RESEARCH AND DEVELOPMENT DAY

JULY 12TH 2012

NASDAQ: VSTM
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, 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 structure of the Company’s planned 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. The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “plan,” “predict,” “project,” “target,” “potential,” “will,” “would,” “could,” “should,” “continue,” 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 may not be predictive of the success of later clinical trials, 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, 2011 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.
Agenda

• Introduction 9:00 – 9:15 AM
• Cancer Stem Cell Seminar (Bob Weinberg) 9:15 – 10:00 AM
• Strategy overview 10:00 – 10:15 AM
• FAK update 10:15 - 10:45 AM
• PI3K/mTOR update 10:45 - 11:00 AM
• Wnt update 11:00 - 11:15 AM
• Diagnostic update 11:15 - 11:30 AM
• Discussion & Questions 11:30 - 12:00 PM
Current Cancer Treatments Often Fail

Current cancer treatments often fail
Relapse often develops into metastatic disease
Metastases are cause of over 90% of cancer deaths

- 5-year relative survival rate (breast cancer)
  - Localized: 99%
  - Regional: 84%
  - Distant: 23%
Targeting Cancer Stem Cells For a Durable Clinical Response

Problem:

Initial Tumor → Tumor reduction but CSCs survive → Recurring Tumor

Current cancer treatments

Goal:

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

CSC drugs + current cancer treatments
Acceleration of FAK Program: In-License of Pfizer Clinical Products

• Background
  – Two Phase 2 ready FAK inhibitors (PF-04554878 and PF-562271)
  – Pfizer program was discontinued due to portfolio review (February 2012)

• Rationale
  – More advanced candidates accelerate our FAK program by 12-18 months
  – Lead compound: VS-6063 (PF-04554878)
  – Capitalize on our FAK/CSC insights
Key Signaling Targets in CSC Survival: FAK, PI3K/mTOR and Wnt

FAK
- Integrins
- FAK
- p130Cas
- Merlin

PI3K/mTOR
- RTKs
- PI3K
- AKT
- mTORC1
- mTORC2

Wnt
- FZD
- LRP5/6
- β-Catenin
- Axin1
- GSK3β
- APC
- CK1α

β-Catenin
Key Signaling Targets in CSC Survival: FAK, PI3K/mTOR and Wnt

FAK
- Integrins
  - VS-6063
  - VS-4718
- Merlin
- FAK
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PI3K/mTOR
- RTKs
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- AKT
- mTORC1
- mTORC2

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- FZD
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- β-Catenin
- GSK3β
- Axin1
- CK1α
- APC

β-Catenin

VS-6063
VS-5584
VS-507
VS-4718
Accelerated Clinical Plan: Three Clinical Products Planned for the Next 12 Months

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<th>2013</th>
<th>2014</th>
<th>2015</th>
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<td>H2</td>
<td>H1</td>
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<td>FAK</td>
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<tr>
<td>VS-6063</td>
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<td>FDA</td>
<td>Phase 2</td>
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<td>PI3K/mTOR</td>
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<td>VS-5584</td>
<td>IND-Tox</td>
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<td>Wnt</td>
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<td>Research Collaboration</td>
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</tbody>
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* Potential regulatory filing for approval

Proposed clinical plans.
Alternatives are being considered
## Scientific Advisory Board

<table>
<thead>
<tr>
<th>Name</th>
<th>Position/Institution</th>
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</thead>
<tbody>
<tr>
<td>Eric Lander, Ph.D.</td>
<td>Broad Institute/MIT/HMS, Co-founder</td>
</tr>
<tr>
<td>Robert Weinberg, Ph.D.</td>
<td>Whitehead Institute/MIT, Co-founder &amp; Chairman of SAB</td>
</tr>
<tr>
<td>Piyush Gupta, Ph.D.</td>
<td>Whitehead Institute/MIT, Co-founder</td>
</tr>
<tr>
<td>Daniel Haber, M.D., Ph.D.</td>
<td>MGH Cancer Center, Harvard Medical School/HHMI</td>
</tr>
<tr>
<td>Phil Sharp, Ph.D.</td>
<td>MIT – 1993 Nobel Prize in Medicine, Cofounder: Biogen, Alnylam; Sirtris SAB</td>
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<td>Roger Tung, Ph.D.</td>
<td>President &amp; CEO/Cofounder – Concert, Vertex (co-invented Lexiva® and Agenerase®)</td>
</tr>
<tr>
<td>Chris Walsh, Ph.D.</td>
<td>Harvard Medical School, Cofounder: Genzyme, Vicuron; Sirtris SAB</td>
</tr>
<tr>
<td>Julian Adams, Ph.D.</td>
<td>President R&amp;D – Infinity Pharmaceuticals, Co-invented/developed Velcade® and Viramune®</td>
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<tr>
<td>Peter Elliott, Ph.D.</td>
<td>Former SVP/Head – R &amp; D, SIRT (now GSK), Millennium (co-developed Velcade®)</td>
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<tr>
<td>Joseph (Yossi) Schlessinger, Ph.D.</td>
<td>Yale Medical School, Cofounder: Sugen (Pfizer), Plexxikon (Daiichi-Sankyo)</td>
</tr>
<tr>
<td>José Baselga, M.D., Ph.D.</td>
<td>Chief – Hematology/Oncology MGH/MGH Cancer Center</td>
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<td>Director – University of Michigan Comprehensive Cancer Center</td>
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## Biopharmaceutical Experience

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## Translational Research

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<td>José Baselga, M.D., Ph.D.</td>
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<tr>
<td>George Daley, M.D., Ph.D.</td>
<td>Director – Stem Cell Program Harvard Medical School/HHMI</td>
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<tr>
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<tr>
<td>Richard Sackler, M.D.</td>
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Bob Weinberg – Whitehead Institute and Verastem Co-Founder

**Finding on Drugs May Help Fight Against Cancer**

**Going After Stem Cells**

Screening Test Detects Chemicals on Attack in Selective Way

By NICHOLAS WADE

Researchers have discovered a way to identify drugs that can specifically attack and kill cancer stem cells, a finding that could lead to a new generation of anti-cancer medicines and a new strategy of treatment.

Many researchers believe that tumor growth is driven by cancerous stem cells that, for reasons not understood, are highly resistant to standard treatments.

**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
## Agenda

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<th>Event</th>
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Key Signaling Targets in CSC Survival: FAK, PI3K/mTOR and Wnt

FAK
- Integrins
- Merlin
- FAK
- VS-6063
- VS-4718
- p130Cas

PI3K/mTOR
- RTKs
- PI3K
- AKT
- mTORC1
- mTORC2
- VS-5584

Wnt
- FZD
- LRP5/6
- VS-507
- β-Catenin

Integrins RTKs
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Key Signaling Targets in CSC Survival: Focal Adhesion Kinase (FAK)

**FAK**
- Integrins → FAK
- Merlin → FAK
- p130Cas

**PI3K/mTOR**
- RTKs → PI3K
- VS-5584
- AKT → VS-5584
- mTORC1
- mTORC2

**Wnt**
- VS-507
- LRP5/6
- FZD
- Axin1
- APC
- GSK3β
- β-Catenin

**β-Catenin**
- CK1α

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Verastem, Inc. Confidential
FAK as a Cancer Stem Cell Target

• FAK inhibitors active in Verastem’s cancer stem cell (CSC) assays

• Cytoplasmic tyrosine kinase that regulates key cellular processes including growth, survival and migration

• FAK is over-expressed in advanced stage cancer (invasive, metastatic) in many tumor types

• Implicated in facilitating CSC self renewal and breast cancer tumor growth in the literature

• Inhibition of FAK expected to reduce both primary tumor and metastatic disease
Clinical Landscape: FAK

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<tr>
<th>Compound</th>
<th>Company</th>
<th>Dev Status</th>
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<tr>
<td>GSK2256098</td>
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<tr>
<td>BI1853520</td>
<td>Boehringer Ingelheim</td>
<td>Ph 1</td>
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FAK Development Candidates: VS-6063 and VS-4718

• VS-6063: Accelerates Verastem’s FAK program by 12-18 months
  – Phase 2 ready (PF-04554878) licensed from Pfizer (July, 2012)
    • Pfizer FAK program deprioritized due to portfolio review (February, 2012)
  – Phase I completed in advanced solid tumors
    • Suitable toxicity profile for long term dosing and combination
    • Signs of clinical activity (stable disease) observed across multiple tumor types
  – Strong IP
    • Composition of matter until 2029

• VS-4718
  – Licensed from Scripps/Poniard (November, 2011)
  – Nominated as a development candidate (May, 2012)
FAK Inhibition Preferentially Reduces CSCs in Multiple Assays

**HMLE: Selective for CSCs**

- % Cell Viability vs. VS-4718, μM
  - Red dots: non-CSCs
  - Green dots: CSCs

**Tumorsphere Formation**

- Normalized Sphere Forming Efficiency (%)

**Aldefluor-Positive CSCs**

- MDA-MB-231
  - Aldefluor-Positive CSCs (% of Control)

**CSCs: Hoechst Dye Exclusion**

- Control vs. 1 μM VS-4718
  - CSCs (14% vs. 0.03%)
Anti-Tumor Efficacy Correlates with Sustained Suppression of Tumor pFAK

**VS-4718 Anti-Tumor Efficacy**

**VS-4718 PK/PD Profile**

Vehicle, BID x 28  
VS-4718 25 mg/kg, BID x 28  
VS-4718 100 mg/kg, BID x 28  
Paclitaxel 15 mg/kg, IP QD x 5
MDA-MB-231 Breast Cancer Cell Line is Most Sensitive to FAK Inhibition

Translational Research: Identification of Patient Selection Markers

Human Breast Cancer Cell Lines

- **NF2-/-**
  - MDA-MB-231
  - **NF2+/+**
  - BT549
  - MDA-MB-453
  - SUM159
  - SUM149
  - MDA-MB-468
  - HCC1937
  - HCC1954

**Relative Growth**

**VS-4718, µM**

**Merlin**

**Actin**

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Key Signaling Targets in CSC Survival: Focal Adhesion Kinase (FAK)

- NF2 (tumor suppressor gene)
- Merlin
- FAK
- p130Cas

Integrins

- VS-6063
- VS-4718
Merlin Negative Breast Cancer Cells are Most Sensitive to FAK Inhibition

Translational Research: Identification of Patient Selection Markers

Merlin (−) MDA-MB-231 Xenograft

Merlin (+) MDA-MB-468 Xenograft

in vitro

in vivo
Merlin Negative Mesothelioma Cell Lines are Especially Sensitive to FAK Inhibition
Cancer Stem Cells in Mesothelioma

- CSCs identified in 90% of human mesothelioma patient samples
- CSCs enriched in pemetrexed-resistant mesothelioma cell lines
- FAK inhibitors reduce CSCs in Merlin negative mesothelioma cell lines
- Pemetrexed increases proportion of mesothelioma CSCs

**H2052 Human Mesothelioma (Merlin Negative)**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Aldefluor-Positive CSCs (% of Control)</th>
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<tbody>
<tr>
<td>Control</td>
<td>100</td>
</tr>
<tr>
<td>VS-6063</td>
<td>80</td>
</tr>
<tr>
<td>Pemetrexed</td>
<td>180</td>
</tr>
<tr>
<td>Pemetrexed + VS-6063</td>
<td>50</td>
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Merlin Loss is Prevalent in Mesothelioma: Potential Clinical Indication for FAK Inhibitor

- Merlin loss is prevalent in ~40% of mesothelioma tumors

- Mesothelioma represents an unmet medical need
  - Usually arises from exposure to asbestos
  - Extremely poor prognosis with most patients dying within 12 months of diagnosis
  - 2,500-3,000 new cases per year in US
  - Incidence is higher (and increasing) in countries like Australia, Britain and Europe

- Chemotherapy is the only treatment for mesothelioma that has been proven to improve survival in randomized and controlled trials
  - Only one approved agent: Alimta (pemetrexed) in combination with cisplatin
    - Approved on a 2.8 month increase in Overall Survival versus cisplatin alone
  - No approved agents in second line setting
    - Median PFS in second line setting is 1.5 months
Additional Tumor Types Under Consideration: Breast and Ovarian Cancer

Over-expression of FAK correlates to a poor prognosis in ovarian cancer
– pFAK (High vs low expression correlated with survival 1.7 vs 3 yrs respectively).

Kaplan-Meier curves of disease-specific mortality for patients with epithelial ovarian carcinoma based on FAK or pFAK expression.

Phase I Study of VS-6063: Good Safety Profile in Patients with Advanced Solid Tumors

Total of 46 patients received doses ranging from 12.5 to 750 mg BID

<table>
<thead>
<tr>
<th>AE*</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>
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</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>14 (30)</td>
<td>3 (7)</td>
<td>0</td>
<td>0</td>
<td>17 (37)</td>
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<tr>
<td>Unconjugated hyperbilirubinemia</td>
<td>6 (13)</td>
<td>9 (20)</td>
<td>2 (4)</td>
<td>0</td>
<td>17 (37)</td>
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<tr>
<td>Fatigue</td>
<td>8 (17)</td>
<td>6 (13)</td>
<td>1 (2)</td>
<td>0</td>
<td>15 (33)</td>
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<tr>
<td>Vomiting</td>
<td>10 (22)</td>
<td>3 (7)</td>
<td>0</td>
<td>0</td>
<td>13 (28)</td>
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<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>

Source: Pfizer, Inc.

*Treatment-Related Adverse Events (≥20%)
43% (16/37) patients enrolled at doses ≥100 mg BID experienced SD

- 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)

7 patients with SD ≥ 6 months

Source: Pfizer, Inc.
VS-6063 Proposed Clinical Development Plan

• Phase 2 study in mesothelioma
  — Randomized, controlled study
  — Patients selected for Merlin status
  — Endpoints: PFS, OS, response rate and biomarkers (FAK & CSC specific markers)
  — Successful Phase 2 study may allow an opportunity for an accelerated approval

• Phase I combination study
  — Dose escalating, combo (VS-6063 plus SOC) study in patients with recurrent disease
  — Endpoints: safety, tolerability, PK, biomarkers (pFAK and CSC) and clinical outcome

• Phase 2 study in breast or ovarian
  — Randomized study (VS-6063 + SOC vs SOC alone) as 2nd/3rd line in recurrent disease
  — Endpoints: PFS, OS, response rate, and biomarkers (FAK & CSC specific markers)

• Phase 3 confirmatory study
  — Randomized study (VS-6063 + SOC vs SOC alone) as 2nd/3rd line in recurrent disease
VS-4718 Proposed Clinical Development Plan

• Phase I healthy volunteer study in Australia
  – Determination of preliminary safety, PK and biomarkers
  – Data can be used as part of a US IND submission
  – Potential for a higher starting dose for Phase I clinical trial in patients
  – 2 dose level savings ~ 3-4 months

• Phase I dose escalation in patients with solid tumors
  – Starting dose will be based upon healthy volunteer study
  – Patient cohorts enriched for tumor types with FAK overexpression e.g. breast, mesothelioma and ovarian
  – Endpoints: safety, tolerability, PK, biomarkers (pFAK & CSC) and clinical outcome
A positive phase 2 in mesothelioma could present an opportunity for an accelerated approval.
FAK Summary

• Absence of Merlin correlates with enhanced sensitivity in both cellular and animal models

• VS-6063 accelerates Phase 2 program by 12-18 months
  – Successful completion of Phase I study in advanced solid tumors
  – Initiation of Phase 2 mesothelioma trial expected Q2, 2013
  – Successful Phase 2 study may allow an opportunity for an accelerated approval

• Nominated VS-4718 as a development candidate
  – Potent inhibition of pFAK and CSC proliferation \textit{in vitro}
  – Inhibits both primary tumor growth and metastasis \textit{in vivo}
  – Phase I (healthy volunteers) study expected to initiate in Q1 2013

Verastem positioned to be the leader in FAK inhibitor clinical development
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Key Signaling Targets in CSC Survival: PI3K/mTOR Pathway

PI3K/mTOR

RTKs

PI3K

AKT

mTORC1

mTORC2

FAK

Integrins

Merlin

p130Cas

VS-5584

Wnt

VS-507

LRP5/6

FZD

β-Catenin

GSK3β

Axin1

APC

β-Catenin

RTKs

Verastem, Inc. Confidential
VS-5584: Pan-PI3K & mTOR Kinase Inhibitor

• Acquired from S-Bio Q2 2012
  — Initial payment of $350,000
  — Total milestones of $21M
  — Tiered low to mid single digit royalties

• IP position
  — Composition of matter to 2028
  — Method of use to 2029
### Clinical Landscape: PI3K/mTOR Dual Inhibitors

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<td>Ph 1</td>
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<tr>
<td>BEZ-235 / BGT226</td>
<td>Novartis</td>
<td>Ph 2</td>
</tr>
<tr>
<td>SAR245409 (XL765)</td>
<td>Sanofi Aventis</td>
<td>Ph 2</td>
</tr>
<tr>
<td>PF4691502</td>
<td>Pfizer</td>
<td>Ph 2</td>
</tr>
<tr>
<td>GDC0980</td>
<td>Genentech</td>
<td>Ph 2</td>
</tr>
<tr>
<td>PWT33597*</td>
<td>Pathway</td>
<td>Ph 1</td>
</tr>
</tbody>
</table>

*PI3Kα/mTOR dual inhibitor*
VS-5584: Candidate Profile

- Potent against mTORC1/2 and all PI3K isoforms
- Highly selective vs. other protein kinases
- Broad and robust anti-tumor efficacy in xenograft models
- Excellent PK properties & target inhibition in tumors
- Differentiation from rapamycin analogs
  - Broader anti-tumor activity, better PK
- Differentiation from other PI3K & mTOR kinase inhibitors
  - Equivalent potency against mTOR & all PI3K isoforms
  - Highly selective for desired targets
  - Excellent PK/PD
VS-5584 Targets Cancer Stem Cells

HMLE CSC assay: VS-5584 preferentially targets CSCs

Aldefluor CSC Assay: VS-5584 reduces CSCs; paclitaxel enriches CSCs
VS-5584 Targets Cancer Stem Cells: Hoechst Dye Exclusion Assay

CSCs

Placebo Control
2.56% CSCs

CSCs

VS-5584 (1.0 µM)
0.038% CSCs

CSCs

VS-5584 (3.0 µM)
0.013% CSCs

% CSCs

DMSO 1.0 µM 3.0 µM
VS-5584
Key Signaling Targets in CSC Survival: PI3K/mTOR

**PI3K/mTOR Activation in Cancer**

- RTK Hyper-Activation

- PI3Kα Mutation
  - ~50% of Breast Cancer
  - ~25% of Colon Cancer

- PTEN Loss
  - Up to 70% of Prostate Cancer
  - ~40% of Glioblastoma
VS-5584 Potently Inhibits PI3K, mTORC1 & mTORC2

### Table: VS-5584 (nM)

<table>
<thead>
<tr>
<th>Target</th>
<th>Marker</th>
<th>VS-5584 (nM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>mTORC1</td>
<td>pS6 (Ser240/244)</td>
<td></td>
</tr>
<tr>
<td>mTORC2</td>
<td>p-Akt (S473)</td>
<td></td>
</tr>
<tr>
<td>PI3K</td>
<td>p-Akt (T308)</td>
<td></td>
</tr>
<tr>
<td>Actin Control</td>
<td>Actin</td>
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</tr>
<tr>
<td></td>
<td>0</td>
<td>4</td>
</tr>
</tbody>
</table>

**IC₅₀ < 100 nM**
VS-5584: Anti-Cancer Activity in Xenograft Models

Prostate Cancer (PC3)  
Colorectal Cancer (Colo205)

Activity also demonstrated in leukemia, hepatocellular and gastric carcinoma xenograft models

† In Colo205 model only
VS-5584: Proposed Clinical Development Plan

• Phase I/ Ib: Dose escalation in patients with advanced cancers
  – Standard 3+3 dose escalation study
  – Phase Ib Expansion: Enriched for PI3K/mTOR relevant tumors (including breast, brain, colon, liver, lung, pancreas, gastric and endometrial cancers)
  – Endpoints: safety, tolerability, PK, biomarkers (PI3K/mTOR and CSC specific markers) and clinical outcome

• Phase I combination study
  – Dose escalating, combination (VS-5584 plus SOC) study in patients with recurrent disease
  – Endpoints: safety, tolerability, PK, biomarkers (PI3K/mTOR & CSC) and clinical outcome

• Phase 2: Combination study in metastatic disease
  – VS-5584 + SOC as second/third line therapy in recurrent disease
  – Endpoints: PFS, OS, response rate and biomarkers (PI3K/mTOR & CSC specific markers)

• Phase 2: Combination study in neo-adjuvant TNBC
  – Randomized, controlled study (VS-5584 plus SOC versus SOC alone)
  – Pathological complete response primary endpoint
Proposed Clinical Study Timelines: PI3K/mTOR Program

**2012**
- Phase I (solid tumors)

**2013**
- Phase Ib (enriching for PI3K/mTOR relevant tumors)
- Phase I combination

**2014**
- Phase 2 (metastatic disease)

**2015**
- Phase 2 (neoadjuvant breast)

**2016**

Proposed clinical plans. Alternatives are being considered.
PI3K/mTOR Summary

• PI3K/mTOR identified as critical node in CSC biology

• VS-5584 shows good potency against mTORC1 / mTORC2 and all PI3K enzymes

• Broad and strong activity in multiple xenograft models

• Good PK / PD properties

• Further defining development strategy based on CSC data

• IND enabling toxicology studies planned for Q4 2012 and clinical trial initiation expected in mid-2013
<table>
<thead>
<tr>
<th>Agenda</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Introduction</td>
<td>9:00 – 9:15 AM</td>
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<tr>
<td>• PI3K/mTOR update</td>
<td>10:45 - 11:00 AM</td>
</tr>
<tr>
<td>• Wnt update</td>
<td>11:00 - 11:15 AM</td>
</tr>
<tr>
<td>• Diagnostic update</td>
<td>11:15 - 11:30 AM</td>
</tr>
<tr>
<td>• Discussion &amp; Questions</td>
<td>11:30 - 12:00 PM</td>
</tr>
</tbody>
</table>
Key Signaling Targets in CSC Survival: Wnt

- **FAK**
  - Integrins
  - VS-4718
  - p130Cas

- **PI3K/mTOR**
  - FAK
  - RTKs
  - VS-5584

- **Wnt**
  - VS-507
  - LRP5/6
  - FZD
  - GSK3β
  - Axin
  - APC
  - CK1α

- **β-Catenin**

- **tp130Cas**

- **AKT**
### Clinical Landscape: Wnt

<table>
<thead>
<tr>
<th>Compound</th>
<th>Company</th>
<th>Mechanism</th>
<th>Dev Status</th>
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</thead>
<tbody>
<tr>
<td>Small Molecules</td>
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<td></td>
</tr>
<tr>
<td>PRI-724</td>
<td>Eisai/Prism</td>
<td>$\beta$-Catenin/CBP</td>
<td>Ph 1</td>
</tr>
<tr>
<td>CWP232291</td>
<td>JW Pharma</td>
<td>Unknown</td>
<td>Ph 1</td>
</tr>
<tr>
<td>LGK974</td>
<td>Novartis</td>
<td>Porcupine Inhibitor</td>
<td>Ph 1</td>
</tr>
<tr>
<td>Antibodies</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OMP-18R5</td>
<td>Oncomed</td>
<td>Pan Frizzled Antagonist</td>
<td>Ph 1</td>
</tr>
</tbody>
</table>
Key Signaling Targets in CSC Survival: Wnt

FZD → LRP5/6 → Wnt

VS-507

Axin1 → GSK3β → β-Catenin

CK1α → APC
Wnt Inhibition

Wnt-Stimulated β-Catenin Signaling

Selective for CSCs

Aldefluor-Positive CSCs

LRP5/6 Protein Levels

Verastem, Inc. Confidential
Eisai Collaboration for Novel Wnt Inhibitors

• Have signed partnership with Eisai to develop proprietary analogs of VS-507

• Eisai has a chemistry team with particular expertise in natural products

• Leverage Eisai chemistry and Verastem CSC/Wnt signaling capabilities

• Verastem will own any new analogs from the partnership
  – Commercial royalty on identified products
  – Eisai has right of first negotiation for limited period of time
Wnt Summary

• Wnt/Beta-catenin signaling is critical in the regulation of CSC proliferation and self-renewal

• Our Wnt inhibitors (e.g. VS-507) provide a unique mechanism to disrupt this pathway and selectively target CSCs

• Deferring VS-507 clinical development

• Key collaboration with Eisai to discover next-generation VS-507 analogs
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</tr>
</tbody>
</table>
Select patients with tumors containing a high percentage of CSCs

Monitor response to therapy
Biomarker Development Strategy

<table>
<thead>
<tr>
<th>Marker Discovery</th>
<th>Assay Identification</th>
<th>Assay Development</th>
<th>Assay Validation</th>
<th>Regulatory Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Literature</td>
<td>in silico, in vitro, in vivo</td>
<td>in vivo, Phase I</td>
<td>Phase I, Phase II</td>
<td>Phase III</td>
</tr>
</tbody>
</table>

Current status

<table>
<thead>
<tr>
<th>Marker</th>
<th>Tumor</th>
<th>Blood/Other Tissue</th>
<th>VSTM Drug</th>
<th>Chemo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stratification marker</td>
<td>e.g. Merlin/NF2</td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PD marker, Effect on target</td>
<td>e.g. Phospho-FAK</td>
<td>e.g. Phospho-FAK Platelets, Hair Follicles, and/or Skin punch</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CSC marker, Effect on CSCs</td>
<td>CSC-specific antibodies, CSC gene signatures</td>
<td>CSC gene signatures, Circulating Tumor Cells (blood)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Biomarker Development Strategy: PD Marker *(Effect on Target)*

**Tumor**

pFAK in Human BrCa Xenograft Tumors

![Bar chart showing pFAK normalized to total protein for different treatments: Vehicle, VS-4718 25 mg/kg BID x28, VS-4718 100 mg/kg BID x28, and Carboplatin 40 mg/kg QD x5.](chart)

- **Vehicle**
- **VS-4718 25 mg/kg BID x28**
- **VS-4718 100 mg/kg BID x28**
- **Carboplatin 40 mg/kg QD x5**

*p < 0.05*  
*p < 0.01*

**Blood/Other Tissue**

pFAK in Human Platelets  
Effect of VS-4718 (ex-vivo)

![Bar chart showing pFAK / Total FAK for different treatments: Vehicle, VS-4718, Vehicle, and VS-4718.](chart)

- **Vehicle**  
- **VS-4718**  
- **Vehicle**  
- **VS-4718**

- **Donor 1**
- **Donor 2**

**VSTM Drug**  
**Chemo**

**PD marker**
Biomarker Development Strategy: CSC Marker (Effect on Cancer Stem Cells)

CSC Marker Discovery

Identify candidate CSC markers through gene array

CSC Marker

High CSC Low CSC

CSC Assay Identification

MDA-MB-231 Breast Cancer Tumorspheres (qPCR measurement)

Relative gene expression levels

0% 50% 100% 150% 200% 250%

Control 1 2 3 4 5

Candidate genes

Test candidate CSC markers for response to treatment with CSC-inhibitors

VSTM Drug Chemo

CSC marker

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Biomarker Summary

• Identified PD markers to measure on-target effect of drug candidates from tumor and tissue samples (e.g. phospho-FAK in platelets)

• Identified initial CSC candidate markers
  – Discovered using gene expression analysis
  – Expression of CSC markers in tumorspheres:
    • Increases due to treatment with paclitaxel
    • Decreases due to treatment with CSC-targeted drugs (e.g. VS-4718)

• Diagnostic development is on track to enter the clinic alongside our therapeutic candidates
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Proposed Clinical Study Timelines

2012
- **VS-6063**
  - FAK
  - CTM manufacture

2013
- **VS-4718**
  - FAK
  - Phase I (healthy volunteers)

2014
- **VS-5584**
  - PI3K/mTOR
  - Phase I (solid tumors)

2015
- Potential regulatory filing for approval
  - FDA meeting
  - Phase I combination
  - Phase 2 (mesothelioma)
  - Phase 2 (recurrent ovarian/breast)

2016

*Proposed clinical plans. Alternatives are being considered.*