UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): January 10, 2023

Revolution Medicines, Inc.

(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-39219**	**47-2029180**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**
700 Saginaw Drive **Redwood City, California** **(Address of Principal Executive Offices)**		**94063** **(Zip Code)**

Registrant's Telephone Number, Including Area Code: 650 481-6801

Not applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock $0.0001 Par Value per Share	RVMD	The NASDAQ Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 2.02 Results of Operations and Financial Condition.

On January 10, 2023, Revolution Medicines, Inc. (the "Company") confirmed to investors that it continues to expect that its net loss for the year ended December 31, 2022 to be between $245 million and $265 million, which includes estimated non-cash stock-based compensation expense of approximately $30 million to $35 million.

The information furnished under this Item 2.02 of this Current Report on Form 8-K shall not be deemed "filed" under the Securities Act of 1934, as amended (the "Exchange Act"), nor shall it be incorporated by reference into any future filings under the Securities Act of 1933, as amended (the "Securities Act"), or under the Exchange Act unless the Company expressly sets forth in such future filing that such information is to be considered "filed" or incorporated by reference therein.

Item 7.01 Regulation FD Disclosure.

On January 10, 2023, the Company provided a corporate presentation relating to its research and development programs by posting an additional corporate presentation to the investor section of the Company's website at: ir.revmed.com/events-and-presentations. The Company's additional corporate presentation is attached hereto as Exhibit 99.1.

The furnishing of the attached presentation is not an admission as to the materiality of any information therein. The information contained in the slides is summary information that is intended to be considered in the context of more complete information included in the Company's filings with the U.S. Securities and Exchange Commission (the "SEC") and other public announcements that the Company has made and may make from time to time by press release or otherwise. The Company undertakes no duty or obligation to update or revise the information contained in this Current Report on Form 8-K, although it may do so from time to time as its management believes is appropriate. Any such updating may be made through the filing of other reports or documents with the SEC, through press releases or through other public disclosures. For important information about forward looking statements, see the slide titled "Legal Disclaimer" in Exhibit 99.1 attached hereto.

The information furnished under this Item 7.01 and in the presentation attached as Exhibit 99.1 to this Current Report on Form 8-K shall not be deemed "filed" for purposes of Section 18 of the Exchange Act or otherwise subject to the liabilities of that section or Sections 11 or 12(a)(2) of the Securities Act. The information contained in this Item 7.01 and in the presentation attached as Exhibit 99.1 to this Current Report on Form 8-K shall not be incorporated by reference into any filing with the SEC made by the Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

Forward-Looking Statements

This Current Report on Form 8-K contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995. Any statements in this report that are not historical facts may be considered "forward-looking statements," including, without limitation, statements regarding the Company's expected net loss and stock-based compensation expense. Forward-looking statements are typically, but not always, identified by the use of words such as "may," "will," "would," "believe," "intend," "plan," "anticipate," "estimate," "expect" and other similar terminology indicating future results. Such forward-looking statements are subject to substantial risks and uncertainties that could cause the Company's development programs, future results, performance or achievements to differ materially from those anticipated in the forward-looking statements. Such risks and uncertainties include, without limitation, risks and uncertainties inherent in the drug development process, including the Company's programs' early stage of development, the process of designing and conducting preclinical and clinical trials, the regulatory approval processes, the timing of regulatory filings, the challenges associated with manufacturing drug products, the Company's ability to successfully establish, protect and defend its intellectual property, other matters that could affect the sufficiency of the Company's capital resources to fund operations, reliance on third parties for manufacturing and development efforts, changes in the competitive landscape and the effects on the Company's business of the COVID-19 pandemic, global events and other macroeconomic conditions. 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 the Company in general, see the Company's Quarterly Report on Form 10-Q filed with the SEC on November 7, 2022, and its future periodic reports to be filed with the SEC. Except as required by law, the Company undertakes no obligation to update any forward-looking statements to reflect new information, events or circumstances, or to reflect the occurrence of unanticipated events.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Company presentation dated January 10, 2023.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

REVOLUTION MEDICINES, INC.

Date: January 10, 2023

By: /s/ Mark A. Goldsmith
Mark A. Goldsmith, M.D., Ph.D.
President and Chief Executive Officer


REVOLUTION
MEDICINES
January 10, 2023
On Target to Outsmart Cancer™
© 2023 Revolution Medicines

Legal Disclaimer

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act. All statements other than statements of historical facts contained in this presentation, including statements regarding our future results of operations and financial position, business strategy, prospective products, availability of funding, ability to manage existing collaborations and establish new strategic collaborations, licensing or other arrangements, the scope, progress, results and costs of developing our product candidates or any other future product candidates, the potential market size and size of the potential patient populations for our product candidates, the timing and likelihood of success of obtaining product approvals, plans and objectives of management for future operations, the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates, future results of anticipated products, and the impact of the COVID-19 pandemic on our business are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. The information included in these materials is provided as of January 10, 2023 and is qualified as such. Except as required by applicable law, we undertake no obligation to update any forward-looking statements or other information contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

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 7, 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.

The fiscal year 2022 financial information contained in this presentation is preliminary and subject to completion of our financial closing and other operational procedures, final adjustments and review by our independent auditors.

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]

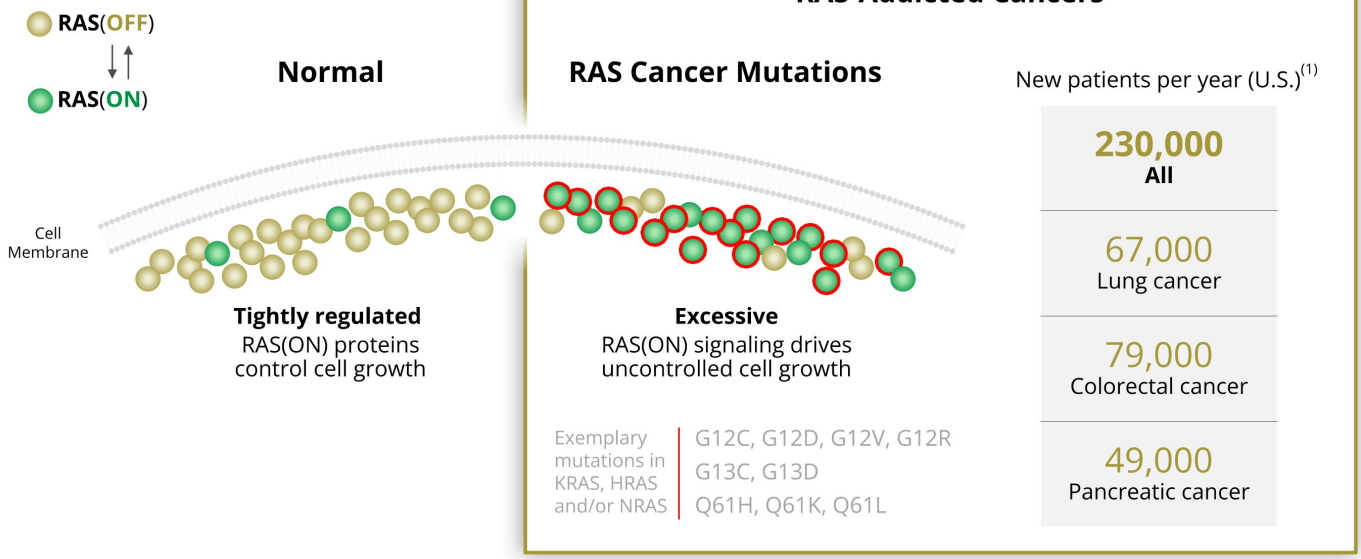
DEEP, SCIENCE-DRIVEN CLINICAL AND PRECLINICAL PIPELINE

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

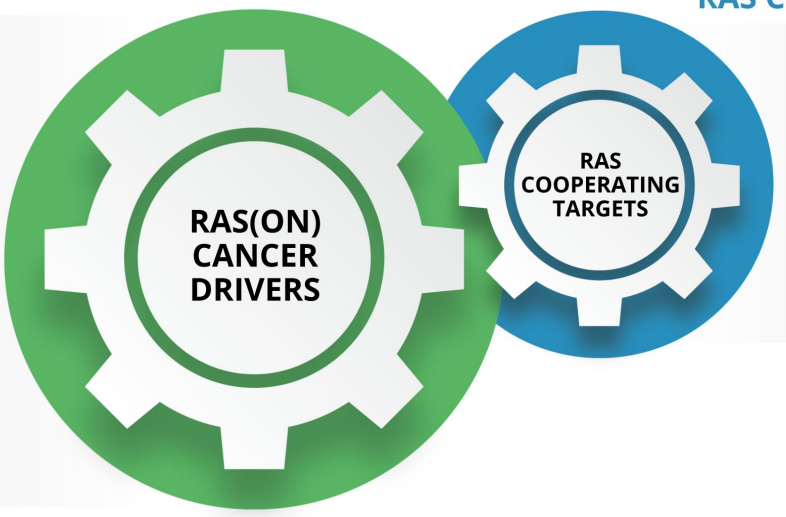


(1) Estimated using tumor mutation frequencies from Foundation Medicine Insights August 2020 and scaled to estimated patient numbers using cancer incidence from ACS *Cancer Facts and Figures* 2020 (see appendix for additional detail); lung cancer = non-small cell lung cancer

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

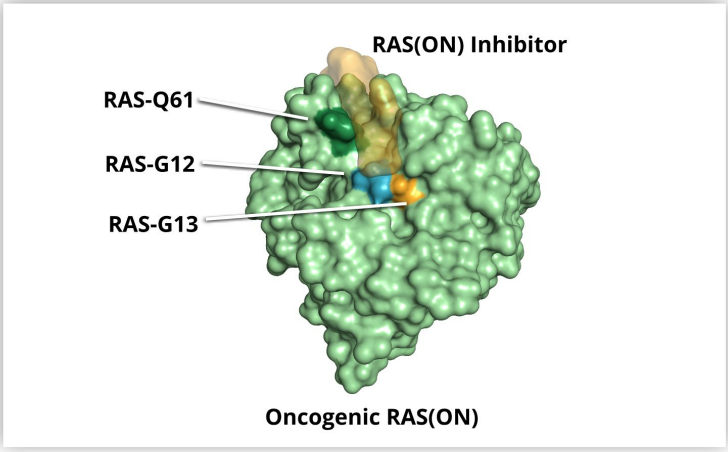


RAS Companion Inhibitors

- 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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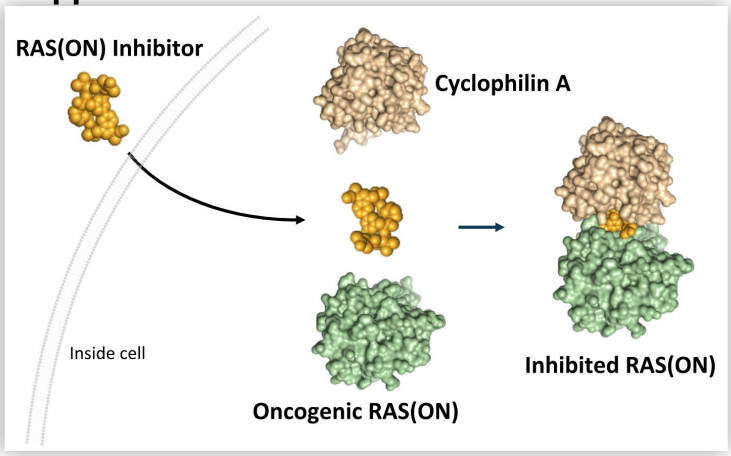


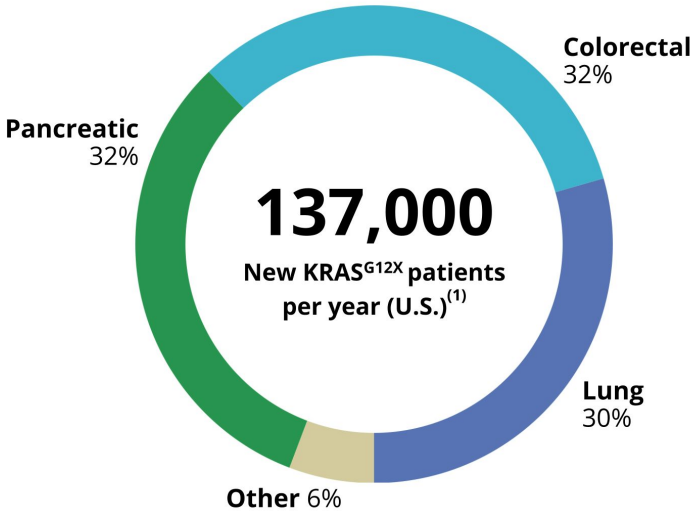
- **Potent, selective, oral and drug-like inhibitors**
- **Deep and sustained suppression of RAS(ON) cancer signaling**

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

Relative Frequency in Human RAS Cancers[1]

(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: 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

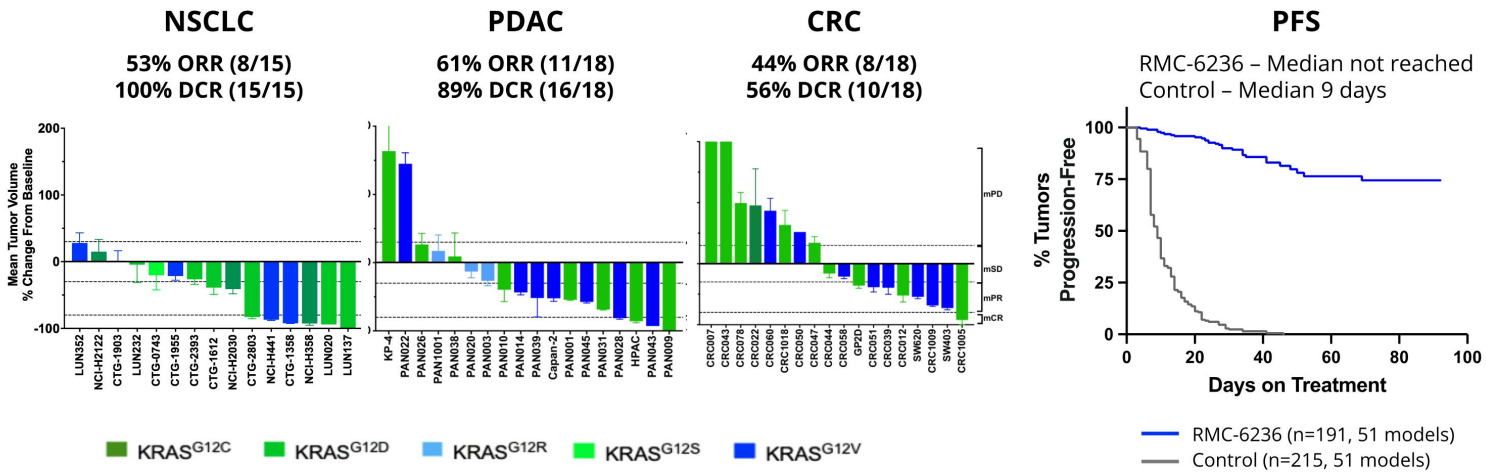
Attractive PK/ADME Profile

- 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



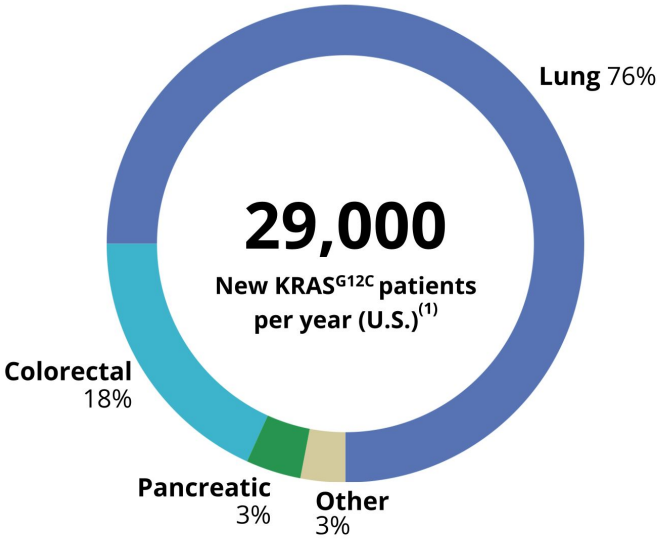
RVMD preclinical research as of 06/01/22
RMC-6236 dosed at 25 mg/kg po qd; n=1-10/group
Progression defined as tumor doubling from baseline
NSCLC = non-small cell lung cancer; PDAC = pancreatic ductal adenocarcinoma; CRC = colorectal cancer
Responses assigned according to mRECIST (see appendix)
ORR = 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 - 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; RP2DS = recommended Phase 2 dose and schedule; ctDNA = circulating tumor DNA

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

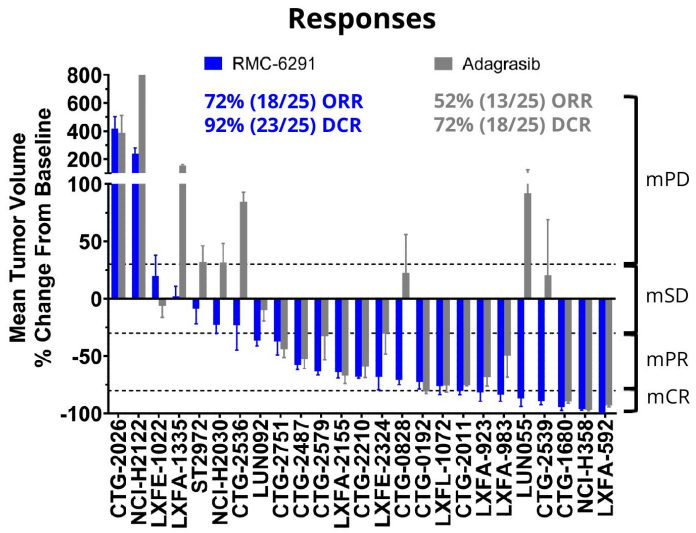
Attractive PK/ADME Profile

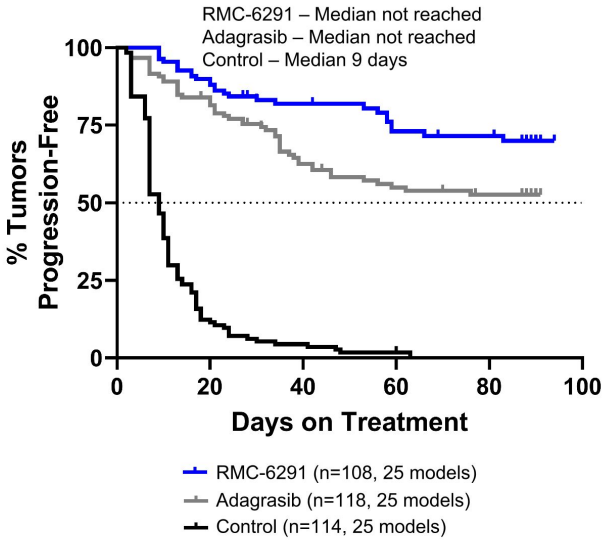
- Favorable *in vivo* oral bioavailability and clearance for effective target coverage in KRAS^{G12C}-addicted cancer cells

(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





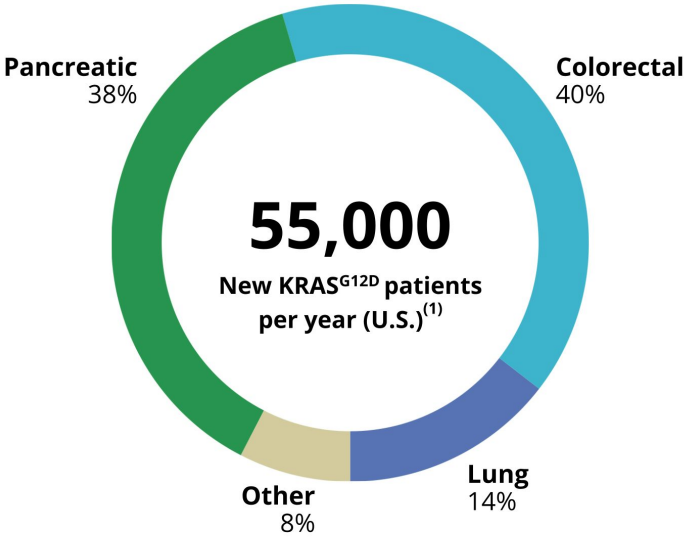
RVMD preclinical research as of 11/20/22
Adagrasib dosed at 100 mg/kg po qd; RMC-6291 dosed at 200 mg/kg po qd; n=3 to 10/group
Progression defined as tumor doubling from baseline
p<0.001 by Log-rank test (RMC-6291 vs adagrasib treatment in the KM analysis)
NSCLC = Non-small cell lung cancer
Responses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

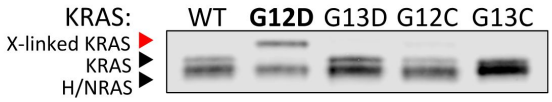
- Favorable *in vivo* oral bioavailability and clearance for effective target coverage in KRAS^{G12D}-addicted cancer cells

(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

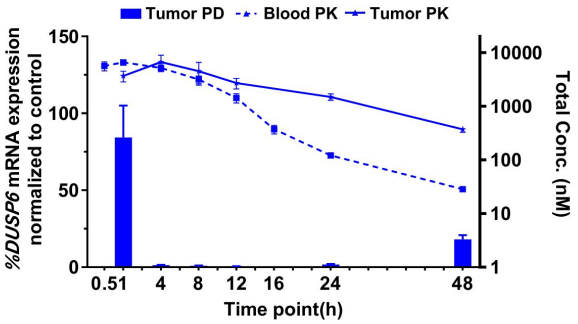
Characterization above is based on RVMD preclinical research

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

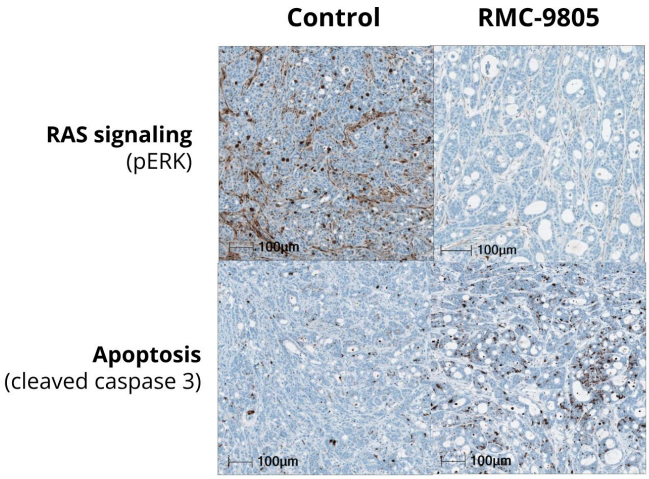
Selective Covalent Binding to KRAS^{G12D}(ON)



Drug Exposure and Pathway Suppression after Oral Dosing[1]



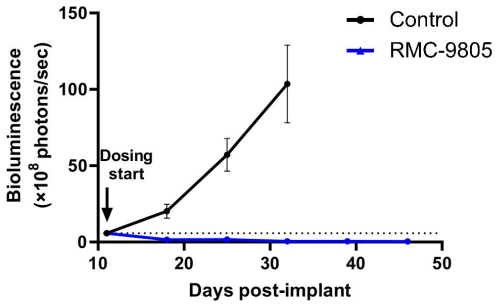
RAS Signaling Inhibition and Apoptosis Induction[2]



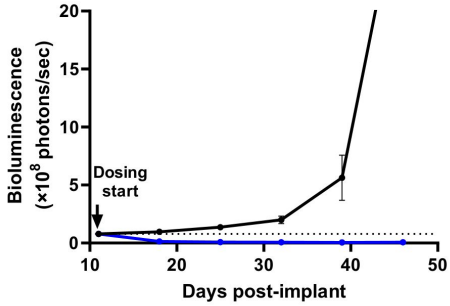
RVMD preclinical research
RMC-9805 dosed at 100 mg/kg po in HPAC subcutaneous xenograft model (PDAC, KRAS$^{G12D/WT}$)
(1) PK/PD data collected at indicated timepoints after a single dose
(2) Histopathology data collected 24h after a single dose

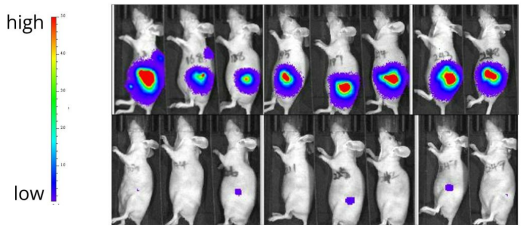
RMC-9805 Drives Deep and Durable Tumor Regressions in Models of Pancreatic Cancer and Brain Metastasis

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



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





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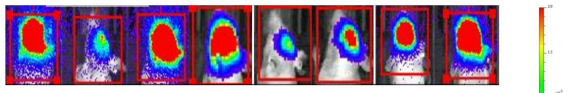
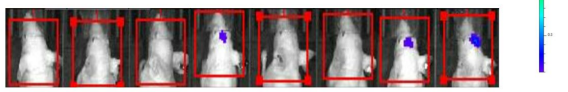
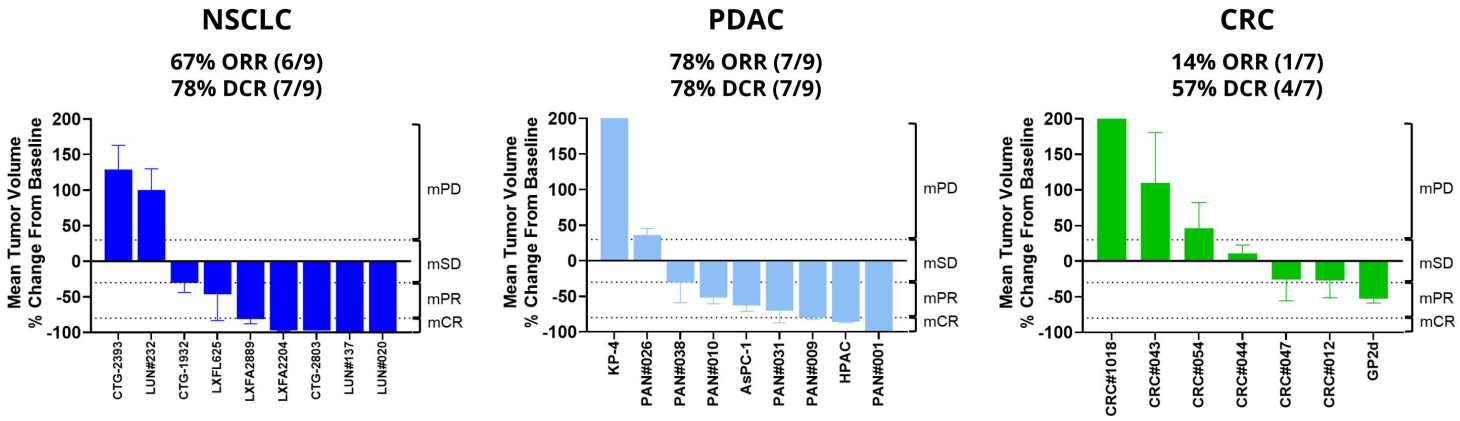


RMC-9805



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



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

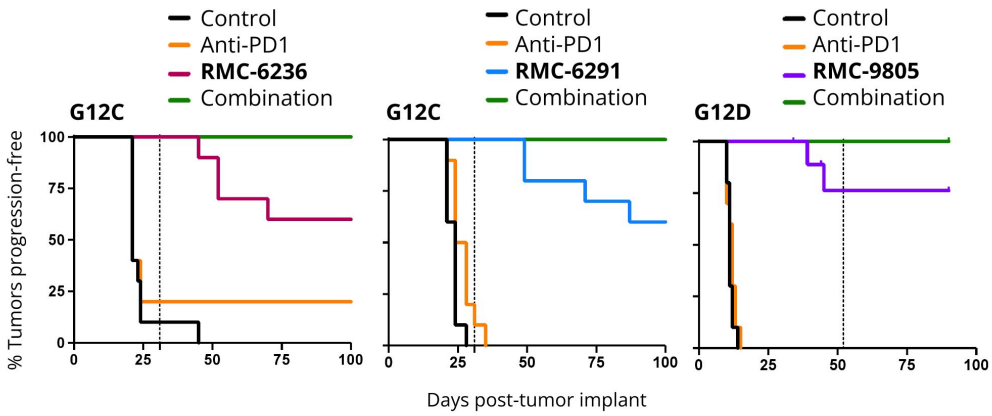
RAS(ON) Inhibitors Induce Anti-Tumor Immunity via Multiple Mechanisms in Immunocompetent Models

Mechanisms of Action

↑ Antigen presentation

↓ Myeloid suppressive cells

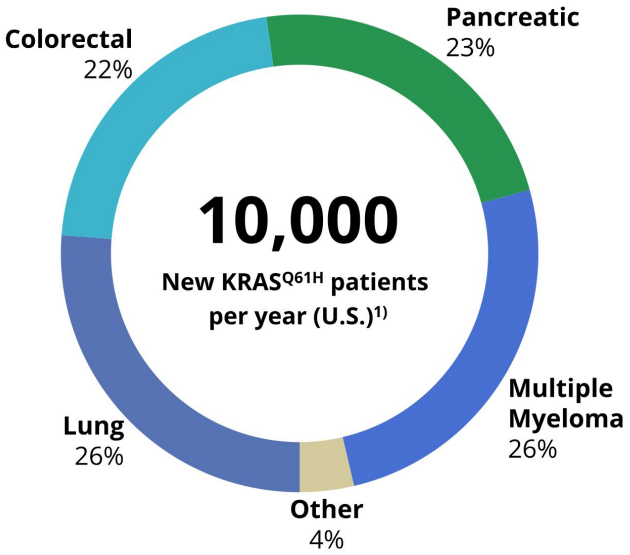
↑ T-cell infiltration



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

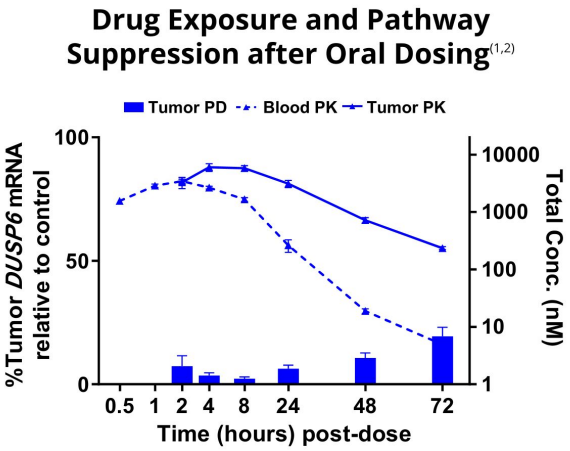
Attractive PK/ADME Profile

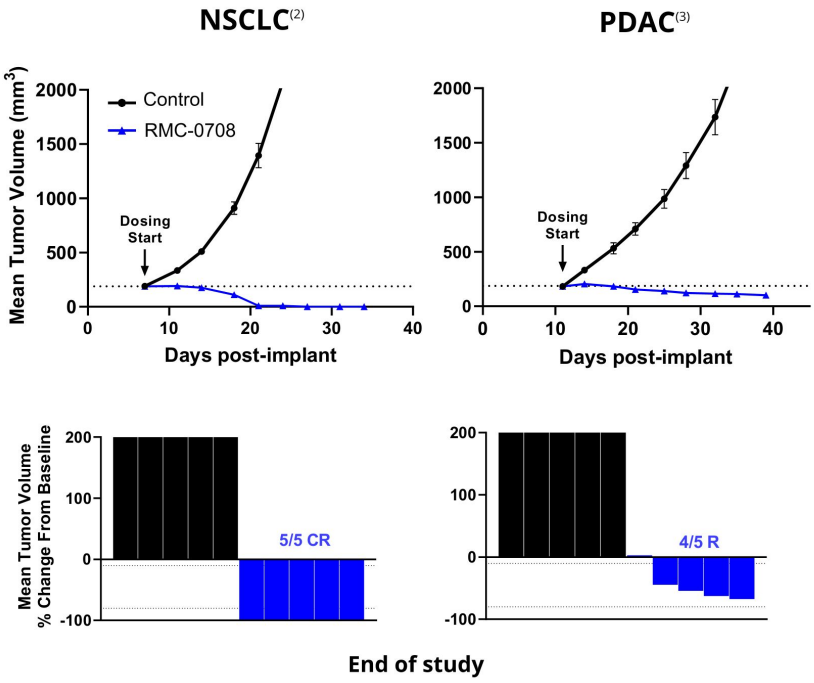
- Favorable *in vivo* oral bioavailability and clearance for effective target coverage in KRAS^{Q61H}-addicted cancer cells

(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





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

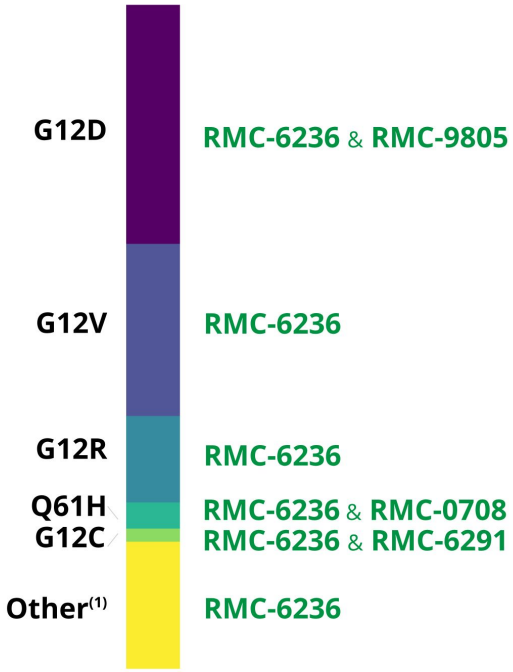
On Target to Outsmart **Pancreatic Cancer**: RAS(ON) Inhibitors Covering All KRAS^{MUTANT} Drivers[1]

Devastating disease
>90% driven by KRAS mutations

49,000

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

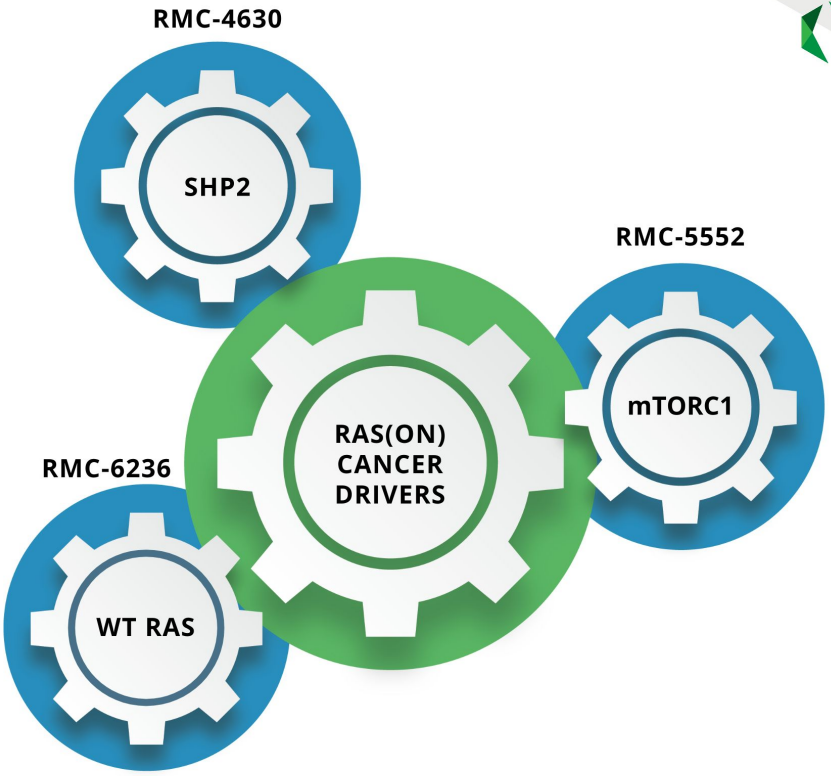
Dismal survival rates
No approved targeted therapies



(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

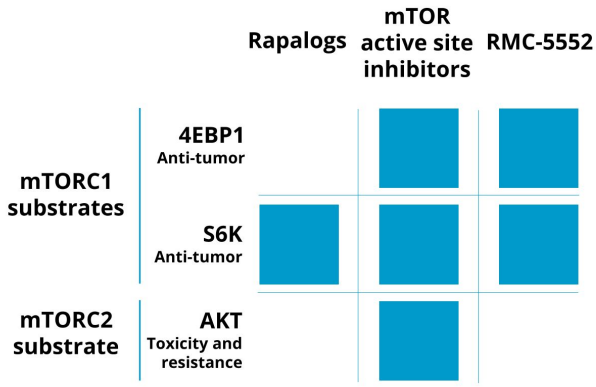
- **Dosing**: Focused primarily on 200 mg D1D2 weekly combined with sotorasib at 960 mg daily
- **Safety**: short- and long-term safety and tolerability

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 - ClinicalTrials.gov Identifier: NCT03634982 https://clinicaltrials.gov/ct2/show/NCT03634982?term=RMC-4630&draw=2&rank=1
(2) Ongoing study - 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 - 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

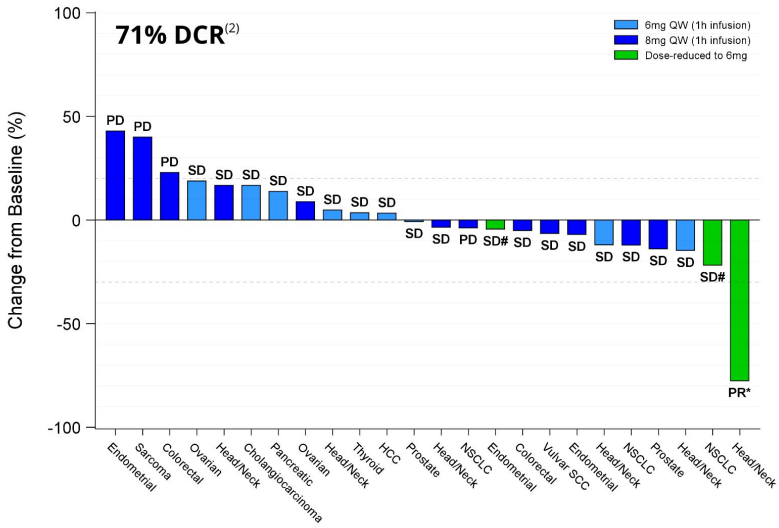
Preliminary radiologic and molecular evidence of activity at tolerated doses:

- 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



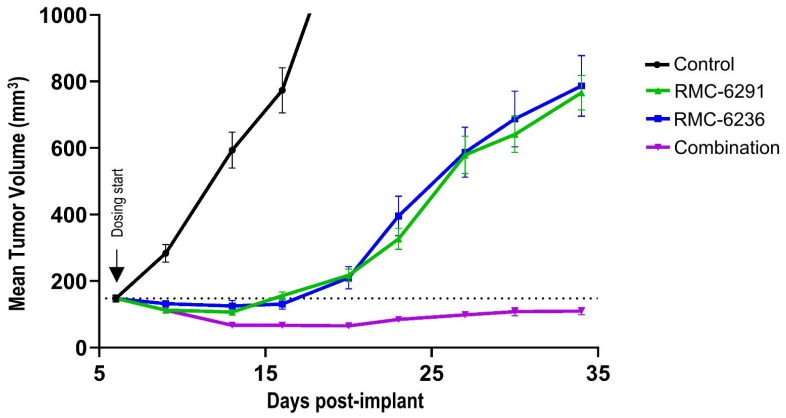
(2) n = 28 efficacy evaluable subjects. DCR = disease control rate.
*Patient received one dose of 12 mg, followed by weekly doses of 6 mg, had complete loss of oncogenic PTEN variant by ctDNA, and has been on RMC-5552 for >12 months.
#Patient received one dose of 10 mg, followed by weekly doses of 6 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 - 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

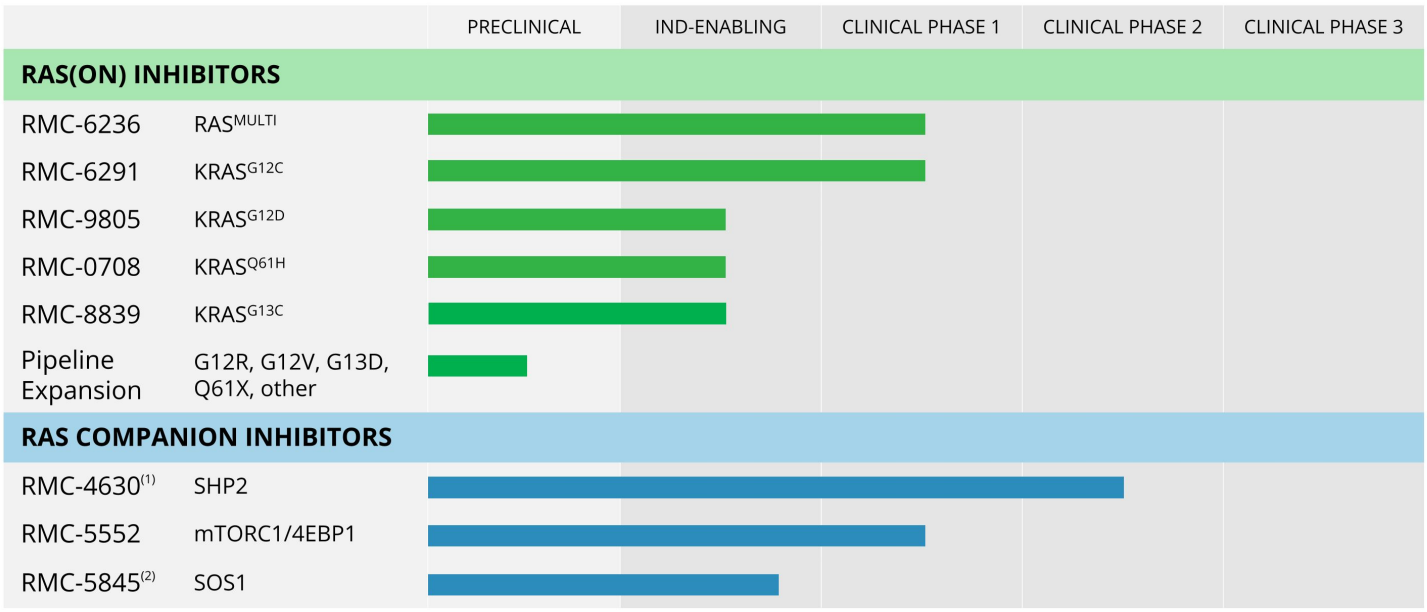
Overcoming Resistance: RMC-6291 + RMC-6236 Combination Induces Regressions in KRAS^{G12C} NSCLC Model



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

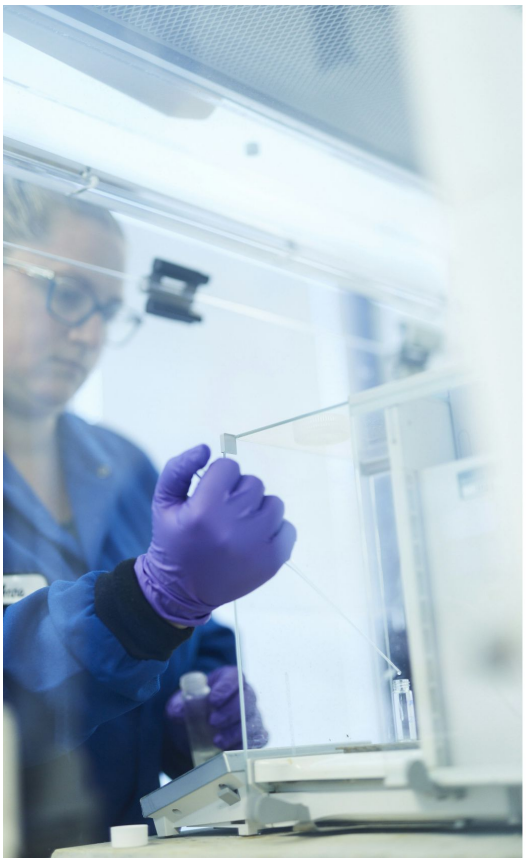
	MILESTONE (EXPECTED TIMING)
RAS(ON) INHIBITORS	
RMC-6236 (RAS^{MULTI})	Provide evidence of first-in-class single agent activity (mid-2023)
RMC-6291 ($KRAS^{G12C}$)	Provide preliminary evidence of superior profile (2H2023)
RMC-9805 ($KRAS^{G12D}$)	Announce dosing of first patient (mid-2023)
RAS COMPANION 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 September 30, 2022	$655.0 million[1]

2022 Financial Guidance
2022 GAAP net loss of $245 million to $265 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 $30 million to $35 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