REVOLUTION MEDICINES

February 27, 2023

On Target to Outsmart Cancer™

Legal Disclaimer

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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' Annual Report on Form 10-K filed with the Securities and Exchange Commission on February 27, 2023, 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.

On Target to Outsmart Cancer

HIGH UNMET NEED IN RAS-ADDICTED CANCERS

30% of human cancers[1], largely unserved by targeted therapeutics

STRONG CLINICAL VALIDATION OF RAS^{MUTANT} AS CANCER DRIVER

Proof-of-principle from first-gen $KRAS^{G12C}$ inhibitors[2]

DEEP, SCIENCE-DRIVEN CLINICAL AND PRECLINICAL PIPELINE

RAS(ON) Inhibitors
Groundbreaking class of drug candidates for robust cancer suppression

RAS Companion Inhibitors
Class-leading drug candidates to counter treatment resistance

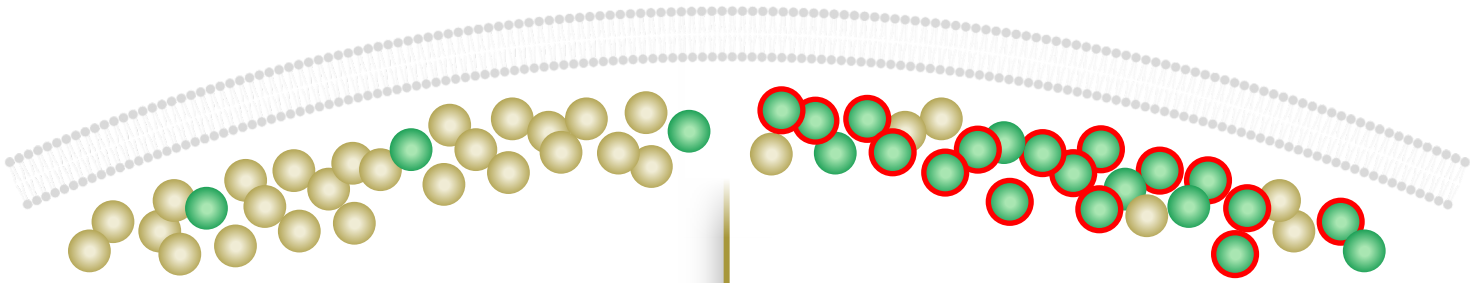
(1) Prior et al., *Cancer Research* 2020
(2) Lumakras approved by the FDA in May 2021, Krazati approved by the FDA in December 2022

Excessive RAS(ON) Signaling Drives 30% of Human Cancers, Targeted by Our Pipeline Strategy

RAS(OFF)

RAS(ON)

Normal



Tightly regulated
RAS(ON) proteins control cell growth

RAS-Addicted Cancers

RAS Cancer Mutations

Excessive
RAS(ON) signaling drives uncontrolled cell growth

Exemplary mutations in KRAS, HRAS and/or NRAS

G12C, G12D, G12V, G12R
G13C, G13D
Q61H, Q61K, Q61L

New patients per year (U.S.)[1]

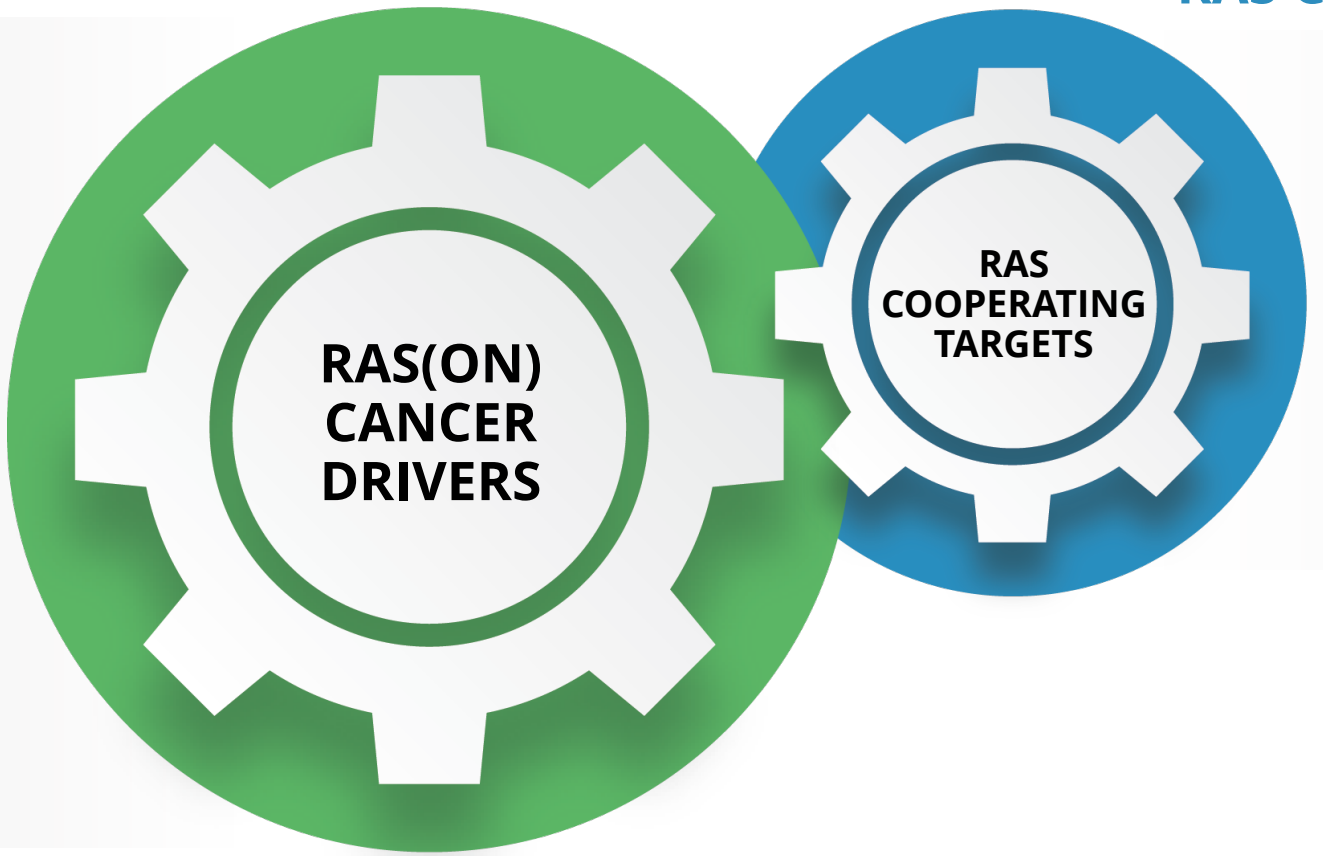
230,000	**All**
67,000	Lung cancer
79,000	Colorectal cancer
49,000	Pancreatic cancer

(1) Estimated using tumor mutation frequencies from Foundation Medicine Insights August 2020 and scaled to estimated patient numbers using cancer incidence from ACS *Cancer Facts and Figures* 2020 (see appendix for additional detail); lung cancer = non-small cell lung cancer

Deep, Science-Driven Clinical and Preclinical Pipeline of Targeted Therapies for RAS-Addicted Cancers

RAS(ON) Inhibitors

- 2 Clinical-stage Drug Candidates
- 3 Development-stage Drug Candidates
- \+ Multiple pipeline expansion programs

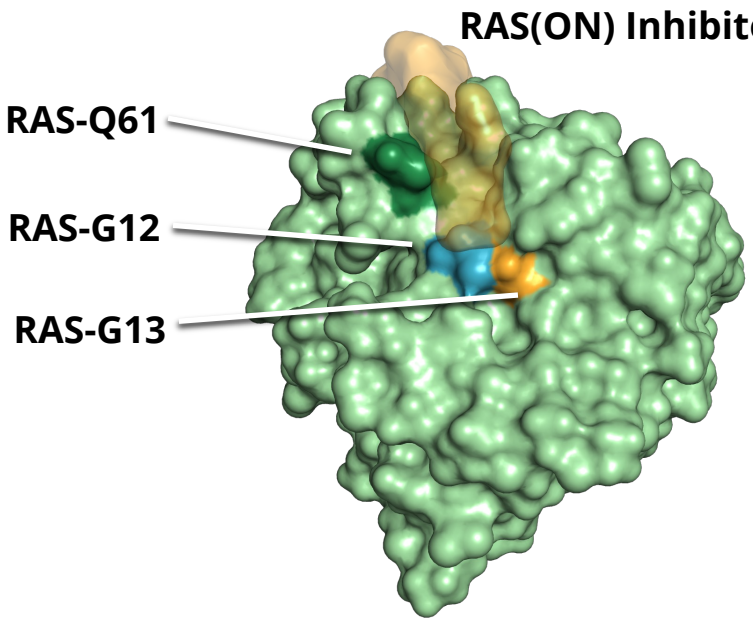


RAS Companion Inhibitors

- 2 Clinical-stage Drug Candidates
- 1 IND-ready Drug Candidate

Groundbreaking RAS(ON) Inhibitors Bind Near RAS Cancer Mutation Hotspots and Suppress Cancer Signaling

Bind



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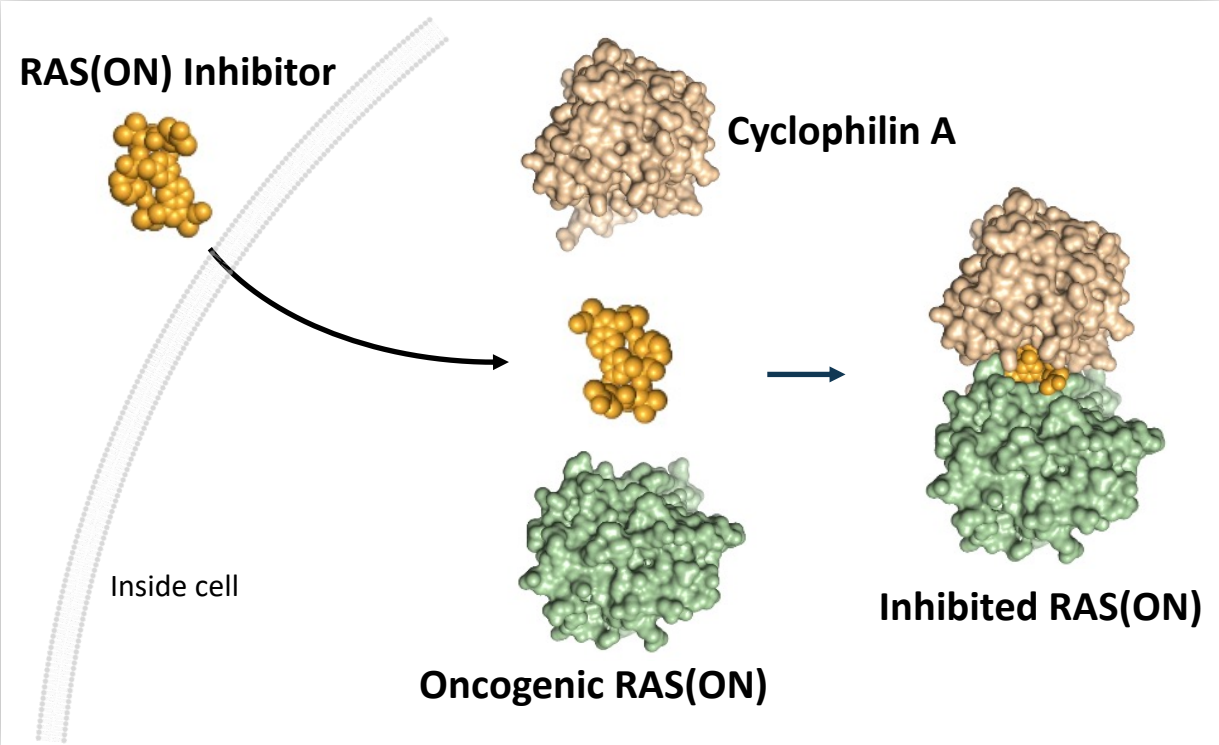


- **Potent, selective, oral and drug-like inhibitors**
- **Deep and sustained suppression of RAS(ON) cancer signaling**

Current Portfolio of RAS(ON) Inhibitors Targets Every RAS Cancer Mutation Hotspot[1]

Relative Frequency in Human RAS Cancers[2]

RMC-6236 MULTI/G12X

RMC-6291 G12C

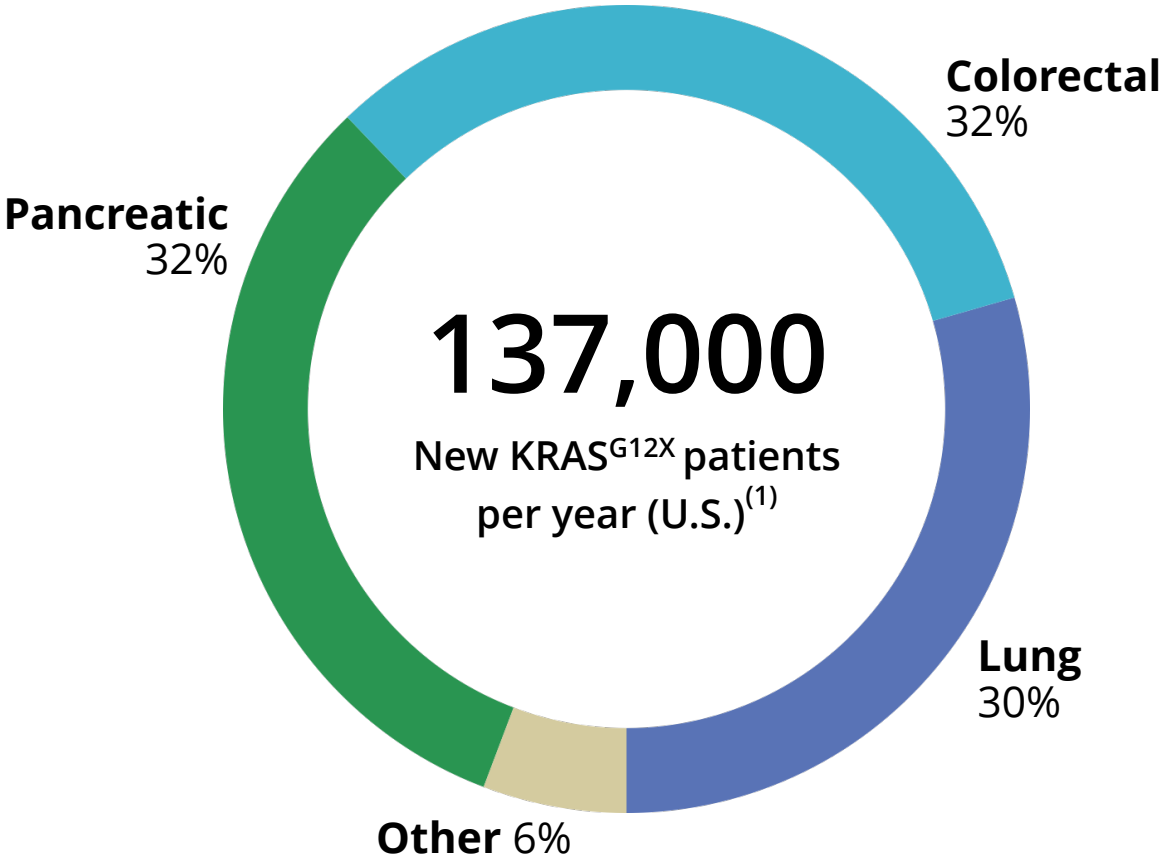
RMC-9805 G12D

RMC-0708 Q61H

RMC-8839 G13C

(1) RAS cancer mutation hotspots defined as G12, G13 and Q61
(2) Calculated using tumor mutation frequencies from Foundation Medicine Insights August 2020 and scaled to estimated patient numbers using cancer incidence from ACS *Cancer Facts and Figures* 2020 (see appendix for additional detail)

RMC-6236: First-in-Class RAS^{MULTI}(ON) Inhibitor with Broad Potential Against RAS-Addicted Cancers



KRAS^{G12X} includes KRAS^{G12D}, KRAS^{G12V}, KRAS^{G12R} and KRAS^{G12C}

Highly Potent and Selective RAS(ON) Inhibitor

- Suppresses diverse mutant RAS cancer drivers and cooperating wild-type RAS proteins

Robust Anti-tumor Activity in Cancer Models

- Deep and sustained inhibition drives durable anti-tumor activity in tumors with common RAS variants

Attractive PK/ADME Profile

- Favorable *in vivo* oral bioavailability, clearance and concentration in tumors for effective target coverage in RAS-addicted cancer cells

(1) Calculated using tumor mutation frequencies from Foundation Medicine Insights August 2020 and scaled to estimated patient numbers using cancer incidence from ACS *Cancer Facts and Figures* 2020 (see appendix for additional detail); lung cancer = non-small cell lung cancer

Characterization above is based on RVMD preclinical research

RMC-6236: Highly Active with Durable Benefit Across *in Vivo* Models of Major Human Cancers with KRAS^{G12X} Drivers

NSCLC

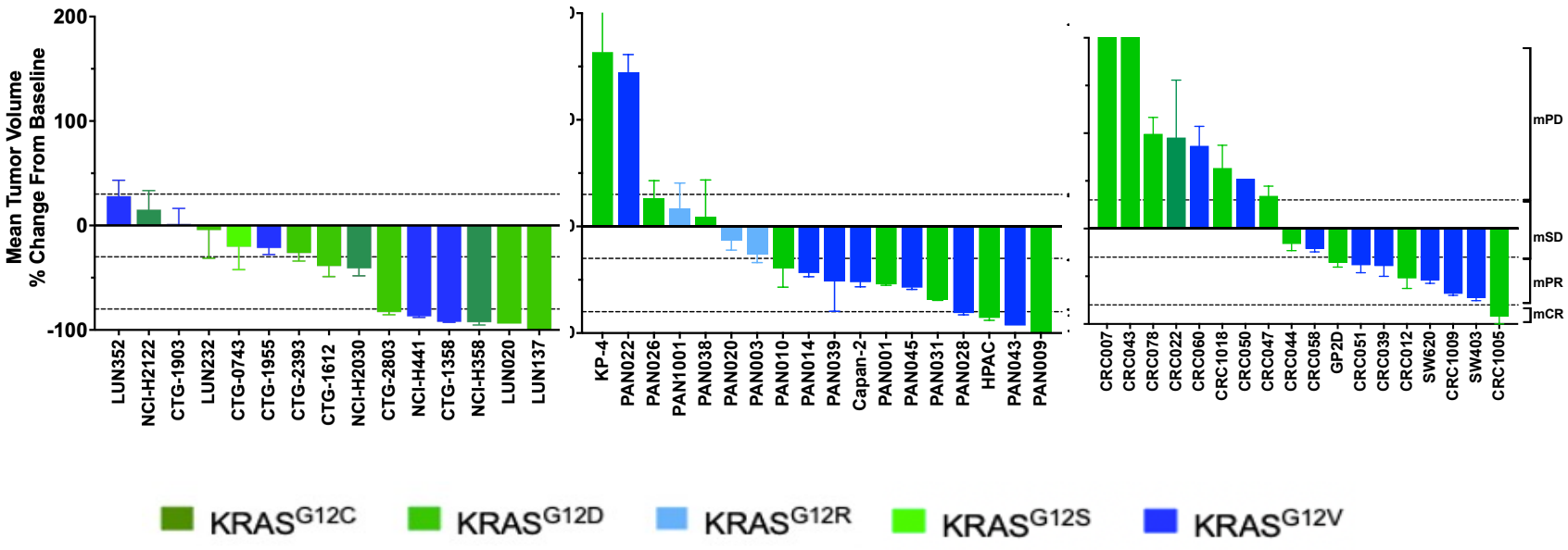
53% ORR (8/15)
100% DCR (15/15)

PDAC

61% ORR (11/18)
89% DCR (16/18)

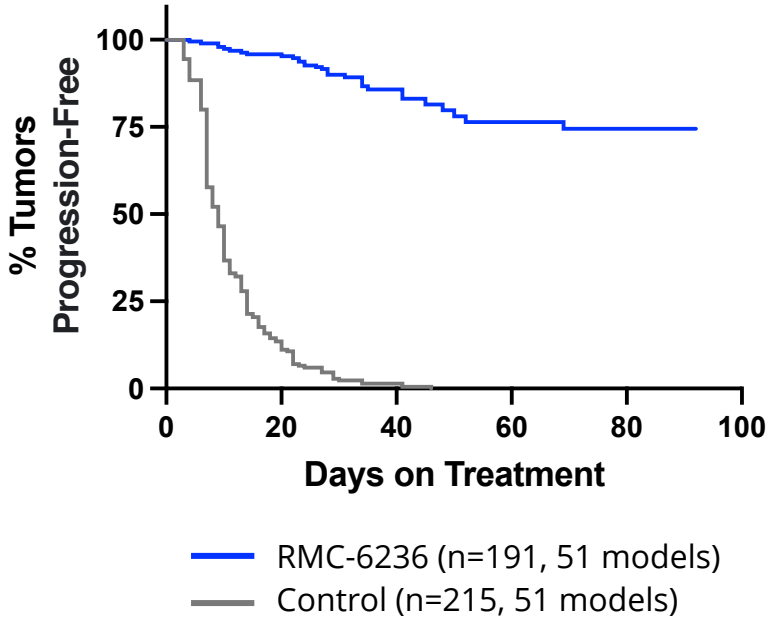
CRC

44% ORR (8/18)
56% DCR (10/18)



PFS

RMC-6236 – Median not reached
Control – Median 9 days



RVMD preclinical research as of 06/01/22
RMC-6236 dosed at 25 mg/kg po qd; n=1-10/group
Progression defined as tumor doubling from baseline
NSCLC = non-small cell lung cancer; PDAC = pancreatic ductal adenocarcinoma; CRC = colorectal cancer
Responses assigned according to mRECIST (see appendix)
ORR = objective response rate; DCR = disease control rate; PFS = progression-free survival

RMC-6236 Phase 1/1b Trial: Clinical Translation of Preclinical Single Agent Profile and Initial Platform Validation

	Preclinical Profile	Aims of Phase 1/1b Clinical Trial[2]
Dosing and Safety	✓ **Oral dosing** (daily and intermittent): drug levels that drive sustained RAS pathway suppression ✓ **Safety**: well-tolerated in active range, dose-limiting toxicities "on target" and reversible ✓ **Long-term treatment**[1] at active doses	○ **Oral dosing**: once daily to reach active exposures + option for intermittent schedule; surrogate markers of activity (ctDNA) ○ **Safety**: short- and long-term safety and tolerability at active exposures ○ **RP2DS**
Anti-Tumor Activity	✓ **Tumor selection**: active in diverse RAS^{MUTANT} NSCLC, pancreatic and CRC models; $KRAS^{G12X}$ most sensitive ✓ **Activity**: deep regressions across $KRAS^{G12X}$ tumors, especially NSCLC and pancreatic models	○ **Patient selection**: signal-seeking across diverse $KRAS^{G12X}$ tumors ○ **Efficacy**: initial clinical responses by RECIST; formal proof-of-concept via expansion cohorts bearing select genotypes/histologies with inadequate SOC

(1) Long-term in mouse models defined as up to 90 days of treatment
(2) Ongoing study, RMC-6236-001 - ClinicalTrials.gov Identifier: NCT05379985 https://clinicaltrials.gov/ct2/show/NCT05379985?term=RMC-6236&draw=2&rank=1
$KRAS^{G12X}$ includes $KRAS^{G12A}$, $KRAS^{G12D}$, $KRAS^{G12R}$, $KRAS^{G12S}$, $KRAS^{G12V}$
MTD = maximum tolerated dose; RP2D = recommended Phase 2 dose and schedule; ctDNA = circulating tumor DNA

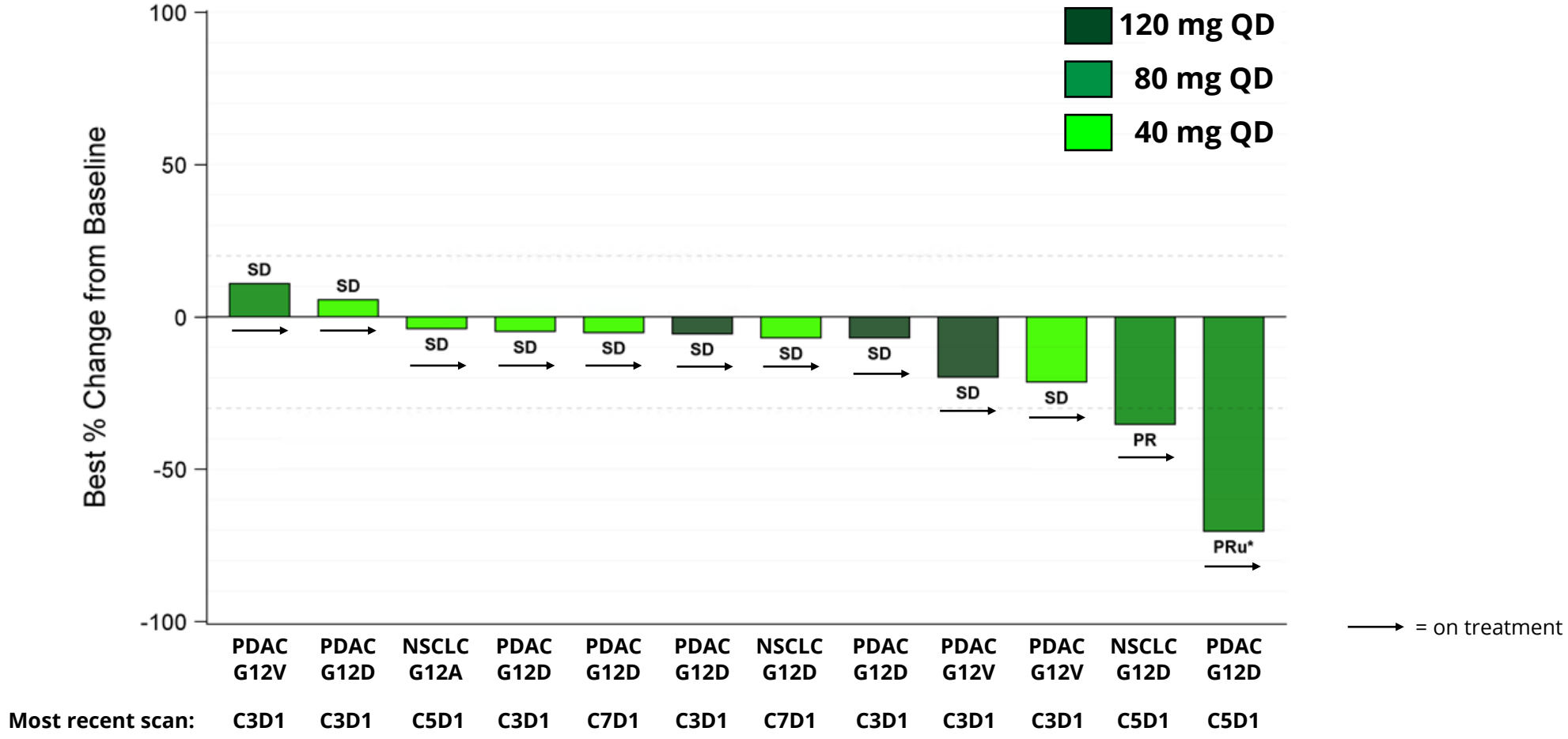
RMC-6236-001: Treatment-Related AEs Occurring in ≥ 10% of All Patients

	10 mg QD (N=3)		20 mg QD (N=13)		40 mg QD (N=9)		80 mg QD (N=7)		120 mg QD (N=4)		Overall (N=36)	
Preferred Term	**Any Grade**	**Grade ≥3**	**Any Grade**	**Grade ≥3**	**Any Grade**	**Grade ≥3**	**Any Grade**	**Grade ≥3**	**Any Grade**	**Grade ≥3**	**Any Grade**	**Grade ≥3**
Rash (CMQ)*	0	0	2 (15.4%)	0	4 (44.4%)	0	6 (85.7%)	0	4 (100%)	0	16 (44.4%)	0
Nausea	1 (33.3%)	0	2 (15.4%)	0	6 (66.7%)	0	2 (28.6%)	0	1 (25.0%)	0	12 (33.3%)	0
Diarrhoea	0	0	1 (7.7%)	0	2 (22.2%)	0	1 (14.3%)	0	2 (50.0%)	0	6 (16.7%)	0
Fatigue	0	0	0	0	2 (22.2%)	0	0	0	2 (50.0%)	0	4 (11.1%)	0
Vomiting	0	0	1 (7.7%)	0	2 (22.2%)	0	0	0	1 (25.0%)	0	4 (11.1%)	0

One related grade 4 adverse event of bowel perforation (also considered a serious adverse event) was reported in a patient receiving 80 mg daily.
The likely cause of the perforation was considered to be shrinkage of metastatic $KRAS^{G12V}$ pancreatic cancer at the site of full-thickness bowel infiltration.

EDC data as of 02/17/2023
CMQ = Customized MedDRA Query
*Consists of dermatitis acneiform, dermatitis psoriasiform, palmar-plantar erythrodysesthesia syndrome, rash maculo-papular, and rash pustular.

RMC-6236-001: Change in Tumor Burden from Patients with KRAS^{G12X} NSCLC or Pancreatic Cancer Treated at ≥ 40 mg Daily



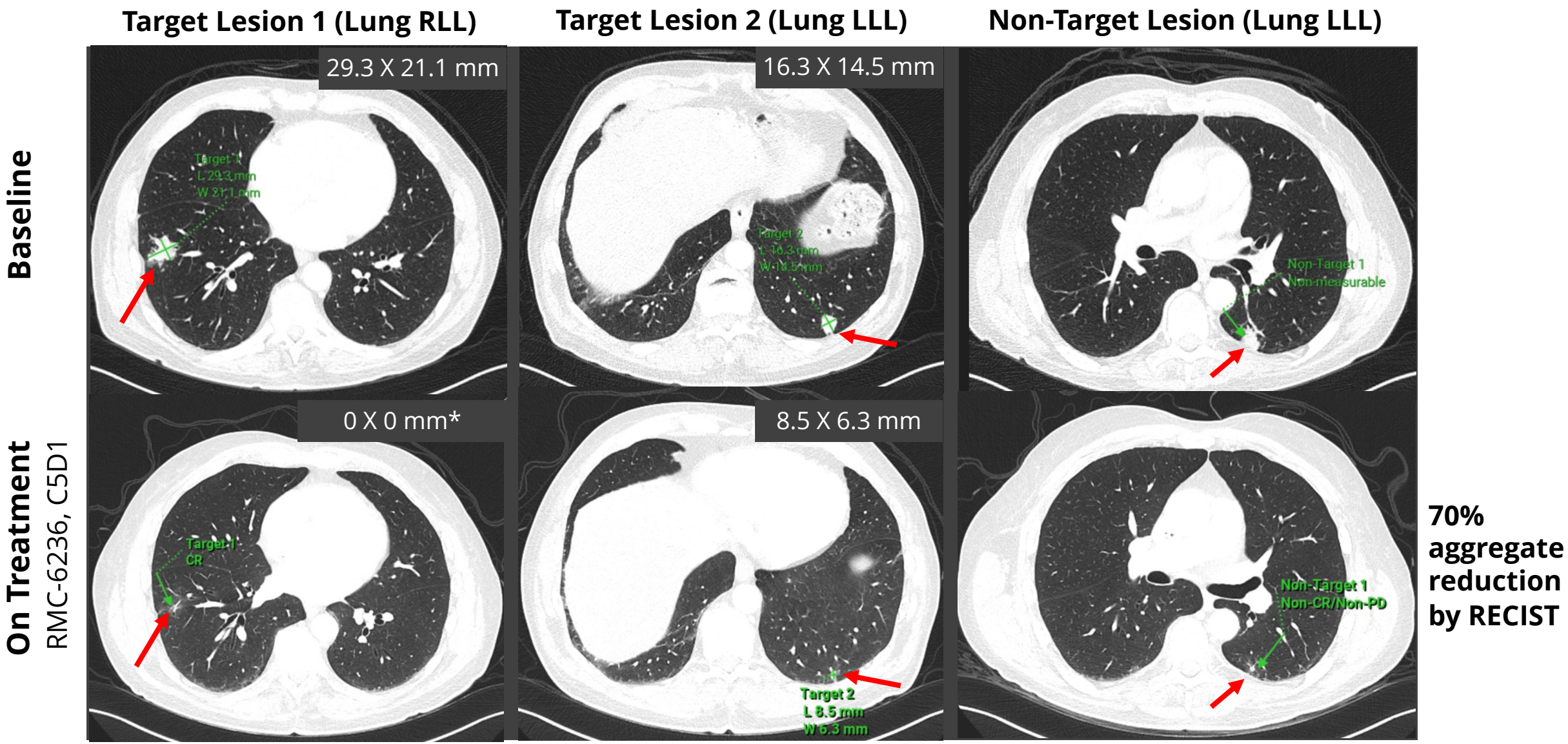
EDC data as of 02/17/2023; efficacy evaluable patients defined as those in this data set with at least one post baseline response assessment or who have died or have experienced clinical progression prior to the first post baseline scan (n=12). Cycle time is 21 days. SD = stable disease, PR = partial response. NSCLC = non-small cell lung cancer; PDAC = pancreatic ductal adenocarcinoma.
*PR unconfirmed as of 02/17/2023.

RMC-6236-001 Case Report: $KRAS^{G12D}$ Pancreatic Cancer Patient

- 76 year-old male
- $KRAS^{G12D}$ pancreatic cancer diagnosed November 2017
- Treated with neoadjuvant chemotherapy, surgery, adjuvant chemotherapy 2018
- Progressed with metastatic disease January 2022; treated with gemcitabine + nab-paclitaxel + investigational therapy with SD as best response

- November 2022 lung metastases
- $KRAS^{G12D}$ with co-occurring loss of P53, CDKN2A, CDKN2B and MTAP
- Treated with RMC-6236 80 mg daily

RMC-6236-001 Case Report: CT Scans for KRAS^{G12D} Pancreatic Cancer Patient

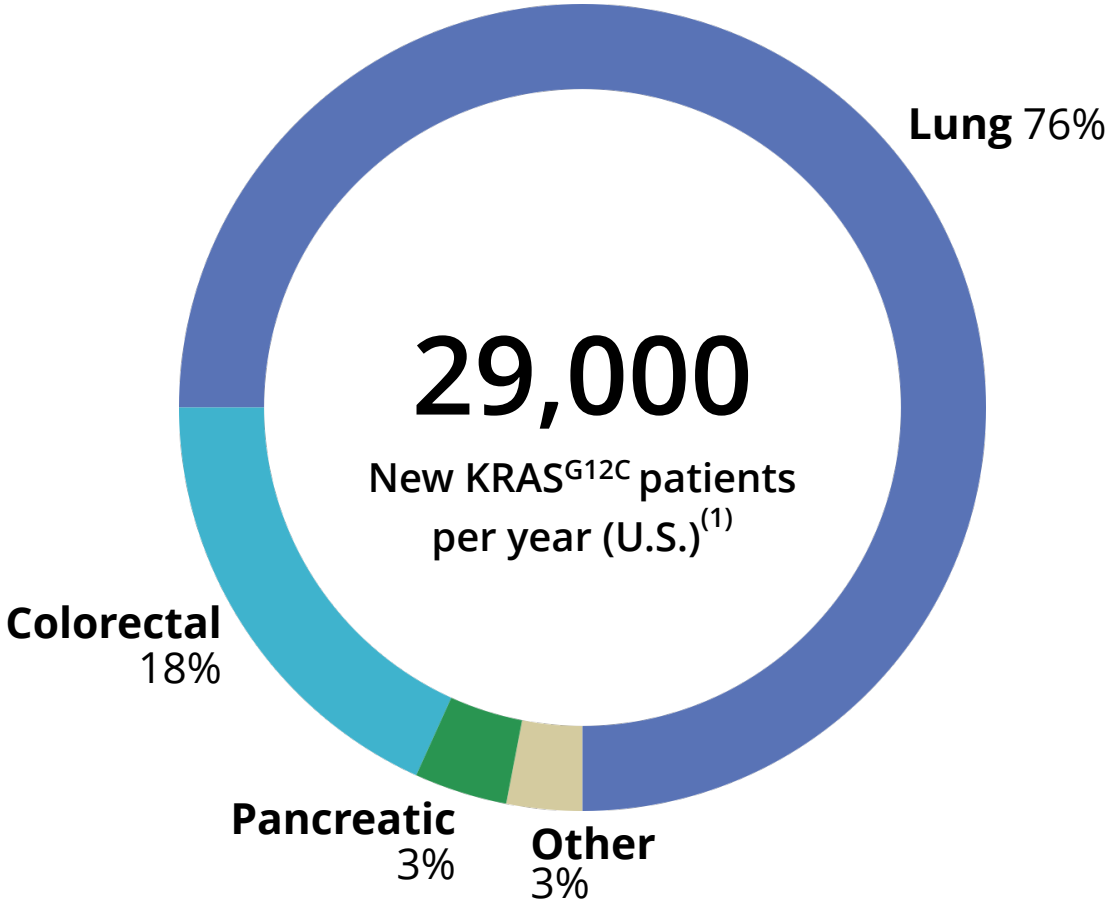


70% aggregate reduction by RECIST

*Per EDC, target lesion #1 on C5D1 was too small to measure; 5 mm used to calculate % reduction in sum of longest diameters of target lesions by RECIST. RLL=right lower lobe; LLL=left lower lobe.

Images courtesy of RMX-6236-001 study site with additional annotation by RVMD (red arrows and target lesion measurements at top right of each scan)

RMC-6291: Mutant-Selective RAS(ON) Inhibitor with Best-in-Class Potential for KRAS^{G12C} Cancers



Highly Potent and Selective RAS(ON) Inhibitor

- Highly active against KRAS^{G12C}
- Covalent for irreversible inhibition
- Low off-target risk and acceptable safety profile

Robust Anti-tumor Activity in Cancer Models

- Rapid, deep and sustained inhibition drives durable anti-tumor effects across multiple KRAS^{G12C} tumor types, with complete responses in some models

Attractive PK/ADME Profile

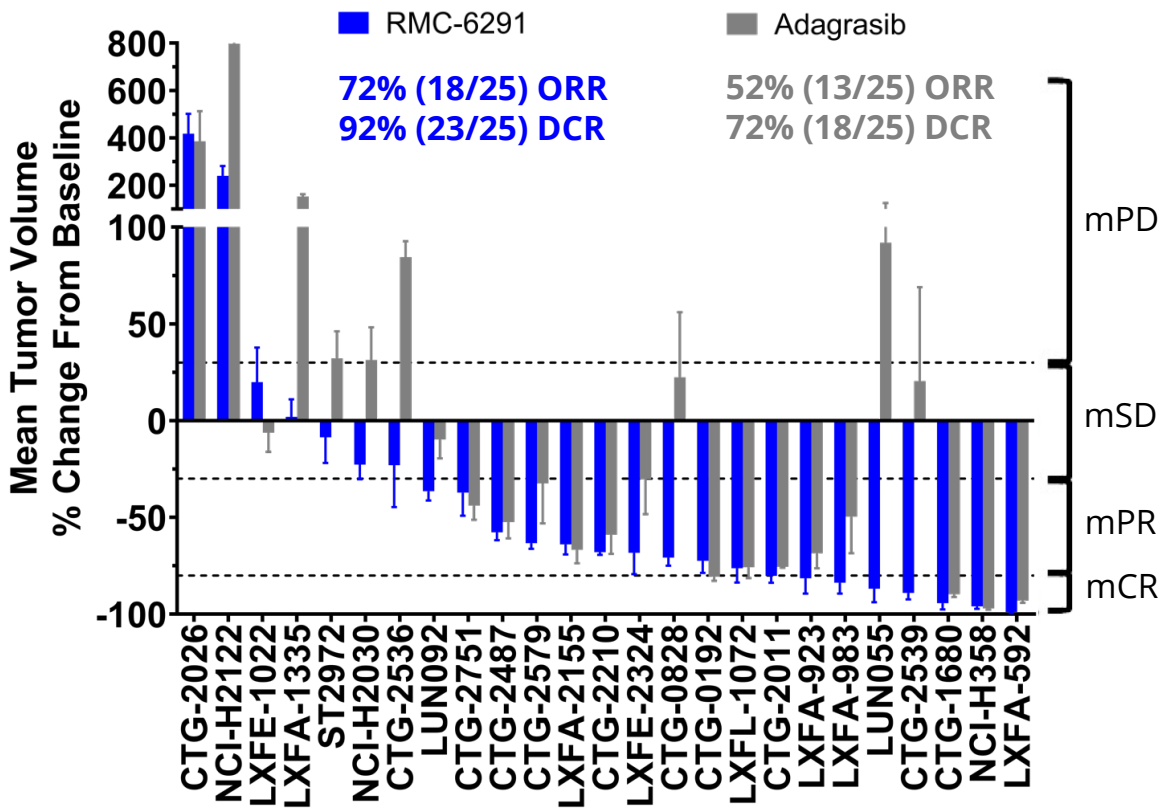
- Favorable *in vivo* oral bioavailability and clearance for effective target coverage in KRAS^{G12C}-addicted cancer cells

(1) Calculated using tumor mutation frequencies from Foundation Medicine Insights August 2020 and scaled to estimated patient numbers using cancer incidence from ACS *Cancer Facts and Figures* 2020 (see appendix for additional detail); lung cancer = non-small cell lung cancer

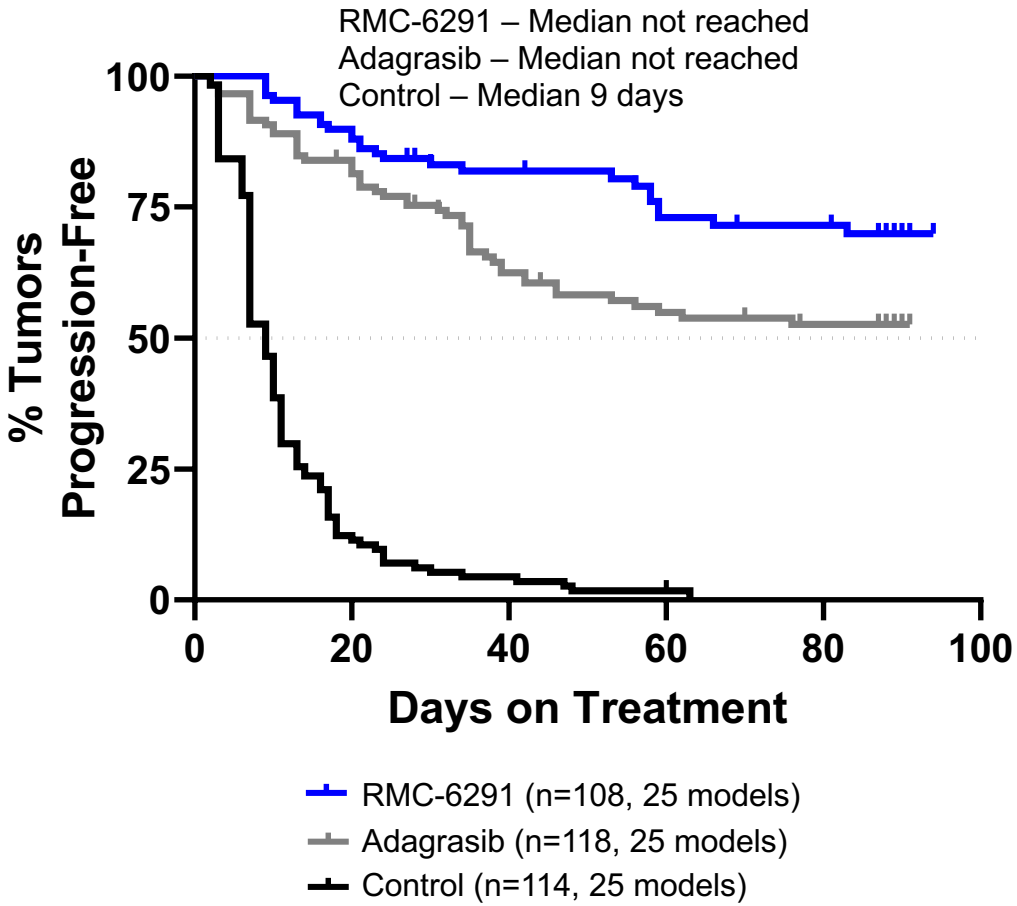
Characterization above is based on RVMD preclinical research

RMC-6291: Superior Response Rates and Durability in Mouse Clinical Trial with 25 KRAS^{G12C} NSCLC Models

Responses



PFS



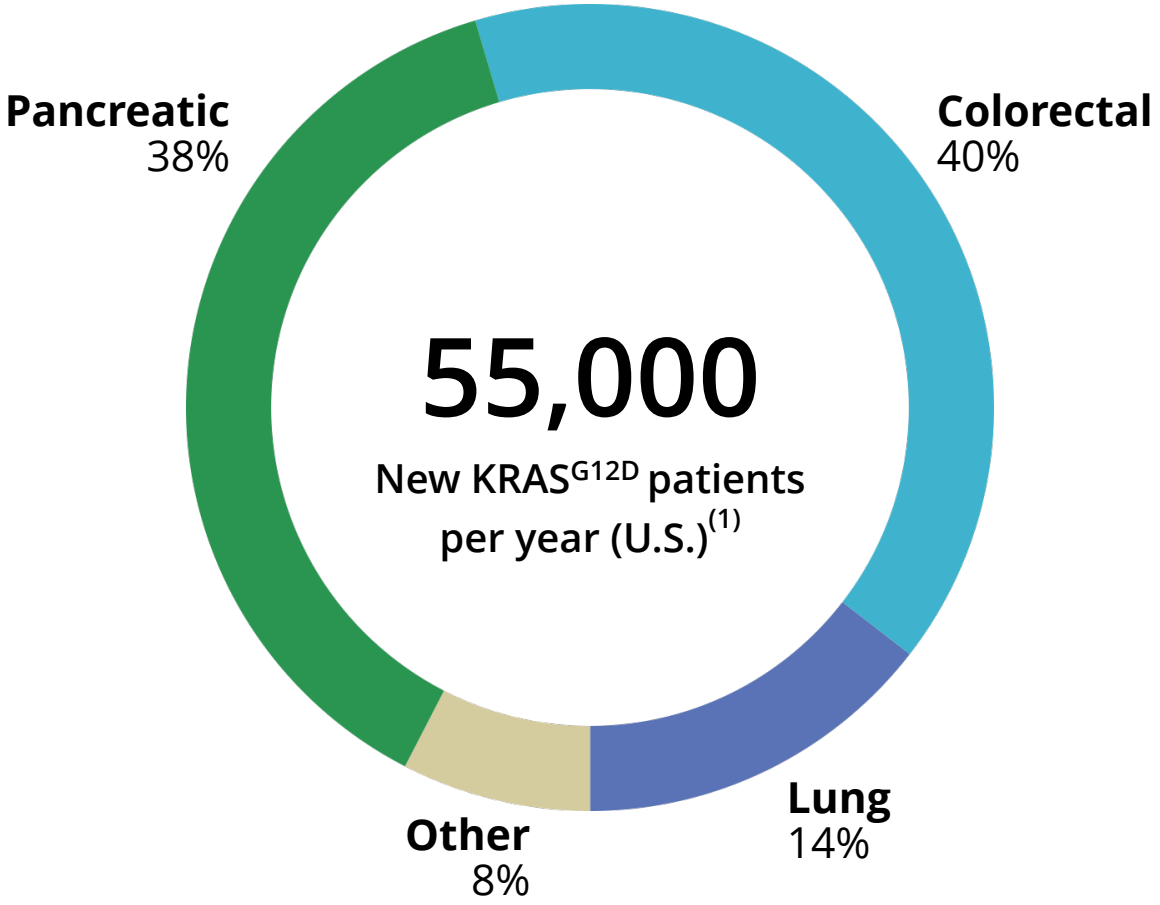
RVMD preclinical research as of 11/20/22
Adagrasib dosed at 100 mg/kg po qd; RMC-6291 dosed at 200 mg/kg po qd; n=3 to 10/group
Progression defined as tumor doubling from baseline
p<0.001 by Log-rank test (RMC-6291 vs adagrasib treatment in the KM analysis)
NSCLC = Non-small cell lung cancer
Responses assigned according to mRECIST (see appendix)

RMC-6291 Phase 1/1b Trial: Clinical Translation of Preclinical Single Agent Profile and Initial Platform Validation

	Preclinical Profile	Aims of Phase 1/1b Clinical Trial[2]
Dosing and Safety	✓ **Oral dosing** (daily): drug levels that drive maximal target crosslinking and sustained RAS pathway suppression ✓ **Safety**: well-tolerated in active range, highly selective for KRAS^{G12C} ✓ **Long-term treatment**[1] at active doses	○ **Oral dosing**: once daily to reach active exposures + option for BID schedule; surrogate markers of activity (ctDNA) ○ **Safety**: short- and long-term safety and tolerability at active exposures ○ **RP2DS**
Anti-Tumor Activity	✓ **Tumor selection**: active in KRAS^{G12C} NSCLC and CRC tumor models, including some resistant to KRAS^{G12C}(OFF) inhibitors ✓ **Activity**: deep and durable regressions across KRAS^{G12C} tumors, especially NSCLC	○ **Patient selection**: KRAS^{G12C} solid tumors; KRAS^{G12C}(OFF) inhibitor-treated patients included in dose escalation ○ **Efficacy**: initial clinical responses by RECIST; formal proof-of-concept via expansion cohorts focused on NSCLC patients without prior KRAS^{G12C}(OFF) inhibitor treatment

(1) Long-term in mouse models defined as up to 90 days of treatment
(2) Ongoing study, RMC-6291-001 - ClinicalTrials.gov Identifier: NCT05462717 https://www.clinicaltrials.gov/ct2/show/NCT05462717?term=RMC-6291&draw=2&rank=1
MTD = maximum tolerated dose; RP2DS = recommended Phase 2 dose and schedule; ctDNA = circulating tumor DNA

RMC-9805: First-in-Class Mutant-Selective RAS(ON) Inhibitor for KRAS^{G12D} Cancers



Highly Potent and Selective RAS(ON) Inhibitor

- Highly active against KRAS^{G12D}
- Covalent for irreversible inhibition
- Low off-target risk and acceptable safety profile

Robust Anti-tumor Activity in Cancer Models

- Rapid, deep and sustained inhibition drives durable regressions in KRAS^{G12D} lung, pancreatic and colorectal cancers

Attractive PK/ADME Profile

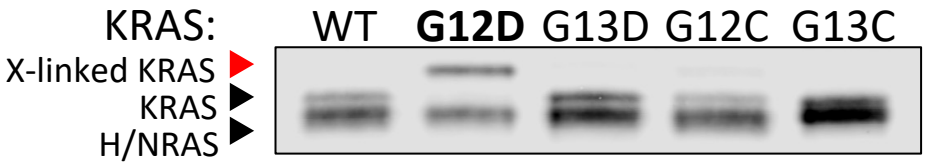
- Favorable *in vivo* oral bioavailability and clearance for effective target coverage in KRAS^{G12D}-addicted cancer cells

(1) Calculated using tumor mutation frequencies from Foundation Medicine Insights August 2020 and scaled to estimated patient numbers using cancer incidence from ACS *Cancer Facts and Figures* 2020 (see appendix for additional detail); lung cancer = non-small cell lung cancer

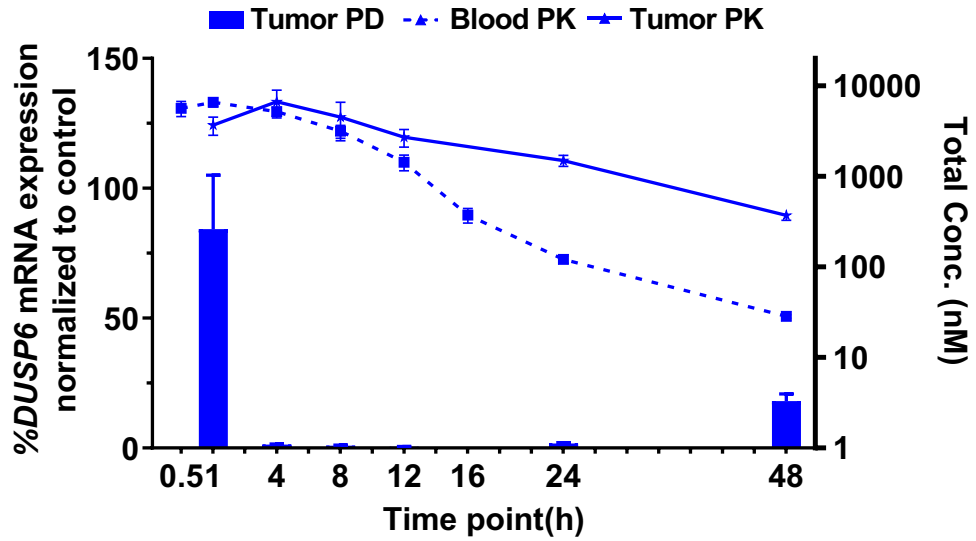
Characterization above is based on RVMD preclinical research

RMC-9805: Selective, Covalent Binding and Inhibition of KRAS^{G12D}(ON) with Apoptosis Induction *in Vivo*

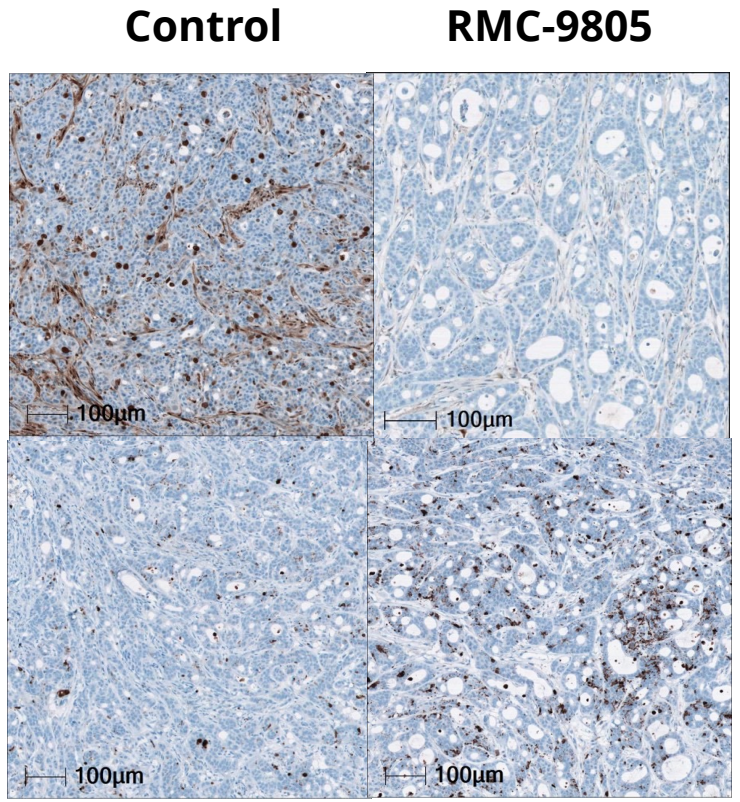
Selective Covalent Binding to KRAS^{G12D}(ON)



Drug Exposure and Pathway Suppression after Oral Dosing(1)



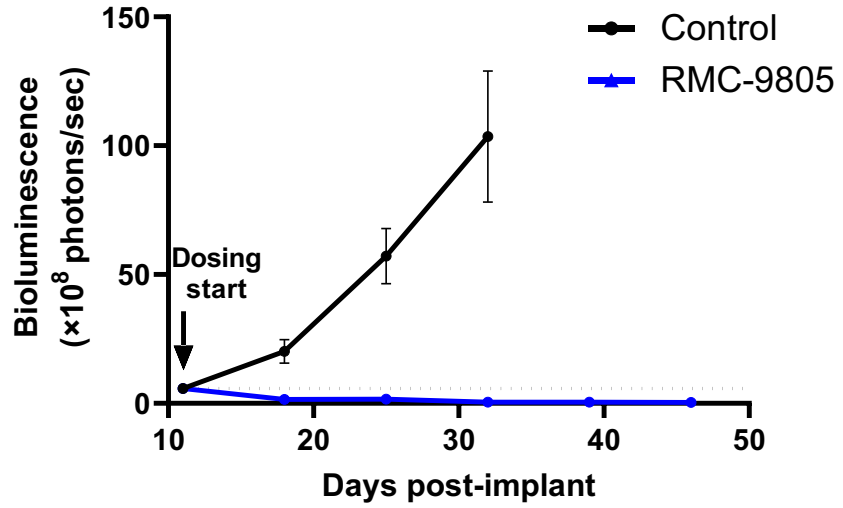
RAS Signaling Inhibition and Apoptosis Induction(2)



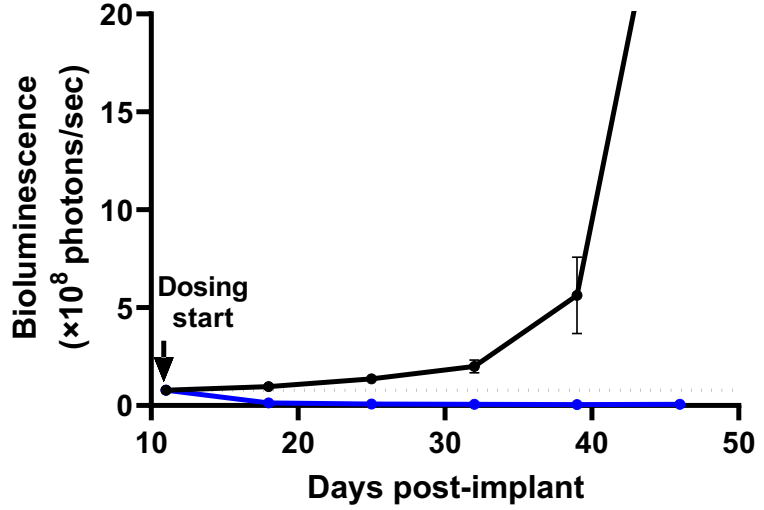
RVMD preclinical research
RMC-9805 dosed at 100 mg/kg po in HPAC subcutaneous xenograft model (PDAC, KRAS$^{G12D/WT}$)
(1) PK/PD data collected at indicated timepoints after a single dose
(2) Histopathology data collected 24h after a single dose

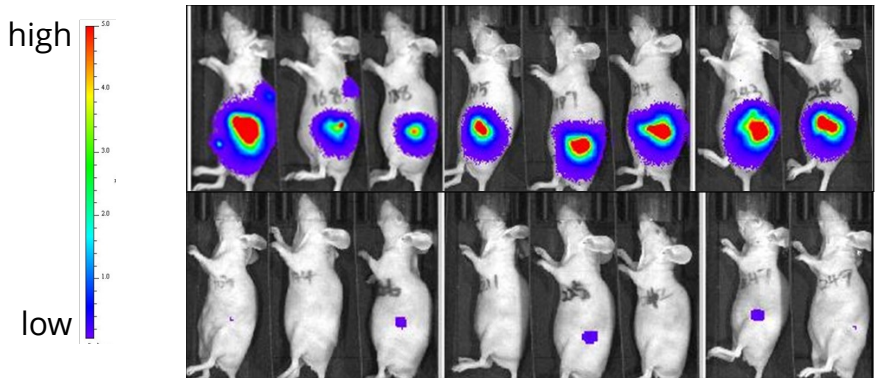
RMC-9805 Drives Deep and Durable Tumor Regressions in Models of Pancreatic Cancer and Brain Metastasis

HPAC ($KRAS^{G12D}$) - Pancreas Xenograft[1]



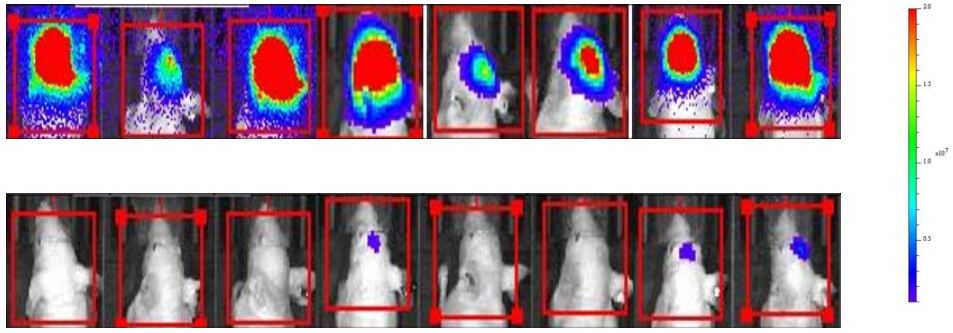
HPAC ($KRAS^{G12D}$) - Brain Xenograft[2]





Control

RMC-9805

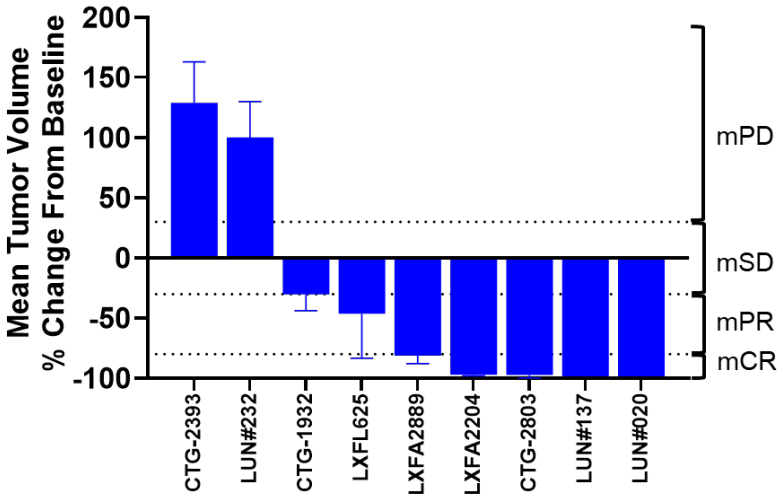


RVMD preclinical research
RMC-9805 dosed at 100 mg/kg po qd
(1) HPAC pancreas orthotopic xenograft model (PDAC, $KRAS^{G12D/WT}$). Mice images were taken on day 21 post implantation.
(2) HPAC intracranial xenograft model (PDAC, $KRAS^{G12D/WT}$). Mice images were taken on day 35 post implantation.

RMC-9805: Highly Active *in Vivo* Across Diverse KRAS^{G12D} Cancer Models

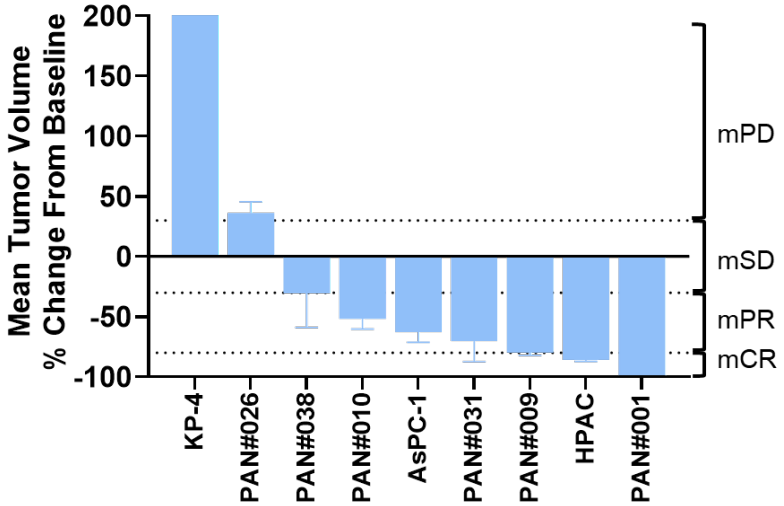
NSCLC

67% ORR (6/9)
78% DCR (7/9)



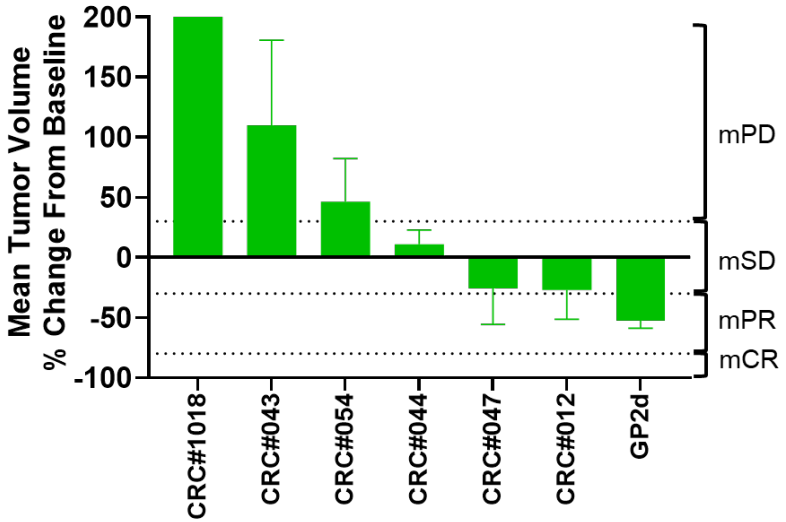
PDAC

78% ORR (7/9)
78% DCR (7/9)



CRC

14% ORR (1/7)
57% DCR (4/7)



RVMD preclinical research as of 11/02/22
RMC-9805 dosed at 100 mg/kg po qd; n=2-8/group
NSCLC = non-small cell lung cancer; PDAC = pancreatic ductal adenocarcinoma; CRC = colorectal cancer
Responses assigned according to mRECIST (see appendix)
ORR = objective response rate; DCR = disease control rate

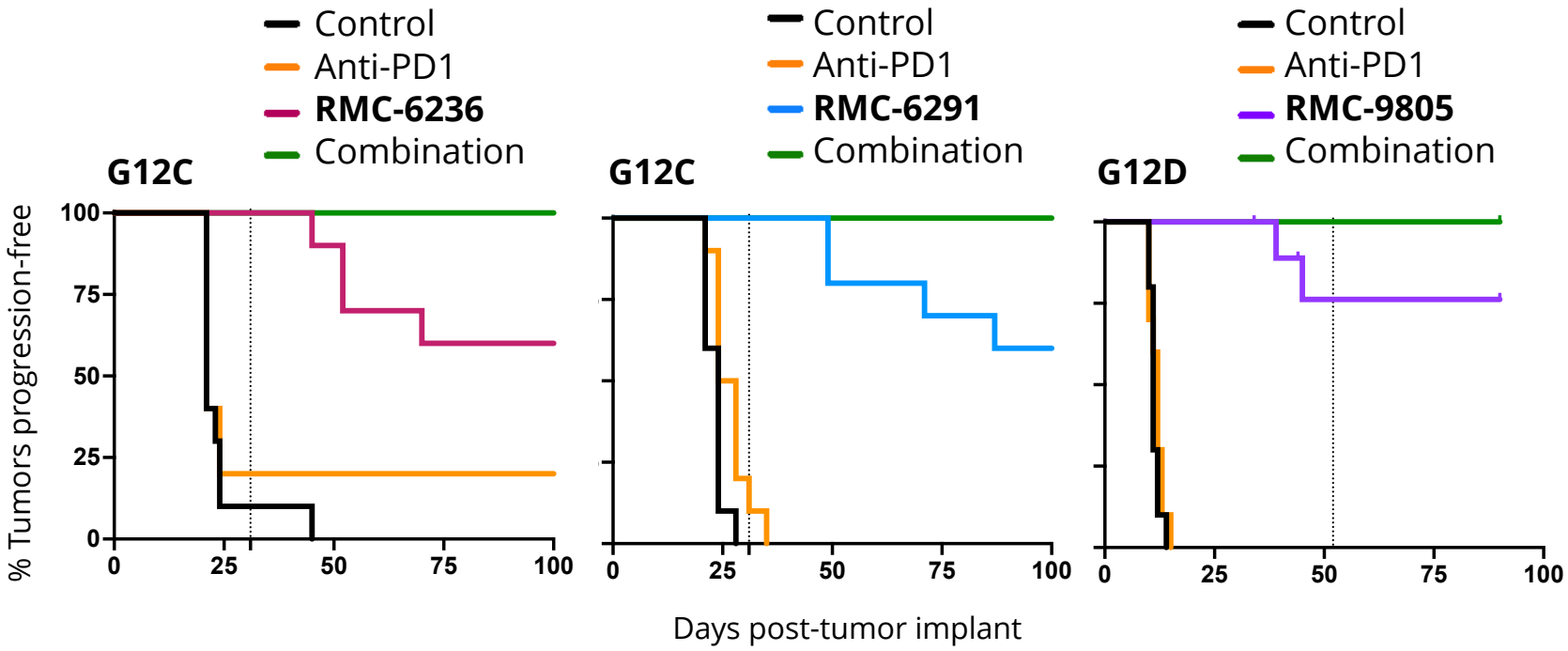
RAS(ON) Inhibitors Induce Anti-Tumor Immunity via Multiple Mechanisms in Immunocompetent Models

Mechanisms of Action

↑ Antigen presentation

↓ Myeloid suppressive cells

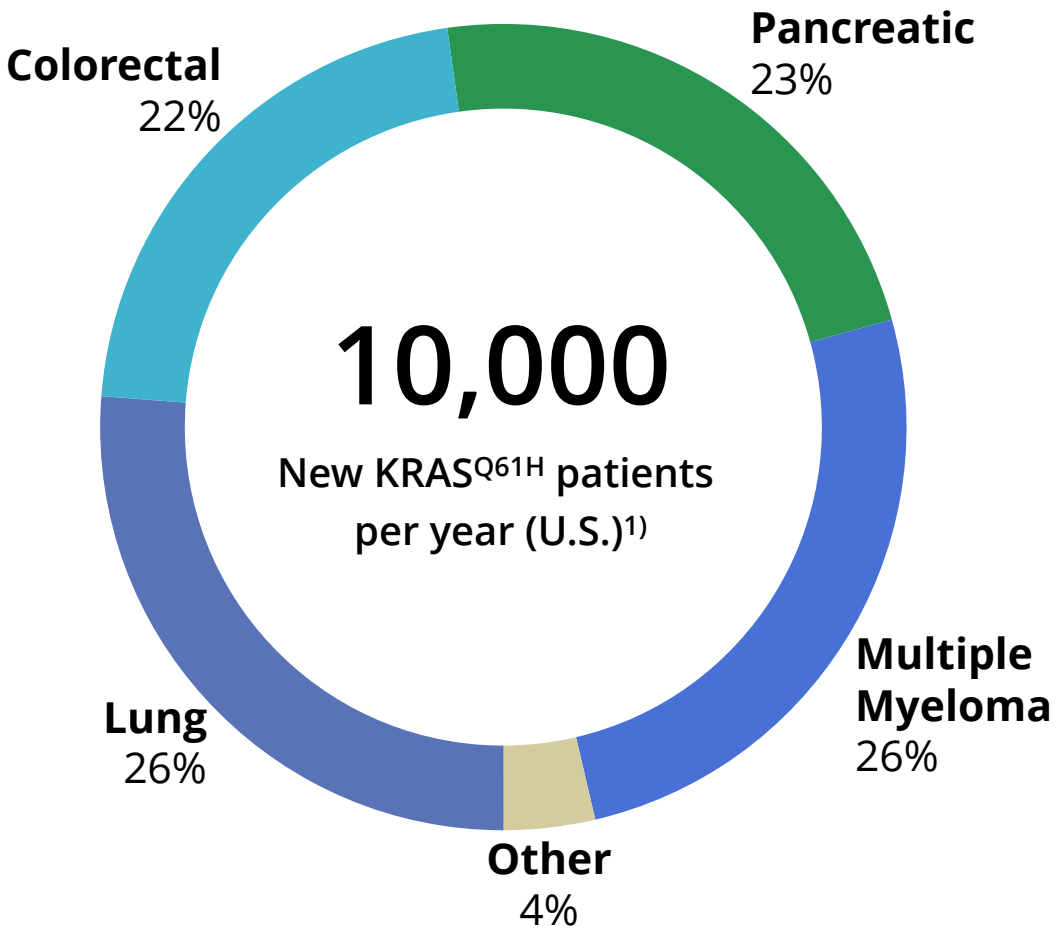
↑ T-cell infiltration



Additive Benefit Supports Clinical Combination Strategies with Immune Therapies

RVMD preclinical research
RMC-9805 experiment conducted in CT26 syngeneic tumor model ($KRAS^{G12D}$); 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; RMC-9805 (100 mg/kg po qd) dosed for 42 days; anti-PD-1 (10 mg/kg ip biw, for 21 days)
Vertical dashed lines represent treatment stop; Kaplan-Meier progression defined as tumor doubling from baseline

RMC-0708: First-in-Class Mutant-Selective RAS(ON) Inhibitor for KRAS^{Q61H} Cancers



Highly Potent and Selective RAS(ON) Inhibitor

- Highly active against KRAS^{Q61H}
- Non-covalent, highly selective over wild-type RAS
- Low off-target risk and acceptable safety profile

Robust Anti-tumor Activity in Cancer Models

- Rapid, deep and sustained inhibition drives durable regressions in KRAS^{Q61H} lung, pancreatic and colorectal cancers

Attractive PK/ADME Profile

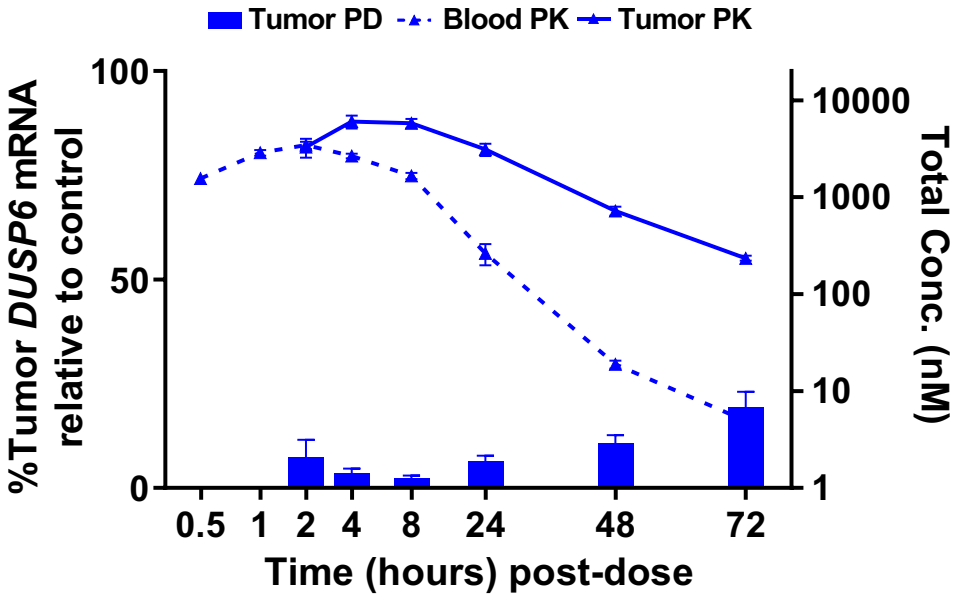
- Favorable *in vivo* oral bioavailability and clearance for effective target coverage in KRAS^{Q61H}-addicted cancer cells

(1) Calculated using tumor mutation frequencies from Foundation Medicine Insights August 2020 and scaled to estimated patient numbers using cancer incidence from ACS *Cancer Facts and Figures* 2020 (see appendix for additional detail); lung cancer = non-small cell lung cancer

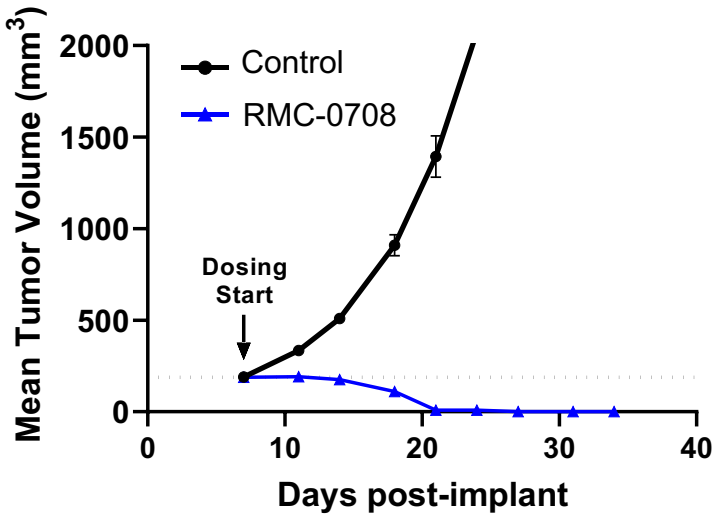
Characterization above is based on RVMD preclinical research

RMC-0708: Sustained Pathway Inhibition *in Vivo* and Tumor Regressions in KRAS^{Q61H} Cancer Models

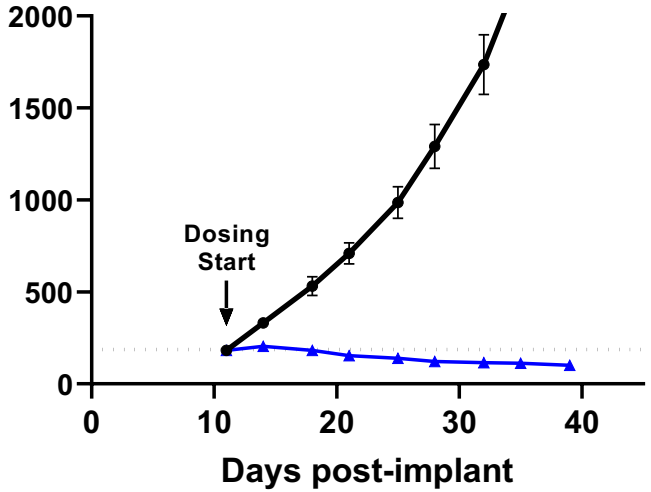
Drug Exposure and Pathway Suppression after Oral Dosing[1,2]

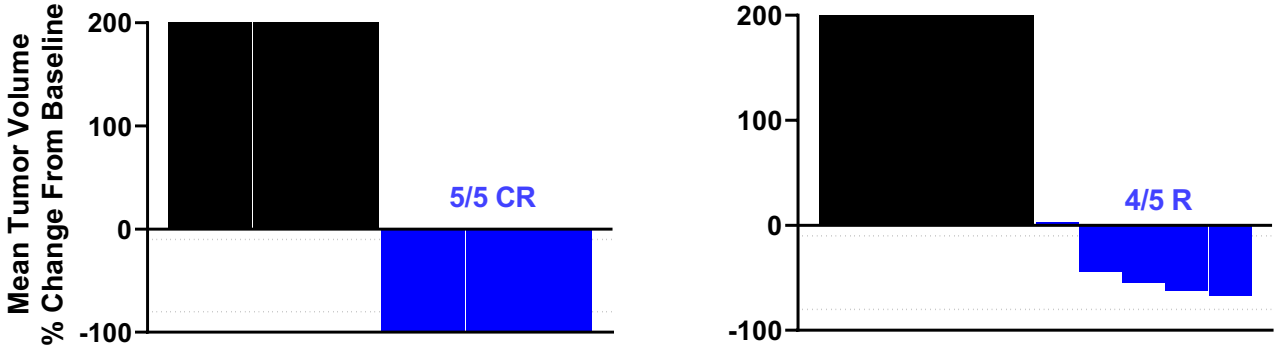


NSCLC[2]



PDAC[3]





RVMD preclinical research
RMC-0708 dosed at 30 mg/kg po qd
(1) PK/PD data collected at indicated timepoints after a single dose
(2) HCC2108 subcutaneous xenograft model (NSCLC, KRAS$^{Q61H/Q61H}$)
(3) T3M-4 subcutaneous xenograft model (PDAC, KRAS$^{Q61H/WT}$)
R = number of regressions >10% from initial; CR = number of regressions ≥80% from initial
Each animal represented as a separate bar in waterfall plots

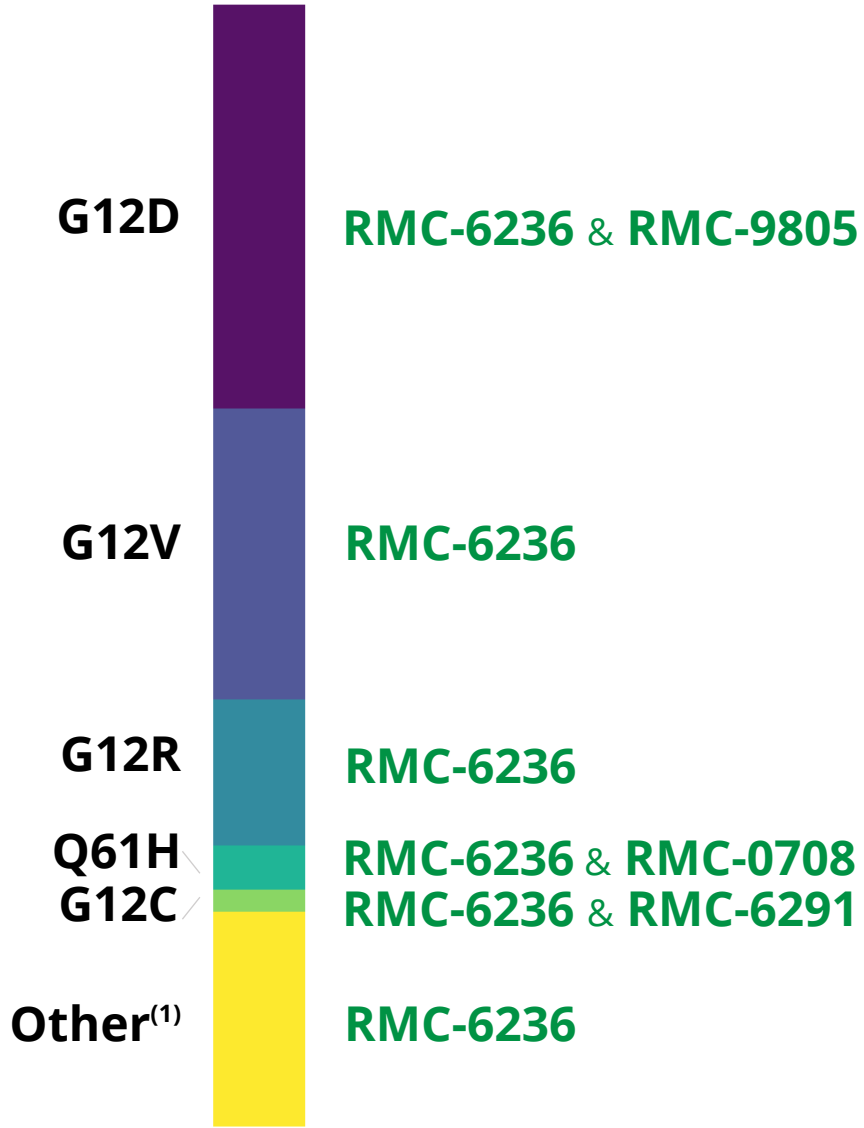
On Target to Outsmart **Pancreatic Cancer**: RAS(ON) Inhibitors Designed to Cover All KRAS^{MUTANT} Drivers[1]

Devastating disease
>90% driven by KRAS mutations

49,000

New KRAS^{MUTANT} pancreatic cancer patients per year (U.S.)[1]

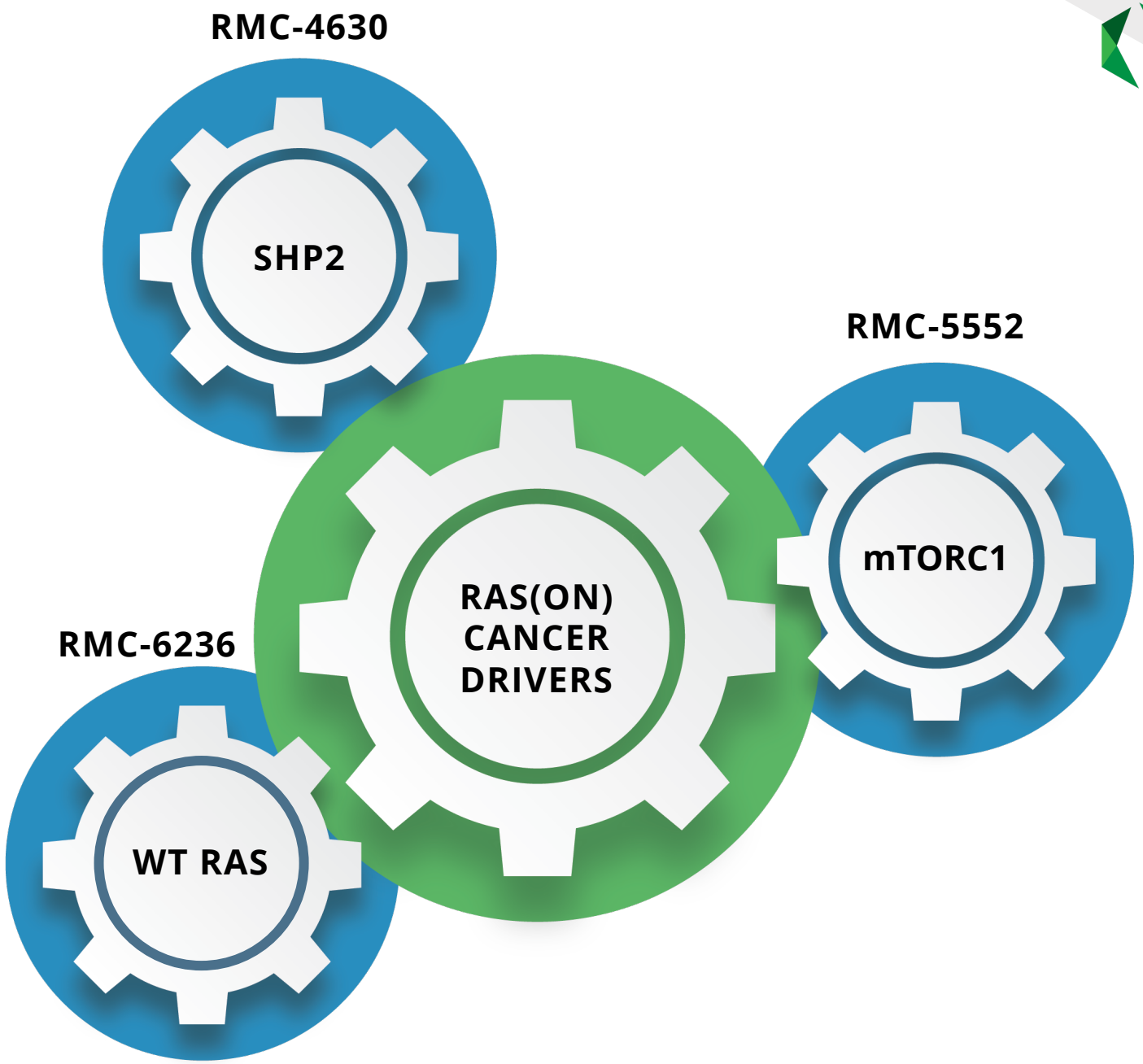
Dismal survival rates
No approved targeted therapies



(1) Calculated using tumor mutation frequencies from Foundation Medicine Insights August 2020 and scaled to estimated patient numbers using cancer incidence from ACS *Cancer Facts and Figures* 2020 (see appendix for additional detail); RMC-6236 tested against all mutations occurring at >2% frequency in pancreatic cancer

RAS Companion Inhibitors

Suppress Cooperating Targets and Pathways that Sustain RAS-Addicted Cancers



Evaluation of RMC-4630 in Combination with Sotorasib in KRAS^{G12C} Cancer Patients

Phase 1/1b Clinical Trial[1]

- ✓ Selected single agent RP2DS: Oral dosing of 200 mg D1D2 weekly: well-tolerated, safety profile consistent with on-pathway inhibition
- ✓ Anti-tumor activity in certain KRAS^{MUTANT} and NF1^{LOF} cancers evidenced by SD, PR and/or CR

Amgen's CodeBreaK 101c Clinical Trial[2]

- ✓ In KRAS^{G12C} patients, "the combination of sotorasib with RMC-4630 was safe and tolerable"[3] with sotorasib at 960 mg po qd and RMC-4630 at 140-200 mg po D1D2 weekly
- ✓ 75% ORR/100% DCR among KRAS^{G12C} inhibitor-naïve NSCLC patients treated at top two doses of RMC-4630 (n=4)

Aims of RMC-4630-03 Phase 2 Trial[4]

Dosing and Safety

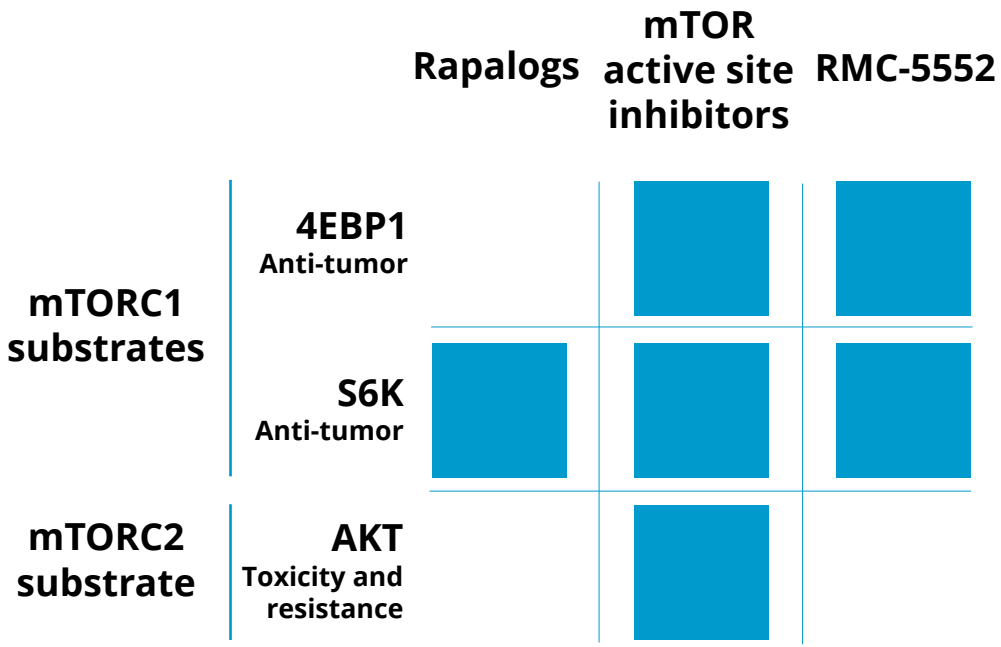
- **Dosing**: Focused primarily on 200 mg D1D2 weekly combined with sotorasib at 960 mg daily
- **Safety**: short- and long-term safety and tolerability

Anti-Tumor Activity

- **Patient Selection**: NSCLC patients without prior KRAS^{G12C} inhibitor treatment stratified into two cohorts: KRAS^{G12C} with or without co-mutations such as KEAP1 or STK11
- **Efficacy**: demonstrate clinical benefit additive to sotorasib

(1) Ongoing study, RMC-4630-01 - ClinicalTrials.gov Identifier: NCT03634982 https://clinicaltrials.gov/ct2/show/NCT03634982?term=RMC-4630&draw=2&rank=1
(2) Ongoing study, CodeBreaK 101c - ClinicalTrials.gov Identifier: NCT04185883 https://clinicaltrials.gov/ct2/show/NCT04185883?term=codebreak+101&draw=2&rank=1
(3) Falchook et. al. Sotorasib in Combination with RMC-4630, a SHP2 Inhibitor, in *KRAS* p.G12C-Mutated NSCLC and Other Solid Tumors. 2022 World Conference on Lung Cancer. August 6-9, 2022. Vienna, Austria. Abstract #OA03.03.
(4) Ongoing study, RMC-4630-03 - ClinicalTrials.gov Identifier: NCT05054725 https://clinicaltrials.gov/ct2/show/NCT05054725?term=RMC-4630&draw=2&rank=2

RMC-5552: First-in-Class Bi-steric mTORC1-Selective Inhibitor for Cancers with Hyperactive mTOR Signaling



Highly Potent and Selective mTORC1 Inhibitor

- Bi-steric mechanism enables selectivity for mTORC1
- Capable of reactivating the tumor suppressor 4EBP1

Robust Anti-tumor Activity in Cancer Models

- Selective inhibition of mTORC1 drives durable regressions in mTOR pathway-mutant models

Attractive PK/ADME Profile

- Weekly dosing provides favorable PK exposure and prolonged target modulation *in vivo*

Characterization above is based on RVMD preclinical research

RMC-5552: Compelling Profile as RAS Companion Inhibitor

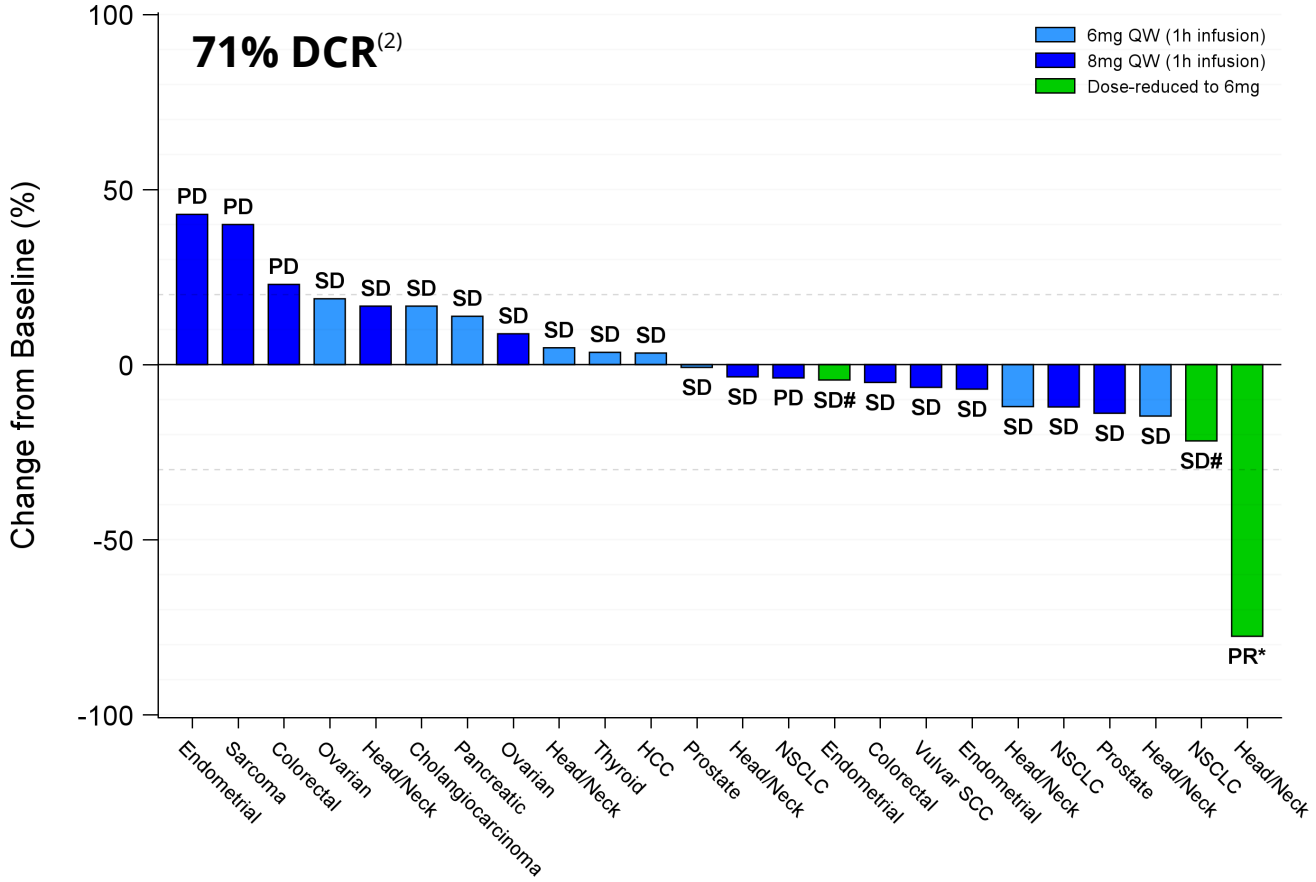
Preliminary radiologic and molecular evidence of activity at tolerated doses:

- Disease control across diverse tumors, including durable stable disease
- Objective response and regressions
- Favorable changes in surrogate markers
  - 3 of 6 patients with stable disease and oncogenic mTOR pathway variants had molecular responses[1]

(1) n = 6 molecular response-evaluable patients with oncogenic mTOR pathway variants detected by ctDNA treated at 6 mg or higher majority dose. "Oncogenic" defined as pathogenic or likely pathogenic by blinded adjudication process using publicly available variant data. Molecular response defined by 50% decrease or greater in mean VAF at C3D1 by Guardant360® Molecular Response algorithm. VAF = variant allele fraction

Phase 1/1b Single Agent Study

Best Tumor Change in Efficacy Evaluable Patients Treated at 6 mg or 8 mg IV Weekly



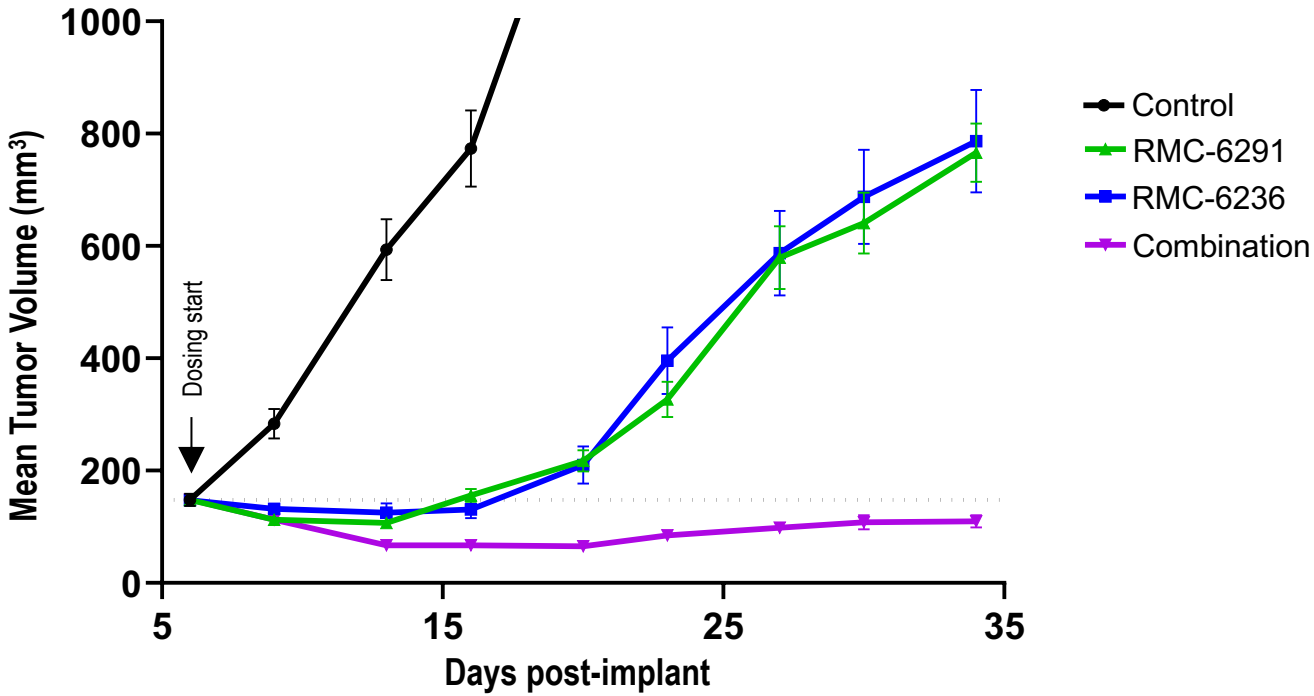
(2) n = 28 efficacy evaluable subjects. DCR = disease control rate.
*Patient received one dose of 12 mg, followed by weekly doses of 6 mg, had complete loss of oncogenic PTEN variant by ctDNA, and has been on RMC-5552 for >12 months.
#Patient received one dose of 10 mg, followed by weekly doses of 6 mg. Both patients were on RMC-5552 for >24 weeks.
Data as of 12/19/2022. PD = progressive disease, SD = stable disease, PR = partial response, mo = months

RMC-5552 Phase 1/1b Trial: Clinical Optimization of Single Agent Profile for Combination with RAS(ON) Inhibitor Portfolio

	Preclinical Profile	Aims of Phase I/Ib Clinical Trial[1]
Dosing and Safety	✓ **Dosing**: Once weekly dosing achieves levels that drive sustained inhibition of mTORC1 signaling and activation of 4EBP1 ✓ **Safety**: Well-tolerated, highly mTORC1 selective	○ **Dosing**: Establish optimal IV regimen based on safety, anti-tumor activity and surrogate markers of activity (ctDNA) ○ **Safety**: Demonstrate short- and long-term safety and tolerability at active exposures
Anti-Tumor Activity	✓ **Single Agent**: Strong activity in tumor models with hyperactivated mTORC1 ✓ **RAS Companion**: Combinatorial activity with RAS(ON) inhibitors	○ **Single Agent**: Evidence of activity at tolerated doses in tumors with hyperactive mTORC1 signaling ○ **RAS Companion**: Identify appropriate dose and schedule for combinations with RAS(ON) inhibitors

(1) Ongoing study, RMC-5552-001 - ClinicalTrials.gov Identifier: NCT04774952 https://clinicaltrials.gov/ct2/show/NCT04774952?term=rmc-5552&draw=2&rank=1
MTD = maximum tolerated dose; RP2DS = recommended Phase 2 dose and schedule; ctDNA = circulating tumor DNA

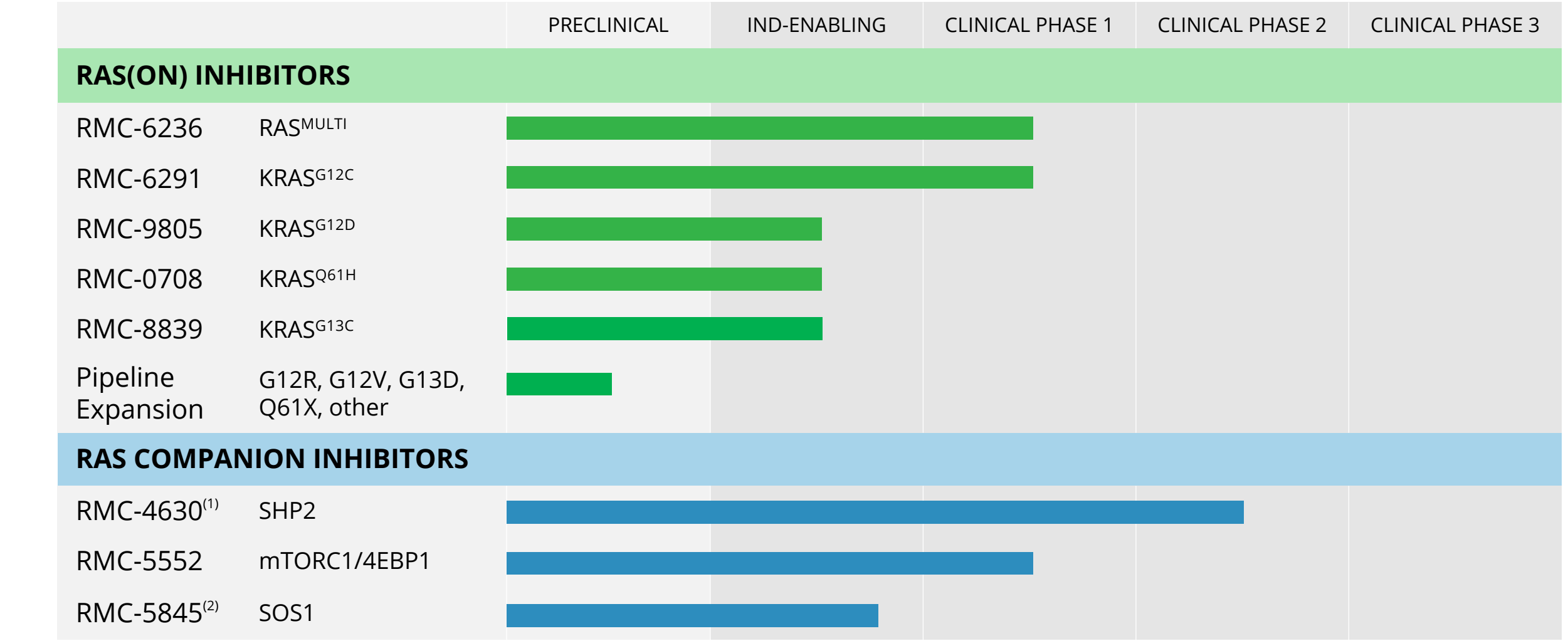
Overcoming Resistance: RMC-6291 + RMC-6236 Combination Induces Regressions in KRAS^{G12C} NSCLC Model



RAS^{MULTI}(ON) Inhibitor Deployed as a RAS Companion Inhibitor

RVMD preclinical research
NCI-H2122 subcutaneous xenograft model (NSCLC, KRAS$^{G12C/G12C}$)
RMC-6291 dosed at 100 mg/kg po qd; RMC-6236 dosed at 10 mg/kg po qd
RMC-6291, RMC-6236 and Combination - n = 15/group, Control – n=8
NSCLC = non-small cell lung cancer

Deep Pipeline of Targeted Therapies for Majority of RAS-Addicted Cancers



(1) Sanofi collaboration on RMC-4630/SAR442720 terminated effective June 2023
(2) IND-ready, active development deferred

Anticipated Milestones

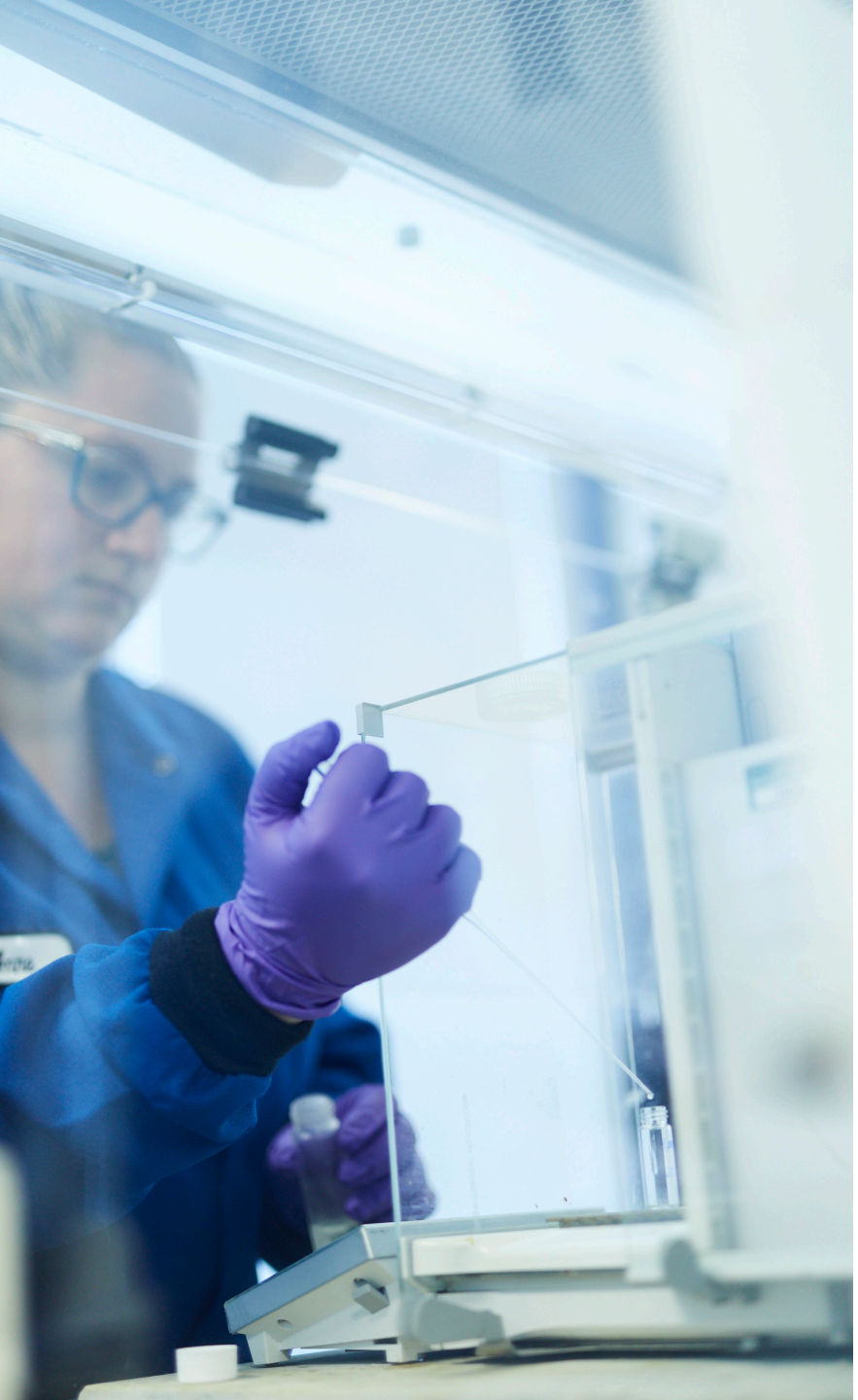
	MILESTONE (EXPECTED TIMING)
RAS(ON) INHIBITORS	
RMC-6236 (RAS^{MULTI})	Provide further evidence of first-in-class single agent activity (mid-2023)
RMC-6291 ($KRAS^{G12C}$)	Provide preliminary evidence of superior profile (2H2023)
RMC-9805 ($KRAS^{G12D}$)	Announce dosing of first patient (mid-2023)
RAS COMPANION INHIBITORS	
RMC-4630 (SHP2)	Provide topline data from RMC-4630-03 (2H2023)
RMC-5552 (mTORC1/4EBP1)	Provide additional evidence of single agent activity (2023)

Financial Information

Financial Position	
Cash, cash equivalents and marketable securities as of December 31, 2022	$644.9 million[(1)]

2023 Financial Guidance
2023 GAAP net loss of $335 million to $365 million[(2)]

(1) With current cash, cash equivalents and marketable securities, the company projects it can fund planned operations through 2024
(2) Includes non-cash stock-based compensation expense of approximately $40 million to $50 million



REVOLUTION MEDICINES

On Target to Outsmart Cancer™

Focused on serving high unmet needs across numerous cancers driven by diverse RAS mutations

Targeted ***RAS(ON) Inhibitors*** with compelling preclinical profiles entered clinic in 2022

Targeted ***RAS Companion Inhibitors*** designed to counter drug resistance have shown initial clinical activity and evaluation continues

Development-stage portfolio covers RAS drivers of all major RAS-addicted cancers

Appendix

- RAS cancer epidemiology statistics are estimated using tumor mutation frequencies from Foundation Medicine Insights August 2020 and scaled to estimated patient numbers using cancer incidence from ACS *Cancer Facts and Figures* 2020:
  - RAS mutations include: KRAS G12(A,C,D,R,S,V), KRAS G13(C,D), KRAS Q61(H, K, L), KRAS A146T, KRAS wild-type amplification, NRAS G12C, NRAS Q61(H,K,L,R,P), HRAS mutations of known/likely function (including HRAS Q61(H,L)), BRAF class 3 mutations, NF1 loss of function mutations, PTPN11 mutations of known/likely function. NF1 LOF mutations = 50% of all NF1 mutations of known/likely function. BRAF class 3 mutations = D287H, D594(A,E,G,H,N,V,Y), F595L, G466(A,E,R,V,E,D,R), N581(I,S), S467L,T599I, V459L.
  - Includes 12 major types: non-small cell lung cancer, colorectal, pancreatic adenocarcinoma, renal, gastroesophageal, head and neck squamous cell, ovarian and biliary cancers, acute myeloid leukemia, and advanced melanoma, bladder and uterine/endometrial cancers causing mortality.
    - $KRAS^{Q61H}$ epidemiology statistics include multiple myeloma in addition to 12 major types named above
  - Est. worldwide annual incidence of RAS-mutated cancers is 3.4 million per Prior et al., *Cancer Research* 2020

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

- Mouse tumor responses on slides 9, 12 and 17 assigned according to mRECIST (modified from Gao et al. Nat Med. 2015):
  - mPD = progressive disease; mSD = stable disease; mPR = partial response; mCR = complete response

- PK = pharmacokinetic; ADME = absorption, distribution, metabolism, and excretion