

INDUSTRY OVERVIEW

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OVERVIEW OF ONCOLOGY MARKET

Overview

Cancer is a group of diseases that involve uncontrolled growth and development of cells in the body. It is the leading cause of death worldwide, resulting in approximately 10 million deaths globally each year. There were 21.9 million new cancer cases globally in 2025, and it was estimated that in 2035, there would be 27.0 million new cancer cases. In 2025, colorectal cancer, lung cancer and pancreatic cancer were among the most common cancers globally, ranking second, fourth and tenth, respectively, in terms of Incidence.

The development of cancer treatment has progressed through several major stages, beginning with surgery and radiotherapy as the earliest foundational treatment modalities, followed by the widespread adoption of chemotherapy as a systemic approach to tumor control. With advances in molecular biology and tumor genomics, oncology entered a new era of more precise and mechanism-driven therapeutic paradigms. Modern oncology therapies primarily comprise targeted therapies and immunotherapies. Targeted therapies include small molecule inhibitors (such as KRAS inhibitors) and antibody-based therapeutics (such as antibody drug conjugates, “ADCs”), while immunotherapies encompass immune checkpoint inhibitors, cell therapies, and emerging innate immune modulators (such as STING agonists). Targeted therapy marked the first major breakthrough in precision oncology by enabling drugs to directly inhibit oncogenic drivers and dysregulated signaling pathways, thereby improving treatment efficacy while reducing systemic toxicity compared with traditional chemotherapy. Building upon this foundation, immunotherapy has introduced a new treatment paradigm by harnessing the patient’s own immune system to recognize and eliminate tumor cells, extending survival outcomes across multiple cancer types. Together, the continued advancement of targeted therapy and immunotherapy has reshaped the modern oncology landscape, shifting cancer treatment from generalized tumor suppression toward selective, mechanism-based and durable therapeutic strategies.

Market Size

The global oncology drug market has expanded significantly in the past and is projected to further grow. The global oncology drug market increased from US\$150.3 billion in 2020 to US\$278.2 billion in 2025 at a CAGR of 13.1%, and is expected to reach US\$683.0 billion in 2035 at a CAGR of 9.4% from 2025 to 2035. Immunotherapies are the primary growth engine, with market share expected to rise from 23.4% in 2020 to 45.7% by 2035, while antibody-based therapies (including ADCs) are projected to account for 56.5% of biologics revenue by 2035.

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China’s oncology drug market also grew rapidly in recent years. The market size increased from RMB197.5 billion in 2020 to RMB279.1 billion in 2025 at a CAGR of 7.2%, and is expected to reach RMB980.0 billion in 2035 at a CAGR of 13.4% from 2025 to 2035. Immuno-oncology drugs’ market share is expected to surge from 7.5% in 2020 to 43.5% by 2035, while chemotherapy’s share will decline from 63.3% to below 10%, underscoring the rapid transformation of China’s oncology treatment landscape.

Growth Drivers and Future Trends

The oncology drug market is being driven and shaped by several fundamental trends, reflecting the continued evolution of cancer treatment toward more effective, durable and patient-centric therapeutic paradigms.

- *Rising demand for more precise and effective therapies.* Advances in molecular biology and tumor genomics have improved understanding of cancer mechanisms, driving growing demand for therapies that are more precise, selective and effective. This has accelerated the shift away from non-specific cytotoxic treatments toward targeted therapies and immunotherapies that offer improved efficacy and safety profiles.
- *Addressing unmet clinical needs, particularly resistance to targeted therapies.* Despite major progress in targeted therapy, drug resistance remains a critical clinical challenge and a key unmet medical need in oncology. The development of novel therapeutic mechanisms and treatment strategies is therefore increasingly focused on overcoming resistance and improving long-term disease control.
- *Improved drug accessibility and affordability.* Ongoing improvements in healthcare systems and reimbursement policies are enhancing the accessibility and affordability of oncology drugs. These developments are expanding patient access to novel therapies and supporting broader utilization across healthcare markets.
- *Longer patient survival driving sustained treatment demand.* Advances in treatment efficacy are leading to longer patient survival, which in turn drives sustained demand for oncology therapies over extended treatment periods.
- *Combination therapy becoming the mainstream treatment paradigm.* Oncology treatment is increasingly shifting toward combination therapy as the mainstream treatment paradigm. Combination regimens improve therapeutic outcomes and play a growing role in the standard of care across multiple cancer indications.

OVERVIEW OF KRAS G12D DRUGS

Overview of KRAS G12D Mutation

RAS is a family of proteins that exhibits a guanosine triphosphatase (“**GTPase**”) activity and cycles between “on” guanosine triphosphate (“**GTP**”)-bound and “off” guanosine diphosphate (“**GDP**”)-bound states. RAS protein regulates multiple signal transductions and plays a central role in the cascade of cell process control, including cell proliferation and cell division.

Three RAS genes encode for protein isoforms, namely Kirsten RAS (“**KRAS**”), Harvey RAS (“**HRAS**”) and Neuroblastoma RAS (“**NRAS**”). KRAS is one of the most frequently mutated oncogenes in human cancers and it represents approximately 75% of all RAS isoforms contributing to cancer. KRAS mutations are detected in approximately 90% of pancreatic cancer, 30-40% of colorectal cancer (“**CRC**”), and 15-20% of lung cancer patients. These mutations are often associated with resistance to targeted therapies and poor outcomes in cancer patients.

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The KRAS G12D mutation represents approximately 30% of all KRAS mutations, making it the most prevalent KRAS variant in human cancers. It occurs with particularly high frequency in PDAC (approximately 38%), CRC (approximately 12%) and non-small cell lung cancer (“NSCLC”) (approximately 4%). Compared with the KRAS G12C mutation, the KRAS G12D mutation leads to a more pronounced impairment of intrinsic GTPase activity, resulting in a higher proportion of constitutively active, GTP-bound KRAS in tumor cells.

The KRAS G12D mutation is a driver genetic alteration that occurs across multiple stages of tumor development, including both early-stage and advanced disease. While this mutation is not restricted to a specific cancer stage, current clinical development of KRAS G12D-targeted therapies is primarily focused on patients with advanced, unresectable, and/or metastatic disease, reflecting the significant unmet medical need within this population. Furthermore, comprehensive biomarker testing, such as next-generation sequencing and other molecular diagnostics, is clinically indicated and routinely conducted primarily in these advanced settings to guide treatment selection. As a result, the screenable target patient pool for these targeted therapies is practically limited to patients with advanced-stage disease.

Major Indications of KRAS G12D Inhibitor

NSCLC

NSCLC is any epithelial lung cancer other than small cell lung cancer, with the most common histological subtypes being adenocarcinoma, squamous cell carcinoma and large cell carcinoma. The global incidence of NSCLC is expected to increase from 2,262.1 thousand cases in 2025 to 2,942.4 thousand cases by 2035. The US incidence of NSCLC is expected to increase from 192.7 thousand cases in 2025 to 208.7 thousand cases by 2035, while the incidence in China is expected to increase from 966.2 thousand cases in 2025 to 1,253.7 thousand cases by 2035. The global drug market of NSCLC is expected to increase from US\$104.3 billion in 2025 to US\$272.4 billion in 2035 at a CAGR of 10.1%. Specifically, China’s drug market of NSCLC is expected to increase from US\$12.3 billion in 2025 to US\$40.6 billion in 2035 at a CAGR of 12.7%, while the market size in U.S. is expected to increase from US\$41.3 billion in 2025 to US\$110.3 billion in 2035 at a CAGR of 10.3%.

According to the Chinese Medical Association Clinical Practice Guidelines for NSCLC (2025 Edition), the standard of care for NSCLC in China differs by disease stage and, for advanced disease, by molecular characteristics, histological subtype and immune biomarker status. In general, earlier-stage NSCLC is treated with local treatment aimed at removing or controlling the tumor, while advanced or metastatic NSCLC is treated mainly with systemic therapies. For early-stage NSCLC, including patients with stage I and II disease, the standard of care generally centers on surgery for patients who are eligible for resection, followed by postoperative adjuvant management where appropriate, including regular follow-up, radiotherapy and chemotherapy. Adjuvant management means additional treatment or monitoring after surgery to reduce the risk of recurrence. For locally advanced NSCLC, including certain patients with stage III disease who are eligible for surgery, treatment may include surgery together with neoadjuvant and/or adjuvant therapies. Neoadjuvant therapy is treatment given before surgery to shrink or control the tumor. For unresectable stage III disease, the standard of care generally includes concurrent chemoradiotherapy, followed by consolidation immunotherapy in eligible patients, which is additional immunotherapy given after chemoradiotherapy to help maintain disease control.

For advanced or metastatic NSCLC, including stage IV NSCLC, treatment is guided primarily by molecular testing (which refers to laboratory analyses of tumor tissue or blood samples to identify genetic or molecular alterations that may guide treatment selection) and biomarker status (which means the presence, absence or expression level of specific molecular features that may affect prognosis or response to treatment). In this setting, standard treatment is selected based on oncogenic driver mutations and immune biomarkers that indicate whether a patient is more likely to benefit from targeted therapy, immunotherapy or chemotherapy-based regimens. Patients with actionable driver alterations, such as EGFR, ALK or ROS1 alterations, may receive corresponding biomarker-driven targeted therapies where available. There are currently no approved targeted therapies specifically for KRAS G12D-mutant tumors in NSCLC. As a result, such patients are primarily treated with standard systemic therapies based on tumor type, including chemotherapy with or without immune checkpoint inhibitors. Systemic therapies are anti-cancer treatments that circulate through the bloodstream and are used to treat cancer cells at both primary and metastatic sites. Eligible patients may also access KRAS G12D-targeted investigational therapies through

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participation in clinical trials. For patients without actionable driver mutations, or with resistant genotypes for which no approved targeted therapy is available, treatment options remain largely chemotherapy- or immunotherapy-based. These treatments may provide clinical benefit but do not directly inhibit the underlying oncogenic signaling pathway, which limits access to precision therapies for certain molecular subgroups, including KRAS G12D-mutant NSCLC.

In the treatment paradigm for stage IV NSCLC without actionable driver mutations, first-line treatment is generally stratified by PD-L1 expression. For patients with PD-L1 expression of 50% or above, first-line treatment may include immune checkpoint inhibitor monotherapy, such as pembrolizumab, atezolizumab or cemiplimab. For patients with PD-L1 expression below 50%, first-line treatment may include chemotherapy in combination with immunotherapy, such as pembrolizumab plus platinum-based chemotherapy with or without anti-angiogenic agents. Upon disease progression, second-line treatment depends in part on whether immunotherapy was used in the first line. If first-line treatment did not include immunotherapy, second-line treatment may include monotherapy with nivolumab, pembrolizumab or atezolizumab. If first-line treatment consisted of chemotherapy plus immunotherapy, second-line treatment may include chemotherapy with or without anti-angiogenic agents, such as docetaxel with or without ramucirumab or nintedanib, or anlotinib.

According to the National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology (“NCCN Guidelines[®]”) for NSCLC (2025, Version 5), for patients with advanced NSCLC harboring KRAS G12D mutations, in the absence of approved KRAS G12D-targeted therapies, the treatment pathway generally follows that for patients without actionable driver mutations. This approach is broadly consistent with the Chinese Society of Clinical Oncology (“CSCO”) guidelines in China and is primarily guided by PD-L1 expression levels. First-line treatment typically comprises immune checkpoint inhibitor-based regimens, including monotherapy in patients with high PD-L1 expression and chemo-immunotherapy combinations in patients with lower PD-L1 expression. Upon disease progression, subsequent treatment determined based on prior therapy exposure and generally involves systemic therapies such as chemotherapy with or without anti-angiogenic agents. Participation in clinical trials is also recommended, particularly in later-line settings.

Against these treatment pathways, TSN1611 monotherapy would be positioned as a targeted investigational treatment option for the biomarker-defined KRAS G12D-mutant subset of NSCLC patients for whom no approved KRAS G12D-directed therapy currently exists, while TSN1611 combination therapy may be positioned to complement established chemo-immunotherapy and anti-cancer regimens and potentially broaden clinical applicability. The addressable patient population for TSN1611, assuming a label limited to KRAS G12D-mutant patients, would represent approximately 4% of NSCLC patients.

CRC

CRC refers to cancers affecting the colon and rectum, and adenocarcinomas of the colon and rectum account for approximately 95% of all CRC cases. The global incidence of CRC is expected to increase from 2,064.4 thousand cases in 2025 to 2,674.4 thousand cases by 2035. The US incidence of CRC is expected to increase from 154.3 thousand cases in 2025 to 175.0 thousand cases by 2035, while the incidence in China is expected to increase from 553.5 thousand cases in 2025 to 714.6 thousand cases by 2035. The global drug market of CRC is expected to increase from US\$27.8 billion in 2025 to US\$63.8 billion in 2035 at a CAGR of 8.7%. Specifically, China’s drug market of CRC is expected to increase from US\$3.8 billion in 2025 to US\$11.9 billion in 2035 at a CAGR of 12.1%, while the market size in U.S. is expected to increase from US\$9.9 billion in 2025 to US\$23.3 billion in 2035 at a CAGR of 9.0%.

According to 2025 CSCO guidelines, the treatment pathway for CRC in China depends on disease stage and resectability. For non-metastatic CRC, treatment generally focuses on removing the tumor through surgery, with chemotherapy before or after surgery where appropriate. For patients with non-metastatic early-stage disease, treatment generally centers on surgery and perioperative chemotherapy. For patients with non-metastatic unresectable disease, treatment may include conversion therapy to facilitate subsequent resection. Conversion therapy aims to shrink or control the tumor so that surgery may become possible.

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For metastatic, or stage IV, CRC, the first-line treatment is based on chemotherapy, and targeted drugs can be used in combination after genetic testing. At this stage, treatment is usually systemic because the cancer has spread beyond the original site. Genetic testing helps determine whether targeted therapies or immunotherapies may be appropriate. Targeted agents, such as cetuximab or bevacizumab, and immune checkpoint inhibitors may be incorporated into treatment regimens depending on patient characteristics and prior treatment exposure. Second line and subsequent treatments are adjusted to different chemotherapy regimens and targeted drugs based on first-line medication choice. Patients with special gene mutation profiles can use corresponding targeted drugs.

According to the NCCN Guidelines[®] for colorectal cancer (2025), the treatment pathway in the United States is broadly aligned with that in China and is determined by disease stage, resectability and biomarker status. For patients with non-metastatic disease, treatment generally centers on surgical resection with perioperative or adjuvant chemotherapy as appropriate. For patients with advanced or metastatic disease, treatment is primarily based on systemic therapy, including chemotherapy regimens such as FOLFOX, FOLFIRI or CAPEOX, in combination with targeted therapies or immunotherapy where applicable. Upon disease progression, subsequent treatment is guided by prior therapy and biomarker status, and may include alternative chemotherapy regimens, biomarker-directed therapies and participation in clinical trials.

Against these treatment pathways, TSN1611 combination therapy may be positioned to complement established systemic regimens and potentially move into earlier treatment settings over time. The addressable patient population for TSN1611, assuming a label limited to KRAS G12D-mutant patients, would represent approximately 12% of CRC patients.

Pancreatic cancer and PDAC

Pancreatic cancer is caused by the abnormal and uncontrolled growth of cells in the pancreas and remains a high-mortality malignancy. The global incidence of pancreatic cancer is expected to increase from 494.0 thousand cases in 2025 to 654.1 thousand cases by 2035, while the incidence in China is expected to increase from 115.0 thousand cases in 2025 to 153.2 thousand cases by 2035.

Pancreatic cancer is a broad term that refers to malignancies arising in the pancreas, including pancreatic ductal adenocarcinoma (“PDAC”), pancreatic neuroendocrine tumors, acinar cell carcinoma and other rare histological subtypes. PDAC is the most common and aggressive form of pancreatic cancer and originates in the exocrine cells that line the pancreatic ducts. PDAC accounts for more than 90% of pancreatic cancer cases and represents the major clinical and commercial segment of pancreatic cancer. Accordingly, references to pancreatic cancer treatment and management in this section are primarily focused on PDAC, unless otherwise specified.

The global incidence of PDAC is expected to increase from 444.6 thousand cases in 2025 to 588.7 thousand cases by 2035. The US incidence of PDAC is expected to increase from 54.6 thousand cases in 2025 to 64.0 thousand cases by 2035, while the incidence in China is expected to increase from 103.5 thousand cases in 2025 to 137.9 thousand cases by 2035. The global drug market of PDAC is expected to increase from US\$2.8 billion in 2025 to US\$6.5 billion in 2035 at a CAGR of 9.0%. Specifically, China’s drug market of PDAC is expected to increase from US\$0.5 billion in 2025 to US\$1.5 billion in 2035 at a CAGR of 12.4%, while the market size in U.S. is expected to increase from US\$1.3 billion in 2025 to US\$3.1 billion in 2035 at a CAGR of 8.9%.

According to the 2025 CSCO guidelines, treatment options for PDAC mainly depend on the disease stage, resectability and patient performance status and overall clinical characteristics. Performance status describes a patient’s general physical condition and ability to tolerate treatment. For purposes of treatment, PDAC is commonly managed by stage and resectability, including resectable disease, borderline resectable disease, locally advanced disease and metastatic disease. For patients with resectable PDAC, the standard of care generally centers on surgical resection, supplemented by perioperative management where appropriate, including adjuvant chemotherapy after surgery. For patients with borderline resectable PDAC, treatment typically involves multidisciplinary management, where specialists in surgical oncology, medical oncology, radiation oncology, radiology and pathology coordinate decisions on neoadjuvant chemotherapy and/or chemoradiotherapy to improve the feasibility and outcome of surgery, followed by surgery and adjuvant therapy where appropriate. For patients with unresectable locally advanced PDAC,

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treatment generally includes systemic chemotherapy and/or chemoradiotherapy, together with supportive care based on patient condition. For patients with metastatic PDAC, treatment is primarily based on systemic chemotherapy-based regimens, with regimen selection guided by patient performance status and overall clinical characteristics.

For patients with unresectable locally advanced or metastatic PDAC, first-line treatment is generally stratified by performance status. In patients with good performance status, first-line treatment generally includes gemcitabine plus albumin-bound paclitaxel, FOLFIRINOX and NALIRIFOX. In patients with poor performance status, first-line treatment may include gemcitabine monotherapy or S-1 monotherapy. For patients with BRCA1/2 mutations receiving platinum-based therapy, if there is no disease progression after 16 weeks of treatment, maintenance therapy with olaparib may also be considered. Upon disease progression, second-line treatment involves switching to another chemotherapy regimen based on first-line treatment. With further disease progression, subsequent treatment may include participation in clinical trials, gemcitabine monotherapy, S-1 monotherapy or best supportive care. Mechanistically, PDAC is characterized by a high prevalence of oncogenic driver mutations such as KRAS mutations, which can lead to continuous activation of downstream cancer-growth signaling pathways. However, current standard treatment options for PDAC remain predominantly chemotherapy-based, with limited availability of effective mutation-directed therapies. This limits access to precision treatment options for most PDAC patients across clinical stages.

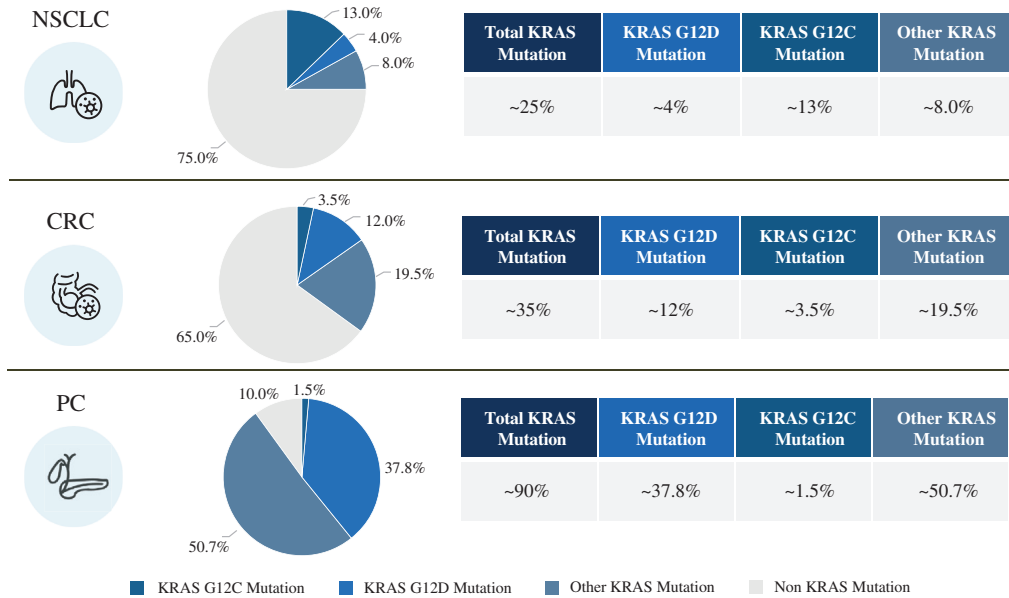
According to the NCCN Guidelines® for pancreatic cancer (2025), the treatment paradigm in the United States is similarly driven by disease stage and resectability, but places greater emphasis on patient performance status and treatment sequencing. For patients with advanced or metastatic PDAC, systemic therapy remains the cornerstone of treatment, with regimen selection primarily guided by performance status. In addition, the NCCN framework highlights the role of maintenance therapy in patients achieving disease control following first-line chemotherapy, as well as the use of biomarker-directed therapies in selected molecularly defined subgroups. Upon disease progression, subsequent treatment is guided by prior therapy exposure and patient condition, with consideration of alternative systemic regimens, clinical trial participation and best supportive care.

Against these treatment pathways, TSN1611 monotherapy would be positioned as a targeted investigational treatment candidate for the biomarker-defined KRAS G12D-mutant subset of PDAC patients for whom current treatment remains largely chemotherapy-based, while TSN1611 combination therapy may be positioned to complement established systemic regimens and potentially broaden clinical applicability over time. The addressable patient population for TSN1611, assuming a label limited to KRAS G12D-mutant patients, would represent approximately 38% of PDAC patients.

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Frequency of KRAS Mutations in Different Cancers

- KRAS mutations are detected in approximately 25% of NSCLC, 35% of CRC and 90% of pancreatic cancer patients.
- The top three cancers with the highest KRAS mutation rates, including NSCLC, CRC and PC.



Source: Literature research and Frost & Sullivan Analysis

Comparative Analysis of KRAS G12D Inhibitors Against Current Standard of Care

Current standards of care for NSCLC, PDAC and CRC remain primarily based on chemotherapy, immunotherapy and, where applicable, other biomarker-directed targeted therapies, rather than KRAS G12D-specific treatment. Against this backdrop, KRAS G12D inhibitors are being developed to provide a biomarker-directed treatment option for patient subsets that are currently treated largely with non-allele-specific regimens.

The oncology market is increasingly focused on addressing resistance to targeted therapies and that combination therapy is becoming the mainstream treatment paradigm. In the KRAS G12D field specifically, future development is increasingly centered on combination treatment approaches, including combinations with chemotherapy and monoclonal antibodies, as monotherapy may face limitations related to resistance and incomplete pathway suppression. Compared with current standard of care, KRAS G12D inhibitors therefore seek to offer a more molecularly targeted treatment approach for KRAS G12D-mutant patient populations, while combination development strategies are intended to enhance therapeutic efficacy, delay resistance development and broaden clinical applicability.

NSCLC

In NSCLC, treatment is stratified based on PD-L1 expression and the presence of actionable driver mutations. For patients without targetable alterations, standard-of-care treatment primarily consists of immunotherapy, either as monotherapy or in combination with chemotherapy. While targeted therapies have significantly improved outcomes in patients with specific driver mutations such as EGFR and ALK, these therapies are not applicable to KRAS G12D-mutant patients.

From a mechanistic perspective, KRAS G12D acts as a key oncogenic driver by constitutively activating downstream signaling pathways. However, existing treatment modalities in NSCLC either act in a non-specific cytotoxic manner (chemotherapy) or modulate the immune response indirectly (immunotherapy), without directly targeting KRAS-driven signaling. As a result, KRAS G12D-mutant NSCLC patients continue to be treated under non-targeted therapeutic frameworks, highlighting the lack of mutation-directed treatment options in this subgroup.

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CRC

In colorectal cancer, treatment is largely based on chemotherapy in combination with targeted agents selected according to molecular characteristics. In particular, anti-EGFR therapies are commonly used in patients with RAS wild-type tumors; however, these agents are not effective in patients with KRAS mutations, including KRAS G12D, thereby limiting access to certain targeted treatment options.

Mechanistically, KRAS G12D drives tumor progression through constitutive activation of downstream signaling pathways. In contrast, current treatment options for KRAS G12D-mutant CRC remain largely chemotherapy-based, with or without anti-angiogenic agents, which do not directly inhibit the KRAS signaling axis. Compared with biomarker-selected populations eligible for targeted therapies, patients harboring KRAS G12D mutations have more limited precision treatment options, underscoring a lack of effective mutation-directed therapies.

PDAC

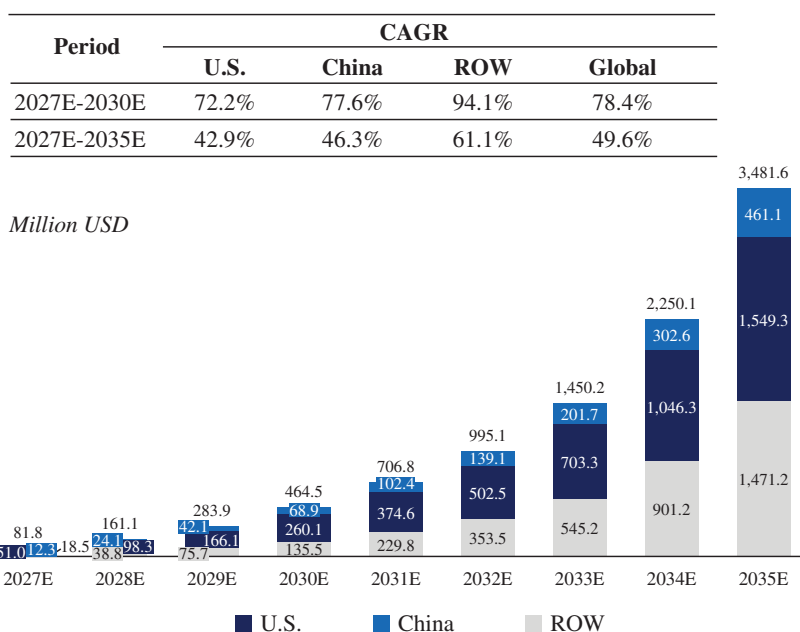
In pancreatic cancer, KRAS mutations are highly prevalent and play a central role in tumor development and progression. Despite this, standard-of-care treatment remains predominantly chemotherapy-based, including regimens such as FOLFIRINOX, NALIRIFOX or gemcitabine plus nab-paclitaxel, with targeted therapies limited to small biomarker-defined subgroups. Immunotherapy has shown limited efficacy in most patients.

From a mechanistic standpoint, KRAS G12D is a key driver mutation in pancreatic cancer; however, current treatment approaches do not directly target this pathway and instead rely on non-specific or indirectly acting mechanisms. As a result, patients with KRAS G12D-mutant PDAC continue to face limited treatment options, highlighting a significant unmet need for therapies that directly target the underlying oncogenic driver.

Market Size of the KRAS G12D Inhibitor Drug Market

With the anticipated commercialization of multiple drug pipelines, the global KRAS G12D inhibitor drug market is expected to increase from US\$81.8 million in 2027 to US\$464.5 million in 2030 at a CAGR of 78.4% from 2027 to 2030, and it will further increase to US\$3,481.6 million in 2035, with CAGR of 49.6% from 2030 to 2035. China's KRAS G12D inhibitor drug market is expected to increase from US\$12.3 million in 2027 to US\$68.9 million in 2030 at a CAGR of 77.6% from 2027 to 2030, and it will further increase to US\$461.1 million in 2035, with CAGR of 46.3% from 2030 to 2035. The US KRAS G12D inhibitor drug market is expected to increase from US\$51.0 million in 2027 to US\$260.1 million in 2030 at a CAGR of 72.2% from 2027 to 2030, and it will further increase to US\$1,549.3 million in 2035, with CAGR of 42.9% from 2030 to 2035.

Global KRAS G12D Inhibitor Drug Market, 2027E-2035E



Source: NMPA, CDE, FDA, ClinicalTrials.gov (“ClinicalTrials”), and Frost & Sullivan Analysis

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The global KRAS G12D inhibitor drug market is expected to begin generating revenue from 2027, primarily due to the continued clinical advancement of leading KRAS G12D inhibitor candidates, including GFH375, HRS-4642 and INCB 161734, which have advanced into Phase III clinical development in the U.S. and other regions and are anticipated to achieve the earliest commercial launches as early as 2027.

The global market growth of KRAS G12D inhibitor drugs is primarily driven by the significant unmet medical needs of biomarker-selected patients with KRAS G12D-mutated tumors, particularly in PDAC, CRC and NSCLC. Although these patients represent defined molecular subgroups within broader cancer populations, currently available therapies generally do not directly inhibit KRAS G12D-driven signaling pathways. KRAS G12D is one of the most prevalent oncogenic driver mutations in PDAC, accounting for approximately 35% of PDAC cases, and is also present in subsets of CRC and NSCLC patients accounting for approximately 12% and 4% of the respective cancer populations, respectively.

Mechanistically, KRAS G12D mutations can continuously activate downstream signaling pathways that promote tumor proliferation and survival. In addition, the aspartate residue in KRAS G12D results in a more pronounced impairment of intrinsic GTPase activity than KRAS G12C, leading to a higher proportion of active, GTP-bound KRAS in tumor cells and contributing to its potent oncogenic potential. In the absence of approved KRAS G12D-targeted therapies, treatment for KRAS G12D-mutated tumors remains largely based on chemotherapy, immunotherapy and other systemic regimens, depending on tumor type and disease stage, with limited availability of effective mutation-directed treatment options. This unmet need supports the commercial potential of KRAS G12D inhibitors, notwithstanding the relatively limited biomarker-selected patient populations in individual tumor types.

The projected growth of the KRAS G12D inhibitor drug market is expected to outpace the growth of the underlying KRAS G12D-mutated patient population, primarily due to (i) increasing clinical advancement and potential commercialization of KRAS G12D-targeted therapies, (ii) expansion into broader indications and treatment settings, (iii) increasing adoption of combination therapies, (iv) improved patient identification through broader molecular diagnostic and next-generation sequencing testing penetration, and (v) the relatively high pricing potential of innovative targeted therapies. In addition, ongoing development of combination strategies, including combinations with immunotherapies and pathway-targeted agents, may further improve therapeutic efficacy and expand clinical applicability. While KRAS G12D mutation prevalence in certain tumor types, such as NSCLC, is relatively low, the large overall incidence of PDAC, CRC and NSCLC, together with a pan-tumor development strategy across these indications, may collectively broaden the addressable patient population and commercial opportunity for KRAS G12D inhibitor drugs.

Competitive Landscape of Pan-RAS and KRAS Inhibitors

The following table summarizes the competitive landscape of pan-RAS and KRAS inhibitors under clinical stage globally.

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Drug	Company	Target	Binding State	Indications	Combination Therapy	Fastest Stages	First Posted Date of Current Clinical Stage	Regions involved	Regulatory Authorities involved
Daraxonrasib	Revolution Medicines	Pan-RAS	ON	1L+ PDAC, 1L 2L 3L NSCLC, 2L+ CRC, 2L+ Advanced Solid Tumor	Mono/Efirontasib/Ivonescimab	NDA	07/22/2026	US	FDA
ZG2001	Zelgen Biopharmaceuticals	Pan-KRAS	N/A	Solid Tumor	Mono	I/II	06/14/2023	China	CDE/FDA
JAB-23E73	AstraZeneca/Jacobio Pharmaceuticals	Pan-KRAS	ON/OFF	2L+ Solid Tumor, 2L+ NSCLC, 2L+ CRC, 1L PDAC	Mono	I/II	11/11/2024	China, US	CDE/FDA
JYP0015	Guangzhou JOYO	Pan-RAS	ON	2L+ Solid Tumor, 2L+ CRC, 2L+ PDAC, 2L+ NSCLC	Mono/Pembrolizumab/Panitumumab	I/II	03/07/2025	China, US	CDE/FDA
GFH276	GenFleet Therapeutics	Pan-RAS	ON	2L+ CRC, 2L+ PDAC, 2L+ NSCLC, 2L+ Solid Tumor	Mono	I/II	09/10/2025	China, Other Region	CDE
HBW-016	Haibowei Pharmaceutical	Pan-KRAS	ON/OFF	2L+ Endometrial cancer, 2L+ PDAC, 2L+ Solid Tumor, 2L+ CRC	Mono	I/II	11/10/2025	China	CDE
BPI-572270	Betta Pharm	Pan-RAS	ON	2L+ CRC, 2L+ PDAC, 2L+ NSCLC, 2L+ Solid Tumor	Mono	I/II	02/11/2026	China	CDE
BLU-924	Sanofi	Pan-KRAS	N/A	2L+ CRC, 2L+ PDAC, 2L+ NSCLC	Mono	I/II	06/04/2026	US	/
BI 3706674	Boehringer Ingelheim	Pan-KRAS	OFF	2L+ Oesophagus Cancer, 2L+ Gastric Cancer	Mono	I	09/12/2023	US, Japan, Korea	N/A
YL-17231	Yingli Pharmaceutical	Pan-KRAS	N/A	2L+ NSCLC, 2L+ CRC, 2L+ Solid Tumor	Mono	I	09/28/2023	China, US	CDE, FDA
QTX3034	Quanta Therapeutics	Pan-KRAS	OFF	2L+ Endometrial cancer, 2L+ PDAC, 2L+ Solid Tumor	Mono	I	01/26/2024	US	FDA
ALTA-3263	Alterome Therapeutics	Pan-KRAS	ON&OFF	2L+ NSCLC, 2L+ CRC, 2L+ PDAC, 2L+ Solid Tumor	Mono/Cetuximab	I	02/19/2025	US	/
RO7673396	Roche	Pan-RAS	N/A	Solid Tumor	Mono	I	03/19/2025	China	CDE
BBO-11818	BridgeBio Pharma	Pan-KRAS	ON/OFF	CRC, PDAC, Solid tumor	Mono/Pembrolizumab/Cis/carboplatin/Pemetrexed	I	04/08/2025	US, Other Region	N/A
AUBE00	Chugai Pharmaceutical	Pan-KRAS	OFF	Solid Tumor	Mono	I	05/12/2025	US, JP	N/A
ERAS-4001	Mingde New Drug Research and Development/Erasca	Pan-KRAS	ON/OFF	2L+ Solid Tumor	Mono/pembrolizumab/panitumumab	I	06/15/2025	US	FDA
AMG 410	Angen	Pan-KRAS	ON/OFF	Solid Tumor	Mono/Pembrolizumab/Panitumumab	I	07/30/2025	China, EU, US, Japan	CDE
HRS-7172	Hengrui Pharma	PAN-RAS	ON	Solid Tumor	Mono	I	08/21/2025	China	CDE
TLN-372	Treeline Biosciences	PAN-KRAS	N/A	Solid Tumor	Mono/cetuximab/pembrolizumab	I	10/05/2025	EU, Austria	N/A
KST-6051	Kestrel Therapeutics	PAN-KRAS	N/A	2L+ Solid Tumor	Mono	I	03/09/2026	US	US
SIM0532	Sincere Pharmaceutical	PAN-RAS	N/A	2L+ PDAC, 2L+ NSCLC, 2L+ Solid Tumor	Mono	I	03/16/2026	China	CDE
TQB3205	Chia Tai-tianqing Pharma	Pan-KRAS	N/A	Solid Tumor	Mono	I	03/16/2026	China	CDE/FDA
ABSK211	Abbisio	Pan-KRAS	N/A	Solid Tumor	Mono	I	07/21/2026	China	CDE/FDA
HZ-V055	HangZhou HealZen	Pan-RAS	ON	2L+ Solid Tumor, 2L+ CRC, 2L+ PDAC, 2L+ NSCLC	Mono	I	07/31/2026	China	CDE

Note: As regulatory authorities such as the FDA and EMA do not publicly disclose whether a specific investigational product has obtained IND clearance or equivalent regulatory status in all cases, the involvement of the FDA or EMA in the competitive landscape is determined based on publicly available disclosures by the respective companies.

Source: CDE, Clinical Trials, Company websites, Frost & Sullivan Analysis

Among these clinical-stage pan-KRAS candidates, daraxonrasib is an NDA stage pan-KRAS candidate. Daraxonrasib stops tumor growth by acting as a molecular roadblock against the cancer-driving RAS protein, specifically targeting it when it is in its active, or “on” state. Rather than attacking the cancer protein directly on its own, the drug first binds to a natural “helper” protein inside the cell called Cyclophilin A. Together, the drug and the helper protein lock onto the active RAS protein to form a bulky, three-part structure (known as a tri-complex). This structure acts like a physical cap over the active RAS protein, preventing it from connecting with other proteins and effectively cutting off the signals that tell the cancer cells to multiply and grow. In contrast, TSN1611 does not rely on a helper protein; instead, it binds directly to the specific KRAS G12D mutation and shuts it down regardless of whether the cancer protein is in its active “on” or inactive “off” state. The following table summarizes comparison of TSN1611, our Core Product, against daraxonrasib.

Category	TSN1611	Daraxonrasib
Drug class	Selective KRAS G12D inhibitor	Pan-RAS(ON) inhibitor
Target coverage	Selectively targets KRAS G12D mutant protein	Directly targets RAS(ON) multi-selective inhibitor
Binding state	Targets both active (GTP-bound) and inactive (GDP-bound) KRAS G12D	Targets active GTP-bound RAS (“RAS(ON)”)

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Category	TSN1611	Daraxonrasib
Mechanism of action .	Inhibition of the KRAS signaling pathway	Binding to an intracellular chaperone protein, Cyclophilin A (CypA), resulting in an inhibitory binary complex that binds active, GTP-bound RAS to form a tri-complex and suppresses RAS signaling by disrupting interactions with effectors such as RAF kinases.
Clinical development focus	Both are being developed for KRAS-mutated solid tumors including PDAC, NSCLC and CRC	
Oral administration . . .	Both are orally administered small-molecule therapies	
Combination potential .	Both may potentially be combined with standard therapies or other targeted agents (e.g. gemcitabine+nab-paclitaxel)	

Competitive Landscape of KRAS G12D Inhibitors

As of the Latest Practicable Date, there was no approved KRAS G12D inhibitor drug globally. The following table sets forth the IND-approved and clinical-stage KRAS G12D inhibitor candidates globally, organized by development stage and, within each stage, by the first posted date of each candidate.

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Drug	Company	Binding State	Indications	Combination Therapy	Development Stages	First Posted Date of Current Clinical Stage	Regulatory Authority involved	Regions Involved
HRS4642	Hengrui Pharma	ON & OFF	1L PDAC	AG	III	10/24/2025	CDE	CN
			Solid Tumor	Mono/ Adebrelimab /chemotherapy/HR-A1921/SHR-9839/Cetuximab	I/II	04/26/2024	CDE	CN
			2L+ NSCLC	Mono	I	09/06/2022	/	CN
GFH375	GenFleet Therapeutics/Vera stem Oncology	ON & OFF	2L+ PDAC	Mono	III	11/11/2025	/	CN
			2L+ NSCLC	Mono	III	05/25/2026	CDE	CN
			1L, 2L+ CRC	Mono, cetuximab, panitumumab, mFOLFOX	II	06/22/2026	CDE/FDA	US, Other Region
INCB161734	Incyte Corporation	ON& OFF	1L PDAC	mFOLFIRINOX GemNabP	III	04/13/2026	/	Global
			2L+ Solid tumor, 2L+ CRC, 2L+ NSCLC	Mono/Cetuximab/Retifanlimab/GEMNabP/mFOLFIRINOX/FOLFOX/FOLFIRI/INCA33890	I	12/21/2023	/	Global
Zoldonrasi	Revolution Medicines	ON	1L PDAC	Mono/Oxaliplatin/Leucovorin/5-Fluorouracil/Irinotecan/Gemcitabine/Nab-paclitaxel	III	06/02/2026	/	US
			2L+ Solid Tumor, 2L+ NSCLC	Mono	II	12/08/2023	/	Global
			2L+ CRC	Ivonescimab	I/II	02/09/2026	/	US
DN022150	De Novo Pharmatech /Kerui Pharmaceutical	N/A	2L+ PDAC	Mono	III	06/17/2026	CDE	CN
			2L+ Solid Tumor, 3L CRC, Mono 2L+ NSCLC		I/II	08/02/2024	CDE	CN
RNN08954	Ranok Therapeutics	OFF	2L+ PDAC	Mono	II	10/24/2025	CDE	CN
			2L+ Solid Tumor, 2L+ CRC, 2L+ NSCLC	Mono	I/II	10/08/2024	CDE	CN
TSN1611	Tyligand	ON & OFF	Solid Tumor, NSCLC, 1L PDAC, 1L CRC	Mono/Cetuximab/mFOLFOX6/Paclitaxel/gemcitabin e/mFOLFOX6	I/II	04/26/2024	CDE	CN, US
Drug	Company	Binding State	Indications	Combination Therapy	Development Stages	First Posted Date of Current Clinical Stage (mm-dd-yy)	Regulatory Authority involved	Regions Involved
GDC-7035	Genentech	N/A	Solid Tumor	Mono/panitumumab	I/II	10/01/2024	/	Global
QLC1101	QILU PHARMACEUTICAL	N/A	2L+ Solid Tumor	Docetaxel/QL1203/QL2107/QL1706	I/II	05/21/2025	CDE	CN
			2L+ CRC, 2L+ PDAC, 2L+ NSCLC	Mono	I	05/08/2024	/	CN
HBW-012336	Haibowei Pharmaceutical	N/A	2L+ Solid Tumor, 2L+ CRC, 2L+ PDAC	Mono	I/II	06/18/2025	CDE	CN
ABSK141	Abbisko Therapeutics	N/A	2L+ Solid Tumor, 2L+ CRC, 2L+ PDAC, 2L+ NSCLC	Mono	I/II	02/04/2026	CDE/FDA	CN
INV-8989	Foshan Yuanli	N/A	Advanced Solid Tumor	Mono	I/II	05/06/2026	CDE	CN
YL-17231	Yingli Pharmaceutical	N/A	2L+ NSCLC, 3L+ CRC, 2L+ Solid Tumor	Mono	I	10/10/2023	CDE/FDA	US, CN
QTX3046	Quanta Therapeutics	ON & OFF	2L+ Solid tumor	Mono/cetuximab	I	05/24/2024	/	US
LY3962673	Eli Lilly	OFF	2L+ Solid Tumor	Mono/Cetuximab/Gemcitabine/nabpaclitaxel/Oxaliplatin/leucovorin/Irinotecan/5-fluorouracil	I	09/19/2024	/	Global
INCB186748	Incyte Corporation	N/A	2L PDAC, 2L+ CRC	Mono/Cetuximab/GEMNabP/mFOLFIRINOX	I	02/10/2025	/	US
HS-10529	Hansoh Pharma	N/A	2L+ Solid Tumor	Mono	I	05/06/2025	CDE	CN
HRS-6093	Hengrui Pharma	ON & OFF	2L+ Solid Tumor	Mono	I	08/21/2025	CDE	CN
KQB548	Bayer AG/Kimquat Biosciences	N/A	2L+ PDAC, 2L+ CRC, 2L+ NSCLC	Mono	I	10/06/2025	FDA	US
ZN-F-6418	Zion Pharma	N/A	2L+ NSCLC, 2L+ CRC, 2L+ PDAC, 2L+ Solid Tumor	Mono	I	11/06/2025	CDE	CN
D3S-003	D3 Bio (Wuxi) Co.	ON & OFF	2L+ Solid Tumor	Mono	I	03/06/2026	CDE/FDA	Global

Source: CDE, ClinicalTrials, company websites, and Frost & Sullivan Analysis

Note: As regulatory authorities such as the FDA and EMA do not publicly disclose whether a specific investigational product has obtained IND clearance or equivalent regulatory status in all cases, the involvement of the FDA or EMA in the competitive landscape is determined based on publicly available disclosures by the respective companies. N/A stands for no binding confirmation is disclosed in the available information. For clinical trials where the line of treatment is not specified, this is because the study eligibility criteria do not explicitly disclose requirements regarding patients’ prior treatment history.

Comparative Analysis Between TSN1611 and other clinical-stage KRAS G12D inhibitors

KRAS normally functions as a molecular switch cycling between an active GTP-bound (“ON”) state and an inactive GDP-bound (“OFF”) state. The KRAS G12D mutation is a genetic alteration and disrupts this switching process by impairing intrinsic GTP hydrolysis, thereby causing KRAS G12D-mutant proteins to remain predominantly in the active GTP-bound (“ON”) state, which continuously activates downstream signaling pathways involved in tumor proliferation and survival.

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Based on their binding mode, KRAS G12D inhibitors can be broadly classified into three categories: OFF-state inhibitors, ON-state inhibitors and dual-state (ON/OFF) inhibitors. In normal cells, the KRAS protein acts as a molecular switch, tightly regulating cell growth by cycling between an inactive ‘off-state’ and an active ‘on-state.’ The KRAS G12D mutation is a genetic alteration that impairs the normal GTP hydrolysis cycle of KRAS, causing the mutant KRAS protein to remain predominantly in its active, GTP-bound “on” state. This continuous activation drives uncontrolled cellular proliferation and tumor growth. Our therapeutic candidates are designed to specifically target and inhibit this aberrant ‘on-state’ of the KRAS G12D mutant protein to halt disease progression.

OFF-state inhibitors are designed to bind the inactive, GDP-bound conformation and may benefit from relatively more defined binding pockets, which could support stable target engagement. However, their activity may be limited by the lower proportion of the inactive state in KRAS G12D-mutant tumors. In particular, because KRAS G12D-mutant proteins predominantly exist in the ON state, OFF-state inhibitors may not fully block the dominant active signaling state unless the protein transitions into the OFF state. ON-state inhibitors are designed to engage the active, GTP-bound conformation, which is more prevalent in KRAS G12D-driven tumors and therefore may enable direct engagement of the dominant signaling state. However, this approach presents structural and biochemical challenges, including the high affinity of KRAS for GTP and the limited availability of well-defined binding sites. In addition, a single-state inhibitor, whether targeting the ON state or the OFF state, is designed to bind only one conformational state and may become less effective if tumor cells shift KRAS proteins toward the non-targeted state through upstream feedback activation or compensatory signaling pathways.

Dual-state inhibitors are designed to engage both ON and OFF conformations of KRAS G12D, which may allow broader coverage of the KRAS signaling cycle, although this approach may introduce additional challenges in drug design, including maintaining selectivity and optimizing pharmacokinetic properties. TSN1611 is designed as a dual-state (ON/OFF) KRAS G12D inhibitor. By binding both the active ON state and the inactive OFF state, dual-state inhibitors, including TSN1611, may provide more comprehensive blockade of KRAS G12D-driven signaling regardless of the conformational status of the mutant protein. This may potentially result in deeper inhibition of downstream signaling pathways and enhanced anti-tumor activity as compared to single-state inhibition. In addition, because dual-state inhibitors may directly bind active KRAS G12D proteins without requiring the protein to transition into the inactive OFF state, they may potentially achieve faster suppression of downstream signaling pathways and more rapid therapeutic responses. Dual-state inhibition may also reduce the likelihood of adaptive or compensatory resistance mechanisms, because inhibitory activity may be maintained even if tumor cells shift KRAS proteins between ON and OFF conformations. These potential advantages may improve durability of response and prolong disease control, subject to further clinical validation.

Given the absence of head-to-head clinical trials across KRAS G12D inhibitor candidates, direct comparisons of clinical efficacy and safety are not available. Nevertheless, clinical data disclosed from individual trials provide a reference framework for understanding the emerging therapeutic profiles of different candidates.

Based on publicly available data, KRAS G12D inhibitor candidates have demonstrated preliminary clinical activity with efficacy outcomes generally within a comparable range across studies. TSN1611 has reported clinical activity in both NSCLC and PDAC cohorts, whereas some other candidates have disclosed data in more limited patient populations.

In terms of safety, TSN1611 has shown a relatively low incidence of grade ≥ 3 treatment-related adverse events based on available data, suggesting a manageable tolerability profile. With respect to anti-tumor activity, TSN1611 demonstrated an objective response rate (“ORR”) of 44.4% and disease control rate (“DCR”) of 88.9% in NSCLC patients treated at 600 -1,200 mg BID, and an ORR of 34.8% and DCR of 82.6% in PDAC patients treated at 1,200 mg BID. While these results compare favorably with certain publicly reported data for other KRAS G12D inhibitors, no direct conclusions regarding relative efficacy can be drawn in the absence of randomized head-to-head studies.

INDUSTRY OVERVIEW

The following table summarizes publicly reported clinical trial data for key KRAS drug candidates. Please note that this presentation is not intended to be a direct comparison. Because the underlying clinical studies differed significantly in their enrolled patient populations, dosing schedules, sample sizes, and reporting standards, no direct conclusions regarding relative efficacy or safety can be drawn in the absence of randomized, head-to-head clinical trials.

Drug	Binding State	Fastest Clinical Progress	Clinical Trials	Safety data	Trial Design	Testing Group	Efficacy Data
Zoldonrasib	On	III	NCT06040541	TRAE (≥ grade3): 13%	1,200 mg PO QD (N=27)	NSCLC Pts	ORR: 52% (95%CI, 32-71) DCR: 93% (95%CI, 76-99)
INCB161734	On & OFF	III	NCT06179160 2023-507091-47-00 JPRN- jRCT2031240694	TRAE (≥ grade 3): 19.7%	1,200 mg (N=41)	PDAC Pts	ORR: 37% DCR: 78%
					600 mg QD + chemotherapy (N=15)		ORR: 27% DCR: 87%
					1,200 mg QD + chemotherapy (N=8)		ORR: 50% DCR: 88%
HRS-4642	On & OFF	III	NCT05533463 CTR20222279	TRAE (≥ grade3): 23.8%	800 mg Q2W/1,200 mg Q2W (N=38)	NSCLC Pts	ORR: 23.7% (95%CI, 11.4-40.2) DCR: 76.3% (95%CI, 59.8-88.6)
					1,200 mg Q2W (N=24)	PDAC Pts	ORR: 20.8% (95%CI, 7.1-42.4) DCR: 79.2% (95%CI, 57.8-92.9)
GFH375	On & OFF	III	NCT06500676 CTR20242253	TRAE (≥ grade3): 26.8%	400, 600 or 750 mg once daily (N=41)	CRC Pts	ORR: 11.0% (90%CI, 2-24) DCR: 77.0% (90%CI, 63-88)
					600 mg QD (N=59)	PDAC Pts	ORR: 40.7% (90%CI, 30-52) DCR: 96.7% (90%CI, 90-99)
					600 mg QD (N=16)	NSCLC Pts	ORR: 68.8% DCR: 93.8%
RNK08954	OFF	II	NCT06667544 CTR20243722	TRAE (≥ grade 3): 25.5%	400-1,200 mg QD (N=47)	NSCLC Pts	ORR: 42.6% DCR: 95.7%
TSN1611	On & OFF	I/II	NCT06385925 CTR20241863	TRAE (≥ grade 3): 6.3%	600-1,200 mg BID (N=27)	NSCLC Pts	ORR: 44.4% DCR: 88.9%
					1,200 mg BID (N=23)	PDAC Pts	ORR: 34.8% DCR: 82.6%

Note: “Fastest clinical progress” refers to the most advanced clinical development stage reached by each drug candidate across all ongoing clinical programs.

Source: Literature review, ClinicalTrials and Frost & Sullivan Analysis

Entry Barriers and Future Trends

The KRAS G12D inhibitor drug market is characterized by high entry barriers, primarily driven by the scientific difficulty of designing a drug that can bind to KRAS G12D effectively, increasing competition among developers, and the substantial cost and long timelines required for drug development. As the developments of leading drug candidates move forward, the threshold for successful market entry continues to increase.

- **Target-specific drug design and development complexity.** Unlike KRAS G12C, KRAS G12D lacks a druggable cysteine residue, which means that drug developers cannot use the same convenient chemical “anchor” used in certain KRAS G12C drugs. This limits the feasibility of covalent inhibition strategies. In addition, the available binding pockets on KRAS G12D are shallow and can change shape, making it difficult for non-covalent drugs to bind to the target strongly and selectively. This inherent structural constraint, together with the biological heterogeneity of KRAS G12D-driven tumors, particularly pancreatic ductal adenocarcinoma and CRC, requires developers to combine advanced structure-based drug design with biomarker-driven patient selection and clinical trial strategies tailored to specific cancer types. These requirements create substantial technical and execution barriers.
- **Increasing competition and first-mover advantages.** The biological validation of KRAS as an oncogenic driver has attracted global R&D investment, leading to a growing number of KRAS-targeted programs across development stages. As existing players advance earlier into clinical development, they accumulate first-mover advantages in clinical data, development experience and strategic positioning. Consequently, new entrants face an increasingly high bar to demonstrate clear differentiation in efficacy, safety or combination potential, further raising market entry thresholds.

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- *High R&D costs and long development timelines.* The development of KRAS G12D inhibitors typically requires substantial capital investment and extended development cycles, driven by intensive preclinical optimization, biomarker-driven clinical trial designs, and iterative molecular refinement. In practice, this means that developers may need to repeatedly optimize the drug molecule, select suitable patient groups based on biomarkers, and adjust clinical development plans as data become available. These factors collectively increase financial barriers and may limit the ability of smaller or less-resourced players to enter the market.

Going forward, the development of the KRAS G12D inhibitor drug market will be characterized by the following trends.

- *Development of multi-candidate R&D platforms and diversified KRAS G12D therapeutic approaches.* Industry focus is gradually shifting from single-asset programs to broader R&D platforms capable of generating multiple drug candidates through standardized and scalable discovery and development capabilities. At the same time, KRAS G12D drug development is moving beyond conventional oral small-molecule inhibitors toward approaches that combine KRAS G12D target biology with multiple therapeutic modalities and delivery technologies, including ADCs, protein degradation technologies and targeted delivery systems. These approaches may drive market development by improving drug delivery and tumor penetration in difficult-to-treat solid tumors, such as PDAC and CRC, where dense tumor tissue and limited drug permeability can make it harder for a drug to reach cancer cells effectively. These approaches may also enhance R&D efficiency through reusable discovery platforms, payloads and linker technologies, and enable companies with integrated capabilities to expand pipelines, diversify development risk and pursue broader commercialization opportunities, including global collaboration and out-licensing arrangements.
- *Increasing focus on combination therapy strategies.* Future development of the KRAS G12D inhibitor drug market is increasingly centered on combination treatment approaches, including combinations with chemotherapy and monoclonal antibodies, as monotherapy may face limitations related to resistance and incomplete pathway suppression. Combination strategies are being actively explored to enhance therapeutic efficacy, delay resistance development and broaden clinical applicability across multiple tumor types. In other words, a KRAS G12D inhibitor may be more effective if used together with other treatments that attack the cancer through different mechanisms. This shift reflects the industry’s growing recognition that durable clinical benefit in KRAS-driven cancers is more likely to be achieved through rational combination regimens rather than single-agent therapies. KRAS G12D inhibitors that demonstrate a tolerable safety profile have the potential to serve as a foundational component for combination therapies.
- *Expansion toward innovative mechanisms and delivery platforms.* Given the complexity of KRAS G12D-driven tumor biology and associated resistance mechanisms, ADC-based approaches targeting KRAS G12D-expressing cells are increasingly viewed as a rational strategy to enhance therapeutic efficacy while mitigating systemic toxicity. ADCs are designed to deliver a therapeutic payload more selectively to cancer cells, rather than exposing the whole body to the same level of drug activity. By leveraging targeted payload delivery and reducing reliance on continuous suppression of the KRAS signaling pathway alone, these approaches have the potential to improve therapeutic index, address resistance challenges and expand clinical applicability across heterogeneous tumor settings.

OVERVIEW OF STING AGONISTS DRUG MARKET

Overview of Immune Agonists

Immune agonists are a heterogeneous class of immunomodulatory agents designed to actively stimulate innate and/or adaptive immune signaling pathways in order to enhance endogenous anti-tumor immune responses. They primarily act by targeting pattern recognition receptors (such as STING, Toll-like receptors (“TLRs”) and RIG-I) or immune costimulatory receptors (such as CD40, OX40 and 4-1BB), thereby promoting dendritic cell activation, improving antigen presentation and enhancing immune effector cell function. Through activation of immune cells including dendritic cells, macrophages and natural killer (“NK”) cells, immune agonists induce the production of type I interferons (“IFN-I”), IL-12, TNF- α and other immune mediators, strengthen T-cell priming and activation, and modulate the tumor immune microenvironment.

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Despite mechanistic validations in preclinical studies, earlier generations of immune agonists have delivered limited clinical success, largely due to challenges in achieving sufficient tumor-localized immune activation while avoiding systemic inflammation and toxicity. These outcomes, however, reflect limitations of earlier delivery strategies and molecular designs, rather than a lack of biological relevance of immune agonism itself. As a result, immune agonists continue to be regarded as a strategically important class of agents, awaiting enabling technologies evolve to better control spatial and temporal immune activation.

Mechanism of Action and Development Evolution of STING Agonists

STING agonists represent one of the most extensively studied and biologically validated subclasses of immune agonists. They are designed to activate the cGAS–STING signaling axis to enhance innate immune activation within the tumor microenvironment. Upon STING activation, downstream signaling through TBK1 and IKK leads to activation of IRF3 and NF-κB, inducing transcription of type I interferons and pro-inflammatory cytokines such as IFN-I and IL-6. This cascade promotes dendritic cell maturation and antigen presentation, thereby facilitating the priming and activation of cytotoxic T cells and strengthening adaptive anti-tumor immunity. Through coordinated activation of innate and adaptive immune responses, STING agonists have the potential to convert immunologically “cold” tumors into immune-inflamed states and enhance the efficacy of cancer immunotherapy.

The development of STING agonists has progressed across multiple technological waves. Early STING agonists, primarily CDNs that mimic endogenous cGAMP, demonstrated innate immune activation and anti-tumor efficacy in preclinical settings; however, clinical translation has been constrained by poor pharmacokinetics, limited tissue penetration and systemic inflammatory toxicity. Subsequent non-CDN small molecule STING agonists were developed to improve drug-like properties and enhance controllability of STING activation; however, achieving sufficiently tumor-selective immune activation remains challenging.

More recent strategies focus on dual mechanism approaches, including STING agonist–antibody drug conjugates (“ADCs”) and dual-mechanism small molecules, which are designed to enhance tumor targeting, confine immune activation to the tumor microenvironment and mitigate systemic toxicity. These advances address key limitations observed in earlier approaches and support the view that, despite historical setbacks, STING agonists, particularly those incorporating dual mechanisms of action.

Competitive Landscape

As of the Latest Practicable Date, there was no approved STING agonists drug globally. The following table sets forth the clinical-stage STING agonists candidates globally.

Drug	Company	Indication	Latest status	Therapeutic strategy	Country/region	First posted date
Ulevostinag	MSD	Recurrent Head and Neck Squamous Cell Carcinoma	Phase II	Mono/Combo with Intravenous	US, EU, Other Regions	2019-12-12
JMKX000197	Jiangxi Jimincare Group	Malignant Pleural Effusion	Phase II	Mono	China	2026-06-15
Dazostinag	Takeda, Curadev Pharma	Advanced or Metastatic Solid Tumors	Phase I/II	Mono/Combo With Pembrolizumab	China, US, Japan, EU, Other regions	2020-06-09
TSN222	Tyligand	Advanced Solid Tumors or Lymphomas	Phase I/II	Mono	China	2023-04-03
DN015089	Shanghai De Novo Pharmatech	N/A	Phase I	Mono	China	2021-10-27
BI 1703880	Boehringer Ingelheim	Solid Tumor	Phase I	Mono	US, Japan, EU,	2022-07-25
KL340399	Sichuan Kelun-Biotech Biopharmaceutical	Advanced Solid tumors	Phase I	Mono	China	2022-07-27
CRD3874	Curadev Pharma	Solid Tumors, AML,	Phase I	Mono	US	2023-09-01
LNP3693	Lupin	Solid tumors and hematological cancers	Phase I	Mono	US	2023-10-26
INCB161734	Incyte Corporation	Advanced Solid tumors, Endometrial cancer, CRC, PC, NSCLC	Phase I	Combo With IO	US, Japan, EU, Other Regions	2023-12-21
cGAMP-ONM-501	OncoNano Medicine	Advanced Solid Tumors and Lymphomas	Phase I	Mono/Combo with Cemiplimab	US, Other regions	2025-05-06

Source: CDE, ClinicalTrials, and Frost & Sullivan Analysis

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Entry Barriers and Future Trends

The STING agonist drug market has following major entry barriers.

- *High druggability and translational challenges.* STING agonists face fundamental druggability constraints and material translational hurdles from preclinical models to human studies. While innate immune activation and antitumor signals have been observed in early research, consistently achieving tumor-restricted immune activation with an acceptable tolerability profile in humans remains challenging, contributing to a relatively low overall translation efficiency.
- *High development cost and clinical risk.* The development of STING agonists typically requires extensive optimization across molecular design and clinical development strategy, which drives R&D expenditure and prolonged timelines. In addition, clinical risk is elevated by the need to balance efficacy with systemic inflammatory toxicity considerations, and the growing emphasis on combination strategies can further increase development complexity, cost and failure risk.
- *Crowded pipeline and high bar for differentiation.* The STING agonist landscape is increasingly competitive, with numerous ongoing development programs. Against this backdrop, differentiation, particularly in terms of efficacy and safety, is critical, and the competitive intensity raises the threshold for new entrants to demonstrate clear advantages in mechanism, delivery, tolerability and/or clinical outcomes.

Going forward, the development of the STING agonist drug market will be characterized by the following trends.

- *Expansion of combination therapy strategies.* STING agonists are increasingly being evaluated in combination regimens to improve response depth and durability and to expand clinical applicability across tumor types, reflecting the industry’s focus on positioning STING activation within multi-modality oncology treatment paradigms.
- *Advancement of delivery systems.* Ongoing efforts are focused on improving delivery approaches to address limitations observed in earlier STING agonist programs, including enhancing tumor localization and controlling the site and magnitude of immune activation to mitigate systemic toxicity risks.
- *Diversification of technological approaches.* The development of STING agonists is increasingly shifting toward non-nucleotide small molecules, dual-mechanism compounds and STING-based ADCs, reflecting a diversification of technological approaches. This multi-modality innovation is expected to continuously enhance STING activation potency, tumor selectivity and drug delivery performance, thereby supporting the advancement of therapeutic designs.

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OVERVIEW OF THE ADC MARKET

Overview of ADC Therapy

ADCs are a class of targeted oncology therapeutics composed of three core components: a monoclonal antibody, a chemical linker, and a highly potent cytotoxic payload. The antibody provides tumor-specific targeting by binding to antigens selectively expressed on cancer cells, the linker controls the stability and release of the payload, and the cytotoxic agent serves as the tumor-killing component.

After binding to tumor cell surface antigens, most ADCs are internalized via endocytosis and trafficked through early and late endosomes before fusion with lysosomes. Within the lysosome, the payload is released through chemical or enzyme-mediated cleavage of the linker, leading to tumor cell apoptosis or death through DNA damage or microtubule disruption. In certain ADCs, membrane-permeable payloads may also induce a bystander effect, enabling the killing of adjacent tumor cells and further enhancing therapeutic efficacy.

ADCs offer several important therapeutic advantages over conventional modalities, including (1) high targeting specificity and selectivity, which reduces off-target toxicity; (2) enhanced cytotoxic potency, as payloads are delivered directly into tumor cells; (3) expanded therapeutic window, which enables improved efficacy and tolerability; and (4) improved resistance management through optimized antibody-payload combinations.

The development of ADCs has progressed through three major technological waves, reflecting continuous improvements in target selection, conjugation technologies and therapeutic scope. The first wave focused primarily on the treatment of hematological cancers, validating the feasibility of antibody-mediated delivery of cytotoxic payloads. However, these early products were constrained by limited payload options and suboptimal safety profiles, which restricted their clinical application. With advances in target selection and conjugation technologies, the second wave expanded into solid tumors with highly and specifically expressed biomarkers, improving clinical efficacy and broadening therapeutic scope. Through optimized linker stability, enhanced bystander effects and improved safety management, third-generation ADCs have demonstrated activity in tumors with both high and low target expression, substantially enlarging the addressable patient population. Looking forward, ADC technology is transitioning toward a next wave of platform-based and functionally integrated formats, featuring bispecific ADCs, dual-payload ADCs, non-cytotoxic targeted payloads, and immune-activating payloads. This evolution marks a shift from the traditional “single-target, single-toxin” paradigm toward a more integrated, multi-functional therapeutic modality, positioning ADCs as an important pillar for future precision oncology.

Market Size of the ADC Market

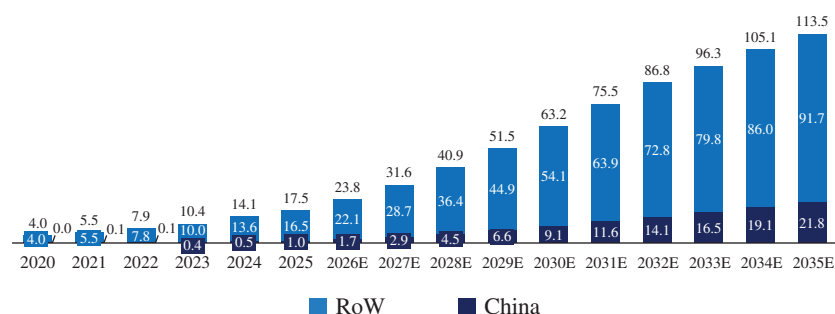
The global ADC market increased from US\$4.1 billion in 2020 to US\$17.5 billion in 2025 representing a CAGR of 33.9%. The market is expected to increase to US\$113.5 billion in 2035 at a CAGR of 20.6% from 2025 to 2035. In China, the ADC market increased from US\$0.02 billion in 2020 to US\$1.0 billion in 2025 at a CAGR of 111.7%, and is expected to increase to US\$21.8 billion in 2035 at a CAGR of 36.1% from 2025 to 2035, outpacing global growth rates.

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Global ADC Market Size and Forecast, 2020-2035E

Period	CAGR		
	China	RoW	Global
2020-2025	111.7%	32.6%	33.9%
2025-2035E	36.1%	18.7%	20.6%

Billion USD



Source: The market data is derived from Frost & Sullivan analysis, which draws on a combination of publicly available information and primary research, including academic publications, sales data of approved products, company disclosures, clinical trial data, and interviews with industry experts.

Entry Barriers and Future Trends

The ADC drug market has following major entry barriers.

- **High R&D and technical barriers.** The development of ADCs involves substantial technical complexity, including antibody selection, linker design for controlled payload release, as well as the screening and validation of novel payloads, especially those of non-cytotoxic nature. Accordingly, successful ADC development typically requires multidisciplinary capabilities across target biology, antibody engineering, medicinal chemistry and translational research, which raises the R&D threshold for new market entrants.
- **Manufacturing complexity and capital-intensive production requirements.** ADC manufacturing is characterized by complex conjugation processes and stringent control requirements, including control of the drug-to-antibody ratio (“DAR”), as well as challenges in process scale-up due to sensitivity to equipment, process parameters and related conditions. Manufacturing requirements are further amplified for ADCs incorporating dual-payload designs or non-traditional targeted payloads, which require more advanced process control and containment systems, as well as higher upfront facility investment.
- **Intensifying competitive landscape.** With the clinical and commercial success of multiple ADC products, the ADC field has attracted extensive participation from global pharmaceutical companies and biopharmaceutical firms. As a result, competition is intensifying across key dimensions such as target selection, payload innovation, manufacturing capabilities and clinical differentiation, increasing the difficulty for late entrants to establish a competitive position.

INDUSTRY OVERVIEW

The future development of the ADC market will be affected by the following trends.

- *Innovation in novel payloads and linker technologies.* While ADCs in current clinical development primarily rely on cytotoxic payloads, such as tubulin inhibitors and topoisomerase inhibitors, with antibody variations, future innovation in payload chemistry and linker technologies is expected to remain a central driver of ADC development. Advances in linker stability, payload potency and controlled release mechanisms are improving the balance between efficacy and safety, thereby enhancing the overall therapeutic index of ADC products. These innovations enable ADCs to deliver antitumor effects while reducing off-target toxicity.
- *Expansion of target coverage and biomarker expression levels.* ADC development is progressively expanding beyond highly expressed tumor antigens toward targets with lower or heterogeneous biomarker expression. Improvements in antibody engineering, linker design and bystander effect mechanisms have enabled newer generations of ADCs to achieve efficacy even in tumors with lower antigen density. This trend enlarges the addressable patient population and extends the clinical applicability of ADC therapies across a wider range of tumor types.
- *Emergence of multi-modal and novel ADC formats.* The ADC field is entering a new stage of structural evolution with the emergence of multi-modal and novel ADC formats, including bispecific ADCs, dual-payload ADCs, non-cytotoxic targeted payloads and immune-activating payloads. These designs transform ADCs from traditional “single-target, single-payload” products into more integrated and functionally diverse therapeutic platforms, creating new opportunities for enhanced efficacy, broader indications and improved treatment durability.

SOURCES OF INFORMATION

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DIRECTORS’ CONFIRMATION

After making reasonable inquiries, our Directors confirm that there has been no adverse change in the market information presented in the F&S Report since the date of the report which may qualify, contradict or have an impact on the information in this document.