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Clinical setback lays bare Vertex’s weakness

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As the company is punished for its failure to diversify, could it be forced into making an acquisition?

Vertex’s $14bn loss in market cap this morning after the failure of a mid-stage rare disease asset looks, on the face of it, a little dramatic. After all the project, VX-814 for alpha-1 antitrypsin deficiency (AATD), was hardly expected to be a big seller.

But the market reaction to the asset’s discontinuation has much to do with sentiment. It seems that investors are finally beginning to wake up to the fact that Vertex has little beyond its marketed cystic fibrosis drugs save a few admittedly interesting, but highly risky pipeline projects.

Vertex’s valuation, which before today sat at over $70bn, now looks very bloated. The company has enjoyed a substantial premium, helped by its reputation as a cystic fibrosis powerhouse. The net present value of the company’s assets, according to *Evaluate Omnium*, is just $26bn – and $25bn of this is accounted for by its CF franchise.

Like many other big biotechs, Vertex now needs to expand beyond its core franchise. And it might need to do more than the small, early-stage deals that it has historically stuck to.

Indeed, the only pipeline projects that have attracted sales forecasts are the now-discontinued VX-814 and CTX001, an ex-vivo gene editing asset being developed with Crispr Therapeutics for sickle cell disease and beta thalassaemia.

The net present value of Vertex's assets			
Product/project	**Description**	**Status**	**NPV ($m)**
Trikafta	CF triplet	Marketed	21,220
Kalydeco	CF drug	Marketed	1,569
Symdeko	CF doublet	Marketed	1,401
Orkambi	CF doublet	Marketed	953
CTX001	Ex-vivo Crispr-edited gene therapy	Ph1/2	788
VX-814	AATD small molecule	Discontinued	197
		Total	**$26.1bn**
Source: EvaluateOmnium.			

So, why the huge disconnect? Vertex has enjoyed a halo effect from its dominance in cystic fibrosis, and has argued that even though it only has a handful of clinical programmes its understanding of biology has meant a high probability of success.

This always seemed a flimsy basis for such a massive premium. Leerink analysts noted that “investors are likely to question whether the heralded Vertex research capability is really validated beyond cystic fibrosis".

In light of VX-814’s failure the company is facing calls to buy something, and fast. But, despite its impressive cash reserves, big deals have never been the group’s style.

Vertex's company acquisitions			
Company	**Area of interest**	**Financials**	**Date**
Semma Therapeutics	Cell therapy for type 1 diabetes	$950m	Sep 2019
Exonics Therapeutics	Gene editing for DMD & DM1	$245m up front	Jun 2019
Virochem Pharma	Hepatitis C therapies	Cash & stock deal worth $370m	Mar 2009
Aurora Biosciences	Drug discovery tech	Stock deal worth $592m	Apr 2001
Source: EvaluatePharma.			

True, it was the acquisition of Aurora in 2001 that set Vertex on the path to becoming the dominant force in CF that it is today. But its most notable purchase since has been of Semma Therapeutics, a developer of a stem-cell therapy for type 1 diabetes (*Vertex spends nearly $1bn on Semma's unproven diabetes cell tech, September 3, 2019*).

The project remains preclinical, according to Vertex’s website.

Vertex has largely preferred to strike research collaborations. The most intriguing is that with Crispr Therapeutics, under which the companies are investigating gene editing in various disorders, with CTX001 being the first to emerge.

Vertex's research collaborations			
Company	**Area of interest**	**Financials**	**Date**
Moderna (expanded collab)	mRNAs for CF	$75m up front	Sep 2020
Affinia Therapeutics	AAV capsids for gene therapies for DMD, DM1 & CF	Not disclosed	Apr 2020
Crispr Therapeutics (expanded collab)	Gene editing for DMD & DM1	$175m up front	Jun 2019
X-Chem (expanded collab)	Novel small molecule therapeutics	Not disclosed	Jan 2019
X-Chem	Novel small molecule therapeutics	Not disclosed	May 2017
Moderna	mRNAs for CF	$40m up front	Jul 2016
Crispr Therapeutics	Gene editing for CF and sickle cell disease	$105m up front	Oct 2015
Parion Sciences	Inhaled ENAC inhibitors for CF (rights returned to Parion in Jan 2020)	$80m up front	Jun 2015

AAV=Adeno-associated virus; CF=Cystic fibrosis; DMD= Duchenne muscular dystrophy; DM1=Myotonic dystrophy type 1; ENAC=Epithelial sodium channel.
Source: EvaluatePharma.

However, Crispr and Semma look like very risky bets. And both are well outside Vertex's core expertise of small molecules.

Still, being a small molecule did not help VX-814. Vertex said yesterday that elevated liver enzymes had been seen in several subjects in a 50-patient phase II trial; this, along with poor drug exposure, suggests that the company has been unable to find a therapeutic window for the project.

Vertex has discontinued VX-814, but it still has another "structurally distinct" small molecule in development for AATD, VX-864. Phase II data are due in the first half of next year, but some analysts have already written off its chances.

"Management hasn't clarified the dose levels being tested for the second AATD programme and how its activity (and liver tox) compare to VX-814," Leerink wrote, saying the whole programme would now "fade into obscurity".

The pressure is now on Vertex, but desperation never makes a good buyer, particularly with valuations currently on the high side.

No wonder investors are heading for the door: picking the right acquisition target is a huge challenge, and here Vertex has little track record to point to.

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