Exhibit 99.1

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

FORM 8-K
CURRENT REPORT

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

Date of report (Date of earliest event reported): **October 4, 2022**

Verastem, Inc.

(Exact Name of Registrant as Specified in Charter)

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

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

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

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

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

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

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

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

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

Emerging growth company ☐

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

Item 7.01. Regulation FD Disclosure

On October 4, 2022, Verastem, Inc. posted its corporate presentation on its website, a copy of which is furnished hereto as Exhibit 99.1 to this Current Report on Form 8-K.

Item 9.01. Financial Statements and Exhibits

Exhibit No.	Description
99.1	Corporate Presentation, dated October 4, 2022
104	Cover Page Interactive Data File (formatted in Inline XBRL)

SIGNATURES

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

VERASTEM, INC.

Dated: October 4, 2022

By: /s/ Brian M. Stuglik
Brian M. Stuglik
Chief Executive Officer

Corporate Presentation

October 2022

Safe Harbor Statement

This presentation includes forward-looking statements about, among other things, Verastem Oncology's programs and product candidates, including anticipated regulatory submissions, approvals, performance and potential benefits of Verastem Oncology's product candidates, that are subject to substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Applicable risks and uncertainties include the risks and uncertainties, among other things, regarding: the success in the development and potential commercialization of our product candidates, including defactinib and other compounds in combination with VS-6766; the occurrence of adverse safety events and/or unexpected concerns that may arise from additional data or analysis or result in unmanageable safety profiles as compared to their levels of efficacy; or our ability to obtain, maintain and enforce patent and other intellectual property protection for our product candidates.

Other risks and uncertainties include those identified under the heading "Risk Factors" in the Company's Annual Report on Form 10-K for the year ended December 31, 2021, as filed with the Securities and Exchange Commission (SEC) on March 28, 2022, 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.

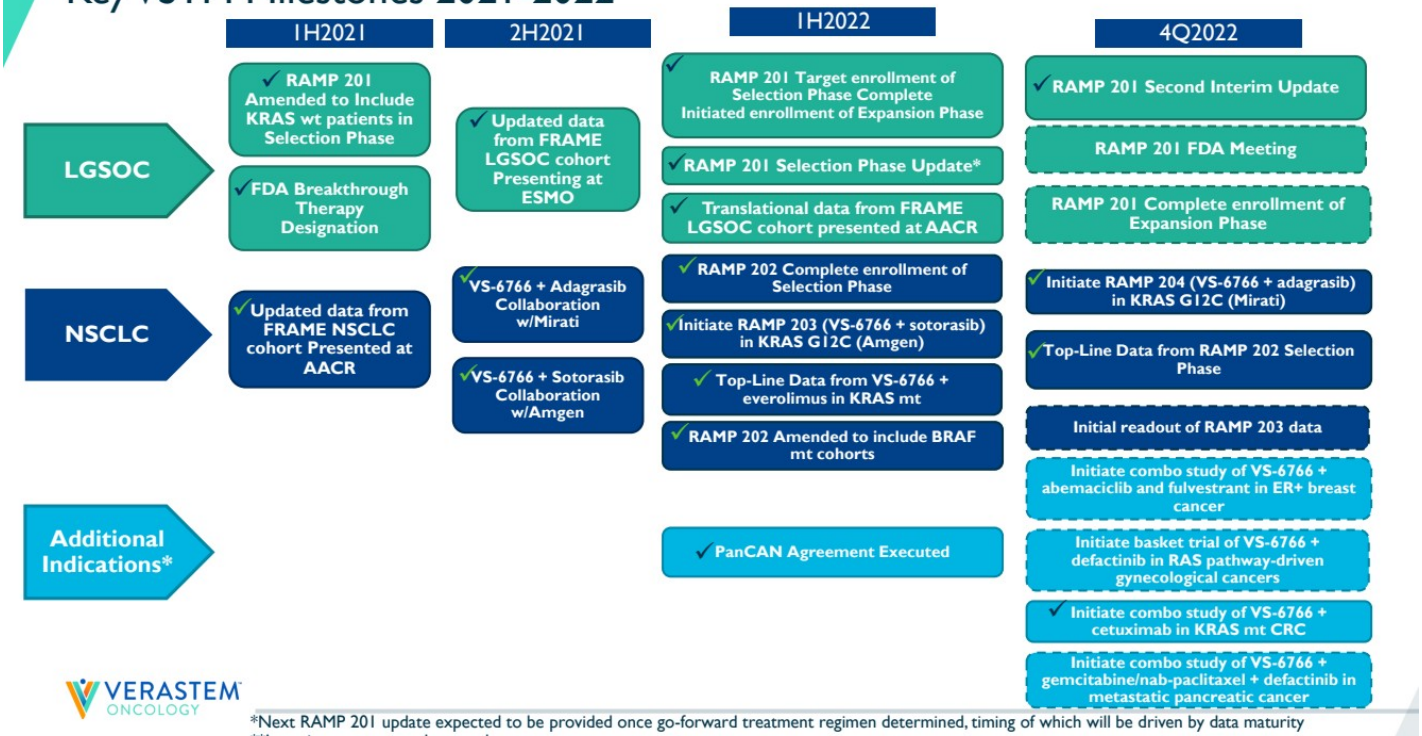
We are a biopharmaceutical company committed to developing and commercializing new medicines for patients battling cancer

Verastem Oncology
Well Positioned to Capitalize on Growth Opportunities

Lead clinical program has best-in-class potential	VS-6766 (RAF/MEK clamp) and defactinib (FAK inhibitor) are clinically active against RAS mutant cancers
Rapid development path to market	**FDA Breakthrough Therapy Designation in LGSOC;** Registration-directed trial initiated in 4Q 2020 in low-grade serous ovarian cancer (LGSOC)
Significant downstream market opportunity and blockbuster potential	**30% of all human cancers are driven by mutations in RAS**; VS-6766 combinations potentially broadly applicable across a variety of tumor types. **Clinical collaborations with Amgen & Mirati** evaluating the combinations of VS-6766 with sotorasib & adagrasib, respectively, in KRAS G12C mutant NSCLC supported by strong pre-clinical rationale **Multiple clinical opportunities** across RAS pathway-driven cancers based on preclinical data
Patent Update	Recently issued intermittent dosing IP for both VS-6766 alone and VS-6766 + defactinib extends patent coverage up to 2038 and 2040
Strong balance sheet	Up to $150 million of non-dilutive funding available from new credit facility Cash balance of $94.3 million as of June 30, 2022 & $110.4 million as of August 31, 2022 Company ended Quarter 2 2022 with $19.6 million non-GAAP operating expenses

* Q2 2022 GAAP operating expenses - $21.4M minus Q2 2022 stock compensation - $1.8M = $19.6M Q2 2022 non-GAAP operating expenses

Key VSTM Milestones 2021-2022



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

VS-6766 is a Differentiated, Potentially Best-in-Class Asset Applicable Across Multiple Patient Populations

- Unique RAF/MEK clamp mechanism of action
- Novel intermittent dosing schedule; convenient oral regimen
- Breakthrough Therapy Designation in recurrent low-grade serous ovarian cancer
- Potential best-in-class safety & tolerability profile relative to marketed MEK inhibitors, with potential for combinability with agents from multiple target classes
- Promising signals of clinical activity in various RAS-driven cancers, including in patients whose tumors previously progressed on other MEK inhibitors
- Preclinical anti-proliferative activity across multiple MAPK pathway alterations (e.g. KRAS, NRAS, BRAF, NF1 mt) and multiple solid tumor indications
- Strong preclinical combination data with other agents targeting RAS pathway and parallel pathways

Robust Clinical Program: VS-6766 in multiple combinations across RAS/MAPK pathway-driven tumors

INDICATION	REGIMEN	STUDY NAME	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	CLINICAL COLLABORATION WITH
LGSOC[1,2]	VS-6766 +/- defactinib	RAMP 201					
R/R LGSOC	VS-6766 + defactinib	FRAME					
R/R endometrioid cancer (RAS/RAF mt)	VS-6766 + defactinib	FRAME					
Gynecological Cancers (RAS Pathway-driven)[4]	VS-6766 + defactinib	IST					
Mesonephric[4]	VS-6766 + defactinib	IST					
R/R NSCLC (BRAF mt)	VS-6766 + defactinib	RAMP 202					
R/R NSCLC (KRAS G12C mt)	VS-6766 + sotorasib	RAMP 203					AMGEN
R/R NSCLC (KRAS G12C mt)[3]	VS-6766 + adagrasib	RAMP 204					MIRATI THERAPEUTICS
Pancreatic Ductal Adenocarcinoma	VS-6766 + gemcitabine/nab-paclitaxel + defactinib	RAMP 205					PANCREATIC CANCER ACTION NETWORK
R/R NSCLC (KRAS mt)	VS-6766 + everolimus (mTORi)	IST					
R/R Colorectal Cancer	VS-6766 + cetuximab (EGFRi)	IST					
ER+ Breast Cancer	VS-6766 + abemaciclib + fulvestrant	IST					

[1] FDA Breakthrough Therapy Designation
[2] Registration-directed trial
[3] In Startup
[4] Preclinical studies underway, ph. 2 investigator-sponsored trials in preparation

Key Financial Statistics

As of and for the quarter ended June 30, 2022

Cash, cash equivalents & investments	$94.3M ($110.4M as of August 31, 2022)
Non-GAAP Operating Expenses	$19.6M
Shares Outstanding	187.6M (210.0M as of August 31, 2022)

Oxford Finance LLC Credit Facility

Loan Tranches		Event
A	$25M	At closing
B	$15M	COPIKTRA PTCL approval in U.S. or $50M equity proceeds
C	$25M	LGSOC accelerated or full approval
D	$35M	$50M product revenue on six months trailing basis
E	$50M	Lender discretion
Total	$150M	

Interest rate: floating rate, which is subject to a floor and a cap; 5% final payment charge, and loan subject to 1-3% early payment fee
Term: 5 Years; Interest only two years initially, extendable up to four years based on achievement of milestones
Financial covenants: None

* Q2 2022 GAAP operating expenses - $21.4M minus Q2 2022 stock compensation - $1.8M = $19.6M Q2 2022 non-GAAP operating expenses

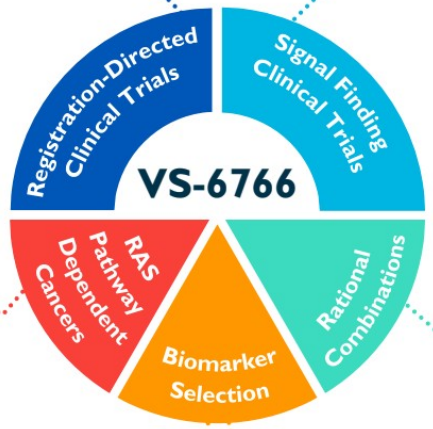
VS-6766 RAF/MEK Clamp Program Overview

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

High Priority Registration Indication

Registration-Directed Trial Initiated in 4Q20

- LGSOC[1,2] (RAMP 201)



Key Signal Finding

- VS-6766 + G12Ci KRAS G12C mt NSCLC[2] (RAMP 203-sotorasib) & (RAMP 204-adagrasib)
- BRAF mt (V600E & non V600E) NSCLC[1,2] (RAMP 202)
- Pancreatic[2]
- RAS/RAF mt endometrioid[1]
- Uveal Melanoma[2]
- VS-6766 + everolimus KRAS mt NSCLC[1,2]
- VS-6766 + cetuximab KRAS mt CRC[2]
- VS-6766 + abemaciclib and fulvestrant in ER+ breast cancer

RAS Pathway Dependent Cancers

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

Biomarker Selection

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

Rational Combinations

- G12Ci[1,2]
- G12Di[2]
- Anti-EGFR[2]
- Everolimus[1,2]
- CDK4/6 inhibitor[2]
- Anti-PD-1[1,2]
- Chemotherapy[2]

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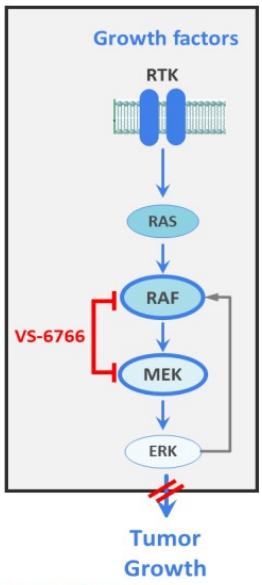
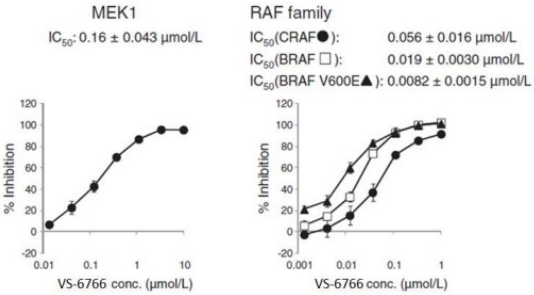
[1] Supported by clinical data

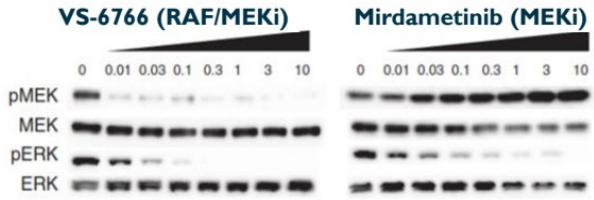
[2] Supported by preclinical data

VS-6766 is a Unique Small Molecule RAF/MEK Clamp



- VS-6766 inhibits MEK, BRAF & CRAF by trapping these molecules in inactive complexes
- MEK inhibitors paradoxically induce MEK phosphorylation (pMEK) by relieving ERK-dependent feedback inhibition of RAF
- By inhibiting RAF phosphorylation of MEK, VS-6766 has advantage of not inducing pMEK
- VS-6766 inhibits ERK signaling more completely; may confer enhanced therapeutic activity

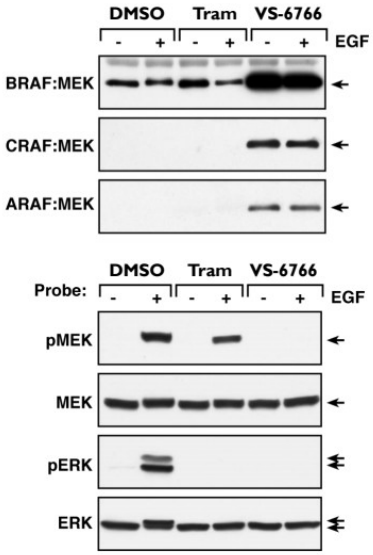


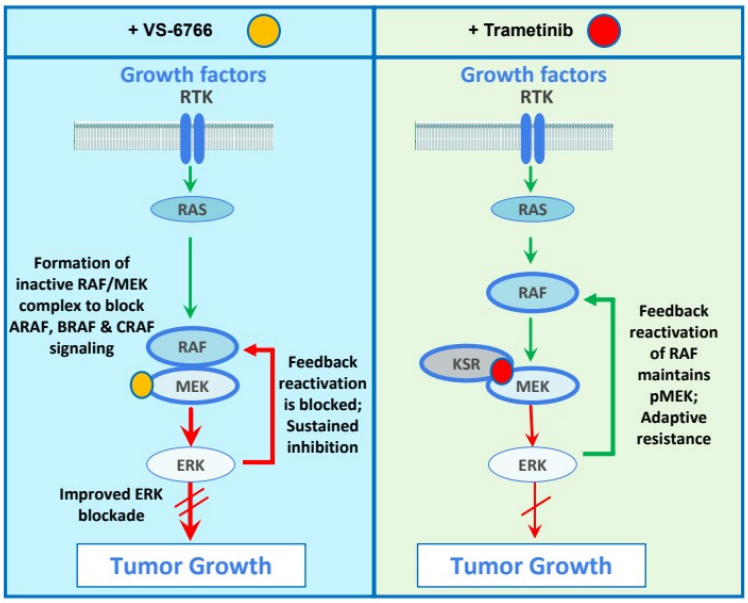


References: Ishii et al., *Cancer Res*, 2013; Lito et al., *Cancer Cell*, 2014

VS-6766 is a Unique RAF/MEK Clamp which Induces Inactive Complexes of MEK with ARAF, BRAF & CRAF

Contrasting mechanism of action vs. trametinib





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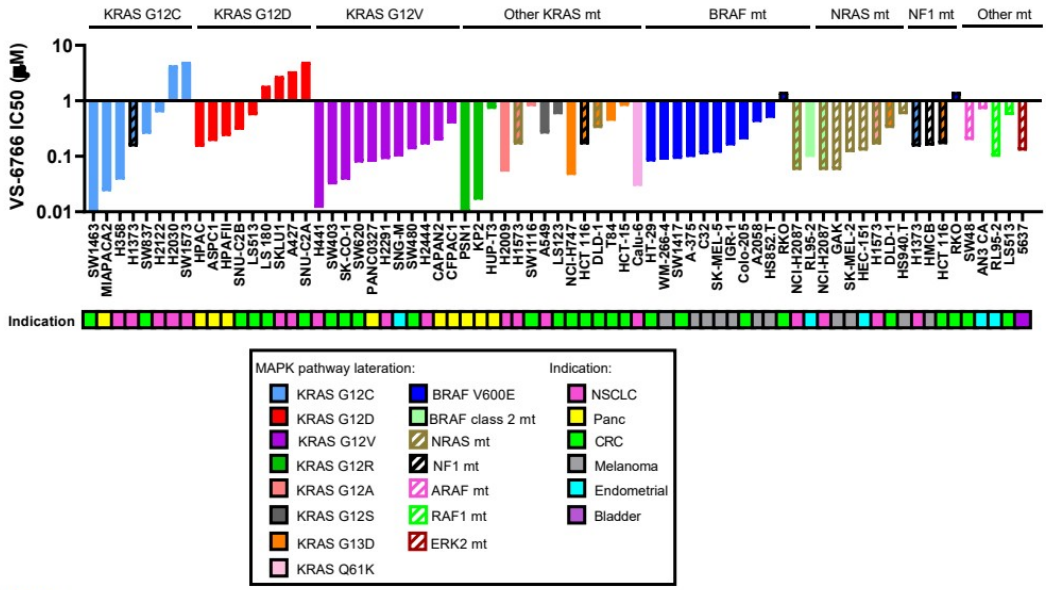
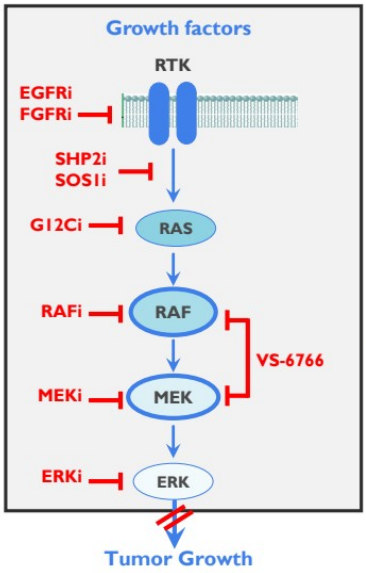
Deborah Morrison unpublished

VS-6766 Inhibits Cell Proliferation Across Multiple RAS/MAPK Pathway Alterations and Multiple Solid Tumor Histologies



Reference: Adapted from Pachter *RAS-Targeted Drug Discovery*, Sep 2021 3D proliferation assay

Vertical Blockade: Establishing VS-6766 as the Backbone of Therapy for RAS/MAPK Pathway-Driven Tumors



- **Current Challenges**
  - Blocking any single target in the pathway is insufficient for maximum depth and duration of anti-tumor efficacy
    - e.g., SHP2i, KRAS-G12Ci, RAFi, MEKi, ERKi
  - Vertical blockade concept is now well established
    - Necessary to block more than 1 target in the pathway
  - Many of these agents (e.g., SHP2i, MEKi) have poor tolerability as monotherapy and in combination

- **Solutions offered by VS-6766**
  - Vertical blockade (RAF and MEK blockade) in a single drug
  - Potential best-in-class tolerability with recommended twice weekly dosing regimen
    - Should enable tolerable combinations
  - Compelling synergy data (preclinical) for VS-6766 combinations (e.g., with KRAS-G12C inhibitors) supporting clinical combinations

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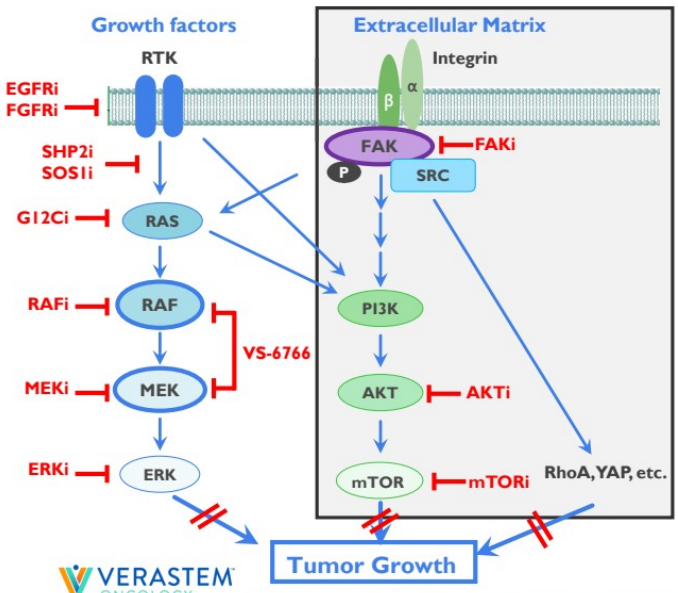
References: [1] Chen, *Mol Cancer Res* 2018; [2] Banerji, BTOG Dublin, Jan 23, 2019

Parallel Pathway Inhibition: Establishing VS-6766 as the Backbone of Therapy for RAS/MAPK Pathway-Driven Tumors



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

- **Solutions offered with VS-6766**
  - Good tolerability with twice weekly VS-6766 opens up intermittent dosing options for combinations
  - Compelling preclinical synergy data with VS-6766 in combination with several key anti-cancer agents
  - RP2D established for VS-6766 + defactinib and for VS-6766 + mTORi (everolimus) with twice weekly regimen

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

Favorable Tolerability Profile with Novel Intermittent Dosing Regimen

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

	VS-6766 monotherapy Daily at MTD N=6 28-day cycle	RP2D VS-6766 monotherapy 4mg twice weekly N=26 28-day cycle	RP2D (VS-6766 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%)

Summary of FRAME Safety Profile

Most Adverse Events (AE) were Grade 1/2

Few patients have discontinued due to AEs in the study

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

Favorable Tolerability Profile at Recommended Phase 2 Dose for VS-6766 plus Defactinib Combination Regimen

Treatment Related Adverse Events Details* (≥10% patients in cohort 3.2mg 6766 and Def 200mg)	VS-6766 4mg Twice Weekly (4 wks of every 4 wks)[1] n=22		VS-6766 3.2mg Twice Weekly Def 200mg BID (3 wks of every 4 wks)[2] n=38	
	Gr1/2	Gr3/4	Gr1/2	Gr3/4
Rash	15	5	32	2
CK Elevation	13	2	19	2
AST Elevation	1		13	
Hyperbilirubinemia			14	1
Visual Disturbance	13		9	
ALT Elevation	2		5	
Diarrhoea	6	1	14	1
Fatigue	5	1	8	1
Oral Mucositis^	7	1	11	
Nausea	5		5	
Vomiting	2		4	
Peripheral Edema	9		10	
Paronychia	3		4	
Thrombocytopenia			6	
Pruritus	3	0	5	

Summary of FRAME Safety Profile

- Most Adverse Events (AE) were Grade 1/2
- Few patients have discontinued due to AEs in the study

RP2D

- **VS-6766 3.2 mg** oral twice wkly (3 wks of every 4 wks)
- **Defactinib 200 mg** oral BID (3 wks of every 4 wks)

*AEs were graded by NCI CTC v4; highest grade only recorded for each patient; AEs presented in ≥10% Patient (cohort 3.2mg 6766 and Def 200mg) data preliminary and subject to change;
^also includes glossitis/mouth ulcers

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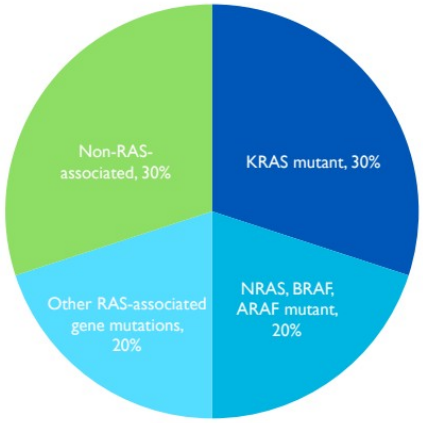
References: [1] Data on file VS-6766 Investigator's Brochure; [2]Banerji, Q4 2020 report

VS-6766 +/- Defactinib in Low-Grade Serous Ovarian Cancer

70% of LGSOC Tumors Driven by Mutations in the RAS/MAPK Pathway

- LGSOC is a type of ovarian cancer that disproportionately affects younger women
- 1,000 to 2,000 patients in the U.S. and 15,000 to 30,000 worldwide diagnosed with LGSOC each year
- A slow growing cancer, that has a median survival of almost 10 years, so patients remain in treatment for a long time (10-yr prevalence ~80,000 worldwide, ~6,000 US)
- Patients often experience significant pain and suffering from their disease over time
- Most prior research has focused on high grade serous ovarian cancer (HGSOC). However, LGSOC is clinically, histologically and molecularly unique from HGSOC with limited treatments available

~30% of LGSOC Patients Have KRAS mt
~70% of LGSOC Shows RAS Pathway-Associated mts

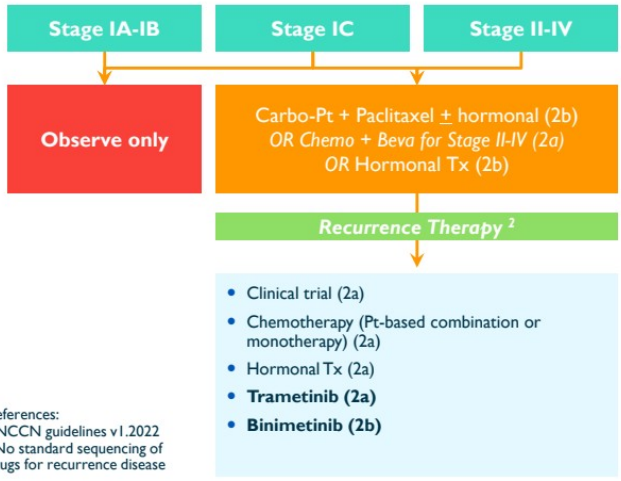


References: AACR Project GENIE Cohort v9.0-public and Verastem unpublished analysis

Reference: 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.

LGSOC: Limited Treatment Options with High Unmet Need

Low-Grade Ovarian Cancer – Treatment Algorithm[1]



References:
[1] NCCN guidelines v1.2022
[2] No standard sequencing of drugs for recurrence disease

Recent Clinical Trials in Recurrent LGSOC

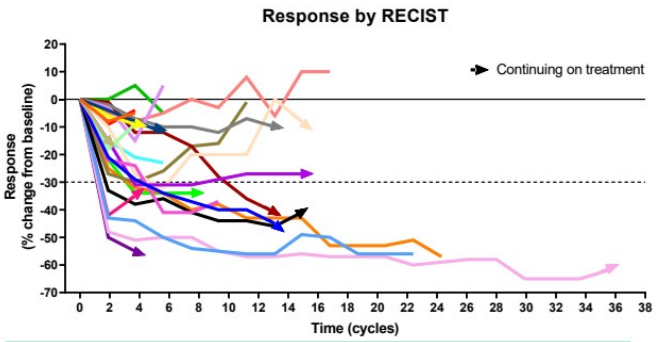
Therapy	Response Rate ORR	Median PFS Months (95% CI)	Discontinuation Rate due to AEs
Standard of Care[1]	6%	7.2 (5.6-9.9)	12 %
Trametinib[1]	26%*	13.0 (9.9-15.0)	35%
Standard of Care[2]	13%	10.6 (9.2 to 14.5)	17%
Binimetinib[2]	16%	9.1 (7.3-11.3)	31%

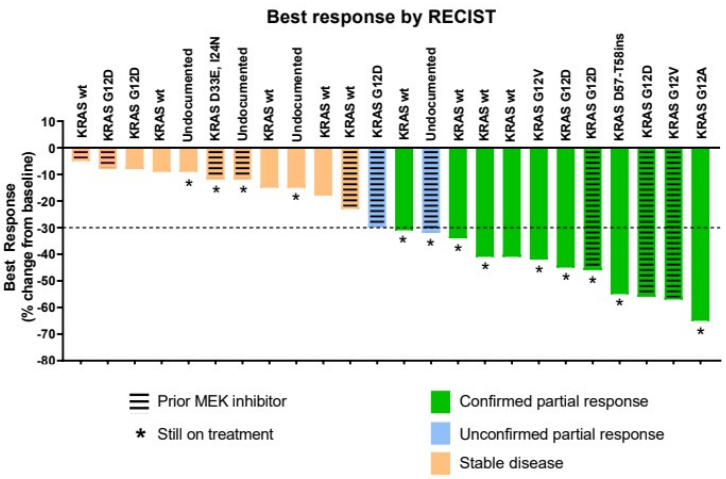
* *Not confirmed by central review*

Standard of Care = letrozole, tamoxifen, chemotherapy
PFS = Progression free survival
CI = confidence interval

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

VS-6766 in Combination with Defactinib (FRAME) Shows Promising ORR with Durability in Refractory LGSOC with Expanded Number of Patients (n=24)





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

Data cut off April 2021
PFS: Progression free survival
NR: Not reached

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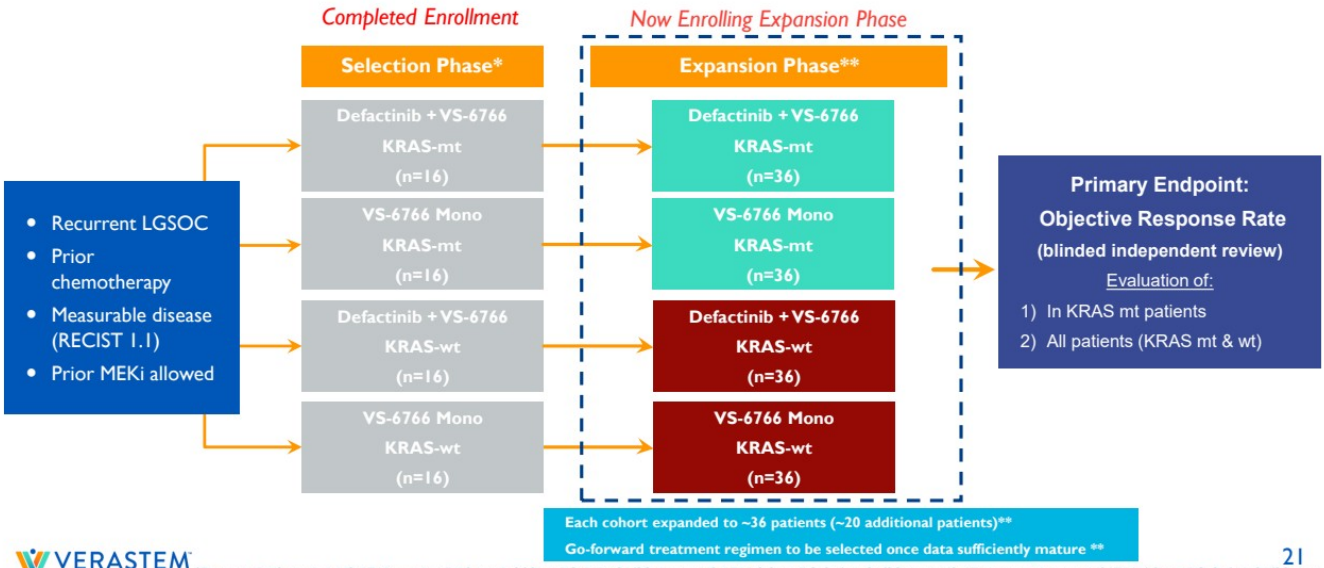
Reference: Banerjee et al., ESMO Sept 2021

RAMP 201 Registration-directed Phase 2 Trial of VS-6766 +/- Defactinib in Recurrent LGSOC - KRAS Mutant (mt) and Wild Type (wt)



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*Dosing: Defactinib + VS-6766 combo: Defactinib 200mg PO BID: 21/28 days + VS-6766 3.2mg PO 2x/wk 21/28 days; VS-6766 monotherapy: VS6766 4.0 mg PO 2x/wk 21/28 days

**Expansion Phase – final sample size to be adjusted based on adaptive design

RAMP 201 Update-October 2022

Update

- Completed second planned interim analysis
- Encouraging efficacy results include independently confirmed responses
- Enrollment continues towards completion of all four cohorts
- No new safety signals, continued favorable safety profile
- Majority of patients remain on treatment

Next Steps

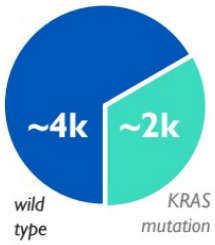
- Full enrollment based on the study protocol on track and expected by the end of the year
- FDA meeting 4Q-22 to align on regulatory path forward and go forward regimen

LGSOC Market Opportunity Larger or Comparable to Other High Unmet Need KRAS Opportunities

Prevalence

~6K

patients US[1]



~80K

patients WW[1]

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

[1] References: Monk, Randall, Grisham, The Evolving Landscape of Chemotherapy in Newly Diagnosed Advanced Epithelial Ovarian Cancer, Am Soc Clin Oncol Educ Book; 2019; Slomovitz, Gourley, Carey, Malpica, Shih, Huntsman, Fader., Grisham et al, Low-Grade serous ovarian cancer: State of the Science; Gynecol Oncol; 2020. Grisham, Iyer, Low-Grade Serous Ovarian Cancer: Current Treatment Paradigms and Future Directions; Curr Treat Options Oncology; 2018; Globocan 2020

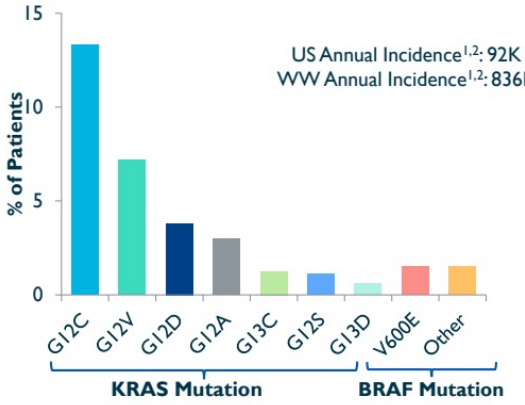
[2] Patient-months of Therapy metric calculated by multiplying relevant incidence/prevalence rate times estimated duration of therapy; represents US market opportunity only; patient population estimates from Globocan 2020, American Cancer Society 2021, AACR Genie Cohort V9.0 public, and scientific publications. Duration of therapy estimates from clinical studies and clinician experience. Patient-months on therapy is for 2nd-line+ patients

[3] NSCLC KRAS G12C 2nd line patients (incidence); Pancreatic RAS/RAF mutant 2nd-line patients (incidence); LGSOC KRAS mutant and wild-type patients (prevalence); Endometrioid RAS/RAF mutant 2nd-line patients (incidence); Uveal melanoma RAS/RAF mutant 2nd-line patients (incidence)

VS-6766 +/- Defactinib in NSCLC

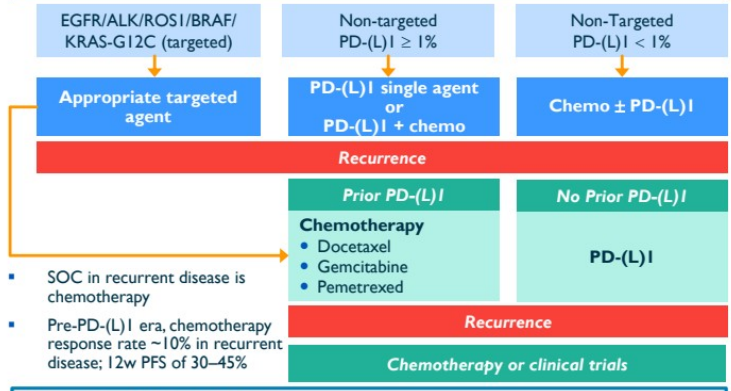
High Unmet Need in Refractory mt NSCLC Adenocarcinoma

NSCLC Adenocarcinoma[3]



KRAS Mutations Represent 25% of Lung Cancer Adenocarcinoma & BRAF Represent 2-4% (EGFR 17%, ALK 7%)[4,6]

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



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

Verastem Clinical Trials:

- RAMP 202:
  - BRAF V600E and BRAF non-V600E—VS-6766 + Defactinib
- RAMP 203—KRAS G12C: VS-6766 + sotorasib
- RAMP 204—KRAS G12C: VS-6766 + adagrasib

References:
[1] Globocan, 2018
[2] https://www.ncbi.nlm.nih.gov/books/NBK519578/
[3] TCGA PanCancer Atlas (cBioPortal analysis)
[4] www.thelancet.com Vol 389 January 21, 2017
[5] Adapted from NCCN Non-small cell lung cancer guidelines Version 3.2020
[6] Clinical Cancer Research DOI 10.1158/1078-0432.CCR-18-2062

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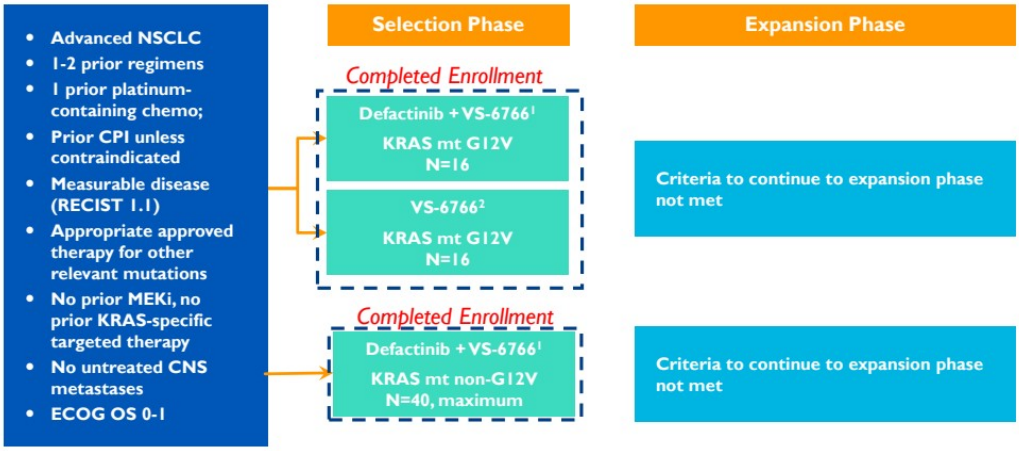
RAMP 202: Phase 2 Trial of VS-6766 +/- Defactinib in Advanced NSCLC Primary Cohort: KRAS G12V mt NSCLC



References:[1] Defactinib 200 mg PO BID (21/28 days) + VS-6766 3.2 mg PO 2x/wk (21/28 days)
[2] VS-6766 4.0 mg PO 2x/wk (21/28 days)

RAMP 202 Results–August 2022

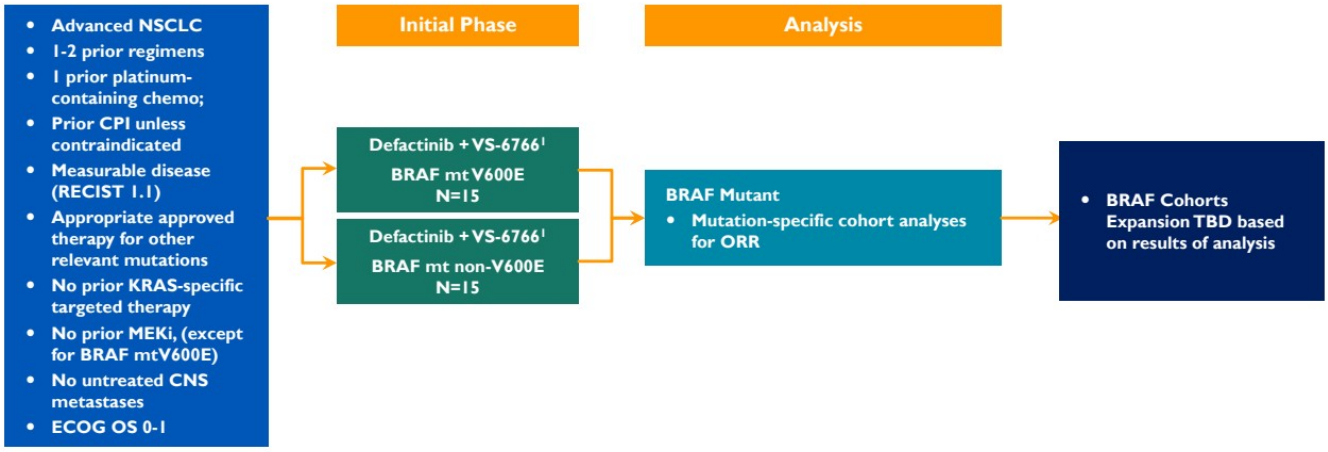
Findings

- The confirmed ORR was 11% (2/19) in KRAS G12V mt NSCLC patients treated with VS-6766 + defactinib with a disease control rate of 37%
- The ORR in non-G12V KRAS mt patients treated with VS-6766 + defactinib was 5% (2/37) with a disease control rate of 54%
    - No subtype was identified for further clinical evaluation of VS-6766 + defactinib in this trial

Next Steps

- Results of Part A of RAMP 202 trial in KRAS-G12V mt NSCLC show VS-6766 ± defactinib did not meet criteria to continue to expansion phase
- Continue to analyze the results of the trial and integrate the findings into our development plans moving forward
- Continuing VS-6766 development in NSCLC with other combinations:
    - Sotorasib
    - Adagrasib
    - Everolimus

RAMP 202: VS-6766 + Defactinib in BRAF mt NSCLC



References:[1] Defactinib 200 mg PO BID (21/28 days) + VS-6766 3.2 mg PO 2x/wk (21/28 days)

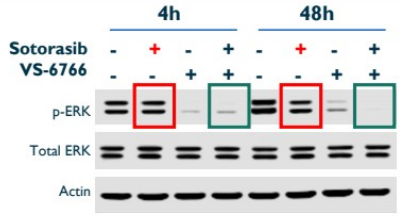
Preclinical Synergy of VS-6766 + G12C Inhibitors in KRAS G12C mt Models

Synergy of VS-6766 + G12C inhibitors across G12C mutant NSCLC, CRC & Pancreatic cancer cell lines

			Combined Synergy Score	
Cell line	**Indication**	**Sensitivity to G12C inhibitors**	**VS-6766 + sotorasib**	**VS-6766 + adagrasib**
H2122	NSCLC	Moderately sensitive	44.7	44.6
H1373	NSCLC	Sensitive	10.0	3.4
SW1573	NSCLC	Insensitive	8.6	12.0
H358	NSCLC	Sensitive	6.9	5.4
H2030	NSCLC	Moderately sensitive	5.1	ND
SW837	CRC	Sensitive	16.1	18.5
MIAPACA2	Panc	Sensitive	2.3	5.3

ND: not determined

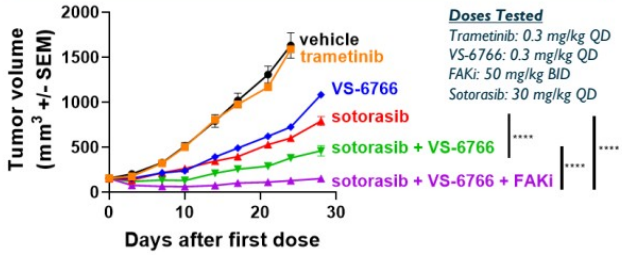
VS-6766 + sotorasib yields deeper and more sustained inhibition of ERK signaling pathway



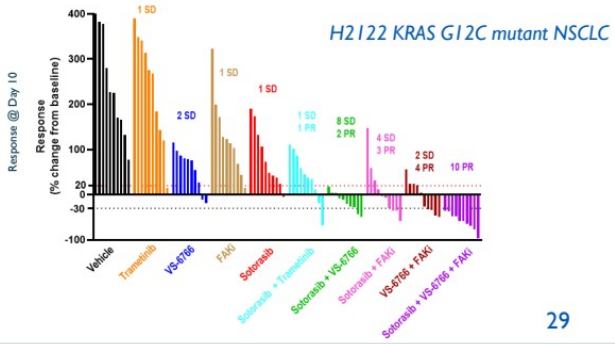
H2122 KRAS G12C mutant NSCLC

Concentrations Tested
Sotorasib: 100 nM
VS-6766: 100 nM

VS-6766 & FAKi potentiate sotorasib efficacy in KRAS G12C mutant NSCLC in vivo; Tumor regression in all mice with triple combination



Doses Tested
Trametinib: 0.3 mg/kg QD
VS-6766: 0.3 mg/kg QD
FAKi: 50 mg/kg BID
Sotorasib: 30 mg/kg QD



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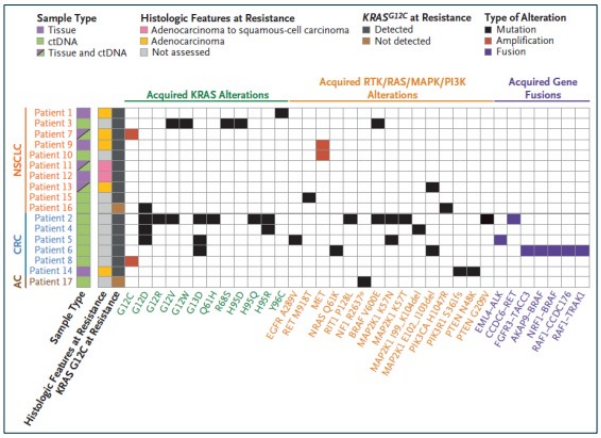
Reference: Coma et al., AACR 2021

Acquired Resistance Mechanisms to KRAS G12Ci Treatment in Patients Further Support Combination of KRAS G12Ci with VS-6766

Summary of Putative Mechanisms of Acquired Resistance to Adagrasib Treatment



- Mechanisms of acquired resistance to KRAS G12Ci adagrasib treatment in patients recently reported[1,2]
- The main resistance alterations occurred in
  - RTK mts or amplifications
  - KRAS mts or amplification
  - NRAS mt
  - BRAF V600E mt, BRAF or CRAF fusions
  - MAP2K1 (MEK1) mt/deletion
- VS-6766 has shown activity against these KRAS, NRAS, BRAF and CRAF modifications

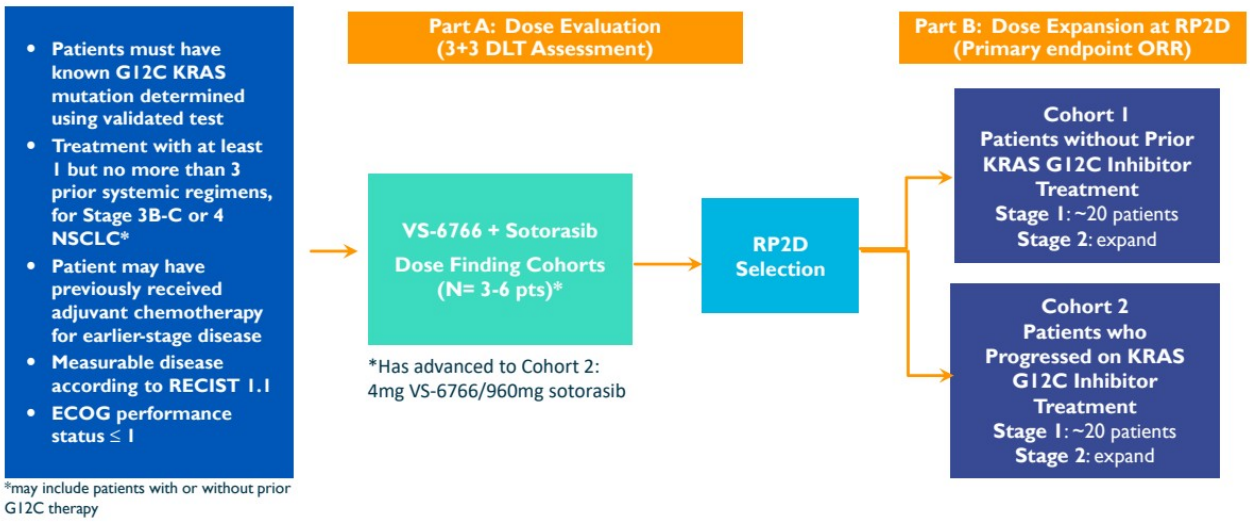
	IC50 (nM)		
Cell Line	Sotorasib	Adagrasib	VS-6766
G12C	29	3	14
G12D	435	382	7
G12C/R68S	157	85	13
G12C/H95D	11	235	10
G12C/Y96C	438	216	4

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

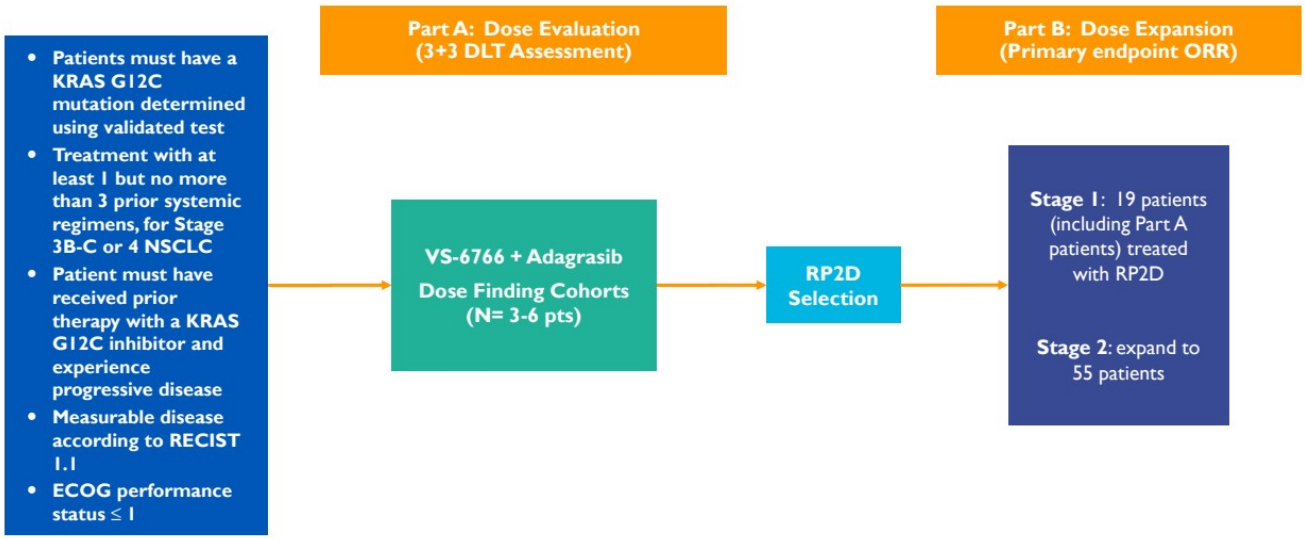
Reference: Andrew Aguirre, unpublished

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

RAMP 203: Phase 1/2 Trial of VS-6766 + LUMAKRAS™ (sotorasib) in KRAS G12C-mutated Advanced NSCLC

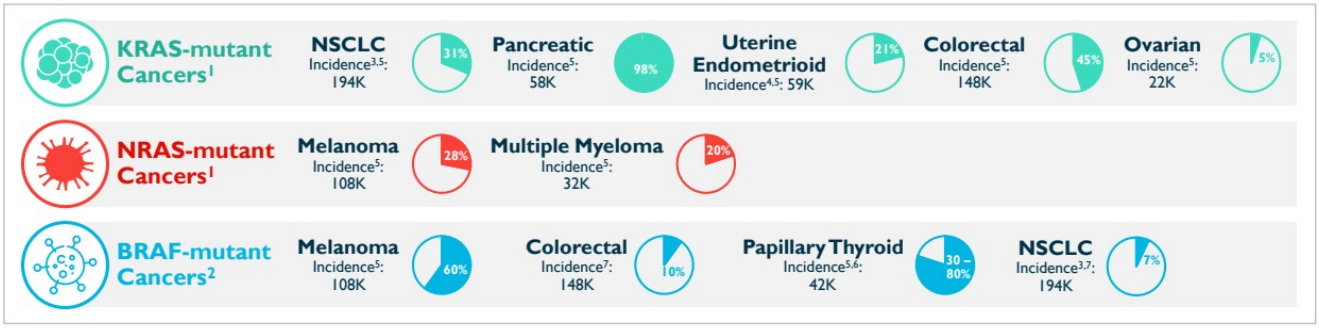


RAMP 204: Phase 1/2 Trial of VS-6766 + Adagrasib in KRAS G12C-mutated Advanced NSCLC



Future Opportunities: VS-6766 as Backbone of RAS Therapy

High Unmet Needs in RAS/MAPK Pathway-Driven Cancers



Breadth of potential opportunity

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

Established prognostic significance

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

Challenges with conventional approaches

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

Incidence References:
[1]Reference for RAS mt frequencies – Cox et al. *Nature Reviews* 13: 828, 2014; [2]Reference for BRAF mt frequencies – Turski et al. *Mol Cancer Ther* 15: 533, 2016
[3]85% of lung cancer is NSCLC (Lu et. al. *Cancer Manag Res.* 2019); [4]90% of all uterine cancers are of the endometrial type (ACS); [5]Cancer Statistics 2020, Siegel et. al. *CA Cancer J Clin* 2020;70:7-30; [6]8 out of 10 thyroid cancers are of the papillary type (ACS)[7]CbioPortal

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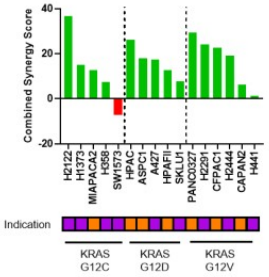
References:
McCormick F Clin Cancer Res 15April2015; [6]Adderley H et al. EBioMedicine 01Mar2019; Papke B et al. Science 17Mar2017; Ryan M et al. *Nature Reviews Clinical Oncology* 01Oct2018; NIH cancer.gov/research/key-initiatives/ras

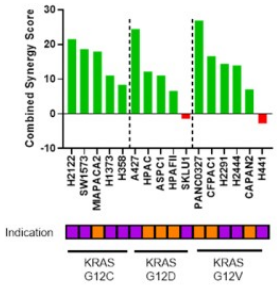
Preclinical Synergy of VS-6766 in Combination with Promising Agents for Clinical Investigation

Vertical MAPK Pathway Inhibition

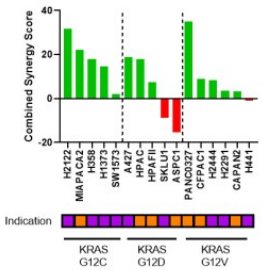
VS-6766 + pan-HERi (Afatinib)



VS-6766 + SHP2i (RMC-4550)

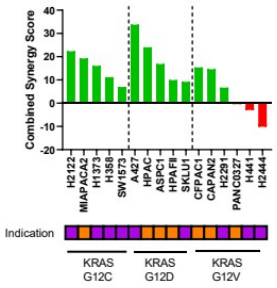


VS-6766 + SOS1i (BI-3406)

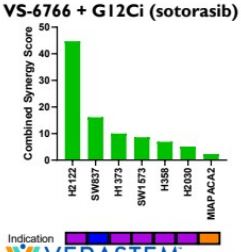


Parallel Pathway Inhibition

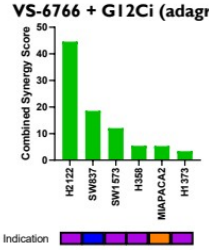
VS-6766 + CDK4/6i (Palbociclib)



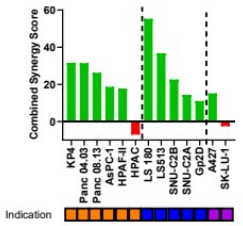
VS-6766 + G12Ci (sotorasib)

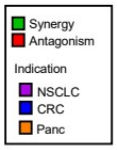


VS-6766 + G12Ci (adagrasib)

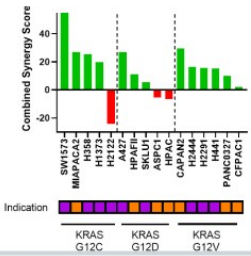


VS-6766 + G12Di (MRTX1133)



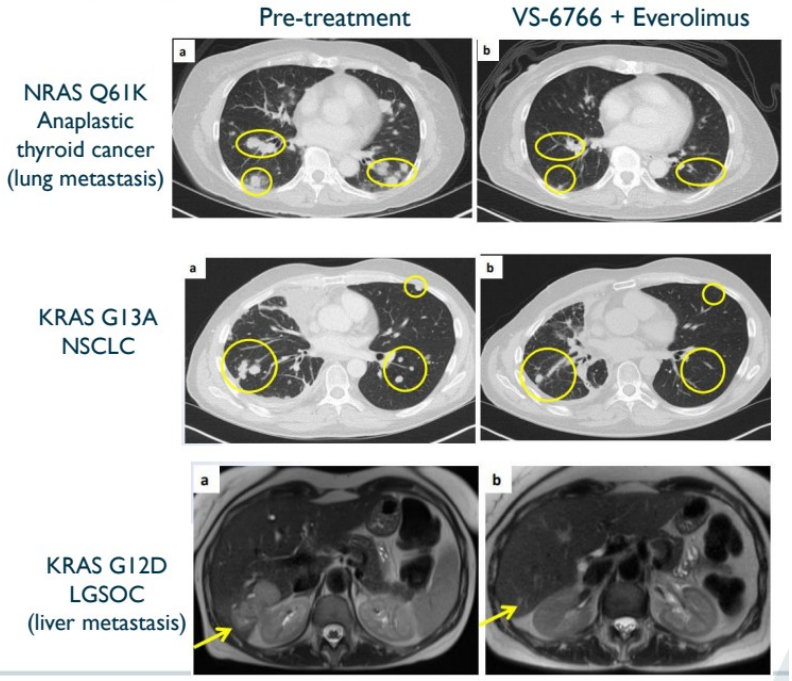


VS-6766 + mTORi (Everolimus)



VS-6766 + Everolimus Clinical Data Presented at ASCO

- Well-tolerated RP2D established for VS-6766 + everolimus with intermittent dosing of both agents (twice weekly; 3 wks on/1 wk off)
  - No DLTs reported at RP2D
- VS-6766 + everolimus combo induced PRs in patients with various RAS mutations in NSCLC, LGSOC and thyroid cancers
- Both LGSOC pts showed PRs with 69% and 79% reduction and have been on treatment for ≥3 years with treatment ongoing
- KRAS mutant NSCLC expansion cohort is currently ongoing – expanding to 20 pts
  - Currently 2 PRs/11
  - Median progression free interval of 6.25 months in heavily pre-treated patients



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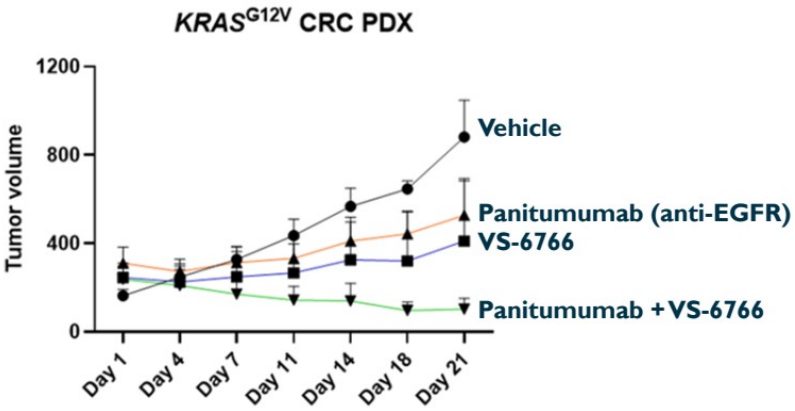
Reference: Minchom et al., ASCO 2022

Combination of VS-6766 with anti-EGFR mAb Induces Tumor Regression in a KRAS mt Colorectal PDX Model



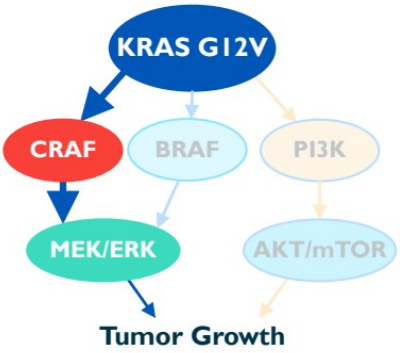
- VS-6766 + anti-EGFR (panitumumab) induces tumor regression in a KRAS G12V mt CRC patient-derived xenograft model
- G12Ci + anti-EGFR (sotorasib + panitumumab and adagrasib + cetuximab) have shown partial responses in KRAS G12C mt CRC (Fakih et al. ESMO 2021; Weiss et al. ESMO 2021)
- **These data support clinical testing of VS-6766 + anti-EGFR (cetuximab) for treatment of KRAS mt CRC (NCT05200442)**

VS-6766 Patent Exclusivity

Backup Slides

VS-6766 Inhibits CRAF - The key driver of KRAS G12V mt NSCLC

A Precision Approach to KRAS G12V Driven NSCLC



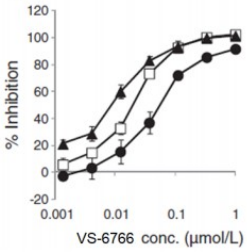
- KRAS G12V signals mainly through RAF/MEK in contrast to other variants, such as KRAS-G12D, which signal more through PI3K/AKT
- KRAS G12V models are especially dependent on CRAF

RAF family

IC_{50}(CRAF●): 0.056 ± 0.016 µmol/L

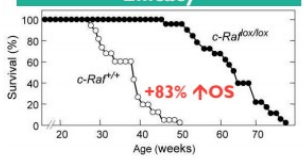
IC_{50}(BRAF □): 0.019 ± 0.0030 µmol/L

IC_{50}(BRAF V600E▲): 0.0082 ± 0.0015 µmol/L

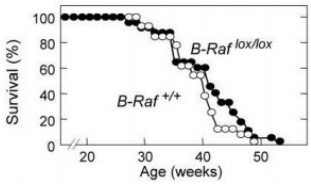


CRAF Drives KRAS G12V mt NSCLC[1]

CRAF KO Shows Strong Efficacy



BRAF KO Has No Effect

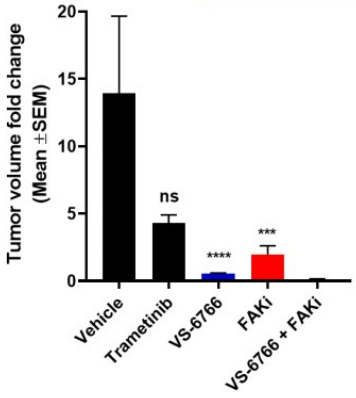


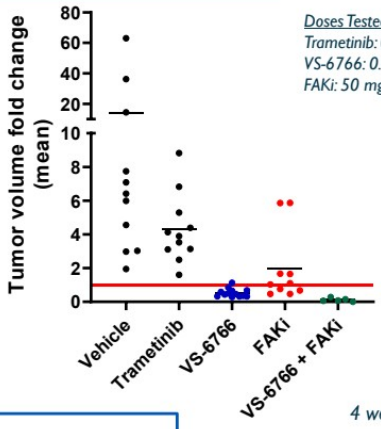
CRAF, but not BRAF, ablation improves survival of mice with KRAS G12V induced lung cancer *in vivo*

References: Ishii et al. *Cancer Res* (2013), Blasco, R. B. et al. *Cancer Cell* (2011), Lito, P. et al. *Cancer Cell* (2014), Sanclemente, M. et al. *Cancer Cell* (2018)

VS-6766 +/- FAKi Induces Significant Tumor Regression in KRAS G12V mt NSCLC in vivo Model, with Clear Differentiation from Trametinib

KRAS G12V mutant;Tp53 KO NSCLC





Doses Tested
Trametinib: 0.1 mg/kg QD (5 days/week)
VS-6766: 0.1 mg/kg QD (5 days/week)
FAKi: 50 mg/kg BID (5 days/week)

- **VS-6766 monotherapy caused tumor regression**
- **VS-6766 + FAKi showed stronger regression**
- **No significant anti-tumor effect of trametinib at same dose level**

4 weeks of treatment

Statistics: Mann-Whitney test

Collaboration with Mariano Barbacid

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Reference: Coma et al. AACR 2021

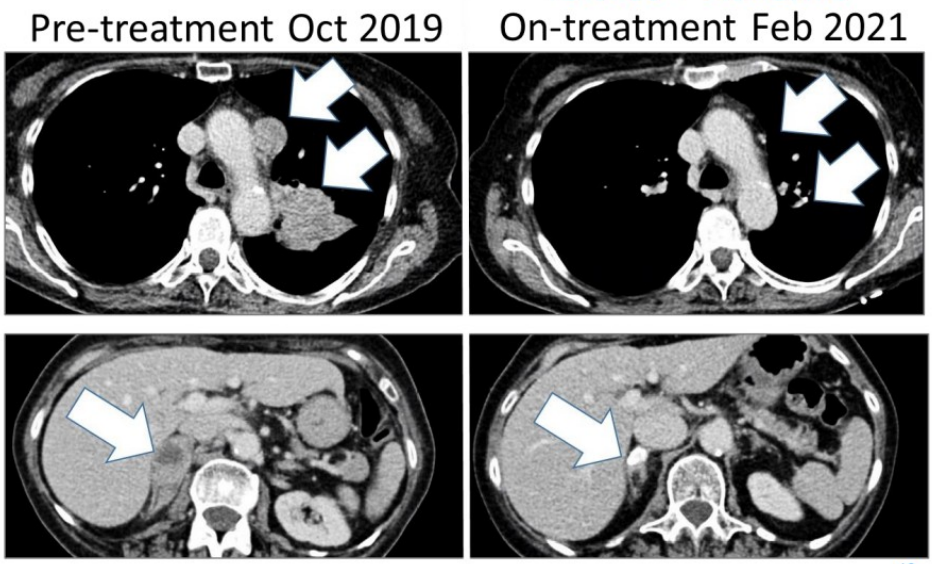
Case Study: Response to VS-6766 + Defactinib in a Patient with KRAS G12V mutant NSCLC

May 2019: Diagnosed with NSCLC

June 2019 - Sept 2019: Treated with first line Carboplatin + Pemetrexed + Pembrolizumab

Oct 2019: Progression, palliative RT to right hip

Nov 2019 – present: On treatment in FRAME study VS-6766 + Defactinib



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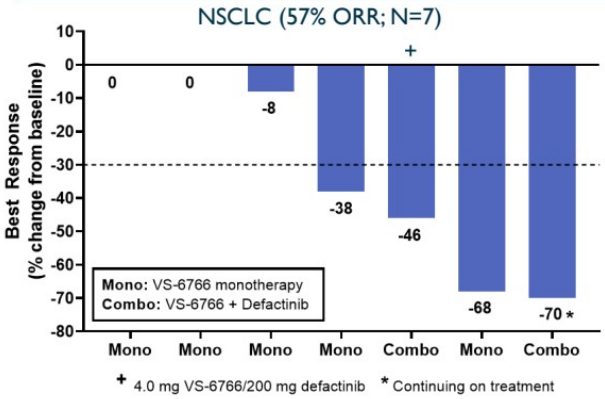
Reference: Krebs et al. AACR 2021

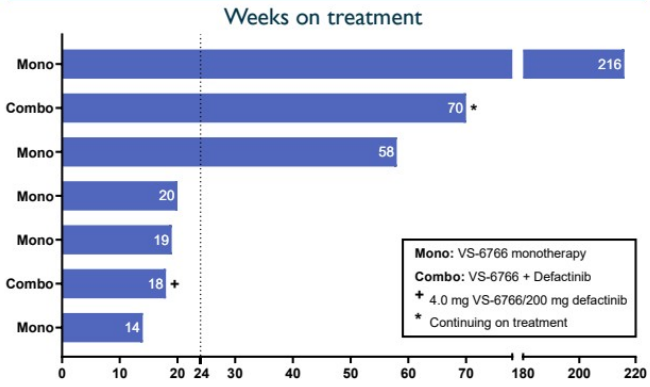
Strong Signal Identified in KRAS G12V NSCLC

VS-6766 ± Defactinib Has Shown a 57% ORR in KRAS G12V mt NSCLC in Integrated Analysis

Best Response by RECIST in KRAS G12V mt NSCLC



Time on Treatment for KRAS G12V mt NSCLC



- **Preclinical evidence suggests combination with Defactinib may improve efficacy in KRAS G12V mt NSCLC**
- **Activity of VS-6766 as a single agent and in combo with Defactinib in KRAS G12V mt NSCLC**

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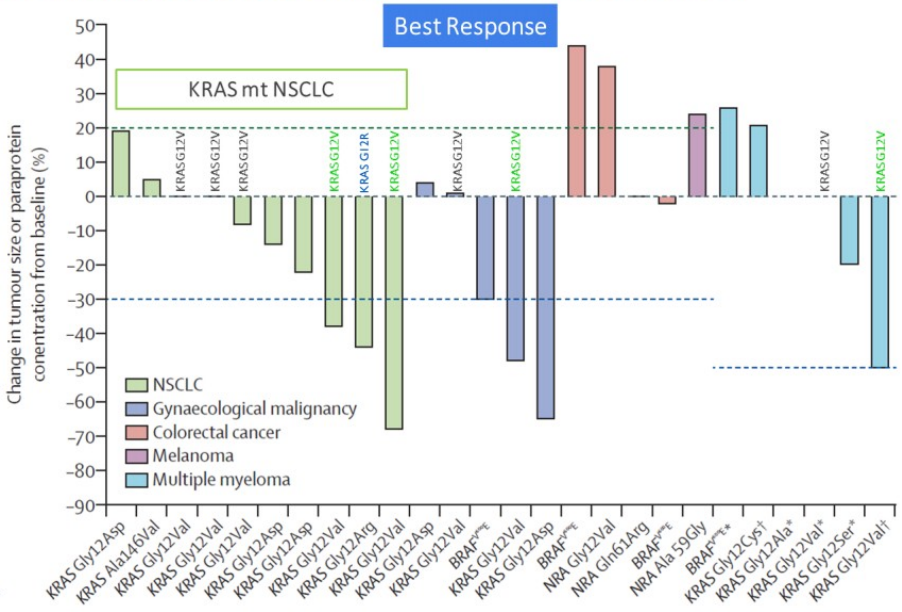
References: [1] Guo, et al Lancet Oncology 2020 [2] Krebs, AACR April 2021(March 18, 2021 cutoff)

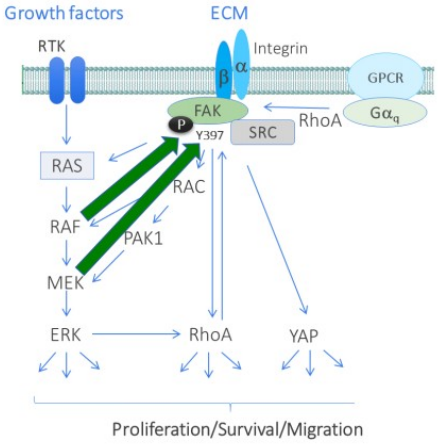
VS-6766 Monotherapy Has Shown Clinical Activity in Several RAS/RAF Mutant Cancer Indications, Including NSCLC and Gynecologic Cancers

Confirmed responses especially in patients with KRAS G12V mutation

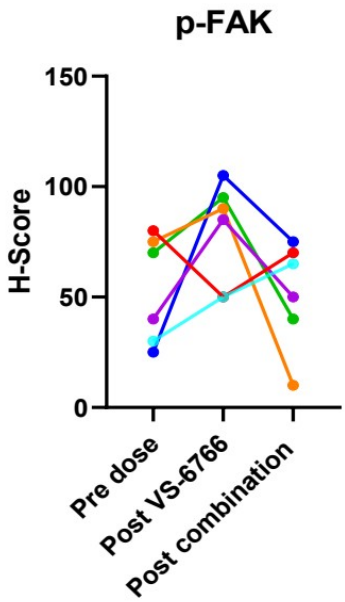


Guo et al., Lancet Oncology 2020

Overcoming Key Resistance Mechanisms to MEK Inhibitors



= Feedback Reactivation



- **MEK inhibition induces compensatory activation of pFAK preclinically and clinically**
  - Trametinib induced ↑ pFAK (Y397) preclinically in KRAS mt NSCLC cell lines
  - **Also observed in patients**
    - **VS-6766 induced ↑ pFAK (Y397) as a potential resistance mechanism in the majority of patients**
    - **Combination with defactinib reduced this compensatory pFAK signal**

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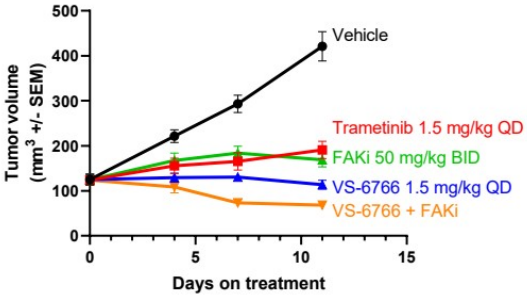
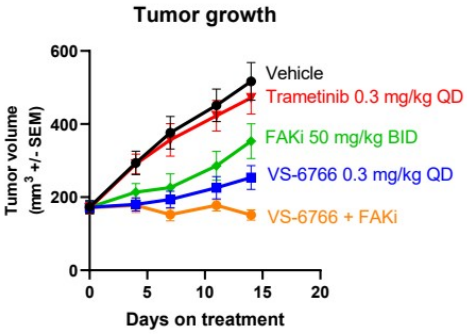
References:
Banerji, BTOG Dublin, Jan 23, 2019
Banerji, AACR VM 1, April 27, 2020, CT143

VS-6766 and FAK Inhibitor Combination Leads to More Robust Anti-Tumor Efficacy in vivo

KRAS^{mt} Ovarian TOV-21G *in vivo* Model[1]



KRAS^{mt} NSCLC H358 *in vivo* Model[2]



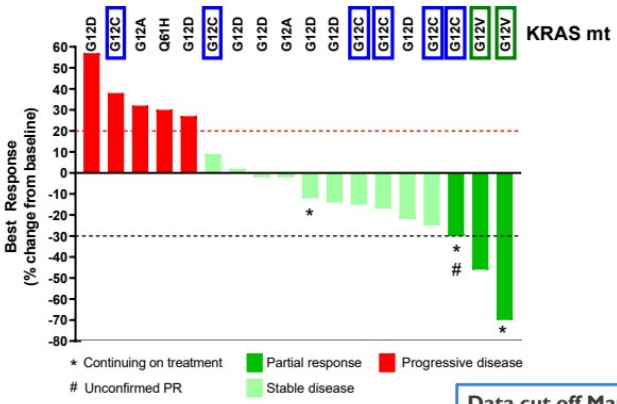
References: [1] Coma AACR 2021; [2] Krebs AACR 2021

NSCLC Responses with VS-6766 + Defactinib Combination (FRAME) (n=20)

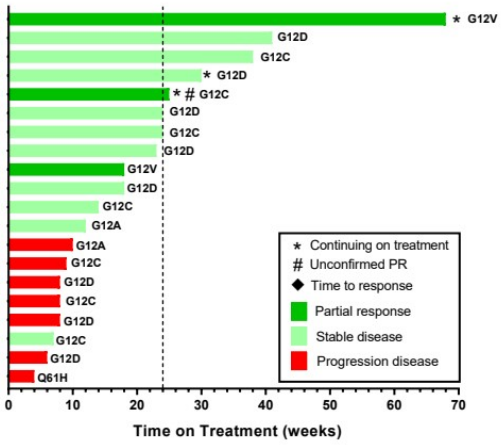
Confirmed responses in 2/2 patients with KRAS G12V mt NSCLC

Tumor reduction in 4/6 patients with KRAS G12C mt NSCLC

Best response by RECIST in KRAS mt NSCLC



Time on Treatment



Data cut off March 5, 2021

- ORR = 15% (3/20)
- ORR in G12V mt = 100% (2/2)
- DCR =65% (13/20)
- 3/20 (15%) still on study
- 7 pts on treatment ≥ 24 weeks

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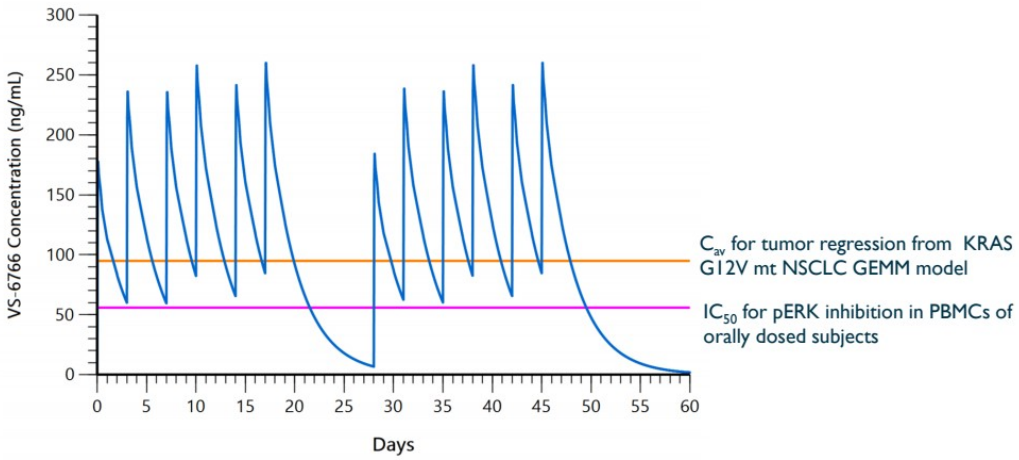
Reference: Krebs et al. AACR 2021

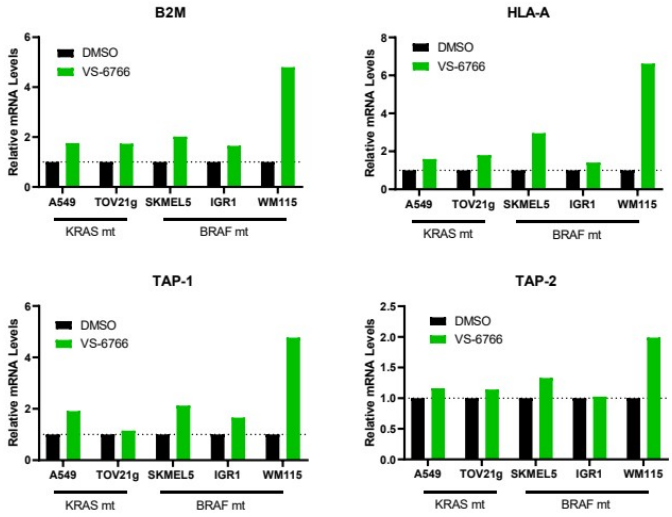
Target exposures for preclinical tumor regression & pERK inhibition in human subjects are covered by twice weekly dosing of 3.2 mg VS-6766, 3 wks on/1 wk off



- Modeling of PK for 3.2 mg VS-6766 2/wk, 3 wks on/1 wk off, based on 3.2 mg single dose PK data (study CCR3808)
- Relationship to average exposure for tumor regression in KRAS G12V mt NSCLC mouse model and IC_{50} against human PBMC pERK activity

References: Martinez-Garcia et al., Clin Cancer Res 2012; Coma et al. AACR 2021

VS-6766 Upregulates MHC Class I Antigens on Tumor Cells: a mechanism for potentiation of I/O efficacy

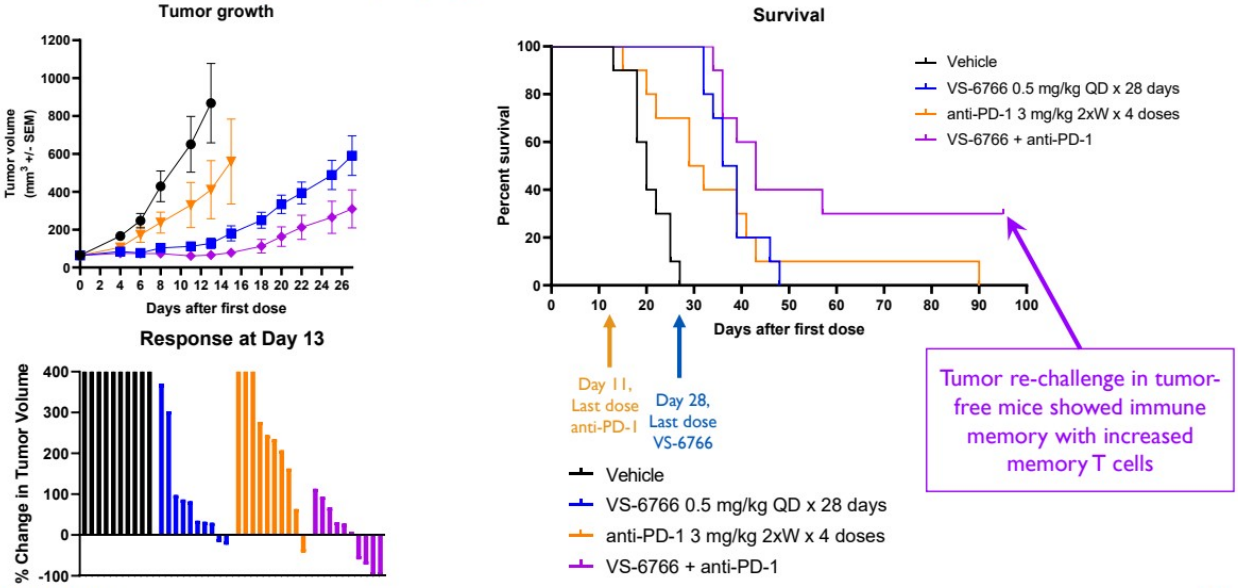


Cell Line	Tumor type	RAS/RAF mutation status
A549	Lung	KRASmt G12S
TOV21g	Ovarian	KRASmt G13C
SKMEL5	Melanoma	BRAFmt V600E
IGR-1	Melanoma	BRAFmt V600E
WM115	Melanoma	BRAFmt V600E

VS-6766 @ 1 μM (except SKMEL5 and IGR-1, 300 nM)

Reference: Pachter, RAS-Targeted Drug Development, Sept 2020

VS-6766 Enhances Tumor Growth Inhibition when Combined with Anti-PD-1 in the CT26 KRAS (G12D) Syngeneic Model



Reference: Pachter, RAS-Targeted Drug Development, Sept 2020

Experienced Senior Management Team

Brian Stuglik
Chief Executive Officer

- Global VP & Chief Marketing Officer – Lilly Oncology
- Founding Member – Proventus Health Solutions

Daniel Paterson
President and Chief Operating Officer

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

Rob Gagnon
Chief Business and Financial Officer

- CFO – Harvard Bioscience, Clean Harbors
- VP of Finance – Biogen Idec

Cathy Carew
Chief Organizational Effectiveness Officer

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

Jonathan Pachter, Ph.D.
Chief Scientific Officer

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

Louis Denis, M.D.
Chief Medical Officer

- CMO, Asana BioSciences
- Boehringer-Ingelheim, Pfizer

Hagop Youssoufian, MSc, M.D.
Head of Medical Strategy

- CMO, BIND Therapeutics, EVP, Progenics,
- CMO & EVP, Ziopharm Oncology, SVP, Imclone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THANK YOU