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PREVALENCE OF CANCER AND EVOLUTION OF ONCOLOGY TREATMENTS

Cancer is a leading cause of death worldwide, and is expected to continue rising due to aging populations, lifestyle-related risk factors, and demographic growth. In 2025, 21.9 million new cancer cases were diagnosed globally, alongside approximately 11 million cancer deaths, highlighting both the high incidence and the severe mortality burden of the disease.

In 2023, a total of 271 million DALYs (disability-adjusted life years) were attributed to cancer, with 97% of these being due to YLLs (years of life lost), reflecting the global burden of cancer mortality. From a global incidence perspective, solid tumors account for the majority of global cancer cases, representing approximately 90% of all new cancer cases worldwide in 2025 and expected to remain at a similar level by 2035. Global new cases of solid tumors are estimated to increase from 20.5 million in 2025 to 25.3 million by 2035. In parallel, hematologic malignancies also represent an important category of malignant diseases.

In 2025, the five most common solid tumors worldwide by incidence are lung, breast, colorectal, prostate, and stomach cancers. Stomach cancer, with approximately 1.0 million new cases, is among the top five solid tumor indications globally in terms of new diagnoses.

Evolution of treatment methods for cancer

Cancer treatment has gone through a long process of development in history, and it will continue to evolve over time. Current treatment modalities include surgery, radiotherapy, chemotherapy, targeted therapy and immunotherapy as well as cell and gene therapy. Together these approaches span curative, disease-controlling and palliative strategies and reflect a shift from broadly cytotoxic treatments toward more precise, biology-driven interventions.

Challenges in current treatments for solid tumors

The principal challenges associated with current cancer treatments include the following:

- ***Limited Opportunity for Radical Surgery.*** A substantial proportion of patients with advanced solid tumors are diagnosed at late stages or present with extensive tumor burden, rendering curative-intent local interventions such as surgery or definitive radiotherapy infeasible.

- ***Mechanistic Barriers to Effective Cancer Therapy.*** Mechanism-driven resistance represents a fundamental barrier to durable disease control in advanced solid tumors. Metastatic dissemination enables tumor cells to colonize anatomically and biologically distinct microenvironments, reducing the effectiveness of localized or pathway-specific therapies. In parallel, the tumor microenvironment (TME) plays a central role in

therapeutic resistance by fostering immune evasion and adaptive tumor evolution under sustained treatment pressure. Multi-drug resistance mechanisms, including enhanced xenobiotic metabolism and active drug efflux, further restrict effective intracellular drug exposure and limit the long-term efficacy of current systemic therapies.

- ***Limited Clinical Outcomes.*** Despite incremental advances, currently available post–standard-of-care systemic therapies, including later-line targeted agents, immune checkpoint inhibitors in refractory settings, antibody-drug conjugates (ADCs), and combination regimens, are rarely curative. Across indications, these approaches are predominantly associated with modest objective response rates and limited durability effects, with long-term remission observed only in a small subset of patients.

- ***Safety and Tolerability Limitations.*** Safety and tolerability limitations arising from cumulative treatment exposure represent a major challenge to sustained clinical benefit, especially in later-line or post–standard-of-care settings. Repeated systemic therapies frequently lead to accumulative toxicities, including bone marrow suppression, neurotoxicity, and organ dysfunction, which progressively limit dosing flexibility, treatment intensity and duration. These safety and tolerability constraints often necessitate dose modification, treatment interruption, or discontinuation, thus compromising real-world effectiveness and limiting the durability of clinical benefit in advanced solid tumors.

OVERVIEW OF CELLULAR IMMUNOTHERAPY AND CAR-T THERAPY MARKET

Immuno-oncology therapy is an emerging pillar of cancer treatment. From 2025 to 2035, immuno-oncology is expected to have the highest CAGR among major cancer treatment modalities, reflecting its rapidly expanding clinical adoption and strategic importance in oncology treatment. The process can be down in either stimulating immune system to attack cancer cells or giving immune system components. According to the market caliber, Immuno-Oncology therapies are primarily classified into cellular immunotherapies (e.g., CAR-T and TCR-T), cytokines, immune checkpoint monoclonal antibodies, oncolytic viruses, T-cell engager (TCE) drugs, and cancer vaccines. These therapeutic modalities aim to enhance anti-tumor immunity by modulating, activating, or redirecting T-cell function. Among these strategies, T cells represent the central effector of adaptive anti-tumor immunity. In particular, genetically engineered T-cell therapies, such as CAR-T cell therapy, directly modify patients' T cells to confer tumor-specific recognition and potent cytotoxic activity, positioning CAR-T as one of the most mature and clinically validated modalities within immuno-oncology.

Cellular immunotherapy

Cellular immunotherapy, also known as adoptive cell transfer (ACT) therapy, is a type of immunotherapy in which immune cells (primarily T cells) are given to a patient for the treatment of cancers. The T cells are usually taken from the patient's own blood or tumor tissues, grown in large numbers in the laboratory, and then infused to the patient to help the immune system kill tumor cells. Cellular immunotherapy can be classified as (i) non-genetically modified cellular immunotherapy (including activated autologous lymphocytes, cytokine induced killer cell and tumor-infiltrating lymphocytes) and (ii) genetically modified immunotherapy (including CAR-T, TCR-T, NK-CAR and Macrophage-CAR).

Barriers to entry in the cellular immunotherapy industry include the following: 1) *High Capital Requirements for R&D* — the cell therapy field demands massive R&D investments, spanning target discovery, preclinical studies, clinical trials, and long-term safety monitoring; 2) *Significant Technology Platform Barriers* — Core technologies in cell therapy require advanced expertise. For example, design of CAR structures and Armored technologies, in particularly, in vivo CAR-T systems require optimized vector designs for efficient T-cell transduction while ensuring tissue-specific targeting; 3) *Stringent Manufacturing and Regulatory Requirements* — CAR-T therapies face particularly complex manufacturing and regulatory compliance due to their novel mechanism of action, and regulatory standards for genetically modified products (e.g., FDA's BLA

or EMA's ATMP rules) vary globally, forcing companies to allocate resources for compliance; and 4) *Process Optimization & Industrialization* — the cell therapy industry is actively advancing process optimization and industrialization to overcome limitations of traditional personalized manufacturing approaches in cycle time, cost, and consistency.

CAR-T cell therapy

Evolution of CAR-T Therapeutic Modalities

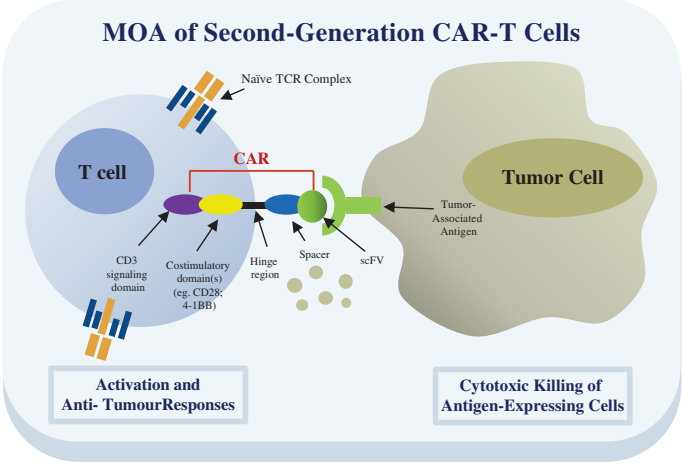
Conventional *ex vivo* CAR-T cell therapy, particularly autologous CAR-T, represents the most clinically established CAR-T modality to date and underpins all currently approved CAR-T products. In this approach, a patient's T cells are collected via leukapheresis, genetically modified *ex vivo* to express a chimeric antigen receptor (CAR), expanded under GMP conditions, and reinfused following lymphodepleting conditioning.

To address manufacturing and availability constraints inherent to individualized production, allogeneic CAR-T therapies based on donor-derived cells have been explored as off-the-shelf alternatives. However, their development remains constrained by fundamental immunological challenges, including graft-versus-host disease and host-mediated rejection, as well as manufacturing bottlenecks associated with large-scale, consistent clinical-grade production and concerns regarding genomic and chromosomal abnormalities arising from extensive *ex vivo* manipulation.

Accordingly, *in vivo* CAR-T therapy is emerging as a more scalable CAR-T implementation paradigm that bypasses *ex vivo* cell manipulation and reduces reliance on individualized manufacturing workflows, enabling direct genetic programming of immune cells within the patient and representing an alternative approach to conventional *ex vivo* CAR-T therapy.

Mechanism of Action

Chimeric antigen receptors (CARs) are engineered receptor proteins that combine antigen-binding and T-cell-activating functions to enable T cells to recognize and eliminate antigen-expressing cancer cells. CAR-T cell therapy involves harvesting a patient's T cells, genetically modifying them via viral vectors carrying the CAR construct and reinfusing the engineered cells as a targeted, cell-based immunotherapy. The following diagram illustrates the mechanism of action for second-generation CAR-T cells:

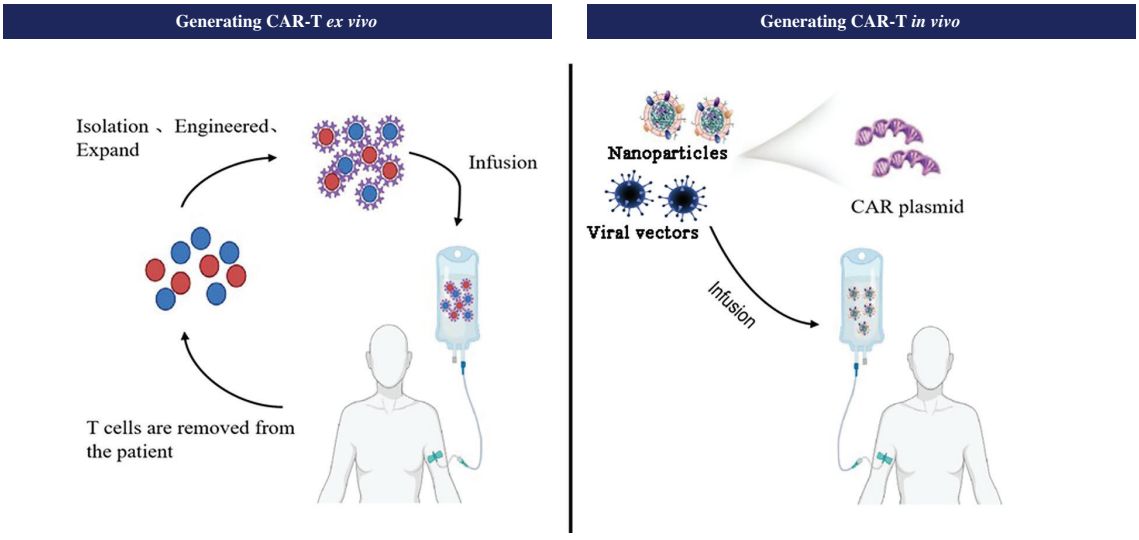


Source: Literature Review, Frost & Sullivan Analysis

Second-generation CAR-T cells exert their therapeutic effects through a sequential and tightly regulated mechanism of action. Upon administration, the extracellular single-chain variable fragment (scFv) of the chimeric antigen receptor specifically recognizes and binds surface antigens expressed on tumor cells in an antibody-like, major histocompatibility complex (MHC)–independent manner, thereby distinguishing CAR-mediated recognition from endogenous T-cell receptor (TCR) signaling. Antigen engagement subsequently induces CAR clustering on the T-cell surface, leading to phosphorylation of CD3ζ immunoreceptor tyrosine-based activation motifs (ITAMs) and activation of downstream signaling cascades mediated by a single costimulatory domain, such as CD28 or 4-1BB, independently of native TCR–MHC interactions. This signaling activation drives transcriptional programs associated with T-cell proliferation, effector function, and cytokine secretion. Ultimately, activated CAR-T cells eliminate antigen-expressing target cells predominantly through perforin- and granzyme-mediated cytotoxicity, with additional contributions from death receptor — mediated pathways, resulting in effective immune-mediated tumor control.

In vivo CAR-T therapy utilizes viral or non-viral delivery systems to introduce CAR-encoding mRNA or vector-based genetic constructs into immune cells *in vivo*, enabling in situ CAR expression and subsequent immune activation. These engineered T cells then circulate, recognize the tumor antigen, activate, and kill cancer cells with high specificity.

The following illustrations demonstrate the key differences between *ex vivo* and *in vivo* CAR-T.



Source: Literature Review, Frost & Sullivan Analysis

In vivo CAR-T therapy is currently transitioning from preclinical exploration to early-stage clinical evaluation. In the United States, a first-in-class *in vivo* CAR-T candidate targeting hematological malignancies, developed by Umoja Biopharma, received FDA IND authorization and subsequently initiated a Phase I clinical study in 2025. Concurrently, a limited number of candidates have entered early-phase clinical studies in other countries, contributing to an emerging body of preliminary human data. This early clinical entry into human studies provides a baseline for assessing the feasibility of in situ T-cell engineering and suggests the modality's potential to address the scalability constraints inherent in traditional *ex vivo* cell therapies.

Clinical advantages of CAR-T cell therapy

CAR-T cell therapy offers the following advantages over other types of cellular immunotherapies:

- ***Avoid Accumulative Toxicity.*** CAR-T therapy is typically administered as a one-time or limited-duration treatment rather than through continuous or repeated dosing over extended periods. As a result, it avoids the prolonged dosing-related drug exposure commonly associated with chronic treatment paradigms, thereby reducing the risk of cumulative toxicity. Treatment-related side effects observed to date remain generally manageable and do not appear to worsen with continued follow-up.

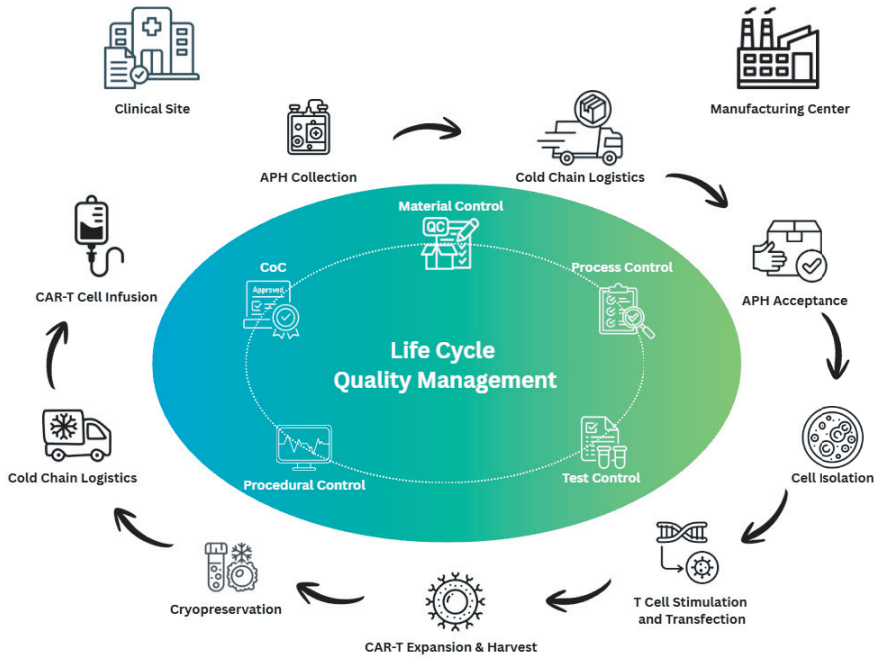
- ***In vivo expansion and long-term durability as a living drug.*** CAR-T therapies are uniquely characterized by their ability to undergo robust *in vivo* expansion and long-term persistence following a single administration. The incorporation of co-stimulatory domains such as CD28 or 4-1BB promotes sustained T-cell proliferation, functional persistence, and the development of memory-like T-cell subsets. These features enable durable anti-tumor activity and prolonged immune surveillance, distinguishing CAR-T therapy from conventional cytotoxic or targeted treatments that rely on continuous drug exposure to maintain efficacy.

- ***Low immune escape.*** CAR-T cells operate independently of MHC recognition requirements, effectively neutralizing the common tumor escape strategy of MHC-I downregulation that often limits conventional T cell therapies, such as TCR-T and TIL.

Ex vivo CAR-T cell manufacturing process

The *ex vivo* CAR-T cell manufacturing process typically involves the collection of leukapheresis material at the clinical site and its transport to the manufacturing facility under controlled cold-chain conditions. Upon receipt, manufacturing activities are initiated, including T-cell isolation and activation, genetic modification via viral transduction, and subsequent cell expansion. Once the target cell dose is achieved, the cell product is harvested, formulated, filled, and cryopreserved. In-process control testing is conducted throughout manufacturing in accordance with predefined SOPs to ensure process consistency and product quality. Following manufacturing completion, lot-release testing is performed based on established quality specifications, covering key attributes such as identity, viability, purity, potency, sterility, endotoxin, mycoplasma, and vector-related parameters. Product release is subject to quality assurance review of batch records, certificates of analysis, and related documentation. The cryopreserved CAR-T product is then transported back to the clinical site under liquid-nitrogen conditions using qualified cold-chain logistics providers. Overall manufacturing timelines may vary by patient; however, *ex vivo* CAR-T cell manufacturing is generally completed within approximately 2-3 weeks, with ongoing advances expected to further shorten manufacturing, testing and release timelines.

The following diagram illustrates the *ex vivo* CAR-T cell manufacturing process:



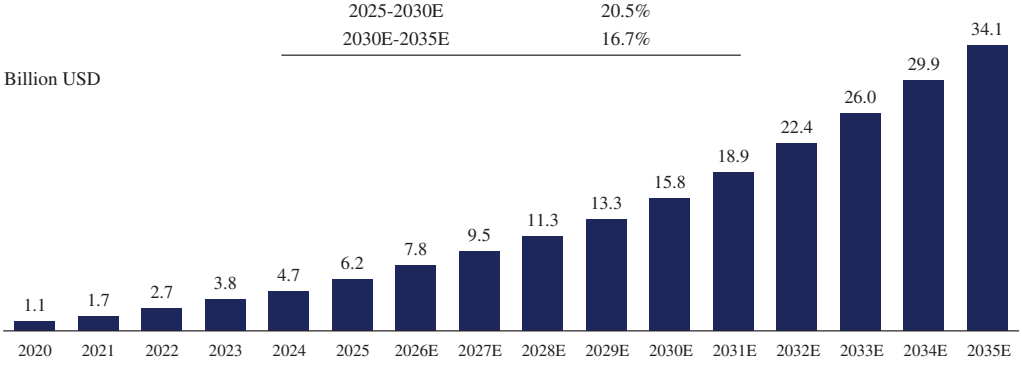
Source: Literature Review, Frost & Sullivan Analysis

Market size of the global and China CAR-T cell therapy markets

The following graphs show historical and forecasted size of the global market and China's market, respectively, for CAR-T cell therapies from 2020 through 2025 and from 2026 through 2035:

Global CAR-T Therapy Market, 2020-2035E

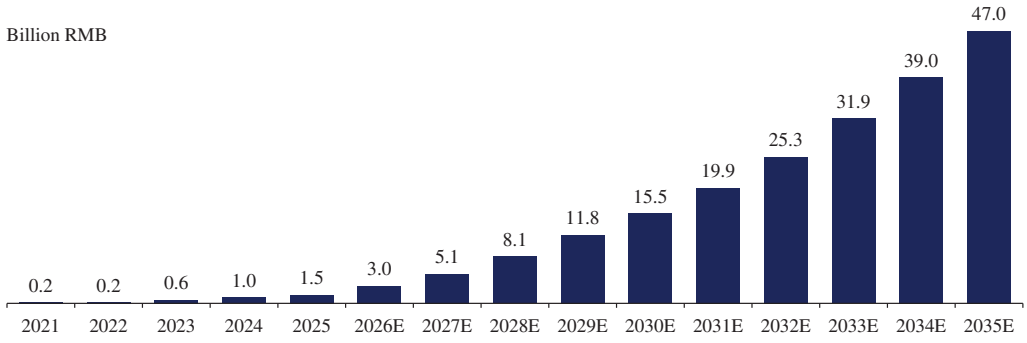
Period	CAGR
2020-2025	41.8%
2025-2030E	20.5%
2030E-2035E	16.7%



Source: Company Annual Reports, Public Information, Frost & Sullivan Analysis

China CAR-T Therapy Market, 2021-2035E

Period	CAGR
2021-2025	78.6%
2025-2030E	58.7%
2030E-2035E	24.8%



Source: Company Annual Reports, Public Information, Frost & Sullivan Analysis

Growth drivers and future trends for the CAR-T cell therapy market

The principal growth drivers and future trends for the CAR-T cell therapy market include the following:

- ***Broadening Therapeutic Applications and Clinical Validation.*** CAR-T therapy is expanding significantly beyond hematologic malignancies into solid tumors and autoimmune diseases. While demonstrating remarkable efficacy in blood cancers, researchers are developing innovative approaches to overcome challenges for treating solid tumors. The therapy also shows promise in autoimmune conditions, where engineered T cells enable targeted immune modulation. This therapeutic expansion substantially broadens the potential patient population and represents a major growth opportunity.

- ***Technology Innovation and Next-Gen Platforms.*** The CAR-T field is evolving through both traditional enhancements and novel platforms. Next-generation CAR designs, including advanced gene editing, continue to improve targeting precision and safety. *In vivo* CAR-T platforms are emerging as a promising approach, using viral and non-viral delivery systems to reprogram T cells directly within patients. These are complemented by multi-target strategies and integrated safety switches, addressing key challenges in relapse prevention and toxicity management while expanding CAR-T's therapeutic potential.

- ***Manufacturing Evolution and Cost Control.*** CAR-T manufacturing is transforming to address cost and scalability challenges. While traditional autologous processes require 2 to 3 weeks with substantial costs, *in vivo* CAR-T approaches offer potential for more standardized, off-the-shelf administration. Process automation through closed-system bioreactors and AI-driven optimization enhances manufacturing consistency and scalability. These advancements are crucial for improving the economic sustainability of CAR-T therapies while maintaining product quality and expanding patient access.

- ***Rising Unmet Clinical Need in Relapsed and Refractory Patients.*** Despite advances in chemotherapy, targeted therapy, and immunotherapy, a substantial proportion of patients with relapsed or refractory malignancies continue to face limited treatment options and poor outcomes. CAR-T therapy has demonstrated differentiated clinical value in these

high-unmet-need populations by delivering deep and durable responses where conventional therapies fail. The growing prevalence of refractory disease across both hematologic and selected solid tumor indications provides a strong demand-side driver for sustained CAR-T market expansion.

- ***Market Access & Commercial Development.*** Since 2017, China's NMPA and CDE have established a regulatory framework for cell therapy products centered on "pharmaceutical management", issuing multiple core guidelines emphasizing the scientific validation of product quality, safety, and efficacy throughout the entire product life cycle, and requiring that manufacturing activities be conducted in compliance with Good Manufacturing Practice (GMP) standards. To accelerate patient access to innovative therapies, China has established regulatory mechanisms such as the Breakthrough Therapy Designation and Priority Review Program. Products that meet the conditions can also be approved for marketing through the Conditional Approval Pathway, based on definite early clinical data to be approved in advance, so as to more quickly meet the clinical needs of serious life-threatening diseases. Furthermore, commercial health insurance (CHI) is increasingly vital in enhancing the affordability of these treatments. The integration of 5 marketed CAR-T products into the Innovative Drug Catalogue for Commercial Health Insurance 《商業健康保險創新藥目錄》 marks a transition toward a more sustainable, multi-tiered reimbursement model, significantly broadening patient access beyond traditional basic medical insurance.

CAR-T CELL THERAPIES FOR GASTRIC CANCER

Overview of Gastric Cancer

Gastric cancer is a malignant disease arising from the gastric mucosa, primarily manifesting as adenocarcinoma derived from the glandular epithelium. The disease disseminates via lymphatic, hematogenous, or transcoelomic pathways, with distant spread most frequently involving the liver, peritoneum, and regional lymph nodes, and less frequently the lungs and bones. The pathogenesis of gastric cancer typically follows a sequential, multi-step progression over several years. Early-stage disease is frequently asymptomatic or presents with non-specific gastrointestinal symptoms, such as epigastric discomfort, nausea, and loss of appetite, which often contributes to diagnostic delays. In contrast, advanced-stage disease is characterized by alarm symptoms, including dysphagia, cachexia, and jaundice, reflecting extensive local invasion or distant metastatic involvement.

Gastric cancer is one of the leading causes of cancer deaths in the world, which has the nature of fast progression and metastasis. The absence of specific symptoms in early-stage disease frequently results in diagnosis at locally advanced or metastatic stages. In terms of incidence in 2025, gastric cancer was among the top five most common cancers globally and in China, reflecting its widespread occurrence and substantial patient base. China represents one of the highest-burden regions for gastric cancer globally, accounting for nearly 40% of newly diagnosed gastric cancer cases worldwide in 2025. Although early-stage gastric cancer could be treated by surgery, the onset of gastric cancer is imperceptible which means that the majority of cases of gastric cancer are diagnosed at a late stage. Late-stage gastric cancer patients usually have poor prognosis with high mortality within one year resulting from stomach dysfunction and other organs being invaded by tumor cells. In China, approximately 79% of gastric cancer patients are diagnosed at a locally advanced or advanced stage. Among patients who experience disease recurrence after surgery, early tumor recurrence, defined as recurrence occurring within 2 years after surgery, accounts for approximately 60-70% of recurrence events, contributing to poor long-term clinical outcomes. As a result, the age-standardized five-year relative survival rate for gastric cancer in China remains low at approximately 5-20%. The broad geographic distribution and large affected population position gastric cancer as a major oncologic indication with significant unmet clinical needs.

Incidence of Gastric Cancer

The annual incidence of gastric cancer worldwide increased from 917.5 thousand in 2020 to 1,036.8 thousand in 2025, representing a CAGR of 2.5%. It is expected to increase to 1,189.7 thousand in 2030, representing a CAGR of 2.8% from 2025 to 2030, and further increase to 1,351.4 thousand in 2035, representing a CAGR of 2.6% from 2030 to 2035.

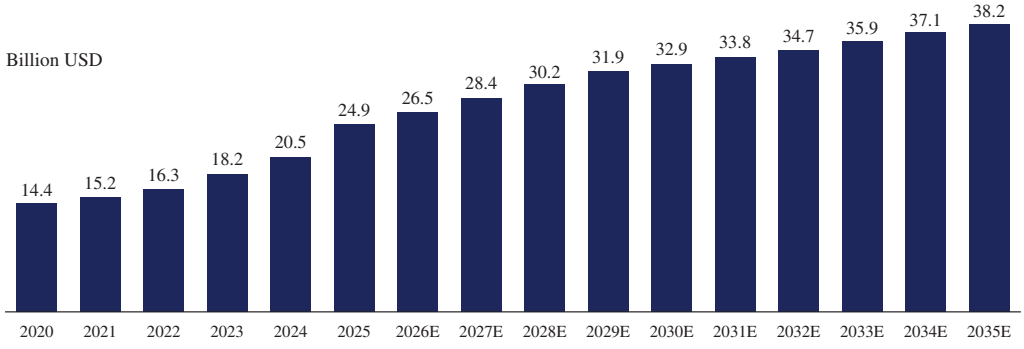
The annual incidence of gastric cancer in China increased from 338.8 thousand in 2020 to 383.1 thousand in 2025, representing a CAGR of 2.5%. It is expected to increase to 442.8 thousand in 2030, representing a CAGR of 2.9% from 2025 to 2030, and further increase to 502.6 thousand in 2035, representing a CAGR of 2.6% from 2030 to 2035.

Market size of gastric cancer drug market

The following graph presents data concerning the historical and forecasted size of the global market for gastric cancer drugs globally:

Historical and Forecasted of Global Gastric Cancer Drug Market Size, 2020-2035E

Period	CAGR
2020-2025	11.6%
2025-2030E	5.7%
2030E-2035E	3.0%

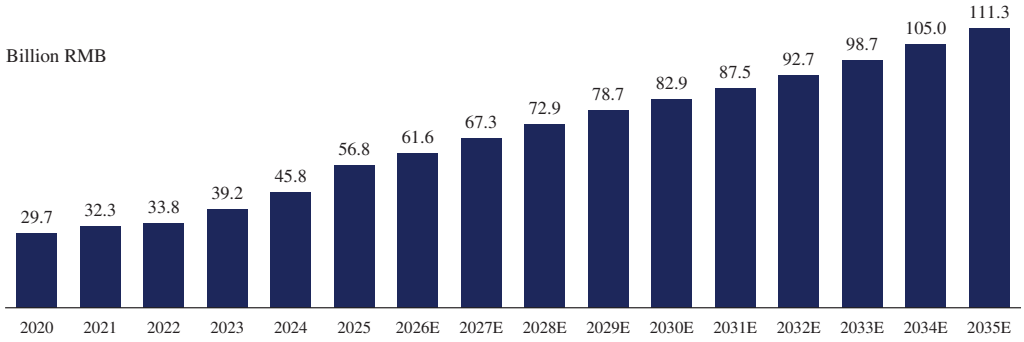


Source: Public Information, Frost & Sullivan Analysis

The following graph presents data concerning the historical and forecasted size of the market for gastric cancer drugs in China:

Historical and Forecasted of China Gastric Cancer Drug Market Size, 2020-2035E

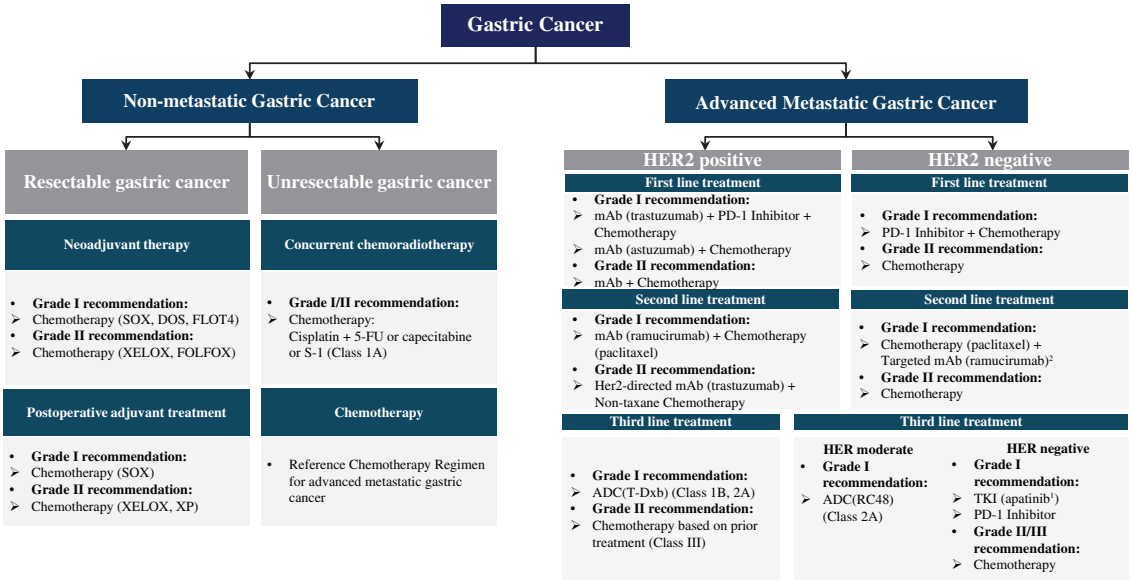
Period	CAGR
2020-2025	13.8%
2025-2030E	7.8%
2030E-2035E	6.1%



Source: Public Information, Frost & Sullivan Analysis

Treatment Paradigm for Gastric Cancer

The following chart illustrates the 2025 CSCO paradigm for gastric cancer treatment:



Source: 2025 CSCO, Frost & Sullivan Analysis

Note: Treatment options beyond first-line therapy for advanced gastric cancer under the current standard of care demonstrate limited clinical efficacy in later-line settings. For example, apatinib[1], one of the few agents approved for third-line treatment of HER2-negative gastric cancer in China, has reported an objective response rate of approximately 3%, with median progression-free survival of around 2-3 months.

In the second-line treatment of advanced gastric cancer, ramucirumab plus paclitaxel represents a commonly used regimen, including in patients with HER2-negative gastric cancer. In the global phase III RAINBOW study, this combination achieved an objective response rate of approximately 28%, with a median progression-free survival of

4.4 months and a median overall survival of 9.6 months. In advanced gastric cancer, median overall survival varies by line of therapy, with approximately 12 to 18 months in the first-line setting, 7 to 11 months in the second-line setting, and less than six months in later lines of treatment.

Unmet Clinical Needs in Current Therapies for Gastric Cancer

The limitations of the current therapies for gastric cancer are:

- ***Lack of Effective Therapeutic Strategies.*** Most patients present with advanced-stage disease at diagnosis, rendering them ineligible for surgery. Conventional treatment modalities, including radiation therapy and cytotoxic chemotherapy, have demonstrated limited efficacy due to inherent challenges such as radio resistance, chemoresistance, and the high proportion of unresectable tumors. These limitations underscore the urgent need for novel therapeutic strategies to improve patient outcomes. Although immunotherapies and targeted medicines have shown great promise, resistance mechanisms, and lack of suitability for various patient populations make it difficult to incorporate them into clinical practice.

- ***Challenges in Patient Stratification and Treatment Personalization.*** Although molecular profiling and biomarker-guided treatment strategies are increasingly incorporated into gastric cancer management, their clinical impact remains limited, as actionable biomarker-defined subgroups represent only a fraction of the overall patient population. In addition, tumor heterogeneity and variability in biomarker expression, together with differences in testing practices, further constrain consistent patient selection for targeted or immunotherapy approaches. As a result, a substantial proportion of patients continue to receive broadly applied chemotherapy-based regimens rather than personalized treatments, underscoring the persistent unmet need for therapeutic strategies capable of benefiting a broader gastric cancer population through more effective and widely applicable targeting approaches.

Comparison of Second- or Later-Line Treatments for Gastric Cancer

The following tables provide information concerning approved second- or later-line treatments and clinical stage product candidates for gastric cancer:

Examples of Marketed Therapies for Gastric Cancer in China and the US:

Type of Treatment	Treatment Option	Approval Date	Indication & Line of Treatment	Clinical Trial		Price	Annual Sales	Treatment Schedule
				Safety	Efficacy			
Small molecule drug: TKI	**Apatinib** Monotherapy	2014.12	• Advanced GC or GEJ • HER negative third line	NCT01512745: (phase III, n=267) (CTR20160019)		Prior to reimbursement: RMB 150 per 250mg; After reimbursement: RMB 105 per 250mg	~1 billion RMB	Recurrent: Once daily 850mg for 28-day cycle
				AE≥3: NM Neutropenia: 5.7%	mPFS: 2.6m ORR: 2.8% mOS:6.5m Disease Control Rate:42.1%			
Chemotherapy	**TAS-102 (Trifluridine/ Tiriracil)** Monotherapy	2019.02	• Advanced GC or GEJ • Third line or later line	TAGS (NCT02500043): (Phase III, n=507)		~$75 per tablet (Trifluridine:15mg/Tipiracil: 6mg)	~700M USD in 2024 (for all indications)	Recurrent: 35 mg/m² twice daily (days 1-5 and days 8-12 of each 28-day cycle)
				AE≥3: 80% Treatment related death: <1%	mOS: 5.7m mPFS:2m DCR: 44.0% ORR:4.0%			

Comparison of Third-line Treatments for Gastric Cancer:

Type	Line of Treatment	Representative Treatment	Strength	Example of Marketed Therapy	Limitation
Chemotherapy	Third-line treatment	• Paclitaxel • Irinotecan,etc	• Systematic reach	• TAS-102 (Trifluridine/ Tipiracil) Monotherapy • Approval date: 2019.02 • Indication: Third line or later line Advanced GC or GEJ • Clinical trial results: (NCT02500043): (Phase III, n=507) ➢ Efficacy: ORR:4.0%; mOS: 5.7m; mPFS:2m ➢ Safety: AE≥3: 80% • Price: ~$75 per tablet • Annual sales: ~750M USD in 2024 • Treatment schedule: Recurrent: 35 mg/m² twice daily	• Requires careful assessment of patients' overall fitness, including performance status, comorbidities, and complications • High toxicity (high rate of Grade ≥3 AEs) • Lacks selectivity and limited efficacy
TKI		• Apatinib	• Oral administration	• Apatinib Monotherapy • Approval date: 2014.12 • Indication: Third line Advanced GC or GEJ • Clinical trial results: NCT01512745: (phase III, n=267) ➢ Efficacy: mPFS : 2.6m; ORR: 2.8%; mOS:6.5m ➢ Safety: AE≥3:NM; Neutropenia: 5.7% • Price: 105 RMB-150 RMB per 250mg • Annual sales: ~1 billion RMB in 2025 • Treatment schedule: Recurrent: Once daily 850mg for 28 -day cycle	• The efficacy is quite limited (ORR 2.8%), with high toxicity rate such as hand-foot syndrome (16%-43%) • Gastric cancer cells can develop resistance to TKIs through gene mutations and reactivation or bypass of signaling pathways, limiting long -term efficacy.
CAR-T		• Satricabtagene Autoleucel (CT041)	• One to three infusions at the recommended dose • Significant efficacy	• CT041 Monotherapy • Approval date: 2026.06 • Indication: Advanced GC or GEJ CLDN18.2 positive third line • Clinical trial results: CT041-ST-01 (ITT n=156, mITT n=136) ➢ Efficacy: mPFS: 3.25m; mOS:7.92m; ORR:30% ➢ Safety: ≥G3 TEAE:99% • Price: 0.99 million per patient	• High treatment cost • Safety concerns: Grade ≥3 TEAEs occurred in 99% of patients, primarily comprising hematologic toxicities
PD-1 inhibitor		• Nivolumab	• Relatively low and manageable incidence of adverse reactions	• Nivolumab Monotherapy • Approval date: 2018.06 • Indication: Third-line or later treatment of advanced GC or GEJ • Clinical trial results: ATTRACTION-2 (NCT02267343): (Phase III, n=493) ➢ Efficacy: mPFS:1.61m; mOS:5.26m; ORR:11.2% ➢ Safety: G3 TRAE: 10.3% • Price: 40 mg/4 mL 4500 RMB/vial • Treatment schedule: 3 mg/kg or 240 mg every two weeks	• Limited eligible patient population (restricted to patients who have not received a PD-1 inhibitor in either prior first- or second-line treatment)

Source: NMPA, Literature review, Frost & Sullivan Analysis

Clinical Data of Clinical Stage Candidates:

Type of Treatment	Treatment Option	Line of treatment	Indication	Clinical Trial		Treatment Schedule
				Safety	Efficacy	
CLDN18.2/4-1BB **bispecific antibody (BsAb)**	Givastomig	Second or later line	• CLDN18.2-positive advanced GC/GEJ	NCT04900818: (phase I, n=55)		Dose-escalation: 0.1, 0.3, 1, 3, 5, 8, 12, 15 mg/kg Q2W (every 2 weeks) Dose expansion: 5, 8, 12, 15 mg/kg
				AE≥3: 18.2%	ORR: 15.0% DCR: 40.0%	
CLDN18.2-targeted **antibody-drug conjugate (ADC)**	CMG901	Second or later line	• CLDN18.2-positive advanced GC/GEJ	KYM901: (phase I, n=134)		Dose-escalation: 0.3-3.4 mg/kg Q3W Dose-expansion: 2.2-3.0 mg/kg Q3W Recommended phase 2 dose: 2.2 mg/kg
				AE≥3: 68% MTD not reached, 1 treatment-related death	ORR: 29%	

• Early-stage clinical development of CMG901, including the Phase I study, was conducted by Keymed and its joint venture KYM Biosciences. Following the global licensing agreement in 2023, AstraZeneca assumed responsibility for further clinical development. Phase III studies are currently ongoing, with no mature clinical data disclosed to date.

Source: Clinical Trial, Literature Review, Frost & Sullivan Analysis

Tumor-associated antigens for treatment of gastric cancer

Claudin-18.2 (CLDN18.2)

Targeted and immunotherapy approaches have progressively reshaped the treatment landscape of gastric cancer, with HER2 and immune checkpoint pathways representing the most established therapeutic targets in current clinical practice. HER2 overexpression, observed in a subset of gastric cancer patients, has enabled the development of HER2-directed monoclonal antibodies and antibody-drug conjugates that are now incorporated into treatment regimens for selected patients. However, HER2 overexpression is detected in fewer than 20% of gastric cancer cases, limiting the applicability of HER2-targeted therapies to a relatively small patient population. In parallel, immune checkpoint inhibition targeting the PD-1/PD-L1 axis has expanded treatment options, particularly in advanced disease settings, often in combination with chemotherapy to enhance response rates. However, objective response rates to PD-1/PD-L1 inhibitors in gastric cancer remain low, limiting the proportion of patients who achieve durable clinical benefit.

Moreover, the proportion of patients eligible for these biomarker-guided therapies remains limited, and treatment outcomes remain heterogeneous due to variability in biomarker expression and tumor biology. Accordingly, increasing attention has turned toward additional tumor-associated antigens with broader expression profiles in gastric cancer, supporting the emergence of CLDN18.2 as a promising therapeutic target across multiple treatment modalities.

Mechanism and Biological Characteristics

CLDN18 is a member of the Claudin family and a component of tight junctions that regulate paracellular barrier function. The CLDN18 gene, located on chromosome 3q22.3, encodes the CLDN18 protein — a non-classical Claudin. Alternative splicing of the gene's first exon generates two distinct splice variants, which encode the tight junction proteins CLDN18.1 and CLDN18.2. These isoforms share high amino acid sequence similarity, differing only in 8 residues within the 51-amino-acid segment of the first extracellular loop. CLDN18.2 is observed in a large fraction of gastric cancers, with approximately 70-80% of patients exhibiting CLDN18.2 expression in tumor tissue.

In non-neoplastic tissues, CLDN18.1 is primarily expressed in normal alveolar epithelium, while CLDN18.2 is specifically expressed in gastric mucosal cells, where it helps maintain gastric barrier integrity. During malignant transformation, tight junction integrity is disrupted, leading to exposure of the CLDN18.2 epitope. Concurrently, CLDN18.2 becomes aberrantly activated and is stably and selectively overexpressed in certain tumor tissues, promoting tumor invasion and metastasis.

Clinical Application

CLDN18.2 has emerged as a major milestone in targeted therapy for gastric cancer. Recent studies show high CLDN18.2 expression in gastric cancer, and targeted therapy can significantly improve survival, offering another potential option for HER2-negative patients. In normal gastric mucosa, CLDN18.2 is specifically localized to tight junctions and plays a critical role in maintaining epithelial barrier integrity. During malignant transformation, disruption of tight junctions leads to aberrant surface exposure of the CLDN18.2 epitope, rendering it an attractive and highly specific therapeutic target.

Currently, a broad range of CLDN18.2-targeted therapeutic modalities have been developed globally, including monoclonal antibodies, bispecific antibodies and T-cell engagers (TCEs), antibody-drug conjugates (ADCs), and CAR-T cell therapies. Among these approaches, monoclonal antibodies represent the most clinically advanced modality to date. Zolbetuximab has demonstrated clinically meaningful benefit in CLDN18.2-positive advanced gastric cancer and has been approved in multiple regions, including the United States and China, in combination with chemotherapy for first-line treatment.

Beyond monoclonal antibodies, other CLDN18.2-targeted modalities are under active clinical investigation. Bispecific antibodies and TCEs are largely in mid-stage clinical development, while multiple CLDN18.2-directed ADCs, have progressed into registrational or late-stage studies as monotherapy for second- or later-line treatment of advanced gastric cancer. However, to date, no CLDN18.2-targeted ADC has received regulatory approval globally.

The high tumor specificity of CLDN18.2 also provides a strong biological rationale for CAR-T cell therapy. By enabling precise T-cell recognition of tumor cells, CLDN18.2-directed CAR-T therapies have demonstrated promising antitumor activity in early clinical studies and represent a potentially transformative treatment strategy for CLDN18.2-positive tumors, particularly gastric cancer, where durable responses remain an unmet clinical need.

Advantages of CLDN18.2 for Gastric Cancer

- ***Enrichment in Immunologically Hot Tumors: Translational Relevance in Immune-Active Settings.*** CLDN18.2 differentiates itself by exhibiting enriched expression in tumors with immunologically hot and immune-active phenotypes. Accumulating clinical and translational evidence indicates that CLDN18.2 expression is frequently observed and retained in immunologically hot tumors. This pattern suggests that CLDN18.2 expression is compatible with immune-active tumor microenvironments and that stable antigen presentation can coexist with immune infiltration.

- ***High Specificity of CLDN18.2 Expression.*** CLDN18.2 is physiologically expressed in differentiated gastric mucosal epithelial cells. Outside of gastric tissue, CLDN18.2 shows little to no expression in most normal tissues and is notably absent from the gastric stem cell compartment. During malignant transformation, CLDN18.2 expression is retained in primary gastric cancer as well as metastatic lesions, and is also observed in tumor cells of selected gastrointestinal malignancies such as pancreatic cancer. This restricted expression pattern in normal tissues, together with tumor-associated expression in gastric and pancreatic cancers, underpins the high target specificity of CLDN18.2 and supports its clinical advantage as a selectively targetable antigen.

- ***High Prevalence of CLDN18.2 Expression.*** In gastric cancer and pancreatic cancer, CLDN18.2 is frequently expressed on tumor cells. In gastric cancer, approximately 70-80% of patients exhibit CLDN18.2 expression, indicating that the majority of gastric cancer cases are CLDN18.2-positive. In pancreatic cancer, CLDN18.2 expression has also been reported in a substantial proportion of patients, with around 60% showing moderate to strong expression. In comparison, an established target such as HER2 is expressed in a smaller subset of gastric cancer patients, which constrains eligibility for the corresponding targeted therapy. The tumor-enriched expression of CLDN18.2, together with its high prevalence in gastric cancer and pancreatic cancer, supports its clinical relevance as a therapeutic target across these indications.

EpCAM

Mechanism and Biological Characteristics

EpCAM (epithelial cell adhesion molecule), also known as CD326, is a type I transmembrane glycoprotein expressed on epithelial cells and originally described as a cell adhesion — related molecule. Structurally, EpCAM consists of an extracellular domain (EpEX), a single transmembrane region, and a short intracellular domain (EpICD), enabling it to function not only as a surface adhesion molecule but also as a signaling component.

In normal epithelial tissues, EpCAM expression is tightly regulated, contributing to epithelial organization and barrier integrity. During malignant transformation, EpCAM expression is aberrantly upregulated, and its intracellular fragment (EpICD) translocates to the nucleus, where it participates in transcriptional regulation. This dysregulation promotes tumor cell proliferation, stemness, invasion, and metastasis. Recent studies have shown that EpCAM is expressed at detectable levels in over 90% of gastric cancer cases. As a result, EpCAM is stably overexpressed in a wide range of epithelial cancers, establishing its role as a tumor-associated antigen.

Circulating tumor cells (CTCs), which are released from primary tumors into the bloodstream, play a critical role in cancer dissemination and are widely recognized as indicators of metastatic progression and disease recurrence across multiple solid tumor types. The molecular characteristics of CTCs often differ from those of primary tumors, including variability or reduction in certain therapeutic target expressions, which presents challenges for sustained treatment efficacy. Among epithelial-derived malignancies, EpCAM has been extensively utilized as a biomarker for the detection and characterization of CTCs, owing to its broad expression in epithelial tumor cells and its association with metastatic disease burden. The frequent detection of EpCAM-positive tumor cells in circulation and metastatic sites highlights its clinical relevance as both a biomarker of tumor dissemination and a potential therapeutic target in solid tumors.

Clinical Application

EpCAM is frequently upregulated in gastric cancer compared to normal gastric mucosa, where baseline expression is typically low or absent, indicating widespread overexpression in tumor tissues relative to non-cancerous gastric mucosa. EpCAM has been explored as an oncology target for several decades, and multiple therapeutic formats have been developed globally, including monoclonal antibodies, bispecific antibodies, and cellular therapies. Among these approaches, EpCAM-CD3 bispecific antibodies represent the most clinically advanced modality to date. Catumaxomab, a trifunctional EpCAM-CD3 antibody, received regulatory approval in Europe in 2009 for the treatment of malignant ascites in patients with EpCAM-positive tumors, where it demonstrated clinical benefit in prolonging the interval between ascites drainage procedures. Although catumaxomab was later withdrawn from the market for commercial reasons, it provided early clinical proof-of-concept for EpCAM-directed T-cell redirection.

While EpCAM-targeted antibodies and T-cell engagers (TCEs) have demonstrated preliminary biological activity and clinical efficacy, their therapeutic utility has remained limited. To date, regulatory approval has been restricted to the intraperitoneal treatment of malignant ascites, with no evidence of durable clinical benefit in the systemic treatment of solid tumors. In addition, transient responses, systemic toxicities, and sub-optimal delivery mechanisms further constrain their broader clinical applicability. Consequently, these limitations support the development of EpCAM-directed CAR-T cell therapies as a potentially more potent modality capable of achieving deeper and more sustained anti-tumor responses in gastric cancer.

EpCAM has the following advantages as a tumor-associated antigen for treatment of gastric cancer:

- ***EpCAM as a CTC Biomarker in Epithelial-Derived Malignancies.*** Early systemic dissemination in epithelial-derived malignancies is closely associated with the presence of circulating tumor cells (CTCs), which are widely implicated in metastatic progression and disease recurrence. EpCAM is extensively utilized as a biomarker for CTC identification due to its frequent and stable expression on circulating tumor cells across epithelial cancers. Clinical evidence from gastrointestinal malignancies, such as gastric cancer, demonstrates that the detection of EpCAM-positive CTCs correlates with tumor burden, advanced disease stage, and unfavorable clinical outcomes. These observations support the clinical relevance of EpCAM in tumor dissemination and underscore its value as a disease-associated target in epithelial-derived solid tumors.

- ***Relevance of EpCAM Targeting in Metastatic Tumor Lesions.*** EpCAM is retained in tumor cells disseminating within serosal and cavity-associated microenvironments. Tumor cells involved in locoregional spread and surface dissemination commonly preserve epithelial phenotypes, as a result, EpCAM is highly expressed in the metastatic tumor lesions. The consistent presence of EpCAM supports its translational relevance as a therapeutic target in advanced disease settings characterized by tumor spread beyond the primary site, independent of specific tumor origin or treatment modality.

- ***High Prevalence of EpCAM Expression Supports Broad Applicability.*** EpCAM is widely expressed across epithelial-derived malignancies and is consistently reported at significantly higher levels in malignant tissues compared with adjacent non-neoplastic counterparts. EpCAM is expressed in >80% of epithelial tumors (e.g., gastric, colorectal, ovarian and breast cancers, among others). For example, EpCAM is expressed at detectable levels in over 90% of gastric cancer patients, over 97% of colorectal cancer (CRC) patients, approximately 73% of ovarian cancer patients, and 62% of triple-negative breast cancer (TNBC) patients. This relatively high and widespread expression profile underpins EpCAM as a broadly applicable therapeutic target across solid tumors.

Global Competitive landscape for CLDN18.2 and EpCAM-Targeted CAR-T Therapies in Gastric Cancer and Others

CLDN18.2

As of the Latest Practicable Date, aside from one CLDN18.2-targeted CAR-T therapy for gastric cancer that has recently been approved for marketing in China, no CLDN18.2-directed CAR-T therapy has been successfully commercialized or approved for market entry worldwide. The following tables provide information concerning the global competitive landscape for CLDN18.2-targeted CAR-T therapies in gastric cancer and others:

Global Clinical-Stage CLDN18.2-Targeted CAR-T Therapies for Gastric Cancer and Others

Global Marketed CLDN18.2-Targeted CAR-T Therapy

Registration Number	Manufacturer	Brand Name	Target	First Approval Date	Marketed Region	Approved Indication
国药准字S20260044	CARsgen	Satricabtagene Autoleucel (CT041)	CLDN-18.2	2026-06-17	China	≥3L advanced G/GEJ adenocarcinoma

Source: NMPA, Frost & Sullivan Analysis

Global Clinical-Staged CLDN18.2-Targeted CAR-T Therapies

Trial/IND Number	Manufacturer	Phase	Generic Name/Code	Target	First Posted Date	Region	Indication
CTR20252202	Immunofoco	III	IMC002	CLDN-18.2	2025-06-18	China (Phase III) US (IND approval from FDA)	GC/GEJ, PC, and other digestive system malignancies
CTR20201940	CARsgen	Ib/II	CT041		2020-10-09	China, US, Canada	PC and other digestive system malignancies
NCT05539430	Legend Biotech	I	LB1908		2022-09-14	US	GC/GEJ and PC
CXSL2400524	Huadao	IND (NMPA)	HD004		2024-08-08	China	Advanced Solid Tumors with Malignant Ascites
CXSL2400479	OriCell Therapeutics	IND (NMPA)	OriC613	MSLN, CLDN-18.2	2024-07-25	China	Advanced Solid Tumors

Source: Clinical Trial, CDE, NMPA, Frost & Sullivan Analysis

EpCAM

The global development of EpCAM-targeted CAR-T therapies remains at an early stage. Although a limited number of EpCAM-directed CAR-T programs have entered early-stage clinical evaluation, no EpCAM-targeted CAR-T therapy has been commercialized to date.

Globally, Immunofoco is currently the only company with a publicly disclosed EpCAM-targeted CAR-T program that has obtained regulatory clearance for clinical development in epithelial-derived solid tumors. Its lead candidate, IMC001, received Investigational New Drug (IND) approvals from both the FDA and China's NMPA in February 2024, covering gastric cancer (GC), gastroesophageal junction adenocarcinoma (GEJ adenocarcinoma), and pancreatic cancer (PC).

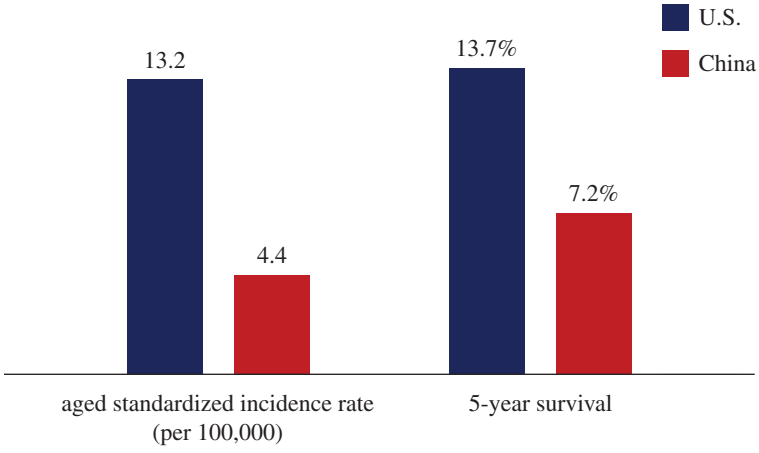
Building on the dual IND approvals, IMC001 further obtained NMPA authorization in March 2025 to initiate a Phase I/IIa basket clinical trial targeting EpCAM-positive, epithelial-derived solid tumors. This study represents the first and, to date, the only EpCAM-targeted CAR-T program globally to receive regulatory approval for clinical evaluation under a basket trial design in this indication, positioning IMC001 at the forefront of EpCAM-directed CAR-T development in gastric cancer.

CAR-T CELL THERAPIES FOR PANCREATIC CANCER

Overview of Pancreatic Cancer

Pancreatic cancer is caused by the abnormal and uncontrolled growth of cells in the pancreas, a large gland that forms part of the digestive system. Pancreatic cancer can be divided into exocrine tumors and endocrine tumors. Most of the pancreas is made of exocrine cells, and most tumors affecting these cells are called adenocarcinomas. Endocrine tumors are less common and are most often benign. Though rare, cancer stemming from a pancreatic endocrine tumor affects the hormone-producing cells. Pancreatic cancer is associated with extremely poor long-term outcomes in both China and the United States. Five-year survival rates remain low, at approximately 13.7% in the U.S. and 7.2% in China, reflecting the aggressive nature of the disease and the limited curative potential of current treatment options. The following chart provides information concerning the age-standardized incidence rate and the five-year survival rate for pancreatic cancer in China and the United States.

ASIR and 5-Year Survival of Pancreatic Cancer in China and U.S.



Source: Literature Review, The Surveillance, Epidemiology, and End Results (SEER) Program, Frost & Sullivan Analysis

Incidence of Pancreatic Cancer

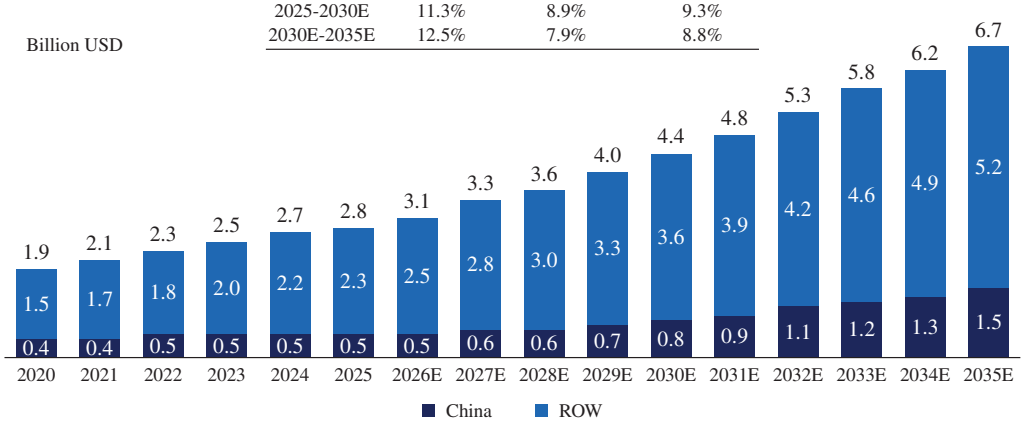
The annual incidence of pancreatic cancer worldwide increased from 495.8 thousand in 2020 to 549.0 thousand in 2025, representing a CAGR of 2.1%. It is expected to increase to 634.3 thousand in 2030, representing a CAGR of 2.9% from 2025 to 2030, and it is expected to further increase to 726.7 thousand in 2035, representing a CAGR of 2.8% from 2030 to 2035. The annual incidence of pancreatic cancer in China increased from 111.8 thousand in 2020 to 127.7 thousand in 2025, representing a CAGR of 2.7%. It is expected to increase to 148.9 thousand in 2030, representing a CAGR of 3.1% from 2025 to 2030, and it is expected to further increase to 170.2 thousand in 2035, representing a CAGR of 2.7% from 2030 to 2035.

Market size of pancreatic cancer drug market

The following graph presents data concerning the historical and forecasted size of the market for pancreatic cancer drugs globally and in China:

Global and China Pancreatic Cancer Drug Market Size, 2020-2035E

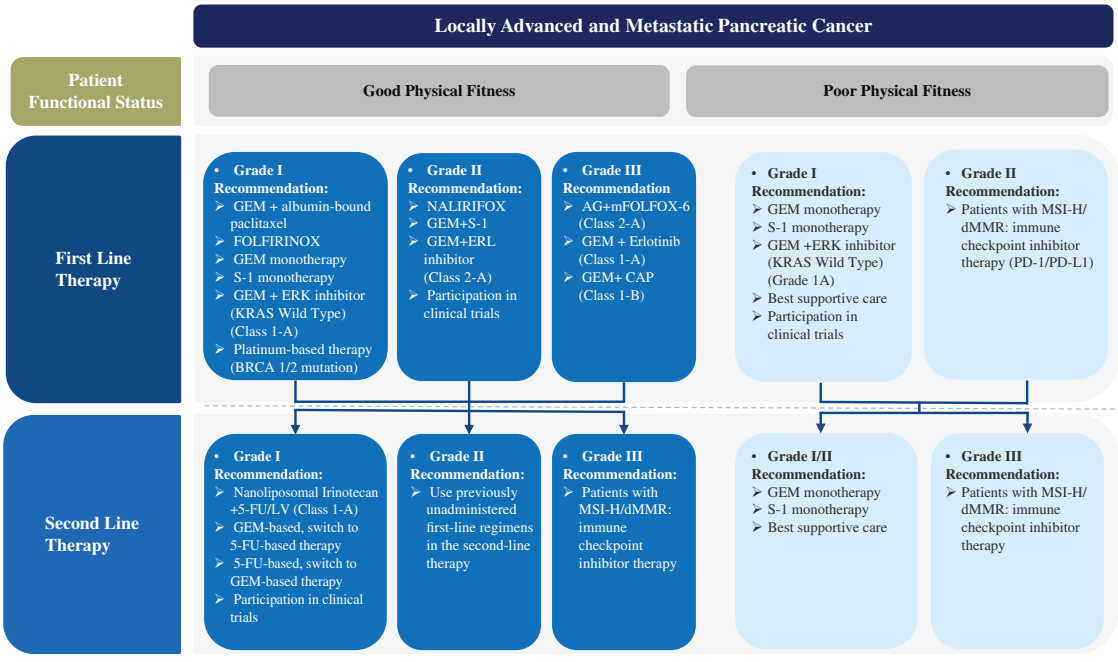
Period	CAGR		
	China	ROW	Global
2020-2025	4.6%	8.5%	7.8%
2025-2030E	11.3%	8.9%	9.3%
2030E-2035E	12.5%	7.9%	8.8%



Source: Public Information, Frost & Sullivan Analysis

Treatment Paradigm for Pancreatic Cancer

The following chart illustrates the 2024 CSCO paradigm for pancreatic cancer treatment:



Source: 2024 CSCO, Frost & Sullivan Analysis

For patients with unresectable locally advanced or metastatic pancreatic cancer, current treatment strategies rely predominantly on systemic chemotherapy, with overall limited response rates, substantial therapeutic challenges, and poor prognosis. In China, commonly used cytotoxic agents include gemcitabine, albumin-bound paclitaxel, 5-fluorouracil with leucovorin (5-FU/LV), platinum compounds, irinotecan, S-1, and capecitabine. Several targeted therapies besides erlotinib have been assessed in combination with gemcitabine, but none has been shown to significantly impact outcomes.

For first-line treatment, patients with good physical fitness are typically treated with combination regimens such as gemcitabine plus albumin-bound paclitaxel (AG) or FOLFIRINOX, as well as gemcitabine or S-1 monotherapy in selected cases. Patients with poor physical fitness generally receive gemcitabine (GEM) or S-1 monotherapy, with gemcitabine plus nimotuzumab considered in KRAS wild-type disease. Across first-line regimens, reported outcomes include an objective response rate (ORR) of approximately 23%-43%, a median progression-free survival (mPFS) of 5.5-7.4 months, and a median overall survival (mOS) of 8.5-11.1 months.

Upon disease progression, second-line treatment options for patients with good physical fitness include liposomal irinotecan plus 5-FU/LV (NAPOLI-1 study), as well as gemcitabine- or 5-FU-based chemotherapy. For patients with poor physical fitness, GEM or fluoropyrimidine monotherapy is commonly used. Overall efficacy in the second-line setting remains modest, with ORR ranging from 12.8% to 16%, mPFS of 2.9-4.2 months, and mOS of 3.3-7.4 months.

Overall, the current treatment paradigm for pancreatic cancer is dominated by chemotherapy, with limited effective targeted therapy options and persistently suboptimal long-term outcomes, underscoring a substantial unmet clinical need. In this case, AG-based chemotherapy followed by CAR-T cell therapy represents a potential therapeutic strategy. Chemotherapy may reduce tumor burden, disrupt the dense stromal barrier, and remodel the immunosuppressive tumor microenvironment, consequently facilitating CAR-T cell infiltration and activation. Sequential cellular therapy may further eradicate residual disease and promote durable immune responses, offering the potential for deeper and more sustained tumor control beyond what is achievable with chemotherapy alone.

Comparison of First- and Second-Line Treatments for Pancreatic Cancer

The following tables provide information concerning approved first- and second-line treatments and clinical stage product candidates for pancreatic cancer:

Examples of Marketed Therapies for Pancreatic Cancer in China and the US:

Type of Treatment	Treatment Option	Approval Date	Indication & Line of Treatment	Clinical Trial		Price	Annual Sales	Treatment Schedule
				Safety	Efficacy			
Combination Chemotherapy	**FOLFIRINOX** vs Gemcitabine (G group)	Around 2010s	• Locally advanced or Metastatic pancreatic cancer • First-line	NCT00112658: (Phase II/III, n=342)		After reimbursement: Oxaliplatin: ~RMB50/50mg; Irinotecan: ~RMB30/40mg; 5-FU: ~RMB 5/ 250mg; LV: ~RMB 10/ 100mg	/	Recurrent: A two-week cycle
				AE related death: 0.6% AE≥3: NM Grade 3 Neutropenia: 45.7%	mOS: 11.1 months mDOR: 5.9m mPFS: 6.4m ORR: 31.6%			
Combination Chemotherapy	**NALIRI + 5-FU/LV** vs 5-FU/LV	2024.02	• Locally advanced or Metastatic pancreatic cancer • Second-line • Prior gemcitabine-based therapy	NCT01494506: (Phase III, n=417)		After reimbursement: RMB985 per 10ml	/	Recurrent: a biweekly schedule (every 2 weeks), within a 6-week treatment cycle
				AE≥3: NM Neutropenia: 27.0%	mOS: 6.1m mPFS: 3.7m			

Source: Clinical Trial, FDA, Frost & Sullivan Analysis

Comparison of First- and Second-line Treatments for Pancreatic Cancer:

Type	Line of Treatment	Representative Treatment	Strength	Example	Limitation
Chemotherapy (Monotherapy & Combination therapy)	First-line treatment Second-line treatment	FOLFIRINOX/ GEM+ Nab -P/S-1 etc.	• Highly effective for patients in good physical fitness • Combination chemotherapy demonstrates improved efficacy compared with chemotherapy monotherapy.	• **Approval Date:** Around 2010s • **NALIRI + 5-FU/LV** • **Indication:** Locally advanced or Metastatic pancreatic cancer • **Efficacy:** mOS: 6.1m; mPFS:3.7m • **Clinical trial:** NCT01494506: (Phase III, n=417) • **Price:** After reimbursement: RMB985 per 10ml • **Safety:** AE≥3:NM • **Treatment schedule:** a biweekly schedule, within a 6-week treatment cycle	• High toxicity • Serious side effects: e.g. hair loss • Efficacy remains limited
Targeted Therapy (Combination therapy with Chemotherapy)	First-line treatment	• Nimotuzumab (mAb) • Erlotinib (TKI)	• Promising strength in specific patient subgroups • Good response rates in patients with high tumor mutational burden	• **Approval Date:** 2008/01 • **Nimotuzumab + Gemcitabine** (NG group) • **Indication:** K–Ras wild-type locally metastatic pancreatic cancer • **Efficacy:** mOS:10.9m; mPFS:4.2m; ORR:7% • **Clinical trial:** NCT00795340 (Phase III, n=82) • **Price:** After reimbursement: ~RMB1200/50mg • **Safety:** AE≥3: 56.8% • **Treatment schedule:** Nimotuzumab 400mg weekly + Gemcitabine 28-day cycle	• Efficacy only present in a small percentage of patients • Efficacy remains limited
Immunotherapy (Immune checkpoint inhibitor)	First-line treatment	• PD-1/PD-L1 inhibitors	• Durable efficacy: long-lasting response • Specific Subgroup Benefit. A salvage option for refractory MSI-H markers	• **Approval Date:** 2018/07 • **Pembrolizumab** • **Indication:** Mismatch repair-deficient (dMMR) advanced solid tumors across 12 different cancer types • **Efficacy:** ORR:34.3%-53%; mOS:23.5m; mPFS:4.1m • **Clinical trial:** NCT01876511 (Phase II, n=86) • **Price:** After reimbursement: RMB18,000 per unit price • **Safety:** AE≥3:14.6% • **Treatment schedule:** Once every three weeks	• Response rates are limited and vary across patient subgroups • PC patients may be resistant to immunotherapy

Source: FDA, Clinical Trial, Literature Review, Frost & Sullivan Analysis

Clinical Data of Clinical-stage Candidates:

Type of Treatment	Treatment Option	Line of Treatment	Indication	Clinical Trial		Treatment Schedule
				Safety	Efficacy	
• CD3/CLDN-18.2 **bispecific antibody (BsAb)** • Chemotherapy	**QLS31905** + Chemotherapy[1]	• PC: First-line	• Previously untreated CLDN18.2-positive metastatic PC	CTR20252978: (Phase III, n=602)		Q3W (every 3 weeks) IV Administration on Day 1/Days 1 and 8
				AE≥3: Decreased lymphocyte count (21.5%)	ORR: 18.2% mOS: 4.2m mPFS: 9.5m	
• CLDN-18.2-targeted **antibody-drug conjugate (ADC)** • Chemotherapy	1. **AZD0901**+ Chemotherapy monotherapy[2] 2. AZD0901 in combination with different chemotherapy agents[4]	• PC: First-line		NCT06219941: (Phase II, n=224)		Intravenous Infusion
				Not disclosed		
• CD3/CLDN-18.2 **bispecific antibody (BsAb)** • Immunotherapy	**IBI389+** Immunotherapy[3]	• PC: Second-line	• Advanced solid tumors refractory to standard treatments (Including PC)	NCT05164458: (Early Phase I, n=121; PC=73)		Dose-escalation: 0.001 to 10 mg/kg Q3W (every 3 weeks) IV
				AE≥3: 35.5% CRS related AE: 59.5%	Not disclosed for PC	
• CLDN-18.2-targeted **antibody-drug conjugate (ADC)**	**IBI343**	• PC: Second-line	• Advanced pancreatic cancer refractory to standard treatment	NCT05458219: (Phase I/Ib, n=83)		Dose-escalation followed by dose-expansion 6-8 mg/kg, Q3W (every 3 weeks) IV
				AE≥3: 50.6% No TEAEs lead to death	CLDN18.2+pts: ORR: 22.7% mOS: 12.1m mPFS: 5.4m	
• Autologous CLDN18.2-targeted **CAR-T cell therapy**	**Satri-cel (CT041)**	• PC: Second-line	• CLDN18.2-Positive Relapsed/Refractory (R/R) pancreatic cancer or GC	NCT04404595: (Phase Ib/II, n=19)		Single infusion
				CRS≥3: 10.5% ICANS (Grade 1): 10.5%	PC group: ORR: 16.7% mDOR: 3.4m CBR[4]: 33.3%	

Note: 1. Gemcitabine Hydrochloride + Paclitaxel, 2. gemcitabine 3. Sintilimab

Source: Clinical Trial, Literature Review, Frost & Sullivan Analysis

Tumor-associated antigens for treatment of pancreatic cancer

Claudin-18.2

Claudin 18.2 (CLDN18.2) has emerged as a highly promising new therapeutic target in pancreatic ductal adenocarcinoma (PDAC). Studies show that CLDN18.2 is expressed in 50%-70% of pancreatic cancer patients, providing a strong rationale for its broad application in targeted therapy. For further information about the mechanism and biological characteristics of CLDN18.2, see "— CAR-T Cell Therapies for Gastric Cancer — Tumor-associated antigens for treatment of gastric cancer — CLDN18.2" above. The advantages of CLDN18.2 as a tumor-associated antigen for the treatment of pancreatic cancer are also discussed in the above section.

EpCAM

Epithelial cell adhesion molecule (EpCAM) is a transmembrane glycoprotein expressed in pancreatic ductal adenocarcinoma and other epithelial malignancies. Studies have shown that EpCAM is upregulated in pancreatic cancer tissues compared with non-malignant pancreatic tissue, supporting its classification as a tumor-associated antigen. As a cell-surface protein with relatively broad expression in tumor cells, EpCAM provides a biologically plausible target for antigen-directed therapeutic strategies, including immunotherapy, in pancreatic cancer. For further information about the mechanism and biological characteristics of EpCAM, see "— CAR-T Cell Therapies for Gastric Cancer — Tumor-associated antigens for treatment of gastric cancer — EpCAM" above. The advantages of EpCAM as a tumor-associated antigen for the treatment of pancreatic cancer are also discussed in the above section.

Global Competitive landscape for CLDN18.2 and EpCAM Targeted CAR-T Therapies in Pancreatic Cancer

As of the Latest Practicable Date, no CLDN18.2-targeted CAR-T therapy in pancreatic cancer has been successfully commercialized or approved for market entry worldwide. The following table provides information concerning the global competitive landscape for CLDN18.2-targeted CAR-T therapies in pancreatic cancer:

Global Clinical-Stage CLDN18.2-Targeted CAR-T Therapies for Pancreatic Cancer

Trial Number	Manufacturer	Phase	Generic Name/Code	Target	First Posted Date	Region	Indication
NCT04404595	CARsgen	I/II	CT041	CLDN-18.2	2020-05-26	US, Canada, China	PC
NCT05539430	Legend Biotech	I	LB1908	CLDN-18.2	2022-09-14	US	
NCT05946226 CTR20231880	Immunofoco	I/IIa	IMC002	CLDN-18.2	2023-06-27	US, China	

Source: Clinical Trial, CDE, Frost & Sullivan Analysis

The global development of EpCAM-targeted CAR-T therapies for pancreatic cancer remains at an early stage. Although a limited number of EpCAM-directed CAR-T programs have entered early-stage clinical evaluation, no EpCAM-targeted CAR-T therapy has been commercialized for pancreatic cancer to date. In mainland China, Immunofoco is currently the only company with a publicly disclosed EpCAM-targeted CAR-T program that has obtained regulatory clearance for clinical development in epithelial-derived solid tumors. Its lead candidate, IMC001, received Investigational New Drug (IND) approvals from both the FDA and China's NMPA in February 2024, covering gastric cancer (GC), gastroesophageal junction adenocarcinoma (GEJ adenocarcinoma), and pancreatic cancer (PC). The following table provides additional information in this respect:

Global Clinical-Staged EpCAM-Targeted CAR-T Therapy

Trial Number	Manufacturer	Phase	Generic Name/Code	Target	First Posted Date	Region	Indication
CTR20260059	Immunofoco	I/IIa	IMC001	EpCAM	2026-01-12	China US (IND approval from FDA)*	Epithelial Solid Tumors (Including GC/GEJ, TNBC, BTC, OC, CC, PC, and GEP-NETs)

* the indication approved by US was EpCAM-Positive Advanced Digestive System Tumors

Note:

1. GC/GEJ: Gastric Cancer/Gastroesophageal Junction Cancer, TNBC: Triple-negative Breast Cancer; BTC: Biliary Tract Cancer; OC: Ovarian Cancer; CC: Colorectal Cancer; PC: Pancreatic Cancer; GEP-NETs: Gastroenteropancreatic Neuroendocrine Tumors

Source: Clinical Trial, CDE, Frost & Sullivan Analysis

CAR-T CELL THERAPIES FOR OTHER EPITHELIAL-DERIVED TUMORS

EpCAM exhibits aberrant expression across multiple epithelial malignancies, reinforcing its relevance beyond pancreatic cancer. In particular, EpCAM dysregulation has been reported in multiple epithelial malignancies, including gastric and gastroesophageal junction (GEJ) adenocarcinoma, colorectal cancer, triple-negative breast cancer (TNBC), and ovarian cancer (OC). In these tumor types, EpCAM overexpression is commonly associated with aggressive disease characteristics and unfavorable clinical outcomes. Many of these indications, especially advanced gastric or GEJ adenocarcinoma and TNBC, continue to face limited effective treatment options and poor long-term prognosis under existing standard-of-care therapies, indicating significant unmet clinical needs. These observations support the relevance of EpCAM as a therapeutic target across a broad range of epithelial tumors and provide a rationale for the development of EpCAM-targeted therapies beyond pancreatic cancer.

The global estimated number of colorectal cancer cases was approximately 2,064.4 thousand in 2025, and is projected to increase to 2,361.2 thousand by 2030, reaching 2,674.4 thousand by 2035, reflecting a steadily expanding disease burden worldwide. In addition, the global estimated number of new breast cancer cases was approximately 2,454.9 thousand in 2025, is expected to rise to 2,698.0 thousand by 2030, and is further projected to reach 2,935.7 thousand by 2035, underscoring the growing clinical impact of this epithelial malignancy. TNBC accounts for 15–20% of incident breast cancers. Moreover, the global estimated number of new ovarian cancer cases was approximately [347.0] thousand in 2025, is expected to rise to 381.6 thousand by 2030, and is further projected to reach 415.6 thousand by 2035, underscoring the growing clinical impact of this epithelial malignancy.

CAR-T CELL THERAPIES FOR AUTOIMMUNE DISEASES

An autoimmune disease is a condition in which the body's immune system mistakenly attacks body, which can be associated with either abnormally low activity or over-activity of the immune system. There are roughly 100 different types of autoimmune disorders, which can affect almost any part of the body, including the heart, brain, nerves, muscles, skin, eyes, joints, lungs, kidneys, glands, the digestive tract, and blood vessels. Traditional treatments for autoimmune diseases are mainly based on hormones and immunosuppression. With the advancement of technology, new therapies like bispecific antibody, antibody fusion protein and CAR-T are gaining more attention due to its potential high remission rate.

Overview of Treatments for Autoimmune Diseases

Current autoimmune diseases treatment can be broadly categorized as (i) biologics-based treatment and (ii) small molecular treatment. Biologics use targeted biological agents — such as antibodies, cell therapies, fusion proteins and MSCs — to modulate the immune system and directly remove or neutralize pathogenic cells. These therapies offer high specificity and longer duration of effect, often reducing dosing frequency and systemic off-target effects. Small-molecule drugs act inside cells to suppress inflammation and interrupt key signaling pathways (e.g., NSAIDs, corticosteroids, DMARDs, JAK/mTOR inhibitors). They provide rapid symptom control, oral dosing flexibility, and options for both short-term relief and long-term disease management.

Mechanism and Advantages of CAR-T for Autoimmune Diseases

CAR-T cell therapy, a cutting-edge cellular immunotherapy with demonstrated efficacy in treating hematologic malignancies, has also demonstrated preliminary clinical efficacy in solid tumors, and exhibits significant promise for addressing autoimmune diseases. This innovative therapeutic approach holds promise for achieving long-term remission in autoimmune diseases, potentially offering significant benefits to affected patients.

CAR-T therapy offers precise targeting and elimination of pathological B cells and plasma cells in autoimmune diseases, directly reducing autoantibody production at its source. Through deep elimination of autoreactive B cells, CAR-T targeted therapy restores the B cell population to a non-reflexive phenotype, gradually rebuilds normal immune tolerance, and reduces the possibility of relapse.

Advantages of CAR-T Cell Therapy for Autoimmune Diseases

- ***Good efficacy enabling long-term treatment-free remission:*** The efficacy of CAR-T cell therapy in autoimmune diseases has been confirmed by multiple clinical studies, especially in refractory or relapsed cases, providing new treatment options. CAR-T cells are capable of persisting *in vivo* and maintaining immunomodulatory activity over extended periods following a single administration. This durable cellular persistence enables a one-time treatment paradigm, supporting prolonged treatment-free remission and long-term disease control in autoimmune diseases.

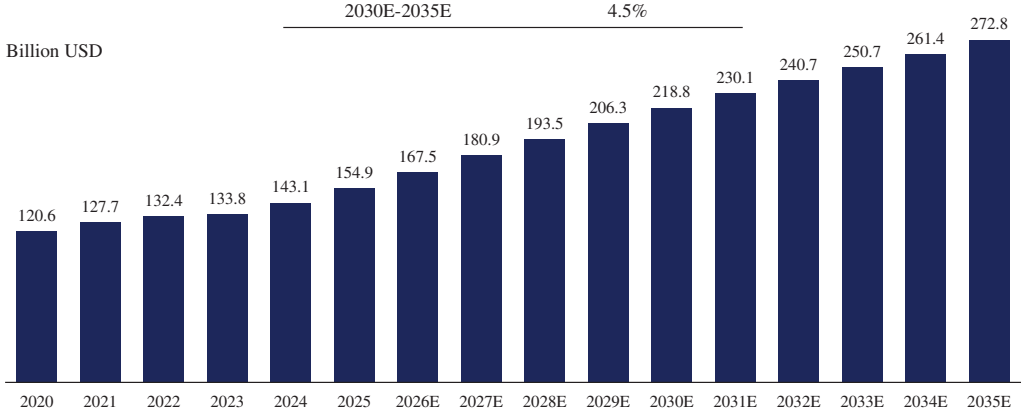
- ***Relatively mild side effects.*** Compared with traditional chemical drugs, CAR-T has lower systemic toxicity, less systemic toxicity, and higher patient tolerance.

Market size of autoimmune drugs market

The following graph shows the historical and forecasted size of the global autoimmune drugs market for the years 2020 through 2035:

Global Autoimmune Drugs Market, 2020-2035E

Period	CAGR
2020-2025	5.1%
2025-2030E	7.2%
2030E-2035E	4.5%

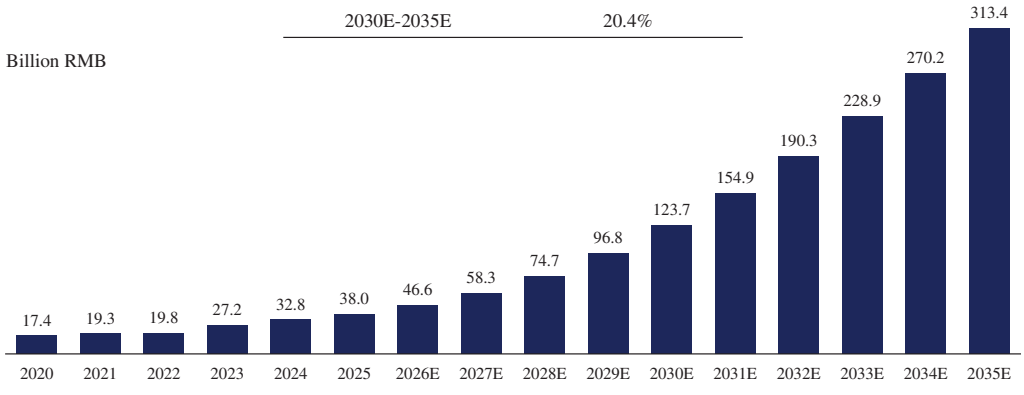


Source: Public Information, Frost & Sullivan Analysis

The following graph shows the historical and forecasted size of the autoimmune drugs market in China for the years 2020 through 2035:

China Autoimmune Drugs Market, 2019-2035E

Period	CAGR
2020-2025	16.9%
2025-2030E	26.6%
2030E-2035E	20.4%



Source: Public Information, Frost & Sullivan Analysis

SOURCES OF INFORMATION

We commissioned Frost & Sullivan, an independent consulting firm, to conduct detailed research on the cellular immunotherapy industry. Frost & Sullivan is an independent global market research and consulting company which was founded in 1961 and is based in the United States. Services provided by Frost & Sullivan include market assessments, competitive benchmarking, and

strategic and market planning for a variety of industries. We have agreed to pay a fee of RMB550,000 to Frost & Sullivan in connection with the preparation of the Frost & Sullivan Report. We have extracted certain information from the Frost & Sullivan Report in this section, as well as in the sections headed "Summary," "Risk Factors," "Business," "Financial Information" and elsewhere in this document to provide our potential investors with a more comprehensive presentation of the industry in which we operate.

During the preparation of the Frost & Sullivan Report, Frost & Sullivan performed both primary and secondary research, and obtained knowledge, statistics, information and industry insights on the industry trends of the cellular immunotherapy industry. Primary research involved discussing the status of the industry with leading industry participants and industry experts. Secondary research involved reviewing annual reports of public companies, independent research reports and Frost & Sullivan's proprietary databases. The Frost & Sullivan Report was compiled based on the assumptions that (i) the overall global social, economic, and political environment is expected to maintain a stable trend over the forecast period, (ii) during the forecast period, related key industry drivers are likely to continue driving growth in China, and (iii) there are no extreme force major event or industry regulations by which the market situation may be affected either dramatically or fundamentally. For the avoidance of doubt, the impacts of COVID-19 have been considered when compiling information in the Frost & Sullivan Report. In this section, Frost & Sullivan presents historical market information for six years (i.e., from 2020 to 2025), which is longer than the Track Record Period and, we believe, is a more accurate reflection of the trends that affect our industry.

Our Directors have confirmed, after taking reasonable care, that as of the Latest Practicable Date there has been no adverse change in the market information set forth herein since the date on which the Frost & Sullivan Report was issued.