Safe Harbor Statement

This presentation includes forward-looking statements about, among other things, Verastem Oncology’s programs and product candidates, including anticipated regulatory submissions, approvals, performance and potential benefits of Verastem Oncology’s product candidates, that are subject to substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Applicable risks and uncertainties include the risks and uncertainties, among other things, regarding: the success in the development and potential commercialization of our product candidates, including defactinib 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, 2020 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.
We are a biopharmaceutical company committed to developing and commercializing new medicines for patients battling cancer.

**Well Positioned to Capitalize on Growth Opportunities**

**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; FDA Breakthrough Therapy Designation in LGSOC.

**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, with preclinical synergy shown with an extensive number of agents including KRAS G12C inhibitors.

**Strong balance sheet**
Monetization of COPIKTRA® (duvelisib) provides funding until at least 2024.
Cash Balance of $127.1 million, as of Mar. 31, 2021
Debt reduced from approx. $185M to $28M (2019-2020)
Annual operating expense forecast of approximately $50 million.
Verastem Oncology Strategic Transformation

- **January 2020**: In-licensed global rights to VS-6766, best-in-class RAF/MEK inhibitor, from Chugai
- **February 2020**: PIPE financing based on data for new clinical program
- **September 2020**: Divested global rights to Copiktra to Secura Bio
- **November 2020**: Initiated registration-directed ph. 2 study in LGSOC
- **December 2020**: Initiated registration-directed ph. 2 study in NSCLC
VS-6766 RAF/MEK Inhibitor Program Overview
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
High Priority Lead Indications with Multiple Growth Opportunities

High Priority Registration Indications
Registration-Directed Trials Initiated in 4Q20
- LGSOC\textsuperscript{1,2}
- KRAS\textsuperscript{G12V} NSCLC\textsuperscript{1,2}

Additional Indication Opportunities
- Pancreatic\textsuperscript{1,2} (10 pt cohort initiated)
- KRAS mt endometrioid\textsuperscript{1} (10 pts initiated)
- Uveal Melanoma\textsuperscript{2} (IST initiated)
- Melanoma\textsuperscript{1,2}
- Colorectal\textsuperscript{1}

Mutation Opportunities
- KRAS mutations\textsuperscript{1,2}
- BRAF & NRAS mutations\textsuperscript{1,2}
- NF1 mutations
- GNAQ mutations\textsuperscript{2}

Other VS-6766 Combinations
- Everolimus\textsuperscript{1,2}
- KRAS G12C inhibitor\textsuperscript{2}
- SHP2 or SOS1 inhibitor\textsuperscript{2}
- CDK4/6 inhibitor\textsuperscript{2}
- EGFR inhibitor\textsuperscript{2}
- Anti-PD-1\textsuperscript{1}

\textsuperscript{1} Supported by clinical data
\textsuperscript{2} Supported by preclinical data
Robust Pipeline Targeting the RAS Pathway and Multiple Growth Opportunities

<table>
<thead>
<tr>
<th>VS-6766 + DEFACTINIB</th>
<th>PRECLINICAL</th>
<th>PHASE 1</th>
<th>PHASE 2</th>
<th>PHASE 3</th>
<th>MARKET</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAMP-201*</td>
<td>KRAS mt/wt LGSOC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAMP-202*</td>
<td>KRAS mt G12V NSCLC</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FRAME study</td>
<td>Advanced LGSOC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FRAME study</td>
<td>Advanced KRAS mt NSCLC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FRAME study</td>
<td>Advanced CRC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FRAME study</td>
<td>Advanced KRAS-G12V mt NSCLC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FRAME study</td>
<td>Advanced pancreatic cancer</td>
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<tr>
<td>FRAME study</td>
<td>Advanced KRAS mt endometrioid cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metastatic uveal melanoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>VS-6766 + OTHER COMBINATIONS</th>
<th>PRECLINICAL</th>
<th>PHASE 1</th>
<th>PHASE 2</th>
<th>PHASE 3</th>
<th>MARKET</th>
</tr>
</thead>
<tbody>
<tr>
<td>KRAS mt NSCLC</td>
<td>VS-6766 + everolimus (mTORi)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Pre-clinical studies ongoing in multiple KRAS mutant tumors

1 Registration-directed trial

RAMP 201 study – NCT04625270
RAMP 202 study – NCT04620330
FRAME study – NCT03875820
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

Growth factors

RTK ➔ RAS ➔ RAF ➔ MEK ➔ ERK ➔ Tumor Growth

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
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
VS-6766 +/- Defactinib in Low-Grade Serous Ovarian Cancer
Favorable Tolerability Profile with Novel Intermittent Dosing Regimen

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

<table>
<thead>
<tr>
<th>Treatment Related Adverse Event</th>
<th>Grade ≥3 (VS-6766 monotherapy)</th>
<th>Grade ≥3 (RP2D)</th>
<th>Grade ≥3 (RP2D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rash</td>
<td>3 (50%)</td>
<td>5 (19%)</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>CK elevation (Creatine phosphokinase)</td>
<td>1 (17%)</td>
<td>2 (8%)</td>
<td>2 (5%)</td>
</tr>
</tbody>
</table>

Summary of FRAME Safety Profile

Most Adverse Events (AE) were Grade 1/2

Few patients have discontinued due to AEs in the study

1 Chenard-Poirier, et al. ASCO 2017
References: Banerji, Q4 2020 report; Data on file
RP2D: recommended phase 2 dosing
## Treatment Related Adverse Events Details*

(≥10% patients in cohort 3.2mg 6766 and Def 200mg)

<table>
<thead>
<tr>
<th></th>
<th>VS-6766 4mg Twice Weekly (4 wks of every 4 wks)$^1$</th>
<th>VS-6766 3.2mg Twice Weekly Def 200mg BID (3 wks of every 4 wks)$^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Gr1/2</td>
<td>Gr3/4</td>
</tr>
<tr>
<td>Rash</td>
<td>15</td>
<td>5</td>
</tr>
<tr>
<td>CK Elevation</td>
<td>13</td>
<td>2</td>
</tr>
<tr>
<td>AST Elevation</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Hyperbilirubinemia</td>
<td>14</td>
<td>1</td>
</tr>
<tr>
<td>Visual Disturbance</td>
<td>13</td>
<td>9</td>
</tr>
<tr>
<td>ALT Elevation</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Fatigue</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Oral Mucositis$^\text{^}\text{^}\text{^}\text{^}$</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Nausea</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Peripheral Edema</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Paronychia</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pruritus</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>

*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; 
$^\text{^}\text{^}\text{^}\text{^}$also includes glossitis/mouth ulcers

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### Summary of FRAME Safety Profile

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

### RP2D

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

References:

$^1$ Data on file VS-6766 Investigator’s Brochure; $^2$Banerji, Q4 2020 report
VS-6766 in Combination with Defactinib Shows Robust ORR with Durability in Refractory LGSOC with Expanded Number of Patients (n=17)

Response by RECIST

- KRAS-G12 mutations ORR = 56% (5/9); data still maturing
- Current ORR = 41% (7/17); data still maturing
- 9/17 (53%) still on study
- 3 pts on treatment for ~2 yrs or more

1 Data cutoff date August 17, 2020
In an updated Dec. 2020 read-out (n=24), ORR data has continued to strengthen, in both KRAS mt and KRAS wt patients, with a consistent safety profile

- Overall response rate (ORR) is 52% (11 of 21 response evaluable patients)
  - KRAS mutant ORR at 70% (7 of 10 response evaluable patients)
  - KRAS wild-type ORR at 44% (4 of 9 response evaluable patients)
  - KRAS status undetermined ORR at 0% (0 of 2 response evaluable patients)

- As reported previously, the most common side effects seen in the study were rash, creatine kinase elevation, nausea, hyperbilirubinemia and diarrhea, most being NCI CTC Grade 1/2 and all were reversible

- Additional data is anticipated to be shared at a medical meeting in 2H 2021
LGSOC: Limited Treatment Options with High Unmet Need

Low-Grade Ovarian Cancer – Treatment Algorithm

Stage IA-IB

Stage IC

Stage II-IV

Observe only

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

Limited Response Rates for Available Treatments:

- Chemotherapy: <10%^2
- Letrozole: 14%^2
- Selumetinib: 15%^3
- Binimetinib: 24%^4
- Trametinib: 26%^2

- 31-35% discontinuation rate with MEK inhibitors due to AEs
- Few discontinuations in the FRAME study due to AEs

^1 NCCN guidelines
KRAS wt patients represent 70% of the LGSOC patient population

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

RAMP 201: KRAS Mutated (mt) and Wild Type (wt), Phase 2, Recurrent LGSOC Adaptive Design for Potential Accelerated Approval

**Selection Phase***
- Defactinib + VS-6766
  - KRAS-mt
    - (n=16)
- VS-6766 Mono
  - KRAS-mt
    - (n=16)

**Expansion Phase**
- Selected Regimen based on ORR
  - Add ~20-30 patients with KRAS mt
  - Add ~20-40 patients with KRAS wt

**Total Expected Range of Patients:** 104-134

*New cohorts added via protocol amendment*

**Primary Endpoint** ORR
Hierarchical evaluation of:
1) In KRAS mt patients
2) All patients (KRASmt & wt)

---

**FDA Was Supportive of Development Strategy, Adaptive Design, and Addition of KRAS wt to Selection Phase**

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

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

**Expansion Phase – final sample size to be adjusted based on adaptive design**
LGSOC market opportunity larger or comparable to other high unmet need KRAS opportunities

Patient-months of Therapy Per Year\(^2\) (across all 2L+ patients)

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Patient-Months Per Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSCLC KRAS G12C(^3)</td>
<td>~6K</td>
</tr>
<tr>
<td>Pancreatic(^3)</td>
<td>~4k</td>
</tr>
<tr>
<td>LGSOC(^3)</td>
<td>~2k</td>
</tr>
<tr>
<td>Endometrioid(^3)</td>
<td>~80K</td>
</tr>
<tr>
<td>Metastatic uveal melanoma(^3)</td>
<td>~4k</td>
</tr>
</tbody>
</table>


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

\(^3\) NSCLC KRAS G12C 2\(^{nd}\) line patients (incidence); Pancreatic RAS/RAF mutant 2\(^{nd}\)-line patients (incidence); LGSOC KRAS mutant and wild-type patients (prevalence); Endometrioid RAS/RAF mutant 2\(^{nd}\), line patients (incidence); Uveal melanoma RAS/RAF mutant 2nd-line patients (incidence)
VS-6766 +/- Defactinib in NSCLC
High Unmet Need in Refractory KRASm NSCLC Adenocarcinoma

**NSCLC Adenocarcinoma**

<table>
<thead>
<tr>
<th>% of Patients</th>
<th>% of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
</tr>
</tbody>
</table>

US Annual Incidence: 92K
WW Annual Incidence: 836K

**KRAS Mutation**

- G12C
- G12V
- G12D
- G12A
- G13C
- G13S
- G13D

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

**Advanced or Metastatic NSCL Cancer Recommend Histologic and Molecular Subtyping**

- EGFR/ALK/ROS1/B
- RAF (targeted)
- Non-targeted PD-(L)1 ≥ 1%
- Non-Targeted PD-(L)1 < 1%
- Appropriate targeted agent
- PD-(L)1 single agent or PD-(L)1 + chemo
- Chemo ± PD-(L)1

**Recurrence**

- Prior PD-(L)1
  - Chemotherapy: Docetaxel, Gemcitabine, Pemetrexed
- No Prior PD-(L)1
  - PD-(L)1

**Chemotherapy or clinical trials**

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

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1. Globocan, 2018
3. TCGA PanCancer Atlas (cBioPortal analysis)
5. Adapted from NCCN Non-small cell lung cancer guidelines Version 3.2020
A Precision Approach to KRAS-G12V Driven NSCLC

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

CRAF, but not BRAF, ablation improves survival of mice with KRAS<sup>G12V</sup> induced lung cancer in vivo

VS-6766 +/- FAKi induces significant tumor regression in KRAS G12V mt NSCLC \textit{in vivo} model, with clear differentiation from trametinib.

**KRAS G12V mutant; Trp53 KO NSCLC**

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

Source: Coma et al. AACR 2021
Case Study: Response to VS-6766 + defactinib in a patient with KRAS G12V mutant NSCLC

May 2019: Diagnosed with NSCLC

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

Oct 2019: Progression, palliative RT to right hip

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

Source: Krebs et al. AACR 2021
Strong Signal Identified in KRAS<sup>G12V</sup> to Be Further Validated

VS-6766 ± Defactinib Has a Confirmed 57% ORR in KRAS<sup>G12V</sup> NSCLC in Integrated Analysis

- Preclinical evidence suggests combination with Defactinib may improve efficacy in KRAS<sup>G12V</sup>
- Activity of VS-6766 as a single agent and in combo with Defactinib in KRAS<sup>G12V</sup>

Time on Treatment for KRAS<sup>G12V</sup> NSCLC

Best Response by RECIST in KRAS<sup>G12V</sup> NSCLC

*4.0 mg VS-6766/200 mg defactinib

Source: 1 Guo, et al Lancet Oncology 2020 2 Banerji, AACR VM 1, April 27, 2020, CT143
Defactinib 200 mg PO BID (21/28 days) + VS-6766 3.2 mg PO 2x/wk (21/28 days)

VS-6766 4.0 mg PO 2x/wk (21/28 days)

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
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

<table>
<thead>
<tr>
<th>Cell line</th>
<th>Indication</th>
<th>Sensitivity to G12C inhibitors</th>
<th>VS-6766 + AMG 510</th>
<th>VS-6766 + MRTX849</th>
</tr>
</thead>
<tbody>
<tr>
<td>H2122</td>
<td>NSCLC</td>
<td>Moderately sensitive</td>
<td>44.7</td>
<td>44.6</td>
</tr>
<tr>
<td>H1373</td>
<td>NSCLC</td>
<td>Sensitive</td>
<td>10.0</td>
<td>3.4</td>
</tr>
<tr>
<td>SW1573</td>
<td>NSCLC</td>
<td>Insensitive</td>
<td>8.6</td>
<td>12.0</td>
</tr>
<tr>
<td>H358</td>
<td>NSCLC</td>
<td>Sensitive</td>
<td>6.9</td>
<td>5.4</td>
</tr>
<tr>
<td>H2030</td>
<td>NSCLC</td>
<td>Moderately sensitive</td>
<td>5.1</td>
<td>ND</td>
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<tr>
<td>SW837</td>
<td>CRC</td>
<td>Sensitive</td>
<td>16.1</td>
<td>18.5</td>
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<td>MIAPA2</td>
<td>Panc</td>
<td>Sensitive</td>
<td>2.3</td>
<td>5.3</td>
</tr>
</tbody>
</table>

Combined Synergy Score

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

H2122 KRAS G12C mutant NSCLC

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**  
(Febuary 23-25, 2021)
Key VSTM Milestones 2020-2022

**Corporate**
- **1H2020**: VS-6766 In-Licensed from Chugai
- **2H2020**: Copiktra divested to Secura Bio
- **1H2021**: RAMP-201 Study Initiated
- **2H2021**: Updated data from FRAME NSCLC cohort
- **1H2022**: RAMP-201 Top-Line Data from Selection Phase & Initiate Expansion Phase

**LGSOC**
- **1H2020**: PIPE Financing for New Clinical Program
- **2H2020**: RAMP-201 Amended to Include KRAS wt patients in Selection Phase
- **1H2021**: FDA Breakthrough Therapy Designation
- **2H2021**: Updated data from FRAME LGSOC cohort
- **1H2022**: RAMP-202 Top-Line Data from Selection Phase & Initiate Expansion Phase

**NSCLC**
- **1H2020**: RAMP-202 Study Initiated
- **2H2020**: Updated data from FRAME NSCLC cohort
# Key Financial Statistics

**As of March 31, 2021**

<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash, cash equivalents &amp; investments as of 3/31/2021</td>
<td>$127.1M</td>
</tr>
<tr>
<td>Shares fully diluted as of 3/31/2021</td>
<td>195.8M</td>
</tr>
<tr>
<td>5.00% Convertible Senior Notes Due 2048 (2018 Notes) as of 3/31/2021</td>
<td>$0.3M*</td>
</tr>
<tr>
<td>5.00% Convertible Senior Notes Due 2048 (2020 Notes) as of 3/31/2021</td>
<td>$28.0M**</td>
</tr>
<tr>
<td>Insider ownership (outstanding / vested) as of 3/31/2021</td>
<td>8.7% / 4.9%</td>
</tr>
</tbody>
</table>

* 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.

** The 2020 Notes have an initial conversion rate of 307.6923 shares of Common Stock per $1,000 which translates to an initial conversion price of $3.25 per share of Common Stock.
Backup Slides
High Unmet Needs in RAS/RAF/MEK/ERK-Driven Cancers

**KRAS-mutant Cancers**
- NSCLC Incidence: 194K
- 31%
- Pancreatic Incidence: 58K
- 98%
- Uterine Endometrioid Incidence: 59K
- 21%
- Colorectal Incidence: 105K
- 45%
- Ovarian Incidence: 22K
- 5%

**NRAS-mutant Cancers**
- Melanoma Incidence: 108K
- 28%
- Multiple Myeloma Incidence: 32K
- 20%

**BRAF-mutant Cancers**
- Melanoma Incidence: 108K
- 60%
- Ovarian Incidence: 22K
- 35 – 60%
- Papillary Thyroid Incidence: 42K
- 30 – 80%

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**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:**

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

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

Pancreatic Adenocarcinoma

Annual Incidence: 58K

Pancreatic Cancer
KRAS Mutation
% of patients

Uterine Endometrioid Carcinoma

Annual Incidence: 59K

Uterine Endometrioid Carcinoma
KRAS Mutation
% of patients

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 \textit{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
Overcoming Key Resistance Mechanisms to MEK Inhibitors

- 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

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

### Defactinib

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Dose (mg)</th>
<th>N</th>
<th>Subject</th>
<th>AUC_{last} (h*ng/mL)</th>
<th>C_{max} (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>200 (with 3.2mg RO)</td>
<td>3</td>
<td>Mean</td>
<td>2071</td>
<td>273</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CV%</td>
<td>103</td>
<td>80</td>
</tr>
<tr>
<td>2a</td>
<td>200 (with 4mg RO)</td>
<td>5</td>
<td>Mean</td>
<td>2252</td>
<td>318</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CV%</td>
<td>124</td>
<td>117</td>
</tr>
<tr>
<td>2b</td>
<td>400 (with 3.2mg RO)</td>
<td>3</td>
<td>Mean</td>
<td>2807</td>
<td>360</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CV%</td>
<td>31</td>
<td>32</td>
</tr>
</tbody>
</table>

Reference: Banerji, AACR VM 1, April 27, 2020, CT143
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

- 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
- 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

<table>
<thead>
<tr>
<th>Cell Line</th>
<th>Tumor type</th>
<th>RAS/RAF mutation status</th>
</tr>
</thead>
<tbody>
<tr>
<td>A549</td>
<td>Lung</td>
<td>KRASmut G12S</td>
</tr>
<tr>
<td>TOV21g</td>
<td>Ovarian</td>
<td>KRASmut G13C</td>
</tr>
<tr>
<td>SKMEL5</td>
<td>Melanoma</td>
<td>BRAFmut V600E</td>
</tr>
<tr>
<td>IGR-1</td>
<td>Melanoma</td>
<td>BRAFmut V600E</td>
</tr>
<tr>
<td>WM115</td>
<td>Melanoma</td>
<td>BRAFmut V600E</td>
</tr>
</tbody>
</table>

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

**Tumor growth**

- **Response at Day 13**
  - Day 11, Last dose anti-PD-1
  - Day 28, Last dose VS-6766

**Survival**

- **Tumor re-challenge in tumor-free mice showed immune memory with increased memory T cells**

- Vehicle
- VS-6766 0.5 mg/kg QD x 28 days
- anti-PD-1 3 mg/kg 2xW x 4 doses
- VS-6766 + anti-PD-1
## LGSOC Market Opportunity – Reference Calculations

<table>
<thead>
<tr>
<th></th>
<th>Number of Patients (2L+)(^2)</th>
<th>Average months on Therapy (per patient)(^2)</th>
<th>Patient-months of Therapy Per Year (across all 2L+ patients)(^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NSCLC KRAS G12C(^3)</strong></td>
<td>![10,000, 20,000, 30,000, 40,000]</td>
<td>![5.00, 10.00, 15.00]</td>
<td>![50,000, 100,000, 150,000]</td>
</tr>
<tr>
<td><strong>Pancreatic(^3)</strong></td>
<td>![10,000, 20,000, 30,000, 40,000]</td>
<td>![5.00, 10.00, 15.00]</td>
<td>![50,000, 100,000, 150,000]</td>
</tr>
<tr>
<td><strong>LGSOC(^1)</strong></td>
<td>![10,000, 20,000, 30,000, 40,000]</td>
<td>![5.00, 10.00, 15.00]</td>
<td>![50,000, 100,000, 150,000]</td>
</tr>
<tr>
<td><strong>Endometrioid(^3)</strong></td>
<td>![10,000, 20,000, 30,000, 40,000]</td>
<td>![5.00, 10.00, 15.00]</td>
<td>![50,000, 100,000, 150,000]</td>
</tr>
<tr>
<td><strong>Metastatic uveal melanoma(^3)</strong></td>
<td>![10,000, 20,000, 30,000, 40,000]</td>
<td>![5.00, 10.00, 15.00]</td>
<td>![50,000, 100,000, 150,000]</td>
</tr>
</tbody>
</table>


2 Patient-months of Therapy metric calculated by multiplying relevant incidence/prevalence rate times estimated duration of therapy; represents US market opportunity only; patient population estimates from Globocan 2020, American Cancer Society 2021, AACR Genie Cohort 9.0 public, and scientific publications. Duration of therapy estimates from clinical studies and clinician experience. Number of patients and months on therapy are for 2nd-line+.

3 NSCLC KRAS G12C 2nd line patients (incidence); Pancreatic RAS/RAF mutant 2nd-line patients (incidence); Endometrioid RAS/RAF mutant 2nd-line patients (incidence); Uveal melanoma RAS/RAF mutant 2nd-line patients (incidence)
A drug with a Breakthrough designation will have...

- Increased communication with FDA during drug development and review

- FDA guidance to ensure that the design of clinical trials are as efficient as practicable

- A cross-disciplinary project lead assigned to the FDA review team and increased involvement of senior managers and experienced review staff

- 29/30 drugs previously granted Breakthrough Therapy designation have been approved by the FDA
Strong Patent Protection

- 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

**Cathy Carew**
Chief People & Organizational Strategy Officer
- Principal – HR Collaborative
- Ironwood, ActiveBiotics, Dynogen, Tufts Health Plan

**Daniel Paterson**
President and Chief Operating Officer
- CEO – The DNA Repair Co. (now On-Q-ity)
- PharMetrics (now IMS), Axion

**Jonathan Pachter, Ph.D.**
Chief Scientific Officer
- Head of Cancer Biology – OSI (now Astellas)

**Rob Gagnon**
Chief Business and Financial Officer
- CFO – Harvard Bioscience, Clean Harbors
- VP of Finance – Biogen Idec

**Hagop Youssoufian, MSc, M.D.**
Head of Medical Strategy
- CMO, BIND Therapeutics, EVP, Progenics
- CMO & EVP, Ziopharm Oncology, SVP, Imclone