

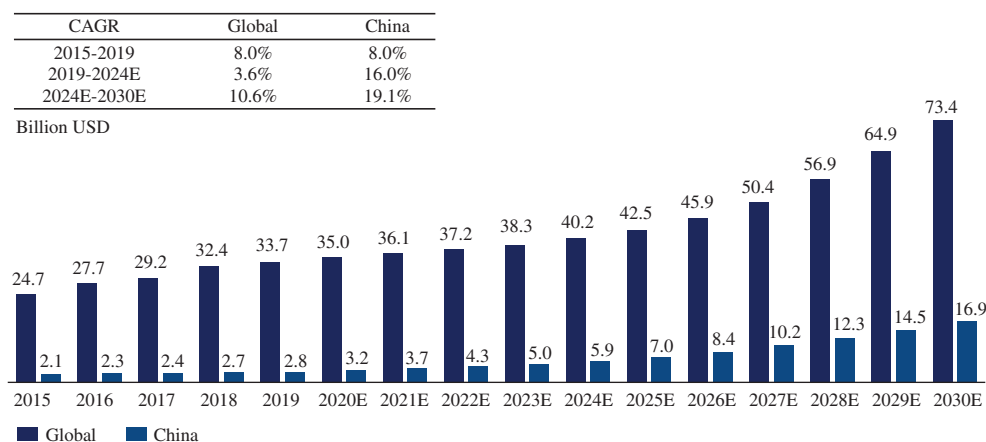
INDUSTRY OVERVIEW

The information and statistics set out in this section and other sections of this document were extracted from different official government publications, available sources from public market research and academic research. In addition, we commissioned Frost & Sullivan to prepare the Frost & Sullivan Report, upon which this section is based. See “—Source of Information.” We believe that the source of this information is an appropriate source for such information and have taken reasonable care in extracting and reproducing such information. We have no reason to believe that such information is false or misleading or that any fact has been omitted that would render such information false or misleading. The information from official and non-official sources has not been independently verified by us, the [REDACTED], Joint Sponsors, [REDACTED], [REDACTED], any of the [REDACTED], any of their respective directors and advisers, or any other persons or parties involved in the [REDACTED], save for Frost & Sullivan, and no representation is given as to its accuracy. Accordingly, the information from official and non-official sources contained herein may not be accurate and should not be unduly relied upon.

OVERVIEW OF CHINA’S OPHTHALMIC DRUG MARKET

China’s ophthalmic drug market has grown rapidly in recent years. The market size of ophthalmic drugs in China grew from US\$2.1 billion in 2015 to US\$2.8 billion in 2019, representing a CAGR of 8.0%. It is estimated to further grow to US\$5.9 billion in 2024 at a CAGR of 16.0% from 2019, and to US\$16.9 billion in 2030 at a CAGR of 19.1% from 2024. The chart below illustrates the historical and estimated size of China’s ophthalmic drug market in comparison with the global ophthalmic drug market:

Global and China Ophthalmic Pharmaceutical Market, 2015-2030E



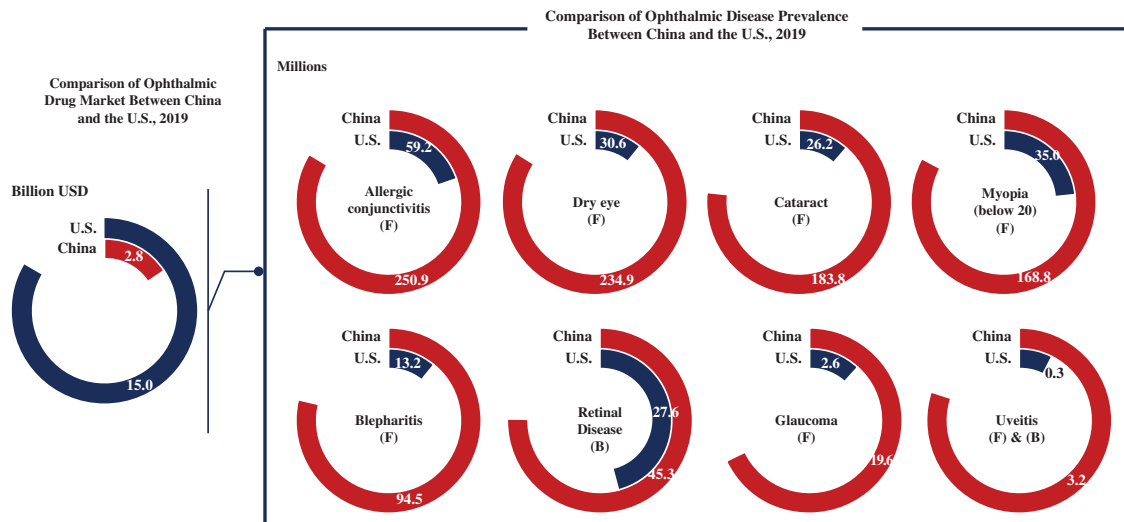
Source: Frost & Sullivan Analysis

Note: Frost & Sullivan confirms that the projection of industry performance has taken into account the COVID-19 outbreak. Patients of serious ophthalmic disease have little obstacles to obtain medicines and the COVID-19 outbreak has not materially impacted the ophthalmic drug market.

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Key Trends in the Treatment of Eye Diseases

Eye diseases refer to the conditions that affect any of the eye components such as cornea, iris, pupil, optic nerve, lens, retina, macula, choroid, conjunctiva or the vitreous. According to Frost & Sullivan, the top 10 most prevalent eye diseases in China in 2019 included refractive errors (including myopia, hyperopia, presbyopia and astigmatism), conjunctivitis, dry eye, cataract, blepharitis, retinal diseases, strabismus, amblyopia, glaucoma and uveitis. Among the top 10 eye diseases, most refractive errors (except for myopia), strabismus and amblyopia are mainly treated by corrective lenses rather than medication. The following diagram sets forth the prevalence of the major eye diseases mainly treated by medication in China and the United States. The comparison indicates that the patient populations of such major eye diseases in China were much larger than those in the United States, whereas the size of China’s ophthalmic drug market was only one-fifth of that of the United States in 2019, indicating a strong growth potential of China’s ophthalmic drug market:



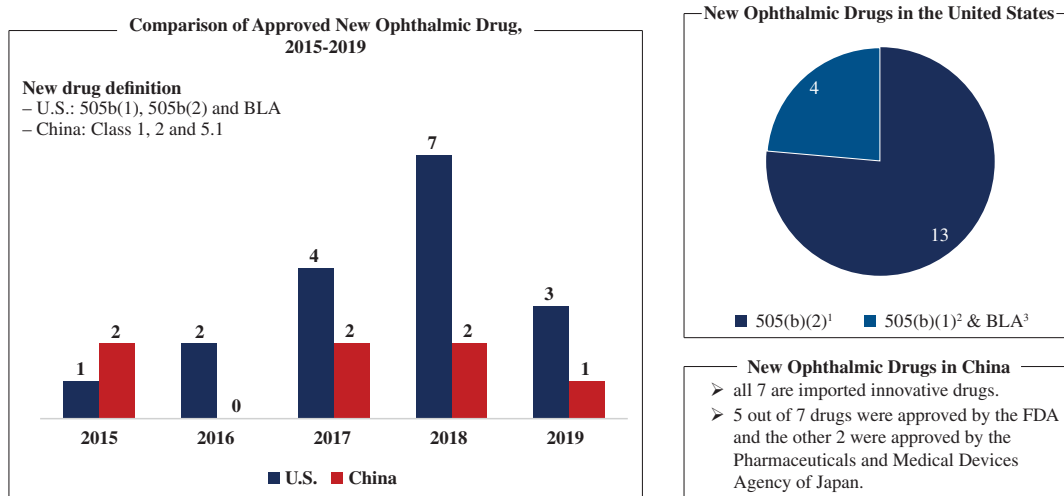
Source: Frost & Sullivan Analysis

Notes:

- (1) “F” refers to front-of-the-eye diseases; “B” refers to back-of-the-eye diseases.
- (2) Frost & Sullivan confirms that all Frost & Sullivan analyses are indicative of the latest updates and published guidelines of the American Academy of Ophthalmology. There are certain differences in the treatment guidelines in the U.S. and in China, but there are no major differences on treatment paradigm.

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Limited by the slow progress in scientific research on the pathogenesis of eye diseases and disorders, the drug discovery efforts of ophthalmic pharmaceutical companies worldwide primarily focus on developing new formulations and new dosage forms that possess advantages over currently approved drug products rather than discovering new targets or new mechanisms of action. Only seven new ophthalmic drugs have been approved in China since 2015, all of which had been developed by MNCs and approved before 2015 outside of China. By comparison, 17 new ophthalmic drugs have been approved in the United States since 2015. Among them, one was discontinued shortly after approval and six are formulation of chemical entities that have been approved and marketed in China. The remaining ten drugs are not yet available in China in any formulation. The charts below set forth details of the new ophthalmic drugs approved in China and the United States since 2015:



Source: FDA, Pharmaceuticals and Medical Devices Agency, NMPA, Frost & Sullivan Analysis

Notes:

1. An NDA submitted under 505(b)(2) is an application that contains full reports of investigations of safety and effectiveness but where at least some of the information required for approval is from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference.
2. An NDA submitted under 505(b)(1) is an application that contains full reports of investigations of safety and effectiveness.
3. A biologics license application (BLA) is an application for permission to introduce, or deliver for introduction, a biologic product into interstate commerce.

The significant unmet medical needs in ophthalmic clinical practice in China are attributable to the limited number of qualified ophthalmologists and effective medications. In 2018, there were only 30.2 ophthalmologists per million population in China, compared to 51.5 in the United States, according to Frost & Sullivan. To address these huge unmet needs, tremendous efforts have been made to train ophthalmologists and encourage new drug discovery. In addition, the PRC government is dedicated to improving access to core treatments through the health insurance programs. These measures are likely to reduce the medical costs substantially and make these drugs more affordable for eye patients.

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Key Drivers of the Ophthalmic Drug Market in China

Expanding patient pool. A large number of people in China suffer from eye diseases and disorders, and this number is expected to further grow because of an accelerating aging population, overuse of electronic screens as well as environmental pollution. Increasing prevalence of eye diseases, together with the broad disease coverage of all age groups, drives the growth of China’s ophthalmic drug market.

Increasing treatment demand. Vision impairment and the associated complications caused by eye diseases not only affect patients’ quality of life, but also impose economic and emotional burdens on their caregivers and the society. As the living standards in China continue to rise, and the public awareness of eye diseases improves, demand for better healthcare in eye diseases will keep growing in the future and drives the overall growth of China’s ophthalmic drug market.

Development of novel therapies. The research in ophthalmology has progressed steadily. Anti-VEGF biologics have been identified as effective therapies for retinal diseases and treatment options using anti-VEGF biologics have continued to expand. Topical PGAs are gradually emerging as better, safer choices for lowering IOP. Substantial advances in ophthalmic treatments are expected in the coming years and will lay the foundation for the overall market growth.

Favorable governmental policies. China has made great efforts in enhancing eye health in the past few decades. In 2016, China adopted a Five-Year National Plan for Eye Health (“十三五”全國眼健康規劃(2016-2020年)), aiming to reduce the burden of major vision-threatening eye diseases. In addition, the Chinese government promulgated a series of policies to shorten the review and approval interval for innovative drugs, which will further accelerate the development and commercialization of drugs with potential to address urgent, unmet clinical needs in the ophthalmic field. The favorable government policies will encourage the ophthalmic drug market to grow rapidly. See “Regulations—PRC Laws and Regulations—Regulation on Pharmaceutical Product Development, Approval and Registration” for details of favorable governmental policies and ongoing health care reforms.

Increasing affordability. In the past five years, the average disposable income of Chinese residents grew significantly to RMB30,733.0 in 2019. In addition, the PRC government is dedicated to improving access to core treatments through the health insurance programs. For example, the NRDL included olopatadine for allergic conjunctivitis patients in 2017, and further incorporated anti-VEGF drugs for wet AMD patients in 2017 as well. Both the increase in disposable income and the expansion of medical reimbursement coverage are expected to make ophthalmic drugs more accessible and present new opportunities for China’s ophthalmic drug market.

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Competitive Landscape of the Ophthalmic Drug Market in China

There are only a limited number of specialized and dedicated ophthalmic pharmaceutical companies in China, such as Santen, Allergan, Bausch & Lomb and Sinqi, most of which are MNCs. Only a few ophthalmic pharmaceutical companies have a drug portfolio that covers both front- and back-of-the-eye diseases. The following table sets forth a comparison of our major competitive peers and their major drug assets:

Company	Market Share 2019	Drug Assets	Chinese Name	Earliest Approval Time	Eye Indication	Addressable Patients(2019)
Company A	12.9%	Tobramycin and Dexamethasone	妥布黴素地塞米松	2013	Ocular inflammation	Blepharitis: 94.5 million Postoperative endophthalmitis prevention: 4.3 million
		Brinzolamide	布林佐胺	2014	Glaucoma	19.6 million
		Olopatadine Hydrochloride	鹽酸奧洛他定	2018	Allergic conjunctivitis	250.9 million
		Travoprost	曲伏前列素	2018	Glaucoma	19.6 million
		Ranibizumab	雷珠單抗	2011	wAMD, DME, mCNV, RVO	18.3 million
Company B	7.3%	Sodium Hyaluronate	玻璃酸鈉	2003	Dry eye	23.5 million
		Levofloxacin	左氧氟沙星	2009	Anti-infection	Bacterial Conjunctivitis: 29.4 million Postoperative endophthalmitis prevention: 4.3 million
		Ofloxacin	氧氟沙星	2007	Anti-infection	Bacterial Conjunctivitis: 29.4 million Postoperative endophthalmitis prevention: 4.3 million
		Fluorometholone	氟米龍	2007	Anti-inflammation	Blepharitis: 94.5 million Postoperative endophthalmitis prevention: 4.3 million Allergic Conjunctivitis: 250.9 million
		Brimonidine Tartrate	酒石酸溴莫尼定	1999	Glaucoma	19.6 million
Company C	3.0%	Prednisolone Acetate	醋酸潑尼松龍	2017	Ocular inflammation	Blepharitis: 94.5 million
		Bimatoprost	貝美前列素	2015	Glaucoma	19.6 million
		Deproteinized Calf Blood Extract	小牛血去蛋白提取物	2007	Anti-inflammation	Allergic Conjunctivitis: 250.9 million
Company D	2.8%	Diclofenac Sodium	雙氯芬酸鈉	1996	Anti-inflammation	Postoperative endophthalmitis prevention: 4.3 million
		Gatifloxacin	加替沙星	2009	Anti-infection	Bacterial Conjunctivitis: 29.4 million Postoperative endophthalmitis prevention: 4.3 million
		Atropine Sulfate	硫酸阿托品	2009	Iridocyclitis, Mydriatic	Refractive error: more than 900 million
		Ofloxacin	氧氟沙星	1994	Anti-infection	Bacterial Conjunctivitis: 29.4 million Postoperative endophthalmitis prevention: 4.3 million
		Sodium Hyaluronate	玻璃酸鈉	2005	Dry eye	23.5 million
Company E	1.1%	Loteprednol Etabonate	氣替潑諾	2011	Anti-inflammation	Blepharitis: 94.5 million

Source: NMPA, Frost & Sullivan Analysis

Licensing is a common business model in the ophthalmology pharmaceutical industry. Four out of seven new ophthalmic drugs approved in China since 2015 were in-licensed, according to Frost & Sullivan. In recent years, other Chinese pharmaceutical companies have in-licensed plenty of ophthalmic drugs from outside China, according to Frost & Sullivan, including, for example, Jiangsu Hengrui Medicine Co., Ltd. (SH.600276), which has in-licensed CyclASol and NOV03 from Novaliq GmbH, Arctic Vision Ltd., which has in-licensed XIPERE from Clearside Biomedical, Inc. (NASDAQ:CLSD), and Essex Bio-Technology Limited (HK.1061), which has in-licensed SkQ1 from Mitotech S.A..

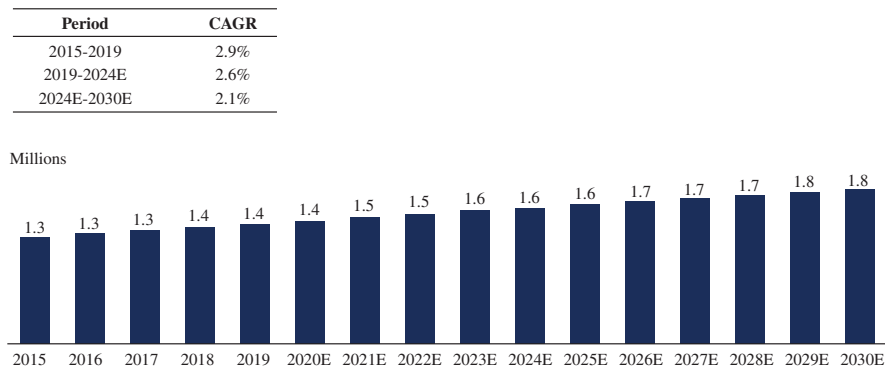
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NIPU

Uveitis is characterized by inflammation of uvea. It produces swelling and destroys eye tissues, and can lead to severe vision loss. There are four types of uveitis depending on the part of uvea that is affected, namely, anterior uveitis, intermediate uveitis, posterior uveitis and panuveitis. Uveitis affecting the posterior segment is one of the major types of eye diseases that causes permanent vision loss, especially in young adults. A retrospective study showed that the mean age of onset of blindness is 34 years old, and blindness is noted in 25.3% of the patients with posterior uveitis and panuveitis. Uveitis can also be categorized into infectious uveitis and non-infectious uveitis. Infectious uveitis is typically caused by bacteria, fungi, parasites or viruses. Non-infectious uveitis is typically caused by problems intrinsic to the eye or conditions associated with systemic autoimmune diseases. The NIPU drug market is expected to continue to grow as driven by innovations in the diagnosis and treatment of uveitis, the increasing affordability of treatments and the increase in the number of qualified practitioners.

Uveitis is one of the leading causes of blindness worldwide, particularly in young adults. The prevalence of NIPU in China grew from 1.3 million in 2015 to 1.4 million in 2019, representing a CAGR of 2.9%. It is estimated to reach 1.6 million in 2024 at a CAGR of 2.6% from 2019, and further grow to 1.8 million in 2030 at a CAGR of 2.1% from 2024. The following chart illustrates the prevalence of NIPU in China:

Prevalence of Non-infectious Uveitis Affecting Posterior Segment in China, 2015-2030E



Source: Frost & Sullivan literature review and analysis

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Treatment Paradigm and Unmet Medical Needs

Early detection and treatment of NIPU is crucial to reduce the risk of vision loss. Currently, there is no standard of care for NIPU in China. The overarching principle for NIPU treatment is to control inflammation at the back of eye. Currently, the mainstay therapy of NIPU generally includes local administration of a corticosteroid, systemic steroid administration or immuno-suppressants if there is a lack of sufficient response. The following table illustrates the comparison of different corticosteroid regimens:

	Periocular/Intravitreal administration	Corticosteroid implants ¹	Oral/Intravenous administration
Type of therapy	Local	Local	Systemic
Frequency of administration	3-4 months	Up to 3 years	Daily
Medication	Triamcinolone acetonide	Fluocinolone acetonide Dexamethasone	Prednisone
Side effects	<ul style="list-style-type: none"> • Ocular side effects • Adverse outcome of repeated injection 	<ul style="list-style-type: none"> • Ocular side effects only 	<ul style="list-style-type: none"> • Systemic side effects • Ocular side effects
Strengths	<ul style="list-style-type: none"> • High-concentration drug with greater ocular penetration • Minimal systemic side effects 	<ul style="list-style-type: none"> • Sustained control of inflammation • Avoids complications associated with repeated injection • Minimal systemic side effects 	<ul style="list-style-type: none"> • Effective when uveitis is related to systemic disease • Non-invasive for oral form
Recurrence	Most patients experience recurrence within 6 months following injection	21.8% of patients experience relapse within 6 months of follow-up	Treatment period < 6 month: ~50% patients experience relapse Treatment period ≥ 6 month: ~5% patients experience relapse

Source: Frost & Sullivan literature review and analysis, Company Information

Note:

1. Currently, no corticosteroid implants indicated for chronic NIU-PS have been approved by the NMPA. Information regarding corticosteroid implants is based in YUTIQ clinical data from FDA-approved label.

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The high rate of recurrence and chronicity of uveitis make the treatment for this disease expensive. The increasing affordability has a positive impact on patients’ willingness for treatment. Particularly, patients are more willing to try novel and efficacious therapies. Local therapy with steroid implants are gaining popularity in the long-term management of posterior uveitis. Globally, there are only three marketed steroid implants indicated for chronic NIU-PS. None of these implants are currently available for uveitis patients in China. OT-401 is the only steroid implant being evaluated under a Phase III clinical trial in China. The following table illustrates a comparison of globally marketed steroid implants:

	Company	FDA Approval Time	Compound	Implantation procedure	Indicated population	Duration of action	Endpoint in clinical study	Treatment Effect (represented by recurrence rates)
OT-401	OcuMension/ Eyepoint	2018	Fluocinolone acetonide 0.18 mg	Preloaded needle applicator that can be administered in the physician’s office	Patients aged 18 and older, with chronic noninfectious uveitis affecting posterior segment of the eye	36 months	Recurrence in the study eye within 6 months following implantation	OT-401 (21.8%); Sham (53.8%)
Retisert	Bausch & Lomb	2005	Fluocinolone acetonide 0.59 mg	Implanted via pars plana incision and secured by a suture in the sclera in an operating room setting	Patients aged 7 and older, with chronic recurrent non-infectious posterior uveitis	30 months	Recurrence of uveitis in the study eye within 34 weeks following implantation	Retisert (14%); Sham (40%)
Ozurdex	Allergan	2009	Dexamethasone 0.7 mg	Given intravitreally via injector in an office-based procedure	Patients aged 18 and older, with noninfectious intermediate or posterior uveitis	6 months	Proportion of patients with vitreous haze score of 0 (no inflammation) at week 8	Ozurdex (53%); Sham (88%)

Source: Frost & Sullivan literature review and analysis, Company Information

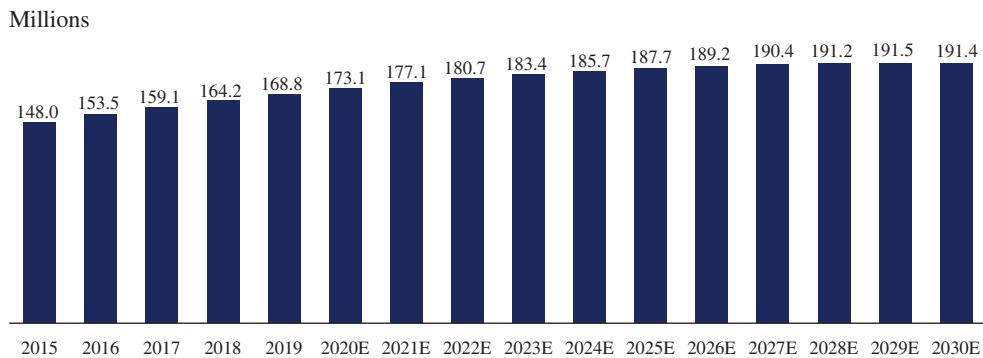
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MYOPIA

Myopia is a vision condition in which close objects are seen clearly, but objects farther away appear blurred. Myopia is usually caused by an elongation of the eyeball, causing the image to be focused in front of the retina. The prevalence of myopia in children and adolescents in China grew from 148.0 million in 2015 to 168.8 million in 2019, representing a CAGR of 3.3%. It is estimated to further grow to 185.7 million in 2024 at a CAGR of 1.9% from 2019, and 191.4 million in 2030 at a CAGR of 0.5% from 2024. The myopia drug market is expected to continue to grow as driven by the large patient population and the proven efficacy of myopia medication. The chart below illustrates the prevalence of myopia in population aged below 20 in China:

Prevalence of Myopia in Population Aged below 20 in China, 2015-2030E

Period	CAGR
2015-2019	3.3%
2019-2024E	1.9%
2024E-2030E	0.5%

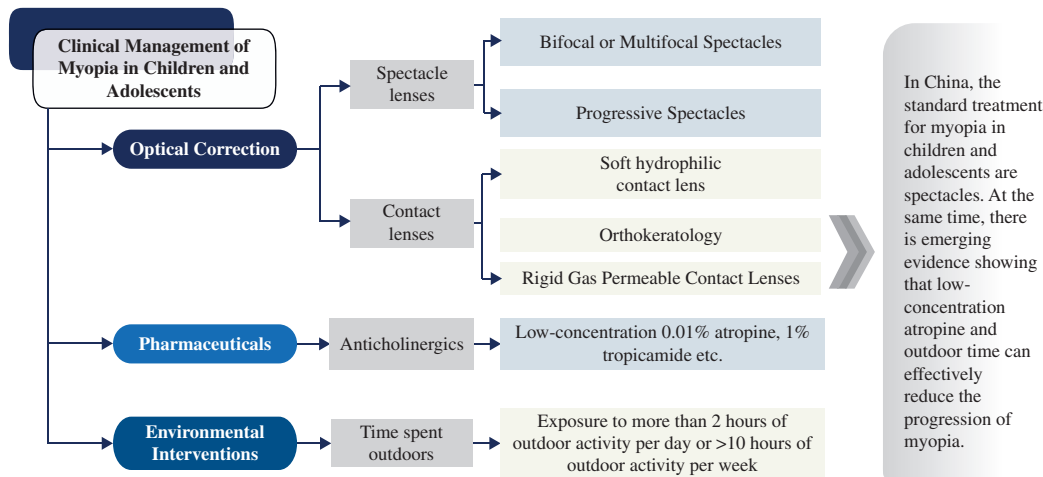


Source: Frost & Sullivan literature review and analysis

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Treatment Paradigm and Unmet Medical Needs

Myopia tends to progress rapidly between the ages of 5 and 15, and usually stabilizes by the end of one’s early 20s. Therefore, prevention or control of the progression of myopia is critical for children and adolescents. Current treatments include (i) optical correction, including spectacle lenses and contact lenses; (ii) use of antimuscarinic eye drops; and (iii) exposure to outdoor activities:



Source: Frost & Sullivan literature review and analysis

While corrective lenses remain the mainstay of vision correction in myopic children and adolescents, its effect in delaying the progression of myopia is limited. Compared to corrective lenses and contact lenses, atropine leads to considerable reduction in myopia progression in terms of refraction change and axial change. The following table sets forth a comparison of corrective lenses and contact lenses and atropine in slowing progression of myopia:

	Subtypes	Mean difference in refraction change, D/yr	Mean difference in axial change, mm/yr	Shortcomings	Strengths
Corrective lenses	Bifocal corrective lenses	0.26	-0.08	<ul style="list-style-type: none"> Distort vision at the edge of the lens if astigmatism exists 	<ul style="list-style-type: none"> Large field of view Less chromatic aberrations High affordability
	Progressive spectacles	0.17	-0.05		
Contact lenses	Soft hydrophilic contact lens	0.06	-0.01	<ul style="list-style-type: none"> Children are less likely to follow hygiene and safety practice May induce problems related to cornea, eyelid and dryness of the eye Relatively expensive 	<ul style="list-style-type: none"> More natural vision compared to glasses Cosmetically acceptable, more easily handled, and more convenient for daily activities
	Orthokeratology	-	-0.15		
	Rigid Gas Permeable Contact Lenses	-0.03	0.02		
Atropine eye drops	High-concentration (1% or 0.5%)	0.68	-0.22	<ul style="list-style-type: none"> Long term high-concentration atropine use may have potential risks including, local allergic and systemic reactions Possible myopic rebound if atropine is stopped suddenly 	<ul style="list-style-type: none"> Clear effects in myopia control, better outcome than corrective lenses and contact lenses
	Moderate-dose (0.1%)	0.53	-0.22		
	Low-concentration (0.01%)	0.53	-0.15		

Source: Frost & Sullivan literature review and analysis

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Note: For all comparisons, the stated values represent the differences in final refraction or axial elongation between the stated intervention and the single vision corrective lenses. In terms of refractive error, a positive indicates that the stated intervention is better. In terms of axial length, a negative indicates the first intervention is better.

Anticholinergic drugs are one of the few effective drugs in myopia control. Although anticholinergic agents have been extensively studied in scientific research, there are only two pharmaceutical agents approved by the NMPA around 30 years ago for use as myopia treatments, namely tropicamide eye drops and raceanisodamine eye drops.

Among ophthalmic anticholinergics, low-concentration atropine is found to have a reliable effect in slowing myopia progression and a good safety profile. In addition, atropine is the only anticholinergic recommended in Appropriate Technical Guidelines for Prevention and Control of Myopia in Children and Adolescents (兒童青少年近視防控適宜技術指南). It has emerged as the most promising myopia-control eye drops. High-concentration (0.5-1%) atropine has been shown to be effective in reducing myopia progression but also proved to have more occurrences of adverse effects. Low-concentration (0.01%) atropine can also effectively control myopia progression, with significantly fewer adverse effects compared to high-concentration atropine. The instability of low-concentration atropine solutions has long been a technical barrier. At 25°C and neutral pH, 0.01% atropine remains stable for only 2-8 weeks, which limited its usage in myopia treatment. Globally, there are a total of four clinical trials investigating the efficacy of atropine for myopia control. Three of them have reached Phase III clinical trial stage. The following table sets forth a comparison between the four clinical-stage drugs and OT-101:

Drug Code/ Name	Sponsor	Age Group	Clinical Phase	Regulatory Authority	First Posted Date
NVK-002	Nevakar , LLC	3 - 17 years	III	FDA	2017/11/22
SYD-101	Sydnexis , Inc.	3 - 14 years	III	FDA	2019/4/18
Atropine 0.01% Ophthalmic Solution	Eyenovia Inc.	3 - 12 years	III	FDA	2019/5/8
Atropine 0.01% Eye Drop	Sinqi	6 – 12 years	III	NMPA	2020/05/27
DE-127 Ophthalmic Solution	Santen Pharmaceutical Co., Ltd.	6 - 11 years	II	Singapore HSA	2017/11/6
OT-101	Ocumension	5 -14 years	Pre -clinical	-	N/A

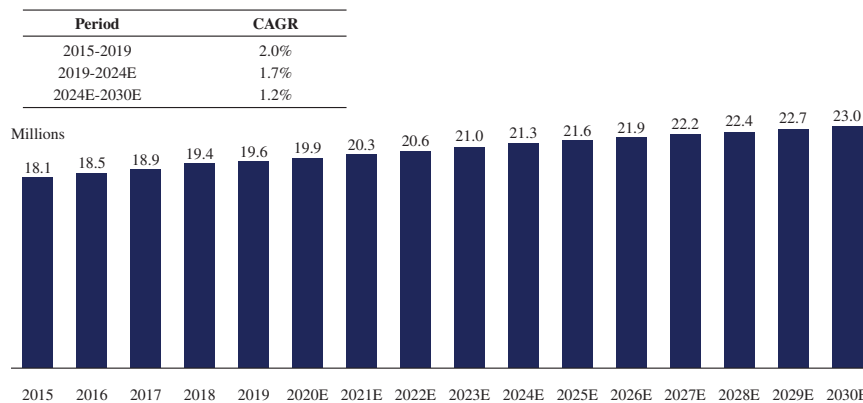
Source: NMPA, FDA, Frost & Sullivan Analysis

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GLAUCOMA

Glaucoma is a group of degenerative diseases due to elevated IOP, which damages the optic nerve and leads to vision loss and eventually blindness if not treated. Glaucoma is the second-leading cause of irreversible blindness worldwide. The prevalence of glaucoma in China increased from 18.1 million in 2015 to 19.6 million in 2019, representing a CAGR of 2.0%. It is estimated to further increase to 21.3 million in 2024 at a CAGR of 1.7% from 2019, and 23.0 million in 2030 at a CAGR of 1.2% from 2024. The glaucoma drug market is expected to continue to grow as driven by the aging population and improvements in diagnostic technology. The following chart illustrates the prevalence of glaucoma in China:

Prevalence of Glaucoma in China, 2015-2030E



Source: Frost & Sullivan literature review and analysis

Glaucoma can be primarily divided into two types, open-angle glaucoma and angle-closure glaucoma, based on whether the anterior chamber angle, which is where the majority of ocular fluid outflow, is open or closed. In contrast to angle-closure glaucoma where patients experience obvious symptoms and signs, individuals with open-angle glaucoma rarely experience symptoms. Thus, open-angle glaucoma is poorly diagnosed and generally detected incidentally during comprehensive ophthalmic examination or at a relatively late stage where the risk of irreversible visual loss is high. Of the 19.6 million patients with glaucoma in China in 2019, 43.9% had open-angle glaucoma and 56.1% had angle-closure glaucoma.

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Treatment Paradigm and Unmet Medical Needs of Glaucoma

The dominant approaches to treating glaucoma encompass pharmacologic therapy, laser therapy and conventional surgery. The ultimate goal of glaucoma treatment is to preserve enough vision during the patient’s lifetime to meet functional needs. Treatment typically aims to delay, stop and ideally reverse the damage to the optic nerve and ganglion cell layer. The only way proven to slow or stop damage from progressing is to reduce IOP to be below the level that will cause continued damage to the optic nerve. Therefore, the overarching principle in many glaucoma treatment guidelines is to reduce IOP to a target level.

Among different types of glaucoma drugs, topical PGAs are considered the mainstream treatments due to their efficacy and safety in lowering IOP. Below is a comparison of common IOP-lowering agents:

	IOP Reduction (%)	Frequency	Adverse Effects	Strengths
Prostaglandin (PGAs)	-25.0-33.0%	Once per day	<ul style="list-style-type: none"> Blurred vision, increased pigmentation of eye color, or irritation of eye. 	<ul style="list-style-type: none"> Strong IOP lowering effect Minimal side effects Less diurnal IOP variation Preferred dosage scheme
Beta-adrenergic antagonists (beta-blockers)	-20.0-25.0%	Once or twice per day	<ul style="list-style-type: none"> Blurred vision, a burning or stinging in the eye. Adverse side effects in individuals with heart problems, lung problems, depression. 	<ul style="list-style-type: none"> Potential neuroprotective effect
Alpha adrenergic agonists	-20.0-25.0%	Three times per day	<ul style="list-style-type: none"> Higher likelihood of allergic reactions Systemic side effects including somnolence and fatigue 	<ul style="list-style-type: none"> Protecting cardio-pulmonary function
Topical carbonic anhydrase inhibitors (CAIs)	-15.0-20.0%	Four times per day when monotherapy, or twice per day as an adjunctive treatment	<ul style="list-style-type: none"> Burning/stinging on instillation, ocular hyperemia, and discharge 	<ul style="list-style-type: none"> Few systemic adverse effects
Cholinergic agonists	-20.0-25.0%	Three times per day when monotherapy, or twice per day as adjunctive treatment	<ul style="list-style-type: none"> Brow-ache, dim vision, blurred vision and headache May cause uveitis and pupil reduction 	<ul style="list-style-type: none"> Relatively inexpensive Comparable IOP-lowering outcome as PGAs

Source: Primary Open-Angle Glaucoma Preferred Practice Pattern, Frost & Sullivan Analysis

Note: These clinical data are collected from different medical publications, not head-to-head research. As a result, these data are only for reference and may not be directly comparable.

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Currently marketed PGA drugs in China include PGA monotherapy eye drops and fixed-dose combination PGA eye drops. The PGA monotherapy eye drops are composed of one type of PGA, while the fixed-dose combination PGA eye drops combine PGAs and other active ingredients in a single dosage form. Fixed-dose combination PGA eye drops usually result in more adverse effects than PGA monotherapy eye drops and have potential teratogenic risks. Under medical guidelines, the PGA monotherapy eye drops are recommended as first-line therapy, the fixed-combination eye drops are only used in patients with progression or who have failed to achieve the target IOP. The following table sets forth a summary of competing PGA eye drops approved by the NMPA:

Generic Name	Representative Product		Number of Other Manufacturers	Earliest NMPA Approval Time	NRDL Inclusion ⁽¹⁾	Price ⁽²⁾ per ml (RMB)
	Trade Name	Manufacturer				
PGA Monotherapy Eye Drops						
Latanoprost	Xalatan®	輝瑞/Pfizer	5	1999	√	53.3
Travoprost	Travatan®	諾華/Novartis	1	2004	√	67.3
Bimatoprost	Lumigan®	艾爾建/Allergan	0	2005	√	47.6
Tafluprost	Tapros®	參天/Santen	0	2015	√	29.9
Fixed-dose Combination PGA Eye Drops						
Latanoprost/Timolol Maleate	Xalacom®	輝瑞/Pfizer	1	2008	×	78.1
Bimatoprost/Timolol Maleate	Ganfort®	艾爾建/Allergan	0	2013	×	50.0
Travoprost/Timolol Maleate	DuoTrav®	諾華/Novartis	0	2014	×	74.3

Source: NMPA, Frost & Sullivan Analysis

Note:

- (1) Refers to the 2020 NRDL which is currently in effect.
- (2) Refers to the hospital procurement price.

Comparison between OT-301 and Other PGA Monotherapy Eye Drops

Compared to other current PGA monotherapy eye drops, OT-301 employs a dual mechanism of action, which allows activation of both the primary and secondary aqueous humor outflows of the eye, leading to a greater IOP-lowering effect for the treatment of glaucoma. It adds NO-mediated efficacy to bimatoprost, which is marketed under the brand name LUMIGAN and considered the most efficacious PGA among those approved to date, according to Frost & Sullivan. In OT-301’s completed Phase II clinical trial, it demonstrated

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both statistically significant non-inferiority for the primary endpoint and superiority for a secondary endpoint over latanoprost (0.005% concentration), the most widely prescribed first-line therapy for glaucoma and ocular hypertension in China, with greater IOP reduction. The table below illustrates a comparison of OT-301 and other PGAs:

	OT-301	VYZULTA (Latanoprostene Bunod 0.024%)	Lumigan (Bimatoprost 0.01%)	Travatan Z (Travoprost 0.004%)	XALATAN (Latanoprost 0.005%)	TAPROS (Tafuprost 0.0015%)
Reduction in Mean IOP	7.6-9.8 mmHg	7.0-9.0 mmHg	≤7.5 mmHg	7.0-8.0 mmHg	6.0-8.0 mmHg	6.0-8.0 mmHg
Patient Mean Baseline IOP	26.8 mmHg	26.7 mmHg	23.5 mmHg	25.0-27.0 mmHg	24.0-25.0 mmHg	23.0-26.0 mmHg
Typical Adverse Events (Incidence ≥5%)	Conjunctival hyperemia (16.8%)	Conjunctival hyperemia (6%)	Conjunctival hyperemia (25%-45%); ocular pruritus (>10%)	Conjunctival hyperemia (30%-50%); decreased visual acuity, foreign body sensation, pain and pruritus (5%-10%)	Blurred vision, burning and stinging, conjunctival hyperemia, foreign body sensation, increased pigmentation of the iris, punctate epithelial keratopathy (5-15%)	Conjunctival hyperemia(4%-20%); ocular stinging and irritation (7%); allergic conjunctivitis (5%)

Source: FDA, Company Information, Frost & Sullivan Analysis

Note: These clinical data are collected from different medical publications, not head-to-head research. As a result, these data are only for reference and may not be directly comparable.

There are only two registered clinical trials for PGAs targeting the glaucoma indication in China. The only indication under Phase III investigation is a fixed-dose combination PGA eye drop, and the other Phase I medication developed by Sinqi is a conventional monotherapy PGA:

Drug Code	Sponsor	Clinical Phase	Regulatory Authority	Initial Publication Date ⁽¹⁾
Fixed-dose Combination PGA Eye Drops				
DE-111A Eye Drops (Tafuprost/timolol maleate)	Santen Pharmaceutical	III	NMPA	2018/11/26
PGA Monotherapy Eye Drops				
Latanoprost Eye Gel	Sinqi Pharmaceutical	I	NMPA	2014/04/02

Source: CDE, Frost & Sullivan Analysis

Note:

(1) Refers to the date on which the information of the respective clinical trial is published for the first time.

Carbonic anhydrase inhibitors, or CAIs, and hyperosmotic agents are the most commonly used drugs prior to surgery to prevent glaucoma due to their marked IOP reduction effect. Both options have a series of systemic side effects and hyperosmotic agents are especially dangerous for patients with predisposing cardiopulmonary risks. Currently, only two systemic CAIs,

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acetazolamide and methazolamide, have been approved by the NMPA and included in the NRDL. Both approved CAIs are in the form of orally administered tablets. There are no injectable systemic CAIs at clinical phase.

Generic Name	Representative Product		Number of Other Manufacturers	Earliest NMPA Approval Time	NRDL Inclusion	Price per Tablet (RMB)
	Trade Name	Manufacturer				
Systemic CAIs Tablets						
Acetazolamide	N.A.	天津力生製藥/ Tianjin Lisheng Pharmaceutical	11	1983	√	0.04
Methazolamide	尼目克司/ NiMuKeSi®	杭州澳醫保靈藥業/ Hangzhou Aoyi Baoling Pharmaceutical	0	2000	√	0.06

Source: NMPA, Frost & Sullivan Analysis

Comparison between Competing Brimonidine Tartrate Eye Drops

Brimonidine tartrate eye drop is indicated for the treatment of open-angle glaucoma and ocular hypertension. Brimonidine tartrate is an alpha-2 adrenergic receptor agonist, which may lower intraocular pressure by reducing aqueous humor formation and enhancing uveoscleral outflow. The following table sets forth a comparison between our brimonidine tartrate eye drops and competing brimonidine tartrate eye drops marketed in China:

Category	Representative Product		Number of Other Manufacturers	Earliest NMPA Approval Time	NRDL Inclusion	Bidding Price of per ml (RMB)	
	Brand Name	Manufacturer					
0.15%	5ml:7.5mg	阿法根 /Alphagan	艾爾建/Allergan	0	2009	√	14.6
	10ml:15mg	阿法根 /Alphagan	艾爾建/Allergan	0	2009	√	x
0.2%	5ml:10mg	阿法根 /Alphagan	艾爾建/Allergan	3	2005	√	6.9
		-	匯恩蘭德 /Huonland		2016	√	

Source: NMPA, Frost & Sullivan Analysis

OT-302

OT-302 is an acetazolamide injection for the treatment of chronic glaucoma and for reducing high IOP after glaucoma and other intraocular surgeries. As an intravenous dosage, OT-302 has similar IOP-lowering outcome as typical oral dosage while it has shorter onset time and can lower IOP immediately after administration.

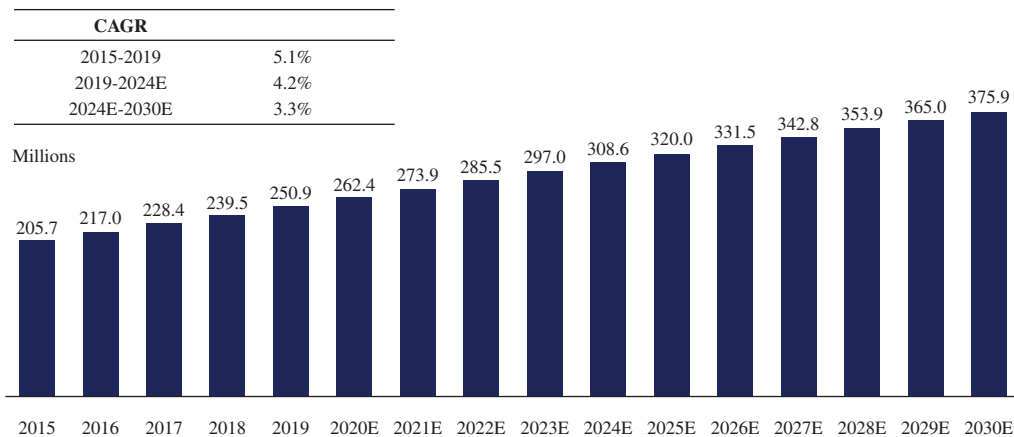
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ALLERGIC CONJUNCTIVITIS

Allergic conjunctivitis occurs when an allergic reaction causes conjunctivitis. It is part of a larger systemic atopic reaction and is usually seasonal with associated upper respiratory tract symptoms and complaints of redness and swelling of the conjunctiva with severe itching and increased lacrimation. The drug market for allergic conjunctivitis is expected to continue to grow, as people have more exposure to allergens due to pet keeping, outing and increased pollution.

The number of allergic conjunctivitis patients in China increased from 205.7 million in 2015 to 250.9 million in 2019, representing a CAGR of 5.1%. It is estimated to reach 308.6 million in 2024 at a CAGR of 4.2% from 2019, and 375.9 million in 2030 at a CAGR of 3.3% from 2024. The following chart sets forth the prevalence of allergic conjunctivitis in China:

China Prevalence of Allergic Conjunctivitis, 2015-2030E



Source: Frost & Sullivan Analysis

Treatment Paradigm and Unmet Medical Needs

Comparison between OT-1001 and Competing Eye Drops for Allergic Conjunctivitis

The treatment principles of allergic conjunctivitis include removing allergens and alleviating symptoms and signs. Due to the limited number of allergic conjunctivitis therapy choices and the lack of potent drugs with long-term safety, it is urgent to discover and develop a wider variety of effective therapies. Currently, mainstream primary therapies of allergic conjunctivitis involve the use of anti-allergic therapeutic agents such as antihistamines,

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multiple-action anti-allergic agents and mast cell stabilizers. Most primary therapies are topical use eye drops. The following table sets forth a comparison of marketed primary eye drops for allergic conjunctivitis in China:

Category	Generic Name	Dosage	NRDL Inclusion	Itching Score Change (3 min post-CAC, placebo baseline)	Age Group	Onset time	Duration time	Price per ml (RMB)
Antihistamines	Cetirizine ¹	1 drop in each affected eye twice daily	x	-1.38	≥2 years old	15 minutes	8 hours	N/A
	Emedastine	1 drop each affected eye up to 4 times daily	√	-1.3	≥3 years old	30 minutes	4 to 8 hours	5.9
Mast cell stabilizers	Pemirolast	1 or 2 drops in each affected eye 4 times daily	x	-1.3	≥3 years old	N.A.	N.A.	4.1
	Cromoglycate	1 drop each affected eye 4 to 6 times daily	√	N.A.	≥4 years old	2 to 3 days	N.A.	1.3
Multiple-action agents	Ketotifen	1 drop every 8 to 12 hours	√	-1.43	≥3 years old	15 minutes	8 to 12 hours	1.4
	Olopatadine	1 drop in each eye twice daily at an interval of 6 to 8 hours	√	-1.43	≥3 years old	<30 minutes	8 hours	17.3
	Azelastine	1 drop each affected eye twice daily	√	-0.85	≥4 years old	3 minutes	8 hours	6.9

Source: Frost & Sullivan literature review and analysis

Note: These clinical data are collected from different medical publications, not head-to-head research. As a result, these data are only for reference and may not be directly comparable.

1. Cetirizine ophthalmic solution, or OT-1001 (ZERVIATE), was approved by the FDA in 2017, and has not been approved in China yet.

The first generation antihistamines are rarely used in clinical practice at present due to the adverse effects that may be caused. Compared with the first-generation antihistamines, the second-generation antihistamines such as cetirizine have the advantages of wider patient coverage, less frequent dosing, shorter onset time, longer duration time and lower AE rate. In contrast, mast cell stabilizers, another group of drugs for allergic conjunctivitis, have longer onset time and only have controlling, but not curative, effects. The following table sets forth a comparison of the first generation and second generation of antihistamines:

	1st generation	2nd generation	Advantages of 2nd generation
Representative drugs	Brompheniramine, diphenhydramine, ketotifen, etc.	Cetirizine, emedastine, azelastine, olopatadine, etc.	Less sedation
Pharmacokinetics	Short half-life, more frequent of administration and large dosage	Most of them are long-acting sustained-release preparations, less frequent of administration and small dosage	Fewer anticholinergic effects
Blood brain permeability	Easy to cross the blood-brain barrier due to lipophilic drugs Produces CNS inhibition	Hard to cross the blood-brain barrier CNS inhibition is not obvious	Less frequent administration
Specificity	Poor H1 receptor selectivity Weak anti-choline and anti-α receptor blockers	Strong H1 receptor selectivity Barely anti-choline and anti-α receptor blockers	Improved adverse effect profile

Source: Frost & Sullivan literature review and analysis

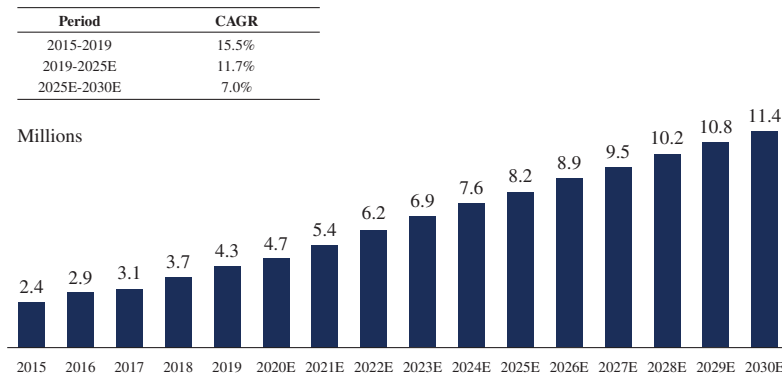
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POSTOPERATIVE INFLAMMATION

Postoperative endophthalmitis is a severe infection involving both the anterior and posterior segments of the eye following intraocular surgery. Postoperative endophthalmitis following cataract surgery is presumed to be caused by bacteria, fungi or, on rare occasions, parasites that enter the eye during the perioperative period. Symptoms of endophthalmitis following cataract surgery vary slightly. Their symptoms depend on whether the infection occurs early (six weeks or less) or late (months or years) after surgery. Early symptoms include a dramatic decrease in vision in the affected eye, eye pain that worsens after surgery, red eyes and swollen eyelids. Late symptoms tend to be milder than early symptoms, which include blurred vision, increased sensitivity to bright light and mild eye pain. The postoperative inflammation drug market, especially, the drug market for inflammations post cataract surgery, is expected to continue to grow as the cataract surgery rate continues to rise and the access to cataract treatment continues to improve.

The total number of patients receiving cataract surgery in China increased from 2.4 million in 2015 to 4.3 million in 2019, representing a CAGR of 15.5%. A large number of such patients have postoperative inflammation following the cataract surgery. Compared to developed countries, postoperative endophthalmitis incident rates in China remain high, especially in small or mid-sized hospitals. Once post-cataract endophthalmitis occurs, 50% of eyes recover with 20/40 vision and 10% are left with no useful vision (5/200 or less). The following chart illustrates the cataract surgery volume in China:

Cataract Surgery Volume in China, 2015-2030E



Source: Frost & Sullivan literature review and analysis

Treatment Paradigm and Unmet Medical Needs

Due to the high rate of blindness of post-operative endophthalmitis, preventive approaches during the operation are of paramount significance. Typical methods to reduce risk of endophthalmitis include placing povidone-iodine to the affected area before surgery, pre-operative and postoperative use of antibiotics and anti-inflammatory agents, and intracameral administration of antibiotics at the conclusion of surgery.

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Fluoroquinolones and aminoglycosides are two topical antibiotic categories that are recommended by medical guidelines for post-operative endophthalmitis prevention. Fluoroquinolones generally have better corneal penetration and broader spectrum coverage, and are more effective in inhibiting postoperative endophthalmitis. Commercially available drugs indicated for postoperative endophthalmitis prevention in China include fluoroquinolone eye drops and aminoglycoside eye drops. The third- and fourth-generation fluoroquinolones are widely used in clinical practice and are preferred over aminoglycosides. The following table illustrates the marketed drugs indicated for postoperative endophthalmitis in China:

Generic Name	Representative Product		Number of Other Manufacturers	Earliest NMPA Approval Time	NRDL Inclusion	Price per Unit (RMB)
	Trade Name	Manufacturer				
Fluoroquinolones Eye Drops						
3rd generation fluoroquinolones	Levofloxacin	Cravit® 参天/Santen	19	2004	√	6.1
4th generation fluoroquinolones	Gatifloxacin	Zhuning® 安徽雙科藥業/Anhui Shuangke Pharmaceutical	8	2005	√	3.1
	Moxifloxacin hydrochloride	Vigamox® 諾華/Novartis	0	2018	√	10.2
Aminoglycosides Eye Drops						
Tobramycin	Tobrex®	諾華/Novartis	31	1999	√	1.0
Tobramycin / Dexamethasone	Tobradex®	諾華/Novartis	8	2001	√	2.4

Source: NMPA, Frost & Sullivan Analysis

Though members of the fourth-generation fluoroquinolones appear to possess similar spectrum of bactericidal activity, the intraocular penetration properties of moxifloxacin and gatifloxacin differ. Compared to gatifloxacin, moxifloxacin has higher concentration in different intraocular sites and thereby has favorable penetration characteristics, which makes it an ideal candidate for ophthalmic indications. Below is a comparison of moxifloxacin and gatifloxacin:

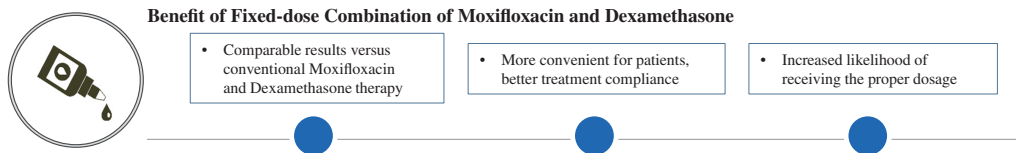
	Intraocular penetration of instilled topical Moxifloxacin and Gatifloxacin		
	Cornea (µg/g)	Aqueous humor (µg/g)	Conjunctiva (µg/g)
Moxifloxacin (0.5%)	12.23 ± 5.33	2.677 ± 1.094	3.15 ± 1.60
Gatifloxacin (0.3%)	6.32 ± 2.47	1.112 ± 0.438	1.84 ± 0.94

Source: Frost & Sullivan literature review and analysis

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The topical antibiotics plus corticosteroids eye drops protocol is credited with keeping infectious and inflammatory complications at their current low rate. Compared to the conventional, separately dosed moxifloxacin and dexamethasone treatment, single-vehicle, fixed-dose combination moxifloxacin/dexamethasone formulation is found to be therapeutically equivalent. In addition, the fixed-dose combination can help patients to receive proper dosage and improve medication adherence. The following chart illustrates the benefit of fixed-dose combination of moxifloxacin and dexamethasone:

	0.5% Moxifloxacin /0.1% Dexamethasone fixed-dose Combination	Conventional 0.5% Moxifloxacin + 0.1% Dexamethasone Therapy
The clinical outcome was evaluated at Day 15		
Ocular pain	0.0%	1.6%
Sign of active ocular Inflammation (redness, edema, tearing, or discharge)	0.0%	1.6%
Number of cells per field in the anterior chamber (>5 cells)	3.1%	3.3%



Source: Frost & Sullivan literature review and analysis

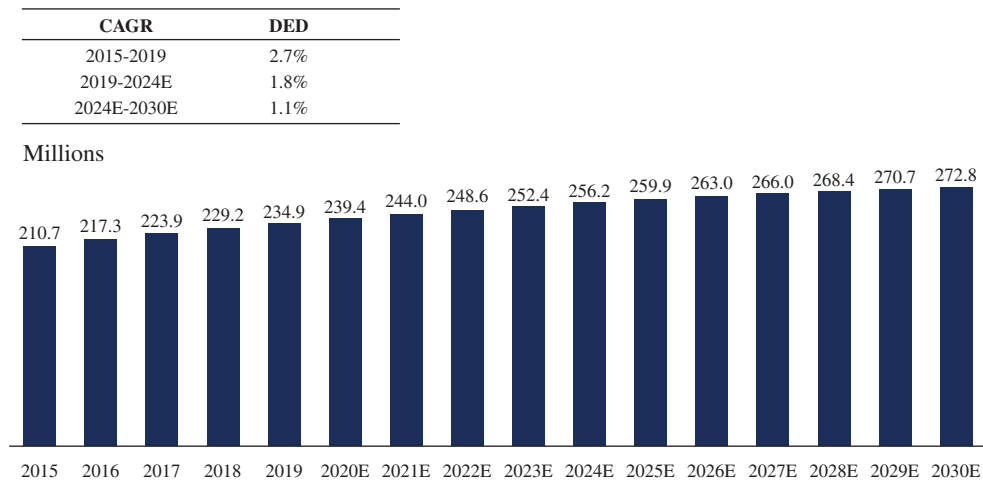
Antibiotic eye drops is a complicated treatment regimen, requiring up to 70 eye drops over three to four weeks on a tapered dosing schedule. Further, cataract surgery patients are often elderly and can have compromised cognitive function, osteoarthritis in their hands and poor eyesight due to the cataract surgery. These complexities can lead to poor compliance due to failure to administer eye drops according to the prescribed schedule, or administering an eye drop but failing to have it go into the eye, and/or not finishing the treatment regimen. Sustained-release intraocular injection has been developed to reduce inconvenience and non-compliance caused by the complicated treatment regimen currently available. OT-502 is a 9% dexamethasone intraocular suspension administered as a single dose into the surgical site at the conclusion of the cataract surgery. It provides a constant release of dexamethasone to control postoperative inflammation. The major benefits of OT-502 include improvement in patient compliance and proper dosing.

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DRY EYE

Dry eye is characterized by inflammation of the ocular surface epithelia due to reduced tear quantity and ocular surface sensitivity. Dry eye has become a common eye condition in modern society. The number of dry eye patients in China grew from 210.7 million in 2015 to 234.9 million in 2019, representing a CAGR of 2.7%. It is estimated that the number may increase to 256.2 million in 2024 at a CAGR of 1.8% from 2019, and 272.8 million in 2030 at a CAGR of 1.1% from 2024. The chart below sets forth the prevalence of dry eye in China:

China Prevalence of Dry Eye Disease, 2015-2030E



Source: Frost & Sullivan literature review and analysis

Treatment Paradigm and Unmet Medical Needs

Treatment options for dry eye mainly include artificial tears and anti-inflammatory drugs. Artificial tears are the first-line therapy, especially for mild dry eye. Although artificial tears relieve symptoms, they cannot cure dry eye. For the treatment of moderate and severe dry eye, artificial tears need to be combined with anti-inflammatory drugs, which address the underlying cause of dry eye, the inflammation of the cornea and conjunctiva.

Artificial Tears

Artificial tears increase tear volume, minimize desiccation and lubricate the ocular surface, thus providing temporary relief of irritation symptoms and reducing the eye surface reaction related to high osmotic pressure of tears. Low viscosity artificial tears are thin and watery, providing quick relief with little or no blurring of vision, but their lubrication effect is short-lived. In contrast, high viscosity artificial tears are more gel-like and can provide longer lubrication. Low viscosity artificial tears are suitable for mild dry eye patients, while moderate to severe dry eye patients benefit more from high viscosity artificial tears. For those patients

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with severe eye surface inflammation and abnormal tear dynamics, or need long term or high frequency use (more than six times daily) of artificial tears, artificial tears without preservatives or with less preservative toxicity are preferred.

Category	Agents	Characteristics	Function
Low viscosity	Polyols	Hydrophilia	<ul style="list-style-type: none"> Increases viscosity Forms protective layer over mucous membrane to relieve irritation
	Polyvinyl alcohol (PVA)	Hydrophilia Film-formation	<ul style="list-style-type: none"> Lowers tear viscosity
High viscosity	Hyaluronic Acid	Hydrophilia Film-formation	<ul style="list-style-type: none"> Binds multiples of its weight in water and lowers tear osmolarity Adheres to ocular surface Stabilizes and evens out the tear film Highly viscous until blink thins it out
	Cellulose derivatives	Hydrophilia Film-formation	<ul style="list-style-type: none"> Cross links upon contact with tear film due to pH difference to increase viscosity Stabilize emulsions
	Oil-based emulsions (mineral and castor oil)	Film-formation	<ul style="list-style-type: none"> Replace or thicken lipid layer to increase tear stability and reduce tear evaporation

Hyaluronic acid has the advantages of high viscosity, dual characteristics of hydrophilia and film-formation, and the function of accelerating corneal wound healing.

Source: Frost & Sullivan Analysis

Comparison between Ou Qin and Competing Hyaluronic Acid Artificial Tears

Hyaluronic acid artificial tears are a high viscosity artificial tears. Currently, there are a total of 18 manufacturers of 22 registered hyaluronic acid artificial tear eye drops:

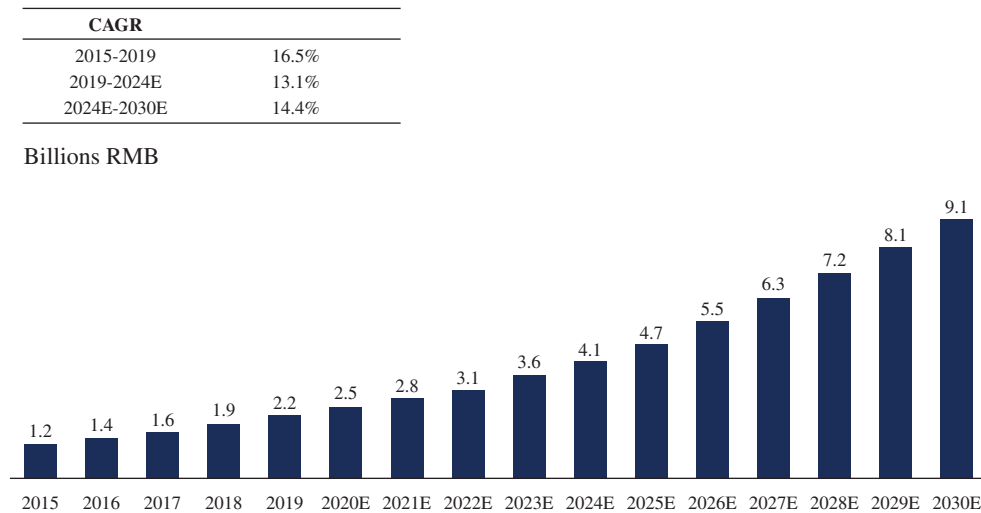
Specification	Representative Product		Number of Other Manufacturers	Earliest NMPA Approval Time	NRDL Inclusion	Price per ml (RMB)
	Brand Name	Manufacturer				
Hyaluronic Acid						
0.1% Mono-dosage	0.4ml	愛麗/Hialid 參天/Santen	3	2003	√	8.6
	0.8ml	潤麗/Run li 博士倫/ Bausch & Lomb	0	2005	√	4.7
0.1% Multi-dosage	5ml	愛麗/Hialid 參天/Santen	11	2000	√	4.5
	7ml	聯邦亮晶晶/ Liangjingjing 珠海聯邦製藥/ United Laboratories	0	2004	√	6.9
	10ml	海露/Hycosan URSAPHARM	0	2003	√	5.7
0.3% Mono-dosage	0.4ml	愛麗/Hialid 參天/Santen	2	2000	√	12.2
	0.8ml	歐沁/Ou Qin 匯恩蘭德/歐康維視 Huonland/OcuMension	0	2019	√	10.0
0.3% Multi-dosage	5ml	愛麗/Hialid 參天/Santen	0	2008	√	7.4

Source: NMPA, Frost & Sullivan Analysis

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The artificial tears market experienced rapid growth in China. The market size increased from RMB1.2 billion in 2015 to RMB2.2 billion in 2019, representing a CAGR of 16.5%. It is estimated to further grow to RMB4.1 billion in 2024 at a CAGR of 13.1% from 2019, and RMB9.1 billion in 2030 at a CAGR of 14.4% from 2024. The following charts illustrates the artificial tears market in China:

China Artificial Tears Market, 2015-2030E



Source: Frost & Sullivan Analysis

Anti-Inflammatory Drugs

For mild to severe dry eye, anti-inflammatory drugs are used to address the underlying cause of dry eye, the inflammation of cornea and conjunctiva. Moderate to severe dry eye patients generally account for 50% of total dry eye patients in China, representing a significant group of patients who are in need for anti-inflammatory drugs. Anti-inflammatory agents used for ocular surface management broadly fall under two categories, namely corticosteroids and immunomodulators. Corticosteroids interfere with expression and transcription of pro-inflammatory genes by targeting receptor and nonreceptor-mediated pathways, respectively. The immunomodulators function by reducing cytokine production to achieve anti-inflammation effects.

As for the development of anti-inflammatory drugs for dry eye, although there are many ongoing studies investigating the efficacy of calcineurin, alpha adrenergic receptor agonists, and TNF- α inhibitors, none of these studies target tyrosine kinases, an enzyme related to the downstream pathway leading to ocular inflammation.

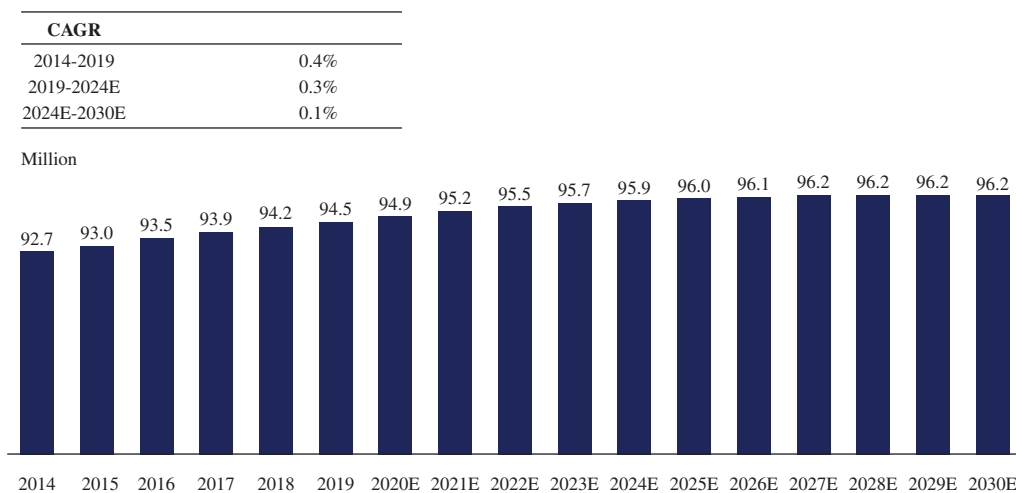
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BLEPHARITIS

Blepharitis is one of the most common eye diseases characterized by eyelid inflammation. It commonly occurs when tiny oil glands located near the base of the eyelashes become clogged and tends to recur. Blepharitis has a significant impact on ocular comfort and quality of life. Symptoms of blepharitis include burning, itchiness, gritty feeling in the eyes, contact lens intolerance, photophobia, redness, swelling and crusting of the eyelid margins. Blepharitis generally is not sight-threatening, but can induce permanent eyelid margin alternations, such as eyelid scarring, loss of eyelashes and in-turning of eyelashes. We expect the blepharitis drug market to continue to grow as driven by the large and increasing patient population, enhanced availability of treatments and the development of novel drug formulations.

The number of blepharitis patients in China increased from 92.7 million in 2015 to 94.5 million in 2019, accounting for nearly 6.8% of the population in China. With the improvement of health awareness and living conditions, the prevalence of blepharitis is slowly decreasing and the total number of blepharitis patients in China is estimated to reach 95.9 million in 2024 at a CAGR of 0.3% from 2019. The following chart illustrates the prevalence of blepharitis in China:

China Prevalence of Blepharitis, 2014-2030E



Source: Frost & Sullivan Analysis

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Treatment Paradigm and Unmet Medical Needs

Currently, there is no treatment solely indicated for blepharitis in China. Topical or systemic administration of antibiotics and topical administration of anti-inflammation drugs are common treatments for blepharitis. Topical cyclosporine and corticosteroid are helpful for eyelid or ocular surface inflammation such as severe conjunctival infection. Several corticosteroid eye drops have been approved by the NMPA for the treatment of steroid-responsive inflammatory ocular conditions. Compared with drugs applied directly to the eyelid margin, corticosteroid eye drops have the limitations of causing increased IOP as discussed below in more detail. The following table illustrates the marketed topical corticosteroid drugs for blepharitis in China:

Category	Generic Name	Representative Product		Number of Other Manufacturers	Earliest NMPA Approval Time	NRDL Inclusion	Price per ml (RMB)
		Brand Name	Manufacturer				
Topical Corticosteroid Drugs							
Monotherapy Drug	Dexamethasone Sodium Phosphate	N.A	廣州白雲山/ Baiyunshan	12	1982	√	4.7
	Fluorometholone	FML	艾爾建/Allergan	2	1999	√	3.4
	Hydrocortisone	N.A	武漢五景藥業/ Wujing Medicine	9	1981	X	0.1
	Loteprednol	Lotemax	博士倫/ Bausch & Lomb	0	2007	X	14.0
	Prednisolone	Pred Forte	艾爾建/Allergan	0	1999	X	5.8
Fixed-dose Combination Drug	Dexamethasone/Tobramycin	Tobradex	諾華/Novartis	8	2001	√	2.4
	Fluorometholone/Gentamicin	Infectoflam	諾華/Novartis	1	1999	X	5.8
	Loteprednol/Tobramycin	Sai Le	博士倫/ Bausch & Lomb	0	2012	X	20.4

Source: NMPA, Frost & Sullivan Analysis

Comparison between OT-503 and Competing Topical Corticosteroid Eye Drops

Eye drops interact with the tears in eyes and spread when eyelids are closed. The eye often eliminates topically applied medications via tear elimination, limiting the penetration of drugs into the ocular tissue. It is difficult to deliver an accurate dosage of eye drops and its long-term use may induce side effects. To overcome the limitation of eye drops, novel formulation drugs that use direct application to eyelid margin may decrease the dosage exposure of eye surface and lower the risk of side effects, such as increased IOP. In addition, another novel formulation is the nanocrystal suspension formulation, which can slow down the drug release rate through improving drug saturation solubility, thus extending the duration of

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action, reducing the peak concentration and side effects. Nanocrystals also increase drug bioavailability and change its administration routes. The following table is a comparison of marketed topical corticosteroid eye drops for blepharitis and OT-503:

Compound	Daily Frequency	Dosage Form	Potency (Duration of Action)	Anti-Inflammatory Potency (Potency relative to Hydrocortisone)	IOP incidence rate (Major AE)	Average IOP increase (mean mmHg)
Loteprednol	2-6 times	Suspension Eye Drop	Long acting	N.A	1.7%	4.1
Fluorometholone	2-5 times	Suspension Eye Drop	Long acting	131	0.13%	6.1
Dexamethasone	3-6 times	Eye Drop & Ointment	Long acting	30	5.2%	8.2
Prednisolone	2-4 times	Suspension Eye Drop	Intermediate acting	4	6.7%	10.0
Hydrocortisone	3-4 times	Suspension Eye Drop	Short acting	1	N.A.	3.2
OT-503	1-2 times	<i>Nanocrystal suspension via an eyelid applicator</i>	Intermediate acting	1-10	None	N.A

Source: Frost & Sullivan literature review and analysis

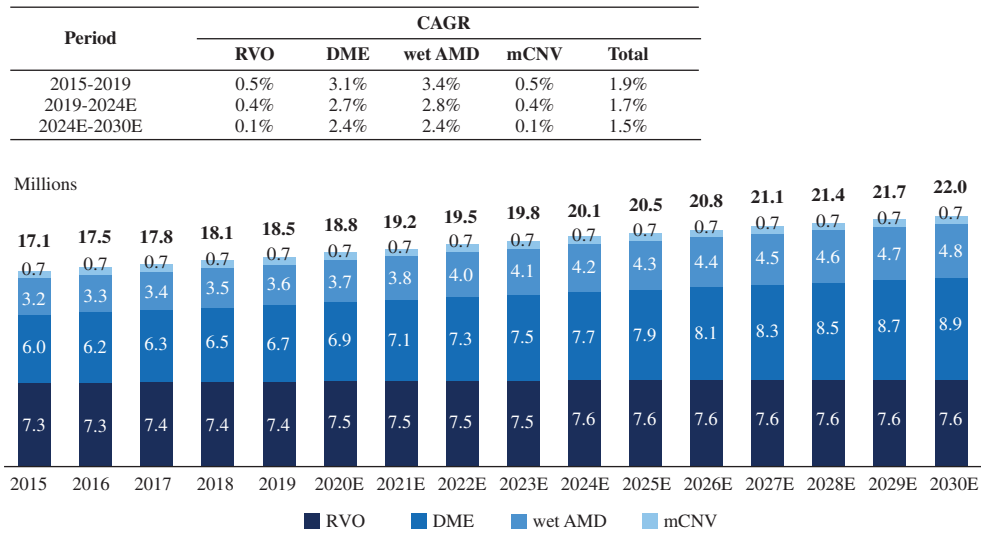
RETINAL DISEASES

Retinal diseases cause damage to the retina, which contains the light-sensitive nerve cells that convert light into signals. They are often characterized by leakage of fluid, hemorrhage and fibrous scarring in the eye. Retinal diseases include wet AMD, DME, RVO and myopic choroidal neovascularization, or mCNV. These diseases are major causes of visual impairment and blindness worldwide. AMD is a degenerative retinal disease that causes progressive loss of central vision. It is a leading cause of irreversible blindness in the elderly. Though wet AMD patients only account for approximately 10% of AMD patients, wet AMD causes 80% to 90% of vision loss among all AMD patients. DME is a complication of diabetes where a diabetic patient loses part or all of the central vision. RVO occurs when the central retinal vein, the blood vessel that drains the retina, or one of its branches becomes blocked. mCNV is a complication of myopia that causes visual impairment. The retinal diseases drug market is expected to continue to grow as driven by an expanding patient population, development of innovative therapy and biosimilar drugs, which further contributes to the drugs’ increasing affordability.

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Among the four types of retinal diseases, prevalence of wet AMD increases more rapidly than the other three because of the aging population. The chart below sets forth the prevalence of retinal diseases in China:

Prevalence of Major Retinal Diseases, 2015-2030E



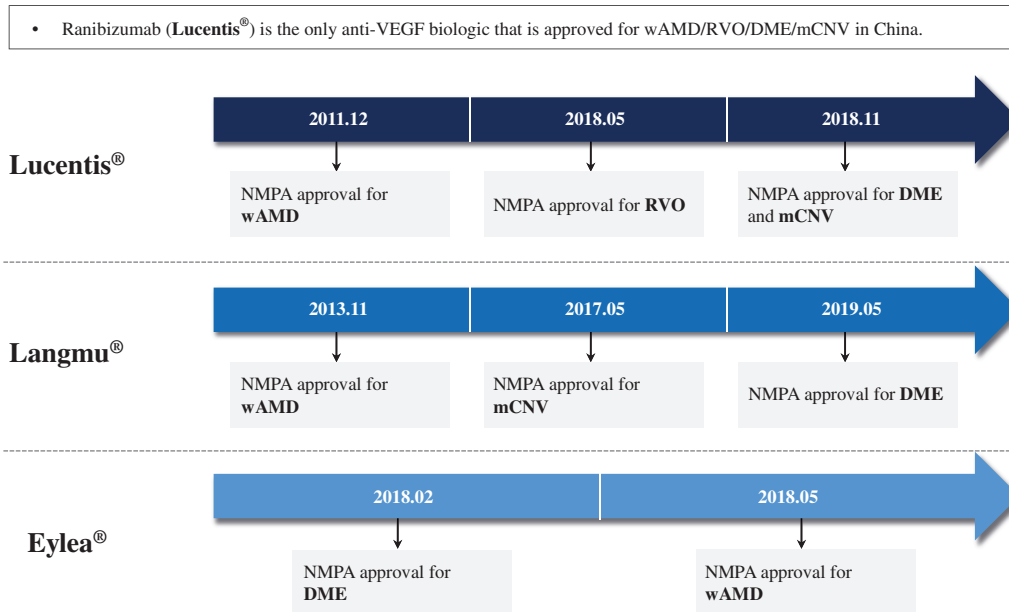
Source: Frost & Sullivan literature review and analysis

INDUSTRY OVERVIEW

Treatment Paradigm and Unmet Medical Needs

Anti-VEGF drugs are currently the first-line therapy for the treatment of wet AMD. Three anti-VEGF biologics have launched in China and all of them have been included in the NRDL. Among these three anti-VEGF biologics, ranibizumab (Lucentis®) is the only anti-VEGF drug that is approved for wet AMD, DME, RVO and mCNV:

NMPA Approval History of Anti-VEGF Biologics



Source: NMPA, Frost & Sullivan Analysis

The three major anti-VEGF drugs, ranibizumab (Lucentis®), Langmu® and aflibercept (Eylea®), had a unit price of RMB9,725, RMB6,725 and RMB5,850, respectively, when they first entered the PRC market. As these three anti-VEGF drugs were included in the NRDL in 2019, their current unit prices decreased to RMB3,950, RMB4,160 and RMB4,100, respectively.

INDUSTRY OVERVIEW

Comparison between OT-701 and Competing Anti-VEGF Drugs

As the PRC patents for aflibercept and ranibizumab will expire between 2020 and 2021, many biosimilar drugs are under development, and are expected to launch within the next two to three years. The launch of these biosimilar drugs are expected to cause general price drops of anti-VEGF drugs and lead to an increase in market availability for anti-VEGF drugs. The following table illustrates a comparison between OT-701 and clinical-stage anti-VEGF drugs that are currently under development in China:

Drug Code	Category	Sponsor	Indication	Clinical Phase	Regulatory Authority	Initial Publication Date ⁽¹⁾
QL1207	Fusion Protein	Qilu Pharma	wAMD	III	NMPA	2019/5/20
			DME	I	NMPA	2018/12/7
QL1205	Monoclonal Antibody	Qilu Pharma	wAMD	III	NMPA	2019/7/17
Faricimab	Bispecifics	Roche	DME	III	NMPA	2019/7/26
Brolucizumab	Monoclonal Antibody	Novartis	wAMD, DME, RVO	III	NMPA	2019/7/29
TK001	Monoclonal Antibody	T-mab Biopharma	wAMD	I	NMPA	2016/1/4
HB002.1M	Fusion Protein	Huabo Biopharma	wAMD	I	NMPA	2018/1/2
TAB014	Monoclonal Antibody	TOT Biopharma	wAMD	I	NMPA	2018/3/21
JY028	Monoclonal Antibody	Eastern Biotech	wAMD	I	NMPA	2018/7/2
601A	Monoclonal Antibody	3S Guojian Pharma	wAMD, DME	I	NMPA	2018/8/13
BAT5906	Monoclonal Antibody	Bio-thera Pharma	wAMD	I	NMPA	2018/10/26
SOLOT-Eye	Monoclonal Antibody	Stainwei Biotech	wAMD	I	NMPA	2018/11/1
IBI302	Bispecifics	Innovent Biologics	wAMD	I	NMPA	2019/1/23
LY09004	Fusion Protein	Luye Pharma	wAMD	I	NMPA	2019/6/20
RC28-E	Fusion Protein	RemeGen Biotech	wAMD	I	NMPA	2020/1/15
OT-701	Fusion Protein	Ocumenion	wAMD	Pre-clinical	–	N/A

Source: CDE, Frost & Sullivan Analysis

Note:

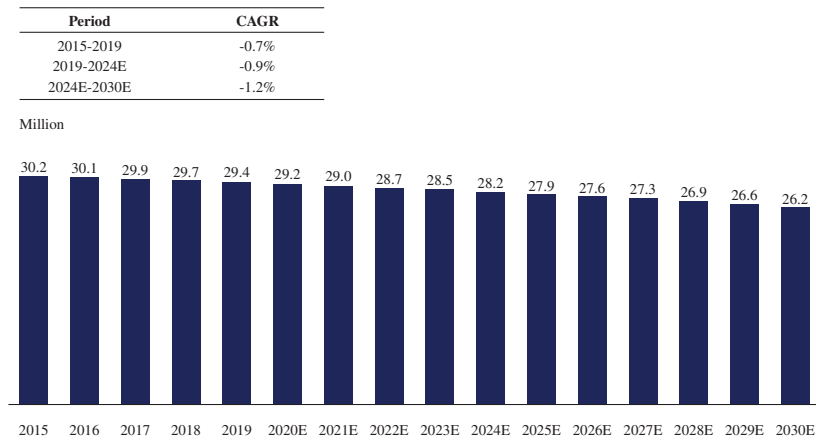
- (1) Refers to the date on which the information of the respective clinical trial is published for the first time.

INDUSTRY OVERVIEW

BACTERIAL CONJUNCTIVITIS

Bacterial conjunctivitis is a common type of conjunctivitis. It is caused by bacteria that infect the eye through various sources of contamination. The incidence of bacterial conjunctivitis in China is slowly decreasing because of improvement in hygiene conditions and personal health awareness. The following chart illustrates the incidence of bacterial conjunctivitis in China:

Incidence of Bacterial Conjunctivitis, 2015-2030E



Source: Frost & Sullivan literature review and analysis

Treatment Paradigm

There is no guideline or consensus for the treatment of bacterial conjunctivitis in China. The core treatment for bacterial conjunctivitis involves topical broad-spectrum antibiotics. Benefits of antibiotic treatment includes quicker recovery and decrease in transmissibility in patients with different levels of severity. The choice of antibiotics usually depends on patients' allergies, resistance patterns and local availability. The following table illustrates the marketed drugs indicated for bacterial conjunctivitis in China:

Generic Name	Representative Product		Number of Other Manufacturers	Earliest NMPA Approval Time	NRDL Inclusion	Price per ml (RMB)
	Brand Name	Manufacturer				
Aminoglycoside						
Amikacin	N.A	成都倍特藥業/ Brilliant Pharmaceutical	0	1990	X	0.8
Neomycin	Poly-Pred	艾爾建/Allergan	12	1984	X	1.2
Tobramycin	Tobrex	諾華/Novartis	30	1999	√	1.0
Gentamycin	Wei Lun	博士倫/Bausch & Lomb	16	1983	√	1.0
Fluoroquinolone						
Moxifloxacin	Vigamox	諾華/Novartis	0	2018	√	10.2
Gatifloxacin	Zhuning	安徽雙科藥業/Anhui Shuangke Pharmaceutical	6	2005	√	3.1
Levofloxacin	Cravit	參天/Santen	18	2004	√	6.1
Ofloxacin	Tarivid	參天/Santen	48	1993	√	0.7
Pazufloxacin	N.A	莎普愛思藥業/ Shapuaisi Pharmaceutical	0	2011	X	10.9
Enoxacin	N.A	遠大天明製藥/Yuanda Tianming Pharmaceutical	9	1996	√	1.0
Ciprofloxacin	Ba Mei Luo	興齊眼藥/Sinqi Pharmaceutical	31	1993	√	0.9
Lomefloxacin	Le Fen	武漢五景藥業/Wujing Medicine	21	1995	X	1.0
Norfloxacin	N.A	武漢五景藥業/Wujing Medicine	30	1991	√	1.8
Chloramphenicol						
Chloramphenicol	Run Shu	博士倫/Bausch & Lomb	60	1981	√	0.8
Others (Sulfonamide, Tetracyclines, etc.)						
Fusidic Acid	Fucithalmic	Amdipharm Limited	0	2011	X	1.1
Sulfamethoxazole	Le Dun Kang	曼秀雷敦/Mentholatum	0	1998	X	1.7

Source: NMPA, Frost & Sullivan Analysis

INDUSTRY OVERVIEW

Among all three antibiotic categories commonly used for bacterial conjunctivitis, fluoroquinolones are the most used category. Fluoroquinolones act by converting their targets, gyrase and topoisomerase IV, into toxic enzymes that fragment the bacterial chromosome. Fluoroquinolones are categorized into four generations according to their spectrum of bactericidal activity. Compared to previous generations, the fourth-generation fluoroquinolones offer considerable advantages, including a wider spectrum of activity, longer duration of activity and a smaller likelihood to provoke antibiotic resistance. Moxifloxacin and gatifloxacin are the two main fourth-generation fluoroquinolone antibiotics. Apart from Vigamox by Novartis which has already been marketed in China, there are another 10 moxifloxacin eye drops that have submitted an abbreviated new drug application, or ANDA:

Company	Submission Date
Shanghai Haohai Biological Technology Co., Ltd.	2019/1/28
Essex Bio-Technology Limited	2019/5/22
China Resources Zizhu Pharmaceutical Co., Ltd.	2019/5/29
Shijiazhuang Great Pharmaceutical Co. Ltd	2019/7/30
Sinqi Pharmaceutical	2019/11/22
Yangtze River Pharmaceutical Group	2019/12/11
Suzhou Industrial Park Tianlong Pharmacy Co., Ltd.	2019/12/31
Jiang Xi Kelun Pharmaceutical Co., Ltd.	2020/1/17
Huonland / Ocumension	2020/2/13
Qilu Pharmaceutical	2020/2/28

Source: CDE, Frost & Sullivan Analysis

SOURCE OF INFORMATION

In connection with the [REDACTED], we have commissioned Frost & Sullivan, an Independent Third Party, to conduct a detailed analysis and to prepare an industry report on the global and PRC ophthalmic drug markets. The Frost & Sullivan Report has been prepared by Frost & Sullivan independent from our influence. We have agreed to pay Frost & Sullivan a fee of RMB680,000 for the preparation of the Frost & Sullivan Report which we consider is in line with the market rates. Except as otherwise noted, all data and forecasts in this section are derived from the Frost & Sullivan Report. Our Directors confirm that, after taking reasonable care, there is no adverse change in the market information since the date of the Frost & Sullivan Report which may qualify, contradict or have an impact on the information disclosed in this section.

INDUSTRY OVERVIEW

Frost & Sullivan prepared its report based on its in-house database, Independent Third Party reports and publicly available data from reputable industry organizations. To prepare the Frost & Sullivan Report, Frost & Sullivan also conducted analysis on projected figures based on historical data, macroeconomic data and specific industry related drivers, and reviewed annual reports of listed companies in the global and PRC ophthalmic drug markets. In compiling and preparing the Frost & Sullivan Report, Frost & Sullivan has adopted the following assumptions: (i) the social, economic and political environments of the PRC will remain stable during the forecast period, which will ensure a sustainable and steady development of the PRC healthcare industry; (ii) the PRC healthcare market will grow as expected due to rising healthcare demand and supply; and (iii) the PRC government will continue to support healthcare reform.