Pharmaceuticals	Topical anesthesia on normal intact skin, genital mucous membranes and ulcer of lower limbs	ANDA	2022/9	Generic drug
Lidocaine/Prilocaine	Zhejiang CDMO Pharmaceutical/ Fuou Pharmaceutical	Topical anesthesia on normal intact skin, genital mucous membranes and ulcer of lower limbs	ANDA	2022/8	Generic drug
Lidocaine/Prilocaine	C&O Pharmaceutical Technology	Epidermal anesthesia for superficial surgery and puncture procedures Topical anesthesia on genital mucous membranes for superficial minor surgery and as pretreatment for infiltration anesthesia in adults and teenagers aged over 12 Local anesthesia on ulcer of lower limbs in adults	ANDA	2022/3	Generic drug

## INDUSTRY OVERVIEW

Generic Name	Company	Major Indications	Product Development Stage	First Posted Date	Drug Types
Lidocaine/Prilocaine	Zhuhai Rundu/ CBC Biotechnological & Pharmaceutical	Epidermal anesthesia for superficial surgery and puncture procedures Topical anesthesia on genital mucous membranes for superficial minor surgery and as pretreatment for infiltration anesthesia	ANDA	2022/2	Generic drug
Lidocaine/Prilocaine	Humanwell Healthcare	Epidermal anesthetic analgesia (for superficial surgery and puncture procedures)	ANDA	2021/12	Generic drug
Lidocaine/Prilocaine	CR.Shunfeng Pharmaceutical/ Shenzhen Yujian	Epidermal anesthesia for superficial surgery and puncture procedures Topical anesthesia on genital mucous membranes for superficial minor surgery and as pretreatment for infiltration anesthesia	ANDA	2021/11	Generic drug
Lidocaine/Prilocaine	Zhuhai Laicci Medical Beauty Technology/ Ruyuan HEC	Epidermal anesthesia for superficial surgery and puncture procedures Topical anesthesia on genital mucous membranes for superficial minor surgery and as pretreatment for infiltration anesthesia	ANDA	2021/8	Generic drug
Lidocaine/Tetracaine	Cutia Therapeutics	Epidermal anesthetic analgesia (for superficial dermatological procedures)	III <sup>(2)</sup>	2023/2	Generic drug
Lidocaine/Tetracaine	Liangfu Pharmaceutical/ Nuobote	Epidermal anesthetic analgesia (for superficial dermatological procedures)	III <sup>(2)</sup>	2023/2	Generic drug
Lidocaine/Prilocaine	Guangzhou Regenex	Topical anesthesia on normal intact skin, genital mucous membranes and ulcer of lower limbs	BE	2023/2	Generic drug
Lidocaine/Prilocaine	CR Double-Crane	Epidermal anesthesia for superficial surgery and puncture procedures Topical anesthesia on genital mucous membranes for superficial minor surgery and as pretreatment for infiltration anesthesia	BE	2023/1	Generic drug
Lidocaine/Prilocaine	Jinan Bairun	Topical anesthetic analgesia (for puncture procedure and superficial surgeries)	BE	2023/1	Generic drug
Lidocaine/Prilocaine	Hangzhou Jingshi	Topical anesthesia on normal intact skin, genital mucous membranes and ulcer of lower limbs	BE	2022/12	Generic drug
Lidocaine/Prilocaine	Zhejiang Puli	Topical anesthesia on normal intact skin, genital mucous membranes and ulcer of lower limbs	BE	2022/11	Generic drug
Lidocaine/Prilocaine	Binhai Meikang	Topical anesthesia on normal intact skin, genital mucous membranes and ulcer of lower limbs	BE	2022/11	Generic drug

## INDUSTRY OVERVIEW

Generic Name	Company	Major Indications	Product Development Stage	First Posted Date	Drug Types
Lidocaine/Prilocaine	Zhejiang Gaozhi	Epidermal anesthesia for superficial surgery and puncture procedures Topical anesthesia on genital mucous membranes for superficial minor surgery and as pretreatment for infiltration anesthesia	BE	2022/9	Generic drug
Lidocaine/Prilocaine	Zhejiang Anglikang	Topical anesthetic analgesia (for puncture procedure and superficial surgeries)	BE	2022/9	Generic drug
Lidocaine/Prilocaine	Ginposome Pharmaceutical	Epidermal anesthesia for superficial surgery and puncture procedures Topical anesthesia on genital mucous membranes for superficial minor surgery and as pretreatment for infiltration anesthesia	BE	2021/11	Generic drug
Lidocaine/Prilocaine	Haisco Pharmaceutical Group	Epidermal anesthetic analgesia for superficial surgery and puncture procedures Topical anesthesia on genital mucous membranes for superficial minor surgery and as pretreatment for infiltration anesthesia	BE	2020/5	Generic drug
Lidocaine/Tetracaine	ADOH B.V/ Juyou Biotech	Epidermal anesthetic analgesia (for superficial dermatological procedures)	IND	2022/11	New drug <sup>(3)</sup>

*Notes:*

- (1) Information as of March 4, 2023; the table only includes the topical anesthesia products for puncture and superficial dermatological procedures.
- (2) The generic lidocaine/tetracaine compound product under clinical trials is classified as Class 3 chemical drug in China. According to the NMPA, Class 3 chemical drug is defined as drugs manufactured by domestic applicants by imitating the original drugs that have been marketed overseas but not yet in China. For such generic products, if bioequivalence data are not available and clinical trials cannot be exempted, Phase III clinical trials of Class 3 chemical drugs are required by the CDE in China.
- (3) Lidocaine/tetracaine compound product developed by ADOH B.V/Juyou Biotech was registered as Class 5.1 chemical drug with the CDE. According to the NMPA, Class 5.1 chemical drug is defined as new drugs including original drugs and modified drugs that have been marketed overseas and are under application for being marketed in China.

*Source: CDE, Frost & Sullivan analysis*

### REPORT COMMISSIONED BY FROST & SULLIVAN

In connection with the [REDACTED], we commissioned Frost & Sullivan, an Independent Third Party, to prepare a report on global and China’s markets regarding localized adipose accumulation management medication, scalp diseases and care, skin diseases and care and topical anesthesia market. Except as otherwise noted, all data and forecasts in this section come from the Frost & Sullivan Report. We have agreed to pay a total of RMB1.05 million in fees for the preparation of the Frost & Sullivan Report. Frost & Sullivan is a market research and consulting company that provides market research on a variety of industries including healthcare. In preparing the report, Frost & Sullivan collected and reviewed publicly available data such as government-derived information, annual reports and industry association statistics, as well as market data collected by conducting interviews with key industry experts and leading industry participants. Frost & Sullivan has exercised due care in collecting and reviewing the information so collected.