

March 7, 2012

## Market Outperform / Speculative Risk

### Ripping Cancer Out By the Root

#### MARKET DATA 3/7/2012

Price	\$10.76
Exchange	NASDAQ
Target Price	\$19.00
52 Wk Hi - Low	\$11.85 - \$10.00
Market Cap(MM)	\$226.6
EV(MM)	\$233.1
Shares Out (MM)	21.1
Public Mkt Float (MM)	21.1
Avg. Daily Vol	NA
Short Interest	171,503

#### BALANCE SHEET METRICS

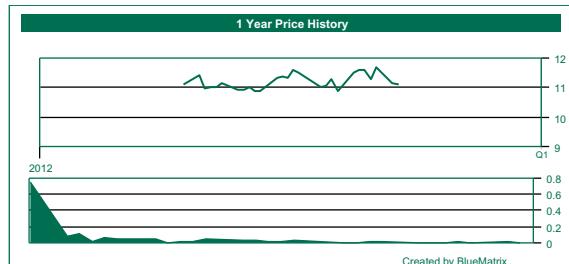
Cash (MM)	\$117.1
LTD (MM)	\$0.0
Total Debt/Capital	NA
Cash/Share	\$5.54
Book Value(MM)	NA
Book Value/Share	NA

#### EARNINGS DATA (\$)

FY - Dec	2011E	2012E	2013E
Q1 (Mar)	--	(0.07)	--
Q2 (Jun)	--	(0.12)	--
Q3 (Sep)	--	(0.15)	--
Q4 (Dec)	(0.26)	(0.18)	--
Full Year EPS	(5.07)	(0.34)	(0.71)

#### INDICES

DJIA	12,776.6
SP-500	1,345.7
NASDAQ	2,598.3
NBI	1,211.2



**Ridding the body of cancer, root and branch.** We are initiating coverage of Verastem, Inc., (VSTM) with a Market Outperform rating and a price target of \$19. VSTM is leveraging the burgeoning knowledge of the biology of the cancer stem cell, which is potentially the most important cell in the tumor milieu as it is both immortal and resistant to most currently-available interventions. In addition, recent research suggest both conventional chemotherapy and certain targeted therapies such as Avastin actually increase the proportion of the tumor cell population that carry "stem-like" properties . VSTM's mission is to use its proprietary technology to develop small molecule compounds that specifically target cancer stem cells.

**Key to success: assembling a world-class scientific team.** VSTM was founded upon the science of a premier team from MIT (from both the Whitehead and Broad Institutes) including Robert Weinberg, PhD, the scientist credited with the discovery of the first oncogene as well as the first tumor suppressor gene. Weinberg is also regarded as the chief proponent of the theory of the endothelial-mesenchymal transition (EMT), the interface between immature, cancer-like cells and mature, normal cells. In addition to Weinberg, the two other scientific founders of VSTM include Eric Lander, PhD, a mathematician turned biologist who was involved in, among other things, the sequencing of the human genome, and Piyush Gupta, Ph.D., who was in large part responsible for the discovery of VSTM's proprietary stem-cell screening assay used to discover the company's lead asset, VS-507.

**VSTM management has an accomplished track record, too.** Founding members of management include President and CEO Christoph Westphal, MD, PhD, who, as a venture capitalist, was responsible for the founding of three highly successful biotechnology companies: Alnylam (ALNY, Market Outperform), Momenta (MNTA, Not Rated) and Sirtris, sold to GlaxoSmithKline (GSK, Not Rated) in 2008 for \$724 million. Other key members of management include COO Robert Forrester, formerly of Coley Pharmaceuticals (sold to Pfizer (PFE, Not Rated) in 2007) and Combinatorix (now Zalicus, ZLCS, Market Outperform) and Jonathan Pachter, PhD, formerly of OSI Pharmaceuticals (now part of Astellas (4503-JP, Not Rated)), where he spent a number of years working on compounds affecting the EMT.

**Expecting multiple drivers over the next 12-24 months that will keep investor attention focused on shares.** In our view, the key driver of VSTM shares will be such items as data publications in peer-review journals, commencement of clinical trials, and potential partnering agreements. We also believe the shares warrant a premium given the company's position in the cancer stem cell land grab.

## Investment Thesis - Front Runner in the Cancer Stem Cell Land Grab

The concept of the cancer stem cell is a recent development in the field of cancer biology, and one that still generates controversy, even amongst respected researchers in the field. However, as the collective effort of scientists in the field advances the understanding, the evidence of the importance of the cancer stem cell in the propagation and maintenance of the tumor accumulates on a regular basis. As such, the work in the field is recapitulating that of other sub-specialties in cancer biology, including the validation of targets that are responsible for the growth and division of cancer stem cells, as well as driver mutations that prove attractive for intervention with small molecule drugs, antibodies as well as other approaches.

VSTM was founded principally on the work of Robert Weinberg, PhD, and the work of his former post-doctoral student, Piyush Gupta, PhD. Dr. Weinberg is an accomplished researcher in the field of cancer biology, and is a founding member of the Whitehead Institute at MIT. He is credited with the discovery of both the first human oncogene - a gene that can transform a normal cell into a cancer cell - as well as the first tumor suppressor gene. He is also credited with giving life to the thesis of the epithelial-mesenchymal transition, the biology of which we will discuss at greater length in this report.

Dr. Gupta, also of the Whitehead Institute, performed his thesis work in the lab of Dr. Weinberg and post-doctoral work in the lab of Dr. Lander. Dr. Gupta developed an assay that enabled the screening of compounds that could inhibit the formation of mammospheres, stem-like precursor cells that give rise to aggressive breast cancer cells. It was this assay that identified the activity of salinomycin, the basis for VSTM's lead program, VS-507. The results of this experiment were published in the August 13, 2009 advanced edition of the peer-reviewed publication, *Cell*.

It is upon these fundamental discoveries and broadly enabling technology that VSTM was founded. Because outstanding science has often been wasted at the hands of inept management in the biotechnology industry, we are greatly comforted and encouraged by the management team that has been gathered at VSTM. President and CEO, Christoph Westphal, is a serial entrepreneur with a proven track record of value creation in the biotech space. In our view, Westphal and his management team will provide VSTM with the kind of leadership that will motivate the team and bring about scientific and clinical value creation despite the company's early stage of development.

### Investment Risks

- Like any biotechnology company, the VSTM investment thesis is subject to a range of risks related to the challenges associated with drug discovery and development. In addition, VSTM's core technology, and the larger cancer stem cell space, is still relatively immature. Thus far, only a small number cancer stem cell therapeutic candidates has reached clinical development.
- The intellectual property landscape in the cancer stem cell space is complex, and many companies hold IP as a result of the rapid and geographically heterogeneous development of the field in academia before industry. While we view VSTM's IP position as enabling the company to have freedom to operate, the IP landscape in the cancer stem cell space continues to carry risk, and this uncertainty could have a negative impact on investor enthusiasm for VSTM shares.
- While the Company has sufficient capital to fund existing operations through the end of 2015, current investors should expect dilution to their existing holdings as a result of future financings, even if VSTM signs agreements that bring in cash in exchange for licenses to its IP or for rights to product candidates.

- Verastem must form partnerships with pharmaceutical companies to further the development of its therapeutic programs. Despite the general belief that pharmaceutical companies are looking to enrich their pipelines through deals with small biotech companies, consolidation in the industry and a desire for products in later-stage clinical trials is making it more difficult for biotech companies to strike lucrative partnerships around their earlier-stage products and technologies. Furthermore, even if VSTM is able to secure such partnerships, these arrangements often require the smaller biotech company to cede control of the clinical development process to its larger partner and, as a result, VSTM could lose control of the timeline for developing its products.
- Drug development is an inherently risky enterprise and VSTM could experience clinical trial failures for one or more its programs. A clinical setback could have a larger-than-normal effect on salvSTM shares, as investors may lose faith in the underlying technology, in addition to the specific program at issue, if there is a negative outcome in one of the Company's clinical programs or in one of its competitors' cancer stem cell programs.

### **Key Upcoming Milestones**

Milestone	Date
• Presentations at AACR Annual Meeting describing potential biomarkers related to VS-507 and VS-4718/5095 development programs	April 1-4, 2012
• Presentations at ASCO	June 1-5 , 2012
• Peer-review scientific journal publication	2H 2012
• IND filing of VS-507 with FDA and initiation of Phase I trial	2H 2012
• IND filing of VS-4718/VS-5095 with the FDA and initiation of Phase I trial	1H 2013

### **Valuation**

We have taken several approaches to arrive at our year-end 2012 price target for VSTM. From a more traditional DCF-based analysis, we derive a \$17.83 valuation using a discount rate of 40%. By CAGR analysis we arrive at a valuation of \$19.16. Taken together we arrive at an overall price target of \$19 and our overall Market Outperform rating. Our methodology and assumptions are described in great detail in the following sections. A select list comparable oncology companies is included at end of our report (Table 17).

### **Forecasting and Valuation Methodology**

In order to arrive at our valuation by DCF analysis, we have forecasted revenue and expenses for VSTM and its two pipeline candidates VS-507 and VS-4718/5095 through 2025 and from thereon assumed a modest growth rate of 7.5% until the expiry of drug patent life in 2032. Based preclinical data and company guidance, we have limited the projected revenues with VS-507 to the neoadjuvant, triple negative breast cancer setting and view the expansion of VS-507 use in maintenance therapy or other cancer indications as potential upside to our valuation. For the FAK inhibitor program (VS-4718/5095) we have projected revenues from second-line use in serous ovarian cancer and neoadjuvant use in inflammatory breast cancer. Again, any expansion of the FAK program into other indications or is regarded as potential upside.

Our DCF analysis and modeling assumptions are presented in further detail on Table 1.

**Table 1. DCF Valuation**

Discount Cash Flow Model	2012E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026-32		
VS-507, US Sales					61.8	158.4	292.4	366.3	409.7	437.5	459.3	478.2	497.7	514.1			
VS-507 Royalties					0.0	5.5	15.6	29.8	39.1	44.0	46.7	48.3	50.2	51.1			
<b>Total VS-507 Revenues</b>	<b>61.8</b>	<b>163.9</b>	<b>308.0</b>	<b>396.2</b>	<b>448.8</b>	<b>481.5</b>	<b>506.0</b>	<b>526.4</b>	<b>547.9</b>	<b>565.2</b>							
VS-4718/5095, US-Sales					133.2	348.7	629.0	777.2	849.3	909.3	955.8	993.7	1,029.6	1,061.3			
VS-4718/5095 Royalties					0.0	13.4	41.3	79.1	102.4	112.8	119.6	124.5	122.5	123.2			
<b>Total VS-507 Revenues</b>	<b>0.0</b>	<b>133.2</b>	<b>362.1</b>	<b>670.3</b>	<b>856.3</b>	<b>951.7</b>	<b>1,022.1</b>	<b>1,075.4</b>	<b>1,118.1</b>	<b>1,152.1</b>	<b>1,184.6</b>						
<b>Total Revenues</b>	<b>0.0</b>	<b>0.0</b>	<b>0.0</b>	<b>0.0</b>	<b>195.0</b>	<b>526.0</b>	<b>978.3</b>	<b>1,252.5</b>	<b>1,400.5</b>	<b>1,503.6</b>	<b>1,581.4</b>	<b>1,644.6</b>	<b>1,700.0</b>	<b>1,749.7</b>			
<b>Cost of product sales</b>	<b>0.0</b>	<b>0.0</b>	<b>0.0</b>	<b>0.0</b>	<b>21.4</b>	<b>53.2</b>	<b>92.1</b>	<b>114.4</b>	<b>125.9</b>	<b>134.7</b>	<b>141.5</b>	<b>147.2</b>	<b>152.7</b>	<b>156.0</b>			
COGS as % US sales					11.0%	10.1%	9.4%	9.1%	9.0%	9.0%	8.9%	8.9%	9.0%	8.9%			
<b>Gross Profit</b>	<b>0.0</b>	<b>0.0</b>	<b>0.0</b>	<b>0.0</b>	<b>173.5</b>	<b>472.8</b>	<b>886.1</b>	<b>1,138.1</b>	<b>1,274.6</b>	<b>1,368.9</b>	<b>1,439.9</b>	<b>1,497.4</b>	<b>1,547.3</b>	<b>1,593.8</b>			
<b>R&amp;D expenses</b>	<b>8.7</b>	<b>15.7</b>	<b>25.8</b>	<b>62.0</b>	<b>89.9</b>	<b>112.4</b>	<b>134.9</b>	<b>155.1</b>	<b>164.3</b>	<b>173.8</b>	<b>178.2</b>	<b>182.6</b>	<b>187.2</b>	<b>191.9</b>			
R&D as % of revenue						21.4%	13.8%	12.4%	11.7%	11.6%	11.3%	11.1%	11.0%	11.0%			
<b>SG&amp;A expenses</b>	<b>2.6</b>	<b>3.5</b>	<b>5.3</b>	<b>15.9</b>	<b>55.8</b>	<b>86.5</b>	<b>106.1</b>	<b>119.0</b>	<b>127.9</b>	<b>134.3</b>	<b>141.0</b>	<b>148.0</b>	<b>155.4</b>	<b>163.2</b>			
SG&A as % of revenue						16.4%	11.1%	9.5%	9.1%	8.9%	8.9%	9.0%	9.1%	9.3%			
<b>Total Operating Expenses</b>	<b>11.3</b>	<b>19.2</b>	<b>31.2</b>	<b>78.0</b>	<b>145.7</b>	<b>198.9</b>	<b>243.0</b>	<b>274.1</b>	<b>292.1</b>	<b>308.1</b>	<b>319.1</b>	<b>330.6</b>	<b>342.6</b>	<b>355.1</b>			
<b>Operating Income (EBIT)</b>	<b>(11.3)</b>	<b>(19.2)</b>	<b>(31.2)</b>	<b>(78.0)</b>	<b>27.8</b>	<b>273.9</b>	<b>643.1</b>	<b>864.1</b>	<b>982.5</b>	<b>1,060.8</b>	<b>1,120.7</b>	<b>1,166.7</b>	<b>1,204.7</b>	<b>1,238.7</b>			
Taxes	0.0	0.0	0.0	0.0	0.0	6.8	128.6	259.2	294.7	318.2	336.2	350.0	361.4	371.6			
Tax Rate	0.0%	0.0%	0.0%	0.0%	0.0%	2.5%	20.0%	30.0%	30.0%	30.0%	30.0%	30.0%	30.0%	30.0%			
<b>After-Tax Operating Income</b>	<b>-11.3</b>	<b>-19.2</b>	<b>-31.2</b>	<b>-78.0</b>	<b>27.8</b>	<b>267.0</b>	<b>514.5</b>	<b>604.8</b>	<b>687.7</b>	<b>742.6</b>	<b>784.5</b>	<b>816.7</b>	<b>843.3</b>	<b>867.1</b>			
Discounting Year					0.75	1.75	2.75	3.75	4.75	5.75	6.75	7.75	8.75	9.75	10.75	11.75	12.75
Discount Factor					1.3	1.8	2.5	3.5	4.9	6.9	9.7	13.6	19.0	26.6	37.2	52.1	73.0
PV					(14.9)	(17.3)	(30.9)	7.9	54.0	74.3	62.4	50.7	39.1	29.5	21.9	16.2	11.9
<b>Residual Cash Flow</b>	<b>360.0</b>																
+ Cash and Cash Equivalents 12/31/12																	
<b>Value Company</b>	<b>467.3</b>																
- Long Term Debt on 12/31/12																	
<b>Value of Equity</b>	<b>467.3</b>																
Fully diluted shares outstanding on 12/31/12																	
<b>Price/Share</b>	<b>\$ 17.83</b>																
Discount Rate					40.0%												
Longer-term growth rate (2026 - Patent expiry)						7.5%											
Source: Rodman and Renshaw Estimates																	

## Company Overview

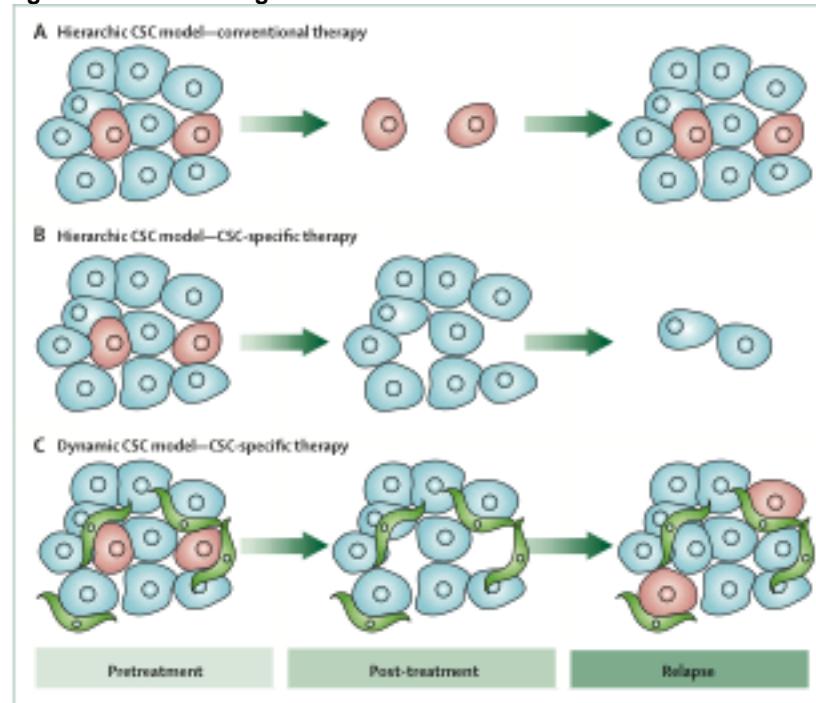
### Cancer Stem Cells Lie at the Root of Residual and Recurrent Disease in Certain Cancers and Limit Results with Conventional Chemotherapy

VSTM is an early stage biotechnology company focused on the discovery and development of small molecule cancer therapies. VSTM is differentiated from the majority of oncology-focused biotechnology companies however, by focusing on drugs that specifically target cancer stem cells and are designed to kill tumors at the root where conventional chemotherapy has had limited impact.

The cancer stem cell (CSC) is an often overlooked and somewhat controversial entity in the present paradigm of cancer treatment and drug development. The concept of the CSC – that a phenotypically distinct cell type within the tumor milieu gives rise to highly proliferative, differentiated progeny while retaining the capacity for self-renewal – has a lengthy history, particularly in the hematologic malignancies. More recently, CSCs have been found to play a role in solid tumors as well.

Pioneering work in this field beginning in leukemia and later in colorectal, breast and brain cancers showed that a subpopulation of tumors cells could be enriched for stem-like properties on the basis of cell surface antigens. These stem-like tumor cells were more capable at seeding new tumors compared with the bulk of tumor cells lacking these surface antigens, and gave rise to tumors that were no longer enriched for CSCs, but comprised mostly of differentiated tumor cells.

Accordingly, it has been proposed CSCs play a critical role in the maintenance and progression of several hematologic and solid malignancies, and in a manner that undermines the efficacy of current cancer therapies. The theory holds that tumors exist in a dynamic equilibrium between CSCs and non-CSCs in which the bulk of tumors cells, comprised of non-CSCs, are sensitive to chemo- and/or targeted therapy, while the CSC fraction remains resistant to therapy and capable of repopulating the tumor from a state of near remission (Figure 1A). If this indeed is case, therapies that are selective for CSCs could offer clinical benefit by depleting a growing tumor of its supply of differentiated cancer cells (Figure 1B). CSC-targeted therapy alone is likely not enough to kill tumors however. In response to certain environmental cues, a differentiated non-CSC can revert to a stem-like cell through the process of epithelial-to-mesenchymal transition (EMT; described in further detail below) (Figure 1C). This process, coupled with the inherent genetic instability of differentiated tumor cells, confers residual tumors with several opportunities to acquire additional genetic aberrations with the potential to yield more aggressive and perhaps drug-resistant disease. Appropriately, the CSC theory has garnered considerable traction among investigators trying to understand the significant rate of breast cancer relapse in women initially achieving remission with current treatment strategies, particularly in women with triple negative disease who are of poorer prognosis.

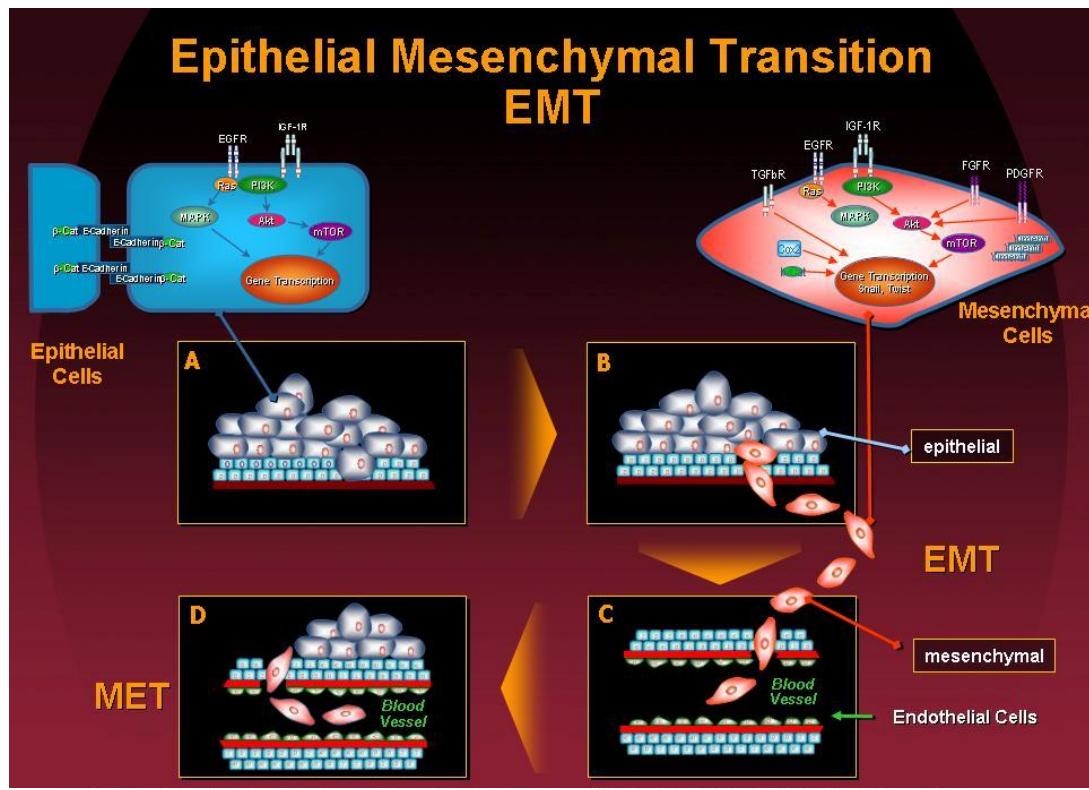
**Figure 1. Paths to Drug Resistance in the Cancer Stem Cell Model.**

Source: Vermeulen, L., et al., *Lancet Oncology*, 2012.

### Epithelial-Mesenchymal Transition (EMT) Underlies Cancer Stem Cell Phenotype and Cancer Metastasis

Central to the cancer stem cell hypothesis is the epithelial-to-mesenchymal transition (EMT). EMT is the process by which epithelial-like tumor cells shed the features that enable polarization, cell-to-cell contact and high proliferative potential in exchange for greater cell motility and invasiveness (80% of all cancers are of an epithelial cell origin). As diagrammed in Figure 2, cells dissolve intracellular adherens junctions by downregulating the expression of the transmembrane protein E-cadherin, and thereby adopt a mesenchymal phenotype which allows them to penetrate endothelial barriers and be carried to distant sites away from the tumor origin. As non-dividing cells, mesenchymal cells can also evade cytotoxic therapies that are generally effective against highly proliferative tissues. Having reached distant sites or following treatment cessation, these cells can undergo a mesenchymal-to-epithelial transition (MET) to repopulate new tumors.

**Figure 2. Epithelial Cancer Cells Can Undergo EMT to Acquire a Stem Cell-like Phenotype in Order to Migrate to Distant Sites and Colonize New Tumors.**



Source: OSI Pharma Company Presentation.

### VS-507: Killing Cancer Stem Cells Through Wnt Pathway Inhibition

#### Wnt/β-Catenin Signaling Contributes to EMT-Induction and CSC Survival

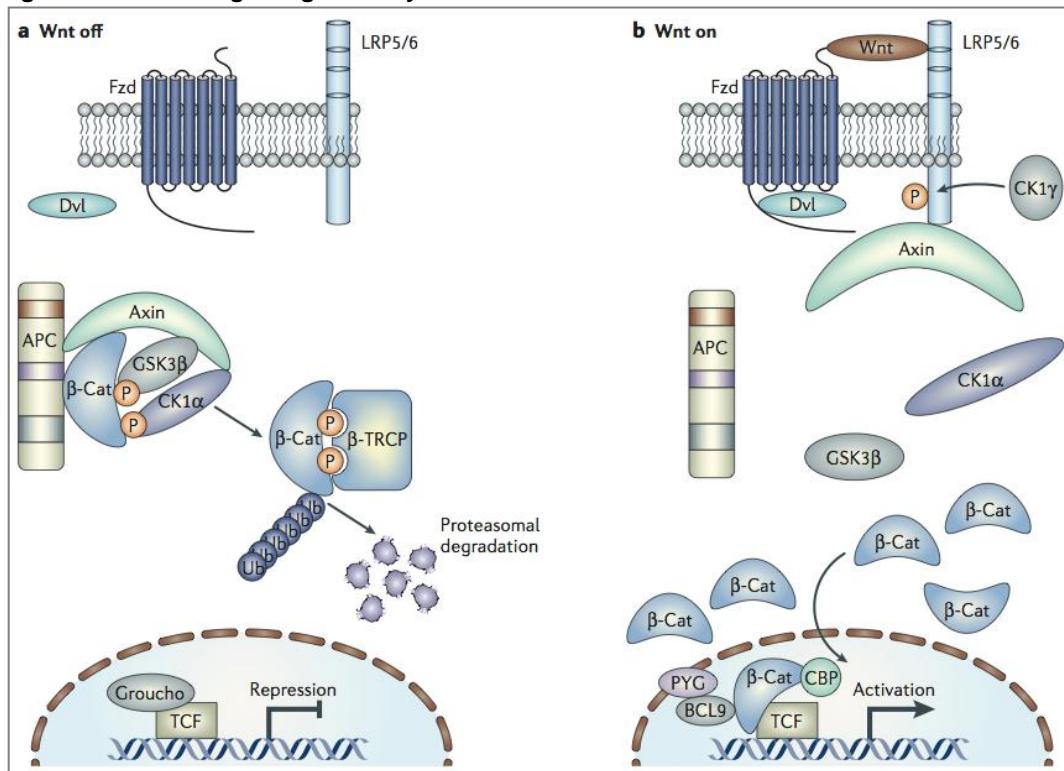
The EMT has primarily been studied in the context of embryonic development, but has been shown more recently to be involved in the conferral of migratory and invasive phenotypes to carcinoma cells, particularly during metastasis. Akin to similar processes during embryogenesis, cancer cells undergoing EMT do so in response to contextual signals secreted by the stromal connective tissue and the surrounding tumor microenvironment that include activators of Wnt signaling and other tumor-initiating, morphogenic pathways including Notch and Hedgehog.

The Wnt (a hybrid abbreviation of the drosophila and mammalian homolog genes *Wg* (Wingless) and *Int* (Integration)) signaling pathway is a key regulator of cell differentiation, proliferation and migration during embryonic development. More recently, it has been shown to exert significant control over tumorigenesis, particularly in colon, breast, endometrial, ovarian and prostate cancers. In this pathway, a family of secreted glycoproteins called Wnts regulates the ability of the transcription factor β-catenin to induce expression of target genes that promote cell proliferation.

In the absence of a Wnt signal, β-catenin is sequestered in an inhibitory complex comprised of the tumor suppressors APC, Axin, GSK3β and CK1. The phosphorylation of β-catenin by CK1 and GSK3β marks it for destruction by poly-ubiquitination by β-TRCP and subsequent degradation by the proteasome (Figure 3A). Upon being secreted from neighboring cells, Wnt proteins bind and form a ternary complex with the target receptor Frizzled (FZD), a seven-pass transmembrane receptor protein, and low density lipoprotein receptor-related protein 5/6

(LRP5/6). This activated receptor complex recruits Axin to the membrane surface, dissociating the  $\beta$ -catenin-CK1-GSK3 $\beta$  turnover complex. The resulting stabilization and accumulation of  $\beta$ -catenin in the cytosol is followed by its translocation to the nucleus where it interacts with T-cell factor (TCF) and others transcription factors to induce the expression of Wnt target genes (*MYC* and *Cyclin D1* among others), and stimulate cell proliferation (Figure 3B).

**Figure 3. The Wnt Signaling Pathway.**



Source: Barker, N., and Clevers, H., *Nature Reviews Drug Discovery*, 2007.

Aberrant activation of the Wnt pathway has been observed in numerous cancers stemming from different lesions within the signaling cascade. Inherited familial adenomatous polyposis (FAP) and spontaneous forms of colorectal cancer were the first contexts in which the link between activated Wnt signaling and cancer was established. Both cancers frequently harbor loss of function mutations in APC, and, less frequently, mutations in Axin2 and  $\beta$ -catenin. Mutations of APC and Axin2 compromise their activities within the  $\beta$ -catenin destruction-box complex, whereas mutations to regulatory phosphorylation sites of  $\beta$ -catenin preclude its ubiquitination and degradation. Genetic silencing of the natural Wnt inhibitory proteins SFRP (secreted frizzled-related protein) and WIF (Wnt inhibitory factor) is also commonly observed in colon cancers. These factors restrain activation of the pathway by binding Wnt proteins and sequestering them away from the target receptors FZD and LRP5/6. In their absence, Wnt ligand receptor activation is able to proceed unabated.

Other cancers have been shown to exhibit activated Wnt signaling, although with less frequency than the colon cancer and rarely due to loss of APC function. More commonly, it is driven by a compilation of mechanisms. Axin 1 mutations have been reported in a small number of medullablastomas and liver cancers, while activating mutations in  $\beta$ -catenin - the more common route of aberrant Wnt signaling - have been observed in liver cancer, endometrial ovarian cancer, prostate cancer and melanoma.

**Table 2. Common Diseases linked with Wnt Pathway Activation.**

Pathway component	Observed alterations	Disease
Wnt ligands	Increased expression	Colon cancer <sup>28,30</sup> ; breast cancer <sup>27,31,40</sup> ; melanoma <sup>30</sup> ; head & neck cancer <sup>41</sup> ; non-small-cell lung cancer <sup>28,42</sup> ; gastric cancer <sup>31</sup> ; mesothelioma <sup>31</sup> ; Barrett's esophagus <sup>31</sup> ; rheumatoid arthritis <sup>33,44</sup> ; schizophrenia <sup>31</sup>
Frizzled receptors	Increased expression	Colon cancer <sup>28,31</sup> ; breast cancer <sup>28</sup> ; head & neck cancer <sup>42</sup> ; gastric cancer <sup>28,37</sup> ; synovial sarcomas <sup>31</sup> ; rheumatoid arthritis <sup>41,44</sup>
Dishevelled family members	Increased expression	Mesothelioma <sup>30</sup> ; non-small-cell lung cancer <sup>30</sup> ; cervical cancer <sup>41</sup>
APC	Loss-of-function mutations/reduced expression	Colon cancer <sup>151–155</sup> ; Barrett's oesophagus <sup>35</sup>
β-catenin	Gain-of-function mutations	Colon cancer; gastric cancer; hepatocellular cancer; hepatoblastoma; Wilms' tumour; endometrial ovarian cancer; adrenocortical tumours; pilomatricoma <sup>34</sup>
Axin 1	Loss-of-function mutations	Hepatocellular cancer <sup>32,156,357</sup> ; hepatoblastomas <sup>31,157</sup>
Axin 2/ Conductin	Loss-of-function mutations	Colon cancer (MSI <sup>+</sup> ) <sup>38,358</sup> ; hepatocellular cancer <sup>156</sup> ; oligodontia (tooth loss) <sup>35</sup>
SFRP family members	Reduced expression	Colon cancer <sup>13,18</sup> ; breast cancer <sup>21,28</sup> ; gastric cancer <sup>18</sup> ; mesothelioma <sup>34</sup> ; non-small-cell lung cancer <sup>13</sup> ; Barrett's oesophagus <sup>38</sup> ; leukaemia <sup>35</sup>
WIF family members	Reduced expression	Colon cancer <sup>18</sup> ; breast cancer <sup>30,34</sup> ; prostate cancer <sup>14</sup> ; lung cancer <sup>32,34</sup> ; bladder cancer <sup>18,34</sup> ; mesothelioma <sup>31</sup>
LRP5	Gain-of-function mutations	Increased bone density <sup>159,358</sup>

APC, adenomatous polyposis coli; LRP, low-density lipoprotein receptor-related protein; MSI<sup>+</sup>, microsatellite instability positive; SFRP, secreted frizzled-related protein; WIF, Wnt Inhibitory factor.

Source: Barker, N., and Clevers, H., *Nature Reviews Drug Discovery*, 2007.

### Triple Negative Breast Cancer is Susceptible to Wnt Pathway Inhibition

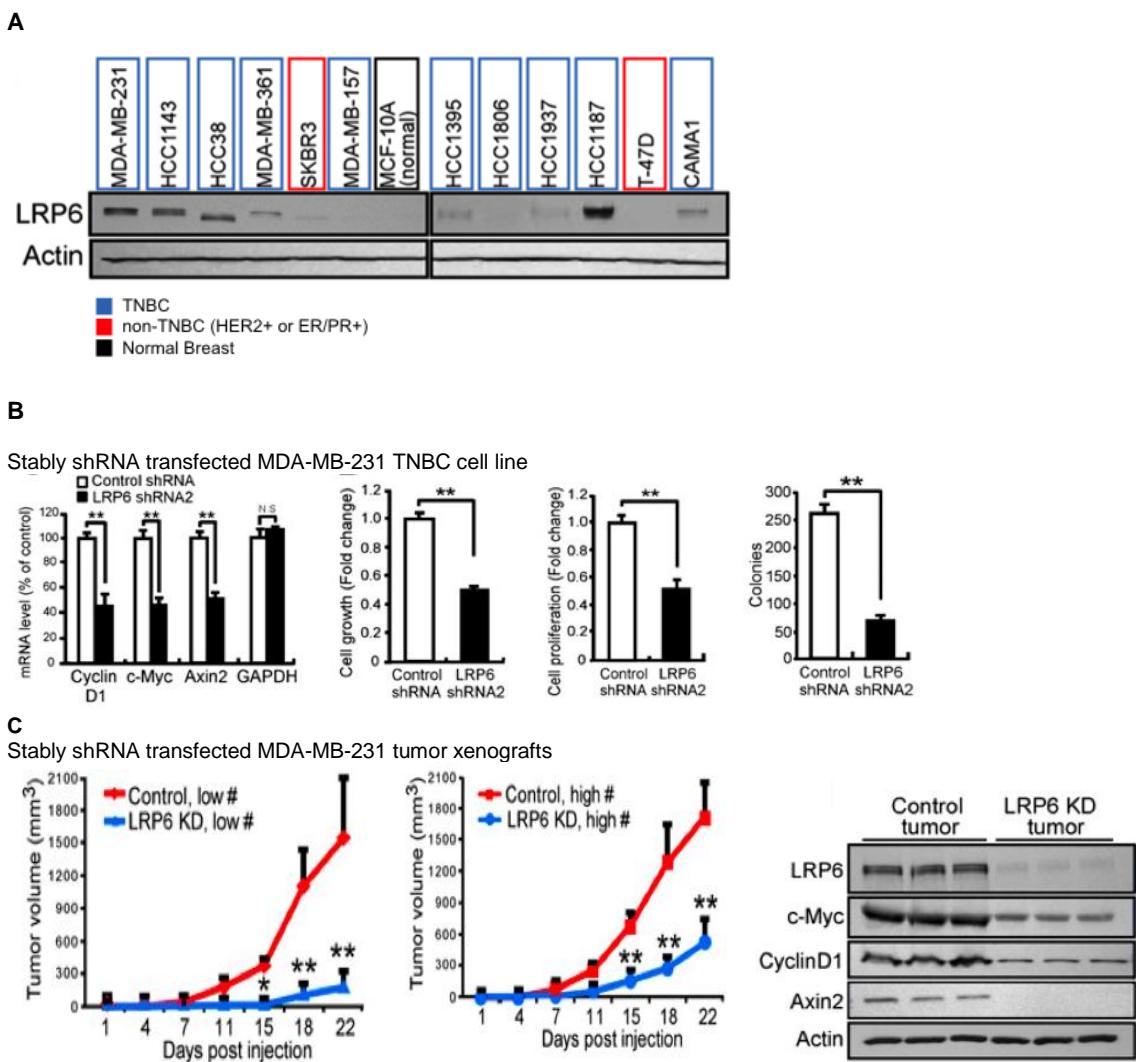
Various solid tumors exhibit Wnt pathway activation stemming from different lesions within the signaling cascade. Recent work suggests tumors of this nature are frequently observed in triple negative breast cancer (TNBC). TNBC is generally defined by the absence of HER2 and/or estrogen/progesterone (ER/PR) histopathology, and is thus refractory to HER2-targeted or hormonal therapy. TNBC is observed in ~15-20% of breast cancer cases, and is most common to African-American, Latino-American and premenopausal women. Part of the paradox surrounding TNBC is that, relative to receptor-positive tumors, TN-tumors are particularly responsive to cytotoxic chemotherapy. Unfortunately, this responsiveness fails to translate into better rates of overall survival, as patients with recurrent or residual TN disease face a higher risk of mortality compared with patients with non-TNBC disease.

The discordance between initial response and overall survival in TNBC has puzzled clinicians and researchers for some time. One hypothesis is that cytotoxics such as taxane chemotherapy, while effective against bulk tumor cells, are ineffective against tumors cells that have undergone EMT and adopted a stem cell phenotype. This mechanism has been studied extensively in model systems of breast cancer and glioblastoma, as is believed to mediate resistance to radiotherapy in addition to chemotherapy.

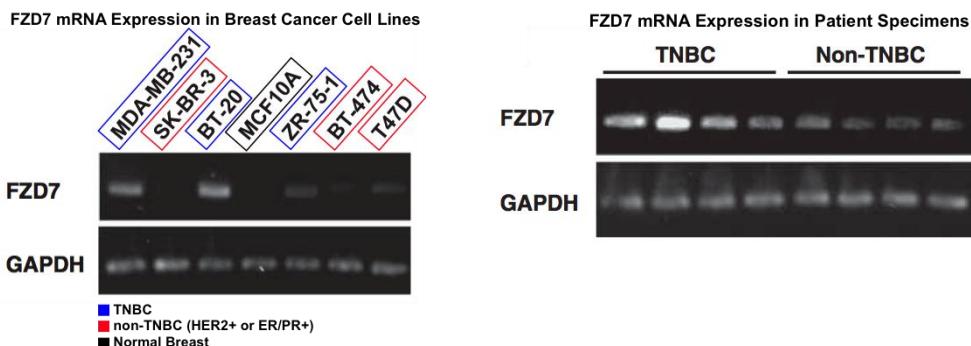
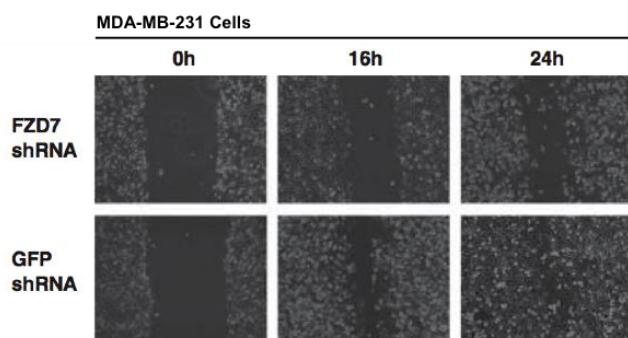
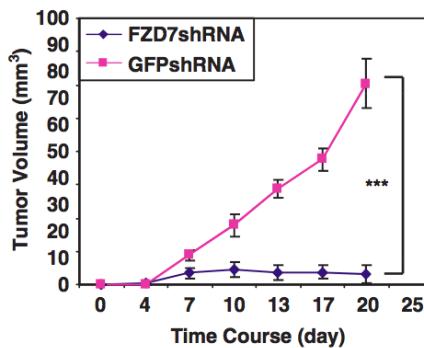
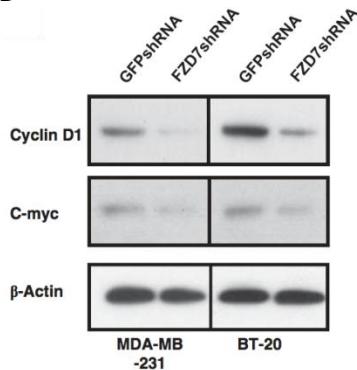
The link between EMT and triple negative breast cancer is further supported by recent evidence showing that TNBC is driven, at least in part, by overactivation of Wnt/β-catenin signaling. Lui and

colleagues, in a 2010 *PNAS* publication, showed that the Wnt receptor LRP6 is frequently overexpressed in TNBC and is absent from HER2/hormone-receptor positive tumor cell lines (Figure 4A). In the same study, depletion of LRP6 message in the TNBC cell line MDA-MB-231 inhibited  $\beta$ -catenin-dependent gene expression and tumor growth in vivo (Figure 4B&C).

**Figure 4. LRP6 is Upregulated in Triple Negative Breast Cancer.**



FZD, the other Wnt co-receptor, was also shown to be involved in the pathogenesis of TNBC. The FZD family is comprised of 10 different protein receptors, of which FZD7 holds the strongest link to breast cancer pathogenesis. Work by Yang et al, published in 2011 in *Oncogene*, shows that FZD7 is over expressed in primary TNBC tumors and in established TNBC cell lines relative to non-TNBC specimens(Figure 5A). By depleting cells of FZD7, TNBC tumor cells can be induced to grow and migrate more slowly following stimulation with Wnt ligand in both culture and tumor xenografts (Figure 5B&C). Downregulation of FZD7 also correlates with decreased accumulation of  $\beta$ -catenin in the nucleus and decreased expression of the  $\beta$ -catenin target genes *Cyclin D1* and *MYC* (Figure 5D).

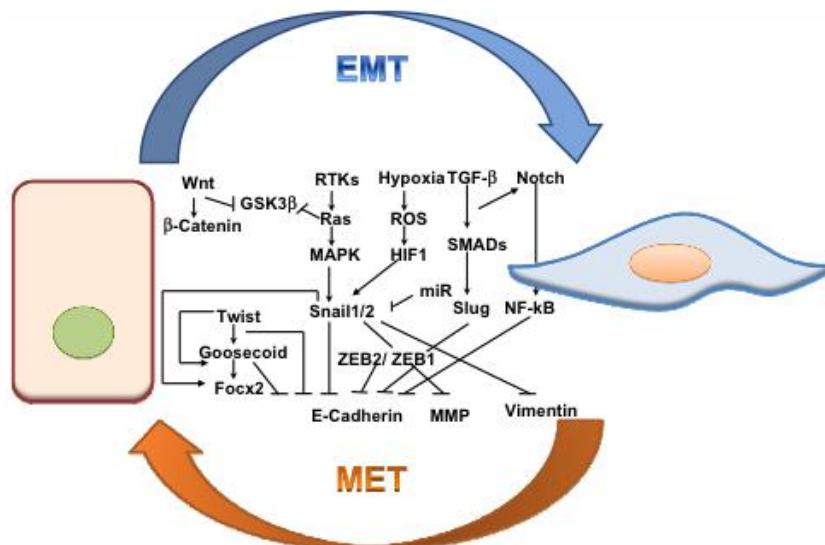
**Figure 5. FZD7 Depletion Slows Breast Tumor Growth and Wnt-Dependent Gene Expression.****A****B****C****D**Source: Adapted from Yang et al., *Oncogene*, 2011.

### Notch and Hedgehog are also involved in TNBC Pathogenesis

Recent data suggest that two additional developmental pathways, the Notch and Hedgehog, also contribute to TNBC growth survival. Activated Notch1 and Notch4 expression has been shown to be elevated in tumor and vascular endothelial cells in a majority of high-grade TNBC compared with hormone positive breast cancer (Speiser J, et al., *Int J Surg Pathol*, In Press, 2011). Notch1 activation has also been linked with the outgrowth of therapy-resistant subpopulation of hormone positive breast cancer cells exhibiting clinical features of triple negative basal-like disease (Haughian, JM, et al, *PNAS*, 109 (8): 2472-7, 2012). Elevated nuclear expression of Hedgehog pathway-regulated transcription factors, GLI1 and FOXC2, has found in association with estrogen-receptor negativity and poor prognosis in patients presenting with basal-like breast cancer. Both Notch and Hedgehog signaling pathways have been shown to mediate the initiation

of EMT programs through the upregulation of transcription factors like Snail, Slug and Twist1, to suppress the expression of E-cadherin, which is essential to epithelial cell phenotype (Figure 6). Studies investigating the link between these pathways, breast cancer, and CSCs more generally are continuing, as are efforts to explore the antitumor activity of Notch and Hedgehog pathway inhibitors in similar contexts.

**Figure 6. Developmental Pathways Mediating EMT – MET Processes.**

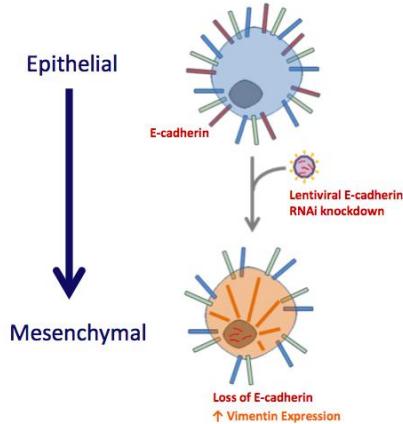


Source: Foroni, C., et al., *Cancer Treat Rev*, 2011.

### VSTM Leverages a Novel Drug Discovery Platform to Identify VS-507 - A CSC-Selective Inhibitor

As an early stage company much of VSTM's value proposition is derived from its drug development platform and its proprietary technology to screen for cancer stem cell-selective agents. The technology relies on patent protected methodology for stably inducing EMT in epithelial tumor cell populations. This methodology was first described in a 2009 *Cell* paper by founding members of VSTM and current members of the company's scientific advisory board Piyush Gupta and Bob Weinberg (Gupta, PB, et al, *Cell*, 138, 645-659, 2009). This paper outlines some of the challenges to identifying CSC-targeted drugs using conventional high-throughput screening techniques: (i) the relative paucity of CSCs compared to the bulk tumor and (ii) and instability of an enriched CSC population which is rapidly lost when cultured in vitro. In an end-run to this problem, VSTM's discovery platform makes use of a non-tumorigenic mammary epithelial cell line (HMEL) that has been experimentally transduced with short hairpin RNA to downregulate the expression of E-cadherin. Depleting the cells of E-cadherin thus induces them to undergo EMT and adopt a mesenchymal phenotype (Figure 6).

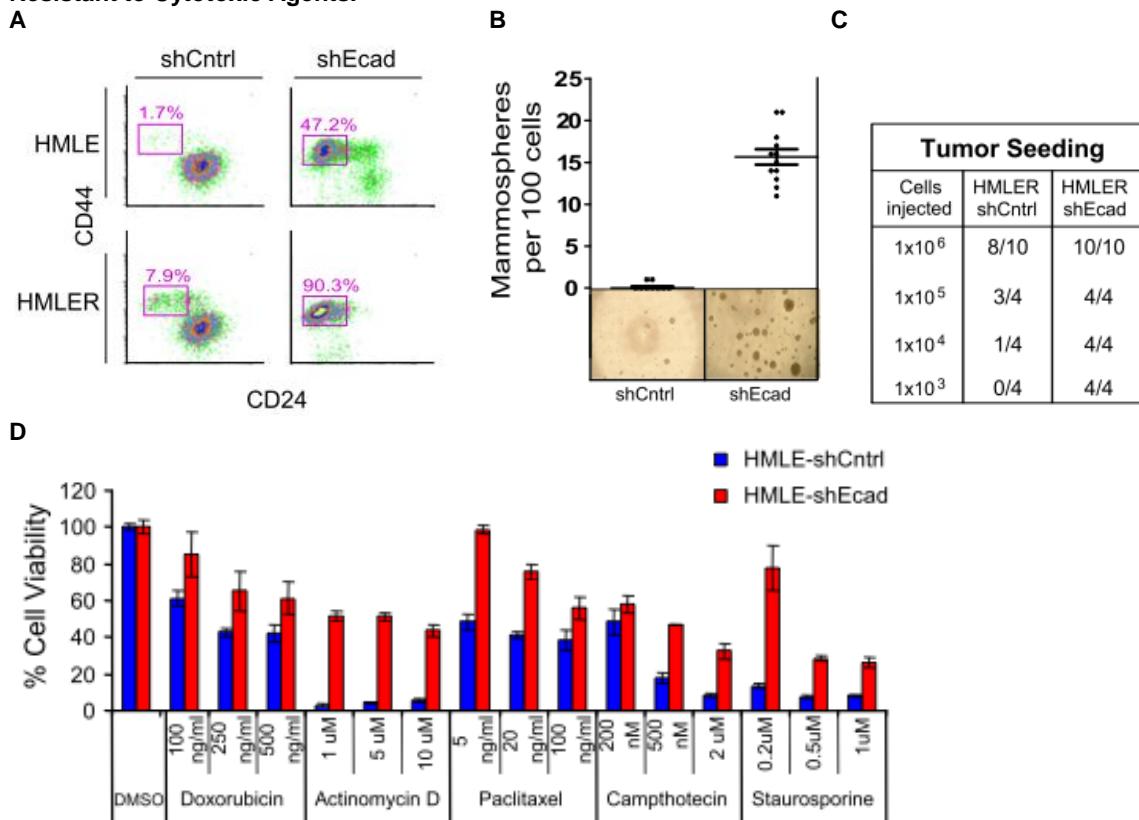
**Figure 6. RNAi Knockdown of E-cadherin Induces Epithelial-to-Mesenchymal Transition in Mammary Epithelial Cells, Creating a Stable Stem-like Cell Population.**



Source: Verastem Company Presentation.

The stem-ness of HMLE<sup>shEcad</sup> has been validated by several experimental analysis showing: (i) enrichment for the cell surface marker profile of CSCs with high CD44 and low CD24 expression (CD44<sup>high</sup>/CD24<sup>low</sup>) (Figure 7A); (ii) increased ability to form tumorspheres, characteristic of CSCs cultured *in vitro* (Figure 7B); and (iii) a 100-fold increase in the ability to seed tumors in mice relative to control HMLE cells (Figure 7C). Importantly, these EMT-induced HMLE<sup>shEcad</sup> cells were shown to be more resistant to standard chemotherapies like paclitaxel and doxorubicin (Figure 7D), consistent with earlier findings that such drugs enrich for CSCs, making them an appropriate model system for CSC-directed drug screens.

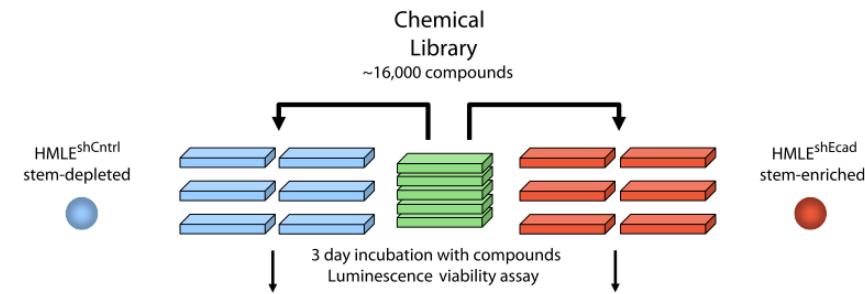
**Figure 7. Mesenchymally-Induced Mammary Epithelial Cells Possess Stem Cell Qualities and are Resistant to Cytotoxic Agents.**



Source: Gupta, P. et al., *Cell*, 2009.

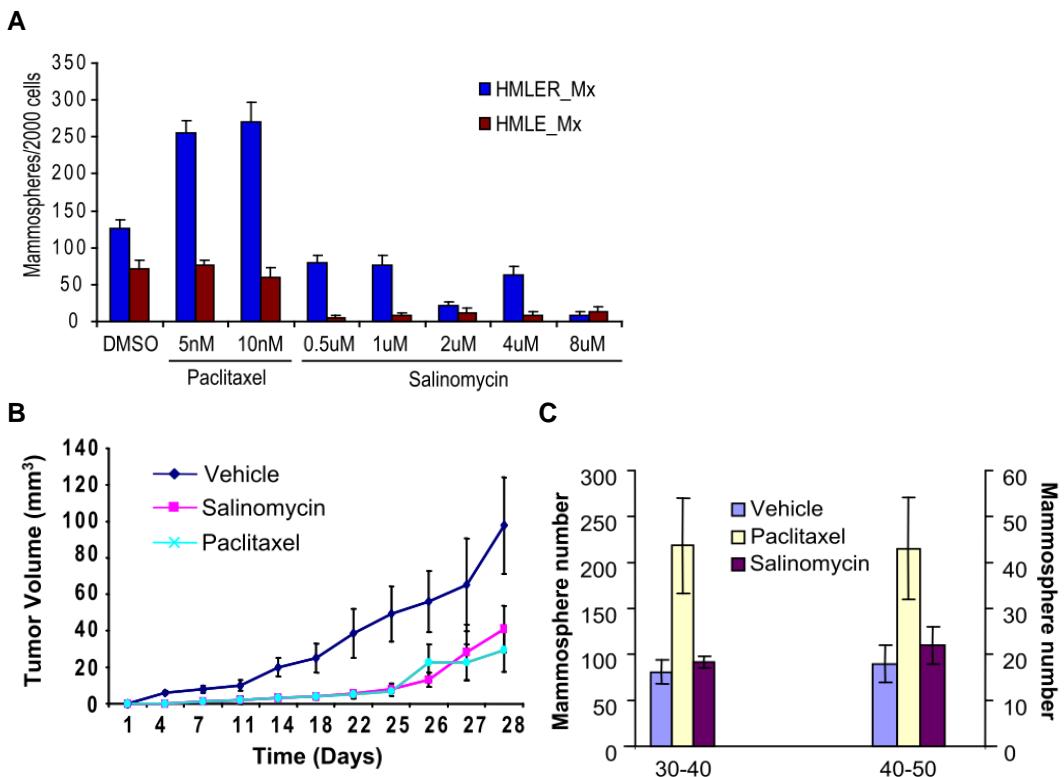
With the biologically appropriate tool in hand, VSTM investigators are able to comparatively screen chemical libraries to identify compounds that selectively kill the CSC-like HMLE<sup>shEcad</sup> cells while leaving the epithelial HMLE<sup>shCrl</sup> cells largely unperturbed (Figure 8). The 2009 Gupta et al *Cell* paper describes a proof-of-concept screen of ~16,000 compounds that delivered four compounds exhibiting greater than 7-fold selectivity for HMLE<sup>shEcad</sup> cells over control cells.

**Figure 8. Design Scheme of VSTM's High Throughput Screen in CSCs.**



Source. Gupta, P., et al., 2009.

Among these compounds, the antibiotic salinomycin held the greatest degree of selective cytotoxicity in EMT-induced CSCs. Follow-up experiments with salinomycin in cell culture and tumor xenografts models were consistent with expected results according to the screen design. Mixed populations of EMT- and non-EMT-induced cells were found to be more sensitive to treatment with salinomycin compared with paclitaxel, with a smaller fraction of remaining cells displaying the CD44<sup>high</sup>/CD24<sup>low</sup> phenotypic hallmark of stem-like epithelial cells and fewer cells able to form mammospheres (Figure 9A). Further evidence that salinomycin was acting on a different cell population from paclitaxel, came from an experiment in which SUM159 breast cancer tumor xenografts were first growth-inhibited by treating mice with either paclitaxel or salinomycin (Figure 9B). When these tumors were then resected after four weeks of treatment and analyzed for the presence of CSCs by an in vitro tumorsphere formation assay, tumors from salinomycin-treated animals formed mammospheres at half the rate of those from paclitaxel treated animals (Figure 9C).

**Figure 9. Salinomycin Kills Breast Cancer Cells In Vivo and Reduces Tumor Seeding Potential.**

Source: Gupta, P. et al., *Cell*, 2009.

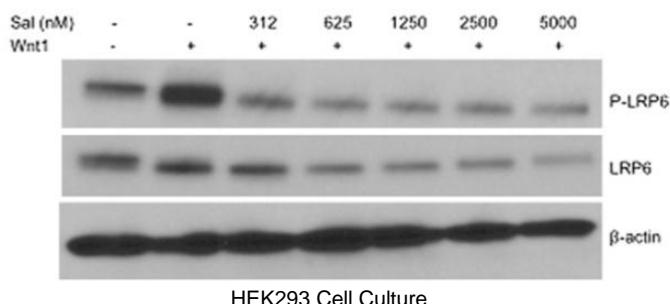
### Salinomycin (VS-507) Targets the Wnt Pathway to Affect Cell Behavior.

Salinomycin has been shown to act as an inhibitor of the Wnt pathway, which comes as a bit of a surprise. Salinomycin is widely used as antibiotic in chicken feed, functionally acting as a potassium ionophore to depolarize and thereby kill various microbes. The discovery that salinomycin could selectively target CSCs certainly suggested repurposing the drug as a potential cancer therapy. VSTM's VS-507 candidate program is a proprietary formulation of salinomycin, with a pending patent application that would grant patent protection into 2032 if issued. Accordingly, hereafter we refer to salinomycin as VS-507.

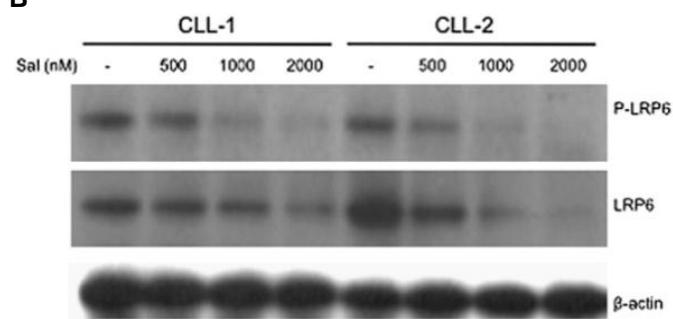
While the discovery that VS-507 could selectively target CSCs was a major finding in itself, little was known about its mechanism of action in this context until Lu et al published their work with the compound in *PNAS* in June, 2011. First, using the non-transformed human embryonic kidney cell line HEK293, the authors showed that VS-507 prevented the phosphorylation of LRP6 following ectopic expression of Wnt1 and stimulated the degradation of LRP6 and  $\beta$ -catenin protein (Figure 9A). Similar results were observed in multiple primary cell lines derived from patients with chronic lymphocytic leukemia (CLL). There, treatment with VS-507 decreased LRP6 phosphorylation and total LRP6 protein expression, as well as the expression of target genes *LEF1*, *Cyclin D1* and *fibronectin*, all previously shown to be upregulated in CLL cells relative to normal lymphocytes (Figure 9B). Using a cytometry-based assay for apoptosis, a differential effect on cell survival was detected in which VS-507 induced apoptosis in CLL cells within 48 hours at an average IC<sub>50</sub> of 230nM, while PBMCs (lymphocytes) collected from healthy donors did not undergo apoptosis even at 100-fold greater concentrations of drug (Figure 9C).

**Figure 10. VS-507 (salinomycin) Disrupts LRP6 Functionality, Downregulates Wnt-Target Gene Expression and Slows Leukemic Tumor Cell Proliferation In Vitro.**

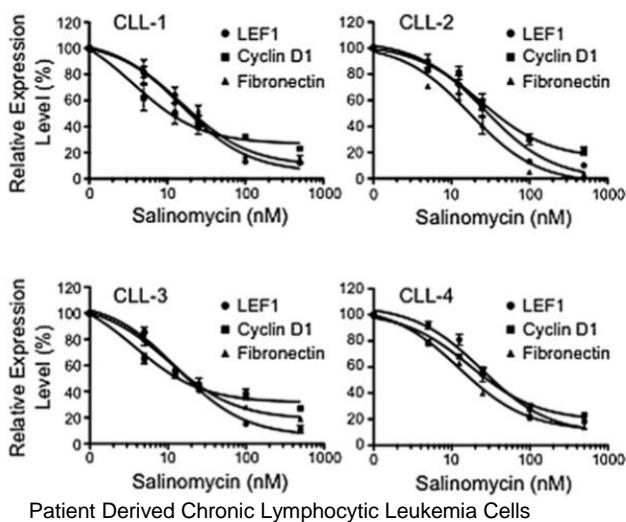
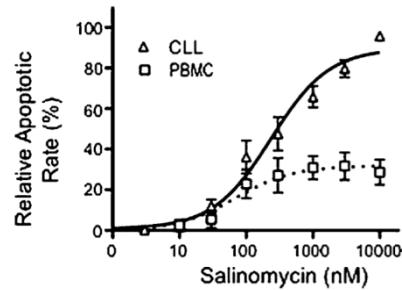
**A**



**B**



**C**



Source: Lu, D., et al., PNAS, 2011.

While these studies show that VS-507 is a modulator of the Wnt pathway, further biochemical and structural analysis are necessary to determine the precise mechanism by which VS-507 disrupts the functionality of LRP6. Tertiary analysis of this sort could prove invaluable to the design of derivative compounds with greater potency and perhaps less off-target activity. Further studies are also required to corroborate suppression of the Wnt pathway as the mechanism by which VS-507 reduces survival of stem-like breast cancer cells, as implied by VSTM investigators.

Other research groups exploring the anti-tumor potential of salinomycin have shown that it may hold utility in other cancer indications and as an enhancer of chemotherapy. Ketola and colleagues (Ketola, K, et al, *Br J Cancer*, 2012) have published work showing that salinomycin inhibited the growth of prostate cancer cell lines, albeit at much higher drug concentrations. Meanwhile, two research groups out of China and S. Korea have each published work indicating that salinomycin sensitized tumors to treatment with standard chemotherapies such as gemcitabine in pancreatic cancer, and any of docetaxel, doxorubicin or etoposide in breast cancer (Zhang, GN., et al, *Cancer Lett*, 2011, and Kim, JH, et al., *Biochem Biophys Res Comm*, 2012 and Kim, JH et al, *Br J.*, 2011).

### **VS-4718/VS-5095: Little FAKkers Bring the Focus to Focal Adhesion Kinase In Solid Tumors**

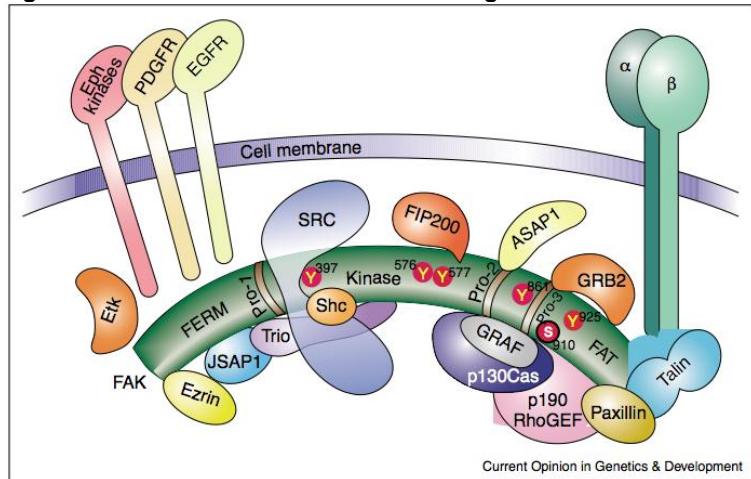
The remaining candidates in VSTM's development pipeline reflect the company's desire to target drug resistant CSCs with alternative approaches. The VS-4718/VS-5095 program takes aim at cancer stem cells by targeting the activity of focal adhesion kinase (FAK) - a molecule of growing importance in the understanding of stem cell self-renewal and proliferation. Unlike VS-507, FAK inhibitors VS-4718 and VS-5095 were not discovered in-house using the EMT-induced CSC drug-screening platform, but rather were acquired in an exclusive worldwide license agreement with the oncology-focused biotechnology company Poniard Pharmaceuticals, Inc. (PARD, Not Rated). Prior studies using a closely related Poniard legacy compound PND-1186 have shown the VS-4718/VS-5095 class of molecules to be potent inhibitors of FAK and FAK-dependent signaling and active against the growth of different pre-clinical tumor models.

Looking beyond Phase I safety analysis, we view the development of VS-4718/VS-5095 much in the same way we view VS-507 – as complement to standard-of-care chemotherapy in indications where CSC survival is likely to mediate recurring disease. The molecular profile of the CSC is an evolving one, and as the data mature we may discover that the survival of particular populations of drug resistant CSCs may be varyingly dependent on the activity of a given signaling pathway. In that respect, we do not view the FAK program as directly competitive with the Wnt program, as ultimately these agents might be administered on the basis of predictive molecular markers or in combination with one another to affect the maximal response. If either FAK inhibitor candidate is shown to be safe and effective in this setting, it too has the potential to be adopted into neoadjuvant treatment regimens and would be expected to have similar market dynamics as VS-507.

The following sections provide an overview of the FAK signaling pathway in the context of cancer pathogenesis and present evidence from preclinical studies supporting the rationale for VS-4718/5095 use in inflammatory breast cancer and serous ovarian cancer.

#### **Focal Adhesion Kinase (FAK) is Functionally Important to Cancer Cell Motility and Survival.**

Focal Adhesion Kinase (FAK) is a non-receptor tyrosine kinase that integrates various growth factor-mediated and mechanical stimuli to regulate cellular migration, proliferation and survival. As the names suggests, FAK is highly enriched at focal adhesion (FA) sites, which are the points of contact between the cell's plasma membrane and the extracellular matrix (ECM). FAK activation is regulated by small surface receptor proteins called integrins that interact with neighboring cells in the surrounding tissue and form contacts with the ECM. In one mechanism of FAK activation (Figure 11), the clustering of integrins during focal adhesion formation condenses integrin-associated proteins talin and paxillin, creating a binding site for FAK via the C-terminal focal adhesion targeting (FAT) domain. Binding of the FAT domain derepresses the FAK kinase domain through mechanisms that are not fully understood but are thought to involve both intermolecular and intramolecular events, resulting in the auto-phosphorylation of FAK at multiple tyrosine residues.

**Figure 11. Protein Interactions Mediating FAK Activation and Downstream Pathway Signaling.**

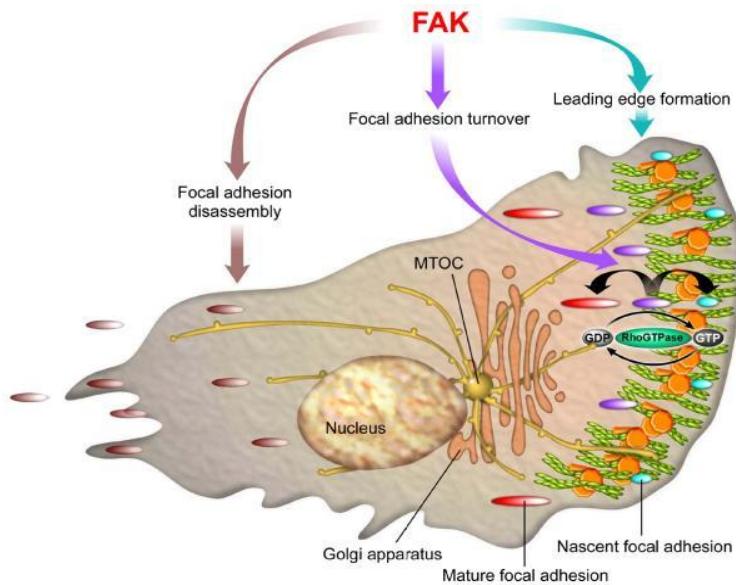
Source: Schlaepfer, D., and Mitra, S., *Curr Opin Gen Dev*, 2004.

The phosphorylation of Tyr-397 produces a high-affinity binding site for several Src-homology 2 (SH2) domain-containing proteins, which include c-Src and the Src family protein kinases (SFKs). The resulting FAK-Src complex is capable of activating several downstream signaling pathways on its own, but it also phosphorylates secondary residues within the FAK kinase domain and C-terminus to facilitate interactions with adaptor proteins to activate downstream pathway signaling. For example, phosphorylated Tyr-925 serves as a binding site for Grb2, an adaptor protein known for its role in the activation of the Ras/MAP kinase signaling cascade. Phosphorylation of Tyr-861 fosters recruitment of the p130Cas-Crk adaptor protein complex required for activation of the Reelin signaling cascade.

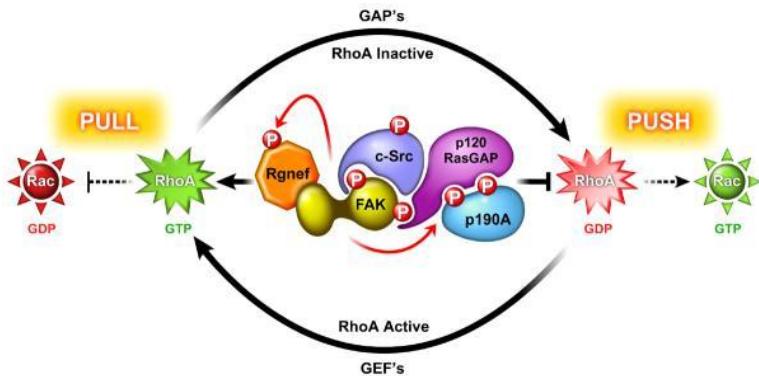
In contrast to other non-receptor tyrosine kinases that mediate survival signaling, FAK holds a key role in the regulation of cell motility. Studies using knockout mouse models point to the importance of FAK in the directional migration of fibroblasts. Complex and dynamic remodeling of the actin cytoskeleton mediates cell migration from point A to B. These events are coordinated by the Rho family GTPases, Rac and Rho, which are themselves regulated by the presence of guanine nucleotide exchange factors (GEFs) and GTPase activating proteins (GAPs). FAK has been shown to regulate RhoGTPase activation by binding and recruiting GEF and GAP proteins to in an alternating manner (Figure 12A and B).

**Figure 12. FAK Regulates RhoGTPase Activity During Directional Cell Migration by Alternatively Binding GEFs and GAPs**

**A**



**B**



Source: Tomar, A., and Schlaepfer, D.D. Curr Opin Cell Biol, 2009.

FAK activation is not entirely downstream of mechanically-mediated integrin signaling. FAK-Src complex formation also occurs in response to the growth factor stimulation of receptor tyrosine kinases (RTKs) such as EGFR, PDGFR and Ephrin receptor. While the precise mechanism of RTK-mediated FAK activation remains elusive, FAK activation in response to EGF is known to be mediated by an indirect interaction of EGFR with the N-terminal FERM (band 4.1, ezrin, radixin, moesin) domain of FAK.

### The Role of FAK in Tumorigenesis, EMT and Breast Cancer Metastasis

Given its role as a positive regulator of cell motility, proliferation and survival, FAK is regarded as a putative oncogene, the deregulated activity of which has the potential drive tumor formation or aggravated tumor phenotypes. Several groups have shown that FAK overexpression negatively correlates with survival and response to therapy in several solid tumors including breast, ovarian, glioma cancers.

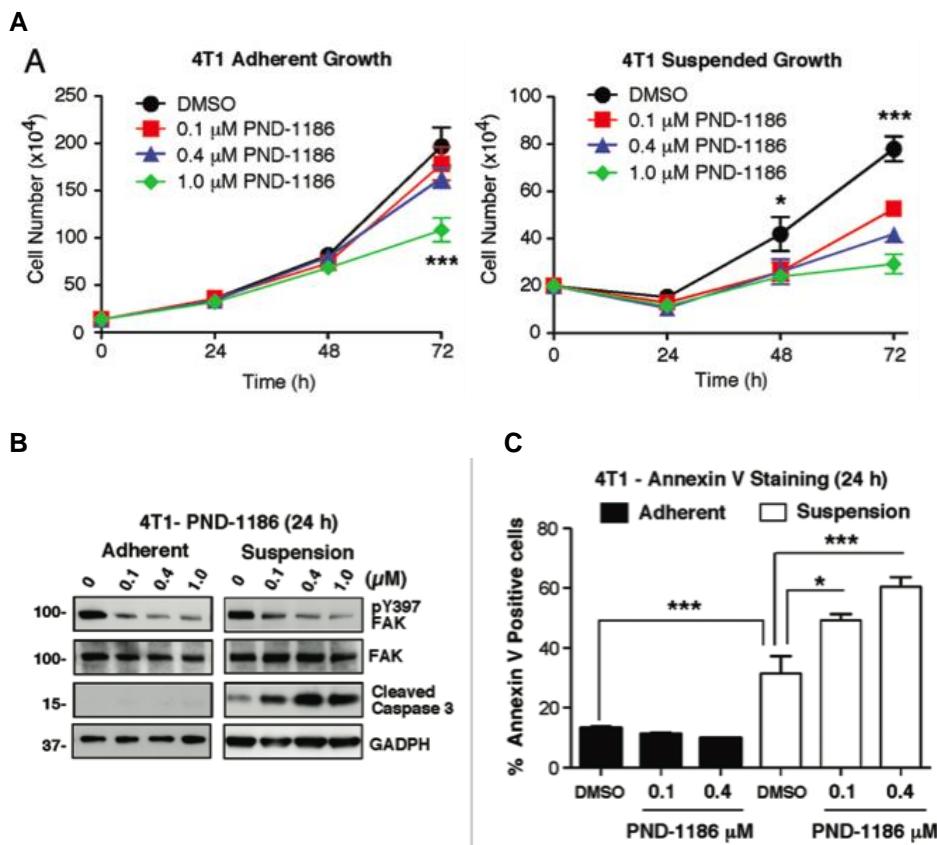
### **VS-4718/VS-5095 Share Class with PND-1186 - A Selective FAK Inhibitor with Low Nanomolar Activity**

As mentioned above, the VS-4718/VS-5095 FAK inhibitor program was acquired through a licensing agreement with Poniard Pharmaceuticals. In evaluating the preclinical activity of these candidates, we have the benefit of two published studies out of the lab of David Schlaepfer in collaboration with Poniard researchers, describing the activity of the structurally related compound PND-1186 (*Tanjoni et al., Can Biol Ther, 2010; and Walsh et al., Can Biol Ther*). PND-1186 is described as a substituted pyridine, ATP-competitive, reversible inhibitor of FAK kinase that targets the purified enzyme with an IC<sub>50</sub> concentration of ~1.5nM *in vitro*. PND-1186 exhibits a high degree of selectivity for FAK. In an activity assay against a panel of 34 kinases at 100nM drug concentration, Flt3 was the only other kinase with diminished activity. In the mouse breast carcinoma cell line 4T1, PND-1186 potently inhibited FAK autophosphorylation at Src-binding binding site Tyr-397 at a minimum concentration of 100nM. Notably, PND-1186 has no effect on the phosphorylation of c-Src, further demonstrating selectivity of the compound.

Results from follow-on cell based experiments with PND-1186 were consistent with the known function of FAK in regulating cell motility and offered interesting insights into the restricted contribution of FAK to cell survival. Treatment with PND-1186 slowed the migration of 4T1 cells in a scratch-wound healing assay, while having little effect on the survival of these cells when grown in 2D culture. Cytotoxic effects with PND-1186 were observed however, when cells were grown in 3D suspension culture and in soft-agar colony formation assays. Some hypothesize that tumors grown in 3D environments more closely mimic the growth of solid tumors as compared to the growth in a 2D monolayer. As shown in Figure 13, increasing the concentration of PND-1186 reduced the rate of suspended cell proliferation in a manner correlating with an induction of apoptosis, as assayed by activated caspase-3 cleavage and annexin-V staining, rather than with a slowed procession through the cell cycle.

Interestingly, only when cells were cultured in non-adherent conditions did PND-1186 begin to inhibit the phosphorylation of the FAK-Src complex substrate p130Cas. During adherent growth, p130Cas phosphorylation was maintained following PND-1186 treatment, suggesting that Src activation by FAK was restricted to anchorage-independent conditions.

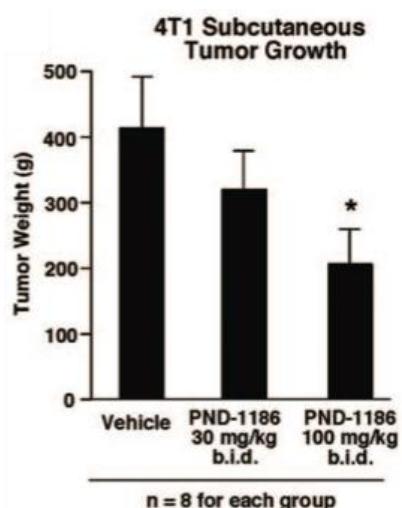
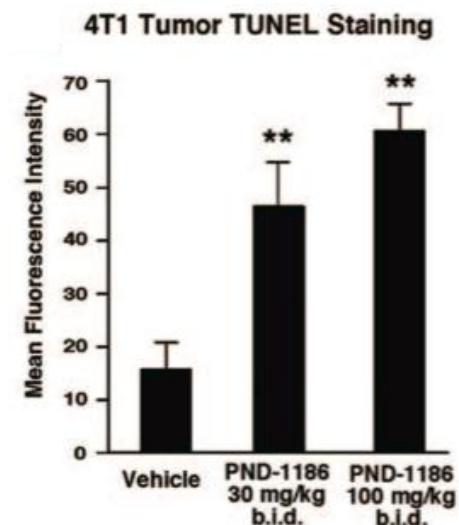
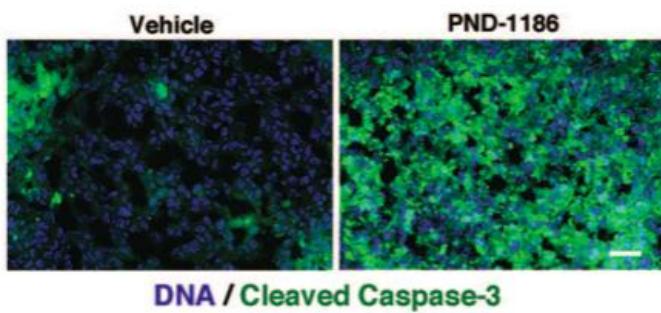
**Figure 13. FAK inhibitor PND-1186 Exhibits In Vitro Anti-Tumor Activity in Cells Grown in 3D but not 2D Environments.**



Source: Tanjoni et al., *Cancer Biology and Therapy*, 2010.

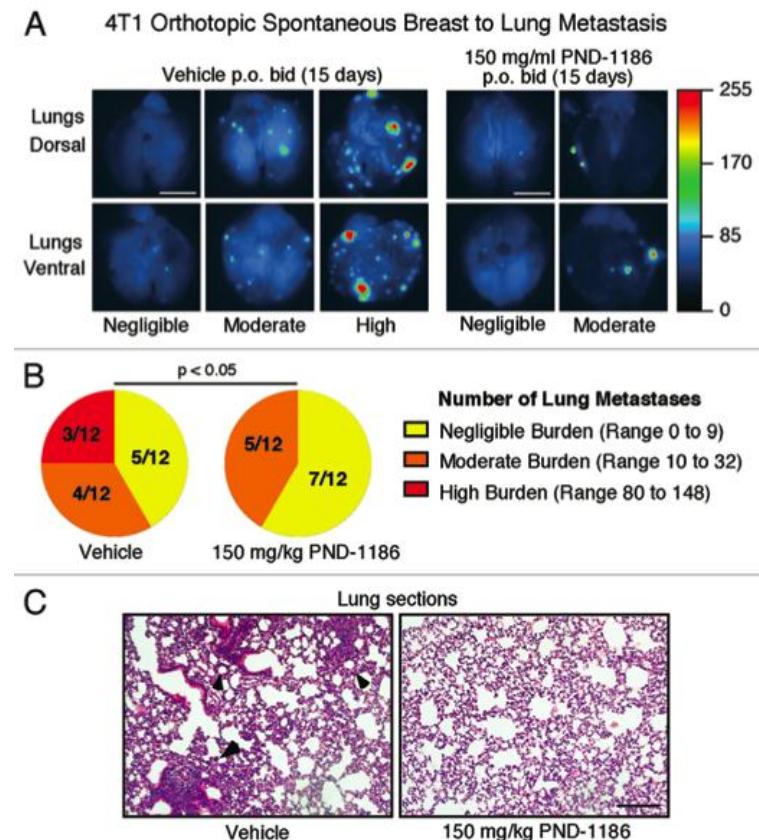
In vivo activity of PND-1186 was assessed in this study using the same 4T1 breast cancer model injected subcutaneously in mice (Figure 14). PND-1186 inhibited subcutaneous 4T1 tumor growth in a dose dependent manner, up to ~ 50% after 5 days of treatment at 100mg/kg, twice daily. Again, tumor growth inhibition correlated with induction of apoptosis as measured by TUNEL staining and caspase-3 activation (Figure 14A-C).

In a companion publication, investigators assessed the anti-metastatic potential of PND-1186. Using an orthotopic mouse model of 4T1 breast carcinoma cells, PND-1186 was shown to inhibit the growth of transplant tumors and reduce the rate of spontaneous spreading of tumor cells to the lungs (Figure 15).

**Figure 14. PND-1186 Inhibits Breast Cancer Tumor Growth and Promotes Apoptosis In Vivo.****A****B****C**

Source: Tanjoni et al., *Cancer Biology and Therapy*, 2010.

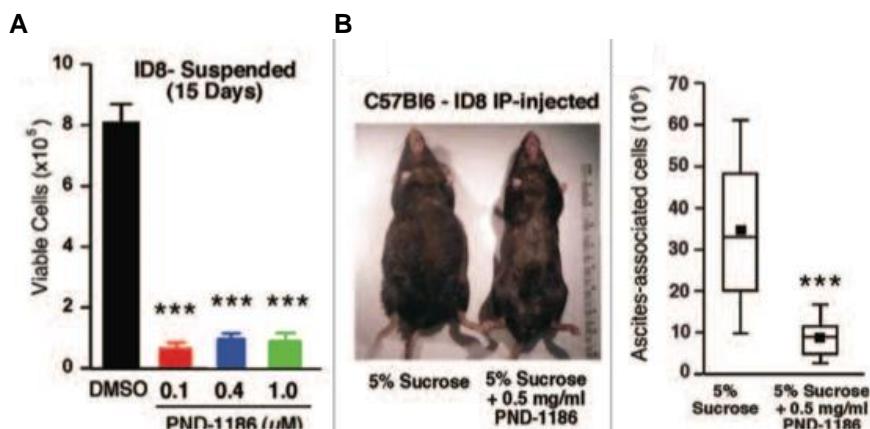
One needs to be wary of over-interpreting results in these studies given the overall positive bend in the data. The majority of the analyses both in vitro and in vivo are carried out using 4T1 cells, which are of murine origin and poorly characterized for genetic aberrations linked to their pathogeneticity.

**Figure 15. PND-1186 Inhibits Spontaneous 4T1 Breast to Lung Metastasis.**

Source: Walsh et al., *Cancer Biology and Therapy*, 2010.

### VS-4718 and VS-5095 Also Hold Promise in Ovarian Cancer

In addition to the growth inhibitory effects demonstrated in the context of breast cancer, PND-1186 has also been tested in a model for ovarian carcinoma under similar experimental conditions. During the progression of serous ovarian cancer, cells are often shed from the primary tumor into the abdominal cavity where they can form spheroids. Left unabated, these spheroids can become implanted in other organs including the uterus, urinary bladder, and bowel. In an *in vitro* analysis, PND-1186 was shown to significantly inhibit the growth of ID8 mouse ovarian carcinoma cells that were grown in suspended culture (Figure 16A). In a complementary set of experiments, mice were intraperitoneally injected (in the abdominal cavity) with ID8 cells in order to model the effects of PND-1186 on ovarian cancer *in vivo*. Treating these mice ad lib with a low dose of PND-1186 (0.5mg/ml) via drinking water prevented the significantly reduced abdominal swelling compared with control mice, and also markedly reduced the detection of tumor spheroids within the abdominal fluid (ascites) (Figure 16B). Importantly, PND-1186 was found to be well tolerated, with no adverse events or losses in body mass detected in treated animals. Similar considerations should be applied in evaluating the strength of these results. Only one ovarian carcinoma cell line was used in these analyses, which was of mouse origin. Nevertheless, the data warrant including ovarian cancer within the purview of potential indications in which to develop the VS-4718/VS-5095 program.

**Figure 16. PND-1186 Inhibits Ovarian Carcinoma Tumor Growth In Vitro and In Vivo.**

Source: Tanjoni et al., *Cancer Biology and Therapy*, 2010.

### Assessing the Clinical Development and Approval Path for VS-507 and VS-4718/5095

VSTM has communicated that it plans to pursue TNBC in the neoadjuvant (that is, the administration of therapy prior to surgery with the objective of achieving cure) setting as a potential approval path for its candidate molecules. For VS-507, this would appear to be a rational approach to approval given that salinomycin was identified from a breast cancer stem cell survival screen and it acts on the Wnt pathway, which is upregulated in TNBC. Furthermore, TNBC has a high rate of recurrence with few available alternative therapies, thus constituting a high unmet medical need. Development in the neoadjuvant setting is also supported by the recent analysis by Esserman and Woodcock published late last year in *JAMA* (*JAMA*, December 21, 2011, Vol. 306, 2608-09), suggesting that pathologic complete response (pCR) may predict recurrence-free survival, with the potential to be an acceptable endpoint for accelerated approval for drugs delivering significantly better pCR rates relative to standard therapy. This approach could meaningfully reduce the time and the clinical risks of development of VS-507.

Like all initial testing in human subjects, the Phase I study of VS-507 will seek to establish a maximum tolerated dose (MTD), safety and tolerability data, and identify biomarker response in tumors of patients treated at the recommended dose within a Phase Ib expansion cohort. As a single agent, we, along with VSTM investigators, do not anticipate dramatic responses with VS-507. The drug exhibits directed activity against a typically chemo-resistant sub-population of cancer cells but only limited activity against cell progenitor cells that compose the bulk of the tumor. Accordingly, a Phase II trial of VS-507 is likely to be a combination study of VS-507 together with standard neoadjuvant therapy (epirubicin plus cyclophosphamide followed by a taxane). Demonstrating a meaningful improvement in pCR rate, a placebo-controlled Phase II of this nature (VS-507 plus standard of care versus standard of care alone) could satisfy the criteria for accelerated approval for use in TNBC while serving as a model for a subsequent Phase III studies in pursuit of full approval. Of course, a second Phase I study evaluating a combined VS-507 plus standard care regimen will be required in order to determine whether preemptive co-toxicities or drug interference exist before initiating later stage clinical trials.

We envision two clinical development paths for VS-4718/5095, the first being second-line or maintenance use in the treatment of serous ovarian cancer and the second, neoadjuvant treatment for inflammatory breast cancer (IBC). There is a growing body of evidence, in addition to that which is presented in this report, linking elevated FAK activity to the severity of ovarian cancer. Emerging evidence also connects FAK with inflammation, which in our view proffers IBC as a suitable indication for clinical development. As with VS-507, we foresee the use of VS-

4718/5095 as being complementary to chemotherapy or standard-of-care, and would therefore anticipate additional Phase I studies with VS-4718/5095 as part of a combined regimen.

### **Revenue Model for VS-507**

Based on the preclinical evidence showing that the Wnt pathway is unregulated in TNBC and sensitive to VS-507, we focus our revenue model on the TNBC indication, specifically in the neo-adjuvant setting. We assume launches coming in 2016 for the US, 2017 in Europe, and 2018 in Japan. Other indications, either in other tumor types or other lines of therapy in TNBC, should be viewed as incremental upside to our model for VS-507.

We derive our addressable population forecasts based on Surveillance Epidemiology and End Results (SEER) database results for breast cancer and assume 15% of breast cancer patients will have TNBC. Based on results from a California Cancer Study Registry in 2007 focused on the TNBC, we assign the non-metastatic patients to their respective staging cohorts and assume a percentage of each cohort will receive neo-adjuvant therapy (Stage I: 20%; Stage II: 50%; Stage III: 90%) in order to arrive at our addressable market calculation. We then model in a market penetration growing from 10% at launch to ~65% by 2023. The duration of therapy assumptions is complicated by the lack of appropriate comparables and that the trial design VSTM would pursue would heavily influence the duration the drug is used for in the neo-adjuvant setting. For these reasons, we assume 3-5 cycles (assuming a cycle is ~ 1 month) of therapy based on the stage of the woman's disease. We then assume a \$10k/month cost in the US and conservative annual price increases of 1.5%. We assume EU pricing at 65% that of the US at launch, and price increases of 1.5% in the next years as the drug launches throughout the EU. In Japan, we model in a price at launch of ~\$8,100 (85% of the US price in that year). For the Ex-US markets, we assume VSTMS collects a royalty of 15% from its future partners.

Based on these assumptions, we assume VS-507 reaches \$670mm in WW sales by 2020, with VSTM recognizing ~\$450 of these revenues. By 2025, we believe the drug could reach \$850mm in the TNBC indication.

**Table 3. VS-507 Revenue Build in the US**

US														
VS-507 (Wnt Inhibitor) Revenue Build - US	2012E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
Breast Cancer Incidence, US	230,480	232,785	235,113	237,464	239,838	242,237	244,659	247,106	249,577	252,073	254,593	257,139	259,711	262,308
% Growth		1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%
% Triple Negative Breast Cancer	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%
# pts with Triple Negative Breast Cancer	34,572	34,918	35,267	35,620	35,976	36,336	36,699	37,066	37,437	37,811	38,189	38,571	38,957	39,346
<b>Neoadjuvant Setting (Invasive diseases Stage I-III)</b>														
<i>Stage I Patients</i>														
% pts with Stage I TNBC					33.5%	33.5%	33.5%	33.5%	33.5%	33.5%	33.5%	33.5%	33.5%	33.5%
# pts with Stage I TNBC					12,052	12,172	12,294	12,417	12,541	12,667	12,793	12,921	13,050	13,181
% receiving neo-adjuvant therapy					20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%
# of Stage I patients receivn neo-adj. therapy					2,410	2,434	2,459	2,483	2,508	2,533	2,559	2,584	2,610	2,636
<i>Stage II Patients</i>														
% pts with Stage II TNBC					50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%
# pts with Stage II TNBC					17,988	18,168	18,349	18,533	18,718	18,905	19,094	19,285	19,478	19,673
% receiving neo-adjuvant therapy					50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%
# of Stage II patients receivn neo-adj. therapy					8,994	9,084	9,175	9,266	9,359	9,453	9,547	9,643	9,739	9,837
<i>Stage III Patients</i>														
% pts with Stage III TNBC					11.5%	11.5%	11.5%	11.5%	11.5%	11.5%	11.5%	11.5%	11.5%	11.5%
# pts with Stage III TNBC					4,137	4,179	4,220	4,263	4,305	4,348	4,392	4,436	4,480	4,525
% receiving neo-adjuvant therapy					90.0%	90.0%	90.0%	90.0%	90.0%	90.0%	90.0%	90.0%	90.0%	90.0%
# of Stage III patients receivn neo-adj. therapy					3,723	3,761	3,798	3,836	3,875	3,913	3,953	3,992	4,032	4,072
<i>Market Share</i>														
Addressable Market (patients receiving neo-adj)	-	-	-	-	15,128	15,279	15,432	15,586	15,742	15,899	16,058	16,219	16,381	16,545
<i>Market Penetration</i>														
Patients on VS-507					1,513	3,820	6,944	8,572	9,445	9,937	10,277	10,542	10,812	11,002
<i>Duration of Therapy</i>														
Stage I					3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
Stage II					4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0
Stage III					5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0
Total Patients Months on Therapy					6,182.4	15,610.6	28,380.2	35,033.7	38,600.8	40,611.3	42,002	43,085	44,185	44,965
Cost per Month of Therapy					\$ 10,000	\$ 10,150	\$ 10,302	\$ 10,457	\$ 10,614	\$ 10,773	\$ 10,934	\$ 11,098	\$ 11,265	\$ 11,434
% Price increase					1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%
<b>US Sales of VS-507</b>														
% Growth					\$ 61.8	\$ 158.4	\$ 292.4	\$ 366.3	\$ 409.7	\$ 437.5	\$ 459.3	\$ 478.2	\$ 497.7	\$ 514.1
					156%	85%	25%	12%	7%	5%	4%	4%	4%	3%

**Table 4. VS-507 Revue Build in Europe**

EUROPE														
VS-507 (Wnt Inhibitor) Revenue Build - EU	2012E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
Breast Cancer Incidence, EU	221,763	223,981	226,221	228,483	230,768	233,075	235,406	237,760	240,138	242,539	244,964	247,414	249,888	252,387
% Growth	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%
% Triple Negative Breast Cancer	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%
# pts with Triple Negative Breast Cancer	33,264	33,597	33,933	34,272	34,615	34,961	35,311	35,664	36,021	36,381	36,745	37,112	37,483	37,858
<b>Neoadjuvant Setting (Invasive diseases Stage I-III)</b>														
<i>Stage I Patients</i>														
% pts with Stage I TNBC							33.5%	33.5%	33.5%	33.5%	33.5%	33.5%	33.5%	33.5%
# pts with Stage I TNBC							11,712	11,829	11,947	12,067	12,188	12,309	12,433	12,557
% receiving neo-adjuvant therapy							20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%
# of Stage I patients receiv neo-adj. therapy							2,342	2,366	2,389	2,413	2,438	2,462	2,487	2,511
<i>Stage II Patients</i>														
% pts with Stage II TNBC							50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%
# pts with Stage II TNBC							17,481	17,655	17,832	18,010	18,190	18,372	18,556	18,742
% receiving neo-adjuvant therapy							50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%
# of Stage II patients receiv neo-adj. therapy							8,740	8,828	8,916	9,005	9,095	9,186	9,278	9,371
<i>Stage III Patients</i>														
% pts with Stage III TNBC							11.5%	11.5%	11.5%	11.5%	11.5%	11.5%	11.5%	11.5%
# pts with Stage III TNBC							4,021	4,061	4,101	4,142	4,184	4,226	4,268	4,311
% receiving neo-adjuvant therapy							90.0%	90.0%	90.0%	90.0%	90.0%	90.0%	90.0%	90.0%
# of Stage III patients receiv neo-adj. therapy							3,618	3,655	3,691	3,728	3,765	3,803	3,841	3,918
<b>Market Share</b>														
Addressable Market (patients receiving neo-adj)	-	-	-	-	-		14,701	14,848	14,997	15,147	15,298	15,451	15,606	15,762
<b>Market Penetration</b>														
Patients on VS-507							1,470	3,712	6,749	8,331	9,179	9,657	9,988	10,403
<i>Duration of Therapy</i>														
Stage I							3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
Stage II							4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0
Stage III							5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0
<b>Total Patients Months on Therapy</b>														
Cost per Month of Therapy							\$ 6,008.1	\$ 15,170.4	\$ 27,579.9	\$ 34,045.8	\$ 37,512.3	\$ 39,466	\$ 40,817	\$ 42,514
% Price increase							\$ 6,090	\$ 6,181	\$ 6,274	\$ 6,274	\$ 6,274	\$ 6,274	\$ 6,274	\$ 6,274
<b>EU Sales of VS-507</b>														
% Growth							\$ 36.6	\$ 93.8	\$ 173.0	\$ 213.6	\$ 235.4	\$ 247.6	\$ 256.1	\$ 266.7
							#DIV/0!	156%	85%	23%	10%	5%	3%	4%
														2%

**Table 5. VS-507 Revenue Build in Japan**

JAPAN														
VS-507 (Wnt Inhibitor) Revenue Build - JPN	2012E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
Breast Cancer Incidence, JPN	46,096	46,557	47,023	47,493	47,968	48,447	48,932	49,421	49,915	50,415	50,919	51,428	51,942	52,462
% Growth	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%
% Triple Negative Breast Cancer	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%
# pts with Triple Negative Breast Cancer	6,914	6,984	7,053	7,124	7,195	7,267	7,340	7,413	7,487	7,562	7,638	7,714	7,791	7,869
<b>Neoadjuvant Setting (Invasive diseases Stage I-III)</b>														
<i>Stage I Patients</i>														
% pts with Stage I TNBC							33.5%	33.5%	33.5%	33.5%	33.5%	33.5%	33.5%	33.5%
# pts with Stage I TNBC							2,434	2,459	2,483	2,508	2,533	2,559	2,584	2,610
% receiving neo-adjuvant therapy							20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%
# of Stage I patients receivn neo-adj. therapy							487	492	502	507	512	517	522	527
<i>Stage II Patients</i>														
% pts with Stage II TNBC							50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%
# pts with Stage II TNBC							3,634	3,670	3,707	3,744	3,781	3,819	3,857	3,896
% receiving neo-adjuvant therapy							50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%
# of Stage II patients receivn neo-adj. therapy							1,817	1,835	1,853	1,872	1,891	1,909	1,929	1,948
<i>Stage III Patients</i>														
% pts with Stage III TNBC							11.5%	11.5%	11.5%	11.5%	11.5%	11.5%	11.5%	11.5%
# pts with Stage III TNBC							836	844	853	861	870	878	887	896
% receiving neo-adjuvant therapy							90.0%	90.0%	90.0%	90.0%	90.0%	90.0%	90.0%	90.0%
# of Stage III patients receivn neo-adj. therapy							752	760	767	775	783	791	798	806
<i>Market Share</i>														
Addressable Market (patients receiving neo-adj)	-	-	-	-	-	-	3,056	3,086	3,117	3,148	3,180	3,212	3,244	3,276
<i>Market Penetration</i>														
Patients on VS-507							-	309	779	1,417	1,749	1,927	2,027	2,097
<i>Duration of Therapy</i>														
Stage I							3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
Stage II							4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0
Stage III							5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0
Total Patients Months on Therapy							0.0	1,261.3	3,184.9	5,790.1	7,147.6	7,875	8,286	8,569
Cost per Month of Therapy							\$ 8,120	\$ 8,120	\$ 8,120	\$ 8,120	\$ 8,120	\$ 8,120	\$ 7,917	\$ 7,719
% Price increase												-2.5%		
<i>JPN Sales of VS-507</i>														
% Growth							\$ -	\$ 10.2	\$ 25.9	\$ 47.0	\$ 58.0	\$ 63.9	\$ 65.6	\$ 67.8
									152.5%	81.8%	23.4%	10.2%	2.6%	3.4%
														1.6%

### **Revenue Model for VS-4718/5095 (FAK Inhibitor Program)**

Based on the preclinical evidence showing that FAK inhibitors have efficacy in serous ovarian cancer and emerging enthusiasm from investigators surrounding a potential role of FAK pathway in inflammatory breast cancer (IBC), we model in those two indications. Given the greater amount of evidence surrounding ovarian cancer, we expect VSTM to prioritize this program over TNBC and as such, assume an earlier launch in this indication. We assume a US launch in 2016 for ovarian, 2017 for the EU and 2018 in Japan.

We derive our addressable population forecasts based on Surveillance Epidemiology and End Results (SEER) database results for ovarian in the US and GLOBOCAN in ex-US geographies, and assume conservatively that 60% of patients will have serous carcinomas. We assume that 25% of patients with Stage I-II ovarian cancer (~20% of all serous ovarian patients) and 75% of patients with Stage III-IV disease will relapse after their initial treatment, and that 40% of all patients will be sensitive to platinum agents upon retreatment. We model in a 10% market share launch, rising to ~70% by 2021. Based on recent studies looking at PARP inhibitors in this setting, we assume a 9 month duration of therapy (assumes 9 cycles). Based on these assumptions, we arrive at ~\$780mm in worldwide sales by 2020.

In assessing the IBC indication, we assume 4% of breast cancer patients have IBC, and assume a market penetration across the entire IBC population. We model in nine month duration of therapy a \$10,000 price per month in the US. We address the ex-US pricing in a manner consistent with that of VS-507. We arrive at sales in the US of ~\$460mm in 2020, and about ~\$300mm ex-US. As was the case with VS-507, we assume VSTM will collect a 15% royalty from its future partner.

**Table 6. US Revenue Build for VS-4718/5095 in Ovarian Cancer.**

US		2012E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
<b>FAK Inhibitor in Ovarian Cancer (\$MM)</b>		22,320	22,655	22,994	23,339	23,689	24,045	24,405	24,772	25,143	25,520	25,903	26,292	26,686	27,086
<b>Ovarian Cancer Incidence, US</b>		22,320	22,655	22,994	23,339	23,689	24,045	24,405	24,772	25,143	25,520	25,903	26,292	26,686	27,086
% Growth		1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%
% with serous ovarian cancer		60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%
# pts with Serous Ovarian Cancer		13,392	13,593	13,797	14,004	14,214	14,427	14,643	14,863	15,086	15,312	15,542	15,775	16,012	16,252
% with Stage I-II Disease		20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%
# of patients with Stage I-II Disease		2,678	2,719	2,759	2,801	2,843	2,885	2,929	2,973	3,017	3,062	3,108	3,155	3,202	3,250
% with Stage III-IV Disease		80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%
# of patients with Stage III-IV Disease		10,714	10,874	11,037	11,203	11,371	11,542	11,715	11,890	12,069	12,250	12,433	12,620	12,809	13,001
<b>Maintenance Setting (Platinum Sensitive)</b>															
% of Stage I-II patients relapsing after 1L Tx		25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%
% of Stage III+ patients relapsing after 1L Tx		70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%
2nd Line Patients - Addressable Market		8,169	8,292	8,416	8,542	8,670	8,800	8,932	9,066	9,202	9,340	9,481	9,623	9,767	9,914
Patients sensitive to Platinum agents upon retreatment		40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%
Duration of Therapy		3,268	3,317	3,366	3,417	3,468	3,520	3,573	3,627	3,681	3,736	3,792	3,849	3,907	3,965
<b>Market Penetration</b>															
Patients on VS-507						346.81	1,232.06	2,143.78	2,357.26	2,484.65	2,615.32	2,711.43	2,790.60	2,851.99	2,915
Duration of Therapy						9.00	9.15	9.40	9.70	9.90	9.95	10.00	10.00	10.00	10.0
Total Patients Months on Therapy						3,121.3	11,273.3	20,151.5	22,865.4	24,598.0	26,022.4	27,114	27,906	28,520	29,146
Cost per Month of Therapy						\$ 15,000	\$ 15,225	\$ 15,453	\$ 15,685	\$ 15,920	\$ 16,159	\$ 16,402	\$ 16,648	\$ 16,897	\$ 17,151
% Price increase						1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%
<b>US Sales of VS-507</b>						\$ 46.8	\$ 171.6	\$ 311.4	\$ 358.6	\$ 391.6	\$ 420.5	\$ 444.7	\$ 464.6	\$ 481.9	\$ 499.9
% Growth						267%	81%	15%	9%	7%	6%	4%	4%	4%	4%

**Table 7. EU Revenue Build for VS-4718/5095 in Ovarian Cancer.**

US		2012E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
<b>FAK Inhibitor in Ovarian Cancer (\$MM)</b>		22,320	22,655	22,994	23,339	23,689	24,045	24,405	24,772	25,143	25,520	25,903	26,292	26,686	27,086
<b>Ovarian Cancer Incidence, US</b>		22,320	22,655	22,994	23,339	23,689	24,045	24,405	24,772	25,143	25,520	25,903	26,292	26,686	27,086
% Growth		1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%
% with serous ovarian cancer		60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%
# pts with Serous Ovarian Cancer		13,392	13,593	13,797	14,004	14,214	14,427	14,643	14,863	15,086	15,312	15,542	15,775	16,012	16,252
% with Stage I-II Disease		20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%
# of patients with Stage I-II Disease		2,678	2,719	2,759	2,801	2,843	2,885	2,929	2,973	3,017	3,062	3,108	3,155	3,202	3,250
% with Stage III-IV Disease		80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%
# of patients with Stage III-IV Disease		10,714	10,874	11,037	11,203	11,371	11,542	11,715	11,890	12,069	12,250	12,433	12,620	12,809	13,001
<b>Maintenance Setting (Platinum Sensitive)</b>															
% of Stage I-II patients relapsing after 1L Tx		25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%
% of Stage III+ patients relapsing after 1L Tx		70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%
2nd Line Patients - Addressable Market		8,169	8,292	8,416	8,542	8,670	8,800	8,932	9,066	9,202	9,340	9,481	9,623	9,767	9,914
Patients sensitive to Platinum agents upon retreatment		40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%
Duration of Therapy		3,268	3,317	3,366	3,417	3,468	3,520	3,573	3,627	3,681	3,736	3,792	3,849	3,907	3,965
<b>Market Penetration</b>															
Patients on VS-507						346.81	1,232.06	2,143.78	2,357.26	2,484.65	2,615.32	2,711.43	2,790.60	2,851.99	2,915
Duration of Therapy						9.00	9.15	9.40	9.70	9.90	9.95	10.00	10.00	10.00	10.0
Total Patients Months on Therapy						3,121.3	11,273.3	20,151.5	22,865.4	24,598.0	26,022.4	27,114	27,906	28,520	29,146
Cost per Month of Therapy						\$ 15,000	\$ 15,225	\$ 15,453	\$ 15,685	\$ 15,920	\$ 16,159	\$ 16,402	\$ 16,648	\$ 16,897	\$ 17,151
% Price increase						1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%
<b>US Sales of VS-507</b>						\$ 46.8	\$ 171.6	\$ 311.4	\$ 358.6	\$ 391.6	\$ 420.5	\$ 444.7	\$ 464.6	\$ 481.9	\$ 499.9
% Growth						267%	81%	15%	9%	7%	6%	4%	4%	4%	4%

**Table 8. Japan Revenue Build for VS-4718/5095 in Ovarian Cancer.**

JPN														
FAK Inhibitor in Ovarian Cancer (\$MM)	2012E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
Ovarian Cancer Incidence, EU	8,839	8,972	9,106	9,243	9,243	8,972	9,106	9,243	9,381	9,522	9,665	9,810	9,957	10,106
% Growth		1.5%	1.5%	1.5%		1.5%	1.5%	1.5%		1.5%	1.5%	1.5%	1.5%	1.5%
% with serous ovarian cancer	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%
# pts with Serous Ovarian Cancer	5,303	5,383	5,464	5,546	5,303	5,383	5,464	5,546	5,629	5,713	5,799	5,886	5,974	6,064
% with Stage I-II Disease	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%
# of patients with Stage I-II Disease	1,061	1,077	1,093	1,109	1,061	1,077	1,093	1,109	1,126	1,143	1,160	1,177	1,195	1,213
% with Stage III-IV Disease	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%	80.0%
# of patients with Stage III-IV Disease	4,243	4,306	4,371	4,437	4,243	4,306	4,371	4,437	4,503	4,571	4,639	4,709	4,779	4,851
<b>Maintenance Setting (Platinum Sensitive)</b>														
% of Stage I-II patients relapsing after 1L Tx	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%
% of Stage III+ patients relapsing after 1L Tx	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%	70%
2nd Line Patients - Addressable Market	3,235	3,284	3,333	3,383	3,235	3,284	3,333	3,383	3,434	3,485	3,537	3,590	3,644	3,699
Patients sensitive to Platinum agents upon retreatment	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%
Market Penetration														
Patients on VS-507					-	-	133	474	824	906	955	1,005	1,042	1,073
Duration of Therapy							9.00	9.15	9.40	9.70	9.90	9.95	10.00	9.0
Total Patients Months on Therapy							1,199.8	4,333.4	7,746.2	8,789.4	9,455	10,003	10,423	9,654
Cost per Month of Therapy							\$ 12,363	\$ 12,363	\$ 12,363	\$ 12,363	\$ 12,363	\$ 12,363	\$ 12,363	\$ 12,363
% Price increase							0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
EU Sales of VS-507					\$ -	\$ -	\$ 14.8	\$ 53.6	\$ 95.8	\$ 108.7	\$ 116.9	\$ 123.7	\$ 128.9	\$ 119.4
% Growth							#DIV/0!	261%	79%	13%	8%	6%	4%	-7%

**Table 9. Revenue Build for VS-4718/5095 in Inflammatory Breast Cancer in the US, EU and Japan**

US															
FAK Inhibitor in IBC - Revenue Build - US	2012E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	
Breast Cancer Incidence, US	230,480	232,785	235,113	237,464	239,838	242,237	244,659	247,106	249,577	252,073	254,593	257,139	259,711	262,308	
% Growth	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	
% Inflammatory Breast Cancer	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	
# pts with IBC	9,219	9,311	9,405	9,499	9,594	9,689	9,786	9,884	9,983	10,083	10,184	10,286	10,388	10,492	
Market Penetration					10.0%	20.0%	35.0%	45.0%	48.0%	50.0%	51.0%	51.5%	52.0%	52.0%	
Patients on FAK Inhibitor					959	1,938	3,425	4,448	4,792	5,041	5,194	5,297	5,402	5,456	
Duration of Therapy					9.0	9.0	9.0	9.0	9.0	9.0	9.0	9.0	9.0	9.0	
Total Patients Months on Therapy					8,634	17,441	30,827	40,031	43,127	45,373	46,743	47,674	48,618	49,104	
Cost per Month of Therapy					\$ 10,000	\$ 10,150	\$ 10,302	\$ 10,457	\$ 10,614	\$ 10,773	\$ 10,934	\$ 11,098	\$ 11,265	\$ 11,434	
% Price increase					1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	
US Sales of VS-507 in IBC					\$ 86.3	\$ 177.0	\$ 317.6	\$ 418.6	\$ 457.7	\$ 488.8	\$ 511.1	\$ 529.1	\$ 547.7	\$ 561.5	
% Growth					105%	79%	32%	9%	7%	5%	4%	4%	4%	3%	
EUROPE															
FAK Inhibitor in IBC - Revenue Build - EU	2012E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	
Breast Cancer Incidence, EU	221,763	223,981	226,221	228,483	230,768	233,075	235,406	237,760	240,138	242,539	244,964	247,414	249,888	252,387	
% Growth	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	
% Inflammatory Breast Cancer	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	
# pts with IBC	8,871	8,959	9,049	9,139	9,231	9,323	9,416	9,510	9,606	9,702	9,799	9,897	9,996	10,095	
Market Penetration					10.0%	20.0%	35.0%	45.0%	48.0%	50.0%	51.0%	51.5%	52.0%	52.0%	
Patients on FAK Inhibitor						932	1,883	3,329	4,322	4,657	4,899	5,047	5,148	5,250	
Duration of Therapy						9.0	9.0	9.0	9.0	9.0	9.0	9.0	9.0	9.0	
Total Patients Months on Therapy						8,391	16,949	29,958	38,902	41,911	44,094	45,425	46,329	47,247	
Cost per Month of Therapy						\$ 6,090	\$ 6,181	\$ 6,274	\$ 6,274	\$ 6,274	\$ 6,274	\$ 6,274	\$ 6,274	\$ 6,274	
% Price increase						1.5%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	
EU Sales of VS-507 in IBC						\$ -	\$ 51.1	\$ 104.8	\$ 188.0	\$ 244.1	\$ 263.0	\$ 276.6	\$ 285.0	\$ 290.7	
% Growth							79%	30%	8%	5%	3%	2%	2%	2%	
JAPAN															
FAK Inhibitor in IBC - Revenue Build - JPN	2012E	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	
Breast Cancer Incidence, JPN	46,096	46,557	47,023	47,493	47,968	48,447	48,932	49,421	49,915	50,415	50,919	51,428	51,942	52,462	
% Growth	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	
% Inflammatory Breast Cancer	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	
# pts with IBC	1,844	1,862	1,881	1,900	1,919	1,938	1,957	1,977	1,997	2,017	2,037	2,057	2,078	2,098	
Market Penetration						10.0%	20.0%	35.0%	45.0%	48.0%	50.0%	50.5%	51.0%	51.0%	
Patients on VS-507							196	395	699	907	978	1,029	1,049	1,070	
Duration of Therapy							9.0	9.0	9.0	9.0	9.0	9.0	9.0	9.0	
Patients on FAK Inhibitor								1,762	3,558	6,289	8,167	8,799	9,257	9,443	9,632
Cost per Month of Therapy								\$ 8,242	\$ 8,242	\$ 8,242	\$ 8,242	\$ 8,242	\$ 8,242	\$ 8,242	\$ 8,242
% Price increase								0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
JPN Sales of VS-507 in IBC							\$ -	\$ -	\$ 14.5	\$ 29.3	\$ 51.8	\$ 67.3	\$ 72.5	\$ 76.3	\$ 77.8
% Growth									102%	77%	30%	8%	5%	2%	2%

**Table 10. Summary of Revenue Builds by Product and Region**

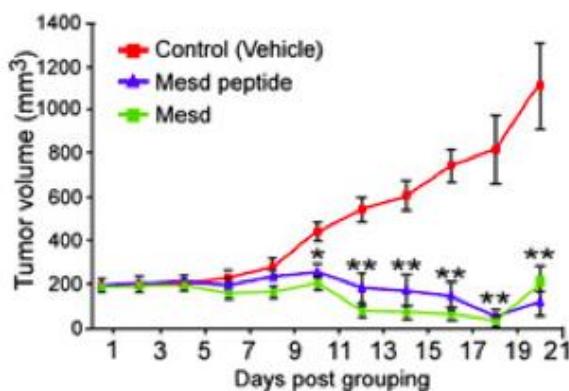
Revenues	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
<b>Total Sales and Royalties to VSTM</b>											
<b>Total Sales US</b>	195.0	507.1	921.4	1,143.6	1,259.0	1,346.8	1,415.1	1,471.8	1,527.3	1,575.5	
% yoy change											
<b>Total Ex-US Royalties</b>	0.0	18.9	56.9	108.9	141.5	156.8	166.3	172.7	172.7	174.3	
% yoy change											
<b>VS-507 Revenues (\$MM)</b>											
<b>VS-507 Total Sales WW</b>	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
<b>Geographical Breakdown of VS-507 Sales</b>											
<b>VS-507 Total Sales, US</b>	61.8	158.4	292.4	366.3	409.7	437.5	459.3	478.2	497.7	514.1	
% yoy change	156%	85%	25%	12%	7%	5%	4%	4%	4%	3%	
<b>VS-507 Total Sales, EU</b>	0.0	36.6	93.8	173.0	213.6	235.4	247.6	256.1	266.7	271.4	
% Royalty Rate	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%
<b>Royalties from EU Sales to Verastem</b>	0.0	5.5	14.1	26.0	32.0	35.3	37.1	38.4	40.0	40.7	
<b>VS-507 Total Sales, JPN</b>	0.0	0.0	10.2	25.9	47.0	58.0	63.9	65.6	67.8	68.9	
% Royalty Rate	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%
<b>Royalties from JPN Sales to Verastem</b>	0.0	0.0	1.5	3.9	7.1	8.7	9.6	9.8	10.2	10.3	
<b>TOTAL WW Sales and Royalties to VSTM for VS-507</b>	61.8	163.9	308.0	396.2	448.8	481.5	506.0	526.4	547.9	565.2	
<b>Revenue by Geography</b>											
<b>US</b>	100%	97%	95%	92%	91%	91%	91%	91%	91%	91%	
<b>EU</b>	0%	3%	5%	7%	7%	7%	7%	7%	7%	7%	
<b>JPN</b>	0%	0%	0%	1%	2%	2%	2%	2%	2%	2%	
<b>VS-4718/5095 Revenues (\$MM)</b>											
<b>VS-4718/5095 Total Sales WW</b>	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
<b>Geographical Breakdown of VS-507 Sales</b>											
<b>VS-4718/5095 Total Sales, US</b>	133.2	348.7	629.0	777.2	849.3	909.3	955.8	993.7	1,029.6	1,061.3	
<b>VS-4718/5095 Total Sales, EU</b>	0.0	89.6	246.0	444.3	534.9	575.8	607.6	629.9	610.1	622.9	
% Royalty Rate	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%
<b>Royalties from EU Sales to Verastem</b>	0.0	13.4	36.9	66.6	80.2	86.4	91.1	94.5	91.5	93.4	
<b>VS-4718/5095 Total Sales, JPN</b>	0.0	0.0	29.4	82.9	147.6	176.0	189.4	200.0	206.7	198.7	
% Royalty Rate	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%
<b>Royalties from JPN Sales to Verastem</b>	0.0	0.0	4.4	12.4	22.1	26.4	28.4	30.0	31.0	29.8	
<b>TOTAL WW Sales and Royalties to VSTM for VS-507</b>	133.2	362.1	670.3	856.3	951.7	1,022.1	1,075.4	1,118.1	1,152.1	1,184.6	
<b>Revenue by Geography</b>											
<b>US</b>	100%	96%	94%	91%	89%	89%	89%	89%	89%	90%	
<b>EU</b>	0%	4%	6%	8%	8%	8%	8%	8%	8%	8%	
<b>JPN</b>	0%	0%	1%	1%	2%	3%	3%	3%	3%	3%	

## Sizing-up the Competitive Landscape for VS-507

The competitive landscape for VS-507 can be viewed from a few different perspective: first, in relation to the various other drug candidates targeting the Wnt pathway; second, in relation to other agents that selectively target cancer stem cells; and third, in relation to other drug candidates or approved therapies currently being explored in the refractory/relapse TNBC setting.

We have identified a number of Wnt pathway inhibitors in development, nearly all of which are in preclinical or early clinical phase clinical assessment. WntTide (Raptor Pharmaceutical; RPTP Not Rated) is a mesoderm development protein (Mesd)-based peptide inhibitor of LRP6 being developed for the treatment of breast cancer. Mesd is a chaperone protein required for the proper folding and stabilization of the Wnt co-receptor LRP6. The preclinical study by Lui et al. referred to above (PNAS, 2010), describes some of the anti-tumor activity of WntTide, showing marked reduction in both tumor growth and the stability of  $\beta$ -catenin and myc in a MMTV-Wnt1 driven murine breast cancer model (Figure 10). And so while WntTide is potential competitor of VS-507, one can argue that VS-507 has benefit from the results with WntTide, validating LRP6 as an anti-cancer target

**Figure 10. MMTV-Wnt1 Driven Transplant Tumor Growth is Sensitive to Treatment with Mesd and the Mesd Peptide Derivative, WntTide.**



Source: Lui et al., PNAS, 2010

OncoMed (Privately held), another leader in the development of therapeutics targeted to CSCs, has two Wnt inhibitor programs in development in collaboration with Bayer (BAYRY.PK, Not Rated). OMP-18R5 is a monoclonal antibody against Frizzled7 currently undergoing evaluation in a Phase I study in solid tumors, initiated in May 2011. OMP-54FZ8, a second Wnt pathway inhibitor, is a soluble peptide chimera of the Frizzled8 cystein rich domain fused to the human Fc domain (FZD8Fc), that acts as receptor decoy to sequester Wnt ligands away from Frizzled receptors in membrane. A potential IND filing with OMP-54FZ8 is anticipated for year end 2012.

**Table 11. Wnt Pathway Competitive Landscape**

Wnt Pathway Inhibitors in Development						
Drug Candidate	Company	Ticker	R&R Rating	Target	Route	Notes
VS-507	Verastem	VSTM	Outperform	LRP6	Unknown	Preclinical
OMP-18R8	OncoMed	Private	N/A	Frizzled 7	IV	Phase I, solid tumors
OMP54FZ8	OncoMed	Private	N/A	Wnt Ligand	IV	Preclinical
WntTide	Raptor Pharma	RPTP	Not Rated	LRP6	IV	Preclinical, breast cancer

Source: Rodman & Renshaw Research

In addition to its Wnt programs, OncoMed has four programs targeting the Notch pathway in either Phase I or preclinical development (with an anticipated IND filing in 2012/2013), and a

burgeoning RSPO-LGR inhibitor program with an IND filing anticipated for 2013. Contributions of the Notch signaling pathway to the maintenance and survival of cancer stem cells have been demonstrated in several preclinical studies (some of which are reviewed here (*Takebe et al., Nature Review Clinical Oncology, 2010*)). OncoMed's leading Notch program demcizumab is an antibody against the Notch activating ligand DLL4, and is currently in expanded Phase I assessment in patients with pancreatic and non-small cell lung cancers.

There are other players in the cancer stem cell targeted therapy space that also deserve some attention. ImmunoCellular Therapeutics (IMUC.OB, Not Rated) is developing a peptide stimulator of the immune response to CD133, an antigen frequently presented by cancer stem cells. ICT-121 is in currently preclinical development in experimental models of glioblastoma multiforme. Stemline Therapeutics (Privately held), is developing SL-401, an IL3R-directed cytotoxic-peptide conjugate directed at cytokine-dependent stem cells. In contrast to its competitors, Stemline has focused primarily in hematologic malignancies. SL-401 is in Phase I clinical evaluation in relapsed/refractory AML.

We would be remiss not to mention Boston Biomedical (Privately held), which was recently acquired by Dainippon Sumitomo Pharma Co. (Tokyo:4506, Not Rated) for \$200MM up front, and up to \$2.4B in development and revenue milestones. BBI608 and BBI503, the principal assets in BBI's product development pipeline, are two oral CSC-directed small molecules, although the molecular targets of either compound have not been disclosed. BBI608 is reportedly entering Phase III trials in colon cancer, while BBI503 is in Phase I evaluation in advanced solid tumors.

**Table 12. Cancer Stem Cell Therapy Competitive Landscape**

Cancer Stem Cell Therapies in Development						
Drug Candidate	Company	Ticker	R&R Rating	Target	Route	Notes
Demcizumab	OncoMed	Private	N/A	DLL4 (Notch Pathway)	IV	Phase I, pancreatic and NSCLC
REGN421	Regeneron	REGN	Not Rated	DLL4 (Notch Pathway)	IV	Phase I initiated
ICT-121	ImmunoCellular Therapeutics	IMUC.OC	Not Rated	CD-133	IV	Preclinical, glioblastoma
SL-401	Stemline Therapeutics	Private	N/A	IL3RR	IV	Phase I, R/R AML
BBI608	Boston Biomedical / Dainippon	Private / Tokyo:4506	Not Rated	Not Disclosed	Oral	Entering Phase III, colon cancer

Source: Rodman & Renshaw Research

With respect to TNBC more generally, there are relatively few developing candidates in this space presenting significant challenges to VS-507. Most of the recent activity has been with poly-ADP ribose polymerase (PARP)-inhibitors that have been predicted to be synthetically lethal with DNA-damage agents in tumors harboring *BRCA1/BRCA2* mutations (Table X). About half of women diagnosed as having high-risk triple negative breast cancer are also positive for *BRCA1/2* mutations, suggesting that VSV-507 could have to share a considerable portion of the TNBC with any number of the PARP inhibitors in development should they reach approval in the similar treatment setting.

**Table 13. PARP Inhibitors In Development in Triple Negative Breast Cancer**

Developing PARP Inhibitors in Triple Negative Breast Cancer					
Drug Candidate	Company	Ticker	R&R Rating	Route	Clinical Trials
Olaparib (AZD2281)	AstraZeneca	AZN	Not Rated	Oral	Phase II, BRCA-associated BC
Iniparib (BSI201)	Sanofi-Aventis	SNY	Not Rated	IV	Phase II, advanced TNBC
Velparib (ABT888)	Abbott	ABT	Not Rated	Oral	Phase II, advanced TNBC, concentrated activity in BRCA-mutant tumors
Rucarparib (AG014699)	Clovis	CLVS	Not Rated	IV	Phase II, Early Stage TNBC and BRCA-associated BC
MK4827	Merck	MRK	Not Rated	Oral	Phase I, solid tumors
CEP8983	Cephalon/Teva	TEVA	Not Rated	Oral	Phase I, solid tumors

Source: Rodman &amp; Renshaw Research

### Competitive Landscape Among FAK inhibitors

The competitive landscape for the VS-4718/VS-5095, apart from the other agents directed toward CSC survival as described above, consists of a handful of small molecules that were developed primarily as FAK inhibitors or one agent shown to target FAK indirectly. Pfizer (PFE, Not Rated) has had two FAK inhibitors in development beginning with PF-0562271, which was halted in favor of the second generation inhibitor PF-4554878. Preclinical studies show that PF4554878 targets FAK and the highly conserved molecule Pyk2 with IC<sub>50</sub> concentrations < 0.6nM. Results of a Phase I dose escalation study with PF-04554878 (NCT00787033) were presented at ASCO in June 2011 and indicated that the drug had an acceptable safety profile. Most adverse events were of low grade and included nausea, vomiting and fatigue. Grade 3 headache was observed in one of three patients and Grade 3 unconjugated hyperbilirubinemia was observed in two of six patients receiving ≤ 425mg BID of drug - the recommended dose for Phase II analysis. These events were manageable and reversible with dose reductions. With respect to clinical benefit, an overall disease stabilization rate of 41% was observed across a variety of solid tumors including NSCLC, ovarian, pancreatic, cholangiocytic, and colon cancers. Phase II trials with PF-04554878 have yet to be initiated.

GlaxoSmithKline (GSK, Not Rated) also has a FAK inhibitor in development. GSK2256098 is currently recruiting patients with solid tumors for a Phase I dose escalation study (NCT01138033). Unfortunately, the absence of preclinical reporting with GSK2256098 makes it difficult to compare to either Pfizer's or VSTM's FAK program.

Other FAK-targeting molecules include Novartis' (NVS, Not Rated) dual FAK/IGF-1R inhibitor NVP-TAE226 and ArQule's (ARQL, Not Rated) Tivantinib – a c-MET inhibitor that indirectly targets FAK with low nanomolar activity. NVP-TAE226 targets both FAK and Pyk2 with a low IC<sub>50</sub> of 5.5nM and prolonged animal survival in xenograft studies with glioma and ovarian cancer models. However, because the compound potently targets IGF-1R it has been considered unsuitable for human trials and was suspended pending further development. Tivantinib (ARQ197) is currently in a Phase III trial in patients with EGFR- and KRAS-driven NSCLC given in combination with erlotinib (Roche, RHHBY, Not Rated) and compared with a control arm of erlotinib plus placebo.

**Table 14. FAK Inhibitor Competitive Landscape**

FAK Inhibitors in Development						
Drug Candidate	Company	Ticker	R&R Rating	Target	Route	Notes
VS-4718/5095	Verastem	VSTM	Outperform	FAK	Oral	Preclinical
PF-562271	Pfizer	PFE	Not Covered	FAK/PYK2	Oral	Phase I completed, 16% SD best response
PF-4554878	Pfizer	PFE	Not Covered	FAK/PYK2	Oral	Phase I completed, 41% SD best response
GSK-2256098	GlaxoSmithKline	GSK	Not Covered	FAK	Oral	Phase I initiated
Tivantinib (ARQ197)	ArQule	ARQL	Not Covered	c-MET/FAK	Oral	Phase III in NSCLC, Phase II initiated in TNBC

Source: Rodman &amp; Renshaw Research

**Table 15. Income Statement**

Income Statement (\$MM)	2010A	1Q - 3Q11A	4Q11E	2011E	1Q12E	2Q12E	3Q12E	4Q12E	2012E	2013E	2014E	2015E	2016E	2017E
<b>Product Sales and Royalties</b>												0.0	61.8	158.4
VS-507, US Sales												0.0	0.0	5.5
VS-507, Ex-US Royalties												0.0	133.2	348.7
FAK Inhibitor, US Sales												0.0	0.0	13.4
FAK Inhibitors, Ex-US Royalties												0.0	0.0	
<b>Total Product Sales and Royalties</b>												0.0	195.0	526.0
<b>License and Milestone Revenue</b>														
<b>Collaboration Revenue</b>														
<b>Total Revenue</b>													195.0	526.0
<b>Cost of Goods Sold</b>													21.4	53.2
% Growth													11.0%	148%
% of Total US Sales													10.5%	
<b>Gross Profit</b>				0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	173.5	472.8
<b>Operating expenses:</b>														
R&D	0.4	5.5	0.4	5.9	0.90	2.00	2.65	3.15	8.7	15.7	25.8	62.0	89.9	112.4
% Growth					122%	33%	19%	47.9%					45.0%	25.0%
% of Total Revenue													46.1%	21.4%
S&A	0.4	2.2	0.4	2.6	0.55	0.63	0.70	0.75	2.6	3.5	5.3	15.9	55.8	86.5
% Growth					14%	12%	7%	1.8%					50.0%	250.0%
% of Total US Sales													28.6%	16.4%
<b>Total operating expenses</b>	0.8	7.7	0.8	8.5	1.5	2.6	3.4	3.9	11.3	19.2	31.2	78.0	145.7	198.9
<b>Operating income (loss)</b>	(0.8)	(7.7)	(0.8)	(8.5)	(1.5)	(2.6)	(3.4)	(3.9)	(11.3)	(19.2)	(31.2)	(78.0)	27.8	273.9
<b>Other income (expense)</b>														
Interest income														
Interest (expense)														
<b>Total other income</b>	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
<b>Pretax Income</b>	(0.8)	(7.7)	(0.8)	(8.5)	(1.5)	(2.6)	(3.4)	(3.9)	(7.3)	(19.2)	(31.2)	(78.0)	27.8	273.9
Provision for Income Tax														6.8
Effective Tax Rate														2.5%
<b>Net income</b>	(0.8)	(7.7)	(0.8)	(8.5)	(1.45)	(2.63)	(3.35)	(3.90)	(7.3)	(19.2)	(31.2)	(78.0)	27.8	267.0
Accretion of preferred stock	(0.0)	(0.0)	0.0	0.0										
<b>Net income applicable to common shareholders</b>	(0.8)	(7.7)	(0.8)	(8.5)	(1.5)	(2.6)	(3.4)	(3.9)	(11.3)	(19.2)	(31.2)	(78.0)	27.8	267.0
<b>Basic EPS to common shareholders</b>	\$ (0.92)	\$ (6.28)	\$ (0.26)	\$ (5.07)	\$ (0.07)	\$ (0.12)	\$ (0.15)	\$ (0.18)	\$ (0.34)	\$ (0.71)	\$ (1.00)	\$ (2.47)	\$ 0.84	\$ 7.87
<b>Diluted EPS to common shareholders</b>	\$ (0.92)	\$ (6.28)	\$ (0.26)	\$ (5.07)	\$ (0.07)	\$ (0.12)	\$ (0.15)	\$ (0.18)	\$ (0.34)	\$ (0.71)	\$ (1.00)	\$ (2.47)	\$ 0.74	\$ 6.91
Basic Shares Outstanding	0.850	1.226	2.993	1.668	21.059	21.375	21.696	22.021	21.377	26.939	31.208	31.521	33.097	33.924
Diluted Shares Outstanding	0.850	1.226	2.993	1.668	21.059	21.375	21.696	22.021	21.377	26.939	31.208	31.521	37.720	38.663
% change in diluted shares outstanding					1.5%	1.5%	1.5%	1.5%	1182%	6.1%	1.0%	1.0%	5.0%	2.5%

**Table**

**Table 16. Balance Sheet**

Balance Sheet (\$MM)	2010A	Q - 3Q11A	4Q11E	2011E	1Q12E	2Q12E	3Q12E	4Q12E	2012E
<b>Current Assets</b>									
Cash and cash equivalents	3.6	41.4	61.8	61.8	117.1	114.5	111.1	107.2	107.2
Prepaid expenses and other current assets	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total current assets	3.6	41.4	61.8	61.8	117.1	114.5	111.1	107.2	107.2
<b>Long-term Assets</b>									
Property and equipment, net	0.0	0.7	0.7	0.7	2.7	2.7	2.7	2.7	2.7
Other long-term assets		0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Restricted cash		0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Total long-term assets	0.0	0.9	0.9	0.9	2.9	2.9	2.9	2.9	2.9
<b>Total Assets</b>	3.6	42.4	62.8	62.8	120.0	117.4	114.0	110.1	110.1
<b>Liabilities and Shareholders' Equity</b>									
<b>Current Liabilities</b>									
Accounts Payable	0.3	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2
Accrued expenses	0.1	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8
Total current liabilities	0.4	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
<b>Long-term liabilities</b>									
Deferred rent	0.0	0.1	0.1	0.08					0.0
Liability for shares subject to repurchase	0.0	0.0	0.0	0.04					0.0
Total Long-term liabilities	0.0	0.1	0.1	0.12	0.0	0.0	0.0	0.0	0.0
Total liabilities	0.4	2.1	2.1	2.13	2.0	2.0	2.0	2.0	2.0
Commitments and contingencies									
Series A redeemable convertible preferred stock	3.9	15.9	0.0	0.00					0.0
Series B redeemable convertible preferred stock									0.0
Series C redeemable convertible preferred stock		31.9		0.00					0.0
Shareholder's Equity									0.0
Common Stock	0.0	0.0	0.0	0.00					0.0
Additional paid-in capital	0.1	0.8	69.1	69.10	127.9	127.9	127.9	127.9	127.9
Accumulated deficit	(0.8)	(8.5)	(8.5)	(8.46)	(9.9)	(12.5)	(15.9)	(19.8)	(19.8)
Total Shareholders' Equity (Deficit)	(0.7)	(7.6)	60.6	60.64	118.0	115.4	112.0	108.1	108.1
<b>Total Liabilities and Shareholders' Equity (Deficit)</b>	3.6	42.36	62.77	62.77	120.0	117.4	114.0	110.1	110.1

**Table 17. Selected Oncology Company Comparables**

Selected Oncology Company Comparables							
Comparable	Ticker	Rating	Price	Market Cap	Cash	Debt	EV
AETerna Zentaris Inc.	AEZS	Market Perform	\$1.86	\$193	\$48	\$0	\$143
Allos Therapeutics Inc.	ALTH	Not Rated	\$1.43	\$151	\$98	\$0	\$51
ArQule Inc.	ARQL	Not Rated	\$7.06	\$380	\$68	\$2	\$275
Array BioPharma Inc.	ARRY	Not Rated	\$2.85	\$175	\$61	\$90	\$235
Astex Pharmaceuticals Inc.	ASTX	Market Outperform	\$1.83	\$170	\$126	\$0	\$44
Celldex Therapeutics Inc.	CLDX	Not Rated	\$3.62	\$160	\$63	\$16	\$113
Clovis Oncology Inc.	CLVS	Not Rated	\$22.52	\$468	\$143	\$0	\$324
Cell Therapeutics Inc.	CTIC	Market Outperform	\$1.25	\$241	\$47	\$0	\$212
Cyclacel Pharmaceuticals Inc.	CYCC	Not Rated	\$0.71	\$39	\$28	\$0	\$24
CytRx Corp.	CYTR	Not Rated	\$0.33	\$49	\$42	\$0	\$7
Delcath Systems Inc.	DCTH	Not Rated	\$3.87	\$186	\$45	\$0	\$141
Endocyte Inc.	ECYT	Not Rated	\$3.44	\$123	\$139	\$12	-\$4
EntreMed Inc.	ENMD	Not Rated	\$2.18	\$27	\$2	\$0	\$58
Exelixis Inc.	EXEL	Not Rated	\$5.20	\$772	\$194	\$182	\$759
GTX Inc.	GTXI	Market Perform	\$3.38	\$212	\$74	\$0	\$138
Immunogen Inc.	IMGN	Not Rated	\$12.89	\$989	\$169	\$0	\$821
Immunomedics Inc.	IMMU	Not Rated	\$3.28	\$248	\$16	\$0	\$231
Infinity Pharmaceuticals Inc.	INFI	Market Perform	\$7.97	\$213	\$75	\$0	\$138
Keryx Biopharmaceuticals Inc.	KERX	Market Outperform	\$4.35	\$309	#N/A	\$0	\$262
Myrexis Inc.	MYRX	Not Rated	\$3.12	\$82	\$81	\$0	\$2
Nektar Therapeutics	NKTR	Not Rated	\$7.49	\$857	\$241	\$230	\$821
Oncogenex Pharmaceuticals Inc.	OGXI	Not Rated	\$15.52	\$151	\$70	\$8	\$90
Oncolytics Biotech Inc.	ONCY	Market Perform	\$4.74	\$338	\$40	\$0	\$296
Oncothreon Inc.	ONTY	Market Outperform	\$5.07	\$213	\$62	\$0	\$151
Oxigene Inc.	OXGN	Not Rated	\$1.28	\$19	\$13	\$0	\$6
Rexahn Pharmaceuticals Inc.	RNN	Market Perform	\$0.48	\$46	\$15	\$0	\$31
Raptor Pharmaceutical Corp.	RPTP	Not Rated	\$7.11	\$340	\$55	\$0	\$285
Sunesis Pharmaceuticals Inc.	SNSS	Not Rated	\$2.26	\$106	\$42	\$0	\$64
Synta Pharmaceuticals Corp.	SNTA	Market Outperform	\$4.22	\$243	\$40	\$17	\$220
Telik Inc.	TELK	Not Rated	\$0.22	\$12	\$11	\$0	\$1
Threshold Pharmaceuticals Inc.	THLD	Not Rated	\$4.56	\$224	\$25	\$0	\$199
YM BioSciences Inc.	YMI	Market Outperform	\$1.91	\$223	\$67	\$0	\$155
ZIOPHARM Oncology Inc.	ZIOP	Not Rated	\$4.68	\$320	\$105	\$0	\$201
Dendreon Corp.	DNDN	Market Outperform	\$11.42	\$1,701	\$539	\$536	\$1,743
<b>Averages</b>				\$293			\$242
Verastem Inc.	VSTM	Market Outperform	\$11.30	\$200	\$101	\$0	\$138

Source: FactSet (as of 3.06.12)

## Senior Management Team

### **Christoph Westphal, M.D., Ph.D., Chairman/CEO**

Dr. Westphal is a Partner of Longwood Founders Fund, which founds and invests in medical companies. He was founder and CEO of Sirtris Pharmaceuticals, since acquired by GlaxoSmithKline in 2008, which he took public and led as Chief Executive Officer until 2010. Dr. Westphal cofounded Alnara Pharmaceuticals (acquired by Eli Lilly (LLY, Not Rated) in 2010), and was co-founder/CEO of Alnylam Pharmaceuticals (ALNY, Market Outperform) and Momenta Pharmaceuticals. Dr. Westphal serves on the board of directors of Ovascience (which he cofounded), and serves on the Board of Fellows of Harvard Medical School, and the Board of Overseers of the Boston Symphony Orchestra. He earned his M.D. from Harvard Medical School and Ph.D. in genetics from Harvard University and he graduated with a B.A. summa cum laude and Phi Beta Kappa from Columbia University.

### **Robert Forrester, LL.B., Chief Operating Officer**

Mr. Forrester has over 10 years experience as the CEO, COO or CFO of both private and public life science companies with Forma Therapeutics, CombinatoRx (now Zalicus) and Coley (acquired by Pfizer). Robert was a managing director of the Proprietary Investment Group at MeesPierson, part of the Fortis Group, investing in life science companies. Prior to MeesPierson, Robert worked for the investment banks, BZW (now Barclays Capital; BARC-GB, Not Rated) and UBS (UBSN-CH, Not Rated), in the corporate finance groups undertaking M&A, and public and private finance transactions. Robert started his career as lawyer with Clifford Chance in London and Singapore. Robert has completed over \$12 billion of transactions. He holds a LL.B. from Bristol University. Robert is a member of the Board of Directors of Myrexis Pharmaceuticals (MYRX, Not Rated).

### **Jonathan Pachter, Ph.D., Head of Research**

Dr. Pachter brings over 20 years of experience in leading discovery of small molecule and monoclonal antibody therapeutics for treatment of cancer. He was previously Head of Cancer Biology at OSI Pharmaceuticals (now Astellas) where his team was responsible for development of models of tumor cell EMT (epithelial-mesenchymal transition) and discovery of drugs disrupting this process. At OSI he advanced five small molecules into development for treatment of cancer, including OSI-906 - a selective IGF-1R/ insulin receptor kinase inhibitor currently in phase III clinical trials and OSI-027 - a selective mTOR kinase inhibitor. Prior to OSI, Dr. Pachter held positions of increasing responsibility at Schering-Plough (now Merck; MRK, Not Rated) where he progressed three agents into development including the monoclonal antibody robatumumab which advanced to phase II clinical evaluation in cancer patients. Dr. Pachter also made key contributions to the regulatory approval of temozolomide for treatment of glioblastoma. He is an author of over 40 peer-reviewed publications and inventor on numerous patents. Dr. Pachter did his postdoctoral work in Pharmacology at Yale University School of Medicine and he holds a Ph.D. from Baylor College of Medicine.

## Board of Directors

### **Christoph Westphal, M.D., Ph.D., Chairman/CEO**

Dr. Westphal is a Partner of Longwood Founders Fund, which founds and invests in medical companies. He was founder and CEO of Sirtris Pharmaceuticals (acquired by GlaxoSmithKline in 2008), which he took public and led as Chief Executive Officer until 2010. Dr. Westphal cofounded Alnara Pharmaceuticals (acquired by Eli Lilly in 2010), and was co-founder/CEO of Alnylam Pharmaceuticals and Momenta Pharmaceuticals. Dr. Westphal serves on the board of directors of Ovascience (which he cofounded), and serves on the Board of Fellows of Harvard Medical School, and the Board of Overseers of the Boston Symphony Orchestra. He earned his M.D. from Harvard Medical School and Ph.D. in genetics from Harvard University and he graduated with a B.A. summa cum laude and Phi Beta Kappa from Columbia University.

**Richard Aldrich**

Mr. Aldrich is a Founder and Partner of Longwood Founders Fund, which funds and invests in biotechnology companies. Mr. Aldrich has co-founded and helped build several successful biotech companies including Sirtris Pharmaceuticals (acquired by GlaxoSmithKline in 2008), Concert Pharmaceuticals, and Alnara Pharmaceuticals (acquired by Eli Lilly in 2010). Prior to co-founding Longwood, he was General Partner of RA Capital, a biotechnology investment fund he founded in 2001. Mr. Aldrich was a co-founding employee of Vertex Pharmaceuticals (VRTX, Not Rated) where he held the position of Senior Vice President and Chief Business Officer and managed all commercial and operating functions from 1989 to 2001. Prior to joining Vertex, Mr. Aldrich held several management positions at Biogen Inc (BIIB, Not Rated). Mr. Aldrich received his undergraduate degree from Boston College, and an MBA from the Amos Tuck School at Dartmouth College.

**John Clarke**

Mr. Clarke co-founded Cardinal Partners in 1997. He currently serves on the Board of Directors of Alnylam Pharmaceuticals, aTyr Pharma, Momenta Pharmaceuticals, Rib-X Pharmaceuticals, Sirtris Pharmaceuticals, (acquired by GlaxoSmithKline in 2008), and Visicu (EICU). He also served as a director for TechRx (Acquired by NDCHealth; NDC, Not Rated). Mr. Clarke has served on the National Venture Capital Association's Board of Directors where he was Chairman of its Regulatory Committee and Membership Committee. Mr. Clarke was a founding director of the Greater Philadelphia Venture Group as well as its past President and Chairman. Mr. Clarke is a past member of the Board of Directors of the Greater Philadelphia Chamber of Commerce and the Board of the Philadelphia Industrial Development Corporation Penn Venture Group. Mr. Clarke has served as a member of the University of Pennsylvania Advisory Panel on Technology Transfer. Mr. Clarke received his A.B. in Economics and Biology from Harvard University and his M.B.A. from the Wharton School at the University of Pennsylvania.

**Ansbert Gadicke, M.D.**

Dr. Ansbert Gadicke is a Co-Founder and Managing Director of MPM Capital. He led MPM's effort to build its Advisory and Investment Banking business from 1992 to 1996 and started its Asset Management business in 1996. MPM Capital is one of the world's largest dedicated investors in life sciences. With committed capital under active management in excess of \$2.0 billion, MPM is uniquely structured to invest globally in healthcare innovation through its BioVentures family of venture capital funds. Prior to founding MPM, Dr. Gadicke was employed by The Boston Consulting Group. Dr. Gadicke received an M.D. from J.W. Goethe University in Frankfurt. He subsequently held research positions in biochemistry and molecular biology at the Whitehead Institute at MIT, Harvard University and the German Cancer Research Center. He has published in leading scientific publications including Nature and Cell. Dr. Gadicke is a Director of Cerimon Pharmaceuticals; Dragonfly Sciences; Radius Health and Solasia Pharma K.K., Tokyo. He previously served as a Director of Arriva Pharmaceuticals, BioMarin (BMRN, Not Rated), Biovitrum, Coelacanth, Idenix (IDIX, Not Rated), Kourion, MediGene (MDG-DE, Not Rated), Omrix Biopharmaceuticals, Pharmasset (since acquired by Gilead; GILD, Not Rated), Inc.; PharmAthene (PIP, Market Perform), Transform, Xanodyne Pharmaceuticals, and ViaCell. He is a member of the Board of Fellows of Harvard Medical School.

**Stephen Kraus**

Mr. Kraus is a Vice President in the Cambridge office of Bessemer Venture Partners. Mr. Kraus covers the healthcare sector, including therapeutics, medical device, healthcare service, and healthcare IT companies. Mr. Kraus is actively involved with BVP's investments in Affymax (AFFY, Not Rated), Oxagen, Aveo (AVEO, Not Rated), Acceleron, Transave, Cerulean, Stromedix, Acorn Cardiovascular, Proteon, and On-Q-ity. Mr. Kraus has served on the boards of Sirtris (acquired by GlaxoSmithKline in 2008) until its IPO, and Restore until its acquisition by Medtronic (MDT, Not Rated) in July 2008. Mr. Kraus currently sits on the boards of Transave and On-Q-ity. Prior to joining Bessemer, Mr. Kraus was Director at the Ironwood Equity Fund, a growth-stage private equity firm, and a management consultant at Bain & Company. In 2002, Mr. Kraus served as Speechwriter and Operations Director for the Democratic nominee for Governor

of Massachusetts. Mr. Kraus graduated summa cum laude from Yale University and earned his MBA from Harvard Business School, where he was a Baker Scholar. He serves on the boards of City on a Hill Public Charter School and Interise.

### **Henri Termeer**

Henri Termeer has served as president and a director of Genzyme Corporation (now Sanofi; SNY, Not Rated) since 1983, its chief executive officer since 1985 and as Chairman of its Board since 1988. In 2008, he was appointed to Massachusetts Governor Deval Patrick's Council of Economic Advisors, and he is a co-chair of the Leadership Council of the Massachusetts Life Sciences Collaborative. Mr. Termeer is also Chairman Emeritus of the New England Healthcare Institute, a nonprofit, applied research health policy organization he was instrumental in founding. Mr. Termeer is Chairman of the Federal Reserve Bank of Boston's Board of Directors, a Board member of ABIOMED Inc. (ABMD, Market Underperform), and a Board member of Massachusetts Institute of Technology Corporation. He is a director of Massachusetts General Hospital, a Board member of Partners HealthCare and a member of the Board of Fellows of Harvard Medical School. He served on the Board of Directors of the Pharmaceutical Research and Manufacturers of America.

### **Scientific Advisory Board**

#### **Robert Weinberg, Ph.D., Co-Chair Scientific Advisory Board**

Dr. Weinberg is a founding member of the Whitehead Institute for Biomedical Research and the Daniel K. Ludwig Professor for Cancer Research in the Department of Biology at MIT. Dr. Weinberg is the internationally recognized authority on the genetic basis of human cancer development. Dr. Weinberg is the author or editor of five books and more than 350 articles. Three of the books are intended for a lay audience; "One Renegade Cell," "Racing to the Beginning of the Road: The Search for the Origin of Cancer" and "Genes and the Biology of Cancer" are co-authored with Dr. Harold E. Varmus, former Director of the National Institutes of Health. More recently, Dr. Weinberg has published a textbook "The Biology of Cancer," which is intended for doctoral students learning about this disease. Dr. Weinberg is a member of the National Academy of Sciences, the Institute of Medicine and a Fellow of the American Academy of Arts and Sciences.

#### **Eric Lander, Ph.D., Co-Chair Scientific Advisory Board**

Dr. Lander is founding director of the Broad Institute and director of its Genome Biology Program. As one of the principal leaders of the Human Genome Project, Dr. Lander and colleagues are using these findings to explore the molecular mechanisms underlying the basis of human disease. A recipient of numerous honors and awards, Dr. Lander has been appointed by President Barack Obama to co-chair the President's Council of Advisors on Science and Technology. He is a professor of biology at MIT and professor of systems biology at Harvard Medical School. In 1990 he founded the Whitehead Institute/MIT Center for Genome Research. The Center became part of the newly founded Broad Institute in 2003. Dr. Lander earned his B.A. in mathematics from Princeton University in 1978 and his Ph.D. in mathematics from Oxford University in 1981 as a Rhodes Scholar. He was an assistant and associate professor of managerial economics at the Harvard Business School from 1981–1990.

#### **Piyush Gupta, Ph.D., Co-Chair Scientific Advisory Board**

Dr. Gupta is Assistant Professor at Whitehead Institute for Biomedical Research. Dr. Gupta is an expert in the application of genomic methods to cancer and has made many contributions to the understanding of cancer metastasis and cancer stem cells. Dr. Gupta received a Bachelor of Science in mathematics from the University of Chicago and a Ph.D. in biology at MIT, where he studied cancer biology with Dr. Robert Weinberg. He conducted post-doctoral research with Dr. Eric Lander at the Broad Institute of MIT and Harvard, where he applied the powerful methods of genomics to problems in cancer biology. Among other accomplishments, Dr. Gupta has developed methods that, for the first time, enable the systematic identification of chemical compounds that selectively kill cancer stem cells. His work has led to the identification of novel

anti-cancer stem cell chemicals of potential therapeutic utility. Dr. Gupta's research has appeared in leading scientific journals and has received international acclaim, including coverage by the MIT Technology Review, Bloomberg News, and as a lead story in the New York Times.

**Julian Adams, Ph.D.**

Dr. Adams is President of Research and Development at Infinity Pharmaceuticals (INFI, Market Perform), Cambridge, MA. Prior to joining Infinity, Dr. Adams was the Senior Vice President, Drug Discovery and Development at Millennium Pharmaceuticals (now owned by Takeda, 4502-JP, Not Rated). In this capacity, Dr. Adams had global responsibility for multiple drug discovery programs, including the successful discovery and development of VELCADE®, a proteasome inhibitor for cancer therapy. Dr. Adams joined Millennium through its acquisition of LeukoSite in 1999 as Senior Vice President, Research and Development. Dr. Adams joined LeukoSite as a result of its acquisition of ProScript, Inc., where he served as a member of the founding management team, as Executive Vice President of Research and Development, and as a member of the Board of Directors. Earlier in his career, Dr. Adams served in various positions, including Director, Medicinal Chemistry, at Boehringer Ingelheim where he successfully discovered the drug Viramune® for HIV. Additionally, Dr. Adams was a Medicinal Chemist at Merck (MRK, Not Rated) from 1982–1987.

**José Baselga, M.D., Ph.D.**

Dr. Baselga is the Bruce A. Chabner Chair and chief of the Division of Hematology/Oncology at Massachusetts General Hospital and associate director of the MGH Cancer Center. His research includes the development of novel molecular targeted agents for cancer therapies, with special emphasis on breast cancer. His research in preclinical and early clinical development of therapies has helped develop a number of new targeted cancer-fighting agents. A breast cancer physician and translational researcher, Baselga was chairman of the Medical Oncology Service and director of the Division of Medical Oncology, Hematology and Radiation Oncology at the Vall d'Hebron Institute of Oncology in Barcelona, Spain before moving to Boston in 2010. He also completed a fellowship in medical oncology at Memorial Sloan-Kettering Cancer Center where he remained as a faculty member of the Breast Medicine Service until returning to Spain in 1996. Dr. Baselga has published more than 250 peer-reviewed articles and over 400 abstracts and book chapters in his career. Dr. Baselga was previously the president of the European Society of Medical Oncology, served on the board of directors of the American Society of Clinical Oncology (ASCO) and is currently a member of the board of directors of the American Association for Cancer Research (AACR).

**George Daley, M.D., Ph.D.**

Dr. Daley is the Samuel E. Lux IV Professor of Hematology/Oncology and the Director of the Stem Cell Transplantation Program at Children's Hospital, Professor of Biological Chemistry and Molecular Pharmacology at Harvard Medical School, investigator of the Howard Hughes Medical Institute, Associate Director of Children's Stem Cell Program and member of the Executive Committee of the Harvard Stem Cell Institute. He received a bachelor's degree magna cum laude from Harvard University, a Ph.D. in biology from the MIT (1989), and an M.D. degree summa cum laude from Harvard Medical School (1991). Dr. Daley's laboratory studies stem cell development and differentiation, emphasizing derivation of functional hematopoietic and germ cell elements from ES cells, and the genetic mechanisms that predispose to malignancy. He has been elected a fellow of the American Association for the Advancement of Science and member of the American Society for Clinical Investigation. He has received research awards from Harvard Medical School, National Institutes of Health, New England Cancer Society, Burroughs Wellcome Fund, Edward Mallinckrodt, Jr. Foundation, and the Leukemia and Lymphoma Society of America. Dr. Daley received the inaugural NIH Directors Pioneer Award, a five-year unrestricted grant to pursue highly innovative research.

**Peter Elliott, Ph.D**

Dr. Elliott was Senior Vice President, Head of Research and Development at Sirtris Pharmaceuticals (acquired by GlaxoSmithKline in 2008). Prior to joining Sirtris, Dr. Elliott was

Executive Vice President of Product Development at CombinatoRx. Dr. Elliott was Vice President of Pharmacology and Drug Development at Millennium Pharmaceuticals and co-developed VELCADE®. Prior to Millennium, Dr. Elliott spent four years at Alkermes (ALKS, Not Rated) and five years at Glaxo in the United Kingdom. Dr. Elliott holds a B.S. in Pharmacology from London University, an M.Phil. in Pharmacology from Cambridge University, and a Ph.D. in Psychopharmacology from Cambridge University.

**Daniel Haber, M.D., Ph.D.**

Dr. Haber is Director of the Massachusetts General Hospital Cancer Center and the Isselbacher/Schwartz Professor of Oncology at Harvard Medical School. He received his medical and doctoral degrees at Stanford in 1983. Following his doctoral studies at Stanford, Dr. Haber completed an internal medicine residency at Massachusetts General Hospital, clinical oncology training at Dana Farber Cancer Institute, and a postdoctoral research fellowship at MIT. Dr. Haber joined the Harvard Medical School faculty in 1991 as assistant professor at the MGH Cancer Center. Dr. Haber's laboratory interests have focused on the area of cancer genetics, including the etiology of pediatric kidney cancer (Wilm's tumor) and genetic predispositions to breast cancer. He has been elected to the American Association of Physicians, the American Society for Clinical Investigation, and the board of directors of the American Association for Cancer Research. Dr. Haber has been honored with the Doris Duke Distinguished Clinical Scholar Award and a Professorship from the National Foundation for Cancer Research, a MERIT Award from the National Cancer Institute, a Dream Team Award from the Prostate Cancer Foundation, the Emil Freireich Award from M. D. Anderson Cancer Center, the Sternlicht Award from Case Western Reserve, and the Hinda Rosenthal Award for Translational Research from AACR. He was appointed to the Howard Hughes Medical Institute in 2008.

**Yossi Schlessinger, Ph.D.**

Dr. Schlessinger is Chairman of the Department of Pharmacology and the William Prusoff Professor at Yale School of Medicine. From 1990 to 2001 he was chairman of the Department of Pharmacology and the Helen and Milton A. Kimmelman Professor at New York University Langone Medical Center. He was also director of the Skirball Institute of NYU from 1998 until 2001. Dr. Schlessinger co-founded SUGEN (acquired by Pharmacia, now Pfizer), Plexxikon, and Kolton Pharmaceuticals. He is a member of the National Academy of Science and serves on the editorial boards of Cell, Molecular Cell, and the Journal of Cellular Biology in addition to many other journals. Dr. Schlessinger received a B.Sc. magna cum laude in chemistry and physics and a M.Sc. magna cum laude in chemistry from the Hebrew University in Jerusalem, Israel. He received a Ph.D. from the Department of Chemical Physics at the Weizmann Institute in Rehovot, Israel, in the field of biophysics.

**Phillip Sharp, Ph.D.**

Dr. Sharp is currently an Institute Professor at the David H. Koch Institute for Integrative Cancer Research, MIT. He was the Founding Director of the McGovern Institute for Brain Research at MIT. Dr. Sharp has been a professor at MIT since 1974. He is a member of the National Academy of Sciences, the Institute of Medicine, and the American Academy of Arts and Sciences. Dr. Sharp received the Nobel Prize for Physiology of Medicine in 1993. He formerly served as a director of Biogen Idec Inc., which he co-founded in 1978. Dr. Sharp is a Director and Founder of Alnylam Pharmaceuticals.

**Roger Tung, Ph.D.**

Dr. Roger Tung is President and Chief Executive Officer of Concert Pharmaceuticals. Before Concert, Dr. Tung worked in venture-backed start-up and major pharmaceutical companies, including Vertex Pharmaceuticals, where he was a founding scientist, Merck, Sharp and Dohme, and E.R. Squibb & Sons (now Bristol-Myers Squibb; BMY, Not Rated). At Vertex, Dr. Tung served as Vice President of Drug Discovery at its San Diego site. He co-invented and headed discovery of Vertex's two commercial HIV protease inhibitor products, Lexiva® and Agenerase®, and led development of Agenerase® in collaboration with Glaxo through FDA and EMEA approval. Dr. Tung has overseen the discovery of numerous clinical candidates. He has

published widely and been granted 47 U.S. patents. Dr. Tung received his Ph.D. in Medicinal Chemistry at the University of Wisconsin-Madison from Professor Daniel H. Rich.

**Christopher Walsh, Ph.D.**

Christopher Walsh is the Hamilton Kuhn Professor at Harvard Medical School, former President of the Dana-Farber Cancer Institute, and Chairman of the Department of Biological Chemistry and Molecular Pharmacology at Harvard Medical School. He is a member of the National Academy of Sciences, the Institute of Medicine, the American Academy of Arts and Sciences, and the American Philosophical Society. Dr. Walsh was also a member of the board of directors at Critical Therapeutics (purchased by Cornerstone therapeutics; CRTX, Not Rated), Kosan Biosciences (purchased by Bristol Myers Squibb), and several private companies. He received a B.A. in Biology from Harvard University and a Ph.D. in Life Sciences from Rockefeller University.

**Eric Winer, M.D.**

Dr. Winer is Director of the Breast Oncology Center at the Dana Farber Cancer Institute and Associate Professor of Medicine at Harvard Medical School. Dr. Winer received his M.D. from Yale University and trained in internal medicine at Yale-New Haven Hospital, where he served as Chief Resident. Dr. Winer was a fellow in Hematology-Oncology at Duke University Medical Center. From 1989 to 1997 Dr. Winer served on the faculty at Duke and co-directed the multidisciplinary breast program. At Dana Farber, Dr. Winer leads a group of investigators researching improved methods of treating women with early-stage and advanced breast cancer, with a focus on identifying more effective treatments that minimize side effects. In addition, several of these studies have included efforts to assess quality of life issues faced by breast cancer survivors. In 2003, Dr. Winer joined Tour de France winner Lance Armstrong on the Tour of Hope cross-country bike ride to raise money for cancer research.

**RODMAN & RENSHAW RATING SYSTEM:** Rodman & Renshaw employs a three tier rating system for evaluating both the potential return and risk associated with owning common equity shares of rated firms. The expected return of any given equity is measured on a RELATIVE basis of other companies in the same sector, as defined by First Call. The price objective is calculated to estimate the potential movement in price a given equity could achieve given certain targets are met over a defined time horizon. Price objectives are subject to exogenous factors including industry events and market volatility. The risk assessment evaluates the company specific risk and accounts for the following factors, maturity of market, maturity of technology, maturity of firm, cash utilization, and valuation considerations. Potential factors contributing to risk: relatively undefined market, new technologies, immature firm, high cash burn rates, intrinsic value weighted toward future earnings or events.

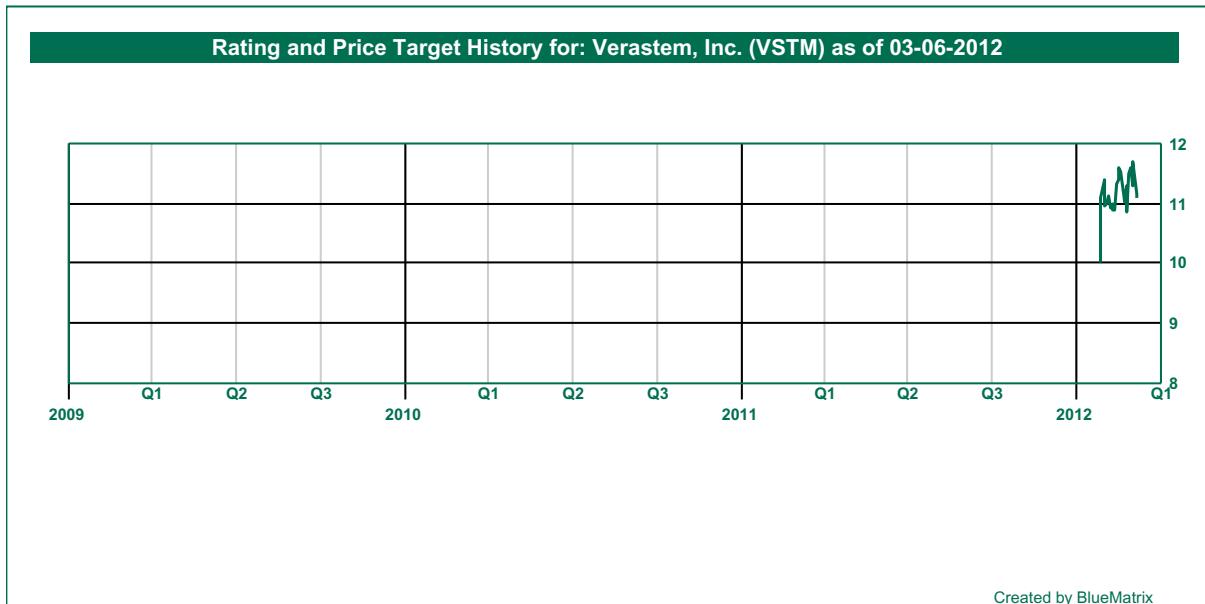
## RETURN ASSESSMENT

- Market Outperform (Buy): The common stock of the company is expected to outperform a passive index comprised of all the common stock of companies within the same sector, as defined by First Call.
- Market Perform (Hold): The common stock of the company is expected to mimic the performance of a passive index comprised of all the common stock of companies within the same sector, as defined by First Call.
- Market Underperform (Sell): The common stock of the company is expected to underperform a passive index comprised of all the common stock of companies within the same sector, as defined by First Call.

## RISK ASSESSMENT

- Speculative - The common stock risk level is significantly greater than market risk. The stock price of these equities is exceptionally volatile.
- Aggressive - The common stock risk level is materially higher than market level risk. The stock price is typically more volatile than the general market.
- Moderate - The common stock is moderately risky, or equivalent to stock market risk. The stock price volatility is typically in-line with movements in the general market.

Rated Companies mentioned in this report					
Company	Ticker	R&R Rating	Price	Mkt Cap (\$ MM)	12 Month Price Target
Æterna Zentaris Inc.	AEZS	Market Outperform	\$1.88	\$197.09	\$3.00
Alnylam Pharmaceuticals Inc.	ALNY	Market Outperform	\$11.81	\$612.15	\$19.00
Array BioPharma Inc.	ARRY	Under Review	\$2.86	\$241.81	NA
Astex Pharmaceuticals, Inc.	ASTX	Market Outperform	\$1.78	\$165.33	\$5.00
Cell Therapeutics Inc.	CTIC	Market Outperform	\$1.30	\$294.36	\$3.00
Dendreon Corp.	DNDN	Market Outperform	\$10.51	\$1,616.51	\$17.00
GTx, Inc.	GTXI	Market Perform	\$3.40	\$213.53	NA
Infinity Pharmaceuticals Inc.	INFI	Market Perform	\$8.16	\$217.70	NA
Keryx Biopharmaceuticals Inc.	KERX	Market Outperform	\$4.34	\$308.10	\$8.00
Medtronic, Inc.	MDT	Market Outperform	\$37.49	\$39,564.74	\$40.00
Myrexis, Inc.	MYRX	Under Review	\$3.10	\$81.77	NA
OncoGenex Pharmaceuticals	OGXI	Under Review	\$15.59	\$151.98	NA
Oncolytics Biotech Inc.	ONCY	Market Perform	\$4.82	\$368.15	NA
Oncothyreon Inc.	ONTY	Market Outperform	\$4.98	\$212.35	\$10.00
PharmAthene, Inc	PIP	Market Perform	1.29	62.28	NA
Poniard Pharmaceuticals Inc.	PARD	Under Review	\$1.02	\$1.53	NA
Rexahn Pharmaceuticals Inc.	RNN	Market Perform	0.48	45.77	NA
Synta Pharmaceuticals Corp.	SNTA	Market Outperform	\$4.26	\$245.37	\$8.00
Verastem, Inc.	VSTM	Market Outperform	\$10.76	\$226.60	\$19.00
YM Biosciences, Inc.	YMI	Market Outperform	\$1.91	\$299.84	\$6.00
Zalucus Inc.	ZLCS	Market Outperform	\$1.02	\$101.22	\$5.00



## RATING SUMMARY

Rating	Distribution of Ratings Table		IB Serv./Past 12 Mos	
	Count	Percent	Count	Percent
Market Outperform(MO)	94	60.30%	14	14.89%
Market Perform(MP)	31	19.90%	3	9.68%
Market Underperform(MU)	6	3.80%	0	0.00%
Under Review(UR)	25	16.00%	4	16.00%
Total	156	100%	21	100%

Investment Banking Services include, but are not limited to, acting as a manager/co-manager in the underwriting or placement of securities, acting as financial advisor, and/or providing corporate finance or capital markets-related services to a company or one of its affiliates or subsidiaries within the past 12 months.

## ADDITIONAL DISCLOSURES

Rodman & Renshaw, LLC. (the "Firm") is a member of FINRA and SIPC and a registered U.S. Broker-Dealer.

## ANALYST CERTIFICATION

I, Michael G. King, Jr., hereby certify that the views expressed in this research report accurately reflect my personal views about the subject company(ies) and its (their) securities.

None of the research analysts or the research analyst's household has a financial interest in the securities of *Æterna Zentaris Inc.*, *Alnylam Pharmaceuticals Inc.*, *Array BioPharma Inc.*, *Astex Pharmaceuticals, Inc.*, *Cell Therapeutics Inc.*, *Dendreon Corp.*, *GTx, Inc.*, *Infinity Pharmaceuticals Inc.*, *Keryx Biopharmaceuticals Inc.*, *Medtronic, Inc.*, *Myrexis, Inc.*, *OncoGenex Pharmaceuticals*, *Oncolytics Biotech Inc.*, *Oncothyreon Inc.*, *Poniard Pharmaceuticals Inc.*, *PharmAthene, Inc.*, *Rexahn Pharmaceuticals Inc.*, *Synta Pharmaceuticals Corp.*, *YM Biosciences, Inc.* and *Zalicus Inc.* (including, without limitation, any option, right, warrant, future, long or short position).

As of Jan 31 2012 neither the Firm nor its affiliates beneficially own 1% or more of any class of common equity securities of *Æterna Zentaris Inc.*, *Alnylam Pharmaceuticals Inc.*, *Array BioPharma Inc.*, *Astex Pharmaceuticals, Inc.*, *Cell Therapeutics Inc.*, *Dendreon Corp.*, *GTx, Inc.*, *Infinity Pharmaceuticals Inc.*, *Keryx Biopharmaceuticals Inc.*, *Medtronic, Inc.*, *Myrexis, Inc.*, *OncoGenex Pharmaceuticals*, *Oncolytics Biotech Inc.*, *Oncothyreon Inc.*, *Poniard Pharmaceuticals Inc.*, *PharmAthene, Inc.*, *Rexahn Pharmaceuticals Inc.*, *Synta Pharmaceuticals Corp.*, *YM Biosciences, Inc.* and *Zalicus Inc.*.

Neither the research analyst nor the Firm has any material conflict of interest with *Æterna Zentaris Inc.*, *Alnylam Pharmaceuticals Inc.*, *Array BioPharma Inc.*, *Astex Pharmaceuticals, Inc.*, *Cell Therapeutics Inc.*, *Dendreon Corp.*, *GTx, Inc.*, *Infinity Pharmaceuticals Inc.*, *Keryx Biopharmaceuticals Inc.*, *Medtronic, Inc.*, *Myrexis, Inc.*, *OncoGenex Pharmaceuticals*, *Oncolytics Biotech Inc.*, *Oncothyreon Inc.*, *Poniard Pharmaceuticals Inc.*, *PharmAthene, Inc.*, *Rexahn Pharmaceuticals Inc.*, *Synta Pharmaceuticals Corp.*, *YM Biosciences, Inc.* and *Zalicus Inc.*, of which the research analyst knows or has reason to know at the time of publication of this research report.

The research analyst principally responsible for preparation of the report does not receive compensation that is based upon any specific investment banking services or transaction but is compensated based on factors including total revenue and profitability of the Firm, a substantial portion of which is derived from investment banking services.

The Firm or its affiliates did not receive compensation from *Æterna Zentaris Inc.*, *Alnylam Pharmaceuticals Inc.*, *Array BioPharma Inc.*, *Astex Pharmaceuticals, Inc.*, *Dendreon Corp.*, *GTX, Inc.*, *Infinity Pharmaceuticals Inc.*, *Medtronic, Inc.*, *Myrexis, Inc.*, *OncoGenex Pharmaceuticals*, *Oncolytics Biotech Inc.*, *Oncothyreon Inc.*, *Poniard Pharmaceuticals Inc.*, *PharmAthene, Inc.*, *Synta Pharmaceuticals Corp.*, *YM Biosciences, Inc.* and *Zalicus Inc.* for any investment banking services within twelve months before, but intends to seek compensation from the companies mentioned in this report for investment banking services within three months, following publication of the research report.

The Firm or its affiliates have received compensation from *Cell Therapeutics Inc.*, *Keryx Biopharmaceuticals Inc.* and *Rexahn Pharmaceuticals Inc.* for investment banking services within twelve months before, and intends to seek compensation from the companies mentioned in this report for investment banking services within three months, following publication of the research report.

Neither the research analyst nor any member of the research analyst's household nor the Firm serves as an officer, director or advisory board member of *Æterna Zentaris Inc.*, *Alnylam Pharmaceuticals Inc.*, *Array BioPharma Inc.*, *Astex Pharmaceuticals, Inc.*, *Cell Therapeutics Inc.*, *Dendreon Corp.*, *GTX, Inc.*, *Infinity Pharmaceuticals Inc.*, *Keryx Biopharmaceuticals Inc.*, *Medtronic, Inc.*, *Myrexis, Inc.*, *OncoGenex Pharmaceuticals*, *Oncolytics Biotech Inc.*, *Oncothyreon Inc.*, *Poniard Pharmaceuticals Inc.*, *PharmAthene, Inc.*, *Rexahn Pharmaceuticals Inc.*, *YM Biosciences, Inc.* and *Zalicus Inc..*

The Firm does not make a market in *YM Biosciences, Inc.* and *Zalicus Inc.* securities as of the date of this research report.

The Firm does make a market in *Æterna Zentaris Inc.*, *Alnylam Pharmaceuticals Inc.*, *Array BioPharma Inc.*, *Astex Pharmaceuticals, Inc.*, *Cell Therapeutics Inc.*, *Dendreon Corp.*, *GTX, Inc.*, *Infinity Pharmaceuticals Inc.*, *Keryx Biopharmaceuticals Inc.*, *Medtronic, Inc.*, *Myrexis, Inc.*, *OncoGenex Pharmaceuticals*, *Oncolytics Biotech Inc.*, *Oncothyreon Inc.*, *Poniard Pharmaceuticals Inc.*, *PharmAthene, Inc.*, *Rexahn Pharmaceuticals Inc.* and *Synta Pharmaceuticals Corp.* securities as of the date of this research report.

Any opinions expressed herein are statements of our judgment as of the date of publication and are subject to change without notice.

Reproduction without written permission is prohibited. The intraday prices of securities mentioned in this report are as of Mar 07 2012. Additional information is available to clients upon written request. For complete research report on Verastem, Inc., please call (212) 356-0500.

Readers are advised that this analysis report is issued solely for informational purposes and is not to be construed as an offer to sell or the solicitation of an offer to buy. The information contained herein is based on sources which we believe to be reliable but is not guaranteed by us as being accurate and does not purport to be a complete statement or summary of the available data. Past performance is no guarantee of future results.