



Delivering Novel Therapies in RAS/MAPK Pathway Driven Cancers

May 2024

Corporate Presentation



Disclaimers

Forward-Looking Statements

This presentation includes forward-looking statements about, among other things, Verastem Oncology's (the "Company") programs and product candidates, strategy, future plans and prospects, including statements related to the timing of the planned rolling New Drug Application (NDA) submission for the avutometinib and defactinib combination in low-grade serous ovarian cancer (LGSOC) the expected outcome and benefits of collaborations, including with GenFleet Therapeutics (Shanghai), Inc. (GenFleet), the potential clinical value of various of the Company's clinical trials, including the RAMP 201, RAMP 205 and RAMP 301 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 the Company's lead compound and the potential market opportunities of our drug candidates. 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.

Applicable risks and uncertainties include the risks and uncertainties, among other things, regarding: the success in the development and potential commercialization of our product candidates, including avutometinib in combination with other compounds, including defactinib, LUMAKRAS™ and others; the uncertainties inherent in research and development, such as negative or unexpected results of clinical trials, the occurrence or timing of applications for our product candidates that may be filed with regulatory authorities in any jurisdictions; whether and when regulatory authorities in any jurisdictions may approve any such applications that may be filed for our product candidates, and, if approved, whether our product candidates will be commercially successful in such jurisdictions; our ability to obtain, maintain and enforce patent and other intellectual property protection for our product candidates; the scope, timing, and outcome of any legal proceedings; decisions by regulatory authorities regarding trial design, labeling and other matters that could affect the timing, availability or commercial potential of our product candidates; whether preclinical testing of our product candidates and preliminary or interim data from clinical trials will be predictive of the results or success of ongoing or later clinical trials; that the timing, scope and rate of reimbursement for our product candidates is uncertain; the market opportunities of our drug candidates are based on internal and third-party estimates which may prove to be incorrect; that third-party payors (including government agencies) may not reimburse; that there may be competitive developments affecting our product candidates; that data may not be available when expected; that enrollment of clinical trials may take longer than expected, which may delay our development programs, including delays in submission or review by the FDA of our NDA submission in recurrent KRAS mutant LGSOC if enrollment in our confirmatory trial is not well underway at the time of submission; that our product candidates will cause adverse safety events and/or unexpected concerns may arise from additional data or analysis, or result in unmanageable safety profiles as compared to their levels of efficacy; that we may be unable to successfully validate, develop and obtain regulatory approval for companion diagnostic tests for our product candidates that require or would commercially benefit from such tests, or experience significant delays in doing so; that our product candidates may experience manufacturing or supply interruptions or failures; that any of our third-party contract research organizations, contract manufacturing organizations, clinical sites, or contractors, among others, who we rely on fail to fully perform; that we face substantial competition, which may result in others developing or commercializing products before or more successfully than we do which could result in reduced market share or market potential for our product candidates; that we will be unable to successfully initiate or complete the clinical development and eventual commercialization of our product candidates; that the development and commercialization of our product candidates will take longer or cost more than planned, including as a result of conducting additional studies; that we may not have sufficient cash to fund our contemplated operations; that we may not attract and retain high quality personnel; that we or Chugai Pharmaceutical Co., Ltd. will fail to fully perform under the avutometinib license agreement; that our target market for our product candidates might be smaller than we are presently estimating; that Secura Bio, Inc. will fail to fully perform under the asset purchase agreement with Secura Bio, Inc., including in relation to milestone payments; that we will not see a return on investment on the payments we have and may continue to make pursuant to the collaboration and option agreement with GenFleet or that GenFleet will fail to fully perform under the agreement; that we may be unable to obtain adequate financing in the future through product licensing, co-promotional arrangements, public or private equity, debt financing or otherwise; that we will not pursue or submit regulatory filings for our product candidates; and that our product candidates will not receive regulatory approval, become commercially successful products, or result in new treatment options being offered to patients.

Other risks and uncertainties include those identified under the heading "Risk Factors" in the Company's Annual Report on Form 10-K for the year ended December 31, 2023, as filed with the Securities and Exchange Commission (SEC) on March 14, 2024, and in any subsequent filings with the SEC, which are available at www.sec.gov and www.verastem.com.

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Verastem Oncology

*Positioned to deliver on
potential 2024 catalysts*

➤ **Potential to be the first approved therapy in LGSOC**

- Topline data from RAMP 201 evaluating avutometinib, a RAF/MEK Clamp in combination with defactinib, a FAK inhibitor, have continued to demonstrate robust responses in patients with recurrent low-grade serous ovarian cancer (LGSOC)
- Initiating rolling NDA for Accelerated Approval in recurrent KRAS mt LGSOC in Q2 2024; anticipated to be completed in H2 2024
- Phase 3 confirmatory study underway with site activations and patient enrollment ongoing in US, Australia, and UK and enrollment planned in Canada, Europe, and South Korea

➤ **Encouraging initial interim data in first-line metastatic pancreatic cancer**

- RAMP 205 study ongoing to evaluate additional dose/schedule combinations of avutometinib + defactinib + gemcitabine + Nab-paclitaxel in first-line metastatic pancreatic cancer

➤ **Ongoing studies in additional indications including NSCLC**

- Expect to report updated interim data from RAMP 203 non-small cell lung cancer (NSCLC) trial evaluating avutometinib plus defactinib with Amgen's KRAS G12C inhibitor, sotorasib, expected in H2 2024
- Expect to report initial interim data from RAMP 204 NSCLC trial evaluating avutometinib with Mirati Therapeutics (Bristol Myers Squibb (BMS)) KRAS G12C inhibitor, adagrasib, expected in H2 2024

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

- GenFleet's IND application for GFH375/VS-7375, an oral KRAS G12D (ON/OFF) inhibitor, was filed in China and accepted for review
- GenFleet expects to initiate Phase I trial for GFH375/VS-7375 in China in H2 2024
- Ongoing discovery/lead optimization for second and third programs

➤ **Balance sheet supports ongoing programs and operations**

- Company ended Q1 2024 with \$110.1M in cash and investments and \$28.1M GAAP operating expenses (\$26.6M non-GAAP operating expenses*)

*Q1 2024 GAAP operating expenses of \$28.06M less Q1 2024 stock-based compensation expense of \$1.48M = \$26.58M Q1 2024 non-GAAP operating expenses;

IND: investigational new drug; NDA: new drug application; RAS: Rat sarcoma; KRAS: Kirsten Rat Sarcoma virus; MAPK: Mitogen-Activated Protein Kinase; RAF: Rapidly Accelerated Fibrosarcoma; MEK: Mitogen-activated extracellular signal-regulated kinase

Clinical Program Designed to Address LGSOC and Beyond

Trial/Regimen	IND-Enabling/ Preclinical	Phase 1	Phase 2	Phase 3	Anticipated Milestones	Collaboration
Avutometinib + Defactinib: Recurrent LGSOC						
RAMP 301 RAF/MEK Clamp + FAKi vs ICT					RAMP 301 Ongoing Enrollment RAMP 201 Mature Dataset Expected to be presented at a Medical Meeting in 2H 2024; Initiate Rolling NDA Submission in Recurrent KRAS mt LGSOC Seeking Accelerated Approval: Q2 2024	
RAMP 201 RAF/MEK Clamp + FAKi						
Avutometinib ± Defactinib + KRAS G12C Inhibitors: mKRAS G12C NSCLC						
RAMP 203 RAF/MEK Clamp ± FAKi + KRAS G12Ci (sotorasib)					RAMP 203 Updated Interim Data: H2 2024	Amgen
RAMP 204 RAF/MEK Clamp + KRAS G12Ci (adagrasib)					RAMP 204 Initial Interim Data: H2 2024	Mirati (BMS)
Avutometinib + Defactinib + Chemotherapy: 1L Metastatic Pancreatic Cancer						
RAMP 205 RAF/MEK Clamp + FAKi + gemcitabine, nab-paclitaxel					RAMP 205 Initial Interim Safety & Efficacy Data at ASCO 2024	PanCAN
GFH375/VS-7375						
KRAS G12D (ON/OFF) inhibitor					IND filed in China and accepted for review; upon clearance expect to initiate Phase 1 in China in H2 2024	GenFleet



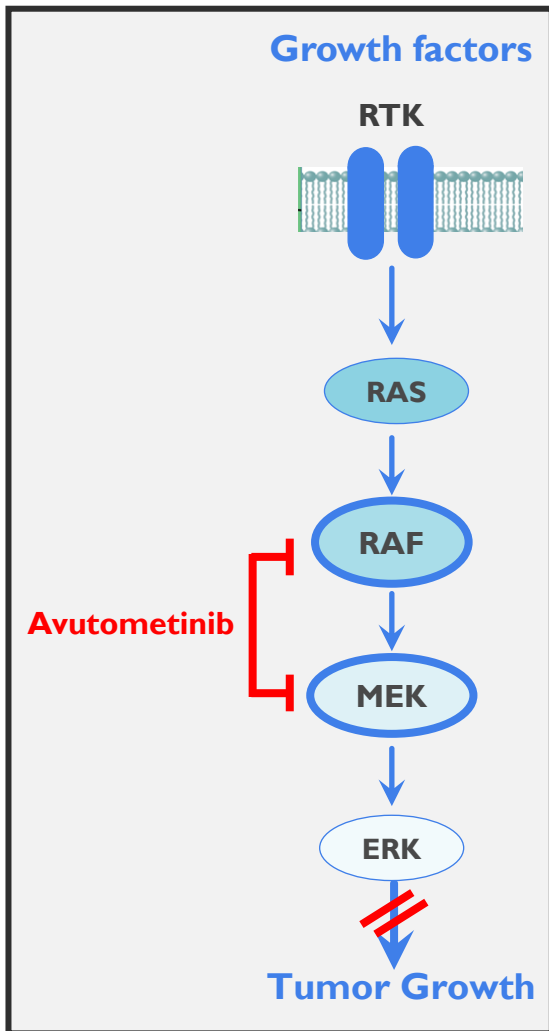
Avutometinib, RAF/MEK Clamp Program Overview

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

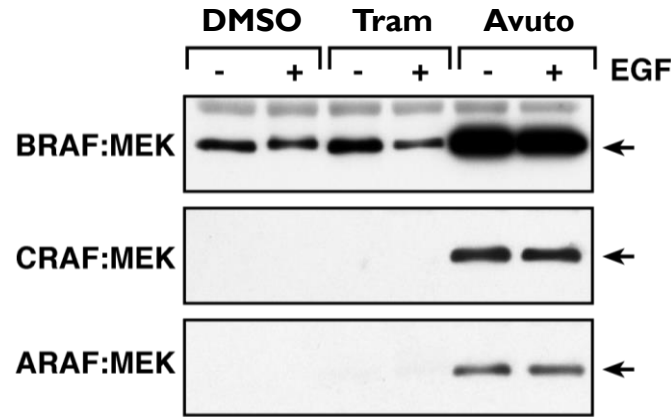
- Differentiated investigational RAF/MEK clamp mechanism of action
- Novel intermittent dosing schedule; convenient oral regimen
- Orphan Drug Designation for avutometinib alone or in combination with defactinib in recurrent LGSOC
- Breakthrough Therapy Designation for combination of avutometinib and 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-mutated metastatic NSCLC
- FDA Fast Track Designation granted for avutometinib plus defactinib in combination with sotorasib for the treatment of KRAS G12C-mutated metastatic NSCLC
- FDA Fast Track Designation granted for avutometinib in combination with Mirati's (BMS) G12C inhibitor adagrasib in KRAS G12C-mutated metastatic 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 Differentiated Small Molecule RAF/MEK Clamp

Contrasting Mechanism of Action vs. MEK-Only Inhibitors

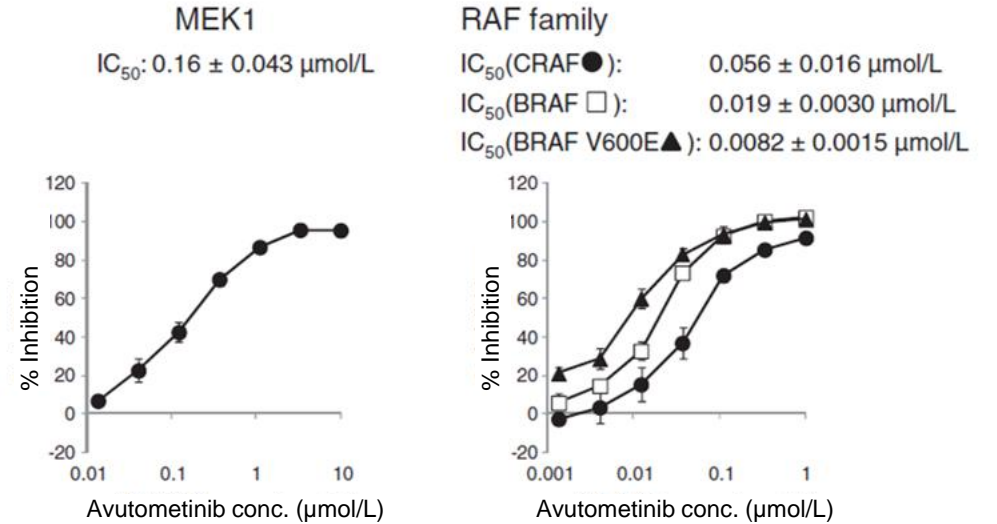


Avutometinib induces dominant negative RAF/MEK complexes



Collaboration with Deborah Morrison, NCI

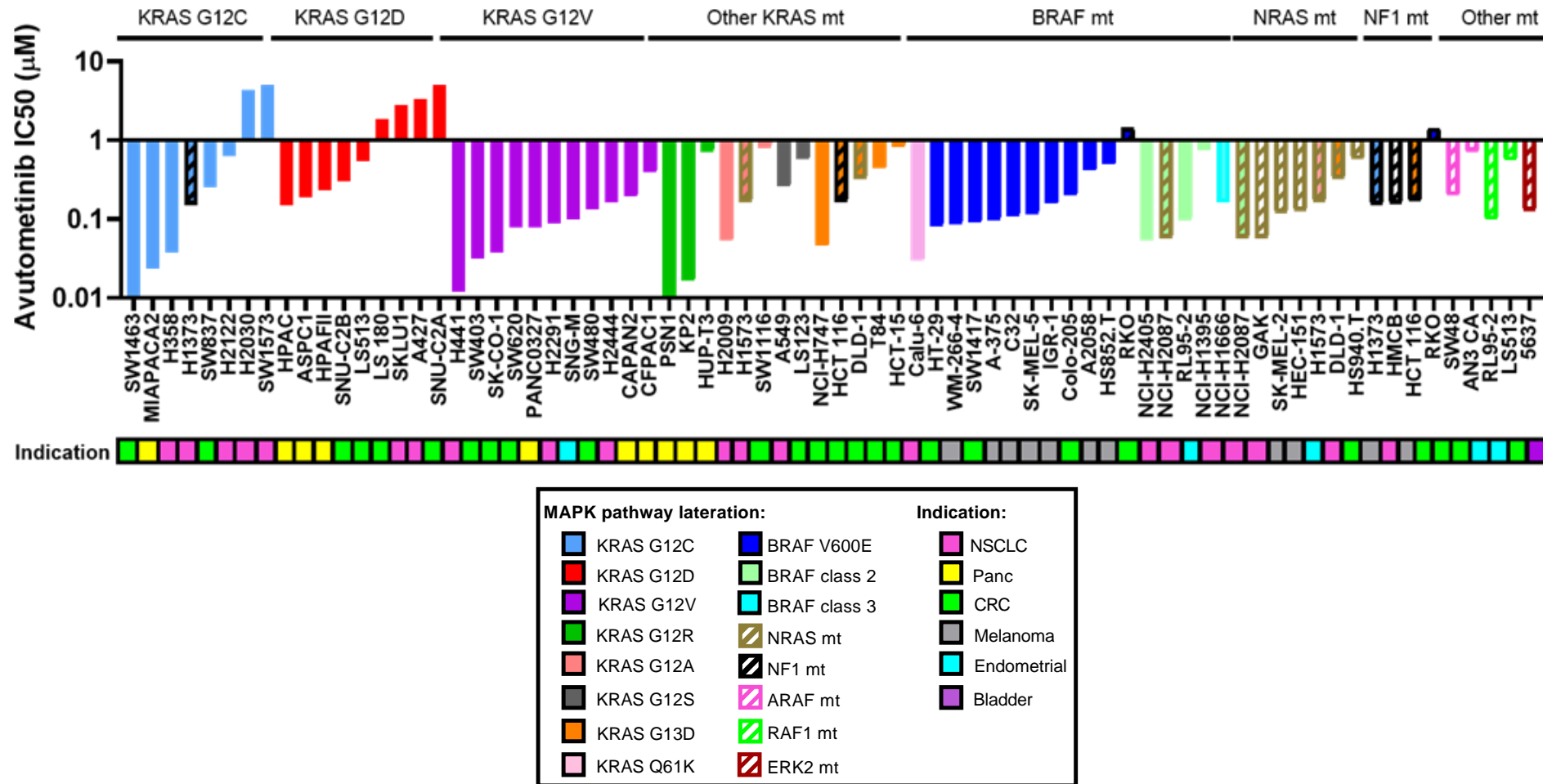
Avutometinib inhibits both RAF and MEK activities



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



Outsmarting Multiple Resistance Mechanisms in the RAS/MAPK Pathway

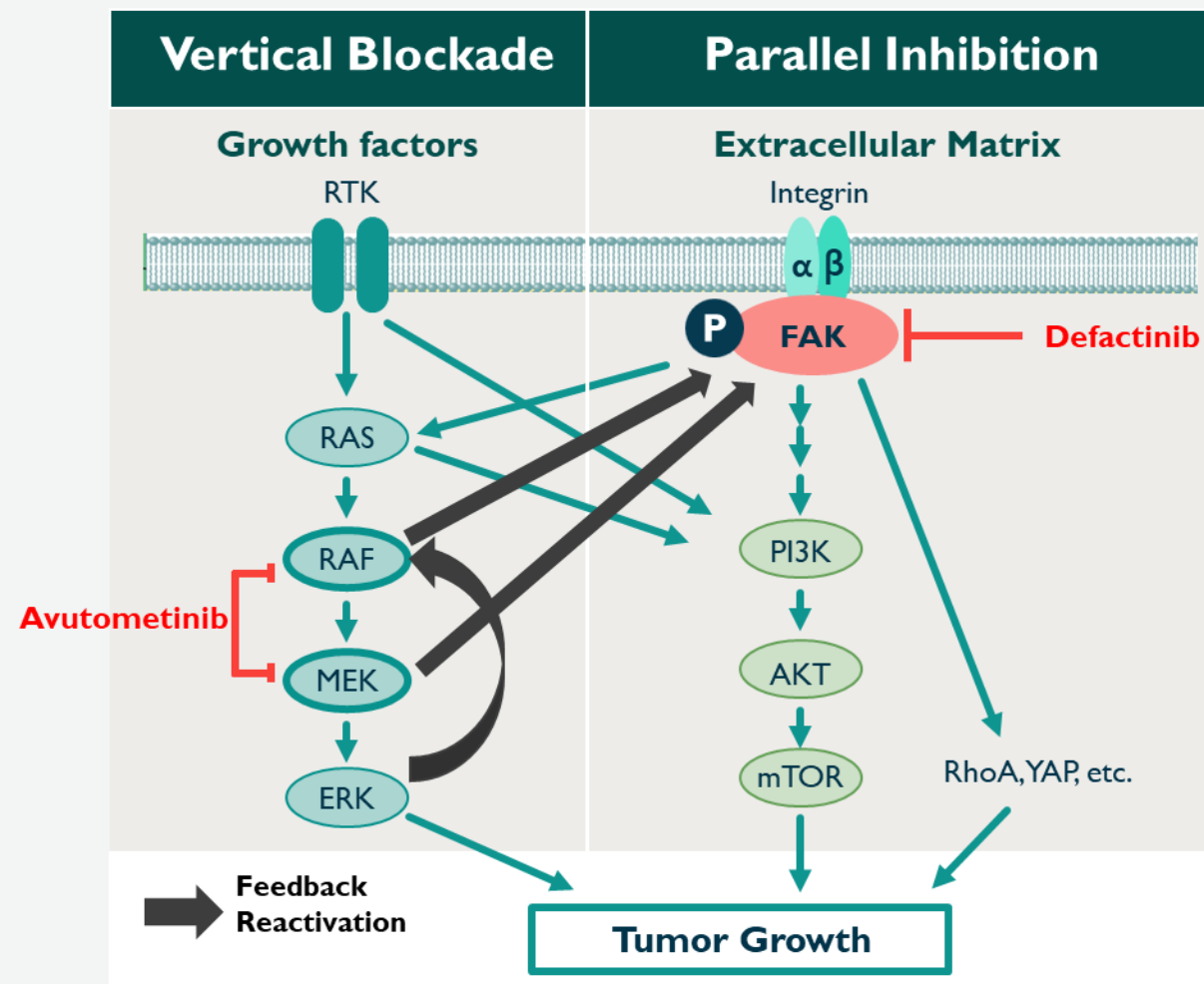
Novel Combination of Investigational Avutometinib + Defactinib with Aim to Improve Patient Outcomes

Avutometinib is an investigational oral RAF/MEK clamp, that confers a vertical blockade of both RAF and MEK

- This differentiated mechanism of action potentially avoids the compensatory reactivation of MEK by RAF enabling more complete pERK inhibition¹⁻³
- Potential best-in-class safety & tolerability profile relative to marketed MEK inhibitors and standard of care for LGSOC⁴⁻⁷
- Promising signals of clinical activity in various RAS pathway-driven cancers, including in patients whose tumors previously progressed on other MEK inhibitors⁶⁻⁸

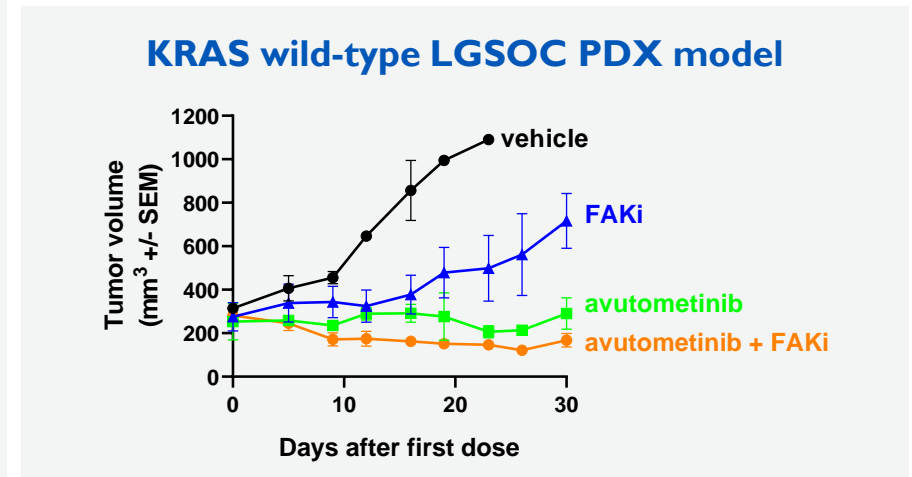
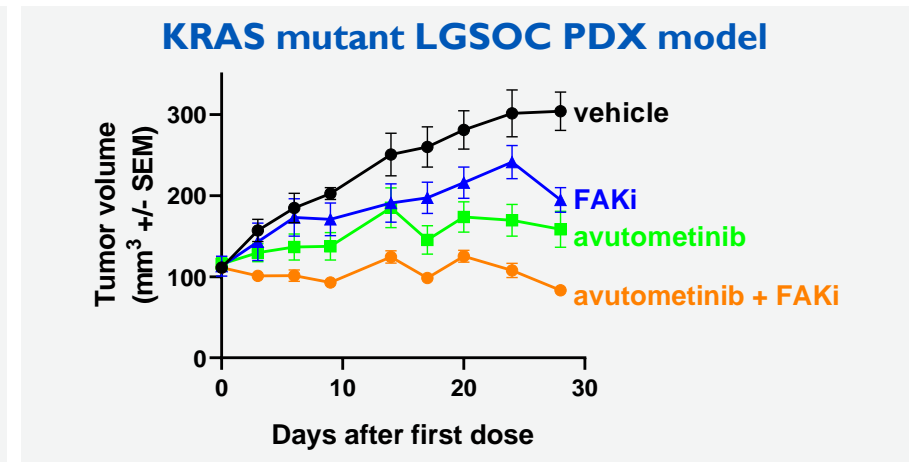
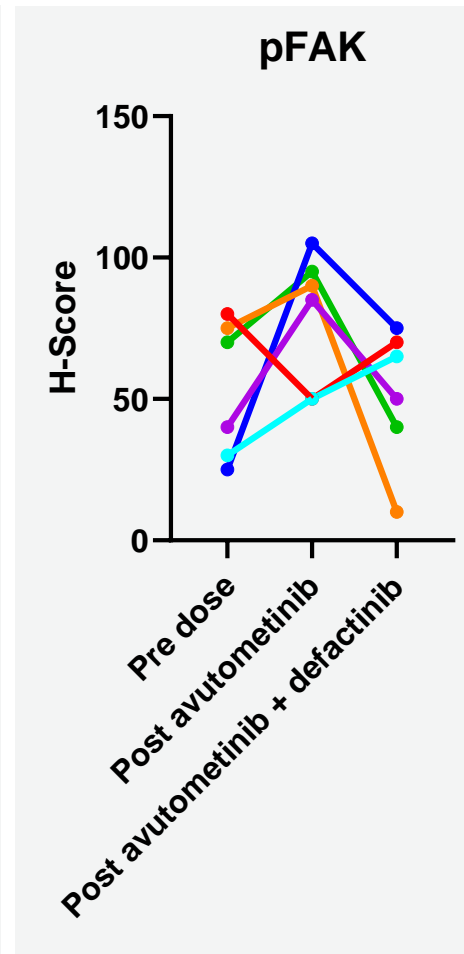
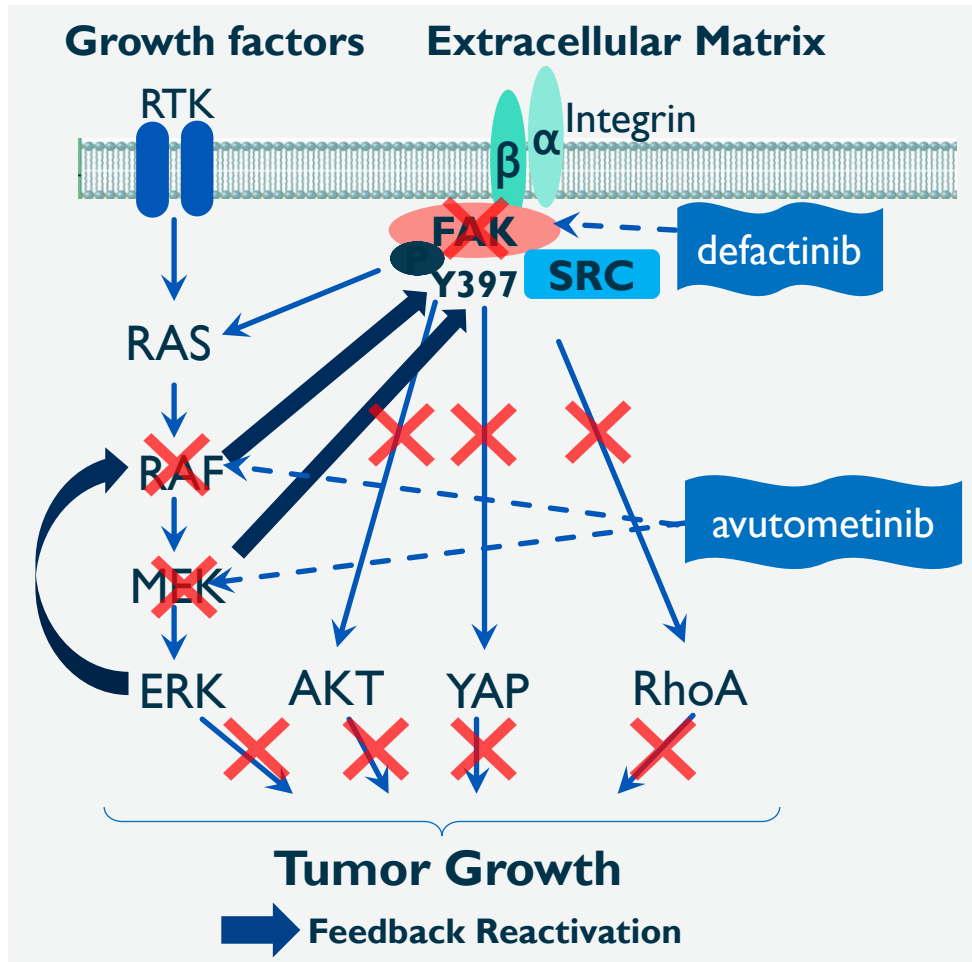
Defactinib is an investigational selective oral inhibitor of FAK, a signal target, which has been show to mediate adaptive resistance to RAS/MAPK pathway inhibition

- Parallel pathway inhibitor demonstrating synergy with avutometinib in multiple tumor models including LGSOC, pancreatic cancer and melanoma⁹⁻¹²
- Monotherapy and combination with other agents such as PD-I inhibitors, and chemotherapy, defactinib demonstrated a manageable safety profile^{13, 14}



Scientific Rationale for Avutometinib and FAK Inhibitor Combination

Anti-Tumor Activity in KRAS Mutant and KRAS 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

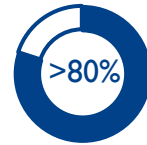
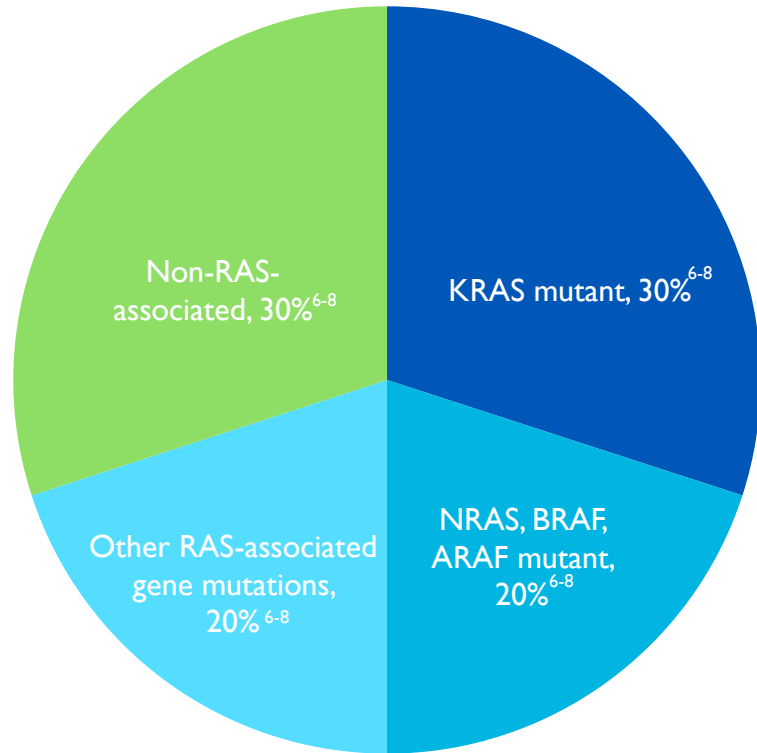
	Avutometinib monotherapy Daily at MTD N=6 28-day cycle	RP2D Avutometinib monotherapy 4mg twice weekly N=26 28-day cycle	RP2D (Avutometinib 3.2mg twice weekly + defactinib 200mg twice daily) N=38 21 days of 28-day cycle
Treatment Related Adverse Event	Grade ≥ 3	Grade ≥ 3	Grade ≥ 3
Rash	3 (50%)	5 (19%)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



Low-Grade Serous Ovarian Cancer (LGSOC)

LGSOC is a Rare Ovarian Cancer that is Insidious, Persistent, and Ultimately Fatal¹⁻⁴

1k-2k¹² incidence of LGSOC with a prevalence of 6k-8k¹³ in the US; 80,000 worldwide



Greater than **80%** of patients with LGSOC will experience a recurrence¹

20-30s

Affects a **younger patient population** and can disproportionately impact **health, fertility, and long-term quality of life**^{9,10}



Current SOC treatments offer **poor to moderate response rates (6-13%)**^{5,9,14}



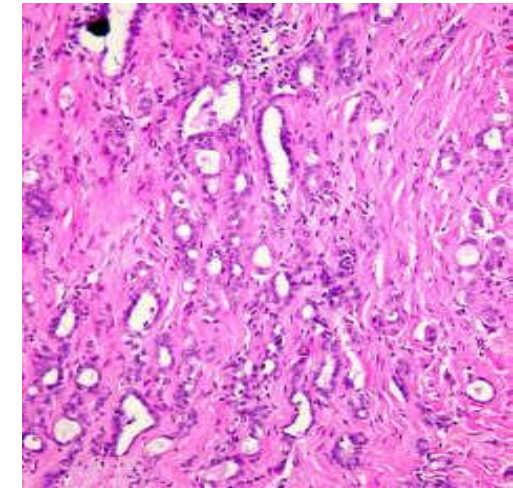
Median overall **survival of ~10 years** from time of diagnosis⁵



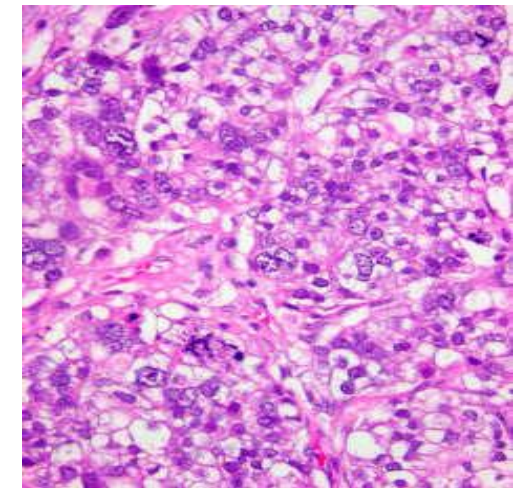
No FDA-approved treatment specifically for LGSOC¹¹

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

	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



Avutometinib ± Defactinib in Low-Grade Serous Ovarian Cancer

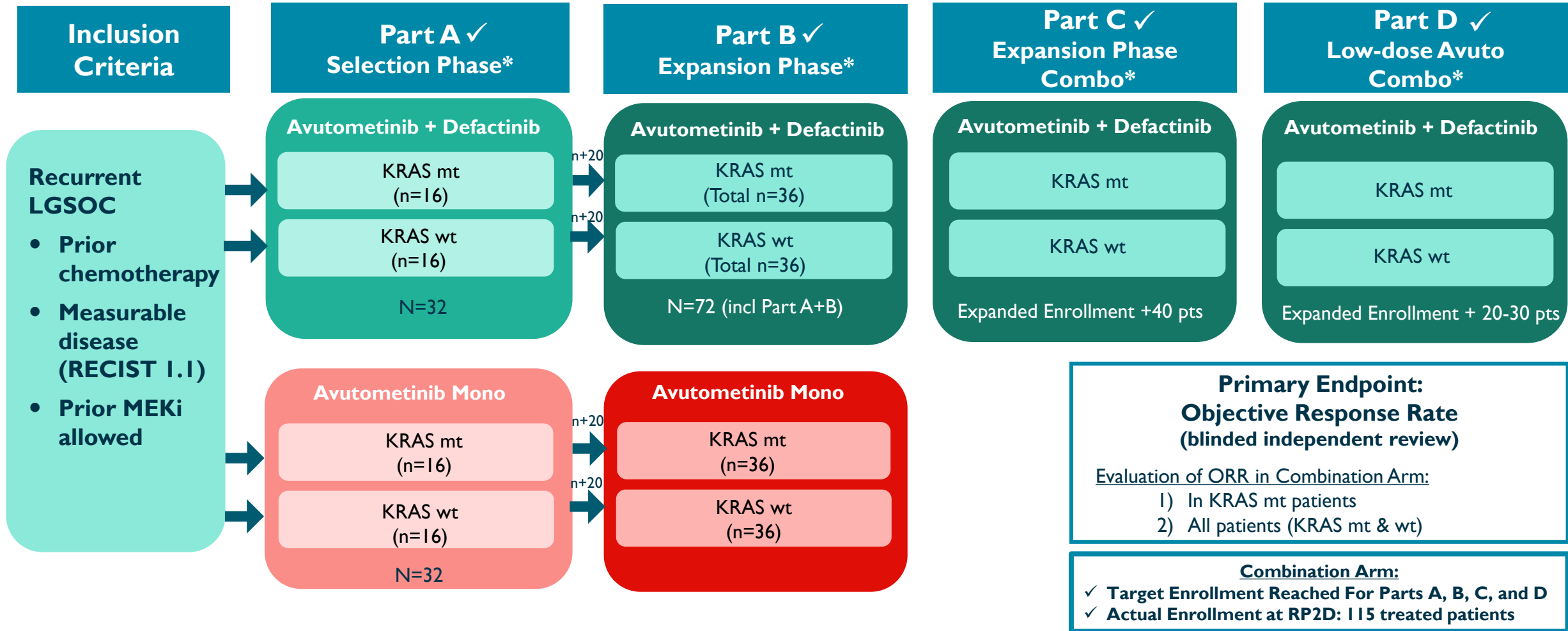
RAMP 201: Topline Data
Parts A + B + C

Topline RAMP 201 Data Support Rolling NDA Submission in Recurrent KRAS mt LGSOC

- RAMP 201 topline data represent larger dataset of patients treated at the RP2D with a minimum follow up of 5 months at last data analysis (Parts A, B and C combined: n=115*; KRAS mt: n=58; KRAS wt: n=57)
- Moving forward with rolling NDA submission for Accelerated Approval in adult patients with recurrent KRAS mt LGSOC who received at least one prior systemic therapy
 - RAMP 201 data with 12-months follow up is needed to complete the submission and drives timeline for final module
 - Path forward for KRAS wt to be discussed with FDA when mature RAMP 201 data available
 - Based on the longer median duration of treatment observed in RAMP 201 Part A, we believe KRAS mt represents $>2/3^{\text{rds}}$ of the revenue opportunity, compared with combined KRAS mt and KRAS wt, without any differential pricing**
- Plan to present mature dataset from RAMP 201 at a medical conference in the second half of 2024
- Expect to complete NDA submission in the second half of 2024

RAMP 201: Ongoing Registration-Directed Phase 2 Trial of Avutometinib ± Defactinib in Patients with Recurrent LGSOC

RAMP 201 (ENGOTov60/GOG3052)



* 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;

RECIST: Response Evaluation Criteria in Solid Tumors; PO: per oral; BID: twice daily; MEKi: Mitogen-activated extracellular signal-regulated kinase inhibitor;

Topline Data: RAMP 201 Continues to Show Robust and Durable Benefit

Topline Data	
Pooled ORR RAMP 201 Parts A + B + C, Data cutoff: Feb. 2024 Minimum follow-up: 5 months	
Avutometinib 3.2 mg + Defactinib 200 mg	
IRC	
ORR Overall Population (Confirmed ORR by BICR)	27% (29/109)*
95% CI	(19%-36%)
KRAS mt	37% (21/57)
KRAS wt	15% (8/52)
Clinical Benefit Rate (CR+PR+SD≥6 months):	60% (65/109)
Discontinuations Due to AEs	9% (10/115)

- Minimum follow-up of 5 months
- 14 patients with stable disease or unconfirmed partial response remain on treatment
- Potential for response rate to further improve with continued follow up
 - Potential responding patients: 29-43 (27%-39%)
 - KRAS mt: 21-30 (37%-53%)
 - KRAS wt: 8-13 (15%-25%)
- No new safety signals
- Plan to present mature dataset at a medical meeting in 2H 2024

Initial Portion of RAMP 201, Part A, Response Rate Improved Through First Year of Follow Up

- Interim results from RAMP 201 Part A were presented at ASCO 2023 annual meeting
- With a minimum of 12 months follow up in Part A at that time, time until objective response were reported
- Approximately 1 year of follow up may be required to fully appreciate the optimal rate of response

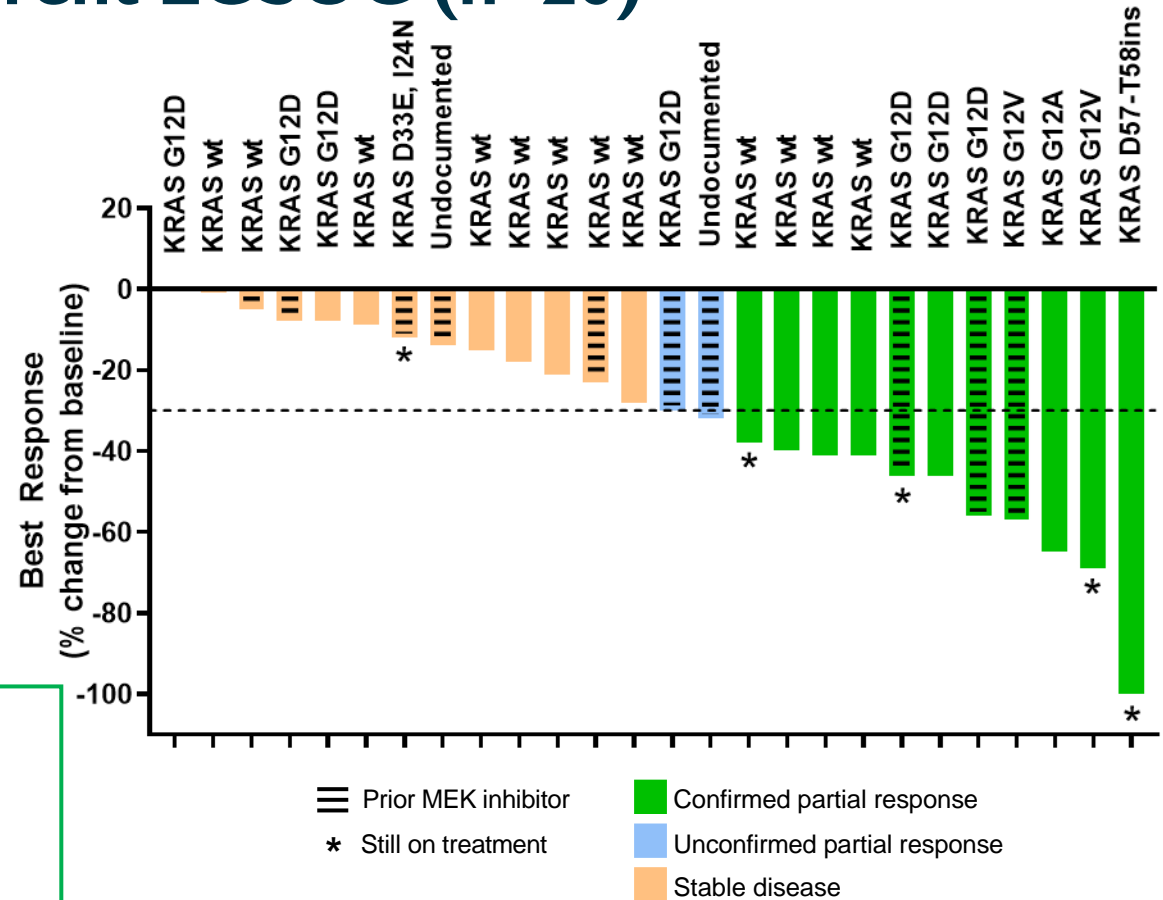
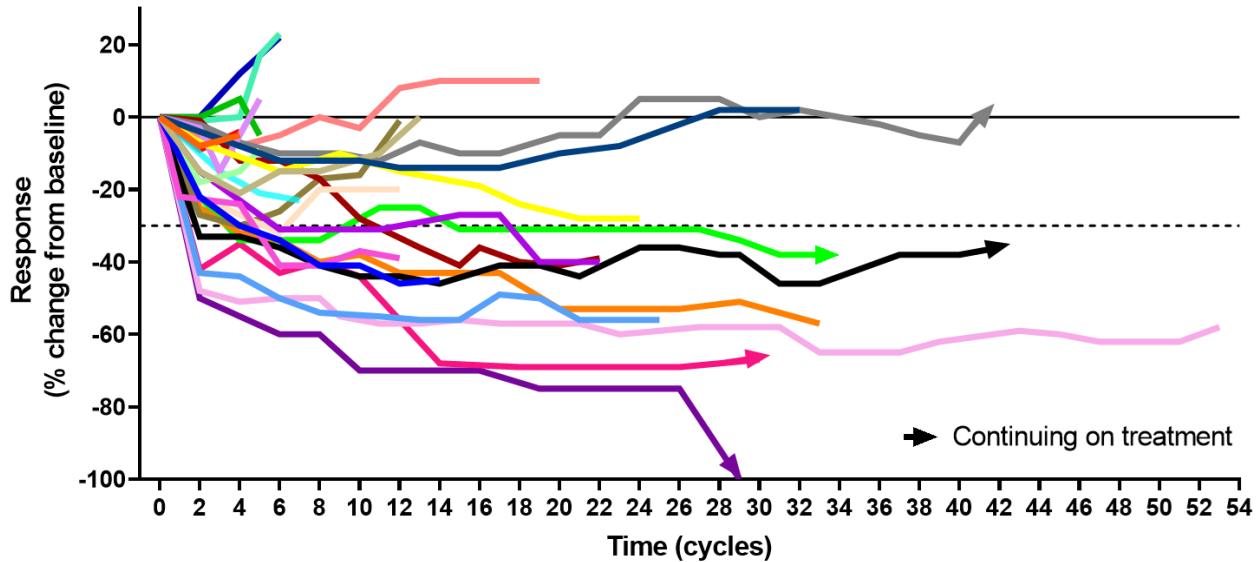
	Avutometinib + Defactinib	
	Total (n=29) Minimum follow-up of 12 months	
	45% (13) 95% CI: (26%, 64%)	
ORR, % (n)	KRAS mt 60% (9/15)	KRAS wt 29% (4/14)
Patients with reduction in tumor, % (n)	86% (25)	
Median Time to Response	5.5 months (range 1.6-14.7 months)	
Median Number of Prior Lines of Therapy	4	

*Median duration of therapy, at subsequent analysis, for patients enrolled to part A:

Median duration of treatment (all patients Part A): 11 months
 KRAS mt median: 18 months KRAS wt median: 8 months

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 number of prior lines of therapy: 3.5
- Responses observed in patients previously treated with MEK inhibitor
- No new safety findings with continued follow-up
- 1 patient discontinued for adverse events as of July 2023 (skin AE)
- Data confirmed via BICR

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



Recent LGSOC Trials Provide Relevant SOC Comparator

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%
MILO ²	2 (1-8)	No	* Low %	SoC (n=101)	13% 95% CI: (7%, 21%)	BICR	10.6 (9.2 - 14.5)	17%

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



Avutometinib + Defactinib in Low-Grade Serous Ovarian Cancer

Regulatory Update

Avutometinib + Defactinib for Recurrent LGSOC: Path to Accelerated Approval

Significant Unmet Medical Need

- No FDA approved therapies specifically for LGSOC
- Urgent need for new treatment options that improve outcomes for patients with LGSOC
- SOC therapy associated with low response rates and high discontinuation rate due to toxicity

Standard of Care (chemo/hormonal therapy)^a

ORR: 6-13%

D/C due to AE: 17-30%

Key Regulatory Achievements & Anticipated Milestones

- ✓ Breakthrough Therapy Designation granted^b
- ✓ Orphan Drug Designation granted for treatment of LGSOC as a distinct disease
- ✓ FDA Pre-NDA meeting 1H 2024
- ✓ Initiating rolling NDA submission for recurrent KRAS mt LGSOC in Q2 2024
- Plan to share RAMP 201 mature dataset with FDA as part of rolling NDA submission
- Expect to complete rolling submission H2 2024, priority review request
- Potential for FDA accelerated approval in 2025
- Ongoing confirmatory study targeting full enrollment by end of 2025

Next Steps: Plans to discuss regulatory path with CHMP and PMDA (EU and Japan)



Commercial Opportunity for
Avutometinib + Defactinib in
Low-Grade Serous Ovarian Cancer

Potential for Avutometinib + Defactinib to Rapidly Penetrate the Current Prevalent Patient Population, if Approved

STAGE II-IV DISEASE¹

→ MOS: ~10 YEARS²

FRONTLINE TREATMENT

± Neoadjuvant platinum/taxane

Debulking surgery

± Platinum/taxane chemotherapy

± Hormone therapy (Mx)

or

± Endocrine therapy



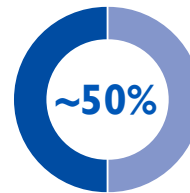
INITIAL RECURRENCE



SUBSEQUENT RECURRENCE

Target Product Profile (TPP) Based on Avutometinib + Defactinib Combination

- 70% of Oncologists surveyed indicate they will initially plan to treat with prevalent patients at their next recurrence³
- 49% of Oncologists surveyed indicate that initial recurrence is the ideal point in the patient journey to initiate treatment with the combination³



Treaters surveyed indicate that based upon approval of the target product profile of the combination, patients with LGSOC previously ineligible for continued treatment would now have a viable option at initial and subsequent recurrences, growing the treatable population³

Anticipate Concentrated Market Opportunity, Potential for Relatively Quick Adoption Given Limitations of SOC

Given the expected longer duration of therapy¹, we believe KRAS mt represents approximately >2/3^{rds} of revenue opportunity compared with combined KRAS mt and KRAS wt, without any differential pricing*

Focused Commercial Launch

Plan for a focused commercial launch, if approved

- Top 400 HCPs and top 100 HCOs collectively cover nearly half of the LGSOC population¹; focused sales force of 14-18 reps

Substantial market preparation activities

- Engaged with 1/3 of prevalent patient population² & ongoing engagement with HCPs³

Excitement for avutometinib + defactinib underscores its potential to address the significant unmet need

- Based on a TPP of avutometinib + defactinib combination:
 - 85% of treaters surveyed say they would adopt within 6 months of receiving FDA approval, suggesting swift uptake of the treatment for eligible patients⁴

Opportunity for active switch to avutometinib + defactinib

- Based on TPP of avutometinib + defactinib combination:
 - 28% of treaters surveyed say they would proactively reach out to switch half of their current LGSOC patients, if approved⁴

Ensuring Patients' Ability to Start and Stay on Therapy

Coverage and access support

- Well-insured patient population will support widespread coverage
- NCCN listing and Medicare protected class status could result in favorable coverage to label
- Comprehensive suite of resources intended to support patients and physicians navigating payer barriers

Ongoing engagement with plans for rapid uptake

- Support of community practices through relationships with Oncology GPOs could facilitate education and adoption
- Focused outreach with HCOs that cover majority of patients in key centers planned now

Patient assistance

- Financial and other insurance barriers, time to coverage, may be mitigated by robust patient service offerings
- High touch Hub and limited distribution network could ensure patients start quickly and stay on therapy

*Based on internal revenue forecasts including potential market penetration of Verastem's product candidates

¹ Based on median duration of therapy from RAMP 201 Part A

NCCN: National Comprehensive Cancer Network; HCP: healthcare professionals; HCO: healthcare organizations; GPO: group purchasing organizations.; 1. VSTM DOF – Claims LGSOC Proxy 2. VSTM DOF. Self-identified LGSOC patients registered via DSE website. 3. VSTM CRM DOF 2024. 4. VSTM DOF, ATU 2024 (n=96, Fielded December 2023 – January 2024)

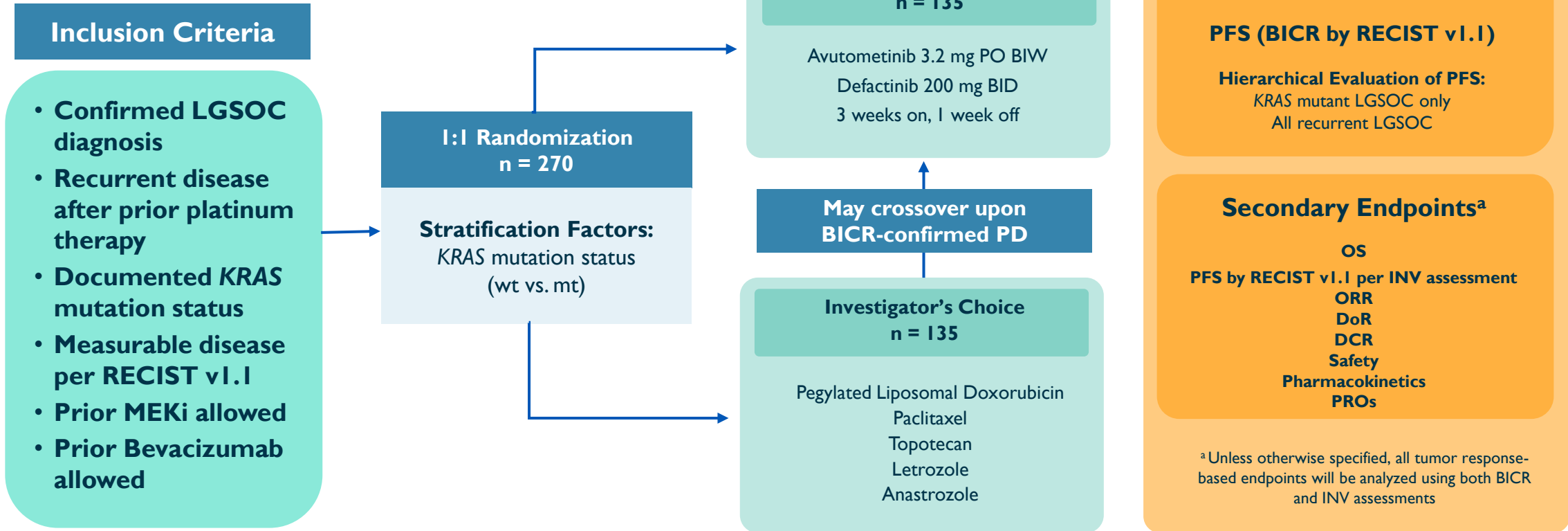


Avutometinib + Defactinib in Low-Grade Serous Ovarian Cancer

RAMP 301: Phase 3 Confirmatory Trial

RAMP 301: International Phase 3 Confirmatory Trial Evaluating Avutometinib + Defactinib in Recurrent LGSOC

RAMP 301 (GOG-3907/ENGOT-ov81/NCRI): Ongoing Randomized Controlled Trial (RCT)

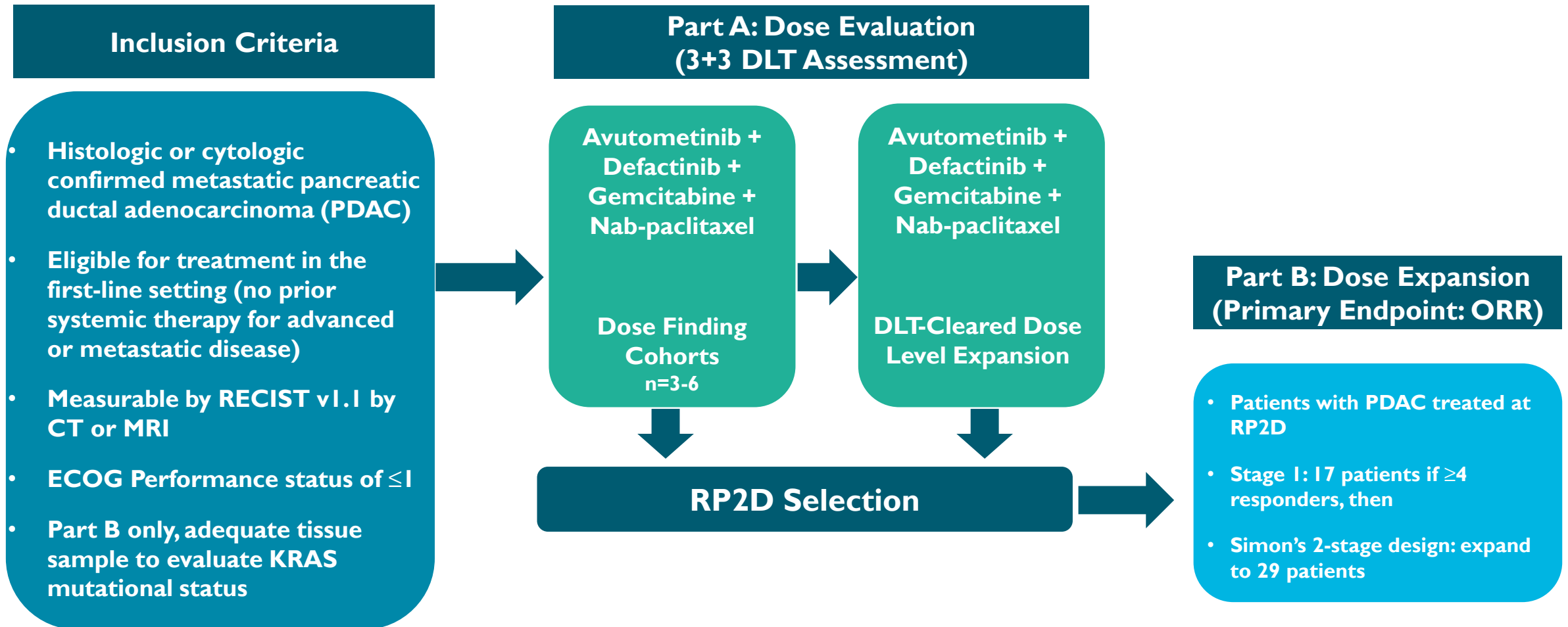




Topline Data from RAMP 205:
Avutometinib + Defactinib + SOC in
First-Line Metastatic Pancreatic
Cancer

RAMP 205: Designed to Identify and Evaluate RP2D in Combination with Chemotherapy for Treatment of Newly Diagnosed mPDAC

RAMP 205: Ongoing Phase 1/2 Evaluating Avutometinib + Defactinib with Gemcitabine and Nab-paclitaxel



RAMP 205: Initial Interim Safety and Efficacy Results

- Encouraging early interim data from ongoing Phase I/2 RAMP 205 study evaluating avutometinib + defactinib + gemcitabine + Nab-paclitaxel in first-line metastatic pancreatic cancer
 - As of data cutoff of May 14, 2024, Dose Level I mature with more than 6 months follow up
 - Confirmed ORR = 83% (5/6)
 - Cohort was DLT cleared, one DLT observed (neutropenic fever)
- Evaluating additional dose/schedule combinations to optimize the dose for safety/tolerability and define RP2D for expansion cohort
- 11 top academic sites currently enrolling and highly engaged
- Presenting RAMP 205 initial interim data at ASCO on June 1, 2024

Dose Level	Avuto	Defactinib	Gem	Nab-Pac
Day 1, 8, 15 chemo dosing:				
-I	2.4 mg BIW	200 mg BID	800 mg/m ²	100 mg/m ²
I	2.4 mg BIW	200 mg BID	800 mg/m ²	125 mg/m ²
Day 1 and 15 chemo dosing:				
Ia	3.2 mg BIW	200 mg BID	800 mg/m ²	125 mg/m ²
2a	3.2 mg BIW	200 mg BID	1000 mg/m ²	125 mg/m ²

Landmark Trials in First-Line Metastatic Pancreatic Cancer

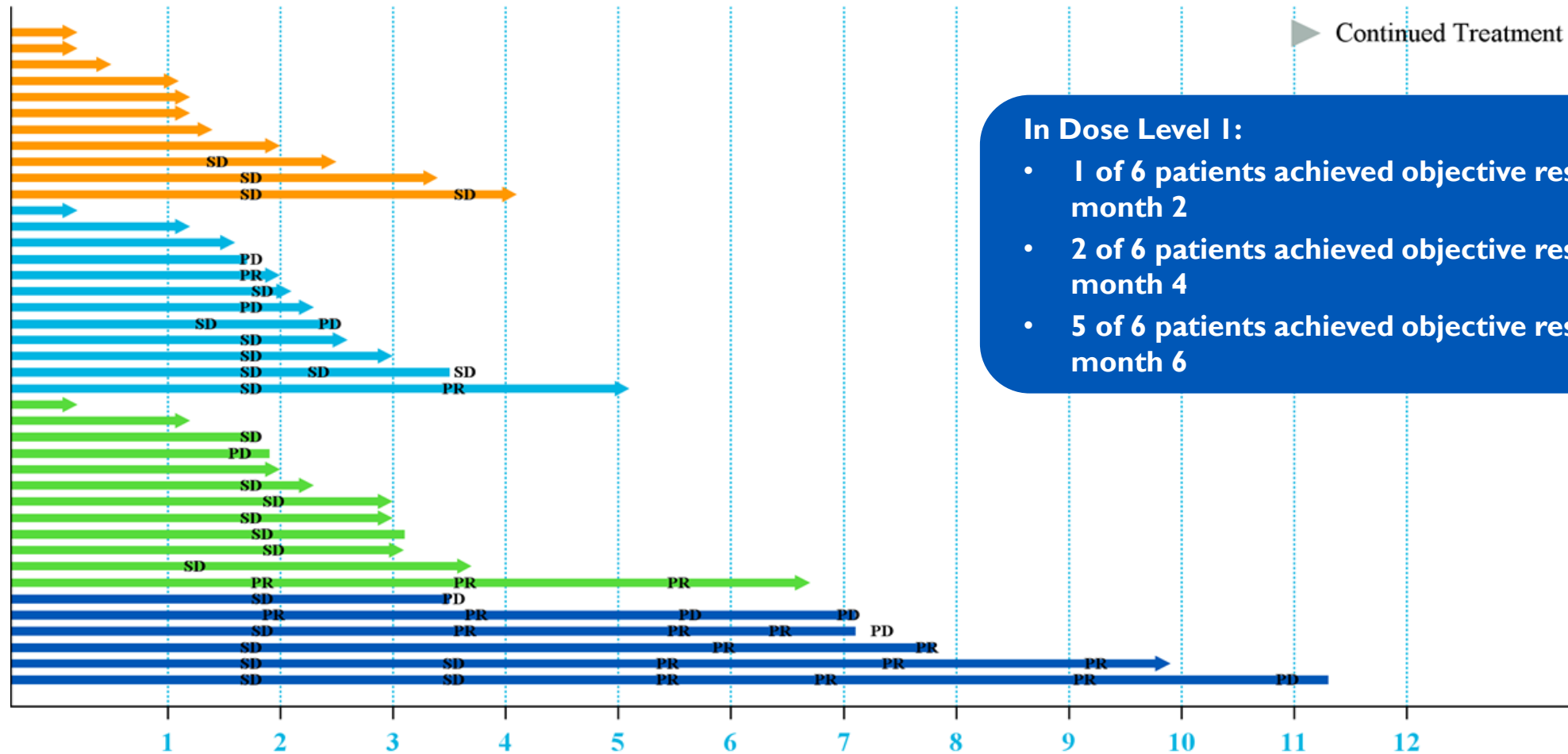
SOC Treatment Landscape:

- ORR is between 23% - 36% for Gem/NabP
- Median overall survival reported between 8.5 – 9.2 months

Trial/PI/Reported (# Patients)	Intervention	Comparator	ORR by Investigator (95% CI)		mPFS (95% CI)	mOS (95% CI)
MPACT Von Hoff 2013 (N=861)	Gem/NabP* (n=431)	Gem (n=430)	Gem/NabP		5.5 months (4.5-5.9)	8.5 months (7.89-9.53)
			29% (25-34)	23% (19-17) IRR**		
NAPOLI 3 O'Reilly 2023 (N=770)	Nalirifox (n=383)	Gem/NabP* (n=387)	Gem/NabP		5.6 Months (5.3-5.8)	9.2 months (8.3-10.6)
			36.2% (31.4-41.2)			
			Nalirifox		7.4 months (6.0-7.7)	11.1 months (10-12.1)
			41.8% (36.8-46.9)			
PRODIGE Conroy 2011 (N=342)	Folfirinox (n=171)	Gem (n=171)	Folfirinox		6.4 months	11.1 months
			31.6% (24.7-39.1)			

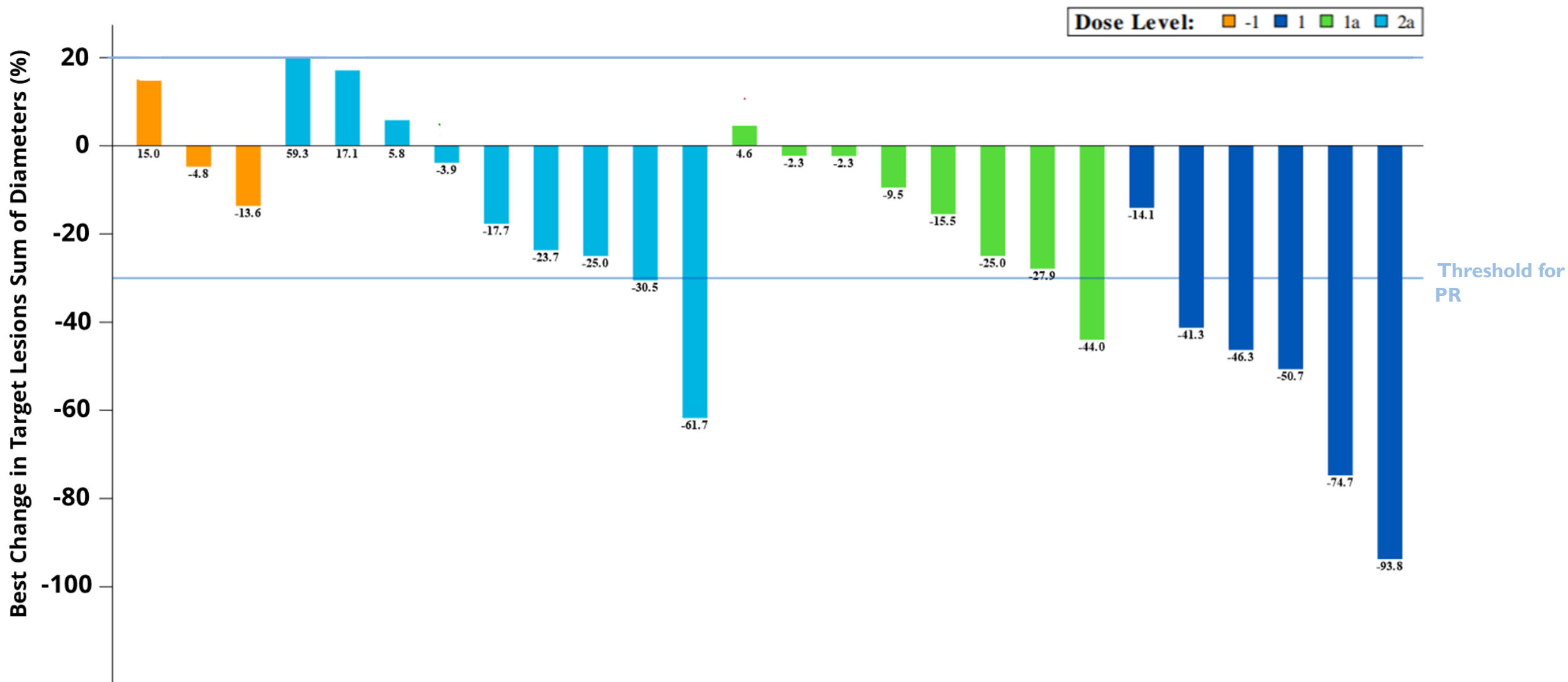
RAMP 205: Evaluating Multiple Regimens in Parallel to Efficiently Identify RP2D in First-Line mPC

Duration of Treatment for All Patients; Safety Population (n=41)



RAMP 205: Best Percent Change in Target Lesion Sum of Diameters

Includes Patients Who Have Had At Least First Scan (n=26)

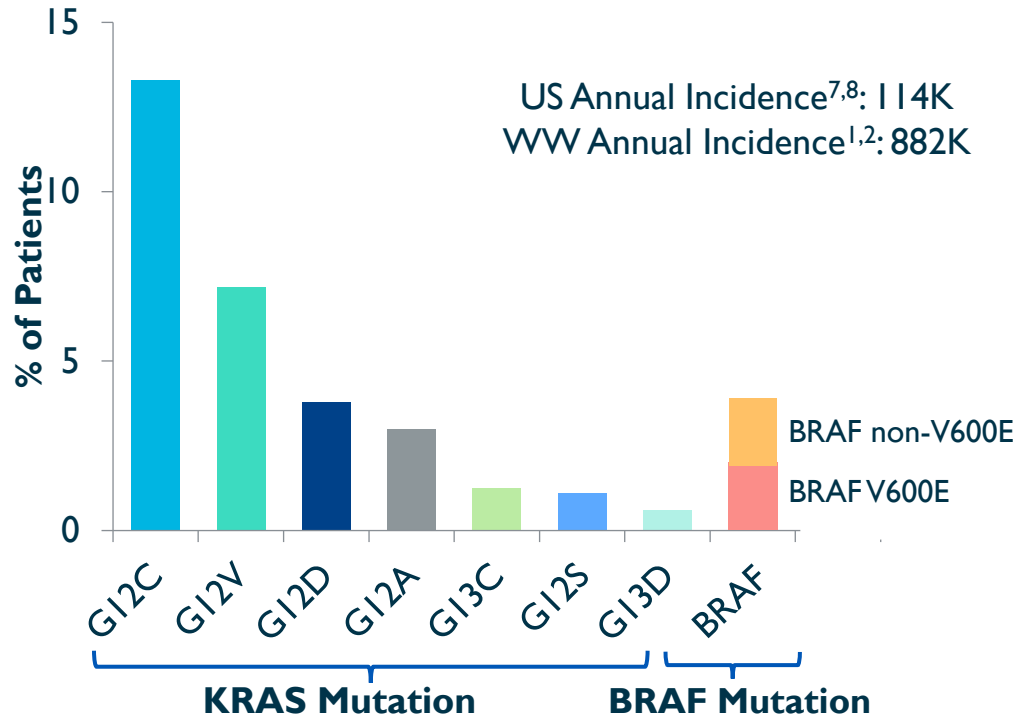




Avutometinib with KRAS G12C Inhibitors in Non-Small Cell Lung Cancer

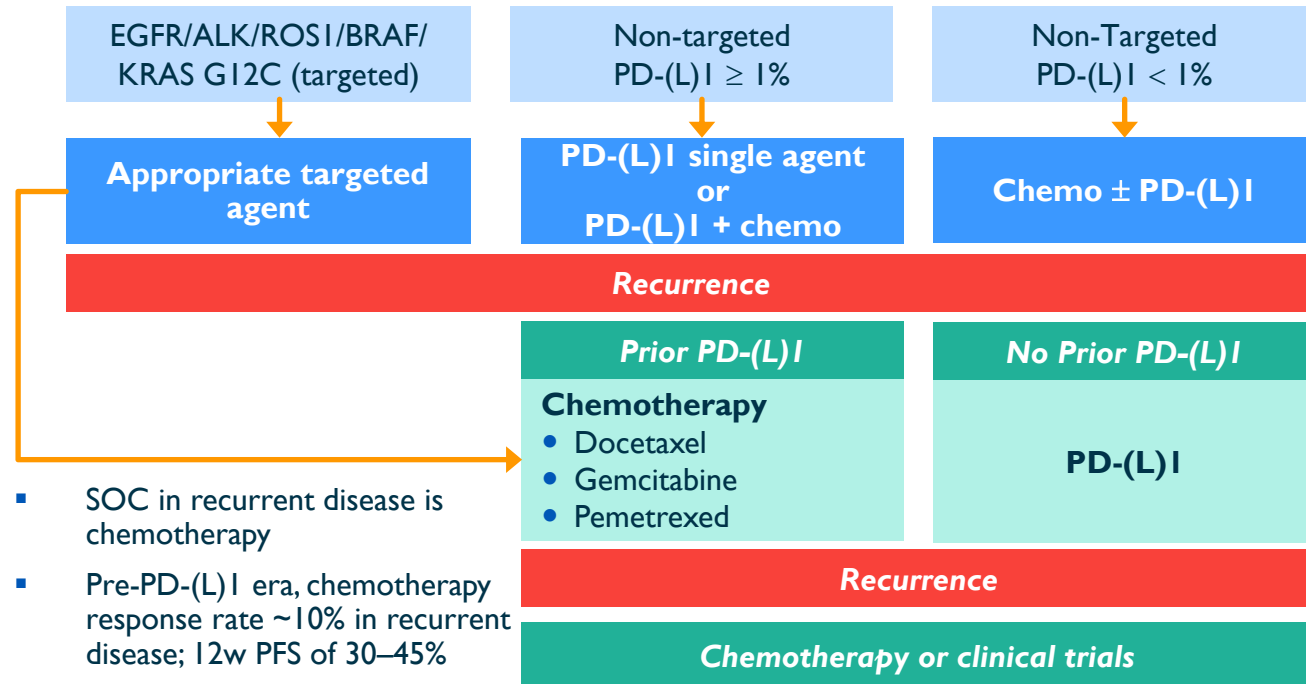
High Unmet Need in Refractory NSCLC Adenocarcinoma

NSCLC Adenocarcinoma³



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

Advanced or Metastatic NSCL Cancer Recommend Histologic and Molecular Subtyping⁵



Verastem Clinical Trials:

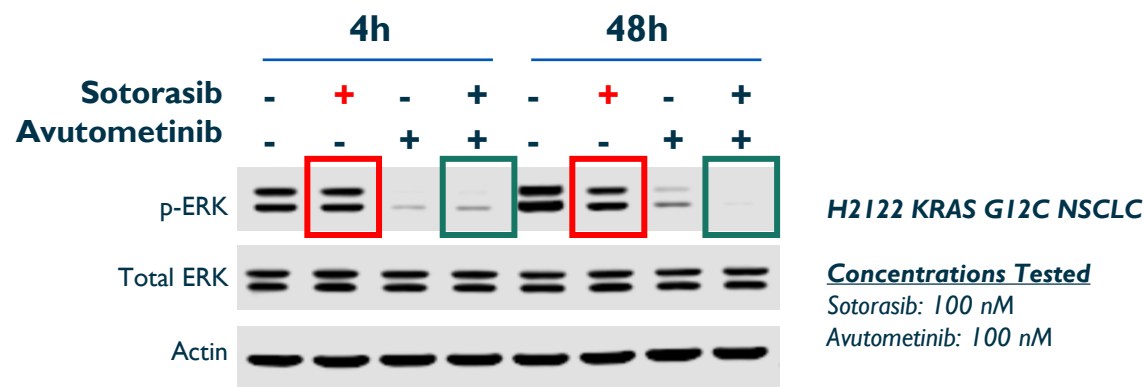
- RAMP 203: Avutometinib ± defactinib + sotorasib in KRAS G12C NSCLC
- RAMP 204: Avutometinib + adagrasib in KRAS G12C NSCLC

Preclinical Synergy of Avutometinib + G12C Inhibitors in KRAS G12C Models

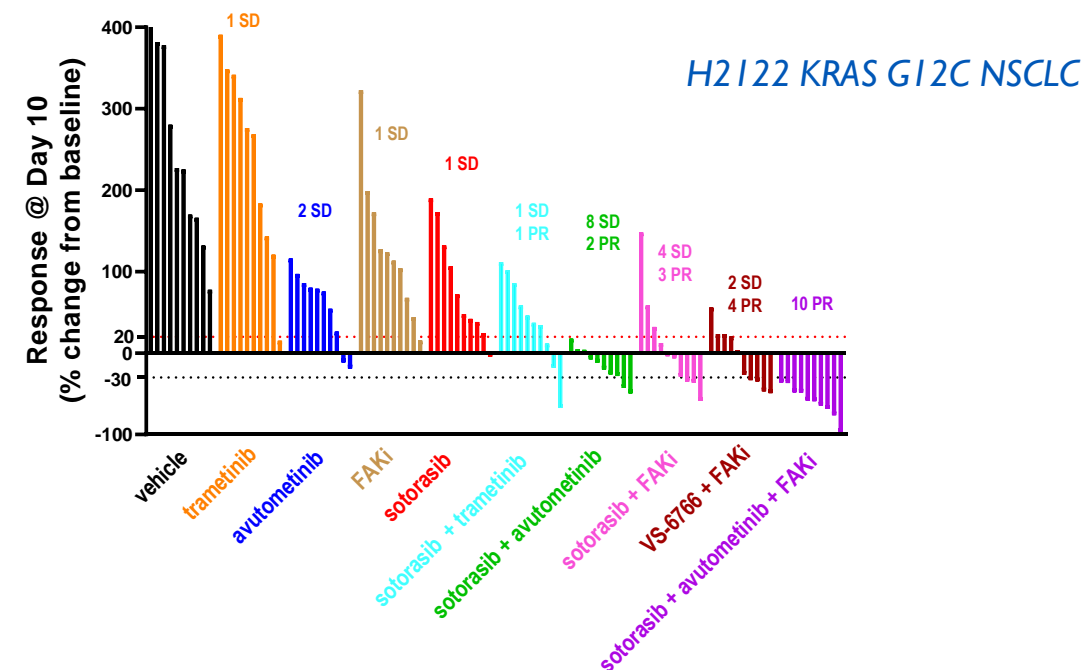
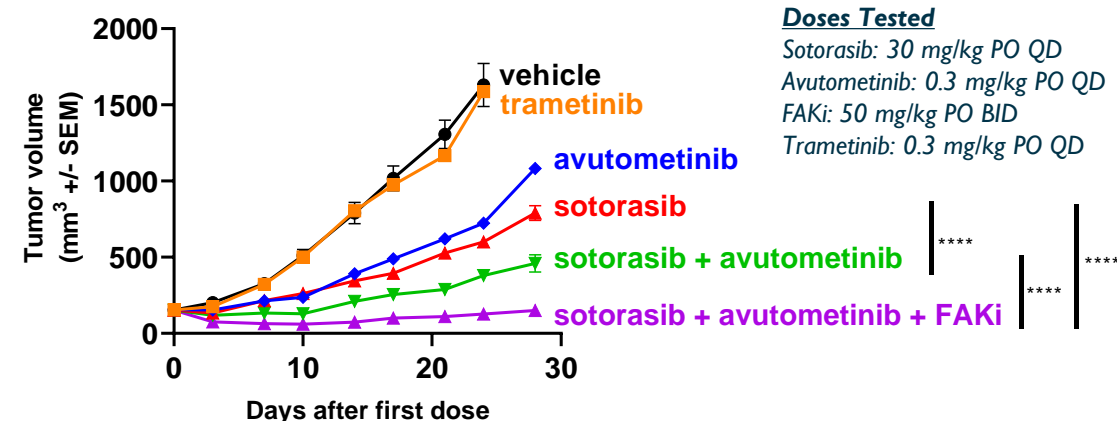
Synergy of avutometinib + G12C inhibitors across G12C mutant NSCLC, CRC & Pancreatic cancer cell lines

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

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 Activity of Sotorasib in G12Ci-Resistant KRAS G12C Models

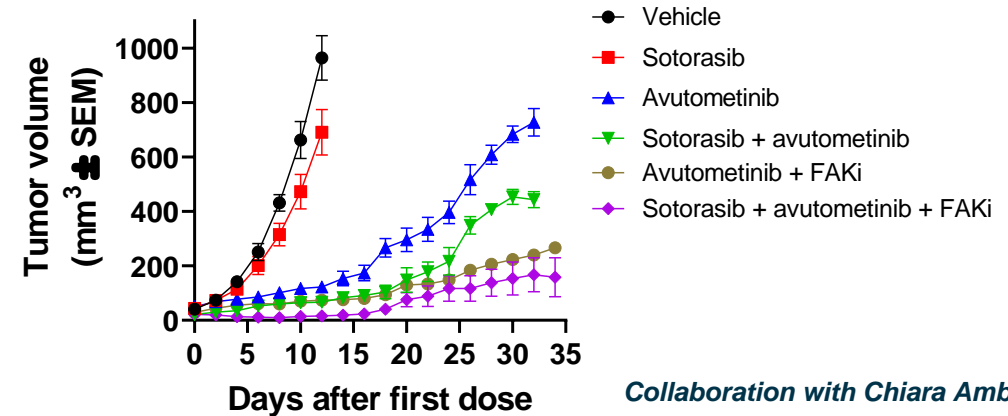
Avutometinib inhibits proliferation of cells harboring acquired KRAS mutations that occur clinically upon progression on G12C inhibitors

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

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

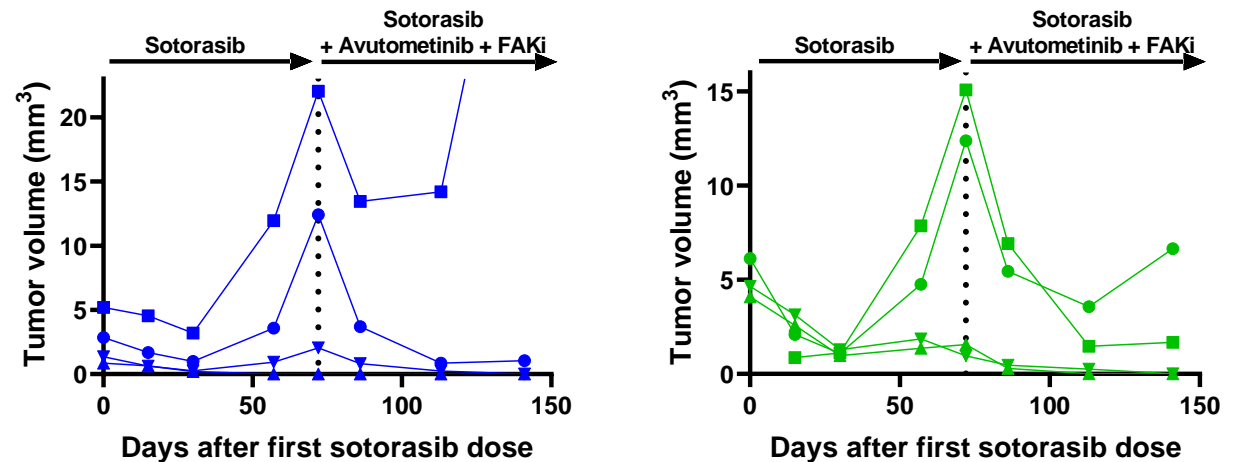
<30 nM 30 - 150 nM >150 nM

Collaboration with Andy Aguirre, DFCI



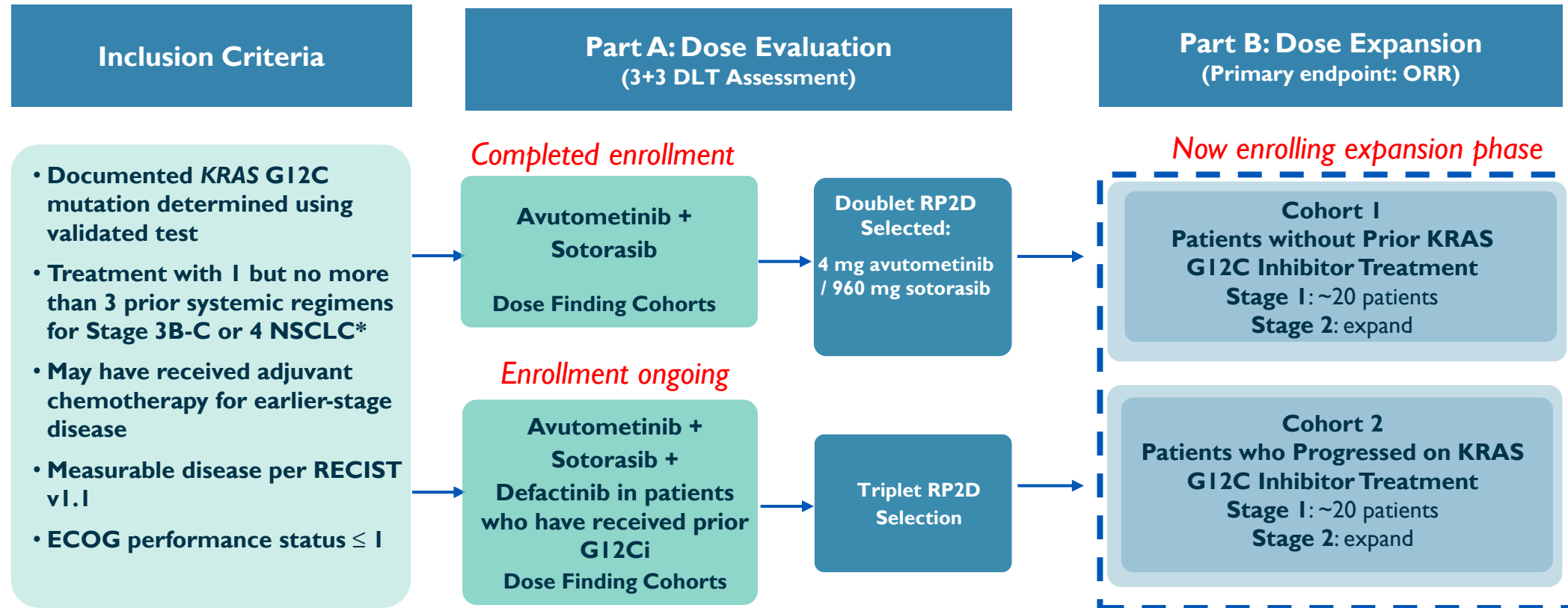
Collaboration with Chiara Ambrogio, U Turin (Italy)

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

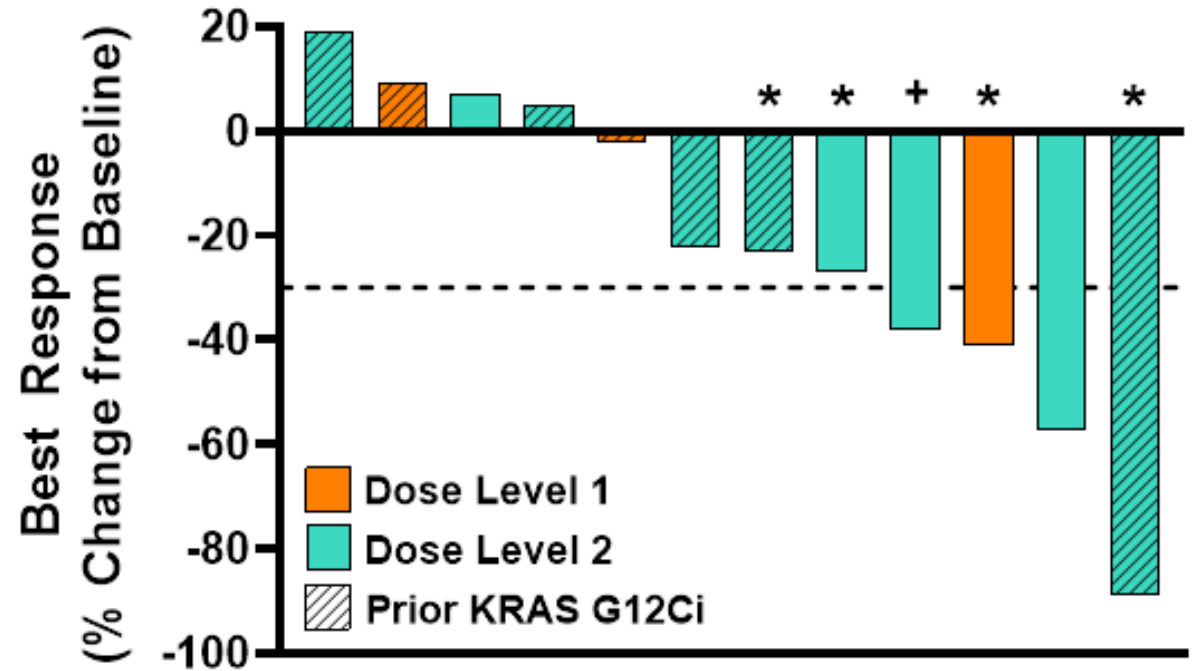
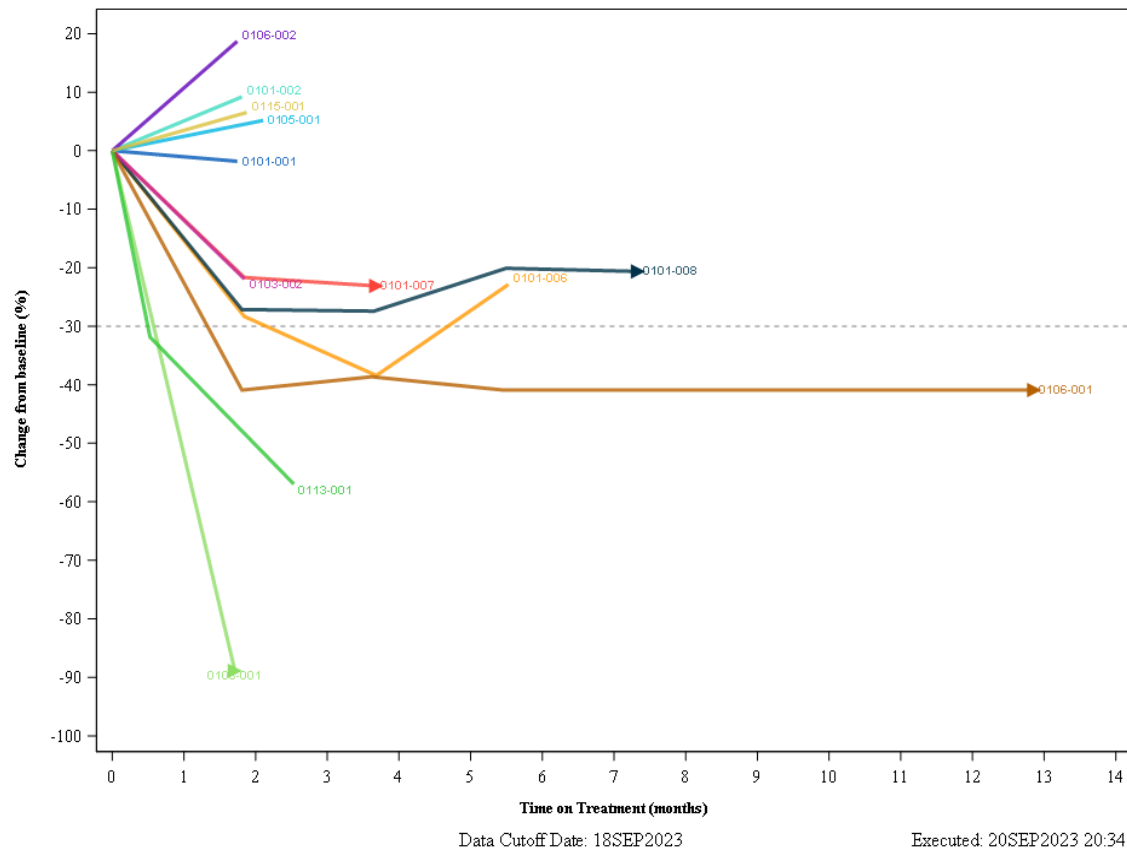


*may include patients with or without prior G12C therapy

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

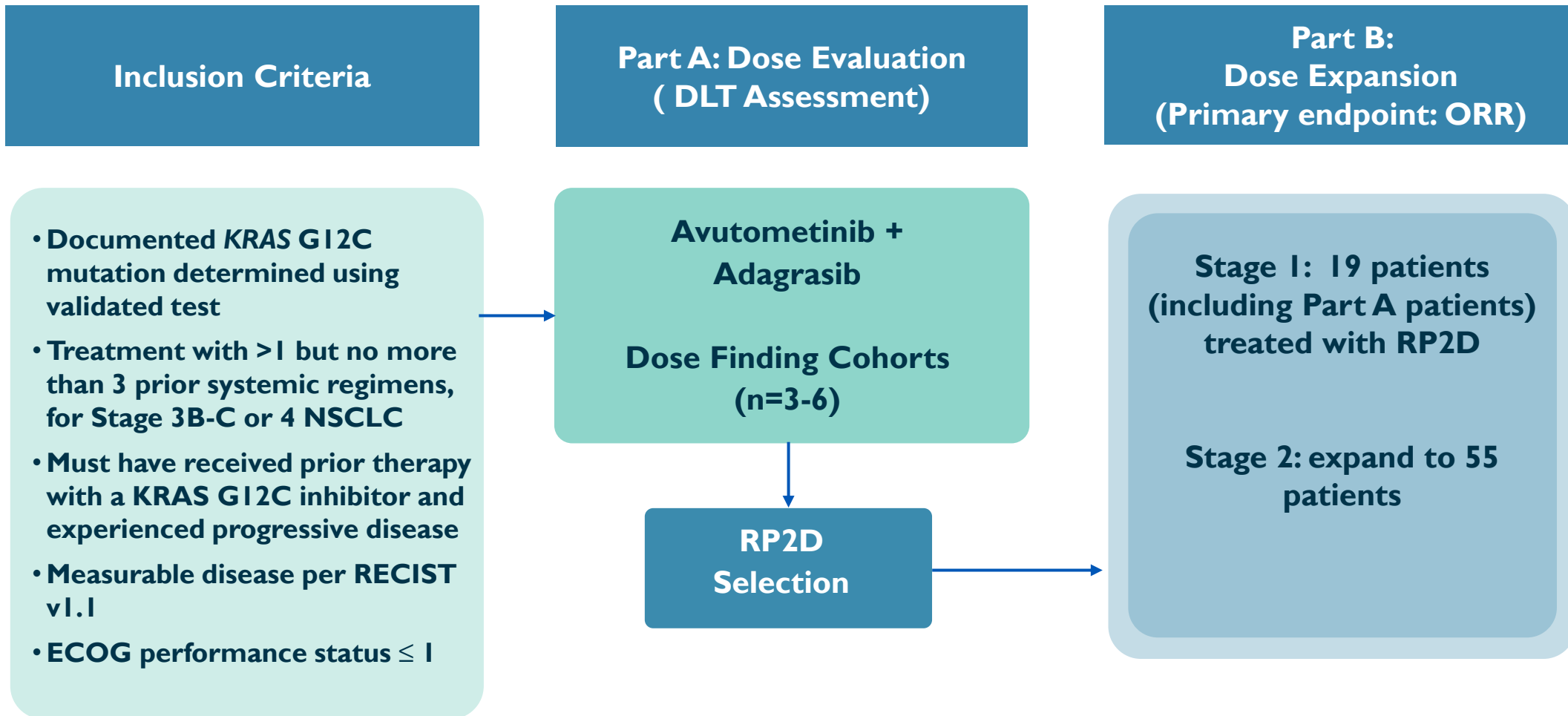
Avutometinib + Sotorasib

Percentage Change in Target Lesion Sum with time on treatment



*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





RAS Pathway-Driven Cancers and Rational Avutometinib Combinations

Investigator-Sponsored Trials Provide Ongoing Comprehensive Approach to Establish More Complete Blockade of RAS Pathway & Resistance Pathways

	Indication	Incidence/ Prevalence	Biomarker %	Regimen	Setting	Phase	Institution
Gynecologic Cancers	LGSOC	Prevalence 6k ¹	70%	Avutometinib + defactinib + letrozole	Low-grade serous ovarian cancer without prior systemic treatment	Phase 1/2	Memorial Sloan Kettering Cancer Center
	Gynecologic Basket	Incidence ⁴⁻⁸ : 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	University of Oklahoma
	Mesonephric	Incidence: ⁹ ~680	96%	Avutometinib + defactinib	Advanced or recurrent mesonephric gynecologic cancer	Phase 2	Memorial Sloan Kettering Cancer Center
CRC	KRAS mt	Incidence ² : 148K	45%	Avutometinib + cetuximab	Recurrent metastatic KRAS mt	Phase 1/2	University of Chicago
	RAS/RAF wt CRC	Incidence ² : 148K	50% ¹²	Avutometinib + defactinib + cetuximab	Unresectable, Anti-EGFR-Refractory Advanced Colorectal Cancer	Phase 1/2	M.D. Anderson Cancer Center
Breast Cancer	ER+/Her2-	Incidence ² : 279K	22.5%	Avutometinib + abemaciclib + fulvestrant	Recurrent ER+/HER2- breast cancer following progression on CDK4/6i + aromatase inhibitor	Phase 1/2	Dana-Farber Cancer Institute
Melanoma	MAPK alterations or wt	Incidence ² : 100K	100%	Avutometinib + defactinib ± encorafenib	Patients with brain metastases from cutaneous melanoma with RAS, RAF or NFI alterations or RAS/RAF/NFI wt	Phase 1/2	University of Utah
Thyroid	MAPK alterations ⁺	Incidence ³ : 44K	35%	Avutometinib + defactinib	Differentiated & anaplastic thyroid cancer	Phase 2	Memorial Sloan Kettering Cancer Center

*excluding BRAFV600E

Discovery Efforts

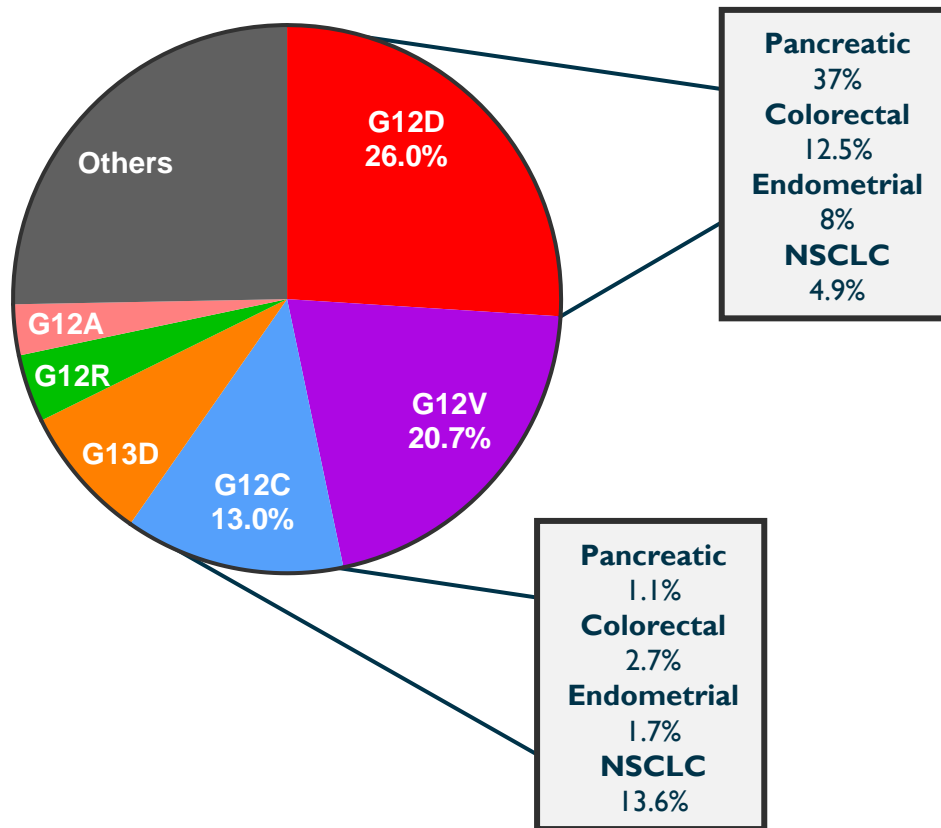
The image features a white background with several diagonal stripes. A large blue stripe runs from the top-left towards the bottom-right. Overlapping this are three narrower stripes: a teal stripe, a white stripe, and an orange stripe, all running parallel to the blue one. At the bottom, a horizontal teal stripe spans the width of the image, overlapping the diagonal stripes.

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

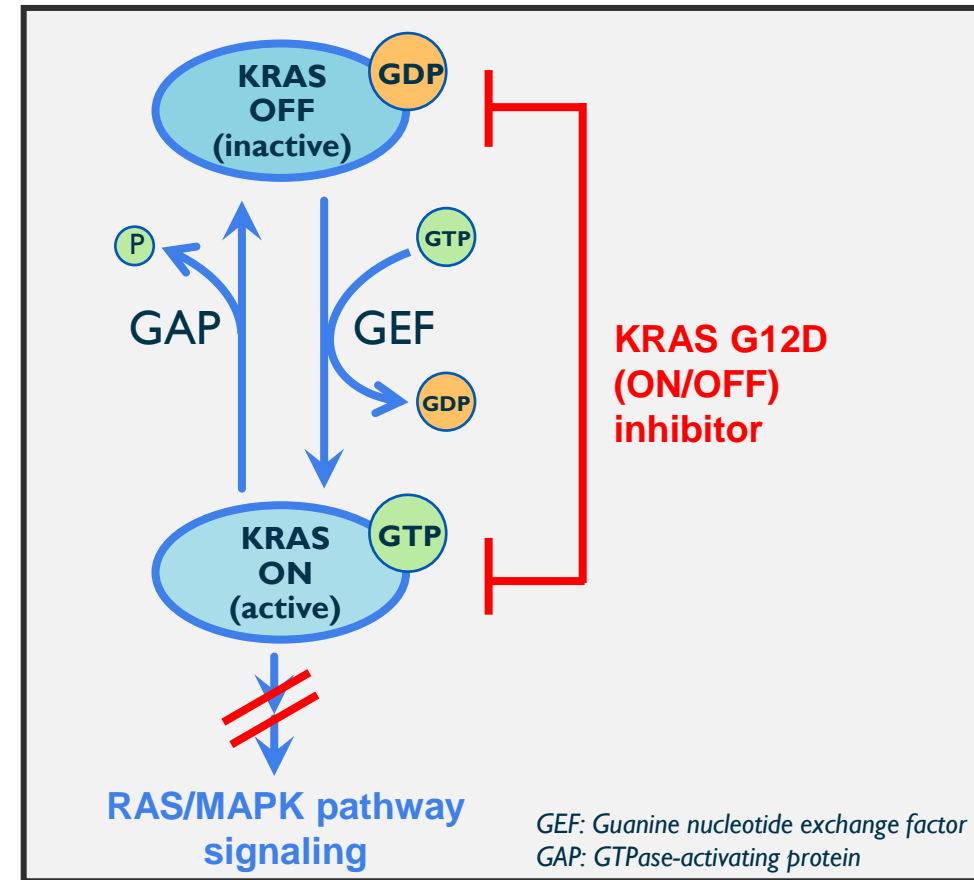
- Increases the breadth of Verastem's oncology pipeline with strategically-aligned RAS pathway focus
 - Exclusive options for Verastem to exclusively license up to 3 programs with development and commercialization rights outside of the GenFleet markets of mainland China, Hong Kong, Macau, and Taiwan
 - 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

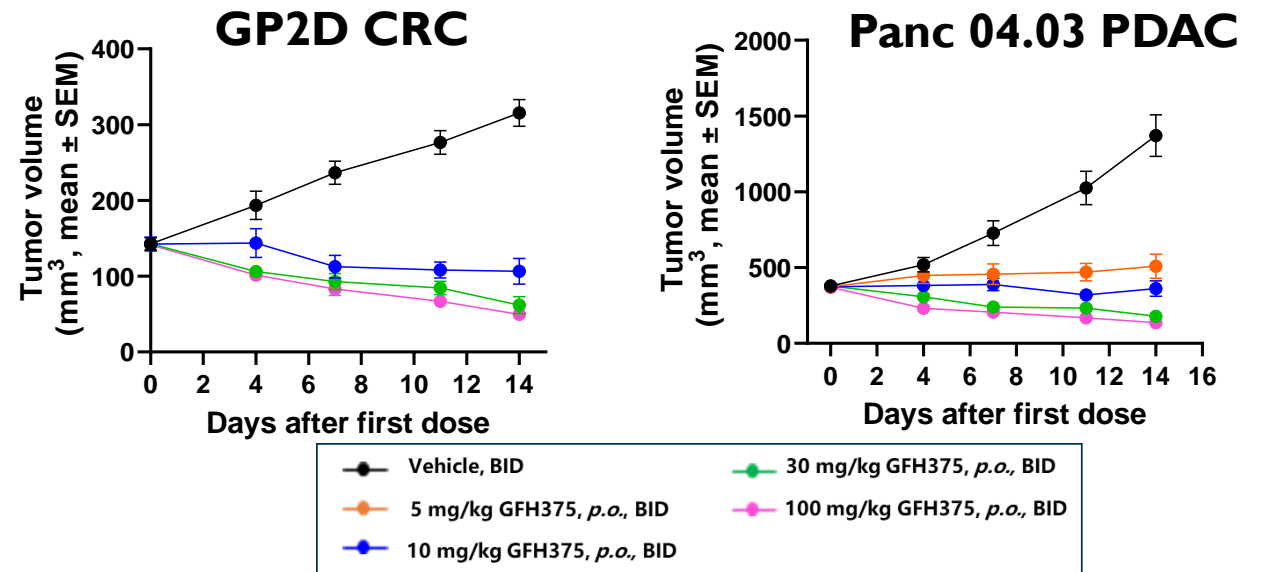
First program from the GenFleet collaboration

- GFH375 (VS-7375) is a potent and selective orally bioavailable inhibitor of KRAS G12D (ON/OFF) with potent anti-tumor activity 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
- Avutemetinib enhances anti-tumor activity 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 activity 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 geometric.

Key Financial Statistics

As of and for the quarter ended March 31, 2024

Cash, cash equivalents & investments	\$110.1M
GAAP Operating Expenses	\$28.1M
Non-GAAP Operating Expenses*	\$26.6M
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
 - \$25M tranche available upon FDA approval of avotometinib for treatment of LGSOC
 - 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

Recent Corporate 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"> ✓ Initiating rolling NDA submission in recurrent KRAS mt LGSOC ✓ Received FDA Orphan Drug Designation ✓ Initiated Phase 3 confirmatory study in Q4'23 ✓ Presented planned subgroup analysis of Part A RAMP 201 trial 	<ul style="list-style-type: none"> ✓ Initial interim safety and efficacy results from RAMP 205 to be presented at ASCO 2024 ✓ Initiated RAMP 205 combo avutometinib + gemcitabine/nab-paclitaxel + defactinib 	<ul style="list-style-type: none"> ✓ Received FDA Fast Track Designation for avutometinib in combination with Mirati's (BMS) G12C inhibitor adagrasib ✓ Received FDA Fast Track Designation and for avutometinib plus defactinib with Amgen's G12C inhibitor sotorasib ✓ Received FDA Fast Track Designation for avutometinib in combo with Amgen's G12C inhibitor sotorasib ✓ Presented initial interim results from Phase I/2 RAMP 203 trial of avutometinib + sotorasib 	<ul style="list-style-type: none"> ✓ Established discovery and development collaboration with GenFleet ✓ Presented preclinical data of GFH375/VS-7375, a potential best-in-class oral KRAS G12D (ON/OFF) inhibitor, at AACR 2024 ✓ IND application was filed in China and accepted for review in Q1'24



THANK YOU

Addendum

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 and overlap, with the orange stripe being the most prominent and widest. The overall design is clean and professional.

Recurrent LGSOC: High Medical Need

No Approved Treatment Options – Limited Benefit from Available Therapies

Recurrent Low-Grade Ovarian Cancer – Treatment Guidelines¹

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)

Avutometinib Patent Exclusivity

Composition of Matter

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



Previous experience:

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

Dan Calkins
Chief Financial Officer



Previous experience:

- Technical Accounting Consultant- CFGI
- PwC LLP

Cathy Carew
Chief Organizational Effectiveness Officer



Previous experience:

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

Mike Crowther
Chief Commercial and Business Strategy Officer



Previous experience:

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

John Hayslip, M.D.
Chief Medical Officer



Previous experience:

- CMO, I-MAB
- Nektar Therapeutics, AbbVie
- Director of clinical research and data management, University of Kentucky's Markey Cancer Center

Jonathan Pachter, Ph.D.
Chief Scientific Officer



Previous experience:

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

Colleen Mockbee
Global Head of Regulatory Affairs and Development



Previous experience:

- Chief Development Officer & SVP of Regulatory, OncXerna
- Head of Global Regulatory, Lilly Oncology