REVOLUTION MEDICINES

July 21, 2022

On Target to Outsmart Cancer™

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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 May 9, 2022, 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

RAS proteins drive 30% of human cancers[(1)], and are largely unserved by targeted therapeutics

STRONG CLINICAL VALIDATION OF RAS AS CANCER DRIVER

Proof-of-principle from first-gen $KRAS^{G12C}$ inhibitors[(2)] predicts favorable impact of targeted inhibitors across numerous RAS cancer drivers

DEEP SCIENCE-DRIVEN PIPELINE

Comprehensive collection of groundbreaking *RAS(ON) Inhibitors* designed to have best-in-class preclinical profiles and/or first-in-class potential tailored to target RAS space broadly; first candidates in the clinic

Leading *RAS Companion Inhibitors* in clinic designed for combination treatment strategies to counter resistance to RAS targeted therapies

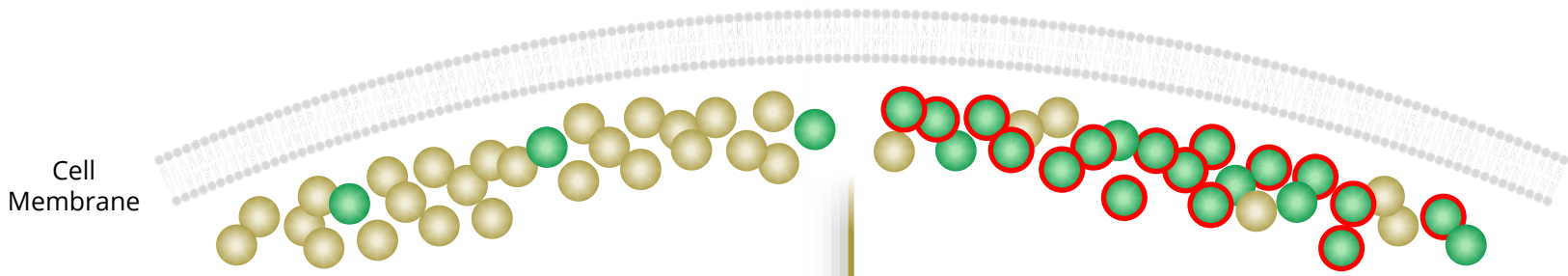
(1) Prior et al., *Cancer Research* 2020
(2) Lumakras approved by the FDA in May 2021

Excessive RAS(ON) Signaling Drives 30% of Human Cancers

RAS(OFF)

RAS(ON)

Normal



Tightly regulated
RAS(ON) proteins control cell growth

Excessive
RAS(ON) signaling drives uncontrolled cell growth

RAS-Addicted Cancers

RAS Cancer Mutations

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

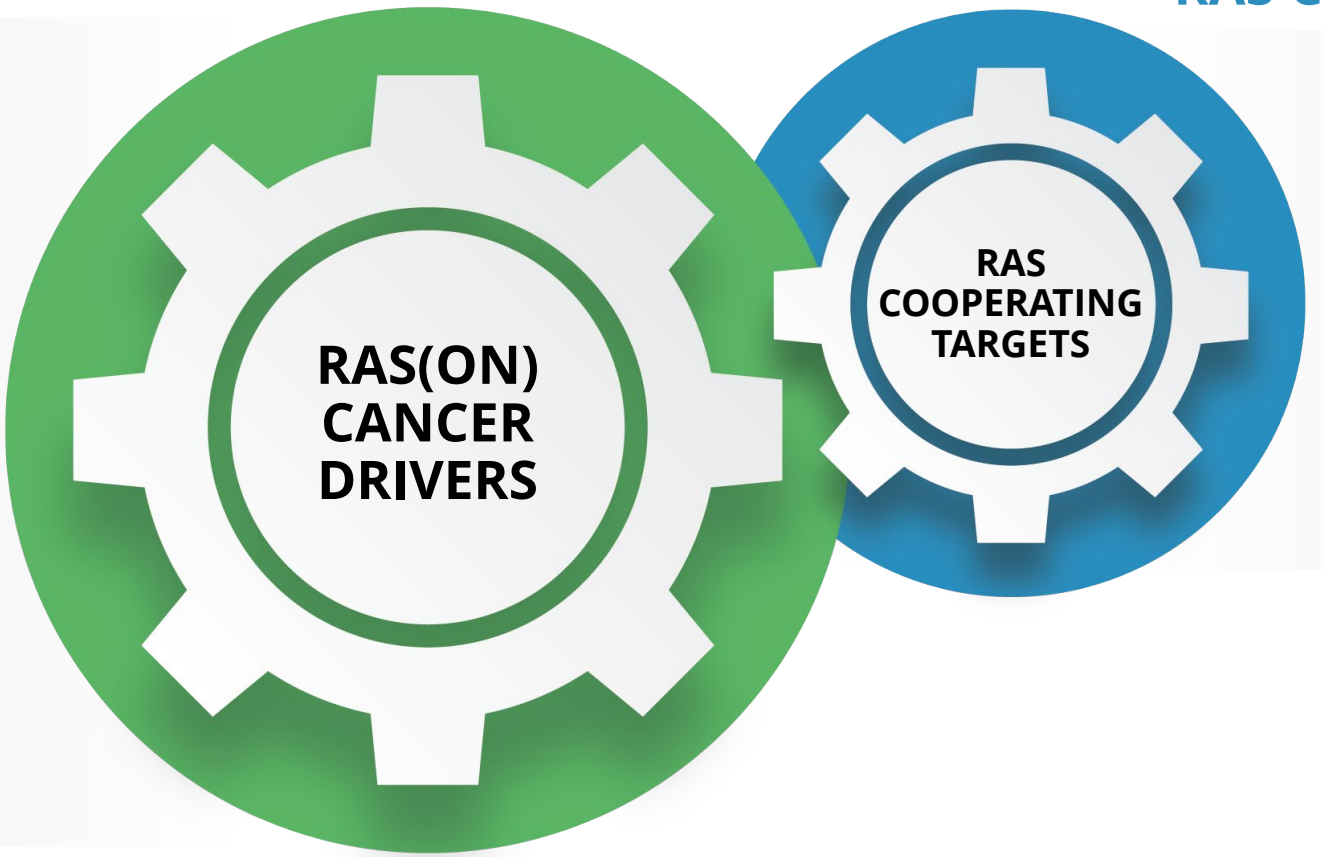
Deep Science-Driven Pipeline of Targeted Therapies for RAS-Addicted Cancers

RAS(ON) Inhibitors

2 Clinical-stage Drug Candidates

2 Drug Candidates in development

4+ Pipeline expansion programs



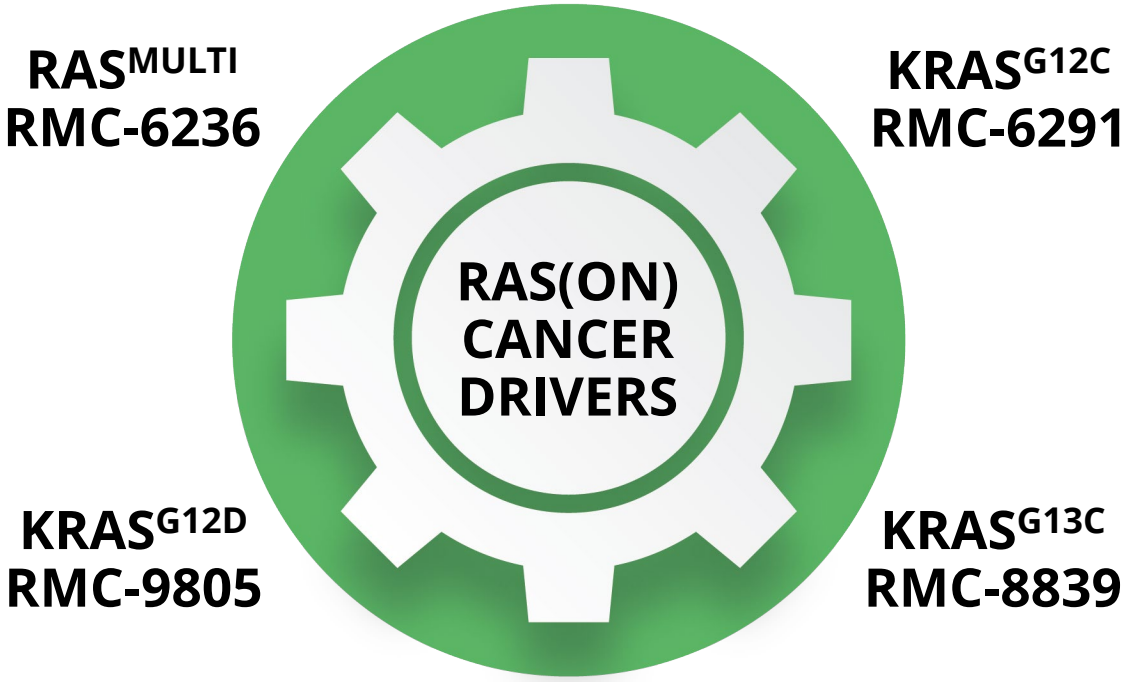
RAS Companion Inhibitors

2 Clinical-stage Drug Candidates

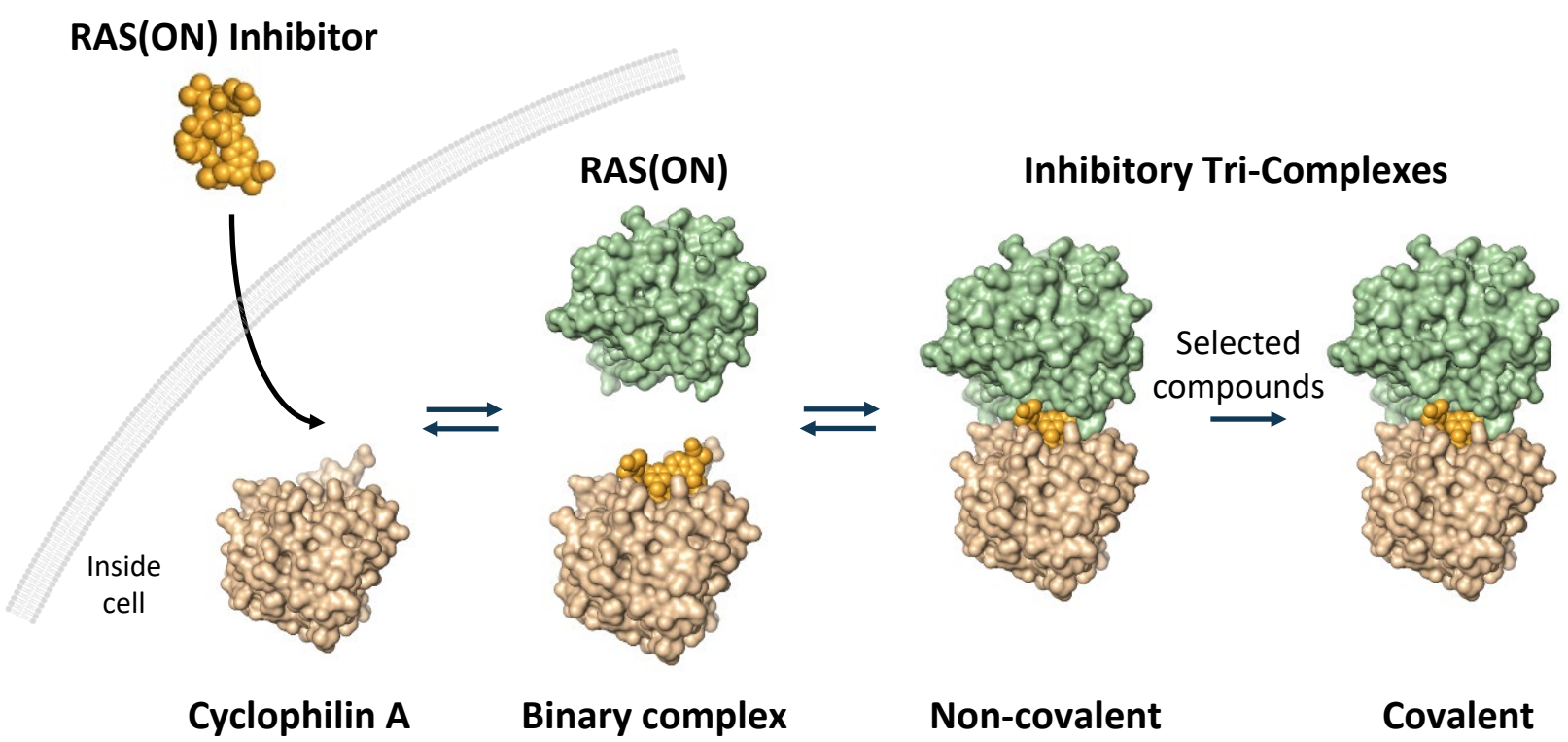
1 IND-ready Drug Candidate

RAS(ON) Inhibitors

Induce Rapid, Deep and Sustained Suppression of RAS(ON) Cancer Drivers



Distinctive RAS Drug Discovery: Innovation Engine Targets Oncogenic RAS(ON) Proteins

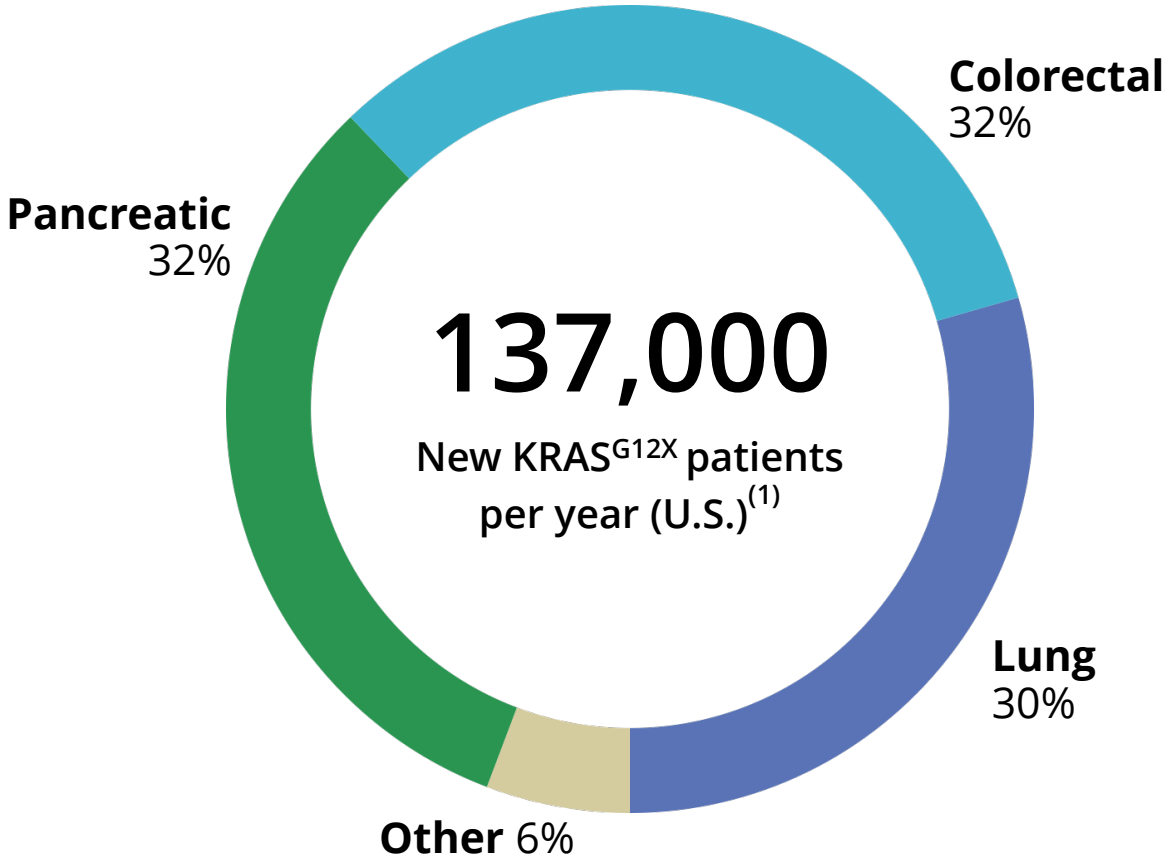


RAS(ON) Inhibitors

Deep and Diverse Collection

- Highly potent and selective
- Oral and drug-like
- Rapid, deep and sustained suppression of RAS(ON) signaling

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

- Inhibits canonical RAS family members, suppressing the mutant cancer driver 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 including KRAS^{G12D}, KRAS^{G12V}, KRAS^{G12R} and KRAS^{G12C}

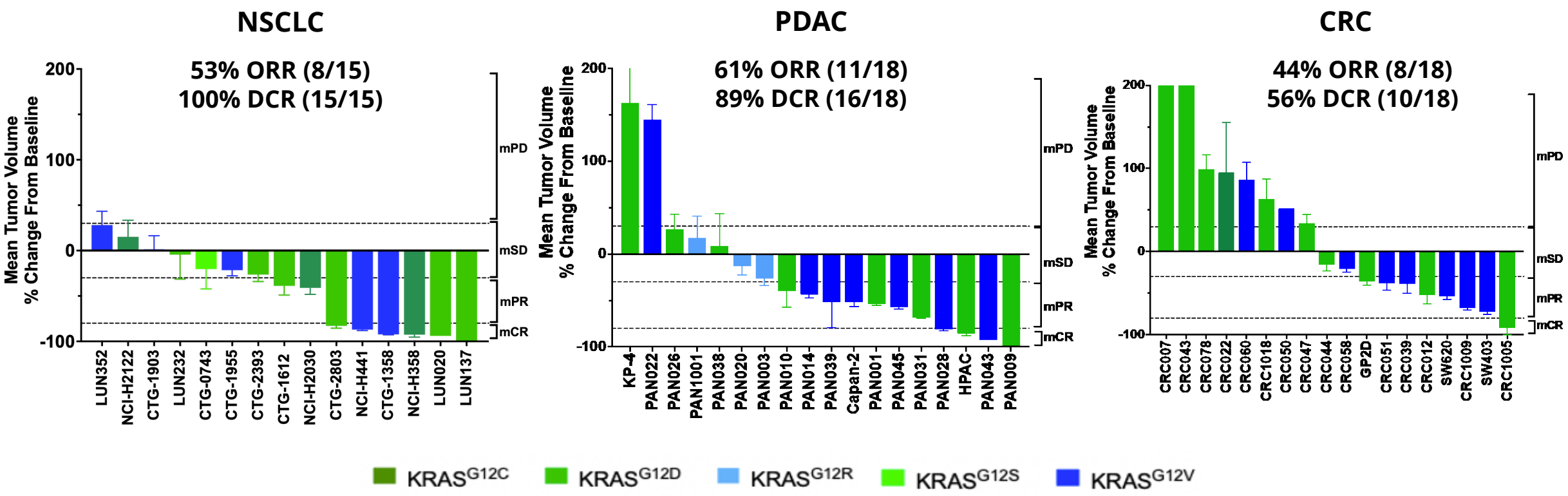
Attractive PK/ADME Profile

- 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

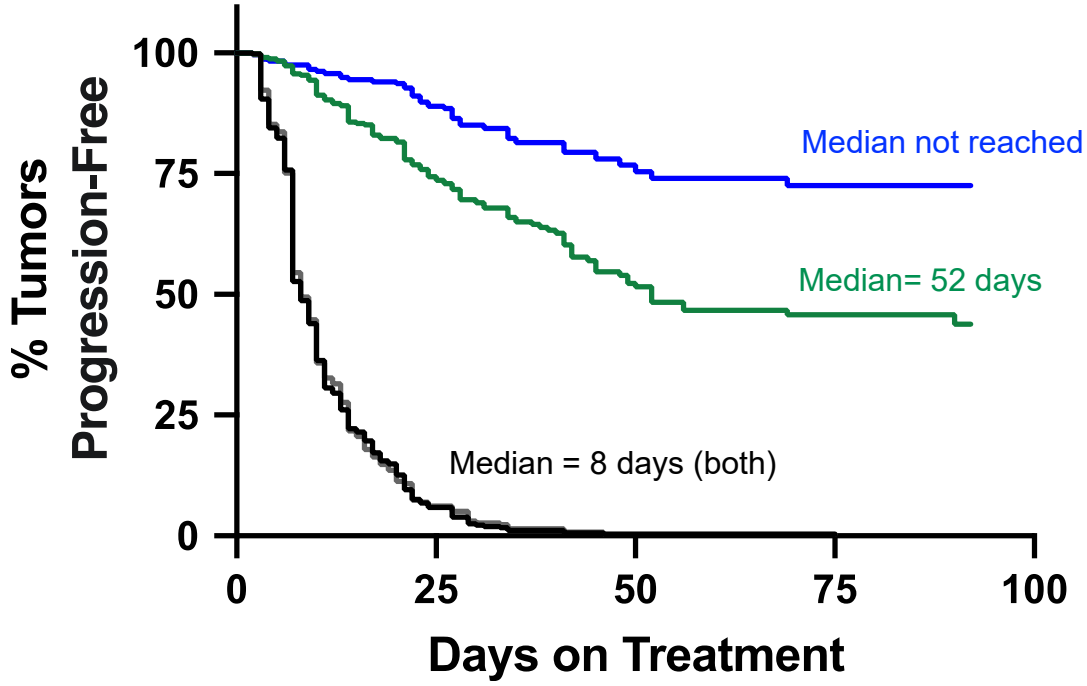
RMC-6236: Highly Active *in Vivo* Across Cancer Models with $KRAS^{G12X}$ Drivers



Deep Tumor Regressions and Complete Responses Observed Across Cancer Models

RVMD preclinical research, as of 03/11/22
RMC-6236 dosed at 25 mg/kg po qd; n = 1-10/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

RMC-6236: Highly Active *in Vivo* Across Cancer Models with Diverse RAS Drivers



KRAS^{G12X} Tumors

- RMC-6236 (n=235, 62 models)
- Control (n=257, 62 models)

RAS Pathway Mutant Tumors

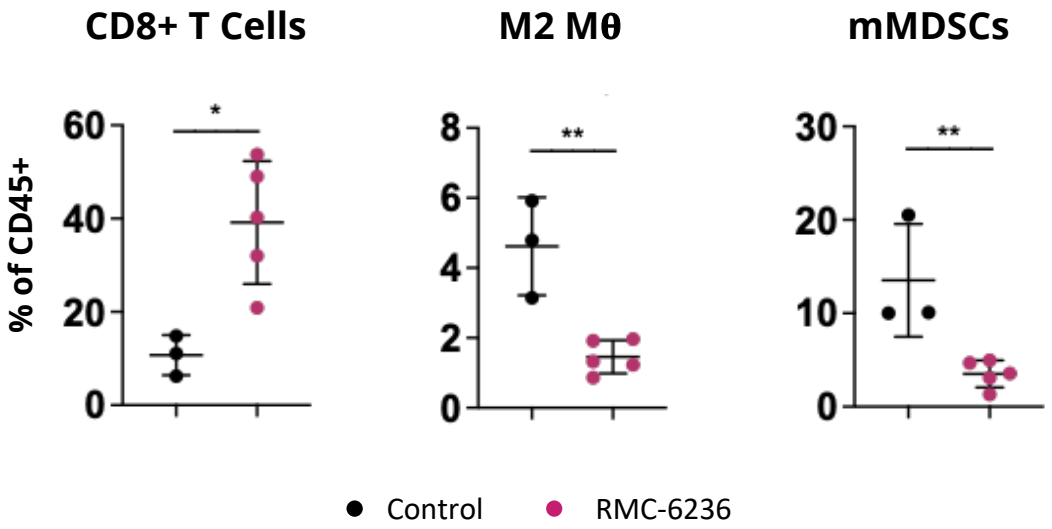
- RMC-6236 (n=411, 97 models)
- Control (n=437, 97 models)

Durable Anti-Tumor Benefit Observed in KRAS^{G12X} Cancer Models and Beyond

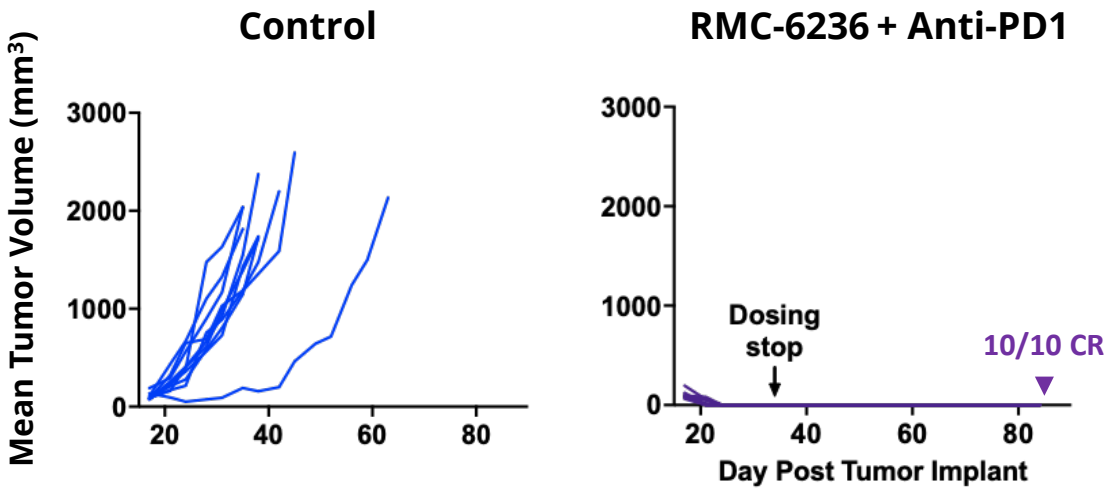
RVMD preclinical research, as of 03/11/22
RMC-6236 dosed at 25 mg/kg po qd
Progression defined as tumor doubling from baseline over 28 days
p<0.0001 by Log-rank test (control vs RMC-6236 treatment)
See appendix for composition of KRAS^{G12X} Tumors and RAS Pathway Mutant Tumors

RMC-6236: Anti-Tumor Immunity *in Vivo* and Strong Additivity with Checkpoint Inhibitor

Favorable Transformation of Tumor Immune Microenvironment



Durable Complete Responses with Checkpoint Inhibitor Combination



Modulation of the Tumor Microenvironment Primes for Anti-Tumor Immunity in Cancer Models

RVMD preclinical research
Syngeneic tumor model with CT26 cell line engineered to express $KRAS^{G12C}$
RMC-6236 dosed at 25 mg/kg po qd; Anti-PD1 dosed at 10 mg/kg ip biw; n = 10/group
M2 Mθ = M2 macrophages; mMDSCs = Monocytic myeloid derived suppressor cells

RMC-6236: Clinical Priorities to Pursue First-in-Class Activity Against KRAS^{G12X} Tumors

Activities (ongoing* or projected)

- Initiated single agent dose escalation in patients with cancers with KRAS^{G12X} mutations (focused on NSCLC, pancreatic cancer and CRC)*
- Include 'below MTD' expansion cohorts in select populations during dose escalation
- Define RP2DS
- Single agent expansion cohorts in KRAS^{G12X} tumors (NSCLC, pancreatic cancer and CRC)
- Combinations in KRAS^{G12X} tumors (NSCLC, pancreatic cancer and CRC)

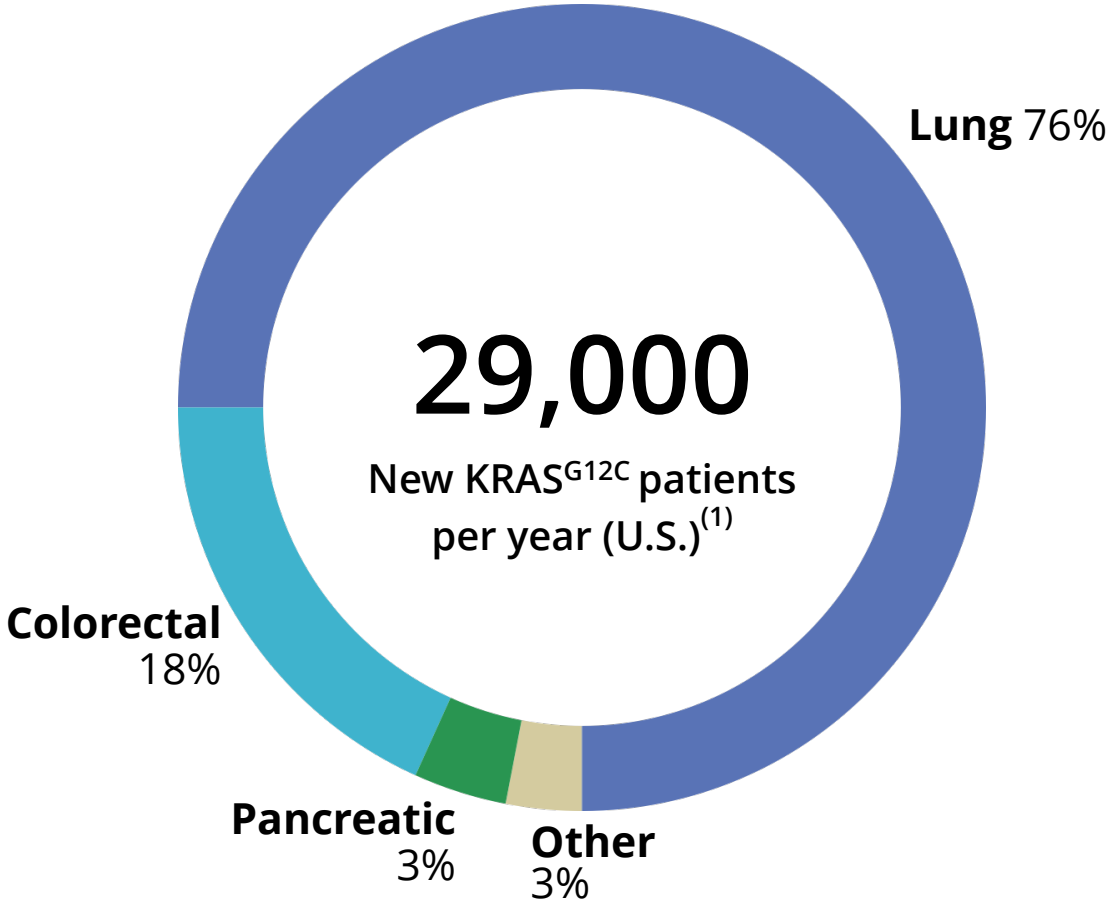
Aims

Evidence of first-in-class single agent activity against KRAS^{G12X} tumors^

^See Anticipated Milestones table

KRAS^{G12X} may include KRAS^{G12D}, KRAS^{G12V}, KRAS^{G12R} and/or KRAS^{G12C}
RP2DS = Recommended Phase 2 dose and schedule
MTD = maximum tolerated dose
NSCLC = non-small cell lung cancer; CRC = colorectal cancer

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

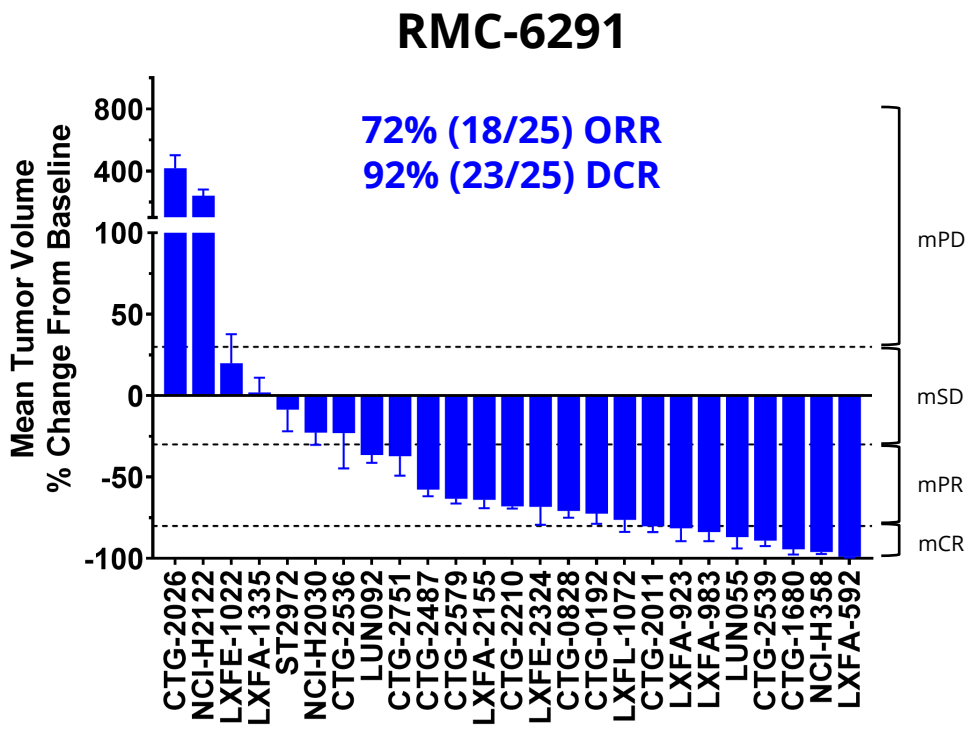
Attractive PK/ADME Profile

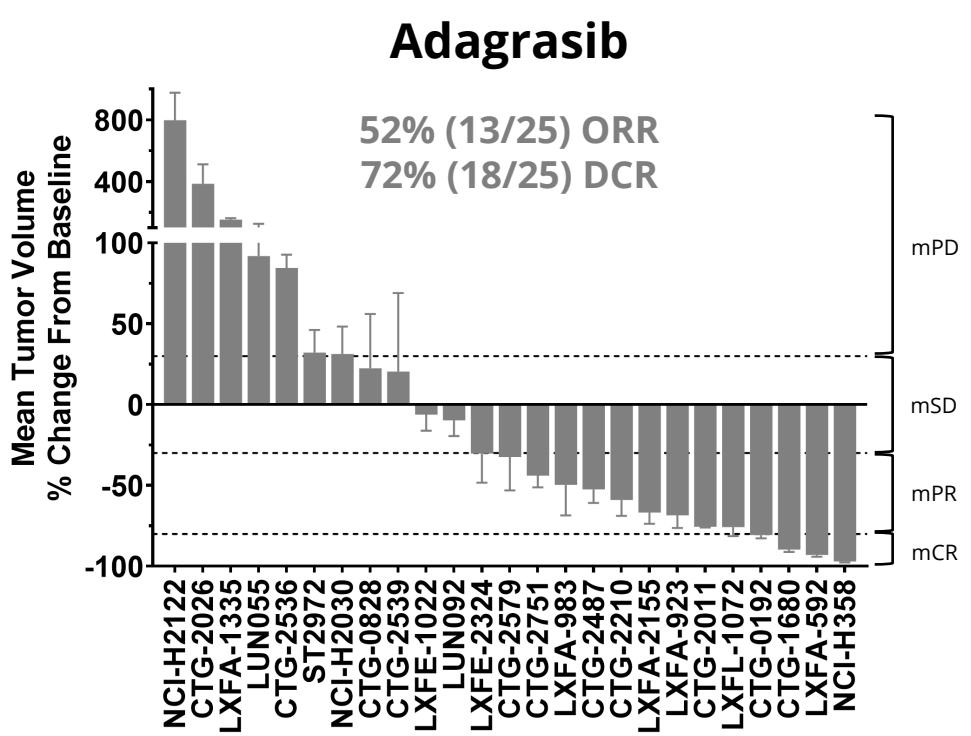
- Favorable *in vivo* oral bioavailability and clearance for effective target coverage in KRAS^{G12C}-addicted cancer cells

(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 Outcomes in Mouse Clinical Trial with KRAS^{G12C} NSCLC Models



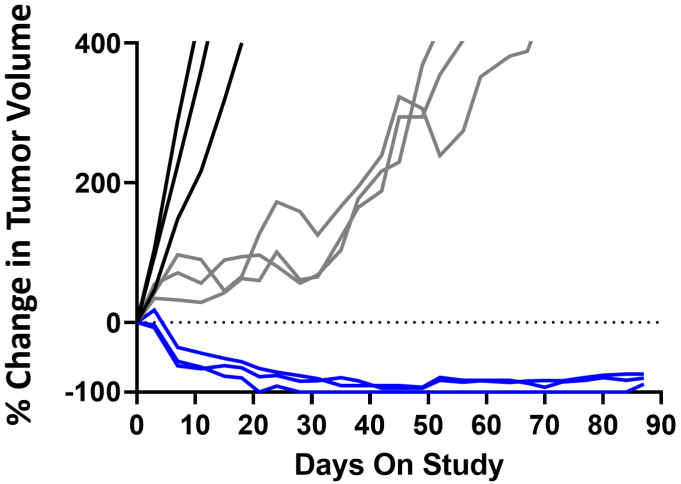


Best-in-Class Potential in KRAS^{G12C} NSCLC

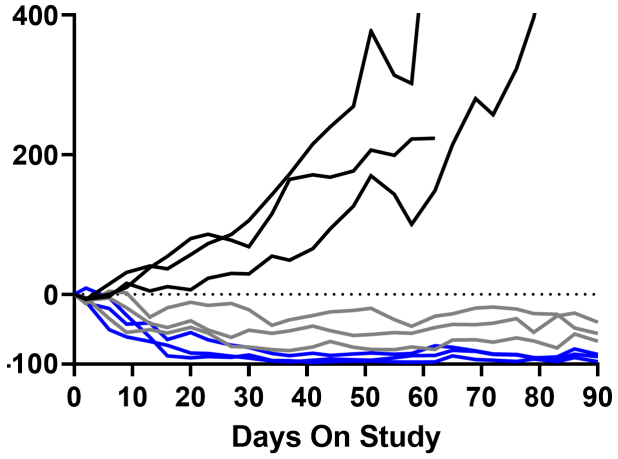
RVMD preclinical research as of 10/21/21
Adagrasib dosed at 100 mg/kg po qd; RMC-6291 dosed at 200 mg/kg po qd; n = 3 to 10/group
NSCLC = Non-small cell lung cancer
Responses assigned according to mRECIST (see appendix)

RMC-6291 May Improve on KRAS^{G12C}(OFF) Inhibitor Class Across Three Outcome Measures in NSCLC

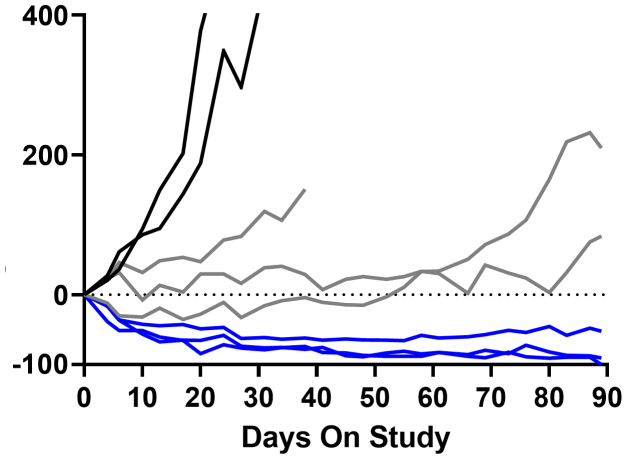
Increased Rate Of Response[(a)]



Increased Depth Of Response[(b)]



Increased Duration Of Response[(c)]



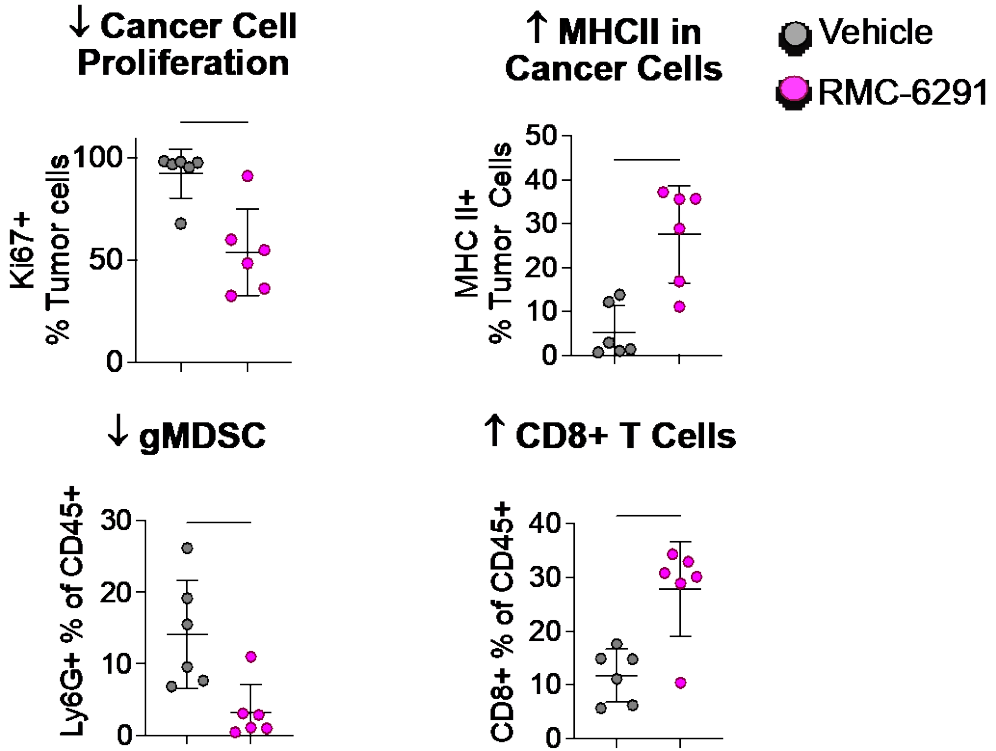
Control RMC-6291 Adagrasib

Best-in-Class Potential in KRAS^{G12C} NSCLC

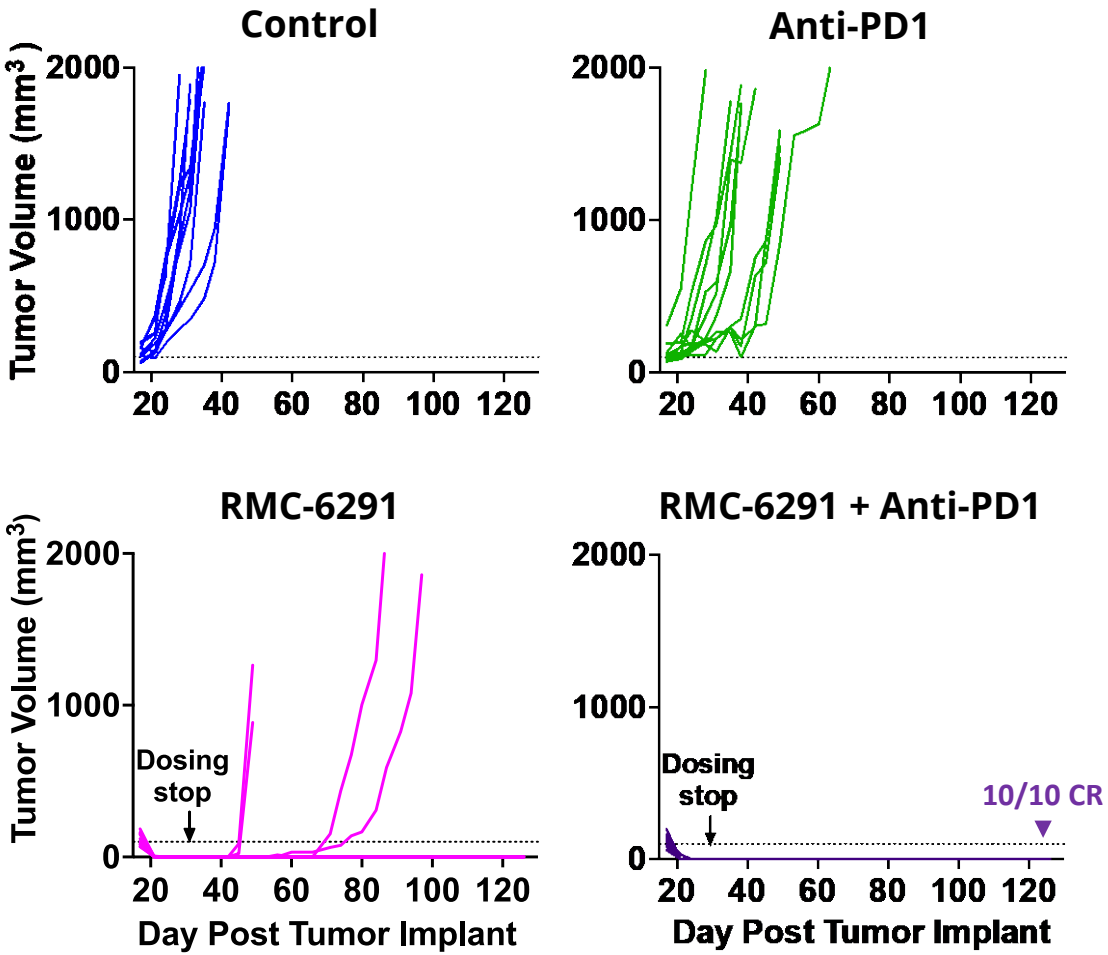
RVMD preclinical research as of 07/28/21
RMC-6291 dosed at 200 mg/kg po qd; Adagrasib dosed at 100 mg/kg po qd
NSCLC = Non-small cell lung cancer
PDX Models: (a) LUN055; (b) LXFA-983; (c) CTG-0828
Nichols. Targeting KRAS^{G12C}(ON) and Potential Application to Overcoming Drug Resistance in RAS-Addicted Tumors. RAS-Targeted Drug Development Summit. Sept. 22, 2021.

RMC-6291: Anti-Tumor Immunity *in Vivo* and Strong Additivity with Checkpoint Inhibitor

Favorable Transformation of Tumor Immune Microenvironment



Durable Complete Responses with Checkpoint Inhibitor Combination



RVMD preclinical research
Syngeneic tumor model with CT26 cell line engineered to express $KRAS^{G12C}$
RMC-6291 dosed at 100 mg/kg po for immuno-PD study; 200 mg/kg po qd for tumor volume study

RMC-6291: Clinical Priorities to Pursue Best-in-Class Activity Against KRAS^{G12C} Tumors

Activities (ongoing* or projected)

- Initiate single agent dose escalation in KRAS^{G12C} tumors^
- Include 'below MTD' expansion cohorts in select populations (e.g., NSCLC) during dose escalation
- Define RP2DS
- Single agent expansion cohorts in KRAS^{G12C} NSCLC and pancreatic cancer (RAS inhibitor naïve +/- failure)
- Combinations in KRAS^{G12C} NSCLC & CRC

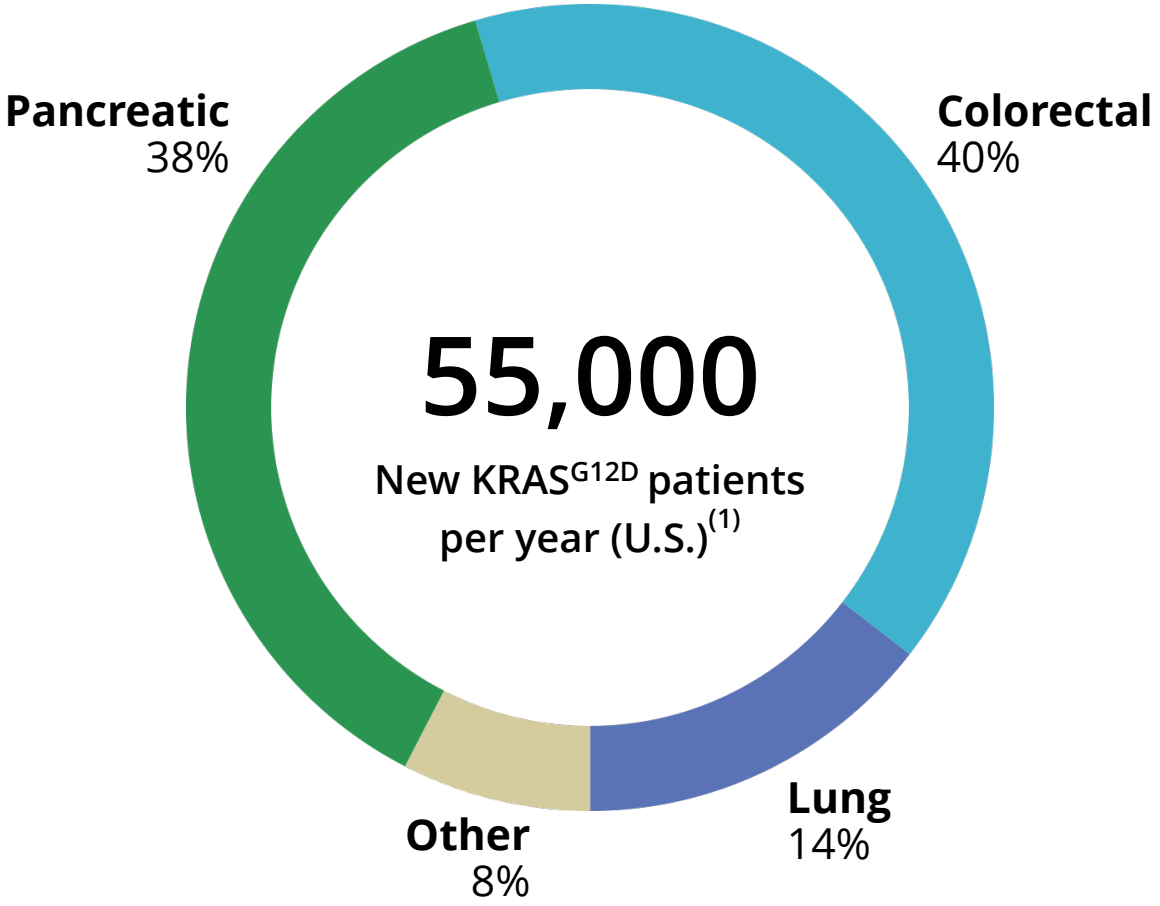
Aims

Preliminary evidence of superior activity against KRAS^{G12C} tumors^

^See Anticipated Milestones table

RP2DS = Recommended Phase 2 dose and schedule
MTD = maximum tolerated dose
NSCLC = non-small cell lung cancer; CRC = colorectal cancer

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

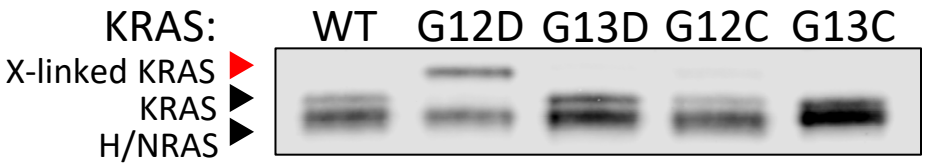
- Favorable *in vivo* oral bioavailability and clearance for effective target coverage in KRAS^{G12D}-addicted cancer cells

(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

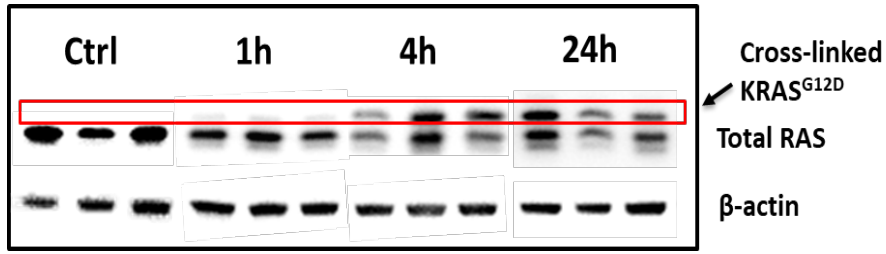
Characterization above is based on RVMD preclinical research

RMC-9805: Selective, Covalent and Orally Active with Sustained Inhibition of KRAS^{G12D} *in Vivo*

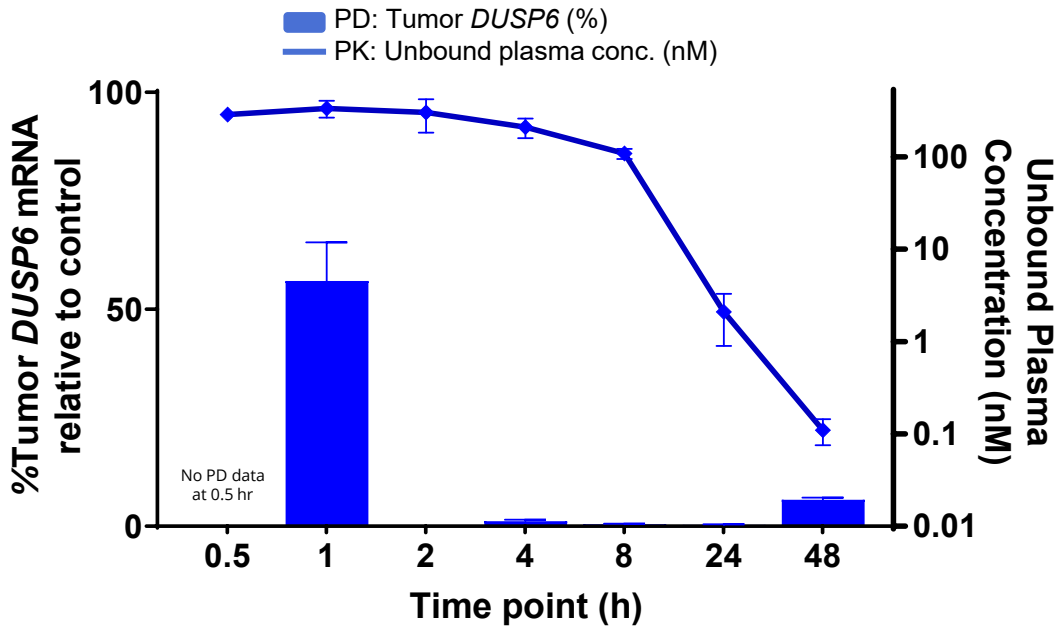
Selective Covalent Modification of KRAS^{G12D}



KRAS^{G12D} Target Engagement HPAC CDX (PDAC, KRAS$^{G12D/WT}$)



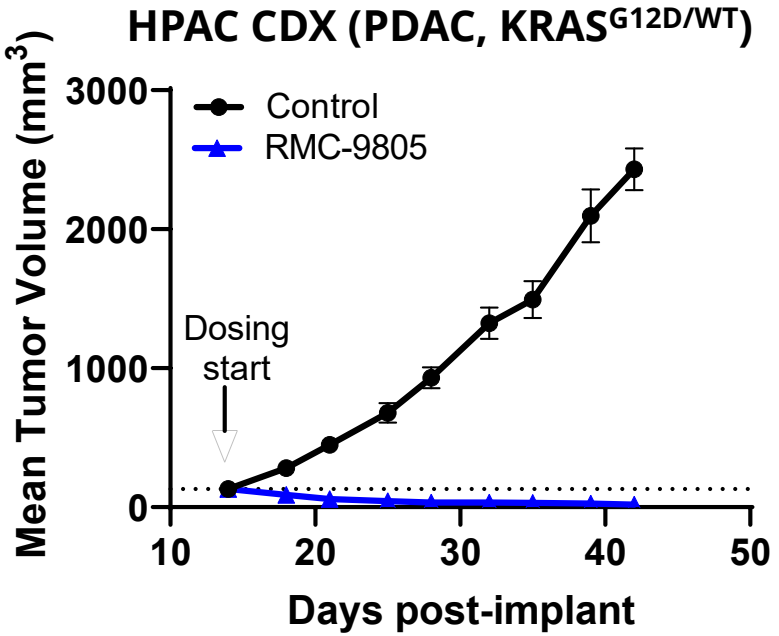
Single Dose PK/PD HPAC CDX (PDAC, KRAS$^{G12D/WT}$)

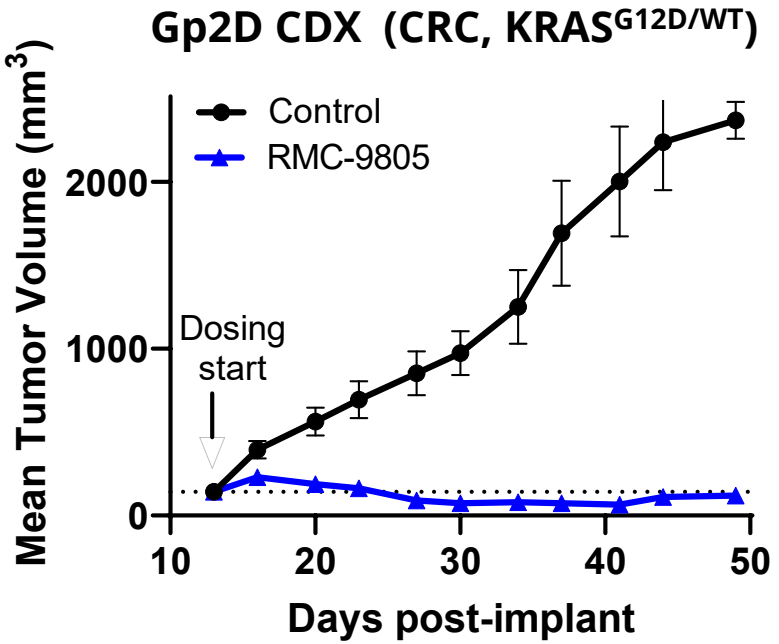


RVMD preclinical research
RMC-9805 dosed at 100 mg/kg po
PDAC = pancreatic ductal adenocarcinoma

RMC-9805: Tumor Regressions in Models of KRAS^{G12D} Cancers

- Designed as first-in-class mutant-selective covalent inhibitor of KRAS^{G12D}
- Deep and durable anti-tumor responses *in vivo* in pancreatic and colorectal cancer models
- Oral dosing, well tolerated

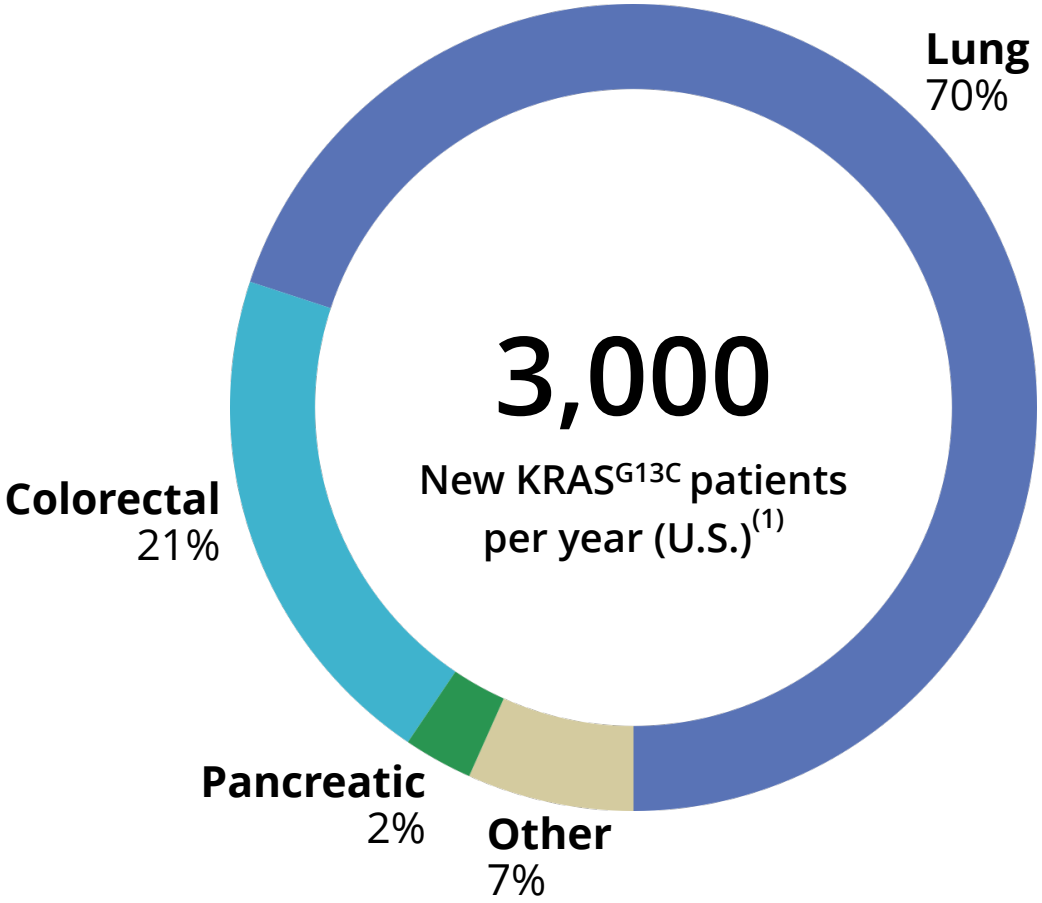




RVMD preclinical research

RMC-9805 dosed at 100 mg/kg po qd; n = 10/group (top), 6/group (bottom); PDAC = pancreatic ductal adenocarcinoma; CRC = colorectal cancer

RMC-8839: First-in-Class Mutant-Selective RAS(ON) Inhibitor for KRAS^{G13C} Cancers



Highly Potent and Selective RAS(ON) Inhibitor

- Highly active against KRAS^{G13C}
- 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^{G13C} lung cancers

Attractive PK/ADME Profile

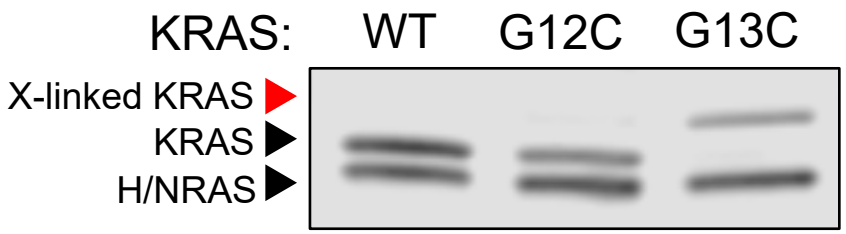
- Favorable *in vivo* oral bioavailability and clearance for effective target coverage in KRAS^{G13C}-addicted cancer cells

(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

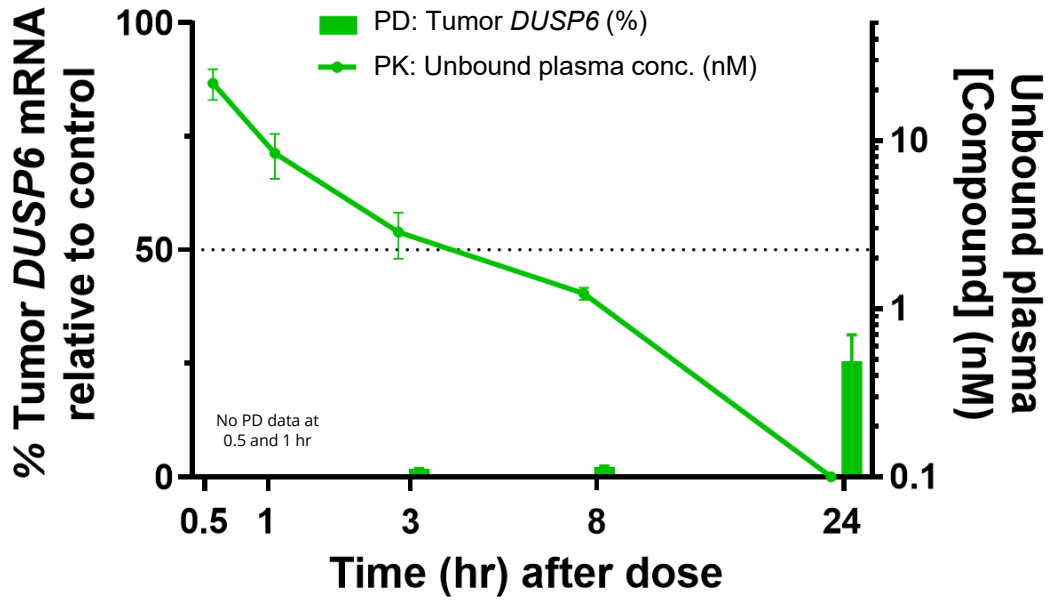
Characterization above is based on RVMD preclinical research

RMC-8839: Selective, Covalent and Orally Active with Sustained Inhibition of KRAS^{G13C} *in Vivo*

Selective Covalent Modification of KRAS^{G13C}



Single Dose PK/PD NCI-H1734 (NSCLC CDX, KRAS^{G13C})

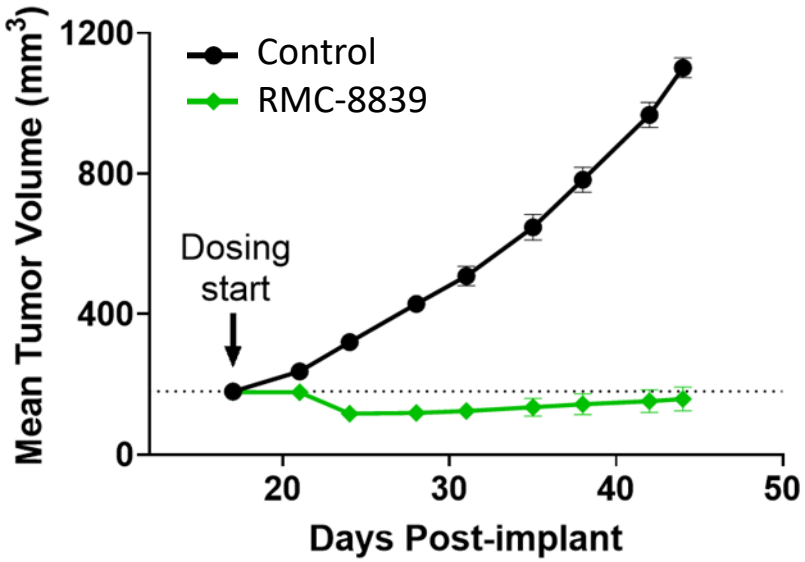


RVMD preclinical research
RMC-8839 dosed at 100 mg/kg po
NSCLC = non-small cell lung cancer

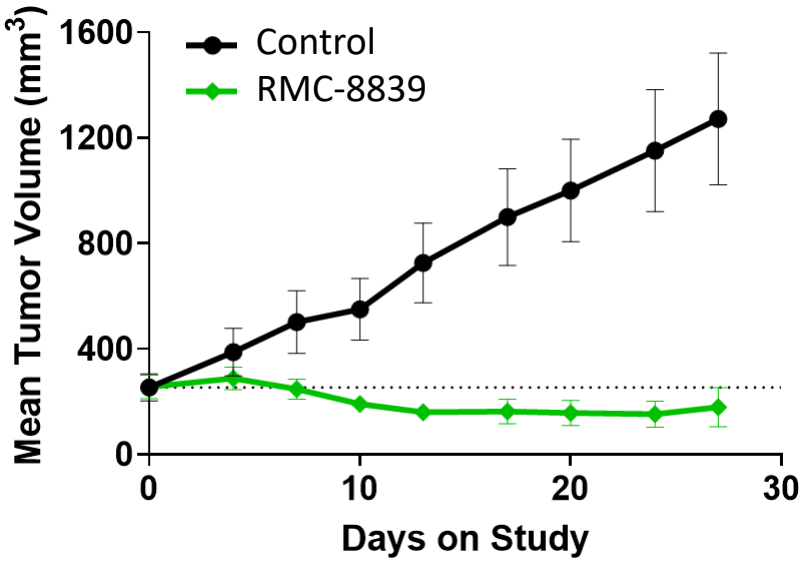
RMC-8839: Tumor Regressions in Models of KRAS^{G13C} Cancers

- Designed as first-in-class mutant-selective covalent inhibitor of KRAS^{G13C}
- Deep anti-tumor responses *in vivo* in non-small cell lung cancer models
- Oral dosing, well tolerated

NCI-H1734 CDX (NSCLC, KRAS$^{G13C/WT}$)



ST2822B PDX (NSCLC, KRAS$^{G13C/WT}$)

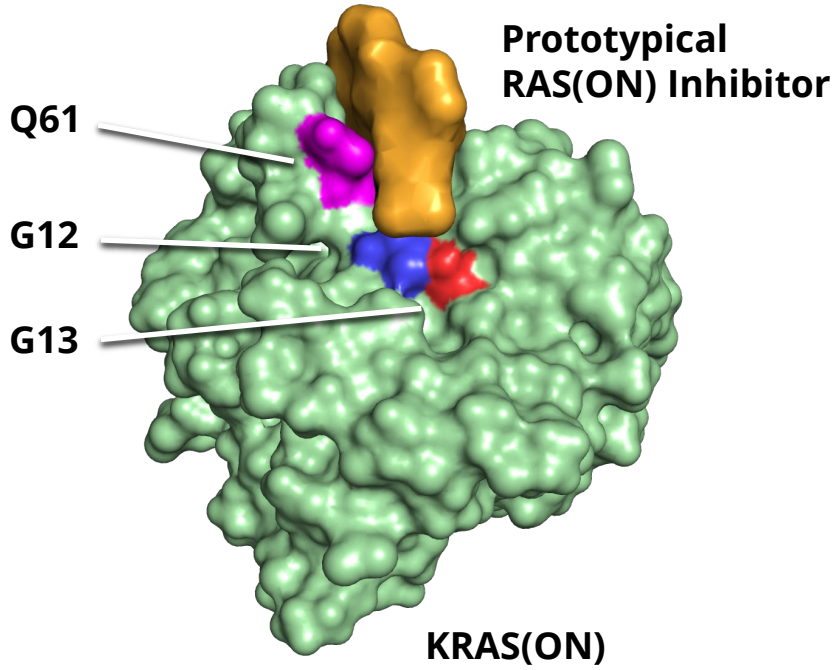


RVMD preclinical research

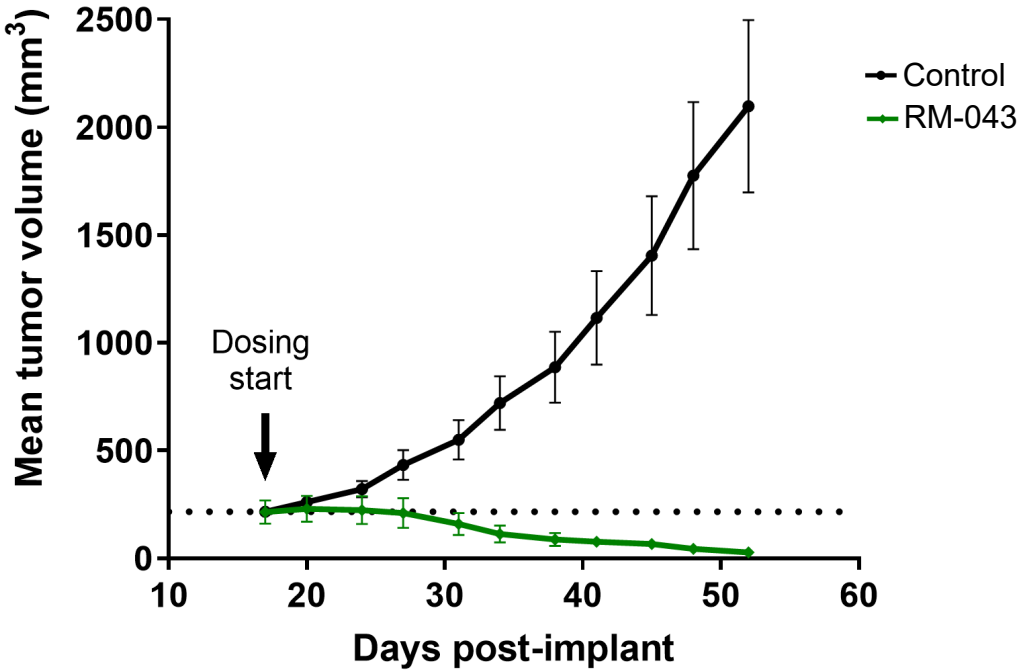
RMC-8839 dosed at 100 mg/kg po qd; n = 5/group; NSCLC = Non-small cell lung cancer

Pipeline Expansion Programs Include Oral, Potent, Selective, Non-Covalent Inhibitors of KRAS^{Q61H}(ON)

RAS(ON) Inhibitor Binding Geometry Enables Targeting of All Three Mutational Hotspots



Hs766T CDX (PDAC, KRAS$^{Q61H/Q61H}$)



RVMD preclinical research
RM-043 dosed at 10 mg/kg po qd; n = 10/group

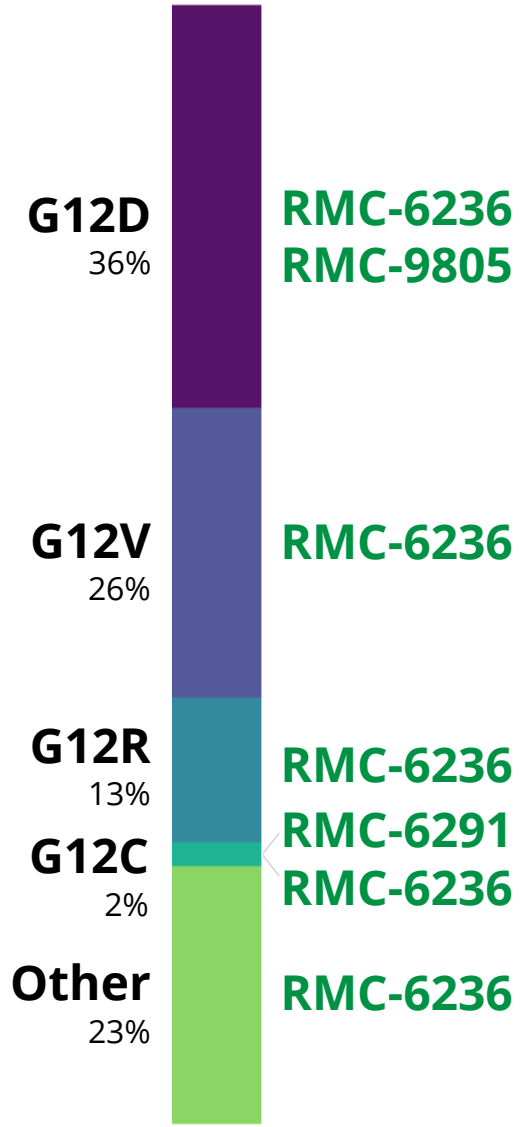
On Target to Outsmart
Pancreatic Cancer

Devastating disease
>90% driven by KRAS mutations

49,000

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

Dismal survival rates
No approved targeted therapies



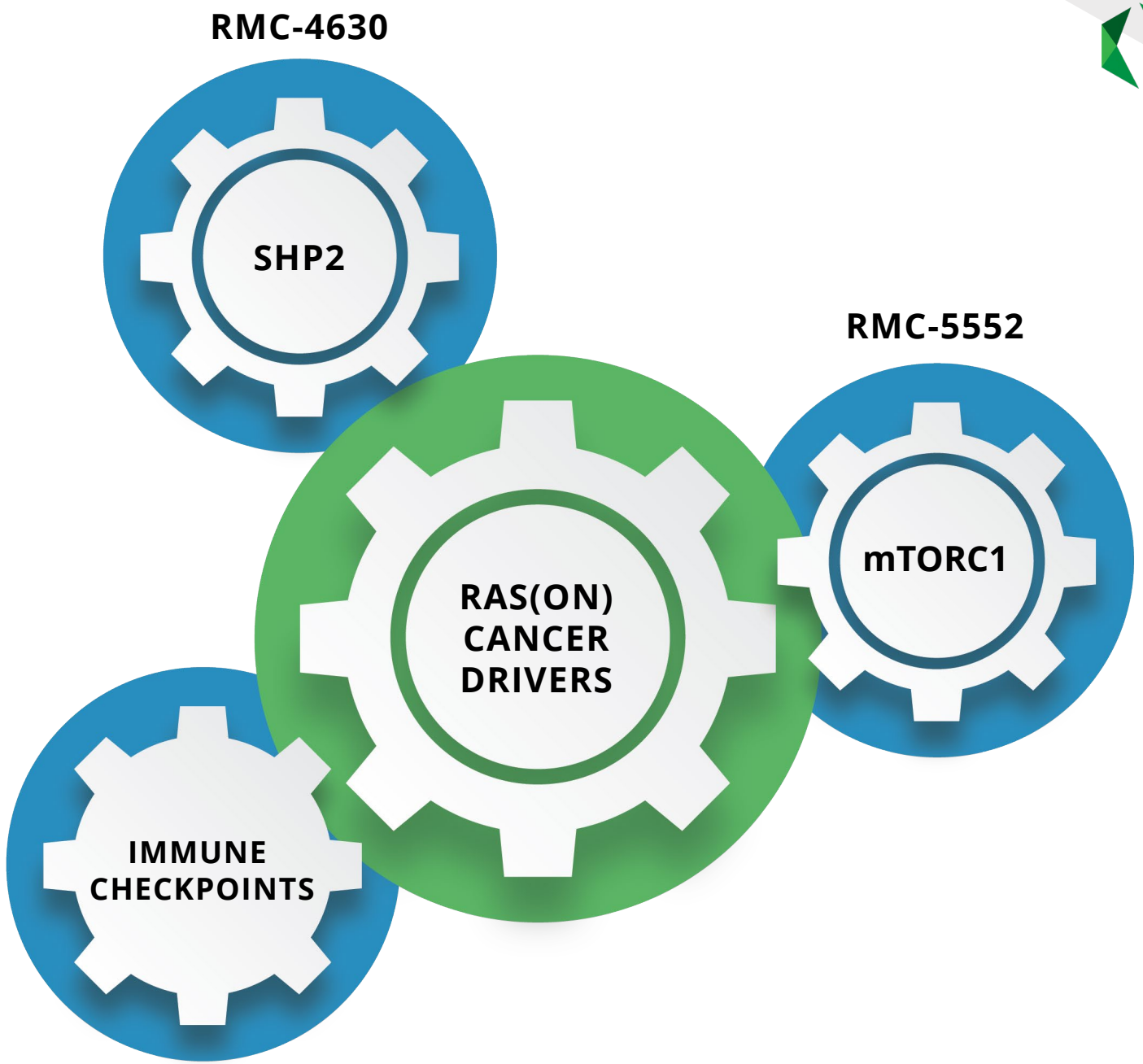
Our development-stage RAS(ON) Inhibitors

- Inhibit >90% of pancreatic cancer drivers in cancer models[1]
- Exhibit strong anti-tumor activity in preclinical models of pancreatic cancer

(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)

RAS Companion Inhibitors

Suppress Cooperating Targets and Pathways that Sustain RAS-Addicted Cancers



RMC-4630: Ongoing and Planned Clinical Combination Studies

STUDY	SPONSOR	COMBINED WITH	INDICATION(S)	STATUS
CodeBreaK 101c (U.S.)	Amgen	sotorasib	2L+ $KRAS^{G12C}$ solid tumors	Ongoing (Phase 1b)
RMC-4630-03 (Global)	RevMed	sotorasib	2L+ $KRAS^{G12C}$ NSCLC	Ongoing (Phase 2)
TCD16210 (Global)	Sanofi	adagrasib	2L+ $KRAS^{G12C}$ NSCLC	In preparation (Phase 1/2)
TBD	RevMed	RMC-6291	$KRAS^{G12C}$ TBD	Planning
TCD16210 (Global)	Sanofi	pembrolizumab	1L $PDL1^{+}$ NSCLC	Ongoing (Phase 2)

sanofi RMC-4630/SAR442720 under 2018 partnership

NSCLC = non-small cell lung cancer

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

"Promising clinical activity was observed"[1] in **CodeBreaK101c**

21 KRAS^{G12C} patients in dose/schedule exploration (all solid tumors, 100-200 mg twice weekly)[2]

"The combination of sotorasib with RMC-4630 was safe and tolerable"[1]

75%/ 100% ORR/DCR among KRAS^{G12C} inhibitor-naïve NSCLC patients treated at top two doses of RMC-4630 (n=4)

+ One patient with progression on sotorasib monotherapy achieved an unconfirmed PR on RMC-4630 combo

https://clinicaltrials.gov/ct2/show/NCT04185883

Currently enrolling patients in **RMC-4630-03**

- Global Phase 2 study of sotorasib + RMC-4630 to complement NSCLC findings of CodeBreaK101c
- Exclusively KRAS^{G12C} inhibitor-naïve NSCLC patients
- Focused on top two doses of RMC-4630 from CodeBreaK101c:
  - 140 and 200 mg D1D2 weekly
- Patients stratified into two cohorts: KRAS^{G12C} +/- co-mutations such as KEAP1 or STK11

https://clinicaltrials.gov/ct2/show/NCT05054725

(1) 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.
(2) Patients were treated with sotorasib (960 mg QD) and RMC-4630, with escalating dose levels of 100 mg, 140 mg, or 200 mg at days 1 and 2 or days 1 and 4 every 7 days. Pharmacokinetic analysis demonstrated that average sotorasib and RMC-4630 exposures were consistent with distributions observed in monotherapy studies, with no clinically meaningful drug-drug interactions noted.
ORR = objective response rate
DCR = disease control rate

RMC-4630: Clinical Priorities to Pursue Best-in-Class Combination Activity in KRAS^{G12C} Tumors

Activities (ongoing* or projected)

- Continue enrollment in RMC-4630-03*
- Registration study in combination with KRAS^{G12C}(OFF) inhibitor in KRAS^{G12C} NSCLC
- Combination study(ies) with KRAS^{G12C}(OFF) inhibitor in KRAS^{G12C} CRC and/or pancreatic cancer
- Combination study(ies) with RMC-6291

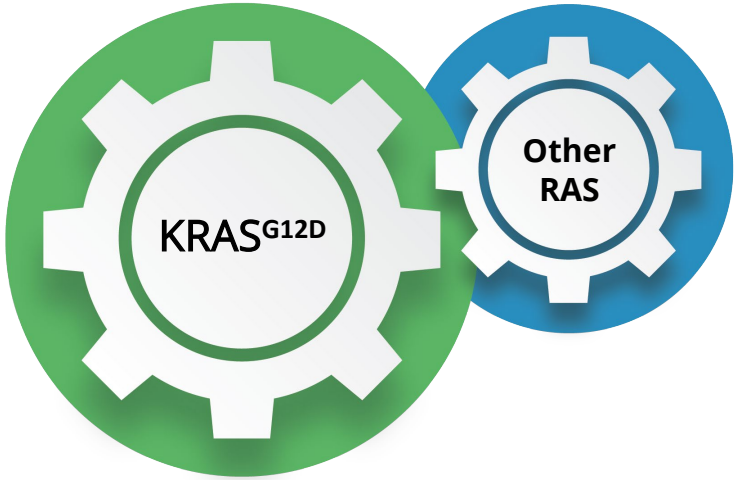
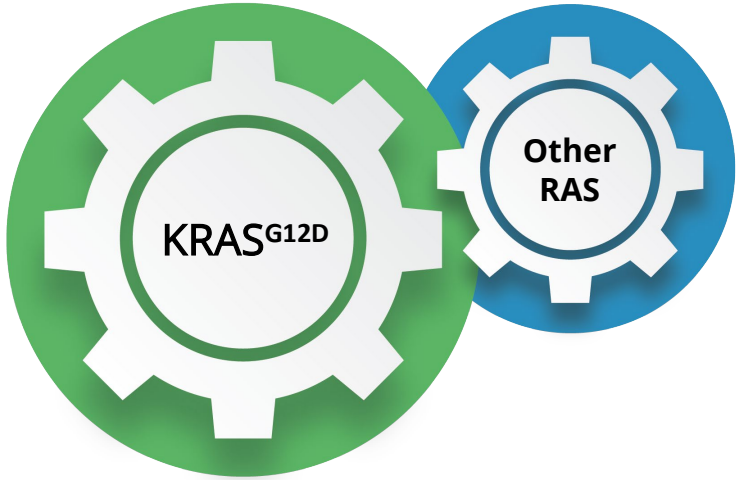
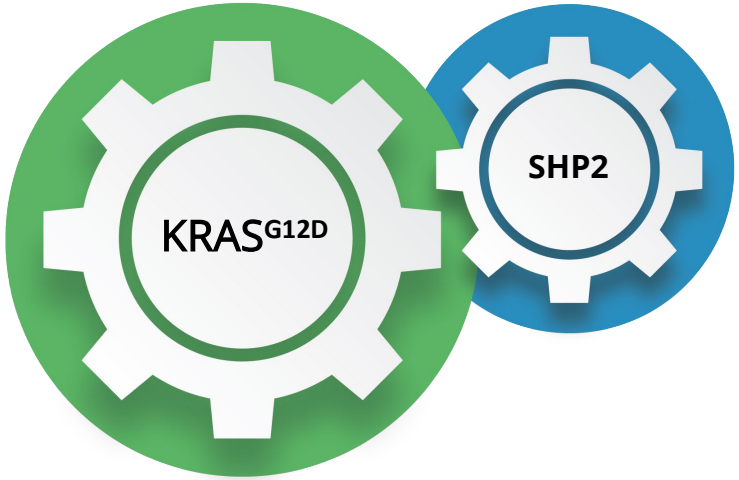
Aims

Evidence of clinical benefit as RAS Companion Inhibitor against KRAS^{G12C} NSCLC
Evidence of clinical benefit as a RAS Companion Inhibitor against additional KRAS^{G12C} tumors

NSCLC = non-small cell lung cancer
CRC = colorectal cancer

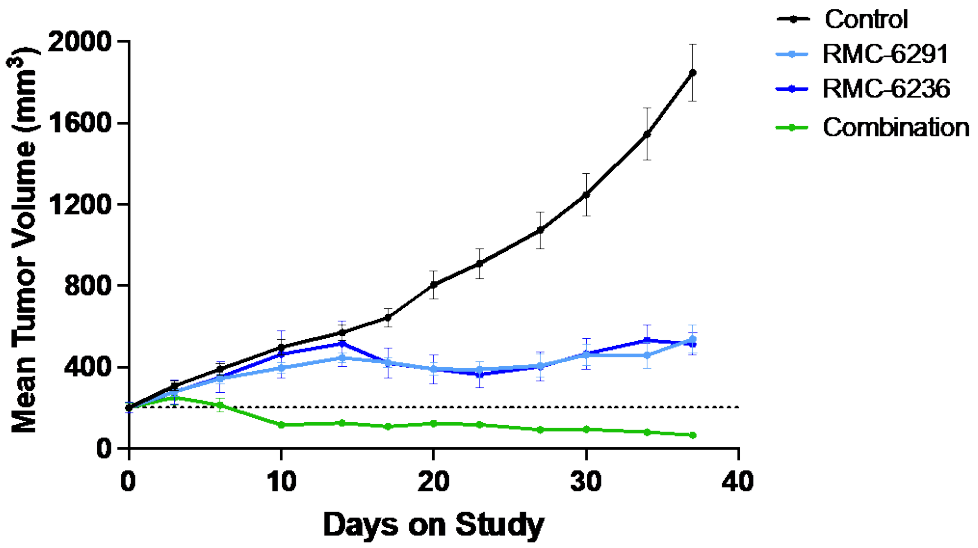
Parallel Treatment Strategies to Outsmart Diverse RAS Inhibitor Resistance Mechanisms

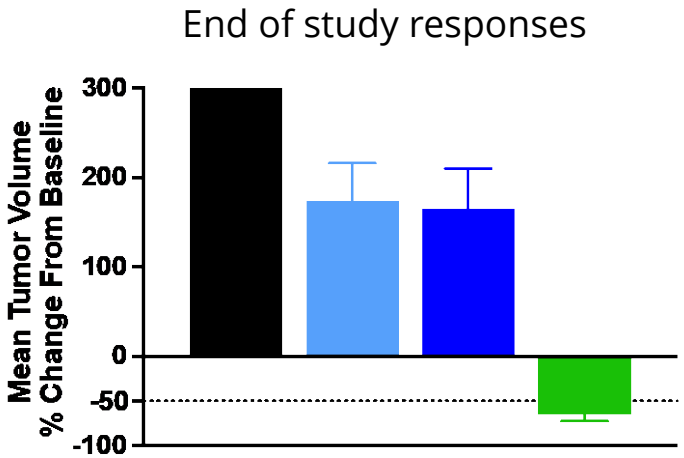
EXAMPLES

RESISTANCE PARADIGMS		
		
TREATMENT STRATEGIES		
RMC-6236	**RMC-9805 + RMC-6236**	**RMC-9805 + RMC-4630**
ALL-IN-ONE	***MAXIMAL DOSING FLEXIBILITY***	***MAXIMAL DOSING FLEXIBILITY***

RMC-6291 + RMC-6236 Combination Induces Tumor Regressions in a Relatively Resistant Model of KRAS^{G12C} CRC

CRC022 PDX (CRC, KRAS$^{G12C/WT}$)

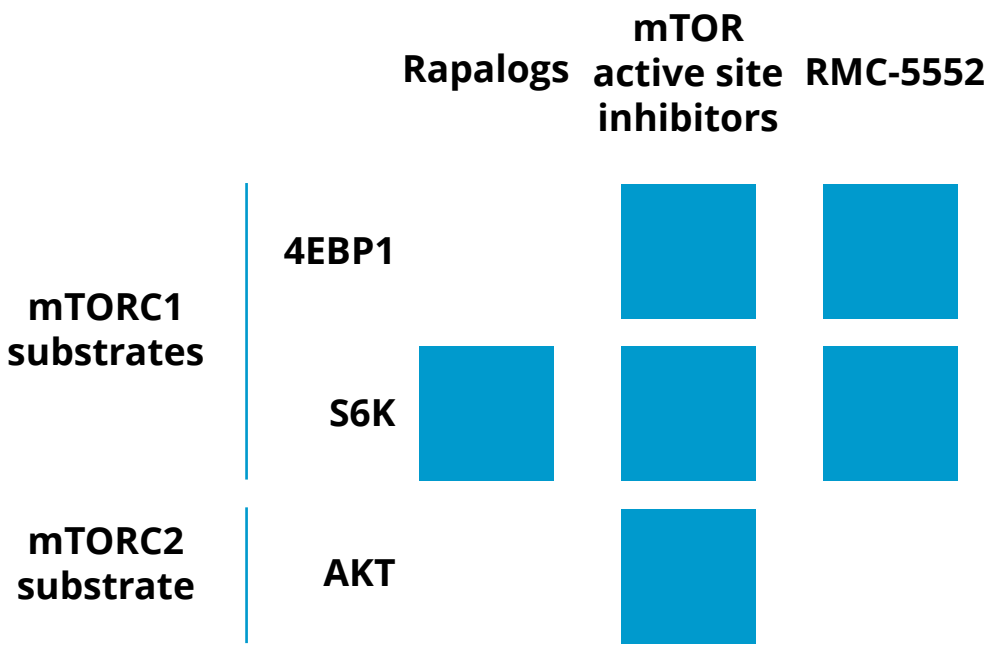




RAS^{MULTI}(ON) Inhibitor Deployed as a RAS Companion Inhibitor

RVMD preclinical research
RMC-6291 dosed at 100 mg/kg po qd; RMC-6236 dosed at 25 mg/kg po qd
Control and RMC-6291 - n = 8/group; RMC-6236 and Combination, n = 3/group; CRC = colorectal cancer

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



Highly Potent and Selective mTORC1 Inhibitor

- Bi-steric structure combines favorable features of rapalogs and active site inhibitors
- Capable of reactivating the tumor suppressor 4EBP1
- Selective over mTORC2, low off-target risk

Robust Anti-tumor Activity in Cancer Models

- Rapid, deep and sustained inhibitor of mTORC1 drives durable regressions in mTOR pathway cancers

Attractive PK/ADME Profile

- Favorable *in vivo* exposure following IV dosing for effective target coverage in mTORC1-dependent cancer cells

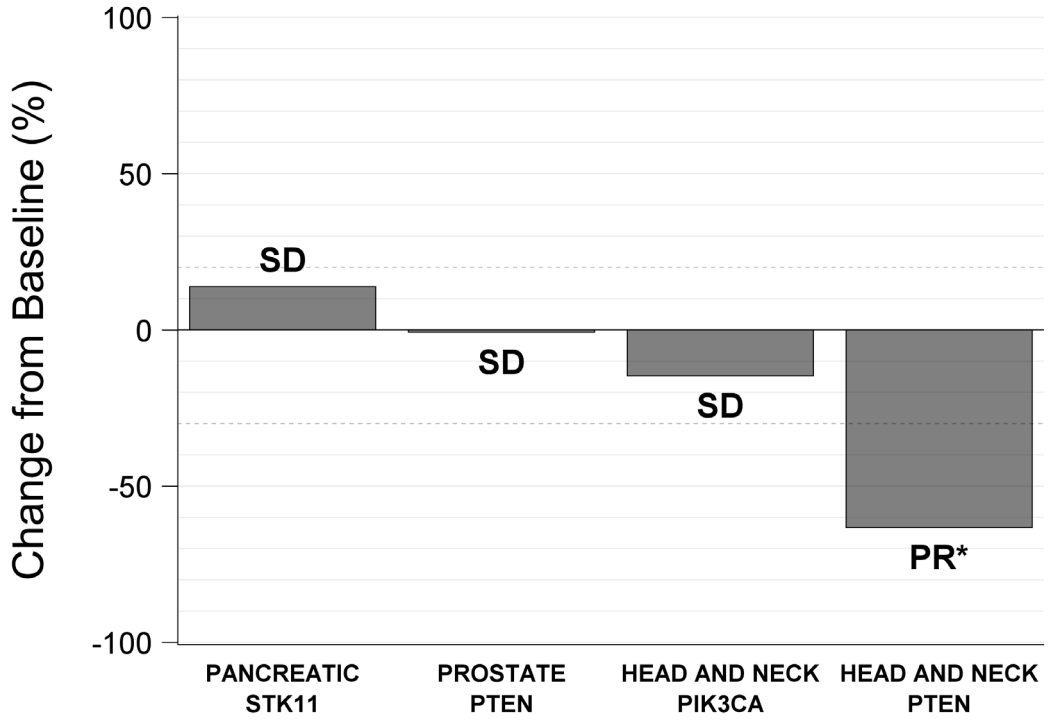
Characterization above is based on RVMD preclinical research

RMC-5552 Clinical Opportunity

- Potent, selective inhibitor of hyperactivated mTORC1 to reactivate the tumor suppressor 4EBP1
- Designed for combination with RAS(ON) inhibitors in patients with cancers harboring RAS/mTOR pathway co-mutations(1)
  - >30,000 new patients per year across lung, colorectal and pancreatic cancers (U.S.)(2)
- Single agent Phase 1b dose escalation underway, focused on tumor genotypes linked to hyperactivated mTORC1 signaling

Preliminary Evidence of Clinical Activity

Best Tumor Change in Efficacy Evaluable Patients Treated with 6 mg IV Weekly(3)



(1) mTOR pathway co-mutations include genetic changes with likely oncogenic activity in one or more of PIK3CA, PTEN, TSC1, TSC2, STK11, and/or mTOR
(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

(3) Preliminary assessments suggest mucositis as the major dose-limiting toxicity. 6 mg weekly was well tolerated. Further enrollment at doses above 6 mg is ongoing to define the RP2DS; *Patient received one dose of 12 mg, followed by weekly doses of 6 mg. Data as of 01/07/2022.

RMC-5552: Clinical Priorities to Pursue Best-in-Class Combination Activity in RAS^{MUTANT}/mTORC1-Activated Tumors

Activities (ongoing* or projected)

- Continue dose optimization and identify RP2DS*
- Initiate single agent expansion cohorts in select tumors with mTOR pathway mutations
- Combinations with RAS(ON) inhibitors from our portfolio in RAS^{MUTANT} tumors with mTOR pathway co-mutations

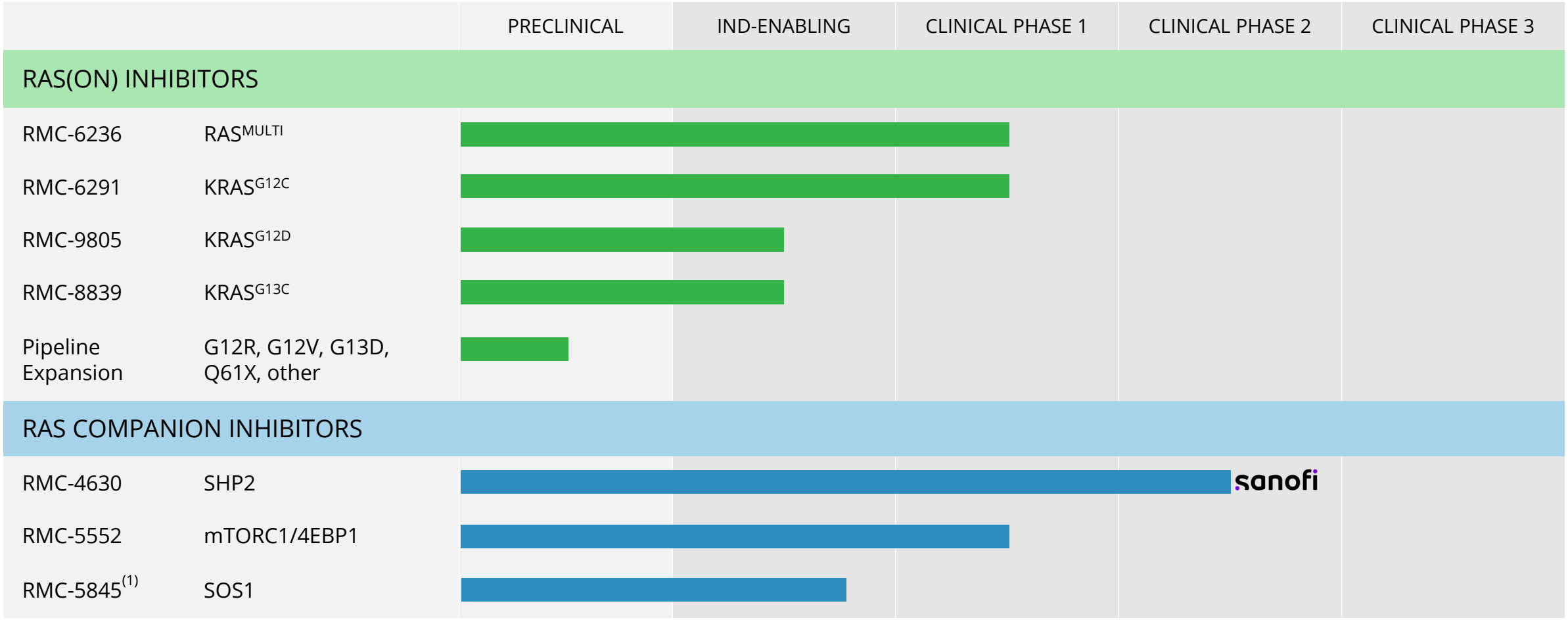
Aims

Additional evidence of single agent activity against tumors with mTOR pathway mutations^

^See Anticipated Milestones table

RP2DS = Recommended Phase 2 dose and schedule

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



(1) IND-ready

Anticipated Milestones

PROGRAM	MILESTONE (EXPECTED TIMING)
RAS(ON) INHIBITORS	
RMC-6236 (RAS^{MULTI})	Provide evidence of first-in-class single agent activity (2023)
RMC-6291 ($KRAS^{G12C}$)	Announce dosing of first patient (2H22); Provide preliminary evidence of superior activity (2023)
RMC-9805 ($KRAS^{G12D}$)	Announce dosing of first patient (mid-2023)
RMC-8839 ($KRAS^{G13C}$)	Announce dosing of first patient (late 2023 or early 2024)
Additional RAS^{MUTANT}-Selective Inhibitor	Nominate development candidate (2H22)
RAS COMPANION INHIBITORS	
RMC-4630 (SHP2)	Provide topline data from RMC-4630-03 (2023)
RMC-5552 (mTORC1/4EBP1)	Provide additional evidence of single agent activity (2023)

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(K,L,R,P), HRAS mutations of known/likely function, 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.
  - 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
- $KRAS^{G12X}$ includes $KRAS^{G12D}$, $KRAS^{G12V}$, $KRAS^{G12R}$ and $KRAS^{G12C}$
- Mouse tumor responses on slides 9 and 14 assigned according to mRECIST (modified from Gao et al. Nat Med. 2015):
  - mPD = progressive disease; mSD = stable disease; mPR = partial response; mCR = complete response
- Kaplan-Meier progression on slide 10 defined as tumor doubling from baseline over 28 days:
  - $KRAS^{G12X}$ Tumors, where X = D,V,C, A or R: n = 207
  - RAS Pathway Mutant Tumors includes $KRAS^{G12X}$ and other RAS and RAS pathway mutant tumors: $KRAS^{G13C}$, $KRAS^{G13D}$, $KRAS^{K117N}$, $KRAS^{Q61H}$, $NF1^{LOF}$, $PTPN11^{E76K\ or\ G503V}$, $BRAF^{Class\ 3\text{-}mutant}$, and $KRAS^{WT\text{-}Amp}$: n = 332
- PDX = patient-derived xenograft; CDX = cell line-derived xenograft
- PK = pharmacokinetic; ADME = absorption, distribution, metabolism, and excretion