REVOLUTION MEDICINES

Translating Frontier Oncology Targets to *Outsmart Cancer*™

June 2020

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 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, future results of anticipated products, are forward-looking statements and the impact of the COVID-19 pandemic on our business. 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.

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.

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 May 14, 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.

Summary

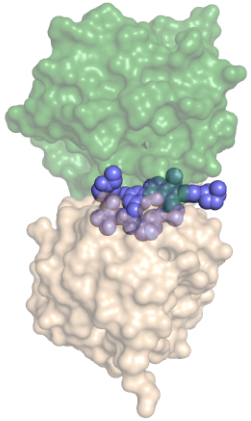
- Clinical-stage precision oncology company with deep focus on RAS cancers; growing clinical momentum
- Cohesive pipeline of complementary investigational products for targeted mono- and combination treatment
- Prolific innovation engine, sophisticated preclinical and clinical capabilities, and seasoned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

Continued Operational Excellence in COVID-19 Environment

- COVID-19 pandemic with profound global impact on health and socioeconomic well-being
- Operational adjustments implemented by RVMD in mid-March have enabled our team to remain healthy, focused and productive. Currently:
  - Limited impact on preclinical productivity and timelines; all projects progressing per expectations
  - No material impact on ongoing clinical study timelines, despite logistical challenges with on-site patient visits and follow up
  - Potential delays associated with planned study initiations, mitigated by active efforts supporting site initiation
- Strong balance sheet
  - $347.9 million in cash, cash equivalents and marketable securities as of 3/31/20

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

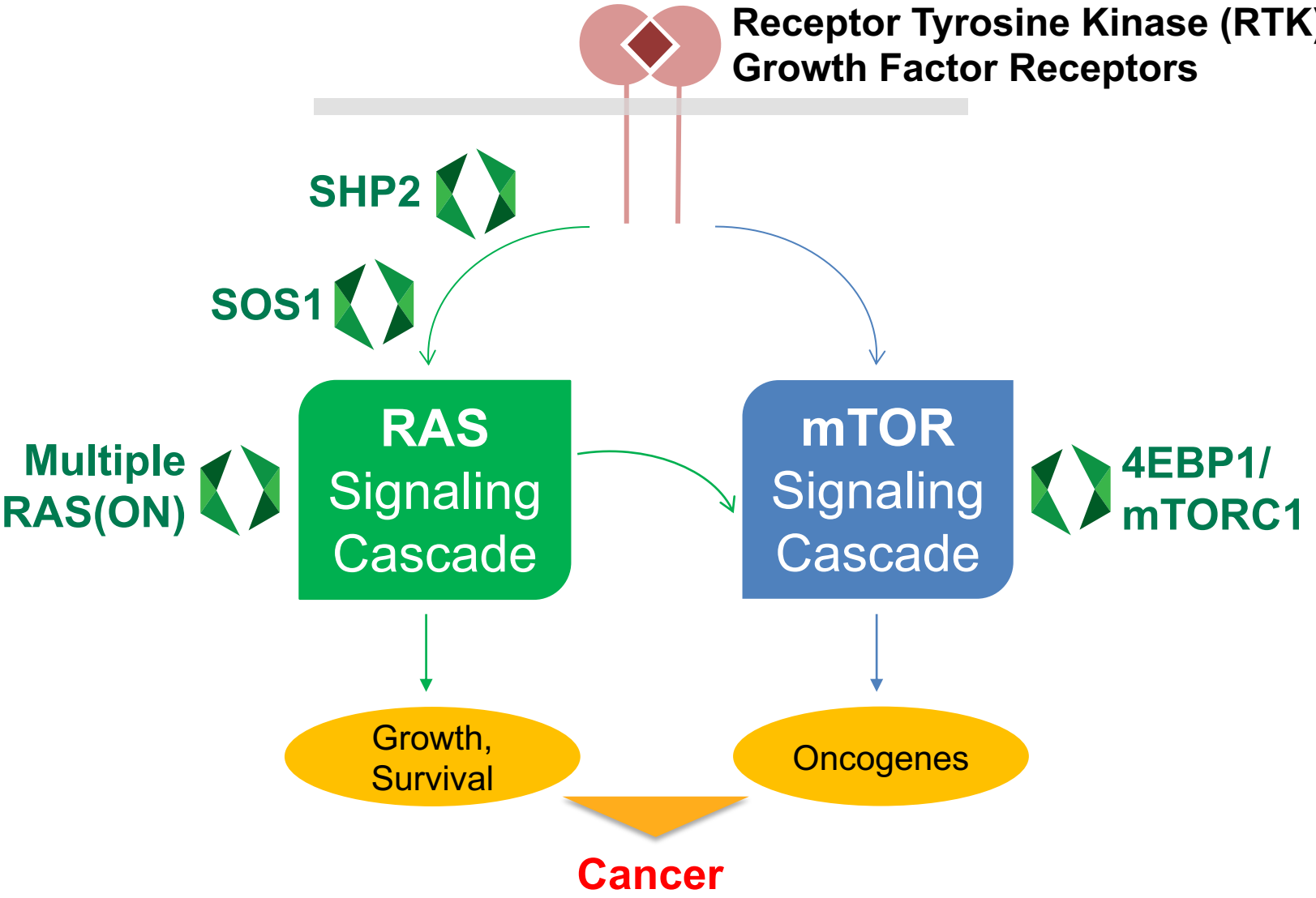
Deep chemical biology and cancer pharmacology know-how to define critical vulnerabilities of *frontier* RAS / mTOR pathway targets and signaling circuits



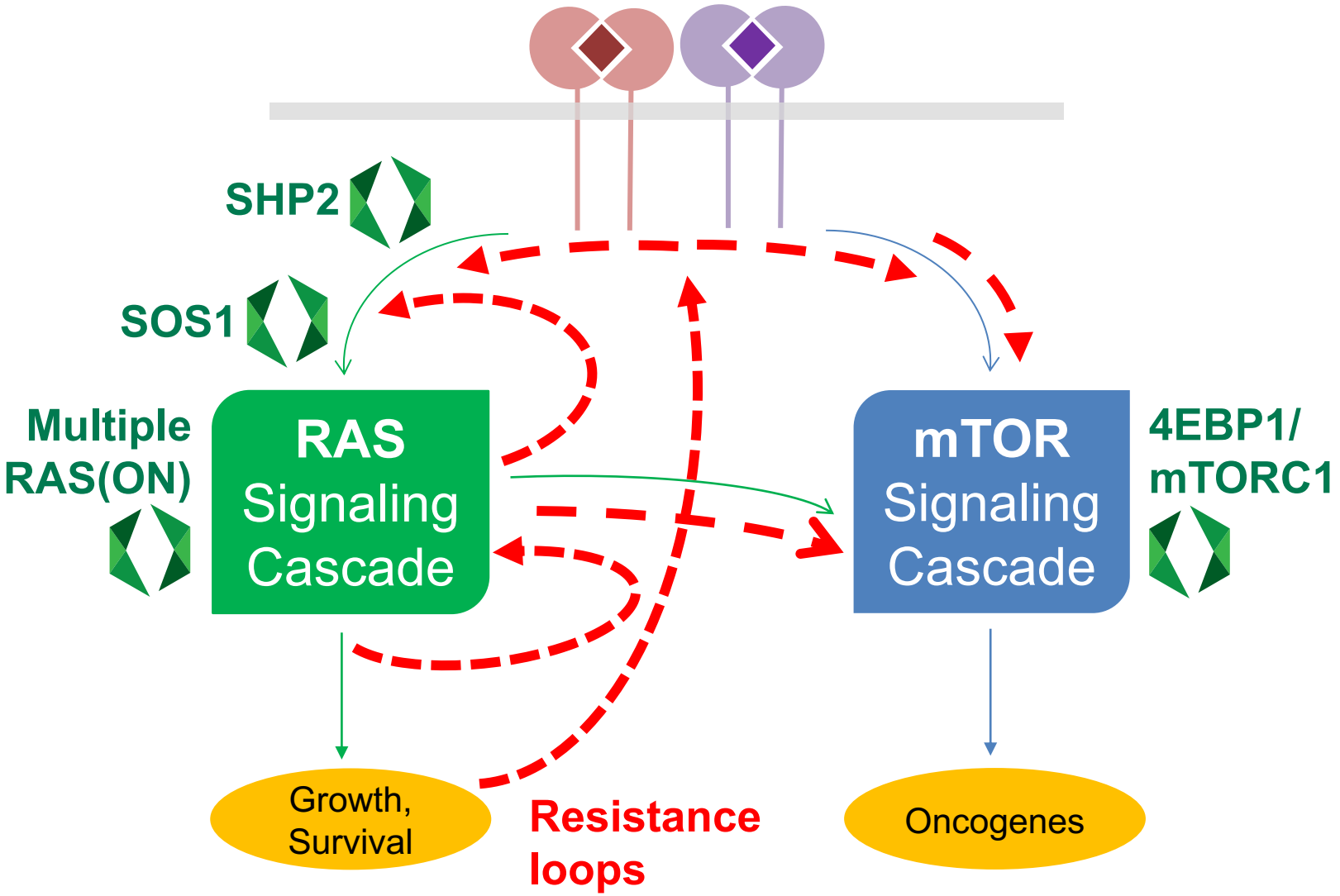
Sophisticated **structure-based drug discovery** capabilities, including proven **access to complex chemical space**, tailored to elusive cancer targets

Astute **precision medicine approach** for patients with genetically-defined cancers addicted to RAS / mTOR pathways

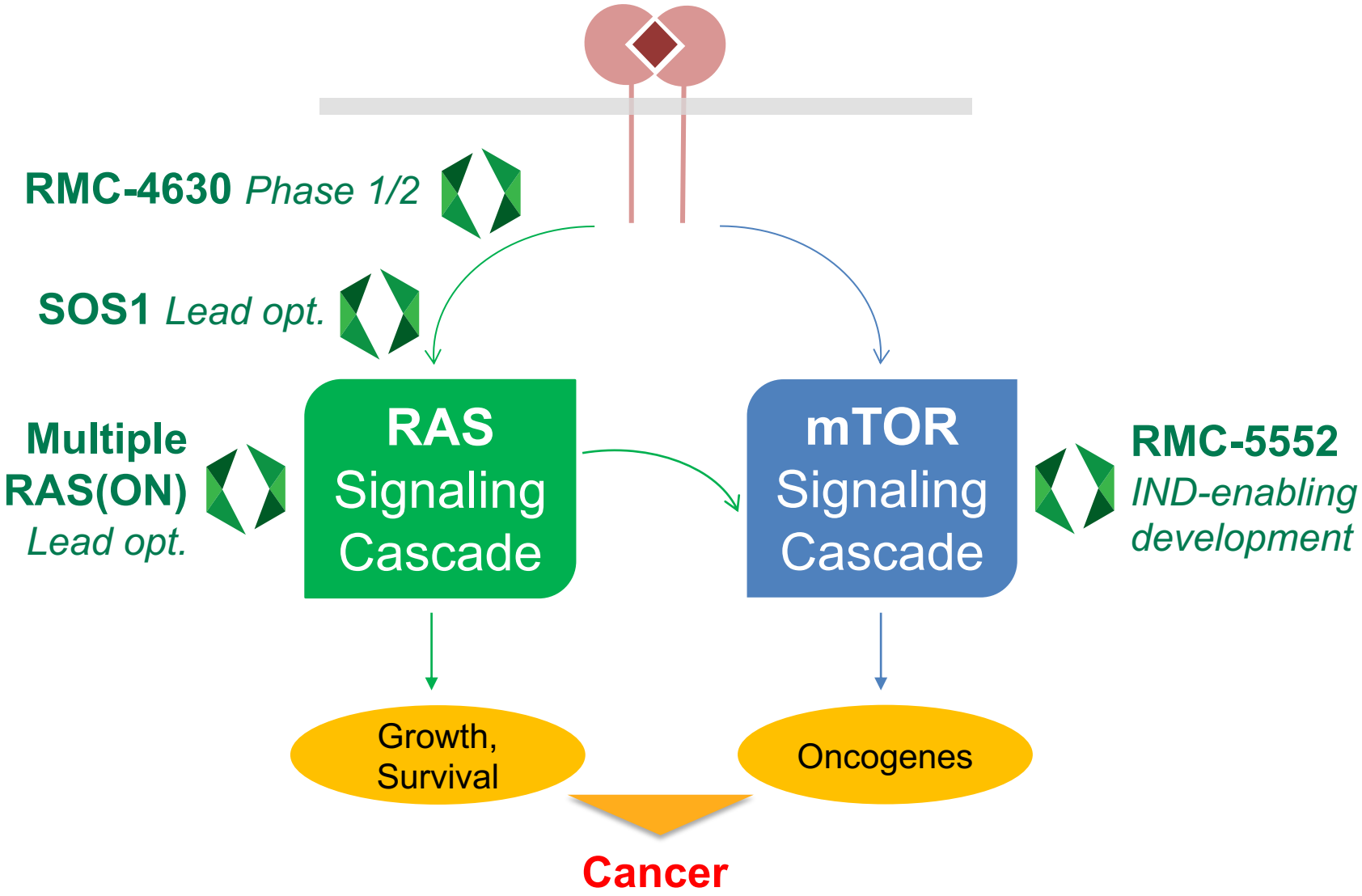
Integrated Pipeline Targets Elusive Drivers of RAS Cancers



Pipeline Drug Combinations to Overcome Resistance Loops that Feed Oncogene Addiction



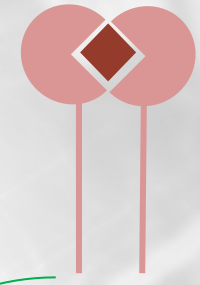
Substantial Progress Spanning Clinical and Preclinical Pipeline



SHP2

RMC-4630

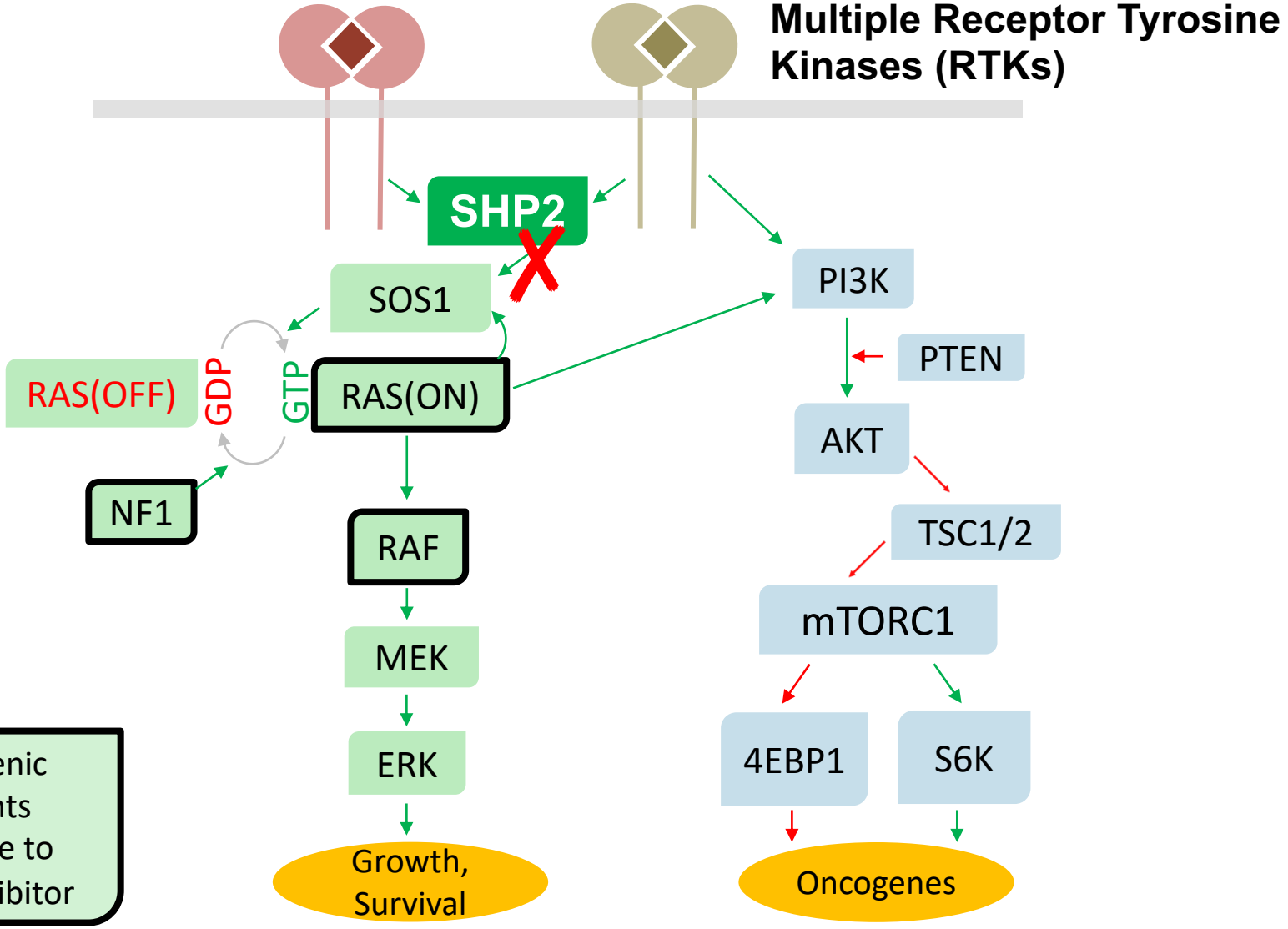
Phase 1/2



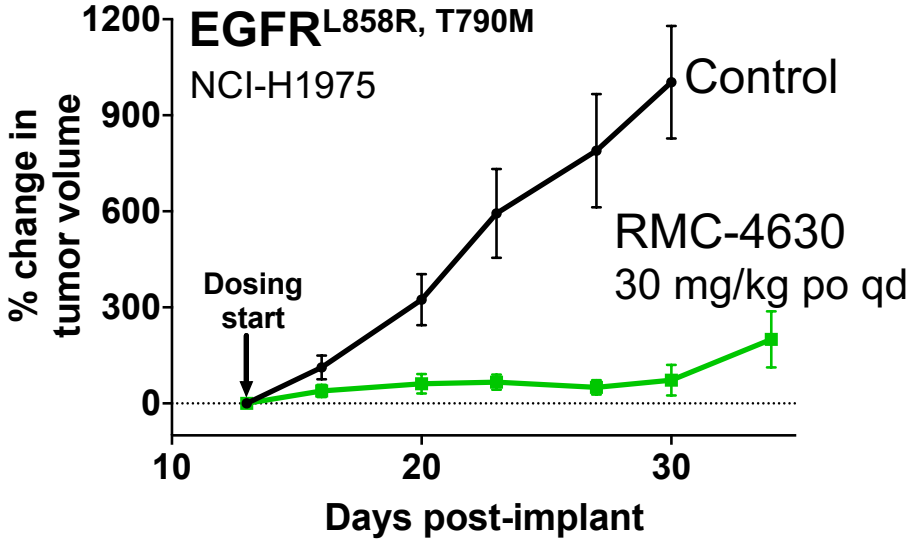
RAS Signaling Cascade

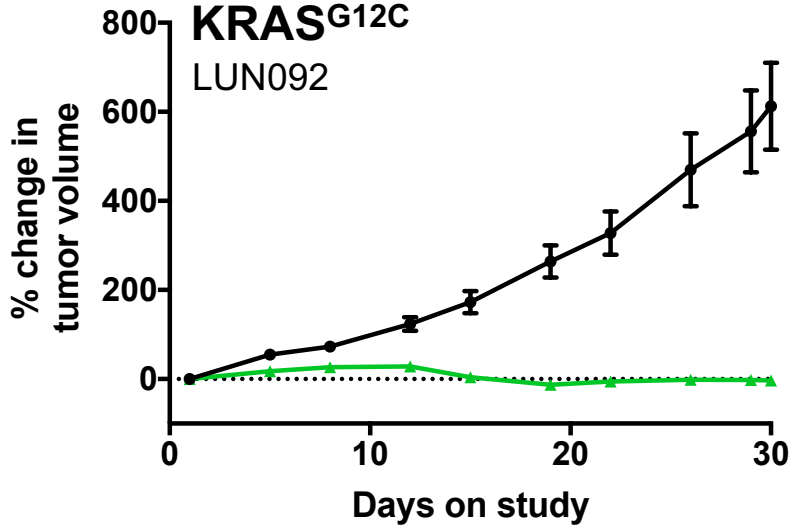
Growth, Survival

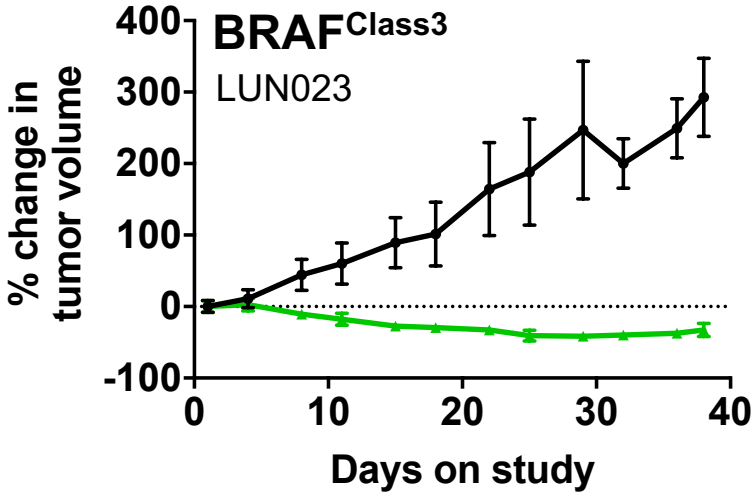
RMC-4630 Inhibits SHP2, a Shared Node that Regulates RAS Signaling Pathway

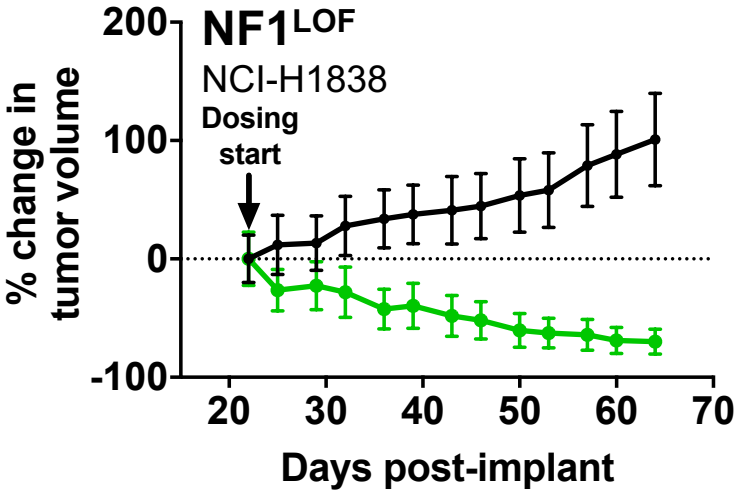


RMC-4630 Drives Stasis and Regressions of NSCLC Xenografts with Select Pathway Mutations

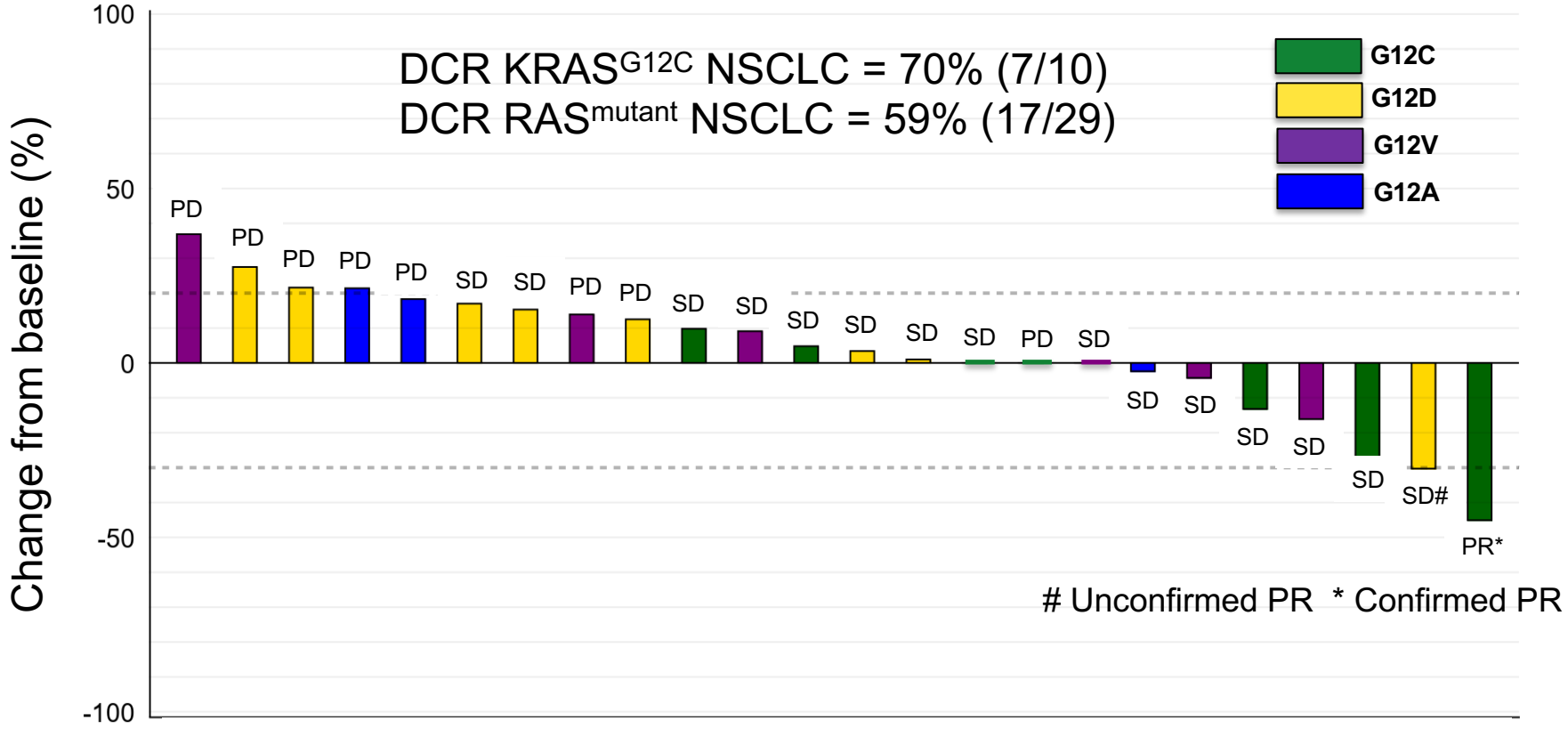








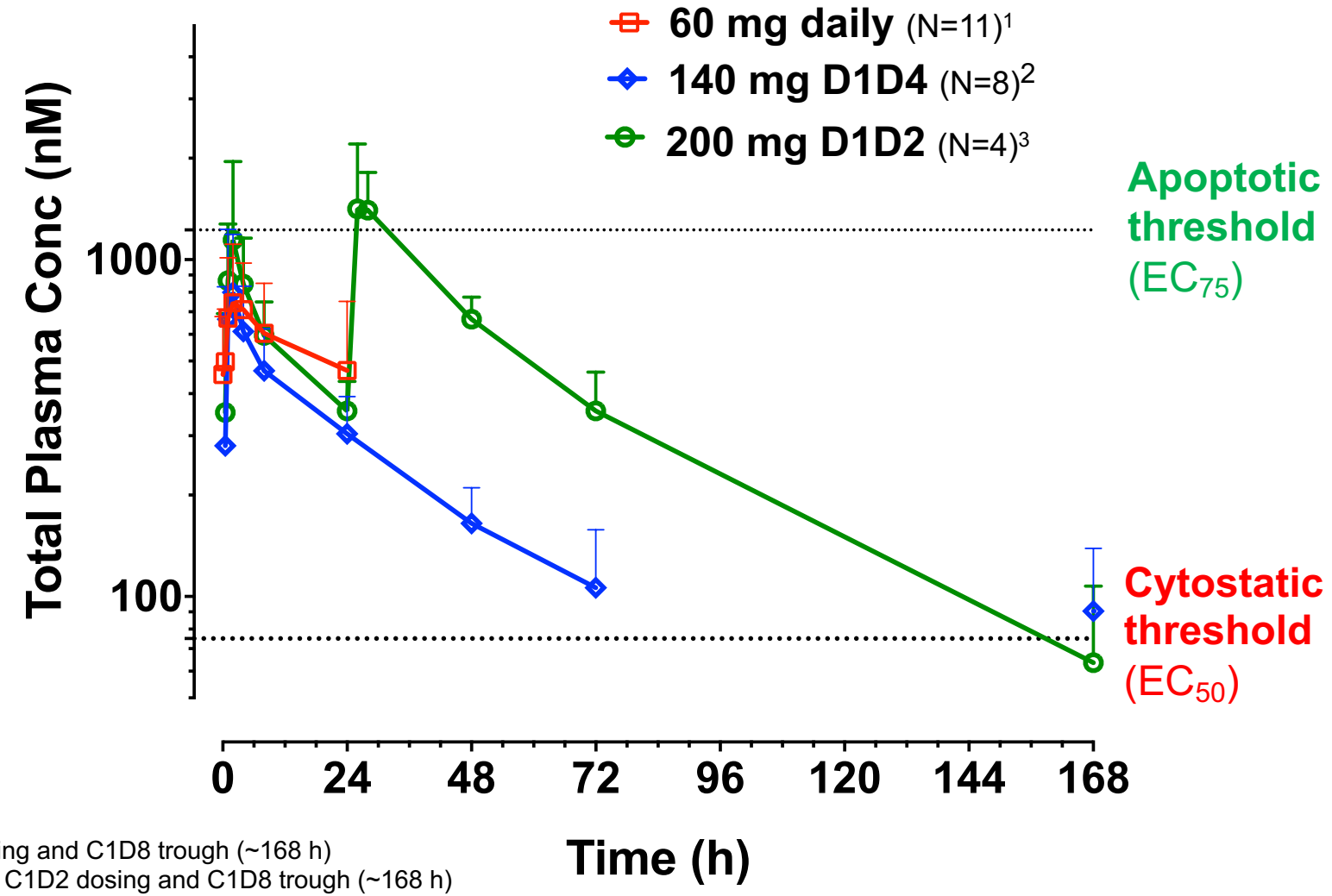
RMC-4630-01: Best Change in Tumor Burden from Baseline in KRAS^{mutant} NSCLC



Data presented for efficacy evaluable 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.
DCR = Disease Control Rate (no PD at first response assessment)

Source: EDC as of 5/4/2020

RMC-4630-01: Further Insights on Intermittent Dosing Paradigm in the Clinic



PK sampled at:
[1]C1D22
[2]Post-C1D1 dosing and C1D8 trough (~168 h)
[3]Post-C1D1 and C1D2 dosing and C1D8 trough (~168 h)

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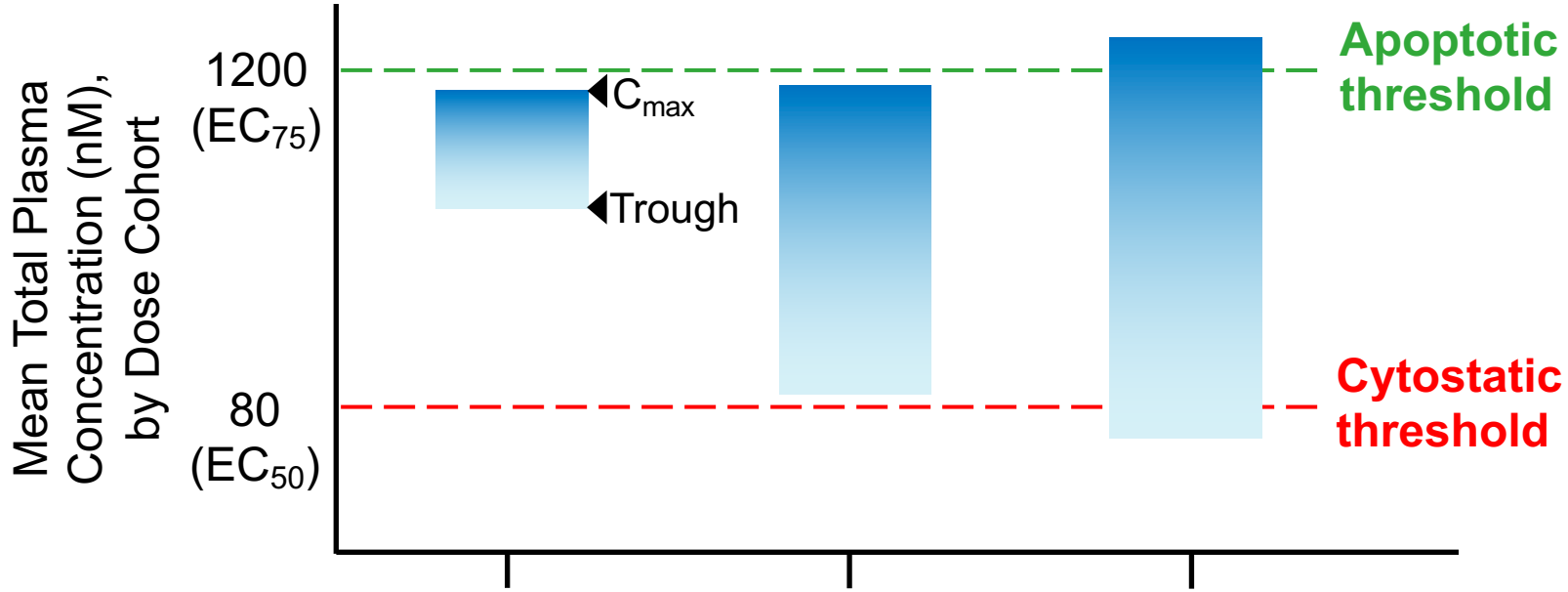
RMC-4630-01: Approaching Dose & Schedule Optimized for Efficacious and Tolerable Exposures



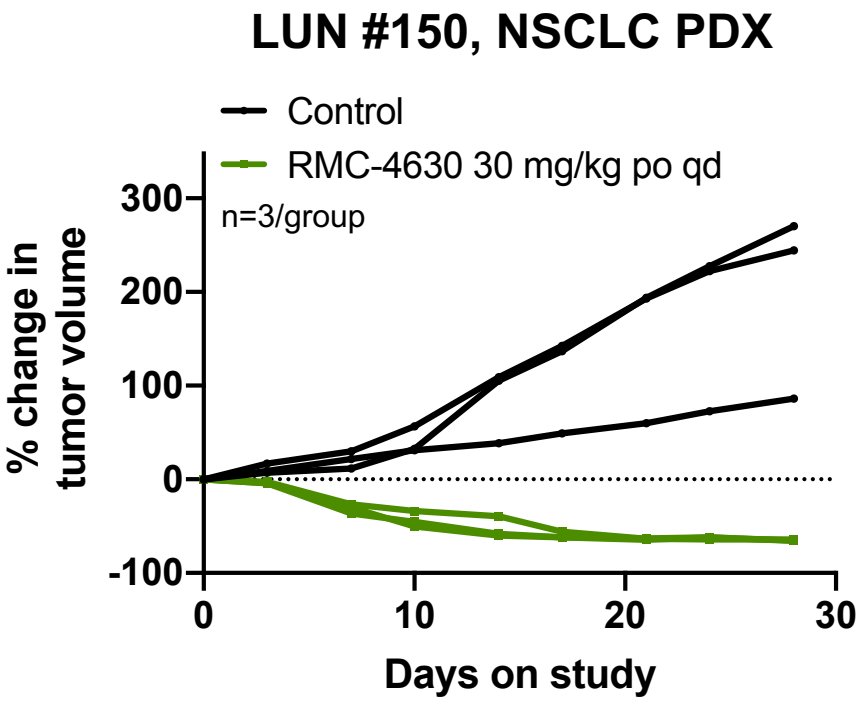
	60 mg daily N=18^	140 mg D1D4* N=8	200 mg D1D2* N=4
Dose cohort:			
With related AEs, grade ≥3:	9/18 (50%)[a]	4/8 (50%)[b]	0/4 (0%)
With AEs Leading to Discontinuation or Dose Reduction:	4/18 (22.2%)	1/8 (12.5%)	0/4 (0%)

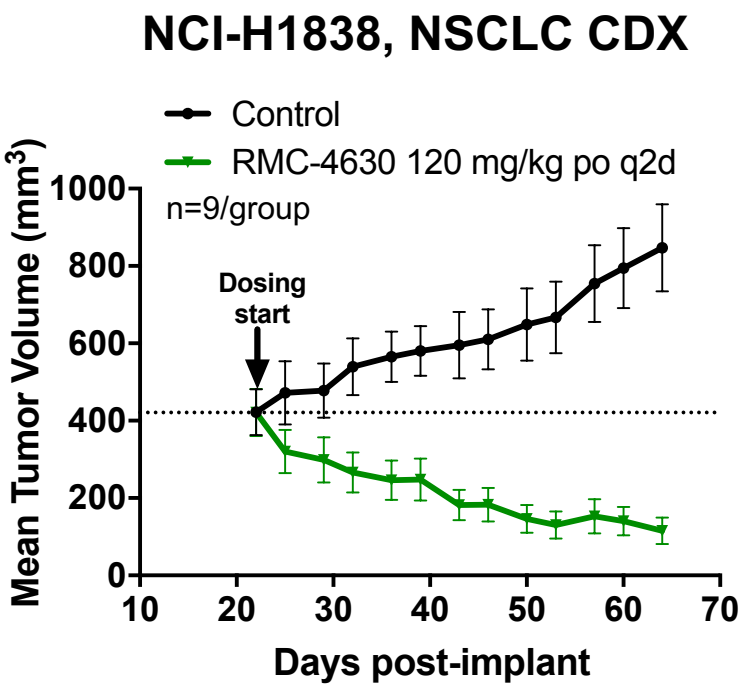
* Each week

^PK available for N=11

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

RMC-4630 Causes Tumor Growth Inhibition and Regressions in Diverse Preclinical NF1$^{LOF\wedge}$ Models





- Anti-tumor effects in numerous NF1^{LOF} PDX models
  - Tumor growth inhibition in 62% (34/55) of models
  - 25% of responses were regressions
- Regressions with intermittent dosing in NF1^{LOF} CDX models

^ NF1^{LOF} (loss-of-function) inferred from deletions, insertions, premature stops and truncations in neurofibromin 1 gene

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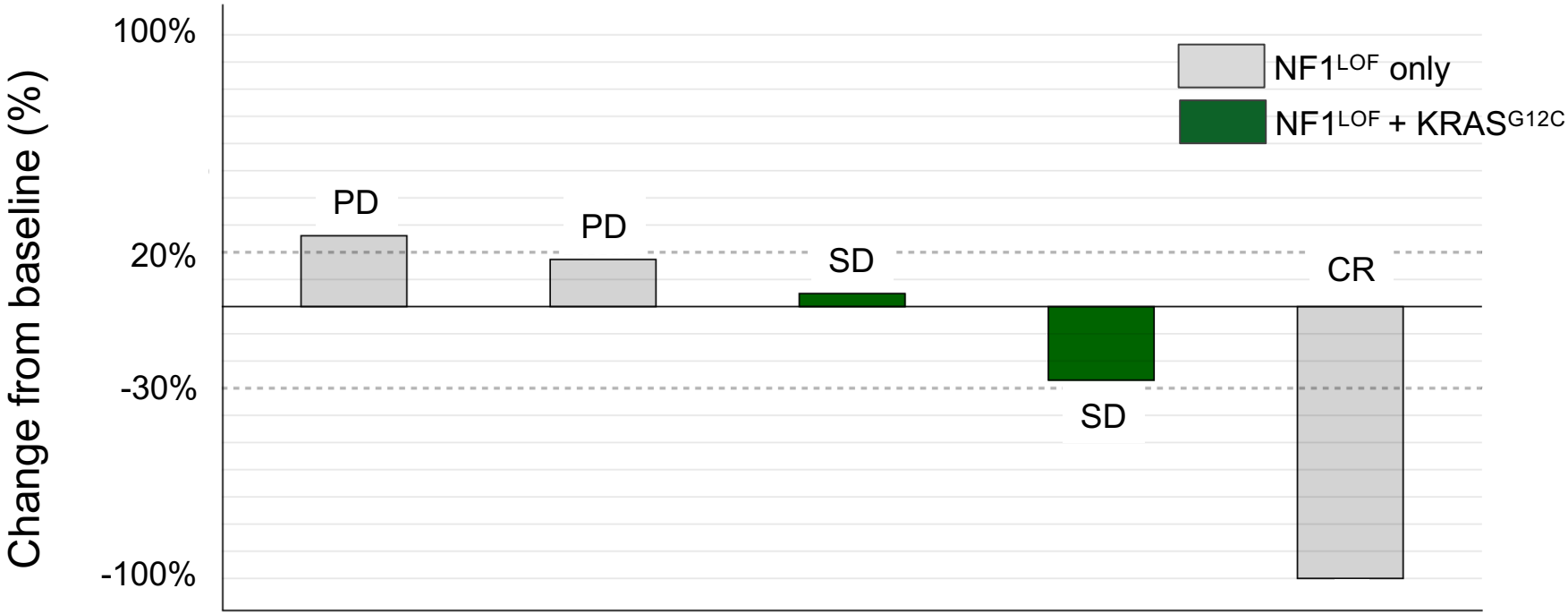
RMC-4630-01: Best Change in Tumor Burden for NSCLC and Gynecologic Tumors with NF1^{LOF}



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

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Complete Response in Patient with Uterine Cancer

- 63yr old with stage IVb poorly differentiated uterine carcinosarcoma
- Diagnosed Oct 2017 – two $NF1^{LOF}$ mutations, POLE (DNA repair) mutation, and ultra-high tumor mutational burden
- Two treatment regimens prior to starting RMC-4630
- Started RMC-4630 200 mg D1D4 reduced to 140 mg D1D4 due to GI toxicity
- Continues in CR at 5 months on study therapy

Target Lesion	Baseline Scan	1st on Treatment Scan
Omental thickening (left upper quadrant)	1.7 cm	0.0 cm
Percent Change from Baseline	-	100% ↓
Overall Response per RECIST V1.1		Complete Response (CR) confirmed

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Rational, Mechanism-driven Combinations as Central Clinical Thesis

Monotherapy
Dose/regimen optimization

SHP2 inhibitor
RMC-4630

Combination therapies

Additive anti-tumor effects + combat adaptive resistance

MEK inhibitors	$KRAS^{G12C}$ inhibitors	RTK inhibitors	Checkpoint inhibitors	ERK inhibitors
Select RAS Pathway Mutations	$KRAS^{G12C}$ Mutation	EGFR Mutations	SOC with Mutations	Select Mutations

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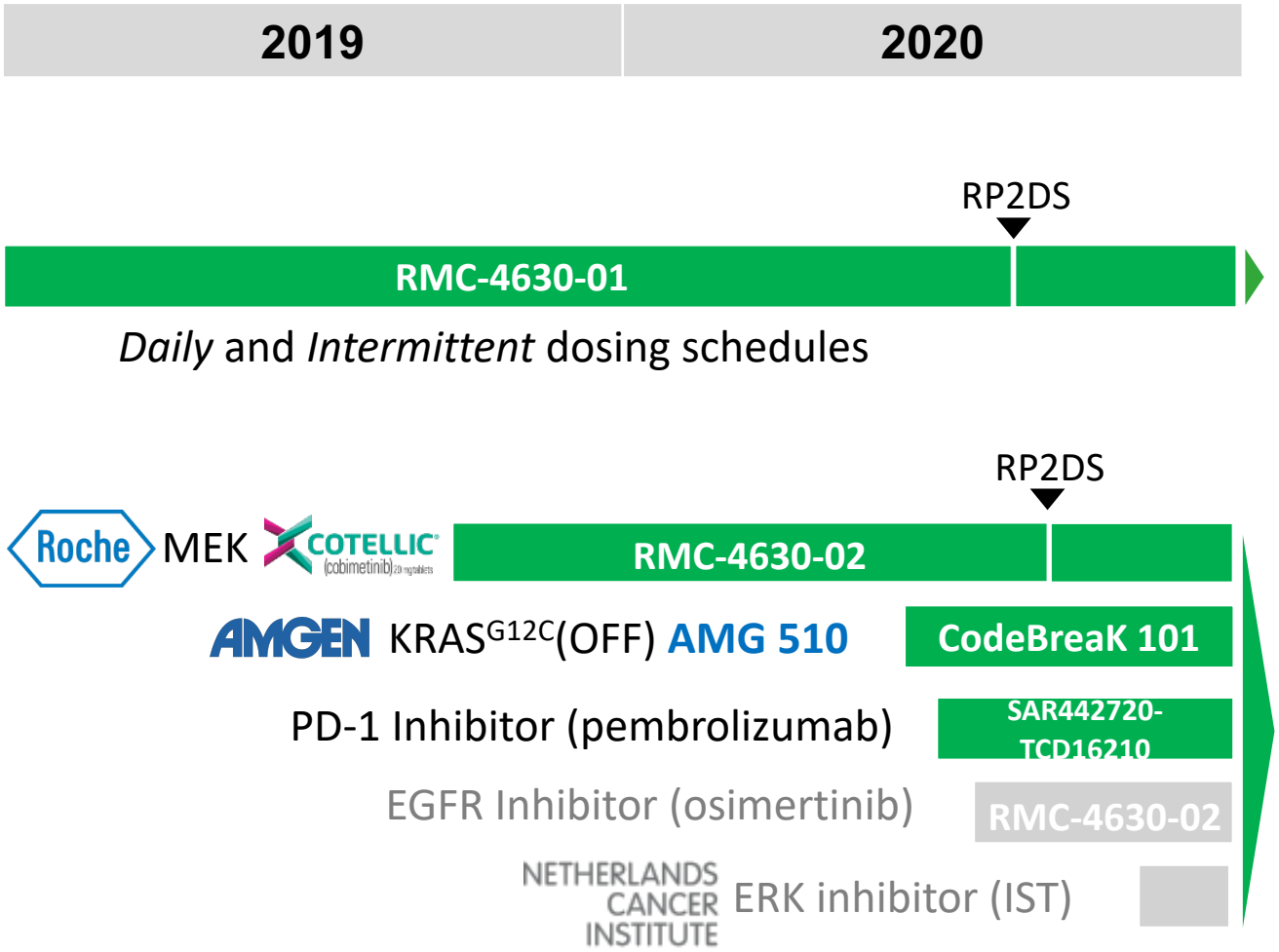
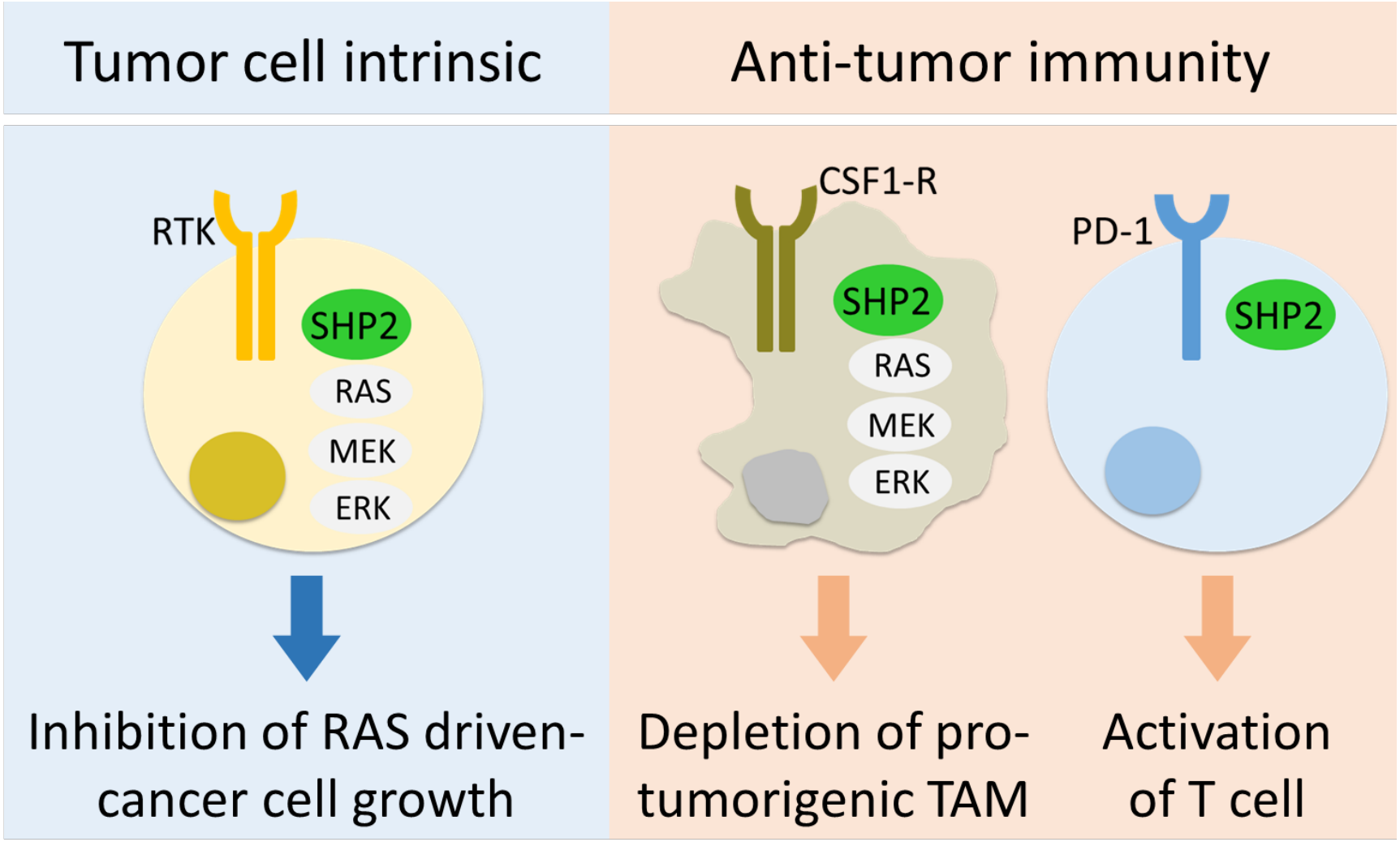
Broad Development Program for RMC-4630 Progressing Well



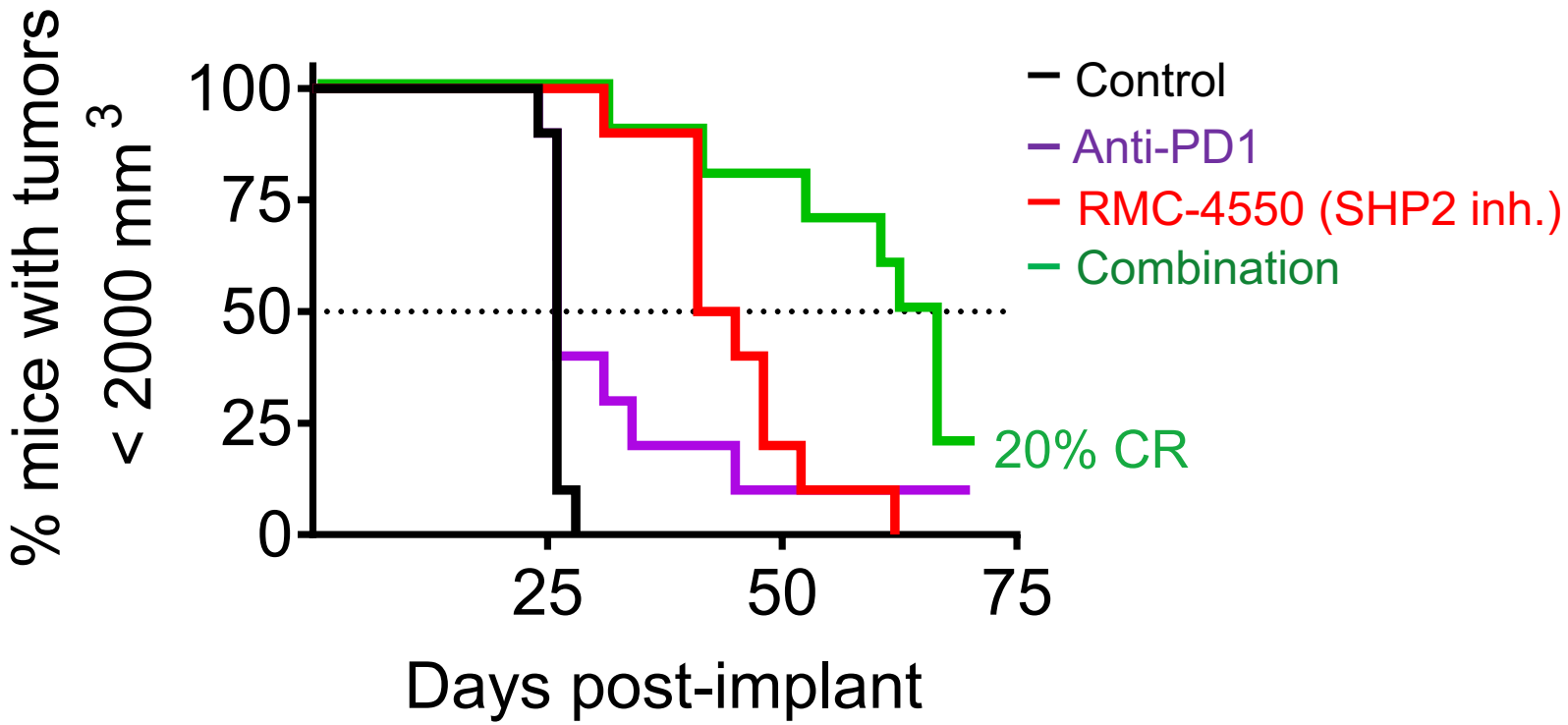
SHP2 Inhibitor Promotes Anti-Tumor Responses via Effects on Innate and Adaptive Immunity



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

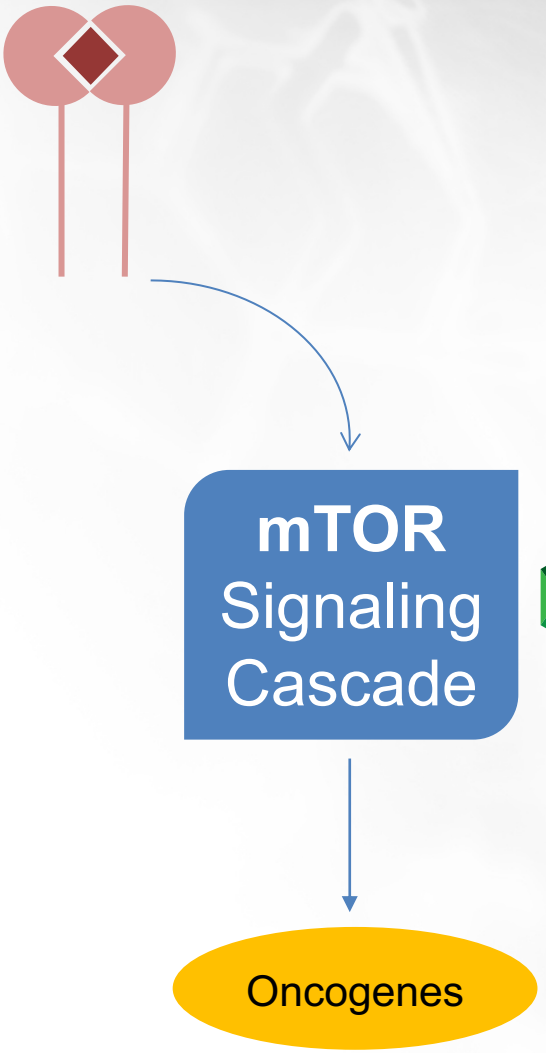
Anti-Tumor Responses from SHP2 Inhibitor Monotherapy and Combination with Anti-PD1

EMT-6 (syngeneic breast cancer, $NF1^{mut}$;$SOS1^{mut}$)



CR: Complete response, with immunological memory

Quintana et al. *Cancer Research* April 2020

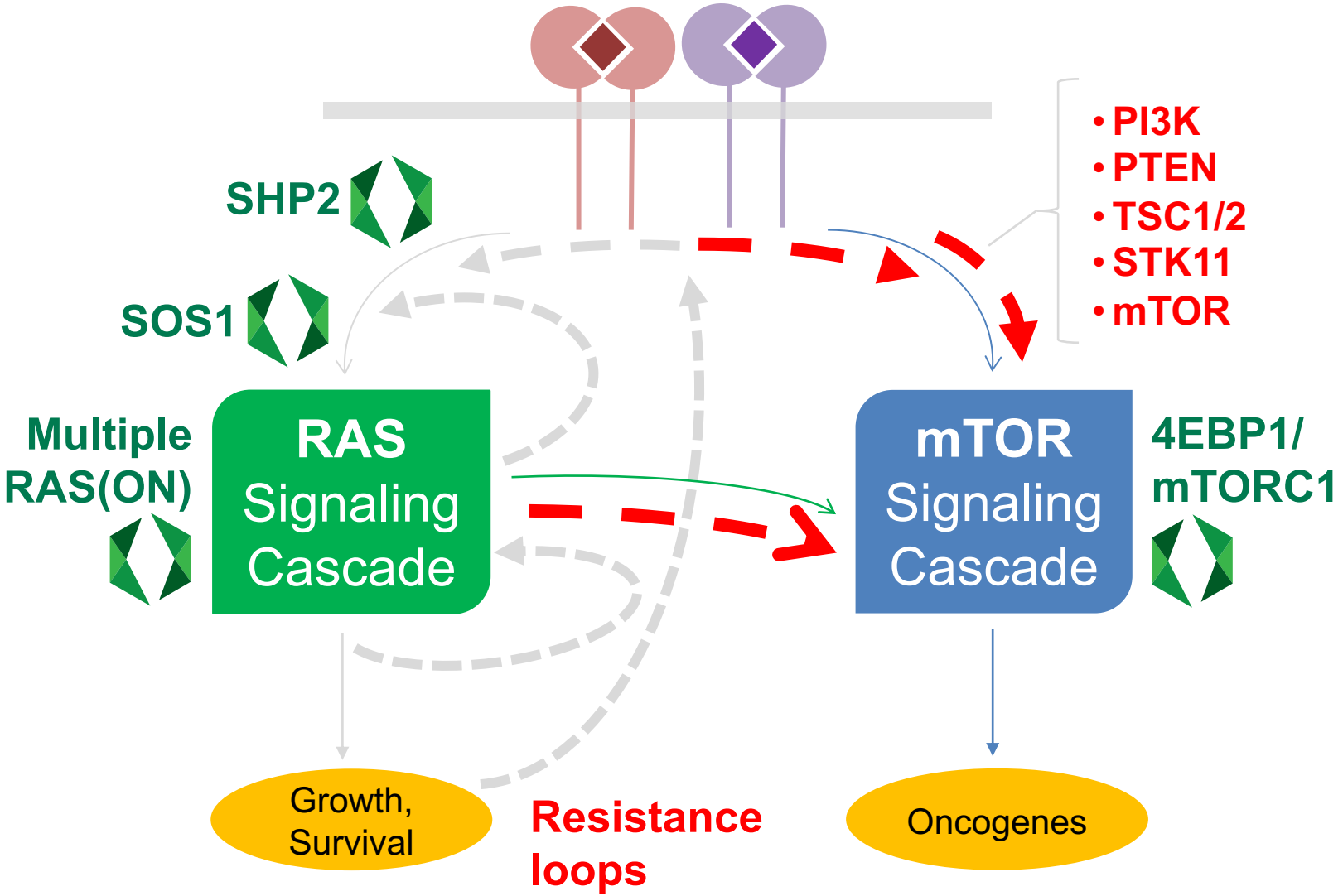


4EBP1/mTORC1

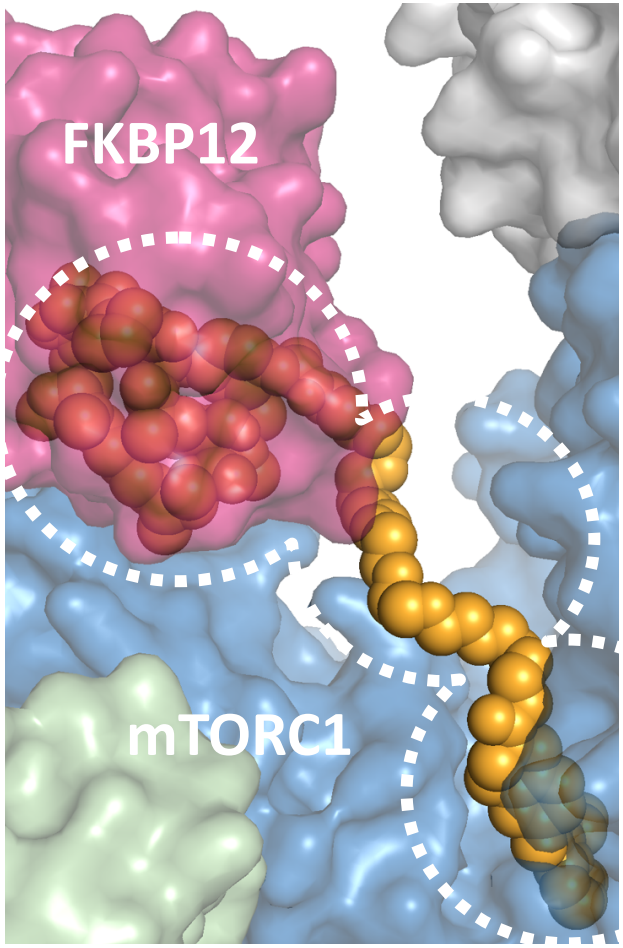
RMC-5552

IND-enabling development

Hyperactivation of mTOR Signaling Frequently Drives Cancer and/or Drug Resistance



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



Allosteric site

Layered structural model

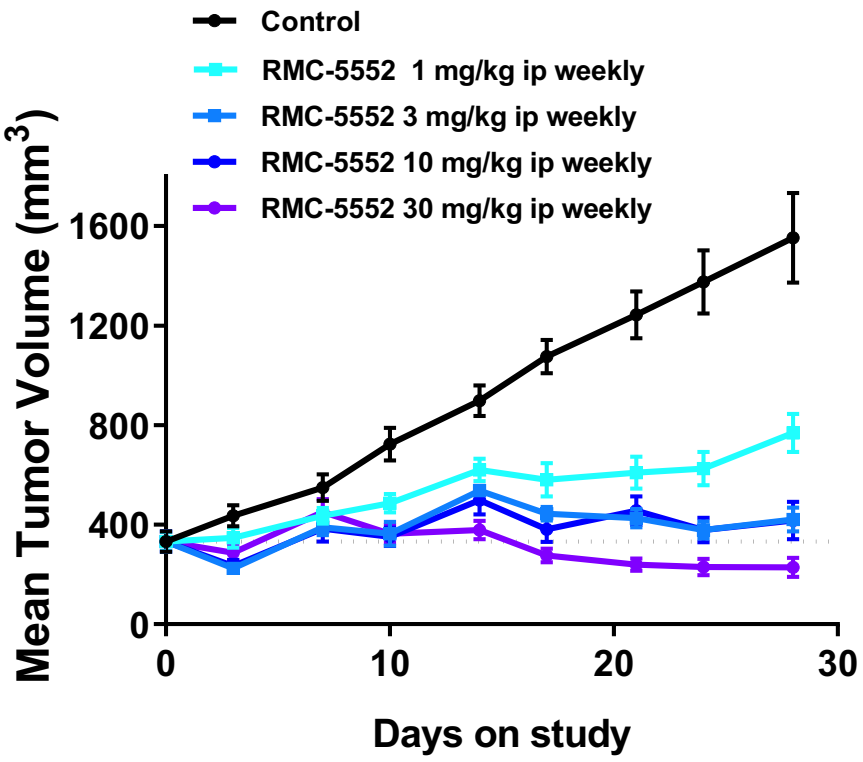
Active site

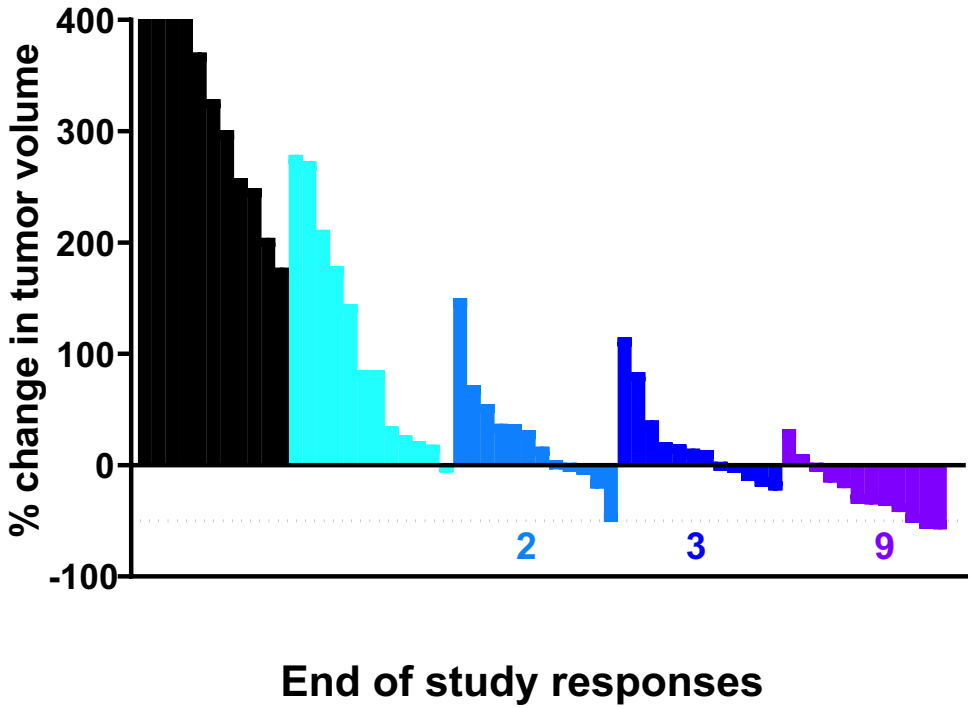
	RMC-5552
Inhibition of mTORC1: pS6K	**0.14 nM**
Inhibition of mTORC1: p4EBP1[1]	**0.48 nM**
Selectivity over mTORC2: AKT[2]	**40X**

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

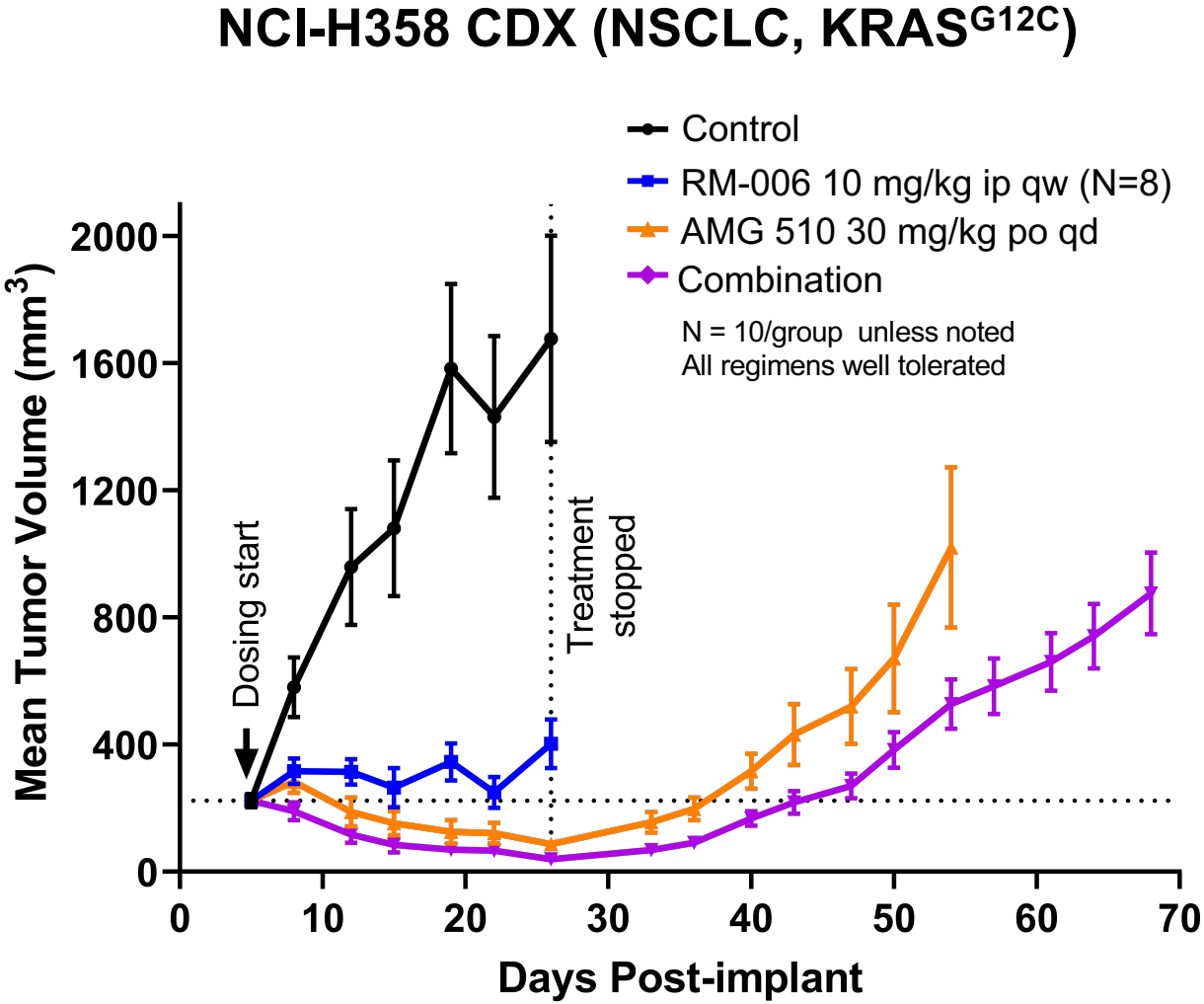
RMC-5552 Monotherapy Drives Regressions in mTORC1-Hyperactivated Tumor Xenografts

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



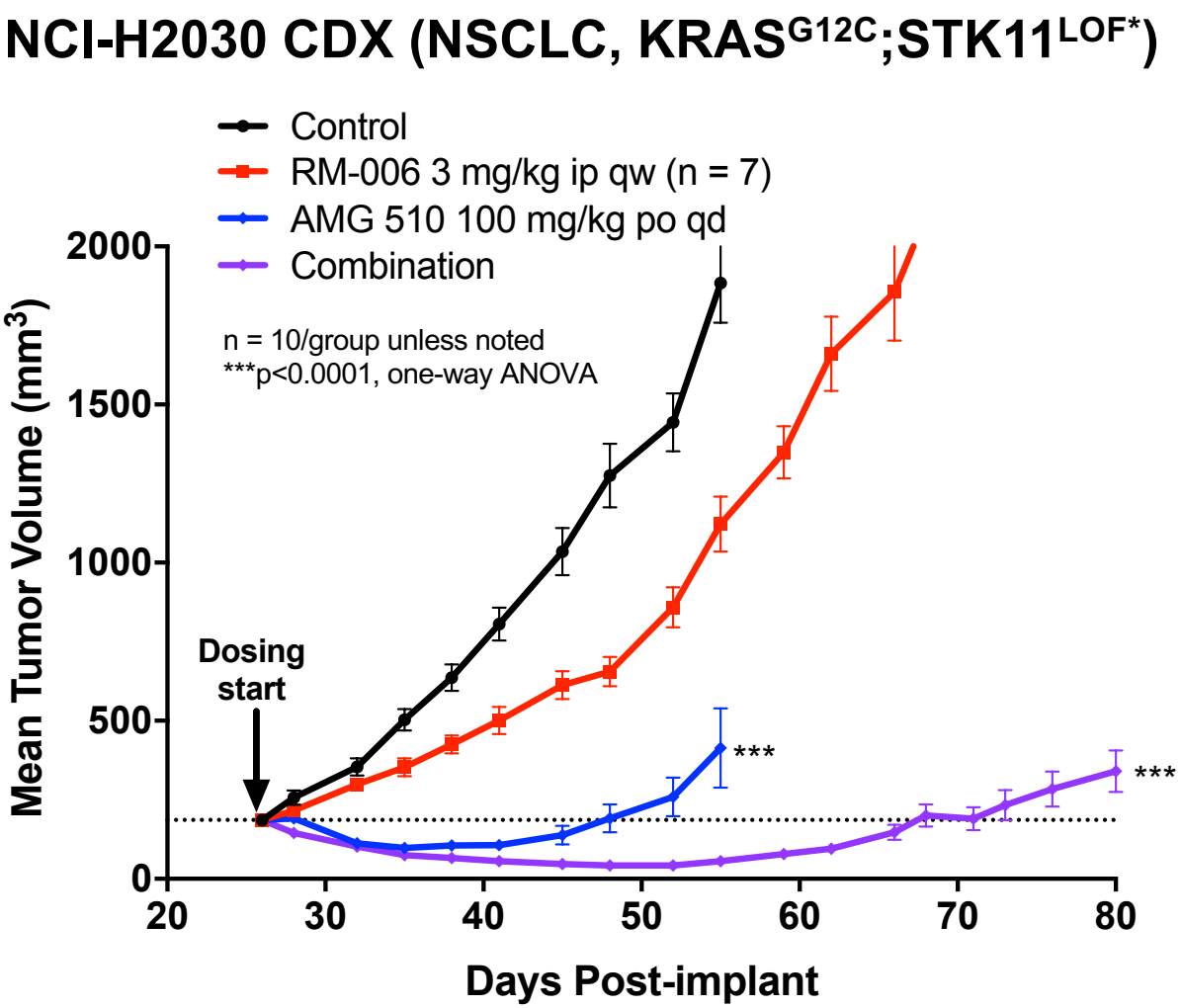


Bi-Steric mTORC1 Inhibitor (RM-006) Exhibits Anti-Tumor Activity in KRAS^{G12C} NSCLC Xenograft



RM-006 = mTORC1-selective bi-steric tool compound

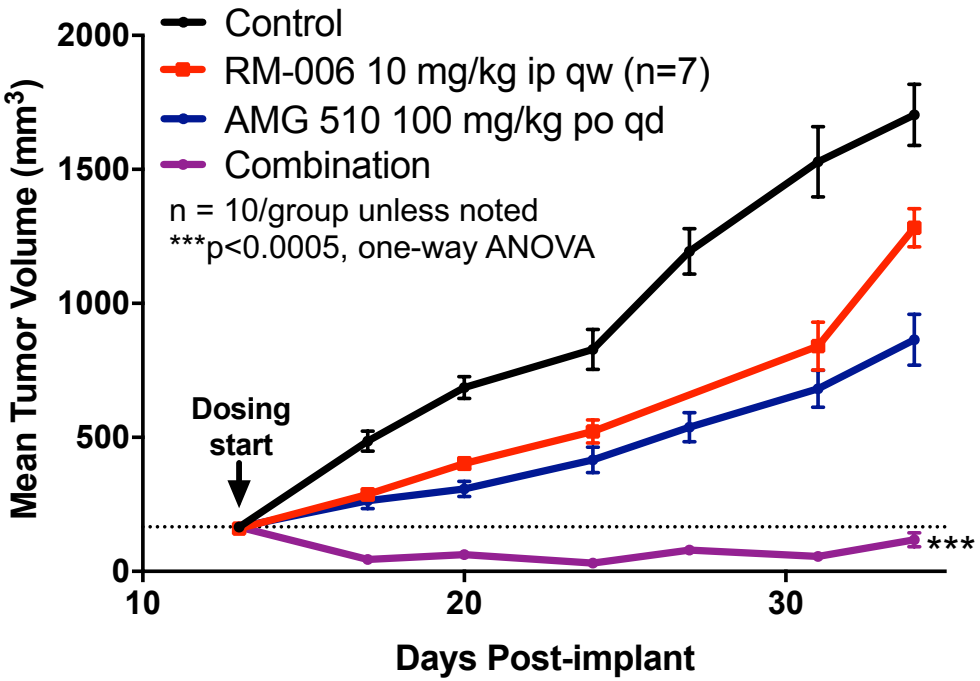
Dual Targeted Therapy for RAS/mTOR Pathway Co-Mutations Delays Acquired Drug Resistance

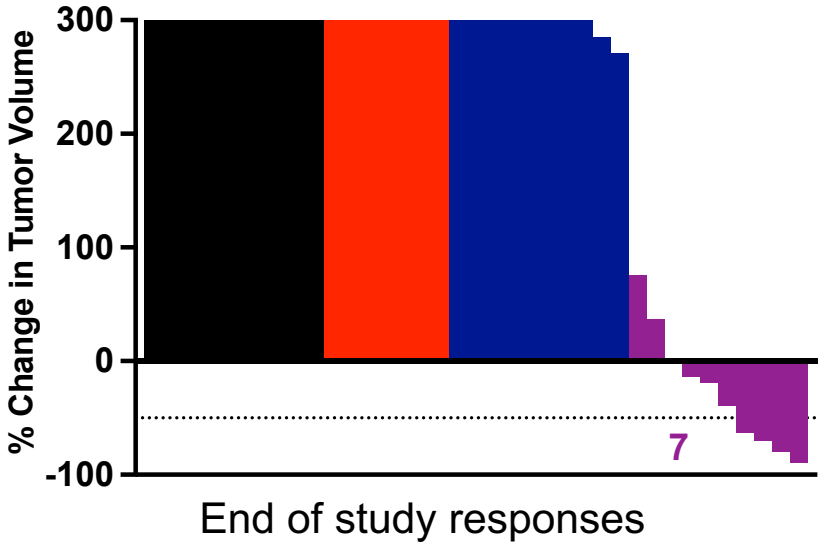


^ $STK11^{LOF}$ (loss-of-function) inferred from deletions, insertions, premature stops and truncations

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

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

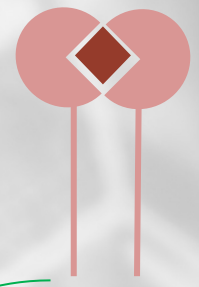




n = number of regressions > 10% from starting volume

^ STK11^{LOF} (loss-of-function) inferred from deletions, insertions, premature stops and truncations

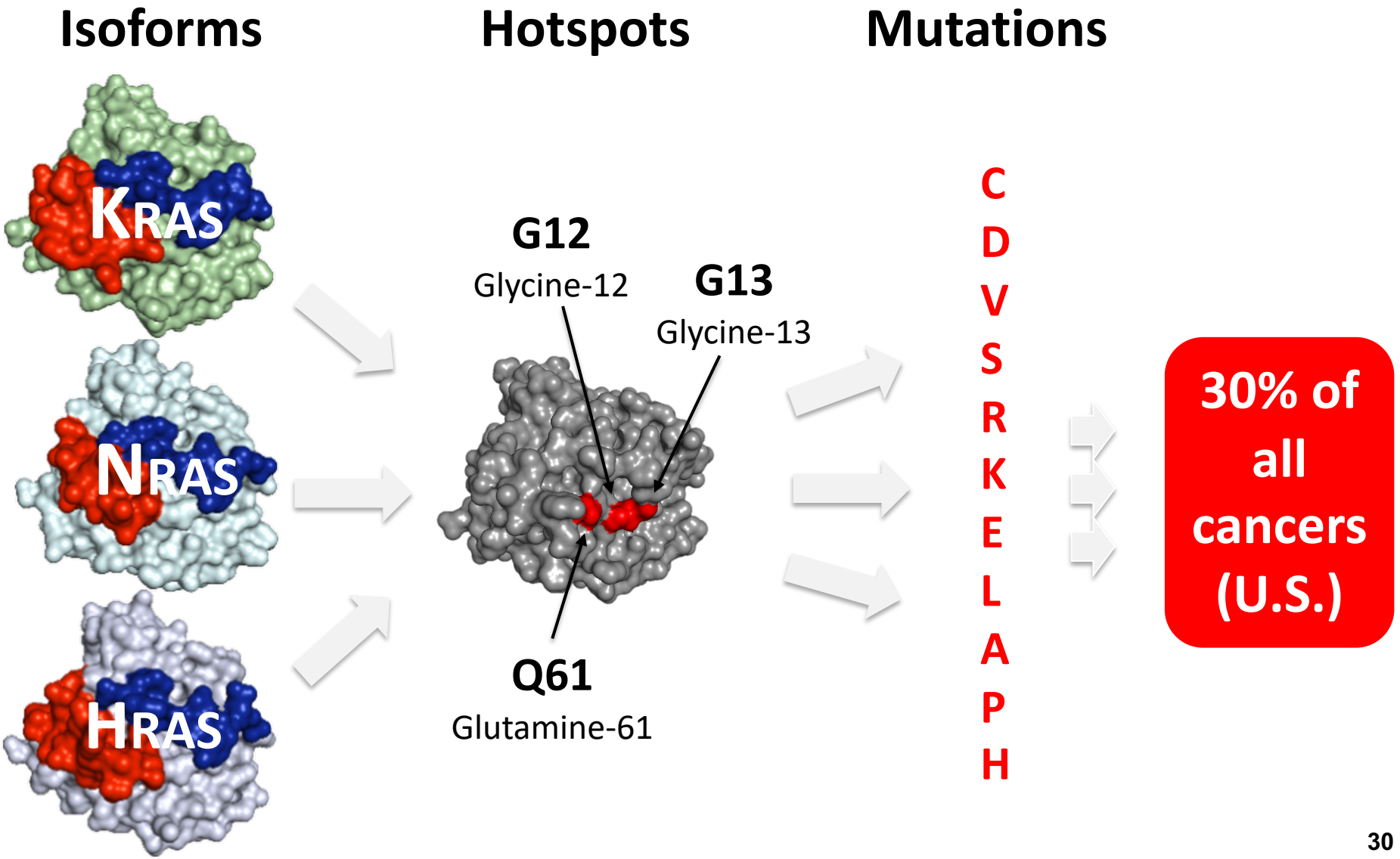
Multiple RAS(ON)
Lead opt.



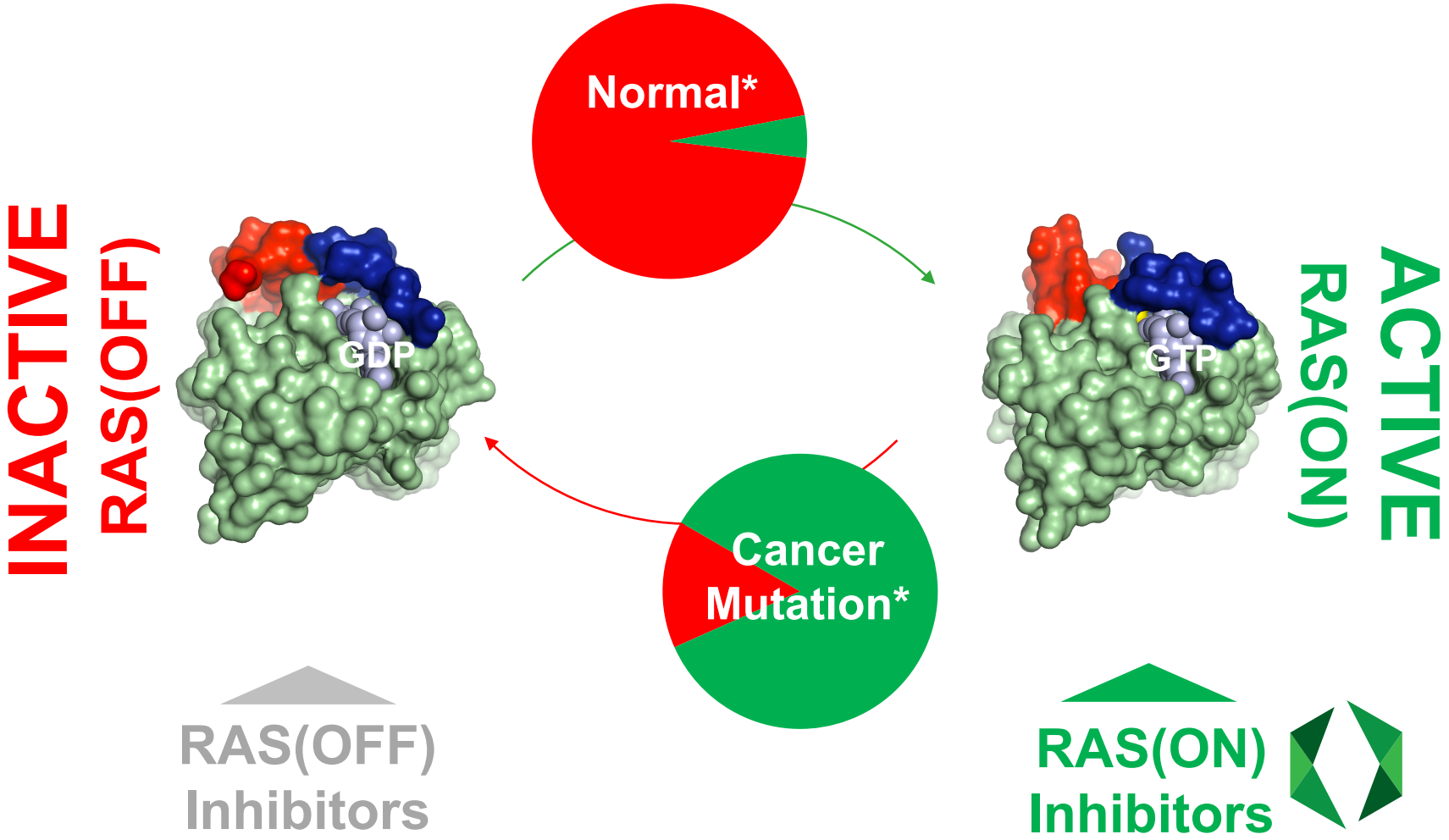
RAS Signaling Cascade

Growth, Survival

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

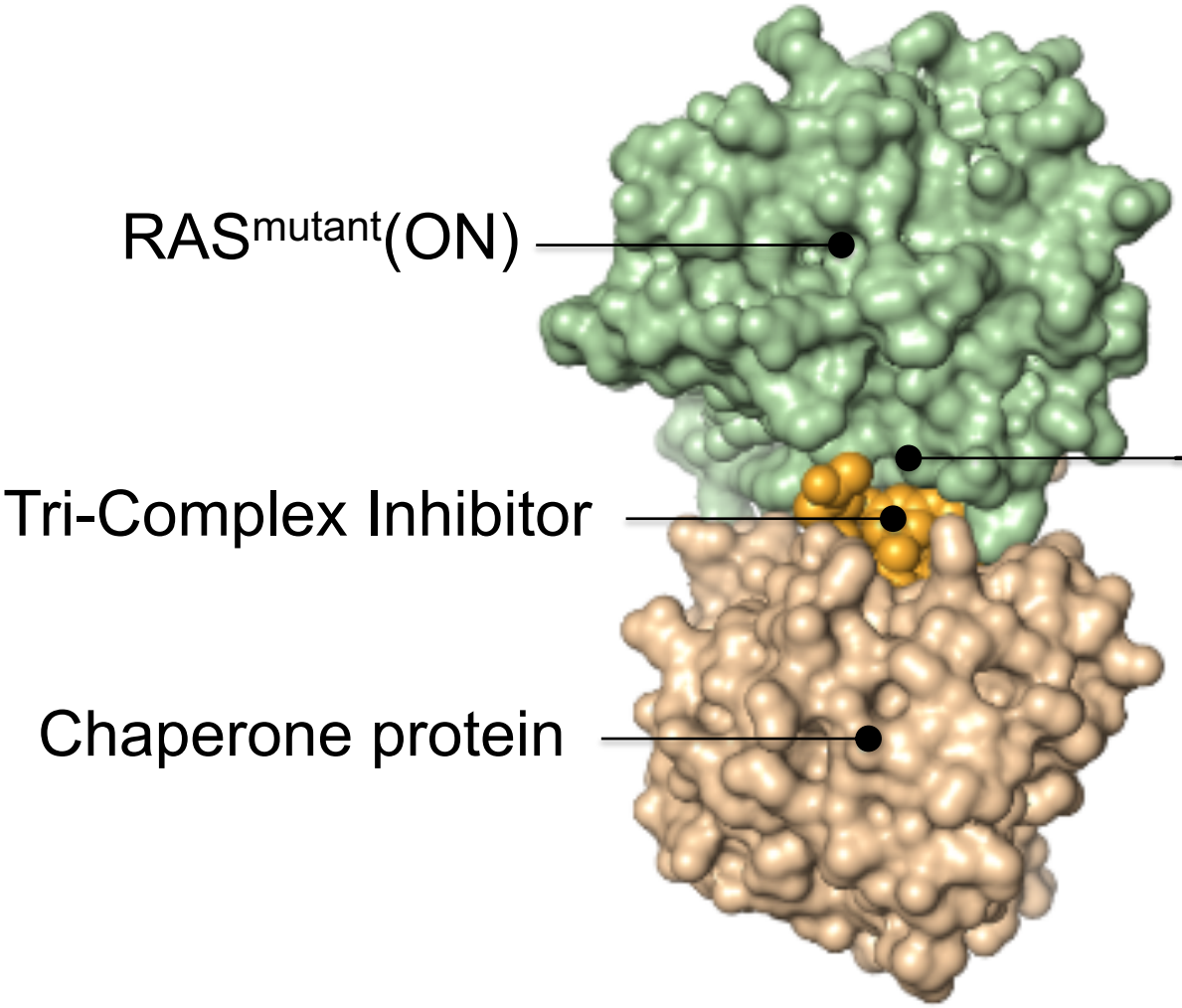


Mutant RAS Tumors are Addicted to, and Tenaciously Maintain, High Levels of RAS(ON)



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

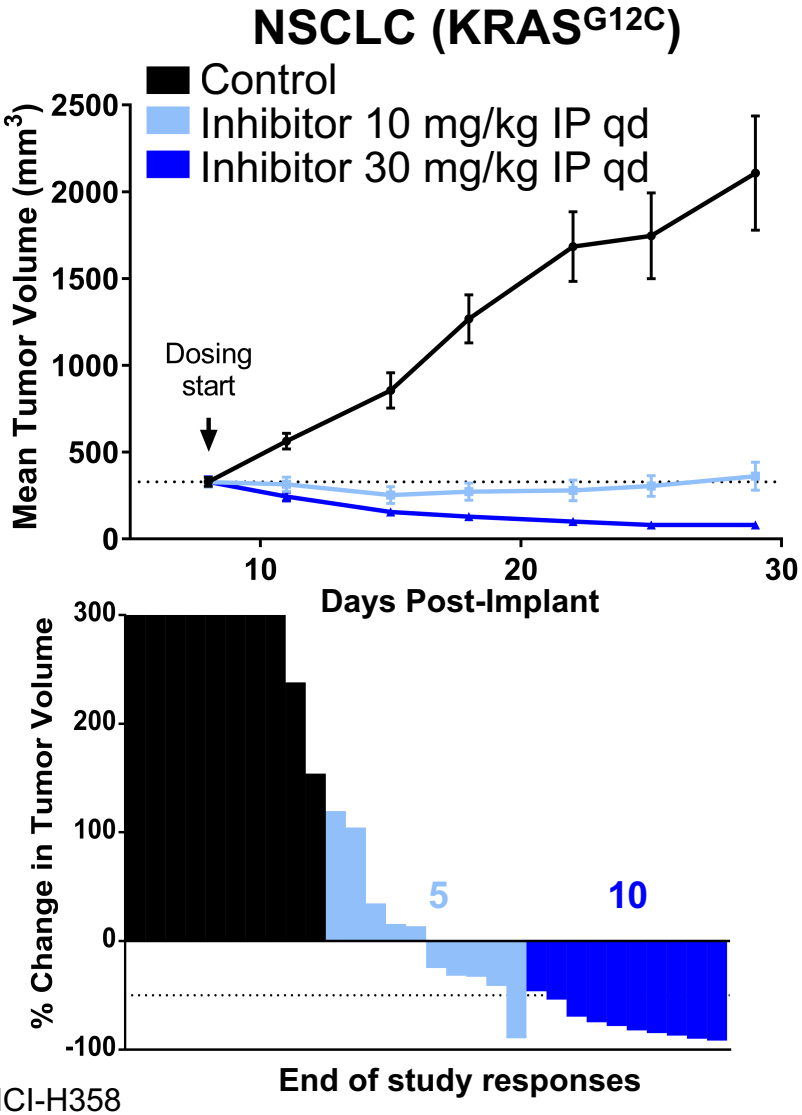
Highly Differentiated Inhibitors of Active Form of Oncogenic RAS Proteins



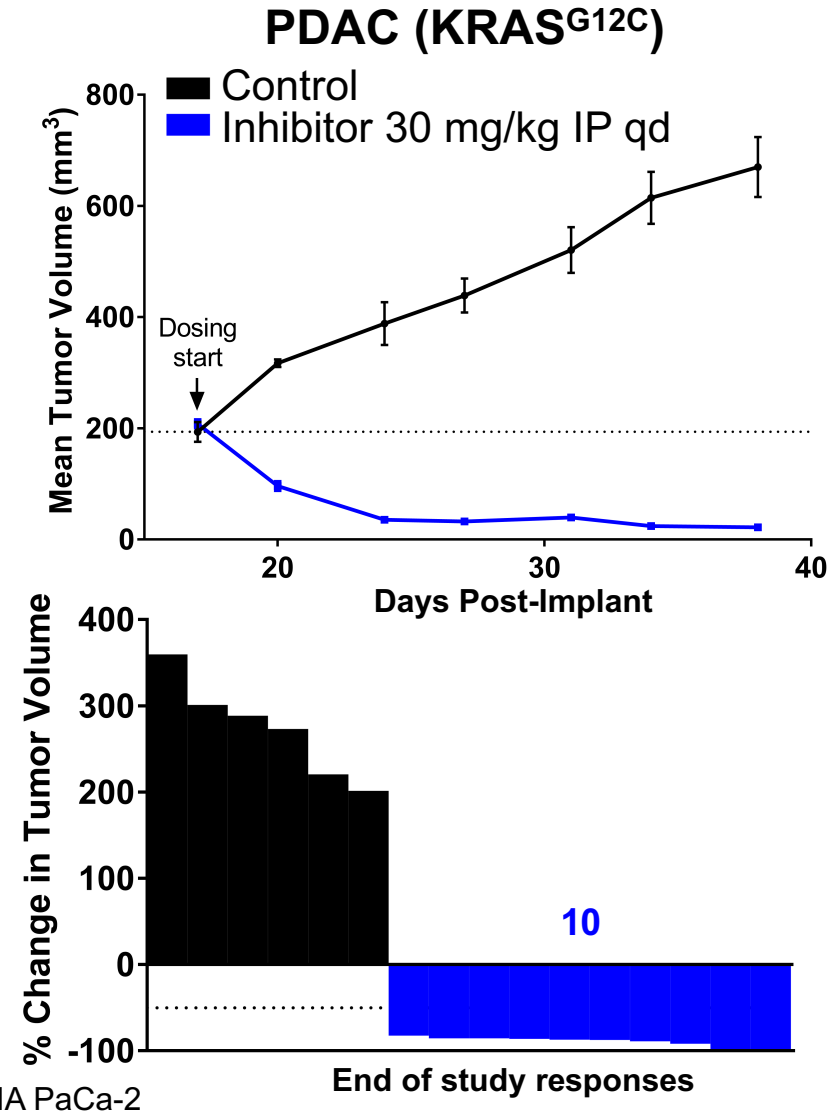
Unique target binding mode

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

KRAS^{G12C}(ON) Inhibitors Drive Tumor Xenograft Regressions *in Vivo*



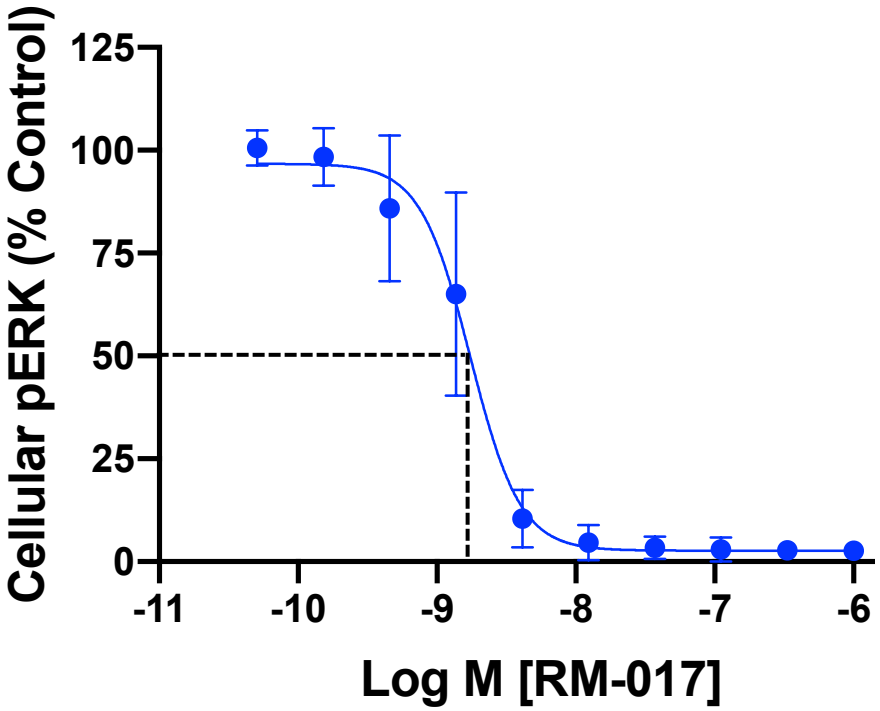
NCI-H358



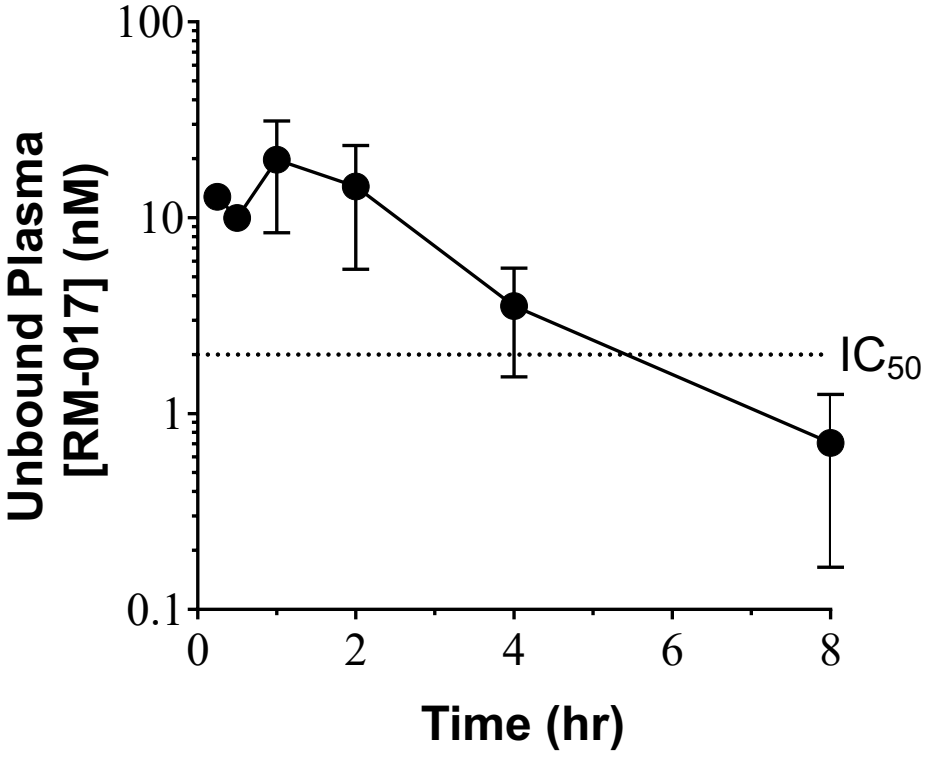
MIA PaCa-2

A Potent, Orally Bioavailable KRAS^{G12C}(ON) Inhibitor from Lead Optimization Series

Suppression of KRAS^{G12C} *in Vitro* (NCI-H358 cells)

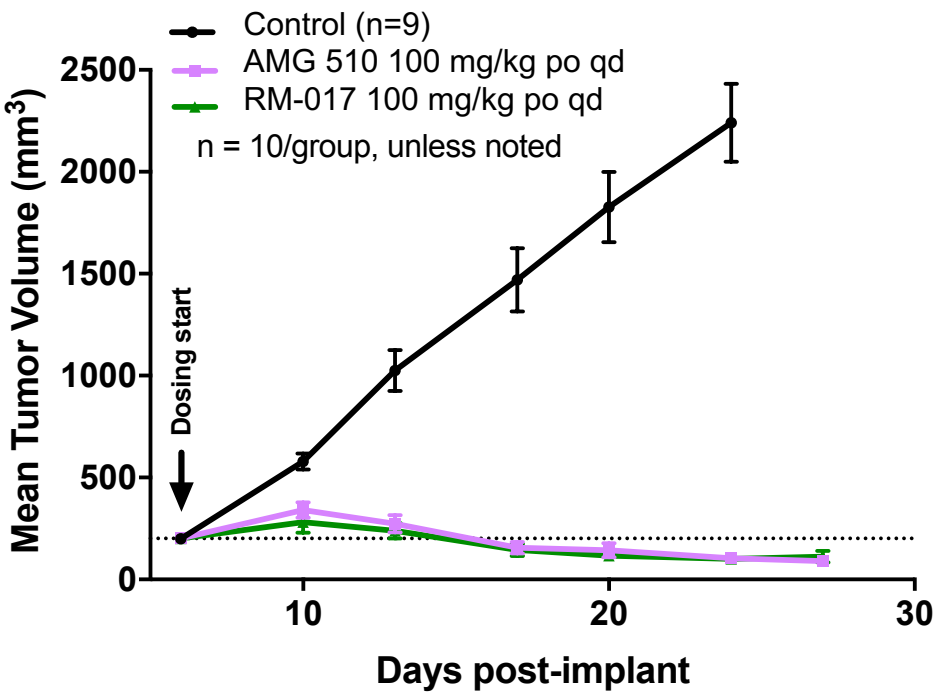


PK After Oral Administration *in Vivo* (mouse)

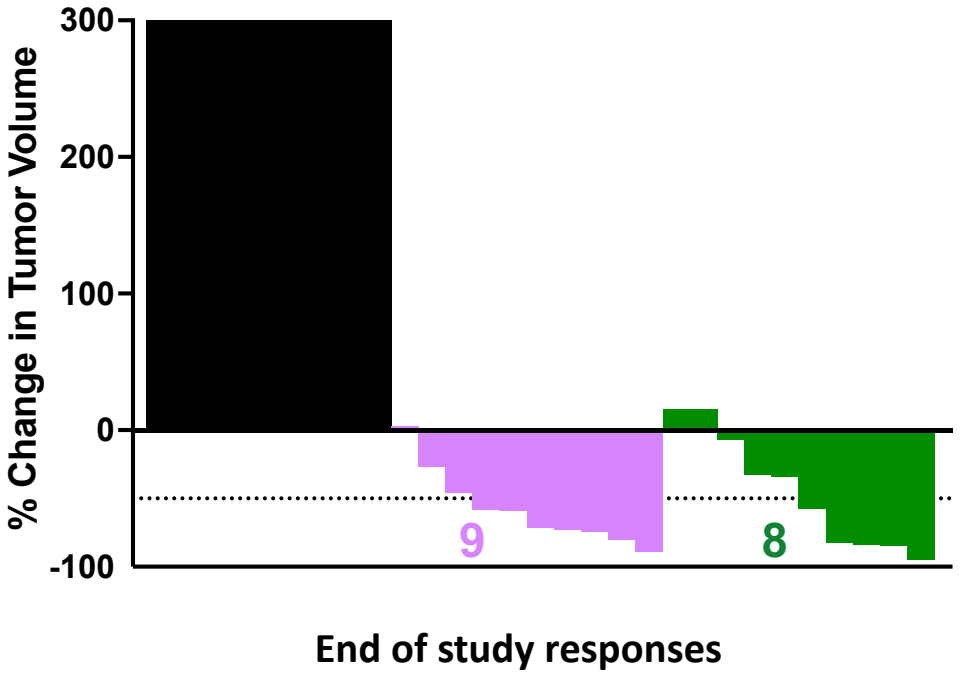


Oral Administration of KRAS^{G12C}(ON) Lead Series Compound Drives Regressions *in Vivo*

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



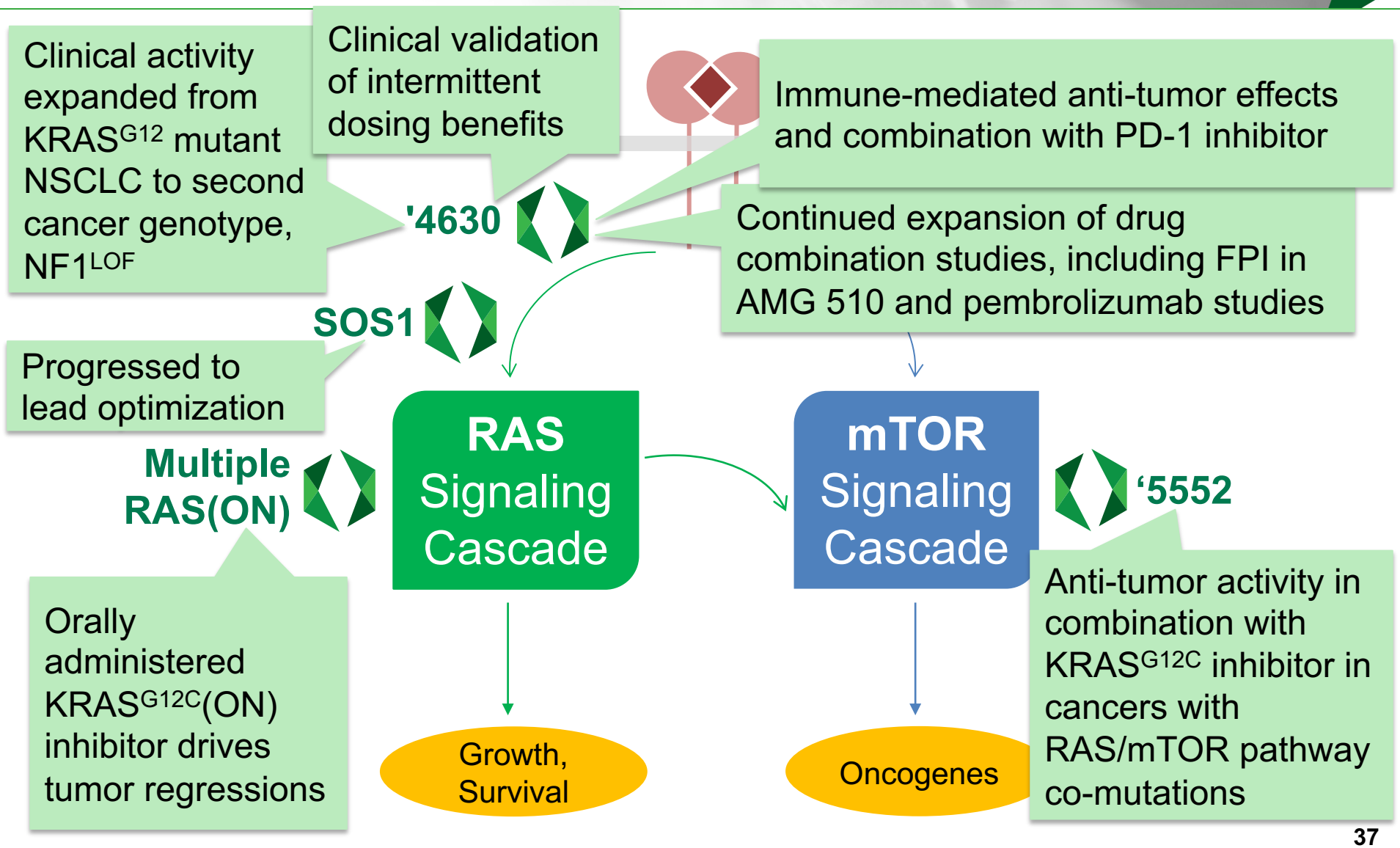
All doses were well tolerated



n = number of regressions > 10% from starting volume

Summary

1H-20: Clinical and Preclinical Pipeline Advances Strengthen Therapeutic Strategies for RAS Tumors



Progress Since IPO and Prospects for 2020

Program	Status
RMC-4630 (SHP2)	✓ **Clinical update** ✓ Intermittent dosing progressing toward RP2DS for mono- and combination therapy ✓ Additional evidence of monotherapy activity in $KRAS^{mutant}$ NSCLC ✓ Initial monotherapy activity in $NF1^{LOF}$ tumors ✓ **Begin treating patients in combination with AMG 510** ✓ FPI June 2020 ✓ **Begin treating patients in combination with anti-PD1** ✓ Cancer Research paper on enhancing immune response ✓ FPI June 2020 • **Begin treating patients in combination with osimertinib**
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 tumor regressions from combination with $KRAS^{G12C}$(OFF) inhibitor

Looking Forward to 2H-2020

Program	Milestones
RMC-4630 (SHP2)	• *Additional* clinical update • Begin treating patients in combination with osimertinib
Mutant RAS(ON)	• Nominate first Development Candidate • Lead compound for second target
RMC-5552 (mTORC1)	• IND-ready

Translating Frontier Oncology Targets to *Outsmart Cancer*™