Evaluate Vantage

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Investors toast Galmed Nash results, but what will the FDA say?

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A couple of months ago, a win for Galmed in Nash looked like the longest of long shots, its drug Aramchol having failed in a fatty liver disease trial in HIV patients. Investors brave enough to double down on their investments after that were rewarded handsomely today when results from a 52-week phase II Nash study pushed shares up threefold.

A closer look at the data suggest that a little more caution is warranted, however. Inconsistent dose response and numerous missed endpoints should have regulators making tough demands when it comes to the design of a pivotal trial to ensure more robust results. If Galmed wants to top up its $16m cash pile, now might be a good time to sell more shares.

Look closely

It is more than a little surprising that Galmed portrayed a study result with so many missed endpoints as a rousing success, but the Israel-based, US-listed group appears to believe it can take the data to the US FDA to discuss a pivotal trial. The two prospective endpoints that were met with a p value of less than 0.05 when compared with placebo were reduction in liver fat based on magnetic resonance spectroscopy (MRS) for patients taking the 400mg daily dose and Nash resolution for the 600mg daily dose.

A post-hoc analysis also found that among those who did show a reduction in MRS liver fat, those taking the 600mg dose saw a 47% absolute change, significantly greater than patients in the placebo arm.

Galmed called Nash resolution a “potentially approvable” endpoint. It also claimed a win on Nash resolution without worsening of fibrosis – another endpoint that it described “potentially approvable” – for the 600mg dose, although with a p value of 0.0514 that is a debatable assertion. Statistical misses for both doses included Nash resolution and fibrosis improvement without worsening of Nash. Both doses at least showed a benefit on liver enzyme levels, although as a safety endpoint that would not be sufficient to justify approval.

These inconsistencies did not seem to worry the investors who pushed shares up from $7 at close on Monday to as much as $25.10. The enthusiasm eased a little as the trading day progressed.

Moving to phase III

Asked in a conference call about a timeline for initiating a pivotal trial, executives would not commit. Chief executive Allen Baharaff said that because this phase II trial was global, expanding to a phase III recruitment should be quick once the trial is off the ground.

Assuming the FDA and EU officials sign off on a design, the expectations for the size and scope of a phase III trial would be akin to Intercept’s phase III for Ocaliva, which seeks to treat 2,370 patients for 18 months. That trial, called Regenerate, is accompanied by a further study in 540 patients with cirrhosis. Regenerate is expected to report in the first half of next year.

With just $16m in the bank at the end of March, Galmed would need a substantial amount of new cash to fund a similar programme. A fundraising seems like a fait accompli, especially since the mixed data would likely have any potential partners waiting for assurances from regulators that a phase III can indeed go ahead.

Today’s share rise suggests that investors have placed a lot of confidence in executives’ talk of a tranquil progression to a pivotal study. Galmed’s valuation depends on this narrative being sustained.

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