Destiny Pharma plc

XF-73 is 'The Real Deal'

20 October 2023

With Destiny's lead drug now licensed to Sebela Pharmaceuticals in preparation for its Phase 3 study, Destiny's second Phase 3-ready drug (XF-73) is next up for partnering and the recent publication and XF Pipeline Update burnished its profile for the benefit of investors and potential partners. As one key opinion leader at the event noted, "XF-73 is the real deal."

Publication enhances XF-73's profile

Destiny announced the publication of a microbiological study that tested XF-73's activity against more than 2,500 clinical isolates of *Staphylococci*. XF-73 was found to be **active against all isolates tested, irrespective of whether they were sensitive or resistant to 22 other antibiotics.** This expands XF-73's existing profile and earlier data that not only showed that it retained activity against a smaller number of recent clinical isolates, including multi-drug resistant (MDR) strains, but that those strains did not develop resistance to XF-73 after repeated passage. In the vernacular of infectious diseases, XF-73 has a low propensity for engineering bacterial resistance.

This is important to regulators since, in contrast to XF-73, the most commonly used antibiotic for nasal decolonisation – mupirocin calcium (Bactroban Nasal) – **does have a resistance problem**, illustrated soon after it became available over the counter in New Zealand (resulting in its withdrawal), and by the very narrow label given to Bactroban Nasal by the FDA (only for the decolonisation by methicillin-resistant *S.aureus* (MRSA) strains as part of an outbreak control intervention). Destiny's publication noted the activity of XF-73 against both MRSA and mupirocin-resistant *S.aureus* strains.

It is also important that the publication demonstrated XF-73's activity not just against MDR *S.aureus* strains, including MRSA, but **against 15 other staphylococcal species**. While most post-surgical infections are the result of autoinfection by the patient's own *S.aureus* strains (and sometimes MRSA strains) that are (probably transient) commensals in the noses of about a third surgical patients, nasal carriage of non-*S.aureus* (or coagulase-negative) staphylococcal can also result in post-operative infections.

Typically, coagulase-negative wound infections are rarer than *S.aureus* infections and in the past have been considered less pathogenic although **biofilm-associated strains are very difficult to eradicate once established**. However, with more elderly and frail patients in hospitals, and the rise in surgical procedures in this patent population, post-operative coagulase-negative staphylococcal infections could be an issue and their decolonisation by XF-73 Nasal should be reassuring to both infectious disease specialists and drug regulators.

XF Pipeline and Valuation

We provide our summary of Destiny's XF Pipeline Update and presentations in the body of this note.

Our fair value for Destiny Pharma plc remains unchanged at £254.7m (or 279 pence per share).

Summary Financials

£'000s, y/e 31 December	2020A	2021A	2022A	2023E	2024E
Revenues					
EBIT	-6,553	-6,287	-7,776	-7,833	-6,353
Basic EPS (p)	-12.0	-8.9	-9.3	-7.4	-5.7
Net Assets	12,436	7,509	7,626	8,487	3,208
Net Cash	9,744	4,646	4,903	5,941	1,795

Source: Company historic data, ED estimates.

Company Data

EPIC	DEST
Price	55p
52 weeks Hi / Lo	61p / 26p
Market cap	£52m
ED Fair Value - per share	£254.7m 279p
Reported cash end H1 23	£9.8m
Avg. daily volume	499k

Share Price, p

Source: ADVFN

Description

Destiny Pharma (Destiny) is an innovative clinical-stage biotechnology company focused on the development and commercialisation of novel medicines that can prevent life-threatening infections.

The company's drug development pipeline includes two late-stage assets, NTCD-M3, a microbiome-based biotherapeutic for the prevention of *C.difficile* infection (CDI) recurrence, which is the leading cause of hospital-acquired infection (HAI) in the US, and XF-73 nasal gel, a proprietary drug targeting the prevention of post-surgical staphylococcal infections including MRSA.

Destiny's shares are listed on AIM.

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Notes from the XF pipeline update meeting

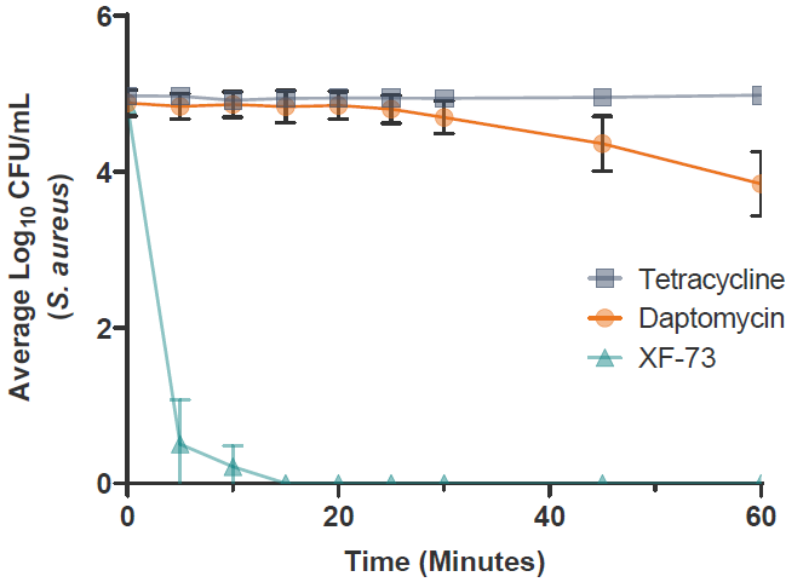
There were some important take-home points in the XF pipeline update. While some of them, like the anti-fungal activity of the XF series and the activity of the XF drug class against bacteria in biofilms, may have been little-known, the combination of the activity of XF drugs against *Candida albicans* in biofilms was new. In addition, the wider discussions gave important context to the development of XF-73 Nasal in particular.

The basics of XF-73

In the last presentation of the day, Destiny's CSO Bill Love reiterated the basic tenants of the XF drug platform. These are new drugs with a novel mechanism of action unrelated to other antimicrobials ("beyond antibiotics" was the phrase that Bill coined). Almost all antimicrobial agents, for example the β-lactam antibiotics like penicillin, **take time to act** because they inhibit bacteria as they grow. The same is true for inhibitors of protein RNA or DNA synthesis like the macrolides and mupirocin because they act only when bacteria grow. By contrast, **XF-73 acts directly on the bacterial membrane so kills bacteria very quickly** and doesn't need bacteria to grow.

This was illustrated in the company's slide below that showed that XF-73 killed more than 99.99% of bacteria within 5 minutes with no survivors after 15 minutes. This helps explain why XF-73 Nasal achieved nasal decolonisation of *S.aureus* in the Phase 2b clinical trial in about a day whereas the dosing schedule for Bactroban Nasal is over 5-days.

XF Drugs kill bacteria very rapidly



Source: Company presentation

Bill went on to discuss the data on studies that have failed to detect bacterial resistance to XF-73 in clinical isolates (in the recent paper discussed earlier in this note), and the inability to generate resistance to XF-73 over 55 passages *in vitro*.

We were reminded that XF-73 has broad-spectrum Gram-positive antimicrobial activity against bacterial strains that are both sensitive and resistant to other antimicrobial agents and that the XF platform has generated data demonstrating anti-fungal activity against *Candida* biofilms as well as activity against bacteria that reside in biofilms and are usually very difficult to treat with conventional antibiotics like mupirocin.

The luxury of choice (of indications)

While XF-73 Nasal's lead indication in the prevention of post-surgical staphylococcal infections has been well-telegraphed by Destiny, its potential use in the **prevention of those infections after reconstruction surgery following breast cancer** provided a useful discussion. Investors will remember that our model for XF-73 Nasal is based on the smaller number of orthopedic, cardiovascular and neurosurgical procedures where the implications of a post-surgical infection can have dire and expensive outcomes.

In many respects, the much larger number of reconstructive breast surgical procedures would make the demonstration of XF-73 to prevent post-surgical infections in a Phase 3 study much easier to conduct. While breast reconstruction surgery may not be perceived as such a high risk from the number of infections – probably because the outcomes of a post-operative infection of a hip replacement may not be as dire or as expensive as a complete surgical revision – their larger number and higher 13.5% rate of post-operative infection, which one of the Key Opinion Leader (KOL) speakers estimated pushes up the cost of a breast reconstructive surgery from $22,000 per patient to $79,000 per patient, makes a compelling pharmacoeconomic case for conducting the Phase 3 study of XF-73 Nasal in this population.

We have included the financial impact slide of surgical site infections (SSIs) in breast reconstruction, below.

Infection resulted in a mean increased cost of $16,737

Possible Additional Costs Associated with Device Infection

	2020 CMS Reimbursed Amount
Admission for postop infection (DRG 856)	$15,142
Expander removal (CPT 11971)	$2,531
Autologous Flap Reconstruction (DRG 582 + CPT 19364)	$24,923
Redo TE-implant reconstruction (DRG 582 + CPT 19357)	$22,336

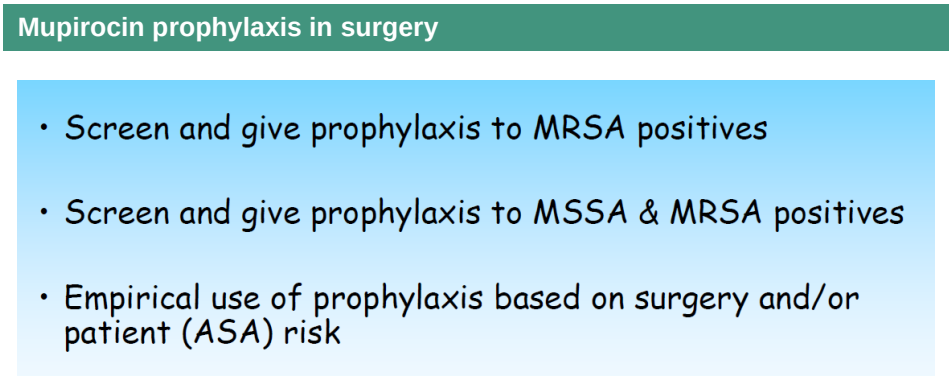
Source: Company presentation

The simple monetary cost of SSIs in breast reconstruction surgical patients underplays the time value and other impacts on patients' quality of life between an uncomplicated breast reconstruction procedure that takes about six months to recover from, and one complicated by a post-operative infection that takes about 15 months until a second surgical procedure can even be considered after a post-surgical infection.

These arguments are likely to be very persuasive to US payers and ex-US single-payer healthcare systems but, more importantly, gives Destiny's potential licensing partners for XF-73 Nasal the luxury of choice of indications, or even a sequence of indications.

Screening or prophylaxis

One of the presenter's slides, included below, discussed the strategies for the current prevention of post-surgical infections or SSIs:



Source: Company presentation

These strategies are also related to the evolution of Destiny's Phase 2b study protocol which was modified as a result of the pandemic to enrich for enrolled surgical patients that were colonised by *S.aureus*. While the slide above related to MRSA screening and prophylaxis as part of an outbreak control protocol (the US label indication for Bactroban Nasal which is also the off-label standard of care (SoC) in the prevention of post-operative staphylococcal infections), the strategy to prevent SSIs caused by sensitive or resistant *S.aureus* strains raises the same issue – that of the cost-effectiveness of screening, and then treating only colonised patients with XF-73 Nasal prior to surgery, or just applying XF-73 Nasal prophylaxis to all indicated surgical patients.

The previous arguments against prophylaxis for all surgical patients were related to the issues of mupirocin – the propensity for resistance, the 5-day before surgery treatment protocol (which, it was noted, results in about 50% compliance) and in the US, the off-label use for the prevention of post-operative surgical infections. **None of these issues are relevant to XF-73 Nasal** because resistance has not been demonstrated or generated with XF-73, treatment is only for about one day before surgery and XF-73 Nasal is expected to be approved in the prevention of post-operative surgical infection indication.

In addition, payers and healthcare providers may take the short treatment phase for XF-73 Nasal compared to mupirocin as another reason to treat all surgical patients with XF-73 Nasal and avoid the cost and time delays of swabbing to detect carriers and delaying surgery. This is also important since nasal carriage of *S.aureus* can be transient (or at least below the level of detection) meaning that a surgical patient would appear to be uncolonized and not be nasally decolonised on one day, but be colonised again on the day of their surgery. With Bactroban Nasal as the flawed Standard of Care (SoC) in the prevention of post-operative staphylococcal infections, as one of the KOLs put it, **XF-73 has the characteristics and potential to replace SoC and become the new SoC.**

In addition, while screening and prophylaxis is likely to continue through XF-73 Nasal's Phase 3 study, there may be good reasons to believe that in clinical practice, XF-73 Nasal prophylaxis could be given to all applicable surgical patients, saving the cost and time delays of screening.

In summary

We were left with a renewed appreciation for the magnitude of post-operative surgical site infections, the difficulties that they pose to clinicians in hospitals and the potentially larger opportunity they present to Destiny and its partners.

FINANCIALS

Income Statement & Forecasts

£'000s, y/e 31 December	2020A	2021A	2022A	2023E	2024E
IFRS Income Statement					
Total revenue					
Administration expenses	-1925	-2200	-2497	-3100	-2500
R&D	-4500	-3816	-4900	-4066	-3600
Other income (expense)		135	154		
Share-based payments & exceptionals	-139	-406	-534	-250	-250
Depreciation & amortisation				-2	-3
Reported EBIT	**-6553**	**-6287**	**-7776**	**-7833**	**-6353**
Reported profit before tax	**-6481**	**-6271**	**-7712**	**-7686**	**-6174**
Taxation	1070	932	1208	950	950
Reported Net income	**-5411**	**-5339**	**-6504**	**-6736**	**-5224**
Basic EPS (p)	-11.97	-8.92	-9.27	-7.38	-5.73
Diluted EPS (p)	-11.97	-8.92	-9.27	-7.38	-5.73

Source: Company historic data, ED estimates

Balance Sheet & Forecasts

£'000s, at y/e 31 December	2020A	2021A	2022A	2023E	2024E
Assets					
Non-current assets					
Tangible assets	18	36	25	25	26
Intangible assets	2261	2261	2261	2261	2261
Total non-current assets	2280	2297	2286	2287	2287
Current assets					
Trade and other receivables	1172	992	1410	1410	227
Cash and equivalents	9744	4646	4903	5941*	1795**
Total current assets	11425	5985	6501	7547	2268
Total assets	13705	8283	8796	9834	4555
Equity and liabilities					
Equity					
Ordinary shares	598	599	733	943	943
Share Premium	27086	27091	33044	39431	39431
Retained earnings	-15247	-20181	-26151	-31887	-37166
Equity attributable to the company	12436	7509	7626	8487	3208
Total equity	12436	7509	7626	8487	3208
Current liabilities					
Trade and other payables	726	218	173	349	349
Total current liabilities	1268	773	1107	1347	1347
Total non-current liabilities					
Total equity and liabilities	13705	8283	8796	9834	4555

*Source: Company historic data, ED estimates. *Including $1m upfront milestone from M3 licensing transaction. **including an estimated $1m milestone from XF-73 licensing transaction*

Cash Flow Statements & Forecasts

£'000s, y/e 31 December	2020A	2021A	2022A	2023E	2024E
Profit before taxation	-6481	-6271	-7712	-7686	-6174
Depreciation & amortisation	17	13	12	2	3
Share-based payments	139	406	534	250	250
Movements in working capital	91	-296	411		
Net cash generated by operating activities	-5492	-5090	-5892	-6631	-5150
Investing activities					
CapEx on tangibles & intangibles	-2264	-30	-1		-1
Acquisitions					
Other investing activities	72	16	65	147	178
Net cash used in investing activities	-2192	-15	64	147	178
Financing activities					
Proceeds from issue of shares	9949	7	6086	6737	
Movements in debt					
Net cash from financing activities	9949	7	6086	7522*	826**
Cash & equivalents at beginning of year	7480	9744	4646	4903	5941
Cash & equivalents at end of year	**9744**	**4646**	**4903**	**5941**	**1795**

*Source: Company historic data, ED estimates. *Including $1m upfront milestone from M3 licensing transaction. **Including an estimated $1m milestone from XF-73 licensing transaction.*

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