Alexza investors right to be agitated over FDA rebuff

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Alexza Pharmaceuticals has a lot to worry about right now. Not only has the FDA refused to grant approval for its lead product, an inhaled version of the schizophrenia drug loxapine, but mutterings are growing louder about partner Valeant Pharmaceuticals’ commitment to the project.

Alexza has yet to sit down with the FDA to discuss the complete response letter and any path forward, but investors clearly fear the worst. Shares in the California company have more than halved in value since the regulator’s decision was announced on Monday, closing at a record low of $1.34 yesterday. A recovery could be hard to come by.

Pulmonary safety

AZ-004 comprises the anti-psychotic loxapine reformulated with the company’s Staccato technology, delivered via an inhaler device. The company filed for approval in December to market the product as a rapid treatment for agitation in patients with schizophrenia or bipolar disorder (Event - Alexza hopes for unhindered approval of inhaled antipsychotic, September 20, 2010).

The FDA’s main safety concerns stem from phase I studies conducted in asthma and COPD patients. In these trials patients in both groups, given either AZ-004 or an inhaled dummy drug using the same device, experienced a decrease in lung function. Alexza anticipates that AZ-004 could affect lung function in these patients, but believes this is easily controlled with a bronchodilator. The reading in the placebo group is harder to explain.

On a conference call Thomas King, the company’s chief executive officer, said they were surprised with the questions on pulmonary safety, considering the FDA has not once raised this as an issue in discussions over the previous few years.

The regulator and Alexza have a fundamentally different view on what the studies show, he said, and this will no doubt be a key topic for debate in any meeting.

Other headaches

Other issues relate to stability studies and manufacturing approval, but it is likely that pulmonary safety is the key concern which could affect the remainder of the company’s pipeline.

Mr King said he did not believe this news “indicts” the whole Staccato platform, but acknowledged pulmonary safety has been an issue recently.

Winning approval for reformulated drugs is certainly not low risk; throw the inhaled issue into the mix and Alexza could have some convincing to do, unfortunately just the sort of hurdles that some have been anticipating (Alexza deals fails to excite but caution may be justified for now, February 11, 2010).

The company probably has around $40m cash, but with analysts saying a one-year delay is the best-case scenario funding could soon become another headache.

Limited interest

Alexza sold US rights to AZ-004 to Biovail earlier this year, now owned by the larger Valeant. Under the terms of the deal no more cash will change hands until approval is granted, and up until then the financial obligations lie with Alexza.

As such Valeant will not be in any hurry to make a decision. Unfortunately, the omens do not look good. In a research note published yesterday analysts at RBC wrote that chief executive Mike Pearson has indicated his interest in AZ-004 is “limited”, because of the extra cost of having to build a hospital sales force.
Analysts who previously followed Biovail were pencilling in sales of $112m by 2016, which would make the product one of the new company's biggest growth drivers, according to EvaluatePharma. The fact that Valeant shares failed to react to the news - the has stock actually climbed since to close at a record high of C$28.28 yesterday - suggests expectations were already low and investor interest is limited.

Unless the FDA makes a swift U-turn, it sounds like Mr Pearson will not need much of an excuse to bid farewell to this deal.