



2026 ESMO LBA: Data Review of GFH276 Monotherapy in RAS-mutant Solid Tumors

Oct. 2026

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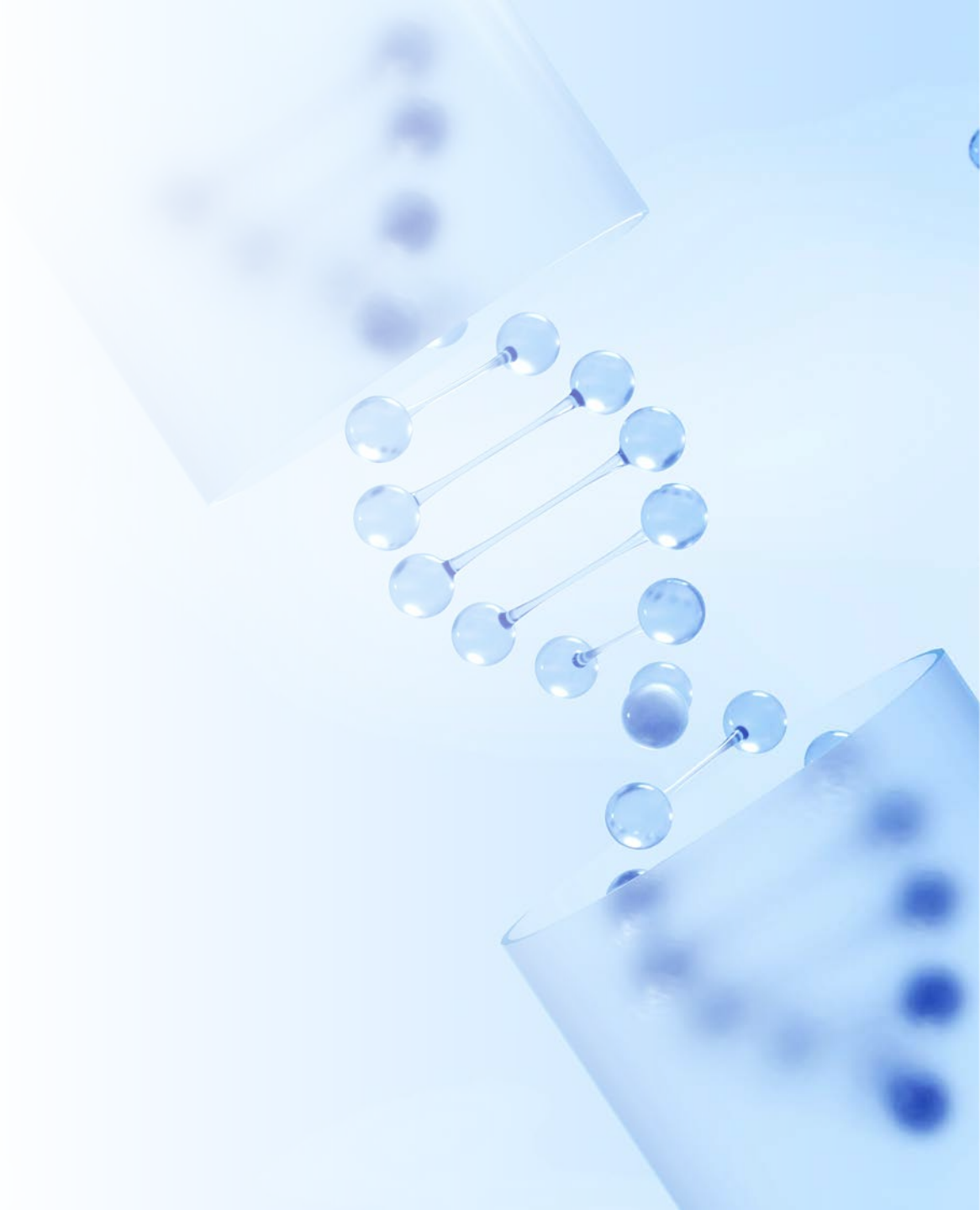
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PART **01**

Study background of GFH276 monotherapy



Leading Position of GenFleet's RAS-inhibiting Therapies across Modalities

Front-runners in China's clinical development

	Target	No.1	No.2	No.3
Switch II pocket inhibitors	KRAS G12C	Fulzerasib (No. 3 globally)	Garsorasib	Glecirasib
	KRAS G12D	GFH375 (global leader in oral G12Di dev't: Ph III mono, other combo trials) HRS-4642 (liposome, IV, Ph III combo with chemo & other therapies)		DN022150 (I/V, Ph III/mono)
	Pan KRAS	JAB-23E73 (mono phase I)	/	/
Molecular glue	Pan RAS	JYP0015/ERAS-0015 (Discontinued after Ph I)	GFH276 (mono ph I/II, multi phase Ib/II combo trials) HRS-7172 (mono ph I, multi phase Ib/II combo trials)	
Other selective inhibitors	KRAS G12V	RO7836748 (Mono phase I registered)	/	/
ADC	Pan RAS ADC (Enrollment not started yet in China)	GFS784 (EGFR-Pan RAS ADC) AN4035 (CEACAM5-Pan RAS ADC)		/

GFH276 (Molecular Glue Pan RAS Inhibitor)

Top-tier in China's Pan RAS Inhibitor Development

First-tier development of Pan RAS inhibitor in China: first patient dosed in Sept. 2025; first-line and late-line combination therapy approved to be initiated in China or abroad, with indications covering PDAC, NSCLC and CRC

Strong IP position and original macrocyclic core structure: "chameleon" effect in molecular design with novel scaffold and robust IP position; broad inhibition of most GTP-bound wildtype and mutant subtypes

Potential to overcome multiple resistances: including secondary KRAS mutations, RTK gene alterations and induced resistance

Significantly wider therapeutic window: equivalent/better efficacy at 1/3-1/10 dosage of RMC-6236; higher bioavailability & dose-dependent activity

Clinical development plan for treatment of major cancer types



Pancreatic
cancer

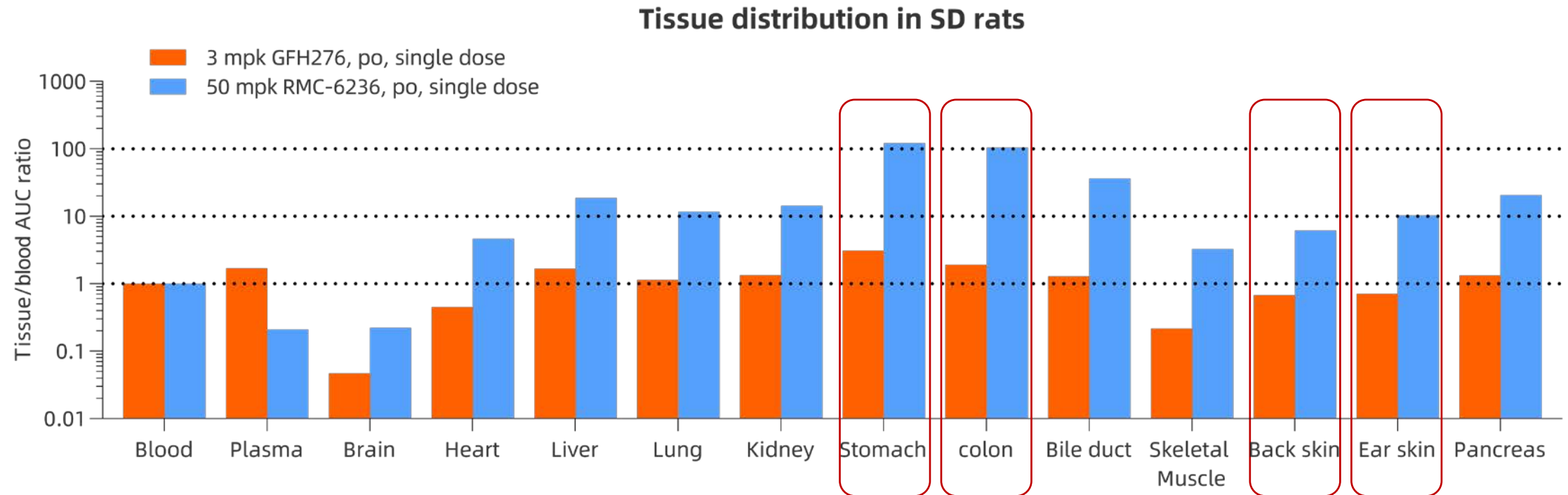


NSCLC



CRC

GFH276: Limited Distribution to Normal Tissues in Rats vs. RMC-6236

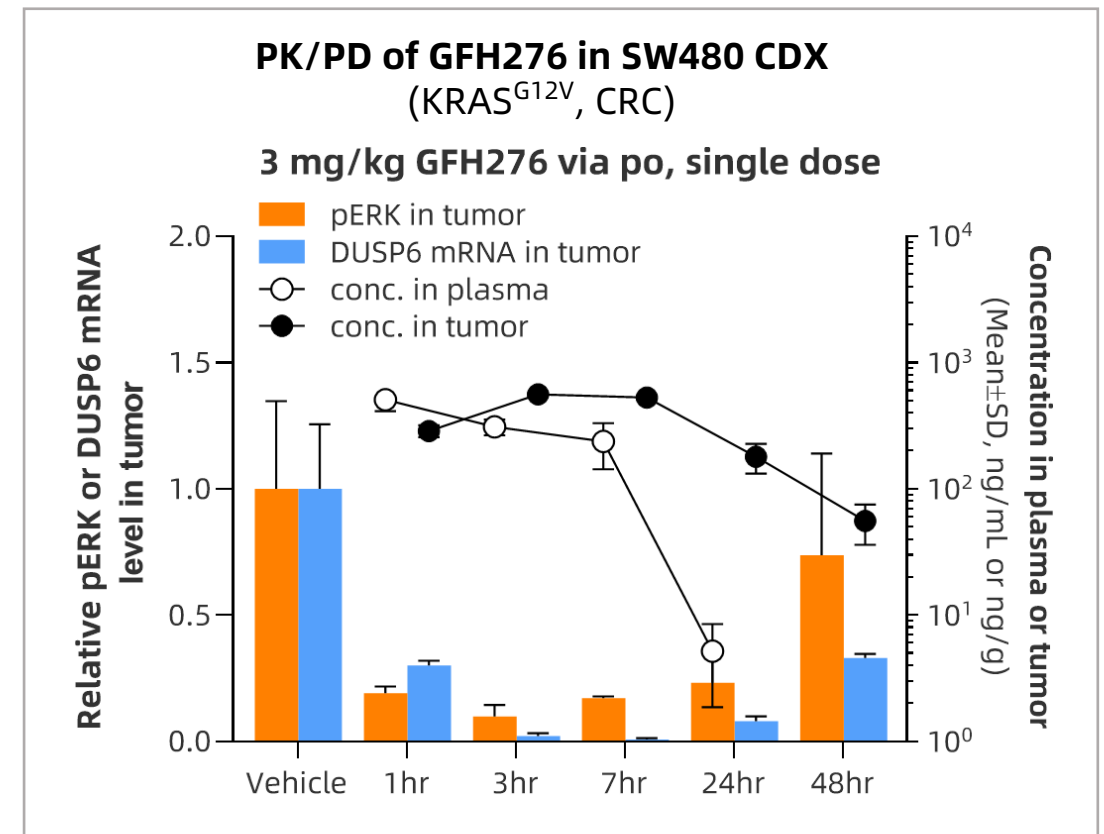
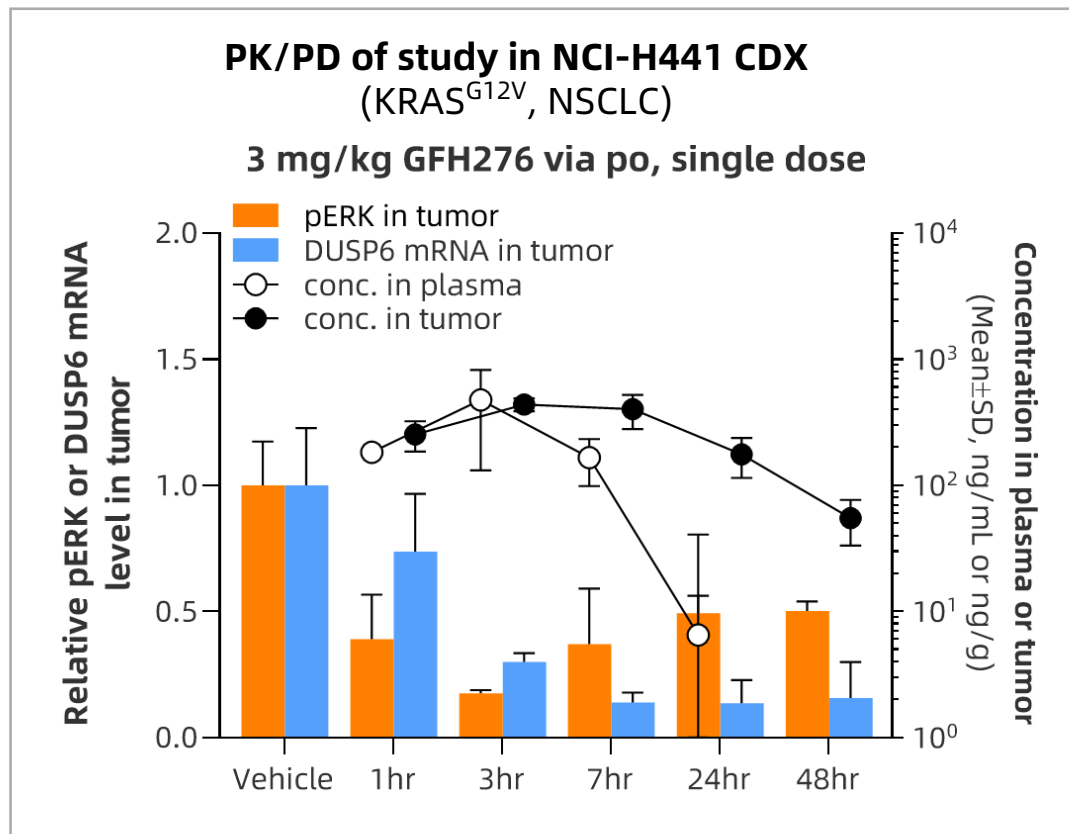


- **Comparable or less exposure of GFH276 in normal tissues vs blood**
- **Dramatically less accumulation in potential toxicity tissues such as skins and GI tracts vs. RMC-6236**

Note: Blood AUC of 3 mpk GFH276 is 10466 ng*h/mL, blood AUC of 50 mpk RMC-6236 is 3285 ng*h/mL

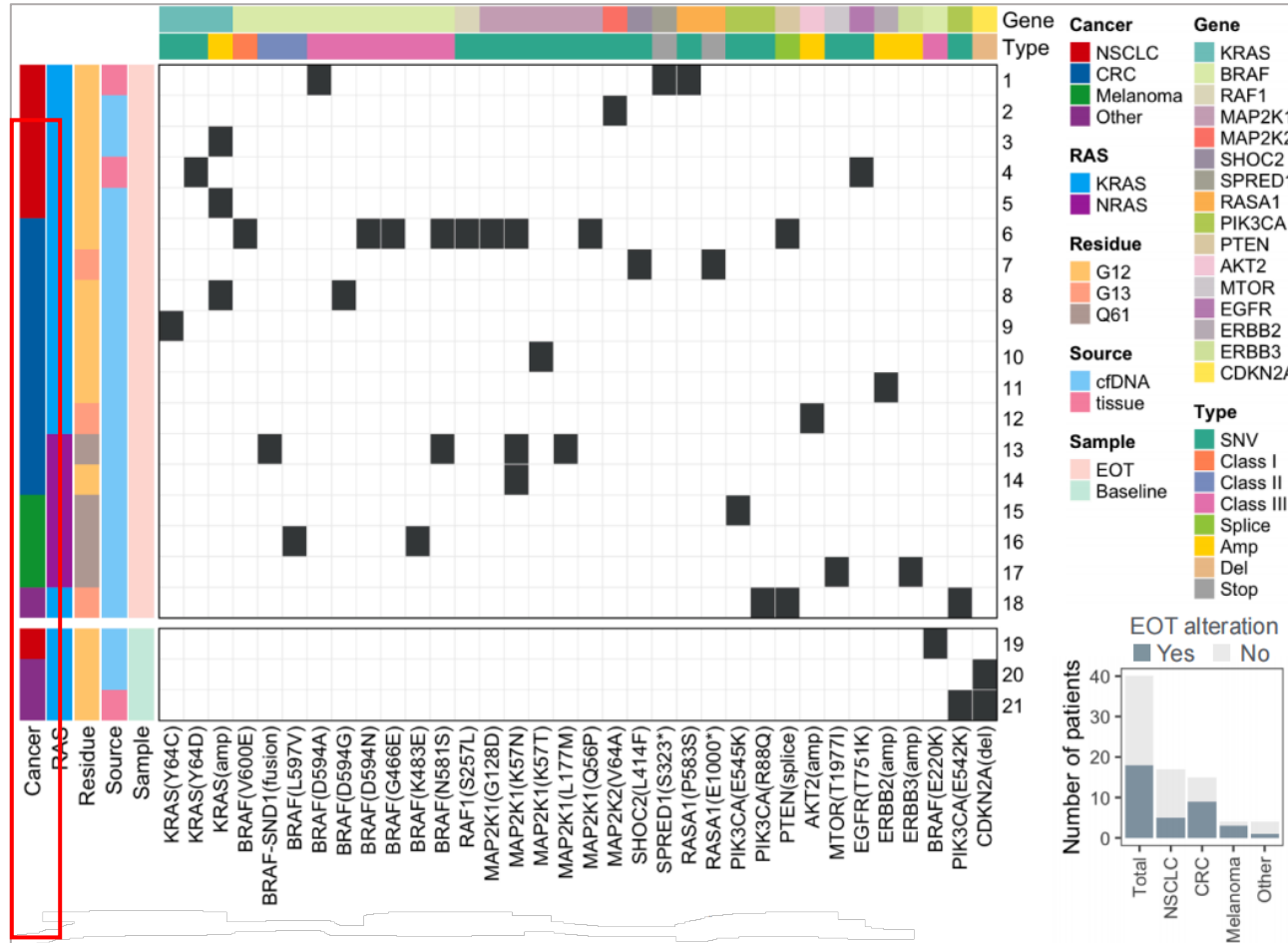
GFH276: Deep and Durable Target Pathway Inhibition In CDX Tumors

- Prolonged GFH276 distribution into KRAS mutated tumors observed after oral administration
- Deep inhibition on MAPK target gene expression starting from 3-7 hours and lasting for up to 48 hours

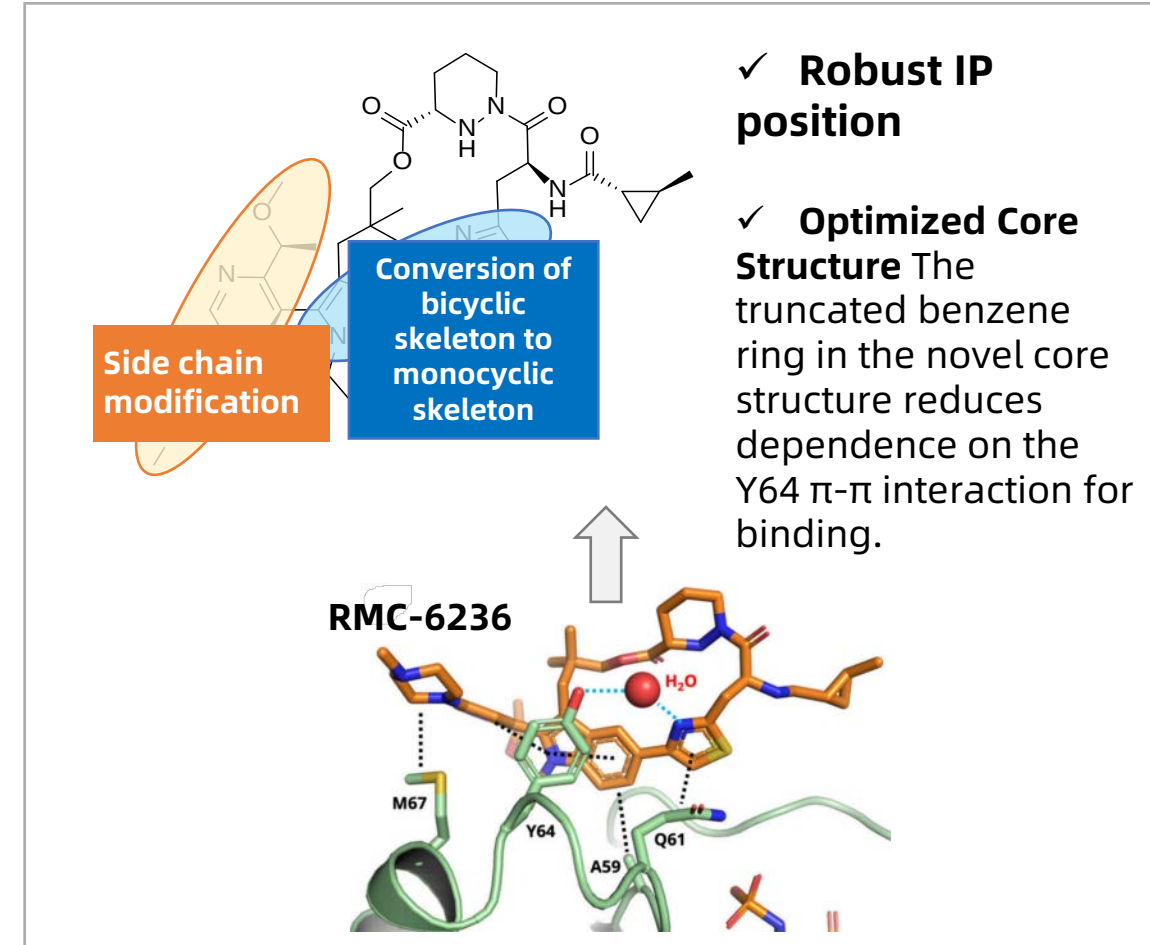


RMC-6236's Clinical Data Reveal KRAS Y64 as One of Key Resistance-associated Mutations for Pan RAS Inhibitors

Y64 mutation is one of the key treatment-emergent alteration in cfDNA or tissue specimens collected after treatment with daraxonrasib

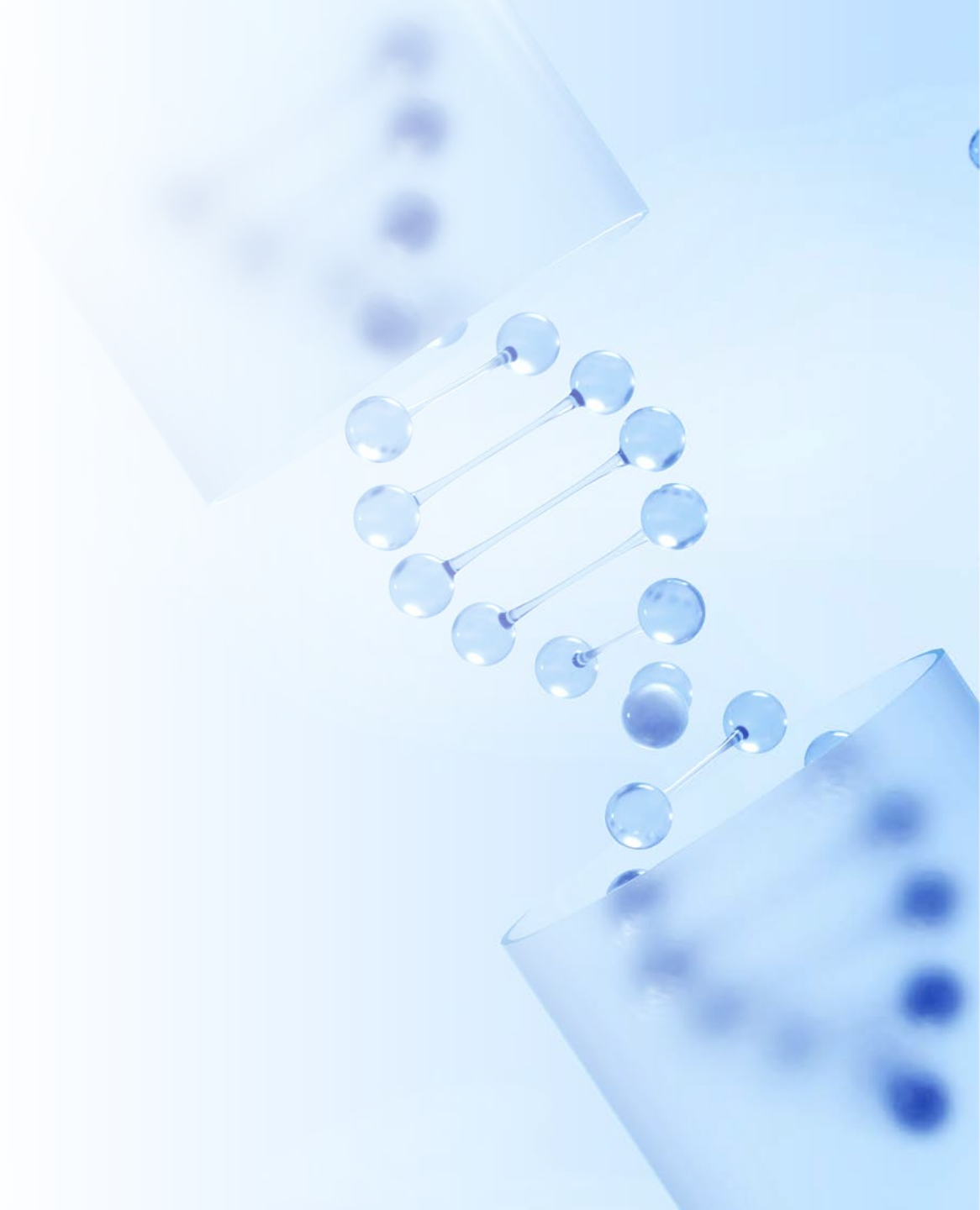


Unique structure features of GFH276 contribute to its ability to overcome resistance



PART 02

GFH375 LBA data review



FIH study of GFH276 (NCT07198321)

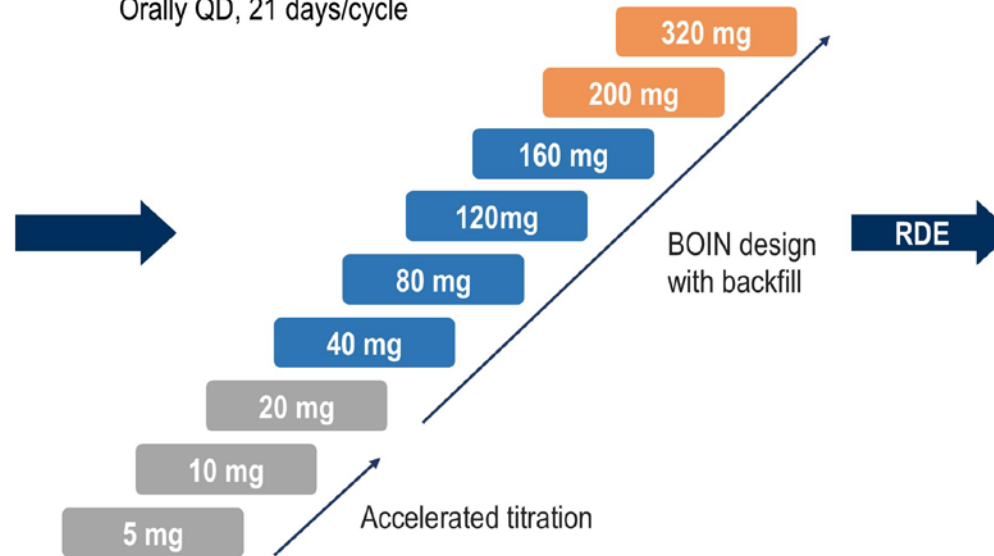
- As of 15 June 2026, a total of **98 patients** were enrolled in the **Phase Ia** study and treat with GFH276 5~320 mg QD, including **73 PDAC**, **18 NSCLC**, 5 CRC and 2 others.

Key eligibility criteria:

- Pathologically confirmed, **advanced solid tumors** harboring **RAS mutations** using local testing results
- Previously treated** with standard therapies
- ECOG PS 0~1

Phase Ia: Dose escalation

Orally QD, 21 days/cycle



Phase Ib: Dose expansion

NSCLC

PC

CRC

Other solid tumors

Treatment until progressive disease, intolerable toxicity or other reasons to withdrawal

Study Endpoints:

- Safety and tolerability
- Investigator-assessed ORR, DoR, DCR, PFS per RECIST v1.1
- Pharmacokinetics
- Exploratory biomarkers

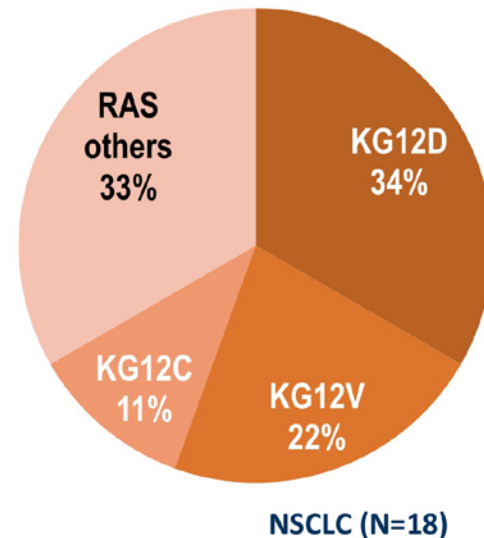
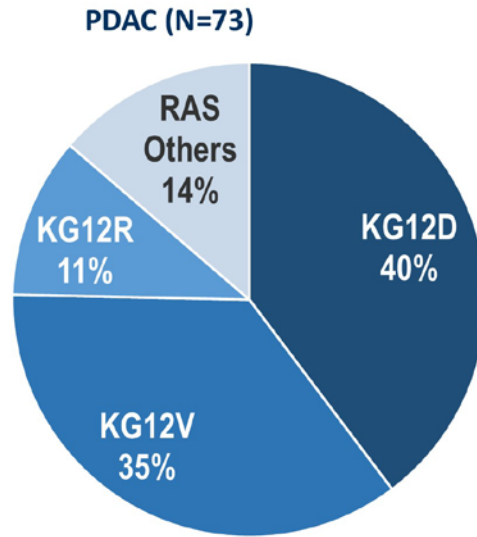
Abbreviations: ECOG, Eastern Cooperative Oncology Group. PS, performance status. QD, once daily. BOIN, Bayesian optimal interval. RDE, recommended dose for expansion. NSCLC, non-small cell lung cancer. PC, pancreatic cancer. CRC, colorectal cancer. DCR, disease control rate. DoR, duration of response. NSCLC, non-small cell lung cancer. ORR, objective response rate. PFS, progression-free survival. PK, pharmacokinetics. RDE, recommended dose for expansion. RECIST 1.1, Response Evaluation Criteria in Solid Tumors 1.1.

Yuxiang Ma, MD

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Demographics and Disease Characteristics

PDAC (N=73)	
Age, median (range), years	61.0 (20.0, 74.0)
≥60, n (%)	43 (58.9)
Male, n (%)	36 (49.3)
ECOG PS 0/1, n (%)	24 (32.9) / 49 (67.1)
Stage IV at study entry, n (%)	71 (97.3)
Baseline metastasis, n (%)	
Liver	57 (78.1)
Peritoneum	23 (31.5)
Lung	12 (16.4)
Bone	6 (8.2)
Number of prior lines of antitumor therapy, median (range)	2 (0, 6+)
0/1/≥2, n (%)	1 (1.4) / 19 (26.0) / 53 (72.6)
Prior antitumor therapy, n (%)	
Chemotherapy	72 (98.6)
Gemcitabine-containing	66 (90.4)
Taxane-containing	63 (78.8)
Fluorouracil-containing	57 (78.1)
Irinotecan-containing	52 (71.2)
Platinum-containing	41 (56.2)
Immune checkpoint inhibitor	24 (32.9)
RAS inhibitor	5 (6.8)

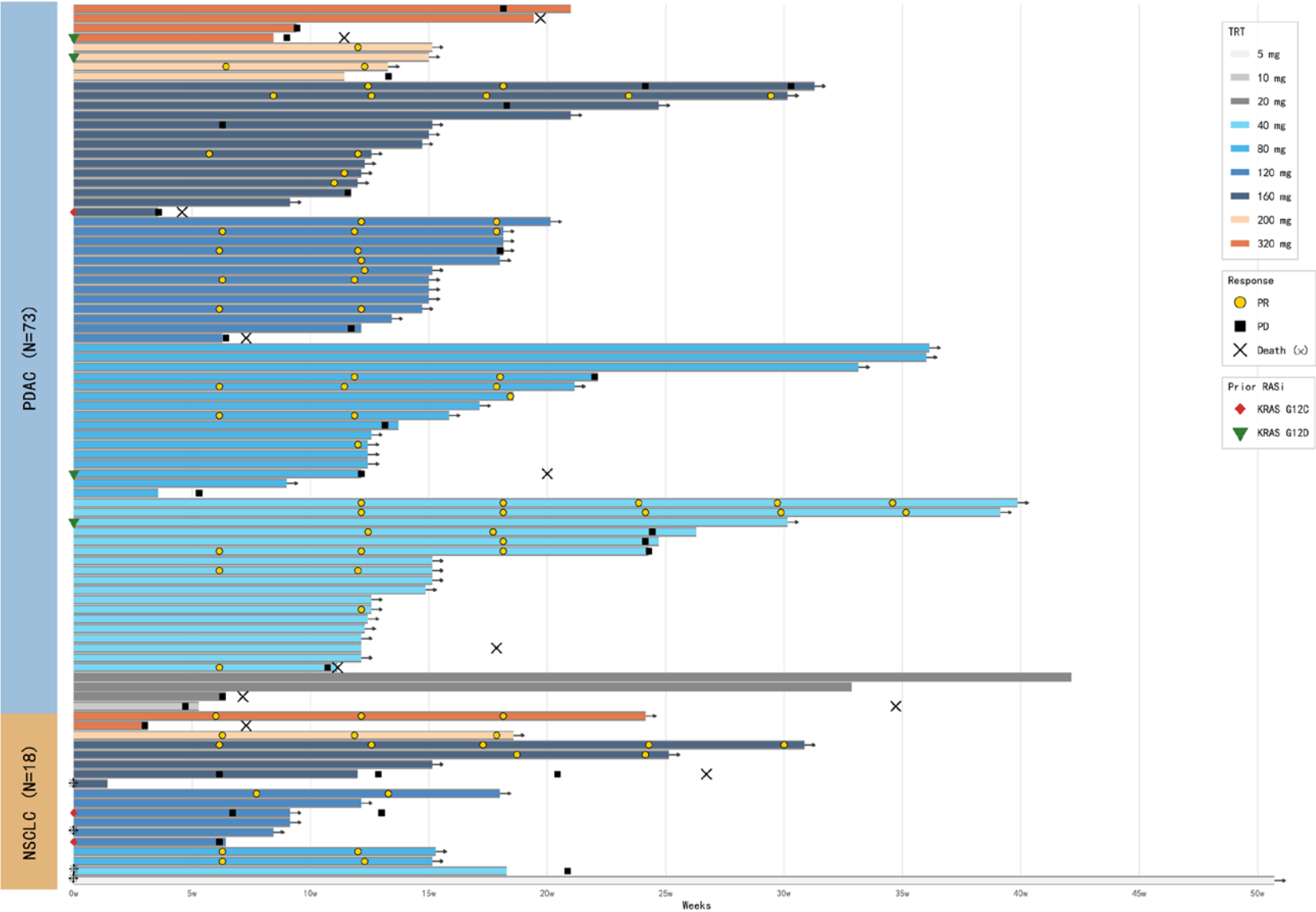


NSCLC (N=18)	
Age, median (range), years	61.5 (53.0, 72.0)
≥60, n (%)	12 (66.7)
Male, n (%)	12 (66.7)
ECOG PS 0/1, n (%)	5 (27.8) / 13 (72.2)
Stage IV at study entry, n (%)	18 (100)
Pathological type	
Adenocarcinoma/squamous carcinoma/other	16 (88.9) / 1 (5.6) / 1 (5.6)
PD-L1 (TPS)	
High/intermediate/ negative/missing	4 (22.2) / 2 (11.1) / 1 (5.6) / 11 (61.1)
Baseline metastasis, n (%)	
Lung	14 (77.8)
Bone	13 (72.2)
Brain	7 (38.9)
Liver	4 (22.2)
Number of prior lines of antitumor therapy, median (range)	2 (0, 6+)
0/1/≥2, n (%)	1 (5.6) / 6 (33.3) / 11 (61.1)
Prior antitumor therapy, n (%)	
Chemotherapy	17 (94.4)
Immune checkpoint inhibitor	15 (83.3)
RAS inhibitor	2 (11.1)

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Duration of Treatment



- Median follow-up time : 18.0 weeks (range: 4.6, 50.7)
- Median duration of treatment : 15.0 weeks (range: 1.4, 50.7) .
- 63 out of 91 were still on treatment.

	PDAC	NSCLC
All	N=73	N=18
Discontinued n(%)	23 (31.5)	5 (27.8)
Disease progression	15 (20.5)	4 (22.2)
Adverse event	-	1 (5.6)
Death	5 (6.8)	-
Physician's decision	1 (1.4)	-
Patient's decision	1 (1.4)	-
Other [#]	1 (1.4)	-
40-160 mg	N=61	N=14
Discontinued n(%)	14 (23.0)	4 (28.6)
Disease progression	9 (14.8)	3 (21.4)
Adverse event	-	1 (7.1)
Death	4 (6.6)	-
Physician's decision	1 (1.6)	-

Data cutoff date: 15 September 2026

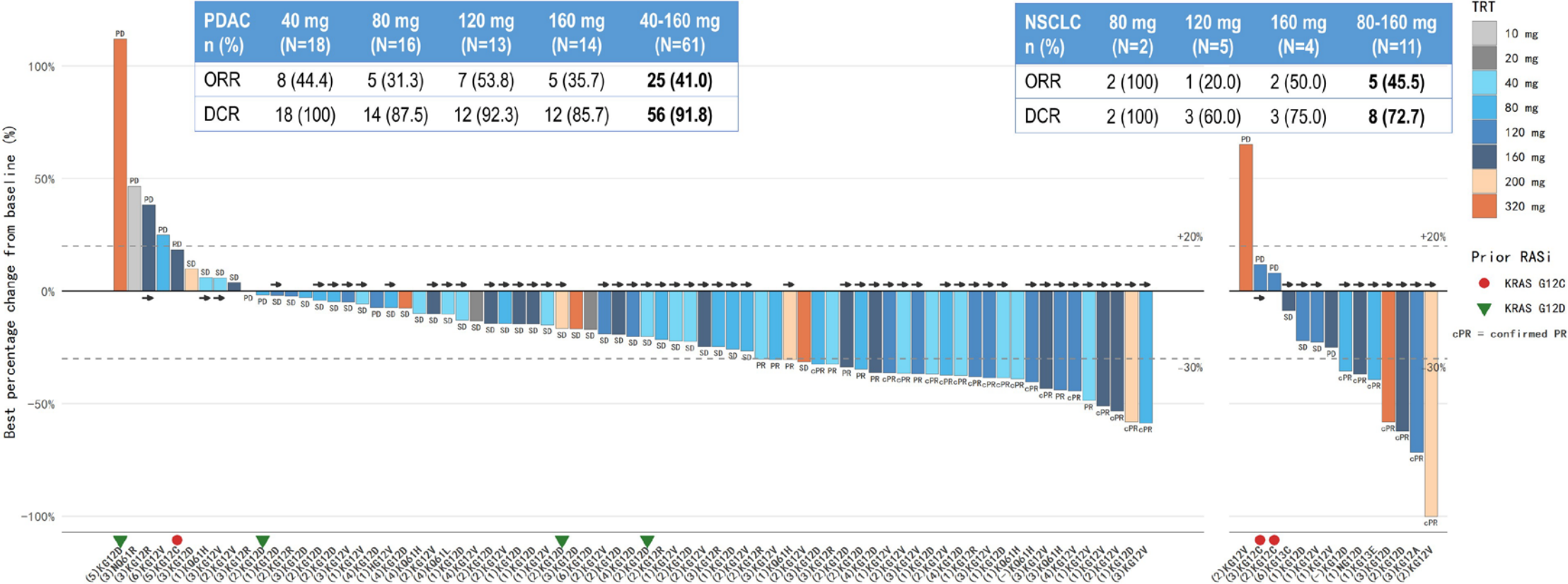
* Represents patients not evaluable for anti-tumor activity: 2 had no target lesions at baseline; 1 discontinued without post-dose tumor assessment due to an AE; 1 had no evaluable post-dose tumor assessment and was remained on treatment.

One patient in the 200 mg cohort discontinued study treatment because of fever and cholecystitis, which resulted in a treatment interruption of more than 28 days; both unrelated to GFH276.

Abbreviations: TRT, treatment. RASi, selective RAS inhibitor

Objective Response

- Partial responses were observed starting from the 40 mg dose cohort.
- 61 PDAC and 14 NSCLC received 40~160 mg:
 - ORR was **41.0%** (25/61, 90% CI: 30.3-52.3) in **PDAC**, and **45.5%** (5/11, 90%CI: 20.0-72.9) in **NSCLC**.
 - In **RAS inhibitor naïve** patients, ORR was **43.1%** (25/58) in **PDAC**, and **55.6%** (5/9) in **NSCLC**.



Data cutoff date: 15 September 2026
ORR and DCR were calculated in the evaluable population, defined as patients with target lesions at baseline and at least one post-dose evaluable tumor assessment. Among the 14 NSCLC, 3 were not evaluable: 1 at 40 mg had no baseline target lesions; 1 at 120 mg had no evaluable post-dose tumor assessment but was still on treatment; 1 at 160 mg dropped out without post-dose tumor assessment due to G3 stomatitis.

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Safety Profile

- No prophylactic medications were used in the Phase Ia part.
- GFH276 is well tolerated in dose range 40-160mg QD without DLTs observed.
- The most common TRAEs were cutaneous, hematological, mucosal, and gastrointestinal, most being grade 1 or 2.
- G3 TRAEs occurred in 27.5%, most commonly rash (7.5%), followed by anemia, diarrhea, platelet count decreased, and WBC count decreased (3.8% each).
- No G4 or G5 TRAEs were observed.

n (%)	40-160 mg (N=80)*	
	Any	G3
TRAE	79 (98.8)	22 (27.5)
TRSAE	9 (11.3)	8 (10.0)
TRAE leading to death	0	0
TRAE leading to dose modifications		
Leading to interruption	18 (22.5)	11 (13.8)
Leading to dose reduction	14 (17.5)	7 (11.3)
Leading to discontinuation	1 (1.3)	1 (1.3)

Data cutoff date: 15 July 2026.

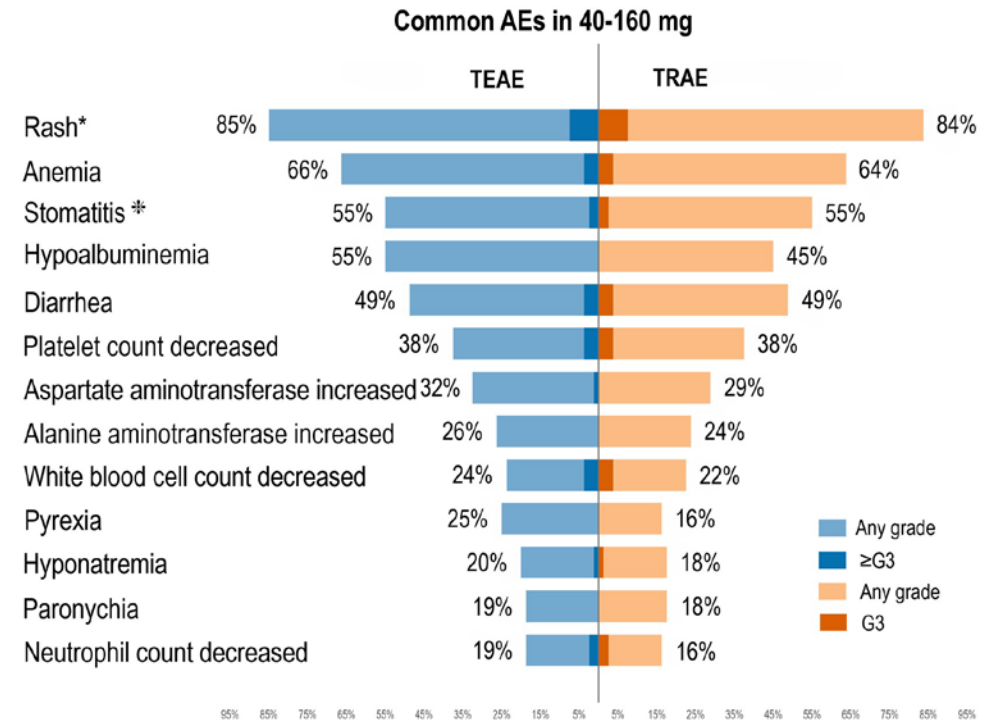
* Including 61 PDAC, 14 NSCLC, 3 CRC, and 2 others.

Median follow-up time (range) was 8.7 (4.4, 31.1) weeks. Median duration of exposure (range) was 8.4 (1.4, 31.0) weeks.

Abbreviations: TRAE, treatment-related adverse event. TRSAE, treatment-related serious adverse event. WBC, white blood cell.

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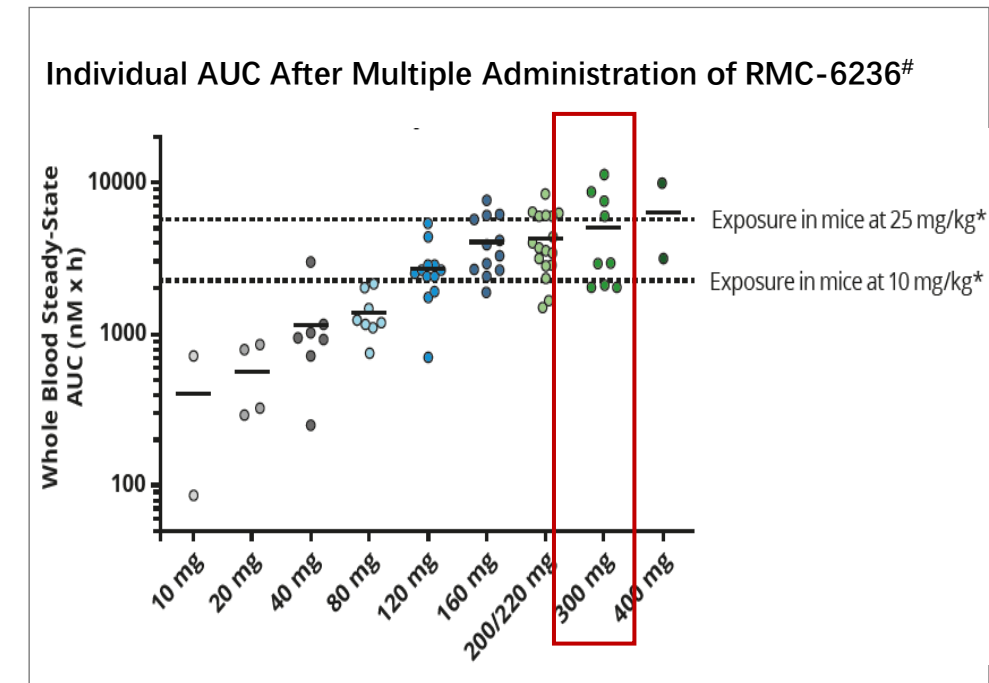
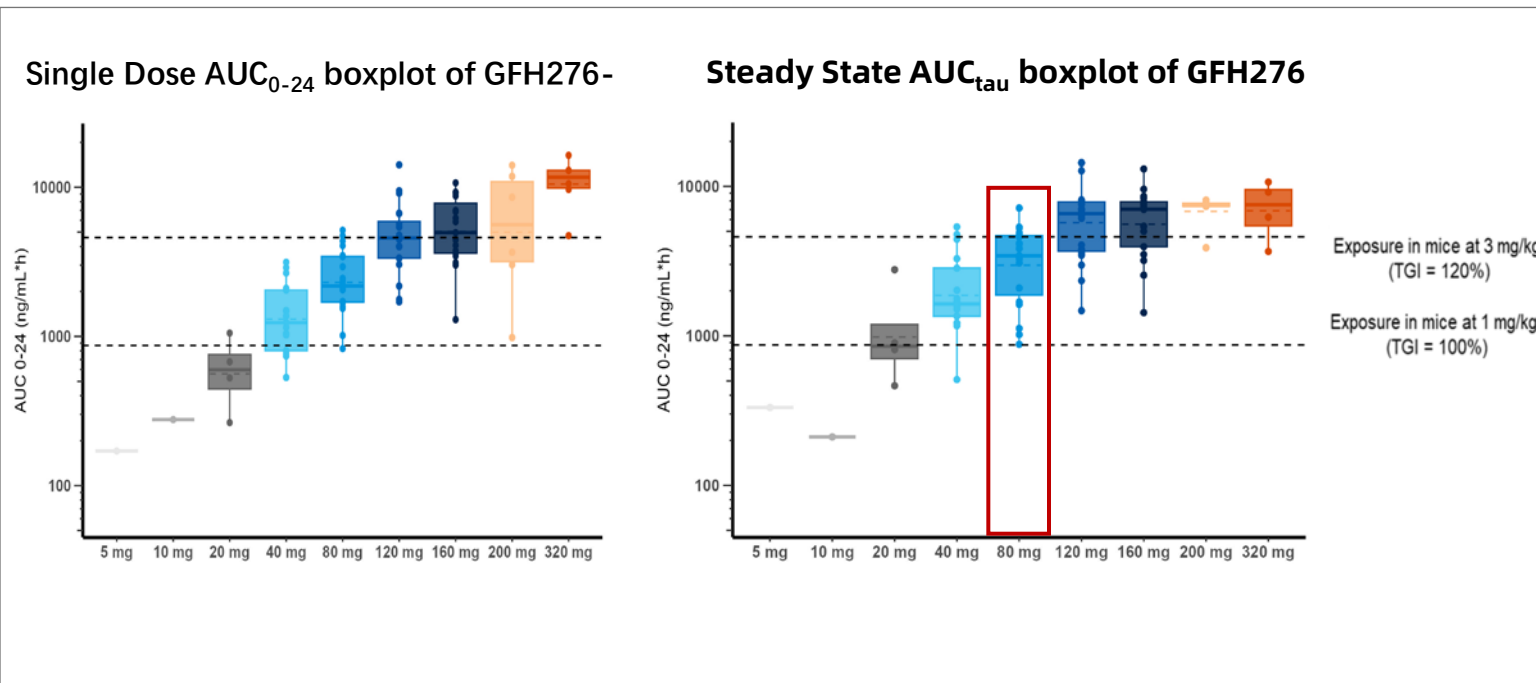
Common AEs were presented by TRAE ≥15%. No G4 or G5 TRAEs were observed.

* Pooled PTs: Rash, dermatitis acneiform, rash maculopapular, erythema nodosum, dermatitis exfoliative generalized, rash pustular, drug eruption, genital rash. Multiple types of rash may have occurred in the same patient.

† Pooled PT: Stomatitis, and mouth ulceration.

GFH276: Linear PK Exposure with No Exposure Plateau

- Approximately **linear PK** exposure with half-life 10.3-19.1 hours.
- **No exposure plateau** or significant accumulation observed.
- Exposure of 40 mg and 120 mg achieved target levels of 100% and 120% TGI in mice AsPC-1 CDX model, respectively.
- Lower dose (GFH276 80mg vs. RMC-6236 300mg) to achieve target exposure



*Exposure corrected with cross-species protein binding and blood/plasma partitioning.

*RMC-6236 10mg/kg QD induces tumor regressions in sensitive models.

*RMC-6236 25mg/kg QD induces tumor regressions in the majority of models.

[#]RVM 2023 AACR Poster

GFH276 human BP ratio=1.05

PDAC Cross-trial Efficacy Comparison

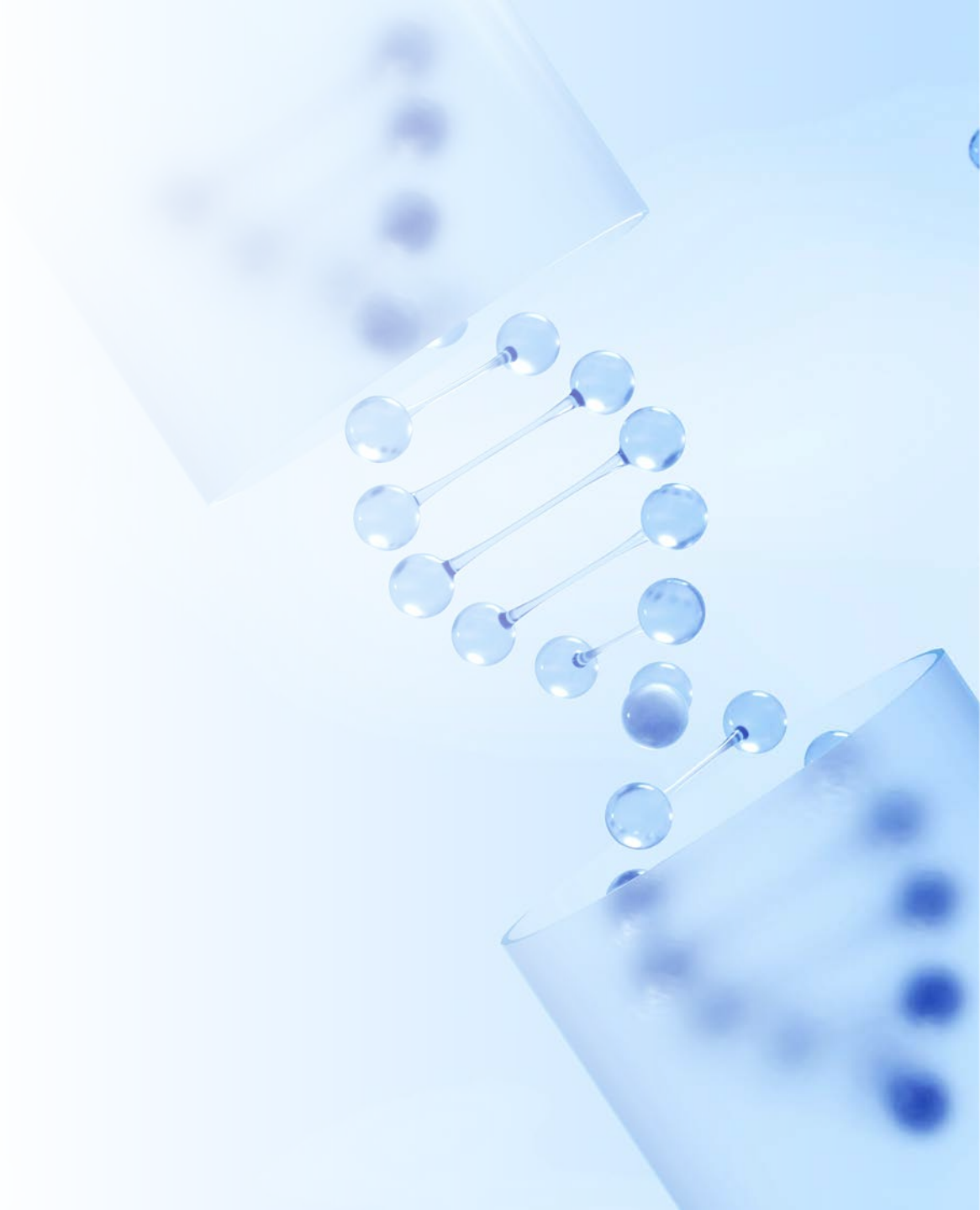
		GFH276	RMC-6236		
Data phase		Phase I	Phase I/II		Phase III
Dose level		40-160 mg QD	300 mg QD (all ORRs are confirmed)		
Overall population		All RAS mutations	All RAS mutations		
	Size	N=61 (2L+)	N=38 (2L)	N=45 (3L+)	N=237 (2L)
	ORR	41%	29%	20%	31.6%
	DCR	91.8%	95%	84%	Not reported
Subgroup efficacy		RAS inhibitor naïve	KRAS G12X-mutant		
	Size	N=58 (2L+)	N=26 (2L)	N=38 (3L+)	N=217 (2L)
	ORR	43.1%	35%	21%	33.2%
	DCR	94.8%	92%	87%	Not reported
Cutoff and source		Cutoff: 2026.9.15 Source: 2026 ESMO	Cutoff: 2025.6.30 Source: 2026 NEJM		Cutoff: 2026.2.10 Source: 2026 ASCO

PDAC Cross-trial Safety Comparison

	GFH276 (40-160 mg QD)		RMC-6236 (300 mg QD)			
Data phase	Phase I		Phase I/II		Phase III	
Sample size	N=61 (2L+)		N=83 (2L+)		N=241 (2L)	
≥3级TRAEs	14.8%		34%		43.6%	
Dose interruption	13.1%		43%		56%	
Dose discontinuation	0		0		1.2%	
Death	0		0		0.4%	
Individual TRAEs	≥ Grade 3	All grades	≥ Grade 3	All grades	≥ Grade 3	All grades
Category of rash	1.6%	78.7%	7%	90%	14%	85%
Anemia	3.3%	60.7%	7%	Not reported	4%	18%
Stomatitis	0	47.5%	4%	54%	12%	53%
Diarrhea	1.6%	41%	4%	52%	5%	58%
Vomiting	0	13.1%	0	36%	< 1%	37%
Nausea	0	9.8%	0	39%	2%	46%
Fatigue	0	1.6%	1%	17%	4%	23%
Cutoff and source	Cutoff: 2026.7.15 Source: 2026 ESMO		Cutoff: 2025.6.30 Source: 2026 NEJM		Cutoff: 2026.2.10 Source: 2026 ASCO	

03 *PART*

Summary and outlook



RAS Inhibitors Define the Fastest-growing Segment in Oncology Market

Pan RAS inhibitor market outlook
(no Pan RASi approved globally)

**Forecast of RMC-6236 peak sales
rising dozens of times over one year**

 GlobalData

Forecast in Dec. 2024

\$230 MM

RBC Capital Markets

Forecast in Sept. 2025

\$4.8 Bn

Bloomberg

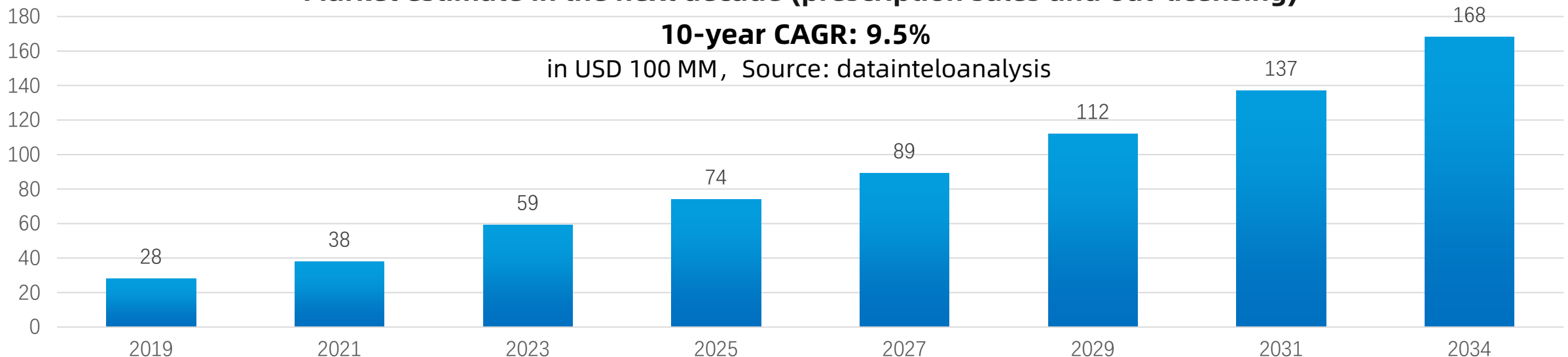
Forecast in May 2026

\$8.3 Bn

Market estimate in the next decade (prescription sales and out-licensing)

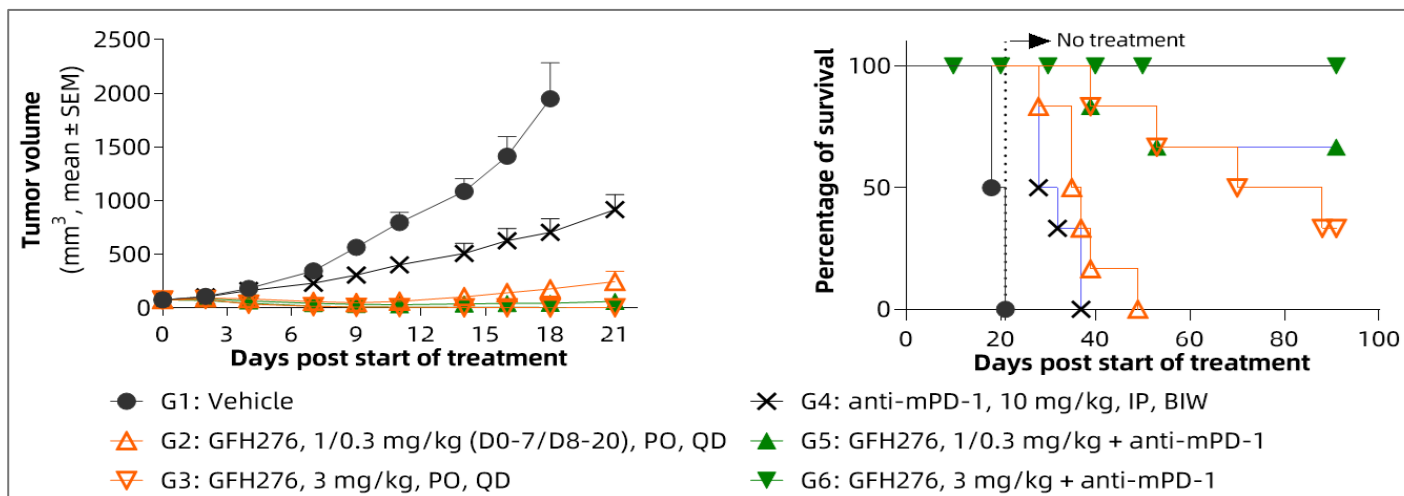
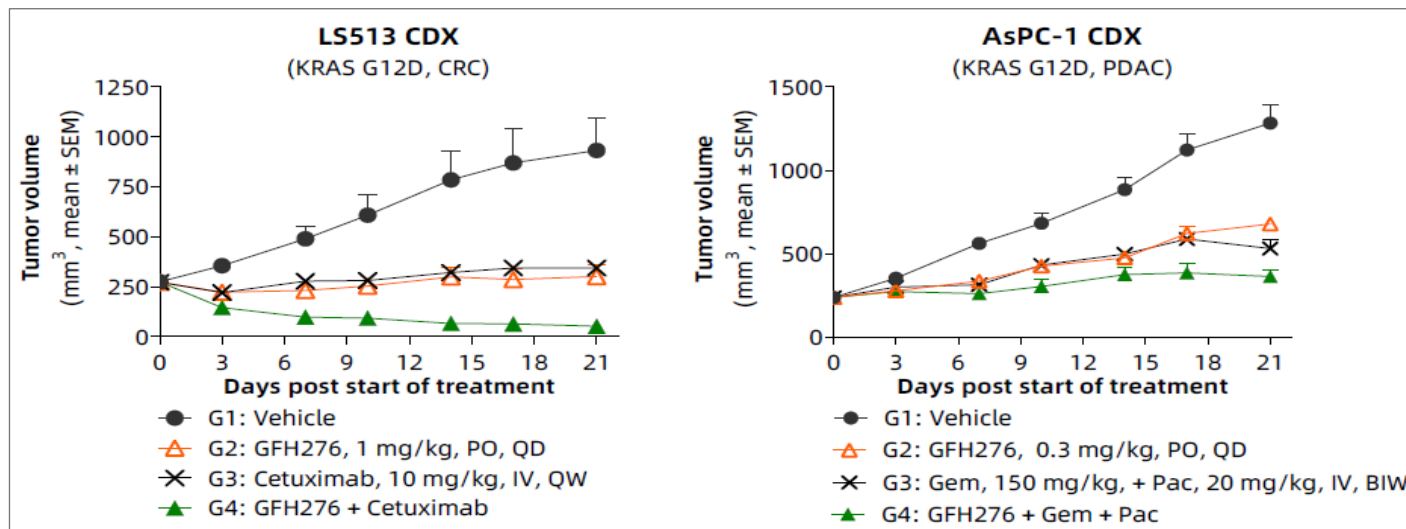
10-year CAGR: 9.5%

in USD 100 MM, Source: dataintelanalysis



Broad Combination Prospects

Animal models of various tumor types (Source: 2026 AACR)



GFH276 combined with cetux

GFH276 with chemo

Preclinical finding: antitumor activity notably exceeding monotherapy

Clinical progress:

- 1L PDAC:** clinical trial approval of GFH276 combined with cetux or chemo (China, Australia)
- 2L+ CRC:** clinical trial approval of GFH276 combined with chemo (±bevacizu), or with cetux (China)

GFH276 combined with PD-1 antibody

Preclinical finding: dose-dependent synergy, tumor-free survival significantly improved even months after treatment cessation

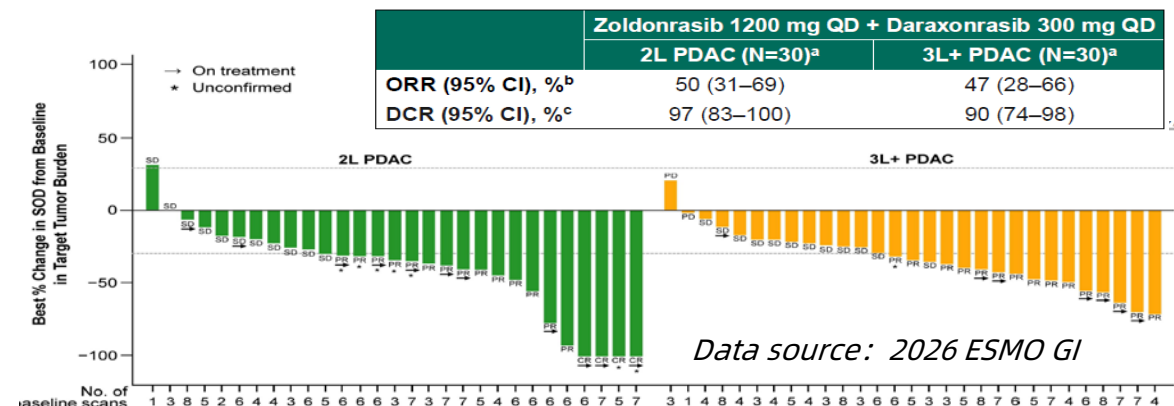
Clinical progress:

- 1L NSCLC:** clinical trial approval of GFH276 combined with PD-1 antibody (China)

GFH375 + GFH276: First-in-world Combo of RAS Inhibitors with Distinct MOA

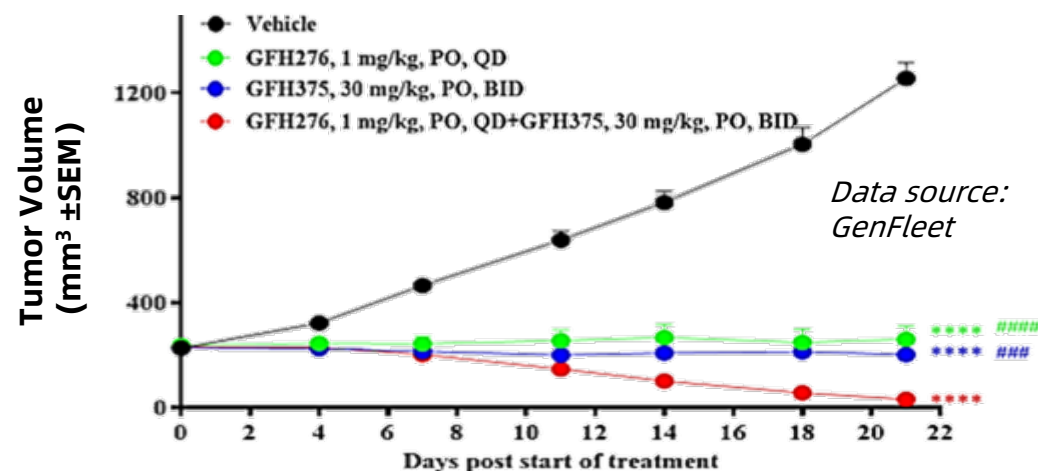
Rev Med trial: dual molecular-glue combination (RMC-9805+RMC-6236)

- ORR: superior to each single-agent monotherapy
- Preliminary clinical validation of combining KRAS G12D + Pan RAS dual inhibition



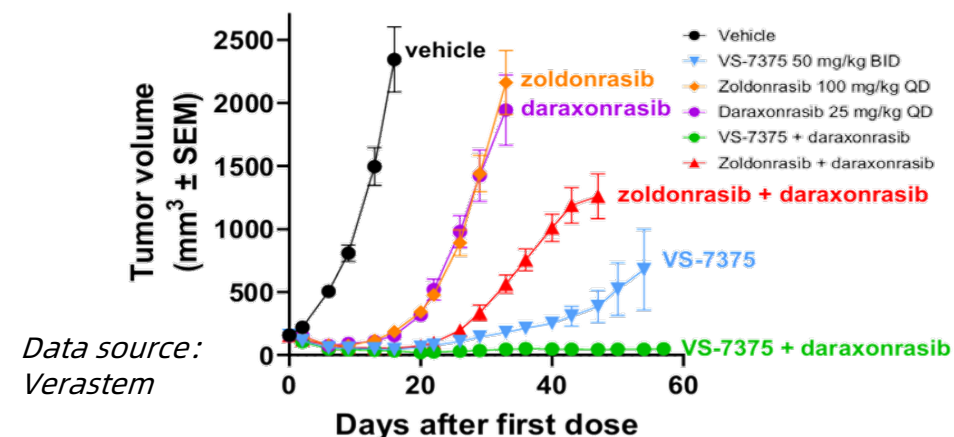
Preclinical PDAC models: GFH375 + RMC-6236

Superior TGI over either monotherapy with obvious synergy



Preclinical PDAC models: GFH375 + RMC-6236

Exhibits superior TGI versus multiple single-agent therapies, surpassing TGI of the RMC-9805 + RMC-6236 combination



Six Launches Support Solid Commercialization Prospects

GFH375 (KRAS G12D inhibitor)

PDAC

BTB

Late-line, mono

1st-line, combo with chemo

NSCLC

BTB

Late-line, mono

CRC

BTB

Late-line, combo with cetux

GFH276 (Pan RAS inhibitor)

PDAC

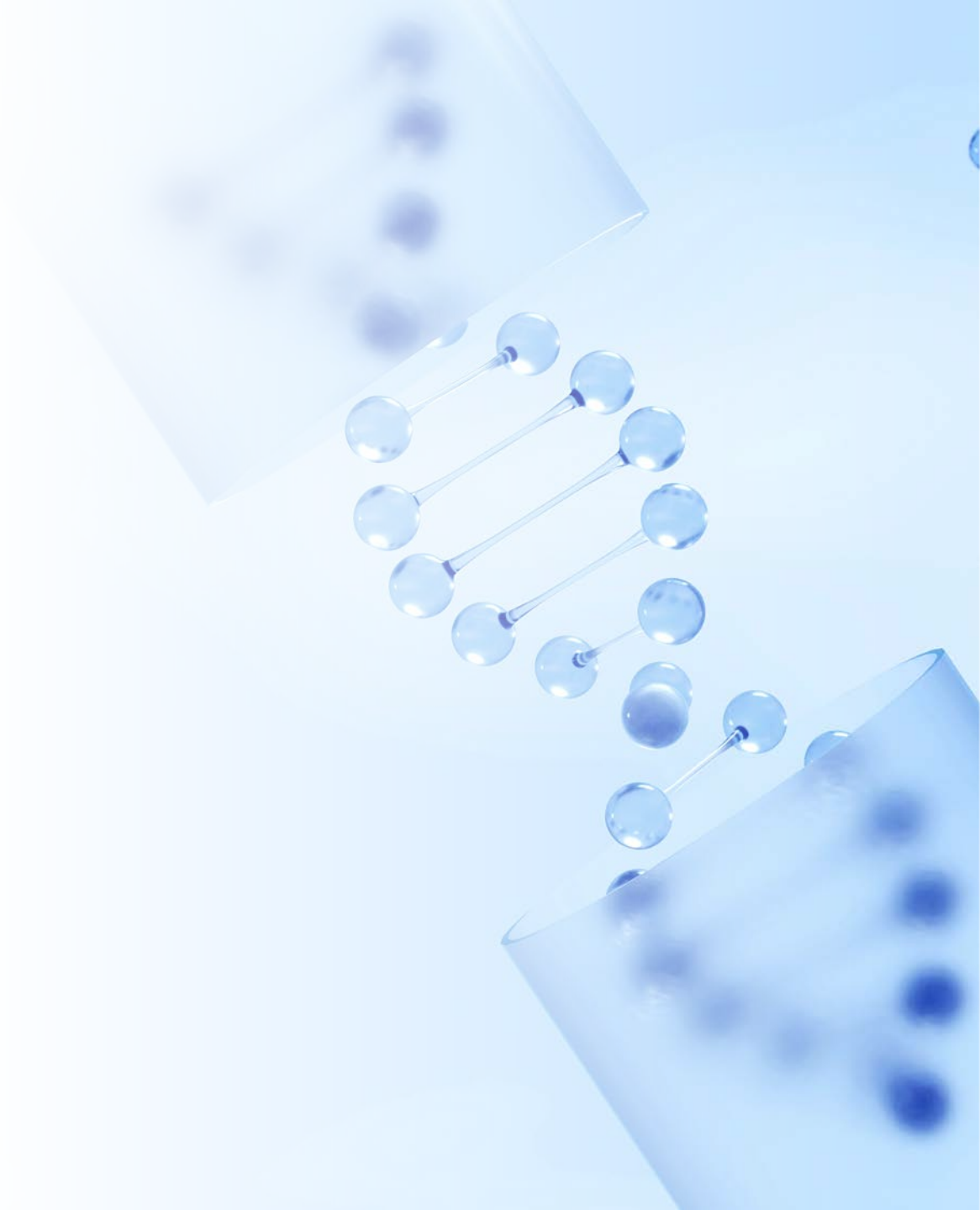
Late-line, mono

1st-line, combo with chemo

PART

04

Q&A





Innovation, in expedition