Exhibit 99.1

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K
CURRENT REPORT

Pursuant to Section 13 or 15(d) of the
Securities Exchange Act of 1934

Date of report (Date of earliest event reported): **September 12, 2023**

Verastem, Inc.

(Exact Name of Registrant as Specified in Charter)

Delaware	**001-35403**	**27-3269467**
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(IRS Employer Identification No.)

117 Kendrick Street, Suite 500, Needham, MA	**02494**
(Address of Principal Executive Offices)	(Zip Code)

Registrant's telephone number, including area code: **(781) 292-4200**

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common stock, $0.0001 par value per share	VSTM	The Nasdaq Capital Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure

On September 12, 2023, Verastem, Inc. posted its corporate presentation on its website, a copy of which is furnished hereto as Exhibit 99.1 to this Current Report on Form 8-K.

Item 9.01. Financial Statements and Exhibits

Exhibit No.	Description
99.1	Corporate Presentation, dated September 12, 2023
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

VERASTEM, INC.

Dated: September 12, 2023

By: /s/ Daniel W. Paterson
Daniel W. Paterson
Chief Executive Officer

VERASTEM ONCOLOGY

Corporate Presentation

September 2023

Disclaimers

This presentation includes forward-looking statements about, among other things, Verastem Oncology's programs and product candidates, including anticipated regulatory submissions, approval 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 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 comparabili 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 interna 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.

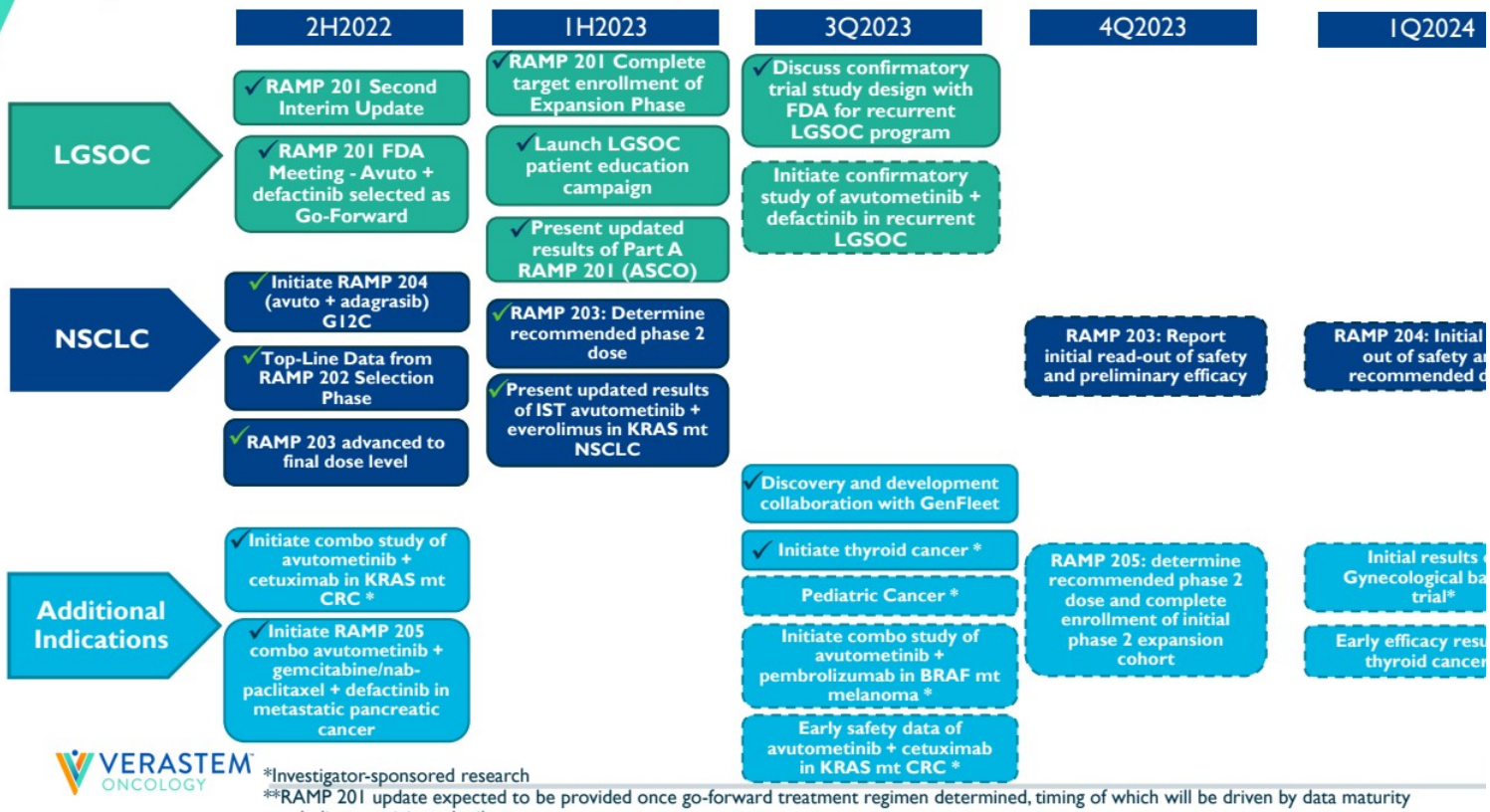
We are a biopharmaceutical company committed to developing and commercializing new medicines for patients battling cancer

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 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 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
Strong balance sheet	Cash and investments balance of $183.1 million as of June 30, 2023 Up to $150 million of non-dilutive funding available from credit facility Company ended Q2 2023 with $20.3 million GAAP operating expense $18.9 million non-GAAP operating expenses*

* Q2 2023 GAAP operating expenses - $20.29M less Q2 2023 stock compensation of $1.43M = $18.86M Q2 2023 non-GAAP operating exper

Key VSTM Achievements & Anticipated Milestones



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*Investigator-sponsored research

**RAMP 201 update expected to be provided once go-forward treatment regimen determined, timing of which will be driven by data maturity

- - - Indicate anticipated milestones

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, NF1 mt) and multiple solid tumor indications
- Strong preclinical combination data with other agents targeting RAS pathway (e.g. KRAS G12C inhibitors) and parall pathways (e.g. FAK inhibitors)

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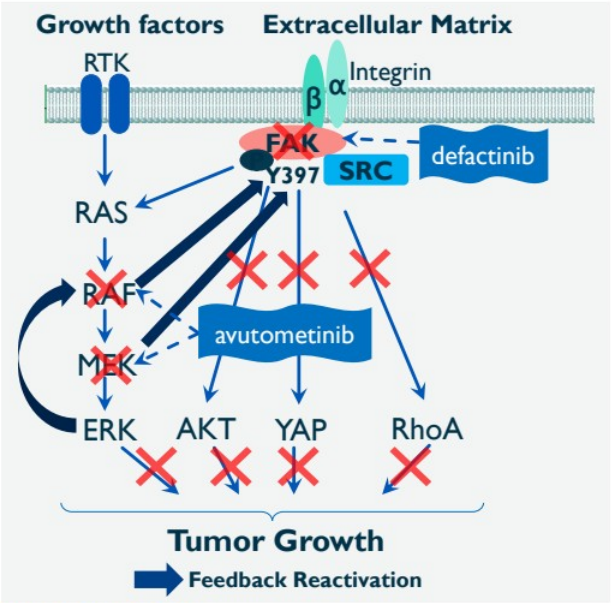
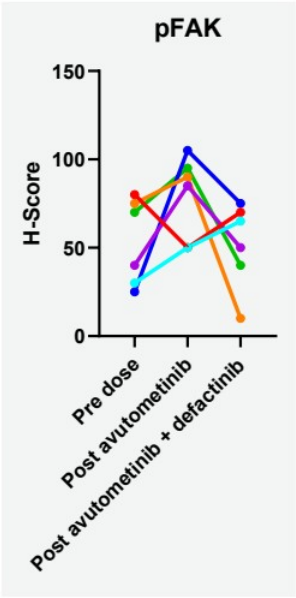
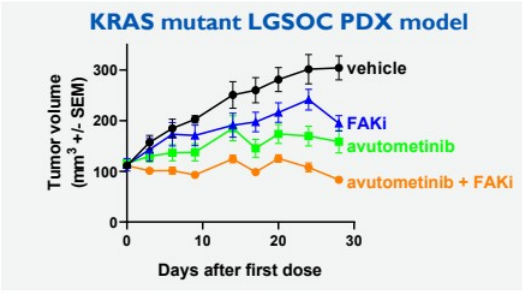
RAF-Rapidly accelerated fibrosarcoma
MEK-Mitogen-activated protein kinase kinase
RAS-Rat sarcoma virus
MAPK-Mitogen-activated protein kinase
KRAS-Kirsten rat sarcoma virus
NRAS-Neuroblastoma RAS viral oncogene homolog
BRAF-v-raf murine sarcoma viral oncogene homolog B1
NF1-Neurofibromatosis type 1

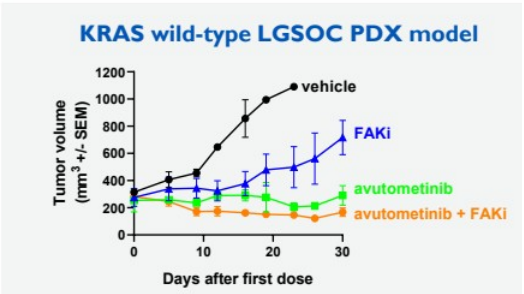
Strong Scientific Rationale for Avutometinib and FAK Inhibitor Combination

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









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References: Banerji, BTOG Dublin, Jan 23, 2019; Banerji, AACR VM 1, April 27, 2020, CT143; Banerji, unpublished; Santin, unpublished

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 appr
  - 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 endocrine therapy are relative 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 ≥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 46% confirmed ORR with durable responses and favorable safety/tolerabil
- 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 8 evaluable patients

➢ Breakthrough Therapy Designation was granted for avutometinib and defactinib in recurrent LGSOC after one or more prior lines of therapy

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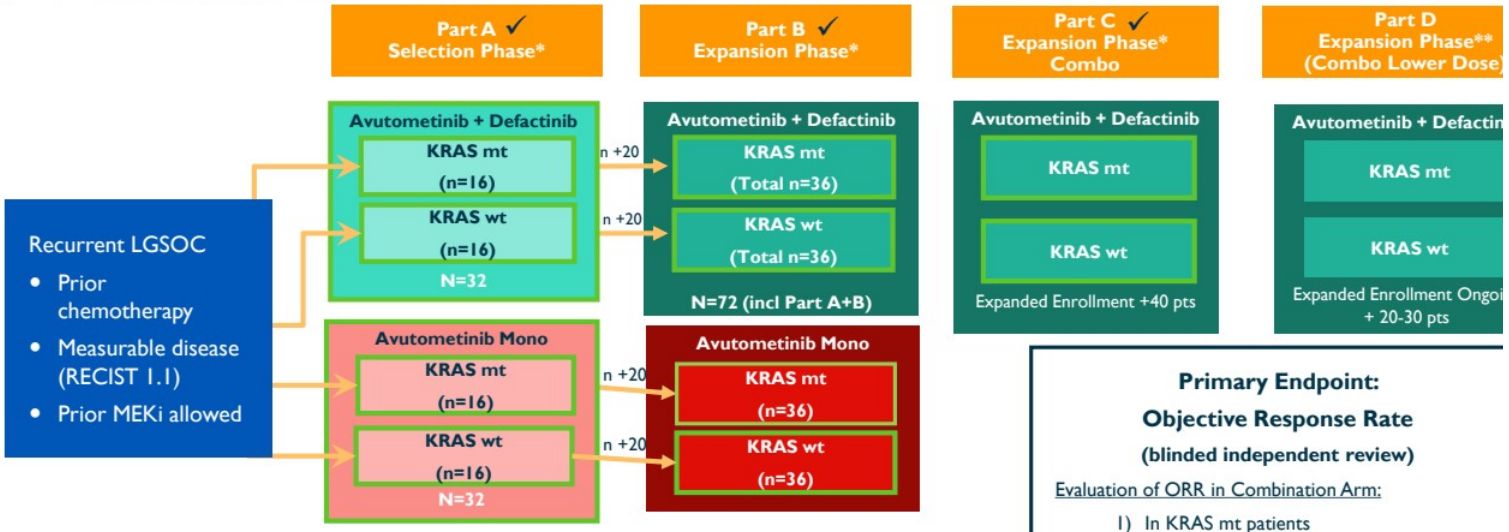
References: Monk et al., The Evolving Landscape of Chemotherapy in Newly Diagnosed Advanced Epithelial Ovarian Cancer, 2019; Slomovitz et al., Low-Grade serous ovarian cancer: State of the Science, 2020; Grisham et al., Low-Grade Serous Ovarian Cancer: Current Treatment Paradigms and Future Directions, 2018; AACR Project GENIE Cohort v9.0-public and Verastem unpublished analysis; Banerjee et al., Phase I study of the combination of the dual RAF/MEK inhibitor VS-6766 and the FAK inhibitor defactinib: Results of efficacy in low grade serous ovarian cancer, ESMO 2021; Malpica et al., Interobserver and intraobserver variability of a two-tier system for grading ovarian serous carcinoma, 2007; NCCN guidelines v1.2023; Zwimpfer et al. Cancer treatment Reviews 112 (2023).

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



Primary Endpoint:
Objective Response Rate
(blinded independent review)

Evaluation of ORR in Combination Arm:
1) In KRAS mt patients
2) All patients (KRAS mt & wt)

Combination Arm:
✓ **Target Enrollment Reached (N=72)**
❖ **Expanded Enrollment Ongoing (Lower Dose)**

* 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

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RAMP 201
ASCO 2023 Update

ASCO 2023 data

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 was12% in the combination overall to date (4.9% due to elevated blood CPK)
- Finalized 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 wit promising safety profile to date. It is particularly encouraging to see extensive tumor shrinkage in women who have had several treatment lin including prior MEK inhibitors. These latest findings suggest the combination may offer a new treatment option for women with this hard-to-tr 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 st Consultant Medical Oncologist at The Royal Marsden NHS Foundation Trust and Team Leader in Women's Cancers at The Institute of Cancer Research, Londor

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Reference: Banerjee et al., ASCO June 2023

Recent LGSOC Trials with Standard of Care Highlight High Unmet Need in Recurrent LGSOC

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 AE
GOG 281[1]	2 (1-10)	No	* Low %	**Standard of Care**	**6% ^ *95% CI: (3%, 12%)***	INV	7.2 (5.6-9.9)	13%
				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%**

[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

GOG 281: *(chemotherapy / endocrine therapy)*
PLD (liposomal doxorubicin), paclitaxel, topotecan, letrozole or tamoxifen

MILO: *(chemotherapy only)*
PLD (liposomal doxorubicin), paclitaxel or topotecan

INV = Investigator
BICR = Blinded independent central revie
PFS = Progression free survival
CI = confidence interval

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Current Trials with Combination of Avutometinib and Defactinib Consistent Overall Response Rate of ~45%

Trial	Median Number of Prior lines of Therapy	Prior MEK Allowed	Prior Bevaciz umab	Therapy	Response Rate ORR	Image Assessment	Median PFS Months (95% CI)	Discontinua Rate Due to A
FRAME[1]	3	Yes	12 %	**Avutometinib + Defactinib**	**46%^** *95% CI: (26%, 67%)*	INV	**23** (11 - NR)	4%
RAMP 201 Part A (ASCO 2023 data)[2]	4	Yes	65%	**Avutometinib + Defactinib**	**45%** **95% CI: (26%, 64%)** **52%***	**BICR**	Not Yet Reached	10%**

[1] Banerjee et al., ESMO Sept 2021

[2] Banerjee et al., ASCO June 2023

** Confirmed + Unconfirmed Objectives res*

***12% discontinuation in all combination pts (Part A + B (n=81): 4.9% due to elevated bloo*

INV = Investigator
BICR = Blinded independent central review
PFS = Progression free survival

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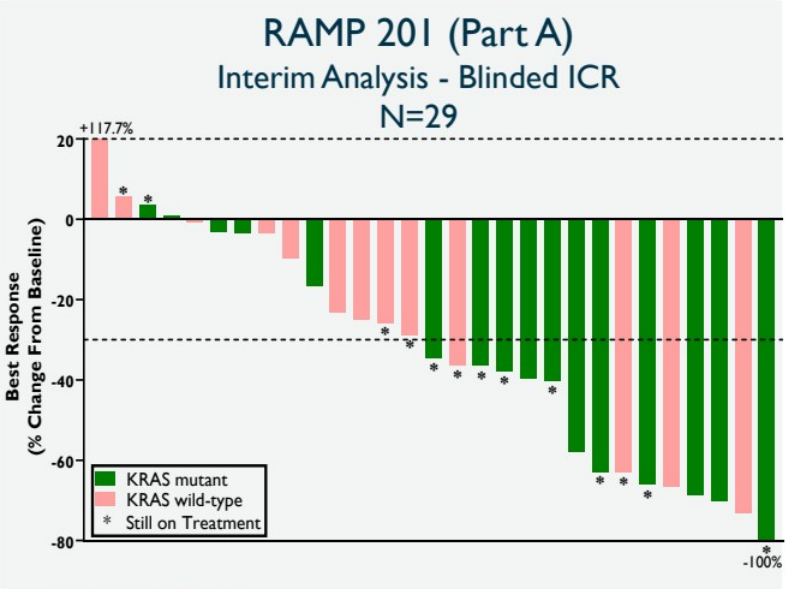
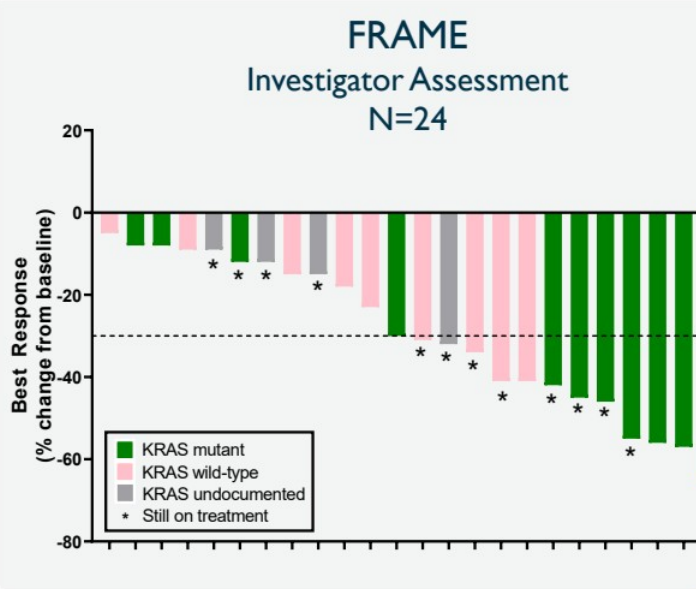
ASCO 2023 data

Combination of Avutometinib and Defactinib
Initial Data from RAMP 201 Trial Reinforce Findings from FRAME Trial





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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/reversible[1]
- Few discontinuations due to adverse events (12.3% in combo due to ≥ 1 TEAE 4.9% due to elevated blood CPK*)
  * No association to date with clinically significant toxicities, including rhabdomyolysis

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

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Reference: Banerjee et al., ASCO June 2023;
[1] J Clin Oncol 41, 2023 (suppl 16; abstr 5515)

Plan to File for Accelerated Approval based on Completed 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 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 confirmatory stu in 2H 2023

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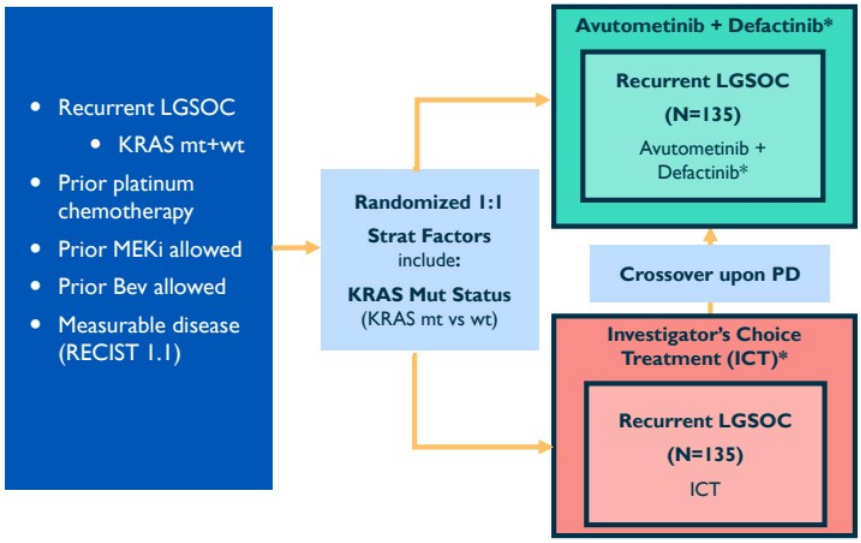
❖**RAMP-301:** Prospective Randomized Controlled Trial

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



Primary Endpoint:
Progression-Free Survival (PFS) by **BICR****

Secondary Endpoints include:

- **Objective Response Rate (ORR)**
- **Duration of Response (DoR)**
- **Disease Control Rate (DCR)**
- **Safety / Tolerability**
- **Patient Reported Outcomes**
- **Overall Survival**

Primary Analysis: Hierarchical Evaluation

1) KRAS mutant LGSOC only
2) All recurrent LGSOC

- **A+D Dosing: Avutometinib 3.2 mg PO 2x/wk 21/28 days + Defactinib 200mg PO BID: 21/28 days**
- **ChemoHormonal ICT: Liposomal doxorubicin (PLD), Paclitaxel, Topotecan, Letrozole, Anastrozole**

** **BICR: Blinded Independent Central R**

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Comprehensive approach to establish more complete blockade of RAS pathway & resistance pathways

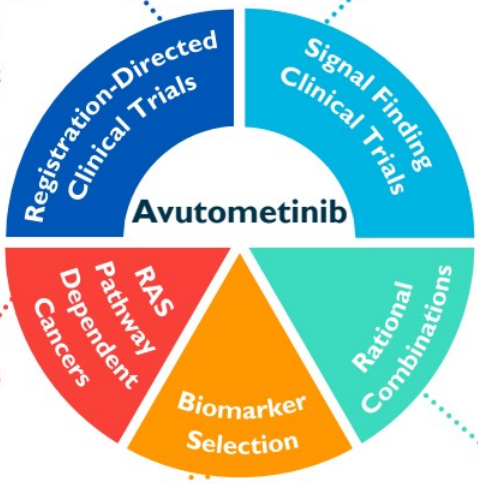
	Indication	Incidence/ Prevalence	Regimen	Setting
Gynecologic Cancers	LGSOC	Prevalence[1]: 6K	Avutometinib + defactinib	Relapsed Refractory molecularly profiled LGSOC
	Gynecologic Basket*	Incidence[6-10]: 85K	Avutometinib + defactinib	Recurrent RAS Pathway-driven (RAS/RAF/NF1) endometrioid cancer, mucinous ovarian cancer, high-grade serous ovarian cancer or cervical cancer
NSCLC Adenocarcinoma	KRAS G12C	Incidence[2,3]: 114K (13%)	Avutometinib + sotorasib (AMGEN)	Recurrent KRAS G12C with prior KRAS G12C inhibitor(i) treatment or KRAS G12Ci naïve
			Avutometinib + adagrasib (MIRATI THERAPEUTICS)	Recurrent KRAS G12C with prior KRAS G12Ci treatment that progressed
	BRAF mt	Incidence[2,3]: 114K (4.5%)	Avutometinib + defactinib	Recurrent BRAF V600E & non-V600E mutant NSCLC
Pancreatic	PDAC	Incidence[4]: 58K (98%)	Avutometinib + defactinib + gemcitabine/nab-paclitaxel (PANCREATIC CANCER ACTION NETWORK)	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
Melanoma	BRAF V600E*	Incidence[4]: 108K (54%)	Avutometinib + pembrolizumab	Recurrent BRAF V600E/K or NRAS (Phase 1 only) mutant Melanoma following progression on prior anti-PD1 therapy

[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 ov 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]Pakkala and Ramalingam JCI Insight 2018); [3]Cancer Statistics 2020, Sieg *Cancer J Clin* 2020;70:7-30; [4]Cancer Statistics 2020, Siegel et. al. *CA Cancer J Clin* 2020;70:7-30 [5]CbioPortal; [6]Uterine cancer is one of the leading gynecologic neoplastic disorders in the US, of which over 80% are endometrioid adenocarcinomas (EA); [7]Endometrioid OC (EnOC for approximately 10% of all OC, with the majority of cases diagnosed as low grade, early stage disease with excellent clinical; [8]Mucinous ovarian cancer: 3-11% of ovarian cancer (Hada et al., 2021); [9]90% 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); [10]HGSOC 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.)

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 signal
- 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 f 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 opti
  - 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

Broad Development Opportunities Across Multiple RAS/MAPK Pathway-Driven Cance



High Priority Registration Indication

Registration-Directed Trial Initiated in 4Q20

- LGSOC[1,2] (RAMP 201)-Target enrollment reached

Key Signal Finding

- Avutometinib + G12Ci in KRAS G12C NSCLC (RAMP 203 - sotorasib) & (RAMP 204 - adagras
- Avutometinib + defactinib in BRAF mt (V600E & V600E) NSCLC[1,2] (RAMP 202)
- Avutometinib + defactinib and gemcitabine/nab-paclitaxel in first line pancreatic cancer (RAMP
- Avutometinib + defactinib in RAS/RAF/NF1 mt gynecological cancers[1,2]
- Avutometinib + cetuximab in KRAS mt CRC[2]
- Avutometinib + abemaciclib and fulvestrant in E breast cancer[2]
- Avutometinib + pembrolizumab in BRAF V600E melanoma[2]

RAS Pathway Dependent Cancers

- Gynecological[1,2]
- NSCLC[1,2]
- Colorectal[1,2]
- Melanoma[1,2]
- Pancreatic[2]
- Thyroid[1,2]

Biomarker Selection

- KRAS mt[1,2]
- BRAF mt (V600 & non-V600)[1,2]
- NRAS mt[1,2]
- CRAF mt/fusions[2]

Rational Combinations

- KRAS inhibitors[2] (G12Ci & G12Di)
- Anti-EGFR[2]
- Everolimus[1,2]
- CDK4/6 inhibitor[2]
- Anti-PD-1[1,2]
- Chemotherapy[2]

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[1] Supported by clinical data

[2] Supported by preclinical data

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 COLLABORAT WITH
LGSOC[1]	Avutometinib + defactinib	RAMP 201	Registration-directed trial: accelerated approva 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		AMGEN
R/R NSCLC (KRAS G12C)	Avutometinib + adagrasib	RAMP 204		MIRATI THERAPEUTICS
Pancreatic Ductal Adenocarcinoma	Avutometinib + gemcitabine/nab-paclitaxel + defactinib	RAMP 205		PANCREATIC CANCER ACTION NETWORK
R/R NSCLC (KRAS mt)	Avutometinib + everolimus (mTORi)	IST		
R/R Colorectal Cancer (KRAS mt)	Avutometinib + cetuximab (EGFRi)	IST		
ER+ Breast Cancer	Avutometinib + abemaciclib + fulvestrant	IST		
BRAF V600E Melanoma[2]	Avutometinib + pembrolizumab	IST		

[1] FDA Breakthrough Therapy Designation
[2] Imminent initiation

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Key Financial Statistics

As of and for the quarter ended June 30, 2023

Cash, cash equivalents & investments	$183.1M
GAAP Operating Expenses	$20.3M
Non-GAAP Operating Expenses*	$18.9M
Shares Outstanding	25.2M**

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

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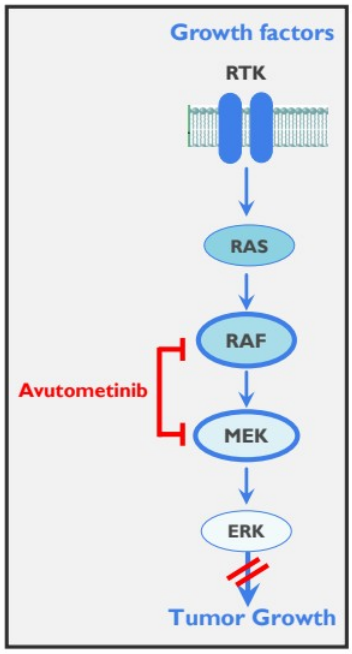
* Q2 2023 GAAP operating expenses - $20.29M less Q2 2023 stock compensation of $1.43M = $18.86M Q2 2023 non-GAAP operating expenses

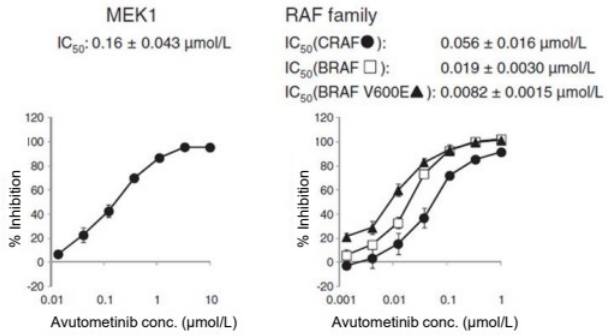
**Excludes Series A Preferred (0.8M Shares on as-converted basis), Series B Preferred (4.2M Shares on as-converted basis), and outstanding unexercised pre-funded warrants (1.5M Shares).

Avutometinib RAF/MEK Clamp Program Overview

Avutometinib is a Unique Small Molecule RAF/MEK Clamp



- Avutometinib inhibits MEK, BRAF & CRAF by trapping these molecules in inactive complexes
- MEK inhibitors paradoxically induce MEK phosphorylation (pMEK) by relieving ERK-dependent feedback inhibition of RAF
- By inhibiting RAF phosphorylation of MEK, avutometinib has advantage of not inducing pMEK
- Avutometinib inhibits ERK signaling more completely; may confer enhanced therapeutic activity



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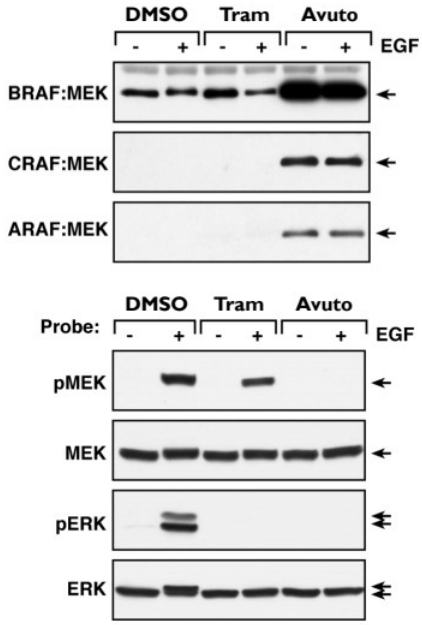
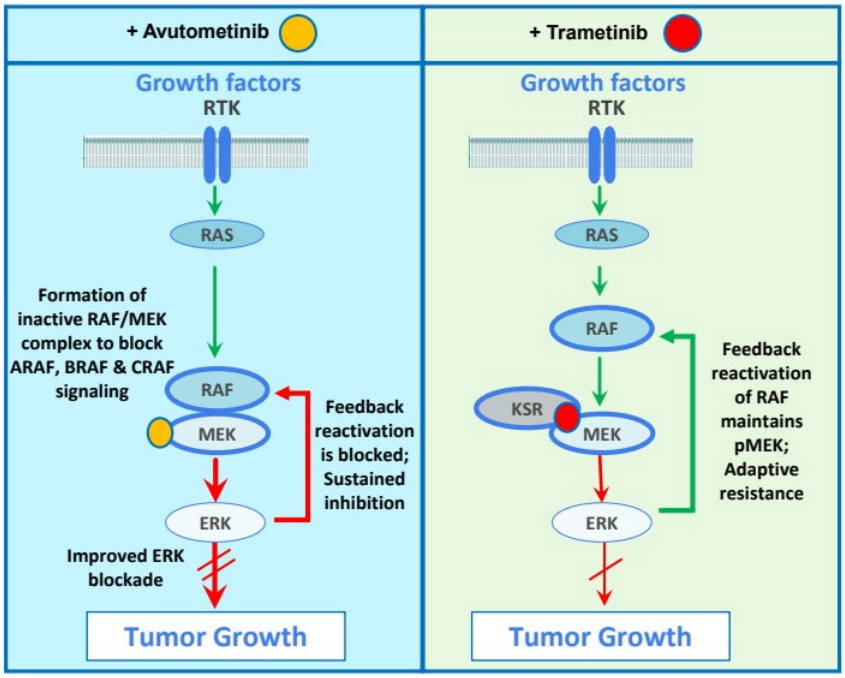
References: Ishii et al., *Cancer Res*, 2013; Lito et al., *Cancer Cell*, 2014

Avutometinib is a Unique RAF/MEK Clamp which Induces Inactive Complexes of MEK with ARAF, BRAF & CRAF

Contrasting mechanism of action vs. trametinib





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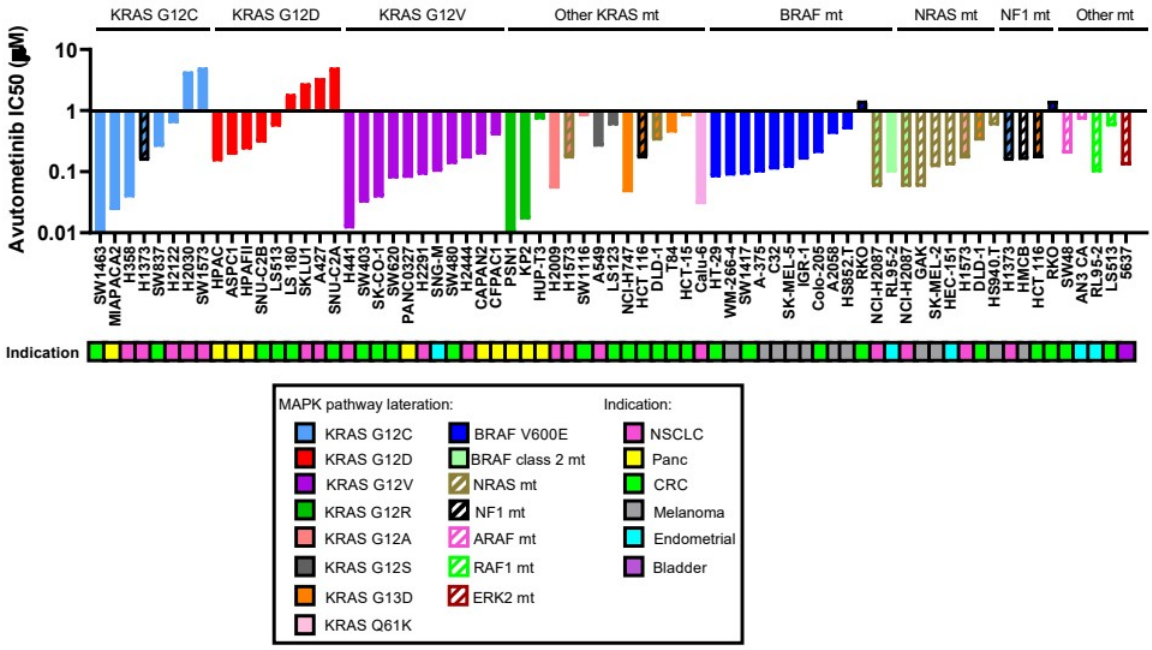
Deborah Morrison unpublished

Reference: Coma et al., AACR 2022

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



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Reference: Pachter *RAS-Targeted Drug Development Summit 2022*; 3D proliferation assay

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

Summary of Adverse Events Grade ≥ 3 Occurring in ≥ 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%)

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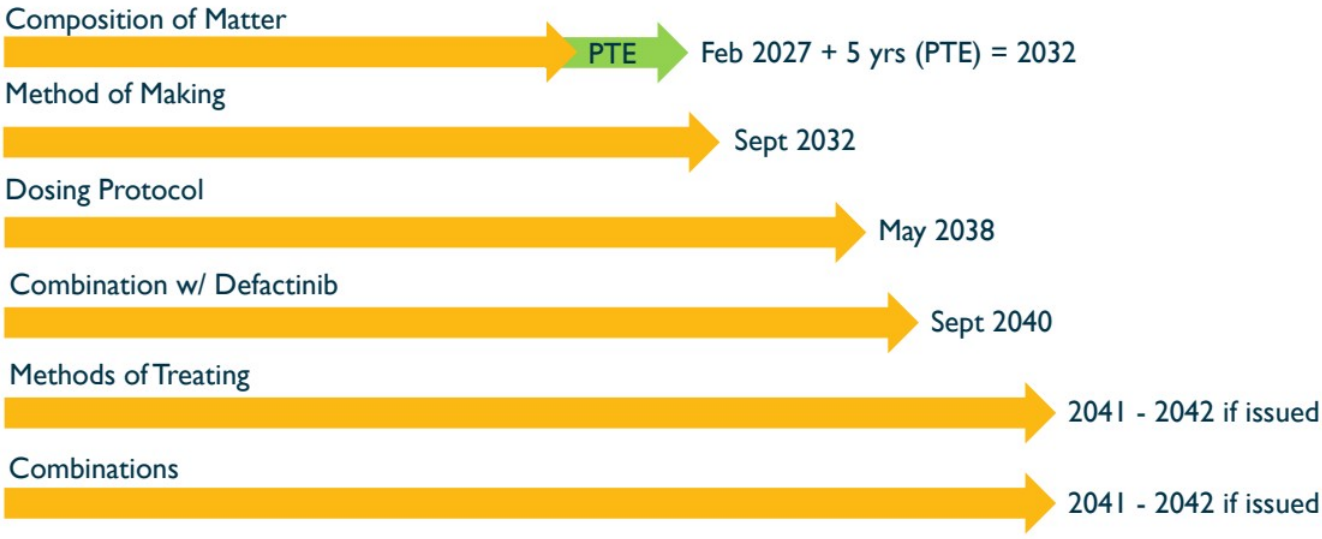
[1] Chenard-Poirier, *et al.* ASCO 2017

References: Banerji, Q4 2020 report; Data on file

RP2D: recommended phase 2 dosing

Avutometinib Patent Exclusivity

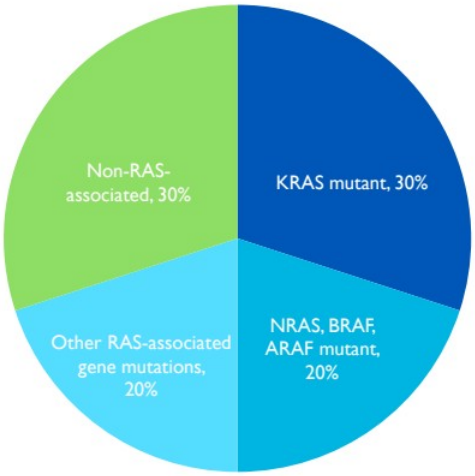


Avutometinib ± Defactinib in Low-Grade Serous Ovarian Cancer

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
- Most prior research has focused 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 r



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

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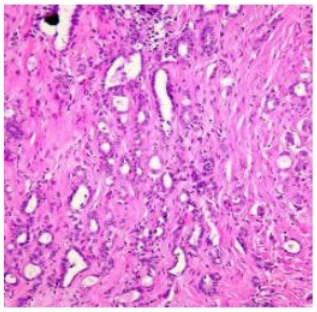
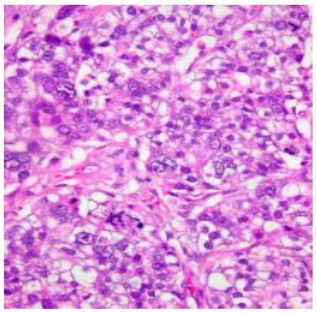
References: Monk, Randall, Grisham, The Evolving Landscape of Chemotherapy in Newly Diagnosed Advanced Epithelial Ovarian Cancer, Am Soc Clin Oncol Educ Book; 201
Slomovitz, Gourley, Carey, Malpica, Shih, Huntsman, Fader., Grisham et al, Low-Grade serous ovarian cancer: State of the Science; Gynecol Oncol; 2020. Grisham, Iyer, Low-
Serous Ovarian Cancer: Current Treatment Paradigms and Future Directions; Curr Treat Options Oncology; 2018; Malpica et al., Am J. Surg Pathol 2007

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

Reference: Malpica et al., Am J. Surg Pathol 2007

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]

No Category 1 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, rel efficacy, and relative toxicity profile.
t: An aromatase inhibitor (i.e., letrozole, anastrozole, exemestane) i preferred if not used previously. Fulvestrant, tamoxifen, or leuprolid acetate is recommended if an aromatase inhibitor was given previc

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**

Preferred Regimens

- Paclitaxel/carboplatin q3weeks[f,g] ± maintenance letrozole (category 2B) or other hormonal therapy (category 2B)[ff]
- Paclitaxel/carboplatin/bevacizumab + maintenance bevacizumab[f,i] (ICON-7 & GOG-218)
- Hormone therapy (aromatase inhibitors: anastrozole, letrozole, exemestane) (category 2B)

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References:
[1] NCCN guidelines v1.2023

Recent LGSOC Trials Highlight High Unmet Need

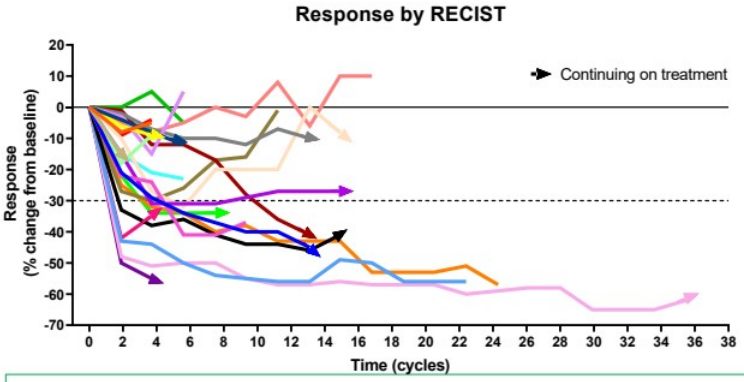
Trial	Number of Prior Systemic Therapies Median (range)	Prior MEK allowed	Prior Bevacizumab	Therapy	Response Rate ORR	Image Assessment	Median PFS Months (95% CI)	Discontinu Rate due to A
GOG 281[1]	**2** (1-10)	No	* Low %	**SoC (n=130)**	**6% 95% CI: (3%, 12%)**	INV	7.2 (5.6-9.9)	13%
				Trametinib (n=130)	**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%**

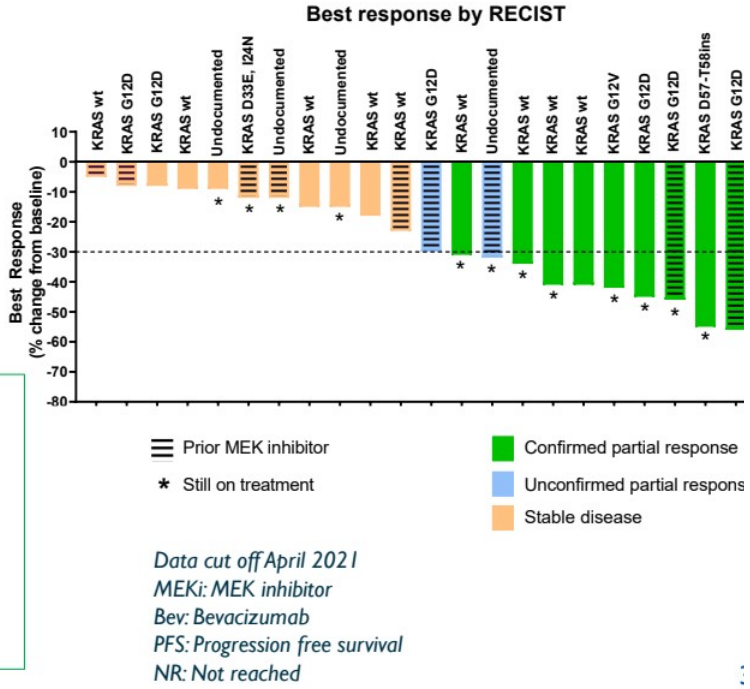
[1] Study GOG 281 trial Gershenson et al., Lancet 2022
[2] MILO Study Monk et al., J Clin Oncol 2020.

** 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
PFS = Progression free survival
CI = confidence interval
NR = Not reached

FRAME Study: Solid Foundation for the Development of Avutometinib in Combination with Defactinib in Recurrent LGSOC (n=24)





- Overall response rate (ORR) = 46% (11 confirmed PRs/24)
  - KRAS mutant ORR = 64% (7 confirmed PRs/11)
  - KRAS wild-type ORR = 44% (4 confirmed PRs/9)
  - KRAS status undetermined (1 unconfirmed PR/4)
- Response too early to determine for 2 pts on study for ≤5 months
- Median 3 lines of Prior Treatment (Prior MEKi 10 pts, Prior Bev 4 pts)
- Responses in patients previously treated with MEKi
- 54% (13/24) patients still on treatment
- 1 patient discontinuing for adverse events as of April 2021
- Median PFS 23 months (95% CI 10.6-NR) across all LGSOC

Data cut off April 2021
MEKi: MEK inhibitor
Bev: Bevacizumab
PFS: Progression free survival
NR: Not reached

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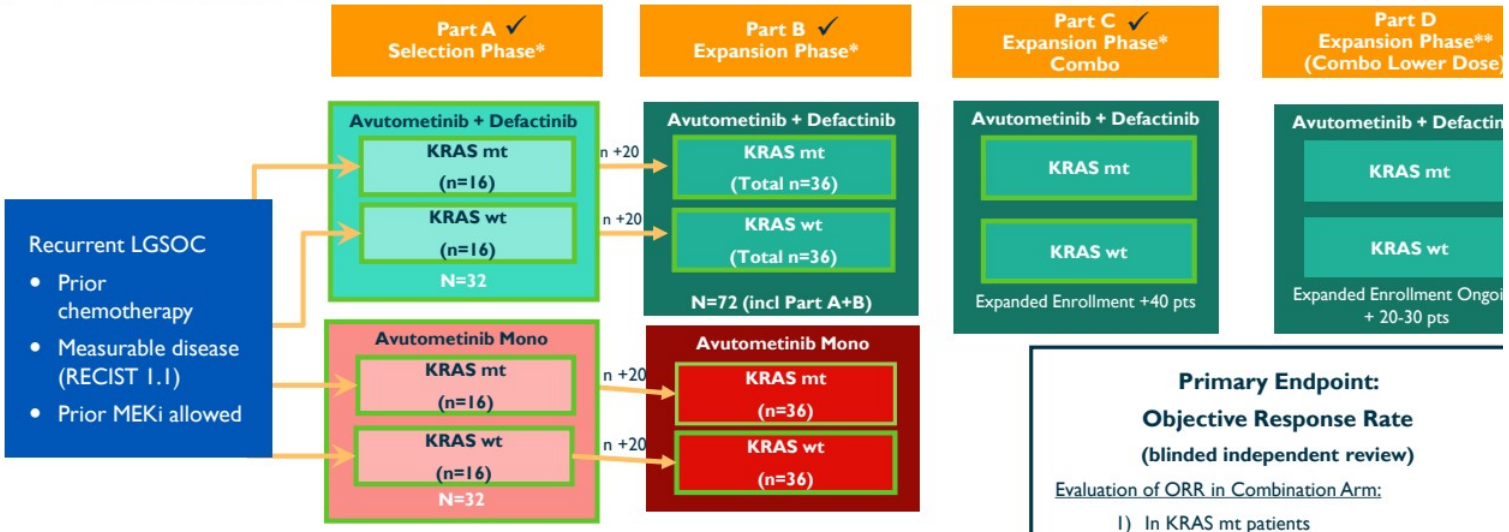
Reference: Banerjee et al., ESMO Sept 2021

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



Primary Endpoint:
Objective Response Rate
(blinded independent review)

Evaluation of ORR in Combination Arm:

1) In KRAS mt patients
2) All patients (KRAS mt & wt)

Combination Arm:
✓ **Target Enrollment Reached (N=72)**
❖ **Expanded Enrollment Ongoing (Lower Dose)**

* 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

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RAMP 201
ASCO 2023 Update

ASCO 2023 data

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 was12% 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 wit promising safety profile to date. It is particularly encouraging to see extensive tumor shrinkage in women who have had several treatment lin including prior MEK inhibitors. These latest findings suggest the combination may offer a new treatment option for women with this hard-to-tr 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 st Consultant Medical Oncologist at The Royal Marsden NHS Foundation Trust and Team Leader in Women's Cancers at The Institute of Cancer Research, Londor

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Recent LGSOC Trials with Standard of Care Highlight High Unmet Need in Recurrent LGSOC

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 AE
GOG 281[1]	**2** (1-10)	No	* Low %	**Standard of Care**	**6% ^ *95% CI: (3%, 12%)***	INV	7.2 (5.6-9.9)	13%
				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%**

[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

GOG 281: *(chemotherapy / endocrine therapy)*
PLD (liposomal doxorubicin), paclitaxel, topotecan, letrozole or tamoxifen

MILO: *(chemotherapy only)*
PLD (liposomal doxorubicin), paclitaxel or topotecan

INV = Investigator
BICR = Blinded independent central revie
PFS = Progression free survival
CI = confidence interval

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Current Trials with Combination of Avutometinib and Defactinib Consistent Overall Response Rate of ~45%

Trial	Median Number of Prior lines of Therapy	Prior MEK Allowed	Prior Bevaciz umab	Therapy	Response Rate ORR	Image Assessment	Median PFS Months (95% CI)	Discontinua Rate Due to A
FRAME[1]	3	Yes	12 %	**Avutometinib + Defactinib**	**46%^** *95% CI: (26%, 67%)*	INV	**23** (11 - NR)	4%
RAMP 201 Part A (ASCO 2023 data)[2]	4	Yes	65%	**Avutometinib + Defactinib**	**45%** **95% CI: (26%, 64%)** **52%***	**BICR**	Not Yet Reached	10%**

[1] Banerjee et al., ESMO Sept 2021

[2] Banerjee et al., ASCO June 2023

** Confirmed + Unconfirmed Objectives res*

***12% discontinuation in all combination pts (Part A + B (n=81): 4.9% due to elevated bloo*

INV = Investigator
BICR = Blinded independent central review
PFS = Progression free survival

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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)	Tota (n=3
Age (yrs), median (min, max)	58 (27, 72)	48 (27, 74)	**51 (27, 74)**	61 (29, 71)	50 (30, 74)	**55 (2**
ECOG PS, n (%)						
0	8 (50)	15 (88)	23 (70)	11 (69)	9 (60)	20 (6
1	8 (50)	2 (12)	10 (30)	5 (31)	6 (40)	11 (3
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,**
Prior platinum-based chemotherapy, n (%)	15 (94)	17 (100)	32 (97)	16 (100)	15 (100)	31 (1
Prior MEK inhibitor therapy, n (%)	5 (31)	5 (29)	10 (30)	2 (13)	2 (13)	4 (1
Prior Bevacizumab, n (%)	8 (50)	8 (47)	16 (48)	7 (44)	13 (87)	20 (6
Prior Hormonal therapy, n (%)	11 (69)	13 (76)	24 (73)	15 (94)	13 (87)	28 (9

ASCO 2023 data

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

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ASCO 2023 data

Combination of Avutometinib and Defactinib

High Disease Control Rate + Tumor Reduction in Recurrent LGSOC

Part A (Evaluable for Efficacy *)

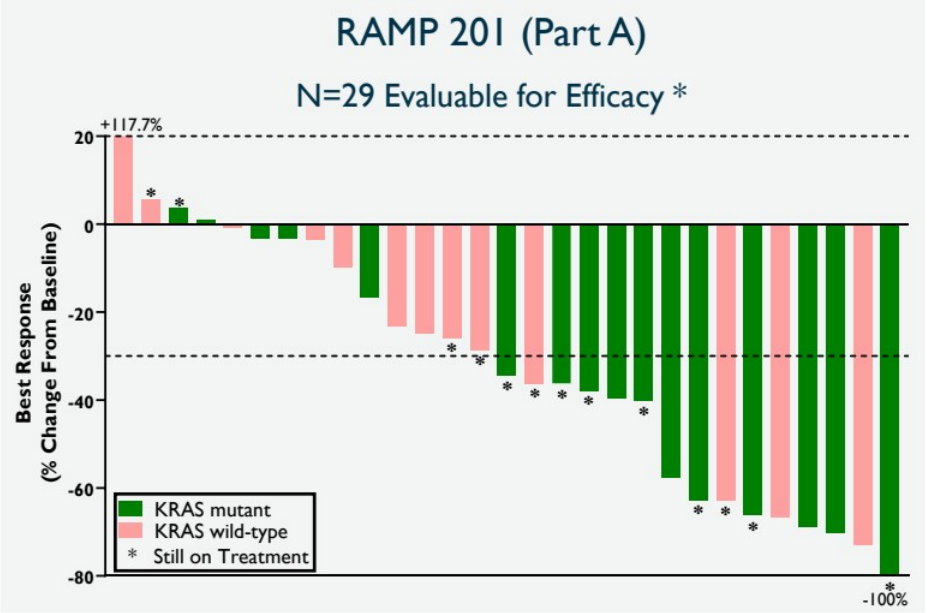
Confirmed ORR: **45%**

Confirmed/Unconfirmed ORR: **52%**

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

Patients still on study treatment: 45%

Minimum follow-up: 12 months



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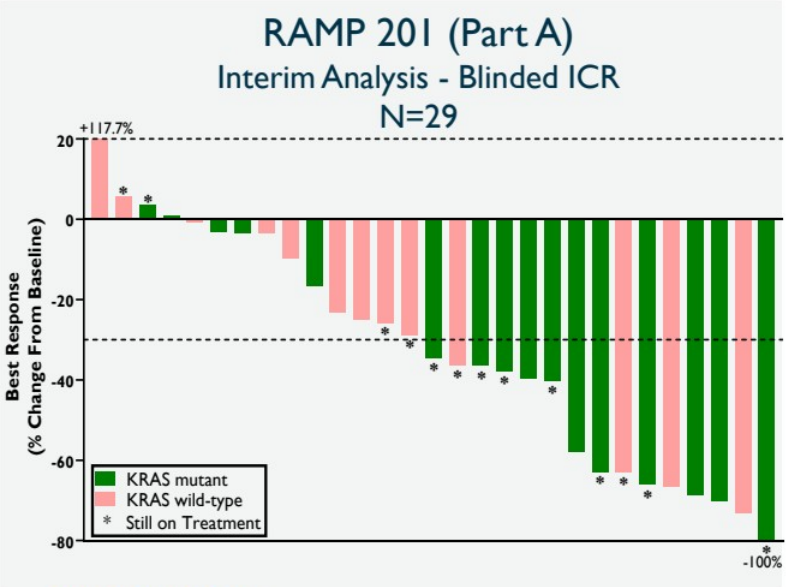
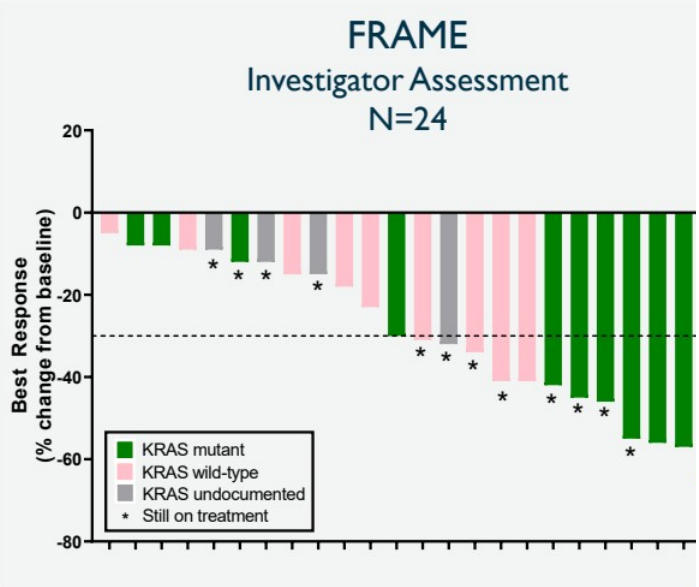
* Evaluable for Efficacy: At least one blinded imaging assessment

Combination of Avutometinib and Defactinib
Initial Data from RAMP 201 Trial Reinforce Findings from FRAME Trial





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/reversible[1]
- Few discontinuations due to adverse events (12.3% in combo due to ≥ 1 TEAE 4.9% due to elevated blood CPK*)
  * No association to date with clinically significant toxicities, including rhabdomyolysis

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

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Reference: Banerjee et al., ASCO June 2023;
[1] J Clin Oncol 41, 2023 (suppl 16; abstr 5515)

Plan to File for Accelerated Approval based on Completed 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 Confirmatory Trial finalized with FDA

Next Steps

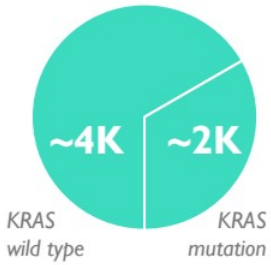
- Target enrollment for primary analysis (n=72) in combination has been achieved
- Plan to file for accelerated approval based on the totality of the data from the RAMP 201 and FRAME studies
- The Company plans to initiate the confirmatory stu in 2H 2023

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

Prevalence

~6K

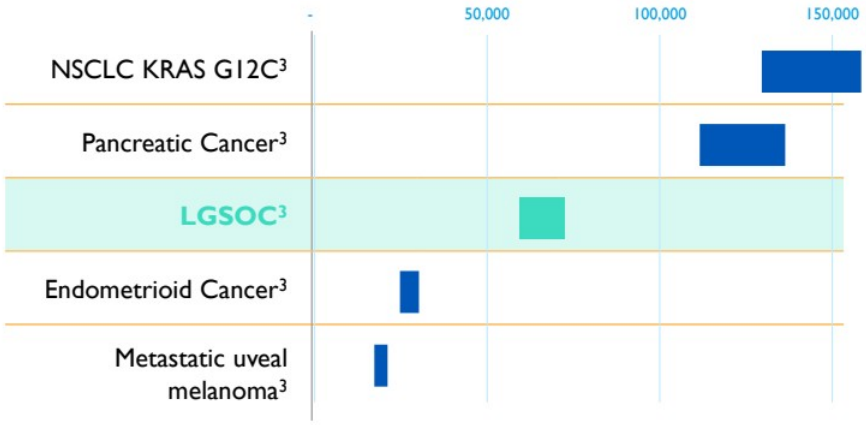
patients US[1]



~80K

patients WW[1]

Patient-months of Therapy Per Year[2] *(across all 2L+ patients)*



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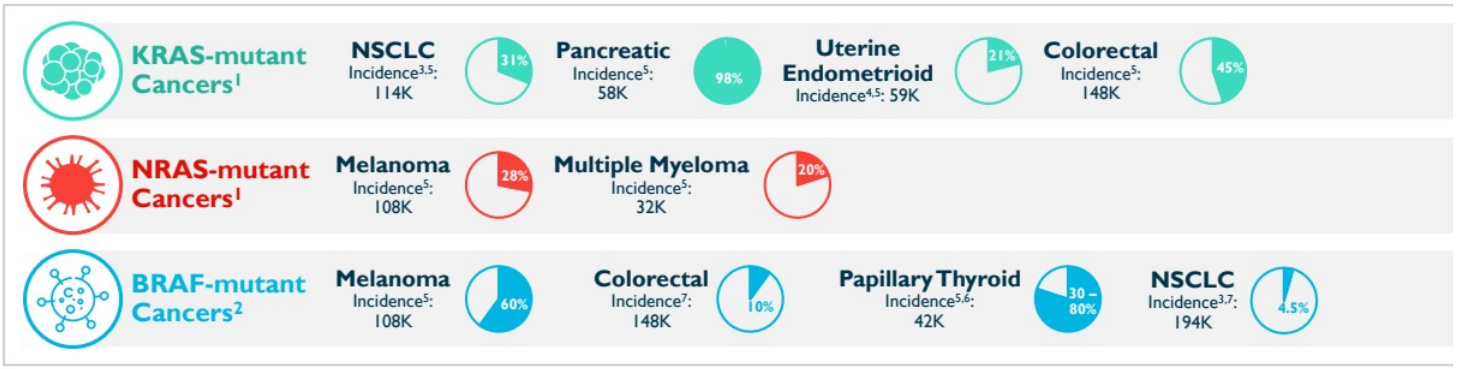
[1] References: Monk, Randall, Grisham, The Evolving Landscape of Chemotherapy in Newly Diagnosed Advanced Epithelial Ovarian Cancer, Am Soc Clin Oncol Educ Book; 2019; Slomovitz, Gourley, Carey, Malpica, Shih, Huntsman, Fader., Grisham et al, Low-Grade serous ovarian cancer: State of the Science; Gynecol 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)

RAS Pathway-Driven Cancers and Rational Avutometinib Combinations

High Unmet Needs in Additional RAS/MAPK Pathway-Driven Cancers



Breadth of potential opportunity

- 30% of all human cancers are driven by mutations of the RAS family of genes[6]

Established prognostic significance

- Patients with mutations of the RAS family have an overall worse prognosis

Challenges with conventional approaches

- Modest progress; limited number of approved therapies
- Single agent therapies (e.g., MEK inhibitors) associated with resistance
- Tolerable combination regimens with MEK inhibitors have been challenging
- Approved RAS inhibitors address only a minority of all RAS mutated cancers (KRAS G12C

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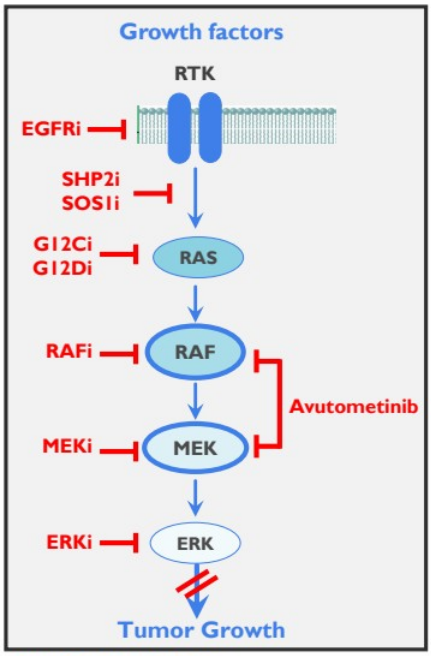
Incidence References:
[1]Reference for RAS mt frequencies – Cox et al. *Nature Reviews* 13: 828, 2014; [2]Reference for BRAF mt frequencies – Turski et al. *Mol Cancer Ther* 15: 533, 2016 [3]50% of NSCLC is adenocarcinoma (Pakkala and Ramalingam JCI Insight 2018); [4]90% of all uterine cancers are of the endometrial type (ACS); [5]Cancer Statistics 2020, Siegel et. al. *CA Cancer J Clin* 2020;70:7-30; [6]8 out of 10 thyroid cancers are of the papillary type (ACS)[7]CbioPortal

References:
McCormick F Clin Cancer Res 15April2015; [6]Adderley H et al. EBioMedicine 01Mar2019; Papke B et al. Science 17Mar2017; Ryan M et al. *Nature Reviews Clinical Oncology* 01Oct2018; NIH cancer.gov/research/key-initiatives/ras

Vertical Blockade: Establishing Avutometinib as the Backbone of Therapy for RAS/MAPK Pathway-Driven Tumors



- **Current Challenges**
  - Blocking any single target in the pathway is insufficient for maximum depth a duration of anti-tumor efficacy
    - e.g. SHP2i, KRAS-G12Ci, KRAS-G12Di, RAFi, MEKi, ERKi
  - Vertical blockade concept is now well established
    - Necessary to block more than 1 target in the pathway
  - Many of these agents (e.g. SHP2i, MEKi) have poor tolerability as monothera and in combination
- **Solutions offered by Avutometinib**
  - Vertical blockade (RAF and MEK blockade) in a single drug
  - Potential best-in-class tolerability with recommended twice weekly dosing regimen
    - Should enable tolerable combinations
  - Compelling synergy data (preclinical) for avutometinib combinations (e.g. wi KRAS G12C inhibitors) supporting clinical combinations
  - Ongoing clinical combination studies with G12Ci (sotorasib, adagrasib), anti-EGFR (cetuximab)

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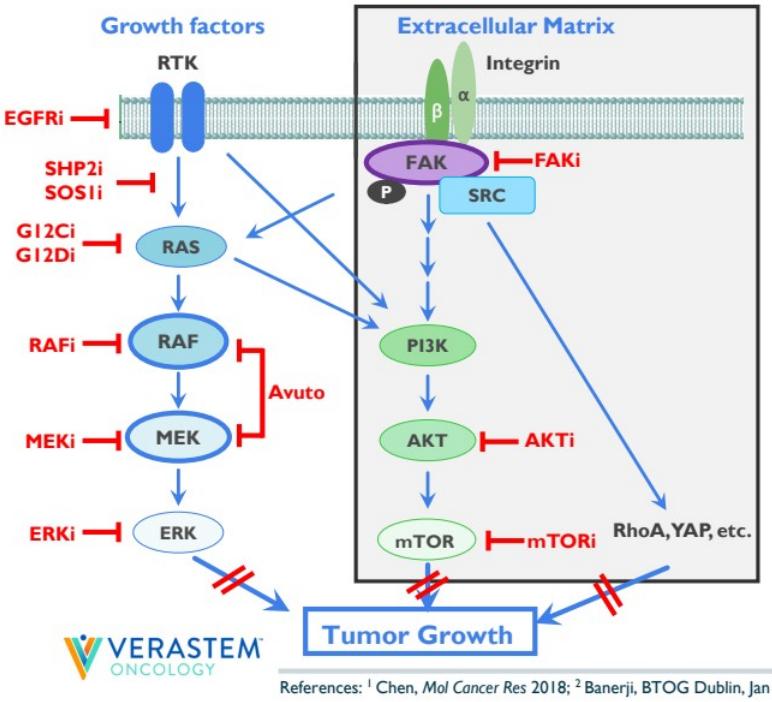
References: [1] Chen, *Mol Cancer Res* 2018; [2] Banerji, BTOG Dublin, Jan 23, 2019

Parallel Pathway Inhibition: Establishing Avutometinib as the Backbone of Therapy for RAS/MAPK Pathway-Driven Tumors



- **Current Challenges**
  - Blocking RAS pathway can be circumvented throug parallel pathways
    - e.g. PI3K/AKT/mTOR, FAK, RhoA, YAP
  - Combinations of MEKi + AKTi have shown poor tolerability

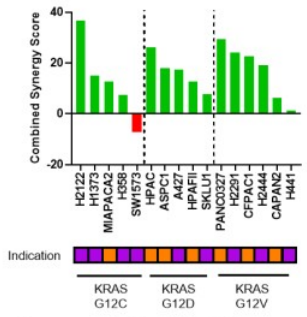
- **Solutions offered with Avutometinib**
  - Promising tolerability and early clinical data with twice weekly avutometinib opens up intermittent dosing options for combinations
  - Compelling preclinical synergy data with avutometinib in combination with several key anti-cancer agents (e.g. FAKi, mTORi)
  - RP2D established for avutometinib + FAKi (defactinib) and for avutometinib + mTORi (everolimus) with twice weekly regimen

References: [1] Chen, *Mol Cancer Res* 2018; [2] Banerji, BTOG Dublin, Jan 23, 2019

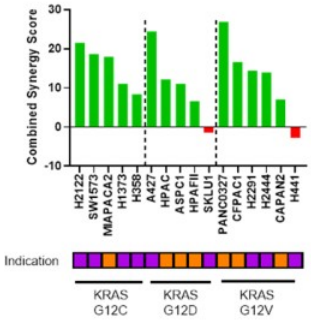
Preclinical Synergy of Avutometinib in Combination with Promising Agents for Clinical Investigation

Vertical RAS/MAPK Pathway Inhibition

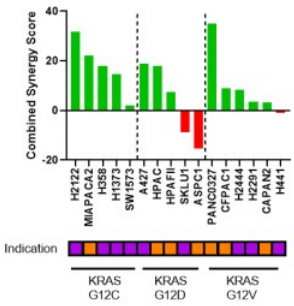
Avutometinib + pan-HERi (afatinib)



Avutometinib + SHP2i (RMC-4550)

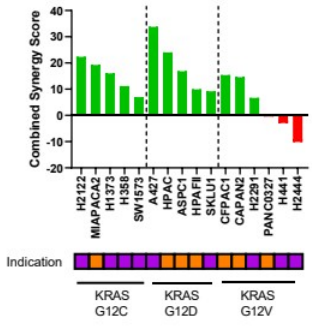


Avutometinib + SOS1i (BI-3406)

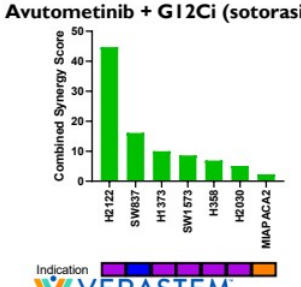


Parallel Pathway Inhibition

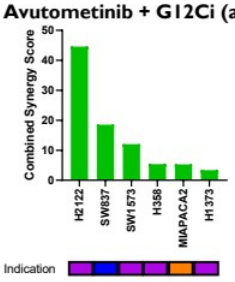
Avutometinib + CDK4/6i (palbocicli



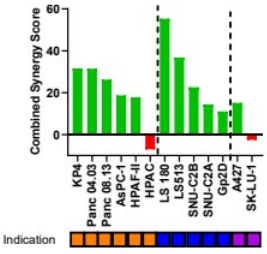
Avutometinib + G12Ci (sotorasib)

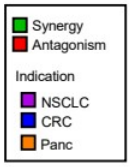


Avutometinib + G12Ci (adagrasib)

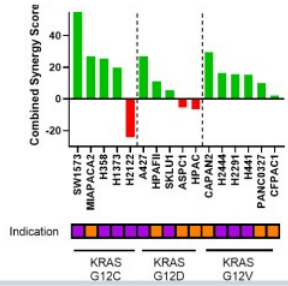


Avutometinib + G12Di (MRTX1133)





Avutometinib + mTORi (everolim



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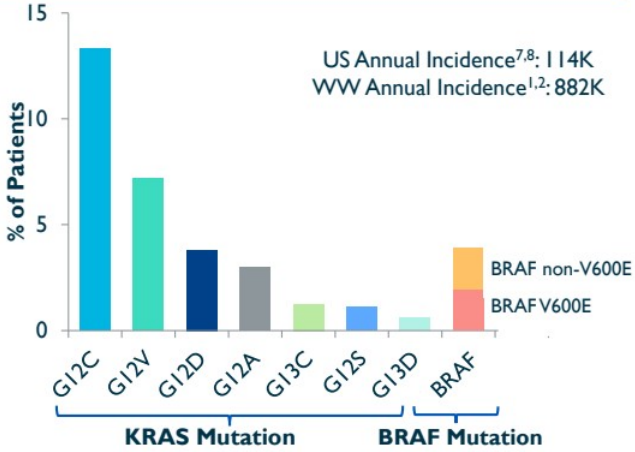
Avutometinib Combinations in Non-Small Cell Lung Cancer

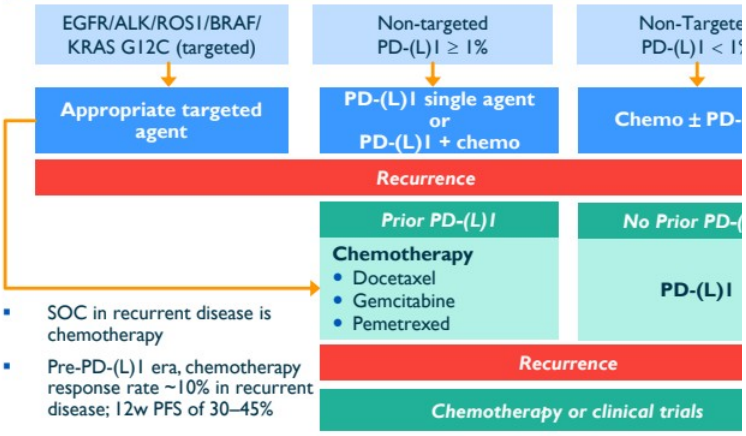
High Unmet Need in Refractory KRAS & BRAF mt NSCLC Adenocarcinoma

NSCLC Adenocarcinoma[3]



KRAS Mutations Represent 25% of Lung Cancer Adenocarcinoma & BRAF Mutations Represent ~4% (EGFR 17%, ALK 7%)[4,6]

Advanced or Metastatic NSCL Cancer Recommend Histologic and Molecular Subtyping[5]



- SOC in recurrent disease is chemotherapy
- Pre-PD-(L)1 era, chemotherapy response rate ~10% in recurrent disease; 12w PFS of 30–45%

Verastem Clinical Trials:

- RAMP 203: Avutometinib + sotorasib in KRAS G12C NSCLC
- RAMP 204: Avutometinib + adagrasib in KRAS G12C NSCLC
- RAMP 202: Avutometinib + defactinib in BRAF V600E and non-V600E N

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

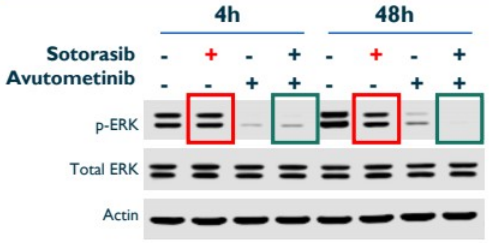
Preclinical Synergy of Avutometinib + G12C Inhibitors in KRAS G12C Models

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	Combined Synergy Score: 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

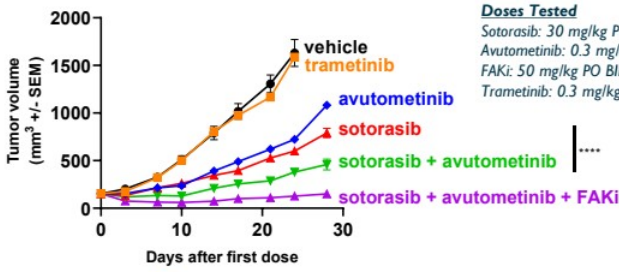
Avutometinib + sotorasib yields deeper and more sustained inhibition of ERK signaling pathway



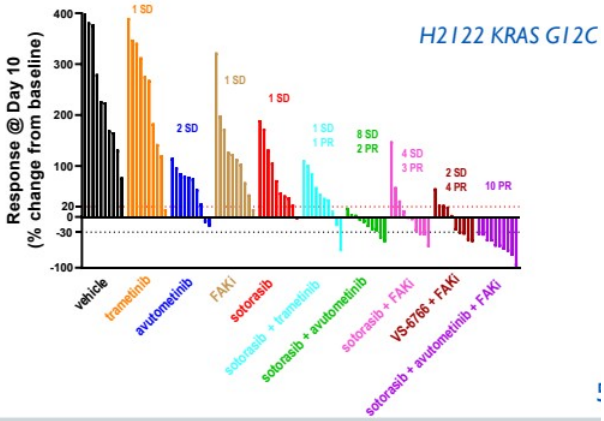
H2122 KRAS G12C NSCLC

Concentrations Tested
Sotorasib: 100 nM
Avutometinib: 100 nM

Avutometinib & FAKi potentiate sotorasib efficacy in KRAS G12 NSCLC in vivo; Tumor regression in all mice with triple combinat



Doses Tested
Sotorasib: 30 mg/kg P
Avutometinib: 0.3 mg/
FAKi: 50 mg/kg PO BI
Trametinib: 0.3 mg/kg



H2122 KRAS G12C

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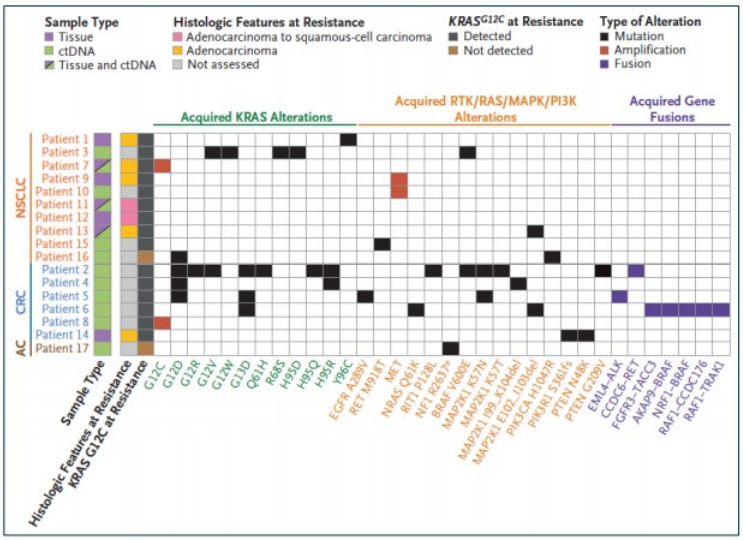
Reference: Coma et al., AACR 2021

Acquired Resistance Mechanisms to KRAS G12Ci Treatment in Patients Further Support Combination of KRAS G12Ci with Avutometinib

Summary of Putative Mechanisms of Acquired Resistance to Adagrasib Treatment



- Mechanisms of acquired resistance to KRAS G12Ci adagrasib treatment in patients recently reported[1,2]
- The main resistance alterations occurred in
  - RTK mts or amplifications
  - KRAS mts or amplification
  - NRAS mt
  - BRAF V600E, BRAF or CRAF fusions
  - MAP2K1 (MEK1) mt/deletion
- Avutometinib has shown activity against these KRAS, NRAS, BRAF and CRAF modifications

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

1 - 30 nM | 30 - 150 nM | 150 - 500 nM

Reference: Andrew Aguirre, unpublished

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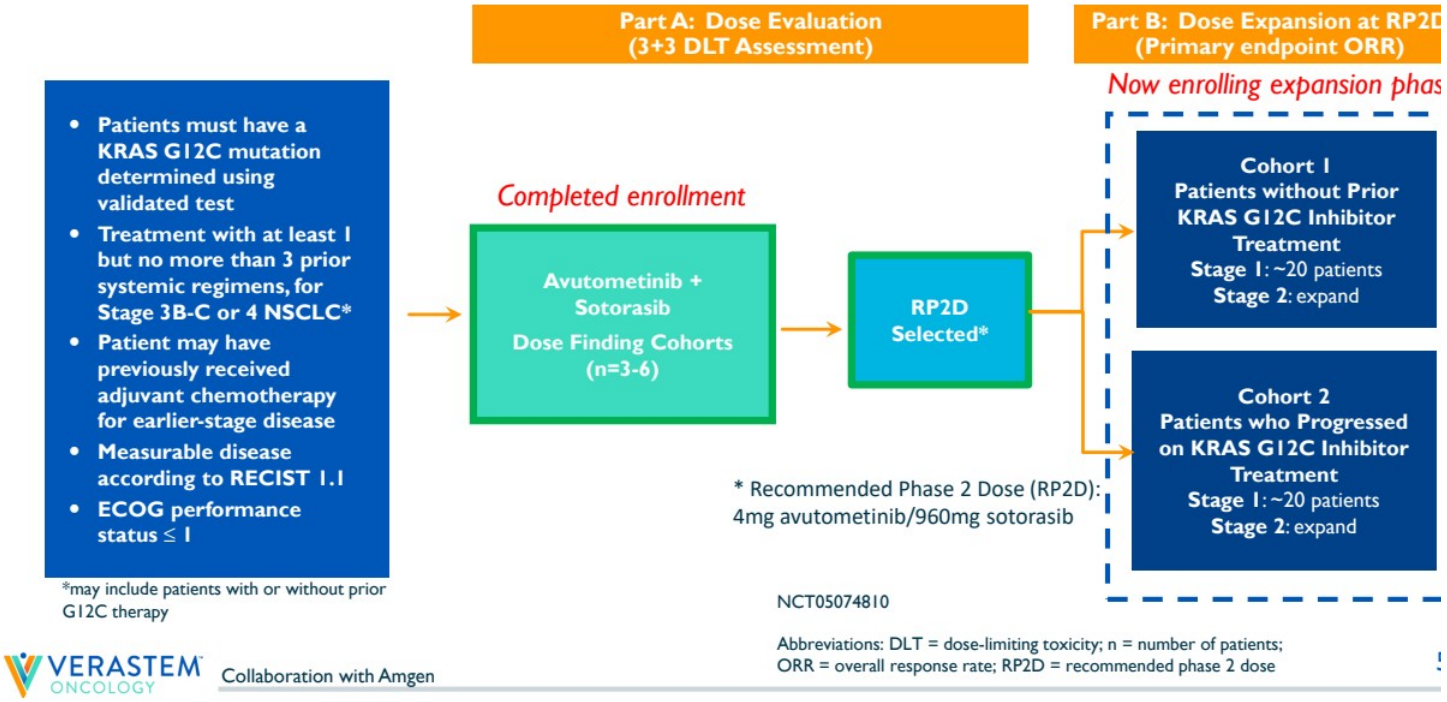
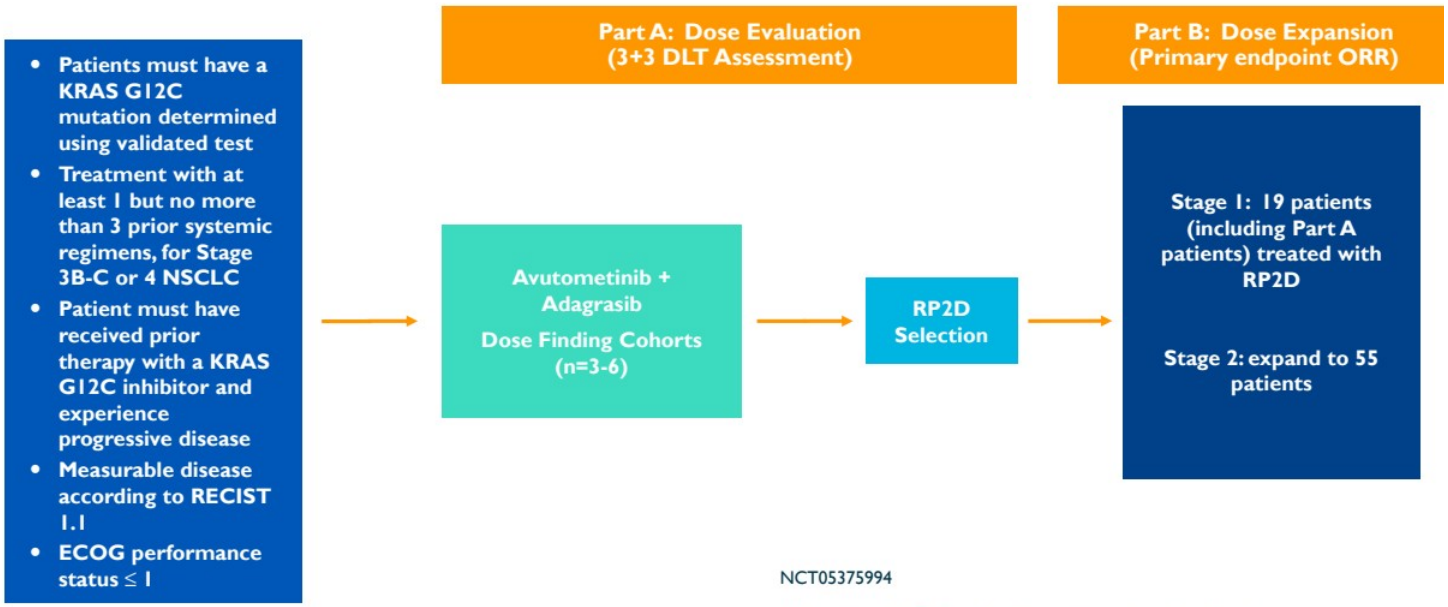
References: [1]Awad MM et al., N Engl J Med 2021; 384: 2382-93; [2]Tanaka et al., Cancer Discov 2021;11:1–10

RAMP 203: Phase 1/2 Trial of Avutometinib + LUMAKRAS™ (Sotorasib) in KRAS G12C Advanced NSCLC



VERASTEM ONCOLOGY Collaboration with Amgen

RAMP 204: Phase 1/2 Trial of Avutometinib + KRAZATI™ (Adagrasib) in KRAS G12C Advanced NSCLC

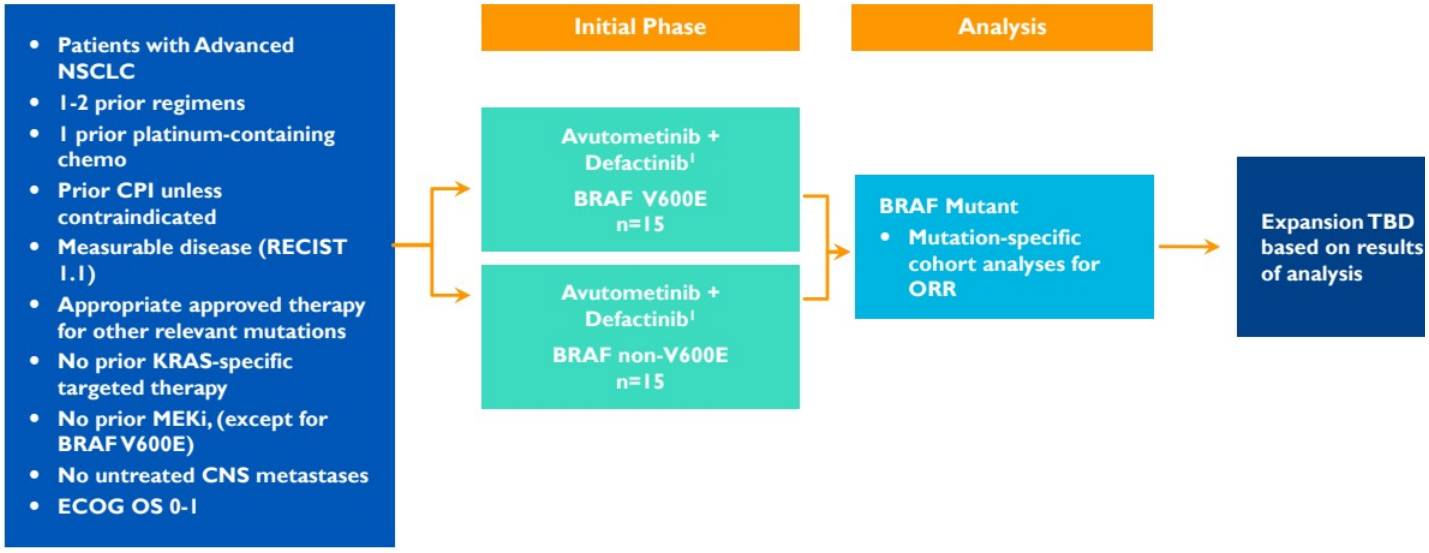


NCT05375994

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

VERASTEM ONCOLOGY Collaboration with Mirati Therapeutics

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



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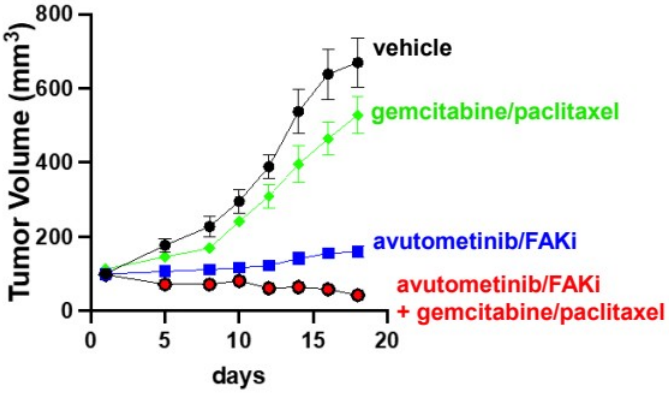
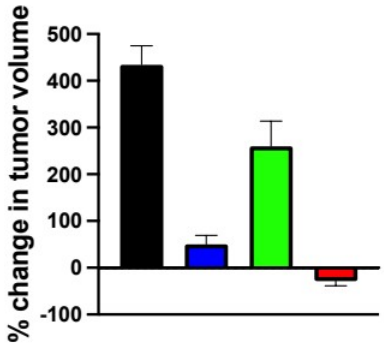
References:[1] Avutometinib 3.2 mg PO 2x/wk (21/28 days) + Defactinib 200 mg PO BID (21/28 days)

NCT04620330

Additional Avutometinib Combinations for Pancreatic, Colorectal and Melanoma

Preclinical Synergy of Avutometinib/FAK Inhibition + Chemotherapy 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

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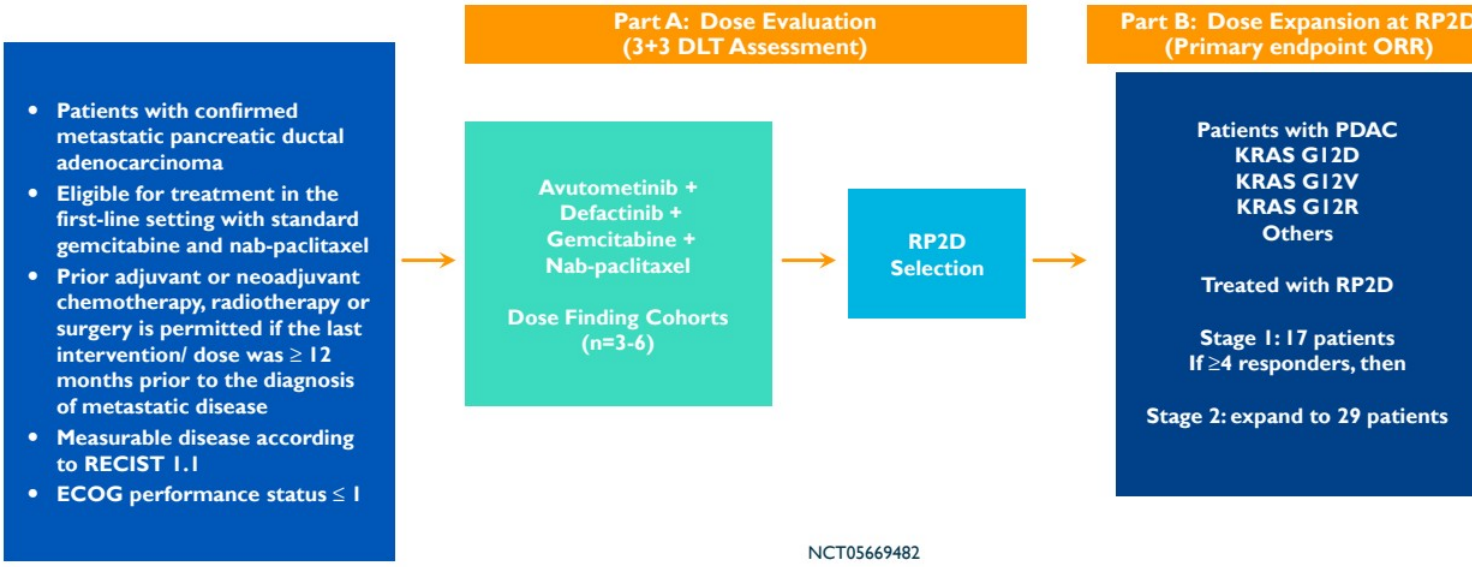
Collaboration with David DeNardo, Washington University; unpublished

RAMP 205: Phase 1/2 Trial of Avutometinib/Defactinib + GEMZAR™ (Gemcitabine)/ABRAXANE™ (Nab-paclitaxel) in Front Line Metastatic Pancreatic Cancer

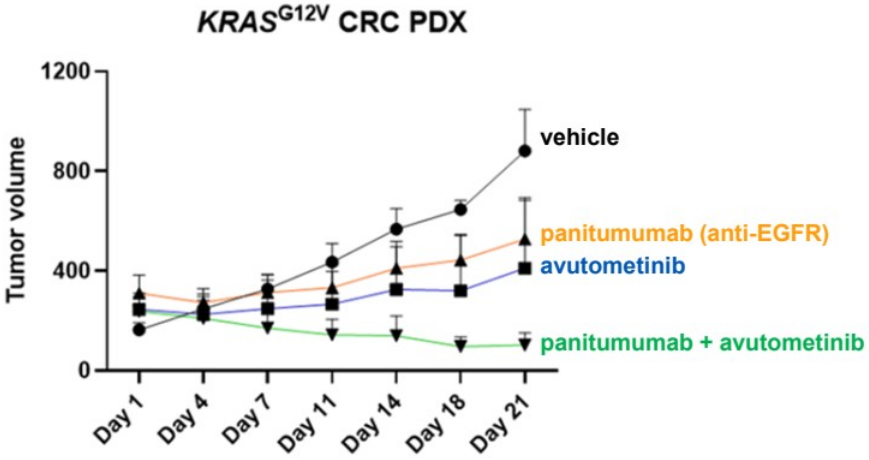


NCT05669482

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

VERASTEM ONCOLOGY Collaboration with PanCAN

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



- 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 G12 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

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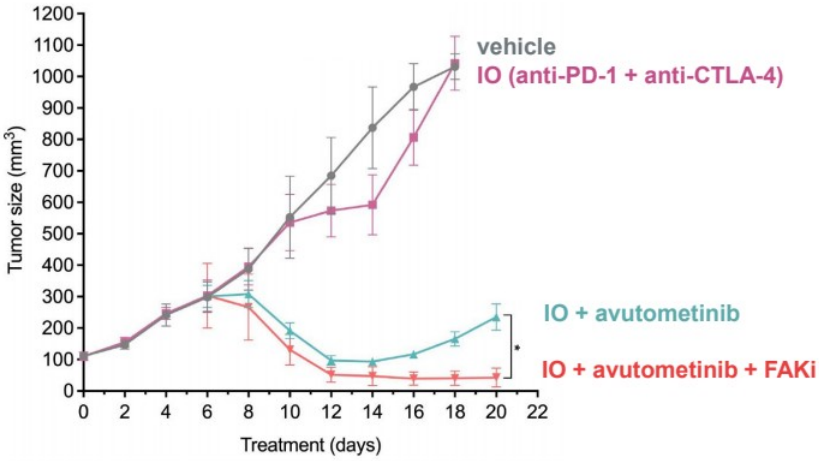
Combination of Avutometinib + FAK Inhibition with Checkpoint Inhibitor Induces Tumor Regression in an IO-resistant BRAF V600E melanoma model



- Avutometinib + IO (anti-PD-1 + anti-CTLA-4 induces tumor regression in an IO-resistant syngeneic BRAF V600E melanoma model (YUMM 1.7)
- FAK inhibition deepens and sustains avutometinib-induced tumor regression
- **These data support the imminent clinic evaluation of avutometinib + pembrolizumab (anti-PD-1) for treatm of BRAF V600E melanoma**

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Collaboration with Silvio Gutkind, UCSD; unpublished

Avutometinib Development in Multiple Combinations Across RAS Pathway-Driven Tumors with Potential Early Read-Outs in 2H 2023

Indication	Study
KRAS G12C NSCLC	RAMP 203: Avutometinib/Sotorasib combo
KRAS G12C NSCLC	RAMP 204: Avutometinib/Adagrasib combo
Pancreatic	RAMP 205: Avutometinib/Gem/Abraxane/Defactinib combo
KRAS mt NSCLC	Avutometinib/Everolimus combo*
KRAS mt CRC	Avutometinib/Cetuximab combo*
ER+ Breast	Avutometinib/Abemaciclib/fulvestrant combo*
RAS/RAF/NF1 Gynecological	Avutometinib/Defactinib combo*
BRAF V600E Melanoma	Avutometinib/Pembrolizumab combo*

*Investigator Sponsored Trials

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