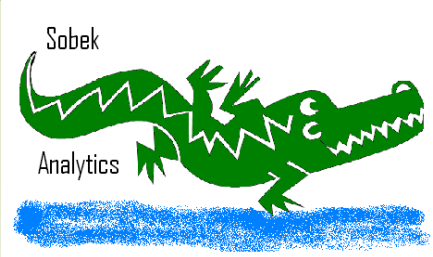

Anacor Pharmaceuticals (ANAC): A Boronic Investment?

Anacor Pharmaceuticals

Anacor Pharmaceuticals (ANAC) is a small cap, biotech company that develops drugs from its proprietary boron platform. The company believes that Boron based drugs have two advantages. First, boron based molecules have unique geometries. Second, boron's reactivity allows these compounds to either interact with targets in a new way or interact with novel targets. The company has four main therapeutic areas. First, its lead program, and wholly owned, is a topical anti-fungal which is current involved in two phase III studies for the treatment of onychomycosis. Second, the company has a couple of compounds that are anti-inflammatory topical treatments, where the lead compound (again wholly owned) is in phase II testing for psoriasis dermatitis. Third, the company has a partnership with GSK to develop novel antibiotics. GSK recently exercised an option to obtain an exclusive license for a treatment of gram-negative bacteria. Finally, Anacor has a number of partnerships (mainly with international organizations) to develop novel treatments for neglected diseases.

AN2690: A Treatment for Onychomycosis

This research note focuses on Anacor's lead program for onychomycosis. I plan on having additional research notes that look at the other therapeutic programs plus the company's boron platform and business development plans.

Contents

What is Onychomycosis?

Onychomycosis is generally a fungal infection of the skin, hair, or nails caused by dermatophytes. Anacor focuses on nail infections, where the fungi attack the nail plate, nail bed and, sometimes, the skin surrounding the nail plate. Onychomycosis most visible effect is that it causes the nails to discolor, become brittle, deform, split, and become separated from the nail bed. Often the nails become so think that trimming becomes difficult and the infection can also lead to pain while wearing shoes.

Current, onychomycosis can be treated in three separate ways. First, Lamisil can be taken as an oral therapy. Second, there are topical treatments such as Penlac Nail Lacquer (ciclopirox). Finally, there is debridement, i.e. the removal of the infected nail.

In general, then, AN2690 appears to have the safety profile of Penlac, a novel anti-fungal activity, and the ability to penetrate the nail and get the drug to the site of the infection.

The Problems Associated with Current Treatments

There are a number of problems associated with current treatments. In general, individuals are faced with choosing between ineffective treatments or an effective treatment with possible severe side effects. The most effective treatment is the oral Lamisil, which has a cure rate of about 38%. The problem is that oral Lamisil can lead to rare but severe kidney toxicity. So the question is whether you want to risk kidney toxicity for a 38% cure rate. That being said, the current market for this treatment is about $1.2 billion.

In contrast both the topical treatments and debridement have no adverse event risks but the cure rates are quite low (5.5% to 8.5% for ciclopirox and virtually 0% for debridement). Despite the ineffectiveness, ciclopirox generally has 350,000 prescriptions a year and there are about 10 million debridements. Clearly there is room in the market for an effective topical treatment with a good cure rate. Source: Company March 2011 Presentation Slide 10

AN2690: A Topical Treatment for Onychomycosis

AN2690 is a topical treatment for onychomycosis developed from Anacor's boron platform. This product differentiates itself in three main ways from current treatments. First, and perhaps most importantly, it has increased nail penetration meaning that more of the drug is actually getting to the fungus. In an in vitro human nail penetration model study, ANZ2690 penetrates the nail 250X more than Penlac (ciclopirox). Over the 15 day study, the mg/sample for Penlac was 0.0088 as compared to 2.24 for AN2690. Given that AN2690 and Penlac have similar anti-fungal efficacy, this increased nail penetration should lead to an increased efficacy.

The second benefit of AN2690 is the novel anti-fungal mechanism of action. In particular, AN2690 inhibits a vital fungal enzyme, leucyl transfer RNA synthetase (LeuRS), which is required for protein synthesis. By inhibiting protein synthesis of the fungus it leads to the termination of cell growth and ultimately cell death. Going after LeuRS, however, required boron within the compound, so this is a target uniquely suited to Anacor's drug discovery platform. For more details on this target, see the following article from the *Journal of Labeled Compounds and Radiopharmaceuticals.*

The third benefit seen with AN2690 is the lack of any systemic side effects. While both Penlac and debridement have benign safety profiles, they are also less effective. Oral Lamisil is effective but runs the risk of rare liver toxicities. Studies have found that topical AN2690 has a safety profile similar to Penlac. In particular, topical treatment with AN2690 lead to little or no levels of the drug in the blood or urine. More importantly, none of the clinical trials had a single case of systemic side effects.

In general, then, AN2690 appears to have the safety profile of Penlac, a novel anti-fungal activity, and the ability to penetrate the nail and get the drug to the site of the infection. So the question, then, is how effective is the treatment?

The Effectiveness of AN2690

Phase II testing of AN2690 has shown the compound to both have the benign safety profile of Penlac but with at least twice the cure rate. The most recent phase IIb study examined the efficacy on AN2690 at 6 months with three doses (2.5%, 5%, and 7.5%). In the study, the vehicle had a response rate of 14%, whereas the response rate for AN2690 ranged from 26% to 32% (statistically significant improvement with a p-value < 0.03). Even at the lowest rate of response it is roughly 3X the cure rate for Penlac. While the oral Lamisil treatment still provides the best chance at a cure, it must be remembered that it also has the least benign safety profile.

Currently, Anacor has an SPA with the FDA and is conducting two parallel phase III studies. These are multi-centered studies that will each enroll 600 patients and be randomized 2:1 into treatment or vehicle. They patients will receive once per day treatment for 48 weeks at the 5% solution (or the vehicle) and the primary data analysis is at 52 weeks, where a cure is defined as a completely clear nail, negative fungal culture and negative fungal KOH. The targeted efficacy is to be at least twice as effective of Penlac (which taking the higher cure rate would be 17%) but approaching that of oral Lamisil (38%). Enrollment of these trials is expected to be completed in the second half of 2011 with data at the second half of 2012.

A Note on AN2690

Currently AN2690 is an un-partnered asset. It was originally partnered to the Schering Corporation, which was bought by Merck. In February 2010, Merck decided to return the rights to Anacor. It seems like this was a decision based on a rationalization of the partnerships of the new Merck and not based on any problems with efficacy. Here is the press release.

Upcoming Milestones for AN2690

There are a number of upcoming milestones for AN2690 over the next 24 months. The two phase III trials were started in the second half of 2010, which should lead to full enrollment in the second half of 2011. This ultimately then will produce final data in the second half of 2012.

The trials take long to collect data because one of the primary endpoints is a completely clear nail, so you have to wait for the nail to grow back. The other primary endpoints are a negative fungal culture and negative fungal KOH. All of which are taken at week 52. The phase III trials have received an FDA SPA on all of the primary endpoints.

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A Little on the Market Opportunity

Obviously the best analogy for market opportunity for AN2690 would be Penlac. Before it went generic in it had US sales of $125 million, which if one accounts for inflation might reasonably be closer to $175 million today. What is interesting, and likely a future research note, is the odds that an AN2690 with a 25% cure rate would be able to steal some market share from Lamisil and debridement. Each 10% share of the oral Lamisil market would add $120 million to the market. Plus, there are likely individuals who would prefer an effective topical treatment to debridement. This would make a reasonable estimate for US sales of at least $300 million if not closer to $500 million. On top of that there is the worldwide market. So it is not impossible for AN2690 to reach peak worldwide sales of $1 billion but a more conservative estimate would have $300 million US and $300 million ex-US for about $600 million worldwide. Of course, this would need to be confirmed by a more detailed analysis.

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 am long shares of ANAC.