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PROGEN, ONE LAST HURDLE

MARC SINATRA'S BIOGUIDE: PROGEN PHARMACEUTICALS

Overview: Progen Pharmaceuticals has been a success story for five years with its share price quadrupling as lead compound, PI-88, has progressed through clinical trials.

PI-88 is an angiogenesis inhibitor. It inhibits the growth of blood vessels into tumors, denying them the elements they need to grow. Angiogenesis inhibitors such as Avastin, Sutent and Nexavar are some of the hottest drugs around. Progen believes PI-88 may have an advantage over other angiogenesis inhibitors because it also inhibits tumor metastases and testing indicates a favourable side-effect profile.

Progen's previous chief executive officer, Lewis Lee, considered it essential to find a partner to develop PI-88. Burrill & Company was appointed in mid-2005 to "advance" partnering discussions after Progen's own efforts stalled. Progen's current CEO, Justus Homburg, has downplayed the importance of partnering and focused on completing the clinical development of PI-88. How should investors interpret this failure to partner and the subsequent change in strategy by the new CEO?

Financials: Market cap: $298 million; cash: $69.7 million; expected 2007-'08 cash burn: $25 million; 2008-'09: $30 million. A recently announced entitlements offer may raise up to $34.1 million.

Directors & Management: executive chairman, Stephen Chang; chief executive officer, Justus Homburg; non-executive director, Dr John R Zalcberg; non-executive director, Patrick Burns; non-executive director, Dr Malvin L Eutick.

Progen's directors and management have a positive mix of start-up, pharmaceutical and venture capital experience.

Technology: Progen's core technological focus is on heparan sulfate and protein-carbohydrate interactions, as evidenced by PI-88 and their other preclinical compounds below. PI-166 was in-licenced from the University of New South Wales.

1.) PI-88 - a heparan sulfate mimic that inhibits heparanase and binds to several proteins involved in angiogenesis, including vascular endothelial growth factor and fibroblast growth factors, limiting their functionality.

2.) PI-166 - a cytotoxic agent that has shown promise in a rat model of hepatoma

3.) Preclinical compounds - Progen has a range of compounds that have been developed in-house and they plan to submit an investigational new drug application with the US Food and Drug Administration on at least one of these compounds as soon as possible.

Products in Development: The following are Progen's main products in development.

PI-88: recurrent liver cancer – phase III trial to begin in the third quarter 2007;
PI-88: advanced melanoma – phase II trial results due end 2007;
PI-88: advanced prostate cancer – phase II trial results due early 2008;
PI-88: non-small cell lung carcinoma – phase II trial results due mid 2007;
PI-166: inoperable liver cancer – phase I results due end 2007.

PI-88's phase II trial results for recurrent liver cancer demonstrated a 25 percent reduction in cancer recurrence and a 78 percent increase in disease-free survival. Progen is preparing to have a special protocol assessment of their phase III trial design to ensure that the results will be acceptable to the FDA, provided endpoints are met.
Progen has obtained orphan drug status for PI-88 for the treatment of melanoma. A previous phase II study in advanced melanoma patients with no treatment options found PI-88 to be well tolerated with signs of efficacy.
The phase Ib trial of PI-166 in inoperable liver cancer patients has been progressing extremely slowly due to the low incidence of liver cancer in Australia and the expected due date for results are a rough guide.

Product markets: Recurrent liver cancer is an unmet indication, so the market is wide open. There are a few treatments for advanced melanoma, but this market is also very open. There are more drugs on the market and in development, such as the highly anticipated Satraplatin, for advanced prostate cancer. The market for non-small cell lung cancer is the most crowded of the four markets, with numerous drugs approved, such as Avastin, and in development.
According to the US National Cancer Institute there are at least 30 angiogenesis inhibiters currently in clinical trials.
Progen puts the addressable market sizes for the indications for which PI-88 is being developed at $US9.1 billion for liver cancer, $US700 million for melanoma, $US8.7 billion for prostate cancer and $US10 billion for non-small cell lung cancer. But UK-based Lead Discovery puts that actual worldwide market for liver cancer drugs at $US286 million (other analysts provide similar numbers); Navigant Consulting puts the melanoma market at around $US250 million; Research and Markets put the worldwide prostate cancer drug market at $US2.6 billion in 2005; analysts say the non-small cell lung cancer therapeutic market won't reach $US4 billion until 2012.

Verdict: Justus Homburg has made some very good changes to Progen's strategy, particularly its regulatory strategy, re-focused the company and got it moving forward. Moreover, the data that has come out of the recurrent liver cancer trial looks very encouraging.
When valuing Progen, the addressable market estimates should be ignored, given they appear exceedingly optimistic. Nonetheless, using the remaining market size data, finding the future income to justify Progen's current market capitalization is fairly easy, despite the number of anti-angiogenesis drugs in development.
I do, however, think that Progen's failure to partner PI-88 is a significant negative signal. Given their extensive efforts, it would appear that they simply couldn't find anyone who believes in PI-88 nearly as much as they do.
Since potential partners, particularly the big ones, are likely to have the clearest view of PI-88, except perhaps Progen itself, one has to ask, if they weren't swayed, why should I be?
I think this negative signal has largely been factored into Progen's share price and I believe Progen is probably pretty fairly priced at the moment. If they were to find a partner, particularly a big one, my opinion would change very quickly.

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