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EP Vantage Interview – Amarin's reinvention bags it a $70m reward

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What a difference two years makes. This week Amarin completed its transformation from one of the worst performing biotechnology stocks in 2007 to a company that had investors scrabbling to get on board to share in what they believe may be a future blockbuster (*The winners and losers of 2007, December 18, 2007*).

The Irish group announced on Tuesday that it had completed a $70m financing from a consortium of current and new investors, which is expected to give it a cash runway all the way to a hoped for 2012 NDA filing of lead drug AMR101, for the control of triglycerides and mixed dyslipidaema.

With cash in the bank to initiate two phase III trials for the drug in lowering high triglycerides and mixed dyslipidaema, it could be expected that the group might want to turn its thoughts to partnering, as the ultimate success of the drug will depend on being able to sell it in the primary care space. Speaking to *EP Vantage* Declan Doogan, interim chief executive, said that Amarin would be considering exploring partnering opportunities, but only at the right terms.

Trial data

Prospective partners may, however, want to wait until the group has reported data from the two phase III studies that AMR101 is expected to initiate by the end of the year. The first study will see the drug examined as a monotherapy in 240 patients with dangerously high triglyceride levels. The second study will be a larger 650 patient trial in combination with a statin to assess its efficacy in mixed dyslipidaema, a condition characterised by high levels of 'bad' LDL cholesterol, high levels of triglyceride and low levels of 'good' HDL cholesterol.

The first data read outs from the respective 12-week studies are due by the end of 2010 and the group is focused on filing the NDA no later than 2012.

Obvious partners would be a group with a large primary care sales force that is already involved in the area of cholesterol, a group that could includes Abbott Laboratories, Merck & Co and Pfizer. Whoever the partner, the strengthening of the group's balance sheet now means that any negotiations will not take place from a position of weakness allowing Amarin to demand better deal terms.

Switching track

Amarin may now be swimming in cash and have caught the eye of new investors, but in April 2007 things were looking dire following the failure of AMR101, then called Miraxion, in Huntington's disease, an event that caused the shares to fall by 82% and left the company looking as if it had few options for survival.

What proved to be the turning point was the decision two years ago by Mr Doogan, then the head of research and development, to switch the focus of AMR101 to a cardiovascular setting.

"It was very clear to me that neuroscience and neuro-degeneration is a high risk business. To take a compound like AMR101 and to hope that it would it work in a condition as poorly understood as Huntington's was a long shot," he says.

If any confidence was needed in the decision, the drug is an ultra-pure ethyl ester of eicosapentaenoic acid (ethyl-EPA), and in Japan ethyl-EPA compounds have been approved for the treatment of hyperlipidaema for over 18 years. "When I looked at the literature and the product history all the signs pointed to cardiovascular," Mr Doogan says.

Booming market

Justification also came from GlaxoSmithKline dipping its toes into the triglyceride waters with the $1.65bn acquisition of Reliant Pharmaceuticals, ostensibly for access to Lovaza, an Omega-3 EPA and docosahexaenoic acid (DHA) treatment, originally licensed for the US market from Pronova BioPharma. For Glaxo this move has paid off; last year Lovaza had sales of $537m, which are due to peak at $1.09bn in 2012 before the product loses patent protection the year after, according to consensus forecasts from EvaluatePharma.

It was this boom in the triglyceride lowering market and growing evidence from long term outcome studies that are showing lowering triglycerides could have a real and meaningful impact on cardiac events and mortality, that convinced new investor Abingworth to come on board, says Joe Anderson, a partner at the UK-based company. Abingworth and other new investors pushed the funding up from the group's original target of $55m to $70m.

Making a difference

Given Lovaza's hold on the market, AMR101 will have to find a big differentiator to give it a fighting chance, especially as generic versions of Lovaza could be on the market by the time AMR101 is launched.

Mr Doogan admits that while the drug will not have first mover advantage it could be a best in class compound. "The literature tells us EPA alone is not associated with an LDL signal and we have seen data from DHA and Lovaza that some patients get an increase in LDL, which is not the direction you want to go in with LDL. Coupled with that we believe we will be able to have a more convenient dose range as we will be targeting half the number of capsules per day," he says.

But it should be remembered that none of these claims have been substantiated. The outcome of the two clinical trials will be pivotal in proving whether Amarin does have a genuinely differentiated product that will be able to become the $1bn selling product that Mr Dougan believes it can, and give its new investors a decent return.