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CRISPR's UK business partner

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Dear *Frontier Tech Investor* subscriber,

Twenty-three years ago a small company spun off from Oxford University in an attempt to commercialise a new kind of biotechnology.

It's been a long road. I'm going to tell you the story today. And I'm going to show you how – at last – the company may have succeeded.

Many of the world's breakthrough medicines of the coming years may ultimately use this little firm's kit. It's deploying a smart solution to a difficult problem, which I believe will see it come out on top of the tech evolution that is going to change the face of healthcare beyond recognition.

This is the kind of change that happened a century ago with the introduction of antibiotics. It introduced something new that both disrupted the previous way of treating bacterial infections but also increased the size of the healthcare market to a size that dwarfed what existed before.

What I see happening today is on a similar scale.

We are on the cusp of an evolution in healthcare that will see a transition to whole life care, focusing on constant monitoring, genetic profiling and lifestyle management rather than what might best be described as disaster management today.

And I think I've spotted the perfect way for British investors to play it.

Why "one shot" biotech firms are failing

When we get sick, the thing we want more than anything else is to get better. That's why we go to the doctor, endure the tests and pay for the medicine. We want to get better.

However, a pharmaceutical company's revenue stream stops when we get better. Businesses are built on repeat customers and if your customer never needs you again that's not a very good business model.

This may sound cynical, but keep in mind that it's better for pharmaceutical companies to focus on how to *ease* our suffering from a condition we will never get better from. That's a much better business model because the revenue stream lasts much longer and provides much greater security for

company earnings.

In other words, you get a lot of repeat business on top of the potential to grow your business, which is what every company wants. As awful as it sounds, curing patients isn't always the best business model for a pharma or biotech firm to pursue.

Let me give you a great example.

Back in 2016, Nick O'Connor and I went to the MIT Technology Review conference in Boston. It was packed with the CEOs of emerging companies who were eager to promote, or perhaps more accurately hype, their products. I was particularly impressed by the president of Spark Therapeutics, Katherine A. High, who was much more interested in relating the difficulties they were trying to overcome in bringing their products to the market.

She was at pains to explain how she had spent the first 25 years of her career painstakingly overcoming one failure after another as they drew progressively closer to understanding how to reprogram the immune system to fight cancer cells.

She said that the introduction of CRISPR Cas-9 gene editing technology was a game-changer for their business. It both reduced the cost and sped up the pace of innovation. It took the painstaking iterative process of drug discovery and put it in overdrive. That allowed the company to IPO in 2015.

Spark Therapeutics' stock ticker is ONCE. That encapsulates the business model. The company is developing one-shot genetic solutions to chronic conditions. In other words, it is dealing in cures rather than treatments.

The kinds of products it wants to bring to market mean that with one injection you will develop a genetic immunity to the lifelong chronic condition you have been dealing with and spending money your whole life on trying to manage.

It's the kind of thing patients are getting really excited about.

The only way it can grow is to develop completely new solutions for other genetic disorders. That's not impossible, but it's not a reason to buy the share for regular investors.

Prior to the release of the company's Luxturna drug, there was no treatment for any form of inherited retinal diseases, many of which eventually end in blindness. With the introduction of the drug, there is a real solution that can provide a genetic repair that arrests the speed of vision impairment.

That is a very different solution than what we are used to. Generally, a drug is designed to treat a bacterial infection or a viral infection or attempts to rebalance blood chemistry, but does not treat the underlying genetic cause of a long-term affliction. Spark Therapeutics is dealing in cures.

Yet at the beginning of last week, the share was trading at the same level as it was at the end of the first day of trading back in 2015. For a company that is developing such an exciting set of products, that's a dismal performance.

In fact, on a relative basis, compared to some of the other exciting companies in the biotech sector, which have multiplied many times over in the same timeframe, it is truly a dismal performance.

So, what is the company doing wrong?

Innovation alone isn't enough: you need a sound business strategy too

When we get down to first principles, it's blindingly obvious.

It is dealing in a suite of rare disorders and by introducing a cure it is reducing the number of potential patients. There is nowhere for it to grow and if it is successful, there will be no more patients and therefore no business.

The only way it can grow is to develop completely new solutions for other genetic disorders. That's not impossible, but it's not a reason to buy the share for regular investors.

However, big pharmaceuticals companies have a very big reason to buy these kinds of companies. Genetics plays a significant role in who develops chronic diseases like Type-2 diabetes, arthritis and cancer. Genetics plays a role in why some people can be lifelong smokers and never get lung cancer. Genetics is why some people develop heart disease from high cholesterol and others can have much higher levels and still live long fruitful lives.

The reason these companies are being bought up is because the big pharmaceuticals companies know that the current concentration on rare disorders is the equivalent of a proof-of-concept effort.

These businesses might not be making a lot of money. But they're proving the innovation side of the equation stacks up. The big pharma companies are likely stepping in to add more

commercial strategy and sound business models.

That could be a very big deal indeed.

Today we are seeing genetic products come to market and companies begin to make money. That's has been the green light for acquisitions because now rather than promises, we have evidence these products can generate revenue.

Now the real work begins, which is to move on to wide market diseases that are global in scope and affect millions of people. That is where the big challenge and opportunity arises for genetics and pharmaceuticals companies.

Large pharmaceuticals companies want to be the ones to develop genetic solutions to chronic diseases and wish to squeeze the maximum revenue from that process while it lasts.

Smaller companies that are full of enthusiasm about the intellectual stimulation they get from creating cures are not receiving love from investors because they have no plan for profitability.

It's a catch-22 because we know that eventually there are going to be genetic solutions to diabetes and arthritis, but they will not reach market until someone figures out a business model to profit from it.

Enter this month's recommendation.

Has this small UK stock built "CRISPR's business partner"?

Oxford BioMedica emerged out of Oxford University in 1996 with the aim of commercialising its LentiVector technology as a delivery system for genetic medicines of the future. That piece of technology is the backbone of the company and informs how it has been able to prosper for so long.

Effectively the LentiVector technology is one innovative way of delivering genetic medicines into the human body.

If you've heard about this sort of thing before, it's because I have written to your previously about CRISPR-Cas 9 gene editing. Lenti are also gene editing vectors and while there is still an acrimonious lawsuit ongoing as to who owns the intellectual property relating to CRISPR, Oxford BioMedica owns the intellectual property relating to Lenti so there is no equivocation on that front which could impact the company.

Lenti have some clear benefits over CRISPR. The first is the large size of the payload (9k) that can be delivered. It is therefore ideally suited to making changes to a subject's DNA that are long or life-long in nature. That does not mean Lenti and CRISPR are competing but rather they are mutually complimentary because Lenti can act as a delivery mechanism for CRISPR packages.

In other words, LentiVector tech may stand in CRISPR's shadow now... but I believe it'll play a key role in the future of genetic medicine. Here is how the company describes the Lenti product:

> *The platform is applicable in many therapeutic areas, and has a number of specific advantages. Lentiviral vectors can genetically modify dividing cells, such as T-cells, as well as non- or rarely dividing cells, such as neurons or early progenitor/stem cells, making it a delivery system of choice in gene and cell therapy. The platform can also integrate genes into non-dividing cells, including in the brain and retina, with ground-breaking long-term studies suggesting gene expression may be maintained indefinitely, offering the prospect of permanent therapeutic benefit following a single administration.*

The clear message is that the lentiviral vector is Oxford BioMedica's key piece of intellectual property and therefore represents a moat around the additional products it creates that rest upon it. That's one of the primary reasons the company has a clear advantage relative to other companies in the gene medicine business.

And I'm clearly not the only one.

The company has pursued a model of building key partnerships and relationships with major pharma firms. Many of these partnerships could lead to genuinely world-changing medicines. So we're not just getting Oxford BioMedica's technology... we're getting the advantages of its partnerships.

Large pharmaceuticals companies want to be the ones to develop genetic solutions to chronic diseases and wish to squeeze the maximum revenue from that process while it lasts.

These partnerships provide Oxford BioMedica with critical revenue

For instance, its relationship with Novartis has delivered Kymriah which is a childhood leukaemia (blood cancer) solution that leads to a cure for the disease. Cancer care is

where the majority of genetic editing companies are focusing because it is a disease that demands a cure rather than symptomatic solution.

It's also where big pharmaceuticals are most willing to co-operate because there is no risk of losing a long-term cash flow, so interests align. Kymriah has the potential to deliver in the region of $100 million in revenue over the next few years.

The drug has been permissioned by the FDA, Canada and the EU for both adults and children. The NHS in England has also permissioned the purchase of the drug but it is not yet available in Scotland. The broad acceptance of Kymriah suggests there is a good chance the revenue forecasts will be achieved.

Haemophilia is a completely different genetic disorder and inhibits the blood's ability to clot. Oxford BioMedica signed a $105.0 million collaboration and licence agreement with Bioverativ. That company was acquired by Sanofi a year ago. That relationship will leverage the use of the LentiVector platform and manufacturing technology Oxford BioMedica possesses.

It has also formed a partnership with the UK Cystic Fibrosis Gene Therapy Consortium. That leverages a relationship with Boehringer Ingelheim and Imperial Innovations which is developing an inhaler aimed at delivering gene therapies directly to the lungs, particularly for cystic fibrosis patients. There is another UK company that was aiming at delivering a similar product, Vectura Plc, so this is a competitive market.

Oxford BioMedica's relationship with Axovant Sciences is an example of cooperation with a somewhat smaller company. This is an example of how the LentiVector system can be leveraged for another disease, this time Parkinson's.

The delivery mechanism involves an injection directly into the brain but the aim is to reactivate dopamine production and therefore remove the symptoms of the disease, permanently. This is a potentially revolutionary development.

The company has agreed a $842.5 million exclusive worldwide agreement for the sale and distribution of the AXO-Lenti-PD product. This is still a development-stage project and a Phase I/II clinical study started last year so there is still a long way to go before it will see a penny of the $842.5 million.

These are the biggest opportunities that the company has highlighted in its annual report, but it has a significant pipeline of potential products that are likely to flesh out revenue growth forecasts in future.

OXB-202, 302, 201, 204 and 208 all focus on ophthalmology and are in various stages of initial testing. Its SAR 422459 and SAR 421869 candidates, which are being developed in conjunction with Sanofi, are further along in the development process and are now in Phase II and Phase I/II trials respectively.

Apart from the royalty agreements discussed above, the company also has a relationship with Orchard Therapeutics which is concentrating on ex vivo solutions to genetic problems. That means it is taking a sample of DNA out of the patient's body, altering it, and putting it back in.

Oxford Biomedica has competence in both ex vivo and in vivo applications (in vivo means injecting new material into the patient). This relationship is an example of how the company is leveraging its intellectual property to develop drugs in its own right, and further the plans of large pharmaceuticals business as well as those of small breakthrough companies.

Cancer care is where the majority of genetic editing companies are focusing because it is a disease that demands a cure rather than symptomatic solution.

How high could this little stock soar?

Now let's look at the share price action.

The company has plenty of back history and we have evidence of both manias and crashes. That gives us a clear idea of just how exciting the biotechnology sector can be but also how punishing investors can be when they are disappointed.

Faced with the long-term history of extraordinary volatility, the obvious objection to investing is that the sector is prone to hype and overpromising. I have a lot of sympathy with that view, which is why I did not want to recommend the share earlier. I did not want to buy until we had seen a significant pullback.

At this time, I want to introduce the hype curve. The outshoot from Oxford was in 1996 and what many people fail to understand is that the true hype factor in the biotech sector was in the late 1990s. That's when all the outlandish promises were being made about the imminence of personalised medicine.

If we look at the long-term history of biotechnology

Oxford BioMedica was one of the survivors. That was 20 years ago. It has taken almost that long to bring the promises made during the excitement of the bubble to fruition.

shares, then many have these massive spikes in the late 1990s which coincide with the TMT bubble (technology, media and telecoms) when anything with a ".com" after the name or claiming to be "new economy" got a free ride from investors willing to big them up to the moon.

That represented the peak of the hype cycle. It's exactly what we saw in 2017 with the cryptocurrency mania.

The inevitable crash ensured that the most hyped companies with the least substance disappeared. Some of the most promising were then either acquired or survived.

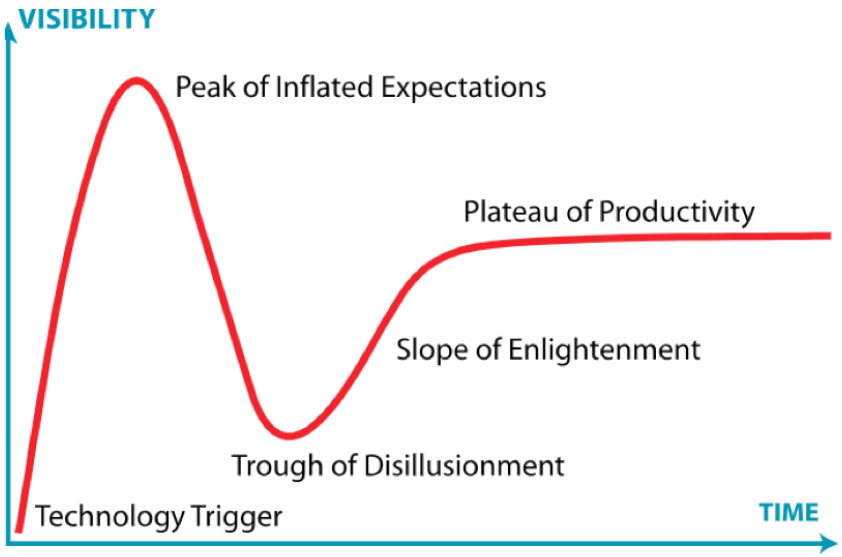
Oxford BioMedica was one of the survivors. That was 20 years ago. It has taken almost that long to bring the promises made during the excitement of the bubble to fruition. Let's look at the hype chart below.

The big question therefore is whether we are in the Technology Trigger, the Peak of Inflated Expectations, the Trough of Disillusionment, the Slope of Enlightenment or Plateau of Productivity.

Since we are only at the dawn of commercial reality, the logical conclusion is that we are now at the slope of enlightenment. This is the time when money starts to flow in and investors can logically begin to expect free cash flow to increase. Oxford BioMedica went earnings positive for the first time in 2018.

If that's the case, then the logical question is, how did it survive so long without earnings? Twenty-three years without earnings is a substantial period of time. That tells us it has had to raise money over the years, even after the slug of cash that came in during the IPO which took place during a bubble.

The company runs a pretty lean operation with just over 300 employees, which is a relatively low overhead for such an impressively innovative company. Nevertheless, it has issued new securities on eight occasions since the original IPO in 1996. The most recent of those was in March 2018 with a fresh £20.49 million share issue.



Right now, the company has £44 million in cash with net debt of £38 million. In the credit markets today, the most common convention is to look at the credit default swap spread because they tend to be more liquid than bonds.

Oxford BioMedica's spread is 65 basis points (0.65%) over gilts, which is very low risk when a comparable index of high-yield companies is currently trading at 385 basis points (3.65%).

The next question any rational investor should be asking is why the share has pulled back so violently since September. Some of the reason will be broad market related but that does not explain why Oxford BioMedica has not participated in the rebound that has taken place since Boxing Day. There must be something else at work.

The reason the company issued more shares in March was to fund additional production facilities for the anti-hemophilia products it is developing in line with Bioverativ. That represents an uncertainty because it has to carry the manufacturing capacity until revenue begins to flow from the investment.

That is why the market has imposed a haircut on the share price, which has taken it down from its June high of 1,062p to last week's low of 581p.

From everything I have read about the share, its capabilities and its plans for the future, not to mention the accelerating pace of M&A activity in the biotech sector, I believe we are very close to a low.

This is why I am writing to you about it today. It is certainly more interesting from an investor's point of view, following a pullback of 45%,

than before.

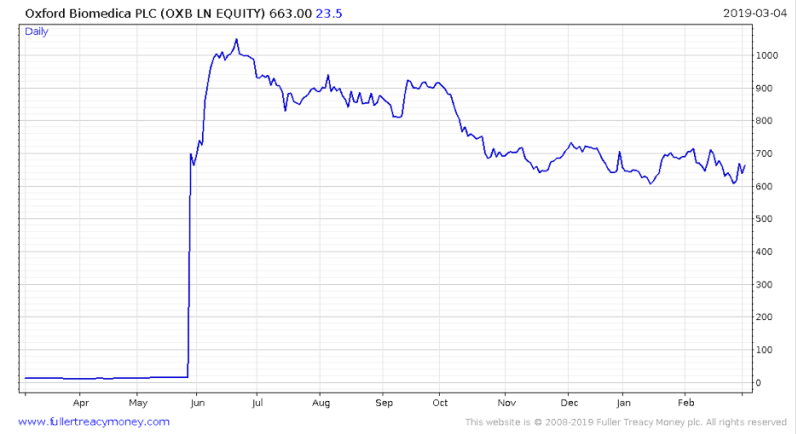
City analysts' estimates for the share range from 800p to 1,450p. The price on Friday was 639p, which tells me that there is a still a lot of support for the share from the City and the selling pressure is overdone.

I expect Oxford BioMedica to be one of the clearest beneficiaries from the future of the genetics industry and for its price to hit 1,450p within the next 18 months. If its Parkinson's solution is successful, and we won't know for a few years, then 5,000p is not unreasonable.

Many thanks,

Eoin Treacy
Investment Director, *Frontier Tech Investor*

Action to take:	**Buy Oxford BioMedica**
Ticker:	**OXB**
Price as of 05.03.2019:	**657.95p**
Buy up to:	**800p**
Market cap:	**435.285m**
52-week high/low:	**1,062/511.00**



Medical

Company	Ticker	Rec Date	Price Then	Price Now	Gain/ loss %
Autodesk	ADSK	19/07/17	$108.83	$157.79	44.99
Illumina	ILMN	05/09/17	$207.22	$307.70	48.49
PureTech Health	PRTC-L	09/01/18	155.75p	167.00p	7.22
Becton Dickinson and Co	BDX	03/05/18	$221.35	$252.86	15.26
Canopy Growth Corp	WEED :CN	21/03/18	C$33.11	C$62.39	88.43
Advanced Oncotherapy	AVO	03/07/18	48p	43.00p	-10.42
Bioquell	BQE :LN	07/08/18	440p	587.00p	33.41
Aurora Cannabis	ACB-T	19/09/18	C$12.35	C$9.60	-22.27

Technology

Company	Ticker	Rec Date	Price Then	Price Now	Gain/ loss %
Garmin	GRMN US	02/08/16	$55.75	$84.74	61.26
Cisco Systems Inc.	CSCO: US	03/04/17	$33.80	$51.16	58.70
Microsoft	MSFT	31/07/17	$73.04	$112.26	57.79
Northrup Grumman	NOC US	07/11/17	$301.66	$283.10	-4.33
Intel Corp	INTC	06/06/18	$57.03	$53.94	-3.81
Activision Blizzard	ATVI: US	02/10/18	$83.29	$41.79	-49.83
Tesla	TSLA	05/11/18	$346.41	$285.36	-17.62
Science Apps Int	SAIC	07/07/16	$58.20	$74.44	33.76
Alphabet	GOOG: US	04/12/18	$1,093	$1147.80	5.01
Visa	V US	08/01/19	$136.06	$147.96	8.93
ZUORA-A	ZUO	05/02/19	$21.39	$22.81	6.64%

Energy

Company	Ticker	Rec Date	Price Then	Price Now	Gain/ loss %
Ormat Technologies	ORA on NYSE	06/06/17	$58.79	$55.92	-3.71
Sherritt International Corp	S CN	06/02/18	C$1.18	C$0.48	-59.32

Moonshot

Company	Ticker	Rec Date	Price Then	Price Now	Gain/ loss %
SolarWindow	WNDW	07/04/16	$3.96	$2.33	-41.16
Alkane Resources Ltd	ALK: AU	05/09/16	AU$ 0.31	AU$ 0.21	-32.79
Superconductor Tech Inc	SCON	03/04/18	$9.60	$1.58	-83.54

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