

Corcept Therapeutics

On Thursday, April 19, 2007, we visited the headquarters of Corcept Therapeutics (CORT) in Menlo Park, California. We met with CEO Joseph Belanoff and new CFO Andrew Galligan. Andrew isn't really a new CFO for Corcept. He was its CFO in its earlier days until he was replaced by Fred Kurland in February 2004. Andrew left for a small private biotech company and ended his stint when that entity was sold to Bayer. In the meantime, ex-CFO Fred Kurland has left to become the CFO at another company. Given Fred's resume, we fully expect his new company to be another biotech in the local area.

In writing this update, we filled in the blanks from the interview. Please don't get the wrong impression - we felt that the executive team was open and candid with us. Everything slid into place, between the interview and our own research.

First and Foremost, What Happened with the Recent Trials?

We have more information and if you want to see our conclusions, skip to the final four paragraphs in this section. In the meantime, let us refresh your memory: the table below is copied from a recent alert to center the discussion. We rang the bell and said that these results were psychotic – that something stank with the administration of the research.

1) **Experienced Centers vs. Newbie Centers (USA Trial)** – There was a statistically significant interaction between treatment sites vs. efficacy. As you might recall, Corcept added trial sites to speed enrollment. Most of the centers were “experienced” having participated in prior Phase II studies. For these experienced centers, there was a statistically significant superiority for Corlux. At the sites that were added later, Corlux patients performed worse than placebo. The placebo remissions rates were *incredibly* high.

2) **Insufficient Blood Levels of Corlux (USA Trial)** – Corlux levels in the plasma were related to symptom improvement. These blood levels were measured on the 7th day of treatment. We think that the adsorption problem is confounded by the inclusion of inappropriate patients (e.g. former Corlux treatment failures).

Nevertheless, even with patients among the “late adds”, there was a rough dose response relationship, if enough Corlux was swimming in the blood stream. At levels greater than 1800 nanograms / ml, patients demonstrated statistically significant effects for Corlux.

There is a binding protein that locks onto Corlux and maintains it for the right length of time so that it has a therapeutic effect. Unfortunately, there is variability between patients and also within the same individual. Hence in the next trial, Corcept will use a higher dose to ensure a high enough blood level.

CORLUX Phase III Trials		
Corcept 07 Study USA Trial	Corcept 06 Study Dose Ranging Trial	Corcept 09 Study European Trial
Target enrollment of 280 pts from about 20 USA sites & 5 European sites. Pts in the treatment arm receive 600 mg of CORLUX daily for 7 days. Neither antidepressants nor antipsychotics are allowed during the 7-day treatment period. Each pt will receive an antidepressant after Day 7.	Target of 443 patients from about 45 sites in the USA and Europe. Pts assigned to one of 4 different arms (placebo; 300 mg; 600 mg; 1,200 mg) for 7 days of treatment. Pts will receive antidepressants (many standard antidepressants are allowed). The FDA mandated the collection of info related to dosage level.	European enrollment of 247 pts. Pts in the treatment arm receive 600 mg of CORLUX daily for 7 days. Neither antidepressants nor antipsychotics are allowed during the 7-day treatment period. Each pt will receive an antidepressant after Day 7.
Primary Endpoint		
% of pts that achieve $\geq 50\%$ improvement in psychotic symptoms ¹ at both Day 7 (treatment) and Day 56 (sustained relief).	% of pts that achieve $\geq 50\%$ improvement in psychotic symptoms ¹ at both Day 7 (treatment) and Day 56 (sustained relief)	% of pts that achieve $\geq 50\%$ improvement in psychotic symptoms ¹ at both Day 7 (treatment) and Day 28 (sustained relief).
Top-line Results		
At day 7, 30.5% of the Corlux patients achieved the primary endpoint criteria while 28.6% of the patients receiving placebo were responders. At day 56, the Corlux and the placebo patients were both experiencing remission rates of approximately 80%.	Failed to achieve primary endpoint. Placebo group had response rates of 34% (Day 7) and about 70% (Day 56). Significant correlation of blood level to response rate. Adequate response rates are achieved with meeting predetermined blood level.	The placebo and treatment groups had an “abnormally high” response rate of about 95% at Day 56.

Our preceding commentary doesn't answer the big issue: from where did these high remission rates hail? These placebo and treatment remission rates are absolutely psychotic, especially in the European trial. We think we have the answer, it's entitled: "how to create the highest placebo rates ever".

The contract research organization is being paid good money for recruiting patients. Corcept wanted to accelerate enrollment and so the company decided to add treatment centers in Central Europe during the last months of the trial. This brings needed cash and prestige to centers in places like Romania. These centers are unused to the rigor of experimental studies. The staff therefore told the patients something like this: *"You are being given a special privilege. You will be given an expensive, state of the art treatment from the United States. It is the best medication available and it is very expensive and extremely effective. You are being given a special honor."*

We did some sniffing around and we're absolutely convinced that is what happened. Knowing this, we told the management that they deserve a special scientific award for discovering the extent to which a placebo effect could be exerted on a self-report of psychotic symptoms.

Here's the rub: if you subtract all patients from the "late add" centers, then the primary endpoints are achieved. If you aggregate the patients across all three Phase III trials from the "normal centers", then the p-value goes out to 5 zeros!

For this reason, however, CEO Joe Belanoff and President Robert Roe have "re-upped" their commitment to the company. They feel that the therapeutic signal is strong, although occluded by the disaster in Europe.

The Clinical Development Plan

The company is still slicing and dicing the data. After it's finished, the company will submit it to the FDA and hopes to have a meeting about eight weeks after this milestone. At this point, then company will know how to proceed forward. Will it require one trial? Two trials? At this point, nothing has been finalized. The management would like to start a pivotal trial by the end this year, so that clinical results can be reported in 2009.

In the meantime, the management feels it's premature to make a decision about developing for an orphan indication. If you look at CEO Belanoff, it's clear that he wants to move as soon as practical into another pivotal trial program.

In the next couple months, we expect top-line results regarding the use of Corlux to prevent Zyprexa related weight-gain. This is a potential mini-blockbuster that hasn't been factored into the stock price. Eli Lilly – the maker of Zyprexa - paid for this "proof of concept" trial but doesn't hold any right of first refusal.

Eli Lilly lost a huge class action lawsuit for this side effect, which is present in a number of antipsychotics. Lastly, the big Pharmas may be able to extend patent life by creating a combination tablet.

If the weight-gain prevention results are good, then clinical development won't focus on Corlux, but on the selective GR-II blockers. These blockers are basically Corlux minus its pregnancy terminating effects (Cortex is also known as RU-486). The development of the selective blockers into the clinic is a special milestone: it should act as a signal to Wall Street and the Big pharmas to watch CORT. For now, we've talked about companies like CORT as a special longshot. The stock price is so low, that the risk reward is still good. It requires *pocket change*.

Financings for 2007

The company recently raised \$9M in a follow-on involving its current institutional investors. This is only enough money to continue current operations for the current year.

We estimate that it costs Corcept about \$30,000 to pay for the treatment associated with each inpatient. We hence estimate that CORT will need to raise about \$35M to \$40M to complete clinical development of Corlux to treat psychotic depression.

We don't expect the company to complete a financing before the arrival of the weight-gain prevention results. There will be a significant upside to good results and a smaller downside for poor results. The company will also be in a position to negotiate a partnership. We don't expect it to involve a ton of upfront cash, but in this case, every few million dollars help.

We wouldn't be surprised if the company initiates two financings in 2007: after the Zyprexa weight-gain prevention results; and with the launch of the pivotal trial(s) for Corlux. We hope that the company will arrange a financing that involve the same quality of investors as in the recent financings.

Milestones

	Apr 2007
Discussion with the FDA	Q3 2007
Corlux Phase III Psychotic Depression – Launch Pivotal Trial(s)	Q4 2007
Corlux Phase I/IIa Weight Gain / Zyprexa Top-line Results	June 2007

Investment Case

Along with ViRexx (REX), we've characterized Corcept as a company to invest only your loose change. This is company that is developing neurological drugs. This is almost always a risky proposition.

If Corcept management reports that Corlux indeed prevents Zyprexa related weight gain, then this changes Corcept's complexion. If the stock doesn't move on these results, then this would present a favorable entry point.

Warm Regards,

The BSR Research Team

(Note: One or more Biotech Stock Research LLC staff members held a position in CORT at the time this was written. For more information, please visit the Disclosure section of our web site.)