Verastem Oncology R&D Investor Event

ASCO 2025

June 2, 2025

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 anticipated timing of a potential launch of avutometinib and defactinib in Low-Grade Serous Ovarian Cancer, the expected outcome and benefits of collaborations, including with GenFleet Therapeutics (Shanghai), Inc. (GenFleet), including the timing of the IND for VS-7375 and the initiation of a Phase 1/2a study with respect to the same, 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," "may," "plan," "target," "potential," "will," "would," "could," "should," "continue," "can" 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; 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; uncertainties related to the recent change in the U.S. presidential administration, including regulatory and policy changes that may adversely affect our business; 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 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 may 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, 2024, as filed with the Securities and Exchange Commission (SEC) on March 20, 2025, and in any subsequent filings with the SEC, which are available at www.sec.gov and www.verastem.com. The forward-looking statements in this presentation speak only as of the original date of this presentation, and we undertake no obligation to update or revise any of these statements whether as a result of new information, future events or otherwise, except as required by law.

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

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

Agenda

Welcome & Overview	Dan Paterson, President & CEO
Pancreatic Cancer Treatment Landscape & RAMP 205 Data Update	Vincent Picozzi, M.D.
VS-7375: KRAS G12D (ON/OFF) Inhibitor with a Differentiated Preclinical Profile	Jon Pachter, Ph.D., CSO
Review of VS-7375 US Phase 1/2a Trial and Supportive Data	David Hong, M.D.
Clinical Development Plans and Timelines for RAMP 205 and VS-7375	John Hayslip, M.D., CMO
Closing Remarks	Dan Paterson
Q&A	

VERASTEM ONCOLOGY

Welcome & Overview

Daniel Paterson
President & CEO

VERASTEM™ ONCOLOGY

Verastem Oncology: Multi-faceted Approach to Improve Outcomes in RAS/MAPK Pathway Driven Cancers

Pursuing unexplored avenues in the RAS/MAPK pathway with novel small molecule drugs that inhibit critical signaling pathways in cancer that promote cancer cell survival and tumor growth.

Synergistic Combinations with Current Pipeline and External Assets

- **RAF/MEK Inhibition**
  - Avutometinib
- **FAK Inhibition**
  - Defactinib
- **KRAS G12D Inhibition**
  - VS-7375
- **2 Undisclosed RAS Pathway-related Targets**

Guiding Principles

- Address cancers with high unmet treatment needs
- Pursue targets with strong biologic rationale
- Drive to clear preclinical evidence and clinical proof-of-concept
- Advance best-in-class molecules
- Enter viable market opportunities

VERASTEM ONCOLOGY

RAF: Rapidly Accelerated Fibrosarcoma; MEK: Mitogen-activated extracellular signal-regulated kinase; RAS: Rat Sarcoma; FAK: Focal Adhesion Kinase; MAPK: Mitogen-activated Protein Kinases;

AVMAPKI FAKZYNJA CO-PACK is the First and Only FDA-Approved Treatment for KRAS-Mutated Recurrent LGSOC

AVMAPKI™
FAKZYNJA™ CO-PACK
(avutometinib capsules; defactinib tablets) 0.8 mg;200 mg

FDA Approved on May 8, 2025

RAS/MAPK Pathway Directed MOA

- AVMAPKI offers dual inhibition of RAF and MEK
- FAKZYNJA mediates drug resistance of activated RAF/MEK
- Together, they offer a more complete blockade of the signaling that drives growth and drug resistance in the RAS/MAPK pathway

Clinically Meaningful Response Rates and Long Duration of Treatment

- 44% ORR, 3.3 to 31.1 months mDOR

Manageable Safety Allows for Treatment Until Progression for Most Patients

Convenient, Two Orally Dosed Treatments

- Novel intermittent dosing schedules

VERASTEM ONCOLOGY

Please see the full Prescribing Information for more information

FDA: Food and Drug Administration; ORR: overall response rate; mDOR: median Duration of Response

Pancreatic Cancer Treatment Landscape & RAMP 205 Data Update

Vincent J. Picozzi, M.D.

Director for the Pancreaticobiliary Program at the Virginia Mason Medical Center

Investigator for RAMP 205 and VS-7375-101 clinical trials

VERASTEM ONCOLOGY

Pancreatic Ductal Adenocarcinoma (PDAC) Represents an Area of High Unmet Need

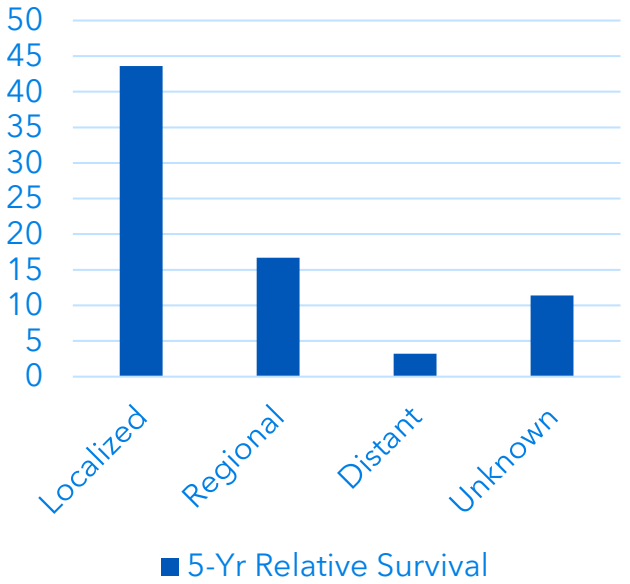
Nearly 180,000 Total Incident PDAC Patients

~59,800[1]

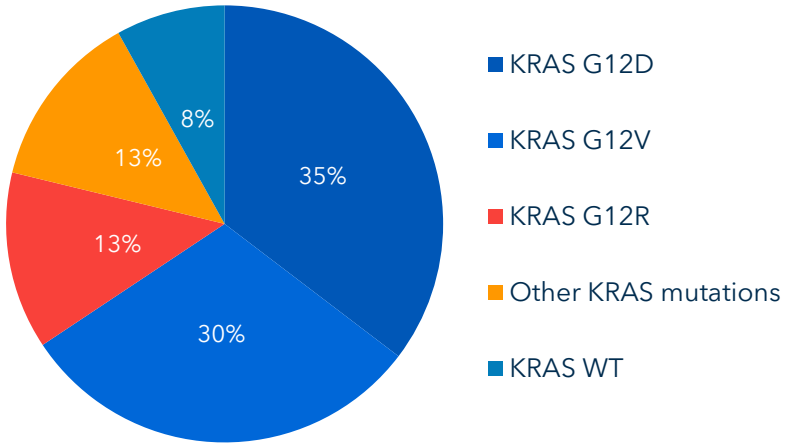
~77,500[2]

~43,200[3]

High Unmet Need Based on 5 Year Relative Survival of 13.3%



KRAS Mutations Are Present in ~90-95% of PDAC [4]



VERASTEM ONCOLOGY

[1]SEER 12;[2]worldometers; [3]Globocan/Japan/factsheet; [4]McIntyre, Cancer Cell, Sept 2023; [5]Yu, Frontiers in Oncology, Jul 2021

Locally Advanced and Metastatic PDAC: 1L and 2L+ Treatment Paradigm

~50-60%[1] metastatic disease at diagnosis

~40-50%[1] local/regional disease at diagnosis

Locally Advanced (LA)/Metastatic PDAC

(50-60%[2] will recur with LA/Metastatic disease)

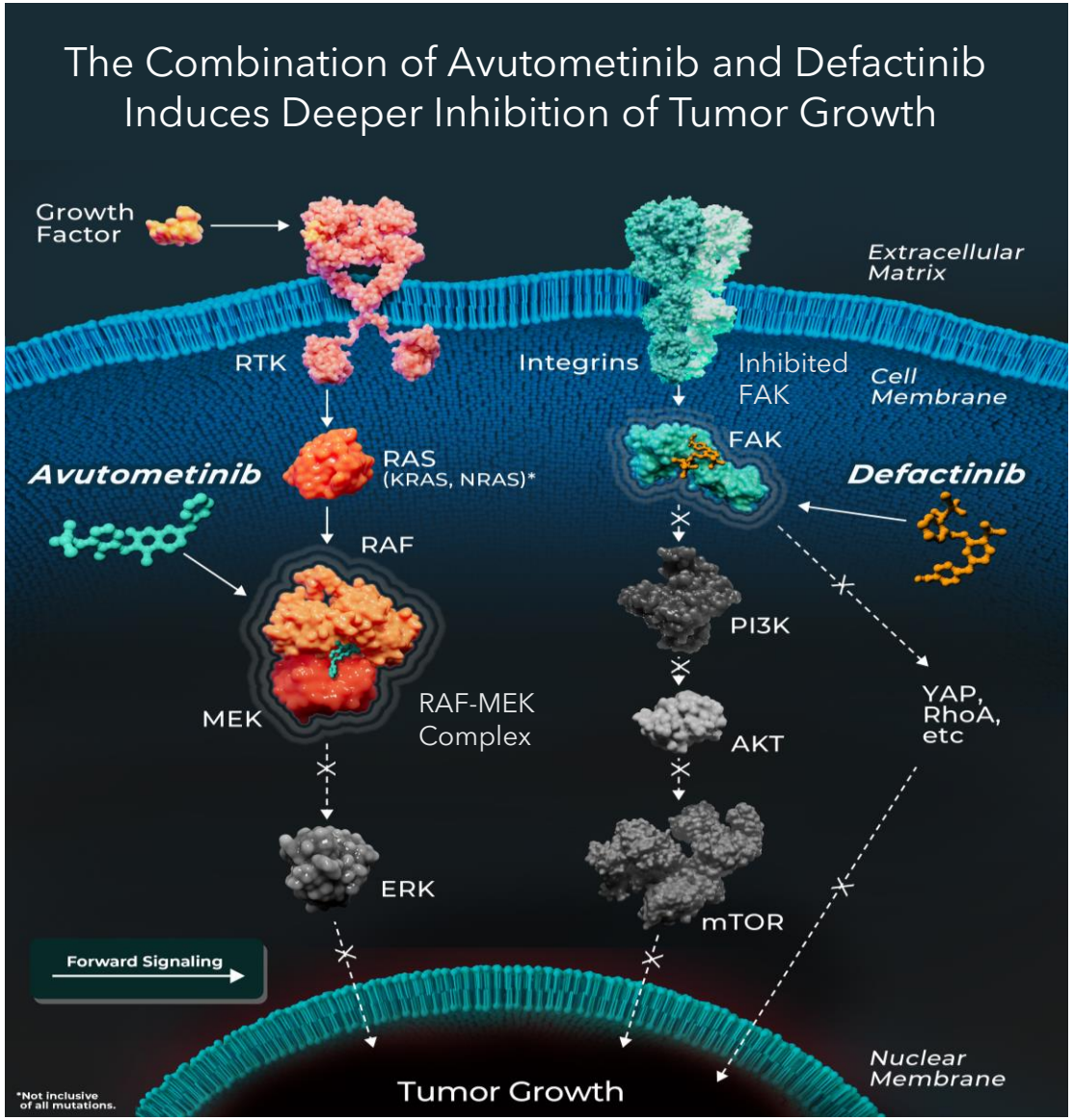
	1L	2L
SOC	**Gem/nab-paclitaxel NALIRIFOX FOLFIRINOX**	**FOLFIRINOX Gem/nab-paclitaxel FOLFOX**
Limitations	• FOLFIRINOX: median overall survival (mOS) = 11.1 months and ORR = 31.6%[3] • Gem/nab-paclitaxel: median overall survival (mOS) = 8.5 - 9.2 months and ORR = 23-36.2%[4,5]	• Gem/nab-paclitaxel: median overall survival (mOS) = 8.6 months and ORR = 15.6%[6]

VERASTEM ONCOLOGY

[1] SEER 21 (2015-20210), [2] Jones, JAMA Surg. Sep 2019, [3] Conroy, 2011·, [4] VonHoff, 2013, [5] O'Reilly, 2023, [6] Sezgin, 2025.

More Complete Blockade of the Signaling that Drives Growth and Resistance of RAS/MAPK Pathway-Dependent Tumors

- Avutometinib inhibits MEK kinase activity while blocking the compensatory reactivation of MEK by upstream RAF[5,6,7]
- Blocking RAF and/or MEK activates FAK, a key mediator of drug resistance[8,9]
- Defactinib, a FAK inhibitor, inhibits parallel pathway signaling[10,11,12]
- Together, avutometinib plus defactinib offer more complete blockade of the signaling that drives the growth of RAS/MAPK pathway-dependent tumors

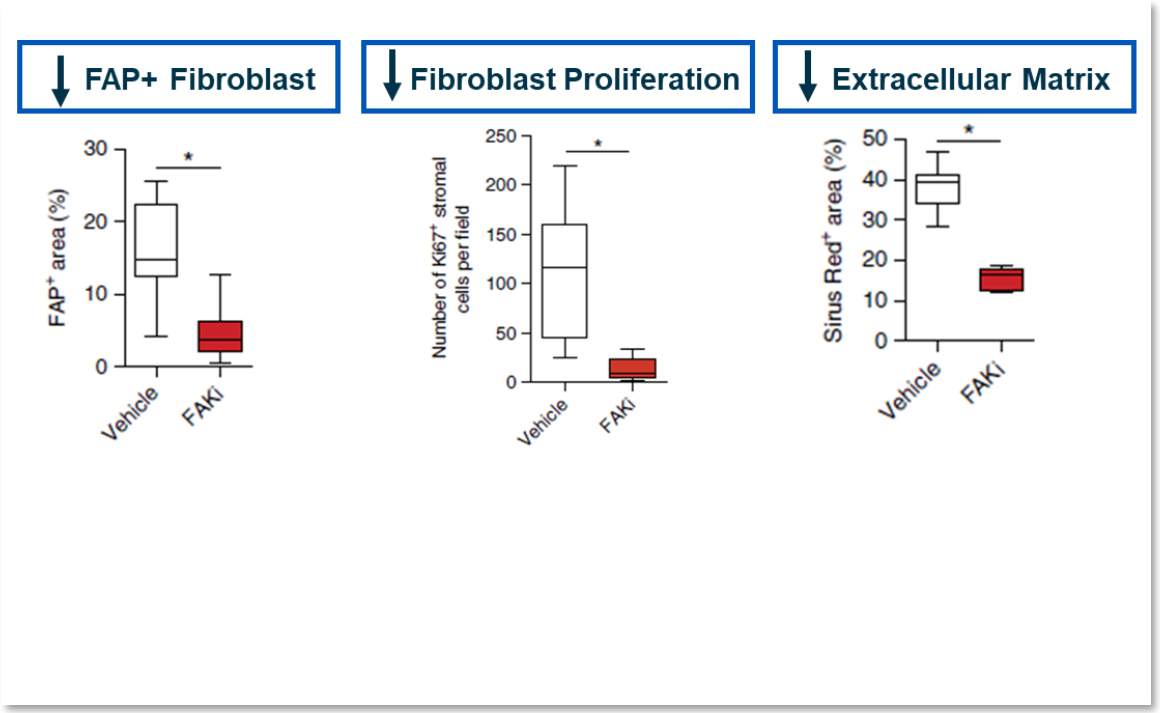


[1]Coma et al., AACR 2022; [2]Ishii et al., Cancer Res, 2013; [3]Lito et al., Cancer Cell, 2014; [4]Lubrano et al., AACR 2024; [5]Banerji et al., AACR 2020; [6]Jones et al., Invest New Drugs 2015; [7]McNamara et al., Gynecol Oncol 2024; [8]Banerjee et al., ASCO 2023

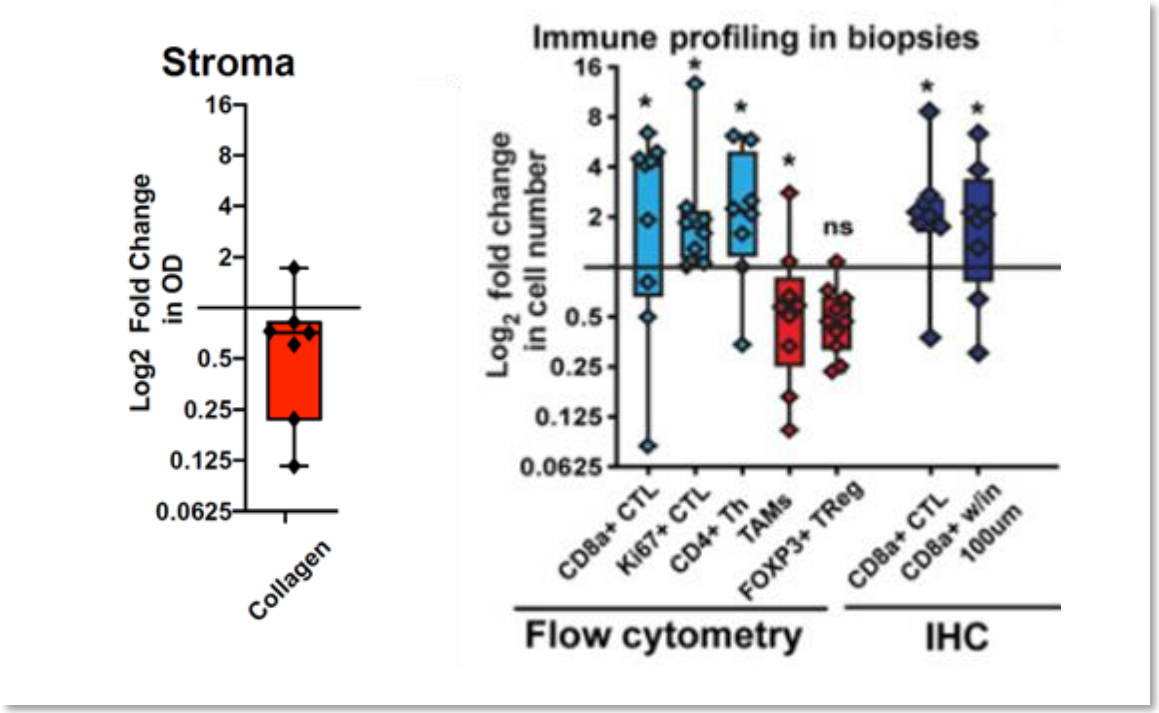
ERK: Extracellular Signal-regulated Kinase; FAK: Focal Adhesion Kinase; MEK, Mitogen-Activated Extracellular Signal-regulated Kinase; mTOR: Mammalian Target of Rapamycin; P: Phosphate; PI3K: Phosphatidylinositol 3-Kinase; RAF: Rapidly Accelerated Fibrosarcoma; RA: Rat Sarcoma Virus; RhoA: Ras Homolog Family Member A; RTK: Receptor Tyrosine Kinase; YAP: Yes-Associated Protein.

FAK inhibitor (Defactinib) Reduces Pancreatic Cancer Stromal Density Preclinically and Clinically

FAKi reduced stromal density in a preclinical (KPC) pancreatic cancer model[1]



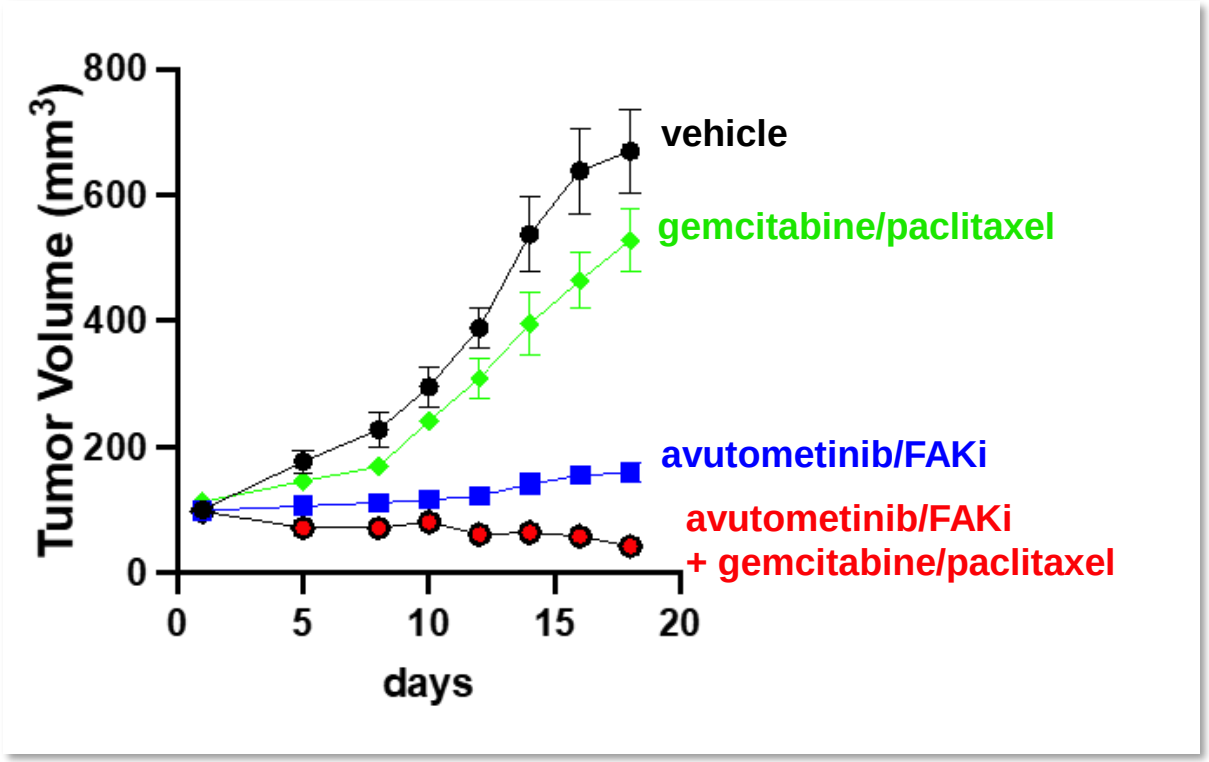
Defactinib + gemcitabine + pembrolizumab reduced stromal density in tumors of patients with pancreatic cancer[2]

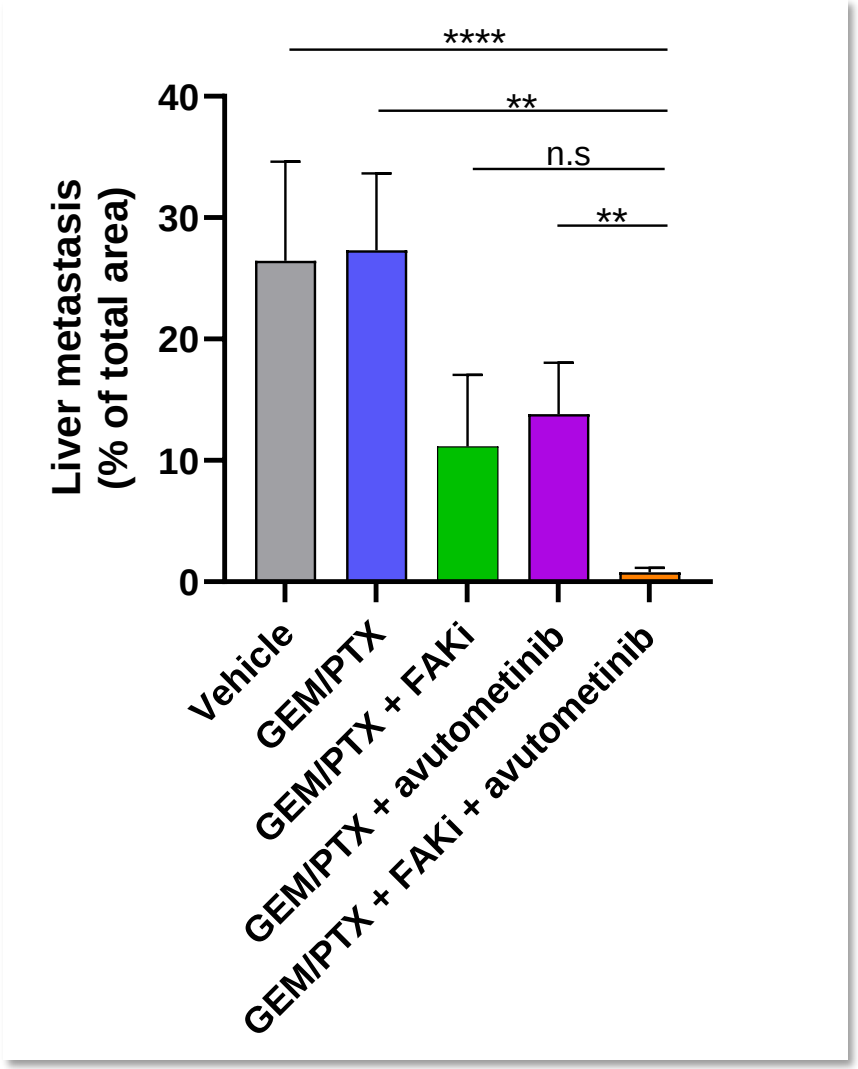


VERASTEM ONCOLOGY

1) Jiang H et al., Nature Med 22: 851, 2016; 2) Wang-Gillam A et al., Clin Cancer Res 28: 5254, 2022

Addition of Avutometinib + FAKi with Chemotherapy Induces Tumor Regression, and Decreases Liver Metastases in a KRAS/p53 Pancreatic Cancer Mouse Model





Liu X et al., Sci Transl Med 2024; GEM: gemcitabine, PTX: paclitaxel

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

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

Inclusion Criteria

- Histologic or cytologic confirmed mPDAC
- Eligible for treatment in the first-line setting (no prior systemic therapy for advanced or metastatic disease)
- Measurable by RECIST v1.1 by CT or MRI
- ECOG Performance status of ≤1
- Part B only, adequate tissue sample to evaluate KRA mutational status

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

Avutometinib + Defactinib + Gemcitabine + Nab-paclitaxel

Dose Finding Cohorts n=3-6

Avutometinib + Defactinib + Gemcitabine + Nab-paclitaxel

DLT-Cleared Dose Level Expansion

RP2D Selection

Part B: Dose Expansion
(Primary Endpoint: ORR)

- Patients with PDAC treated at RP2D
- Stage 1: 17 patients if ≥4 responders, then
- Simon's 2-stage design: expand to 29 patients

Collaboration with PanCAN, NCT05669482

VERASTEM ONCOLOGY

DLT: dose-limiting toxicity; RP2D: recommended phase 2 dose; CT: computed tomography; ECOG: European Cooperative Oncology Group; MRI: magnetic resonance imaging

RAMP 205: 12 Patients Enrolled in Each Dose Cohort

Dose level 1 selected as the RP2D

PART A Enrollment Summary Dose Levels & Administration Schedule (28-day) Cycle

- **Enrolled:** (n=60)
- **Treatment Ongoing:** (n=19)
- **Ended Study:** (n=30)
- **Survival Follow Up:** (n=11)

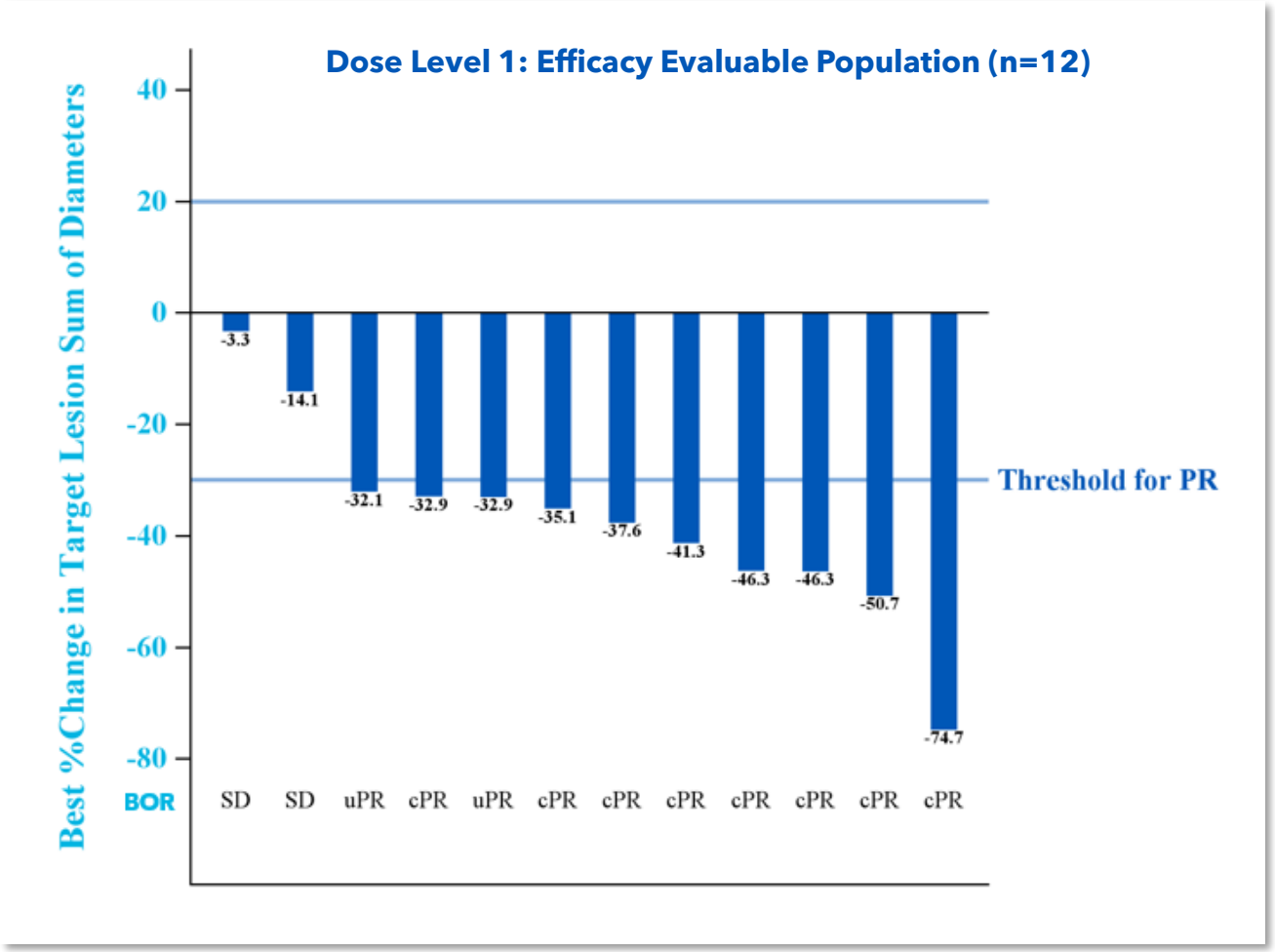
Dose Level	Avutometinib	Defactinib	Gemcitabine	Nab-Paclitaxel	Days Chemo Dosing	Enrolled N=60
1	2.4	200	800	125	1-8-15	12
0	3.2	200	800	100	1-8-15	12
-1	2.4	200	800	100	1-8-15	12
1a	3.2	200	800	125	1-15	12
2a	3.2	200	1000	125	1-15	12

VERASTEM ONCOLOGY

Updated 05/01/25

Dose Level 1 Demonstrated an 83% ORR with Tumor Shrinkage Observed in All Patients

As of April 30, 9th patient confirmed responses, 1 unconfirmed response

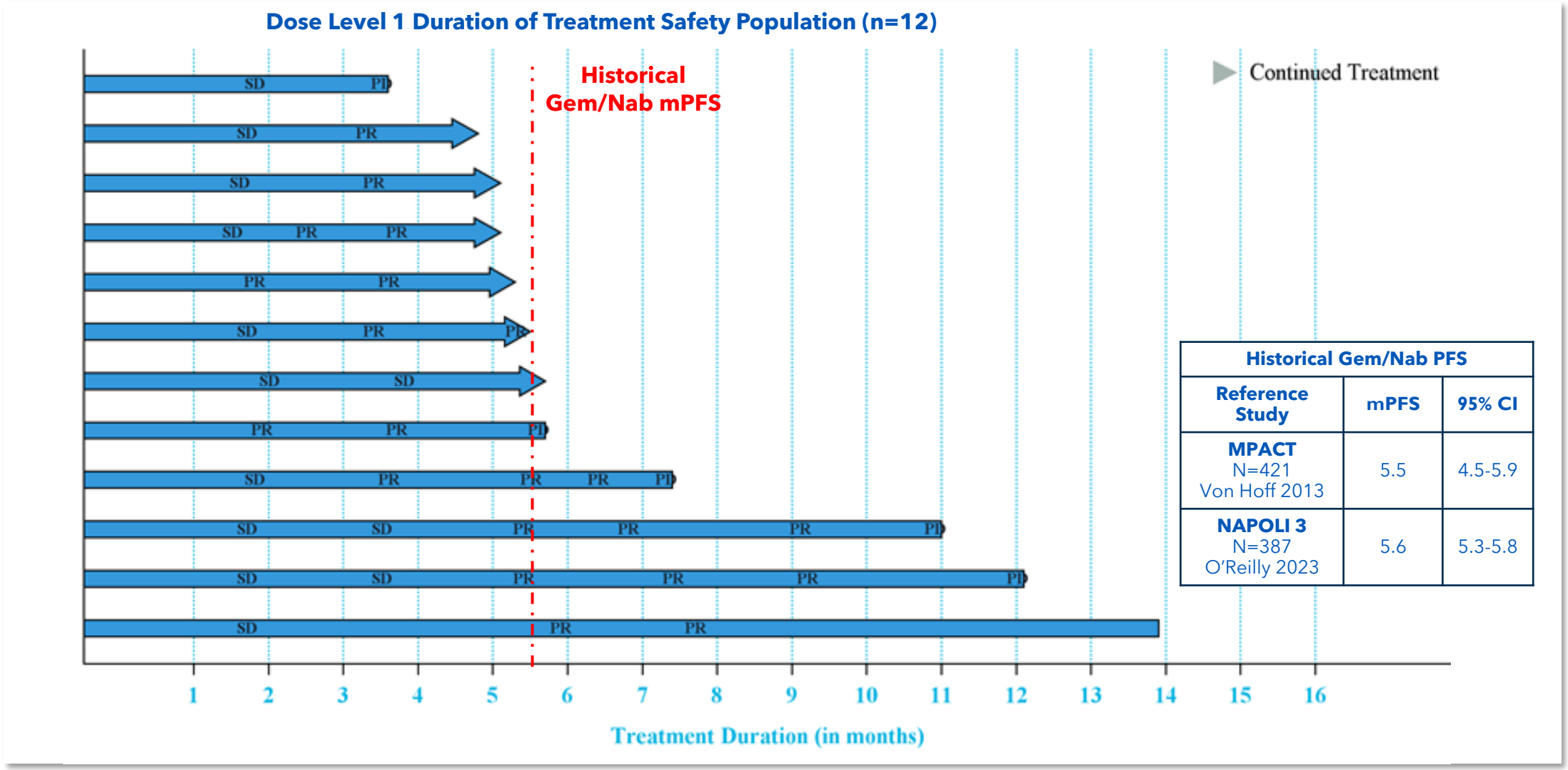


Dose Level 1: Response & Disease Control Rate as of April 25, 2025	
Unconfirmed ORR, n (%)	**83.3%** (10/12)
Confirmed ORR, n (%)	66.7% (8/12)
PR, n (%)	8 (66.7)
uPR, n (%)	2 (16.7)
SD, n (%)	2 (16.7)
PD, n (%)	0
DCR, n (%) ≥ 4 cycles	**92%** (11/12)

VERASTEM ONCOLOGY

Source: F_TR_WATERFALL.sas Data Cut: 25 APR 25

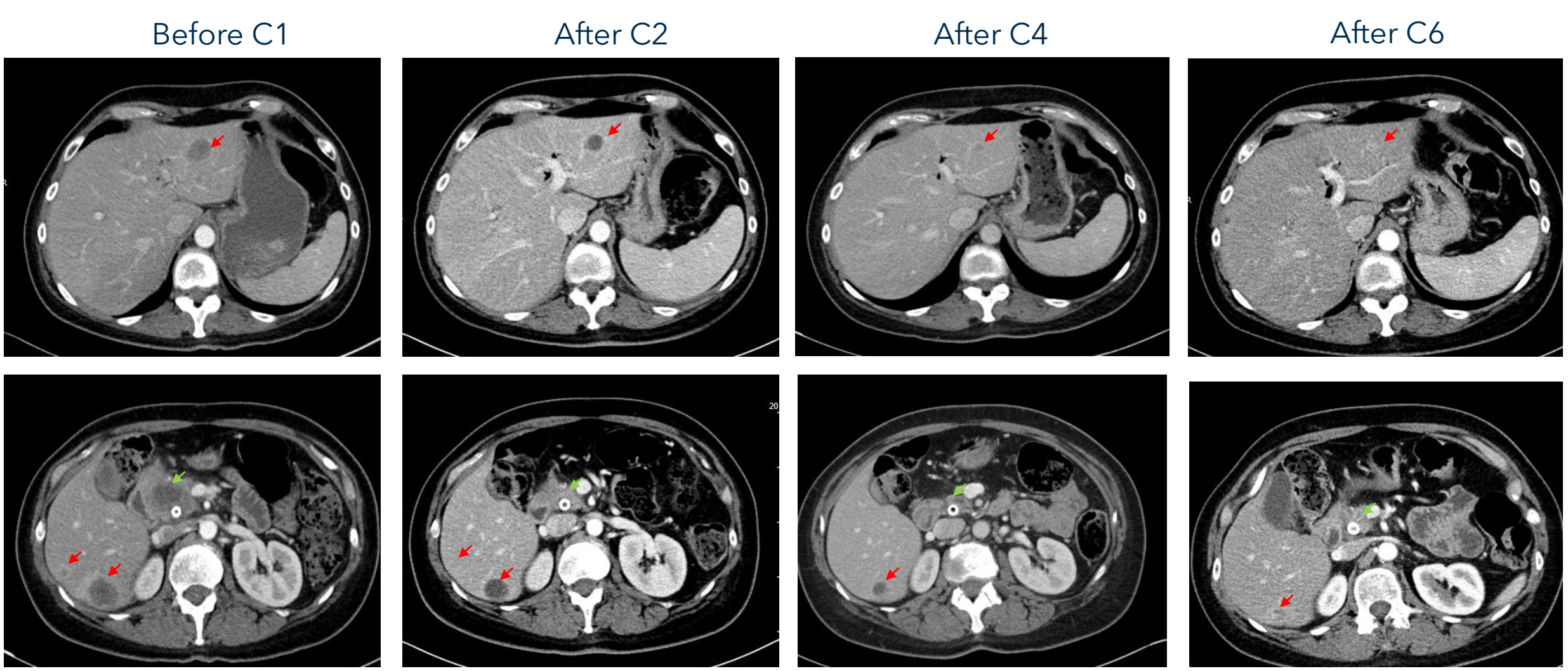
Encouraging Duration of Treatment Observed to Date for Dose Level 1



Historical Gem/Nab PFS		
Reference Study	**mPFS**	**95% CI**
MPACT N=421 Von Hoff 2013	5.5	4.5-5.9
NAPOLI 3 N=387 O'Reilly 2023	5.6	5.3-5.8

Source: Program:F_TX_RS_SWIMMER_DL1.sas Data Cut: 25 APR 25

63yo Female with mPDAC in Dose Level 1



Source: Dr. Lim, Siteman Cancer Center 7

AEs were Generally Manageable, Allowing Patients to Remain on Treatment

DL1 Treatment Emergent AE All Grades ≥ 25% / Non-laboratory AEs				
TEAEs	**Dose Level 1 (n=12)**		**NAPOLI 3* (N=379)**	
Preferred term	**All Grades n (%)**	**Grade ≥3 n (%)**	**All Grades n (%)**	**Grade ≥3 n (%)**
Nausea	10 (83)	0	162 (43)	10 (3)
Diarrhoea	9 (75)	0	139 (37)	17 (4)
Fatigue	9 (75)	0	143 (38)	20 (5)
Alopecia	8 (67)	0	119 (31)	Not Listed**
Constipation	8 (67)	0	113 (30)	8 (2)
Oedema peripheral	7 (58)	2 (17)	108 (29)	Not Listed**
Rash maculo-papular	7 (58)	0	Not Listed**	Not Listed**
Stomatitis	7 (58)	1 (8)	45 (12)	Not Listed**
Vomiting	7 (58)	1 (8)	100 (26)	8 (2)
Dysgeusia	6 (50)	0	58 (15)	Not Listed**
Hypotension	6 (50)	0	Not Listed**	Not Listed**
Pyrexia	6 (50)	1 (8)	87 (23)	Not Listed**
Decreased appetite	5 (42)	0	106 (28)	10 (3)
Hypertension	5 (42)	1 (8)	Not Listed**	8 (2)
Neuropathy peripheral	5 (42)	1 (8)	66 (17)	22 (6)
Cough	4 (33)	0	Not Listed**	Not Listed**
Dyspepsia	4 (33)	0	Not Listed**	Not Listed**
Dyspnoea	4 (33)	0	47 (12)	8 (2)
Retinopathy	4 (33)	1 (8)	Not Listed**	Not Listed**
Vision blurred	4 (33)	1 (8)	Not Listed**	Not Listed**
Abdominal Distension	3 (25)	0	Not Listed**	Not Listed**
Abdominal Pain	3 (25)	0	77 (20)	14 (4)
Depression	3 (25)	0	Not Listed**	Not Listed**
Epistaxis	3 (25)	0	43 (11)	Not Listed**
Febrile Neutropenia	3 (25)	3 (25)	Not Listed**	9 (2)
Rash	3 (25)	0	Not Listed**	Not Listed**

- No new or unexpected AEs observed
- Most non-laboratory AEs were grade 1 or 2
- AEs were generally manageable, allowing patients to remain on treatment
- The rates and severities of most AEs are consistent with the individual rates reported for Gem/Nab and Avutometinib/Defactinib
- Nausea, diarrhea, constipation, febrile neutropenia, and anemia may be increased in comparison to those expected with Gem/Nab

DL1 Treatment Emergent AE All Grades ≥ 25% / Laboratory-related AEs				
TEAEs	**Dose Level (n=12)**		**NAPOLI 3* (N=379)**	
Preferred term	**All Grades n (%)**	**Grade ≥3 n (%)**	**All Grades n (%)**	**Grade ≥3 n (%)**
Anaemia	8 (67)	5 (42)	153 (40)	66 (17)
Neutropenia***	8 (67)	6 (50)	192 (51)	144 (38)
Hyperbilirubinaemia***	7 (58)	2 (17)	Not Listed**	11 (3)
Thrombocytopenia***	5 (42)	1 (8)	154 (41)	23 (6)
Aspartate aminotransferase increased	3 (25)	1 (8)	40 (11)	8 (2)
Hypokalemia	3 (25)	0	49 (13)	15 (4)

VERASTEM ONCOLOGY

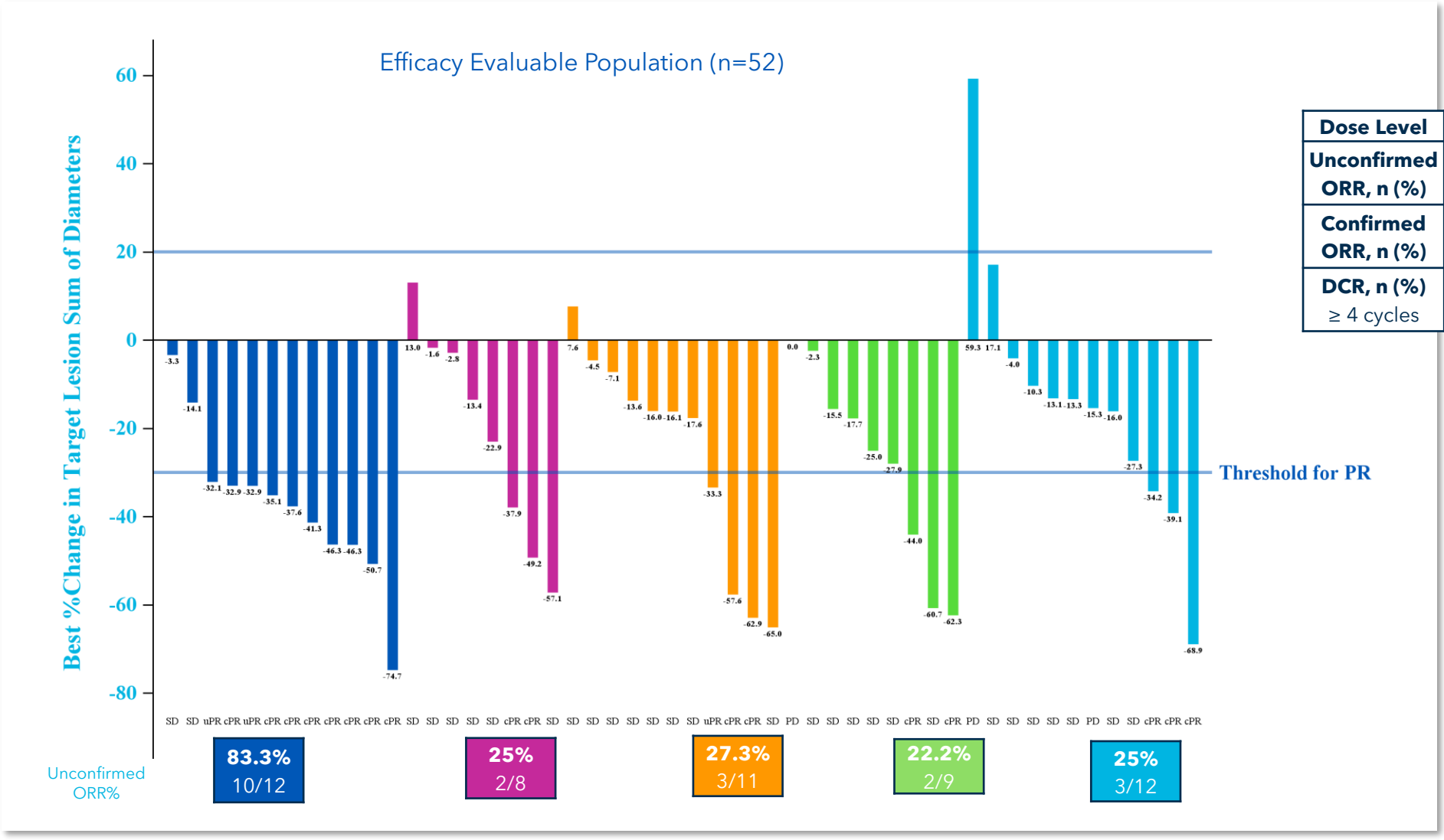
RAMP 205 data source:T_AE_GRADE_PT.sas : Data Cut: 11 APR 25

*Supplement Appendix: (NAPOLI 3). Wainberg et al. The Lancet, Volume 402, Issue 10409, 1272 – 1281

**If "Not Listed" then adverse event is either not reported or did not meet threshold of <10% all grade TEAE or <2% G3 or higher TEAE.

***'Neutropenia' and 'Neutrophil count decreased' are grouped as 'Neutropenia'. 'Thrombocytopenia' and 'Platelet count decreased' are grouped as 'Thrombocytopenia'. 'Hyperbilirubinaemia' and 'Blood bilirubin increased' are grouped as 'Hyperbilirubinaemia''. AE, adverse event;

92% (48/52) of Patients Showed Tumor Reduction Across All Dose Cohorts



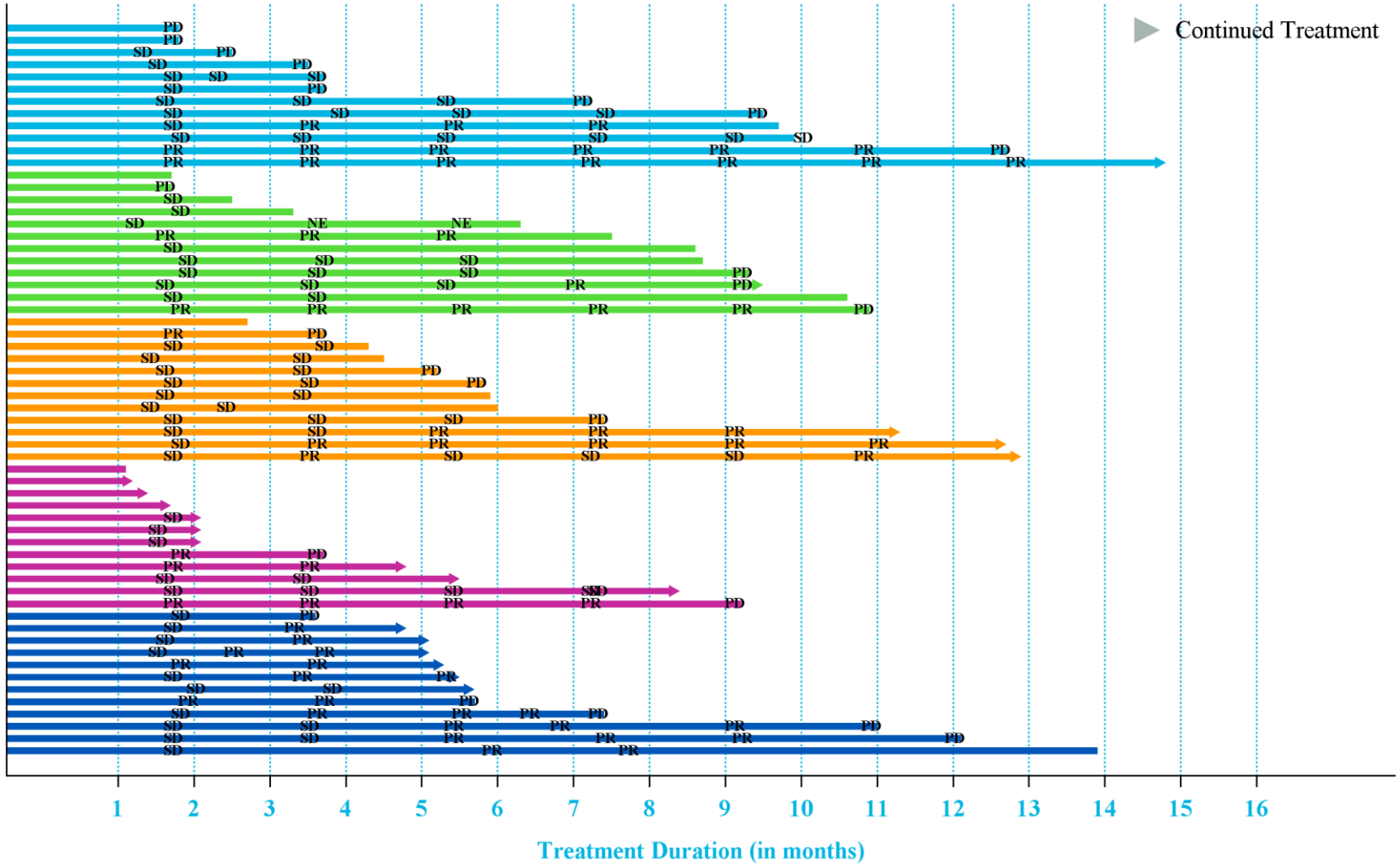
Dose Level	1	0	-1	1a	2a
Unconfirmed ORR, n (%)	83.3% 10/12	25% 2/8	27.3% 3/11	22.2% 2/9	25% 3/12
Confirmed ORR, n (%)	66.7% 8/12	25% 2/8	18.2% 2/11	22.2% 2/9	25% 3/12
DCR, n (%) ≥ 4 cycles	83.3% 10	50% 4	81.8% 9	55.6% 5	58.3% 7

VERASTEM ONCOLOGY

Source: F_TR_WATERFALL.sas Data Cut: 25 APR 25
2 patients excluded from efficacy evaluable population due to no post baseline scan. Change from baseline at each visit is calculated for the lesions that were measured at both baseline and post-baseline visit. One patient in DL1 came off study treatment in Cycle 3, but continued to receive Nab-paclitaxel and gemcitabine and is counted in the efficacy population.

Many Patients in DL1 & DL0 Remain on Treatment with Responses Still Developing

Duration of Treatment for All Patients: Safety Population (N=60)



Dose Level	Treatment Ongoing N=19
2a	1
1a	0
-1	3
0	9
1	6

Response assessment after first PD are not shown.

Note: Subject 0151-008 came off study treatment in Cycle 3, but continued to receive Nab-paclitaxel and gemcitabine and is counted in the efficacy population

Source: Program: F_TR_NADIR_PCHG_SERIES.sas Data Cut: 25 APR 25

Conclusions

- Impressive efficacy signals and a manageable safety profile
  - Dose level 1 selected as the RP2D
  - 10/12 patients in dose level 1 achieved an objective response
  - Preliminary observations suggest increased Nab-paclitaxel dose intensity, along with optimizing avutometinib, defactinib, and gemcitabine correlates with efficacy
  - Most patients poised to exceed historical estimates of mPFS
  - Expansion enrollment underway to 29 patients

VERASTEM ONCOLOGY

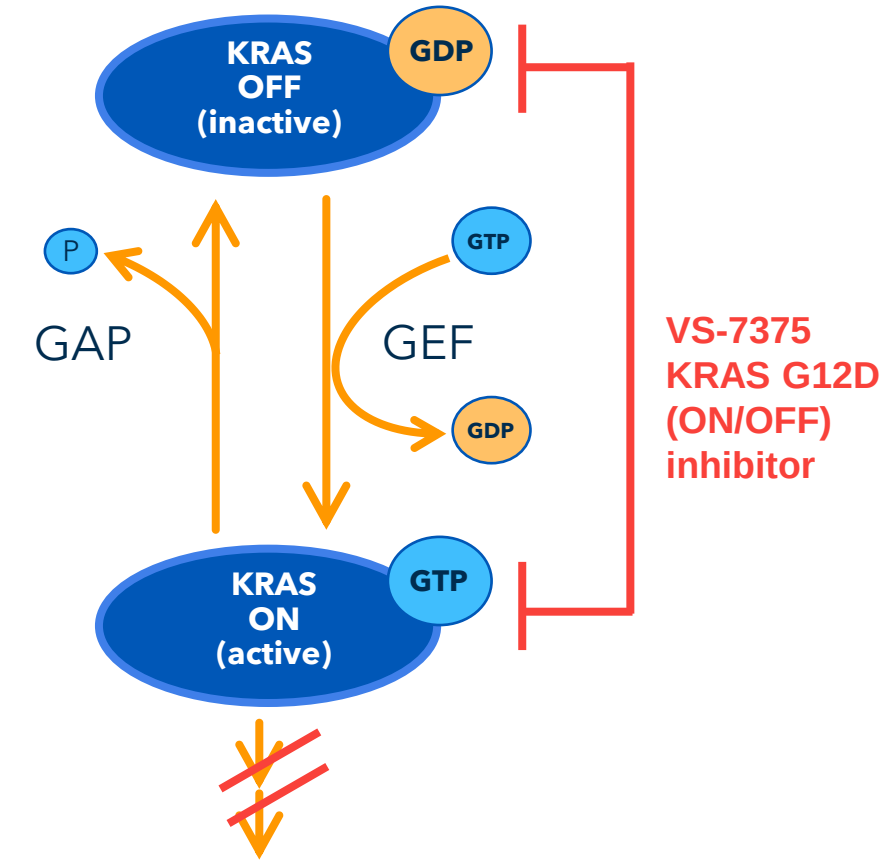
VS-7375: KRAS G12D (ON/OFF) Inhibitor with a Differentiated Preclinical Profile

Jonathan Pachter, PhD
Chief Scientific Officer

VERASTEM™ ONCOLOGY

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



- 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

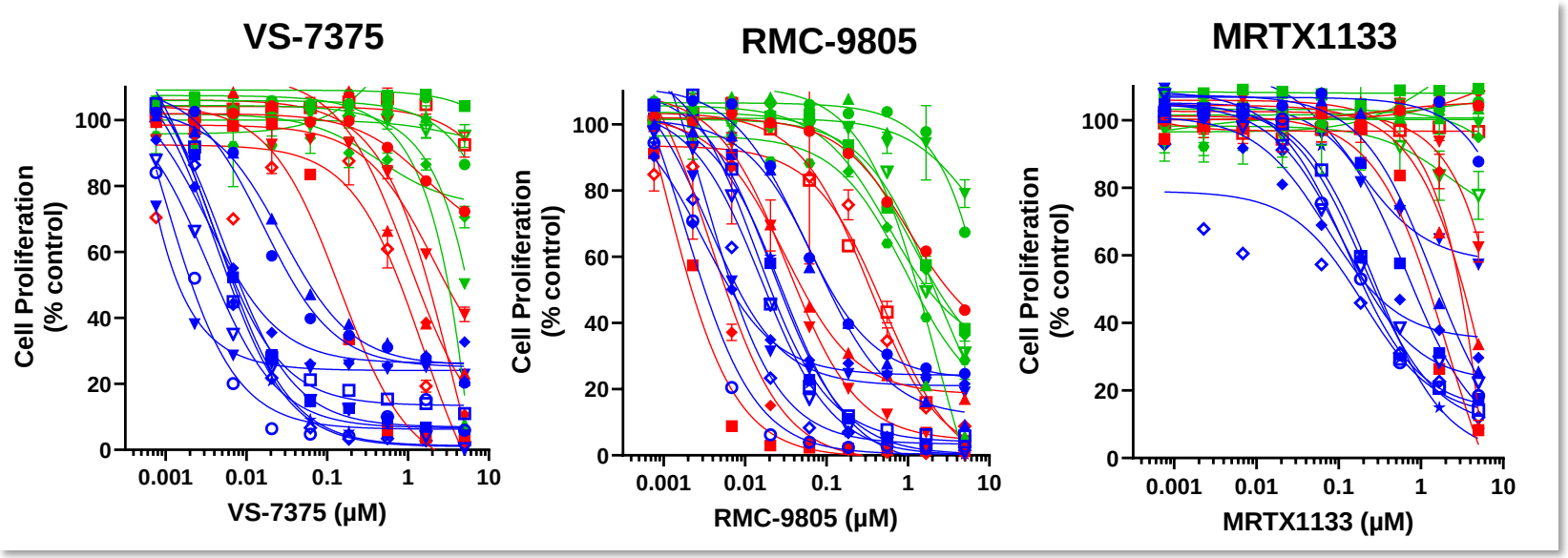
VS-7375 is a dual inhibitor of ON (GTP) and OFF (GDP) states of KRAS G12D*

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

VERASTEM ONCOLOGY

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

VS-7375 Shows Improved KRAS G12D Selectivity and Potency vs Other KRAS G12D inhibitors



KRAS G12D-mutant
- SKLU1 (KRAS G12D)
- AsPC1 (KRAS G12D)
- HPAF-II (KRAS G12D)
- KP4 (KRAS G12D)
- GP2D (KRAS G12D)
- Panc08.13 (KRAS G12D)
- HPAC (KRAS G12D)
- LS513 (KRAS G12D)
- LS180 (KRAS G12D)
- Panc04.03 (KRAS G12D)

KRAS non-G12D-mutant
- MiaPaca2 (KRAS G12C)
- H358 (KRAS G12C)
- H1373 (KRAS G12C)
- H2122 (KRAS G12C)
- H441 (KRAS G12V)
- A549 (KRAS G12S)
- HCT116 (KRAS G13D)

KRAS wild-type
- HT1299 (KRAS wt)
- GAK (KRAS wt)
- SKMEL2 (KRAS wt)
- PC9 (KRAS wt)
- H1975 (KRAS wt)
- A375 (KRAS wt)
- HT29 (KRAS wt)

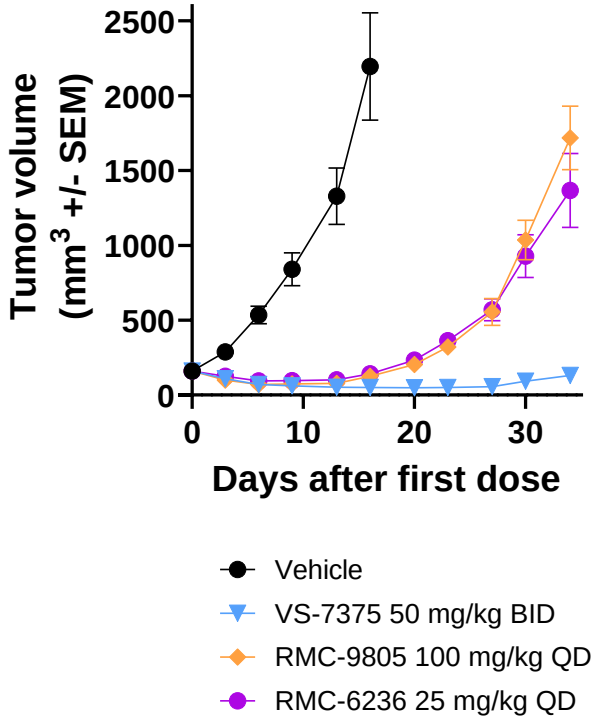
Cell Line	KRAS status	VS-7375 IC50 (nM)	RMC-9805 IC50 (nM)	MRTX1133 IC50 (nM)
SKLU1	G12D	8	7	414
KP4	G12D	2	4	187
GP2D	G12D	2	8	>5000
HPAC	G12D	7	9	156
HPAF-II	G12D	5	18	124
AsPC1	G12D	7	19	248
Panc08.13	G12D	8	26	739
LS513	G12D	7	28	265
LS180	G12D	33	96	>5000
Panc04.03	G12D	63	111	1332
MiaPaca2	G12C	133	3	1052
H358	G12C	1471	6	2277
H1373	G12C	3069	43	>5000
H2122	G12C	>5000	334	>5000
H441	G12V	828	51	2487
A549	G12S	>5000	3337	>5000
HCT116	G13D	756	358	>5000
H1299	wild-type	>5000	1003	>5000
GAK	wild-type	3287	1109	>5000
SKMEL2	wild-type	>5000	1600	>5000
PC9	wild-type	>5000	1986	>5000
H1975	wild-type	>5000	2514	>5000
A375	wild-type	>5000	>5000	>5000
HT29	wild-type	>5000	>5000	>5000

< 65 nM	65-125 nM	> 125 nM

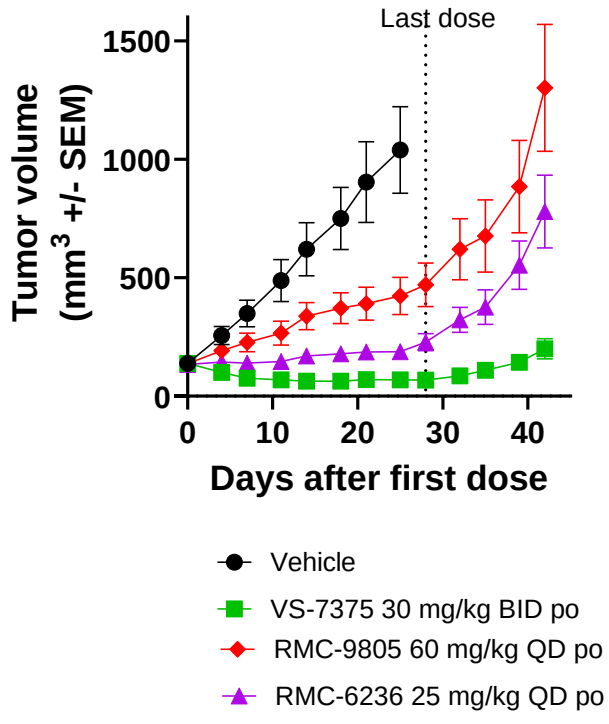
VERASTEM ONCOLOGY

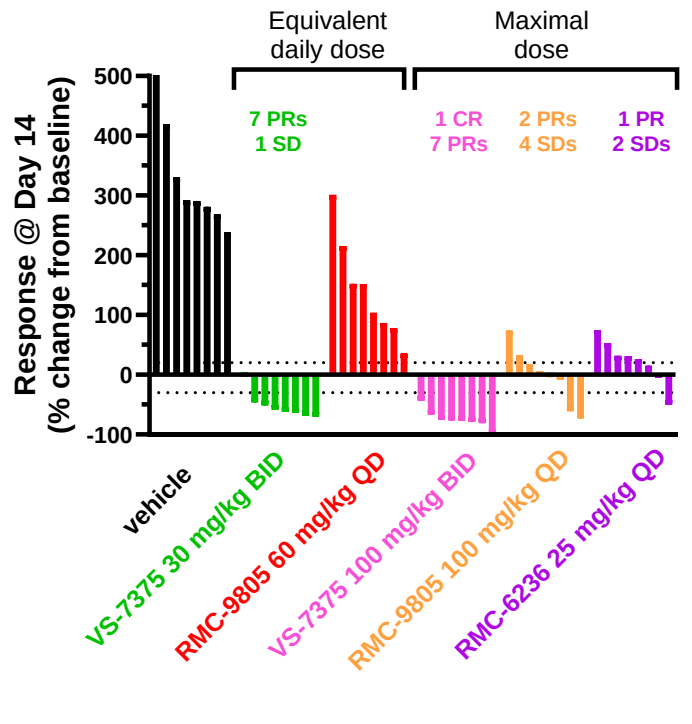
VS-7375 (G12D ON/OFF inhibitor) is More Efficacious than KRAS ON Inhibitors in Reducing Tumor Growth in KRAS G12D Models

KP4 KRAS G12D PDAC model



LS513 KRAS G12D CRC model

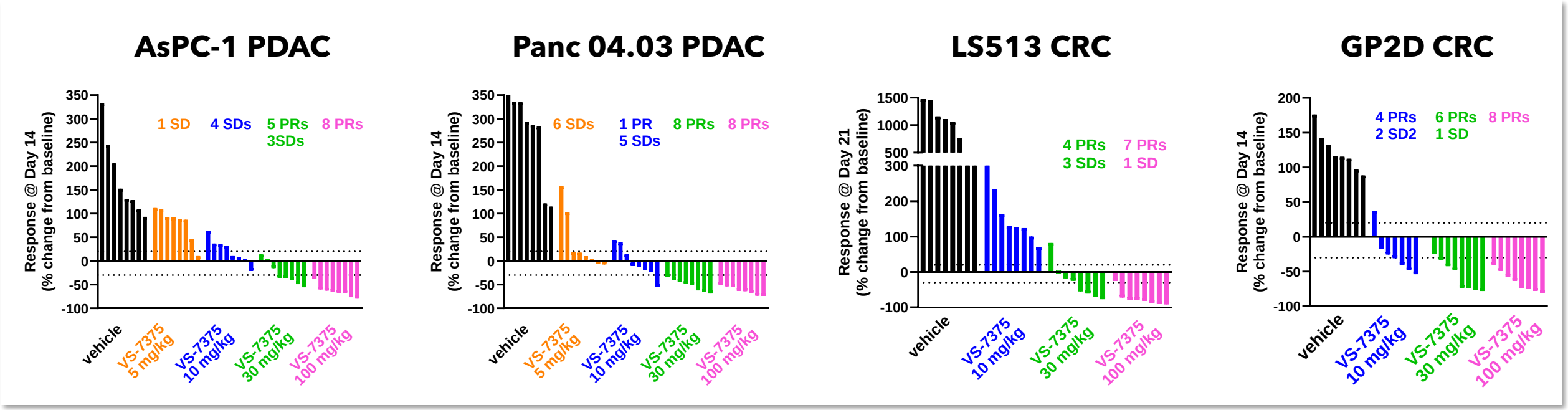




VERASTEM ONCOLOGY

VSTM Data on File.

Oral Administration of VS-7375 Inhibits Tumor Growth in a Dose-Dependent Manner in KRAS G12D models

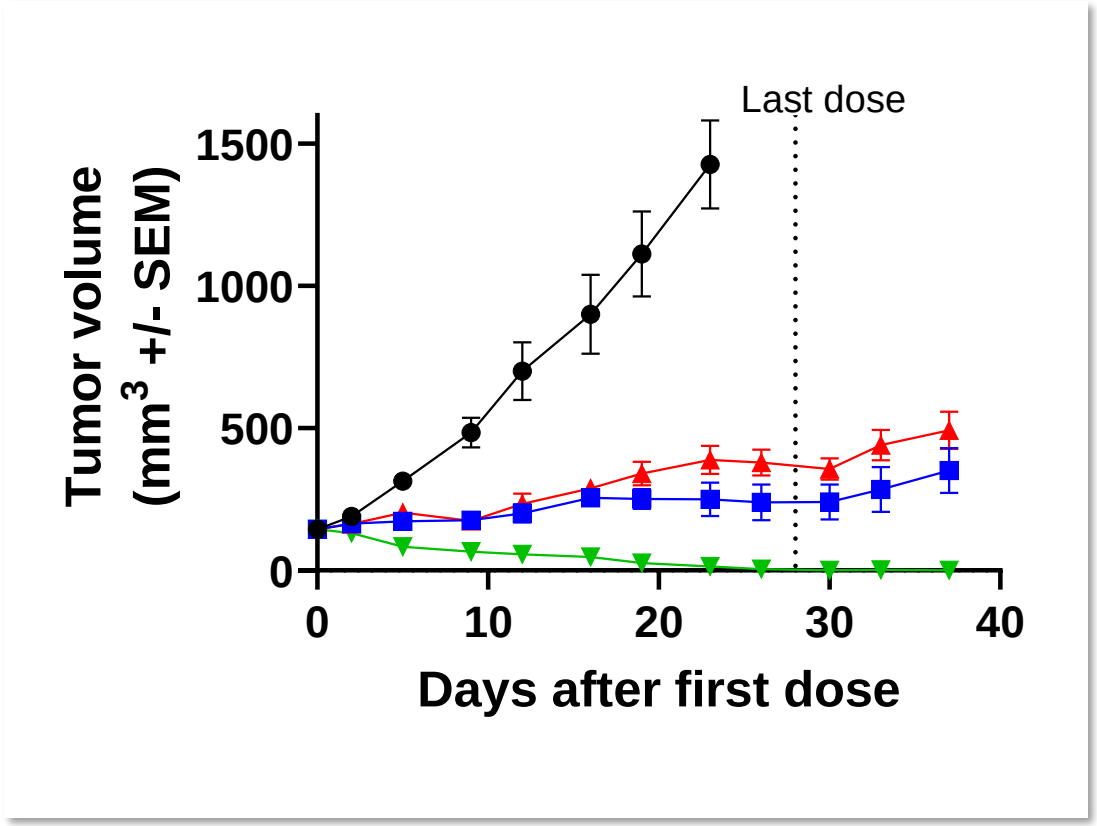


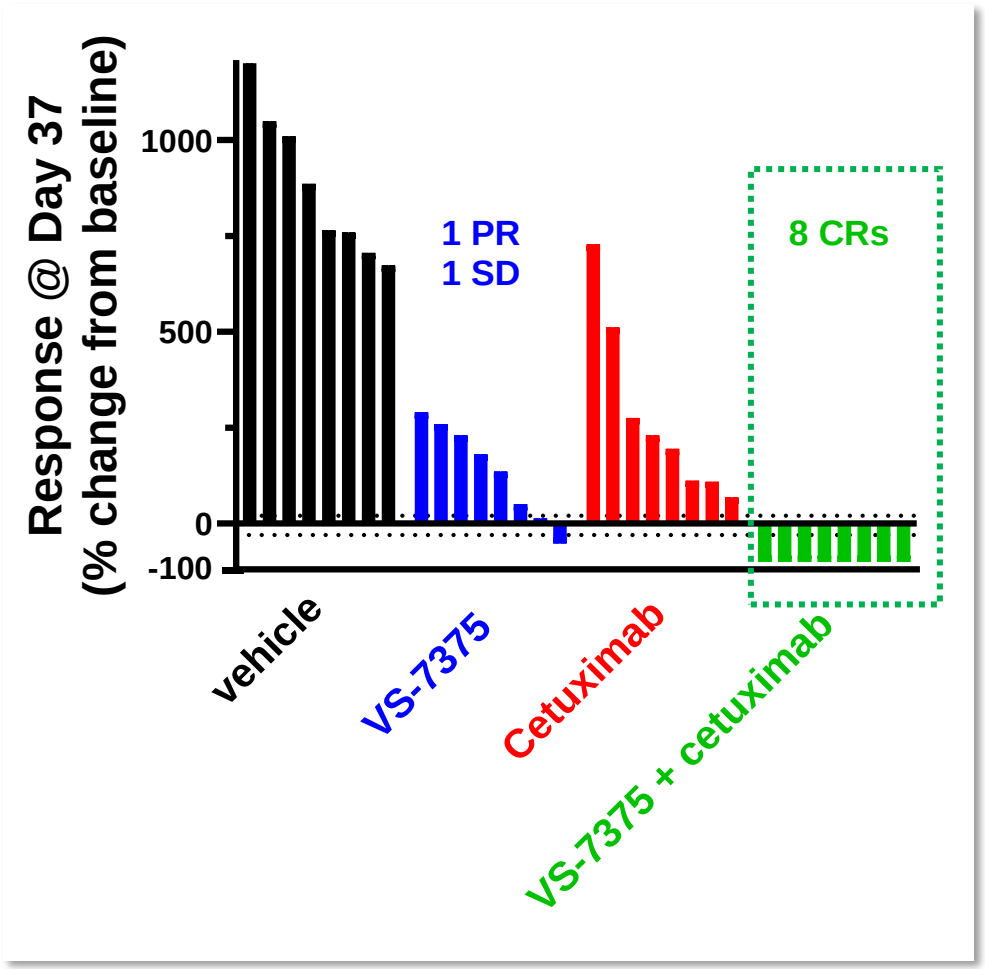
- 10 mg/kg conferred strong tumor regressions in the most sensitive model (GP2D)
- 30 mg/kg conferred strong tumor regressions across all models
- 100 mg/kg conferred partial responses (>30% reduction) in >95% of all mice

VERASTEM ONCOLOGY

Presented at AACR 2024

Addition of Cetuximab with VS-7375 Induces Complete Responses in All Mice in a KRAS G12D Colorectal Cancer Model





LS513 Colorectal Cancer Model

- Vehicle *p.o.*, BID
- VS-7375 10 mg/kg *p.o.*, BID
- Cetuximab 0.25 mg/mouse IP Q3D
- VS-7375 + cetuximab

VERASTEM ONCOLOGY

Presented at AACR 2025

Review of VS-7375 US Phase 1/2a Trial and Supportive Data

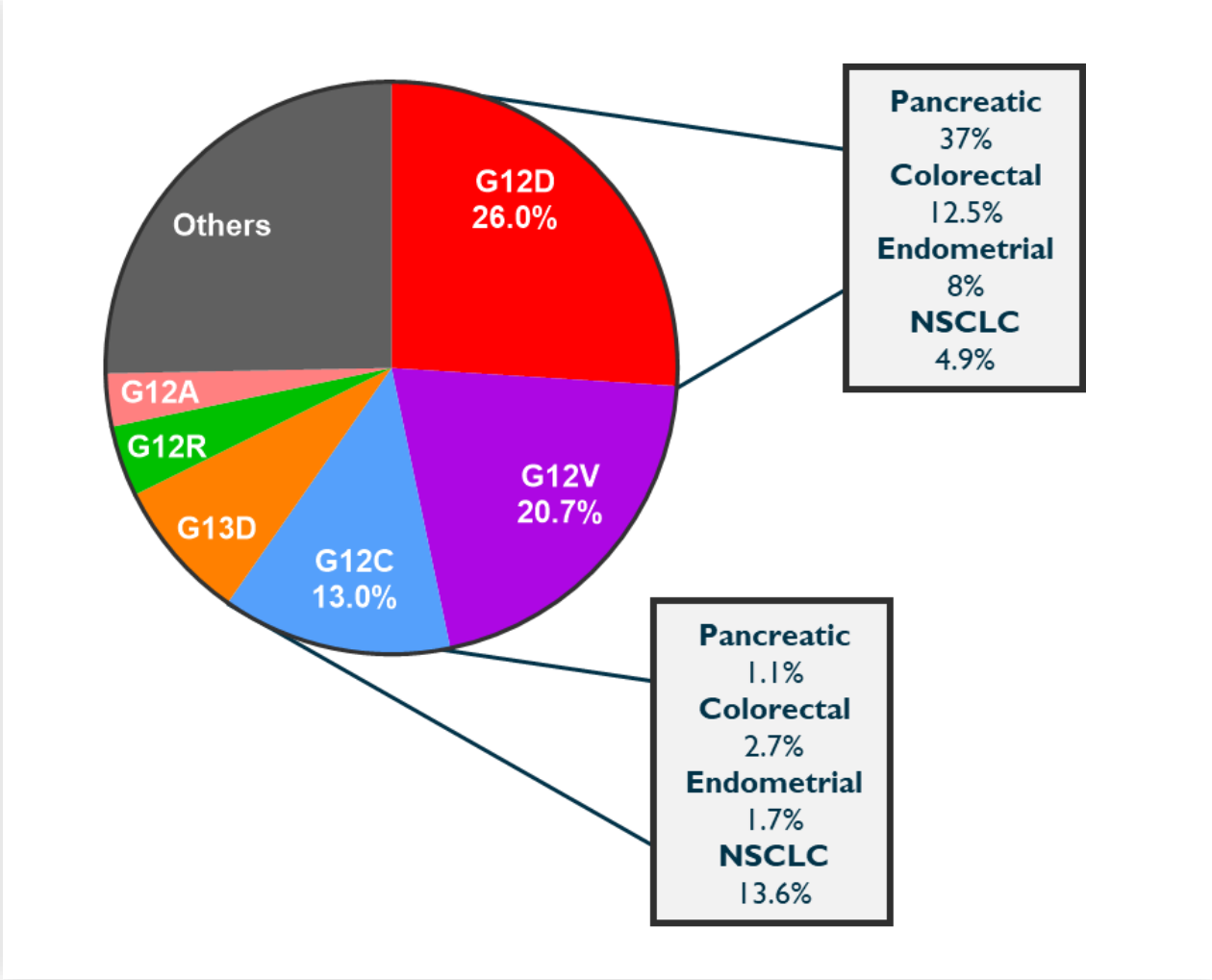
David S. Hong, M.D.
Douglas E. Johnson Endowed Professor
Deputy Chair of the Department of Investigational Cancer Therapeutics [A Phase I Program]
Division of Cancer Medicine
Clinical Medical Director of the Clinical and Translational Research Center (CTRC)
University of Texas M.D. Anderson Cancer Center

Investigator: VS-7375-101 trial

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



VERASTEM ONCOLOGY

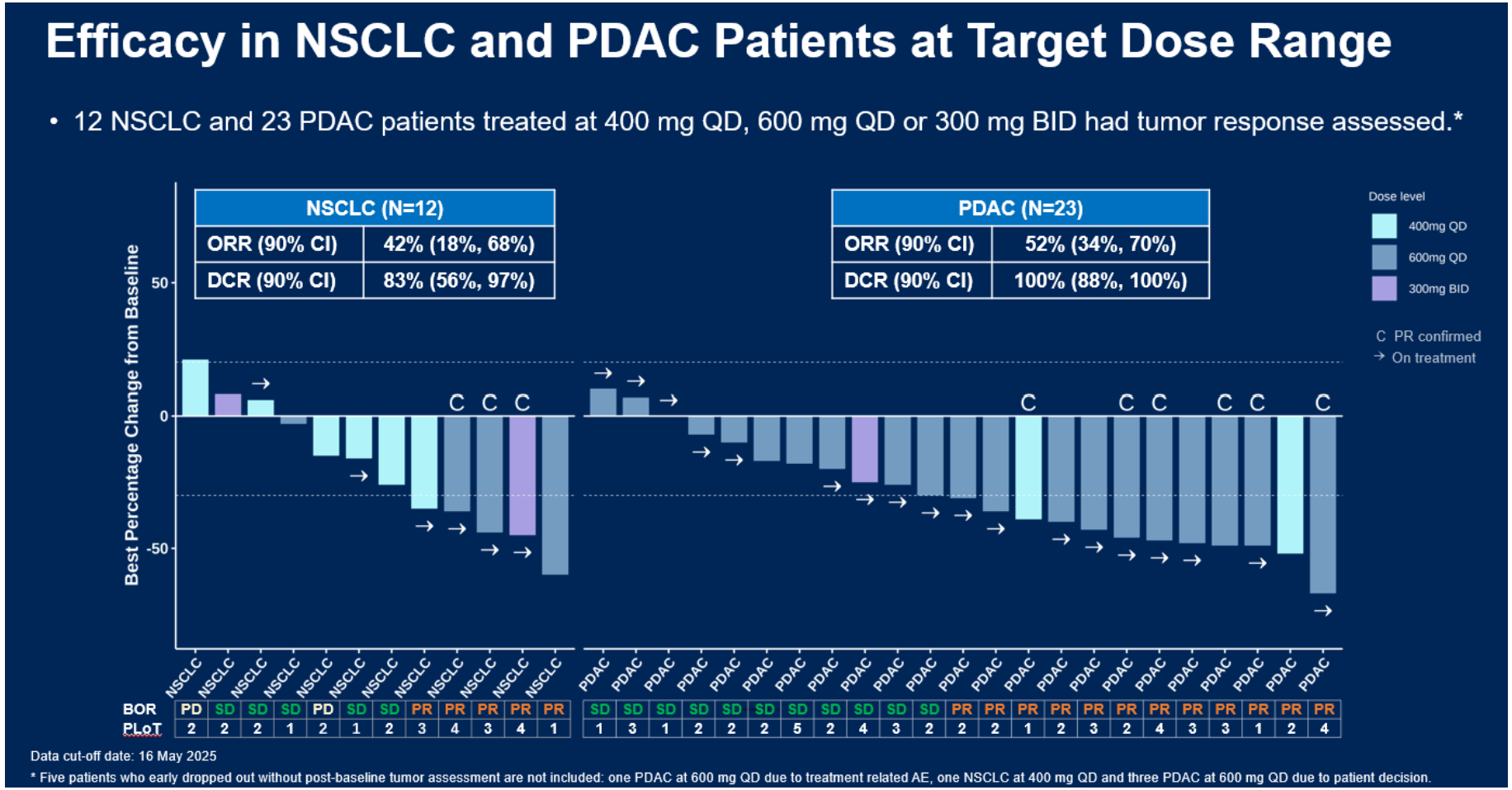
Adapted from Hofmann et al., Cancer Discovery 2022

GFH375 Demonstrated Encouraging Initial Efficacy in Lung and Pancreatic Cancers

42% ORR in NSCLC, 83% DCR

52% ORR in PDAC, 100% DCR

- 62 patients were enrolled in the Phase 1 monotherapy portion of the study in China
- Oral doses ranging from 100 to 900 mg daily
- Patients with advanced KRAS G12D mutant solid tumors
- Previously treated with standard therapies



VERASTEM ONCOLOGY

Source: GenFleet Therapeutics ASCO 2025 Rapid Oral Presentation June 2, 2025; A First-in-human Phase I/II Study of GFH375, a Highly Selective and Potent Oral KRAS G12D Inhibitor in Patients in KRAS G12D Mutant Advanced Solid Tumors

Initial AE Profile Demonstrates that GFH375 is Tolerable with a Manageable Safety Profile

Treatment Related Adverse Events (TRAEs)

- GFH375 is tolerable with a manageable safety profile
- No DLT observed at all tested dose levels.
- No treatment related death.
- Most frequent G3/4 TRAEs were neutrophil count decreased (8%) and diarrhea (5%).

	All Patients (N=62)		400mg QD + 600mg QD + 300 mg BID (N=49)	
	Any Grade	≥ Grade 3	Any Grade	≥ Grade 3
Any TRAE	62 (100%)	18 (29%)	49 (100%)	15 (31%)
TRAEs occurring in ≥ 20% of patients, n(%)				
Diarrhea	43 (69%)	3 (5%)	34 (69%)	2 (4%)
Nausea	42 (68%)	0 (0%)	34 (69%)	0 (0%)
Vomiting	38 (61%)	1 (2%)	29 (59%)	1 (2%)
Anemia	32 (52%)	0 (0%)	26 (53%)	0 (0%)
Decreased appetite	24 (39%)	0 (0%)	20 (41%)	0 (0%)
Neutrophil count decreased	21 (34%)	5 (8%)	17 (35%)	4 (8%)
White blood cell count decreased	20 (32%)	1 (2%)	15 (31%)	1 (2%)
AST increased	20 (32%)	1 (2%)	16 (33%)	0 (0%)
Hypoalbuminaemia	17 (27%)	0 (0%)	12 (24%)	0 (0%)
Asthenia	17 (27%)	1 (2%)	15 (31%)	1 (2%)
ALT increase	15 (24%)	0 (0%)	13 (27%)	0 (0%)
TRAEs leading to dose reduction, n(%)	7 (11%)	3 (5%)	5 (10%)	1 (2%)
TRAEs leading to dose interruption, n(%)	13 (21%)	7 (11%)	9 (18%)	6 (12%)
TRAEs leading to treatment discontinuation, n(%)	2 (3%)#	2 (3%)	2 (4%)	2 (4%)
Treatment Related SAEs, n(%)	6 (10%)	5 (8%)	5 (10%)	4 (8%)

Percentage (%) is rounded to the nearest whole number.
Time from first dosing to safety data cutoff is at least 26 days. Median time on treatment was 6.4 weeks (range: 0.1-38.0).
The two patients discontinued treatment due to G3/4 hepatic function abnormality, both were treated at 600 mg QD.

Data cut-off date: 31 Mar 2025

Abbreviations: ALT, alanine transaminase; AST, aspartate transferase; DLT, dose-limiting toxicity; SAE, serious adverse event; TRAE, treatment related adverse event.

VERASTEM ONCOLOGY

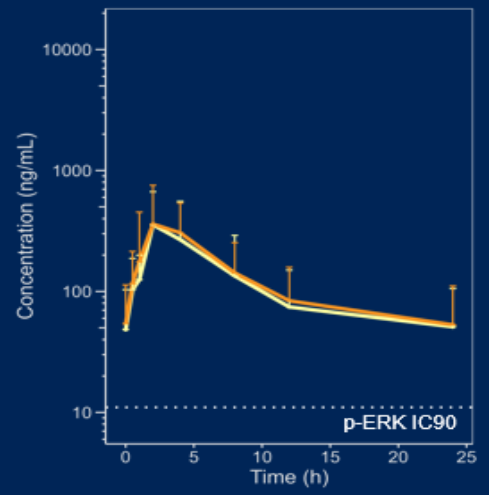
Source: GenFleet Therapeutics ASCO 2025 Rapid Oral Presentation June 2, 2025; A First-in-human Phase I/II Study of GFH375, a Highly Selective and Potent Oral KRAS G12D Inhibitor in Patients in KRAS G12D Mutant Advanced Solid Tumors

Convenient Once Daily Dosing Achieves Trough Concentrations 3x the IC_{90} for pERK inhibition in KRAS G12D cell lines

Pharmacokinetics

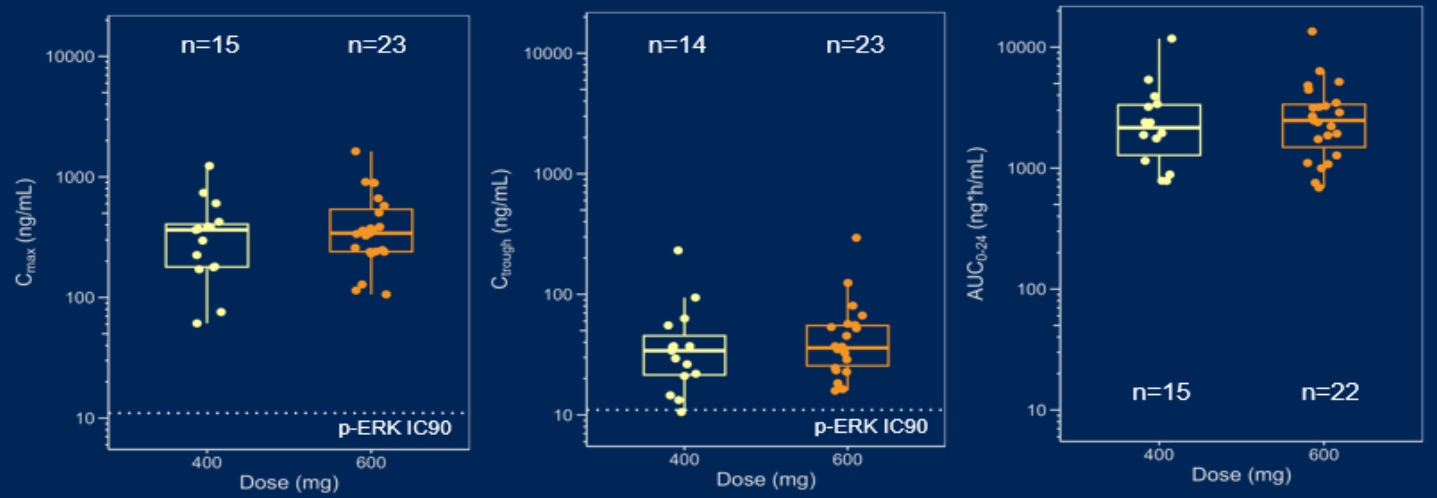
- Following a single dose of GFH375, mean $t_{1/2}$ ranged from 16.3-21.1 hours, compatible with QD dosing.
- 400 mg and 600 mg QD can maintain the mean trough concentration three times above the IC_{90} for inhibiting p-ERK in AsPC-1 cells.
- 600 mg QD was recommended as the phase II dose.

GFH375 24-h concentrations at steady state



Error bar: standard deviation

Exposure of GFH375 at steady state (C_{max}, C_{trough}, AUC_{0-24})

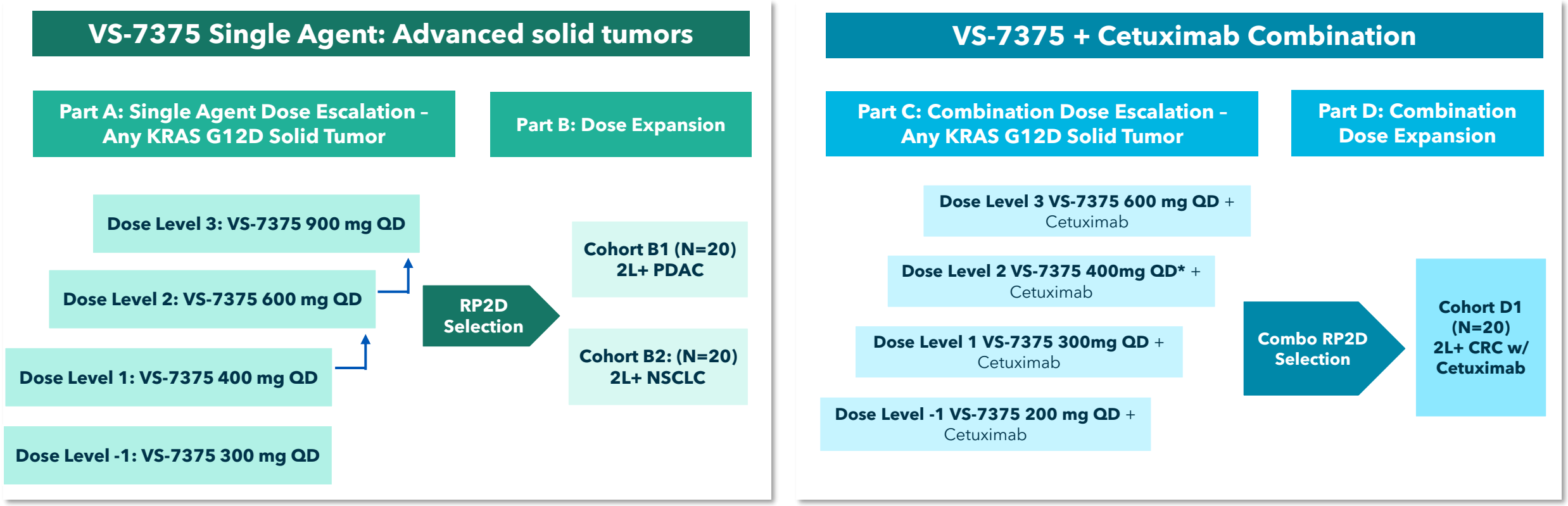


Parameters: C_{max} - maximum concentration; C_{trough} - trough concentration; AUC_{0-24} - area under the curve from 0h to 24h

VERASTEM ONCOLOGY

Source: GenFleet Therapeutics ASCO 2025 Rapid Oral Presentation June 2, 2025; A First-in-human Phase I/II Study of GFH375, a Highly Selective and Potent Oral KRAS G12D Inhibitor in Patients in KRAS G12D Mutant Advanced Solid Tumors

Verastem Phase 1/2a Study Includes Monotherapy Expansion Cohorts in PDAC and NSCLC and Cetuximab Combination in CRC



The study will evaluate dosing with meals and utilize prophylactic anti-emetics

VERASTEM ONCOLOGY

*Anticipated starting dose level for cetuximab combination once the monotherapy clears 600 mg dose level

Conclusions

- **With promising early results, VS-7375 has the potential to meet a significant unmet need in solid tumor cancers**
  - The unmet need is high: 61,000 metastatic KRAS G12D patients are diagnosed every year across pancreatic, lung, colorectal and other solid tumor cancers
- **In the initial Phase 1 study in China, GFH375/VS-7375 demonstrated:**
  - Pharmacokinetics showed good oral bioavailability and a half-life that supports once daily dosing
  - Proof of concept in humans with encouraging initial data in pancreatic & lung cancers
- **Potential for unique combinations with VS-7375, including:**
  - Avutometinib (RAF/MEKi)
  - Defactinib (FAKi)

Key questions remain for the G12D inhibitor space

- What will be the impact of ON-selective, ON/OFF dual or OFF-selective KRAS inhibitors on efficacy/safety profile?
- Which asset has brain penetration for potential treatment of lung mets?

VERASTEM ONCOLOGY

Clinical Development Plans and Timelines

John Hayslip, M.D.
Chief Medical Officer

VERASTEM™ ONCOLOGY

Opportunity for Avutometinib Plus Defactinib with SOC Chemo to Reshape Expectations in Advanced Pancreatic Cancer

- **Our Opportunity:**
  - A novel regimen for metastatic PDAC, with most patients achieving objective responses

- **Target Product Profile:**
  - **Efficacy:** Preliminary efficacy suggests this combination may be amongst the most efficacious treatments in development for newly diagnosed metastatic PDAC
  - **Safety/Tolerability:** GI and heme effects may be increased compared to traditional Gem/Nab, though manageable for most patients to date
  - Convenient regimen without increased chemo chair time

Clinical Focus:

•Phase 2 RAMP 205 IL mPDAC

•Expand to Simon's 2-stage design: expand to 29 patients

•Phase 3 study in IL PDAC

•Plan to launch Phase 3 pivotal study in 1L PDAC in 2026

•Additional Expansion Opportunities:

•Evaluate two potential treatment indications:

•Newly diagnosed metastatic PDAC

•Newly diagnosed borderline resectable PDAC

•Plan for further regulatory interactions to align on plans

•Continue to evaluate combination strategies with current pipeline and external assets to improve outcomes in mPDAC

VERASTEM ONCOLOGY

Emerging VS-7375 KRAS G12D (ON/OFF) Inhibitor Clinical Findings and Planned Next Steps

- **Our Opportunity:**

High Responses Rates | **Deeper Regressions**

- **Target Product Profile:**
  - Once-daily oral administration
  - Highly potent and selective for KRAS G12D with binding to ON/OFF states
  - Efficacy: potential for best-in-class response rates and durability
  - Safety: MTD not yet declared and potential to further improve the GI profile with prophylaxis

Clinical Focus:

- **US Trial: VS-7375-101 Phase 1/2a**
  - First three sites initiated in May 2025
  - Initiating enrollment with an efficacious dose level – 400 mg QD
  - Planned expansion cohorts in PDAC and NSCLC
  - Planned expansion cohort with cetuximab in CRC
- **Additional Combinations and Tumor Types**
  - Planning to evaluate VS-7375 in additional combinations and tumor types
    - Newly diagnosed PDAC
    - Newly diagnosed NSCLC
    - Additional KRAS G12D mutated tumor types including recurrent endometrial cancer

VERASTEM ONCOLOGY

Closing Remarks

Daniel Paterson
President & CEO

VERASTEM ONCOLOGY

Delivering on Our Multi-Faceted Approach to Advance Novel Therapies for RAS/MAPK Pathway Driven Cancers

RAMP 205

- ~180,000 PDAC patients globally with 5-year relative survival of 13.3%
- Avutometinib plus defactinib offer more complete blockade of signaling that drives growth of RAS/MAPK pathway-dependent tumors
- Dose level 1 demonstrated ORR of 83% (10/12) in frontline mPDAC with a manageable side effect profile
- Plans to launch Phase 3 study in 1L mPDAC in 2026

Address Unmet Need

Differentiated Treatment

Benefits over Standard of Care

Next Steps

VS-7375

- 61,000 metastatic KRAS G12D diagnoses annually across pancreatic, lung, colorectal and other solid tumor cancers
- Highly potent and selective oral KRAS G12D inhibitor capable of targeting both ON and OFF states to maintain inhibition, aiming for maximum efficacy and more durable benefit
- Demonstrated oral bioavailability and ORR of 52% in pancreatic and 43% in lung cancers; manageable side effect profile
- Activating sites for Phase 1/2a trial in advanced solid tumors in the U.S.

VERASTEM ONCOLOGY

Q&A

VERASTEM ONCOLOGY