# INDUSTRY OVERVIEW

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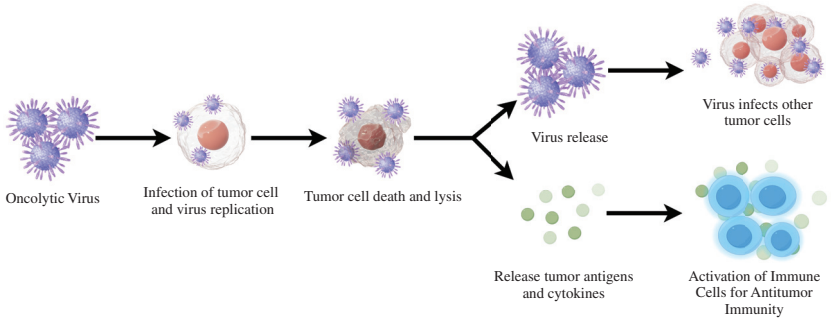
## OVERVIEW OF ONCOLYTIC VIRUS THERAPIES

### Overview and Mechanism of Action of Oncolytic Virus

Oncolytic viruses are tumor-selective immunotherapies that replicate within and lyse cancer cells, expose tumor-associated antigens, and reshape the tumor microenvironment to activate systemic immune responses. Since their early discovery, the field has advanced significantly, highlighted by the FDA's 2015 approval of IMLYGIC® (T-VEC), the first oncolytic virus therapy in the U.S. Their antitumor activity arises from multiple mechanisms: selective viral replication in metabolically dysregulated, immune-evasive tumor cells; direct tumor cell lysis and spread to neighboring malignant cells; and induction of immunogenic cell death that enhances antigen exposure. Oncolytic viruses also convert immunologically "cold" tumors into "hot" tumors by releasing pro-inflammatory signals and recruiting immune effector cells, strengthening antigen presentation, T-cell priming, and immune infiltration. By releasing tumor antigens in situ, they can further act as personalized tumor vaccines, generating durable systemic immunity and potentially preventing recurrence. The following diagram illustrates the mechanism of action of oncolytic virus:




*Source: Literature Review, Frost & Sullivan Report*

Oncolytic viruses preferentially replicate in cancer cells with impaired antiviral defenses, causing direct tumor-cell lysis and release of progeny virions. This lytic process exposes tumor-associated antigens, neoantigens, and danger signals (such as ATP and HMGB1), triggering immunogenic cell death that drives dendritic-cell maturation and efficient MHC-I cross-presentation, thereby activating cytotoxic T lymphocytes through classic TCR pathways. At the same time, the tumor microenvironment becomes enriched with pro-inflammatory cytokines and chemokines that recruit NK cells, macrophages, and effector T cells while reducing suppressive populations like MDSCs and Tregs — effectively converting "cold" tumors into "hot" tumors responsive to immunotherapy. By continually supplying diverse patient-specific antigens in situ, oncolytic viruses function as an in-vivo TCR-based immunotherapy platform, avoiding the manufacturing and antigen-loss limitations of ex-vivo engineered TCR-T products and enabling durable systemic antitumor immunity with lower relapse risk.

### Technological Pathway of Oncolytic Virus Therapies

Oncolytic viral vectors differ significantly in their engineering strategies, therapeutic advantages, representative viral platforms, clinical development stages, and applicable indications as demonstrated in the following table.

**Comparison of Oncolytic Viral Vector**

| Viral Vector | Key Characteristics | Typical Modification Methods | Example |
|---|---|---|---|
| **HSV** | a large viral capacity suitable for multi-factor payloads, with extensive engineering experience and a well-established safety profile | commonly engineered via ICP34.5/ICP47 deletion | T-VEC, G47Δ, RP1, BS001 |
| **Adenovirus** | high replication efficiency and mature manufacturing processes, making it suitable for large-scale production | often modified at E1/E3 regions or with tumor-specific promoters | ONYX-015, CG0070 |
| **Vaccinia Virus** | broad infection with strong cell lysis capabilities, ideal for short-term, high-intensity immune activation | strong lytic capacity and immune activation | Pexa-Vec |
| **Reovirus** | strong cytolytic activity enable targeted oncolysis in solid tumors | selective for Ras-activated tumor cells | Pelareorep |
| **NDV (Newcastle Disease Virus)** | tumor-selective replication and potent immunostimulant support robust anti-tumor immunity with low toxicity | natural tumor selectivity, especially in immunocompromised tumor environments | MTH-68/H, PV701 |
| **VSV (Vesicular Stomatitis Virus)** | rapid replication and high immunogenicity make it well-suited for swift tumor control | strong lytic ability, often used with immune payload insertion (e.g. IFN, NIS) | VSV-IFN β-NIS |

*Source: Frost & Sullivan Report*

Among all viral vector platforms, HSV stands out for its exceptionally large viral capacity, mature engineering flexibility, and well-established safety profile, making it ideal for complex therapeutic applications. HSV has a relatively large genome of approximately 150 kb, reflecting its greater biological complexity, including the ability to establish latency and evade host immune responses. The larger genomic size enables HSV to encode a broader range of proteins, providing multiple potential sites for genetic modification and facilitating the incorporation of therapeutic transgenes. Owing to its large about 152 kb double-stranded genome, HSV provides superior payload capacity and engineering flexibility, accommodating at least approximately 30 kb of inserted sequences and, in amplicon systems, transgene units approaching around 150 kb, substantially exceeding the capacities of E1/E3-deleted adenoviral vectors (approximately 8 kb with genomes constrained to approximately 105% of wild-type length), adeno-associated virus ("**AAV**") (approximately 4.7 kb), and vesicular stomatitis virus ("**VSV**") (an approximately11 kb negative-sense genome comprising only five core genes, which severely limits available insertion space). In addition, the large and stable HSV genome enables efficient and precise engineering through targeted cleavage and homologous recombination directly in infected cells, often combined with fluorescent markers for rapid enrichment and clonal isolation, resulting in high engineering throughput. By contrast, adenoviral vector construction is constrained by relatively low homologous recombination efficiency and labor-intensive plaque purification despite advances such as bacterial recombination systems; AAV cloning, while straightforward at the plasmid level, is practically limited by stringent packaging constraints that frequently necessitate dual-vector strategies; and VSV engineering via reverse genetics is restricted by genome size, transcriptional gradients, and replication fitness costs that may compromise genetic stability. From a safety perspective, reported data indicate that HSV exhibits the lowest incidence of severe adverse events (1.35%, 95% CI: 0.93–1.85) among these platforms, compared with higher rates observed for VSV (5.40%, 95% CI: 1.67–10.99). HSV-1 backbones are already clinically validated, while HSV-2 is increasingly recognized for advantages in replication, immunomodulation, and manufacturability, especially in

solid tumors. HSV-2's ability to suppress apoptosis supports a longer replication cycle, promoting sustained viral persistence and stronger oncolytic activity. Although HSV-1 and HSV-2 have similarly large genomes, certain HSV-2 strains achieve higher yield and stability in bioreactors and show better intracellular retention, improving downstream concentration and purification.

Oncolytic virus platforms have advanced through sequential generations of engineering. Early versions used natural or lightly modified viruses with limited control over safety and selectivity. Second-generation designs introduced deletions such as ICP34.5 and ICP47 to improve tumor specificity, while third-generation viruses added immunomodulatory cytokines (e.g., GM-CSF, IL-12, anti-CD3, anti-PD-L1) to couple oncolysis with stronger immune activation.

**Comparison of Armed Oncolytic Virus Therapies**

| Dimension | 1st Generation | 2nd Generation | 3rd Generation |
|---|---|---|---|
| **Design Principle** | Natural defects in tumor antiviral response for selective replication | Engineered to improve tumor targeting and replication | Armed with immunostimulatory nucleic acid sequence to boost immune response and enhance safety |
| **Key Mechanism** | Spontaneous tumor-selective replication | Insertion/deletion of viral nucleic acid sequence for better tumor tropism and reduced toxicity | Incorporation of cytokines, chemokines, ligands, or bispecific T-cell engagers ("**TCEs**") to stimulate anti-tumor immunity |
| **Immune Activation** | Indirect immune activation via tumor lysis | Enhanced antigen release and presentation | Direct immune stimulation (GM-CSF, IL-12, CD40L, chemokines, bispecific TCEs) |
| **Safety Profile** | Limited safety due to wild-type backbones | Improved safety through attenuation and modifications | Further enhanced safety by rational design and immune-modulating payloads |
| **Clinical Status** | Early clinical exploration; limited approvals | Established clinical validation (T-VEC, G47Δ approved) | Ongoing clinical development; the most advanced candidates have reached Phase III, such as our Company's BS001 and BS006 |

*Source: Frost & Sullivan Report*

Emerging approaches now emphasize modular payload design, novel viral vector, and deep engineering of immunosuppressive pathways, reflecting a transition toward platform-based, precision-engineered solutions for multi-indication and combination therapies, where once a safe backbone is established, it can be rationally and repeatedly engineered for specific tumor-immune contexts and deployed across multiple indications, most often in combination with checkpoint inhibitors or other immunotherapies. In addition to the direct tumor lysis and immune activation of oncolytic viruses, armed oncolytic viruses which are engineered to express immune-stimulatory nucleic acid sequence further enhance immune cell infiltration and synergize with other agents such as immune checkpoint inhibitors ("**ICIs**"), resulting in multiple complementary anti-tumor mechanisms.

### Applications for Oncolytic Virus Therapies

Oncolytic viruses offer broad therapeutic versatility through engineered payloads, strategic combinations, and perioperative use. As monotherapies, they can deliver antigens, cytokines, chemokines, or bispecific T-cell engagers to boost innate and adaptive immunity, with early studies showing safety and preliminary efficacy across solid and CNS tumors. When combined with immune checkpoint inhibitors, oncolytic viruses drive immunogenic cell death, enhance TIL infiltration, and upregulate PD-L1, converting "cold" tumors into "hot" tumors and improving ICI responsiveness. They also synergize with Chimeric Antigen Receptor T-cell therapy (CAR-T) and Chimeric Antigen Receptor Natural Killer cell therapy (CAR-NK) therapies by promoting antigen release, dendritic-cell maturation, and effector-cell activation. In perioperative settings, oncolytic viruses can be used in adjuvant or neoadjuvant regimens to strengthen local control, reduce recurrence, and improve long-term surgical outcomes.

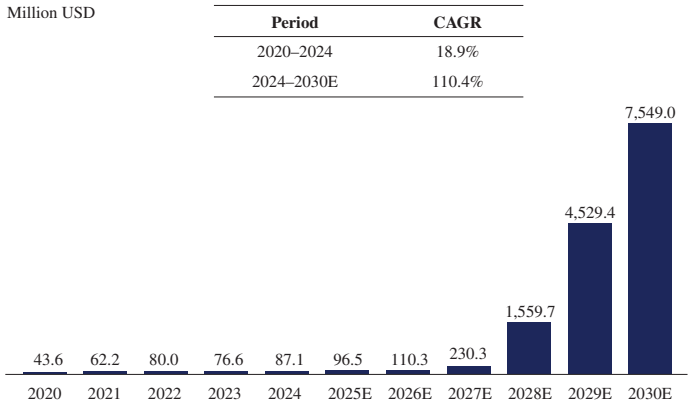
Oncolytic viruses have shown activity across a broad range of solid tumors, including melanoma, CRC, GBM, STS, and BTC, with more than 150 active clinical trials worldwide evaluating both monotherapy and combination approaches. This breadth highlights their potential as a scalable platform therapy capable of addressing significant unmet needs in oncology. That said, clinical adoption may face practical constraints, as live viral products often require specialized handling, storage, and institutional protocols. As clinical data, guidelines, and reimbursement frameworks mature, the Company expects the use of oncolytic virus therapies to expand over time.

## OVERVIEW OF ONCOLYTIC VIRUS MARKET

### Market Size of Oncolytic Virus

The global oncolytic virus market has experienced strong growth in recent years, driven by the unique mechanism of action of oncolytic viruses in cancer immunotherapy and the expanding landscape of clinical indications.

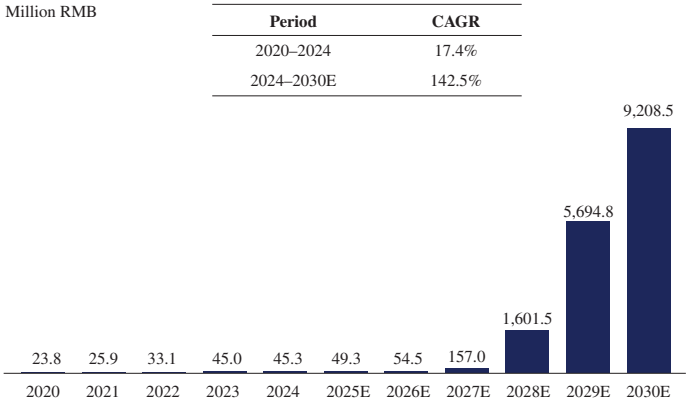
**Global Oncolytic Virus Market Size, 2020–2030E**




*Source: Frost & Sullivan Report*

Driven by growing research and development commitments from domestic enterprises, a consistent uptick in clinical trial approvals, favorable policy support for innovative biologics, and an increasingly defined commercialization roadmap, China's oncolytic virus market is transitioning from its nascent stage into a period of rapid growth.

**China's Oncolytic Virus Market Size, 2020–2030E**




*Source: Frost & Sullivan Report*

## Competitive Landscape of Oncolytic Virus

Globally, the number of approved oncolytic virus drugs remains limited, with indications focused on only a few tumor types. As of the Latest Practicable Date, only four oncolytic virus drugs had received regulatory approval globally, represented by Amgen's IMLYGIC® (T-VEC) and Daiichi Sankyo's DELYTACT® (G47Δ). The following tables set out the details of these approved products.

**Global Marketed Oncolytic Virus Drugs**

| Drug Name | Company | Vector | Indications | Drug Delivery Method | Approved region | Approved Date |
|---|---|---|---|---|---|---|
| Rigvir | Latima | ECHO-7 | Melanoma | Intramuscular injection | Armenia, Georgia, Latvia, Uzbekistan | 2004–04 |
| H101, 安柯瑞 | Shanghai Pharma | Ad5 | Nasopharyngeal carcinoma | Intratumoral | China | 2005–11 |
| T-VEC, Imlygic | Amgen | HSV-1 | Melanoma | Intralesional injection | US, Europe, Israel, Australia | 2015–10 |
| Delytact/G47Δ | Daiichi Sankyo | HSV-1 | Malignant Glioma | Intratumoral | Japan | 2021–06 |

*Note:* Globally approved and marketed pharmaceutical products (including FDA-approved products, but excluding those approved only in any single country, such as China or Japan), only T-VEC.

*Source: Clinical trials (as of 02/2026), Frost & Sullivan analysis*

As of the Latest Practicable Date, only four oncolytic virus drug candidates had advanced into the Phase III clinical stage globally, including our Company's BS001. As the only candidate currently in Phase III in China, BS001 is positioned to address a critical unmet need in the domestic market, significantly enhance patient accessibility, and establish a strong competitive moat. The following tables illustrate the global and China's competitive landscape of oncolytic virus drug candidates under clinical development.

**Global Competitive Landscape of Oncolytic Virus Pipeline (Phase III or above)**

| Pipeline Name | Originator Company | Highest Clinical Phase | Virus Type | First Disclosure Date | Indications |
|---|---|---|---|---|---|
| BS001 | Binhui Biopharm | Phase 3 | HSV-2 | 2023–03–08 | Melanoma, CRC* |
| RP1 | Replimune | Phase 3 | HSV–1 | 2024–02–09 | Melanoma |
| CG0070 | CG Oncology | Phase 3 | Adenovirus | 2020–10–27 | NMIBC |
| Olvi-Vec | Genelux Corporation | Phase 3 | Poxviridae | 2022–03–07 | Epithelial ovarian cancer, NSCLC, solid tumors |

**China's Competitive Landscape of Oncolytic Virus Pipeline (Phase III or above)**

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|---|---|---|---|---|---|
| BS001 | Binhui Biopharm | Phase 3 | HSV-2 | 2023–01–10 | Melanoma |

*Notes:*

1. Indications refer to all clinical trials initiated for each investigational drug within the past three years; not all indications are under development at the most advanced clinical phase. Only clinical programs that have remained active during this period are included.

2. For drugs with multiple trials at the same phase, the earliest publicly disclosed trial initiation date is used.

* *FDA clearance has been obtained for a Phase III trial in this indication; however, the trial has not yet commenced.*

*Source: Clinicaltrials.gov, NMPA, Frost & Sullivan Report*

**Growth Drivers of Oncolytic Virus Market**

The continued expansion of the oncolytic virus therapy market is supported by several key growth drivers.

- ***Expansion of market.*** Melanoma remains an attractive indication for oncolytic virus therapy due to the continued presence of unmet medical need despite the availability of established standard-of-care treatments. Current treatment options include surgery, immune checkpoint inhibitors, targeted therapies for selected patients, and local treatment modalities; however, a substantial proportion of patients do not achieve durable clinical benefit. Oncolytic viruses are relevant in melanoma both as monotherapy and in combination regimens, particularly for patients with injectable cutaneous, subcutaneous or nodal lesions. The clinical rationale for monotherapy use is supported by T-VEC, the first approved oncolytic virus for melanoma, which demonstrated an improved durable response rate in the pivotal OPTiM trial. In addition, oncolytic viruses have been shown to enhance antitumor immune responses through tumor cell lysis and induction of systemic immune activation, thereby supporting their continued development in combination with other therapeutic modalities.

- ***Technological progress.*** Advances in engineering and synthetic biology have enhanced the precision and flexibility of viral design, enabling more differentiated pipelines and wider indication coverage. At the same time, delivery innovations, particularly lipid nanoparticles ("**LNPs**") — are facilitating systemic administration by encapsulating oncolytic virus, derived nucleic acids for intravenous delivery, addressing the constraints of intratumoral injection. When paired with targeted ligands, these platforms further improve delivery efficiency and specificity, supporting the development of next-generation oncolytic virus therapies.

- ***Diagnostics and predictive tools advancements.*** The development of companion diagnostics and biomarker-based screening is improving patient stratification and clinical trial efficiency. These tools enable more precise identification of responsive populations, accelerating development timelines and enhancing therapeutic outcomes for oncolytic virus therapies.

- ***Supportive policy environment.*** In China, although no oncolytic virus product has been included in the National Reimbursement Drug List (NRDL) to our knowledge, the reimbursement landscape for innovative cancer immunotherapies has become increasingly supportive. For example, toripalimab has been included in the NRDL for multiple oncology indications, including unresectable or metastatic melanoma following failure of prior systemic therapy. Such precedents suggest that innovative immuno-oncology therapies may obtain reimbursement coverage in China where supported by demonstrated clinical value and successful price negotiation. In the United States,

regulatory programs such as Breakthrough Therapy designation and Regenerative Medicine Advanced Therapy (RMAT) designation may further facilitate a more efficient and predictable development pathway for oncolytic virus therapies.

**Future Trends in the Oncolytic Virus Market Addressing Current Development Challenges**

Several development challenges remain in the oncolytic virus field, acting as barriers to entry or bottlenecks in progress. Addressing these challenges not only reflects current limitations but also highlights emerging trends shaping the future of this sector.

- ***Breakthroughs in delivery technologies.*** Most oncolytic virus therapies require intratumoral or intracavitary injection, restricting use to accessible lesions and limiting efficacy against metastatic or deep-seated tumors. Intravenous delivery could broaden reach but remains challenged by immune clearance, circulation instability, and limited tumor targeting. Emerging approaches, such as LNP-encapsulated oncolytic virus, derived nucleic acids and ligand-based targeting — are showing promising early clinical results in improving systemic delivery and expanding therapeutic impact.

- ***Safety and selectivity enhancement.*** Despite attenuation strategies, concerns remain regarding neurotoxicity, uncontrolled viral replication, and systemic inflammation, especially when immune stimulatory nucleic acid sequences are introduced. Achieving selective replication in tumor cells while sparing healthy tissue remains a key challenge. Current approaches such as deleting essential viral sequences and using tumor specific promoters show promise, but maintaining stable and safe payload expression continues to be technically demanding.

- ***Precision medicine integration.*** Biomarkers are increasingly shaping the development of personalized oncolytic virus therapies. Predictive biomarkers, including those identified by our Company, help pinpoint patients who are more likely to respond, enabling more targeted treatment and improving clinical trial efficiency. Companion diagnostics are also being integrated earlier in development to support the selection of high-benefit populations and enhance overall efficiency.

- ***Manufacturing and quality control.*** Under GMP standards, developers must ensure consistent viral purity, potency, and activity, while minimizing batch-to-batch variation and process drift. To address these challenges, oncolytic virus producers are increasingly exploring new directions in manufacturing and quality control aimed at improving consistency, reducing costs, and accelerating time-to-market.

- ***Platform multifunctionality.*** Developing oncolytic virus therapies demands integrated expertise in molecular biology, immunology, virology, and bioengineering, making platform level innovation a key differentiator and barrier to entry. Leading companies are building standardized platforms that support not only oncolysis but also applications such as protein replacement and enhancement of cell therapies, enabling more streamlined development and rapid iteration across multiple assets.

- ***Global collaboration.*** Oncolytic virus therapies often require coordination across hospital departments, complex reimbursement negotiations, and expertise in international registration. As a result, international multi center trials, regional manufacturing hubs, and overseas commercialization networks are becoming standard practice, positioning oncolytic virus therapies for global clinical validation and market access.

## MARKET OPPORTUNITIES FOR ONCOLYTIC VIRUS THERAPIES

The global cancer burden continues to rise, placing long term pressure on healthcare systems and highlighting persistent unmet needs. Worldwide cancer incidence increased from 19.3 million in 2020 to 21.3 million in 2024 at a CAGR of 2.5% and is expected to reach 24.5 million by 2030, reflecting a CAGR of 2.3%. In China, new cancer cases grew from 4.6 million in 2020 to 5.0 million in 2024 at a CAGR of 2.2% and are projected to reach 5.6 million by 2030 at a CAGR of 1.9%. This growing patient base, together with improved diagnosis and treatment access, continues to drive steady market expansion. Globally, the cancer drug market increased from US$150.3 billion in 2020 to US$253.3 billion in 2024 at a CAGR of 13.9% and is expected to reach US$452.5 billion by 2030 at a CAGR of 10.2%. China's market is expanding even faster, rising from RMB197.5 billion in 2020 to RMB258.2 billion in 2024 at a CAGR of 6.9%, and is projected to reach RMB527.3 billion by 2030 at a CAGR of 12.6%. Against this backdrop, oncolytic viruses are emerging as a differentiated treatment modality. Their use has expanded from superficial tumors to deeper and more complex solid tumors, with strategies shifting toward systemic and precision oriented applications. Clinical studies have shown activity in melanoma, colorectal cancer, glioma, soft tissue sarcoma, and biliary tract cancer, and more than 150 active trials worldwide reflect the growing interest and future potential of this modality.

### Melanoma

#### *Overview of Melanoma*

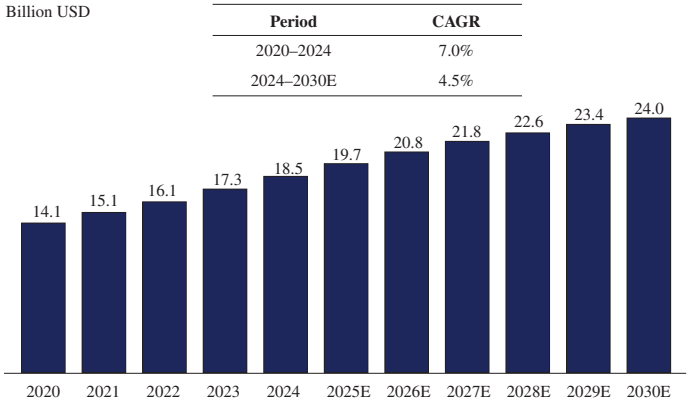
Melanoma is an aggressive malignancy arising from melanocytes, most often in the skin. It metastasizes readily and carries high mortality when not detected early. Ultraviolet radiation is the primary risk factor, alongside genetic susceptibility and immunosuppression. Melanoma is classified into cutaneous, acral, mucosal, and uveal subtypes. Cutaneous melanoma frequently carries the BRAFV600 mutation, which drives tumor growth through the MAPK pathway. In contrast, acral and mucosal melanoma more often show KIT mutations or a triple wild type profile, resulting in poorer responses to standard targeted therapies. Acral melanoma, which is more common in Asian populations and typically appears on the palms, soles, and nail beds, is especially challenging due to delayed diagnosis, distinct biological features, and limited treatment responsiveness.

Global melanoma incidence rose from about 324.6 thousand cases in 2020 to 351.6 thousand in 2024 at a CAGR of 2.0% and is expected to reach 376.6 thousand by 2030, reflecting a CAGR of 1.2%. In China, new melanoma cases increased from about 8.3 thousand in 2020 to 9.2 thousand in 2024 at a CAGR of 2.6% and are projected to reach 10.3 thousand by 2030 at a CAGR of 1.9%. This steady rise highlights the continuing public health burden and the importance of improved prevention and early detection. Meanwhile, for patients with unresectable and/or metastatic or recurrent melanoma who meet clinical trial criteria for third-line therapy, the addressable patient population for melanoma was approximately 3.3 thousand in China and 101.0 thousand globally in 2024, and is projected to increase to approximately 3.7 thousand in China and 106.7 thousand globally by 2030. Melanoma management includes surgery, radiotherapy, chemotherapy, targeted therapy, immunotherapy, and emerging modalities such as oncolytic virus therapies. In the U.S., PD-1 based immunotherapy (such as pembrolizumab, nivolumab, or nivolumab plus ipilimumab) is the standard first-line treatment for cutaneous melanoma. Patients with BRAFV600 mutations are typically treated with BRAF and MEK targeted combinations such as dabrafenib plus trametinib. In China, first-line options similarly include immune checkpoint inhibitors, targeted therapies for BRAFV600 mutations, and tyrosine kinase inhibitors such as imatinib for KIT mutated cases. Anti angiogenic agents including bevacizumab or endostar are often used with chemotherapy or immunotherapy.

#### *Market Size of Melanoma Therapeutics*

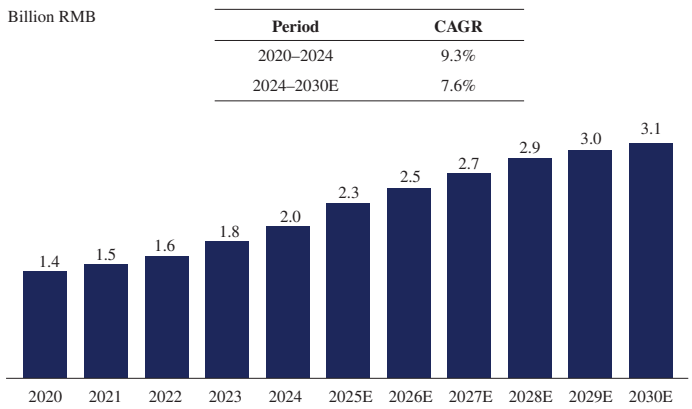
Driven by rising global demand for innovative therapies, improved diagnostics, and more effective targeted treatments, the melanoma therapeutics market has experienced steady growth both globally and in China. The melanoma therapeutics market is expected to maintain its upward trajectory in the near future.

**Global Melanoma Therapeutics Market Size, 2020–2030E**




*Source: Frost & Sullivan Report*

**China's Melanoma Therapeutics Market Size, 2020–2030E**




*Source: Frost & Sullivan Report*

***Market Opportunities and Competitive Landscape for Oncolytic Virus Therapy in Melanoma***

While immune checkpoint inhibitors have improved outcomes in melanoma, meaningful unmet medical needs remain. In global phase III studies of PD-1 and CTLA-4 combination therapy in advanced melanoma, the objective response rate was approximately 58%, indicating that around 40% of patients did not achieve an objective response at initial tumor assessment. In addition, a proportion of patients who initially respond may subsequently develop acquired resistance during follow-up. Certain melanoma subtypes, including mucosal melanoma, acral melanoma and melanoma with brain metastases, generally respond less favorably to standard immunotherapy. Moreover, combination checkpoint inhibitor regimens are associated with relatively high rates of immune-related adverse events, which may limit tolerability, particularly in clinically vulnerable patients. Melanoma's strong inherent immunogenicity makes it particularly suitable for oncolytic virus therapy. Oncolytic viruses induce direct tumor cell lysis, release tumor associated antigens, and activate dendritic cells, thereby amplifying T cell-mediated immunity. Clinically, they may be used as salvage treatments or combined with immune checkpoint inhibitors to enhance both local and systemic antitumor responses, improving overall response rates and durability of benefit. Intratumoral injection remains the primary mode of delivery, especially for cutaneous lesions, enabling localized viral replication with minimal systemic toxicity. Taken together, these features position melanoma as a strategically attractive indication for oncolytic virus therapy, with meaningful opportunities in both monotherapy and combination settings to address unmet clinical needs.

T-VEC remains the only approved oncolytic virus therapy for melanoma globally, demonstrating improved durable response rates in patients with unresectable disease. As of the Latest Practicable Date, no other oncolytic virus therapies had obtained regulatory approval, and the limited number of marketed products offers significant opportunities for differentiated therapies. As of the Latest Practicable Date, globally, there were 20 oncolytic virus drug candidates for melanoma in clinical development, including two in Phase III, four in Phase II, three in Phase I/II and 11 in Phase I. In China, there were four oncolytic virus drug candidates for melanoma in clinical development, including one in Phase III, one in Phase II, one in Phase I/II and one in Phase I. Among them, our Core Product, BS001, is the only oncolytic virus candidate in Phase III clinical development in China. The following tables summarize the global and China competitive landscape of oncolytic virus candidates under clinical development for melanoma.

**Global Competitive Landscape of Oncolytic Virus Pipeline for Melanoma (Phase III or above)**

| Drug Name | Company | Indication | Virus Type | Clinical Stage | First Posted Date |
|---|---|---|---|---|---|
| RP1 | Replimune | Melanoma | HSV-1 | Phase 3 | 2024–02–09 |
| BS001 | Binhui Biopharm | Melanoma | HSV-2 | Phase 3 | 2023–03–08 |

**China's Competitive Landscape of Oncolytic Virus Pipeline for Melanoma (Phase III or above)**

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|---|---|---|---|---|---|
| BS001 | Binhui Biopharm | Melanoma | HSV-2 | Phase 3 | 2023–01–10 |

*Notes:*

1. Excluding trials terminated at the investigator's initiative.
2. Only includes pipelines active within the past three years.

*Source: Clinicaltrials.gov, CDE, Frost & Sullivan Report*

The BS001 has demonstrated better efficacy results for treating melanoma. The table below sets forth the comparison of major clinical results between BS001 and T-VEC.

**Comparison of Major Clinical Results Between BS001 and T-VEC in Treating Melanoma**

| | T-VEC | BS001 |
|---|---|---|
| Virus vector and administration | HSV-1; intratumoral | HSV-2 expressing GM-CSF; intratumoral |
| Major clinical results in treating melanoma | The Phase III clinical trial demonstrated good efficacy results of T-VEC in treating unresectable advanced melanoma. While its ORR was 26.4%, its mOS reached 23.3 months, 4.4 months longer than the 18.9 months observed in the control group. | The Phase Ia/Ib clinical trial as of August 15, 2025 manifested a robust efficacy profile, with the ORR of 34.48%. In terms of survival rate, a one-year survival rate of 91.0% and a two-year survival rate of 72.0% were observed. The current mOS has achieved 46.6 months. |

*Source: Company data, National Center for Biotechnology Information, Frost & Sullivan Report*

## Colorectal Cancer

### *Overview of Colorectal Cancer*

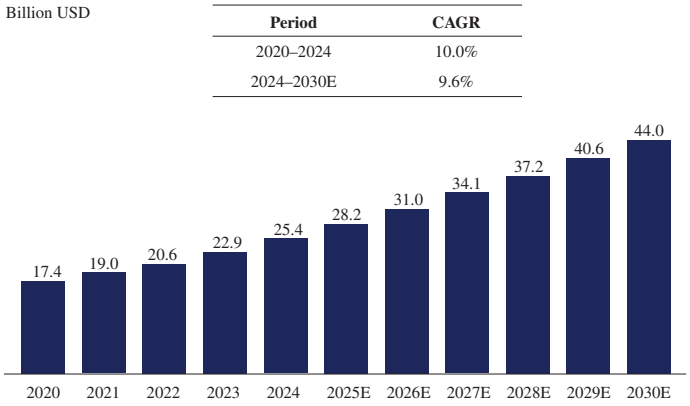
Colorectal cancer, a malignant tumor of the colon or rectum, is among the most common gastrointestinal cancers worldwide. It is generally categorized into non-metastatic and metastatic disease, with the liver being the most frequent site of metastasis. Liver metastasis occurs in up to 64% of patients and is associated with poorer prognosis, shorter overall survival, and fewer treatment options, underscoring the high clinical burden and unmet need in metastatic colorectal cancer. Globally, the incidence of colorectal cancer rose from approximately 1.9 million cases in 2020 to 2.1 million in 2024 (CAGR of 2.2%) and is projected to reach 2.3 million by 2030 (CAGR of 2.0%). In China, incidence increased from about 489.8 thousand cases in 2020 to 542.4 thousand in 2024 (CAGR of 2.6%) and is expected to reach 608.4 thousand by 2030 (CAGR of 1.9%). Among these patients, approximately 0.74 million globally and 195.3 thousand in China had liver metastases in 2024, with numbers projected to rise to about 0.8 million worldwide and 219.0 thousand in China by 2030, reflecting a growing patient population and expanding clinical need. Meanwhile, for patients requiring subsequent systemic therapy after standard treatment and meeting clinical trial criteria for second-line therapy, the addressable patient population for colorectal cancer was approximately 414.9 thousand in China and 1.6 million globally in 2024, and is projected to increase to approximately 465.4 thousand in China and 1.8 million globally by 2030.

The standard treatment for colorectal cancer in the U.S. is generally stratified based on disease stage, e.g., non-metastatic versus metastatic. Within these categories, further treatment decisions are guided by tumor resectability and may involve chemotherapy alone or in combination with targeted therapies or immunotherapy. In contrast, treatment strategies in China are primarily determined by the cancer stage. Early-stage colorectal cancer is typically managed with surgery, chemotherapy, and radiotherapy, while advanced-stage disease involves systemic therapy and chemotherapy, in addition to surgical intervention. Additionally, biomarker testing is commonly conducted prior to initiating first-line therapy to inform personalized treatment planning.

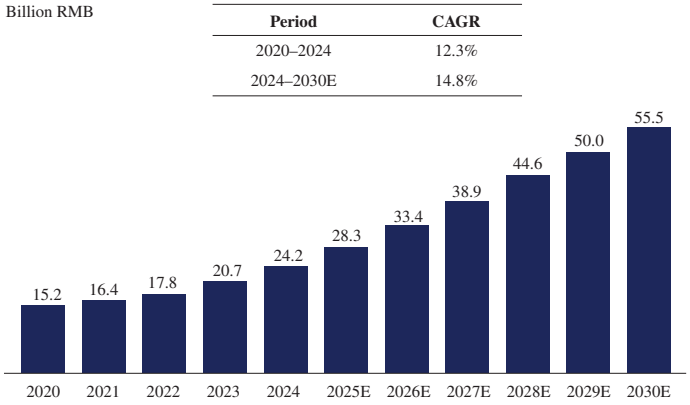
### *Market Size of Colorectal Cancer Therapeutics*

Driven by rising incidence rates, the increasing adoption of early screening technologies, and the commercialization of innovative therapies, including immunotherapies, targeted agents, and oncolytic viruses, the global colorectal cancer therapeutics market has experienced steady expansion in recent years and continues to demonstrate strong long-term growth potential. Within the global colorectal cancer market, China is experiencing faster growth, driven by expanded screening coverage, accelerated drug approvals, and increasingly diverse treatment options. As clinical practices become more standardized and healthcare reimbursement improves, China's colorectal cancer therapeutics market is expected to maintain strong growth.

**Global Colorectal Cancer Therapeutics Market Size, 2020–2030E**



**China's Colorectal Cancer Therapeutics Market Size, 2020–2030E**




*Source: Frost & Sullivan Report*

***Market Opportunities and Competitive Landscape for Oncolytic Virus Therapy in Colorectal Cancer***

Over 90% of metastatic colorectal cancer patients are microsatellite stable, an immunologically "cold" subtype that responds poorly to ICIs. Existing immunotherapies provide only modest survival benefits, and chemotherapy or targeted agents offer limited response rates and durability, particularly in liver-dominant disease. Liver metastases frequently require locoregional treatment, yet few immune-based approaches adequately address this need. Oncolytic viruses help convert "cold" tumors into "hot" ones by enhancing immune cell infiltration and antigen presentation, thereby overcoming immune resistance. They can also be engineered with immune-stimulatory payloads or used in combination with PD-1/PD-L1 inhibitors to further boost activity. Broader adoption of screening tools such as FOBT and colonoscopy supports earlier diagnosis, increasing the feasibility of intratumoral therapies. For patients with liver metastases, intratumoral or intra-arterial approaches, including hepatic artery infusion, offer localized treatment with reduced systemic toxicity, further expanding the potential of oncolytic virus therapies.

However, as of the Latest Practicable Date, there were no oncolytic virus therapies approved for the treatment of colorectal cancer, underscoring the significant untapped market potential in this area. As of the Latest Practicable Date, globally, there were 15 oncolytic virus drug candidates for colorectal cancer in clinical development, including one in Phase III, one in Phase II, four in Phase I/II and nine in Phase I. In China, there were two oncolytic virus drug candidates for colorectal cancer in clinical development, including one in Phase I/II and one in Phase I. Among them, BS001 is the only oncolytic virus candidate for colorectal cancer in Phase I/II or above clinical development in China. The following tables illustrate the global and China's competitive landscape of oncolytic virus drug candidates under clinical development for colorectal cancer.

**Global Competitive Landscape of Oncolytic Virus Pipeline for Colorectal Cancer (Phase II or above)**

| Drug Name | Company | Indication | Clinical Stage | First Posted Date |
|---|---|---|---|---|
| BS001 | Binhui Biopharm | Colorectal cancer* | Phase 3 | 2025–09–09** |
| Voyager V1 | Vyriad | Colorectal cancer | Phase 2 | 2020–02–28 |

**China's Competitive Landscape of Oncolytic Virus Pipeline for Colorectal Cancer (Phase I/II or above)**

| Drug Name | Company | Indication | Clinical Stage | First Posted Date |
|---|---|---|---|---|
| BS001 | Binhui Biopharm | Colorectal cancer | Phase 1/2 | 2019-03-05*** |

*Notes:*

1. Excluding trials terminated at the investigator's initiative.
2. Only includes pipelines active within the past three years.

* *FDA clearance has been obtained for a Phase III trial in this indication; however, the trial has not yet commenced.*

** *Represents the date on which FDA clearance was received for the Phase III trial in this indication.*

*** *Represents the initiation date of its Phase I/II basket trial including colorectal cancer cohort; the first patient in this cohort was enrolled in July 2020.*

*Source: Clinicaltrials.gov, CDE, Frost & Sullivan Report*

**Glioma**

***Overview of Glioma***

Glioma is a heterogeneous primary brain tumor arising from glial cells, ranging from low-grade lesions to highly aggressive forms such as glioblastoma ("**GBM**"). Globally, incidence increased from approximately 488.5 thousand cases in 2020 to 531.5 thousand in 2024 (CAGR of 2.1%) and is projected to reach 600.6 thousand by 2030 (CAGR of 2.1%). In China, incidence rose from about 65.8 thousand in 2020 to 75.1 thousand in 2024 (CAGR of 3.3%) and is expected to reach 87.5 thousand by 2030 (CAGR of 2.6%). Meanwhile, for patients who have failed standard-of-care and meet clinical trial criteria, the addressable patient population for glioma was approximately 36.5 thousand in China and 258.3 thousand globally in 2024, and is projected to increase to approximately 42.5 thousand in China and 291.9 thousand globally by 2030. Despite incremental advances in surgery, radiotherapy, and temozolomide-based regimens, recurrence remains common — occurring in roughly 90% of high-grade and 52–62% of low-grade gliomas within two years — highlighting significant unmet need. Treatment decisions in both the U.S. and China are commonly guided by the Karnofsky Performance Status ("**KPS**"). For patients with KPS $\geq$ 60, MGMT promoter methylation is a key biomarker for first-line therapy: methylated patients generally benefit more from temozolomide-based chemoradiotherapy, while unmethylated patients may be directed to alternative regimens or clinical trials. Patients with KPS $<$60 are typically considered for reduced-intensity therapy or palliative care. Second-line treatment is initiated upon progression and may include alternative chemotherapy, re-irradiation, surgery, or clinical trial participation, tailored to molecular features and functional status.

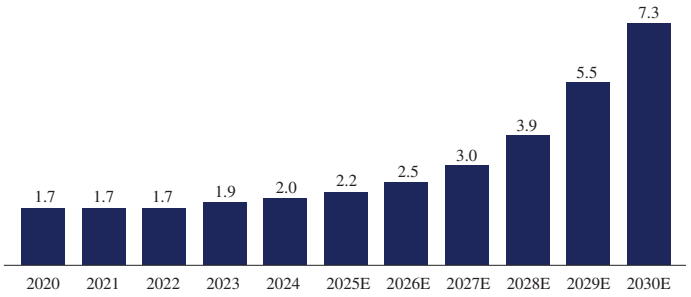
***Market Size of Glioma Therapeutics***

Over the past few years, the global glioma therapeutics market has grown at a moderate pace. With continued innovation in therapeutic approaches and expanding patient access, both the global and Chinese glioma therapeutics markets are expected to experience significant growth in the coming years.

**Global Glioma Therapeutics Market Size, 2020–2030E**

Billion USD

| Period | CAGR |
|---|---|
| 2020–2024 | 4.1% |
| 2024–2030E | 24.1% |

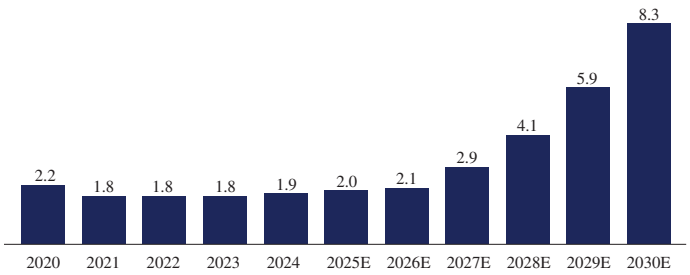



*Source: Frost & Sullivan Report*

**China's Glioma Therapeutics Market Size, 2020–2030E**

Billion RMB

| Period | CAGR |
|---|---|
| 2020–2024 | –3.9% |
| 2024–2030E | 27.8% |




*Source: Frost & Sullivan Report*

***Market Opportunities and Competitive Landscape for Oncolytic Virus Therapy in Glioma***

Glioma is a highly challenging and life-threatening disease with limited treatment options and poor prognosis. GBM represents the most aggressive and lethal subtype, yet effective therapies remain elusive. A major obstacle is the blood-brain barrier ("**BBB**"), which restricts the delivery of most systemic treatments, including monoclonal antibodies and small-molecule inhibitors. ICIs have also shown limited benefit in central nervous system tumors due to their immunologically "cold" microenvironment. As a result, outcomes remain poor, with high recurrence rates and few effective options after progression. This is especially true for recurrent gliomas, where no established standard of care exists and response rates to ICIs and targeted therapies remain low, underscoring a substantial unmet medical need and a clear opportunity for novel therapeutic approaches.

Unlike conventional therapies constrained by the BBB and the immune-privileged nature of the central nervous system, oncolytic viruses offer a differentiated therapeutic approach. They can be administered directly into the tumor or ventricular system via stereotactic injection or intrathecal catheter, bypassing the BBB. Once inside the CNS, they selectively replicate within tumor cells, inducing lysis and releasing pro-inflammatory cytokines that recruit immune effector cells and initiate a localized antitumor response. Engineered constructs expressing immunostimulatory molecules such as GM-CSF, IL-12, or bispecific TCEs may further enhance T-cell-mediated activity. Advances in HSV-2-based platforms have shown stable replication and favorable safety in early CNS studies, supporting their potential for clinical translation.

Globally, glioma treatment is receiving increasing attention. In China, gliomas are included in the fast-track review pathway for innovative drugs, especially those targeting rare and high-burden cancers, which significantly accelerates development timelines. However, as of the Latest Practicable Date, only one oncolytic virus therapy had been approved for glioma, i.e., Daiichi Sankyo's DELYTACT® (G47Δ) approved in Japan, highlighting a substantial unmet need and significant market potential in this therapeutic area. As of the Latest Practicable Date, globally, there were 13 oncolytic virus drug candidates for glioma in clinical development, including one in Phase II, three in Phase I/II and nine in Phase I. In China, there were four oncolytic virus drug candidates for glioma in clinical development, including three in Phase I/II and one in Phase I. Among them, BS001 is one of the three oncolytic virus candidates for glioma in Phase I/II clinical development in China. The following tables illustrate the global and China's competitive landscape of oncolytic virus drug candidates under clinical development for glioma.

**Global Competitive Landscape of Oncolytic Virus Pipeline for Glioma (Phase I/II or above)**

| Drug Name | Company | Indication | Clinical Stage | First Posted Date |
|---|---|---|---|---|
| BS001 | Binhuì Bio | Glioblastoma | Phase 1/2 | 2022-02-08 |
| Leraptolutev | Istari Oncology | Glioblastoma | Phase 2 | 2020-07-16 |
| BioTTT001 | BioTTT | Anaplastic glioma | Phase 1/2 | 2025-01-02 |
| C5252 | Immivira | Glioma, Malignant | Phase1/2 | 2025-11-21 |

**China's Competitive Landscape of Oncolytic Virus Pipeline for Glioma (Phase I/II or above)**

| Drug Name | Company | Indication | Clinical Stage | First Posted Date |
|---|---|---|---|---|
| BS001 | Binhuì Bio | Glioblastoma | Phase 1/2 | 2021-07-30 |
| BioTTT001 | BioTTT | Anaplastic glioma | Phase 1/2 | 2024-12-10 |
| JL15003 | Jechcbio | Glioblastoma | Phase 1/2 | 2025-04-28 |

*Notes:*

1. Excluding trials terminated at the investigator's initiative.
2. Only includes pipelines active within the past three years.

*Source: Clinicaltrials.gov, CDE, Frost & Sullivan Report*

## Soft Tissue Sarcoma

### *Overview of Soft Tissue Sarcoma*

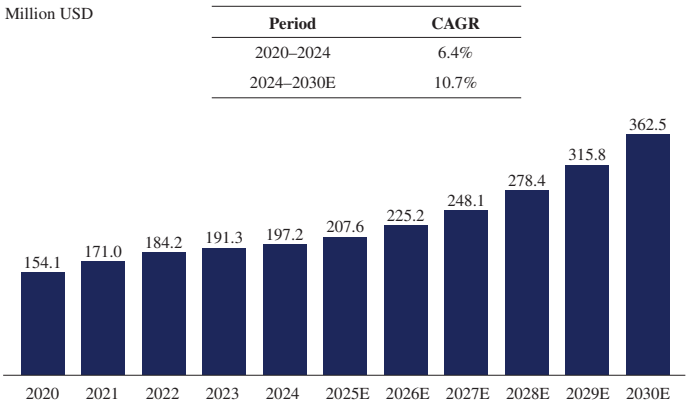
Soft tissue sarcoma is a rare and heterogeneous group of malignant tumors arising from mesenchymal tissues, including fat, muscle, nerves, blood vessels, and fibrous tissue. With more than 50 histological subtypes, it can occur throughout the body, most commonly in the extremities and retroperitoneum. Globally, incidence increased from approximately 185.3 thousand cases in 2020 to 207.1 thousand in 2024 (CAGR of 2.8%) and is projected to reach 239.1 thousand by 2030 (CAGR of 2.4%). In China, newly diagnosed cases rose from about 44.5 thousand in 2020 to 50.3 thousand in 2024 (CAGR of 3.1%) and are expected to reach 59.2 thousand by 2030 (CAGR of 2.8%). Meanwhile, for unresectable or recurrent/metastatic STS patients receiving second-line or later systemic therapy, the addressable patient population for soft tissue sarcoma was approximately 26.3 thousand in China and 108.1 thousand globally in 2024, and is projected to increase to approximately 30.9 thousand in China and 124.8 thousand globally by 2030.

Due to its aggressive nature and potential for local recurrence and distant metastasis, soft tissue sarcoma presents significant clinical challenges and often requires a multidisciplinary treatment approach, including surgery, radiotherapy, chemotherapy, and increasingly, targeted and immunotherapies. For resectable tumors, surgery remains the cornerstone, often combined with neoadjuvant radiotherapy to preserve function and improve local control. In cases of unresectable disease, systemic therapy becomes the mainstay, with anthracycline-based chemotherapy serving as the standard first-line regimen across most histological subtypes. Upon disease progression or in histologically distinct subtypes, treatment may shift toward targeted therapies (e.g., anlotinib, pazopanib) and immunotherapies, reflecting an evolving paradigm that balances tumor control with functional preservation and quality of life.

***Market Size of Soft Tissue Sarcoma Therapeutics***

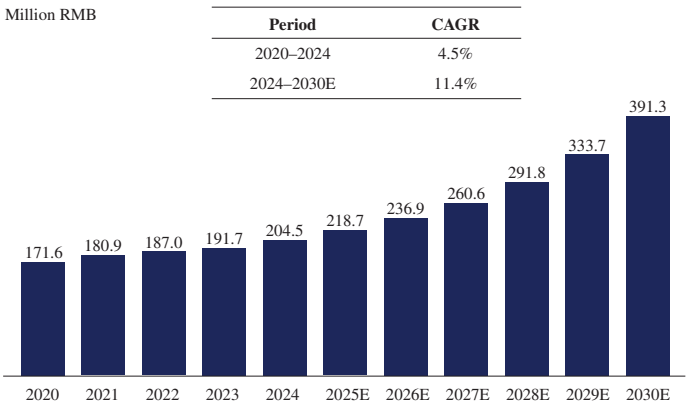
The global soft tissue sarcoma therapeutics market has grown steadily, driven by advances in diagnostics, longer patient survival, and broader treatment options. Emerging modalities, including novel agents, immunotherapies, and oncolytic viruses, are reshaping the treatment landscape and creating new opportunities for market expansion. In China, systemic treatment options have expanded with the introduction of targeted therapies and immunotherapies. The inclusion of certain soft tissue sarcoma drugs in the NRDL and their designation for priority review have further accelerated the uptake of innovative therapies.

**Global Soft Tissue Sarcoma Market Size, 2020–2030E**




*Source: Frost & Sullivan Report*

**China's Soft Tissue Sarcoma Therapeutics Market Size, 2020–2030E**




*Source: Frost & Sullivan Report*

***Market Opportunities and Competitive Landscape for Oncolytic Virus Therapy in Soft Tissue Sarcoma***

Soft tissue sarcoma encompasses more than 50 histologic subtypes and exhibits high inter-tumoral heterogeneity, creating substantial treatment challenges. Responses vary widely, resistance to conventional therapies is common, and no universally accepted second-line standard exists. Anthracycline-based chemotherapy, typically doxorubicin, remains the first-line regimen but provides limited benefit in advanced or metastatic disease, with modest response rates and poor long-term outcomes. ICIs have also shown mixed efficacy, with meaningful benefit confined to select subtypes such as undifferentiated pleomorphic sarcoma and alveolar soft part sarcoma. These limitations highlight a clear need for novel therapeutic approaches. Oncolytic viruses offer a subtype-agnostic immune-activation platform suitable for this heterogeneous disease. Intratumoral delivery can enhance local control, particularly in superficial or extremity tumors and in post-surgical settings. In combination regimens, oncolytic viruses may synergize with tyrosine kinase inhibitors (such as pazopanib or anlotinib) by improving vascular permeability and promoting T-cell infiltration. Pairing oncolytic viruses with ICIs may also enhance immune recognition in immunologically "cold" subtypes, including synovial sarcoma and undifferentiated pleomorphic sarcoma.

Further engineering oncolytic viruses to express immunostimulatory molecules can enhance both local and systemic antitumor activity. Such armed oncolytic viruses are being investigated in synovial sarcoma and other immune-cold soft tissue sarcoma subtypes, with early data showing manageable safety across histologies. As soft tissue sarcoma qualifies under rare disease regulatory frameworks, novel modalities such as oncolytic viruses may benefit from accelerated pathways, including breakthrough therapy designation and priority review, creating an avenue for therapeutic innovation in this difficult-to-treat disease.

As of the Latest Practicable Date, no oncolytic virus for soft tissue sarcoma treatment had been approved globally. As of the same date, globally, there were eight oncolytic virus drug candidates in this area in clinical development, including one in Phase II, one in Phase I/II and six in Phase I. In China, there were two oncolytic virus drug candidates in clinical development in this area, including one in Phase II and one in Phase I/II. Among them, BS001 is one of the oncolytic virus candidates in Phase I/II clinical development in China. The following tables illustrate the global and China's competitive landscape of oncolytic virus drug candidates under clinical development for soft tissue sarcoma.

**Global Competitive Landscape of Oncolytic Virus Pipeline for Soft Tissue Sarcoma (Phase I/II or above)**

| Drug Name | Company | Indication | Clinical Stage | First Posted Date |
|---|---|---|---|---|
| VG161 | Virogin Biotech | Sarcoma | Phase 2 | 2023–05–24 |
| BS001 | Binhui Bio | Soft tissue sarcoma | Phase 1/2 | 2019–03–05 |

**China's Competitive Landscape of Oncolytic Virus Pipeline for Soft Tissue Sarcoma (Phase I/II or above)**

| Drug Name | Company | Indication | Clinical Stage | First Posted Date |
|---|---|---|---|---|
| VG161 | Virogin Biotech | Soft tissue sarcoma | Phase 2 | 2023–05–24 |
| BS001 | Binhui Biopharm | Soft tissue sarcoma | Phase 1/2 | 2019–03–05* |

*Notes:*

1. Excluding trials terminated at the investigator's initiative.
2. Only includes pipelines active within the past three years.

* *Represents the initiation date of its Phase I/II basket trial including soft tissue sarcoma cohort; the first patient in this cohort was enrolled in January 2021.*

*Source: Clinicaltrials.gov, CDE, Frost & Sullivan Report*

## Biliary Tract Cancer

### *Overview of Biliary Tract Cancer*

Biliary tract cancer comprises a group of aggressive malignancies arising from the bile ducts and gallbladder, characterized by poor prognosis and limited treatment options. Because early symptoms are nonspecific, most patients present with advanced disease, highlighting the urgent need for more effective therapies. Globally, incidence increased from approximately 367.9 thousand cases in 2020 to 419.1 thousand in 2024 (CAGR of 3.3%) and is projected to reach 505.0 thousand by 2030 (CAGR of 3.2%). In China, newly diagnosed cases rose from about 126.0 thousand in 2020 to 139.8 thousand in 2024 (CAGR of 2.6%) and are expected to reach 161.1 thousand by 2030 (CAGR of 2.4%). Meanwhile, for patients who have progressed after standard therapy and qualify for third-line treatment, the addressable patient population for biliary tract cancer was approximately 67.9 thousand in China and 203.7 thousand globally in 2024, and is projected to increase to approximately 78.3 thousand in China and 245.4 thousand globally by 2030.

In the U.S., treatment for biliary tract cancer is mainly divided into systemic therapy and other options like radiation. First-line treatments often involve immunotherapy combined with chemotherapy, like durvalumab or pembrolizumab plus chemotherapy. If the disease progresses, second-line options include FOLFOX or other chemotherapy regimens. In China, chemotherapy remains the primary first-line treatment, while second-line therapies increasingly include targeted agents. For patients with specific mutations—such as FGFR, IDH1, HER2, or NTRK—targeted therapies like pemigatinib, futibatinib, ivosidenib, and trastuzumab combinations are available, and may be used in both first- and second-line settings, sometimes in combination with immunotherapies like nivolumab + ipilimumab.

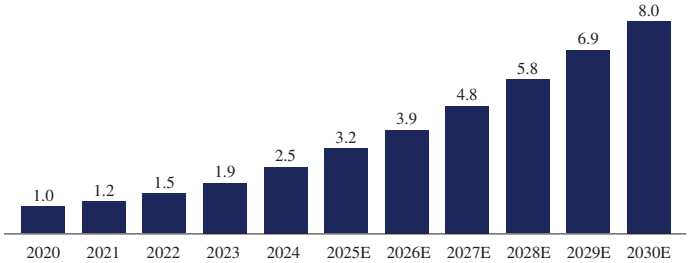
### *Market Size of Biliary Tract Cancer Therapeutics*

Despite its relatively small market size, biliary tract cancer carries a high unmet clinical need. Market penetration has accelerated in recent years, driven by advances in diagnostics, improved early detection, and the introduction of innovative therapies. Both the global and China markets have experienced notable growth, reflecting the release of previously unmet treatment demand and a rapidly evolving therapeutic landscape.

**Global Biliary Tract Cancer Therapeutics Market Size, 2020–2030E**

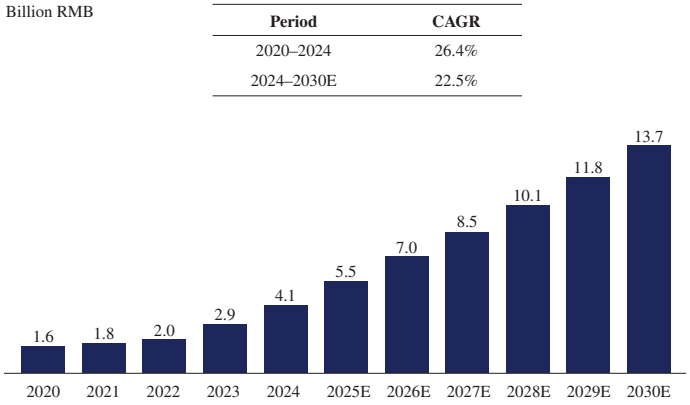
Billion USD

| Period | CAGR |
|---|---|
| 2020–2024 | 25.8% |
| 2024–2030E | 21.4% |




*Source: Frost & Sullivan Report*

**China's Biliary Tract Cancer Therapeutics Market Size, 2020–2030E**




*Source: Frost & Sullivan Report*

***Market Opportunities and Competitive Landscape for Oncolytic Virus Therapy in Biliary Tract Cancer***

Patients with malignant biliary tract cancer generally have poor prognosis, with limited benefit even from first-line therapy. Traditional chemotherapy and recently approved PD-1 inhibitors provide only modest improvements, and median overall survival typically remains under one year. Targeted therapies apply only to a small subset of patients with actionable mutations, leaving most with few effective options. Oncolytic viruses offer an approach by altering the tumor microenvironment, inducing pro-inflammatory signaling, and enhancing immune-cell infiltration to improve responsiveness to ICIs. They may also act as immunologic primers for chemotherapy or FGFR/IDH1-targeted agents, potentially broadening the patient population that can benefit. Given the localized nature of many biliary tract tumors, oncolytic viruses can be delivered regionally through hepatic artery infusion or percutaneous intratumoral injection. Multimodal delivery — combining deep-tumor injection with intravenous administration — may further improve intratumoral concentration and distribution, supporting better therapeutic outcomes.

Biliary tract cancer qualifies for orphan drug designation and may benefit from accelerated regulatory pathways such as fast-track and breakthrough therapy review. As of the Latest Practicable Date, no oncolytic virus had been approved for this indication. However, next-generation, payload-armed oncolytic viruses are advancing into preclinical and early clinical development, offering new therapeutic opportunities for this high-need population. As of the Latest Practicable Date, globally, there were two oncolytic virus drug candidates for biliary tract cancer in clinical development, including one in Phase II and one in Phase I/II. In China, there were also two oncolytic virus drug candidates for biliary tract cancer in clinical development, including one in Phase II and one in Phase I/II. Among them, BS001 is one of the oncolytic virus candidates in Phase I/II clinical development in China. The following tables summarize the global and China competitive landscape of oncolytic virus candidates under clinical development for biliary tract cancer.

**Global Competitive Landscape of Oncolytic Virus Pipeline for Biliary Tract Cancer (Phase I/II or above)**

| Drug Name | Company | Indication | Clinical Stage | First Posted Date |
|---|---|---|---|---|
| VG161 | Virogin Biotech | Intrahepatic cholangiocarcinoma | Phase 2 | 2022–01–24 |
| BS001 | Binhui Biopharm | Biliary tract cancer | Phase 1/2 | 2019–03–05 |

**China's Competitive Landscape of Oncolytic Virus Pipeline for Biliary Tract Cancer (Phase I/II or above)**

| Drug Name | Company | Indication | Clinical Stage | First Posted Date |
|---|---|---|---|---|
| VG161 | Virogin Biotech | Intrahepatic cholangiocarcinoma | Phase 2 | 2021–12–02 |
| BS001 | Binhui Biopharm | Biliary tract cancer | Phase 1/2 | 2019–03–05* |

*Notes:*

1. Excluding trials terminated at the investigator's initiative.
2. Only includes pipelines active within the past three years.

* *Represents the initiation date of its Phase I/II basket trial including biliary tract cancer cohort; the first patient in this cohort was enrolled in March 2021.*

*Source: Clinicaltrials.gov, CDE, Frost & Sullivan Report*

## SYSTEMIC DELIVERY OF ONCOLYTIC VIRUSES

### Overview of LNP Delivery

LNPs are nanoscale, lipid-based vesicles that encapsulate nucleic acids for highly efficient intravenous delivery. First validated through their success as vaccine delivery platforms, LNPs have demonstrated strong clinical safety and scalable manufacturing. Beyond infectious-disease vaccines, their ability to enable transient protein expression supports broad therapeutic applications, including cancer vaccines, protein-replacement therapies, and treatments for rare genetic disorders. In oncolytic virus development, LNPs add further value by packaging OV-derived nucleic acids for systemic administration. This approach helps overcome the limitations of intratumoral injection, increases delivery efficiency, broadens therapeutic reach, and supports the development of next-generation oncolytic virus therapies.

### Comparative Methods for Systemic Delivery of Oncolytic Viruses

Systemic delivery of oncolytic viruses is being advanced through three primary strategies: (i) LNP delivery, which encapsulates OV-derived nucleic acids in lipid vesicles optimized for intravenous administration; (ii) structural modification of the virus, including capsid-stabilizing peptides or polymer coatings that help intact virions survive in circulation and reach tumors; and (iii) cell-based carriers, which load whole virus into living cells or cell-derived vesicles to leverage natural immune-evasion mechanisms for systemic transport.

**Comparison of Systemic Delivery Methods for Oncolytic Viruses**

| Method | Features | Advantages | Limitations |
|---|---|---|---|
| **LNP Delivery** | • Encapsulating nucleic acids<br>• Validated intravenous delivery<br>• Scalable manufacturing | • High delivery efficiency<br>• Clinical validation<br>• Manufacturing scalability<br>• Versatility and modifiability | • Inherent potential toxicity associated with LNPs |
| **Structural Modification of Oncolytic Viruses** | • Modifies capsid for stability<br>• Extends circulation time | • Extended circulation time | • Complex engineering<br>• Low translation potential |
| **Cell Vectors** | • Uses cells<br>• Natural immune evasion | • Excellent immune evasion capabilities<br>• High safety | • Difficult large-scale cultivation<br>• Complex CMC process<br>• Substantial barriers to industrialization |

Among these approaches, LNPs offer the most industrially viable pathway. They already have clinical proof of concept in humans, demonstrating scalable, reproducible manufacturing and a favorable safety profile. LNPs provide high encapsulation efficiency and rapid endosomal release, achieving superior transfection compared with capsid engineering or cell-based carriers. Their modular lipid composition also enables straightforward payload swapping, tumor-targeting ligand attachment, and co-formulation with immunomodulators, without the cell-culture or CMC complexities of carrier platforms or the extensive engineering required for capsid redesign. These advantages position LNP delivery as the most practical and differentiated solution for next-generation oncolytic virus therapies.

**Applications of LNP Delivery Beyond Oncolytic Viruses**

Beyond their use in oncolytic virus delivery, LNPs support a wide range of therapeutic applications. They enable vaccine delivery, including personalized cancer vaccines that present patient-specific neoantigens and induce strong antitumor immunity. LNPs also facilitate liver-targeted nucleic acid delivery for rare hereditary diseases and transient protein replacement in regenerative medicine, demonstrating broad therapeutic versatility.

## SOURCE OF INFORMATION

We engaged Frost & Sullivan, a market research consultant, to prepare the Frost & Sullivan Report for use in this document. The information from Frost & Sullivan disclosed in this document is extracted from the Frost & Sullivan Report and is disclosed with the consent of Frost & Sullivan. In preparing the Frost & Sullivan Report, Frost & Sullivan collected and reviewed publicly available data such as government-derived information, annual reports, trade and medical journals, industry reports and other available information gathered by not-for-profit organizations as well as market data collected by conducting interviews with industry key opinion leaders. Frost & Sullivan has exercised due care in collecting and reviewing the information so collected and independently analyzed the information, but the accuracy of the conclusions of its review largely relies on the accuracy of the information collected. We agreed to pay Frost & Sullivan a fee of US$105,403 for the preparation and update of the Frost & Sullivan Report, which is not contingent on the [REDACTED] proceeding. Our Directors confirm that, after making reasonable enquiries, there is no material adverse change in the market information since the date of the Frost & Sullivan Report which may qualify, contradict or have an impact on the information in this section.