Progress Update and 2015 Outlook

January 8, 2015

NASDAQ: VSTM

Forward-Looking Statements

This presentation and other matters discussed today, or answers that may be given to questions asked, include forward-looking statements about the Company's strategy, future plans and prospects, including statements regarding the development of the Company's compounds, including VS-6063, VS-4718, VS-5584 and VS-507, and the Company's FAK, PI3K/mTOR, Wnt and diagnostics programs generally, the timeline for clinical development and regulatory approval of the Company's compounds, the expected timing for the reporting of data from on-going trials and for the COMMAND interim analysis, the expected timing of completion of COMMAND enrollment, the structure of the Company's planned or pending clinical trials, the Company's rights to develop or commercialize its compounds and the ability of the Company to finance contemplated development activities and to fund operations for a specified period. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," "proposed," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Each forward-looking statement is subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statement. Applicable risks and uncertainties include the risks that the preclinical testing of the Company's compounds and preliminary data from clinical trials may not be predictive of the results or success of pending or later clinical trials, that data may not be available when we expect it to be, that enrollment will take longer than expected, that our compounds will cause unexpected safety events, that the Company will be unable to successfully initiate or complete the clinical development of its compounds, including VS-6063, VS-4718, and VS-5584, that the development of the Company's compounds will take longer or cost more than planned, and that the Company's compounds will not receive regulatory approval or become commercially successful products. Other risks and uncertainties include those identified under the heading "Risk Factors" in the Company's Annual Report on Form 10-K for the year ended December 31, 2013 and in any subsequent SEC filings. The forward-looking statements contained in this presentation reflect the Company's current views with respect to future events, and the Company does not undertake and specifically disclaims any obligation to update any forward-looking statements.

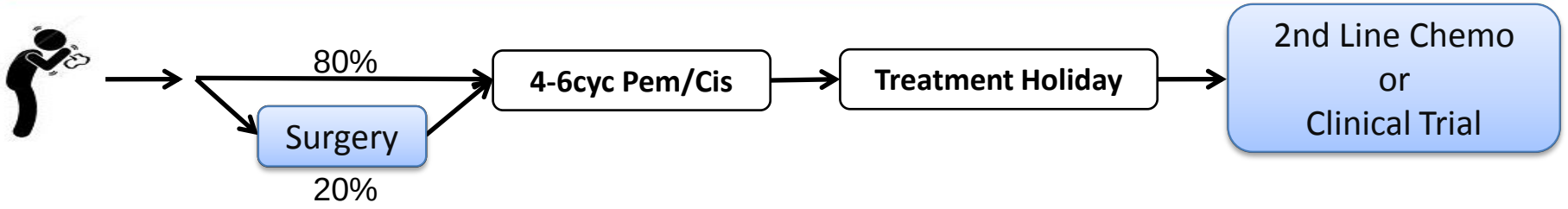
Pipeline Progress in 2014: Building Momentum

VS-6063	VS-4718	VS-5584
✓ Opened COMMAND in 13 countries. Enrollment is on track with interim expected Q2 2015	✓ Phase 1 trial is on track and enrolling well	✓ Phase 1 trial is on track and enrolling well
✓ Completing the Japanese Phase 1 opened COMMAND in Japan	✓ No DLTs to date and encouraging signs of clinical activity	✓ Well into active range with encouraging signs of clinical activity
✓ Mesothelioma: "Window of Opportunity" data	✓ Reported supportive preclinical data at AACR, EORTC, and ASH	✓ Reported supportive preclinical data at AACR, iMig, EORTC
✓ Ovarian: Phase 1/1b data with paclitaxel	✓ Published in Science Translational Medicine	✓ Published in *Molecular Cancer Therapeutics*
✓ NSCLC: 12 week PFS rate at interim analysis met in 2 cohorts	✓ Published in *Blood*	

VS-6063

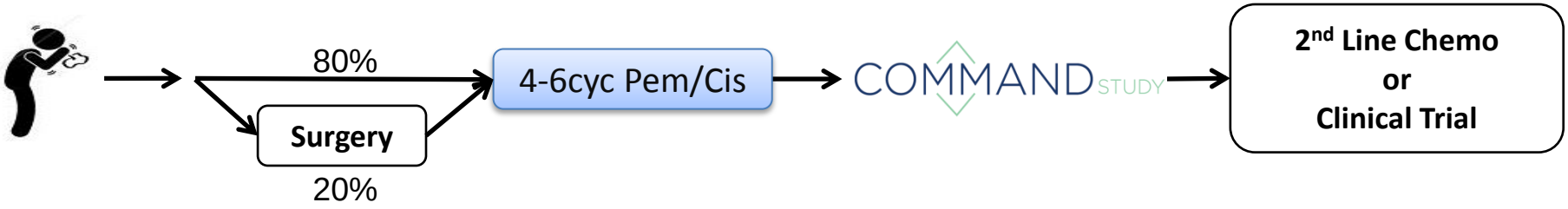
Oral Focal Adhesion Kinase Inhibitor

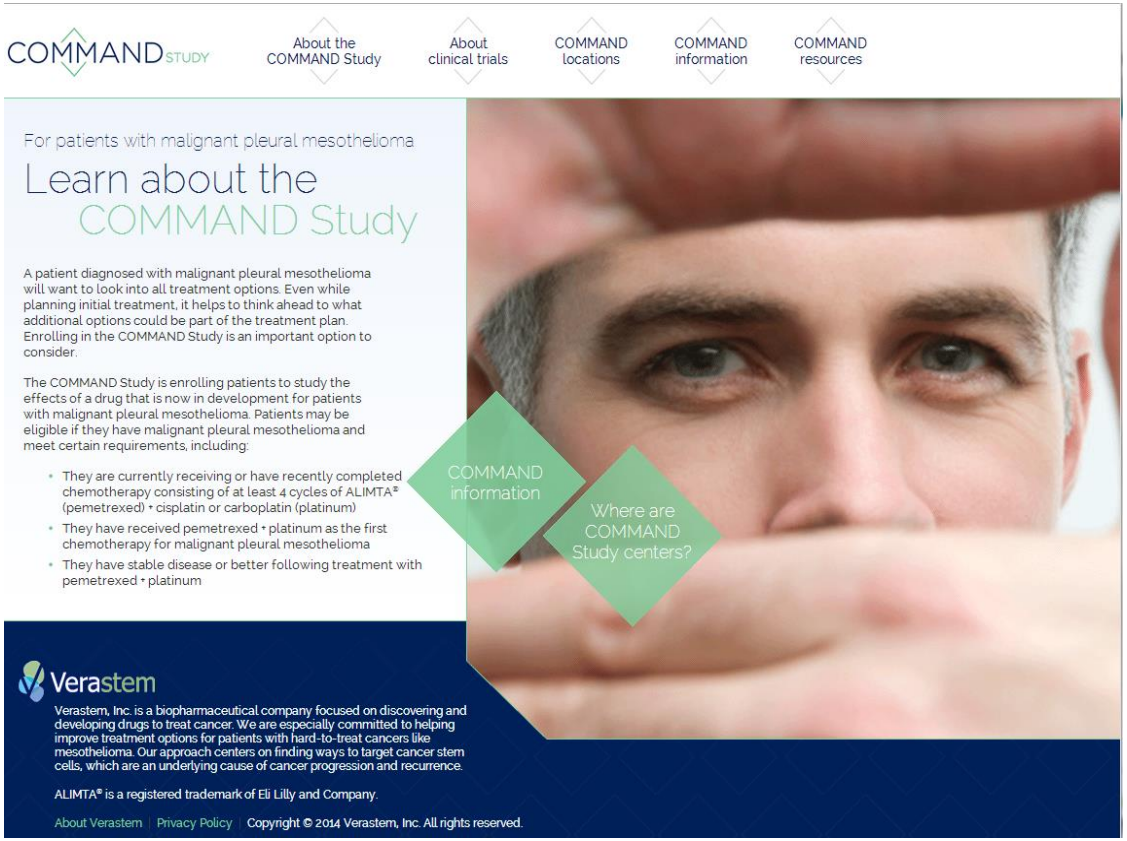
Demonstrated Activity of FAK Inhibitors in Mesothelioma



- VS-6063 has demonstrated activity in the neo-adjuvant setting
- VS-6063 Phase 1 in Japanese subjects included 1 patient with relapsed mesothelioma
  - Symptom improvement and PFS of 5.6 months
- VS-4718 Phase 1 has enrolled 3 mesothelioma patients to date
  - Two patients have had disease stabilization of greater than 5 months
- GSK evaluated 29 patients with their FAK inhibitor (GSK2256098) in the relapsed setting
  - Treatment resulted in median PFS of 4.5 months vs historical control of 1.5 months
  - Increased activity observed in merlin low (median PFS = 6 months)

COMMAND: A Registration-Directed Study of VS-6063 as Switch Maintenance in Mesothelioma





International Mesothelioma Steering Committee

Anna Nowak, Australia

Dean Fennell, United Kingdom

Hedy Kindler, USA

Larry Schwartz, USA

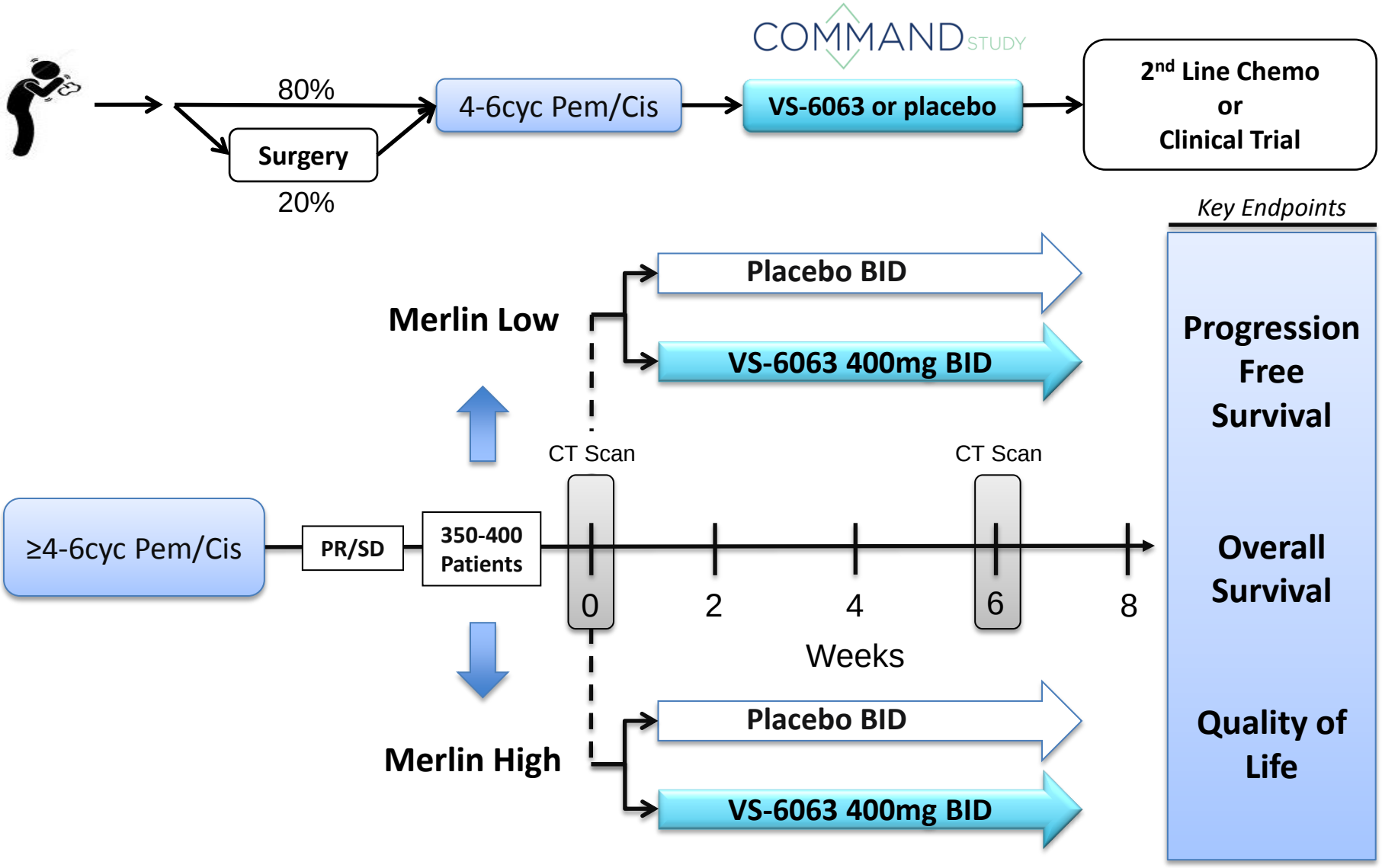
Lee Krug, USA

Paul Baas, Netherlands

Richard Gralla, USA

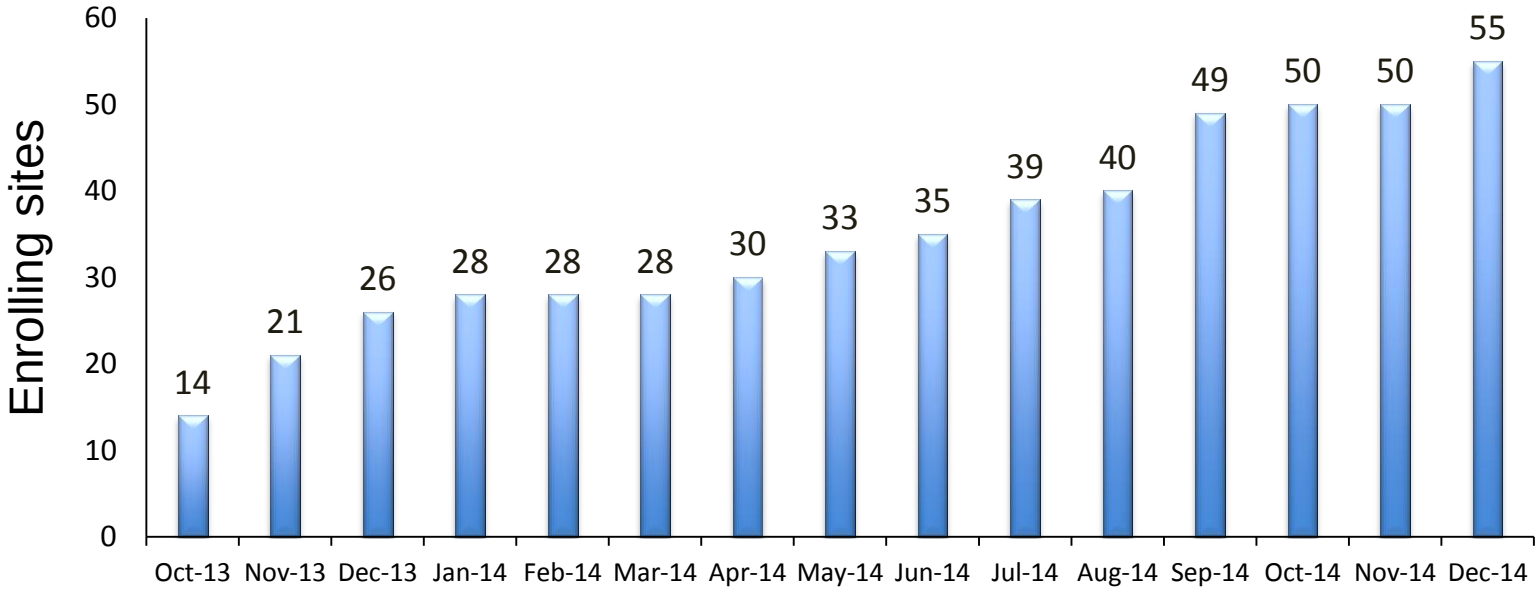
Takashi Nakano, Japan

COMMAND: A Registration-Directed Study of VS-6063 as Switch Maintenance in Mesothelioma



COMMAND: A Simultaneous, Multinational Development Strategy

- 13 countries activated
- 55 sites open and enrolling



COMMAND: Enrollment is Currently On-Track for Completion by YE 2015

Data Safety Monitoring Board

Has met twice and has not interrupted or modified the study

Patient Enrollment

Targeting 372 patients

180 patients randomized

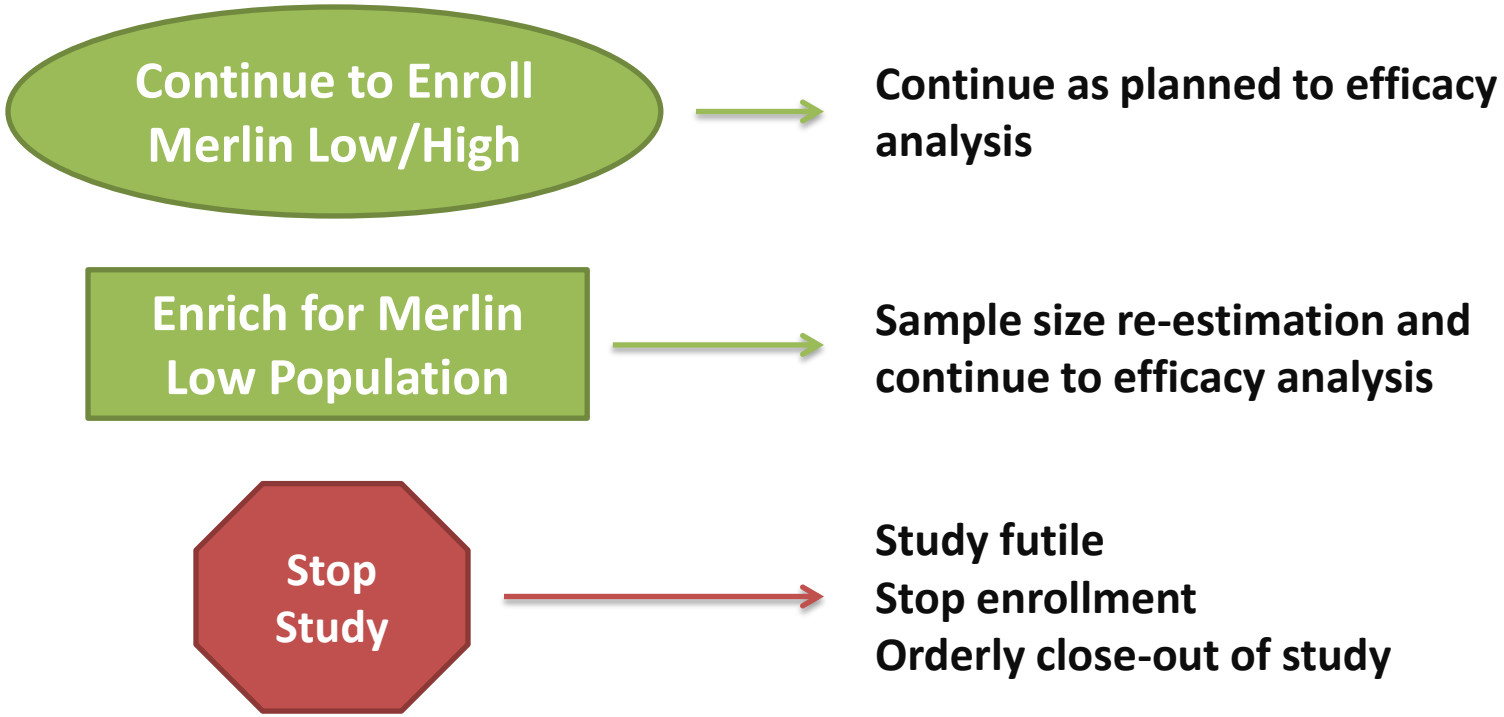
On track

Merlin Status

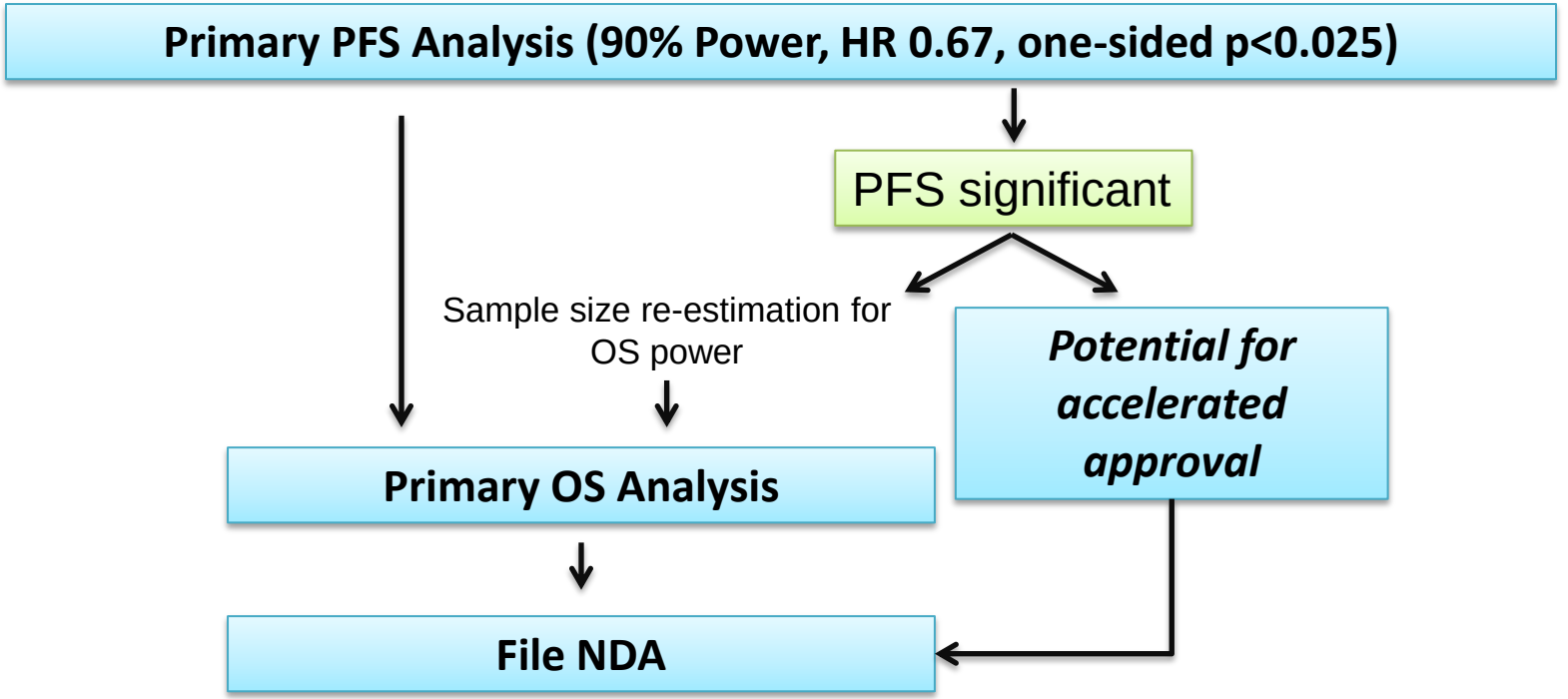
To date: 41% of patients have tumors that are merlin-low which is consistent with our assumptions

COMMAND Interim Analysis to Define Patient Population – Expected Q2 2015

- The interim analysis will occur when 50% of progression events are reported
- Decision rules for the interim analysis are based on the conditional power to detect a difference in PFS between active and placebo groups
- Conditional power levels set in conjunction with two separate, independent, statistical teams

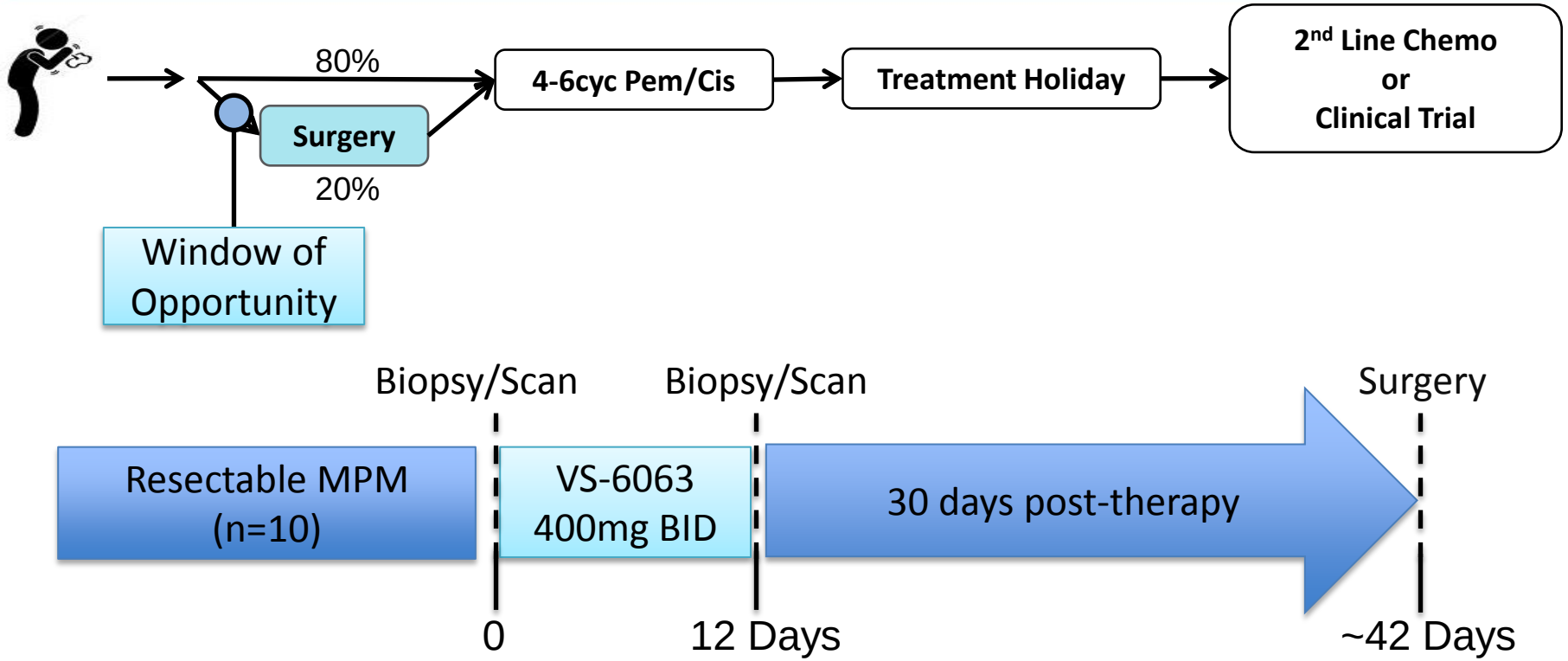


COMMAND is Designed to Support Worldwide Regulatory Filing



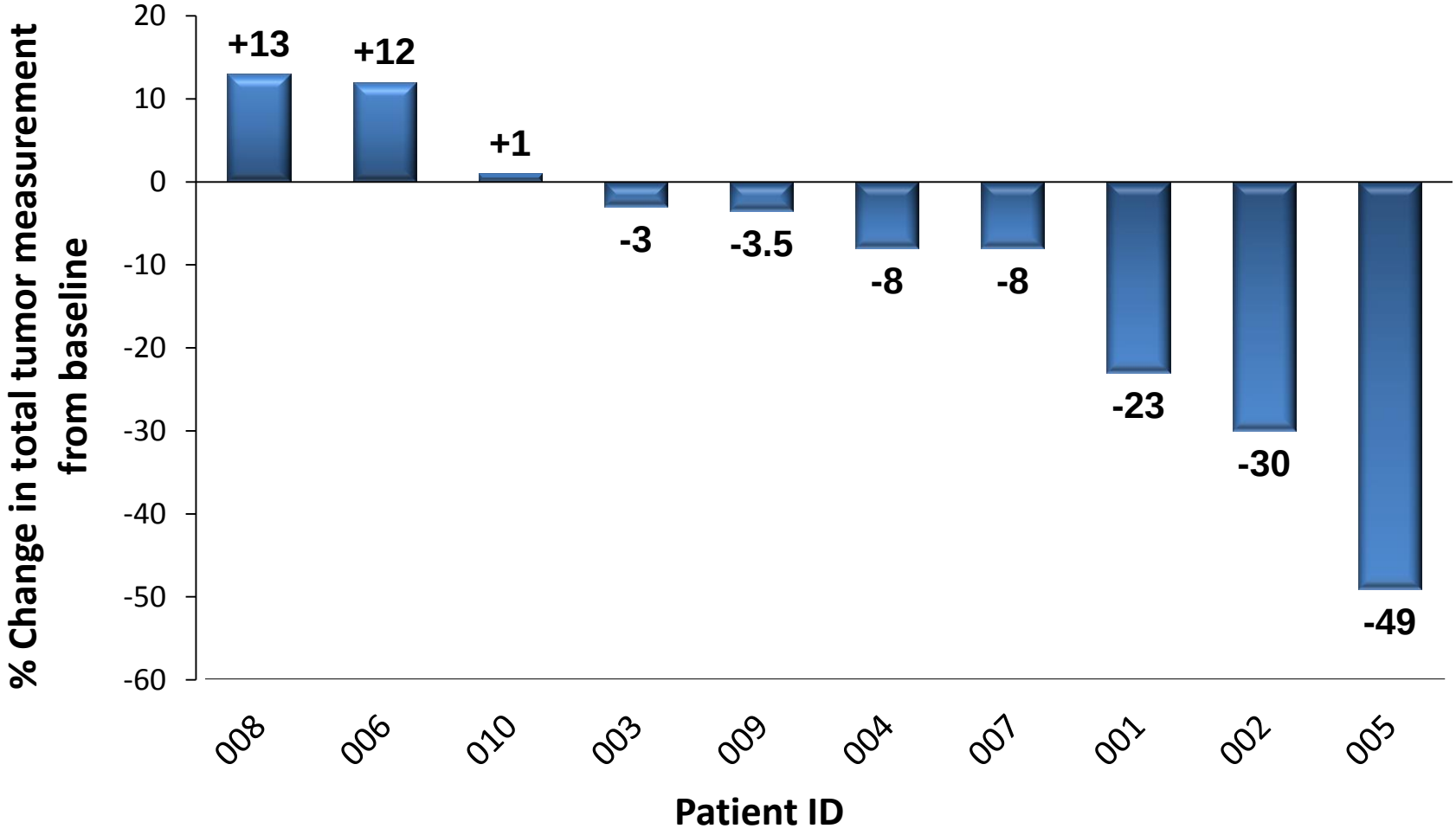
- If the primary PFS endpoint is significant, we will discuss filing strategies with the FDA and other agencies
- Continue study to OS analysis

Biomarker Study in Patients with Surgically-Eligible Mesothelioma (Window of Opportunity)



- VS-6063 inhibited FAK activity by 70% in evaluable biopsies
- VS-6063 reduced markers of cancer stem cells in 5 of 7 evaluable biopsies
- Tumor response evaluated by PET/CT using RECIST modified for mesothelioma
- Protocol amendment approved for 35 day dosing

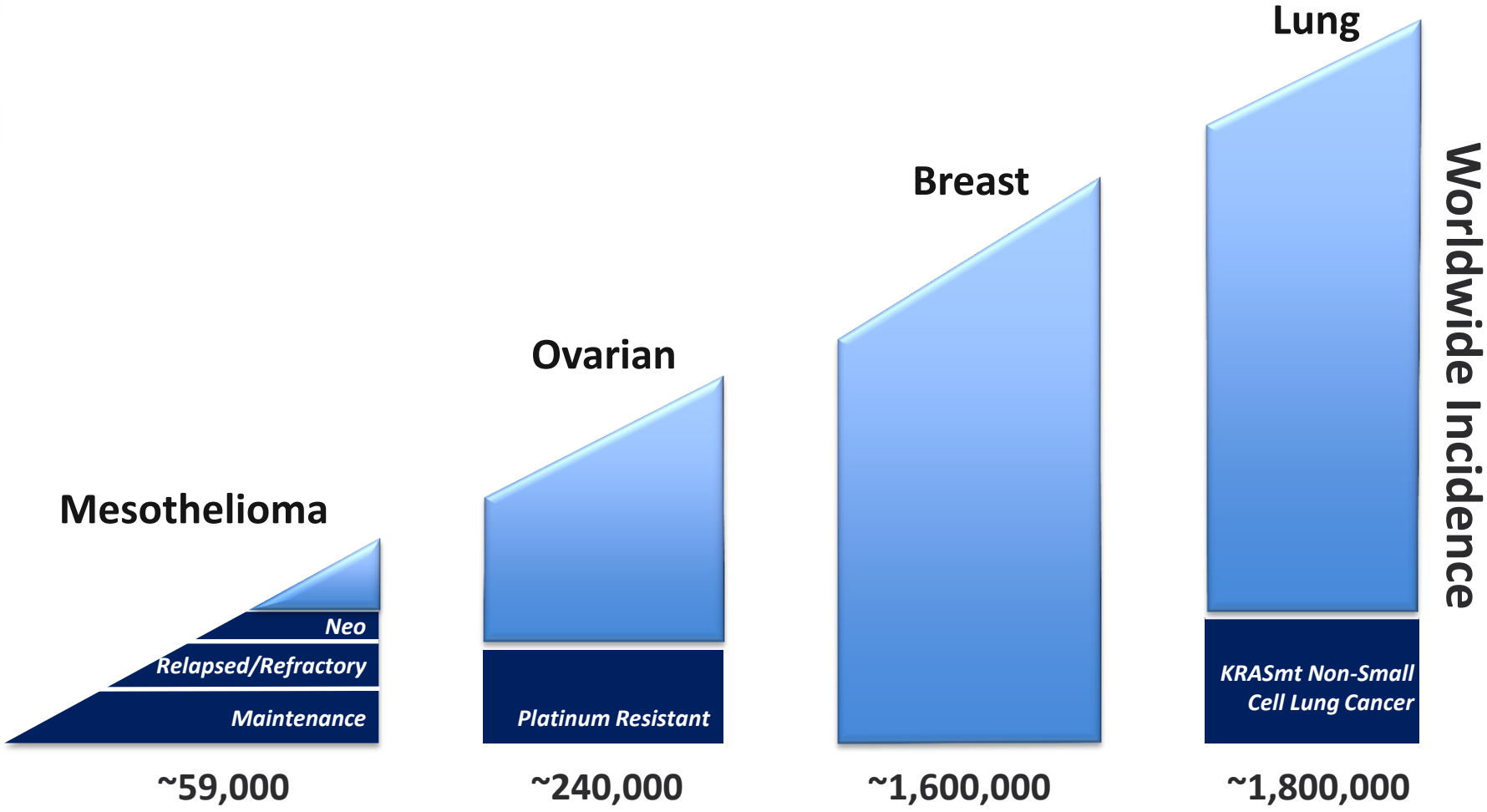
Encouraging Early Signal After 12 Days of Treatment with VS-6063



PET/CT performed to guide biopsy
Tumor response assessed using RECIST modified for mesothelioma
Unlocked, in-progress data as of Aug 2014

Bueno et al., iMig 2014

Approval in Mesothelioma is a Potential Gateway to Many Cancers



VS-6063: Well Tolerated and Signs of Activity in Phase 1 as Single Agent

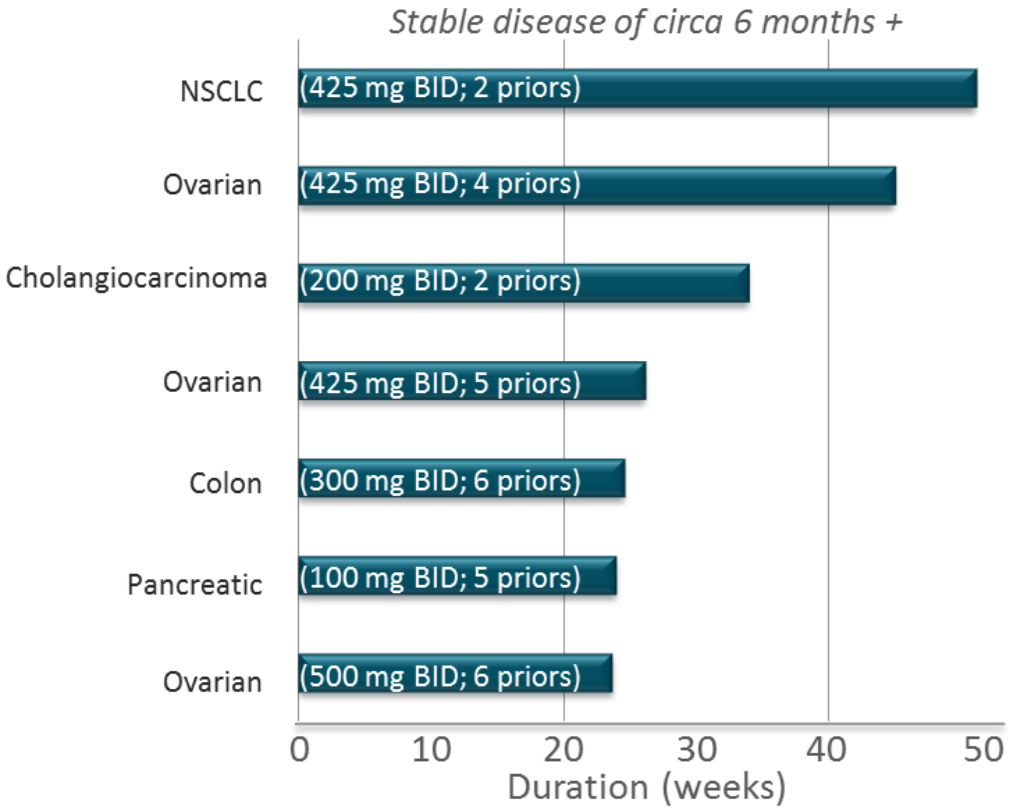
Generally Well Tolerated

	Grade				
	1	2	3	4	Total
Adverse Events*	**N (%)**	**N (%)**	**N (%)**	**N (%)**	**N (%)**
Nausea	14 (30)	3 (7)	0	0	17 (37)
Unconjugated hyperbilirubinemia	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)

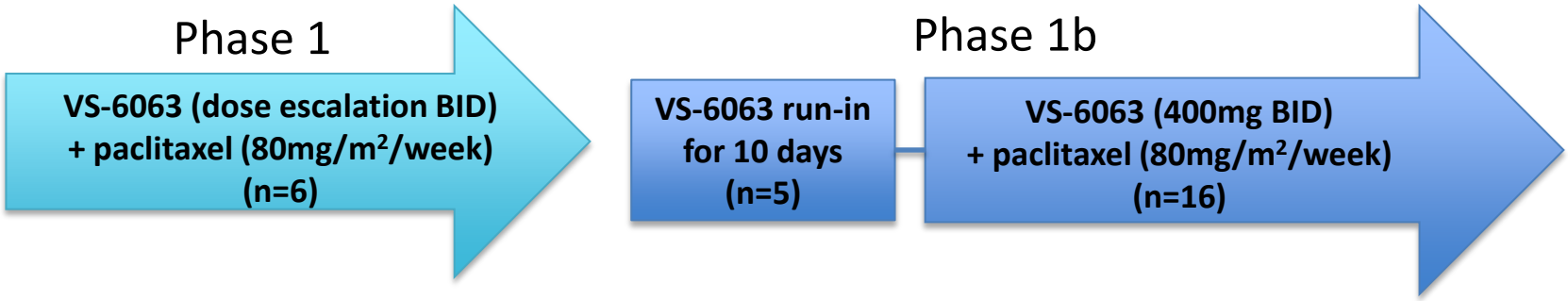
*Treatment-Related Adverse Events (≥20%)

Jones SF J Clin Oncol 2011 29:1 (suppl; abstr 3002)

Initial Signs of Clinical Activity



VS-6063 and Paclitaxel in Patients with Ovarian Cancer: A Combinable Regimen with Potential for Many Indications



Design

- A Phase 1 dose escalation of VS-6063 with weekly paclitaxel
- 5 patients in Phase 1b had a 10-day run in with single agent VS-6063 with pre/post biopsies

Status

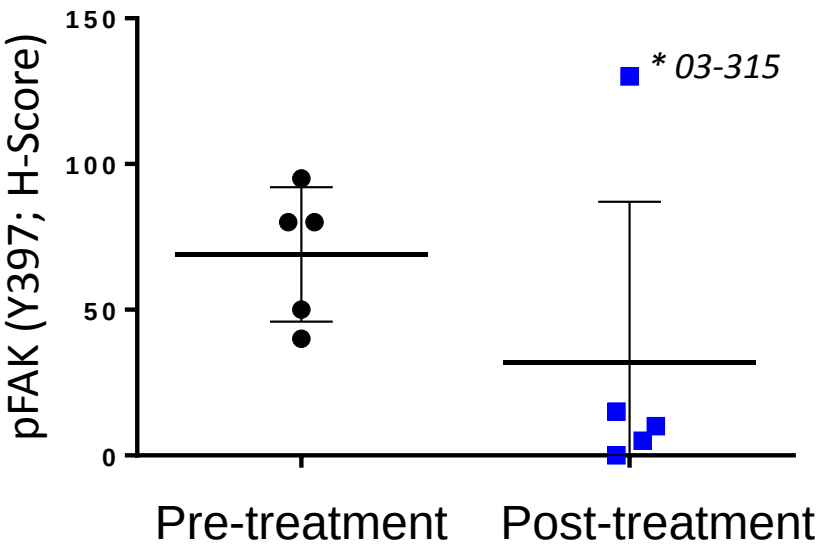
- Enrollment complete: 22 patients with relapsed ovarian cancer (6 on dose escalation and 16 in expansion cohort)

Results

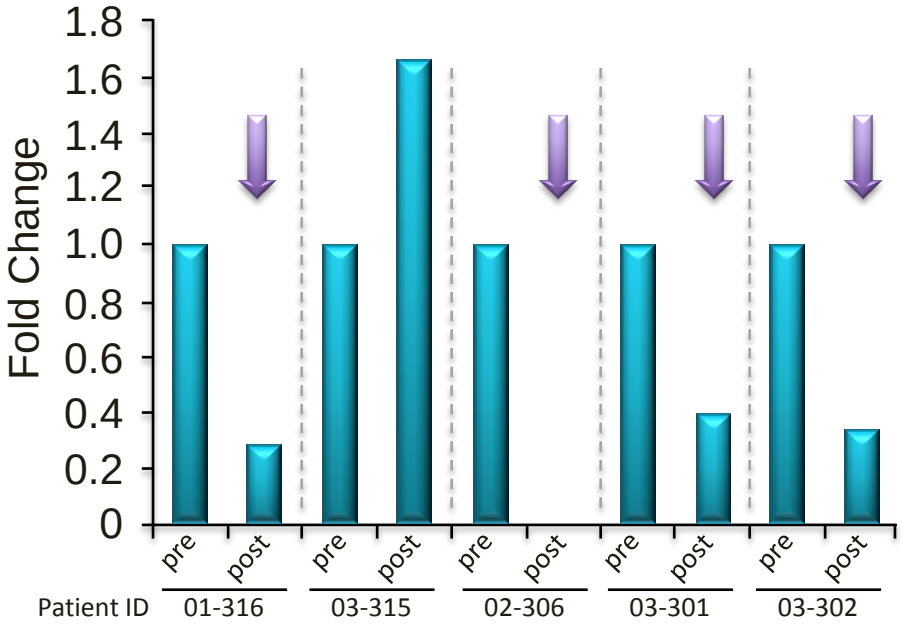
- The combination of VS-6063 and weekly paclitaxel was generally well tolerated and did not alter the pharmacokinetics of paclitaxel exposure
- Paves the way to several other indications where paclitaxel is standard of care

VS-6063 Has On-Target Effects in Patient Biopsies: Reductions in FAK Activity & Cancer Stem Cell Markers Observed

FAK Activity



Cancer Stem Cells

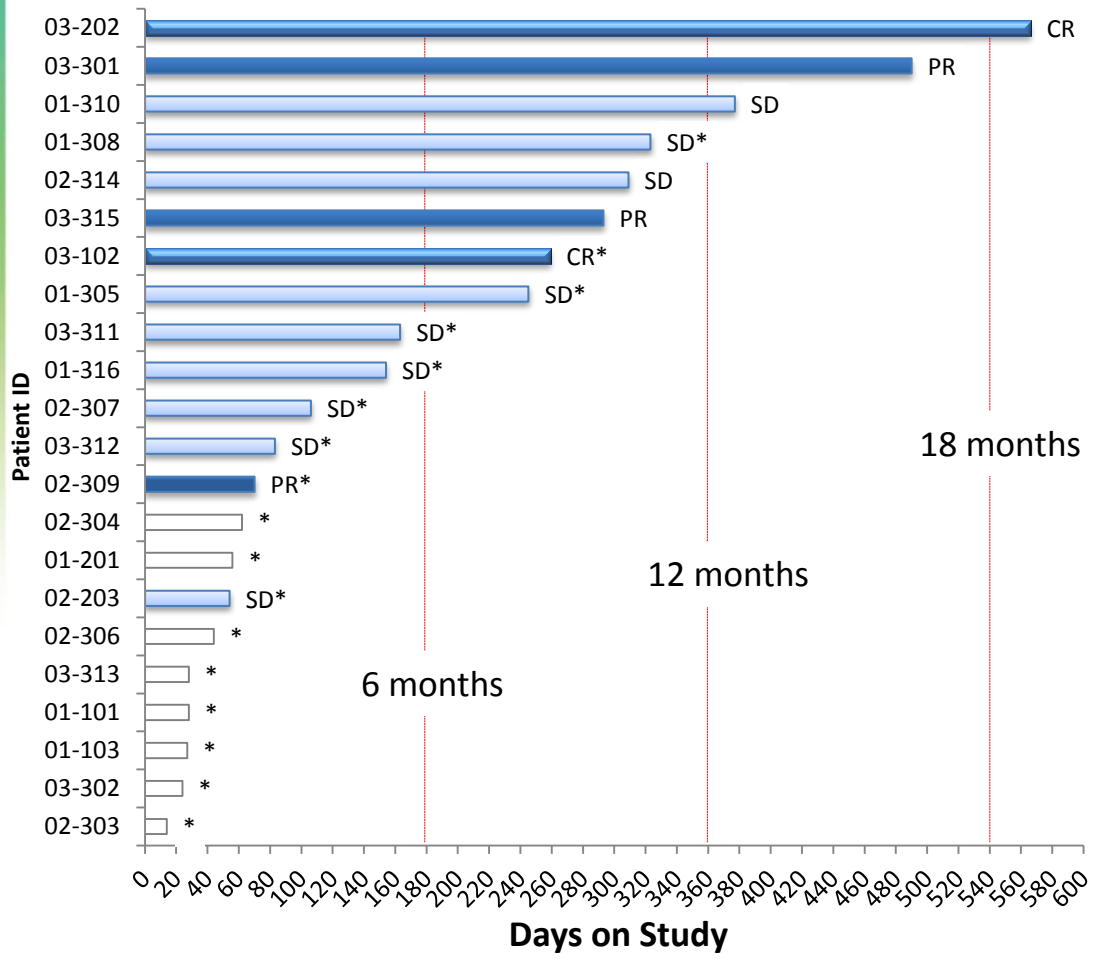


- Paired tumor biopsies were obtained in five patients following 10 days of VS-6063 administration (400 mg BID)
- The same 4 patients with reductions in FAK activity also had a reduction in markers of cancer stem cells

Unlocked, in-progress data as of 15 Dec 2014

VS-6063 and Paclitaxel Combination Shows Activity in Ovarian Cancer

Overall Best Response of at least Stable Disease of ≥8 weeks: 64%



Objective Response or Stable Disease ≥6 months	N (%)
Complete Response (CR)	2 (9%)
Partial Response (PR)	3 (14%)
Stable Disease ≥6 months	4 (18%)
Overall	**9 (41%)**

N=22 (80% Platinum Resistant)

5 patients still on study

1 Complete Response

2 Partial Response

2 Stable Disease (≥6 months)

CR

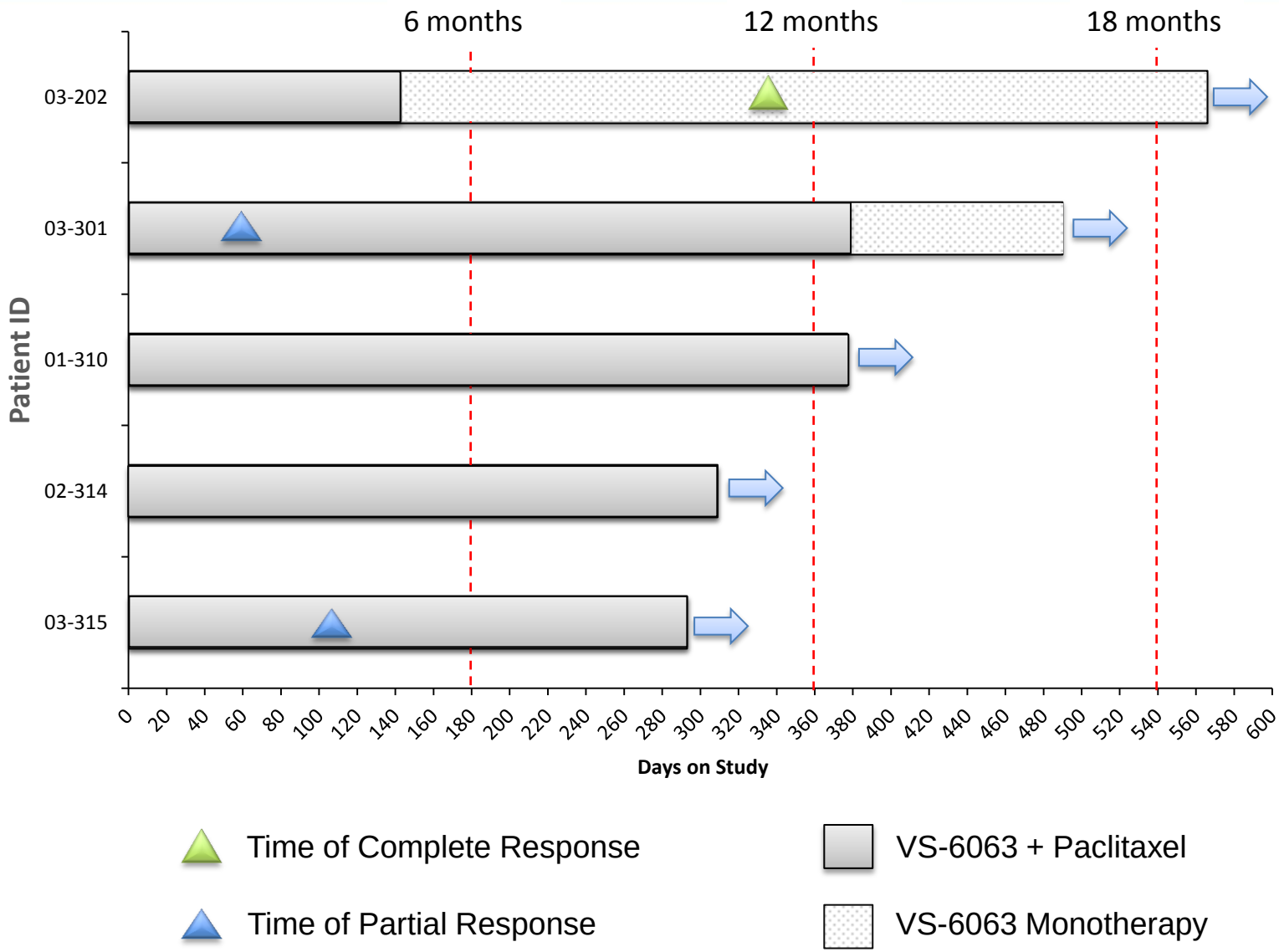
PR

SD

* Off study

Unlocked, in-progress data as of 15 Dec 2014

Five Patients Remain on Study with Durable Disease Control: Three Over 12 Months to Date



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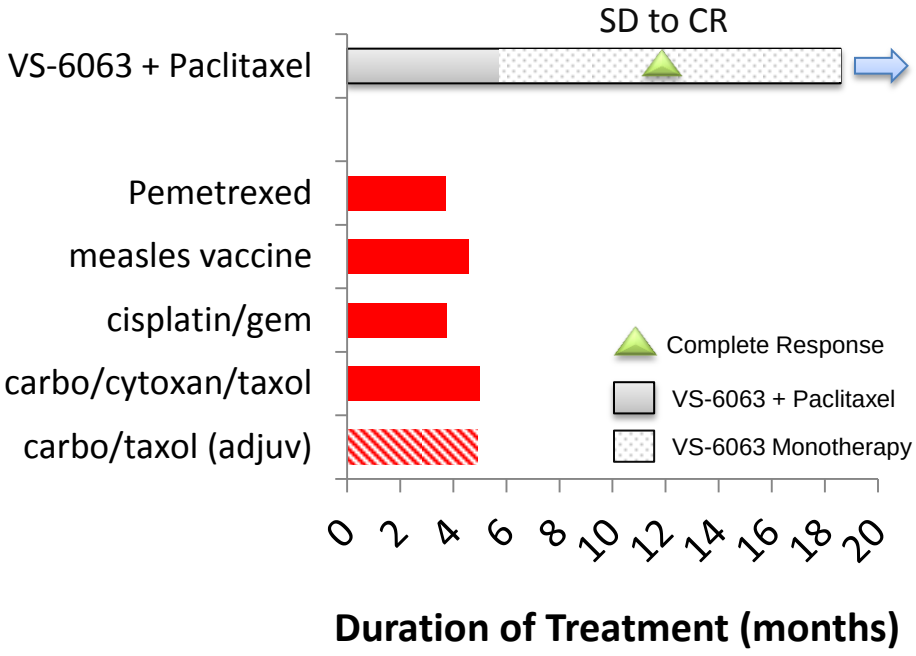
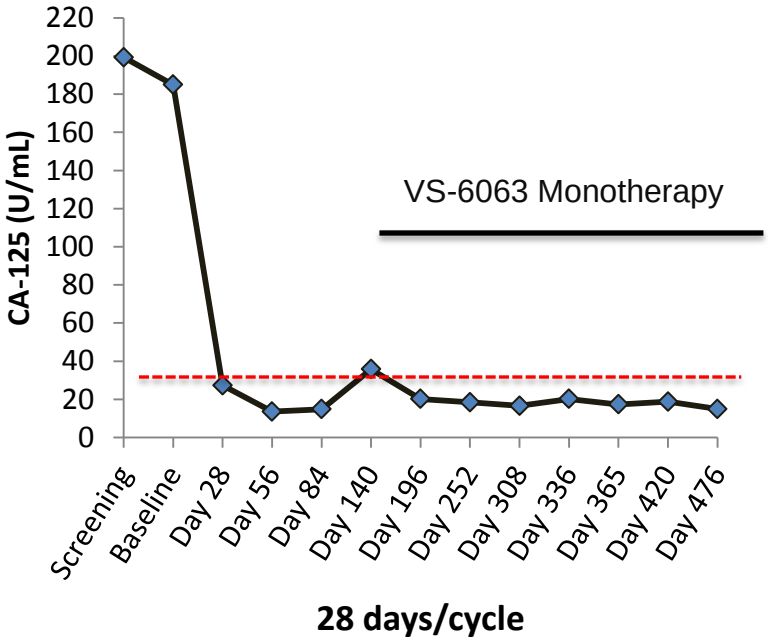
Patient 03-202: Achieved Complete Response on Single Agent VS-6063

- 71 year old patient at screening with stage IV platinum-resistant serous ovarian cancer. Had 4 prior lines of therapy for recurrent disease
- Disease stabilization on combination treatment but discontinued paclitaxel because of toxicity at 4.5 months. Continued on VS-6063 monotherapy
- While on VS-6063 monotherapy the two remaining lesions disappeared at 11.8 months
- On study for >18 months and is tolerating VS-6063 well

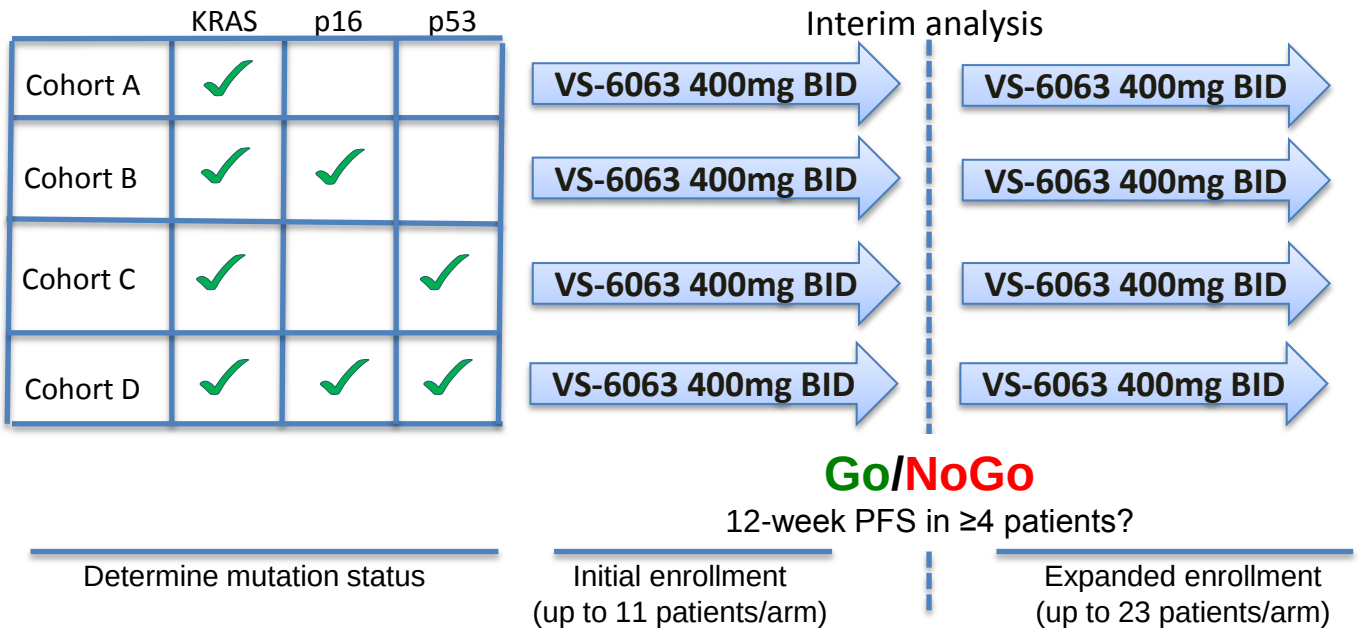




 *Unlocked, in-progress data as of 15 Dec 2014

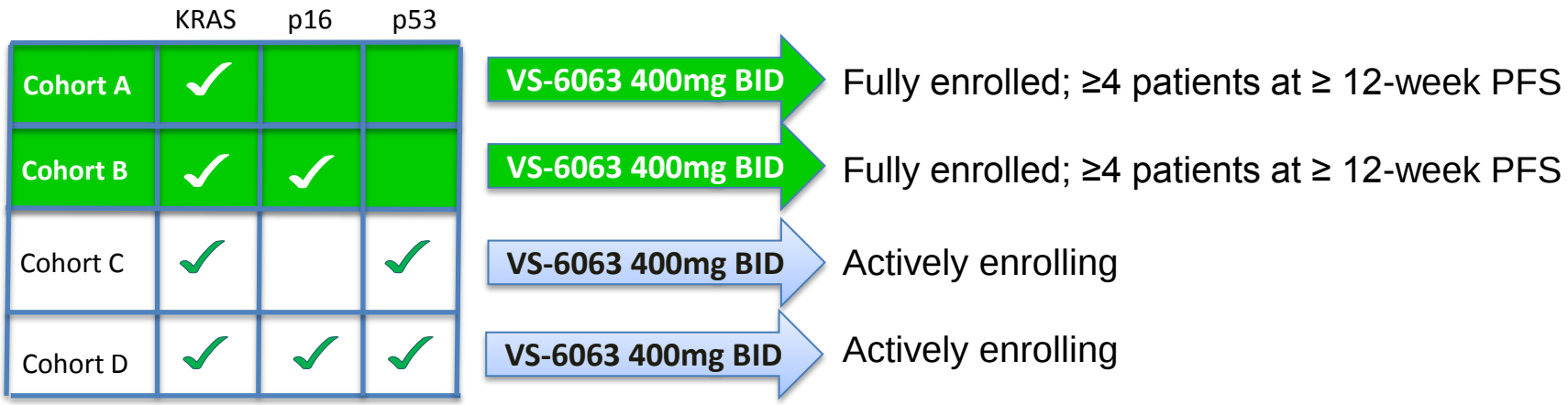
Phase 2 Study of Single Agent VS-6063 in Patients with KRAS-mutated Non-Small Cell Lung Cancer

- NSCLC patients stratified by KRAS/p16/p53 mutation status
  - Poor prognosis and limited treatment options: Median OS of ~6mo and PFS of 6 weeks
- A key study endpoint is single-agent VS-6063 safety for potential mesothelioma NDA
- Simon two-stage design with an interim analysis of ≥12 week PFS in ≥4/11 patients



Encouraging Signals To Date in NSCLC: Two Cohorts Achieved the Interim Analysis Threshold

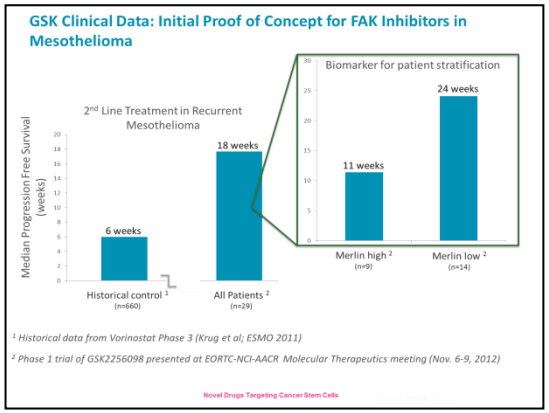
- Study accruing well at 9 US sites
- Long-term use proving generally well tolerated with some patients on study for over 6 months
- Accrual has completed in 2 cohorts and expect to fill remaining cohorts in H1 2015
- The fully accrued cohorts have both achieved the interim threshold

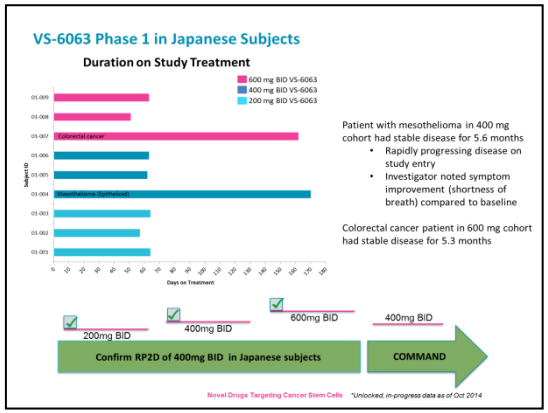


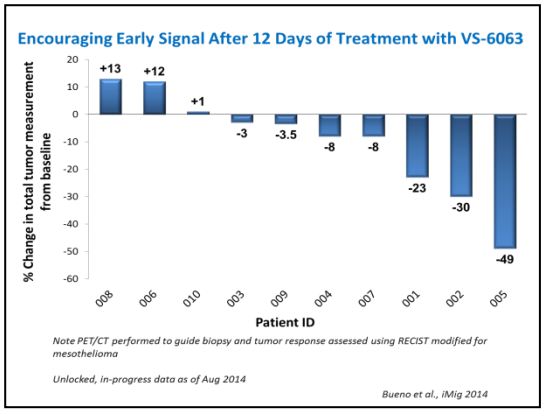
Will decide on potential next steps once all of the cohorts are completed

*Unlocked, in-progress data as of 5 Jan 2015

Increasing Evidence Supports our Confidence in 6063







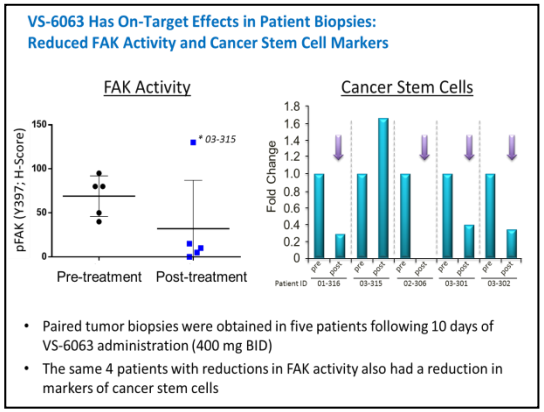
FAK Inhibitors in relapsed mesothelioma

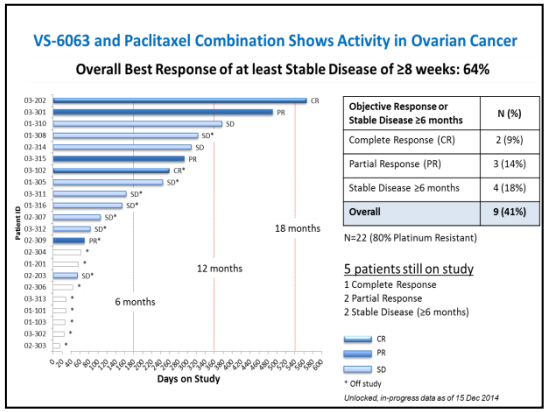
VS-6063 in ovarian cancer

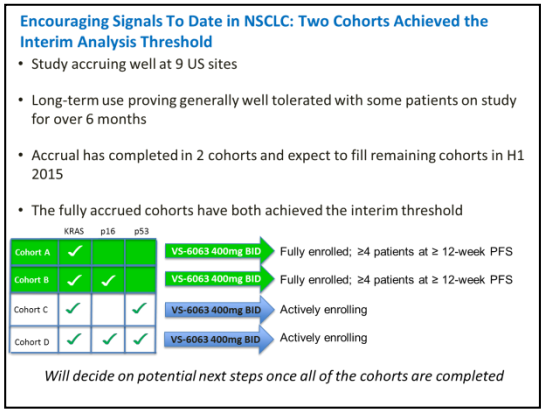
Verastem

VS-6063 in neo-adjuvant mesothelioma

VS-6063 non-small cell lung cancer







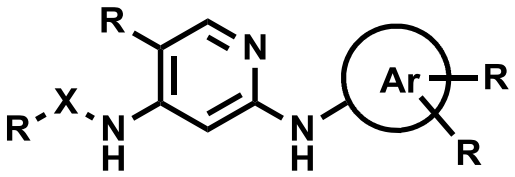
VS-4718

Oral Focal Adhesion Kinase Inhibitor

VS-4718 – FAK Inhibitor Structurally Distinct from Lead

- Orally available, potent, low nanomolar inhibition of FAK kinase
- Targets cancer stem cells in *in vitro* and *in vivo* models of cancer

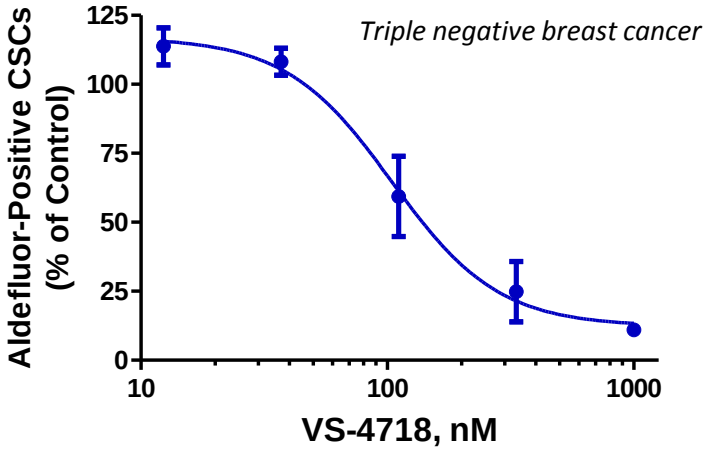
Biochemical Properties



FAK Enzymatic IC_{50} = 42 nM
FAK Cellular EC_{50} = 31 nM

Composition of matter though 2028

Cancer Stem Cells



VS-4718: Phase 1 is Progressing Well Through Dose Escalation

Design

- Biopsy-driven Phase 1 dose escalation study in solid tumors

Status

- Generally well-tolerated to date
- MTD has not yet been reached
- Expect to report preliminary data in H2 2015

Observations

- Two patients with mesothelioma have had disease stabilization for greater than 5 months

*Unlocked, in-progress data as of 5 Jan 2015

VS-5584

Oral Dual mTORC1/2 and PI3K Inhibitor

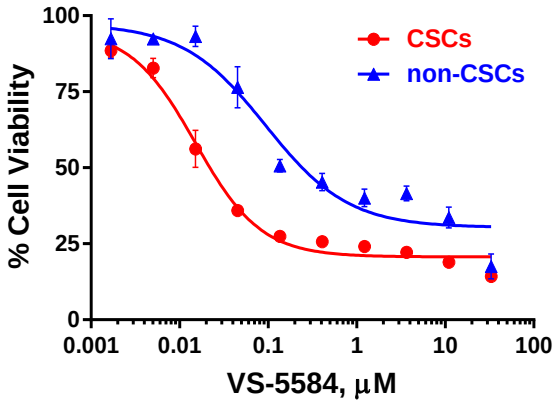
VS-5584 – Dual mTORC1/2 and Pan-PI3K Inhibitor

- Orally available, potent dual mTORC1/2 & pan-PI3K inhibitor
- Demonstrated preferential activity against cancer stem cells in preclinical models *in vitro* & *in vivo*
- Utilizing an intermittent dosing schedule of 3x/week

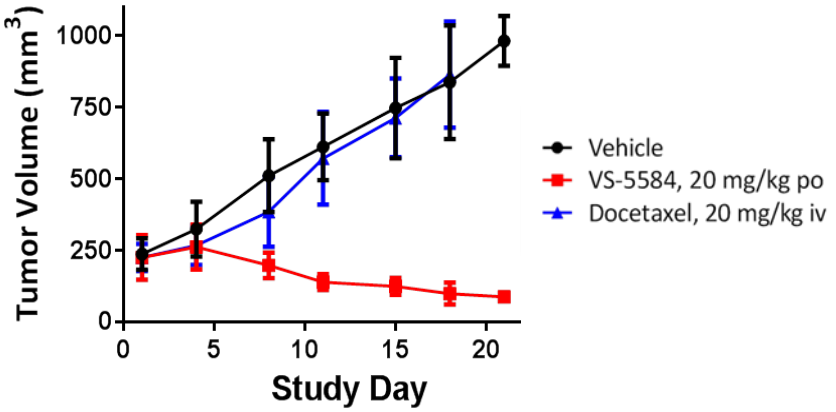
VS-5584 Biochemical Potencies (nM)

mTOR	PI3K-Alpha	PI3K-Beta	PI3K-Delta	PI3K-Gamma
3.4	2.6	21	3.0	2.7

Preferential Inhibition of CSCs



Chemo-resistant Breast Cancer



VS-5584: Building Confidence in the Potential for a Therapeutic Window

Design

- Phase 1 dose escalation study in solid tumors

Status

- Generally well tolerated to date and the expected on-target effects are clinically manageable
- MTD has not yet been reached
- Expect to report preliminary data in H2 2015

Observations

- Well within active dose range based on PD biomarker measurements
- Initial clinical activity in mesothelioma and other tumors
- Disease control of 6 months or more has been observed

Confidence to initiate combination of VS-5584 and VS-6063 in relapsed/refractory mesothelioma Q1 2015

*Unlocked, in-progress data as of 5 Jan 2015

2015 Is a Pivotal Year for Verastem

COMMAND Interim Analysis: Q2 2015

Anticipated company updates

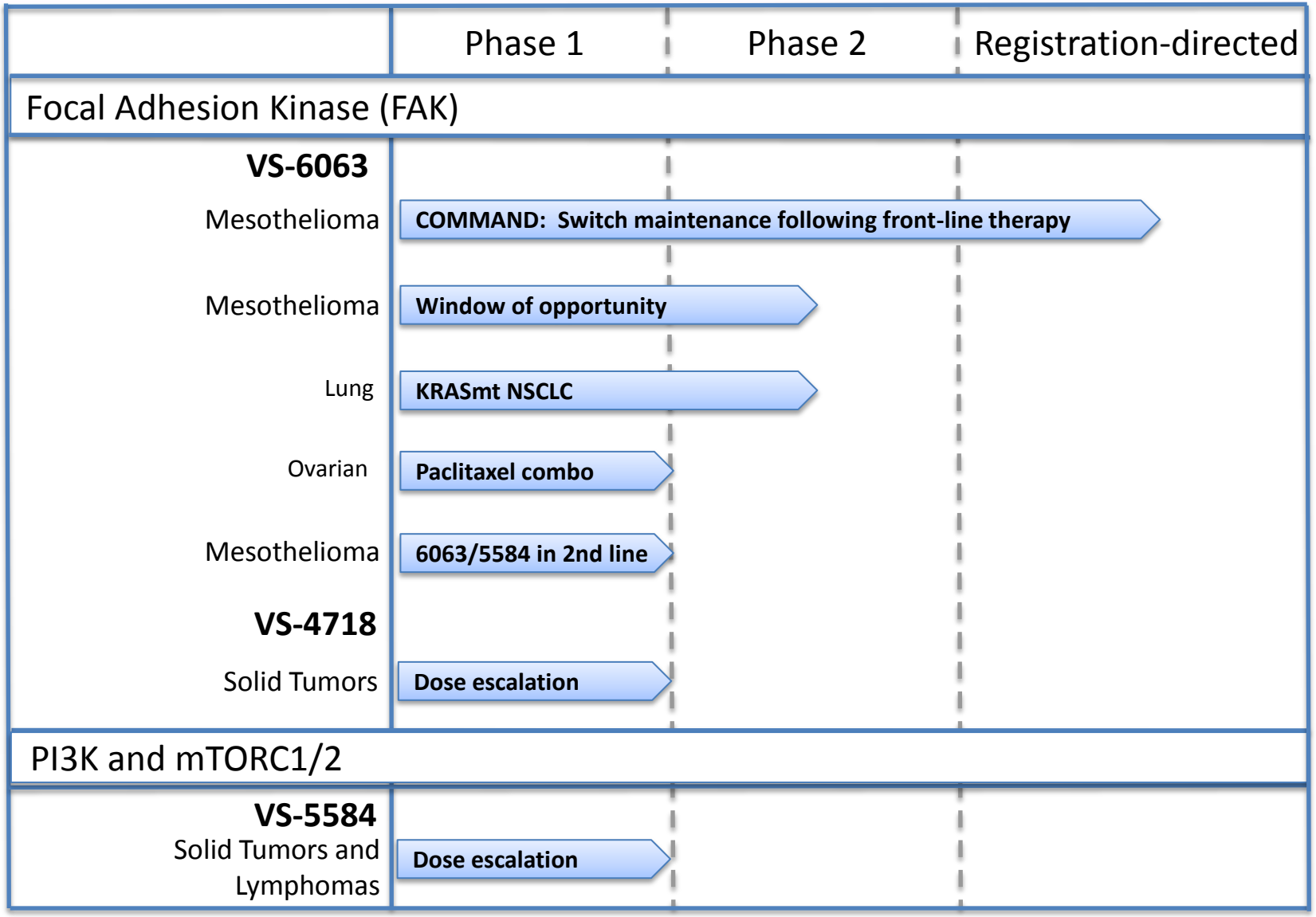
- 2014 Year End Financials: March, 2015
- ASCO Analyst and Investor Breakfast, Sunday, May 31, 2015

Data expected to be disclosed at major medical meetings

- VS-6063
  - VS-6063 Phase 2 KRASm NSCLC: H2 2015
  - VS-6063 Phase 2 Meso Window of Opportunity study: H1 2016
  - VS-6063/Paclitaxel combination in ovarian cancer: H2 2015
- VS-4718
  - VS-4718 Phase 1: H2 2015
- VS-5584
  - VS-5584 Phase 1: H2 2015

Note: Will update on ongoing trials as appropriate at company events

Portfolio of Product Candidates Targeting Cancer Stem Cells



Question and Answer Session