Merck takes charge of vernakalant

All good things come to those who wait and yesterday Cardiome got the news it was waiting for. Merck & Co has purchased North American rights to Cardiome’s emergency atrial fibrillation therapy vernakalant from Astellas Pharma, consolidating the global development programme for both the intravenous and oral versions of the drug under the New Jersey company’s umbrella.

Investors took the deal as a sign that Merck was fully committed to the anti-arrhythmic and boosted Cardiome shares by 28% to C$5.29 yesterday. The hope is that the deal will jump-start US clinical development of the IV version, now under a clinical hold by the FDA, as well as accelerate into phase III trials the oral version for chronic treatment.

Heart stopping

Marketed in Europe as Brinavess, IV vernakalant has been subject to a series of regulatory delays. The most damaging was in 2008 when following a positive advisory committee vote the FDA asked for an additional trial to determine whether its risk-benefit profile favoured it over electrical cardioversion in patients with serious heart disease (Cardiome’s regulatory delay prompts nervousness, August 13, 2008).

The Act V trial that emerged from that decision then suspended enrolment following a single case of cardiogenic shock. In the meantime, Merck informed Cardiome that it had not made any decisions about the development plan for the vernakalant pill - dubbed RSD1235 po and MK-6621- to which it already owned global rights (Merck calls a go-slow on oral vernakalant, August 12, 2010).

Given that there had been no dialogue between Astellas and the FDA since last year on IV vernakalant, analysts believe Merck’s assumption of the license is a sign that Cardiome’s new North American partner sees a path to market and that there will be resolution soon on questions about cardiogenic shock.

Analysts from Leerink Swann write that Cardiome would like the development path to be clear by the end of 2011, although that may not be possible.

Restarting Act V, initiating a new phase III trial or combining the existing Act V data with EU registry data all are possible ways to resolve the safety questions. If a whole new trial is ordered, it will add some burden to Cardiome’s balance sheet as the Canadian company is responsible for 25% of development costs.

As it is Cardiome’s only product in active clinical development, the long US delays have clearly been damaging. At one time, analysts had pencilled in US sales of more than $300m in sales for IV vernakalant in 2011, with Cardiome expected to pull in 20-30% royalties.

As it is only on the market in Europe, current forecasts put global sales at just $17m this year, and will only breach $200m in 2016, according to EvaluatePharma forecasts.

Given that Merck’s assumption of the US license clears a path toward approval in the world’s largest drug market, the 28% jump in share price appears to be justified.

Pill progress

As for oral vernakalant, approval for maintenance of regular heartbeat in patients with atrial fibrillation makes it potentially a much bigger product. For now, equity analysts covering Merck are not forecasting sales although analysts that cover Cardiome estimate royalty and income from US co-promotion at $78m in 2016, following a launch in 2013 - estimates that look highly optimistic.

Analysts from RBC noted in April that Merck needed to control the IV vernakalant programme to restart late-stage research on oral vernakalant. Merck now has an opportunity to present a consistent message in negotiating with the FDA over the design of both the confirmatory safety trials for the IV product and the pivotal trials for the pill.
With Merck now in full control of the molecule, Cardiome's prospects are looking better than they have in months. News on the progress of the oral programme is now anticipated in the autumn as Merck draws up its 2012 plans, confirmation on which could mean further share price gains.