

# Medical Technology Stock Letter



## **This Issue: Bydureon Sinks on Data while Novavax Jumps on BARDA Funding**

Issue No. 699

March 3, 2011



**Pulse of the Market by Jim McCamant**

**BTK: 1,294.26, NBI: 998.77**

Over the last two weeks, the Nasdaq was down 1.2% or 32.84 points, the S&P 500 was down 1.3% or 17.68 points and the BTK Index was down 0.47% or 6.1 points. The Model Portfolio was down 2.8% and the Trader's Portfolio was down 6.1%.

This week we have seen an unusual stock market. The good economic news will control one day, or part of a day, and then the higher price for oil will drive stocks lower. Within this conflict the market is willing to ignore profits, which have remained excellent. The bears justify this by pointing out that much higher oil prices could slow economies and reduce future earnings. This strange market is increasing volatility and short-term risk, but it is unlikely to impact the market on a longer-term basis. As long as the short-term weirdness does not stop the economic recovery, stocks will work their way higher. The strong consumer confidence and the excellent ISM numbers were particularly impressive. The eventual reduction in short-term worries will result in an increased interest in biotech stocks and many of them have very large potential in comparison to modest risk. While biotech stocks are definitely held under the sway of the larger markets, eventually individual stocks percolate to the top based on fundamentals, and these will continue to be our focus.

### **Vertex Pharmaceuticals**

Looking back over much of the hype of the last 15 years, most people would say that the promise of biotechnology is largely undelivered. However, for people living with cystic fibrosis the medical advances of the biotech age have transformed their lives. Fifty years ago a person born with the genetic disorder would not be likely to live past elementary school. Today, cystic fibrosis (CF) patients live relatively normal lives, and the introduction of bronchodilators, mucolytics and inhaled antibiotics have greatly improved their quality of life. On the other side of the coin, for no-one is the promise of biotech left so deeply unfulfilled as it is for CF patients. The average life expectancy for CF patients is still only in the mid-30s, and while multiple new therapies have been developed to treat the symptoms of CF, none yet has tackled the underlying cause of the disease. Furthermore, the available treatments are not easy for patients. Most patients must inhale medications from an inhaler for hours each day, and since therapy is needed from an early age this often involves parents and families having to wrestle each day with truculent infants. To put it lightly, the burden of therapy is heavy.

Cystic fibrosis is caused by a malfunction in the formation of a particular protein, the cystic fibrosis transmembrane conductance regulator (CFTR). For most CF patients, a genetic defect encodes a modified, defective version of the protein so instead of doing its job, which is to help transfer ions into and out of cells, the protein is degraded. This leads to patients having problems with digestion and with their lungs. The digestive problems, caused by a deficiency in enzymes that should be made by the pancreas, are mostly controlled by particular diets and by adding in the needed enzymes. The pulmonary problems, characterized by thick mucous in the lungs that harbors infection and makes breathing difficult, are tougher to treat. The most common genetic difference leading to CF is called  $\Delta F508$ , referring to the deletion of three nucleotides and subsequent loss of phenylalanine at the 508th position of the CFTR protein. About 90% of the 70,000 CF patients worldwide have this mutation. There are, however, hundreds of other mutations that lead to similar problems with the CFTR protein. For a small percentage of patients, about 5% who have the G551D mutation, life may soon be looking up.

Last week, Vertex Pharmaceuticals (VRTX) released data from a Phase III study of their experimental CF drug VX-770. The drug, known as a potentiator, acts on the defective CFTR protein to make it work properly as a cell ion channel. In the trial, VRTX demonstrated huge significance by delivering a 10.6% improvement, from 64% to 75%, in FEV1, the patient's forced expiratory volume in one second, a standard measure of pulmonary health. This compared to no change in placebo patients, and an improvement of just under 5% would have been significant. Those in the treatment arm also experienced an average weight gain of about 7 pounds, compared to 1 pound for placebo, and were 55% less likely to have a pulmonary exacerbation. The data released so far was for adolescent and adult patients, and data from another Phase III trial of juvenile patients is expected later this year. VX-770 is the most advanced clinical program of disease modifying CF therapies. PTC Therapeutics is testing Ataluren (PTC124) in patients with nonsense mutation CF, another subset of the overall population. VRTX has another disease modifying CF program that combines VX-770 with VX-809, called a corrector, that moves the CFTR protein to the proper place. Trials of the combination in CF patients with the most common  $\Delta F508$  mutation are ongoing.

Analysts have predicted that VX-770, if approved for use in approximately 5% of the CF population, has the potential to generate sales between \$400K and \$1 billion annually. The CF Foundation helped in the development of the drug and will likely be owed royalty payments upon approval. VRTX stock responded accordingly, with a 17% jump when the news was released, and multiple new 52-week highs established this week. We think that the maximum annual sales fall more on the lower end of the estimates, and the data and sales were quickly incorporated into the price of this popular stock. The overall evaluation of VRTX is of course being driven by the hepatitis C candidate telaprevir, so this significant success in CF is a nice cherry on top for the company. It certainly makes VRTX a more attractive takeover target. We have believed that the value of VRTX's programs has been fully realized by the market and this is not a good entry point for the stock. More than anything, we are happy to see some CF patients finally receiving the disease-modifying therapies they need. As for VRTX, the news this week pushed the company's market capitalization over \$10 billion. Careful investors should keep an eye out for a correction.



## Company Updates

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**FOCUS: ALTH, ASTM, ALKS, AMLN, ARQL, CELG, NVAX, ONXX, SGMO.**

**Allos Therapeutics** (ALTH) released their fourth-quarter and year-end results for 2010 this week, and announced regulatory progress for *Folotyn* in peripheral T-cell lymphoma (PTCL), a form of blood cancer. The company reported quarterly and yearly losses of \$18.1 and \$74.1 million, respectively. Quarterly and yearly revenues for *Folotyn*, which was launched commercially in January 2010, were \$11.7 and \$35.2 million, respectively. The company ended the year with cash and investments totaling almost \$99 million. *Folotyn* sales should continue to grow in 2011, especially if ALTH is able to gain marketing approval in Europe. The application to the EMA for the use of *Folotyn* to treat relapsed and refractory PTCL was completed in

December 2010. Additionally, Phase II trials of the drug in bladder cancer and breast cancer should be completed this year. At the same time, the company did say earlier this year that they will not pursue Phase III trials of the drug in NSCLC.

In the lymphoma space, ALTH is seeking approval for *Folotyn* to treat newly diagnosed PTCL patients who have achieved a response following initial treatment with a CHOP-based therapy (cyclophosphamide, doxorubicin, vincristine and prednisone). The company has reached an agreement on an SPA for a Phase III trial in this population with co-primary endpoints of progression-free survival and overall survival. The trial is expected to begin enrolling patients this year. The original *Folotyn* approval was based on patient response in the Phase II PROPEL trial under an accelerated timeline. That means that survival has never been demonstrated with *Folotyn*, so this Phase III trial is very important for the company both to gain approval for first-line therapy and as a required post-approval study. The company is also planning a Phase III trial of *Folotyn* plus bexarotene (*Targretin*) in patients with relapsed or refractory cutaneous T-cell lymphoma (CTCL).

Now that they have an approved drug with growing sales, the investment picture for ALTH going forward is healthy. The company has a revenue stream and is vigorously pursuing expansion of the market for their drug, both geographically and in terms of disease indications. We have multiple catalysts to look forward to with ALTH in 2011, including potential EU marketing approval and ongoing clinical results. The presence of an approved oncology drug and relatively small market cap continue to make ALTH a possible takeover target. **ALTH is a Buy under \$5.**

**Aastrom** reported their year end and quarterly financials this past week, which are discussed below. More importantly, management provided updates what to expect in 2011. The catalysts we'll be looking for this year are:

- Report final results (12 month data) from the ongoing Phase II CLI study in Q2
- Launch the first Phase III studies in CLI "no option" patients mid-year
- Report interim data from the IMPACT-DCM study (12 month data) and present the ongoing Phase II Catheter DCM trial (six month data) in Q3 and launch the next phase of clinical testing in DCM by the end of the year
- Finalized SPA in Q2 2011 for the "no option" trial, and in Q3 of 2011 for the "poor option" trial.

The first Phase III trial will seek to treat 500 patients with severe CLI. These "no option" patients must have confirmed tissue loss and disease progression to qualify for enrollment. We expect the primary endpoint of the program to be amputation-free survival at 12-months (AFS-12). Other endpoints will include major amputation (above the ankle), de novo gangrene, wound size, and all cause mortality. Management has taken a number of steps to improve the Phase III trial design and patient selection compared to the Phase 2b RESTORE trial. We think patient selection is particularly important and management emphasized these points during the call:

- ASTM will employ an independent steering committee of outside physicians who have direct experience with CLI programs to help oversee and monitor the trial.
- Aastrom will utilize a centralized review committee comprised of experienced vascular surgeons to screen and monitor patients and set a standardized disease progression and amputation criteria.
- Management has established rigorous entry criteria to help standardize the baseline characteristics of each "no option" patient. This establishes a second layer of qualification beyond the treating physician.
- To limit geographical variability and standard of care variability, the trial will be conducted in only North America at sites in the U.S. and Canada. A recent Phase III failure in CLI was run worldwide and showed wide variability by geography.
- Management has significant experience including many new hires with CLI trial experience, in addition their CRO is also experienced in conducting CLI trials.

All of the above changes will also be incorporated into the second Phase III trial in the CLI program which is to treat 200 patients with moderate CLI, aka, "poor option." These patients have disease progression with a clear path toward amputation, and are easier to find than "no option" patients. In fact, the FDA has encouraged ASTM to pursue "poor option" patients as there is large unmet medical need in this population. We believe the FDA wants to see AFS-12 as the primary endpoint, and ASTM's management is hoping to include revascularization or MALEFS (major adverse limb event free survival) as an endpoint. At this point we are unsure just how important the inclusion of MALEFS will be to the success of the trial, and it is possible that the company and the FDA agree on two endpoints. It is clear that the event rate will be lower than in the "no option" group, and including revascularization may lead to a more clinically relevant endpoint for patients that have not yet progressed to only surgical options. Management is hoping to secure an SPA around this second Phase III trial sometime in the third quarter 2011. We expect that this trial will start late in the year.

ASTM also discussed their recent dilated cardiomyopathy (DCM) Phase II data on the conference call with their VP of clinical and regulatory, Dr. Sharon Watley, leading the discussion. The Phase II DCM data showed they could effectively deliver the therapy directly into the left ventricle without any major safety issues. Still, the other ongoing DCM trial is delivering the therapy via a catheter and is much less invasive than surgery. They also believe that the therapy may work better in ischemic patients which will allow for a finite target patient population. Thus, the next trial will utilize catheter delivery into a more select DCM patient population that is ischemic (restricted blood flow to the heart). This indication has received orphan drug designation from the FDA and we are eager to see what endpoints they can agree on with the Agency. The endpoints that are currently being considered include measures of cardio fitness including the six minute walk test, cardio-pulmonary function, and exercise capacity. The company uses the NY Heart scale (1-4) to determine how severe the DCM patients are before enrollment, usually enrolling 3s or 4s, and this measure of quality of life may also be incorporated into upcoming the Phase IIb trial. Because the drug candidate has been granted orphan drug status by the FDA, there is the potential for the Phase IIb trial to be a registration trial if the data is strong enough.

ASTM has reported operating results for the quarter and six months ended December 31, 2010, reflecting the recent change in the company's fiscal year end from June 30 to December 31. Net loss for the quarter and six months ended December 31, 2010 was \$13.3 million, or \$0.44 per share, and \$19.3 million, or \$0.66 per share, compared to a net loss of \$4.3 million, or \$0.20 per share, and \$8.1 million, or \$0.38 per share, for the same periods a year ago. The company had a total of \$31.2 million in cash and cash equivalents, compared to \$14.7 million in cash and cash equivalents at December 31, 2009. This gives the company enough many for 2011 and should put them into a good position to negotiate partnerships.

While we believe that ASTM has a solid cash position, there have been recent rumors that the company is going to finance again soon. The rumors started when the company recently announced that they will hold a special meeting of shareholders on Monday, March 21, 2011 to approve an increase the number of authorized shares of common stock from 62.5 million to 150 million. The current number of shares outstanding is 38.6 million as of December 31, 2010, and adding in the 4.5 million options and 15.3 million warrants, and total authorized (fully diluted) shares total 58.3 million. This is less than 4 million from the total 62.5 allowed under the current shareholder authorization. While this has provided some fuel for short-sellers over the past month, the reality is that ASTM has many options to raise additional funds and a partnership is certainly possible. The increase to 150 million shares should be seen as what may eventually be needed years down the road, not the number of shares the company intends to offer. We continue to believe in ASTM and their management team's ability to deliver value, and the current price weakness is providing an excellent entry point. **ASTM is a buy under \$3.50.**

**Amylin** and **Alkermes'** stock prices were both down this week after releasing top-line results from DURATION-6, a head-to-head study designed to compare weekly *Bydureon* to Novo Nordisk's once-daily *Victoza*. The disappointing results showed that patients receiving *Bydureon* experienced a reduction in A1C of 1.3% from baseline, compared to a reduction of 1.5% for *Victoza*, and did not meet the pre-specified primary endpoint of non-inferiority to *Victoza*. This was a risky trial that would

have been a huge marketing tool, but now it will be used against *Bydureon*. Given that *Bydureon* is not yet on the market and will have to play catch up, the risk was probably worth taking. If *Bydureon* had been shown to be superior, everyone would hale the companies' boldness and foresight instead of saying that they'd made a mistake. While the top-line efficacy endpoint was not as good as *Victoza*, the data was still good and the peripherals actually tilt towards *Bydureon*.

AMLN's stock was down over 25% and ALKS stock was down over 10% on good data that wasn't quite as good as their competitor's. We believe that the 25% sell-off is an over-reaction as *Bydureon* is much closer to approval and the path is much clearer than it was last year when the FDA requested more information on *Bydureon*. In previous trials *Bydureon*'s A1C was better than *Victoza* and A1C is not the only criteria for an effective diabetes drug. *Bydureon* has consistently provided better weight loss than *Victoza* and has shown about half the side-effects. Most importantly, *Bydureon* is a once-weekly injection vs. a daily injection for *Victoza*, (one needle stick vs. seven needle sticks a week), which is very important to patients. While doctor's certainly understand the importance of biomarkers like A1C, a patient's comfort and compliance are also considered, and we think that this data will not discourage doctors from trying *Bydureon*.

We are going to change our recommendation on AMLN from a Hold to a Buy under \$11.50. We believe that this week's decline has more than discounted the disappointment from DURATION 6 which did show *Bydureon* to highly effective, just not quite as good as *Victoza*. We are also much closer to the re-filing of *Bydureon* with the FDA than we were in October. We also have added clarity as the NDA will be re-filed by year end. Therefore, we are raising our buy limit on ALKS from \$12 to \$13 to take advantage of today's opportunity. ALKS has done a tremendous job creating value in their pipeline, and *Bydureon* still represents significant revenue growth for both ALKS and AMLN. While we are disappointed in the news, we believe that both stocks have been over-sold and urge subscribers to either add or establish positions in AMLN and ALKS.

**AMLN is now a Buy under \$11.50 and ALKS is now a Buy under \$13.**

**ArQule** announced their 2010 financial results this week and gave guidance as to what we should expect in 2011. The company reported a net loss of \$30 million or \$0.68 per share, for the year ended December 31, 2010, compared with a net loss of \$36 million or \$0.82 per share, for the year ended December 31, 2009. At the end of the year, ARQL had a total of almost \$83 million in cash and marketable securities. The main reason for the decrease in costs year-on-year was due to the shift of clinical costs to partners Daiichi Sankyo and Kyowa Hakko Kirin, although some of the savings were smartly reinvested in earlier stage clinical and pre-clinical programs. ARQL completed an offering in January with net proceeds of around \$46.5 million and also received a milestone payment from Daiichi Sankyo in February after dosing commenced in the pivotal Phase III trial of ARQ 197/tivantinib (in combination with erlotinib) for patients with non-squamous, NSCLC who have received one or two prior systemic anti-cancer therapies.

Now that the Phase III trial is underway, ARQL outlined the following goals for tivantinib in 2011:

- Opening of all of the clinical trial sites in the pivotal Phase III combination trial with erlotinib in NSCLC.
- Communication of data from the randomized Phase II single-agent trial in liver cancer in the 2H 2011.
- Continuation of patient enrollment in a randomized Phase II combination trial with irinotecan and cetuximab in colorectal cancer.
- Evaluation of data from the open-label Phase I combination trials with gemcitabine and with sorafenib in multiple tumor types that may inform further clinical trials.

Tivantinib (ARQ 197) is a selective small molecule inhibitor of c-Met receptor tyrosine kinase, which appears to play many roles in cancer cell proliferation, tumor spread, new blood vessel formation and drug resistance. In late January the company presented data from a Phase I combination trial with irinotecan and cetuximab in patients with metastatic colorectal cancer

at the ASCO 2011 Gastrointestinal Cancers Symposium. The data supports the ongoing Phase II trial, which is enrolling CRC patients with the wild-type form of the KRAS gene who have received front-line systemic therapy.

ARQL completed fundraising at a good time from a position of strength, and combined with ongoing milestone revenue the company appears to have enough cash on hand to last until the end of 2013. In addition the lead program, ARQL is also pursuing multiple earlier programs that should continue to provide good news flow throughout this year. Without much fanfare, ARQL continues to push ahead with their programs and have put themselves in a strong position financially. We will continue to monitor the tivantinib program, especially looking forward to Phase II liver data later this year. **ARQL is a Buy under \$6.**

**Celgene** announced this week that the company has received priority review for *Istodax* for the treatment of relapsed or refractory peripheral T-cell lymphoma. The priority status means that the FDA will review the *Istodax* NDA within six months, providing an opportunity for CELG to have the drug approved by mid-year, with a PDUFA date set for June 17. Also, last week the company announced that it has settled a lawsuit with Elan over patent infringement related to *Abraxane*, legal troubles purchased from Abraxis along with the drug last year. Under the terms of the settlement, CELG will pay Elan \$78 million and receive a portfolio of patents related to *Abraxane*. Elan will not receive any future royalties or payments. Later this month the company is expected to release top-line data from the Phase II trial of amrubicin in small-cell lung cancer. **CELG is a Buy under \$60.**

**Novavax** stock was up nicely earlier in the week before trading off after two value-creating announcements. First and most important, BARDA granted NVAX a contract for \$97 million over three years, which can be extended for an additional two years, for a total contract value of \$179.1 million. That's \$97 million in non-dilutive financing that significantly bolsters NVAX valuation and ability to fully develop their technology. The company also inked a VLP vaccine partnership with LG Life Sciences (LGLS) of Korea, which includes an upfront payment, milestone payments, and most importantly double digit royalties.

The BARDA contract is part of a national pandemic vaccine preparedness strategy, which includes the advanced development of new types influenza vaccines as well as expanding and diversifying domestic influenza vaccine production, and establishing and testing stockpiles of pre-pandemic vaccine. In addition, the recombinant flu vaccine may enhance pandemic vaccine manufacturing surge capacity in the United States. Under its contract, NVAX is to continue to develop new technology to produce vaccines using insect cells to express influenza proteins and create virus-like particles that stimulate a strong immune response in humans.

During the contract's base period, funded activities would include:

- Three clinical trials utilizing NVAX' pandemic influenza VLP vaccine candidate with adjuvants (including Novavax's proprietary adjuvant).
- Phase II dose-ranging trial and Phase III registration trial utilizing the NVAX seasonal influenza VLP vaccine candidate which should allow the company to file their BLA in 2012.
- Development of a manufacturing facility plan that has the capability to produce finished vaccine within twelve weeks and at least 50 million doses within six months of an influenza pandemic declaration.

On the same day as the BARDA contract was received, NVAX' also announced an agreement with LGLS, who received an exclusive license to manufacture, develop and commercialize influenza vaccines using NVAX recombinant VLP technology in South Korea. LGLS also receives a non-exclusive license to manufacture, develop and commercialize influenza VLP vaccines

in certain undisclosed emerging market countries. NVAX will receive upfront and milestone payments from LGLS in addition to double-digit royalty rate payments from commercial sales. The company will also provide VLP technology transfer and manufacturing support for LGLS's new vaccine production facility. Finally, LGLS will be responsible for funding clinical development and licensure of influenza VLP vaccines in South Korea and other countries, and for construction of a new VLP vaccine manufacturing facility that can produce 30 million doses planned at LGLS's Osong campus in South Korea (which has already begun).

In sum, these are two huge value creating events for NVAX as they have secured at \$97 million in non-dilutive funding that should allow the company to fully develop their seasonal flu vaccine and file for FDA approval in 2012. We also mentioned in the last Issue that securing BARDA funding would validate NVAX's platform technology and lead to additional corporate partnerships. However, we certainly did not expect them to deliver a two-fer on the news front in one day. We believe that the LGLS partnership is underappreciated today because of the bigger BARDA news and also because there were no dollar amounts revealed in the press release. NVAX is in the driver's seat for negotiating their next partnership as they now have the cash to drive better deals. Also, Big Pharma is lurking and they could swoop and try to buy NVAX at a premium. We are buyers on any dips below \$3 as the current price does not reflect the \$97 million in non-dilutive financing or the value created with LGLS partnership. **NVAX is a buy on dips below \$3.**

We recommended **Onyx** as a buy at \$5.97 about 15 years ago and have been recommended investments in the stock at various points since then. Over that time, we have been pleased to watch ONXX mature into a biopharmaceutical company with a drug on the market and a legitimate pipeline. We now believe we have reached another inflection point and the risk/reward has shifted to the negative. There is a good chance that their accelerated NDA filing for carfilzomib will be delayed by the FDA. This negative event may have been foreshadowed by last year's manufacturing problems, and the FDA still hasn't signed-off on this issue with ONXX saying they are still in scale-up. Our "Spidey Sense" is tingling as a number of subtle factors detailed below have lead to our conclusion that here is good chance that the FDA will want to wait until 2013 for the Phase III data. Thus, we are recommending a sale of ONXX at current prices with the possibility of re-recommending ONXX in the future at a lower price.

ONXX has reported their 4th Quarter and year end financial results. The company reported non-GAAP net income of \$39.2 million, or \$.63 per diluted share, for the full year 2010 compared to non-GAAP net income of \$54.4 million, or \$0.89 per diluted share, for the same period in 2009. ONXX reported a non-GAAP net loss of \$17.4 million, or \$0.28 per diluted share, for the fourth quarter 2010 compared to non-GAAP net income of \$8.8 million, or \$0.14 per diluted share, for the same period in 2009. Nexavar net sales were \$934 million and \$257.4 million for the full year and fourth quarter 2010, respectively, an increase of 11% and 9%, compared to \$843.5 million and \$235.2 million in the same periods in 2009. Nexavar's growth has primarily come from Asia where sales for liver cancer have begun to grow in China even though it is not currently reimbursed there. South Korea approved Nexavar reimbursement for liver cancer late in 2010 and this will have a positive impact going forward.

On the earnings conference call, ONXX management emphasized their goals for 2011:

- Goal 1. File the carfilzomib NDA with the FDA. The drug candidate is eligible for a fast track review and a rolling NDA was started last month which allows them submit the NDA in modules. Manufacturing is still a big question with ONXX saying that they are still in the scale-up phase. The Oncological Drugs Advisory Committee (ODAC) recently discussed accelerated approvals and stated that they need randomized confirmatory trials (i.e. completed Phase III trials) to at least be underway before they grant accelerated approval. ONXX may need to start an additional Phase III study before the FDA even considers accepting their accelerated NDA. A pointed question from the conference call was: Why are they not pursuing an accelerated European approval, given

that the EMEA is more inclined to accept an accelerated approval than the FDA? ONXX answered that Proteolix (whom they acquired to access carfilzomib) had previously made a commitment to the EMEA to run the Phase III trial before ONXX owned the asset. ONXX has helped feed investor's expectations as they are expecting \$2.5 billion in peak sales from the franchise.

- Goal 2. Grow Nexavar sales in liver cancer, expect double digit growth in Asia. While we believe that growth in Asia is materializing, it is taking time to ramp up and we do not expect huge growth this year.
- Goal 3. Start Phase II trial for '0912, their oral proteome inhibitor. Clearly they need to start this trial if they are going to create \$2.5 billion in sales from this class of drug candidates.

In other news, ONXX and partner Bayer have begun enrolling patients in a Phase III trial evaluating Nexavar in combination with the oral chemotherapy capecitabine vs. capecitabine alone for the treatment of patients with advanced breast cancer. The RESILIENCE Trial (Phase III TRial Comparing CapecitabinE in Combination with SorafenIb or PLacebo for Treatment of Locally Advanced or Metastatic HER2-Negative Breast CancEr) is a randomized, double-blind, placebo-controlled study with expected enrollment of 519 patients in more than 20 countries including the United States, Brazil, Japan and Australia. The primary endpoint of the study is progression-free survival. Secondary endpoints include overall survival, time to progression, and safety.

Starting this Phase III study is a positive for ONXX. However, after mixed results of other Nexavar breast cancer trials, we do not have a lot of confidence in this trial being a difference maker for the company.

**NDA filing at risk:** We have been cautiously optimistic regarding ONXX' plan to file carfilzomib for accelerated approval ever since last year's manufacturing problems. Since then we have become concerned with the company's goal of filing the NDA by mid-year. First, while the rolling NDA can be advantageous, in this case it sounds like a way for the FDA to delay or prolong the process. Second, it was the manufacturing situation that caused the original delay last year, the company saying they are still in the scale-up stage makes us nervous that all the manufacturing issues have not yet been resolved with the FDA. Third, we find it highly unusual that the EMA, which is usually more lenient than the FDA, has already asked for a Phase III trial. It is important to remember that Roche/IMGN had this exact strategy back fire on them last year when the FDA refused their accelerated NDA for T-DM1 despite delivery of very promising Phase IIb data in metastatic breast cancer.

While carfilzomib may be an approvable drug in multiple myeloma (MM), the fact that there are three drugs already approved for MM means it may no longer be considered a large unmet medical need. Meanwhile, ONXX assures us that they can still file carfilzomib for accelerated approval by mid-year. We believe there are too many question marks for a smooth NDA filing, and a more cautious FDA will likely just wait for the Phase III results from ASPIRE that will be available in 2013. If carfilzomib gets delayed, ONXX stock will probably trade back down to the \$25 level as the company has created huge expectations for the drug candidate this year. We will not be unwilling to re-recommend the stock at such a point, as we still like carfilzomib's potential, and Nexavar's growth potential in the years to come. For now, however, it is time to take some healthy profits from this stock and wait to see what happens next. **ONXX is a now a sell.**

**Sangamo BioSciences** (SGMO) helped kick-off the 2011 Conference on Retroviruses and Opportunistic Infections (CROI) in Boston this week with an investigator presentation on the Phase I SB-728-902 trial of the company's treatment for HIV infection (SB-728). As you may recall, this therapy was designed on the idea that certain people are immune to HIV infection because their T-cells do not express the protein (CCR5) that the virus uses to identify and infect the cells. Clinicians remove a sample of the patient's blood, and certain white blood cells are separated and then treated with the zinc finger nuclease technology (ZFN). The ZFN actually modifies the genetic code of the cells (around 25% of them, anyway), turning off the gene that encodes for the protein CCR5. These cells are then re-injected into the patient. The idea is that the injected cells,

because they do not express CCR5, will not be susceptible to HIV infection. The cells are therefore available to carry out their important immunological functions, protecting the patients from infection. Investigators and SGMO hope that this therapy will eventually be considered a “functional cure” for HIV/AIDS.

Before getting into the data, the news released today is definitely exciting. However, we should all keep in mind that these data show that the therapy appears to be safe and offer proof of concept that the therapy may be effective in HIV patients. More trials will obviously be needed to show this is actually an effective therapy. With that in mind, though, we are very happy with this initial presentation. Most importantly but not surprisingly since this is an autologous procedure, the treatment appears to be safe and well tolerated. The injected cells were found to persist and even multiply in the patients' bodies. Five of the six patients in the two cohorts discussed today experienced a durable improvement in CD4+ T-cell count after 12 months. These patients also had sustained improvement in CD4:CD8 T-cell ratio, an indicator of immunological health. Finally, the modified T-cells persisted and multiplied, especially in the gut mucosa which is an important spot for the immune response and also a reservoir for the HIV virus. In the sixth patient, it is believed that the patient's immune system fought the virus used to deliver the ZFN therapy.

The data presented today was from the first six patients, and up to 13 will eventually be enrolled in the trial. The first two cohorts of three patients each are made up of patients who have been on continuous highly active antiretroviral therapy (HAART) and who have no detectable viral load. This group represents about 30% of all HIV/AIDS patients. The third cohort will enroll similar patients, but SGMO has expanded the trial so that the final 3-4 patients will consist of those who are on long term HAART but who still have active viral infections. A second Phase I trial is ongoing, and the important difference between the two trials is that in the second some of the patients will discontinue HAART treatment after the ZFN therapy. The gold standard will be if the therapy can actually lower viral levels in these patients. This will be a better test of the actual efficacy of the therapy, however preliminary results are not expected until later this year. We had hoped that another presentation later in the conference would shed more light on the efficacy question, however all of the data presented so far primarily addressed the safety and tolerability of the treatment.

All week, SGMO has been receiving the kind of news that biotech companies dream of, with multiple main-stream news outlets picking up the story that the company is developing what may be a “functional cure” for AIDS. Over the last six months, SGMO has had enough success to come on to the radar screens of major investors, and since the company has solid science to back up their clinical progress, the stock price has responded to the attention. The treatments that SGMO is developing are exciting, and we see this stock going much higher this year and in subsequent years based on clinical progress. At this time, we do not recommend chasing the stock. However, considering the excitement that this and SGMO's diabetic neuropathy therapy are generating, we do recommend adding to your position on dips under \$8, which continued throughout the week after the conference and may persist for the foreseeable future. **SGMO is a buy under \$8.**

## PORTFOLIO CHANGES

### Transactions to be completed on Monday, March 7th

Using the closing prices of **Monday, March 7**, we will sell all positions of **ONXX** in both portfolios. A 1% commission will be charged on each transaction.

**"THE BACK PAGE"**

Symbol	Company	PRICE				Target	# of shrs. (m)	Mkt. Value (\$ mil.)	Recommendation
		Orig. Rec.	Lo (52-Week)	Hi	Current				
ASTM *	Aastrom	1.43	1.32	4.45	2.17	7	38.6	83.8	BUY under \$3.50
ALKS *	Alkermes	10.13	9.81	16.10	12.56	25	95.0	1,193.2	BUY under \$13 *
ALTH	Allos	3.43	3.05	8.79	3.10	10	80.8	250.5	BUY under \$5
AMLN *	Amylin	7.88	9.51	24.21	11.20	30	137.3	1,537.8	BUY under \$11.50 *
ARQL	Arqule	7.99	3.25	7.49	6.24	12	43.9	273.9	BUY under \$6
BMRN	BioMarin	12.68	17.70	28.42	24.37	30	99.9	2,434.6	BUY under \$21
CELG	Celgene	49.93	48.02	65.79	54.04	75	468.9	25,339.4	BUY under \$60
ELN	Elan Corp.	20.05	4.25	8.24	6.48	25	474.6	3,075.4	BUY under \$10
IMGN	ImmunoGen	4.86	4.96	10.90	9.27	17	50.8	470.9	BUY under \$7
INCY	Incyte	5.88	8.50	17.48	13.94	24	92.4	1,288.1	BUY under \$15
ISIS	Isis	7.63	7.59	11.43	8.96	30	100.2	897.8	BUY under \$12
NEOP	Neoprobe Corp.	1.86	1.42	4.71	4.19	2.6	79.7	333.9	BUY under \$2
NVAX	Novavax	2.44	1.94	3.50	2.68	6	107.3	287.6	BUY under \$3
OGXI	OncoGenex	36.82	11.83	22.71	15.45	75	9.6	148.1	BUY under \$35
ONXX *	Onyx	5.97	19.54	37.85	35.90	N/A	57.2	2,053.5	SELL *
PVCT.OB	Provectus	1.38	0.78	1.76	0.92	5	70.2	64.6	BUY under \$1.50
SGMO	Sangamo	4.77	2.81	9.15	7.86	20	41.1	322.7	BUY under \$8

**THE MODEL PORTFOLIO**

Company	Shares Owned	Total Cost	Today's Value
<i>LONG positions</i>			
Aastrom	15,000	21,968	32,550
Alkermes	4,000	52,312	50,240
Allos	835	3,189	2,589
Amylin	510	1,595	5,712
ArQule	2,000	11,413	12,480
BioMarin	1,000	12,270	24,370
Celgene	1,000	58,227	54,040
ImmunoGen	2,000	9,938	18,540
Incyte	2,062	13,792	28,744
Isis	2,500	22,575	22,400
Novavax	25,000	61,610	67,000
OncoGenex	3,000	63,892	46,350
Onyx	750	21,500	26,925
Provectus	40,000	46,056	36,800
Sangamo	5,000	23,250	39,300

<b>3-Mar-11</b>	Equities	\$468,040
	Cash	-\$5,001
	<b>Portfolio Value</b>	<b>\$463,039</b>

**THE TRADER'S PORTFOLIO**

Company	Shares Owned	Total Cost	Today's Value
<i>LONG positions</i>			
Alkermes	2000	27189.2	25,120
Allos	758	4,859	2,348
Amylin	938	28,179	10,500
ArQule	1,563	10,247	9,753
Incyte	1,139	6,978	15,878
Novavax	10,000	24,644	26,800
OncoGenex	2,000	62,495	30,900
Onyx	375	9,870	13,463
Provectus	5,000	6,969	4,600
Sangamo	5,000	23,250	39,300
	Position total		\$178,662
	Margin		-\$38,753
	<b>Portfolio Value</b>		<b>\$139,909</b>

**BENCHMARKS**

	NASDAQ	S&P500	Model	Trader's
Last 2 weeks	-1.2%	-1.3%	-2.8%	-6.1%
2011 year to date	5.5%	5.2%	-3.6%	-0.9%
Calendar Year 2010	16.9%	12.8%	19.6%	4.3%
Calendar Year 2009	43.9%	23.5%	9.9%	-16.9%

**THE MEDICAL TECHNOLOGY STOCK LETTER**

John McCamant, Editor  
 Jim McCamant, Editor at Large  
 Jerry Isaacson, Ph.D., Research Analyst  
 Mahalet Solomon, Associate

\* Changed recommendation

**MODEL PORTFOLIO:** The Model Portfolio is designed to reflect specific recommendations. We began the Model Portfolio on 12/23/83 with \$100,000. On 4/13/84, we became fully invested. All profits are reinvested. Stocks recommended since then may be equally attractive, but may not be in the Model Portfolio. Transactions and positions are valued at closing prices. No dividends are created, and a 1% commission is charged. We don't use margin. Interest income is credited only on large cash balances.

**TRADER'S PORTFOLIO:** The Trader's Portfolio joined the Model Portfolio on 1/6/05 with \$500,000 and is designed to take advantage of short-term opportunities throughout the biotech sector. The Trader's Portfolio will hold both long and short positions in stocks, trade in options, and use margin. These strategies increase risk. Although there is no limit on the time any purchase can be held, the timeframe for most investments will be weeks to months.

**NEW MONEY BUYS (when under our buy limit)**

1st tier: ALKS, CELG, BMRN  
 2nd tier: ALTH, IMGN, INCY, ISIS  
 3rd tier: ARQL, ASTM, IMGN, NVAX, OGXI, PVCT.OB, SGMO