

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): **May 24, 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:

<b>Title of each class</b>	<b>Trading Symbol(s)</b>	<b>Name of each exchange on which registered</b>
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 May 24, 2024, Verastem, Inc. (the “Company” or “Verastem”) issued a press release announcing the initiation of a rolling submission of a New Drug Application (“NDA”) to the U.S. Food and Drug Administration (“FDA”) for Accelerated Approval of the combination of avutometinib and defactinib for adult patients with recurrent KRAS mutant (“KRAS mt”) low-grade serious ovarian cancer (“LGSOC”);

A copy of the press release is furnished hereto as Exhibit 99.1 to this Current Report on Form 8-K.

On May 24, 2024, the Company also posted its corporate presentation on its website, a copy of which is furnished hereto as Exhibit 99.2 to this Current Report on Form 8-K.

**Item 8.01 Other Events.**

***Recent Developments***

RAMP-201 (ENGO/Tov60/GOG3052)

The Company recently announced that it has initiated the rolling submission of an NDA to the FDA seeking accelerated approval of the combination of avutometinib and defactinib for patients with recurrent KRAS mt LGSOC who received at least one prior systemic therapy. The rolling review process allows Verastem to submit completed sections of an application for review by the FDA before all sections become available. The initial sections of the application will include the nonclinical and quality sections. Based on discussions with the FDA, the primary efficacy analysis will be based on the RAMP 201 study with 12 months of follow up and that the proposed indication for final submission of the clinical module can be expanded in the event the Company provides data that would be considered a substantial improvement over available therapy in the KRAS wildtype (“KRAS wt”) population. Previously, the FDA granted Orphan Drug Designation for the combination in LGSOC and Breakthrough Therapy Designation for the combination for treatment of patients with LGSOC with recurrent disease after one or more prior lines of therapy, including platinum-based chemotherapy. The Company plans to request a priority review of the NDA. Currently, there are no FDA-approved treatments specifically for recurrent LGSOC.

In the RAMP 201 trial, 115 patients with recurrent LGSOC were treated with the combination of avutometinib and defactinib, of which 109 patients had measurable tumor masses at baseline and were eligible for formal efficacy evaluation as of the data cutoff (February 2024). As of the data cutoff, all patients had a minimum follow-up of five months since enrollment. Confirmed objective response rates by blinded independent central review for patients evaluable for efficacy were 27% in all patients, and 37% and 15% in KRAS mt (n=57) and KRAS wt (n=52) LGSOC, respectively. Of the 32 patients who remained on study treatment at the data cutoff, 14 achieved a best response rate of stable disease or unconfirmed partial response and therefore have the potential to achieve a formal objective response upon further treatment. 60% of evaluable patients (65/109) achieved either a complete response, partial response, or stable disease response for 6 months or longer (Clinical Benefit Rate  $\geq$  6 months). The safety results were consistent with previously reported safety data, and the discontinuation rate due to adverse events was 9% in the trial overall, as of the cutoff date.

The Company previously announced results from Part A of the RAMP 201 trial, which were presented at the American Society of Clinical Oncology Annual Meeting in 2023. For the patients in Part A, as of the February 2024 cutoff date, median duration of therapy for all patients was 11 months, and for patients with KRAS mt and KRAS wt LGSOC, median duration of treatment was 18 months and 8 months, respectively.

---

Based on internal revenue forecasts, including potential market penetration of the Company's product candidates and the longer median duration of treatment observed in RAMP 201 Part A, the Company believes that KRAS mt represents over two-thirds of the revenue opportunity, compared with combined KRAS mt and KRAS wt, without any differential pricing. According to awareness trial usage survey results conducted by the Company, using a target product profile based on the avutemetinib and defactinib combination, 70% of oncologists surveyed indicated they would plan to treat prevalent patients with the combination at the patients' next recurrence, and 49% indicated that initial recurrence would be the ideal time to introduce the combination treatment in the patient journey. The Company plans to have a focused commercial launch targeting the top 400 healthcare providers and top 100 healthcare organizations which are estimated to cover nearly half of the LGSOC population with a target sales force of between 14-18 representatives.

***Note Regarding Recent Developments***

The potential market opportunity for The Company's product candidates is difficult to estimate precisely. Management of the Company makes estimates, including those contained in this Current Report on Form 8-K, regarding the incidence and prevalence of target patient populations, the rate of recurrence and the median survival for particular diseases, including with respect to LGSOC, based on various third-party sources and internally generated analysis and use such estimates in making decisions regarding the Company's drug development strategy determining indications on which to focus in preclinical or clinical trials.

---

Management's estimates of the patient population, pricing and revenue opportunities for the Company's product candidates, including KRAS mt and KRAS wt for patients with LGSOC, are based on a number of internal and third-party estimates that may be inaccurate or based on imprecise data. For example, if approved by the FDA, the market opportunity of the Company's product candidates will depend on, among other things, acceptance by the medical community, patient access, drug pricing and reimbursement. The number of patients in the addressable market may turn out to be lower than expected, patients may not be otherwise amenable to treatment with the Company's drugs, or new patients may become increasingly difficult to identify or gain access to, all of which may significantly harm the Company's business, financial condition, results of operations, and prospects. Further, if any approval that the Company obtains is based on a narrower definition of patient populations than the Company had anticipated, the potential market for the Company's product candidates will be smaller than management's current estimates, which could have a materially adverse effect on the Company's ability to achieve commercialization and generate revenues.

In addition, the FDA and other comparable regulatory authorities could require clearance or approval of an in vitro diagnostic or companion diagnostic device as a condition of approval for any product candidates that require from such tests, including the combination of avutemetinib and defactinib. If the Company is unable to successfully validate, develop and obtain regulatory approval for companion diagnostic tests for the Company's product candidates that require such tests, or experience significant delays in doing so, the Company may not realize the full commercial potential of these product candidates and the Company's drug development strategy and operational results may be harmed.

The development programs for some of the Company's product candidates contemplate working with developers or obtaining access to marketed companion diagnostic tests, which are assays or tests to identify an appropriate patient population. For example, in connection with the Company's planned rolling NDA submission for the combination of avutemetinib and defactinib for patients with recurrent KRAS mt LGSOC, the Company may be required to obtain FDA approval or clearance of a companion diagnostic. If safe and effective use of any of the Company's product candidates the Company may develop depends on a companion diagnostic, the Company may not receive marketing approval, or marketing approval may be delayed, if the Company is unable to or is delayed in developing, identifying, or obtaining regulatory approval or clearance any such the companion diagnostic product for use with the Company's product candidate. The process of obtaining or creating such companion diagnostics is time consuming and costly and the Company, and/or future collaborators, may encounter difficulties in developing and obtaining regulatory clearance or approval for the companion diagnostics.

***Note Regarding Forward-Looking Statements***

This Current Report on Form 8-K includes forward-looking statements about, among other things, the Company's programs and product candidates, strategy, future plans and prospects, the potential clinical value of various of its clinical trials, including the RAMP 201 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 the Company's 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 avotemetinib 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, or that the FDA may require the Company to have completed enrollment or to enroll additional patients in the Company's ongoing RAMP-301 confirmatory Phase 3 clinical trial prior to Verastem submitting or the FDA taking action on our NDA seeking accelerated approval; that our product candidates will cause adverse safety events and/or unexpected concerns may arise from additional data or analysis, or result in unmanageable safety profiles as compared to their levels of efficacy; that we may be unable to successfully validate, develop and obtain regulatory approval for companion diagnostic tests for our product candidates that require or would commercially benefit from such tests, or experience significant delays in doing so; that our product candidates may experience manufacturing or supply interruptions or failures; that any of our third-party contract research organizations, contract manufacturing organizations, clinical sites, or contractors, among others, who we rely on fail to fully perform; that we face substantial competition, which may result in others developing or commercializing products before or more successfully than we do which could result in reduced market share or market potential for our product candidates; that we will be unable to successfully initiate or complete the clinical development and eventual commercialization of our product candidates; that the development and commercialization of our product candidates will take longer or cost more than planned, including as a result of conducting additional studies; that we may not have sufficient cash to fund our contemplated operations; that we may not attract and retain high quality personnel; that we or Chugai Pharmaceutical Co., Ltd. will fail to fully perform under the avotemetinib license agreement; that our target market for our product candidates might be smaller than we are presently estimating; that Secura Bio, Inc. will fail to fully perform under the asset purchase agreement with Secura Bio, Inc., including in relation to milestone payments; that we will not see a return on investment on the payments we have and may continue to make pursuant to the collaboration and option agreement with GenFleet Therapeutics (Shanghai), Inc. ("GenFleet"), or that GenFleet will fail to fully perform under the agreement; that we may be unable to obtain adequate financing in the future through product licensing, co-promotional arrangements, public or private equity, debt financing or otherwise; that we will not pursue or submit regulatory filings for our product candidates; and that our product candidates will not receive regulatory approval, become commercially successful products, or result in new treatment options being offered to patients.

Other risks and uncertainties include those identified under the heading "Risk Factors" in the Company's Annual Report on Form 10-K for the year ended December 31, 2023, as filed with the Securities and Exchange Commission (the "SEC") on March 14, 2024, and in any subsequent filings with the SEC, including in this Current Report on Form 8-K, which are available at [www.sec.gov](http://www.sec.gov) and [www.verastem.com](http://www.verastem.com).

As a result of these and other factors, we may not achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. The forward-looking statements contained in this Current Report on Form 8-K reflect the Company's views as of the date hereof, and the Company does not assume and specifically disclaims any obligation to update any forward-looking statements whether as a result of new information, future events or otherwise, except as required by law.

#### Item 9.01. Financial Statements and Exhibits

<u>Exhibit No.</u>	<u>Description</u>
<a href="#">99.1</a>	<a href="#">Press Release, dated May 24, 2024 relating to Verastem's Regulatory Update</a>
<a href="#">99.2</a>	<a href="#">Corporate Presentation, dated May 24, 2024</a>
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: May 24, 2024

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

---

**Verastem Oncology Announces the Initiation of a Rolling Submission of NDA to FDA Seeking Accelerated Approval of Avutometinib and Defactinib Combination for the Treatment of Adult Patients with Recurrent KRAS Mutant Low-Grade Serous Ovarian Cancer**

*Plan to complete NDA submission with the mature RAMP 201 dataset, anticipated to include 12 months of follow-up, in the second half of 2024*

*Plan to present the mature dataset from RAMP 201 at a medical conference in the second half of 2024*

*Avutometinib and defactinib combination have continued to show robust and durable response rates in ongoing RAMP 201 trial in patients with recurrent low-grade serous ovarian cancer*

*Company to host investor conference call and webcast on Friday, May 24, 2024 at 8:00 am EDT to provide update on RAMP 201 and rolling NDA submission*

BOSTON--(BUSINESS WIRE)--May 24, 2024--Verastem Oncology (Nasdaq: VSTM), a biopharmaceutical company committed to advancing new medicines for patients with cancer, today announced that it has initiated the rolling submission of a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) seeking accelerated approval of the combination of avutometinib, a RAF/MEK clamp, and defactinib, a selective FAK inhibitor, for adult patients with recurrent KRAS mutant (KRAS mt) low-grade serous ovarian cancer (LGSOC), who received at least one prior systemic therapy. The rolling review process allows the Company to submit completed sections of an application for review by the FDA before all sections become available. The initial sections of the application will include the nonclinical and quality sections. In discussions with the FDA, Verastem reached agreement to submit a primary efficacy analysis based on the RAMP 201 study with 12 months of follow up. Based on discussions with the FDA, we understand that the proposed indication for final submission of the clinical module can be expanded in the event Verastem provides data that demonstrates a substantial improvement over available therapy in the KRAS wild-type (KRAS wt) population. FDA has accepted Verastem's plan to submit the clinical module in the second half of 2024 to complete the NDA application. Previously, the FDA granted Breakthrough Therapy Designation (BTD) for the combination for treatment of patients with recurrent LGSOC, regardless of KRAS status, following one or more previous lines of therapy and Orphan Drug Designation (ODD) for the combination in certain LGSOC indications. The Company plans to request a priority review of the NDA. Currently, there are no FDA-approved treatments specifically for recurrent LGSOC.

"The initiation of our rolling NDA submission of the avutometinib and defactinib combination for accelerated approval, is an important step towards addressing the significant unmet needs that patients face living with KRAS mutant low-grade serous ovarian cancer," said Dan Paterson, president and chief executive officer of Verastem Oncology. "The data from our ongoing RAMP 201 trial continues to support our belief that the avutometinib and defactinib combination has the potential to be a new standard of care in patients with recurrent low-grade serous ovarian cancer, if approved. In the second half of this year, we anticipate completing our NDA submission with the mature data from the RAMP 201 trial and discussing with the FDA a path forward for patients with KRAS wild-type disease. We also expect to present the mature dataset at a medical meeting in the second half of 2024."

RAMP 201 is a Phase 2 registration-directed study evaluating avutometinib and defactinib combination in patients with recurrent LGSOC. The enrollment in RAMP 201 is completed, with 115 patients being treated at the recommended Phase 2 dose (RP2D) of avutometinib 3.2 mg twice weekly and defactinib 200 mg twice daily for 3 out of every 4 weeks, and follow-up continues. Verastem expects to complete the NDA submission after obtaining mature safety and efficacy data from the RAMP 201 trial, including 12 months of follow-up, anticipated in the second half of 2024. Verastem also plans to further discuss the KRAS wt data with FDA to inform the potential path forward for approval for this patient population. The Company plans to present the mature dataset from RAMP 201 at a medical meeting in the second half of 2024. As of February 2024, the interim data continued to show robust overall response rates (ORR) and durable responses with low discontinuation rates due to adverse events (AEs) in patients from RAMP 201 Parts A, B, C, who had a minimum follow-up of five (5) months.

---

The FDA granted Breakthrough Therapy Designation of the investigational combination of avutometinib and defactinib for the treatment of all patients with recurrent LGSOC regardless of KRAS status after one or more prior lines of therapy, including platinum-based chemotherapy in May 2021. Avutometinib alone or in combination with defactinib was also granted Orphan Drug Designation by the FDA for the treatment of LGSOC in March 2024. The Company believes that this Orphan Drug Designation signifies that LGSOC is a rare ovarian cancer that is a distinct and different disease from other forms of ovarian cancer such as high-grade serous ovarian cancer (HGSOC). LGSOC is highly recurrent and fatal, with no FDA-approved treatment options, and the current standard of care treatments include hormonal therapy or chemotherapy, which have demonstrated an ORR between 6-13% with discontinuation due to AEs of 17-30%.

The Company is currently enrolling patients and activating sites for RAMP 301, an international confirmatory Phase 3 trial, evaluating the avutometinib and defactinib combination versus standard of care chemotherapy or hormonal therapy for the treatment of patients with KRAS mt and KRAS wt recurrent LGSOC.

#### **Conference Call and Webcast Information**

Verastem will hold an investor conference call and webcast on Friday, May 24 at 8:00 am EDT, to review the initiation of the NDA submission and limited, topline data from the RAMP 201 trial, with a minimum follow-up of five (5) months and the RAMP 205 data. The call will feature members of Verastem's management team. To access the conference call, please dial (844) 763-8274 (local) or (412) 717-9224 (international) at least 10 minutes prior to the start time and ask to be joined into the Verastem Oncology conference call. A live audio webcast of the call, along with accompany slides, will be accessible [here](#). The Company expects to file an 8-K pertaining to this update.

#### **About RAMP 201**

RAMP 201 (ENGOTov60/GOG3052) is an adaptive, two-part multicenter, parallel cohort, randomized, open-label trial to evaluate the efficacy and safety of avutometinib alone and in combination with defactinib in patients with recurrent low-grade serous ovarian cancer. The first part of the study (Part A) determined the selection of the go forward regimen, which was the combination of avutometinib and defactinib versus avutometinib alone, based on overall response rates. The expansion phases of the trial (Parts B and C) are evaluating the safety and efficacy of the go forward regimen of avutometinib 3.2 mg twice weekly and defactinib 200 mg twice daily. The Part D portion of the trial is evaluating a low dose of avutometinib in combination with defactinib to inform individualized dose reduction.

---



### **About RAMP 301**

RAMP 301 (GOG-3097; ENGOT-ov81/NCRI) is an international collaboration between The GOG Foundation, Inc. (GOG) and the European Network of Gynaecological Oncological Trial groups (ENGOT) sponsored by Verastem Oncology. The trial is expected to enroll a total of 270 patients in the U.S., Canada, the United Kingdom, Europe, Australia and South Korea, who will be randomized to either the combination of avutometinib and defactinib or investigator's choice chemotherapy (pegylated liposomal doxorubicin, paclitaxel, topotecan) or hormone therapy (letrozole, anastrozole). The primary endpoint is progression free survival (PFS) by Blinded Independent Central Review. Secondary endpoints include ORR, duration of response, disease control rate, safety and tolerability, patient reported outcomes, and overall survival.

### **About Low-Grade Serous Ovarian Cancer (LGSOC)**

LGSOC is a rare ovarian cancer that is insidious, persistent and ultimately fatal. LGSOC is distinct and different from high-grade serous ovarian cancer (HGSOC) and requires different treatment. LGSOC is highly recurrent and less sensitive to chemotherapy compared to HGSOC. Approximately 6,000-8,000 women in the U.S. and 80,000 worldwide are living with this disease. LGSOC affects younger women with bimodal peaks of diagnosis at ages between 20-30 and 50-60 and has a median survival of approximately ten years. The majority of patients report negative impact of LGSOC on their mental and physical health, fertility, and long-term quality of life. The current standard of care for this disease includes hormone therapy and chemotherapy, but there are no treatments specifically approved by the U.S. Food and Drug Administration to treat LGSOC.

### **About the Avutometinib and Defactinib Combination**

Avutometinib is a n investigational RAF/MEK clamp that is designed to induce inactive complexes of MEK with ARAF, BRAF and CRAF potentially creating a more complete and durable anti-tumor response through maximal RAS/MAPK pathway inhibition. Avutometinib is designed to block both MEK kinase activity and the ability of RAF to phosphorylate MEK. This differentiated proposed mechanism potentially allows avutometinib to block MEK signaling without the compensatory activation of MEK that appears to limit the efficacy of other MEK-only inhibitors. The U.S. Food and Drug Administration (FDA) granted Breakthrough Therapy Designation of the investigational combination of avutometinib and defactinib, a selective FAK inhibitor, for the treatment of all patients with recurrent low-grade serous ovarian cancer (LGSOC) regardless of KRAS status after one or more prior lines of therapy, including platinum-based chemotherapy. Avutometinib alone or in combination with defactinib was also granted Orphan Drug Designation by the FDA for the treatment of LGSOC.

Verastem Oncology is currently conducting clinical trials with avutometinib in RAS/MAPK driven tumors as part of its **Raf And Mek Program** or RAMP. RAMP 301 (NCT06072781) is an international Phase 3 confirmatory trial evaluating the combination of avutometinib and defactinib versus standard chemotherapy or hormonal therapy for the treatment of recurrent LGSOC. RAMP 201 (NCT04625270) is a Phase 2 registration-directed trial of avutometinib in combination with defactinib in patients with recurrent LGSOC and enrollment has been completed in each of the dose optimization and expansion phases and the low-dose evaluation.

Verastem Oncology has established clinical collaborations with Amgen and Mirati to evaluate LUMAKRAS™ (sotorasib) in combination with avutometinib and defactinib and KRAZATI™ (adagrasib) in combination with avutometinib in KRAS G12C mutant NSCLC as part of the RAMP 203 (NCT05074810) and RAMP 204 (NCT05375994) trials, respectively. The RAMP 205 (NCT05669482), a Phase 1b/2 clinical trial evaluating avutometinib and defactinib with gemcitabine/Nab-paclitaxel in patients with front-line metastatic pancreatic cancer, is supported by a PanCAN Therapeutic Accelerator Award.

---

## About Verastem Oncology

Verastem Oncology (Nasdaq: VSTM) is a late-stage development biopharmaceutical company committed to the development and commercialization of new medicines to improve the lives of patients diagnosed with cancer. Our pipeline is focused on RAS/MAPK-driven cancers, specifically novel small molecule drugs that inhibit critical signaling pathways in cancer that promote cancer cell survival and tumor growth, including RAF/MEK inhibition and FAK inhibition. For more information, please visit [www.verastem.com](http://www.verastem.com) and follow us on [LinkedIn](#).

## Forward Looking Statements

This press release includes forward-looking statements about, among other things, Verastem Oncology's programs and product candidates, strategy, future plans and prospects, including statements related to the expected timing of the planned rolling New Drug Application (NDA) submission for the avutometinib and defactinib combination in low-grade serous ovarian cancer, 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 Verastem Oncology's lead compound. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," "can," "promising" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Forward-looking statements are not guarantees of future performance and are 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 recurring KRAS mutant LGSOC if enrollment in our confirmatory trial is not well underway at the time of submission, or that the FDA may require the Company to have completed enrollment or to enroll additional patients in the Company's ongoing RAMP-301 confirmatory Phase 3 clinical trial prior to Verastem submitting or the FDA taking action on our NDA seeking accelerated approval; that our product candidates will cause adverse safety events and/or unexpected concerns may arise from additional data or analysis, or result in unmanageable safety profiles as compared to their levels of efficacy; that we may be unable to successfully validate, develop and obtain regulatory approval for companion diagnostic tests for our product candidates that require or would commercially benefit from such tests, or experience significant delays in doing so; that our product candidates may experience manufacturing or supply interruptions or failures; that any of our third party contract research organizations, contract manufacturing organizations, clinical sites, or contractors, among others, who we rely on fail to fully perform; that we face substantial competition, which may result in others developing or commercializing products before or more successfully than we do which could result in reduced market share or market potential for our product candidates; that we will be unable to successfully initiate or complete the clinical development and eventual commercialization of our product candidates; that the development and commercialization of our product candidates will take longer or cost more than planned, including as a result of conducting additional studies; that we may not have sufficient cash to fund our contemplated operations; that we may not attract and retain high quality personnel; that we or Chugai Pharmaceutical Co., Ltd. will fail to fully perform under the avutometinib license agreement; that our target market for our product candidates might be smaller than we are presently estimating; that Secura Bio, Inc. will fail to fully perform under the asset purchase agreement with Secura Bio, Inc., including in relation to milestone payments; that we will not see a return on investment on the payments we have and may continue to make pursuant to the collaboration and option agreement with GenFleet Therapeutics (Shanghai), Inc. (GenFleet), or that GenFleet will fail to fully perform under the agreement; that we may be unable to obtain adequate financing in the future through product licensing, co-promotional arrangements, public or private equity, debt financing or otherwise; that we will not pursue or submit regulatory filings for our product candidates; and that our product candidates will not receive regulatory approval, become commercially successful products, or result in new treatment options being offered to patients.

---

As a result of these and other factors, we may not achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. 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. The forward-looking statements contained in this press release reflect Verastem Oncology's views as of the date hereof, and the Company does not assume and specifically disclaims any obligation to update any forward-looking statements whether as a result of new information, future events or otherwise, except as required by law.

**For Investor and Media Inquiries:**

Julissa Viana

Vice President, Corporate Communications and Investor Relations

[investors@verastem.com](mailto:investors@verastem.com) or

[media@verastem.com](mailto:media@verastem.com)

---



# Delivering Novel Therapies in RAS/MAPK Pathway Driven Cancers

May 2024

Corporate Presentation



# Disclaimers

## Forward-Looking Statements

This presentation includes forward-looking statements about, among other things, Verastem Oncology's (the "Company") programs and product candidates, strategy, future plans and prospects, including statements relating to the Company's pending 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 (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, the potential for and timing of commercialization of product candidates and potential for additional development programs involving the Company's lead compound and the potential market opportunities of our drug candidates. Forward-looking statements include words such as "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. 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 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 avutometinib in combination with 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 to 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 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 on 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 our 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 clinical trials 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 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 counterparts; 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 the development and commercialization of our product candidates; that any of our third-party contract research organizations, contract manufacturing organizations, clinical sites, or contractors, among others, with whom we have entered into agreements, may not perform as expected; 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 may not have sufficient cash to fund our contemplated operations; that we may not attract and retain high quality personnel; that we or Chugai Pharmaceutical Co., Ltd. will fail to fully perform under the asset purchase agreement with GenFleet; that our target market for our product candidates might be smaller than we are presently estimating; that Secura Bio, Inc. will fail to fully perform under the asset purchase agreement with GenFleet; 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 make milestone payments; 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 applications 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 and in any subsequent filings with the SEC, which are available at [www.sec.gov](http://www.sec.gov) and [www.verastem.com](http://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 or events that occur after the date of this presentation, 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 is derived from GAAP 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 measures, to provide 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 non-GAAP information, 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 in conjunction with the Company's GAAP financial measures. Non-GAAP information is not intended to be a substitute for, or superior to, financial information prepared and presented in accordance with GAAP. In addition, this non-GAAP information 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 on 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.

## 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, 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 or accuracy 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 completeness of such information.



# Verastem Oncology

Positioned to deliver on  
potential 2024 catalysts

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

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

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

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

## ➤ Ongoing studies in additional indications including NSCLC

- Expect to report updated interim data from RAMP 203 non-small cell lung cancer (NSCLC) trial evaluating avutometinib plus defactinib with Amgen's KRAS G12C inhibitor, sotorasib, expected in Q3 2024
- Expect to report initial interim data from RAMP 204 NSCLC trial evaluating avutometinib plus sotorasib with Bristol Myers Squibb (BMS) KRAS G12C inhibitor, adagrasib, expected in Q3 2024

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

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

## ➤ Balance sheet supports ongoing programs and operations

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

\*Q1 2024 GAAP operating expenses of \$28.06M less Q1 2024 stock-based compensation expense of \$1.48M = \$26.58M Q1 2024 non-GAAP operating expenses  
IND: investigational new drug; NDA: new drug application; RAS: Rat sarcoma; KRAS: Kirsten Rat Sarcoma virus; MAPK: Mitogen-Activated Protein Kinase; RAF: Rapi

# Clinical Program Designed to Address LGSOC and Beyond

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



ASCO: American Society of Clinical Oncologist; FAKi: focal adhesion kinase inhibitor; ICT: investigator choice of treatment



# Avutometinib, RAF/MEK Clamp Program Overview

---



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

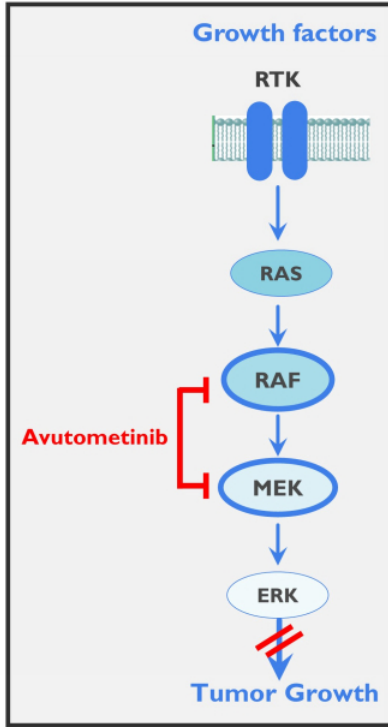
- Differentiated investigational RAF/MEK clamp mechanism of action
- Novel intermittent dosing schedule; convenient oral regimen
- Orphan Drug Designation for avutometinib alone or in combination with defactinib in recurrent LGSC
- Breakthrough Therapy Designation for combination of avutometinib and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



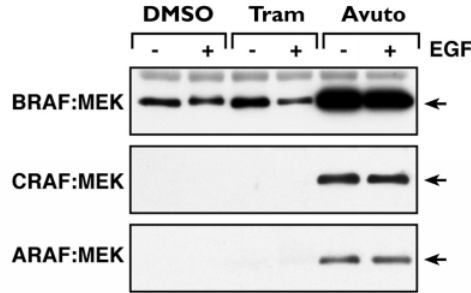
RAF-Rapidly accelerated fibrosarcoma, MEK-Mitogen-activated protein kinase kinase, RAS-Rat sarcoma virus MAPK-Mitogen-activated protein kinase KRAS-KRAS NRAS-Neuroblastoma RAS viral oncogene homolog, BRAF-v-raf murine sarcoma viral oncogene homolog B1, NFI-Neurofibromatosis type I

# Avutometinib is a Differentiated Small Molecule RAF/MEK

Contrasting Mechanism of Action vs. MEK-Only Inhibitors

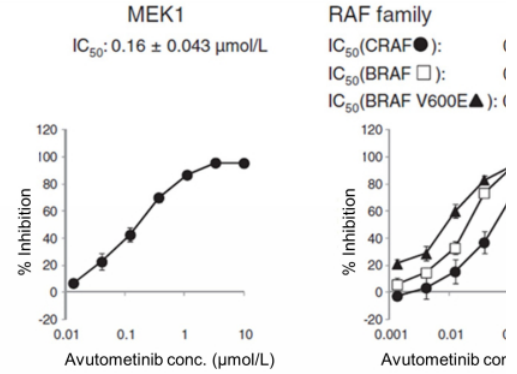


**Avutometinib induces dominant negative RAF/MEK complexes**

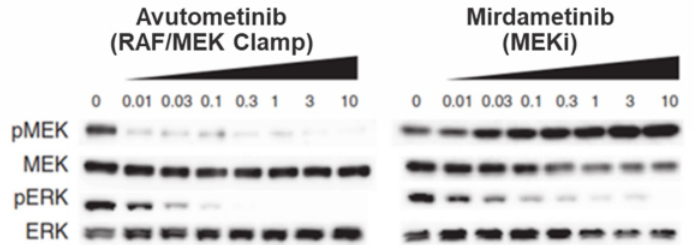


*Collaboration with Deborah Morrison, NCI*

**Avutometinib inhibits both RAF and MEK**

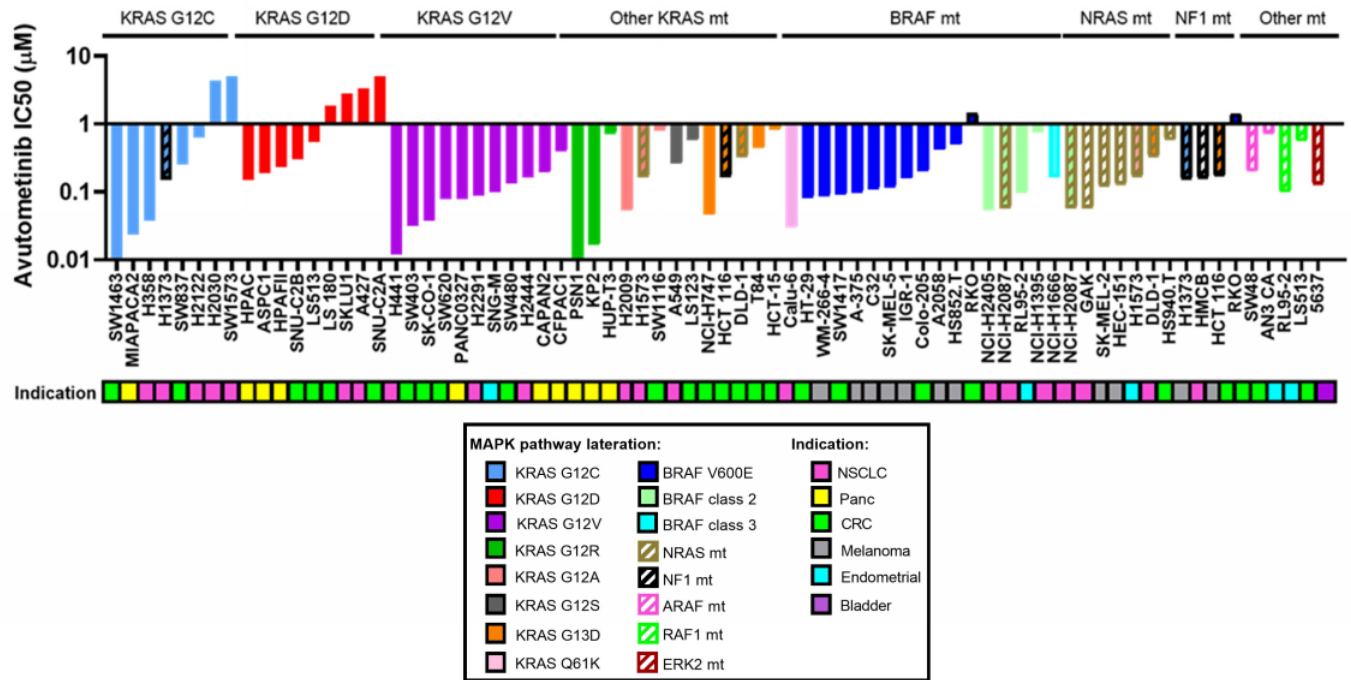


**The RAF/MEK clamp mechanism avoids the compensatory activation of pMEK enabling more complete pERK inhibition**



Coma et al., AACR 2022; Ishii et al., *Cancer Res*, 2013; Lito et al., *Cancer Cell*, 2014

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



# Outsmarting Multiple Resistance Mechanisms in the RAS/MAPK Pathway

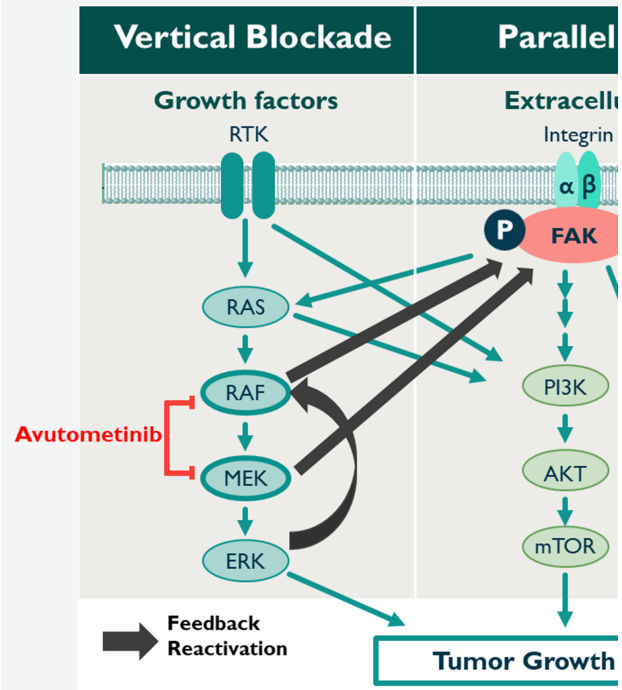
Novel Combination of Investigational Avutometinib + Defactinib with Aim to Improve Patient Outcomes

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

- This differentiated mechanism of action potentially avoids the compensatory reactivation of MEK by RAF enabling more complete pERK inhibition<sup>1-3</sup>
- Potential best-in-class safety & tolerability profile relative to marketed MEK inhibitors and standard of care for LGSOC<sup>4-7</sup>
- Promising signals of clinical activity in various RAS pathway-driven cancers, including in patients whose tumors previously progressed on other MEK inhibitors<sup>6-8</sup>

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

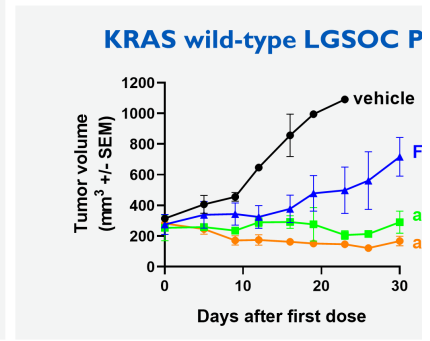
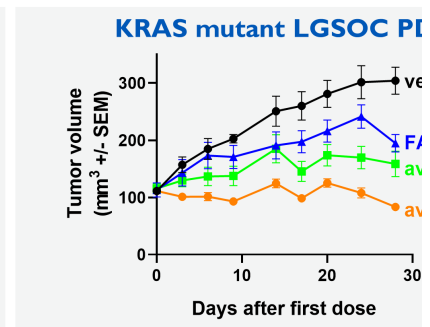
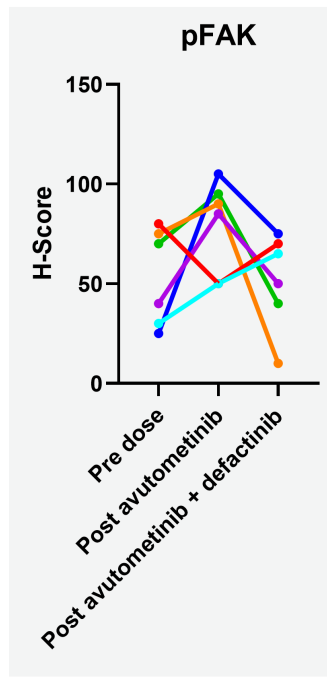
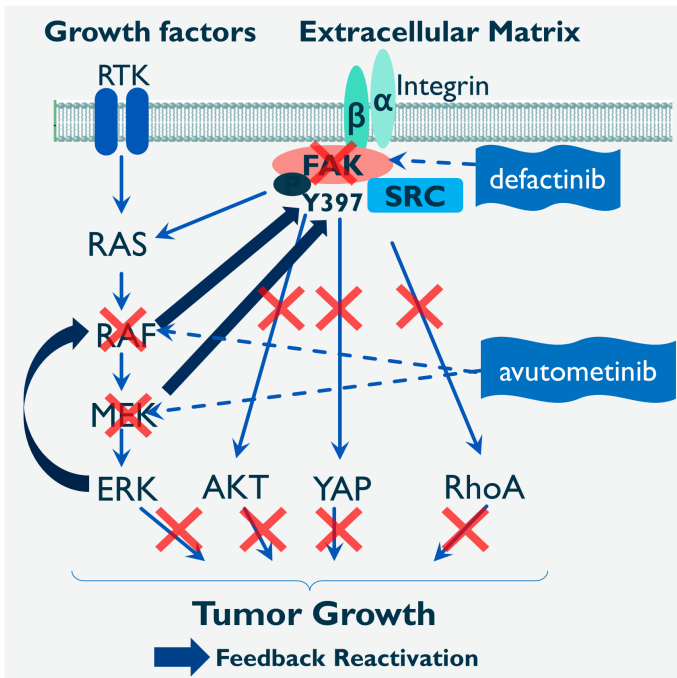
- Parallel pathway inhibitor demonstrating synergy with avutometinib in multiple tumor models including LGSOC, pancreatic cancer and melanoma<sup>9-12</sup>
- Monotherapy and combination with other agents such as PD-1 inhibitors, and chemotherapy, defactinib demonstrated a manageable safety profile<sup>13, 14</sup>



<sup>1</sup>Coma et al., AACR 2022; <sup>2</sup>Ishii et al., Cancer Res, 2013; <sup>3</sup>Lito et al., Cancer Cell, 2014; <sup>4</sup>Gershenson et al., Lancet 2022 (Study GOG 281); <sup>5</sup>Monk et al., J Clin Oncol 2020 (MILO Study); <sup>6</sup>Banerjee et al., FRAME; <sup>7</sup>Banerjee et al., ASCO June 2023 (Study RAMP 201); <sup>8</sup>Awad et al., EORTC- NCI – AACR Conference Oct 2023 (Study RAMP 203); <sup>9</sup>McNamara et al., Gynecol Oncol 2024; <sup>10</sup>Liu et al., AACR 2024; <sup>11</sup>Stanley et al., AACR 2024; <sup>12</sup>Fennell et al., J Clin Oncol 2019; <sup>13</sup>Wang-Gillam et al., Clin Cancer Res 2022

# 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 I, April 27, 2020, CT143; Banerji, unpublished; Santin, unpublished

# Optimized Dosing Schedule Defined: Favorable Tolerability Profile with Novel Intermittent Dosing Regime

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	(Avutometinib weekly + ... twice weekly 21 days on / 7 days off)
Treatment Related Adverse Event	Grade $\geq 3$	Grade $\geq 3$	Grade $\geq 3$
Rash	3 (50%)	5 (19%)	2 (8%)
CK elevation (Creatine phosphokinase)	1 (17%)	2 (8%)	2 (8%)



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

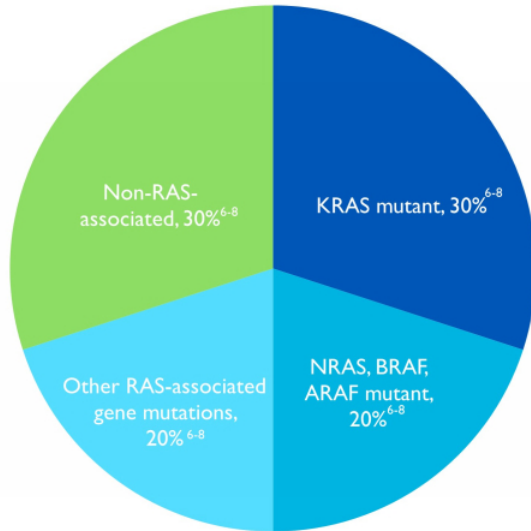


# Low-Grade Serous Ovarian Cancer (LGSOC)

---

# LGSOC is a Rare Ovarian Cancer that is Insidious, Persistent and Ultimately Fatal<sup>1-4</sup>

1k-2k<sup>12</sup> incidence of LGSOC with a prevalence of 6k-8k<sup>13</sup> in the US; 80,000 worldwide



Greater than **80%** of patients with LGSOC experience a recurrence<sup>1</sup>

**20-30s**

Affects a **younger patient population** and disproportionately **impact health, fertility quality of life**<sup>9,10</sup>



Current SOC treatments **offer poor to no response rates** (6-13%)<sup>5,9,14</sup>



Median overall **survival of ~10 years from diagnosis**<sup>5</sup>



**No FDA-approved treatment** specifically for LGSOC

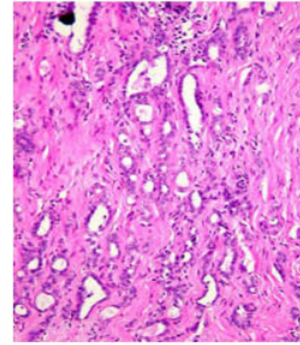


1. Babaier 2022/p1/para1/ln6,7; 2. Gadducci 2020/p4/para2/ln16,7; 3. Gershenson Lancet 2022/p545/col2/para2/ln6-9; 4. Gershenson 2015/p2681/fig1; 5. Gershenson Gynecol Oncol 2022; 6. Manning Naggar Gynecol Oncol 2022; 7. AACR GENIE v9.0 VSTM unpublished analysis (data on file); 8. AACR GENIE v9.0 VSTM unpublished analysis (data on file); 9. Slomovitz Gynecol Oncol 2020; 10. Manning-Geist B et al. Clin Cancer Res 2022;28(20):4456-4465;11.16\_suppl (June 1, 2023) 5515-5515;12. Verastem DOF; 13. US Cancer Statistics. Accessed 2024. 14. Monk 2020/p3758/table2/footnote-b

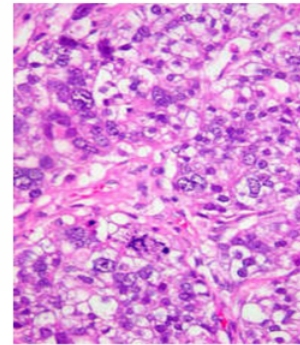


# Low-Grade and High-Grade Serous Ovarian Cancer Are Distinct Diseases

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



**LGSOC**



**HGSOC**



Avutometinib ± Defactinib in  
Low-Grade Serous Ovarian Cancer

RAMP 201: Topline Data  
Parts A + B + C

---

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

- RAMP 201 topline data represent larger dataset of patients treated at the RP2D with a min up of 5 months at last data analysis (Parts A, B and C combined: n=115\*; KRAS mt: n=58; KRAS w
- Moving forward with rolling NDA submission for Accelerated Approval in adult patients with KRAS mt LGSOC who received at least one prior systemic therapy
  - RAMP 201 data with 12-months follow up is needed to complete the submission and drives time module
  - Path forward for KRAS wt to be discussed with FDA when mature RAMP 201 data available
  - Based on the longer median duration of treatment observed in RAMP 201 Part A, we believe KR represents  $>2/3^{\text{rds}}$  of the revenue opportunity, compared with combined KRAS mt and KRAS wt differential pricing\*\*
- Plan to present mature dataset from RAMP 201 at a medical conference in the second half
- Expect to complete NDA submission in the second half of 2024

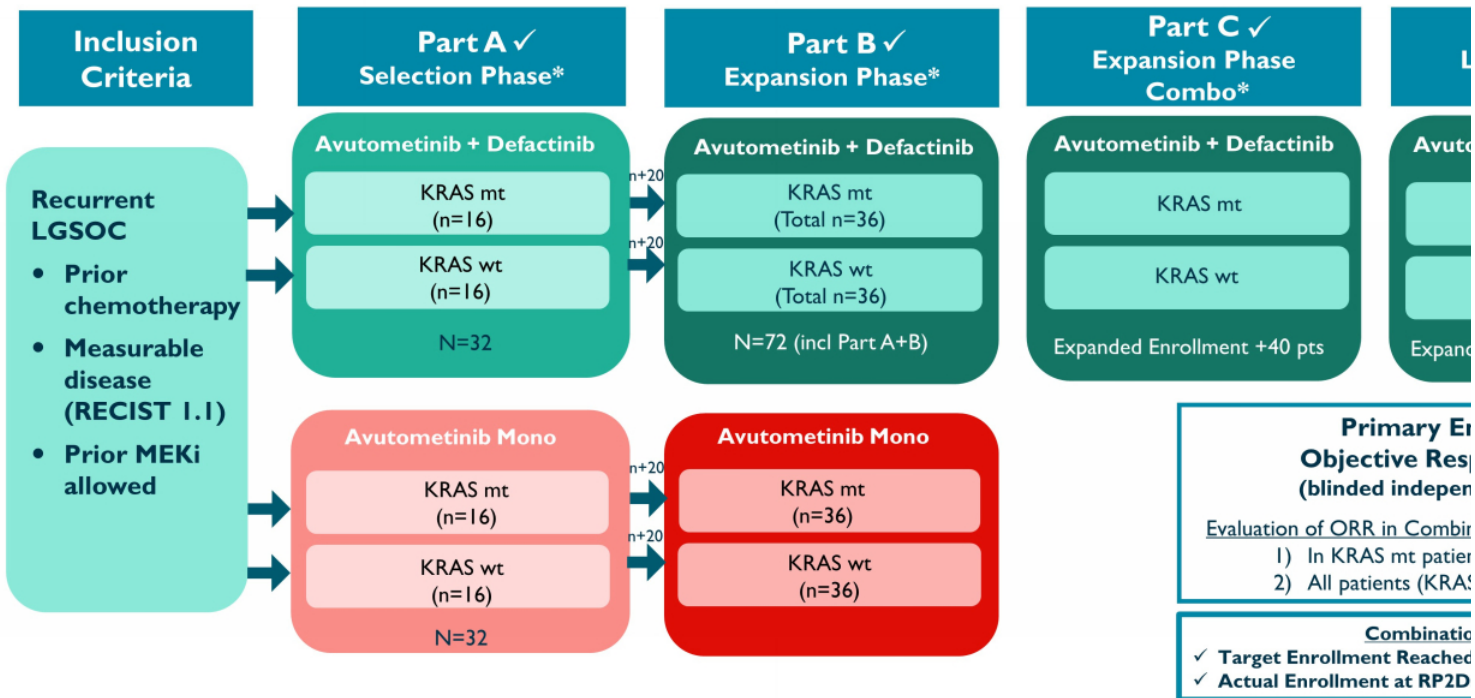


\*6 patients with no baseline measurable disease per independent review committee (IRC); KRAS wt: kirsten rat sarcoma virus; wt: wild type

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

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

RAMP 201 (ENGOTov60/GOG3052)



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

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

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

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

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

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

- Minimum follow-up of 5 months
- 14 patients with stable unconfirmed partial response on treatment
- Potential for response to improve with continued treatment
  - Potential response rate (27%-39%)
  - KRAS mt: 21-30 (37%)
  - KRAS wt: 8-13 (15%)
- No new safety signals
- Plan to present mature data at upcoming medical meeting in 2H2024



All information based on data cutoff as of Feb. 23, 2024; \*6 patients with no baseline measurable disease per IRC

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

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

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

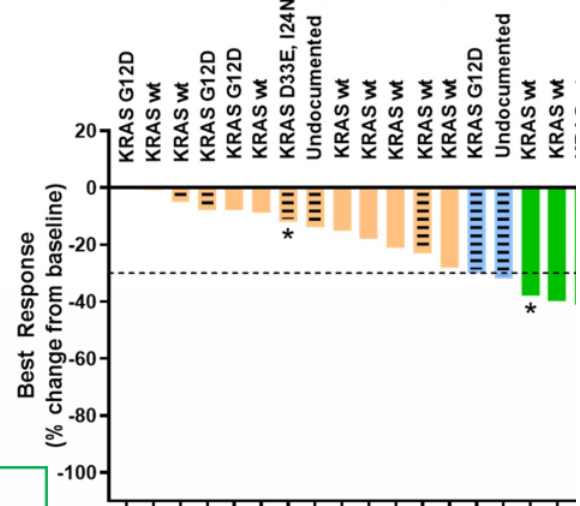
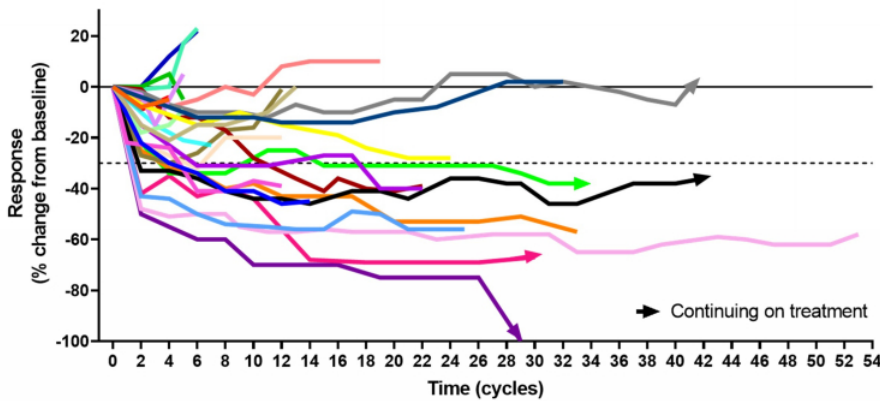
\*Median duration of therapy, at subsequent analysis, for patients enr

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

\*As of 23Feb2024 data cutoff

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

Response by RECIST



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

Prior MEK inhibitor  
 Still on treatment  
 Confirmed p  
 Unconfirmed  
 Stable disea

28-day cy  
 DoR: Durc  
 PFS: Progr  
 NR: Not r



# Recent LGSOC Trials Provide Relevant SOC Comparator

Trial	Number of Prior Systemic Therapies Median (range)	Prior MEK allowed	Prior Bevacizumab	Therapy	Response Rate ORR	Image Assessment	Median PFS Months (95% CI)
GOG 281 <sup>1</sup>	2 (1-10)	No	* Low %	SoC (n=130)	6% 95% CI: (3%, 12%)	INV	7.2 (5.6-9.9)
MILO <sup>2</sup>	2 (1-8)	No	* Low %	SoC (n=101)	13% 95% CI: (7%, 21%)	BICR	10.6 (9.2 - 14.5)

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



<sup>1</sup> Study GOG 281 trial Gershenson et al., Lancet 2022; <sup>2</sup> MILO Study Monk et al., J Clin Oncol 2020.

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





# Avutometinib + Defactinib in Low-Grade Serous Ovarian Cancer

## Regulatory Update

---

# Avutometinib + Defactinib for Recurrent LGSOC: Path to Accelerated Approval

## Significant Unmet Medical Need

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

### Standard of Care (chemo/hormonal therapy)<sup>a</sup>

ORR: 6-13%

D/C due to AE: 17-30%

## Key Regulatory Achievements Anticipated Milestones

- ✓ Breakthrough Therapy Designation granted
- ✓ Orphan Drug Designation granted for treatment of LGSOC as a distinct disease
- ✓ FDA Pre-NDA meeting 1H 2024
- ✓ Initiating rolling NDA submission for recurrent LGSOC in Q2 2024
- Plan to share RAMP 201 mature dataset of rolling NDA submission
- Expect to complete rolling submission H1 2025 review request
- Potential for FDA accelerated approval in H2 2025
- Ongoing confirmatory study targeting full approval by end of 2025

**Next Steps:** Plans to discuss regulatory pathways with EMA and PMDA (EU and Japan)



<sup>a</sup> Gershenson et al, Lancet 2022; Monk et al, JCO 2020

<sup>b</sup> 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. Administration; CHMP: Committee for Medicinal Products for Human Use; PMDA: Pharmaceutical and Medical Devices Agency; EU: European Union



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

---

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

STAGE II-IV DISEASE<sup>1</sup>

MOS: ~10

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 treat with prevalent patients at their next recurrence
- 49% of Oncologists surveyed indicate that initial recurrence is the ideal point in the patient journey to initiate treatment with the combination<sup>3</sup>



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



1. NCCN: National Comprehensive Cancer Network; NCCN guidelines v1.2023 / 2. Gershenson Gynecol Oncol 2022;p1/Abstract/Results/In1-2 / 3. VSTM DOF, ATU 2024 (n=96, Fielded December 2023)

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

Given the expected longer duration of therapy<sup>1</sup>, we believe KRAS mt represents approximately >2/3<sup>rds</sup> of revenue opp compared with combined KRAS mt and KRAS wt, without any differential pricing\*

## Focused Commercial Launch

### Plan for a focused commercial launch, if approved

- Top 400 HCPs and top 100 HCOs collectively cover nearly half of the LGSOC population<sup>1</sup>; focused sales force of 14-18 reps

### Substantial market preparation activities

- Engaged with 1/3 of prevalent patient population<sup>2</sup> & ongoing engagement with HCPs<sup>3</sup>

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

- Based on a TPP of avutometinib + defactinib combination:
  - 85% of treaters surveyed say they would adopt within 6 months of receiving FDA approval, suggesting swift uptake of the treatment for eligible patients<sup>4</sup>

### Opportunity for active switch to avutometinib + defactinib

- Based on TPP of avutometinib + defactinib combination:
  - 28% of treaters surveyed say they would proactively reach out to switch half of their current LGSOC patients, if approved<sup>4</sup>

## Ensuring Patients' Ability to Start and Stay on Therapy

### Coverage and access support

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

### Ongoing engagement with plans for rapid uptake

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

### Patient assistance

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

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

<sup>1</sup> Based on median duration of therapy from RAMP 201 Part A

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



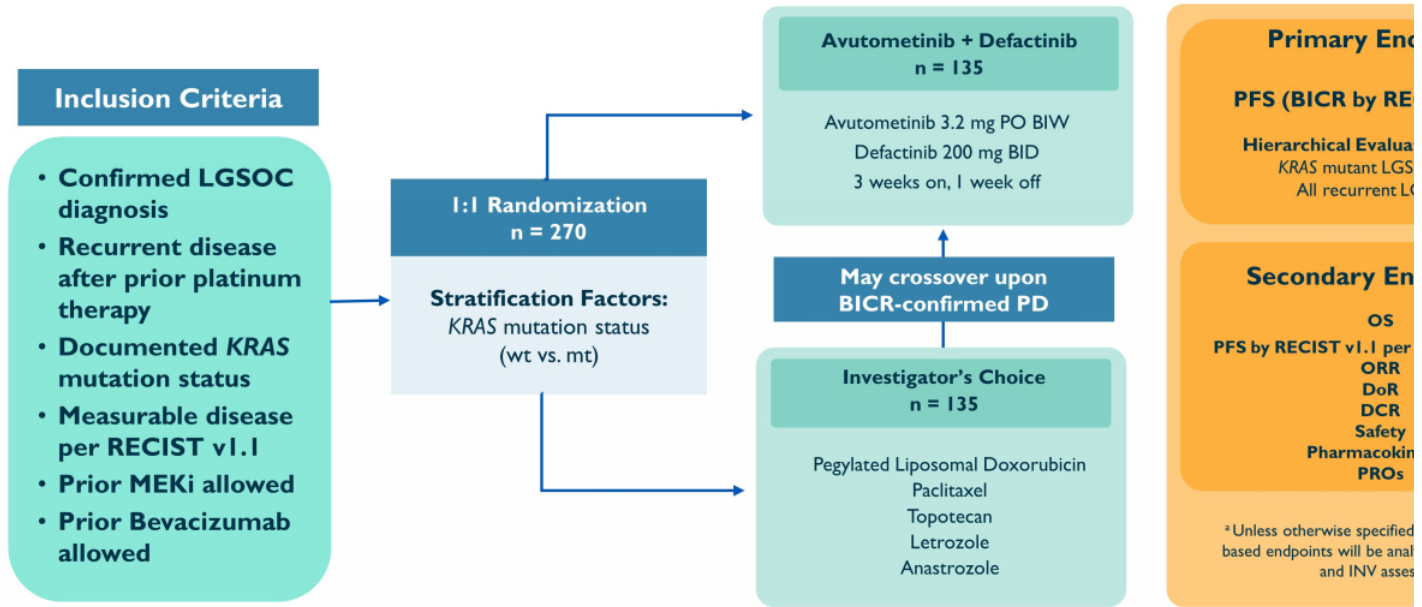
Avutometinib + Defactinib in  
Low-Grade Serous Ovarian Cancer

RAMP 301: Phase 3 Confirmatory  
Trial

---

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

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



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 outcome response evaluation criteria in solid tumors; wt: wild type.



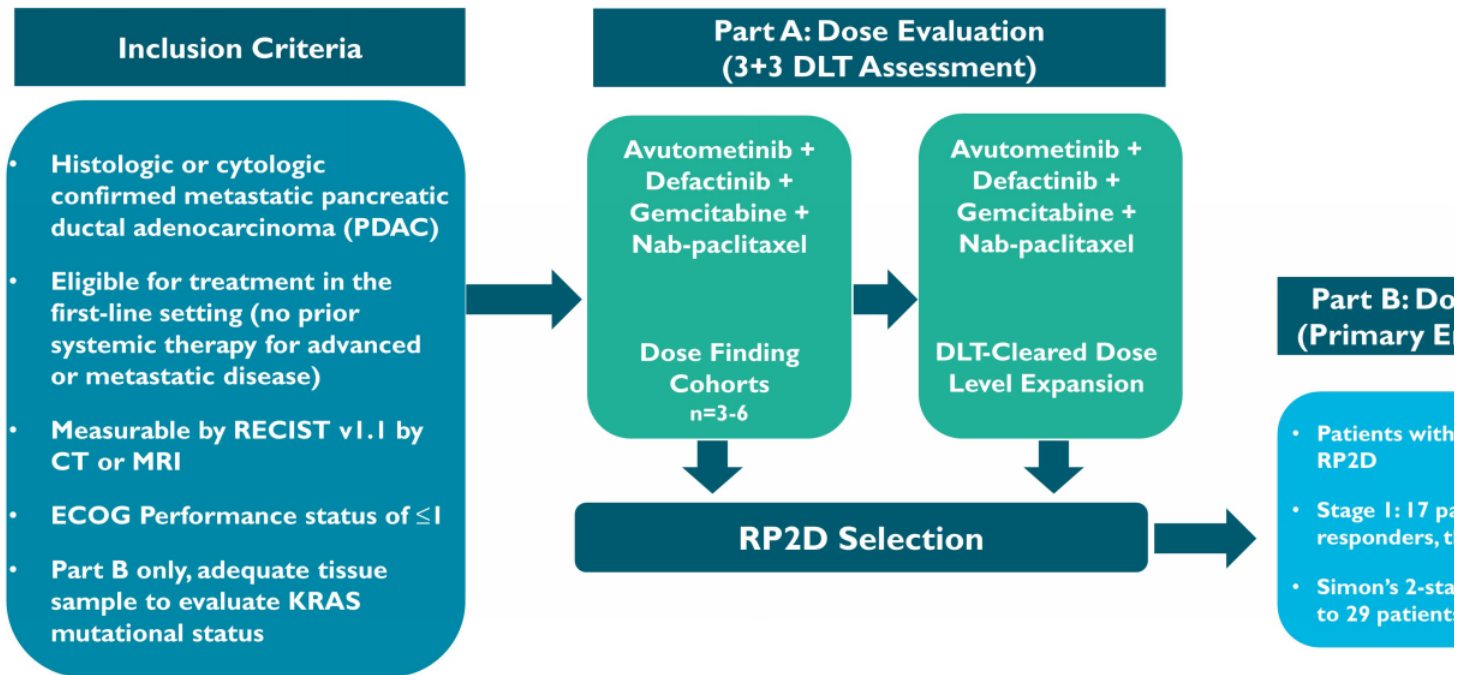
Topline Data from RAMP 205:  
Avutometinib + Defactinib + SOC in  
First-Line Metastatic Pancreatic  
Cancer

---



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

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 avutome 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
    - 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 RP2D for expansion cohort
- 11 top academic sites currently enrolling and highly engaged
- Presenting RAMP 205 initial interim data at ASCO on June 1, 2024

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



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

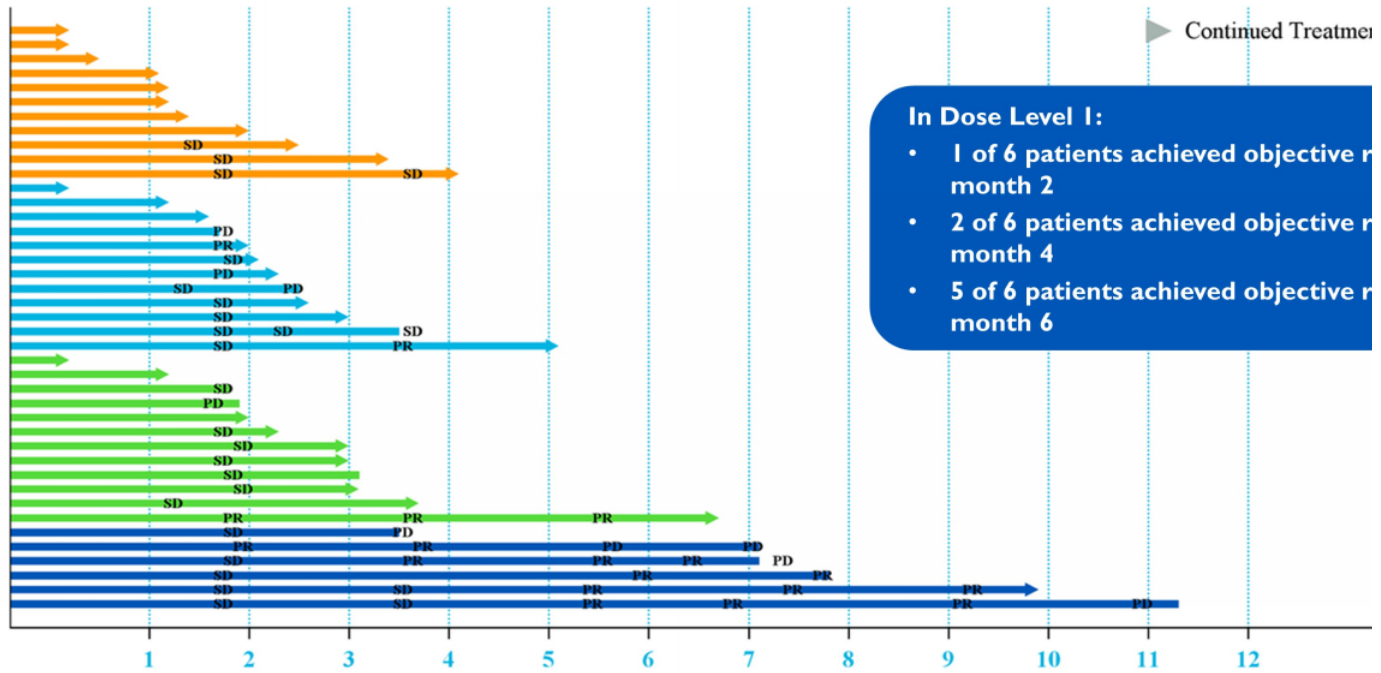
Trial/PI/Reported (# Patients)	Intervention	Comparator	ORR by Investigator (95% CI)		mPFS (95% CI)
<b>MPACT</b> Von Hoff 2013 (N=861)	<b>Gem/NabP*</b> (n=431)	Gem (n=430)	<b>Gem/NabP</b>		<b>5.5</b> months (4.5-5.9)
			<b>29%</b> (25-34)	<b>23%</b> (19-17) IRR**	
<b>NAPOLI 3</b> O'Reilly 2023 (N=770)	<b>Nalirifox</b> (n=383)	<b>Gem/NabP*</b> (n=387)	<b>Gem/NabP</b>		<b>5.6</b> Months (5.3-5.8)
			<b>Nalirifox</b>		<b>7.4</b> months (6.0-7.7)
<b>PRODIGE</b> Conroy 2011 (N=342)	<b>Folfinirox</b> (n=171)	Gem (n=171)	<b>Folfinirox</b>		<b>6.4</b> months
			<b>31.6%</b> (24.7-39.1)		



For Reference only: No cross-trial comparison made.\*Dosing schedule in Gem/NabP arms above= 1000/125(mg/m<sup>2</sup>) D1,8,15 q 4w, \*\*Secondary endpoint of ORR based on Review), \*\*\*NR: Not Reported.

# 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)

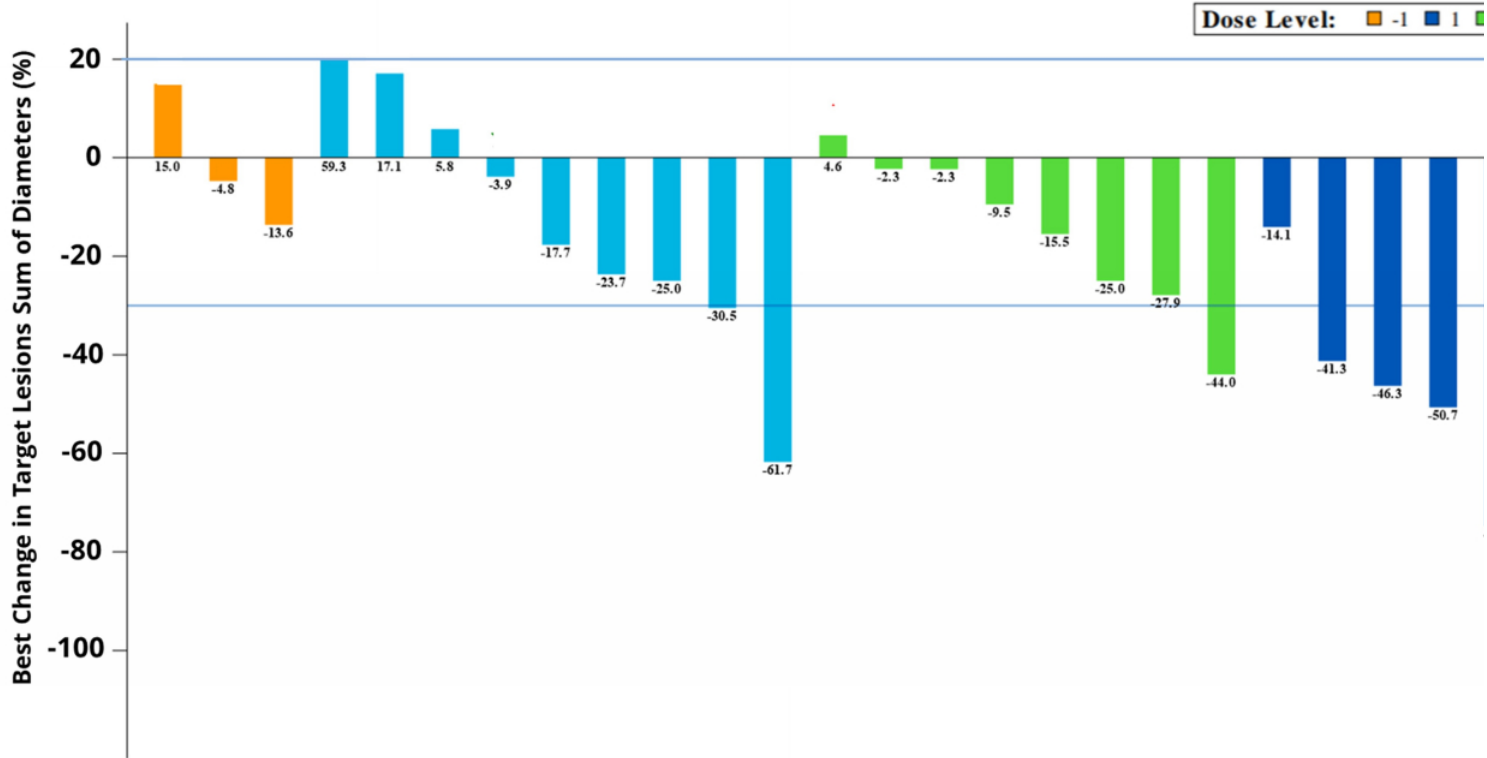


Data Cutoff Date: 14 MAY 2024

Source: Program: F\_TR\_SWIMMER.sas

# RAMP 205: Best Percent Change in Target Lesion Sum of D

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



Data Cutoff Date: 14 MAY 2024

Source: Program: F\_TR\_WATERFALL\_BYDOSE2

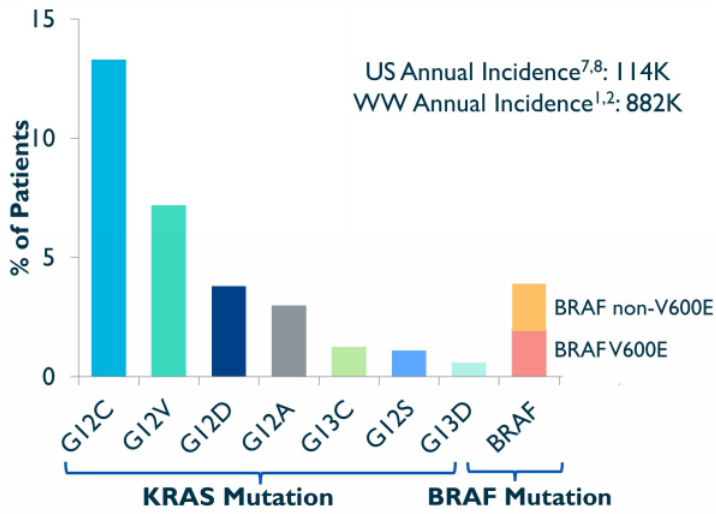


# Avutometinib with KRAS G12C Inhibitors in Non-Small Cell Lung Cancer

---

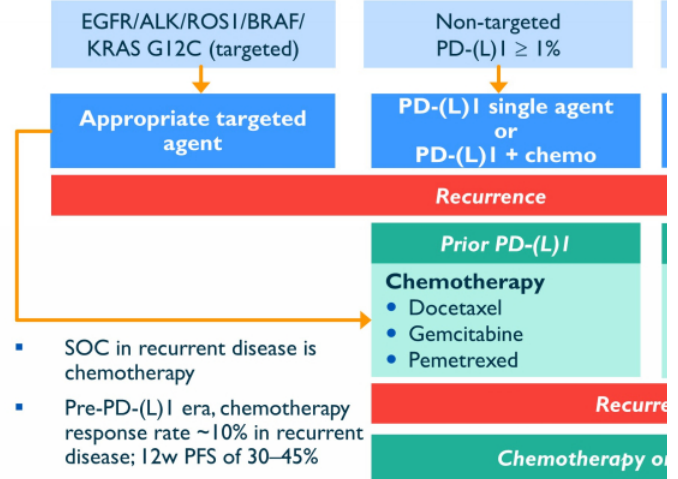
# High Unmet Need in Refractory NSCLC Adenocarcinoma

## NSCLC Adenocarcinoma<sup>3</sup>



KRAS Mutations Represent 25% of Lung Adenocarcinoma & BRAF Mutations Represent ~4% (EGFR 17%, ALK 7%)<sup>4,6</sup>

## Advanced or Metastatic NSCLC Recommend Histologic and Molecular S



### Verastem Clinical Trials:

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



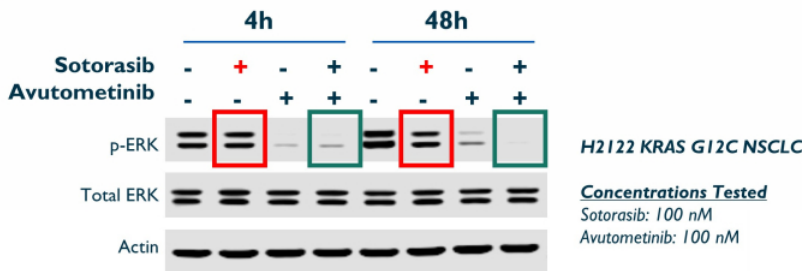
<sup>1</sup> Globocan, 2020; <sup>2</sup> <https://www.ncbi.nlm.nih.gov/books/NBK519578/>; <sup>3</sup> TCGA PanCancer Atlas (cBioPortal analysis); <sup>4</sup> www.thelancet.com Vol 389 January 21, 2017; <sup>5</sup> Adapted from lung cancer guidelines Version 3.2020; <sup>6</sup> Clinical Cancer Research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

# Preclinical Synergy of Avutometinib + G12C Inhibitors in KRAS G12C

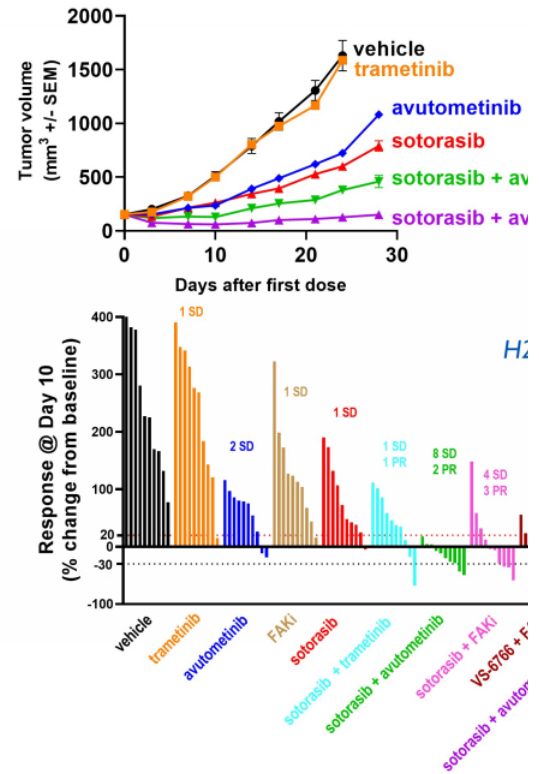
Synergy of avutometinib + G12C inhibitors across G12C mutant NSCLC, CRC & Pancreatic cancer cell lines

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 NSCLC in vivo; Tumor regression in all mice with





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

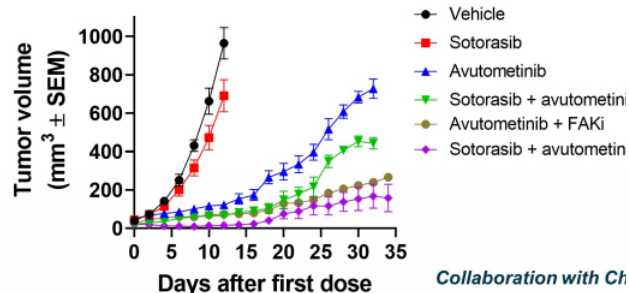
Avutometinib inhibits proliferation of cells harboring acquired KRAS mutations that occur clinically upon progression on G12C inhibitors

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

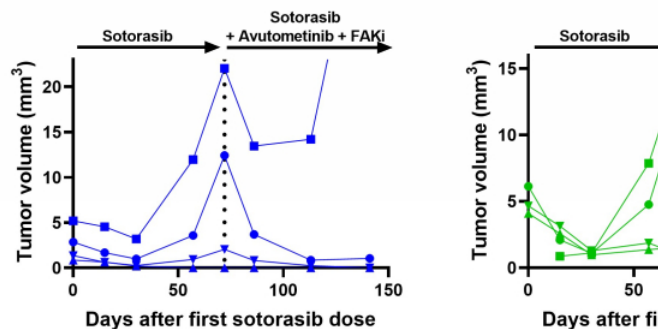
Collaboration with Andy Aguirre, DFCI

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



Collaboration with Ch...

Addition of avutometinib + FAKi restores anti-tumor activity of sotorasib monotherapy in a KRAS G12C NSCLC GEM model

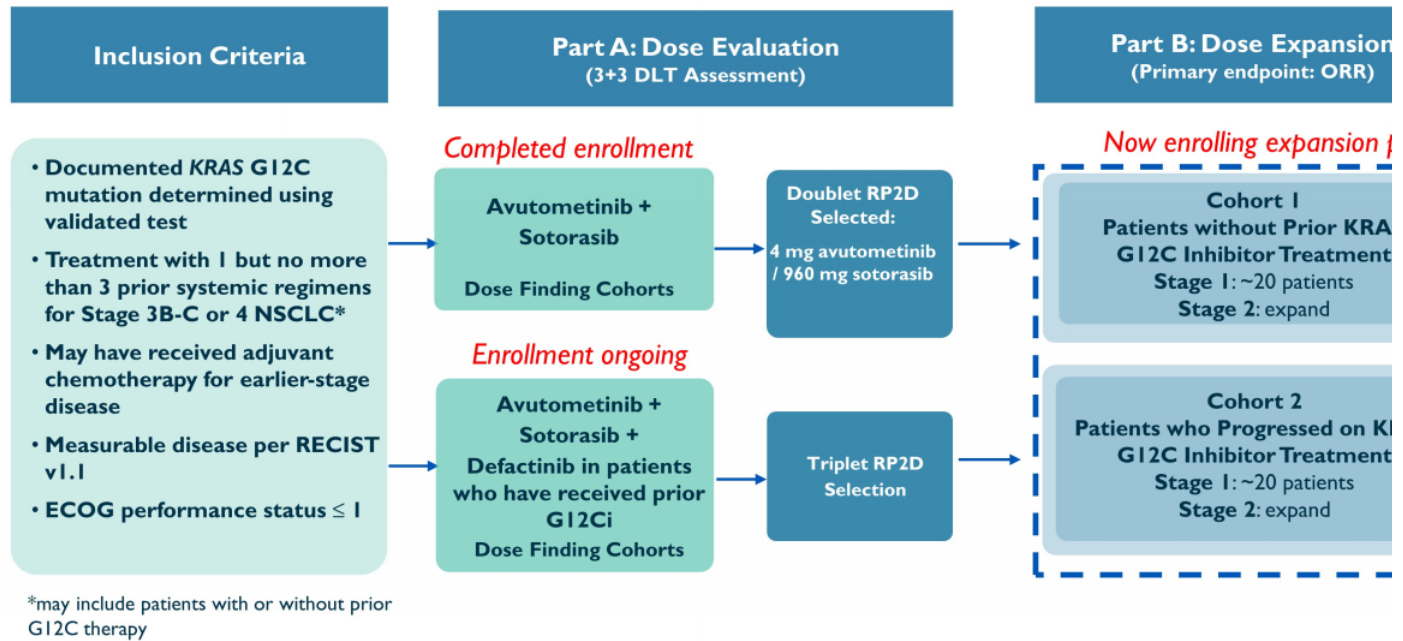


Collaboration with Mariano Barbacid, CNIO (S)



Reference: Coma et al., AACR RAS meeting 2023

# RAMP 203: Phase I/2 Trial of Avutometinib + LUMAKRAS<sup>®</sup> (Sotorasib) ± Defactinib in KRAS G12C Advanced NSCLC



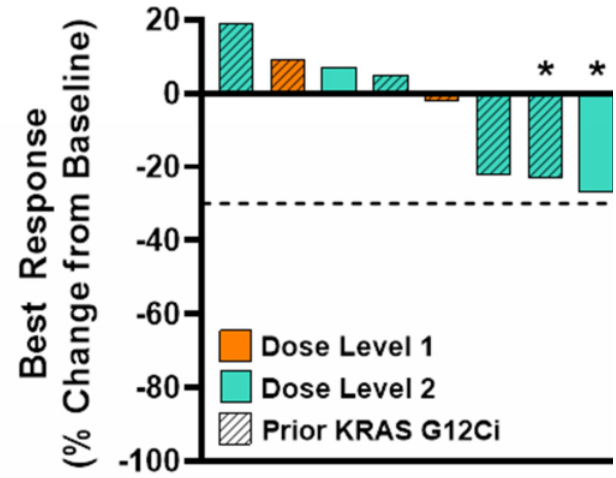
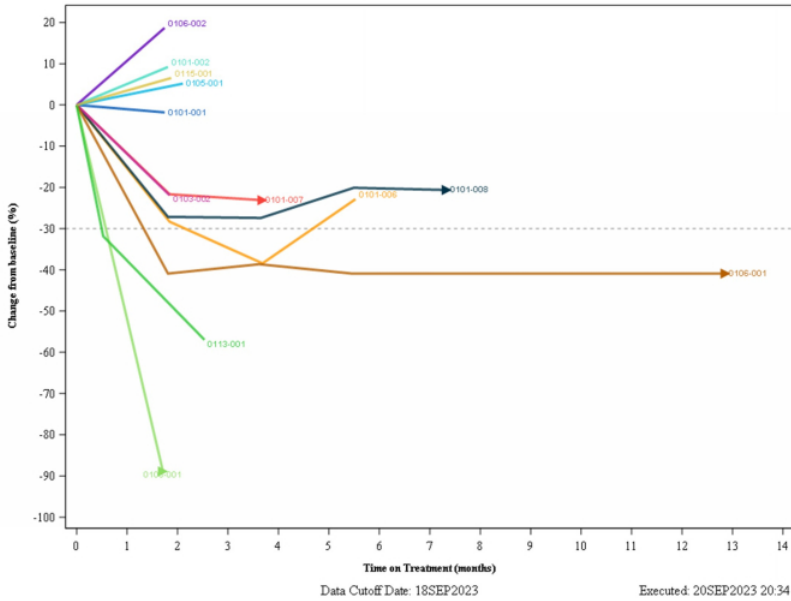
Collaboration with Amgen, NCT05074810

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, phase 2 dose.

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

## Avutometinib + Sotorasib

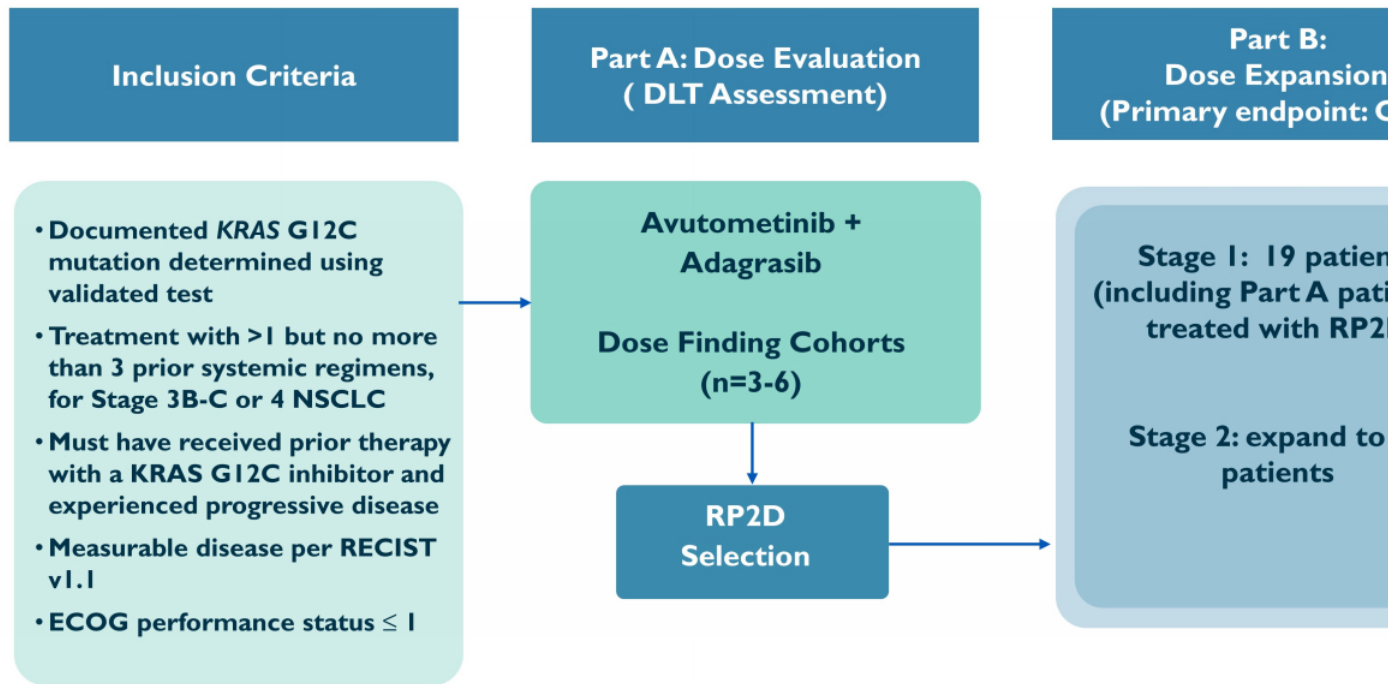
Percentage Change in Target Lesion Sum with time on treatment



\*On treatment at time of data cutoff; + Patient with -31 classified as SD due to disease progression prior to cor



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



Collaboration with Mirati (BMS) NCT05375994

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 tumors recommended phase 2 dose.



# RAS Pathway-Driven Cancers and Rational Avutometinib Combinations

---

# Investigator-Sponsored Trials Provide Ongoing Comprehensive Appr Establish More Complete Blockade of RAS Pathway & Resistance Pa

	Indication	Incidence/ Prevalence	Biomarker %	Regimen	Setting	Phas
<b>Gynecologic Cancers</b>	LGSOC	Prevalence 6k <sup>1</sup>	70%	Avutometinib + defactinib + letrozole	Low-grade serous ovarian cancer without prior systemic treatment	Phase 1/2
	Gynecologic Basket	Incidence <sup>4-8</sup> : 85K	25%	Avutometinib + defactinib	Recurrent RAS Pathway-driven (RAS/RAF/NFI) endometrioid cancer, mucinous ovarian cancer, high-grade serous ovarian cancer or cervical cancer	Phase 2
	Mesonephric	Incidence: <sup>9</sup> ~680	96%	Avutometinib + defactinib	Advanced or recurrent mesonephric gynecologic cancer	Phase 2
<b>CRC</b>	KRAS mt	Incidence <sup>2</sup> : 148K	45%	Avutometinib + cetuximab	Recurrent metastatic KRAS mt	Phase 1/2
	RAS/RAF wt CRC	Incidence <sup>2</sup> : 148K	50% <sup>12</sup>	Avutometinib + defactinib + cetuximab	Unresectable, Anti-EGFR-Refractory Advanced Colorectal Cancer	Phase 1/2
<b>Breast Cancer</b>	ER+/Her2-	Incidence <sup>2</sup> : 279K	22.5%	Avutometinib + abemaciclib + fulvestrant	Recurrent ER+/HER2- breast cancer following progression on CDK4/6i + aromatase inhibitor	Phase 1/2
<b>Melanoma</b>	MAPK alterations or wt	Incidence <sup>2</sup> : 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
<b>Thyroid</b>	MAPK alterations <sup>†</sup>	Incidence <sup>3</sup> : 44K	35%	Avutometinib + defactinib	Differentiated & anaplastic thyroid cancer	Phase 2

<sup>†</sup>excluding BRAFV600E



<sup>1</sup> 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 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 20: Siegel et. al. CA Cancer J Clin 2020;70:7-30; <sup>2</sup>Cancer Statistics 2020, Siegel et. al. CA Cancer J Clin 2020;70:7-30 <sup>4</sup>Uterine cancer is one of the leading gynecologic neoplastic disorders in the US, of which over 80% are endometri <sup>5</sup>Endometrioid OC (EnOC) accounts for approximately 10% of all OC, with the majority of cases diagnosed as low grade, early stage disease with excellent clinical; <sup>6</sup>ucinous ovarian cancer: 3-11% of ovarian cancer (Hada et: 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>); <sup>8</sup>HGSOC the most common t accounting for approximately 75% of epithelial ovarian cancers. (<https://ocrahope.org/news/high-grade-serous-carcinoma/>) <sup>9</sup>Ji Son (David Hong) ASCO 2023

# Discovery Efforts



---

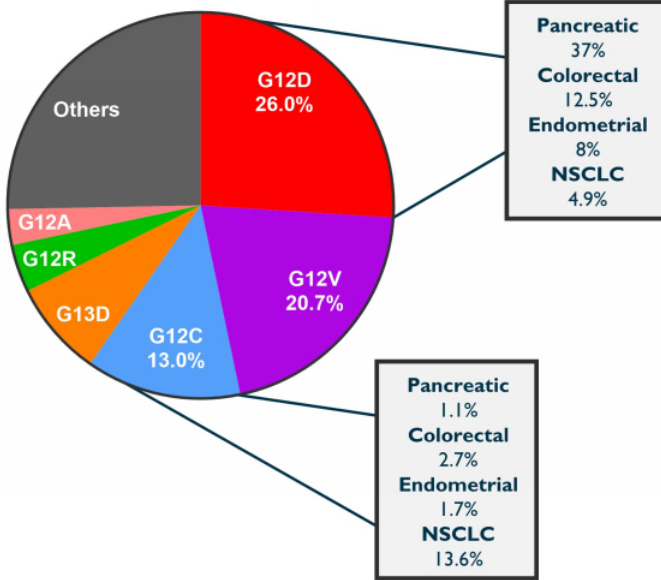
# Discovery and Development Collaboration with GenFleet Strengthens Pipeline Targeting RAS Pathway-Driven Canc

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

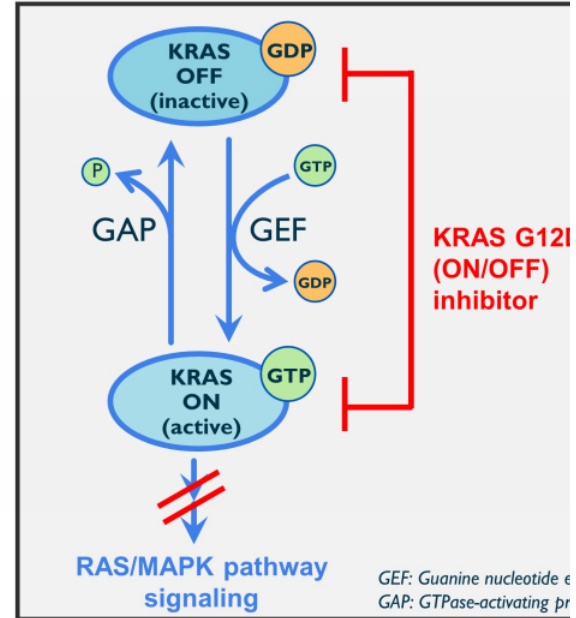


# Rationale for Designing a Potent and Selective Orally Bioavailable In KRAS G12D (ON/OFF) for the Treatment of Patients with KRAS G1

KRAS G12D is the most frequent KRAS mutation in human cancer



Ideal to inhibit both the active (ON) & inactive of KRAS for deep and durable inhibition of t



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

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

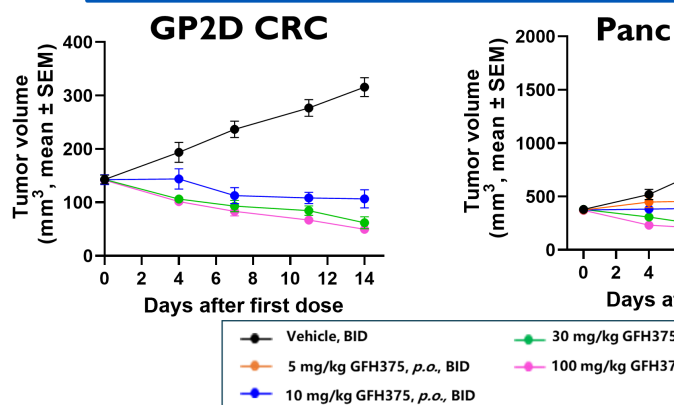
First program from the GenFleet collaboration

- 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
- Avutometinib enhances anti-tumor activity of GFH375 (VS-7375) in preclinical models
- IND-enabling GLP toxicology studies complete
- IND application filed in China and accepted for review; upon clearance expect to initiate Phase I trial in China in H2 2024

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

KRAS G12D State	GFH375 IC <sub>50</sub> (KRAS G12D)
GppNp-bound (ON/active)	2 ± 1
GDP-bound (OFF/inactive)	6 ± 1

Potent anti-tumor activity demonstrated across preclinical models



Zhou et al., AACR 2024

# Financials



---

# 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 avutometinib 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 penalty
- 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-expenses

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

# Recent Corporate Achievements

Avutometinib + Defactinib: Recurrent LGSOC	Avutometinib + Defactinib: Metastatic Pancreatic Cancer	Avutometinib + KRAS G12C Inhibitors: NSCLC	GFH375/M Oral G12D Inhib
<ul style="list-style-type: none"> <li>✓ Initiating rolling NDA submission in recurrent KRAS mt LGSOC</li> <li>✓ Received FDA Orphan Drug Designation</li> <li>✓ Initiated Phase 3 confirmatory study in Q4'23</li> <li>✓ Presented planned subgroup analysis of Part A RAMP 201 trial</li> </ul>	<ul style="list-style-type: none"> <li>✓ Initial interim safety and efficacy results from RAMP 205 to be presented at ASCO 2024</li> <li>✓ Initiated RAMP 205 combo avutometinib + gemcitabine/nab-paclitaxel + defactinib</li> </ul>	<ul style="list-style-type: none"> <li>✓ Received FDA Fast Track Designation for avutometinib in combination with Mirati's (BMS) G12C inhibitor adagrasib</li> <li>✓ Received FDA Fast Track Designation and for avutometinib plus defactinib with Amgen's G12C inhibitor sotorasib</li> <li>✓ Received FDA Fast Track Designation for avutometinib in combo with Amgen's G12C inhibitor sotorasib</li> <li>✓ Presented initial interim results from Phase 1/2 RAMP 203 trial of avutometinib + sotorasib</li> </ul>	<ul style="list-style-type: none"> <li>✓ Established development with GenFlee</li> <li>✓ Presented pre of GFH375/M potential best KRAS G12D inhibitor, at A</li> <li>✓ IND applicati China and acc in Q1'24</li> </ul>

THANK YOU

---

# Addendum



---

# Recurrent LGSOC: High Medical Need

No Approved Treatment Options – Limited Benefit from Available Therapies

## Recurrent Low-Grade Ovarian Cancer – Treatment Guidelines<sup>1</sup>

### RECURRENCE THERAPY<sup>f</sup>

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

No Category I recommendations (high-level evidence) or Category 2a (lower-level evidence with uniform N) unless otherwise indicated

<sup>f</sup>: There is no standard sequencing of drugs for recurrent disease. Considerations include prior therapies, drug efficacy, and relative toxicity profile.

<sup>t</sup>: An aromatase inhibitor (i.e., letrozole, anastrozole) is preferred if not used previously. Fulvestrant, tamoxifen, or toremifene is recommended if an aromatase inhibitor is not used.

#### Preferred Regimens

- Paclitaxel/carboplatin q3weeks<sup>f,9</sup> ± maintenance letrozole (category 2B) or other hormonal therapy (category 2B)<sup>11</sup>
- Paclitaxel/carboplatin/bevacizumab + maintenance bevacizumab<sup>1,1</sup> (ICON-7 & GOG-218)
- Hormone therapy (aromatase inhibitors: anastrozole, letrozole, exemestane) (category 2B)





# Avutometinib Patent Exclusivity

Composition of Matter

Feb 2027 + 5 yrs (PTE) = 2032

Method of Making

Sept 2032

Dosing Protocol

May 2038

Combination w/ Defactinib

Sept 2040

Solid Form

Dec 2042

Methods or Treating; Combinations

2041 - 2042 if iss

# Experienced Senior Management Team

**Daniel Paterson**  
President and Chief  
Executive Officer



Previous experience:

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

**Dan Calkins**  
Chief Financial  
Officer



Previous experience:

- Technical Accounting Consultant- CFGI
- PwC LLP

**Cathy Carew**  
Chief Organizational  
Effectiveness Officer



Previous experience:

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

**Mike Crowther**  
Chief Commercial and  
Business Strategy  
Officer



Previous experience:

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

**John Hayslip, M.D.**  
Chief Medical Officer



Previous experience:

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

**Jonathan Pachter  
Ph.D.**  
Chief Scientific Officer



Previous experience:

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