

# Good Data from CROI

## First Look is a Good Look

Sangamo provided the first look at its CROI data this morning with its press release ([Sangamo BioSciences Announces Presentation of Positive Clinical Data From Novel ZFN Therapeutic Approach for the Treatment of HIV/AIDs at Conference for Retroviral and Opportunistic Infections](#)). There is a lot of information in the release, so let us go through the main points.

First, and for a phase I most importantly, the treatment appears safe. In fact, the safety profile seems about as clean as one could expect. While most everyone expected a safe treatment, it is nice to get confirmation. One of the short theses going into this was that the modified T-cells would be treated as an outsider and would generate a rejection response. This did not happen and is both important and undermines one of the short arguments.

Second, the modified T-cells trafficked normally and were observed in the gut mucosa. The gut mucosa generally has a reservoir of the virus and seeing the modified T-cells there is evidence that the modified T-cells are able to resist the virus. So not only does the body accept the modified T-cells as its own but they are able to resist the virus and essentially act as a normal T-cell.

Third, and most exciting from my perspective, five of the six patients achieved a normalization of the CD4:CD8 ratio. A normalized CD4:CD8 ratio implies that the immune system of these individuals is being protected by the treatment. Clearly more work needs to be done but a sustained normalization would defend these individuals from a number of opportunistic infections that generally lead to a series of co-morbidities in AIDS.

Overall, the data are precisely what one would hope for and provide strong evidence that this treatment will ultimately be a success.

## These are Not the Droids You are Looking For

While one would hope that the share price would rocket higher on the news, it is important to keep in mind that immediate price actions are not the measuring stick. It remains possible that the price will move significantly higher this week but it has had a strong run and a sell the news reaction is possible as well. The key for long term investors is the data. So pay less attention to the near term price action and dig into the data.

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Monday, February 28, 2011



## How Now Brown Cow?

It is important to keep in mind that these data are only the start. Much more work needs to be done and additional questions have to be answered. So what are key questions?

--How durable is the response?

In order to turn this treatment into a viable commercial opportunity, the treatment has to have some durability. To be clear, this is not a critique of the study or data but a guide to what we need to look for going forward. In my view, a normalization of the CD4:CD8 ratio that last over a year would be sufficient. In other words, if you

could normalize the immune system for at least a year with a single treatment, you create a nice commercial opportunity. My hunch is that a lot of HIV patients would be willing to undergo a once a year treatment to keep their immune systems healthy. Again, it is not clear the durability of the response and it might be even longer than a year, so we need to wait for more data on this issue. In general, however, the more durable the response, the more likely that this treatment would be commercially viable.

*I think Sangamo will get there, it is just a question as to what treatment would be needed to achieve it.*

### Quotes about the Results

"These compelling data provide a mechanistic 'proof of concept' for this novel approach to HIV therapy which shows the most promise of any yet tested,"

-- Carl June M.D., Director of Translational Research at the Abramson Family Cancer Research Institute at the University of Pennsylvania School of Medicine

"These results are about as good as you could hope for. . . . Unequivocally, the safety looks good. But it could all amount to nothing unless we move viral load. Then it's just an interesting experiment."

-- Jacob Lalezari, director of [Quest Clinical Research](#), a San Francisco clinical trial center.

"When that data comes at the end of this year, we should have an idea whether the efficacy is durable enough and potent enough,"

- Moussatos, a biotechnology analyst

These appeared in a [Bloomberg article](#) or [Sangamo's press release](#).

## How Now Brown Cow?- Continued

--What about the one non-responder?

Getting five out of six to respond to treatment is a great accomplishment but what about number six? According to a [Bloomberg article](#), the non-responder had a muted response because their immune system attacked the virus used to deliver the treatment. To be clear, the immune system did not attack the modified T-cells but the virus used to modify the T-cells. As such, the patient likely received a minimal amount of modified T-cells. So the good news is that five out of six is a really high success ratio. Also good is that the immune system did not react to the T-cells but more needs to be done to better understand why the immune system reacted to the virus used to modify the T-cells. Is there a way to predict who will respond in this way and who will not? What percent of patients would have a similar response? Again, this is not to be critical but to highlight questions that will be answered going forward.

--What about Viral Loads?

The data presented today would not have an effect on the viral loads because these patients remained on HAART, i.e. you cannot decrease viral loads in patients with a limited viral load. So the open question is what will happen to the viral loads when this treatment is used in a population with higher viral loads? That is still an open question. An ability to lower viral loads or decrease the need to use HAART would be a great result for this treatment. Odds are that the Sangamo treatment will get there but it is not clear when or how. There are three chances for Sangamo to get to this point. First, the current treatment (altering T-cells and reinfusing once) might be enough. We may get data on this later, so it remains a possibility. Second, the current treatment (modified T-cells reinfused) will work but at a higher level. In this case, modified T-cells are sufficient but are needed in greater numbers than a single dose can generate. The company is working on a [dose escalating trial](#) to figure out the number of modified T-cells needed to create a critical mass of protected T-cells. Finally, to protect the system and eliminate the virus, the company may need to treat all blood cells and the hematopoietic stem cell (HSC) pre-clinical work would accomplish this. The HSC work has real world proof of concept in the Berlin patient and the HSC treatment would essentially replicate what happened in that case (without the bone marrow transplant). Again, it is not clear which of these treatment regimes would be most effective in decreasing viral loads. What I think is clear that given today's data, it is only a matter of time before Sangamo gets a treatment that takes out the virus.

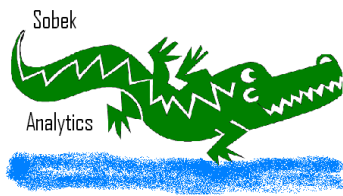
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## Disclaimer

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 SGMO shares and March \$8 calls.

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