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 on-going 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**
  - *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*
  - *Jonathan Pachter, Ph.D. - Verastem Head of Research*
  - *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*
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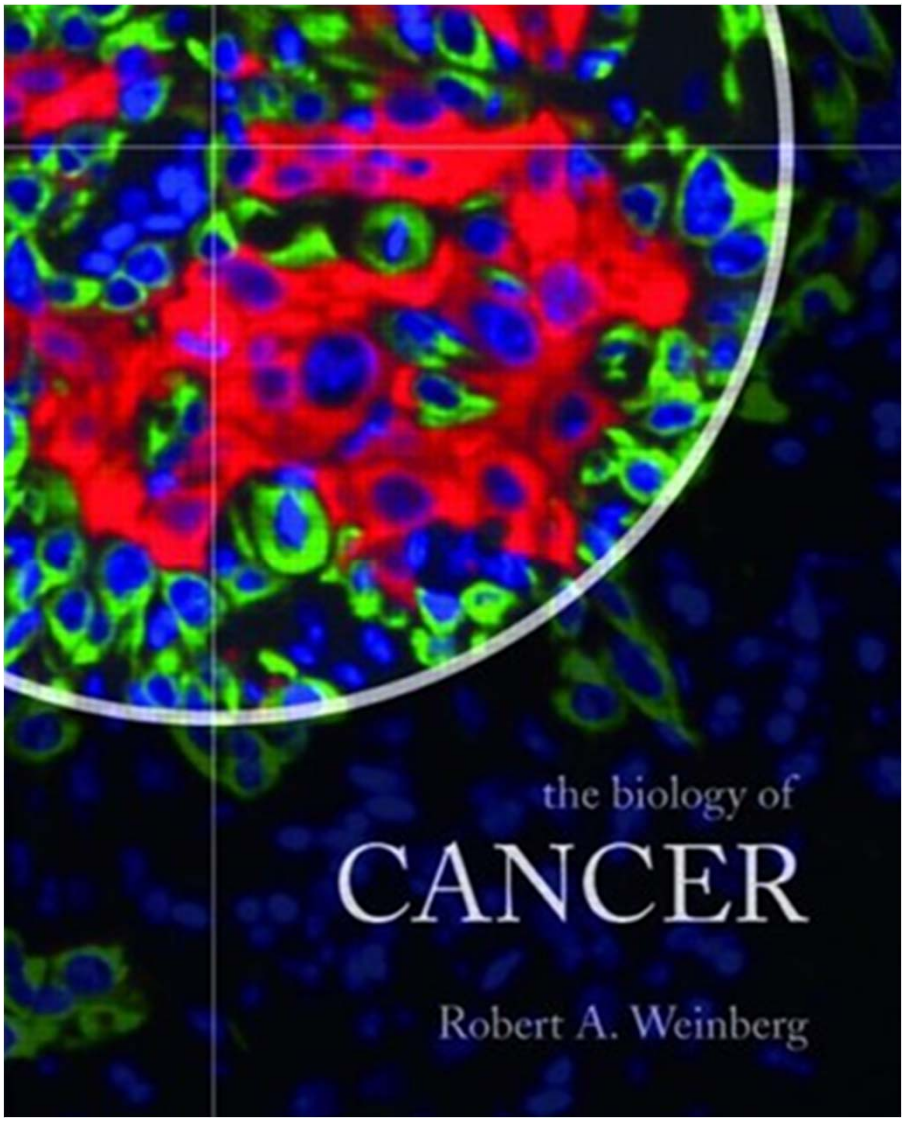
- **Question and Answer Session**
  - *Speakers and panelists*
- **NASDAQ Closing Bell**
  - *All attendees*
- **Reception and Networking**
  - *All attendees*


END
SPEED
LIMIT

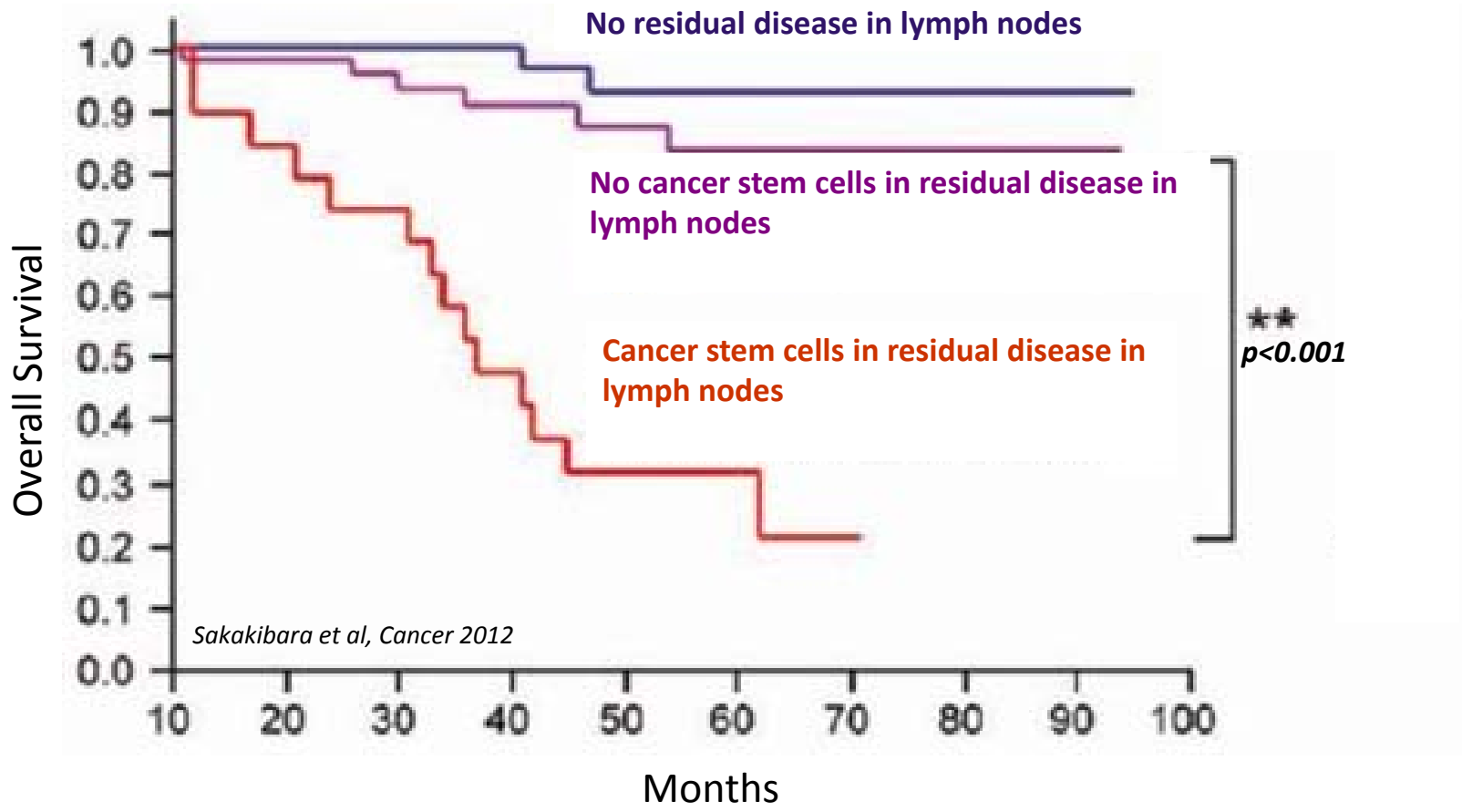

We want to change the way cancer is treated by targeting cancer stem cells

Cancer Stem Cells Drive Disease Progression and Metastasis




What does this mean for patients?

Cancer Stem Cells Predict Poor Survival in Breast Cancer

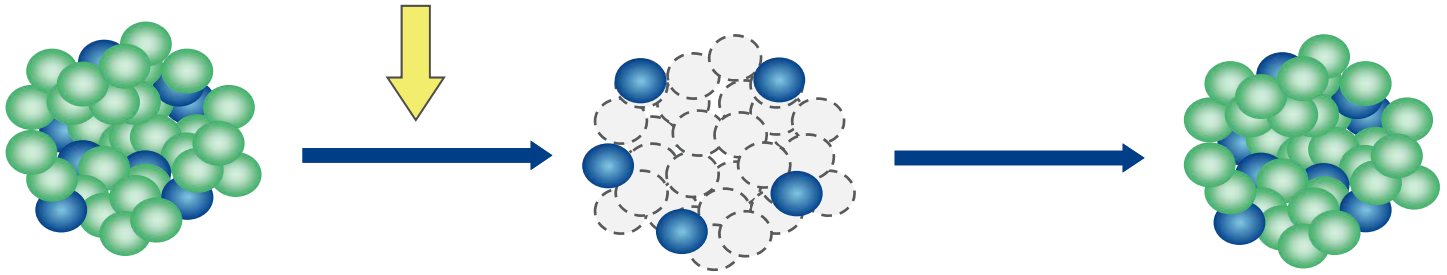


- N = 115 patients
- Standard neoadjuvant chemotherapy of 4 cycles anthracycline & cyclophosphamide + 12 weeks of paclitaxel

Targeting Cancer Stem Cells for a Durable Clinical Response

PROBLEM:

Current cancer treatments



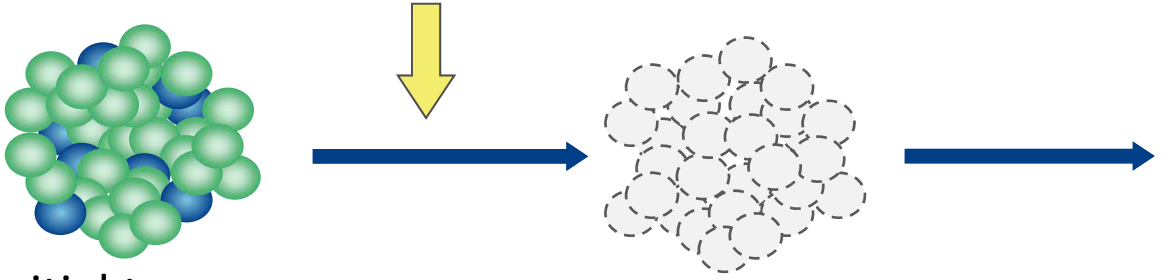
Initial tumor

Tumor reduction but CSCs survive

Recurring tumor

SOLUTION :

CSC drugs + current cancer treatments



Initial tumor

Tumor reduction and elimination of CSCs

More durable clinical response

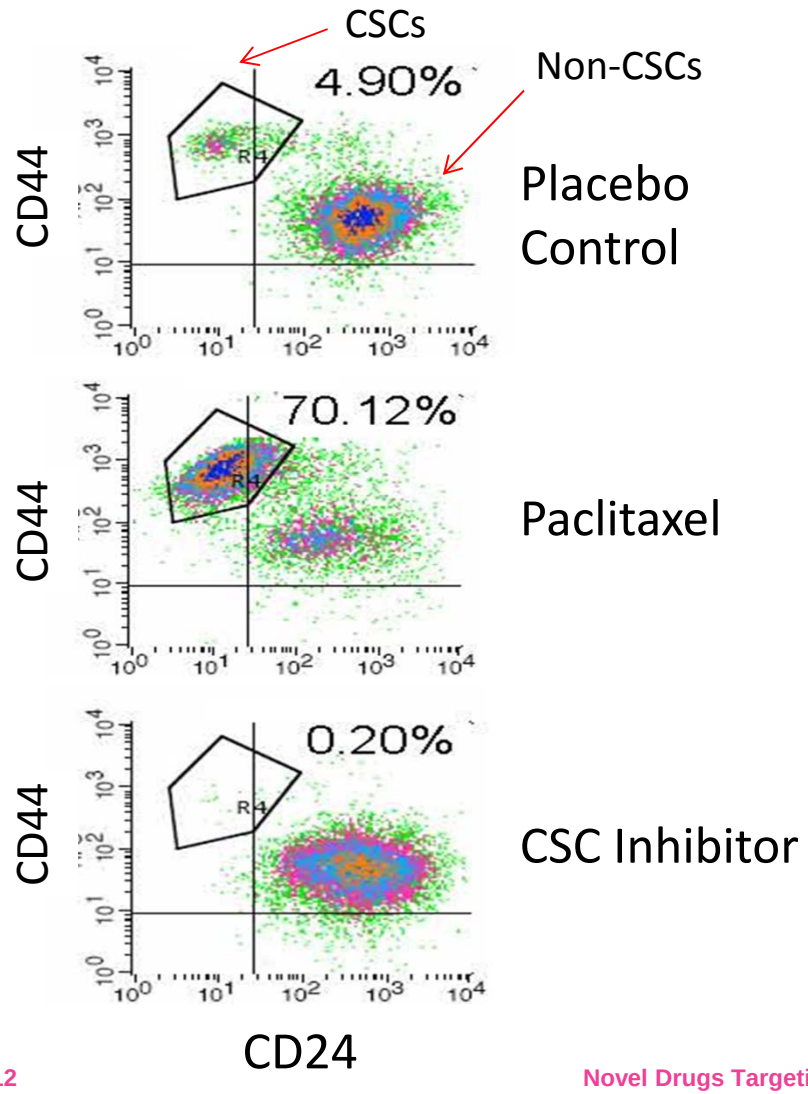

How can we do this?

Path to a Portfolio of Drugs Targeting Cancer Stem Cells

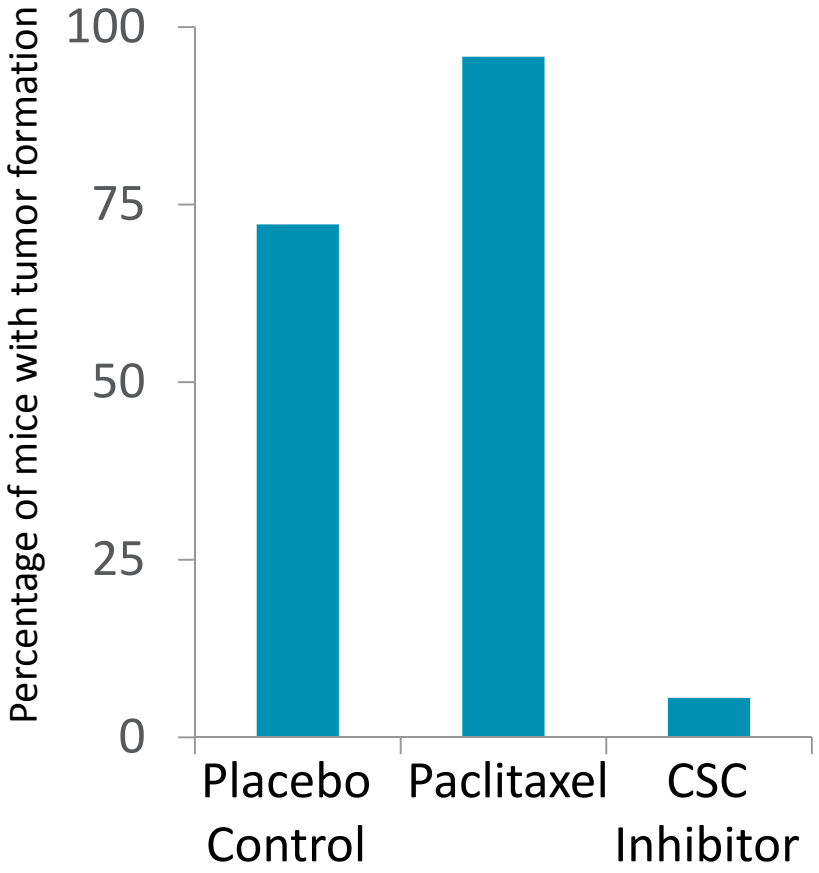
Screening technology

Our Platform Identifies Product Candidates that Kill Cancer Stem Cells

Breast cancer cells in vitro



Breast cancer cells in vivo

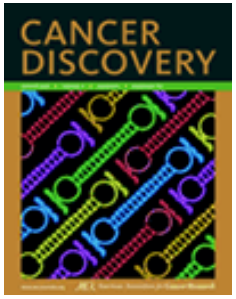


Gupta et al., Cell 2009

Verastem

Path to a Portfolio of Drugs Targeting Cancer Stem Cells

Screening technology



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

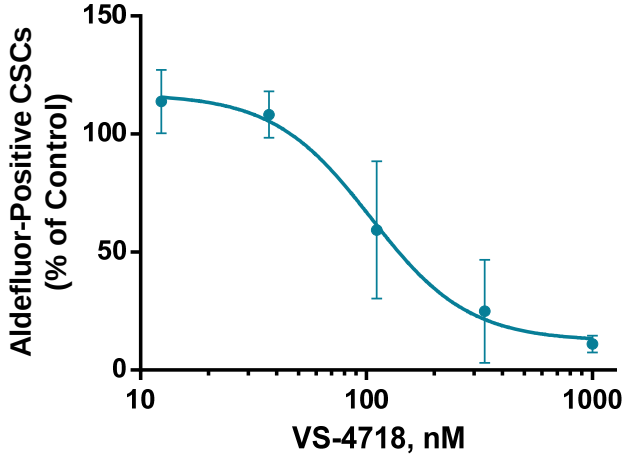
Identification of the Key Pathways for Cancer Stem Cells

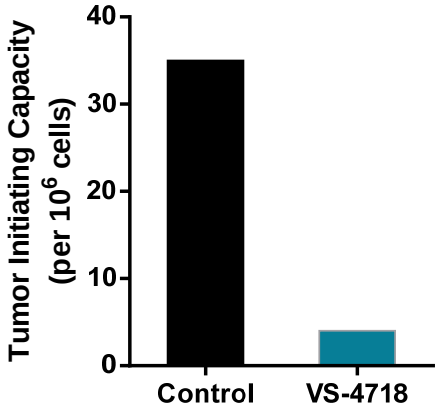
Focal Adhesion Kinase

VS-4718

FAK Enzymatic IC_{50} = 42 nM

FAK Cellular EC_{50} = 31 nM



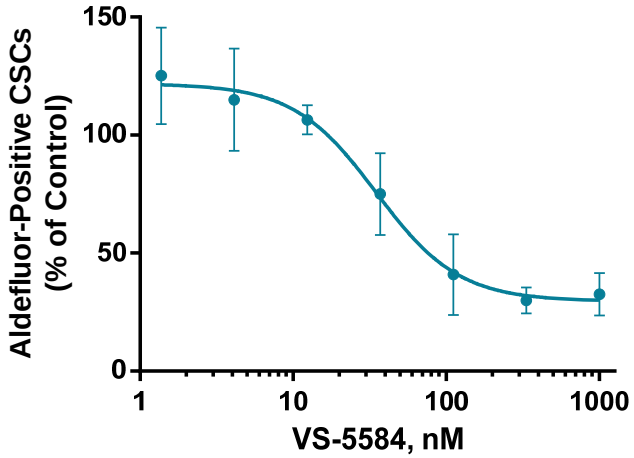


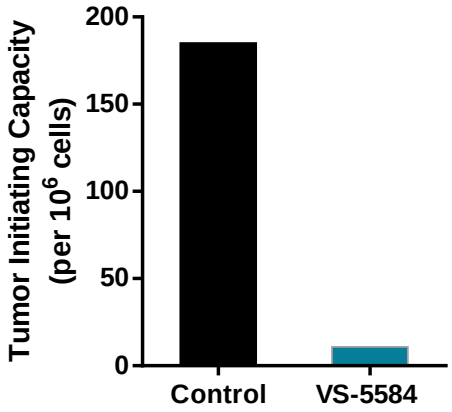
PI3K/mTOR

VS-5584

PI3K/mTOR Enzymatic IC_{50} ~3 nM

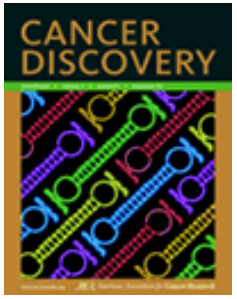
PI3K/mTOR Cellular EC_{50} ~ 40 nM





Path to a Portfolio of Drugs Targeting Cancer Stem Cells

Screening technology



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

***Accelerated** FAK*
*program **with VS-6063***

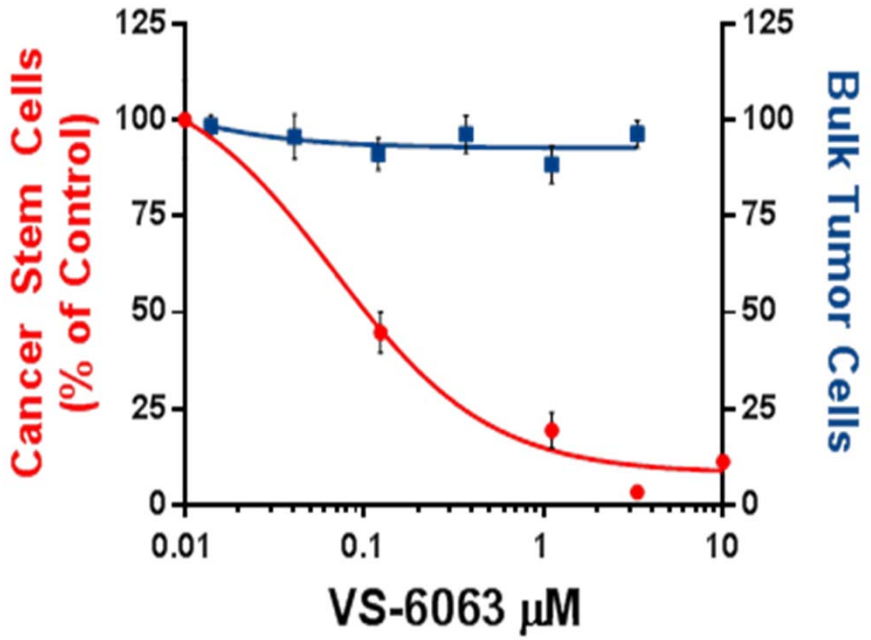
Acquisition of VS-6063 Accelerated our Existing Program Targeting Cancer Stem Cells Through FAK Inhibition

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

	Grade				
	1	2	3	4	Total
Adverse Events*	N (%)	N (%)	N (%)	N (%)	N (%)
Nausea	14 (30)	3 (7)	0	0	17 (37)
Increased serum bilirubin	6 (13)	9 (20)	2 (4)	0	17 (37)
Fatigue	8 (17)	6 (13)	1 (2)	0	15 (33)
Vomiting	10 (22)	3 (7)	0	0	13 (28)
Headache	9 (20)	0	1 (2)	0	10 (22)
Diarrhea	8 (17)	2 (4)	0	0	10 (22)
Decreased appetite	8 (17)	1 (2)	0	0	9 (20)

*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

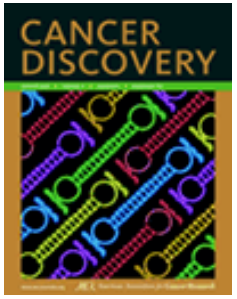
Phase 1
VS-4718

Phase 1
GSK & BI

Registration-directed
VS-6063

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***

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:

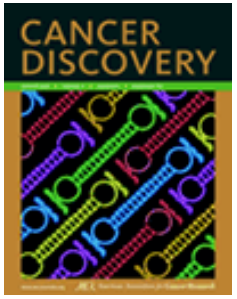
- They are currently receiving or have recently completed chemotherapy consisting of at least 4 cycles of ALIMTA® (pemetrexed) + cisplatin or carboplatin (platinum)
- They have received pemetrexed + platinum as the first chemotherapy for malignant pleural mesothelioma
- They have stable disease or better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

Path to a Portfolio of Drugs Targeting Cancer Stem Cells

Screening technology



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Pfizer

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*Received **orphan drug designation** status in US and EU*

COMMAND STUDY

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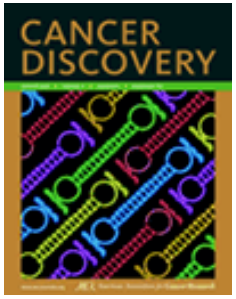
VS-6063 has Orphan Drug Status in the US and Europe

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



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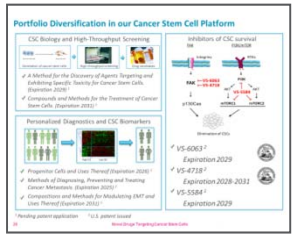
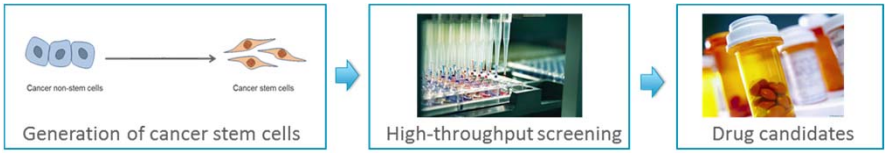


*Portfolio **diversification***

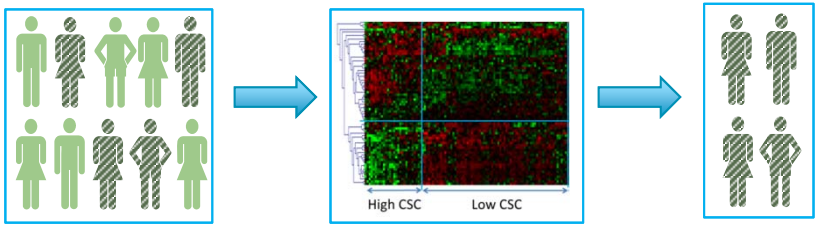
Portfolio Diversification in our Cancer Stem Cell Platform

CSC Biology and High-Throughput Screening



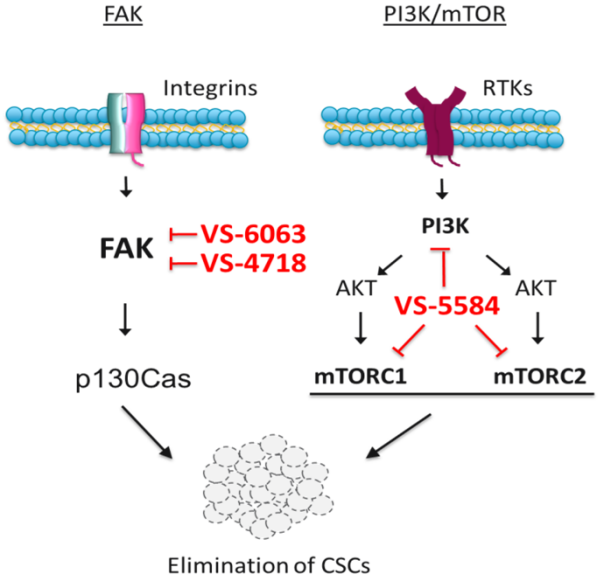
- ✓ *A Method for the Discovery of Agents Targeting and Exhibiting Specific Toxicity for Cancer Stem Cells. (Expiration 2029)* [1]
- ✓ *Compounds and Methods for the Treatment of Cancer Stem Cells. (Expiration 2031)* [1]

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]

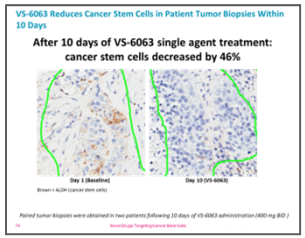
Inhibitors of CSC survival



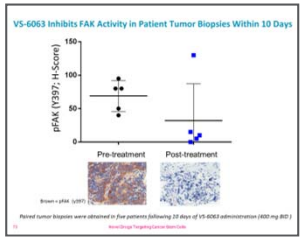
- ✓ *VS-6063* [2]
  Expiration 2029
- ✓ *VS-4718* [2]
  Expiration 2028-2031
- ✓ *VS-5584* [1]
  Expiration 2029

[1] *Pending patent application* [2] *U.S. patent issued*

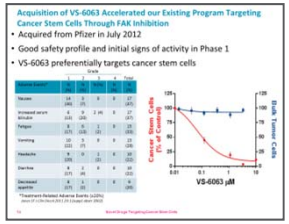
Path to Confidence in the Cancer Stem Cell Targeting Drug VS-6063



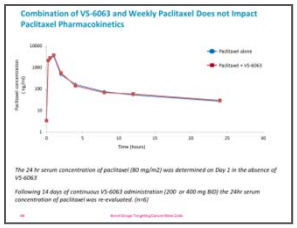
Reduction of CSCs *in patient biopsies*



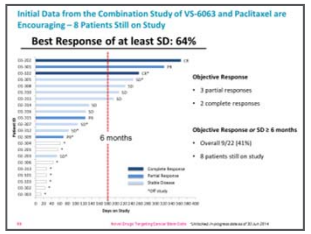
Good ***target inhibition***



Good safety profile



Combinable *with paclitaxel*



Initial signs of ***clinical activity***

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Mesothelioma Applied® Research Foundation

research - education - support - advocacy

UNMET NEEDS OF THE MESOTHELIOMA PATIENT AND FAMILY

Mary Hesdorffer, NP, Executive Director

Mesothelioma Applied Research Foundation

OVERVIEW

- 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

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THE DISEASE

- 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

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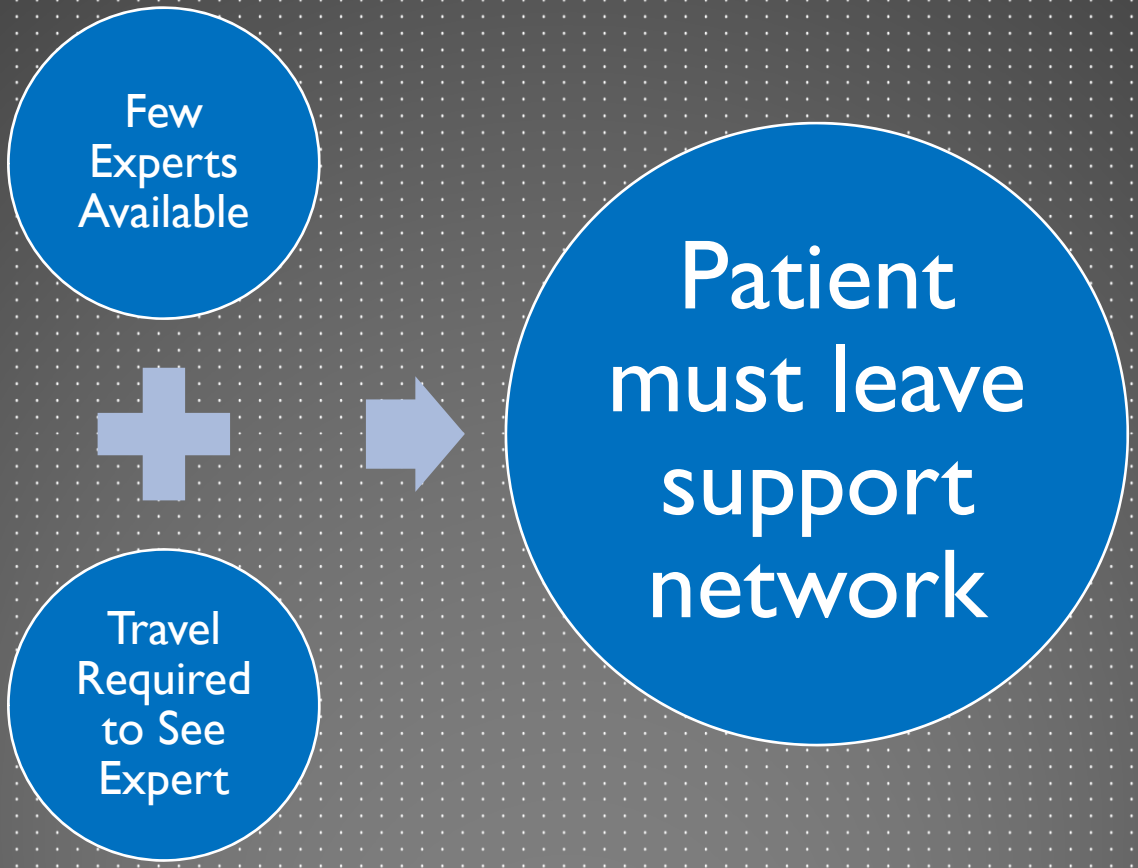
HEALTHCARE SYSTEM

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



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URGENCY IN DECISION-MAKING

Rush to invasive tests

Decisions made in a highly emotional state

Mandatory time frame to sort through info?

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PROVIDER WEAKNESSES

- 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

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INSURANCE AND COVERAGE ISSUES

Medicare

- State specific and often inadequate
- Attached to HMOs

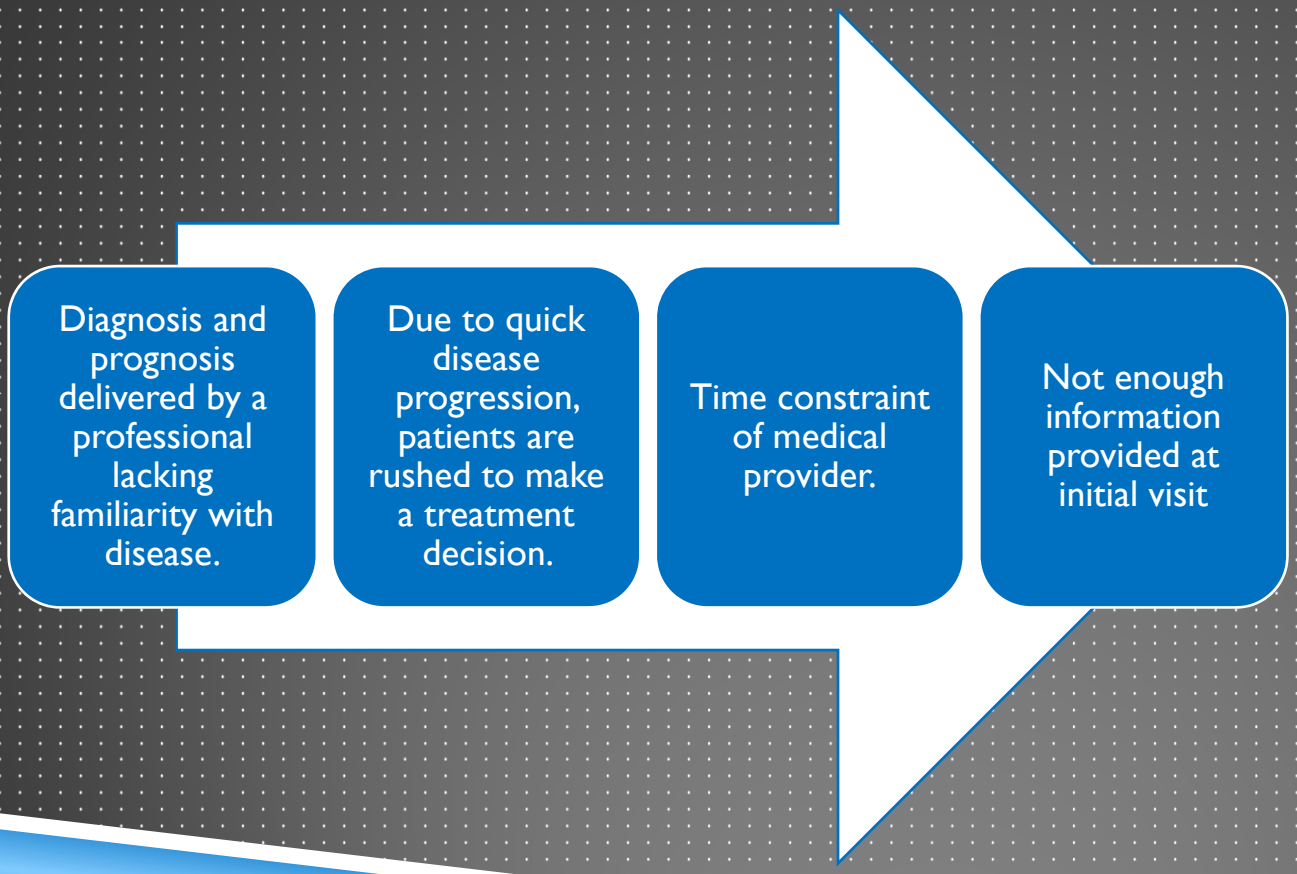
Private Insurance

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

Uninsured or Underinsured

- Incredible difficulty obtaining timely and quality care

SUMMARY PATIENT CHALLENGES AND RESULTS



Mesothelioma family often falls victim to predators.

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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)

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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

MEETING THE NEEDS

- 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

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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

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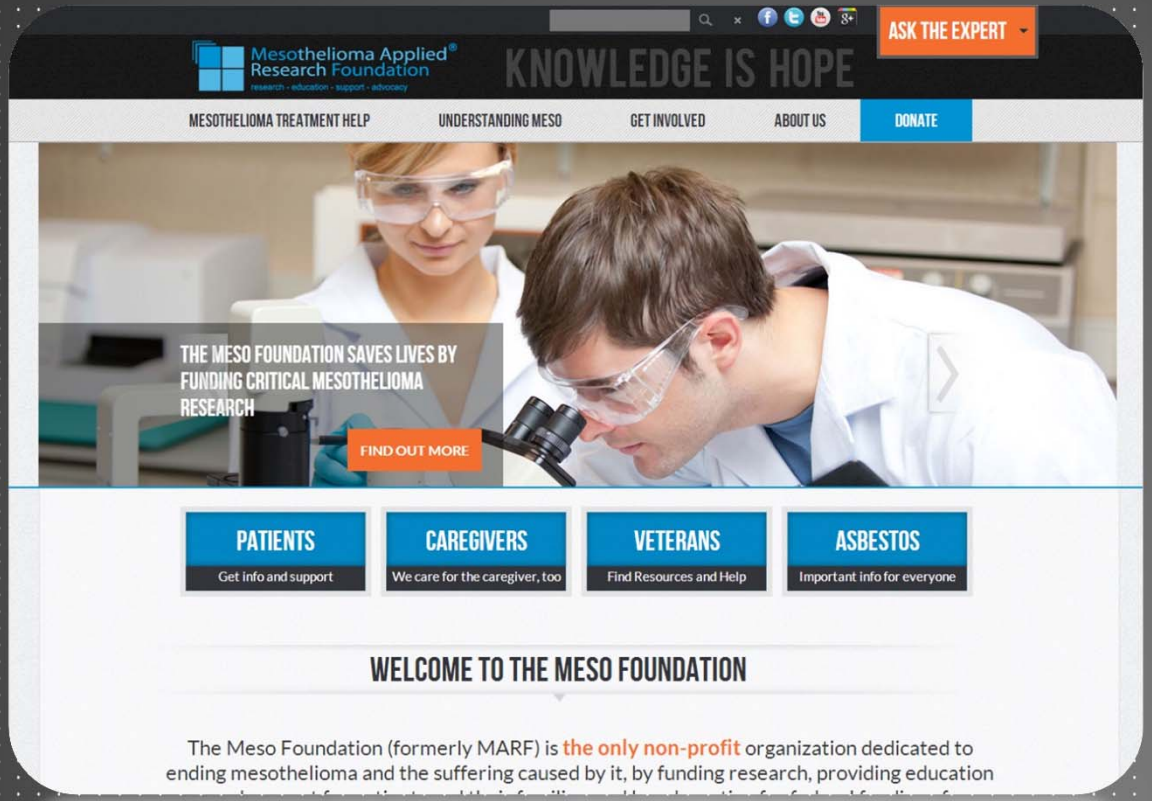
research - education - support - advocacy

THE MESO FOUNDATION



- Learn more by visiting our website at **curemeso.org**

Mesothelioma Applied® Research Foundation
research - education - support - advocacy

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*
  - *Jonathan Pachter, Ph.D. - Verastem Head of Research*
  - *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*
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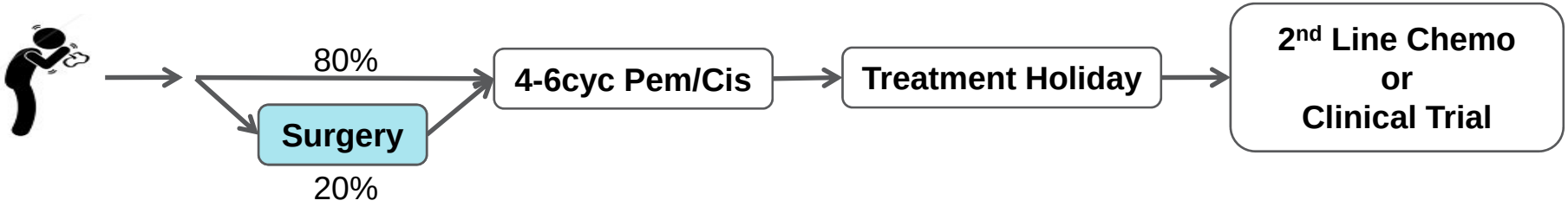
- Question and Answer Session
  - *Speakers and panelists*
- NASDAQ Closing Bell
  - *All attendees*
- Reception and Networking
  - *All attendees*

Mesothelioma Patient Journey



Surgical Options

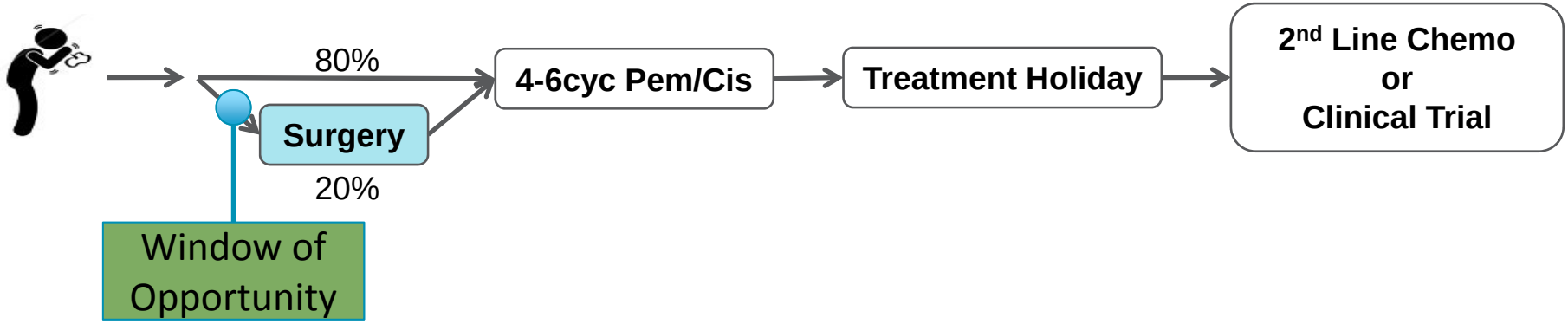
- Approximately 20% of patients diagnosed with MPM are eligible for surgery
- Stage of disease and performance status are primary factors
- No approved agents or treatment modality as neo-adjuvant or adjuvant therapy

Raphael Bueno, M.D.

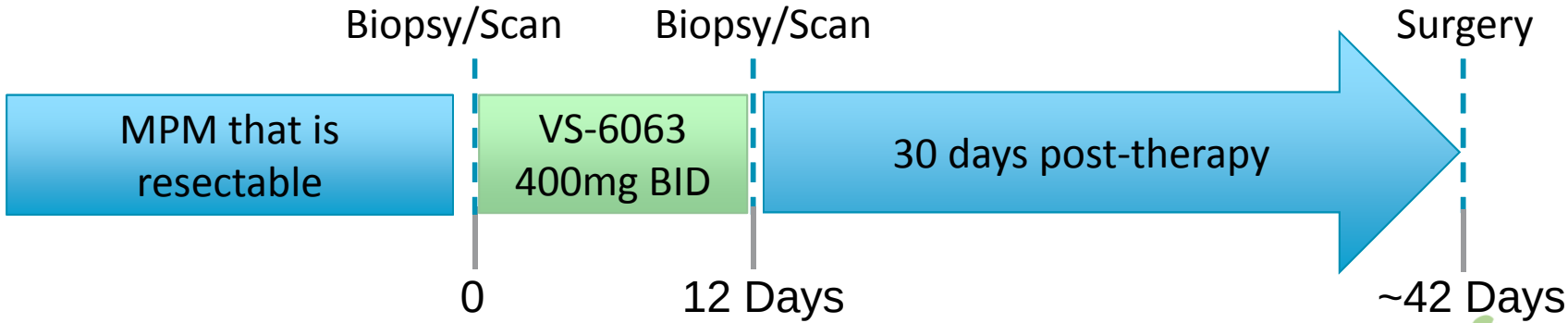
Chief, Thoracic Oncology, Brigham and Women's Hospital

Professor, Harvard Medical School

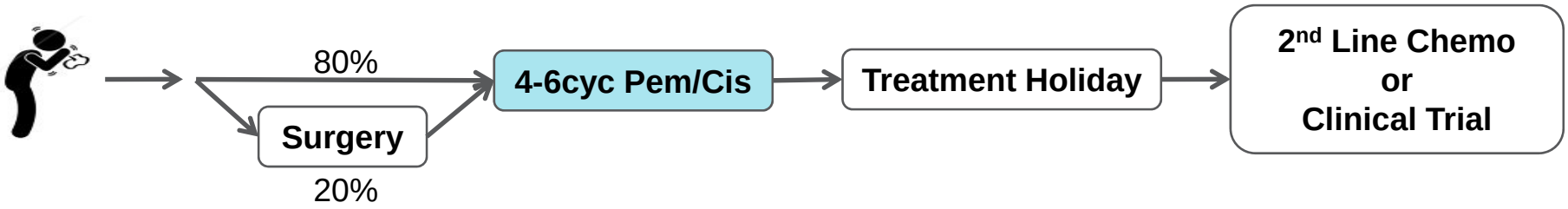
Window of Opportunity Study in Surgery-Eligible Patients



- 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



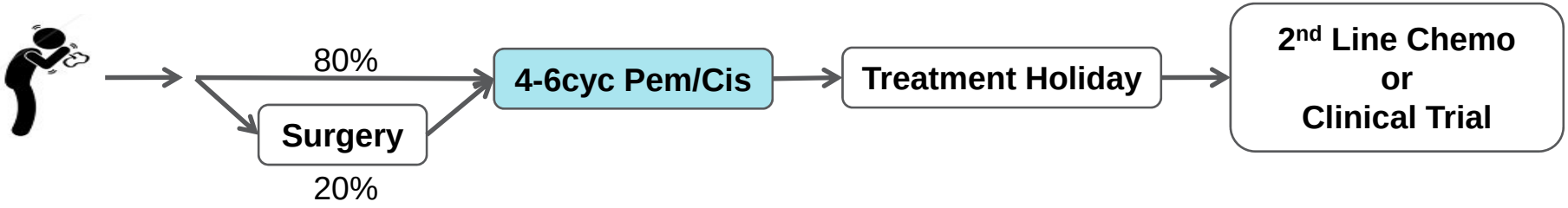
Phase 3 study of Pemetrexed (Alimta) in Combination with Cisplatin



- 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

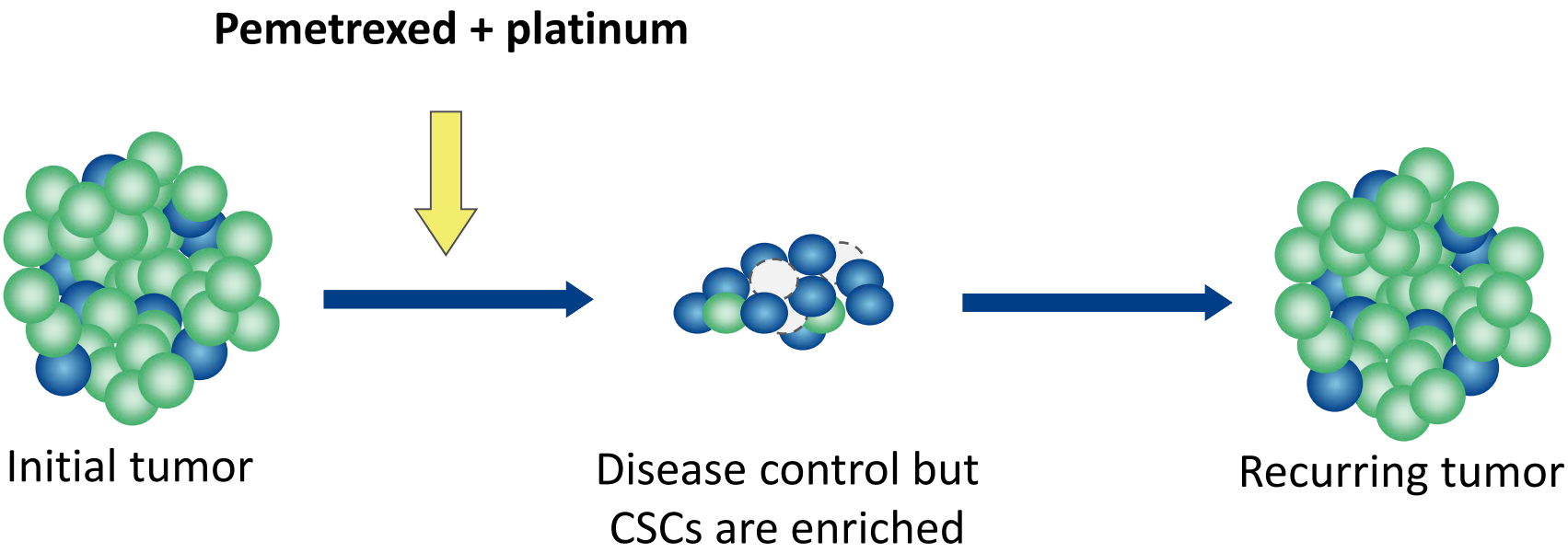
Endpoint	Cisplatin	Pem/Cis	HR	P Value
Response rate, %	16.7	41.3		< .001
Median TTP, months	3.9	5.7	0.68	< .001
Median OS, months	9.3	12.1	0.77	.028
Global QoL score	38	45		.012
Improved symptom distress	44	51		.009

No Advances in Standard Therapy for Over 12 Years



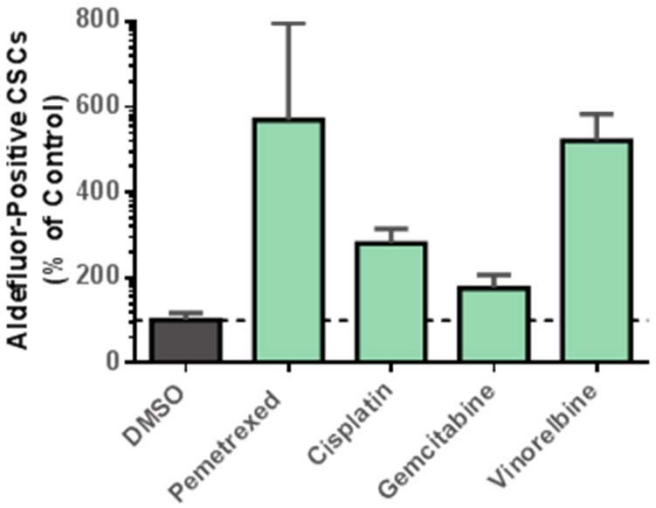
- Pemetrexed remains the ONLY approved drug for MPM worldwide
- Limited effect of pemetrexed+cisplatin on patient response

The Current Therapy for Mesothelioma Enriches Cancer Stem Cells



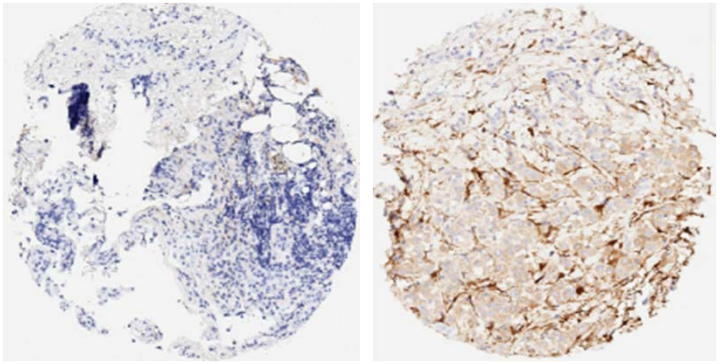
Standard of Care Treatment Increases Cancer Stem Cells

Mesothelioma Cancer Stem Cells *in vitro*



Mesothelioma Cancer Stem Cells in Patient Biopsies

Pre-treatment	Post-treatment with pem/cis



Brown = ALDH+ (cancer stem cells)

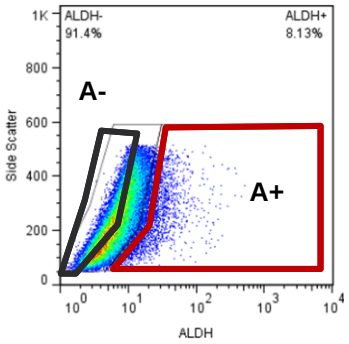
Treatment of human MPM cell lines with pemetrexed enriches cancer stem cells

Canino et al. Oncogene 2011

Tumor Initiating Assay – The Gold Standard for Cancer Stem Functionality

Mesothelioma cells

Aldefluor Assay



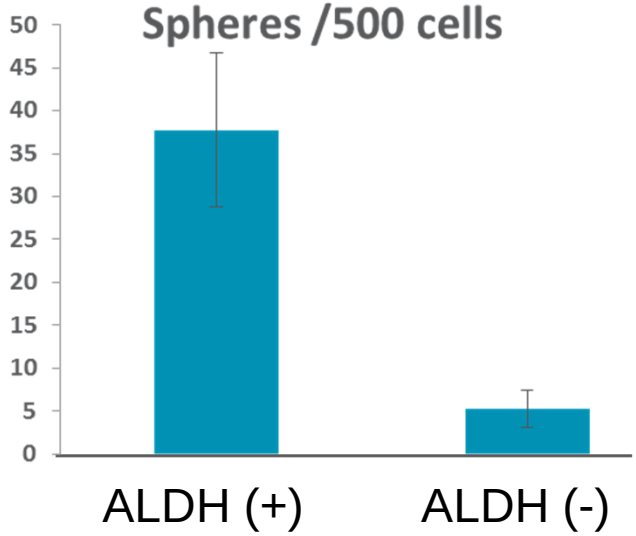
Functional Tests

1^0 Tumorsphere assay

Limiting dilutions *in vivo*

Measure tumor volume

1^0 Tumorsphere assay



Tumor Initiating Frequency

(ALDH+): 1/174

(ALDH-): 1/6063

35x Increase

p value: $2x10^{-7}$

VS-6063 Inhibits Tumor Initiation in Mouse Mesothelioma Models

Mesothelioma cells

Drug Treatment

Control

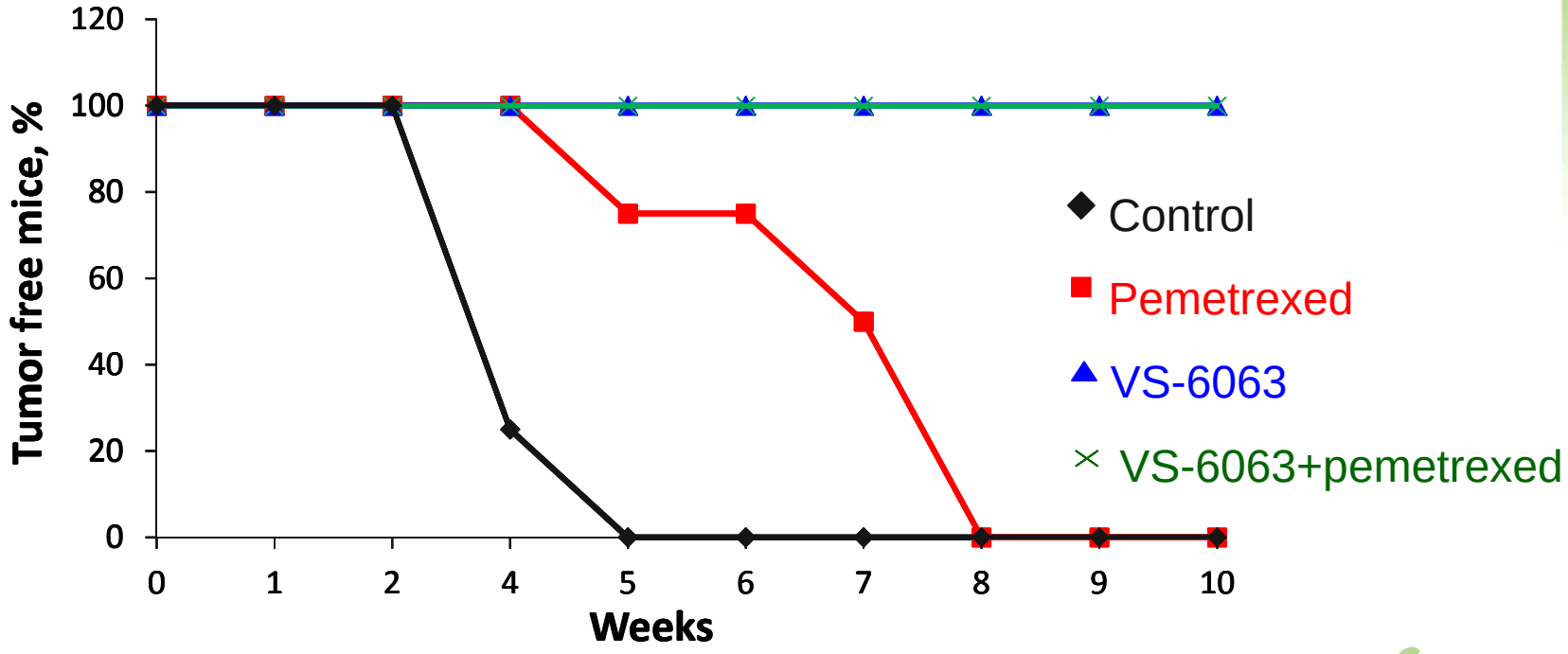
Pemetrexed

VS-6063

VS-6063+pemetrexed

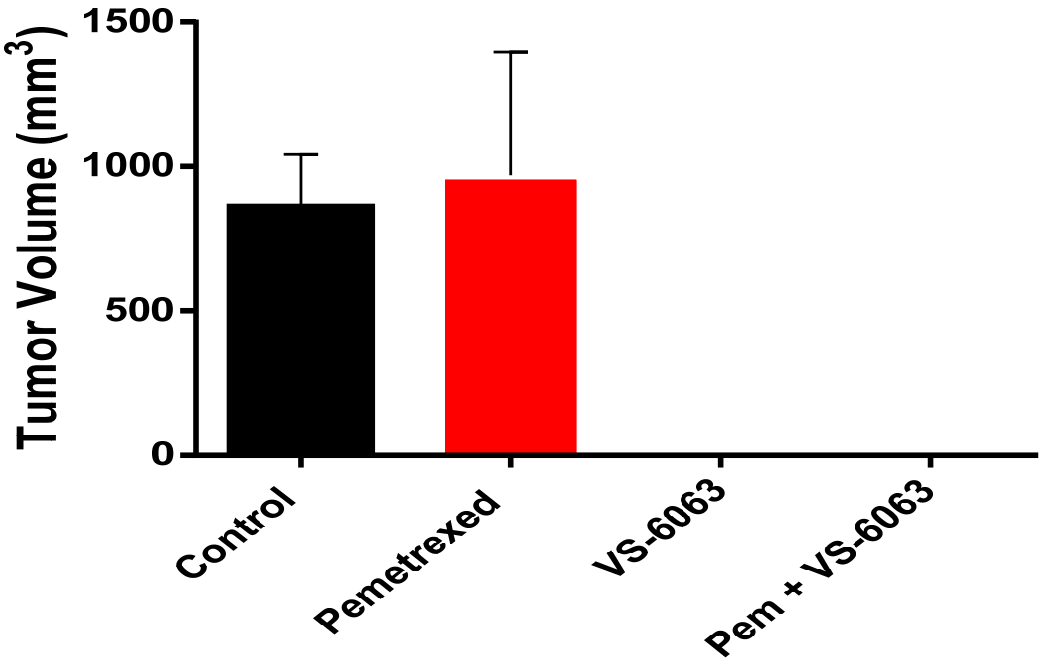
Functional Tests

Tumor Initiation *in vivo*

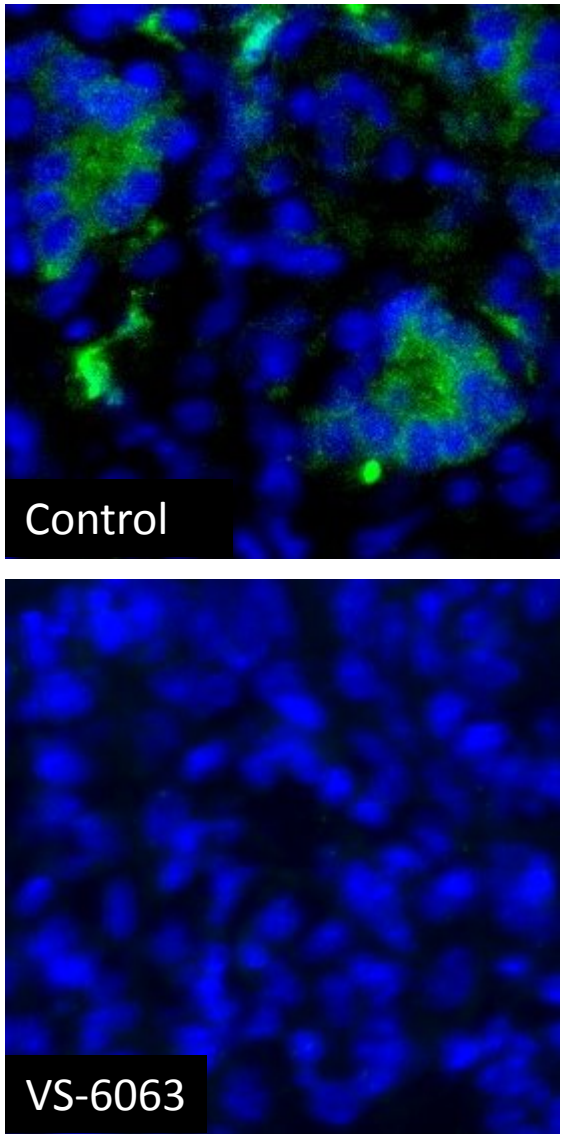


VS-6063 Inhibits Tumor Initiation/Growth in Mesothelioma Models

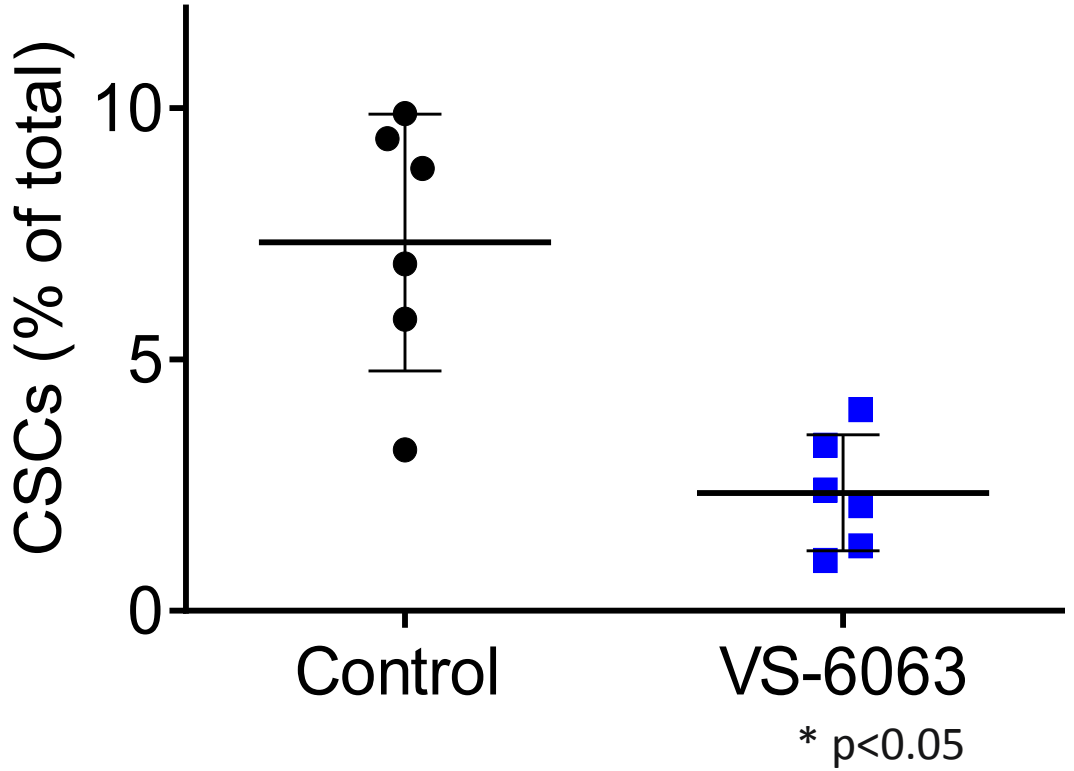
Mesothelioma cells	Drug Treatment	Functional Tests
	Control Pemetrexed VS-6063 VS-6063+pemetrexed	Measure tumor volume



Oral Administration of VS-6063 Targets Cancer Stem Cells in Mesothelioma Tumors Grown in Mouse Lungs



50 mg/kg, po BID x 2 wks

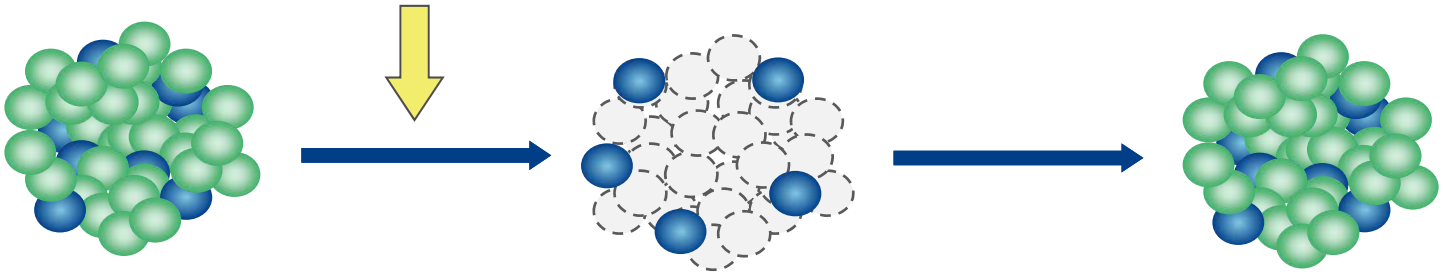


CSCs (ALDH+)
DAPI

COMMAND: Targeting Cancer Stem Cells for a More Durable Clinical Response

PROBLEM:

Current cancer treatments



Initial tumor

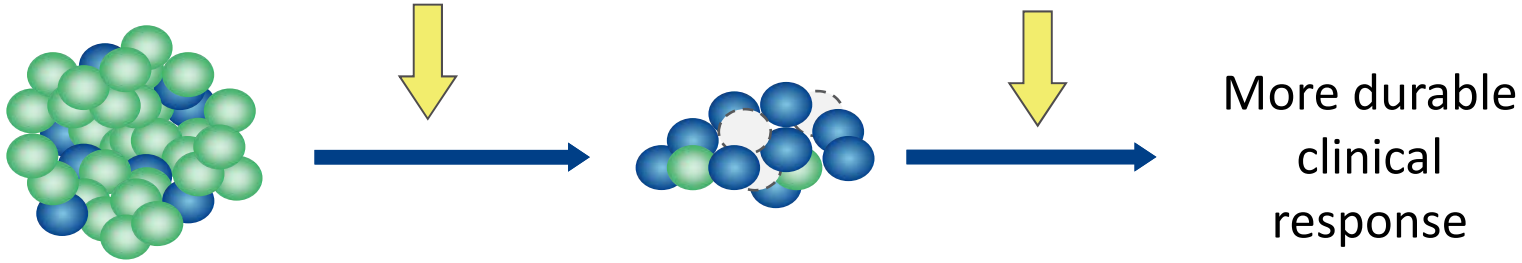
Tumor reduction but CSCs survive

Recurring tumor

SOLUTION :

Pemetrexed + platinum

VS-6063

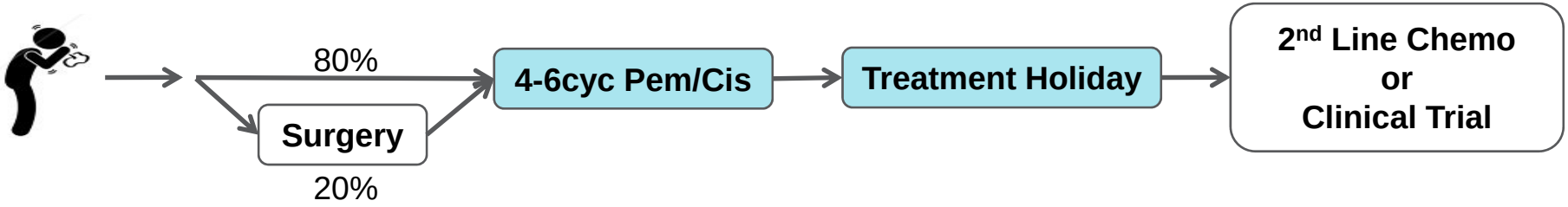


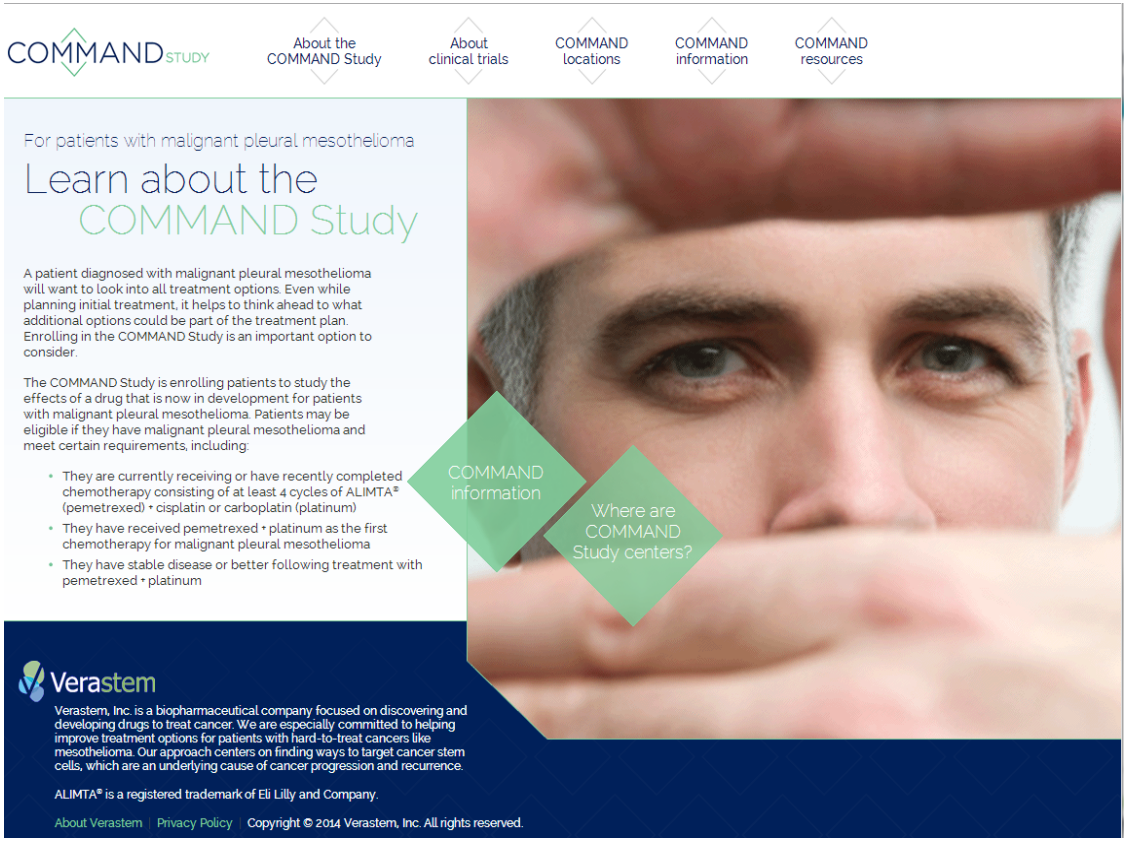
Initial tumor

Disease control but CSCs are enriched

More durable clinical response

COMMAND: Targeting Cancer Stem Cells in the Switch Maintenance Setting





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=~350-400)

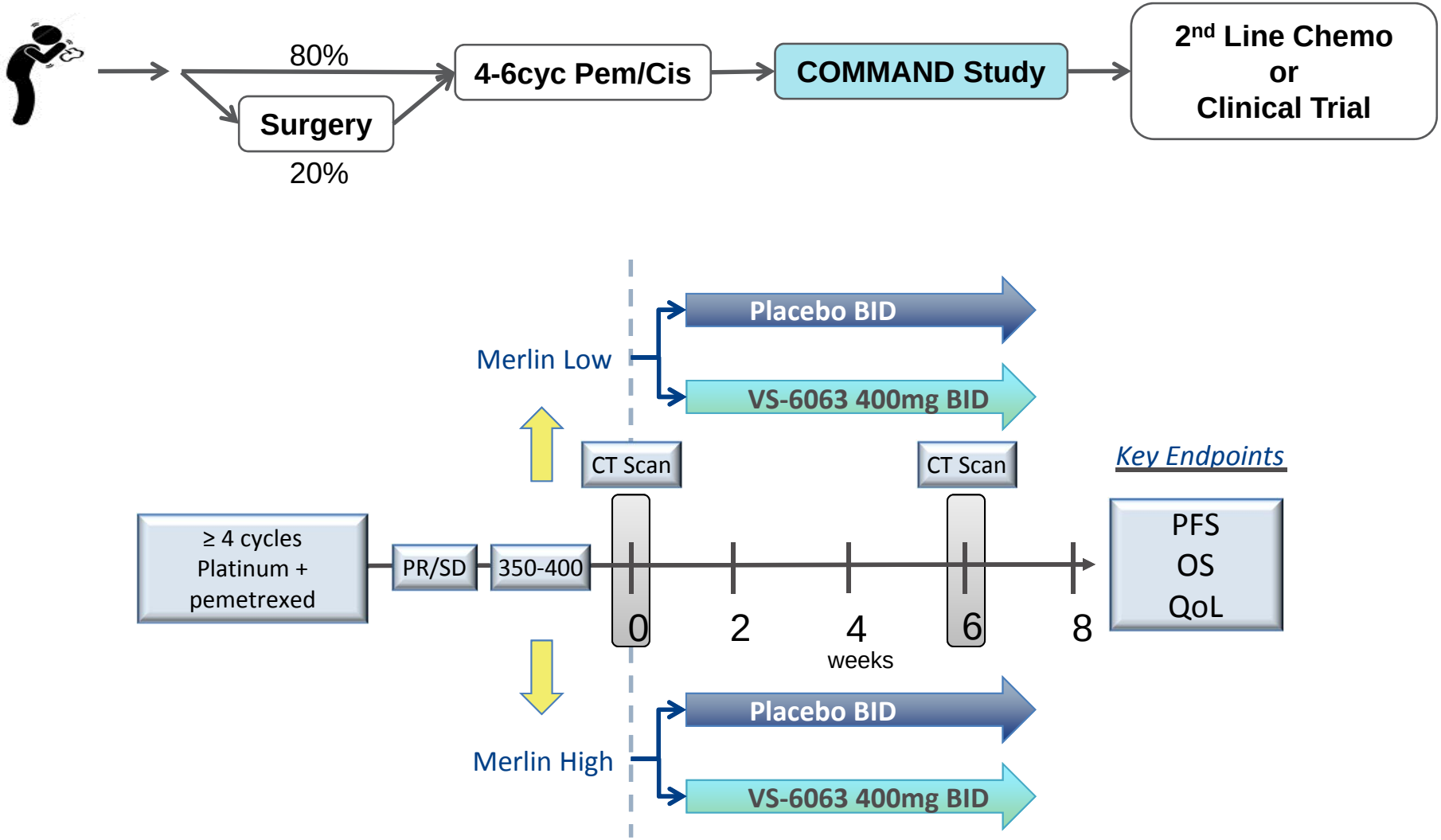
- Measurable or Evaluable Disease per RECIST v1.1
- One prior regimen (≥4 cycles) pem/cis or pem/carbo with documented ongoing response (PR or SD)

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

Primary Objectives	Secondary Objectives	Exploratory Objectives
Overall Survival (OS)	Quality of Life (QoL) (LCSS-Meso)	Time to new lesion
Progression Free Survival (PFS)	Objective Response Rate (ORR)	Relationship of VS-6063 PK and outcome
	Safety and tolerability	Population PK of VS-6063

COMMAND: A Registration-Directed Study of VS-6063 to Maintain Tumor Control in Mesothelioma



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

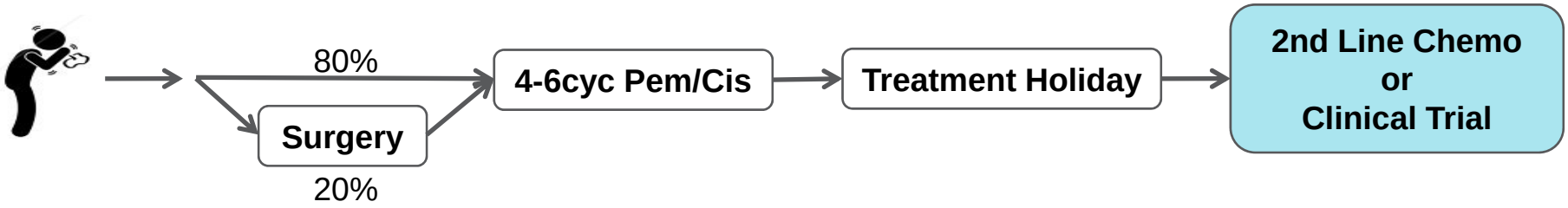
- **5** interviews on **prime time UK regional news channels** – ITV and BBC
- **141 radio interviews** including *Sky News Radio, BBC Three Counties* and *Imagine FM*
- **2** items of print coverage
- **8** items of online coverage
- **Advertorial** in the UK national newspaper The Independent

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*

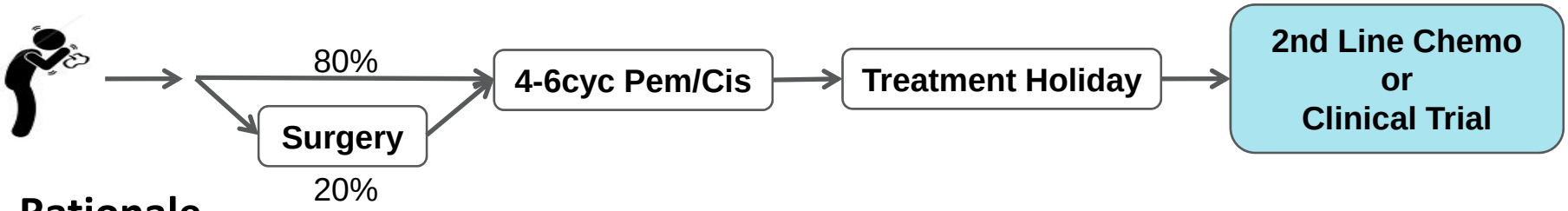
    AND
  - *Promising results are NOT observed among the full sample*
- If the trial is adapted:
  - *The required number of patients to maintain 90% power will be re-estimated*
- At the primary analysis:
  - *PFS, QOL and tolerability data will be assessed for potential to file as basis for accelerated 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

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



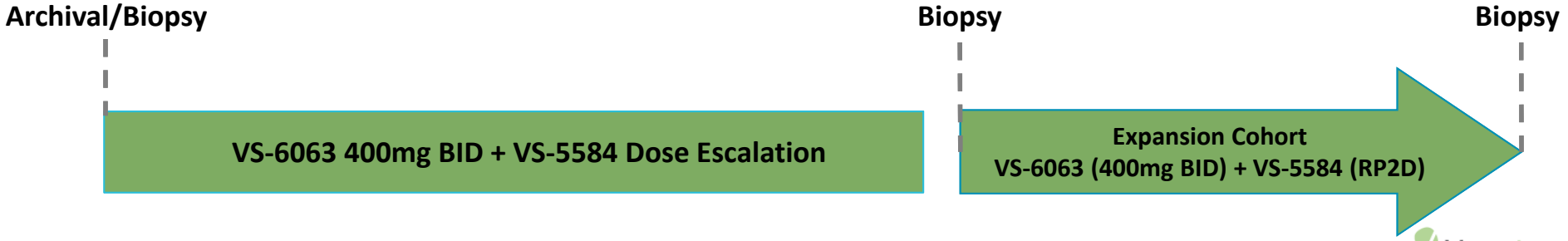
Rationale

- 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

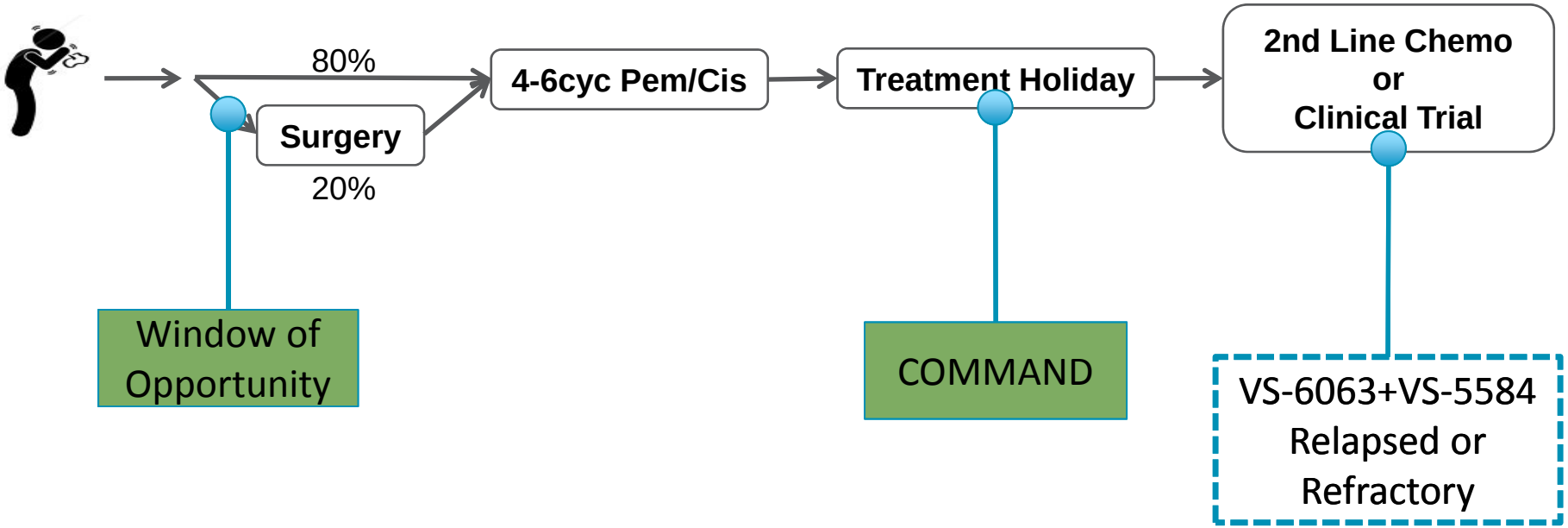
Goals

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

Enrollment (N=~40)



Developing Potential Treatment Options Throughout the Patient Journey



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

Ongoing

Planned

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- **Question and Answer Session**
  - *Speakers and panelists*
- **NASDAQ Closing Bell**
  - *All attendees*
- **Reception and Networking**
  - *All attendees*

Cancer Stem Cells Drive Ovarian Cancer Progression and Recurrence

Presence of CSCs in ovarian cancer correlates with poor PFS & OS

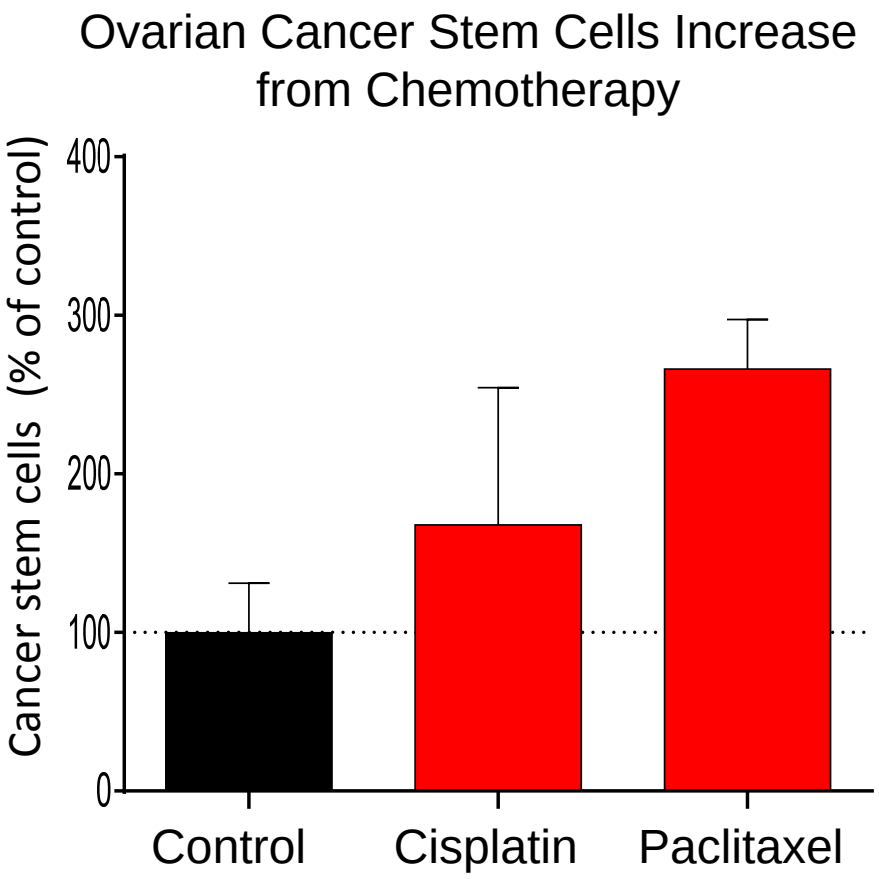
Silva et al., Cancer Res 2011

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 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

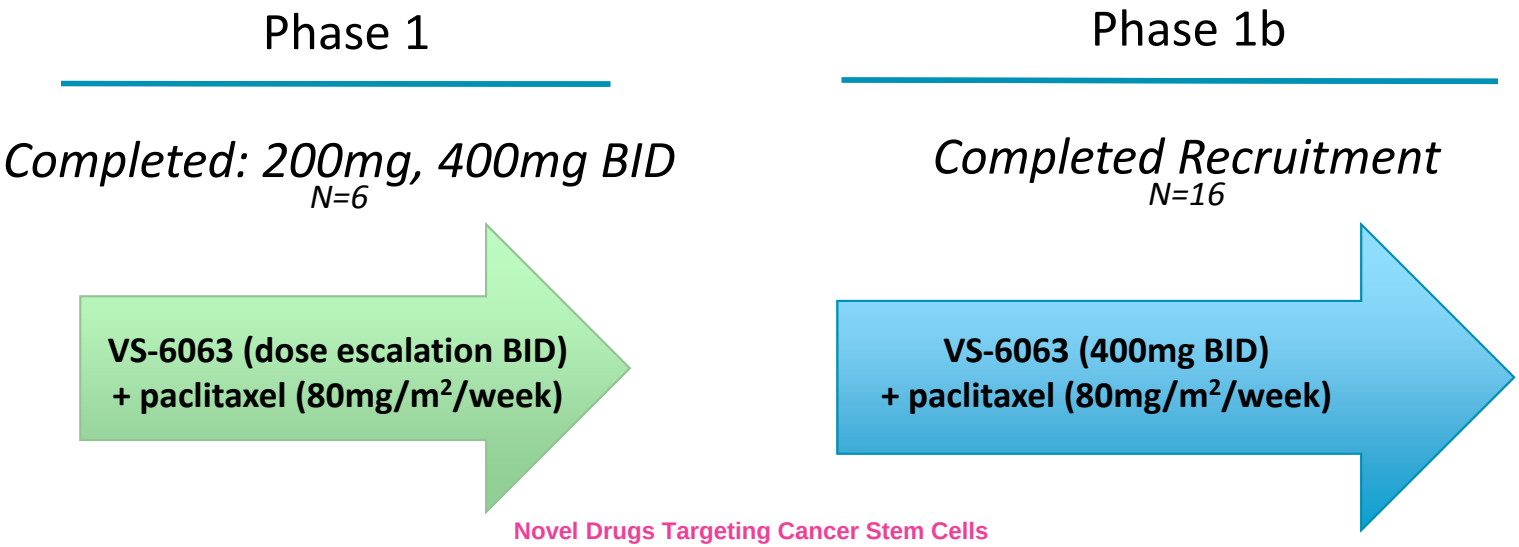
Goals

- 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

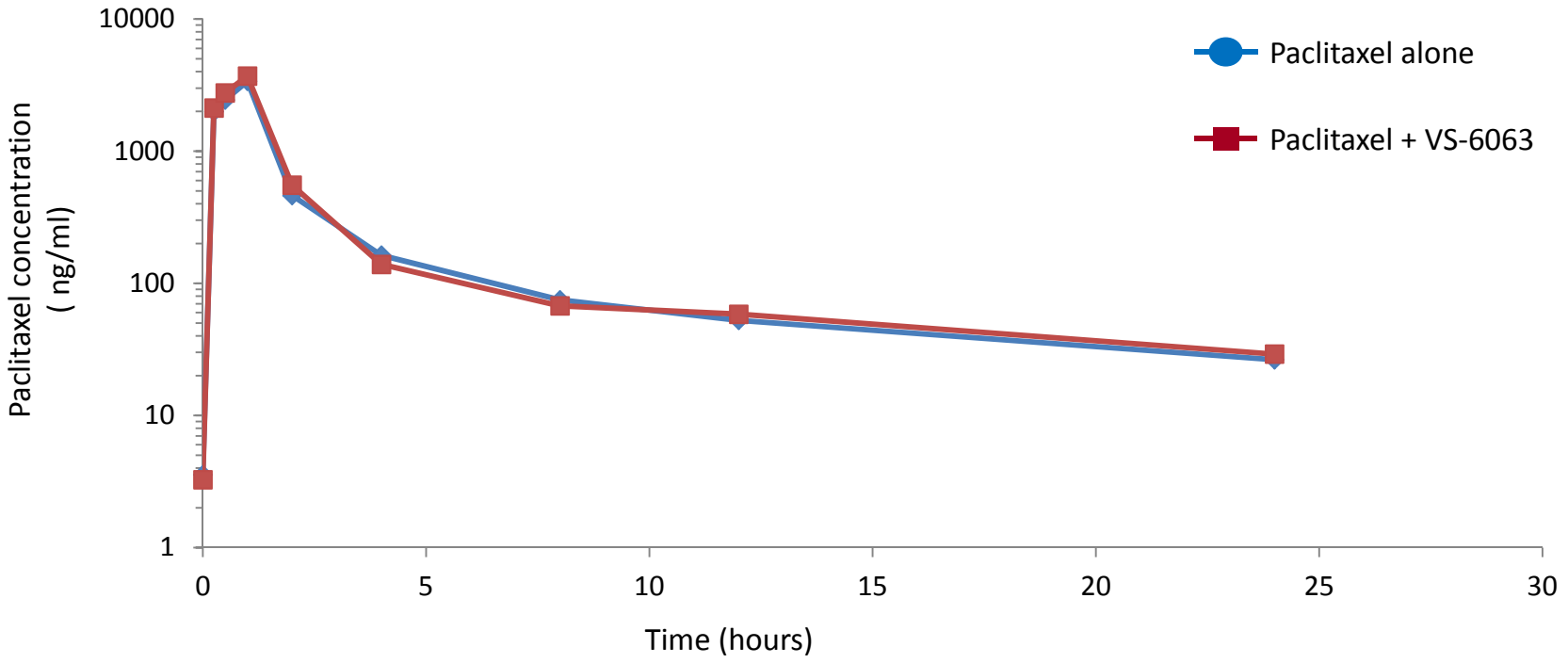


80% of Patients on Study Have Platinum Resistant Ovarian Cancer

	Phase I		Phase Ib
	200 mg defactinib BID + 80 mg/m² paclitaxel weekly	400 mg defactinib BID + 80 mg/m² paclitaxel weekly	400 mg defactinib BID + 80 mg/m² paclitaxel weekly
Patients, n	3	3	16
Median age, years (range)	59.0 (53-69)	74.0 (65-75)	67.5 (26-81)
Median time since initial diagnosis, years	2.00 (1.2-2-4)	3.24 (3.1-5.0)	2.32 (0.6-13.4)
Histology Serous Endometriod Other	 1 (33.3%) 1 (33.3%) 1 (33.3%)	 3 (100%) 0 (00.0%) 0 (00.0%)	 12 (75.0%) 0 (00.0%) 4 (25.0%)
ECOG PFS 0 1	 1 (33.3%) 2 (66.7%)	 2 (66.7%) 1 (33.3%)	 11 (68.8%) 5 (31.3%)
Prior chemotherapy regimens 1 2 3 ≥4	 0 (0.00%) 0 (0.00%) 3 (100%) 0 (0.00%)	 0 (0.00%) 0 (0.00%) 0 (0.00%) 3 (100%)	 5 (31.3%) 4 (25.0%) 4 (25.0%) 3 (18.8%)
Platinum Resistant	1 (33.3%)	3 (100%)	13 (81.3%)

**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

	Phase I		Phase Ib	
Adverse Event	200 mg defactinib BID + 80 mg/m^2 paclitaxel weekly (n=3)	400 mg defactinib BID + 80 mg/m^2 paclitaxel weekly (n=3)	400 mg defactinib BID + 80 mg/m^2 paclitaxel weekly (n=16)	Total (n=22)
Anemia	3 (100%)	1 (33.3%)	6 (37.5%)	10 (45.5%)
Fatigue	2 (66.7%)	3 (100%)	5 (31.3%)	10 (45.5%)
Bilirubin Increased	2 (66.7%)	0 (00.0%)	6 (37.5%)	8 (36.4%)
Nausea	2 (66.7%)	1 (33.3%)	4 (25.0%)	7 (31.8%)
Pyrexia	1 (33.3%)	2 (66.7%)	4 (25.0%)	7 (31.8%)
Vomiting	1 (33.3%)	2 (66.7%)	4 (25.0%)	7 (31.8%)
Neutropenia	1 (33.3%)	2 (66.7%)	3 (18.8%)	6 (27.3%)
Peripheral Edema	1 (33.3%)	1 (33.3%)	4 (25.0%)	6 (27.3%)
Peripheral Neuropathy	1 (33.3%)	2 (66.7%)	3 (18.8%)	6 (27.3%)
Diarrhea	0 (00.0%)	1 (33.3%)	4 (25.0%)	5 (22.7%)
Urinary Tract Infection	1 (33.3%)	1 (33.3%)	3 (18.8%)	5 (22.7%)

Most Frequently Reported Adverse Events ≥20%

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

Literature: Weekly Paclitaxel Alone Results in Limited Clinical Activity

Efficacy

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

*95% CI for difference in proportions alive and progression free at 6 months

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

1 patient had a complete response

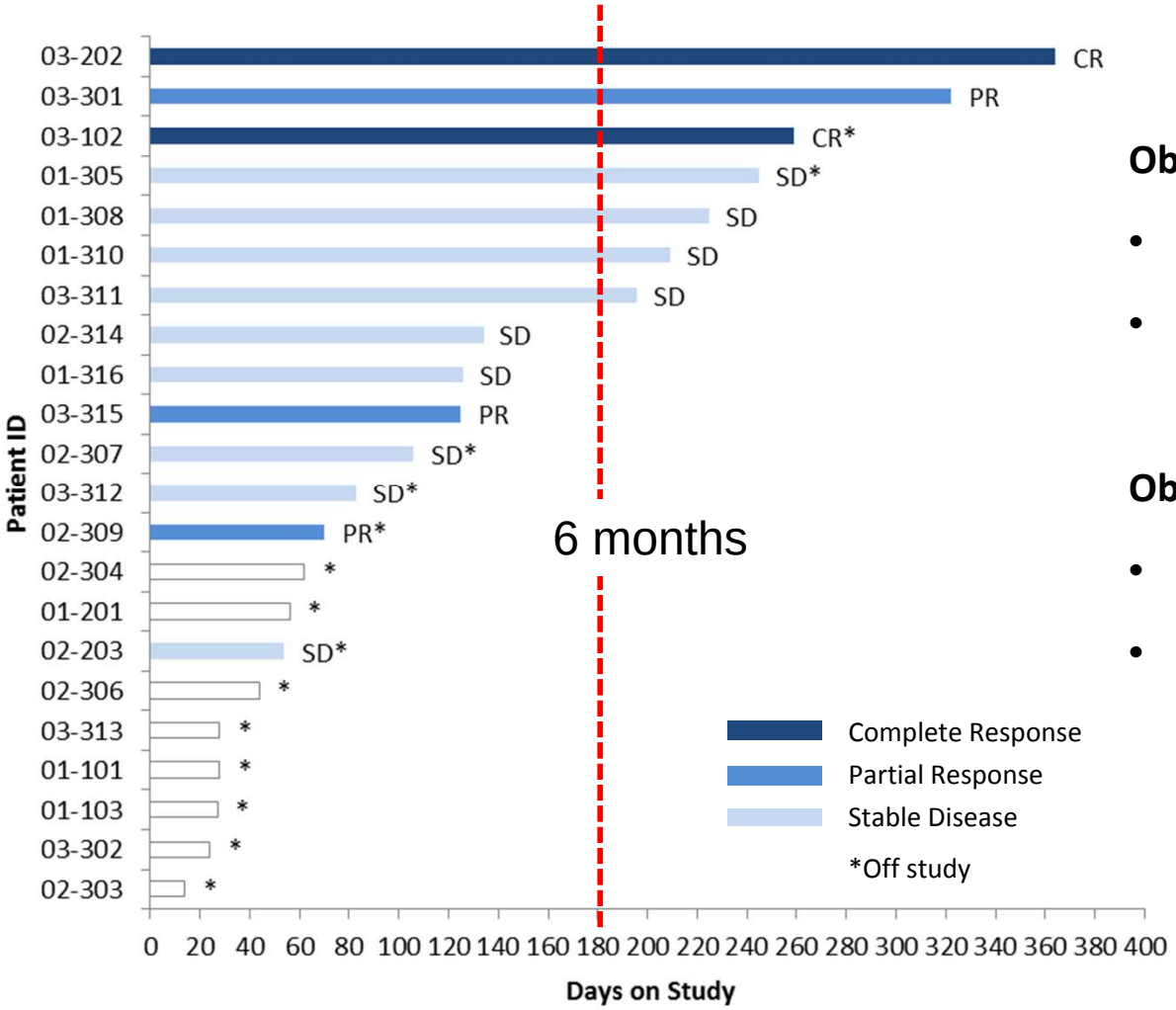
Results consistent with Phase 3 AURELIA study

(Pujade-Lauraine et al, J Clin Oncol 32, 2014)

McNeish et al., ASCO 2012

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

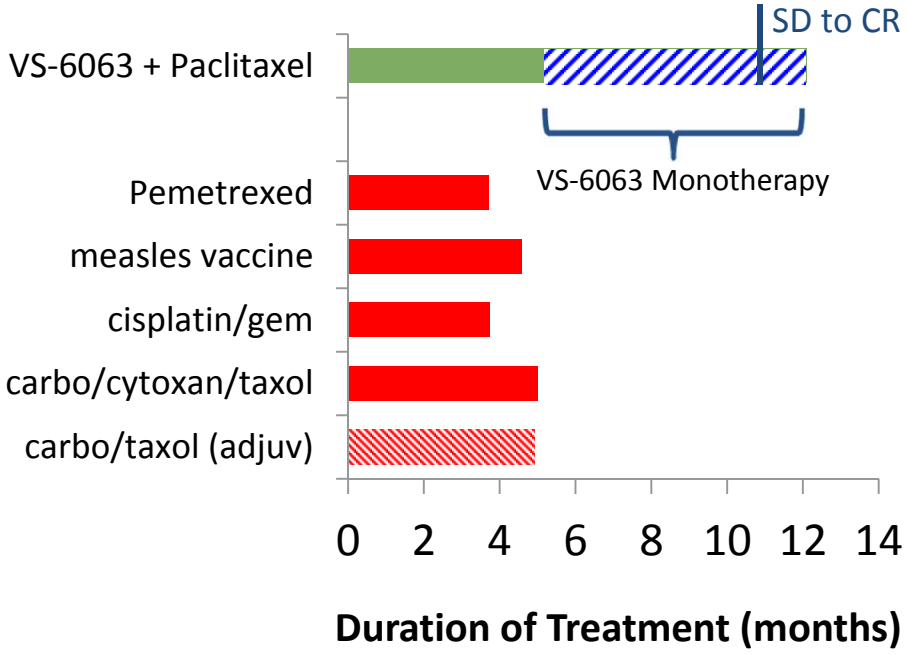
Objective Response *or* SD ≥ 6 months

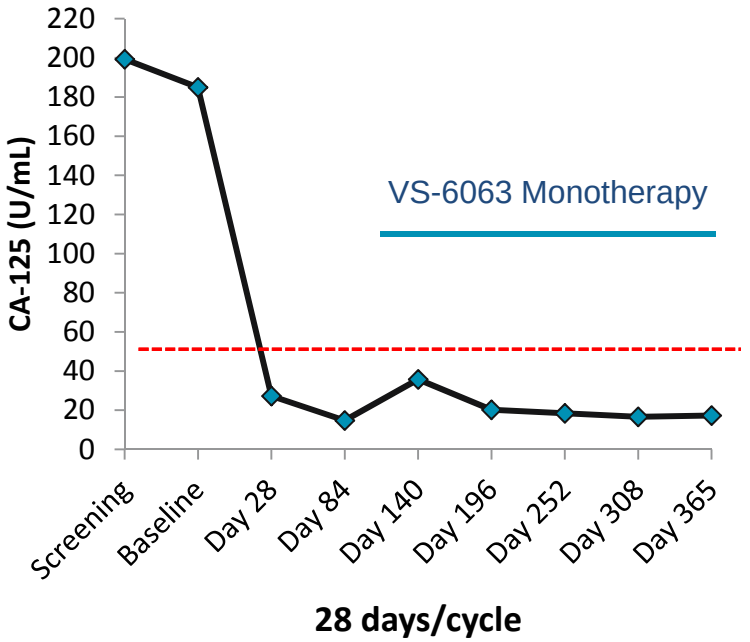
- Overall 9/22 (41%)
- 8 patients still on study

 **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



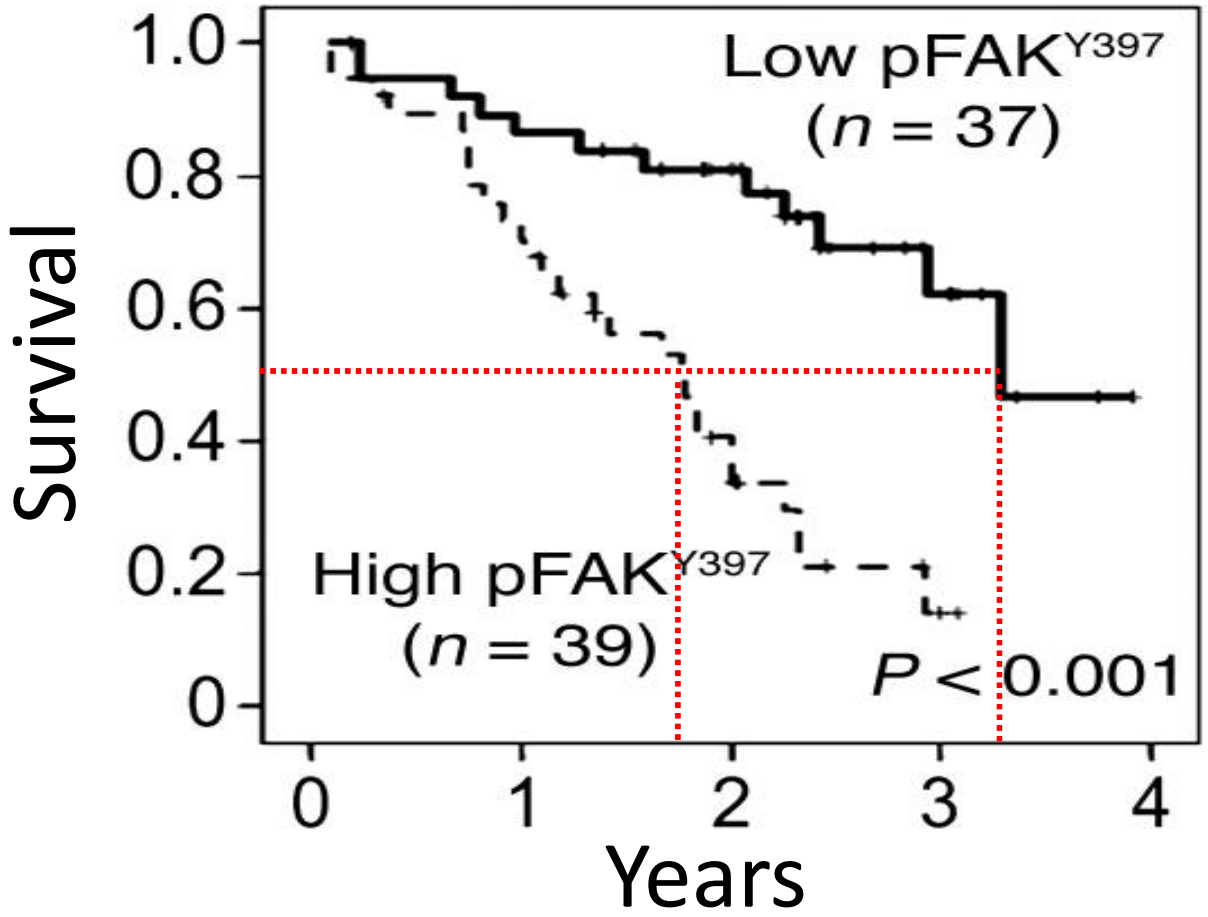


 *Unlocked, in-progress data as of 30 Jun 2014

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

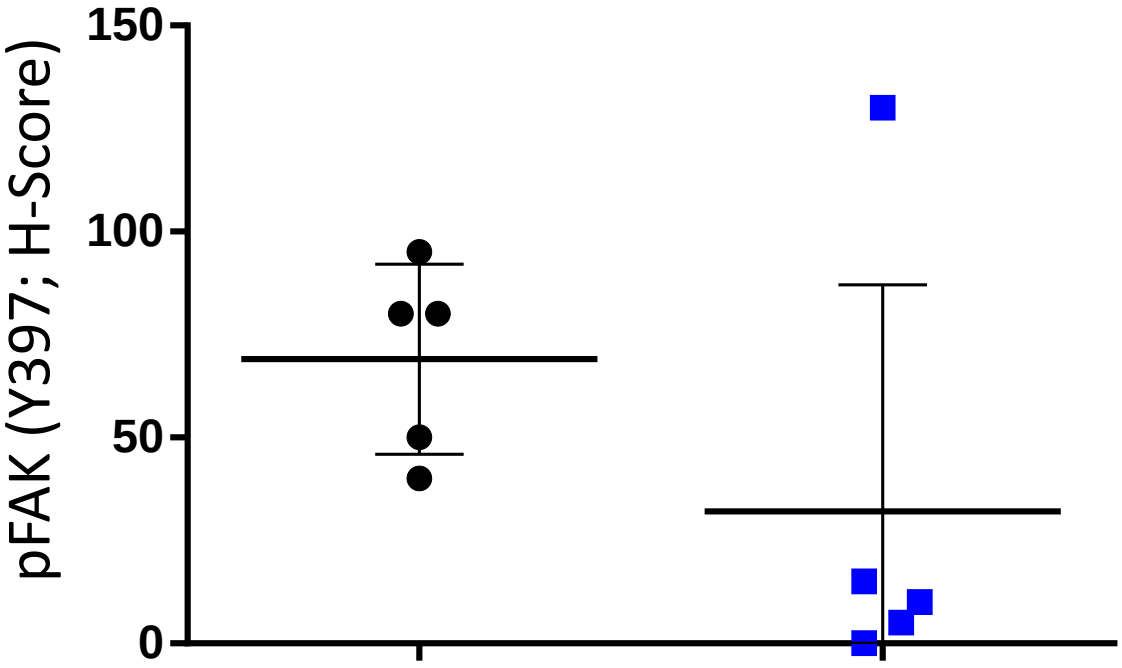
FAK Activity is Correlated with Poor Prognosis in Ovarian Cancer



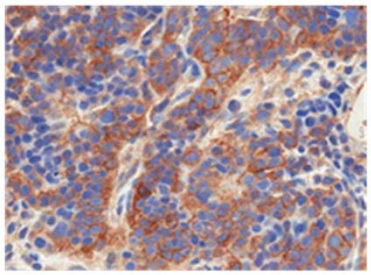
Mean survival (high/low) 1.7 vs 3.2yrs

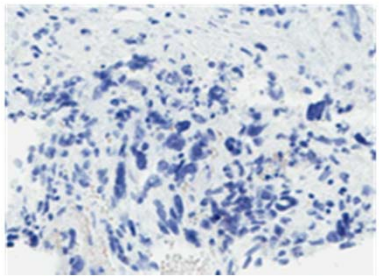
Sood et al., J Clin Invest 2010

VS-6063 Inhibits FAK Activity in Patient Tumor Biopsies Within 10 Days



Brown = pFAK (y397)

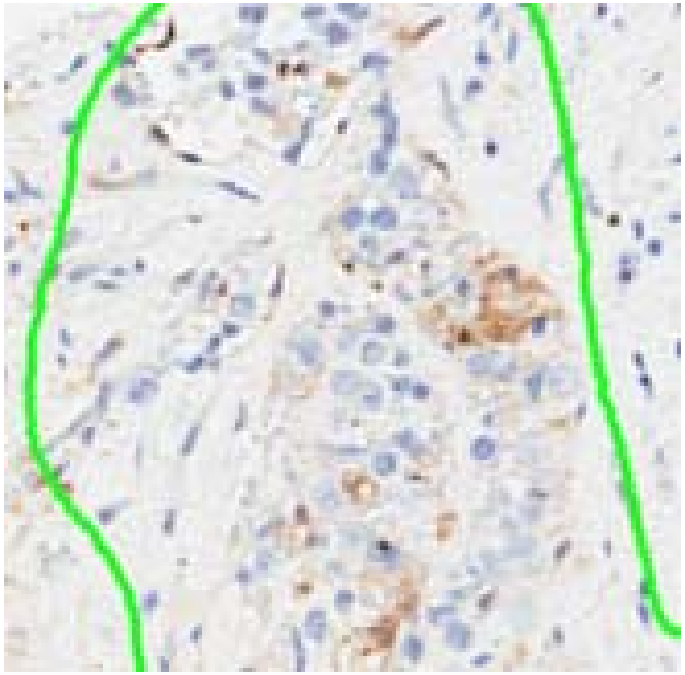




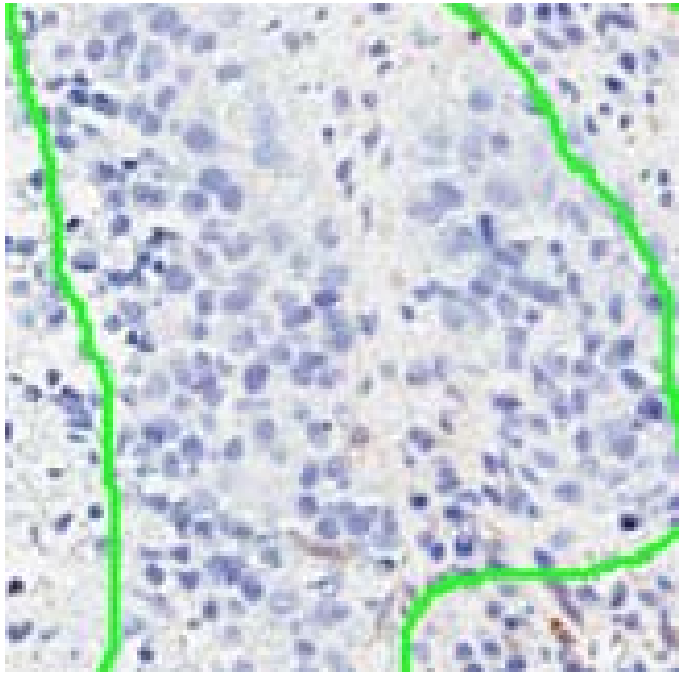
Paired tumor biopsies were obtained in five patients following 10 days of VS-6063 administration (400 mg BID)

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%



Day 1 (Baseline)



Day 10 (VS-6063)

Brown = ALDH (cancer stem cells)

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

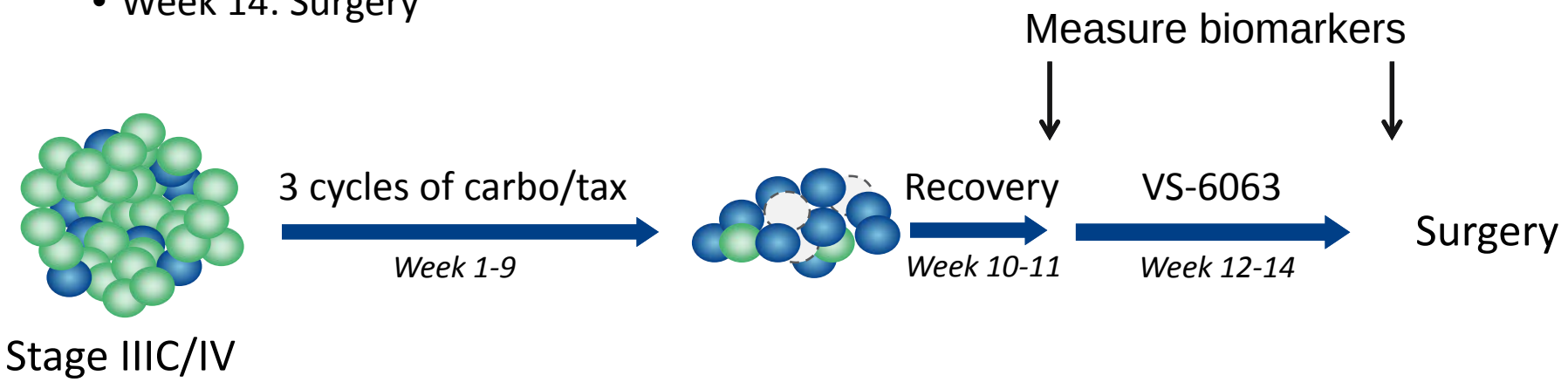
- Measure cancer stem cell biomarkers

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



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

Primary Objective	Secondary Objectives	Exploratory Objective
Progression Free Survival (PFS)	Objective Response Rate (ORR)	Overall Survival (OS)
	QOL	

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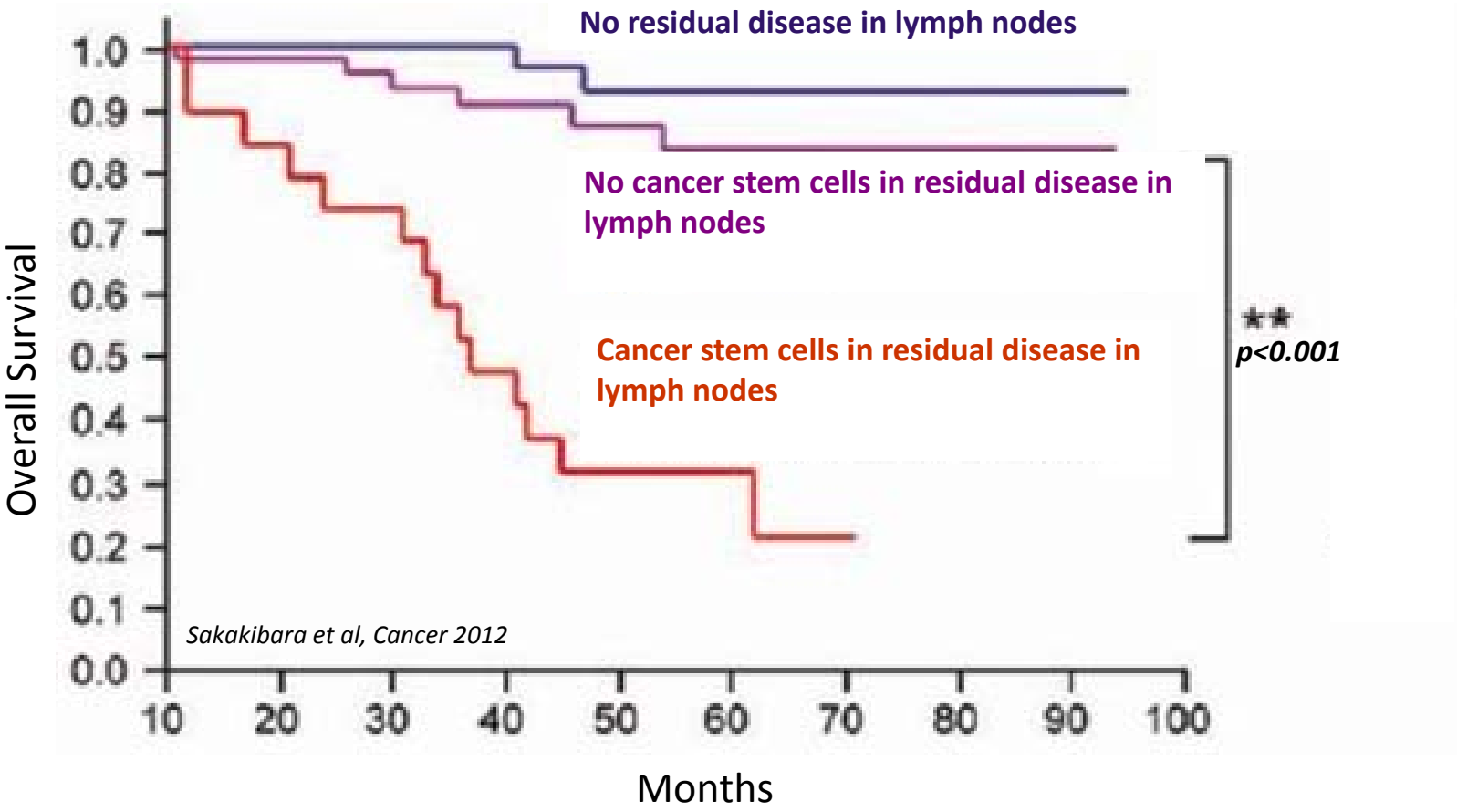
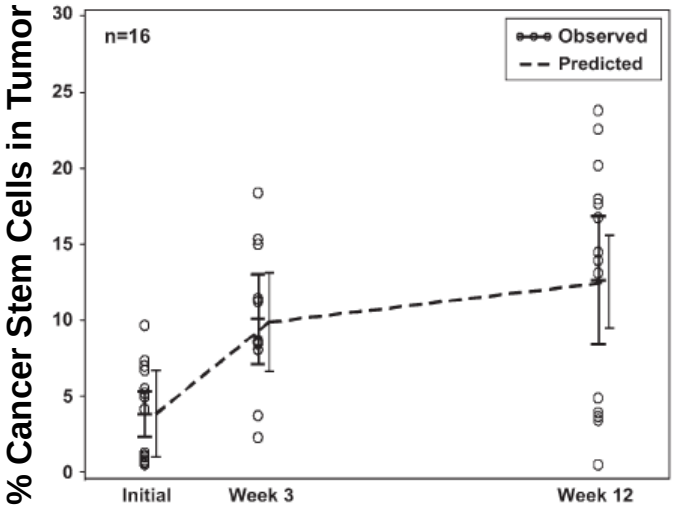
Cancer Stem Cells Predict Poor Survival in Breast Cancer



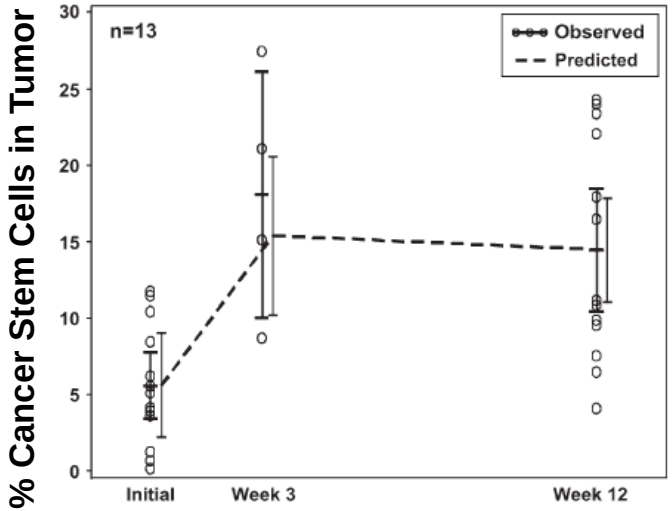
- N = 115 patients
- Standard neoadjuvant chemotherapy of 4 cycles anthracycline & cyclophosphamide + 12 weeks of paclitaxel

Cancer Stem Cells Emerge In Response to Chemotherapy

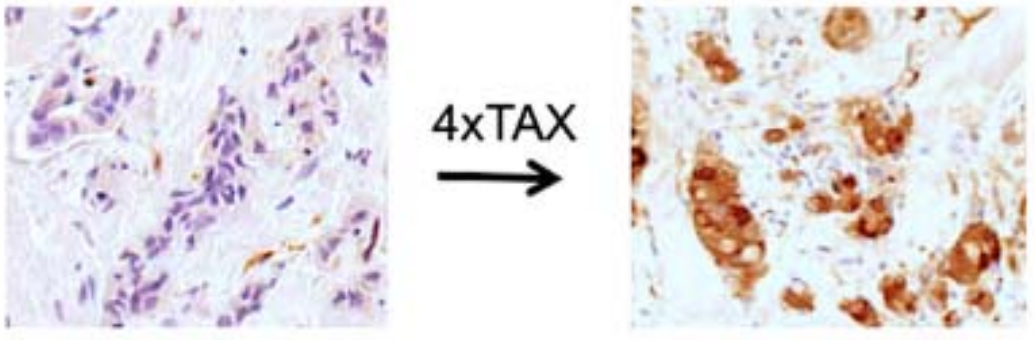
Triple Negative Breast Cancer



ER+ Breast Cancer



Li et al., JNCI 2008

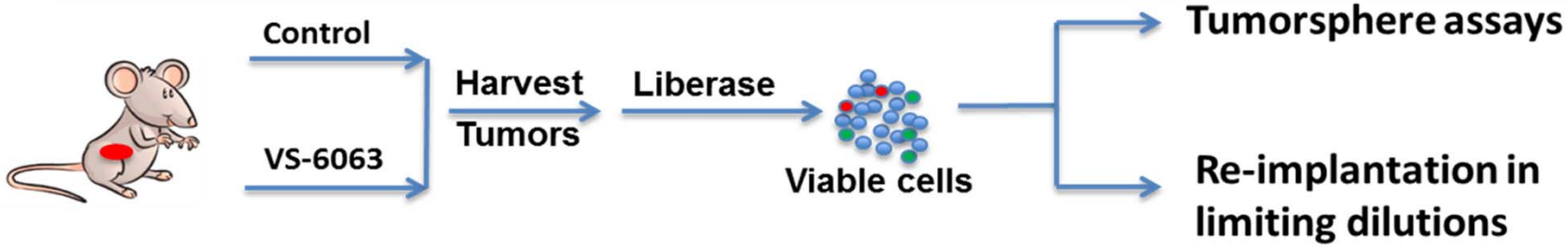


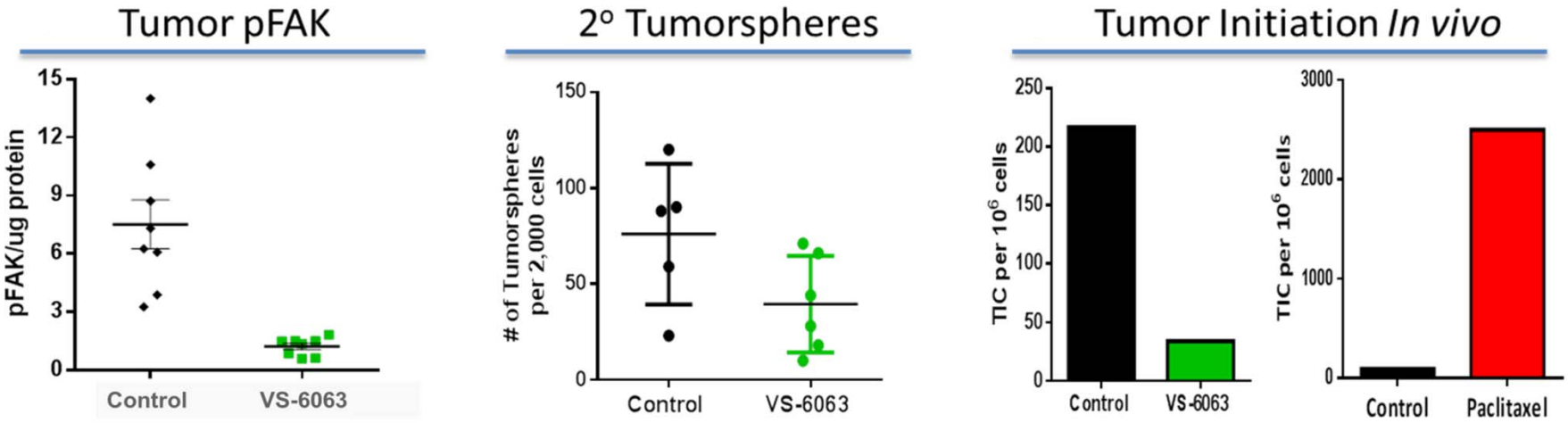
Baseline

Docetaxel

Alamgeer et al., Breast Cancer Research 2014

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=~100)

- Newly diagnosed, locally advanced triple negative breast cancer

Design:

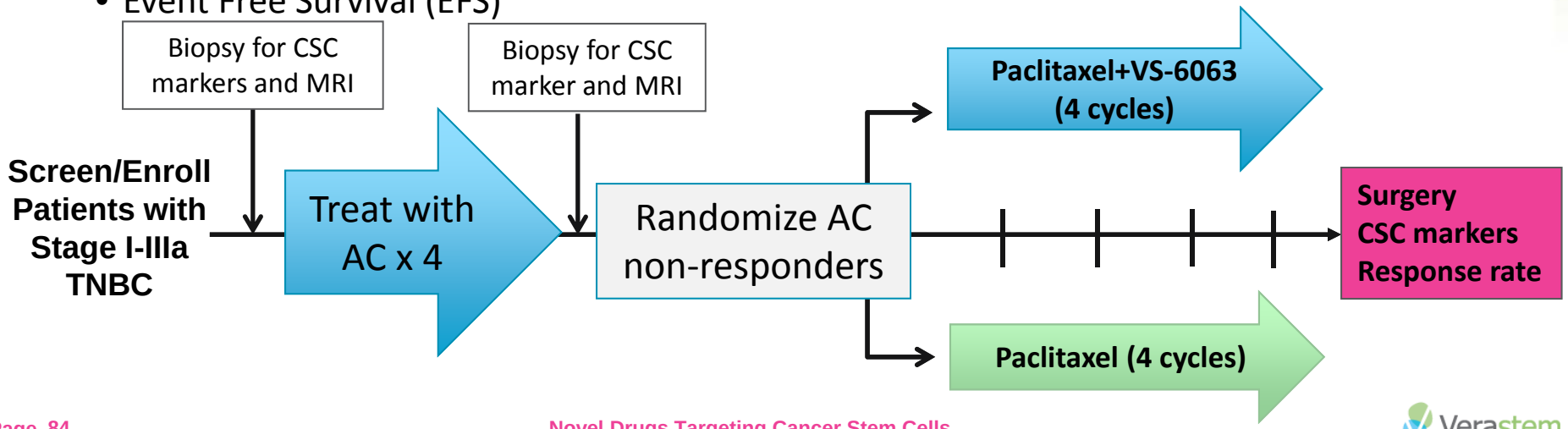
Open Label, Randomized, Multi Center

Primary Endpoints

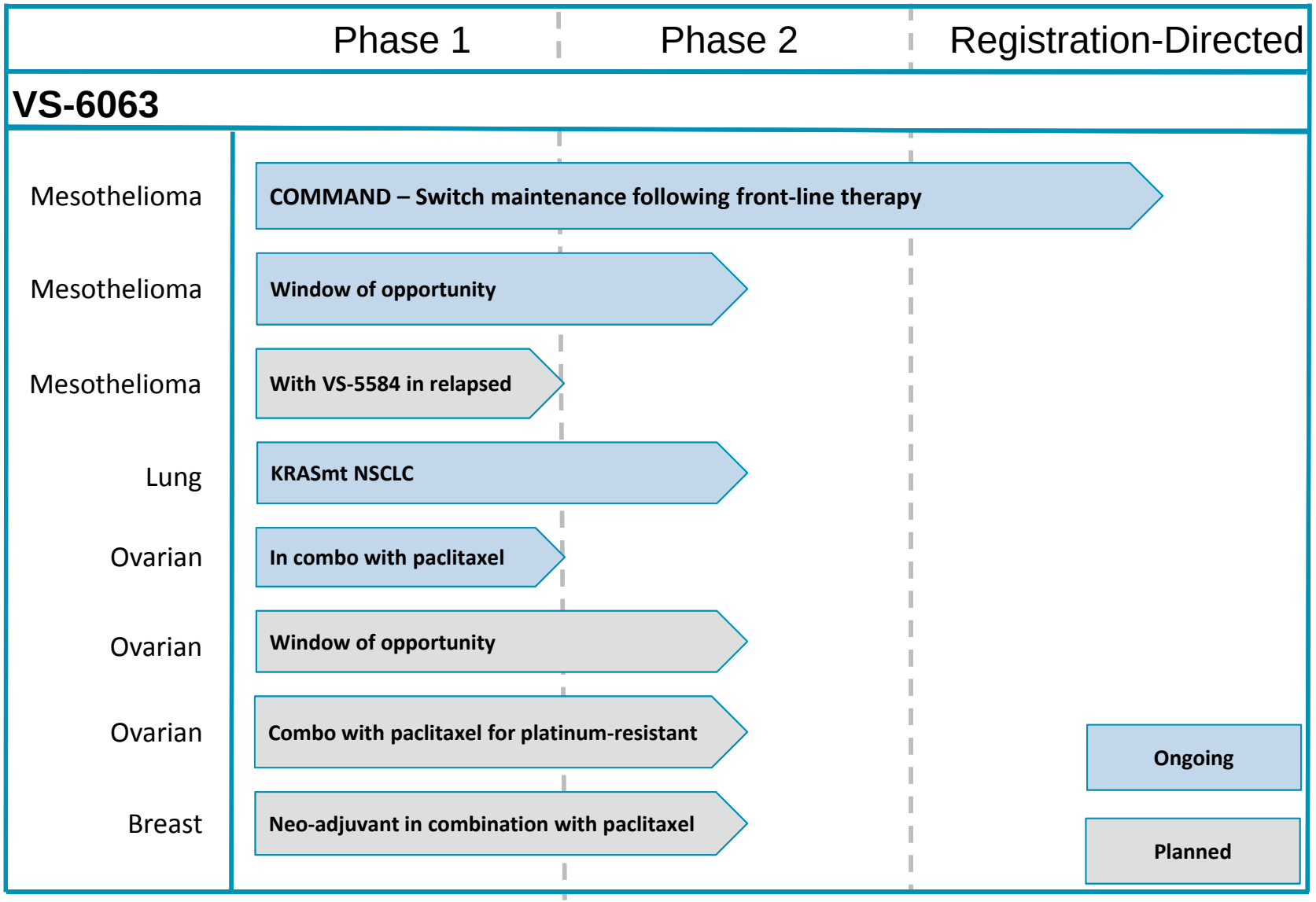
- Cancer stem cell "Response" rate (CSCR)
- Safety and tolerability

Exploratory Endpoint

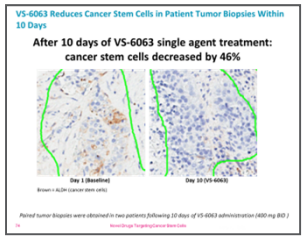
- Event Free Survival (EFS)



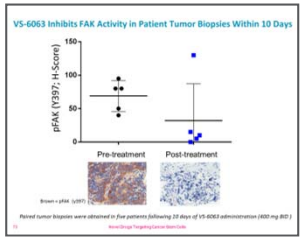
Clinical Development of VS-6063



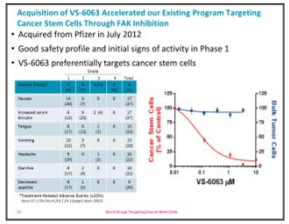
Path to Confidence in the Cancer Stem Cell Targeting Drug VS-6063



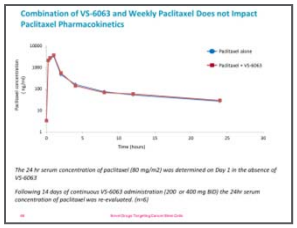
Reduction of CSCs *in patient biopsies*



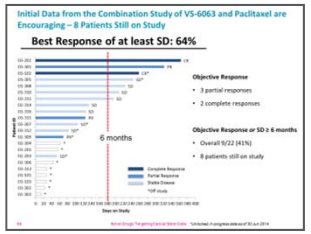
Good ***target inhibition***



Good safety profile

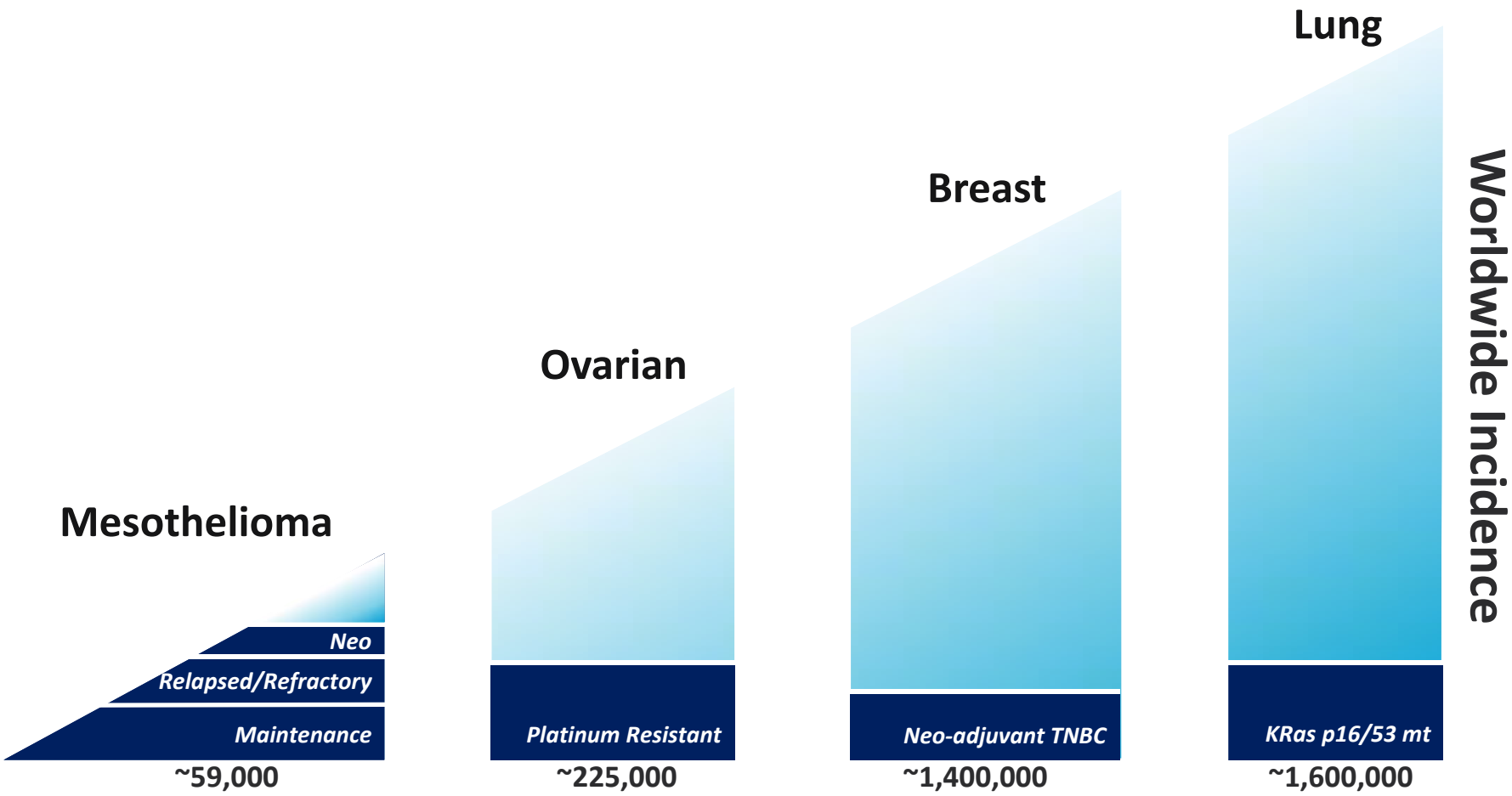


Combinable *with paclitaxel*



Initial signs of ***clinical activity***

Pursuing the Potential of Targeting Cancer Stem Cells for Patients Worldwide




We want to change the way cancer is treated by targeting cancer stem cells

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