



Delivering Novel Therapies in RAS/MAPK Pathway Driven Cancers

April 2024

Corporate Presentation



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This presentation includes forward-looking statements about Verastem Oncology's programs and product candidates, strategy, future plans and prospects, including statements related to the expected outcome and benefits of collaborations, including with GenFleet Therapeutics (Shanghai), Inc. ("GenFleet"), the potential clinical value of various of its clinical trials, the timing of commencing and completing trials, including topline data reports, interactions with regulators, the potential for and timing of commercialization of product candidates and potential for additional development programs involving Verastem Oncology's lead compound. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," "can," "promising" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Each forward-looking statement is subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statement.

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Verastem Oncology

*Strong progress in 2023
sets up multiple value-
creation opportunities*

Well-Positioned To Deliver on 2024 Catalysts

➤ On track to deliver the first approved therapy in LGSOC

- Data at ASCO 2023 of avutometinib, a RAF/MEK Clamp in combination with defactinib, a FAK inhibitor, demonstrated robust responses in patients with recurrent low-grade serous ovarian cancer (LGSOC)
- Phase 3 confirmatory study underway with plans to report updated topline data from RAMP 201 trial in H1 2024
- Commence rolling NDA for Accelerated Approval in H1 2024

➤ Ongoing studies in additional indications including Pancreatic Cancer and NSCLC

- Report initial safety and efficacy results from RAMP 205 trial of avutometinib + gemcitabine/nab-paclitaxel + defactinib in first-line metastatic pancreatic cancer in H1 2024
- Report updated data from both non-small cell lung cancer (NSCLC) trials - RAMP 203 (sotorasib-Amgen) and RAMP 204 (adagrasib-Mirati) trials in Mid-2024

➤ GenFleet collaboration furthers pipeline potential in RAS/MAPK driven cancers

- GenFleet's IND application for GFH375/VS-7375, a potential best-in-class oral KRAS G12D (ON/OFF) inhibitor, was filed in China and accepted for review; upon clearance expect to initiate Phase I trial in China in H2 2024
- Expect to initiate Phase I trial for GFH375/VS-7375 in China in H2 2024
- Ongoing discovery/lead optimization for second and third programs

➤ Strong balance sheet to support ongoing programs and operations

- Company ended Q4 2023 with \$137.1M in cash and investments and \$31.1 million GAAP operating expenses (\$29.5 million non-GAAP operating expenses*)

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* Q4 2023 GAAP operating expenses - \$31.14M less Q4 2023 stock compensation of \$1.60M = \$29.54M Q4 2023 non-GAAP operating expenses;
IND: investigational new drug application; NDA: new drug application

Driving Momentum in 2024: Recap of Recent Key Achievements

Avutometinib + Defactinib: Recurrent LGSOC	Avutometinib + Defactinib: Metastatic Pancreatic Cancer	Avutometinib + KRAS G12C Inhibitors: NSCLC	GFH375/VS-7375: Oral G12D (ON/OFF) Inhibitor
<ul style="list-style-type: none">✓ Received FDA Orphan Drug Designation✓ Initiated Phase 3 confirmatory study✓ Presented planned subgroup analysis of Part A RAMP 201 trial✓ RAMP 201 FDA meeting – combination selected as go-forward regimen	<ul style="list-style-type: none">✓ Initiated RAMP 205 combo avutometinib + gemcitabine/nab-paclitaxel + defactinib	<ul style="list-style-type: none">✓ Received FDA Fast Track Designation for avutometinib in combo with Amgen's G12C inhibitor sotorasib✓ Presented initial results from Phase I/2 RAMP 203 trial of avutometinib + sotorasib in KRAS G12C mutant NSCLC✓ Added defactinib to avutometinib and sotorasib combination in the RAMP 203 trial	<ul style="list-style-type: none">✓ Established discovery and development collaboration with GenFleet✓ Selected GFH375/VS-7375, a potential best-in-class oral KRAS G12D (ON/OFF) inhibitor✓ IND application was filed in China and accepted for review

Clinical Program Designed for Success in LGSOC, Signal Generation

Regimen	IND-Enabling/ Preclinical	Phase 1	Phase 2	Phase 3	Anticipated Milestones	Collaboration
Avutometinib + Defactinib: Recurrent LGSOC						
RAF/MEK Clamp + FAKi					RAMP 301 Ongoing Enrollment	
RAF/MEK Clamp + FAKi					RAMP 201 Topline Data; Rolling NDA Submission Seeking Accelerated Approval: H12024	
Avutometinib + KRAS G12C Inhibitors: NSCLC						
RAF/MEK Clamp + KRAS G12Ci (sotorasib) + FAKi					RAMP 203 Updated Data Mid-2024	Amgen
RAF/MEK Clamp + KRAS G12Ci (adagrasib)					RAMP 204 Updated Data Mid-2024	Mirati/BMS
Avutometinib + Defactinib: Metastatic Pancreatic Cancer						
RAF/MEK Clamp + FAKi + gemcitabine, nab-paclitaxel					RAMP 205 Initial Safety/Efficacy H12024	PanCAN
GFH375/VS-7375						
G12D (ON/OFF) inhibitor					IND filed in China and accepted for review; upon clearance expect to initiate Phase 1 in China in H22024	GenFleet



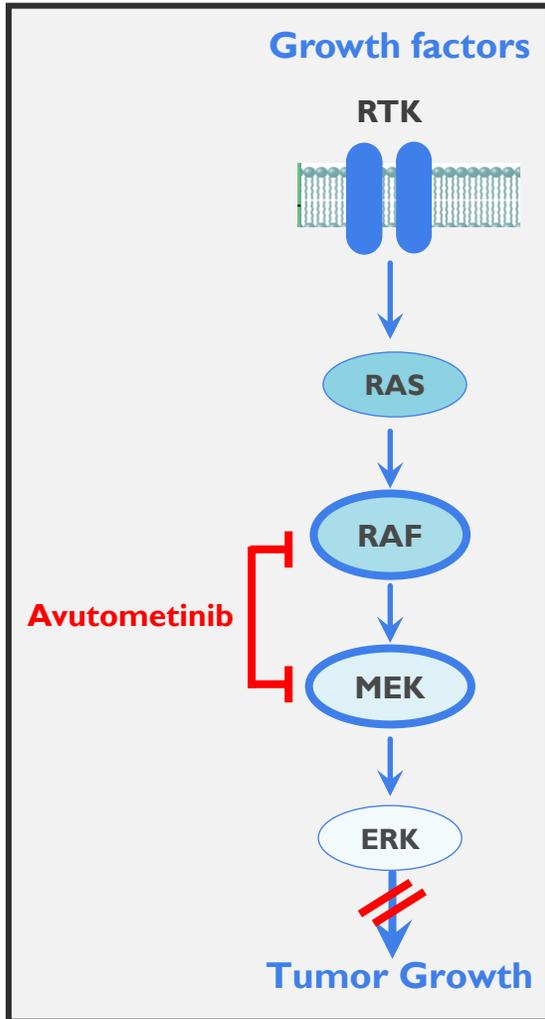
Avutometinib RAF/MEK Clamp Program Overview

Avutometinib is a Differentiated Agent with the Potential to Serve as the Backbone for Combinations Across RAS Pathway-Driven Cancers

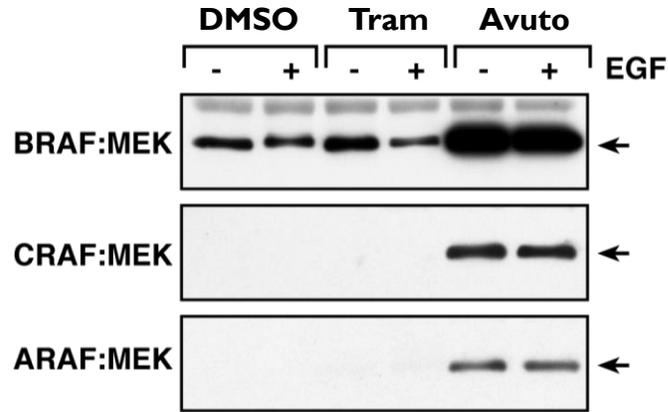
- Unique RAF/MEK clamp mechanism of action
- Novel intermittent dosing schedule; convenient oral regimen
- Orphan Drug Designation for avutometinib alone or in combination with defactinib in recurrent LGSOC
- Breakthrough Therapy Designation for combination of avutometinib and defactinib for treatment of recurrent LGSOC after one or more prior lines of therapy including platinum-based chemotherapy
- Received FDA Fast Track Designation for avutometinib in combination with Amgen's G12C inhibitor sotorasib in KRAS G12C-mutant NSCLC
- Potential best-in-class safety & tolerability profile relative to marketed MEK inhibitors, with potential for combinability with agents from multiple target classes
- Promising signals of clinical activity in various RAS pathway-driven cancers, including in patients whose tumors previously progressed on other MEK inhibitors

Avutometinib is a Unique Small Molecule RAF/MEK Clamp

Contrasting Mechanism of Action vs. MEK-Only Inhibitors

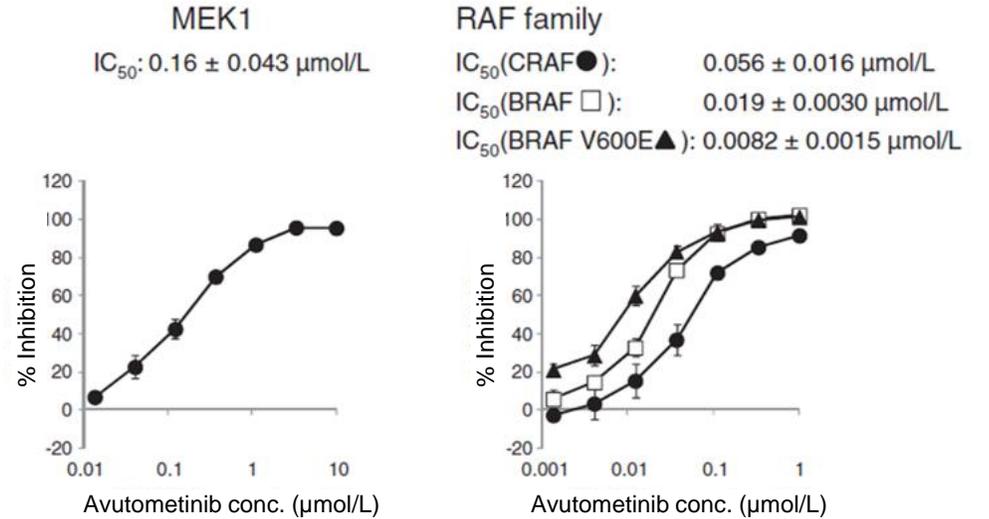


Avutometinib induces dominant negative RAF/MEK complexes

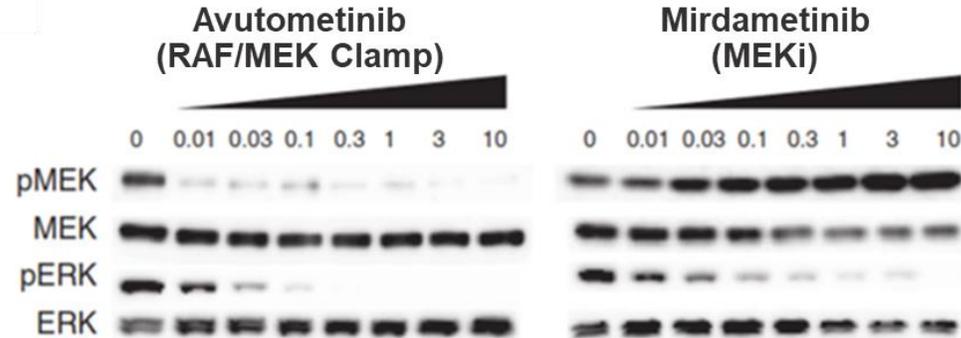


Collaboration with Deborah Morrison, NCI

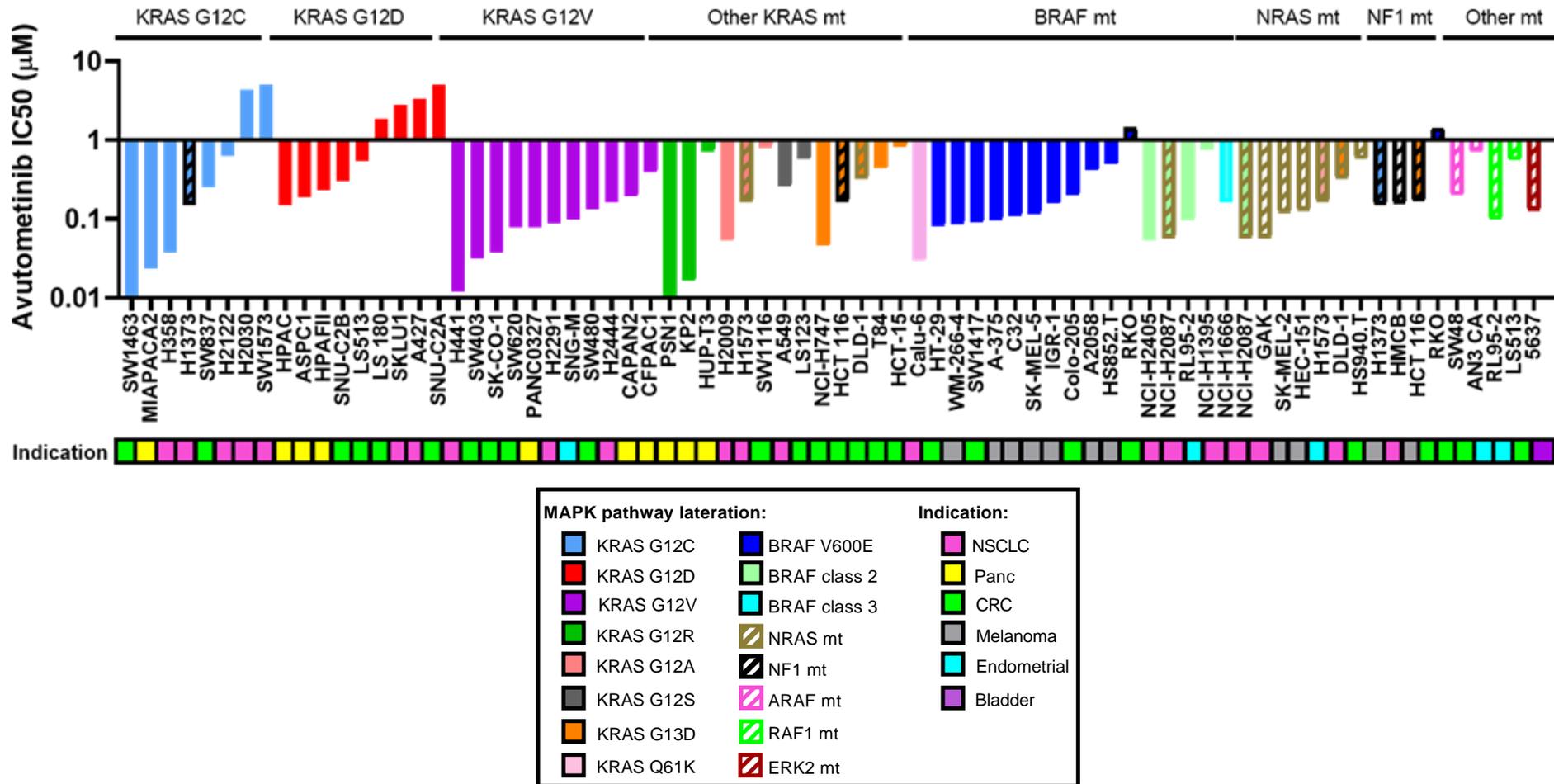
Avutometinib inhibits both RAF and MEK activities



The RAF/MEK clamp mechanism avoids the compensatory activation of pMEK enabling more complete pERK inhibition

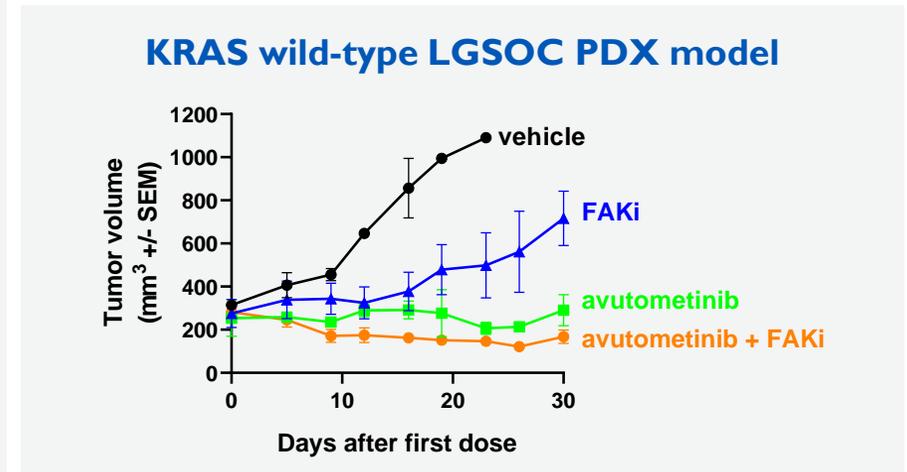
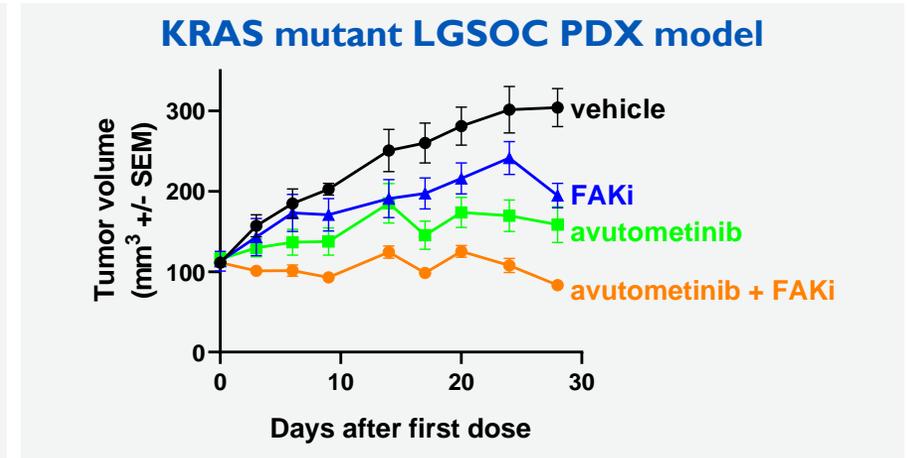
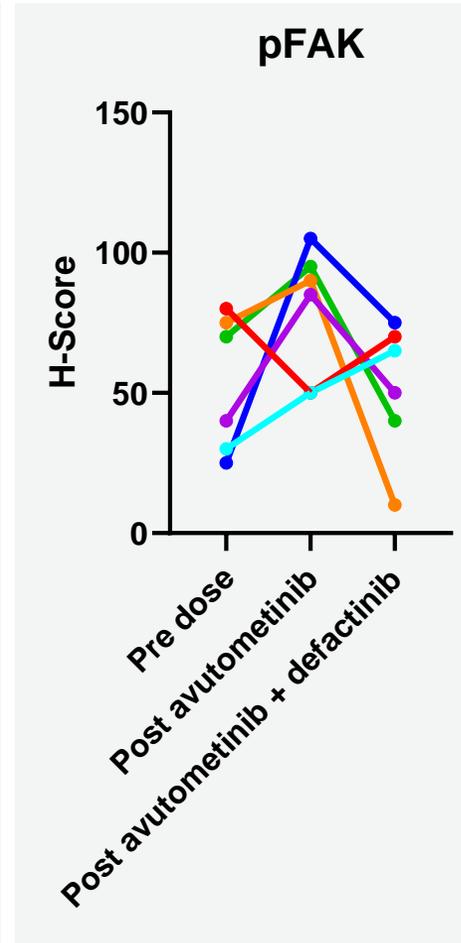
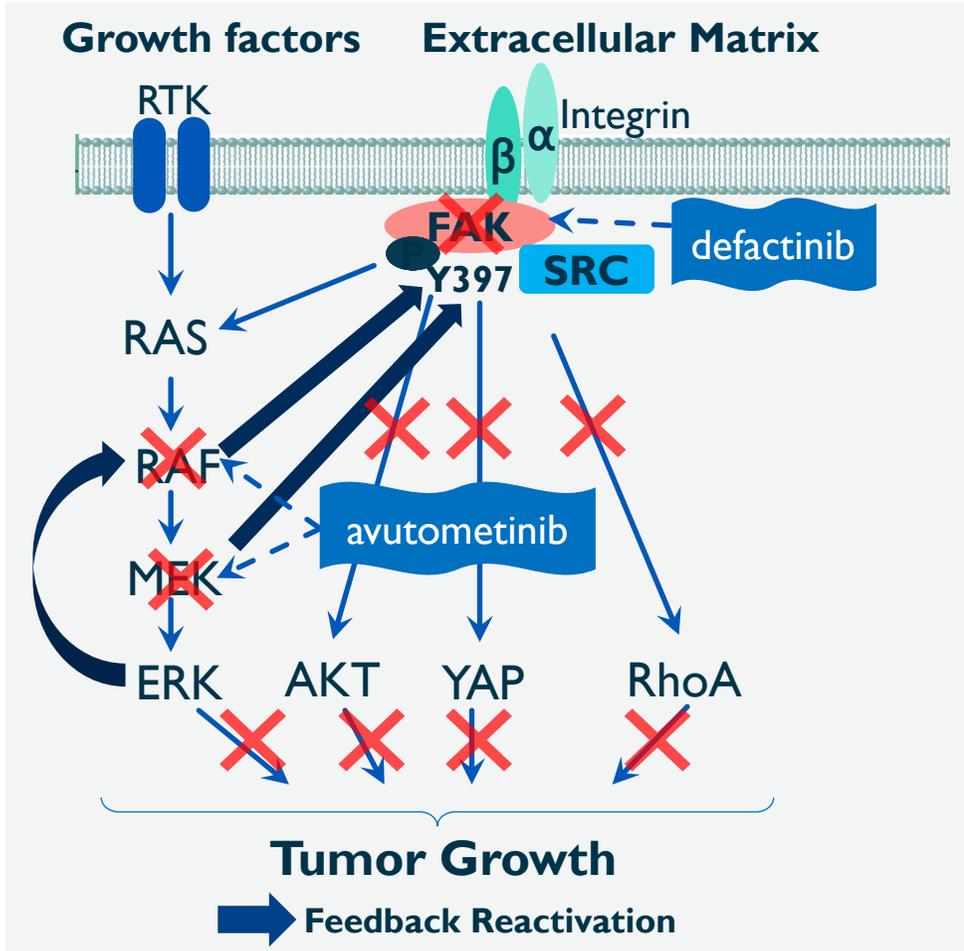


Avutometinib Inhibits Cell Proliferation Across Multiple RAS/MAPK Pathway Alterations and Multiple Solid Tumor Histologies



Strong Scientific Rationale for Avutometinib and FAK Inhibitor Combination

Anti-Tumor Efficacy in KRAS Mutant and Wild-Type LGSOC models



Optimized Dosing Schedule Defined: Favorable Tolerability Profile with Novel Intermittent Dosing Regimen

Summary of Adverse Events Grade ≥ 3 Occurring in $\geq 5\%$ of patients

	Avutometinib monotherapy Daily at MTD N=6 28-day cycle	RP2D Avutometinib monotherapy 4mg twice weekly N=26 28-day cycle	RP2D (Avutometinib 3.2mg twice weekly + defactinib 200mg twice daily) N=38 21 days of 28-day cycle
Treatment Related Adverse Event	Grade ≥ 3	Grade ≥ 3	Grade ≥ 3
Rash	3 (50%)	5 (19%)	2 (5%)
CK elevation (Creatine phosphokinase)	1 (17%)	2 (8%)	2 (5%)



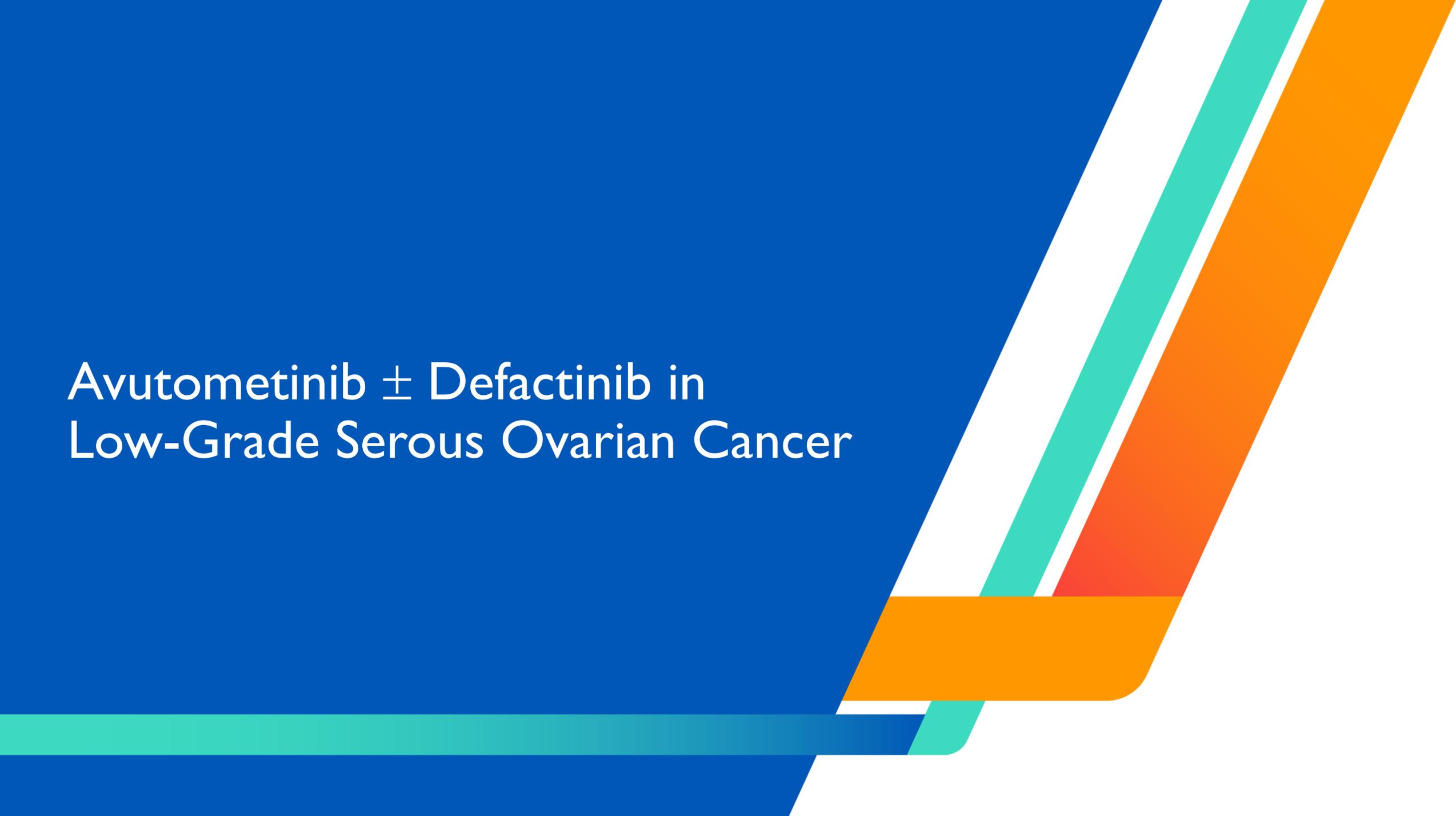
RAS Pathway-Driven Cancers and Rational Avutometinib Combinations

Ongoing Comprehensive Approach to Establish More Complete Blockade of RAS Pathway & Resistance Pathways

	Indication	Incidence/ Prevalence	Biomarker %	Regimen	Setting	Phase	Collaborator
Gynecologic Cancers	RAMP301 LGSOC	Prevalence ¹ : 6K	 70%	Avutometinib + defactinib	Relapsed Refractory molecularly profiled LGSOC	Phase 3 Confirmatory trial	
	RAMP201 LGSOC	Prevalence ¹ : 6K	 70%	Avutometinib + defactinib	Relapsed Refractory molecularly profiled LGSOC	Phase 2 Registration-directed. AA cohort fully enrolled	
	Gynecologic Basket*	Incidence ⁶⁻¹⁰ : 85K	 25%	Avutometinib + defactinib	Recurrent RAS Pathway-driven (RAS/RAF/NFI) endometrioid cancer, mucinous ovarian cancer, high-grade serous ovarian cancer or cervical cancer	Phase 2	
	Mesonephric	Incidence: ¹¹ ~680	 96%	Avutometinib + defactinib	Advanced or recurrent mesonephric gynecologic cancer	Phase 2	
NSCLC Adenocarcinoma	RAMP203 KRAS G12C	Incidence ^{2,3} : 114K	 13%	Avutometinib + sotorasib ± defactinib	Recurrent KRAS G12C with prior KRAS G12C inhibitor(i) treatment or KRAS G12Ci naïve	Phase 1/2	
	RAMP204 KRAS G12C			Avutometinib + adagrasib	Recurrent KRAS G12C with prior KRAS G12Ci treatment that progressed	Phase 1/2	
Pancreatic	RAMP205 PDAC	Incidence ⁴ : 58K	 98%	Avutometinib + defactinib + gemcitabine/nab-paclitaxel	Previously untreated (front-line) metastatic pancreatic ductal adenocarcinoma (PDAC)	Phase 1/2	
CRC	KRAS mt*	Incidence ⁵ : 148K	 45%	Avutometinib + cetuximab	Recurrent metastatic KRAS mt	Phase 1	
Breast Cancer	ER+*	Incidence ⁵ : 279K	 22.5%	Avutometinib + abemaciclib + fulvestrant	Recurrent ER+/HER2- breast cancer following progression on CDK4/6i + aromatase inhibitor	Phase 1	
Thyroid	MAPK alterations**	Incidence ⁴ : 44K	 35%	Avutometinib + defactinib	Differentiated & anaplastic thyroid cancer	Phase 2	

*IST **excluding BRAFV600E

¹ Monk, Randall, Grisham, The Evolving Landscape of Chemotherapy in Newly Diagnosed Advanced Epithelial Ovarian Cancer, Am Soc Clin Oncol Educ Book; 2019; Slomovitz, Gourley, Carey, Malpica, Shih, Huntsman, Fader., Grisham et al, Low-Grade serous ovarian cancer: State of the Science; Gynecol Oncol; 2020. Grisham, Iyer, Low-Grade Serous Ovarian Cancer: Current Treatment Paradigms and Future Directions; Curr Treat Options Oncology; 2018; Globocan 2020; ²Pakkala and Ramalingam JCI Insight 2018); ³Cancer Statistics 2020, Siegel et. al. CA Cancer J Clin 2020;70:7-30; ⁴Cancer Statistics 2020, Siegel et. al. CA Cancer J Clin 2020;70:7-30 ⁵CbioPortal; ⁶Uterine cancer is one of the leading gynecologic neoplastic disorders in the US, of which over 80% are endometrioid adenocarcinomas (EA); ⁷Endometrioid OC (EnOC) accounts for approximately 10% of all OC, with the majority of cases diagnosed as low grade, early stage disease with excellent clinical; ⁸Mucinous ovarian cancer: 3-11% of ovarian cancer (Hada et al., 2021); ⁹90% of Ovarian Cancer is Epithelial Ovarian Cancer (<https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2018/cancer-facts-and-figures-2018.pdf>); ¹⁰HGSOC the most common type of ovarian cancer, accounting for approximately 75% of epithelial ovarian cancers. (<https://ocrahope.org/news/high-grade-serous-carcinoma/>) ¹¹Ji Son (David Hong) ASCO 2023



Avutometinib ± Defactinib in
Low-Grade Serous Ovarian Cancer

LGSOC Unmet Need & Opportunity

- LGSOC is a less common type of ovarian cancer that is often diagnosed in younger women
 - LGSOC is a unique disease that is distinct from high-grade serous ovarian cancer (HGSOC) in its pathology, protracted clinical course and low response to chemotherapy and thus requires a more tailored therapeutic approach
 - An estimated 1,000-2,000 patients are diagnosed with LGSOC per year in the U.S., with prevalence of ~6,000
- There are currently no approved therapies specifically indicated for recurrent LGSOC
 - Recent clinical trials in recurrent LGSOC showed that standard-of-care chemo and hormonal therapy are relatively ineffective (6-13% ORR).
 - LGSOC has a chemo-resistant nature and optimal treatment has not yet been defined. NCCN guidelines include clinical trials and observation highlighting the lack of approved & effective therapies
- LGSOC is known to be driven by the MAPK (RAS) pathway in $\geq 70\%$ of patients
- A phase I/II study in the UK (FRAME) evaluated the combination of avutometinib and defactinib
 - Results in recurrent LGSOC showed a 42% confirmed ORR with durable responses and favorable safety/tolerability
- RAMP 201: A registration-directed Phase 2 trial of avutometinib and avutometinib + defactinib in recurrent LGSOC
 - Updated data from ASCO 2023 showed a 45% confirmed ORR in the combination arm with tumor shrinkage in 86% of evaluable patients
- RAMP 301: A confirmatory Phase 3 trial evaluating the combination of avutometinib and defactinib versus standard chemotherapy or hormonal therapy for the treatment of recurrent LGSOC

- **Orphan Drug Designation** for avutometinib alone or in combination with defactinib in recurrent LGSOC
- **Breakthrough Therapy Designation** granted for avutometinib and defactinib in recurrent LGSOC after one or more prior lines of therapy

LGSOC is a Unique RAS Pathway-Driven Cancer with a High Unmet Need

● LGSOC is a type of ovarian cancer that disproportionately affects younger women

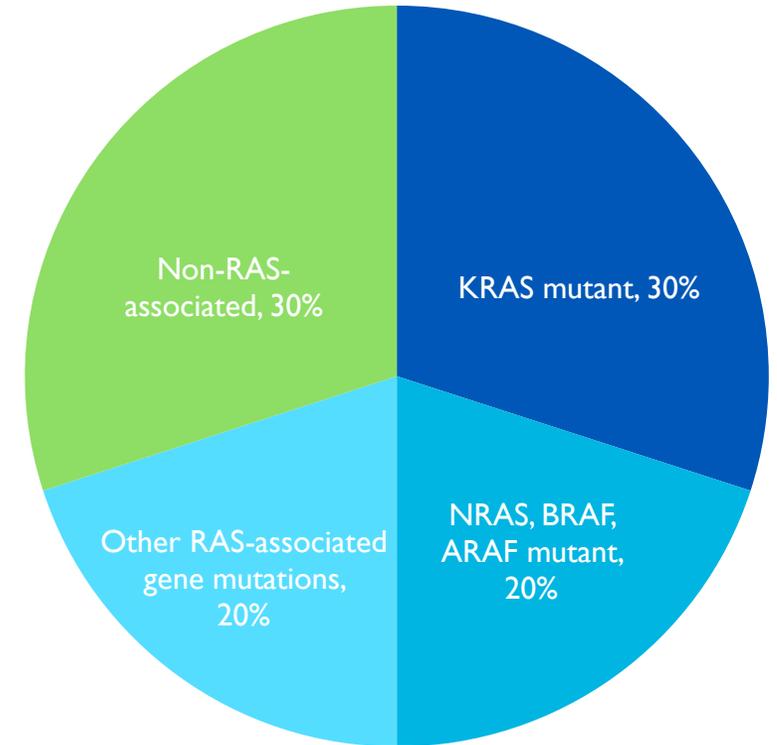
● 1,000 to 2,000 patients in the U.S. and 15,000 to 30,000 worldwide diagnosed with LGSOC each year

● A slow growing cancer, that has a median survival of almost 10 years, so patients remain in treatment for a long time (10-yr prevalence ~80,000 worldwide, ~6,000 US)

● Patients often experience significant pain and suffering from their disease over time

● Prior research has focused primarily on HGSOC. However, LGSOC is clinically, histologically and molecularly unique from HGSOC with limited treatments available

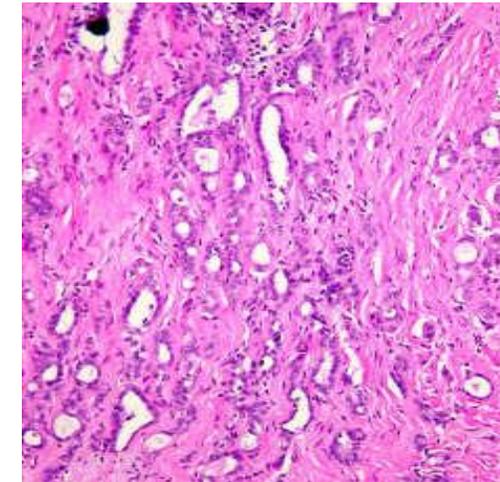
~30% of LGSOC Patients Have KRAS mt
~70% of LGSOC Shows RAS Pathway-Associated mts



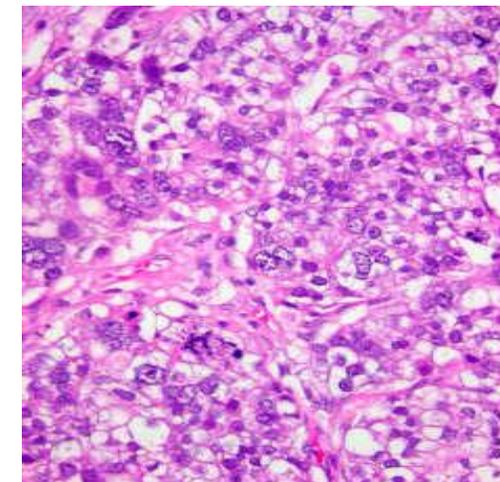
References: AACR Project GENIE Cohort v9.0-public and Verastem unpublished analysis

Low-Grade and High-Grade Serous Ovarian Cancer Are Different Diseases

Variable	LGSOC	HGSOC
Nuclear atypia	Uniform round to oval with little variation	+++ Marked variation
Mitotic Index	<12 mitoses per 10 hpf	>12 mitoses per 10 hpf
Chromatin and variation in size of nucleus	Little	Marked (nuclear size ratio ≥ 3)
Mutation	KRAS ++ BRAF + ER/PR +++	P53 +++ BRCA 1/2 +
Precursor	Serous borderline tumor	Tubal intraepithelial neoplasia



LGSOC



HGSOC

Recurrent LGSOC: High Medical Need

No Approved Treatment Options – Limited Benefit from Available Therapies

Recurrent Low-Grade Ovarian Cancer – Treatment Guidelines ¹

RECURRENCE THERAPY^r

Recurrent disease^s

Clinical trial
 or
 Trametinib^f
 or
 Binimetinib (category 2B)^f
 or
 Dabrafenib + trametinib (for *BRAF* V600E-positive tumors)^f
 or
 Hormonal therapy^t
 or
 Chemotherapy (if not previously used), [see OV-C \(6 of 11\)](#)
 or
 Other systemic therapy^{f,u}
 • For platinum-sensitive disease, [see OV-C \(8 of 11\)](#)
 • For platinum-resistant disease, [see OV-C \(9 of 11\)](#)
 or
 Observation

No Category I recommendations (high-level evidence).
 Category 2a (lower-level evidence with uniform NCCN consensus) unless otherwise indicated
 f: There is no standard sequencing of drugs for recurrent disease. Considerations include prior therapies, disease burden, relative efficacy, and relative toxicity profile.
 t: An aromatase inhibitor (i.e., letrozole, anastrozole, exemestane) is preferred if not used previously. Fulvestrant, tamoxifen, or leuprolide acetate is recommended if an aromatase inhibitor was given previously.

Preferred Regimens

- Paclitaxel/carboplatin q3weeks^{f,9} ± maintenance letrozole (category 2B) or other hormonal therapy (category 2B)¹¹
- Paclitaxel/carboplatin/bevacizumab + maintenance bevacizumab¹¹ (ICON-7 & GOG-218)
- Hormone therapy (aromatase inhibitors: anastrozole, letrozole, exemestane) (category 2B)

Recent LGSOC Trials Highlight High Unmet Need

Trial	Number of Prior Systemic Therapies Median (range)	Prior MEK allowed	Prior Bevacizumab	Therapy	Response Rate ORR	Image Assessment	Median PFS Months (95% CI)	Discontinuation Rate due to AEs
GOG 281 ¹	2 (1-10)	No	* Low %	SoC (n=130)	6% 95% CI: (3%, 12%)	INV	7.2 (5.6-9.9)	30%
				Trametinib (n=130)	26% 95% CI: (19%, 35%)	INV	13.0 (9.9-15.0)	36%
MILO ²	2 (1-8)	No	* Low %	SoC (n=101)	13% 95% CI: (7%, 21%)	BICR	10.6 (9.2 - 14.5)	17%
				Binimetinib ² (n=198)	16% 95% CI: (11%, 22%)	BICR	9.1 (7.3-11.3)	31%

¹ Study GOG 281 trial Gershenson et al., Lancet 2022

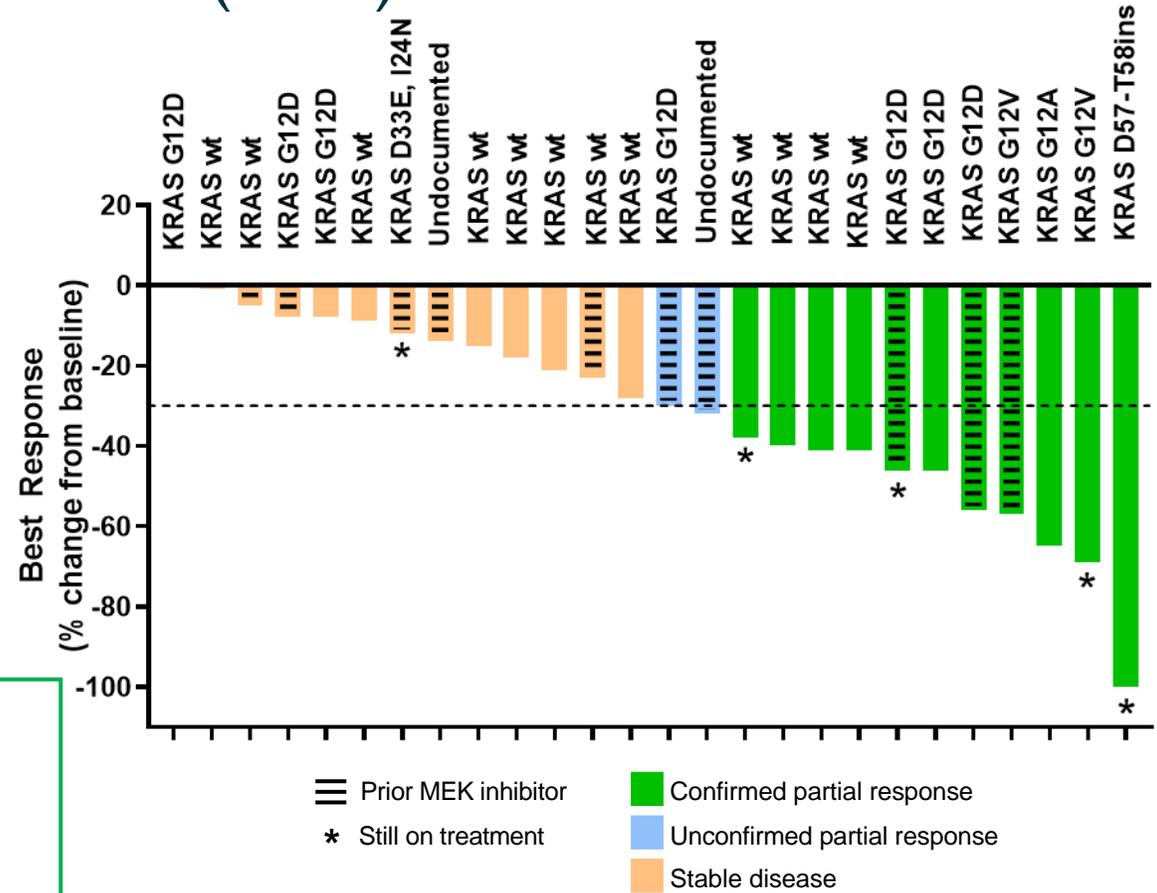
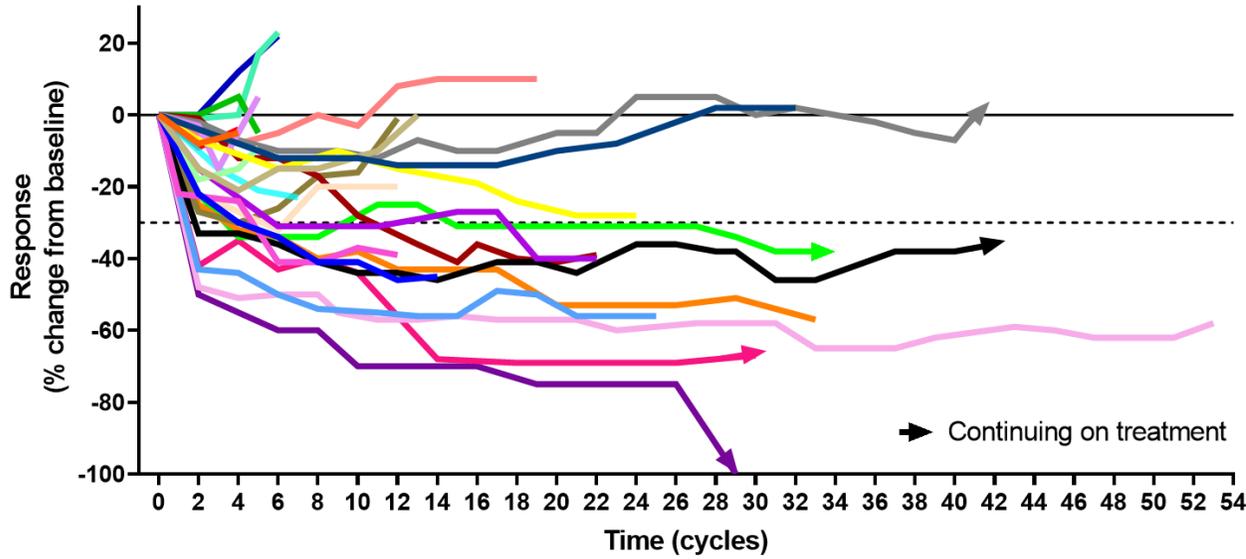
² MILO Study Monk et al., J Clin Oncol 2020.

* Low historical use of bevacizumab during trial conduct. % not reported
MILO: no more than 3 lines of prior chemotherapy

SoC = Standard of Care (endocrine / chemotherapy)
INV = Investigator
BICR = Blinded independent central review
PFS = Progression free survival
CI = confidence interval
NR = Not reached

FRAME Study: High Rate of Durable Responses with the Combination of Avutometinib and Defactinib in Recurrent LGSOC (n=26)

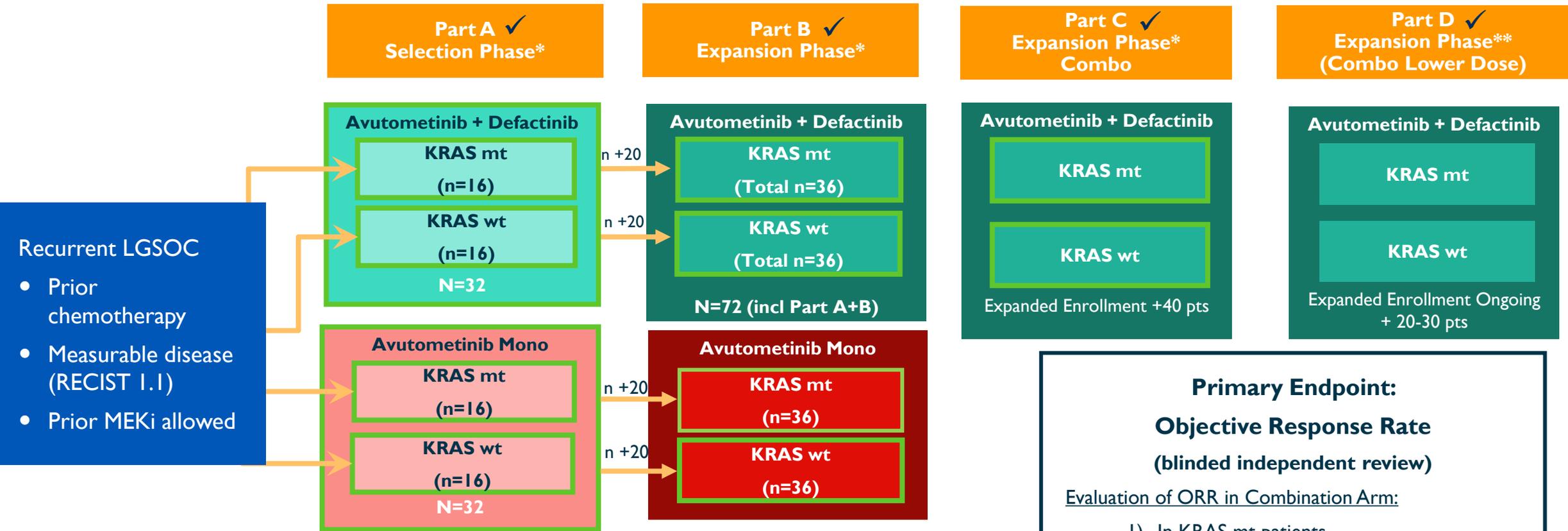
Response by RECIST



- Overall response rate (ORR) = 42% (11 confirmed PRs/26)
 - KRAS mutant ORR = 58% (7 confirmed PRs/12)
 - KRAS wild-type ORR = 33% (4 confirmed PRs/12)
- Median DoR 26.9 months (95% CI 8.5-47.3) across all LGSOC patients
- Median PFS 20.0 months (95% CI 11.1 – 31.2) across all LGSOC per RECIST 1.1
- Median 3.5 prior lines of treatment (n=26)
- Responses observed in patients previously treated with MEK inhibitor
- 19% (5/26) patients still on treatment as of July 2023 (minimum follow up: ~17 months)
- No new safety findings with continued follow-up
- 1 patient discontinued for adverse events as of July 2023 (skin AE)

28-day cycles
 DoR: Duration of Response
 PFS: Progression free survival
 NR: Not reached

RAMP 201 (ENGOTov60/GOG3052): Registration-Directed Phase 2 Trial of Avutometinib ± Defactinib in Patients with Recurrent LGSOC



* Dosing: Avutometinib + Defactinib combo: Avutometinib 3.2 mg PO 2x/wk 21/28 days + Defactinib 200 mg PO BID: 21/28 days;
 Avutometinib monotherapy: Avutometinib 4.0 mg PO 2x/wk 21/28 days

** Lower Dose: Avutometinib + Defactinib combo: Avutometinib 1.6 mg PO 2x/wk 21/28 days + Defactinib 200 mg PO BID: 21/28 days;

✓ Completed Enrollment

Updated Data from Part A of RAMP 201

“These results demonstrate avutometinib in combination with defactinib can deliver high response rates for patients with recurrent LGSOC with a promising safety profile to date. It is particularly encouraging to see extensive tumor shrinkage in women who have had several treatment lines, including prior MEK inhibitors. These latest findings suggest the combination may offer a new treatment option for women with this hard-to-treat cancer, and we are hopeful it will become the new standard of care.”

–**Dr. Susana Banerjee, MBBS, MA PhD, FRCP**, *global and lead investigator of the study, Consultant Medical Oncologist at The Royal Marsden NHS Foundation Trust and Team Leader in Women’s Cancers at The Institute of Cancer Research, London*

	Avutometinib + Defactinib	
	Total (n=29)	
	45% (13) 95% CI: (26%, 64%)	
ORR, % (n)	KRAS mt 60% (9/15)	KRAS wt 29% (4/14)
Tumor shrinkage, % (n)	86% (25)	
Median Time to Response	5.5 months (range 1.6-14.7 months)	
Relative avutometinib Dose Intensity	83% ± 20%	

- 29 patients were evaluable for efficacy with a minimum follow-up of 12 months and 13 (45%) patients remain on study treatment
- Patients were heavily pretreated with a median of 4 prior systemic regimens (up to 11)
 - 3 out of 4 patients who received prior MEK inhibitors responded to the combination
- Median duration of response and median progression free survival have not been reached
- Safety and tolerability continued to be favorable and consistent with previously reported data
 - The discontinuation rate due to ≥ 1 adverse event was 12% in the combination overall to date (4.9% due to elevated blood CPK)

Recent LGSOC Trials with Standard of Care Highlight High Unmet Need: Current Trials with Avutometinib + Defactinib Show Overall Response Rate >40%

Trial	Median Number of Prior lines of Therapy	Prior MEK Allowed	Prior Bevacizumab	Therapy	Response Rate ORR	Image Assessment	Median PFS Months (95% CI)	Discontinuation Rate Due to AEs
GOG 281 ¹	2 (1-10)	No	* Low %	Standard of Care	6% ^ 95% CI: (3%, 12%)	INV	7.2 (5.6-9.9)	30%
				Trametinib	26%^ 95% CI: (19%, 35%)	INV	13.0 (9.9-15.0)	36%
MILO ²	2 (1-8)	No	* Low %	Standard of Care	13% 95% CI: (7%, 21%)	BICR	10.6 (9.2 to 14.5)	17%
				Binimetinib	16% 95% CI: (11%, 22%)	BICR	9.1 (7.3-11.3)	31%
FRAME ³	3.5	Yes	19 %	Avutometinib + Defactinib	42%^ 95% CI: (23%, 63%)	INV	20 (11 - 31)	4%
RAMP 201 Part A (ASCO 2023 data) ⁴	4	Yes	65%	Avutometinib + Defactinib	45% 95% CI: (26%, 64%) 52%***	BICR	Not Yet Reached	10%**

¹Study GOG 281 trial Gershenson et al., Lancet 2022

²MILO Study Monk et al., J Clin Oncol 2020.

³ Banerjee et al., ESMO Sept 2021

⁴ Banerjee et al., ASCO June 2023

* Low historical use of bevacizumab during trial conduct. % not reported

MILO: no more than 3 lines of prior chemotherapy

SoC = Standard of Care

GOG 281: (chemotherapy / endocrine therapy)

PLD (liposomal doxorubicin), paclitaxel, topotecan, letrozole or tamoxifen

MILO: (chemotherapy only)

PLD (liposomal doxorubicin), paclitaxel or topotecan

*** Confirmed + Unconfirmed Objectives responses

** | 2% discontinuation in all combination pts (Part A + B (n=81): 4.9% due to elevated blood CPK)

INV = Investigator

BICR = Blinded independent central review

PFS = Progression free survival

CI = confidence interval

AE = adverse event

RAMP 201 Part A: Heavily Pre-Treated Patient Population

*Prior Platinum-Based Chemotherapy, Endocrine Therapy, Bevacizumab in Most Patients;
Prior MEK Inhibitor Therapy was Permitted*

	Avutometinib Monotherapy			Avutometinib + Defactinib		
	KRAS mt (n=16)	KRAS wt (n=17)	Total (n=33)	KRAS mt (n=16)	KRAS wt (n=15)	Total (n=31)
Age (yrs), median (min, max)	58 (27, 72)	48 (27, 74)	51 (27, 74)	61 (29, 71)	50 (30, 74)	55 (29, 74)
ECOG PS, n (%)						
0	8 (50)	15 (88)	23 (70)	11 (69)	9 (60)	20 (65)
I	8 (50)	2 (12)	10 (30)	5 (31)	6 (40)	11 (35)
Number of Prior Systemic Regimens, median (min, max)	4 (1, 10)	3 (1, 9)	3 (1, 10)	4 (1, 8)	5 (2, 11)	4 (1, 11)
Prior platinum-based chemotherapy, n (%)	15 (94)	17 (100)	32 (97)	16 (100)	15 (100)	31 (100)
Prior MEK inhibitor therapy, n (%)	5 (31)	5 (29)	10 (30)	2 (13)	2 (13)	4 (13)
Prior Bevacizumab, n (%)	8 (50)	8 (47)	16 (48)	7 (44)	13 (87)	20 (64)
Prior Hormonal therapy, n (%)	11 (69)	13 (76)	24 (73)	15 (94)	13 (87)	28 (90)

RAMP 201 Part A: Evaluable Patient Population*

Positive ORR Confirmed by Blinded Independent Central Review (BICR) Support Avutometinib + Defactinib as Go Forward Regimen in LGSOC - Regardless of KRAS Status

	Avutometinib			Avutometinib + Defactinib		
	KRAS mt (n=15)	KRAS wt (n=15)	Total (n=30)	KRAS mt (n=15)	KRAS wt (n=14)	Total (n=29)
Confirmed ORR, n (%)	2 (13)	1 (6)	3 (10) 95% CI (2%, 24%)	9 (60)	4 (29)	13 (45) 95% CI (26%, 64%)
CR, n (%)	1 (7)	0	1 (3)	0	0	0
PR, n (%)	1 (7)	1 (6)	2 (7)	9** (60)	4 (29)	13 (45)
SD, n (%)	12 (80)	13 (81)	25 (83)	6 (40)	7 (50)	13 (45)
Disease control rate***, n (%)	14 (93)	14 (88)	28 (93)	15 (100)	11 (79)	26 (90)
PD, n (%)	1 (7)	2 (13)	3 (10)	0	3 (21)	3 (10)
Confirmed + unconfirmed ORR, n (%)	2 (13)	1 (6)	3 (10)	11 (73)	4 (29)	15 (52)

* Evaluable for Efficacy: At least one blinded imaging assessment in 31 of 33 and 29 of 31 patients enrolled in respective treatment arms

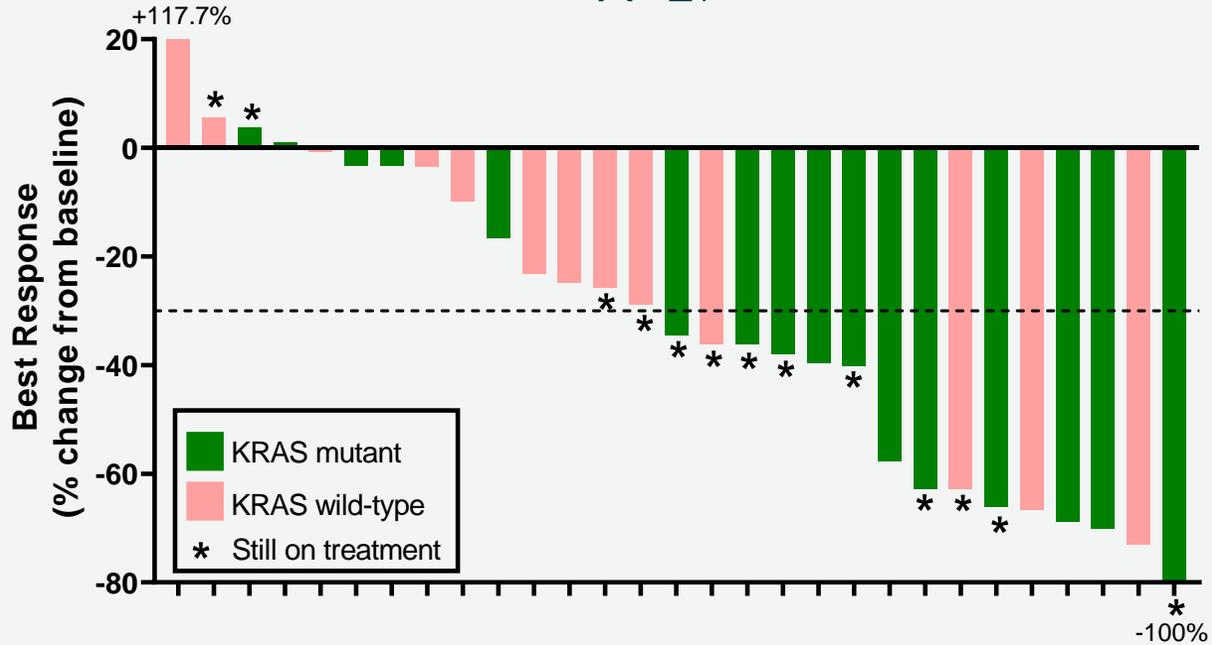
** Includes patient deepened to CR at last assessment; CR not yet confirmed

***Disease control rate (SD + PR + CR) at 8 weeks.

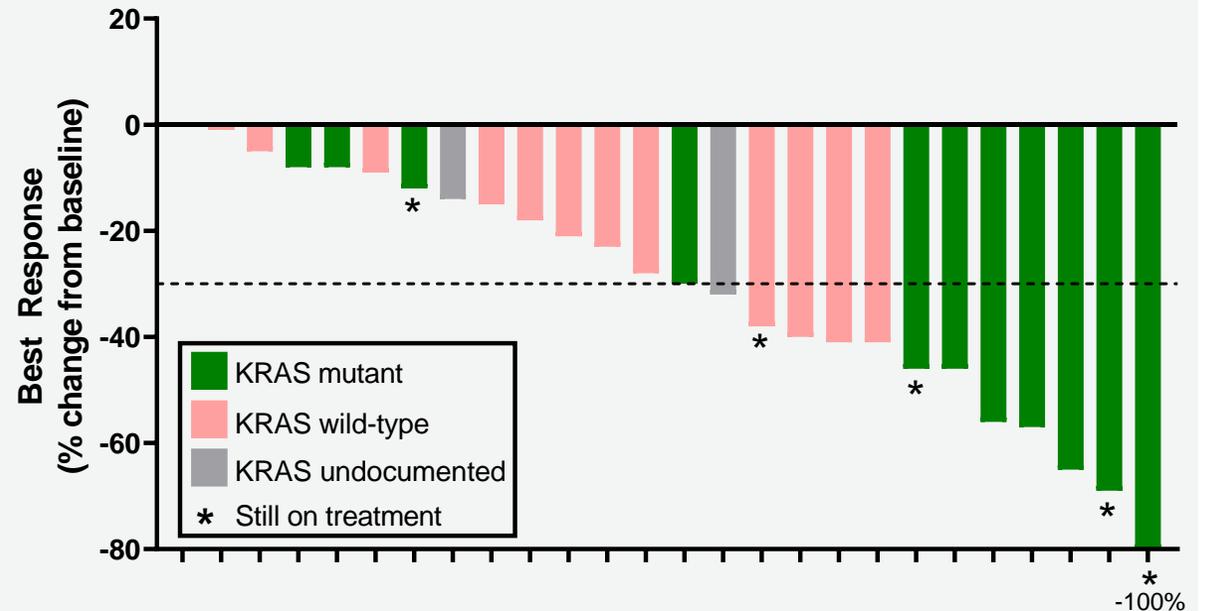
Combination of Avutometinib and Defactinib

Initial Data from RAMP 201 Trial Reinforce Findings from FRAME Trial

RAMP 201 (Part A) Interim Analysis - Blinded ICR N=29



FRAME Investigator Assessment N=26



RAMP 201: Safety and Tolerability Profile of Avutometinib + Defactinib

No New Safety Signals; Few Discontinuations Due to Adverse Events

Most Common Treatment-Related Adverse Events (>20%) in All Treated Patients

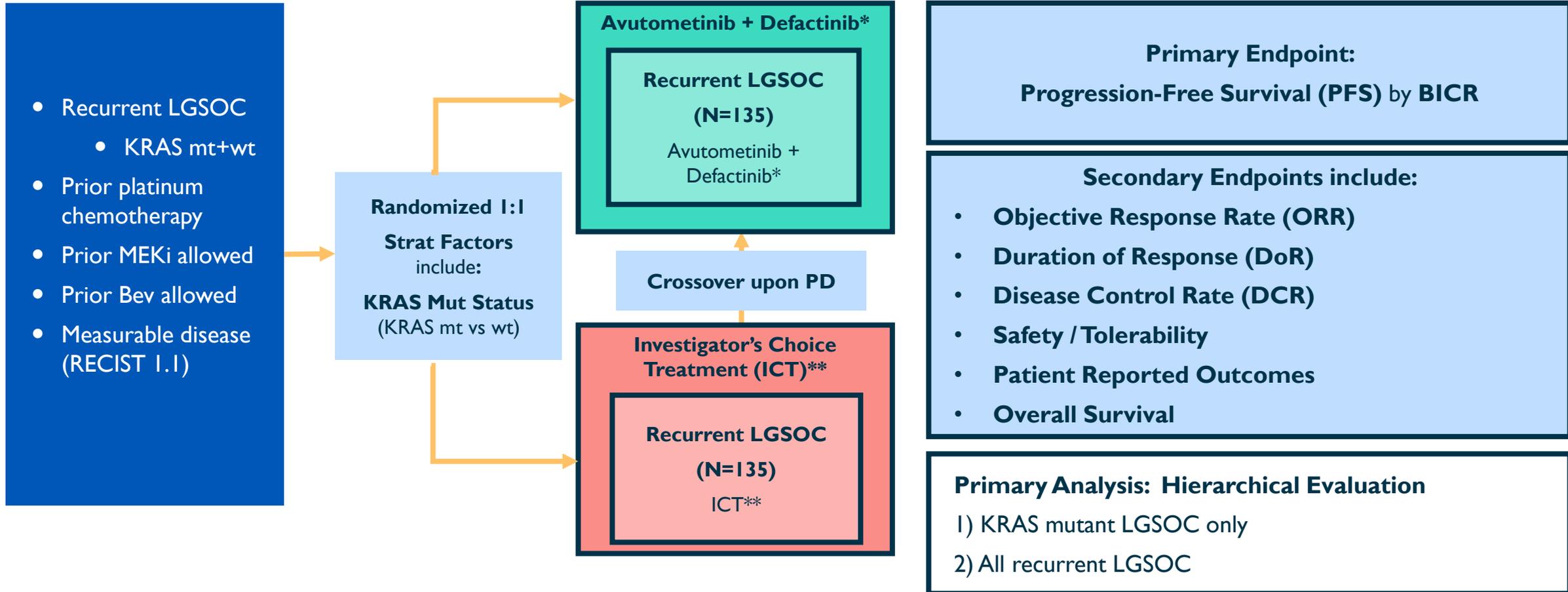
- Majority of adverse events are mild to moderate and manageable/reversible¹
- Few discontinuations due to adverse events (12.3% in combo due to ≥ 1 TEAE 4.9% due to elevated blood CPK*)

* No association to date with clinically significant toxicities, including rhabdomyolysis

Avutometinib + Defactinib (n=81)		
	Any Grade	Grade ≥3
Nausea, n (%)	50 (61.7)	0
Diarrhea, n (%)	40 (49.4)	3 (3.7)
Blood CPK increased, n (%)	39 (48.1)	15 (18.5)
Oedema peripheral, n (%)	34 (42.0)	1 (1.2)
Vomiting, n (%)	30 (37.0)	0
Vision blurred, n (%)	29 (35.8)	0
Dermatitis acneiform, n (%)	28 (34.6)	2 (2.5)
Fatigue, n (%)	27 (33.3)	3 (3.7)
Rash, n (%)	25 (30.9)	2 (2.5)
Dry skin, n (%)	18 (22.2)	0
Anemia, n (%)	14 (17.3)	3 (3.7)

❖ RAMP-301: Avutometinib + Defactinib

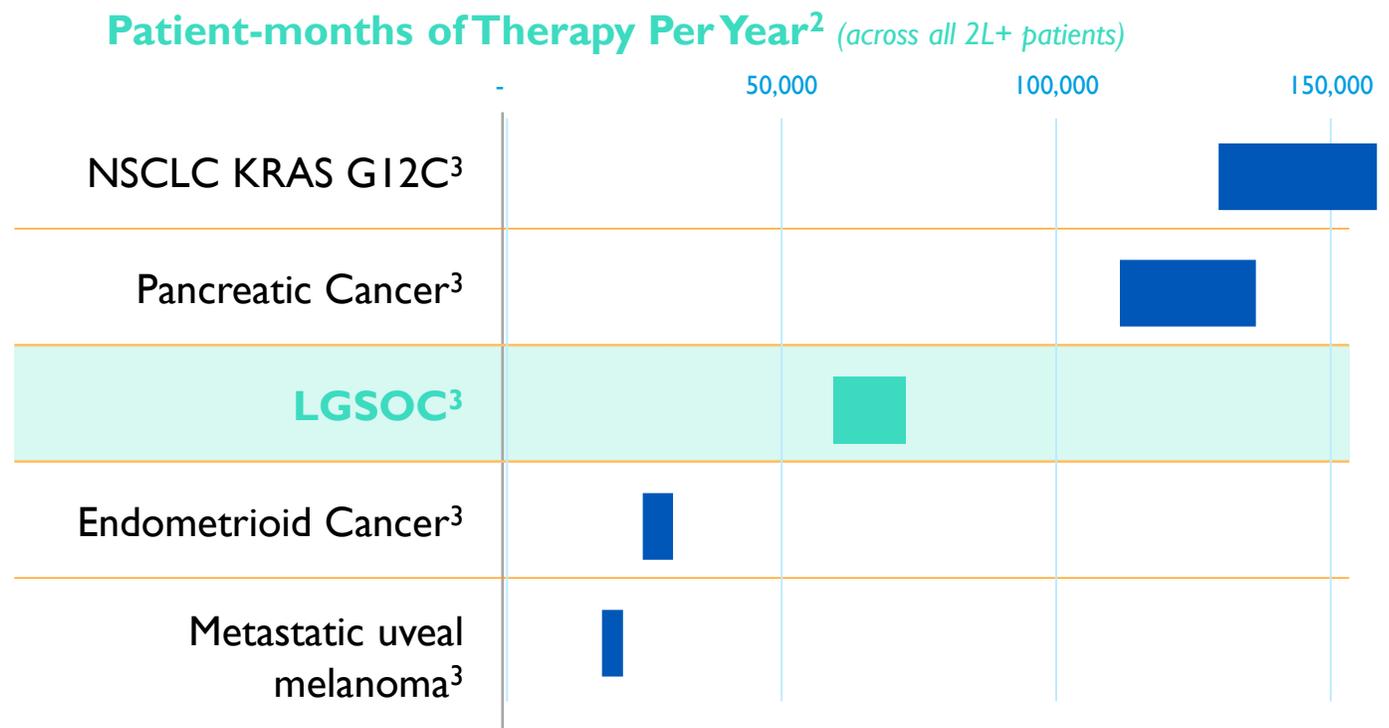
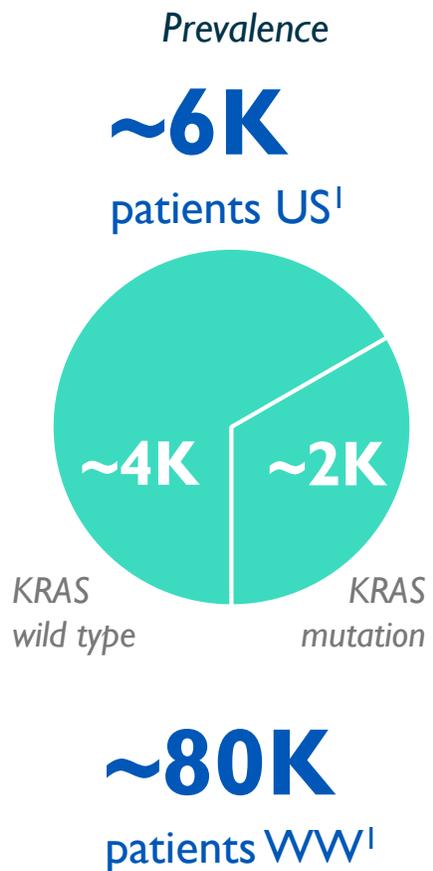
Phase 3 Confirmatory Trial – Randomized Controlled Trial (RCT)



*A+D Dosing: Avutometinib 3.2 mg PO 2x/wk 21/28 days + Defactinib 200mg PO BID: 21/28 days

**Chemo Hormonal ICT: Liposomal doxorubicin (PLD), Paclitaxel, Topotecan, Letrozole, Anastrozole

RAMP 201 Part A Interim Data Support Meaningful Market Potential for All Recurrent LGSOC Regardless of KRAS Status with Long Duration of Therapy



¹ Monk, Randall, Grisham, The Evolving Landscape of Chemotherapy in Newly Diagnosed Advanced Epithelial Ovarian Cancer, Am Soc Clin Oncol Educ Book; 2019; Slomovitz, Gourley, Carey, Malpica, Shih, Huntsman, Fader., Grisham et al, Low-Grade serous ovarian cancer: State of the Science; Gynecol Oncol; 2020. Grisham, Iyer, Low-Grade Serous Ovarian Cancer: Current Treatment Paradigms and Future Directions; Curr Treat Options Oncology; 2018; Globocan 2020

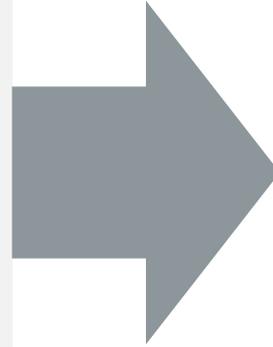
² Patient-months of Therapy metric calculated by multiplying relevant incidence/prevalence rate times estimated duration of therapy; represents US market opportunity only; patient population estimates from Globocan 2020, American Cancer Society 2021, AACR Genie Cohort V9.0 public, and scientific publications. Duration of therapy estimates from clinical studies and clinician experience. Patient-months on therapy is for 2nd-line+ patients

³ NSCLC KRAS G12C 2nd line patients (incidence); Pancreatic RAS/RAF mutant 2nd-line patients (incidence); LGSOC KRAS mutant and wild-type patients (prevalence); Endometrioid RAS/RAF mutant 2nd-line patients (incidence); Uveal melanoma RAS/RAF mutant 2nd-line patients (incidence)

Plan to File for Accelerated Approval with Mature RAMP 201 and FRAME Study Results

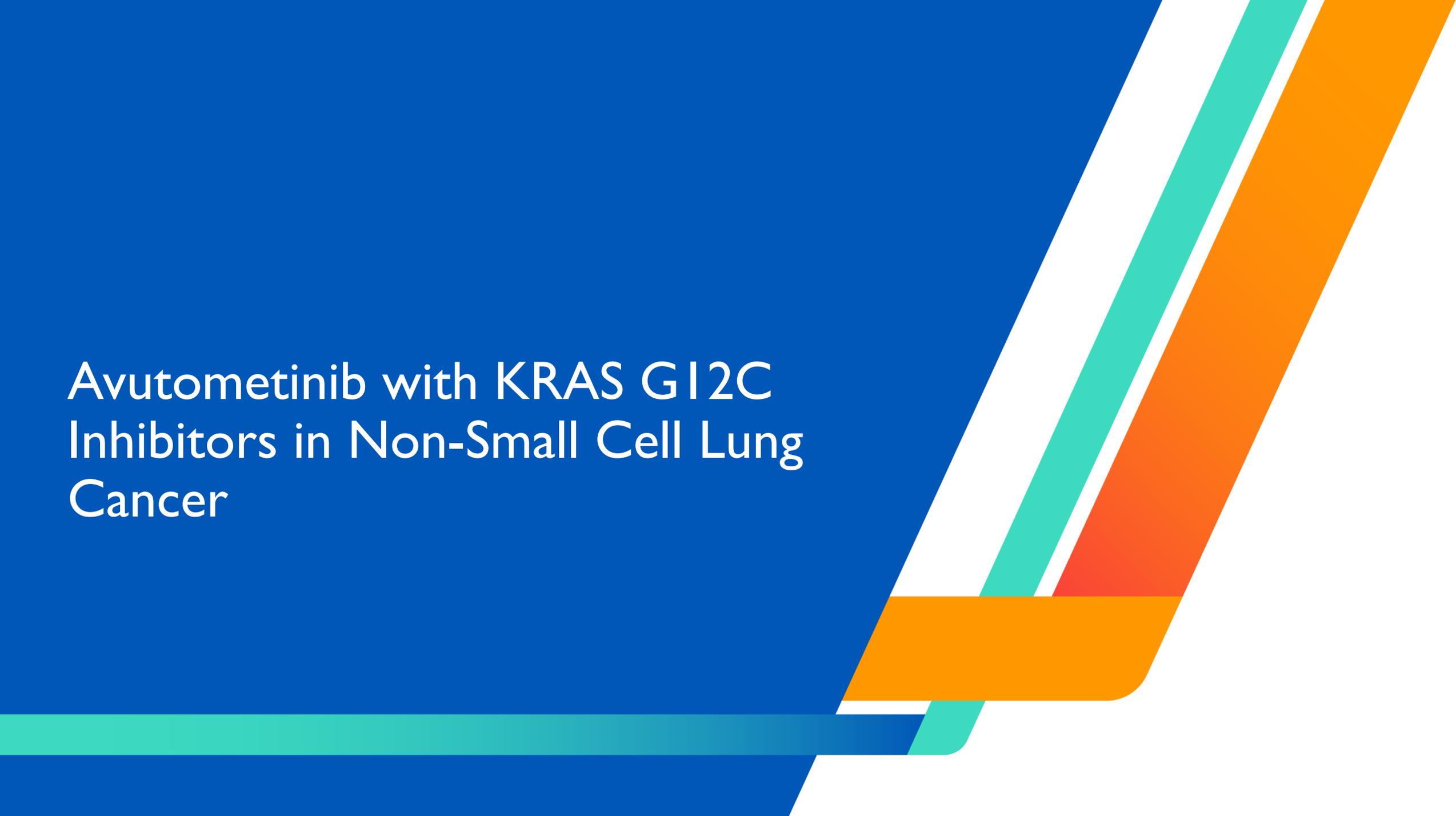
Recent Achievements/Milestones

- Encouraging efficacy results include independently confirmed responses (FRAME study)
- RAMP 201 Part A data at ASCO 2023 demonstrated ORR of 45% (13/29) and tumor shrinkage in 86% (25/29) of evaluable patients
- No new safety signals; few discontinuations due to adverse events
- Initiated RAMP 301, a Phase 3 confirmatory trial
- High unmet need in rare ovarian cancer with no currently FDA approved therapies specifically for recurrent LGSOC
- Received FDA Breakthrough Therapy Designation and Orphan Drug Designation for avutometinib in combination with defactinib in LGSOC



Next Milestones

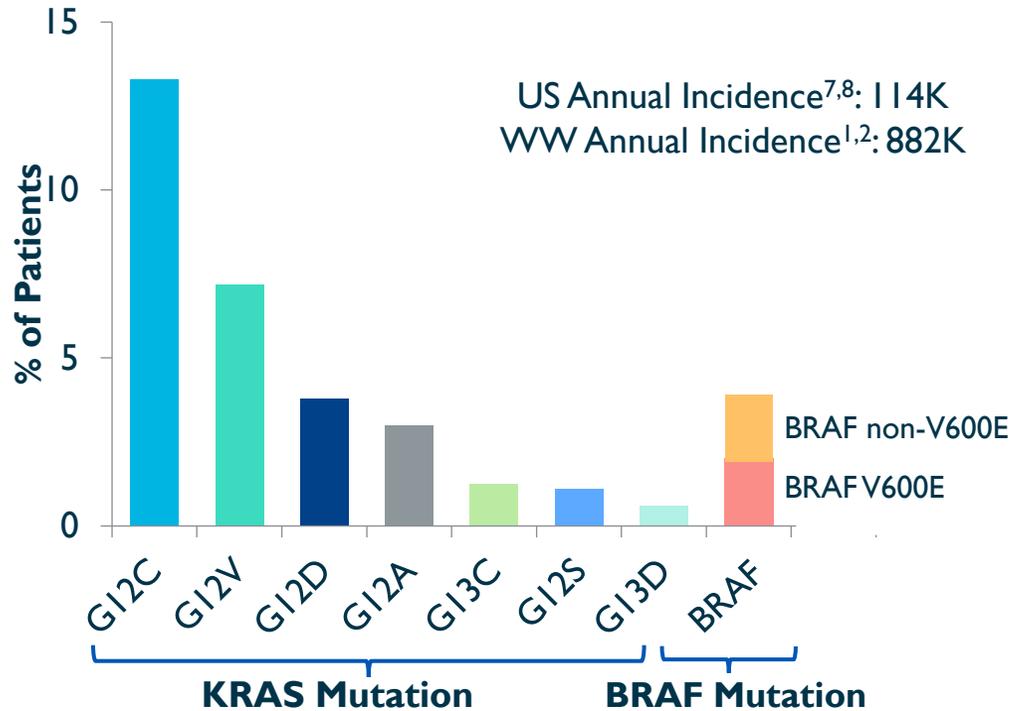
- Plan to file for accelerated approval based on the totality of the data from the RAMP 201 and FRAME studies
- Report updated topline data from RAMP 201 trial in H1 2024
- Continue site activation (sites currently open in US and Australia) and enrollment of RAMP 301, a Phase 3 confirmatory study



Avutometinib with KRAS G12C Inhibitors in Non-Small Cell Lung Cancer

High Unmet Need in Refractory NSCLC Adenocarcinoma

NSCLC Adenocarcinoma³

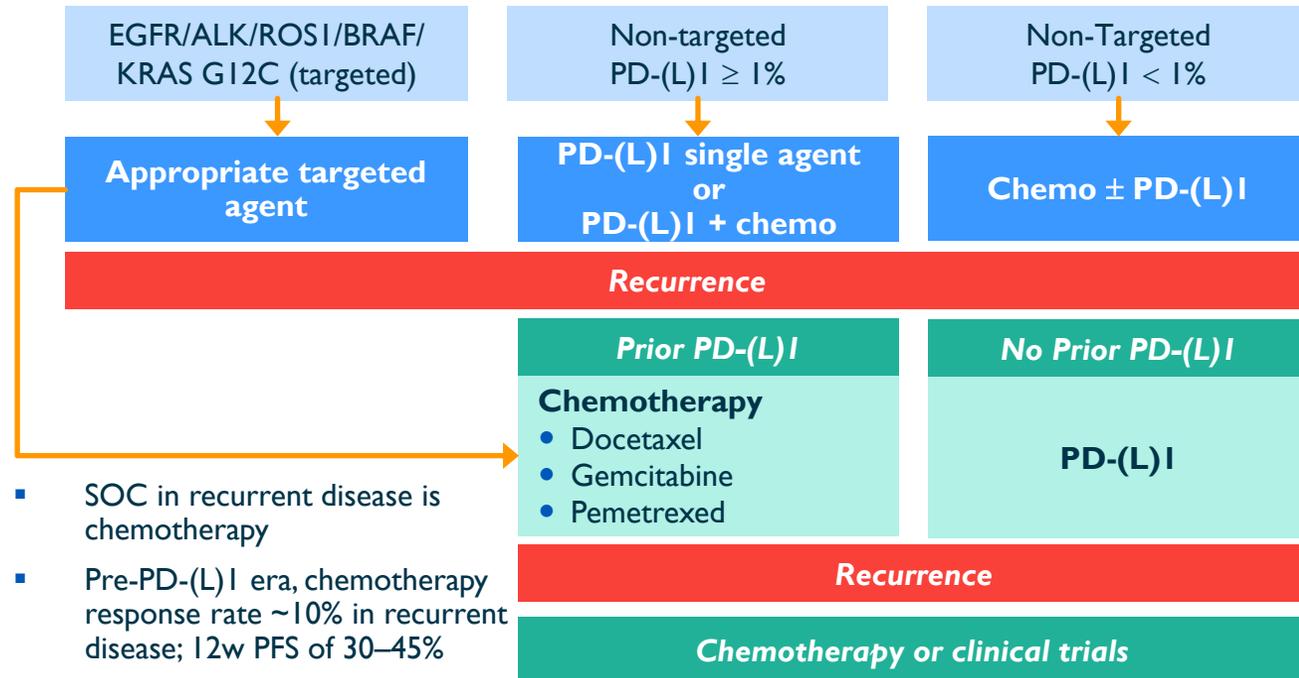


KRAS Mutations Represent 25% of Lung Adenocarcinoma & BRAF Mutations Represent ~4% (EGFR 17%, ALK 7%)^{4,6}

References:

- ¹ Globocan, 2020
- ² <https://www.ncbi.nlm.nih.gov/books/NBK519578/>
- ³ TCGA PanCancer Atlas (cBioPortal analysis)
- ⁴ www.thelancet.com Vol 389 January 21, 2017
- ⁵ Adapted from NCCN Non-small cell lung cancer guidelines Version 3.2020
- ⁶ Clinical Cancer Research DOI 10.1158/1078-0432.CCR-18-2062
- ⁷ 50% of NSCLC is adenocarcinoma (Pakkala and Ramalingam JCI Insight 2018)
- ⁸ Cancer Statistics 2020, Siegel et. al. CA Cancer J Clin 2020;70:7-30

Advanced or Metastatic NSCL Cancer Recommend Histologic and Molecular Subtyping⁵



Verastem Clinical Trials:

- RAMP 203: Avutometinib + sotorasib in KRAS G12C NSCLC
- RAMP 204: Avutometinib + adagrasib in KRAS G12C NSCLC

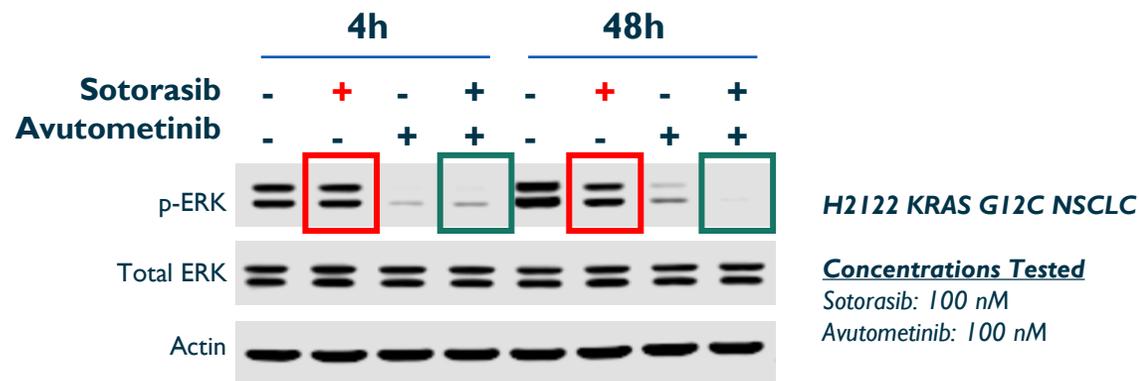
Preclinical Synergy of Avutometinib + G12C Inhibitors in KRAS G12C Models

Synergy of avutometinib + G12C inhibitors across G12C mutant NSCLC, CRC & Pancreatic cancer cell lines

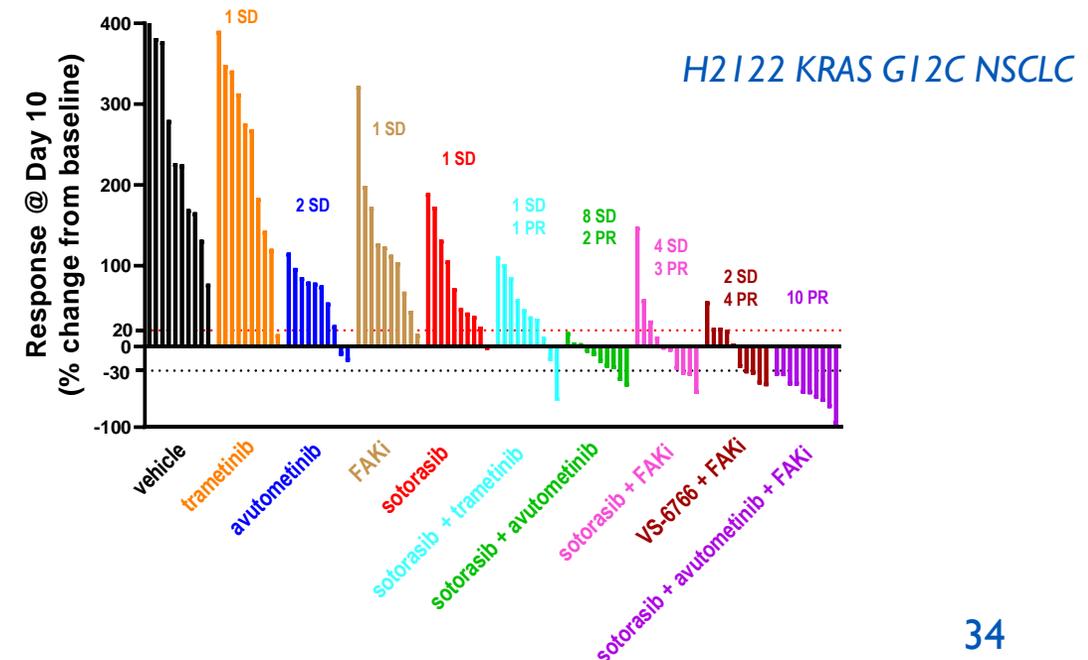
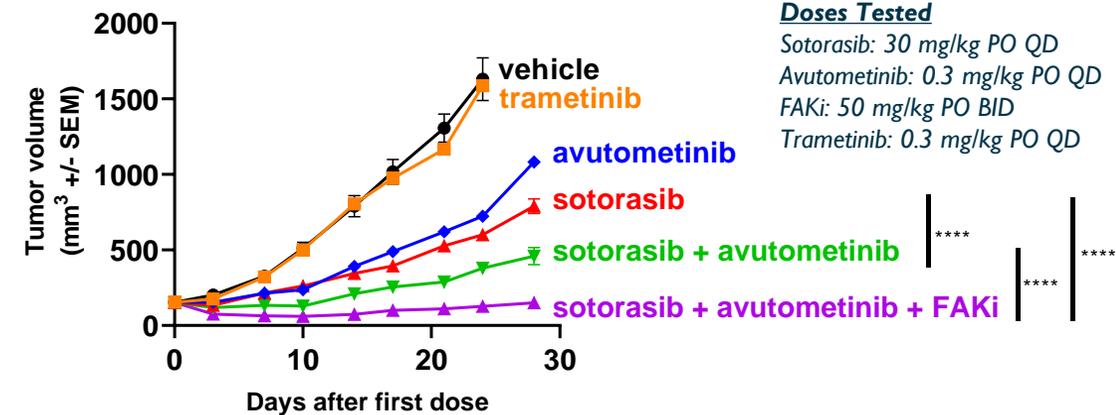
Cell line	Indication	Sensitivity to G12C inhibitors	Combined Synergy Score	
			Avutometinib + sotorasib	Avutometinib + adagrasib
H2122	NSCLC	Moderately sensitive	44.7	44.6
H1373	NSCLC	Sensitive	10.0	3.4
SW1573	NSCLC	Insensitive	8.6	12.0
H358	NSCLC	Sensitive	6.9	5.4
H2030	NSCLC	Moderately sensitive	5.1	ND
SW837	CRC	Sensitive	16.1	18.5
MIAPACA2	Panc	Sensitive	2.3	5.3

ND: not determined

Avutometinib + sotorasib yields deeper and more sustained inhibition of ERK signaling pathway



Avutometinib & FAKi potentiate sotorasib efficacy in KRAS G12C NSCLC in vivo; Tumor regression in all mice with triple combination



Avutometinib ± FAKi Restores Anti-Tumor Efficacy of Sotorasib in G12Ci-Resistant KRAS G12C Models

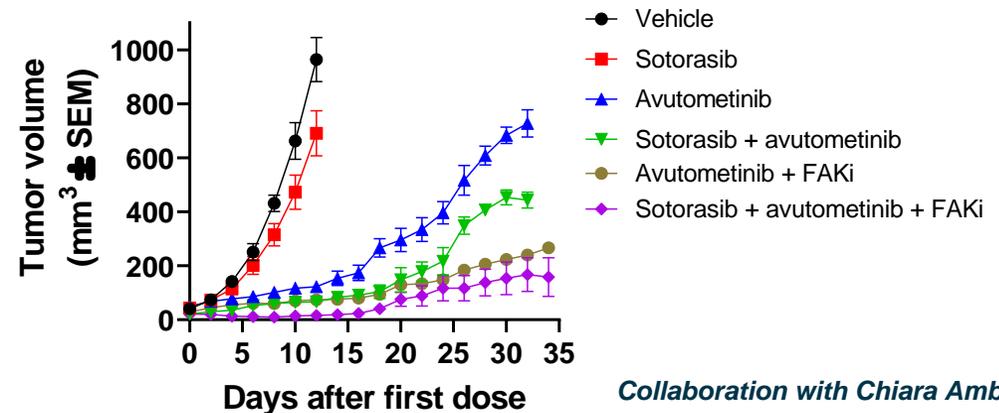
Avutometinib is effective against acquired KRAS mutations that occur clinically upon progression on G12C inhibitors

Cell Line	IC50 (nM)		
	Sotorasib	Adagrasib	Avutometinib
G12C	29	3	14
G12D	435	382	7
G12C/R68S	157	85	13
G12C/H95D	11	235	10
G12C/Y96C	438	216	4
G12C/Y96D	>5000	578	17

<30 nM 30 - 150 nM >150 nM

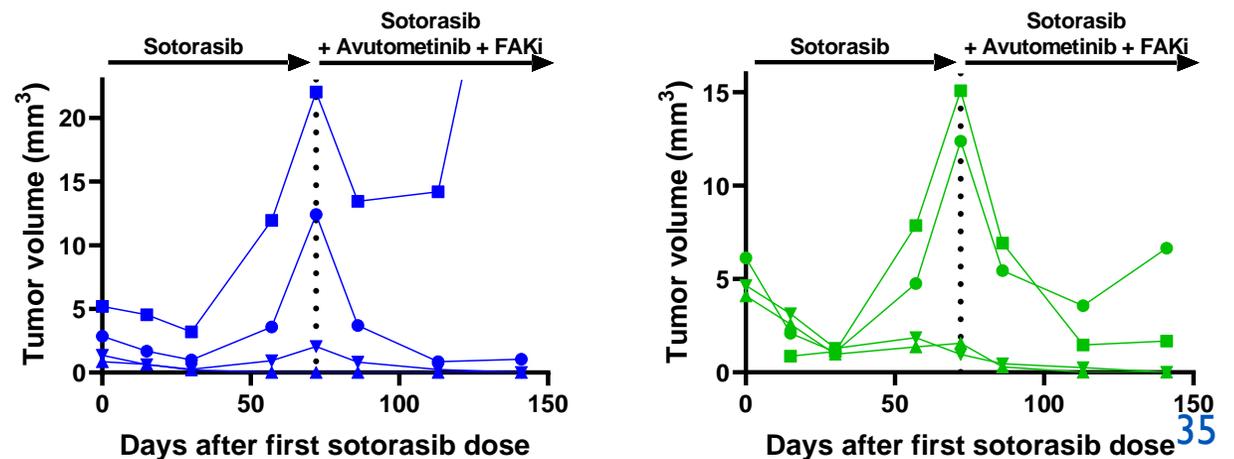
Collaboration with Andy Aguirre, DFCI

Addition of avutometinib + FAK inhibitor to sotorasib increases tumor growth inhibition in a sotorasib-resistant KRAS G12C/Y96D model



Collaboration with Chiara Ambrogio, U Turin (Italy)

Addition of avutometinib + FAKi restores anti-tumor activity after progression on sotorasib monotherapy in a KRAS G12C NSCLC GEMM model



Collaboration with Mariano Barbacid, CNIO (Spain)

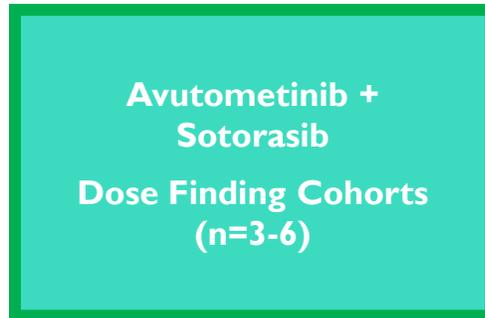
RAMP 203: Phase I/2 Trial of Avutometinib + LUMAKRAS™ (Sotorasib) ± Defactinib in KRAS G12C Advanced NSCLC

- Patients must have a KRAS G12C mutation determined using validated test
- Treatment with at least 1 but no more than 3 prior systemic regimens, for Stage 3B-C or 4 NSCLC*
- Patient may have previously received adjuvant chemotherapy for earlier-stage disease
- Measurable disease according to RECIST 1.1
- ECOG performance status ≤ 1

*may include patients with or without prior G12C therapy

Part A: Dose Evaluation (3+3 DLT Assessment)

Completed enrollment



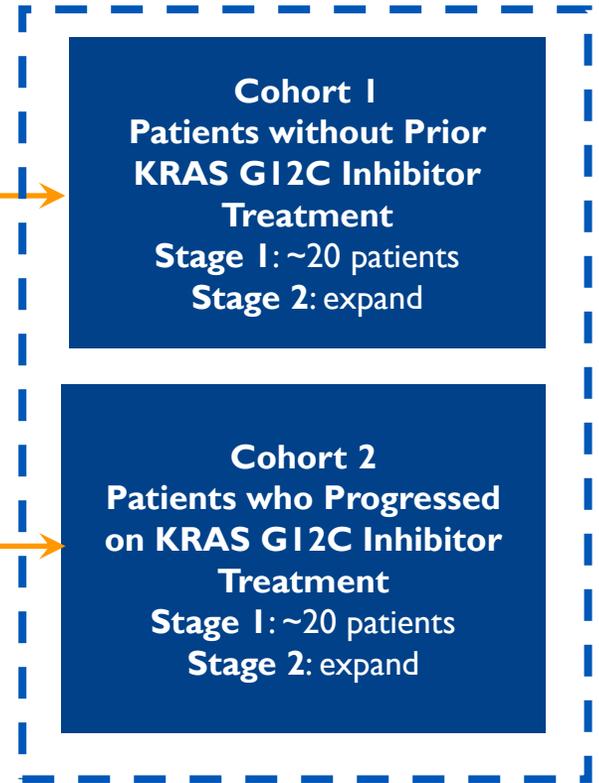
Recently added PART A dose escalation with avutometinib + defactinib + sotorasib



* Recommended Phase 2 Dose (RP2D): 4mg avutometinib / 960mg sotorasib

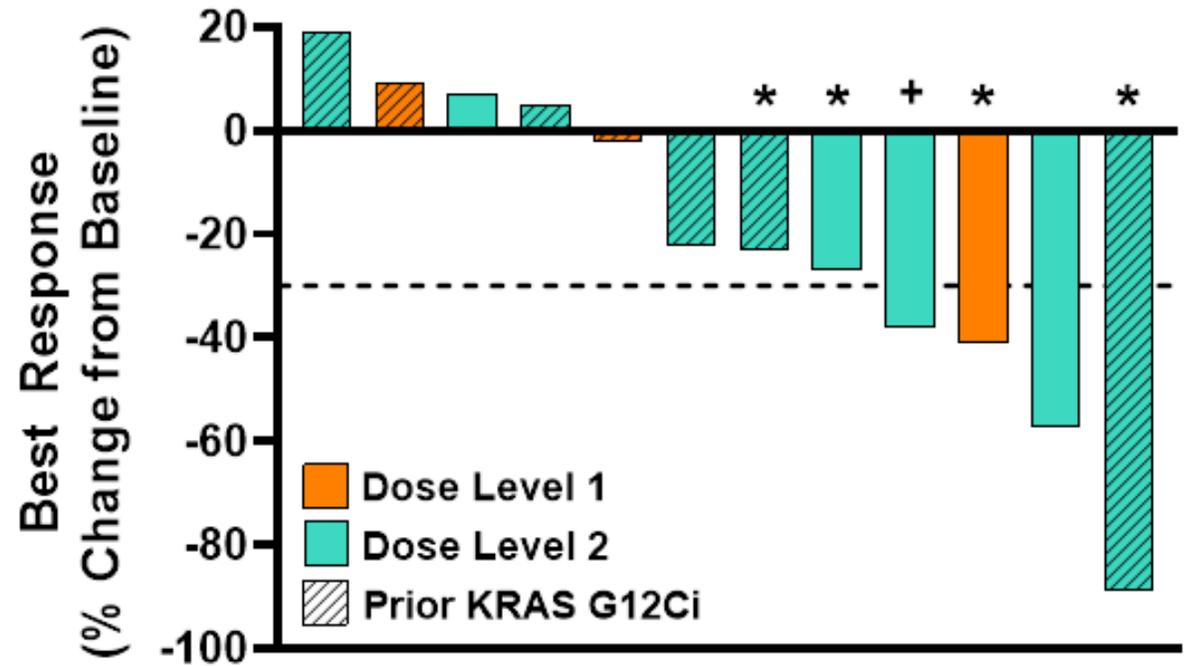
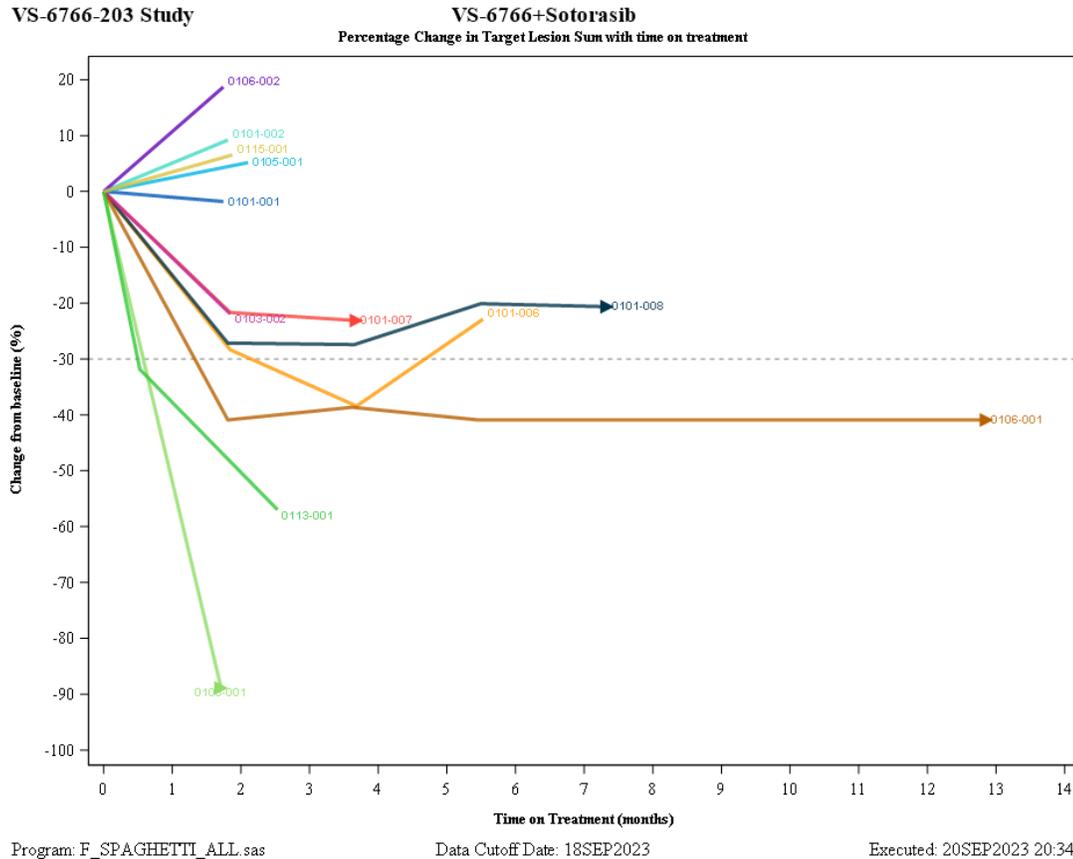
Part B: Dose Expansion at RP2D (Primary endpoint ORR)

Now enrolling expansion phase



NCT05074810

RAMP 203: Objective Responses in KRAS G12C NSCLC Sotorasib + Avutometinib Combination



*On treatment at time of data cutoff; + Patient with -38.4% tumor reduction classified as SD due to disease progression prior to confirmatory scan.

RAMP 204: Phase I/2 Trial of Avutometinib + KRAZATI™ (Adagrasib) in KRAS G12C Advanced NSCLC

- Patients must have a **KRAS G12C** mutation determined using validated test
- Treatment with at least 1 but no more than 3 prior systemic regimens, for Stage 3B-C or 4 NSCLC
- Patient must have received prior therapy with a **KRAS G12C** inhibitor and experience progressive disease
- Measurable disease according to **RECIST 1.1**
- **ECOG** performance status ≤ 1

Part A: Dose Evaluation
(3+3 DLT Assessment)

Part B: Dose Expansion
(Primary endpoint ORR)

Avutometinib +
Adagrasib
Dose Finding Cohorts
(n=3-6)

RP2D
Selection

Stage 1: 19 patients
(including Part A
patients) treated with
RP2D

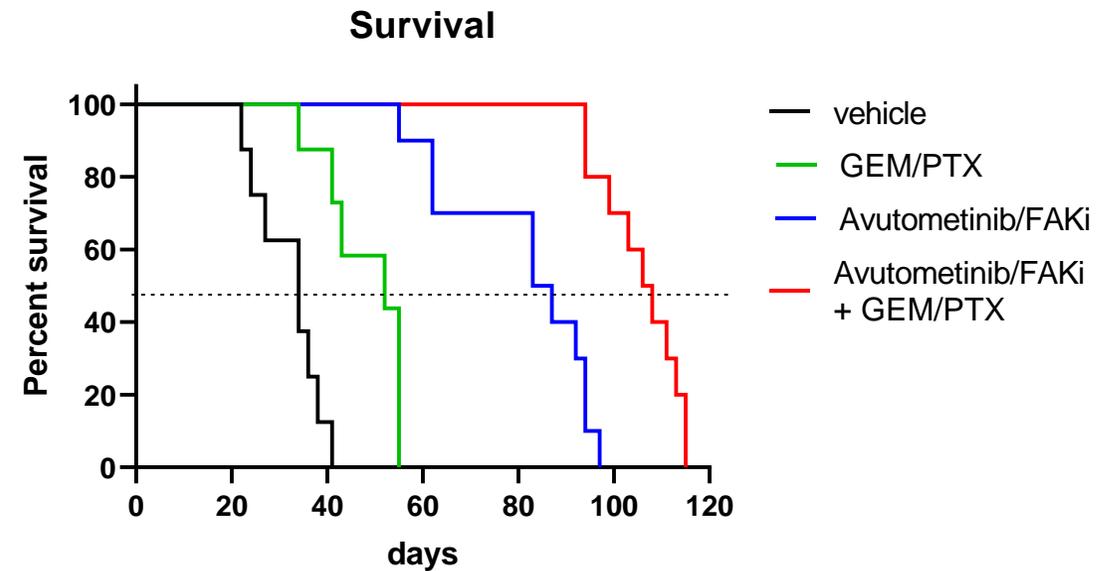
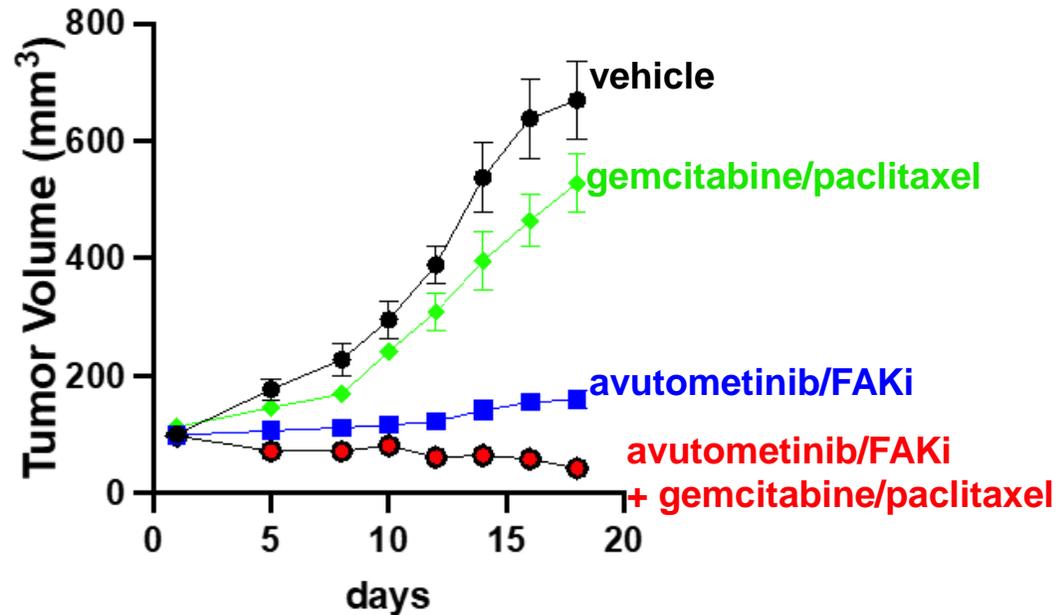
Stage 2: expand to 55
patients

NCT05375994



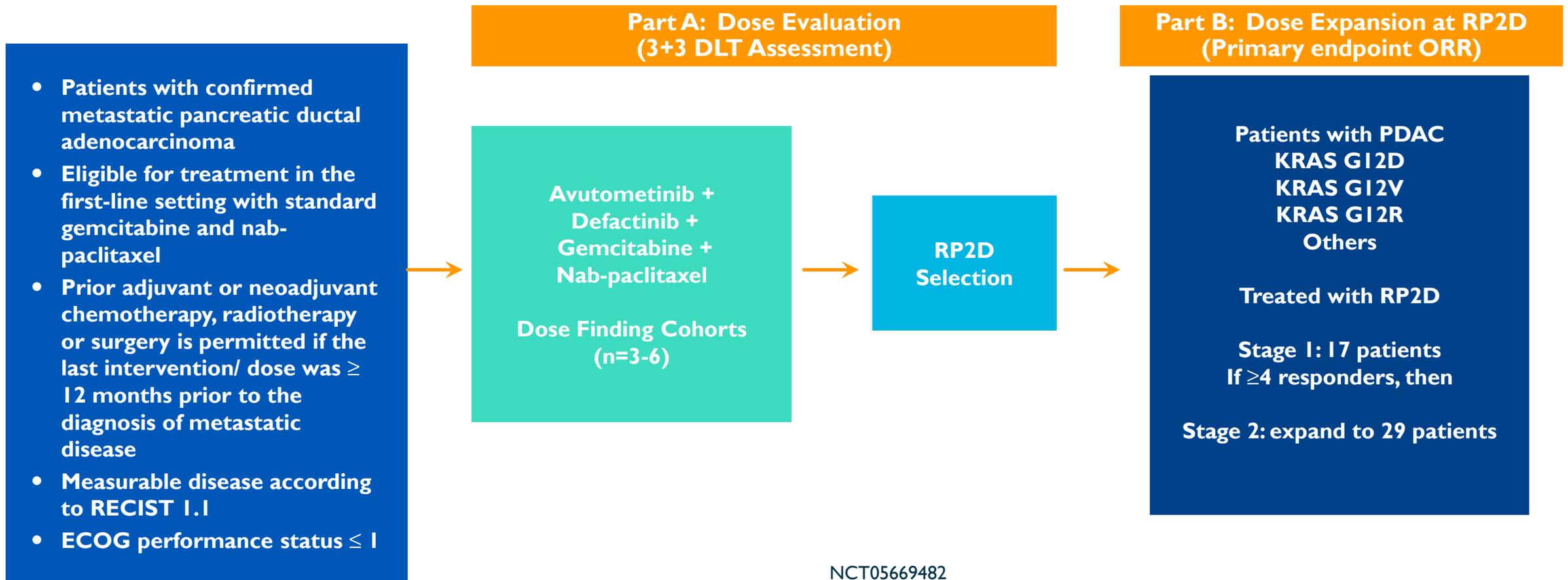
Avutometinib Combinations in Pancreatic Cancer and Colorectal Cancer

Addition of Avutometinib + FAKi to Chemotherapy Induces Tumor Regression and Increases Survival in a KRAS/p53 Pancreatic Cancer Mouse Model



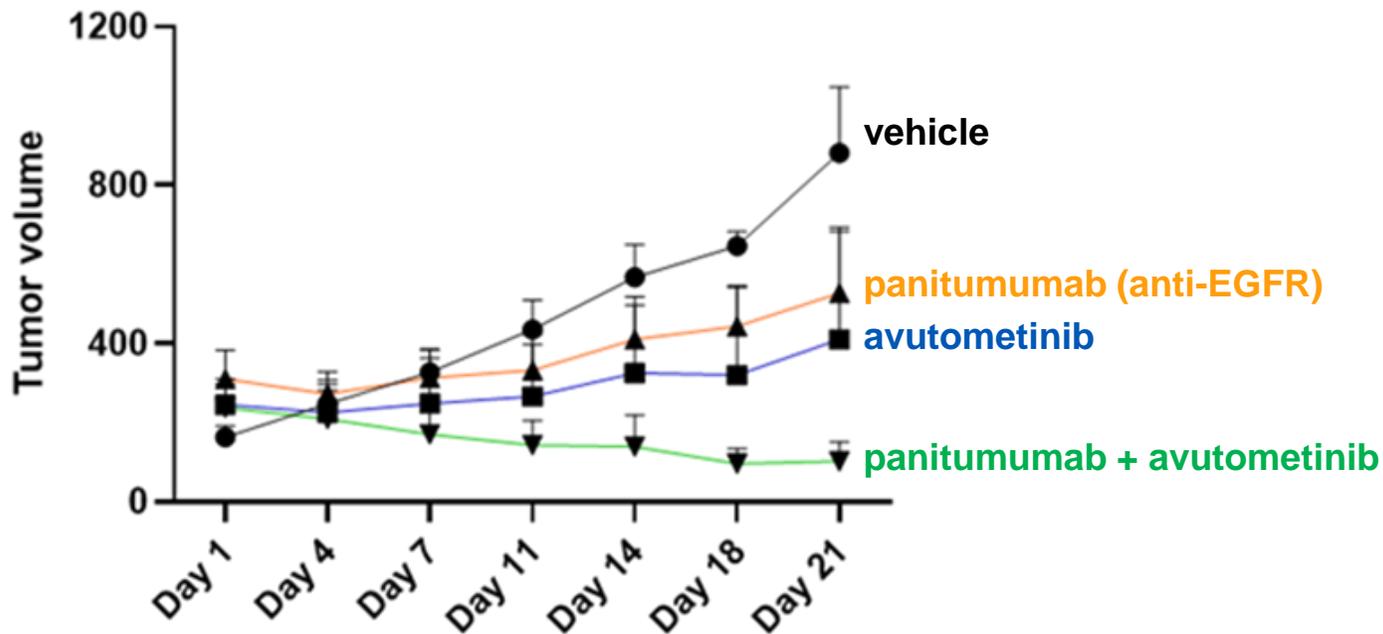
- ✓ The combination of avutometinib + FAKi induces tumor growth inhibition and increases survival but does not induce tumor regression
- ✓ Addition of chemo (gemcitabine + paclitaxel) to avutometinib/FAKi induces tumor regression

RAMP 205: Phase I/2 Trial of Avutometinib/Defactinib + GEMZAR™ (Gemcitabine)/ABRAXANE™ (Nab-paclitaxel) in Front Line Metastatic Pancreatic Cancer



Combination of Avutometinib with anti-EGFR mAb Induces Tumor Regression in a KRAS mt Colorectal PDX Model

KRAS^{G12V} CRC PDX



- Avutometinib + anti-EGFR (panitumumab) induces tumor regression in a KRAS mutant CRC patient-derived xenograft model
- G12Ci + anti-EGFR (sotorasib + panitumumab and adagrasib + cetuximab) have shown partial responses in KRAS G12C CRC (Fakih et al. ESMO 2021; Weiss et al. ESMO 2021)
- **These data support the ongoing clinical evaluation of avutometinib + cetuximab (anti-EGFR) for treatment of KRAS mt CRC (NCT05200442)**

Collaboration with Marwan Fakih, City of Hope

Pachter, RAS Development Summit, 2021

Discovery Efforts

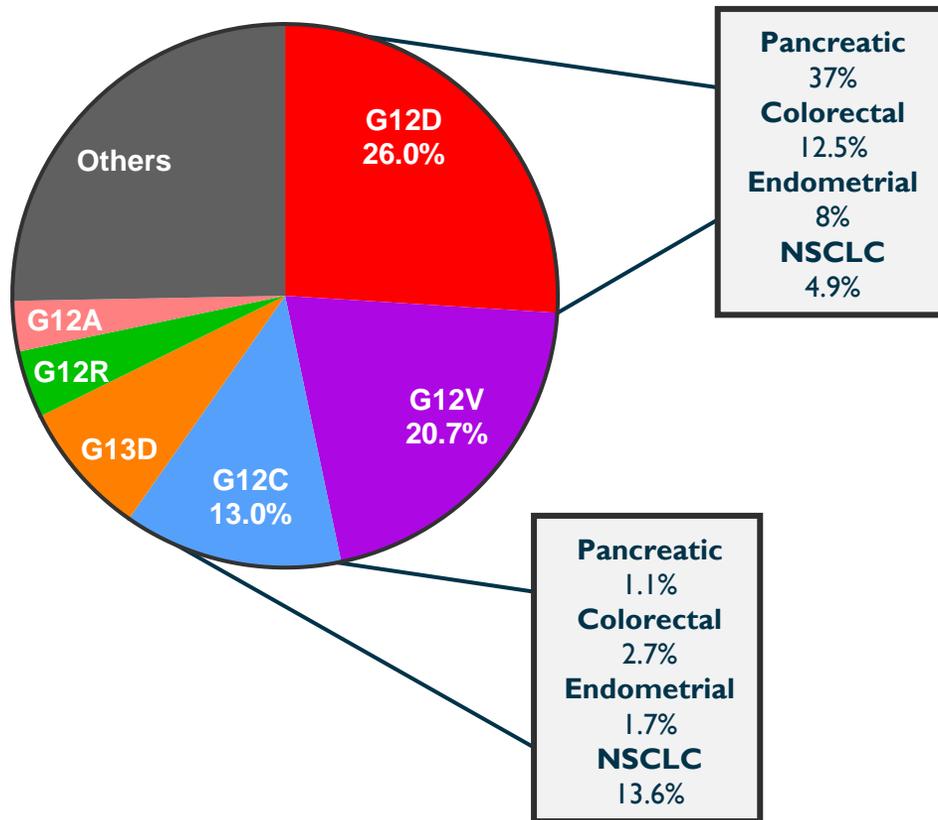
The image features a solid blue background on the left side. On the right side, there are several diagonal stripes in shades of blue, teal, and orange, creating a dynamic, modern look. The stripes are layered, with the orange stripe being the most prominent and extending from the bottom right towards the top right. A horizontal teal stripe runs across the bottom of the image, overlapping the diagonal stripes.

Discovery and Development Collaboration with GenFleet Strengthens Pipeline Targeting RAS Pathway-Driven Cancers

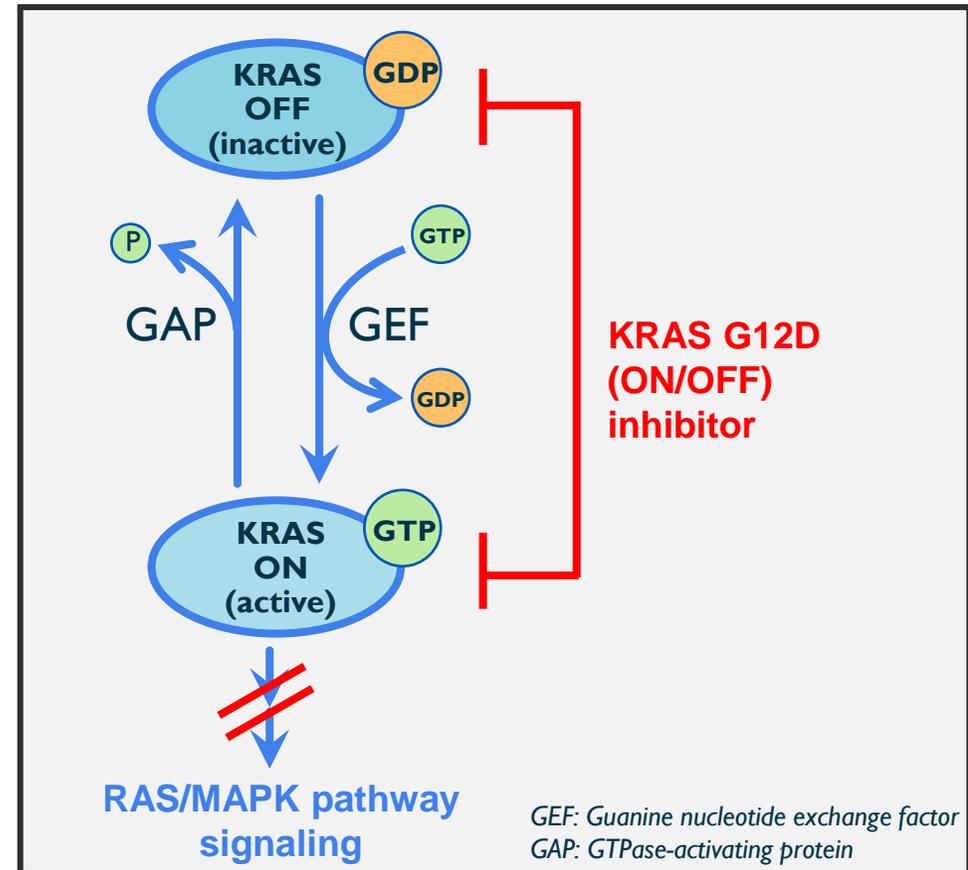
- Increases the breadth of Verastem's oncology pipeline with strategically-aligned RAS pathway focus
 - Exclusive options for Verastem to exclusively license up to 3 programs with development and commercialization rights outside of the GenFleet markets of mainland China, Hong Kong, Macau, and Taiwan
 - Potential development in combination with Verastem's current pipeline
 - Selected GFH375 (VS-7375), an oral KRAS G12D (ON/OFF) inhibitor as lead program; programs 2 & 3 in discovery phase
 - Small molecule programs focused on anti-cancer targets related to the RAS/MAPK pathway or surrounding cancer cell signaling
- Strategic collaboration builds on Verastem Oncology and GenFleet's experience in RAS pathway-driven cancers
 - Collective worldwide strengths in RAS pathway discovery and development
 - Established network of collaborators, including leading scientific and clinical experts
 - Leverages experience from GenFleet's KRAS G12C inhibitor program and Verastem's avutometinib/defactinib program
- Risk-sharing structure of the collaboration with milestone-based options provides capital efficient approach
 - At execution, Verastem paid GenFleet an upfront payment for options to obtain exclusive right to 3 programs on a program by program basis
 - Combined with the upfront amount, payments for future annual R&D support, development milestones and option payment for first program through completion of Phase I trial could equal up to \$11.5 million
 - Potential total deal size across all 3 programs up to \$625.5 million excluding royalties if Verastem exercises its in-license options
 - Includes exclusive rights for Verastem to obtain a license to each of the compounds after successful completion of pre-determined milestones in Phase I trials

Rationale for Designing a Potent and Selective Orally Bioavailable Inhibitor of KRAS G12D (ON/OFF) for the Treatment of Patients with KRAS G12D Cancers

KRAS G12D is the most frequent KRAS mutation in human cancer



Ideal to inhibit both the active (ON) & inactive (OFF) states of KRAS for deep and durable inhibition of tumor growth



GFH375 (VS-7375) is an Oral KRAS G12D (ON/OFF) Inhibitor

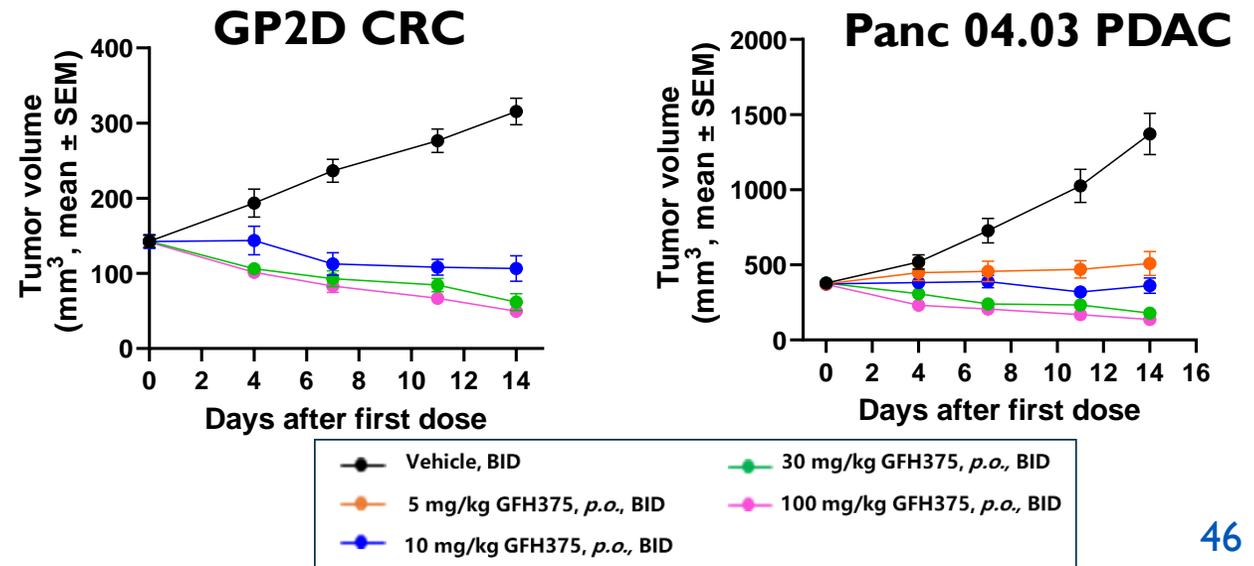
First program from the GenFleet collaboration

- GFH375 (VS-7375) is a potent and selective orally bioavailable inhibitor of KRAS G12D (ON/OFF) with potent anti-tumor efficacy demonstrated across preclinical models
- Dual inhibitor of ON (GTP) and OFF (GDP) states of KRAS G12D
- Orally bioavailable across preclinical species
- Potent against intracranial tumor models suggesting potential to treat brain metastases
- Avutometinib enhances anti-tumor efficacy of GFH375 (VS-7375) in preclinical models
- IND-enabling GLP toxicology studies complete
- IND application filed in China and accepted for review; upon clearance expect to initiate Phase I trial in China in H2 2024

Dual inhibitor of ON (GTP) and OFF (GDP) states of KRAS G12D

KRAS G12D State	GFH375 IC50 (nM) (KRAS G12D binding)
GppNp-bound (ON/active)	2 ± 1
GDP-bound (OFF/inactive)	6 ± 1

Potent anti-tumor efficacy demonstrated across preclinical models



Financials

The image features a solid blue background on the left side. On the right side, there are several overlapping diagonal stripes in shades of teal and orange. A horizontal teal bar is positioned at the bottom, overlapping the diagonal stripes. The overall design is modern and minimalist.

Key Financial Statistics

As of and for the quarter ended December 31, 2023

Cash, cash equivalents & investments	\$137.1M
GAAP Operating Expenses	\$31.1M
Non-GAAP Operating Expenses*	\$29.5M
Shares Outstanding	25.3M**

Sources of Non-Dilutive Capital

- **Oxford Finance LLC Credit Facility**
 - Up to \$150M available in a series of term loans
 - \$40M term loans outstanding
 - Remaining \$110M available upon achievement of pre-defined milestones or at lender's discretion
 - Floating interest rate, subject to a floor and a cap; 5% final payment charge, and loan subject to 1-3% early payment fee
 - Interest only payments through April 2025
 - No financial covenants
- **Secura Bio, Inc. (Secura) Asset Purchase Agreement – COPIKTRA**
 - Regulatory and commercial milestone payments up to \$95M
 - Entitled to receive 50% of royalties, milestones, and sublicensee revenue payments made to Secura related to COPIKTRA
 - Low double-digit royalties on annual net sales over \$100M in US, EU, and UK

Avutometinib Patent Exclusivity

Composition of Matter

→ PTE → Feb 2027 + 5 yrs (PTE) = 2032

Method of Making

→ Sept 2032

Dosing Protocol

→ May 2038

Combination w/ Defactinib

→ Sept 2040

Solid Form

→ Dec 2042

Methods or Treating; Combinations

→ 2041 - 2042 if issued

Experienced Senior Management Team



Daniel Paterson
President and Chief Executive Officer

- CEO – The DNA Repair Co. (now On-Q-ity)
- PharMetrics (now IMS), Axion



Dan Calkins
Chief Financial Officer

- Technical Accounting Consultant- CFGI
- PwC LLP



Cathy Carew
Chief Organizational Effectiveness Officer

- Principal – HR Collaborative
- Ironwood, ActiveBiotics, Dynogen, Tufts Health Plan



Mike Crowther
Chief Commercial and Business Strategy Officer

- CBO, Minerva Biotechnologies
- Interim US lead and VP of US Marketing, Kite Pharma
- Celgene



Jonathan Pachter, Ph.D.
Chief Scientific Officer

- Head of Cancer Biology – OSI (now Astellas)
- Schering-Plough



Hagop Youssoufian, MSc, M.D.
Head of Medical Strategy

- CMO, BIND Therapeutics, EVP, Progenics,
- CMO & EVP, Ziopharm Oncology, SVP, Imclone



THANK YOU