REVOLUTION MEDICINES

Translating Frontier Oncology Targets to *Outsmart Cancer*™

Corporate Overview
Q4-2020
November 12, 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 November 12, 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 or other information contained herein 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.

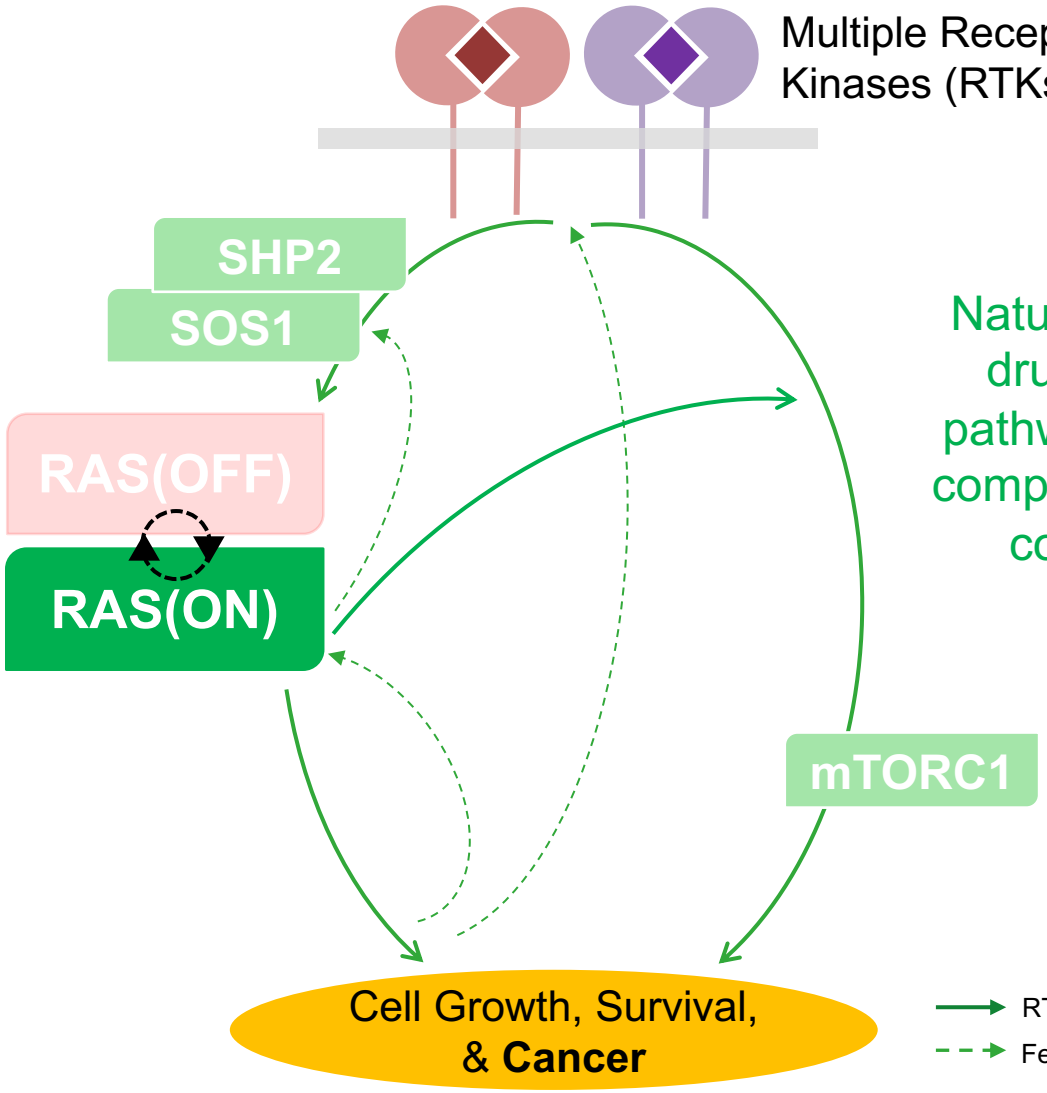
Summary

- Clinical-stage precision oncology company focused on large unmet needs in RAS-addicted cancers
- RAS(ON) Inhibitors target diverse oncogenic RAS variants via highly differentiated profiles
- RAS Companion Inhibitors are potential backbones of targeted combinations to maximize clinical benefit
- Strong financial condition and history of corporate transactions that enable mission and build value

RAS(ON) Proteins Cause Cancer, RAS Addiction and Drug Resistance

1.
Many mutant and wild-type RAS family variants underlie addiction

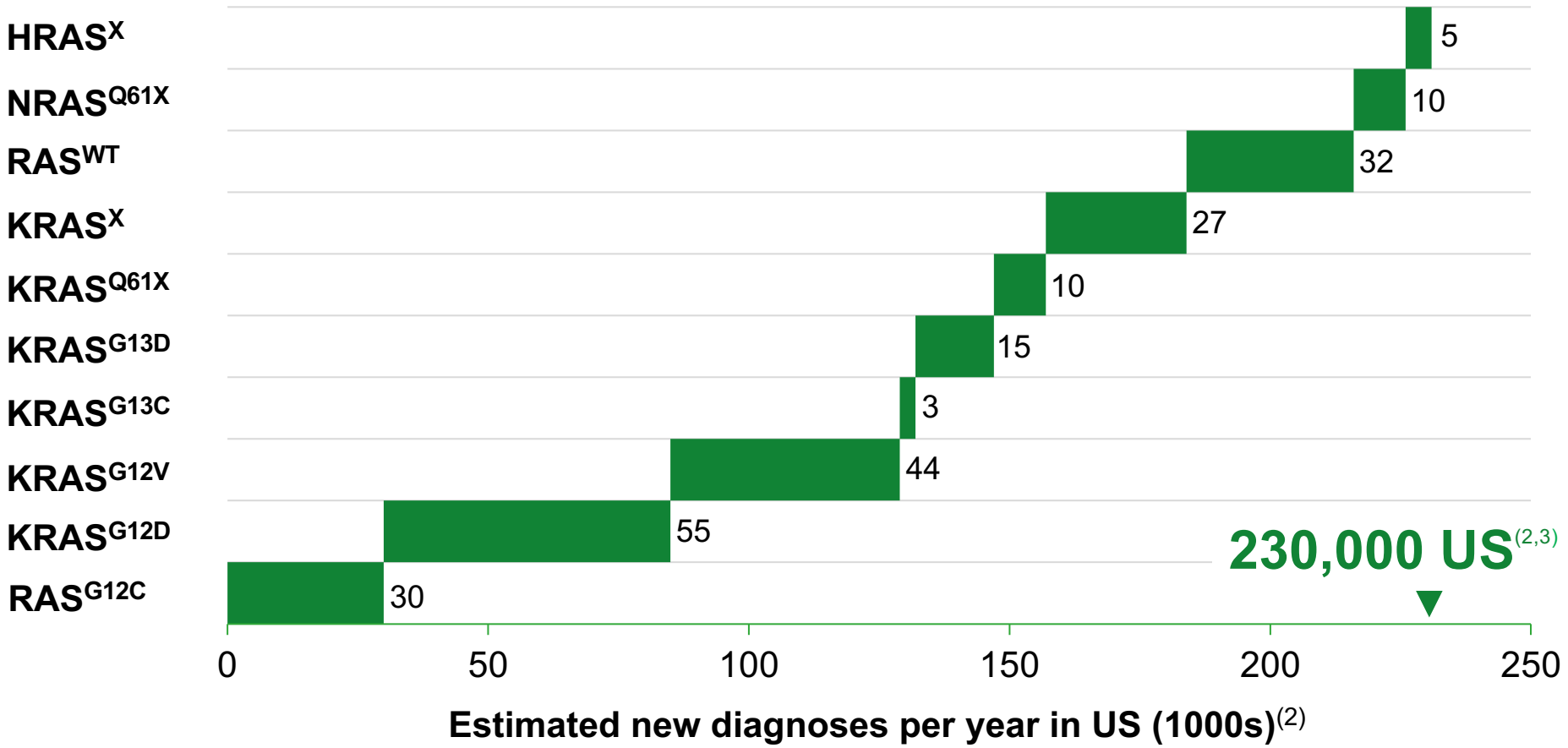
2.
RAS(ON) form drives oncogenic signaling



3.
Natural circuits are drug resistance pathways, requiring companion drugs for combinations

Targeted Therapies Needed for Common, Serious, Genetically-Defined RAS-Addicted Cancers

Tumor Addiction[1]:



(1) $HRAS^{X}$ = all HRAS mutants; $NRAS^{Q61X}$ X = H, K, L, R, P; RAS^{WT} = $NF1^{LOF}$, RAS^{WTamp}, $BRAF^{class3,}$ and $PTPN11^{MUT}$; $KRAS^{X}$ X = G12A, G12R, G12S and A146T; $KRAS^{Q61X}$ X = H, K, L; RAS^{G12C} includes $KRAS^{G12C}$ and $NRAS^{G12C}$

(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. 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.

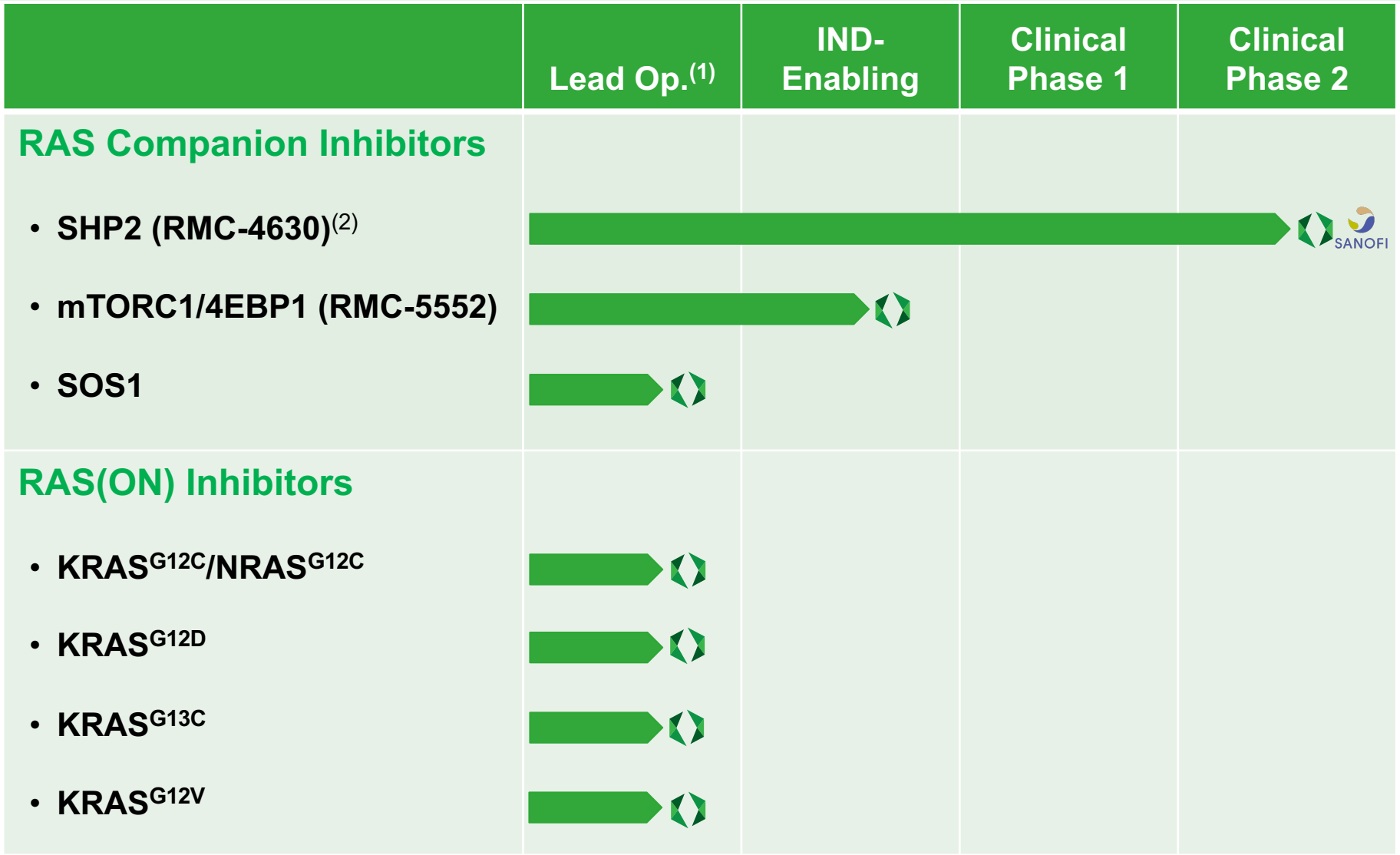
(3) Est. worldwide annual incidence of RAS-mutated cancers is 3.4 million per Prior et al., *Cancer Research* 2020

Potent, Cell-Active RAS(ON) Inhibitors for Variants Driving Vast Majority of RAS-Addicted Cancers

Tumor Addiction:	RVMD RAS(ON) Inhibitor[1]
$HRAS^{X}$	$HRAS^{Q61H}$, $HRAS^{Q61L}$
$NRAS^{Q61X}$	$NRAS^{Q61H}$, $NRAS^{Q61K}$, $NRAS^{Q61L}$, $NRAS^{Q61P}$, $NRAS^{Q61R}$
RAS^{WT}	RAS wild-type
$KRAS^{X}$	$KRAS^{G12R}$, $KRAS^{G12S}$
$KRAS^{Q61X}$	$KRAS^{Q61H}$, $KRAS^{Q61K}$, $KRAS^{Q61L}$
$KRAS^{G13D}$	$KRAS^{G13D}$
$KRAS^{G13C}$	$KRAS^{G13C}$
$KRAS^{G12V}$	$KRAS^{G12V}$
$KRAS^{G12D}$	$KRAS^{G12D}$
RAS^{G12C}	$KRAS^{G12C}$, $NRAS^{G12C}$

(1) Defined as tumor cell growth EC_{50} < 75 nM. Some inhibitors are active against more than one RAS variant.
List is representative as of 11/1/20 but does not necessarily include all discovery compounds.

Expansive and Strategic RVMD Pipeline of Targeted Drugs to Defeat RAS-Addicted Cancers



(1) Entry into Lead Optimization stage requires drug-like molecules exhibiting preclinical *in vivo* activity
(2) Expansion at RP2DS for RMC-4630 + cobimetinib portion of RMC-4630-02 study represents Phase 2

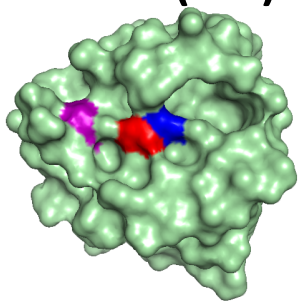
RAS(ON) Inhibitors: Target Diverse RAS Variants via Highly Differentiated Profiles

	Lead Op.(1)	IND-Enabling	Clinical Phase 1	Clinical Phase 2
RAS Companion Inhibitors				
• SHP2 (RMC-4630)(2)				
• mTORC1/4EBP1 (RMC-5552)				
• SOS1				
RAS(ON) Inhibitors				
• **$KRAS^{G12C}/NRAS^{G12C}$**				
• **$KRAS^{G12D}$**				
• **$KRAS^{G13C}$**				
• **$KRAS^{G12V}$**				

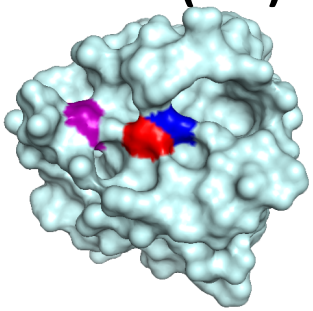
(1) Entry into Lead Optimization stage requires drug-like molecules exhibiting preclinical *in vivo* activity
(2) Expansion at RP2DS for RMC-4630 + cobimetinib portion of RMC-4630-02 study represents Phase 2

Numerous RAS(ON) Variants are Major Therapeutic Opportunities for RAS-Addicted Cancers

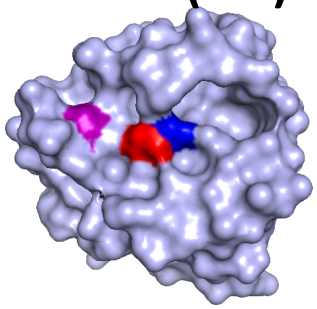
KRAS(ON)



NRAS(ON)

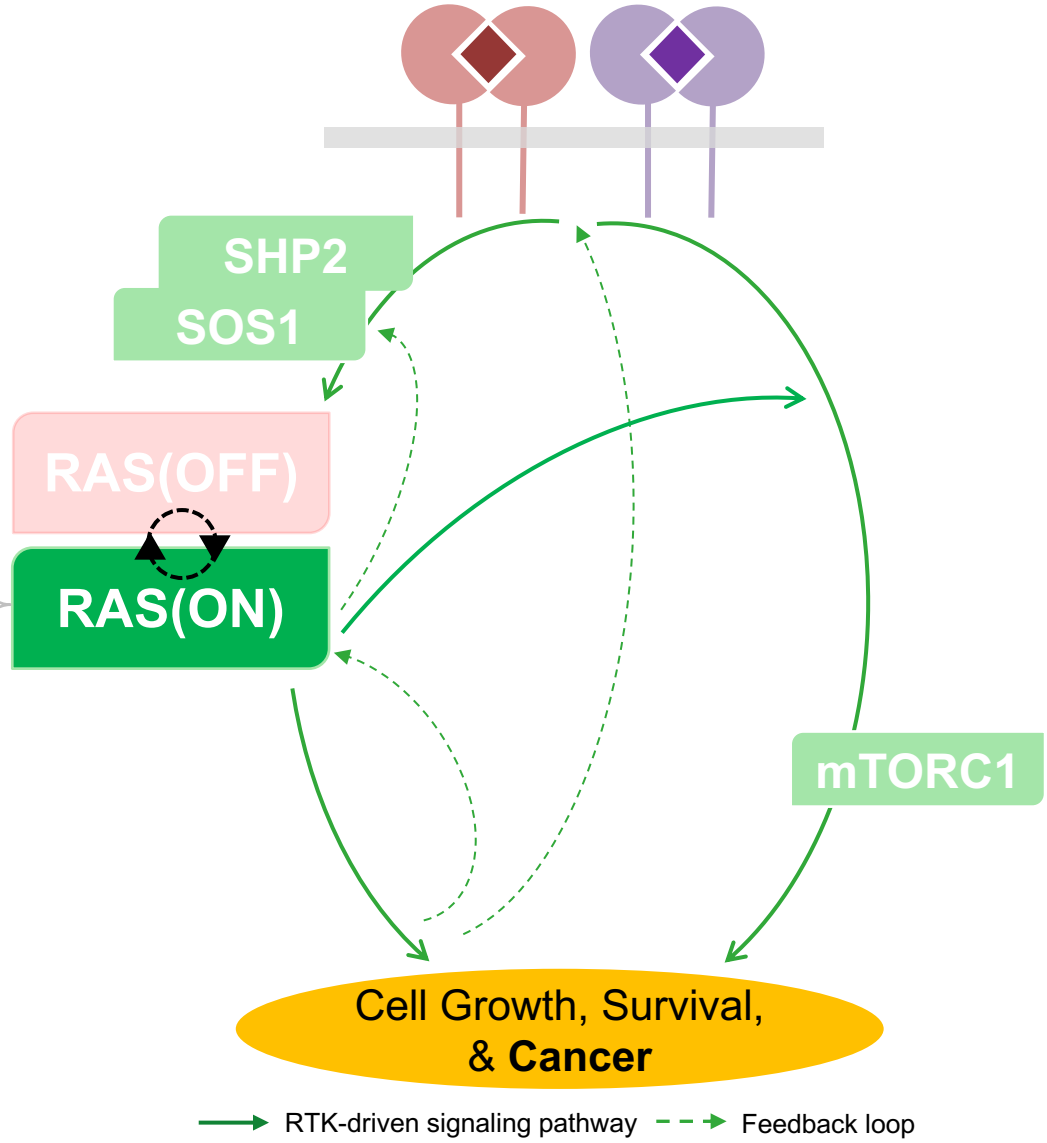


HRAS(ON)

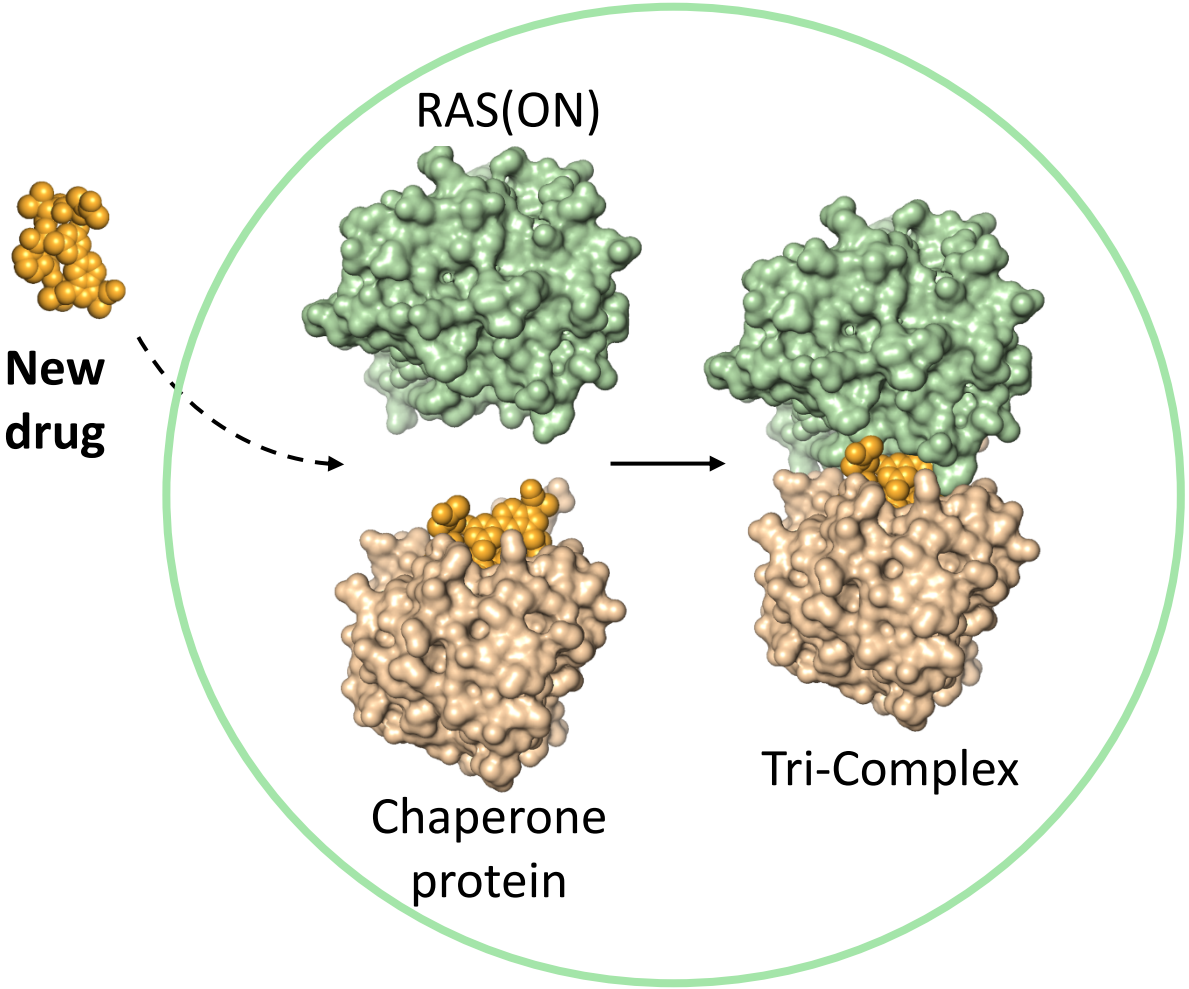


Mutation Hotspots

- G12
- G13
- Q61



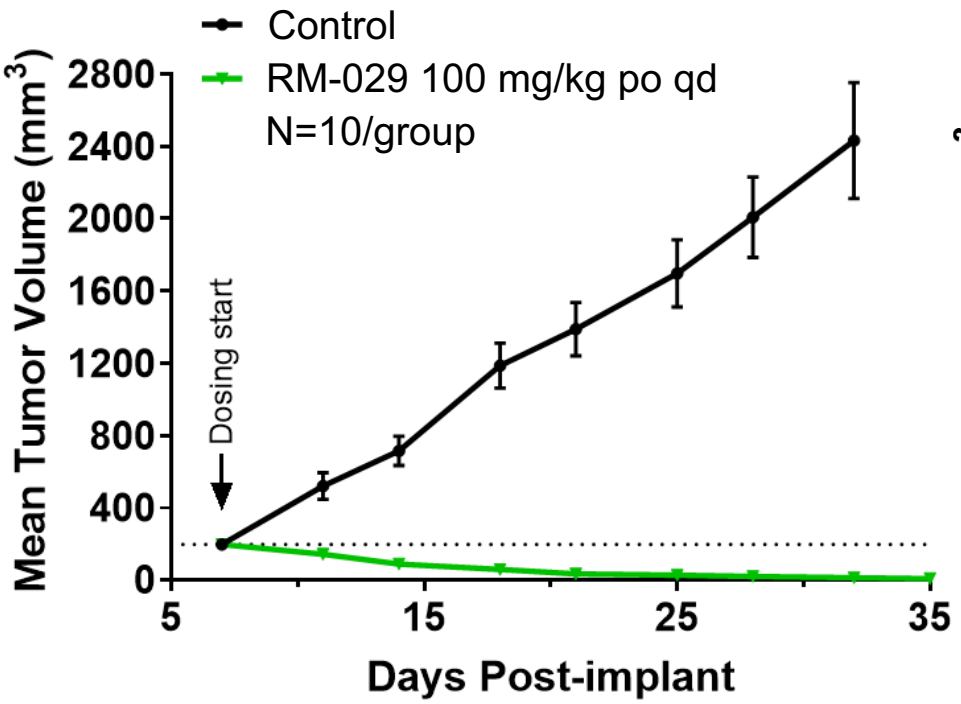
Tri-Complex Inhibitors Block Signaling by RAS(ON) Proteins and Offer Potential Advantages

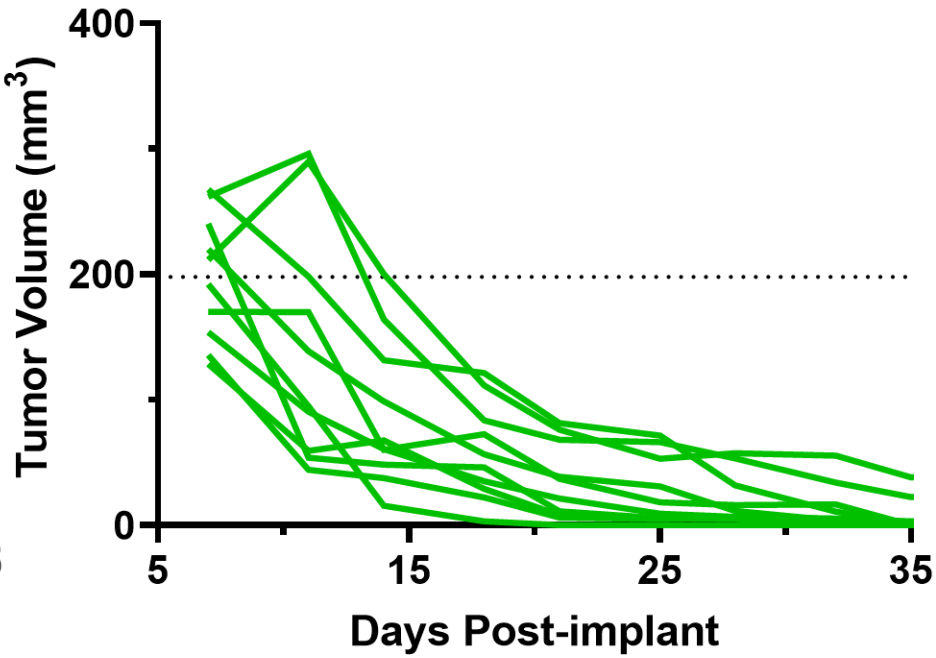


- Proven reach to broad range of oncogenic RAS variants
- Compelling mono and combination anti-tumor activity in preclinical *in vivo* models
- Hypothesized clinical benefits: breadth, depth and/or duration of anti-tumor impact

KRAS^{G12C}/NRAS^{G12C}(ON) Inhibitor Drives Deep Regressions of KRAS^{G12C} Tumors *in Vivo*

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





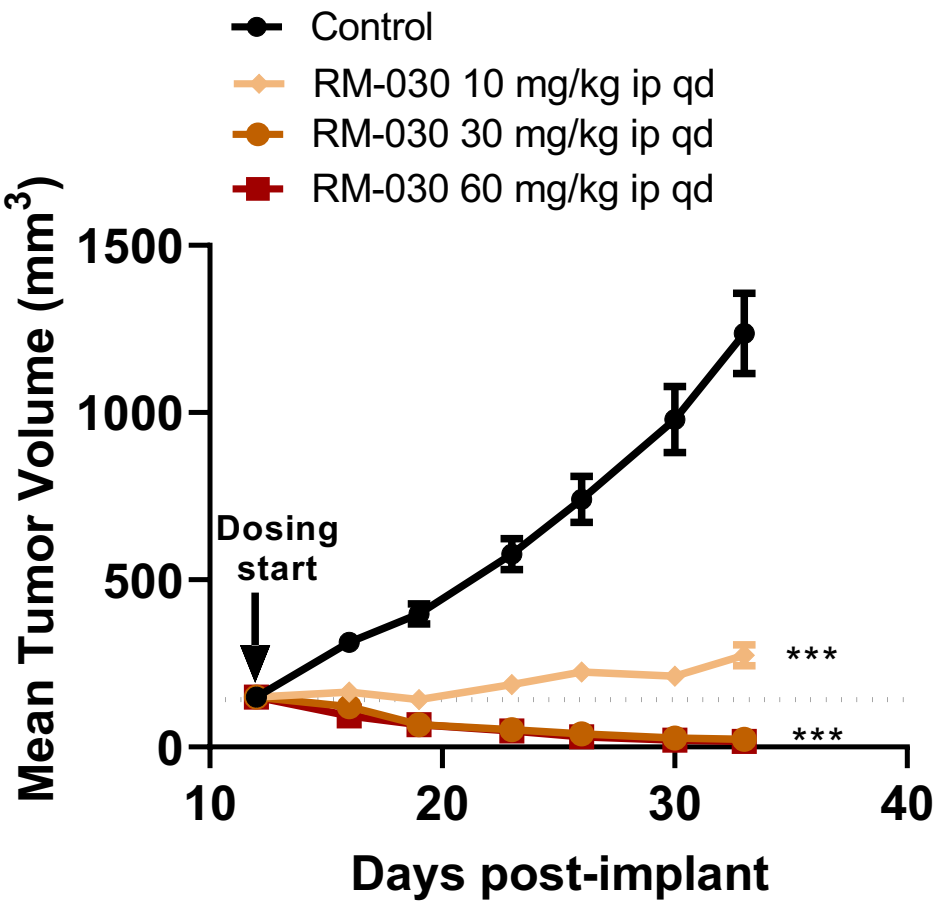
Treatment was well tolerated

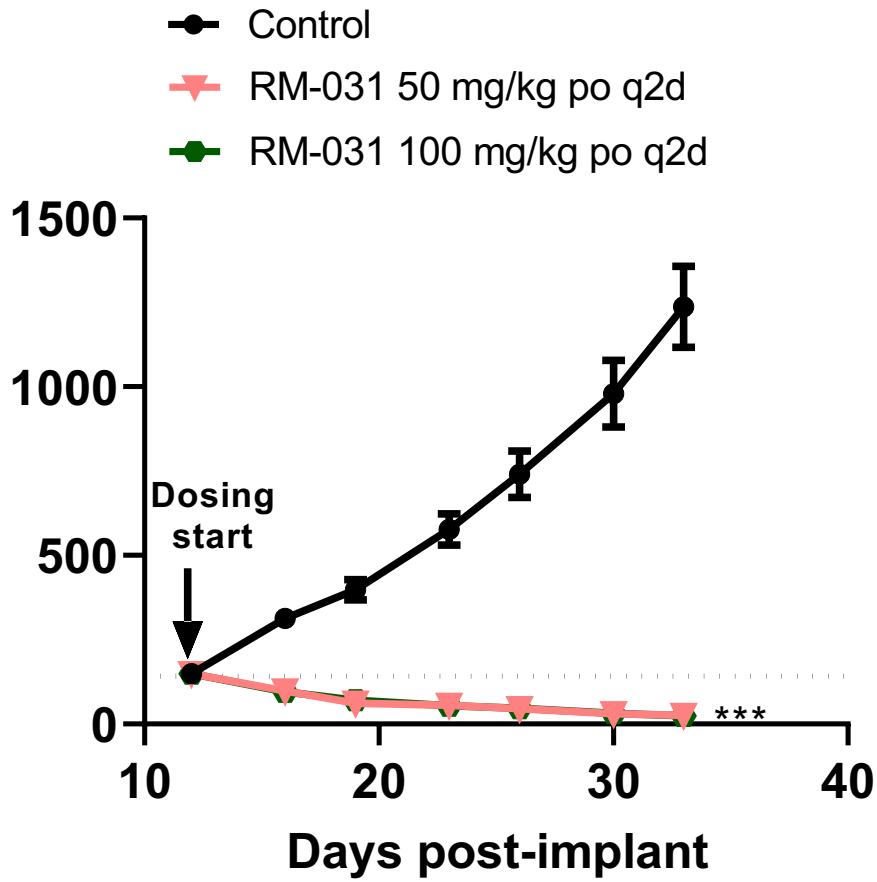
Some animals exhibited complete responses (CR) = 3 consecutive tumor measurements ≤ 30 mm^3

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

KRAS^{G12D}(ON) Inhibitors Drive Deep Regressions of KRAS^{G12D} Tumors *in Vivo*

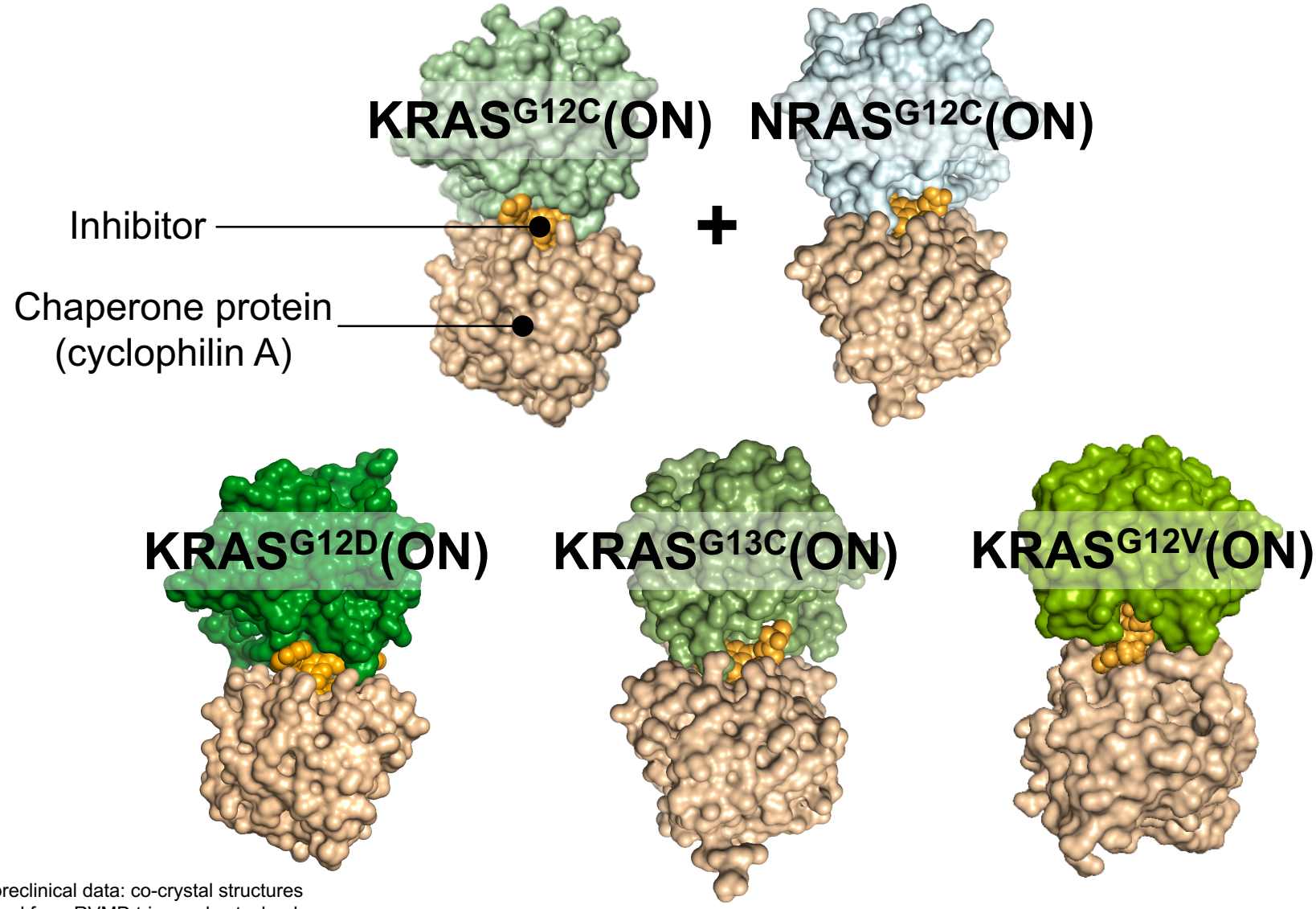
HPAC CDX (Pancreatic adenocarcinoma, KRAS$^{G12D/WT}$)





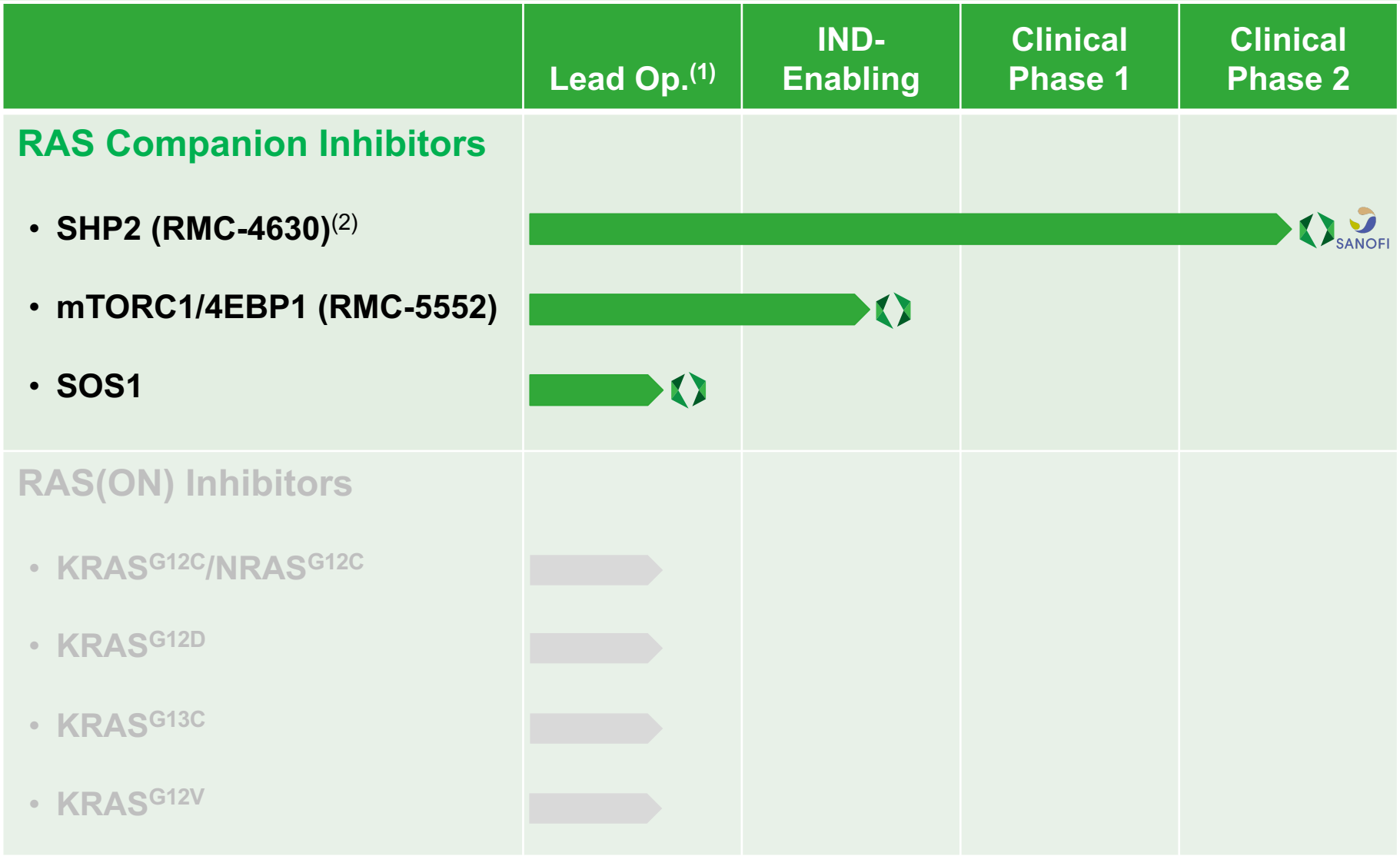
RVMD preclinical data
n = 10/group ***p<0.001
All dose levels well tolerated

First-in-Class RAS(ON) Inhibitors[1] Advanced to Lead Optimization for Five Oncogenic Variants



RVMD preclinical data: co-crystal structures
(1) Derived from RVMD tri-complex technology

RAS Companion Inhibitors: Potential Backbones of Targeted Combinations to Maximize Benefit

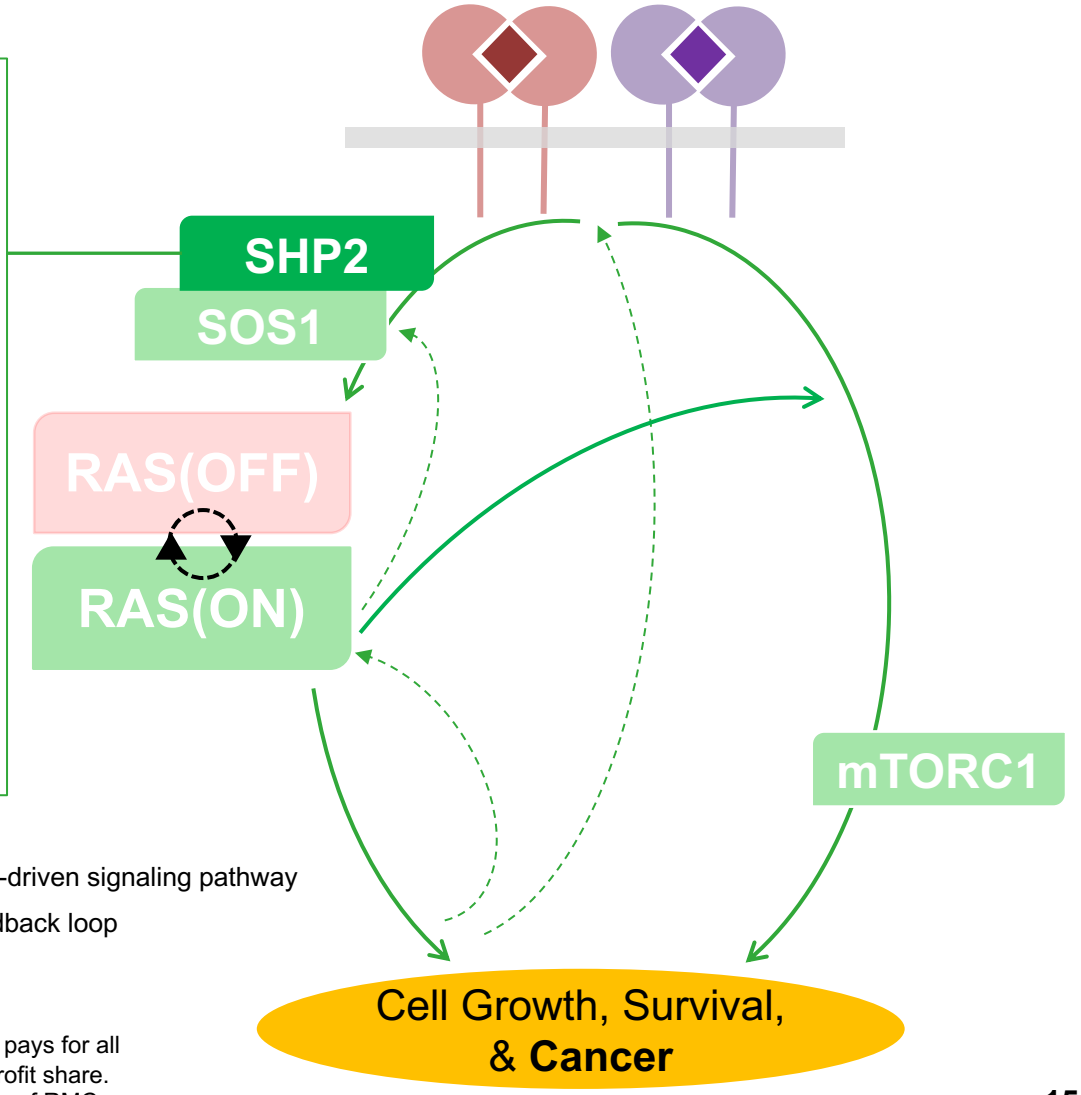


(1) Entry into Lead Optimization stage requires drug-like molecules exhibiting preclinical *in vivo* activity
(2) Expansion at RP2DS for RMC-4630 + cobimetinib portion of RMC-4630-02 study represents Phase 2

RMC-4630: Potent, Oral Inhibitor of SHP2 – Master Regulator of RAS Signaling Pathway

RMC-4630[1]

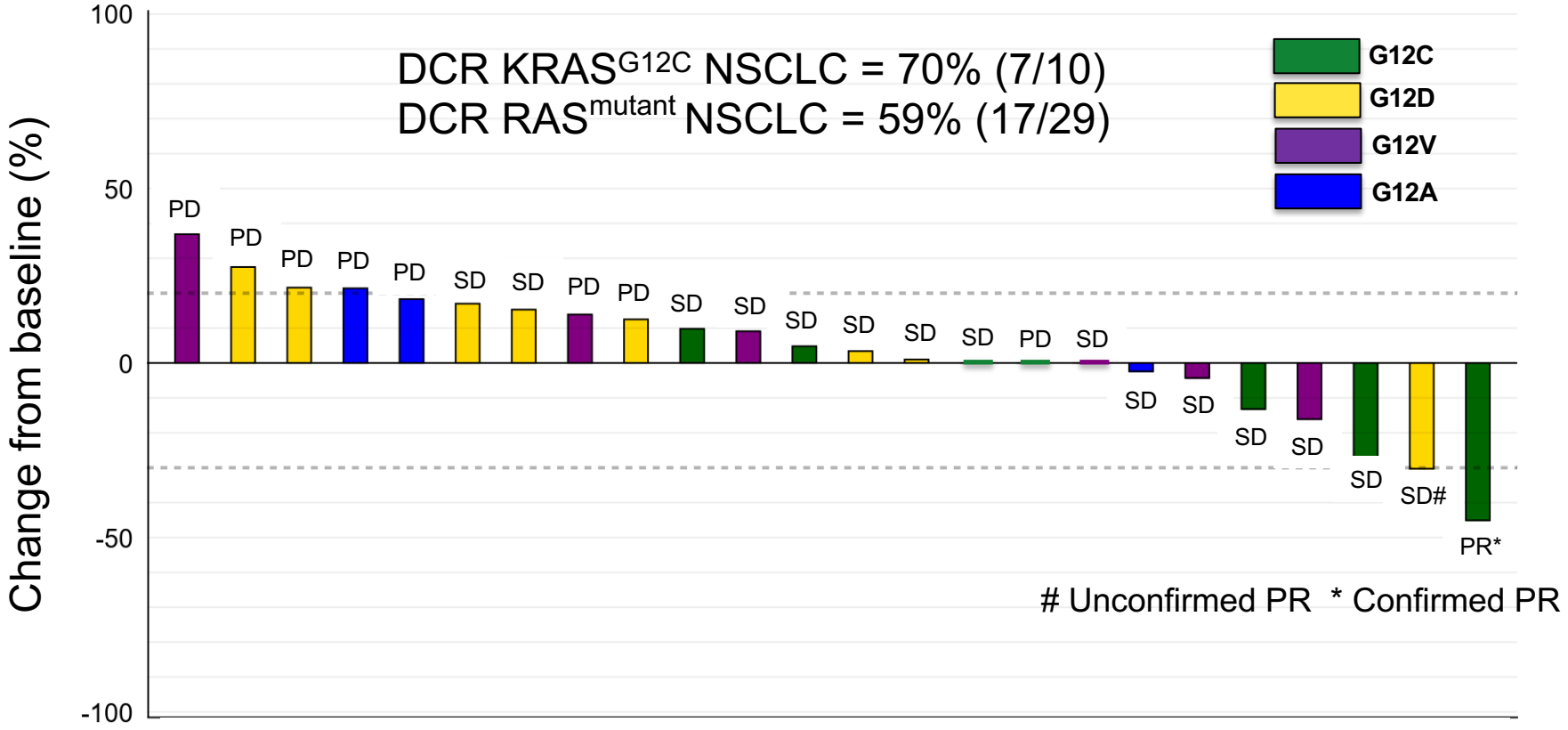
- Clinical Phase 2[2]
- Monotherapy and "backbone" for combinations
- Initial monotherapy activity in multiple cancers with defined tumor genotypes
- Initial combo activity with MEK inhibitor in RAS^{mut} colorectal cancer
- Initial clinical evidence of immune enhancement in tumors



(1) RMC-4630/SAR442720. Under 2018 partnership, Sanofi pays for all development costs and RVMD/Sanofi have 50/50 U.S. profit share.
(2) Expansion at RP2DS for RMC-4630 + cobimetinib portion of RMC-4630-02 study represents Phase 2

SANOFI

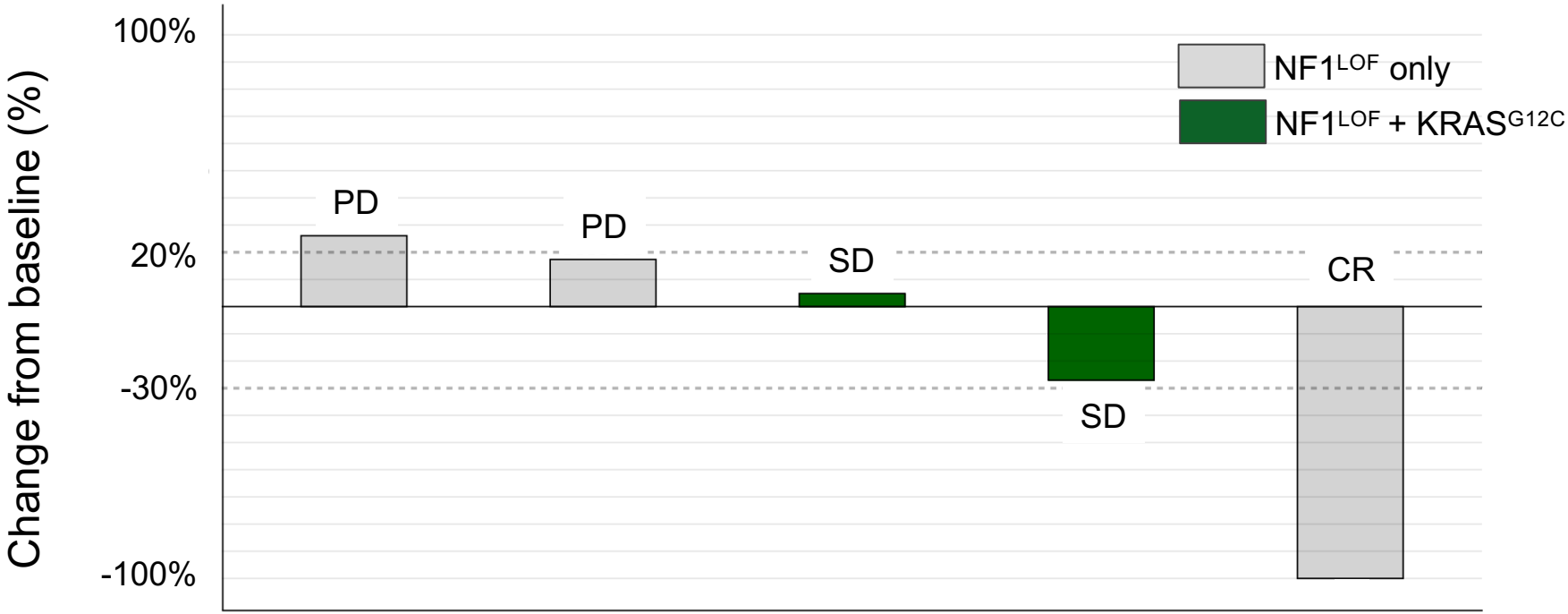
RMC-4630-01: Best Change in Tumor Burden from Baseline in KRAS^{mutant} NSCLC



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.

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

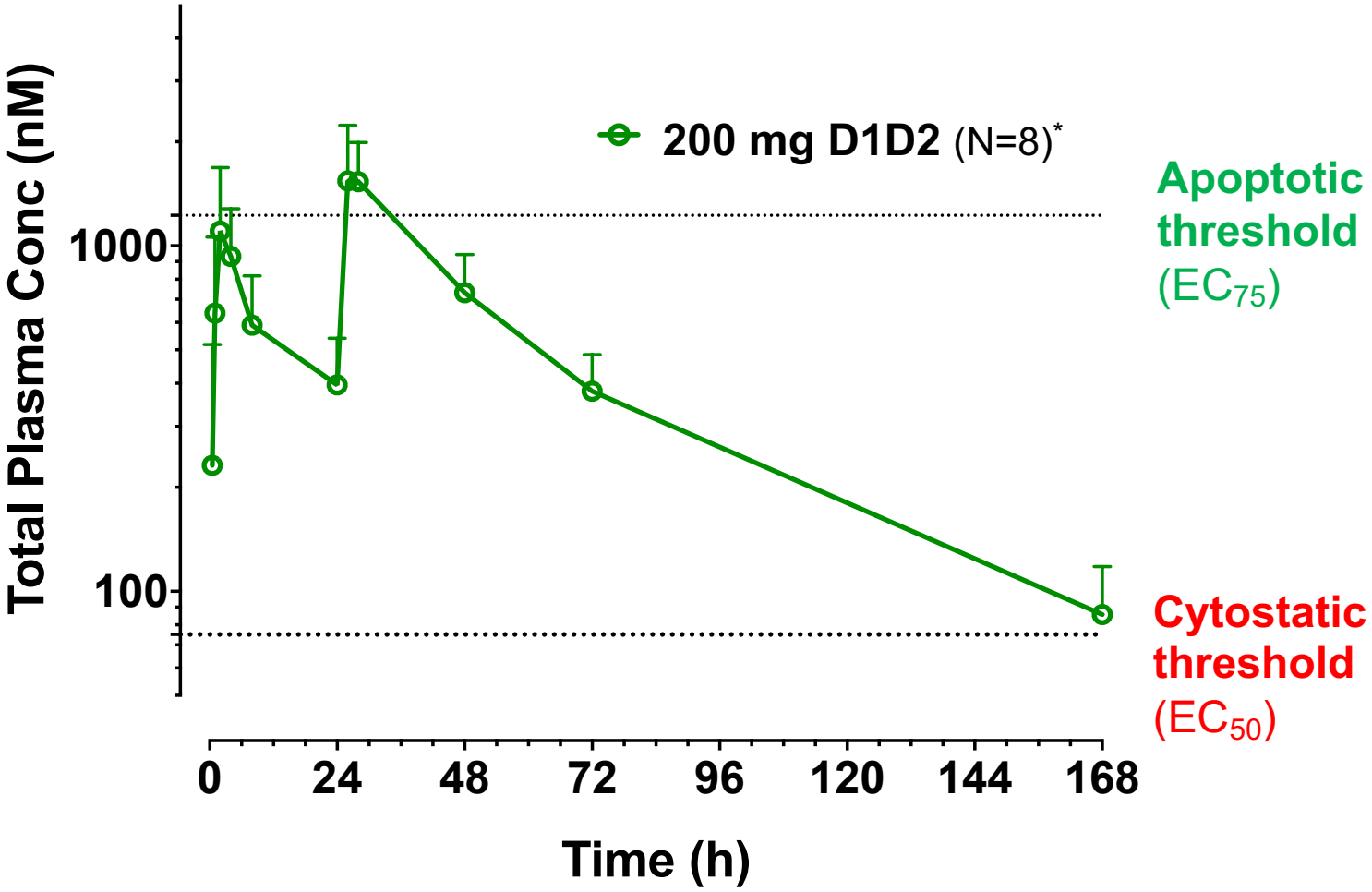


Dose:	80mg	80mg	60mg	200mg	200mg
Schedule:	Daily	Daily	Daily	D1D4	D1D4
Type:	Ovarian	Ovarian	NSCLC	NSCLC	Uterine

- 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-4630-01: Attractive Exposure Profile of RP2DS for RMC-4630 Single Agent

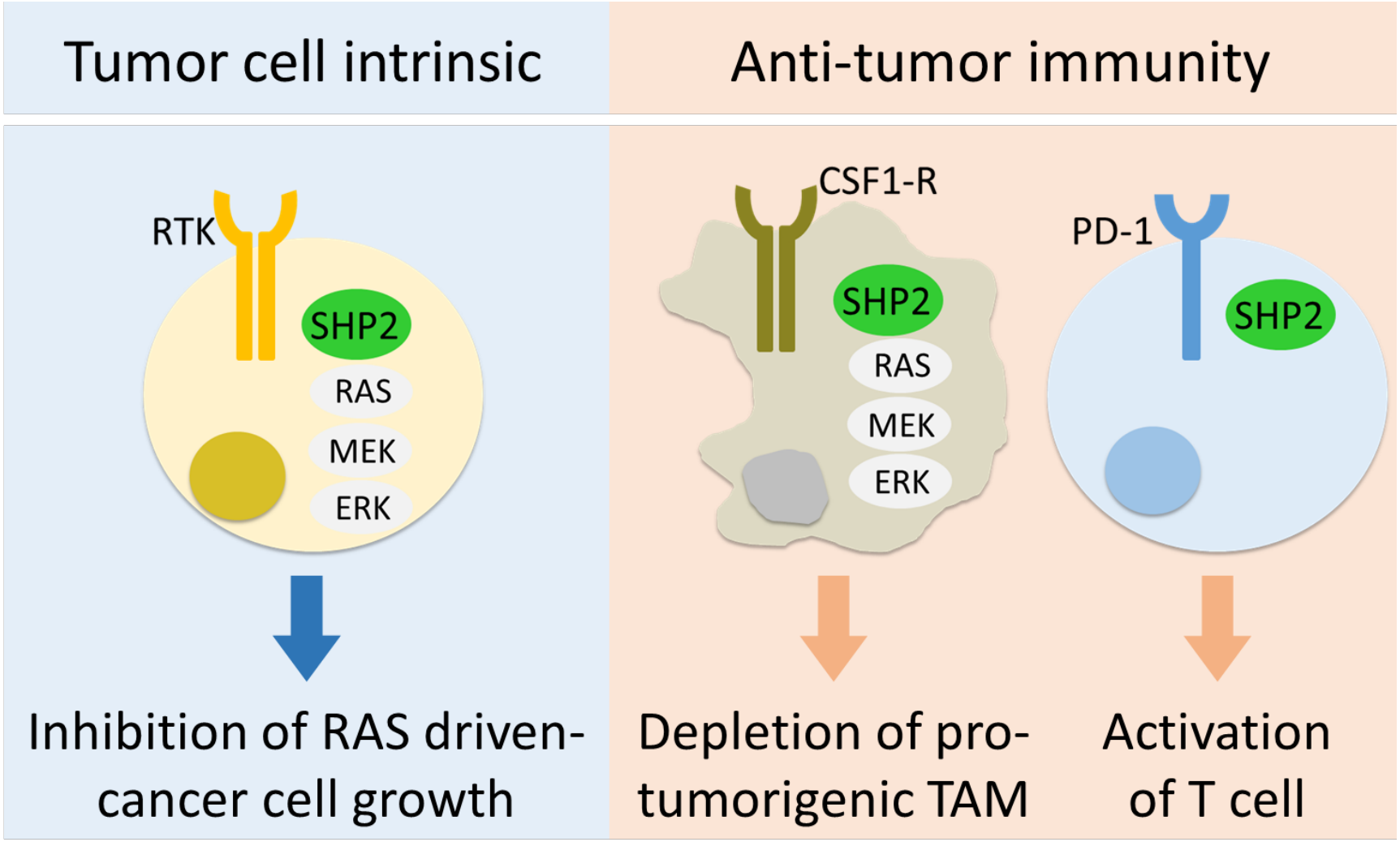


RP2DS = recommended Phase 2 dose and schedule

* PK for all patients in the 200 mg D1D2 twice weekly dose escalation cohort where PK sampling timepoints are post-C1D1 and C1D2 dosing and C1D8 trough (~168 h).

Data cutoff 10/23/2020

Preclinical[(1)] and Clinical[(2)] Evidence Supports Two Mechanisms of Anti-Tumor Benefit from RMC-4630



(1) Nichols et al., *Nature Cell Biology*, August 2018; Quintana et al. *Cancer Research.* April 2020
(2) Ou et al., *Sixth AACR-IASLC International Joint Conference*, 2020; Kelsey, S. *RAS Targeted Drug Development*, September 2020

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

Combinations with RMC-4630:

Induce additive anti-tumor effects[(1)]

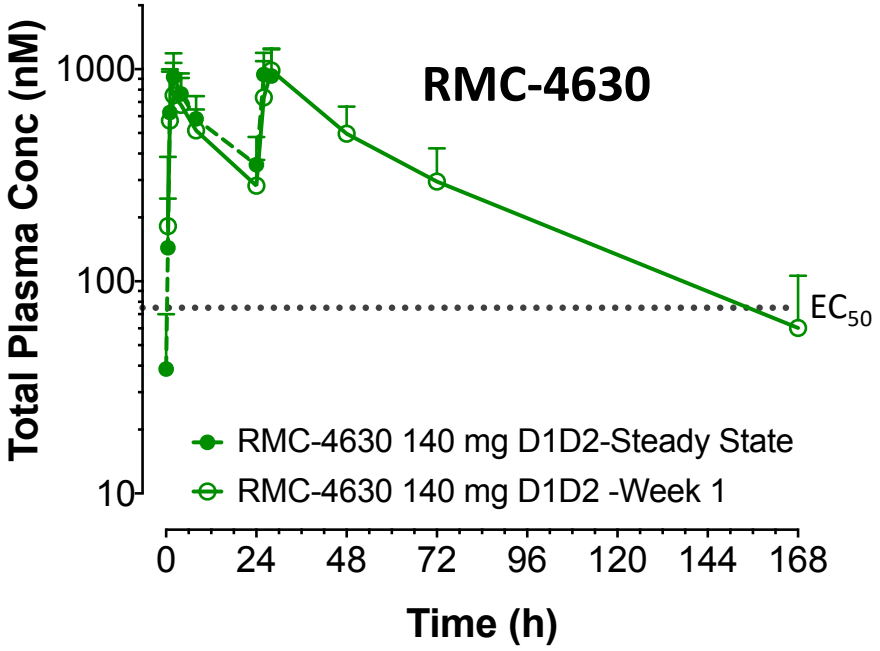
Combat adaptive resistance[(2)]

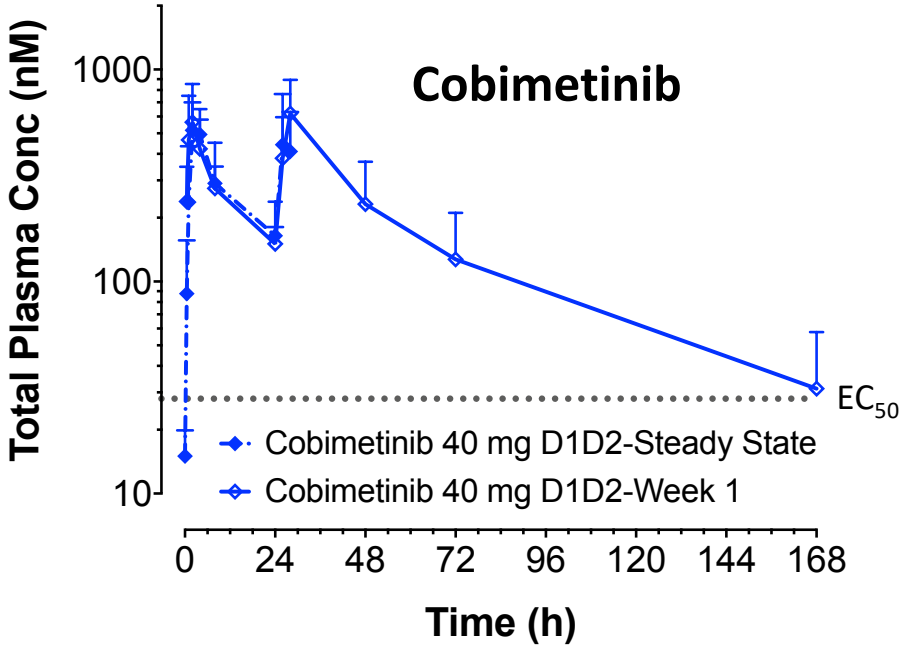
MEK inhibitors	ERK inhibitors	KRAS^{G12C} inhibitors	RTK inhibitors	Checkpoint inhibitors
Inhibit RAS pathway nodes		Inhibit driver mutations		Inhibit immune suppressors
Combination for RAS-addicted tumors		Combination for tumors carrying KRAS^{G12C}	Combination for tumors carrying EGFR^{mutation}	Combination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

RMC-4630-02: Attractive Exposure Profile of RP2DS for RMC-4630/Cobimetinib Combination

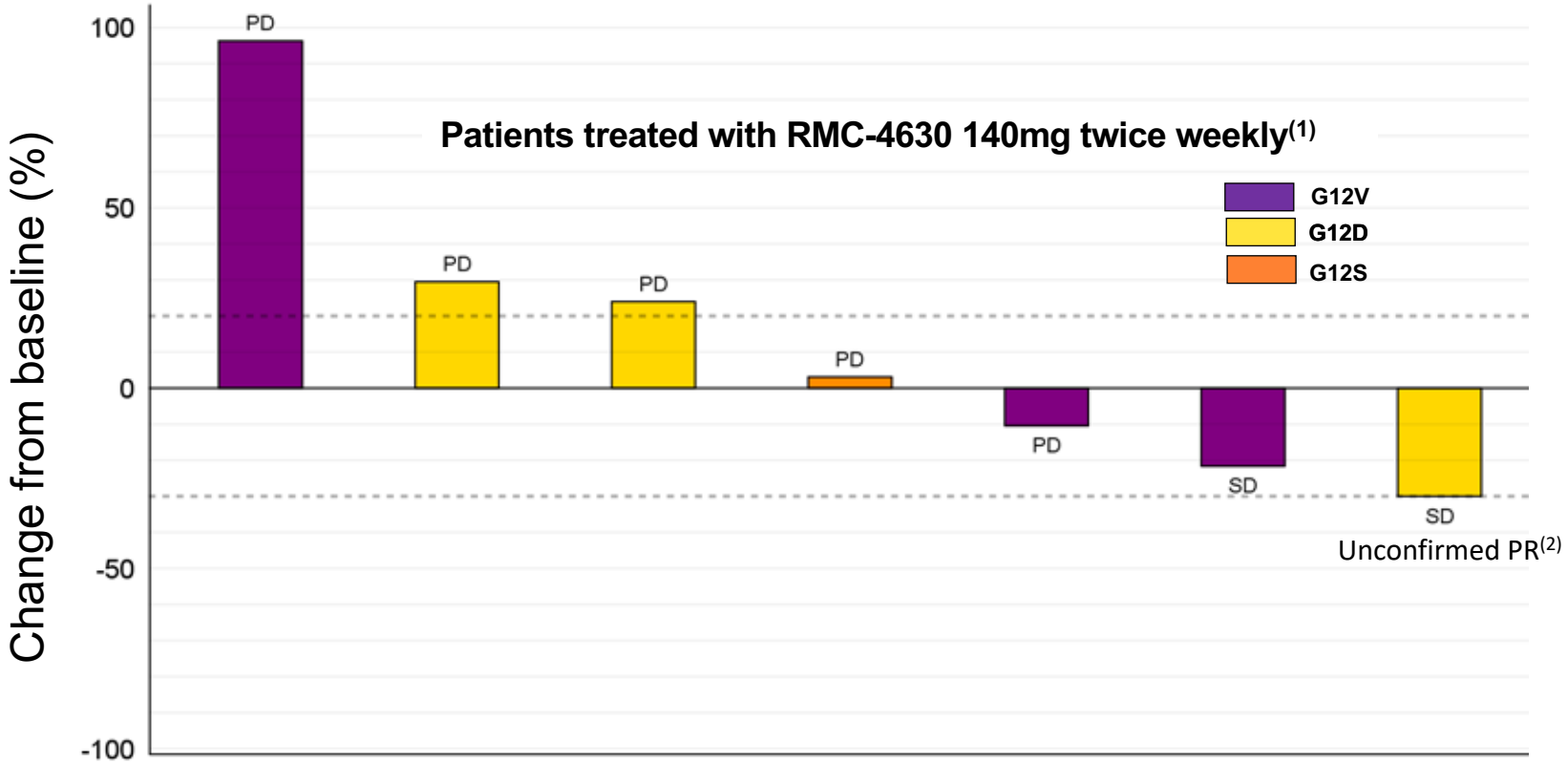




pERK EC_{50} in NCI-H358 CDX (NSCLC $KRAS^{G12C/WT}$)

RP2DS = recommended Phase 2 dose and schedule
Data as of 9/21/20; Bendell et al., *ENA 2020*

RMC-4630-02: Best Change in Tumor Burden from Baseline in KRAS^{mutant} Colorectal Cancer



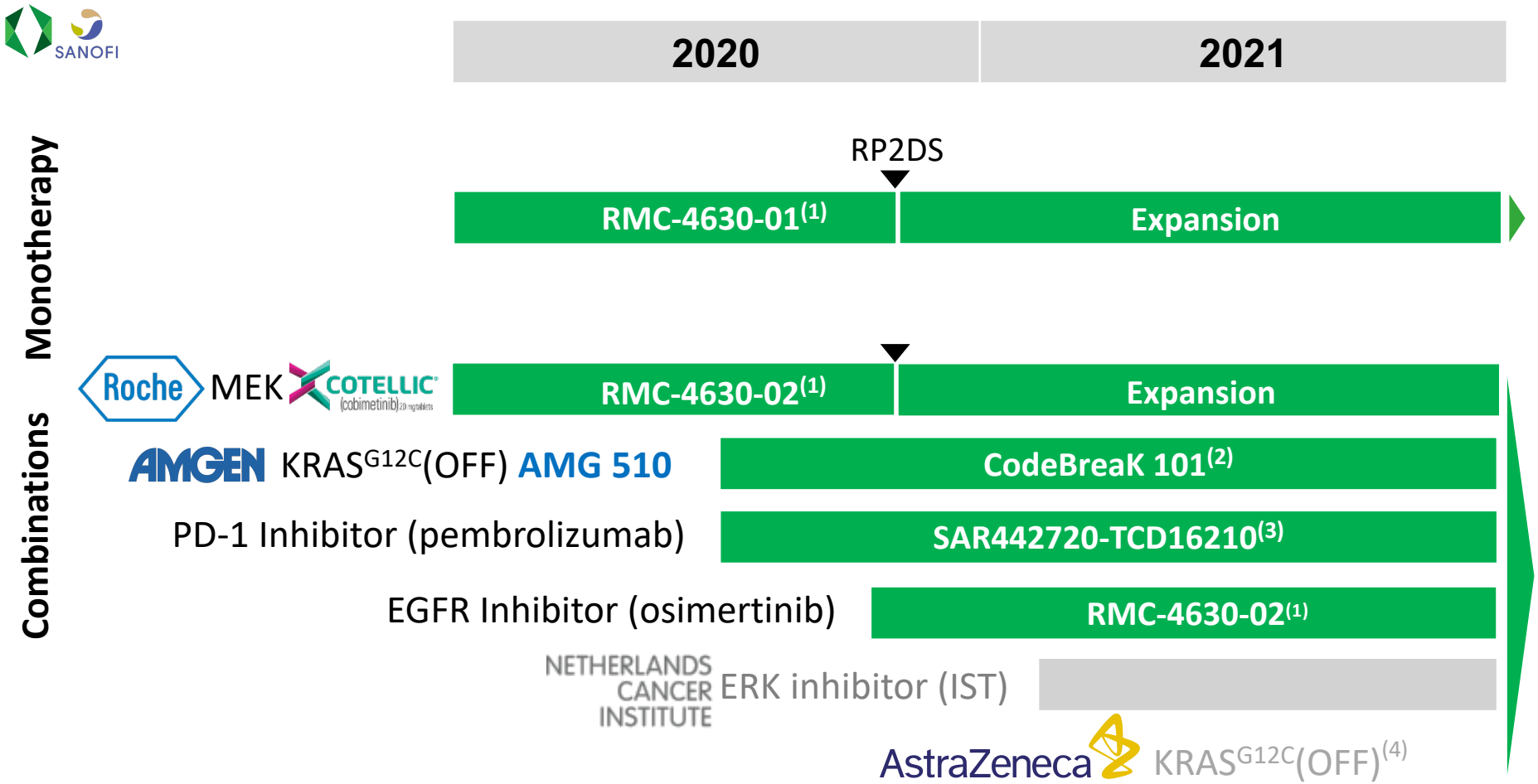
RMC-4630	140 mg D1D2	140 mg D1D2	140 mg D1D2	140 mg D1D2	140 mg D1D4	140 mg D1D4	140 mg D1D2
cobimetinib	20 mg daily	60 mg D1D2	60 mg D1D2	20 mg daily	20 mg daily	20 mg daily	60 mg D1D2

(1) Data presented for the 7 patients with KRAS mutant colorectal cancer treated with RMC-4630 140 mg twice weekly and varying cobimetinib dose and schedules out of the efficacy evaluable population of 8 patients (excluding 1 patient for whom there was no post-baseline scan)

(2) Unconfirmed PR achieved 30% reduction in tumor burden at end of cycle 2 and 25% reduction at end of cycle 4 (28-day cycles)

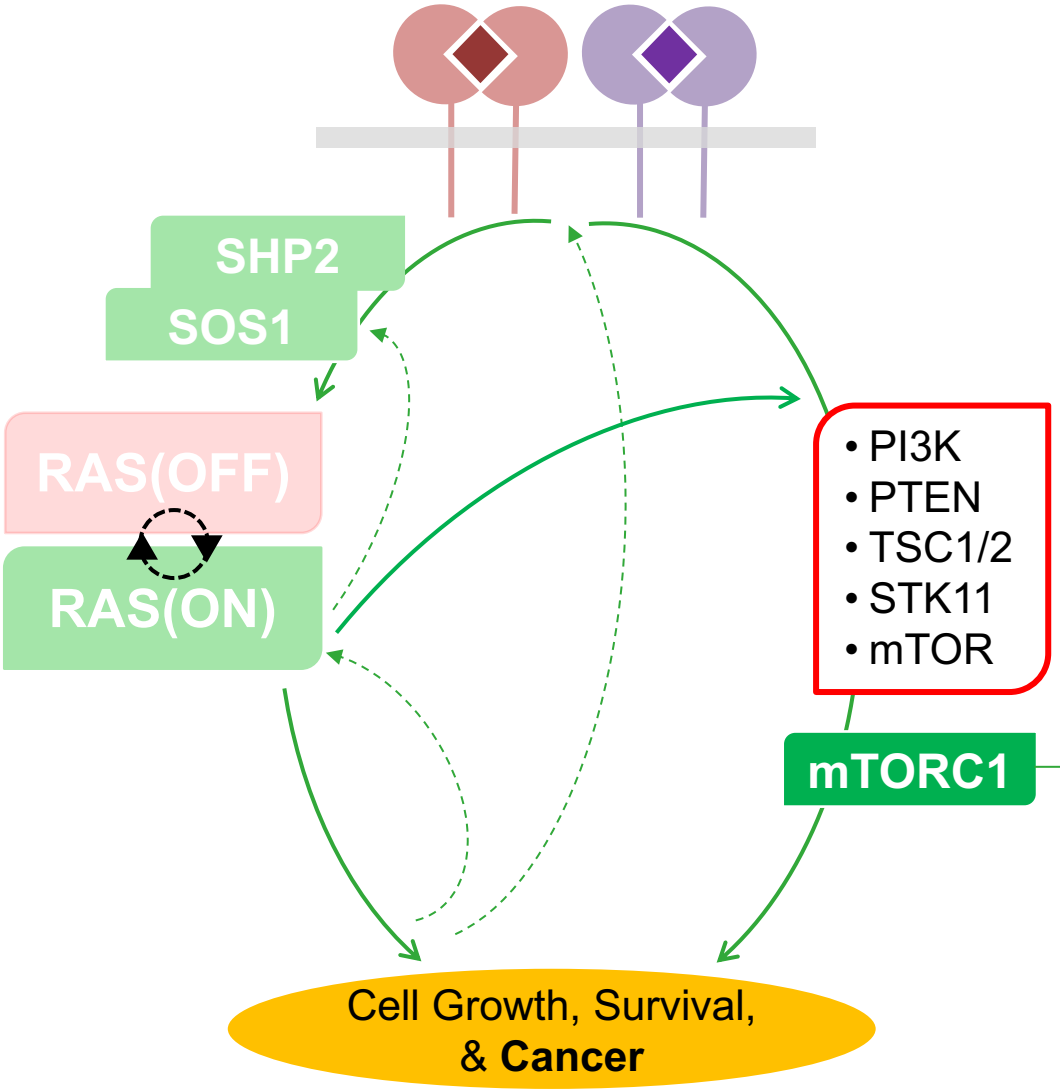
Data as of 9/21/2020; Bendell et al., *ENA 2020;* PD = Progressive Disease; SD = Stable Disease; PR = Partial Response; PD, SD and PR each per RECIST 1.1

Broad Development Program for RMC-4630 Testing Multiple Clinical Hypotheses



(1) Sponsored by RVMD
(2) Sponsored by Amgen
(3) Sponsored by Sanofi
(4) To be sponsored by AZ
Green bars represent ongoing studies
Gray bars and text represent planned studies

RMC-5552: Potent, Selective Inhibitor of Hyperactivated mTORC1 Signaling in Cancer



RMC-5552

- Completing IND-enabling development
- Monotherapy for selected tumor genotypes
- Combinations with RAS inhibitors for patients with cancers harboring RAS/mTOR signaling co-mutations

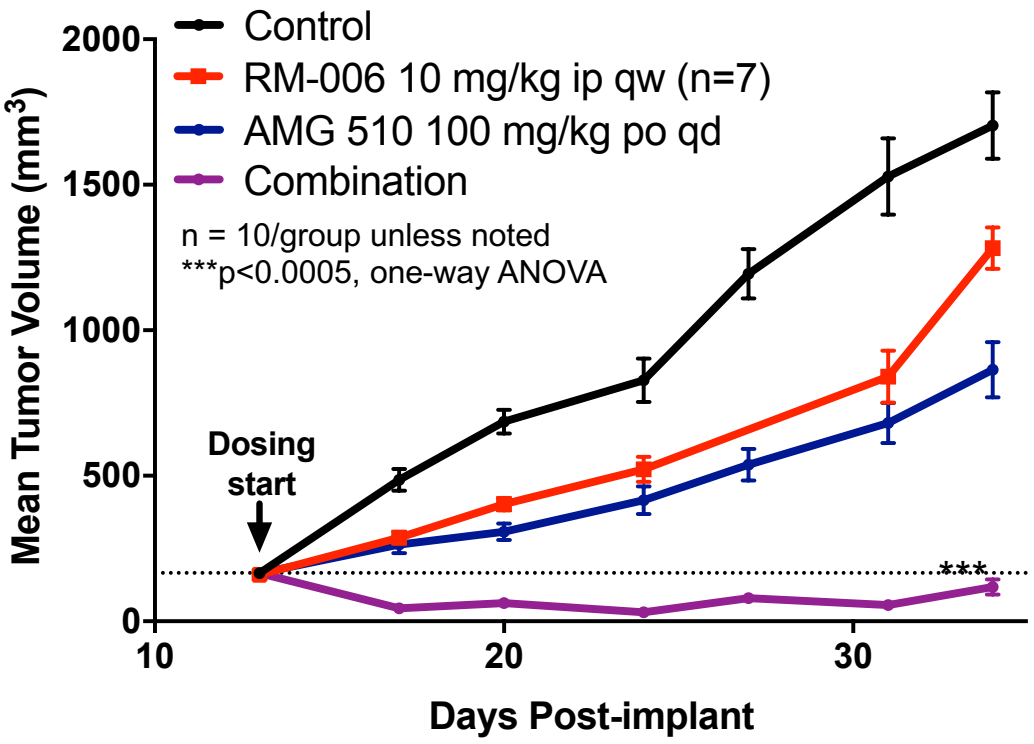
Genomic alterations of these proteins hyperactivate mTORC1 and can drive cancer

RTK-driven signaling pathway

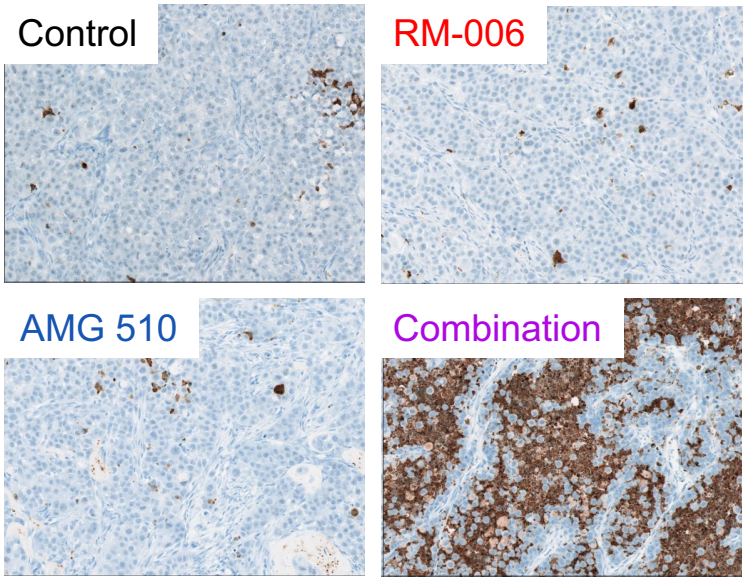
Feedback loop

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

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



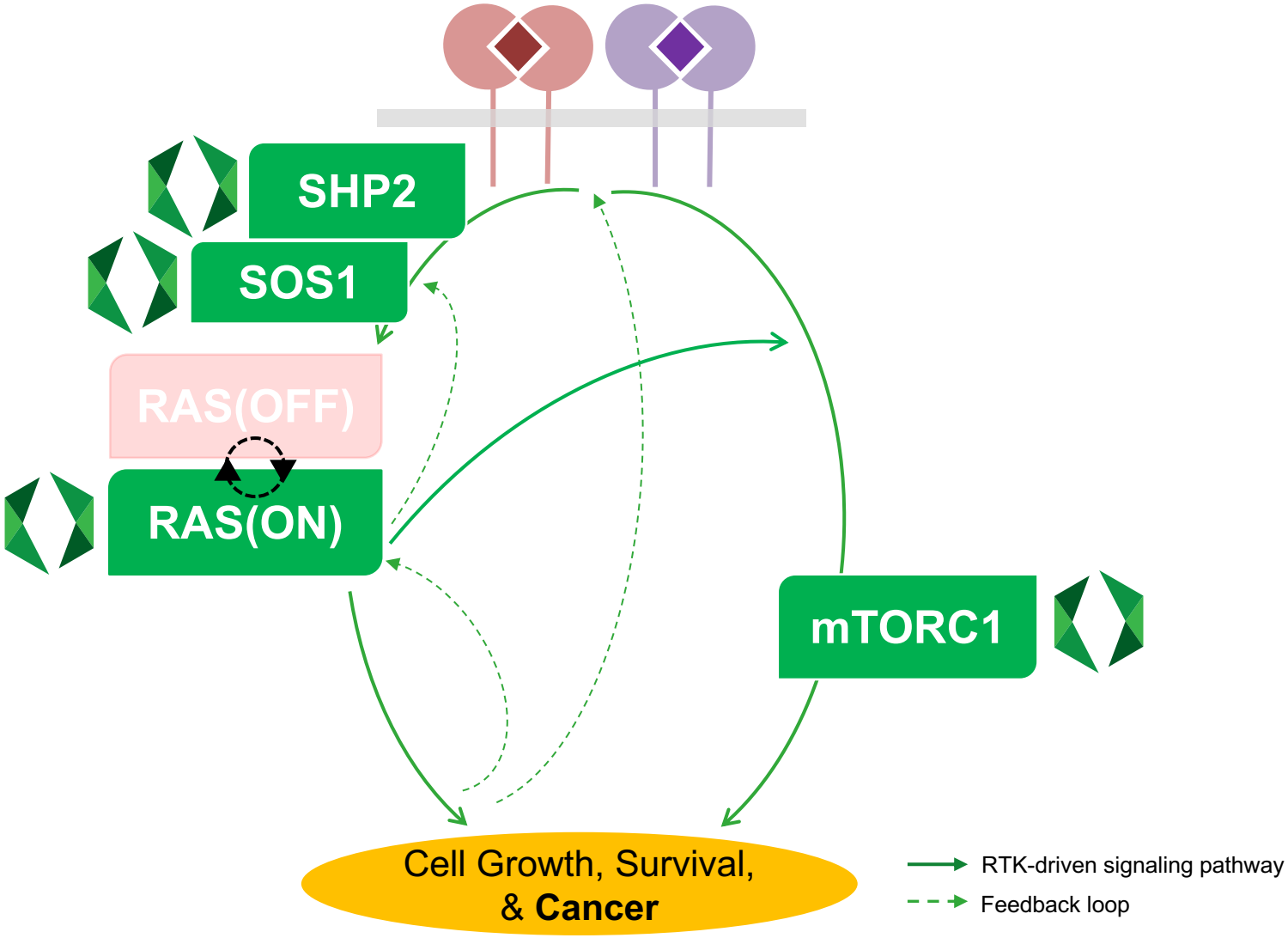
Apoptosis*



*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

Strategic R&D Pipeline Targets Key Players that Drive RAS Addiction and Drug Resistance



2020 Year-to-Date

- **RAS(ON) Inhibitors**
  - ✓ Produced potent and cell-active first-in-class inhibitors targeting all major oncogenic RAS variants
  - ✓ Regressions in xenograft tumor models driven by $KRAS^{G12C}$ or $KRAS^{G12D}$
  - ✓ Inhibitors advanced to lead optimization for 5 oncogenic RAS variants

- **RAS Companion Inhibitors**
  - ✓ Initial anti-tumor activity observed in patients treated with RMC-4630
    - Monotherapy ($KRAS^{mutant}$ NSCLC and $NF1^{LOF}$ uterine cancer); completed dose-escalation and entered expansion at RP2DS
    - Evidence of immune enhancement
    - Combination with cobimetinib ($KRAS^{mutant}$ CRC); completed dose-escalation and entered expansion at RP2DS
    - Combination studies underway with: AMG 510 (sotorasib), pembrolizumab and osimertinib
  - ✓ RMC-5552 continues on track to IND

- **Corporate**
  - ✓ Successful IPO and first follow-on financing, with strong balance sheet

Corporate Milestones

Milestone	Expected Delivery
RAS(ON) Inhibitors	
Nominate first Development Candidate	Q420
Identify lead compound for second target	✓
Nominate second Development Candidate	1H21
RAS Companion Inhibitors	
• SHP2 (RMC-4630)	
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	✓
Monotherapy dose escalation safety data set	1H21
Preliminary activity data for combination with cobimetinib	2H21
Initial tolerability and PK data for combination with osimertinib	2H21
• mTORC1/4EBP1 (RMC-5552)	
IND-ready	Q420
Begin treating patients with RMC-5552 monotherapy	1H21

Financial Information

Financial Position	
Cash, cash equivalents and marketable securities @ 9/30/2020	$466.1M(1)

(1) Includes $167.8 million in net proceeds from the July 2020 public offering of common stock.

Translating Frontier Oncology Targets to *Outsmart Cancer*™