Vical (VICL) and its Pipeline

Vical: Summary
Special report written by Juan P. R. Serrate

Vical’s stock price has rallied the last few weeks. At the time of this writing the company has a market cap of roughly $180M and a price per share of $2.50. At the end of 2010, total cash was $60M after raising $37M in September 2010 in a stock offering that cut the stock price almost by half. It is worth pointing out that at the time of the offering, Vical had less than $15M cash. According to the recently published annual report, Vical burned $28.2M in 2010 and it expects to burn between $22M and $27M in 2011. Vical’s main catalyst for this year is the data release from its phase III trial of Allovectin-7 in the second half. Insider activity shows that it is a buy under $2, however, insiders have sold at various prices in the past. For instance, they sold at $3.5 well in advance of the stock offering and they have recently been selling shares at $2.28. Therefore, it would not be strange to see a correction but this may also be the start point of a consistent run-up to the data release.
It has two drugs in ongoing Phase I trials:
- H1N1 vaccine: it is a Vaxfectin-formulated plasmid DNA vaccine for the potential treatment or prevention of swine-origin pandemic influenza H1N1 in collaboration with the US Naval Medical Research Center, with data expected in 1Q2011.
- Avian H5N1 influenza vaccine: a three-component plasmid DNA vaccine, comprising nucleoprotein (NP), an ion channel protein (M2), a hemagglutinin surface protein from H5N1 influenza virus strains, plus Vical’s proprietary Vaxfectin adjuvant, for the potential prevention of avian influenza. After positive preliminary results presented in 2008, the company was planning a larger trial in 2009 and looking for funding sources for its future development.

Company overview and pipeline

Vical, formed in April 1987, is a company that discovers and develops vaccine and gene therapy products based on its plasmid DNA delivery technologies for the prevention and treatment of life-threatening or serious diseases.

Vical’s independent program comprises:
- Allovectin-7 for metastatic melanoma. Currently undergoing phase III trials. A detailed explanation on the technology and the clinical trials is provided below.
- TransVax (VCL-CB01) is in phase II trials. It is an injectable intramuscular bivalent plasmid DNA vaccine, consisting of one plasmid encoding CMV phosphoprotein 65 and another encoding CMV glycoprotein B (gB), for the potential treatment of cytomegalovirus (CMV) infection. After September 2010’s positive results, a phase III trial is expected to start in 2H2011.

Allovectin-7 is an immunotherapeutic which is made of a lipid DNA plasmid that contains the genes that encode HLA-B7 and b2-globulin.

What is Allovectin-7?
Vical is developing Allovectin-7 (veligene alloplasmid) for the potential treatment of metastatic melanoma. Allovectin-7 is an immunotherapeutic which is made of a lipid DNA plasmid that contains the genes that encode HLA-B7 and b2-globulin. Melanoma cells have reduced expression of the Major Histocompatibility Complex class I (MHC-I) therefore, they are able to avoid the immune system recognition and thus can migrate through the body causing damaging effects without being targeted by T-cells. HLA-B7 works as an immune-potentiator. Since it is expressed only in 20% of the American population, it allows an allogenic immune response. B2-globulin mutations have been pointed out as a possible cause for the reduction of MHC-I expression in tumor cells. If the drug works as expected, tumor cells will express MHC-I and will be subject to immune system destruction. Furthermore, a foreign immune stimulation will boost the immune response.

Allovectin-7 has undergone clinical trials since 1993 for metastatic melanoma and other cancer indications such as head and neck cancer (discontinued due to poor enrollment), renal carcinoma, colorectal cancer. In 1999 Vical decided to prioritize the “most promising indications” i.e. metastatic melanoma.

Phase III trial of low dose A-7
Focusing on phase III trials for melanoma types III and IV, Vical started enrollment in 2000 in what would be an open-label, multicenter, randomized, controlled trial at more than 50 centers across the US. The trials were designed to determine the effectiveness of a low dose (10 μg) of velimogene aliplasmid and dacarbazine chemotherapy versus dacarbazine alone in delaying disease progression. Enrollment was completed in September 2001. However, in September 2002, Vical revealed that its low-dose phase III registration trial with velimogene aliplasmid in patients with metastatic melanoma “would not advance to an independent endpoint assessment and adjudication committee because an initial review of investigator-determined efficacy by an external consultant indicated that the study would not meet statistical significance of its primary endpoints; objective response rate and/or time to disease progression” ([1Q file here](#)). Remember, that was with the LOW DOSE. Now, higher doses of up to 2mg have been essayed in the past in several trials, including the phase III one from which data will be released in 2H2011.
Phase II and III trials of high-dose A-7

The phase II trial presented interim results in June 2003. A-7 was dosed at 500, 1,000 and 2,000 micrograms intratumorally in a single lesion or multiple lesions. At that time, among 91 patients, there were 2 complete responses, 10 partial responses, 22 had stable disease and 57 had progressive disease. In November 2003, the study produced a median duration of response of at least 6.4 months. These data have been increasing with time as more patients were being included in the outcome. In June 2004, data from 127 patients revealed 2CR, 11 PR, 34 SD and 80 cases of PD. At that point, the MDR was over 8.7 months. Over time, there was an increase until January 2011 when the last PR indicates a duration increased to 13.8 months.

Particularly, the publication released on Jan 11 this year stated: “The most recently completed Phase 2 trial was a single-arm, open-label study in which 127 chemo-refractory or chemo-intolerant subjects were treated with high-dose Allovectin-7. There were no treatment-related Grade 3 or Grade 4 adverse events, and no withdrawals from the trial for tolerability. The overall response rate for the 127 patients receiving the high-dose treatment was 11.8%, with 4 complete responders and 11 partial responders. The median duration of response was 13.8 months and median survival was 18.8 months. These data compare favorably against historical controls from other studies in metastatic melanoma.”

The OS data looked good at first glance, however, as biotech analyst Patrick Crutcher points out, that was only measured with responders (see reference here). If you looked over this article, you already know the percentage of patients responding to A7 and you can draw your own conclusions. Surprisingly, Vical claims in its company presentations that the OS data is even better than the recently approved antibody Ipilimumab which is a misleading statement for investors to say the least.

The phill high-dose trial began in January 2007 when the company announced the enrollment of its first patient in the trial. The open-label, multicenter trial enrolled 390 patients with recurrent metastatic melanoma who had been treated with surgery, adjuvant therapy, and/or biotherapy, but not with chemotherapy. A total of 260 patients would receive high-dose (2 mg) velimogene aliplasmid and 130 would receive chemotherapy in the form of either dacarbazine or temozolomide. The primary endpoint was objective response rates after 24 weeks, and survival, safety and tolerability was also assessed. After some delays in recruiting patients and four positive safety analyses, enrollment was completed in February 2010. At that time, the company expected to complete patient follow-up in 2011. Have a look at clinicaltrials.gov (study identifier NCT00395070). The primary completion date is February 2011 and the study completion date is expected for Aug 2011. According to Vical’s PR and corporate presentations, the database will be locked in the second half, therefore data release will follow a few weeks after the announcement.

Licensing

Vical started contacting companies to discuss potential license agreements in 2004. In May 2006 AnGes licensed the compound for marketing in several Asian countries. In December 2008 Vical signed an agreement for marketing and sales rights with Ecizabasi in Turkey. Since August 2009 Teva has had marketing rights in Israel.
Investment Summary
A-7 has demonstrated itself to be safe and efficacious in terms of survival. However, this is not so in regard to the overall response as it has shown pretty similar results to Dacarbazine. Whereas the low dose had to be discontinued, doses over 1,000 times higher showed better activity, but still there was no improvement in the overall response. A phase III trial with a larger number of patients enrolled is not likely to show an outright improvement in the overall response (which happens to be its primary endpoint). The market knows this and has consequently kept the stock price low. Nevertheless, a moderate run-up could start as the date of the database lock and the subsequent data release approaches. A profitable strategy could be to be long the run-up and short the news.

Disclaimer
I am not a certified financial analyst. All the information provided in this report is my interpretation and may contain errors. Please, do not invest based solely on my opinions as it is critical for all investors to conduct their own due diligence and invest in ways that best fit their own needs. In addition, I have own no shares or options of VICL.

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