RESEARCH AND DEVELOPMENT DAY

JULY 10, 2014

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, 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 ongoing trials, the structure of the Company’s planned or pending clinical trials, additional planned studies, the Company’s rights to develop or commercialize its compounds, the Company’s obligations to make milestone payments and royalties, potential indications for clinical development, 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, that the Company will be unable to start additional studies as 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.
Verastem Research and Development Day 2014 Agenda

• Changing the Way Cancer is Treated by Targeting Cancer Stem Cells
  — Robert Forrester - Verastem President and Chief Executive Officer

• From the Front Line: Mesothelioma Care and the Patient Experience
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• Question and Answer Session
  — Speakers and panelists

• NASDAQ Closing Bell
  — All attendees

• Reception and Networking
  — All attendees
We want to change the way cancer is treated by targeting cancer stem cells
Cancer Stem Cells Drive Disease Progression and Metastasis
What does this mean for patients?
Cancer Stem Cells Predict Poor Survival in Breast Cancer

- **N** = 115 patients
- Standard neoadjuvant chemotherapy of 4 cycles anthracycline & cyclophosphamide + 12 weeks of paclitaxel

*Sakakibara et al, Cancer 2012*
Targeting Cancer Stem Cells for a Durable Clinical Response

**PROBLEM:**

*Current cancer treatments*

Initial tumor $\rightarrow$ Tumor reduction but CSCs survive $\rightarrow$ Recurring tumor

**SOLUTION:**

*CSC drugs + current cancer treatments*

Initial tumor $\rightarrow$ Tumor reduction and elimination of CSCs $\rightarrow$ More durable clinical response
How can we do this?
Path to a Portfolio of Drugs Targeting Cancer Stem Cells

Screening technology
Our Platform Identifies Product Candidates that Kill Cancer Stem Cells

Breast cancer cells in vitro

CD44

Placebo Control

CD44

Paclitaxel

CD44

CSC Inhibitor

Breast cancer cells in vivo

CD24

Gupta et al., Cell 2009
Path to a Portfolio of Drugs Targeting Cancer Stem Cells

Screening technology

Identified critical CSC pathways: FAK and PI3K/mTOR
Identification of the Key Pathways for Cancer Stem Cells

**Focal Adhesion Kinase**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Enzymatic IC₅₀</th>
<th>Cellular EC₅₀</th>
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</thead>
<tbody>
<tr>
<td>VS-4718</td>
<td>42 nM</td>
<td>31 nM</td>
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</table>

**PI3K/mTOR**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Enzymatic IC₅₀</th>
<th>Cellular EC₅₀</th>
</tr>
</thead>
<tbody>
<tr>
<td>VS-5584</td>
<td>3 nM</td>
<td>40 nM</td>
</tr>
</tbody>
</table>

Bar graphs showing Tumor Initiating Capacity (per 10⁶ cells) and Aldefluor-Positive CSCs (% of Control) for VS-4718 and VS-5584.
Screening technology

Identified critical CSC pathways: FAK and PI3K/mTOR

Accelerated FAK program with VS-6063
Acquisition of VS-6063 Accelerated our Existing Program Targeting Cancer Stem Cells Through FAK Inhibition

• Acquired from Pfizer in July 2012
• Good safety profile and initial signs of activity in Phase 1
• VS-6063 preferentially targets cancer stem cells

<table>
<thead>
<tr>
<th>Adverse Events*</th>
<th>Grade</th>
<th>1 (%)</th>
<th>2 (%)</th>
<th>3 (%)</th>
<th>4 (%)</th>
<th>Total</th>
</tr>
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<tbody>
<tr>
<td>Nausea</td>
<td></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>Increased serum bilirubin</td>
<td></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></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></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>
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<td>9 (20)</td>
<td>0</td>
<td>1 (2)</td>
<td>0</td>
<td>10 (22)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td></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></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%)

Jones SF J Clin Oncol 2011 29:1 (suppl; abstr 3002)
Acquisition of VS-6063 – Acceleration to First-in-Class

Phase 1 VS-4718 → Phase 1 GSK & BI → Registration-directed VS-6063
Screening technology

Identified critical CSC pathways: FAK and PI3K/mTOR

Accelerated FAK program with VS-6063

Initiated registration-directed study targeting cancer stem cells in mesothelioma
For patients with malignant pleural mesothelioma

Learn about the COMMAND Study

A patient diagnosed with malignant pleural mesothelioma will want to look into all treatment options. Even while planning initial treatment, it helps to think ahead to what additional options could be part of the treatment plan. Enrolling in the COMMAND Study is an important option to consider.

The COMMAND Study is enrolling patients to study the effects of a drug that is now in development for patients with malignant pleural mesothelioma. Patients may be eligible if they have malignant pleural mesothelioma and meet certain requirements, including:

- They are currently receiving or have recently completed chemotherapy consisting of at least 4 cycles of ALIMTA® (pemetrexed) + cisplatin or carboplatin (platinum)
- They have received pemetrexed + platinum as the first chemotherapy for malignant pleural mesothelioma
- They have stable disease or better following treatment with pemetrexed + platinum

Verastem

Verastem, Inc. is a biopharmaceutical company focused on discovering and developing drugs to treat cancer. We are especially committed to helping improve treatment options for patients with hard-to-treat cancers like mesothelioma. Our approach centers on finding ways to target cancer stem cells, which are an underlying cause of cancer progression and recurrence.

ALIMTA® is a registered trademark of Eli Lilly and Company

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Path to a Portfolio of Drugs Targeting Cancer Stem Cells

**Screening technology**

*Identified critical CSC pathways: FAK and PI3K/mTOR*

**Pfizer**

*Accelerated FAK program with VS-6063*

**COMMAND STUDY**

*Initiated registration-directed study targeting cancer stem cells in mesothelioma*

**Received orphan drug designation status in US and EU**
VS-6063 has Orphan Drug Status in the US and Europe

A recognition of the unmet need in mesothelioma and desire for innovative new treatments for patients
Path to a Portfolio of Drugs Targeting Cancer Stem Cells

Screening technology

Accelerated FAK program with VS-6063

Received orphan drug designation status in US and EU

Identified critical CSC pathways: FAK and PI3K/mTOR

Initiated registration-directed study targeting cancer stem cells in mesothelioma

Portfolio diversification
Portfolio Diversification in our 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

- **FAK**
  - VS-6063 ²
  - VS-5584 ¹
  - VS-4718 ²

- **PI3K/mTOR**
  - VS-6063 ²
  - VS-4718 ²

¹ Pending patent application ² U.S. patent issued
Path to Confidence in the Cancer Stem Cell Targeting Drug VS-6063

Good target inhibition

Reduction of CSCs in patient biopsies

Good safety profile

Combinable with paclitaxel

Initial signs of clinical activity

24 Novel Drugs Targeting Cancer Stem Cells
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UNMET NEEDS OF THE MESOTHELIOMA PATIENT AND FAMILY

Mary Hesdorffer, NP, Executive Director
Mesothelioma Applied Research Foundation
Disease

Challenges
- Healthcare system
- Mesothelioma-specific logistics of treatment
- Urgency in decision-making
- Provider weaknesses
- Insurance and coverage issues
- Predators unique to mesothelioma
  - Who are they and why do they exist?
  - Predator tactics
  - How they hurt mesothelioma patients

What patients must know?

Needs of the mesothelioma patient and family and how we can meet them:
- Easy access to accurate, comprehensive, credible source of information
- Easy access to medical coverage
- Help with travel to treatment centers
- Less urgency and more support with crucial decision-making
- Accurate “translation” of scientific info
- Ability to compare physicians, treatments, side-effects, outcomes
- Peer and professional support
- Understanding of economic and legal interests surrounding mesothelioma
- Offer effective treatments
Mesothelioma is aggressive and rare
- Disease progresses quickly
- Lack of proximity to peer and professional support

Patients are especially vulnerable immediately following diagnosis
- They are afraid, demoralized, and often become depressed

Patients want and need availability of treatments

Lack of funding for mesothelioma research impedes scientifically driven clinical breakthroughs
The United States has one of the most complex healthcare systems globally.

In crisis, families must:

- navigate the system;
- become successful in their pursuit of receiving appropriate state-of-the-art care;
- sort out the pretenders from the experts they encounter along the way
MESOTHELIOMA-SPECIFIC LOGISTICS OF TREATMENT

- Few Experts Available
- Travel Required to See Expert

Patient must leave support network
URGENCY IN DECISION-MAKING

Rush to invasive tests

Decisions made in a highly emotional state

Mandatory time frame to sort through info?
We forget the long road to the expert and the pitfalls along the way.

We fail to ask questions about coverage and if it is of concern to them.

We often do not refer to social worker who can team with us.

We often fail to assess for coping skills or for depression despite there being abbreviated scales to measure these areas.
INSURANCE AND COVERAGE ISSUES

Medicare
- State specific and often inadequate
- Attached to HMOs

Private Insurance
- High copays, inadequate prescription coverage
- Which member of family is the main insured?

Uninsured or Underinsured
- Incredible difficulty obtaining timely and quality care
Diagnosis and prognosis delivered by a professional lacking familiarity with disease.

Due to quick disease progression, patients are rushed to make a treatment decision.

Time constraint of medical provider.

Not enough information provided at initial visit.

Mesothelioma family often falls victim to predators.
WHAT PATIENTS NEED TO KNOW

Must get second opinion

Treatments are different at each center

Data is presented differently at each center

All patients should see medical oncologist AND thoracic surgeon (unless without doubt inoperable)
SUMMARY: NEEDS OF THE MESOTHELIOMA PATIENT

- Information
  - Accurate “translation” of scientific info
  - Ability to compare physicians, treatments, side-effects, outcomes
- Medical coverage
- Travel
- Less urgency during crucial decision-making
- Peer and professional support
- Understanding of economic and legal interests surrounding mesothelioma
- Effective treatments
The Mesothelioma Applied Research Foundation works to meet the needs of mesothelioma patients.

Services include:
- Medical consultations
- Credible and comprehensive information on all potential treatments and centers that provide them
- Unbiased and independent
- Travel grants
- Individual and group support for the patient and his/her family
- Help with decision-making
- Funding of research to spur development of new and effective treatments
THE MESO FOUNDATION

- The Mesothelioma Applied Research Foundation (also known as the Meso Foundation) is the only 501(c)3, nonprofit organization dedicated to eradicating mesothelioma and the suffering caused by it.

- Research
  - $8.2 million in peer-reviewed mesothelioma research funded to date
  - 166 published articles in peer-reviewed journals as a result of this funding

- Education

- Support

- Advocacy
Learn more by visiting our website at curemeso.org
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Surgical Options

- Approximately 20% of patients diagnosed with MPM are eligible for surgery
- Stage of disease and performance status are primary factors
- No approved agents or treatment modality as neo-adjuvant or adjuvant therapy
Raphael Bueno, M.D.

Chief, Thoracic Oncology, Brigham and Women’s Hospital
Professor, Harvard Medical School
Window of Opportunity Study in Surgery-Eligible Patients

- Up to 20 patients receive VS-6063 (400 mg BID) for 12 days prior to surgery
- Measure biomarkers in tumor biopsies
- Evaluate tumor response by PET/CT
- Provide guidance for future studies

MPM that is resectable

Surgery

0 12 Days

Biopsy/Scan

Biopsy/Scan

VS-6063 400mg BID

30 days post-therapy

~42 Days

2nd Line Chemo or Clinical Trial
Phase 3 study of Pemetrexed (Alimta) in Combination with Cisplatin

- Phase 3 randomized, single-blind study: multi center, multinational
- Conducted 1999-2001
- Chemo-naïve patients not eligible for curative surgery: N=446
- Pemetrexed 500mg/m2 and cisplatin 75mg/m2 versus cisplatin alone

### Endpoint Results

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Cisplatin</th>
<th>Pem/Cis</th>
<th>HR</th>
<th>P Value</th>
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</thead>
<tbody>
<tr>
<td>Response rate, %</td>
<td>16.7</td>
<td>41.3</td>
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<td>&lt; .001</td>
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<tr>
<td>Median TTP, months</td>
<td>3.9</td>
<td>5.7</td>
<td>0.68</td>
<td>&lt; .001</td>
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<tr>
<td>Median OS, months</td>
<td>9.3</td>
<td>12.1</td>
<td>0.77</td>
<td>.028</td>
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<tr>
<td>Global QoL score</td>
<td>38</td>
<td>45</td>
<td></td>
<td>.012</td>
</tr>
<tr>
<td>Improved symptom distress</td>
<td>44</td>
<td>51</td>
<td></td>
<td>.009</td>
</tr>
</tbody>
</table>
• Pemetrexed remains the ONLY approved drug for MPM worldwide

• Limited effect of pemetrexed+cisplatin on patient response
The Current Therapy for Mesothelioma Enriches Cancer Stem Cells

Pemetrexed + platinum

Initial tumor → Disease control but CSCs are enriched → Recurring tumor

Recurring tumor
Standard of Care Treatment Increases Cancer Stem Cells

Mesothelioma Cancer Stem Cells

\textit{in vitro}

![Graph showing the effect of different treatments on cancer stem cells](image)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>ALDH-Positive CSCs (% of Control)</th>
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<tbody>
<tr>
<td>DMSO</td>
<td>200</td>
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<tr>
<td>Pemetrexed</td>
<td>600</td>
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<tr>
<td>Cisplatin</td>
<td>800</td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>600</td>
</tr>
<tr>
<td>Vinorelbine</td>
<td>400</td>
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</table>

Mesothelioma Cancer Stem Cells

\textit{in Patient Biopsies}

<table>
<thead>
<tr>
<th>Pre-treatment</th>
<th>Post-treatment with pem/cis</th>
</tr>
</thead>
</table>

Brown = ALDH+ (cancer stem cells)

Treatment of human MPM cell lines with pemetrexed enriches cancer stem cells

\textit{Canino et al. Oncogene 2011}
Tumor Initiating Assay – The Gold Standard for Cancer Stem Functionality

Mesothelioma cells → Aldefluor Assay → Functional Tests

1^0 Tumorsphere assay
Limiting dilutions *in vivo*
Measure tumor volume

1^0 Tumorsphere assay
Spheres /500 cells

<table>
<thead>
<tr>
<th>ALDH(+)</th>
<th>ALDH(-)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 ALDH+ Cells</td>
<td>1/174</td>
</tr>
<tr>
<td>(ALDH+)</td>
<td>(ALDH-)</td>
</tr>
<tr>
<td>35x Increase</td>
<td>p value: $2 \times 10^{-7}$</td>
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</table>
VS-6063 Inhibits Tumor Initiation in Mouse Mesothelioma Models

<table>
<thead>
<tr>
<th>Mesothelioma cells</th>
<th>Drug Treatment</th>
<th>Functional Tests</th>
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<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Tumor Initiation in vivo</td>
</tr>
<tr>
<td></td>
<td>Pemetrexed</td>
<td></td>
</tr>
<tr>
<td></td>
<td>VS-6063</td>
<td></td>
</tr>
<tr>
<td></td>
<td>VS-6063+pemetrexed</td>
<td></td>
</tr>
</tbody>
</table>

Tumor free mice, %

Weeks

- Control
- Pemetrexed
- VS-6063
- VS-6063+pemetrexed

Novel Drugs Targeting Cancer Stem Cells
VS-6063 Inhibits Tumor Initiation/Growth in Mesothelioma Models

<table>
<thead>
<tr>
<th>Mesothelioma cells</th>
<th>Drug Treatment</th>
<th>Functional Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Measure tumor volume</td>
</tr>
<tr>
<td></td>
<td>Pemetrexed</td>
<td></td>
</tr>
<tr>
<td></td>
<td>VS-6063</td>
<td></td>
</tr>
<tr>
<td></td>
<td>VS-6063+pemetrexed</td>
<td></td>
</tr>
</tbody>
</table>

Measure tumor volume

![Graph showing tumor volume comparisons between control, pemetrexed, VS-6063, and VS-6063+pemetrexed.]
Oral Administration of VS-6063 Targets Cancer Stem Cells in Mesothelioma Tumors Grown in Mouse Lungs

Control

VS-6063

50 mg/kg, po BID x 2 wks

CSCs (ALDH+)

DAPI

CSCs (% of total)

Control

VS-6063

* p<0.05
COMMAND: Targeting Cancer Stem Cells for a More Durable Clinical Response

**PROBLEM:**

Current cancer treatments

Initial tumor ➔ Tumor reduction but CSCs survive ➔ Recurring tumor

**SOLUTION:**

Pemetrexed + platinum

Initial tumor ➔ Disease control but CSCs are enriched

VS-6063 ➔ More durable clinical response
COMMAND: Targeting Cancer Stem Cells in the Switch Maintenance Setting

80%
Surgery
4-6cyc Pem/Cis
Treatment Holiday
2nd Line Chemo or Clinical Trial

80%
20%

International Mesothelioma Steering Committee

Anna Nowak, Australia
Dean Fennell, United Kingdom
Hedy Kindler, USA
Larry Schwartz, USA
Lee Krug, USA
Paul Baas, Netherlands
Richard Gralla, USA
Takashi Nakano, Japan
**COMMAND: A Registration-Directed Study of VS-6063 to Maintain Tumor Control in Mesothelioma**

**Goal**
- To support approval of VS-6063 on a global basis

**Patients (N=\sim 350-400)**
- Measurable or Evaluable Disease per RECIST v1.1
- One prior regimen (≥4 cycles) pem/cis or pem/carbo with documented ongoing response (PR or SD)

**Design**
- Multinational, randomized, double blind, placebo controlled
- Stratification based on merlin status with an adaptive enrichment design
- No cross-over allowed
- Conducted and monitored as a pivotal study

<table>
<thead>
<tr>
<th>Primary Objectives</th>
<th>Secondary Objectives</th>
<th>Exploratory Objectives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Survival (OS)</td>
<td>Quality of Life (QoL) (LCSS-Meso)</td>
<td>Time to new lesion</td>
</tr>
<tr>
<td>Progression Free Survival (PFS)</td>
<td>Objective Response Rate (ORR)</td>
<td>Relationship of VS-6063 PK and outcome</td>
</tr>
<tr>
<td></td>
<td>Safety and tolerability</td>
<td>Population PK of VS-6063</td>
</tr>
</tbody>
</table>
COMMAND: A Registration-Directed Study of VS-6063 to Maintain Tumor Control in Mesothelioma

- **Surgery**
  - 80%
  - 20%

- **4-6cyc Pem/Cis**
  - COMMAND Study

- **2nd Line Chemo or Clinical Trial**

**Merlin Low**
- Placebo BID
- VS-6063 400mg BID

**Merlin High**
- Placebo BID
- VS-6063 400mg BID

**Key Endpoints**
- PFS
- OS
- QoL

- ≥ 4 cycles Platnum + pemetrexed
- PR/SD 350-400
- CT Scan

**2nd Line Chemo or Clinical Trial**
COMMAND: A Simultaneous, Multinational Development Strategy

- 34 sites open and enrolling
- 24 month accrual anticipated
There is a Significant Desire for New Treatments in Mesothelioma

ACTIVITIES

New study, harnessing ground-breaking science, offers hope to British mesothelioma patients

• Feb 24th - Interviews with UK TV, radio and newspapers discussing the current unmet needs in mesothelioma and new clinical trials underway in the UK

Saatchi Bill: enabling medical innovation for all patients

• Feb 24th - Professor Fennell and Mavis Nye spoke at a public consultation at UK Parliament in the House of Lords

• Feb 24th - University of Leicester issued a press release announcing Prof Fennell’s involvement

RESULTS

152 individual news articles have been generated across the UK with a reach in excess of 29.5 million

• 5 interviews on prime time UK regional news channels – ITV and BBC

• 141 radio interviews including Sky News Radio, BBC Three Counties and Imagine FM

• 2 items of print coverage

• 8 items of online coverage

• Advertorial in the UK national newspaper The Independent
COMMAND Permits Patient Enrichment While Maintaining Power for Potential Registration Submission

- Interim analysis will be conducted after 50% (N=128) of expected PFS events occur

- The trial will adapt to enroll only the biomarker-selected population if:
  - *Promising results are observed among the subpopulation*
    - AND
  - *Promising results are NOT observed among the full sample*

- If the trial is adapted:
  - *The required number of patients to maintain 90% power will be re-estimated*

- At the primary analysis:
  - *PFS, QOL and tolerability data will be assessed for potential to file as basis for accelerated approval (follow OS for full approval)*
There is No Standard Second-line Therapy for Patients

- Patients requiring second-line therapy may be referred to clinical trials
- Median progression free survival in second line is only 6 weeks

4-6cyc Pem/Cis → Treatment Holiday → 2nd Line Chemo or Clinical Trial

Surgery

80%

20%
Evaluating a Potential Treatment for the Relapsed/Refractory Mesothelioma Patient Population (Patients not eligible for COMMAND)

Rationale

- Strong pre-clinical data demonstrating synergy of VS-6063 and VS-5584 in pre-clinical mesothelioma models
- GSK FAKi demonstrated SD in patients with relapsed disease
- PI3k/mTOR inhibitor GDC-0980 demonstrated ORR in patients with relapsed disease

Goals

- Safety of combination
- Biomarker analysis
- Assess potential activity in mesothelioma

Enrollment (N=40)

Archival/Biopsy

VS-6063 400mg BID + VS-5584 Dose Escalation

Biopsy

Expansion Cohort

VS-6063 (400mg BID) + VS-5584 (RP2D)
Developing Potential Treatment Options Throughout the Patient Journey

- Surgery
  - 80%
  - 20%

Window of Opportunity

- 4-6cyc Pem/Cis
- Treatment Holiday

Command

- 2nd Line Chemo or Clinical Trial
- VS-6063+VS-5584
  - Relapsed or Refractory

We want to maximize the potential treatment options for patients with mesothelioma

Ongoing

Planned
Verastem Research and Development Day 2014 Agenda

• Changing the Way Cancer is Treated by Targeting Cancer Stem Cells
  – Robert Forrester - Verastem President and Chief Executive Officer

• From the Front Line: Mesothelioma Care and the Patient Experience
  – Mary Hesdorffer, N.P. – Executive Director, Mesothelioma Applied Research Foundation

• Targeting Cancer Stem Cells in Multiple Clinical Settings for the Treatment of Mesothelioma
  – Raphael Bueno, M.D. – Chief, Thoracic Oncology, Brigham and Women’s Hospital
  – Professor Dean Fennell, Ph.D., FRCP – Chair, Thoracic Oncology, University of Leicester
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  – Joanna Horobin, M.B., Ch.B. – Verastem Chief Medical Officer

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• Question and Answer Session
  – Speakers and panelists

• NASDAQ Closing Bell
  – All attendees

• Reception and Networking
  – All attendees

62 Novel Drugs Targeting Cancer Stem Cells
Cancer Stem Cells Drive Ovarian Cancer Progression and Recurrence

Presence of CSCs in ovarian cancer correlates with poor PFS & OS
Silva et al., Cancer Res 2011

VS-6063 re-sensitized drug-resistant ovarian models to paclitaxel
Kang et al., JNCI 2013

High tumor FAK and pFAK expression correlate with poor survival
Sood et al., J Clin Invest 2010

Ovarian Cancer Stem Cells Increase from Chemotherapy

Cancer stem cells (% of control)

Control  Cisplatin  Paclitaxel

0  100  200  300  400
Ovarian Cancer is the Most Lethal Gynecological Malignancy

• >225,000 new diagnoses per year globally

• The majority of patients present late with metastatic disease (stage III/IV)

• Standard of care treatment is cytoreductive surgery to remove all visible disease – usually followed by adjuvant chemotherapy with carboplatin and paclitaxel/docetaxel for at least 6 cycles

• A relapse within 6 months after platinum containing therapy is categorized as platinum-resistant

• At first relapse ~25% of patients have platinum resistant disease
Platinum Resistant Ovarian Cancer

• Combining chemotherapy adds toxicity without improving efficacy
  – Median PFS generally less than 6 months
  – Median OS approximately 12 months

• Combination with novel agents under evaluation
  – Bevacizumab with chemotherapy recently shown to improve PFS but did not show a statistically significant effect on OS (AURELIA study)

• Sequential use of single chemotherapeutic agents recommended
  – Most active single agents are paclitaxel, pegylated liposomal doxorubicin and topotecan

• Chemotherapy treatment increases cancer stem cells
Combining VS-6063 with Paclitaxel for Patients with Ovarian Cancer

Goals

- Target cancer stem cells concurrently with chemotherapy
- Evaluate feasibility of combination of VS-6063 with weekly paclitaxel - paves the way to several other indications where paclitaxel is standard of care

Objectives

- Evaluate safety and tolerability of combination of VS-6063 with weekly paclitaxel
- Measure pharmacokinetics of paclitaxel in combination with VS-6063
- Confirm pharmacodynamic effect of VS-6063 on pFAK target

Protocol permits single agent VS-6063 “maintenance” following paclitaxel

Phase 1

*Completed: 200mg, 400mg BID*

\[N=6\]

VS-6063 (dose escalation BID) + paclitaxel (80mg/m²/week)

Phase 1b

*Completed Recruitment*

\[N=16\]

VS-6063 (400mg BID) + paclitaxel (80mg/m²/week)
80% of Patients on Study Have Platinum Resistant Ovarian Cancer

<table>
<thead>
<tr>
<th></th>
<th>Phase I</th>
<th>Phase Ib</th>
<th>Phase Ib</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>200 mg defactinib BID + 80 mg/m² paclitaxel weekly</td>
<td>400 mg defactinib BID + 80 mg/m² paclitaxel weekly</td>
<td>400 mg defactinib BID + 80 mg/m² paclitaxel weekly</td>
</tr>
<tr>
<td>Patients, n</td>
<td>3</td>
<td>3</td>
<td>16</td>
</tr>
<tr>
<td>Median age, years (range)</td>
<td>59.0 (53-69)</td>
<td>74.0 (65-75)</td>
<td>67.5 (26-81)</td>
</tr>
<tr>
<td>Median time since initial diagnosis, years</td>
<td>2.00 (1.2-2-4)</td>
<td>3.24 (3.1-5.0)</td>
<td>2.32 (0.6-13.4)</td>
</tr>
<tr>
<td>Histology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serous</td>
<td>1 (33.3%)</td>
<td>3 (100%)</td>
<td>12 (75.0%)</td>
</tr>
<tr>
<td>Endometrioid</td>
<td>1 (33.3%)</td>
<td>0 (00.0%)</td>
<td>0 (00.0%)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (33.3%)</td>
<td>0 (00.0%)</td>
<td>4 (25.0%)</td>
</tr>
<tr>
<td>ECOG PFS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1 (33.3%)</td>
<td>2 (66.7%)</td>
<td>11 (68.8%)</td>
</tr>
<tr>
<td>1</td>
<td>2 (66.7%)</td>
<td>1 (33.3%)</td>
<td>5 (31.3%)</td>
</tr>
<tr>
<td>Prior chemotherapy regimens</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0 (00.0%)</td>
<td>0 (00.0%)</td>
<td>5 (31.3%)</td>
</tr>
<tr>
<td>2</td>
<td>0 (00.0%)</td>
<td>0 (00.0%)</td>
<td>4 (25.0%)</td>
</tr>
<tr>
<td>3</td>
<td>3 (100%)</td>
<td>0 (00.0%)</td>
<td>4 (25.0%)</td>
</tr>
<tr>
<td>≥4</td>
<td>0 (00.0%)</td>
<td>3 (100%)</td>
<td>3 (18.8%)</td>
</tr>
<tr>
<td>Platinum Resistant</td>
<td>1 (33.3%)</td>
<td>3 (100%)</td>
<td>13 (81.3%)</td>
</tr>
</tbody>
</table>

*Unlocked, in progress data, as presented at ASCO 2014
Combination of VS-6063 and Weekly Paclitaxel Does not Impact 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)
Combination of VS-6063 and Weekly Paclitaxel Does not Worsen the Well-Known Side Effect Profile of Paclitaxel Alone

<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></td>
<td>200 mg defactinib BID + 80 mg/m² paclitaxel weekly (n=3)</td>
<td>400 mg defactinib BID + 80 mg/m² paclitaxel weekly (n=16)</td>
<td></td>
</tr>
<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>

*Unlocked, in progress data, as presented at ASCO 2014

Most Frequently Reported Adverse Events ≥20%
### Literature: Weekly Paclitaxel Alone Results in Limited Clinical Activity

#### Efficacy

<table>
<thead>
<tr>
<th></th>
<th>Saracatinib (N=69)</th>
<th>Placebo (N=34)</th>
<th>HR (95% CI; P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median PFS (months)</td>
<td>3.9</td>
<td>5.4</td>
<td>1.14 (0.74, 1.77; p=0.55)</td>
</tr>
<tr>
<td>PFS at 6 months (%)*</td>
<td>29%</td>
<td>38%</td>
<td>-9% (-28%, 12%; p=0.28)</td>
</tr>
<tr>
<td>Median OS (months)</td>
<td>12.7</td>
<td>12.8</td>
<td>1.37 (0.70, 2.71; p=0.36)</td>
</tr>
<tr>
<td>Median TTP (months)</td>
<td>4.0</td>
<td>5.4</td>
<td>1.13 (0.72, 1.75; p=0.60)</td>
</tr>
<tr>
<td>Response n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CR</td>
<td>0</td>
<td>1 (2.9%)</td>
<td></td>
</tr>
<tr>
<td>PR</td>
<td>8 (11.6%)</td>
<td>4 (11.8%)</td>
<td></td>
</tr>
<tr>
<td>SD</td>
<td>13 (18.8%)</td>
<td>3 (8.8%)</td>
<td></td>
</tr>
<tr>
<td>Duration of response (months)</td>
<td>5.6</td>
<td>4.5</td>
<td></td>
</tr>
</tbody>
</table>

*Best Response of at least SD on weekly paclitaxel: 24%

1 patient had a complete response

Results consistent with Phase 3 AURELIA study

*(Pujade-Lauraine et al, J Clin Oncol 32, 2014)*
Initial Data from the Combination Study of VS-6063 and Paclitaxel are Encouraging – 8 Patients Still on Study

Best Response of at least SD: 64%

Objective Response
- 3 partial responses
- 2 complete responses

Objective Response or SD ≥ 6 months
- Overall 9/22 (41%)
- 8 patients still on study

*Unlocked, in-progress data as of 30 Jun 2014
Patient 03-202: Platinum Resistant Disease with 5 Prior Treatments

- Presented at screening with stage IV platinum-resistant serous ovarian cancer
- Had stable disease on combination treatment and went on VS-6063 monotherapy after 4.5 months
- While on VS-6063 monotherapy the two remaining lesions disappeared at 11.8 months
- Continues on study and is tolerating VS-6063 well

**Duration of Treatment (months)**

- VS-6063 + Paclitaxel
- Pemetrexed
- Measles vaccine
- Cisplatin/gem
- Carbo/cytoxan/taxol
- Carbo/taxol (adjuv)

**Graphs:**
- SD to CR
- VS-6063 Monotherapy
- CA-125 (U/mL)

*Unlocked, in-progress data as of 30 Jun 2014*
Key Takeaways from the Ongoing Combination Study in Ovarian Cancer

• VS-6063 plus weekly paclitaxel is a combinable regimen

• Encouraging signs of clinical activity observed
  – 64% Best Response (SD+)
  – 5 Objective Responses (3PR and 2CR) to date

• Data supportive of further clinical development
FAK Activity is Correlated with Poor Prognosis in Ovarian Cancer

Mean survival (high/low) 1.7 vs 3.2yrs

Low pFAK\(^{Y397}\)
(n = 37)

High pFAK\(^{Y397}\)
(n = 39)

\(P < 0.001\)
Paired tumor biopsies were obtained in five patients following 10 days of VS-6063 administration (400 mg BID)
VS-6063 Reduces Cancer Stem Cells in Patient Tumor Biopsies Within 10 Days

After 10 days of VS-6063 single agent treatment: cancer stem cells decreased by 46%

Paired tumor biopsies were obtained in two patients following 10 days of VS-6063 administration (400 mg BID)
VS-6063: “Window of Opportunity” Study in Ovarian Cancer

Goal
• Measure cancer stem cell biomarkers

Patients (N~20)
• Newly diagnosed stage IIIC/IV disease undergoing primary surgery
• Routinely administered 3 cycles of chemo prior to surgery

Design
• Time 0: Diagnostic laparoscopy to confirm staging yields baseline tissue
• Weeks 1-9: Administer 3 cycles of carbo tax (paclitaxel or docetaxel)
• Weeks 10-11: Post chemo recovery period
• Weeks 12-14: 14 days of VS-6063 400mg BID
• Week 14: Surgery

Stage IIIC/IV

3 cycles of carbo/tax

Week 1-9

Recovery

Week 10-11

VS-6063

Week 12-14

Surgery

Measure biomarkers
VS-6063: Phase 2 Study in Platinum-Resistant Ovarian Cancer

Goal
• POC to provide baseline for potential registration-directed study

Patients (N=~100)
• Platinum resistant; ≤2 prior chemotherapy regimens
• Measurable or Evaluable Disease per RECIST v1.1

Design
• Randomized, placebo-controlled, weekly paclitaxel 80mg/kg/m2 (D1,8,15 of 28 day cycle) +/- defactinib 400mg BID
• Stratification – treatment free interval <3 months vs. 3-6 months; prior bevacizumab
• No crossover allowed
• Permit single agent VS-6063 “maintenance” following paclitaxel discontinuation for toxicity

Key Endpoints

<table>
<thead>
<tr>
<th>Primary Objective</th>
<th>Secondary Objectives</th>
<th>Exploratory Objective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progression Free Survival (PFS)</td>
<td>Objective Response Rate (ORR)</td>
<td>Overall Survival (OS)</td>
</tr>
<tr>
<td></td>
<td>QOL</td>
<td></td>
</tr>
</tbody>
</table>

Novel Drugs Targeting Cancer Stem Cells
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  - Speakers and panelists

- NASDAQ Closing Bell
  - All attendees

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  - All attendees
Cancer Stem Cells Predict Poor Survival in Breast Cancer

- N = 115 patients
- Standard neoadjuvant chemotherapy of 4 cycles anthracycline & cyclophosphamide + 12 weeks of paclitaxel

Sakakibara et al, Cancer 2012
Cancer Stem Cells Emerge In Response to Chemotherapy

Triple Negative Breast Cancer

ER\(^+\) Breast Cancer

Li et al., JNCI 2008

Alamgeer et al., Breast Cancer Research 2014

Baseline

Docetaxel

Novel Drugs Targeting Cancer Stem Cells
VS-6063 Reduces CSCs & Tumor-Initiating Capability In Xenograft Tumor Model in Contrast to Paclitaxel

- Mice bearing MDA-MB-231 tumors were treated with 50 mg/kg VS-6063 po BID or vehicle control for 25 days and CSC endpoints were assessed.
- Tumor initiating capability in 2° mice was decreased by VS-6063, but increased by paclitaxel treatment.
Triple Negative Breast Cancer (TNBC)

• Defined primarily by what it lacks:
  – Estrogen (ER) and progesterone (PR) receptors
  – Overexpression/amplification of the HER2 gene

• 15% to 20% of breast cancers (US) but a disproportionate share of morbidity and mortality
  – Highly aggressive
  – Increased incidence in younger women and women of African origin
  – Lack of effective targeted therapies

• Neoadjuvant chemotherapy (AC followed by taxane) is widely used prior to surgery for primary disease
  – 30 – 40% pCR rate (depending on study)
**VS-6063: Neo-adjuvant Study in Early Stage TNBC**

**Goals**
- Determine effect of VS-6063 on cancer stem cells in TNBC

**Patients (N=\sim 100)**
- Newly diagnosed, locally advanced triple negative breast cancer

**Design:**
Open Label, Randomized, Multi Center

**Primary Endpoints**
- Cancer stem cell “Response” rate (CSCR)
- Safety and tolerability

**Exploratory Endpoint**
- Event Free Survival (EFS)

- Screen/Enroll Patients with Stage I-IIla TNBC
- Biopsy for CSC markers and MRI
- Treat with AC x 4
- Biopsy for CSC marker and MRI
- Randomize AC non-responders
- Paclitaxel+VS-6063 (4 cycles)
- Paclitaxel (4 cycles)
- Surgery CSC markers Response rate
### Clinical Development of VS-6063

<table>
<thead>
<tr>
<th>VS-6063</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Registration-Directed</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mesothelioma</strong></td>
<td>COMMAND – Switch maintenance following front-line therapy</td>
<td>Window of opportunity</td>
<td>With VS-5584 in relapsed</td>
</tr>
<tr>
<td><strong>Lung</strong></td>
<td>KRASmt NSCLC</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ovarian</strong></td>
<td>In combo with paclitaxel</td>
<td></td>
<td>Window of opportunity</td>
</tr>
<tr>
<td><strong>Ovarian</strong></td>
<td></td>
<td></td>
<td>Combo with paclitaxel for platinum-resistant</td>
</tr>
<tr>
<td><strong>Breast</strong></td>
<td></td>
<td></td>
<td>Neo-adjuvant in combination with paclitaxel</td>
</tr>
</tbody>
</table>

- **Ongoing**
- **Planned**
Path to Confidence in the Cancer Stem Cell Targeting Drug VS-6063

**Reduction of CSCs in patient biopsies**

**Good target inhibition**

**Good safety profile**

**Combinable with paclitaxel**

**Initial signs of clinical activity**

- **Good target inhibition**
- **Reduction of CSCs in patient biopsies**
- **Good safety profile**
- **Combinable with paclitaxel**
- **Initial signs of clinical activity**
Pursuing the Potential of Targeting Cancer Stem Cells for Patients Worldwide

Mesothelioma

- Neo
- Relapsed/Refractory
- Maintenance
- ~59,000

Breast

- Neo-adjuvant TNBC
- ~1,400,000

Ovarian

- Platinum Resistant
- ~225,000

Lung

- KRas p16/53 mt
- ~1,600,000

Worldwide Incidence
We want to change the way cancer is treated by targeting cancer stem cells
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  – Professor Dean Fennell, Ph.D., FRCP – Chair, Thoracic Oncology, University of Leicester
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  – Joanna Horobin, M.B., Ch.B. – Verastem Chief Medical Officer

• Targeting Cancer Stem Cells with Combination Treatment in Ovarian Cancer
  – Manish Patel, M.D. – Associate Director, Florida Cancer Specialists/Sarah Cannon Research Institute
  – Joanna Horobin, M.B., Ch.B. – Verastem Chief Medical Officer

• Targeting Cancer Stem Cells Through the Neo-Adjuvant Treatment of Breast Cancer
  – José Baselga, M.D., Ph.D. – Physician in Chief, Memorial Sloan Kettering Cancer Center
  – Jonathan Pachter, Ph.D. - Verastem Head of Research
  – Joanna Horobin, M.B., Ch.B. – Verastem Chief Medical Officer

• Question and Answer Session
  – Speakers and panelists

• NASDAQ Closing Bell
  – All attendees

• Reception and Networking
  – All attendees