Revolution Medicines

On Target to Outsmart Cancer

November 6, 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 November 6, 2024, and its future periodic reports to be filed with the Securities and Exchange Commission.

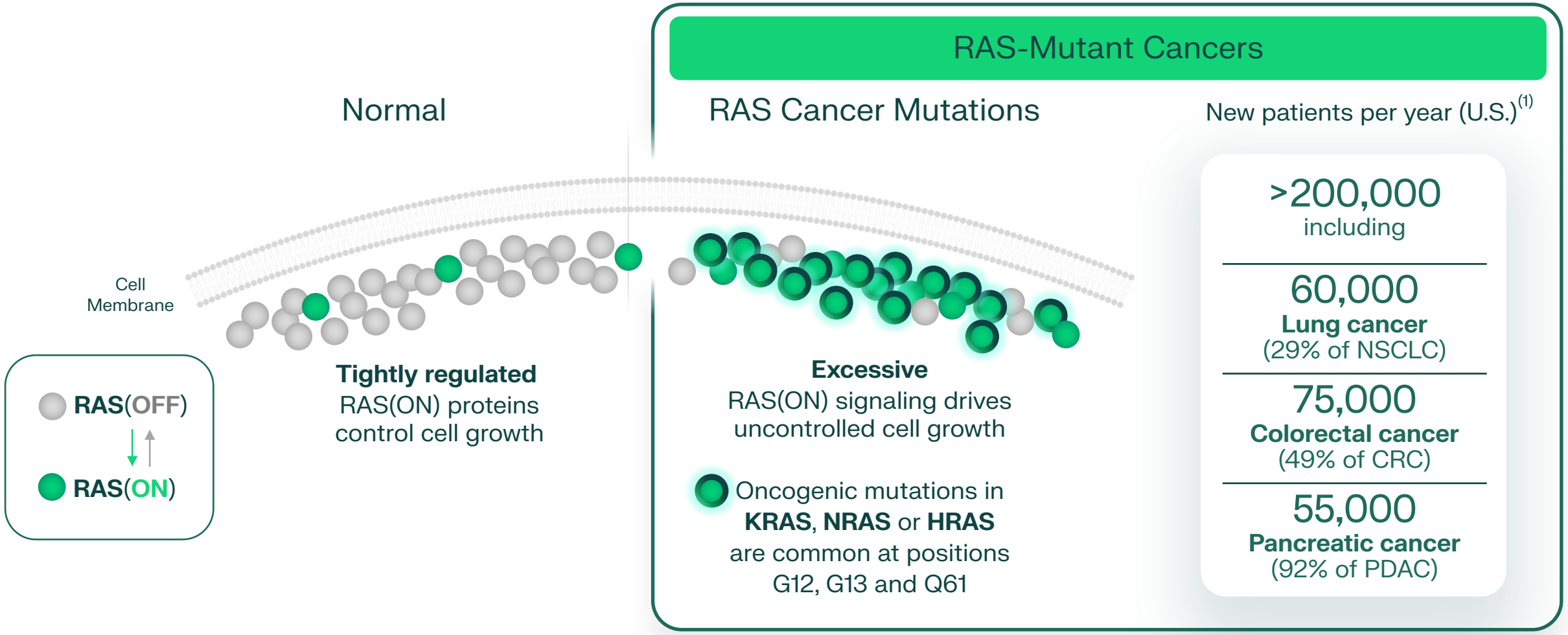
This presentation concerns product candidates that are under clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration (FDA). These product candidates are currently limited by Federal law to investigational use, and no representation is made as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

Revolution Medicines

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**
  - RASolute 302, a global, randomized Phase 3 study in 2L metastatic PDAC patients, is ongoing
  - Continuing monotherapy and combination exploration for 1L PDAC and other indications
- **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
  - Encouraging initial clinical proof-of-concept for RMC-6291 and RMC-9805 monotherapy

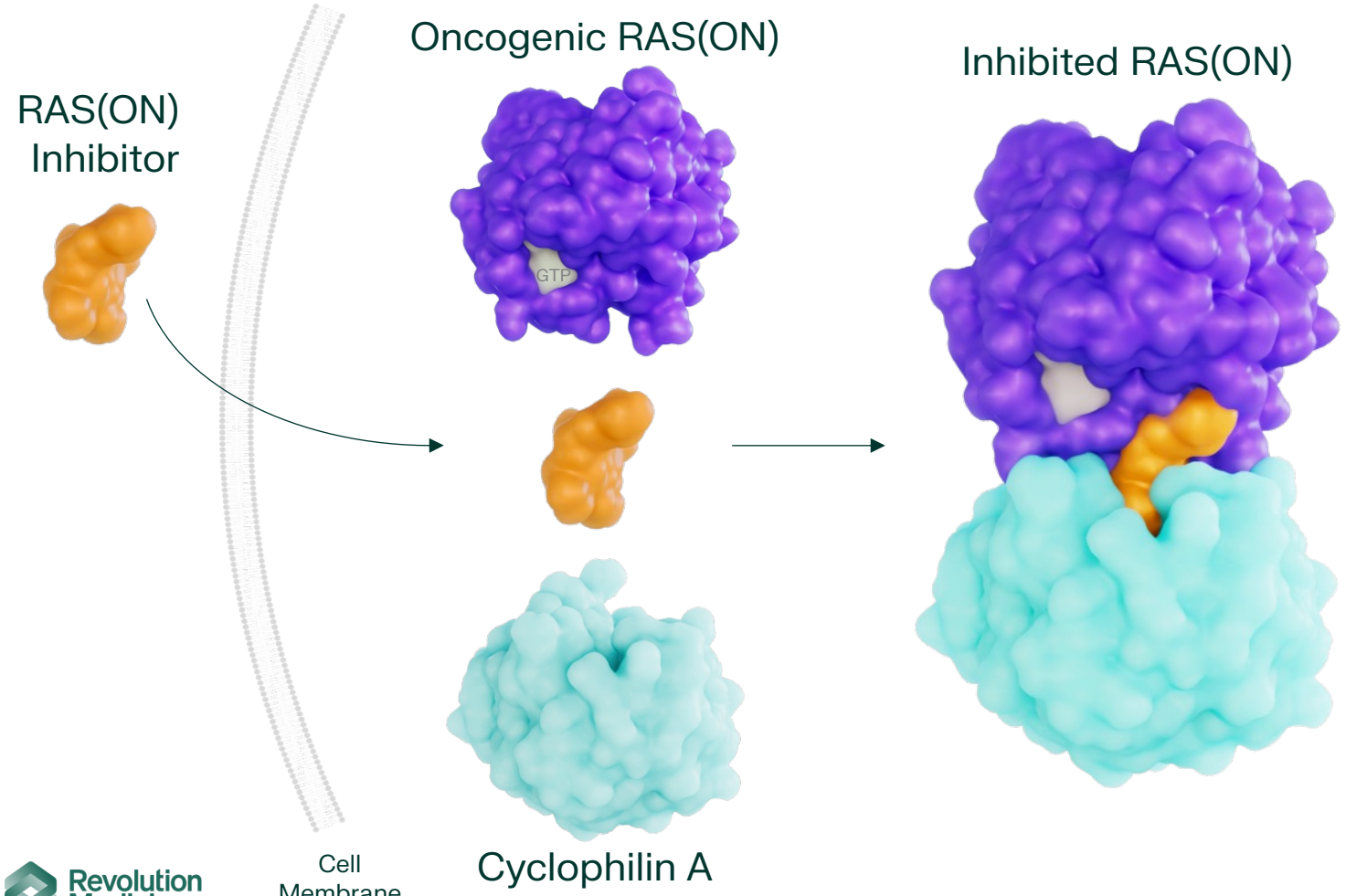
Portfolio of RAS(ON) Inhibitors Designed to Target Significant Number of Human Cancers



Revolution Medicines

(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; 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 Antitumor 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 three 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	Currently enrolling Phase 3 PDAC study[1] Initiation of Phase 3 NSCLC study expected in Q1 2025	**G12X and expansion**
Mutant-Selective		
RMC-6291	Evidence of differentiated clinical antitumor activity in NSCLC and CRC	**G12C**
RMC-9805	Evidence of encouraging clinical tolerability and antitumor activity in PDAC	**G12D**

(1) RAS G12X, non-synonymous mutations in KRAS, HRAS or NRAS at codon 12 (G12); expansion also includes G13X and Q61X, non-synonymous mutations in KRAS, HRAS or NRAS at codons 13 and 61, respectively and RAS wild-type.

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[2]

Most patients diagnosed with metastatic disease[3]

- 5-year survival is 3%[2]

Multi-agent chemotherapy is the primary treatment for most patients[2]

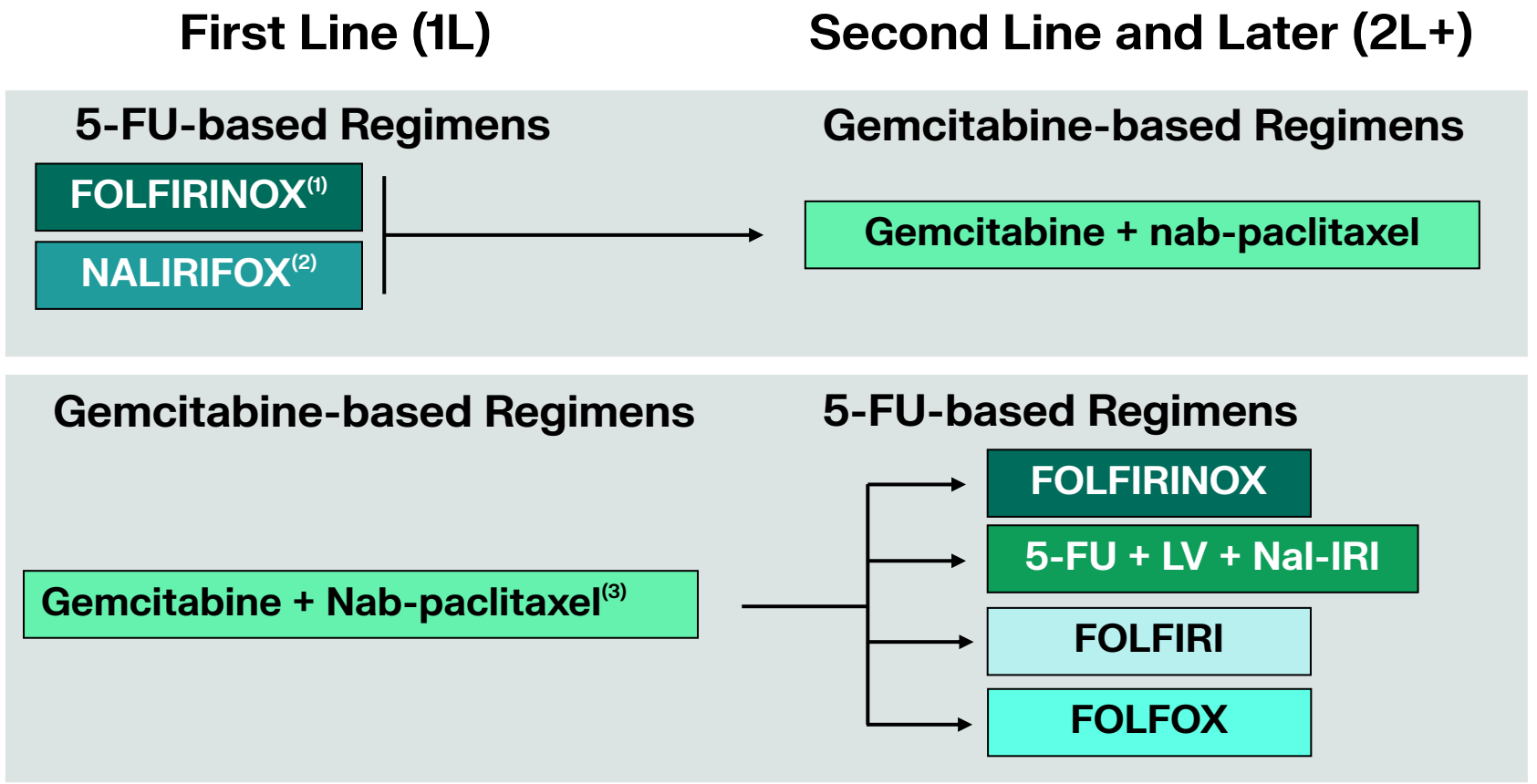
- Current targeted therapies benefit minority of patients[2]

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

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

(1) Incidence from ACS Cancer Facts and Figures 2024, adjusted for PDAC only. Includes all stages of disease. (2) CancerMPact 2022. (3) JAMA (2021) 326: 851-862. (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

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

Significant Need for Treatment(s) with Improved Efficacy and Tolerability for Patients with Previously Treated Metastatic PDAC

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]

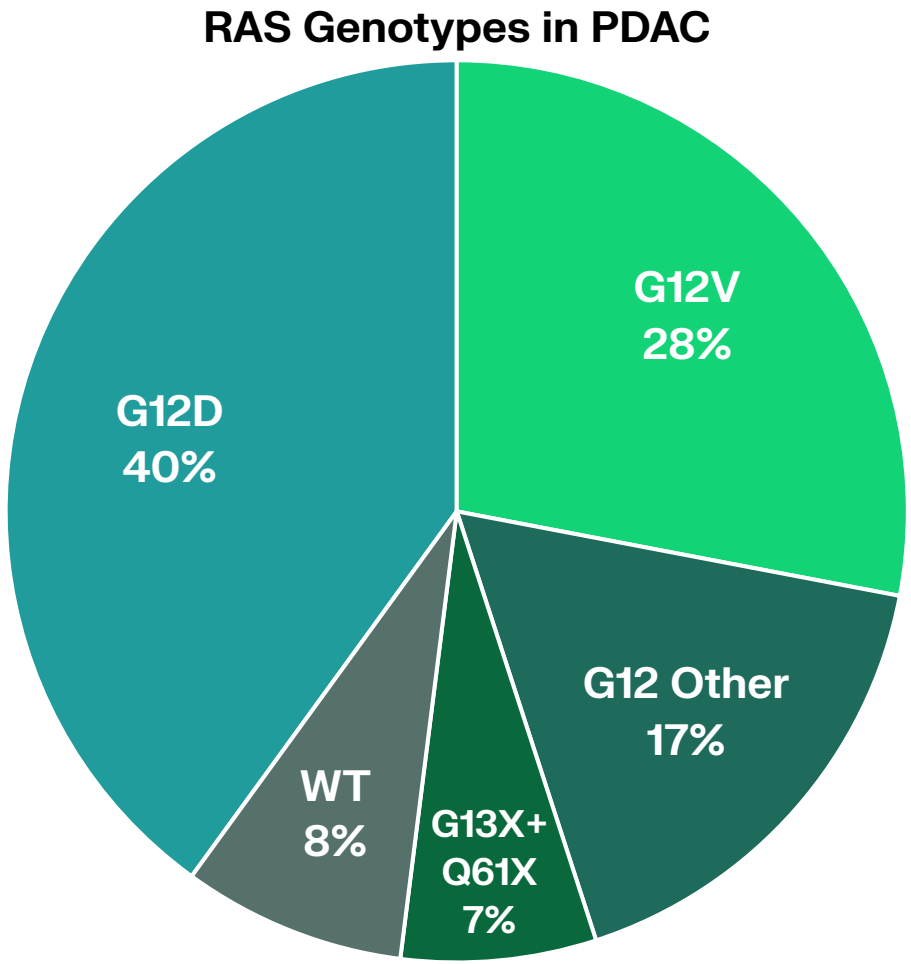
(1) Onivyde USPI. (2) Chiorean EG, et al. Clin Cancer Res 2021:27:6314–33. (3) Chung V, et al. JAMA Oncol 2017;3:516–22. (4) Hecht JR, et al. J Clin Oncol 2021;39:1108–18. (5) Huffman BM, et al. JAMA Network Open 2023;6:e2249720. (6) Hammel P, et al. ASCO GI 2022. (7) Fouchardiere C, et al. J Clin Oncol 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.
ORR, objective response rate. PFS, progression-free survival. OS, overall survival. NA, not available.

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]

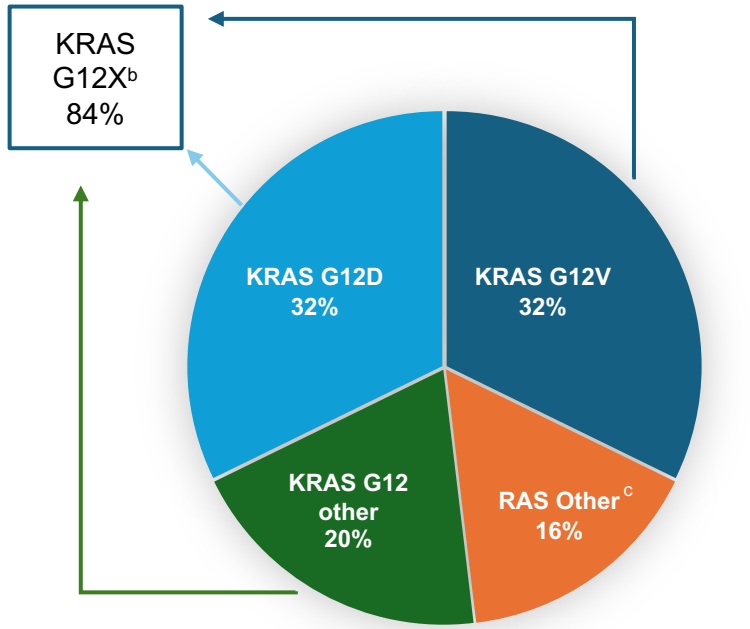


(1) ACS Cancer Facts and Figures 2024 adjusted for PDAC only.
(2) Estimated using tumor mutation frequencies from Foundation Medicine Insights March 2022.
RAS G12X, non-synonymous mutations in KRAS, HRAS or NRAS at codon 12 (G12). G13X and Q61X, non-synonymous mutations in KRAS, HRAS or NRAS at codons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

Phase 1 Study Demographics and Baseline Characteristics in PDAC Patients Representative of Phase 3 Study Population

PDAC Patients, RMC-6236 160–300 mg QD (N = 127)	
Age, years, median (range)	64 (30–86)
Male, n (%)	71 (56)
ECOG PS 1, n (%)	81 (64)
Number of prior anticancer therapies, median (range)	2 (1-11)
Number of prior anticancer therapies in metastatic setting, n (%)[a]	
0	2 (1)
1	57 (45)
2+	68 (54)
Liver metastases at baseline, n (%)	85 (67)
Metastatic at diagnosis [Stage IV], n (%)	66 (52)

RAS Genotypes Among Patients with PDAC 160–300 mg



Data cutoff: July 23, 2024.

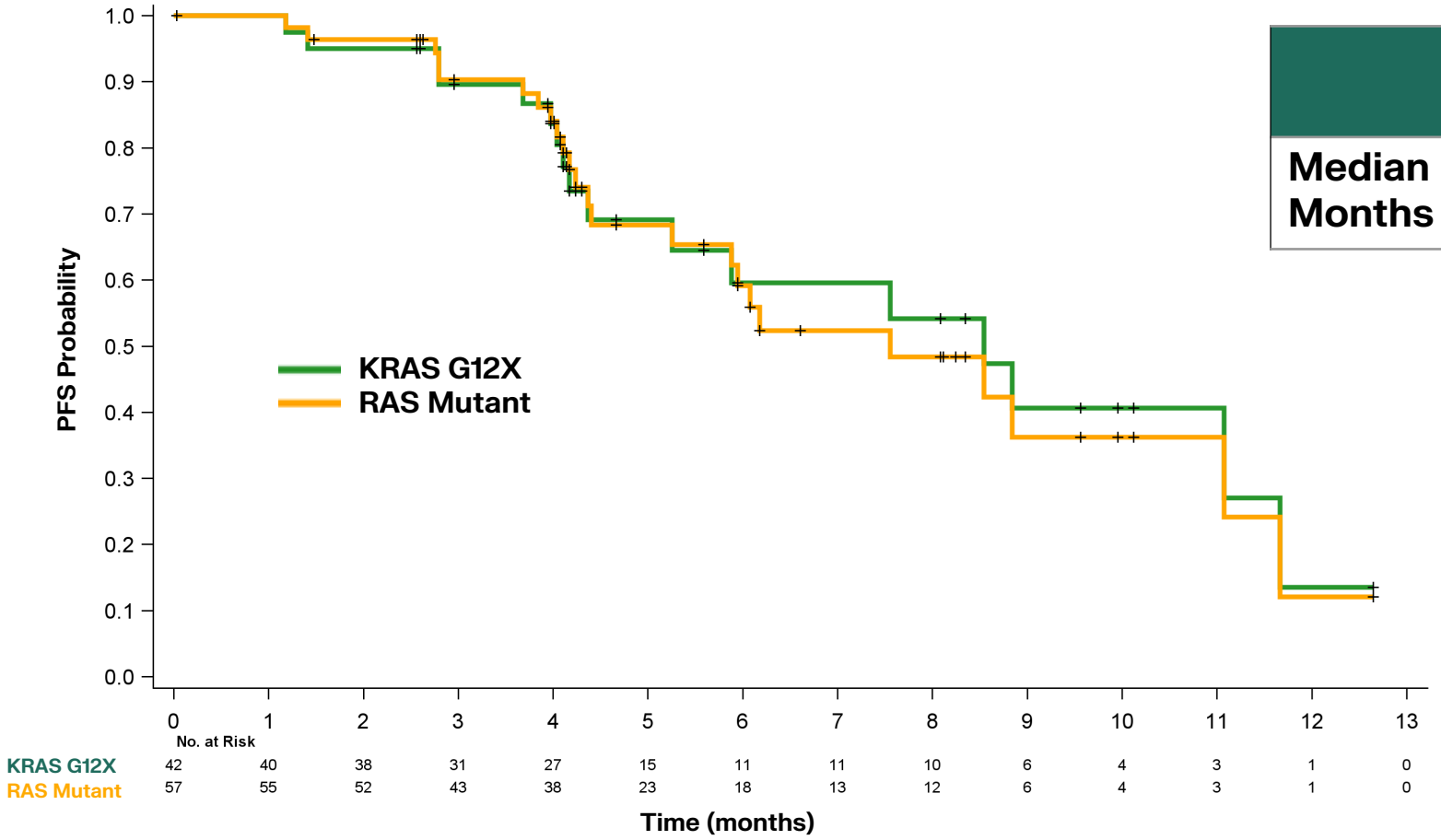
[a]Patients with locally advanced or metastatic PDAC; 1 prior line of therapy in the metastatic setting included patients who progressed on prior therapy in an earlier setting within 6 months of last dose.

[b]KRAS G12X mutations are defined by nonsynonymous mutations in KRAS codon 12 (G12).

[c]RAS Other includes mutations in KRAS G13X, KRAS Q61X, or mutations in HRAS or NRAS at codons G12X, G13X, or Q61X.

ECOG PS, Eastern Cooperative Oncology Group Performance Status. PDAC, pancreatic ductal adenocarcinoma. QD, daily.

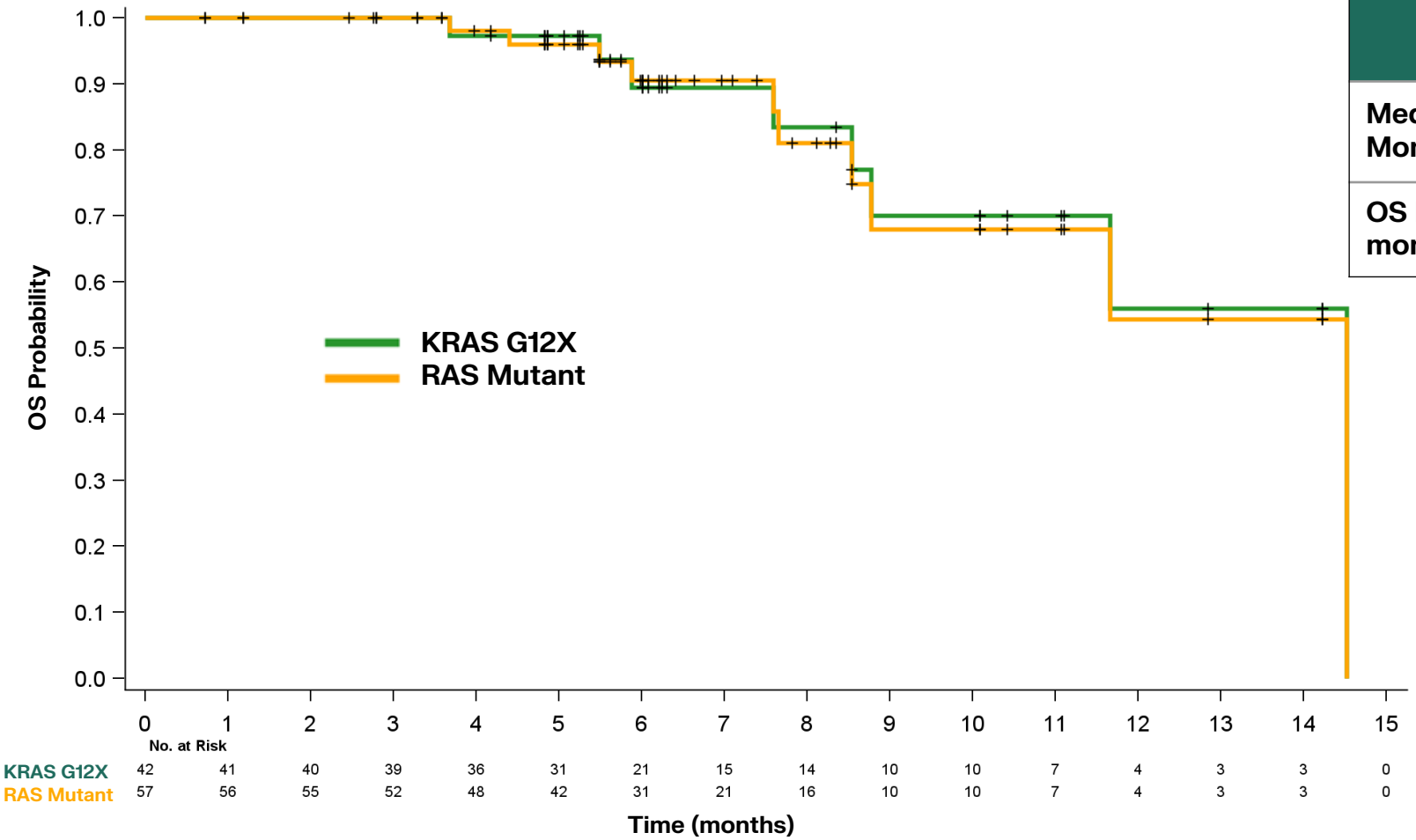
Compelling PFS in PDAC Patients Treated with RMC-6236 160-300 mg as 2L Therapy



	KRAS G12X[a] (N = 42)	RAS Mutant[b] (N = 57)
Median PFS, Months (95% CI)	**8.5** (5.3-11.7)	**7.6** (5.9-11.1)

Data cutoff: July 23, 2024.
2L in the metastatic setting includes patients who progressed within 6 months of the last dose of a prior therapy in an earlier setting.
Median follow-up is 6 months for KRAS G12 and 6.2 months for RAS mutant.
[a]KRAS G12X mutation includes any KRAS mutation where glycine (G) at position 12 is substituted by any other amino acid.
[b]RAS mutant includes any G12, G13, or Q61 substitution mutation in metastatic PDAC.
2L, second line. PDAC, pancreatic ductal adenocarcinoma. PFS, progression-free survival.

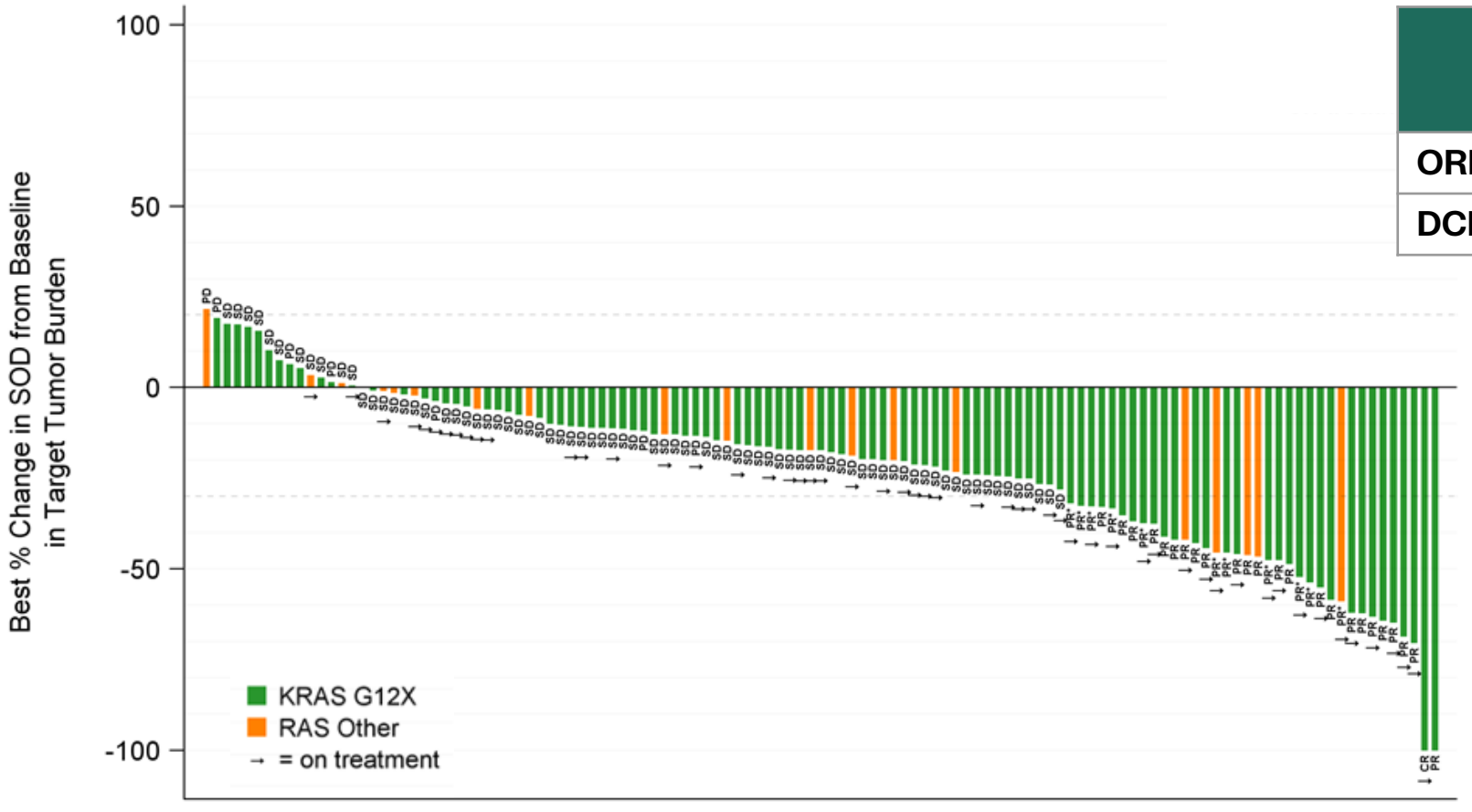
Compelling OS in PDAC Patients Treated with RMC-6236 160-300 mg as 2L Therapy



	KRAS G12X[a] (N = 42)	RAS Mutant[b] (N = 57)
Median OS, Months (95% CI)	**14.5** (8.8, NE)	**14.5** (8.8, NE)
OS Rate at 6 months, % (95% CI)[c]	**89** (70, 97)	**91** (77, 96)

Data cutoff: July 23, 2024.
Median follow-up is 6 months for KRAS G12X and 6.2 months for RAS mutant.
[a]KRAS G12X mutation includes any KRAS mutation where glycine (G) at position 12 is substituted by any other amino acid.
[b]RAS mutant includes any G12, G13, or Q61 substitution mutation in metastatic PDAC.
[c]OS rate at 6 months and 95% CI are from Kaplan-Meier analysis.
2L, second line. PDAC, pancreatic ductal adenocarcinoma. NE, not evaluable. OS, overall survival.

ORR and DCR in PDAC Patients Treated with RMC-6236 160-300 mg



	KRAS G12X[a], 160-300 mg	
	2L (N = 42)	3L+ (N = 63)
ORR[b]	29%	22%
DCR[b]	91%	89%

Data cutoff: July 23, 2024.

Among patients with an objective response (confirmed or unconfirmed), 50% of initial response occurred after 2 months of RMC-6236 treatment.

[a]KRAS G12X mutation includes any KRAS mutation where glycine (G) at position 12 is substituted by another amino acid. RAS Other includes mutations in KRAS G13X, KRAS Q61X, or mutations in HRAS or NRAS at codons G12X, G13X, or Q61X.

[b]ORR and DCR analyses included all patients who received first dose of RMC-6236 at least 14 weeks prior to data cutoff date (to allow 2 potential scans). Unconfirmed PRs (PR*) with treatment discontinued (will never confirm) were not considered responders but remained in the denominator; ORR (by RECIST v1.1) included confirmed CRs/PRs and unconfirmed CRs/PRs who were still on treatment and may yet be confirmed. 2L in the metastatic setting included patients who progressed on prior therapy in an earlier setting within 6 months of last dose.

CR, complete response. DCR, disease control rate. ORR, objective response rate. PD, progressive disease. PDAC, pancreatic ductal adenocarcinoma. PR, partial response. SD, stable disease. SOD, sum of diameters.

RMC-6236 Generally Well Tolerated in Patients with PDAC

Maximum severity of treatment-related AEs (TRAEs)	RMC-6236 160-300 mg QD (N = 127)	
	Any Grade	Grade ≥ 3
Any TRAE	124 (98)	37 (29)
TRAEs occurring in ≥ 10% of patients, n (%)		
Rash[a]	115 (91)	10 (8)
Diarrhea	61 (48)	3 (2)
Nausea[b]	54 (43)	0 (0)
Vomiting[b]	39 (31)	0 (0)
Stomatitis	39 (31)	4 (3)
Fatigue	25 (20)	1 (1)
Paronychia	17 (13)	0 (0)
Mucosal inflammation	16 (13)	1 (1)
Thrombocytopenia/platelet count decreased	14 (11)	3 (2)
Decreased appetite	14 (11)	1 (1)
Peripheral edema	13 (10)	0 (0)
Other select TRAEs, n (%)		
Anemia	11 (9)	7 (6)
ALT elevation	10 (8)	3 (2)
AST elevation	9 (7)	2 (2)
Neutropenia/neutrophil count decreased	7 (6)	2 (2)

- Majority of TRAEs were Grade 1 - 2
- One Grade 4 TRAE observed (platelet count decreased); no Grade 5 TRAEs

Data cutoff: July 23, 2024.

[a]Includes preferred terms of dermatitis, 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.

[b]No prophylaxis for nausea or vomiting was administered.

Median duration of treatment is 5.3 months in 160-300 mg population.

AE, adverse event. ALT, alanine transaminase. AST, aspartate transferase. TRAE, treatment-related adverse event.

RMC-6236 Achieves High Dose Intensity at Therapeutic Doses in Patients with PDAC

	RMC-6236 160–300 mg QD (N = 127)
TRAEs leading to dose modification, n (%)	45 (35)
Dose interruption	43 (34)
Dose reduction	24 (19)
Dose discontinuation	0 (0)
Specific TRAEs leading to dose reduction in >10% patients, n (%)	
Rash[a]	14 (11)
Mean dose intensity	92%

Data cutoff: July 23, 2024.
[a]Includes preferred terms of dermatitis acneiform, rash, rash maculopapular.
Median duration of treatment is 5.3 months in 160-300 mg population.
PDAC, pancreatic ductal adenocarcinoma. QD, daily. TRAE, treatment-related adverse event.

Design of Ongoing RASolute 302 Study: 2L Metastatic PDAC

Key Eligibility Criteria

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

NCT06625320

N = 460

R
1:1

- RMC-6236 300 mg PO 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

(1) SOC chemotherapy options: Gemcitabine + nab-paclitaxel, modified FOLFIRINOX, NAL-IRI+5-FU+LV, or FOLFOX.
2L, second line. PDAC, pancreatic ductal adenocarcinoma. ECOG PS, Eastern Cooperative Oncology Group Performance Status. R, randomized. PO, oral administration. QD, once daily. SOC, standard of care. PFS, progression-free survival. OS, overall survival. ORR, objective response rate. DOR, duration of response. QoL, quality of life.

Need and Opportunity for Improved Outcomes in 1L Metastatic PDAC

Treatment	Trial	Median Survival
FOLFIRINOX	Conroy et al. (*Prodige-4 Intergroup trial*)	11.1 months
Gemcitabine plus nab-paclitaxel	Von Hoff et al. (*MPACT trial*)	8.5 months
NALIRIFOX	Wainberg et al. (NAPOLI-3)	11.1 months

- Currently designing Phase 3 study of RMC-6236 in 1L treatment of patients with metastatic PDAC

Gemcitabine: 1000 mg/m^2 weekly for 7 of 8 weeks and then weekly for 3 of 4 weeks (days 1, 8, and 15).
FOLFIRINOX: oxaliplatin 85 mg/m^2, irinotecan 180 mg/m^2, leucovorin 400 mg/m^2, and fluorouracil 400 mg/m2 given as a bolus followed by 2400 mg/m2 given as a 46-hour continuous infusion, every 2-weeks.
Gemcitabine plus nab-paclitaxel: nab-paclitaxel 125 mg/m^2 + gemcitabine 1000 mg/m^2 on days 1, 8, and 15 every 4 weeks.
NALIRIFOX: liposomal irinotecan 50 mg/m2, oxaliplatin 60 mg/m^2, leucovorin 400 mg/m^2, and fluorouracil 2400 mg/m^2 administered sequentially as a continuous IV infusion over 46-hour, every 2-weeks (days 1 and 15).

Highlights of RMC-6236 PDAC Program

- RMC-6236 is the first targeted investigational drug designed to directly inhibit all major forms of oncogenic RAS(ON), the common drivers of PDAC
- RMC-6236 exhibited a manageable safety profile, favorable dose intensity and compelling antitumor activity as measured by PFS and OS in a broad population of previously treated patients with RAS mutant metastatic PDAC
- These data support our ongoing global, randomized Phase 3 clinical study (RASolute 302) of RMC-6236 versus SOC chemotherapy as 2L treatment in patients with previously treated metastatic PDAC
- Aiming to accelerate potential registrational studies 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
2L, second line. PDAC, pancreatic ductal adenocarcinoma. PFS, progression-free survival. OS, overall survival. SOC, standard of care.

RMC-6236 in NSCLC and Other Solid Tumors

Highlights of RMC-6236 in NSCLC & Other Solid Tumors

- RMC-6236 is being evaluated in solid tumors beyond PDAC, including NSCLC and CRC
- Initial results for RMC-6236 monotherapy demonstrated encouraging clinical antitumor activity in patients with advanced RAS mutant NSCLC at generally well tolerated doses
  - Plans to share updated clinical data and initiate Phase 3 trial
- Multiple combinations have potential to enable advancement into additional tumor types and earlier lines therapy
  - RMC-6236 combinations being evaluated in GI cancers include standard of care therapies (i.e., chemotherapies) and doublets with RAS(ON) mutant-selective inhibitors
  - RMC-6236 combinations being evaluated in NSCLC include immunotherapies (e.g., pembrolizumab) and doublets with RAS(ON) mutant-selective inhibitors

NSCLC, non-small cell lung cancer. CRC, colorectal cancer. GI, gastrointestinal.

RAS(ON) G12C-Selective Inhibitor RMC-6291

Highlights of RMC-6291 Program

- RMC-6291 is the first reported G12C-selective inhibitor with a mechanism of action driven by targeting the RAS(ON) state
- Initial results for RMC-6291 monotherapy demonstrated encouraging clinical antitumor activity in patients with KRAS G12C at generally well tolerated doses
  - Clinical responses observed in both KRAS(OFF) G12C inhibitor-experienced and -naïve patients
- Combination strategies for RMC-6291 under exploration include RAS(ON) inhibitor doublets with multi-selective inhibitor RMC-6236 and with standard of care therapies, including immunotherapies

NSCLC, non-small cell lung cancer. CRC, colorectal cancer.

RAS(ON) G12D-Selective Inhibitor RMC-9805

RMC-9805-001 Phase 1 Study Design (RMC-9805 Monotherapy)

Key Eligibility Criteria

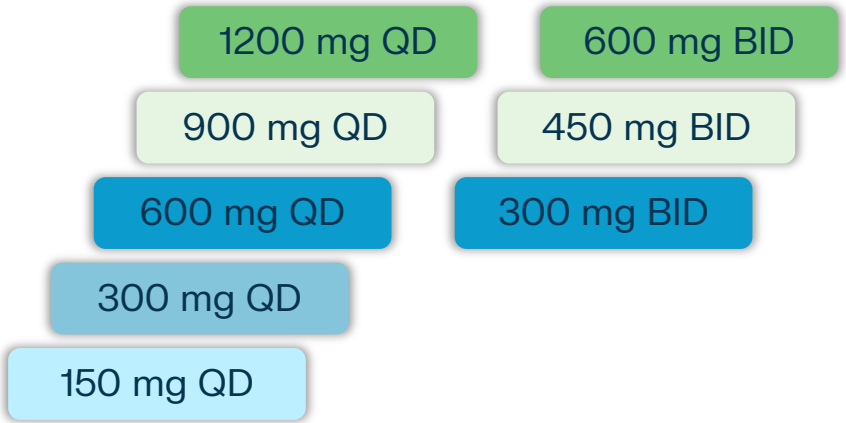
- Advanced solid tumors with KRAS G12D mutations
- Received prior standard therapy appropriate for tumor type and stage
- ECOG PS 0–1
- No active brain metastases

Key Endpoints

- Safety and tolerability
- Pharmacokinetics
- Anti-tumor activity

Part 1: Dose Escalation

RMC-9805 administered orally QD or BID, 21-day treatment cycle

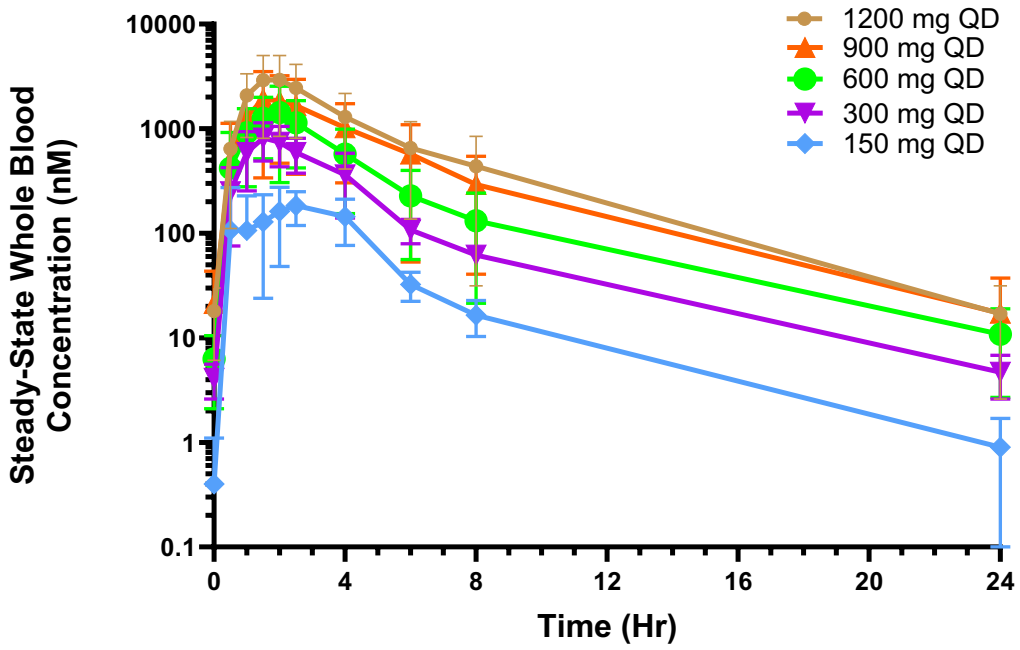


Part 2: Expansion and Dose Optimization in PDAC

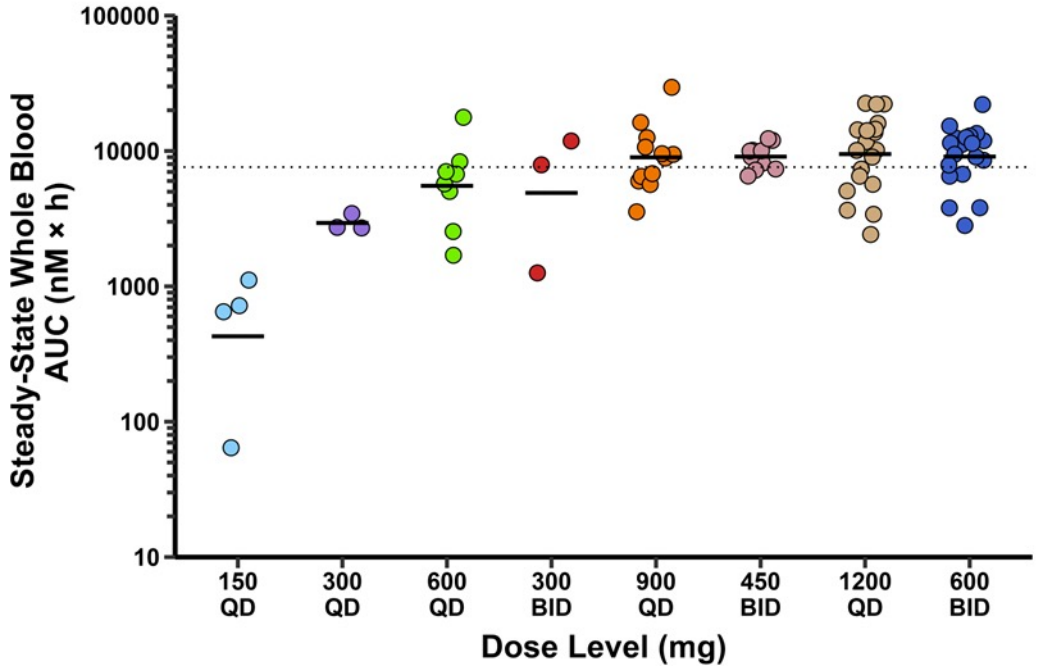
ECOG PS, Eastern Cooperative Oncology Group Performance Status. PDAC, pancreatic ductal adenocarcinoma. QD, once daily. BID, twice daily.

Dose-Dependent Exposure Increases for RMC-9805 Reach Levels Predicted to Induce Tumor Regressions

Mean Steady-State Blood PK Profiles



Individual Steady-State Blood AUC



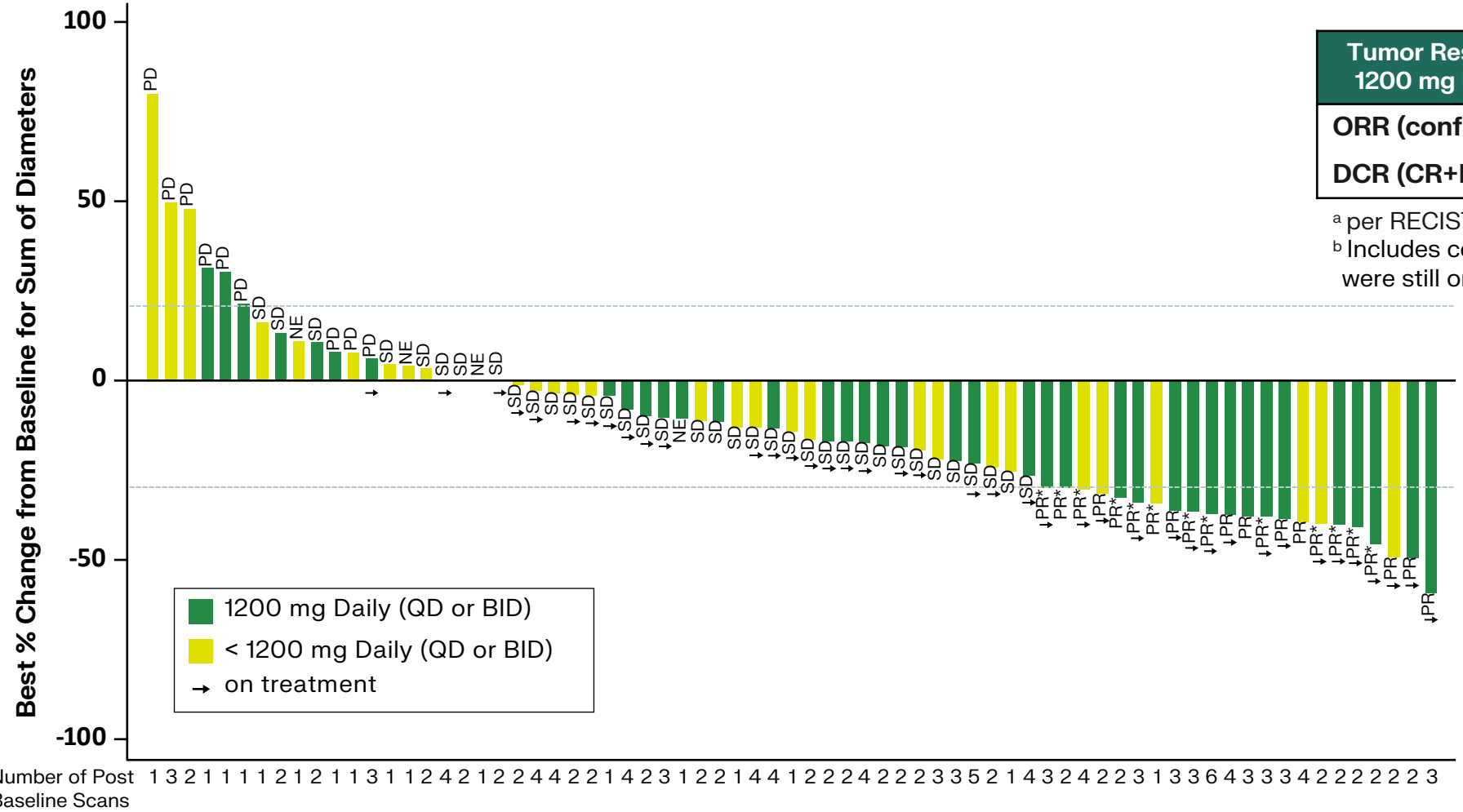
Exposure in mice at 100 mg/kg

- Dose that induces tumor regressions in majority of preclinical PDAC models

- PK supports 1200 mg QD as a candidate RP2DS in PDAC

PK data as of July 16, 2024.
Left: steady-state concentrations from Cycle 1 Day 15. Error bars represent standard deviation. Right: steady-state AUC in Cycle 1 Day 15. Each circle represents an individual patient AUC.
AUC, area under the curve. QD, once daily. BID, twice daily. PDAC, pancreatic ductal adenocarcinoma. PK, Pharmacokinetics. RP2DS, recommended Phase 2 dose and schedule.

Encouraging Initial Antitumor Activity in PDAC Patients Treated with RMC-9805



Tumor Response for PDAC Patients Treated with 1200 mg Daily Dose (QD, N = 20 or BID, N = 20)[a]	
ORR (confirmed or pending)[b], % (n)	30% (12)
DCR (CR+PR+SD), % (n)	80% (32)

[a] per RECIST v1.1
[b] Includes confirmed PRs and unconfirmed PRs who were still on treatment and may yet be confirmed

Data cutoff: September 2, 2024. All treated patients with PDAC who received a first daily dose at least 14 weeks prior to data cutoff date (applies to Waterfall plot and ORR table).
Includes confirmed PRs and unconfirmed PRs who were still on treatment and may yet be confirmed. Two patients (1200 mg daily dose) who progressed after initial PR without a confirmation and who remained on treatment at the data cut-off date were not counted as responders. Three additional patients (N=2 at 1200 mg daily; N=1 at < 1200 mg daily) are not displayed on the Waterfall plot due to withdrawal of consent or clinical progression. Among patients with a response (confirmed or unconfirmed), 55% of first responses occurred after 2 months of RMC-9805 treatment (all dose levels).
CR, complete response. DCR, disease control rate. NE, not evaluable. PD, progressive disease. PR, partial response. PR*, unconfirmed partial response. SD, stable disease. ORR, objective response rate. RECIST, response evaluation criteria in solid tumors.

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RMC-9805 Generally Well Tolerated at 1200 mg Daily

Patients Treated with RMC-9805 1200 mg Daily (1200 mg QD, N = 60 or 600 mg BID, N = 39)				
Maximum Severity of Treatment-Related AEs	**Grade 1**	**Grade 2**	**Grade 3**	**Any Grade**
TRAEs occurring in ≥10% of patients, n (%)				
Nausea	23 (23%)	4 (4%)	0	27 (27%)
Diarrhea	16 (16%)	4 (4%)	0	20 (20%)
Vomiting	13 (13%)	2 (2%)	0	15 (15%)
Rash[a]	10 (10%)	0	0	10 (10%)
Other select TRAEs, n(%)				
ALT elevation	5 (5%)	0	1 (1%)	6 (6%)
AST elevation	3 (3%)	1 (1%)	0	4 (4%)
Stomatitis	0	0	0	0
TRAEs leading to dose reduction, n (%)	4 (4%)	0	0	4 (4%)
TRAEs leading to treatment discontinuation, n (%)	0	0	0	0

- No treatment-related Grade 4 or 5 AEs or SAEs have been reported

Data cutoff: September 2, 2024.
Median time on treatment was 2.8 months (range: 0.2–6.7).
[a]Includes preferred terms of dermatitis, dermatitis acneiform, dermatitis psoriasiform, eczema, erythema, rash, rash erythematous, rash macular, rash maculo-papular, rash papular, rash pruritic, and rash pustular.
AE, adverse event. ALT, alanine transaminase. AST, aspartate transferase. SAE, serious adverse event. TRAE, treatment-related adverse event. QD, once daily. BID, twice daily.

Highlights of RMC-9805 Program

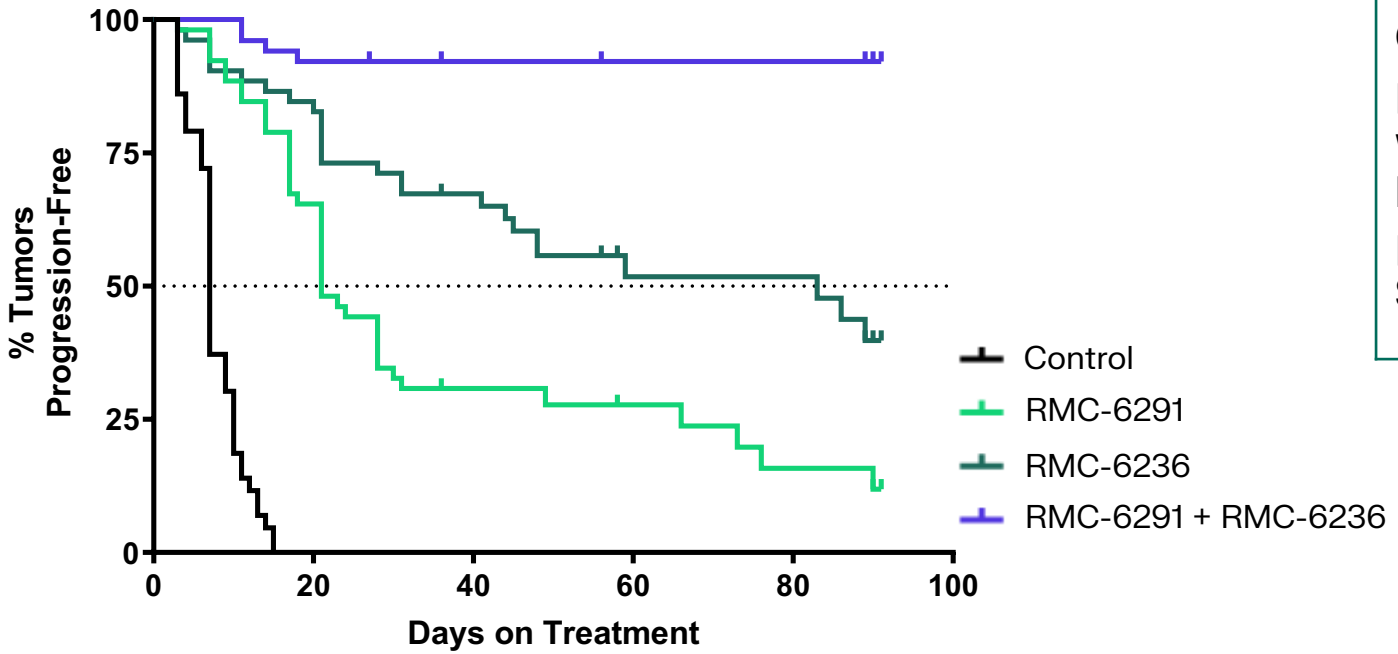
- RMC-9805 has demonstrated promising initial clinical profile in patients with KRAS G12D PDAC
  - Orally administered and well tolerated
  - Encouraging antitumor activity as demonstrated by tumor regressions
  - Durability assessment pending longer follow-up
- Dose optimization in KRAS G12D PDAC and other solid tumors is ongoing – 1200 mg QD identified as a candidate RP2DS in PDAC
- Observations to date support ongoing development as a single agent and in combination with other therapies, including the RAS(ON) multi-selective inhibitor RMC-6236

PDAC, pancreatic ductal adenocarcinoma. QD, once daily. RP2DS, recommended Phase 2 dose and schedule.

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]



RMC-6291-101 Clinical Trial[2]

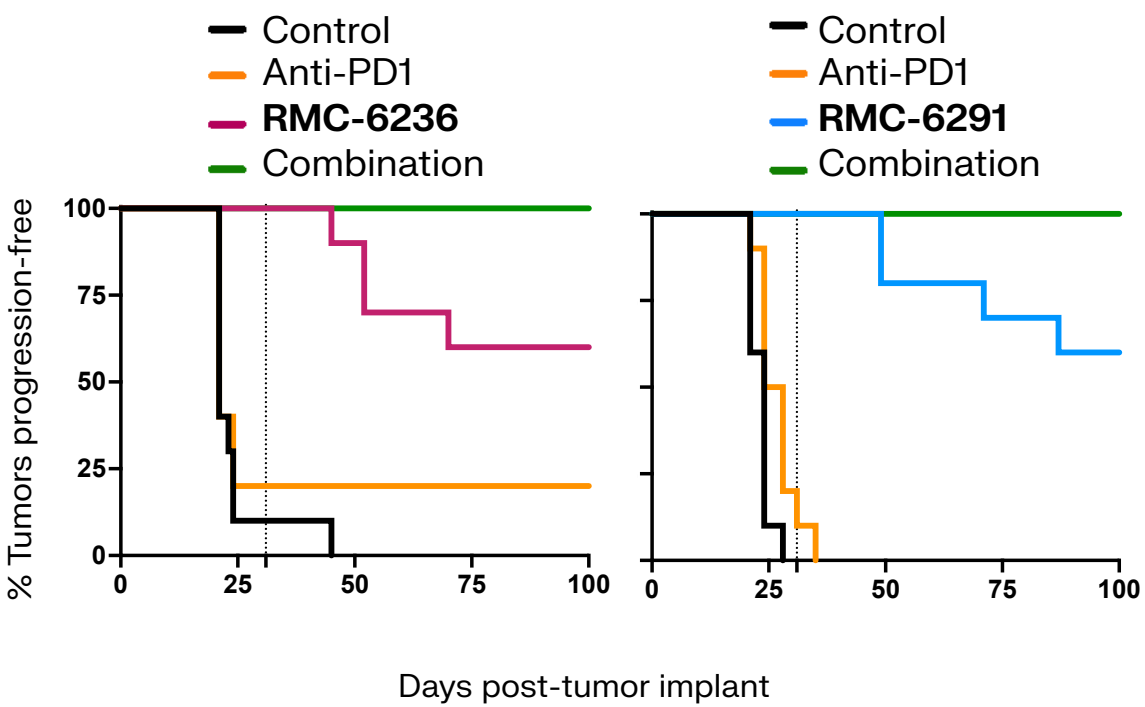
Objectives: evaluate safety, tolerability and preliminary activity of RMC-6236 combined with RMC-6291
Patient Population: KRAS G12C solid tumors, primarily NSCLC and CRC
Study Status: Dosing

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

(1) RVMD preclinical research. 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.
NSCLC, non-small cell lung cancer.

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

(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.
NSCLC, non-small cell lung cancer.

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	Dosing	Qualification for potential 1L

(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.
NSCLC, non-small cell lung cancer. PDAC, pancreatic ductal adenocarcinoma. CRC, colorectal cancer. 1L, first line.

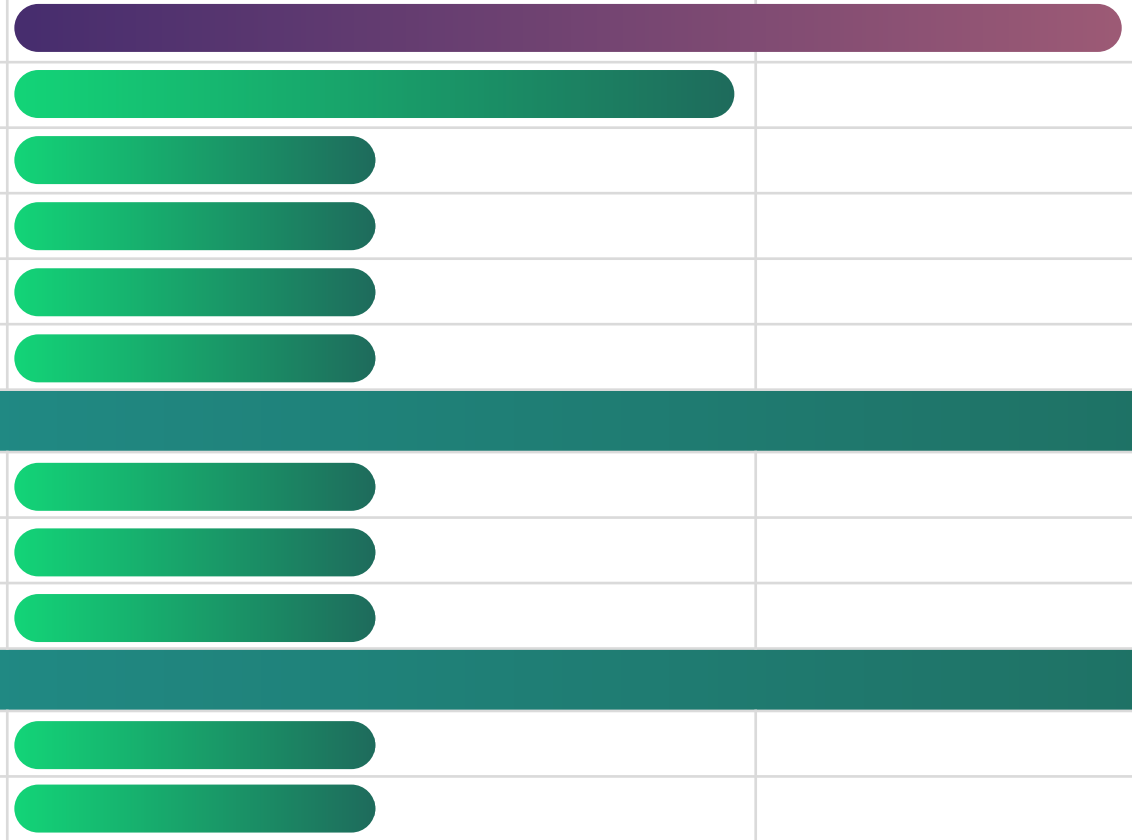
Corporate Priorities & Anticipated Milestones

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 (Disclosed October 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 (Q1 2025)
Expand reach of RMC-6236	✓ Disclose initial data from Phase 1 expansion monotherapy cohort for additional tumor types and genotypes (Disclosed at AACR 2024) • Disclose initial combination RMC-6236 + pembrolizumab clinical PK, safety, tolerability and activity data (Q4 2024)
Qualify mutant-selective inhibitors for late-stage development	<u>RMC-6291 | G12C-selective inhibitor</u> • Disclose initial combination RMC-6291 + RMC-6236 clinical PK, safety, tolerability and activity data (Q4 2024) • Disclose initial combination RMC-6291 + pembrolizumab clinical PK, safety, tolerability and activity data (1H 2025) <u>RMC-9805 | G12D-selective inhibitor</u> ✓ Disclose initial monotherapy clinical PK, safety, tolerability and activity data from ongoing Phase 1 study (Disclosed October 2024)

PDAC, pancreatic ductal adenocarcinoma. 2L, second line. NSCLC, non-small cell lung cancer. PK, Pharmacokinetics..

RAS(ON) Inhibitor Clinical Development Pipeline

APPROACH	FOCUS	EARLY CLINICAL DEVELOPMENT[1]	REGISTRATIONAL TRIAL
RMC-6236 (MULTI: G12X, G13X, Q61X)			
Monotherapy	PDAC RASolute		
	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)

NSCLC, non-small cell lung cancer. PDAC, pancreatic ductal adenocarcinoma. CRC, colorectal cancer.

Financial Information

Financial Position	
Cash, cash equivalents and marketable securities as of September 30, 2024	$1.55 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.

Revolution Medicines™

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