Edison investment research

Targeting cancer stem cells

Pharma & biotech

Verastem will shortly begin a series of studies that should provide definitive proof-of-concept for its cancer stem cell (CSC) hypothesis. The company plans to initiate Phase II trials of its lead compound, VS-6063, a FAK inhibitor that preclinical tests suggest is CSC-directed in mesothelioma and ovarian cancer. It also expects to advance VS-4718 and VS-5584, two CSC-directed compounds, into human clinical studies and decide on suitable indications thereafter. Verastem is well funded (>$90m cash) to reach the significant value inflection points associated with the results of these studies.

Year end	Revenue ($m)	PBT* ($m)	EPS* (c)	DPS (c)	P/E (x)	Yield (%)
12/11	0.0	(13.7)	(10.6)	0.0	N/A	N/A
12/12e	0.0	(34.5)	(1.7)	0.0	N/A	N/A
12/13e	0.0	(42.4)	(1.9)	0.0	N/A	N/A
12/14e	0.0	(43.6)	(2.0)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding intangible amortisation and exceptional items.

Novel cancer targeting approach

Using a proprietary screening platform and its deep understanding of CSC biology, Verastem identifies and develops drugs that target selectively to CSCs. CSC-targeting anti-cancer drugs could potentially overcome the shortcomings of traditional cancer drugs that are ineffective against CSCs, possibly the root cause of cancer treatment failure. Although unproven in clinics, when combined with traditional cancer drugs, CSC-targeting drugs could potentially bring a cure for cancer.

Possible accelerated path to approval

Verastem's VS-6063, a focal adhesion kinase (FAK) inhibitor and a CSC-targeting drug based on the company's various assay for CSC-targeting features, could enter a Phase II trial in midyear 2013 in maintenance setting of mesothelioma after a meeting with the FDA. A competitor's drug in the same class has shown robust efficacy in this disease setting, suggesting high probability of clinical success. Given the lack of treatment options for patients with this disease, a strong efficacy of VS-6063 in a well-defined sub-population could potentially lead to an accelerated approval by 2016.

More clinical data expected

Additional clinical data, such as for VS-6063 in ovarian cancer, VS-4178 and VS-5084 in solid tumours, should provide more direct evidence of how CSC-targeting drugs work in clinics.

Valuation: NPV of $203m

We value the company using a DCF model of product pipeline, arriving at an NPV of $203m for VS-6063, VS-4178 and VS-5584. Our valuation is $295m, or $13.5 per share, which includes $92m of cash, marketable securities and long-term investments at the end of 2012.

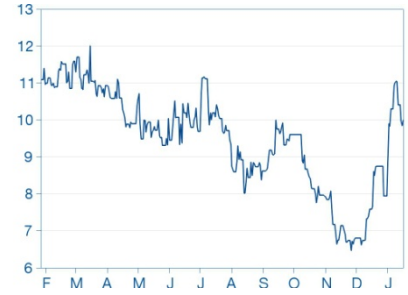
Verastem is a research client of Edison Investment Research Limited

17 January 2013

Price	$10.0
Market cap	$213m

Shares in issue	21.3m
Free float	51%
Code	VSTM
Primary exchange	NASDAQ
Other exchanges	N/A

Share price performance



%	1m	3m	12m
Abs	31.8	18.1	N/A
Rel (local)	26.5	16.6	N/A
52-week high/low		$12.01	$6.27

Business description

Verastem is a biopharmaceutical company focused on discovering and developing novel drugs that selectively target cancer stem cells (CSCs). Its lead drug is VS-6063, a FAK inhibitor, currently in Phase II testing. Its pipeline also includes VS-4718, another FAK inhibitor and VS-5584, a PI3K/mTOR inhibitor, both entering Phase I testing this year.

Next events

VS-6063 Ph II in mesothelioma	Mid-13
VS-6063 Ph I/II in second/third-line ovarian cancer	H113
VS-5584/4718 Phase I solid tumours	H213

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Edison profile page

Investment summary

Company description: Turning cutting-edge science into products

Verastem is a leader in the discovery and development of drugs that selectively target CSCs. Co-founded by Robert Weinberg, Eric Lander and Piyush Gupta, three leading CSC researchers associated with MIT and/or Harvard, the company established a proprietary screening and assay platform and through it discovered CSC-specific targets and compounds. Its lead drug VS-6063, a FAK inhibitor, will enter Phase II testing for maintenance in mesothelioma and second-line ovarian cancer in 2013. Its pipeline also includes VS-4718, another FAK inhibitor, and VS-5584, a PI3K/mTOR dual inhibitor, both in IND-enabling toxicicology studies. The company has raised a total of c $130m since its inception, including $68m before and $63m during its IPO in January 2012.

Exhibit 1: Verastem pipeline

Compound	Target	Indication(s)	Note
VS-6063	FAK	Mesothelioma	Phase II trial in maintenance mesothelioma; also stratifying for merlin negative patients; potential as registration trial: Initiation mid-13.
		Ovarian cancer	Phase I/II In combination with paclitaxel: Initiation H113.
VS-4718	FAK	Solid tumour	Phase I/Ib: Initiation H113.
VS-5584	PI3/mTOR	Solid tumour	Phase I: Initiation H213.

Source: Verastem

Valuation: DCF value of $295m, including cash and pipeline value

We value Verastem at $295m, or $13.5 per share, based on a sum-of-the-parts DCF valuation, using a standard discount rate of 12.5%. This includes a product pipeline value of $203m and year end cash and equivalents of $92m. For product pipeline valuation, we have estimated peak sales of $829m for VS-6063 in mesothelioma and ovarian cancer and peak sales of $346m for VS-4718 and VS-5584 (modest in our view, because indications have not been determined for these two drugs). We apply clinical success rates of 15% for VS-4718 and VS-5584, 25% for VS-6063 in ovarian cancer and 35% in mesothelioma. Our rNPV calculation subtracts the royalty pay-outs Verastem owes to licensors of each compound, including Pfizer, Poniard/Scripps and S*Bio.

Sensitivities: Main risks are in clinical trials

Verastem is subject to the risks typically associated with biotech company drug development, including the possibility of unfavourable or ambiguous outcomes in clinical trials, the success of competitors and commercial decisions by partners or potential partners. Verastem may carry higher risks than its peers because 1) the CSC theory is new and no drugs specifically targeting CSCs have been proven in the clinics; 2) Verastem's drug candidates are in the early stage of development, and early stage drugs not only have lower clinical success rates, but also face more development challenges as treatment standards change; and 3) Verastem's cash may only support its operation until 2015 and it needs to raise additional funds before then.

Financials: Cash of $91.8m at end-2012

Cash and equivalents at the end of Q312 were $97.4m and our model suggests this will be $91.8m at 30 December. Based on our projection of cash burn, we estimate that this should support the company's operation until Q415, at which time (or preferably earlier) the company would need to raise additional funds, either from the capital market or from strategic players, to continue its development efforts.

Outlook: A new way of targeting cancer

Verastem expects shortly to begin a series of studies that should provide definitive proof-of-concept for its cancer stem cell (CSC) hypothesis. The company plans to initiate Phase II trials of its lead compound, VS-6063, a FAK inhibitor that preclinical tests suggest is CSC-directed, in mesothelioma and ovarian cancer. It also expects to advance VS-4718 and VS-5584, two CSC-targeting compounds, into human clinical studies and to decide on suitable indications thereafter.

Exhibit 2: Verastem licence agreements

Drug	Licensor	Date	Upfront payment	Milestone payments	Royalty pay-out	Patent expiry
VS-5584	S*Bio	May 2012	$300,000	Up to $21m	Mid-to-high single digit	2029
VS-6063	Pfizer	July 2012	$1.5m and $2m worth of stocks	$2m development; $125m regulatory and commercial	High-single to mid-double digit on sales	2029
VS-4718/ 5059	Poniard/ Scripps	Nov 2011	$250,000	Up to $13.25m; warrants of 142,857 shares upon first human dosing	Low-to-mid single digit	2028
VS-507	Whitehead Institute	Oct 2010	$104,000, 166,664 shares	$1.56m	Low-single digit	No COM patent protection
VS-507 analogues	Eisai	July 2012	None	None	Low-single digit	N/A

Source: Edison Investment Research, Verastem

Cancer stem cells: A new frontier in cancer research

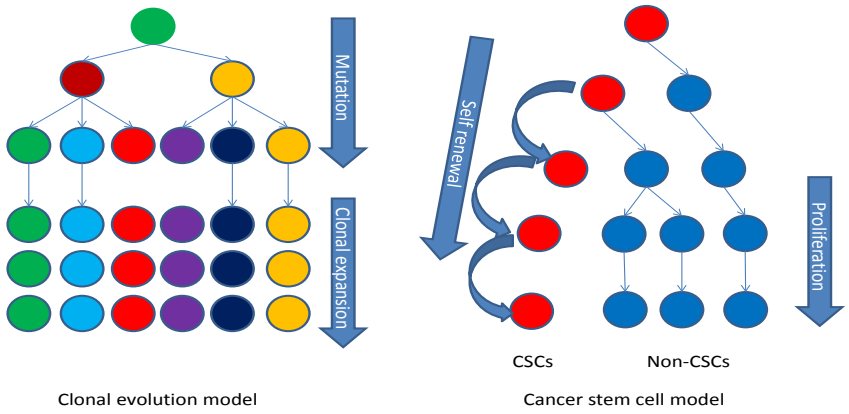
Traditional cancer biology views tumours as a collection of abnormal cells of enhanced capacity of proliferation, resulting from a process called clonal evolution. It is thought that germline and/or somatic genetic mutations caused by internal as well as external stimuli give certain cells a selective advantage, leading to propagation of these "clones" that compose the bulk of tumour. This view resulted in the identification of most chemotherapy drugs, because fast-dividing cancer cells are more susceptible to chemotherapy drugs' damage on the basic mechanism of cell division (DNA replication and synthesis, cell cycle, cytoskeleton changes, etc) than normal cells. Examples include nitrogen mustards and antifolates,[1] which first became available in the early-1940s. In some cases, such as in childhood leukaemia and testicular cancer, this has brought cures. By and large, chemotherapy has brought only incremental survival benefit, as relapses ultimately occur in most cancers. Furthermore, most chemotherapy drugs have significant toxicities, since as a result of their mechanism they also damage fast-dividing normal cells, such as those in bone marrow, the gastrointestinal tract and hair follicles.

The emergence of molecular biology since the 1950s has greatly enhanced knowledge of cancer at the molecular level, leading to the identification of oncogenes that are responsible for the transformation of normal cells to tumour cells through a phased accumulation of mutations in, or amplification of, oncogenes. This ushered in a new era of cancer drug development, dubbed targeted therapy, in the 1990s. Targeted cancer therapies exploit the differences between normal and tumour cells at the molecular level and attack tumour cells based on their differentiated molecular make-up from normal cells. These drugs, the best examples of which are Herceptin (trastuzumab, Roche) and Gleevec (imatinib, Novartis), bring significantly fewer toxicities to patients than chemotherapy drugs and in some cases have resulted in profound responses in patients that carry the target.

Despite the success of chemotherapy and targeted therapy, the reality of cancer treatment is far from perfect. Most cancer therapies only bring incremental survival benefit, because a majority of patients succumb to drug resistance and eventually relapse. Therefore, a fundamentally new approach to cancer drug development is needed if a cure for cancer is ultimately to be achieved.

1 | Sanchez-Garcia *et al*, BioEssays 2007, 29:1269-1280.

Exhibit 3: Two cancer theories



Source: Edison Investment Research, Verastem

The CSC theory

The CSC theory, which dates back to the early-1930s, claims that tumours are organised in a hierarchal order, which resembles normal tissues such as skin, colon and blood, with a minor population of self-renewable cells sitting on top (see Exhibit 3), from which a variety of heterogeneous mature cells capable of only limited proliferation are derived. The self-renewable cells have the characteristics of self-initiation, heterogeneity, ie, potential for multidirectional differentiation, and resistance to apoptosis. Since these are also characteristics of normal stem cells, the self-renewable cells in tumour are also called cancer stem cells. Similar to normal tissues, it is not the bulk of the differentiated tumour cells but the rare CSCs that fuel the sustained growth of a tumour.

The revival of CSC research started with direct evidence of the existence of CSCs shown by D Bonnet and JE Dick[2] in 1997. In a study of human acute myeloid leukaemia (AML) cells, they found that only a small fraction (one per 10,000) of AML cells are capable of generating tumours after various fractions are transplanted into mice with an altered immunological system (NOD/SCID mice: non-obese/severe-combined immunedeficient). The small, renewable fraction has two key criteria that also define stem cells: proliferation and differentiation, as millions of mature AML cells can be obtained from a mouse that is transplanted with one single CSC (proof of enormous proliferation capability) and the tumours formed in the recipient mice are identical to that in the human donor (proof of differentiation and formation of tumour heterogeneity). The approach pioneered by Bonnet and Dick was applied to other types of cancer and led to the identification of CSCs in breast, lung, ovarian, prostate, gastric, colorectal, brain and pancreatic cancer.[3]

According to the traditional cancer theory, cancer drugs kill the bulk of tumour cells, resulting in tumour shrinkage or responses. Treatment failure is due to pre-existing or acquired tumour cells that are insensitive (resistant) to therapy. These resistant cells can overtake sensitive cells under the pressure of treatment, leading to relapse either locally or distantly. In the light of the CSC theory, traditional cancer drugs target only fast-dividing tumour cells, but leave the quiescent, slow-dividing CSCs untouched. It is these CSCs that will re-start the growth of the tumour, resulting in treatment failure and tumour relapses. If this theory is true, traditional therapies are by design imperfect because they do not reach the source of the cancer. One study by the Baylor College of Medicine showed that the treatment of breast cancer with docetaxel does not kill CSCs because biopsies taken 12 weeks after treatment had

2 D Bonnet and JE Dick, 1997 Nature Medicine, 3, 730-737.
3 J Gil *et al*, 2008, J. App. Genet, 49, 193-199.

increased expression of biomarkers for CSCs compared with those at the beginning of treatment.[4] They also observed an increase in functional CSCs, ie, higher tumorsphere initiating capacity after treatment. A new and potentially better approach is to use agents that specifically target CSCs, or the combination of CSC-targeting and traditional drugs, to de-bulk the tumour and eliminate CSCs simultaneously. Theoretically, such an approach may represent a cure for cancer.

CSC theory: Challenges and controversies

Like any biology theory, the CSC theory is not without its challenges and controversies. Few people question the existence of a small number of cells in a tumour that harbour the capacity to re-initiate tumour growth. However, whether the existence of such cells truly points to a hierarchal structure of tumour is yet to be definitively proven. Furthermore, at least in some solid tumours such as melanoma, CSCs are not rare but rather abundant. Therefore in these systems, the tumour hierarchal structure consisting of rare CSCs is questionable. There are also questions about what really constitute a CSC, because most experimental approaches used today to separate CSCs from non-CSCs are so-called surface biomarkers. Not only do these biomarkers differ greatly from one type of tumour to another, their biological roles in rendering a cell's stemness are not always clear. Finally, new study results, which show that CSCs and non-CSCs inside tumours exist in a phenotypic equilibrium, challenge the notion of the hierarchal order of the tumour. In these systems, CSCs and non-CSCs cycle back and forth in direct contrast to the hierarchal model in which non-CSCs are derived from CSCs, but not vice versa.

There are also challenges in applying the CSC theory to the practice of drug development. One essential requirement for drug discovery is the supply of cells that can be used to screen drug candidates. CSCs are rare and slow growing and therefore not naturally suitable for screening assays. In this respect, Verastem's proprietary platform is unique and offers the company an advantage over others. However, the biggest challenges are in the development of CSC-targeting drugs. Because CSC-targeting agents are unlikely to work on fast-dividing cells, they are unlikely to result in fast shrinkage of tumours, the hallmark of today's drug efficacy evaluation. Therefore, the evaluation of CSC-targeting drugs may involve more mechanism-based tests than simply relying on tumour responses.

Verastem's proprietary CSC-targeting drug discovery platform

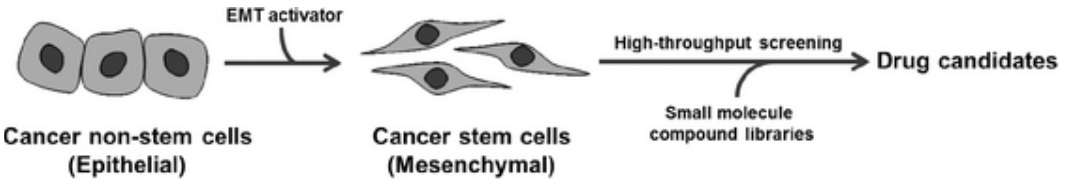
Verastem was based on work by Robert A Weinberg, Eric S Lander and Piyush B Gupta, who was a doctoral student in the Weinberg lab and a post-doctoral fellow in the Lander lab, to specifically discover and develop small molecule drugs targeting CSCs.

The proprietary technology that Verastem licensed from the Whitehead and Broad institutes is based on two important findings discovered by the three scientific founders: 1) Epithelial-to-mesenchymal transition (EMT), a biological process that normally happens during the development of tissues and organs before birth, also occurs in solid tumour development and the resulting mesenchyme-like tumour cells have the capability to invade through local barriers and metastasise to other sites in the body; and 2) mesenchymal tumour cells share many traits of CSCs, such as resistance to chemotherapy and the enrichment of biomarkers typically found on CSCs. These scientists developed a technique that activates the EMT in epithelial tumour cells by genetically knocking down the E-cadherin gene. As a result they can grow large quantities of CSC-like mesenchymal cells. This overcomes two critical challenges of applying CSCs theory to drug development: the rarity and the instability of CSCs. By obtaining large quantities of stable mesenchymal cells that resemble CSCs,

4 CJ Creighton *et al*, 2009, Proc Natl Acad Sci U S A. 106:13820-13825.

high-throughput screening of compounds can be carried out. The first compound that Verastem brought into preclinical development, VS-507, was discovered through such a process.

Exhibit 4: Verastem's platform for searching CSC-targeting drugs



Source: Verastem 10 K 2011

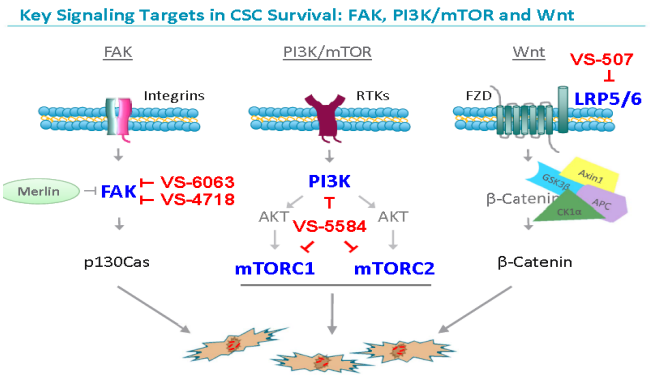
Once a putative compound is identified, Verastem subjects it to a variety of tests to verify the compound's CSC-targeting features. These tests typically include the HMLE assay, the Aldefluor-positive CSC assay, the tumorsphere formation assay and the Hoechst Dye exclusion test.

Verastem's CSC-targeting drug-discovery/development strategy

Using the platform mentioned above, Verastem and its collaborators have screened more than 300,000 compounds and identified approximately a dozen that passed the tests described above. Some of these, such as VS-507, were also shown to target known pathways critical for CSC survival. The company has conducted additional preclinical studies of VS-507, which at one point was its lead drug candidate.

Simultaneously, Verastem also conducts research to discover possible biological pathways with which these putative CSC-targeting compounds might be interfering, so that further clinical development can be guided by biomarkers. One added benefit of this approach is that Verastem can look outside the company for drug candidates that target the relevant pathway. Research by Verastem's scientific founders and others has shown (see Exhibit 5) that three targets and their associated pathways, FAK, PI3K/mTOR and Wnt, are key signalling targets in CSC survival and therefore viable targets for CSC-targeting drugs. This unique insight has led Verastem to in-license several compounds targeting these pathways from other companies and advanced the company's development timeline significantly. The best example of this approach is the FAK pathway and the in-licensing of VS-6063 and VS-4718. Verastem's screening has identified many compounds that could be targeting FAK. At the same time, internal and external research has linked the FAK pathway to CSCs. Verastem subsequently looked outside and found that two candidates, VS-4718 from Poniard and VS-6063 from Pfizer, are proven FAK inhibitors. It licensed these two compounds, which moved up the company's developmental timeline by more than 12-18 months.

Exhibit 5: Key pathways in CSC that Verastem drugs are targeting



Source: Verastem reports

Pipeline drug analysis

FAK in CSC survival and metastasis

FAK is an enzyme that plays a major role in the regulation of cell adhesion, migration and survival in a variety of cells. Ablation of FAK in skin cells prevents the mobilisation of stem cells,[5] suggesting a key role in stem cell migration. FAK expression is greater in many tumour types compared to normal tissue, particularly in cancers that have a high invasive and metastatic capability, suggesting a role in tumour invasion or metastasises. Shibue and Weinberg provided direct evidence[6] that FAK expression is required for lung cancer metastasis. Furthermore, analysis of breast tumour samples showed the amplification or increase in number of the gene-encoding FAK exists in a large percentage of breast cancers[7] and population analysis demonstrated a direct correlation between FAK intensity score and poor prognoses in breast[8] and ovarian[9] cancer patients. These data combined suggest that FAK is involved in CSC survival and tumour metastasis and a potentially good target for drug development.

Another tumour suppressor gene, NF-2, and the protein it encodes, merlin, also play an important role in tumour cell adhesion, invasion and cell motility. Studies by Verastem scientists and others have shown that merlin- cells are more sensitive to FAK inhibitors than merlin+ cells and restoration of merlin function desensitises cells to FAK inhibition, therefore linking NF-2/merlin to the FAK pathway.

VS-6063

VS-6063 was licensed from Pfizer in July 2012 after Pfizer deprioritised this compound following Phase I testing (see Exhibit 2). Verastem sees VS-6063 as promising because of the company's understanding of CSC theory and FAK's role in CSC and tumour metastasis, This gave Verastem the opportunity to license in VS-6063, thus accelerating its FAK programme by 12-18 months.

Phase I and preclinical data

In a Phase I study conducted by Pfizer in various tumour types, VS-6063 was given to 46 patients at doses from 12.5mg to 750mg orally and twice daily (BID). No grade 4 adverse events (AEs) were seen with the drug and only four patients (8%) had developed grade 3 AEs. Although no objective responses were seen, 43% (16/37) of patients given the drug at ≥100 mg BID experienced stable disease (SD), with seven patients having SD longer than six months.

Internally, Verastem has conducted tests that show VS-6063 preferentially targets CSCs and we expect more data to be presented in 2013. Work published by the company on another FAK inhibitor, VS-4718, clearly demonstrated that a FAK inhibitor inhibits growth of CSCs in HMLE and Aldefluor assay, arrests tumorsphere formation and eliminates "side population" in the Hoechst exclusion test. Furthermore, the drug is profoundly more effective in tumour cell lines that lack merlin, suggesting FAK inhibitors could be particularly potent in merlin- tumour, such as mesothelioma, in which up to 45-50% of tumour cells have lost merlin expression.

Phase II trial and path forward

Verastem has chosen mesothelioma and ovarian cancer, and possibly breast cancer, as leading indications for VS-6063. The decision to focus on mesothelioma is based on two lines of evidence. Firstly, Verastem showed that VS-6063 and VS-4718, also a FAK inhibitor, preferentially attenuate

5 RA Ridgway *et al,* Carcinogenesis 2012, 33.
6 T Shibue and RA Weinberg, PNAS 2009, 106:10290-10295.
7 Y Pylayeva *et al*, J of Clin Invest., 2009 119:252-266.
8 AL Lark *et al*, Modern pathology, 2005, 18:1289-1294.
9 Sood *et* al, J Clin Invest., 2010, 120:1515-1523.

growth of malignant mesotheliomas with NF2 mutation (merlin-). Secondly, GSK's GSK2256098, a FAK inhibitor, demonstrated almost a threefold progression-free survival (PFS) rate than the historical standard (17.7 vs 6.1 weeks; placebo arm in VANTAGE 014 Phase III trial) in second-line mesothelioma. It also showed a doubling (24.1 vs 11.4 weeks) of PFS in merlin- than in merlin+ mesothelioma patients, providing direct evidence that FAK inhibition could be merlin-dependent. It is estimated that approximately 46% of mesothelioma are merlin negative. These data have prompted Verastem to focus on mesothelioma as VS-6063's first indication. Current standard first-line treatment for mesothelioma is Alimta plus cisplatin, which was approved based on 2.8 months of increase in OS vs cisplatin. In the Phase III EMPHACIS trial,[10] Alimta and cisplatin was shown to have ORR in 41% of patients and SD of 25%. However, only 53% and 5% of patients were able to finish six or eight cycles of treatments, respectively, mostly due to toxicity of the Alimta/cisplatin regimen. If a well-tolerated drug, such as VS-6063, can extend the duration of response or stable disease after first-line therapy, these patients may have even longer overall survival. That is exactly the setting where the first Phase II trial of VS-6063 will be.

The company is planning a meeting with the FDA in early-2013 to discuss the Phase II trial design for maintenance mesothelioma. The trial will be a placebo-controlled, 300-350 patient, randomised study testing VS-6063 in patients who are stable (response or SD) after first-line treatment, with PFS as the primary end point. Patients will also be stratified for merlin status, a potential subgroup for accelerated approval. A major upside of this meeting would be the FDA's buy-in of the trial result as the basis for a conditional approval, if the efficacy result is "substantial". Verastem expects to initiate the trial in mid-2013 and finish the study in 2015, and obtain an approval as early as 2016.

The choice of ovarian cancer and possibly breast cancer as other indications for VS-6063 is based on the finding that increased FAK activity correlates with decreased survival in these two cancer types. A retrospective analysis[11] of 61 ovarian cancer patients found that those with high FAK had an OS of 1.7 years, whereas those with low FAK had an OS of three years. Various studies[12] have also shown FAK over-expression correlates with breast cancer invasiveness and metastasis.

Verastem's ovarian cancer trial is a combined Phase I/II trial. During the Phase I stage, VS-6063 will be tested with paclitaxel in ovarian cancer patients to determine a Phase II dose. Once the Phase II dose is determined, the trial will enter the Phase II, randomised stage, comparing VS-6063 plus paclitaxel vs placebo plus paclitaxel, in platinum-resistant ovarian cancer with the primary end point of PFS. The outcome of this trial, if positive, would guide a Phase III trial design.

Although the company has not specifically mapped the strategy in breast cancer, the Phase I ovarian cancer trial could be very informative because how well VS-6063 is combined with paclitaxel would be crucial information for future breast cancer trials since paclitaxel is so widely used in breast cancer treatment. Given that VS-6063 is targeting the CSCs, the root cause for cancer recurrence and possibly metastasis, Verastem believes that VS-6063 could be particularly suitable for treatment at the neoadjuvant setting, where increases of pathological complete response rates would certainly result in significant clinical benefit (pathological complete response leads to increased OS). That setting is also clinically practical because results could be quickly obtained, after four to six cycles of treatment before surgery, vs a long clinical testing period in the adjuvant or advanced breast cancer setting.

10 NJ Vogelzang *et al*, J. Clin Oncol 2003, 21:2634-2644.
11 Sood *et al*, 2010, J Clin Invest., 120:1515-1523.
12 M Luo and JL Guan, 2010, Cancer Letter 28:127-139.

VS-4718

Verastem licensed VS-4718 from Scripps Institute and Poniard Pharmaceuticals in November 2011 (see Exhibit 2). Verastem has presented or published various test results that showed VS-4718 preferentially inhibits growth of CSCs, attenuates breast CSC function and in vivo growth and renders high potency against malignant mesothelioma with NF2 mutation. Verastem proposes initiating a Phase I trial in solid tumour types with FAK over-expression, such as breast, mesothelioma and ovarian cancer, in early-2013.

Competitive landscape in mesothelioma and FAK inhibition

While there are quite a few ongoing trials for mesothelioma (see Exhibit 6), only one is in a Phase III trial (pemetrexed/cisplatin ± Avastin) in the first-line setting. The Avastin trial, if positive, could change the standard care of first-line treatment and make VS-6063's positioning as a choice of maintenance a little challenging because VS-6063 is not tested after treatment with Avastin/Alimta/cisplatin. However, if NSCLC is a good guidance, we would expect Avastin to be only effective in a subset of mesothelioma patients and accepted as a first-line choice in limited geographic regions, and leaving Alimta/cisplatin as a first-line treatment choice to most mesothelioma patients.

There are currently two drugs tested as a maintenance treatment in Phase II trials, including MolMed's NGR-hTNF and Lilly's (NCI-sponsored) Alimta. NGR-hTNF could be a direct competition to VS-6063 if it is positive in the Phase II maintenance trial. In a Phase II trial, NGR-hTNF alone produced partial response (PR) and stable disease (SD) in 2% and 40% of patients, respectively, and a median PFS of 2.8 months (12 weeks), less than GSK2256098's 17.7 weeks of PFS in the same setting. Since MolMed is also conducting a Phase III trial of the same drug in the second-line setting, we would think the company's focus is in the second-line, not the maintenance setting. We view the Phase III, second-line NGR015 trial as having a low probability of generating a positive outcome because the comparison arm is the BIC and there is no Phase II combination data in the same disease setting. Whether Alimta can be used as a maintenance after Alimta/cisplatin in the first-line is questionable. In addition, we are not sure that Eli Lilly would be conducting Phase III trials for Alimta in this setting while the drug's patent protection is already expired.

The most advanced FAK inhibitor in development is GSK's GSK2256098. In a Phase I trial (see Exhibit 7, overleaf), the drug was tested at 80 to 1,500mg bd in advanced cancer patients. While the drug was generally well tolerated, no objective response was seen. Instead, SDs in mesothelioma, melanoma, and naso/pharyngeal cancer and renal cell were observed. Later, analysis of PFS in mesothelioma found the drug's efficacy correlated with merlin expression status: PFS was 17.7 weeks, 24.1 weeks and 11.4 weeks in overall, merlin negative and merlin positive patients, respectively.

Although GSK2256098 is the most advanced FAK inhibitor in clinical development and the data of that drug in mesothelioma as reported in November 2012 (see Exhibit 7) was ground-breaking, Verastem may jump ahead of GSK in developing VS-6063 by moving into maintenance in mid-2013 after its FDA meeting in early-2013. GSK is still enrolling patients in the ongoing, five-arm Phase Ib study (see Exhibit 7) to find the optimal dose for multiple tumour types. Furthermore, the ultra-orphan status of mesothelioma may not be as interesting to GSK as to Verastem. VS-6063 and GSK2256098 are comparable in terms of efficacy, with VS-6063 having better tolerability, based on analysis of Phase I data. Therefore, we think that VS-6063 is better suited for maintenance in mesothelioma than GSK2256098.

PI3K/mTOR pathway and CSCs

The PI3K/mTOR pathway and its involvement in cancer development have been extensively studied over the years. Drugs targeting this pathway, such as Torisel (temsirolimus, Pfizer) and Afinitor (everolimus, Novartis), have already been approved. More are in various stages of clinical development. However, most of the drug candidates in this class target individual components of the pathway.

Exhibit 6: Competitive landscape in mesothelioma

Compound/ technology	Company	Trial
NGR-hTNF/ hTNF- CNGRCG peptide conjugate NGR-hTNF	MolMed	390-pt Phase III trial (NGR015) of NGR-hTNF plus BIC (doxorubicin, gemcitabine, or vinorelbine]) vs placebo plus BIC in second-line (results: February 2013). Results of 57-patient Phase II study presented at ASCO 2010.
		100-pt Phase II study of NGR-hTNF vs pbo as maintenance in pts treated with Alimta/cisplatin (result: March 2013).
Avastin/VEGF mab	Roche	445-pt Phase II/III study of pemetrexed/cisplatin ± Avastin in first-line (result: December 2014).
Alimta	Lilly/NCI	96-pt Phase II of Alimta vs. observation as maintenance in pts treated with Alimta/cisplatin (result: April 2012)
Amatuximab/mesothelin mab	Morphotek	86-pt Phase II, single-arm study in first-line (result: December 2011).
Recentin (cedirinib)/VEGFR inhibitor	AstraZeneca	NCI-sponsored 116-pt Phase I/II study of pemetrexed/cisplatin ± cedirinib in first-line (result: 6/2014); 50-pt academic sponsored study.
CBP501/ G2 checkpoint inh.	CanBas	72-pt Phase I/II study of pemetrexed/cisplatin ± CBP501 in first-line (results: April 2012).
Affinitor (everolimus)/mTOR inh.	Novartis	55-pt Phase II study in second-line (results: February 2011); 9-pt Phase II study in second- or third-line patients with Merlin/NF2 loss (complete).
Cixutumumab/IGFR mab	Lilly	20-pt Phase II, single-arm study in second-line (results: April 2012).
Erbitux/EGFR mab	Lilly	18-pt Phase II, single-arm study in first-line (result: September 2013).
Rilotumumab/HGF mab	Amgen	55-pt Phase II study in combination pemetrexed/cisplatin in first-line (results: October 2012).
ADI-PEG 20/ peg-arginine deiminase	Polaris	66-pt Phase II study in ASS-negative, second-line (results: July 2012).
HSV1716/oncolytic virus	Virttu Biologics	12-pt Phase II study (results: April 2014).
Fresolimumab/TGF-β mab	Sanofi	20-pt Phase II study in second-line (results: October 2012).
CRS-207/vaccine	Aduro BioTech	16-pt Phase Ib study in combination with pemetrexed/cisplatin in first-line (result: June 2014).
Oshadi D and R/unknown	Oshadi	17-pt Phase IIa study (result: December 2014).
Tremelimumab/CTLA-4 mab	AstraZeneca	29-pt Phase II, single arm study in second-line (result: January 2014).
TroVax/Vaccine	Oxford BioMedica	26-pt Phase II, single arm study in first-line (result: March 2013).
PF-03446962/ALK1 mab	Pfizer	26-pt Phase II, single arm study in second-line (result: January 2014).
Oncolytic measles/vaccine	Mayo Clinic	36-pt Phase I study in first-line (result: November 2013).

Source: Edison Investment Research

Exhibit 7: FAK inhibitors under development

Compound	Company	Targets	Development status	Data
GSK2256098	GSK	FAK	Phase I, 138-pts trial ongoing	Phase I at ASCO 2012: 80 to 1,500 mg BID, SD in mesothelioma, melanoma, naso/pharyngeal and kidney cancer; EORTC-NCI-AACR 2012: recurrent mesothelioma, PFS 17.7 wks, 24.1 wks and 11.4 wks in overall, merlin- and merlin+; IC_{50} 2-15nM
BI 853520	Boehringer Ingelheim	FAK	Phase I, 90-pts trial ongoing	Preclinical at AACR_NIC-RORTC 2011: anti-tumour activity in vitro and in vivo; EC_{50} of 1-3nM
VS-6063	Verastem	FAK	Phase I, 46-pts trial complete; Phase II planned	ASCO 2011: SD in 16 (43%) pts for dose ≥100 mg BID
TAE226	Novartis	FAK and IGF1R	Phase I	IC_{50}: 6.24±0.51nM
Y15	Roswell Park Cancer Inst	Y397 of FAK	Preclinical	Inhibition of Y397 autophophorylation site of FAK
CEP-37440	Teva (Cephalon)	ALK and FAK	Preclinical	N/A
VS-4718	Verastem	FAK	Preclinical	EC_{50} 1μM
CTx-0294945	Cancer Therapeutics CRC	FAK	Preclinical	AACR 2012: IC_{50} 6.6 nM
CTx-0294886	Cancer Therapeutics CRC	FAK, VEGFR3, FLT3	Preclinical	EACR-22: IC_{50} 36 nm

Source: Edison Investment Research

The first evidence that the PI3K/mTOR pathway is important for CSC came with the finding that when PTEN, a component of the PI3K/mTOR pathway, is inactivated, mouse haematopoietic stem cells started to move out of the bone marrow, colonise distant organs and result in first a myeloproliferative disorder (MPD) and then an acute myeloid/lymphoid leukemic-like disease.[13] Similarly, PTEN inactivation or PI3K activation in solid tumour cell lines confers stem cell-like characteristics.[14] These results show that the PI3K/mTOR pathway is a critical component of CSC survival and suggest that targeting this pathway is an attractive approach to attack CSCs.

VS-5584

Verastem's screening for CSC-targeting compounds showed that when PI3K, mTORC1 and mTORC2 are all substantially inhibited growth of CSCs is attenuated. Therefore, dual inhibitors of PI3K/mTORC1/2 (or in theory, a combination of PI3K and mTOR inhibitors) would be the most potent CSC-targeting drug candidates. VS-5584, licensed from S*Bio in November 2011, showed strong potency to all sub-types of PI3K, as well as mTORC1 and 2, exhibiting nM range IC_{50} in in vitro assays to all these targets. Verastem has shown that VS-5584 passes all the tests designed to show a compound is CSC-targeting. Furthermore, VS-5584 was shown to perform as well as or better than other compounds that target the PI3K/mTOR pathway. For example, VS-5584 performed as well as Everolimus in a prostate cancer model, but better in a colorectal model (see Exhibit 8, left panel). The drug also induced tumour regression in a docetaxel-resistant patient-derived breast cancer model where decataxel, as expected, showed no efficacy (see Exhibit 8, right panel). With the caveat that these are preclinical data, the results nonetheless showed that VS-5584 could be a unique compound, which may find clinical application in many types of cancer that are difficult to treat with conventional cancer drugs.

Verastem proposes starting a Phase I/Ib trial in H213 to find a safe dose and initial signs of activity. Possible subsequent studies include Phase I combination studies in solid tumour, possibly in PI3K/mTOR enriched patient population. Phase II trials in either metastatic or neoadjuvant breast cancer patients may start as early as 2014 or 2015.

Competitive landscape in PI3K/mTOR

There are more than 35 PI3K, mTOR or dual PI3K/mTOR inhibitors in development for cancer (see Exhibit 9, not all data shown). As illustrated in Exhibit 5, there are multiple family members of PI3K (alpha, delta, gamma and beta) and mTOR (C1 and C2) involved in the pathway in tumour cells. The compounds listed in Exhibit 9 vary in their inhibitory potency on various components of the pathway, with some potent on all members and others more specific on a particular member. Research by Verastem showed that only when all members of the pathway are inhibited is growth of CSCs stopped. This suggests that only dual PI3K/mTOR inhibitors such as VS-5584 will be worthy CSC-targeting drug candidates.

Wnt pathway

The Wnt signalling pathways play a key role in embryonic development and maintenance of homeostasis in mature tissues, suggesting its importance in stem cell biology. Aberrant regulation of the Wnt pathway in the gut leads to self-renewal and cancer, thus linking the pathway to CSCs. Furthermore, many of the cell surface markers that were used for sorting CSCs are direct Wnt targets, providing more evidence that the Wnt pathway is critical for CSCs.

13 J Zhang *et al*, Nature 2006, 441: 518–522 ; OH Yilmaz *et al*, Nature 2006, 441: 475–482.
14 H Zheng *et al*, Nature 2008, 455, 1129–1133; A Dubrovska et al, PANS, 2009, 106:268–273; J Zhou,. *et al*, 2007, PANS 104:16158–16163.

Exhibit 8: VS-5584 anti-tumour activity in preclinical models

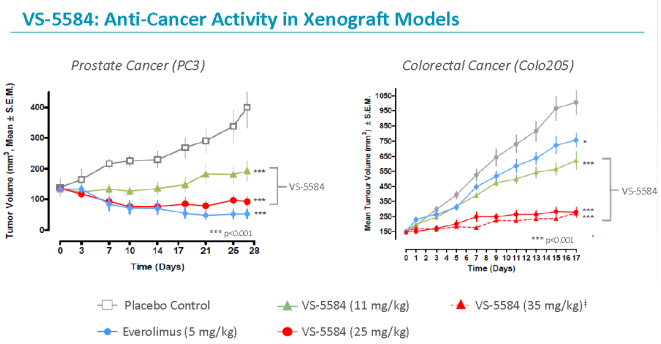
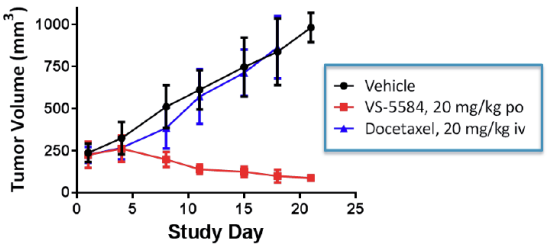


Fig 6: Oral VS-5584 induces tumor regression in a docetaxel-resistant patient-derived breast cancer model



Mice were implanted with tumor fragments from a docetaxel-resistant patient-derived triple negative breast cancer. Mice were treated with VS-5584 (20 mg/kg, po, qd) or docetaxel (20 mg/kg, i.v.) as indicated.

Source: Verastem reports

Exhibit 9: Selected PI3K, mTOR or dual PI3K/mTOR inhibitors in development for cancer

Compound	Company	Target(s)	Status	Route of administration; main indication(s)
PF-05212384	Pfizer	PI3K/mTOR	Phase II	IV; endometrial and solid tumour
PF-4691502	Pfizer	PI3K/mTOR	Phase II	Oral; endometrial and solid tumour
RG7422/GDC-0980	Roche	PI3K/mTOR	Phase II	Oral; prostate, breast, NHL, RCC
SAR245409/XL765	Exelixis/Sanofi	PI3K/mTOR	Phase I/II	Oral: brain, breast, NSCLC
BEZ235	Novartis	PI3K/mTOR	Phase I/II	Oral; breast, prostate, RCC cancer, solid tumour
BGT226	Novartis	PI3K/mTOR	Phase I/II	Oral; breast cancer
GSK2126458	GSK	PI3K/mTOR	Phase I	Oral; cancer
SF1126	Semafore Pharma	PI3K/mTOR	Phase I	IV; CLL, MCL, MM and solid tumour
DS-7423	Daiichi Sankyo	PI3K/mTOR	Phase I	Oral: solid tumours
PWT33597	Pathway Therap.	PI3K alpha/mTOR	Phase I	Oral; solid tumours
VS-5584	Verastem	PI3K/mTOR	Preclinical	Oral; cancer
P7170	Piramal Life Sciences	PI3K/mTOR	Preclinical	Oral; cancer

Source: Edison Investment Research, BioCentury and Verastem

Exhibit 10: Drugs targeting Wnt pathway in development

Compound	Company	Target(s)	Status	Route of administration; main indication(s)
LGK974	Novartis	Porcupine (acyltransferase)	Phase I	Oral; melanoma, breast
PRI-724	Eisai/Prism Pharma	β-catenin/CBP	Phase I	IV; haematological and solid tumour
CWP232291	JW Pharma	Unknown	Phase I	IV; AML, MM
OMP-18R5	Oncomed	MAb against Frizzled	Phase I	IV; solid tumour
OMP-54F28	Oncomed	FZD8 fusion protein	Phase I	IV; solid tumour
OTSA101	OncoTherapy	Yttrium 90 conjugated MAb against FZD10	Phase I	IV; solid tumour

Source: Edison Investment Research, Verastem

VS-507, the first drug candidate that came out of the screen using the proprietary platform devised by the company's scientific co-founders, was found to inhibit LRP5/6, a Wnt pathway component. In preclinical models, VS-507 was shown to inhibit β-catenin signalling, the hallmark of the Wnt pathway activation. As VS-507 preferentially inhibits growth of CSCs but not non-CSCs, these data therefore directly prove that β-catenin signalling and Wnt pathway activation is required for CSC survival.

Despite VS-507's role in killing CSCs, Verastem is delaying the development of this drug, opting for any second-generation compounds that may come out of collaboration with Eisai. The collaboration was set up to develop analogues of VS-507, leveraging Eisai's chemistry capabilities. Verastem will own the new analogues from the collaboration with Eisai eligible for commercial royalties on identified products and a limited time of first right of negotiation.

Competitive landscape in Wnt pathway

There are currently six drugs targeting the Wnt pathway in human clinical testing. Of these, only LGK974, Novartis, a Porcupine (acyltransferase) inhibitor, is an oral drug. As Verastem has delayed VS-

507's clinical development, opting for better analogues that may come out of the Eisai collaboration, it is behind various competitors in the development timeline.

Competitive landscape of CSC-targeting drug development

There are seven companies (see Exhibit 11) that specifically focus on developing CSC-targeting cancer therapies. The most advanced drug is Boston Biomedical's BBI608, expected to enter Phase III testing for colorectal cancer in 2013. However, very little is known about the drug's MOA and clinical data. The other company that has a robust CSC-targeting pipeline is OncoMed with five in clinical studies. OncoMed has established collaborations with GSK and Bayer in developing CSC-targeting drug candidates. The Bayer deal includes $40m upfront payments and up to $387.5m per programme for a total of five, and double-digit royalties on net product sales, a good example of big pharma's strong interest in CSC-targeting drugs. Recently, OncoMed moved OMP-52M51 into Phase I testing, which triggered a $4m milestone payment from GSK. OncoMed's focus on antibodies differs from Verastem's focus on small molecules, making them less direct competitors. We believe Verastem's platform is very robust and its pipeline valuable among all these companies.

Exhibit 11: Companies involved in CSC-targeting drug development

Company	Technology platform	Lead drug/indication
Verastem	Stable CSC-like HELM based high-throughput screening; CSC functional assay	VS-6063/mesothelioma, ovarian; VS-4718/solid tumour; VS-5584/solid tumour
Stemline Therapeutics	Three-step platform, which includes CSC isolation and target identification, in silico screen for compound and anti-CSC functional assays	SL-401/AML; SL-701/glioma
OncoMed Pharmaceuticals	Surface markers and flow cytometry-based platform to isolate CSCs and targets; developing antibodies directed against CSC targets	OMP-21M18/NSCLC; OMP-59R5/pancreatic; OMP-18R5 and OMP-54F28/solid tumour
Stemergie Biotechnology S.A.	Methodology to identify and enrich CIC without the use of any marker; long-term culture of primary cells	N/A
Bionomics (Eclipse)	CSC Rx discovery platform to identify antibody therapeutics that inhibit the growth of CSCs	ET-101(preclinical, Phase I in 2014)
Dainippon (Boston Biomedical)	N/A	BBI608/colorectal
Fate Therapeutics	A cellular reprogramming and differentiation technologies for generating cell types of interest for target discovery and high-throughput screening	ProHema/stem cell transplantation (Phase Ib)

Source: Edison Investment Research

Sensitivities

Verastem is subject to the risks typically associated with biotech company drug development, including the possibility of unfavourable or ambiguous outcomes in clinical trials, the success of competitors and commercial decisions by partners or potential partners. Verastem may carry higher risks than its peers because 1) the CSC theory is new and unproven and no drugs specifically targeting CSCs have been proven in the clinics; 2) Verastem's drug candidates are in the early stage of development and early stage drugs not only have lower clinical success rates, but also face more development challenges as treatment standards change; and 3) Verastem's cash may only support its operation by 2015 and it needs to raise additional funds before then.

Specifically, Verastem shares may be sensitive to VS-6063's clinical progress in mesothelioma, including whether the FDA will accept to the company's Phase II trial design, the speed at which the company can enrol enough patients in a potentially "pivotal" trial and the robustness of the drug's efficacy in the trial. Furthermore, the outcome of other drugs in development for this disease, in particular Roche's Avastin and MolMed's NGR-hTNF, could affect's VS-6063's market potential as a maintenance therapy for mesothelioma initially.

In addition, investors should also be mindful of GSK's development effort of GSK2256098, which is the closest FAK inhibitor competitor to VS-6063. If GSK decides to move aggressively to mesothelioma, it could also be a major setback for Verastem given GSK's substantially stronger financial capability.

Valuation

We value Verastem at $295m, or $13.5 per share, based on a sum-of-the-parts DCF valuation, using a standard discount rate of 12.5%. This includes product pipeline value of $203m and end-2012 cash, marketable securities and long-term investments at $92m. For product pipeline valuation, we have estimated peak sales of $829m for VS-6063 in mesothelioma and ovarian cancer and peak sales of $346m for VS-4718 and VS-5584 (modest in our view, as indications have not been determined for these two drugs). We apply clinical success rates of 15% for VS4718 and VS-5584, 25% for VS-6063 in ovarian cancer and 35% in mesothelioma. Our rNPV calculation subtracts the royalty pay-outs Verastem owes to licensors of each compound, including Pfizer, Poniard/Scrippts and S*Bio.

We apply a probability of clinical rate of 35%, higher than the average, for VS-6063 in the Phase II maintenance setting of mesothelioma. This is based on our view that VS-6063 could generate GSK2256098-like efficacy in the disease: doubling and tripling of PFS comparing to historical standard in ITT and merlin-negative patients, respectively. In addition, the Phase II trial could be designated pivotal, therefore justifying for a higher success date.

Exhibit 12: Verastem DCF model

($m except for per share data)	rNPV ($m)	rNPV / share ($)	Prob. of success	Launch	Peak sales	Royalty pay-out	Patent expiry	Key assumptions
VS-6063, maintenance mesothelioma	$73.8	$3.38	35%	2016	$297	-10%	2029	US treatable pts: 2,250 annually; full-course treatment cost: $37.500 in 2016.
VS-6063, second-line ovarian cancer	$76.8	$3.52	25%	2018	$532	-10%	2029	US treatable pts: 8,912 annually; full-course treatment cost: $31,212 in 2018.
VS-4178, cancer	$26.5	$1.21	15%	2019	$346	-3.5%	2029	
VS-5584, cancer	$26.0	$1.19	15%	2019	$346	-5.5%	2029	
Total pipeline value	$203	$9.30						
Net cash (2012 YE)	$92	$4.19						
Total firm value	$295							
Total diluted shares (m)	21.8							
Value per share ($)	$13.5							

Source: Edison Investment Research. Note: Net cash includes marketable securities and long-term investments.

Financials: Cash of $91.8m at end-2012

Verastem reported a loss of $10.4m in Q312, while net cash used in operating activities was $6.7m. Cash and equivalents at the end of Q312 amounted to $97.4m. We expect the company's cash and cash equivalents, marketable securities and long-term investments at the end of 2012 to be $91.8m. Based on our projection of cash burn, we estimate that this cash should support the company's operations into Q415, at which time (or preferably earlier) the company would need to raise additional funds, either from the capital market or from strategic players, to continue its development efforts. As per Edison's policy, no revenue from potential future licensing agreements is assumed in the financial model.

Exhibit 13: Financial summary

$'000s	2010	2011	2012e	2013e	2014e
Year end 31 December					
PROFIT & LOSS					
Revenue	0	0	0	0	0
Cost of Sales	0	0	0	0	0
Gross Profit	0	0	0	0	0
EBITDA	(784)	(13,698)	(34,749)	(42,630)	(43,670)
Operating Profit (before amort. and except.)	(784)	(13,698)	(34,749)	(42,630)	(43,670)
Intangible Amortisation	0	0	0	0	0
Exceptionals	(2)	(32)	(6)	0	0
Other	0	0	0	0	0
Operating Profit	(786)	(13,730)	(34,755)	(42,630)	(43,670)
Net Interest	0	15	251	190	110
Profit Before Tax (norm)	(784)	(13,683)	(34,498)	(42,440)	(43,560)
Profit Before Tax (FRS 3)	(786)	(13,715)	(34,504)	(42,440)	(43,560)
Tax	0	0	0	0	0
Profit After Tax (norm)	(784)	(13,683)	(34,498)	(42,440)	(43,560)
Profit After Tax (FRS 3)	(786)	(13,715)	(34,504)	(42,440)	(43,560)
Average Number of Shares Outstanding (m)	0.9	1.3	18.8	20.8	21.4
EPS - normalised and fully diluted (c)	(0.9)	(10.6)	(1.7)	(1.9)	(2.0)
EPS - (IFRS) (c)	(0.9)	(10.6)	(1.8)	(2.0)	(2.0)
Dividend per share (c)	0.0	0.0	0.0	0.0	0.0
Gross Margin (%)	N/A	N/A	N/A	N/A	N/A
EBITDA Margin (%)	N/A	N/A	N/A	N/A	N/A
Operating Margin (before GW and except.) (%)	N/A	N/A	N/A	N/A	N/A
BALANCE SHEET					
Fixed Assets	0	11,096	51,695	9,719	2,512
Long-term investment	0	8,994	50,579	8,000	0
Property Plant & Equipment	0	709	884	944	1,144
Other	0	1,393	232	775	1,368
Current Assets	3,596	47,941	41,709	50,872	24,420
Cash and cash equivalents	3,584	20,954	5,557	14,620	31,068
Marketable securities-short term	0	26,857	35,703	35,703	(7,297)
Prepaid expenses and other current assets	12	130	449	549	649
Other	0	0	0	0	0
Current Liabilities	(368)	(3,146)	(6,149)	(7,549)	(8,949)
Creditors	(368)	(3,146)	(6,149)	(7,549)	(8,949)
Short term borrowings	0	0	0	0	0
Long Term Liabilities	0	(516)	(64)	(7)	(4)
Long term borrowings	0	0	0	0	0
Other long term liabilities	0	(516)	(64)	(7)	(4)
Net Assets	3,228	55,375	87,191	53,035	17,979
CASH FLOW					
Operating Cash Flow	(330)	(10,147)	(22,497)	(33,646)	(34,462)
Net Interest	0	15	251	190	110
Tax	0	0	0	0	0
Capex	(8)	(785)	(321)	(60)	(200)
Acquisitions/disposals	0	0	0	0	0
Financing	3,922	64,224	57,601	0	0
Dividends	0	0	0	0	0
Net Cash Flow	3,584	53,307	35,034	(33,516)	(34,552)
Opening net debt/(cash)	0	(3,584)	(56,805)	(91,839)	(58,323)
HP finance leases initiated	0	0	0	0	0
Other	0	(86)	0	0	0
Closing net debt/(cash)	(3,584)	(56,805)	(91,839)	(58,323)	(23,771)

Source: Edison Investment Research, Verastem

Contact details	Revenue by geography
215 First Street, Suite 440, Cambridge, Massachusetts 02142 US +1 617-252-9300 www.verastem.com	N/A

CAGR metrics		Profitability metrics		Balance sheet metrics		Sensitivities evaluation	
EPS10-14e	N/A	ROCE 13e	N/A	Gearing 13e	N/A	Litigation/regulatory	●
EPS 12-14e	N/A	Avg ROCE 10-14e	N/A	Interest cover 13e	N/A	Pensions	○
EBITDA 10-14e	N/A	ROE 13e	N/A	CA/CL 13e	N/A	Currency	○
EBITDA 12-14e	N/A	Gross margin 13e	N/A	Stock turn 13e	N/A	Stock overhang	○
Sales 10-14e	N/A	Operating margin 13e	N/A	Debtor days 13e	N/A	Interest rates	○
Sales 12-14e	N/A	Gr mgn / Op mgn 13e	N/A	Creditor days 13e	N/A	Oil/commodity prices	○

Management team

Chairman/CEO: Christoph Westphal, MD, PhD

Dr Westphal is a partner of Longwood Fund. He was founder, co-founder or CEO of several biotech companies, including Sirtris, Alnara and Alnylam. He earned his MD and PhD from Harvard University and BA from Columbia University.

Chief operating officer: Robert Forrester, LLB

Before Verastem, Mr Forrester was CEO, COO or CFO of Forma Therapeutics, CombinatoRx and Coley. He worked at investment firms including Fortis Group, BZW and UBS and is a member of the board of directors of Myrexis Pharmaceuticals.

Chief medical officer: Joanna Horobin, MB, ChB

Dr Horobin was president of Syndax Pharma, VP of oncology at RPR (now part of Sanofi), COO of CombinatoRx and EVP at EntreMed. She received her medical degree from the University of Manchester, and holds a diploma of pharmaceutical medicine from the Royal College of Physicians in the UK.

Head of research: Jonathan Pachter, PhD

Dr Pachter was previously head of cancer biology at OSI Pharmaceuticals. He did his postdoctoral work in pharmacology at Yale University School of Medicine and holds a PhD from Baylor College of Medicine.

Principal shareholders	(%)
Longwood Fund LP	13.5%
CHP III LP	10.5%
MPM Asset Management	9.57%
Bessemer Venture Partners	9.39%
Eastern Capital Ltd	5.38%
Hambrecht & Wuist Capital Management	4.16%

Companies named in this report

Amgen (AMGN), Astellas (ALPMF), Bionomics(BNO.AX), Celgene (CELG), Daiichi (DSKYF), Dainippon (DNPUF), Eisai (ESALY), Exelixis (EXEL), Fate Therapeutics, GSK (GSK), Infinity (INFI), Novartis (NVS), Novogen (NVGN), Oncothyreon (ONTY), Oncomed, Oncotherapy, Pfizer(PFY), Roche (ROG.VX), S*Bio, Stemline (STML), Takeda (TKPYY), Teva (TEVA).

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