Evaluate Vantage

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Prostate cancer results power Cougar Biotech's shares

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Companies developing experimental treatments for prostate cancer have given investors a white knuckle ride this year, and disappointing clinical results at GPC Biotech, Novacea and Dendreon have left many nursing losses.

Despite these setbacks, investors are still backing companies with promising looking therapies, attracted by the scale of the opportunity for a treatment that can demonstrate real efficacy in the disease. One of the hopefuls is Cougar Biotechnology, whose shares have tripled since they were listed this February on the OTC Bulletin Board, an electronic quotation system for unlisted securities, making them one of the best performing biotech stocks this year.

The company's lead candidate CB7630, generically known as abiraterone acetate, is an inhibitor of testosterone biosynthesis. It is in phase II trials for the treatment of various stages of prostate cancer, and has shown promise in difficult to treat, hormone refractory prostate cancer (HRPC) patients.

Hormone dependent

Testosterone plays a vital role in the development of prostate cancer, fuelling tumour growth. First-line therapies, known as androgen deprivation therapy (ADT), deprive the body of the hormone by stopping the testes producing testosterone, preventing the cancer from growing and delaying disease progression.

Sooner or later, however, the tumour becomes resistant to ADT and can grow without hormones, at which stage the disease becomes classified as HRPC. However, before this stage is reached tumours often adapt, gaining the ability to grow using the very low levels of androgen produced by the adrenal gland.

At this point, second-line agents can be used to block the adrenal androgens, before the patient requires chemotherapy. But because there is no FDA approved second-line hormonal treatment, the substantial proportion of HRPC that remains hormone driven is very hard to treat.

In the US, the anti-fungal ketoconazole is mostly commonly used, off-label, to knock out the adrenal gland, but at high and often toxic doses with limited efficacy, which is why the drug is not approved for this use in many countries, including the UK.

Double action

Because Cougar's CB7630 acts on both the testes and adrenal gland, it reduces circulating hormones more effectively than current therapies. The company hopes it will yield a new treatment option for patients who fail ADT, but whose tumours remain dependent on testosterone.

There is a substantial market for hormone-based therapies. The biggest selling anti-androgen and LHRH (luteinizing hormone-releasing hormone) analogue, AstraZeneca's Casodex and Zoladex respectively, generated sales of $1.21bn and $1.0bn in 2006. A large proportion of patients receiving these drugs would benefit from an effective second-line hormone treatment, if one was available. The rise in Cougar's share price reflects this, with shares in the company closing at $30.5 on Tuesday 27, November, valuing the company at $534m.

Phase I/II trials have demonstrated that CB7630 is capable of delaying progression in patients who have progressed on ADT, and in those with more advanced disease who have relapsed following chemotherapy. It has also demonstrated tumour shrinkage, and efficacy in terms of PSA decline (a marker of prostate cancer) is better than other HRPC drugs on the market. On top of that, the safety profile has been favourable and high doses have been used without toxicity.

The company now needs to demonstrate a definite effect on survival, and plans to starts a phase III trial in the first half of 2008. News on the final design of the trial, which is likely to be in a post-chemotherapy setting, and go-ahead from regulators, are key events on the horizon.

Data is unlikely to available until 2010 at the earliest, particularly as the FDA seems increasingly comfortable with overall survival, as opposed to progression-free survival, as an end point.

Funding

Shareholders in Cougar, the biggest being biotechnology venture capitalist Lindsay Rosenwald with a 23% stake, according to a filing in March, could have some interesting events on the horizon. Aside from clinical progress, the company may need to raise additional capital.

Cougar ended the third-quarter with $62m in cash, which will be stretched, if not depleted, after funding a full phase III trial. The company also plans to start a phase I/II trial in breast cancer this year, although this is being funded by an external grant.

In August there was talk of Cougar's shares progressing to a full Nasdaq listing, which while increasing liquidity and visibility, could be carried out alongside a fundraising. Another route could be a licensing deal, as the group has retained full commercial rights to the product. However, comments from management indicate the group is keen to keep the value in the company.

The company could not be reached for comment.