Geron bets its stake in haematological disease

Investors have rewarded Geron for its never-say-die strategy. Shares have doubled to more than $3 in the last month as readout approaches for the twice-failed candidate imetelstat in haematological disease.

Investors have not been deterred by the fact the most-advanced trial of the telomerase inhibitor is in myelofibrosis, a disease area that looks to be well served by Jak inhibitors like Incyte's Jakafi in coming years, or that Geron has given up in solid tumours after multiple setbacks (Geron revives imetelstat as brain cancer drug bombs out, December 4, 2012). Supporting the investment case, if marginally, is a lower-risk approach to development than in the past, as the California group has slashed costs and relied on academic researchers for this last-chance trial.

Laser-like focus

Geron was once known as much for its work in stem cells as for telomerase inhibition, but it has over the past two years trimmed the cell therapies from its portfolio and focused on the one area in which its lead candidate shows promise: haematological disease. Activity in essential thrombocythaemia has given some hope of activity in myelofibrosis, to which many thrombocythaemia patients progress.

Telomerase inhibition, on the other hand, has not in general delivered on its promise as a cancer treatment. Telomerase hinders normal cell aging and death, and is active in many types of malignant disease – thus it is an attractive target for drug developers. Only two products have made it into the clinic, however, with imetelstat the most advanced (Geron blow could put final nail in telomerase inhibitor coffin, September 11, 2012).

The key catalyst for investors today is a Mayo Clinic-sponsored phase II proof-of-concept trial in 29 patients, measuring an overall response rate in primary and secondary myelofibrosis patients. An initial cohort of 11 patients was expanded after the pre-specified criterion of at least two responders was met, and subsequent cohorts will receive a higher dose, similar to that received by patients in an essential thrombocythaemia trial.

The company hopes that data will be presented at the Ash haematology conference in December. Final results from the trial, if the compound succeeds in showing a benefit, will assist in designing a company-sponsored multicentre trial.

Eye-popping

Even by biotech bubble standards, Geron’s recent uplift has been stunning. In the past month, shares are up 108% – an impressive uplift compared with the 8% of the Nasdaq biotechnology index, or even the 42% of investor darling Sarepta. Granted, Geron was starting from a low base – it closed at a record low $1.02 on April 17 – but there can be no disputing that it has caught fire with developments from the Mayo trial.

Such a rise would make Geron an almost sure bet to top up its war chest through a share offering, even though it is not in any immediate need. Its $71.6m of cash should be sufficient to fund it through late 2015 if it is not running phase III trials, according to analysts from Piper Jaffray. Cash is being conserved by decisions to slash staffing by three quarters, to just 44 employees after divestment of stem cell research, internal discovery and companion diagnostics work.

But strong activity in myelofibrosis could be a spur for work in leukaemia and multiple myeloma, and an expanded phase II programme will not come cheap – a partnership seems a long shot. In the event of complete failure, the executive team might want to come up with a plan B, which means Geron will need to re-enter the partnership or M&A game, a proposition that will demand cash.

Given the high-risk nature of imetelstat, Geron’s management would be wise to make the most of the valuation rise.
<table>
<thead>
<tr>
<th>Trial</th>
<th>ID</th>
</tr>
</thead>
<tbody>
<tr>
<td>29 patients with primary or secondary myelofibrosis</td>
<td>NCT01731951</td>
</tr>
</tbody>
</table>

To contact the writer of this story email Jonathan Gardner in London at jonathang@epvantage.com or follow @JonEPVantage on Twitter

© Copyright 2019 Evaluate Ltd.