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): **September 16, 2020**

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 September 16, 2020, Verastem, Inc. (the "Company") issued a press release and posted a presentation, which the Company will be presenting at the Second Annual RAS-Targeted Drug Development Summit on September 16, 2020 (the "Presentation"), announcing updated clinical data from the low-grade serous ovarian cancer cohort of the ongoing investigator-initiated Phase 1/2 FRAME study. Copies of the press release and the Presentation are furnished hereto as Exhibits 99.1 and 99.2.

On September 16, 2020, the Company also posted its corporate presentation, a copy of which is furnished hereto as Exhibit 99.3.

Item 9.01. Financial Statements and Exhibits

Exhibit No.	Description
99.1	Press Release, dated September 16, 2020
99.2	Presentation for Second Annual RAS-Targeted Drug Development Summit
99.3	Corporate Presentation, dated September 16, 2020
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: September 16, 2020

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

Exhibit 99.1

Verastem Oncology Announces Presentation of Updated Phase 1/2 FRAME Study Data at the 2nd Annual RAS-Targeted Drug Development Summit

Preliminary Data on VS-6766 and Defactinib Combination Continues to Show Encouraging Response Rates, Durability and a Favorable Safety Profile in KRAS Mutant Low-Grade Serous Ovarian Cancer in Investigator-Initiated Trial

New Preclinical Data Demonstrating Synergy and Tumor Regression with G12C Inhibitors in Combination with VS-6766 and FAK Inhibitor In Vitro and In Vivo Also Presented

Management to Host Investor Conference Call Today at 8:00 AM ET

BOSTON, MA – September 16, 2020 – Verastem, Inc. (Nasdaq:VSTM) (also known as Verastem Oncology), a biopharmaceutical company committed to advancing new medicines for patients battling cancer, today announced updated results from the ongoing investigator-initiated Phase 1/2 FRAME study evaluating VS-6766, its RAF/MEK inhibitor, in combination with defactinib, its FAK inhibitor, which demonstrated robust response rates, duration of response and a favorable safety profile in patients with low-grade serous ovarian cancer (LGSOC). These data will be presented in a virtual oral presentation today by Dr. Udai Banerji from The Institute of Cancer Research and The Royal Marsden at the 2nd Annual RAS-Targeted Drug Development Summit.

"Existing treatments for patients with LGSOC are limited by either 10-25% response rates and/or increased toxicities, leading to high discontinuation rates. The FRAME data being presented today continue to demonstrate that RAF/MEK inhibition combined with FAK inhibition is well tolerated with a 56% overall response rate (ORR) in patients with KRAS-G12 mutant LGSOC and a 41% ORR in the overall LGSOC population. These data are still actively maturing with more than half of the patients still on treatment as of the data cutoff date, and responses in this patient population tend to deepen over time," said Dan Paterson, President and Chief Operating Officer of Verastem Oncology. "The response rates from this expanded data set are highly encouraging, consistent with the prior positive data from this study, and continue to speak to the significant potential of the VS-6766/defactinib combination for patients battling LGSOC."

Verastem recently met with the Food and Drug Administration (FDA), and the FDA is supportive of the Company's adaptive study design for the planned Phase 2 registration-directed trials evaluating VS-6766 and defactinib in patients with recurrent LGSOC. Verastem expects to commence registration-directed clinical trials in both recurrent LGSOC and KRAS mutant non-small cell lung cancer by the end of 2020. Assuming a positive outcome from these registration-directed trials, Verastem expects to submit New Drug Applications to the FDA requesting accelerated approval for the VS-6766/defactinib combination in both LGSOC and KRAS mutant NSCLC.

Updated Phase 1/2 FRAME Study Results in Patients with LGSOC

Among the patients with LGSOC (n=17), the overall response rate (ORR) was 41% (7 of 17 patients), all partial responses (PRs). Among the patients with KRAS-G12 mutant LGSOC (n=9), the ORR was 56% (5 of 9 patients). Of the seven patients who responded, five had received one or more prior MEK inhibitors. In patients with KRAS mutant LGSOC receiving the recommended Phase 2 dosing (RP2D) regimen, the ORR was 50% (3 of 6 patients). The LGSOC cohort of the FRAME study remains ongoing, with 53% (9 of 17 patients) still on study as of the data cutoff date of August 17, 2020, with three patients on treatment for two years or more.

The most common Grade ≥3 treatment-related adverse events (TEAEs) observed for the recommended Phase 2 dosing regimen were rash (4%) and elevated creatine kinase (4%). No patients discontinued from the FRAME study due to TEAEs.

The novel, intermittent, combination dosing schedule used in the FRAME study continues to show encouraging clinical activity in patients with KRAS mutant LGSOC, including in patients who had previously progressed following treatment with a MEK inhibitor.

“These updated safety and efficacy results in both KRAS mutant LGSOC as well as the overall LGSOC population are highly encouraging. Of particular note in this early look at the data, is the strong, 50% response rate, durability, and tumor reduction seen in patients with KRAS mutant LGSOC receiving the recommended Phase 2 dosing (RP2D) regimen, which is the regimen we will be taking into our upcoming registration-directed study,” said Brian Stuglik, Chief Executive Officer of Verastem Oncology. “With nine out of 11 patients at RP2D active in the study and responses still developing, we look forward to continued data outputs from this study and we remain on track to commence Phase 2 registration-directed trials in both LGSOC and KRAS mutant NSCLC by the end of this year.”

Preclinical Results from Studies Investigating VS-6766 and Defactinib in Combination with G12C Inhibitors

KRAS-G12C inhibitors may benefit from novel combination approaches to enhance their inhibition of the ERK signaling pathway. In the preclinical results that will be presented today at the meeting, VS-6766 showed synergy with KRAS-G12C inhibitors in reducing cancer cell viability across a panel of KRAS-G12C mutant NSCLC and colorectal cancer (CRC) cell lines. This enhanced cellular anti-cancer activity of the combination correlated with deeper and more durable inhibition of ERK pathway signaling relative to G12C inhibition alone. In KRAS-G12C mutant NSCLC models in mice, the RAF/MEK dual inhibitor VS-6766 was more effective than trametinib when compared at equal dose level both alone and in combination with a G12C inhibitor. In the KRAS-G12C NSCLC models tested, the combination of G12C inhibitor with VS-6766 and FAK inhibitor induced tumor regressions of ≥30% in all mice.

“The anti-tumor effects of VS-6766 were generally comparable to those of KRAS-G12C inhibitors in KRAS-G12C NSCLC models in mice and were stronger than the effects of trametinib at a comparable dose,” said Jonathan Pachter, Ph.D., Chief Scientific Officer of Verastem Oncology. “The tumor regressions observed with the triple combination of VS-6766, FAK inhibitor and G12C inhibitor were particularly striking. These data support clinical evaluation of VS-6766 and defactinib with G12C inhibitors in patients with KRAS-G12C mutant tumors.”

About the Phase 1/2 FRAME Study

The FRAME study is an open-label, investigator-initiated study that is designed to assess safety, dose response and preliminary efficacy of the VS-6766/defactinib combination in patients with KRAS mutant solid tumors, including LGSOC, non-small cell lung cancer (NSCLC) and colorectal cancer (CRC). The FRAME study is being led by Dr. Banerji and is being conducted in the United Kingdom. In this study, VS-6766 was administered using a twice-weekly dose escalation schedule and was administered three out of every four weeks. Defactinib was administered using a twice-daily dose escalation schedule, also three out of every four weeks. Dose levels were assessed in three cohorts: cohort 1 (VS-6766 3.2mg, defactinib 200mg); cohort 2a (VS-6766 4mg, defactinib 200mg); and cohort 2b (VS-6766 3.2mg, defactinib 400mg). The recommended Phase 2 dose was determined to be VS-6766 3.2mg, defactinib 200mg. The FRAME study is now expanding to include new cohorts in pancreatic cancer, KRAS mutant endometrial cancer and KRAS-G12V mutant NSCLC.

Details for the RAS-Targeted Drug Development Summit oral presentation are as follows:

Title: Clinical Combinations: Dual RAF-MEK Inhibitor & FAK for Treatment of KRAS Mutant Cancers With a Focus on Low Grade Ovarian Cancer
Lead author: Udai Banerji, The Institute of Cancer Research and The Royal Marsden
Date and Time: Wednesday, September 16, 2020; 3:35 p.m. ET (12:35 p.m. PT)

Title: Synergistic Combinations with the Dual RAF/MEK Inhibitor VS-6766 to Overcome Resistance Mechanisms
Lead author: Jonathan Pachter, Verastem Oncology
Date and Time: Wednesday, September 16, 2020; 12:10 p.m. ET (9:10 a.m. PT)

Conference Call and Webcast Information

The Verastem Oncology management team will host a conference call and webcast on Wednesday, September 16, 2020, at 8:00 AM ET to discuss the updated Phase 1/2 FRAME study data. The call can be accessed by dialing (877) 341-5660 (US and Canada) or (315) 625-3226 (international), five minutes prior to the start of the call and providing the passcode 5278200.

The live, listen-only webcast of the conference call can be accessed by visiting the investors section of the Company's website at www.verastem.com. A replay of the webcast will be archived on the Company's website for 90 days following the call.

About VS-6766

VS-6766 (formerly known as CH5126766, CKI27 and RO5126766) is a unique inhibitor of the RAF/MEK signaling pathway. In contrast to other MEK inhibitors in development, VS-6766 blocks both MEK kinase activity and the ability of RAF to phosphorylate MEK. This unique mechanism allows VS-6766 to block MEK signaling without the compensatory activation of MEK that appears to limit the efficacy of other inhibitors.

About Defactinib

Defactinib (VS-6063) is an oral small molecule inhibitor of FAK and PYK2 that is currently being evaluated as a potential combination therapy for various solid tumors. The Company has received Orphan Drug designation for defactinib in ovarian cancer and mesothelioma in the US, EU and Australia. Preclinical research by Verastem Oncology scientists and collaborators at world-renowned research institutions has described the effect of FAK inhibition to enhance immune response by decreasing immuno-suppressive cells, increasing cytotoxic T cells, and reducing stromal density, which allows tumor-killing immune cells to enter the tumor.[1,2]

About the VS-6766/Defactinib Combination

RAS mutant tumors are present in ~30% of all human cancers, have historically presented a difficult treatment challenge and are often associated with significantly worse prognosis. Challenges associated with identifying new treatment options for these types of cancers include resistance to single agents, identifying tolerable combination regimens with MEK inhibitors and new RAS inhibitors in development addressing only a minority of all RAS mutated cancers.

The combination of VS-6766 and defactinib has been found to be clinically active in patients with KRAS mt tumors. In an ongoing investigator-initiated Phase 1/2 FRAME study, the combination of VS-6766 and defactinib is being evaluated in patients with LGSOC, KRASmt NSCLC and colorectal cancer (CRC). Updated data from this study presented at the 2nd Annual RAS-Targeted Drug Development Summit in September 2020 demonstrated a 56% overall response rate and long duration of therapy among patients with KRAS-G12 mt LGSOC. Based on an observation of higher response rates seen in NSCLC patients with KRAS-G12V mutations in the study, Verastem will also be further exploring the role of VS-6766 and defactinib in KRAS-G12V NSCLC. The FRAME study was expanded in August 2020 to include new cohorts in pancreatic cancer, KRASmt endometrial cancer and KRAS-G12V NSCLC.

About Verastem Oncology

Verastem Oncology (Nasdaq: VSTM) is a development-stage biopharmaceutical company committed to the development and commercialization of new medicines to improve the lives of patients diagnosed with cancer. Our pipeline is focused on novel small molecule drugs that inhibit critical signaling pathways in cancer that promote cancer cell survival and tumor growth, including RAF/MEK inhibition and focal adhesion kinase (FAK) inhibition. For more information, please visit www.verastem.com.

Forward-Looking Statements Notice

This press release includes forward-looking statements about Verastem Oncology's strategy, future plans and prospects, including statements related to the potential clinical value of the RAF/MEK/FAK combination and the timing of commencing a registration-directed trial for the RAF/MEK/FAK combination. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," "can," "promising" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Each forward-looking statement is subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statement.

Applicable risks and uncertainties include the risks and uncertainties, among other things, regarding: the success in the development and potential commercialization of our product candidates, including 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; 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 labeling and other matters that could affect the 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 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; that our product candidates will experience manufacturing or supply interruptions or failures; 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; that we or Chugai Pharmaceutical Co., Ltd. will fail to fully perform under the VS-6766 license agreement; that we may not have sufficient cash to fund our contemplated operations; that we may be unable to make additional draws under our debt facility or obtain adequate financing in the future through product licensing, co-promotional arrangements, public or private equity, debt financing or otherwise; that we will be unable to execute on our partnering strategies for defactinib in combination with VS-6766; that we will not pursue or submit regulatory filings for our product candidates; and that our product candidates will not receive regulatory approval, become commercially successful products, or result in new treatment options being offered to patients.

Other risks and uncertainties include those identified under the heading "Risk Factors" in the Company's Annual Report on Form 10-K for the year ended December 31, 2019 as filed with the Securities and Exchange Commission (SEC) on March 11, 2020 and in any subsequent filings with the SEC. The forward-looking statements contained in this press release reflect Verastem Oncology's views as of the date hereof, and the Company does not assume and specifically disclaims any obligation to update any forward-looking statements whether as a result of new information, future events or otherwise, except as required by law.

References

[1] Chénard-Poirier, M. et al. Results from the biomarker-driven basket trial of RO5126766 (CH5127566), a potent RAF/MEK inhibitor, in RAS- or RAF-mutated malignancies including multiple myeloma. Journal of Clinical Oncology 2017: 35. 10.1200/JCO.2017.35.15_suppl.2506.

[2] https://clinicaltrials.gov, NCT03875820

Contacts

Investors:
John Doyle
Vice President, Investor Relations & Finance
+1 781-469-1546
jdoyle@verastem.com

Media:
Lisa Buffington
Corporate Communications
+1 781-292-4205
lbuffington@verastem.com

Exhibit 99.2


Verastem
Oncology
Synergistic Combinations with the Dual RAF/MEK Inhibitor VS-6766 to Overcome Resistance Mechanisms
Jonathan Pachter, PhD, Chief Scientific Officer – Verastem Oncology
RAS-Targeted Drug Development, Sept 16, 2020
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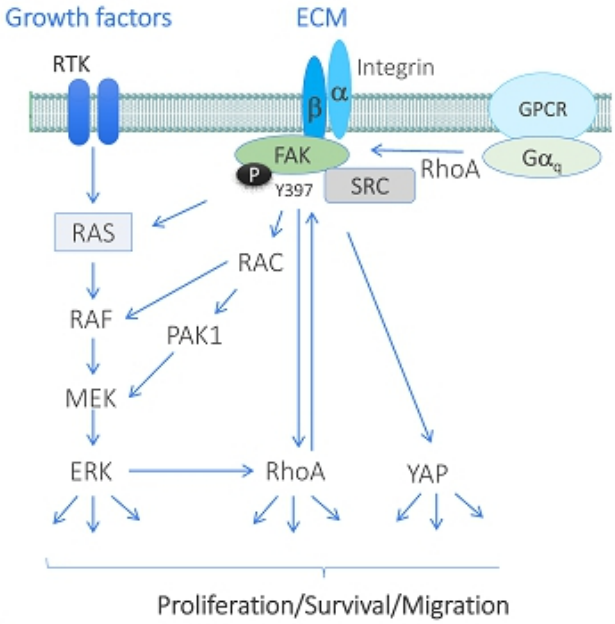
Disclosures

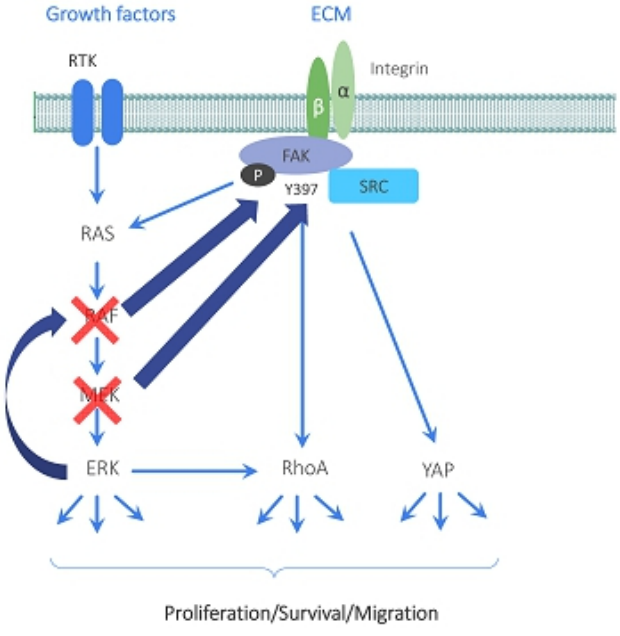
- I am an employee of Verastem Oncology
- I will be discussing investigational/off-label uses of VS-6766 (RAF/MEK inhibitor) and defactinib (focal adhesion kinase inhibitor)

More Complete Shutdown of RAS Pathway-Driven Tumor Growth Requires Addressing Multiple Resistance Mechanisms



- BRAF & MEK inhibitors can block Growth Factor-stimulated ERK signaling, but Cell Attachment can also stimulate ERK signaling through a FAK-dependent pathway (Slack-Davis, JCB 162:281, 2003)
- GPCR-mediated activation of RhoA and YAP pathways through FAK (Feng, Cancer Cell, 2019) may also confer cancer cell proliferation and survival bypassing the ERK pathway
- Signaling through a RhoA-FAK axis is required for maintenance of KRAS-dependent lung adenocarcinomas (Konstantinou, Cancer Discovery 3:444, 2013)
- BRAF inhibition generates a drug-tolerant microenvironment for melanoma cells which can be abolished by FAK inhibition (Hirata, Cancer Cell 27:574, 2015)

More Complete Shutdown of RAS Pathway-Driven Tumor Growth Requires Addressing Multiple Resistance Mechanisms



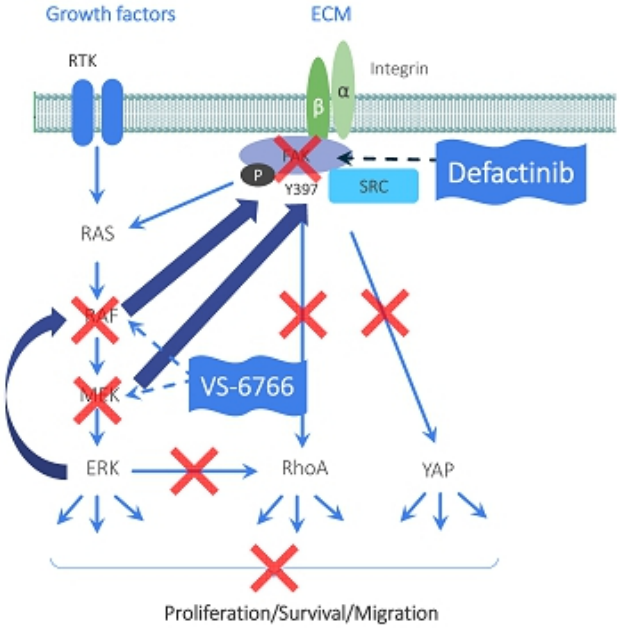
- BRAF inhibition induces compensatory activation of pFAK[1]
- MEK inhibition induces compensatory activation of pFAK preclinically and clinically[2]
  - Trametinib induced ↑ pFAK (Y397) preclinically in KRAS mt NSCLC cell lines
  - Also observed in patients
    - VS-6766 induced ↑ pFAK (Y397) as a potential resistance mechanism in the majority of patients
    - Combination with defactinib reduced this compensatory pFAK signal
- Upon MEK blockade, ERK feeds back to activate RAF kinase

➡ = Feedback Reactivation

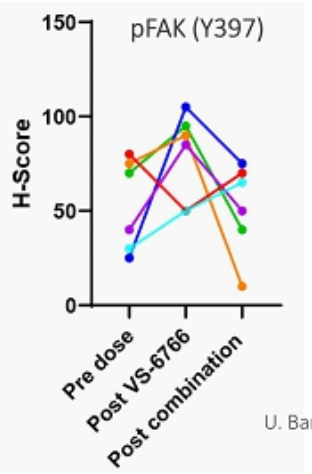
Verastem Oncology

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

More Complete Shutdown of RAS Pathway-Driven Tumor Growth Requires Addressing Multiple Resistance Mechanisms



- In patients with KRAS mt tumors
  - VS-6766 induced ↑ pFAK (Y397) as a potential resistance mechanism in the majority of patients
  - Combination of VS-6766 with defactinib reduced this compensatory pFAK signal

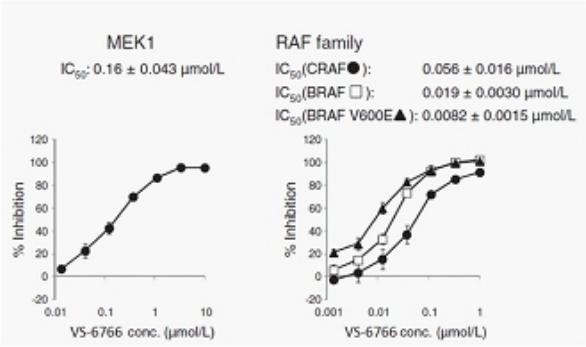


U. Banerji, AACR 2020

Verastem Oncology

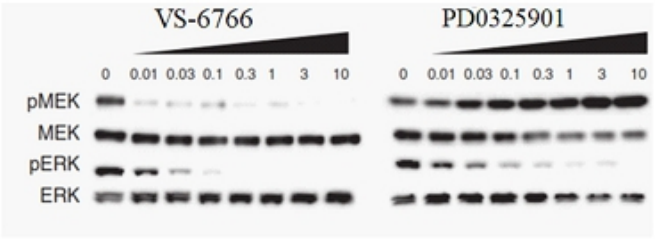
VS-6766 is a Unique Small Molecule RAF/MEK Dual Inhibitor

- VS-6766 inhibits both MEK & RAF kinase activities



- Most 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

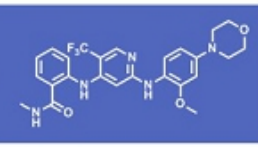


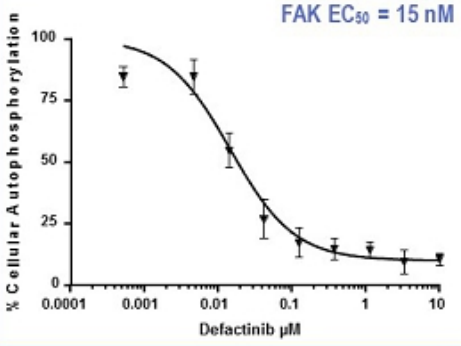
Reference:
Ishii et al., *Cancer Res*, 2013; Lito et al., Cancer Cell, 2014; Blasco, R. B. *et al. Cancer Cell* (2011); Sanclemente, M. *et al. Cancer Cell* (2018)

Verastem Oncology

Defactinib (VS-6063) – Selective FAK Inhibitor

Defactinib

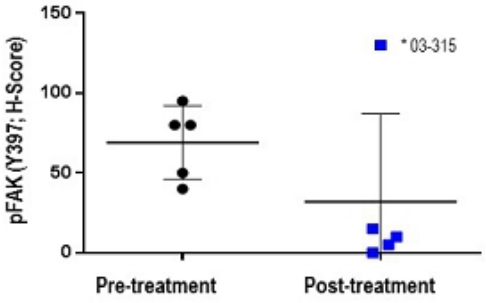




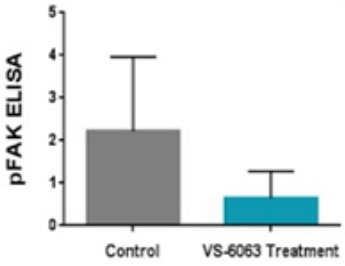
Dosage: Oral, 400mg BID

- Studied in 500+ patients with good safety profile observed to date
- DLT not reached
- Early signs of clinical efficacy
- Well established safety profile as a single agent and in combination:
  - RAF/MEKi, PD-1i, Chemotherapy

OVARIAN CANCER: TUMOR BIOPSIES



MESOTHELIOMA: TUMOR BIOPSIES

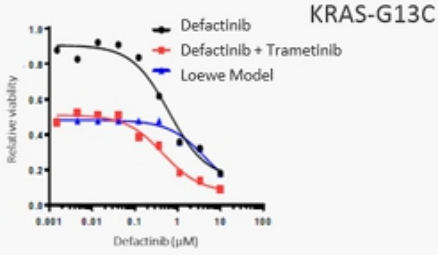


Verastem Oncology

Combination of defactinib with VS-6766 or trametinib shows synergy in KRAS mt and BRAF mt cell lines

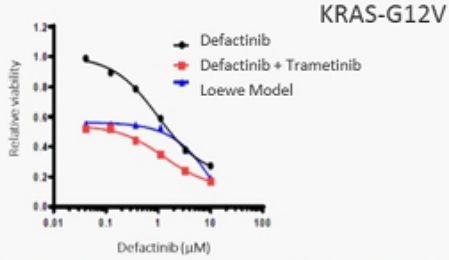
TOV-21G CELLS KRAS-MUTANT OVARIAN CANCER

KRAS-G13C

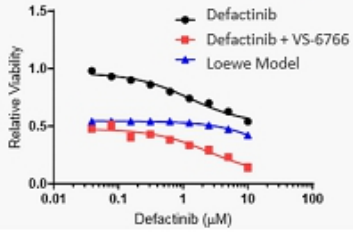


H441 CELLS KRAS-MUTANT NON-SMALL-CELL LUNG CANCER

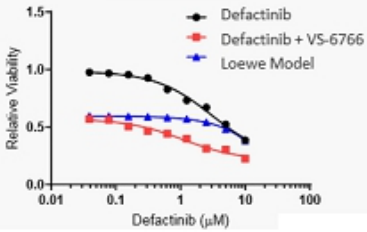
KRAS-G12V



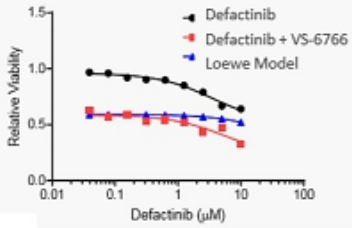
SW982 CELLS SARCOMA BRAF:pV600E



MERO-14 CELLS MESOTHELIOMA



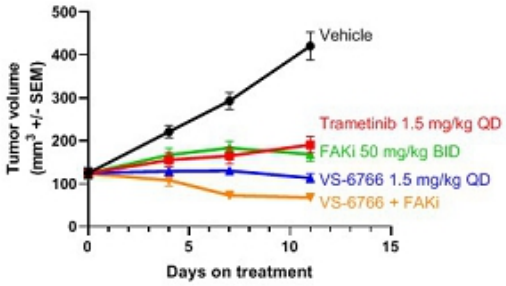
CAL-51 CELLS TRIPLE NEGATIVE BREAST CANCER



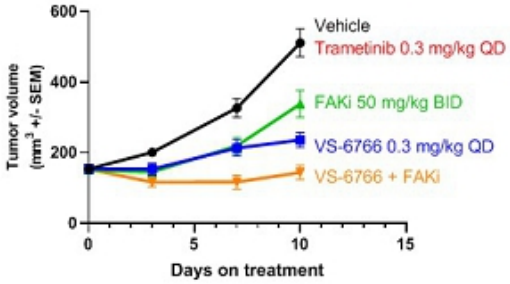
Verastem Oncology

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

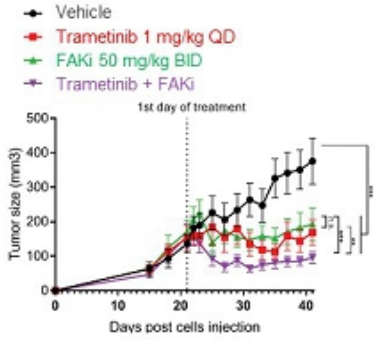
Ovarian cancer model
(TOV-21g KRAS(G13C) mutant)



NSCLC cancer model
(H2122 KRAS(G12C) mutant)



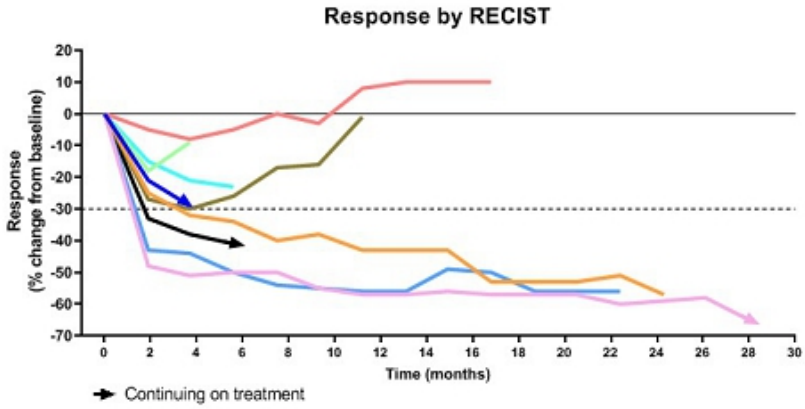
Uveal melanoma model
(92.1 GNAQ mutant)

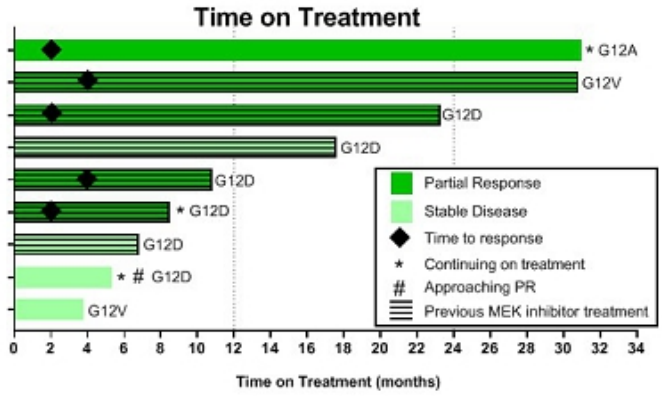


J. Paradis, AACR 2020

Verastem Oncology

VS-6766 in Combination with Defactinib Shows Robust ORR with Durability in Patients with Refractory KRAS Mutant Low Grade Serous Ovarian Cancer





Udai Banerji, RAS-Targeted Drug Development, 2020
9/16/20, 3:35 pm ET

- 9 pts with KRAS-G12 mutations
- ORR = 56% (5/9); data still maturing
- 4/5 PRs in pts who had previous MEKi
- 2 pts on treatment for 2.5 yrs

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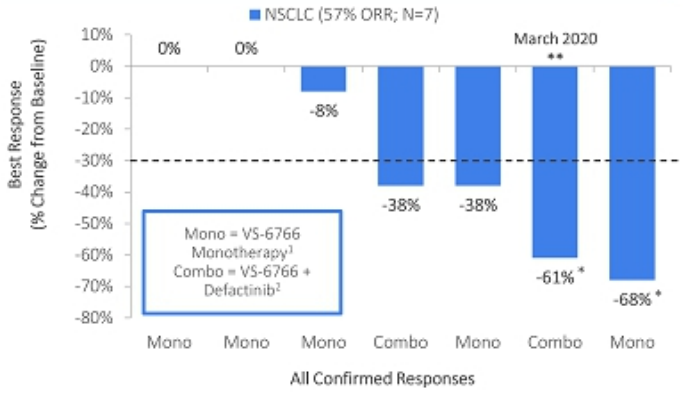
Cut-off August 17, 2020

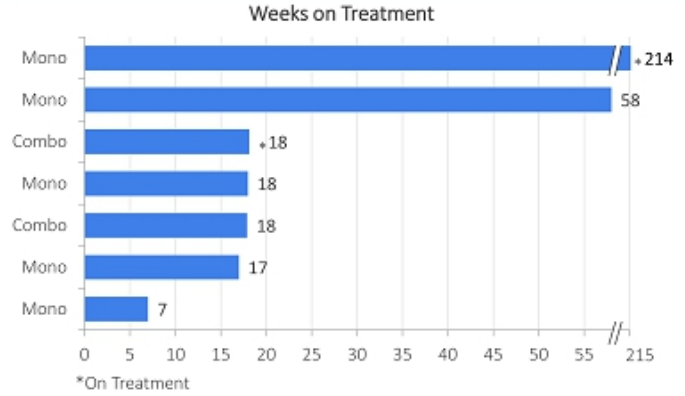
Strong Signal Identified in KRAS^{G12V} NSCLC to Be Further Validated

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}
- 1 additional confirmed PR in KRAS^{G12V} mutant patient as of Mar-2020

Source: [1] Martinez-Garcia, M. et al. *Clin. Cancer Res.* (2012); [2] Banerji, AACR VM 1, April 27, 2020, CT143

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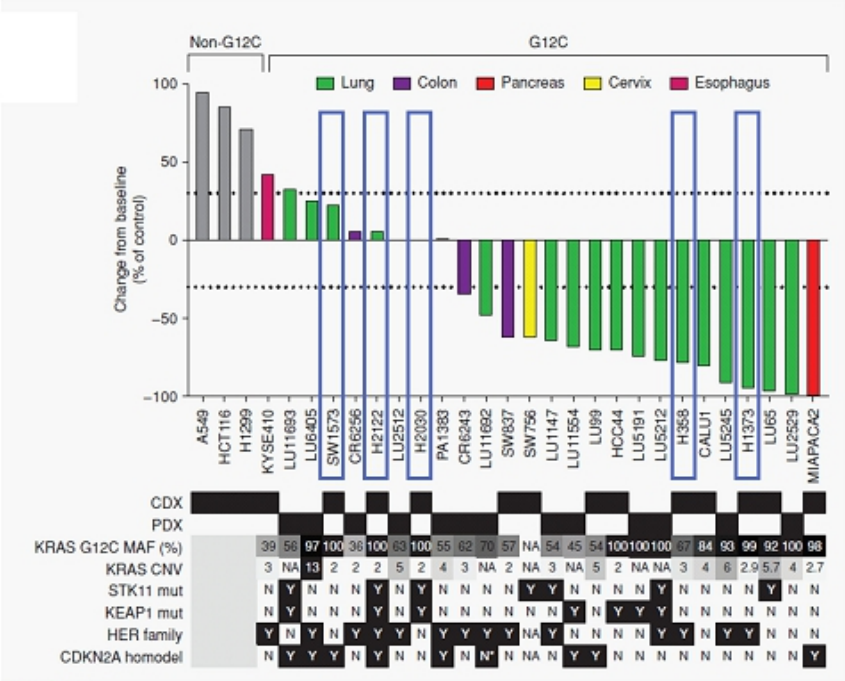
KRAS-G12C mutant tumor models differ in their sensitivity to G12C inhibitors



MRTX849
100 mg/kg QD

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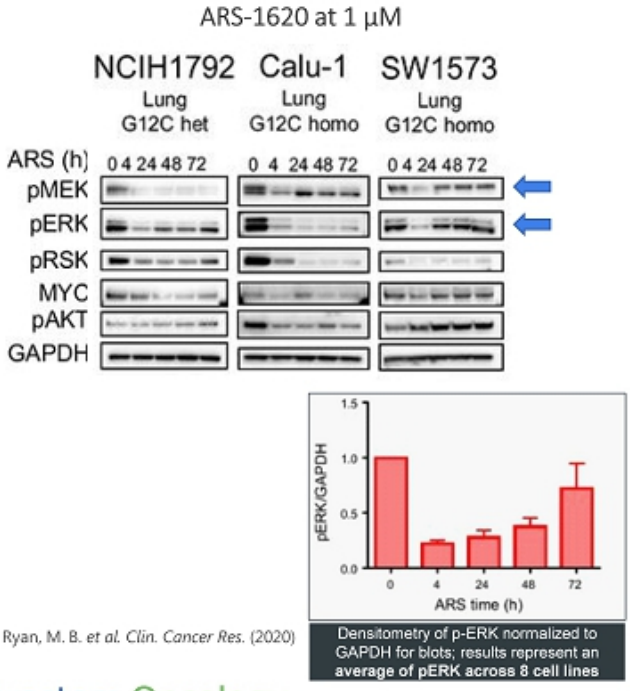
Hallin et al., Cancer Discovery 2020

G12C inhibitors do not maintain sustained inhibition of pMEK & pERK



Densitometry of p-ERK normalized to GAPDH for blots; results represent an average of pERK across 8 cell lines

Source: Ryan, M. B. *et al. Clin. Cancer Res.* (2020)

- Sustained inhibition of pMEK & pERK may be essential for durable response in KRAS-G12C mutant NSCLC & colorectal cancer
- KRAS-G12C inhibitors as monotherapy transiently inhibit pMEK & pERK *in vitro*

- VS-6766 yields more complete blockade of pMEK & pERK than other MEKi in preclinical models
- Tested hypothesis that VS-6766 combination with G12C inhibitors should yield deeper & durable inhibition of ERK pathway signaling with corresponding synergy in KRAS-G12C tumor cell lines

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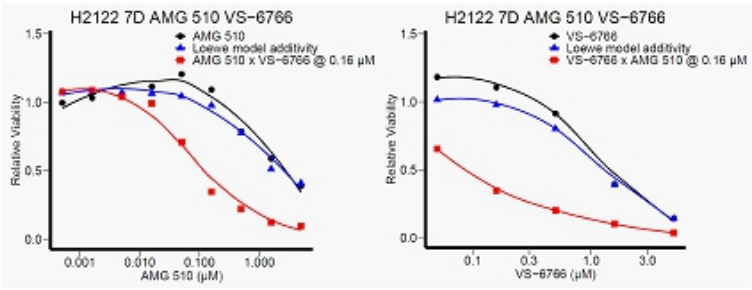
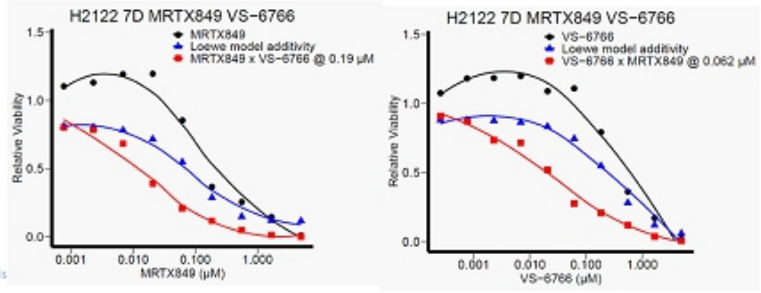
G12C inhibition is synergistic with VS-6766 in KRAS G12C mutant NSCLC & CRC cell lines

Cell line	Indication	Sensitivity to G12C inhibitors	Synergy Score (Loewe model)	
			VS-6766 + AMG 510	VS-6766 + MRTX849
H2122	NSCLC	Moderately sensitive	43.9	46.9
H358	NSCLC	Sensitive	14.5	11.9
H2030	NSCLC	Moderately sensitive	12.1	ND
H1373	NSCLC	Sensitive	9.3	9.6
SW1573	NSCLC	Insensitive	5	ND
SW837	CRC	Sensitive	14.9	ND
SW1463	CRC	Moderately sensitive	11.5	ND

H2122: AMG 510 + VS-6766 (RAF/MEKi)



H2122: MRTX849 + VS-6766 (RAF/MEKi)



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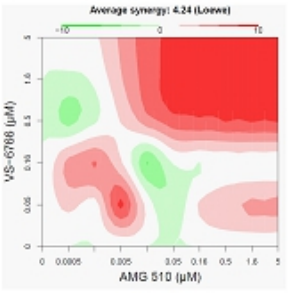
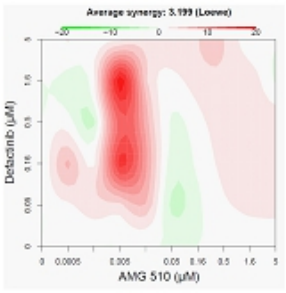
G12C inhibition is synergistic with VS-6766 & defactinib in KRAS G12C mutant NSCLC & CRC cell lines

H358 (KRAS G12C NSCLC)

AMG 510 + VS-6766

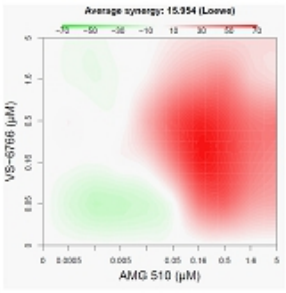


AMG 510 + Defactinib

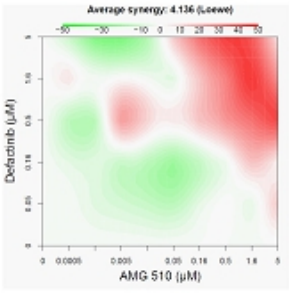


H2122 (KRAS G12C NSCLC)

AMG 510 + VS-6766

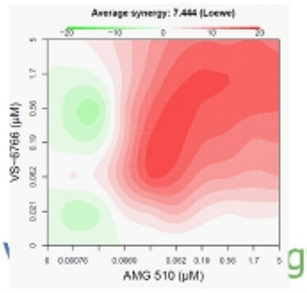


AMG 510 + Defactinib

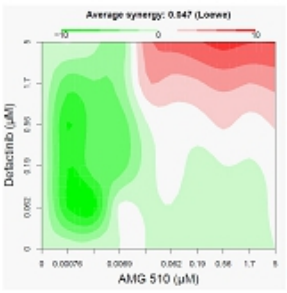


SW837 (KRAS G12C CRC)

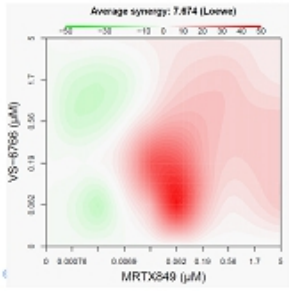
AMG 510 + VS-6766



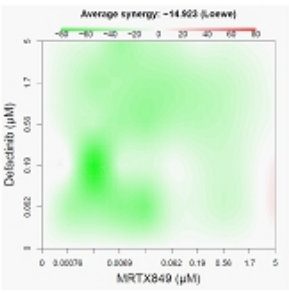
AMG 510 + Defactinib



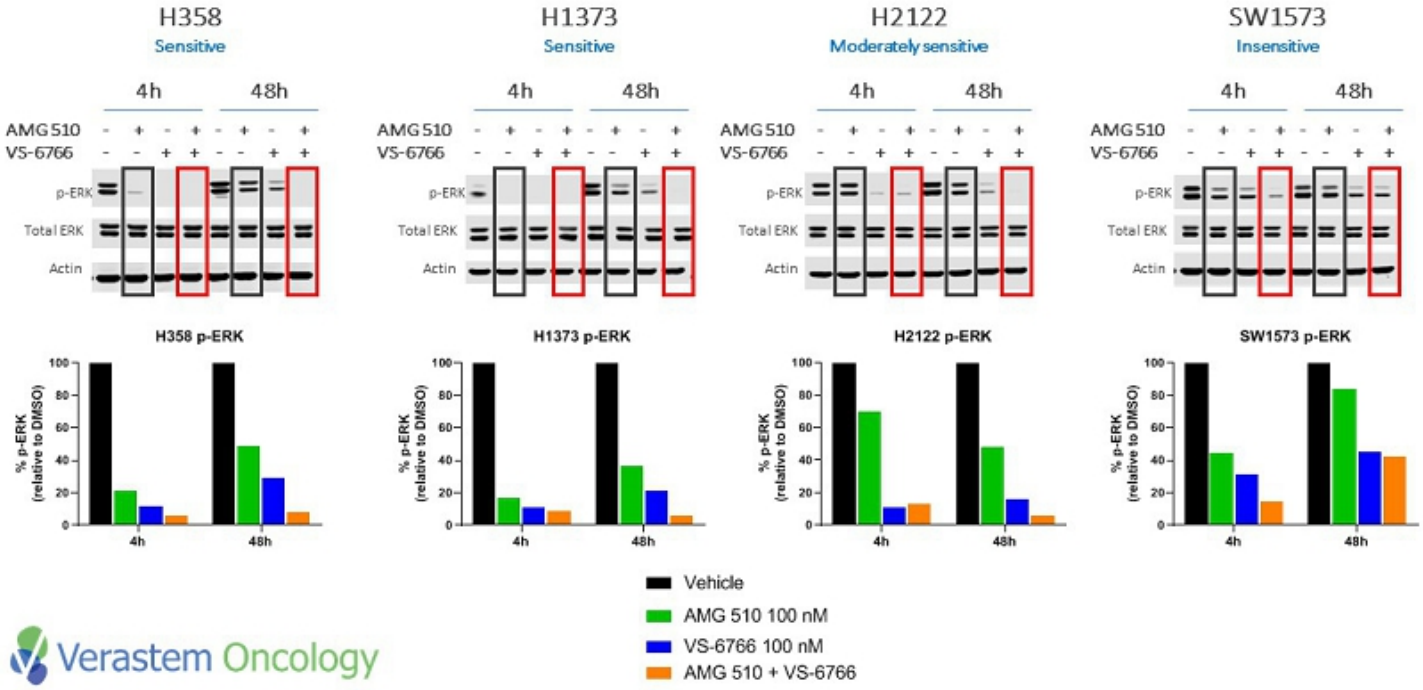
MRTX849+ VS-6766



MRTX849 + Defactinib



Addition of VS-6766 to AMG 510 increases depth & duration of inhibition of p-ERK relative to AMG 510 across a panel of KRAS-G12C mt NSCLC cell lines



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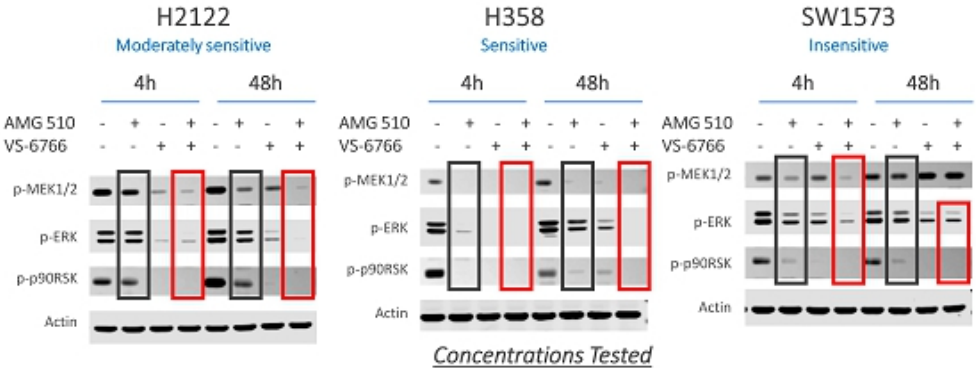
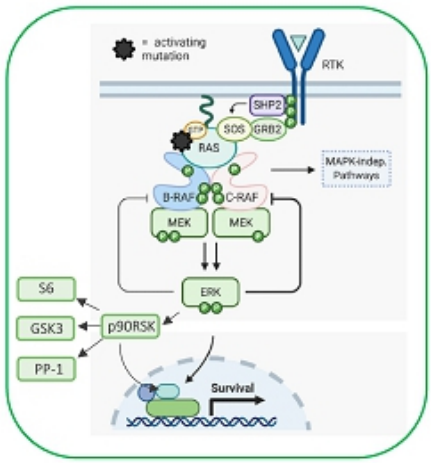
Addition of VS-6766 to AMG 510 increases depth & duration of inhibition of MEK/ERK signaling relative to AMG 510 across a panel of KRAS-G12C mt NSCLC cell lines



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



- In G12C cell lines sensitive to AMG 510 (e.g. H358), addition of VS-6766 to AMG 510 increases duration of inhibition of the MEK/ERK/RSK pathway
- In G12C cell lines less sensitive to AMG 510 (e.g. H2122), addition of VS-6766 to AMG 510 increases inhibition of the MEK/ERK/RSK pathway at both early and late time points

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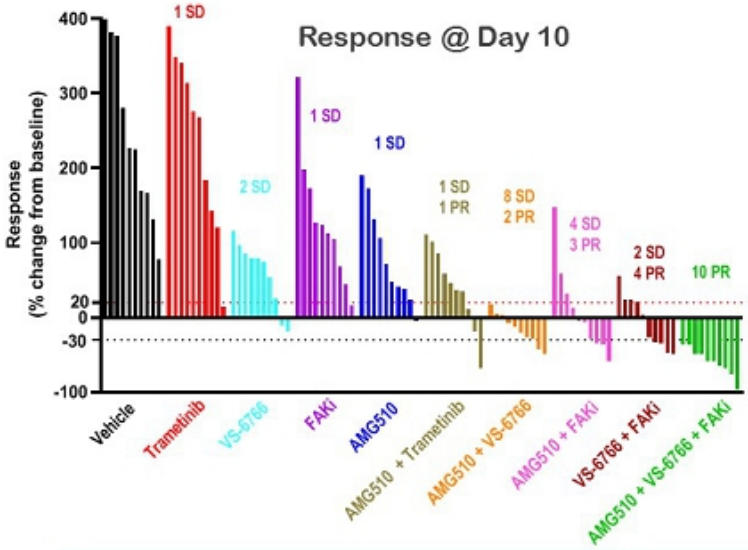
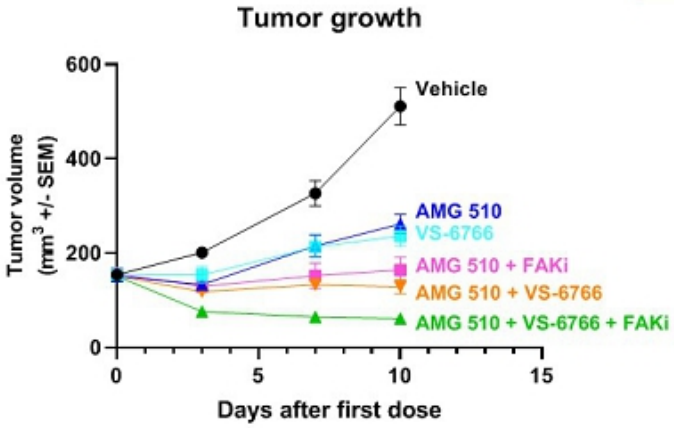
VS-6766 & FAKi potentiate AMG 510 efficacy in KRAS G12C mutant NSCLC in vivo

Tumor regression in all mice with triple combination

H2122 KRAS G12C mutant NSCLC





- VS-6766 is more effective than trametinib at equal dose
- VS-6766 or FAKi each potentiate the efficacy of AMG 510
- Triple combination of AMG 510 + VS-6766 + FAKi yields tumor regression in all mice

Doses Tested

Trametinib: 0.3 mg/kg QD
VS-6766: 0.3 mg/kg QD
FAKi: 50 mg/kg BID
AMG 510: 30 mg/kg QD

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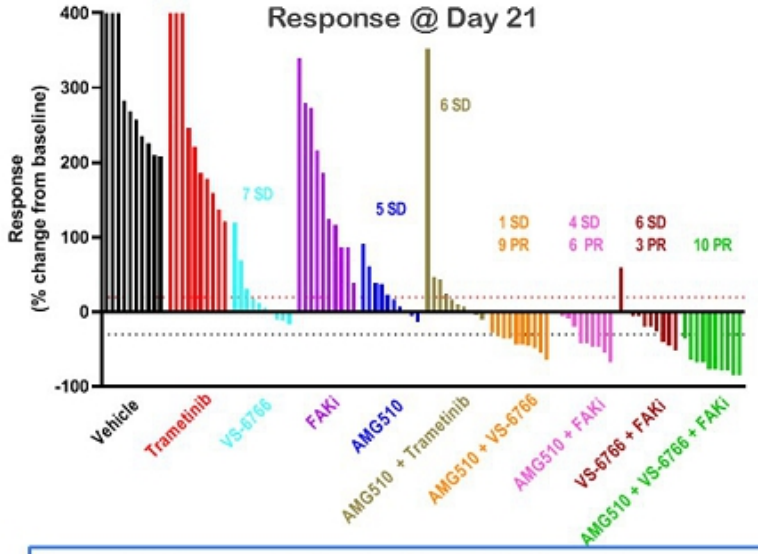
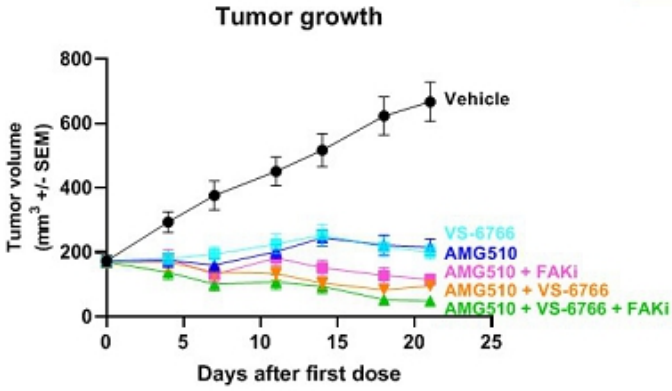
VS-6766 & FAKi potentiate AMG 510 efficacy in KRAS G12C mutant NSCLC in vivo

Tumor regression in all mice with triple combination

H358 KRAS G12C mutant NSCLC





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Doses Tested

Trametinib: 0.3 mg/kg QD
VS-6766: 0.3 mg/kg QD
FAKi: 50 mg/kg BID
AMG 510: 10 mg/kg QD

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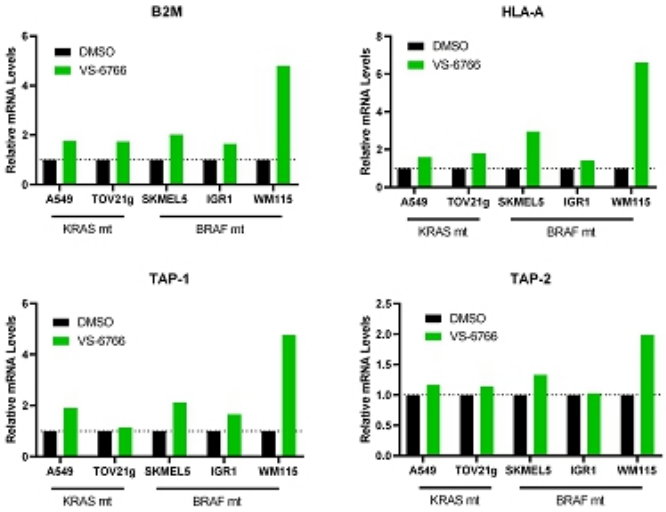
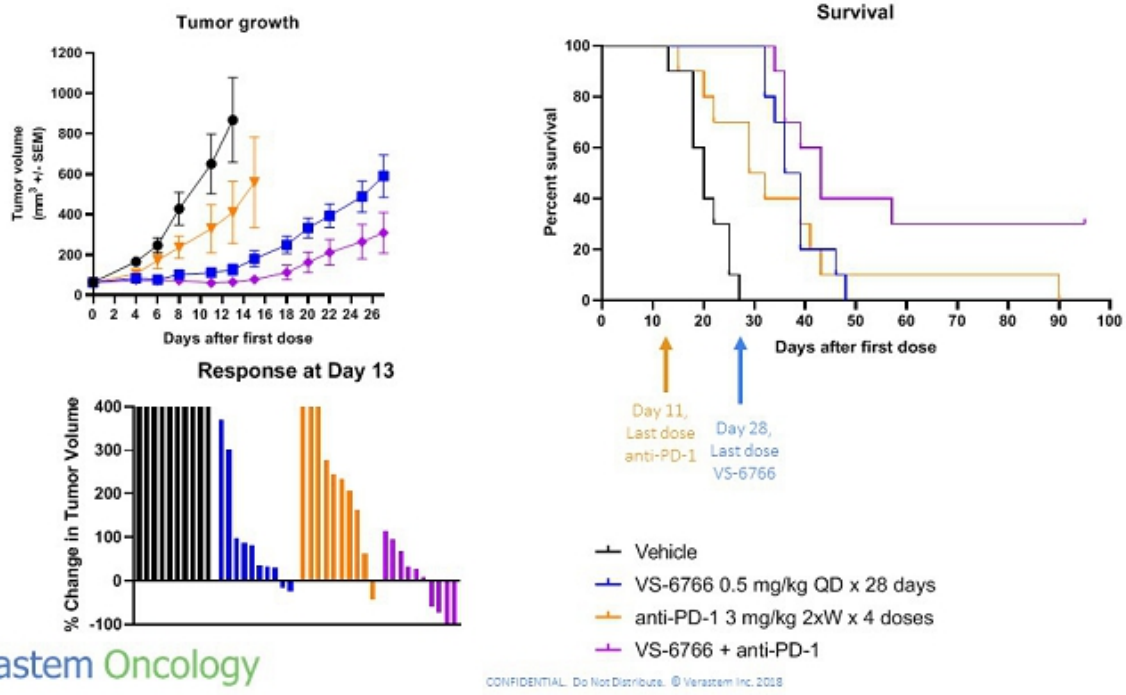
Role of VS-6766 in Immuno-Oncology: VS-6766 upregulates antigen presentation machinery (MHC-I) including β2 microglobulin



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

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

VS-6766 enhances tumor growth inhibition when combined with anti-PD-1 in the CT26 KRAS (G12D) syngeneic model



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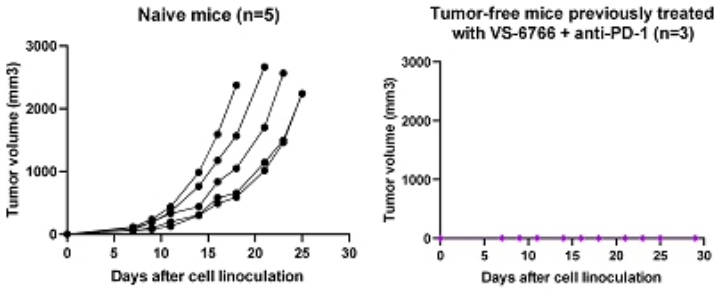
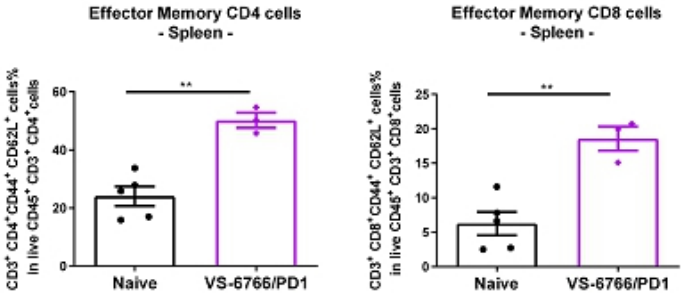
Combination of VS-6766 + anti-PD-1 induces long-lasting immune memory in the CT26 colorectal cancer model

Tumor re-challenge: Tumor-free mice show durable immune memory



Tumor-free mice show increase in effector memory T cells



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VS-6766 Combinations to Overcome Resistance Mechanisms: Conclusions

- **Combination of dual RAF/MEK inhibitor VS-6766 + FAKi may yield more complete RAS pathway shutdown**
  - Synergy in cellular models with tumor regression *in vivo*
  - Clinical activity in KRAS mt ovarian cancer & KRAS G12V mt NSCLC patients

- **Combination of RAF/MEK inhibitor VS-6766 is synergistic with KRAS-G12C inhibitors across G12C mt NSCLC & CRC cell lines**
  - Strong & durable inhibition of pERK pathway signaling
  - Tumor regressions in KRAS G12C mt NSCLC models *in vivo*
  - In KRAS G12C NSCLC models, triple combination of G12Ci + VS-6766 + FAKi yields PRs in all mice

- **Combination of RAF/MEK inhibitor with anti-PD-1 yields enhanced efficacy & immune memory *in vivo***
  - VS-6766 increases MHC-I expression across KRAS & BRAF mt cell lines

VS-6766 Combinations: Next Steps

- Registration-directed phase II study of VS-6766 + defactinib vs. VS-6766 monotherapy in Low Grade Serous Ovarian Cancer
- Registration-directed phase II study of VS-6766 + defactinib vs. VS-6766 monotherapy in KRAS-G12V mt NSCLC
- Potential for a combination study of VS-6766 ± defactinib with a G12C inhibitor in patients with KRAS-G12C mt NSCLC and/or CRC

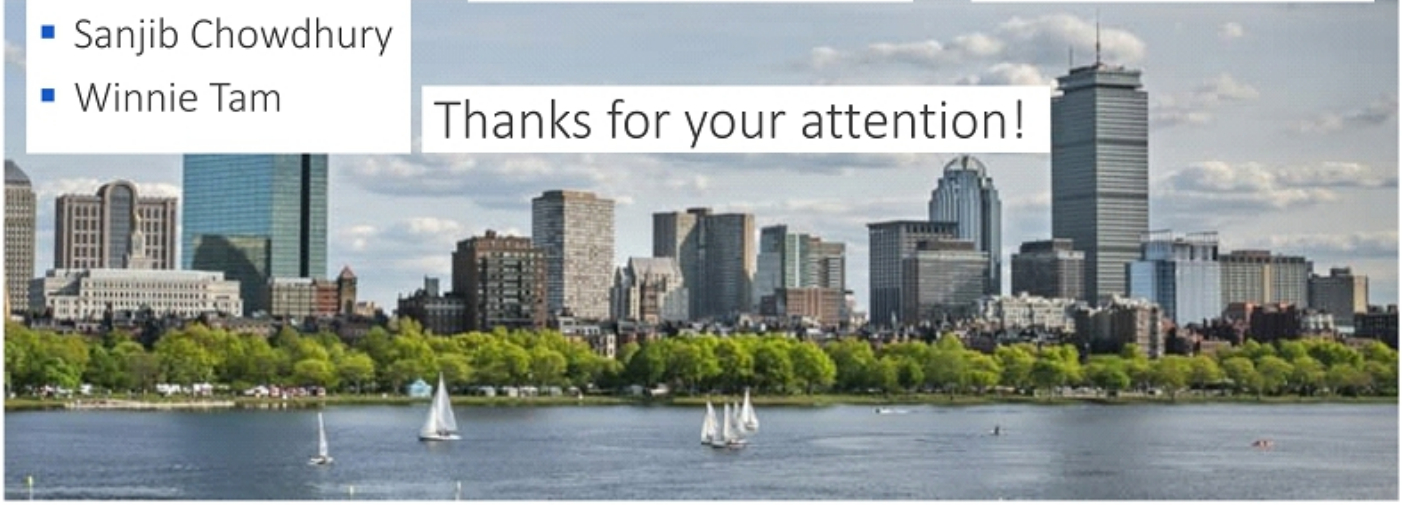
Acknowledgments

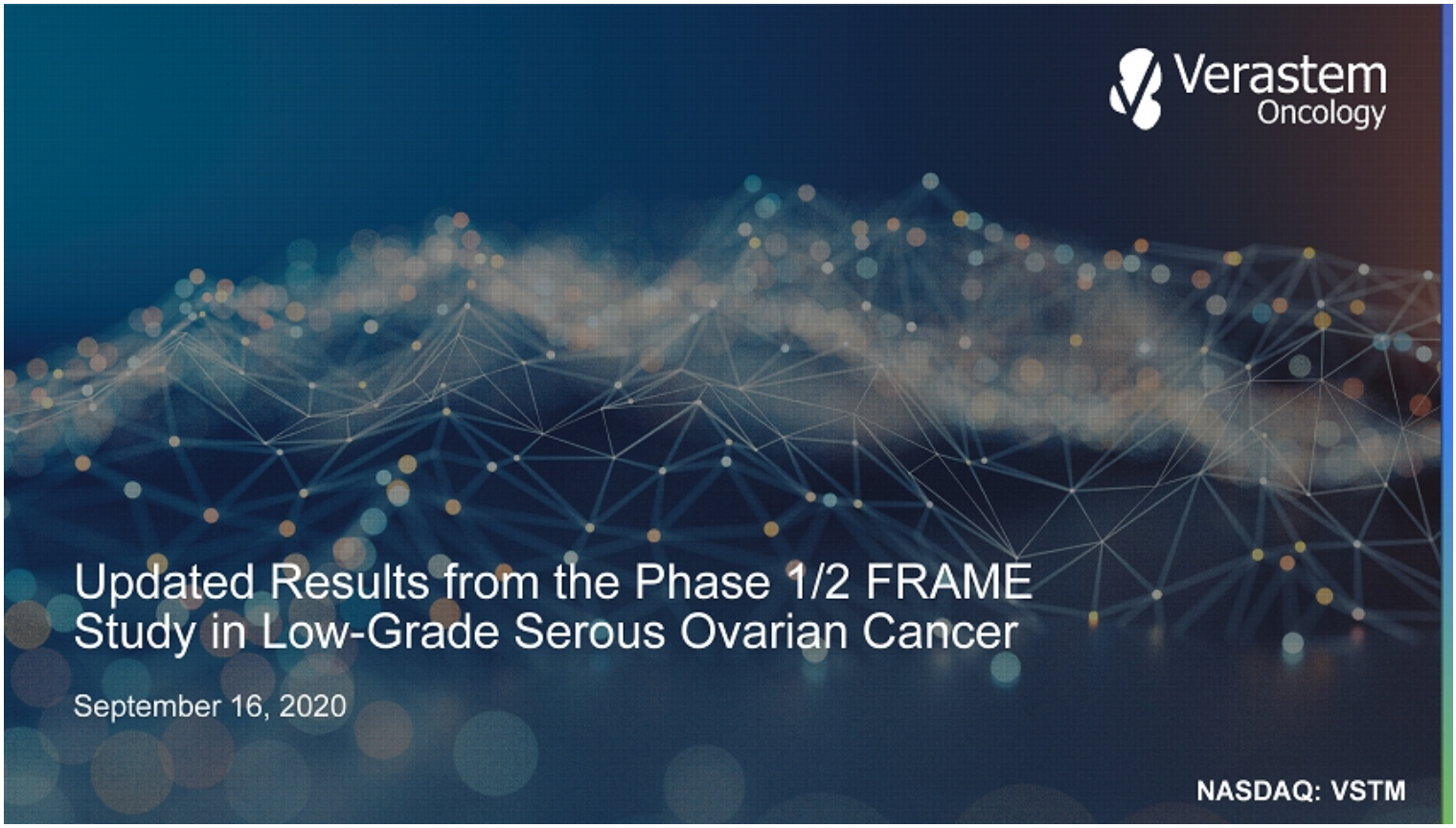
Verastem Oncology
- Silvia Coma
- Sanjib Chowdhury
- Winnie Tam

Royal Marsden Hospital
- Udai Banerji

UCSD
- J. Silvio Gutkind

Thanks for your attention!




Verastem
Oncology
Updated Results from the Phase 1/2 FRAME Study in Low-Grade Serous Ovarian Cancer
September 16, 2020
NASDAQ: VSTM

On Today's Call

Prepared Remarks

- John Doyle, *Vice President, Investor Relations and Finance*
- Dan Paterson, *Chief Operating Officer*
- Rachel Grisham, MD, *Medical Oncologist, Memorial Sloan Kettering Cancer Center*
- Brian Stuglik, *Chief Executive Officer*
- Rob Gagnon, *Chief Financial Officer*

Joining for Q&A Session

- Jonathan Pachter, PhD, *Chief Scientific Officer*

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 satisfaction of closing conditions with respect to the sale of the COPIKTRA assets to Secura Bio; the ability of Secura Bio to achieve the clinical and sales milestones necessary to result in additional consideration payable to Verastem.

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.

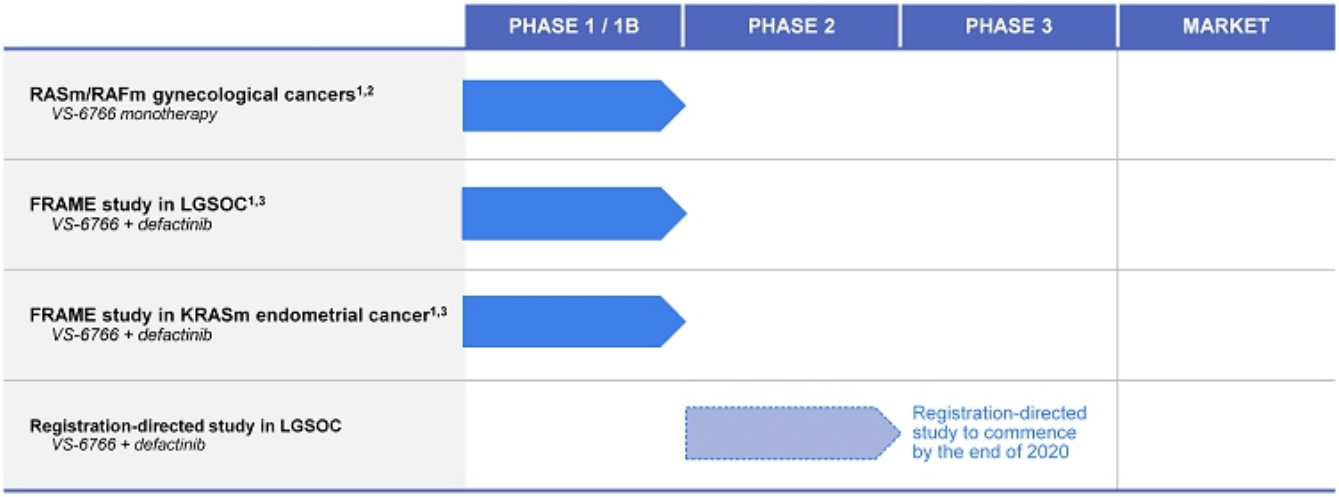
The forward-looking statements in this presentation speak only as of the original date of this presentation, and we undertake no obligation to update or revise any of these statements.

Updated Phase 1/2 FRAME Study Data in Low-Grade Serous Ovarian Cancer

Dan Paterson
President and Chief Operating Officer

Verastem Oncology

RAF/MEK Inhibitor VS-6766 in Gynecological Malignancies



[1] Investigator-sponsored trial
[2] Chénard-Poirier, M. et al. Results from the biomarker-driven basket trial of RO5126766 (CH5127566), a potent RAF/MEK inhibitor, in RAS- or RAF-mutated malignancies including multiple myeloma. *Journal of Clinical Oncology* 2017: 35
[3] NCT03875820

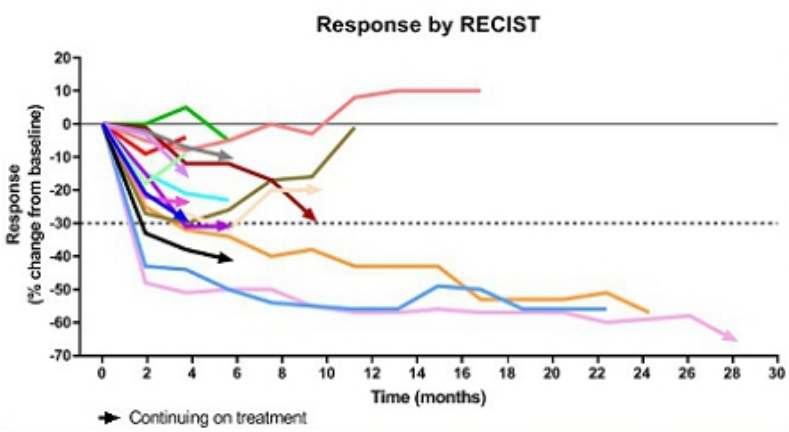
Favorable Tolerability Profile for Novel Intermittent Dosing Regimen of VS-6766 plus Defactinib

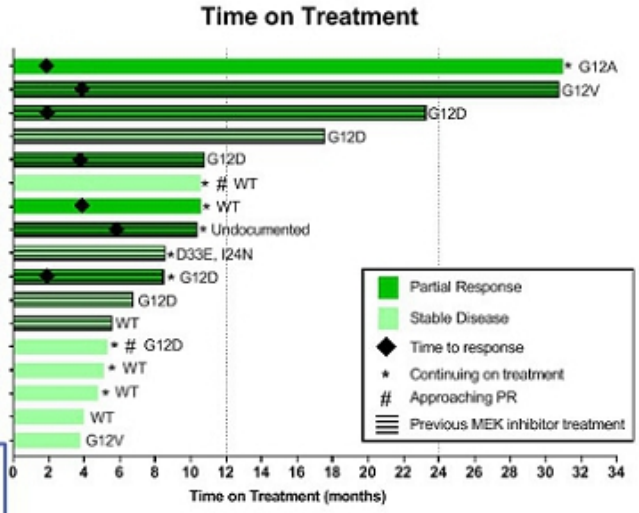
	Daily at MTD N=6 28-day cycle	4mg twice weekly N=26 28-day cycle	RP2D (VS-6766 3.2mg twice weekly + defactinib 200mg twice daily) N=26 21 days of 28-day cycle
Adverse Event	**Grade ≥3**	**Grade ≥3**	**Grade ≥3**
Rash related	3 (50%)	5 (19%)	1 (4%)
CK elevation	1 (17%)	2 (8%)	1 (4%)
Blurred vision	-	-	-
Peripheral edema	-	-	-
Diarrhea	-	1 (4%)	-
Mucositis	-	1 (4%)	-
Fatigue	-	1 (4%)	-
Nausea	-	-	-

[1] Chenard-Poirier, *et al.* ASCO 2017.

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

Verastem Oncology





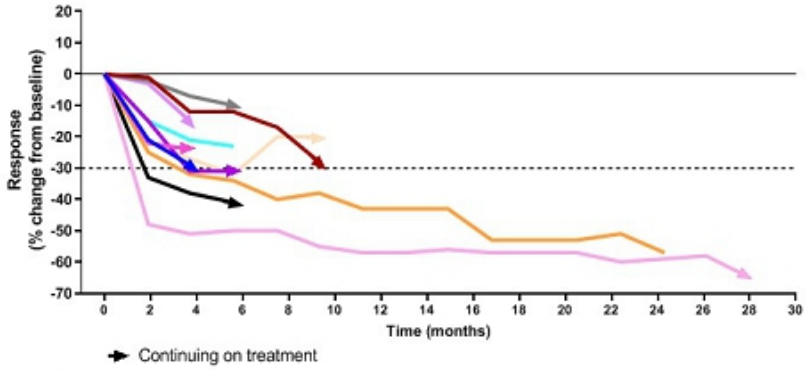
- KRAS-G12 mutations ORR = 56% (5/9); data still maturing
- Current ORR = 41% (7/17); data still maturing
- 5/7 PRs in pts who had previous MEKi[1]
- 9/17 (53%) still on study[2]
- 3 pts on treatment for ~2 yrs or more

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

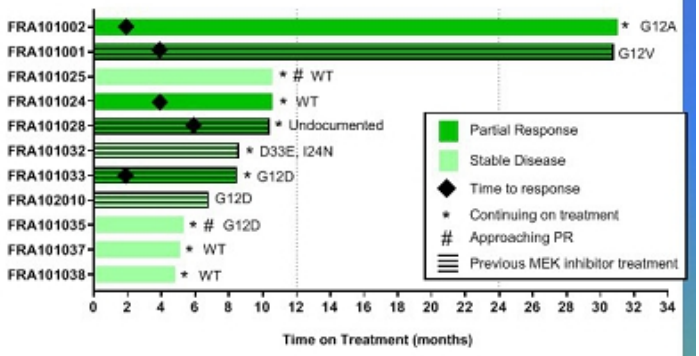
VS-6766 in Combination with Defactinib Shows Robust ORR with Durability in Refractory LGSOC at Phase 2 Dose Level

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

Response by RECIST



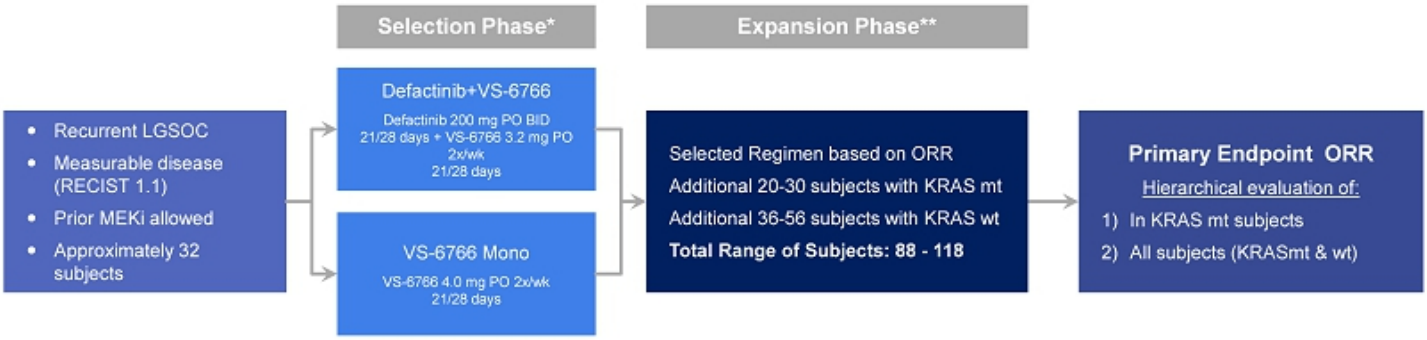
Time on Treatment



- 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

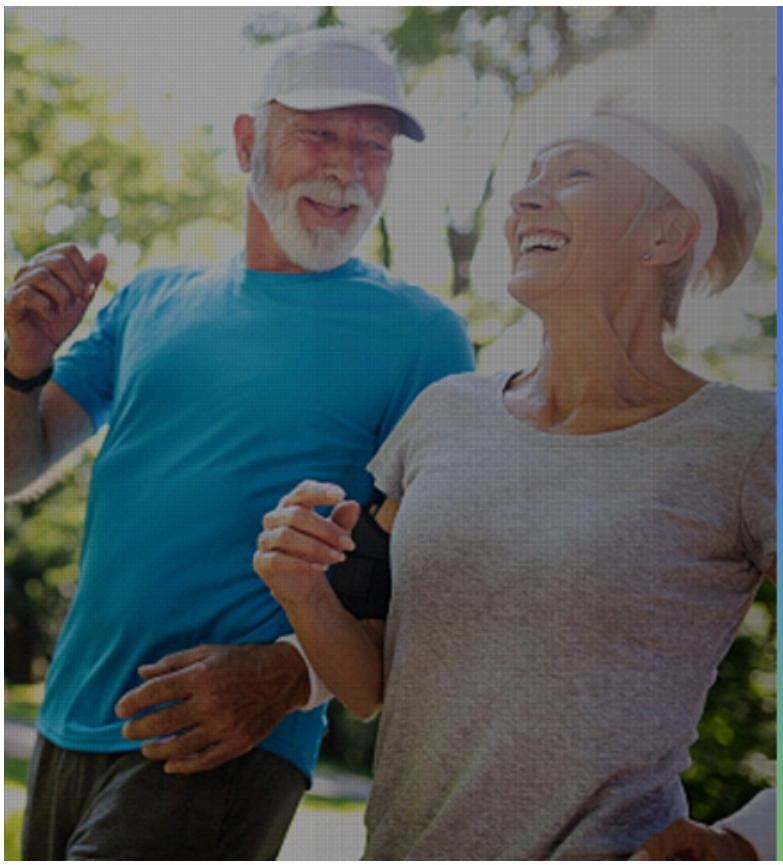
KRAS Mutated (mt) and Wild Type (wt), Phase 2, Recurrent LGSOC Adaptive Design for Potential Accelerated Approval



FDA Was Supportive of Development Strategy and Adaptive Design

This Registration-directed Phase 2 Study is Expected to Commence by Year End 2020

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



Low-Grade Serous Ovarian Cancer

Treatment Landscape and Clinical Perspective

Rachel Grisham, MD
Memorial Sloan Kettering Cancer Center

Verastem Oncology

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

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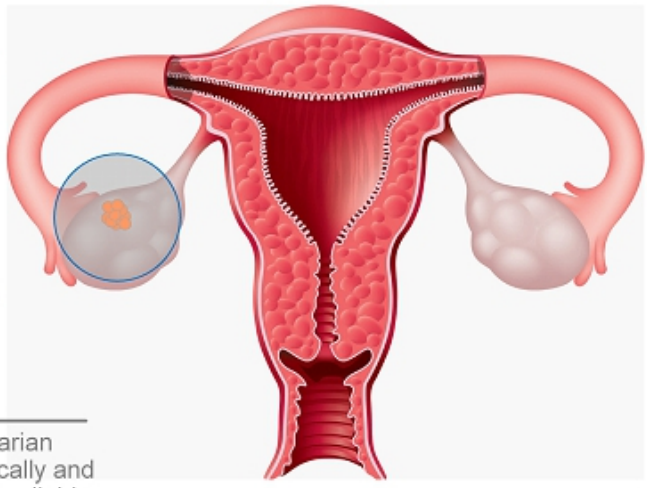
- LGSOC is a type of ovarian cancer that disproportionately affects younger women
- 1,000 to 2,000 patients in the U.S. and 15,000 to 30,000 worldwide diagnosed with LGSOC each year
- A slow growing cancer, that has a median survival of almost 10 years, so patients remain in treatment for a long time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



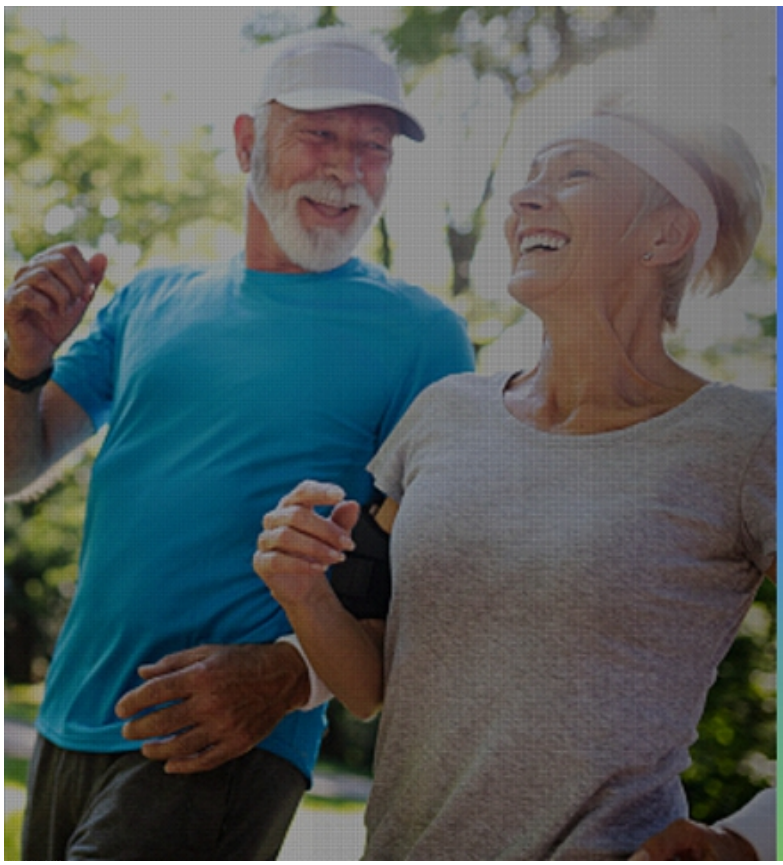
Source: Monk, Randall, Grisham, The Evolving Landscape of Chemotherapy in Newly Diagnosed Advanced Epithelial Ovarian Cancer, Am Soc Clin Oncol Educ Book; 2019; Slomovitz, Gourley, Carey, Malpica, Shih, Huntsman, Fader., Grisham et al, Low-Grade serous ovarian cancer: State of the Science; Gynecol Oncol;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

Treatment Landscape and Clinical Perspective

Rachel Grisham, MD
Memorial Sloan Kettering Cancer Center

Memorial Sloan-Kettering Cancer Center
The Best Cancer Care. Anywhere.

Bio: Dr. Grisham is a medical oncologist with clinical expertise in the diagnosis and treatment of women with gynecologic malignancies including ovarian, uterine, and cervical cancers as well as other less common tumors. Her clinical research focuses on developing novel treatments and improving treatment strategies for women with gynecologic malignancies. She has a particular interest in the use of targeted therapies for the treatment of recurrent ovarian cancer. She has developed, and serves as the principal investigator for, ongoing clinical trials in this area. Dr. Grisham earned her M.D. degree from Duke University School of Medicine. She completed her residency at Massachusetts General Hospital and subsequently held fellowships at Weill Cornell Medical College and Memorial Sloan Kettering Cancer Center.



Low-Grade Serous Ovarian Cancer

Market Opportunity

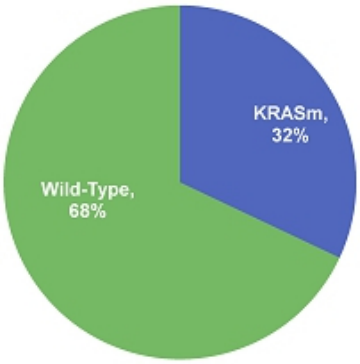
Brian Stuglik
Chief Executive Officer

Verastem Oncology

LGSOC: Key Drivers Are KRAS/NRAS/BRAF Mutations

	Incidence	10 Yr Prevalence
Worldwide	~15,000 – 30,000	~80,000
US	~1,000 – 2,000	~6,000

32% of LGSOC Patient Have KRAS Mutations



- Wild-type KRAS includes NRAS and BRAF mutations, among others

*Based on LGSOC representing 5-10% of epithelial ovarian cancer

LGSOC: Limited Treatment Options With High Unmet Need

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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

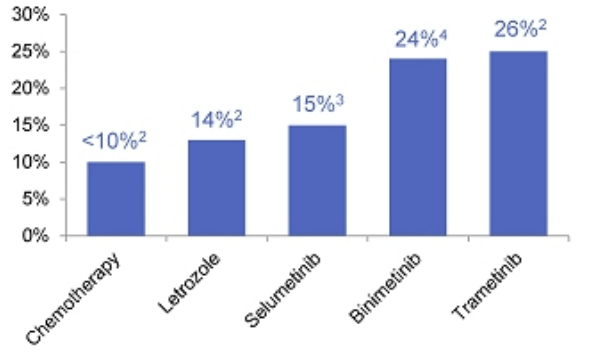
- Pt-Chemo combo +/- Beva
- **Trametinib**
- **Fulvestrant**

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

Validating Clinical Data in LGSOC
VS-6766 ± Defactinib Represents Best in Class Market Opportunity in LGSOC

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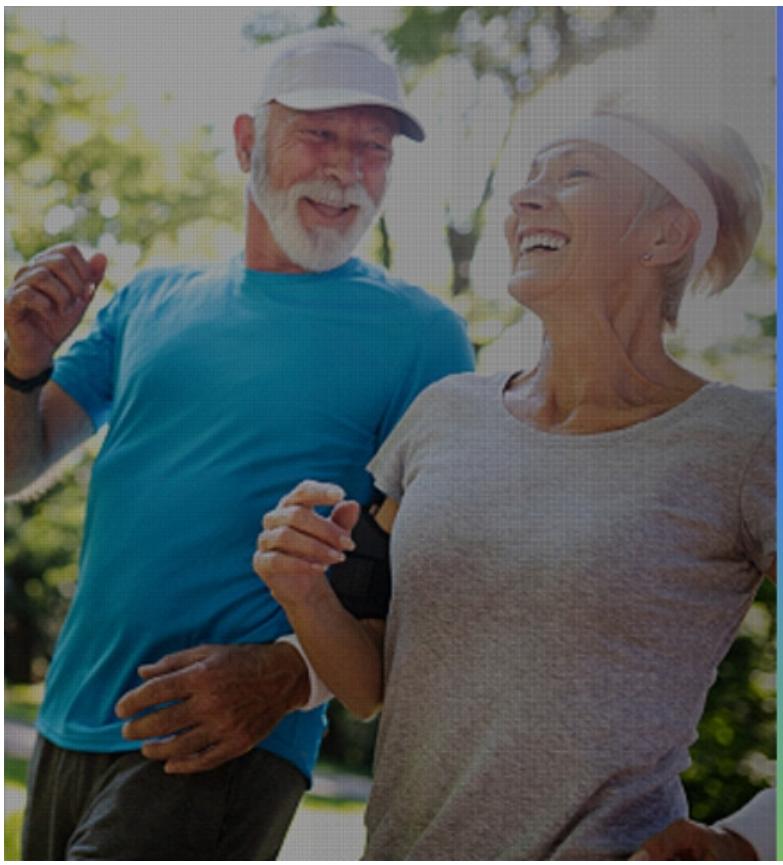
Key Takeaways

- KRAS mutations account for 32%[1] of LGSOC cases
- No FDA-approved therapy; limited treatment options
- Unmet medical need creates large market opportunity
- ~6,000 patients living with the disease; ultra-orphan opportunity
- FRAME study: 56% ORR in KRAS-G12m LGSOC and 41% ORR in overall LGSOC represents best-in-class opportunity
- FDA supportive of development strategy and registration trial design

Next Steps

- Commence Phase 2 registration-directed trial by the end of 2020
- Report updated data from FRAME LGSOC cohort in mid-2021

[1] AACR Project Genie, cBioportal



Other Program Updates

Brian Stuglik
Chief Executive Officer

Verastem Oncology

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

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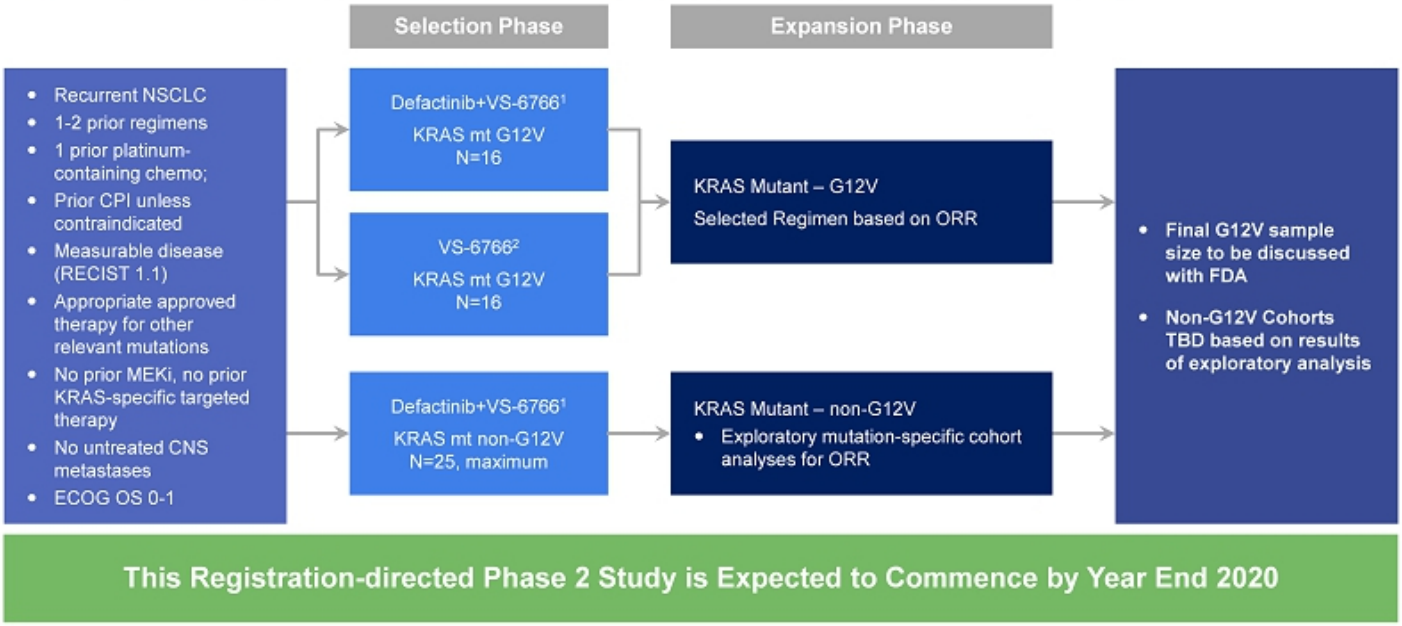

This Registration-directed Phase 2 Study is Expected to Commence by Year End 2020

[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)

Continuing to Move VS-6766 Forward Aggressively With Additional Opportunities

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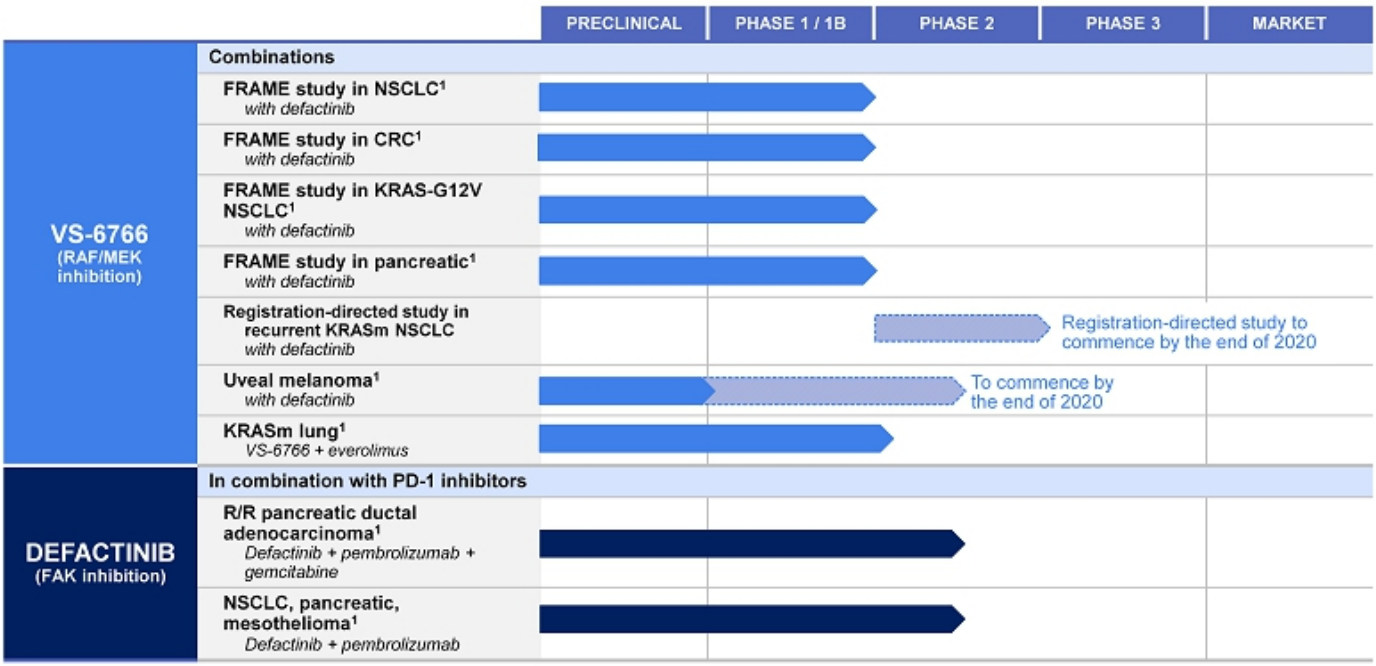
NSCLC

- Go-forward strategy is to focus primarily on KRAS G12V patients in NSCLC given clinical signals to-date
- KRAS G12V cohort added to ongoing FRAME study
- Completing Phase 1 investigating VS-6766 in combination with everolimus; plan to advance to Phase 2 in KRASm non-G12V NSCLC
- Reported new preclinical data demonstrating strong synergy and tumor regression with G12C inhibitors in combination with VS-6766 and FAK inhibitor *in vitro* and *in vivo*

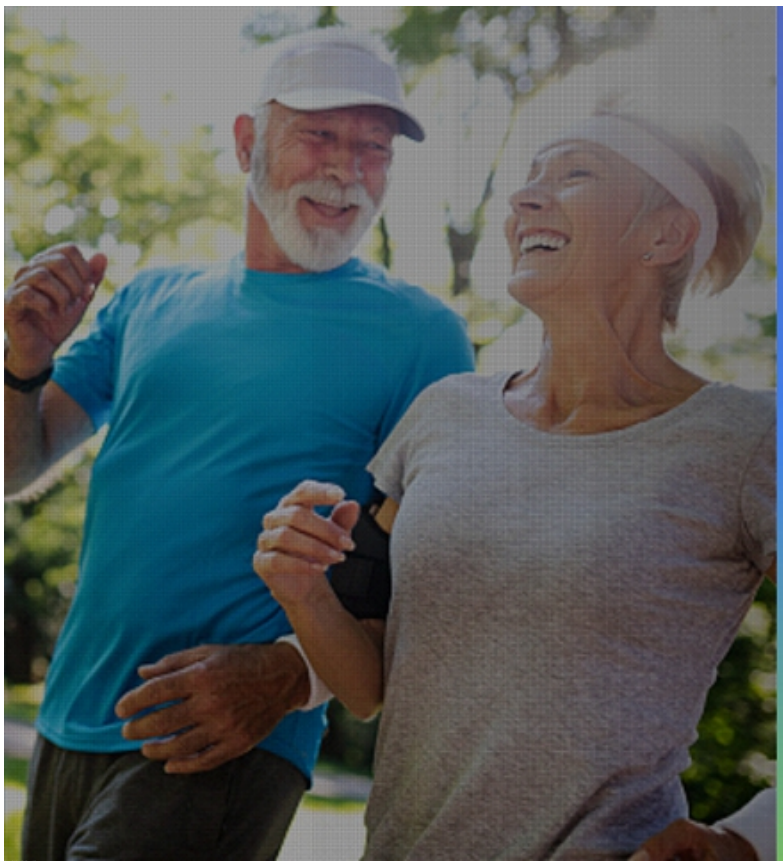
Other Tumor Areas

- Expanded FRAME study to include pancreatic and KRASm endometrial patient cohorts to provide early efficacy signals
- Uveal melanoma IST expected to commence by the end of 2020
- VS-6766 enhances efficacy of anti-PD-1 in preclinical models

Other High Priority Lead Indications with Multiple Growth Opportunities



[1] Investigator-sponsored study



Corporate

Rob Gagnon
Chief Financial Officer

Verastem Oncology

Selling COPIKTRA® (duvelisib) Rights to Secura Bio

- Total Deal Value Up to $311 Million, Plus Royalties
- Provides Cash Runway Through at Least 2024
- New Verastem Headcount of ~50
- Beginning in 2021 Annual OPEX Expected to be ~$50 Million
- Secura Bio to Assume All Operational and Financial Responsibilities, Including Existing Royalty Obligations

Key Financial Statistics

Cash, cash equivalents & short-term investments as of 6/30/2020	**$160.8M**
Proforma cash (as of June 30, 2020) of $230 million *Inclusive of $70 million received upfront at closing*	**$230M**
Shares fully diluted as of 6/30/2020	188.2M
Hercules Term Loan Facility as of 6/30/2020	$35.0M*
5.00% Convertible Senior Notes Due 2048 (2018 Notes) as of 6/30/2020	$28.3M**
Insider ownership (outstanding / vested) as of 6/30/2020	8.3% / 4.3%

* On April 23, 2019, we entered into a 4th Amendment to our existing Agreement with Hercules Capital, Inc. whereas we may borrow up to an aggregate amount of $75.0 million, of which $35.0 million was outstanding as of the date of amendment and 6/30/2020.

** The 2018 Notes have an initial conversion rate of 139.5771 shares of Common Stock per $1,000 which translates to an initial conversion price of $7.16 per share of Common Stock.

Key Upcoming Milestones for Remainder of 2020

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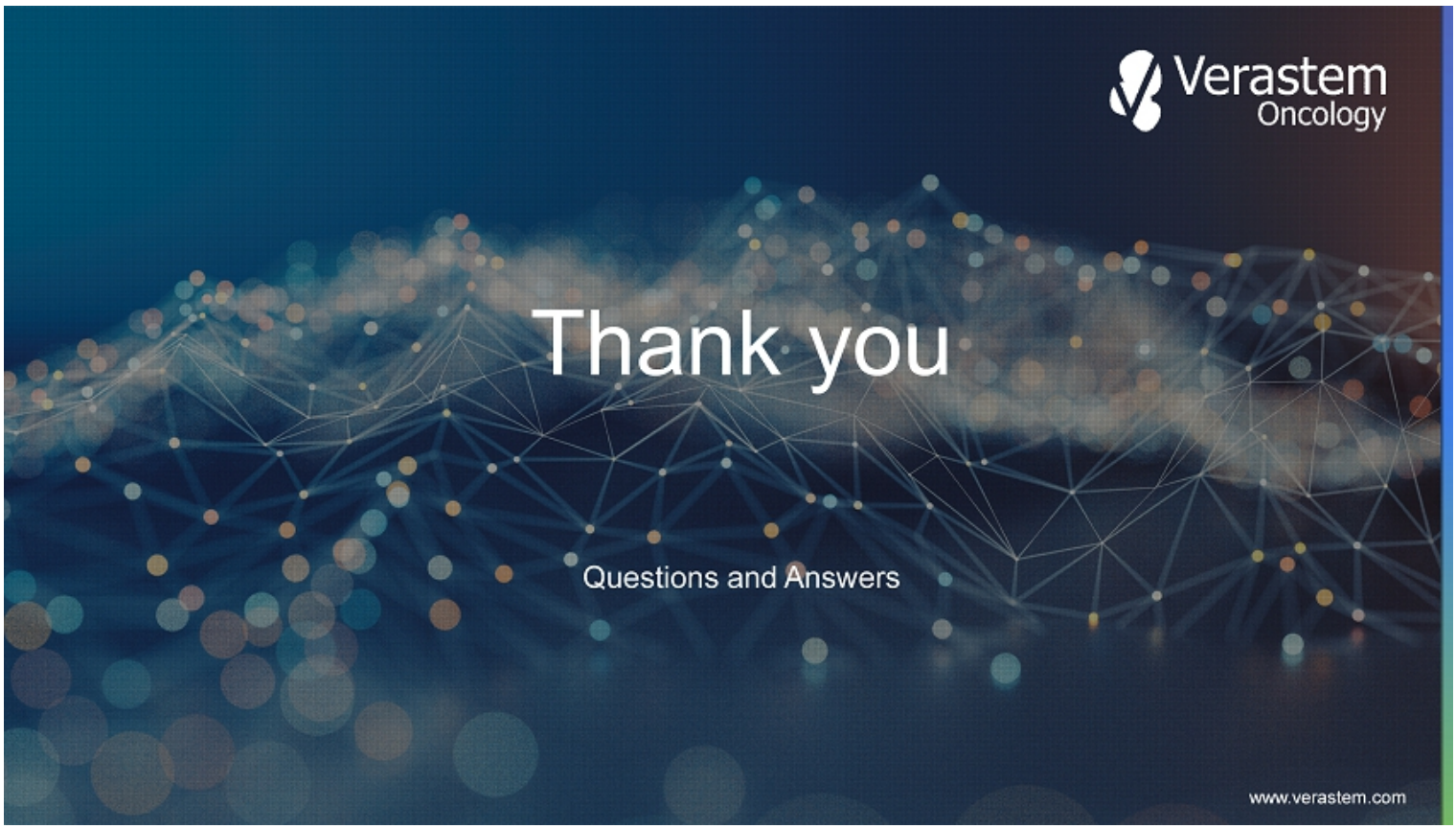
VS-6766 & Defactinib

- ✓ Regulatory path forward in LGSOC and KRAS mutant NSCLC during the 3Q 2020
- ✓ Expand Phase 1/2 FRAME study to include new cohorts in pancreatic cancer, KRASm endometrial cancer and KRAS-G12V NSCLC
- ✓ Present updated data from the LGSOC cohort of the Phase 1/2 FRAME study in Sept 2020
- ✓ Present preclinical findings in combination w/G12C inhibitors in Sept 2020
- ○ Commence registration-directed trial in recurrent LGSOC by year end 2020
- ○ Commence registration-directed trial in recurrent KRASm NSCLC by year end 2020

Corporate

- ✓ Monetize COPIKTRA; extend cash runway through at least 2024
- ✓ Reduce OPEX for 2021
- ○ Close Secura Bio transaction in 3Q 2020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Oncology
Thank you
Questions and Answers
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