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Savient experiences severe gout pain

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In what must be the most nervy markets in living memory and a regulatory climate in the pharmaceutical industry that is ultra wary of even the slightest hint of safety concerns, it was perhaps inevitable that news of a potential increased cardiovascular risk for patients taking gout treatment Puricase would have a calamitous effect on the shares in Savient Pharmaceuticals.

Yesterday shares in the group fell 73% to $3.07, their lowest level in two and a half years, as numerous analysts downgraded their forecasts following the discovery that 5% of patients had reported adverse cardiovascular events, findings that had not previously been revealed in interim data analyses. This sparked investor fears that the drug, which is due to be filed in the next few weeks, will not get approval first time round and that uptake will be slow and limited to only the most severely affected patients.

The drug had been forecast to report sales of $382m in 2012, according to consensus forecasts by EvaluatePharma, but the news could spark a wave of downgrades. Yesterday Cowen said it was now expecting 2012 sales of the drug to be $172m.

Few bright spots

Eun Yang, a healthcare analyst at Jeffries, said that the news also means there is little hope of any near term recovery in the shares. “Since Puricase is the only product they have, if you have concerns over approvability, the stock could remain at this level. I think it is an approvable drug, but I don't think it will get through the FDA in the first review cycle.”

In addition, the safety concerns are likely to stymie any chance Savient has of finding a European partner for the drug ahead of eventual approval, meaning that without the licensing cash it might have to raise funds. With shares at their current level this will cause significant dilution.

The negative speculation could be unfair given that the cardiovascular events may have been overdone, considering five of the eight patients that reported heart problems continued on the drug without further incident, indicating that Puricase might not be responsible. Today the shares were up 5% in early morning trading, to $3.24.

Historic doubts

Even before yesterday’s dramatic falls there had been nagging doubts about how approvable Puricase really is. What had previously worried some investors was the imbalance of deaths between the treatment and placebo arms and the high, almost unacceptable, number of infusion reactions for Puricase, including 20% of patients suffering anaphylaxis-like reactions. As previously reported by EP Vantage - *Savient flying high but not risk free, January 14, 2008*- all this had prompted questions whether the treatment’s undoubted efficacy and orphan drug status was enough to offset safety concerns.

Questions still also remain over patients developing antibodies to the drug and a current lack of re-treatment data, which will not be available before the second half of 2009. Many are now predicting an advisory committee, expected in the first quarter of 2009, will recommend delaying approval until the results of these studies are released.

New challengers

With Puricase’s future now looking uncertain and some only predicting sales in a smaller hard-to-treat market, the field would appear wide open for another challenger to come in and grab a large slice of a market that until recently has not seen a new drug approved for over 30 years.

The particularly hard to treat nature of gout has deterred many from starting development, and as such other than standard gout treatment allopurinol, the only other marketed product is febuxostat. Originally developed by Teijin in Japan, the drug was launched in Japan in June and recently received marketing permission in Europe through Ipsen, which licensed the drug in 2003. Launch is expected by the end of the year and sales in 2014 are predicted to be $108m.

But the drug has had less success in the US, where it was originally filed in 2004 under the name TMX-67, by the collaboration of Takeda and Abbott Laboratories which in-licensed the drug in the US. Since the dissolving of this partnership, Takeda has been trying to win approval, but the drug, which has had two approvable letters, is now filed, called Uloric and is up before an advisory committee on November 24.

Late Stage Gout Pipeline					
	Product	**Company**	**Genericname**	**PharmacologicalClass**	**2014 Sales ($m)**
Filed	Uloric	Takeda	febuxostat	Xanthine oxidase inhibitor	228
PhaseIII	Puricase	Savient Pharmaceuticals	pegloticase	Urate oxidase	600
PhaseII	Arcalyst	Regeneron Pharmaceuticals	rilonacept	IL-1 antagonist	
	RDEA806	Ardea Biosciences		NNRTI	
Total					**828**

The next new drugs on the horizon are URL Pharma’s treatment MPC-004, which will come up before US regulators for approval at the end of June 2009. Ardea Biosciences' RDEA806, is also being developed for the disorder as a secondary indication after HIV.

More interesting is Regeneron Pharmaceuticals' Arcalyst, which in September reported phase II results that showed an 81% reduction in gout flares. The drug is expected to enter phase III trials by the middle of next year. This is the drug that on the surface looks like it might be the one to provide a much-needed alternative in what is a very stagnant field.