Four Biotech Names with Major Market Potential: Michael Higgins

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COMPANIES MENTIONED

- ADVENTRX Pharmaceuticals Inc.
- Akorn Inc.
- BioDelivery Sciences Inc.
- CytRX Corporation
- Endo Pharmaceuticals Inc.
- MannKind Corp.
- Nektar Therapeutics
- Pfizer Inc.
- Reckitt Benckiser Pharmaceuticals Inc.
- Titan Pharmaceuticals Inc.

A bit of luck and a lot of capital: Drug companies need both to navigate the seemingly perpetual path leading to the market debut of a new drug. Brinson Patrick Securities Managing Director Michael Higgins uses his experience as a drug marketer with big pharma to identify investment opportunities in companies with new drugs that address unmet needs. Higgins serves up his very best ideas to *The Life Sciences Report* and explains in detail why four growth stocks can rack up huge gains for investors gutsy enough to bet on smaller companies.

Source: George S. Mack of *The Life Sciences Report*

The Life Sciences Report: Michael, we live with a regulatory process in drug development that lasts for years. It seems to consume investors as we watch a molecule go through the pipeline. Do you think investors place too much emphasis on pivotal trial data, advisory committee votes and Prescription Drug User Fee Act (PDUFA) outcomes when, in some cases, a product's market potential might not even merit that amount of due diligence?

Michael Higgins: Yes. I think you're dead on. The clinical and regulatory boxes have to be checked, of course, but quite often investors haven't done the depth of the work required to figure out what a launch will look like, how long it will take for a drug to reach peak sales and what competitors' reactions may be once a drug is on the market. We often find ourselves looking at two different companies: a clinical phase company, which then becomes a marketing company. In the process you might see executives change, strategies change and personnel change, but most of that has little to do with where the stock is going to go. That is more frequently a matter of need in the market, and how a new drug may fill that need.

TLSR: We sometimes see stocks sell off after a drug is approved, or even after a very successful advisory committee meeting. I'm wondering if the realization of market opportunity really only sets in after a drug is approved or after we know it's likely to be approved. Can this kind of disappointment be anticipated or mitigated by the analyst or investor?

MH: Absolutely. It's a matter of timing. For example, investors may not like the consensus estimates or the potential valuation versus the drug's marketing outlook at the time of drug launch. That does not mean they shouldn't own the stock in the regulatory/development stage. Investors should look at what the next event is. That said, some companies will never have a burst during clinical development because the marketing outlook is weak. In other cases, the company may not have made its case effectively, and analysts with Buy ratings on the stock may not have been effective in stating the case either. Certainly, every positive regulatory decision is not followed by the stock selling off. It is on a case-by-case basis.

TLSR: And a lot of times when a product is marketed, we see pretty decent sales that don't seem to move the shares. What's happening here?

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MH: What's happening is, typically, a change of investor base. More clinical investors versus development investors are in the stock, and other things may have changed as well. Potential patent challenges may be lingering over a drug. In addition, a company may be a couple of quarters away from a report of actual sales, and during that time there is speculation and uncertainty. Having the next event or catalyst several quarters away has a tendency to push stock lower, which creates its own perception. It's a "prove-it" scenario and that is a tough situation, especially if there are competitors in the space. The company, and even covering analysts, may not talk about it, but the buy-siders know full well that there may be another story lingering on the side. Many things can keep shares depressed until there is an actual revenue trajectory projection.

"When I'm picking up a company, I go to the end of every road I possibly can before I feel like I've checked all the boxes imaginable."

TLSR: Michael, you've got companies in your coverage that range from a penny-stock $25 million ($25M) valuation to $1.25 billion ($1.25B). The issues with marketability of shares on the low end of this range are obvious and well known. Although the risk is typically very high on the low end, sophisticated institutional investors cannot buy these shares by virtue of their size. Who, then, are the ideal or right investors for that penny-stock category?

MH: This is a tough business and it behooves investors to stay one step ahead. One way to do that is to understand what's happening in the micro-cap space, whether an investor owns micro caps or not. The way I look at it, if you're investing in $500M market cap companies and higher, you need to follow what's happening in the micro-cap space because those companies are in categories and in a regulatory environment that impacts larger companies as well. Also, analysts covering the small companies give investors greater detail and insights into those categories. An analyst covering $25–30M market cap names is required to follow what's going on in the weeds, whereas these details may be less relevant to $3–5B market cap companies with a dozen products in the pipeline.

TLSR: I have noticed more in-depth sellside research going on in micro-cap companies. It's really interesting to see an analyst do a 75-page report on a tiny valuation company, which is what I have seen in your coverage. What does this mean for this micro-cap biotech sector?

MH: I can't speak for others. I know that when I'm picking up a company, I go to the end of every road I possibly can before I feel like I've checked all the boxes imaginable. For instance, I had previously covered ADVENTRX Pharmaceuticals Inc. (ANX:AMEX)—you just referred to that 75-page report. I have picked it up again. I have taken a deeper look at it, and I believe ANX-188 (purified poloxamer 188) is going to succeed in sickle cell disease.

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The pathways that affect sickle cell patients are complex, and there are so many products available that an investor won't find many "me-too" products. The subject really does require a 75-pager, written as tightly as possible with a lot of footnotes, to accurately cover what's going on in and around the company. But for other companies, it's a one-stop story and it's pretty quick research. It really varies.

TLSR: Go ahead and continue with ADVENTRX, since you've mentioned it and you obviously like it.

MH: ADVENTRX has an improved, purified poloxamer, which acts as a surfactant to reduce the adhesion of the sickled cells and increases blood flow. A decade ago CytRX Corporation (CYTR:NASDAQ) did a phase 3 study with the compound that just barely missed a primary endpoint. The study was in patients of all ages, but the therapy worked very well in the pediatric group. ADVENTRX is about to initiate a phase 3 trial in that pediatric group. We expect some very positive results roughly two years out, but I am doing the analysis work up front, rather than grabbing for it later. I plan to continue to follow ADVENTRX and the entire space.

TLSR: What is your investment thesis surrounding ANX-188?

MH: There are roughly 100,000 (100K) sickle cell patients in the U.S. and an equal number in Europe, with about 13M worldwide. About two times each year these patients experience excruciating pain crises, for which they are hospitalized and must take very high doses of opioids. Their pain thresholds and respiratory conditions must be monitored closely because narcotics depress respiration. There are not a lot of options for these patients. One drug, hydroxyurea (brands Droxia, Hydrea) has been approved and helps reduce the number of pain events per year. It requires monthly monitoring, which makes it very expensive for the patient and provider, and it isn't used much at all. ANX-188 can reduce the severity and duration of the very painful vaso-occlusive crises that occur in sickle cell disease.

TLSR: Just to be clear, ANX-188 is intended as therapy for an acute vaso-occlusive episode, right? It is not intended as a chronic therapy, is it?

MH: No, it is not a chronic therapy. ANX-188 would be infused in the hospital over a 48-hour period to patients admitted with excruciating painful vaso-occlusive crises. The average duration of hospitalization is five to six days, and the drug is intended to reduce the amount of opioids used during that time.

TLSR: Sickle cell disease is a small market. My understanding is that in the U.S., 69K patients per year present to the emergency department. I got this number from the ADVENTRX website. Your investment theory really has to hinge on the fact that the company has such a small market cap that any revenues will move the shares pretty well. Is that it?

MH: Yes. For now, I am rather conservative on the revenues of the drug per course of treatment, but it is more than twice the size of cystic fibrosis. While this is not a curative regimen, it is for a very symptomatic condition and one in which the marketed option is not in question.

TLSR: ANX-188 improves blood cell movement through small vasculature, where the sickle- or crescent-shaped cells might otherwise adhere and cause an occlusion. Are there other potential indications that you can see this product being developed for?

MH: There could be applications completely outside of sickle cell. It looks like the company will be outlining those additional indications in the near term. Acute coronary syndrome (ACS) will likely be one of those. We will wait to see what unfolds.

TLSR: The company said that it intended to begin its phase 3 trial before the end of this year. We're nearly there. Do you think it's going to hurt shares if ADVENTRX doesn't meet that goal?

MH: Any time you miss a time point can hurt shares. I would expect some detrimental impact, but at this point, we're expecting a start by year-end. I haven't heard anything different.

TLSR: Would you mention another company?

MH: BioDelivery Sciences Inc. (BDSI:NASDAQ) is a small company with two phase 3 trials in progress, one of which is partnered with Endo Pharmaceuticals (ENDP:NASDAQ). Both products are sublingual formulations that include buprenorphine. The difference between the two is that one is buprenorphine by itself, intended for low back pain, and is partnered with Endo. The other includes naloxone; it is very similar to Reckitt Benckiser Pharmaceuticals Inc.'s (RBGPY:OTCPK) Suboxone (buprenorphine + naloxone), which is a treatment for patients struggling with opioid addiction and is on track to record $2B in U.S. sales next year. Its patent has expired, and there are no generics.

TLSR: The first thing you notice when you look at this company is that the share price has quadrupled over the past 12 months. It makes me wonder if it could be perfectly priced now. Is there upside left?

MH: Given its $135M market cap, I don't think investors have clued into the opioid-addiction product's upside, or to the upside for the Endo-partnered drug for low back pain. BDSI could see revenues much higher than its current market cap. With the financing from Endo behind it, this is an excellent time for investors to take a look and understand the marketability of its two phase 3 assets. The next events are relatively low risk clinically. We could see a partnership for the Suboxone-similar product within the next six to nine months. That would be a huge catalyst.

That said, I really think it is in the company's best long-term interest to keep the Suboxone-similar product and market it to the 5K-doctor market by itself—to be selfish with the revenues. Now is an excellent time for investors to take a look. The company is very well capitalized.

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TLSR: Titan Pharmaceuticals Inc. (TTNP:OTC) is developing a six-month duration subdermal implant containing buprenorphine by itself. But, as another sublingually administered product like original Suboxone, do you think BDSI's product is differentiated enough to take market share?

MH: Taste and speed of dissolution are big deals with this patient group because patients are quite often just starting to reduce their opioid addiction. The caregiver currently is required to watch the patient for 15–30 minutes, until the film product has dissolved completely under the tongue. That is something both patients and doctors don't appreciate. If a company can avoid or reduce that dissolution time, it may have a better product. If a new product has improved compliance features over Suboxone, which is currently on the market, it could be a whole new ballgame. That's what BDSI has.

TLSR: Another name?

MH: Another one I'd point to is a much more controversial call, and that's MannKind Corp. (MNKD:NASDAQ). It has had two complete response letters from the U.S. Food and Drug Administration (FDA) on its inhalable insulin product, Afrezza (human insulin of recombinant DNA origin), but that was for an older device that the company thought was not approvable due to requirements placed on it by the FDA. The new Dreamboat device is smaller, more convenient and requires less insulin to be inhaled to produce the same bioequivalent blood levels as the previous device. It is a product that can meet the FDA's requirements. The next event will be phase 3

results, due in mid- to late 2013, the most notable being in type 2 diabetics. This trial basically requires proof that inhalation of the product will reduce hemoglobin A1c (HbA1c or A1c) levels by 0.5% or more. [Note: A1c testing is a standard assay to determine if diabetes is being managed properly; the higher the A1c level, the poorer the blood sugar control.] This should be a relatively low-risk trial for the company.

I've followed every comment the company has made in the last several years and every filing that it has produced, and I do not see any reason why the FDA won't approve Afrezza with the new Dreamboat inhaler in early 2014. From there, it's an inhalable insulin competing with subcutaneous injectable insulins. So far, the data we have seen with Afrezza show no change in weight or weight loss versus the rapid-acting analogs that are injected. The biggest benefit will be the ability to pull a whistle-sized device from a pocket and take a brief inhalation versus taking out a pen and sticking yourself three times a day.

TLSR: Nektar Therapeutics (NKTR:NASDAQ) had an inhalable insulin product approved called Exubera (human insulin of recombinant DNA origin) that was marketed for a short period. Its partner was Pfizer Inc. (PFE:NYSE), which returned the product and all rights back to Nektar after marketing the product for less than a year. Could you tell me how Afrezza will be a better product and why it will be more marketable if it is approved?

MH: Lung function tests are very different between the two products, not just in the amount of insulin inhaled but also in the overall metabolic effects that both devices produce. Also, the two drug delivery devices are very different if you look at them. The Exubera device was a tall tube.

TLSR: It looked like a bong.

MH: Yes, you could say that it looked like a big bong that Pfizer was asking the patient to pull out at a restaurant or at home on a daily basis and get comfortable with. Afrezza, with the Dreamboat device, will fit in the palm of your hand. It would look like you're covering your mouth while coughing, when in fact you are inhaling insulin. Nobody in the room will even know that you just took a dose of insulin. It is a dramatically different product, not just by its optics but also in terms of how it affects the body metabolically.

TLSR: Another company?

MH: Akorn Inc. (AKRX:NASDAQ) is a great example of why investors who follow $500M market cap companies and bigger should be looking downstream. Akorn's market cap is roughly $1.3B today, gaining more than $1B in market value over the last three years. Its market cap was under $200M three years ago. The company simply executed on its niche generic plan, by which it produces injectable products for hospitals that are relatively difficult to reverse engineer and get approval on. The company has also benefitted from the drug shortage phenomenon that cropped up in the last two years. Akorn has a growing pipeline, and many of its products have been at the FDA for longer than 30 months. In 2013, we should see a handful of meaningful products get approved and launched. At that point, we may be back in the situation we were two or three years ago, when the revenues started to escalate significantly.

TLSR: This company has so many different product lines and individual products. What would be the drivers?

MH: When I initiated coverage in March, I outlined a dozen or so products that the

company could potentially be working on. Akorn doesn't specify which product it is waiting for and when it may get approved. It is up to the analyst to turn over the rocks and find what may be in the pipeline. At this point, what I like about the company is that it doesn't have one big bolus product that we're all waiting for, a product that the stock heads higher on and then sells off on later. We are looking for continued execution to move shares higher.

TLSR: This is, of course, an operating company, not a holding company, right?

MH: Right.

TLSR: Thank you very much, Michael. We have spoken about several companies not covered previously here at *The Life Sciences Report.*

MH: Thank you. I appreciate it.

Michael Higgins is a life sciences analyst at Brinson Patrick Securities Corp. He provides significant experience working with and covering life sciences companies. Prior to joining Brinson Patrick, Higgins was a managing director and senior specialty pharmaceuticals analyst at Rodman & Renshaw LLC. Prior to joining Rodman & Renshaw, Higgins gained 10 years of drug marketing experience with Procter & Gamble Pharmaceuticals, followed by nine years as a research analyst. He has worked as an analyst with Dafna Capital Management LLC, Wedbush Securities and an independent research firm he founded, 4sight Research Partners LLP. Higgins has earned a four-star rating from StarMine for stock recommendation performance. He is most recognized for his coverage of "drug launch" companies, as well as drug delivery technologies and patents. He received a bachelor's degree in finance from the University of Wisconsin and his master's degree in business administration from Marquette University.

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