

4D pharma PLC

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4D pharma: A clinical stage innovator and pioneer of Live Biotherapeutics

To understand 4D pharma plc (LON:DDDD), it is first worth trying to get your head around the technology that has spawned drug candidates in cancer, gastrointestinal and respiratory ailments and autoimmune disease.

Working in the emerging area of the human microbiome (the bacteria that reside mainly in the gut), 4D has developed Live Biotherapeutics — products that contain live organisms such as human commensal bacteria.

The approach focuses on single strains to assess specific mechanisms of action targeting a defined disease pathway.

Even variations between different strains of bacteria of the same species are assessed and exploited.

4D's chief executive, Duncan Peyton, says superficially identical bacteria can sometimes differ up to 20% in their gene content, and therefore may have highly different functional profiles.

Attractive safety profiles

Toxicity has always been a major impediment to the success of new drugs.

In developing its Live Biotherapeutics, 4D has isolated bacteria from healthy human donors which are expected to have "highly attractive safety profiles".

"A lot of the safety issues encountered in novel drug development are due to the off-target effects," explains Peyton.

"As bacteria derived from the human gut, and which are restricted to the gut following administration, we first approached Live Biotherapeutics from that angle - the potential to create safe and efficacious drugs."

Early studies assessed the impact of these Live Biotherapeutics on the immune system.

While early programmes investigated ways to suppress the immune system, one strain, now known as MRx0518, was found to be a significant stimulator of it.

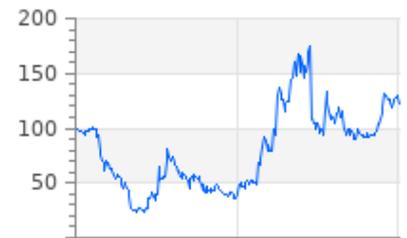
Important breakthrough

That was an important breakthrough, particularly in this era of immuno-oncology, where the body's defences are used to battle and beat the disease.

Now in the early phase of clinical development, MRx0518 is being trialled as a single therapy for solid tumours and pancreatic cancer.

Sexier, to the lay investor at least, will be its collaboration with Merck & Co. trialling 4D's breakthrough with the American giant's blockbuster checkpoint inhibitor Keytruda.

1 Year Share Price Graph



January 2020 July 2020 January 2021

Share Information

Code: DDDD
Listing: LSE
Sector: Pharma & Biotech
Website: www.4dpharmapl.com

Company Synopsis:

4D are pioneers in harnessing bacteria as a revolutionary new class of medicines - called live biotherapeutics.

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Checkpoint inhibitors are big business. By 2022 sales are expected to be around US\$25bn a year, while Keytruda alone generated revenues of US\$11.1bn in 2019, up 55%.

But this class of drug, which works to unmask cancer to the immune system, currently has its limitations.

First, the likes of Keytruda work for probably only 30% of the population. When they do work, they work exceptionally well.

Sadly, over time the effect can wane.

MRx0518 is being trialled to assess its potential to work synergistically with Keytruda to reengage the immune system.

Significant tumour reduction

The latest update (on June 5) revealed that five of the 12 solid tumour patients constituting Part A of the phase I/II trial continued to receive the combination treatment of Keytruda and MRx0518, including two who have had a partial response to the drugs, showing significant reductions in their tumours.

This was a difficult-to-treat, end-of-life group, who had previously lost response to checkpoint inhibitors such as Keytruda, so the results should be seen in this context.

Of these two patients, one had previously received three lines of treatment, the other seven before enrolling on 4D's trial.

The former, who has metastatic renal cell carcinoma, has now been on the study for over a year, while the latter, a lung cancer sufferer, started treatment 49 weeks ago.

"What we have seen so far we have been pleased with," says Peyton with a degree of understatement.

Oncology is just one part of the business. It has clinical-phase drugs in gastrointestinal and respiratory conditions, the most advanced of which is Blautix, its phase II treatment of irritable bowel syndrome (IBS).

In April, 4D received fast-track clinical trial authorisation from the UK regulator to carry out a phase II assessment of its single-strain live biotherapeutic immune modulator MRx-4DP0004 in 90 people hospitalised with COVID-19.

Recruitment starts soon

Having received ethics approval, 4D expects to start recruiting patients in June, with preliminary data expected in the fourth quarter of this year.

"If we see a signal in the data, we might consider starting dosing patients earlier in the disease progression, before people get to the hospital," says Peyton of the programme.

"The earlier we dose, the greater the likelihood we'll be able to stop the progression of the hyperinflammatory condition [associated with COVID]."

4D pharma has found itself bucking the recent positive trend in the healthcare sector as its shares have marked time around February's 50p placing price in recent weeks.

With around £20m in the bank, the company has an enterprise value of £40m.

For that, you get four clinical-stage assets and four clinical readouts (including two phase II studies) expected by the end of the year.

Not just that, 4D is blazing a trail in the field in Live Biotherapeutics, which CEO Peyton describes as a "revolutionary new class of medicines" that appear uniquely safe.

And it has perfected the manufacturing process at scale, something that sets 4D apart from others in the microbiome therapeutics space.

Bargain territory?

A catalyst for a more realistic valuation might be a partnership of some description, adding to 4D's research collaboration with MSD Merck & Co in the vaccines space.

A licensing deal in the oncology space would seem an ideal place to start, though Peyton believes MRx0518 has the potential to work with other immune checkpoint inhibitors, not just Keytruda.

"Of course, MSD is a ready-made partner and we like working with them, but there are others out there," he adds.

"We have multiple conversations ongoing around IBS and we've done a lot of pre-clinical work in autoimmune and oncology too.

"We have conversations in all those areas, and conversations about the platform itself."

Let's hope those conversations help crystallise value.

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