

INDUSTRY OVERVIEW

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ONCOLOGY DRUG MARKET

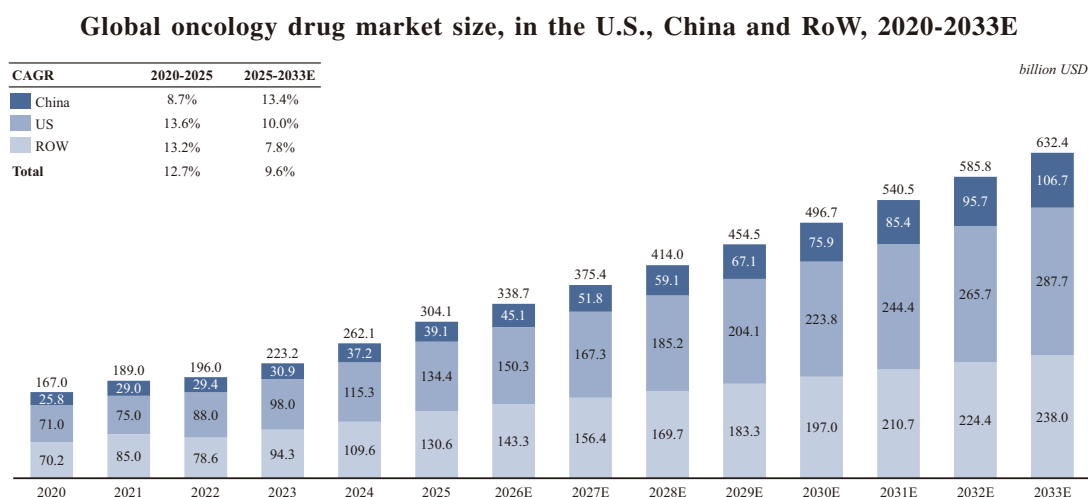
Overview of Oncology Drug Market

Oncology Drug Market Size Globally and in China

The market size of the global oncology drug market increased from US\$167.0 billion in 2020 to US\$304.1 billion in 2025, representing a CAGR of 12.7% during the period. The market size of the global oncology drug market is expected to increase to US\$632.4 billion by 2033, representing a CAGR of 9.6% from 2025 to 2033.

The market size of the China oncology drug market increased from US\$25.8 billion in 2020 to US\$39.1 billion in 2025, representing a CAGR of 8.7% during the period. The market size of the China oncology drug market is expected to increase to US\$106.7 billion by 2033, representing a CAGR of 13.4% from 2025 to 2033.

The chart below sets out the oncology drug market size globally, in China, the U.S., and the rest of the world from 2020 to 2033.



Source: International Agency for Research on Cancer (IARC), NCCR, NCCN, CSCO, CIC

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Evolution of Cancer Therapy and Small-molecule Drugs

- Shift toward precision oncology. Cancer therapy has evolved from local interventions and systemic chemotherapy to precision oncology, with treatment selection increasingly guided by tumour biology and molecular features.
- Small molecules remain a key treatment modality. Small-molecule drugs continue to play a central role in oncology due to their ability to target intracellular pathways and their suitability for combination regimens.
- Small-molecule innovation is expanding treatment options. New small-molecule approaches are expanding the range of addressable targets and providing additional options to overcome resistance.

Entry Barriers of the Oncology Drug Market

- Regulatory complexity. Oncology drug development is subject to stringent and evolving regulatory requirements, requiring substantial compliance capabilities, extensive documentation and rigorous clinical validation.
- Clinical capability restrictions. Oncology trials depend on specialised clinical infrastructure, biomarker-driven patient recruitment and established investigator networks, creating high execution barriers for new entrants.

Drivers and Development Trends of Oncology Drug Market

- Increasing focus on key signalling pathways. Oncology R&D is increasingly centred on major signalling pathways to identify new targets and therapeutic opportunities.
- Increasing development of combination therapies. Combination strategies are being advanced to enhance efficacy, delay resistance and broaden clinical applicability.
- Continued optimisation of drug profiles. Developers are seeking improved efficacy, safety and tolerability to enhance product differentiation within established mechanisms.
- Growing interest in novel mechanisms. New therapeutic approaches are being explored to address difficult-to-treat genetic alterations and unmet needs beyond established targets.
- Advanced platforms supporting more efficient drug development. Technology-enabled platforms are helping improve discovery and development efficiency for oncology therapies.

Market Challenges of the Oncology Drug Market

- Pricing pressure. Intensifying payer cost controls, government price negotiations and biosimilar competition are compressing pricing power and reducing returns on oncology innovation.
- Increasing drug resistance in patients. The frequent emergence of acquired resistance shortens product durability and forces companies to continuously develop next-generation therapies.

MARKET POTENTIAL OF SHP2 INHIBITOR

SHP2

Overview of SHP2

SHP2 is a signalling protein involved in multiple intracellular pathways, including RAS/ERK, PI3K/AKT and JAK/STAT, and plays an important role in regulating cell growth, survival and migration. In oncology, SHP2 has attracted increasing interest as a therapeutic target due to its role in tumour-related signalling across multiple cancer types, particularly those associated with dysregulated MAPK pathway signalling.

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SHP2 inhibitors are also being actively explored in combination therapies, particularly with KRAS inhibitors and receptor tyrosine kinase-targeted therapies such as EGFR-TKIs. Such combinations may improve treatment response and help address certain resistance mechanisms, and are supported by mechanistic rationale, pre-clinical findings and ongoing clinical evaluation. Exploratory combinations with immunotherapies are also under investigation.

Development Challenges and Market Threats for SHP2 Inhibitors

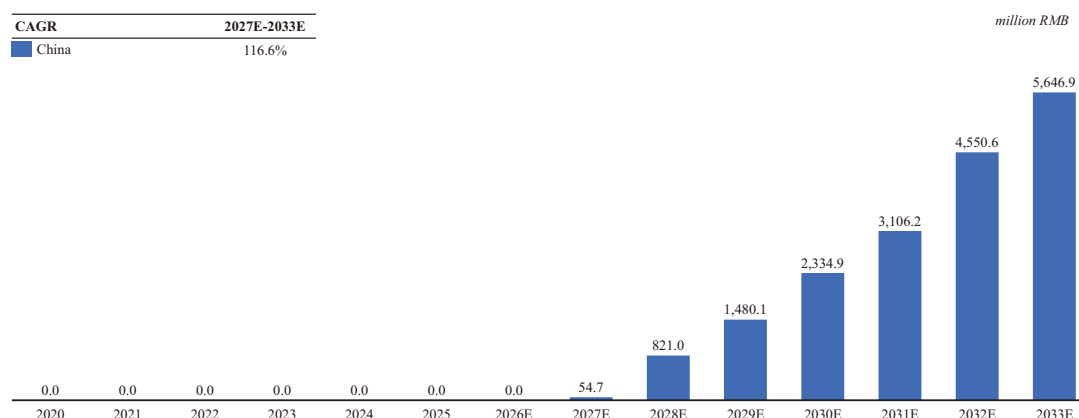
- **Drugability and biological complexity.** SHP2 presents significant development challenges due to its conserved phosphatase structure, selectivity difficulties, suboptimal drug-like property requirements and context-dependent biological functions, all of which complicate inhibitor design and clinical development.
- **Selectivity and safety risks.** Structural homology with other phosphatases and SHP2’s broad physiological roles increase the risk of off-target toxicity and unpredictable adverse events.
- **Late-entrant competition.** Later entrants may face meaningful commercial disadvantage once first-in class therapies establish guideline positioning, physician adoption and payer access.

SHP2 Inhibitors Market Size in China

The market of SHP2 inhibitors in China is expected to exist commencing from 2027. The market size is expected to increase from RMB54.7 million in 2027 to RMB5,646.9 million in 2033, representing a CAGR of 116.6%. According to CIC, by 2033, KRAS inhibitor-based combinations and EGFR-TKI-based combinations are estimated to account for approximately 60% and 24%, respectively, of the overall market potential of SHP2 inhibitor-based regimens, while the remaining market potential is expected to be distributed across other SHP2 inhibitor-based therapeutic settings.

The chart below sets out the SHP2 inhibitors market size in China, from 2027 to 2033.

SHP2 inhibitors market size in China



Source: Annual reports, NMPA, CIC

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Competitive Landscape of SHP2 Inhibitors

The table below sets out the global competitive landscape of SHP2 inhibitors as of the Latest Practicable Date.

Drug	Company	Target	Treatment	Globally Most Advanced Indications	Highest Clinical Stage	First Posted Date	Location
Sitnepatofib	Jacobio	SHP2	Combo with glecirasib	KRAS ^{G12C} mutated locally advanced or metastatic NSCLC	Phase III	2024-05-14	China
GH21	Our Company	SHP2	Combo with Garsorasib	KRAS ^{G12C} mutated solid tumour incl. NSCLC	Phase II	2025-12-31	China
ERAS601	Erasca	SHP2	Combo with ERKi	Advanced or metastatic solid tumour	Phase I/II	2021-04-29	Global excl. China
BR790	Qingfeng / Gopherwood	SHP2	Combo with Tislelizumab	Solid tumour incl. NSCLC, CRC, esophageal squamous cell carcinoma, head/neck squamous cell carcinoma, etc.	Phase I/II	2022-07-20	China
RG001	Ringene	SHP2	Mono	Advanced malignant solid tumour	Phase I	2021-08-20	China
ET0038	Etern	SHP2	Mono	Advanced solid tumour	Phase I	2021-09-29	Global
ICP189	Nocturne	SHP2	Mono	Advanced solid tumour	Phase I	2022-03-11	China
HS-10381	Hansoh	SHP2	Mono	Advanced solid tumour	Phase I	2022-04-18	China
HMP1415S1	Hutchison	SHP2	Mono	Advanced malignant solid tumour	Phase I	2023-04-20	China
MK0472	Merck	SHP2	Mono / Combo with MK3475 / Combo with MK1084	Advanced or metastatic solid tumour	Phase I	2023-05-10	Global excl. China

Source: FDA, NMPA, clinicaltrials.gov, CDE, CIC

The table below sets out the competitive landscape of key SHP2 inhibitors, namely, GH21, BBP-398 and Migoprotafib (ERAS-601).

Product	GH21	BBP-398	Migoprotafib (ERAS-601)
Target	SHP2	SHP2	SHP2
Clinical stage	Phase 1 monotherapy study	Phase 1 (dose-escalation 1a + dose-expansion 1b)	Phase 1a open-label dose-escalation/expansion study
Enrolled indications	Advanced solid tumour mainly including NSCLC, CRC, HNSCC, ESC	Advanced solid tumours harbouring MAPK-pathway mutations	Locally advanced or metastatic solid tumours
Prior-treatment status	Heavily pretreated advanced solid tumour population	Heavily pretreated advanced solid tumours	Heavily pretreated advanced solid tumours
Regimen	GH21 monotherapy : Two dose regimens, QD and BIW D1D2, were explored in dose escalation part with 3–30 mg QD and 18–30 mg BIW D1D2	BBP-398 monotherapy : QD: 350–550 mg QD in phase 1a; expansion at 350 mg and 450 mg QD in phase 1b	ERAS-601 monotherapy : 10–150 mg QD; MTD 100 mg, RP2D 60 mg QD
Enrolled patient number	70	72	56
Efficacy	Overall DCR 41.7% (25/60): <ul style="list-style-type: none"> KRAS^{G12C} NSCLC: DCR 60% (1 PR + 5 SD /10) EGFR-mut/high NSCLC: DCR 57% (4 SD /7) HNSCC: DCR 100% (4 SD /4) ESC: DCR 75% (3 SD /4) In the 9 mg QD cohort, 15/22 (68.2%) achieved SD, with longest SD about 13 months	Phase 1a: 26% SD among 23 evaluable; mPFS1.8 mo Phase 1b: 30% SD among 27 evaluable; SD 31% at 350 mg and 27% at 450 mg; mPFS2.2 mo (350 mg) and 1.9 mo (450 mg)	10/56 SD (18%)
Safety	Reported no DLTs, and no TRAEs leading to dose reduction, discontinuation, or death; 9 mg QD described as having favourable safety/tolerability	Acceptable safety profile up to 450 mg QD; dose escalation to 550 mg was halted due to increased thrombocytopenia and edema	Generally well tolerated; most frequent AEs were diarrhoea, peripheral edema, dyspnea, anaemia, constipation, fatigue, AST increase, platelet count decrease
Source	ASCO 2025	NPJ Precision Oncology 2026	Molecular Cancer Therapeutics 2025

Source: ASCO 2025, NPJ Precision Oncology 2026, Molecular Cancer Therapeutics 2025, Clinicaltrials.gov

Market Drivers and Trends of the SHP2 Inhibitor Market

- Precision pathway targeting. Biomarker-driven patient selection is supporting the development of more targeted SHP2 therapies for tumours with high SHP2 pathway dependence.
- Combination therapy synergy. SHP2 inhibitors are emerging as important combination partners with KRAS^{G12C} inhibitors and EGFR-TKIs by helping overcome bypass signalling and treatment resistance.

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- Accelerated approval. Expedited regulatory pathways for SHP2 programs addressing high unmet needs are helping accelerate clinical development and potential commercialisation.

SHP2 Inhibitors in Oncology: Rationale for Targeting the MAPK Pathway

Overview of MAPK Pathway

The MAPK pathway is a conserved signalling cascade comprising RAS, RAF, MEK and ERK, and plays a key role in regulating cell proliferation, differentiation, survival and apoptosis. Activation of this pathway begins with upstream receptor stimulation and sequentially transmits signals through RAS, RAF, MEK and ERK to intracellular effectors. According to CIC, RAS is one of the most frequently mutated oncogenes and is mutated in about one-third of cancers, while KRAS is the most commonly mutated RAS isoform and is found in over 20% of all human cancers.

Overview of KRAS-mutated Cancers

KRAS is a small GTPase that cycles between inactive and active states and transmits signals through the MAPK pathway and other downstream routes. KRAS mutations impair normal GTP hydrolysis and result in persistent downstream pathway activation, thereby promoting tumour initiation and progression.

KRAS mutations are particularly common in PDAC, CRC and NSCLC. Mutation subtypes vary by tumour type, with KRAS^{G12D} being most common in PDAC and CRC, and KRAS^{G12C} being the predominant subtype in NSCLC. Across KRAS-mutated adenocarcinomas overall, KRAS^{G12C} is the most common variant, accounting for approximately 40% of KRAS-mutated cases.

Major Indications for SHP2 Inhibitors

KRAS^{G12C} Mutated NSCLC

Overview of NSCLC

Within NSCLC, adenocarcinoma and squamous cell carcinoma are the two most common subtypes. In the Chinese population, adenocarcinoma, squamous cell carcinoma and other histologies account for approximately 71%, 28% and 1% of NSCLC, respectively. In the U.S., the approximate distribution is 57%, 28% and 15%, respectively. From a molecular perspective, NSCLC is biologically diverse and can be further characterised by distinct genomic alterations that contribute to tumour initiation and progression, including mutations affecting key oncogenic signalling networks such as the KRAS/ERK/MAPK pathway as well as EGFR mutations, among others. This underlying heterogeneity has become an important framework for understanding disease biology and informing clinical research and drug development in NSCLC.

According to CIC, NSCLC accounted for approximately 85% of total lung cancer incidence. Among all NSCLC patients, approximately 70% were advanced NSCLC patients. Among advanced NSCLC patients, approximately 60% were AGA-positive. Of such NSCLC patients in China, approximately 19% had MAPK-activated pathway mutations, approximately 4.5% had KRAS^{G12C} mutations, and approximately 50% had EGFR mutations.

Incidence of KRAS^{G12C} Mutated NSCLC in China

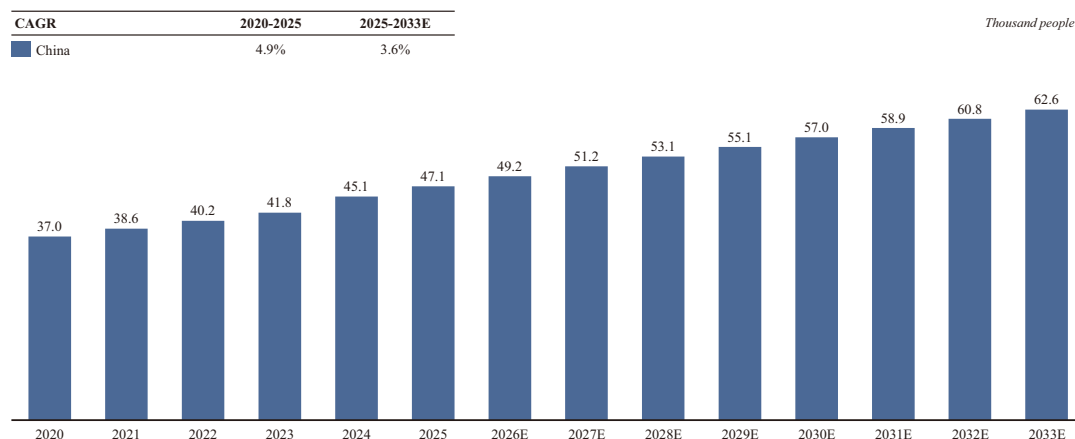
In NSCLC, KRAS mutations accounted for approximately 10.3% of incidence in China. KRAS^{G12C} is among the most clinically important KRAS mutation subtypes in NSCLC given its meaningful prevalence and therapeutic relevance. In 2025, KRAS^{G12C} mutated NSCLC accounted for approximately 4.5% in China.

The incidence of KRAS^{G12C} mutated NSCLC in China increased from 37.0 thousand in 2020 to 47.1 thousand in 2025, representing a CAGR of 4.9% during the period. The incidence of KRAS^{G12C} NSCLC in China is expected to increase to 62.6 thousand by 2033, representing a CAGR of 3.6% from 2025 to 2033.

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The chart below sets out the incidence of KRAS^{G12C} mutated NSCLC in China, from 2020 to 2033.

Incidence of KRAS^{G12C} Mutated NSCLC in China, 2020–2033E

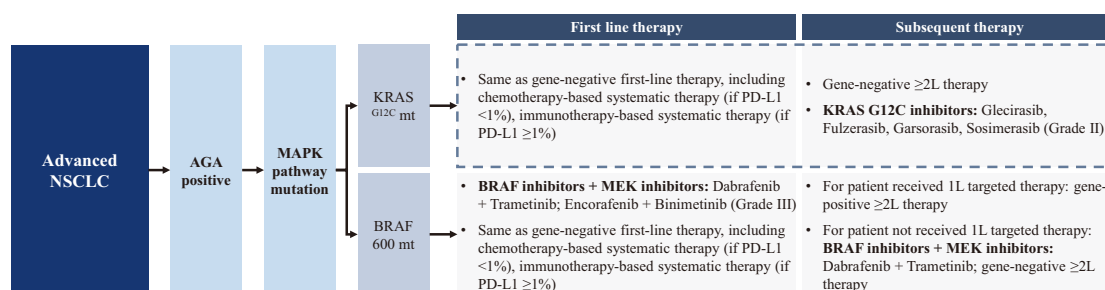


Source: GLOBOCAN, WHO, CIC

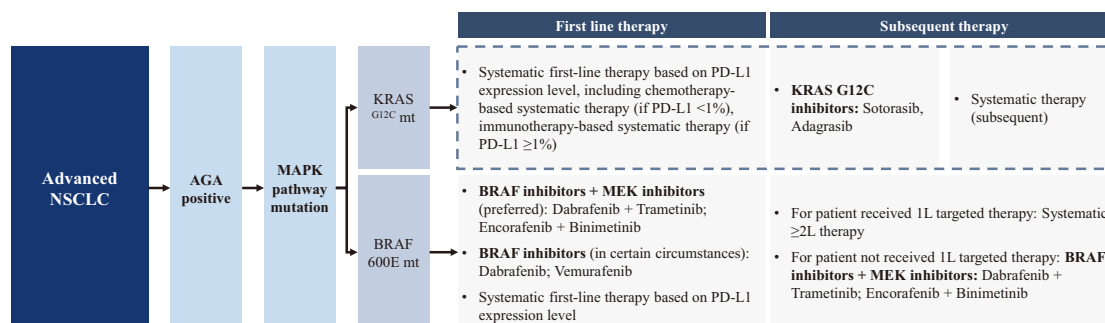
Treatment Paradigm and Clinical Unmet Needs for KRAS^{G12C} Mutated NSCLC

Treatment frameworks for advanced NSCLC incorporate KRAS mutation status within standard systemic therapy algorithms. The first line treatment in both the U.S. and China is generally chemotherapy- or immunotherapy-based systematic therapy, and KRAS^{G12C} inhibitors are only recommended to use for the subsequent therapy.

Treatment paradigm of MAPK pathway mutated NSCLC, CSCO



Treatment paradigm of MAPK pathway mutated NSCLC, NCCN



Source: NCCN, CSCO, CIC

Despite meaningful progress, current KRAS^{G12C} targeted therapy still faces substantial unmet needs. Among advanced NSCLC patients with KRAS^{G12C} mutations, approximately 90% had failed first-line (or 1L) therapy, approximately 25% had failed 1L therapy and received KRAS^{G12C} inhibitors

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as second-line (or 2L) therapy, and approximately 50% had failed KRAS^{G12C} inhibitors as 2L therapy. Across studies, most patients ultimately develop resistance with disease progression, underscoring the need for more durable disease control and rational combination strategies that can delay or overcome resistance mechanisms. Clinical benefit from single agent KRAS^{G12C} inhibition has been viewed as constrained in depth and durability in routine practice, and positioning has largely remained in second line and later, leaving an ongoing need to improve outcomes earlier in the treatment course.

The Company intends to position the GH21’s combination with Garsorasib (“GH21-KRASI CoTx”) for NSCLC patients harbouring KRAS^{G12C} mutations, with an addressable market of approximately 47.1 thousand incident cases in China in 2025, representing approximately 4.5% of overall NSCLC incidences.

KRAS^{G12C} Mutated CRC

Overview of CRC

CRC arises in the colon or rectum and is described as the third most common malignancy globally. In China, diagnosis frequently occurs at advanced stages due to non-specific early symptoms, with more obvious manifestations such as blood in the stool, palpable abdominal mass and persistent pelvic or lower-abdominal pain appearing as disease progresses.

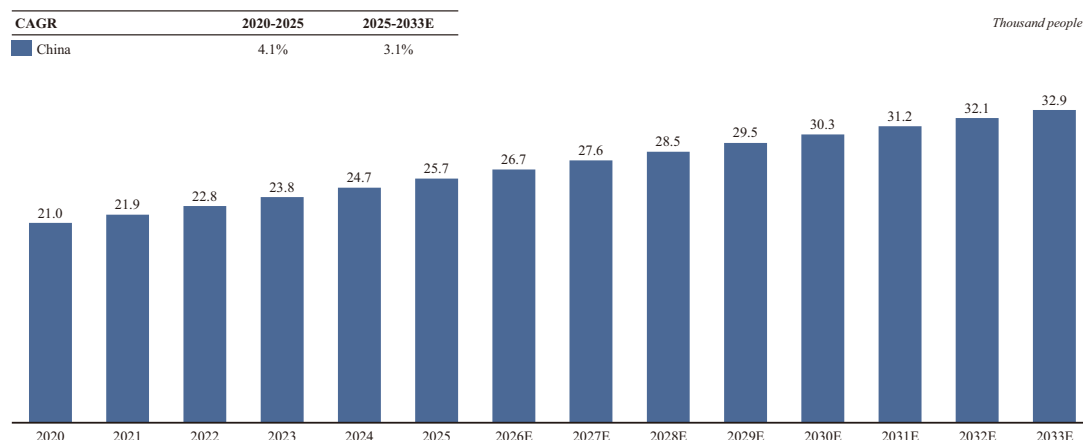
KRAS are commonly detected in advanced CRC in up to 40–50% of all CRC cases. The KRAS^{G12C} mutation shows minor racial or regional differences and accounts for approximately 3%–4% of CRC incidence.

Incidence of KRAS^{G12C} Mutated CRC in China

The incidence of KRAS^{G12C} mutated CRC in China increased from 21.0 thousand in 2020 to 25.7 thousand in 2025, representing a CAGR of 4.1% during the period. The incidence of KRAS^{G12C} CRC in China is expected to increase to 32.9 thousand by 2033, representing a CAGR of 3.1% from 2025 to 2033.

The chart below sets out the incidence of KRAS^{G12C} mutated CRC in China, in 2020 to 2033.

Incidence of KRAS^{G12C} Mutated CRC, in China, 2020–2033E



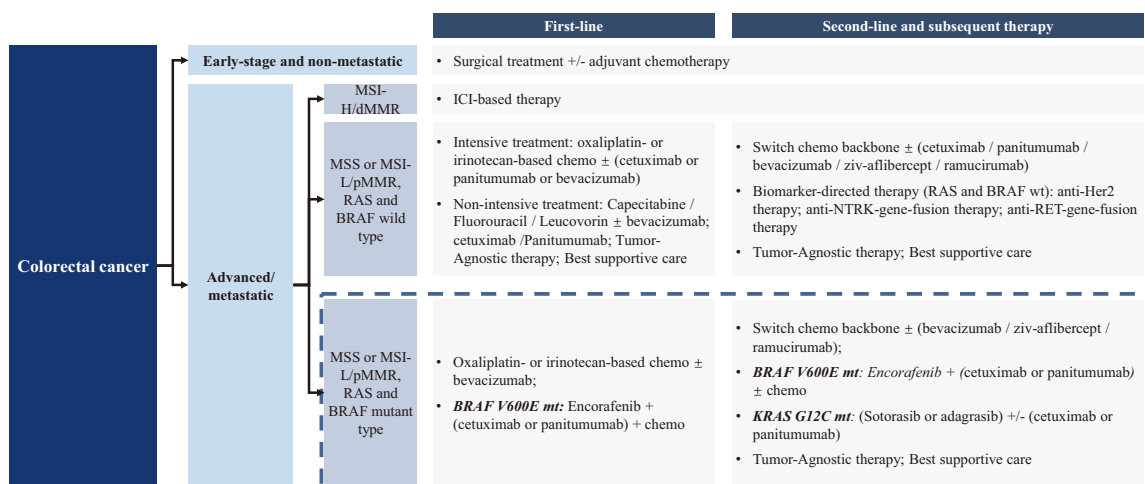
Source: GLOBOCAN, WHO, CIC

Treatment Paradigm and Unmet Clinical Needs for KRAS^{G12C} Mutated CRC

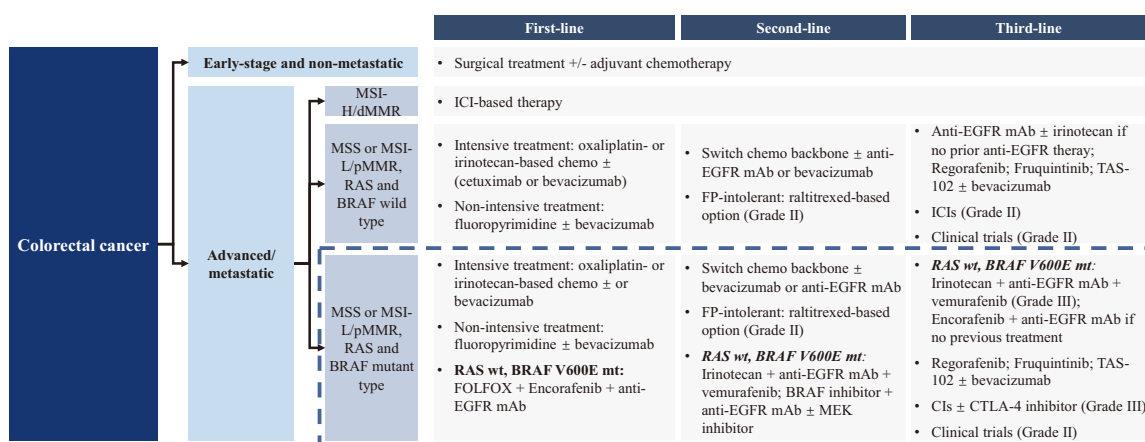
For early-stage and non-metastatic disease, treatment typically comprises surgery and adjuvant chemotherapy. For advanced or metastatic disease, systemic regimens are stratified by tumour biology and treatment intensity. For first-line therapy, CSCO recommend doublet or triplet chemotherapy with or without bevacizumab. In second-line and beyond, CSCO prioritises chemotherapy with or without bevacizumab or regorafenib/trifluridine-tipiracil in second-line and beyond, without KRAS^{G12C} inhibitor formal approval in China.

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Treatment Paradigm of CRC, NCCN



Treatment Paradigm of CRC, CSCO



Source: NCCN, CSCO, CIC

In the U.S., KRAS^{G12C} inhibitors are approved only from 2L onward, leaving 1L reliant on chemotherapy with or without bevacizumab. In China, no KRAS^{G12C} inhibitors hold approval for CRC, compelling reliance on non-targeted chemotherapy regimens and exposing critical access gaps. However, in the US, although KRAS^{G12C} inhibitor combinations with EGFR inhibitors elevate ORR to 26-62.5% and mPFS to 3.9-8.1 months in pretreated KRAS^{G12C}-mutated CRC compared to monotherapy's 7.1-29.1% ORR and 4-5.6 months mPFS, substantial unmet needs endure, including curtailed response durability (mOS around 10-13 months), high G3-4 TRAE rates (22%-45%), and both primary resistance through EGFR-mediated MAPK pathway reactivation plus acquired resistance from secondary KRAS mutations or RTK amplifications. These gaps underscore the pressing demand for therapies offering sustained disease control, refined biomarkers for optimal sequencing and partner selection, and options viable earlier in treatment lines beyond late-stage use.

The Company intends to position the GH21-KRASi CoTx for CRC patients harbouring KRAS^{G12C} mutations, with an addressable market of approximately 25.7 thousand incident cases in China in 2025, representing approximately 4.4% of overall CRC incidences.

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KRAS^{G12C} Mutated Pancreatic Ductal Adenocarcinoma (“PDAC”)

Overview of PDAC

PDAC, accounting for approximately 90% of pancreatic cancers, is presented as one of the most lethal malignancies, with a 5-year survival rate of only 13%. Surgical resection is described as the only curative option. However, only a minority of patients present with resectable disease at diagnosis, and in China more than 80% of patients are diagnosed at an advanced stage. This reflects limited effective treatment options.

Reported risk factors include smoking, type II diabetes, chronic pancreatitis, family history of pancreatic cancer or pathogenic variants, obesity, older age and heavy alcohol consumption.

Incidence of KRAS^{G12C} Mutated PDAC in China

In PDAC, KRAS mutations accounted for approximately over 80% of incidence and KRAS^{G12C} represents approximately 1% to 3% of all PDAC cases.

The incidence of KRAS^{G12C} PDAC in China increased from 2.6 thousand in 2020 to 2.9 thousand in 2025, representing a CAGR of 2.2% during the period. The incidence of KRAS^{G12C} PDAC in China is expected to increase to 3.4 thousand by 2033, representing a CAGR of 1.7% from 2025 to 2033.

Treatment Paradigm and Clinical Unmet Needs for KRAS^{G12C} Mutated PDAC

Treatment of PDAC is primarily determined by disease stage and resectability. For most patients with advanced or metastatic disease, systemic chemotherapy remains the standard of care, while targeted treatment options remain limited.

Currently, there is no approved KRAS^{G12C} inhibitor specifically for KRAS^{G12C} mutated PDAC in China, leaving chemotherapy as the dominant option across lines. In the U.S., KRAS^{G12C} targeted therapy remains principally a post chemotherapy consideration in previously treated KRAS^{G12C} mutated PDAC patients rather than routine 1L use.

The Company intends to position the GH21-KRASi CoTx for PDAC patients harbouring KRAS^{G12C} mutations, with an addressable market of approximately 2.9 thousand incidences in China in 2025, representing approximately 2.6% of overall PDAC incidences.

Overview of treatment path of pancreatic cancer, NCCN

Locally Advanced or Metastatic Pancreatic Cancer	Performance Status	Good	Intermediate	Poor
	First-line treatment	<ul style="list-style-type: none"> AG (Gemcitabine + Albumin-bound Paclitaxel) ± Cisplatin FOLFIRINOX NALIRIFOX Gemcitabine monotherapy Gemcitabine + Capecitabine Gemcitabine + Erlotinib 	<ul style="list-style-type: none"> AG (Gemcitabine + Albumin-bound Paclitaxel) Gemcitabine monotherapy Capecitabine monotherapy Only for metastatic pancreatic cancer <ul style="list-style-type: none"> CAPEOX FOLFIRI FOLFOX 	<ul style="list-style-type: none"> Palliative and Best Supportive Care Gemcitabine monotherapy PD-1/PD-L1 immune checkpoint inhibitors (MSI-H/dMMR)
	Second-line treatment	<ul style="list-style-type: none"> Re-use 1L regimen if relapse >6mo post-adjuvant therapy For 1L using Gemcitabine-based regimen, 2L treatment with 5-FU-based regimen recommended, vice versa 		<ul style="list-style-type: none"> Palliative and Best Supportive Care For 1L using 5-FU-based regimen, 2L treatment with Gemcitabine monotherapy recommended

		<ul style="list-style-type: none"> Use 1L unused regimen for 2L treatment PD-1/PD-L1 immune checkpoint inhibitors (MSI-H/dMMR) Adagrasib/Sotorasib (KRAS G12C mutation-positive) Only for locally advanced pancreatic cancer: <ul style="list-style-type: none"> Induction Chemotherapy; Chemoradiation; Clinical trials
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Overview of treatment path of pancreatic cancer, CSCO

Locally Advanced Pancreatic Cancer		• Best Supportive Care; Transformative Radiotherapy; Interventional Therapy; Palliative Chemotherapy, Traditional Chinese Medicine	
Locally Advanced or Metastatic Pancreatic Cancer	Performance Status	Good	Poor
	First-line treatment	<ul style="list-style-type: none">GEM + Nab-Paclitaxel (AG Regimen)GEM MonotherapyS-1 MonotherapyFOLFIRINOXNALIRIFOXGEM + S-1/ Erlotinib/CAP RegimenGEM + Nimotuzumab (KRAS WT)	<ul style="list-style-type: none">GEM MonotherapyS-1 MonotherapyGEM + Nimotuzumab (KRAS WT)Best Supportive CareClinical TrialsPD-1/PD-L1 immune checkpoint inhibitors (MSI-H/dMMR)
	Second-line treatment	<ul style="list-style-type: none">Nanoliposomal Irinotecan + 5-FU/LV1L Treatment Using Gemcitabine-Based Regimen; 2L Treatment with 5-FU-Based Regimen Recommended, vice versaFor postoperative distant metastasis >6 months after adjuvant therapy, original or alternative chemotherapy may be usedClinical Trials	<ul style="list-style-type: none">GEM MonotherapyFluoropyrimidine-Based Monotherapy ChemotherapyBest Supportive Care
		<ul style="list-style-type: none">Use 1L unused regimen for 2L treatmentPD-1/PD-L1 immune checkpoint inhibitors (MSI-H/dMMR)	

Source: NCCN, CSCO, CIC

Pancreatic cancers are typically diagnosed at advanced stages when the only available treatments are palliative. Around 40% of patients are found to have metastatic disease at the time of diagnosis. For advanced PDAC, typical first-line systemic therapy yields a mOS of around 11 months, depending on regimen and patient selection. Although the Chemo-Radiotherapy for Pancreatic cancer followed by Surgery Study and docetaxel-based triplet (fluorouracil plus leucovorin, oxaliplatin, and docetaxel) improved the rate to 47% and 45%, respectively, it remains an important public health and clinical issue due to its aggressive nature and low survival rate.

Although recent advances in treatment have improved survival outcomes to some extent, clinical outcomes in pancreatic adenocarcinoma remain unsatisfactory compared with many other cancers. The limited efficacy of targeted therapies in this setting continues to highlight significant clinical unmet needs.

EGFR Mutated NSCLC

Overview of EGFR Mutations in NSCLC

EGFR is a receptor tyrosine kinase that regulates key downstream signalling pathways involved in cell proliferation, differentiation and survival. In NSCLC, activating EGFR mutations represent a major molecular subset, with an overall prevalence of approximately 30% globally and close to 50% in China, and are important oncogenic drivers in this disease.

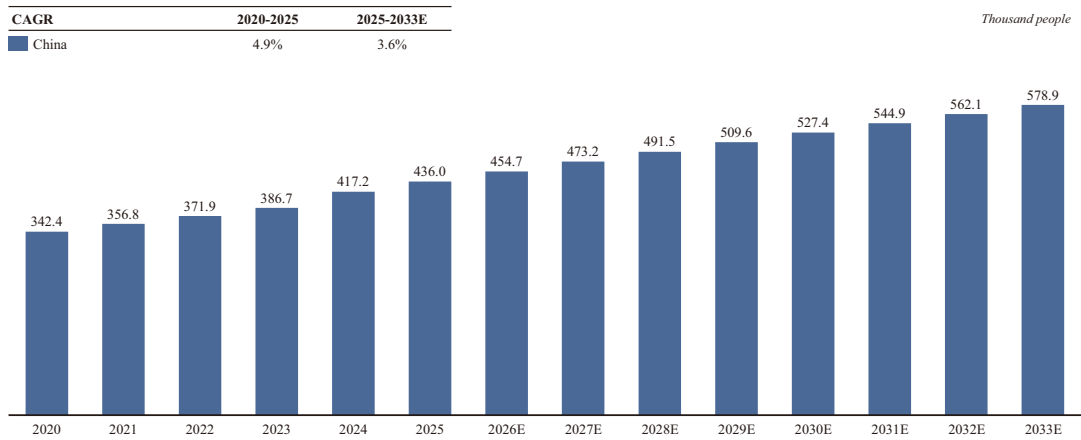
Incidence of EGFR-mutated NSCLC in China

The incidence of EGFR-mutated NSCLC in China increased from 342.4 thousand in 2020 to 436.0 thousand in 2025, representing a CAGR of 4.9% during the period. The incidence of EGFR-mutated NSCLC in China is expected to increase to 578.9 thousand by 2033, representing a CAGR of 3.6% from 2025 to 2033.

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The chart below sets out the incidence of EGFR-mutated NSCLC in China in 2020 to 2033.

Incidence of EGFRmut NSCLC in China, 2020-2033E



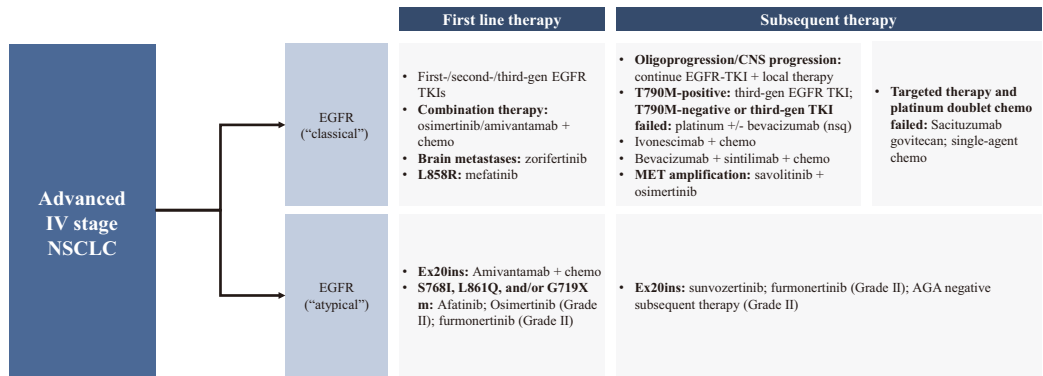
Source: GLOBOCAN, WHO, CIC

Treatment Paradigm and Clinical Unmet Needs for EGFR-mutated NSCLC

For advanced stage IV NSCLC with classical EGFR mutations, category I first-line recommendations include third-generation TKIs (e.g., osimertinib, almonertinib, firmonertinib, befotertinib, rezivertinib, rilertinib), second-generation TKIs (afatinib, dacomitinib) and first-generation TKIs (gefitinib, erlotinib, icotinib), with zorifertinib noted for brain metastases and combination options such as osimertinib plus chemotherapy. Subsequent therapy is determined by progression type. For oligoprogression or CNS progression, continuation of the prior EGFR-TKI with local therapy is recommended. For widespread progression, if first or second generation fails with T790M-positive status, third-generation TKIs are recommended. For T790M-negative or post-third-generation TKI failure, platinum-doublet chemotherapy with or without bevacizumab (non-squamous) is recommended, with additional targeted combinations and re-biopsy to explore resistance mechanisms.

The following table sets out the treatment paradigm for EGFR mutated NSCLC recommended by CSCO.

Treatment paradigm of EGFRmut NSCLC, CSCO



Source: CSCO, CIC

Resistance to EGFR-TKIs is described as inevitable following initial responses. After failure of first or second generation EGFR-TKIs, approximately 50% develop T790M-positive resistance. Among those who are T790M-negative after developing resistance, around 55% exhibit bypass pathway abnormalities (e.g., MET, BRAF, and HER2). Post-progression options, including chemotherapy, targeted therapies and immunotherapy, have generally demonstrated limited outcomes.

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Unmet clinical needs for EGFR-mutated NSCLC include:

- Limited efficacy in certain mutations. While classical EGFR mutations respond well to third-generation TKIs, uncommon variants such as G719X, L861Q and S768I demonstrate comparatively less ideal activity, reflecting molecular heterogeneity. Among advanced NSCLC patients with EGFR mutations, approximately 50% had failed third-generation EGFR-TKIs.
- Drug resistance. Subsequent treatment options following targeted therapy resistance are limited. Chemotherapy-based palliative regimens typically report objective response rates of approximately 30% to 40%, median progression-free survival of 5.3 months and median overall survival of 9.6 months (carboplatin/pemetrexed).

The Company intends to position the GH21’s combination with Osimertinib (“**GH21-EGFR-TKI CoTx**”) for NSCLC patients with EGFR mutations, with an addressable market of approximately 436.0 thousand incidences in China in 2025, representing approximately 41.3% of overall NSCLC incidences.

MARKET POTENTIAL OF ERK1/2 INHIBITORS

ERK Inhibitors and the MAPK Pathway

The MAPK pathway is a conserved signalling cascade regulating cell proliferation, differentiation, apoptosis and other fundamental processes. In the canonical sequence, upstream inputs activate RAS via GEFs, shifting it from a GDP-bound inactive state to a GTP-bound active state. Active RAS recruits and activates RAF, which phosphorylates MEK1/2. MEK then phosphorylates and activates ERK1/2. Activated ERK translocates to the nucleus, where it phosphorylates substrates including RSK, CREB, Elk-1 and NF-κB, altering gene expression and cell-cycle progression.

Dysregulation and mutations in MAPK pathway components are prevalent in solid tumours. KRAS mutations occur in over 20% of all cancers, while BRAF mutations are common in melanoma and papillary thyroid cancer. MEK/ERK alterations are also observed across gastrointestinal and pulmonary malignancies. By directly suppressing ERK signalling, ERK inhibitors (“**ERKi**”) can block pathway reactivation and help overcome resistance to RAF and MEK inhibitors, restoring sensitivity in MEK-resistant settings and improving pathway control. ERK inhibitor classes include ATP-competitive, covalent and allosteric ERK1/2 inhibitors, as well as ERK5 and dual-targeting ERK agents.

MAPK PATHWAY MUTATIONS IN SOLID TUMOURS

See “ — Market Potential of SHP2 Inhibitors — SHP2 Inhibitors in Oncology: Rationale for Targeting the MAPK Pathway — Overview of MAPK Pathway” for details.

Global Competitive Landscape of ERK1/2 Inhibitors

The table below sets out the competitive landscape of ERK1/2 inhibitors globally as of the Latest Practicable Date.

Competitive landscape of ERK1/2 inhibitors globally

Drug	Company	Target	Globally Most Advanced Indications	Highest Clinical Stage	First Posted Date	Location
Ulixertinib	BioMed Valley	ERK1/2	Solid tumour and haematology tumours incl. CNS, MM, Lymphoma, UC, GBM, BC, PC, EOC, Prostate cancer, UCS, Melanoma, ESCC, CRC, GC, BTC, Cell histiocytosis	Phase II	2015-06-08	Global excl. China
Rineterkib	Novartis	ERK1/2	Melanoma	Phase II	2020-06-04	Global excl. China
Beroterkib	Astex	ERK1/2	Advanced solid tumour	Phase I/II	2018-05-09	Global excl. China
ERAS-007	Erasca	ERK1/2	Advanced or metastatic solid tumour	Phase I/II	2021-04-29	US
GH55	Our Company	ERK1/2	Solid tumour	Phase I/II	2022-10-27	China
D3S-002	D3 Bio	ERK1/2	Advanced solid tumours with MAPK pathway mutations	Phase I/II	2023-06-02	Global
IPN01194	Ipsen	ERK1/2	Advanced solid tumour, incl. CRC, PDAC, HNSCC	Phase I/II	2024-03-12	Global excl. China
HMPL-295	HutchMed	ERK1/2	Advanced malignant solid tumour	Phase I	2021-04-15	China

Source: clinicaltrials.gov, CDE, CIC

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Major Indications for MAPK Pathway Mutations

MAPK Pathway Mutated NSCLC

Overview of NSCLC

Alterations affecting the MAPK signalling cascade are common in NSCLC and include recurrent driver mutations in genes such as KRAS and BRAF, which promote tumour growth through sustained pathway activation. Because these mutations often act as foundational oncogenic events, MAPK pathway status is routinely assessed in molecular profiling and can influence treatment selection in defined patient subsets. Among NSCLC patients, MAPK pathway mutations represent in approximately 24% globally and 19% in China. See “ — Major Indications for SHP2 Inhibitors — KRAS^{G12C} Mutated NSCLC — Overview of NSCLC”.

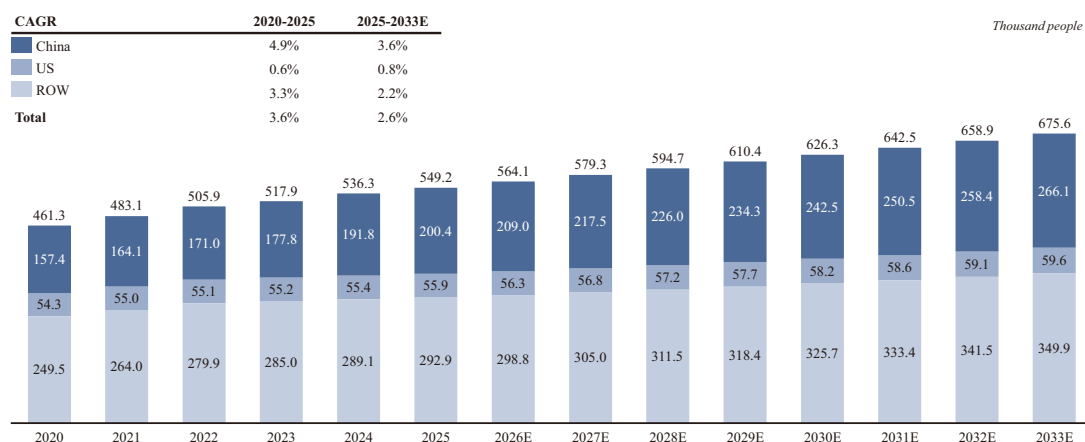
Global Incidence of MAPK Pathway Mutated NSCLC

The global incidence of MAPK pathway mutated NSCLC increased from 461.3 thousand in 2020 to 549.2 thousand in 2025, representing a CAGR of 3.6% during the period. The global incidence of MAPK pathway mutated NSCLC is expected to increase to 675.6 thousand by 2033, representing a CAGR of 2.6% from 2025 to 2033.

The incidence of MAPK pathway mutated NSCLC in China increased from 157.4 thousand in 2020 to 200.4 thousand in 2025, representing a CAGR of 4.9% during the period. The incidence of MAPK pathway mutated NSCLC in China is expected to increase to 266.1 thousand by 2033, representing a CAGR of 3.6% from 2025 to 2033.

The chart below sets out the incidence of MAPK pathway mutated NSCLC globally, in China, the U.S., and the rest of the world in 2020 to 2033.

Global incidence of MAPK pathway mutated NSCLC, 2020-2033E



Source: GLOBOCAN, WHO, CIC

Treatment Paradigm and Clinical Unmet Needs for MAPK Pathway Mutated NSCLC

In current clinical practice in both the U.S. and China, actionable clinical subtyping of MAPK pathway mutated NSCLC is largely limited to KRAS^{G12C} and BRAF V600/V600E mutations. Treatment paradigm for MAPK pathway mutated NSCLC. See “ — Major Indications for SHP2 Inhibitors — KRAS^{G12C} Mutated NSCLC — Treatment Paradigm and Clinical Unmet Needs for KRAS^{G12C} mutated NSCLC”.

The treatment pathway for KRAS^{G12C}-mutated NSCLC is described in “ — Major Indications for SHP2 Inhibitors — KRAS^{G12C} Mutated NSCLC — Treatment Paradigm and Clinical Unmet Needs for KRAS^{G12C} mutated NSCLC”.

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For BRAF V600/V600E mutated NSCLC, guidelines in both countries generally recommend a BRAF inhibitor in combination with a MEK inhibitor as first-line therapy, and upon disease progression, patients are typically managed using the same subsequent-line approaches applied to mutation-negative NSCLC, primarily immunotherapy-based regimens and/or chemotherapy depending on PD-L1 expression level and clinical status. For patients with other MAPK pathway alterations outside KRAS^{G12C} and BRAF V600/V600E, there are currently no approved targeted therapies, and management generally follows standard AGA-negative NSCLC systemic treatment paradigms and clinical trial participation where available.

The Company intends to position the GH21’s combination with GH55 (“GH21-GH55 CoTx”) for NSCLC patients with MAPK pathway mutations, with an addressable market of approximately 200.4 thousand incidences in China in 2025, representing approximately 19.0% of overall NSCLC incidences.

MAPK Pathway Mutated CRC

Overview of CRC

Among CRC patients, MAPK pathway mutations represent in approximately 66% globally and 58% in China. See “ — Major Indications for SHP2 Inhibitors — KRAS^{G12C} Mutated CRC — Overview of CRC”.

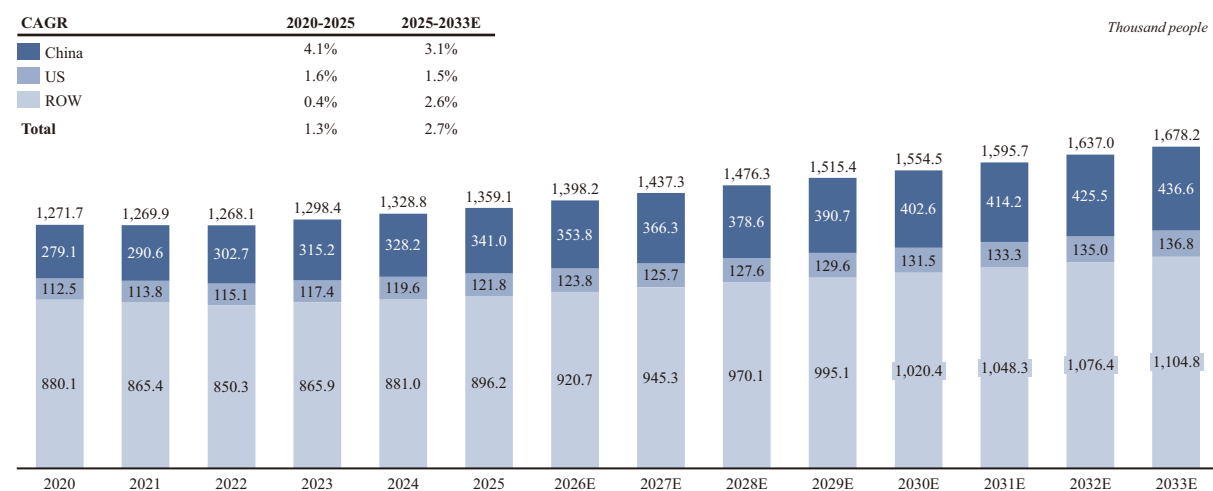
Global Incidence of MAPK Pathway Mutated CRC

The global incidence of MAPK pathway mutated CRC increased from 1,271.7 thousand in 2020 to 1,359.1 thousand in 2025, representing a CAGR of 1.3% during the period. The global incidence of MAPK pathway mutated CRC is expected to increase to 1,678.2 thousand by 2033, representing a CAGR of 2.7% from 2025 to 2033.

The incidence of MAPK pathway mutated CRC in China increased from 279.1 thousand in 2020 to 341.0 thousand in 2025, representing a CAGR of 4.1% during the period. The incidence of MAPK pathway mutated CRC in China is expected to increase to 436.6 thousand by 2033, representing a CAGR of 3.1% from 2025 to 2033.

The chart below sets out the incidence of MAPK pathway mutated CRC globally, in China, the U.S., and the rest of the world in 2020 to 2033.

Global incidence of MAPK pathway mutated CRC, 2020-2033E



Source: GLOBOCAN, WHO, CIC

Treatment Paradigm and Clinical Unmet Needs for MAPK Pathway Mutated CRC

In current clinical practice in both the United States and China, clinically actionable categorisation of MAPK pathway mutated CRC is only anchored on RAS and RAF status, but approved precision options remain confined to narrow subtypes. Specifically, within RAS-mutated CRC, only the KRAS^{G12C} subgroup has approved targeted therapies, and within RAF-mutated CRC, approved targeted

INDUSTRY OVERVIEW

therapies are limited to the BRAF V600E subgroup. Treatment paradigm for MAPK pathway mutated CRC see “ — Major Indications for SHP2 Inhibitors — KRAS^{G12C} Mutated CRC — Treatment Paradigm and Clinical Unmet Needs for KRAS^{G12C} mutated CRC”.

The treatment approach for KRAS^{G12C}-mutated CRC is described in “— Major Indications for SHP2 Inhibitors — KRAS^{G12C} Mutated CRC — Treatment Paradigm and Clinical Unmet Needs for KRAS^{G12C} mutated CRC”.

For BRAF V600E-mutated CRC, management is more heterogeneous and differs by country. In the United States, selected patients may receive a BRAF inhibitor combined with EGFR blockade such as cetuximab, with or without chemotherapy, as an early systemic option, and a MEK inhibitor plus a BRAF inhibitor may also be used in practice as an off-label approach in certain circumstances; after progression, care typically returns to established CRC standard of care, including chemotherapy-based regimens. In China, first-line therapy for BRAF V600E-mutated CRC generally remains chemotherapy-based, while BRAF-targeted strategies in combination with EGFR blockade, with or without chemotherapy, are more commonly positioned in the second-line setting. For MAPK pathway alterations outside KRAS^{G12C} and BRAF V600E, there are currently no approved targeted therapies, and patients are typically treated with standard CRC systemic regimens and encouraged to enrol in clinical trials where available.

The Company intends to position the GH21-GH55 CoTx for CRC patients with MAPK pathway mutations, with an addressable market of approximately 341.0 thousand incidences in China in 2025, representing approximately 58.4% of overall CRC incidences.

MAPK Pathway Mutated PDAC

Overview of PDAC

Among PDAC patients, MAPK pathway mutations represent in approximately 94% globally and 87% in China. See “ — Major Indications for SHP2 Inhibitors — KRAS^{G12C} Mutated PDAC — Overview of PDAC”.

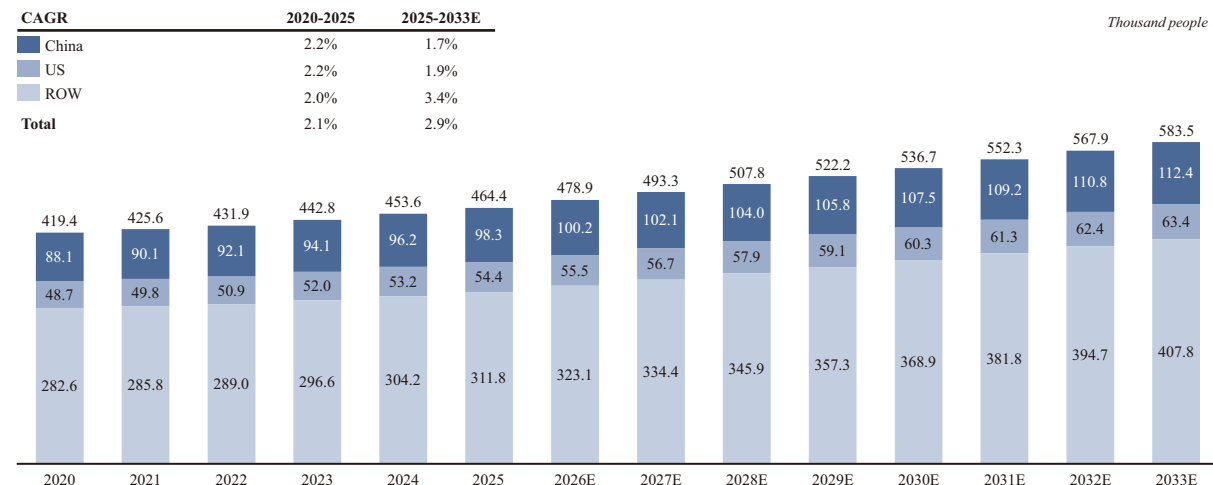
Global Incidence of MAPK Pathway Mutated PDAC

The global incidence of MAPK pathway mutated PDAC increased from 419.4 thousand in 2020 to 464.4 thousand in 2025, representing a CAGR of 2.1% during the period. The global incidence of MAPK pathway mutated PDAC is expected to increase to 583.5 thousand by 2033, representing a CAGR of 2.9% from 2025 to 2033.

The incidence of MAPK pathway mutated PDAC in China increased from 88.1 thousand in 2020 to 98.3 thousand in 2025, representing a CAGR of 2.2% during the period. The incidence of MAPK pathway mutated PDAC in China is expected to increase to 112.4 thousand by 2033, representing a CAGR of 1.7% from 2025 to 2033.

The chart below sets out the incidence of MAPK pathway mutated PDAC globally, in China, the U.S., and the rest of the world in 2020 to 2033.

Global incidence of MAPK pathway mutated PDAC, 2020-2033E



Source: GLOBOCAN, WHO, CIC

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Treatment Paradigm and Clinical Unmet Needs for MAPK Pathway Mutated PDAC

In current clinical practice, among the US and China, NCCN is the only guideline that operationalised MAPK pathway mutation in PDAC as a distinct clinical subgrouping framework, and this remains largely limited to KRAS^{G12C} and BRAF V600E. Treatment paradigm for MAPK pathway mutated PDAC see “ — Major Indications for SHP2 Inhibitors — KRAS^{G12C} Mutated PDAC — Treatment Paradigm and Clinical Unmet Needs for KRAS^{G12C} mutated PDAC”.

The treatment approach for KRAS^{G12C}-mutated PDAC is described in “— Major Indications for SHP2 Inhibitors — KRAS^{G12C} Mutated PDAC — Treatment Paradigm and Clinical Unmet Needs for KRAS^{G12C} mutated PDAC”.

For BRAF V600E mutated PDAC, US practice may consider combined BRAF and MEK inhibition, such as dabrafenib plus trametinib, in the first line or second line setting in selected patients and have no satisfactory alternative treatment options; after progression, patients are generally managed with chemotherapy-based regimens consistent with the broader PDAC treatment regimens. In China, pancreatic cancer guidance does not currently provide MAPK pathway subtype specific recommendations, such that MAPK pathway directed approaches in PDAC are generally confined to clinical trials or off label use and patients otherwise receive standard chemotherapy-based care.

The Company intends to position the GH21-GH55 CoTx for PDAC patients with MAPK pathway mutations, with an addressable market of approximately 98.3 thousand incidences in China in 2025, representing approximately 87.2% of overall PDAC incidences.

OVERVIEW OF SYNTHETIC LETHALITY DRUG MARKET

Overview of Synthetic Lethal Drugs

Synthetic lethality describes a genetic relationship in which loss of either of two pathways alone is compatible with cell survival, but simultaneous impairment of both becomes lethal. A synthetic lethal drug targets the cancer cells that remaining dependency, so the cancer cell loses its last effective route to cope with damage and dies, while normal cells, which retain the originally impaired pathway, are less affected. This logic supports precision treatment based on the tumour’s molecular defects rather than solely on tissue origin.

According to CIC, synthetic lethality is a well-researched and validated mechanism, testified by the remarkable finding of BRCA1/2-mutant tumour cells to poly-(ADP-ribose) polymerase (“**PARP**”) inhibitors. Several PARP inhibitors were approved by the FDA for the treatment of breast cancer and ovarian cancer in clinical practice. The world’s first PARP inhibitor was approved for the treatment of ovarian cancer.

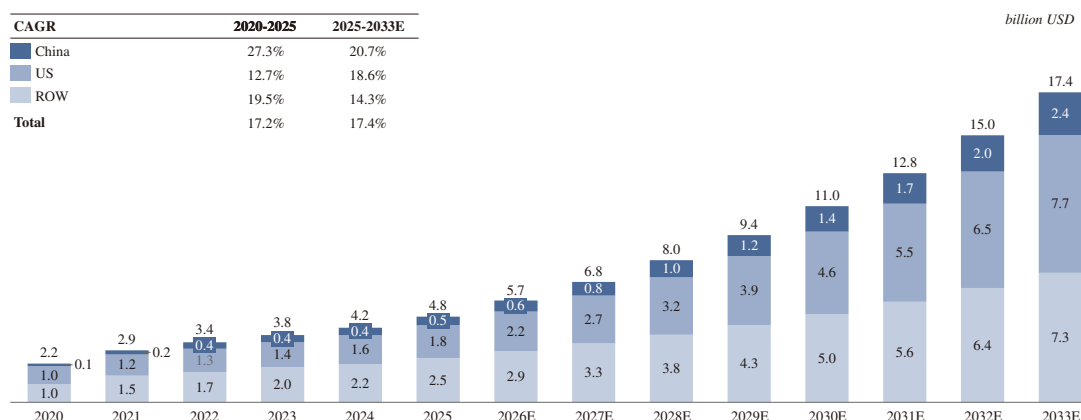
Synthetic Lethal Drug Market Size Globally and in China

The market size of the global synthetic lethal drug market increased from US\$2.2 billion in 2020 to US\$4.8 billion in 2025, representing a CAGR of 17.2% during the period. The market size of the global synthetic lethal drug market is expected to increase to US\$17.4 billion by 2033, representing a CAGR of 17.4% from 2025 to 2033.

The market size of the China synthetic lethal drug market increased from US\$0.1 billion in 2020 to US\$0.5 billion in 2025, representing a CAGR of 27.3% during the period. The market size of the China synthetic lethal drug market is expected to increase to US\$2.4 billion by 2033, representing a CAGR of 20.7% from 2025 to 2033. The chart below sets out the synthetic lethal drug market size in China, the U.S. and the rest of the world from 2020 to 2033.

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Global Synthetic lethal drug market size



Source: Annual reports, NMPA, FDA, CIC

MARKET POTENTIAL OF PRMT5 INHIBITORS

PRMT5 / MTAP Synthetic Lethality

Homozygous deletion of Methylthioadenosine Phosphorylase (“**MTAP**”) is observed in approximately 15% of solid tumours. In MTAP-deleted tumour cells, loss of MTAP function leads to accumulation of 5'-deoxy-5'-methylthioadenosine (“**MTA**”), which creates a selective vulnerability to Protein Arginine Methyltransferase 5 (“**PRMT5**”) inhibition. This provides a rationale for the development of PRMT5 inhibitors in this genetically defined patient population.

PRMT5 inhibitors have evolved from earlier non-selective agents to next-generation, biomarker-selective molecules designed to improve the therapeutic index. Compared with first-generation PRMT5 inhibitors, which broadly inhibit PRMT5 in both tumour and normal tissues and are therefore associated with dose-limiting toxicities, next-generation PRMT5 inhibitors are designed to achieve greater selectivity in MTAP-deleted tumours while reducing inhibition of PRMT5 in normal tissues, with the aim of improving tolerability and expanding the therapeutic window.

Competitive Landscape of Next-generation PRMT5 Inhibitors

PRMT5 inhibitors have undergone a clear mechanistic evolution from earlier, broadly acting agents to next-generation, highly biomarker-selective molecules designed to improve therapeutic index. First-generation PRMT5 inhibitors generally suppress PRMT5 activity in a largely non-selective manner, inhibiting PRMT5 not only in MTAP-deleted tumour cells but also in normal tissues, including those with intact MTAP, thereby limiting dosing and clinical utility. This on-target, systemic PRMT5 blockade has been associated with clinically meaningful toxicities including hematologic suppression, reproductive toxicity, and cardiovascular effects. In contrast, next-generation PRMT5 inhibitors are engineered to achieve high functional selectivity by preferentially targeting the PRMT5 biology that is enriched in MTAP-deleted tumours, while largely preserving PRMT5 function in normal tissues. By reducing inhibition of PRMT5 in healthy cells, these selective approaches are intended to mitigate normal-tissue cytotoxicity, enable more sustained target engagement, and expand the therapeutic window for MTAP-deleted malignancies.

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The table below sets out the competitive landscape of next-generation PRMT5 inhibitors indicated for MTA cooperative cancers globally as of the Latest Practicable Date.

Drug	Company	Target	Globally Most Advanced Indications	Highest Clinical Stage	First Posted Date	Location
MRTX1719	Mirati / Bristol-Myers Squibb	PRMT5	Metastatic NSCLC with homozygous MTAP deletion	Phase II/III	2025-07-14	Global
			Untreated metastatic PDAC with homozygous MTAP deletion	Phase II/III	2025-07-21	Global
Vopimetostat	Tango	PRMT5	MTAP-deleted solid tumours incl. NSCLC, mesothelioma, PDAC, sarcoma	Phase I/II	2023-02-17	Global excl. China
AZD3470	AstraZeneca	PRMT5	MTAP deficient advanced/metastatic solid tumours	Phase I/II	2023-11-14	Global
CTS3497	CytosinLab	PRMT5	MTAP deleted solid tumours incl. ESCC, PAAD, BTC, NSCLC, MPM	Phase I/II	2024-12-03	China
TNG456	Tango	PRMT5	NSCLC, GBM with MTAP loss	Phase I/II	2025-02-05	US
PH020	Bayer	PRMT5	MTAP-deleted solid tumours	Phase I/II	2025-04-06	Global
HRS-6719	Hengrui	PRMT5	MTAP-deficient advanced solid tumours	Phase I/II	2025-04-08	China
BGB-58067	BeiGene	PRMT5	MTAP-deleted advanced solid tumour	Phase I	2024-09-19	Global
GTA182	Apeiron	PRMT5	MTAP null/lost advanced solid tumour	Phase I	2024-10-14	China
GH56	Our Company	PRMT5	MTAP-deleted advanced solid tumour	Phase I	2025-01-20	China
HSK41959	Haisco	PRMT5	MTAP-deleted solid tumour	Phase I	2025-03-31	China
ABSK131	Abbisko	PRMT5	MTAP-deleted advanced or metastatic solid tumour	Phase I	2025-04-02	China
DC50292A	Beijing Double-Crane Runchuang	PRMT5	MTAP-deleted advanced or metastatic solid tumour	Phase I	2025-04-29	China
PEP08	PharmaEngine	PRMT5	MTAP-deleted advanced or metastatic solid tumour	Phase I	2025-05-15	Global excl. China
GS-5319	Gilead	PRMT5	MTAP-deleted advanced solid tumour	Phase I	2025-08-17	Global excl. China
CS08399	Chipscreen	PRMT5	MTAP-deleted advanced solid tumour and lymphoma	Phase I	2026-04-15	China
HS-10587	Hansoh	PRMT5	MTAP-deleted advanced solid tumour	Phase I	2026-04-20	China

Source: FDA, NMPA, clinicaltrials.gov, CDE, CIC

Major Indications for PRMT5 Inhibitors

MTAP-Deleted NSCLC

Overview of NSCLC

Among NSCLC patients, MTAP deletion represents in approximately 15% in China and global. See “ — Major Indications for SHP2 Inhibitors — KRAS^{G12C} Mutated NSCLC — Overview of NSCLC”.

Global Incidence of MTAP-Deleted NSCLC

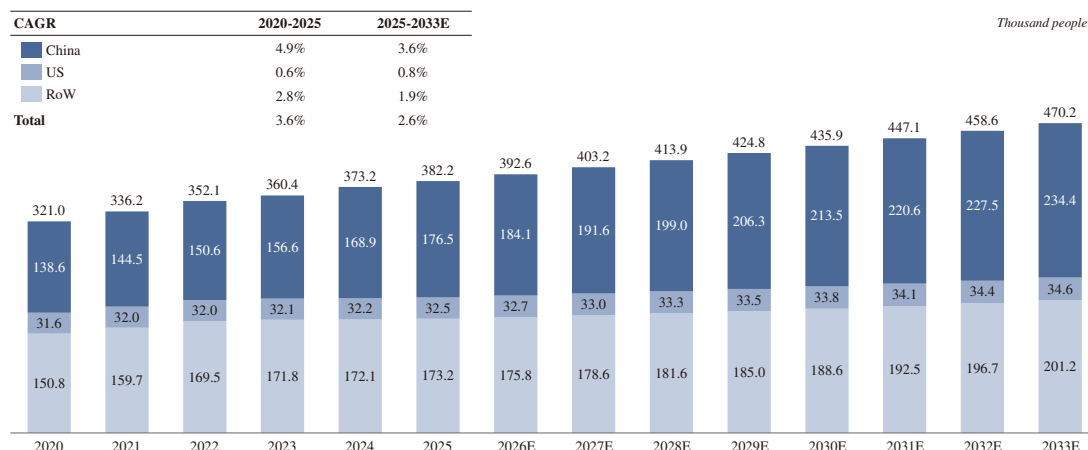
The global incidence of MTAP-deleted NSCLC increased from 321.0 thousand in 2020 to 382.2 thousand in 2025, representing a CAGR of 3.6% during the period. The global incidence of MTAP-deleted NSCLC is expected to increase to 470.2 thousand by 2033, representing a CAGR of 2.6% from 2025 to 2033.

The incidence of MTAP-deleted NSCLC in China increased from 138.6 thousand in 2020 to 176.5 thousand in 2025, representing a CAGR of 4.9% during the period. The incidence of MTAP-deleted NSCLC in China is expected to increase to 234.4 thousand by 2033, representing a CAGR of 3.6% from 2025 to 2033.

INDUSTRY OVERVIEW

The chart below sets out the incidence of MTAP-deleted NSCLC globally, in China, the U.S., and the rest of the world in 2020 to 2033.

Incidence of MTAP-deleted NSCLC in global, 2020-2033E



Source: GLOBOCAN, WHO, CIC

Treatment Paradigm and Unmet Clinical Needs for MTAP-Deleted NSCLC

Neither China’s CSCO guidelines nor U.S. NCCN guideline frameworks currently recognise MTAP-deleted NSCLC as a formal diagnostic/therapeutic subtype or a standard treatment-defining biomarker; instead, they stratify advanced NSCLC primarily by actionable oncogenic drivers (e.g., EGFR, KRAS, BRAF V600, HER2, etc.) and immunotherapy markers such as PD-L1, without incorporating MTAP status into routine pathway branching. Importantly, MTAP loss is not rare: multiple datasets indicate approximately 15% MTAP loss, implying a sizeable global molecularly defined subgroup. Given the large baseline incidence of NSCLC and the absence of a guideline-embedded, approved MTAP-directed standard of care today, MTAP-deleted NSCLC represents a substantial “unserved/underserved” segment with clear room for targeted innovation, supporting the view that it carries significant market potential as MTAP-synthetic-lethality strategies advance through clinical development.

MTAP-Deleted Digestive Cancers

Overview of Digestive Cancers

Digestive cancers represent a major oncology category characterised by high clinical complexity, substantial morbidity and mortality, and significant healthcare resource utilisation. Key digestive cancer types commonly include colorectal cancer (CRC), esophageal cancer, gastric cancer, liver cancer, and pancreatic cancer. These malignancies frequently present with heterogeneous biology, limited early detection, and high rates of recurrence or metastatic disease, resulting in persistently challenging outcomes despite advances in surgery, radiotherapy, systemic chemotherapy, targeted therapies, and immuno-oncology. Accordingly, digestive cancers continue to impose a meaningful disease burden and underscore the ongoing need for more effective, biomarker-driven and accessible treatment options.

Across major digestive cancers, MTAP deletion represents in approximately 8% of digestive cancers overall. Within individual indications, reported MTAP loss is particularly enriched in pancreatic cancer (approximately 22%) and esophageal cancer (approximately 20%), and remains notable in gastric cancer (approximately 11%). Collectively, these prevalence patterns support MTAP deletion as a cross-indication biomarker that can define sizable patient segments in select high-need digestive tumours, underscoring the potential value of developing MTAP-directed therapeutic strategies in this area.

Global Incidence of MTAP-Deleted Digestive Cancers

The global incidence of MTAP-deleted digestive cancers increased from 375.1 thousand in 2020 to 415.8 thousand in 2025, representing a CAGR of 2.1% during the period. The global incidence of MTAP-deleted digestive cancers is expected to increase to 514.5 thousand by 2033, representing a CAGR of 2.7% from 2025 to 2033.

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The incidence of MTAP-deleted digestive cancer in China increased from 122.7 thousand in 2020 to 128.4 thousand in 2025, representing a CAGR of 0.9% during the period. The incidence of MTAP-deleted digestive cancers in China is expected to increase to 138.7 thousand by 2033, representing a CAGR of 1.0% from 2025 to 2033.

Treatment Paradigm and Unmet Clinical Needs for MTAP-Deleted Digestive Cancers

In digestive cancers, treatment selection is primarily guided by tumour site, stage, resectability, and a limited set of validated biomarkers (e.g., HER2, MSI-H/dMMR, PD-L1, FGFR2, CLDN18.2, select driver alterations), with management typically spanning surgery and locoregional approaches in earlier disease and multi-agent systemic regimens in the advanced setting. MTAP deletion is not currently embedded as a routine classification or treatment-defining decision point in standard clinical pathways, and patients with MTAP-deleted disease are generally treated according to the prevailing standards for each tumour type rather than a biomarker-directed algorithm. Against this backdrop, MTAP deletion appears across multiple digestive malignancies creating a cross-indication, molecularly defined addressable population. As MTAP-linked synthetic-lethality approaches advance clinically, the combination of substantial unmet need in metastatic digestive tumours and a repeatable biomarker footprint across several large indications support attractive market potential for MTAP-directed therapies in digestive cancers.

MARKET POTENTIAL OF KIF18A INHIBITORS

Overview of KIF18A Inhibitors

TP53 encodes the tumour suppressor protein, a key regulator of cell-cycle arrest, DNA repair and apoptosis. Somatic TP53 mutations occur across multiple tumour types, particularly in aggressive subtypes and advanced disease stages. Loss of p53 function removes a key anti-proliferative checkpoint and may promote DNA damage propagation and clonal evolution.

Ploidy abnormalities are a hallmark of cancer. WGD occurs in approximately 30% to 40% of human cancers and is associated with aneuploidy, chromosomal instability (“CIN”), disease progression and metastasis.

KIF18A is a mitotic kinesin essential for spindle function. Inhibition of KIF18A has demonstrated selective anti-tumour activity in cancers with ploidy-related features such as aneuploidy, WGD and CIN, with limited effects on normal diploid cells. Sensitivity to KIF18A inhibition appears to be enriched in TP53-mutated and/or WGD-positive settings, including tumour types with high CIN prevalence such as high-grade serous ovarian cancer and triple-negative breast cancer (“TNBC”).

Global Competitive Landscape of KIF18A Inhibitors

The table below sets out the competitive landscape of KIF18A inhibitors globally as of the Latest Practicable Date.

Competitive landscape of KIF18A inhibitors globally

Drug	Company	Target	Globally Most Advanced Indications	Highest Clinical Stage	First Posted Date	Location
VLS-1488	Volastra	KIF18A	HGSOC, squamous NSCLC, TNBC, gastric adenocarcinoma (not EBV+), colorectal, ESCC, esophageal adenocarcinoma, GEJ, bladder, head and neck squamous cell carcinomas, OC, CN-high endometrial/uterine	Phase I/II	2023-06-15	US
Sovilnesib	Volastra	KIF18A	TNBC, HGSOC, primary peritoneal cancer and/or fallopian-tube cancer, serous endometrial cancer, solid tumour with TP53 mutation	Phase I	2020-03-02	Global excl. China
GH2616	Our Company	KIF18A	Solid tumour with TP53 mutant and WGD positive, incl. HGSOC, UCS, LUAD, LUSC, TNBC, BLCA, CRC, etc.	Phase I	2024-01-26	China
GenSci122	GeneScience	KIF18A	Recurrent or metastatic advanced solid tumours with TP53 mutant and WGD positive	Phase I	2025-01-08	China
ATX-295	Accent	KIF18A	Recurrent or metastatic advanced solid tumours incl. HGSOC	Phase I	2025-01-29	US
HS387	Hisun	KIF18A	Advanced solid tumour	Phase I	2025-07-07	China
MEN2501	Menarini	KIF18A	Platinum-resistant OC	Phase I	2025-11-10	Global excl. China
HW221043	Humanwell Healthcare	KIF18A	Advanced solid tumor	Phase I	2026-06-01	China

Source: clinicaltrials.gov, CDE, CIC

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Major Indications for KIF18A Inhibitors

TNBC

Overview of TNBC

Breast cancer is a leading malignancy among women worldwide. Major clinical subtypes include HR+/HER2-, HER2+, and TNBC. TNBC is defined by the absence of oestrogen receptor and progesterone receptor expression (<1% for each) and HER2 negativity by immunohistochemistry/in situ hybridisation.

TNBC accounts for approximately 15% of breast cancers and is more prevalent among younger women. Relative to other subtypes, TNBC is characterised by poor differentiation, higher aggressiveness, and earlier, more frequent recurrence and metastasis. In advanced TNBC, chemotherapy remains foundational, with the choice between single-agent and combination regimens tailored to disease stage and clinical context. Novel agents, including PARP inhibitors, immune checkpoint inhibitors and ADCs, have been incorporated for biomarker-defined populations and selected treatment settings.

Global Incidence of TNBC

The global incidence of TNBC increased from 339.2 thousand in 2020 to 368.2 thousand in 2025, representing a CAGR of 1.9% during the period. The global incidence of TNBC is expected to increase to 426.1 thousand by 2033, representing a CAGR of 1.8% from 2025 to 2033.

The incidence of TNBC in China increased from 50.9 thousand in 2020 to 57.5 thousand in 2025, representing a CAGR of 2.5% during the period. The incidence of TNBC in China is expected to increase to 67.0 thousand by 2033, representing a CAGR of 1.9% from 2025 to 2033.

Treatment Paradigm and Clinical Unmet Needs for TNBC

For TNBC, first-line regimens frequently employ taxanes, with combination or single-agent chemotherapy in subsequent lines (e.g. eribulin, vinorelbine, gemcitabine, capecitabine). In PD-L1-positive metastatic TNBC, checkpoint inhibitors are used. PARP inhibitors are options for patients with germline BRCA1/2 mutations. ADCs are used in later lines according to biomarker and label.

Under current practice, chemotherapy remains the standard of care for most patients. Immunotherapy benefits a subset only. Real-world data indicate short first-line treatment duration, early mortality and high attrition between lines. A proportion of patients do not receive second-line therapy due to progression or performance decline. Although ADCs improve outcomes in pre-treated settings, durable responses are limited, indicating a continued need for more effective and tolerable agents across lines.

Ovarian Cancer

Overview of Ovarian Cancer

Ovarian cancer often presents insidiously, with a high proportion of patients diagnosed at advanced stages. Debulking surgery and platinum-based chemotherapy remain central in management.

High-grade serous carcinoma (HGSOC) commonly associated with serous tubal intraepithelial carcinoma precursor lesions, accounting for approximately 80% of OC. TP53 mutation prevalence is approximately 95% in HGSOC. Also, WGD prevalence in OC is approximately 38%.

Global Incidence of Ovarian Cancer

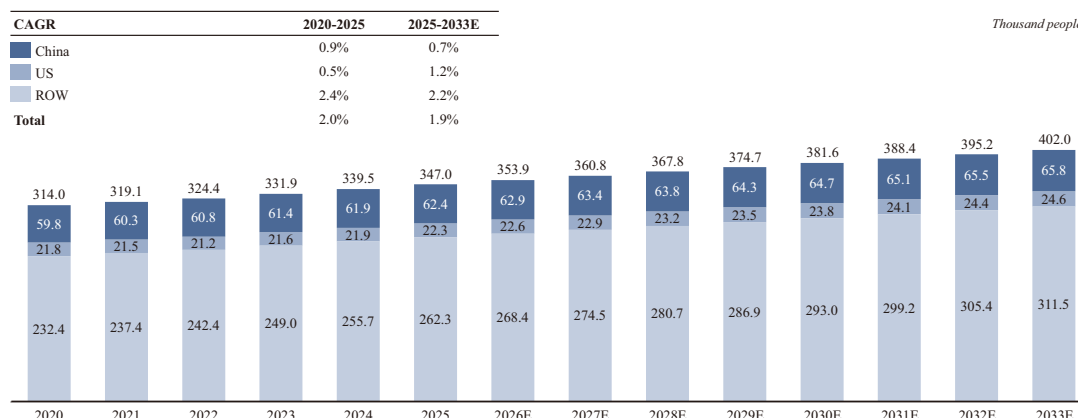
The global incidence of ovarian cancer increased from 314.0 thousand in 2020 to 347.0 thousand in 2025, representing a CAGR of 2.0% during the period. The global incidence of ovarian cancer is expected to increase to 402.0 thousand by 2033, representing a CAGR of 1.9% from 2025 to 2033.

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The incidence of ovarian cancer in China increased from 59.8 thousand in 2020 to 62.4 thousand in 2025, representing a CAGR of approximately 0.9% during the period. The incidence in China is expected to increase to 65.8 thousand by 2033, representing a CAGR of approximately 0.7% from 2025 to 2033.

The chart below sets out the incidence of ovarian cancer in China, the U.S. and the rest of the world from 2020 to 2033.

Global incidence of ovarian cancer, in the U.S., China and RoW, 2020-2033E



Source: the Lancet, Globocan, CIC

Treatment Paradigm and Clinical Unmet Needs for Ovarian Cancer

According to both CSCO and NCCN, In stage II-IV epithelial disease, first-line treatment typically comprises platinum-based chemotherapy with or without bevacizumab, followed by biomarker-guided maintenance. PARP inhibitors are used in maintenance according to BRCA1/2 and homologous recombination deficiency (“**HRD**”) status, alone or in combination with bevacizumab as indicated. In earlier stages, adjuvant platinum-based chemotherapy is administered according to risk features.

On relapse, treatment is stratified by platinum sensitivity. Platinum-sensitive disease is typically re-treated with platinum-based combinations (with optional bevacizumab) followed by maintenance. Platinum-resistant disease is treated with non-platinum single agents (with or without anti-angiogenics) and other targeted regimens as appropriate.

MARKET POTENTIAL OF MAT2A INHIBITORS

MAT2A / MTAP SYNTHETIC LETHALITY

Methionine adenosyltransferase 2A (“**MAT2A**”) is a key enzyme that produces S-adenosyl-L-methionine (“**SAM**”), the body’s primary methyl donor, which supports DNA and protein methylation as well as other cellular processes involved in gene expression and cell survival. In certain cancer settings, elevated methylation demand makes SAM supply an important metabolic dependency, providing a rationale for MAT2A inhibition.

The relevance of MAT2A inhibition is particularly evident in cancers with MTAP deletion, which is frequently co-deleted with CDKN2A in several solid tumours. Loss of MTAP disrupts the methionine salvage pathway and leads to accumulation of methylthioadenosine (“**MTA**”), creating a synthetic lethality rationale whereby further reduction of SAM through MAT2A inhibition may selectively stress MTAP-deleted tumour cells while sparing MTAP-intact normal tissues. As a result, MAT2A inhibitors are being developed as a biomarker-driven approach for MTAP-deleted cancers.

INDUSTRY OVERVIEW

Major Indications for MAT2A Inhibitors

MTAP-Deleted NSCLC

See “ — Market Potential of PRMT5 Inhibitors — Major Indications for PRMT5 inhibitors — MTAP-Deleted NSCLC” for details.

MTAP-Deleted Urothelial Cancer

Overview of MTAP-Deleted Urothelial Cancer

Urothelial cancer (UC) is a malignancy arising from the urothelial lining of the urinary tract, most commonly in the bladder but also in the renal pelvis and ureter. Clinically, UC spans a broad spectrum from non-muscle-invasive disease, which is often managed with endoscopic resection and intravesical therapy but has a high recurrence risk, to muscle-invasive and metastatic disease, where outcomes are driven by the risk of progression and the availability of effective systemic regimens. Over the past decade, the treatment landscape for advanced UC has expanded beyond platinum-based chemotherapy to include immune checkpoint inhibitors and, increasingly, targeted and antibody–drug conjugate options in selected patient populations, reinforcing the direction toward biomarker-informed treatment pathways.

MTAP-deletion represents a recurrent, clinically relevant molecular subset in UC. MTAP loss typically results from deletions at chromosome 9p21, often occurring alongside CDKN2A loss, and it is frequently cited as affecting approximately 26% of UC cases.

Global Incidence of MTAP-Deleted Urothelial Cancer

The global incidence of MTAP-deleted UC increased from 165.6 thousand in 2020 to 189.6 thousand in 2025, representing a CAGR of 2.7% during the period. The global incidence of MTAP-deleted UC is expected to increase to 240.8 thousand by 2033, representing a CAGR of 3.0% from 2024 to 2033.

The incidence of MTAP-deleted UC in China increased from 25.8 thousand in 2020 to 30.1 thousand in 2025, representing a CAGR of 3.1% during the period. The incidence of MTAP-deleted UC in China is expected to increase to 36.3 thousand by 2033, representing a CAGR of 2.4% from 2025 to 2033.

Treatment Paradigm and Unmet Clinical Needs for MTAP-Deleted Urothelial Cancer

Same as MTAP-deleted NSCLC, current treatment pathways for urothelial cancer in both China and the U.S. are not built around MTAP status as a formal diagnostic or treatment-defining subtype. Publicly available summaries of CSCO and NCCN guideline updates similarly emphasise chemotherapy, immunotherapy and ADC-based regimens, and targeted options such as FGFR-directed approaches, without routine pathway branching by MTAP.

Against this backdrop, MTAP-deleted urothelial cancer represents a sizeable molecularly defined segment with meaningful unmet need and clear commercial headroom. MTAP loss is a relatively common event in urothelial carcinoma, with reported 26% MTAP deletion in UC. This prevalence, combined with the substantial baseline incidence of urothelial cancer in China, underpins a large potential addressable population. As MTAP synthetic-lethality strategies mature clinically, they have the potential to create a new biomarker-driven treatment segment in urothelial cancer that is both clinically differentiated and commercially attractive.

INDUSTRY OVERVIEW

SOURCE OF INFORMATION

In connection with the [REDACTED], we have commissioned CIC, an independent third party, to conduct a detailed analysis and prepare an industry report on the China pharmaceutical market. The CIC Report has been prepared by CIC independently and without our influence. We have agreed to pay CIC a fee of RMB1.1 million for the preparation of the CIC Report, which we consider to be in line with market rates. Except as otherwise noted, all data and forecasts in this section are derived from the CIC Report. Our Directors confirm that, after taking reasonable care, there has been no adverse change in the market information since the date of the CIC Report that may qualify, contradict, or materially impact the information disclosed in this section.

CIC prepared its report based on its in-house database, independent third party reports, and publicly available data from reputable industry organisations. To prepare the CIC Report, CIC also conducted analysis on projected figures using historical data, macroeconomic data, and specific industry-related drivers, and reviewed annual reports of listed companies in the Chinese pharmaceutical markets. In compiling and preparing the CIC Report, CIC adopted the following assumptions: (i) the social, economic, and political environments in global will remain stable during the forecast period, ensuring sustainable and steady development of the healthcare industry in global; (ii) the healthcare markets in global will grow as expected due to rising healthcare demand and supply; and (iii) global governments will continue to support healthcare reform.