Delivering Novel Therapies for RAS/MAPK Pathway Driven Cancers

January 2025
Corporate Presentation

VERASTEM ONCOLOGY

Disclaimers

Forward-Looking Statements
This presentation includes forward-looking statements about, among other things, Verastem Oncology's (the "Company") programs and product candidates, strategy, future plans and prospects, including statements related to the scope and expecting timing for the FDA's review of the rolling New Drug Application (NDA) submission for the avutometinib and defactinib combination in LGSOC, the ongoing discussions with the FDA and the ability to obtain Accelerated Approval and Priority Review of the mature RAMP 201 data, the potential of the combination of avutometinib and defactinib to change the way patients with recurrent LGSOC are treated, the expected outcome and benefits of collaborations, including with GenFleet Therapeutics (Shanghai), Inc. (GenFleet), the status of enrollments for and potential of the results of the RAMP 301 Phase 3 trial to expand the indication regardless of KRAS mutation status, the structure of our planned and pending clinical trials, 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 timeline and indications for clinical development, regulatory submissions, the potential for and timing of commercialization of product candidates and potential for additional development programs involving the Company's lead compound and the potential market opportunities of, and estimated addressable markets for, our drug candidates. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," "can," "promising" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Each forward-looking statement is subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statement.

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

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

The forward-looking statements in this presentation speak only as of the original date of this presentation, and we undertake no obligation to update or revise any of these stateme nts whether as a result of new information, future events or otherwise, except as required by law.

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

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Verastem Oncology: Preparing to Commercialize First Novel RAS/MAPK/FAK Combo Asset with Billion-Dollar Addressable Market Opportunity

Transition to commercial-stage company in 2025 focused on RAS/MAPK-driven cancers

Avutometinib and defactinib combo has the potential to become the first and only FDA approved treatment for recurrent KRAS mutant Low-Grade Serous Ovarian Cancer (LGSOC)

FDA granted Priority Review with June 30, 2025, PDUFA Date

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

Discovery partnership with GenFleet Therapeutics on novel, potential best-in-class RAS pathway-related programs, including clinical stage KRAS G12D inhibitor, for **additional value creation**

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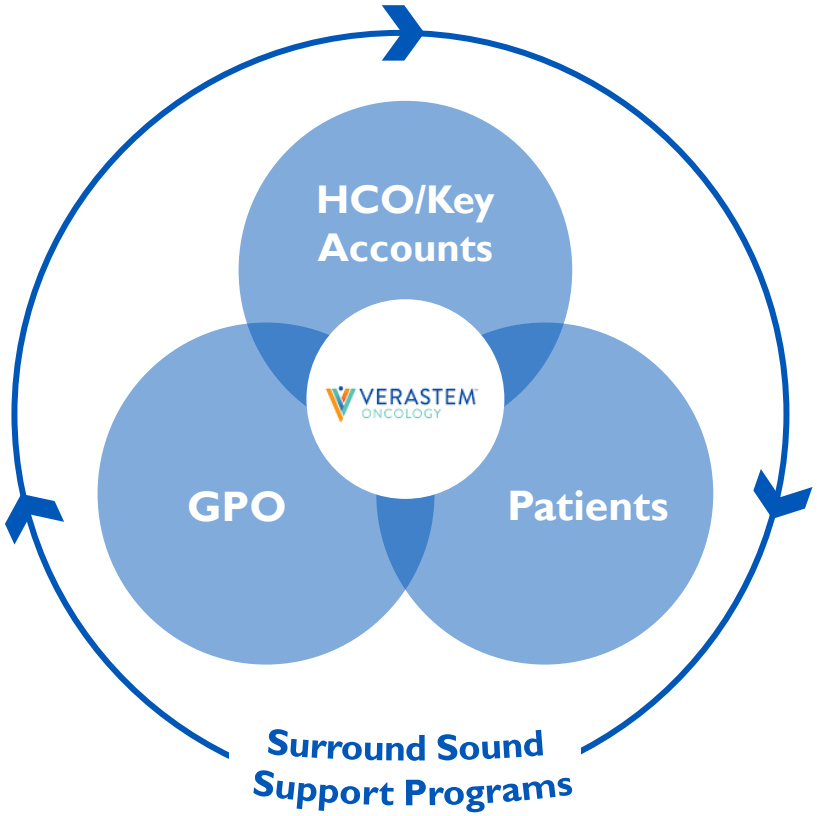
RAS: Rat Sarcoma; MAPK: Mitogen-activated protein kinases; FDA: Food and Drug Administration; LGSOC: Low-grade Serous Ovarian Cancer

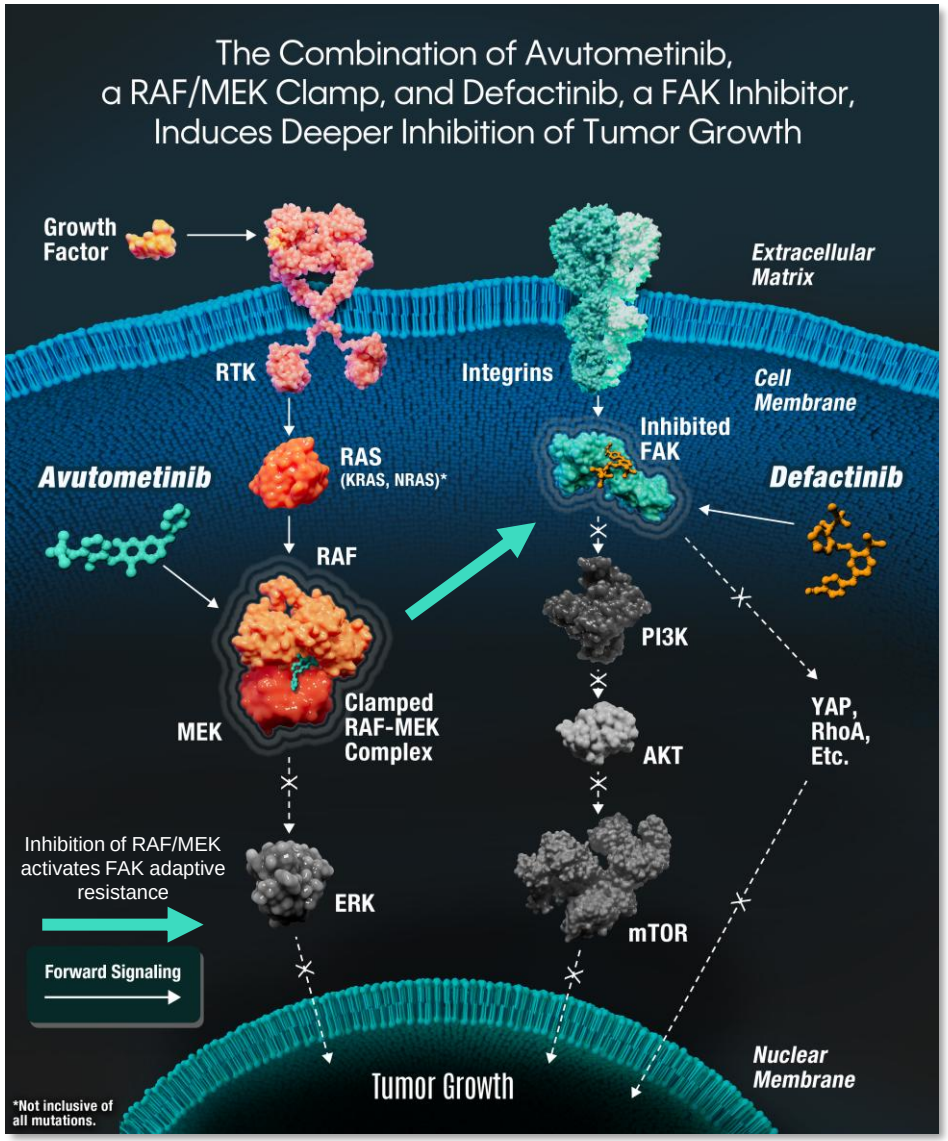
Efficiently Scaled Launch Model to Deliver Best-in-Class Launch for Recurrent KRAS mutant LGSOC in Mid-2025



Mid-year Launch June 30, 2025 PDUFA Date	Novel/novel combination being reviewed under the Accelerated Approval pathway with Priority Review
Potential New Standard of Care	Avutometinib plus defactinib is differentiated on multiple efficacy measures, favorable tolerability leading to relatively low rates of discontinuation due to AEs
Concentrated Launch Focus	Lean and focused field team for access, scientific exchange, and sales
Significant Market Opportunity	Anticipate high market penetration in recurrent KRAS mt LGSOC in both prevalent and newly recurrent population

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

- 70% of LGSOC tumors are driven by RAS/MAPK pathway-associated mutations[1-4]
  - 30% are KRAS mutant with other mutations including NRAS, BRAF, NF1, and other RAS pathway-associated gene mutations
- Avutometinib is an oral RAF/MEK clamp that potently inhibits MEK kinase activity while also blocking the compensatory reactivation of MEK by upstream RAF[5-7]
- FAK is activated in response to MAPK pathway inhibition by avutometinib as well as by RAF inhibitors and MEK-only inhibitors[8, 9]
- Defactinib is an oral selective FAK inhibitor that inhibits parallel pathway signaling and FAK inhibition has been demonstrated to enhance the antitumor efficacy of avutometinib both preclinically and clinically[10-12]
- Together, avutometinib and defactinib have the potential to offer more complete blockade of the signaling that drives the growth of RAS/MAPK pathway-dependent tumors with the objective of deeper and more durable responses



1 AACR Genie v16.1; 2 Cheasley et al., J Pathol 2021; 3 Thomson et al., Gynecol Oncol 2023; 4 Gershenson et al., Gynecol Oncol 2022; 5 Coma et al., AACR 2022; 6 Ishii et al., Cancer Res, 2013; 7 Lito et al., Cancer Cell, 2014; 8 Lubrano et al., AACR 2024; 9 Banerji et al., AACR 2020; 10 Jones et al., Invest New Drugs 2015; 11 McNamara et al., Gynecol Oncol 2024; 12 Banerjee et al., ASCO 2023

ERK; extracellular signal-regulated kinase; FAK, focal adhesion kinase; MAPK, mitogen-activated protein kinase; MEK, mitogen-activated extracellular signal-regulated kinase; mTOR, mammalian target of rapamycin; P, phosphate; PI3K, phosphatidylinositol 3-kinase; RAF, rapidly accelerated fibrosarcoma; RAS, rat sarcoma virus; RhoA, Ras homolog family member A; RTK, receptor tyrosine kinase; YAP, Yes-associated protein.

Clinical Program Designed to Address LGSOC and Beyond

Trial/Regimen	Discovery Phase	IND-Enabling/ Preclinical	Phase 1	Phase 2	Phase 3	Anticipated Milestones
Avutometinib + Defactinib: Recurrent LGSOC						
RAMP 301 RAF/MEK Clamp + FAKi vs ICT						Complete enrollment in RAMP 301 by end of 2025
RAMP 201 RAF/MEK Clamp + FAKi						PDUFA Action Date: June 30, 2025
Avutometinib ± Defactinib + Sotorasib (KRAS G12C Inhibitor): KRAS G12C NSCLC						
RAMP 203 RAF/MEK Clamp ± FAKi + KRAS G12Ci (sotorasib) Amgen Collaboration						An interim update is planned to be presented at a medical meeting in the second half of 2025
Avutometinib + Defactinib + Chemotherapy: 1L Metastatic Pancreatic Cancer						
RAMP 205 RAF/MEK Clamp + FAKi + gemcitabine, nab-paclitaxel PanCAN Collaboration						Expect to report updated safety and efficacy data in Q1 2025
GenFleet Collaboration of RAS/MAPK-Pathway Targeted Assets						
VS-7375/GFH375 KRAS G12D (ON/OFF) inhibitor						Anticipate filing U.S. IND during Q1 2025; Expect to initiate Phase 1/2a trial in U.S. in mid-2025; updated data from Phase 1 study in China expected in mid-2025
Undisclosed						
Undisclosed						

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

Avutometinib Plus Defactinib to Generate Near-Term Growth, while Pipeline Has Potential to Become Significant Driver for Long-Term Growth

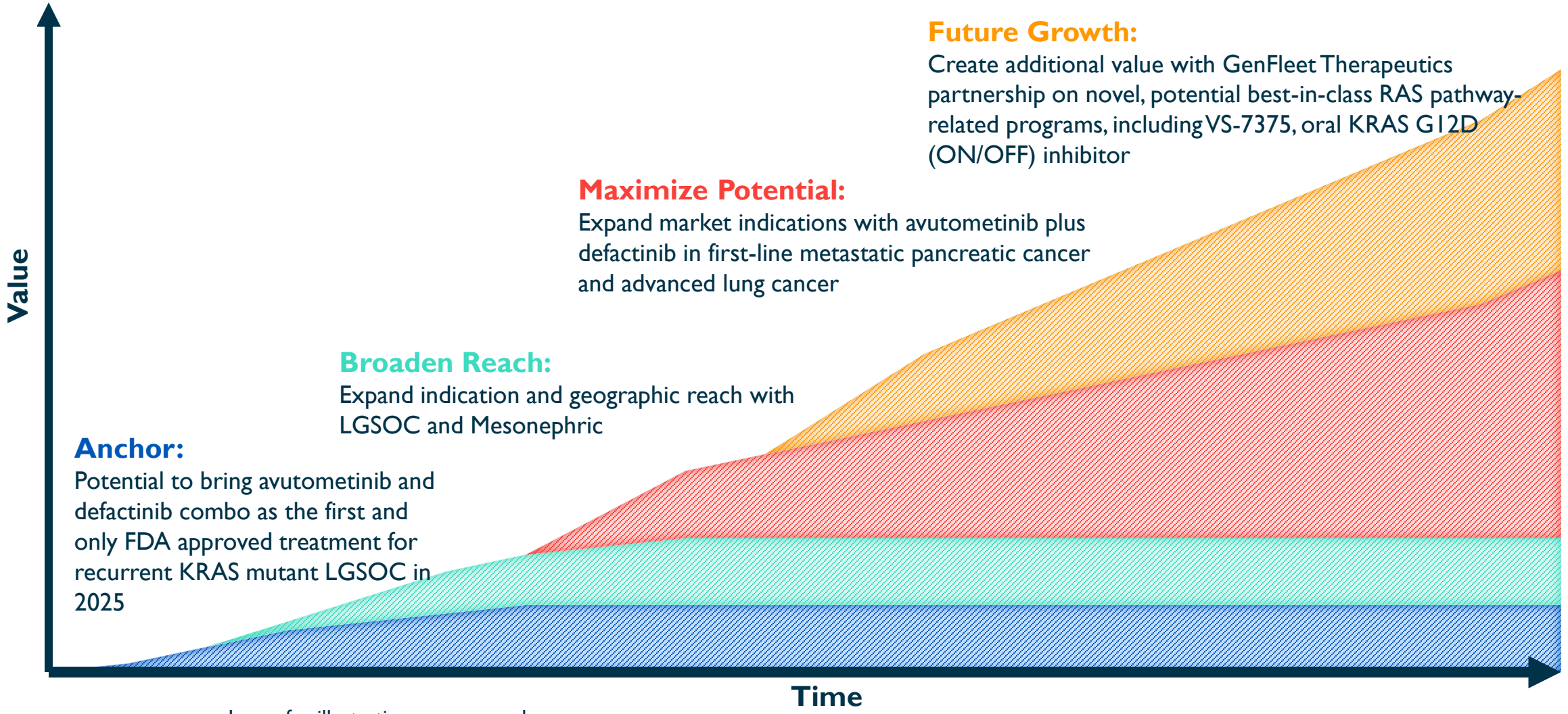

Image for illustrative purposes only.

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

Avutometinib and Defactinib in Recurrent Low-Grade Serous Ovarian Cancer (LGSOC)

PDUFA Action Date: June 30, 2025
Potential Launch in Recurrent KRAS mutant LGSOC in mid-2025

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Amanda, real patient living with recurrent LGSOC
Diagnosed at 26 with LGSOC

Verastem Aims to Deliver First FDA-Approved Treatment Specifically for Recurrent KRAS mutant LGSOC in mid-2025

Avutometinib + Defactinib Demonstrated Durable Results Across Various Efficacy Measures in Heavily Pretreated Patients in RAMP 201

- 31% Overall ORR, 44% in KRAS mt, 17% in KRAS wt
- 82% of all patients had tumor shrinkage
  - 14.5 months estimated mean DoT, 18.3 months in KRAS mt and 10.7 months in KRAS wt
- 12.9 months median PFS, 22 months in KRAS mt, 12.8 months in KRAS wt
- 10% discontinuation rates due to adverse events

Clear Regulatory Path for KRAS Mutant

- Under the Accelerated Approval pathway received Priority Review and June 30, 2025 PDUFA Action Date for recurrent KRAS mutant LGSOC
- RAMP 301 enrollment remains on track and will continue enrolling all comers
- Committed to make the combination available to patients with KRAS wild-type in several ways, including a path for regulatory approval

Significant Market Opportunity in Area of High Unmet Need

- SoC (Chemo/Hormonal) is associated with low response rates (6-13%) with PFS below 12 months and high discontinuation rates due to toxicity
- Plan to be launch ready in first-half of 2025 to maximize market opportunity in recurrent KRAS mutant LGSOC
- Plan to submit RAMP 201 for NCCN guideline review
- NCCN guideline inclusion may enable patients with KRAS wild-type LGSOC to access therapy, if FDA-approved

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The combination of Avutometinib and Defactinib is an investigational drug. It has not been proven to be safe or effective and has not been approved by FDA or any other comparable regulatory authority.

Source for all data: RAMP 201 data cut off as of June 30, 2024; LGSOC: Low-grade serous ovarian cancer; ORR: Objective Response Rate; KRAS, kirsten rat sarcoma virus; KRAS mt: mutant; KRAS wt: wild-type; PFS: Progression-free Survival; NDA: New Drug Application; SOC: Standard of Care; NCCN: National Comprehensive Cancer Network;

High Unmet Need for an Effective & Tolerable Therapy in Recurrent LGSOC

- **U.S. Incidence / Prevalence:** 1k-2k[1] / 6k-8k[2] / **Worldwide:** 80,000
- **70% of LGSOC tumors are driven by RAS/MAPK pathway-associated mutations[3-6]**
  - ~30% are KRAS mutant, with other mutations including NRAS, BRAF, NF1, and other RAS pathway-associated gene mutations
- Affects **younger population** (20-30s) and disproportionately **impacts health, fertility, and long-term quality of life[7,8]**
- **80%+ of patients will experience a recurrence[9]**
- **Disease currently managed by NCCN guidelines,** with no FDA approved treatments
- Current SoC **offer poor to moderate response rates** (6-13%) and patients cycle through therapy[10.11,12]
- **Median OS of ~10 years** from time of diagnosis[13]
  - KRAS mt – ~12 years[14] and KRAS wt – ~7 years[14]

"When you get told that you have a recurrence, the mental load is a lot. You're thinking, okay, what did I have to do for treatment the first time? Now I have to repeat that. And will there even be something available for me to take for a second, or a third recurrence?"

- Amanda, real patient living with recurrent LGSOC
Diagnosed at 26 with LGSOC

1.Verastem DOF; 2. US Cancer Statistics. Accessed 2024. 3. AACR Genie v16.1; 4. Cheasley et al., J Pathol 2021; 5 Thomson et al., Gynecol Oncol 2023; 6 Gershenson et al., Gynecol Oncol 2022;7. Slomovitz *Gynecol Oncol* 2020; 8. Manning-Geist B et al. Clin Cancer Res 2022;28(20):4456-4465; 9. Babaier 2022/p1/para1/ln6,7; 10. Gershenson Gynecol Oncol 2022; 11. Slomovitz *Gynecol Oncol* 2020; 12. Monk 2020/p3758/table2/footnote-b; 13. Banerjee SN). J Clin Oncol. 41. No 16_suppl (June 1, 2023) 5515-5515; 14. Manning-Geist B et al. Clin Cancer Res 2022;28(20):4456-4465; Calculated using figures in Gershenson Gynecol Oncol 2022.

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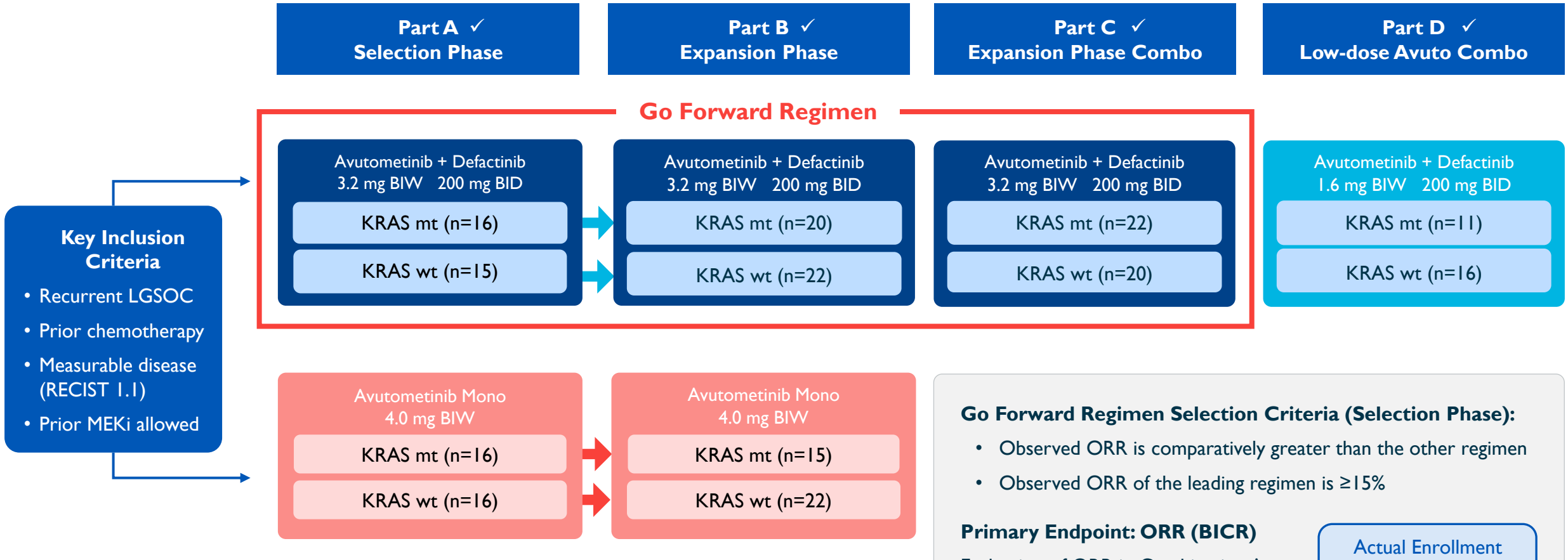
RAMP 201: Registration-Directed Phase 2 Trial of Avutometinib ± Defactinib in Patients with Recurrent LGSOC

RAMP 201 (ENGOT-ov60/GOG-3052)



Go Forward Regimen Selection Criteria (Selection Phase):

- Observed ORR is comparatively greater than the other regimen
- Observed ORR of the leading regimen is ≥15%

Primary Endpoint: ORR (BICR)

Evaluation of ORR in Combination Arm:

- In KRAS mt patients
- All patients (KRAS mt & wt)

Actual Enrollment at RP2D: **115 Treated Patients**

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Numbers represent patients treated on study. RECIST: Response Evaluation Criteria in Solid Tumors; MEKi: Mitogen-activated extracellular signal-regulated kinase inhibitor; BICR, blinded independent central review; BID, twice daily; BIW, twice weekly; RP2D: Recommended Phase 2 Dose

Avutometinib + Defactinib Demonstrate Durable Results in Efficacy Measures & Low Discontinuation Rates Due to AEs, Regardless of KRAS Status

Primary analysis of entire RAMP 201 dataset supports go-forward regimen as optimal dose

Avutometinib (3.2 mg BIW) + Defactinib (200 mg BID) Regimen
Parts A+B+C

ORR: 31% overall	**DOR at 6 months: 81% overall**	**Median PFS: 12.9 months overall**
44% in KRAS mt	87% in KRAS mt	22.0 months in KRAS mt
17% in KRAS wt	63% in KRAS wt	12.8 months in KRAS wt

- Patients with more prior regimens (>3) including prior bevacizumab and MEK-only therapy had lower response rates
- The combination was well tolerated allowing for prolonged exposure to therapy
- 10% discontinued due to adverse events

Monotherapy: Avutometinib (4.0 BIW)
Part A+B

- Protocol evaluated avutometinib 4 mg monotherapy vs avutometinib 3.2 mg + defactinib combination
- ORR: 17% overall
  - 23% in KRAS mt and 13% in KRAS wt
- Go-Forward Regimen demonstrated higher ORR
- TEAEs leading to D/C was 16%

Low-Dose: Avutometinib (1.6 mg BIW) + Defactinib (200 mg BID)
Part D

- Disease progression by 4 months 22% in Low-Dose Part D
  - Disease progression by 4 months 12% with Go-Forward Regimen
- TEAEs leading to discontinuation: 15%
  - Not lower than Go-Forward Regimen

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The combination of Avutometinib and Defactinib is an investigational drug. It has not been proven to be safe or effective and has not been approved by FDA or any other comparable regulatory authority.

Source for all data: RAMP 201 data cut off as of June 30, 2024; DOR: Duration of Response; TEAEs: treatment-emergent adverse events; AEs: adverse events

RAMP 201 Enrolled Heavily Pretreated Patients with a Median of 3 Prior Systemic Regimens

- Most patients received prior platinum-based chemotherapy and endocrine therapy
- 51% of all patients received prior bevacizumab and about 1 in 5 received prior MEK-only inhibitor therapy

RAMP 201: Parts A+B+C Baseline Patient Characteristics	Avutometinib + Defactinib Regimen 3.2 mg BIW + 200 mg BID 3 weeks on / 1 week off*		
	All patients N=115	**KRAS mt N=58**	**KRAS wt N=57**
Age (years), Median (min, max)	54 (21, 87)	60 (29, 87)	45 (21, 80)
ECOG PS, n (%)			
0	78 (68)	42 (72)	36 (63)
1	37 (32)	16 (28)	21 (37)
Median number of prior systemic regimens (min, max)	**3** (1, 9)	**3** (1, 9)	**3** (1, 9)
Prior platinum-based chemotherapy, n (%)*	114 (99)	58 (100)	56 (98)
Prior Hormonal therapy, n (%)	99 (86)	49 (84)	50 (88)
Prior Bevacizumab, n (%)	**59** (51)	**23** (40)	**36** (63)
Prior MEK inhibitor therapy, n (%)	**25** (22)	**12** (21)	**13** (23)

In the avutometinib + defactinib group: 77% of patients were White; 4% Asian; 4% Black or African American; 4% other; 11% not reported

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Source for all data: RAMP 201 data cut off as of June 30, 2024 *2 pts without prior platinum received anastrazole only (1 in the monotherapy and 1 in combination arm); ECOG PS, Eastern Cooperative Oncology Group performance status

Mature Data from RAMP 201 Continue to Show Robust Responses

- Overall: **31% ORR** in all evaluable patients
  - **44% ORR in KRAS mt** and **17% ORR in KRAS wt**

Response Rate: Parts A, B, and C	Avutometinib + Defactinib Regimen 3.2 mg BIW + 200 mg BID 3 weeks on / 1 week off		
	All patients N=109	**KRAS mt N=57**	**KRAS wt N=52**
Confirmed* ORR, n (%)	**34 (31)**	**25 (44)**	**9 (17)**
CR	2 (2)	2 (4)	0
PR	32 (29)	23 (40)	9 (17)
SD†, n (%)	62 (57)	28 (49)	34 (65)
PD, n (%)	9 (8)	2 (4)	7 (13)
Not Evaluable, n (%)	4 (4)	2 (4)	2 (4)

Efficacy evaluable population includes patients who received at least one dose of study drug and had measurable disease at baseline by BICR.
Patients not evaluable for response did not have a postbaseline assessment but are included in the denominator for the efficacy evaluable population.

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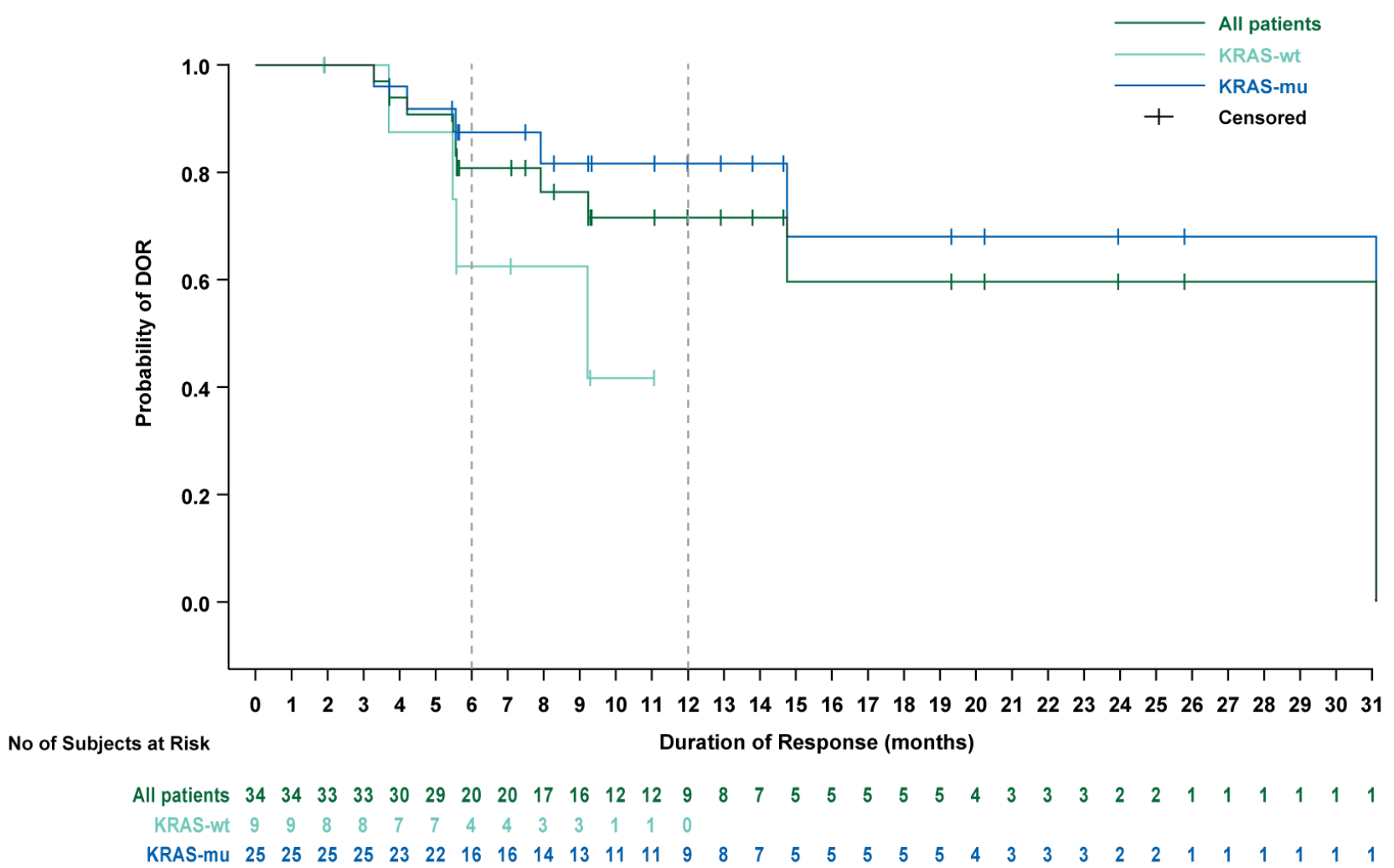
Source for all data: RAMP 201 data cut off as of June 30, 2024 ; * By RECIST 1.1 Objective Response by BICR: blinded independent central review 9primary endpoint); Includes Unconfirmed PR; SD (or unconfirmed PR) must occur at least 53 days after first dose date; ‡ PD, progressive disease; PR, partial response; SD, stable disease.

81% of Patients Achieved a Duration of Response of at Least 6 Months

Avutometinib + Defactinib Regimen: Duration of Response



3.7 MONTHS

Median time to response
(range, 1.7-19.2)

87%

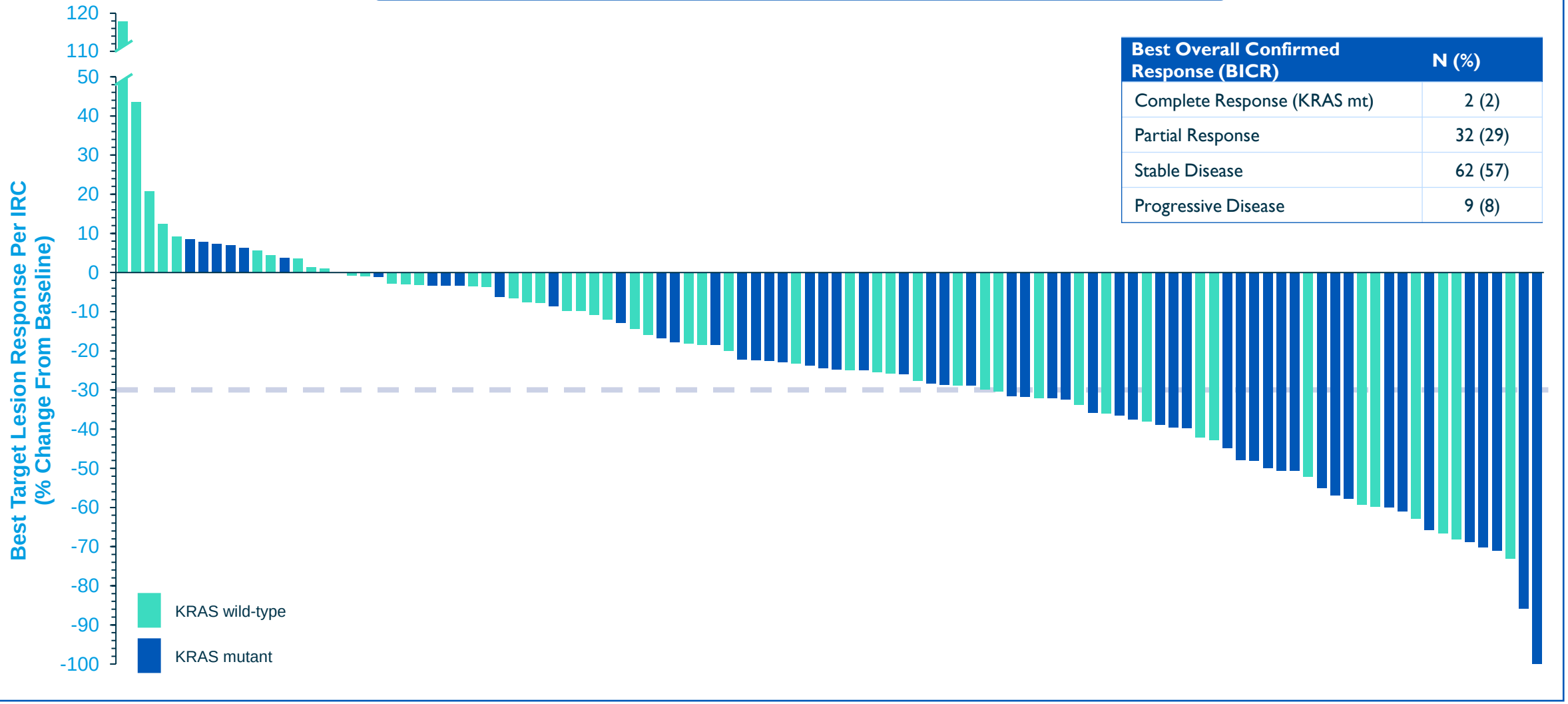
DOR for KRAS mt and
63% for KRAS wt at 6 months

	Avutometinib + Defactinib 3.2 mg BIW + 200 mg BID 3 weeks on / 1 week off		
	All Patients N=34	**KRAS mt N=25**	**KRAS wt N=9**
DOR (mo), median (range)	**31.1** (14.8, 31.1)	**31.1** (14.8, 31.1)	**9.2** (5.5, NE)
DOR >= 6 mo* (95% CI)	81% (62%, 91%)	87% (66%, 96%)	63% (23%, 86%)
DOR >= 12 mo* (95% CI)	72% (54%, 89%)	82% (65%, 98%)	NE

Source for all data: RAMP 201 data cut off as of June 30, 2024 ***KM estimates;** NE = Could not be estimated based on number of patients with loss of response.

82% of All Patients Had a Reduction in Target Lesions, Regardless of KRAS Status

Avutometinib + Defactinib Regimen: Best Overall Response



Best Overall Confirmed Response (BICR)	N (%)
Complete Response (KRAS mt)	2 (2)
Partial Response	32 (29)
Stable Disease	62 (57)
Progressive Disease	9 (8)

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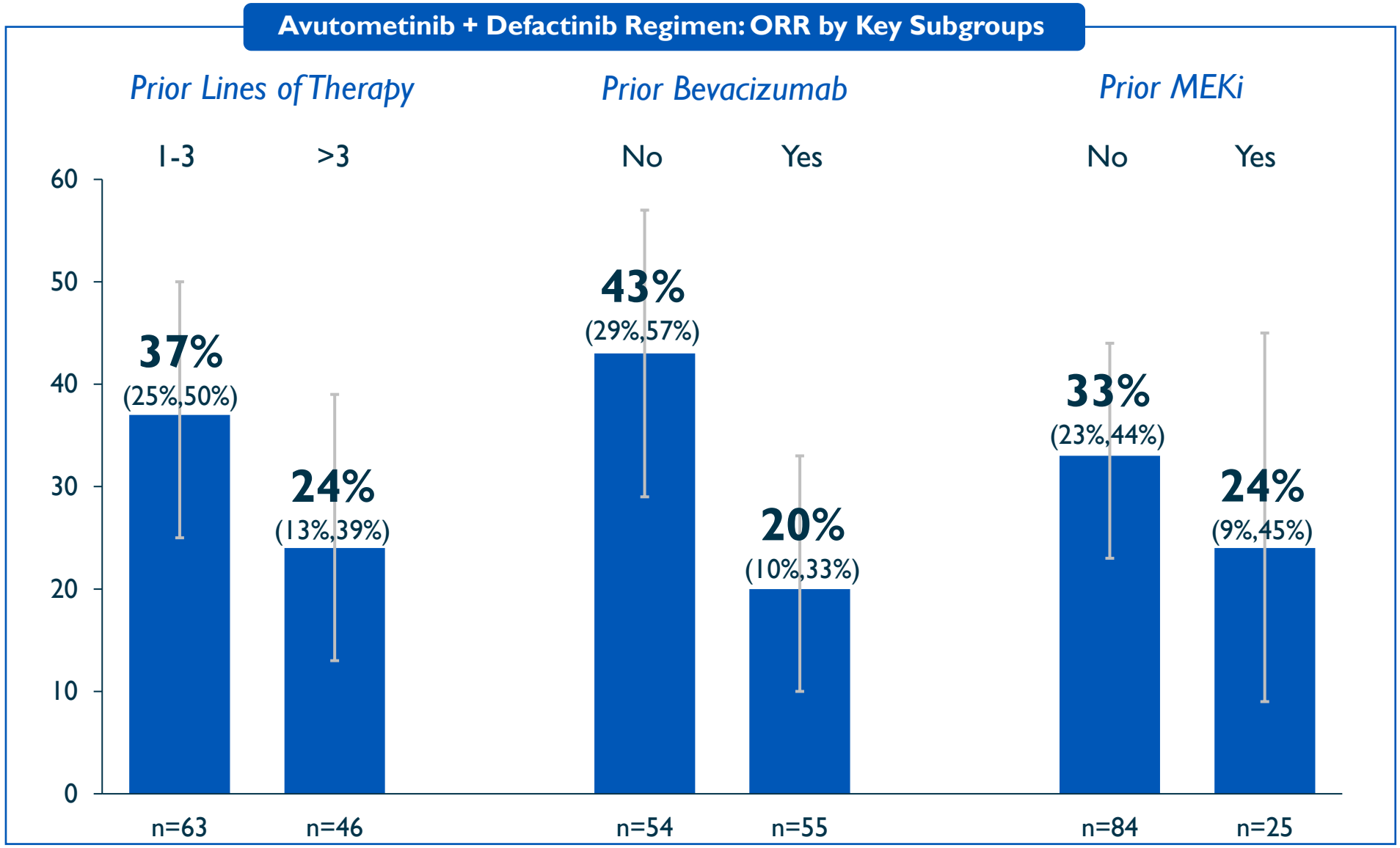
Source for all data: RAMP 201 data cut off as of June 30, 2024; Responses for 3 patients (KRAS wild type, n=1; KRAS mutant, n=2) were unknown. IRC, Independent Review Committee.

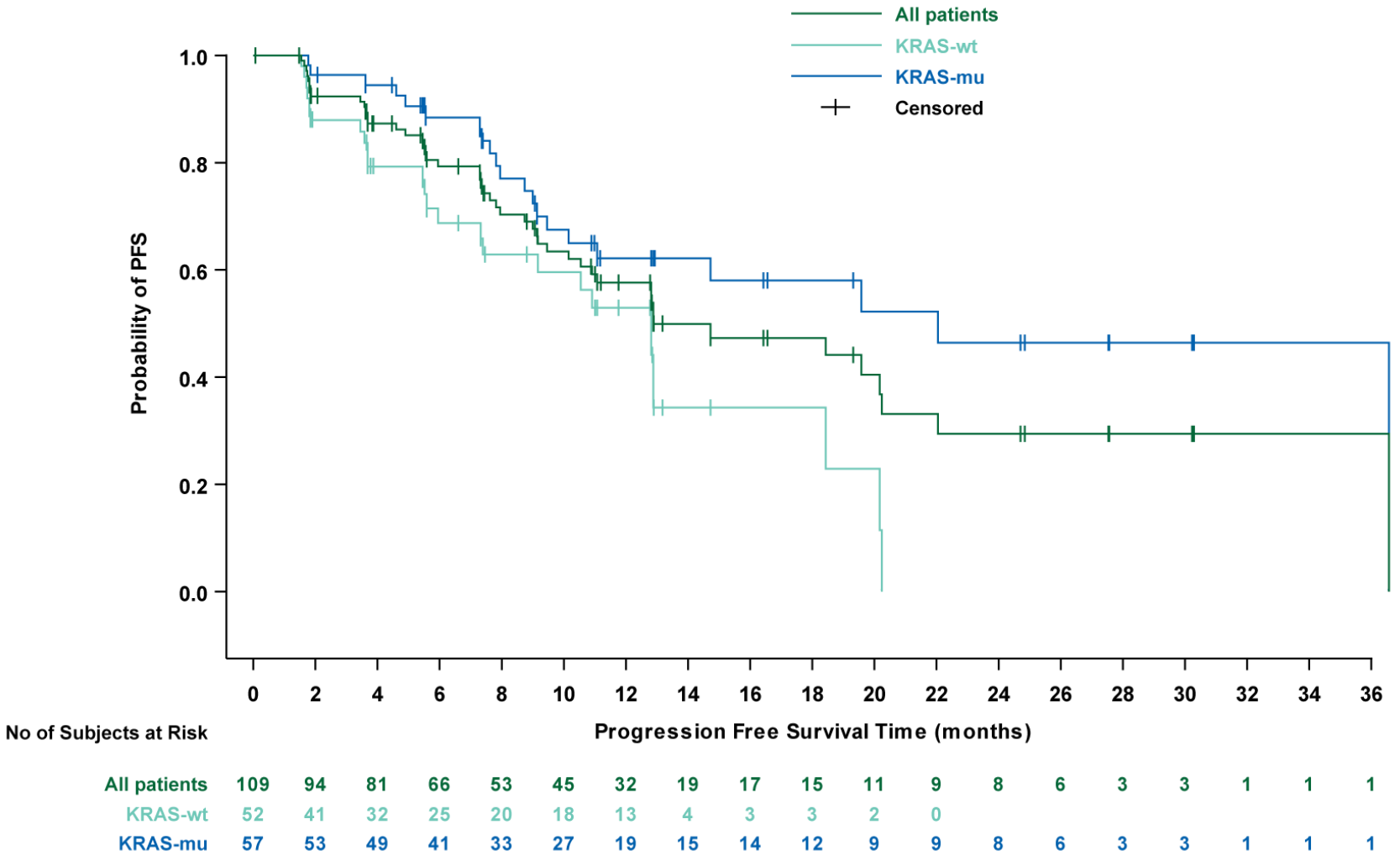
Receiving Avutometinib and Defactinib Earlier in the Course of Therapy was Associated with Higher Rates of Response



Source for all data: RAMP 201 data cut off as of June 30, 2024; Bars show 95% confidence intervals

Patients Achieved an Overall mPFS of 12.9 Months

Avutometinib + Defactinib Regimen: Progression Free Survival (PFS)



At 6 Months

79% OVERALL

88% in KRAS mt and
69% in KRAS wt

At 12 Months

58% OVERALL

62% in KRAS mt and
53% in KRAS wt

PFS, median (95% CI)

Total N=109	KRAS mt N=57	KRAS wt N=52
12.9 mos (10.9, 20.2)	22 mos (11.1, 36.6)	12.8 mos (7.4, 18.4)

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Source for all data: RAMP 201 data cut off as of June 30, 2024

Low Discontinuation Rate of 10% Due to Adverse Events, No New Safety Signals

	Avutometinib + Defactinib Regimen 3.2 mg BIW + 200 mg BID 3 weeks on / 1 week off		
	All patients	KRAS mt	KRAS wt
Patients Treated	115	58	57
Patients on Treatment, n (%)	32 (28)	24 (41)	8 (14)
Patients Discontinued Treatment, n (%)	83 (72)	34 (59)	49 (86)
Primary Reason for Discontinuation			
RECIST v1.1 Disease Progression	46 (40)	18 (31)	28 (49)
Adverse Event/Unacceptable Toxicity	12 (10)	4 (7)	8 (14)
Withdrawal of Informed Consent	10 (9)	4 (7)	6 (11)
Other*	10 (9)	5 (9)	5 (9)
Clinical Deterioration	5 (4)	3 (5)	2 (4)
Death	0	0	0

Median follow-up = 13.6 mo (range, 1.4 – 39.5)

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Source for all data: RAMP 201 data cut off as of June 30, 2024; *Other includes: clinical progression (n=8) and progression confirmed by biopsy/pathology report, progression by confirmation of cytology from pleural effusion showing malignant etiology, debulking surgery, patient noncompliance, patient withdrawal with agreement to follow-up, physician decision (1 each).;

Avutometinib Plus Defactinib Continue to Demonstrate a Well-Tolerated Safety Profile

Treatment-Related Adverse Events (>20% of patients)* n (%)	Avutometinib + Defactinib Regimen 3.2 mg BIW + 200 mg BID 3 weeks on/1 week off N= 115	
Preferred term	**All Grades**	**Grade ≥3**
Non-laboratory AEs		
Nausea	77 (67.0)	3 (2.6)
Diarrhea	67 (58.3)	9 (7.8)
Oedema peripheral	61 (53.0)	1 (0.9)
Fatigue	50 (43.5)	3 (2.6)
Vomiting	49 (42.6)	3 (2.6)
Vision blurred	47 (40.9)	0
Rash	41 (35.7)	2 (1.7)
Dermatitis acneiform	39 (33.9)	5 (4.3)
Dry skin	30 (26.1)	0
Anemia	26 (22.6)	6 (5.2)
Laboratory-related AEs		
Increased blood CPK	69 (60.0)	28 (24.3)
Increased blood bilirubin increased/ hyperbilirubinemia	38 (33.0)	5 (4.3)
AST increased	36 (31.3)	2 (1.7)

Severe adverse events are generally uncommon and typically managed by a treatment pause

10% (12/115) discontinued for AEs (any cause); most common increased CPK (n=4)

80% (92/115) had AEs leading to dose interruption

- 38% (44/115) for elevations in CPK

36.5% (42/115) had AEs leading to dose reduction

- Mean relative dose intensity of 0.84 for avutometinib and 0.77 for defactinib

7% (8/115) of patients had serious AEs considered by the investigator to be related to study treatment: the only event occurring in more than 1 patient was abdominal pain

4 deaths (within 30 days of discontinuation) but were not considered related to the study treatment:

- GI hemorrhage, large intestine perforation, clinical progression, clinical deterioration

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Source for all data: RAMP 201 data cut off as of June 30, 2024; *Most common adverse events (preferred term) considered by the investigator to be related to study drug (either avutometinib or defactinib); AE, adverse event; AST; aspartate aminotransferase; CPK, creatine phosphokinase; GI, gastrointestinal.

RAMP 301: First Randomized Prospective Study to Fully Characterize KRAS Status of all Enrolled LGSOC Patients

RAMP 301:
Phase 3 International Confirmatory Trial

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

Enrollment is on track, targeting full enrollment by end of 2025

Changing the Treatment Paradigm in Recurrent LGSOC

PDUFA Action Date: June 30, 2025
Potential Launch in Recurrent KRAS mutant LGSOC in mid-2025

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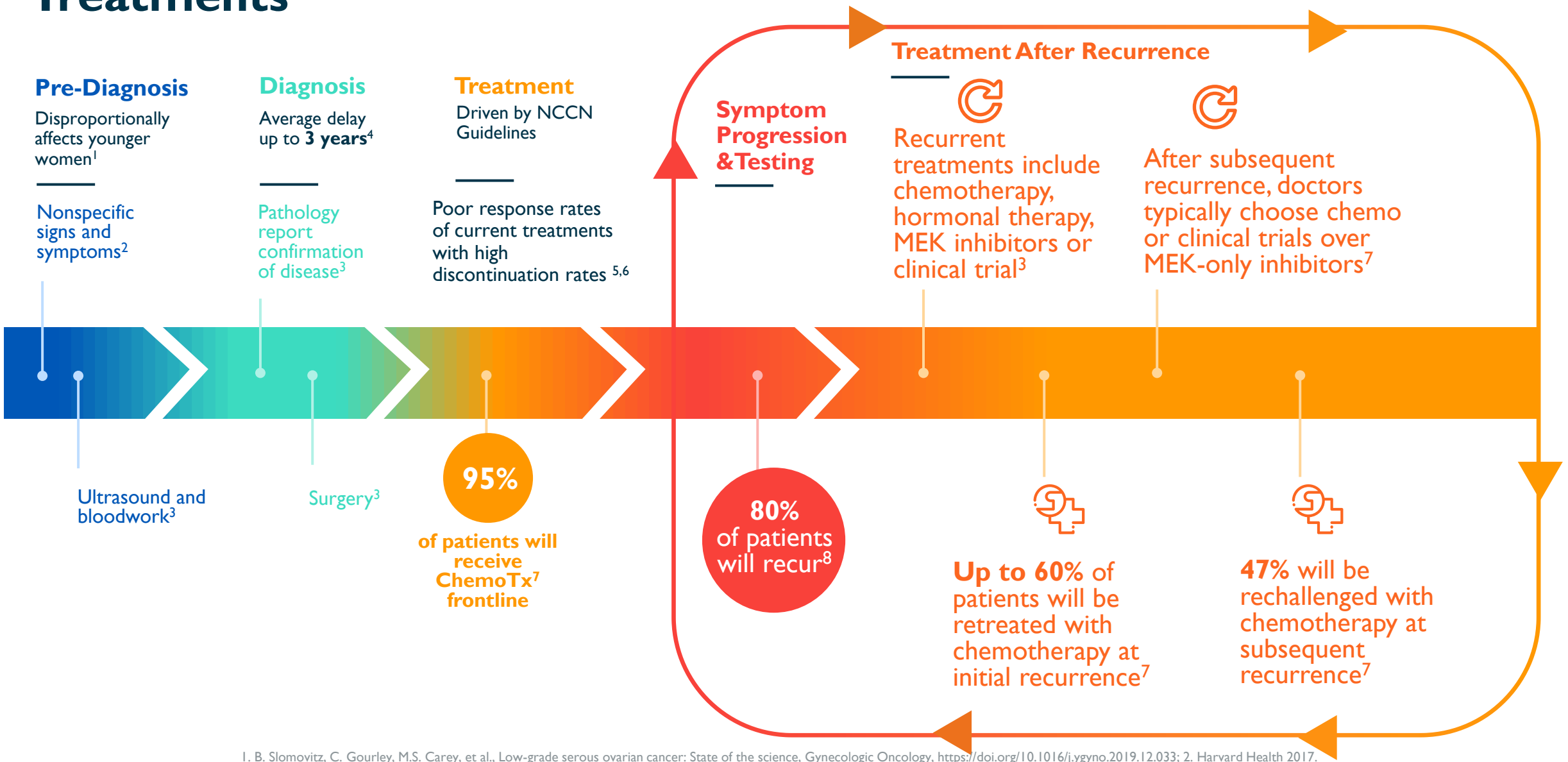
80% of Patients with LGSOC Recur and Often Cycle Through Treatments



1. B. Slomovitz, C. Gourley, M.S. Carey, et al., Low-grade serous ovarian cancer: State of the science, Gynecologic Oncology, https://doi.org/10.1016/j.ygyno.2019.12.033; 2. Harvard Health 2017. https://www.health.harvard.edu/cancer/certain-symptoms-may-be-early-signs-of-ovarian-cancer. Assessed October 8, 2024; 3. NCCN Clinical Practice Guidelines in Oncology: (NCCN Guidelines®) for Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer V. 3.2024; 4. LGSOC Patient Impact Survey Research Findings, Harris Poll 2023. https://www.businesswire.com/news/home/20231107926726/en/; 5. Monk BJ et al. J Clin Oncol 2020 (MILO); 6. Gershenson DM et al. Lancet 2022 (GOG 281); 7. Verastem DOF. Demand Study March 2024.\; 8. Gershenson et al J Clin Oncol 2015.

Current Available Therapies Offer Relatively Poor Response Rates, High Discontinuation Rates

- These studies started in 2013 and 2014
- Both MILO and GOG studies had low historical use of bevacizumab during trial conduct; % not reported
- Mutation category is KRAS/BRAF/NRAS rather than just KRAS for GOG 281
  - In both studies, not all patients had mutation status available
- In the MILO study no more than 3 lines of prior chemotherapy
- No prior MEK inhibitors were allowed in either GOG 281 or MILO
- The number of prior systemic therapies median (range) were 2 (1-10) in GOG 281 and 2 (1-8) in MILO

Trial	Therapy	Image assessment	Response Rate ORR	ORR KRAS mt	ORR KRAS wt	Median PFS Months (95% CI)	mPFS KRAS mt	mPFS KRAS wt	Discontinuation Rate due to AEs
GOG 281[1]	**SoC** (n=130) (n=22 KRAS/NRAS/ BRAF mt; n=42 KRAS/NRAS/ BRAF wt)	INV	**6%** 95% CI: (3%, 12%)	**9.1%,** 95% CI: (1.9%, 26.1%)	**7.1%,** 95% CI: (2.1%, 17.9%)	**7.2** (5.6-9.9)	**11.4** 95% CI: (3.7, 13.3)	**6.3** 95% CI: (3.7, 9.9)	**30%**
	Trametinib (n=130) (n=22 KRAS/NRAS/ BRAF mt; n=42 KRAS/NRAS/ BRAF wt)	INV	**26%** 95% CI: (19%, 35%)	**50%,** 95% CI: (30.2%, 69.8%)	**8.3%,** 95% CI: (2.9%, 18.6%)	**13.0** (9.9-15.0)	**13.2** 95% CI: (9.4, 20.8)	**7.3** 95% CI: (5.6, 12.7)	**36%**
MILO[2]	**SoC** (n=101) (n=24 KRAS mt; n=42 KRAS wt)	BICR	**13%** 95% CI: (7%, 21%)	**33%,** 95% CI: (16%, 55%)	**19%** (8.6%, 34%)	**10.6** (9.2 - 14.5)	**14.6** (9.4, NA)	**11.5** (5.7, 26.6)	**17%**
	Binimetinib[2] (n=198) (n=45 KRAS mt; n=90 KRAS wt)	BICR	**16%** 95% CI: (11%, 22%)	**44%,** 95% CI: (30%, 60%)	**19%,** 95% CI: (11%, 29%)	**9.1** (7.3-11.3)	**17.7** (12, NR)	**10.8** (5.5, 16.7)	**31%**

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[1]Study GOG 281 trial Gershenson et al., Lancet 2022; [2]MILO Study. Grisham et al Clinical Cancer Research 2023, [3]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 Combo Has the Potential to Address Key Treatment Needs

To date, avutometinib + defactinib combination data in recurrent LGSOC show[1]:

- Clinically meaningful response rates and durable benefit in both KRAS mutant and wild-type tumors
- Long progression-free survival and duration of treatment
- Favorable tolerability profile, supported by novel intermittent dosing schedule, with oral treatments[2]
- Low discontinuation rates due to adverse events

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[1]Data from RAMP 201 study June 30. 2024 cutoff; [2]Chenard-Poirier, et al. ASCO 2017; References: Banerji, Q4 2020 report

LGSOC Represents a Significant Market Opportunity

Total Addressable Market Opportunity	KRAS mutant – Initial Launch	KRAS wild-type
Estimated Annual **Incident** Addressable Opportunity[1]	**$300M+**	**$374M+**
Incident Population[2]	~500	~1,000
Avg. Duration of Therapy[3]	18 months	11 months
Estimated **Prevalent** Addressable Opportunity[1] *(Target to Address in First 3-5 Years)*	**$1.7B+**	**$1.6B+**
Prevalent Population[2]	~2,800	~4,200
Avg. Duration of Therapy[3]	18 months	11 months

Anticipate high market penetration in LGSOC KRAS mt population given:

- No FDA approved therapies for LGSOC

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

- Patients cycle through therapies
  - Median of 3 prior therapies in RAMP 201
- Long overall survival in LGSOC patients at ~10 years
  - KRAS mt – ~12 years
  - KRAS wt – ~7 years

1. Estimated total addressable market opportunity based on incident / prevalent populations, average duration of therapy (as observed in VSTM clinical trials) and cost of therapy of $34,000 per month, consistent with other recent oncology drug launches (e.g. OJEMDA - $33,916 OGSIVEO - $29,000; www.dayonebio.com/wp-content/uploads/Ojemda-Connecticut_VF.pdf; www.hhs.texas.gov/sites/default/files/documents/apr-2024-durb-agenda-item8d.pdf) 2. Verastem DOF – Based on 30% KRAS mt and 70% KRAS wt in incident population assumed of 1,500 annually and 40% KRAS mt and 60% KRAS wt (calculation on file based on weighted average longer overall survival in KRAS mt compared to KRAS wt) initial prevalent population of 7,000; 3. RAMP 201 data cutoff as of June 30, 2024

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Current Treatments on NCCN Guidelines

- Plan to submit RAMP 201, inclusive of entire patient population, for publication and NCCN consideration
- There are no FDA-approved treatments and no standard sequencing of drugs for recurrent disease

	NCCN Category 1	NCCN Category 2a	NCCN Category 2b	NCCN Category 3
General % Commercial Payer Coverage				
Recurrent LGSOC Treatment NCCN Recommendations and Contemporary Clinical Data in LGSOC	**No category 1 recommendation**	**Hormonal therapy (e.g., Anastrozole, Letrozole) & chemotherapy** • 6-13% ORR and 17-30% discontinuation rate due to AEs • Based on GOG 281 and MILO studies **Trametinib** (2-4% U.S, utilization rate[1]) • 13 months PFS, 95% CI: (9.9-15.0) vs SoC • 26% ORR based on INV assessment of comparator arm of all patients not BICR • 36% discontinuation rate due to AEs • Based on GOG 281[2]	**Binimetinib** • Study stopped due to futility • PFS 12.5 vs 11.6 (HR 0.87) • 16% ORR based on BICR of comparator arm and 31% discontinuation rate due to AEs • Based on MILO study[3]	

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

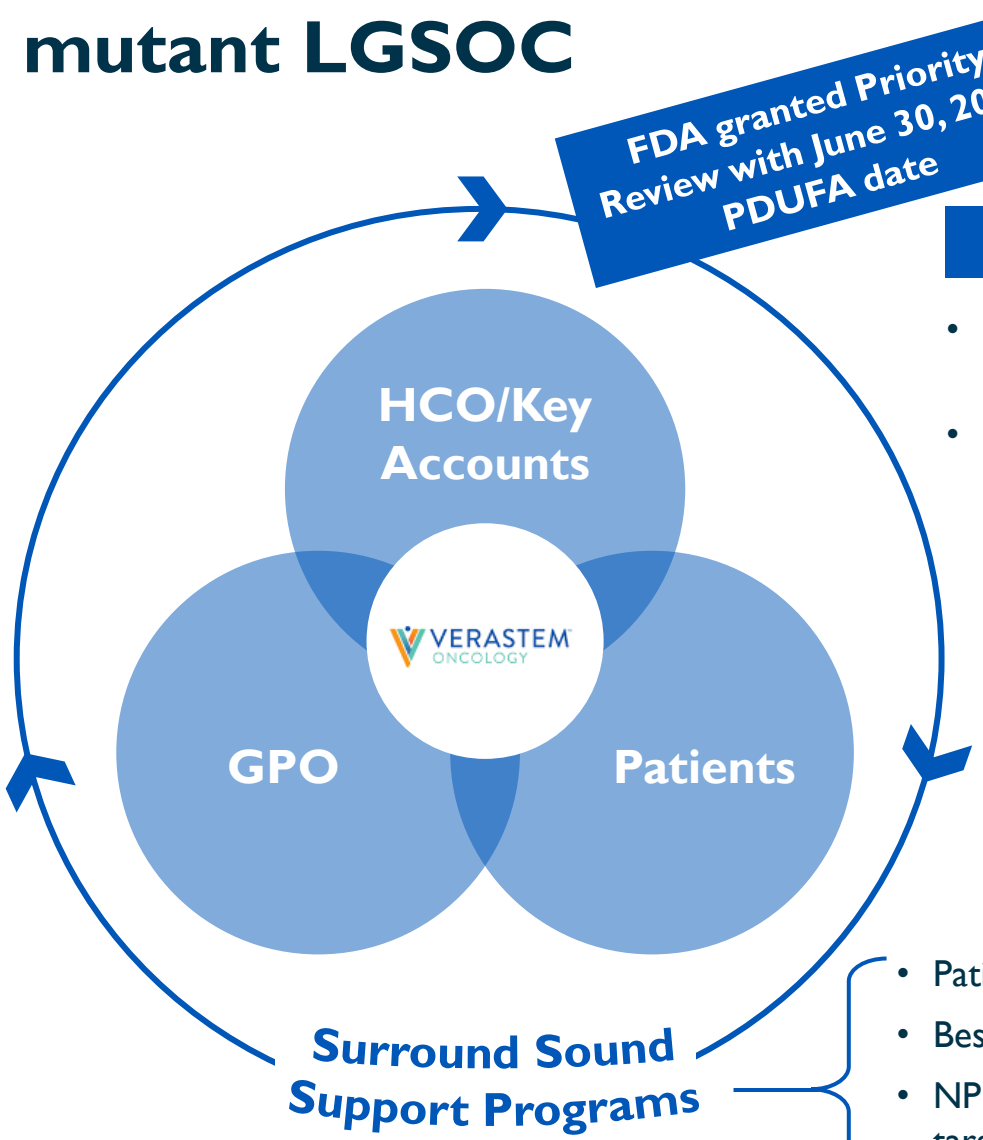
Efficiently Scaled Launch Model to Deliver Best-in-Class Launch for Recurrent KRAS mutant LGSOC

HCO/Key Account Focus

- Top 100 commercial HCOs contribute 49.4% of patient claims[1]
- ~400 HCPs manage these patients[1]
- Deploy lean, focused field sales team (~14-18 reps) for access and scientific exchange

GPO/Large Affiliated Practices

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



Patient Focused

- More than 2,500 patients have registered on disease education website[2]
- Robust program for ongoing education and resources

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

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

Potential to Change Treat Paradigm and Improve Patient Outcomes

1k-2k incidence with a prevalence of 6k-8k; **potential for high market penetration in KRAS mutant** at launch enriching overtime with the prevalent patient population

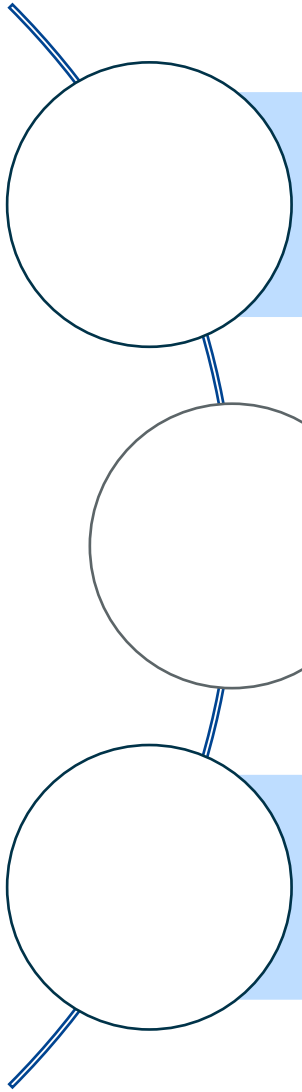
Current available therapies offer limited efficacy, relatively high discontinuation rates due to AEs; **no FDA-approved therapies and no active promotion**

NCCN guidelines help to drive treatment decision; will submit entire RAMP 201 dataset for NCCN consideration

Avutometinib in combination with defactinib is differentiated on multiple efficacy measures, relatively low rates of discontinuation due to AEs and favorable tolerability

Efficiently scaled launch model to deliver best-in-class launch for recurrent KRAS mutant LGSOC

Next Steps in LGSOC Clinical Program and NDA



FDA decision: June 30, 2025, PDUFA action date

Publish RAMP 201 primary analysis for all patients and then submit for NCCN consideration

Complete enrollment in RAMP 301 Phase 3 confirmatory study by end of 2025

Avutometinib ± Defactinib

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

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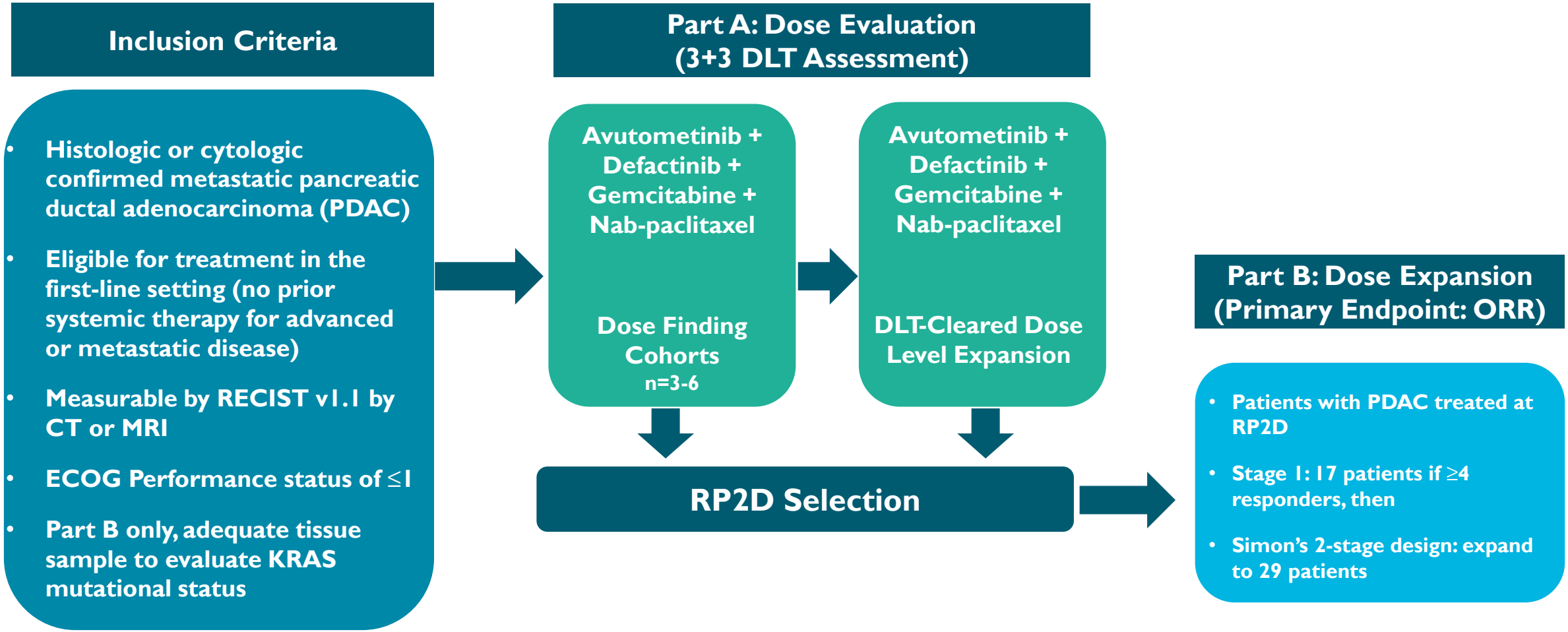
Topline Data from RAMP 205: Avutometinib + Defactinib + SOC in First-Line Metastatic Pancreatic Cancer

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

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



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

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

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

Landmark Trials in First-Line Metastatic Pancreatic Cancer

SOC Treatment Landscape:

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

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

For Reference only: No cross-trial comparison made.*Dosing schedule in Gem/NabP arms above= 1000/125(mg/m^2) D1,8,15 q 4w, **Secondary endpoint of ORR based on IRR (Independent Radiology Review),

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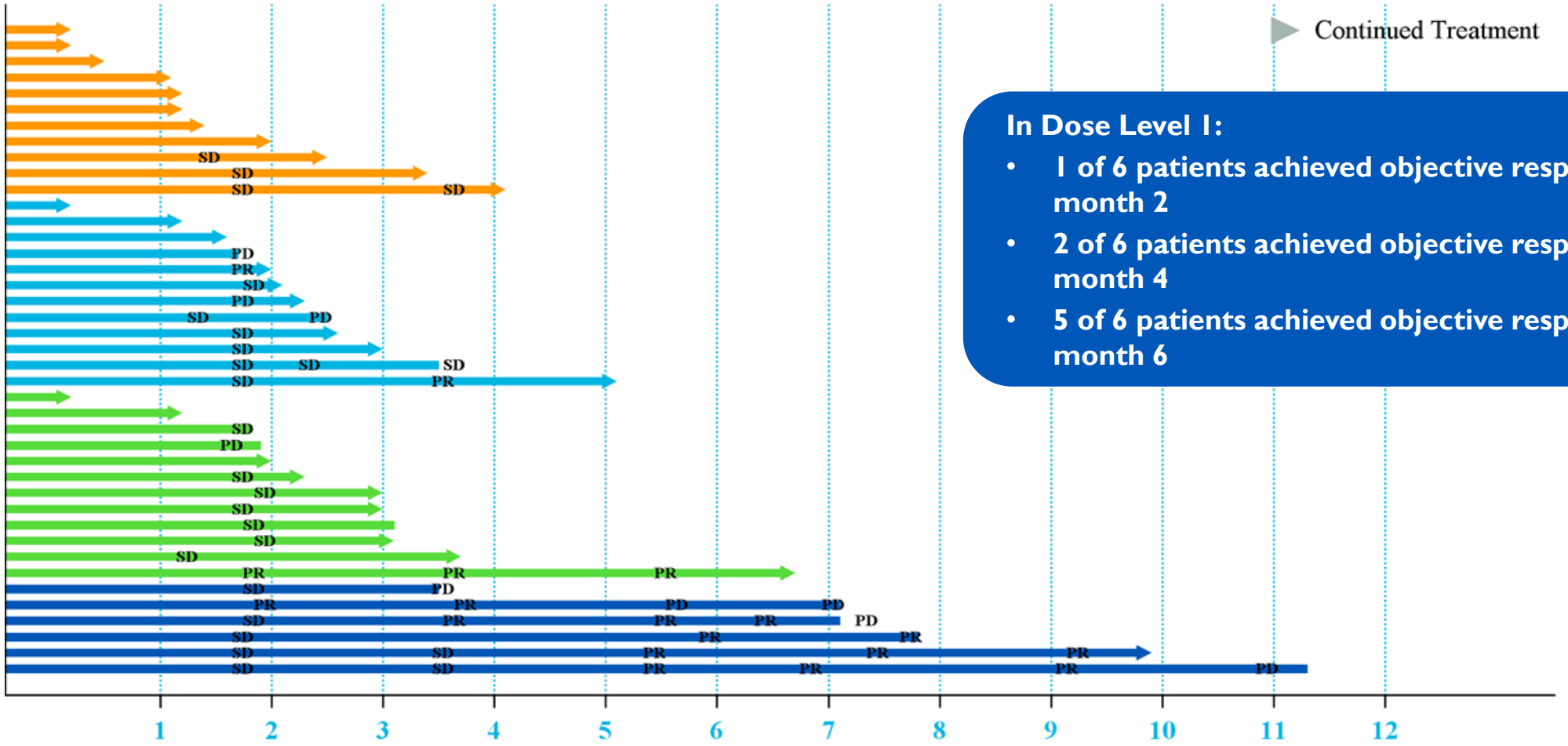
RAMP 205: Evaluating Multiple Regimens in Parallel to Efficiently Identify RP2D in First-Line mPC

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

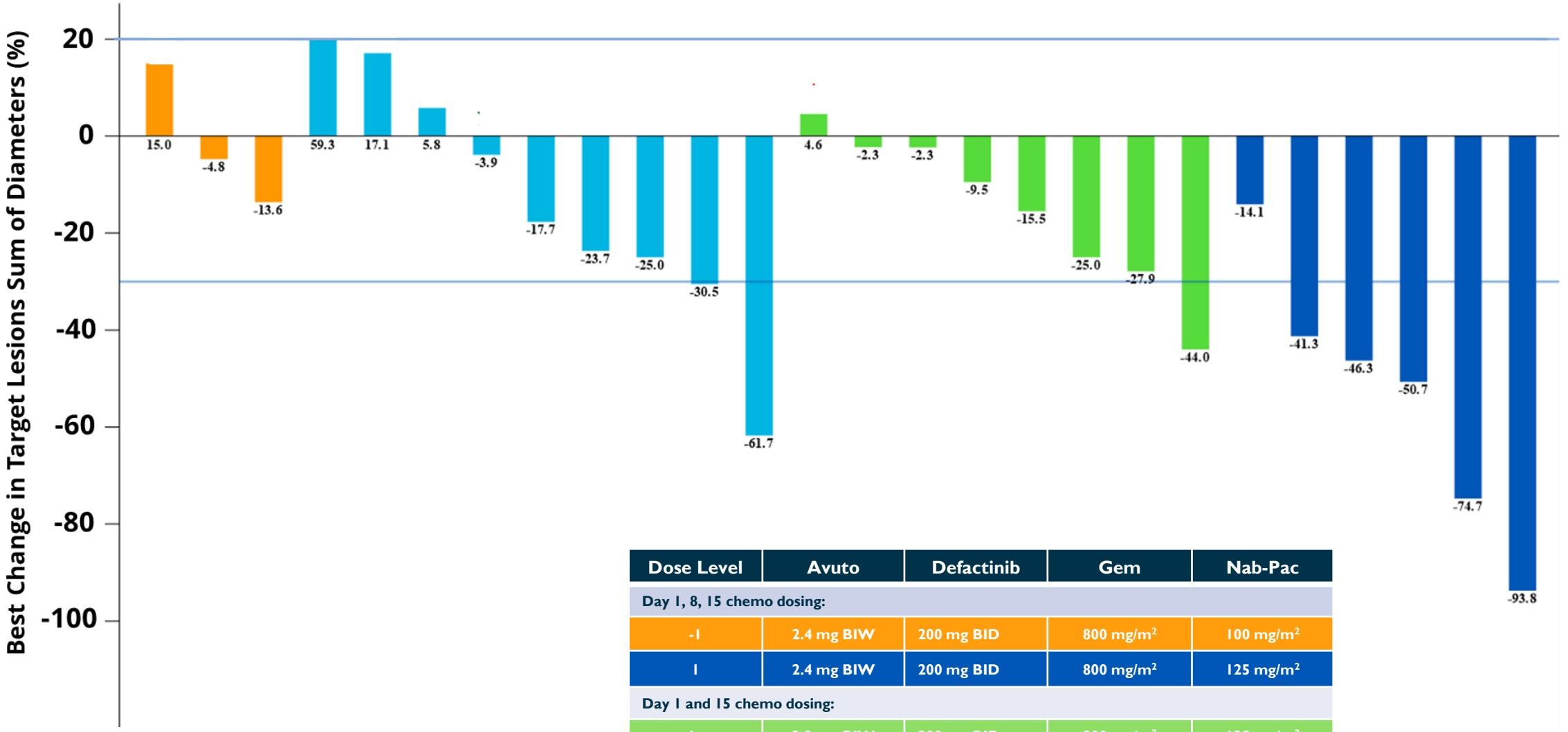


In Dose Level 1:

- 1 of 6 patients achieved objective response by month 2
- 2 of 6 patients achieved objective response by month 4
- 5 of 6 patients achieved objective response by month 6

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

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



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

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Data Cutoff Date:14 MAY 2024

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

- Any grade TEAEs occurring in ≥20% or grade ≥3 occurring in ≥5% of patients[1]

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

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

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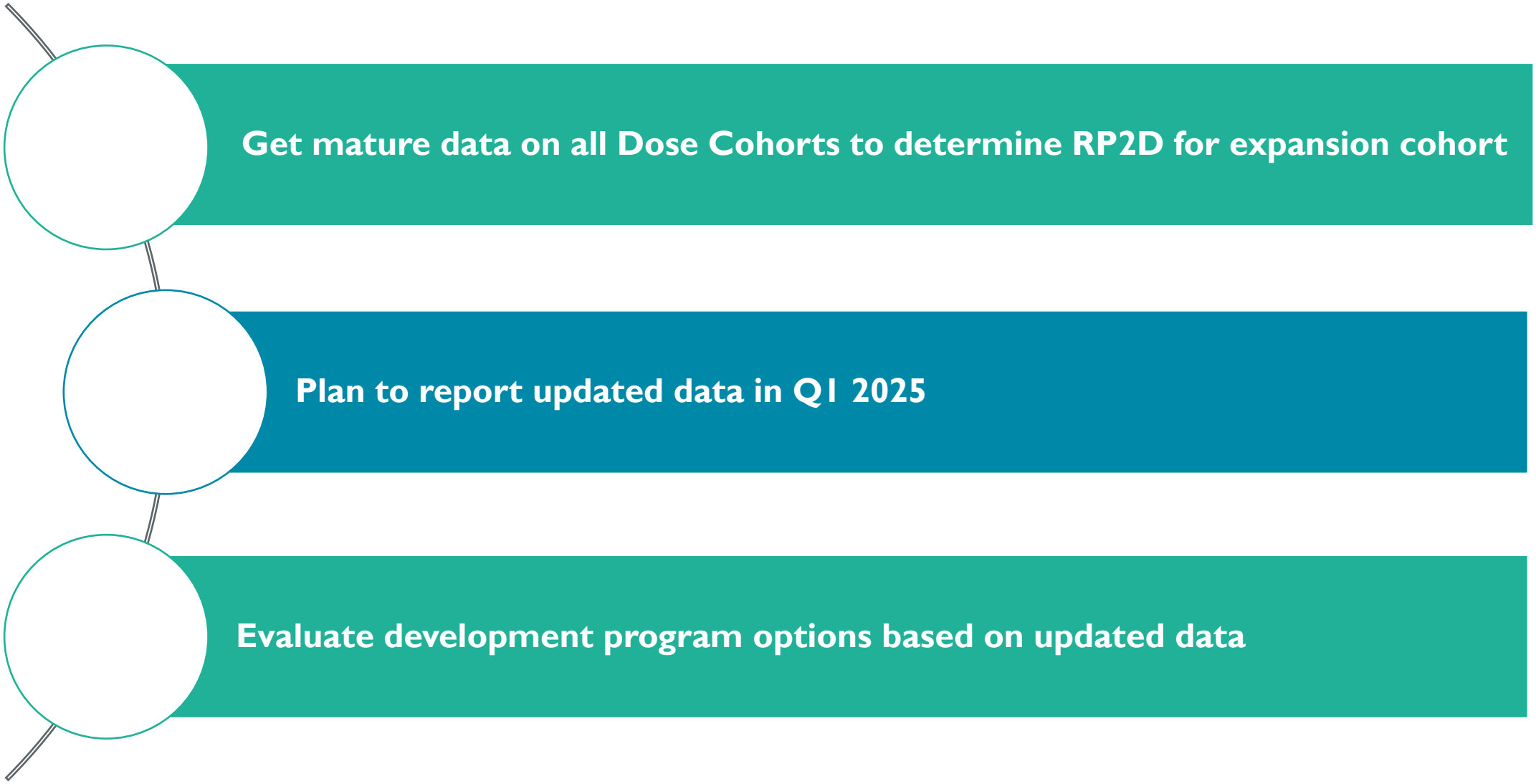
No head-to-head clinical trials have been conducted between avutometinib and defactinib combination and gemcitabine and Nab-paclitaxel.

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

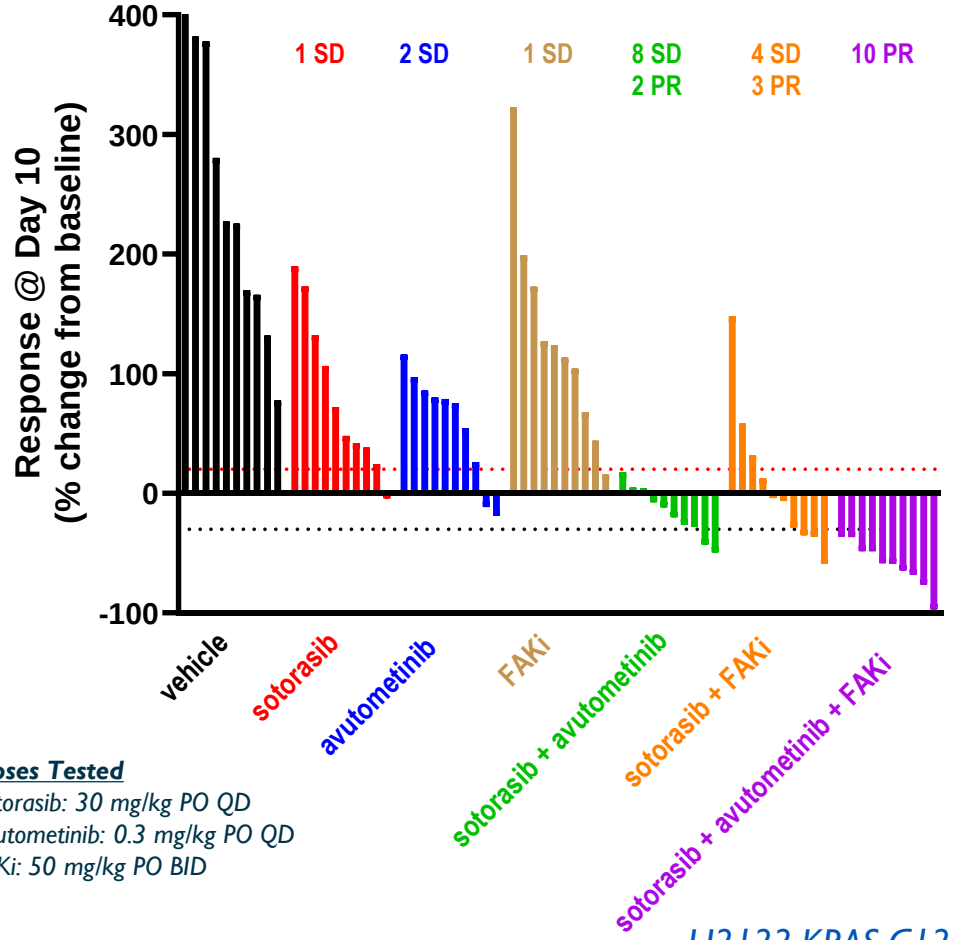
Next Steps for RAMP 205



Avutometinib ± Defactinib with Sotorasib (G12Ci) in KRAS G12C mutant NSCLC

Addition of FAK inhibitor Augments the Efficacy of Sotorasib + Avutometinib and Reverses Sotorasib Resistance in KRAS G12C NSCLC Preclinical Models

Avutometinib enhances sotorasib efficacy. Addition of FAK inhibitor induces deep tumor regressions in all treated mice

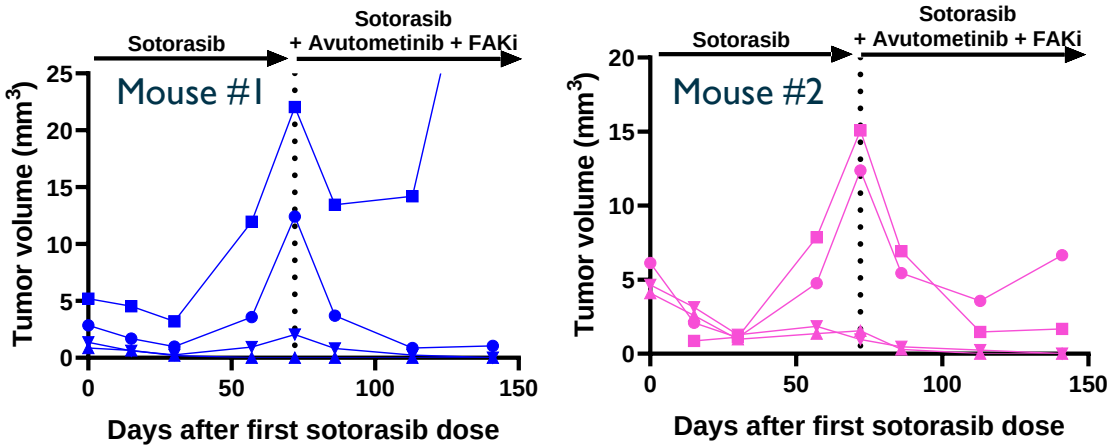


Doses Tested

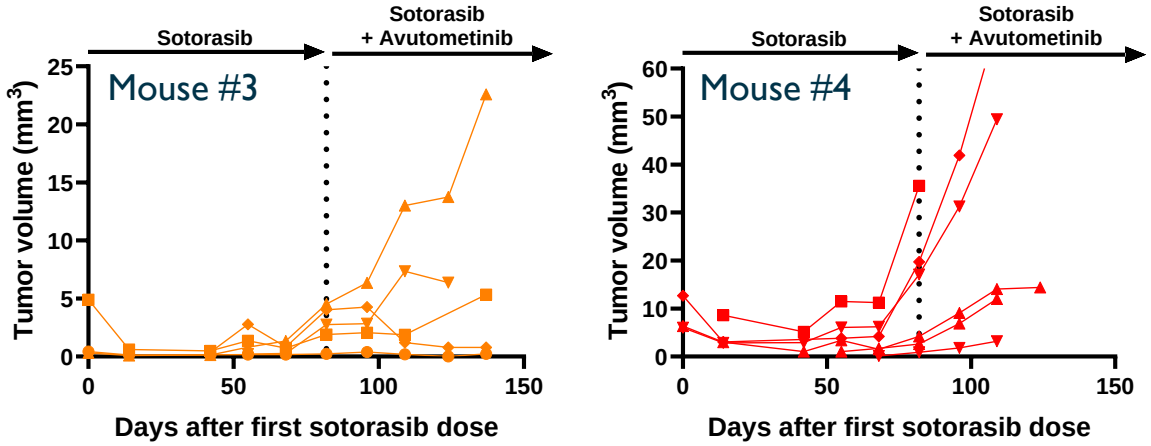
Sotorasib: 30 mg/kg PO QD
Avutometinib: 0.3 mg/kg PO QD
FAKi: 50 mg/kg PO BID

H2122 KRAS G12C NSCLC

Addition of FAKi + avutometinib reverses sotorasib resistance



Addition of avutometinib is insufficient to reverse sotorasib resistance



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Collaboration Verastem & Mariano Barbacid, CNIO (Spain)

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

Inclusion Criteria

- Documented *KRAS* G12C mutation determined using validated test
- Treatment with 1 but no more than 3 prior systemic regimens for Stage 3B-C or 4 NSCLC*
- May have received adjuvant chemotherapy for earlier-stage disease
- Measurable disease per RECIST v1.1
- ECOG performance status ≤ 1

*may include patients with or without prior G12C therapy

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

KRAS G12C inhibitor-naive → **Avutometinib + Sotorasib** Dose Finding Cohort → **RP2D Selected:** 4 mg avutometinib / 960 mg sotorasib

Progressed on KRAS G12C inhibitor → *Now enrolling* **Avutometinib + Sotorasib + Defactinib** Dose Finding Cohort → **Alt-RP2D Selection**

Part B: Dose Expansion
(Primary endpoint: ORR)

Treatment with RP2D and/or Alt-RP2D

Enrollment Complete for Stage 1

Cohort 1
Patients without Prior KRAS G12C Inhibitor Treatment
Stage 1: ~20 patients
Stage 2: expand to 54

Now enrolling

Cohort 2
Patients who Progressed on Prior KRAS G12C Inhibitor Treatment
Stage 1: ~19 patients
Stage 2: expand to 55

Cohort 1
Patients without Prior KRAS G12C Inhibitor Treatment
Stage 1: ~20 patients
Stage 2: expand to 54

Cohort 2
Patients who Progressed on Prior KRAS G12C Inhibitor Treatment
Stage 1: ~19 patients
Stage 2: expand to 55

Collaboration with Amgen, NCT05074810

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

RAMP 203: No DLTs Were Observed in the First Triplet Combination Cohort in Patients Previously Treated with a G12C Inhibitor

Triplet Combination Update:

- As of a November 21, 2024, data cutoff, 3 patients whose cancer previously progressed on a G12C inhibitor have been treated with the triplet combination of sotorasib 960 mg administered daily on a continuous schedule and avutometinib 3.2 mg twice-weekly (BIW) plus defactinib 200 mg twice-daily (BID). Avutometinib and defactinib are administered on a three out of four weeks schedule.
- 2 of the 3 patients demonstrated initial tumor reductions of at least 20% at the first scan. As of the data cutoff, all three patients remain on treatment.
- With no DLTs observed in the first triplet combination cohort, enrollment of additional patients to the triplet combination continues.

Doublet Combination Update:

- As previously reported, the doublet combination of avutometinib with sotorasib has completed enrollment (n=28) in the G12C inhibitor treatment-naïve Stage 1 Part B cohort.
- The KRAS G12C inhibitor prior-treated Stage 1 Part B cohort is still enrolling patients and is anticipated to complete enrollment in early 2025.
- Patients in both cohorts continue to be followed for safety and efficacy to determine if observed efficacy supports expanded enrollment.
- Plan to complete enrollment and evaluate the safety and efficacy of the triplet combination before expanding either of the doublet cohorts.

Next Steps for RAMP 203

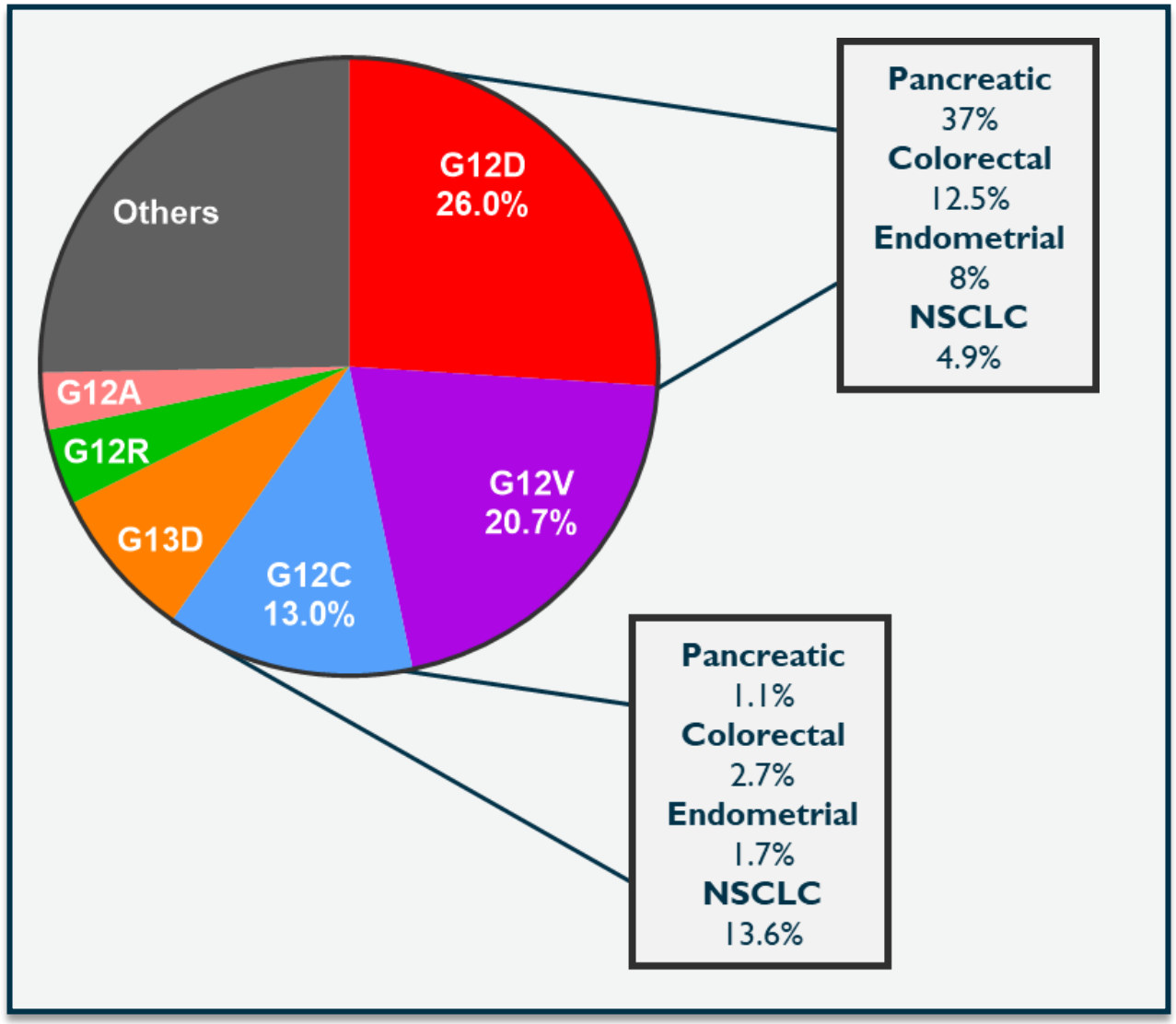
- Complete enrollment in the KRAS G12C inhibitor prior treated Stage 1 Part B cohort in Q1 2025
- Complete enrollment and evaluate the safety and efficacy of the triplet combination in H1 2025
- Present an interim update at a medical meeting in the second half of 2025

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

VERASTEM ONCOLOGY

KRAS G12D is the Most Frequent KRAS Mutation in Human Cancers

- The only approved KRAS inhibitors target KRAS G12C which is largely restricted to NSCLC
- KRAS G12D accounts for 26% of all KRAS mutations
- KRAS G12D mutations are especially prevalent in pancreatic and colorectal cancers
- Targeting KRAS G12D has historically been challenging due to the shallow pocket for drug interaction and lack of a cysteine for covalent binding



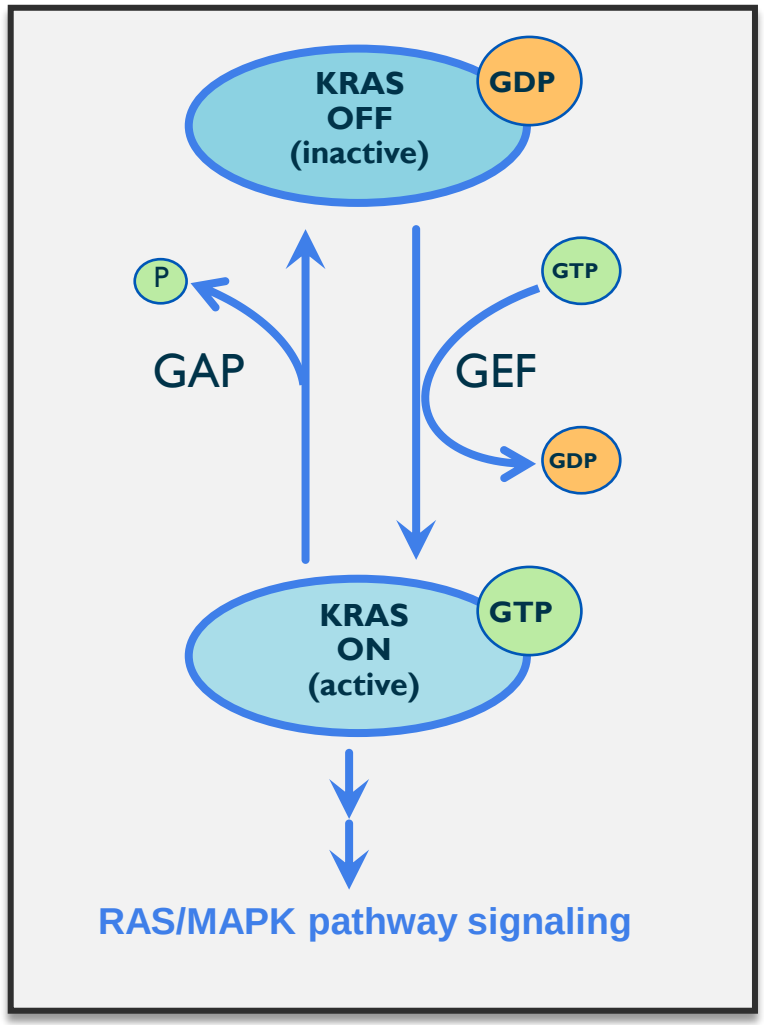
Adapted from Hofmann et al., Cancer Discovery 2022

Target Profile for a Best-in-Class KRAS G12D inhibitor

Categories	Criteria/Rationale
ON/OFF Dual Inhibition	Potent inhibition of both KRAS-GTP (ON) and KRAS-GDP (OFF) states for deep and durable inhibition of tumor growth
Potency	Inhibition of KRAS G12D signaling with sub-nanomolar potency
KRAS G12D Selectivity	Selectivity for KRAS G12D may enable avoidance of rash for dosing to maximal target inhibition and better combinability with other agents
Oral Bioavailability	Oral bioavailability to enable convenient round-the-clock target coverage
Anti-Tumor Efficacy	Deep tumor regressions in preclinical KRAS G12D models at low oral doses
Blood Brain Barrier	Activity in intracranial tumor models may indicate potential to treat brain metastases (e.g. in NSCLC)

Target profile based on the Company's internal analysis and framework

Importance of Inhibiting Both the Active (ON) & Inactive (OFF) States of KRAS for Deep and Durable Inhibition of Tumor Growth

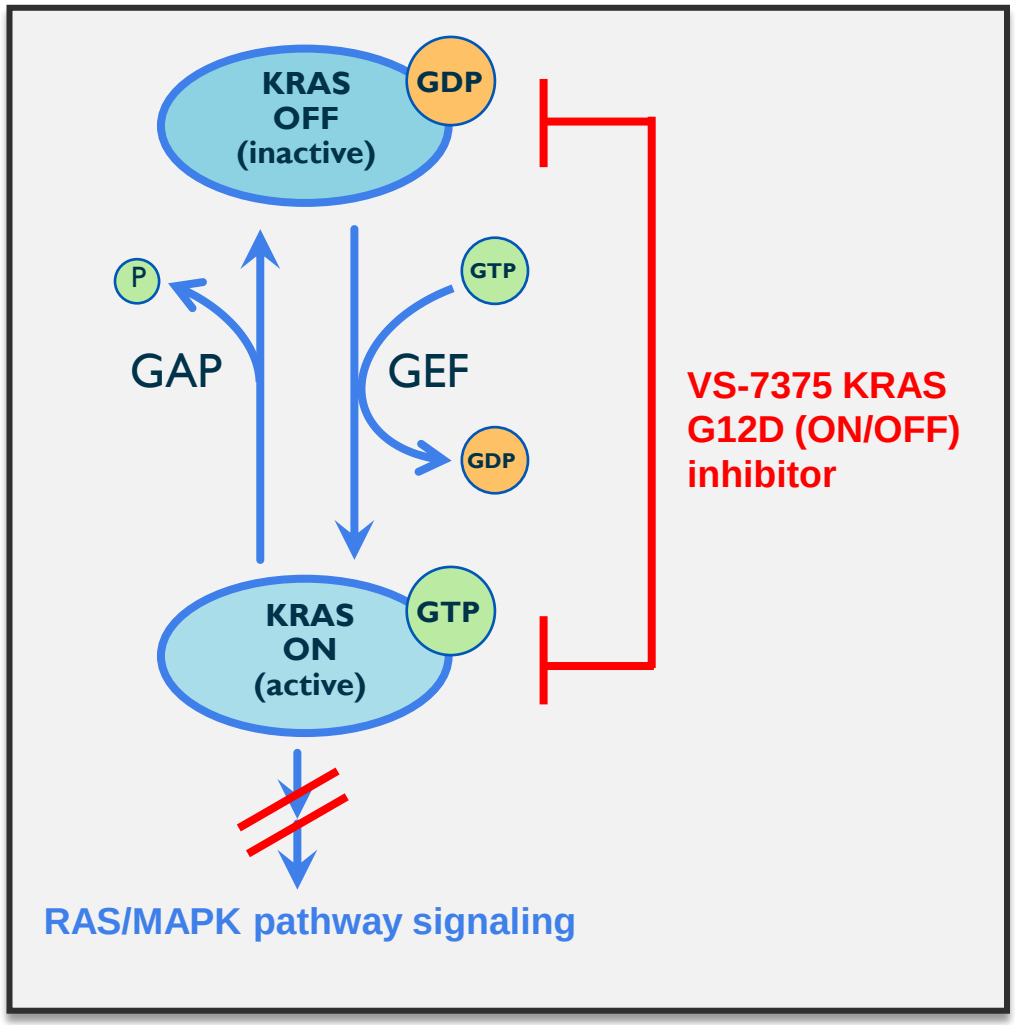


- KRAS-GTP is the active (ON) state which drives cancer growth
- KRAS-GDP is the inactive (OFF) state and represents a KRAS pool that will cycle back to the active ON state
- OFF-state selective agents (e.g., approved G12C inhibitors) may give sub-optimal efficacy because they do not target the active ON state
- ON-state selective agents (e.g., RMC-6236) can also drive GTP hydrolysis to the OFF state which they can no longer bind*
- May be ideal to have an inhibitor capable of targeting both the ON and OFF states of KRAS to maintain inhibition around the clock, aiming for maximum efficacy

*Piro Lito, RAS Initiative Conference 2024; GEF: Guanine nucleotide exchange factor; GAP: GTPase-activating protein

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

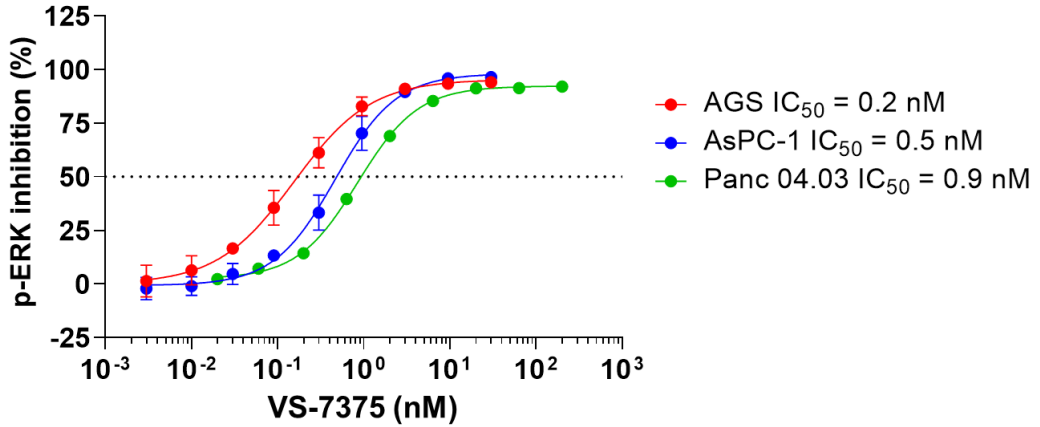
Non-covalent inhibitor of KRAS G12D (ON/OFF) with potent anti-tumor efficacy across preclinical models



VS-7375 is a dual inhibitor of ON (GTP) and OFF (GDP) states of KRAS G12D*

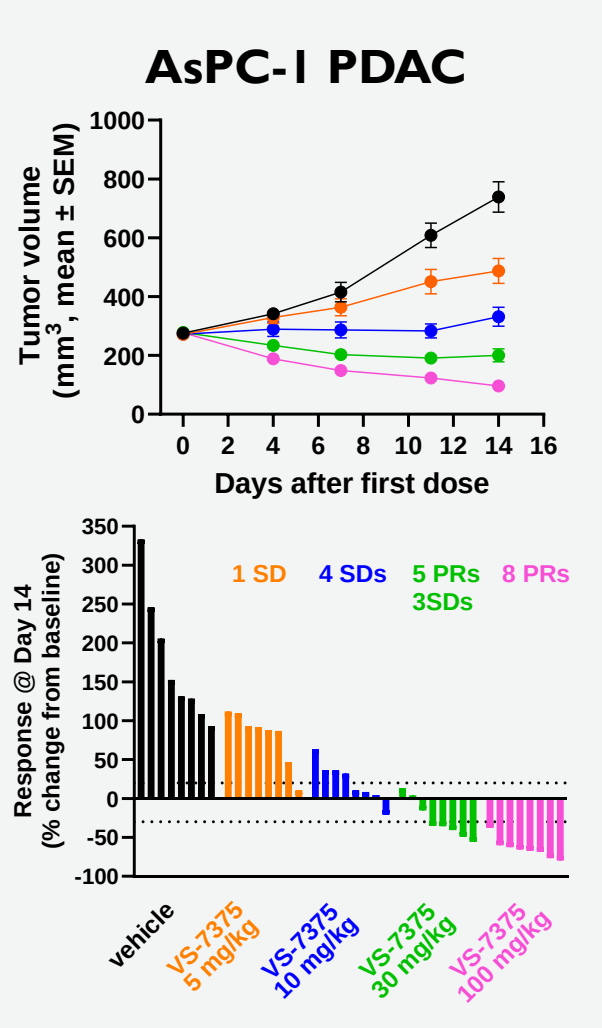
KRAS G12D State	VS-7375 IC50 (nM) (KRAS G12D binding)
GppNp-bound (ON/active)	2 ± 1
GDP-bound (OFF/inactive)	6 ± 1

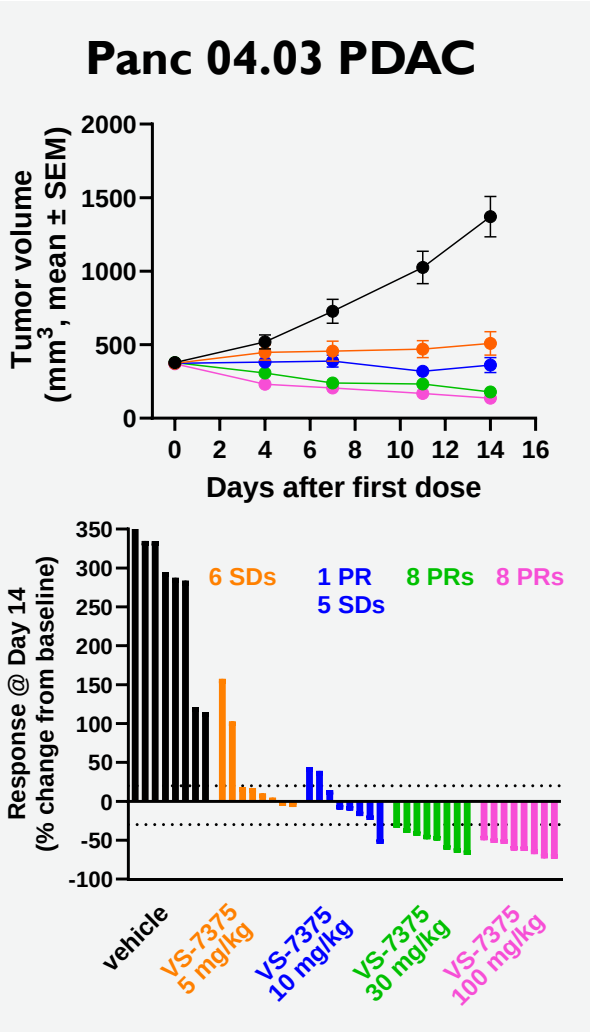
VS-7375 potently inhibits pERK signaling in KRAS G12D tumor cells*

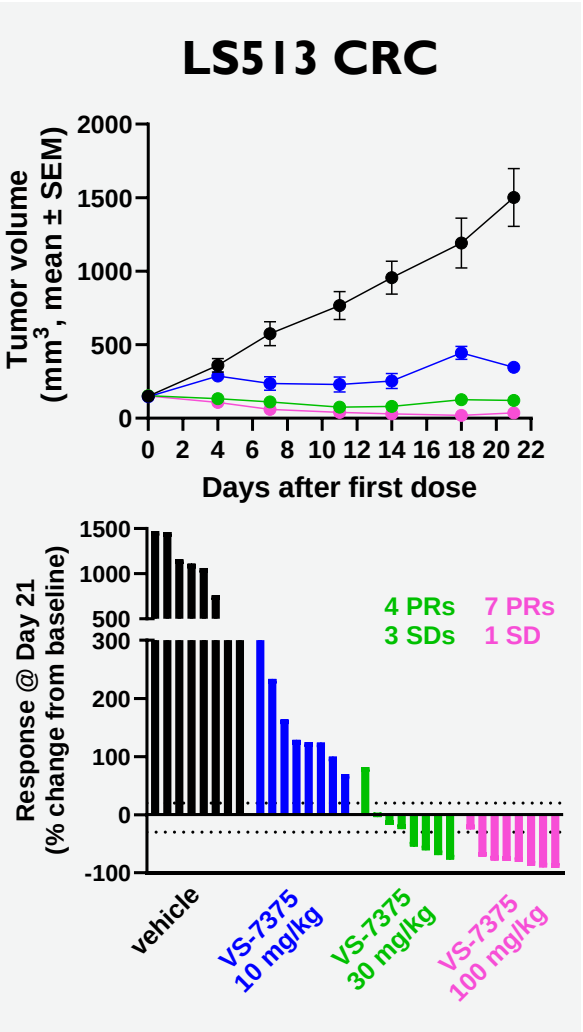


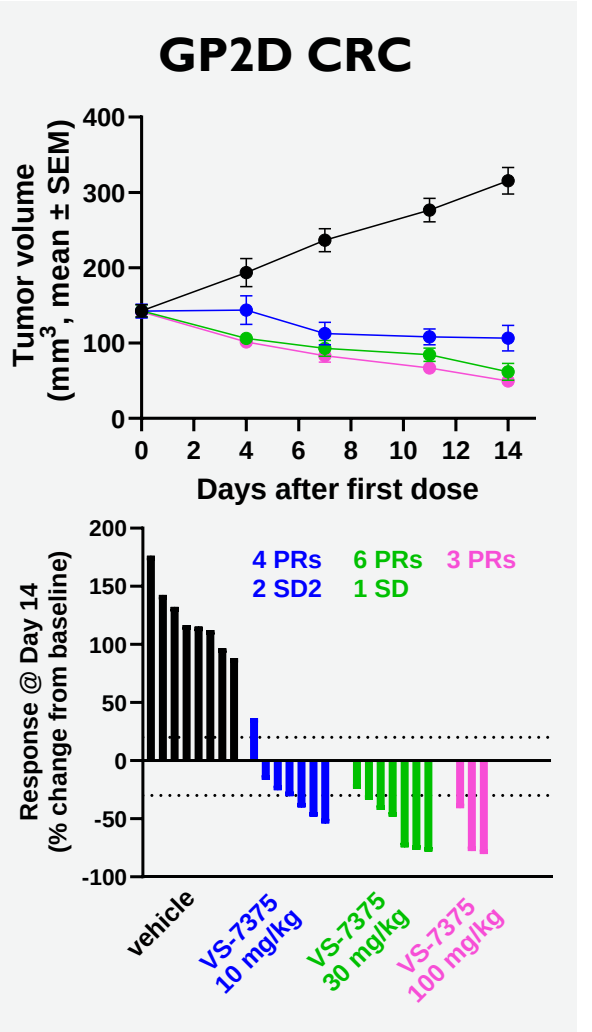
*Zhou et al., AACR 2024

VS-7375 Induces Tumor Regression in Multiple KRAS G12D Tumor Models via Oral Administration









- Vehicle, BID
- 5 mg/kg VS-7375, *p.o.*, BID
- 10 mg/kg VS-7375, *p.o.*, BID
- 30 mg/kg VS-7375, *p.o.*, BID
- 100 mg/kg VS-7375, *p.o.*, BID

Source for all data: Zhou et al., AACR 2024

VS-7375 Positively Addresses the Key Criteria for a Potential Best-in-Class G12D Inhibitor

Categories	Criteria/Rationale	VS-7375*
ON/OFF Dual Inhibition	Potent inhibition of both KRAS-GTP (ON) and KRAS-GDP (OFF) states for deep and durable inhibition of tumor growth	**Yes** IC_{50} = 2 nM (KRAS G12D ON) IC_{50} = 6 nM (KRAS G12D OFF)
Potency	Inhibition of KRAS G12D signaling with sub-nanomolar potency	**Yes** pERK IC_{50} = 0.2 – 0.9 nM
KRAS G12D Selectivity	Selectivity for KRAS G12D may enable avoidance of rash for dosing to maximal target inhibition and better combinability with other agents	**Yes** Inhibits proliferation of KRAS G12D cell lines more potently than other KRAS mutations or KRAS wild-type
Oral Bioavailability	Oral bioavailability to enable convenient round-the-clock target coverage	**Yes** Across preclinical species
Anti-Tumor Efficacy	Deep tumor regressions in preclinical KRAS G12D models at low oral doses	**Yes** Tumor regressions @ 10-30 mg/kg PO BID
Blood Brain Barrier	Activity in intracranial tumor models may indicate potential to treat brain metastases (e.g. in NSCLC)	**Yes** Efficacy @ 10 mg/kg PO BID in intracranial model

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*Zhou et al., AACR 2024;
Best-in-class target profile based on the Company's internal analysis and framework.

VS-7375: Initial Data Demonstrate Oral Bioavailability and Clinical Activity

- 26 patients have been treated with VS-7375 in a Phase 1 dose escalation study being conducted in China[1]
- Both confirmed and unconfirmed partial responses have been observed, including patients with metastatic pancreatic cancer and advanced non-small cell lung cancer[2]
- Six dose cohorts have been cleared with no dose-limiting toxicities (DLTs) observed[2]
- Oral dosing of VS-7375 has achieved plasma levels in patients that correlate with efficacious exposures that induced deep tumor regressions across all preclinical KRAS G12D tumor models (preclinical data presented in collaboration with GenFleet at the AACR 2024 annual meeting)[2]
- Companies expect to share updated preclinical and clinical data at upcoming medical meetings in mid-2025

1. GenFleet Stock Exchanged of Hong Kong Limited Application in Dec. 2024: https://www1.hkexnews.hk/app/sehk/2024/107026/documents/sehk24122701307.pdf; 2. VSTM DOF.

VS-7375 Shows Potential Best-in-Class Properties Relative to Other G12D Inhibitors

	Criteria	VSTM/ GenFleet VS-7375	Mirati/BMS MRTX1133	RevMed RMC-9805	Lilly LY3962673	AZ AZD0022	Incyte INCB161734	Quanta QTX3046	Tyligand TSN1611	Betta BPI-501836	Hengrui HRS-4642
On/Off	ON/OFF selectivity ratio	3x	0.2x	NR	0.016x	NR	1.2x	0.0003x	1.2x	NR	NR
Oral	Oral availability in preclinical models	Y	N	Y	Y	Y	Y	Y	Y	N	N
Potency	AsPC-1 pERK IC50	0.5 nM	NR	23 nM	NR	NR	7 nM	30 nM	NR	0.8 nM	NR
	Panc 04.03 pERK IC50	0.9 nM	NR	NR	NR	NR	19 nM	NR	NR	2.7 nM	NR
Tumor regression	GP2D Oral dose for tumor regression	10 mg/kg PO BID	30 mg/kg IP BID	100 mg/kg PO QD	30 mg/kg PO BID	NR	No regression @ 30 mg/kg PO QD	100 mg/kg PO BID	10 mg/kg PO BID	NR	Slight regression @ 15 mg/kg IV QW
	Panc 04.03 Oral dose for tumor regression	10 mg/kg PO BID	30 mg/kg IP BID	NR	NR	Tumor stasis @ 150 mg/kg PO BID	Slight regression @ 30 mg/kg PO QD	NR	NR	Regression @ 6 mg/kg IV BIW	NR
BBB	Efficacy demonstrated in intracranial model	Y	NR	Y	NR	NR	NR	NR	NR	NR	NR

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NR: not reported ; PO = oral administration; IP = intraperitoneal admiration; BID = twice per day; QD = once per day; QW = once per week; BIW = twice per weekReferences: GenFleet/Verastem AACR 2024; Hallin et al (Mirati) 2022; RevMed AACR 2023; RevMed AACR 2024; Lilly ENA 2023; Lilly AACR 2024; AstraZeneca (AZ) AACR 2024; Incyte AACR 2024; Quanta AACR 2023; Tyligand AACR 2024; Betta AACR 2024; Zhou et al (Hengrui) 2024

Next Steps for VS-7375 & GenFleet Collaboration

- GenFleet plans to continue to enroll patients into Phase 1/2 trial for VS-7375/ GFH375 in China in patients with KRAS G12D-mutated advanced solid tumors
- Anticipate filing U.S. IND for VS-7375 during Q1 2025 and initiate a Phase 1/2a study in mid-2025
- GenFleet/Verastem expect to share updated preclinical and clinical data at medical meetings in mid-2025
- Ongoing discovery/lead optimization in 2nd and 3rd programs

Achievements, Anticipated Milestones & Financials

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Planned Near-Term LGSOC Commercial Launch, Followed by Meaningful Catalysts to Expand Into Larger, Underserved Patient Populations

Program	Anticipated Milestones & Activities
Avutometinib + Defactinib in Recurrent Low-grade Serous Ovarian Cancer (LGSOC)	✓ Completed rolling NDA submission in KRAS mutant LGSOC in October 2024 ✓ Announced mature data from RAMP 201 at IGCS Annual Meeting in October 2024 ❑ June 30, 2025 PDUFA action date; U.S. commercial launch in recurrent KRAS mutant LGSOC in mid-2025 • Continue site activations and patient enrollment in international Phase 3 confirmatory study
Avutometinib + Defactinib + SOC in First-Line Metastatic Pancreatic Cancer	• Continue RAMP 205 study follow up on all dose cohort levels to determine RP2D go forward regimen ❑ Plan to report updated data from the ongoing RAMP 205 in Q1 2025
Avutometinib ± Defactinib + Sotorasib: mKRAS G12C Non-small Cell Lung Cancer (NSCLC)	❑ Complete enrollment in the KRAS G12C inhibitor prior treated Stage 1 Part B cohort in Q1 2025 ❑ Complete enrollment and evaluate the safety and efficacy of the triplet combination in H1 2025 ❑ Present an interim update at a medical meeting in the second half of 2025
VS-7375, KRAS G12D (ON/OFF) Inhibitor	• GenFleet plans to continue to enroll patients into Phase 1/2 trial for VS-7375/GFH375 in China in patients with KRAS G12D-mutated advanced solid tumors ✓ Initial data readout of VS-7375/GFH375 study in China expected in 2025 ❑ Anticipate filing U.S. IND VS-7375/GFH375 during Q1 2025 ❑ Expect to initiate Phase 1/2a trial in U.S. in mid-2025 ❑ The Companies expect to share updated preclinical and clinical data at medical meetings in mid-2025 • Ongoing discovery/lead optimization in second and third programs

Key Financial Statistics

As of and for the quarter ended September 30, 2024

Cash, cash equivalents & short-term investments	$113.2M
GAAP Operating Expenses	$37.0M
Non-GAAP Operating Expenses	$35.1M*
Shares Outstanding	40.3M**

Select financials as of December 31, 2024

Cash, cash equivalents & short-term investments	$88.8M
Cash, cash equivalents & short-term investments – pro-forma	$128.6M***

Sources of Non-Dilutive Capital

- **Oberland Finance Credit Facility**
  - Up to $150M available in a series of notes
    - $75M principal of notes outstanding
    - Remaining $75M available at Company's option upon achievement of pre-defined milestones
      - $25M tranche upon FDA approval of avutometinib and defactinib for treatment of LGSOC
      - $50M tranche upon trailing six months revenue of at least $55M
  - Floating interest rate, subject to a floor and a cap
  - Interest only payments through January 2031
  - No financial covenants

* Q3 2024 GAAP operating expenses of $37.03M less Q3 2024 stock-based compensation expense of $1.94M = $35.09M Q3 2024 non-GAAP operating expenses;

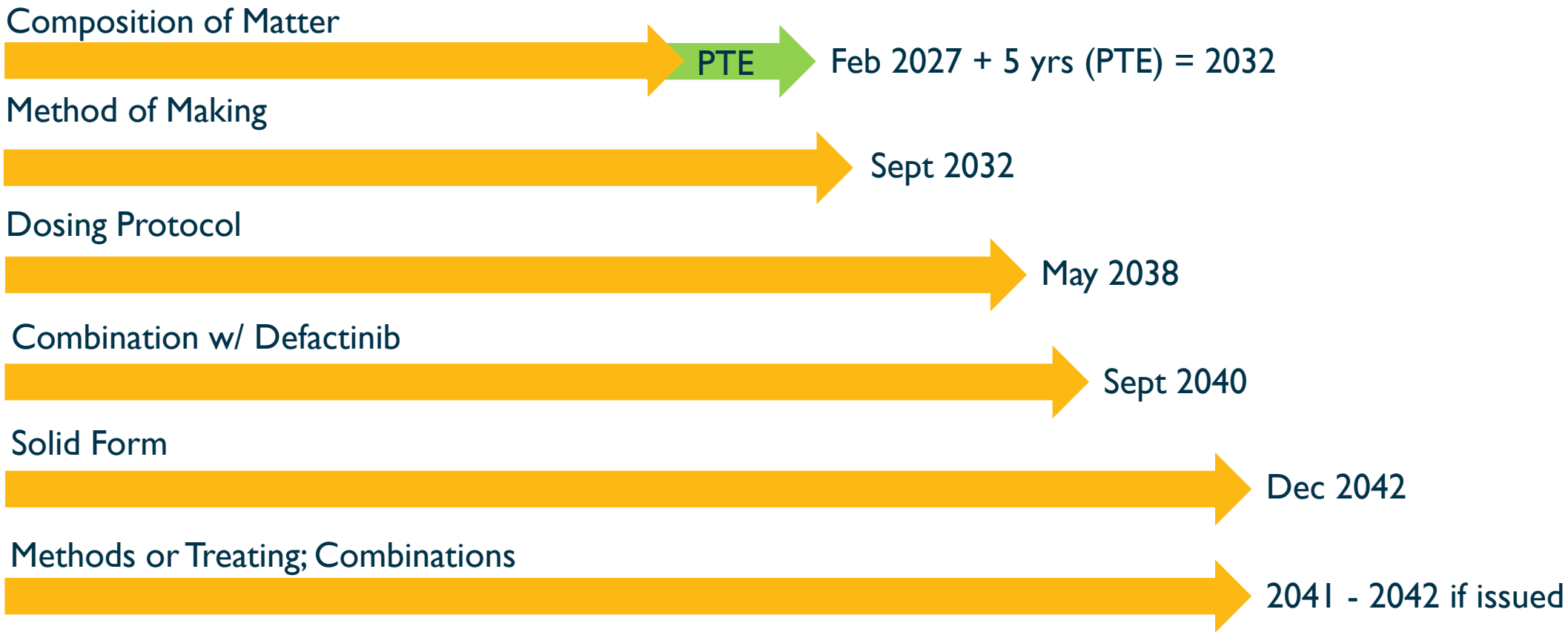
**Excludes Series A Preferred (0.8M Shares on as-converted basis), Series B Preferred (4.2M Shares on as-converted basis), unexercised Warrants (18.3M shares upon exercise) and unexercised Pre-Funded Warrants (5.0M shares upon exercise)

***Cash, cash equivalents, & short-term investments of $88.8M as of December 31, 2024, plus proceeds of $32.3M in January 2025 from Oberland Finance credit facility after repayment of Oxford facility, and equity purchase from Oberland Finance of $7.5M in January 2025

Thank You

Addendum

Avutometinib Patent Exclusivity



Experienced Senior Management Team

Daniel Paterson
President and Chief Executive Officer

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

John Hayslip, M.D.
Chief Medical Officer

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

Dan Calkins
Chief Financial Officer

Previous experience:
- Technical Accounting Consultant- CFGI
- PwC LLP

Colleen Mockbee
Global Head of Regulatory Affairs and Development

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

Cathy Carew
Chief Organizational Effectiveness Officer

Previous experience:
- Principal – HR Collaborative
- Ironwood
- ActiveBiotics
- Dynogen
- Tufts Health Plan

Jonathan Pachter, Ph.D.
Chief Scientific Officer

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

Mike Crowther
Chief Commercial and Strategy Officer

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

Nate Sanburn
Chief Business Officer

Previous experience:
- Associate VP, Head of Collaborations & Late Phase BD, Lilly Oncology
- National Gene Vector Lab, Indiana University

Avutometinib Monotherapy Provided Lower Rate of Response

- Patients enrolled had comparable baseline characteristics as patients randomized to avutometinib plus defactinib regimen
  - Median of 3 prior lines of therapy, 49% had prior bevacizumab, 26% had prior MEKi
- ORR: 17% in all patients, 23% KRAS mt and 13% KRAS wt
- TEAEs leading to D/C: comparable between monotherapy (16%) and combination (10%)

	Avutometinib Monotherapy 4.0 mg BIW 3 weeks on / 1 week off		
	All patients N=69	KRAS mt N=30	KRAS wt N=39
Confirmed* ORR, n (%)	**12 (17)**	**7 (23)**	**5 (13)**
CR	1 (1)	1 (3)	0
PR	11 (16)	6 (20)	5 (13)
SD†, n (%)	43 (62)	17 (57)	26 (67)
PD, n (%)	7 (10)	3 (10)	4 (10)
Not Evaluable, n (%)	7 (10)	3 (10)	4 (10)

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Source for all data: RAMP 201 data cut off as of June 30, 2024

Low-Dose Regimen (Part D) Determined to be Suboptimal Based on Pre-Defined Analysis

Low-dose regimen will not be pursued as a starting dose in the treatment of recurrent LGSOC

- Patients enrolled in Part D had comparable baseline characteristics as patients randomized to the avutometinib plus defactinib regimen
  - Median of 3 prior lines of therapy, 40% had prior bevacizumab, 37% had prior MEKi
- Suboptimal threshold: disease progression by 2nd scheduled assessment (Cycle 5 Day 1) >50% higher than that observed with avutometinib 3.2 mg BIW + defactinib
- TEAEs leading to D/C: comparable between 3.2 mg dose (10%) and 1.6 mg dose (15%)

IRC Assessment	Avutometinib 3.2 mg + 200 mg Defactinib Regimen 3 weeks on / 1 week off N=109	Avutometinib 1.6 mg + 200 mg Defactinib 3 weeks on / 1 week off N=23	% Difference
RECIST v1.1 Progressive Disease within 4 months	13 (12%)	5 (22%)	**+83%**

Source for all data: RAMP 201 data cut off as of June 30, 2024; D/C discontinuation

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

Summary of Adverse Events Grade ≥ 3 Occurring in ≥ 5% of patients

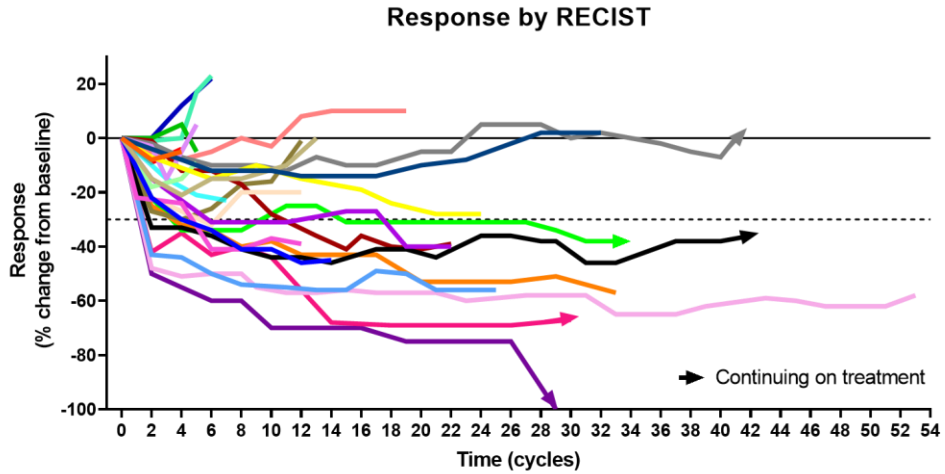
	Avutometinib monotherapy Daily at MTD N=6 28-day cycle	**RP2D Avutometinib monotherapy 4mg twice weekly N=26 28-day cycle**	**RP2D** (Avutometinib 3.2mg twice weekly + defactinib 200mg twice daily) **N=38 21 days of 28-day cycle**
Treatment Related Adverse Event	**Grade ≥3**	**Grade ≥3**	**Grade ≥3**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

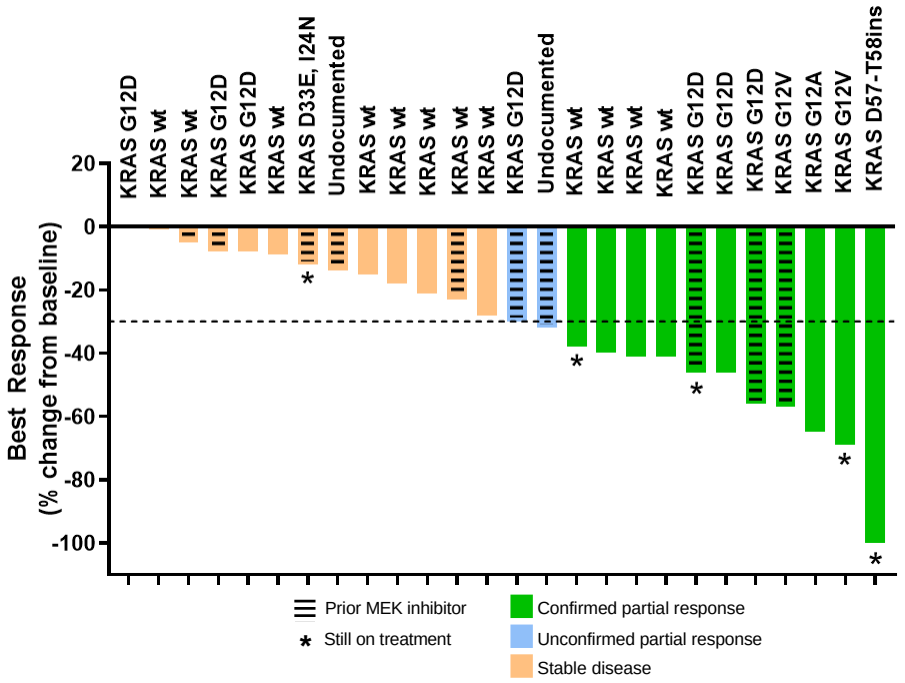
[1] Chenard-Poirier, *et al.* ASCO 2017; References: Banerji, Q4 2020 report; Data on file; RP2D: recommended phase 2 dosing

FDA Breakthrough Designation Based on FRAME Data

FRAME*

ORR Overall Population (Confirmed ORR by BICR)	**42%** (11 confirmed PRs/26)
95% CI	(19%, 36%)
KRAS mt	**58%** (7 confirmed PRs/12)
KRAS wt	**33%** (4 confirmed PRs/12)
Median Duration of Response (DoR) (95% CI 8.5-47.3) across all LGSOC patients	**26.9 months**
Median Progression Free Survival (PFS) (95% CI 11.1 – 31.2) across all LGSOC per RECIST 1.1	**20.0 months**
Median number of prior lines of therapy	**3.5 lines**
Responses observed in patients previously treated with MEK inhibitor	
No new safety findings with continued follow-up	
One (1) patient discontinued for adverse events as of July 2023 (skin AE)	



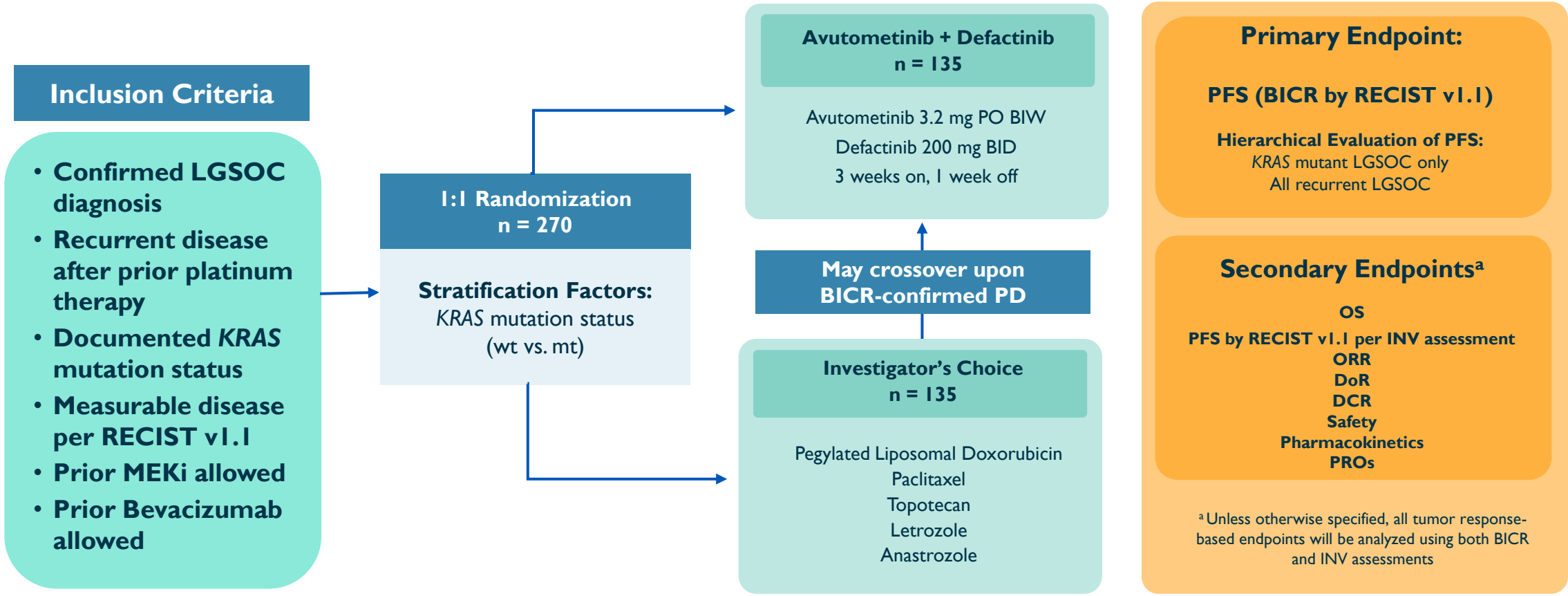


Breakthrough Through Therapy Designation for combination of avutometinib and defactinib for treatment of recurrent LGSOC after one or more prior lines of therapy including platinum-based chemotherapy

*Denis, 5th Annual RAS-Targeted Drug Development Sept 2023; (Data cut off July 2023: Data on file); BICR: Blinded independent central review

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

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

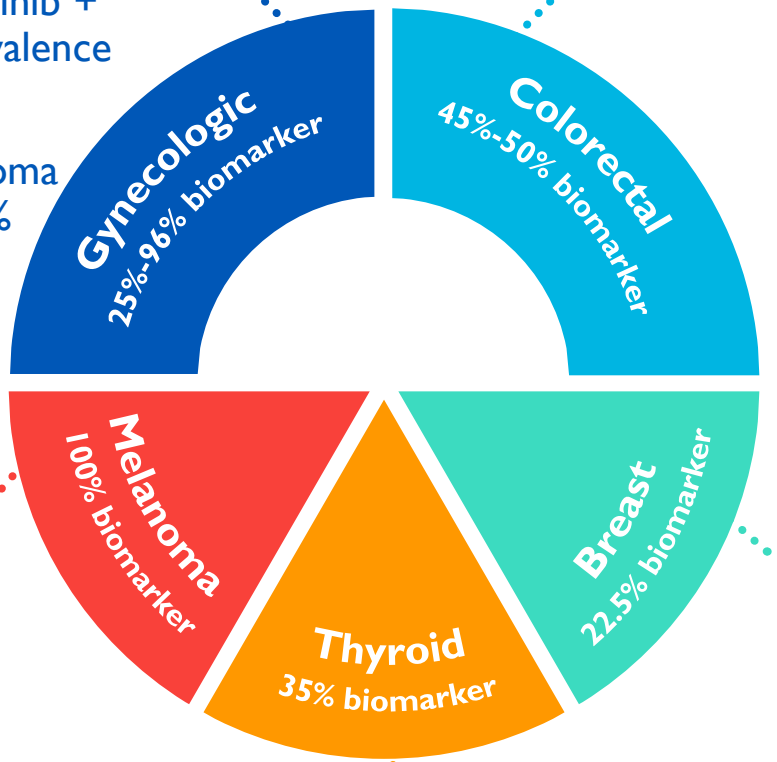


NCT06072781

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

Robust Investigator-Sponsored Trials Evaluates Multiple Potential Indications

- **LGSOC:** MSKCC Phase 1/2 with Avutometinib + Defactinib + Letrozole; 70% biomarker; Prevalence 6k[1]
- **Gynecologic Basket:** University of Oklahoma Phase 2 with Avutometinib + Defactinib; 25% biomarker; Incidence[4-8]: 85K
- **Mesonephric:** MSKCC Phase 2 with Avutometinib + Defactinib; 96% biomarker; Incidence[9]:~680



- **KRAS mt:** University of Chicago Phase 1/2 with Avutometinib + Cetuximab; 45% biomarker; Incidence[2]: 148K
- **RAS/RAF wt:** MDACC Phase 1/2 with Avutometinib + Defactinib + Cetuximab; 50% biomarker; Incidence[2]: 148K

- **MAPK Alterations or wt:** University of Utah Phase 1/2 with Avutometinib + Defactinib + Encorafenib; 100% biomarker; Incidence[2]: 100K

- **ER+/Her2-:** Dana-Farber Cancer Institute Phase 1/2 with Avutometinib + Abemaciclib + Fulvestrant; 22.5% biomarker; Incidence[2]: 279K

- **MAPK Alterations:** MSKCC Phase 2 with Avutometinib + Defactinib; 35% biomarker; Incidence[3]: 44K

[1] Monk, Randall, Grisham, The Evolving Landscape of Chemotherapy in Newly Diagnosed Advanced Epithelial Ovarian Cancer, Am Soc Clin Oncol Educ Book; 2019; Slomovitz, Gourley, Carey, Malpica, Shih, Huntsman, Fader., Grisham et al, Low-Grade serous ovarian cancer: State of the Science; Gynecol Oncol; 2020. Grisham, Iyer, Low-Grade Serous Ovarian Cancer: Current Treatment Paradigms and Future Directions; Curr Treat Options Oncology; 2018; Globocan 2020; [2]Cancer Statistics 2020, Siegel et. al. *CA Cancer J Clin* 2020;70:7-30; [3]Cancer Statistics 2020, Siegel et. al. *CA Cancer J Clin* 2020;70:7-30 [4]Uterine cancer is one of the leading gynecologic neoplastic disorders in the US, of which over 80% are endometrioid adenocarcinomas (EA); [5]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; [6]ucinous ovarian cancer: 3-11% of ovarian cancer (Hada et al., 2021); [7]90% of Ovarian Cancer is Epithelial Ovarian Cancer (https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2018/cancer-facts-and-figures-2018.pdf); [8]HGSOC the most common type of ovarian cancer, accounting for approximately 75% of epithelial ovarian cancers. (https://ocrahope.org/news/high-grade-serous-carcinoma/) [9]Ji Son (David Hong) ASCO 2023

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