Revolution Medicines

On Target to Outsmart Cancer

43rd Annual J.P. Morgan Healthcare Conference

January 13, 2025

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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.

This presentation includes certain information regarding publicly available results from clinical trials by third parties evaluating other product candidates. Such trials were not head-to-head trials with any of Revolution Medicines' product candidates and include differences in study protocols, patient populations and reporting standards, and caution should be exercised when comparing data across trials.

Our Mission

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

Daraxonrasib
RMC-6236 | MULTI

Elironrasib
RMC-6291 | G12C

Zoldonrasib
RMC-9805 | G12D

Compelling pipeline from pioneering science

Proven execution and patient-centric strategy

Financial strength to enable vision

Our Strategy

To maximize the impact of our RAS(ON) inhibitor portfolio for patients with RAS-addicted cancers by:

01 — Commercializing daraxonrasib (RMC-6236) initially in **late-stage** disease

02 — Moving aggressively to develop RAS(ON) inhibitors in **earlier lines** of therapy (first line metastatic, locally-advanced unresectable, adjuvant)

03 — Developing optimal, biologically rational RAS(ON) inhibitor **combinations** for earlier lines

04 — Continuously innovating for patients by producing new, **differentiated drug candidates**

2025 Priorities Toward Creating Industry-Leading Targeted Medicines Franchise for Patients with RAS-Addicted Cancers

Discovery

Sophisticated RAS cancer drug discovery and biological sciences

- Advance fourth development candidate to clinic readiness
- Progress next-generation programs

Development

Pioneering drug candidates and proven capabilities

- Execute daraxonrasib (RMC-6236) pivotal trials in 2L PDAC and NSCLC
- Advance daraxonrasib into 1L PDAC pivotal trial
- Commit to initial pivotal trial(s) with mutant-selective inhibitor

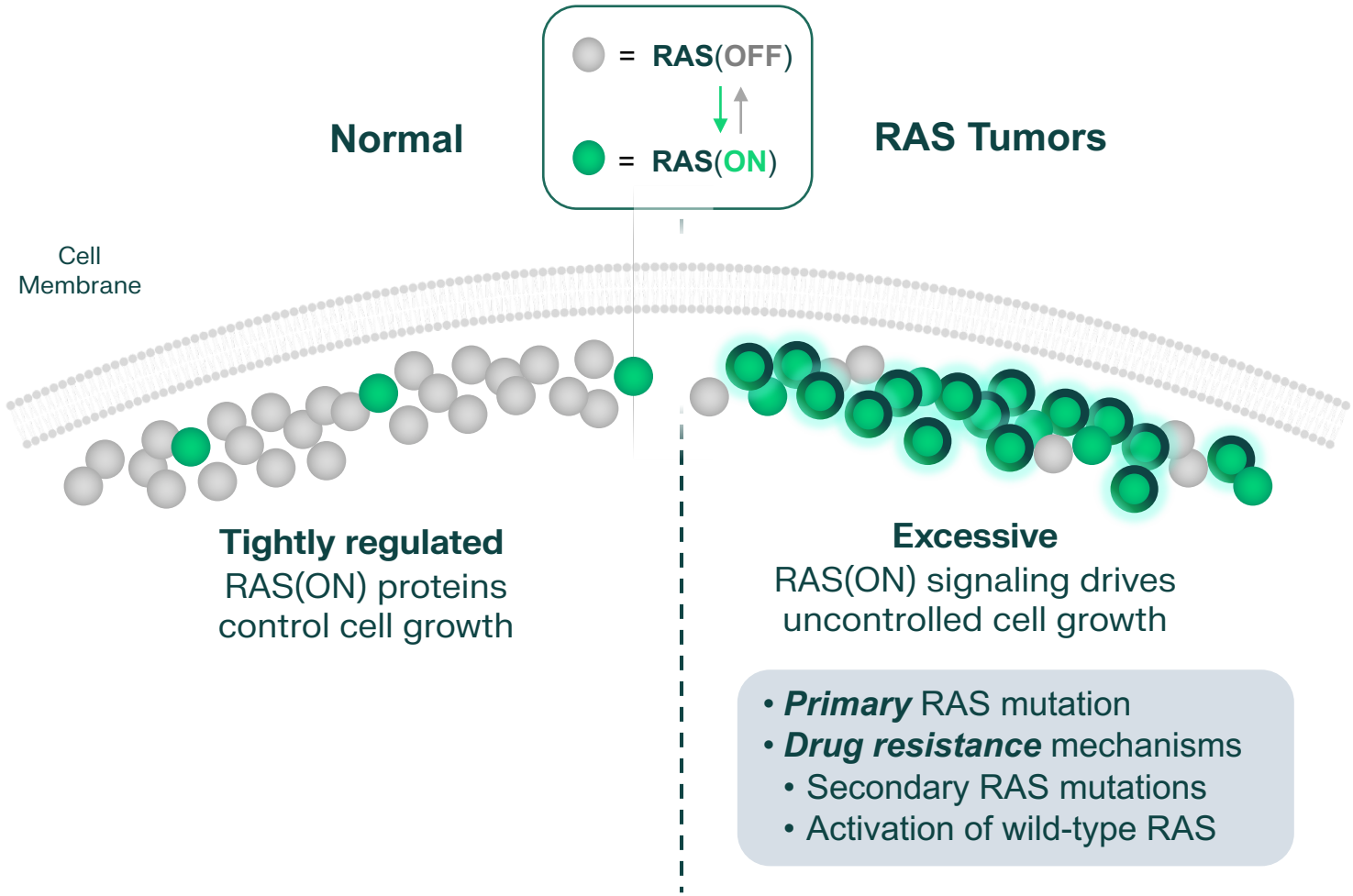
Delivery

Established select partnerships; manufacturing daraxonrasib at commercial scale

- Grow commercial and operational capabilities in support of U.S. launch
- Expand and reinforce select partnerships

2L, second line; 1L first line; PDAC, pancreatic ductal adenocarcinoma; NSCLC, non-small cell lung cancer.

RAS(ON) Proteins are Key Therapeutic Targets in RAS-Addicted Cancers

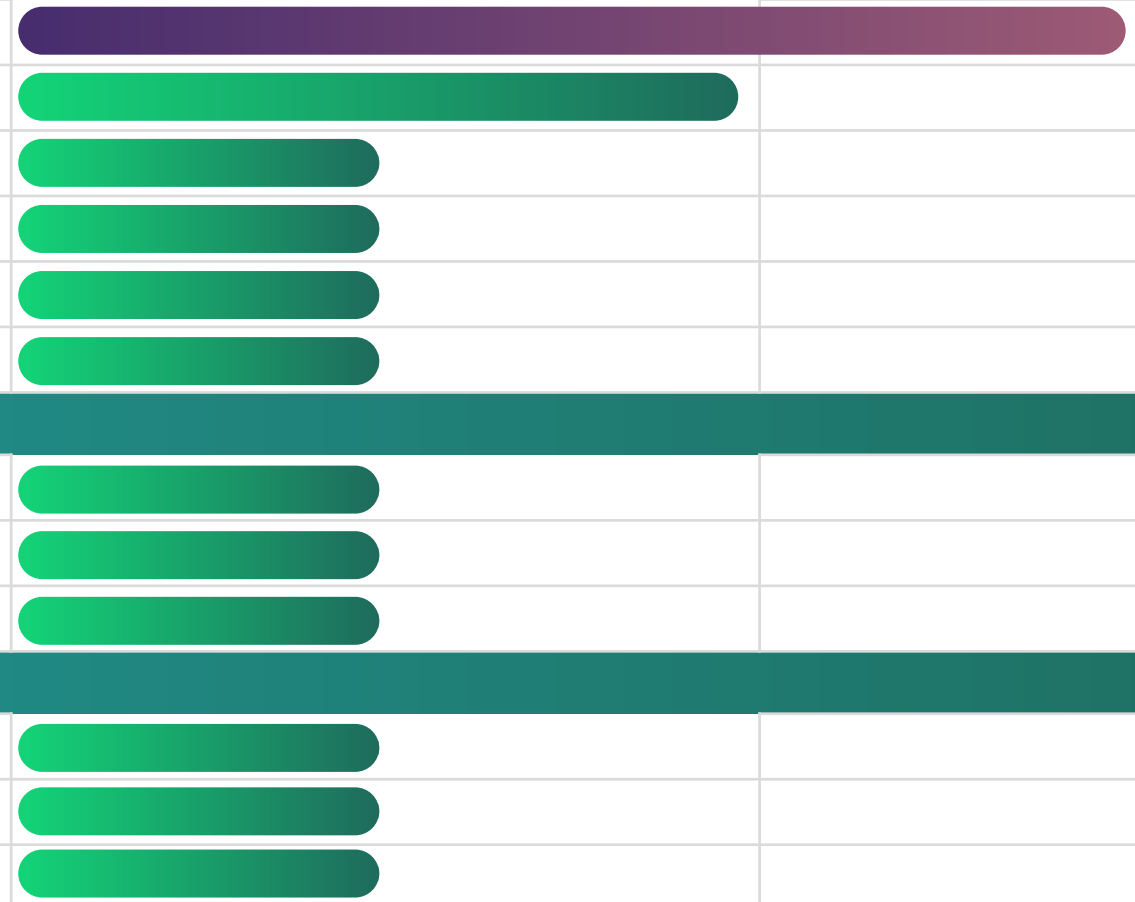


- **Major cancers with RAS drivers**[1]
  - Pancreatic ductal adenocarcinoma (>90%)
  - Non-small cell lung cancer (~30%)
  - Colorectal cancer (~50%)
- **Optimized clinical impact**
  - One or more RAS inhibitors
  - Deep and durable inhibition of RAS(ON) signaling
  - Suppression of dominant RAS-mediated drug resistance

[1] Estimated using tumor mutation frequencies from Foundation Medicine Insights March 2022.

Pipeline Led by Three Pioneering, Clinical-Stage RAS(ON) Inhibitors

APPROACH	FOCUS	EARLY CLINICAL DEVELOPMENT[1]	REGISTRATIONAL TRIAL
Daraxonrasib (RMC-6236 | MULTI)			
Monotherapy	PDAC RASolute		
	NSCLC		
	Other solid tumors		
Combination	+ Chemotherapy, PDAC and CRC		
	+ Pembrolizumab, NSCLC		
	+ anti-EGFR, CRC		
Elironrasib (RMC-6291 | G12C)			
Monotherapy	Solid tumors		
Combination	+ Pembrolizumab, NSCLC		
	+ daraxonrasib, solid tumors		
Zoldonrasib (RMC-9805 | G12D)			
Monotherapy	Solid tumors		
Combination	+ SOC therapies, solid tumors		
	+ daraxonrasib, solid tumors		



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

Additional RAS(ON) Mutant-Selective Inhibitors (RMC-5127 (G12V), RMC-0708 (Q61H) and RMC-8839 (G13C)) and **next-generation programs**

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PDAC, pancreatic ductal adenocarcinoma; NSCLC, non-small cell lung cancer; CRC, colorectal cancer. SOC, standard of care.

Daraxonrasib (RMC-6236): RAS(ON) Multi-Selective Inhibitor

Active against

Diverse RAS driver mutations

Multiple drug resistance mechanisms, including secondary RAS mutations and wildtype RAS

PDAC (~55,000 new RAS U.S. patients per year)(1)

- 2L monotherapy POC: median PFS 8.8 mo | OS Rate at 6 mo: 100%(2)
- 2L monotherapy registrational study is enrolling
- Evaluating multiple combinations in 1L

NSCLC (~60,000 new RAS U.S. patients per year)(1)

- 2/3L monotherapy POC : median PFS 9.8 mo | mOS 17.7 mo(3)
- 2/3L monotherapy registrational study pending
- Initial combinability with pembrolizumab has been demonstrated
- Evaluating multiple combinations in 1L

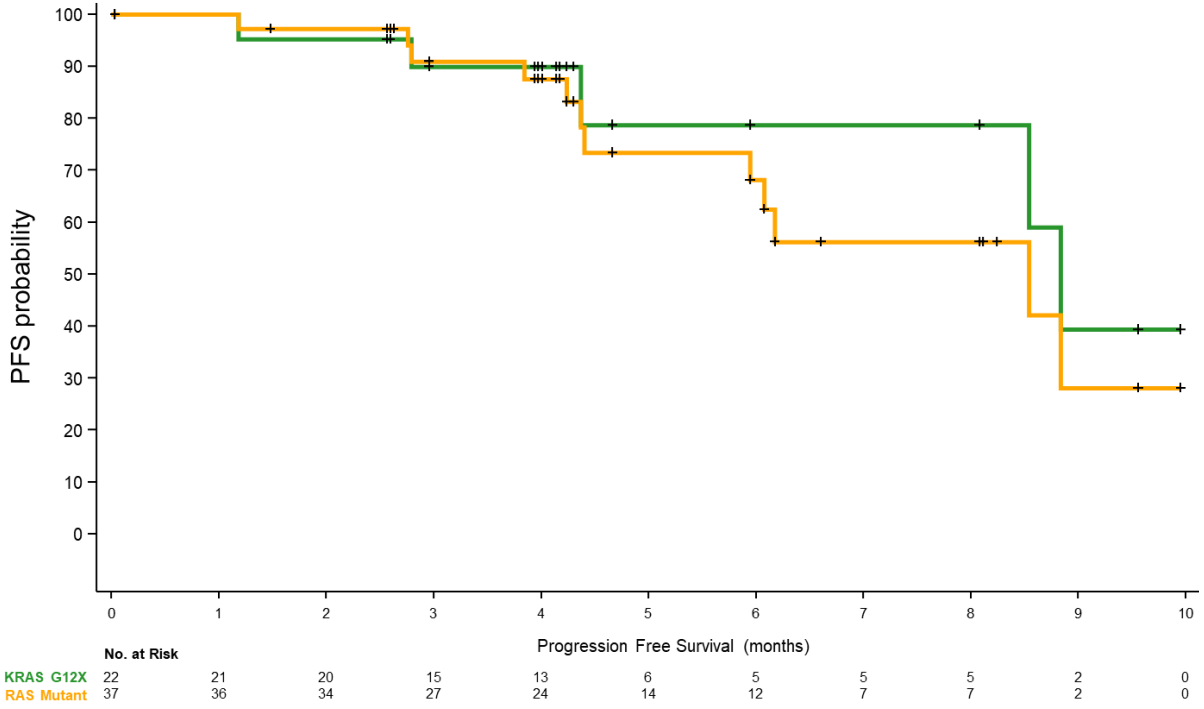
Other RAS-Addicted Tumors

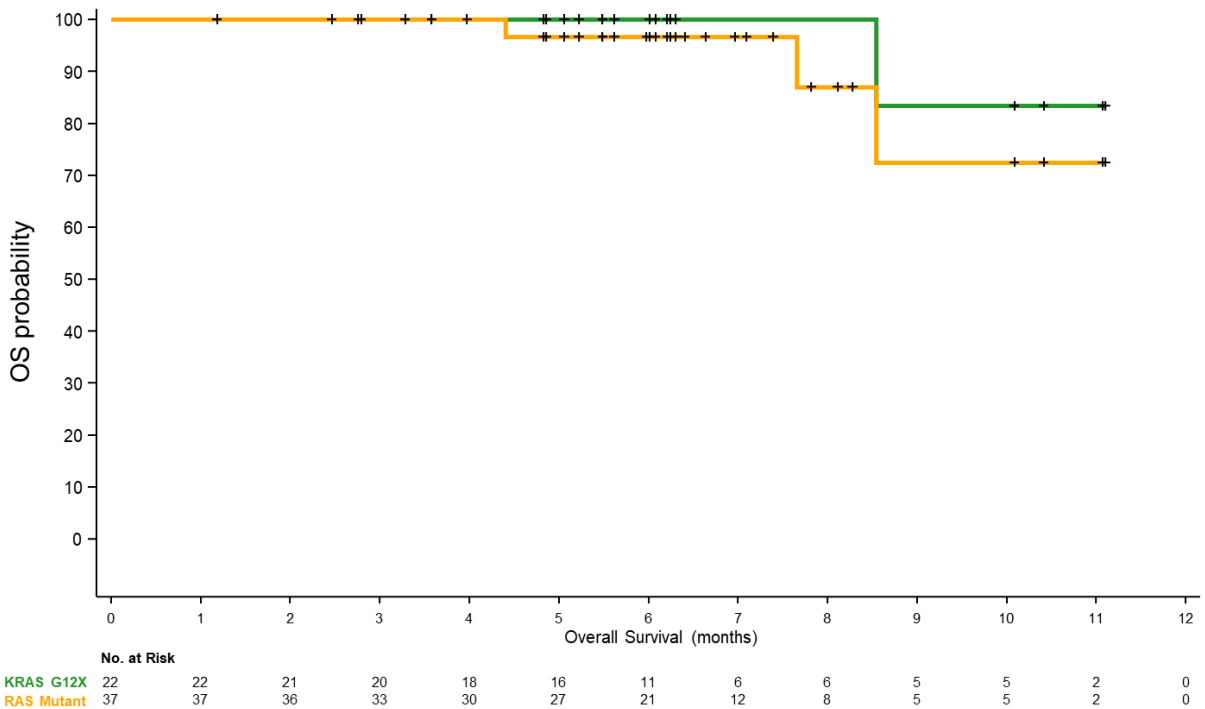
- Combination strategies in colorectal cancer
- Ongoing evaluation of antitumor activity in additional solid tumors

(1) Incidence from ACS Cancer Facts and Figures 2024, includes all stages of disease.
(2) RMC-6236-001: 2L patients with KRAS G12X PDAC treated with RMC-6236 300 mg daily (data cutoff: 7/23/2024).
(3) RMC-6236-001: 2L/3L patients with RAS G12X NSCLC treated with RMC-6236 at 120-220 mg daily. (data cutoff: 9/30/2024).
PDAC, pancreatic ductal adenocarcinoma; POC, proof-of-concept; 2L, second line; PFS, progression-free survival; OS, overall survival; 3L, third line; 1L, first line, NSCLC, non-small cell lung cancer.

Encouraging Durability in 2L Patients with PDAC Treated with Daraxonrasib at 300 mg Daily

	Median PFS, months (95% CI)	Median OS, Months (95% CI)	OS Rate at 6 months, % (95% CI)
KRAS G12X	**8.8** (8.5, NE)	**NE** (NE, NE)	**100** (100, 100)
RAS Mutant[(1)]	**8.5** (5.9, NE)	**NE** (8.5, NE)	**97** (79, 100)





(1) RAS Mutant defined as patients with G12X, G13X or Q61X PDAC.
2L in the metastatic setting includes patients who progressed on prior therapy in an earlier setting within 6 months of last dose.
Median follow-up is 6.1m and 6.6m for KRAS G12 and RAS mutant in the 2L setting at 300mg, respectively.
2L, second line; PDAC, pancreatic ductal adenocarcinoma; PFS, progression-free survival; OS, overall survival, CI, confidence interval; NE, not estimable.

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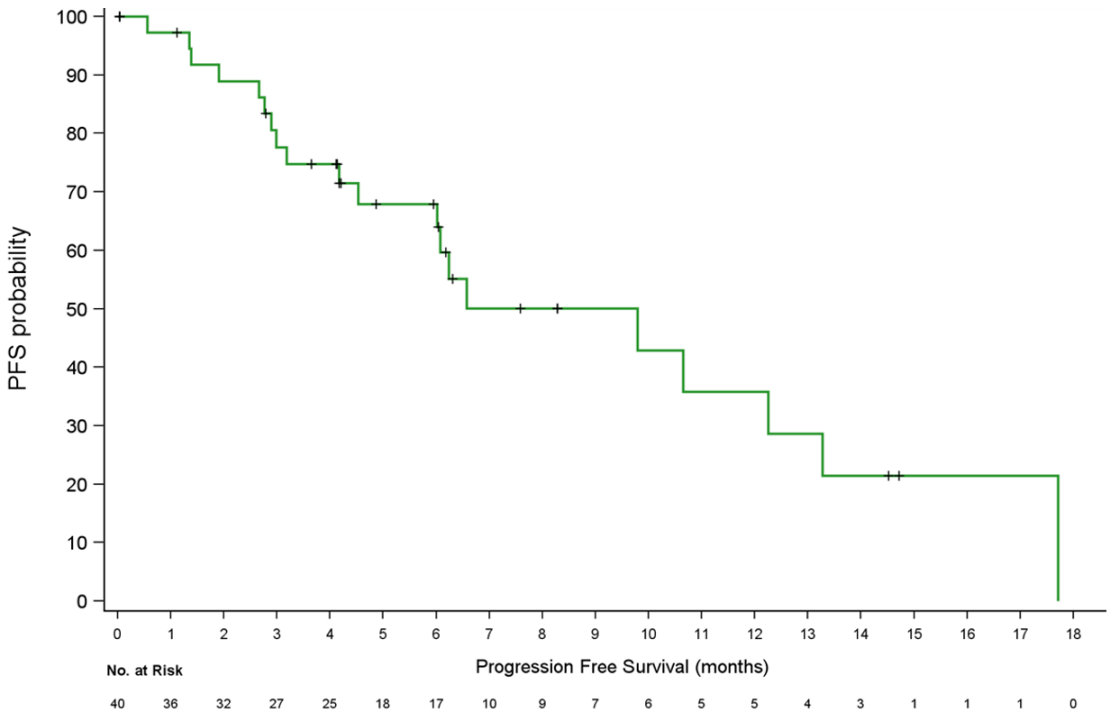
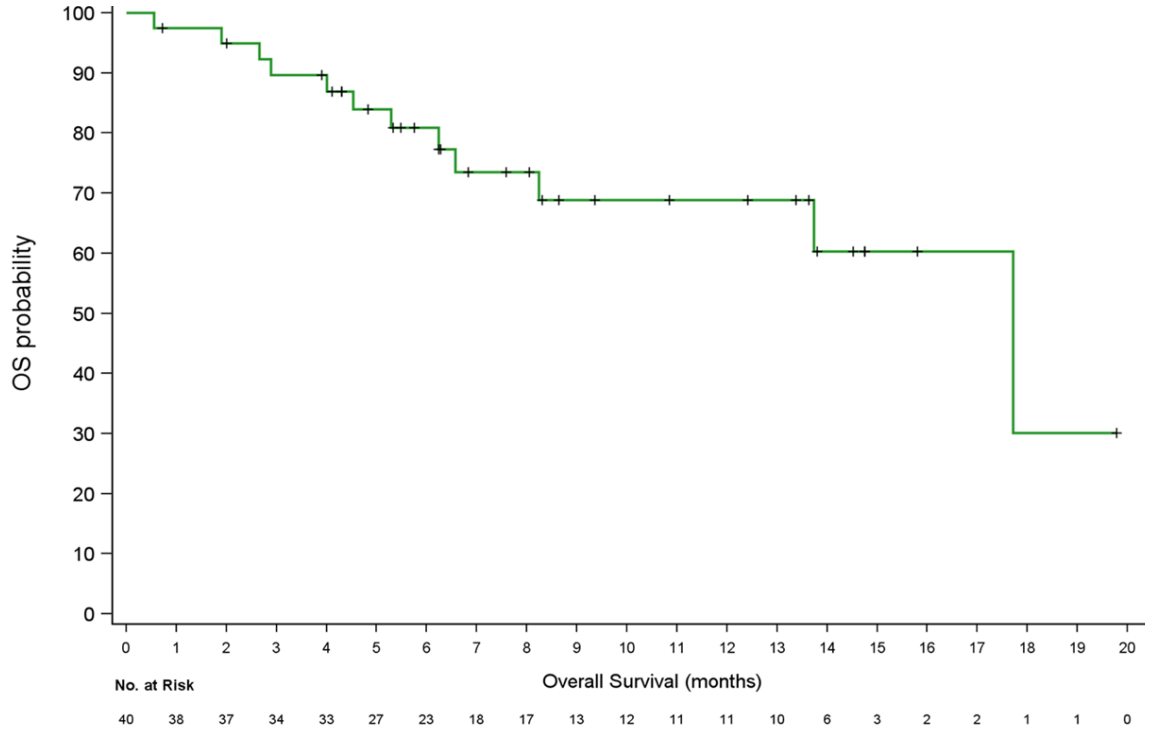
ENA 2024 data set
(Data cutoff: Jul 23, 2024)

Encouraging Durability in 2L/3L Patients with RAS G12X NSCLC Treated with Daraxonrasib at 120-220 mg Daily

Median PFS, months (95% CI)	Median OS, Months (95% CI)
9.8 (6, 12.3)	**17.7** (13.7, NE)





Population includes patients with RAS G12X mutant NSCLC who have received 1 or 2 prior lines of therapy which must include prior immunotherapy and platinum chemotherapy administered either concurrently or sequentially, and have not received docetaxel previously. Adjuvant therapy or multimodal therapy with curative intent is considered prior therapy if disease progression occurred or treatment completion was within 6 months of first dose of RMC-6236. Median follow-up is 10.8 months.

2L, second line; 3L, third line; NSCLC, non-small cell lung cancer; PFS, progression-free survival; OS, overall survival, CI, confidence interval; NE, not estimable.

Data cutoff: Sept 30, 2024.

Elironrasib (RMC-6291): RAS(ON) G12C-Selective Inhibitor

Active against

Primary RAS G12C mutation

Tumors in patients naïve to, or previously treated with, first generation RAS(OFF) inhibitors

NSCLC (~60,000 new RAS U.S. patients per year, ~12% G12C mutations)(1)

- Highly active in patients both naïve to and previously treated with G12C(OFF) inhibitors(2)
- Initial tolerability observed in combination with pembrolizumab(3)

CRC (~75,000 new RAS U.S. patients per year, ~4% G12C mutations)(4)

- Initial validation of RAS(ON) inhibitor doublet, with daraxonrasib, in patients previously treated with G12C(OFF) inhibitors(5)

Exploring Combination Strategies

- Early data with pairwise combinations provides support for triplet combination (elironrasib + daraxonrasib + pembrolizumab) in 1L NSCLC(3)
- Combination studies ongoing with SOC

(1) Incidence from ACS Cancer Facts and Figures 2024, includes all stages of disease.
(2) P. Janne et al, Preliminary Safety and Anti-Tumor Activity of RMC-6291, a First-in-Class, Tri-Complex KRASG12C(ON) Inhibitor in Patients With or Without Prior KRASG12C(OFF) Inhibitor Treatment, ENA 2023.
(3) RMC-LUNG-101 (data cutoff: 10/28/2024).
(4) Incidence from ACS Cancer Facts and Figures 2023; includes all stages of disease.
(5) RMC-6291-101 (data cutoff: 10/28/2024).
NSCLC, non-small cell lung cancer; CRC, colorectal cancer; 1L, first line; SOC, standard of care.

Elironrasib + Daraxonrasib Case Report: Patient with KRAS G12C CRC

Baseline Characteristics

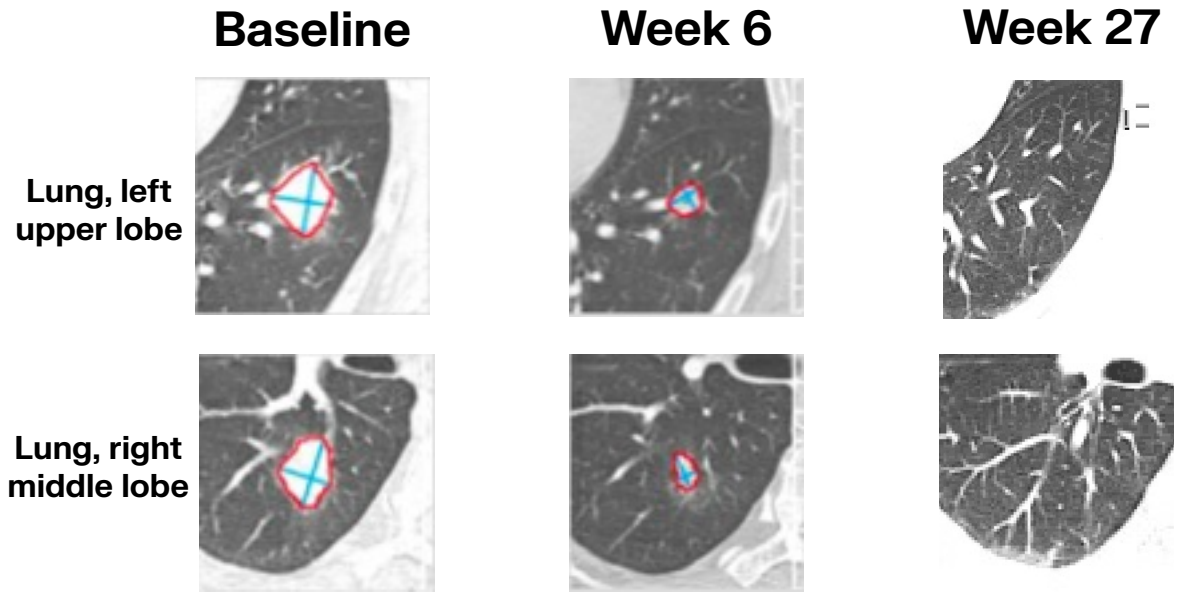
- 55 year-old male initially diagnosed with colorectal adenocarcinoma in 2019
- ECOG 1
- KRAS G12C, KRAS Y96N and RTK rearrangements (ALK and MET fusions) detected in baseline ctDNA

Treatment History

- Laparoscopic low anterior resection in 2019 (Stage I)
- Metastatic recurrence and left hepatectomy in 2021
- FOLFIRINOX + bevacizumab
- Adagrasib + cetuximab
- Investigational agent + pembrolizumab

RAS(ON) Doublet Treatment Course

- Started treatment with RMC-6291 100 mg BID + daraxonrasib 200 mg QD on Mar 11, 2024 in Dose Exploration Phase
- C3D1: Partial Response
- C5D1: Confirmed Partial Response with complete resolution of all non-target lesions
- C10D1: Complete Response
- Continued on treatment with no Grade 3 or higher TRAEs



Target Lesion	Baseline (mm)	Week 6 (mm)	Week 27 (mm)
Lung, left upper lobe	28.8	14.1	0
Lung, right middle lobe	25	13.4	0
Sum of Diameters	53.8	27.5 (-49%)	**0 (-100%)**
Overall Response	-	**PR**	**CR**

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CRC, colorectal cancer; ECOG, Eastern Cooperative Oncology Group; BID, twice daily; QD, once daily; TRAE, treatment-related adverse event, PR, partial response, CR, complete response.

Data cutoff: Oct 28, 2024.

Zoldonrasib (RMC-9805): RAS(ON) G12D-Selective Inhibitor

Active against

Primary RAS G12D mutation – the single most common RAS driver in solid tumors

PDAC (~55,000 new RAS U.S. patients per year, ~40% with G12D mutations)(1)

- Promising initial monotherapy clinical profile in PDAC (30% ORR)(2); follow-up ongoing for durability assessment
- Highly encouraging initial tolerability

Executing Monotherapy Opportunities

- 1200 mg QD identified as a recommended Phase 2 dose in PDAC
- Monotherapy studies ongoing across multiple tumors

Exploring Combination Strategies

- Compelling profile also supports development in combination with chemotherapies and targeted agents, including RAS(ON) inhibitor doublet with daraxonrasib

(1) Incidence from ACS Cancer Facts and Figures 2024, includes all stages of disease.
(2) David S. Hong et al., Preliminary Safety, Pharmacokinetics, and Antitumor Activity of RMC-9805, an Oral, RAS(ON) G12D-Selective, Tri-Complex Inhibitor in Patients with KRAS G12D Pancreatic Ductal Adenocarcinoma (PDAC) from a Phase 1 Study in Advanced Solid Tumors, ENA 2024.
PDAC, pancreatic ductal adenocarcinoma; ORR, objective response rate; QD, once daily.

Zoldonrasib Case Report: Patient with KRAS G12D NSCLC

Demographics and Baseline Characteristics

- 36-year-old Asian woman
- Diagnosed with KRAS G12D NSCLC in Sept 2022
- Metastatic progression after 2023

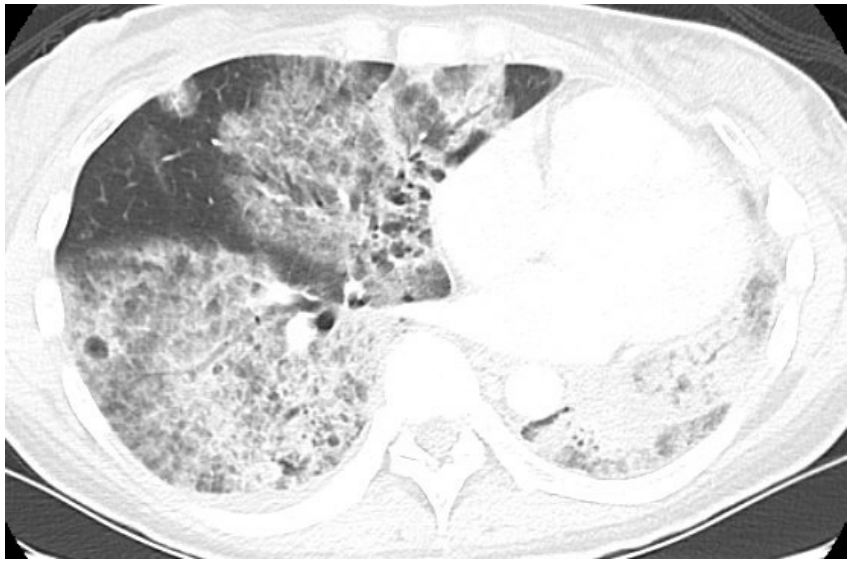
Treatment History

- Carboplatin, pemetrexed, nivolumab (neoadjuvant)
- VATS lobectomy LLL, LUL wedge resection MLND in 2022
- Atezolizumab (adjuvant)
- Left lung radiotherapy (neoadjuvant)
- Carboplatin, paclitaxel, atezolizumab, bevacizumab (1L)

RMC-9805 Treatment Course

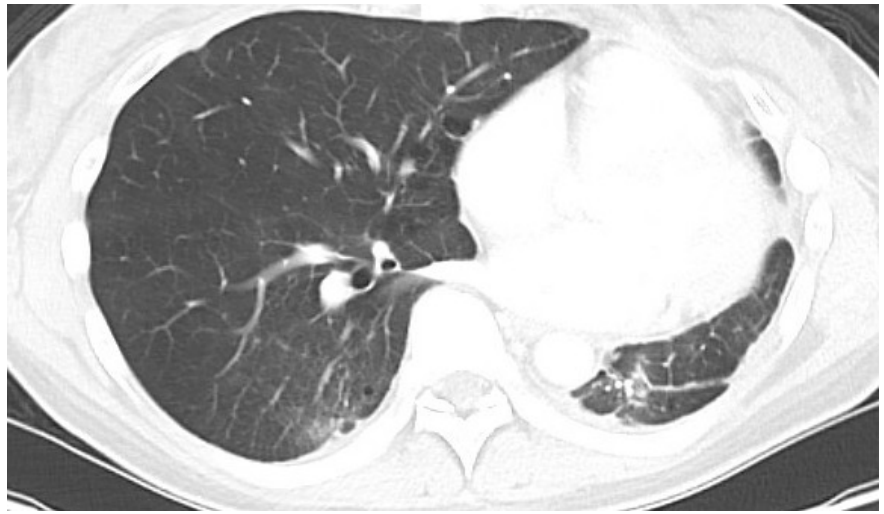
- C1D1: Received RMC-9805 at 1200 mg QD
- C3D1: Partial Response per RECIST 1.1 (-70%)
- C5D1: Confirmed Partial Response (-84%)
- C7D1: Confirmed Partial Response (-84%)
- C9D1: Confirmed Partial Response (-84%)
- Treatment-emergent G3 increase in CPK, dose held and resumed at 900 mg QD suspected due to vigorous exercise
- Within 1 week of C1D1, came off oxygen with resolved cough
- Exercising daily in the gym

Baseline CT



Resolution of extensive lung and lymphangitic carcinomatosis

C3D1 CT



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NSCLC, non-small cell lung cancer; VATS, video-assisted thoracic surgery; LLL, left lower lobe; LU, left upper lobe; MLND, mediastinal lymph node dissection; CPK, creatine phosphokinase; QD, once daily, RECIST, Response Evaluation Criteria in Solid Tumors.

Data as of 1/6/2025 EDC

Highly Active RAS(ON) Inhibitors Drive Combination Opportunities to Support Development in Earlier Lines of Therapy

RAS(ON) inhibitor doublets
Daraxonrasib (RMC-6236) + mutant-selective inhibitors

- Initial POC with elironrasib (RMC-6291) in CRC
- Evaluation underway with zoldonrasib (RMC-9805)
- RMC-5127 (G12V) offers third planned doublet partner

Immunotherapy
Daraxonrasib or mutant-selective inhibitor + checkpoint inhibitor

- Initial combinability demonstrated for daraxonrasib or elironrasib + pembrolizumab in previously treated patients
- Evaluation underway in 1L NSCLC
- Safety assessment underway for zoldonrasib + pembrolizumab

Targeted agents
Daraxonrasib or mutant-selective inhibitor + targeted agents

- Collaboration to evaluate RAS(ON) inhibitors + PRMT5 inhibitor, TNG462
- Collaboration to evaluate RAS(ON) inhibitors + cetuximab

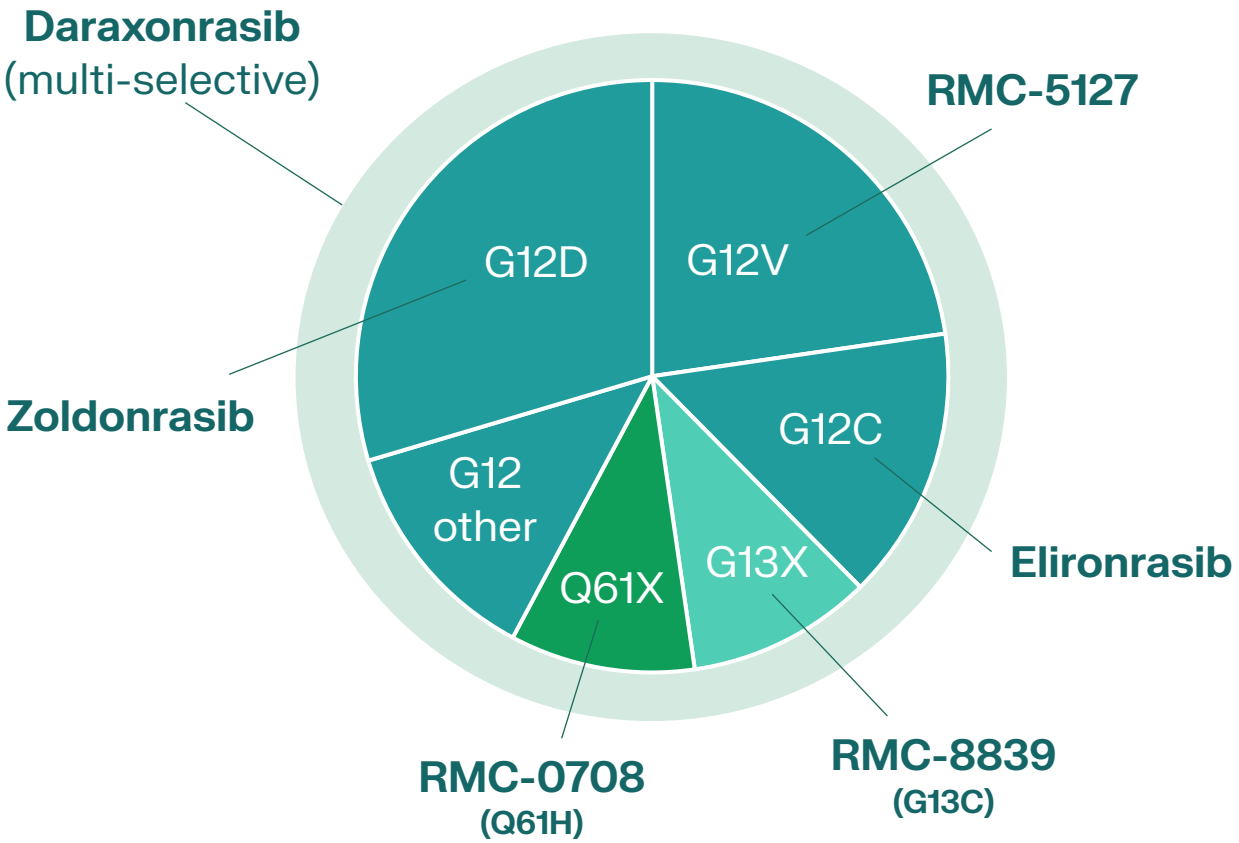
Chemotherapy
Daraxonrasib or mutant-selective inhibitor + SOC

- Safety evaluation underway for daraxonrasib or zoldonrasib with 1L chemotherapies

POC, proof-of-concept; CRC, colorectal cancer; NSCLC, non-small cell lung cancer; SOC, standard of care; 1L, first line.

Track Record of Innovation Against RAS Cancers Signals Great Promise of Pipeline and Organization

Frequency of RAS Variants Among RAS Mutant Solid Tumors



Pipeline and Organizational Progress

- Pioneered RAS(ON) inhibitor class
- Compelling daraxonrasib POC in PDAC and NSCLC
- Compelling zoldonrasib activity and safety in PDAC
- Mechanistic POC for first RAS(ON) inhibitor doublet
- Combinability of daraxonrasib or elironrasib with pembrolizumab
- Manufacturing daraxonrasib at commercial scale
- Forged broad range of select partnerships
- Exceptionally strong balance sheet

Q61H represents ~40% of Q61X. G13C represents ~14% of G13X.
POC, proof-of-concept; PDAC, pancreatic ductal adenocarcinoma; NSCLC, non-small cell lung cancer.

Entering 2025 with Momentum and Conviction to Embrace Responsibility

Robust pipeline, capabilities and financial capital fuel vision to create industry-leading targeted medicines franchise for patients with RAS-addicted cancers

2025 priorities include:

- Executing daraxonrasib pivotal trials in previously treated PDAC and NSCLC
- Advancing daraxonrasib into pivotal trial in 1L PDAC
- Committing to first pivotal trial(s) with mutant-selective inhibitor(s)
- Data-driven prioritization of combination strategies for early lines of therapy
- Advancing fourth RAS(ON) inhibitor development candidate to clinic readiness
- Growing commercial and operational capabilities in support of U.S. launch
- Progressing next-generation programs

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

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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 (unless otherwise noted).
  - 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