NOVEL DRUGS TARGETING CANCER STEM CELLS

NASDAQ: VSTM

JUNE 4, 2014
Forward-Looking Statements

This presentation and other matters discussed today, or answers that may be given to questions asked, include forward-looking statements about the Company’s strategy, future plans and prospects, including statements regarding the development of the Company’s compounds, including VS-6063, or defactinib, VS-4718, VS-5584 and VS-507, and the Company’s FAK, PI3K/mTOR, Wnt and diagnostics programs generally, the timeline for clinical development and regulatory approval of the Company’s compounds, the expected timing for the reporting of data from on-going trials, the structure of the Company’s planned or pending clinical trials, the Company’s rights to develop or commercialize its compounds, the Company’s obligations to make milestone payments and royalties and the ability of the Company to finance contemplated development activities and to fund operations for a specified period. The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “plan,” “predict,” “project,” “target,” “potential,” “will,” “would,” “could,” “should,” “continue,” “proposed,” 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 that the preclinical testing of the Company’s compounds and preliminary data from clinical trials may not be predictive of the results or success of pending or later clinical trials, that data may not be available when we expect it to be, that enrollment of clinical trials may take longer than expected, that the Company will be unable to successfully complete the clinical development of its compounds, including VS-6063, VS-4718, and VS-5584, that the development of the Company’s compounds will take longer or cost more than planned, and that the Company’s compounds will not receive regulatory approval or become commercially successful products. 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, 2013 and in any subsequent SEC filings. The forward-looking statements contained in this presentation reflect the Company’s current views with respect to future events, and the Company does not undertake and specifically disclaims any obligation to update any forward-looking statements.
Targeting Cancer Stem Cells to Improve Patient Outcomes

**OPPORTUNITY**
- Discovery platform at the forefront of cancer stem cell biology
- Pipeline of clinical candidates targeting cancer stem cells in early and late-stage clinical trials

**STRATEGY**
- VS-6063 lead program: registration-directed trial with orphan drug designation
- Therapeutic indication expansion for the treatment of many cancer types

**LEADERSHIP**
- Experienced leadership and advisory team to guide strategy and execute development plan
- Strong record of execution → Key clinical and data milestones expected in 2014

**CAPITAL**
- $113.9 million as of 3/31/14
- Sufficient capital to fund operations into 2016

*Estimates based on currently proposed clinical plans and subject to change*
Targeting Cancer Stem Cells for a Durable Clinical Response

Problem:

Initial tumor → Tumor reduction but CSCs survive → Recurring tumor

Solution:

Initial tumor → Tumor reduction and elimination of CSCs → Durable clinical response

Current cancer treatments

CSC drug + current cancer treatments

June 4, 2014

Novel Drugs Targeting Cancer Stem Cells
Clinical Evidence: Presence of Cancer Stem Cells Associated with Poor Prognosis in Early Breast Cancer

No cancer stem cells in residual disease in lymph nodes

Cancer stem cells in residual disease in lymph nodes

N = 115 patients

Standard neoadjuvant chemotherapy of 4 cycles of anthracycline & cyclophosphamide + 12 weeks of paclitaxel

CSCs identified by ALDH1

Sakakibara et al, Cancer 2012
Our Product Candidates Target and Kill Cancer Stem Cells

Breast cancer cells in vitro

- CD44
- CD24
- CSCs: 4.90%
- Non-CSCs: 70.12%
- CSC Inhibitor: 0.20%

Breast cancer cells in vivo

- Placebo
- Paclitaxel
- CSC Inhibitor

Gupta et al., Cell 2009

Percentage of mice with tumor formation

0 25 50 75 100
Placebo Paclitaxel CSC Inhibitor
Cancer Stem Cells May Drive Disease Progression in Epithelial Solid Tumors: 80% of All Cancers

Mesothelioma
Registration-directed
WW Incidence
~59,000

Ovarian
Phase 1b in combo
WW Incidence
~225,000

Breast
WW Incidence
~1,400,000

Lung
Phase 2 in NSCLC
WW Incidence
~1,600,000

Mesothelioma is a potentially rapid path to regulatory filing
# Portfolio of Product Candidates Targeting Cancer Stem Cells

<table>
<thead>
<tr>
<th>Focal Adhesion Kinase (FAK)</th>
<th>PreClin</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>VS-6063</td>
<td></td>
<td></td>
<td>COMMAND: A Registration-directed trial</td>
<td></td>
</tr>
<tr>
<td>Mesothelioma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung (KRASmt NSCLC)</td>
<td></td>
<td></td>
<td>Phase 2</td>
<td></td>
</tr>
<tr>
<td>Ovarian</td>
<td></td>
<td></td>
<td>Phase 1/1b in combo with paclitaxel</td>
<td></td>
</tr>
<tr>
<td>VS-4718</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solid Tumors</td>
<td></td>
<td></td>
<td>Phase 1/1b</td>
<td></td>
</tr>
</tbody>
</table>

| PI3K and mTORC1/2          |         |         |         |         |
| VS-5584                    |         |         |         |         |
| Solid Tumors and Lymphomas|         |         | Phase 1/1b |         |

| Wnt/β-Catenin              |         |         |         |         |
| Eisai                      |         |         |         |         |
| Research Collaboration     |         |         |         |         |
FAK is Critical for Cancer Stem Cells

- FAK is a critical pathway for cancer stem cells and disease progression

  Shibue et. al.; Cancer Discovery 2012 Aug;2(8):706-21

- Targeted deletion of FAK shown to reduce tumor-initiating capability

  Figure adapted from Luo et. al.; Cancer Res (2009) 69:466
VS-6063 – Targeting Cancer Stem Cells Through FAK Inhibition

- Oral compound with good safety profile and initial signs of activity in Phase 1
- Orphan designation in US and EU for mesothelioma
- Two clinical FAK competitors
  - Boehringer Ingelheim: Phase 1
  - GlaxoSmithKline: Phase 1b

VS-6063 Preferentially Targets Cancer Stem Cells in vitro

Composition of matter though 2029

FAK Enzymatic IC$_{50}$ = 24 nM
FAK Cellular EC$_{50}$ = 28 nM

![Chemical structure of VS-6063](image)
Mesothelioma Incidence Continues to Rise Worldwide

• Highly aggressive and lethal cancer
  – High percentage of tumors with cancer stem cells resistant to standard of care
  – 12 month median survival on standard of care

• Asbestos exposure is primary risk factor with latency > 20 years
  – Approximately 2 million tons of asbestos continues to be consumed per year
  – Many countries have yet to ban asbestos

• WHO estimates total worldwide fatalities of 59,000/year
  – Most rapidly increasing cancer in women in Britain
  – New diagnoses increased 250% since 2006 in Japan
Merlin as a Potential Patient Enrichment Marker: A Tumor Suppressor Lost in ~50% of Mesothelioma Tumors

- Mesothelioma tumors with merlin loss are enriched in cancer stem cells & more aggressive

Menges et al. (Fox Chase Cancer Center) Cancer Res. 2014

**Merlin Loss Increases Potency of VS-6063 in Bulk Tumor Cells**

VS-6063 Reduces Tumor Initiating Capability

VS-6063 Reduces Tumor Bulk in Merlin low Mesothelioma
GSK Clinical Data: Initial Proof of Concept for FAK Inhibitors in Mesothelioma

**2nd Line Treatment in Recurrent Mesothelioma**

- **Historical control:** 6 weeks (n=660)
- **All Patients:** 18 weeks (n=29)
- **Merlin high:** 11 weeks (n=9)
- **Merlin low:** 24 weeks (n=14)

**Biomarker for patient stratification**

---

1. **Historical data from Vorinostat Phase 3 (Krug et al; ESMO 2011)**

2. **Phase 1 trial of GSK2256098 presented at EORTC-NCI-AACR Molecular Therapeutics meeting (Nov. 6-9, 2012)**
COMMAND: A Registration-Directed Study of VS-6063 to Maintain Tumor Control in Mesothelioma

1\textsuperscript{st} line
4-6 cycles Alimta + cisplatin
Median PFS: 5.7 mos\textsuperscript{1}

2\textsuperscript{nd} line
No SoC
PFS: 6wks\textsuperscript{3}

\textbf{VS-6063 immediately following 1\textsuperscript{st} line chemotherapy}
Baseline PFS: 4 mos\textsuperscript{2}

\textbf{Key Endpoints}
PFS
OS
QoL

\textbf{Merlin Low}
≥ 4 cycles Platinum/Alimta

CT Scan
0
2
4
weeks
6
8

PR/SD
350-400

\textbf{Merlin High}

CT Scan

\textbf{Placebo BID}

\textbf{VS-6063 400mg BID}

\textbf{Placebo BID}

\textbf{VS-6063 400mg BID}

\textsuperscript{1}Vogelzang et al; JCO Vol 21, No 14 (July 15), 2003: pp 2636-2644
\textsuperscript{2}Buikheisen et al., Lancet Oncol 2013; 14: 543-51
\textsuperscript{3}Krug et al; ESMO 2011

Novel Drugs Targeting Cancer Stem Cells
Enrichment Design of COMMAND Enables Multiple Potential Paths to Registration

- **Interim PFS Analysis at 50% PFS Events**
  - **Futile**
    - Stop study
  - **Enroll all patients**
  - **Enrich merlin-low only**
    - Sample size re-estimation for PFS power

- **Primary PFS Analysis (90% Power)**
  - PFS significant
    - Sample size re-estimation for OS power
    - **Potential for accelerated approval**
  - **Primary OS Analysis**
  - **File NDA**
**COMMAND: A Simultaneous, Multinational Development Strategy**

- 33 sites open and enrolling

<table>
<thead>
<tr>
<th>Australia</th>
<th>Belgium</th>
<th>Canada</th>
<th>France</th>
<th>Netherlands</th>
<th>New Zealand</th>
<th>South Africa</th>
<th>Spain</th>
<th>Sweden</th>
<th>UK</th>
<th>USA</th>
<th>Japan</th>
</tr>
</thead>
<tbody>
<tr>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
</tr>
</tbody>
</table>

- Estimated time to full enrollment: 24 months
- Study update at R&D Day on Thursday, July 10th in New York
Motivated investigators due to unmet need and ‘drug lag’

In Phase 1, VS-6063 was generally well tolerated at all dose levels with similar side effects to western patients

One patient (1/9) on the Phase 1 study has mesothelioma and had stable disease with symptomatic improvement for over 5 months on study

Goal is to pursue development in major markets simultaneously
Phase 1/1b Interim Results: Combination of VS-6063 and Weekly Paclitaxel in Patients with Ovarian Cancer

No Impact on Paclitaxel Pharmacokinetics

The 24 hr serum concentration of paclitaxel (80 mg/m2) was determined on Day 1 in the absence of VS-6063.

Following 14 days of continuous VS-6063 administration (200 or 400 mg BID) the 24hr serum concentration of paclitaxel was re-evaluated. (n=6)

VS-6063 Reduces FAK Activity in Tumor Biopsies at Day 10

Paclitaxel alone
Paclitaxel + VS-6063

Phospho-FAK levels were compared between Day 1 and Day 10 biopsy samples by immunohistochemistry.

Paired tumor biopsies were obtained in five patients following 10 days of defactinib administration (400 mg BID).
Phase 1/1b Interim Results: Combination of VS-6063 and Weekly Paclitaxel in Patients with Ovarian Cancer

Clinical activity and no worsening of the well characterized side effects of paclitaxel

Best overall response and duration on study

14 of 22 (64%) patients have a best overall response of at least SD in this ongoing study

400 mg BID defactinib
200 mg BID defactinib

* Subject remains on study treatment
# Subject discontinued due to AE

CR - Complete Response; PR - Partial Response; SD - Stable Disease; PD - Progressive Disease; NE – Not Evaluable

As reported on June 2nd, 2014 at ASCO
Key IP Supports Cancer Stem Cell Platform

CSC Biology and High-Throughput Screening

✓ A Method for the Discovery of Agents Targeting and Exhibiting Specific Toxicity for Cancer Stem Cells. (Expiration 2029)¹
✓ Compounds and Methods for the Treatment of Cancer Stem Cells. (Expiration 2031)¹

Personalized Diagnostics and CSC Biomarkers

✓ Progenitor Cells and Uses Thereof (Expiration 2026)¹
✓ Methods of Diagnosing, Preventing and Treating Cancer Metastasis. (Expiration 2025)²
✓ Compositions and Methods for Modulating EMT and Uses Thereof (Expiration 2031)¹

Inhibitors of CSC survival

PI3K/mTOR

FAK

Integrins

RTKs

VS-6063

VS-4718

VS-5584

p130Cas

mTORC1    mTORC2

Elimination of CSCs

✓ VS-6063 ²
Expiration 2029

✓ VS-4718 ²
Expiration 2028-2031

✓ VS-5584 ¹
Expiration 2029

¹ Pending patent application ² U.S. patent issued
Verastem is at the Forefront of Cancer Stem Cell Biology

Identification of Selective Inhibitors of Cancer Stem Cells by High-Throughput Screening

The Epithelial-Mesenchymal Transition Generates Cells With Properties of Stem Cells
Mani, Weinberg, et al. 2008

Paracrine and autocrine signals induce and maintain mesenchymal and stem cell states in the breast
Scheel, Weinberg, et al. 2011

Identification of Selective Inhibitors of Cancer Stem Cells by High-Throughput Screening

Hallmarks of Cancer: The Next Generation
Hanahan, Weinberg. 2011

The outgrowth of micrometastases is enabled by the formation of filopodium-like protrusions.

Stochastic State Transitions Give Rise to Phenotypic Equilibrium in Populations of Cancer Cells
Gupta, Lander, et al. 2011

The New York Times

The Wall Street Journal.

Other companies involved in cancer stem cell drug development
Scientific Advisory Board

Robert Weinberg, Ph.D.
*Whitehead Institute/MIT*
*Co-founder & Chairman of SAB*

Peter Elliott, Ph.D.
*Former SVP/Head – R & D, SIRT (now GSK)*
*Millennium (co-developed Velcade®)*

Eric Lander, Ph.D.
*Broad Institute/MIT/HMS*
*Pioneer of Human Genome Project*

Richard Sackler, M.D.
*Chairman – Purdue Pharma*

Phil Sharp, Ph.D.
*MIT – 1993 Nobel Prize in Medicine*
*Cofounder: Biogen, Alnylam; Sirtris SAB*

Chris Walsh, Ph.D.
*Harvard Medical School*
*Cofounder: Genzyme, Vicuron; Sirtris SAB*

Joseph (Yossi) Schlessinger, Ph.D.
*Yale Medical School*
*Cofounder: Sugen (Pfizer), Plexxikon (Daiichi-Sankyo)*

Translational Research

José Baselga, M.D., Ph.D.
*Physician in Chief; MSKCC*
*Senior Medical Advisor*

George Daley, M.D., Ph.D.
*Director – Stem Cell Program*
*Harvard Medical School/HHMI*

Max Wicha, M.D.
*Director – University of Michigan Comprehensive Cancer Center*

Eric Winer, M.D.
*Director – Breast Oncology Center*
*Dana Farber Cancer Institute/HMS*
Verastem Team

Executive Management

Robert Forrester
President/CEO, BOD
CEO/CFO, CombinatoRx/COLY
MeesPierson, Barclays, UBS

Christoph Westphal, M.D., Ph.D.
Executive Chairman of BOD, Cofounder
Cofounder/CEO: MNTA, ALNY, XLRN, SIRT, VSTM
Cofounder: Alnara (now Lilly), OvaScience (OVAS)

Jack Green
Chief Financial Officer
CFO, Genzyme Transgenics Corporation (GTC)

Joanna Horobin, M.B., Ch.B.
Chief Medical Officer
President/CEO, Syndax
10 marketed drugs (Taxotere®, Camptosar®)
Breakthrough designation for Entinostat

Jonathan Pachter, Ph.D.
VP, Head of Research
Head of Cancer Biology, OSI (now Astellas)
Schering-Plough (now Merck)

Daniel Paterson
Chief Business Officer
CEO: The DNA Repair Co. (now On-Q-ity)
PharMetrics (now IMS), Axion

Board of Directors

Richard Aldrich
Longwood Fund

Timothy Barberich
Former CEO/Chair Sepracor (SEPR)

Michael Kauffman, M.D., Ph.D.
CEO Karyopharm (KPTI), former CMO Onyx

Henri Termeer
Lead Director
Former CEO/Chair Genzyme

Paul Friedman, M.D.
Former President/CEO Incyte (INCY)

Alison Lawton
Former Genzyme (now Sanofi)

Louise Phanstiel
BOD: Cedars Sinai, MYGN

Stephen Sherwin, M.D.
BOD: BIIB; NBIX, RIGL
### Portfolio of Product Candidates Targeting Cancer Stem Cells

<table>
<thead>
<tr>
<th></th>
<th>PreClin</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Focal Adhesion Kinase (FAK)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>VS-6063</strong></td>
<td></td>
<td>COMMAN: A Registration-directed trial</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mesothelioma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung (KRASmt NSCLC)</td>
<td></td>
<td></td>
<td>Phase 2</td>
<td></td>
</tr>
<tr>
<td>Ovarian</td>
<td></td>
<td>Phase 1/1b in combo with paclitaxel</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>VS-4718</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solid Tumors</td>
<td></td>
<td>Phase 1/1b</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PI3K and mTORC1/2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>VS-5584</strong></td>
<td></td>
<td></td>
<td>Phase 1/1b</td>
<td></td>
</tr>
<tr>
<td>Solid Tumors and Lymphomas</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wnt/β-Catenin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eisai</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Research Collaboration</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Cash, cash equivalents and marketable securities balance: $113.9m**  
*(As of 3/31/14)*
### Key Achievements in 2013
- Completed 4 IND Filings
- Orphan Drug status in US and EU for VS-6063 in mesothelioma
- Obtained clinical allowance in 12 countries for VS-6063 trials
- VS-6063 COMMAND Study in mesothelioma
- VS-6063 Japanese Phase 1
- VS-6063 + paclitaxel Phase 1/1b combination in ovarian cancer
- VS-6063 Phase 2 NSCLC
- VS-4718 Phase 1
- VS-5584 Phase 1
- VS-6063 Phase 1 + paclitaxel combination dose escalation

### Key Milestones Expected in 2014
- Progress COMMAND towards interim analysis
- Open COMMAND in Japan
- VS-6063 Japanese Phase 1
- VS-6063 + paclitaxel Phase 1/1b combination in ovarian cancer
- VS-6063 Phase 2 NSCLC interim analysis
- VS-5584 Phase 1 interim data
- VS-4718 Phase 1 interim data
- AACR, ASCO, EORTC, SABCS, iMIG

Estimates based on currently proposed clinical plans and are subject to change
## Targeting Cancer Stem Cells to Improve Patient Outcomes

### OPPORTUNITY
- Discovery platform at the **forefront of cancer stem cell biology**
- **Pipeline of clinical candidates** targeting cancer stem cells in early and late-stage clinical trials

### STRATEGY
- VS-6063 lead program: **registration-directed trial** with orphan drug designation
- **Therapeutic indication expansion** for the treatment of many cancer types

### LEADERSHIP
- Experienced leadership and advisory team to guide strategy and execute development plan
- Strong record of execution → **Key clinical and data milestones expected in 2014**

### CAPITAL
- **$113.9 million** as of 3/31/14
- Sufficient capital to fund operations into 2016

*Estimates based on currently proposed clinical plans and subject to change*
Appendix
FAK Inhibition Preferentially Reduces CSCs in Multiple Assays

**Aldefluor Assay**

![Graph showing Aldefluor-Positive CSCs (% of Control) vs. VS-4718, nM]

**Tumorsphere Formation**

![Graph showing Secondary Spheres (% of Control) vs. VS-4718]

**Hoechst Dye Exclusion (SP)**

![Graph comparing Control and 1 μM VS-4718]

Novel Drugs Targeting Cancer Stem Cells
### Primary Endpoint: Safety and Tolerability

<table>
<thead>
<tr>
<th>Adverse Events*</th>
<th>Grade 1 (N, %)</th>
<th>Grade 2 (N, %)</th>
<th>Grade 3 (N, %)</th>
<th>Grade 4 (N, %)</th>
<th>Total (N, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>14 (30)</td>
<td>3 (7)</td>
<td>0</td>
<td>0</td>
<td>17 (37)</td>
</tr>
<tr>
<td>Unconjugated hyperbilirubinemia</td>
<td>6 (13)</td>
<td>9 (20)</td>
<td>2 (4)</td>
<td>0</td>
<td>17 (37)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>8 (17)</td>
<td>6 (13)</td>
<td>1 (2)</td>
<td>0</td>
<td>15 (33)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>10 (22)</td>
<td>3 (7)</td>
<td>0</td>
<td>0</td>
<td>13 (28)</td>
</tr>
<tr>
<td>Headache</td>
<td>9 (20)</td>
<td>0</td>
<td>1 (2)</td>
<td>0</td>
<td>10 (22)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>8 (17)</td>
<td>2 (4)</td>
<td>0</td>
<td>0</td>
<td>10 (22)</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>8 (17)</td>
<td>1 (2)</td>
<td>0</td>
<td>0</td>
<td>9 (20)</td>
</tr>
</tbody>
</table>

* Treatment-Related Adverse Events (≥ 20%)

### Initial Signs of Clinical Activity

- **Stable disease of circa 6 months +**
  - NSCLC: (425 mg BID; 2 priors)
  - Ovarian: (425 mg BID; 4 priors)
  - Cholangiocarcinoma: (200 mg BID; 2 priors)
  - Ovarian: (425 mg BID; 5 priors)
  - Colon: (300 mg BID; 6 priors)
  - Pancreatic: (100 mg BID; 5 priors)
  - Ovarian: (500 mg BID; 6 priors)

**-4 out of 8 ovarian patients had SD**

*Jones SF J Clin Oncol 2011 29:1 (suppl; abstr 3002)*
## Phase 1/1b Combination Study in Patients with Ovarian Cancer - Safety

### Treatment-Emergent Adverse Events in ≥20% patients

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Phase I: 200 mg defactinib BID + 80 mg/m² paclitaxel weekly (n=3)</th>
<th>Phase Ib: 400 mg defactinib BID + 80 mg/m² paclitaxel weekly (n=16)</th>
<th>Total (n=22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>3 (100%)</td>
<td>6 (37.5%)</td>
<td>10 (45.5%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>2 (66.7%)</td>
<td>5 (31.3%)</td>
<td>10 (45.5%)</td>
</tr>
<tr>
<td>Bilirubin Increased</td>
<td>2 (66.7%)</td>
<td>6 (37.5%)</td>
<td>8 (36.4%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>2 (66.7%)</td>
<td>4 (25.0%)</td>
<td>7 (31.8%)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>1 (33.3%)</td>
<td>4 (25.0%)</td>
<td>7 (31.8%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1 (33.3%)</td>
<td>4 (25.0%)</td>
<td>7 (31.8%)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>1 (33.3%)</td>
<td>3 (18.8%)</td>
<td>6 (27.3%)</td>
</tr>
<tr>
<td>Peripheral Edema</td>
<td>1 (33.3%)</td>
<td>4 (25.0%)</td>
<td>6 (27.3%)</td>
</tr>
<tr>
<td>Peripheral Neuropathy</td>
<td>1 (33.3%)</td>
<td>3 (18.8%)</td>
<td>6 (27.3%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>0 (00.0%)</td>
<td>4 (25.0%)</td>
<td>5 (22.7%)</td>
</tr>
<tr>
<td>Urinary Tract Infection</td>
<td>1 (33.3%)</td>
<td>3 (18.8%)</td>
<td>5 (22.7%)</td>
</tr>
</tbody>
</table>
VS-6063: Phase 2 Study in KRAS-mutated NSCLC

- Increase safety database for VS-6063
- Hypothesis-driven design based on work from UT Southwestern

Preclinical Rationale

**Double mutation in KRAS + p16 or p53 leads to increased sensitivity to FAK inhibition**

**Simon Two-Stage Clinical Trial Design**

<table>
<thead>
<tr>
<th>Mutation Status</th>
<th>Interim Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>KRAS</strong></td>
<td><strong>p16</strong></td>
</tr>
<tr>
<td>Cohort A</td>
<td>✓</td>
</tr>
<tr>
<td>Cohort B</td>
<td>✓</td>
</tr>
<tr>
<td>Cohort C</td>
<td>✓</td>
</tr>
<tr>
<td>Cohort D</td>
<td>✓</td>
</tr>
</tbody>
</table>

PFS of ≥ 12 weeks in ≥4 patients?

- 11 patients/arm
- 23 patients/arm
VS-4718 – FAK Inhibitor Structurally Distinct from Lead

- Potent, low nanomolar inhibition of FAK kinase
- Targets cancer stem cells in *in vitro* and *in vivo* models of cancer
- Phase 1 dose escalation in patients with advanced cancers ongoing

Biochemical Properties

![Chemical Structure](image)

FAK Enzymatic IC<sub>50</sub> = 42 nM  
FAK Cellular EC<sub>50</sub> = 31 nM

*Composition of matter though 2028*

Cancer Stem Cells

![Graph](image)

*Triple negative breast cancer*
**VS-5584: Dual mTORC1/2 and pan-PI3K Inhibitor**

<table>
<thead>
<tr>
<th>IC$_{50}$ (nM)</th>
<th>mTOR</th>
<th>PI3K-Alpha</th>
<th>PI3K-Beta</th>
<th>PI3K-Delta</th>
<th>PI3K-Gamma</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3.4</td>
<td>2.6</td>
<td>21</td>
<td>3.0</td>
<td>2.7</td>
</tr>
</tbody>
</table>

- Oral formulation
- Phase 1 dose escalation in patients with solid tumors and lymphomas ongoing

**PI3K/mTOR**

**RTKs**

**PI3K**

**AKT**

**VS-5584**

**AKT**

**mTORC1**

**mTORC2**

Elimination of CSCs