Evaluate Vantage

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From zero to hero, Endocyte completes a remarkable transformation

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The US biotech claims an unexpected victory, scoring a $2.1bn takeover by Novartis on the strength of an asset it had bought for just $12m.

Four years ago Endocyte was the laughing stock of biotech. Yet it somehow managed to draw a line under its mistakes and find a new lead asset under a new chief executive. But even its most exuberant followers could hardly have expected that this would lead to today's $2.1bn takeover offer from Novartis.

Given Novartis's recent success with Lutathera the Swiss group's interest makes sense: Endocyte's new lead, 177Lu-PSMA-617, is like Lutathera a lutetium-labelled therapeutic. But this does not help answer questions about the takeover's curious timing – well before pivotal data readout – or about why an asset bought for $2.1bn was apparently worth just $12m one year ago.

$12m is effectively what Endocyte had paid in cash in September 2017 to license 177Lu-PSMA-617, a prostate cancer therapeutic, from ABX Biomedizinische Forschungsreagenzien, a private German nuclear medicine specialist. The deal also involved $3.8m of stock and warrants, and Endocyte later acquired clinical data, plus a US IND from a Houston-based company called Radiomedix.

Until that point Endocyte had spent three years languishing in an existential crisis occasioned by the failure of its previous lead, the folate receptor-targeting molecule vintafolide (*Esmo – Missed Target leaves Endocyte clutching at straws, September 28, 2014*). Between vintafolide's pivotal data presentation at Esmo 2014 and last year's ABX deal Endocyte stock lost some 70% of its value.

But then the incredible transformation began, and as of yesterday the shares were up nearly 300% year to date, and Endocyte was a billion-dollar company, having even managed to pull off a $189m equity raise. The Novartis deal announced today represents a further premium of 54% on top of yesterday's closing price.

Why?

This is where the questions begin. It is not clear, for instance, why Novartis is paying such a huge premium for an asset that has yet to provide definitive clinical proof; 177Lu-PSMA-617's pivotal Vision study will not yield radiographic progression-free survival data until the end of 2019.

The Swiss firm could lose either way. If Vision fails it will have thrown $2.1bn down the drain; if it succeeds it opens itself up to questions about what precisely its business development team was doing last year when

ABX was willing to sell 177Lu-PSMA-617 for just $12m.

And how likely is Vision to succeed? The precedent is not great. The antigen targeted by 177Lu-PSMA-617 is PSMA, which is expressed in 70-80% of prostate cancer patients, but is also present on tissues other than prostate cancer, so the project is unlikely to offer a benefit devoid of toxicity.

The broader question is how realistic an opportunity prostate cancer is right now. In this morning's statement Novartis calls metastatic castration-resistant prostate cancer (mCRPC) a "disease with limited treatment options". Yet this ignores the fact that new drugs like Johnson & Johnson's Zytiga and Pfizer's Xtandi have completely revolutionised treatment of this cancer.

It will not go unnoticed that several players wanting to enter mCRPC have found it impossible to run successful clinical trials because Zytiga and Xtandi had changed the treatment paradigm. Assets that fell by the wayside include Active Biotech/Ipsen's tasquinimod, Takeda's ortoronel, Oncogenex/Teva's custirsen and Exelixis's cabozantinib.

Novartis argues that 177Lu-PSMA-617's phase II data were strong; the Vision study has the asset given on top of best supportive care, Zytiga or Xtandi. Other radiotherapeutics in prostate cancer, such as Bayer's Xofigo, have underwhelmed, though Novartis correctly points out that this alpha-emitter targets not mCRPC but the bone metastases resulting from the disease.

At least there is no doubt as to what drove Novartis's thinking in going after Endocyte. In today's third-quarter presentation the Swiss firm referred to Lutathera, a drug that delivers the same radioactive lutetium-177 isotope as 177Lu-PSMA-617 and is approved for neuroendocrine tumours, as a "potential blockbuster".

Lutathera came into Novartis's hands through last year's takeover of Advanced Accelerator Applications for $3.9bn. Clearly the company thinks it can repeat the trick with Endocyte, offering the markets another salutary lesson about the risks of shorting even the most questionable biotech stocks.

Study	Detail	Timing	Trial ID
Vision	750 mCRPC pts, given 177Lu-PSMA-617 + best supportive care/Zytiga/Xtandi, vs best supportive care/Zytiga/Xtandi alone	rPFS data end 2019; OS data end 2020	NCT03511664