Evaluate Vantage

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EP Vantage Interview – Opexa touts potential of disease-modifying MS drug

Breakthroughs in MS are pharma's flavour of the moment - each developer vying to commercialise its product with an ever-more-unique selling point. Small Texas company Opexa Therapeutics is throwing its hat into the ring once more, as chief executive Neil Warma tells *EP Vantage* about potential disease-modifying cellular immunotherapy Tovaxin.

Following positive meetings with the FDA, Opexa believes it is on course to start phase III trials in a matter of months. The announcement caused shares in the $44m market cap company to surge 88% to $2.82 at peak in trading last Wednesday; the stock is currently trading at $2.40. While much attention has been levied on oral MS pills lately, Mr Warma reckons Tovaxin's approach of infrequent subcutaneous injections, disability-stabilising action, and personalised, selective targeting could set it apart, although uncertainty remains over weak phase II results two years ago. In any case, with just $4.7m in cash as of the third quarter, Opexa is in urgent need of a partner or fresh financing if these phase III goals are to become reality.

Luring partners

Opexa is still discussing study design with the FDA, and the company has not yet set a date. Nevertheless, news that FDA supported the proposed clinical design, and agreed that manufacturing optimisation was sufficient, was enough to send shares skyrocketing.

"The important thing for us was getting the clear direction from the FDA," says Mr Warma. "It's always pleasing to see an appreciation in the stock market. I think for us the milestone is significant."

Opexa is currently assessing all its strategic options. That partnership discussions are ongoing, and with hope the phase III moniker will lure more collaborators to the table, indicates this is the company's preferred route.

"We'll move aggressively forward on the partnering path," Mr Warma says. "But at the same time we don't want to be beholden to any partner either, so we'll look at other financing options."

Investors would be most comfortable with a big pharma partner with MS interests, though Mr Warma does not rule out retaining Tovaxin in-house at this stage, instead securing a higher-value commercialisation partnership on the back of good data.

Tovaxin, like Dendreon's prostate cancer success story Provenge, is a cellular immunotherapy customised to a patient's individual disease profile. MS is the result of autoreactive immunological T-cells targeting a patient's own myelin layer, which protects nerve fibres.

In an approach likened to vaccination, these malfunctioning T-cells are isolated and extracted from a patient's blood, their activity attenuated using radiation, and then subcutaneously injected back into the patient to illicit an immune response.

Mixed efficacy, good safety

Mr Warma says that efficacy data so far puts Tovaxin "at least as good as the best on the market."

Phase IIb Terms trial results in relapse-remitting MS patients who had not received any prior treatment, showed over 83% remained relapse-free after 12 months, with a 64% decrease in annualised relapse rate (ARR) compared to placebo, comparable to Novartis' Gilenya.

Top-line results from this study were presented over two years ago, and in the broader treatment-naïve and previously-treated population there was a non-significant 37% ARR reduction.

Opexa stated at the time that all the observed relapse rates were nevertheless comparable with those achievable by marketed therapies, and that results may have been skewed because the Tovaxin arm used patients with more severe disease.

However, while Tovaxin is meant as a first-line therapy, a significant 55% reduction was observed in patients

treated previously with MS agents.

This may not necessarily be a limiting factor, perhaps providing a viable alternative to patients unsatisfied by other therapies. Mr Warma thinks it likely the phase III trial will target treatment-naïve patients, but believes Tovaxin's mechanism of action will be effective in all MS patients, potentially including secondary-progressive MS.

Disease-modifying

Crucially, Mr Warma remarks, Tovaxin has shown signs of significantly improving patient disability – Tovaxin-treated patients demonstrated a 28.1% improvement measured using the Expanded Disability Status Scale (EDSS), compared with 5.6% in the placebo group.

"Most drugs we have seen have focused on slowing down progression [of disability]," says Mr Warma.

Despite the impressive efficacy of novel MS therapies, broad immunosuppressive activity gives rise to sometimes serious problems like infections. As Tovaxin uses a patient's own immune cells, immunosuppression is specifically targeted, and importantly no serious side effects have yet been reported.

"That benefit/risk [profile] is really overweighted thus far on the benefit side," says Mr Warma, remarking that Tovaxin appears to be ticking all the requisite regulatory boxes.

"Up to 50% of MS patients stop taking therapies because of side effects and compliance," adds Mr Warma.

With only five subcutaneous injections per year, Tovaxin is preferable to hospital infusions. And while tablets like Novartis' Gilenya have been dubbed somewhat of a formulation 'holy grail', Mr Warma says the infrequent and non-invasive protocol may yet prove more favourable.

According to Mr Warma, one physician quizzed by Opexa on the potential adoption of Tovaxin versus Gilenya said he would pick five annual subcutaneous injections over a lifelong daily pill.

Great strides

Interestingly with Provenge paving the way in cancer, success with Tovaxin could signal a new path for cellular immunotherapies in autoimmune disease and immune disorders. Certainly Mr Warma is able to see a clearer regulatory path for Tovaxin because of Provenge:

"[Dendreon] have done great strides for the cell therapy industry, and have knocked down a lot of the barriers moving forward with the health authorities."

While efficacy might be strongest in a specific population, the risk/benefit profile can still potentially surpass existing treatments, and with favourable compliance. How Tovaxin fares from here depends on decent financing and a partner that can see potential through any previous shortcomings.