Destiny Pharma Plc

New Model Anti-Infectives

27 July 2020

Destiny Pharma is not just developing novel anti-infective drugs - its lead product XF-73 is in the US and European Phase 2b study for a new preventative indication that had not been awarded to <u>any</u> other drug before. The clinical study of XF-73, which has proven antimicrobial activity, is expected to report an interim review in August 2020. As anti-infectives have higher probabilities of success than other therapeutic areas, Destiny's destiny looks bright.

Not making the same mistakes

Many august healthcare organisations such as the World Health Organisation and US Centers for Disease Control have warned about the shortage of new antimicrobial agents to fight the global threat of antimicrobial resistance (AMR). However, many biotech companies have fallen into the trap of developing new anti-infective **treatments** in indications where there is **no unmet medical need**, or where generic **competition already exists**. Destiny Pharma's novel first drug neatly side-steps all of these issues by developing XF-73 for **the prevention** of post-surgical staphylococcal infections.

Destiny's near-term focus is on the Phase 2b clinical study of XF-73 cardiovascular surgery patients. Due to the coronavirus pandemic, Destiny had paused the study recruitment at 68 patients randomised out of a total of 200. Following the FDA's recent guidelines to drug sponsors on the conduct of clinical trials during the coronavirus pandemic, Destiny's fruitful discussions with the FDA have resulted in **recruitment recommencing** in earnest and is now up to 77 patients. A smart protocol adaption has been agreed which reduces enrolment to 125 patients without compromising the power of the study's primary endpoint. The study is now about two thirds enrolled.

This is a **positive development** since it saves Destiny money and time; and should ensure recruitment completion by the end of 2020. As an antimicrobial agent that has demonstrated the rapid reduction of nasal staphylococcal carriage in healthy volunteers, we regard the **probability** of demonstrating statistical significance in the primary microbiological endpoint in the placebo-controlled Phase 2b study, **as very high**.

We use a risk-adjusted NPV (rNPV) model to value Destiny Pharma based only on the development costs, our expectations of future milestone and licensing revenues for XF-73, and Destiny's cash. We discuss later the key valuation drivers and assumptions in our model which assumes that Destiny will license XF-73 in 2021 and the product will launch in 2024 with the US as the first market.

We value Destiny Pharma at £86.3m or 197p per share.

Summary Financials

£'000s, y/e 31 December	2017A	2018A	2019A	2020E	2021E
Revenues			306		
EBIT	-3,222	-6,084	-5,585	-5,927	-2,877
Basic EPS (p)	-8.45	-11.86	-10.75	-11.98	-4.68
Net Assets	16,686	12,257	7,759	2,539	515
Net Cash	16,724	12,061	7,480	2,534	511

Source: Company historic data, ED estimates

EPIC	DEST
Price (last close)	31p
52 weeks Hi/Lo	66p / 30p
Market cap	£14m
ED value / share	£86.3m / 197p
Net cash Dec '19	£7.5m
Avg. daily volume	64,418

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.

Destiny's proprietary drug discovery platform has generated a number of active antimicrobials including its lead drug XF-73. XF-73 is currently in a Phase 2b clinical study under a US IND for the prevention of staphylococcal post-operative infections.

Destiny's shares are listed on the UK London Stock Exchange's Alternative Investment Market.

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Investment proposition

Destiny Pharma is a clinical-stage biotechnology company developing novel anti-infectives to prevent and treat infections caused by sensitive and resistant bacteria. Destiny's proprietary drug discovery XF platform has generated a number of active antimicrobials including its lead drug XF-73. XF-73 is in a Phase 2b clinical study under a US IND for the prevention of staphylococcal post-operative infections. XF-73 is also active against many AMR bacteria.

Destiny listed its shares on AIM in September 2017, raising £15.2m to develop XF-73. This was followed by a regional development and commercialisation agreement for China and other Asian countries (excluding Japan) with **China Medical Systems Holdings** (CMS) that included an additional £3m investment. Destiny are a virtual clinical discovery and development company which means that the cash burn is typically low, despite the costs of clinical trials. Destiny achieves this low operating cash outflow (which was £4.6m and £4.7m in 2018 and 2019, respectively) by having a small infrastructure footprint and out-sourcing other non-proprietary discovery and developments tasks to contractors and collaborators, the relationships with whom, are managed by Destiny's clinical and discovery project managers. Destiny's earlier research programmes are also largely funded by non-dilutive grant funding.

Destiny are at a critical stage in their history where the top-line results of its Phase 2b clinical study are expected in 2020. We expect these to generate **partnerships for XF-73's Phase 3 development and commercialisation**. XF-73 has proven to be a potent topical anti-staphylococcal agent that reduces nasal colonisation to microbiologically undetectable levels in a day or so in healthy volunteers. As such, the Phase 2b clinical study in surgical patients with nasal staphylococcal carriage is expected to achieve its primary microbiological endpoint.

Recent financial results

Destiny's ongoing US and European Phase 2b study largely dictated its FY 2019 financial results with total operating expenses of £5.6m (£6.1m in FY 2018), comprising of £3.8m in R&D costs and £1.9m in other administrative costs (£3.5m and £1.8m in FY 2018, respectively). This outflow was lessened by a £0.8m R&D tax credit, and £0.3m in grant income (£0.8m and £0m in FY 2018, respectively). Grant income from four collaborations make Destiny's earlier stage discovery pipeline highly cost-effective.

Destiny's cash balance at the end of FY 2019 was **£7.5m** (vs £12.1m at end FY 2018 and £9.1m at the end of H1 19). As a company with few major costs outside of the Phase 2b clinical study, Destiny's prudent management can stretch its financial resources at least to the end of Q4 2021. The coronavirus pandemic has brought swings and roundabouts for Destiny: a pause to the Phase 2b study and therefore a delay in licensing the product, but a raised profile for AMR hospital infections, that would make a licensing transaction more likely.

Our valuation

We have linked an epidemiological model of high-risk surgeries in the US, EU, Japan and China to forecast the number of patients that could form the market for XF-73. In addition to pricing and other assumptions, we have produced a risk-adjusted NPV model of the value to Destiny's shareholders of the future milestones and royalties from a partnered XF-73.

After adding Destiny's cash at the end of December 2019, we determine a risk adjusted NPV valuation of £86.3m or 197 pence per share.

Introduction

Destiny Pharma is a clinical development-stage biotechnology company developing novel anti-infectives to prevent and treat infections that are caused by sensitive and resistant bacteria. Destiny's proprietary drug discovery platform has generated a number of active antimicrobials including its lead drug XF-73. XF-73 is currently in a Phase 2b clinical study under a US IND for the prevention of staphylococcal post-operative infections. The Phase 2b clinical study – which was paused due to the coronavirus pandemic – is nevertheless expected to complete recruitment by the end of 2020 which gives Destiny **about a year to partner** the product.

The old model of antimicrobial agent development

Antimicrobial agents comprise a large group of molecules that either inhibit or kill bacteria, fungi, viruses or protozoa. Antibacterial agents, like Destiny's XF-73 can be further classified in many ways. Those (like XF-73) that kill the bacteria exposed to the drug are termed bactericidal while those (like vancomycin, for example) that just inhibit bacteria until the host's immune system can eliminate them, are termed bacteriostatic.

Alternatively, antimicrobial agents can be classified by their source. Antibiotics (like penicillin and streptomycin) are produced by the fermentation of either fungi and bacteria respectively, while antimicrobial agents like XF-73 and nitrofurantoin, for example are synthetic, typically with a lower cost of goods than antibiotics, and made in a short chemical synthesis. The golden age of antibiotics that lasted until the 1980s was characterised by the discovery and development of many new classes of antimicrobial agents and their derivatives. These were able to be prescribed to treat a wide variety of community- and hospital-acquired infections like pneumonia or urinary tract infections, sexually transmitted diseases and even meningitis or septicaemia.

Two dynamics brought this golden age to an end however – the sequential expiry of the patents of the original antibiotics, and AMR. AMR, as typified by the methicillin-resistant *Staphylococcus aureus* (MRSA) was largely a hospital phenomenon for many years because of the selection pressure that came about from antibiotic use, concentrated in institutions with very sick and fragile patients. Over time, the selection of resistant strains brought about by continued antimicrobial agent use in nursing homes and smaller hospitals resulted in MRSA at least, appearing in the community. **AMR is frequently associated with treatment failure and higher costs**.

The sequential expiry of the patents on antibiotics contributed to the decline of pharmaceutical primary care field forces in many countries because the promotion of drugs that were generic generated no revenue for the originator company. Even before AMR rose to prominence, the reduction in branded antimicrobial agent sales in turn reduced the investment in pharmaceutical R&D and few novel antimicrobial agents were developed after the late 1980s.

Thus, the perfect storm was generated whereby AMR increased as a result of the continued usage of the existing antimicrobial agents, but big pharmaceutical companies had already closed down their discovery and developments efforts, so few new antimicrobial agents were available.

This is where biotechnology companies would typically fill the void and since the primary care (or retail) market was not viable, many companies stepped forward to address AMR infections in hospitals.

The track record of biotechnology company-developed antimicrobial agents has been patchy and in more recent times, because of the negative investment drivers listed in the table below, has been associated with bankruptcy filings, take-under transactions and serving as a cash shell by US anti-infective companies Archogen Inc., Optimer Pharmaceuticals Inc. and Tetraphase Pharmaceuticals, Inc..

Fortunately for Destiny, they have developed antimicrobial agents that **are unaffected by the clinical, regulatory and commercial issues** that have hindered these other anti-infective companies which developed **treatments** for bacterial infections, rather than, like Destiny, the **prevention** of infections.

A new model in anti-infectives

Destiny Pharma is an anti-infectives discovery and development company. Although the recent history of biotech companies in the anti-infective space has not been good, few of the anti-infective companies remaining other than Destiny have learned from these mistakes. There remain positive and negative drivers for anti-infective drug development which we summarise in the table below.

Positive and negative investment drivers in anti-infectives

Positive	Negative
Few new anti-infectives discovered	Short-course therapies are commercially challenging
Increasing antimicrobial resistance (AMR)	Indication-specific approvals
Effective, short-course treatment is curative	Frequent generic standard of care
Government and charitable funding of AMR	Many infections remain sensitive
COVID-19 raises AMR profile	Pharmacoeconomic arguments challenging
Preclinical activity is very predictive	Resistance can emerge & treatment fail
Hospital anti-infective cost is DRG absorbed	Primary care is infrequently detailed
Approval can be on microbiological endpoints	Antibiotics require fermentation to manufacture
Few preventative indications	Non-empiric therapy needs sensitivity testing
Compliance better for hospital-administered drugs	New agents reserved for later therapy lines

Source: ED

The right-hand side of the table comprises a litany of the drivers that caused the failures of the anti-infective companies in the last twenty years and, thankfully, **they do not largely apply to Destiny**. Indeed, Destiny are taking the short-course administration aspect – that makes it difficult for a single antimicrobial product to be commercially viable – head-on with their preventative indication which is by definition a shorter course than for most drugs, but in large numbers of pre-operative patients. On the positive side, most of those drivers apply to Destiny.

Destiny are developing an anti-infective series of drugs that are synthetic (cheap to manufacture) and have never been encountered in nature before. This latter point means that even recent clinical isolates of multi-drug resistant bacterial pathogens have not been found that are resistant to Destiny's XF-series of drugs. In addition, laboratory experiments have failed to train bacteria to become resistant to the XF series, in the same way as can be done with fusidic acid or streptomycin, for example.

Thus, an important aspect of Destiny's drugs is that **resistance to them is unlikely to be an issue** and this makes them ideal for empiric prescribing: prescribed to patients without the need to isolate and determine the antimicrobial sensitivity of the infecting or colonising organism.

For the treatment of sensitive infections, antimicrobial therapies are almost always short-course treatments that are curative. While this is a positive in the table above, it has made them much less commercially attractive than is the case for drugs to treat chronic diseases that have to be taken by the patient for the rest of their lives. Once again, Destiny's indication for its first drug XF-73 is a preventative one, meaning it can be administered to all patients undergoing high risk surgery, rather than waiting to treat the 0.3-2.3% of surgical patients who develop an infection which can be difficult and expensive to treat.

There are pharmacoeconomic arguments for not just treating the 30% of high-risk surgical patients who have been detected to carry *Staphylococcus aureus* in their noses, but the larger number of all high-risk surgical patients since staphylococcal nasal carriage can be transient (possibly below the level of detection), and there would be costs for screening all patients. In addition, the consequent delay to surgical procedures while the screening results are awaited is not compatible with typical surgical schedules.

When operating normally, hospitals tend to admit patients for elective surgical procedures and conduct the procedure either that same day, or the day after admission. XF-73 can be dosed on the day of admission and the day following surgery to align with this schedule. An unapproved competitor to XF-73 – Bactroban Nasal, ***mupirocin***) – has to be dosed **for five days before surgery** and is not compatible with normal surgical routines. The requirement for patients to self-administer Bactroban Nasal at home before hospital admission and the high level of pre-existing mupirocin resistance makes it an unpopular and unapproved competitor to XF-73.

The use of an unapproved (or off-label) drug is discouraged if an approved drug is also available, particularly in the US where the spectre of litigation would linger over a physician that prescribed an unapproved drug over XF-73, once approved for this indication, and the patient subsequently developed a post-surgical infection.

The focus of biotechnology companies developing antimicrobial agents to treat hospital infections is both a positive and negative driver.

Positive, because patients with either community-acquired infections that require hospitalisation like pneumonia or meningitis, or hospital acquired infections like post-surgical infections are serious and rarely go untreated.

The unmet need is therefore high. For hospital patients in the US, for example, each indication has a diagnosis related group (DRG) code, that determines the amount of money to cover the patient's treatment (which is either reimbursed by a health insurer or by one of the federal schemes) under the inpatient prospective payment system IPPS.

The more serious the condition or procedure, the higher the value of the DRG code. So, for neurological or cardiovascular surgical procedures, the drug costs are usually a tiny part of the total amount reimbursed (often running to **hundreds of thousands of dollars**).

This is a good thing because the cost of the antimicrobial agents rarely appears on the radar of payers as an issue.

However, new antimicrobial agents have been the victims off their own success since their use over short periods of time usually results in a cure. Adding to this, the so-called antibiotic stewardship, where new agents are kept in reserve until patients have failed the first- or second- line (and usually cheaper and generic) antimicrobial agents, has contributed to the failure of many anti-infective biotechnology companies.

Under these conditions where AMR infections are treated by new agents, the number of patients with resistant infections and the price premium (to generics) that the drugs can demand, has largely been the cause of **the failures of biotechnology-developed antibiotics** like dalbavancin, plazomicin and eravacycline.

Destiny Pharma has learned from the mistakes of others in developing an antimicrobial agent in a preventative indication (where no infection needs to be diagnosed) with an agent that is active to sensitive and AMR bacteria and is administered over 1-2 days to a large number of patients prior to their surgical procedure.

The value of antimicrobial agent companies

Despite the factors on the negative side of the investment drivers table above, antimicrobial agents remain an active area for investment, **and more so in 2020 than previously**.

AMR remains as an important threat to public health as the widespread use of antimicrobial agents provides the selection pressure for AMR bacteria to develop. The coronavirus pandemic has upped the tempo on the recognition on AMR. Indeed, those organisations like the WHO, CDC and Wellcome Trust who had highlighted AMR before the pandemic, have been warning that the large number of patients hospitalised as a result of coronavirus infections, often with secondary pneumonias, provide additional selection pressure.

The high-profile aspect of AMR also adds a public relations aspect to any investment (by acquisition or collaboration) by bigger pharmaceutical companies. Thus, antimicrobials remain valued assets for example, Merck & Co. acquired Cubist Pharmaceuticals Inc. for **$8.4bn** and Pfizer Inc. acquired Vicuron Pharmaceuticals Inc. for **$1.9bn**.

In addition, even though some of the more recent antimicrobial agent biotechnology companies have failed to successfully commercialise their new treatments, they have been acquired for significant sums. Tetraphase Pharmaceuticals Inc., the developer of eravacycline was recently acquired for **$43m upfront** and $16m in contingent value rights.

All three companies had existing classes (and therefore not new) antibiotic therapies approved by the FDA.

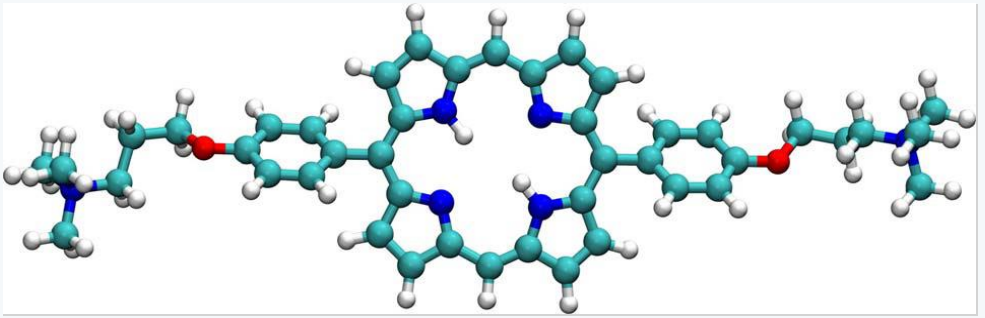
The XF-series of drugs and XF-73

The XF-series of synthetic antimicrobial agents are a novel group of microbiologically active drugs with and (like XF-73) without the addition of photodynamic (light-activated) activity, that are rapidly bactericidal and against many Gram-positive, and some Gram-negative bacterial pathogens.

The XF-series have demonstrated pre-clinical and clinical activity against sensitive and resistant Gram-positive pathogens including MRSA and vancomycin-insensitive *S.aureus* (VISA). A lack of resistance and bactericidal activity are important for preventive and empiric indications where a drug can be prescribed without first determining the antimicrobial sensitivity of the infecting pathogen (or, in the case of prevention, the presence of one). The XF-series have a broad spectrum bactericidal Gram-positive, and some Gram-negative activity that appears to be similar in effect to bactericidal antibiotics in the days before AMR.

A structure called a porphyrin ring lies at the centre of the XF series of drugs (the square in the molecular structure XF-73, below) and binds to the bacterial membrane resulting in lysis. The porphyrin ring is also what enables Destiny's expanded series of related drugs which are earlier in development, to have photodynamic antibacterial activity in addition to the non-photodynamic intrinsic antimicrobial activity of the XF-73.

Structure of XF-73 (exeporfinium chloride)



Source: Destiny Pharma

XF-73, the lead product in Destiny's pipeline (below) is in a Phase 2b clinical study for the prevention of post-operative surgical infections. This is a new indication, for which there is only off-label competition that has issues with AMR. XF-73 has been shown to be active against sensitive and resistant currently circulating clinical isolates of *S.aureus* – which are asymptomatically carried in the noses of about a third of people and can autoinfect wounds in up to about 2% of surgical patients – and nasal administration of XF-73 has been shown to reduce staphylococcal carriage down to below delectable levels in healthy volunteers.

The Phase 2b Clinical study of XF-73

Destiny is currently conducting a Phase 2b clinical study under a US IND for the prevention of post-surgical staphylococcal infections in (high-risk) cardiovascular surgical patients by intranasal administration of XF-73 (NCT03915470). Earlier studies have shown that XF-73 is active against a wide variety of Gram-positive and some Gram-negative bacterial pathogens, irrespective of whether they are resistant or sensitive to other antimicrobial agents. A previous study (NCT02282605) demonstrated a statistically-significant reduction in nasal *S.aureus* carriage by both XF-73 doses (0.5 and 2.0mg/g of nasal gel, given up to three times daily) over placebo in healthy volunteers.

Apart from the larger numbers of patients in the Phase 2b study, the main differences between the Phase 1/2a and Phase 2b protocols were the substitution of healthy volunteers with cardiovascular surgery patients and the use of only the higher 2mg/g dose, twice daily.

While there is no approved drug for the nasal decolonisation of *S.aureus* prior to surgery to prevent post-surgical infections, there is some off-label competition. GlaxoSmithKline's Bactroban Nasal (mupirocin calcium) is restricted in the US for the nasal decolonisation of only MRSA carriage as part of measures in controlling an MRSA outbreak. While some larger hospitals use it as non-MRSA *S.aureus* nasal decolonisation prior to surgery, it is not FDA approved for that indication and has been associated with an increasing prevalence of mupirocin resistance. In Europe, the label for Bactroban Nasal is more broadly based on *S.aureus* nasal decolonisation (originally in hospital outbreaks) so could be used for nasal decolonisation prior to surgery if, like in the US, mupirocin resistance were not a concern.

In addition to both markets, Bactroban Nasal's labelled treatment duration is for five days to achieve decolonisation. XF-73 has been, and is being, administered on the day of admission (in hospital) and the day after surgery. The reliance of patients to treat themselves for up to five days before hospital administration is a **significant compliance barrier** to Bactroban Nasal's use in the prevention of staphylococcal post-surgical infections.

XF-73 and the microbiome

In previous clinical studies of XF-73, administration has demonstrated rapid knock-down of *S.aureus* nasal colonisation in the first and second days of treatment, and then the gradual re-colonisation over longer observation periods. Investors may not appreciate that this is a good thing from a healthy microbiome perspective. The microbiome is the total bacterial colonisation of the body which in almost all people results in a positive balanced ecosystem.

So while complete sterilisation of the nose before infection to prevent post-operative infections may be a naïve aspiration, the less severe knock-down of Gram-positive bacteria including *S.aureus*, to below detectable (and auto-infectious) levels is preferable from a holistic perspective that allows the normal protective flora to be reconstituted, once the prophylactic course has completed. In earlier studies, this is exactly what XF-73 has demonstrated.

Recent protocol developments

The Phase 2b clinical study protocol was posted on clinicaltrials.gov in April 2019 and by the time Destiny's interim results announced in September 2019, the study had started enrolling subjects in the US and Europe. Recruitment at US sites was slower than expected and consequently, recruitment was expected to complete in early 2020, with a results announcement shifted from Q4 2019 to mid-2020. Ironically, we regard this delay as **mostly positive** since the slow US recruitment was due to study sites in larger teaching hospitals already using off-label Bactroban Nasal to prevent post-surgical staphylococcal infections.

These sites were unwilling to host a placebo-controlled study (which may have increased their incidence of post-operative infection). This meant a delay to the study results while sites were located that did not have an existing preventative protocol (possibly with a higher baseline rate of surgical infections, another positive point). But it should mean that once XF-73 is the only FDA-approved product for this indication, it would be enthusiastically endorsed by larger teaching hospitals without the **mupirocin resistance issues** of off-label Bactroban Nasal.

As a result of the coronavirus pandemic - which had effectively closed many hospitals and reduced surgical procedures down to minimal emergency procedures - most clinical trials were paused. At Destiny's full-year results in April 2020, it was announced that recruitment into the Phase 2b study had been paused at 68 patients out of a 200 target, but that, subject to the ongoing pandemic, study recruitment is expected to complete by the end of 2020 with an interim safety review in August 2020.

Destiny's recent announcement on the FDA's agreement of a study protocol amendment comes only weeks after the FDA had reached out to companies conducting clinical studies during the pandemic to discuss any alterations to study their protocols that would maintain the power of the studies, but enable enrolment and recruitment in a timely manner.

The FDA have agreed a number of protocol amendments with Destiny:

- Patients can be recruited into the study in a home nurse visit, rather than having to attend a hospital. At the peak, with up to 40% of UK coronavirus infections being contracted in institutions, the avoidance of an additional hospital visit should ease this recruitment constraint.
- Local polymerase chain reaction (PCR) screening tests at study sites can be conducted, rather than at central sites after Destiny provided validation data on the satellite site use of commercial test that is being used.
- The definition of microbiological intent-to-treat (micro-ITT) population was allowed.

The addition of the micro-ITT population is probably the most significant protocol amendment since it has the silver-lining for the study that adjusts the primary population for the efficiency analyses from modified-ITT to micro-ITT.

As the primary endpoint of the study remains microbiological – the significant reduction in *S.aureus* numbers between baseline and just before surgery – there may previously have been a mismatch between the larger number of patients that were positive by the very sensitive PCR test at baseline, but not microbiologically (as culture-positive has a much lower level of detection than PCR) just before surgery. The definition of the micro-ITT population defines a smaller number of patients that are culture-positive for *S.aureus* carriage at both time points to be included in the study, rather than a larger number of PCR-positive patients at baseline in order to have enough that were culture-positive just before surgery.

This protocol amendment therefore has the effect of **reducing (and actually enriching) the study population numbers** from an enrolment of 200 previously down to 125 that are culture-positive just before surgery. The transient nature of *S.aureus* nasal colonisation means that there may still be pre-operative patients that were culture-positive and enrolled in the study at recruitment, but were culture negative at baseline. The revised number of 125 patients recruited has been designed to have 80 culture-positive patients at baseline that would retain the statistical power of the study to detect the difference in the primary endpoint with 80 culture-positive patients just before surgery.

Now that the study has restarted, there are already 77 patients enrolled, or about two thirds of the new enrolment total has now completed. Thus, this amendment will save Destiny time in the completion of the study and at least the costs of screening a larger number of patients without compromising the power of the study on the primary endpoint.

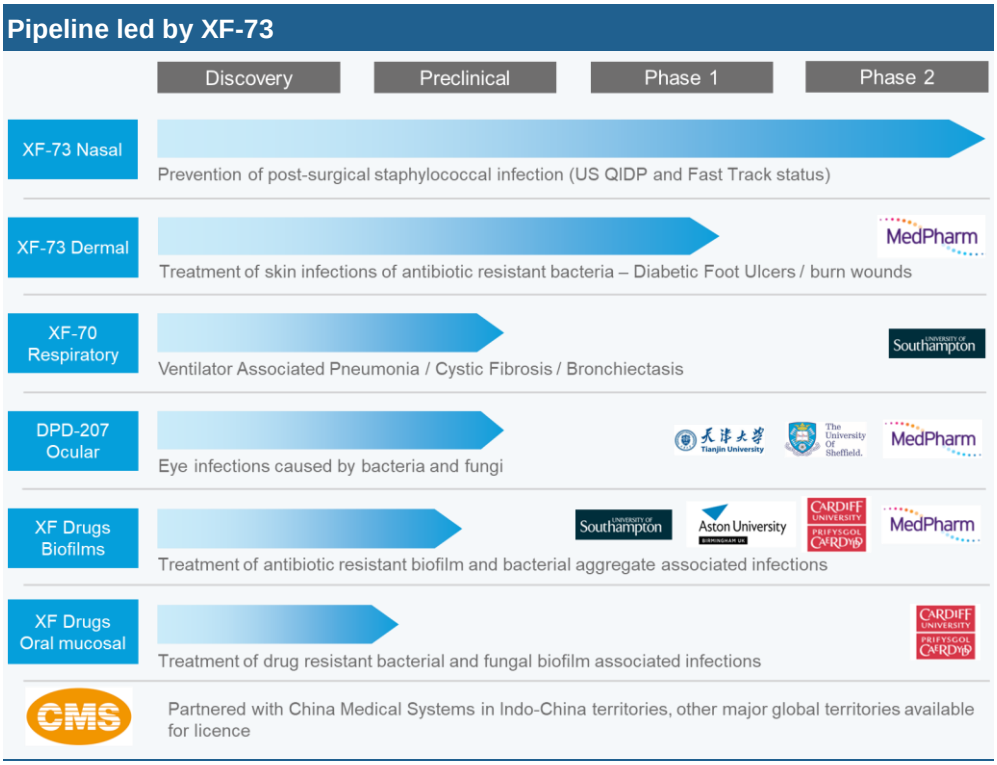
The study is also measuring a larger number of secondary endpoints including the number of post-operative infections and the use of rescue antibiotics after surgery if an infection is suspected, even if it is not detected (for example, if a post-operative patient spikes a fever). Even at 200 patients, it was probably not possible to show a statistically significant difference between XF-73 and placebo in these secondary endpoints but the direction of the data (how many more post-surgical infections in placebo patients) will aid the sizing and overall design of the Phase 3 study.

Destiny's Pipeline: cost-effective and not just XF-73

Beyond XF-73 Nasal for the prevention of post-operative surgical infections undergoing high-risk surgical procedures, Destiny's pipeline includes XF-73 for dermal (skin infection and colonisation) indications, and then other products, for example in ocular and biofilm indications. Destiny's pipeline beyond XF-73 is largely funded by collaborative and grant revenue and currently comprises of four collaborations.

In June 2020 Destiny announced a grant-funded collaboration with the University of Cardiff on the treatment of MDR bacterial and fungal infections that have a biofilm element. The ability for Destiny's drugs to be surface-active – able to kill both growing and more sedentary microorganisms like those protected from the host response in a biofilm – is the impetus behind these collaborations. Infections associated with biofilms like endocarditis or those associated with cystic fibrosis and dental infections with a plaque involvement, **are amongst the most difficult to treat.**

In September 2019, Destiny has received a grant award to support a new ophthalmic infection collaboration at Sheffield University and as the chairman pointed out in Destiny's annual report, Destiny continues to review new collaboration opportunities including those created by the coronavirus pandemic.



Source: Destiny Pharma

Financials

Destiny's IPO on London's AIM market in 2017 raised £15.2m and this was quickly followed by a £3m investment by China Medical Systems Holdings Limited (CMS) in December 2017. The CMS investment was part of a regional development and commercialisation agreement for Destiny's products in Asian markets, excluding Japan.

Destiny's FY 2019 results noted cash and equivalents of £7.5m (vs £12.1m at end FY 2018 and £9.1m at the end of H1 2019). As a semi-virtual company with few major costs outside of the now resumed Phase 2b clinical study, Destiny's prudent management can stretch its financial resources at least through Q4 2021. Our financial forecasts confirm at least a similar cash runway.

Conducting the clinical study largely dictated its FY 2019 financial results with total operating expenses of £5.6m (£6.1m in FY 2018). Operating expense that comprised R&D costs of £3.8m and other administrative costs of £1.9m (£3.5m and £1.8m in FY 2018, respectively). This was buffered by a £0.8m R&D tax credit and £0.3m in grant income (£0.8m and £0m in FY 2018, respectively).

The coronavirus pandemic has brought swings and roundabouts for Destiny: a pause to the Phase 2b study and therefore a delay in licensing the product, but a raised profile for antimicrobial resistant (AMR) hospital infections, that now **makes a licensing transaction more likely.**

Now the Phase 2b study is again underway, and completion expected in 2020, Destiny's cash runway extends beyond the year in which they have partner XF-73 on the basis of those results. Our assumption is that on the basis of positive Phase 2b results before the end of 2020, XF-73 is partnered during 2021 and that transaction includes $10m in up-front, and a $5m milestone payment to accompany the start of Phase 3. This is illustrated as an £8m debt (and a corresponding cash inflow) in our 2021 financial forecasts.

Valuation

We have used a risk-adjusted NPV model to value Destiny Pharma which results in a valuation of £86.3m, or 197p per share based only on the use of XF-73 in the prevention of staphylococcal post-surgical infections in high-risk surgical patients.

While Destiny's Phase 2b clinical study is in cardiovascular surgical patients – who are at high risk of the complications of a post-operative staphylococcal infection – we have included in our patient populations (and expectations for the Phase 3 study) two other high-risk surgical patients. These are neurosurgical and orthopaedic surgical procedures, where the morbidity and cost of a post-operative infection is at least as high as that of a cardiovascular surgery patient. We have however, excluded lower-risk surgical procedures such as percutaneous coronary interventions (which are effectively minimally invasive procedures, with small incisions), spinal anaesthetic procedures, carpel tunnel corrections and knee arthroscopies (which are all, effectively minimally invasive).

There is good US data on the number of these surgical procedures which we have extrapolated to Europe on a population basis, but reduced significantly in China to correlate with a lower penetration rate and lower number of high-risk surgeries there.

We have assumed that 90% of all high-risk surgical patients are treated prophylactically with an antibiotic prior to surgery - including off-label single systemic antibiotic doses - in all markets except China (where we have forecasted only 25%), since the morbidity and mortality costs of a post-surgical infection in cardiovascular, neurosurgical or orthopaedic patients, including the extra days of hospital stay, far outweigh the costs of prophylactically treating all high-risk surgical patients.

However, we have assumed that XF-73 only achieves a maximum of **60% market share (30% in China)** which initially builds very slowly (at 0.6% at launch in the US in 2024) before reaching 60% in 2034 before patent expiry in the US 2036 (including QIDP and other extensions). In all other markets we assume loss of exclusivity (LoE) in 2034 after which, we have assumed generic erosion.

A prevention of infection indication (which the FDA has agreed to) avoids the commercial issues associated with treating infections with short course therapies described above in the old model of anti-infective commercialisation. Instead, the preventative population includes a larger number of asymptomatic surgical patients prophylactically treated for a short course where a post-surgical infection could be costly and associated with significant morbidity.

We have forecasted the first launch of XF-73 in the US in 2024 and, as a Phase 2 asset, apply a 35% probability of success compounded with a 70% chance of a licensing deal (since there is already an Asian commercialisation and development deal with CMS). A breakdown of our rNPV analysis of Destiny Pharma is given in the table below:

Risk-adjusted NPV valuation summary

	NPV (£m)	Probability of success	Probability of license	rNPV (£m)	rNPV (p/share)
XF-73 royalty payments (£190m over 2024-35)	381.7	35%	70%	73.9	169
XF-73 milestone payments between 2021 & 2028	74.1	35%	70%	14.3	33
Costs of XF-73 development & R&D up to 2036	(9.5)	100%		(9.5)	(22)
Net Cash	7.5	100%		7.5	17
Total valuation	**453.8**			**86.3**	**197**

Source: Company data and ED estimates

The key assumptions in our model include:

- We have assumed the US price for a course of XF-73 to be $450. This is marginally above Bactroban Nasal's 2020 price of $374 per course, but Bactroban Nasal does not have the indication for the prevention of post-surgical infections, is associated with AMR and is a five-day self-administered in the community, rather than XF-73's two-day-hospital administered course. In addition, this compares well with Destiny's US pricing and market access study which suggested a US price of about $400 per course in 2018 when the Bactroban Nasal price was $221 per five-day course.

- We have correlated the prices of XF-73 in other markets to those of other hospital-administrated drugs and their US prices. This results in the pricing assumptions for Japan, the EU and China being $400, $250 and $100 per course, respectively.

Our pricing assumptions also include progressive gross-to-net discounts starting between four and five years after launch, depending on the market.

- We expect XF-73 to be partnered on the basis of the Phase 2b study results in 2021. Along with a modest 10% royalty rate on global sales, which we estimate starting at £1.9m in FY 2024, our estimation of XF-73's licensing terms include a schedule of milestone payments totalling £190m earned over five years, the last $10m milestone being paid in 2028 when we estimate that XF-73's global sales will have exceeded $1bn.

Commercialising XF-73

We have assumed that within the year following the Phase 2b results, Destiny will license XF-73 on a global basis ex-China, although regional deals may occur. We have reduced our estimates of R&D and other administrative expenses from £5.70m in 2020 to £2.65m from 2021 onwards as Destiny's marketing partner takes on the cost of Phase 3 development and commercialisation.

Our peak end-market sales estimations of the sales of XF-73 by Destiny's partner are $1.8bn in the US, $372m in Europe, and $44 and $50m in Japan and China, respectively.

Conclusions

Destiny Pharma present investors with an interesting opportunity. The development of antimicrobial agents typically involves **much lower risk** than other therapeutic areas. The most recent track-record of biotech companies developing antimicrobial agents has not been good because they have conformed with the old model of anti-infective development: developing **treatments** for which there is an existing, often generic standard of care.

Destiny has carefully avoided these pitfalls by developing XF-73 for the prevention of infections, an indication without on-label competition. The global pandemic has resulted in a temporary delay to the results of Destiny's Phase 2b study, although the study restart has recently come with protocol amendment that gives the hiatus a silver lining.

Using a rNPV analysis, we value Destiny Pharma at £86.3m or 197p per share.

Forecasts

Consolidated Income Statement & Forecasts					
£'000s, y/e 31 December	**2017A**	**2018A**	**2019A**	**2020E**	**2021E**
IFRS Income Statement					
Total revenue			306		
Administration expenses	-1011	-1800	-1030	-1900	-1900
R&D	-387	-3546	-3800	-4000	-950
Other income (expense)	-613				
Share-based payments & exceptionals	-710	-738	-204	-25	-25
Depreciation & amortisation	-2	-4		-2	-2
Reported EBIT	**-3222**	**-6084**	**-5585**	**-5927**	**-2877**
Reported profit before tax	**-3211**	**-6008**	**-5521**	**-5845**	**-2849**
Taxation	234	841	813	600	800
Reported Net income	**-2977**	**-5167**	**-4708**	**-5245**	**-2049**
Basic EPS (c before 2019, p after 2019)	-8.45	-11.86	-10.75	-11.98	-4.68
Diluted EPS (c before 2019, p after 2019)	-8.45	-11.86	-10.75	-11.98	-4.68

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	31	29
Intangible assets					
Total non-current assets	22	30	33	31	29
Current assets					
Trade and other receivables	277	931	911	277	277
Cash and equivalents	11724	7061	7480	2534	8511
Total current assets	17061	13028	8525	2944	8922
Total assets	**17083**	**13058**	**8557**	**2975**	**8951**
Equity and liabilities					
Equity					
Ordinary shares	436	436	439	439	439
Share Premium	17292	17292	17296	17321	17346
Retained earnings	-1042	-5471	-9976	-15221	-17270
Equity attributable to the company	16686	12257	7759	3139	1361
Total equity	16686	12257	7759	2539	515
Current liabilities					
Trade and other payables	-152	-404	-514	-152	-152
Total current liabilities	-397	-802	-798	-436	-436
Total non-current liabilities					-8000
Total equity and liabilities	17083	13058	8557	2975	8951

Source: Company historic data, ED estimates

Consolidated Cash flow Statement & Forecasts					
£'000s, y/e 31 December	**2017A**	**2018A**	**2019A**	**2020E**	**2021E**
Profit before taxation	-3211	-6008	-5521	-5845	-2849
Adjustment for:					
Depreciation & amortisation	2	10	18	2	2
Movements in working capital	165	381	-83	272	0
Share-based payments	710	738	204	25	25
Net cash generated by operating activities	-2153	-4721	-4631	-5028	-2050
Investing activities					
Capital expenditure on tangibles	-23	-18	-21		
Other investing activities	-4990	76	5063	82	28
Net cash used in investing activities	-5013	58	5043	82	27
Financing activities					
Net proceeds from issue of shares	17409		7		
Movements in debt					8000
Net cash from financing activities	17409		7		8000
Cash & equivalents at beginning of year	1481	11724	7061	7480	2534
Cash & equivalents at end of year	**11724**	**7061**	**7480**	**2534**	**8511**

Source: Company historic data, ED estimates

Investor Access

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