REVOLUTION MEDICINES

Translating Frontier Oncology Targets to *Outsmart Cancer*™

Corporate Overview
Q3-2020

August 20, 2020

Legal Disclaimer

This presentation contains forward-looking statements. 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 maintain existing collaborations, including with Sanofi, 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, and future results of anticipated products, 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. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements 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 filed with the Securities and Exchange Commission on August 10, 2020, and its future periodic reports to be filed with the Securities and Exchange Commission. Except as required by law, Revolution Medicines undertakes no obligation to update any forward-looking statements to reflect new information, events or circumstances, or to reflect the occurrence of unanticipated events.

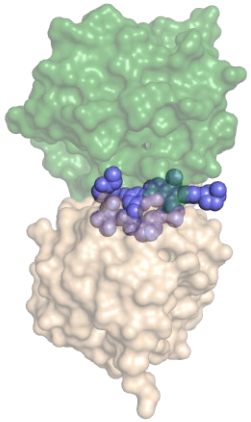
This presentation concerns anticipated products that are under clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration (FDA). It is currently limited by Federal law to investigational use, and no representation is made as to its safety or effectiveness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

Summary

- Clinical-stage precision oncology company focused on RAS-addicted cancers; growing clinical momentum
- Cohesive pipeline of complementary investigational products for targeted mono- and combination treatment
- Prolific innovation engine, sophisticated preclinical and clinical capabilities, and seasoned company leadership
- Strong financial condition and corporate transactions that build value

Our Innovation Engine Focused on Genetic Drivers of RAS-Dependent Cancers

Deep chemical biology and cancer pharmacology know-how to define critical vulnerabilities of *frontier* targets and signaling circuits



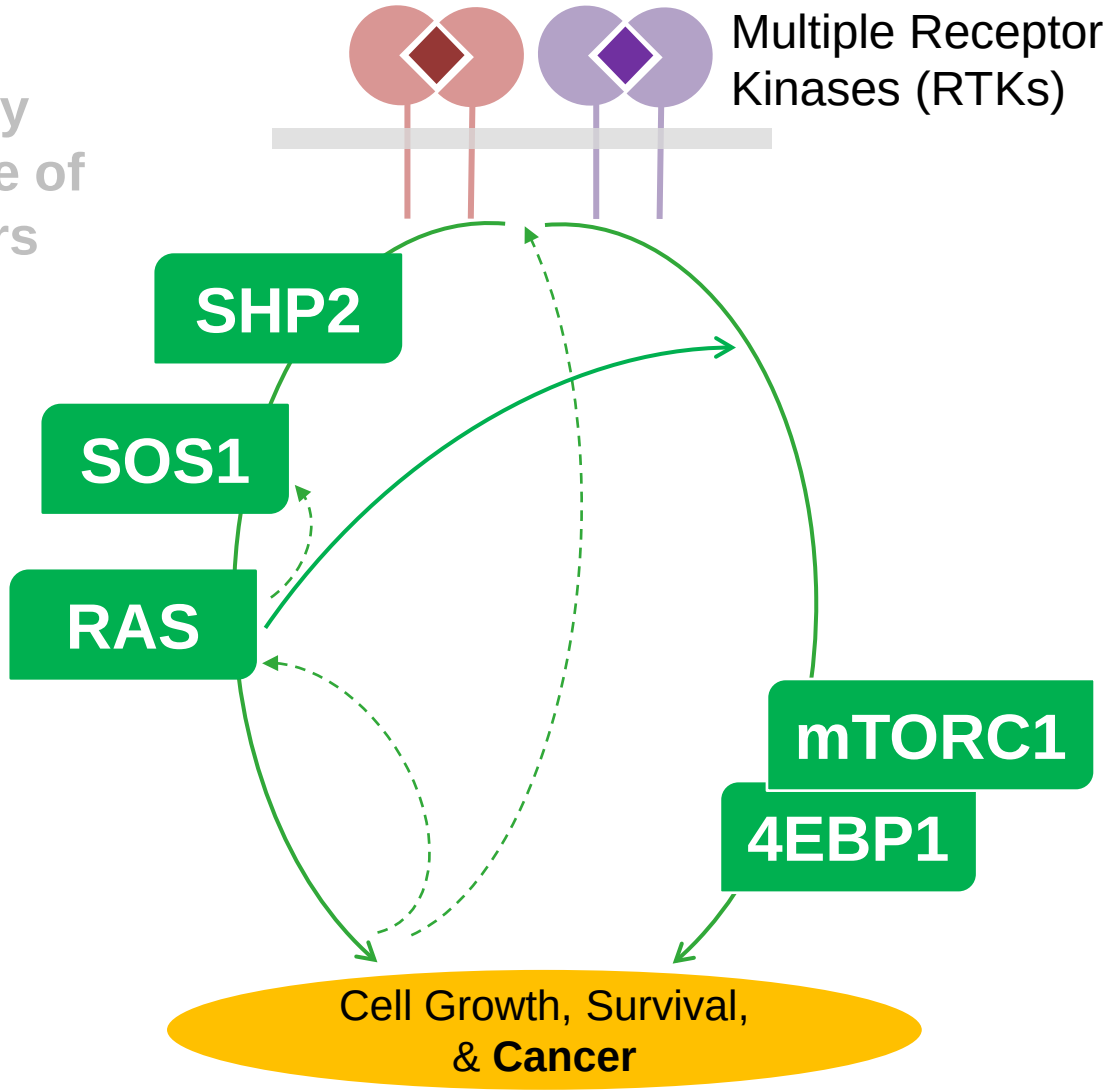
Sophisticated **structure-based drug discovery** capabilities, including proven **access to complex chemical space**, tailored to elusive cancer targets

Astute **precision medicine approach** for patients with genetically-defined cancers addicted to RAS or related circuits

Nodes that Control Cell Growth in RAS-Addicted Cancers are RVMD Frontier Drug Targets

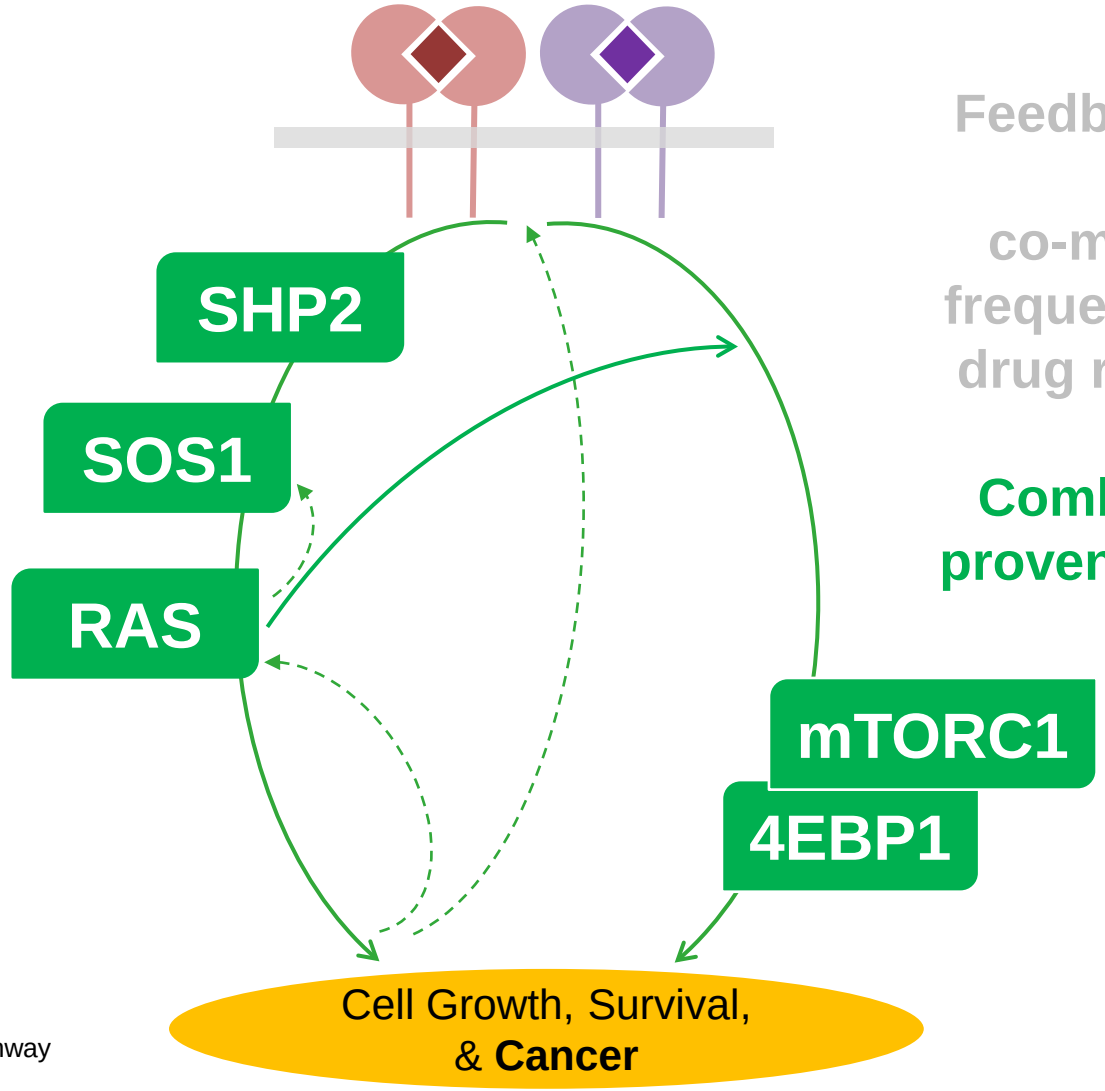
RAS pathway common cause of major cancers

RAS mutations drive ~30% of all cancers(1)



(1) Hobbs et al. *Journal of Cell Science* 2016

Multiple Resistance Pathways Feed RAS Addiction and Often Require Combination Strategies



Feedback loops and co-mutations frequently cause drug resistance

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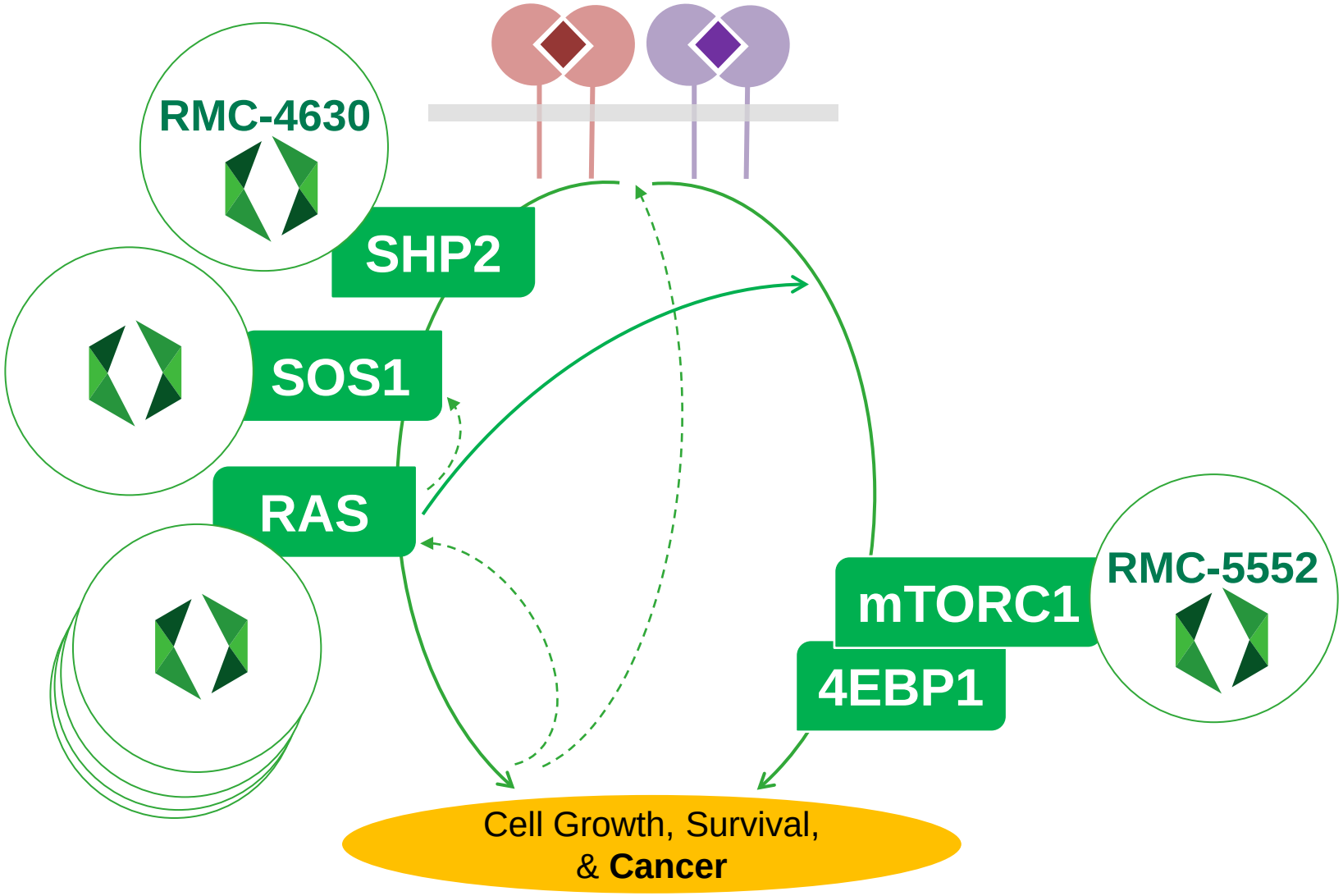
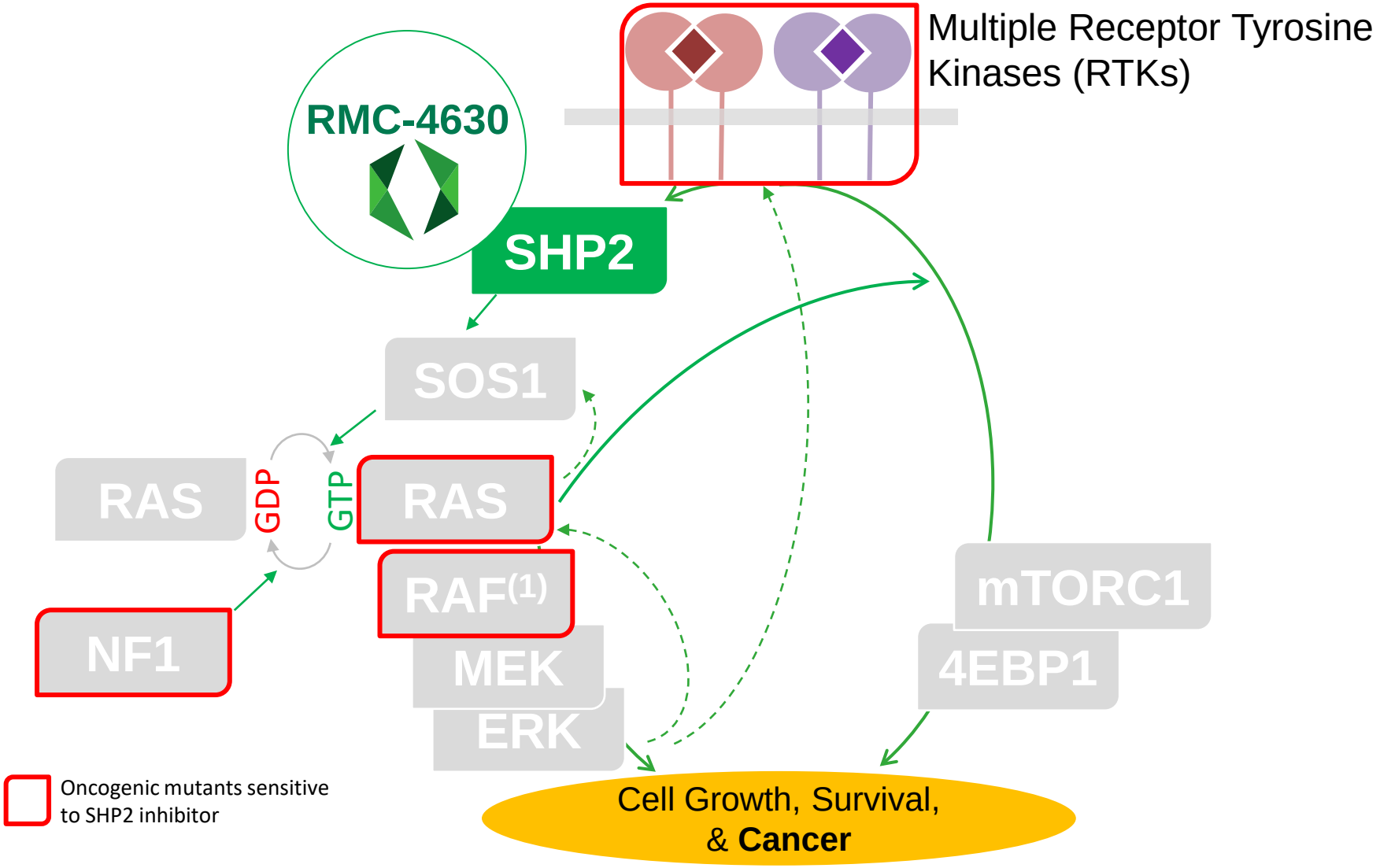
Combinations proven approach

Pipeline Designed for Targeted Drug Combinations to Defeat Resistance in RAS-Addicted Cancer



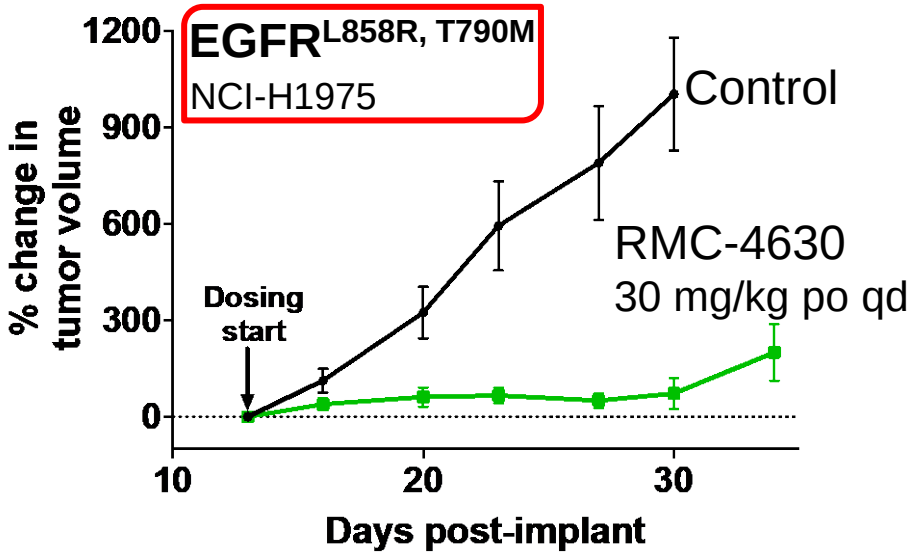
Phase 1/2

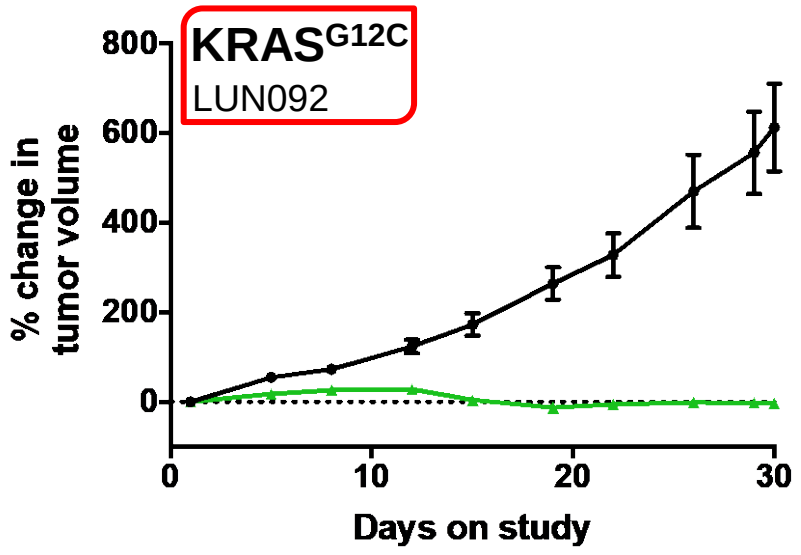
RMC-4630 Inhibits SHP2, a Shared Node that Regulates RAS Signaling Pathway

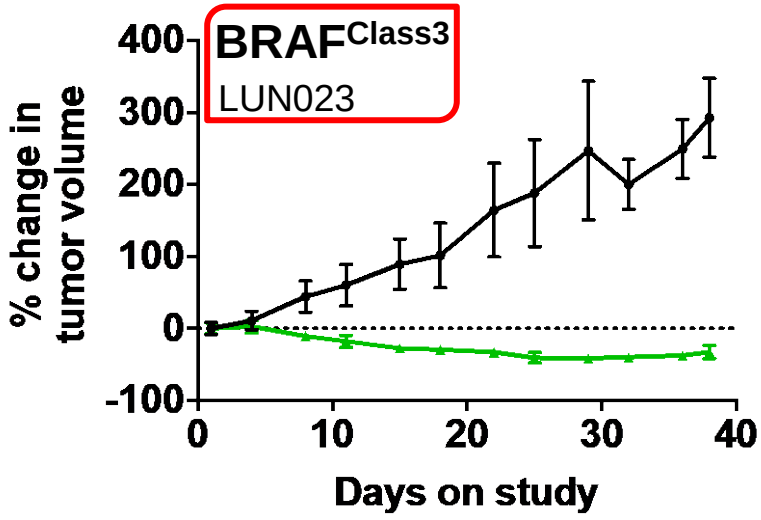


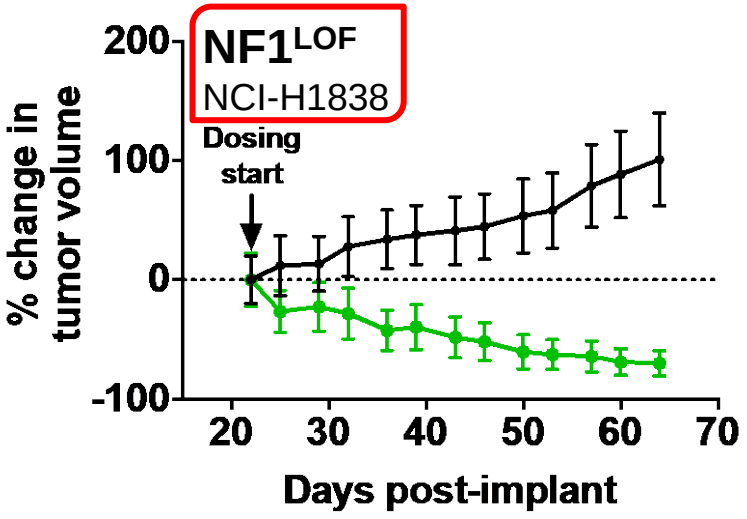
(1) Class 3 mutations of BRAF ($BRAF^{Class3}$)

RMC-4630 Drives Stasis and Regressions of NSCLC Xenografts with Select Pathway Mutations



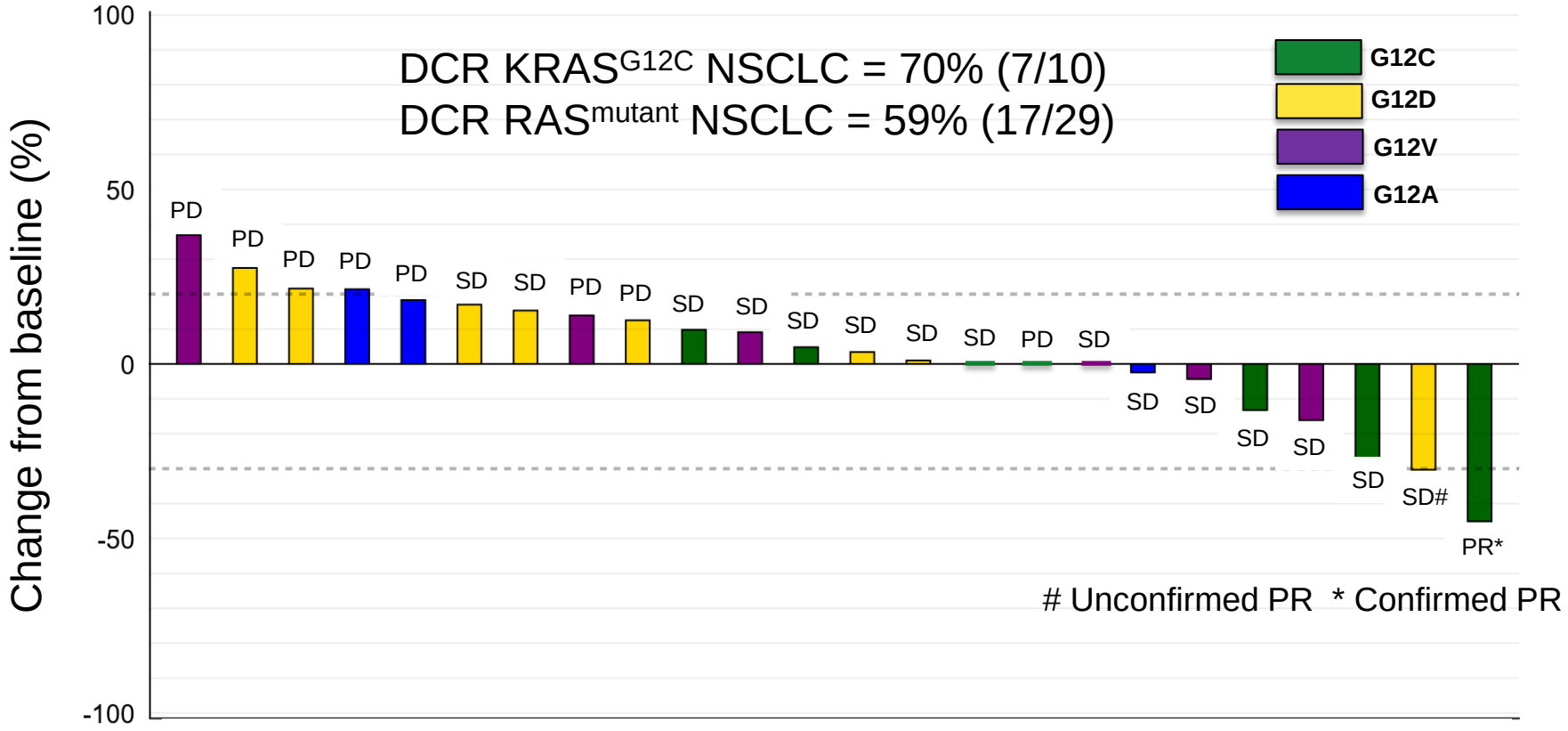






RVMD preclinical data; NSCLC = Non-small cell lung cancer

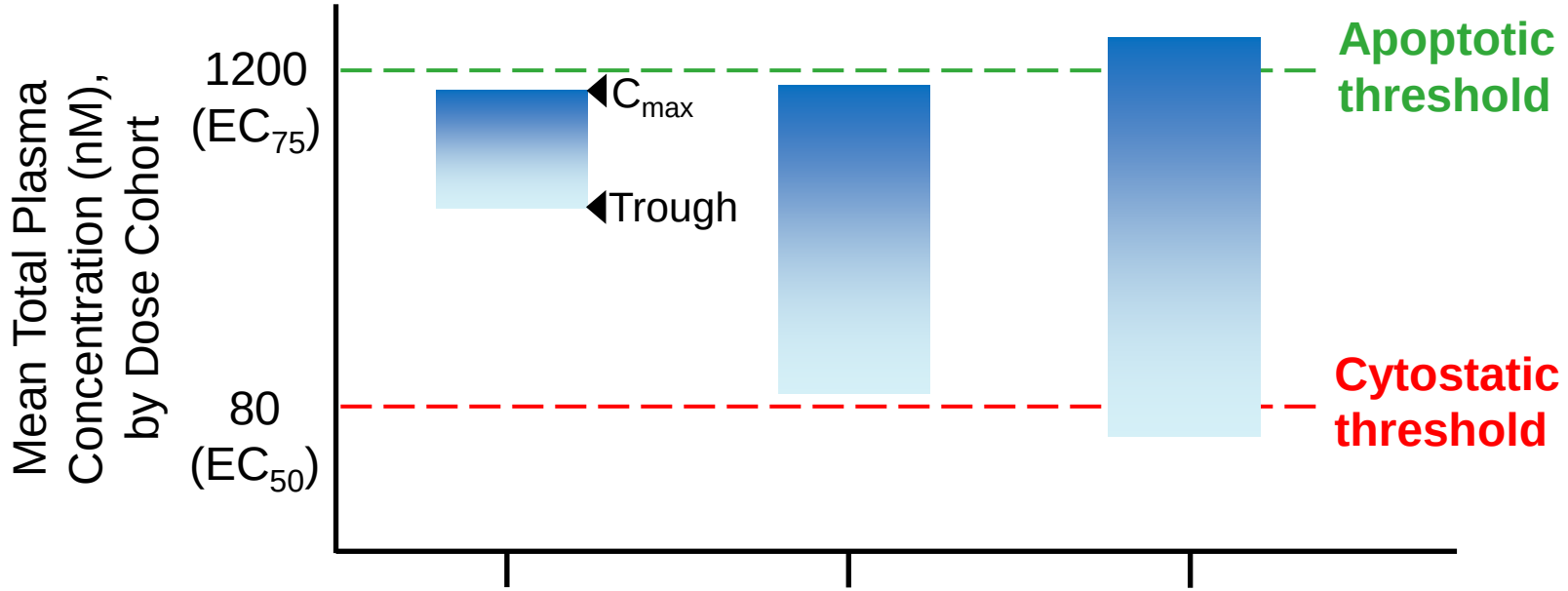
RMC-4630-01: Best Change in Tumor Burden from Baseline in KRAS^{mutant} NSCLC



Data presented for <u>efficacy evaluable</u> population **(N=29)** defined as patients with baseline and at least one post-baseline scan or who died or had clinical progression prior to first post-baseline scan.
Five patients are not represented in this figure: 4 patients had clinical progression prior to first scan, and 1 patient died due to disease progression at the time of data extract.

Data as of 5/4/2020; NSCLC = Non-small cell lung cancer; DCR = Disease Control Rate (no PD at first response assessment); PD = Progressive Disease; SD = Stable Disease; PR = Partial Response; PD, SD and PR each per RECIST 1.1

RMC-4630-01: Approaching Dose & Schedule Optimized for Efficacious and Tolerable Exposures



Dose cohort:	**60 mg daily** **N=18^**	**140 mg D1D4*** **N=8**	**200 mg D1D2*** **N=4**
With related AEs, grade ≥3:	9/18 (50%)[a]	4/8 (50%)[b]	0/4 (0%)
With AEs Leading to Discontinuation or Dose Reduction:	4/18 (22.2%)	1/8 (12.5%)	0/4 (0%)

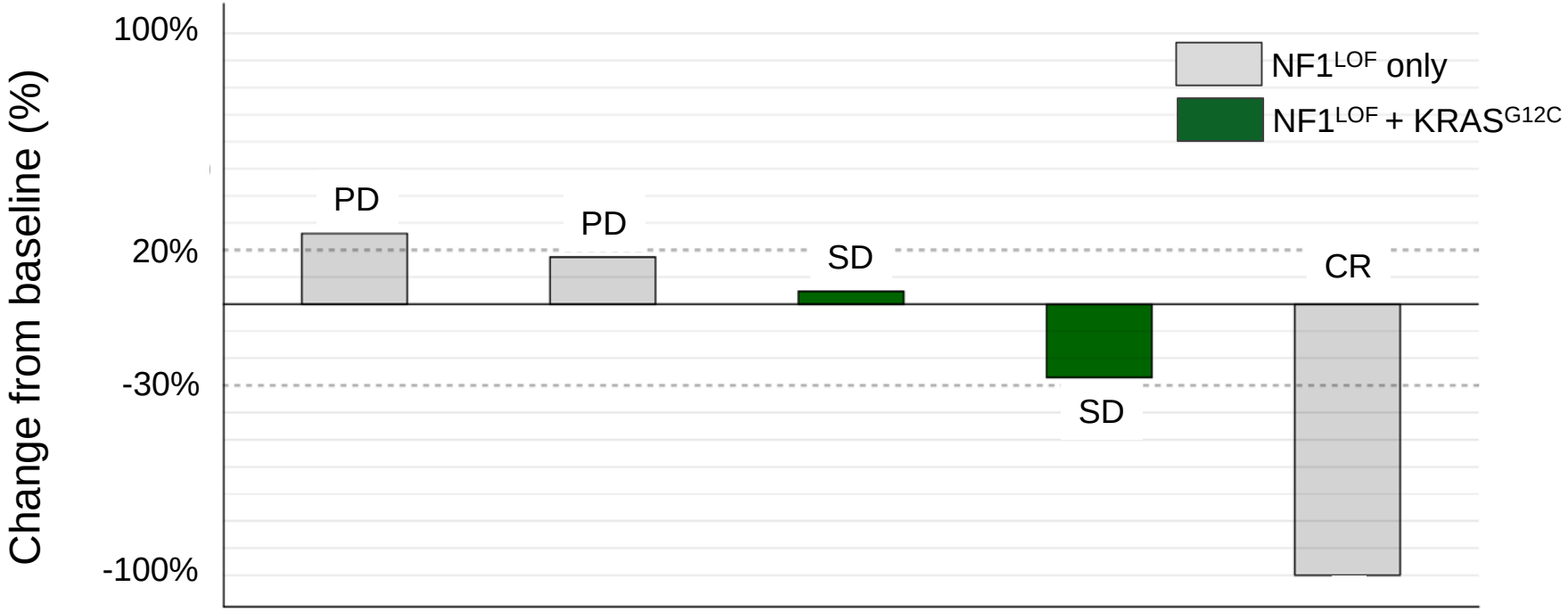
* Each week

^PK available for N=11

[a] 2 grade 4
[b] 0 grade 4

Data as of 5/4/2020

RMC-4630-01: Best Change in Tumor Burden for NSCLC and Gynecologic Tumors with NF1^{LOF}

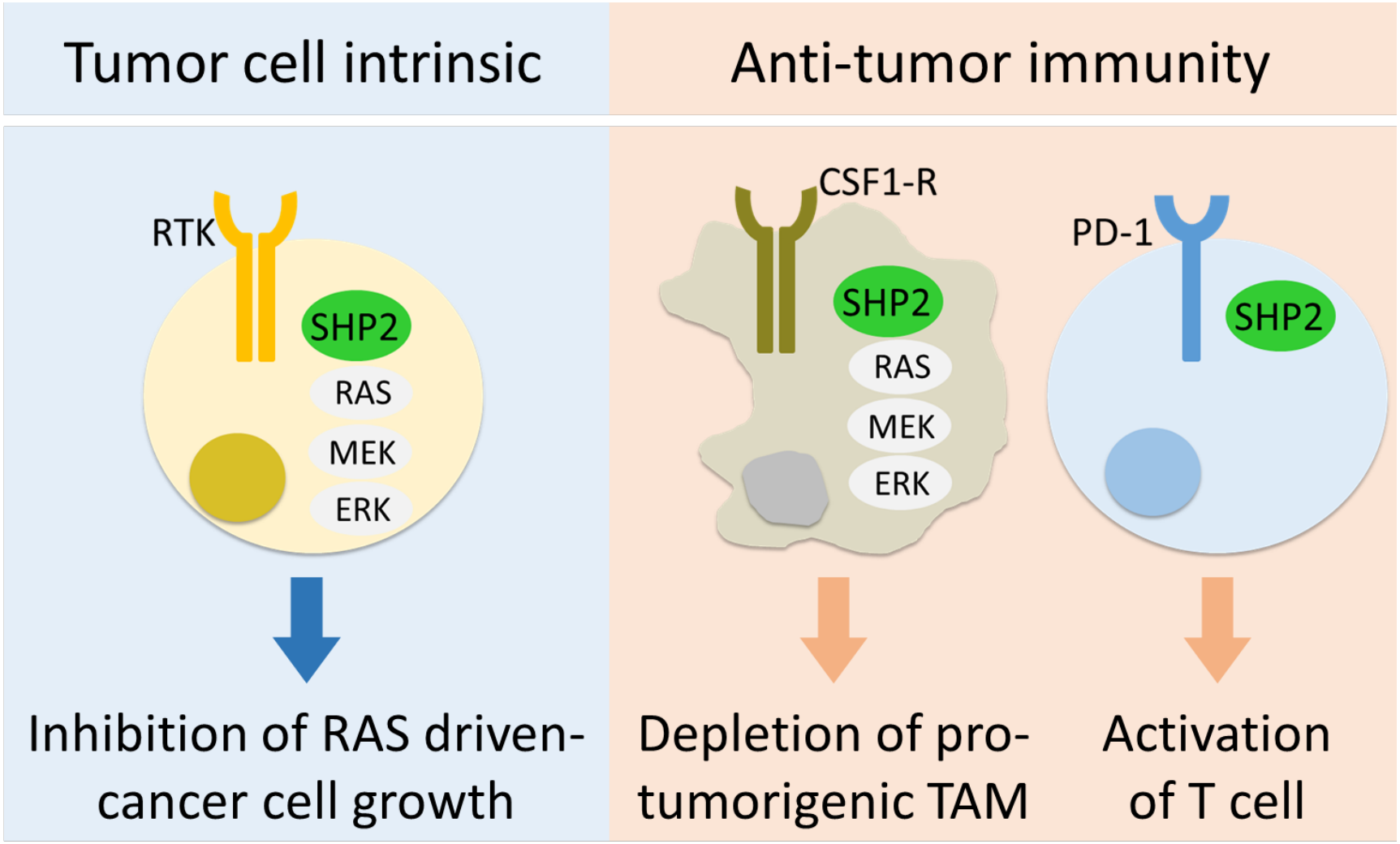


Dose:	80mg	80mg	60mg	200mg	200mg
Schedule:	Daily	Daily	Daily	D1D4	D1D4
Type:	Ovarian	Ovarian	NSCLC	NSCLC	Uterine

- 1 patient (NSCLC) with death due to clinical PD is not represented in this figure
- NF1^{LOF} (loss-of-function) inferred from deletions, insertions, premature stops and truncations in neurofibromin 1 gene

Data as of 5/4/2020; NSCLC = Non-small cell lung cancer

RMC-4630 Drives Anti-Tumor Benefit via Both Cell-Intrinsic and Immune System Mechanisms



Based on Quintana et al. *Cancer Research* April 2020

Central Clinical Thesis: RMC-4630 as Backbone for Rational, Mechanism-Based Combinations

Combinations with RMC-4630:

Induce additive anti-tumor effects (1)

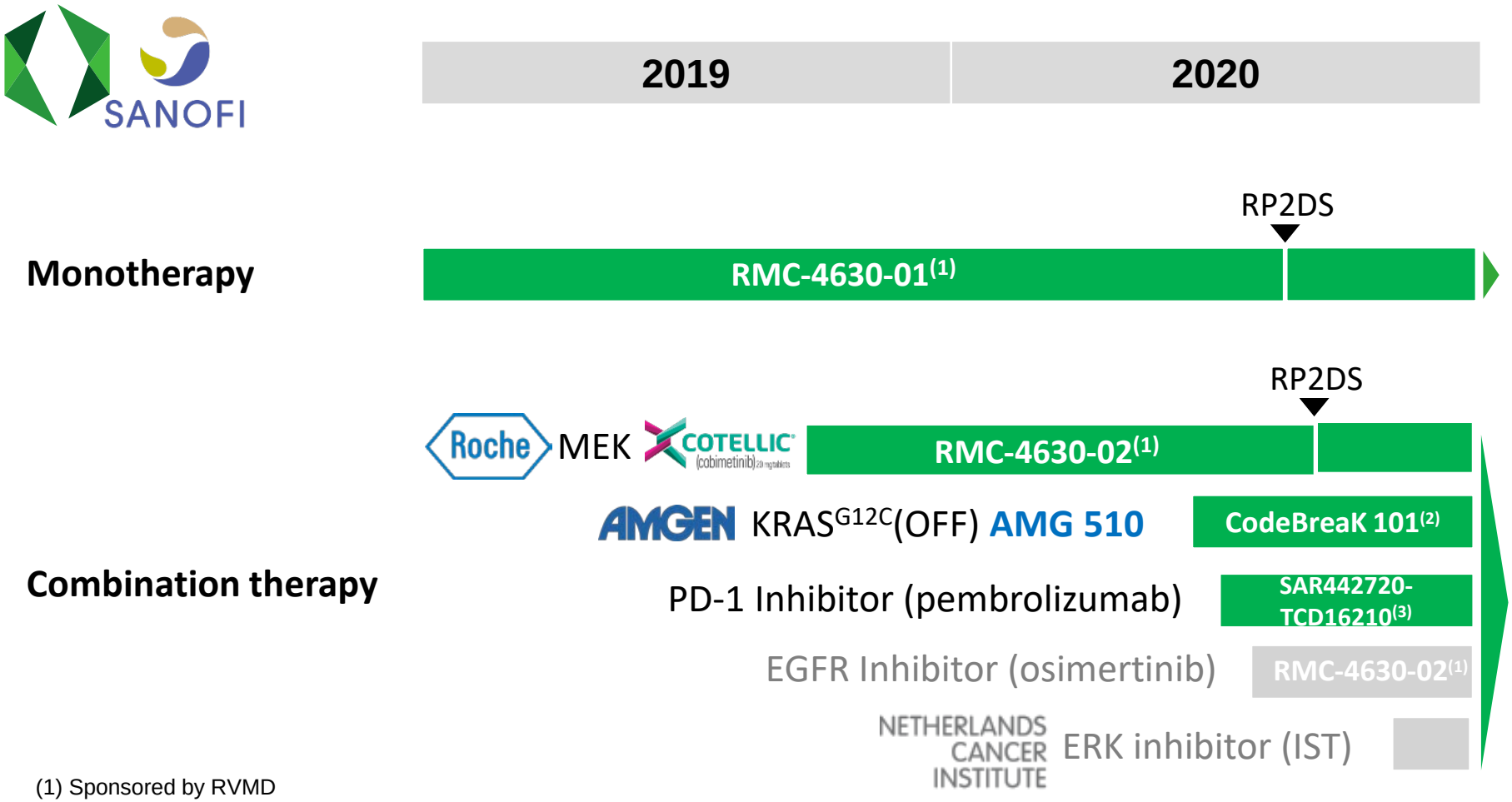
Combat adaptive resistance (2)

MEK inhibitors	ERK inhibitors	$KRAS^{G12C}$ inhibitors	RTK inhibitors	Checkpoint inhibitors
Inhibit RAS pathway nodes		Inhibit driver mutations		Inhibit immune suppressors
Combination for RAS-addicted tumors		Combination for tumors carrying $KRAS^{G12C}$	Combination for tumors carrying $EGFR^{mutation}$	Combination for RAS-addicted tumors

(1) RVMD preclinical research; Singh et al., *CSHL* 2018; Mainardi et al., *Nature Medicine* 2018; Lu et al., *Molecular Cancer Therapeutics* 2019; Hallin et al., *Cancer Discovery* 2020; Liu et al., *AACR* 2020; Smith et al., *AACR* 2020; Quintana et al. *Cancer Research* 2020

(2) RVMD preclinical research; Fedele et al., *BioRxiv* 2018; Ahmed et al., *Cell Reports* 2018; Mainardi et al., *Nature Medicine* 2018; Lu et al., *Molecular Cancer Therapeutics* 2019; Liu et al., *AACR* 2020; Hallin et al., *Cancer Discovery* 2020; Smith et al., *AACR* 2020

Broad Development Program for RMC-4630 Progressing Well

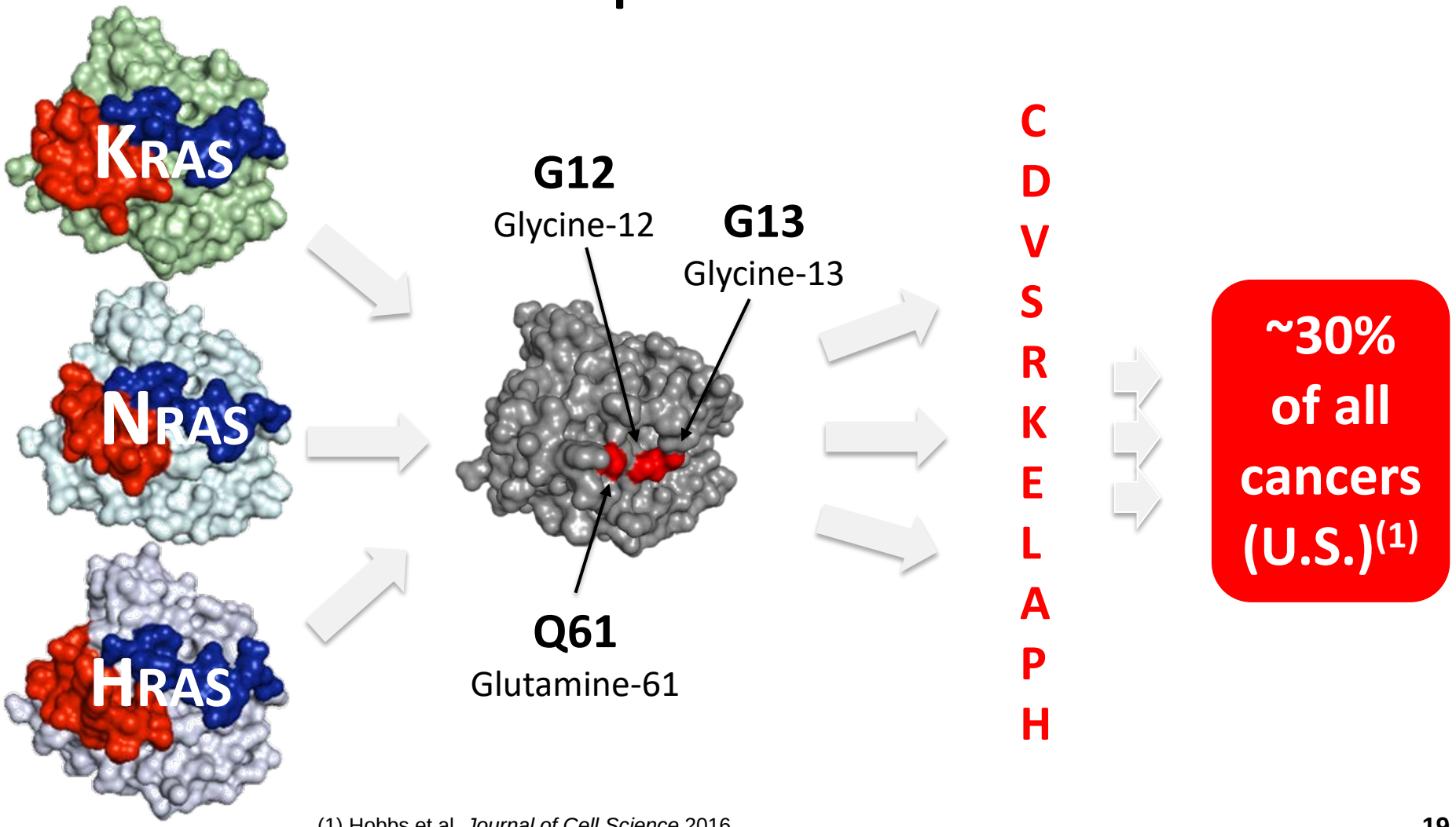


(1) Sponsored by RVMD
(2) Sponsored by Amgen
(3) Sponsored by Sanofi
Green bars represent ongoing studies
Gray bars represent planned studies

Partnership (2018) Enables Broad Opportunity for Success in RMC-4630 Clinical Program

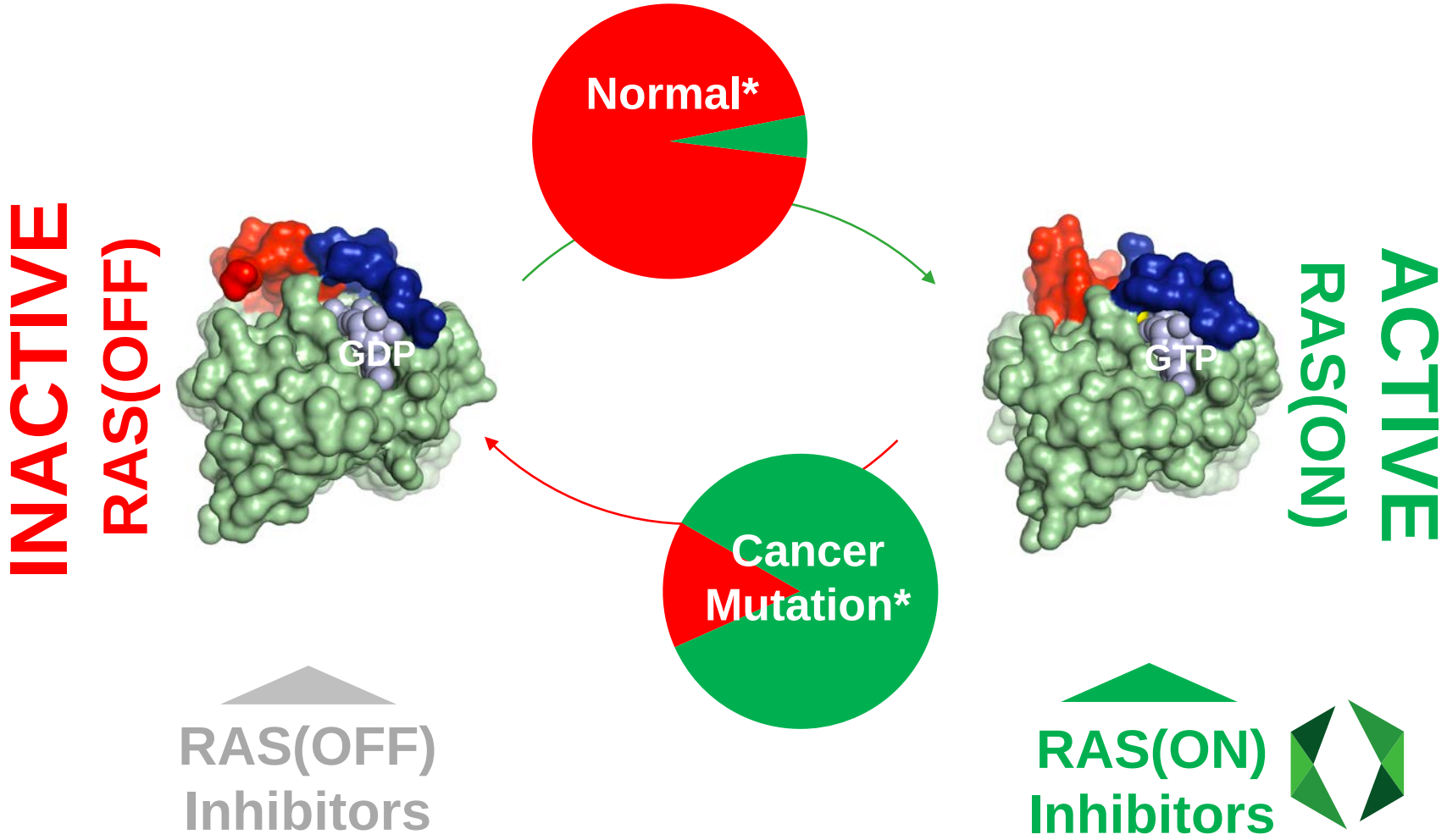
	REVOLUTION MEDICINES	SANOFI
Funding	• Received $50M upfront fee • Eligible for > $500M in pre-commercial milestones	• Pays for substantially all research and all development costs (including combinations)
Commercial	• 50/50 profit share in US • Tiered royalty ex-US • Right to co-promote in US	• Leads global commercialization • 50/50 profit share in US
R&D	• Leads research and early clinical development	• Leads later clinical development

Numerous RAS Mutants Commonly Drive Human Cancers and are Important Disease Targets



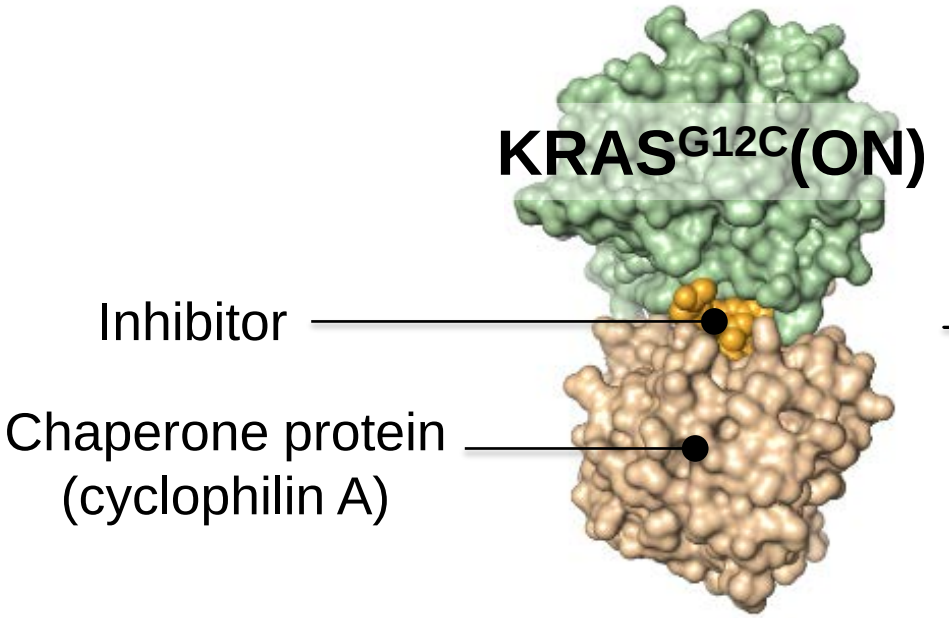
(1) Hobbs et al. *Journal of Cell Science* 2016

Mutant RAS Tumors are Addicted to, and Tenaciously Maintain, High Levels of RAS(ON)



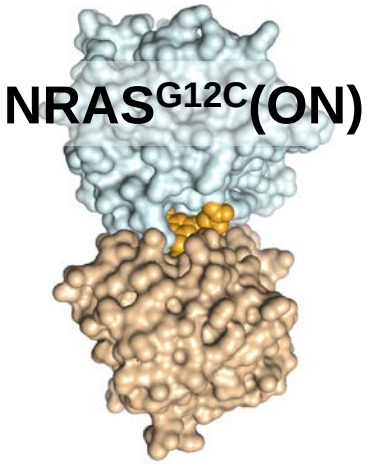
*Adapted from Patricelli et al., *Cancer Discovery* 2016

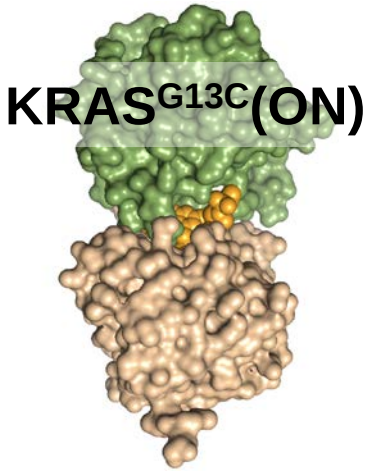
Highly Differentiated Inhibitors of Diverse Oncogenic RAS(ON) Mutants

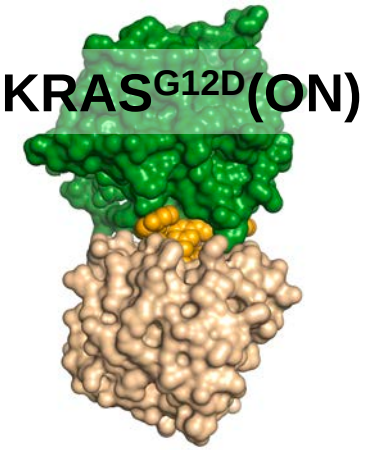


Unique binding mode

- Active RAS form
- Near hotspot mutations
- Forms tri-complex
- Directly inhibits oncogenic signaling

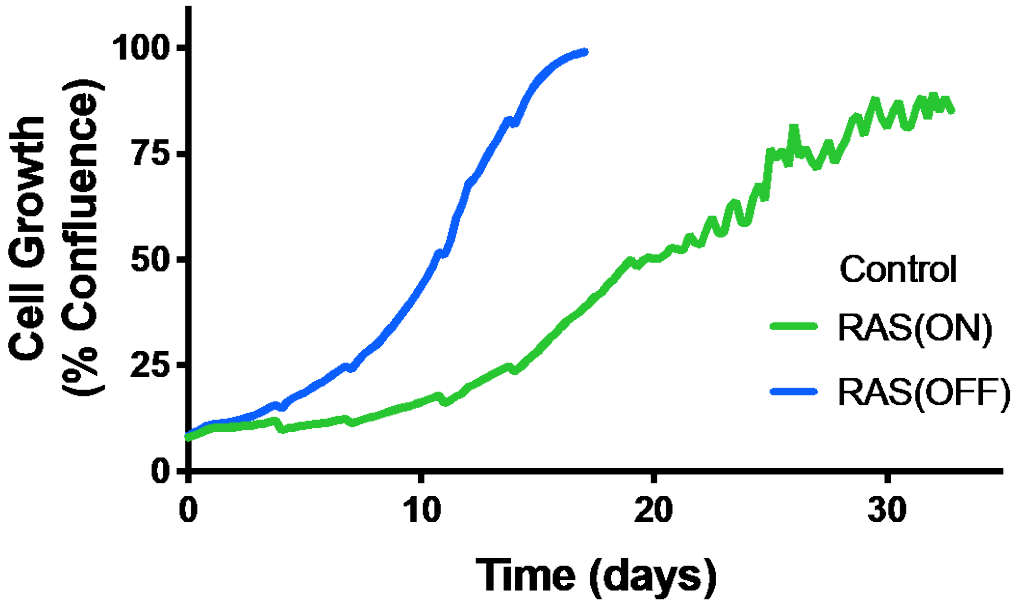






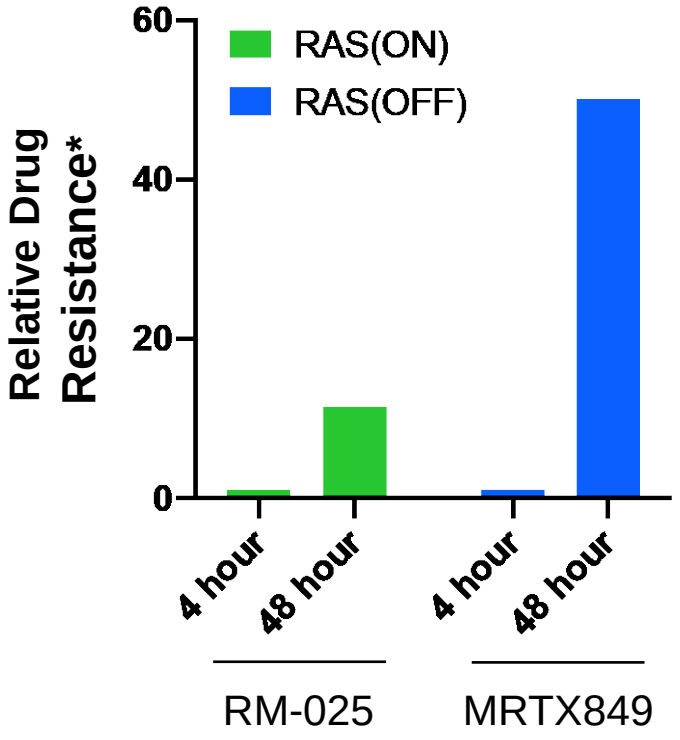
KRAS^{G12C}(ON) Inhibitors Induce Sustained Tumor Cell Suppression *in Vitro*

NCI-H358 (NSCLC, KRAS^{G12C})



RAS(OFF) = Mirati-11
RAS(ON) = RM-007
Concentrations normalized based on pathway suppression.

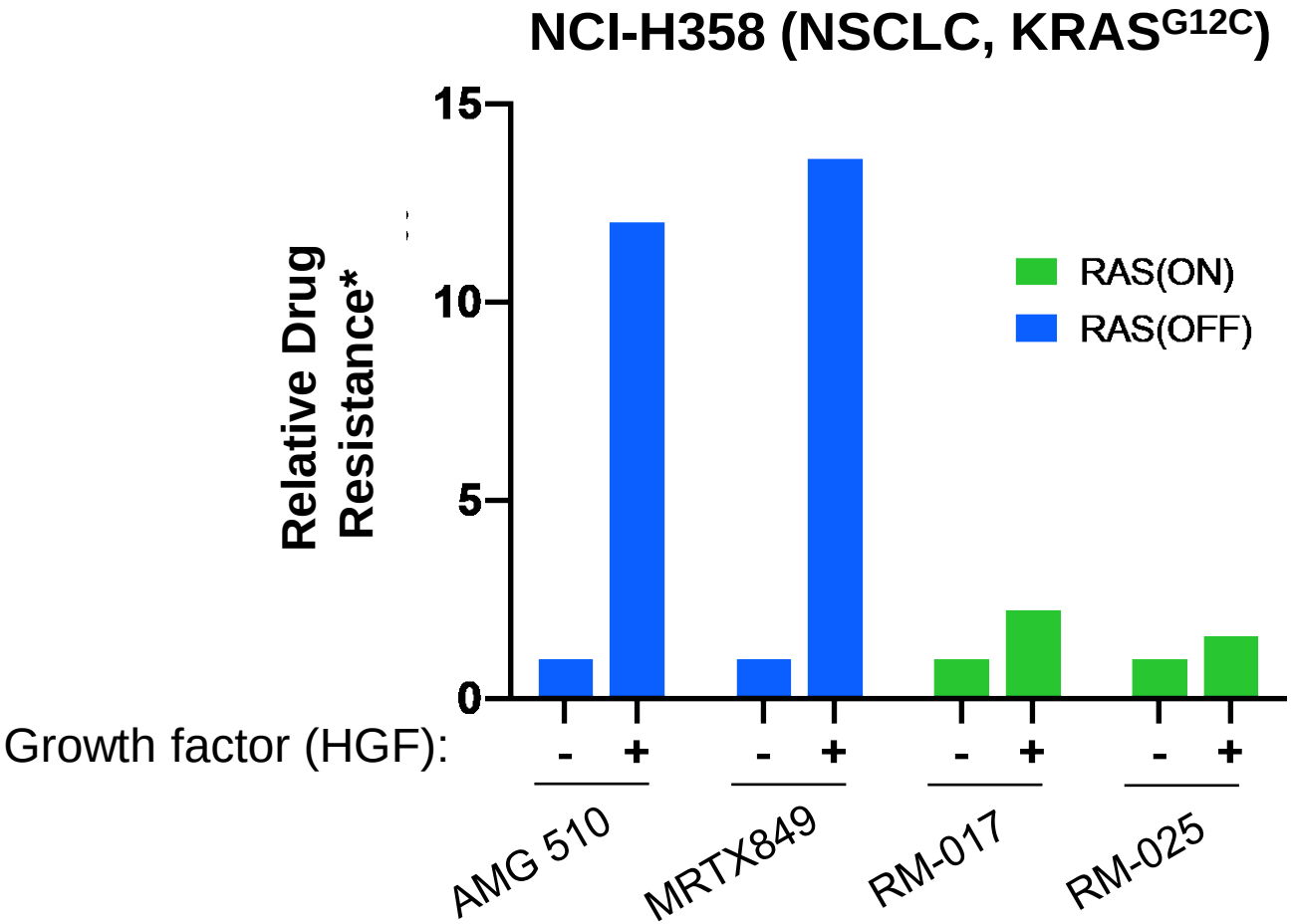
SW1463 (CRC, KRAS^{G12C})



*Fold increase in IC_{50} (pERK)

RMVD preclinical data; NSCLC = Non-small cell lung cancer;
CRC = Colorectal cancer

KRAS^{G12C}(ON) Inhibitors Minimally Affected by Resistance via RTK Activation *in Vitro*

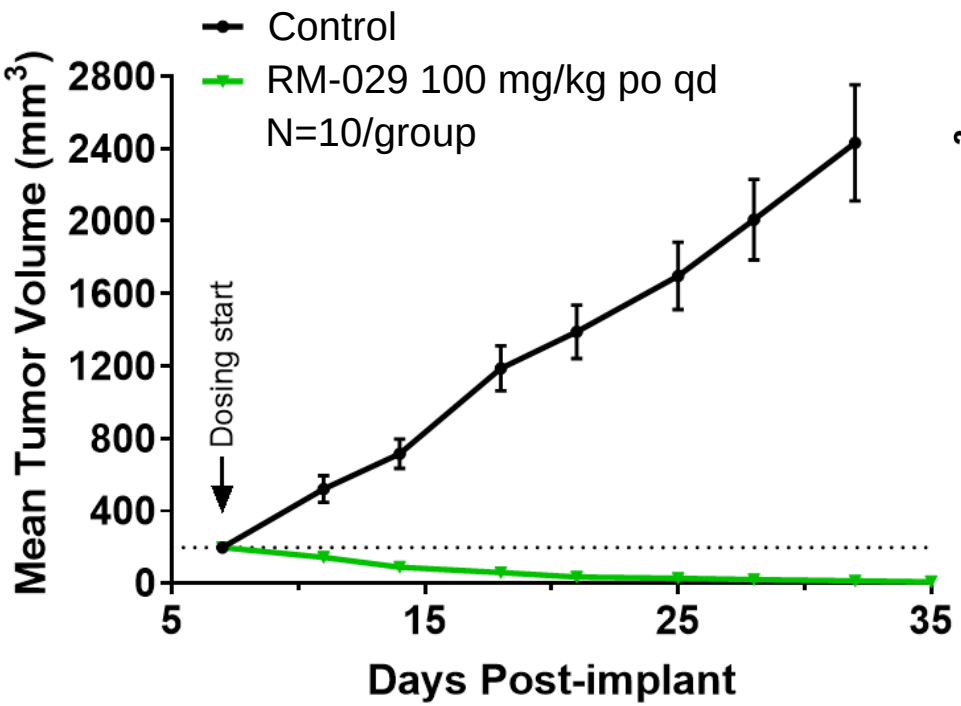


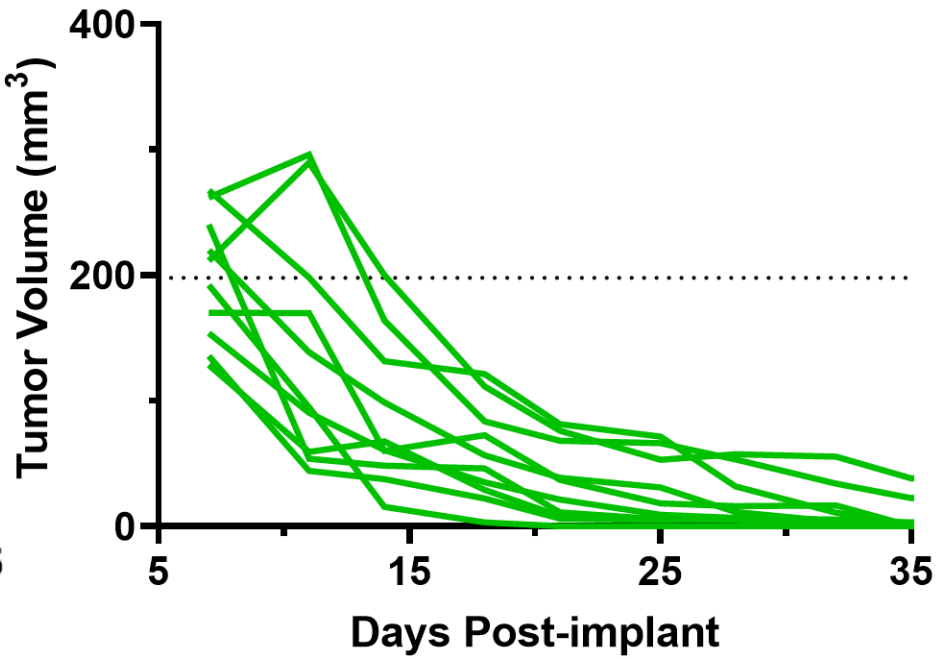
* Fold increase in IC_{50} (cell growth)

RVMD preclinical data; NSCLC = Non-small cell lung cancer

Oral KRAS^{G12C}(ON) Lead Series Compound Drives Deep Regressions *in Vivo*

NCI-H358 CDX (NSCLC, KRAS^{G12C})





Treatment was well tolerated

Some animals exhibited complete responses (CR) = 3 consecutive tumor measurements ≤ 30 mm^3

RVMD preclinical data
CDX = cell line-derived xenograft
NSCLC = Non-small cell lung cancer

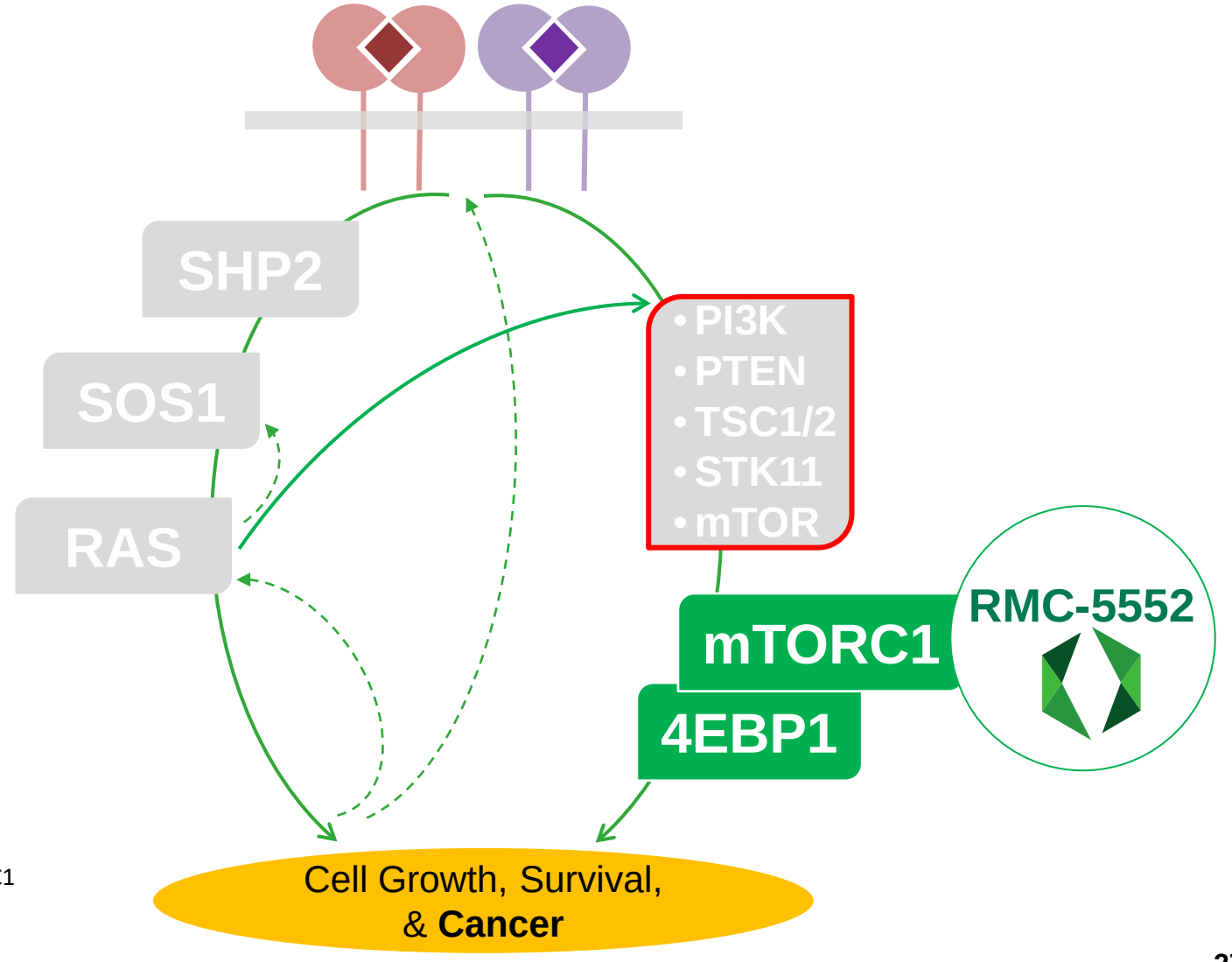
Preclinical Features of RAS(ON) Class of Inhibitors Suggest Possible Clinical Advantages

Mechanism of action of RAS(ON) inhibitors is hypothesized to permit one or more of:

- Higher response rates
- Deeper anti-tumor activity
- Greater duration of clinical benefit
- Beneficial combinations with other upstream and downstream pathway inhibitors

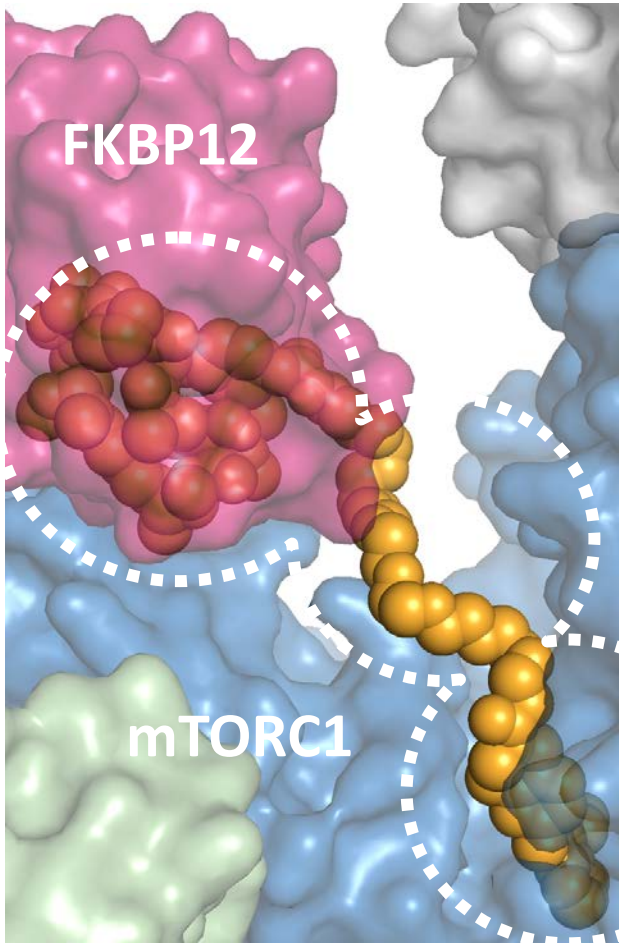
IND-enabling development

Hyperactivation of mTOR Signaling Drives Cancer and/or Drug Resistance in RAS-Addicted Tumors



Genomic alterations of these proteins hyperactivate mTORC1 and can drive cancer

Attractive Profile of Bi-Steric mTORC1 Inhibitors, including Development Candidate RMC-5552



Allosteric site

Layered structural model

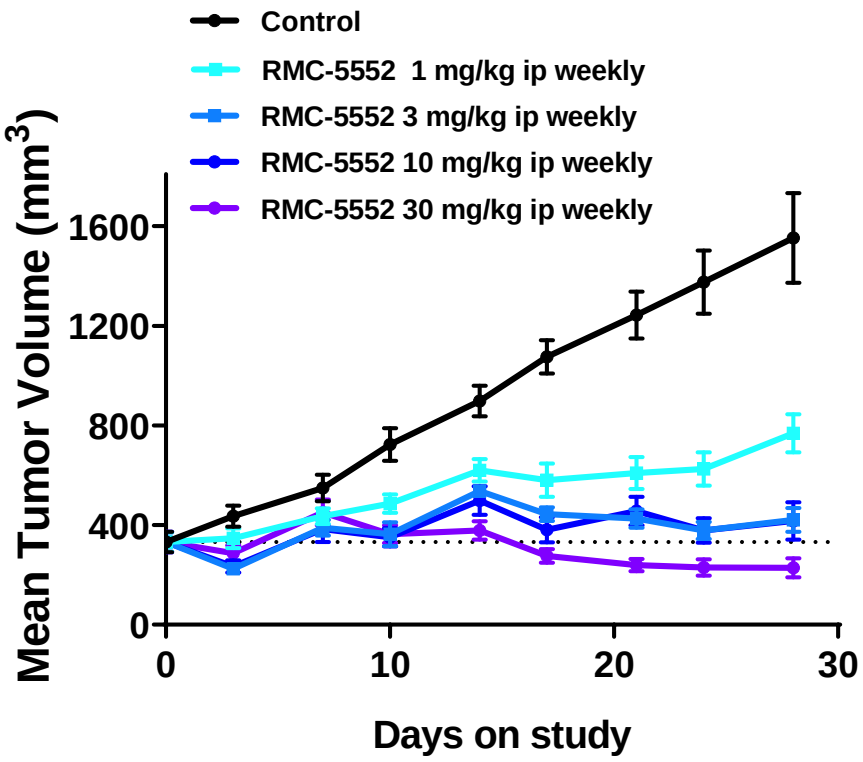
Active site

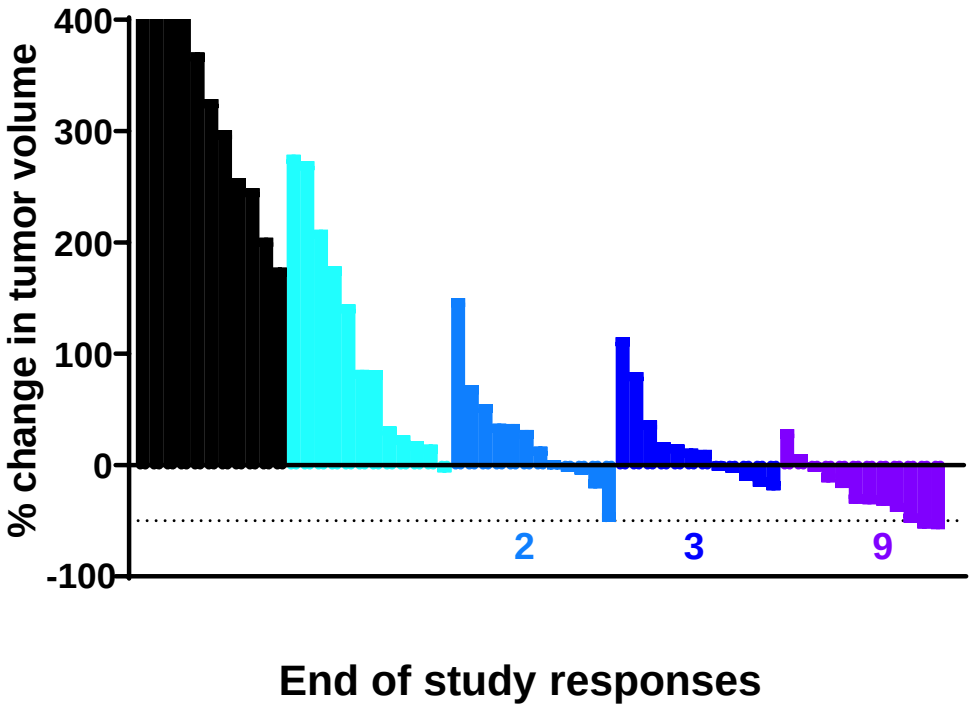
	RMC-5552
Inhibition of mTORC1: pS6K	**0.14 nM**
Inhibition of mTORC1: p4EBP1[1]	**0.48 nM**
Selectivity over mTORC2: AKT[2]	**40X**

[1] **Rapamycin** is not considered an inhibitor.
[2] **Active site inhibitors** are not considered selective.

RMC-5552 Monotherapy Drives Regressions in mTORC1-Hyperactivated Tumor Xenografts

MCF7 CDX (Breast cancer, PIK3CA^{mutant}; ER$^{+/}$HER2^{-})



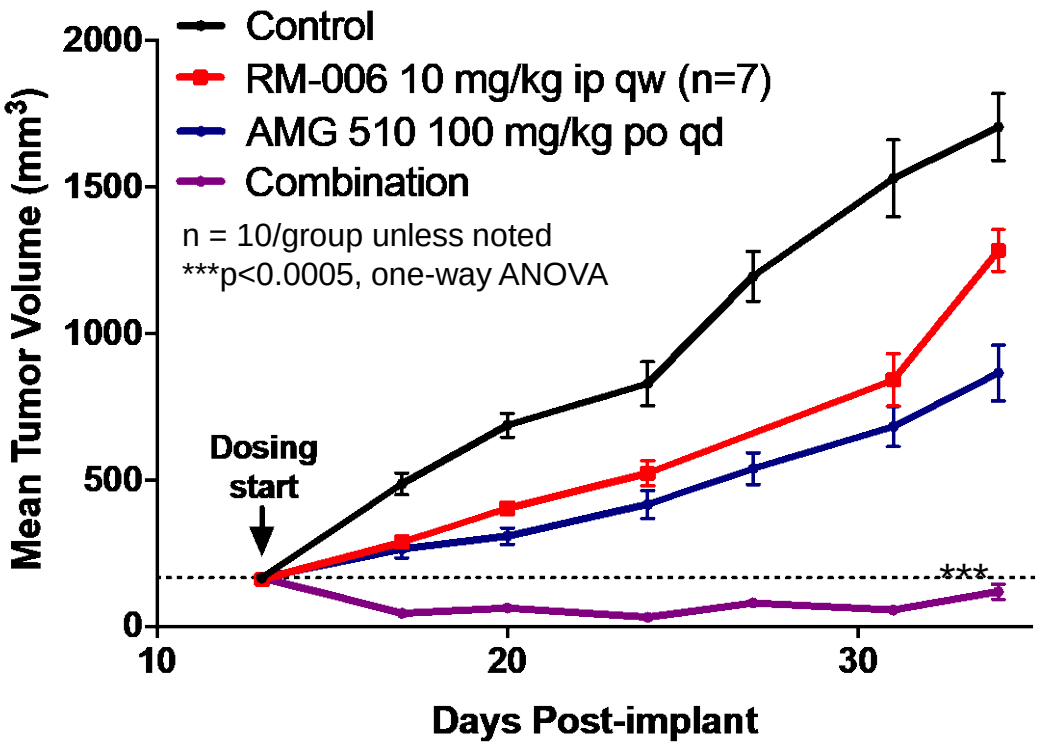


n = number of regressions > 10% from starting tumor volume

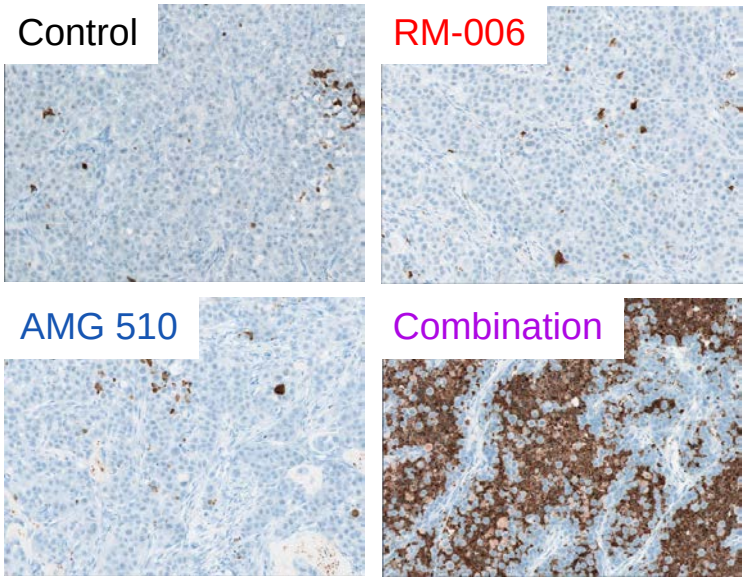
RVMD preclinical data
CDX = cell line-derived xenograft

Dual Targeted Therapy for RAS/mTOR Signaling Co-Mutations Overcomes Primary Resistance

NCI-H2122 NSCLC CDX ($KRAS^{G12C}$; $STK11^{LOF}$)



Apoptosis*

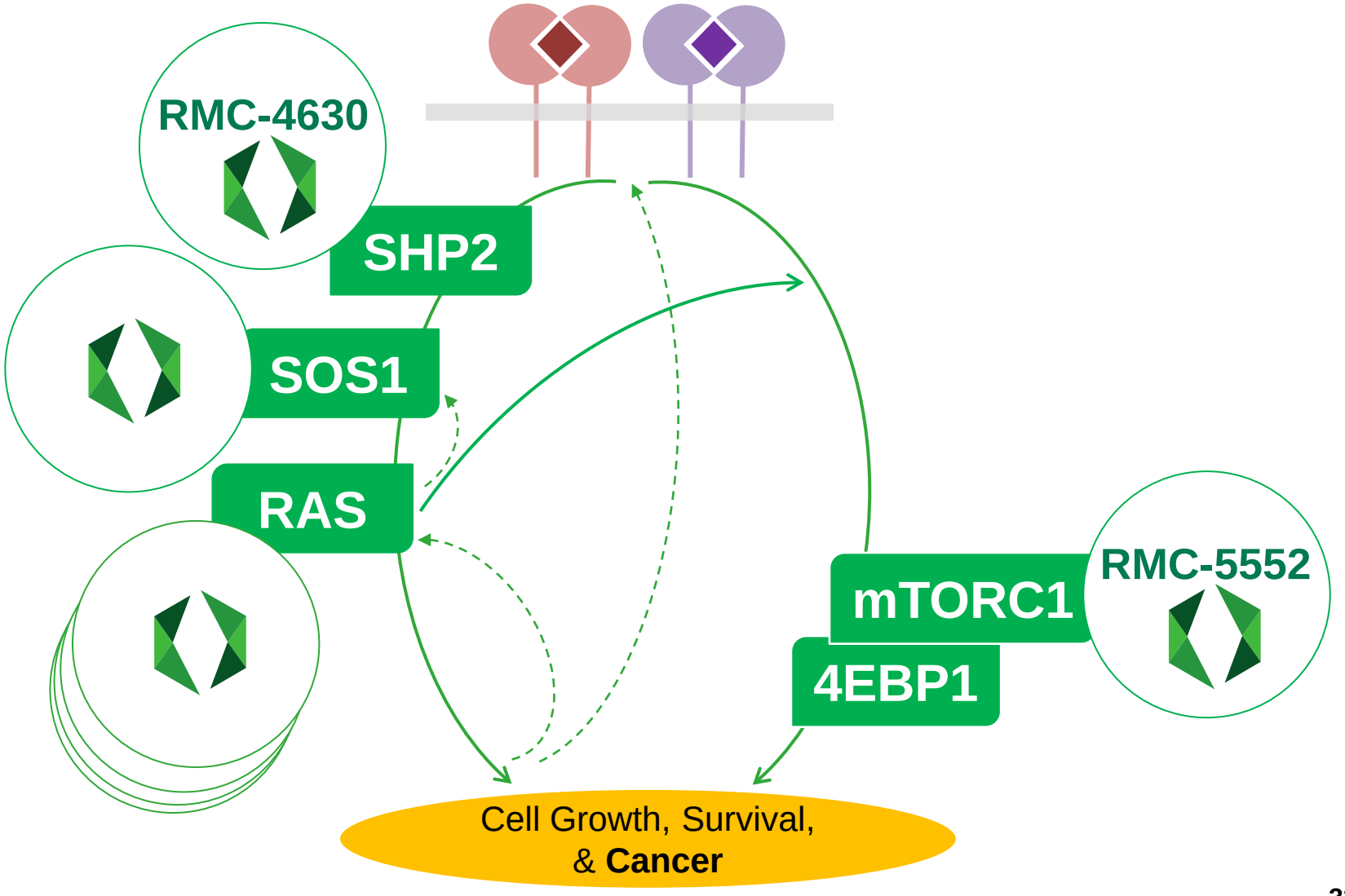


*Cleaved Caspase-3, 24 hr. post-treatment

RVMD preclinical data; Yang et al. *AACR* 2020
CDX = cell line-derived xenograft
$STK11^{LOF}$ (loss-of-function) inferred from deletions, insertions, premature stops and truncations
NSCLC = Non-small cell lung cancer

Summary

Pipeline Designed for Targeted Drug Combinations to Defeat Resistance in RAS-Addicted Cancer



2020 Milestones

Program	Status
RMC-4630 (SHP2)	✓ **Clinical update** ✓ **Begin treating patients in combination with AMG 510** ✓ **Begin treating patients in combination with anti-PD1** • **Begin treating patients in combination with osimertinib** • **Additional clinical update**
Mutant RAS(ON)	• **Nominate first Development Candidate** ✓ Preclinical regressions from oral $KRAS^{G12C}$(ON) inhibitor • **Lead compound for second target**
RMC-5552 (mTORC1)	• **IND-ready** ✓ Preclinical regressions from combination with $KRAS^{G12C}$(OFF) inhibitor

Financial Information

Financial Position	
Cash, cash equivalents and marketable securities @ 6/30/2020 (1)	$325.4M

(1) Amount does not include proceeds from the July 2020 public offering of common stock, whereby the Company issued and sold 6.9 million shares of its common stock at a price of $26.00 per share for net proceeds of $167.9 million, after deducting underwriting discounts and commissions and offering expenses

Translating Frontier Oncology Targets to *Outsmart Cancer*™