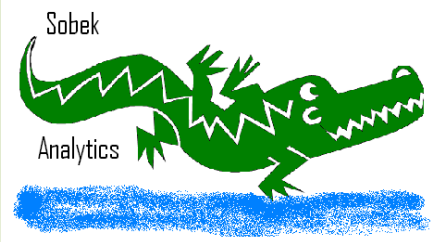

Anacor Pharmaceuticals (ANAC): A Topical Investment

Anacor Pharmaceuticals: Part II

Anacor Pharmaceuticals (ANAC) is a small cap, biotech company that develops drugs from its proprietary boron platform. The previous note on Anacor concentrated on it topical treatment for Onychomycosis. As part of the ongoing series, this note examines AN2728, the company's lead topical compound for psoriasis. In general, AN2728 is a topical boron based product that inhibits PDE4 and reduces the production of TNF-α, IL-12, and IL-23. It is being developed to treat mild to moderate patients, which is 80% of the psoriasis market. Of the 4 million prescriptions written for mild- to moderate psoriasis each year about 87% are for topical treatments. Anacor is attempting to frame AN2728 as an effective and safer topical treatment than is currently available thereby hoping to capture a significant portion of the $2.8 billion psoriasis market. Assuming that AN2728 makes it to market with such a profile, it could be quite lucrative especially since Anacor retains worldwide rights for the compound. Even if the company only keeps the United States rights, it still could be a profitable opportunity.

AN2728: The Road Ahead

There should be a steady flow of information on AN2728 over the next couple of years. Below is a list of these clinical milestones:

1H2011: Start Phase IIb trial- Completed
2H2011: Final Phase IIb data
2H2011: Start Phase III trial
1H2012: Complete enrollment in Phase III trial
2H2011: Phase III data

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What is Psoriasis?

Psoriasis is a chronic autoimmune disease that affects over 100 million people worldwide and 7.5 million in the United States alone. The key to the disease is that the immune system sends out faulty signals that speed to the production of skin cells. Psoriasis often presents itself as scaly red and white patches on the skin, although some people can have psoriasis with limited to no dermatological symptoms. While it is a chronic disease, it does cycle through periods of increased and decreased activity.

While the causes of psoriasis are still under investigation, a couple of points can be made about its epidemiology. First, immune cells move into the epidermis and secret chemical signals that lead to inflammation (tumor necrosis factor-α, interleukin-1β, and interleukin-6) and other that cause keratinocytes to proliferate (interleukin-22). Second, like many inflammatory diseases, PDE (and its associated family) are validated targets for treatment. It is the PDE that AN2728 targets and thereby reduces tumor necrosis factor-α.

At week 12, the 2% BID treatment showed a 54% improvement rate as compared to 19% for the vehicle. In addition, this improvement was measured with an approvable endpoint (proportion of plaques achieving clear or almost clear with ≥ 2-Grade improvement from baseline).

The Problems Associated with Current Psoriasis Treatments

While the targeting of PDE is a common approach for the treatment of psoriasis, the problem is the associated side effects, such as emesis. In addition, PDE inhibitors can lead to vomiting, nausea, arteritis and immunosuppression. These effects are exacerbated with systemic deliveries of the PDE inhibitor and leads to problems in the brain, gastrointestinal tract, arteries or whole body. One solution to these systemic effects is the use of a topical treatment.

The current topical treatments are not without problems. For instance, long-term use of topical corticosteroids can cause the skin to thin. Vitamin D derivatives can irritate the skin and retinoids can both irritate and lead to birth defects.

Overall, then, even the topical options, which are less effective but perhaps safer than the systemic drugs, have serious side effects that limit their usage.

AN2728: A Topical Treatment for Psoriasis

AN2728 has shown to be an effective and safe treatment for mild to moderate psoriasis through a series of phase II trials. Most recently, in a phase II dose ranging study, AN2728 achieved its primary endpoint of a statistically significant improvement in overall target plaque severity than vehicle-treated plaques at day 42. While these results were achieved with the 2% BID treatment regime, it seems like all doses except the lowest (0.05% QD) had similar levels of efficacy. The results were also significant over the longer-term. At week 12, the 2% BID treatment showed a 54% improvement rate as compared to 19% for the vehicle. In addition, this improvement was measured with an approvable endpoint (proportion of plaques achieving clear or almost clear with ≥ 2-Grade improvement from baseline).

While the statistically significant improvements are nice, what is more important is how these responses measure up to the competition. Using the same endpoint as above (proportion of plaques achieving clear or almost clear with ≥ 2-Grade improvement from baseline) Taclonex (Betamethasone Dipropionate plus Calciprotriene) only achieved a 48% success rate in its phase III trial. Vectical, in its phase III trial, was even worse with a 22% success rate. These comparison are shown in the company presentation on slide 22. It is important to note as well that the results from Taclonex were with 4 weeks of treatment, Vectical with 8 weeks, and AN2728 with 12 weeks. While this might not seem like a fair comparison, it is important to note that these lengths are the complete treatment time. For instance, Taclonex cannot be used for more than 4 weeks based on its side effects. This is a critical point because even if AN2728 needs to be dosed for 12 weeks, it can be done because of its relatively benign safety profile. In this way, these comparisons are fair as they represent a full treatment regime for each compound.

In terms of development, the phase IIb trial should readout later this year and the company expects to meet with the FDA to develop the final protocol for the phase II trials. These should start in the second half of 2011. Given the length of the trials, this implies data from the phase III trial would be available in the second half of 2012. So while it is not clear the precise timing and design of the trials, it is clear that the company (assuming that the data in the phase IIb trial is consistent with previous results) is on course to have critical data on this program in the second half of next year. What is less clear is if the company will run two phase III trials at the same time or if the FDA would even require two phase III trials. These questions, however, should be answered by the end of 2011 and we should have a better sense of how and when this compound will make it to market.

A Second Indication: Atopic dermatitis

Aside from psoriasis, Anacor is looking at AN2728 for the treatment of atopic dermatitis, which is a chronic rash characterized by itchiness and inflammation. This is large market with about 70 million people in the major world markets and one that mainly afflicts children. As with the treatment for psoriasis, the currently available treatments have a number of side effects that limit their use. This is especially the case given that atopic dermatitis usually occurs in children, where issues of safety become especially important.

Currently, Anacor plans to initiate a phase II trial in atopic dermatitis in the first half of 2011 with results by the end of the year. If the trials are successful, then a phase IIb trial would start soon thereafter with data by the end of 2012. The trial is unique in that Anacor is looking at both AN2728 and AN2898. The company is not sure which compound would be most effective, so the phase II trial will have 3-arms (AN2728, AN2898, and vehicle). At the end of the trial, the company will then decide which compound to use in the next clinical trial.

Atopic dermatitis in some ways is a bonus indication for AN2728 (or AN2898). There is pre-clinical evidence that indicates that these compounds can safely address atopic dermatitis but proof of concept in a human trial is lacking. As such, this trial will act as a no/no go point for further development in this indication. Given the size of the potential market, it makes sense to expend some resources to determine the effectiveness of these compounds in the treatment of atopic dermatitis.

Recent Data

There was a poster recently presented at the 2011 Society for Investigative Dermatology (SID) Annual Meeting entitled "Safety and efficacy of AN2728 ointment in a phase 2b dose-ranging bilateral study of mild-to-moderate plaque psoriasis." In general, the poster confirms that AN2728 is both and effective and safe treatment for psoriasis. It is useful to quote the safety portion of the poster:

"No serious adverse events were reported. Overall, 51 patients (35.4%) experienced at least one AE during the study. The majority (86%) of AEs were considered unrelated or unlikely to be treatment related and most (82%) were mild in severity. None of the treatment-related events was severe."

"Table 1. Most Common AEs by Frequency

Preferred Term	n (%)
Pruritus	10 (6.9%)
Influenza	7 (4.9%)
Dermatitis contact	5 (3.5%)
Pharyngitis	5 (3.5%)"

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