Destiny Pharma plc

Support on both fronts

8 November 2021

The autumn of 2021 appears to be the zenith, so far, for the profile of *C.difficile* infection (CDI) with conference presentations and *C.difficile* awareness month. We have collated data on these recent presentations, and results from competitors to Destiny Pharma's NTCD-M3 product for the prevention of recurrent CDIs, and find M3 to be superior in almost all respects. We continue to expect a licensing transaction for at least one of Destiny's Phase 3-ready products.

NTCD-M3 remains at the forefront

Destiny's most recently acquired Phase 3-ready product, the non-toxigenic *Clostridioides difficile* strain M3 (NTCD-M3), appears to be **in the right place, at the right time**. November is *C.difficile* awareness month and Destiny's consultant and Advisory Board member Professor Dale Gerding has just presented at the *C.difficile* International Conference. There have also been posters and presentations at the recent IDWeek conference in US, including some from Destiny's competitors, and some competitor data was summarised in Professor Gerding's presentation.

The presentation on Friday November 5 included an efficacy ranking of treatments to prevent CDIs with Destiny's NTCD-M3 product ranking in second place, just below oligofructose. Destiny's more direct competitor in the microbiome space, SER-109 from Seres Therapeutics, lies back in eighth place. In addition, in Professor Gerding's comparison of the safety of many of the proposed and available treatments for CDIs, Destiny's NTCD-M3 ranked highest (safest), while SER-109 appeared down the list in sixth place. Oligofructose, which has been associated with diarrhoea and abdominal pain, did not appear in the first eight places on the safety ranking of CDI treatments.

Nasal decolonisation also rises to the fore

A recent clinical study noted in an announcement by Destiny highlighted the role of nasal decolonisation in the prevention of post-surgical staphylococcal infections. Investors will remember that Destiny's home-grown Phase 3-ready product, XF-73 has been successful in Phase 2b in this indication and the results were summarized in our note.

While the large and successful study presented at the recent IDWeek virtual conference demonstrated the superior nasal decolonisation of a nasal antibiotic compared to a nasal antiseptic, the antibiotic used has been associated with the selection of resistance, which we explore further in this note.

Valuation unchanged

Our valuation for Destiny Pharma remains unchanged despite the recent supportive news flow as we await news on partnering and the Phase 3 studies. The fair value of Destiny Pharma remains at £200.2m or 335p per share.

Summary Financials

£'000s, y/e 31 December	2017A	2018A	2019A	2020A	2021E
Revenues					
EBIT	-3,222	-6.084	-5,585	-6,553	-5,947
Basic EPS (p)	-8.5	-11.9	-10.8	-12.0	-8.6
Net Assets	16,686	12,257	7,759	12,436	7,893
Net Cash	16,724	12,061	7,480	9,744	5,329*

*Source: Company historic data, ED estimates. *Including illustrative debt simulating a $10m up-licensing payment*

Company Data

EPIC	DEST
Price (last close)	112p
52 weeks Hi/Lo	189p / 62p
Market cap	£67m
ED Fair Value - per share	£200.2m 335p
Net cash H1'21	£7.1m
Avg. daily volume	48,828

Share Price, p

Source: ADVFN

Description

Destiny Pharma (Destiny) is a clinical development-stage biotech company developing novel anti-infectives to prevent and treat infections caused by sensitive and resistant bacteria and viruses.

Destiny's proprietary drug discovery platform has generated a number of active antimicrobials including its lead drug XF-73. XF-73 has successfully completed a Phase 2b clinical study under a US IND for the prevention of staphylococcal post-operative infections. In September 2020, Destiny started a preclinical collaboration to prevent COVID-19 diseases by stimulating innate immunity. In November 2020, Destiny acquired the Phase 3-ready asset NTCD strain M3 for the prevention of *C.difficile* infections (CDI).

Destiny's shares are listed on AIM.

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Destiny's lead product shines against the competition

Investors will remember that Destiny Pharma acquired exclusive worldwide rights to NTCD-M3, the only single strain microbiome product in development for the treatment or prevention of recurrent CDIs, in November 2020. Partly due to the pandemic – where many more fragile patients are hospitalised – there has been **a growing appreciation** of the importance of CDIs amongst hospitalised patients.

There is a good reason for this because **CDIs are the most common cause of healthcare-associated infections in US hospitals**. Part of the burden of CDIs is related their recurrence as a sequence of infections, in the same patient. This is the result of the hardiness of *C.difficile* spores, which can resist first-line treatments such as antibiotics, that appear to be active against the vegetative (non-spore) form of *C.difficile*, but are not active against its metabolically inert spores.

Competitors to Destiny's NTCD-M3 product include antibiotics, which largely retain their first-line status because not all patients recur, they are cheap, generic and are known pharmaceutical entities. After first-line antibiotics, treatment options include the branded antibiotic Dificid (fidaxomicin) which, like Zinplava below, is an expensive product. At the other end of the spectrum is the very expensive monoclonal antibody Zinplava (bezlotoxumab) which was approved by the FDA in 2016. Because of Zinplava's cost, it is reserved for the most recurrent of patients and has to be administered intravenously in hospital. Sales of both branded products have been limited and Merck did not report either Dificid or Zinplava revenues in 2020.

More passive than antibiotics, microbiome-directed approaches include single sugars such as oligofructose (see below), that are largely metabolised by commensal anaerobic bowel bacteria to suppress toxigenic *C.difficile* strains, the faecal matter-derived and single or mixed bacterial approaches to modulating the lower bowel microbiome.

NTCD-M3's advantages against microbiome competitors

Destiny's consultant and Advisory Board member Professor Dale Gerding presented at the *C.difficile* International Conference on Friday November 5, and his presentation included an efficacy spectrum of adjunctive treatments to treat or prevent CDI recurrences where Destiny's single-strain NTCD-M3 microbiome-directed approach ranked in second place.

Microbiome approaches to treating CDI recurrences are either a single-species (like NTCD-M3), multi-species consortia (like VE303, below) or less defined faecal-derived bacterial mixes (like SER-109, below), which either inhabit the ecological niche that would be occupied by toxigenic *C.difficile* strains, or supply a more normal microbiome, respectively. In Professor Gerding's efficacy analysis, NTCD-M3 ranked second highest, just below oligofructose. Oligofructose is a food additive oligosaccharide which is not metabolised until the lower bowel and seems to have been considered for the primary prevention of CDI's, rather than the secondary prevention of the first or multiple CDI recurrences.

Furthermore, in Professor Gerding's comparison of the safety of the proposed and available treatments for CDIs, Destiny's NTCD-M3 ranked highest on the clinical safety assessment while oligofructose – which has been associated with diarrhoea and abdominal pain – did not appear in the first eight places on the safety list of CDI treatments. The last clinical trial with oligofructose was reported in 2005 and the product may not now be in development for CDI.

Destiny's more direct competitor in the microbiome space, SER-109 from Seres Therapeutics, was back in eighth place in Professor Gerding's efficacy analysis, and, in the safety comparison, SER-109 appeared down the list in sixth place. SER-109 created a stir in the summer of 2020 when Seres reported the first successful Phase 3 microbiome intervention in the treatment of recurrent CDIs. However, SER-109 is a faecal matter transplant (FMT)-derived, and less defined microbiome product, where faecal matter is treated with alcohol to kill vegetative cells to leave the remaining spores.

FMT-derived products have been criticised as having variable yields of spores that are dependent on the characteristics of the donors. SER-109 demonstrated an 11.1% recurrence rate in the single Phase 3 study of 182 patients randomised 1:1 to placebo, with the placebo arm having a 41.3% recurrence rate. By comparison, NTCD-M3's superior 5% recurrence rate was seen in a study of 157 patients, randomised 3:1 active to placebo arms, and a 30% recurrence rate in placebo patients in Phase 2. In addition, more than a year after their Phase 3 results, Seres have not yet filed SER-109 for FDA approval, almost certainly because the study was too small to determine safety on a new FMT-derived product and the FDA is probably awaiting the read-out of Seres's larger, open-label extension study.

Other competitors to Destiny's single-strain NTCD-M3 microbiome product, (where Destiny has already negotiated the size, end points and other parameters of the Phase 3 study with the FDA), are at earlier stages. Finch Therapeutics' Phase 2 Data for CP101 for the prevention of CDI is an FMT-derived product which demonstrated a 25.5% CDI recurrence (in 101 patients) at 8 weeks, against a placebo arm (of 96 patients) with a 38.8% recurrence rate.

Vedanta Biosciences, a private US biotech company recently presented data on its 79-patient Phase 2 study of VE303, randomised 2:1 active *vs.* placebo groups. VE303 achieved a 13.8% recurrence rate against 45.5% for placebo (*cf.* NTCD-M3's 5% recurrence rate and 30% recurrences in placebo patients). Vedanta has not yet agreed a Phase 3 protocol with the FDA for VE303; an eight-strain defined bacterial spore consortium. While safety and efficacy will be the most important facets of a microbiome (or non-microbiome) product to treat CDIs, manufacturing complexity (and therefore cost) and dosing will also have significant roles to play.

Mixed species products will have much higher manufacturing costs than Destiny's NTCD-M3 single strain spore product. In addition, while NTCD-M3 is dosed as a single capsule for seven days, Vedanta's VE3030 Phase 2 study involved patients ingesting ten capsules daily for 14 days.

XF-73's profile supported by recent data

The profile of Destiny's home-grown product – **the antibacterial agent XF-73 for the nasal decolonisation of staphylococci prior to surgery** – has also benefitted from recently published supporting data.

A clinical study noted in an announcement by Destiny highlighted the role of nasal decolonisation in the prevention of post-surgical staphylococcal infections. This large and successful study was presented at the recent US IDWeek virtual conference and demonstrated the superior nasal decolonisation of a nasally-administered antibiotic, compared to a nasal antiseptic. The antibiotic used however, was mupirocin calcium nasal ointment (Bactroban Nasal), which, while it remains a branded product, has an unfortunate association with the development of resistance. Mupirocin is unique in its class of antibiotics and the free base active ingredient has been available for many years as a dermal ointment for the treatment of primary and secondary skin infections.

To address an impending patent expiry, Bactroban Ointment was moved to over-the-counter (OTC) status in some markets like New Zealand but this unrestricted use resulted in high levels of community mupirocin resistance. OTC status was subsequently reversed in New Zealand. Prior to these events, the FDA, had never approved the Bactroban Nasal formulation for more general nasal decolonisation, such as the prevention of post-surgical infections, because of the fear of generating mupirocin resistance in hospitals. In the US, for this reason, Bactroban Nasal remains indicated only for the eradication of nasal colonisation as a result of an MRSA (for example) hospital outbreak.

This backdrop reinforces XF-73's profile as an active antimicrobial agent that has demonstrated in a Phase 2b study that it can effectively decolonise the nasal carriage of staphylococci in surgical patients. Furthermore, as a new agent, resistance against XF-73 has not been observed or generated experimentally.

While the recent study on mupirocin highlights the clinical need and efficacy of nasal decolonisation, regulators and infectious disease physicians are unlikely to favour the product used, Bactroban Nasal, in that role as an approved product. However, without mupirocin's resistance baggage, XF-73's role in that indication has been supported by the recent study.

Licensing prospects

In both cases, XF-73 and NTCD-M3 are Phase 3-ready products, although unlike NTCD-M3, the agreement of the FDA and details of the XF-73 Phase 3 protocol have yet to be announced. But when the profiles of both products are compared to their competition, **we remain confident in assuming at least one licensing transaction** in our model.

Income Statement & Forecasts

£'000s, y/e 31 December	2017A	2018A	2019A	2020A	2021E
IFRS Income Statement					
Total revenue					
Administration expenses	-1011	-1800	-1887	-1925	-2100
R&D	-387	-3546	-3800	-4500	-3816
Other income (expense)	-613		306	12	
Share-base payments & exceptionals	-710	-738	-204	-139	-25
Depreciation & amortisation	-2	-4			-6
Reported EBIT	**-3222**	**-6084**	**-5585**	**-6553**	**-5947**
Reported profit before tax	**-3211**	**-6008**	**-5521**	**-6481**	**-5929**
Taxation	234	841	813	1070	800
Reported Net income	**-2977**	**-5167**	**-4708**	**-5411**	**-5129**
Basic EPS (p)	-8.45	-11.86	-10.75	-11.97	-8.58
Diluted EPS (p)	-8.45	-11.86	-10.75	-11.97	-8.58

Source: Company historic data, ED estimates

Balance Sheet & Forecasts

£'000s, at y/e 31 December	2017A	2018A	2019A	2020A	2021E
Assets					
Non-current assets					
Tangible assets	22	30	33	26	40
Intangible assets				2261	2261
Total non-current assets	22	30	33	2280	2301
Current assets					
Trade and other receivables	277	931	911	1172	547
Cash and equivalents	11724	7061	7480	9744	12524
Total current assets	17061	13028	8525	11425	13678
Total assets	17083	13058	8557	13705	15979
Equity and liabilities					
Equity					
Ordinary shares	436	436	439	598	598
Share Premium	17292	17292	17296	27086	27091
Retained earnings	-1042	-5471	-9976	-15247	-19796
Equity attributable to the company	16686	12257	7759	12436	7893
Total equity	16866	12257	7759	12436	7893
Current liabilities					
Trade and other payables	152	404	514	726	349
Total current liabilities	397	802	798	1268	892
Total non-current liabilities					-7194*
Total equity and liabilities	17083	13058	8557	13705	15979

*Source: Company historic data, ED estimates, * Illustrative debt representing a $10m upfront licensing transaction payment*

Cash Flow Statements & Forecasts

£'000s, y/e 31 December	2017A	2018A	2019A	2020A	2021E
Profit before taxation	-3211	-6008	-5521	-6481	-5929
Depreciation & amortisation	2	10	18	17	6
Share-based payments	710	738	204	139	211
Movements in working capital	165	381	-83	91	249
Net cash generated by operating activities	-2153	-4721	-4631	-5492	-4411
Investing activities					
CapEx on tangibles & intangibles	-23	-18	-21	-2264	-28
Other investing activities	-4990	76	5063	27	18
Net cash used in investing activities	-5013	58	5043	-2192	-10
Financing activities					
Proceeds from issue of shares	17406		7	9949	6
Movements in debt					7194*
Net cash from financing activities	17409		7	9949	7201
Cash & equivalents at beginning of year	1481	11724	7061	7480	9744
Cash & equivalents at end of year	**11724**	**7061**	**7480**	**9744**	**12524**

*Source: Company historic data, ED estimates, * Illustrative debt representing a $10m upfront licensing transaction payment*

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