Evaluate Vantage

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ARYx seeking knight in shining armour

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This week, ARYx Therapeutics received the sort of news that nightmares are made of for small biotechs; key partner Procter & Gamble decided to hand back the rights to its experimental constipation drug, depriving the group of an essential milestone payment and raising the prospect of a dilutive fundraising.

If it wants to avoid going cap in hand to investors, the US group will be forced to sign away the rights to one or both of its two other pipeline projects earlier than hoped, an unfortunate situation to be in when trying to maximise the value of a project. Unsurprisingly, shares in the company, which have only been listed since November, fell 20% to a record low of $5.27 on the news.

P&G signed the rights to ATI-7505, a prokinetic agent in phase 2 clinical trials for chronic constipation and functional dyspepsia, two years ago. Like ARYx's other candidates, it has been created using its proprietary RetroMetabolic Drug Design technology to create structurally related molecules to drugs already on the market that retain efficacy of the original version, but are metabolised through safer pathways to avoid side effects.

ATI-7505 was modelled after cisapride, a Johnson & Johnson product which generated sales of over $1bn until it was withdrawn in 2000 due to serious cardiovascular side effects. Its other two products are ATI-5923, an oral anti-coagulant based on warfarin and ATI-2042, an oral anti-arrhythmic based on amiodarone.

Be still my beating heart

The P&G decision was based on a Thorough QTc study, which measures heart rate changes and are used as an indication of cardiac safety, carried out to establish whether the drug carried the same cardiovascular side effects as cisapride. The drug is a 5HT4 agonist like Novartis’s Zelnorm, which was withdrawn from the US market after it was linked to cardiovascular events, so P&G would have been looking for a completely clean safety profile to consider progressing with the project.

The trial, as ARYx read it, was a success. The only mildly concerning result was a subset read out in women, which appeared to show an elevated risk, but which the company put down to errors in study conduct. It concluded the result – which would be the first time a difference in gender had been noted in any such study – was anomalous.

P&G clearly took a different view point. It said the decision to terminate was based on their view of certain commercial and technical criteria, and that the program no longer fitted into their future plans. With cardiac safety currently at the top of the list of concerns at the FDA at the moment, the company maybe took a view that the project would be too risky, expensive and drawn out to pursue.

One year of cash

For ARYx, meanwhile, financial guidance was based on a substantial milestone payment due on successful conclusion of the study, but only if P&G decided to continue with the collaboration. With the termination of two ongoing phase II trials of ATI-7505, the $60m in cash at the end of the first quarter will last through the second quarter of next year, the company's finance director revealed on a conference call on Wednesday.

While a new partner will be sought for ATI-7505, all efforts will now be placed on progressing its other two candidates. However, with results due from trials that would have formed the basis of partnership deals due around the time money runs out, the clock is ticking loudly and ominously.

The results from a phase II, head-to-head study of ATI-5923 versus warfarin in 600 patients are due at the end of the second quarter of 2009, which the company said may qualify as a pivotal trial with the FDA. Talks with big pharma partners have been held, but whether an acceptable deal can be completed within the timeframe is questionable, executives said.

Data from a phase II trial of ATI-2042 are due by year-end, and although interest has been shown, doing a deal without the data would not achieve the best terms.

Limited options

ARYx may not have any choice. A worse than hoped for deal might look more appealing than trying to raise funds through other means, and risk putting out already disgruntled investors. The group floated last November at $10, and the performance since has not been pretty. The shares plunged 19% on their first day of trading, while the IPO itself was priced much lower than initial expectations of $14-$16.

In after market trade on Thursday, the stock jumped back 50% to $8.36, suggesting that some investors are willing to bet ARYx will benefit in the long term from this setback. However, unless a knight in shining armour appears on the horizon pretty soon with a short term remedy, shareholders are going to become increasingly nervous.