Revolution Medicines

On Target to Outsmart Cancer

August 7, 2024

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For a further description of the risks and uncertainties that could cause actual results to differ from those anticipated in these forward-looking statements, as well as risks relating to the business of Revolution Medicines in general, see Revolution Medicines' Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on August 7, 2024, and its future periodic reports to be filed with the Securities and Exchange Commission.

This presentation concerns product candidates that are under clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration (FDA). These product candidates are currently limited by Federal law to investigational use, and no representation is made as to their safety or effectiveness for the purposes for which they are is being investigated.

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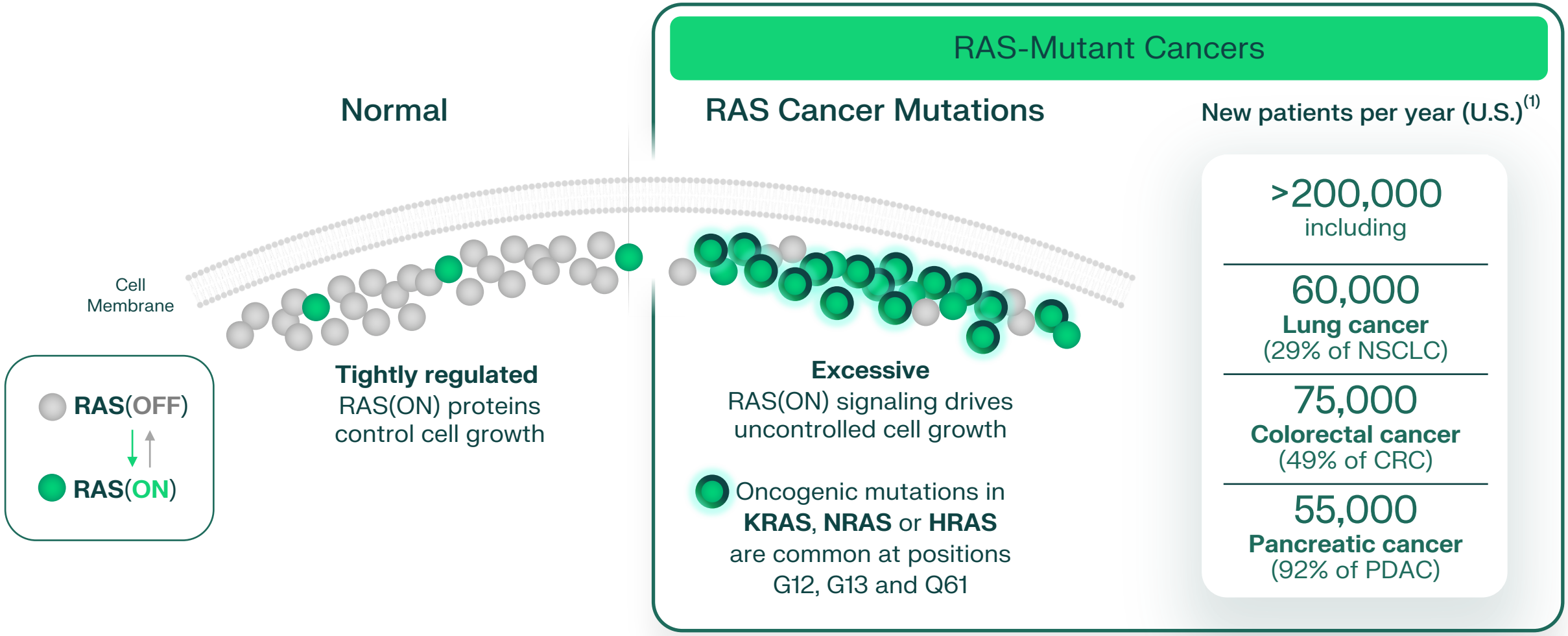
Mission: to revolutionize treatment for patients with RAS-addicted cancers through the discovery, development and delivery of innovative, targeted medicines.

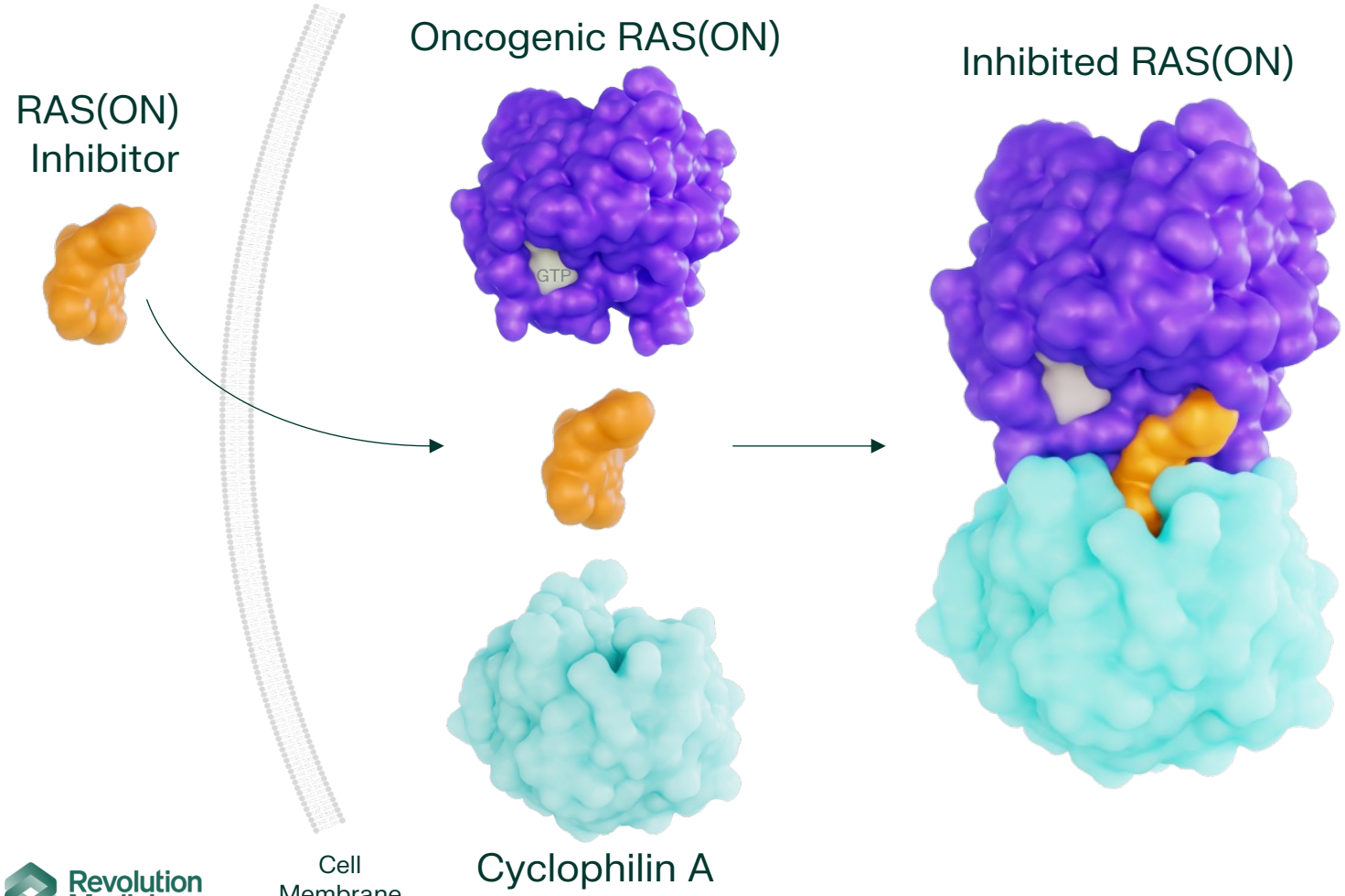
- **Pioneering class of RAS(ON) inhibitor drug candidates** targeting oncogenic drivers of life-threatening cancers
- **RMC-6236 is a groundbreaking RAS(ON) multi-selective inhibitor:**
  - Advancing to RASolute 302, a global, randomized Phase 3 trial in 2L metastatic PDAC patients
  - Continuing monotherapy and combination exploration for 1L PDAC and other indications
- **Early clinical development underway for RMC-6291 (G12C) and RMC-9805 (G12D),** mutant-selective, covalent RAS(ON) inhibitors designed for monotherapy and combination therapies, including with RMC-6236

Portfolio of RAS(ON) Inhibitors Designed to Target 30% of Human Cancers



(1) Estimated using tumor mutation frequencies from Foundation Medicine Insights March 2022 and scaled to estimated patient numbers using cancer incidence from ACS Cancer Facts and Figures 2023, PDAC based on ACS Cancer Facts and Figures 2024 (see appendix for additional detail); NSCLC = non-small cell lung cancer; CRC = colorectal cancer; PDAC = pancreatic ductal adenocarcinoma

Pioneering Tri-complex RAS(ON) Inhibitors Designed to Deliver Robust and Durable Anti-tumor Activity



- **Direct inhibition of RAS(ON) cancer drivers**
- **Deep and durable suppression of RAS cancer signaling designed to defy common drug resistance mechanisms**
- **Clinical validation of first two RAS(ON) Inhibitors studied as single agents**

Initial Clinical Profiles of RAS(ON) Inhibitors Support Broad Set of Potential Opportunities to Treat RAS-Addicted Cancers

		Target Genotypes
Multi-Selective		
RMC-6236	Clinical validation in NSCLC and PDAC; Advancing to Phase 3 in PDAC	**G12X and expansion**[(1)]
Mutant-Selective		
RMC-6291	Evidence of differentiated clinical activity in NSCLC and CRC	**G12C**
RMC-9805	Dose optimization ongoing	**G12D**

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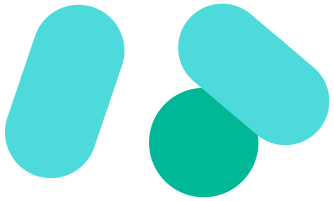
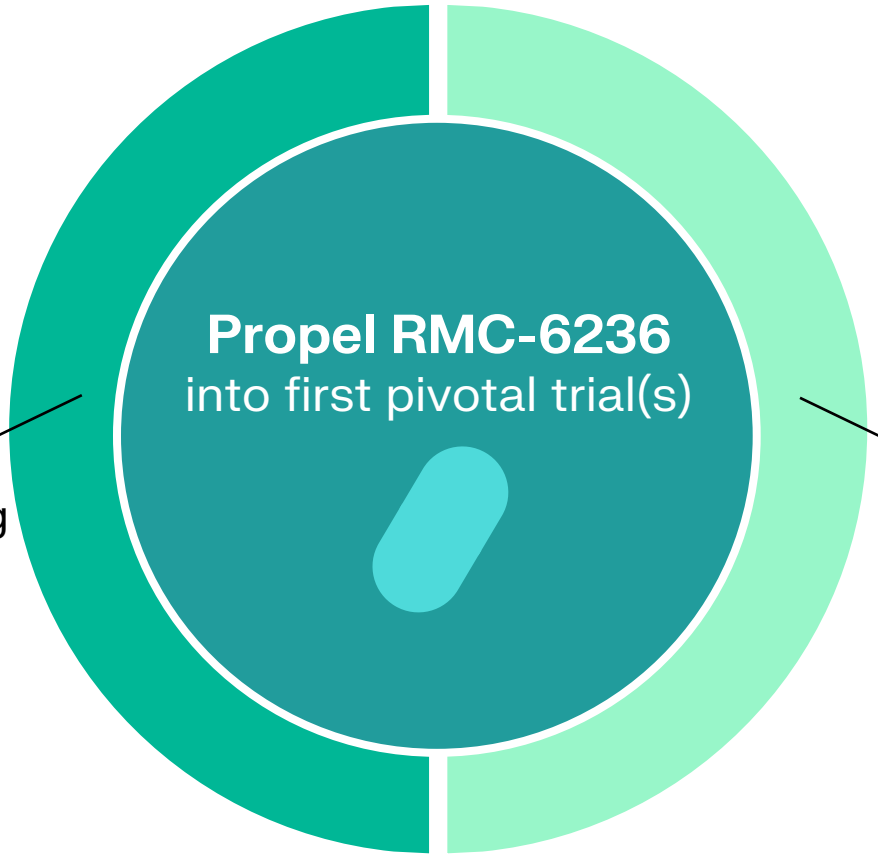
(1) KRAS G12X initially defined as mutation at codon 12 which encodes glycine (G) to X where X = A, D, R, S, or V. RMC-6236-001 protocol amended in August 2023 to broaden enrollment, now allowing patients with tumors bearing mutations in any of the three hotspots (G12X/G13X/Q61X) in any of the three major RAS isoforms (KRAS/NRAS/HRAS); G12X broadened to include G12C.

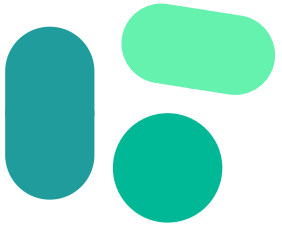
2024 Capital Allocation Priorities to Advance Pioneering RAS(ON) Inhibitor Pipeline …

Expand reach of RMC-6236
by clinically assessing opportunities (1L, types, mutations)





Qualify mutant-selective inhibitors
led by RMC-6291 and RMC-9805 for late-stage development



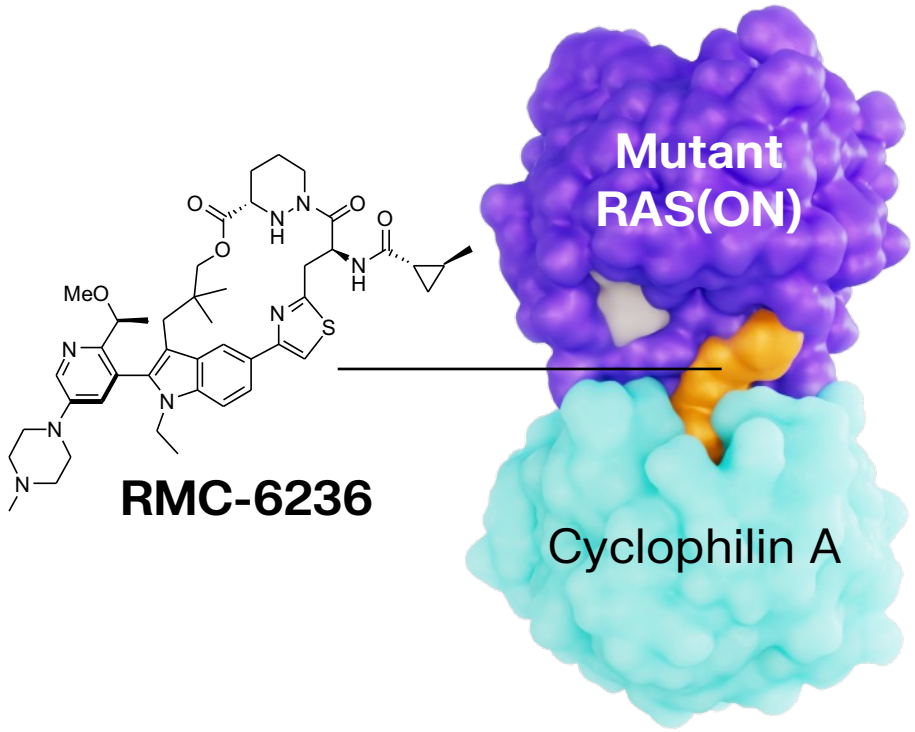
… driving to

Industry-Leading Targeted Medicines Franchise for RAS-Addicted Cancers

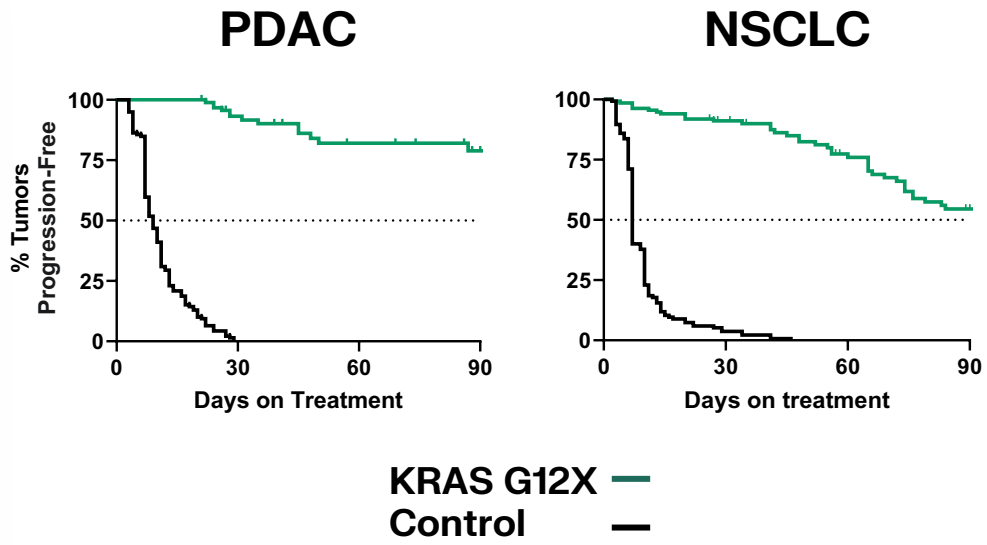
RAS(ON) Multi-Selective Inhibitor RMC-6236

RMC-6236: RAS(ON) Multi-Selective Inhibitor Designed to Directly Inhibit Oncogenic State of Common RAS Drivers of Cancer

Pioneering Drug Design and Mechanism of Action



Induces Durable Progression-Free Survival in RAS G12X Models[1]

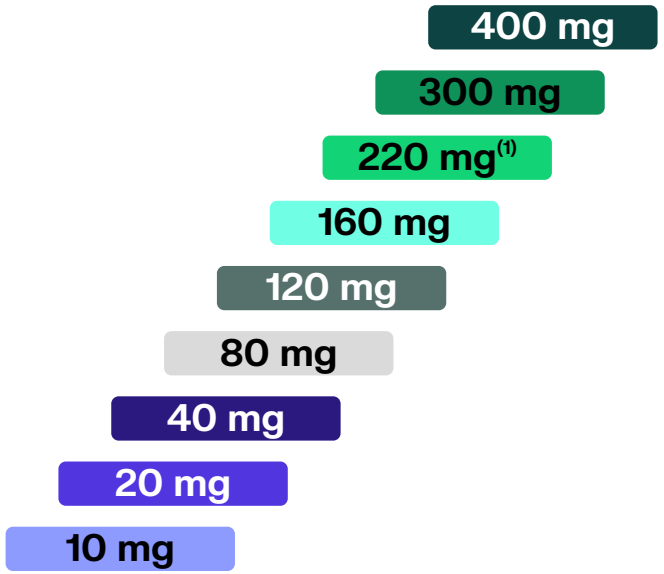


(1) RVMD preclinical data, Jiang et. al. Cancer Discovery 2024:14:1-24.

RMC-6236 has been Evaluated Across a Large Number of Patients with Advanced RAS Mutant Solid Tumors in the First-in-Human Trial

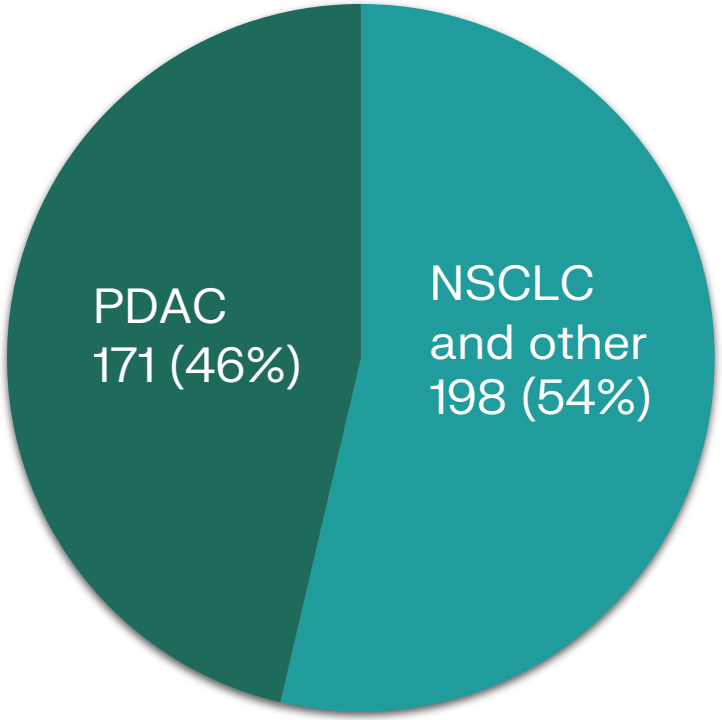
Dose Escalation in Solid Tumors

RMC-6236 administered orally QD



Tumor Types in FIH Trial

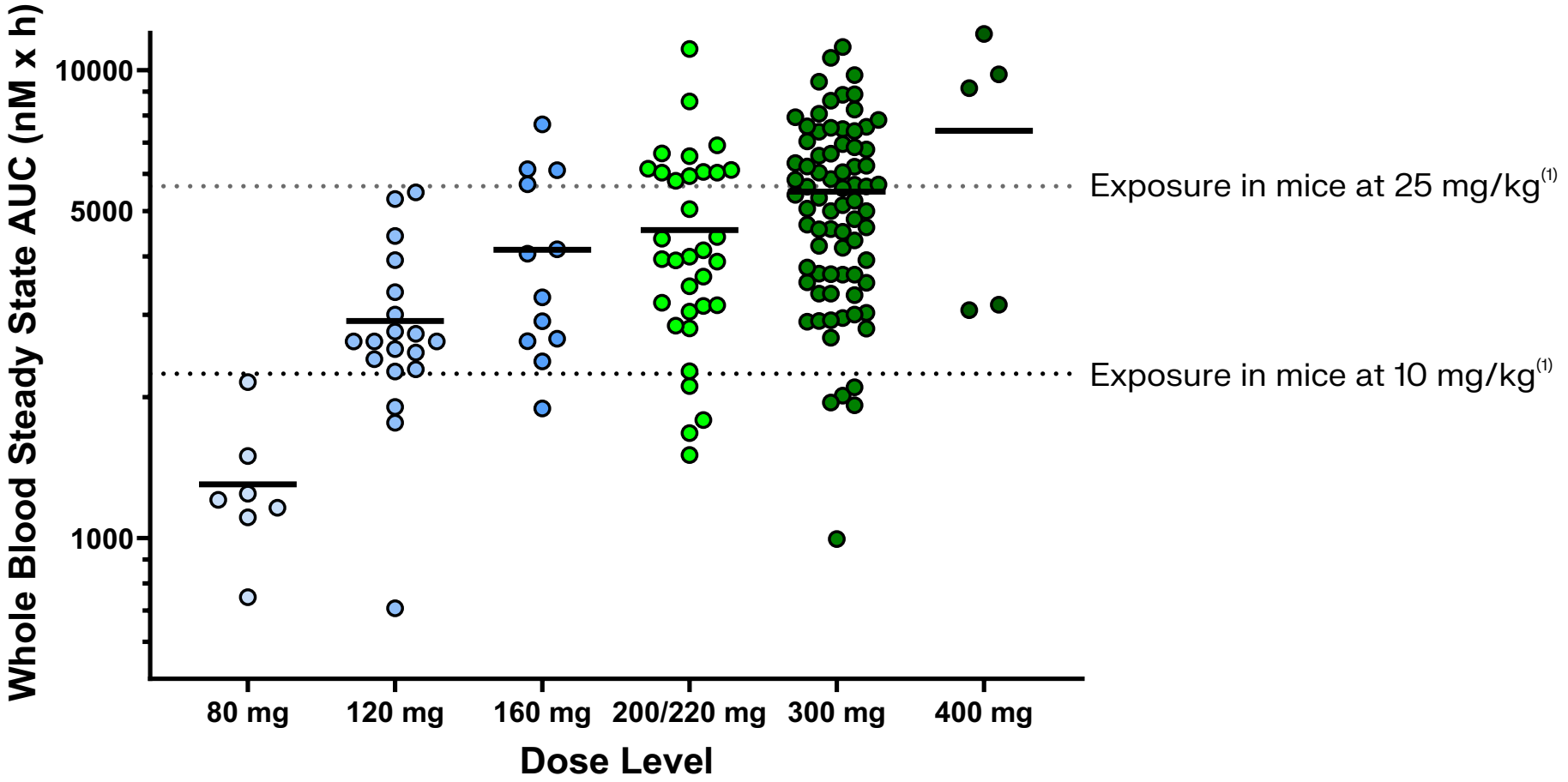
N = 369



RMC-6236-001 Clinical Trial: https://clinicaltrials.gov/study/NCT05379985
(1) 220 mg cleared dose limiting toxicity (DLT) evaluation and a dose of 200 mg was selected for further expansion/optimization.
FIH, first-in-human; QD, once daily.

5/11/24 data cutoff

Dose Levels of 160-300 mg QD Achieved Target Exposures in Almost All Patients



(1) Exposures corrected with cross-species protein binding and blood/plasma partitioning. 10 mg/kg/day induces tumor regressions in sensitive preclinical models while 25 mg/kg/day induces regressions in the majority of preclinical models (Jiang et. al. Cancer Discovery 2024:14:1-24).

3/26/24 data cutoff

RMC-6236 in Pancreatic Cancer

PDAC is a Devastating, RAS-Driven Disease with Major Unmet Medical Needs

60K new cases estimated to be diagnosed in the US in 2024[1]

- 3rd leading cause of cancer deaths[1]

Most patients diagnosed with metastatic disease[2]

- 5-year survival is 3%[2]

Multi-agent chemotherapy is the primary treatment for most patients[3]

- Current targeted therapies benefit minority of patients[3]

Pancreatic cancer is the most RAS-addicted of all major cancers

- Over 90% of patients with PDAC have RAS mutant tumors[4]

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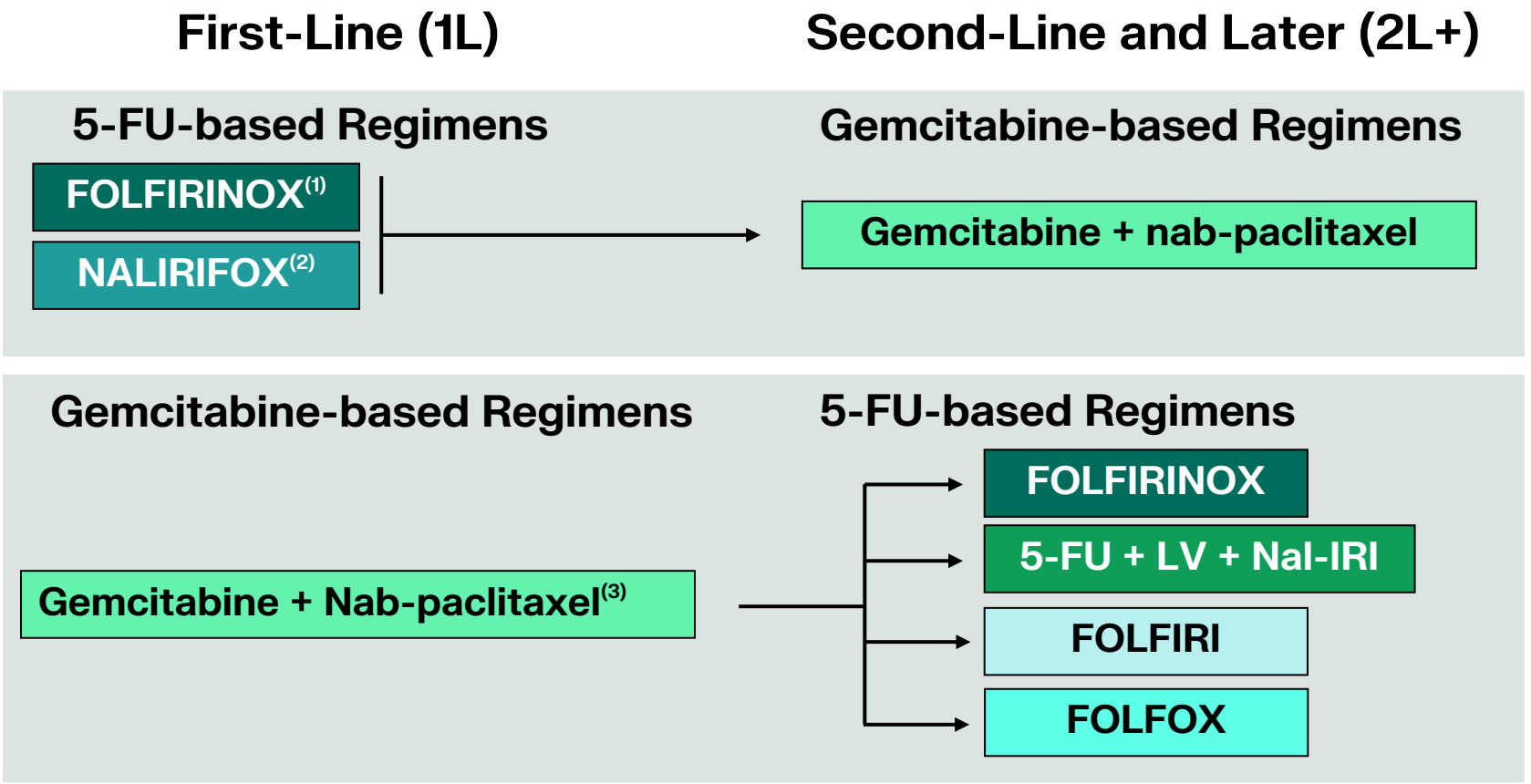
(1) Incidence from ACS Cancer Facts and Figures 2024, adjusted for PDAC only. Includes all stages of disease. (2) ACS Cancer Facts and Figures 2024 adjusted for metastatic stage only. (3) CancerMPact 2022. (4) Estimated using tumor mutation frequencies from Foundation Medicine Insights March 2022.

Current Treatment Paradigm for Metastatic PDAC



Supportive care measures: IV port-a-cath, steroids, G-CSF, GI toxicity management

5-FU, fluorouracil; LV, leucovorin; Nal-IRI, nanoliposomal irinotecan; GI, gastrointestinal

(1) Conroy T, et al. *NEJM* 2011;364:1817-25. (2) Wainberg AZ, et al. *Lancet* 2023;402:1272–81; (3) Von Hoff DD, et al. *NEJM* 2013;369:1691-703.

Chemotherapy in Previously Treated Metastatic PDAC Provides Limited Clinical Benefit with Significant Toxicity

Reported Efficacy

Study	Regimen	Treatment line	No. of patients	ORR (%)	Median PFS (months)	Median OS (months)
NAPOLI 1[1]	**5-FU+LV+Nal-IRI**	2L+	117	8	**3.1**	**6.1**
SWOG S1513[2]	**FOLFIRI**	2L	58	10	**2.9**	**6.5**
SWOG S1115[3]	**FOLFOX**	2L	62	7	**2.0**	**6.7**
SEQUOIA[4]	**FOLFOX**	2L	284	6	**2.1**	**6.3**
QUILT-3.010[5]	**Gemcitabine + nab-paclitaxel**	2L	40	3	**2.7**	**6.6**
Trybeca-1[6]	**Gemcitabine + nab-paclitaxel**	2L	148	NA	**3.5**	**6.9**
GEMPAX[7]	**Gemcitabine + paclitaxel**	2L	140	17	**3.1**	**6.4**
Gupta et al.[8]	**5-FU+LV+Nal-IRI**	3L+	30	3	**1.9**	**5.0**
Enzler et al.[9]	**CBP501+cisplatin+nivolumab**	3L+	36	6	**1.9**	**5.1**

Reported Safety and Dose Modifications

- 5-FU/LV/Nal-IRI dose interruptions required in 62% of patients, dose reductions in 33%, and discontinuations in 11%[1]
- Gemcitabine + nab-paclitaxel dose modifications required in 63%[6]

ORR, objective response rate; PFS, progression-free survival; OS, overall survival; NA, not available.

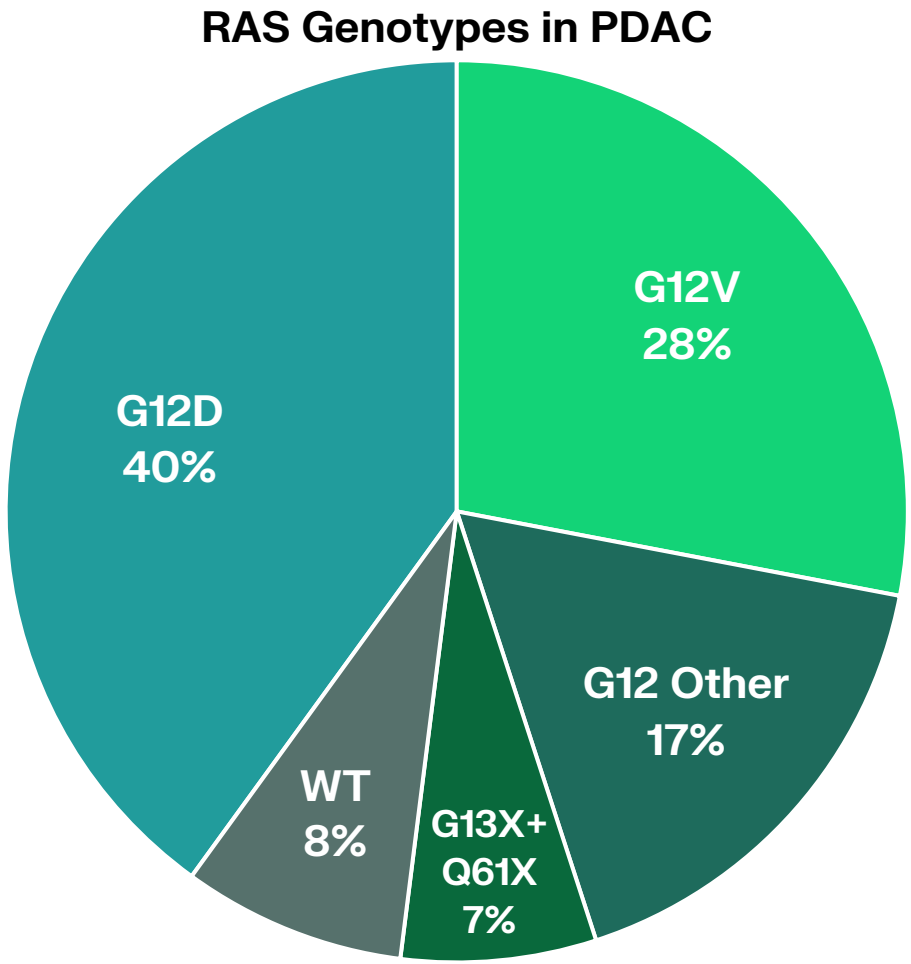
(1) Onivyde USPI; (2) Chiorean EG, et al. Clin Cancer Res 2021:27:6314–33; (3) Chung V, et al. JAMA Oncol 2017;3:516–22; (4) Hecht JR, et al. J Clin Oncol 2021;39:1108–18; (5) Huffman BM, et al. JAMA Network Open 2023;6:e2249720. (6) Hammel P, et al. ASCO GI 2022; (7) Fouchardiere C, et al. J Clin Oncol 2024;42:1055-1066; (8) Gupta A, et al. Frontiers Oncol 2023: 13:1250136; (9) Enzler T, et al. Eur J Cancer 2024: 113950, means of median PFS and median OS from four experimental regimens provided

RAS-Targeted Therapies Have the Potential to Address Large Unmet Needs and Transform Treatment for PDAC

60,000
new PDAC cases per year (U.S.)[1]

92%
have RAS driver mutations[2]

85%
have RAS G12X driver mutations, <2% are G12C[2]



WT, wild type
(1) ACS Cancer Facts and Figures 2024 adjusted for PDAC only.
(2) Estimated using tumor mutation frequencies from Foundation Medicine Insights March 2022.
RAS G12X, non-synonymous mutations in KRAS, HRAS or NRAS at codon 12 (G12). G13X and Q61X, non-synonymous mutations in KRAS, HRAS or NRAS at codons 13 and 61, respectively.

Patient Demographics and Baseline Characteristics: PDAC (160–300 mg)

Baseline Characteristics	N=127
Age, median (range), years	64 (30-86)
Male, n (%)	71 (56%)
ECOG PS 1, n (%)	82 (65%)
Number of prior anti-cancer therapies, median (range)	2 (1-11)
Select type of prior anti-cancer regimens, n (%)	
(m)FOLFIRINOX	95 (75%)
Gemcitabine + nab-paclitaxel	91 (72%)
Number of prior anti-cancer therapies in metastatic setting, median (range)	2 (0-5)
Number of prior anti-cancer therapies in metastatic setting[1]	
0	2 (2%)
1	56 (44%)
2+	68 (54%)
Liver metastases at baseline	86 (68%)
Metastatic at diagnosis (Stage IV)	67 (53%)

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(1) First-in-human study enrolled patients with locally advanced or metastatic PDAC; 1 prior line of therapy in the metastatic setting includes patients who progressed on prior therapy in an earlier setting within 6 months of last dose; 1 patient with data missing for line of therapy
ECOG PS, Eastern Cooperative Oncology Group Performance Status.

5/11/24 data cutoff

Treatment-Related Adverse Events: PDAC (160-300 mg)

	N = 127	
Maximum Severity of Treatment-Related AEs (TRAEs)	**Any Grade**	**Grade ≥3**
Any TRAE	122 (96%)	28 (22%)
TRAEs occurring in ≥10% of patients, n (%)		
Rash[1]	111 (87%)	8 (6%)
Diarrhea	58 (46%)	2 (2%)
Nausea	54 (43%)	0 (0%)
Stomatitis/mucositis	48 (38%)	3 (2%)
Vomiting	36 (28%)	0 (0%)
Fatigue	21 (17%)	1 (1%)
Paronychia	13 (10%)	0 (0%)
Other select TRAEs, n (%)		
ALT elevation	6 (5%)	0 (0%)
AST elevation	8 (6%)	0 (0%)
Electrocardiogram QT prolonged	1 (1%)	1 (1%)
Neutropenia/neutrophil count decreased	6 (5%)	1 (1%)
Thrombocytopenia/platelet count decreased	14 (11%)	3 (2%)

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(1) Includes preferred terms of dermatitis acneiform, eczema, erythema, rash, rash erythematous, rash maculopapular, rash pruritic and rash pustular; multiple types of rash may have occurred in the same patient.
ALT, alanine transaminase; AST, aspartate transferase.

5/11/24 data cutoff

Treatment-Related Adverse Events Leading to Dose Modifications: PDAC (160–300 mg)

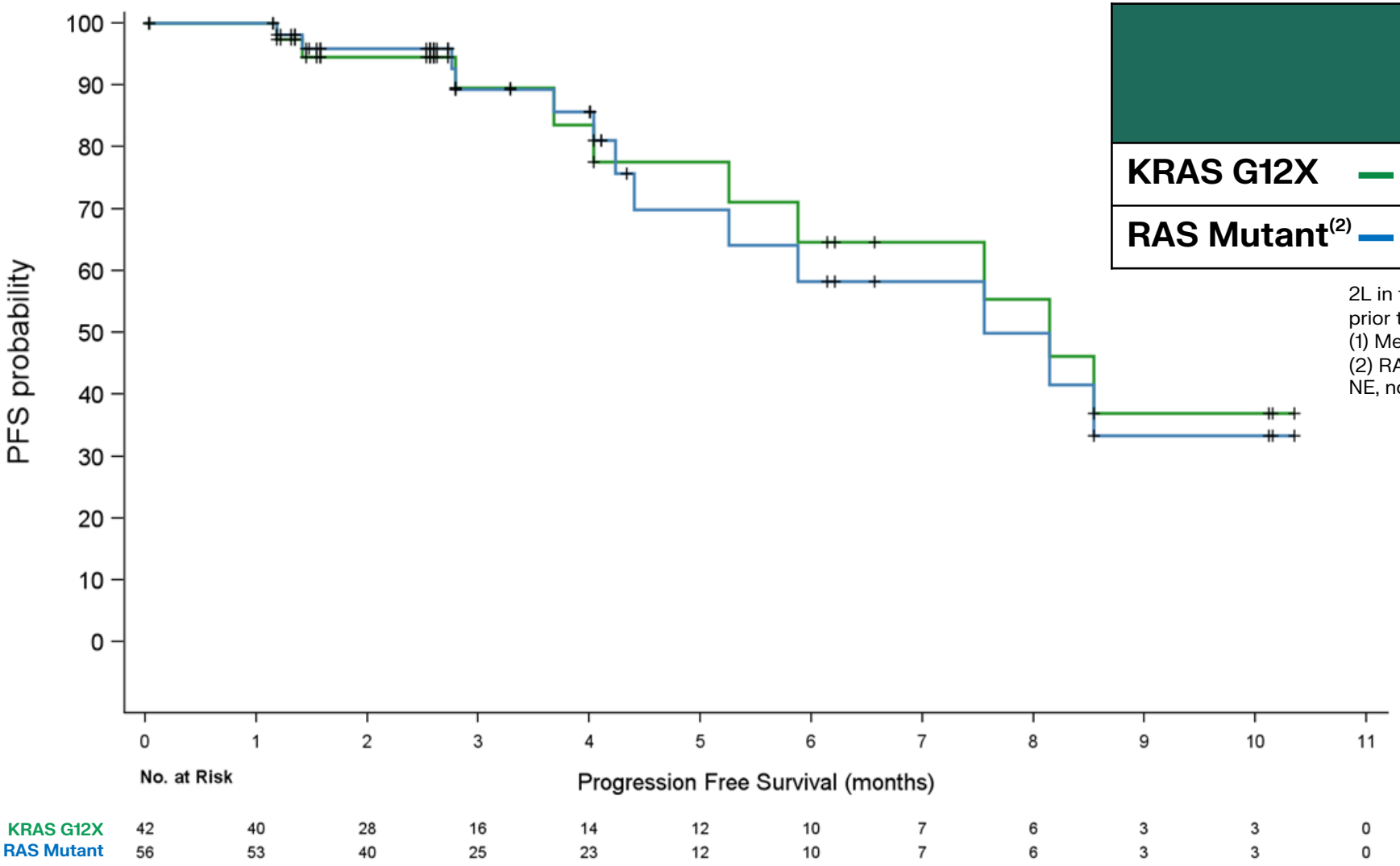
	N = 127
TRAEs leading to dose modification, n (%)	35 (28%)
Dose interruption	34 (27%)
Dose reduction	14 (11%)
Dosing discontinuation	0 (0%)
Specific TRAEs leading to dose reduction (≥2 patients) by preferred term	
Rash[1]	7 (6%)
Stomatitis/mucositis	4 (3%)
Decreased appetite	2 (2%)
Diarrhea	2 (2%)
Platelet count decreased	2 (2%)

- Dose intensity was ≥ 92% at each dose level with an average of 94% across the 160-300 mg cohorts

(1) Includes preferred terms of dermatitis acneiform and rash maculopapular; multiple types of rash may have occurred in the same patient.

5/11/24 data cutoff

Observed PFS in 2L Metastatic PDAC on RMC-6236 (160-300 mg)



	Median PFS Months (95% CI)	Benchmark Median PFS[1] Months
KRAS G12X	**8.1** (5.9-NE)	2.0-3.5
RAS Mutant[2]	**7.6** (5.3-NE)	

2L in the metastatic setting includes patients who progressed on prior therapy in an earlier setting within 6 months of last dose
(1) Median PFS benchmark from published reports (see slide 15)
(2) RAS Mutant defined as patients with G12X, G13X or Q61X PDAC.
NE, not estimable.

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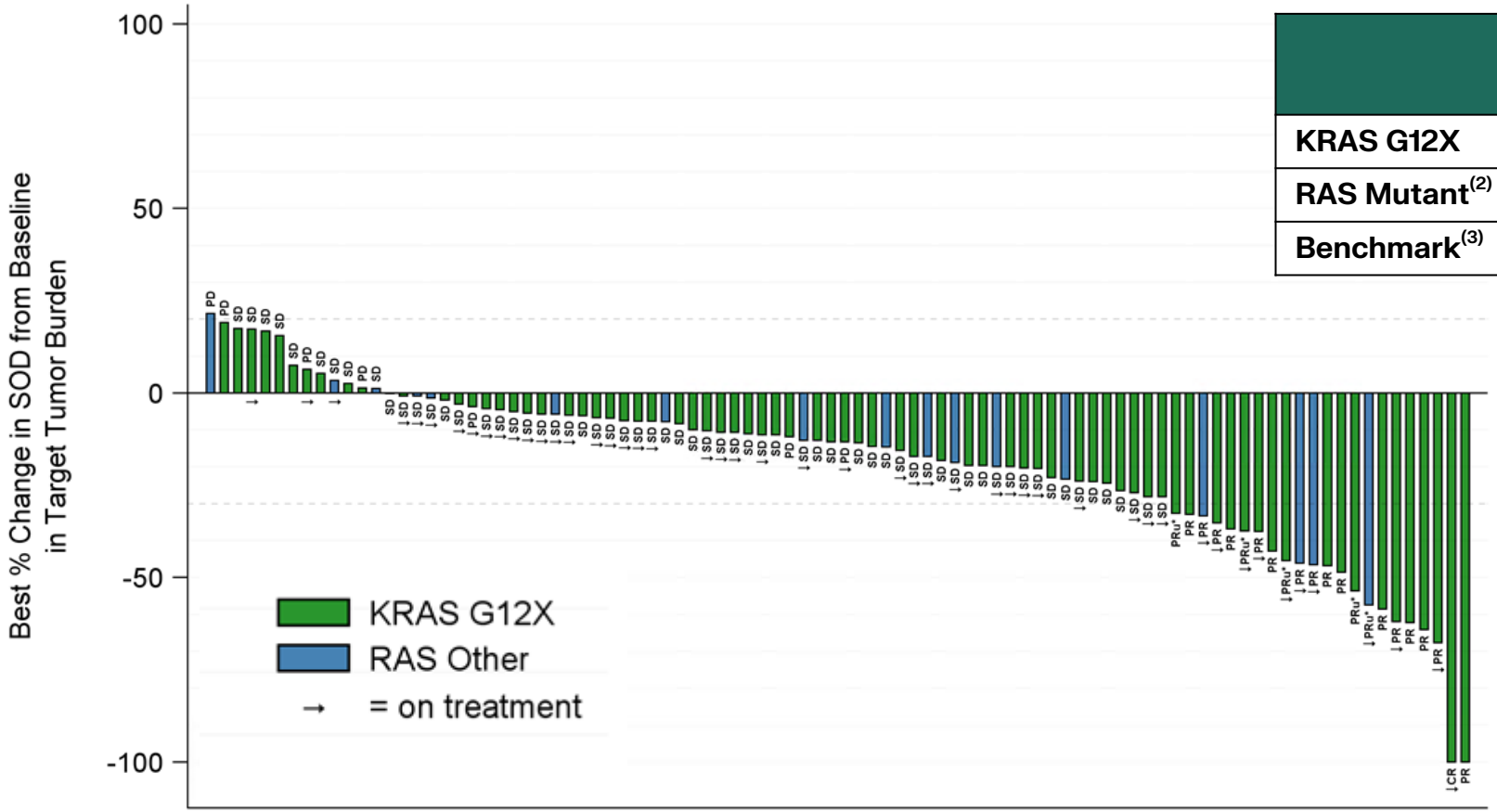
5/11/24 data cutoff

Best Percentage Change in Tumor Size from Baseline and Objective Response Rate in 2L+ PDAC (RMC-6236 160-300 mg)

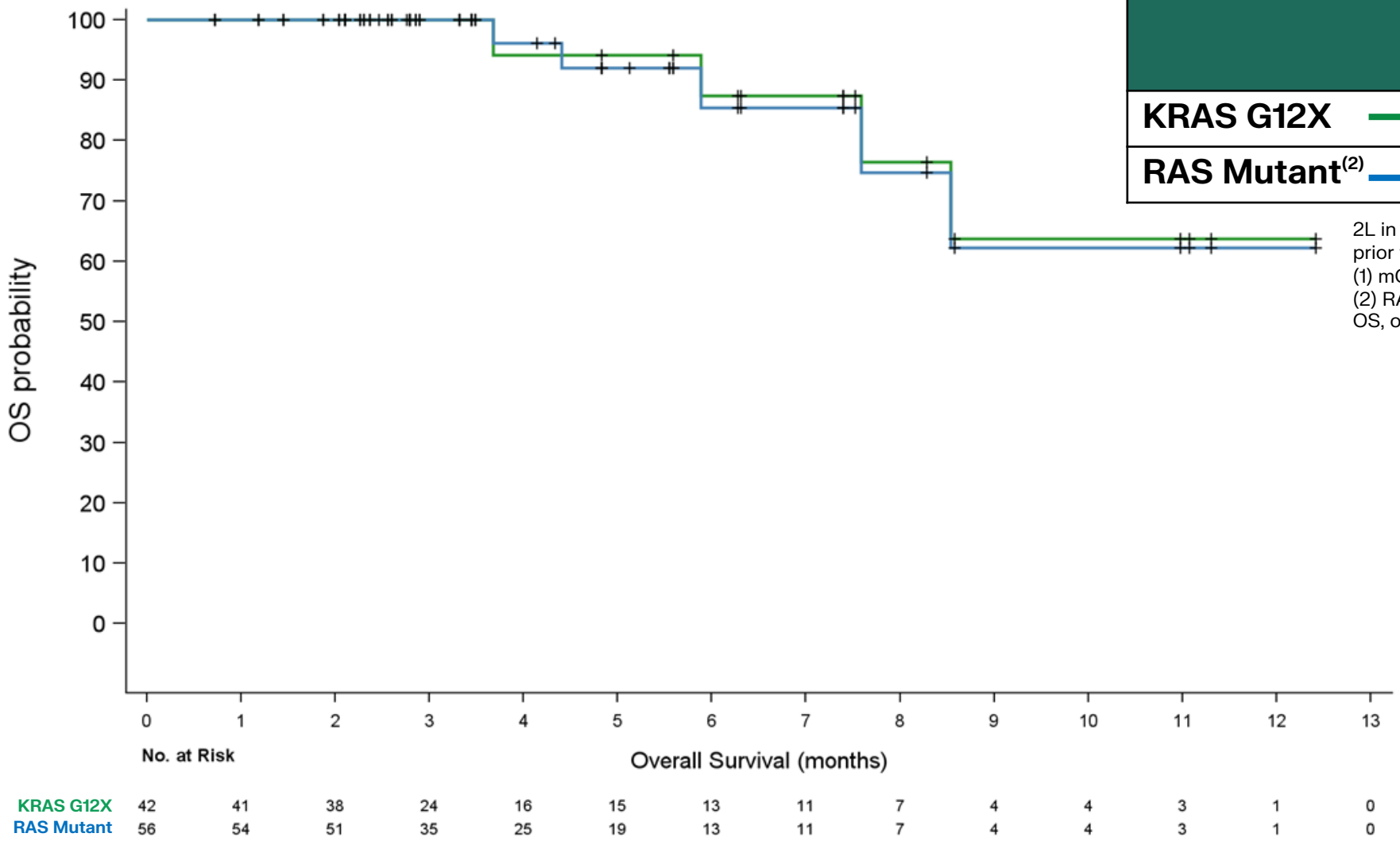


	ORR 14+ week[1]	ORR 20+ week[1]	DCR 14+ week[1]
KRAS G12X	20% (16/79)	27% (13/48)	87% (69/79)
RAS Mutant[2]	21% (20/97)	26% (16/61)	88% (85/97)
Benchmark[3]	9%		NA

(1) "ORR 14+ week" and "DCR 14+ week" analyses include all patients who received first dose of RMC-6236 at least 14 weeks prior to data cutoff date (to allow 2 potential scans). "ORR 20+ week" analysis is similarly defined to allow 3 potential scans. 5 patients included in the denominator of the '14+ week' analyses are not displayed on waterfall due to lack of post-baseline target lesion assessment (4 patients discontinued treatment without post-baseline scans: 3 3L+ patients discontinued due to death, 1 due to subject request to withdraw from treatment, and 1 patient had documented PD due to new lesion without target lesion assessment); *Unconfirmed PRs (PRu) with treatment discontinued (will never confirm) are not considered responders but remain in the denominator (n=5); ORR (by RECISTv1.1) includes confirmed CRs/PRs and unconfirmed CRs/PRs who are still on treatment and may yet confirm; As per convention, 2L in the metastatic setting includes patients who progressed on prior therapy in an earlier setting within 6 months of last dose; ORR, objective response rate; DCR, disease control rate; PD, progressive disease; SD, stable disease; PR, partial response; CR, complete response; RAS Other, non-G12X RAS mutations.
(2) RAS Mutant defined as patients with G12X, G13X or Q61X PDAC.
(3) Benchmark mean ORR derived from published reports (see slide 15); NA, not available.

5/11/24 data cutoff

Interim Observed OS in 2L Metastatic PDAC on RMC-6236 (160-300 mg)



	Median OS Months (95% CI)	Benchmark Median OS[1] Months
KRAS G12X	NE (8.5, NE)	6.1-6.9
RAS Mutant[2]	NE (8.5, NE)	

2L in the metastatic setting includes patients who progressed on prior therapy in an earlier setting within 6 months of last dose
(1) mOS benchmark from published reports (see slide 15)
(2) RAS Mutant defined as patients with G12X, G13X or Q61X PDAC.
OS, overall survival; NE, not estimable

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5/11/24 data cutoff

RASolute 302 Phase 3 Trial

Global, randomized, controlled Phase 3 trial comparing RMC-6236 to chemotherapy in 2L treatment of patients with metastatic PDAC

Trial Design for RASolute 302: 2L Metastatic PDAC

Key Eligibility Criteria

- Confirmed PDAC
- 1 prior line of therapy in the metastatic setting
- ECOG PS 0-1

N = 460

R
1:1

- RMC-6236 300 mg p.o. QD (N = 230)
- Investigator's Choice SOC Chemotherapy[1] (N = 230)

Primary Endpoints
(RAS G12X)

- PFS, OS

Secondary Endpoints
(All Patients)

- PFS, OS
- ORR, DOR
- QoL

SOC, standard of care; WT, wild type; p.o., oral administration; QD, once daily, DOR, duration of response; QoL, quality of life.
Trial design and dose selection based on FDA meeting. Finalization of design details pending final protocol submission.
(1) SOC chemotherapy options: Gemcitabine + nab-paclitaxel, modified FOLFIRINOX, NAL-IRI+5-FU+LV, or FOLFOX

Nested Trial Design with Hierarchical Testing Aims to Maximize Probability of Success and Potentially Enable Broad Label

Primary Analysis: ***Core study population***

RAS G12X patients

Secondary Analysis: ***Expanded study population***

RAS G12X, G13X and Q61X patients

+

RAS WT patients who do not have other non-RAS, 'actionable' mutations[1]

WT, wild type

(1) RAS(ON) multi-selective inhibitors exhibit anti-tumor activity In preclinical models of PDAC with RAS WT (Wasko et. al, Nature 2024: 629: 927-936)

Estimated Timeline for RASolute 302 Phase 3 Trial

2024		2025		2026		2027	
1H	2H	1H	2H	1H	2H	1H	2H

Anticipated study initiation

Anticipated Primary Endpoint PFS read-out

Anticipated Primary Endpoint OS read-out

Parallel Development of RMC-6236 in Earlier Lines of PDAC Therapy

- Given large unmet need in early stage PDAC and compelling clinical validation of RMC-6236 in 2L PDAC, advancing RMC-6236 into earlier lines of treatment has emerged as a priority, including:
  - 1L metastatic
  - Locally advanced, unresectable
  - Resectable

- Aiming to accelerate potential registrational trials in earlier lines of PDAC therapy, evaluation of RMC-6236 monotherapy and combination approaches is ongoing:
  - RMC-6236 + chemotherapy[1]
  - RMC-6236 + RAS(ON) mutant-selective inhibitors[2]

(1) RMC-GI-102 Clinical Trial: https://clinicaltrials.gov/study/NCT06445062
(2) RMC-6291-101 Clinical Trial: https://clinicaltrials.gov/study/NCT06128551; RMC-9805-001 Clinical Trial: https://clinicaltrials.gov/study/NCT06040541

RMC-6236 in NSCLC and Other Solid Tumors

RMC-6236-001: Summary of Treatment-Related Adverse Events (All Patients)

	Total (n=131)				
Maximum severity of TRAEs	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Any Grade**
TRAEs occurring in ≥10% of patients, n (%)					
Rash*	57 (44)	29 (22)	6 (5)	0	92 (70)
Nausea	41 (31)	14 (11)	0	0	55 (42)
Diarrhea	32 (24)	9 (7)	1 (1)	0	42 (32)
Vomiting	27 (21)	9 (7)	0	0	36 (28)
Stomatitis	10 (8)	9 (7)	2 (2)	0	21 (16)
Fatigue	12 (9)	4 (3)	0	0	16 (12)
Other select TRAEs, n (%)					
ALT elevation	6 (5)	1 (1)	1 (1)‡	0	8 (6)
AST elevation	6 (5)	0	1 (1)‡	0	7 (5)
Electrocardiogram QT prolonged	1 (1)	0	0	0	1 (1)
TRAEs leading to dose reduction†, n (%)	0	9 (7)	2 (2)	0	11 (8)
TRAEs leading to treatment discontinuation, n (%)	0	0	0	1 (1)	1 (1)

- Median duration of treatment at the time of data extraction was 2.27 months (range: 0.2–14)
- One Grade 4 TRAE occurred in a patient with PDAC treated at 80 mg who had a large intestine perforation at the site of an invasive tumor that reduced in size while on treatment (TRAE leading to treatment discontinuation)
- No fatal TRAEs were observed. Two patients discontinued study treatment due to death: one patient with PDAC (120 mg) died due to PD; one patient with NSCLC (200 mg) died due to unknown cause reported as unrelated to RMC-6236

‡ Post-data extraction, the Grade 3 ALT and AST elevations in the table above were associated with biliary obstruction and reported as unrelated to RMC-6236

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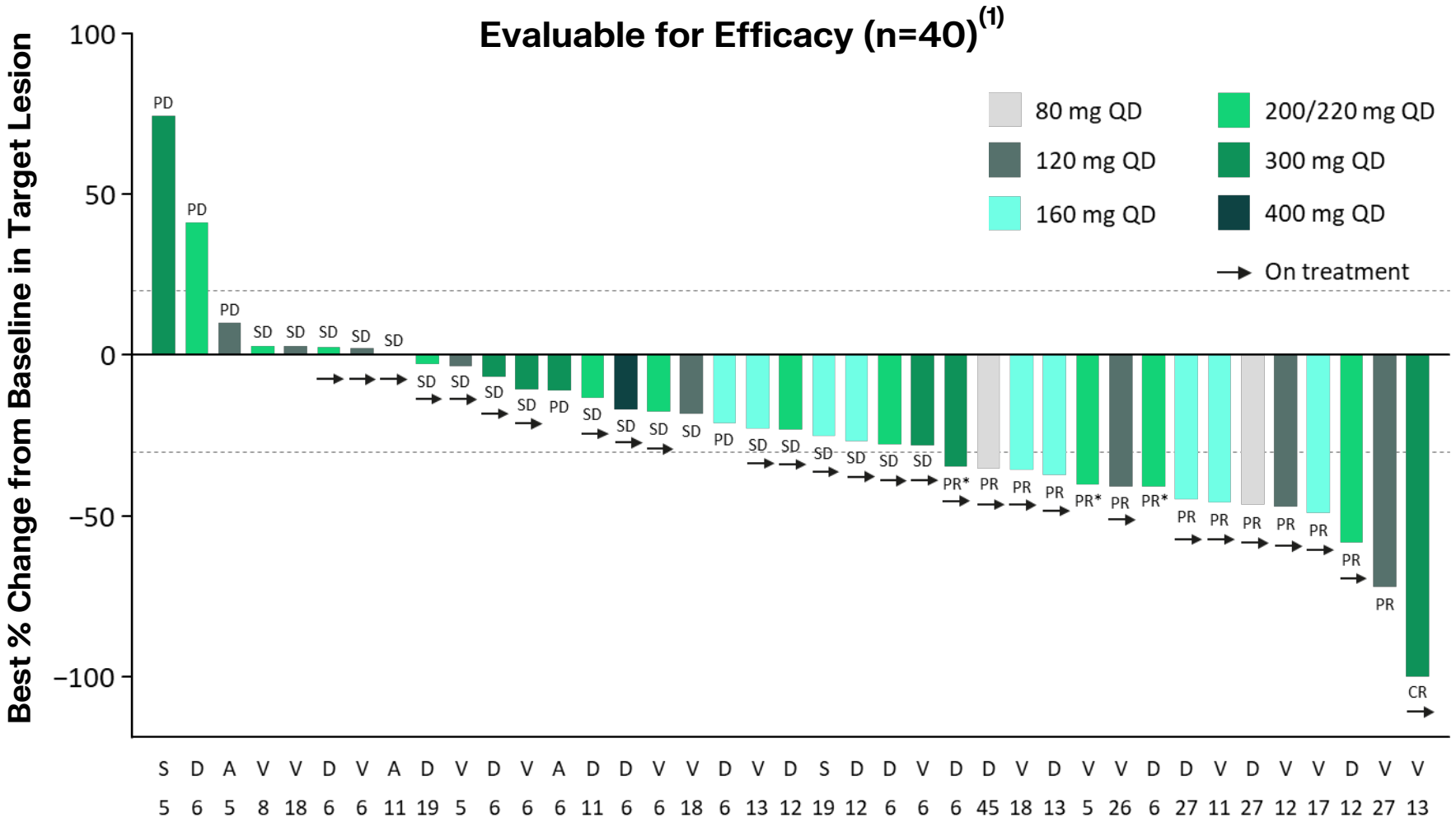
*Includes preferred terms of dermatitis acneiform, rash maculopapular, rash, rash pustular, dermatitis psoriasiform, erythema, rash erythematous; multiple types of rash may have occurred in the same patient; †The most common TRAE leading to dose reduction was rash (acneiform or maculopapular); there were no reductions at doses ≤80 mg. AE, adverse event; ALT, alanine transaminase; AST, aspartate transferase; PD, progressive disease; TRAEs, treatment-related adverse events.

Data Extracted 11 Sep 2023.

KRAS G12X NSCLC: Best Overall Response to RMC-6236



RMC-6236-001: Clinical Activity in KRAS G12X NSCLC(2)	
Best overall response, n (%)	
Complete response	1 (3)
Partial response	14 (35)
Stable disease	19 (48)
Progressive disease	5 (13)
Not evaluable(3)	1 (3)
ORR, n (%)	15 (38)
Confirmed, n	12
DCR (CR+PR+SD), n (%)	34 (85)
SOC Benchmark(4)	
Docetaxel, ORR (%)	(13)
DCR (%)	(60)

(1) Patients who received first dose of RMC-6236 at least 8 weeks prior to data extract date.
(2) Tumor response per RECIST 1.1.
(3) One subject withdrew from study without post-baseline scans.
(4) SOC=standard of care; efficacy benchmark for docetaxel taken from CodeBreaK 200, Lancet (2023) 401: 733-746.
*Unconfirmed PR per RECIST 1.1.

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Data Extracted 12 Oct 2023.

Proposed Global Randomized Phase 3 Trial in Patients with Previously-Treated RAS Mutant NSCLC

Trial Design[1]

R

RMC-6236

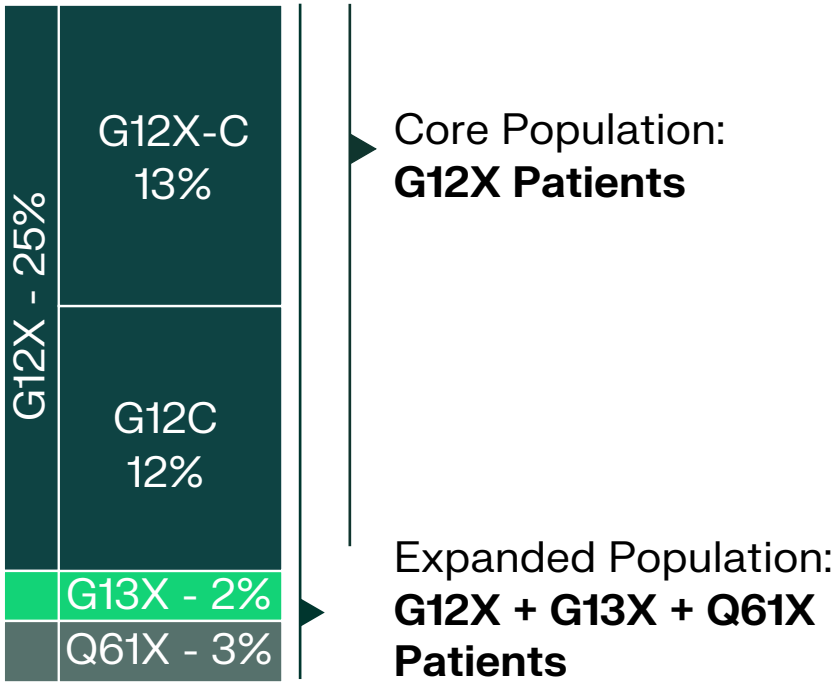
Docetaxel

Endpoints

PFS
OS
Patient Reported Outcomes

- **N** > 400 patients
- **Prior therapies**: Anti-PD-(L)1 and platinum-containing regimen in metastatic setting; RAS inhibitor naïve (including G12C inhibitor)
- **Biomarker**: RAS G12X, G13X, or Q61X mutation
- **Study Initiation**: Aiming for 2024

Potential Patient Populations[1,2]



- Potential for nested trial design to enable evaluation of core and expanded patient populations[1]

R = Randomized
(1) Study design subject to change based on regulatory authority feedback
(2) Percentages of all NSCLC patients with tumors bearing RAS G12X, G13X, or Q61X genotypes; estimated using tumor mutation frequencies from Foundation Medicine Insights March 2022 and scaled to estimated patient numbers using cancer incidence from ACS Cancer Facts and Figures 2023 (see appendix for additional detail)

Key RMC-6236-001 Monotherapy Expansion Cohorts Underway

Corporate Priority	Cohort	Dosing	Purpose
Expand reach of RMC-6236	**NSCLC**		
	G12X dose optimization (300 mg and below)	✓	Dose selection for pivotal trial
	RAS G13X and Q61X expansion (300 mg)	✓	Pivotal trial design
	CRC		
	G12X expansion (300 mg)	✓	Signal seeking
	RAS G13X and Q61X expansion (300 mg)	✓	Signal seeking

- G12C included in G12X across all tumor types and cohorts

RMC-6236-001 protocol amended in August 2023 to broaden enrollment, now allowing patients with tumors bearing mutations in any of the three hotspots (G12X/G13X/Q61X) in any of the three major RAS isoforms (KRAS/NRAS/HRAS); G12X broadened to include G12C

Complementary RAS(ON) Inhibitors Designed for Monotherapy and Combination Strategies Against RAS-Addicted Cancers

RAS Multi-Selective

- Monotherapy with broad potential for RAS-addicted cancers
- Backbone of RAS(ON) inhibitor doublets with mutant-selective RAS(ON) inhibitors
- Targeted agent for SOC combinations, including immunotherapies

RAS Mutant-Selective

- Alternative monotherapy approaches
- Complementary to RAS multi-selective inhibitor in RAS(ON) inhibitor doublets
- Differentiated targeted agent profiles for SOC combinations, including immunotherapies

RAS(ON) G12C-Selective Inhibitor RMC-6291

RMC-6291-001: Summary of Treatment-Related Adverse Events

Total (n=63)				
Maximum Severity of TRAEs	**Grade 1**	**Grade 2**	**Grade 3**	**Any Grade**
TRAEs occurring in ≥10% of patients, n (%)				
Diarrhea	10 (16)	7 (11)	1 (2)	18 (29)
Nausea	14 (22)	3 (5)	0	17 (27)
ECG QT prolonged	8 (13)	1 (2)	7 (11)	16 (25)
QTcF* ≥501 ms	–	–	1 (2)	–
Fatigue	4 (6)	4 (6)	0	8 (13)
Vomiting	6 (10)	2 (3)	0	8 (13)
AST increased	7 (11)	0	0	7 (11)
TRAEs leading to dose reduction, n (%)	0	1 (2)	8 (13)	9 (14)
TRAEs leading to treatment discontinuation, n (%)	0	0	1 (2)	1 (2)

- No treatment-related Grade 4 or 5 AEs or SAEs were reported
- No patients had cardiac sequelae (e.g., torsade de pointes) associated with an ECG QT prolonged event

RMC-6291-001 Clinical Trial: https://clinicaltrials.gov/study/NCT05462717
*QTcF refers to QT interval corrected for heart rate by Fridericia's formula.
AE, adverse event; AST, aspartate transferase; ECG, electrocardiogram; SAE, serious adverse event, TRAE, treatment-related adverse event.

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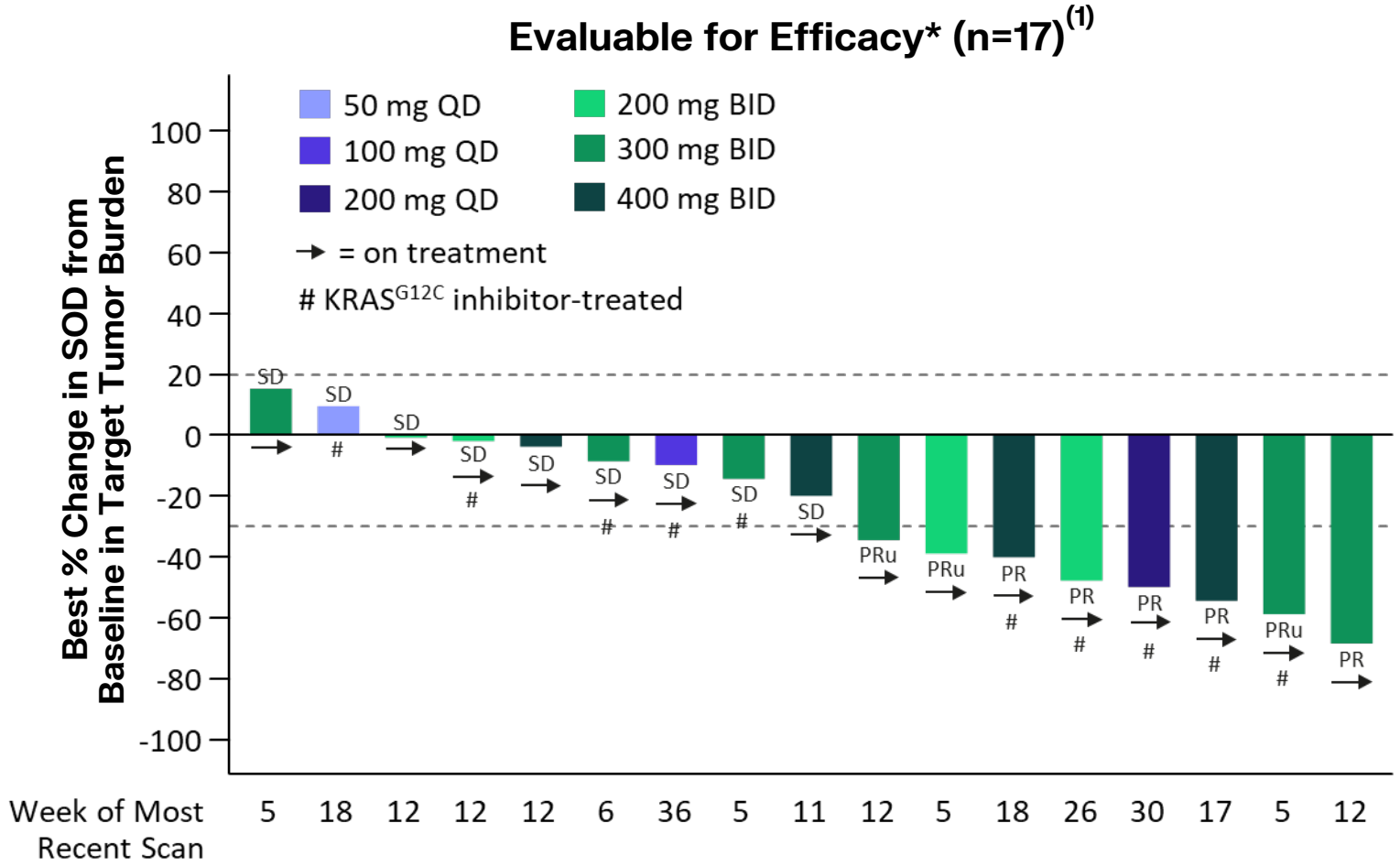
Data Extracted 05 October 2023.

KRAS^{G12C} NSCLC Previously Treated with or Naïve to a KRAS^{G12C}(OFF) Inhibitor: Best Overall Response to RMC-6291



RMC-6291-001: Clinical Activity in KRAS G12C NSCLC(2)

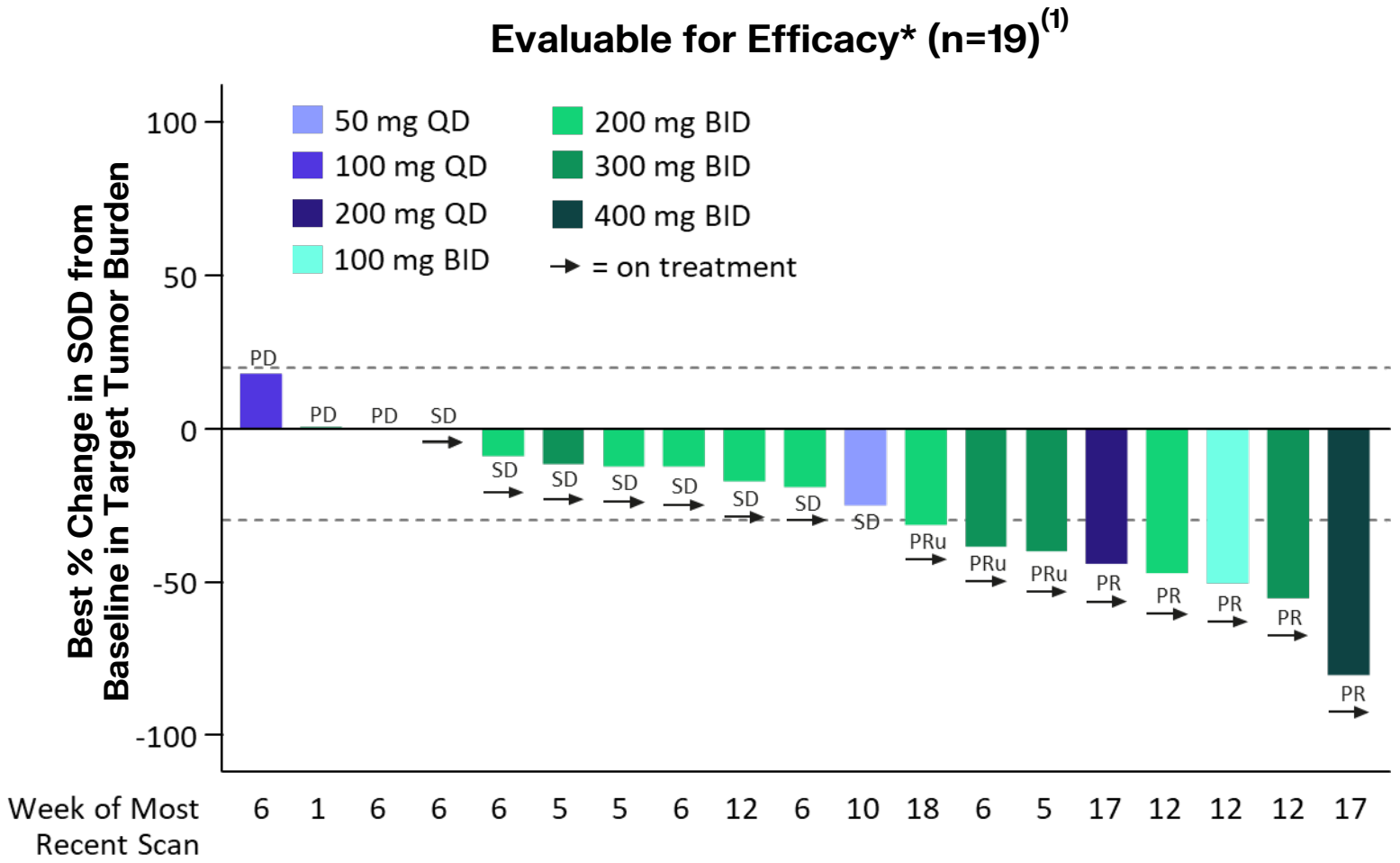
Best overall response, n (%)	Prior G12Ci (n=10)	Naïve to G12Ci (n=7)
Partial response(3)	5 (50)	3 (43)
Stable disease	5 (50)	4 (57)
Progressive disease	0	0
ORR, n (%)	5 (50)	3 (43)
DCR (CR+PR+SD), n (%)	10 (100)	7 (100)

(1) All treated patients who received a first dose of RMC-6291 at least 8 weeks prior to data extract date.
(2) Tumor response per RECIST 1.1.
(3) PR includes 5 confirmed and 3 unconfirmed.
Pru=Unconfirmed PR per RECIST 1.1; G12Ci=G12C inhibitor.

Revolution Medicines

Data Extracted 05 October 2023.

KRAS^{G12C} CRC Naïve to KRAS^{G12C}(OFF) Inhibitor: Best Overall Response to RMC-6291



RMC-6291-001: Clinical Activity in KRAS G12C CRC[2]	
Best overall response, n (%)	**n=20†**
Partial response[3]	8 (40)
Stable disease	8 (40)
Progressive disease[4]	4 (20)
ORR, n (%)	8 (40)
DCR (CR+PR+SD), n (%)	16 (80)

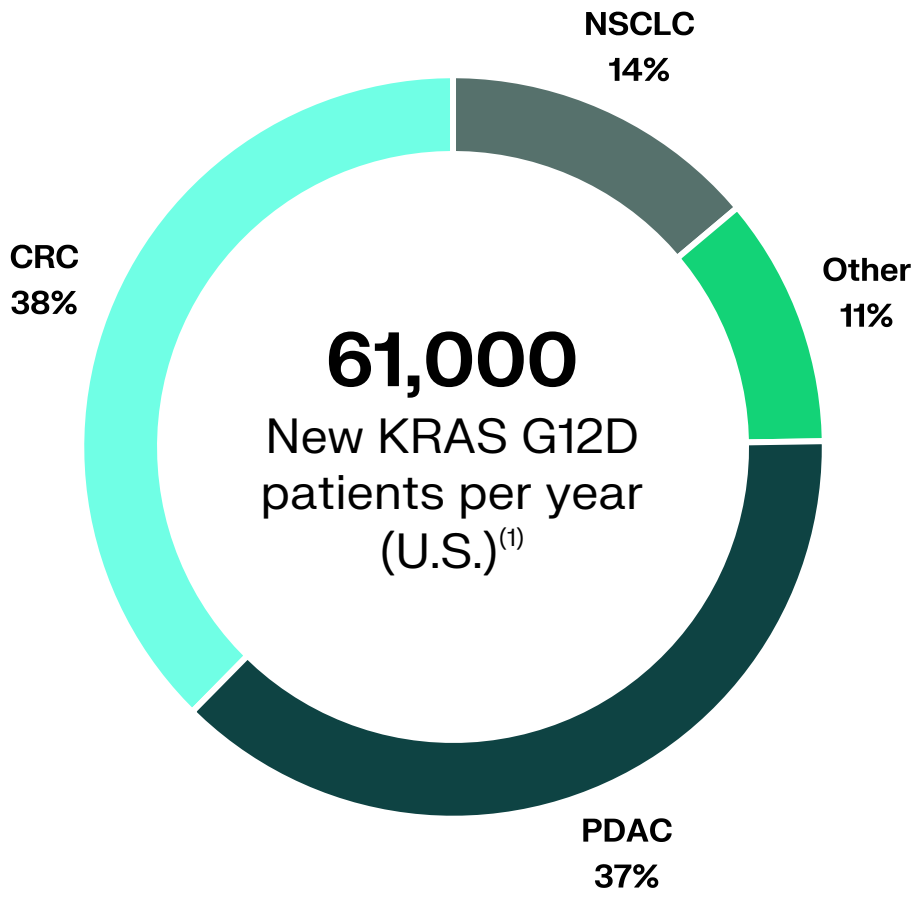
(1) All treated patients who received first dose of RMC-6291 at least 8 weeks prior to data extract date.
(2) Tumor response per RECIST 1.1.
(3) PR includes 5 confirmed and 3 unconfirmed.
(4) One patient had PD due to a new lesion and target lesion measurements were not available.
Pru=Unconfirmed PR per RECIST 1.1.

Revolution Medicines

Data Extracted 05 October 2023.

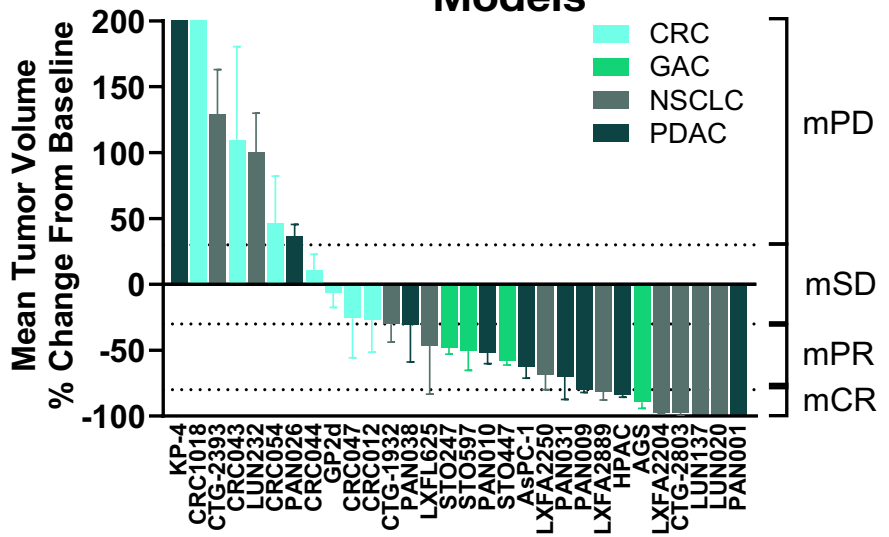
RAS(ON) G12D-Selective Inhibitor RMC-9805

RMC-9805: Clinical-Stage, RAS(ON) Mutant-Selective, Covalent Inhibitor for RAS G12D Cancers



Selective Covalent Binding to RAS G12D

In Vivo Anti-Tumor Activity across KRAS G12D Cancer Models



(1) Estimated using tumor mutation frequencies from Foundation Medicine Insights March 2022 and scaled to estimated patient numbers using cancer incidence from ACS Cancer Facts and Figures 2023 (see appendix for additional detail)

RVMD preclinical research as of 11/02/22; NSCLC = non-small cell lung cancer; PDAC = pancreatic ductal adenocarcinoma; CRC = colorectal cancer; GAC = Gastric adenocarcinoma

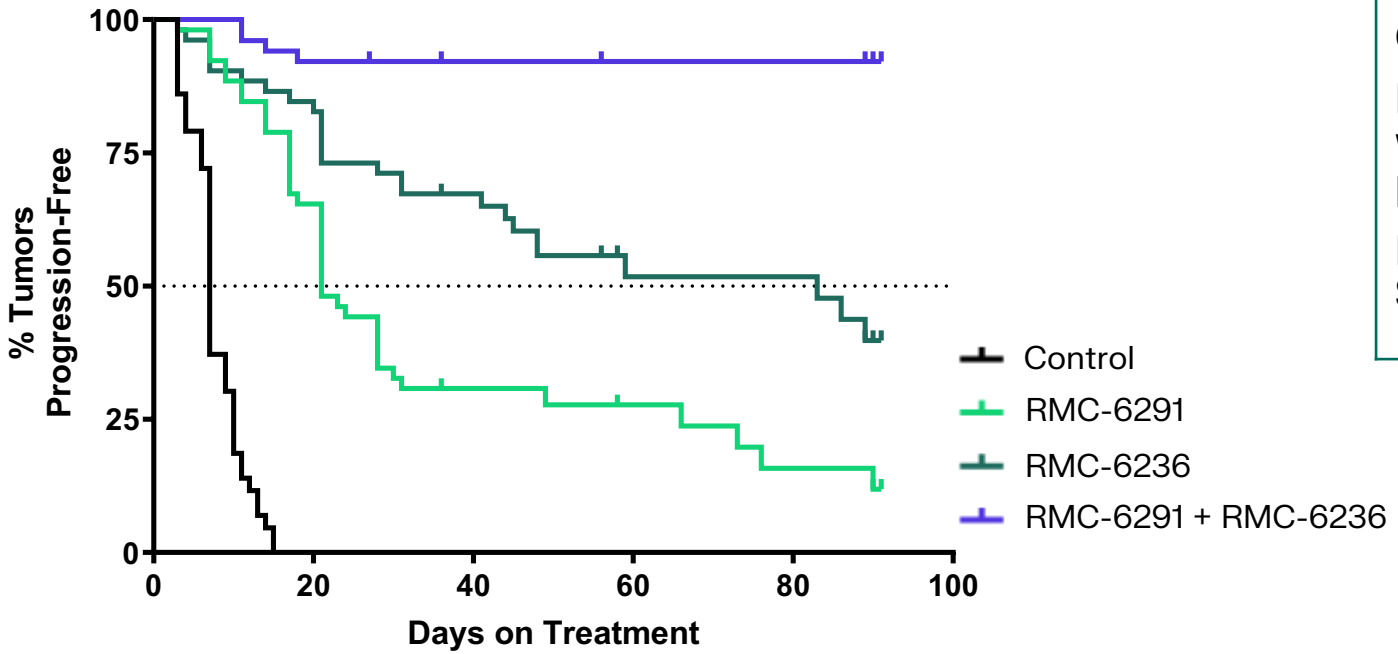
RMC-9805 dosed at 100 mg/kg po qd; n=3-8/group; Responses assigned according to mRECIST: mPD = progressive disease; mSD = stable disease; mPR = partial response; mCR = complete response

RMC-9805-001 Clinical Trial: https://clinicaltrials.gov/study/NCT06040541

RAS(ON) Inhibitor Combinations to Enable Potential First Line Treatment Development

Phase 1b Combo: RMC-6236 + RMC-6291 Doublet Designed to Overcome Resistance and Prolong Durability in KRAS G12C NSCLC

Preclinical Validation[1]



- RAS(ON) inhibitor doublet evaluated across seven models, including five identified as resistant to RMC-6291 monotherapy

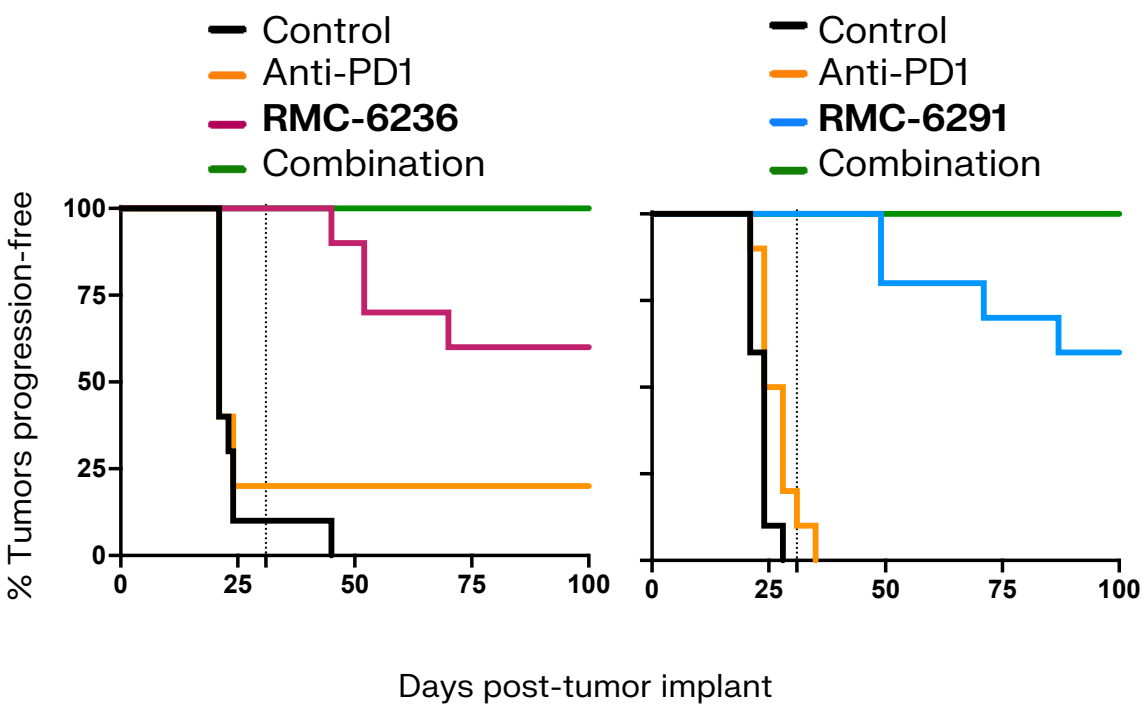
RMC-6291-101 Clinical Trial[2]

Objectives: evaluate safety, tolerability and preliminary activity of RMC-6236 combined with RMC-6291
Patient Population: KRAS G12C solid tumors, primarily NSCLC and CRC
Study Status: Dosing

(1) RVMD preclinical research; NSCLC = non-small cell lung cancer; RMC-6236 dosed at 25 mg/kg po qd (n=52); RMC-6291 dosed at 100 or 200 mg/kg po qd (n=52); Combination (n=51). For each group, n = total number of animals from the seven models that comprise the dataset. Progression defined as tumor doubling from baseline.
(2) RMC-6291-101 Clinical Trial: https://clinicaltrials.gov/study/NCT06128551

Phase 1b Combos: RAS(ON) Inhibitor Combinations with Pembrolizumab to Inform Potential Evaluation in 1L NSCLC

Preclinical Validation[1]



RMC-LUNG-101 Clinical Trial: Pembrolizumab[2]

Objectives: evaluate safety, tolerability and preliminary activity of RMC-6236 and RMC-6291 each combined with pembrolizumab
Patient Population: RMC-6236 in RAS-mutant NSCLC, RMC-6291 in KRAS G12C NSCLC
Study Status: Dosing

Revolution Medicines

(1) RVMD preclinical research; RMC-6236 and RMC-6291 experiments conducted in CT26 model engineered to express $KRAS^{G12C}$; RMC-6236 (25 mg/kg po qd) or RMC-6291 (200 mg/kg po qd) dosed for 14 days; Vertical dashed lines represent treatment stop; Kaplan-Meier progression defined as tumor doubling from baseline
(2) RMC-LUNG-101 Clinical Trial: https://clinicaltrials.gov/study/NCT06162221

Key RAS(ON) Inhibitor Combination Cohorts

Corporate Priority	Cohort	Status	Purpose
Expand reach of RMC-6236	**NSCLC**[1]		
	RMC-6236 + pembrolizumab +/- chemotherapy	dosing	qualification for potential 1L
	PDAC[2]		
	RMC-6236 + chemotherapy	dosing	qualification for potential 1L
	CRC[2]		
	RMC-6236 + anti-EGFR	dosing	signal seeking
	RMC-6236 + chemotherapy	initiated	signal seeking
Qualify mutant-selective inhibitors for late-stage development	**NSCLC**[1]		
	RMC-6291 + pembrolizumab +/- chemotherapy	dosing	qualification for potential 1L
	Solid tumors[3]		
	RMC-6291 + RMC-6236	dosing	qualification for potential 1L
	RMC-9805 + RMC-6236	initiated	qualification for potential 1L

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(1) RMC-LUNG-101 Clinical Trial: https://www.clinicaltrials.gov/study/NCT06162221
(2) RMC-GI-102 Clinical Trial: https://clinicaltrials.gov/study/NCT06445062
(3) RMC-6291-101 Clinical Trial: https://www.clinicaltrials.gov/study/NCT06128551, RMC-9805-001 Clinical Trial https://clinicaltrials.gov/study/NCT06040541

RAS(ON) Inhibitor Development Highlights

Preparing for Late-Stage Development of RAS(ON) Multi-Selective Inhibitor

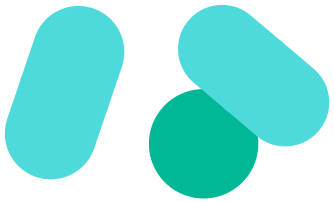
- **RMC-6236 Monotherapy in 2L RAS Mutant Tumors**
  - Updated safety, tolerability and antitumor activity profile in PDAC support advancement to a Phase 3 registrational trial in 2L treatment of patients with metastatic PDAC
  - Initial profile in NSCLC supports plan to advance to registrational study
- **RMC-6236 Combinations in 1L RAS Mutant Tumors**
  - Exploratory combination studies initiated in PDAC and NSCLC to qualify options for potential development in 1L settings

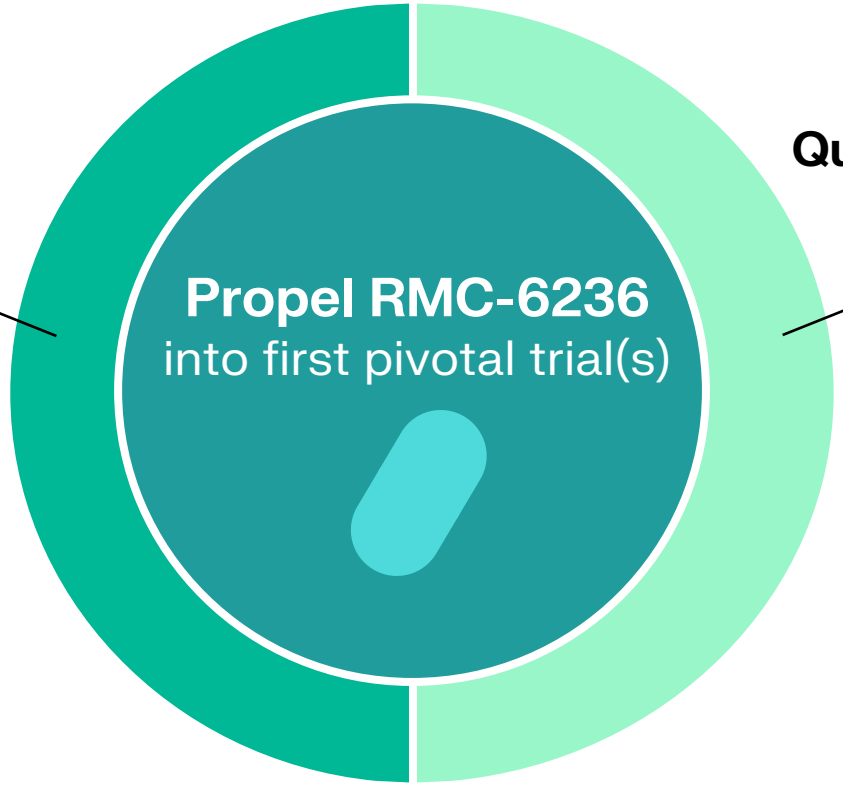
Clinical Studies of RAS(ON) Mutant-Selective Inhibitors to Define Late-Stage Development Options

- **RMC-6291 in RAS G12C Tumors**
  - Exploratory combination studies underway for RMC-6291 with RMC-6236 and RMC-6291 with pembrolizumab to qualify treatment options for potential development in 1L settings
- **RMC-9805 in RAS G12D Tumors**
  - Monotherapy dose optimization underway and combination with RMC-6236 initiated

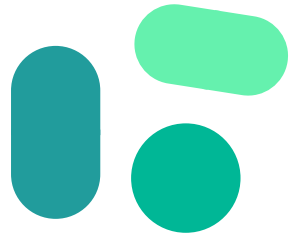
Broad Clinical Validation Across RAS Genotypes and Tumor Types Driving Late-Stage Development

Expand reach of RMC-6236
by clinically assessing opportunities
(1L, types, mutations)





Qualify mutant-selective inhibitors
led by RMC-6291 and RMC-9805 for late-stage development



- Mono cohorts
- Combination cohorts

- Dose selection
- Durability of response
- Trial designs

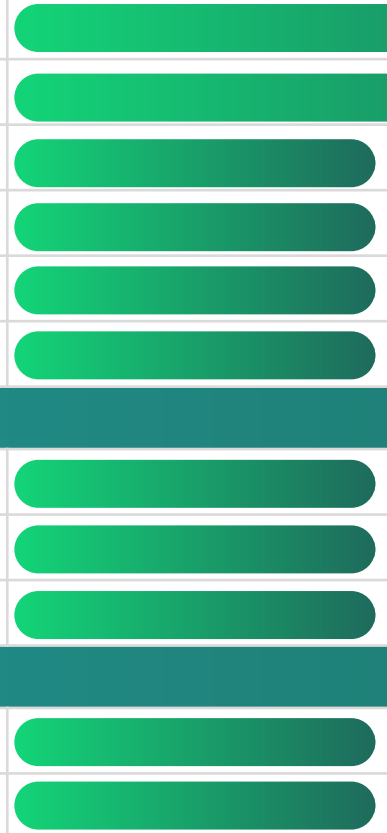
- Mono profiles and dose selection
- Combination cohorts
- Late-stage plans

Corporate Priorities & Anticipated Milestones

Corporate Priorities	Milestone (Expected Timing)
Begin first RMC-6236 monotherapy pivotal trials	✓ Disclose updated clinical safety, tolerability and activity data from ongoing Phase 1 study in patients with PDAC (Disclosed July 2024) • Initiate Phase 3 2L PDAC study (2H 2024) • Disclose updated clinical safety, tolerability and activity data from ongoing Phase 1 study in patients with NSCLC (Q4 2024) • Initiate Phase 3 2L NSCLC study (Q4 2024)
Expand reach of RMC-6236	• Disclose initial combination RMC-6236 + pembrolizumab clinical PK, safety, tolerability and activity data (Q4 2024) ✓ Disclose initial data from Phase 1 expansion monotherapy cohort for additional tumor types and genotypes (Disclosed at AACR 2024)
Qualify mutant-selective inhibitors for late-stage development	<u>RMC-6291 | G12C-selective inhibitor</u> • Disclose initial combination RMC-6291 + pembrolizumab clinical PK, safety, tolerability and activity data (1H 2025) • Disclose initial combination RMC-6291 + RMC-6236 clinical PK, safety, tolerability and activity data (Q4 2024) <u>RMC-9805 | G12D-selective inhibitor</u> • Disclose initial monotherapy clinical PK, safety, tolerability and activity data from ongoing Phase 1 study (Q4 2024)

Clinical Development Pipeline

APPROACH	FOCUS	EARLY CLINICAL DEVELOPMENT[1]	REGISTRATIONAL TRIAL
RMC-6236 (MULTI: G12X, G13X, Q61X)			
Monotherapy	PDAC		
	NSCLC		
	Other solid tumors		
Combination	+ Chemotherapy, PDAC and CRC		
	+ Pembrolizumab, NSCLC		
	+ anti-EGFR, CRC		
RMC-6291 (G12C)			
Monotherapy	Solid tumors		
Combination	+ Pembrolizumab, NSCLC		
	+ RMC-6236, solid tumors		
RMC-9805 (G12D)			
Monotherapy	Solid tumors		
Combination	+ RMC-6236, solid tumors		



(1) Long bar indicates that registrational intent has been announced.

Additional Clinical Development Opportunities (next steps subject to portfolio priority decisions):

RAS(ON) Mutant-Selective Inhibitors: RMC-5127 (G12V), RMC-0708 (Q61H) and RMC-8839 (G13C)

RAS Companion Inhibitors: RMC-4630 (SHP2) and RMC-5552 (mTORC1/4EBP1)

Financial Information

Financial Position	
Cash, cash equivalents and marketable securities as of June 30, 2024	$1.6 billion[(1)]

2024 Financial Guidance
2024 GAAP Net Loss of $560 million to $600 million[(2)]

(1) With current cash, cash equivalents and marketable securities, the company projects it can fund planned operations into 2027, based on its current operating plan.
(2) Includes non-cash stock-based compensation expense of approximately $70 million to $80 million.

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Appendix

- All RAS cancer epidemiology statistics are estimated using tumor mutation frequencies from Foundation Medicine Insights March 2022 and scaled to estimated patient numbers using cancer incidence from ACS Cancer Facts and Figures 2023:
  - RAS mutations include: KRAS G12(A,C,D,F,L,R,S,V), KRAS G13(C,D,R,V), KRAS Q61(E,H,K,L,P,R) NRAS G12(A,C,D,R,S,V), NRAS G13(C,D,R,V), NRAS Q61(H,K,L,R), HRASG12(C,D,S,V), HRASG13(C,D,N,R,S,V), HRASQ61(K,L,R).
  - Includes 13 major solid cancer types: non-small cell lung cancer, colorectal, pancreatic ductal adenocarcinoma, renal, esophageal, head and neck squamous cell, ovarian, stomach, biliary, and carcinomas of unknown primary (CUP), and advanced melanoma, bladder and endometrial cancers causing mortality.
    - KRAS Q61H epidemiology statistics include multiple myeloma in addition to 13 major solid cancer types named above

- RAS mutations drive 30% of human cancers per Prior et al., *Cancer Research* 2020

- Mouse tumor responses assigned according to mRECIST (modified from Gao et al. Nat Med. 2015):
  - mPD = progressive disease; mSD = stable disease; mPR = partial response; mCR = complete response