Evaluate Vantage

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Vertex’s second transformation: Duchenne time

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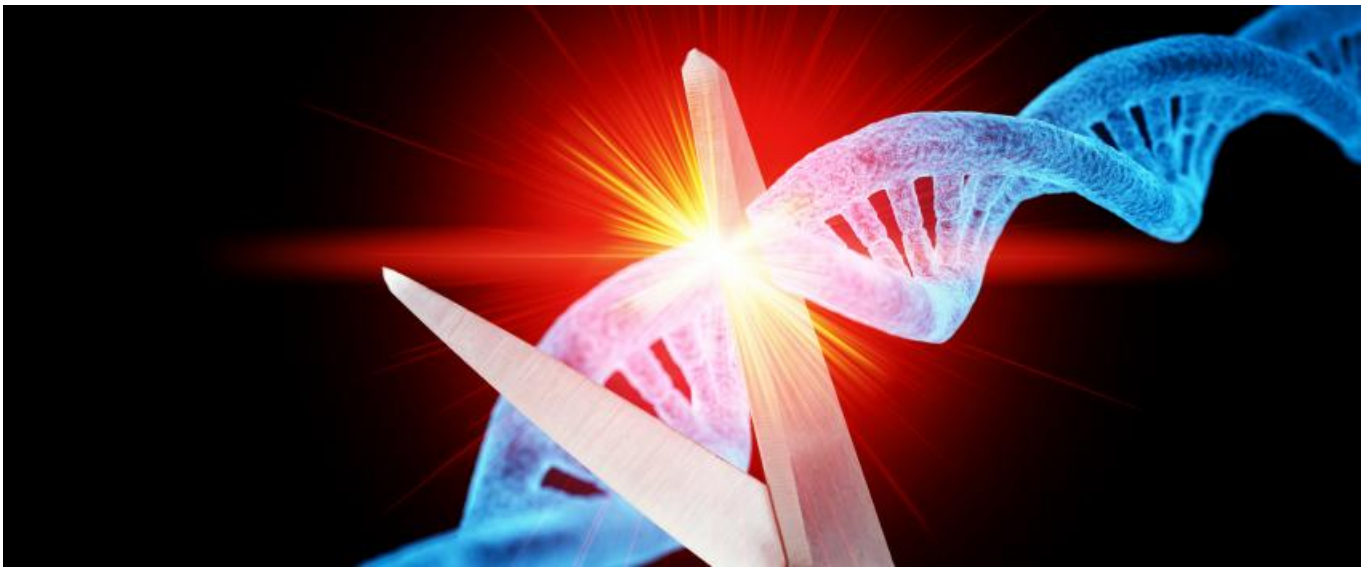

The cystic fibrosis player does deals with Crispr and Exonics to launch itself into a highly competitive rare disease area.

Vertex is no stranger to makeovers, having already switched from hepatitis C to become a highly successful cystic fibrosis player. Yesterday it sowed the seeds for what could become its second transformation – into a company specialising in treatments for Duchenne muscular dystrophy.

Its basis for building a pipeline here is two deals that together cost the company $420m. The fact that there are at present still just two not particularly effective DMD treatments on the US market illustrates the opportunity, but unlike in cystic fibrosis Vertex will have to pedal hard to catch up with the DMD leaders.

This is because since the controversial approval of the first treatment, Sarepta’s Exondys 51, the industry pipeline for DMD has mushroomed. Indeed, *EvaluatePharma* reveals over 30 projects in phase II-III clinical trials alone.

Selected Duchenne muscular dystrophy projects			
Project	**Company**	**Mechanism**	**2024e sales ($m)**
Filed			
Golodirsen	Sarepta Therapeutics	Exon 53 binding oligonucleotide RNAi	331
Phase III			
Casimersen	Sarepta Therapeutics	Exon 45 binding oligonucleotide	250
Suvodirsen	Wave Life Sciences	Exon 51 binding oligonucleotide	235
Edasalonexent	Catabasis Pharmaceuticals	NF-kB inhibitor	227
RG6206	Roche/Bristol-Myers Squibb	Myostatin (GDF8) inhibitor	-
Givinostat	Italfarmaco	HDAC inhibitor	-
Phase II			
SRP-9001	Sarepta Therapeutics	Microdystrophin gene therapy	1,820
SGT-001	Solid Biosciences	Microdystrophin gene therapy	577
Pamrevlumab	Fibrogen	Connective tissue growth factor MAb	381
Vamorolone	Santhera/Idorsia	NF-kB inhibitor	293
NS-065	Nippon Shinyaku	Exon 53 binding oligonucleotide RNAi	218
PB1046	Phasebio Pharmaceuticals	VIP2 agonist	87
GALGT2	Sarepta Therapeutics	GALGT2 gene therapy	3
ATL1102	Antisense Therapeutics/Ionis	Alpha-4 integrin antisense	-
TXA127	Constant Therapeutics	GPCR peptide agonist	-
AAV1-Follistatin	Milo Biotechnology	Myostatin (GDF8) inhibitor	-
MNK-1411	Mallinckrodt	Melanocortin-2 receptor agonist	-
Phase I			
PF-06939926	Pfizer (ex Bamboo)	Microdystrophin gene therapy	-

Vertex's bid to compete will come courtesy of a $175m technology licence from Crispr Therapeutics, with which it already collaborates on sickle cell disease and beta-thalassaemia, and the $245m acquisition of the private gene editing business Exonics Therapeutics.

Together, these two tie-ups will give Vertex the scientific tools to work on new treatments for DMD and myotonic dystrophy type 1. These tools comprise Crispr's Crispr/Cas9 technology, endonucleases, single and double-cut RNAs and AAV vectors, and the single-cut Crispr tech Exonics licensed from UT Southwestern Medical Center.

Vertex's most important competitors will be Sarepta, Solid Biosciences, Pfizer and Wave Life Sciences, but numerous others are waiting in the wings too. This is quite the turnaround from just a few years ago, as the life sciences investor Brad Loncar pointed out yesterday.

> Did you ever think you'd see a day where DMD was starting to get crowded. High quality problem!
>
> — Brad Loncar (@bradloncar) June 6, 2019

Having launched Exondys 51 Sarepta is now awaiting US approval of its second exon-skipper, golodirsen, In the gene therapy space that Vertex is entering, meanwhile, Sarepta's biggest immediate hope is the microdystrophin project SRP-9001, while the first data from Pfizer's PF-06939926, acquired with Bamboo Therapeutics for $150m, are due later this month.

Vertex said that along with DMD it would be seeking to develop treatments for myotonic dystrophy type 1, another muscle function disorder that has a different genetic cause. The competitor pipeline here is much thinner, with clinical projects comprising AMO Pharma’s AMO-02 and Ionis’s baliforsen, and Avidity Biosciences, Expansion Therapeutics and Audentes working on preclinical assets.

Evercore ISI analysts yesterday wrote that myotonic dystrophy type 1 might represent a larger prevalent population than DMD. If this is the case, and considering the competitor landscape, perhaps the former disease has the greatest potential for Vertex to make its mark.