Ophthalmic Pharmaceutical Market

Independent Market Research

Confidential For

Date : 24 June 2025

For and on behalf of
Frost & Sullivan Limited

Name: Terry Tse
Title: Consulting Director

Frost & Sullivan
Jun, 2025

Overview of Ophthalmic Disease

- Ophthalmic disease refers the conditions that affect any of the eye components such as cornea, optic nerve, lens, retina, choroid, and ocular surface. The eye is anatomically divided into the anterior and posterior segments with the lens-iris barrier roughly demarcating the two segments. The anterior segment of the eye mainly consists of cornea, conjunctiva, iris, and lens. The posterior segment mainly consists of vitreous body, retina, choroid and optic nerve. Common disease affecting the anterior segment of the eye are dry eye disease, glaucoma, uveitis, allergic conjunctivitis, pterygium and pinguecula. Prominent disease affecting the posterior segment of the eye include wet age-related macular degeneration and diabetic retinopathy.
- Delivery to the anterior segment of the eye may be achieved through topical and subconjunctival routes, or injected intracamerally. Posterior segment delivery can be achieved topically, systemically, and periocularly, via the suprachoroidal space, and via intraocular injections.

Vitreous body

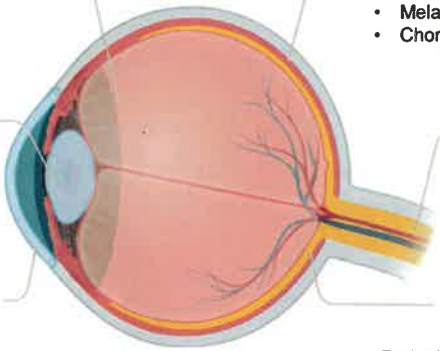
- Vitreous Hemorrhage
- Posterior Vitreous Detachment
- Vitreous Opacity

Lens

- Cataract
- Ectopia lens

Cornea & Ocular surface

- Allergic conjunctivitis
- Pterygium & Pinguecula
- Meibomian gland dysfunction (MGD) and Dry eye disease
- Corneal dystrophy
- Blepharitis



Choroid

- Choroidal detachment
- Melanoma of Choroid
- Choroiditis

Optic nerve

- Glaucoma
- Optic Neuritis
- Optic atrophy

Retina

- Retinal detachment
- Diabetic retinopathy
- Macular hole
- Retinopathy of prematurity (ROP)
- Wet Age-Related Macular Degeneration (wAMD)

Source: Frost & Sullivan Analysis

Introduction to Common Ophthalmic Diseases

- According to WHO report on vision, ophthalmic diseases are categorized by non-vision threatening and vision threatening. Eye conditions that typically do not threaten vision include conjunctivitis, pterygium, pinguecula, blepharitis, and dry eye disease. Although the harm caused by non-vision-threatening eye diseases is relatively low, they can still impact people's daily lives in the long term. In the absence of timely treatment, some non-vision-threatening eye diseases may lead to a variety of severe complications and carry the risk of vision loss.
- Eye conditions that can cause vision impairment and blindness include retinal diseases, cataract, glaucoma, uveitis, juvenile myopia and presbyopia.

Non-Vision-Threatening Eye Diseases

Blepharitis: Inflammation of the eyelids near the base of the eyelashes characterized by redness and irritation of the eye and eyelid.

Chalazion and hordeolum (stye): Common eyelid disorders resulting from a blocked gland or localized infection that can cause pain.

Conjunctivitis: Inflammation of the conjunctiva (the clear membrane lining the inside of the eyelids and covers the white part of the eye) most commonly caused by allergy or infection.

Dry eye: Due to an inadequate tear production that can result in irritation and blurred vision.

Pinguecula: A yellowish-raised benign growth on the conjunctiva meaning it is non-cancerous and not life-threatening or sight-threatening.

Subconjunctival haemorrhage: Broken blood vessels underneath the conjunctiva.

Vision-Threatening Eye Diseases

Age-related macular degeneration: Damage to the central part of the retina responsible for detailed vision leads to dark patches, shadows or distortion of the central vision.

Cataract: Cloudiness in the lens of the eye, leading to increasingly blurred vision. The risk of developing cataract increases with age.

Glaucoma: Progressive damage to the optic nerve. Initially, loss of vision occurs in the periphery and can progress to severe vision.

Refractive error: Due to an abnormal shape or length of the eye ball; light does not focus on the retina resulting in blurred vision. Common types include myopia and presbyopia.

Uveitis: A general term for inflammation of the iris, ciliary body and choroid, which can cause serious complications and sequelae, even blindness.

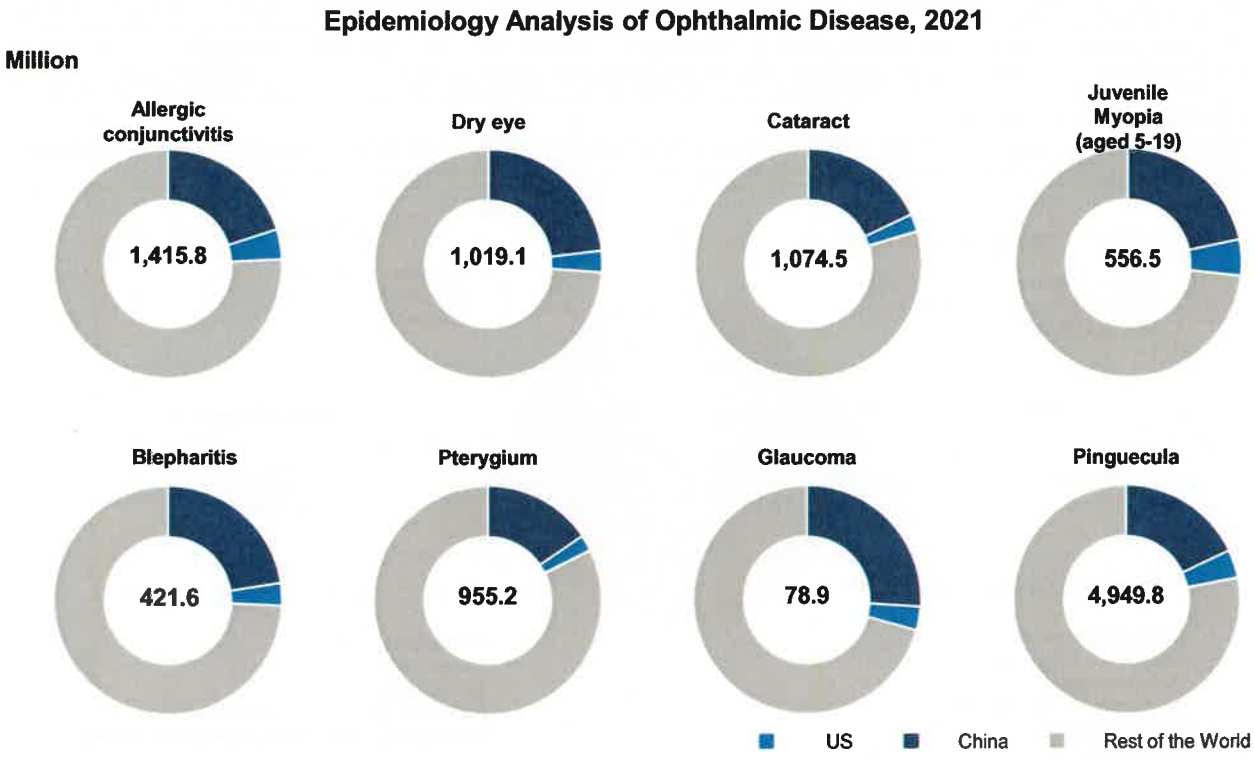
Trachoma: Caused by a bacterial infection. After many years of repeated infections, the eyelashes can turn inwards (known as trichiasis) which can lead to corneal scarring and, in some cases, blindness.

Diabetic retinopathy: Damage to blood vessels in the retina which become leaky or blocked. Swollen central retina commonly causes vision loss. Abnormal blood vessels can also grow from the retina, which cause retina scarring and blindness.

Pterygium: Abnormal growths on the conjunctiva that can cause pain. In advanced cases, pterygium can encroach on the cornea and cause vision loss.

Source: WHO Report on Vision, Frost & Sullivan

Epidemiology Analysis of Ophthalmic Disease, 2021



Source: Literature Review, Frost & Sullivan Analysis

Drug Application Pathways in the U.S.

- In the U.S., drug application has three pathways, 505(b)(1) and 505(b)(2) for NDA and 505(b)(j) for ANDA. The new drug definition includes novel drugs and modified new drugs. 505(b)(2) is frequently applied across the pharmaceutical industry to increase the likelihood of success and substantially lower development cost and reduce commercialization timeline.

Application Type	Drug Type	Application Pathway
NDA (new drug applications)	• New molecular entities (NMEs)	505(b)(1): An application that contains full reports of investigations of safety and efficacy.
	• Modified new drug, including new dosage and formulation, new combination product, new indication, new route of administration, etc.	505(b)(2): An application that contains full reports of investigations of safety and efficacy but where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference.
ANDA (abbreviated new drug applications)ANDA	• Generics	505(j): An application that contains information to show that the proposed product is identical in active ingredient, dosage form, strength, route of administration, labeling, quality, performance characteristics, and intended use, among other things, to a previously approved product.

Source: FDA, Frost & Sullivan Analysis

Ophthalmic Drugs Approved via 505(b)(2) Pathway

- The 505(b)(1) NDA pathway requires a great deal of time, resources and capital, and has a considerable failure rate.
- The 505(b)(2) pathway was created to help avoid unnecessary duplication of studies, including nonclinical and clinical studies, already performed on an existing or previously approved drugs, to fulfill various registration requirements. Thus, the 505(b)(2) pathway allows for a less expensive and faster approval compared to 505(b)(1) pathway.

	505(b)(1)	505(b)(2)
Duration from Drug Discovery to Approval	10-15 years	3-6 years
Cost	>US$ 2.5 billion	NA
Success Rate from Phase I to Approval	6.2%	22.6%
Patent and Market Exclusivity[1]	5 years	3 years

Note: 1. A 5-year period of exclusivity is granted to new drug applications for products containing chemical entities never previously approved by FDA. No 505(b)(2) application or ANDA may be submitted during the 5-year exclusivity period except that such applications may be submitted after 4 years if they contain a certification of patent invalidity or noninfringement. A 3-year period of exclusivity is granted for a drug product that contains an active moiety that has been previously approved.

The 505(b)(2) pathway offers potential advantages not afforded by the other two pathways:

1. Reduced timeline and lower development cost because of avoided self-generated pre-clinical and clinical data required for approval;
2. Approval success rates are typically greater than for 505(b)(1) NDA programs because safety and efficacy profiles of the drug substance are typically well-characterized;
3. Comparable patent and market exclusivity to 505(b)(1) pathway.

Benefits of Ophthalmic 505(b)(2) Approvals

- Ocular structures possess distinctive anatomical and physiological barriers. Due to the outer and inner blood-ocular barrier (BOB), the influx of a drug into the retina and vitreous region is limited, requiring the systemic administration of high doses to achieve therapeutic concentrations within the eye, thereby increasing the risk of side effects. Thus, off-label use of systemic drugs for ophthalmic diseases is rarely recommended in the clinical practice, due to safety concerns and lack of efficacy.
- Many therapeutical mechanisms of ocular diseases share similarities with those in systemic diseases. Thus, 505(b)(2) pathway offers an attractive and de-risked pathway to repurposing an approved systemic drug to treat ocular diseases.

Source: Literature Review, Frost & Sullivan Analysis

Chemical Drug Application Category in China

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

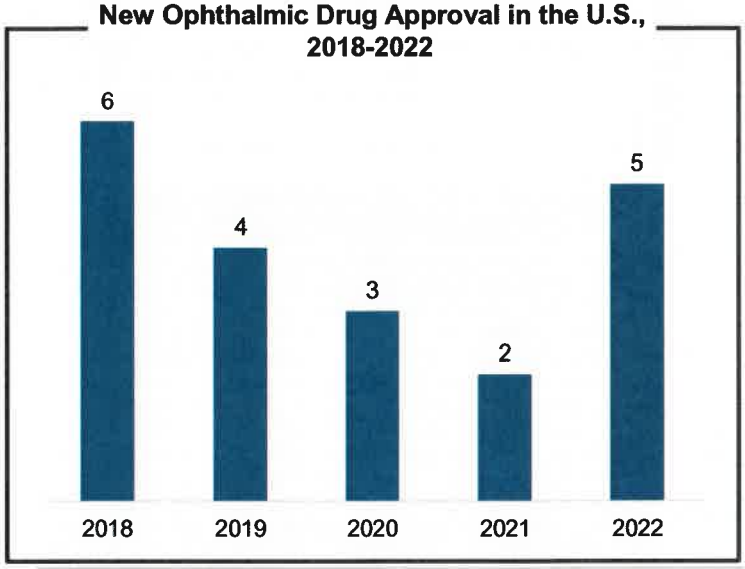
Category	Classification	Definition / Scope
New drugs	Class 1 Innovative new drugs which have never been marketed within or outside China	Active ingredients and their formulations which have clinical value and contain compounds with new structure and pharmacological effects.
	Class 2 Improved new drugs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

Source: NMPA, Frost & Sullivan Analysis

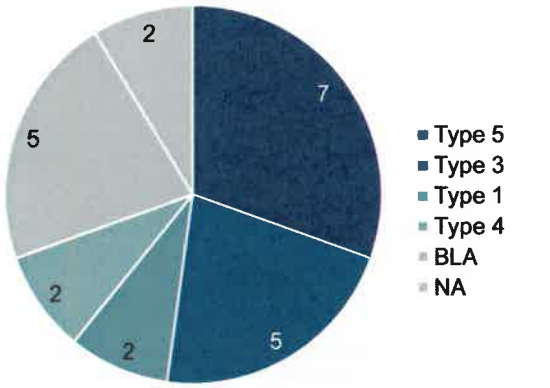
Approved New Ophthalmic Drugs in U.S., 2018-2022

- New drug is defined to be drugs that got approved via submission of new drug application (505b(1) and 505b(2)) and BLA. The FDA Biologics License Application (BLA) is a request for permission to introduce, or deliver for introduction, a biologic product into interstate commerce. Among 20 new ophthalmic drugs approved from 2018 to 2022, 11 of which are approved through 505(b)(2) pathway.

New Ophthalmic Drug Approval in the U.S., 2018-2022



Breakdown of New Ophthalmic Drug by Application Type



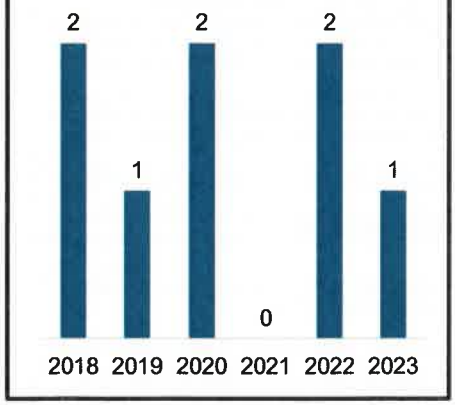
- Type 1-New Molecular Entity
- Type 3-New Dosage Form
- Type 4-New Combination
- Type 5-New Formulation
- BLA-Biologic License Application

Source: FDA, Frost & Sullivan Analysis

Approved New Ophthalmic Drugs in China, 2018-2023

- There are 8 new ophthalmic drugs approved in China from 2018 to 2023.

New Ophthalmic Drug Approval in China, 2018-2022



Drug Name	Company	Indication	Submission Classification	First Approval Time	
				NMPA	FDA
Eylea	Regeneron/Bayer	DME, wAMD	Category 3 of therapeutic biological products[1]	2018	2011
Vigamox	Novartis Pharmaceuticals	Conjunctivitis	Class 5.1	2018	2003
Simbrinza	Novartis Pharmaceuticals	Open-angle glaucoma and high intraocular pressure	Class 5.1	2019	2013
Oxervate	Dompé farmaceutici S.p.A	Neurotrophic keratitis	Class 5.1	2020	2018
Pataday	Novartis	Allergic conjunctivitis	Class 5.1	2020	2004
Yutiq	EyePoint Pharmaceuticals/Ocumension	Chronic non-infectious uveitis	Class 5.1	2022	2018
Verkazia	Santen	Vernal keratoconjunctivitis	Class 5.1	2022	2021
Vabysmo	Roche Pharma	DME, wAMD, BRVO	Category 3 of therapeutic biological products	2023	2022

Note: 1. Biological product marketed oversea but not marketed in China yet.
2.Chinese medicine is not included.
Source: NMPA, Frost & Sullivan Analysis

Approved New Ophthalmic Drugs in U.S., 2018.01-2024.05 (1/3)

- Below is a listing of new ophthalmic drugs approved by CDER. New drugs can be classified by novel drugs, whose active moieties that FDA had not previously approved, and modified new drugs, contain active moieties that are closely related to active moieties in products that FDA has previously approved. Yutiq, Lotemax Sm, and Durysta were approved by FDA via 505(b)(1) pathway, whose active moiety that has been previously approved.
- 505(b)(2) regulatory pathway is a common R&D development approach adopted by ophthalmic biotechnology companies. For example, Dextenza, indicated for ocular itching associated with allergic conjunctivitis, was approved by FDA in 2018 through 505(b)(2) pathway. Dextenza product revenue for 2022 was US$ 50.5 billion versus US$ 42.0 billion for 2021. And Lumify, manufactured by Bausch and Lomb, was approved by FDA in 2017. Lumify product revenue for 2022 reached US$ 131 million.
- The global top 3 sale ophthalmic drugs approved via 505(b)(2) pathways in are Restasis, Lumigan, Combigan, with the global sales revenue of US$666 million, US$514 million and US$346 million in 2022.

Novel Ophthalmic Drugs in the U.S., 2018.01-2024.05

Drug Name	Company	Active Compound	Indication	Approval Date	Drug Application	Submission Classification
Oxervate	Dompe Farmaceutici S.P.A.	Cenegermin-Bkbj	Neurotrophic keratitis	2018	BLA	/[1]
Beovu	Novartis Pharmaceuticals Corporation	Brolucizumab-Dbll	• Neovascular (Wet) Age-Related Macular Degeneration (AMD) • Diabetic Macular Edema (DME)	2019	BLA	/
Tepezza	Horizon Therapeutics Ireland Dac	Teprotumumab-Trbw	Thyroid Eye Disease	2020	BLA	/
Kimmtrak	Immunocore Limited	Tebentafusp-Tebn	HLA-A*02:01-positive adult patients with unresectable or metastatic uveal melanoma	2022	BLA	/
Vabysmo	Genentech, Inc.	Faricimab-Svoa	• Neovascular (Wet) Age-Related Macular Degeneration (nAMD) • Diabetic Macular Edema (DME)	2022	BLA	/
Omlonti	Santen	Omidenepag Isopropyl	Reduction of IOP in patients with open-angle glaucoma, or ocular hypertension	2022	505(b)(1)	Type 1
Miebo	Bausch and Lomb	Perfluorhexyloctane	Dry Eye Disease	2023	505(b)(1)	Type 1
Xdemvy	Tarsus	Lotilaner	Demodex blepharitis	2023	505(b)(1)	Type 1
Izervay	Iveric Bio	Avacincaptad pegol	Geographic atrophy secondary to age-related macular degeneration	2023	505(b)(1)	Type 1

Source: FDA, CDER, Frost & Sullivan Analysis

Approved New Ophthalmic Drugs in U.S., 2018.01-2024.05 (2/3)

Modified New Ophthalmic Drugs in the U.S., 2018.01-2024.05

Drug Name	Company	Active Compound	Reference Listed Drug	Indication	Approval Date	Drug Application	Submission Classification
Cequa	Sun Pharma Global	Cyclosporine	Neoral and Sandimmune	Keratoconjunctivitis sicca (dry eye)	2018	505(b)(2)	Type 5
Inveltys	Kala Pharmaceuticals	Loteprednol Etabonate	Lotemax	Post-operative inflammation and pain	2018	505(b)(2)	Type 5
Xelpros	Sun Pharma Global	Latanoprost	Xalatan	Reduction of IOP in patients with open-angle glaucoma, or ocular hypertension	2018	505(b)(2)	Type 3
Yutiq	Fluocinolone Acetonide Intravitreal Implant	Fluocinolone Acetonide	/	Chronic non-infectious uveitis	2018	505(b)(1)	Type 5
Dextenza	Ocular Therapeutix	Dexamethasone	Maxidex	Ocular itching associated with allergic conjunctivitis	2018	505(b)(2)	Type 3
Lotemax Sm	Bausch and Lomb	Loteprednol Etabonate	/	Post-operative inflammation and pain	2019	505(b)(1)	Type 5
Rocklatan	Aerie Pharmaceuticals	Latanoprost	Xalatan	Reduction of IOP in patients with open-angle glaucoma, or ocular hypertension	2019	505(b)(2)	Type 4 and 5
Avaclyr	Fera Pharmaceuticals	Acyclovir	Zovirax	Acute herpetic keratitis	2019	505(b)(2)	Type 3
Durysta	Allergan	Bimatoprost	/	Reduction of IOP in patients with open-angle glaucoma, or ocular hypertension	2020	505(b)(1)	Type 3
Eysuvis	Kala Pharmaceuticals	Loteprednol Etabonate	Lotemax	Short-term treatment of signs and symptoms of dry eye disease	2020	505(b)(2)	NA
Verkazia	Santen	Cyclosporine	NA	Vernal keratoconjunctivitis	2021	505(b)(2)	Type 5
Vuity	Abbvie	Pilocarpine Hydrochloride	NA	Presbyopia	2021	505(b)(2)	Type 5
Acuvue Theravision with Ketotifen	Johnson and Johnson Vision Care	Ketotifen Fumarate	NA	Prevention of ocular itch	2022	505(b)(2)	Type 3 and 4
Atropine Sulfate Ophthalmic Solution	Paragon Bioteck	Atropine Sulfate	NA	Dilation of the pupil before eye exams	2022	505(b)(2)	NA
Vevye	Novaliq	Cyclosporine	Cequa	Dry Eye Disease	2023	505(b)(2)	Type 5

Source: FDA, CDER, Frost & Sullivan Analysis

Approved New Ophthalmic Drugs in U.S., 2018.01-2024.05 (3/3)

Drug Name	Company	Active Compound	Reference Listed Drug	Indication	Approval Date	Drug Application	Submission Classification
Qlosi	Orasis Pharmaceuticals	Pilocarpine hydrochloride	NA	Presbyopia	2023	505(b)(2)	Type 3
Ryzumvi	Ocuphire Pharma Inc	Phentolamine	NA	Pharmacologically-induced mydriasis produced by adrenergic agonists or parasympatholytic agents	2023	505(b)(2)	Type 3
Mydcombi	Eyenovia	Tropicamide and phenylephrine	NA	Pupil dilation	2023	505(b)(2)	Type 5

Note: 1, / means information is not applicable.
2, Type 1-New molecular entity, Type 2-New active ingredient, Type 3-New dosage form, Type 4-New combination, Type 5-New Formulation or Other Differences (e.g., new indication, new applicant, new manufacturer)
3, NA means public information is not available.

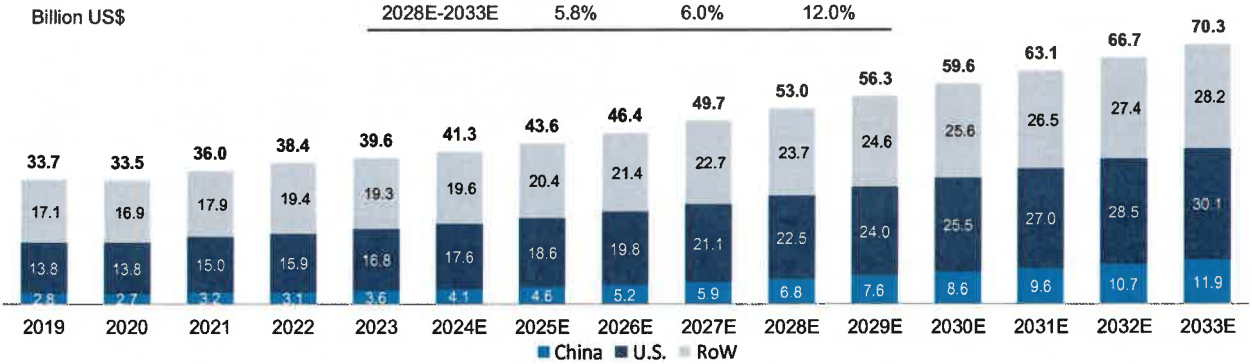
- *Source: FDA, CDER, Frost & Sullivan Analysis*

Global Ophthalmic Drug Therapies Market Size and Forecast, 2019-2033E

- Global ophthalmic drug therapies market size increased from US$33.7 billion in 2019 to US$39.6 billion in 2023 with a CAGR of 4.1%. It is expected to continue to increase to US$53.0 billion in 2028 and US$70.3 billion in 2033 with a CAGR of 6.0% and 5.8% from 2023 to 2028 and from 2028 to 2033 respectively.
- U.S. ophthalmic drug therapies market size increased from US$13.8 billion in 2019 to US$16.8 billion in 2023 with a CAGR of 5.1%. It is expected to continue to increase to US$22.5 billion in 2028 and US$30.1 billion in 2033 with a CAGR of 6.1% and 6.0% from 2023 to 2028 and from 2028 to 2033 respectively.
- China ophthalmic drug therapies market size increased from US$2.8 billion in 2019 to US$3.6 billion in 2023 with a CAGR of 6.2%. It is expected to continue to increase to US$6.8 billion in 2028 and US$11.9 billion in 2033 with a CAGR of 13.6% and 12.0%, from 2023 to 2028 and from 2028 to 2033 respectively.

Global Ophthalmic Drug Therapies Market Size and Forecast, 2019-2033E

Period	CAGR		
	Global	U.S.	China
2019-2023	4.1%	5.1%	6.2%
2023-2028E	6.0%	6.1%	13.6%
2028E-2033E	5.8%	6.0%	12.0%



Source: Literature Review, Expert Interview, Annual Report, and Frost & Sullivan Analysis

Introduction of Protein Kinase Inhibitors

- Protein kinases can be specifically involved in cell growth, proliferation and differentiation and mutations may lead to unregulated growth and proliferation. They act by adding a phosphate group to a protein (phosphorylation), usually on a specific amino acid which often makes the protein or enzyme "active". Some kinase inhibitors have specificity for multiple kinases and are called "multi-kinase inhibitors" (MKI). The limitations of many single kinase inhibitors can be overcome by agents with multi-target action.

Protein Kinase

1 Introduction

Protein kinases are ubiquitous intracellular and cell surface proteins that play critical roles in cell signaling pathways involved in metabolism, injury responses, adaption, growth and differentiation. A range of receptor kinases are involved in these processes, including vascular endothelial growth factor receptor (VEGF), platelet-derived growth factor receptor (PDGFR), stem cell factor (c-KIT), Flt3, fibroblast growth factor receptor (FGFR) and so on.

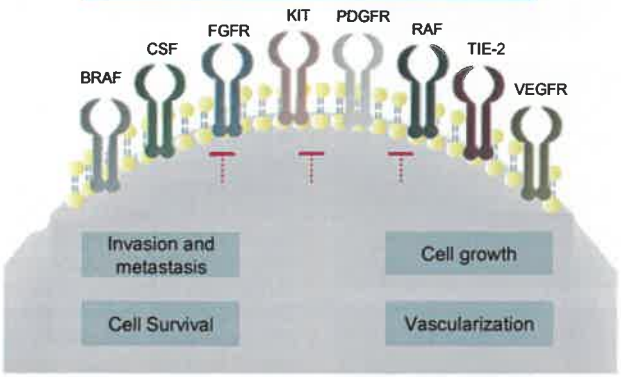
2 Classification

The protein kinases can be categorized based upon the amino acid that they phosphorylate: either serine, threonine or tyrosine.

3 Clinical Benefits of MKI

MKI may pose higher selectivity, efficacy, resistance and lower toxicity than single kinase inhibitor.

MOA of Kinase Inhibitors



Case of MKI in Posterior Eye Disease

Pazopanib is a small multi-tyrosine kinase inhibitor (TKI) that targets VEGF and PDGF receptors and inhibits angiogenesis. Pazopanib was first approved by the Food and Drug Administration (FDA) for the treatment of advanced renal cell carcinoma and more recently for treatment of soft tissue sarcoma. Clinical studies conducted by GSK have proved the ocular potential of pazopanib in macular degeneration since 2007.

Source: Literature Review, Frost & Sullivan Analysis

Growth Drivers for Ophthalmic Drug Market

Enlarging Patient Pool

- Poor eye health and impaired vision have a negative effect on quality of life and restrict equitable access to and achievement in education and the workplace. The number of people with major eye diseases continues to increase across the globe. In 2023, juvenile myopia and dry eye disease affect over 550 million and 900 million patients globally, due to prevalent use of digital devices. Additionally, the overall growth of the aging population and increasing prevalence of diabetes and hypertension have also boosted the prevalence of pterygium, pinguecula, age-related eye diseases such as diabetic retinopathy, and glaucoma. With the soaring prevalence of eye diseases and the related increase in disability-adjusted life years (DALYs), the demand for proper treatment is expected to increase in the coming years. This, in turn, will facilitate the growth of the market.

Unmet Clinical Needs

- As the living standards continue to rise, and the public awareness of ophthalmic disease improves due to consistent efforts on patients education, demand for better healthcare in ophthalmic disease will keep growing in the future and drive the overall ophthalmic pharmaceutical market. However, currently, the research and development focus of multinational ophthalmic players is mainly retinal diseases and glaucoma. There are also much clinical needs of ophthalmic patients that are not being addressed, such as pterygium, pinguecula, juvenile myopia and meibomian gland dysfunction, for which there is no effective treatment, due to high discovery, clinical and regulatory barriers.

Innovative Ophthalmic Therapy

- With strengthened knowledge and advancing research, the field of ophthalmology has progressed steadily. Decades ago, anti-VEGFs have retained their status in eye disease for the foreseeable future, now these options have expanded beyond original indication wAMD and are approved for a slew of retinal diseases, involving DME, mCNV and RVO. Moreover, looking ahead, the next decade of ophthalmic treatment will hold a bounty of advances and will lay the foundation for the overall market growth. For instance, the majority of multi-kinase inhibitors are used for oncology treatment, and as further clinical studies reveal proven safety and efficacy in the treatment of ocular diseases, more possibilities for the treatment of ocular diseases are available.

Favorable Policy Environment

- Many countries have made large strides in enhancing eye health in the past few decades. The gravity of eye disease control and management has raised authority attention. The seventy-forth World Health Assembly, having considered the consolidated report of the Director-General, decided to endorse the global targets for effective coverage of refractive errors and effective coverage of cataract surgery to be achieved by 2030. In addition, in 2022, China issued a new Five-year-National Plan for Eye Heath (*《"十四五"全国眼健康规划(2021-2025)》*), proposing to reduce the burden of major vision-threatening diseases. Work to prevent blindness is led by the government, with prestigious public hospitals across the country contributing to research and programming.

Future Trends for Ophthalmic Drug Market

Broader Therapeutic Indications	• Anti-allergic, anti-inflammatory, retinal and dry eye disease segments have been dominating the global ophthalmic drug market, owing to factors such as the increasing high prevalence and successful development and commercialization of therapeutic medications of these diseases. However, only symptomatic relieving treatment is available for many eye conditions, involving pterygium, pinguecula, dry eye disease, and so on, for which there is no effective and safe treatment options. Researches has demonstrated that the treatment of these conditions can pose a substantial economic burden on the patient and on society. In the future, unmet clinical demands for these conditions are expected to be solved.
Investigation on Innovative Drugs	• Innovative ophthalmic medication, involving novel drug mechanism, drug dosage forms and drug delivery routes, targeting a variety of eye diseases are being developed and trialed. Novel drug mechanism, new delivery system and forms of administration will help to yield better effectiveness, compliance and safety. There exists multiple biologics for the treatment of ophthalmic diseases. For instance, anti-VEGF agents have shown high specificity. However, they are limited in treating posterior ophthalmic diseases as it is difficult for biologics to penetrate through vitreous humor and might require high frequency of intraocular injection that significantly impacts patient compliance and introduces side effects. Innovative technical platforms may increase the response rate and efficacy in treating posterior ophthalmic diseases.
Increasing Penetration Rate of Eye Care Services	• The prevalence of eye conditions and associated complications is influenced by the affordability and accessibility of eye care services. In the recent tears, many barriers related to gender, socioeconomic status, perceived cost of eye care, health insurance conditions have been continually eliminated or addressed to increase accessibility to and affordability for eye services. For instance, the unmet clinical needs in ophthalmic clinical practice in China attributed to both the lack of ophthalmologists and medication, which result in a larger under-treated population than other specialties in medicine. According to National Health Commission of the People's Republic of China, the number of eye hospitals in China increased from 761 in 2018 to 1,203 in 2021 and the number of specialized doctors increased from 14,024 in 2018 to 21,173 in 2021. Together with growing awareness of eye health and disposable income, the penetration rate of eye care services will ultimately grow in the future.

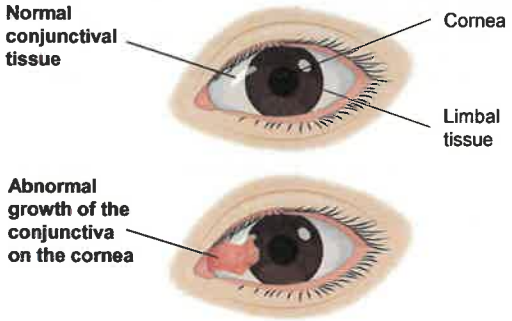
Entry Barriers of Ophthalmic Drug Market

Product Development Capabilities	• The field of ophthalmology is quite specialized. The eye has an intricate assembly of different cells, specialized vasculature, and intricate structural organization that result in different functions, unlike other therapeutic areas that have significant organ system interactions and/or overlap, allowing greater mobility of the skill-set from one specialty to another. Therefore, domain-specific knowledge and skills are crucial for the effective development of ophthalmic medicines. The development of ophthalmic medications is knowledge-intensive, which creates a greater barrier for small or emerging businesses to enter the ophthalmic drug industry.
Complicated Therapeutic System Design	• Depending on the anatomical area, eye tissues are exposed to distinct and frequently heterogeneous biochemical microenvironments. Additionally, both in health and sickness, different eye areas have different permeability characteristics. Ophthalmic drug development is consequently extremely complicated and varies depending on the field of use with regard to successful formulation development and dosage forms. When taken as a whole, these characteristics provide a serious obstacle to the creation of efficient ophthalmic treatment.
Manufacturing and Quality Management Capabilities	• The ability to manufacture ophthalmic medications has a direct impact on their effectiveness. Facilities that adhere to GMP standards, skilled production team, validated production process, good quality management system are essential. Significant entrance barriers are present for businesses lacking qualified manufacturing capabilities.
Brand Recognition	• Naturally, doctors and hospitals are more likely to suggest well-known products that have been shown to be secure and efficient. As a result, developing a well-known brand with substantial involvement among doctors and hospitals may take years of work and investment on the part of new entrants.

Overview of Pterygium

- Pterygium is a benign proliferative ocular surface disease characterized mainly by wing-shaped and fibrovascular growth of the limbal and conjunctival tissue over the adjacent cornea. While the body of the pterygium remains on the sclera, the head advances unto the cornea in many cases affecting vision, causing general discomfort, and becoming a cosmetic nuisance. Exposure to ultraviolet light (UVB) is generally believed to be a strong risk factor for the development of pterygium. As a result of alterations in local ocular surface homeostasis, the main components of pterygium include proliferative clusters of limbal stem cells, active fibrovascular tissue, epithelial metaplasia, altered extracellular matrix with accumulation of collagen and elastin fibers and inflammatory infiltration. Common symptoms include hyperemia, irritation, foreign body sensation, and visual impairment due to its damage to the corneal.
- Pterygium can cause hyperemia, growing onto the cornea, disrupting the normal tear film and leading to dryness, irritation and blindness if untreated in rare cases. Hyperemia can also be caused by the body's immune response to the pterygium, which can lead to inflammation and redness. The symptoms of pterygium associated hyperemia may include eye redness, irritation, tearing, and a sensation of a foreign body in the eye.

Pterygium



Risk Factors

- UV radiation
- Environmental irritants, such as dust and smog
- Age
- Familial and hereditary factors
- History of eye irritation
- Viral etiology

Mechanism of Pterygium caused Hyperemia

The abnormal tissue of pterygium can physically block the tear film from reaching the cornea, causing dryness and irritation and can produce inflammatory mediators that cause blood vessels to dilate, leading to hyperemia.

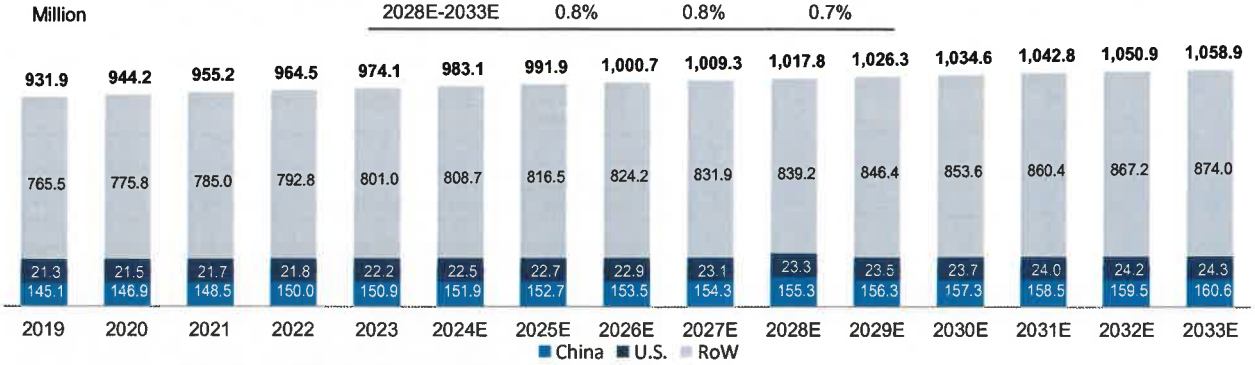
Source: Literature Review, Frost & Sullivan Analysis

Global Prevalence of Pterygium, 2019-2033E

- Global prevalence of pterygium increased from 931.9 million in 2019 to 974.1 million in 2023 with a CAGR of 1.1%. It is expected to continue to increase to 1,017.8 million in 2028 and 1,058.9 million in 2033 with a CAGR of 0.9% and 0.8% from 2023 to 2028 and from 2028 to 2033 respectively.
- Prevalence of pterygium in the U.S. increased from 21.3 million in 2019 to 22.2 million in 2023 with a CAGR of 1.1%. It is expected to continue to increase to 23.3 million in 2028 and 24.3 million in 2033 with a CAGR of 0.9% and 0.8% from 2023 to 2028 and from 2028 to 2033 respectively.
- Prevalence of pterygium in China increased from 145.1 million in 2019 to 150.9 million in 2023 with a CAGR of 1.0%. It is expected to continue to increase to 155.3 million in 2028 and 160.6 billion in 2033 with a CAGR of 0.6% and 0.7%, from 2023 to 2028 and from 2028 to 2033 respectively.

Global Prevalence of Pterygium, 2019-2033E

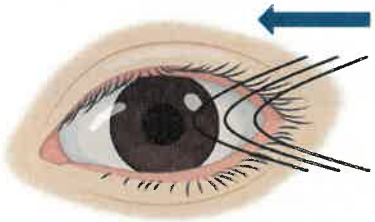
Period	CAGR		
	Global	U.S.	China
2019-2023	1.1%	1.1%	1.0%
2023-2028E	0.9%	0.9%	0.6%
2028E-2033E	0.8%	0.8%	0.7%



Source: Literature Review, Expert Interview, Frost & Sullivan Analysis

Current Treatment Options and Unmet Clinical Needs for Pterygium

- In the U.S., topical eyedrops to manage pterygium symptoms were used in around 60% of pterygium patients. Surgical excision was performed in around 5% of patients. Around 30% of pterygium patients was estimated that did not seek any medical treatment due to mild symptoms at their early stage.
- In China, the proportion of pterygium who used topical eyedrops and surgical excision were around 5% and 0.4% in China. Over 90% of pterygium patients in China did not seek any medical treatment.



Stage Progression of Pterygium	Symptoms	Treatment Options	Penetration Rate
Stage 1: The head of pterygia did not reach the midline between the limbus and pupillary margin	Asymptomatic Signs of dry eye, such as burning, itching or tearing Hyperemia associated eye redness, irritation, tearing, and a sensation of a foreign body in the eye	Pharmaceuticals (off-label use)	~60% in the U.S. ~5% in China
Stage 2: The head of pterygia passed the midline but did not reach the pupil			
Stage 3: The head of pterygia passed the pupillary margin	Visual symptoms due to induced astigmatism or direct encroachment onto the visual axis	Surgery + Adjunctive Therapy	~5% in the U.S. ~0.4% in China

Note: Penetration rate of different treatment options are among total pterygium patients.

Source: Literature review, expert interview, Frost & Sullivan analysis

Current Treatment Options and Unmet Clinical Needs for Pterygium

- There is no effective drug launched on the market to treat pterygium globally and in China. Currently, the most common treatment for pterygium that cause visual disturbances is surgical excision. Any off-label drug use is mainly for symptomatic relieve, involving artificial tears, non-preserved lubricant eye ointment or short term anti-inflammatory eye drop, which may arise safety and effectiveness concerns for long-term use and usually adopted in early stages.
- Pterygium may be responsible for a vision-impairing astigmatism even before reaching to the corneal center, and it may persuade the surgeon for an early surgery with the purpose of correcting the patient's refractive error. Various adjuvant therapies, such as beta irritation, mitomycin, anti-VEGF agents and cyclosporine A, have been used in pterygium surgery to decrease the postoperative recurrence. However, the recurrence rate remains high after surgical removal.
- It is difficult to detect pterygium at the early stage, especially for patients without proper awareness of disease prevention and control. Slit-lamp microscope observations and anterior segment photographs taken by ophthalmologists are main methods to detect pterygium. The condition of pterygium is often asymptomatic, especially early in its development. Additionally, the severity of pterygium is mainly based on the subjective evaluation of ophthalmologists. However, due to the lack of primary ophthalmologists, screening for pterygium still faces a huge gap in remote or rural areas with relatively limited medical resources. Therefore, there are unmet clinical needs to develop a drug therapy to reduce pterygium associated hyperemia and relieve relevant symptoms.

Management of Pterygium

Pharmacological intervention

- **Artificial Tears**
- **Non-preserved lubricant eye ointment**

- **Anti-inflammatory eye drops**

Only for symptomatic and temporary use

Surgical intervention

- **Bare sclera:** excise the head and body of pterygium and allow the bare scleral bed to re-epithelialize
- **Conjunctival or conjunctiva-limbal autografting:** obtain an autograft and suture the graft over the exposed scleral bed after excision
- **Amniotic membrane transplantation:** suture the amniotic membrane over the exposed scleral bed after excision

+

Adjunctive therapy:
- Mitomycin-C (MMC), Beta irradiation, Anti-VEGF, Cyclosporine A

Common complications of surgical intervention include subconjunctival hemorrhage, graft edema, graft loss, retraction, graft sliding, and granuloma
Recurrence rate of surgical intervention can vary from 6.7%-88%.
The average reported cost for pterygium surgery and associated treatment ranges from $5,000 to $10,000 in the U.S. and around RMB3,000 in China.

Source: Literature review, Frost & Sullivan analysis

Current Treatment Options and Unmet Clinical Needs for Pterygium

- There is no effective drug launched on the market to treat pterygium globally and in China. Currently, the most common treatment for pterygium is surgical excision. Surgical excision of the pterygium offers a definitive solution by removing the abnormal tissue and also has a long history of clinical practice. While surgical intervention carries risks such as infection or recurrence, these are generally outweighed by its long-term effectiveness in restoring ocular health and appearance.
- Any off-label drug use is mainly for symptomatic relieve, involving artificial tears, non-preserved lubricant eye ointment or short term anti-inflammatory eye drop, which may arise safety and effectiveness concerns for long-term use and usually adopted in early stages.
- Pterygium may be responsible for a vision-impairing astigmatism even before reaching to the corneal center, and it may persuade the surgeon for an early surgery with the purpose of correcting the patient's refractive error. Various adjuvant therapies, such as beta irritation, mitomycin, anti-VEGF agents and cyclosporine A, have been used in pterygium surgery to decrease the postoperative recurrence. However, the recurrence rate remains high after surgical removal.

Method	Treatment Options	Mechanism of Action	Limitation	Cost
Pharmaceuticals	Artificial Tears Non-preserved lubricant eye ointment	• keep the eye lubricated and relieve minor discomfort	• Off-label use • Only for symptomatic and temporary use	/[1]
	Anti-inflammatory eye drops	• inhibit inflammatory reaction		
Surgery	Bare sclera	• excise the head and body of pterygium and allow the bare scleral bed to re-epithelialize	• Common complications of surgical intervention include subconjunctival hemorrhage, graft edema, graft loss, retraction, graft sliding, and granuloma	• $5,000~$10,000 in the U.S • Around RMB3,000 in China
	Conjunctival or conjunctiva-limbal autografting	• obtain an autograft and suture the graft over the exposed scleral bed after excision		
	Amniotic membrane transplantation	• suture the amniotic membrane over the exposed scleral bed after excision		
Adjunctive therapy	Mitomycin-C (MMC), Beta irradiation, Anti-VEGF, Cyclosporine A	• Inhibit neovascular and inflammatory eye conditions		

Note: 1, The off-label drug use is mainly for symptomatic relieve, which shows no minimal therapeutic goods. It is not applicable to calculate the annual cost per patient of off-label drug use, because the drug label doesn't clarify the recommended dosage and duration of its off-label use.

Source: Drug Discovery Today, Frost & Sullivan Analysis

Recurrence Rate Analysis of Pterygium Surgery

- Conjunctival or conjunctiva-limbal autografting with intraoperative and postoperative mitomycin (MMC) remains the preferred method because it provides a lower recurrence rate and better cosmetic result. Recurrence rate of this method was reported to be within the range of 0-9% and 6.5-21%, with intraoperative and postoperative MMC respectively. Wide range of recurrence rate may result from different preoperative features and patient selection of previous studies. Young age has been reported to be associated with a higher recurrence rate. Other features may include pterygium size, ethnicity and gender. Individual surgery results may differs due to surgeons' experience.

Surgical Technique	Advantages	Drawbacks	Adjunctive Therapy	Recurrence Rate (%)
Bare sclera	• Easy to perform • Short surgical time	• High recurrence rates • Possible discomfort and pain (related to pterygium extension)	None	24%-89%
			Beta irradiation	0-52%
			Intraoperative subconjunctival bevacizumab injection	57.6%
			Postoperative topical bevacizumab	0-41.7%
			Postoperative MMC injection	0-38%
			Intraoperative MMC	3%-38%
Conjunctival or conjunctiva-limbal autografting	• Low recurrence rates • Easy to perform (in comparison with transpositional flap) • Good cosmetic results	• Long surgical time (especially in suture-assisted fixation) • Possible discomfort and pain (especially in suture-assisted fixation) • Risk of graft loss/displacement • Difficulty in covering of large defects	None	1%-40%
			Subconjunctival bevacizumab injection	0-18.8%
			Postoperative topical cyclosporine 0.05%	3.4%-7.5%
			Postoperative MMC	6.5%-21%
			Intraoperative MMC	0-9%
Amniotic membrane	• Easier to perform (in comparison with conjunctival autografting) • Useful to cover large defects • Conjunctival sparing • Short surgical time • Can be applied in patients with insufficient conjunctiva	• Higher recurrence rates (in comparison with conjunctival autografting) • Risk of graft loss/displacement • Possible discomfort and pain (suture-assisted fixation)	None	2.6%-42.3%
			Intraoperative MMC	16%-21%

Source: Drug Discovery Today, Frost & Sullivan Analysis

Competitive Landscape of Pterygium

- There is no drug launched on the market to treat pterygium globally and in China. The table below listed the current clinical-staged pipeline of pterygium therapies globally and in China. Both CBT-001 and AG-86893 are nintedanib (MKI). The active compound of RMP-A03 is not disclosed. All the listed pterygium pharmaceutical candidates are administrated by topical routes.
- Ofev (nintedanib), manufactured by Boehringer Ingelheim, is the reference listed drug for CBT-001. Ofev, initially approved by FDA in 2014, is indicated for the treatment of idiopathic pulmonary fibrosis, chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype, and Slowing the rate of decline in pulmonary function in patients with systemic sclerosis-associated interstitial lung disease. Nintedanib is a small molecule that inhibits multiple receptor tyrosine kinases (RTKs) and non-receptor tyrosine kinases (nRTKs). Nintedanib inhibits the following RTKs: platelet-derived growth factor receptor (PDGFR) α and β, fibroblast growth factor receptor (FGFR) 1-3, vascular endothelial growth factor receptor (VEGFR) 1-3, colony stimulating factor 1 receptor (CSF1R), and Fms-like tyrosine kinase-3 (FLT-3). These kinases except for FLT-3 have been implicated in pathogenesis of interstitial lung diseases (ILD). Nintedanib binds competitively to the adenosine triphosphate (ATP) binding pocket of these kinases and blocks the intracellular signaling cascades, which have been demonstrated to be involved in the pathogenesis of fibrotic tissue remodeling in ILD. Nintedanib, pharmacologically targeting the angiogenic and fibrotic pathogenesis of pterygium, has the potential to eliminate or postpone the need for surgery.
- In China, Ofev has entered the National Reimbursement Drug List-B, the end user price of which has been decreased to around RMB 4,500 for a supply of 30 capsules. In the U.S., the listed price of Ofev oral capsule is around $13,695 for a supply of 60 capsules. The end user price of Ofev varies from $0 to $243 per capsule depending on patient's medical insurance plans, treatment plans and different pharmacies.

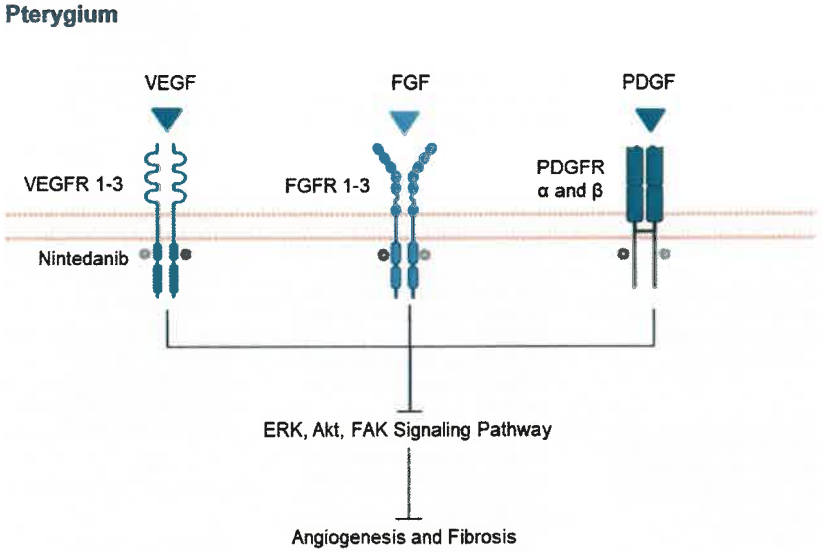
Drug Name/Code	Company	Region	Phase	Indications	Active Compound	Mechanism	First Posted Date
CBT-001	Cloudbreak Therapeutics, LLC	US	Phase 3	Prevention of pterygium progression and reduction of conjunctival hyperaemia	Nintedanib	Tyrosine kinase inhibitor	2022-07-13
		China	Phase 3	Prevention of pterygium progression and reduction of conjunctival hyperaemia			2023-09-04
AG-86893	Allgenesis Biotherapeutics Inc.	Australia	Phase 2	Prevention of pterygium progression and reduction of conjunctival hyperaemia	Nintedanib	Tyrosine kinase inhibitor	2018-05-23
RMP-A03	Suzhou Raymon Pharmaceuticals Company, Ltd.	US	Phase 2	Prevention of pterygium progression and reduction of conjunctival hyperaemia	NA	NA	2023-04-03

*Competitive landscape as of 2025/05/30

Note: 1, The phase 2 trial of RMP-A03 is not yet recruiting. And the clinical site is not available.
2, three drug candidates indicated for pterygium are expected to be approved and launched in 2026,2029 and 2036respectively.
Source: CDE, ClinicalTrials.gov, Frost & Sullivan Analysis

Mechanism of Nintedanib in the Treatment of Pterygium

- Nintedanib competitively binds to the intracellular adenosine triphosphate (ATP)-binding site of fibroblast growth factor receptors (FGFRs), platelet-derived growth factor receptors (PDGFRs) and vascular endothelial growth factor receptors (VEGFRs) resulting in blockage of the autophosphorylation of these receptors and the downstream signaling cascades, which have been demonstrated to be involved in the the angiogenic and fibrotic pathogenesis of pterygium.



Source: Literature Review, Frost & Sullivan Analysis

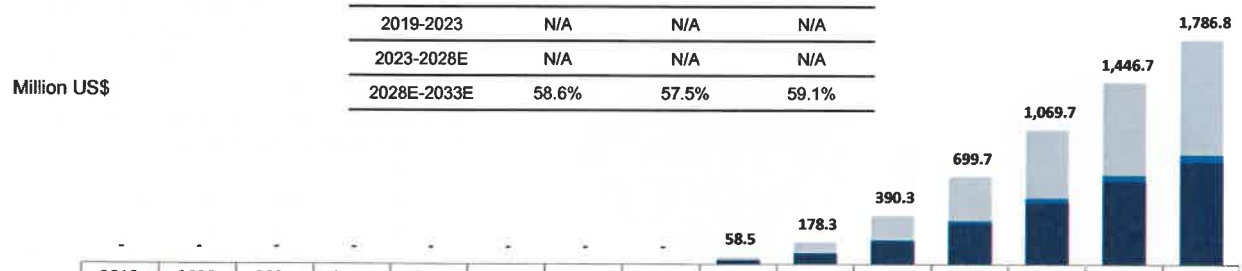
Historical and Forecasted Market Size of Global Pterygium Drug Therapies, 2019-2033E

- The market size of global pterygium drug therapies will start to expand in 2027, and is estimated to reach US$178.3 million in 2028. And it has a market potential of US$1,786.8 million until 2033 with a CAGR of 58.6% from 2028 to 2033. U.S. pterygium drug therapies market size is expected to increased from US$84.2 million in 2028 to US$815.0 million in 2033 with a CAGR of 57.5% from 2028 to 2033. China pterygium drug therapies market size is expected to increased from US$2.1 million in 2028 to US$59.9 million in 2033 with a CAGR of 59.1% from 2028 to 2033.

Historical and Forecasted Market Size of Global Pterygium Drug Therapies, 2019-2033E

Period	CAGR		
	Global	U.S.	China
2019-2023	N/A	N/A	N/A
2023-2028E	N/A	N/A	N/A
2028E-2033E	58.6%	57.5%	59.1%

Million US$



	2019	2020	2021	2022	2023	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E
Global	-	-	-	-	-	-	-	-	58.5	178.3	390.3	699.7	1,069.7	1,446.7	1,786.8
RoW		-	-	-	-	-	-	-	25.8	88.2	195.0	352.3	541.8	736.0	911.9
China	-	-	-	-	-	-	-	-	2.1	5.9	12.9	23.3	35.7	48.4	59.9
U.S.	-	-	-	-	-	-	-	-	30.6	84.2	182.3	324.1	492.2	662.3	815.0

Source: Literature Review, Expert Interview, and Frost & Sullivan Analysis

Growth Drivers and Entry Barriers of Pterygium Drug Therapy Market

Expanding Patient Pool

- Pterygium is a common eye condition that affects millions of people worldwide. As the prevalence of pterygium continues to rise, the demand for effective pharmaceutical treatments is also increasing. Global prevalence of pterygium increased from 919.4 million in 2018 to 964.5 million in 2022 with a CAGR of 1.2%. It is expected to continue to increase to 1,021.2 million in 2027 and 1,077.1 million in 2032 with a CAGR of 1.1% and 1.1% from 2022 to 2027 and from 2027 to 2032 respectively. This presents a significant opportunity for pharmaceutical companies to develop and commercialize new treatments for pterygium, as the demand for effective therapies is likely to increase in tandem with the growing number of affected individuals.

Unmet Medical Needs

- Increasing awareness about eye health and the availability of treatment options are also contributing to the growth of the pterygium pharmaceuticals market. As more people become aware of pterygium and its potential impact on vision and quality of life, there is a growing demand for effective pharmaceutical interventions to manage this condition. This heightened awareness is driving patients to seek effective treatment for pterygium, creating a larger patient pool for pharmaceutical companies to target with their products. A Brazilian Amazon region survey stated that the prevalence of pterygium as cause of visual impairment and blindness was 14.3% and 3.9%, respectively.

Necessity of Early-stage Medication

- There is no effective drug therapy, approved to treat pterygium globally. Currently, the most common treatment for pterygium is surgical excision. Any off-label drug use is mainly for symptomatic relieve, which may arise safety and effectiveness concerns for long-term use. However, the recurrence rate of modern surgery excision can be as high as around 10%. By addressing pterygium in its early stages, patient outcomes can be significantly enhanced, with reducing need for more invasive interventions.

R&D as a Barrier to Entry

- The R&D obstacles of developing drug therapies indicated for pterygium lie in identifying and developing appropriate (i) modality to target pathogenesis of the disease, (ii) drug delivery method and (iii) formulation for the delivery. Developing and obtaining patents for the method of use by inhibiting relevant growth factors to prevent pterygium growth and nano-emulsion as an eye drop to treat pterygium, based upon the fibrovascular nature of disease create a greater barrier for small or emerging businesses to enter the pterygium drug therapy market.

Source: Frost & Sullivan Analysis

Overview of Juvenile Myopia

- Juvenile myopia refers to the rapid progress of myopia in children and adolescents. As children aged 5-19 are at a critical stage of visual development, myopia develops rapidly at this stage. Different from refractive myopia caused by ciliary muscle fatigue and ciliary contraction, juvenile myopia is characterized by rapid increase of the axis length (AL) and growth of the eyeball year by year. Even if the ciliary muscle is healthy, it cannot accurately image. Juvenile myopia can lead to high myopia and degenerative changes of the eyeball, and patients may suffer retinal choroidal atrophy, choroidal neovascularization, macular hole, retinal detachment, etc., which will cause severe damage to vision and is the leading cause of blindless. Therefore, children and adolescents with moderate to high myopia are in urgent need to effectively control the rapid increase of AL and prevent complications.

Progressive Myopia

Moderate to high myopia

Axis length increase

Juvenile Myopia

- ***Genetic factors:*** Genetic evidence suggests that the prevalence of myopia in children increases with the number of myopic parents.
- Most cases of myopia may have defects involved in the control of structural proteins.
- ***Environmental factors:*** Urbanization and educational attainment may contribute to the development of myopia.
- Distance work has been identified as a risk factor, but the correlation is weak and difficult to quantify.

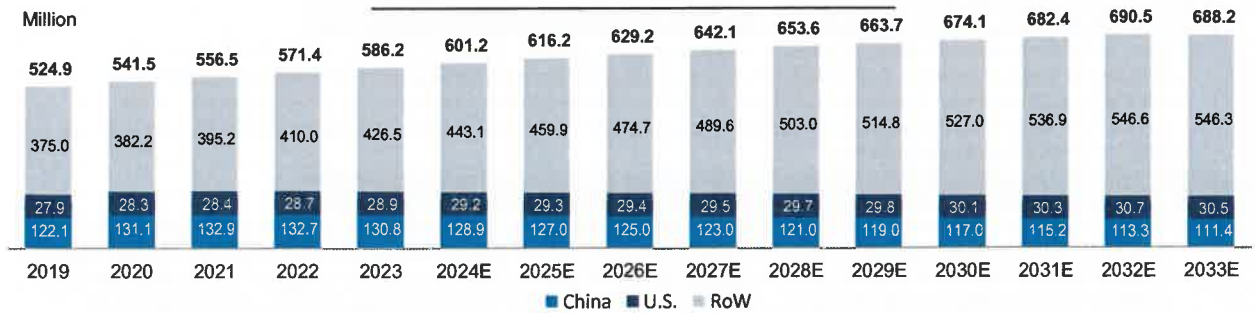
Source: Literature Review, Frost & Sullivan Analysis

Global Prevalence of Juvenile Myopia, 2019-2033E

- Global prevalence of juvenile myopia increased from 524.9 million in 2019 to 586.2 million in 2023 with a CAGR of 2.8%. It is expected to continue to increase to 653.6 million in 2028 and 688.2 million in 2033 with a CAGR of 2.2% and 1.0% from 2023 to 2028 and from 2028 to 2033 respectively.
- Prevalence of juvenile myopia in the U.S. increased from 27.9 million in 2019 to 28.9 million in 2023 with a CAGR of 1.0%. It is expected to continue to increase to 29.7 million in 2028 and 30.5 million in 2033 with a CAGR of 0.5% and 0.6% from 2023 to 2028 and from 2028 to 2033 respectively.
- Prevalence of juvenile myopia in China increased from 122.1 million in 2019 to 130.8 million in 2023 with a CAGR of 1.7%. It is expected to decrease to 121.0 million in 2028 and 111.4 billion in 2033 with a CAGR of -1.5% and -1.6%, from 2023 to 2028 and from 2028 to 2033 respectively.

Global Prevalence of Juvenile Myopia, 2019-2033E

Period	CAGR		
	Global	U.S.	China
2019-2023	2.8%	1.0%	1.7%
2023-2028E	2.2%	0.5%	-1.5%
2028E-2033E	1.0%	0.6%	-1.6%

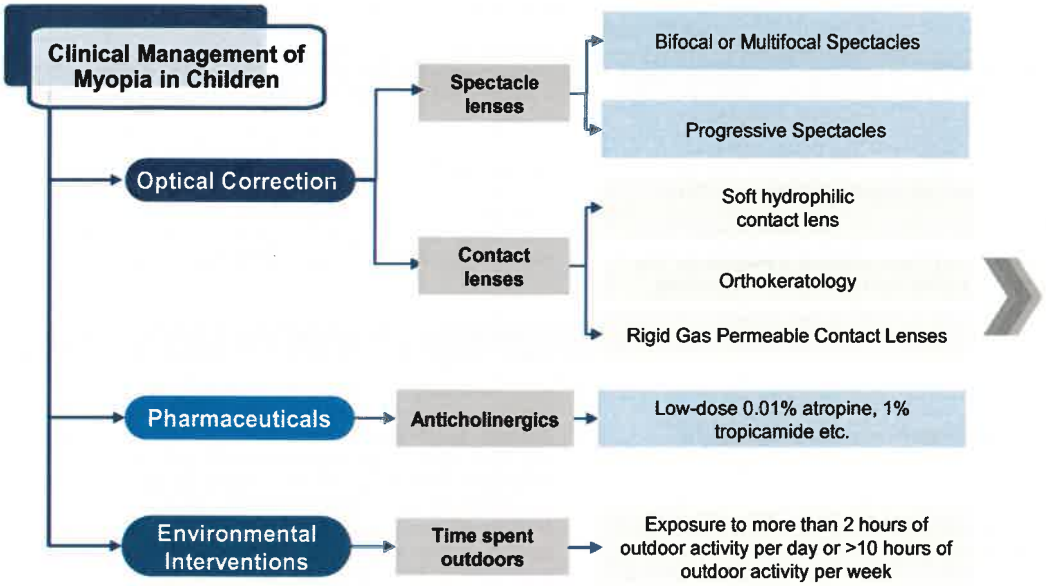


Note: The jump in prevalence with juvenile myopia in 2020 is due to an increase in the overall juvenile population in 2020, which NBS says is due to the fact that the 2019 population numbers are based on a sample made from 2010 census data and therefore differ significantly from the 2020 census data.

Source: Literature Review, Expert Interview, Frost & Sullivan Analysis

Current Treatment Paradigm of Myopia in Children and Adolescents

- Slowing progression of myopia has a considerable public health impact, and thus the field of myopia control has been developed rapidly. Treatments proposed to prevent or reduce the progression of myopia include optical correction, use of antimuscarinic eyedrop, contact lenses, and other approaches.
- In China, atropine is the only anticholinergic got recommended in the guideline. Atropine is the currently available anticholinergic drug for off-label use in myopia treatment with demonstrated consistent efficacy.



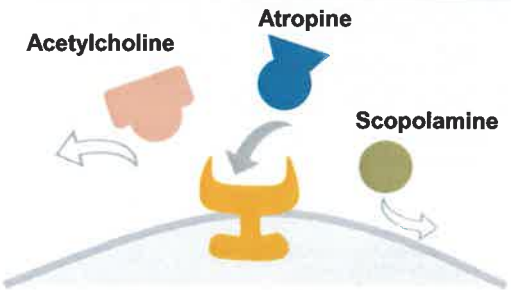
In China, the standard treatment for myopia in children are spectacles. At the same time, there is emerging evidence that low-concentration atropine and outdoor time can effectively minimize the progression of myopia.

Source: Literature Review, Frost & Sullivan Analysis

Mechanism of Action of Atropine

- Currently, atropine is the only medication that has been demonstrated to be consistently effective in slowing myopic progression. Higher concentrations of atropine such as 1% or 0.5% have been show to be very effective, but the high rate of photophobia side-effect has been associated with high dropout rate. In the past years, publications from Asia have reported of low-concentration atropine in myopia control while having lower rates of adverse effects. And low dose atropine for myopia control has largely been sourced off-label by eyecare professionals. Therefore, there have been renewed interests in the clinical implementation of atropine for myopia retardation.

Potential Mechanism of Action



- The exact mechanism of topical atropine is still not known, Currently there are three possible mechanisms of action.
- Atropine targets biological receptors in both the retina and sclera, to curtail myopia progression .

MOA1

- Binding of atropine to the muscarinic receptors of amacrine cells **in retina** increases the **release of dopamine**, which is an inhibitory chemical mediator for eye growth

MOA2

- **Reduction of γ-aminobutyric acid levels** was shown to be downregulated following the atropine treatment in myopia-induced mice

MOA3

- Scleral fibroblast cells carry all five muscarinic receptors on their cell membrane and binding to atropine may interfere with **scleral remodeling**

Source: Literature Review, Frost & Sullivan Analysis

The Current Treatment Methods and Limitations for Myopia and Progressive Myopia

- The current treatment methods for progressive myopia are optical correction (Spectacle Lens and contact lens), anticholinergics therapy (low dose Atropine sulfate eye drops) and refractive surgery (non-laser surgery and laser surgery, laser surgery includes excimer laser and femtosecond laser). Laser-assisted in situ keratomileusis (LASIK) is the best known and most commonly performed refractive surgery. Around 60% of the patients who met the criteria are eligible for refractive surgery. Refractive surgery, is a surgical procedure that reshapes the cornea to improve vision and reduce the need for spectacle or contact lenses. It is typically recommended for adults with stable vision who are looking for a long-term solution to their vision problems. One of the primary benefits of LASIK is a short procedure that results in lasting vision improvement.

Limitations

Optical Correction

Spectacle Lenses

- **Myopia exacerbation.** Because the corneal is aspherical, peripheral vision will fall behind the retina and the axial length increases. Thus, myopia will exacerbate.
- **Discomfort:** Glasses with high diopter strength is heavy and they will squeeze noses and ears which may cause allergies. Safety issues: The lens and frame may scratch face under the scene of intense exercise etc.
- **Poor aesthetics.**

Contact lens

- **Inconvenience:** Patients need to clean and disinfect contact lens before wearing.
- Long time wearing, or non-fit contact lens **may cause corneal hypoxia.**
- **Potential risk of infection and complications:** the contact lens are contaminated, there will be deposit in the lens which will cause damage to eyes and induce complications.
- **High expense.**

Pharmaceutical

- **Adverse reaction.** Low concentration atropine may also have adverse reactions including photophobia, vision blurring, changes in intraocular pressure (IOP), rebound effect, and local allergy. Among them, photophobia is the most common one. Also, there may be systematic adverse reaction.

Refractive Surgery

- **Refractive surgery has age limit.** Whether patients are qualified for surgery depends on corneal thickness, pupil diameter, eye disease history, etc.
- Refractive surgery can only be performed once, and it is **possible of future myopia.** Also, myopia progression aging, and presbyopia will all offset the surgery effect.
- **High surgery expense.** Most healthcare insurance plans don't cover refractive surgery. The average cost of LASIK eye surgery is $4,400 and RMB4,000-6,000 for two eyes in the U.S. and China, respectively.

Source: Literature Review, Frost & Sullivan Analysis

Treatment Paradigm of Juvenile Myopia

- Treatments proposed to prevent or reduce the progression of myopia and the current treatment methods for juvenile myopia are listed in the chart below.

	Method	Subtype	Indication	Limitations	Annual Cost per Patient in the U.S., US$	Annual Cost per Patient in China, RMB
Lifestyle Intervention	**Environmental Interventions**	• Time spent outdoors • Exposure to more than 2 hours of outdoor activity per day or >10 hours of outdoor activity per week	Juvenile myopia	NA	NA	NA
Pharmaceuticals Intervention	**Anticholinergics**	• Low-dose 0.01% atropine • 1% tropicamide etc.	• slow the progression of myopia in children aged from 6 to 12 years, have a refraction of **-0.75 D to -4.00 D**	• **Adverse reaction.** Including photophobia vision blurring, changes in intraocular pressure (IOP), rebound effect, and local allergy.	~660	~3,600
Optical Correction	**Spectacle lenses**	• Bifocal or Multifocal Spectacles	• myopia with fast refractive progression	• **Myopia exacerbation.** The corneal is aspherical, peripheral vision will fall behind the retina and the axial length increases. • **Discomfort** • **Poor aesthetics**	200 - 400	500 – 2,000
		• Progressive Spectacles			150 - 250	200 – 2,000
	Contact lenses	• Soft hydrophilic contact lens	• slow the progression of myopia in children aged 8-12 at the initiation of treatment, have a refraction of -0.75 D to -4.00 D (spherical equivalent) with ≤ 0.75 diopters of astigmatism	• Inconvenience • Long time wearing, or non-fit contact lens may cause corneal hypoxia. • Potential risk of infection and complications • High expense	200 – 1,000	1,000 - 7,000
		• Orthokeratology	• Slow the progression of myopia in children with up to about -6.00D of myopia and no more than -1.75D of astigmatism		1,000 - 4,000	4,000 - 15,000
		• Rigid Gas Permeable Contact Lenses	• correction of refractive error (myopia, hyperopia, presbyopia and/or astigmatism) in aphakic and non-aphakic persons with non-diseased eyes		~200	2,000 – 4,000
Refractive Surgery	**Laser Surgery**	• Excimer laser • Femtosecond laser	• Stable eye prescription for normally -0.5 D to -8.0 D myopia	• Refractive surgery has age limit. • Refractive surgery can only be performed once, and it is possible of future myopia. Also, myopia progression aging, and presbyopia will all offset the surgery effect • High surgery expense	~4,400	4,000-6,000

Note: The annual cost of spectacle lenses and contact lenses can significantly vary depending on various factors such as the brand, quality of lenses, additional coatings (like anti-glare or blue light protection), replacement frequency, and the place of purchase (online, retail store, optometrist's office).

Source: China Ministry of Education, Eye (Lond), NVISION, Frost & Sullivan Analysis

Comparison of Interventions to Slow Progression of Myopia

- While spectacles remain the mainstay of vision correction in myopic children, it effect in delaying the progression of myopia is still limited. Compared to spectacles, orthokeratology and atropine lead to considerable reduction in myopia progression in terms of refraction change and axial change.
- In the recent years, around 90% of juvenile myopia patients have worn spectacle lenses in most of the countries, involving the U.S. and in China. The high penetration rate will maintain in the future. The penetration rate of orthokeratology have reached around 5% and 2% in the U.S. and China respectively. In the next 10 years, the penetration rate of orthokeratology is expected to reach over 15% and 10% in the U.S. and China respectively.
- It should be noted that for all comparisons, the stated values represent the differences in final refraction or axial elongation between the stated intervention and the single vision spectacle lenses. In terms of refractive error, a positive mean difference therefore indicates that the stated intervention is better. In terms of axial length, a negative mean difference indicates the first intervention is better.

	Subtypes	Mean difference in refraction change, D/yr	Mean difference in axial change, mm/yr	Shortcomings	Strengths
Spectacle lenses	Bifocal spectacle lens	0.26	-0.08	• Distort vision at the edge of the lens if astigmatism exists	• 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	• Children are less likely to follow hygiene and safety practice • May induce problems related to cornea, eyelid and dryness of the eye • Relatively expensive	• 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-dose(1% or 0.5%)	0.68	-0.22	• Long term high-dose atropine use may have potential risks including, local allergic and systemic reactions • Possible myopic rebound if atropine is stopped suddenly	• Clear effects in myopia control, better outcome than spectacle lenses and contact lenses
	Moderate-dose(0.1%)	0.53	-0.22		
	Low-dose(0.01%)	0.53	-0.15		

1. Huang J, Wen D, Wang Q, et al. Efficacy Comparison of 16 Interventions for Myopia Control in Children: A Network Meta-analysis. Ophthalmology 2016;123(4):697–708.

Source: Ophthalmology, Frost & Sullivan Analysis

Competitive Landscape of Marketed Anticholinergics in China

- Tropicamide has been approved to dilate pupils for diagnostic procedures in many countries and have reported to be an effective cycloplegic agent in children with pseudomyopia. Raceanisodamine has been approved to treating pseudomyopia. The two pharmaceutical agents, which approved around 1990 by NMPA, are relatively outdated, and may cause side effects such as allergy, elevated IOP and nausea.
- Pseudomyopia is a condition where a person experiences blurred vision due to excessive focusing or accommodative spasm, rather than the eyeball being too long or the cornea being too curved as in myopia. If the factors contributing to pseudomyopia are not addressed and the eyes continue to experience strain from excessive near work, there is a risk that it could lead to the development or progression of true myopia over time.
- Since 2019, 0.01% atropine eyedrops has been applied as in-house preparation to slow down the progression of myopia in China. According to Shenyang Xinqi Pharmaceuticals, the sales revenue of its atropine sulphate eyedrops prepared by Sinqi Eye Hospital in 2022 has reached RMB400 million, which represented at least 100 thousand juvenile myopia patients has adopted atropine eye drops. Till the end of 2023, there is no atropine drug therapy have been approved in the U.S. and China, the historical proportion of atropine drug therapy is nil. The penetration rate of atropine among juvenile myopia patients group in the U.S. and China is expected to reach approximately 20% and 10% in 2033, respectively.

Generic Name	Representative Product		Indications	Number of Other Manufacturers	Earliest NMPA Approval Time	Annual Cost per patient, RMB
	Brand Name	Manufacturer				
Anticholinergics Eye Drops						
Tropicamide	N.A.	济民可信/Jemincare	• Induce mydriasis (dilation of the pupil) for diagnostic procedures • Pseudomyopia	1	1989	~9
Raceanisodamine	N.A.	五景药业/Wuhan Wujing Medicine	• Pseudomyopia	7	1990	~18
Atropine Sulphate	Meioupin	沈阳兴齐/Shenyang Xinqi	• Juvenile myopia	0	2024	3,625

Note: Tropicamide and raceanisodamine are not recommended to use over 3 months.

Source: NMPA, Frost & Sullivan Analysis

Comparation of Aqueous and Non-aqueous Atropine Drug Therapy

- Compared with aqueous type, non-aqueous atropine eye drops have advantages including better stability, lower incidence of side effect, and higher bioavailability.

Aqueous Atropine drug therapy

Advantage -

- ***Effective hydration:*** Aqueous eye drops are formulated to mimic the natural composition of tears, providing effective hydration to the eyes and more easier to distribute evenly across the ocular surface.
- ***Comfortable application:*** Aqueous eye drops are typically well-tolerated by most individuals and can be applied easily without causing discomfort or stinging.

Disadvantage -

- ***Degradation:*** Atropine is an ester drug. Due to the existence of an ester bond in its structure, aqueous atropine solution tends to be hydrolyzed at neutral pH (6.6-7.8), which most ophthalmic solutions are close to, and relatively more stable at low pH (2-4) in the aqueous formulation. The low pH formulations are known to cause irritation to the eyes. Aqueous atropine eye drops are unstable and easily decomposed, which could potentially affect the efficacy and safety of eye drops.
- ***Expcipients:*** Aqueous eyedrops typically require additional excipients, including buffers and salts, viscosity builders and surfactants, which may increase local adverse events, such as stinging, burning and excessive tearing.
- ***Preservatives:*** The buffering agent in atropine eye drops may promote microbe growth. Preservatives are commonly used to counter this issue, but prolonged use may harm the cornea. An alternative option is to use preservative-free formulations or single-use packaging or filtering systems, albeit at a higher cost.

Non-aqueous Atropine Drug therapy

Advantage –

- ***Higher stability:*** The degradation of atropine is significantly reduced in non-aqueous solutions due to the absence of free hydroxide ions. This reduction in degradation results in a decrease in the production of impurities, which ultimately enhances the efficacy and safety of atropine.
- ***No preservatives are required:*** Atropine in a non-aqueous solution can lower bacterial production without the need for preservatives or single-dose packaging.
- ***Lower dosage:*** Non-aqueous atropine requires a lower dose than aqueous atropine, which can reduce the risk of adverse effects.
- ***Higher bioavailability:*** Low volume drop, low surface tension when drug contact with eye surface, increase drug's residence time.

Disadvantage –

- ***Potential for blurred vision:*** Non-aqueous eye drops may have a tendency to cause temporary blurred vision upon application.
- ***Limited compatibility with contact lenses:*** Individuals who wear contact lenses may find non-aqueous eye drops to be less compatible with their lenses, leading to potential interactions or discomfort.

Source: Literature Review, Frost & Sullivan Analysis

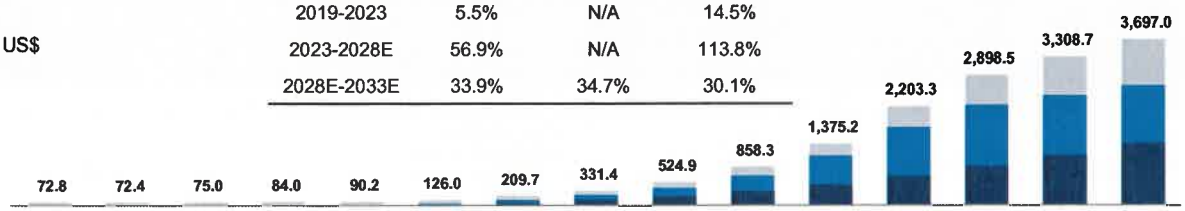
Historical and Forecasted Market Size of Global Juvenile Myopia Drug Therapies, 2019-2033E

- Global juvenile myopia drug therapies market size increased from US$72.8 million in 2019 to US$90.2 million in 2023 with a CAGR of 5.5%. It is expected to continue to increase to US$858.3 million in 2028 and US$3,697.0 million in 2033 with a CAGR of 56.9% and 33.9% from 2023 to 2028 and from 2028 to 2033 respectively.
- U.S. juvenile myopia drug therapies market size is expected to increased from US$308.4 million in 2028 to US$1,370.0 million in 2033 with a CAGR of 34.7% from 2028 to 2033 .
- China juvenile myopia drug therapies market size increased from US$3.0 million in 2019 to US$5.2 million in 2023 with a CAGR of 14.5%. It is expected to continue to increase to US$347.9 million in 2028 and US$1,299.0 million in 2033 with a CAGR of 113.8% and 30.1%, from 2023 to 2028 and from 2028 to 2033 respectively.

Historical and Forecasted Market Size of Global Juvenile Myopia Drug Therapies, 2019-2033E

Period	CAGR		
	Global	U.S.	China
2019-2023	5.5%	N/A	14.5%
2023-2028E	56.9%	N/A	113.8%
2028E-2033E	33.9%	34.7%	30.1%

Million US$



	2019	2020	2021	2022	2023	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E
Global	72.8	72.4	75.0	84.0	90.2	126.0	209.7	331.4	524.9	858.3	1,375.2	2,203.3	2,898.5	3,308.7	3,697.0
RoW	69.8	69.5	71.7	79.2	85.0	90.2	95.6	101.2	134.6	202.0	272.7	463.5	666.3	860.6	1,028.0
China	3.0	2.9	3.3	4.8	5.2	35.8	68.6	115.9	195.8	347.9	643.6	1,094.0	1,367.6	1,339.1	1,299.0
U.S.	-	-	-	-	-	-	45.5	114.2	194.5	308.4	459.0	645.7	864.7	1,108.9	1,370.0

Source: Literature Review, Expert Interview, and Frost & Sullivan Analysis

Global Competitive Landscape of Atropine Drug Therapy Indicated for Progressive Myopia

- There is currently no approved atropine drug therapy indicated for juvenile myopia in the United States. Across the globe, 3 atropine drug therapy has been approved for slowing the progression of myopia. Eikance 0.01% eye drop approved by Australia Therapeutic Goods Administration (TGA) is the first atropine for children aged 4 to 14 years on March 19th, 2021, as a treatment to slow the progression of myopia. Meioupin 0.01% eye drop was approved by NMPA in China for children aged 6-12 years as a treatment to slow the progression of myopia on March 5th, 2024. Ryjusea 0.025% eye drop was first approved in Japan for children aged 3 to 14 years as a treatment to slow the progression of myopia on December 27th, 2024, and in the European Union on June 5th, 2025. However, the limited shelf life due to atropine's instability in the aqueous formulation has prevented aqueous atropine eye drops from being widely recognised as a treatment option. The shelf lifetime of approved Eikance and Meioupin are 36 months and 18 months respectively. The listed price of Eikance in Australia is around AU$40. The annual cost per patient is estimated to be around AU$480 per patient. In the U.S., diluted atropine eye drops are often sold directly by eye care professionals to their patients for approximately $58.3 to $91.7 for a monthly supply ($700 to $1,100 for an entire year supply).

Formulation	Drug Name/Code	Company	Region	Phase	Dosage[1]	Indications	First Posted/Approved Date
Non-aqueous	CBT-009	Cloudbreak Therapeutics, LLC/Novotech (Australia) Pty Limited	Australia	Phase 1/2	NA[2]	Juvenile myopia	2022-05-13
Aqueous	**Eikance**	**Aspen Pharmacare Australia Pty Ltd**	**Australia**	**Approved**	**0.01%**	**Juvenile myopia**	**2021-03-19**
	Ryjusea	**Santen Pharmaceutical Co., Ltd.**	**Japan/EU**	**Approved**	**0.025%**	**Juvenile myopia**	**2024-12-27**
	NVK-002	Vyluma, Inc./Syneos Health/Nevakar, Inc.	US	NDA	0.01%	Juvenile myopia	/
	SYD-101	Sydnexis, Inc.	US	Phase 3	0.01%/0.03%	Juvenile myopia	2019-04-18
	Atropine	Bausch & Lomb Incorporated	US	Phase 3	0.01%	Juvenile myopia	2019-05-08
	OT-101	Ocumension (Hong Kong) Limited/ORA, Inc./Statistics & Data Corporation	US	Phase 3	0.01%	Juvenile myopia	2021-02-25
	Atropine Sulfate	LitePharmTech Co., Ltd.	Korea	Phase 3	NA	Juvenile myopia	2022-09-06
	Alleance®	Laboratorios Sophia S.A de C.V.	NA	Phase 3	0.01%	Juvenile myopia	2024-04-29
	SHJ002	Sunhawk Vision Biotech, Inc.	Taiwan	Phase 2	NA	Juvenile myopia	2024-08-30
	BHVI	Hai Yen Eye Care/Brien Holden Vision Institute	Vietnam	Phase 1/2	0.02%	Juvenile myopia	2020-03-10
	IVMED-85	iVeena Delivery Systems, Inc.	NA	Phase 1/2	NA	Juvenile myopia	2023-03-09

Note: 1, Dosage of approved atropine drug therapy refers to the dosage approved by each regulatory authority. Dosage of atropine drug therapy at clinical stage refers to the dosage investigated under each clinical trial.
2, NA means public information is not available.

Source: ClinicalTrials.gov, Frost & Sullivan Analysis

China Competitive Landscape of Atropine Drug Therapy Indicated for Progressive Myopia

- The table below lists the current clinical-staged pipeline of progressive myopia therapies in China.

Formulation	Drug Name/Code	Company	Phase	Dosage	Indications	First Posted Date/Approved Date
Aqueous	**Meioupin**	**Shenyang Xinqi Pharmaceutical Co.,Ltd.**	**Approved**	**0.01%**	**Juvenile myopia**	**2024-03-12**
	HR19034	Chengdu Suncadia Pharmaceuticals Co., Ltd.	NDA	NA	Juvenile myopia	/
	NVK-002	Zhaoke Ophthalmology Ltd	NDA	NA	Juvenile myopia	/
	NA	Shenyang Xinqi Pharmaceutical Co.,Ltd.	Phase 3	0.02%/0.04%	Juvenile myopia	2021-09-27
	OT-101	Ocumension Therapeutics/Lyophilization Technology, Inc	Phase 3	0.01%	Juvenile myopia	2021-12-17
	ARVN002	Arctic Vision Shanghai Biotechnology Co Ltd/Alcami Corporation	Phase 3	0.01%	Juvenile myopia	2022-09-14
	QLM3004	Qilu Pharmaceutical Co Ltd	Phase 3	0.01%/0.02%/0.04%	Juvenile myopia	2023-08-02
	NA	Zhejiang Shapuaisi Pharmaceutical Co., Ltd.	Phase 3	0.02%	Juvenile myopia	2023-11-27
	NA	BrightGene Pharmaceuutical Co.,Ltd	Phase 3	0.01%/0.02%	Juvenile myopia	2024-03-15
	NA	Seefunge Pharmaceutical Technology Co., Ltd.	Phase 3	0.01%/0.02%	Juvenile myopia	2024-11-27
	DE-127	Santen Pharmaceutical Co Ltd	Phase 2/3	0.025%	Juvenile myopia	2022-3-28
	NA	Hangzhou Hels Technology	Phase 2/3	NA	Juvenile myopia	2023-04-23
	DA001	Wuhan Docan Pharmaceutical	Phase 2	NA	Juvenile myopia	2025-01-20
	NA	Aier Health Ophthalmology (Liaoning) Co., Ltd	Phase 1	NA	Juvenile myopia	2022-10-27
	STN1013400	Santen Pharmaceutical Co.,Ltd.	Phase 1	NA	Juvenile myopia	2023-03-27
	DA001	Wuhan Docan Pharmaceutical Co., Ltd.	Phase 1	NA	Juvenile myopia	2023-11-22
	GPN00884	EBE PHARMACEUTICAL CO.,LTD./Grand Pharmaceutical Co.,Ltd.	Phase 1	NA	Juvenile myopia	2024-04-23
	NA	Lepu Medical	Phase 1	0.01%/0.03%	Juvenile myopia	2024-05-10

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

Growth Drivers of Progressive Myopia Drug Therapy Market

Expanding Myopic Population

- Myopia had emerged as a major public health issue throughout the world. The prevalence of progressive myopia, and in particular in East Asia, has markedly increased over the past half-century, partially owing to urbanization, lifestyle changes, and longer study years. **Global prevalence of juvenile myopia increased from 506.1 million in 2018 to 571.4 million in 2022 with a CAGR of 3.1%. It is expected to continue to increase to 642.2 million in 2027 and 690.7 million in 2032 with a CAGR of 2.4% and 1.5% from 2022 to 2027 and from 2027 to 2032 respectively.** The increasing number of myopic children and adolescents generates strong, growing demand for pharmaceuticals targeting slowing progression of myopia in addition to conventional measures and promote the growth of progressive myopia pharmaceutical market.

National Strategy for Myopia Prevention

- It is indicated that myopia might become one of the most common causes of irreversible vision loss in East Asians. With China being the most populous country in the world, the prevalence of myopia in younger generation is of high interest and importance. In 2018, the Ministry of Education released Comprehensive Plan to Prevent Shortsightedness among Children (综合防控儿童青少年近视实施方案), this initiative stated the myopia rate for **primary school students should be below 38%, for middle school students, below 60%, and for high school students, below 70% till 2030**. These policy will raise the awareness of myopia control and facilitate the overall progressive myopia pharmaceutical market.

Proven Efficacy of Atropine Eye Drop

- Currently only a limited number of non-atropine-based drug therapies were approved globally for delaying myopia progression, whose effect in delaying the progression of myopia is still limited. Extensive research has shown atropine eye drop have promising clinical outcome and good profile of tolerance even in a long-term follow-up period. Also, topical low-dose atropine has been used off-label globally for decades and incorporated into the routine management of myopia. Guideline for Appropriate Techniques for the Prevention and Control of Myopia in Children and Adolescents（《兒童青少年近視防控適宜技術指南》）in China has recommended 0.01% atropine eye drop as a therapy added to conventional optical correction. Proven efficacy of the pharmacological agents, combined with its increasingly wider adoption in clinical practice, once been approved, ultimately will sustain the development of the myopia pharmaceutical market.

Source: Frost & Sullivan Analysis

Entry Barrier of Progressive Myopia Drug Therapy Market

R&D as a Barrier to Entry

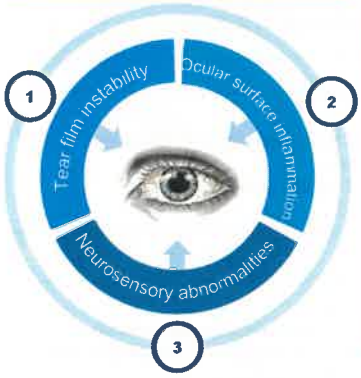
- The R&D obstacles of developing drug therapies indicated for juvenile myopia lie in developing appropriate formulation to overcome the instability of atropine in aqueous formulations, commonly used as commercial eye drop products, to maintain reasonable drug product shelf life. Due to the chemical structure of atropine with internal ester bond linkage, atropine molecule tends to decompose in water. In addition, atropine aqueous formulation tends to cause eye irritation which could have an impact on patient compliance for chronic usage in children and adolescent, the target patient population. Developing and obtaining patents for the non-aqueous formulation as an eye drop to potentially overcome the instability of atropine, and adopting an approved artificial tear as the major excipient of the non-aqueous formulation which could potentially increase the comfort level of eyes, could be an obstacle for new entrants.

Source: Frost & Sullivan Analysis

Overview of Dry Eye Disease (DED)

- Dry eye disease (DED), a multifactorial disease of the tear film, characterized by increased tear film osmolarity, ocular inflammation, deterioration of ocular surface and neurosensory abnormalities, can cause some ocular symptoms such as ocular discomfort and visual disturbance.
- Patients are diagnosed with DED based on their symptoms and tear film stability. Patients with moderate to severe dry eye often complain of significant itching, limitation of daily activities, deterioration in the quality of life and even depression. Patients with clogged meibomian glands and mites have less stable tear film. Therefore, preventing and relieve meibomian glands clog and mites are effective ways of decreasing prevalence of DED.

DED Mechanism



DED Signs

- **Tear film instability**
- **Meibomian glands clog**
- **Demodicid Mites**

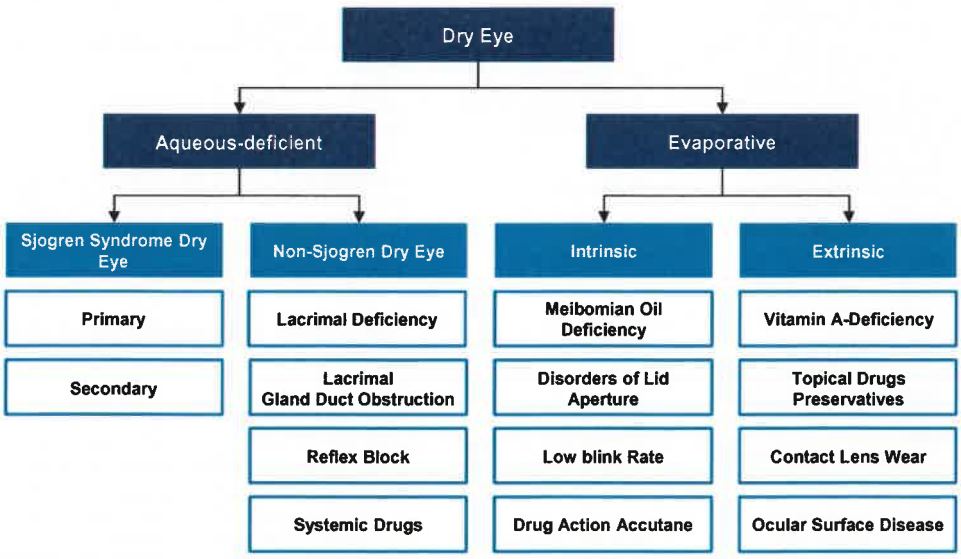
Risk Factors

- Low Blink Rate
- Wide Lid Aperture
- Aging
- Low Androgen Pool
- Systemic Drugs
- Low Relative Humidity
- High Wind Velocity
- Occupational Environment
- Prevalent Use of Digital Devices

Source: Literature Review, AAO, Frost & Sullivan Analysis

Classification of Dry Eye Disease

- The classification system of the DEWS report is the most used one, with aqueous-deficient DED and evaporative dry eye as the major two subtypes. Aqueous-deficient was further classified into Sjogren and non-Sjogren categories. Evaporative dry eye was subclassified into intrinsic and extrinsic categories, and they were further classified as resulting from a range of causes. MGD is the leading cause of evaporative DED.

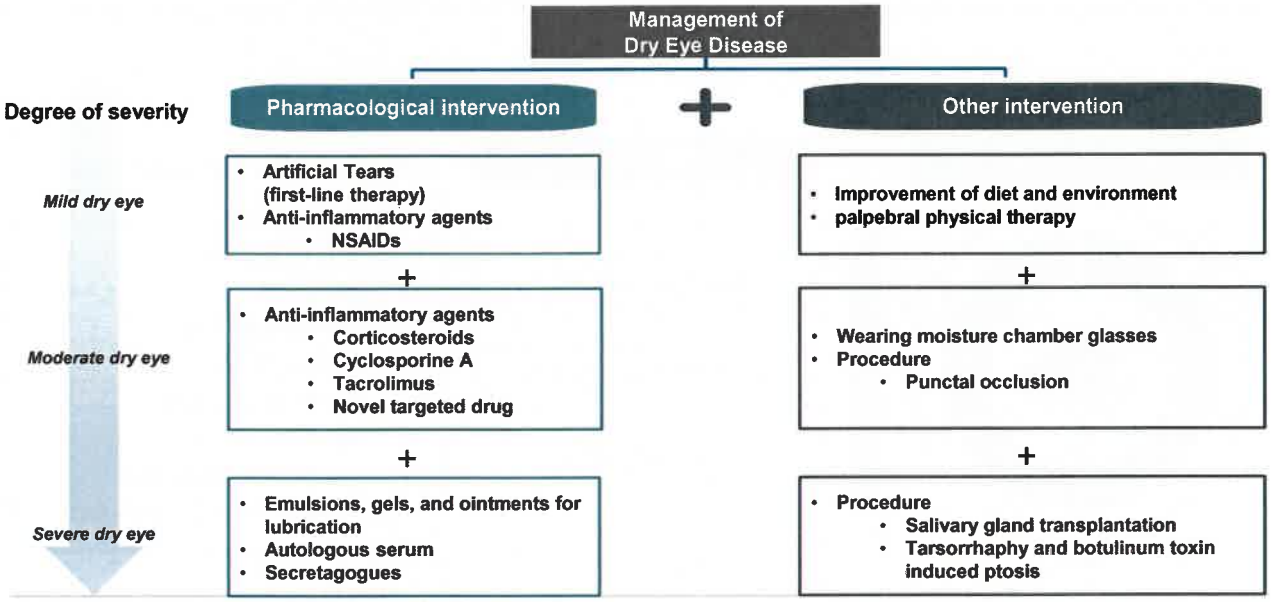


1. Jun, & Shimazaki. (2018). Definition and diagnostic criteria of dry eye disease: historical overview and future directions. Investigative ophthalmology & visual science.

Source: Literature Review, Frost & Sullivan Analysis

Current Treatment Paradigm of DED

- DED is a complex ocular surface multifactorial disease, and inflammation is the major pathological result of such tear film abnormality.
- Artificial tears are essential therapy to symptomatic relief of dry eye and may be subject to further combined use with other drugs when dry eye disease progression to moderate and severe. However, they can provide only temporary symptomatic relieve without addressing the underlying disease causes. For severe DED patients who haven't achieved improvement with the forecasting treatments, surgeries are required.



Source: American Academy of Ophthalmology, Frost & Sullivan analysis

The Current Treatment Methods and Limitations for DED

- Treatment for DED consists of pharmaceuticals, devices and surgery.

Method	Mechanism	Example	Limitation
Pharmaceuticals	**Artificial tears:** replenish tears, lubricate the ocular surface, and dilute the soluble inflammatory mediators on the surface	• Hyaluronic acid sodium eye drops	• Adverse Reaction: temporary blurry vision • Long term use may cause lacrimal gland malfunction
	Anti-inflammatory: inhibit inflammatory reaction and treat immune-related DED.	• Cyclosporine A (immunosuppressant)	• Requires long-term use • The main side effect is ocular surface pain (aching, burning) and irritation
	Corneal repair: Boost the tissue repair and regeneration in the mesoderm and ectoderm	• Recombinant Bovine Basic Fibroblast Growth Factor Eye Drop	• Allergy • Not easy for storage (It should be kept at 2-8℃ and cannot be used after 2 weeks if the eye drop is opened)
	Stimulate mucoprotein secretion: Stimulate the secretion of mucin in ocular epithelial cells and also the secretion of water and lipids	• Diquas (P2Y2 agonist)	• Repeated medication in one day may reduce patient compliance (It should be used 6 times a day according to the manual) • Not easy for storage (The eye drop will expire within 28 days) • Adverse reaction: eye irritation, itching and increasing eye discharge
	Mite removal	• Terpinenol-4 wipe	• Hard to achieve therapeutic effect in short term (The overall treatment period lasts 1-2months)
	Reduce evaporation: Form a monolayer at the air-liquid interface of the tear film which can be expected to reduce evaporation.	• MIEBO (perfluorohexyloctane)	• Adverse reaction: blurred vision (less than 4% of individuals)
Therapeutic device	Therapeutic contact lenses (Soft): For DED with corneal injury	• Purevision 2 bangage lens	• Long time wearing may cause corneal edema and hyperemia
	Therapeutic neurostimulation device	• iTEAR®100, TrueTear	• It may cause nasal irritation and lower the comfort
Surgery	Lacrimal duct embolism: embolize lacrimal duct to keep tears and artificial tears on eyes and relive the symptom	• SmartPlug punctual plug	• Adverse reaction: rejection, local inflammation, redness, pain • Unfit for patients with inflammatory in eyes and patients with poor tear duct conditions (ectropion, narrow) • Induce chronic eye disease. (When the tear duct is blocked for a long time, bacteria and tear fluids gathered in the tear sac and cause chronic dacryadeitis)

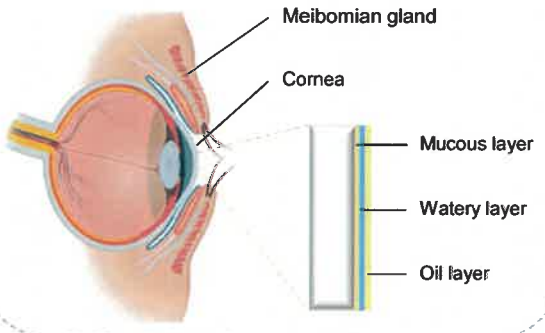
Source: American Academy of Ophthalmology, Frost & Sullivan analysis

Overview of Meibomian Gland Dysfunction (MGD)

- Meibomian glands are large sebaceous glands present in eyelids which secrete lipids that form the superficial layer of tear film to protect evaporation of the aqueous phase. MGD, a chronic diffuse abnormality of the meibomian glands, characterized by terminal duct obstruction along with qualitative or quantitative changes in the glandular secretion. The obstruction of the terminal duct occurs because of hyper keratinization of the duct epithelium and the viscous nature of the meibum. These can result in atrophy and drop out of the meibomian glands, thus decreasing secretion. The symptoms of MGD can be observed in the forms of tear film abnormalities, which can cause evaporative DED, ocular surface irritation, inflammation, or ocular surface disease. MGD is the leading cause of dry eye disease, s meibomian glands play an important role in providing lipids to the tear film, which helps to retard the evaporation of tears from the ocular surface.
- Meibomian gland dysfunction commonly occurs with an eyelid problem called blepharitis, which causes inflamed eyelids and a crusty discharge at the base of the eyelashes.

Meibomian Gland Dysfunction

Meibomian glands are oil glands along the edge of the eyelids where the eyelashes are located.



Risk Factors

- Age
- Diet
- Androgen depletion
- Desiccating stress
- Microbiome alterations
- Wearing contact lens
- Wearing eye makeup

MGD ➤ DED

The tear film is composed of mucous layer, water layer and oil layer, which play an important role in the stability of ocular surface. Changes in the quality or quantity of the tear film composition may lead to reduced stability of the tear film, leading to rapid evaporation of tears, finally inducing in DED. MGD is a contributing factor in 70% to 86% of DED cases globally. DED is a common public health concern with a prevalence rate of near 10% out of total global population, and the number of patient population with DED achieved 923.2 million in 2022 globally.

Source: Literature Review, Frost & Sullivan Analysis

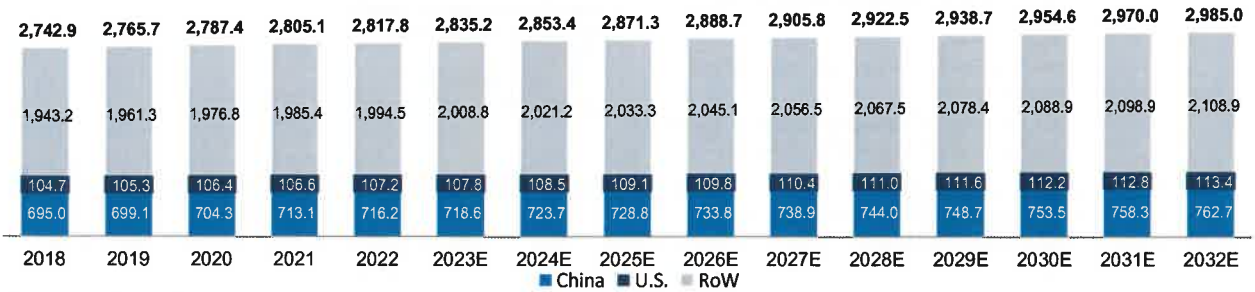
Global Prevalence of MGD, 2018-2032E

- Global prevalence of MGD increased from 2,742.9 million in 2018 to 2,817.8 million in 2022 with a CAGR of 0.7%. It is expected to continue to increase to 2,905.8 million in 2027 and 2,985.0 million in 2032 with a CAGR of 0.6% and 0.5% from 2022 to 2027 and from 2027 to 2032 respectively.
- U.S. prevalence of MGD increased from 104.7 million in 2018 to 107.2 million in 2022 with a CAGR of 0.6%. It is expected to continue to increase to 110.4 million in 2027 and 113.4 million in 2032 with a CAGR of 0.6% and 0.5% from 2022 to 2027 and from 2027 to 2032 respectively.
- China prevalence of MGD increased from 695.0 million in 2018 to 716.2 million in 2022 with a CAGR of 0.8%. It is expected to continue to increase to 738.9 million in 2027 and 762.7 million in 2032 with a CAGR of 0.6% and 0.6%, from 2022 to 2027 and from 2027 to 2032 respectively.

Global Prevalence of MGD, 2018-2032E

Period	CAGR		
	Global	U.S.	China
2018-2022	0.7%	0.6%	0.8%
2022-2027E	0.6%	0.6%	0.6%
2027E-2032E	0.5%	0.5%	0.6%

Million



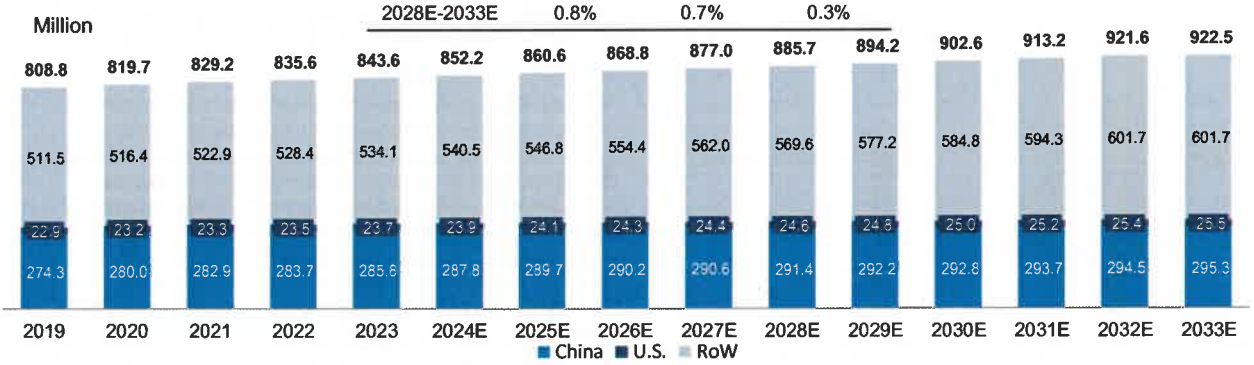
Source: Literature Review, Expert Interview, Frost & Sullivan Analysis

Global Prevalence of MGD associated DED, 2019-2033E

- Global prevalence of MGD associated DED increased from 808.8 million in 2019 to 843.6 million in 2023 with a CAGR of 1.1%. It is expected to continue to increase to 885.7 million in 2028 and 922.5 million in 2033 with a CAGR of 1.0% and 0.8% from 2023 to 2028 and from 2028 to 2033 respectively.
- U.S. prevalence of MGD associated DED increased from 22.9 million in 2019 to 23.7 million in 2023 with a CAGR of 0.8%. It is expected to continue to increase to 24.6 million in 2028 and 25.5 million in 2033 with a CAGR of 0.8% and 0.7% from 2023 to 2028 and from 2028 to 2033 respectively.
- China prevalence of MGD associated DED increased from 274.3 million in 2019 to 285.8 million in 2023 with a CAGR of 1.0%. It is expected to continue to increase to 291.4 million in 2028 and 295.3 million in 2032 with a CAGR of 0.4% and 0.3%, from 2023 to 2028 and from 2028 to 2033 respectively.

Global Prevalence of MGD associated DED, 2019-2033E

Period	CAGR		
	Global	U.S.	China
2019-2023	1.1%	0.8%	1.0%
2023-2028E	1.0%	0.8%	0.4%
2028E-2033E	0.8%	0.7%	0.3%



Source: Literature Review, Expert Interview, Frost & Sullivan Analysis

Treatment Paradigm of MGD associated DED

- In the staging of disease, it is recognized that it is difficult clinically to separate the effects of MGD and the effects of aqueous deficiency on the ocular surface. In addition, co-morbid diseases are often present. Below listed the evidence-based approach to the management of MGD.

Stage	Clinical Description	Pharmacological Intervention	Other Intervention
1	• No symptoms of ocular discomfort, itching, or photophobia • No ocular surface staining	• NA	• Improvement of diet and environment
2	• Minimal to mild symptoms of ocular discomfort, itching, or photophobia • Scattered lid margin features • None to limited ocular surface staining	• Artificial lubricants • Topical azithromycin • Topical emollient lubricant or liposomal spray • Consider oral tetracycline derivatives	• All the above • Palpebral physical therapy • Advise improving ambient humidity, optimizing workstations, and increasing dietary omega-3 fatty acid intake
3	• Moderate symptoms of ocular discomfort, itching, or photophobia with limitations of activities • Plugging lid margin • Mild to moderate conjunctival and peripheral corneal staining	• All the above • Oral tetracycline derivatives • Lubricant ointment at bedtime • Anti-inflammatory therapy for dry eye • Therapy targeting tear evaporation	• All the above
4	• Marked symptoms of ocular discomfort, itching or photophobia with definite limitation of activities • Dropout lid margin • Increased conjunctival and corneal staining , including central staining	• All the above	• All the above

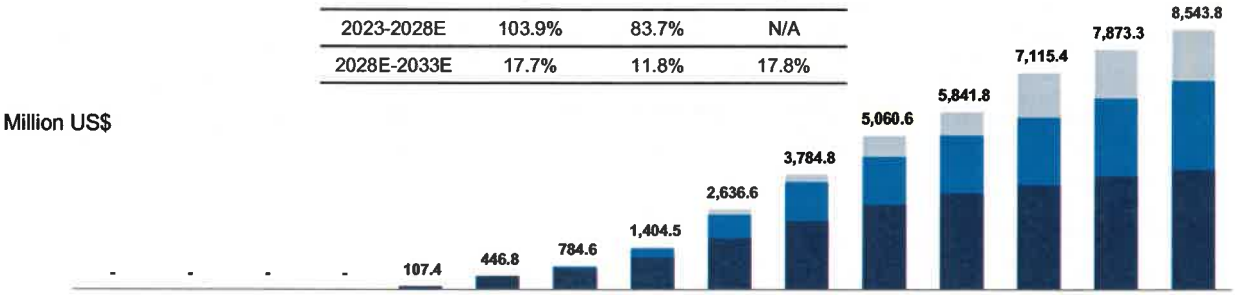
Source: American Academy of Ophthalmology, Invest. Ophthalmol. Vis. Sci., Frost & Sullivan analysis

Historical and Forecasted Market Size of Global MGD associated DED Pharmaceuticals, 2019-2033E

- The market size of global MGD associated DED pharmaceuticals will start to expand in 2023, is expected to increased from US$3,784.8 million in 2028 to US$8,543.8 million in 2033 with a CAGR of 17.7% from 2028 to 2033.
- The market size of U.S. MGD associated DED pharmaceuticals is expected to increased from US$2,246.7 million in 2028 to US$3,932.1 million in 2033 with a CAGR of 11.8%.
- The market size of China MGD associated DED pharmaceuticals is expected to increased from US$1,288.5 million in 2028 to US$2,926.6 million in 2033 with a CAGR of 17.8%.

Historical and Forecasted Market Size of Global MGD associated DED Pharmaceuticals, 2019-2033E

Period	CAGR		
	Global	U.S.	China
2019-2023	N/A	N/A	N/A
2023-2028E	103.9%	83.7%	N/A
2028E-2033E	17.7%	11.8%	17.8%



	2019	2020	2021	2022	2023	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E
Global	-	-	-	-	107.4	446.8	784.6	1,404.5	2,636.6	3,784.8	5,060.6	5,841.8	7,115.4	7,873.3	8,543.8
RoW	-	-	-	-	-	4.5	35.9	55.3	185.9	249.6	696.2	790.8	1,470.0	1,593.6	1,685.2
China	-	-	-	-	-	0.5	67.0	297.6	777.5	1,288.5	1,579.8	1,887.6	2,215.6	2,561.3	2,926.6
U.S.	-	-	-	-	107.4	441.8	681.7	1,051.5	1,673.2	2,246.7	2,784.6	3,163.4	3,429.9	3,718.4	3,932.1

Source: Literature Review, Expert Interview, and Frost & Sullivan Analysis

Competitive Landscape of Meibomian Gland Dysfunction

- Tear film evaporation causes tear film instability, tear hyperosmolarity, and ocular surface inflammation and cell apoptosis, resulting in a continuing cycle of DED. The primary goal of treatment for DED associated with MGD is to restore the tear film lipid layer and decrease evaporation, thereby reducing ocular signs and symptoms. Although a wide range of treatments are available for DED, before the approval of MIEBO™ by FDA, topical ophthalmic prescription medications only attempt to alter various factors that may contribute to DED, such as inflammation, bacterial growth, inadequate tear production). These medications approved for the treatment of DED do not target the key driver of the disease (i.e., excessive evaporation).
- MIEBO™ (perfluorohexyloctane ophthalmic solution), indicated for the treatment of the signs and symptoms of dry eye disease (DED), was approved by FDA in 18th May 2023. MIEBO is the first and only FDA-approved treatment for dry eye disease that directly targets tear evaporation, often associated with MGD. Perfluorohexyloctane forms a monolayer at the air-liquid interface of the tear film which can be expected to reduce evaporation. The exact mechanism of action for MIEBO™ in DED is not known.
- The list price of MIEBO is approximately US$771 per month in the U.S.

Brand Name	Company	Region/Authority	Indications	Active Compound	Mechanism	Approved Date	Annual Cost per Patient[2], USD$	Patent Expiry Date
MIEBO (NOV03)	Bausch & Lomb Inc.	U.S./FDA, EU/EMA[3]	DED	Perfluorohexyloctane[1]	N/A	2023-05-18	9,252	2037-06-21

*Competitive landscape as of *2025/05/30*

Note: 1, In December 2019, Bausch + Lomb acquired the rights from Novaliq GmbH to pursue development and commercialization of NOV03 for DED and combination products based on NOV03 in additional ophthalmic indications in the United States and Canada.
2, The product label of Miebo has not clarified the recommended administration duration. KALAHARI study, the multi-center, open-label, single-arm, 12-month safety extension trial (NCT04140227) tracked the long-term use of Miebo. Overall, participants showed sustained safety and efficacy throughout the study duration.
3, In Europe, Miebo is commercialised by Ursapharm, under the name EvoTears.

Source: FDA, Frost & Sullivan Analysis

Competitive Landscape of MGD associated DED

Drug Name/Code	Company	Region	Phase	Indications	Active Compound	Mechanism	First Posted Date
SHR8058/ NOV03 eye drops[1,2]	Jiangsu Hengrui Pharmaceuticals Co Ltd	China	NDA	MGD associated DED	Perfluorohexyloctane	N/A	/
AZR-MD-001[3]	Azura Ophthalmics Ltd/ORA, Inc.	US	Phase 3	MGD associated DED	Selenium Disulfide	Keratolytic agent	2024-03-26
HY02[3]	Hovione Scientia Ltd	US	Phase 2	MGD associated DED	Minocycline	N/A	2019-03-25
AXR-270[3]	AxeroVision, Inc.	US	Phase 2	MGD associated DED	NA	Glucocorticoid receptor agonist[3]	2020-07-14
CBT-006	**Cloudbreak Therapeutics, LLC**	**US**	**Phase 2**	MGD associated DED	**Cyclodextrin**	**Supramolecular catalysts**	**2021-05-12**
CBT-008	**Cloudbreak Therapeutics, LLC**	**US**	**Phase 2**	MGD associated DED	**Cyclodextrin**	**Supramolecular catalysts**	**2022-03-02**
TP-03[4]	Tarsus Pharmaceuticals, Inc.	US	Phase 2	MGD associated DED	Lotilaner	Non-competitive gamma-aminobutyric acid receptor antagonist	2022/07/12

*Competitive landscape as of *2025/05/30*

Note:
1, Bausch & Lomb acquired the rights to develop and commercialise NOV03 from Novaliq in the United States and Canada in December 2019.
2, Although on FDA approved label, the indication of Miebo™ is DED, the patients in their clinical information were patients with MGD associated DED.
3, Perfluorohexyloctane is a novel substance that has been approved as a medical device NovaTears®, as a nonblurring wetting agent for the ocular surface.
4, In China, Novaliq has a strategic cooperation with Jiangsu Hengrui Pharmaceuticals to develop, manufacture and commercialize NOV03 for the treatment of MGD associated DED.
5, AZR-MD-001, HY02, AXR-270 are anti-inflammatory antibiotics.
6, TP-03 is an antiparasitic agent.

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

Growth Drivers of MGD associated DED Drug Therapy Market

Expanding MGD associated DED Population

- MGD is highly prevalent, which has led to a greater awareness of the condition among both patients and healthcare professionals, driving the demand for effective pharmaceutical treatments. Studies have shown that MGD is a contributing factor in 70% to 86% of DED cases globally. **Global prevalence of MGD associated DED increased from 800.1 million in 2018 to 835.6 million in 2022 with a CAGR of 1.1%. It is expected to continue to increase to 885.4 million in 2027 and 938.8 million in 2032 with a CAGR of 1.2% and 1.2% from 2022 to 2027 and from 2027 to 2032 respectively.** As a result, there has been a growing demand for pharmaceutical treatments that target the underlying causes of MGD and provide relief for those affected by this condition.

Recognitive Enhancement in Causes of Disease

- In addition to the high prevalence of MGD associated DED, also a growing understanding of the underlying causes of the condition will continuously boost the market growth of MGD associated DED pharmaceutical. In the past, DED patients were mainly diagnosed and treated based on their unstable tear film. In the recent years, DED has been recognized as a multifactorial disease and been clearly classified as aqueous-deficient DED and evaporative dry eye as the major two subtypes. **The increased understanding has led to a greater focus on developing drug therapies that target these underlying causes, offering more targeted and effective solutions for patients.**

Significant Shift in Treatment Approach

- Furthermore, there has been a significant shift in the approach to treating MGD in recent years. While traditional treatments focused primarily on managing symptoms, there is now a greater emphasis on addressing the root causes of the condition. This shift has created a demand for pharmaceuticals that not only provide symptomatic relief but also target the underlying mechanisms of MGD, offering more comprehensive and long-lasting solutions for patients. In 2023, MIEBO™ was approved by FDA, which is the first and only FDA-approved treatment for dry eye disease that directly targets evaporative DED. **According to the 2023 Quarter 3 financial report of Bausch & Lomb Inc., the total prescriptions of MIEBO, involving first time prescription and refilling, was reported to reach 9,600 in the first month post launch.**

Source: Frost & Sullivan Analysis

Entry Barrier of MGD associated DED Drug Therapy Market

R&D as a Barrier to Entry

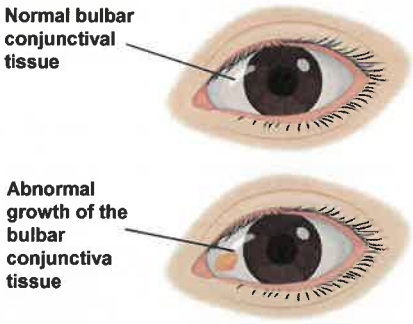
- The R&D obstacles of developing drug therapies indicated for MGD associated DED lie in the lack of clear understanding on the pathogenesis of the disease and appropriate method to address the underlining cause of disease. Discovering and obtaining patents for the mechanism of action to dissolve cholesterol, the key component believed to contribute to the lipid accumulation at meibomian gland orifice, could be an obstacle for new entrants.

Source: Frost & Sullivan Analysis

Overview of Pinguecula

- Pinguecula is characterized as raised yellow-white fibrovascular growth of the interpalpebral bulbar conjunctiva that does not involve the cornea and represents elastotic degeneration of subepithelial collagen with hyalinized connective tissue. It may cause cosmetic blemish or irritation if vascularised due to inflammation. Evidence suggests that VEGF promotes angiogenesis and vascularization, making it a highly significant therapeutic target. Pinguecula is thought to arise as a result of the effects of environmental irritants such as wind and dust, and are associated with UV-light exposure and aging, however the evidence of the association between UV-light exposure and pinguecula remains limited. Pinguecula is distinguished from pterygium by its lack of corneal invasion.
- As a pinguecula is a raised bump, the natural tear film spreads unevenly over the surface of the eye, thus causing a break in the tear film. This leads to dryness of eyes, burning sensation, itching, constant rubbing of the eyes due to foreign body sensation, blurry vision and stinging.

Pinguecula



Risk Factors

- Age
- UV radiation
- Environmental irritants, such as dust and smog
- Familial and hereditary factors
- Male gender
- Diabetes mellitus
- Contact lense wear

Dry Eye Symptoms

- When a pinguecula is inflamed, it is known as pingueculitis.
- The surface of the conjunctiva overlying the pinguecula will interfere with the normal spreading of the tear film. Thus dry eye symptoms such as burning sensation, itching, and foreign body sensation occur. Dellen may appear near the pinguecula. Tear break-up time may diminish in patients with pinguecula.

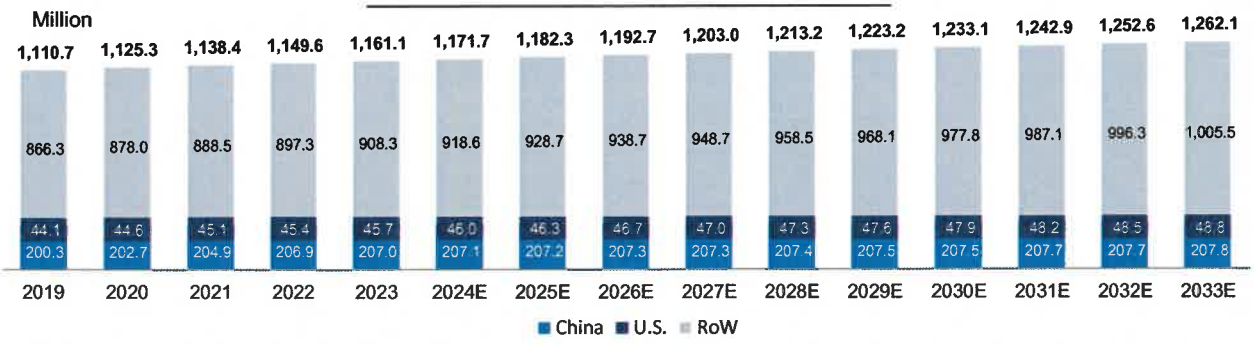
Source: Literature Review, Frost & Sullivan Analysis

Global Prevalence of Vascularised Pinguecula, 2019-2033E

- Global prevalence of vascularised pinguecula increased from 1,110.7 million in 2019 to 1,161.1 million in 2023 with a CAGR of 1.1%. It is expected to continue to increase to 1,213.2 million in 2028 and 1,262.1 million in 2033 with a CAGR of 0.9% and 0.8% from 2023 to 2028 and from 2028 to 2033 respectively.
- Prevalence of vascularised pinguecula in the U.S. increased from 44.1 million in 2019 to 45.7 million in 2023 with a CAGR of 0.9%. It is expected to continue to increase to 47.3 million in 2028 and 48.8 million in 2033 with a CAGR of 0.7% and 0.6% from 2023 to 2028 and from 2028 to 2033 respectively.
- Prevalence of vascularised pinguecula in China increased from 200.3 million in 2019 to 207.0 million in 2023 with a CAGR of 0.8%. It is expected to decrease to 207.4 million in 2028 and 207.8 billion in 2033 with a CAGR of 0%, and 0%, from 2023 to 2028 and from 2028 to 2033 respectively.

Global Prevalence of Vascularised Pinguecula, 2019-2033E

Period	CAGR		
	Global	U.S.	China
2019-2023	1.1%	0.9%	0.8%
2023-2028E	0.9%	0.7%	0%
2028E-2033E	0.8%	0.6%	0%



Source: Literature Review, Expert Interview, Frost & Sullivan Analysis

Current Treatment Options and Unmet Clinical Needs for Vascularised Pinguecula

- There is no drug launched on the market to treat vascularised pinguecula globally and in China. Below listed off-label pharmacological treatment, are only used for symptomatic relieve. Lubrication with artificial tears and ointment can only help with mild cases of dryness or foreign body sensation. If inflammation is more severe, a short course of topical steroids or topical antibiotic-steroid in tapering dose may be indicated. Topical non-steroidal anti-inflammatory drugs are also effective in treating pingueculitis. Long-term use of topical steroid therapy should be discouraged due to adverse side-effects, such as intraocular pressure elevation, cataract formation and increased risk of infection. Cold compresses may help patients with inflamed pinguecula.
- Surgical excision is considered only for cosmetic reasons.

Management of Pinguecula

Pharmacological intervention

- **Artificial Tears**
- **Non-preserved lubricant eye ointment**

- **Topical steroids/antibiotic-steroid/non-steroidal anti-inflammatory drugs**

Only for symptomatic and temporary use

Surgical intervention

- **Conjunctival autografting**: obtain an autograft and suture the graft over the exposed scleral bed after excision
- **Argon laser photocoagulation**: provide control of the extent and depth of removal of tissue
- **Cryotherapy**

+

Adjunctive therapy:
- Topical antibiotic-steroid eye drops

- Common complications of surgical intervention include recurrence of pinguecula and pigmentary changes at the site of removal.
- The average reported cost for pinguecula surgery and associated treatment can range from $1,000 to $5,000 in the U.S and around RMB2,000 in China.

Source: NVISION, Frost & Sullivan Analysis

Current Treatment Options and Unmet Clinical Needs for Vascularised Pinguecula

- There is no drug launched on the market to treat vascularised pinguecula globally and in China. Below listed off-label pharmacological treatment, are only used for symptomatic relieve. Lubrication with artificial tears and ointment can only help with mild cases of dryness or foreign body sensation. If inflammation is more severe, a short course of topical steroids or topical antibiotic-steroid in tapering dose may be indicated. Topical non-steroidal anti-inflammatory drugs are also effective in treating pingueculitis. Long-term use of topical steroid therapy should be discouraged due to adverse side-effects, such as intraocular pressure elevation, cataract formation and increased risk of infection. Cold compresses may help patients with inflamed pinguecula.
- Surgical excision is considered only for cosmetic reasons.

Method	Treatment Options	Mechanism of Action	Limitation	Cost
Pharmaceuticals	Artificial Tears Non-preserved lubricant eye ointment	• keep the eye lubricated and relieve minor discomfort	• Off-label use • Only for symptomatic and temporary use	/[1]
	Anti-inflammatory drugs	• inhibit inflammatory reaction		
Surgery	Conjunctival autografting	• obtain an autograft and suture the graft over the exposed scleral bed after excision	• Common complications of surgical intervention include recurrence of pinguecula and pigmentary changes at the site of removal	• $1,000 to $5,000 in the U.S • Around RMB2,000 in China
	Argon laser photocoagulation	• provide control of the extent and depth of removal of tissue		
	Cryotherapy	• suture the amniotic membrane over the exposed scleral bed after excision		
Adjunctive therapy	Topical antibiotic-steroid eye drops	• Inhibit neovascular and inflammatory eye conditions		

Note: 1, The off-label drug use is mainly for symptomatic relieve, which shows no minimal therapeutic goods. It is not applicable to calculate the annual cost per patient of off-label drug use, because the drug label doesn't clarify the recommended dosage and duration of its off-label use.

Source: NVISION, Frost & Sullivan Analysis

Competitive Landscape of Vascularised Pinguecula

- There is no drugs launched on the market to treat vascularised pinguecula globally and in China.
- The table below lists the current clinical-staged pipeline of vascularised pinguecula therapies globally and in China.
- Inlyta (axitinib), manufactured by Pfizer is the reference listed drug for CBT-004. Inlyta, initially approved by FDA in 2012, is indicated for the treatment of advanced renal cell carcinoma. Axitinib, a small molecule multi-receptor tyrosine kinase inhibitor, have the advantage of blocking VEGF receptors, and blocking platelet derived growth factor receptors, which play a role in neovascularization and pathologic angiogenesis.

Drug Name/Code	Company	Region	Phase	Indications	Active Compound	Mechanism	First Posted Date
CBT-004	Cloudbreak Therapeutics	US	Phase 2	Vascularised pinguecula	Axitinib	Tyrosine kinase inhibitor	2021-05-12

*Competitive landscape as of 2025/05/30

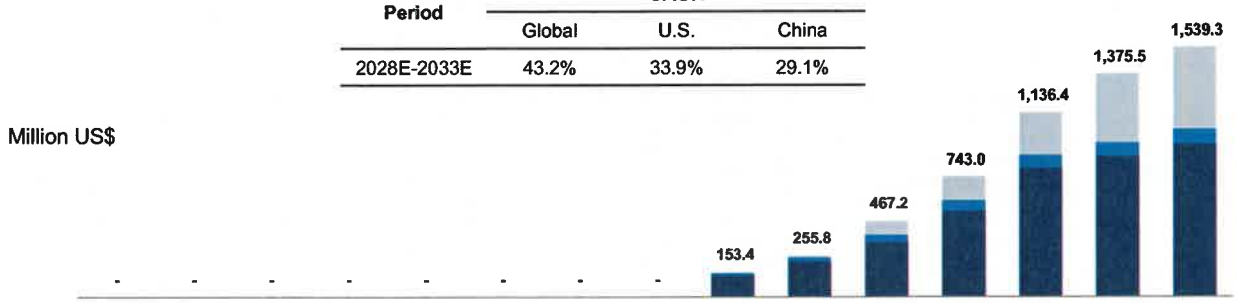
Source: CDE, ClinicalTrials.gov, Frost & Sullivan Analysis

Historical and Forecasted Market Size of Global Vascularised Pinguecula Drug Therapies, 2019-2033E

- The market size of global vascularised pinguecula drug therapies will start to expand in 2027, and is expected to increased from US$255.8 million in 2028 to US$1,539.3 million in 2033 with a CAGR of 43.2% from 2028 to 2033.
- U.S. vascularised pinguecula drug therapies market size is expected to increased from US$218.6 million in 2028 to US$940.6 million in 2033 with a CAGR of 33.9% from 2028 to 2033.
- China vascularised pinguecula drug therapies market size is expected to increased from US$25.7 million in 2028 to US$92.2 million in 2033 with a CAGR of 29.1% from 2028 to 2033.

Historical and Forecasted Market Size of Global Vascularised Pinguecula Drug Therapies, 2019-2033E

Period	CAGR		
	Global	U.S.	China
2028E-2033E	43.2%	33.9%	29.1%



	2019	2020	2021	2022	2023	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E
Global	-	-	-	-	-	-	-	-	153.4	255.8	467.2	743.0	1,136.4	1,375.5	1,539.3
RoW	-	-	-	-	-	-	-	-	6.9	11.5	85.0	149.1	264.8	425.8	506.5
China	-	-	-	-	-	-	-	-	14.7	25.7	42.3	65.3	77.2	85.3	92.2
U.S.	-	-	-	-	-	-	-	-	131.8	218.6	339.9	528.6	794.4	864.5	940.6

Source: Literature Review, Expert Interview, and Frost & Sullivan Analysis

Growth Drivers and Entry Barrier of Vascularised Pinguecula Drug Therapy Market

Enlarging Patient Pool

- Vascularized pinguecula is a common condition characterized by the presence of a yellowish, raised lesion on the conjunctiva, often near the cornea. This condition is frequently observed in individuals with prolonged exposure to ultraviolet light, dust, wind, and other environmental factors. The large patient pool affected by vascularized pinguecula presents an opportunity for further research and clinical intervention to better understand the underlying mechanisms and develop effective treatment strategies.

Unmet Medical Needs

- There is no drug launched on the market to treat vascularised pinguecula globally. Current treatment options for vascularised pinguecula are limited, often focusing on alleviating symptoms rather than addressing the underlying angiogenesis and vascularization. As a result, there is a clear need for innovative therapeutic interventions that target the angiogenesis and inflammation associated with this condition. Advancements in this area could significantly improve the quality of life for individuals affected by vascularised pinguecula, offering hope for more effective management and potential resolution of this challenging ocular condition.

R&D as a Barrier to Entry

- The R&D obstacles of developing drug therapies indicated for vascularised pinguecula lie in identifying appropriate (i) modality to target pathogenesis of the disease, (ii) drug delivery method and (iii) formulation for the delivery. Developing and obtaining patents for the method of use by inhibiting relevant growth factors to reduce vascularised pinguecula, and appropriate formulation as an eye drop to treat the disease, based upon the vascular nature of disease, could be an obstacle for new entrants.

Source: Frost & Sullivan Analysis

Overview of Glaucoma

Category and Risk Factors

- Glaucoma is a group of eye diseases that are usually characterized by progressive structural and functional changes of the optic nerve, leading to glaucomatous appearing optic disc and visual field damage if untreated.
- Glaucoma is often associated with a long and asymptomatic initial phase, and is usually unnoticed until its later stages. Worldwide, glaucoma is the second-leading cause of blindness after cataracts.

Category of Glaucoma

Primary Glaucoma

- Primary Open-Angle Glaucoma(POAG) is an optic neuropathy characterized by progressive peripheral visual field loss followed by central field loss in a typical pattern. It is usually but not always in the presence of elevated intraocular pressure (IOP).
- Primary Angle-Closure Glaucoma (PACG) is characterized by narrowing or closure of the anterior chamber angle. The normal anterior chamber angle provides drainage for the aqueous humor. When this drainage pathway is narrowed or closed, inadequate drainage leads to elevated IOP and damage to the optic nerve.

Secondary Glaucoma

- Secondary forms of glaucoma are characterized by the involvement of predisposing ocular or systemic diseases such as uveitis, trauma, and diabetes thereby resulting in an alteration of aqueous humor dynamics.

Risk Factors of Glaucoma

- Elevated intraocular pressure is the most critical risk factor for open-angle glaucoma, most patients with glaucoma have an IOP measurement of greater than 21mm Hg. East Asian ethnic background and elder age are more closely associated with the development of angle-closure glaucoma.
- Other risk factors in related to one or more types of glaucoma include: gender, hypertension, diabetes, family history of condition, hyperopia, certain biometric characteristics.

Source: Literature Review, Frost & Sullivan Analysis

Overview of Glaucoma

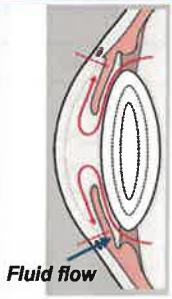
Pathogenesis and Symptoms

- The pathogenesis of open-angle glaucoma is not fully elucidated, but it is believed that the elevation of intraocular pressure due to the imbalance between secretion of aqueous humor by ciliary body and its drainage can cause retinal ganglion cell death. For angle-closure glaucoma, pupillary block is the most common mechanism of angle closure and is caused by resistance to aqueous humor flow from the posterior to anterior chambers at the pupil.

Pathogenesis

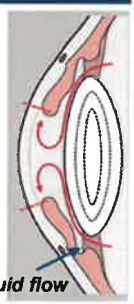
Open-Angle Glaucoma

- The pathogenesis of primary open-angle glaucoma is not clear. Optic nerve axon loss may be related to ganglion cell susceptibility, microcirculatory deficiency at the optic nerve head, or extracellular matrix factors.
- These factors may play a combined role: circulatory or extracellular matrix factors could account for both high pressures and axon loss; variation in axon susceptibility might explain why the disease state does not correlate well with elevated IOP.



Angle-Closure Glaucoma

- In primary angle-closure, the lens is located far forward anatomically and rests against the iris. Aqueous humor can't flow normally through the pupil. Pressure builds up behind the iris, causing the peripheral iris to bow forward and cover all or part of the anterior chamber angle.
- Prolonged or repeated contact between the iris and the angle can lead to scarring and functional damage to the trabecular meshwork, the tissue in the angle that acts as a sieve through which the aqueous humor drains.



Symptoms

- Individuals with open-angle glaucoma rarely experience symptoms. Thus, open-angle glaucoma is generally detected incidentally during comprehensive ophthalmic examination. This is in contrast to angle-closure glaucoma in which patients present with obvious symptoms and signs.
- Central visual field loss is a late manifestation of open-angle glaucoma, usually preceded by ganglion cell loss and optic nerve damage.

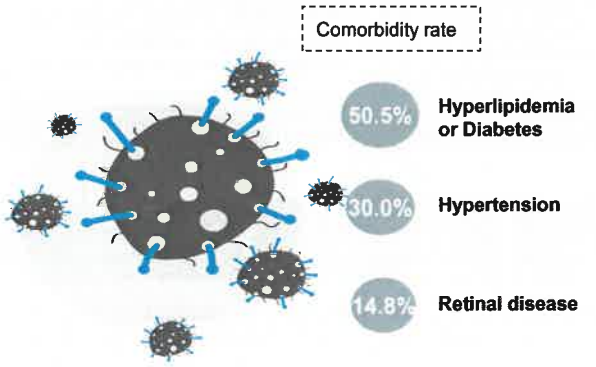
- The degree of the IOP elevation from angle-closure determines whether symptoms occur. If the IOP rises quickly, as is typical of acute primary angle-closure glaucoma, patients may experience some of the following symptoms:
  - Decreased vision
  - Halos around lights
  - Headache
  - Severe eye pain
  - Nausea and vomiting

Source: Literature Review, Frost & Sullivan Analysis

Analysis of Burden Caused by Glaucoma

- Glaucoma is a leading cause of blindness in the developed and developing world. Not only is the clinical impact of this disease considerable, but associated economic and humanistic burdens – affecting patients, caregivers, and communities are substantial.

- Comorbidities also influence the management of glaucoma. Patients with glaucoma have a higher risk of retinal disease and systemic diseases including hypertension and diabetes. It is also found that patients with glaucoma had higher mean triglyceride levels.



Blind Rate of Glaucoma

A retrospective meta analysis shows the rate of binocular or monocular blindness caused by glaucoma is about 38.3 in the mainland of China.

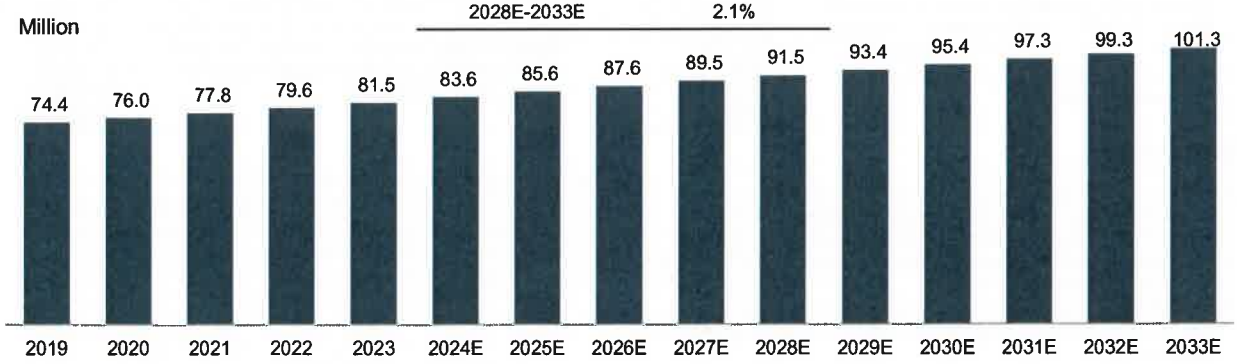
Source: Literature Review, Frost & Sullivan Analysis

Global Prevalence of Glaucoma, 2019-2033E

- Global prevalence of glaucoma increased from 74.4 million in 2019 to 81.5 million in 2023 with a CAGR of 2.3%. It is expected to continue to increase to 91.5 million in 2028 and 101.3 million in 2033 with a CAGR of 2.3% and 2.1% from 2023 to 2028 and from 2028 to 2033 respectively.

Global Prevalence of Glaucoma, 2019-2033E

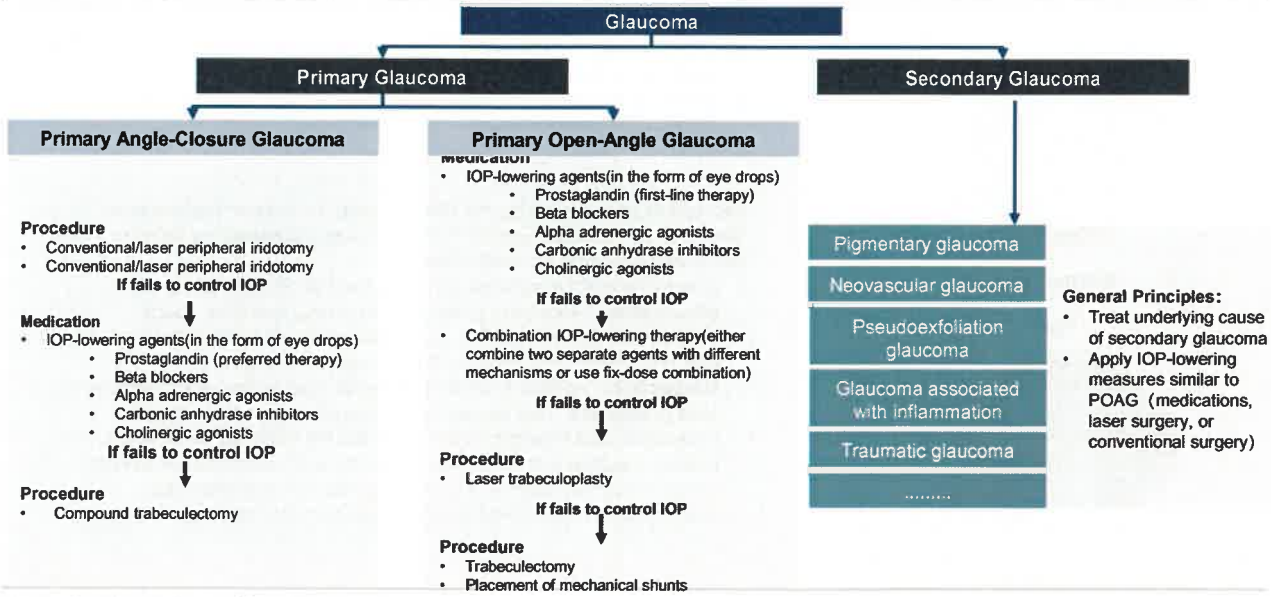
Period	CAGR
2019-2023	2.3%
2023-2028E	2.3%
2028E-2033E	2.1%



Source: Literature Review, Frost & Sullivan Analysis

Current Treatment Paradigm of Glaucoma

- In glaucoma practice today, the dominant approaches to treatment 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 should delay, stop, and ideally reverse the damage to the optic nerve and ganglion cell layer. The only clinically proven way to slow or stop damage from progressing is to reduce IOP below the level that will cause continued damage to optic nerve. Therefore, the overarching principle in many glaucoma treatment guidelines is to set a target IOP.
- Glaucoma filtration surgery ("GFS") is believed to be an effective way to lower high IOP in patients with glaucoma. However, excess scarring and fibrosis after surgery can lead to blockage of the drainage and cause failure of GFS over time. The usage of anti-fibrotic cytotoxic antimetabolite drugs such as mitomycin C can improve the success rate of GFS but these cytotoxic drugs can also cause various adverse complications.



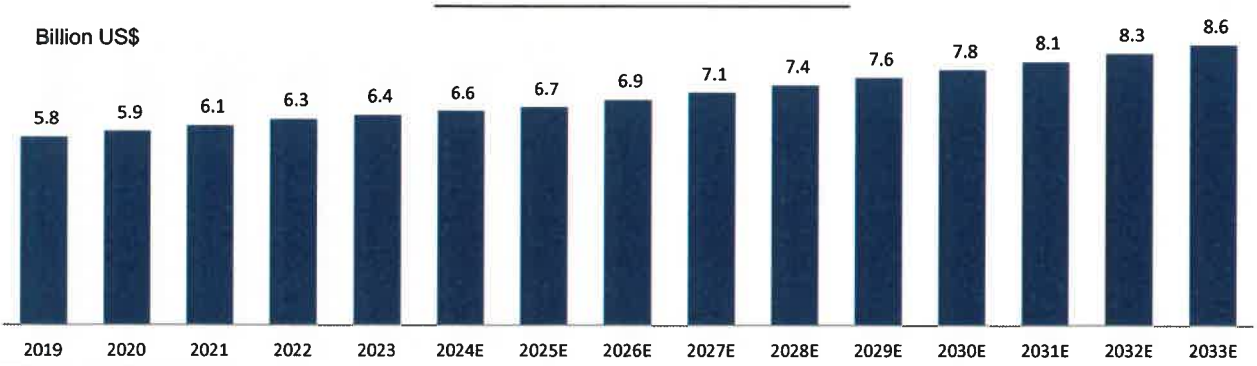
Source: Literature Review, Frost & Sullivan Analysis

Historical and Forecasted Market Size of Global Glaucoma Drug Therapies, 2019-2033E

- The market size of global glaucoma drug therapies increased from US$5.8 billion in 2019 to US$6.4 billion in 2023 with a CAGR of 2.8%. It is expected to continue to increase to US$7.4 billion in 2028 and US$8.6 billion in 2033 with a CAGR of 2.7% and 3.2% from 2023 to 2028 and from 2028 to 2033 respectively.

Historical and Forecasted Market Size of Global Glaucoma Drug Therapies, 2019-2033E

Period	CAGR
2019-2023	2.8%
2023-2028E	2.7%
2028E-2033E	3.2%

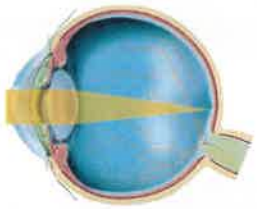


Source: Literature Review, Expert Interview, Annual Report, and Frost & Sullivan Analysis

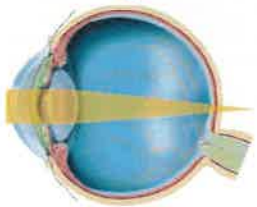
Overview of Presbyopia

- During aging, the lens in the eye gradually becomes thicker and loses flexibility. With less elasticity, it will be difficult for the eye to focus up close. Another proposed cause is the gradual loss of function of the ciliary muscles. Presbyopia is a refractive condition, whereby the progressive loss of accommodation results in loss of the visual ability to focus on objects located at different distance. In other words, presbyopia reduces an individual's ability to perform visual tasks at near distance. Symptoms begin to appear after the age of 40. As the world's population is aging, presbyopia is one of the most pressing visual concerns in the future.

Presbyopia



Normal Eye



Presbyopia

The mechanism of pharmacological presbyopia treatment

1. **Pinhole effect:** Pupillary miotics increase the depth of focus by creating a pinhole effect.
2. **Lens softening**: Assume that lens stiffening and loss of flexibility are presbyopia's main causes.

Muscarinic agonists cause the ciliary muscle to contract and the lens thickness to increase, and the induced miosis increases the depth of focus and creates pseudo accommodation.

- One of the main muscarinic agonists used in clinical trials is **1% pilocarpine.** Pilocarpine provides both miosis and ciliary body contraction, thus stimulating accommodation and potentially improving tear production by stimulating lacrimal gland secretion.
- **Carbachol** is another muscarinic agonist used in drug combinations to treat presbyopia. This parasympathomimetic agent stimulates the muscarinic and nicotinic receptors on the iris sphincter muscle to create miosis, resulting in a smaller pupil aperture, which increases the depth of focus. Unlike pilocarpine, it is a full agonist that also promotes acetylcholine release from parasympathetic nerve endings.

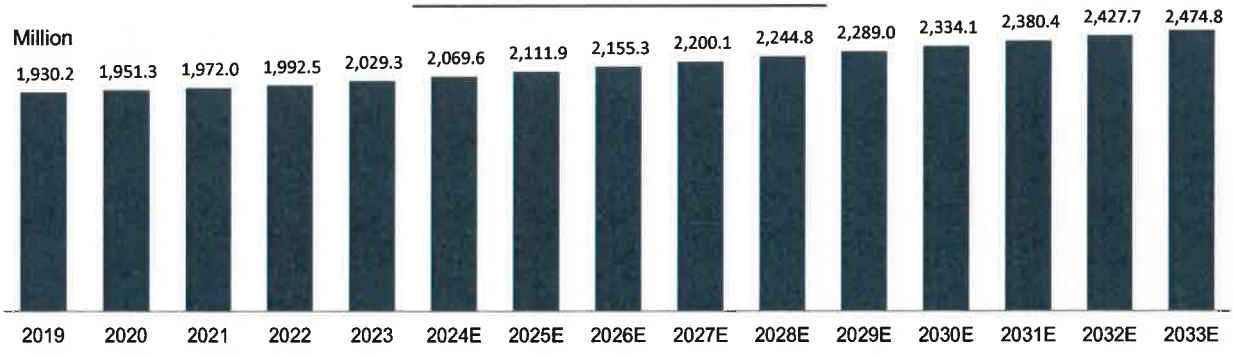
Source: Literature Review, Frost & Sullivan Analysis

Global Prevalence of Presbyopia, 2019-2033E

- Global prevalence of presbyopia increased from 1,930.2 million in 2019 to 2,029.2 million in 2023 with a CAGR of 1.3%. It is expected to continue to increase to 2,244.8 million in 2028 and 2,474.8 million in 2033 with a CAGR of 2.0% and 2.0% from 2023 to 2028 and from 2028 to 2033 respectively.

Global Prevalence of Presbyopia, 2019-2033E

Period	CAGR
2019-2023	1.3%
2023-2028E	2.0%
2028E-2033E	2.0%



Source: Literature Review, Frost & Sullivan Analysis

Current Treatment Methods and Limitations for Presbyopia

- Current treatment for presbyopia includes optical correction, pharmaceuticals and refractive surgery. Spectacles and contact lenses are two major options for optical correction. Muscarinic agonists which has pupillary miotic effect is used for presbyopia such as pilocarpine. As for refractive surgery, it includes laser surgery, intracorneal inlays, and intraocular lens implantation.
- Vuity and Qlosi are the only 2 FDA-approved eye drops to treat presbyopia. Both of them are pilocarpine hydrochloride. Pilocarpine hydrochloride is a muscarinic receptor agonist. Its mechanism of action is to stimulate cholinergic receptors on smooth muscle cells of the ciliary and iris sphincter muscles to shrink pupil. The contraction of the ciliary body results in decreased zonular tension which allows the crystalline lens to thicken, and contraction of the iris sphincter muscle results in pupillary miosis, which increases depth of focus by way of aperture optics. Most of the other drug candidates also exploit this miotic mechanism.

Limitations

Optical Correction	Pharmaceuticals	Refractive Surgery
Spectacle Lenses • **Inadequate vision** at intermediate or very close distances • **Poor aesthetics** • **Inconvenience:** patients should always have them to hand, which is a particular problem for the forgetful elderly presbyope **Contact lens** • **Age-dependent ocular changes** such as decreased tonus of eyelids, a reduced palpebral aperture, and decreased lacrimal production and tear stability may all influence the success of wearing contact lenses. • **Hygiene issues and proper care** also limit use of contact lenses	• **Adverse reaction:** it can cause chronic inflammation and stimulation of the fixed pupil, posterior synechiae and spasmodic contractions of the iris, pigment dispersion, and myopic shift. • Its effect only lasts for about 6 hours and requires use everyday. • It improves the vision but cannot cure presbyopia.	• Laser surgery always compromises near vision or far vision. It also limits future intraocular lens implantation, and **the surgery is irreversible.** • Intracorneal inlays have **late complications** that include corneal stromal opacity, late hyperopic shift, and inadequate visual performance caused by corneal irregularity. • Intraocular lens implantation depends on the **unpredictable neuroadaptation process** and may lead to prolonged postoperative recovery. It may also produce halos and glare and result in loss of stereopsis and a decrease of contrast sensitivity.

Source: Literature Review, Frost & Sullivan Analysis

Historical and Forecasted Market Size of Global Presbyopia Drug Therapies, 2019-2033E

- The market size of global presbyopia drug therapies started expanding in 2021, and is expected to increase from US$0.2 billion in 2023 to US$3.4 million in 2028 with a CAGR of 86.6% from 2023 to 2028. It is expected to continue to increase to US$5.6 million in 2033 with a CAGR of 10.3% from 2028 to 2033.

Forecasted Market Size of Global Presbyopia Drug Therapies, 2019-2033E

Period	CAGR
2019-2023	N/A
2023-2028E	86.6%
2028E-2033E	10.3%

Source: Literature Review, Expert Interview, Annual Report, and Frost & Sullivan Analysis

Overview of Retinal Diseases

- Retinal diseases, which are often characterized by leakage of fluid, hemorrhage and fibrous scarring in the eye, and develop from the back surface of the eye (i.e. fungus) and the vitreous around, include wet age-related macular degeneration (wAMD), diabetic macular edema (DME), retinal vein occlusion (RVO) and myopic choroidal neovascularization (mCNV) not secondary to AMD. These diseases are major causes of visual impairment and blindness worldwide. Retinal diseases can cause irreversible loss of visual acuity, which can have a major impact on patients' vision-related quality of life and overall wellbeing.

wAMD

- Age-related macular degeneration (AMD) is a degenerative retinal disease that causes progressive loss of central vision. It's the leading cause of irreversible blindness in aged people
- In AMD patients, approximately 10% are wAMD. However, 80%~90% cases of vision loss are from wAMD patients.
- In the wAMD, new blood vessels grow and leak blood and fluid under the macula. This can lead to retinal detachment, scarring, and irreversible vision loss.
- Although AMD tends to occur in one eye at a time, approximately 50% of patients who have wAMD in one eye will also develop this condition in their second eye within 5 years.
- Major risk factors of wAMD includes: aging, genetics, smoking, AMD in one eye, etc.

DME

- DME is a complication of diabetes wherein the patient loses the central vision to a certain degree. The condition occurs due to leakage of intraretinal fluid or lipid into the macular area from microaneurysms or damaged blood vessels.
- Before the development of DME, diabetic retinopathy (DR) firstly occurs, which damages the blood vessels in the retina, resulting in vision impairment. These blood vessels continue to build up pressure in the eye and leak fluid, leading to DME.
- The prevalence of DME is rapidly accelerating along with the increasing number of diabetic patients, which becomes a growing healthcare concern.
- Major risk factors of DME includes: diabetes, hypertension, hyperpermeability of the retinal vasculature, etc.

RVO

- RVO occurs when the central retinal vein, the blood vessel that drains the retina, or one of its branches becomes blocked, which can lead to blurry vision or loss of vision in the eyes.
- RVO may be categorized by the anatomy of the occluded vein and the degree of ischemia produced. The two major RVO types are central retinal vein occlusion (CRVO) and branch retinal vein occlusion (BRVO).
- Major risk factors of RVO includes: aging, hypertension, arteriosclerosis, hyperlipidemia, etc.

mCNV

- mCNV is a complication of myopia that causes visual impairment. In myopic eyes, the elongation of the anteroposterior axis causes stress, which induces the creation of new blood vessels in the choroid. It is this neovascularistion that causes the decrease in visual acuity.
- mCNV can happen in one or both eyes. More than 30% with mCNV in one eye will develop it in the other eye within 8 years.
- Major risk factors of mCNV includes: myopia, aging, female gender, macular changes, etc.

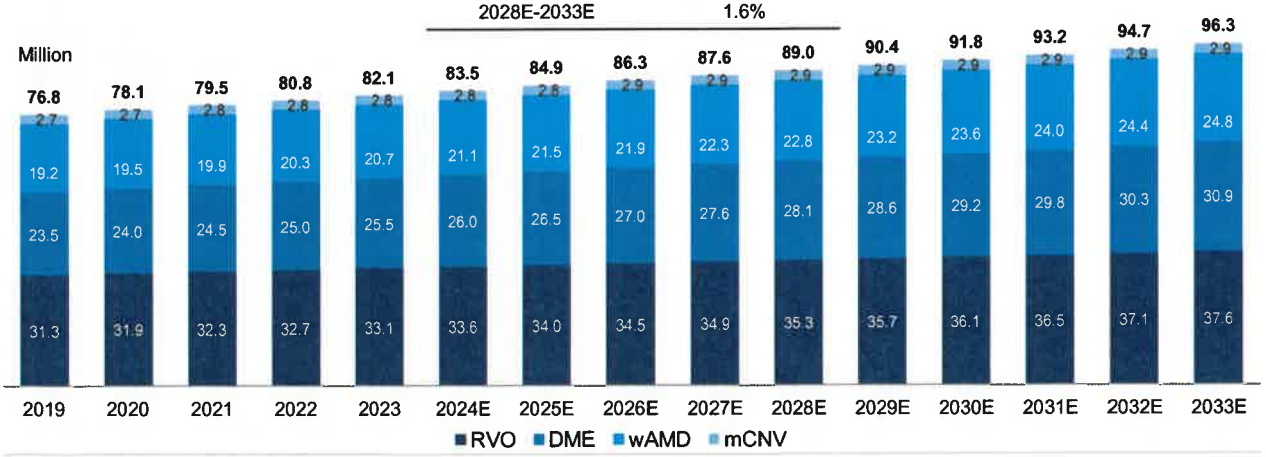
Source: Literature Review, Frost & Sullivan Analysis

Global Epidemiology Analysis of Major Retinal Diseases, 2019-2033E

- Among the major 4 types of retina diseases, prevalence of wAMD and DME increase more rapidly than the others, which are mainly caused by risk factors such as the aging population, increasing prevalence of diabetes, etc. In 2023, the number of wAMD patients reached 20.7 million, and it is expected to reach 24.8 million in 2033. The number of DME patients reached 25.5 million in 2023 and is forecasted to reach 30.9 million in 2033.

Global Epidemiology Analysis of Major Retinal Diseases, 2019-2033E

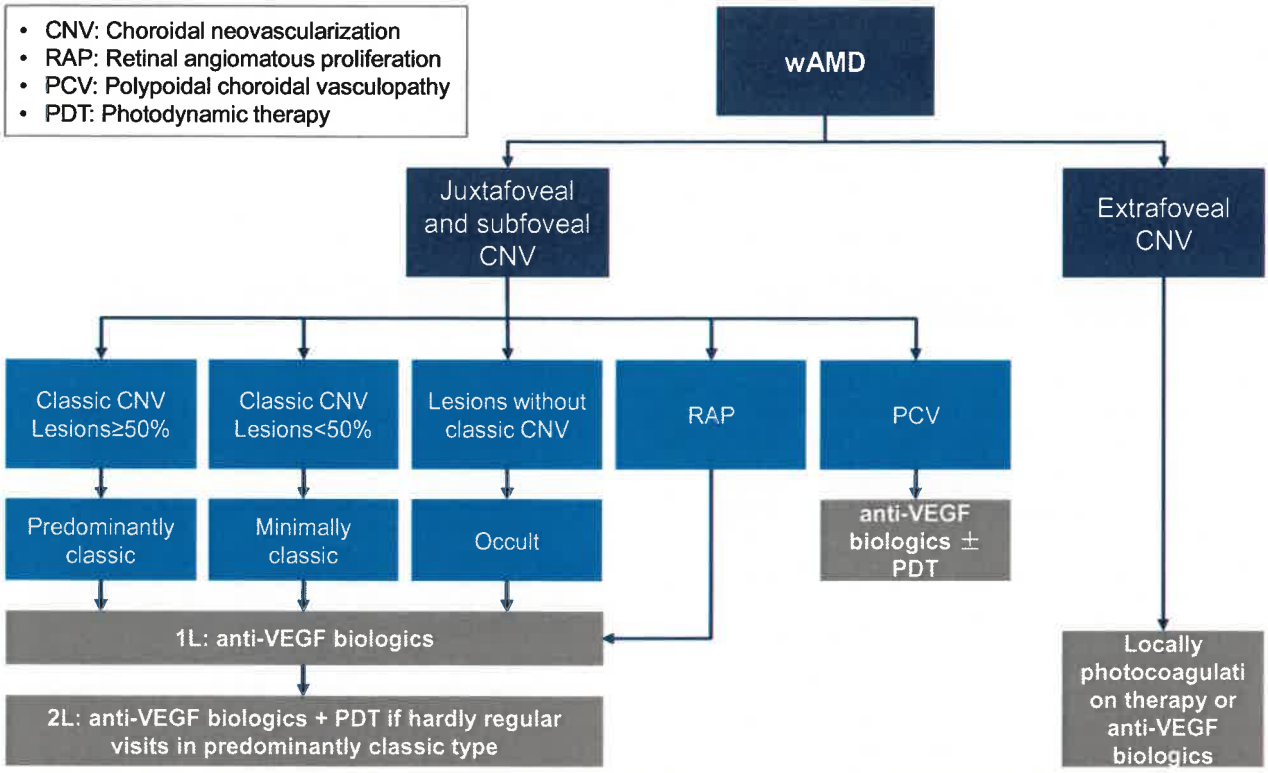
Period	CAGR
2019-2023	1.7%
2023-2028E	1.6%
2028E-2033E	1.6%



Source: Literature Review, Frost & Sullivan Analysis

Treatment Paradigm of wAMD

- CNV: Choroidal neovascularization
- RAP: Retinal angiomatous proliferation
- PCV: Polypoidal choroidal vasculopathy
- PDT: Photodynamic therapy

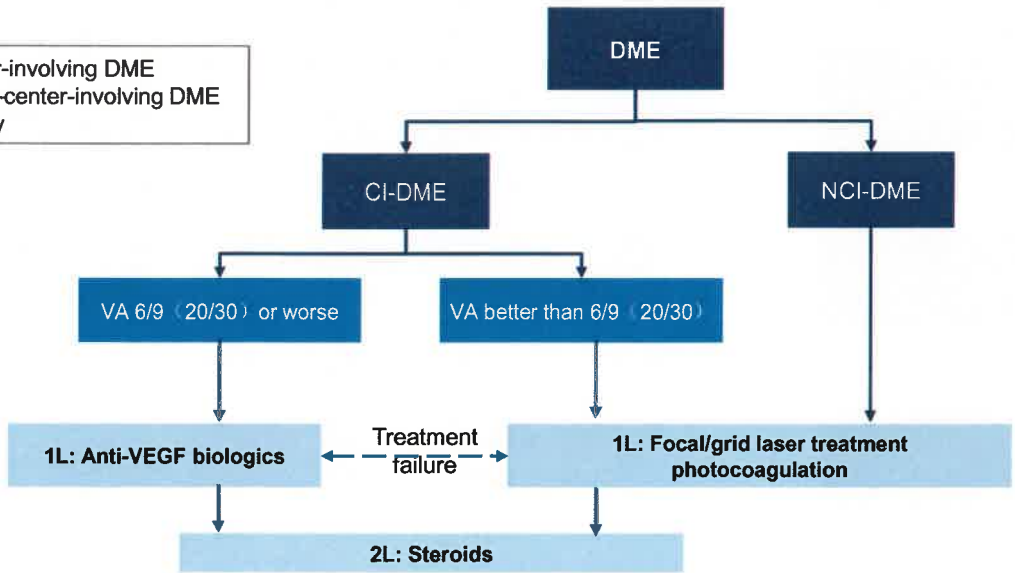


Source: Literature Review, Frost & Sullivan Analysis

Treatment Paradigm of DME

- The pathology of DME involves both VEGF and inflammation. Intravitreal anti-vascular endothelial growth factor (anti-VEGF) agents are effective in the treatment of center-involved diabetic macular edema with vision loss. For eyes with persistent retinal thickening despite anti-VEGF therapy, consider laser treatment after 24 weeks. At the same time, laser photocoagulation surgery remains the preferred treatment for non-center-involved diabetic macular edema. Treatment with intravitreal steroid may also be considered, but they are usually used as second-line treatment of DME due to their side effects, including cataract progression and elevated intraocular pressure.

- CI-DME：Center-involving DME
- NCI-DME：Non–center-involving DME
- VA：visual acuity



Source: IDF, Literature Review, Frost & Sullivan Analysis

The Current Treatment Limitations for DME and wAMD (Pharmaceuticals)

- Due to DR treatment is approved after guideline, anti-VEGF biologics is not regarded as first line therapy, but is the priority in clinical practice.
- For both DME and wAMD patients, anti-VEGF is the first-line therapy, such as ranibizumab and aflibercept etc., which are administered via intravitreal injections. Corticosteroid therapy by vitreous inserts (sustained delivery) is the second-line treatment for patients for whom anti-VEGF therapy is ineffective.

Limitations

Biologics（Anti-VEGF)

- Intravitreal administration of anti-VEGF therapy is generally considered safe, and ocular complications are rare. However, potential side effects include: Pain, inflammation, increased intraocular pressure, peripheral wound healing, thromboembolic events, myocardial infarction, stroke, hypertension, gastrointestinal perforations, and kidney disease
- It has a short-term effect and thus requires repeated treatment.
- Biologics are expensive and long- term usage also increases the cost.
- The antigen-antibody interaction and the signaling regulation of biologics are unpredictable. The experience of using biologics to treat UME is still insufficient.

Corticosteroid

- Adverse reaction: After long-term use of glucocorticoids, patients may have a full moon-shaped face, buffalo hump, obesity or acne.
- Inducing the local or systematic lesions: multiple intravitreal injections will cause vitreous turbidity and increase IOP. It may also subsequently cause local lesions in ocular such as cataracts, glaucoma, or even systematic lesions including hypertension and diabetes.
- Its effect is short-termed, so patients need inject repeatedly which increases the risk of complications and side effects. It also increases patients' burden.

Source: Literature Review, Frost & Sullivan Analysis

Indications of Marketed Anti-VEGF Biologics

	FDA Approved	NMPA Approved
wAMD	2006—Lucentis® 2011—Eylea® 2019—BEOVU® 2022—Vabysmo ™	2011—Lucentis® 2013—Lumitin® 2018—Eylea®
DME	2012—Lucentis® 2014—Eylea® 2022—Vabysmo ™	2018—Lucentis® 2018—Eylea®
mCNV	2017—Lucentis®	2017—Lumitin® 2018—Lucentis®
RVO	2010—Lucentis® 2014—Eylea®	2018—Lucentis®

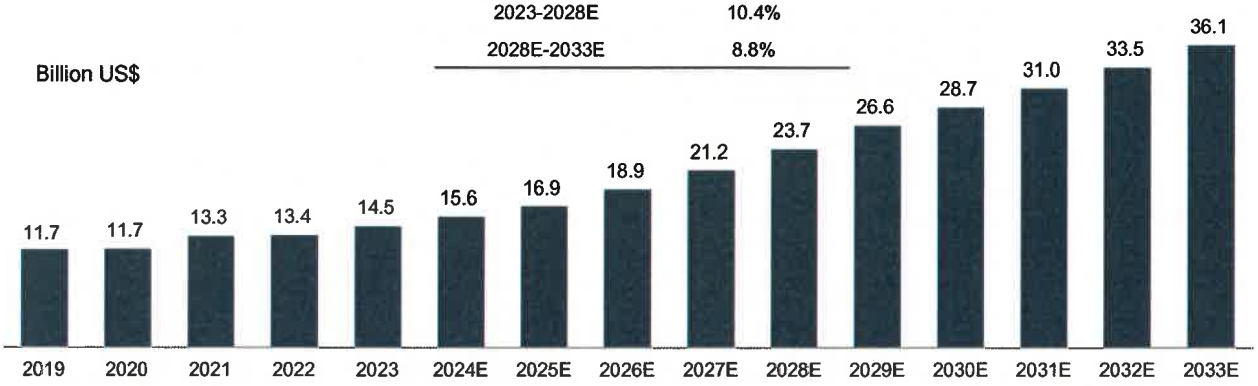
Source: NMPA, FDA, Frost & Sullivan Analysis

Historical and Forecasted Market Size of Global Anti-VEGF Agents, 2019-2033E

- The market size of global anti-VEGF agents increased from US$11.7 billion in 2019 to US$14.5 billion in 2023 with a CAGR of 5.5% from 2019 to 2023. It is expected to continue to increase to US$23.7 billion in 2028 and US$36.1 billion in 2033 with a CAGR of 10.4% and 8.8% from 2023 to 2028 and from 2028 to 2033 respectively.

Historical and Forecasted Market Size of Global Anti-VEGF Agents, 2019-2033E

Period	CAGR
2019-2023	5.5%
2023-2028E	10.4%
2028E-2033E	8.8%



Source: Literature Review, Expert Interview, Annual Report, and Frost & Sullivan Analysis

Global and China Marketed Anti-VEGF Biologics Indicated for Retinal Diseases

- The anti-VEGF biologics provide a non-surgical way to treat retinal diseases.

Generic Name	Brand Name	Maufacturers	First Approved Year and Authority	Annual Cost Per Patient in the U.S.	Global Sales Revenue Initial Year Post-Launch	Global Sales Revenue After 5 Year Post-launch
Ranibizumab	Lucentis®	Novartis/Genentech (Roche)	2006.06/FDA	US$3,726-US$14,904	US$1,208 million (2007)	US$ 2,820.5 million (2010)
Aflibercept	Eylea®	Regeneron/Bayer/Santen	2011.11/FDA	US$15,664-US$25,454	US$ 856.0 million (2012)	US$ 4,294.6 million (2015)
Brolucizumab	BEOVU®	Novartis	2019.10/FDA	US$14,826-US$16,944	US$190.0 million (2020)	Not disclosed (2023)
Faricimab	Vabysmo™	Genentech (Roche)	2022.01/FDA	US$14,172-US$33,068	US$671.0 million (2022)	US$ 2,623.3 million (2023)
Conbercept	Lumitin	Kanghong Pharmaceutical	2013.12/NMPA	/	RMB 74.0 million (2014)	RMB 882.0 million (2018)

Note:
Annual costs will vary based on several factors, including type of retinal disease and a patient's prescribed dosing schedule.

Source: FDA, Frost & Sullivan Analysis

Glossary

"abbreviated NDA"	abbreviated new drug application, an application for a generic drug to an approved drug]
"active pharmaceutical ingredient" or "API"	active pharmaceutical ingredient, the substance in a pharmaceutical drug that is biologically active
"ADS" or "ADS platform"	antibody-drug synergism or antibody-drug synergism platform, an innovative technology designed by the Group to either improve the efficacy or extend the duration of drug effect for intravitreally administered drugs by involving conjugating an antibody drug to a small molecule drug, using a linker designed to be enzymatically hydrolysed in the vitreous humour in a controlled manner
"AE"	adverse event, any untoward medical occurrence in a patient or clinical trial subject associated with the use of a drug or other therapy
"amblyopia"	Reduced vision typically in one eye that results from the brain suppressing input from the affected eye due to the unequal visual signals from each eye leading to poor development of visual acuity in the affected eye
"allergen"	a substance that causes an allergic reaction]
"AMD"	age-related macular degeneration, a disease that causes damage to the macula and leads to progressive loss of central vision
"best-in-class"	the drug with the best clinical advantage within a drug class
"BLA"	biologic license application, an application in the United States for permission to introduce a biologic product into U.S. inter-state commerce
"DME"	diabetic macular edema, a complication of diabetes wherein the patient loses the central vision to a certain degree
"CDMO"	contract development and manufacturing organisation, a company that provides comprehensive drug manufacturing services and drug development services for other companies on a contract basis
"Clinical trial region"	the place of conducting clinical trials
"CMC"	chemistry, manufacturing and controls, a process which mainly includes defining a drug product's characteristics, formulation development and product testing to ensure that the product is safe, effective and consistent between batches]
"CMO"	contract manufacturing organisation, a company that manufactures drug products for other companies on a contract basis]
"Compazine"	a brand name for the medication prochlorperazine, which belongs to a class of drugs called phenothiazines, primarily used to treat nausea and vomiting, particularly in patients undergoing chemotherapy or radiation therapy
"CRO"	contract research organisation, a company that provides support to pharmaceutical companies by providing a range of professional research services on a contract basis
"Cycloplegia"	paralysis of the ciliary muscle of the eye resulting in dilatation of the pupil and paralysis of accommodation
"disability-adjusted life years"	a measure of overall disease burden, expressed as the number of years lost due to ill-health, disability or early death.
"double-masked clinical trial"	a type of clinical trial in which neither the participants nor the research team know which treatment a specific participant is receiving, which helps prevent bias or expectations from influencing the results of the study
"dry eye"	a condition associated with inadequate tear production and marked by redness, itching and burning of the eye

Glossary

"DED"	dry eye disease, a multifactorial disease of the tear film, characterised by increased tear film osmolarity, ocular inflammation, deterioration of ocular surface and neurosensory abnormalities, can cause some ocular symptoms such as ocular discomfort and visual disturbance
"diagnosis rate"	the percentage of individuals with the disease who is identified in healthcare institutions
"diagnosis and treatment rate"	the percentage of individuals with the disease who is identified in healthcare institutions and receive appropriate medical care or intervention
"ECPs"	eye care professionals
"First posted date"	the date on which www.ClinicalTrials.gov or www.chinadrugtrials.org.cn.
"FGFRs"	fibroblast growth factor receptors, membrane-spanning proteins that are a subgroup of the family of tyrosine kinase receptor
"first-in-class"	a drug that uses a new and unique mechanism of action for treating a medical condition
"GCP"	good clinical practice, an international ethical and scientific quality standard developed by International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use for designing, conducting, recording and reporting trials that involve the participation of human subjects
"generic drug"	a drug that is chemically identical to an original drug and is generally available in the same strength and dosage forms as the original
"GLP"	good laboratory practice, a quality system of management controls for research laboratories and organizations to try to ensure the uniformity, consistency, reliability, reproducibility, quality and integrity of chemical and pharmaceuticals non-clinical safety tests
"GMP"	good manufacturing practice, a system for ensuring that products are consistently produced and controlled according to quality standards
"IND"	investigational new drug, the application for which is the first step in the drug review process by regulatory authorities to decide whether to permit clinical trials. Also known as clinical trial application, or CTA, in China
"juvenile myopia"	myopia in children and adolescents aged 5 to 19 years old
"KOLs"	key opinion leaders, individuals or organisations who have expert product knowledge and influence in a particular field, and who are trusted by relevant interest groups and have significant effects on consumer behaviour
"mCNV"	myopic choroidal neovascularization, a complication of myopia, which causes the creation of new blood vessels in the choroid, a vascular membrane of the eyeball
"MGD"	meibomian gland dysfunction, a chronic diffuse abnormality of the meibomian glands, characterised by terminal duct obstruction along with qualitative or quantitative changes in the glandular secretion
"MRCT"	multi-regional clinical trial, a clinical trial that is conducted in different regions under a common trial design for simultaneous global new drug development

Glossary

"MKI" or "MKI platform"	multi-kinase inhibitor or multi-kinase inhibitor platform
"Mydriasis"	excessive or prolonged dilatation of the pupil of the eye
"NDA"	new drug application, an application through which the drug sponsor formally proposes that the relevant regulatory authority approve a new drug for sales and marketing
"off-label use"	medication which is being used in a manner not specified in the approved packaging label
"ophthalmology"	a branch of medical science dealing with the structure, functions and diseases of the eye
"OTC drugs" or "OTC products"	over-the-counter drugs or products, drugs or products that are sold directly to a consumer without a prescription
"PDGFRs"	platelet-derived growth factor receptors, cell surface tyrosine kinase receptors for members of the platelet-derived growth factor family
"penetration rate"	the percentage of the target population that has adopted or is using the therapy
"Phase I clinical trial"	a study in which a drug is introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion, and if possible, to gain an early indication of its effectiveness
"Phase II clinical trial"	a study in which a drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the drug for specific targeted diseases, and to determine dosage tolerance and optimal dosage
"Phase III clinical trial"	a study in which a drug is administered to an expanded patient population at geographically dispersed clinical trial sites to generate statistically sufficient data to evaluate the efficacy and safety of the drug for regulatory approval and to provide adequate information for the labelling of the product
"pharmacokinetics" or "PK"	the study of the bodily absorption, distribution, metabolism, and excretion of drugs
"PI"	principal investigator, the scientist in charge an experiment or research report
"pre-clinical research"	research that tests a drug candidate on non-human subjects to gather efficacy and safety information to decide whether the drug candidate is ready for clinical trials in human subjects
"pterygium"	a benign proliferative ocular surface disease characterised mainly by wing-shaped and fibrovascular growth of the limbal and conjunctival tissue over the adjacent cornea
"randomised clinical trial"	a study in which the participants are divided by chance into separate groups that compare different treatments or other interventions

Glossary

"retina"	a thin layer of tissue that lines the back of the eye on the inside
"RVO"	Retinal vein occlusion, a disease due to the blockage of the retinal vein which can led to blurry vision or loss of vision
"SAEs"	serious adverse events, AEs that result in death, or is life-threatening, or require in-patient hospitalisation or cause prolongation of existing hospitalisation, or result in persistent or significant disability or incapacity, or is a congenital anomaly or birth defect
"standard of care"	a treatment that is accepted and widely used by medical experts as a proper and standard treatment for a certain disease
"TEAE"	treatment-emergent adverse event, an undesirable event not present prior to medical treatment, or an already present event that worsens either in intensity or frequency following the treatment]
"translational science"	a process of accelerating and turning biomedical research discoveries into real-world applications that improves people's health, such as diagnostics, treatments and cures
"treatment rate"	the percentage of individuals with the disease who receive appropriate medical care or intervention
"VEGF"	vascular endothelial growth factor, a signal protein produced by cells that stimulates the formation of blood vessels
"VEGFRs"	vascular endothelial growth factor receptors, tyrosine kinase receptors responsible for binding with VEGF to initiate signal cascades that stimulate angiogenesis among other effects

Verification Notes

- Each of Cloudbreak Therapeutics' MKI and ADS platforms is a leading platform for developing drug candidates targeting anterior and posterior ophthalmic diseases, respectively.
- Cloudbreak Therapeutics is one of the very few ophthalmology-focused biotech companies globally with R&D capabilities that cover the entire lifecycle of drug translational science - from early-stage discovery through to large-scale multi-region clinical trials and global product registration process.
- There exists multiple biologics for the treatment of ophthalmic diseases.
- The FDA Biologics License Application (BLA) is a request for permission to introduce, or deliver for introduction, a biologic product into interstate commerce.
- Patents are a property right granted by the United States Patent and Trademark Office anytime during the development of a drug and can encompass a wide range of claims. Currently, the term of a new patent is 20 years from the date on which the application for the patent was filed in the United States.
- Exclusivity refers to certain delays and prohibitions on approval of competitor drugs available under the statute that attach upon approval of a drug or of certain supplements. A new drug application (NDA) or abbreviated new drug application (ANDA) holder is eligible for exclusivity if statutory requirements are met. A 5-year period of exclusivity is granted to new drug applications for products containing chemical entities never previously approved by FDA. No 505(b)(2) application or ANDA may be submitted during the 5-year exclusivity period except that such applications may be submitted after 4 years if they contain a certification of patent invalidity or noninfringement. A 3-year period of exclusivity is granted for a drug product that contains an active moiety that has been previously approved.
- Growth drivers of China juvenile myopia drug therapy market include large potential market demand, atropine advances over other approaches, state focus and policy for myopia. Prevention and control implementation plan: Due to this drastic increase in both the prevalence and severity of myopia, on August 30, 2018, eight national departments jointly issued the "Comprehensive Prevention and Control of Myopia in Children and Adolescents Implementation Plan" with the goal of controlling the prevalence of myopia in the high school populations at about 70 percent by 2030.
- Cloudbreak Therapeutics is one of the few ophthalmology companies worldwide working with the FDA and the NMPA to set new global standards for treatment, regulatory review and clinical trial for pterygium and vascularised pinguecula.
- Australia is a preferred destination for early-stage clinical trials, due to its cost-efficiency, time-saving and high-quality benefits. At later stage, clinical trials will be conducted in the regions where the regulatory approval is going to be pursued.

Verification Notes

- Some countries require approvals of the sale price of a drug before it can be marketed, and the pricing review period may not begin until after marketing or licensing approval is granted. In some markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted.
- A primary trend in the global healthcare industry is cost containment. Government authorities and these third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products.
- Many pharmaceutical companies have developed worldwide patent portfolios of varying sizes and breadth. Many patents may cover a marketed product, including but not limited to, the composition of the product, methods of use, formulations and production processes. Not all such patents have expired globally, including potentially in the jurisdictions where we are developing and intend to commercialise our drug candidates.
- Periodic maintenance fees, renewal fees, annual fees and various other governmental fees on patents and patent applications are due to be paid to the USPTO, the CNIPA and other patent agencies in other jurisdictions in several stages over the lifetime of a patent. The USPTO, the CNIPA and other governmental patent agencies also require compliance with a number of procedural, documentary, and other similar provisions during the patent application process.
- Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications are typically not published until at least several months after filing.
- Off-label use refers to the unapproved use of an approved drug.
- Ofev (nintedanib), manufactured by Boehringer Ingelheim, is the reference listed drug for CBT-001. Ofev, initially approved by FDA in 2014, is indicated for the treatment of idiopathic pulmonary fibrosis, chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype, and Slowing the rate of decline in pulmonary function in patients with systemic sclerosis-associated interstitial lung disease. Nintedanib is a small molecule that inhibits multiple receptor tyrosine kinases (RTKs) and non-receptor tyrosine kinases (nRTKs). Nintedanib inhibits the following RTKs: platelet-derived growth factor receptor (PDGFR) α and β, fibroblast growth factor receptor (FGFR) 1-3, vascular endothelial growth factor receptor (VEGFR) 1-3, colony stimulating factor 1 receptor (CSF1R), and Fms-like tyrosine kinase-3 (FLT-3). These kinases except for FLT-3 have been implicated in pathogenesis of interstitial lung diseases (ILD). Nintedanib binds competitively to the adenosine triphosphate (ATP) binding pocket of these kinases and blocks the intracellular signaling cascades, which have been demonstrated to be involved in the pathogenesis of fibrotic tissue remodeling in ILD. Nintedanib, pharmacologically targeting the angiogenic and fibrotic pathogenesis of pterygium, has the potential to eliminate or postpone the need for surgery.

Verification Notes

- Inlyta (axitinib), manufactured by Pfizer is the reference listed drug for CBT-004. Inlyta, initially approved by FDA in 2012, is indicated for the treatment of advanced renal cell carcinoma. Axitinib, a small molecule multi-receptor tyrosine kinase inhibitor, have the advantage of blocking VEGF receptors, and blocking platelet derived growth factor receptors, which play a role in neovascularization and pathologic angiogenesis.
- The list price of Restasis and Xiidra is approximately US$600 per month in the U.S.
- In the U.S. and China, orthokeratology costs (for both eyes) can range between $1,000 to $4,000, and between RMB 8,000 to RMB 15,000, based on the complexity and progression of the patient's myopia. The lifespan of ortho-k lenses can vary based on the individual wearer's care and use, normally 1 to 2 years.
- The end user price of ISOPTO ATROPINE 1%, manufactured by Alcon, indicated for mydriasis, cycloplegia, penalization of the healthy eye in the treatment of amblyopia in the U.S., is around $67 for a supply of 5 milliliters. As ISOPTO ATROPINE 1% is usually used during the eye examination, it is not applicable to calculate the annual cost per patient.
- Even though the ophthalmic emulsion may potentially cause temporarily blurred vision due to its less effective hydration comparing to aqueous drug therapy, no significant limitation and disadvantage of the ophthalmic emulsion has been identified, that could effect the patients' acceptance. Restasis, an ophthalmic emulsion has been approved for dry eye treatment by the FDA. Restasis has gained good acceptance by patients and achieved commercial success over the years.
- The listed price of Eylea intravitreal solution (40 mg/mL) is around US$1,958 and RMB 6,000 for a supply of 0.05 milliliters in the U.S. and in China.
- Atropine Sulfate Injection, given intramuscularly, intravenously or subcutaneously, has been approved by FDA for temporary blockade of severe or life threatening muscarinic effects.
- As low dose (0.01%) atropine eyedrops is more well-tolerated by patients, it has been demonstrated to be safe and effective in slowing myopia progression. Both of the approved atropine indicated for juvenile myopia (i.e. Eikance and Xinqi Meioupin) are prescibed for low dose.
- In the United States and China, the diagnosis and treatment rate of progressive myopia is expected to increase slightly and still remain over 90% in 2025.and reach approximately 100% in 2030.
- .The annual cost of juvenile myopia drug therapies in the United States and China is estimated be around US$600 based on the price of Eikance and several in-hospital preparations and RMB3,600 based on the price of Xingi Meioupin, respectively.

Verification Notes

- The diagnosis rate and treatment rate of pterygium is expected to reach 3.5% and 0.9% in the United States and China, respectively, in 2027 and 6.1% and 2.8% in the United States and China, respectively, in 2033. And the expected penetration rate of pterygium drug therapies being 0.5% and 0.2% in the United States and China, respectively, in 2027; and 7.6% and 1.5% in the United States and China, respectively, in 2033.
- The growth rate of the expected market size for pterygium drug therapies was also agents currently approved for retina benchmarked with that of the surging market size of anti-VEGF diseases, mainly because the market for anti-VEG;F agents indicated for retinal diseases has observed several blockbuster drugs in recent years before there was no approved drug therapy. The similarity of such anti-VEGF agents with 0BT.00l includes the following aspects: (i) comparable first-in-class potential/feature, (ii)comparable disease nature, and (iii) comparable drug price.
- The penetration rate of myopia drug therapies (representing the penetration rate of myopia drug therapies among patients who currently require optical correction and refractive surgery)among juvenile myopia patient group was nil up to 2023 in the United States and China, and is expected to reach approximately 10.2% and 8.9% in 2033, respectively.

Requested Drug Information

Brand Name	Active Compound	Manufacturer	Regulatory Authority	Initial Approval	Indications	Patent Applicant Holder
Ofev	Nintedanib	Boehringer Ingelheim	FDA	2014.10	Idiopathic pulmonary fibrosis, chronic fibrosing interstitial lung diseases (ILDs), and systemic sclerosis-associated interstitial lung disease	Boehringer Ingelheim
Inlyta	Axitinib	Pfizer	FDA	2012	Advanced renal cell carcinoma	PF PRISM CV
Mitozytrex	Mitomycin	Supergen	FDA	2002	Disseminated adenocarcinoma of the stomach or pancreas	Supergen
Sporanox	Itraconazole	Janssen	FDA	1992	Oropharyngeal and esophageal candidiasis	Janssen
Dexacort	Dexamethasone sodium phosphate	UCB	FDA	1982	Endocrine disorders, rheumatic disorders, collagen diseases, dermatologic diseases, allergic states and so on	UCB
Vibativ	Telavanvancin hydrochloride	Cumberland Pharmaceuticals	FDA	2009	Complicated skin and skin structure infections caused by susceptible Gram-positive bacteria	Cumberland Pharmaceuticals
Indocollyre	Indomethacin	BAUSCH & LOMB	EMA	1989	Ocular inflammatory processes of various origin	BAUSCH & LOMB
ISOPTO ATROPINE	Atropine Sulfate	Alcon	FDA	2016.12	Mydriasis, cycloplegia, penalization of the healthy eye in the treatment of amblyopia	Alcon

Note:
The molecule patent of Ofev expires in September 2026.
The molecule patent of ISOPTO ATROPINE has expired.

Source: FDA, Frost & Sullivan Analysis