Destiny Pharma

The best possible scenario

29 March 2021

As promised, Destiny has announced the top-line results of its Phase 2b clinical study of XF-73 in the prevention of staphylococcal post-surgical infection. As an active antimicrobial agent, we had expected XF-73 to have efficacy in this indication, but the strength of the data was an outstanding result. Specifically, there was a greater than 99% reduction in nasal carriage achieved in just 24 hours, the primary endpoint of the study, compared to placebo. Destiny is now in the attractive but unusual situation (amongst UK biotech companies) of having two Phase 3-ready assets: XF-73 and also NTCD-M3 targeting prevention of *C.difficile* infection recurrence.

In Destiny's Phase 2b study of the XF-73 nasal formulation, the primary endpoint of microbiological eradication of *Staphylococcus aureus (S.aureus),* including MRSA*,* nasal carriage just before surgery, compared to placebo, was **met with high statistical significance** (p<0.0001). As expected, the XF-73 nasal formulation was **safe, with no treatment-related adverse events**. Investors will remember that the coronavirus pandemic had delayed this study and had also resulted in fewer patients treated. In retrospect, the pandemic and protocol revisions did Destiny a favour by treating a smaller number of patients, but enriching them by recruiting only those with proven *S.aureus* carriage. This is one of the learnings from the study, which we discuss further in the body of this note.

Work on the design of a Phase 3 program following **the success of the Phase 2b study is now underway and will be important for partnering discussions**. On partnering, our model assumes a single global licensing transaction for the XF-73 nasal product later this year. Those assumptions remain unchanged, although we now recognise that the success of the Phase 2b study may encourage Destiny to sign regional licensing transactions that fund the Phase 3 program, while retaining rights in other markets until a later stage, in order to generate higher shareholder value.

Cost-effective R&D

Destiny have also recently announced an agreement with the US National Institute of Allergy and Infectious Diseases (NIAID) to evaluate the preclinical safety of a dermal formulation of XF-73. The NIAID know XF-73 very well, having conducted the previous Phase 2a study on the nasal formulation of XF-73, and this new collaboration should provide continued validation of XF-73 as a novel antimicrobial. We have not made any changes to our financials as a result of this cost-effective outsourcing of R&D to the NIAID as Destiny's costs will largely be limited to clinical trial supplies.

Valuation updated for progress

Our financial forecasts will not change until Destiny's FY 2020 results due on April 14, but our valuation has been updated after the XF-73 clinical trial results. **Our fair value of Destiny Pharma has increased to £213.6m (357p per share) from £156.9m (262p per share) as a result of Destiny becoming a company with two Phase 3-ready programs.**

Summary Financials

£'000s, y/e 31 December	2017A	2018A	2019A	2020E	2021E
Revenues					
EBIT	-3,222	-6.084	-5,585	-6,659	-5,944
Basic EPS (p)	-8.45	-11.86	-10.75	-9.68	-8.40
Net Assets	16,686	12,257	7,759	12,367	7,364
Net Cash	16,724	12,061	7,480	10,559	5,175

Source: Company historic data, ED estimates

Company Data

EPIC	DEST
Price (last close)	159.5p
52 weeks Hi/Lo	162p / 31p
Market cap	£95m
ED Fair Value - per share	£213.6m 357p
Est. net cash FY'20*	£10.6m
Avg. daily volume	131,080

*Based on last offering and estimated costs.

Share Price, p

Source: ADVFN

Description

Destiny Pharma (Destiny) is a clinical development-stage biotechnology 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).

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XF-73's Phase 2b results exceed expectations

Destiny Pharma have successfully completed the Phase 2b study of the nasal formulation of the novel antimicrobial agent, XF-73, in the eradication of post-surgical infections in high-risk, open-heart surgery patients.

In XF-73-treated patients, mean *S.aureus* nasal carriage was reduced by 99.5%, or more than 99% compared to placebo ($p<0.0001$) with high statistical significance maintained in both the per protocol, and intent to treat (the latter including any drop-outs) populations. The secondary endpoints that included the measurement in the reduction in *S.aureus* carriage 24 hours before surgery, also favoured the XF-73 treatment arm. The administration of XF-73 in the study protocol used four doses of XF-73 in the 24 hours prior to surgery, and one just after wound closure.

This compares very favourably in terms of surgical scheduling, with the off-label and now discontinued competitor, Bactroban Nasal, which is administered twice daily (morning and evening) for five days before surgery, usually prior to hospital admission.

The XF-73 nasal formulation is safe and well-tolerated with no treatment-related adverse effects.

While the coronavirus pandemic had resulted in a delay to this study's top line results announcement, the amendments of the protocol have also provided some advantages. Originally, 200 patients could have been admitted to the study and may or may not have been colonised by *S.aureus*. The protocol modifications resulted in an enriched culture-confirmed study population of 124 patients and probably assisted in the demonstration of the dramatic benefit over placebo.

One of the other effects of treating a smaller number of patients is that the number of surgical infections was likely to be co-ordinately smaller. Indeed, no post-operative surgical infections were detected in the study. The Phase 2b study therefore provides clear-cut microbiological validation that XF-73 can rapidly eliminate nasal *S.aureus* carriage in high-risk surgical patients if administered prior to, and just after surgery.

It is virtually inconceivable that, after demonstrating such a statistically significant difference over placebo in the primary microbiological endpoint, a reduction in post-operative infections would also be observed if the Phase 3 includes enough patients. The study also gives Destiny and its partners, additional insight into the size and patient selection for the Phase 3 study.

All eyes turn to partnering options

We continue to assume that Destiny will partner XF-73 nasal and we have forecasted a $10m (£7.69m) upfront payment (illustrated as debt in our financials) before the end of FY 2021. This would be a considerable validation of Destiny's development heritage, and a track record on which to develop and partner the other assets in its portfolio. While the positive Phase 2b study results now make this transaction more likely, it could be argued that Destiny have more than just binary partnering options, after the Phase 2b study.

The question outstanding from the Phase 2b study is how many patients have to be treated in order to demonstrate a statistically significant reduction in post-surgical staphylococcal infections. This is an important number for Destiny's partners, since it determines their investment in the product in addition to the upfront, milestones and royalties payable to Destiny.

It is also an important reimbursable endpoint for payers since the costs of post-surgical infections, including the extra days of hospitalisation, are easily quantifiable. Logically, for an active antimicrobial that has already demonstrated microbiological success in Phase 2b, success in demonstrating reduced post-surgical infections should logically follow, as long as the Phase 3 study is large enough to detect a difference between active and placebo arms.

Investors will remember from our initiation note that about a third of surgical patients are colonised by *S.aureus* in their noses, while in about 2% of surgical patients, this colonisation goes on to autoinfect the patients' surgical incisions. Ironically, the pandemic, which brought about a delay to the Phase 2b study also provided an upside since the FDA signed-off of a protocol amendment that reduced the number (and costs) of patients in the study from 200 to 124. The recruitment criteria were also altered to exclude those patients who were not colonised by *S.aureus* at the start of dosing.

Since Destiny's Phase 2b study has demonstrated that the XF-73 nasal product can eliminate *S.aureus* nasal colonisation after application of four doses in the 24 hours prior to surgery, and then one dose after, it would be pointless to delay surgical procedures by a day or more in determining which patients are culture-positive, since the cost of treating all high-risk surgical patients is likely to be less than the costs and delays in testing.

All these learnings and more from the Phase 2b study will help Destiny's potential partners cost up their financial commitments in developing the XF-73 nasal product. Since these results are so compelling, we have wondered if partnering has to be so binary as licensing the XF-73 nasal product to one partner for all markets. An alternative would be to license one or two individual markets initially, in order to fund the Phase 3 study, while keeping other markets for a later transaction, for example, after the Phase 3 study results. Thus, a higher valuation transaction could accrue to Destiny's shareholders. We have however, maintained our valuation model of XF-73 as a single, global transaction for now.

XF-73 indication expansion continues to dermal infections

The potential for XF-73 may not just be in the nasal product. Destiny recently announced an agreement with the US National Institute of Allergy and Infectious Diseases (NIAID) to evaluate the preclinical safety of a dermal formulation of XF-73 for the treatment of skin infections. The NIAID know XF-73 very well, having conducted the US Phase 2a study on the nasal formulation of XF-73 and this new collaboration should provide continued validation of XF-73 as a novel antimicrobial. We have not made any changes to our financials as a result of this cost-effective outsourcing of R&D to the NIAID as Destiny's costs will largely be limited to clinical trial supplies.

Continued pipeline expansion into CDI and COVID-19 prevention products

Destiny's biotherapetic or "microbiome" pipeline also continues to progress and includes the NTCD M3 biotherapeutic for the prevention of recurrent *C.difficile* infection (CDI), which, like the XF-73 nasal product, is also a Phase 3-ready asset, and the earlier-stage SPOR-COV grant funded co-development project for the prevention of COVID-19 and other respiratory infections.

Valuation implications of the positive Phase 2b study

Destiny's success, as measured by the elimination of microbiological carriage in the primary endpoint of the Phase 2b study, demands that we update our valuation to reflect that Destiny Pharma is now a rare case amongst UK biotech companies by having two fully-owned Phase 3-ready assets. A recent publication has updated the probabilities of success for small molecule drugs and one of the few reasons for an upward adjustment for a product in development was listed as the meeting of a primary endpoint in a clinical trial.

Prior to the Phase 2b study results for the XF-73 nasal product, our probability adjustment was 35%; from which our previous £156.9m, or 262p per share valuation was derived. The recent update to small molecule probabilities of success do not exactly define a revised probability of success for Destiny's XF-73 nasal product since average historical rates for small molecules have been 59% in Phase 1, dipping to 33% in Phase 2 (due to the greater number of failures in Phase 2), and rising again to 59% between Phase 3 and before product registration.

With Destiny's XF-73 Nasal product now firmly out of Phase 2, but in planning for Phase 3, we have used an interim probability of success of the asset of 45% which leaves us scope for a further increase, once there is more visibility on the start of the Phase 3 study.

The positive Phase 2b study results for Destiny's XF-73 nasal product have resulted in our valuation increasing to £213.6m, or 357p per share.

Financials

Consolidated Income Statement & Forecasts

£'000s, y/e 31 December	2017A	2018A	2019A	2020E	2021E
IFRS Income Statement					
Total revenue					
Administration expenses	-1011	-1800	-1887	-1850	-2100
R&D	-387	-3546	-3800	-4000	-3816
Other income (expense)	-613		306	25	
Share-base payments & exceptionals	-710	-738	-204	-117	-25
Depreciation & amortisation	-2	-4		-9	-2
Reported EBIT	**-3222**	**-6084**	**-5585**	**-6659**	**-5944**
Reported profit before tax	**-3211**	**-6008**	**-5521**	**-6632**	**-5828**
Taxation	234	841	813	839	800
Reported Net income	**-2977**	**-5167**	**-4708**	**-5793**	**-5028**
Basic EPS (p)	-8.45	-11.86	-10.75	-9.68	-8.40
Diluted EPS (p)	-8.45	-11.86	-10.75	-9.68	-8.40

Source: Company historic data, ED estimates

Consolidated Balance Sheet & Forecasts

£'000s, at y/e 31 December	2017A	2018A	2019A	2020E	2021E
Assets					
Non-current assets					
Tangible assets	22	30	33	26	24
Goodwill				2308	2308
Total non-current assets	22	30	33	2333	2332
Current assets					
Trade and other receivables	277	931	911	560	277
Cash and equivalents	11724	7061	7480	10559	12868
Total current assets	17061	13028	8525	11135	13161
Total assets	17083	13058	8557	13469	15493
Equity and liabilities					
Equity					
Ordinary shares	436	436	439	696	696
Share Premium	17292	17292	17296	27439	27464
Retained earnings	-1042	-5471	-9976	-15768	-20796
Equity attributable to the company	16686	12257	7759	12367	7364
Total equity	16866	12257	7759	12367	7364
Current liabilities					
Trade and other payables	152	404	514	818	152
Total current liabilities	397	802	798	1102	436
Total non-current liabilities					-7692
Total equity and liabilities	17083	13058	8557	13469	15493

Source: Company historic data, ED estimates

Consolidated Cash Flow Statements & Forecasts

£'000s, y/e 31 December	2017A	2018A	2019A	2020E	2021E
Profit before taxation	-3211	-6008	-5521	-6632	-5828
Depreciation & amortisation	2	10	18	9	2
Share-based payments	710	738	204	117	25
Movements in working capital	165	381	-83	656	-383
Net cash generated by operating activities	-2153	-4721	-4631	-5038	-5500
Investing activities					
Acquisitions				-2308	
Capital expenditure on tangibles	-23	-18	-21	-2	
Other investing activities	-4990	76	5063	27	116
Net cash used in investing activities	-5013	58	5043	-2283	116
Financing activities					
Proceeds from issue of shares	17406		7	10400	
Movements in debt					7692
Net cash from financing activities	17409		7	10400	7692
Cash & equivalents at beginning of year	1481	11724	7061	7480	10559
Cash & equivalents at end of year	**11724**	**7061**	**7480**	**10559**	**12868**

Source: Company historic data, ED estimates

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