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): **February 24, 2021**

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. Other Events

On February 24, 2021, Verastem, Inc. posted its corporate presentation, a copy of which is furnished hereto as Exhibit 99.1.

Item 9.01. Financial Statements and Exhibits

Exhibit No.	Description
99.1	Corporate Presentation, dated February 24, 2021
104	Cover Page Interactive Data File (formatted in Inline XBRL and contained in Exhibit 101)

SIGNATURE

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.

Date: February 24, 2021

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


Verastem
Oncology
Corporate Presentation
February 2021
NASDAQ: VSTM

Safe Harbor Statement

This presentation includes forward-looking statements about, among other things, Verastem Oncology's products and product candidates, including anticipated regulatory submissions, approvals, performance and potential benefits of Verastem Oncology products and 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 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

Additional information regarding these factors can be found in Verastem Oncology's Annual Report on Form 10-K for the fiscal year ended December 31, 2019 and in any subsequent filings with the SEC, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors that May Affect Future Results," as well as in our subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission (SEC) and 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.

Well Positioned to Capitalize on Growth Opportunities

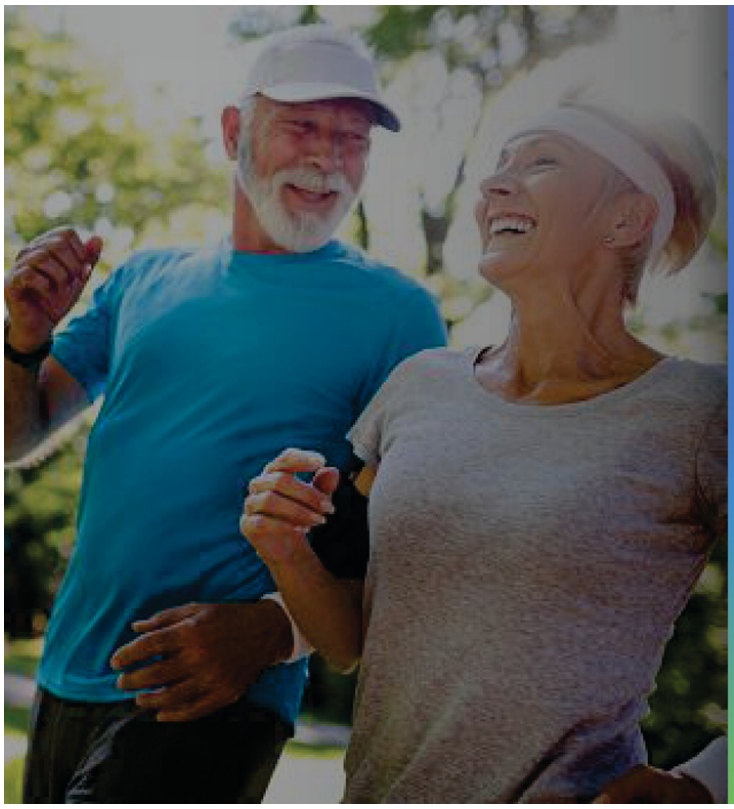
Verastem Oncology

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

New lead clinical program has best-in-class potential	VS-6766 (RAF/MEKi) and defactinib (FAKi) are clinically active against RAS mutant cancers
Rapid development paths to market	Validating clinical results achieved in KRAS mutant low-grade serous ovarian cancer (LGSOC), strong signal in KRAS mutant G12V NSCLC; registration-directed trials initiated in 4Q 2020
Significant downstream market opportunity and blockbuster potential	30% of all human cancers are driven by mutations in RAS family of genes; VS-6766 combinations broadly applicable across a variety of tumor types
Strong balance sheet	Monetization of COPIKTRA® (duvelisib) provides funding until at least 2024 Proforma Cash Balance of $168.3 million, after Hercules Debt Repayment Starting in 2021, annual operating expense forecast $50 million

2020 Highlights: A Transformative Year for Verastem Oncology

- January: In-licensed global rights to VS-6766, best-in-class RAF/MEK inhibitor, from Chugai
- February: PIPE financing based on data for new clinical program
- September: Divested global rights to Copiktra to Secura Bio
- November: Initiated registration-directed ph. 2 study in LGSOC
- December: Initiated registration-directed ph. 2 study in NSCLC



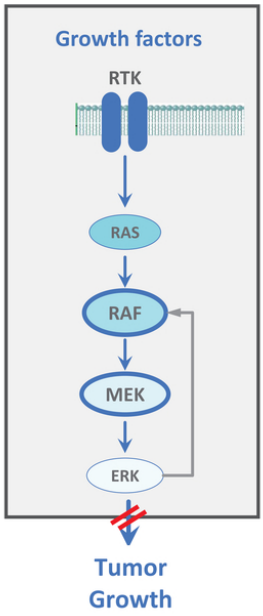
VS-6766 RAF/MEK Inhibitor Program Overview

Verastem Oncology

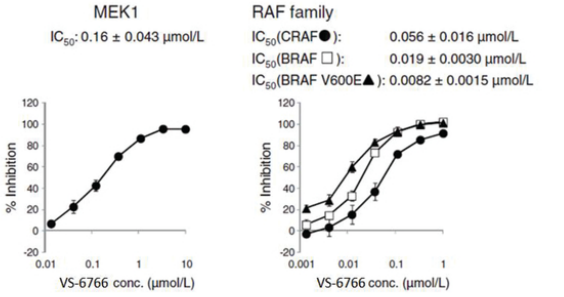
VS-6766 is a differentiated, best-in-class asset potentially applicable across multiple patient populations

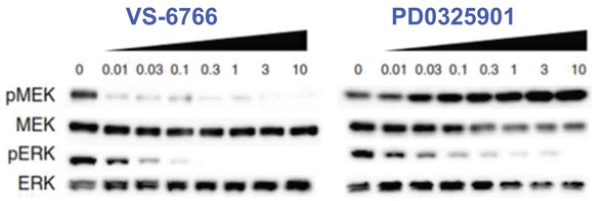
- Unique dual RAF/MEK targeting mechanism of action
- Best-in-class safety & tolerability profile relative to marketed MEK inhibitors, with potential for combinability with agents from multiple target classes
- Novel intermittent dosing schedule; convenient oral regimen
- Clear signals of clinical activity in various RAS-driven cancers, including in patients whose tumors previously progressed on other MEK inhibitors
- Strong preclinical and clinical synergy data in combination with other agents targeting RAS pathway and parallel pathways

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



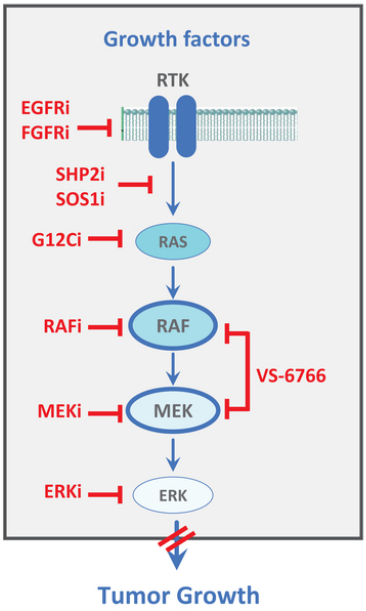
- VS-6766 inhibits both MEK & RAF kinase activities
- MEK inhibitors paradoxically induce MEK phosphorylation (pMEK) by relieving ERK-dependent feedback inhibition of RAF
- By inhibiting RAF phosphorylation of MEK, VS-6766 has advantage of not inducing pMEK
- VS-6766 inhibits ERK signaling more completely; may confer enhanced therapeutic activity





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

Vertical Blockade: Establishing VS-6766 as the backbone of therapy for RAS pathway-driven tumors

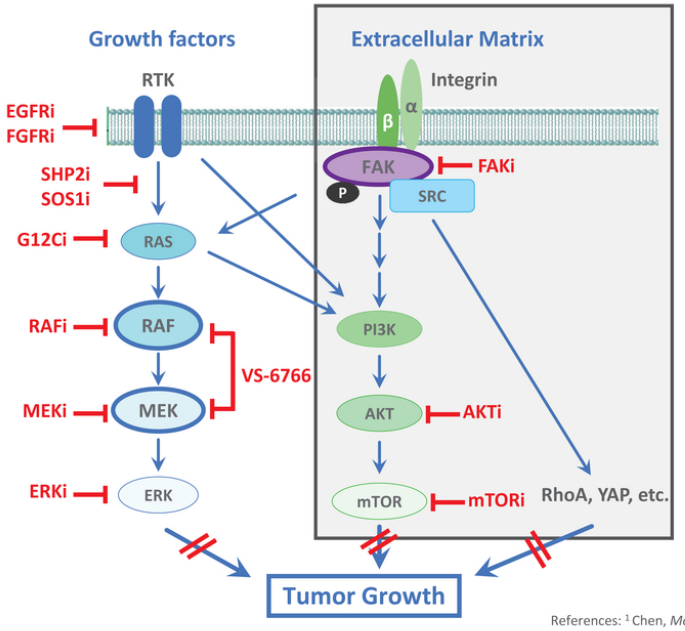


- Current Challenges
  - Blocking any single target in the pathway is insufficient for maximum depth and duration of anti-tumor efficacy
    - e.g.,, SHP2i, KRAS-G12Ci, RAFi, MEKi, ERKi
  - Vertical inhibition concept is now well established
    - Necessary to block more than 1 target in the pathway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

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

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

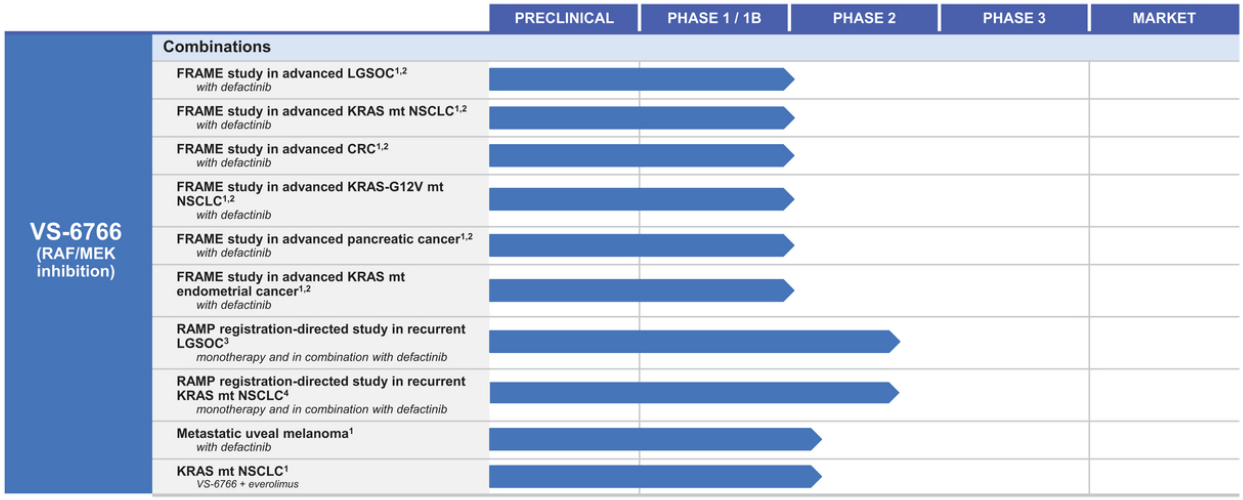
Parallel Pathway Blockade: Establishing VS-6766 as the backbone of therapy for RAS pathway-driven tumors



- 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 FAK inhibition and with AKT pathway inhibition (e.g. everolimus)
  - RP2D established for VS-6766 + defactinib and for VS-6766 + mTORi (everolimus) with twice weekly regimen (Udai Banerji, 3Q20)

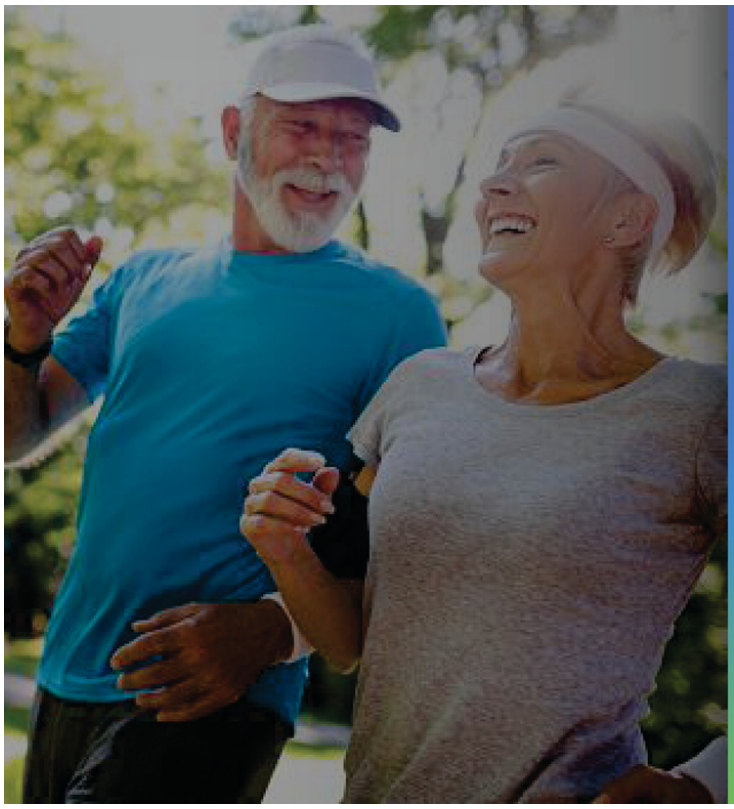
References: [1] Chen, *Mol Cancer Res* 2018; [2] Banerji, BTOG Dublin, Jan 23, 2019

Robust Pipeline Targeting the RAS Pathway and Multiple Growth Opportunities



**Pre-clinical studies ongoing in multiple KRAS mutant tumors*

[1] Investigator-sponsored trial
[2] NCT03875820
[3] NCT04625270
[4] NCT04620330



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

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What is Low-Grade Serous Ovarian Cancer (LGSOC)?

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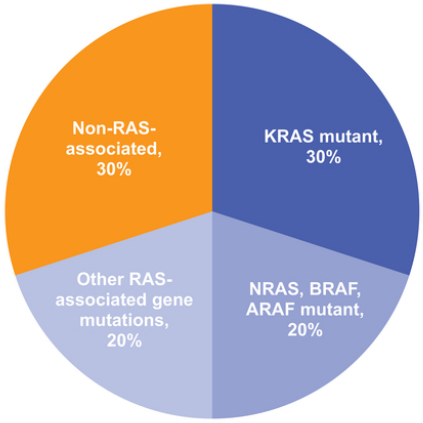
- LGSOC is a type of ovarian cancer that disproportionately affects younger women
- 1,000 to 2,000 patients in the U.S. and 15,000 to 30,000 worldwide diagnosed with LGSOC each year
- A slow growing cancer, that has a median survival of almost 10 years, so patients remain in treatment for a long time (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



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

Source: 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]

Stage IA-IB

Observe only

Stage IC

Stage II-IV

Pt Chemo Combo:
Carbo-Pt + Paclitaxel (preferred)
+ Beva for Stage II-IV (incl maintenance Beva)
OR Hormonal Tx (2B)

Recurrence

Pt-Sensitive

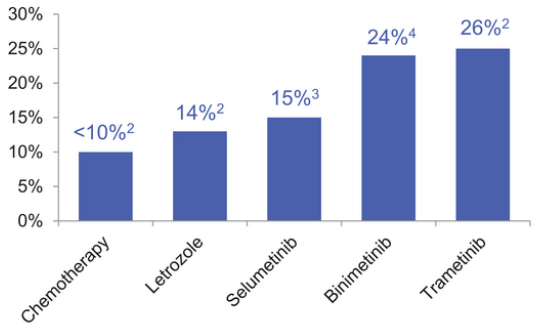
- Pt-Chemo combo +/- Beva
- **Trametinib**
- **Fulvestrant**

Pt-Resistance

- Taxane or gemcitabine, or doxorubicine, or topotecan +/- Beva
- **Trametinib**
- **Fulvestrant**

[1] NCCN guidelines
[2] Gershenson, et al. ESMO 2019.
[3] Farley, et al. Lancet Oncology, 2013.
[4] Grisham, Monk, Banerjee, et al. IGCS 2019.

Limited Response Rates for Available Treatments:



- 31-35% discontinuation rate with MEK inhibitors due to AEs
- No discontinuations in the FRAME study due to AEs

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%)

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

VS-6766 3.2 mg + Defactinib 200 mg Selected as RP2D

Treatment Related Adverse Events Occurring in ≥ 10 Patients (Total) Q4 2020 Update

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Treatment Related Adverse Events Details* (≥10% patients in cohort 3.2mg 6766 and Def 200mg)	VS-6766 3.2mg Def 400mg Cohort 2b n=3		VS-6766 4mg Def 200mg Cohort 2a n=23		RP2D VS-6766 3.2mg Def 200mg n=38	
	Gr1/2	Gr3/4	Gr1/2	Gr3/4	Gr1/2	Gr3/4
Rash	3		18	3	32	2
CK Elevation	1		10	4	19	2
AST Elevation	1		11	1	13	
Hyperbilirubinemia	1		8	1	14	1
Visual Disturbance	2		7		9	
ALT Elevation	1		10		5	
Diarrhoea	1		6		14	1
Fatigue			10		8	1
Oral Mucositis^			7	2	11	
Nausea	2		9		5	
Peripheral Edema			6		10	
Thrombocytopenia			4		6	
Pruritus			3	1	5	

- Most Adverse Events (AE) were Grade 1/2
  - All changes were reversible
- No DLTs in Cohort 1 or 2a
- DLTs Cohort 2b: Gr 2 rash in 2/3 of patients; MTD not reached
- Chronic Grade 2 AEs in patients on treatment > 6 months
- To date, no patients have discontinued due to AEs in expansion phase (cohort 3.2mg VS-6766 and Def 200mg)

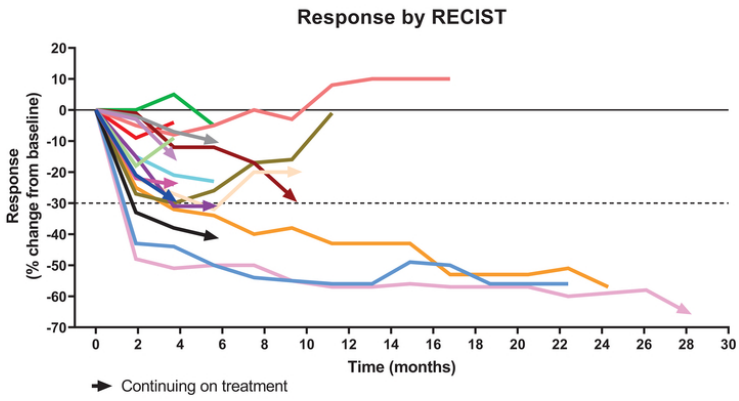
RP2D

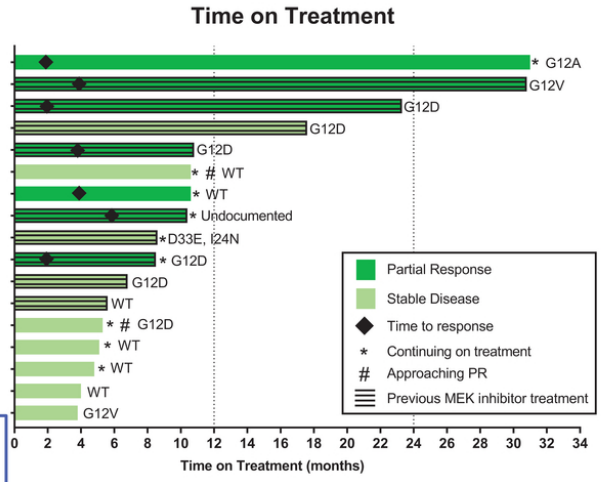
- **VS-6766 3.2 mg** oral twice wkly (3 wks of every 4 wks)
- **Defactinib 200 mg** oral BID (3 wks of every 4 wks)

*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
References: Banerji, Q4 2020 report; Data on file

VS-6766 in Combination with Defactinib Shows Robust ORR with Durability in Refractory LGSOC with Expanded Number of Patients (n=17)

Verastem Oncology

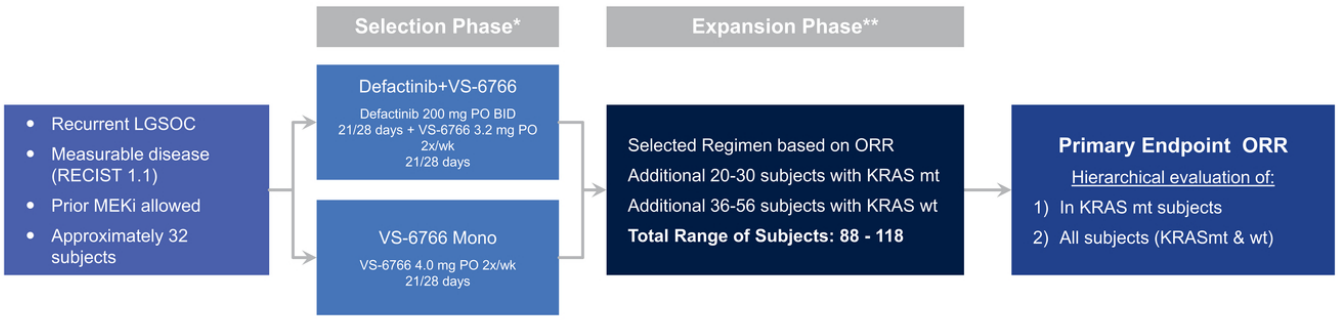




- KRAS-G12 mutations ORR = 56% (5/9); data still maturing
- Current ORR = 41% (7/17); data still maturing
- 5/9 PRs in pts who had previous MEKi[1]
- 9/17 (53%) still on study[2]
- 3 pts on treatment for ~2 yrs or more

[1] Patients came off prior MEKi treatment primarily for progression
[2] Data cutoff date August 17, 2020

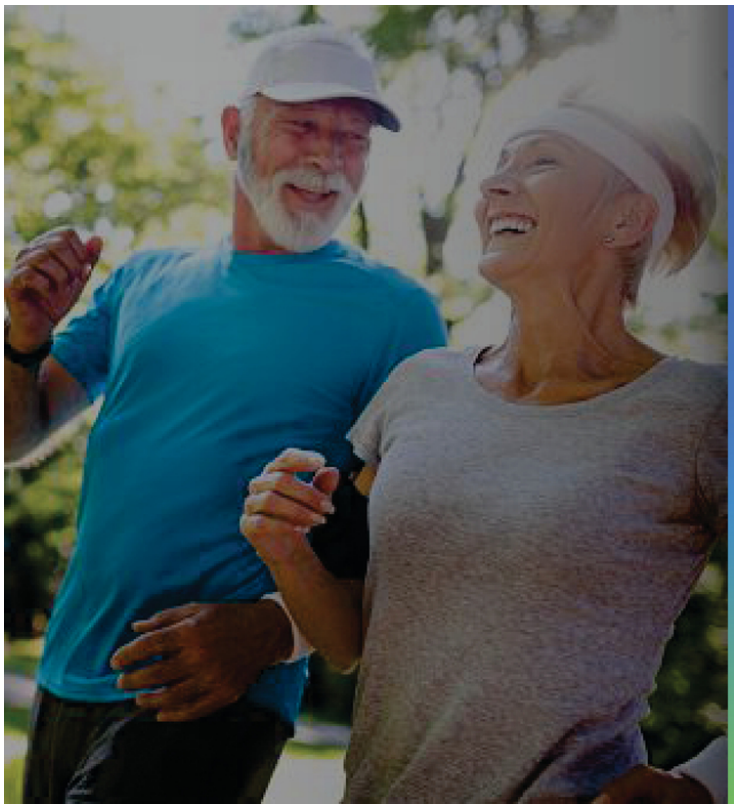
KRAS Mutated (mt) and Wild Type (wt), Phase 2, Recurrent LGSOC Adaptive Design for Potential Accelerated Approval



FDA Was Supportive of Development Strategy and Adaptive Design

This Registration-directed Phase 2 Study Commenced in November 2020 with an estimated Primary Completion Date for the Expansion Phase of June 2023 (clinicaltrials.gov)

* Selection Phase – KRAS mt only
** Expansion Phase – final sample size to be adjusted based on adaptive design



VS-6766 +/- Defactinib in NSCLC

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High Unmet Need in Refractory KRASm NSCLC Adenocarcinoma

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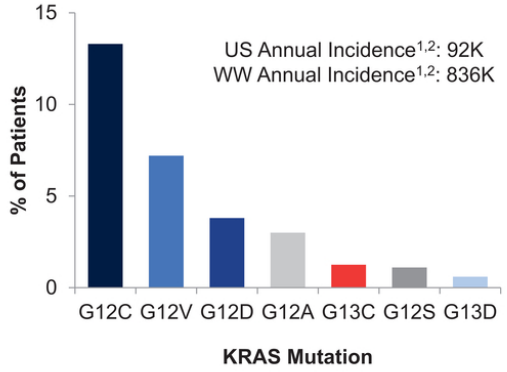
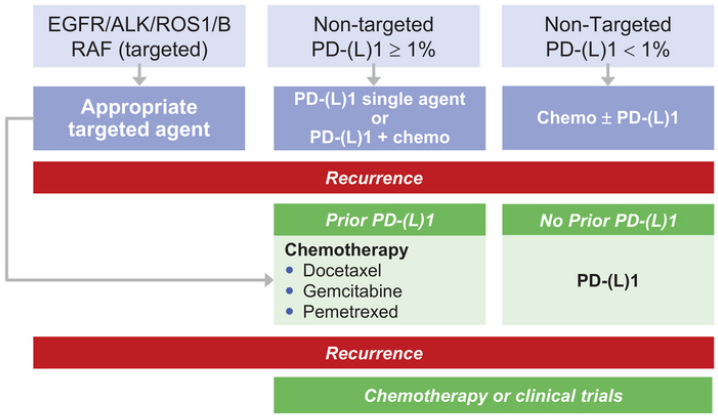
NSCLC Adenocarcinoma[3]



KRAS Mutations Represent 25% of Lung Cancer Adenocarcinoma (EGFR 17%, ALK 7%)[4]

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



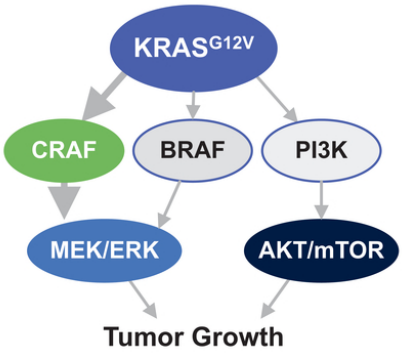
- SOC in recurrent disease is chemotherapy
- Pre-PD-(L)1 era, chemotherapy response rate ~10% in recurrent disease; 12w PFS of 30–45%

[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

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

Verastem Oncology

A Precision Approach to KRAS-G12V Driven NSCLC



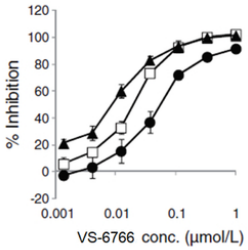
- $KRAS^{G12V}$ signals mainly through RAF/MEK in contrast to other variants, such as KRAS-G12D, which signal more through PI3K/AKT
- $KRAS^{G12V}$ models are especially dependent on CRAF

RAF family

IC_{50}(CRAF●): 0.056 ± 0.016 µmol/L

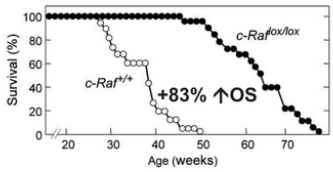
IC_{50}(BRAF □): 0.019 ± 0.0030 µmol/L

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

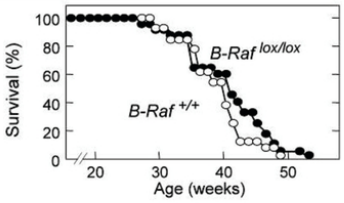


CRAF Drives $KRAS^{G12V}$ NSCLC[1,3]

CRAF KO vs. WT



BRAF KO vs. WT



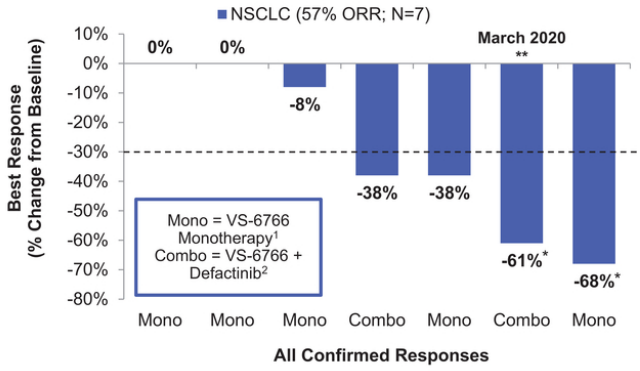
CRAF, but not BRAF, ablation improves survival of mice with $KRAS^{G12V}$ induced lung cancer *in vivo*

Source: 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)

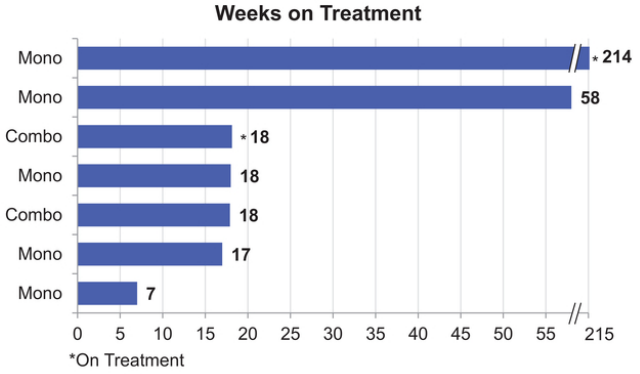
Strong Signal Identified in KRAS^{G12V} to Be Further Validated

VS-6766 ± Defactinib Has a Confirmed 57% ORR in KRAS^{G12V} NSCLC in Integrated Analysis

Best Response by RECIST in KRAS^{G12V} NSCLC



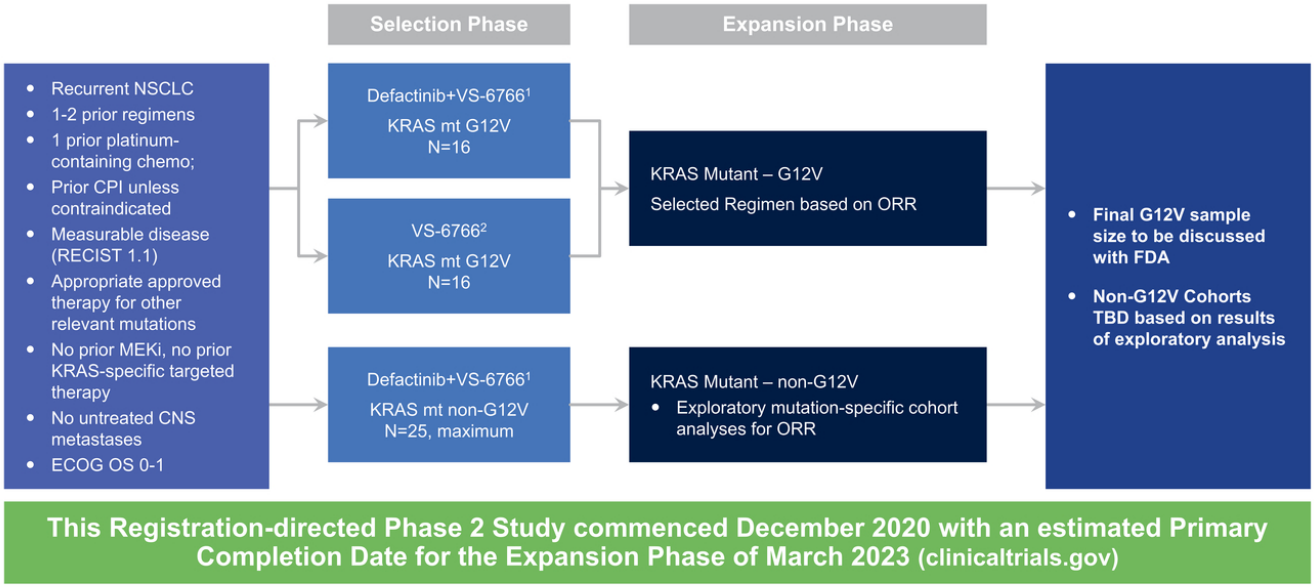
Time on Treatment for KRAS^{G12V} NSCLC



- Preclinical evidence suggests combination with Defactinib may improve efficacy in KRAS^{G12V}
- Activity of VS-6766 as a single agent and in combo with Defactinib in KRAS^{G12V}

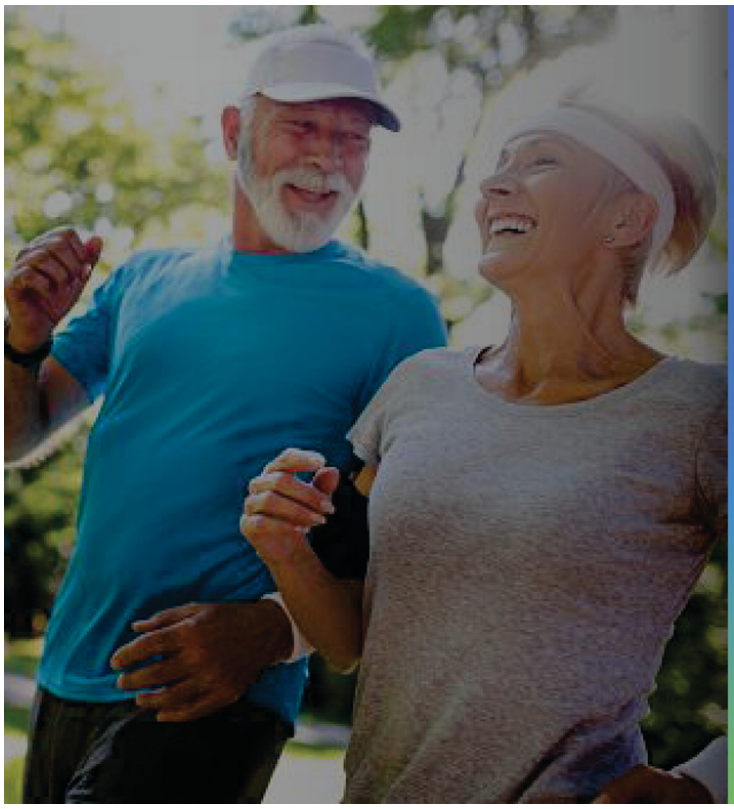
Source: [1] Guo, et al Lancet Oncology 2020 [2] Banerji, AACR VM 1, April 27, 2020, CT143

NSCLC Clinical Strategy: KRAS Mutant (mt), Enriched G12V, Phase 2, Recurrent NSCLC for Potential Accelerated Approval



This Registration-directed Phase 2 Study commenced December 2020 with an estimated Primary Completion Date for the Expansion Phase of March 2023 (clinicaltrials.gov)

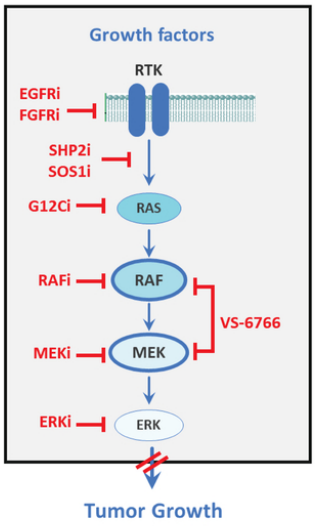
[1] Defactinib 200 mg PO BID (21/28 days) + VS-6766 3.2 mg PO 2x/wk (21/28 days)
[2] VS-6766 4.0 mg PO 2x/wk (21/28 days)

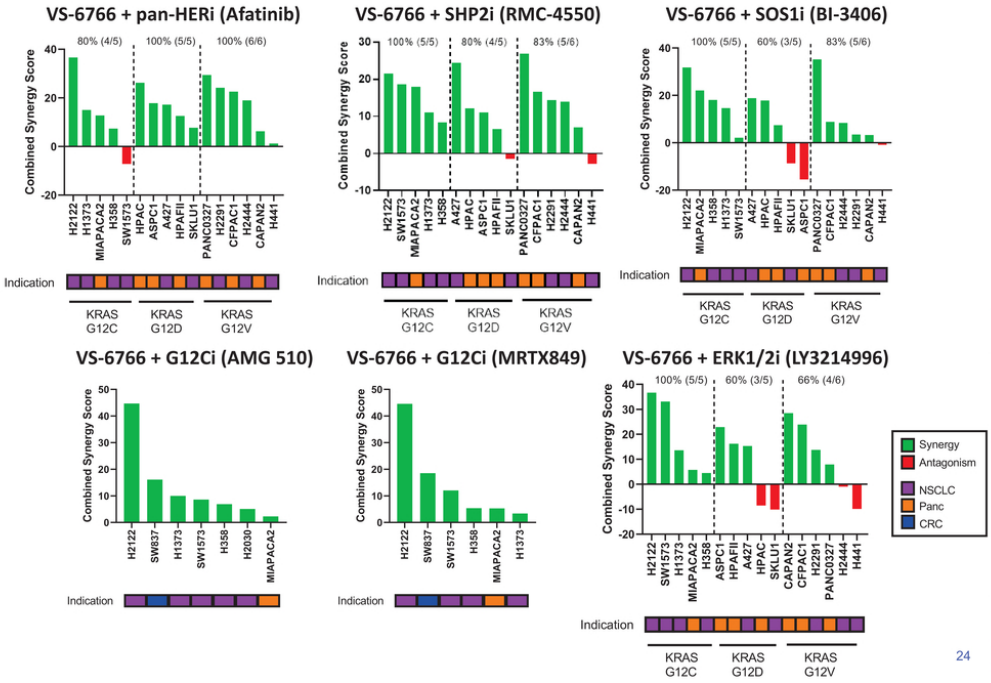


Future Opportunities: VS-6766 as Backbone of RAS Therapy

Verastem Oncology

Vertical Blockade: Preclinical synergy in combination with several promising targets





Presented at RAS-Targeted Drug Discovery (February 23-25, 2021)

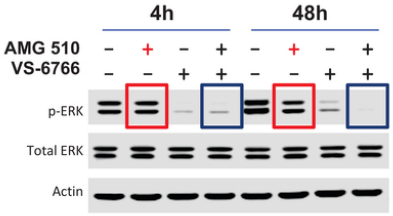
Preclinical synergy of VS-6766 + G12C inhibitors in KRAS G12C mt models

Synergy of VS-6766 + G12C inhibitor AMG 510 across G12C mutant NSCLC, CRC & Pancreatic cancer cell lines

			Combined Synergy Score	
Cell line	Indication	Sensitivity to G12C inhibitors	VS-6766 + AMG 510	VS-6766 + MRTX849
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

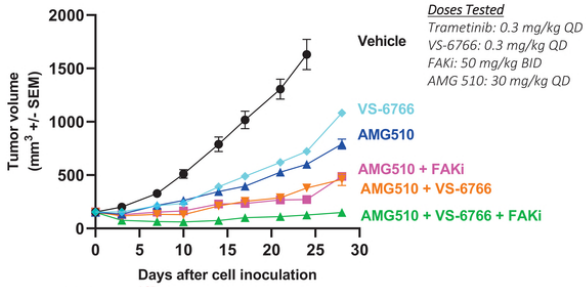
VS-6766 + AMG 510 yields deeper and more sustained inhibition of ERK signaling pathway

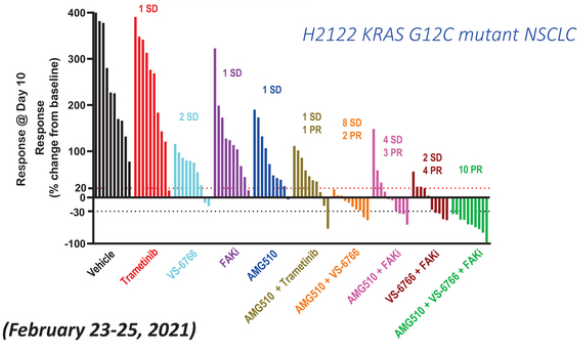


H2122 KRAS G12C mutant NSCLC

Concentrations Tested
AMG 510: 100 nM
VS-6766: 100 nM

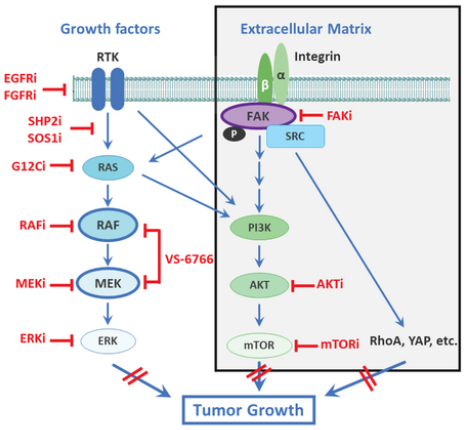
VS-6766 & FAKi potentiate AMG 510 efficacy in KRAS G12C mutant NSCLC in vivo; Tumor regression in all mice with triple combination





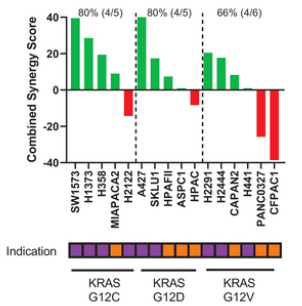
Presented at RAS-Targeted Drug Discovery (February 23-25, 2021)

Parallel Pathway Blockade: Two synergistic combinations already progressed to clinical stage

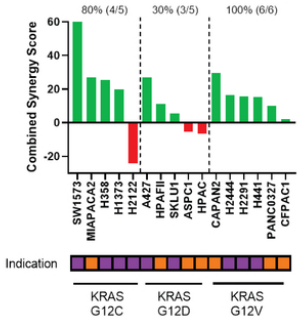


Presented at RAS-Targeted Drug Discovery (February 23-25, 2021)

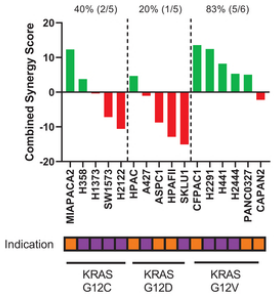
VS-6766 + p70S6K/AKTi (M2698)



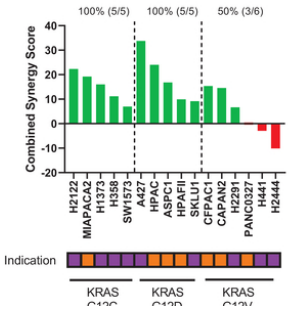
VS-6766 + mTORi (Everolimus)



VS-6766 + FAKi (Defactinib)



VS-6766 + CDK4/6i (Palbociclib)



High Priority Lead Indications with Multiple Growth Opportunities

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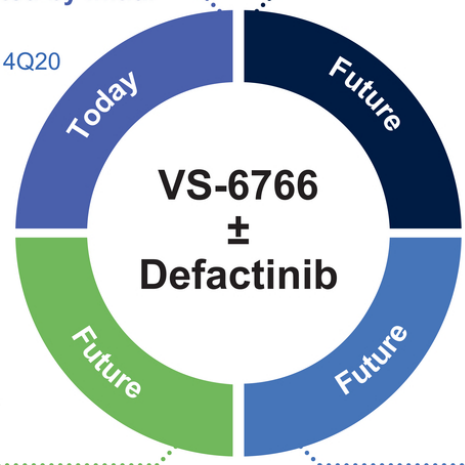
High Priority Indications Supported by Initial Data

Registration-Directed Trials Initiating in 4Q20

- LGSOC[1,2]
- $KRAS^{G12V}$ NSCLC[1,2]

Other Mutation Opportunities

- GNAQ mutations in uveal melanoma2
- NF1 mutations in melanoma
- MAP3K1 mutations in breast cancer



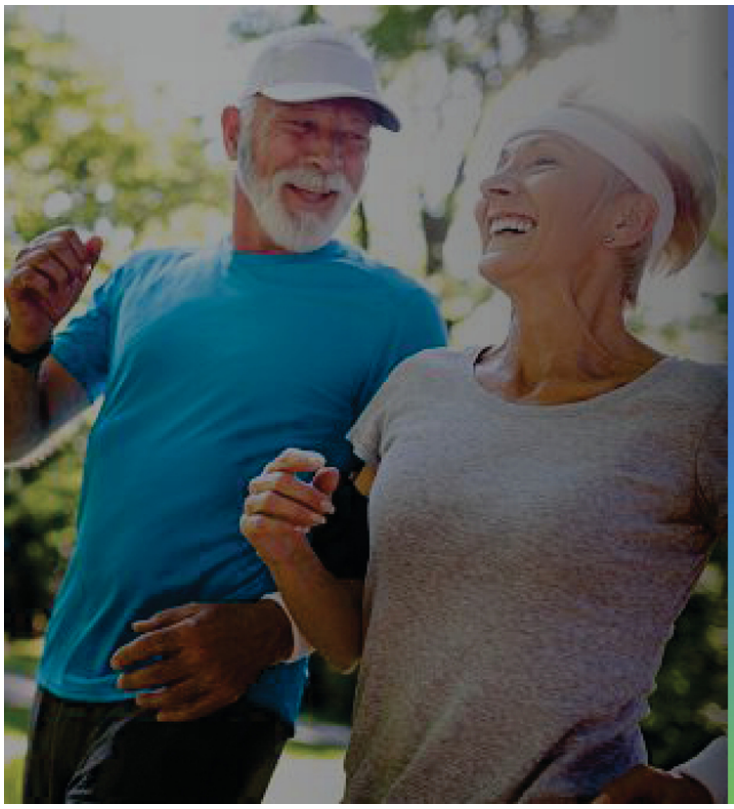
Expansion Opportunities

- Pancreatic[1,2] (10 pt cohort initiated)
- KRAS mt endometrial[1] (10 pts initiated)
- Uveal Melanoma[2] (IST initiated)
- BRAF mt melanoma[1,2]
- NRAS mt melanoma
- RAF mt prostate[2]

Other Combinations

- Anti-PD-1[1,2]
- $KRAS^{G12C}$ inhibitors[2]
- Everolimus[1,2]
- SHP2 inhibitors[2]

[1] Supported by clinical data
[2] Supported by preclinical data



Corporate

Verastem Oncology

Key Financial Statistics

As of September 30, 2020

Cash, cash equivalents & short-term investments as of 9/30/2020	$205.7M
Shares fully diluted as of 9/30/2020	190.2M
Hercules Term Loan Facility as of 9/30/2020	$35.0M
5.00% Convertible Senior Notes Due 2048 (2018 Notes) as of 9/30/2020	$28.3M
Insider ownership (outstanding / vested) as of 9/30/2020	9.2% / 5.0%

Revised to include Hercules Debt Repayment

Proforma Cash after Hercules Repayment	$168.3M
5.00% Convertible Senior Notes Due 2048 as of 11/09/2020	$28.3M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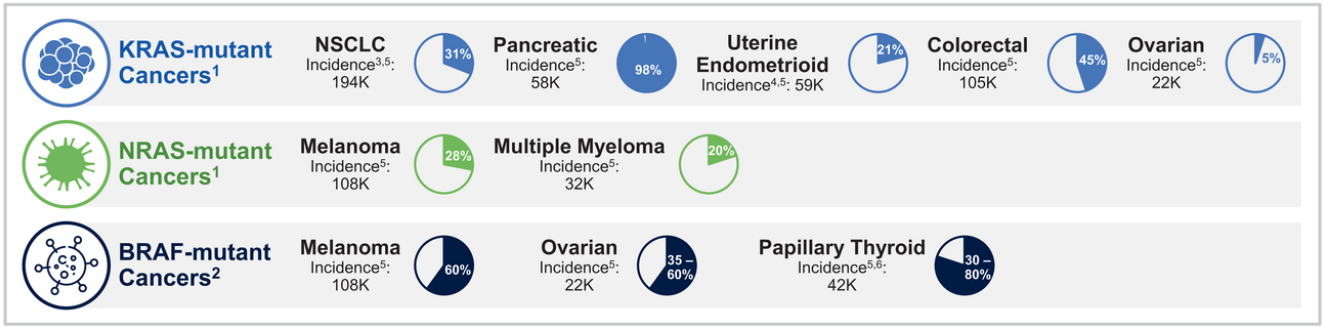
High Unmet Needs in RAS/RAF/MEK/ERK-Driven Cancers



Breadth of potential opportunity

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

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 Sources:

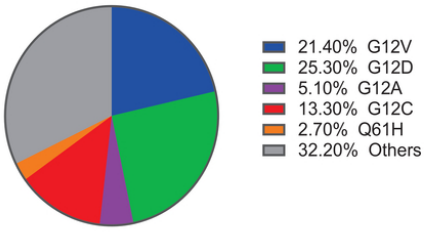
[1]Reference for RAS mt frequencies – Cox et al. *Nature Reviews* 13: 828, 2014; [2]Reference for BRAF mt frequencies – Turski et al. *Mol Cancer Ther* 15: 533, 2016
[3]85% of lung cancer is NSCLC (Lu et. al. *Cancer Manag Res.* 2019); [4]90% of all uterine cancers are of the endometrial type (ACS); [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)

References:

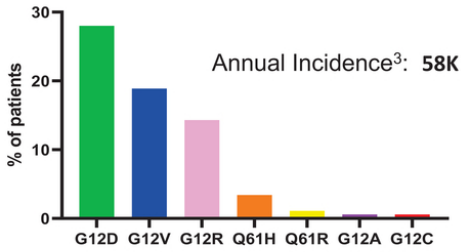
McCormick F Clin Cancer Res 15April2015; Adderley H et al. EBioMedicine 01Mar2019; Papke B et al. Science 17Mar2017; Ryan M et al. *Nature Reviews Clinical Oncology* 01Oct2018; NIH cancer.gov/research/key-initiatives/ras

KRAS G12V and G12D Represent ~50% of KRAS Mutations across Human Cancers

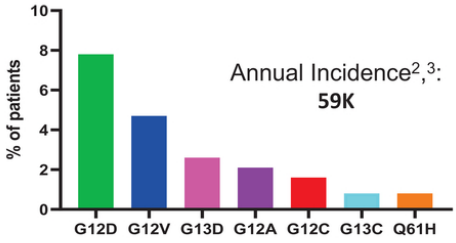
% frequency in a total of 780 cancer patients with KRAS mutations[1]



Pancreatic Adenocarcinoma[1]



Uterine Endometrioid Carcinoma[1]



[1] TCGA PanCancer Atlas (cBioPortal analysis)
[2] 90% of all uterine cancers are of the endometrial type (ACS)
[3] Cancer Statistics 2020 (Siegel et al. CA Cancer J Clin 2020; 70:7-30)

VS-6766 and FAK inhibitor combination leads to more robust anti-tumor efficacy *in vivo*

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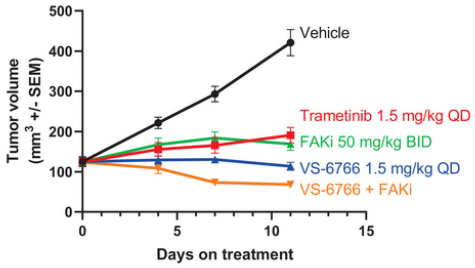
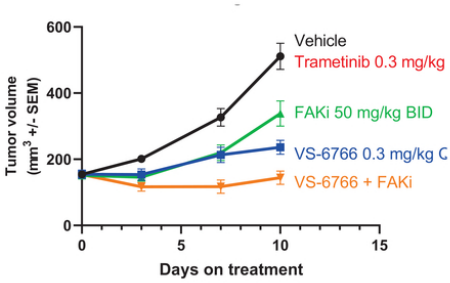
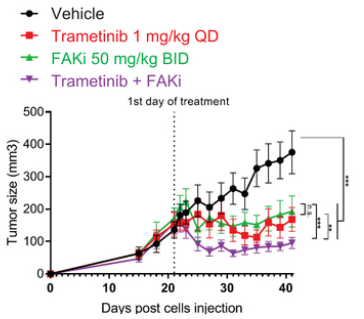
Ovarian cancer model
(TOV-21g KRAS(G13C) mutant)



NSCLC cancer model
(H2122 KRAS(G12C) mutant)

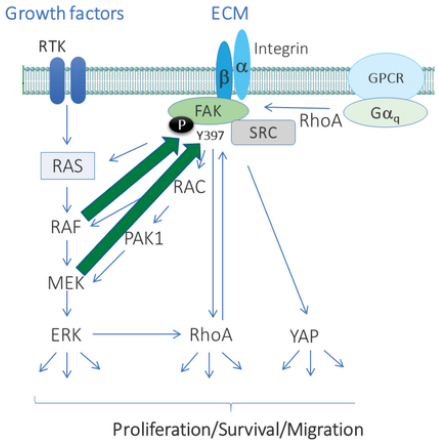


Uveal melanoma model
(92.1 GNAQ mutant)

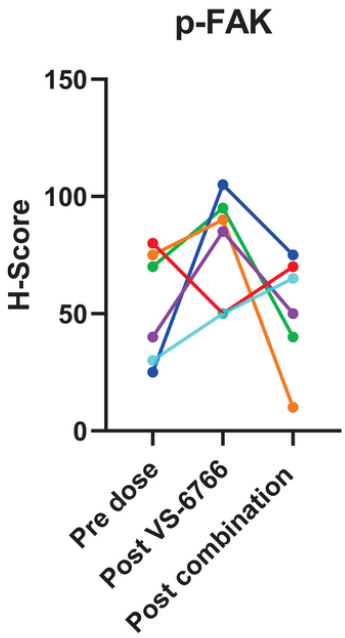


J. Paradis, AACR 2020

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**

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

Pharmacokinetic Profiles of VS-6766 + Defactinib in Combination Similar to that seen in Single Agent Studies

VS-6766

Cohort	Dose (mg)	N	Subject	$AUC_{0\text{-}24h}$ (h*ng/mL)	C_{max} (ng/mL)
1	3.2 (with 200mg VS)	3	Mean	6179	354
			CV%	32.1	30.4
2a	4 (with 200mg VS)	5	Mean	5353	289
			CV%	15.8	16.0
2b	3.2 (with 400mg VS)	1	FRA101-007	3302	229

Defactinib

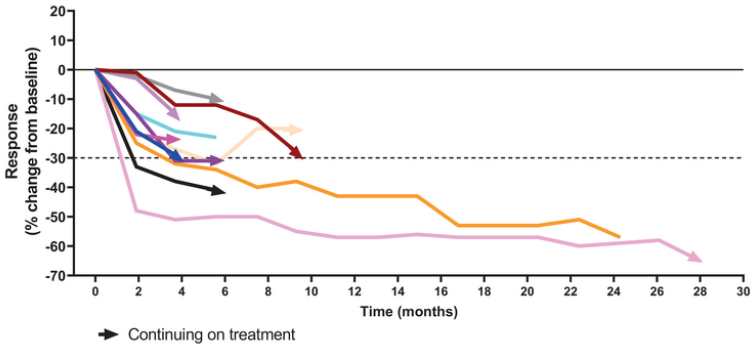
Cohort	Dose (mg)	N	Subject	AUClast (h*ng/mL)	Cmax (ng/mL)
1	200 (with 3.2mg RO)	3	Mean	2071	273
			CV%	103	80
2a	200 (with 4mg RO)	5	Mean	2252	318
			CV%	124	117
2b	400 (with 3.2mg RO)	3	Mean	2807	360
			CV%	31	32

Reference: Banerji, AACR VM 1, April 27, 2020, CT1

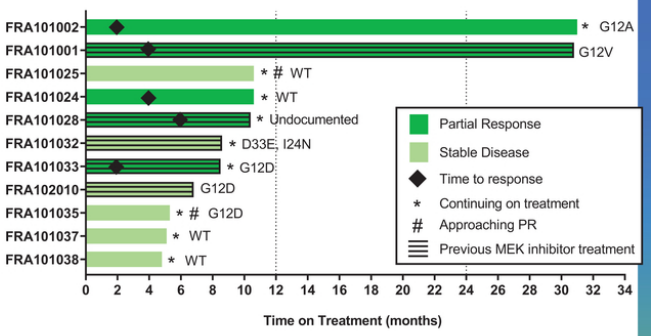
VS-6766 in Combination with Defactinib Shows Robust ORR with Durability in Refractory LGSOC at Phase 2 Dose Level

All patients on RP2D: 3.2 mg VS-6766 (2x/wk) + 200 mg Defactinib (BID) q3/4 wks

Response by RECIST



Time on Treatment

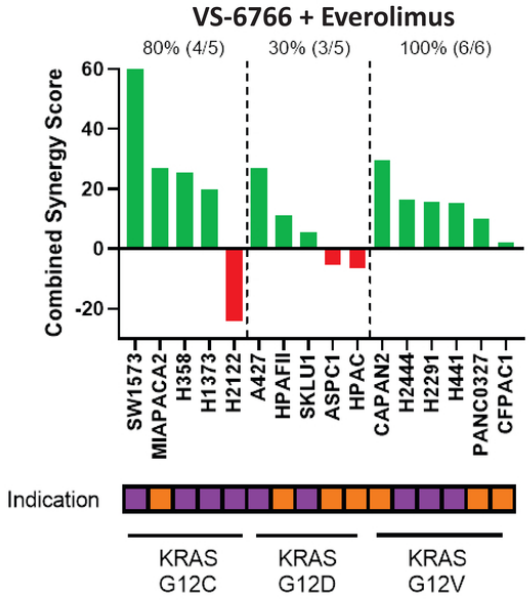


- ORR in KRAS mt = 50% (3/6); data still maturing
- Current overall ORR = 45% (5/11); data still maturing
- 9/11 (82%) still on study at RP2D[1]
- 2 pts on treatment for 2.5 yrs

[1] Data cutoff date August 17, 2020

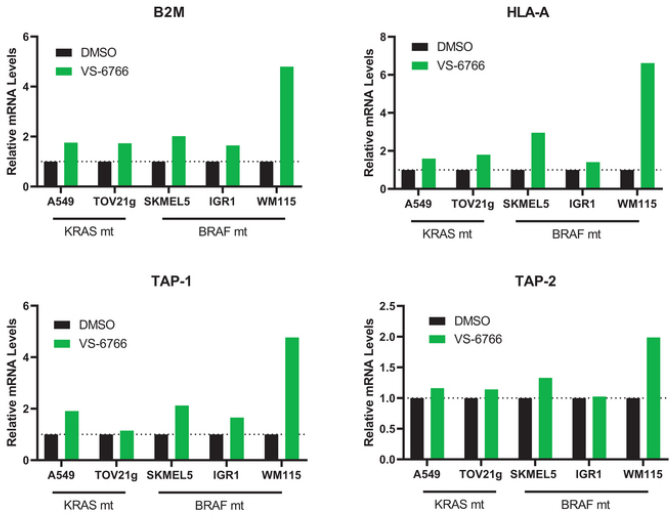
Status: Combination of VS-6766 with Everolimus (mTOR inhibitor)

- Synergy of VS-6766 + everolimus observed broadly across cancer cell lines with various KRAS mutation variants
- *A well-tolerated RP2D for VS-6766 + everolimus has been established with intermittent dosing of both agents (twice weekly; 3 wks on/1 wk off)*
- *KRAS mutant NSCLC expansion cohort is currently ongoing with VS-6766 + everolimus*



Presented at RAS-Targeted Drug Discovery (February 23-25, 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	KRASmut G12S
TOV21g	Ovarian	KRASmut G13C
SKMEL5	Melanoma	BRAFmut V600E
IGR-1	Melanoma	BRAFmut V600E
WM115	Melanoma	BRAFmut V600E

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

Strong Patent Protection for VS-6766 ± Defactinib

- COM for VS-6766 to 2027 & defactinib to 2028, Hatch Waxman should extend to 2032
- VS-6766 intermittent dosing regimen until 2038 if granted
- FAK/MEK combination to 2035
- VS-6766/defactinib combination until 2040 if granted
- Method of manufacture for VS-6766 to 2032
- Other activity related to patent protection is ongoing and will continue into the future

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 People & Organizational Strategy Officer

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

Jonathan Pachter, Ph.D.
Chief Scientific Officer

- Head of Cancer Biology – OSI (now Astellas)

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

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