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Marc Sinatra's Bioguide

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BIOGUIDE: CLINUVEL – PHARMACEUTICAL TO COSMETIC … AND BACK

Overview: The journey of Clinuvel's afamelanotide has been a long one since its discovery as a potential skin cancer preventative in the 1980s. But its potential cosmetic use has become a main focus for investors, helped by a previous CEO often referring to the $US5 billion US tanning market.

Under current chief executive officer, Dr Philippe Wolgen, the cosmetic focus has been shelved and the potential clinical indications for afamelanotide have been expanded. The one question most investors ask is: "Which market is Clinuvel really targeting?"

Financials: Market cap: $67 million; cash: $46 million; last quarter burn: $2.8 million.

Directors: Non-executive chair, Brenda Shanahan; CEO, Dr Philippe Wolgen; chief scientific officer, Dr Helmer Agersborg; non-executive directors Dr Roger Aston, Stanley McLiesh and Jack Wood.
Clinuvel has a quality board with experience covering each of the required areas.

Products in Development:
Afamelanotide is an analogue of alpha-melanocyte stimulating hormone. It stimulates production of photo-protectant melanin by melanocytes in the skin and is being developed to treat the following five indications:
1) Polymorphic light eruption (PLE) - a common rash affecting some individuals' skin upon sun exposure. A phase II study showed a significant reduction in the use of rescue medications in the test group, but not a reduction in symptoms. A European phase III PLE study should report next year.
2) Erythropoietic protoporphyria (EPP) - a disease where protoporphyrin accumulates in the skin causing severe, long-term, photosensitivity to strong light sources. Significantly increased time to photo-provocation in EPP patients on afamelanotide has been shown. The drug has orphan status for EPP in Europe and the US. A European phase III study should report in mid 2009.
3) Photodynamic therapy (PDT) side effects – In some PDT procedures the photo-sensitizers used cause photosensitivity in the same way EPP does for up to 90 days. A phase II study in PDT patients on afamelanotide, which also has European orphan status for this indication, is due to report in early 2009.
4) Actinic keratoses (AK) - are precancerous skin lesions which develop due to sun exposure. Transplant patients are 100 times more likely to develop skin cancer and their actinic keratoses are three times more likely to develop into cancer than for normal individuals. A European phase II AK prevention trial of afamelanotide in transplant patients should report in 2010.
5) Solar urticaria (SU) - is a form of hives that appears rapidly after sun exposure and often dissipates quickly. Afamelanotide is currently in a European pilot trial of 10 patients, with results expected in 2009.

Sunscreens are of no real use to EPP patients and those who have undergone PDT. They are of somewhat limited use to patients with PLE and SU. Clinuvel's previous regime submitted an IND for afamelanotide to the US FDA for sunburn prevention and PLE. After feedback from the agency, it was withdrawn.

Significant Product Markets: In Europe and the US, EPP and SU are rare affecting 5,000 to 15,000 and 30,000 individuals, respectively. PLE is common, affecting one hundred million people in these locations. IMS Health has put the markets for EPP, SU and PLE in 2006 at $US25 million, $US12 million and $US40 million, respectively.

At the end of 2005, there were 164,000 living transplant patients in the US. IMS put the market size for transplant patients at $US240 million.

It is difficult to derive solid figures for PDT. A common photo-sensitizer, Photofrin, generated $US5.9 million dollars in 2007, enough sales to treat about 1200 patients.

There is little product development in these markets.

Opinion: It is clear that Clinuvel is focused on the clinical benefits of afamelanotide, which are likely to be greatest for EPP and PDT side-effects.

The photosensitivity suffered by such patients is and can be extreme. Small improvements in quality of life would be significant and it is for these groups that I believe Clinuvel will submit an investigational new drug application to the US Food and Drug Administration.

Submission of the application has been continually pushed back, almost certainly as a result of the previous aborted application attempt which may have raised some red flags with regulators. Clinuvel must be certain this time. The good news is given the photodynamic therapy side effects indication requires only short term therapy; the delay in submission is likely to be off-set by shorter clinical trial requirements.

Afamelanotide's likely impact on the other indications is less clear, as the inability to significantly reduce symptoms in the phase II polymorphic light eruption study showed. With the actinic keratoses study, the drug seems unlikely to obviate the need for aggressive sun protection for, and skin cancer screening of, transplant patients.

To be a blockbuster, afamelanotide must make inroads into some combination of the combined polymorphic light eruption, actinic keratoses and off-label areas. Off-label use may occur in skin cancer survivors to more peripheral use in areas such as patients allergic to sunscreens.

The cosmetic use of afamelanotide is problematic since doctors will need to balance all of the risks relative to only a cosmetic benefit before prescribing it, but significant sales could occur in this area.

I have arrived at a discounted cash flow valuation for Clinuvel of 54 cents a share, but I have only factored in low penetrations into the PLE, AK and off-label markets. Should any or all of these three take-off, the company could benefit considerably.

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marc@biotechdaily.com.au www.biotechdaily.com.au