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THE GENE THERAPY MARKET

Overview of Gene Therapy

Gene therapy is a novel and disruptive treatment method that uses various genetic altering techniques to treat diseases at their source. Its treatment mechanisms include, among others, gene replacement, gene addition, gene expression alteration, and gene editing. Compared with traditional medicines that generally treat symptoms or modulate physiological pathways, gene therapy goes upstream and targets the root genetic defect or blocks the pathogenic mechanism, offering curative potential to inherited diseases with no existing treatment options, and long-lasting benefit with a single treatment for refractory diseases.

While the adoption of gene therapy used to be constrained by its limited application scenarios and high costs, advances in gene therapy in recent years have enabled it to gradually pivot from ultra-rare, monogenic disorders towards more prevalent, large-market indications. Developments in the manufacturing process of gene therapy drugs are also enabling early-movers in the industry to reduce product cost and improve accessibility of gene therapy treatments. While there are already more than a dozen gene therapy products approved by regulators globally, recent developments have created significant opportunities for fast-moving and sophisticated gene therapy companies.

Gene therapy typically utilizes vectors to deliver genetic materials into target cells where they are transcribed and translated into functional proteins. Gene therapy vectors are primarily divided into viral and non-viral vectors. Viral vectors, which account for over 90% of gene therapies with a known delivery method, exploit their natural infection and fusion mechanisms to achieve high transduction efficiency and long-term expression in target cells. In comparison, non-viral vectors offer benefits such as lower immunogenicity and larger cargo capacity, but generally exhibit lower delivery efficiency and shorter duration of expression.

Commonly used viral vectors include adeno-associated viruses ("**AAV**"), adenoviruses, herpes simplex viruses, lentiviruses, and retroviruses. The following diagram sets forth a comparison of commonly used viral vectors. In particular, AAV enjoys advantages including wide host range, long-term *in vivo* expression and low immunogenicity, although it also tends to have low loading capacity. For details, see "— rAAV Gene Therapy Drugs and CMC Platforms — Overview of rAAV Gene Therapy".

Comparative Analysis of Commonly Used Viral Vectors in Gene Therapy

	AAV	Adenovirus	Herpes Simplex Virus	Lentivirus	Retrovirus
Genome	Single-stranded DNA	Double-stranded DNA	Double-stranded DNA	Single-stranded RNA	Single-stranded RNA
Size	18-26nm	70-90nm	150-200nm	80-130nm	80-130nm
Host Species	Primarily non-dividing cells	Dividing/Non-dividing Cells	Dividing/Non-dividing Cells	Dividing/Non-dividing Cells	Dividing Cells
Cargo Gene Capacity	5kb	8kb	>30kb	8kb	8kb
Host Integration	✗	✗	✗	✓	✓
Long-term Expression	✓	✗	✓	✓	✓
Immunogenicity	Low	High	High	Moderate	Moderate
Advantages	• Wide host range • Long-term in vivo expression • Low immunogenicity	• Suitable for almost all cell lines and primary cells • Target specific cell-surface receptors	• High virus titer • Large capacity for exogenous genes • Wide range of host cells	• Wide range of infected hosts • High gene expression level	• Low toxicity • Stable cell line for the target gene
Disadvantages	• Low loading capacity	• Short gene expression time • Multiple infections can trigger an immune response	• Can trigger an immune response • Cytotoxic	• Poor in-vivo transfection performance • Risk of mutation	• Poor in-vivo infection efficiency • Risk of oncogene activation/insertional mutation

Source: Frost & Sullivan Report

Development Pathway and Clinical Application Scenarios

The development of gene therapy has achieved significant milestones since its early days. The discovery of AAV as a replication-defective virus dates back to 1965. The concept of gene therapy was subsequently proposed in 1971 and rAAV was first used as a gene delivery vector in 1974. The FDA approved the world's first clinical trial of gene therapy in humans in 1990. In 2017, Luxturna® became the first FDA-approved rAAV gene therapy for the treatment of IRD associated with biallelic RPE65 mutations. The approval rate for gene therapy drugs accelerated greatly since 2022, mainly driven by the maturation of underlying technologies and a more established regulatory framework. Among the 16 gene therapy drugs approved in the United States since 2015, 14 were approved since 2022, such as Hemgenix® in 2022, Roctavian®, Casgevy® and Vyjuvek® in 2023, and Begvez® in 2024.

Currently, approved gene therapy drugs are primarily used for rare diseases. The FDA defines rare diseases as those affecting fewer than 200,000 people in the United States, and the National Health Commission ("**NHC**") of the PRC maintains a list of designated rare diseases based on miscellaneous factors. Among the 16 gene therapy drugs approved in the United States and one gene therapy drug approved in China since 2015, 15 drugs, or 88.2%, target rare diseases as defined by the FDA or designated by the NHC. However, there has been a trend for gene therapy research and development to pivot from rare diseases towards more prevalent, large-market indications. Among the 178 and 110 gene therapy drugs under clinical stage development in the United States and China, 38% and 46% of them target more prevalent indications, respectively.

In terms of the therapeutic areas targeted by gene therapy drugs, ophthalmic disease is the most targeted area among all gene therapy drugs under clinical stage development in the United States and in China. There are 39 and 40 gene therapy drugs under clinical stage development targeting ophthalmic diseases in the United States and China, respectively, representing 24% and 36% of the total number of gene therapy drugs under development. Ophthalmic diseases have received major attention since the eye is an ideal target for gene therapy due to its immune-privileged status, compartmentalization, and accessibility for local delivery. In 2017, Luxturna® was approved in the United States as an rAAV gene therapy for the treatment of RPE65-mediated IRD, validating gene therapy as a viable treatment option for ophthalmic diseases. Gene therapy drugs currently under development for ophthalmic diseases target not only monogenic IRDs such as Leber congenital amaurosis ("**LCA**") but also high-prevalence, multifactorial refractory diseases like neovascular nAMD, DME and DR.

Gene therapy drugs also offer great potential to other therapeutic areas such as nervous system, cardiovascular and hematologic diseases. With cardiovascular diseases as an example, while traditional drugs are primarily palliative and require lifelong administration, gene therapy may achieve sustained transgene expression over multiple years with a single administration.

Approved Drugs and Drugs under Development

Since 2015 and up to the Latest Practicable Date, the United States has approved 16 gene therapy products, of which 14 were approved since 2022. Since 2015 and up to the Latest Practicable Date, China has approved one gene therapy product. Recent regulatory changes have raised expectations that more drug candidates will be approved in the near future.

The following table sets forth certain details of these approved gene therapy drugs.

Approved Gene Therapy Drug in China

Brand Name	Drug Name	Company	Vector type	Target	Indication	NMPA First Approval Time	Therapeutic Area	Treatment Cost (RMB in millions)	2024 Annual Sales (US$ in million)
信玖凝®	Dalnacogene ponparvovec	Belief Biomed Inc	Adeno-associated virus vector rAAV	FIX	Hemophilia B	2025-04-08	Hematological disorders, rare disease	2.8	NA

Source: CDE, Frost & Sullivan Report

Approved Gene Therapy Drugs in the United States

Brand Name	Drug Name	Company	Vector type	Target	Indication	FDA Approval Time	Therapeutic Area	Treatment Cost (US$ in millions)	2024 Annual Sales (US$ in million)
Papzimeos®	Zopapogene imadenovec	Precigen	Adenovirus vector AdV	HPV	Recurrent respiratory papillomatosis	2025-08-14	Respiratory Diseases, rare disease	0.5*	NA
Zevaskyn®	Prademagene zamikeracel	Abeona Therapeutics	Retroviral vector (RV)	COL7A1	Recessive dystrophic epidermolysis bullosa	2025-04-29	Rare disease, skin disorders	3.1	NA
Upstaza®	Eladocagene exuparvovec	PTC Therapeutics	Adeno-associated virus vector AAV2	AADC	Aromatic L-amino-acid decarboxylase deficiency	2024-11-13	Neurological disorders, rare disease	3.7	NA
Beqvez®	Fidanacogene elaparvovec	Roche	Adeno-associated virus vector AAVrh74	FIX	Hemophilia B	2024-04-26	Hematological disorders, rare disease	3.5	NA
Lenmeldy®	Atidarsagene autotemcel	Orchard Therapeutics	Lentiviral vector (LV)	ARSA	Metachromatic leukodystrophy	2024-03-18	Rare disease, neurological disorders, endocrine & metabolic disorders	4.3	21.8
Casgevy®	Exagamglogene autotemcel	CRISPR Therapeutics/ Vertex Pharmaceuticals	Electroporation	BCL11A	β-thalassemia	2024-01-16	Hematological disorders	2.2	10
	Exagamglogene autotemcel	CRISPR Therapeutics/ Vertex Pharmaceuticals	Electroporation	BCL11A	Sickle cell disease	2023-12-08	Hematological disorders, rare disease		
Lyfgenia®	Lovotibeglogene autotemcel	Bluebird Bio	Lentiviral vector (LV)	HBB	Sickle cell disease	2023-12-08	Hematological disorders, rare disease	3.1	11.6

Brand Name	Drug Name	Company	Vector type	Target	Indication	FDA Approval Time	Therapeutic Area	Treatment Cost (RMB in millions)	2024 Annual Sales (US$ in millions)
Roctavian®	Valoctocogene Roxaparvovec	BioMarin Pharmaceutical	Adeno-associated virus vector AAV5	FVIII	Hemophilia A	2023-06-29	Hematological disorders, rare disease	2.9	26.0
Elevidys®	Delandistrogene moxeparvovec	Sarepta Therapeutics	Adeno-associated virus vector AAVrh74	Microdystrophin	Duchenne muscular dystrophy	2023-06-23	Rare disease, musculoskeletal disorders	3.2	820.8
Vyjuvek®	Bercolagene telserpavec	Krystal Biotech	Herpes simplex virus vector (HSV1)	COL7A1	Dystrophic epidermolysis bullosa	2023-05-19	Rare disease, skin disorders	0.6*	290.5
Adstiladrin®	Nadofaragene firadenovec	Merck & Co./ Ferring Pharmaceuticals	Adenoviral vector (AdV)	IFNA2	Non-muscle-invasive bladder cancer	2022-12-16	Oncology	0.2*	75.6
Hemgenix®	Etranacogene dezaparvovec	uniQure Biopharma/CSL	Adeno-associated virus vector AAV5	FIX	Hemophilia B	2022-11-22	Hematological disorders, rare disease	3.5	NA
Skysona®	Elivaldogene autotemcel	Bluebird Bio	Lentiviral vector (LV)	ABCD1	Cerebral adrenoleukodystrophy	2022-09-16	Rare disease, neurological disorders, endocrine & metabolic disorders	3.0	9.9
Zynteglo®	Betibeglogene autotemcel	Bluebird Bio	Lentiviral vector (LV)	HBB	β-thalassemia	2022-08-17	Hematological disorders	2.8	62.3
Zolgensma®	Onasemnogene abeparvovec	Novartis	Adeno-associated virus vector AAV9	SMN1	Spinal muscular atrophy	2019-05-24	Rare disease, musculoskeletal disorders, neurological disorders	2.1	1,214.0
Luxturna®	Voretigene neparvovec	Roche/Novartis	Adeno-associated virus vector AAV2	RPE65	Inherited retinal dystrophy due to biallelic RPE65 mutations	2017-12-19	Ophthalmic disorders, rare disease	0.9	NA

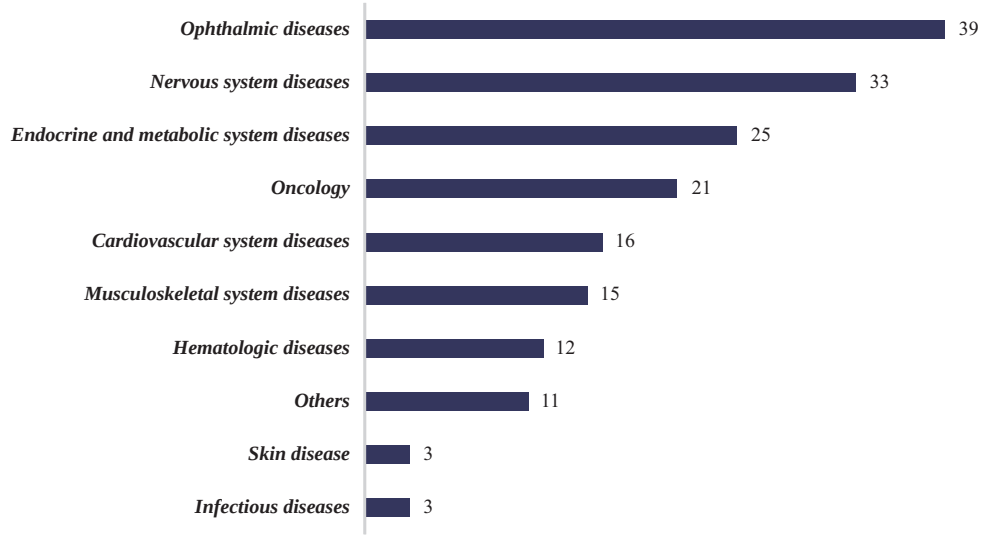
Note:

* Denotes annual treatment cost instead of total treatment cost, as the number of years required for treatment vary by patient.

Source: FDA, Frost & Sullivan Report

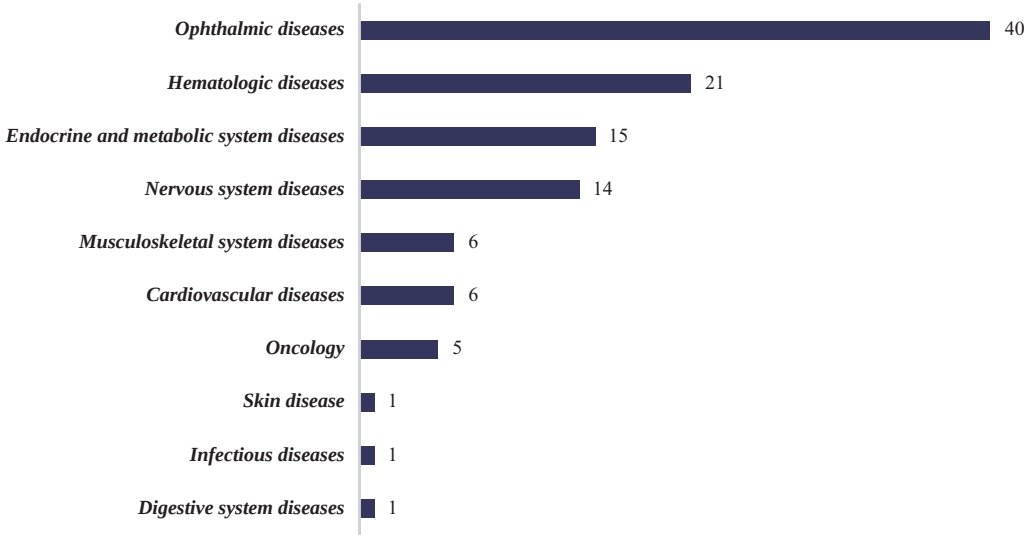
There is currently a robust and diverse development pipeline for gene therapy drugs, including 178 clinical stage candidates in the United States and 110 clinical stage candidates in China as of the Latest Practicable Date. The following charts set forth a breakdown of the drug candidates by therapeutic area.

Gene Therapy Drugs under Development in the United States



Source: Frost & Sullivan Report

Gene Therapy Drugs under Development in China

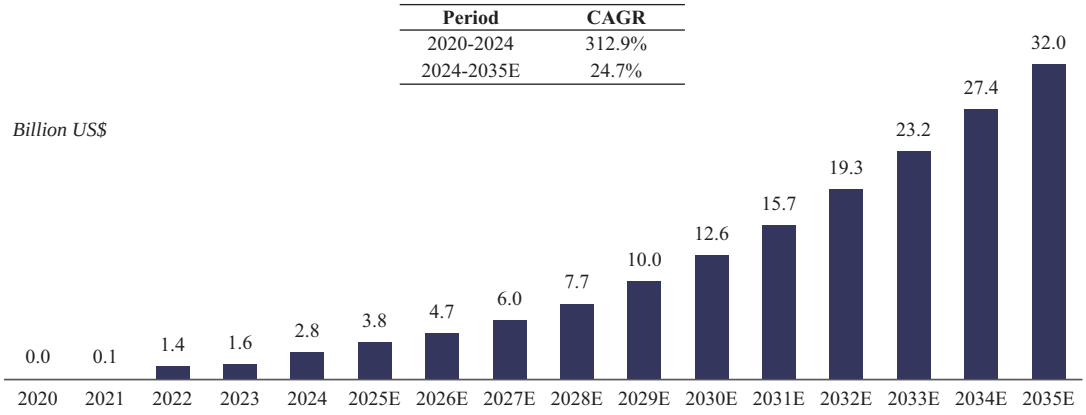


Source: Frost & Sullivan Report

Gene Therapy Market Size

The global gene therapy market has witnessed rapid growth in the last few years, reaching a market size of US$2.8 billion in 2024. The market has gone through a period of exponential growth from 2020 to 2024 with a CAGR of 312.9%. Going forward, the global market is expected to grow at a CAGR of 24.7% from 2024 to 2035 and reach a market size of US$32.0 billion in 2035. The following diagram illustrates the growth of the global gene therapy market.

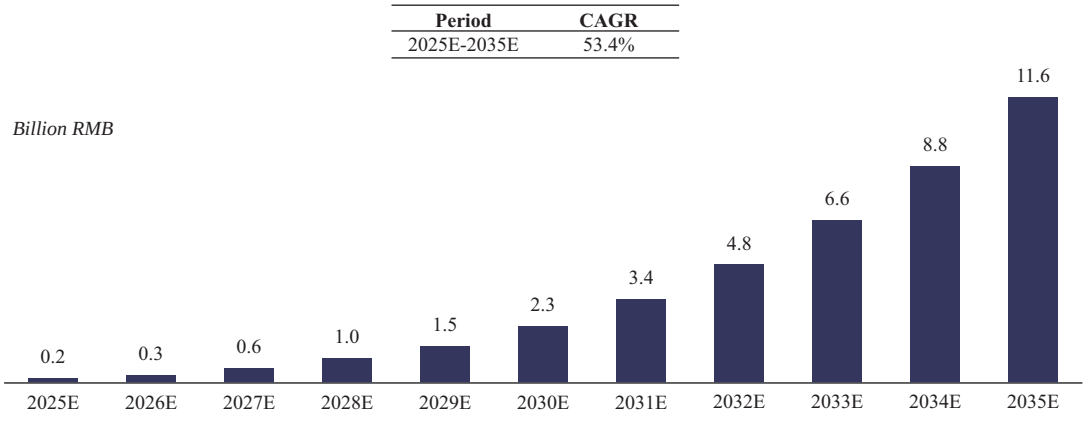
Global Gene Therapy Market, 2020-2035E



Source: Frost & Sullivan Report

The gene therapy market in China is also poised for a period of rapid growth. In 2024, the gene therapy market in China had a minimal scale. It is expected to grow at a CAGR of 53.4% from 2025 to 2035 and reach a market size of RMB11.6 billion in 2035. The following diagram illustrates the growth of the China gene therapy market.

Gene Therapy Market in China, 2025E-2035E



Source: Frost & Sullivan Report

Challenges and Entry Barriers to the Gene Therapy Market

The major challenges and entry barriers to the gene therapy market are set forth as follows:

- ***Manufacturing capacity and cost constraints.*** The gene therapy market is confronting a severe manufacturing capacity constraint, driven by the rapid expansion of clinical pipelines and the inherent complexity of production processes. These therapies require specialized equipment, highly trained personnel, and intricate steps such as viral vector production, leading to exorbitant upfront costs and prolonged development timelines. Moreover, the current lack of scalable and standardized manufacturing methods poses significant challenges for smaller biotechnology companies, restricting market entry and ultimately limiting patient access to these transformative treatments.

- ***Regulatory, safety and long-term efficacy uncertainties.*** As a novel therapeutic approach, gene therapy still faces significant uncertainties in both regulatory oversight and clinical implementation. Long-term data regarding treatment durability and potential delayed adverse effects remain insufficient, impacting physicians' willingness to adopt these therapies and patients' confidence in them. Given the long-lasting nature of genetic interventions, their regulatory framework is exceptionally stringent and continuously evolving, demanding extensive preclinical and clinical evidence. This dynamic environment heightens research and development risks and prolongs time-to-market cycles.

- ***High price and limited market acceptance.*** There is a fundamental tension between research and development costs and market accessibility. Most approved therapies target ultra-rare diseases affecting small patient populations, necessitating high prices to recoup investments. For example, Luxturna®, the only gene therapy treatment option for RPE65-mediated IRD approved in the United States and Europe, is priced at approximately US$850,000 per treatment. However, healthcare systems and payers struggle to bear such costs, resulting in fragmented reimbursement policies with limited coverage.

Growth Drivers and Future Trends of the Gene Therapy Market

The growth of the gene therapy market is expected to be driven by the following factors:

- ***Innovation in vector delivery technology.*** Innovations in vector delivery systems and the use of gene-editing tools to improve existing gene-therapy methods are major drivers of the gene therapy market. The iterative upgrading of gene-delivery technologies is closely linked to the innovation of gene-delivery vectors. Specifically, the employment of artificial intelligence is accelerating the development of rAAV vectors. AI models analyze vast datasets to design novel AAV capsids with enhanced tissue targeting, reduced immunogenicity, and improved yield.

- ***Advances in detection technology drive target discovery and screening.*** Improved detection technologies, particularly gene sequencing, have enabled more effective target discovery. In addition, genome breakthroughs have sped up drug screening, creating more pharmaceutical opportunities.

- ***Favorable government policies.*** Countries globally have rolled out numerous supportive policies for basic biomedical research and gene drug development. These involve boosting basic research investment, promoting advanced biotech such as gene and cell therapy, and prioritizing the review of innovative gene-related drugs.

- ***Growing investment in research and development and capital support.*** The global gene therapy market is experiencing significant growth thanks largely to the increased research and development investment and capital support. These have enabled companies and research institutes to expand and improve their gene therapy platforms and operations by leveraging the latest research and development technologies, substantial project experience, and the increasingly sophisticated industry support systems.

In China, the growth of the gene therapy market is expected to be further driven by public-private collaborations that promote the development of commercial insurances that cover gene therapy drugs. In December 2025, the National Healthcare Security Administration published the Innovative Drug Directory for Commercial Health Insurances, covering 19 innovative drugs that offer significant clinical benefits but are not covered by public health insurances, including several gene therapy drugs. Drugs listed on the Innovative Drug Directory are expected to supplement public health insurances and receive coverage from commercial health insurances, including the government-supervised, privately-operated Hui Min Bao (惠民保).

The future development of the gene therapy market is likely to witness the following trends:

- ***Expanding application of gene therapy.*** Gene therapy is shifting from rare diseases to more prevalent indications. Early successes in the treatment of rare diseases such as spinal-muscular atrophy and LCA validated the treatment method, but pipelines are now targeting large-market conditions including heart failure, type 2 diabetes, hypertension, chronic pain and Alzheimer's disease. This strategic shift is expected to move gene therapy from a niche intervention to a mainstream therapeutic modality across the spectrum of refractory and inherited illnesses.

- ***Increasingly cost-effective platforms for research and development and production.*** Currently, there are two major cell culture platforms for gene therapy: the Bac/Sf9 system and HEK293 system. Depending on the type of cell growth, they are further divided into suspension, adherent, and microcarrier-based cultures. Suspension culture is widely used and has become the mainstream choice due to its ease of scale-up. Companies are constantly exploring and iteratively improving various culture process platforms. These platforms are suitable for the production of different types of viral vectors and can meet the requirements of large-scale production through process optimization. Domestic manufacturers, by continuously refining their processes, have been able to reduce costs while steadily increasing viral titers and single-cell yields.

- ***Affordability and accessibility.*** The gene therapy market is expected to experience improving affordability and accessibility, driven by (i) biotech companies' ongoing efforts to enhance the cost-effectiveness of research and development and manufacturing processes, (ii) the government's support for increasingly flexible and diversified payment options, such as the expansion of commercial health insurance coverage and policy-supported reimbursement mechanisms, and (iii) higher patient volume and economies of scale which may allow more patient-friendly pricing.

- ***Enhancing safety profile.*** Future gene therapy development is expected to enhance safety through refined vector designs, reduced immunogenicity, and improved targeting specificity. Innovations such as transient expression systems, controllable gene switches, and lower-integration-risk vectors aim to minimize off-target effects and long-term adverse events, supporting broader patient access and regulatory acceptance.

- ***Increasingly stringent quality control standards.*** To improve product safety and efficacy when manufacturing at scale, it is crucial to conduct quality research on gene therapy products, establish corresponding manufacturing and quality control methods and standards, carry out systematic non-clinical studies, and evaluate safety risks as well as effectiveness of action mechanisms.

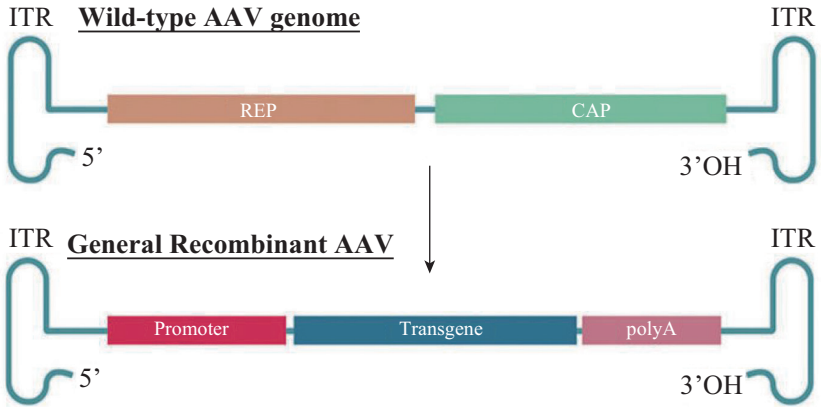
rAAV GENE THERAPY DRUGS AND CMC PLATFORMS

Overview of rAAV Gene Therapy

AAV is a single-stranded DNA virus, and the two ends of its genomic DNA are inverted terminal repeat ("**ITR**") sequences which are required for DNA replication initiation and packaging of recombinant AAV virus particles. Between the ITR sequences lies the viral coding region, which contains two genes, Rep and Cap. Among them, the Rep gene mainly functions in the replication of the viral genome and its integration with the host genome, while the Cap gene mainly functions in the packaging of the viral genome and its secretion from host cells.

For rAAV gene therapy, wild-type AAV genomes are packaged into rAAV and used as vectors in gene therapies. The most widely used packaging method for rAAV relies on the triple transfection of HEK293 cells. This system employs three plasmids: a transfer plasmid carrying the gene of interest flanked by ITRs, a Rep/Cap plasmid providing AAV replication and capsid proteins, and an adenoviral helper plasmid supplying essential viral functions. However, for scalable manufacturing, the Bac/Sf9 system offers a compelling alternative. In this platform, recombinant baculoviruses deliver specially designed insect-promoter-driven Rep and Cap expression cassettes along with the ITR-flanked gene of interest to Sf9 insect cells. This method is particularly advantageous for large-scale production due to its superior scalability, as it utilizes viral infection rather than plasmid transfection, and lower cost, as it utilizes viral expansion instead of large-scale plasmid preparation. For details, see "— CMC Platforms for rAAV Vectors" below.

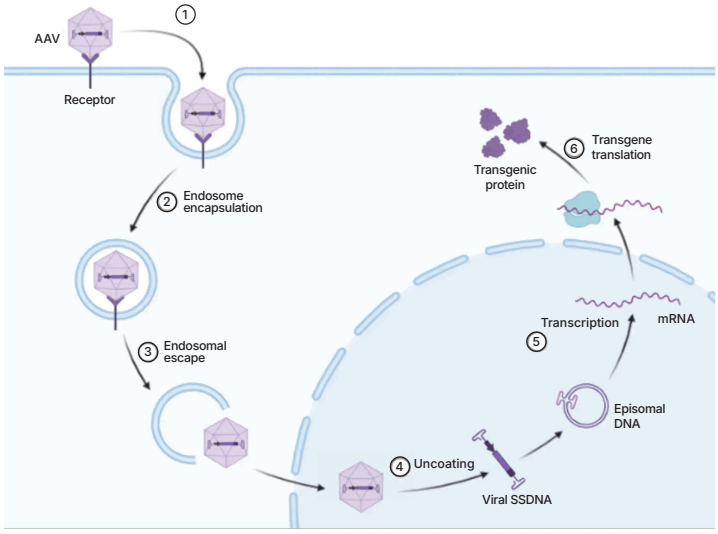
The following chart sets forth the structure of wild-type AAV genomes and general recombinant AAVs.



Source: Literature Review, Frost & Sullivan Report

Compared with other viral vectors, rAAV vector enjoys a number of advantages including being non-pathogenic, enabling efficient and sustained transgene expression, easy manipulation, and low immunogenicity. As a replication-defective DNA virus without autonomous replication ability, AAV can only replicate when other helper viruses simultaneously infect the host. Moreover, it barely integrates into the host genome.

rAAV gene therapy utilizes rAAV vectors to deliver genes of interest into target cells, where they are transcribed and translated into functional proteins. The following diagram illustrates the mechanisms of action of rAAV gene therapies when applied to treat target diseases.



Notes:

(1) Steps 1 through 3: rAAV vectors bind to cell surface receptors and are then internalized by vesicles and transported to the nuclear membrane.

(2) Steps 4 through 6: After detaching from the vesicles, rAAV transports its single-stranded genome into the cell nucleus, where it is converted into DNA, and then the expression of the target protein is completed through transcription and translation.

Source: Literature Review, Frost & Sullivan Report

AAV can be classified into different serotypes based on genetic sequencing and functional characteristics (designated AAV1 through AAV13). Different serotypes may have different tissue tropism, that is, tissue specificity for infection. Therefore, different serotypes may be used for different diseases and targeted tissues to achieve the best effect. For example, specific serotypes can be used to target photoreceptor cells or retinal pigment epithelium, making them ideal for treating ophthalmic diseases.

Approved Drugs and Drugs under Development

As of the Latest Practicable Date, there were nine rAAV gene therapy drugs approved globally. These drugs generally focus on rare diseases and have high production cost and treatment cost. Six of the approved drugs were produced with the HEK293 system and three were produced with the Bac/Sf9 system.

The following table sets forth certain details of these rAAV gene therapy drugs.

Drug Name	Company	Vector type	Target	Indication	Regulatory Approval Time	Therapeutic Area	Production System
Alipogene tiparvovec(1)	uniQure Biopharma, Cassie Pharma, Amsterdam Molecular Therapeutics, Xenon Pharma	Adeno-associated virus vector AAV1	LPL	Familial chylomicronemia syndrome	EMA: 2012-10-25	Cardiovascular disease, rare disease	Bac/Sf9
Voretigene neparvovec	Roche/Novartis	Adeno-associated virus vector AAV2	RPE65	Retinal dystrophy caused by biallelic RPE65 mutations	FDA: 2017-12-19 EMA: 2018-11-22 PMDA: 2023-06-26	Ophthalmologic disease, rare disease	HEK293
Onasemnogene abeparvovec	Novartis/Regenxbio	Adeno-associated virus vector AAV9	SMN1	Spinal muscular atrophy	FDA: 2019-05-24 PMDA: 2020-03-19 EMA: 2020-05-18	Musculoskeletal system disorder, neurological disease, rare disease	HEK293
Eladocagene exuparvovec	PTC Therapeutics	Adeno-associated virus vector AAV2	AADC	Aromatic L-amino acid decarboxylase deficiency	EMA: 2022-07-20 FDA: 2024-11-13	Neurological disease, rare disease	HEK293
Valoctocogene Roxaparvovec	BioMarin Pharma	Adeno-associated virus vector AAV5	FVIII	Hemophilia A	EMA: 2022-08-24 FDA: 2023-06-29	Hematologic disease, rare disease	Bac/Sf9
Etranacogene dezaparvovec	uniQure Biopharma/CSL	Adeno-associated virus vector AAV5	FIX	Hemophilia B	FDA: 2022-11-22 EMA: 2023-02-20	Hematologic disease, rare disease	Bac/Sf9
Delandistrogene moxeparvovec	Roche, Sarepta Therapeutics	Adeno-associated virus vector AAVrh74	Microdystrophin	Duchenne muscular dystrophy	FDA: 2023-06-23 PMDA: 2025-05-13	musculoskeletal system disorder, rare disease	HEK293
Fidanacogene elaparvovec	Roche	Adeno-associated virus vector AAVrh74	FIX	Hemophilia B	FDA: 2024-04-26 EMA: 2024-07-25	Hematologic disease, rare disease	HEK293
Dalnacogene Ponparvovec	Belief BioMed; Shanghai Belief-Delivery BioMed	Adeno-associated virus vector AAV	FIX	Hemophilia B	NMPA: 2025-04-08	Hematologic disease, rare disease	HEK293

Note:

(1) Alipogene tiparvovec was voluntarily withdrawn in 2017 following its commercial unsustainability, which was driven by an high price and limited market uptake in Europe.

Source: Clinicaltrial.gov, Frost & Sullivan Report

There are over 200 rAAV gene therapy drugs under development globally. However, most of these candidates are still in early clinical exploration, with approximately 57% in combined phase I /II clinical trials and 22% in standalone phase I trials. Late-stage activities are emerging but the numbers remain relatively modest. Approximately 6% of the pipeline is in phase II clinical trials; approximately 10% is in phase III trials; approximately 3% is in phase II/III trials; and only four drugs have reached the biologics license application stage.

Rare diseases and ophthalmic diseases constitute a significant portion of the global rAAV gene therapy pipeline. Treatment for rare diseases account for over half of all rAAV gene therapy drugs under development. Meanwhile, in terms of therapeutic areas, ophthalmic disease is the most targeted area, and other promising areas include neoromuscular, cardiovascular and hematologic diseases.

CMC Platforms for rAAV Vectors

The CMC of rAAV vectors present significant challenges to the rAAV gene therapy market. Some of these challenges include:

- ***High manufacturing cost.*** rAAV production remains one of the most expensive manufacturing platforms in the biologics field. Costs are driven by low volumetric productivity, dependence on complex cell-based production systems, high cost of plasmids, and labor-intensive downstream purification steps. In addition, rAAV requires extensive quality testing, which further increases per-batch and per-dose costs.

- ***Batch-to-batch consistency.*** rAAV potency is highly sensitive to the manufacturing process, and small variations in upstream or downstream operations can significantly affect biological activity. Low potency is often driven by factors such as incomplete genome packaging, damaged or oxidized capsids, aggregation, vector genome truncation, and suboptimal transduction efficiency. Variability in potency directly impacts clinical efficacy and may require higher doses, compounding safety risks.

- ***High empty capsid rates.*** Empty capsids inflate the total capsid burden without therapeutic benefit, tipping the immune balance towards neutralizing antibodies and complement activation. Removing these impurities is essential to secure potency, minimize reactogenicity, and achieve a clean safety profile.

- ***Limited scalability.*** Most traditional rAAV manufacturing platforms are difficult to scale linearly due to limitations in transfection efficiency, oxygen transfer, plasmid mass requirements, and vessel size. The lack of robust, high-yield, industrial-scale processes hinders commercial readiness and drives up cost, lead time, and facility requirements.

Currently, there are two primary manufacturing systems for rAAV vectors. The HEK293 system utilizes plasmid transfection into HEK293 cells, and the Bac/Sf9 system utilizes baculovirus infection of Spodoptera frugiperda insect cells. While the HEK293 system has traditionally been widely used due to its ease of setup and relatively low technical barrier, the Bac/Sf9 system is attracting interest in recent years due to its low manufacturing cost, high batch-to-batch consistency, low empty capsid rates, and high scalability and volumetric yield, all of which are potentially crucial advantages that may help overcome the key challenges to the gene therapy market. In addition, some rAAV gene therapy drugs under development use the HSV/BHK system, although to date there has been no approved rAAV gene therapy drug globally produced with this system.

The following table sets forth a comparison of the two primary manufacturing systems.

Category	Bac/Sf9 System	HEK293 System	Descriptions
Manufacturing Cost	Relatively low	Relatively high	The cost of rAAV manufacturing in Bac/Sf9 is generally lower, driven by inexpensive media and efficient infection-based production. HEK293 production is more expensive due to the need for large quantities of high-quality plasmids, costly transfection reagents, and more demanding mammalian cell culture processes.
Batch-to-Batch Consistency	High	Moderate	Batch-to-batch consistency is a key advantage of the Bac/Sf9 platform. Once the baculovirus master bank is established, production under consistent multiplicity of infection conditions results in minimal variability between batches. In contrast, the HEK293 system, relying on transient transfection, exhibits greater batch-to-batch variation due to inherent differences in transfection efficiency and plasmid quality in each production run.
Empty Capsid Rates	Relatively low	Relatively high	The Bac/Sf9 system generally results in lower empty capsid rates. In a head-to-head study in which rAAV2.N54-aflibercept vectors were produced in Bac/Sf9 and HEK293 platforms under matched upstream/downstream protocols, rAAV from the HEK293 platform had a full/empty capsid ratio of 70.8%, while rAAV from the Bac/Sf9 system had a full/empty capsid ratio of 93.2%, demonstrating a markedly lower empty capsid rate for the Bac/Sf9 system.
Scalability	High (100–2000+ L)	Moderate; limited by transfection	The Bac/Sf9 system is highly scalable, with insect cells readily expanding in large stirred-tank bioreactors reaching up to 2,000 liters, making it well suited for large-scale GMP manufacturing. In comparison, the scaling of the HEK293 system is limited by the efficiency and cost of plasmid transfection.
Yield per Liter	High and scalable	Moderate	The Bac/Sf9 system typically achieves high volumetric yields, benefiting from efficient infection and good scalability. HEK293 yields are moderate and more sensitive to transfection efficiency and plasmid quality. In the same head-to-head study discussed above, rAAV from Bac/Sf9 cells had approximately 40-fold higher yields than rAAV from HEK293 cells.

Source: Frost & Sullivan Report

THE OPHTHALMIC DRUG MARKET

Overview of Ophthalmic Diseases

Ophthalmic disease refers to a class of disorders that anatomically occur in the eyes. There are more than one hundred recognized ophthalmic diseases. According to the anatomy of the eye, ophthalmic diseases can be divided into anterior segment diseases such as cataracts, glaucoma, dry eye and myopia, and posterior segment diseases such as AMD and DME. In addition, eye conditions caused by genetic defects are collectively referred to as inherited ophthalmic diseases, which include, among others, retinal degenerations such as XLRP, LCA and others.

Ophthalmic diseases can result in an irreversible loss of vision and blindness. In particular, based on an estimate from 2020, the leading causes of blindness in adults aged over 50 years old are, in the order of prevalence, cataracts, glaucoma, undercorrected refractive error, AMD, and diabetic eye diseases (including DR and DME).

Treatment Paradigm

A wide range of treatment options have been developed for ophthalmic diseases. Among them, anti-VEGF therapy is a standard treatment drug for fundus neovascular diseases, which include DME, nAMD, myopic choroidal neovascularization and retinal vein occlusion, as well as retinopathy of prematurity.

VEGF, or vascular endothelial growth factor, is a protein secreted by the endothelial cells, immune cells, epithelial cells or tumor cells that promotes the growth of blood vessels. Fundus neovascular diseases can lead to an overexpression of VEGF protein in cells, which stimulates neoangiogenesis and results in retinopathy and impaired vision. Anti-VEGF drugs inhibit VEGF-guided neoangiogenesis and alleviate disease progression.

As of the Latest Practicable Date, a number of anti-VEGF drugs have been approved in China and the United States for the treatment of fundus neovascular diseases. The following chart sets forth a breakdown of approved drugs by targeted indication.

	FDA Approved	NMPA Approved
nAMD	2006—Lucentis® 2011—Eylea® 2019—Beovu® 2022—Vabysmo® 2023—Eylea HD®	2011—Lucentis® 2013—Lumitin® 2018—Eylea® 2024—Vabysmo® 2025—Eylea HD®
DME	2012—Lucentis® 2014—Eylea® 2022—Vabysmo® 2022—Beovu® 2023—Eylea HD®	2018—Lucentis® 2018—Eylea® 2019—Lumitin® 2023—Vabysmo® 2025—Beovu®
mCNV	2017—Lucentis®	2017—Lumitin® 2018—Lucentis®
RVO	2010—Lucentis® 2014—Eylea® 2023—Vabysmo® 2025—Eylea HD®	2018—Lucentis® 2022—Lumitin® 2024—Vabysmo®
DR	2015—Eylea® 2017—Lucentis® 2023—Eylea HD®	2021—Lucentis®\
ROP	2023—Eylea®	2021—Lucentis®

Source: NMPA, FDA, Frost & Sullivan Report

Unmet Medical Needs

Despite steady advances in the treatment methods for ophthalmic diseases, significant unmet medical needs remain.

With respect to anti-VEGF therapies, due to the short half-life of anti-VEGF antibodies or proteins, frequent repeated injections are required to maintain therapeutic efficacy. This creates both a high economic burden to patients and the health systems and results in low patient adherence over time subsequently resulting in poor long-term outcomes. In addition, frequent injections also result in increased risk of developing fibrosis, retinal scarring, and geographic atrophy.

More generally, there is an insufficient number of therapies available, as the pathogenesis of certain ophthalmic diseases such as IRDs are not yet fully understood. Challenges remain in ophthalmic drug delivery, as complex delivery methods such as subretinal or intraretinal injections are often beyond the capacity of hospitals in less developed regions. There is limited access to innovative drugs, particularly outside of the United States and Europe. Finally, there is insufficient drug development for rare diseases, as their limited market size often discourages investment, resulting in a lack of effective treatment.

rAAV Gene Therapy in Ophthalmic Disease Treatment

In recent years, rAAV gene therapy has emerged as a promising treatment option for certain ophthalmic diseases, particularly fundus neovascular diseases. Compared with other treatment options, rAAV gene therapy possesses several key advantages which may enable it to address existing unmet medical needs.

Higher Safety Profile

rAAV vectors have low immunogenicity and are less likely to trigger strong immune responses when introduced into the body. This characteristic significantly reduces the risk of the body's immune system attacking the vector and the introduced gene. Additionally, rAAV is non-pathogenic to humans, does not naturally cause disease, and barely integrate into the host patient's genome.

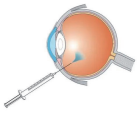
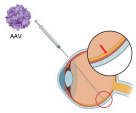
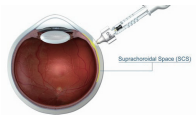
Stable Gene Expression

rAAV vectors can achieve long-term transgene expression in dividing and non-dividing cells. Moreover, rAAV vectors are highly efficient in transducing various cell types in the eye. Therefore, one injection of rAAV gene therapy can provide long-lasting benefits. Engineered serotypes of AAV can target specific ocular tissues, such as retinal pigment epithelium and photoreceptors, which is crucial for effective gene therapy.

Targeted and Efficient Delivery

By engineering the viral capsid or using cell-specific promoters, rAAV vectors can deliver genes specifically to certain cell types in the eye. This not only minimizes off-target effects but also enhances therapeutic efficacy by ensuring that the therapeutic gene is expressed only in the desired cells.

Furthermore, the relatively small tissue area and accessible nature of the eye allow rAAV vectors to be administered directly with low doses. The retina-blood barrier reduces systemic exposure and the risk of immune responses, making the delivery process more controllable and precise. Currently, depending on the therapeutic purpose, rAAV vectors are mainly delivered through intravitreal injection, subretinal injection, and suprachoroidal injection. The following diagram sets forth a comparison of the main delivery methods for rAAV vectors. Intravitreal injection is relatively non-invasive and has low requirements for the operation environment and the doctor's expertise, but also requires rAAV vectors to be able to penetrate multiple layers of cells.

	Intravitreal Injection	Subretinal Injection	Suprachoroidal Injection
Type of Injection			
Infecting Cell	• Mainly infects ganglion cells and Müller glial cells	• Mainly infects retinal pigment epithelial (RPE) cells and photoreceptor cells	• Mainly infects retinal pigment epithelial (RPE) cells and Photoreceptors (rods and cones)
Advantages	✓ Less invasive ✓ Operation is more convenient, safer, has lower requirements for the doctor's operation, and has high clinical applicability ✓ Fewer postoperative complications	✓ Subretinal injection allows the viral vector to more easily approach RPE cells, and it also results in a relatively reduced immune response.	✓ Minimally invasive, in-office procedure ✓ Broad circumferential coverage ✓ Bypasses inner barriers
Disadvantages	✘ Intravitreal injection requires the viral vector to travel from the vitreous cavity to the RPE cells, moving from the inner retina to the outer retina. rAAV may need to effectively penetrate the entire retina, crossing through multiple layers of cells, hence there is a relatively high requirement for the penetrating ability of the rAAV vector, especially for expessing non-secreted therapeutic proteins.	✘ Some patients might experience thinning of the central retina and vision loss, with decreased retinal thickness observed in certain cases, posing significant safety risks. ✘ Subretinal injection is a special surgery and has a risk of retina detachment. It faces challenges in achieving uniform and precise delivery, with some medication potentially leaking from the retinal incision, making it difficult to deliver the vector volume accurately and evenly.	✘ Immune exposure and inflammation: The suprachoroidal space is outside the blood-retinal barrier, so gene vectors there are exposed to immune surveillance ✘ Rapid choroidal clearance: The choriocapillaris has extremely high blood flow, so vector particles in the SCS can be quickly washed away. This rapid clearance may limit the fraction of vector that penetrates into retina. Much higher dose is needed. ✘ Technical challenges of injection: Delivering into the thin SCS requires precision and a special device.

Source: Literature Review, Frost & Sullivan Report

Increasing Clinical Applications

So far, a total of nine rAAV gene therapy drugs have received regulatory approval. For instance, Luxturna® is an rAAV gene therapy that has been approved for treating RPE65-mediated IRD. Currently, a significant amount of research and clinical trials are ongoing to explore the potential applications of rAAV vectors in ophthalmic diseases.

As a result of the above advantages of rAAV vectors, there have been many high-profile transactions involving rAAV vectors. For example, in October 2025, Eli Lily acquired Adverum Biotechnologies, including its lead product candidate, ixo-vec, for US$262 million. Ixo-vec, or ixoberogene soroparvovec and formerly ADVM-022, is an rAAV gene therapy candidate in Phase III clinical trials targeting nAMD. In November 2025, Eli Lily obtained the worldwide exclusive rights to MeiraGTx Holdings' AAV-AIPL1, an rAAV gene therapy candidate for LCA4, with an upfront payment of US$75 million and total milestone payments of US$475 million. Also in October 2025, Otsuka Pharmaceutical entered into a license agreement with 4D Molecular Therapeutics to obtain exclusive rights in Asia-Pacific for 4D-150, an rAAV gene therapy in Phase III clinical trials targeting nAMD and DME, for US$471 million. Meanwhile, AbbVie is progressing its development of sura-vec, or surabgene lomparvovec and formerly ABBV-RGX-314, an rAAV gene therapy for nAMD and DR, towards Phase III clinical trials, after entering into a collaboration and licensing agreement for the candidate in 2021 with an upfront payment of US$370 million and total milestone payment of up to US$1.38 billion.

Growth Drivers of the Ophthalmic Drug Market

The growth of the ophthalmic drug market is expected to be driven by the following factors:

- ***Enlarging Patient Pool.*** Retinal disease-related vision loss negatively affects patients' quality of life and limits participation in education and the workforce. The number of people affected by major retinal diseases continues to increase globally. nAMD represents a substantial disease burden, with patient numbers reaching 21.2 million in 2024 globally. DR driven by the growing prevalence of diabetes affects an even larger population, with 124.2 million patients worldwide in 2024. The rising prevalence of nAMD and DR, largely attributable to population aging and metabolic disease trends, has led to a continued increase in disability-adjusted life years. As a result, demand for effective and durable ophthalmic treatments is expected to grow in the coming years, thereby facilitating sustained expansion of the global ophthalmic drug market.

- ***Broader Therapeutic Indications.*** Refractory retinal diseases such as DR and nAMD require long-term treatment, and the high injection burden of anti-VEGF therapies has driven demand for durable therapies. Meanwhile, advances in gene therapy are enabling single-administration treatments with durable efficacy. Although Luxturna® remains the only globally marketed ophthalmic gene therapy to date approved for RPE65-mediated IRD, a growing pipeline is rapidly emerging. In China, 39 ophthalmic gene therapy candidates are currently in clinical development, with over 20 targeting chronic retinal diseases such as AMD and DME rather than rare inherited conditions. This expanding pipeline underscores the transition of gene therapy toward broader therapeutic indications, supporting continued growth of the ophthalmic drug market.

- ***Favorable global regulatory environment.*** Supportive regulatory frameworks across major markets have contributed to the growth of the ophthalmic drug market. In the United States, the FDA has issued disease-specific and modality-focused guidance for ophthalmic drug development, including recommendations for nAMD, while regulatory mechanisms such as treatment INDs and expanded access programs have facilitated the development and availability of innovative therapies. In parallel, China has strengthened national eye health policies under the 14th Five-Year National Eye Health Plan, focusing on expanded ophthalmic healthcare capacity and improved disease screening and treatment coverage. Together with increasing regulatory clarity on quality, safety, and efficacy requirements, these measures have supported sustained investment and the long-term expansion of the global ophthalmic drug market.

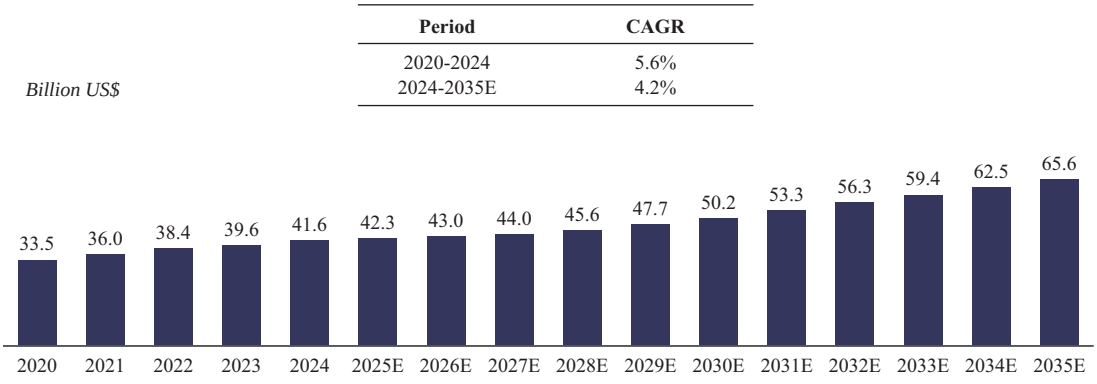
The Ophthalmic Drug Market Size

The global ophthalmic drug market grew from US$33.5 billion in 2020 to US$41.6 billion in 2024 with a CAGR of 5.6%. It is expected to continue growing at a CAGR of 4.2% from 2024 to 2035, and reach US$65.6 billion in size in 2035.

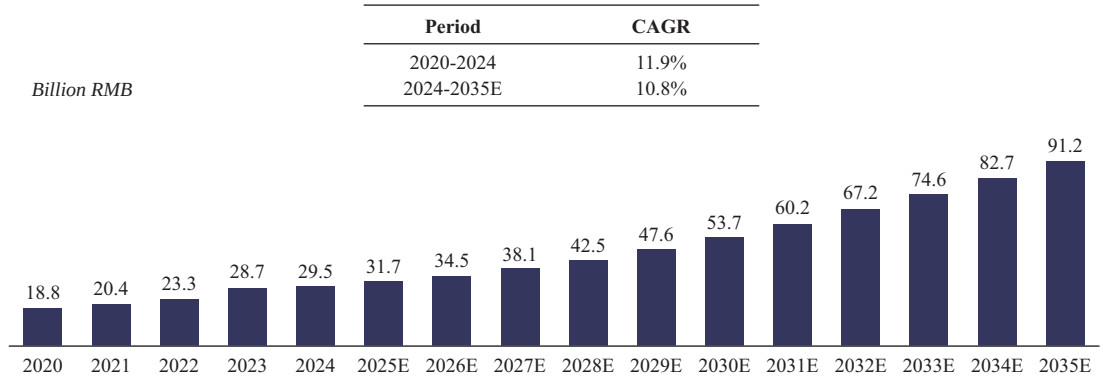
In comparison, the China ophthalmic drug market has grown at a faster pace and is projected to keep up its momentum. Tremendous effort has been invested in research and development of ophthalmic drugs in China. Consistent with worldwide trends, an increasing number of ophthalmic drugs with new and user-friendly formulations and dosing schedules have been in development. In addition, benefiting from drug registration reforms, an increasing number of innovative drugs are expected to enter the Chinese market at an expedited pace. Moreover, with the fast-growing innovation capabilities of domestic developers, the development efforts on drugs with innovative targets is expected to increase. The China ophthalmic drug market was RMB18.8 billion in 2020 and has reached RMB29.5 billion in 2024 with a CAGR of 11.9% from 2020 to 2024. The market is expected to reach RMB91.2 billion in 2035, representing a CAGR of 10.8% from 2024 to 2035.

The following diagram illustrates the growth of the global and China ophthalmic drug market.

Global Ophthalmic Drug Market, 2020-2035E



China Ophthalmic Drug Market, 2020-2035E



Source: Frost & Sullivan Report

The RPGR-associated XLRP Market

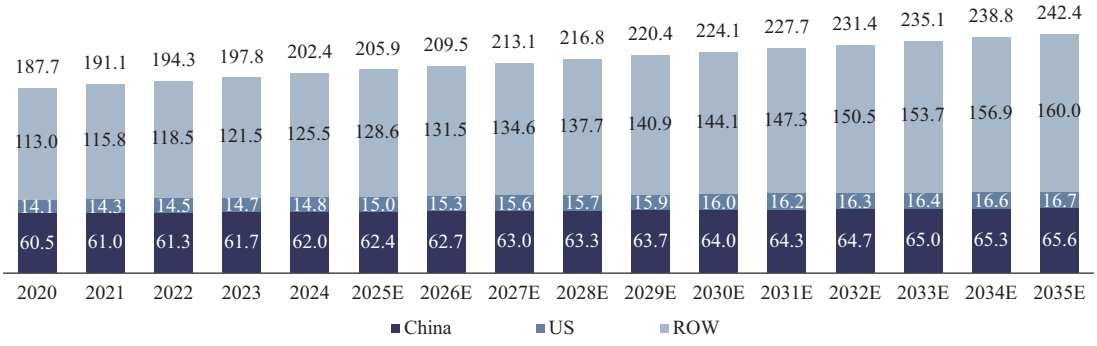
RP is a form of IRD. It is characterized by primary degeneration of rod photoreceptors, followed by secondary loss of cones, leading to progressive night blindness and visual field constriction, usually resulting in legal and often complete blindness.

RPs generally consist of autosomal dominant RP, XLRP, and autosomal recessive, with XLRP being the most severe subtype and accounting for approximately 5% to 15% of all RPs. Among XLRPs, mutations in the RPGR gene are the most common causes, with RPGR-associated XLRP representing over 70% of XLRPs.

The number of XLRP patients globally reached 202.4 thousand in 2024 and is forecasted to reach 242.2 thousand in 2035. In China, the number of XLRP patients was 62.0 thousand in 2024, which is expected to grow to 65.6 thousand in 2035. In the United States, the number of XLRP patients was 14.8 thousand in 2024, which is expected to grow to 16.7 thousand in 2035. The following chart sets forth certain additional details regarding the global prevalence of XLRP.

Global Prevalence of XLRP, 2020-2035E

Period	CAGR			
	China	US	ROW	Total
2020-2024	0.6%	1.2%	2.7%	1.9%
2024-2035E	0.5%	1.1%	2.2%	1.7%



Source: Frost & Sullivan Report

The current treatment paradigm for RPGR-associated XLRP is extremely limited. China's latest clinical guidelines emphasize that there is no therapy that can cure or halt RPs. Patients are counseled to avoid intense light, limit visual fatigue, and maintain regular sleep and healthy dietary habits to modestly slow disease progression. There is an urgent need to develop innovative and effective disease-modifying strategies to address RPs, particularly its most severe subtype, XLRP.

As of the Latest Practicable Date, no gene therapy drug for XLRP has been approved globally and there were two rAAV gene therapy drugs for XLRP treatment in clinical development globally. The following table illustrates the competitive landscape of rAAV gene therapy drugs for XLRP treatment as of the Latest Practicable Date.

Drug Name	Company	Target	Phase	First Posted Date	Country	Production Platform
Laruparetigene zosaparvovec (laru-zova, AGTC-501)	Beacon Therapeutics	RPGR	Phase II/III	2021-04-20	UK, US, Australia	HSV/BHK
FT-002	**Frontera Therapeutics**	**RPGR**	**Phase I/II**	**2024-02-07**	**China**	**Bac/Sf9**
			Phase II IND Approval	**2024-09-23**	**US**	

Source: Frost & Sullivan Report

The nAMD Market

AMD, a degenerative retinal disease that causes progressive loss of central vision, is the leading cause of irreversible blindness in aged people. The disease affects the central area in the ocular posterior segment, known as the macula lutea, which is essential for the vision of fine details and image resolution. Symptoms of AMD include blurriness in central vision, trouble seeing in low lighting, and extra sensitivity to glare, among others.

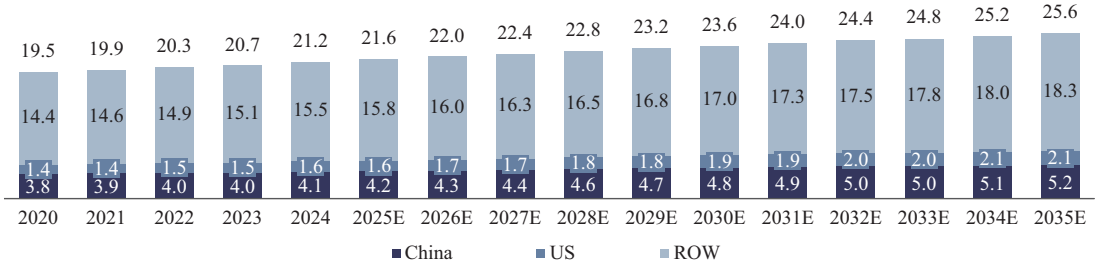
AMD can be categorized as either dry AMD or neovascular AMD, also known as wet AMD or nAMD. While nAMD only accounts for approximately 10% to 20% of AMD cases, it is responsible for approximately 80% to 90% of all vision loss attributable to AMDs.

The number of patients with nAMD globally reached 21.2 million in 2024, and is expected to reach 25.6 million in 2035. In China, the number of nAMD patients was 4.1 million in 2024, which is expected to grow to 5.2 million in 2035. In the United States, the number of nAMD patients was 1.6 million in 2024, which is expected to grow to 2.1 million in 2035. The following charts set forth certain additional details regarding the global prevalence of nAMD.

Global Prevalence of nAMD, 2020-2035E

Period	CAGR			
	China	US	ROW	Total
2020-2024	2.1%	3.2%	1.9%	2.1%
2024-2035E	2.1%	2.7%	1.5%	1.7%

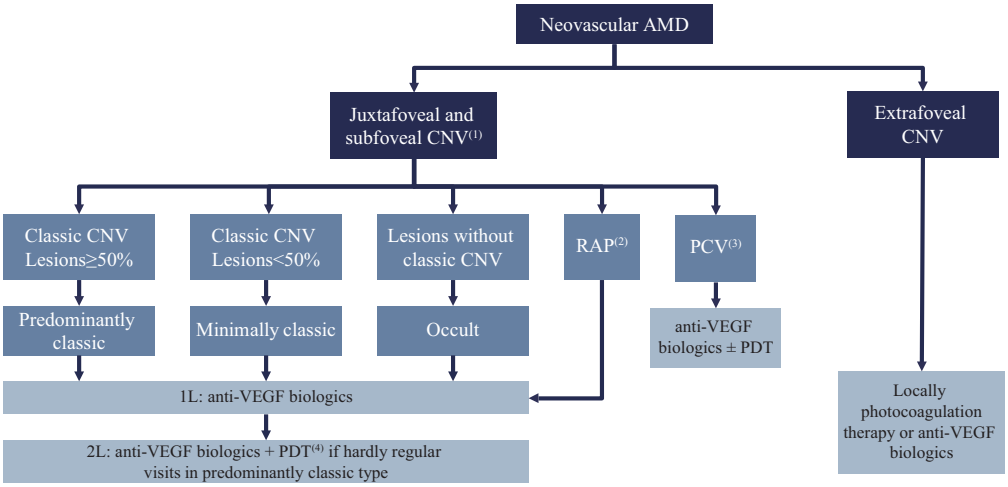
Million



Source: Frost & Sullivan Report

The current treatment paradigm of nAMD primarily relies on the intravitreal injection of anti-VEGF agents. In addition, verteporfin with PDT or thermal laser therapies are also used, although less commonly. The charts below set forth the treatment paradigm for nAMD in China and the United States.

Treatment Paradigm for nAMD in China



Notes:

(1) CNV: choroidal neovascularization.

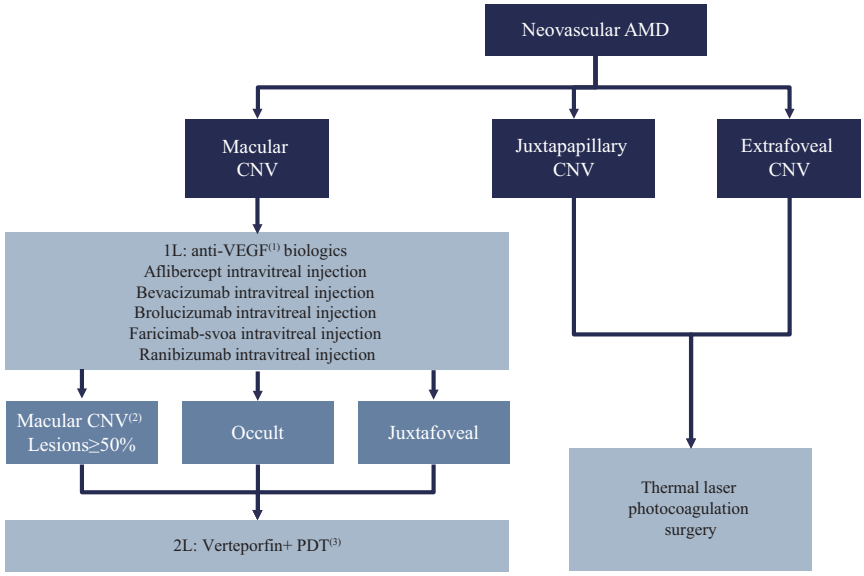
(2) RAP: retinal angiomatous proliferation.

(3) PCV: polypodal choroidal vsculopathy.

(4) PDT: photodynamic therapy.

Source: Literature Review, Frost & Sullivan Report

Treatment Paradigm for nAMD in the United States



Notes:

(1) VEGF: vascular endothelial growth factor.

(2) CNV: choroidal neovascularization.

(3) PDT: photodynamic therapy.

Source: Literature Review, Frost & Sullivan Report

These existing treatment options have significant limitations, including poor patient compliance and high treatment burden. As discussed above, anti-VEGF treatment manages the symptoms of nAMD but does not alter the underlying disease course, thus requiring lifelong intervention. nAMD patients have to receive nine intravitreal anti-VEGF injections in the first year alone and continue at three to six injections annually. This frequent injection need creates a long-term logistical burden on patients as well as caregivers, and results in poor patient compliance. There is also a significant economic cost. According to a published cost-effectiveness study in the UK, long-term anti-VEGF therapy is estimated to average a total of 9.2 quality-adjusted life years. On this basis, the total treatment costs of anti-VEGF therapy are calculated to be up to US$304,000 in the United States and up to RMB403,000 in China.

Gene therapy represents a promising approach to address the above limitations by enabling the continuous, endogenous production of anti-angiogenic proteins, potentially offering a one-time, durable treatment solution. As of the Latest Practicable Date, there were 22 rAAV gene therapy drugs for nAMD treatment in clinical development globally, including nine that are administered through intravitreal injections. The following table illustrates the competitive landscape of rAAV gene therapy drugs for nAMD treatment as of the Latest Practicable Date.

Route of Administration	Drug Name	Company	Target	Phase	First Posted Date	Country
Intravitreal	Ixoberogene soroparvovec (Ixo-vec , ADVM-022)	Eli Lilly /Adverum	VEGF	Phase III	2025/3/4	US
	4D-150	4D Molecular Therapeutics	VEGFA; VEGFB; VEGFC; PLGF	Phase III	2025/3/7	US, Canada
	SKG0106	Skyline Therapeutics	VEGFA	Phase I/II	2023/8/3	China, US
	FT-003	**Frontera Therapeutics**	**VEGF**	**Phase I/II**	**2023/8/21**	**China**
				Phase II IND Approval	**2024/11/11**	**US**
	XMVA09	Starrygene Therapeutics Company Limited	ANGPT2, VEGF	Phase I/II	2024/4/12	China
	ABI-110	Avirmax Biopharma	VEGF	Phase I/II	2024/8/8	US
	GZ402663	Sanofi	VEGF	Phase I/II	2024/10/28	US
	IVB-103	Innovec Biotherapeutics	Not disclosed	Phase I/II	2024/11/29	China
	EXG202	Hangzhou Jiayin Biotechnology Co., Ltd	ANGPT2, VEGF	Phase I/II	2025/9/18	China
Subretinal	Surabgene lomparvovec (Sura-vec, ABBV-RGX-314)	Abbvie / Regenxbio	AAV8-VEGF	Phase III	2022/6/7	US,UK, Japan, etc.
	LX102	Innostellar Biotherapeutics	VEGF	Phase II	2024/1/9	China
	KH631	Chengdu Kanghong Pharmaceutical Group Co., Ltd.	VEGF	Phase I/II	2023/1/5	China
				Phase I	2022/12/10	US
	JWK001	Chengdu Gene Vector Biotechnology	VEGF	Phase I/II	2023/3/2	China
	EXG102 -031	Hangzhou Jiayin Biotechnology Co., Ltd	ANGPT2, VEGFA, VEGFC	Phase I/II	2023/10/12	China
				Phase I	2023/6/6	US
	NG101	Reyon Pharmaceutical, Neuracle Genetics	VEGF	Phase I/II	2023/8/9	US, Canada
	RRG001	Shanghai Refreshgene Therapeutics	VEGF	Phase I/II	2023/11/21	China
	NGGT007	Next Generation Gene Therapeutics	CYP4V2	Phase I/II	2025/1/16	China
	CRG-B191	Shanghai Keruike Pharmaceutical Technology Co., Ltd	VEGF	Phase I/II	2025/11/6	China
	HG202	HuidaGene Therapeutics Co., Ltd.	VEGF	Phase I	2023/9/4	China
	RGL-2201	Shanghai Regenelead Therapies Co., Ltd.	VEGF	Phase I	2025/3/3	China
Suprachoroidal	AL-001	Beijing Anlong Biopharmaceutical Co., Ltd	VEGF	Phase II	2025/2/17	China
	KH658	Chengdu Kanghong Pharmaceutical Group Co., Ltd.	VEGF	Phase I/II	2024/6/13	China

Source: Clinicaltrial.gov, CDE, Frost & Sullivan Report

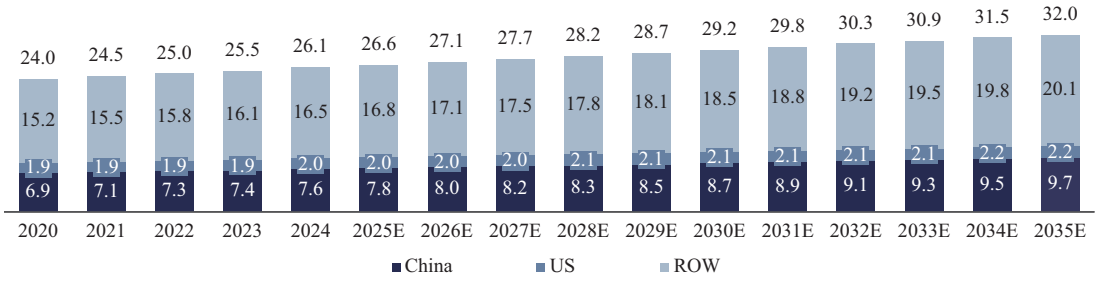
The DME Market

DME is one of the most common fundus neovascularization diseases in China and one of the serious complications of diabetic retinopathy. DME causes the retina to thicken within the diameter of the optic disc in the center of the macula, and the fluid leakage or exudation caused by the lesion can enter the retina, resulting in the destruction of the blood-retinal barrier.

The number of patients with DME globally reached 26.1 million in 2024, and is expected to reach 32.0 million in 2035. In China, the number of DME patients was 7.6 million in 2024, which is expected to grow to 9.0 million in 2035. In the United States, the number of DME patients was 2.0 million in 2024, which is expected to grow to 2.2 million in 2035. The following charts set forth certain additional details regarding the global prevalence of DME.

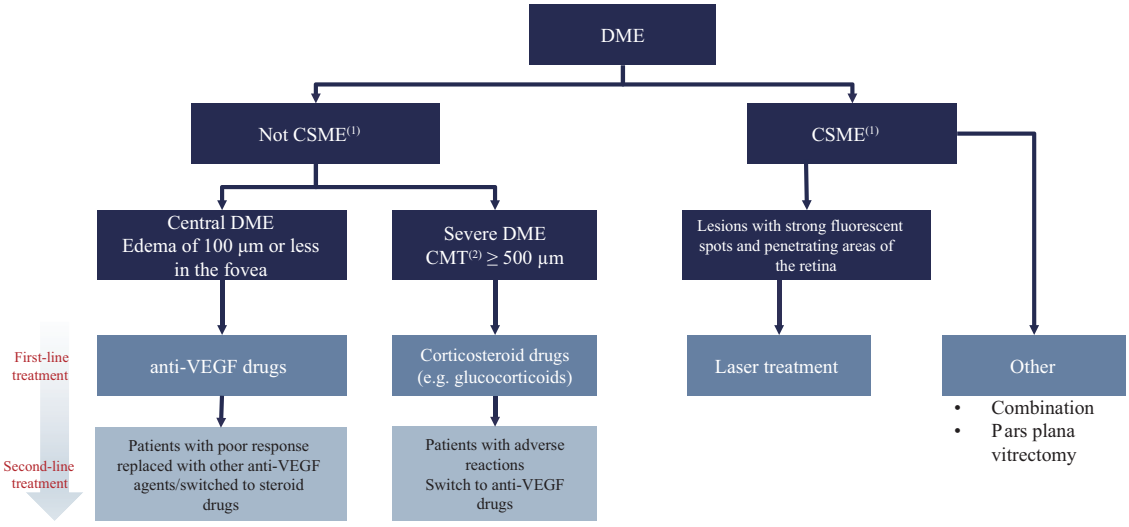
Global Prevalence of DME, 2020-2035E

Period	CAGR			
	China	US	ROW	Total
2020-2024	2.5%	1.2%	2.1%	2.1%
2024-2035E	2.2%	0.9%	1.8%	1.9%



Source: Frost & Sullivan Report

Anti-VEGF drugs are currently the recommended therapy for DME treatment. However, they are subject to the downsides associated with their limited duration of action, including high treatment burden, poor patient compliance and unsatisfactory long-term outcomes. The chart below sets forth the treatment paradigm for DME.



Notes:

(1) CSME: clinically significant DME, the highest grade lesion type in the clinical diagnosis and treatment of the macula.

(2) CMT: macular central retinal thickness.

Source: Frost & Sullivan Report

Similar to nAMD, rAAV gene therapy is a promising solution for DME treatment given its ability to accomplish long-lasting results through a single injection and substantially improves upon the deficiencies of standard anti-VEGF therapy. As of the Latest Practicable Date, there were four rAAV gene therapy drugs for DME treatment under clinical development globally. The following table illustrates the competitive landscape of rAAV gene therapy drugs for DME treatment as of the Latest Practicable Date.

Route of Administration	Drug Name	Company	Target	Phase	First Posted Date	Country
Intravitreal	4D-150	4D Molecular Therapeutics	VEGFA, VEGFB, VEGFC, PLGF	Phase II	2023 -07-05	US, Puerto Rico
	FT-003	**Frontera Therapeutics**	**VEGF**	**Phase I/II**	**2023 -10-27**	**China**
				Phase II IND Approval	**2024 -12-25**	**US**
	SKG0106	Skyline Therapeutics	VEGFA	Phase I	2024 -01-25	China
Suprachoroidal	Surabgene lomparvovec (Sura-vec, ABBV-RGX-314)	Abbvie / Regenxbio	VEGF	Phase II	2025 -04-16	US

Source: Clinicaltrial.gov, CDE, Frost & Sullivan Report

The DR Market

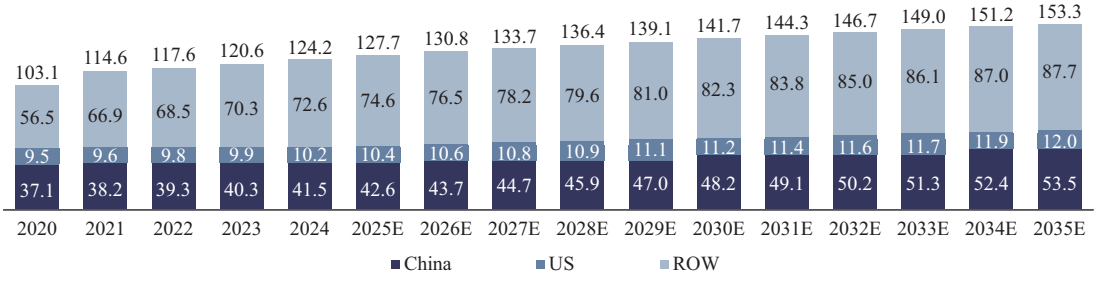
DR is a microvascular and neurodegenerative complication of diabetes mellitus, characterized by pericyte loss, basement membrane thickening, microaneurysm formation, neovascularization, and blood–retinal barrier disruption. DR progresses through distinct stages, primarily categorized as non-proliferative DR ("**NPDR**") and proliferative DR ("**PDR**"). NPDR represents the earlier, non-sight-threatening stage, characterized by weakened retinal blood vessels that may leak, causing swelling or edema. In contrast, PDR is the advanced, sight-threatening stage defined by the growth of abnormal, fragile new blood vessels on the retinal which can lead to severe bleeding and retinal detachment.

The number of patients with DR globally reached 124.2 million in 2024, and is expected to reach 153.3 million in 2035. In China, the number of patients with DR was 41.5 million in 2024, and is expected to reach 53.5 million in 2035. In the United States, the number of patients with DR was 10.2 million in 2024, and is forecasted to reach 12.0 million in 2035. The following chart sets forth certain additional details regarding the prevalence of DR globally.

Global Prevalence of DR, 2020-2035E

Period	CAGR			
	China	US	ROW	Total
2020-2024	2.8%	1.8%	6.4%	4.8%
2024-2035E	2.3%	1.5%	1.7%	1.9%

Million



Source: Frost & Sullivan Report

While NPDR is generally managed with close observation and control of blood glucose, blood pressure and lipids, PDR requires more targeted treatment methods, including panretinal photocoagulation ("**PRP**"), the core and standard treatment for high-risk PDR, pars plana vitrectomy ("**PPV**"), and anti-VEGF therapy. The chart below sets forth the treatment paradigm for DR according to standard guidelines in China.

Disease Stage	First-Line Recommendation	Second-Line/Alternative Options
NPDR	• **Systemic Management:** Strict control of blood glucose, blood pressure, and lipids.	• **Close Observation:** For mild/moderate NPDR without macular edema.
PDR	• **PRP:** The core, standard treatment for high-risk PDR.	• **PPV:** For sight-threatening complications such as non-clearing vitreous hemorrhage or tractional retinal detachment. • **Anti-VEGF Therapy:** Used for active neovascularization, vitreous hemorrhage, or as pre-operative adjunct.
DME	• **Anti-VEGF Therapy:** First-line treatment for center-involving DME.	• **Focal/Grid Laser Photocoagulation:** For non-center-involving DME or as a supplement. • **Intravitreal Corticosteroids:** Consider for cases with an inadequate response to anti-VEGF or a significant inflammatory component.

Source: Frost & Sullivan Report

There are significant medical needs that remain unmet by existing treatment options. Neither PRP, PPV nor anti-VEGF therapy offers a cure for DR. Patients require long-term, in many cases lifelong, treatment and monitoring. Frequent intravitreal injections and follow-ups impose significant time, financial and psychological burdens, resulting in undertreatment and suboptimal outcomes in the long run. In addition, PRP, the standard treatment for PDR, works by ablating hypoxic retinal tissue to inhibit neovascularization. This is a destructive approach that often leads to irreversible side effects such as peripheral visual field loss and impaired night vision.

As of the Latest Practicable Date, there was only one approved drug for DR treatment globally and 20 drugs for DR treatment under clinical development globally, including only one rAAV gene therapy drug.

The RPE65-related LCA/RP Market

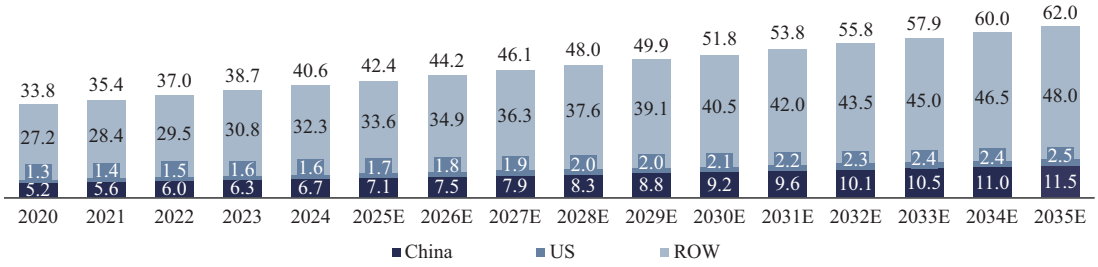
LCA is a form of IRD, meaning a group of heterogeneous disorders caused by gene mutations primarily affecting retinal photoreceptors. LCA is characterized by severe visual impairment from birth or the first few months of life, roving eye movements or nystagmus, poor pupillary light responses, oculodigital sign, and undetectable or severely abnormal full-field electroretinogram. The primary pathogenic genes of LCA include CEP290, GUCY2D, and RPE65, among others. Like LCA, RP is also a form of IRD and refers to a group of rare eye diseases that are characterized by the gradual breakdown of cells in the retina, causing progressive vision loss. RP can be caused by mutations in the RPE65 gene, among other factors.

The number of patients with RPE65 mutation-associated LCA/RP globally had reached 40.6 thousand in 2024, and is expected to reach 62.0 thousand in 2035. The number of patients with RPE65 mutation-associated LCA/RP in China had reached 6.7 thousand in 2024, and is expected to reach 11.5 thousand in 2035. The number of RPE65 mutation-associated LCA/RP patients in the US reached 1.6 thousand in 2024, and is forecasted to reach 2.5 thousand in 2035.

Global Prevalence of RPE65 mutation-associated LCA/RP, 2020-2035E

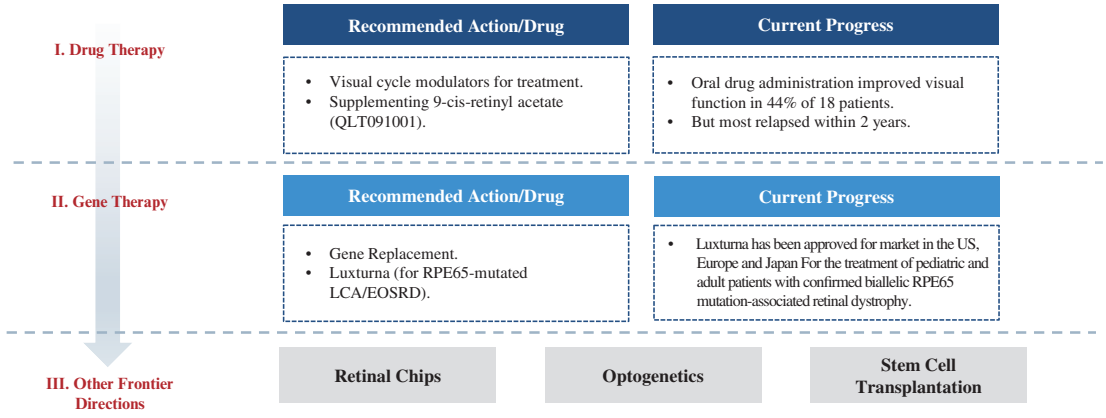
Period	CAGR			
	China	US	ROW	Total
2020-2024	6.5%	5.0%	4.4%	4.7%
2024-2035E	5.0%	4.0%	3.7%	3.9%

Thousand



Source: Frost & Sullivan Report

There are currently limited treatment options available for LCA. Patients accepting standard drug therapies typically relapse within 2 years. The chart below sets forth the treatment paradigm for LCA.



Source: Literature Review, Frost & Sullivan Report

For RPE65-related LCA/RP, the only approved gene therapy, Luxturna®, is priced at approximately US$850,000 per treatment and has not yet been approved in China.

As of the Latest Practicable Date, there was one rAAV gene therapy drug approved for RPE65-related LCA/RP treatment treatment globally, and four rAAV gene therapy drugs in the clinical development stage for RPE65-related LCA/RP treatment globally. The following tables illustrate the competitive landscape of rAAV gene therapy drugs for RPE65-related LCA/RP treatment as of the Latest Practicable Date.

Approved Drug

Brand Name	Drug Name	Company	Target	First Approved Date	Country	Route of Administration	Strength	Treatment Cost (US$ in millions)	Annual Sales in 2024 (US$ in millions)
LUXTURNA®	Voretigene neparvovec	Roche	RPE65	2017-12-19	US	Subretinal	0.5 ml	0.9	20.4
				2018-11-22	Europe				
				2023-06-01	Japan				

Source: Frost & Sullivan Report

Drugs under Development

Route of Administration	Drug Name	Company	Target	Phase	First Posted Date	Country
Subretinal	LX101	Innostellar Biotherapeutics	RPE65	Phase III	2024-10-10	China
	Cevaretigene ritoparvovec	MeiraGTx	RPE65	Phase I/II	2016-05-24	US, UK
	FT-001	**Frontera Therapeutics**	**RPE65**	**Phase I/II**	**2022-11-07**	**China**
				Phase I IND Approval	**2022-07-19**	**US**
	HG-004	HuidaGene Therapeutics Co., Ltd.	RPE65	Phase I/II	2023-06-18	China, US

Source: Clinicaltrial.gov, CDE, Frost & Sullivan Report

THE CARDIOVASCULAR DRUG MARKET

Overview of Cardiovascular Diseases

Cardiovascular disease is a group of diseases affecting the patients' heart and blood vessels. Its signs and symptoms include chest pain, shortness of breath, dizziness, fatigue, and palpitation, among others. Typical indications include arrhythmia, coronary artery diseases, heart failures, peripheral artery diseases, congenital heart diseases, and deep vein thrombosis.

rAAV Gene Therapy in Cardiovascular Disease Treatment

Current drugs for congenital cardiovascular diseases, including ACE inhibitors, β-blockers, mineralocorticoid antagonists, as well as devices, are palliative in nature and do not correct the underlying genetic defect. As a result, they require long-term patient compliance. Gene therapy, on the other hand, offers curative potential to cardiovascular diseases and has received increasing attention.

Within gene therapy, rAAV gene therapy benefits from numerous advantages including targeted and efficient delivery and stable gene expression. Certain serotypes of AAV, especially AAV8 and AAV9, exhibit a natural tropism for cardiomyocytes, meaning they can efficiently cross the vascular endothelium and specifically transduce cardiomyocytes after injections via the vein. In addition, as cardiomyocytes are terminally differentiated cells that rarely divide, rAAV vectors, with their genomes existing as circular episomes within the cell nucleus, can continuously express therapeutic proteins throughout the target cell's life cycle, with minimal dilutions due to cell division.

rAAV Gene Therapy Drugs under Development

As of the Latest Practicable Date, there were currently 16 rAAV gene therapy drugs for cardiovascular disease treatment under clinical development globally. The following table illustrates the competitive landscape of rAAV gene therapy drugs for cardiovascular disease treatment as of the Latest Practicable Date.

Drug Name	Company	Target	Indication	Country	Phase	First Posted Date
SRD-001	Eiger BioPharmaceuticals; Celladon; Medera; Sardocor	ATP2A2	Cardiac failure	Europe	Phase II	2007-09-26
			Duchenne Muscular Dystrophy Associated Cardiomyopathy	US	Phase I	2024-01-24
Encoberminogene Rezmadenovec	XyloCor Therapeutics	VEGF	Angina	US	Phase II	2018-11-21
			Coronary artery disease	US	Phase II	2025-08-12
RGX 501	Regenxbio	LDLR	Homozygous familial hypercholesterolemia	US, Netherlands, Canada	Phase II	2019-09-06
AB-1002	Bayer AG; Asklepios Bio Pharmaceutical	PP1	Cardiac failure	US, Europe	Phase II	2022-10-28
LX2006	Adverum Biotechnologies; Lexeo Therapeutics	FXN	Cardiomyopathy Associated With Friedreich's Ataxia	US	Phase I/II	2022-06-30
TN-201	Tenaya Therapeutics	MYBPC3	Hypertrophic cardiomyopathy	US	Phase I/II	2023-05-01
LX2020	Lexeo Therapeutics; Stelios Therapeutics	PKP2	Arrhythmogenic cardiomyopathy	US	Phase I/II	2023-10-31
TN-401	Tenaya Therapeutics	PKP2	Arrhythmogenic Right Ventricular Cardiomyopathy	US	Phase I/II	2024-01-18
ALXN2350	AstraZeneca	BAG3	Dilated cardiomyopathy	US	Phase I/II	2025-10-16
GC304	Beijing Jinlan Gene	LPL	Hyperlipidemia	China	Phase I	2023-05-16
RP-A601	Rocket Pharmaceuticals; Renovacor	PKP2	Arrhythmogenic cardiomyopathy	US	Phase I	2023-05-22
NGGT006	Next Generation Gene Therapeutics	LDLR	Hyperlipidemia	China	Phase I	2023-11-09
NXL001	NeuExcell Therapeutics	NEUROD1	Ischemic Stroke	China	Phase I	2024-12-30
YAP-101	Medley Therapeutics	SAV1	Cardiac failure	US	Phase I	2025-02-12
RP-A701	Rocket Pharmaceuticals; Renovacor	BAG3	Dilated cardiomyopathy	US	Phase I	2025-08-22
SGT-501	Solid Biosciences	CASQ2	Catecholaminergic polymorphic ventricular tachycardia	US	Phase I	2025-08-29

Source: clinicaltrials.gov, Frost & Sullivan Report

Growth Drivers and Future Trend of the Cardiovascular Drug Market

The growth of the cardiovascular drug market is expected to be driven by the following factors:

- ***Global Disease Burden and Unmet Medical Needs.*** Cardiovascular diseases are the leading cause of death globally and impose a substantial disease burden worldwide, highlighting significant unmet medical needs. According to *Global, Regional, and National Burden of Cardiovascular Diseases and Risk Factors in 204 Countries and Territories, 1990-2023*, published by the ACC, the number of cardiovascular disease deaths globally has increased markedly over recent decades, rising from approximately 13.1 million deaths in 1990 to around 19.2 million deaths in 2023. Despite the widespread use of established therapies, this sustained and growing disease burden underscores a persistent lack of effective treatment options, particularly for advanced and progressive cardiac conditions, supporting continued global demand for innovative therapeutic approaches.

- ***Favorable government policies.*** In the United States, the FDA has taken disease-specific actions to support innovation in cardiovascular therapies, including issuing draft guidance on *Treatment for Heart Failure: Endpoints for Drug Development*, which allows improvements in symptoms or physical function to support regulatory approval and encourages the use of biomarkers and hospitalization outcomes in clinical trial design. In parallel, China has made sustained strategic investments under the "Healthy China 2030" initiative, adopting the *Cardiovascular and Cerebrovascular Disease Prevention and Treatment Action Implementation Plan (2023–2030)* to systematically reduce disease incidence and mortality. Together, these policy and regulatory efforts reflect a supportive environment for continued development of innovative cardiovascular therapies.

A defining future trend in the cardiovascular drug market is expected to be the paradigm shift from the lifelong management of refractory symptoms towards curative or disease-modifying genetic therapies. A prime example is the development of gene therapy for HCM caused by mutations in the MYBPC3 gene, a common genetic form of heart disease. Current standard care - β-blockers, implantable defibrillators, and surgery - only manage complications without correcting the underlying shortage of functional protein. Pioneering gene therapies in development aim to introduce a functional copy of the MYBPC3 gene via a single intravenous infusion of a cardiotropic viral vector such as an rAAV vector, thereby treating HCM caused by mutations in the MYBPC3 gene.

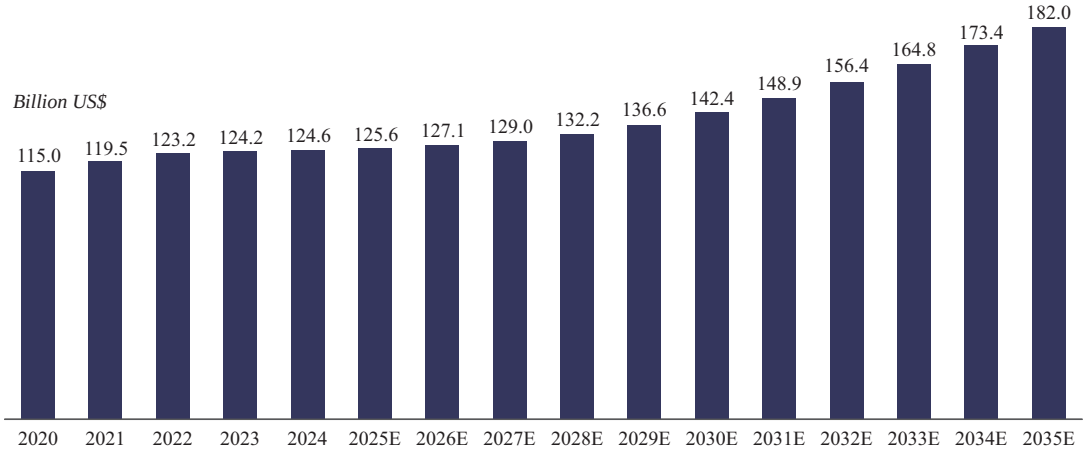
The Cardiovascular Drug Market Size

The global cardiovascular drug market grew from US$115.0 billion in 2020 to US$124.6 billion in 2024 with a CAGR of 2.0%. It is expected to continue growing at a CAGR of 3.5% from 2024 to 2035, and reach US$182.0 billion in size in 2035. The cardiovascular disease drug market in China grew from RMB176.1 billion in 2020 to RMB178.7 billion in 2024 with a CAGR of 0.4%. It is expected to continue growing at a CAGR of 3.7% from 2024 to 2035, and reach RMB265.1 billion in size in 2035.

The following diagram illustrates the growth of the global and China cardiovascular drug market.

Global Cardiovascular Drug Market, 2020-2035E

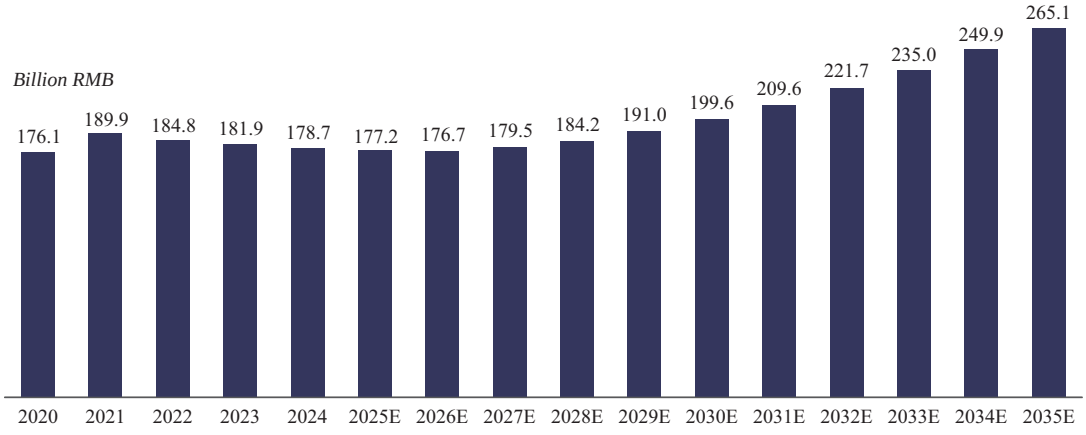
Period	CAGR
2020-2024	2.0%
2024-2035E	3.5%



Source: Frost & Sullivan Report

Cardiovascular Drug Market in China, 2020-2035E

Period	CAGR
2020-2024	0.4%
2024-2035E	3.7%



Source: Frost & Sullivan Report

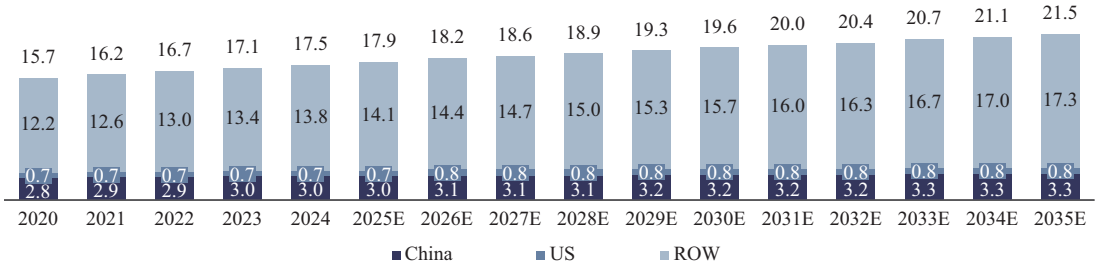
The HCM Market

HCM is a form of myocardial hypertrophy, usually left-ventricular, that is often due to sarcomere-gene variants. Its symptoms include exertional dyspnea, chest pain, palpitations, fatigue, and presyncope or syncope, among others.

The number of patients with HCM globally reached 17.5 million in 2024, and is expected to reach 21.5 million in 2035. In China, the number of HCM patients was 3.0 million in 2024, which is expected to grow to 3.3 million in 2035. In the United States, the number of HCM patients was 0.7 million in 2024, which is expected to grow to 0.9 million in 2035. The following charts set forth certain additional details regarding the global prevalence of HCM.

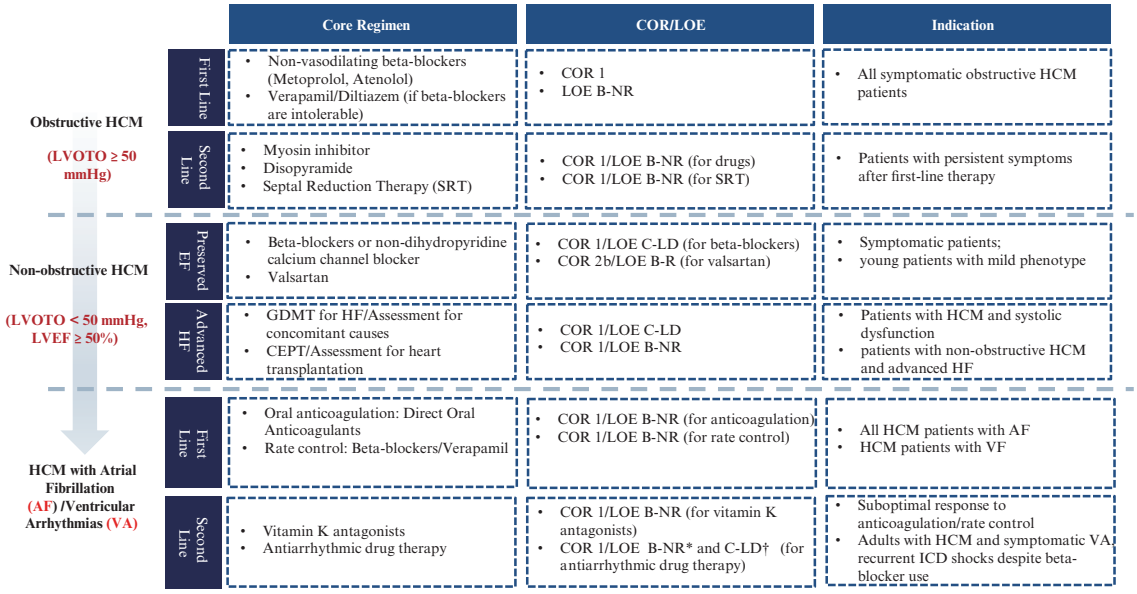
Global Prevalence of HCM, 2020-2035E

Period	CAGR			
	China	US	ROW	Total
2020-2024	1.7%	2.5%	3.0%	2.8%
2024-2035E	0.9%	1.3%	2.1%	1.9%



Source: Frost & Sullivan Report

The recommended treatments for HCM are phenotype-based, meaning that therapies vary for obstructive HCM, non-obstructive HCM, and HCM with atrial fibrillation or ventricular arrhythmias. The chart below sets forth the treatment paradigm for HCM in the United States.



Source: Frost & Sullivan Report

Given the limitations of existing treatment options, namely that they blunt symptoms and slow disease progression but do not correct the underlying defect, gene therapy has a potential to become a disruptive treatment method for HCM. Clinical development of rAAV gene therapy drugs for HCM is ongoing but relatively new. As of the Latest Practicable Date, only one rAAV gene therapy candidate for HCM treatment had entered clinical development globally. Its details, together with details of our FT-017, are set forth in the table below.

Route of Administration	Drug Name	Company	Modality	Target	Highest Phase	Country	First Posted Date
Intravenous	TN-201	Tenaya Therapeutics	Gene Therapy	MYBPC3	Phase I/II	US	2023-05-01
	FT-017	**Frontera Therapeutics**	**Gene Therapy**	**MYBPC3**	**Phase I/II IND Approval**	**China, US**	**2025-04-28**

Source: Clinicaltrial.gov, CDE, Frost & Sullivan Report

The Arrhythmogenic Right Ventricular Cardiomyopathy ("ARVC") Market

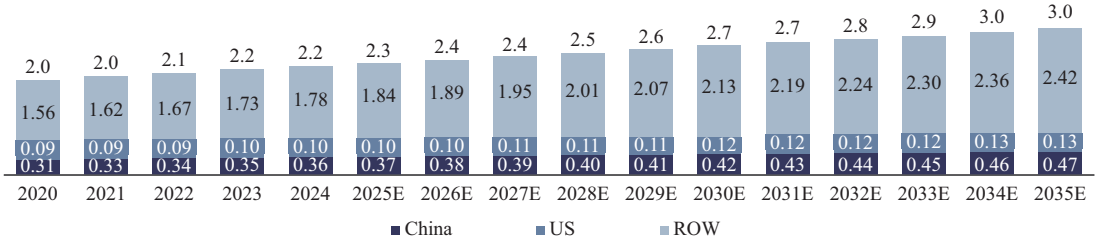
ARVC is a genetically determined heart muscle disease characterized by progressively fibrofatty replacement of the right ventricular myocardium. Patients may be asymptomatic, but symptomatic patients usually first present with ventricular tachycardia or ventricular fibrillation. Both symptomatic and asymptomatic individuals may experience sudden death. ARVC is responsible for approximately 10% of sudden deaths in young adults.

The number of patients with ARVC globally reached 2.2 million in 2024, and is expected to reach 3.0 million in 2035. The number of patients with ARVC in China was 0.36 million in 2024, and is expected to reach 0.47 million in 2035. The number of patients with ARVC in the United States was 0.10 million in 2024, and is expected to reach 0.13 million in 2035. The following charts set forth certain additional details regarding the global prevalence of ARVC.

Global Prevalence of ARVC, 2020-2035E

Period	CAGR			
	China	US	ROW	Total
2020-2024	3.4%	3.2%	3.3%	3.3%
2024-2035E	2.6%	2.5%	2.9%	2.8%

Million



Source: Frost & Sullivan Report

There is currently no approved drug for ARVC. The management of ARVC primarily rests on the off-label use of β-blockers, amiodarone or sotalol to curb arrhythmia, retard remodeling and prevent sudden death. As of the Latest Practicable Date, there were three rAAV gene therapy drugs for ARVC under clinical development globally.

SOURCE OF INFORMATION

In connection with the [**REDACTED**], we have engaged Frost & Sullivan to conduct a detailed analysis and prepare an industry report on the major markets for which our drug candidates are positioned. Frost & Sullivan is an independent global market research and consulting company which was founded in 1961 and is based in the United States. We have agreed to pay Frost & Sullivan a total fee of approximately RMB680,000 for the preparation of the Frost & Sullivan Report, and we believe that such fees are consistent with the market rate. The payment of such amount is not contingent upon our successful [**REDACTED**] or on the results of the Frost & Sullivan Report. Except for the Frost & Sullivan Report, we did not commission any other industry report in connection with the [**REDACTED**].

The market projections in the Frost & Sullivan Report were based on the following key assumptions: (i) the overall social, economic and political environment globally and in China is expected to remain stable during the forecast period; (ii) the economic and industrial development globally and in China is likely to maintain a steady growth trend over the next decade; (iii) related key industry drivers are likely to continue driving the growth of the market during the forecast period; and (iv) there is no extreme force majeure or industry regulation in which the market may be affected dramatically or fundamentally. The reliability of the Frost & Sullivan Report may be affected by the accuracy of the foregoing key assumptions.

The Directors have exercised reasonable care in selecting and identifying the named information sources, in compiling, extracting and reproducing the information, and in ensuring that there is no material omission of the information.