



Corporate Presentation

November 2023



Disclaimers

This presentation includes forward-looking statements about, among other things, Verastem Oncology's programs and product candidates, including anticipated regulatory submissions, approvals, performance and potential benefits of Verastem Oncology's product candidates, as well as Verastem Oncology's potential income under its asset purchase agreement with Secura Bio. Inc. and borrowings under its credit facility, that are subject to substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. 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 defactinib and other compounds in combination with avutometinib (VS-6766); the occurrence of adverse safety events and/or unexpected concerns that may arise from additional data or analysis or result in unmanageable safety profiles as compared to their levels of efficacy; or our ability to obtain, maintain and enforce patent and other intellectual property protection for our product candidates.

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, 2022, as filed with the Securities and Exchange Commission (SEC) on March 14, 2023, and in any subsequent filings with the SEC, which are available at www.sec.gov and www.verastem.com.

The forward-looking statements in this presentation speak only as of the original date of this presentation, and we undertake no obligation to update or revise any of these statements.

This presentation contains references to our non-GAAP operating expense, a financial measure that is not calculated in accordance with generally accepted accounting principles in the US ("GAAP"). This non-GAAP financial measure excludes certain amounts or expenses from the corresponding financial measures determined in accordance with GAAP. Management believes this non-GAAP information is useful for investors, taken in conjunction with the Company's GAAP financial statements, because it provides greater transparency and period-over-period comparability with respect to the Company's operating performance and can enhance investors' ability to identify operating trends in the Company's business. Management uses these measures, among other factors, to assess and analyze operational results and trends and to make financial and operational decisions. Non-GAAP information is not prepared under a comprehensive set of accounting rules and should only be used to supplement an understanding of the Company's operating results as reported under GAAP, not in isolation or as a substitute for, or superior to, financial information prepared and presented in accordance with GAAP. In addition, this non-GAAP financial measure is unlikely to be comparable with non-GAAP information provided by other companies. The determination of the amounts that are excluded from non-GAAP financial measures is a matter of management judgment and depends upon, among other factors, the nature of the underlying expense or income amounts. Reconciliations between these non-GAAP financial measures and the most comparable GAAP financial measures are included in the footnotes to the slides in this presentation on which a non-GAAP number appears.

Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third party sources and Verastem Oncology's own internal estimates and research. While Verastem Oncology believes these third party sources to be reliable as of the date of this presentation, it has not independently verified, and makes no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third party sources. In addition, all of the market data included in this presentation involves a number of assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions.

Verastem Oncology

Well Positioned to Capitalize on Growth Opportunities

Lead clinical program has best-in-class potential

Avutometinib (VS-6766; RAF/MEK clamp) and defactinib (FAK inhibitor) are clinically active against RAS pathway-driven cancers

Rapid development path to market in LGSOC

FDA Breakthrough Therapy Designation; Updated data from Part A of RAMP 201 trial show a confirmed objective response rate of 45% in patients with recurrent low-grade serous ovarian cancer treated with avutometinib and defactinib; target enrollment was achieved in January 2023; timing of accelerated approval filing to be based on data maturity and finalization of confirmatory study plans

Significant downstream market opportunity and blockbuster potential

30% of all human cancers are driven by mutations in RAS; Avutometinib combinations potentially broadly applicable across a variety of tumor types.

Clinical collaborations with Amgen & Mirati evaluating the combinations of avutometinib with sotorasib & adagrasib, respectively, in KRAS G12C NSCLC supported by strong pre-clinical rationale
Multiple clinical studies in progress evaluating avutometinib combinations across RAS pathway-driven cancers

Additional Discovery Programs

The collaboration with GenFleet Therapeutics adds the potential for 3 small molecule programs to the discovery pipeline

Strong balance sheet

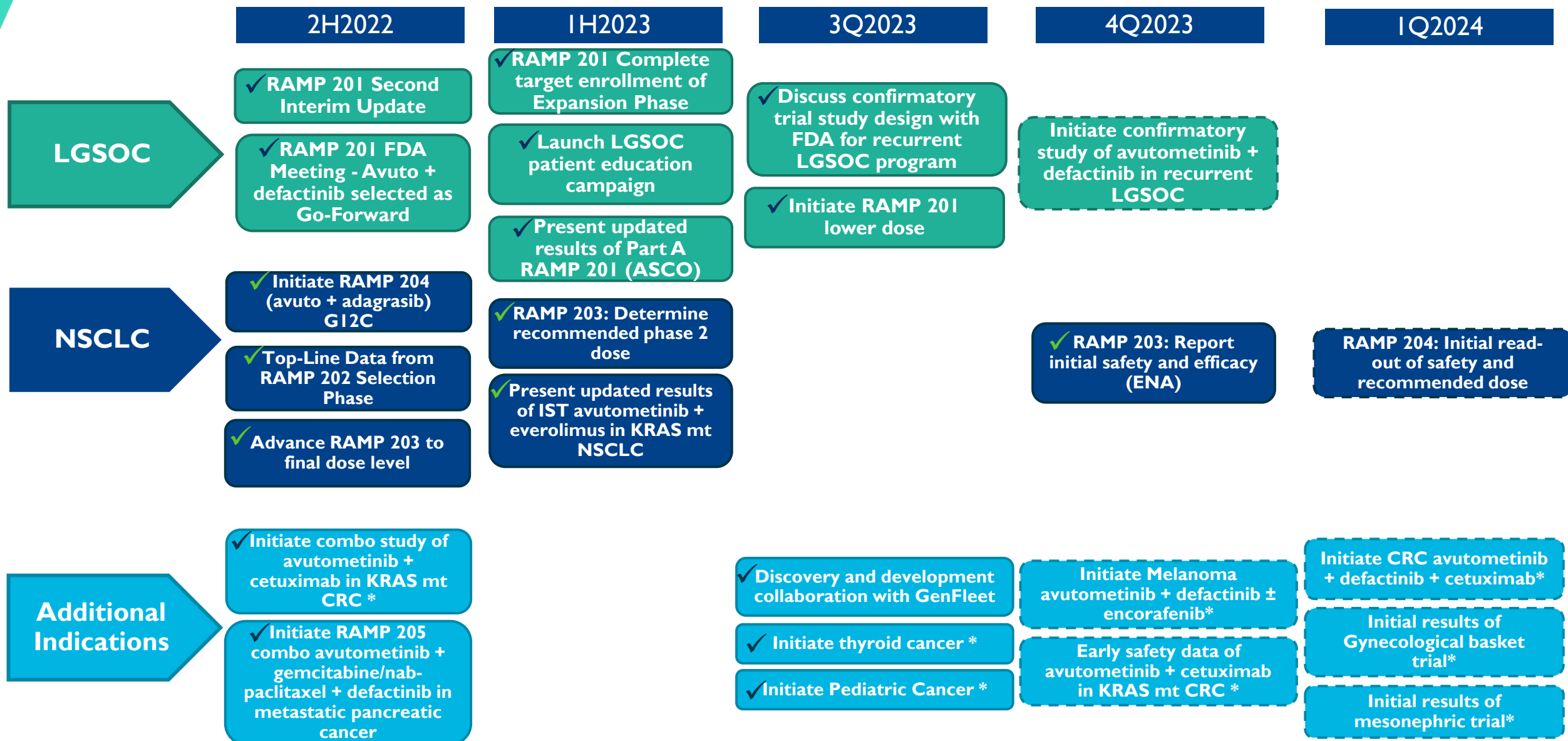
Cash and investments balance of \$165.7 million as of September 30, 2023
Up to \$150 million of non-dilutive funding available from credit facility

Company ended Q3 2023 with \$21.3 million GAAP operating expenses and \$19.8 million non-GAAP operating expenses* 3

We are a biopharmaceutical company committed to developing and commercializing new medicines for patients battling cancer

* Q3 2023 GAAP operating expenses - \$21.31M less Q3 2023 stock compensation of \$1.52M = \$19.79M Q3 2023 non-GAAP operating expenses

Key VSTM Achievements & Anticipated Milestones





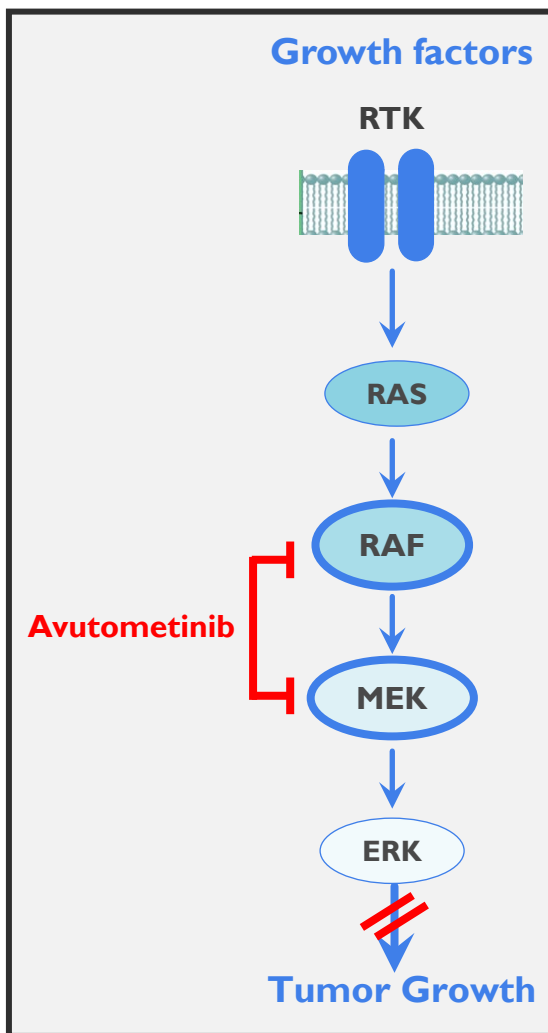
Avutometinib RAF/MEK Clamp Program Overview

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

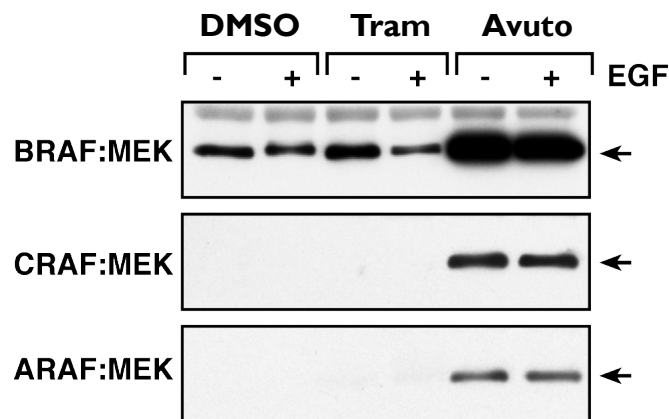
- Unique RAF/MEK clamp mechanism of action
- Novel intermittent dosing schedule; convenient oral regimen
- Breakthrough Therapy Designation for combination of avutometinib and defactinib for treatment of recurrent low-grade serous ovarian cancer (LGSOC) after one or more prior lines of therapy including platinum-based chemotherapy
- 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
- Preclinical anti-proliferative activity across multiple MAPK pathway alterations (e.g. KRAS, NRAS, BRAF, NFI mt) and multiple solid tumor indications
- Strong preclinical combination data with other agents targeting RAS pathway (e.g. KRAS G12C inhibitors) and parallel pathways (e.g. FAK inhibitors)

Avutometinib is a Unique Small Molecule RAF/MEK Clamp

Contrasting Mechanism of Action vs. MEK-Only Inhibitors



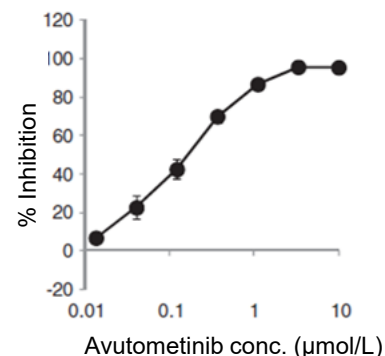
Avutometinib induces dominant negative RAF/MEK complexes



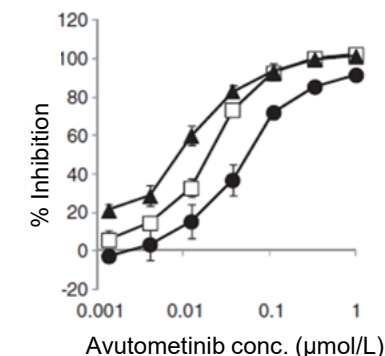
Collaboration with Deborah Morrison, NCI

Avutometinib inhibits both RAF and MEK activities

MEK1
IC₅₀: 0.16 ± 0.043 μmol/L



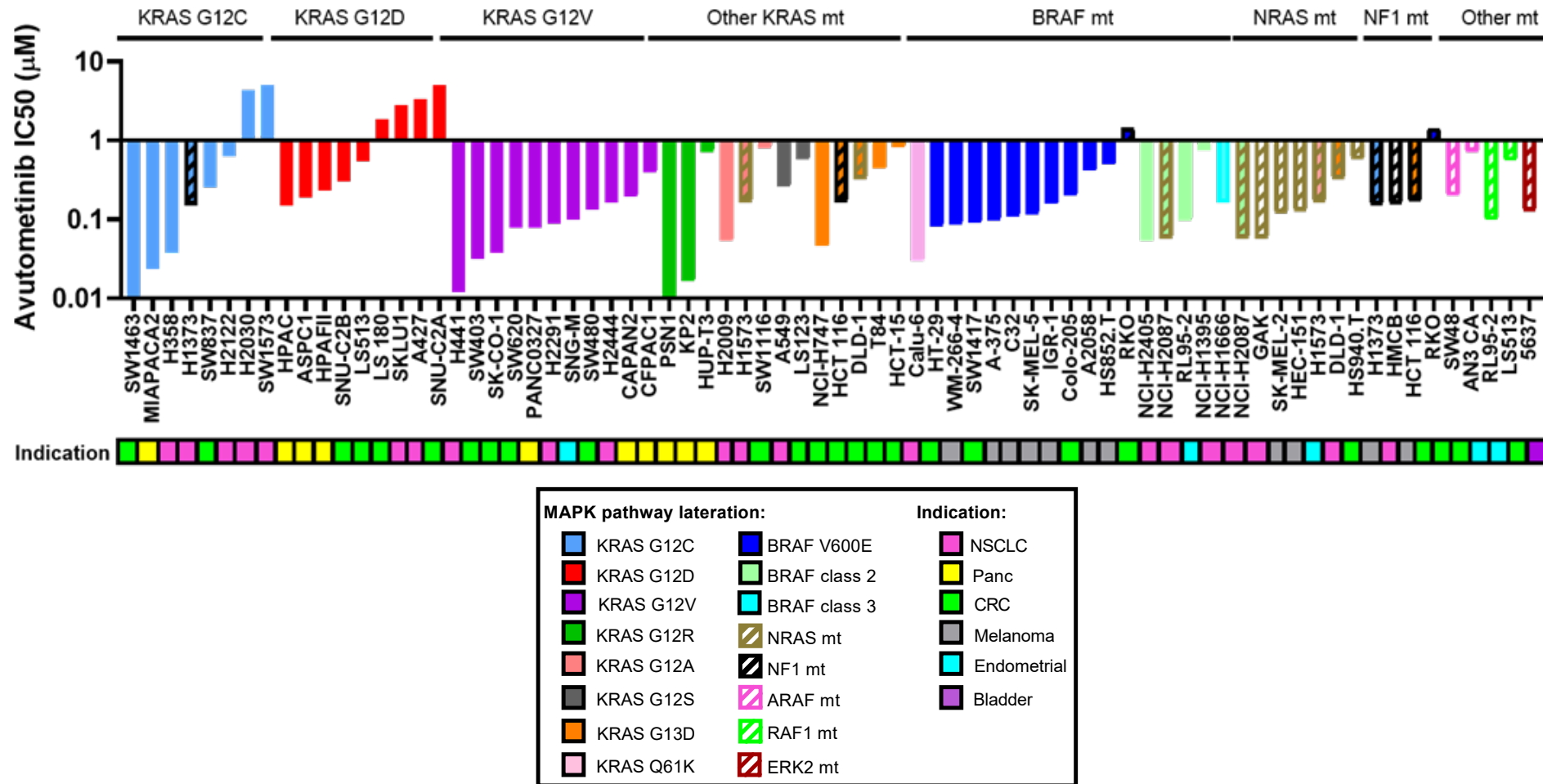
RAF family
IC₅₀(CRAF●): 0.056 ± 0.016 μmol/L
IC₅₀(BRAF□): 0.019 ± 0.0030 μmol/L
IC₅₀(BRAF V600E▲): 0.0082 ± 0.0015 μmol/L



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



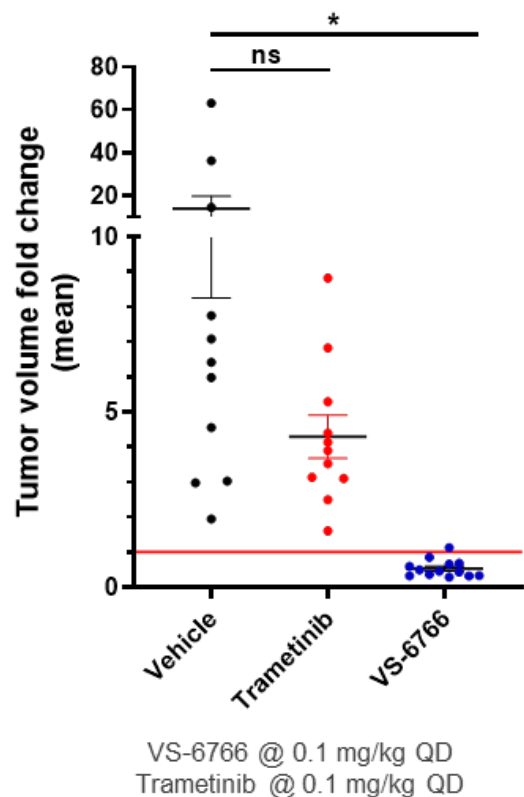
Avutometinib Inhibits Cell Proliferation Across Multiple RAS/MAPK Pathway Alterations and Multiple Solid Tumor Histologies



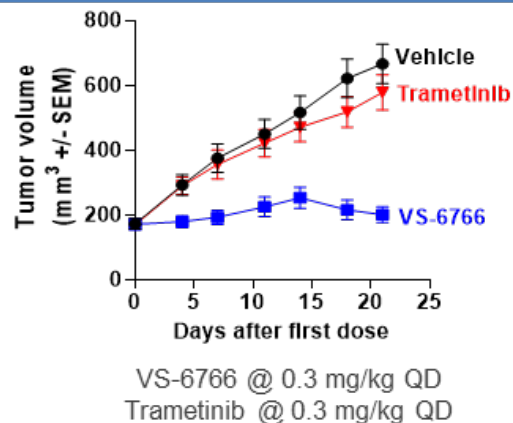
Avutometinib (VS-6766) Anti-Tumor Activity in KRAS Mutant Models

Superiority vs. Trametinib

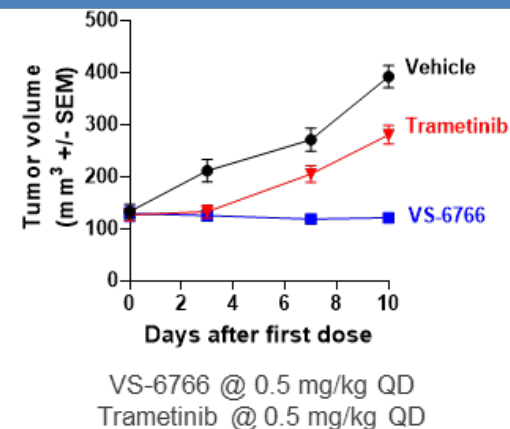
KRAS G12V mt/Trp53KO NSCLC GEMM



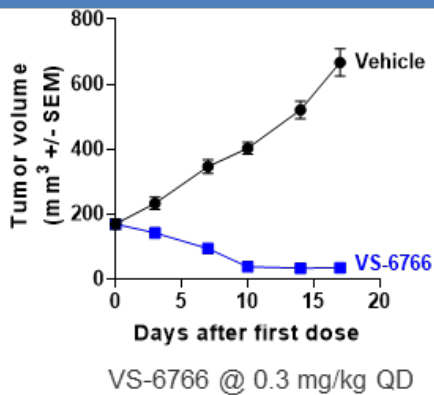
H358 KRAS G12C mt NSCLC



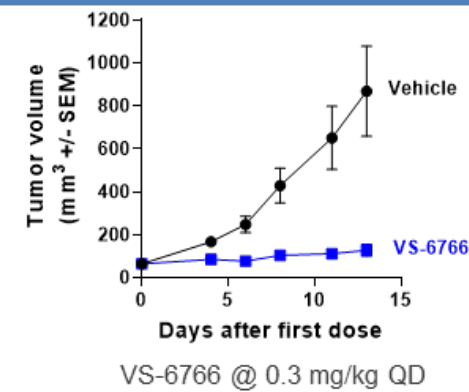
TOV21G KRAS G13D mt ovarian cancer



MiaPaca2 KRAS G12C mt pancreatic cancer



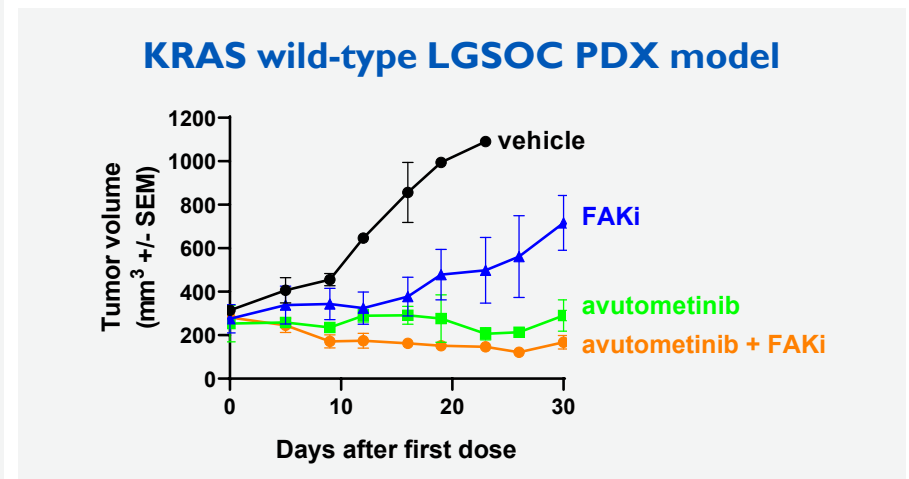
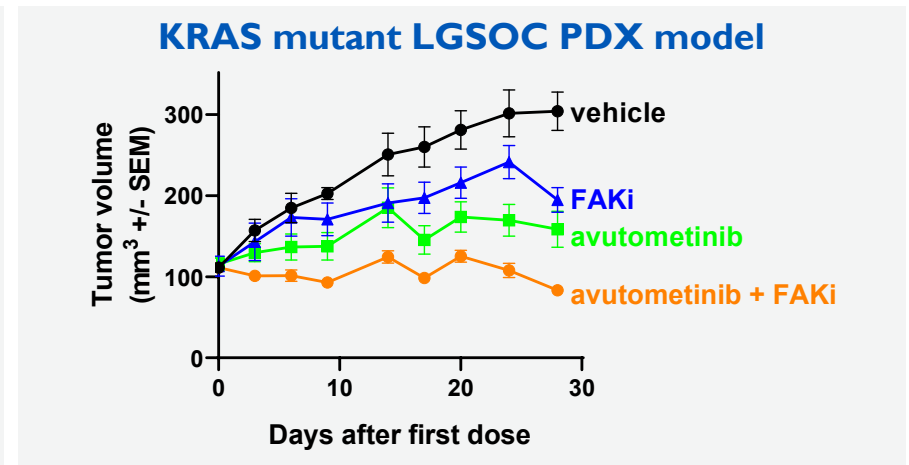
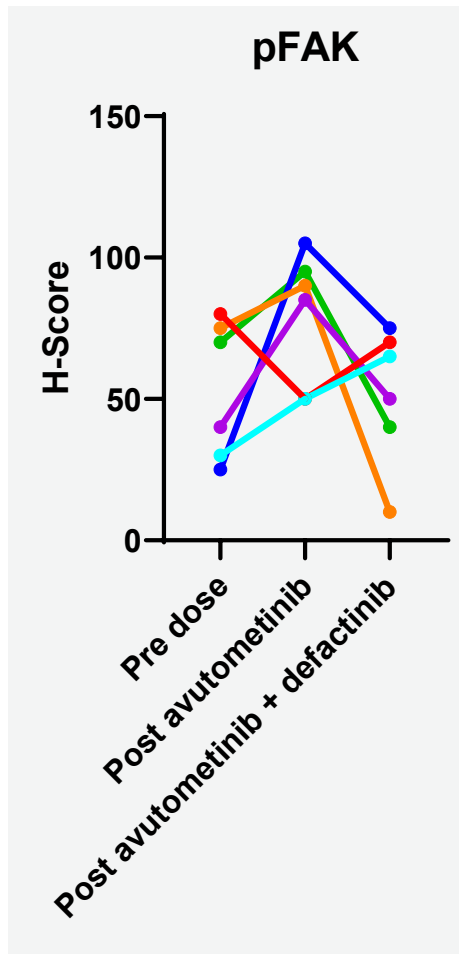
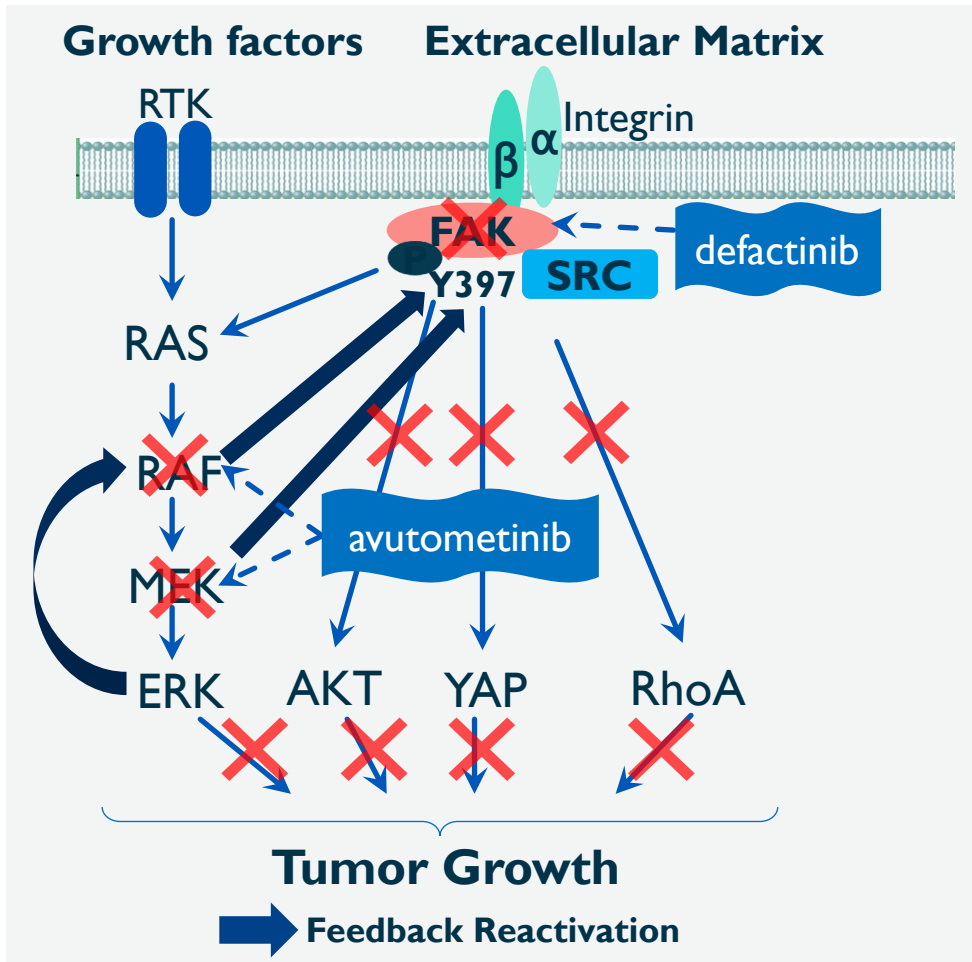
CT26 KRAS G12D mt colorectal cancer



Collaboration with Mariano Barbacid, CNIO (Spain)

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	Collaborator
Gynecologic Cancers	RAMP201 LGSOC	Prevalence ¹ : 6K	 70%	Avutometinib + defactinib	Relapsed Refractory molecularly profiled LGSOC	
	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	
NSCLC Adenocarcinoma	RAMP203 and 204 KRAS G12C	Incidence ^{2,3} : 114K	 13%	Avutometinib + sotorasib	Recurrent KRAS G12C with prior KRAS G12C inhibitor(i) treatment or KRAS G12Ci naïve	
	RAMP202 BRAF mt	Incidence ^{2,3} : 114K	 4.5%	Avutometinib + adagrasib	Recurrent KRAS G12C with prior KRAS G12Ci treatment that progressed	
Pancreatic	RAMP205 PDAC	Incidence ⁴ : 58K	 98%	Avutometinib + defactinib + gemcitabine/nab-paclitaxel	Previously untreated (front-line) metastatic pancreatic ductal adenocarcinoma (PDAC)	
CRC	KRAS mt*	Incidence ⁵ : 148K	 45%	Avutometinib + cetuximab	Recurrent metastatic KRAS mt	
Breast Cancer	ER+*	Incidence ⁵ : 279K	 22.5%	Avutometinib + abemaciclib + fulvestrant	Recurrent ER+/HER2- breast cancer following progression on CDK4/6i + aromatase inhibitor	
Thyroid	MAPK alterations*+	Incidence ⁴ : 44K	 35%	Avutometinib + defactinib	Differentiated & anaplastic thyroid cancer	

*IST †excluding BRAFV600E

¹References: 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/#:~:text=High%2Dgrade%20serous%20carcinoma%20is,unless%20another%20type%20is%20specified.>)

Robust Clinical Program: Avutometinib in multiple combinations across RAS/MAPK pathway-driven tumors

INDICATION	REGIMEN	STUDY NAME	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	CLINICAL COLLABORATION WITH
LGSOC ¹	Avutometinib + defactinib	RAMP 201				Registration-directed trial: accelerated approval cohort fully enrolled	
R/R LGSOC	Avutometinib + defactinib	IST-FRAME					
Gynecological Cancers (RAS Pathway-driven)	Avutometinib + defactinib	IST					
Mesonephric ²	Avutometinib + defactinib	IST					
R/R NSCLC (BRAF mt)	Avutometinib + defactinib	RAMP 202				 	
R/R NSCLC (KRAS G12C)	Avutometinib + sotorasib	RAMP 203					
R/R NSCLC (KRAS G12C)	Avutometinib + adagrasib	RAMP 204					
Pancreatic Ductal Adenocarcinoma	Avutometinib + gemcitabine/nab-paclitaxel + defactinib	RAMP 205					
R/R Colorectal Cancer (KRAS mt)	Avutometinib + cetuximab (EGFRi)	IST					
ER+ Breast Cancer	Avutometinib + abemaciclib + fulvestrant	IST					
Thyroid Cancer ²	Avutometinib + defactinib	IST					



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

➤ Breakthrough Therapy Designation was 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

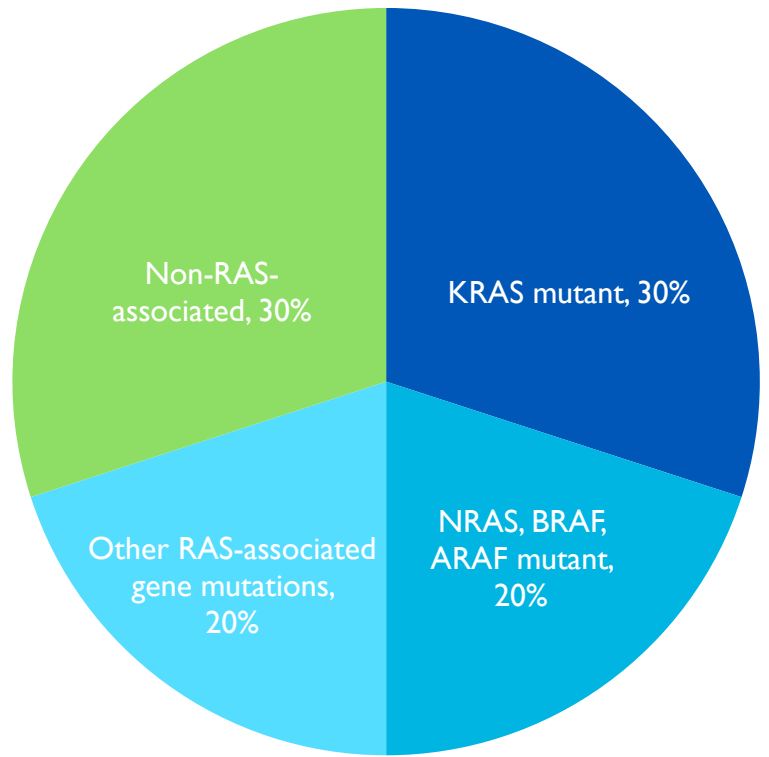
● 1,000 to 2,000 patients in the U.S. and 15,000 to 30,000 worldwide diagnosed with LGSOC each year

● 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 high grade serous ovarian cancer (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

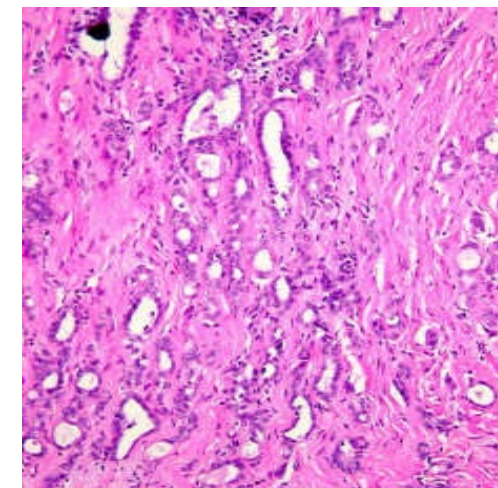


References: AACR Project GENIE Cohort v9.0-public and Verastem unpublished analysis

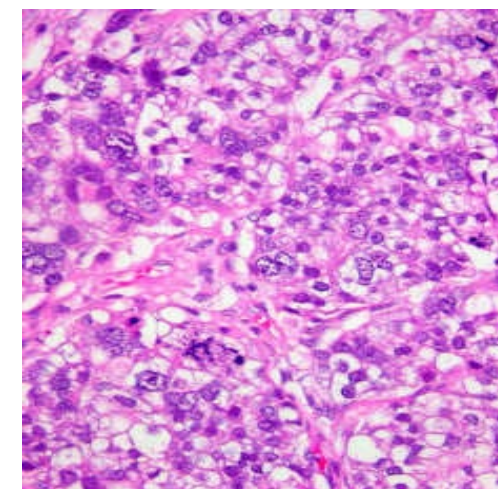


Low-Grade and High-Grade Serous Ovarian Cancer Are Different Diseases

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 +++ BRCA1/2 +
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 bevacizumab^{1,11} (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

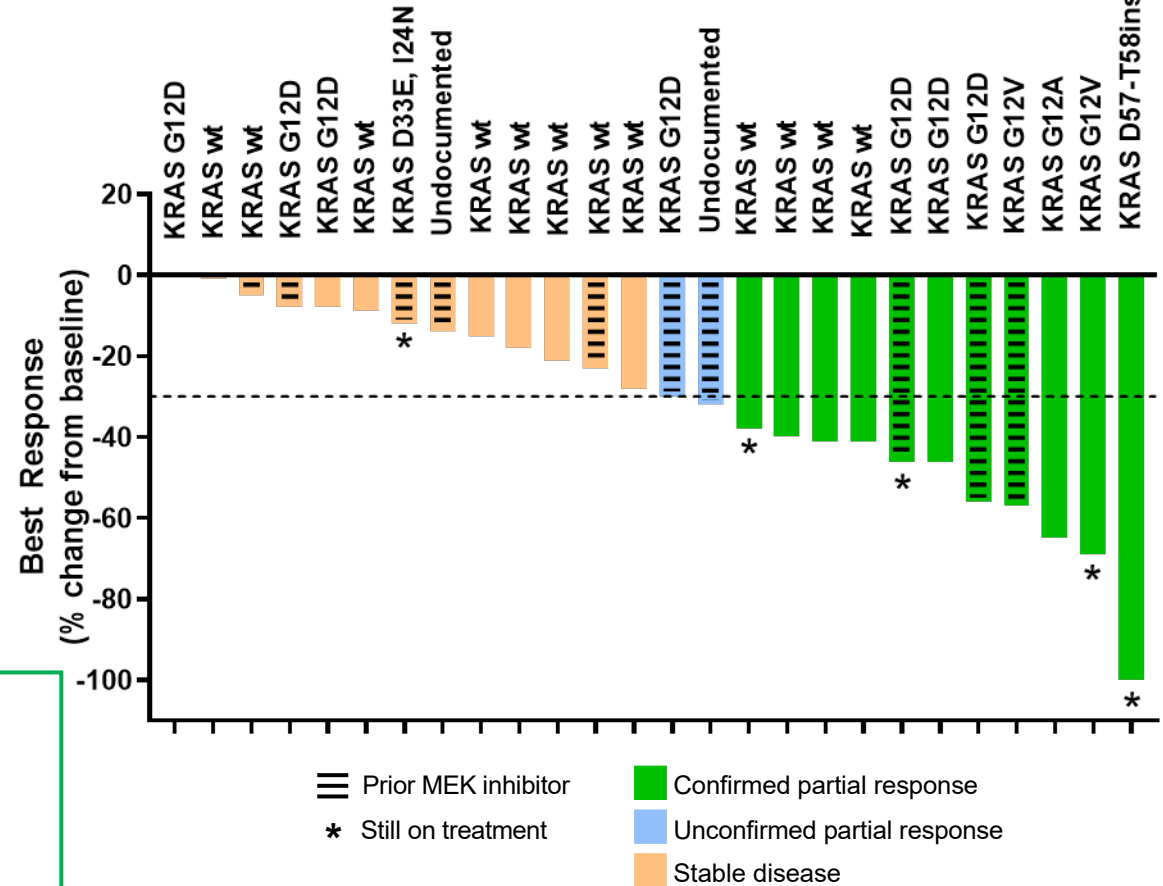
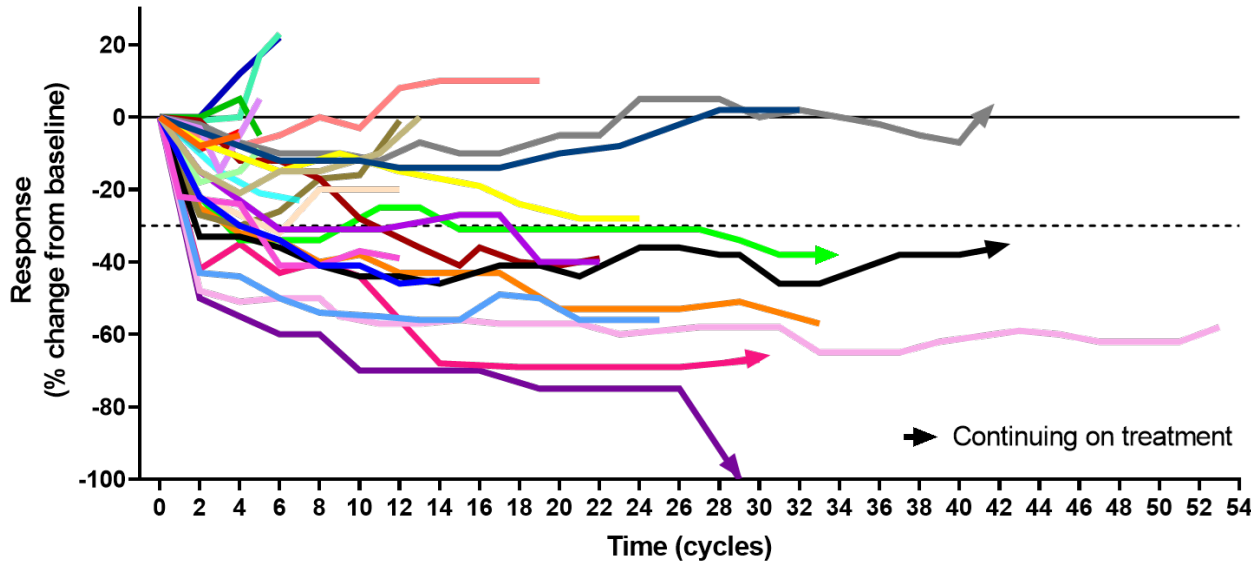
² MILO Study Monk et al., J Clin Oncol 2020.

* 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 Low Grade Serous Ovarian Cancer (n=26)

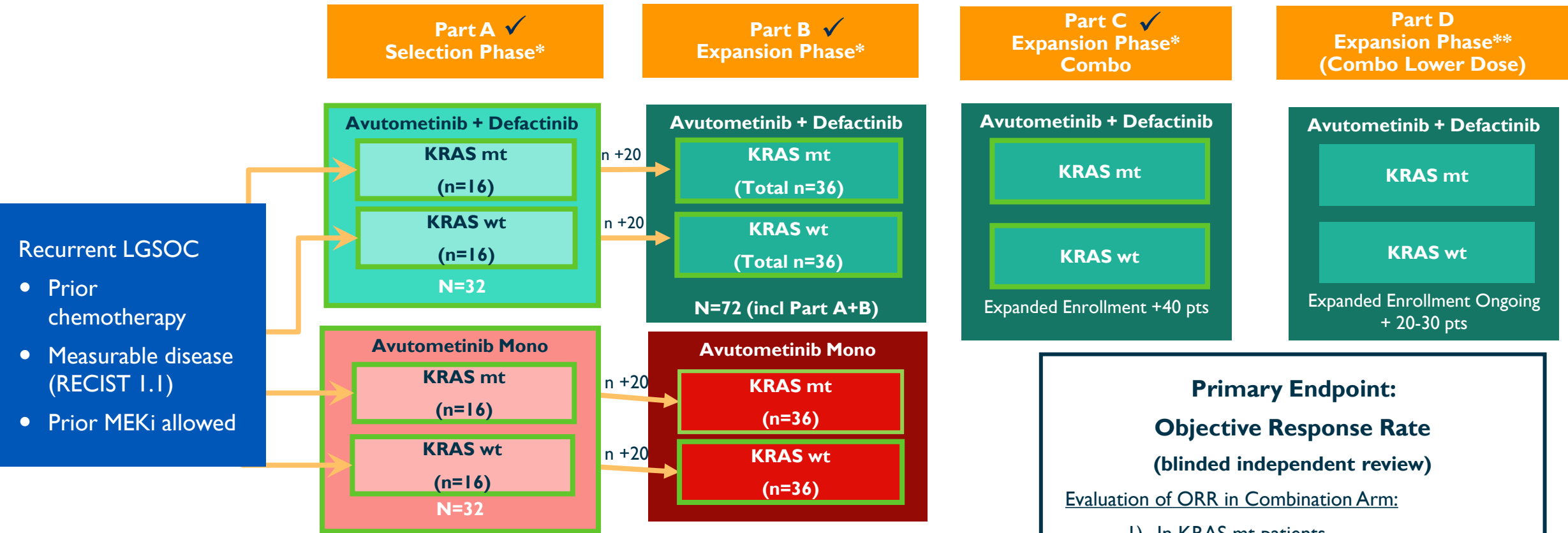
Response by RECIST



- 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 (ENGOT060/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

Combination Arm:

- ✓ Target Enrollment Reached (N=72)
- ❖ Expanded Enrollment Ongoing (Lower Dose)

Updated Data from Part A of RAMP 201

	Avutometinib + Defactinib	
	Total (n=29)	
ORR, % (n)	45% (13) 95% CI: (26%, 64%)	
	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 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)
- Finalizing the design of a randomized confirmatory trial with the FDA, which is planned to begin in the second half of 2023

“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

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

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)
1	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.

BICR, blinded independent central review; mt, mutant; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease; wt, wild type

Combination of Avutometinib and Defactinib

High Disease Control Rate + Tumor Reduction in Recurrent LGSOC

Part A (Evaluable for Efficacy *)

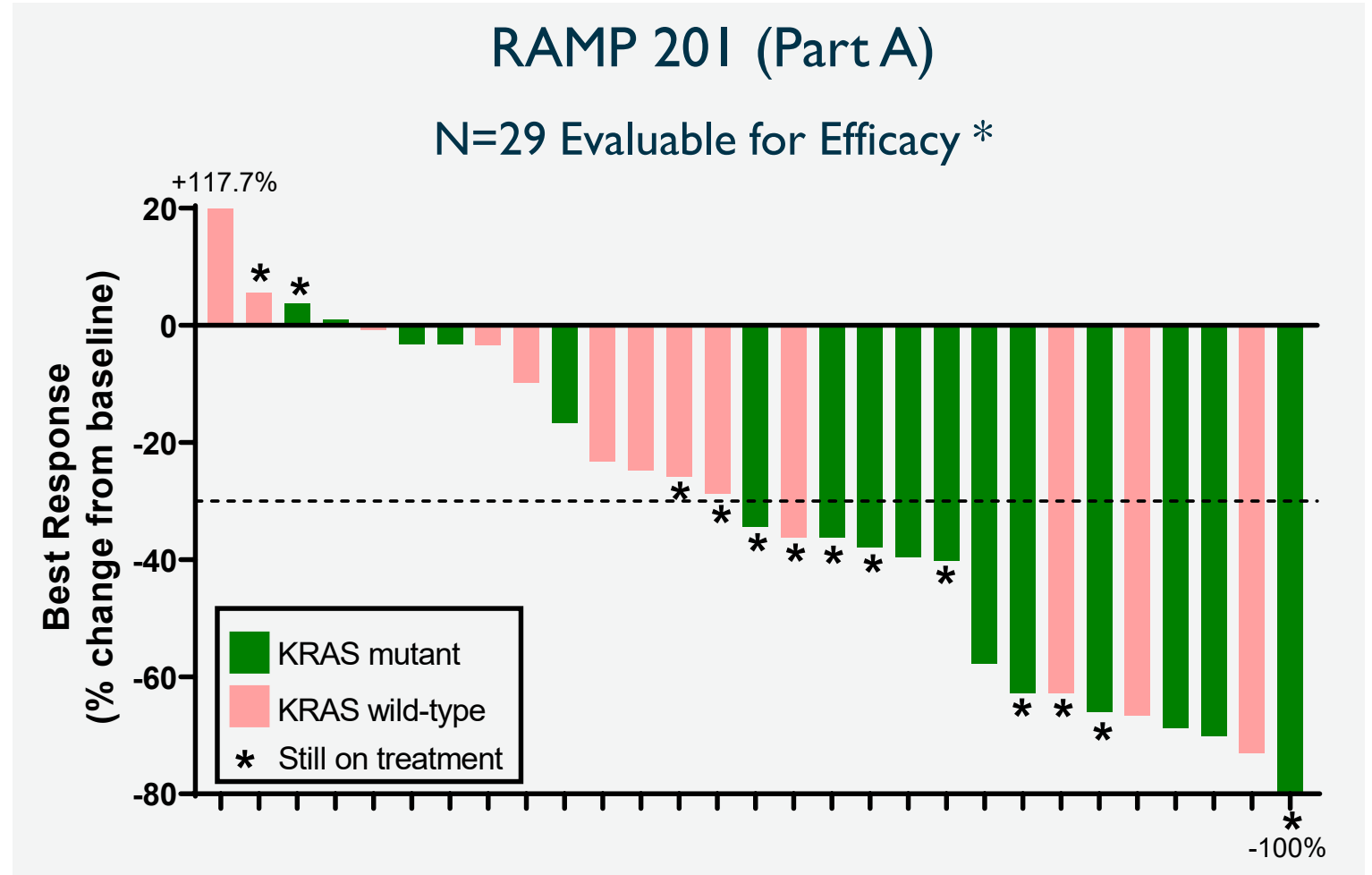
Confirmed ORR: **45%**

Confirmed/Unconfirmed ORR: **52%**

Disease Control Rate (SD+PR): **90%**

Patients still on study treatment: 45%

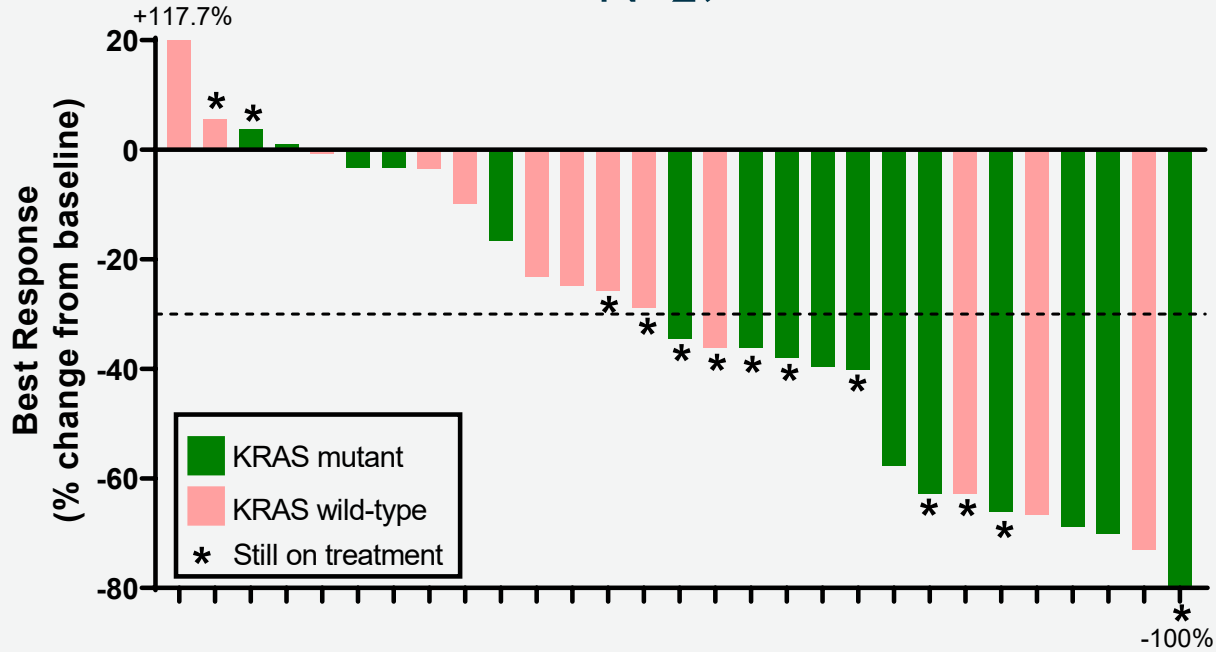
Minimum follow-up: 12 months



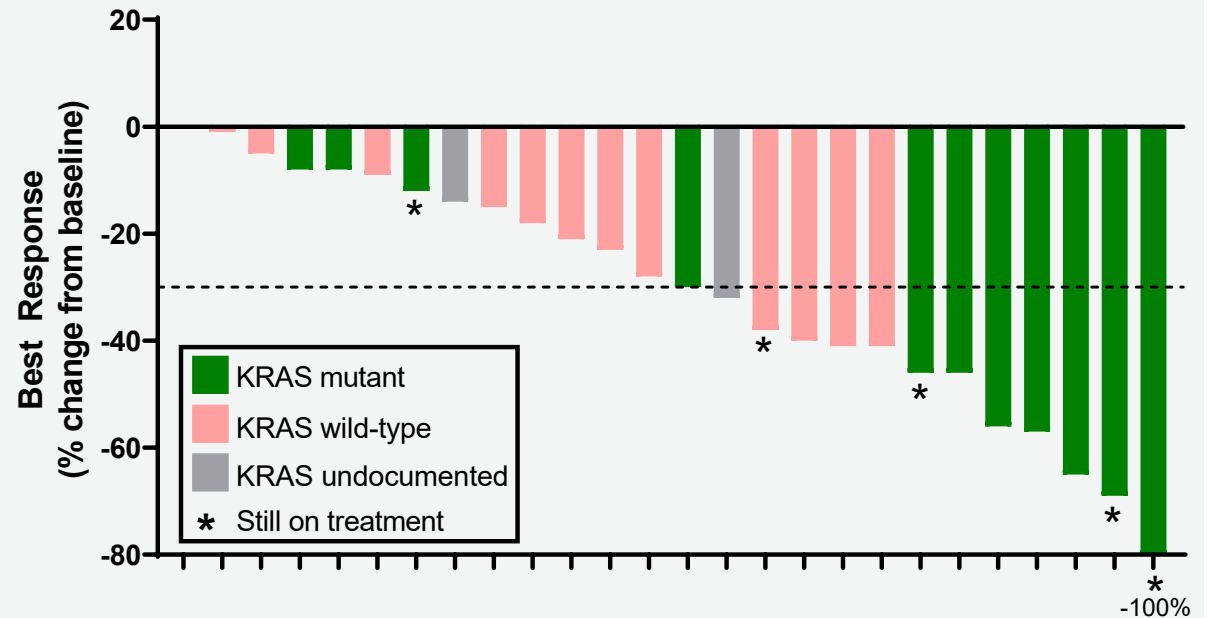
Combination of Avutometinib and Defactinib

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

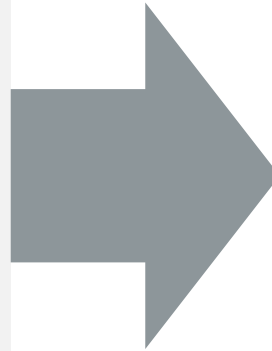
- Majority of adverse events are mild to moderate and manageable/reversible¹
- Few discontinuations due to adverse events (12.3% in combo due to \geq 1 TEAE 4.9% due to elevated blood CPK*)
 - * No association to date with clinically significant toxicities, including rhabdomyolysis

Avutometinib + Defactinib (n=81)		
	Any Grade	Grade \geq 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)

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

Update

- Combination of avutometinib with defactinib selected as go forward treatment regimen
- Combination development continues in all recurrent LGSOC, regardless of KRAS status
- Encouraging efficacy results include independently confirmed responses
- No new safety signals; few discontinuations due to adverse events
- Updated RAMP 201 Part A data presented at ASCO 2023
- Design of Phase 3 Confirmatory Trial finalized with FDA

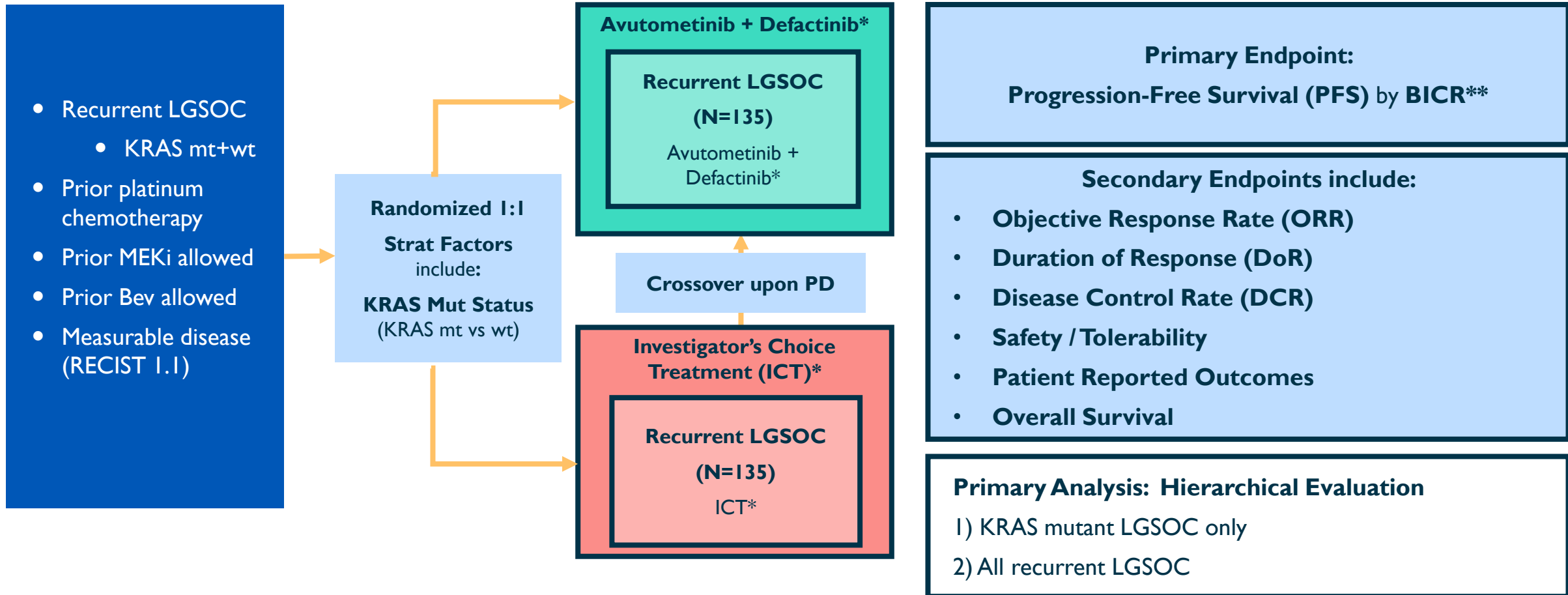


Next Steps

- Target enrollment for primary analysis (n=72) in combination has been achieved
- Plan to file for accelerated approval based on the totality of the data from the RAMP 201 and FRAME studies
- The Company plans to initiate the phase 3 confirmatory study in 2H 2023

❖ RAMP-301: Prospective Randomized Controlled Trial

Forward Plan: **Confirmatory Trial** – Randomized Controlled Trial (RCT)

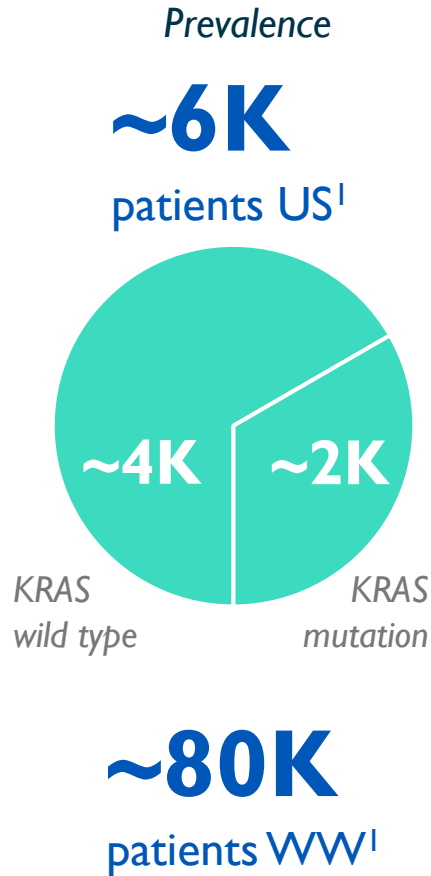


*A+D Dosing: Avutometinib 3.2 mg PO 2x/wk 21/28 days + Defactinib 200mg PO BID: 21/28 days

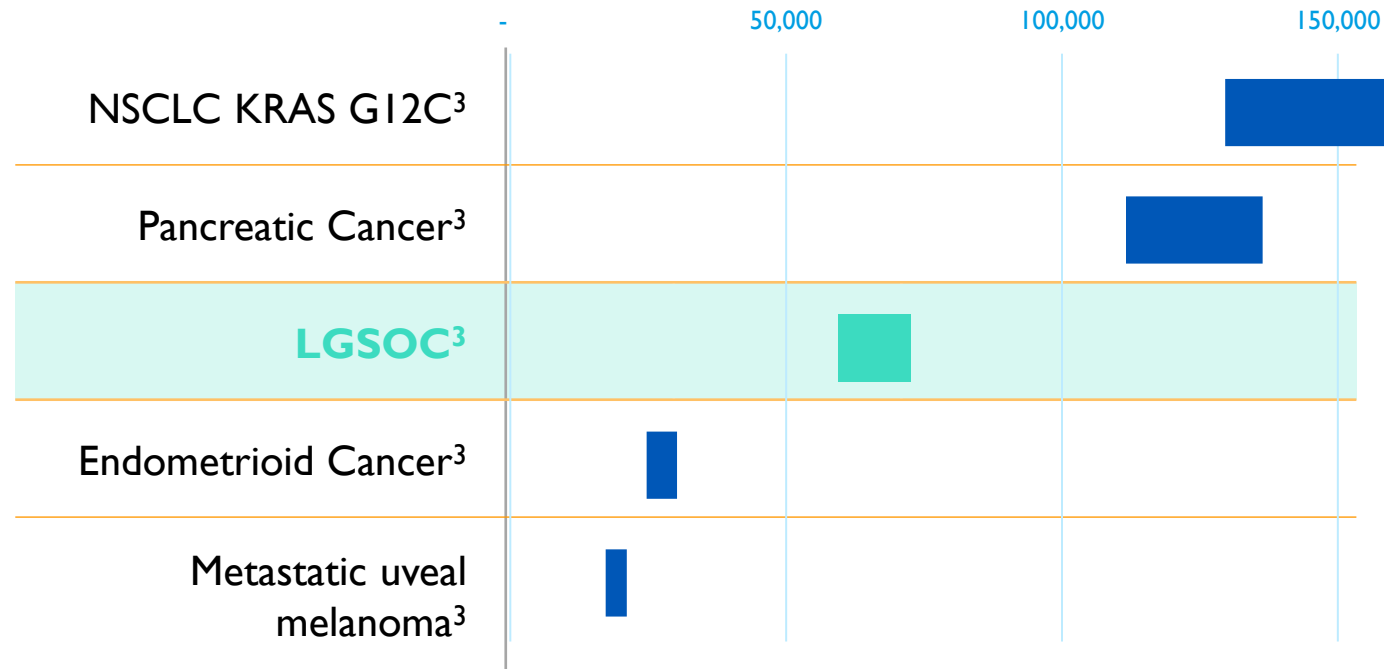
*Chemo Hormonal ICT: Liposomal doxorubicin (PLD), Paclitaxel, Topotecan, Letrozole, Anastrozole

** BICR: Blinded Independent Central Review

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



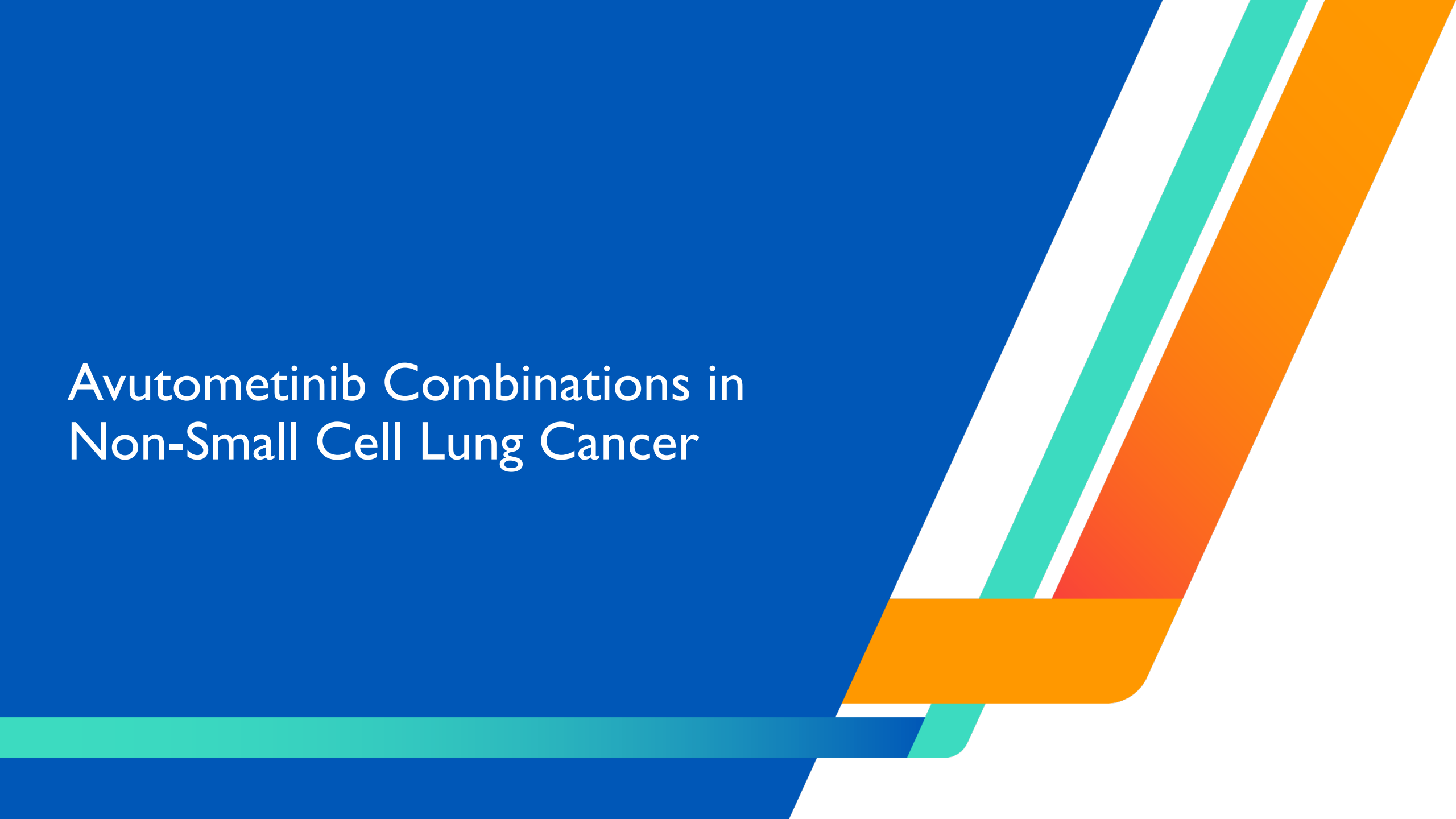
Patient-months of Therapy Per Year² (across all 2L+ patients)



¹ References: 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

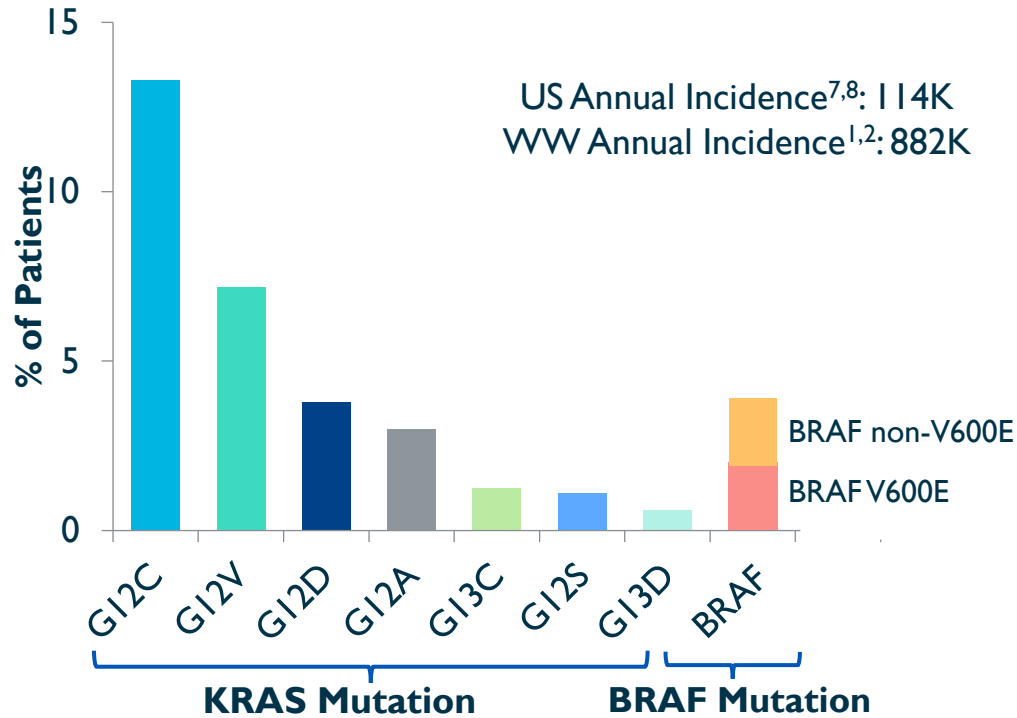
³ NSCLC KRAS G12C 2nd line patients (incidence); Pancreatic RAS/RAF mutant 2nd-line patients (incidence); LGSOC KRAS mutant and wild-type patients (prevalence); Endometrioid RAS/RAF mutant 2nd-line patients (incidence); Uveal melanoma RAS/RAF mutant 2nd-line patients (incidence)



Avutometinib Combinations in Non-Small Cell Lung Cancer

High Unmet Need in Refractory KRAS & BRAF mt NSCLC Adenocarcinoma

NSCLC Adenocarcinoma³

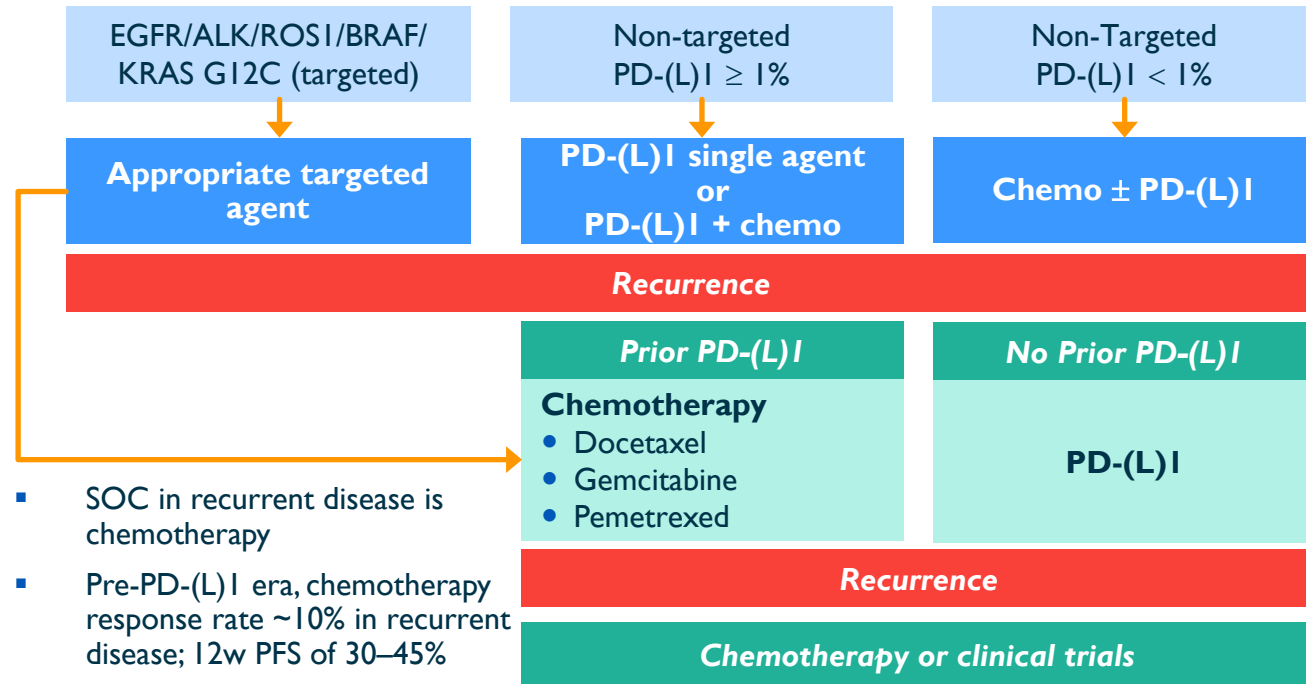


KRAS Mutations Represent 25% of Lung Adenocarcinoma & BRAF Mutations Represent ~4% (EGFR 17%, ALK 7%)^{4,6}

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
- RAMP 202: Avutometinib + defactinib in BRAFV600E and non-V600E NSCLC

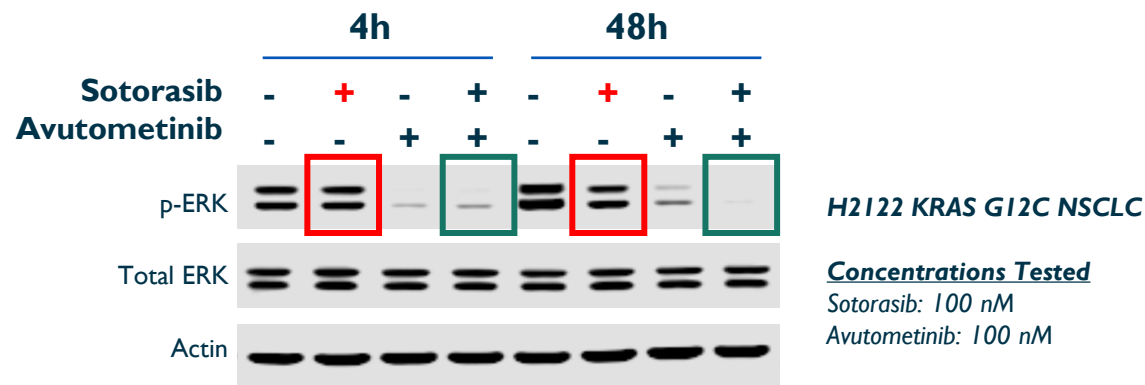
Preclinical Synergy of Avutometinib + G12C Inhibitors in KRAS G12C Models

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

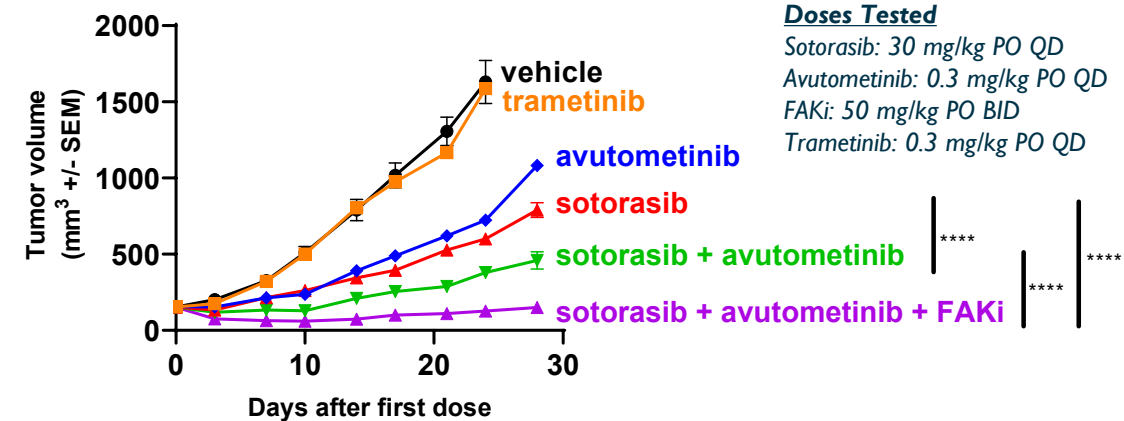
Cell line	Indication	Sensitivity to G12C inhibitors	Combined Synergy Score	
			Avutometinib + sotorasib	Avutometinib + adagrasib
H2122	NSCLC	Moderately sensitive	44.7	44.6
H1373	NSCLC	Sensitive	10.0	3.4
SW1573	NSCLC	Insensitive	8.6	12.0
H358	NSCLC	Sensitive	6.9	5.4
H2030	NSCLC	Moderately sensitive	5.1	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

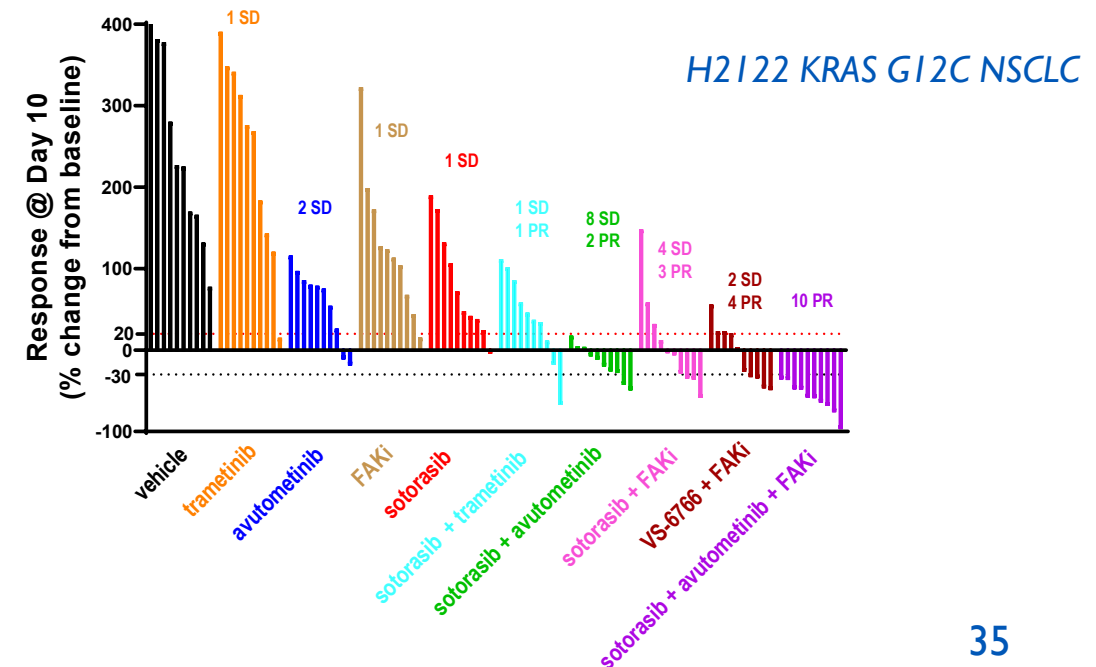


Avutometinib & FAKi potentiate sotorasib efficacy in KRAS G12C NSCLC in vivo; Tumor regression in all mice with triple combination



Doses Tested

Sotorasib: 30 mg/kg PO QD
 Avutometinib: 0.3 mg/kg PO QD
 FAKi: 50 mg/kg PO BID
 Trametinib: 0.3 mg/kg PO QD



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

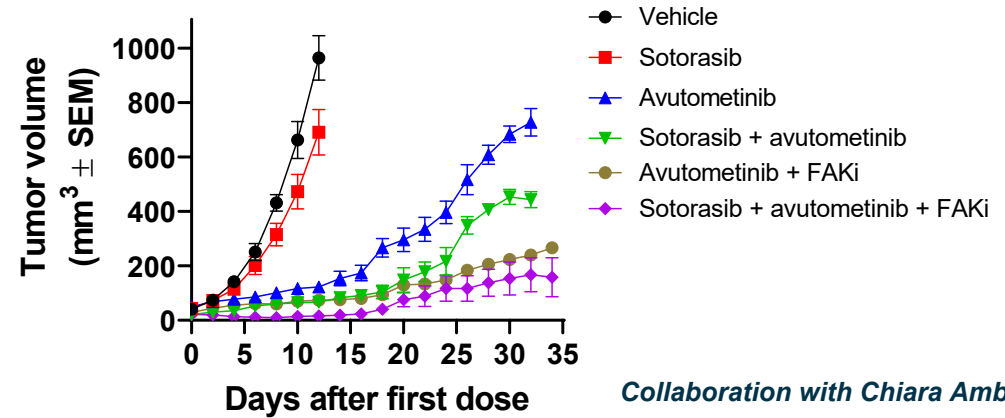
Avutometinib is effective against acquired KRAS mutations that occur clinically upon progression on G12C inhibitors

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

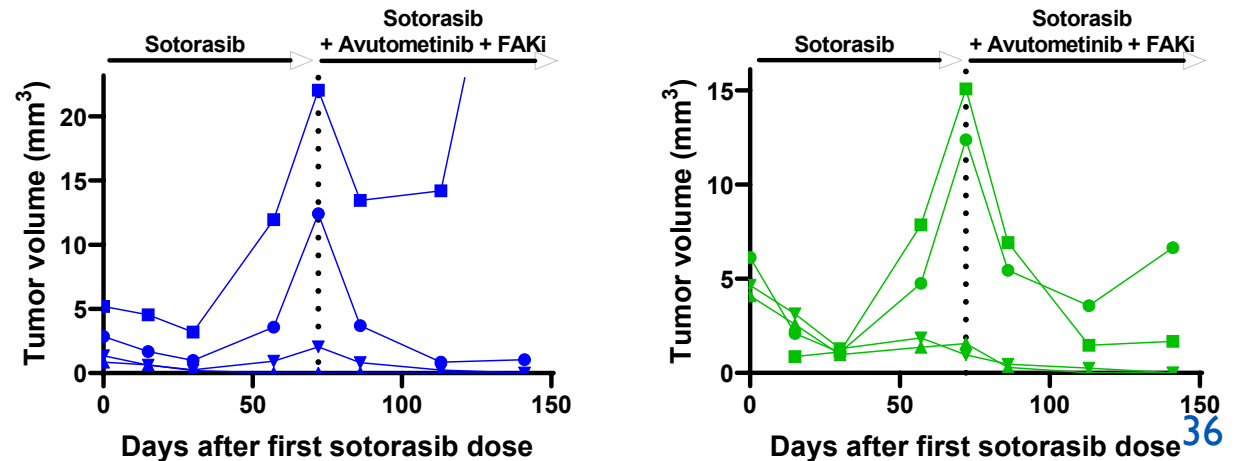
<30 nM 30 - 150 nM >150 nM

Collaboration with Andy Aguirre, DFCI

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



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



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

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

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

- 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

Completed enrollment

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

RP2D Selected*

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

Now enrolling expansion phase

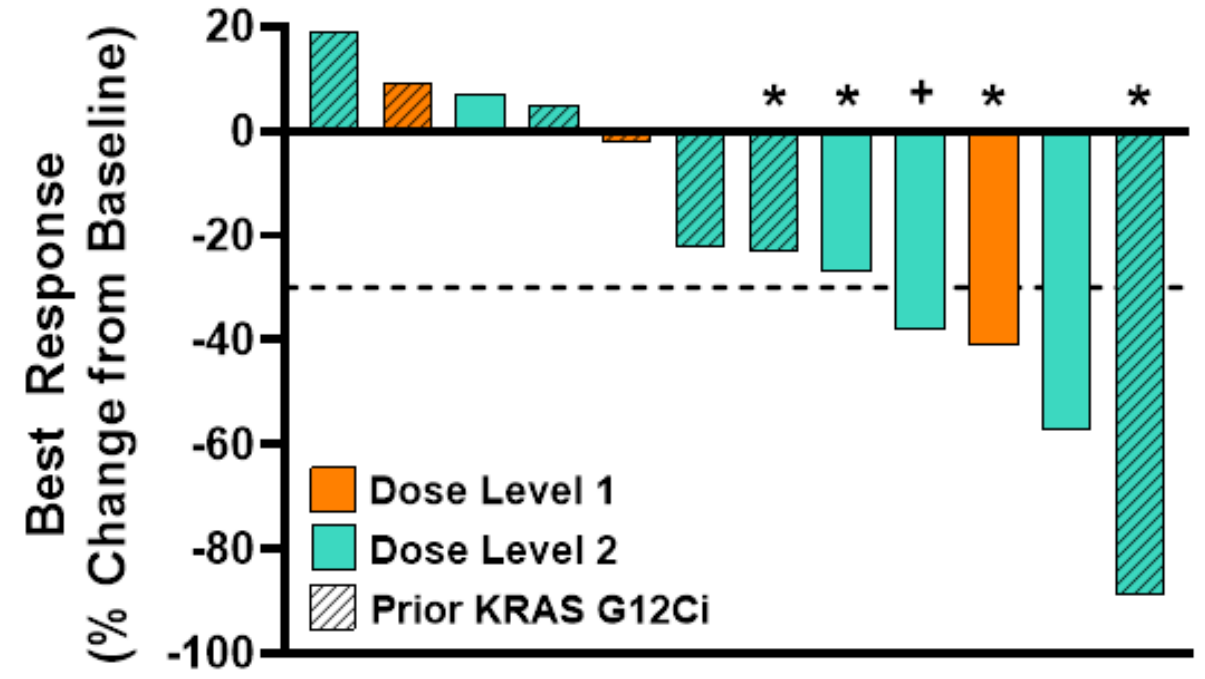
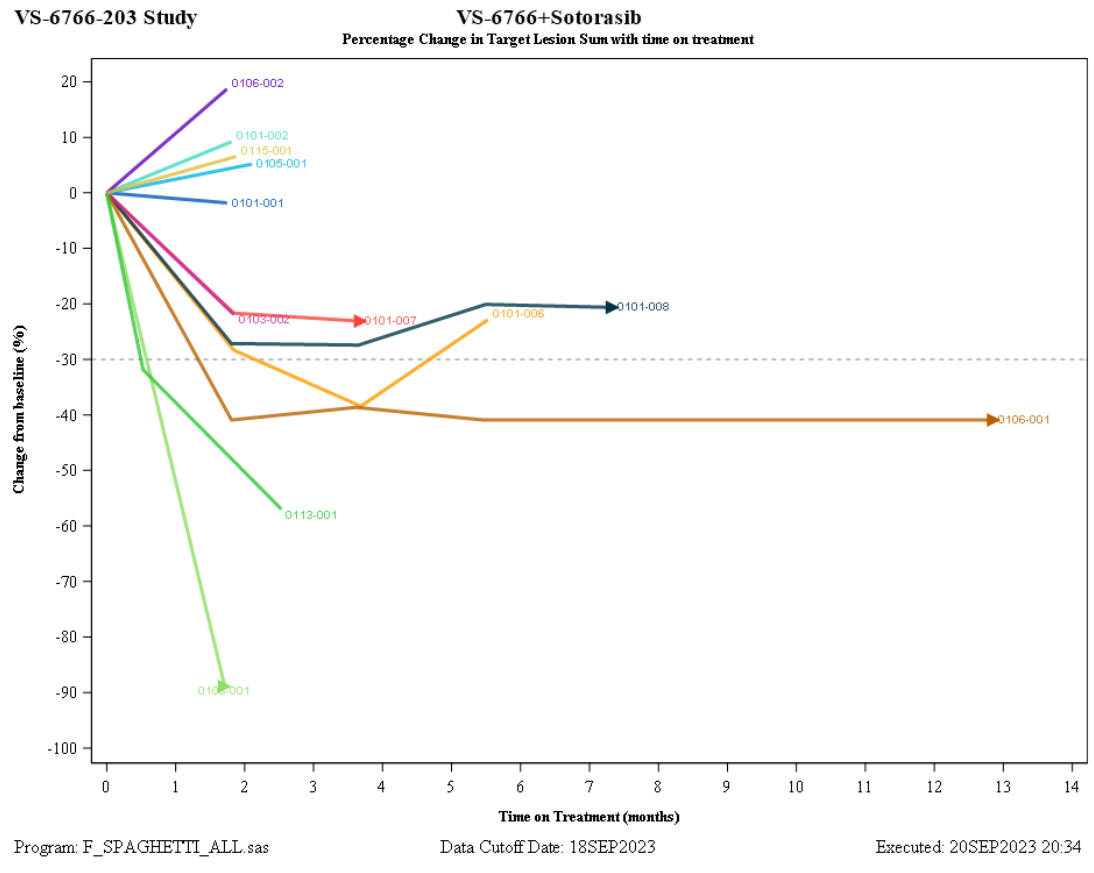
Cohort 1
Patients without Prior KRAS G12C Inhibitor Treatment
Stage 1: ~20 patients
Stage 2: expand

Cohort 2
Patients who Progressed on KRAS G12C Inhibitor Treatment
Stage 1: ~20 patients
Stage 2: expand

NCT05074810

Abbreviations: DLT = dose-limiting toxicity; n = number of patients;
ORR = overall response rate; RP2D = recommended phase 2 dose

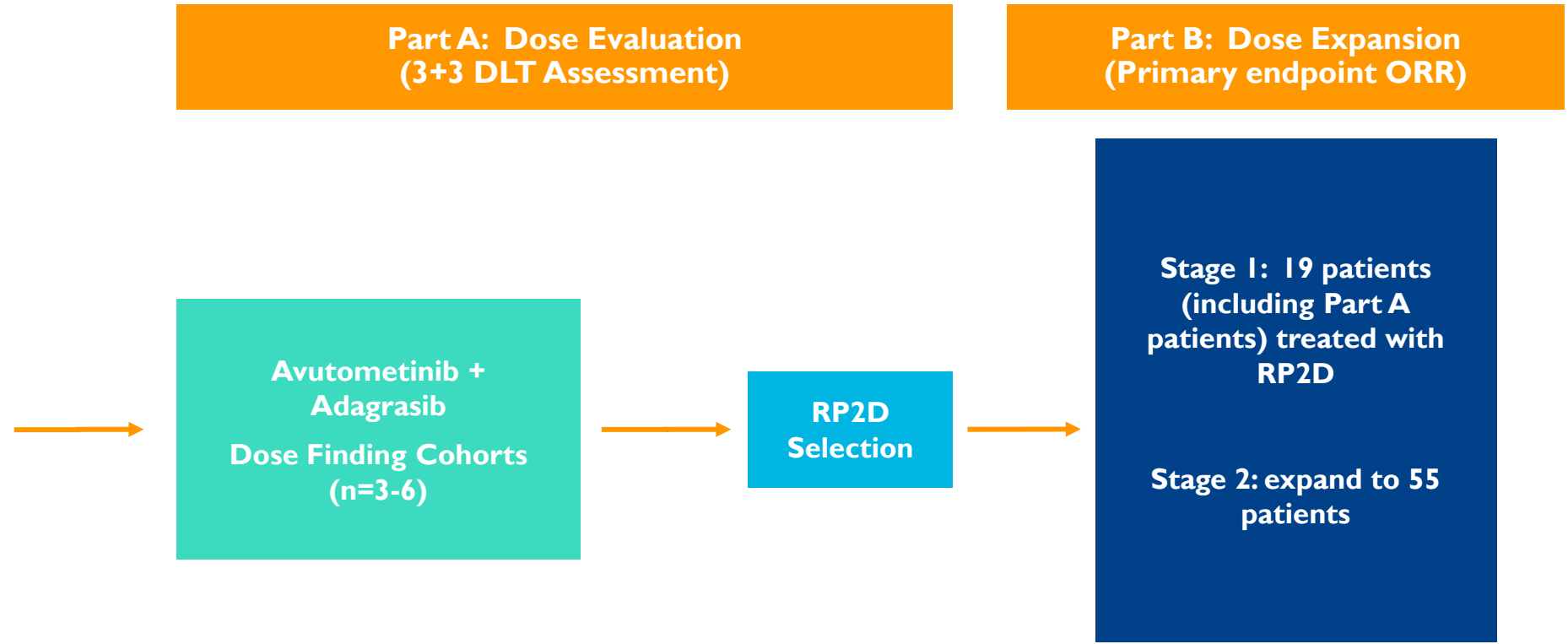
RAMP 203: Objective Responses in KRASG12C NSCLC Sotorasib + Avutometinib Combination



*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

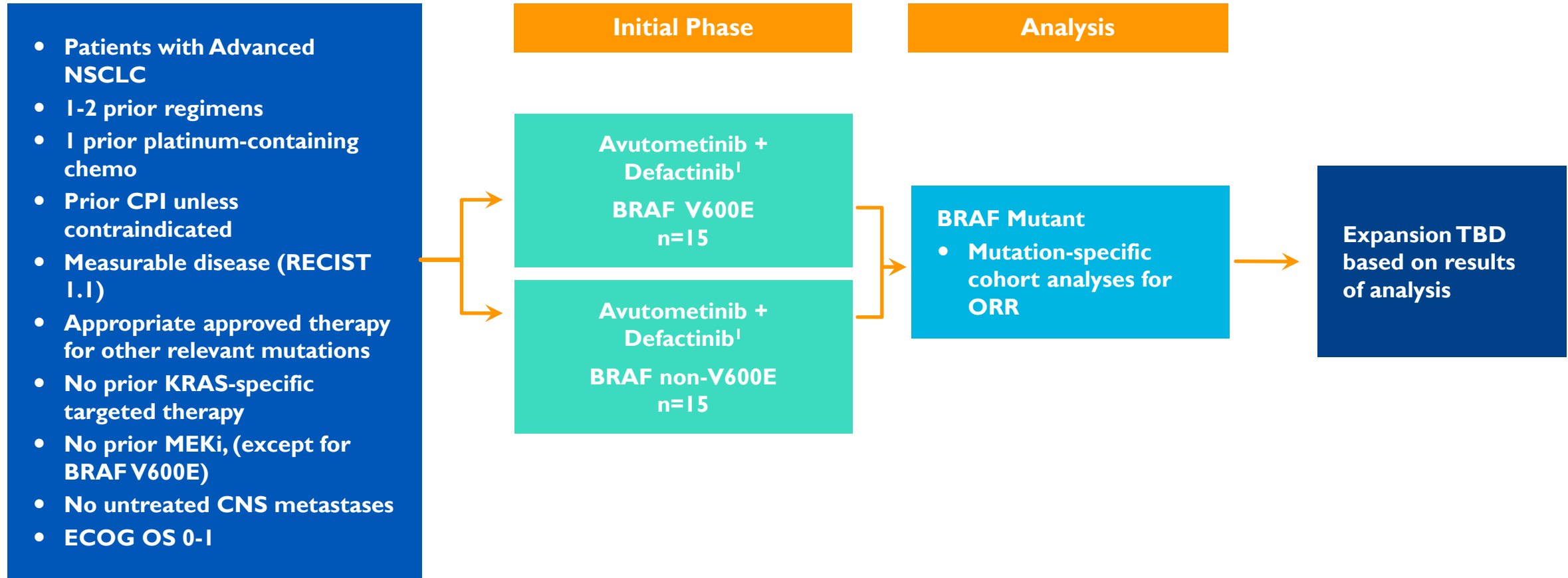
- Patients must have a **KRAS G12C** mutation determined using validated test
- Treatment with at least 1 but no more than 3 prior systemic regimens, for Stage 3B-C or 4 NSCLC
- Patient must have received prior therapy with a **KRAS G12C** inhibitor and experience progressive disease
- Measurable disease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



NCT05375994

Abbreviations: DLT = dose-limiting toxicity; n = number of patients; ORR = overall response rate; RP2D = recommended phase 2 dose

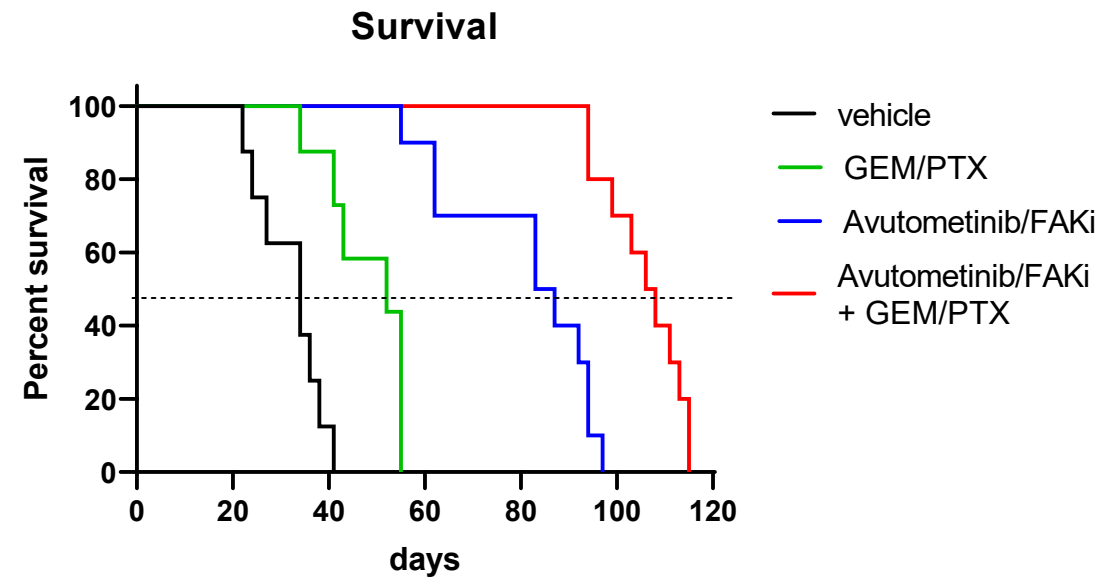
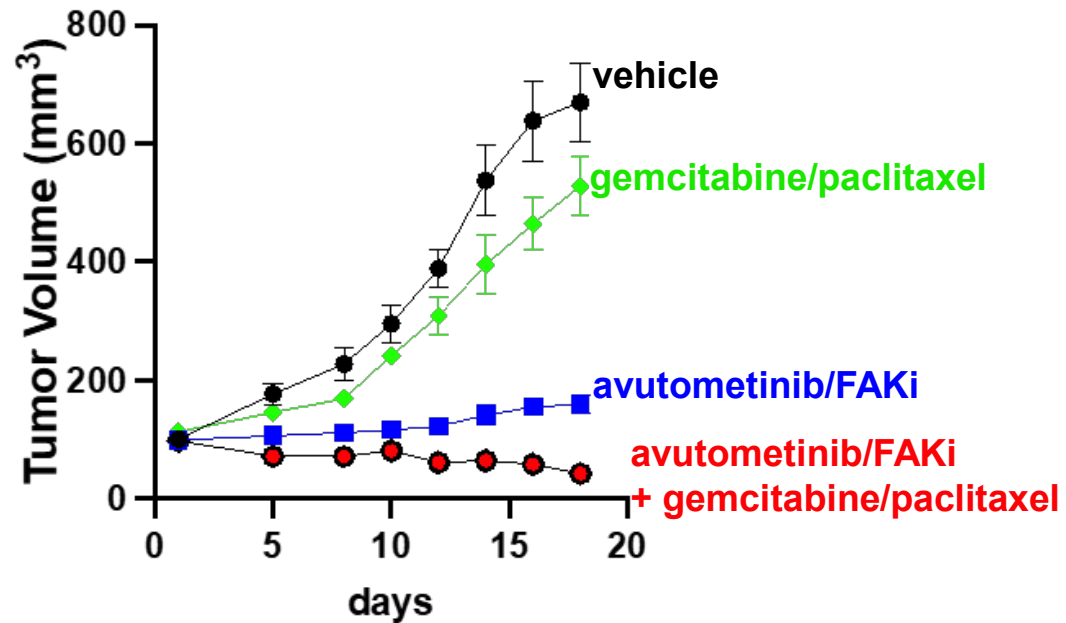
RAMP 202: Phase 2 Trial of Avutometinib + Defactinib in BRAF mt NSCLC



Additional Combinations and Programs

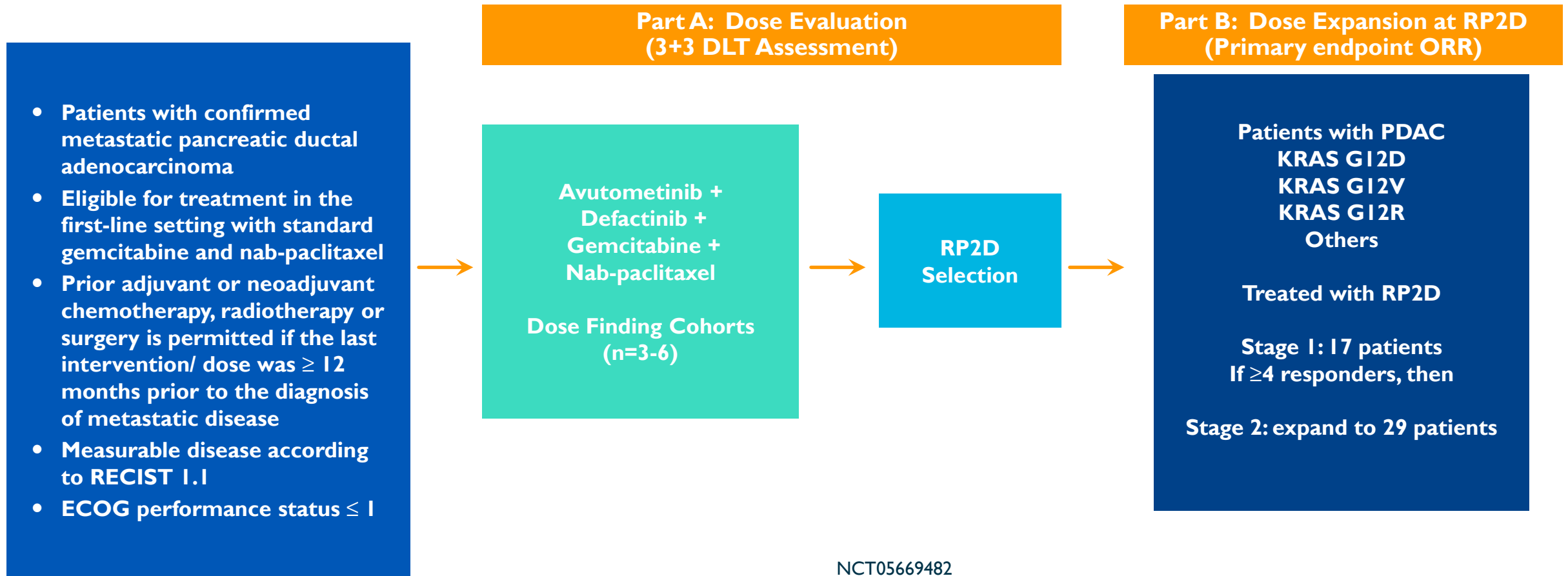
The background features a large blue area on the left. On the right, there are several diagonal stripes in blue, teal, and orange. A horizontal teal stripe runs across the bottom of the page, overlapping the diagonal stripes.

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

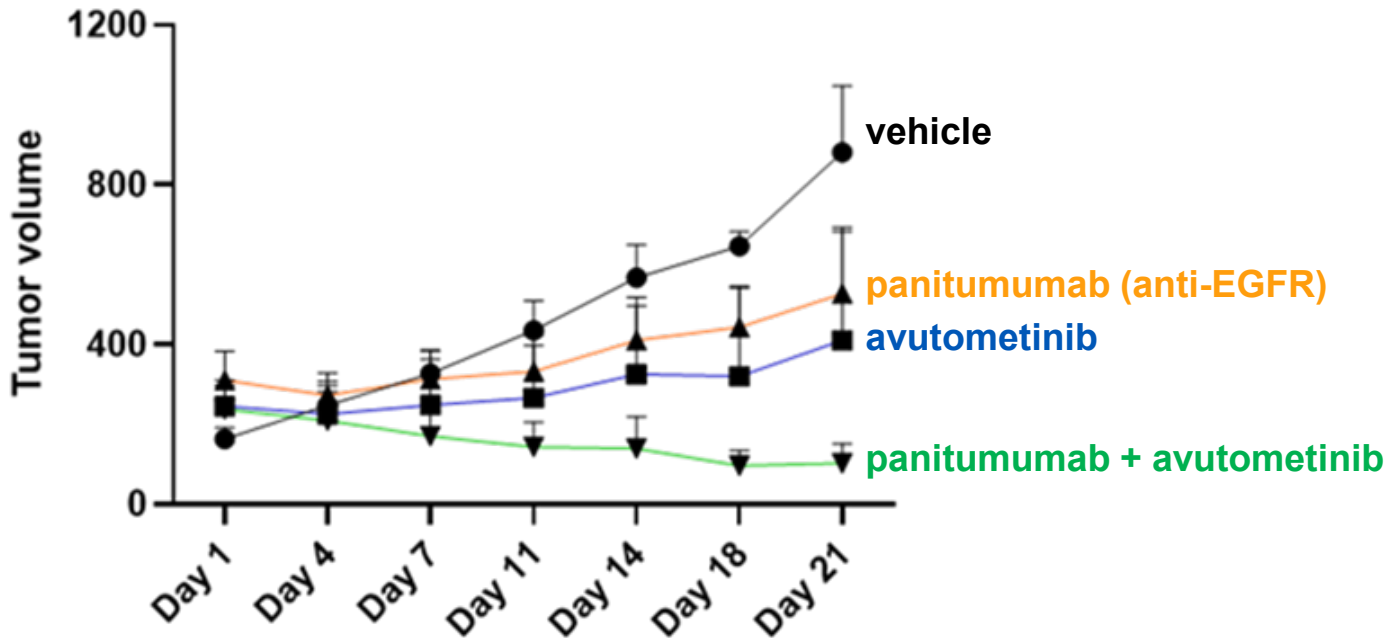


NCT05669482

Abbreviations: DLT = dose-limiting toxicity; n = number of patients;
ORR = overall response rate; RP2D = recommended phase 2 dose

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 and Financials

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 overlapping the others. The overall design is clean and professional.

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 option for Verastem to license up to 3 programs with development and commercialization rights outside China
 - Potential development in combination with Verastem's current pipeline
 - Lead program in IND enabling studies; 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 to pay GenFleet an upfront payment to obtain exclusive option right to 3 programs
 - 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

Key Financial Statistics

As of and for the quarter ended September 30, 2023

Cash, cash equivalents & investments	\$165.7M
GAAP Operating Expenses	\$21.3M
Non-GAAP Operating Expenses*	\$19.8M
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

Methods of Treating

→ 2041 - 2042 if issued

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



Louis Denis, M.D.

Chief Medical Officer

- CMO, Asana BioSciences
- Boehringer-Ingelheim, Pfizer



Jonathan Pachter, Ph.D.

Chief Scientific Officer

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



David C. Mitchell

Senior Vice President and Head of Regulatory Affairs

- Senior VP and Head of Regulatory Affairs-Sumitovant Biopharma
- Roivant Sciences, Aeglea Pharmaceuticals, Aquinox Pharmaceuticals, AbbVie



Hagop Youssoufian, MSc, M.D.

Head of Medical Strategy

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



THANK YOU