

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): **June 26, 2024**

Verastem, Inc.

(Exact Name of Registrant as Specified in Charter)

Delaware
(State or Other Jurisdiction
of Incorporation)

001-35403
(Commission
File Number)

27-3269467
(IRS Employer
Identification No.)

117 Kendrick Street, Suite 500, Needham, MA
(Address of Principal Executive Offices)

02494
(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 June 26, 2024, Verastem, Inc. posted its updated 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
99.1 104	Corporate Presentation dated June 26, 2024 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: June 26, 2024

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



Delivering Novel Therapies in RAS/MAPK Pathway Driven Cancers

June 2024

Corporate Presentation



Disclaimers

Forward-Looking Statements

This presentation includes forward-looking statements about, among other things, Verastem Oncology's (the "Company") programs and product candidates, strategy, future plans and prospects, including statements related to the timing, scope and progress of the rolling New Drug Application (NDA) submission for the avutometinib and defactinib combination in low-grade serous ovarian cancer (LGSOC); the expected outcome and benefits of collaborations, including with GenFleet Therapeutics (Shanghai), Inc. (GenFleet), the potential clinical value of various of the Company's clinical trials, including the RAMP 201, RAMP 205 and RAMP 301 trials, the timing of commencing and completing trials, including topline data reports, interactions with regulators, the potential for and timing of commercialization of product candidates and potential for additional development programs involving the Company's lead compound and the potential market opportunities of, and estimated addressable markets for, our drug candidates. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," "can," "promising" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Each forward-looking statement is subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statement.

Applicable risks and uncertainties include the risks and uncertainties, among other things, regarding: the success in the development and potential commercialization of our product candidates, including avutometinib in combination with other compounds, including defactinib, LUMAKRAS™ and others; the uncertainties inherent in research and development, such as negative or unexpected results of clinical trials, the occurrence or timing of applications for our product candidates that may be filed with regulatory authorities in any jurisdictions; whether and when regulatory authorities in any jurisdictions may approve any such applications that may be filed for our product candidates, and, if approved, whether our product candidates will be commercially successful in such jurisdictions; our ability to obtain, maintain and enforce patent and other intellectual property protection for our product candidates; the scope, timing, and outcome of any legal proceedings; decisions by regulatory authorities regarding trial design, labeling and other matters that could affect the timing, availability or commercial potential of our product candidates; whether preclinical testing of our product candidates and preliminary or interim data from clinical trials will be predictive of the results or success of ongoing or later clinical trials; that the timing, scope and rate of reimbursement for our product candidates is uncertain; the market opportunities of our drug candidates are based on internal and third-party estimates which may prove to be incorrect; that third-party payors (including government agencies) may not reimburse; that there may be competitive developments affecting our product candidates; that data may not be available when expected; that enrollment of clinical trials may take longer than expected, which may delay our development programs, including delays in submission or review by the FDA of our NDA submission in recurrent KRAS mutant LGSOC; if enrollment in our confirmatory trial is not well underway at the time of submission; that our product candidates will cause adverse safety events and/or unexpected concerns may arise from additional data or analysis, or result in unmanageable safety profiles as compared to their levels of efficacy; that we may be unable to successfully validate, develop and obtain regulatory approval for companion diagnostic tests for our product candidates that require or would commercially benefit from such tests, or experience significant delays in doing so; that the mature RAMP 201 data and associated discussions with the FDA may not support the scope of our rolling NDA submission for the avutometinib and defactinib combination in LGSOC, including with respect to KRAS wild type LGSOC; that our product candidates may experience manufacturing or supply interruptions or failures; that any of our third-party contract research organizations, contract manufacturing organizations, clinical sites, or contractors, among others, who we rely on fail to fully perform; that we face substantial competition, which may result in others developing or commercializing products before or more successfully than we do which could result in reduced market share or market potential for our product candidates; that we will be unable to successfully initiate or complete the clinical development and eventual commercialization of our product candidates; that the development and commercialization of our product candidates will take longer or cost more than planned, including as a result of conducting additional studies or our decisions regarding execution of such commercialization; that we may not have sufficient cash to fund our contemplated operations, including certain of our product development programs; that we may not attract and retain high quality personnel; that we or Chugai Pharmaceutical Co., Ltd. will fail to fully perform under the avutometinib license agreement; that our total addressable and target markets for our product candidates might be smaller than we are presently estimating; that Secura Bio, Inc. will fail to fully perform under the asset purchase agreement with Secura Bio, Inc., including in relation to milestone payments; that we will not see a return on investment on the payments we have and may continue to make pursuant to the collaboration and option agreement with GenFleet or that GenFleet will fail to fully perform under the agreement; that we may not be able to establish new or expand on existing collaborations or partnerships, including with respect to licensing of our product candidates, on favorable terms, or at all; that we may be unable to obtain adequate financing in the future through product licensing, co-promotional arrangements, public or private equity, debt financing or otherwise; that we will not pursue or submit regulatory filings for our product candidates; and that our product candidates will not receive regulatory approval, become commercially successful products, or result in new treatment options being offered to patients.

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

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 whether as a result of new information, future events or otherwise, except as required by law.

Use of Non-GAAP Financial Measures

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 this measure, 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 this non-GAAP financial measure and the most comparable GAAP financial measure are included in the footnotes to the slides in this presentation on which such non-GAAP number appears.

Third-Party Sources

Certain information contained in this presentation, including industry and market data and other statistical information, relates to or is based on studies, publications, surveys and other data obtained from third-party sources and the Company's own internal estimates and research. While the Company 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: Preparing to Commercialize First Novel RAS/MAPK Combo Asset with Billion-Dollar Addressable Market Opportunity

Transition to commercial-stage company focused on RAS/MAPK-driven cancers

Avutometinib and defactinib combo has the potential to become the first and only FDA approved treatment for recurrent LGSOC as soon as 2025

Market expansion with avutometinib + defactinib in first-line metastatic pancreatic cancer and advanced lung cancer

Partnership with GenFleet Therapeutics on novel, potential best-in-class RAS pathway programs for additional value creation

Pipeline Assets Have the Potential to Provide Significant Market Opportunity in Both Short- and Long-Term

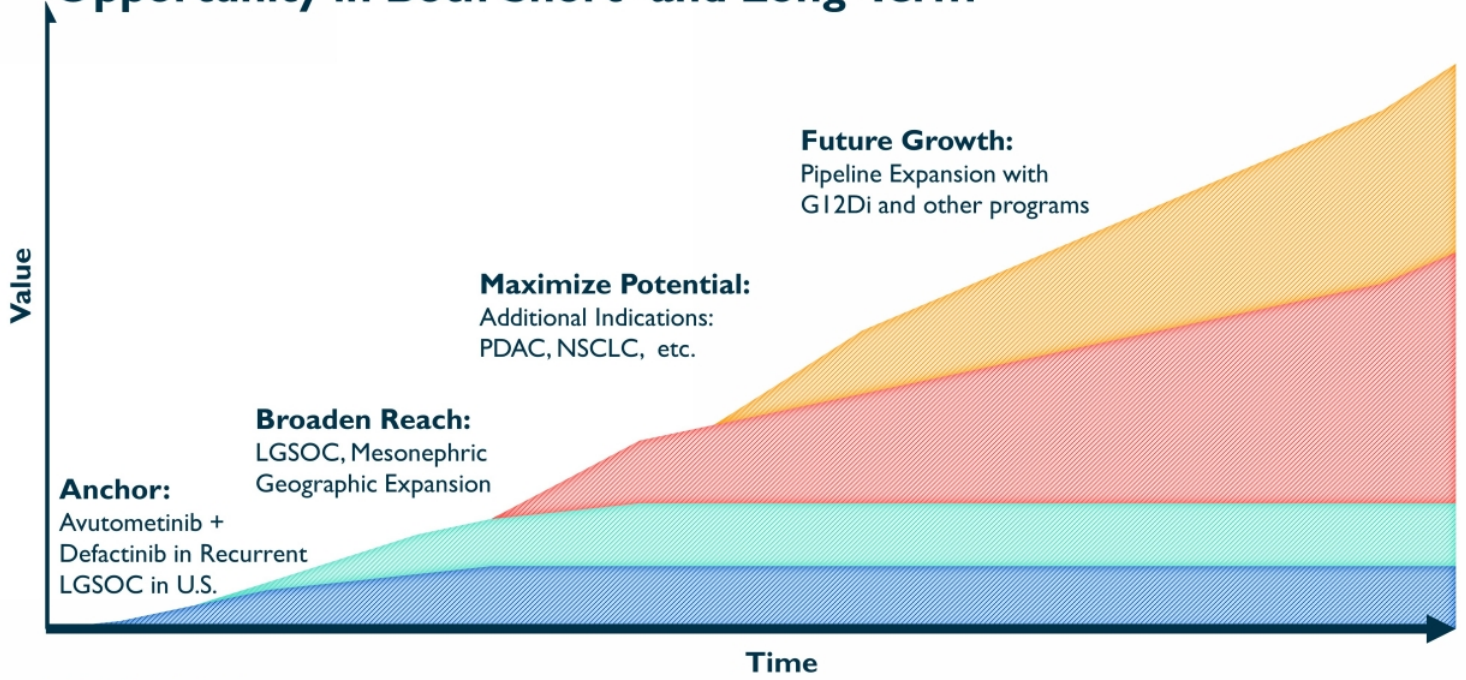
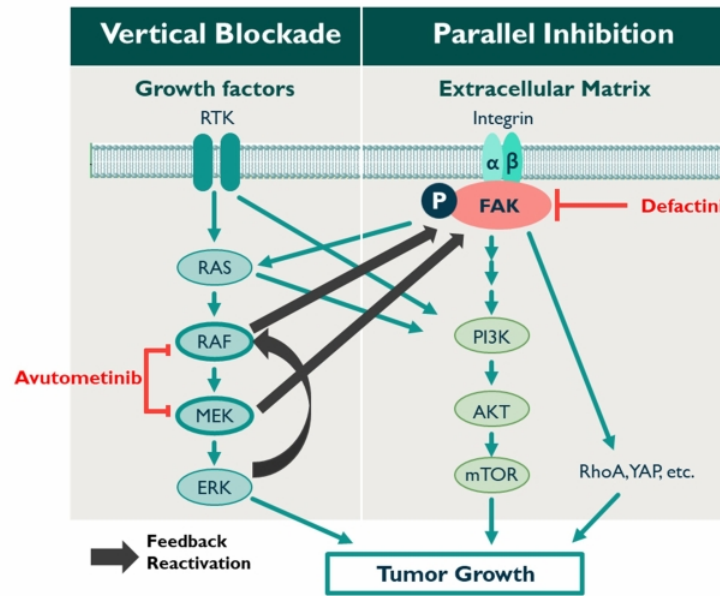


Image for illustrative purposes only.

PDAC: pancreatic ductal adenocarcinoma cancer; NSCLC: non-small cell lung cancer

Lead Program: Avutometinib + Defactinib Aims to Inhibit Multiple Resistance Mechanisms in the RAS/MAPK Pathway to Improve Patient Outcomes

- Novel combination of avutometinib, a RAF/MEK clamp, and defactinib, a FAK inhibitor, offers a complementary MOA not achievable with previous MEK-only inhibitors
- Clinical activity in various RAS pathway-driven cancers, including in patients whose tumors previously progressed on other MEK inhibitors³⁻⁵
- Clinical data demonstrate potential best-in-class safety & tolerability profile relative to marketed MEK-only inhibitors and standard of care therapies for LGSOC¹⁻⁴



¹Gershenson et al., Lancet 2022 (Study GOG 281); ²Monk et al., J Clin Oncol 2020 (MILO Study); ³Banerjee et al., ESMO Sept 2021 (Study FRAME); ⁴Banerjee et al., ASCO June 2023 (Study RAMP 201); ⁵Awad et al., EORTC-NCI – AACR Conference Oct 2023 (Study RAMP 203); MOA: mechanism of action;

Clinical Program Designed to Address LGSOC and Beyond

Trial/Regimen	IND-Enabling/ Preclinical	Phase 1	Phase 2	Phase 3	Anticipated Milestones	Collaboration
Avutemetinib + Defactinib: Recurrent LGSOC						
RAMP 301 RAF/MEK Clamp + FAKi vs ICT	[Progress bar]				RAMP 301 Ongoing Enrollment	
RAMP 201 RAF/MEK Clamp + FAKi	[Progress bar]				Plan to announce RAMP 201 mature dataset in H2 2024; Expect to complete rolling NDA Submission in Recurrent LGSOC: H2 2024	
Avutemetinib ± Defactinib + KRAS G12C Inhibitors: mKRAS G12C NSCLC						
RAMP 203 RAF/MEK Clamp ± FAKi + KRAS G12Ci (sotorasib)	[Progress bar]				RAMP 203 Updated Interim Data: H2 2024	Amgen
RAMP 204 RAF/MEK Clamp + KRAS G12Ci (adagrasib)	[Progress bar]				RAMP 204 Initial Interim Data: H2 2024	Mirati (BMS)
Avutemetinib + Defactinib + Chemotherapy: 1L Metastatic Pancreatic Cancer						
RAMP 205 RAF/MEK Clamp + FAKi + gemcitabine, nab-paclitaxel	[Progress bar]				RAMP 205 Updated Safety & Efficacy Data: H1 2025	PanCAN
GFH375/VS-7375						
KRAS G12D (ON/OFF) inhibitor	[Progress bar]				IND cleared and initiating Phase 1/2 trial in China	GenFleet



RAF: Rapidly Accelerated Fibrosarcoma; MEK: Mitogen-activated extracellular signal-regulated kinase; FAKi: focal adhesion kinase inhibitor; KRAS: Kirsten Rat Sarcoma virus; ICT: investigator choice of treatment; NSCLC: non-small cell lung cancer; NDA: New Drug Application

Avutometinib + Defactinib

Potential Approval in 2025 for Recurrent Low-Grade Serous Ovarian Cancer

Potential to Bring a New Treatment Option for Recurrent LGSOC with Substantially Improved Outcomes on an Accelerated Timeline

Avutemetinib + Defactinib combo has the potential to be first and only FDA approved treatment specifically for recurrent LGSC



- **Initiated rolling NDA submission** based on the strength of the preliminary RAMP 201 data with minimum of 5 months follow up in KRAS mt population¹

- **Anticipate patients in U.S. achieving broad and rapid access to therapy regardless of KRAS status** (either through label or NCCN)

- **Seeking broadest label possible** with mature RAMP 201 data to inform final indication
- Recent **SoC LGSOC studies provide best data to benchmark** against

• **Substantial Opportunity with Total Addressable Market²:**

- Initial focus on prevalence population: KRAS mt \$1.2B+, KRAS wt \$1.0B+
- Annual opportunity of \$570M

- **Efficacy and safety data package has potential to show advantage across subgroups** and favorable benefit/risk profile

- **If approved, expect rapid adoption and high market penetration** given no FDA approved therapies and based on oncologist survey¹



1. Feb. 2024 data cutoff; 1. VSTM DOF, ATU 2024 (n=96, Fielded December 2023 – January 2024); 2. Refer to breakdown of market opportunity on slide 11. SoC: Standard of Care; mt: mutant; wt: wild-type; NCCN: National Comprehensive Cancer Network

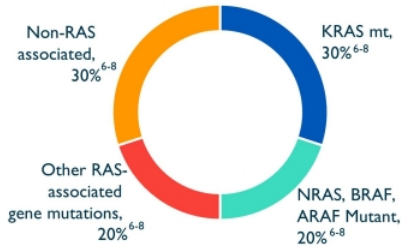
High Unmet Need for an Effective Therapy in Recurrent LGSOC That is Also Tolerable and Offers Better Outcomes

LGSOC is a rare ovarian cancer that is insidious, persistent and ultimately fatal with no FDA approved treatments¹⁻⁴

U.S. Incidence: 1k-2k¹²

U.S. Prevalence: 6k-8k¹³

Worldwide: 80,000



20-30s

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



Nonspecific signs and symptoms include bloating, pelvic or abdominal pain, back pain, fatigue, upset stomach and more¹⁵

6-13%

Current SoC treatments (hormone/chemotherapy) **offer poor to moderate response rates** and patients will cycle through therapy⁵



80%+ of patients will experience a recurrence¹



Median OS of ~10 years from time of diagnosis¹¹

- KRAS mt – 12 years¹⁶
- KRAS wt – 7 years¹⁶



1. Babsier 2022; 2. Gadducci 2020; 3. Gershenson Lancet 2022; 4. Gershenson 2015; 5. Gershenson Gynecol Oncol 2022; 6. Manning-Geist Clin Cancer Res 2022; 7. El Naggar Gynecol Oncol 2022; 8. AA GENIE v9.0 VSTM unpublished analysis (data on file); 9. Slomovitz Gynecol Oncol 2020; 10. Manning-Geist B et al. Clin Cancer Res 2022; 11. Banerjee SN. J Clin Oncol 41, No. 16, suppl (June 1, 2023) 551S-551S; 12. Verastem DOF; 13. US Cancer Statisticians 2024; 14. Monk 2020; 15. Ferrell B, et al. Symptom concerns of women with ovarian cancer. J Pain Symptom Manage. 2003;25(6):528-538; SoC: Standard of Care; OS: Overall Survival. 16. Calculated using figures in Gershenson Gynecol Oncol 2022.

Avutometinib + Defactinib Combo Has the Potential to Address Key Treatment Needs

- To date, avutometinib + defactinib combination data in recurrent LGSOC show:
 - Clinically meaningful response rates and durable benefit¹
 - Strong Clinical Benefit Rate in patients with KRAS mutant or wild-type tumors,² which supports treatment decisions
 - Long progression-free survival (PFS) and duration of response (DoR) are achievable in patients who have received multiple lines of therapy, including prior MEK inhibitor¹
 - Low discontinuation rates due to adverse events²
 - Novel intermittent dosing schedule, with oral treatments, supports favorable tolerability profile³



1. Data from RAMP 201 study Feb. 2024 cutoff 2. Data from FRAME study; 3. Chenard-Poirier, et al. ASCO 2017; References: Banerji, Q4 2020 report; ; 4. VSTM DOF, ATU 2024 (n=96, Fielded December 2023 – January 2024); ORR: Objective Response Rates

When treating recurrent LGSOC, doctors place most importance on efficacy and safety, while adhering to NCCN guidelines:⁴

Improves outcomes: PFS, ORR

Has meaningful disease control rate

Has tolerable side effect profile

Has good access coverage

Start of Rolling NDA Submission Supported by RAMP 201 Initial Topline Results with Minimum of 5 Months Follow Up

RAMP 201 Shows Robust Early Responses, May Continue to Deepen with Mature Follow Up

Data cutoff: Feb. 2024, minimum of 5 months of follow up. Avutometinib 3.2 mg + Defactinib 200 mg

ORR Overall Population (Confirmed ORR by BICR)	27% (29/109) ¹
95% CI	(19%, 36%)
KRAS mt	37% (21/57)
KRAS wt	15% (8/52)

Clinical Benefit Rate Is a Key Driver of Treatment Decisions Among Physicians²

Clinical Benefit Rate (CR+PR+SD \geq 6 months):	60% (65/109)
Clinical Benefit Rate KRAS mt:	68% (39/57)
Clinical Benefit Rate KRAS wt:	50% (26/52)

Discontinuation Rates Due to Adverse Events Remain Low²

Discontinuations Due to AEs No new safety signals	9% (10/115)
---	--------------------

In RAMP 201, 14 Patients with Stable Disease or Unconfirmed Partial Response Remain on Treatment²

Potential responding patients:	29-43 (27%-39%)
Potential responding KRAS mt patients:	21-30 (37%-53%)
Potential responding KRAS wt patients:	8-13 (15%-25%)



1. 6 patients with no baseline measurable disease per IRC; 2. All information based on data cutoff of Feb. 2024. Minimum of 5 months follow up. Avutometinib 3.2 mg + Defactinib 200 mg; BICR: Blinded independent central review

Recent LGSOC Trials with Standard of Care Highlight High Unmet Need

Trial	Image Assessment	Median Number of Prior lines of Therapy	Prior MEK Allowed	Therapy	Response Rate ORR	Discontinuation Rate Due to AEs
GOG 281 ¹	INV	2 (1-10)	No	Standard of Care**	6% ^ 95% CI: (3%, 12%)	30%
MILO ²	BICR	2* (1-8)	No	Standard of Care**	13% 95% CI: (7%, 21%)	17%

* MILO: no more than 3 lines of prior chemotherapy

**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

Opportunity to Improve Upon Standard of Care

Trial	Image Assessment	Median Number of Prior lines of Therapy	Prior MEK Allowed	Therapy	Response Rate ORR	Discontinuation Rate Due to AEs
RAMP 201 ⁴	BICR	4	Yes	Avutometinib + Defactinib	27% 95% CI: (19%, 36%)	9%
FRAME	BICR	3.5	Yes	Avutometinib + Defactinib	42% 95% CI: (23%, 63%)	4%



No head-to-head clinical trials have been conducted between avutometinib and defactinib combination and SoC. Comparisons are made from different clinical trials at different points in time, with different trial design and patient populations. As a result, cross-trial comparison cannot be made.

¹Study GOG 281 trial Gershenson et al., Lancet 2022; ²MILO Study Monk et al., J Clin Oncol 2020; ³Banerjee et al., ESMO Sept 202; ⁴Data cutoff: Feb. 2024, minimum of 5 months of follow up. Avutometinib 3.2 mg + Defactinib 200 mg
SoC = Standard of Care (endocrine / chemotherapy). INV = Investigator, BICR = Blinded independent central review, PFS = Progression free survival; CI = confidence interval, NR = Not reached

KOL Feedback on Avutometinib + Defactinib in Recurrent LGSOC Reinforces Opportunity to Address Unmet Treatment Needs

'Current RAMP 201 ORR in heavily pretreated patients is better than any treatment options available'

"We are very excited about the recent data reported for the RAMP 201 study and initiation of the rolling submission. An overall response rate of close to 30% in heavily pretreated patients is better than any treatment options we have available for LGSOC patients today and line of therapy matters as we've learned from other studies in LGSOC. Response rates are higher in KRAS-mutated patients compared to KRAS wild-type disease and this is what we would expect since KRAS wild-type has a less favorable prognosis."

'Response rates with SoC are disappointing and tolerability with MEK inhibitors was an issue'

"What is important here is how this compares to what we currently have available for patients with standard-of-care treatments where response rates are disappointing. We continue to use chemotherapy and hormonal therapy in spite of low response rates of 6-13%. In terms of the MEK inhibitors, binimetinib had a response rate of 16% and did not beat standard of care, and for trametinib response rates were 26% but not independently reviewed and tolerability was an issue. In the end, the MEK inhibitors did not get reviewed by the FDA and there are still no FDA approved treatments for LGSOC."

'If approved, [Avutometinib + Defactinib] will change the Standard of Care'

"Overall, the RAMP 201 update is good news for patients and seeing this now under review by the FDA is an important milestone. If approved, this will change the standard of care."

Bradley J. Monk, MD, FACS, FACOG

Florida Cancer Specialists and Research Institute, Medical Director Late-Phase Clinical Research
Vice President and Member Board of Directors GOG-Foundation, Director GOG-Partners
RAMP 201, RAMP 301 investigator

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

STAGE II-IV DISEASE¹

→ MOS: ~10 YEARS²

FRONTLINE TREATMENT

→ INITIAL RECURRENCE

→ SUBSEQUENT RECURRENCE

± Neoadjuvant platinum/taxane
Debulking surgery
± Platinum/taxane chemotherapy
± Hormone therapy (Mx)
or
± Endocrine therapy

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

- 70% of Oncologists surveyed indicate they **will initially plan to treat with prevalent patients at their next recurrence**³
- 49% of Oncologists surveyed indicate that **initial recurrence is the ideal point** in the patient journey to initiate treatment with the combination³

85% of treaters surveyed say they **would adopt within 6 months of receiving FDA approval**, suggesting swift uptake of the treatment for eligible patients³

28% of treaters surveyed say they **would proactively reach out to switch** half of their current LGSOC patients, if approved³



1. NCCN: National Comprehensive Cancer Network; NCCN guidelines v1.2023; 2. Gershenson Gynecol Oncol 2022/p11/Abstract/Results/In1-2; 3. VSTM DOF, ATU 2024 (n=96, Fielded December 2023 – January 2024); Mx: maintenance

LGSOC Indication Represents Significant Market Opportunity

Total Addressable Market Opportunity	KRAS mutant	+	KRAS wild-type
Estimated Annual Incident Addressable Opportunity ¹	\$300M+		\$270M+
Incident Population ²	~500		~1,000
Avg. Duration of Therapy ³	18 months		8 months
Estimated Prevalent Addressable Opportunity ¹ (Target to Address in First 3-5 Years)	\$1.7B+		\$1.1B+
Prevalent Population ²	~2,800		~4,200
Avg. Duration of Therapy ³	18 months		8 months

Anticipate high market penetration in LGSOC KRAS mt population given:

- No FDA approved therapies for LGSOC
- High adoption rate based on Survey of Oncologists⁴

Plan to address prevalent population over 3-5 years from launch:

- Patients cycle through therapies
 - Median of 4 prior therapies in RAMP 201
- Long overall survival in LGSOC patients at ~10 years
 - KRAS mt – 12 years
 - KRAS wt – 7 years



1. Estimated total addressable market opportunity based on incident / prevalent populations, average duration of therapy (as observed in VSTM clinical trials) and cost of therapy of \$34,000 per month, consistent with other recent oncology drug launches (e.g. OJEM \$33,916 OGSIVEO - \$29,000; www.dsayonebio.com/wp-content/uploads/Ojemida-Connecticut_VF.pdf; www.hhs.texas.gov/sites/default/files/documents/apr-2024-durb-agenda-item8d.pdf) 2. Verastem DOF – Based on 30% KRAS mt and 70% KRAS wt in incident popl assumed of 1,500 annually and 40% KRAS mt and 60% KRAS wt (calculation on file based on weighted average longer overall survival in KRAS mt compared to KRAS wt) initial prevalent population of 7,000; 3. RAMP 201 Part A data cutoff 23FEB2024; 4. Based on V DOF, ATU 2024 (n=96, Fielded December 2023 – January 2024) 70% of Oncologists surveyed would treat with A&D at next recurrence; kept 70% for KRAS mt, and assumed 50% discount for KRAS wt.

Efficiently Scaled Commercial Model to Deliver Best-In-Class Launch

HCO/Key Account Focus

Top 100 commercial HCOs contribute 49.4% of patient claims¹
 ~400 HCPs manage these patients!
 Deploy lean, focused field team (14-18 reps)

Patient Focused

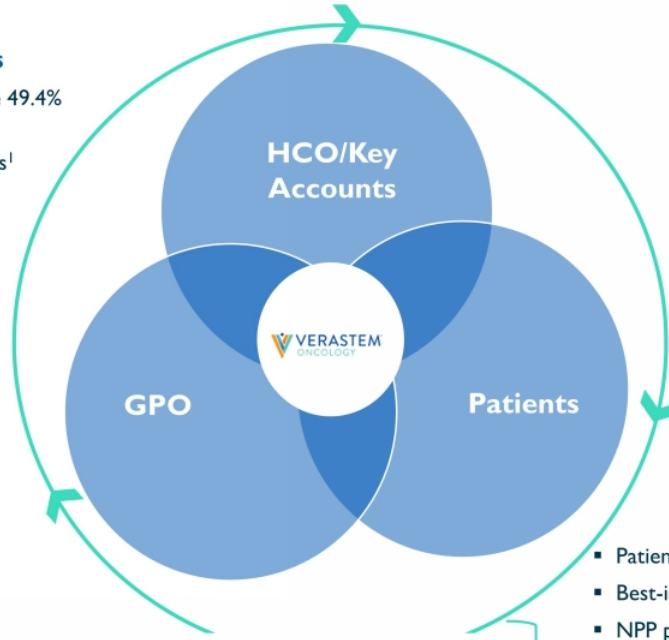
YTD more than 2,100+ patients have registered on DSE website, which represents 35% of the population²



Robust program for ongoing education and resources

GPO/Large Affiliated Practices

Ensuring inclusion in all relevant pathways and EMR systems
 Access is based on group provided programs and/or opportunities



Surround Sound Support Programs

- Patient support and access programs
- Best-in-class multichannel marketing
- NPP pull through and reinforcement to targeted customers and white space territories
- Inside Sales Reps will bolster Field Force efforts



1. VSTM DOF – Claims LGSOC Proxy; 2. VSTM DOF. Self-identified patients with LGSOC registered via DSE (disease) website; YTD: Year-to-date; NPP: Non-personal promotion

Pursuing Broadest Label Possible with Mature Data from RAMP 201

Expect to Complete Rolling NDA Submission in H2 2024

Regulatory Approach

- Seeking Accelerated Approval, ORR and DoR are main efficacy outcomes
- No FDA approved treatments
- Current SoC therapy is associated with low response rates and high discontinuation rate due to toxicity

SoC¹: ORR: 6-13%
D/C Due to AE: 17-30%

- Avutometinib + Defactinib clinical data shows advantage over available therapy

Avutometinib + Defactinib:
ORR: 27%*
KRAS mt: 37%, KRAS wt: 15%
D/C Due to AE: 9%

Upcoming Milestones

- Submit final NDA module to include efficacy & safety from mature RAMP 201 to complete rolling submission and data from overall population to inform final indication
- Expect to complete rolling submission in H2 2024, priority review request
- Target to complete full enrollment by end of 2025 for ongoing Phase 3 (RAMP 301) confirmatory study
- Plans to discuss regulatory path with CHMP and PMDA (EU and Japan)

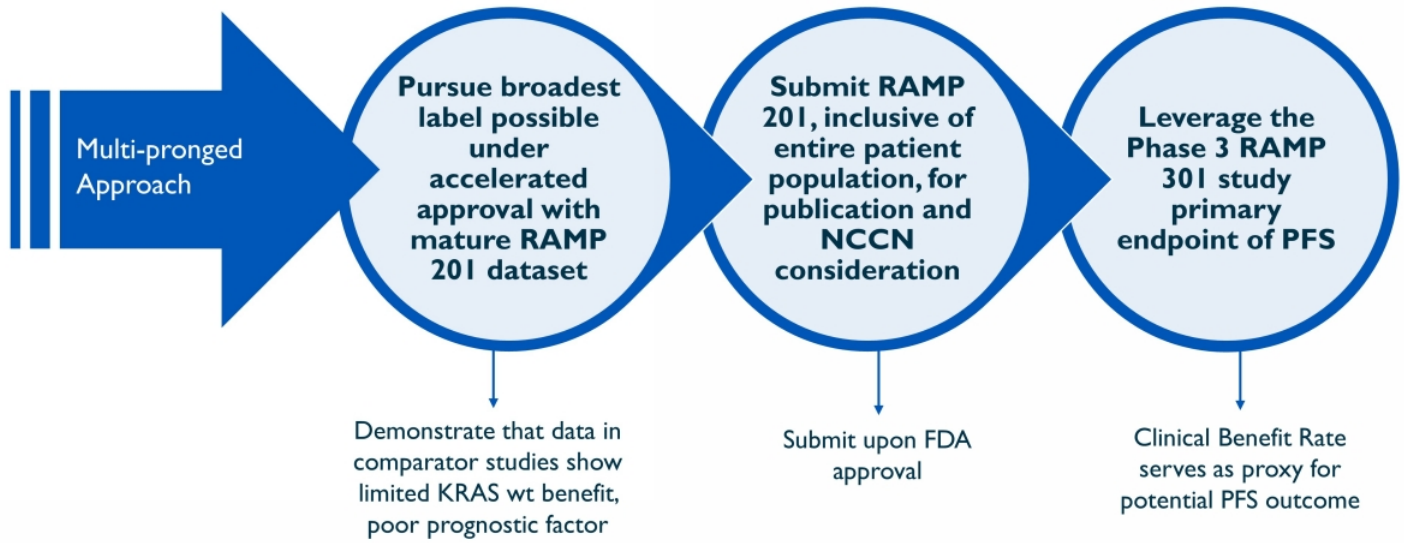
**Potential for FDA
accelerated
approval in 2025**

*RAMP 201 Parts A,B, C, Feb. 2024 cutoff – minimum of 5 months follow up



These data are derived from different clinical trials at different points in time, with differences in trial design and patient populations, cross-trial comparison cannot be made, and no head-to-head clinical trials have been conducted.
Breakthrough Therapy Designation for combination of avutometinib and defactinib for treatment of recurrent LGSOC after one or more prior lines of therapy including platinum-based chemotherapy; I. Gershenson et al, Lancet 2022; Monk et al, JCO 2020; CHMP: Committee for Medicinal Products for Human Use; PMDA: Pharmaceutical and Medical Devices Agency; EU: European Union; D/C: discontinuation

Multi-Pronged Approach to Ensure Patients with Recurrent KRAS Wild-Type LGSOC Will Have Access to Avutometinib + Defactinib, if Approved



Leverage RAMP 301 to Support Regulatory Path in the U.S., ROW

RAMP 201: Phase 2 Registration-Directed Trial Target Enrollment Completed

- Patients enrolled with recurrent KRAS mt and KRAS wt LGSOC; prior chemo and MEKi use allowed
 - Primary Endpoint: ORR
- Determined avutometinib 3.2 mg BIW + defactinib 200 mg BID combination as go forward regimen based on greater antitumor activity and tolerability profile vs avutometinib 4.0 mg BIW monotherapy
- Expansion phase of combo includes 115 patients at RP2D
- Low-dose evaluation of avutometinib of 1.6 mg BIW and defactinib 200 mg BID to be submitted to FDA as part of Project Optimus
- Mature data expected in H2 2024

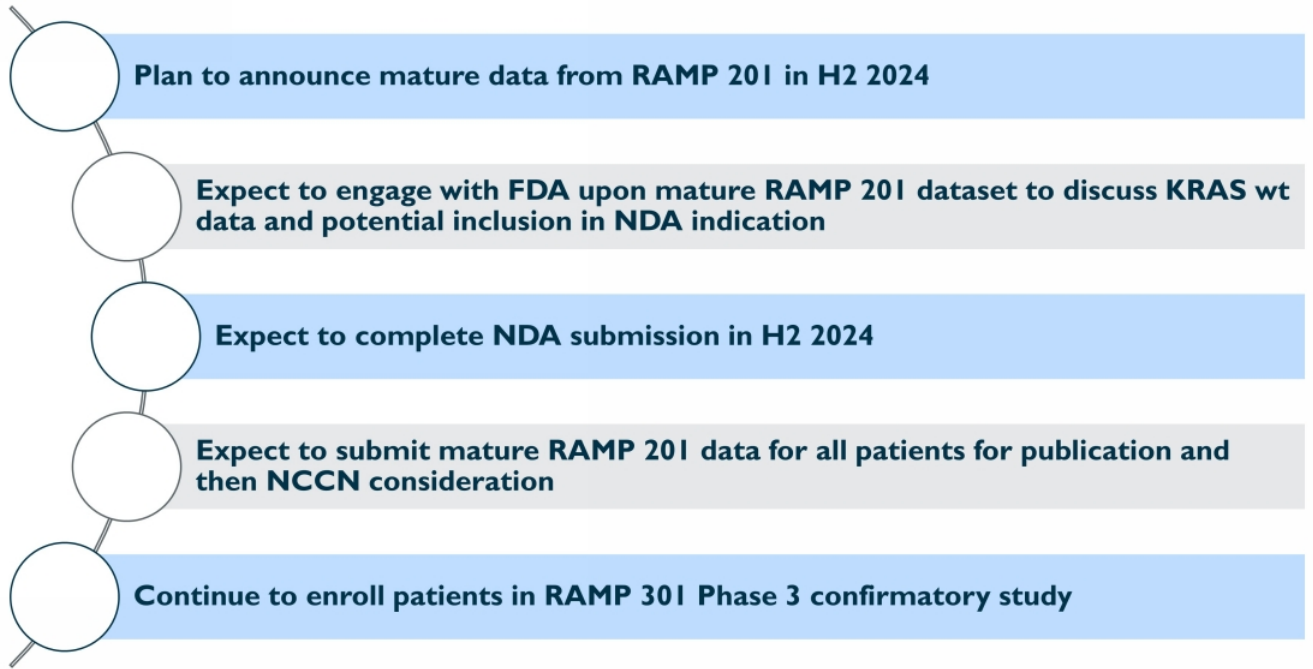
RAMP 301: Phase 3 International Confirmatory Trial Enrollment Ongoing

- Patients enrolling is similar to patient population in RAMP 201, with recurrent KRAS mt and KRAS wt LGSOC; prior MEKi and bevacizumab use allowed and post one line of platinum chemotherapy
 - Primary Endpoint: PFS
- Stratification Factors: KRAS mutation status (wt vs. mt)
- Investigator choice of treatment
 - May crossover to avutometinib + defactinib arm upon BICR-confirmed progressive disease (PD)
- Study sites include the U.S., Australia, UK, Canada, Europe, and South Korea
 - Targeting full enrollment by end of 2025



BIW: twice a week; BID: twice a day

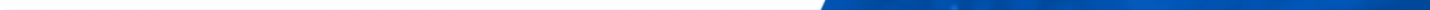
Next Steps in LGSOC Clinical Program and NDA



Avutometinib ± Defactinib

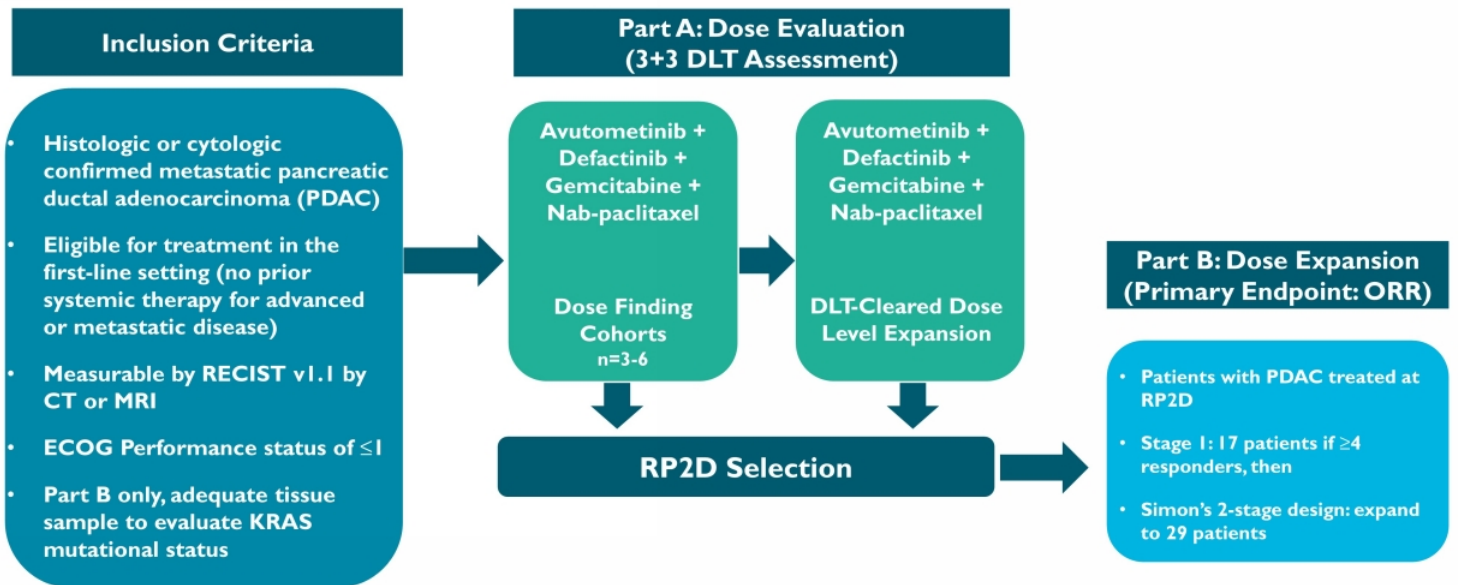
Potential Market Expansion Opportunities in First-line
Metastatic Pancreatic Cancer and Advanced Lung
Cancer

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



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

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



Collaboration with PanCAN, NCT05669482

DLT: dose-limiting toxicity; n: number of patients; ORR: overall response rate; RP2D: recommended phase 2 dose; CT: computed tomography; ECOG: European Cooperative Oncology Group; MRI: magnetic resonance imaging

RAMP 205: Initial Interim Safety and Efficacy Results

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

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



DLT: dose-limiting toxicity; ASCO: American Society of Clinical Oncology

Landmark Trials in First-Line Metastatic Pancreatic Cancer

SOC Treatment Landscape:

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

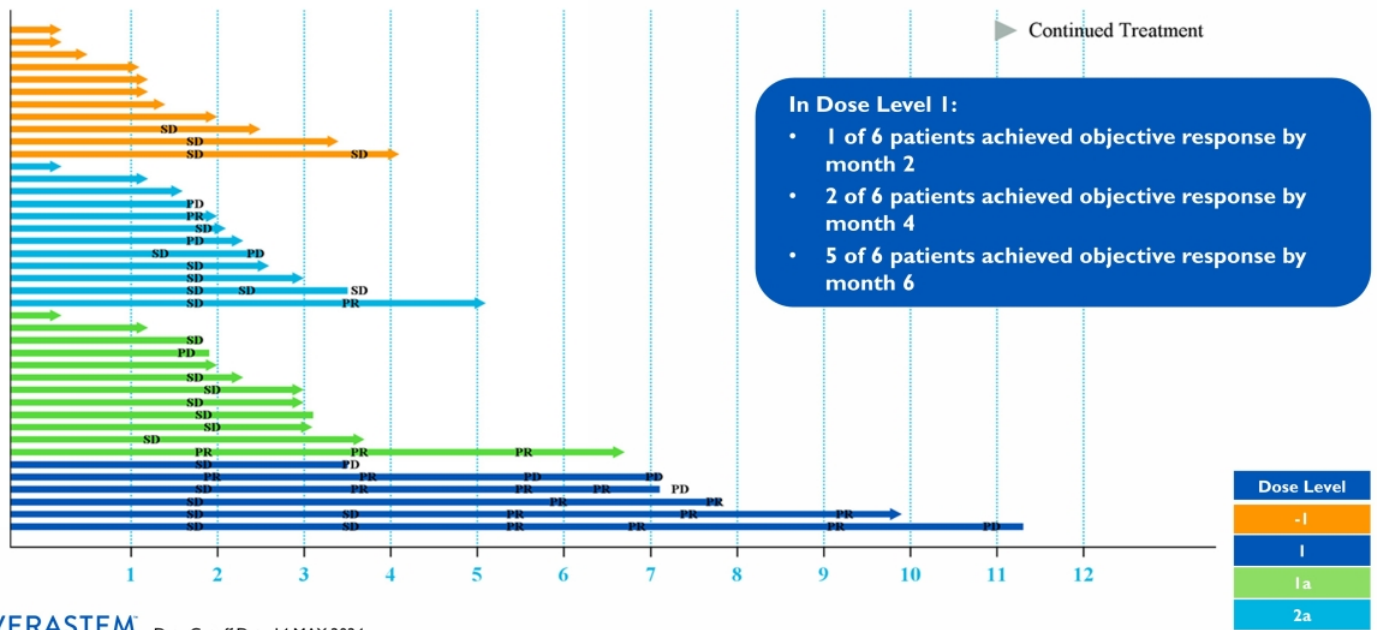
Trial/PI/Reported (# Patients)	Intervention	Comparator	ORR by Investigator (95% CI)		mPFS (95% CI)	mOS (95% CI)
MPACT Von Hoff 2013 (N=861)	Gem/NabP* (n=431)	Gem (n=430)	Gem/NabP		5.5 months (4.5-5.9)	8.5 months (7.89-9.53)
			29% (25-34)	23% (19-17) IRR**		
NAPOLI 3 O'Reilly 2023 (N=770)	Nalirifox (n=383)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



For Reference only: No cross-trial comparison made.*Dosing schedule in Gem/NabP arms above= 1000/125(mg/m²) D1,8,15 q 4w, **Secondary endpoint of ORR based on IRR (Independent Radiology Review).

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

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



Data Cutoff Date: 14 MAY 2024
Source: Program: F_TR_SWIMMER.sas

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

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



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



Data Cutoff Date: 14 MAY 2024

Source: Program: F_TR_WATERFALL_BYDOSE2

RAMP 205: AE Profile Generally Comparable with Gem/Nab-P

- Any grade TEAEs occurring in $\geq 20\%$ or grade ≥ 3 occurring in $\geq 5\%$ of patients¹

	DL-1 (n=11)		DL1 (n=6)		DL1a (n=12)		DL2a (n=12)		Total (N=41)	
	Any Grade, n (%)	Grade ≥ 3 , n (%)	Any Grade, n (%)	Grade ≥ 3 , n (%)	Any Grade, n (%)	Grade ≥ 3 , n (%)	Any Grade, n (%)	Grade ≥ 3 , n (%)	Any Grade, n (%)	Grade ≥ 3 , n (%)
Nausea	6 (54.5)	0 (0)	5 (83.3)	0 (0)	7 (58.3)	0 (0)	6 (50.0)	0 (0)	24 (58.5)	0 (0)
Fatigue	5 (45.5)	0 (0)	5 (83.3)	0 (0)	5 (41.7)	1 (8.3)	7 (58.3)	0 (0)	22 (53.7)	1 (2.4)
Constipation	4 (36.4)	0 (0)	5 (83.3)	0 (0)	7 (58.3)	0 (0)	4 (33.3)	0 (0)	20 (48.8)	0 (0)
Diarrhoea	1 (9.1)	0 (0)	4 (66.7)	0 (0)	6 (50.0)	0 (0)	6 (50.0)	0 (0)	17 (41.5)	0 (0)
Alopecia	3 (27.3)	0 (0)	6 (100.0)	0 (0)	3 (25.0)	0 (0)	2 (16.7)	0 (0)	14 (34.1)	0 (0)
Neutrophil count decreased	2 (18.2)	2 (18.2)	4 (66.7)	4 (66.7)	4 (33.3)	3 (25.0)	3 (25)	2 (16.7)	13 (31.7)	11 (26.8)
Rash maculo-papular	4 (36.4)	0 (0)	5 (83.3)	0 (0)	3 (25.0)	0 (0)	1 (8.3)	0 (0)	13 (31.7)	0 (0)
Vomiting	3 (27.3)	0 (0)	4 (66.7)	0 (0)	4 (33.3)	1 (8.3)	2 (16.7)	0 (0)	13 (31.7)	1 (2.4)
Anaemia	2 (18.2)	1 (9.1)	2 (33.3)	2 (33.3)	2 (16.7)	2 (16.7)	3 (25.0)	1 (8.3)	9 (22.0)	6 (14.6)
Decreased appetite	2 (18.2)	0 (0)	3 (50.0)	0 (0)	3 (50.0)	0 (0)	1 (8.3)	0 (0)	9 (22.0)	0 (0)
Alanine aminotransferase increased	1 (9.1)	1 (9.1)	2 (33.3)	2 (33.3)	3 (25.0)	1 (8.3)	1 (8.3)	0 (0)	7 (17.1)	4 (9.8)

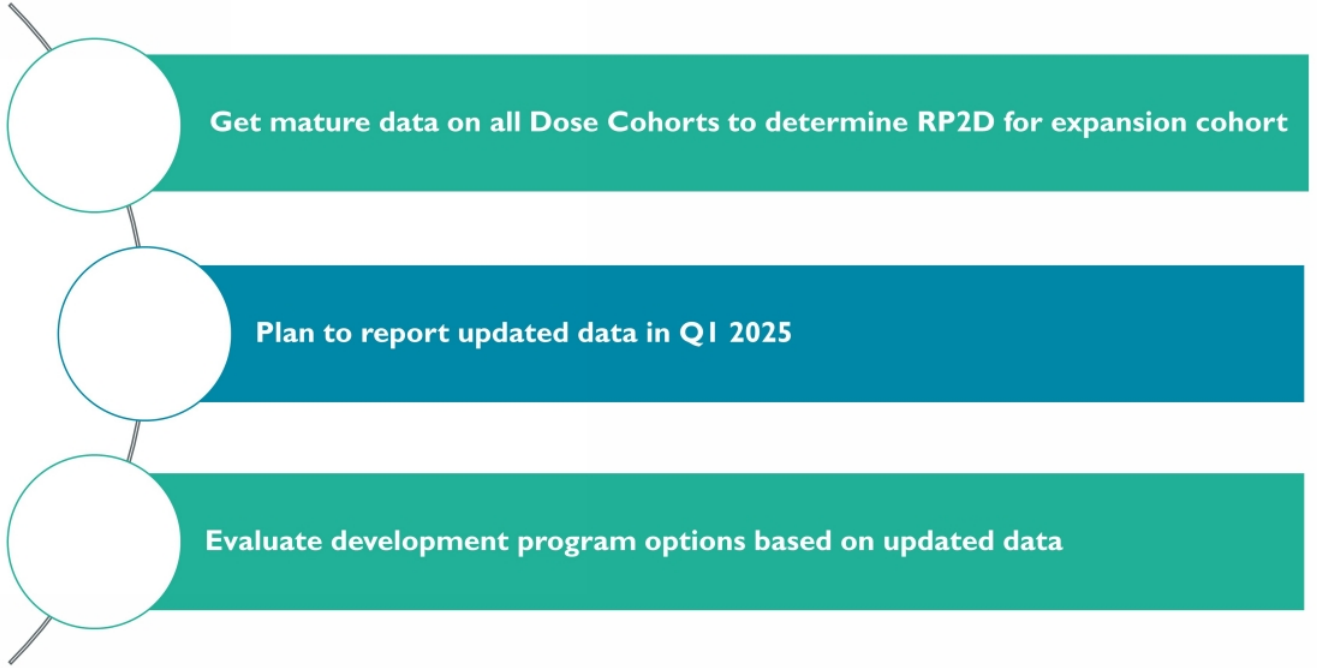
- Inclusion of avutometinib plus defactinib may increase rates of neutropenia and rash



No head-to-head clinical trials have been conducted between avutometinib and defactinib combination and gemcitabine and Nab-paclitaxel.

¹ Lim et al. ASCO 2024 Abstract #4140; Data Cutoff: May 14, 2024. TEAEs were graded based on guidelines provided in CTCAE v5.0. CTCAE v5.0, Common Terminology Criteria for Adverse Events version 5.0; DL, dose level; TEI, treatment emergent adverse event.

Next Steps for RAMP 205



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

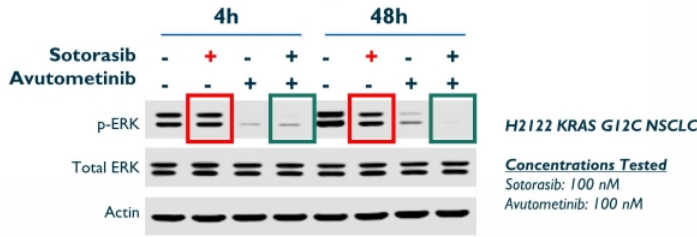


Preclinical Synergy of Avutometinib + G12C Inhibitors in KRAS G12C Models

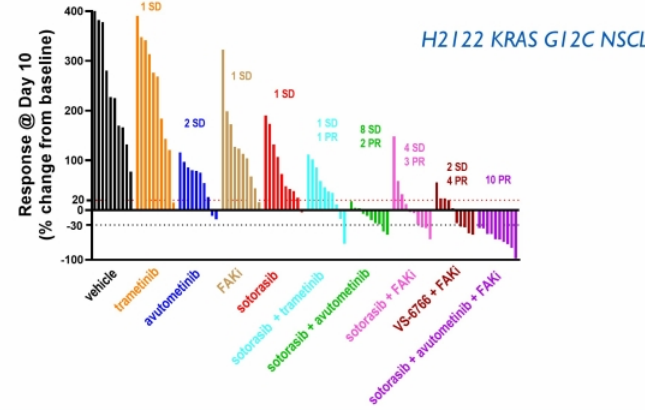
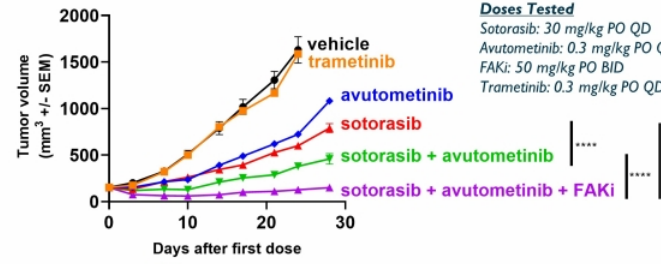
Synergy of avutometinib + G12C inhibitors across G12C mutant NSCLC, CRC & Pancreatic cancer cell lines

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

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



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



Coma et al., AACR 2021; ND: not determined

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

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

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

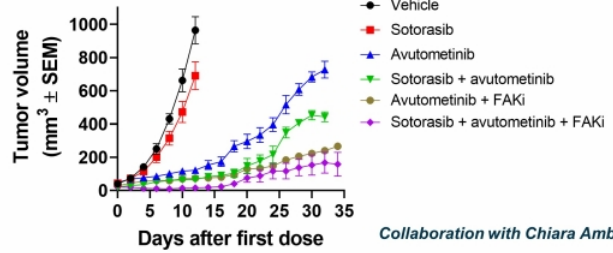
<30 nM 30 - 150 nM >150 nM

Collaboration with Andy Aguirre, DFCI



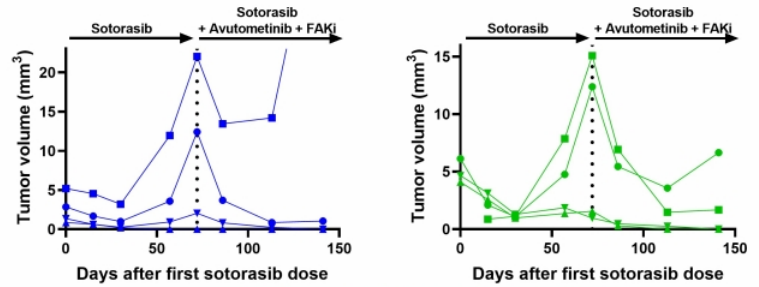
Coma et al., AACR RAS meeting 2023

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



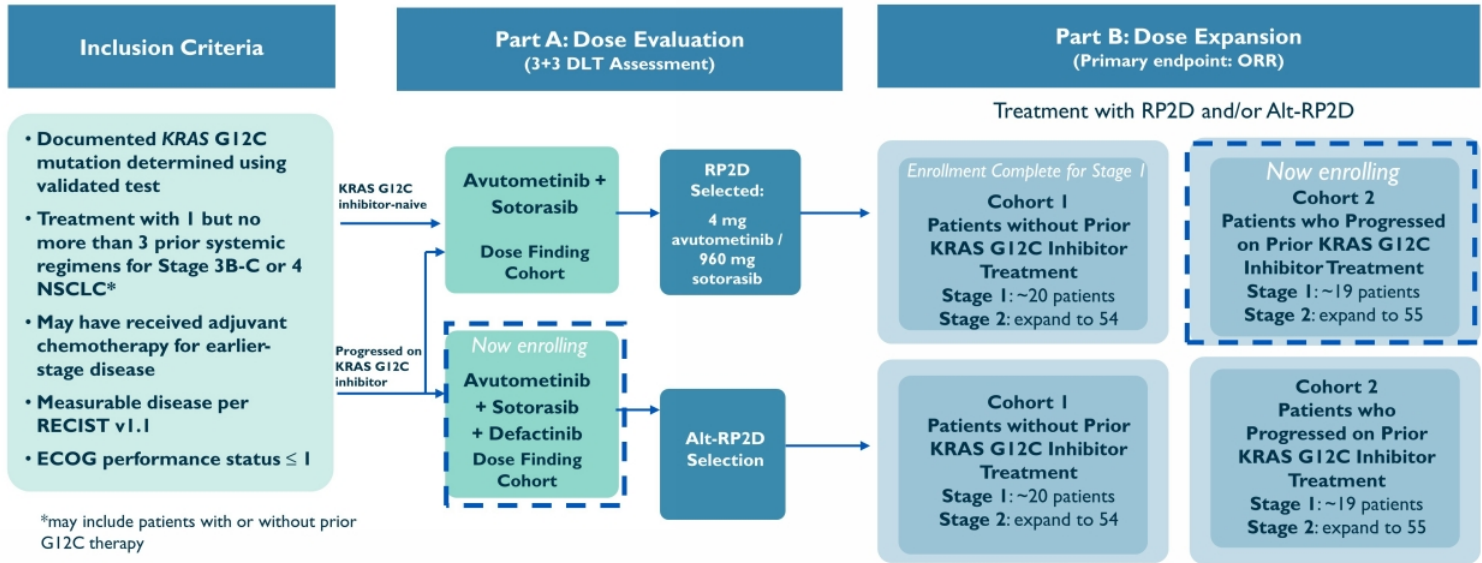
Collaboration with Chiara Ambrogio, U Turin (It)

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



Collaboration with Mariano Barbacid, CNIO (Spain)

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



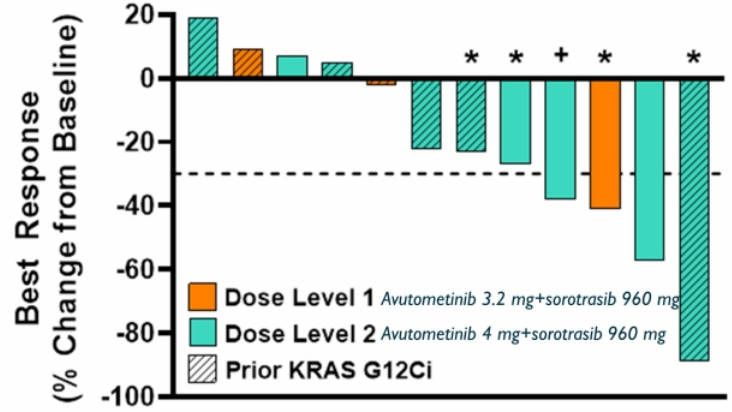
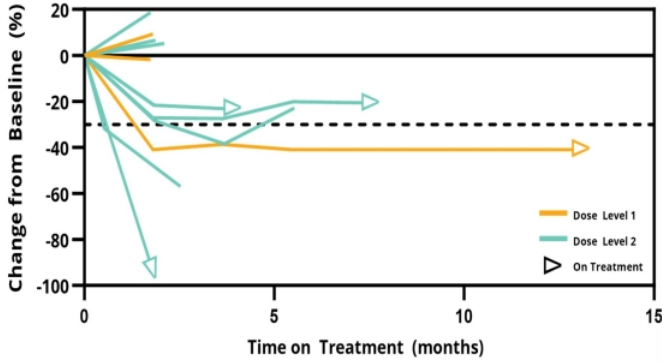
Collaboration with Amgen, NCT05074810

DLT, dose-limiting toxicity; KRAS, kristen rat sarcoma virus; NSCLC, non-small cell lung cancer; ORR, objective response rate; RECIST v1.1, response evaluation criteria in solid tumours version 1.1; RP2D, recommended phase 2 dose.

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

Avutometinib + Sotorasib

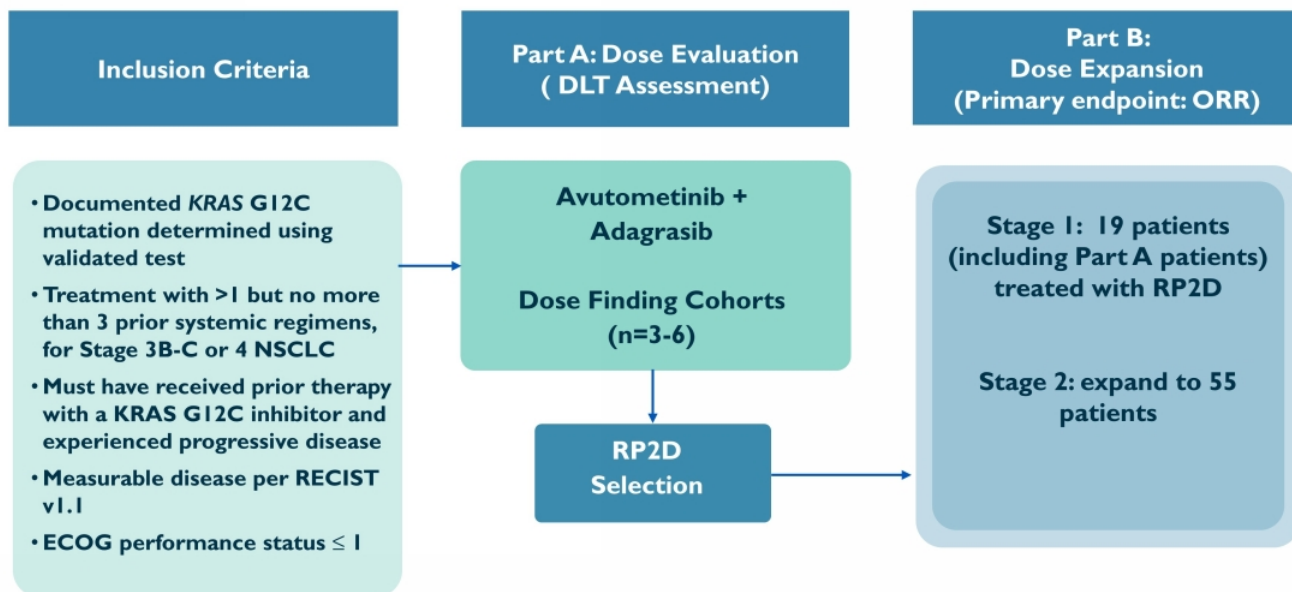
Percentage Change in Target Lesion Sum with time on treatment



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



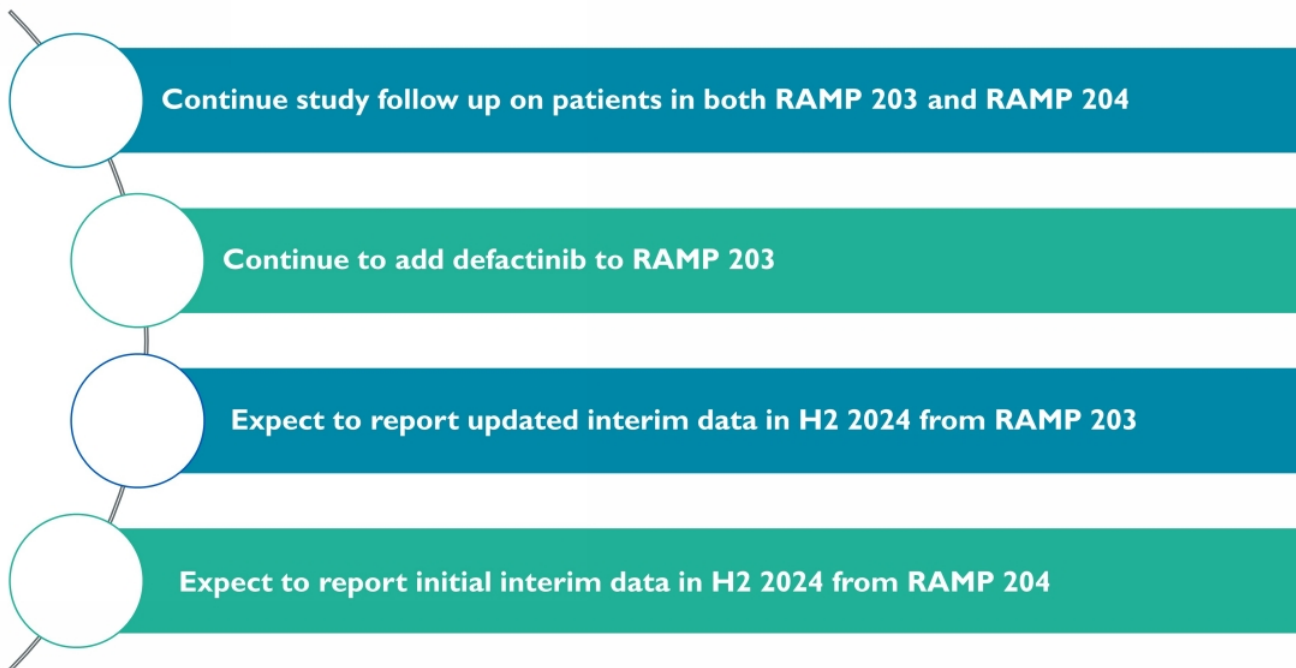
RAMP 204: Phase I/2 Trial of Avutometinib + KRAZATI™ (Adagrasib) in KRAS G12C Advanced NSCLC



Collaboration with Mirati (BMS) NCT05375994

DLT, dose-limiting toxicity; RECIST v1.1, response evaluation criteria in solid tumors version 1.1; RP2D, recommended phase 2 dose.

Next Steps for RAMP 203 and RAMP 204



Ongoing Investigator-
Sponsored Studies to Expand
Avutometinib Indications and
Combinations



Investigator-Sponsored Trials Provide Cost-Efficient Approach to Identify Future Development Directions

	Indication	Incidence/Prevalence	Biomarker %	Regimen	Setting	Phase	Institution
Gynecologic Cancers	LGSOC	Prevalence 6k ¹	70%	Avutometinib + defactinib + letrozole	Low-grade serous ovarian cancer without prior systemic treatment	Phase 1/2	Memorial Sloan Kettering Cancer Center
	Gynecologic Basket	Incidence ⁴⁻⁸ : 85K	25%	Avutometinib + defactinib	Recurrent RAS Pathway-driven (RAS/RAF/NFI) endometrioid cancer, mucinous ovarian cancer, high-grade serous ovarian cancer or cervical cancer	Phase 2	University of Oklahoma
	Mesonephric	Incidence ⁹ : ~680	96%	Avutometinib + defactinib	Advanced or recurrent mesonephric gynecologic cancer	Phase 2	Memorial Sloan Kettering Cancer Center
CRC	KRAS mt	Incidence ² : 148K	45%	Avutometinib + cetuximab	Recurrent metastatic KRAS mt	Phase 1/2	University of Chicago
	RAS/RAF wt CRC	Incidence ² : 148K	50% ¹²	Avutometinib + defactinib + cetuximab	Unresectable, Anti-EGFR-Refractory Advanced Colorectal Cancer	Phase 1/2	M.D. Anderson Cancer Center
Breast Cancer	ER+/Her2-	Incidence ² : 279K	22.5%	Avutometinib + abemaciclib + fulvestrant	Recurrent ER+/HER2- breast cancer following progression on CDK4/6i + aromatase inhibitor	Phase 1/2	Dana-Farber Cancer Institute
Melanoma	MAPK alterations or wt	Incidence ² : 100K	100%	Avutometinib + defactinib ± encorafenib	Patients with brain metastases from cutaneous melanoma with RAS, RAF or NFI alterations or RAS/RAF/NFI wt	Phase 1/2	University of Utah
Thyroid	MAPK alterations ⁺	Incidence ³ : 44K	35%	Avutometinib + defactinib	Differentiated & anaplastic thyroid cancer	Phase 2	Memorial Sloan Kettering Cancer Center

⁺excluding BRAFV600E



¹ Monk, Randall, Grisham, The Evolving Landscape of Chemotherapy in Newly Diagnosed Advanced Epithelial Ovarian Cancer, Am Soc Clin Oncol Educ Book; 2019; Stomovitz, 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; ²Cancer Statistics 2020, Siegel et. al. CA Cancer J Clin 2020;70:7-30; ³Cancer Statistics 2020, Siegel et. al. CA Cancer J Clin 2020;70:7-30 ⁴Uterine cancer is one of the leading gynecologic neoplastic disorders in the US, of which over 80% are endometrioid adenocarcinomas (EA); ⁵Endometrioid OC (EnOC) accounts for approximately 10% of all OC, with the majority of cases diagnosed as low grade, early stage disease with excellent clinical; ⁶mucinous ovarian cancer: 3-11% of ovarian cancer (Hadi et al., 2021); ⁷90% 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>); ⁸HGSOC the most common type of ovarian cancer, accounting for approximately 75% of epithelial ovarian cancers. (<https://ocrahope.org/news/high-grade-serous-carcinoma/>) ⁹ Son (David Hong) ASCO 2023



Partnership with GenFleet
Therapeutics on Novel, Potential Best-
in-Class RAS Pathway Programs

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

- Increases the breadth of Verastem's oncology pipeline with strategically-aligned RAS pathway focus
 - Exclusive options to license up to 3 programs with development and commercialization rights outside of the GenFleet markets of mainland China, Hong Kong, Macau, and Taiwan
 - Potential development in combination with Verastem's pipeline
 - Selected GFH375 (VS-7375), an oral KRAS G12D (ON/OFF) inhibitor is the first program; programs 2 & 3 in discovery phase
 - Small molecule programs focused on anti-cancer targets related to the RAS/MAPK pathway or surrounding cancer cell signaling
- Strategic collaboration builds on Verastem Oncology and GenFleet's experience in RAS pathway-driven cancers
 - Collective worldwide strengths in RAS pathway discovery and development
 - Established network of collaborators, including leading scientific and clinical experts
 - Leverages experience from GenFleet's KRAS G12C inhibitor program and Verastem's avometinib/defactinib program
- Risk-sharing structure of the collaboration with milestone-based options provides capital efficient approach
 - At execution, Verastem paid GenFleet an upfront payment for options to obtain exclusive right to 3 programs
 - 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
 - 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

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

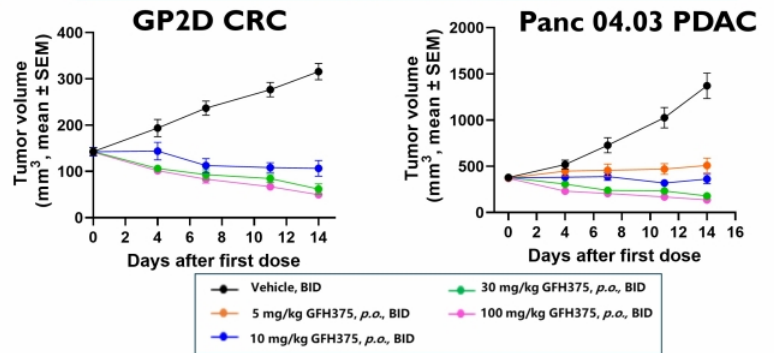
First program from the GenFleet collaboration

- GFH375 (VS-7375) is a potent and selective orally bioavailable inhibitor of KRAS G12D (ON/OFF) with potent anti-tumor activity demonstrated across preclinical models
- Dual inhibitor of ON (GTP) and OFF (GDP) states of KRAS G12D
- Orally bioavailable across preclinical species
- Potent against intracranial tumor models suggesting potential to treat brain metastases
- Avutemetinib enhances anti-tumor activity of GFH375 (VS-7375) in preclinical models
- IND-enabling GLP toxicology studies complete
- Phase I/2 trial initiated in China in an open-label, multi-center study of patients with G12D-mutant advanced solid tumors

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

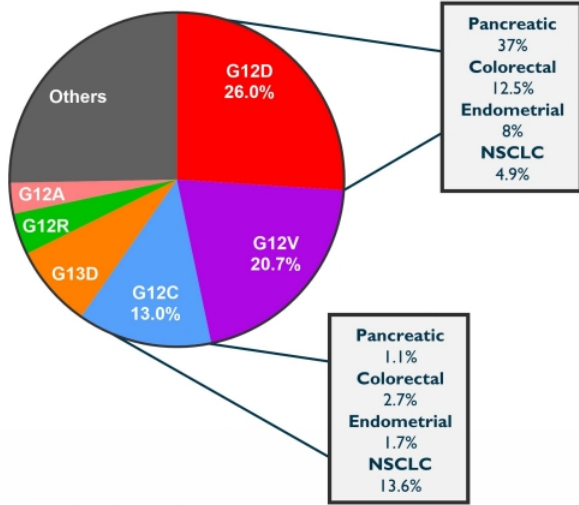
KRAS G12D State	GFH375 IC50 (nM) (KRAS G12D binding)
GppNp-bound (ON/active)	2 ± 1
GDP-bound (OFF/inactive)	6 ± 1

Potent anti-tumor activity demonstrated across preclinical models

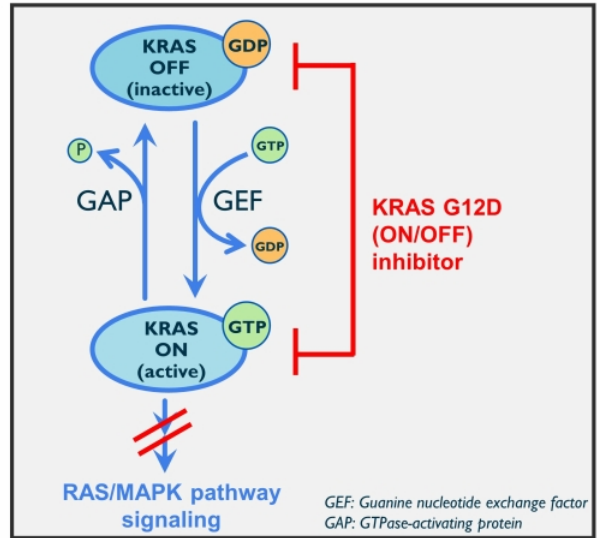


Potent, Selective, Orally Bioavailable Inhibitor of KRAS G12D (ON/OFF) Provides Multiple Options for Clinical Development

KRAS G12D is the most frequent KRAS mutation in human cancer



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



Reference: Adapted from Hofmann et al., Cancer Discovery 2022

Next Steps for GFH375/VS-7375 & GenFleet Collaboration





Achievements, Anticipated Milestones
& Financials

Verastem Poised to Become a Commercial-Stage Company with Significant Short- to Long-Term Opportunity

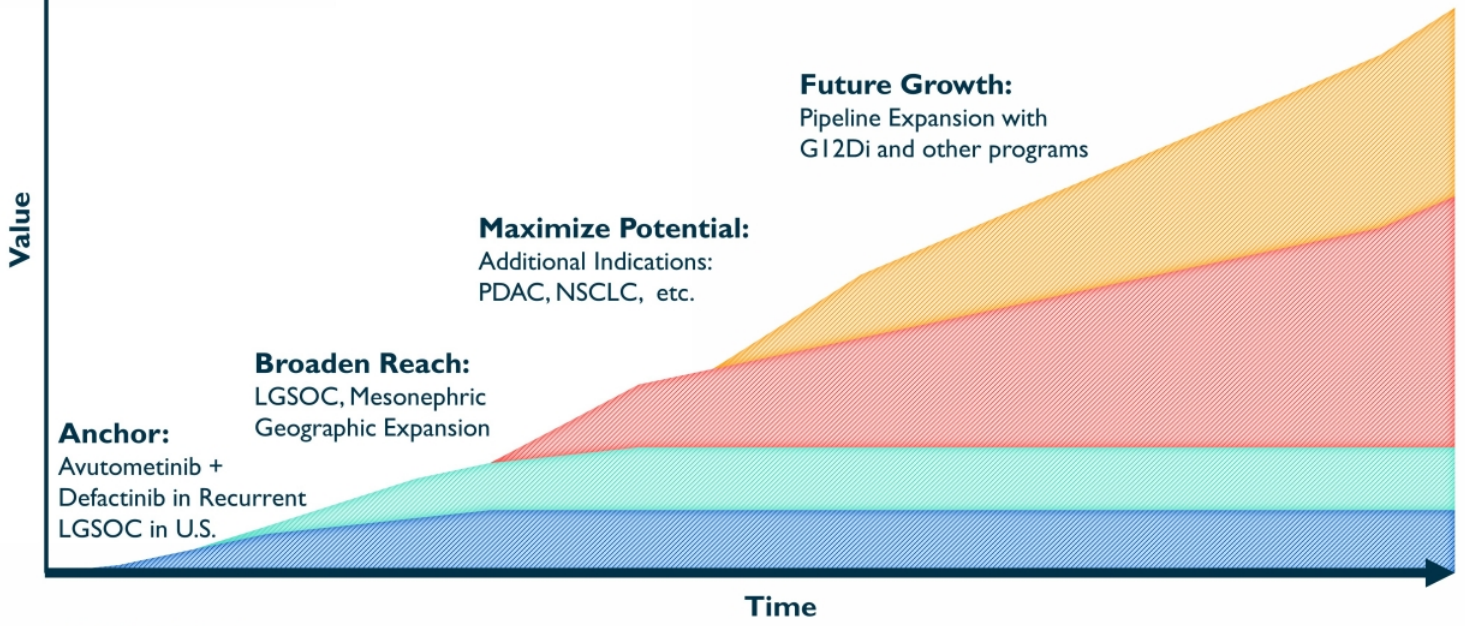


Image for illustrative purposes only.

PDAC: pancreatic ductal adenocarcinoma cancer; CRC: colorectal cancer

Recent Corporate Achievements

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

Anticipated Milestones and Activities in H2 2024

Program	Anticipated Milestones & Activities
Avutometinib + Defactinib in Recurrent Low-grade Serous Ovarian Cancer (LGSOC)	<ul style="list-style-type: none"> <input type="checkbox"/> Plan to complete rolling NDA in H2 2024 <input type="checkbox"/> Plan to announce mature data from RAMP 201 in H2 2024 • Continue site activations and patient enrollment in international Phase 3 confirmatory study in US, Australia, and UK and enrollment planned in Canada, Europe, and South Korea
Avutometinib + Defactinib + SOC in First-Line Metastatic Pancreatic Cancer	<ul style="list-style-type: none"> • Continue RAMP 205 study follow up on all dose cohort levels to determine RP2D go forward regimen <input type="checkbox"/> Plan to present updated results from RAMP 205 in Q1 2025
Avutometinib ± Defactinib + KRAS G12C Inhibitors: mKRAS G12C Non-small Cell Lung Cancer (NSCLC)	<ul style="list-style-type: none"> <input type="checkbox"/> Expect to report updated interim data in H2 2024 from RAMP 203 NSCLC trial evaluating avutometinib plus defactinib with Amgen's KRAS G12C inhibitor, sotorasib <input type="checkbox"/> Expect to report initial interim data in H2 2024 from RAMP 204 NSCLC trial evaluating avutometinib with Mirati Therapeutics (Bristol Myers Squibb (BMS)) KRAS G12C inhibitor, adagrasib
GenFleet's GFH375/VS-7375, KRAS G12D (ON/OFF) Inhibitor	<ul style="list-style-type: none"> • Ongoing discovery/lead optimization for second and third programs

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



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

ASCO: American Society of Clinical Oncology

Key Financial Statistics

As of and for the quarter ended March 31, 2024

Cash, cash equivalents & investments	\$110.1M
GAAP Operating Expenses	\$28.1M
Non-GAAP Operating Expenses*	\$26.6M
Shares Outstanding	25.3M**

Sources of Non-Dilutive Capital

- **Oxford Finance LLC Credit Facility**

- Up to \$150M available in a series of term loans
 - \$40M term loans outstanding
 - Remaining \$110M available upon achievement of pre-defined milestones or at lender's discretion
 - \$25M tranche available upon FDA approval of avotemetinib for treatment of LGSOC
- Floating interest rate, subject to a floor and a cap; 5% final payment charge, and loan subject to 1-3% early payment fee
- Interest only payments through April 2025
- No financial covenants



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

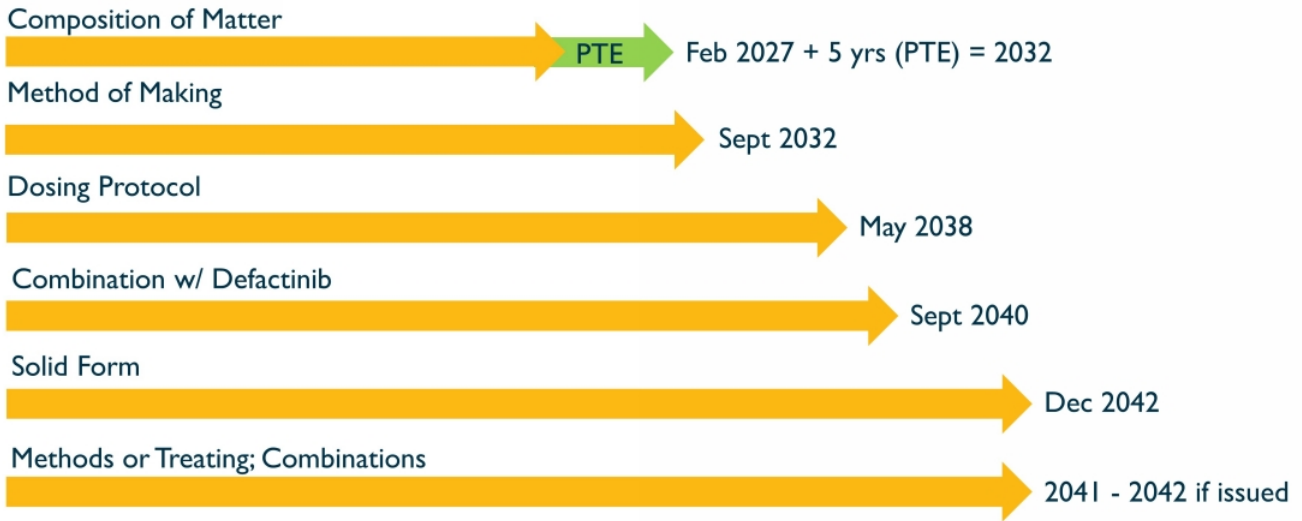
**Excludes Series A Preferred (0.8M Shares on as-converted basis), Series B Preferred (4.2M Shares on as-converted basis), and outstanding unexercised pre-funded warrants (1.5M Shares).

THANK YOU



Addendum

Avutometinib Patent Exclusivity



Experienced Senior Management Team

Daniel Paterson
President and Chief Executive Officer



Previous experience:

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

John Hayslip, M.D.
Chief Medical Officer



Previous experience:

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

Dan Calkins
Chief Financial Officer



Previous experience:

- Technical Accounting Consultant- CFGI
- PwC LLP

Colleen Mockbee
Global Head of Regulatory Affairs and Development



Previous experience:

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

Cathy Carew
Chief Organizational Effectiveness Officer



Previous experience:

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

Jonathan Pachter, Ph.D.
Chief Scientific Officer



Previous experience:

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

Mike Crowther
Chief Commercial and Strategy Officer



Previous experience:

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

Nate Sanburn
Chief Business Officer

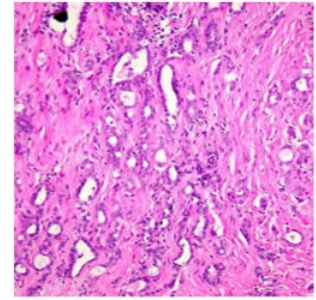


Previous experience:

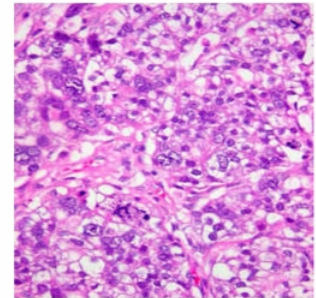
- Associate VP, Head Collaborations & L Phase BD, Lilly Oncology
- National Gene Vector Lab, Indiana University

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

	LGSOC	HGSOC
Nuclear atypia	Uniform round to oval with little variation	+++ Marked variation
Mitotic Index	<12 mitoses per 10 hpf	>12 mitoses per 10 hpf
Chromatin and variation in size of nucleus	Little	Marked (nuclear size ratio ≥ 3)
Mutation	KRAS ++ BRAF + ER/PR +++	P53 +++ BRCA1/2 +
Precursor	Serous borderline tumor	Tubal intraepithelial neoplasia



LGSOC



HGSOC

FDA Breakthrough Designation Based on FRAME Data

FRAME*

ORR Overall Population (Confirmed ORR by BICR)	42% (11 confirmed PRs/26)
95% CI	(19%, 36%)
KRAS mt	58% (7 confirmed PRs/12)
KRAS wt	33% (4 confirmed PRs/12)

Median Duration of Response (DoR)
(95% CI 8.5-47.3) across all LGSOC patients **26.9 months**

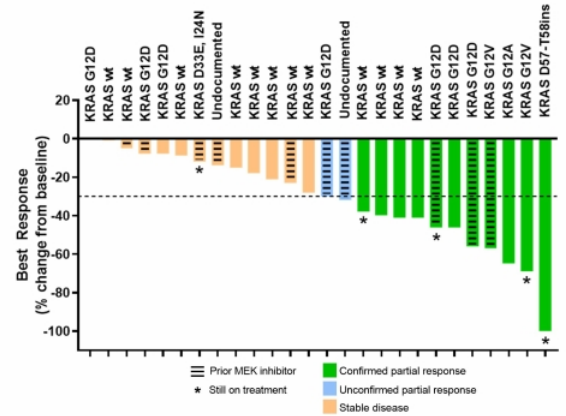
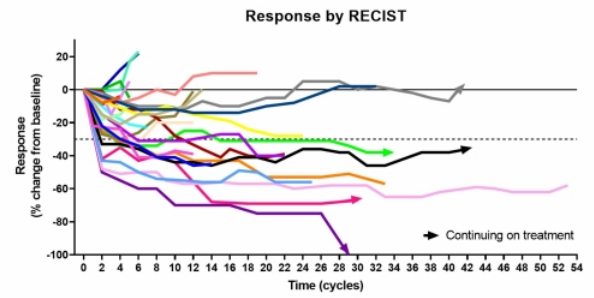
Median Progression Free Survival (PFS)
(95% CI 11.1 – 31.2) across all LGSOC per RECIST 1.1 **20.0 months**

Median number of prior lines of therapy **3.5 lines**

Responses observed in patients previously treated with MEK inhibitor

No new safety findings with continued follow-up

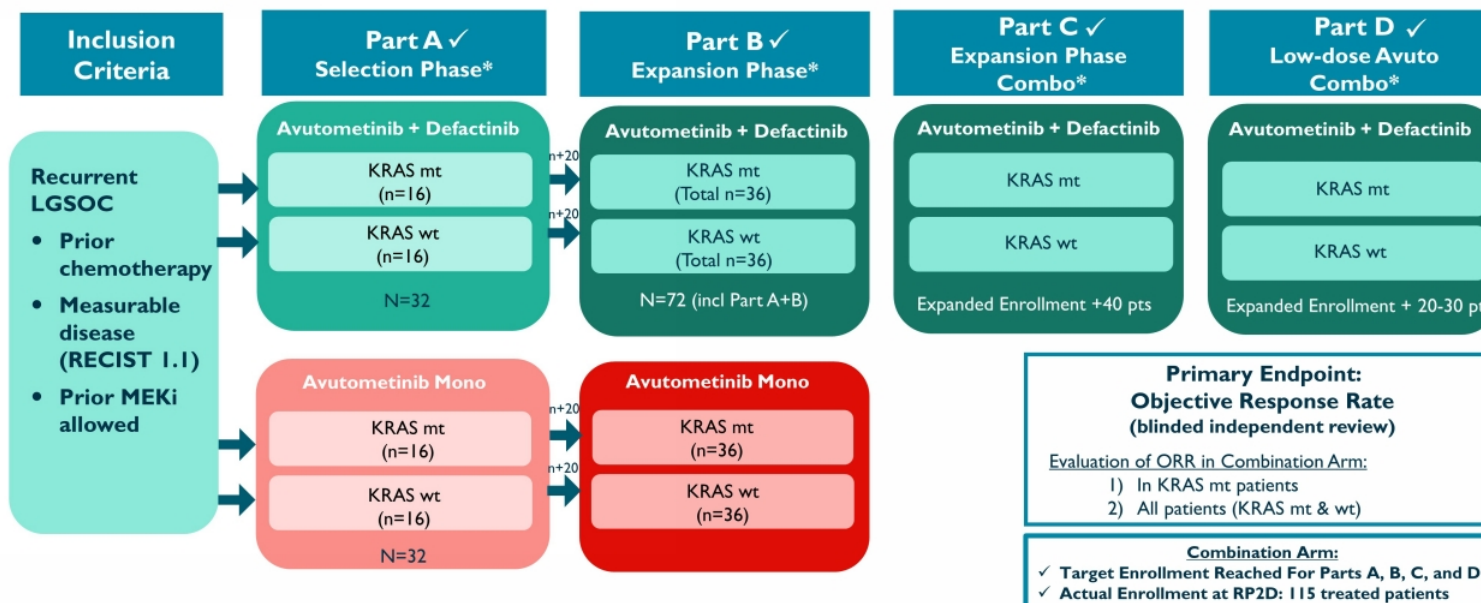
One (1) patient discontinued for adverse events as of July 2023 (skin AE)



Breakthrough Through Therapy Designation for combination of avotemetinib and defactinib for treatment of recurrent LGSOC after one or more prior lines of therapy including platinum-based chemotherapy
*Denis, 5th Annual RAS-Targeted Drug Development Sept 2023; (Data cut off July 2023; Data on file); BICR: Blinded independent central review

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

RAMP 201 (ENGOTv60/GOG3052)



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

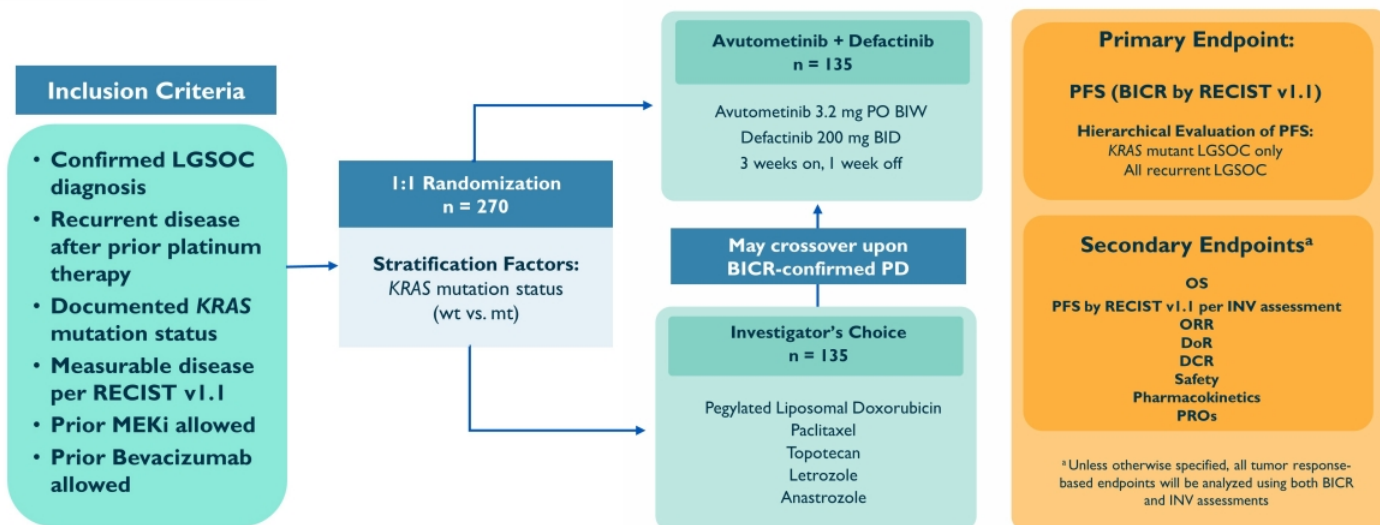
Avutometinib monotherapy: Avutometinib 4.0 mg PO 2x/wk 21/28 days

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

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

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

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

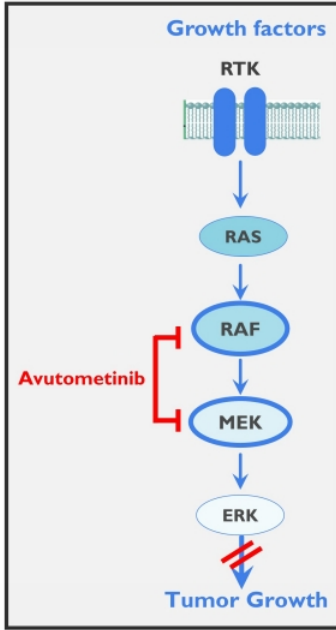


VERASTEM ONCOLOGY NCT06072781

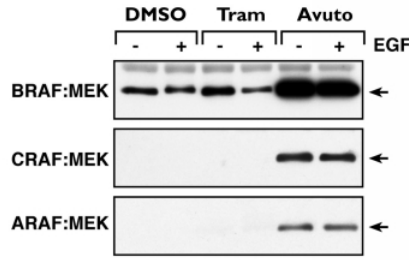
BICR: blinded independent central review; BID: twice a day; BIW: twice a week; DCR: disease control rate; DoR: duration of response; INV: investigator; KRAS: Kirsten rat sarcoma virus; MEKi: MEK inhibitor; mt: mutant; PO: per oral; pts: patients; ORR: objective response rate; OS: overall survival; PD: progressive disease; PFS: progression-free survival; PROs: patient-reported outcomes; RECIST: response evaluation criteria in solid tumors; wt: wild type.

Avutometinib is a Differentiated Small Molecule RAF/MEK Clamp

Contrasting Mechanism of Action vs. MEK-Only Inhibitors

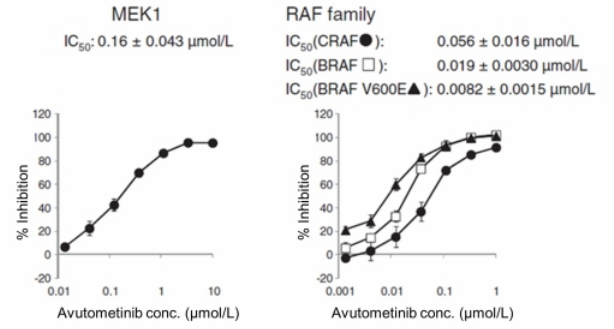


Avutometinib induces dominant negative RAF/MEK complexes

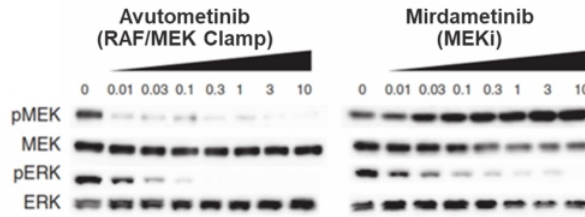


Collaboration with Deborah Morrison, NCI

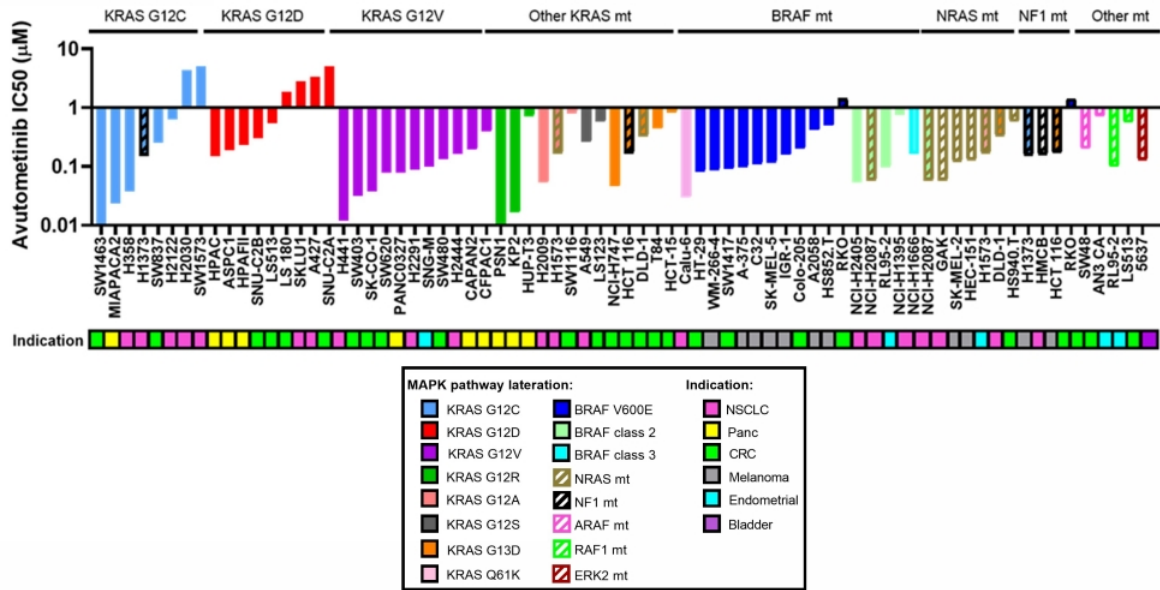
Avutometinib inhibits both RAF and MEK activities



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



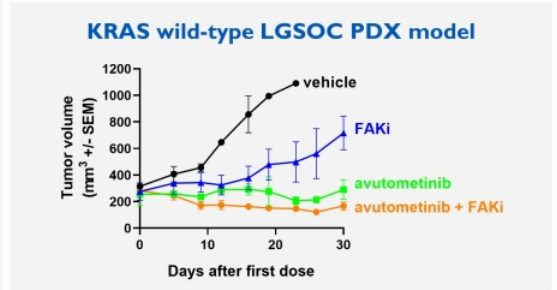
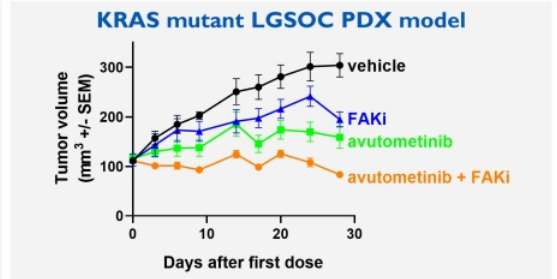
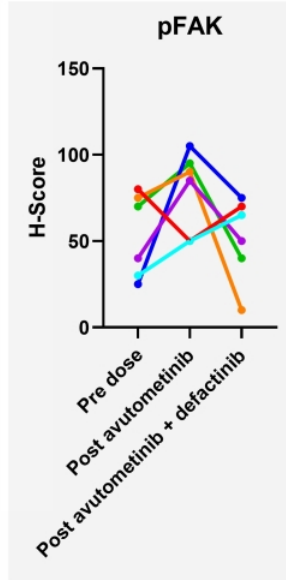
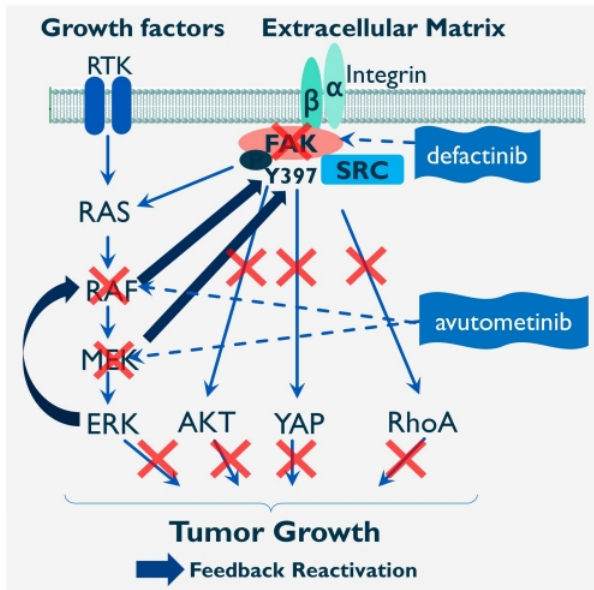
Avutometinib Inhibits Cell Proliferation Across Multiple RAS/MAPK Pathway Alterations and Multiple Solid Tumor Histologies



Verastem, unpublished data

Scientific Rationale for Avutometinib and FAK Inhibitor Combination

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



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

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

Summary of Adverse Events Grade \geq 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 \geq 3	Grade \geq 3	Grade \geq 3
Rash	3 (50%)	5 (19%)	2 (5%)
CK elevation (Creatine phosphokinase)	1 (17%)	2 (8%)	2 (5%)



¹ Chenard-Poirier, et al. ASCO 2017; References: Banerji, Q4 2020 report; Data on file; RP2D: recommended phase 2 dosing

Plan to Seek Comparable, If Not Better, Coverage as SoC at Time of Approval

- Available treatments for recurrent LGSOC offer low response rates and frequent discontinuations due to toxicity
- There are no FDA-approved treatments and no standard sequencing of drugs for recurrent disease

	NCCN Category 1	NCCN Category 2a	NCCN Category 2b	NCCN Category 3
General % Commercial Payer Coverage				
Recurrent LGSOC Treatment NCCN Recommendations and Contemporary Clinical Data in LGSOC	No category I recommendation	<p>Hormonal therapy (e.g., Anastrozole, Letrozole) & chemotherapy</p> <ul style="list-style-type: none"> • 6-13% ORR and 17-30% discontinuation rate due to AEs • Based on GOG 281 and MILO studies <p>-----</p> <p>Trametinib (2-4% U.S. utilization rate⁶)</p> <ul style="list-style-type: none"> • 13 months PFS, 95% CI: (9.9-15.0) vs SoC • 26% ORR based on INV assessment of comparator arm of all patients not BICR • 36% discontinuation rate due to AEs • Based on GOG 281⁴ 	<p>Binimetinib</p> <ul style="list-style-type: none"> • Study stopped due to fertility • PFS 12.5 vs 11.6 (HR 0.87) • 16% ORR based on BICR of comparator arm and 31% discontinuation rate due to AEs • Based on MILO study⁵ 	



General source: NCCN; McGivney Global Advisory research and analysis; L.E.K. research and analysis
 1) NCCN categories of preference: Preferred intervention, Other recommended intervention, Useful in certain circumstances. 2) High-level of evidence generally means large randomized controlled Phased 3 trials; 3) Coverage by all major commercial payers; 4) GOG 281 trial Gershenson et al., Lancet 2022 5) MILO Study Monk et al., J Clin Oncol 2020; 6) Data on File.