Destiny Pharma plc

In a class of its own

9 January, 2018

Collectively, candidates from Destiny Pharma's novel XF platform have demonstrated activity against a range of highly prevalent bacteria responsible for causing serious and multi-drug resistant healthcare acquired infections. These include the most virulent and difficult to target, with eight so far tested that appear on the World Health Organisation and US Centers for Disease Control and Prevention (CDC)'s list of priority pathogens including MRSA (methicillin-resistant *Staphylococcus aureus*).

Destiny is prioritising XF-73 which has potential to be first to **a $1.2bn core market,** in a new FDA-backed indication for prevention of post-surgical *S aureus* infection. CDC estimates that people with MRSA are **64% more likely to die** than those with a non-resistant form of infection.

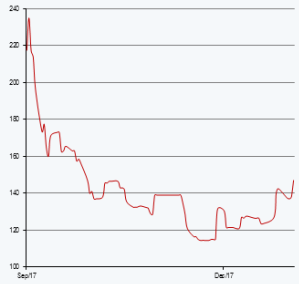
- The XF platform is based on **a novel chemical class** which offers the potential to rapidly kill bacteria via mechanisms that differentiate the XF candidates from standard antimicrobial treatments. The commercial potential of such drugs is enhanced, not only to treat or prevent infection, but with low propensity for bacteria such as *S aureus* to develop resistance as seen in standard microbiology models even after 50-plus exposures to XF-73. Anti-Microbial Resistance (AMR) is **a major limiting factor with standard antibiotic treatments.** The low potential for resistance to XF-73 could support wider adoption, tripling the core patient pool.
- If the data are borne out in the Phase IIb study, then **XF-73 has potential to be first to market in a new FDA-backed indication, setting a new standard and gaining a strong foothold in the market.** There appears to be limited competition in later stage pipelines in the preventative space and with no approved drugs in the US. Furthermore, it seems that Destiny's XF-73 is likely to be a more convenient presentation compared to currently used off-label antibiotic, mupirocin.
- The company is focused on **the fastest route** to a Phase III ready data package, first for XF-73 and the next three products in the pipeline, rather than eyeing up a slot as a specialty pharma company. Destiny is already well-funded because of its recent £15.3m fund raise together with a further £3m investment from **China Medical Systems**, this is sufficient to complete the Phase II program for XF-73 in our forecasts. This route could be accelerated by a range of drivers and policy-led incentives, plus potential to benefit from alternative, non-dilutive sources of funding.
- Looking forward, we consider **the probability of securing a deal post-Phase II is high**, if efficacy already seen in 166 subjects is confirmed, given the apparent scarcity of novel treatments and recent high-profile vaccines failures.
- **China Medical Systems** is an ideal partner / investor with access to huge markets.

Our DCF valuation using a 12.5% discount rate is £115m or 263p/share. NB at this stage this only reflects the current clinical candidate XF-73 in the US market, and includes our estimated net cash of £16.8m at end of 2017. Consequently, we see the current market value as a fair entry point into a novel pipeline with further upside potential if additional candidates enter clinical development.

Company Data

EPIC	**AIM: DEST**
Price (last close)	163p
Market cap	£70m
ED value/share	263p

Share price since IPO, p



Source: ADVFN

Description

Destiny Pharma is a UK-based clinical stage developer of medicines for the prevention and treatment of infections caused by drug-resistant bacteria.

There are four candidates in development from the XF Drug series, the most advanced is about to enter Phase IIb studies in Prevention of post-surgical Staphylococcal infection.

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Background

Destiny Pharma (DEST) is a drug development company based in Brighton, UK focused on developing innovative drugs with the potential to prevent or treat prevalent forms of drug resistant infection. Its XF drug platform is based on a new chemical class which acts to kill bacteria via mechanisms that are distinct from antibiotics. Studies to date demonstrated rapid action against drug resistant strains of *Staphylococcus*, including Methicillin Resistant *Staphylococcus aureus* (MRSA), which is the leading cause of healthcare-acquired infection.

The Company was founded in 1997 by the current Chief Scientific Officer (CSO) Dr Bill Love, originally as a contract research organisation (CRO) focused on photodynamic anti-bacterial treatments, it switched strategy to target drug development in 2003 after the discovery of the anti-bacterial XF drugs. DEST has raised c £37m since inception, including £15.3m gross on admission to the London AIM in September 2017, and £3m subsequently. The Company has received c £5m of non-dilutive funding including support from National Institute of Allergy and Infectious Diseases (NIAID) which funded and conducted a US study of XF-73.

Preventing and treating drug resistant infection

Destiny Pharma's XF drug series is based on a novel chemical class which offers the potential to kill bacteria rapidly via mechanisms that differentiate the XF candidates from standard antimicrobial treatments, notably antibiotics. In fact, early stage studies to date with the lead program XF-73 suggest that antimicrobial resistance (AMR) the chief treatment-limiting factor associated with antimicrobial drugs such as antibiotics, is avoided with XF-73 even after multiple exposures to the product.

Product/Indication/Mode of delivery	Development Status
XF-73/Prevention of post-surgical Staphylococcal infection/Intra-nasal	Phase IIa data/ next step Phase IIb
XF-73/Prevention of hospital/ventilator-associated Staphylococcal pneumonia/Throat	Pre-clinical
XF-70/Treatment of skin burn wound infections of antibiotic resistant bacteria/Dermal	Pre-clinical
XF-70/Treatment of bacterial biofilm infections/Lung	Early pre-clinical

Source: Destiny Pharma

A truly urgent need to tackle drug-resistant infection

While healthcare providers across the globe have made progress in reducing healthcare-acquired infection, through increased awareness of the role of antimicrobial treatments in perpetuating disease and stewardship of antibiotics for example, **there remains a persistent shortage of new and effective treatments to overcome drug resistant bacteria.**

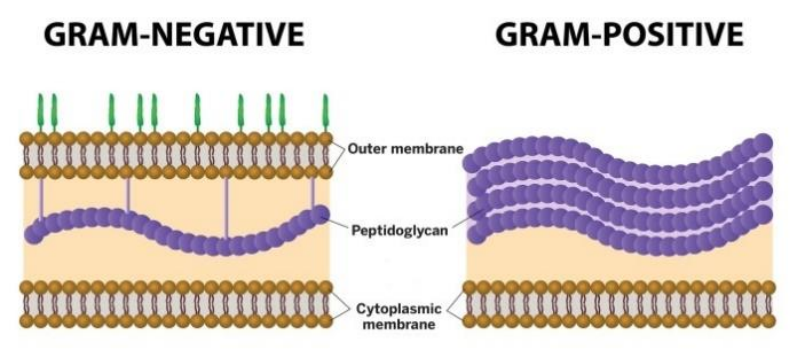
This is despite incentives to encourage new treatments and healthcare provider-led initiatives aimed to minimise the risk of AMR. In 2017 the World Health Organisation (WHO) released its list of the top 12 (or so called 'dirty dozen') most threatening pathogens, drawn up using a series of criteria which include: **urgency in terms of threat to human health, the limited number of drugs in development, ease of transmission and level of resistance to antibiotics.**

WHO pathogens: priority list for R&D		
CRITICAL	**URGENT**	**CONCERNING**
Acinetobacter baumannii, carbapenem- resistant	*Enterococcus faecium, vancomycin- resistant*	*Streptococcus pneumoniae, penicillin- resistant*
Pseudomonas aeruginosa, carbapenem- resistant	*Staphylococcus aureus, methicillin- resistant*	*Haemophilus influenzae, ampicillin- resistant*
Enterobacteriaceae, carbapenem- resistant	*Helicobacter pylori, clarithromycin- resistant*	*Shigella spp., fluoroquinolone-resistant*
	Campylobacter spp., fluoroquinolone- resistant	
	Salmonellae, fluoroquinolone-resistant	
	Neisseria gonorrhoeae, cephalosporin- resistant	

Source: World Health Organisation

Unsurprisingly, the three critical pathogens fall into the **Gram-negative class** which are the deadliest and most resistant to drug treatment. Gram-negative bacteria have an impermeable outer membrane that forms a strong barrier and which promotes antimicrobial drug resistance.

The structure of bacteria



Source: Chemical & Engineering News

XF-73 has been shown to be effective against **all Gram-positive bacteria** tested including both the drug resistant and susceptible strains of *S aureus* (MRSA and MSSA). It is thought that this is because of the ability to disrupt the peptidoglycan layer and to permeate the cytoplasmic membrane hence leading to cell disruption and death[1].

It is also active against a number of Gram-negative bacteria tested including *Pseudomonas aeruginosa* which is commonly responsible for hospital-related infections such as pneumonia and urinary tract infections (UTIs).

As a group, candidates from Destiny Pharma's XF platform have demonstrated activity against a range of highly prevalent bacteria responsible for causing serious and multi-drug resistant healthcare acquired infections. That includes the most virulent and difficult to target, with eight that appear on the World Health Organisation and the CDC's list of priority pathogens for antibiotics development.

[1]XF-73, a novel anti-staphylococcal membrane-active agent with rapid bactericidal activity; Chopra et al, Journal of Antimicrobial Chemotherapy 2009.

XF drugs demonstrate a broad range of activity	
Gram-positive	**Gram-negative**
*Staphylococcus aureus**	*Acinetobacter baumannii**
Propionibacterium acnes	*Pseudomonas aeruginosa**
*Mycobacterium tuberculosis**	
*Bacillus anthracis**	*Yersinia pestis**
*Clostridium difficile**	
Listeria monocytogenes	
Group G Streptococcus	
*Streptococcus pneumoniae**	

*Source: Destiny Pharma taken from preclinical studies *Pathogen is an R&D priority*

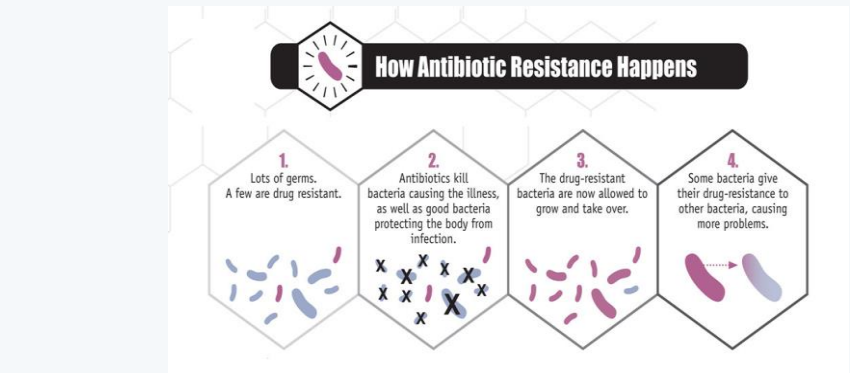
Initially, Destiny Pharma is investigating XF-73, its most advanced product, in prevention of post-surgical Staphylococcal infection where XF-73 has shown clinical evidence of **rapid and effective kill** of *S aureus* (classed as an urgent threat by WHO). Around 11,500 of the 80,500 or 15% of people in the US who contract MRSA related infections each year die as a result according to the CDC.

Antibiotics and antimicrobials

Antibiotics are the most established antimicrobials in the category and are the mainstay of treatment for infection, often used in combination with disinfectants in the hospital environment. *Grand View* market research estimates that the value of the antibiotics market reached **$39bn** in 2015. The launch of penicillin in 1943 revolutionised the treatment of infection. However, the advent of **resistance** around 20 years later has been a feature for all antibiotics approved since that time across six key classes.

Antimicrobial resistance (AMR) is a major threat to human health and summed up by Lord Jim O'Neill in his AMR review commissioned by the UK government in 2016 – ***'if AMR is not dealt with, it will lead to one death every three seconds***' or put another way, up to **10 million** lives will be lost per annum by 2050.

Development of resistance



Source: CDC

Strong drivers and unmet need

Some of the recommendations issuing from the 2016 AMR Review exemplify the response needed, notably incentives for the pharmaceutical industry to start developing new drugs, coupled with further encouragement and the ongoing supportive legislation being issued worldwide.

Event	Relevance for Destiny
Generating Antibiotics Incentives Now (GAIN) Act 2012, Food & Drug Administration FDA, US	Range of incentives under Qualified Infectious Disease Product QIDP designation Eligibility for fast track designation, Expedited review, Potential extension of existing marketing exclusivity period by five years. Destiny Pharma's lead drug XF-73 has QIDP status.
New Technology Add on payment, NTAP US	Medicare add-on payments to top-up or substitute full reimbursement.
Independent review on AMR, May 2016, UK	Prioritisation, recommendations and heightened awareness of need for alternative treatments.
UN meeting on AMR September 2016	Global action plan to fight AMR
FDA - 21st Century Cures Act, signed into law, December 2016	To facilitate the development of medical products, fostering use of real world evidence in drug trials, establishing Limited Populations development pathway for antibacterial/antifungal drugs, finalisation targeted for December 2018.

Sources: various sites; AMR = antimicrobial resistance

Tackling the threat of drug resistant bacteria

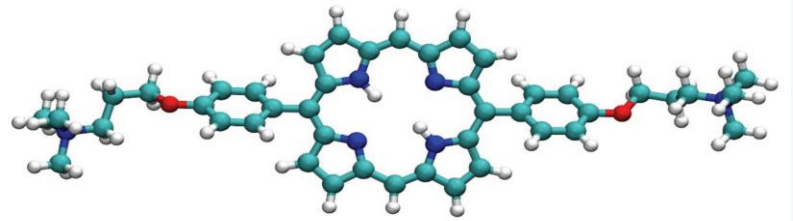
Destiny Pharma is developing a portfolio of drug candidates in this area of very high unmet need which demonstrate a wide spectrum of antimicrobial activity. Conclusions drawn over the course of five clinical studies (which we will later describe in greater detail) and a range of preclinical studies with lead candidate XF-73 are that it demonstrates mechanisms that:

- **Present rapid and potent bacterial kill taking effect within minutes;**
- **Show sustained efficacy against MRSA, seen in preclinical studies, resistance did not develop even after 55 exposures to XF-73;**
- **Are effective against all types of Gram-positive bacteria tested and with activity against certain strains of Gram-negative bacteria;**
- **Act at all stages tested, including during dormancy, growth period, and in drug-resistant Biofilms;**
- **Act to weaken and disrupt bacterial cell walls leading to cell death, without causing lysis (breaking down the cell wall).**

Provided that follow-on studies are consistent, these properties and mechanisms offer exciting potential for the XF products to meet the urgent unmet need for new antimicrobial drugs that cover a broad spectrum of bacteria.

Furthermore, the low potential for resistance to develop can accelerate finding a long-term solution to a critical healthcare problem of our time.

Molecular structure of XF-73



Source: Destiny Pharma

The most advanced candidate is XF-73, defined by the chemical name exeporfinium chloride, which is a synthetic dicationic porphyrin derivative, and has a unique structure that sets it apart from standard antimicrobials.

XF-73 potentially first to an 18m patient market

XF-73 is a clinical stage product and the Company is now well-funded to take XF-73 into US Phase IIb studies in a new FDA-defined indication, 'Prevention of post-surgical Staphylococcal infection'. The reward for successful development is treating **a primary patient population of up to 6 million in the US alone, worth up to $1.2bn** counting the high-risk category of patients and who are also carriers of *S aureus.* We view that XF-73 has potential to be more broadly adopted for universal use (i.e. no screening) to treat all 18 million high risk surgical patients if the low potential for resistance is borne out, tripling the potential market size. Currently there is no approved drug in the US in the preventative setting.

XF-73 was designated as a Qualified Infectious Disease Product (QIDP) by US Food and Drug Administration (FDA) in 2015. The FDA's QIDP designation, ratified under the GAIN provisions of the Food and Drug Administration Safety and Innovation Act of 2012, confers a range of benefits to incentivise the development of new antimicrobial drugs. Key features are:

- Eligibility for fast track designation, maybe allowing Destiny more interaction with FDA;
- Expedited review, reducing the FDA's target review period from 10 months to 6 months;
- Potential extension of existing marketing exclusivity period by five years.

Destiny Pharma has developed broad IP around the XF drugs platform in its focus markets (US, Europe and Japan) lasting up to 2023-2029, which can potentially be extended under the terms of the QIDP by a further five years from approval taking the total patent duration up to 2028-2035. The IP is notably covering:

- Composition of matter which covers the novel molecular structure of XF drugs;
- New uses arising from novel mechanism of action;
- Activity against biofilms –to combat a leading challenge in treating chronic infection.

The dearth of new treatments in pipelines is partly due to the self-limiting nature of antibiotic treatments which means the return on investment in antibiotics in traditional and existing indications can be limited. This is not the case for Destiny Pharma because it is developing XF drugs that demonstrate low resistance generation to date and it has identified areas of high unmet need in a new lead indication with a very broad commercial potential given the number of patients that would benefit.

Destiny Pharma has a genuinely novel approach

XF-73 is the Company's most advanced program, having been trialled in ≥160 volunteer subjects in five studies, most recently in the US National Institute of Allergy and Infectious Diseases (NIAID) sponsored trial. If the results of these studies are seen to be sustained in larger patient groups, then XF-73 is in line to be the first treatment in the setting - Prevention of post-surgical Staphylococcal infection – increasing the probability of it being widely adopted.

Alternative approaches, including vaccines, have so far failed to yield success – there have been high profile disappointments including those of Nabi Biopharmaceutical's StaphVAX and Merck's V710 which both failed at Phase III – while other developers of alternative **prophylactic**, or **preventative** *S aureus* treatments appear to be at an earlier stage than XF-73.

Staphylococcus aureus is a form of bacteria with known resistance to major groups of antibiotics, MRSA being the most notorious strain (methicillin resistant) however others exist such as VISA and VRSA (vancomycin intermediate and vancomycin resistant). MRSA is one of the most important bacterial pathogens in health care-associated infection in terms of virulence, prevalence, diversity of disease spectrum, and propensity for widespread transmission.[2]

The main surgical groups at risk are those undergoing cardiothoracic, neurosurgical and orthopaedic procedures. There are **over 40 million people in the US alone** who undergo surgery. Up to 18 million people fall into the higher risk category, but that leaves a potentially huge patient population that would benefit from XF-73, if approved. Furthermore, the economic burden caused by antibiotic-resistant infections in the US has been estimated to be as high as **$20 billion**.[3]

Tackling settings with heightened MRSA risk

In a healthcare location, such as a hospital or nursing home, MRSA can cause severe problems such as bloodstream infections, pneumonia and surgical site infections. If not treated quickly, MRSA infections can cause sepsis and death (www.cdc.gov).

In the postoperative setting, the risk of contracting MRSA is significantly raised. The symptoms of MRSA infection include boils or abscesses, foul smelling and painful wound sites, fever or chills and redness. The risk factors for contracting infection include:

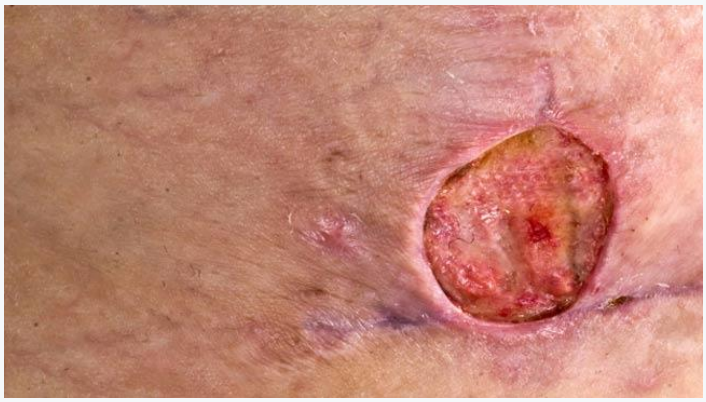
- Length and type of surgery - more invasive procedures over two hours being higher risk;
- Age, smoking status and diabetes;
- Having a compromised immune system.

[2]AHRQ: Agency for Healthcare Research and Quality.

[3]The Antibiotic Resistance Crisis

The incidence of *S aureus* is linked to a high of 42% greater risk of mortality[4] while extended **hospital stays of up to 130% longer** for patients with *S aureus* contribute to the excess cost burden of care.

Example of MRSA infection



Source: Healthline.com

One study[5] showed that in 82.2% of MRSA infections the *S aureus* originated from the patients themselves, transmitting the bacteria into their own bloodstream. **Other analyses show that about one in three people carry *S aureus* in their nose, usually without harm, while two in 100 people carry MRSA – up to a third of carriers go on to develop surgical site infection (SSI).** *S aureus* has been shown to be responsible for >60% of SSIs.[6]

XF-73 fits into established infection control methods

The rationale and evidence for nasal decolonisation is well-established in hospital settings. Although it is not a standard procedure in all hospitals, decolonisation is an important feature of the pre-surgical hygiene routine and in 2016 featured in WHO recommendations and those of many US hospital groups, owing to the link between nasal carriage of *S aureus* and infection. This is clearly supportive of adoption of XF-73 by healthcare providers.

There is widespread off-label use of the topical intranasal antibiotic mupirocin (mupirocin calcium) in its generic form and known under brand names including Bactroban nasal ointment/GSK in the US. **But mupirocin is not approved by the FDA in the prevention setting.** There is therefore a lack of formal clinical data for mupirocin in the setting. The topical antibiotic is frequently used in conjunction with screening and disinfectant scrubs prior to surgery to prevent post-surgical infection.

In fact, there are **no topical antibiotics approved** for prevention of auto-infection of post-surgical staphylococcus in the US.

[4]Postoperative *Staphylococcus Aureus* Infections in Medicare Beneficiaries; 2014 Razavi et al PLOS One

[5] Nasal carriage as a source of *Staphylococcus aureus* bacteremia. Study Group in NEJM – von If et al.

[6] Nasal carriage of *S aureus* increases the risk of surgical site infection after major heart surgery in Journal of Hospital Infection 2008 Munoz et al.

Indeed, despite screening to rule out non-carriers, to narrow down the patient group and to minimise exposure to antibiotic usage, mupirocin use is limited by:

- The risk of increase in resistance which has been linked to widespread use of mupirocin in healthcare settings[7];
- Risk of developing *Clostridium difficile* infection is listed as a side effect;
- Mupirocin dosing is required to commence five days prior to surgery to take effect which is limiting in urgent or emergency cases;
- Mupirocin has not been formally FDA approved and studied in full length clinical trials for this indication so there is a lack of standard data on outcomes.

Whereas XF-73 has already been shown to be **immediately effective** in killing bacteria and in the planned Phase IIb study Destiny Pharma is developing it specifically for the new FDA-backed indication for prevention of post-surgical Staph infection.

Notably, initial data show that bacteria did not develop resistance - after 55 repeat passages of exposure to XF-73 *in vitro* – suggesting a very clear rationale for developing XF-73 to combat drug resistant bacteria including MRSA. Vancomycin is the mainstay of treatment of Gram-positive infection such as MRSA but resistance is an emerging and concerning threat according to CDC and with few or no approved alternative treatment options.

XF-73: the clinical evidence

Destiny Pharma is due to take XF-73 (in intranasal gel form) into US Phase IIb FDA studies in 2018. The strategy is to complete the Phase II development stage for XF-73 which comprises a further two studies; a placebo controlled Phase IIb efficacy study in up to 200 patients and a standard Phase I dermal safety study, required by FDA to satisfy the requirement for all topical drugs.

Trial results to 2016	
XF-73A01	First in man, 5-day dosing, 0.075mg/g, safe
XF-73B01	5-day dosing, 0.5mg/g dose, safe
XF-73B02	5-day dosing, 2mg/g dose, enhanced anti *S aureus* effect, safe
XF-73B03	NCT02282605 UK placebo-controlled Phase I/II study in 60 subjects, 2-day dosing /2 treatment arms at 1.2mg/0.3mg per g doses, rapid anti *S aureus* effect, safe
DMID-11-0007	NCT01592214US Phase I placebo-controlled study in 48 subjects, 5-day dosing, met primary outcome safe and rapid effect.

Source: Destiny Pharma

Looking first at the existing body of data, there are five completed studies of XF-73, the most recent being the US government, NIAID-sponsored controlled study which was published in September 2016. Results to date demonstrate that XF-73 has ***rapid and effective anti-bacterial activity***, including a statistically significant result compared to placebo in the

7 Mupirocin Resistance in Patients Colonized with Methicillin- Resistant *Staphylococcus aureus* in a Surgical Intensive Care Unit; Jones et al. Clinical Infectious Diseases

NIAID-sponsored study, against *S aureus* supported by a good safety profile derived from over 160 subjects.

The US study was designed to test the overall safety profile and efficacy of XF-73 and it used higher than previously tested concentrations of XF-73 over a five-day period and was entitled;

'A Two-Part Phase I Study to Establish and Compare the Safety and Local Tolerability of Two Nasal Formulations of XF-73 for Decolonization of *Staphylococcus Aureus*: A Previously Investigated 0.5 mg/g Viscosified Gel Formulation versus a Modified Formulation',

The two-stages comprised:

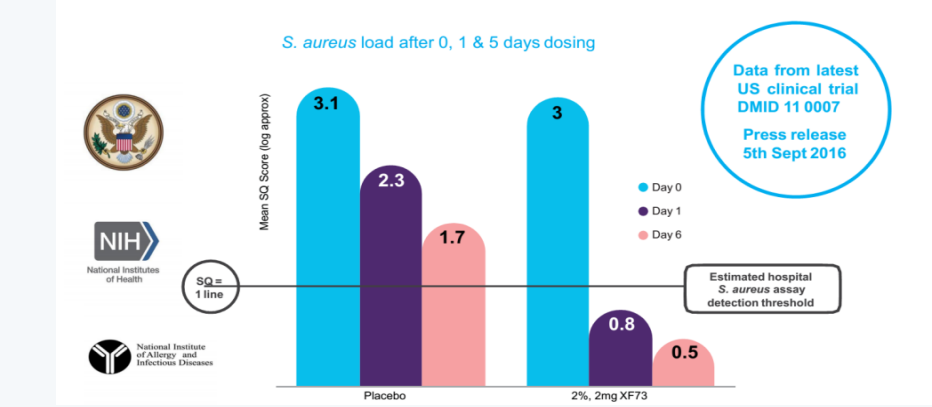
- Part 1 - a safety trial in eight healthy volunteers progressing to,
- Part 2 - in 48 healthy volunteers testing positive as carriers of nasal *S aureus* bacteria. Part 2 was double-blinded, placebo-controlled studying two concentrations of XF-73 of 0.5 & 2.0mg/g and two viscosities over a 5-day period.

The NIAID/DMID study outcome that was announced in a press release September 2016 concluded that **both concentrations of XF-73 were deemed safe and well-tolerated**, and no drug was detected as being absorbed into the bloodstream with a consistent safety profile between placebo and treatment arms.

Overall, XF-73 demonstrated a rapid, anti-staphylococcal effect after one day, with the 2.0mg/g gel showing a statistical difference against placebo, which was sustained throughout the dosing period.

S aureus burden was measured using a microbiological unit of Colony Forming Units (CFUs) and the outcomes show that with the higher dose gel, this measure fell below the estimated hospital assay detection threshold. Bacterial load is generally tested using gold standard method of nasal swab cultures measuring the number of CFUs/ml.

XF-73 shows rapid effect against MRSA in NIAID-sponsored trial

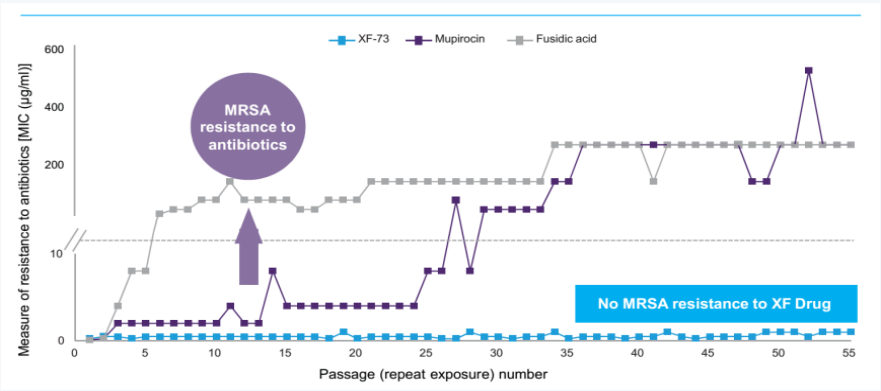


Source: Destiny Pharma

In the XF-73, 2mg/g, 2% group, the average measure of CFU's (log approx.) fell from the base point of 3.0 to 0.8 on day one and to 0.5 by day six showing that the XF-73 2mg/g, 2% mg gel caused *S aureus* levels to fall rapidly below the hospital detection threshold. In the placebo group, there was a much lower average drop on day one and which by day six, remained above the estimated hospital detection threshold.

In a separate, *in vitro* study entitled –Investigation for potential mutational resistance to XF-73- the resistance of MRSA to XF-73, and the topical antibiotics mupirocin, steroidal antibiotic, fusidic acid, vancomycin and retapamulin were tested using minimum inhibitory concentration [MIC] as a unit of measurement over 55 repeated exposures to MRSA. Generally speaking, a rise in MIC demonstrates that bacterial resistance is developing. The study demonstrated the outcomes in the following chart.

Durable effect of XF-73 – no resistance after 55 exposures to MRSA



Source: Investigation of the potential for mutational resistance to XF-73, retapamulin, mupirocin, fusidic acid, daptomycin and vancomycin in MRSA isolates during a 55 Passage Study, Farrell et al, Antimicrobial agents and Chemotherapy 2011.

Notably, no MRSA resistance was seen to develop to XF-73 throughout the period of exposure after 55 passages.

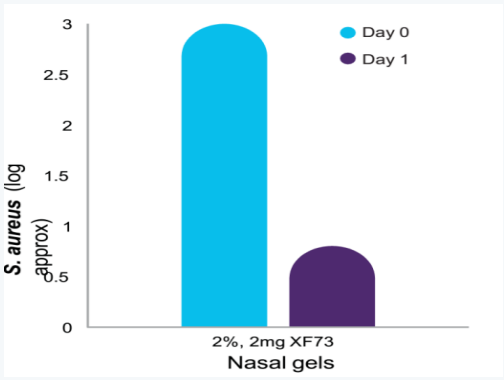
In contrast, MRSA resistance to fusidic acid and mupirocin occurred at days two and day three, respectively, after exposure to these drugs: **demonstrating a marked divergence between XF-73 and the antibiotics tested.**

Furthermore, a measure of the potency of XF-73 in terms of MIC on clinical trial nasal *S aureus* swabs prior to and post exposure to XF-73 showed a consistent result of 0.25-2 µg/ml suggesting that *S aureus* remained susceptible to XF-73 at both points measured.

In summary, XF-73 demonstrates in studies to-date a good safety and efficacy profile in clinical trials involving 216 subjects. Significantly, there is **no systemic absorption** which is supportive of the use of XF-73 in the preventative setting.

Efficacy of the 2mg/g, 2% concentration of XF-73 demonstrated **rapid 1 day efficacy** – after 2-3 doses with duration of the effect throughout the treatment period. The following chart measures *S aureus* load and summarises the average level at baseline and day one of dosing from the latest US NIAID trial:

Summary of clinical studies of XF-73 in NIAID Trial



Source: Destiny Pharma

In context, XF-73 is being measured against a placebo as there are no standard approved treatments to benchmark it against in the prevention setting in the US. In studies so far, XF-73 demonstrates a good safety profile and efficacy at the higher dose suggesting that the drug can be used in the setting. If the immediate effect is seen in ongoing studies, then this presents a potential advantage for XF-73 as it appears more convenient and easier to administer than mupirocin which requires 5-day dosing to take effect both for elective surgeries and in emergency cases when there is less time to prepare for procedure. In addition, the low propensity for resistance to develop differentiates XF-73 from marketed antibiotics such as mupirocin.

Ongoing steps – phase IIb studies XF-73

The next steps are for Destiny Pharma to take XF-73 into larger studies to provide additional data on efficacy and safety in Prevention of post-surgical *S aureus* infection – first, a standard dermal sensitivity trial is required in the US, followed by a c 200 patient trial to test the efficacy of XF-73 vs placebo in pre-surgical candidates (rather than in healthy volunteers as before).

The trial is anticipated to commence in 2018 and we estimate that the timeline for completing the studies will be up to 18 months at a cost, including Chemistry Manufacturing and Controls (CMC) work, of up to £8.5m, with **potential readout of the final study data in 2019.**

The Phase IIb endpoint will be microbiological, that means the load of *S aureus* in the anterior nares (nasal passages) will be measured before and after exposure to the drug, as in the previous studies, rather than measuring a clinical outcome such as subsequent infection transmission rate. We anticipate that the outcomes of these studies will be used to support ongoing studies in other indications. Notably, the dermal sensitivity trial could be used to determine decision-making for the other dermal indications being studied or evaluated. Another significant measure would be to monitor potential resistance to XF-73 although this is unlikely to be proven in the trial setting.

Focus on being first-to-market in prevention setting

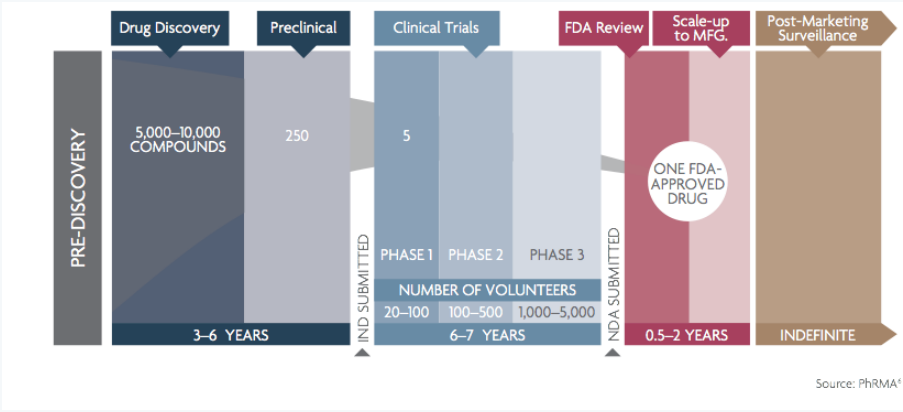
Destiny Pharma has said its strategy is to work towards creating a Phase III-ready clinical data package for the drugs in the XF pipeline – i.e. to take the products through to the end of Phase II.

Most likely it will seek a partner or license deal before the Phase III stage, focusing current resources on the ongoing Phase II development rather than starting the process of building a proprietary speciality sales force.

Clearly the key priority and near-term focus for the Company is on the lead candidate XF-73, and post-IPO there is now sufficient funding in place to complete the Phase II program – which is targeted by 2019. The typical approval timeline and process for drugs is illustrated in the following graphic, suggesting that XF-73 could be registered as early as 2021, assuming the plan runs to schedule and if it benefits from expedited review under QIDP.

Destiny Pharma has therefore already passed the halfway point in the clinical development process.

Approval timeline



Source: PhRMA

Starting with the lead indication - Prevention of post-surgical *S aureus* infection – we calculate that there are around **18 million high risk surgeries per annum** in the focus market of the US – as a reminder this population constitutes the highest unmet need. Since XF-73 is potentially a first in a new indication, we have evaluated the potential for it being used in a targeted setting i.e. in *S aureus* carriers and for Universal Decolonisation.

If we assume that patients will be routinely screened, with an average of one third being carriers of *S aureus* and therefore candidates for targeted decolonisation, then that narrows the market down to **a pool of c 6m patients in the potential core market for XF-73.**

We assume that XF-73 will be priced at the average cost of a five-day course of nasal mupirocin of $200 (source: GoodRx) so that equates to **a total annual market of over $1.2bn**. Since there are no standard approved treatments and given potential competitive advantages for XF-73 (because of its immediate action) and assuming the absence of resistance to XF-73 seen in earlier studies is borne out in clinical trials, it stands to garner **a significant proportion of this pool**. The requirement for hospitals to comply with infection control and to report cases of infection in order to qualify for value-based reimbursement means that XF-73 is **likely to qualify for reimbursement** if priced in line with mupirocin.

Therefore, if XF-73 is the first product to reach the market in the indication (it does appear to be more advanced than peers) then it could achieve 50% of the market: giving us a **peak sales figure of $602m**. We assume launch in 2022 and that with QIDP status the period of patented commercialisation extends out to 2035.

Looking at the pool of c 12m non-carriers of *S aureus*, it is probable that there will be take up into this section given the low propensity for resistance to develop to XF-73, the expense and delay (it takes between one to three days to get test results) caused by screening and because of the inaccuracies of swab testing; some studies show that the negative predictive value of screening is good, i.e. it correctly rules out non-carriers in most cases, however its positive predictive accuracy is less reliable, that is to say a significant number of *S aureus* carriers are missed.

We therefore think that this Universal Decolonisation will be a secondary market for XF-73 and we calculate **peak sales of $244m** at 10% penetration in Universal Decolonisation.

Finally, we view that XF-73 will have high utility for Universal Decolonisation in the 0.5m annual emergency surgery cases carried out in the US each year, notably because of its very rapid bactericidal activity, and we calculate peak sales of **$50m in this setting** at 50% market penetration.

A natural extension for XF-73 into critical care setting

The Company has identified that XF-73 also has potential as a decolonisation in the high-risk group of Intensive Care Unit (ICU) patients. There is a growing recognition of the preventative approach of Universal Decolonisation (UD) of ICU patients on admission which has been shown to **reduce the incidence of infection by over 40%.**

With MRSA already a serious threat, ICU patients are exposed to yet higher levels of the bacteria. So much so that previously unaffected patients are at risk of infection within an ICU.[8] In 2011, an estimated 14,156 hospital-onset invasive MRSA infections occurred in the United States, 26% of which were in ICUs.[9]

There is broad evidence - including from the large REDUCE MRSA Trial – that shows Universal Decolonisation was more effective than screening or isolation of patients for example. Universal ICU decolonisation significantly reduced MRSA-positive clinical cultures by 37%, and all-cause bloodstream infection by 44%.

The practice of universal ICU decolonisation is becoming increasingly widespread and guidelines from many influential bodies including the Infectious Disease Society of America (IDSA), Surgical Society of America and the Agency for Healthcare Research and Quality - recommend implementation.

[8]Ziakas PD, Zacharioudakis IM, Zervou FN et al. Methicillin-resistant *Staphylococcus aureus* prevention strategies in the ICU: a clinical decision analysis. *Crit Care Med*. 2015

[9]Dantes R, Mu Y, Belflower R et al. National burden of invasive methicillin-resistant *Staphylococcus aureus* infections, United States, 2011. *JAMA Intern Med*. 2013

There are up to 8 million ICU admissions per annum in the US and we estimate that between 10-25% of healthcare facilities are implementing the protocol at present with potential for this proportion to increase as guidelines are accepted.

Many studies including one comparing the cost of Universal Decolonisation in the ICU setting showed that *'it outperforms other strategies and is likely to be cost-effective even at low willingness-to-pay thresholds'*.

Furthermore, the study concluded that for an average 700 annual ICU admissions in a typical 12-bed ICU, the projected annual savings could reach $129,500 to $135,100 if Universal Decolonisation is enacted'.[10]

Therefore, there is strong clinical and economic evidence to support Universal Decolonisation, endorsed by key opinion-leading bodies, although this has not yet been confirmed by studies conducted by Destiny Pharma. However, we believe that, if clinical data confirms efficacy in the post-surgical setting, XF-73 could also be adopted as a treatment **in the ICU setting**.

In this case it would again replace mupirocin, which is the most frequently used, off-label medication in decolonisation – and the low probability of *S aureus* resistance developing could be strongly supportive of XF-73.

We opine that a further Phase II study would be required to test XF-73 in the ICU setting; it could be supported by the safety and efficacy data from the post-surgical setting, although in a real-world situation there could be **off-label adoption** of XF-73 in Universal Decolonisation, as is the case with mupirocin given the low potential for *S aureus* resistance to develop. Meanwhile, the enactment of the US Cures Act recommendations, anticipated by the end of 2018, could be supportive of an abbreviated development pathway in this indication.

For the time being, we await further visibility on timeline for a study and are assuming that QIDP status would be sought before taking this indication forward, before we add projections into our model.

[10]Methicillin-resistant Staphylococcus aureus prevention strategies in the ICU: a clinical decision analysis – in Critical Care in Medicine Ziakis et al 2015

CMS agreement brings financial + strategic benefits

In November 2017, Destiny Pharma confirmed the key elements its Regional Development and Commercialisation framework agreement with a wholly owned subsidiary of Hong Kong-listed **China Medical Systems Holdings (CMS).**

On finalising the agreement, CMS made a further £3m equity investment in Destiny Pharma shares (added to its £3m investment in the £15.3m September placing) taking its share ownership to 8.77% of the enlarged share capital. The total proceeds of £18.3m will be used to accelerate the development of the XF drug pipeline.

CMS, which has a market capitalisation of c US$ 6bn, is a respected participant in a huge Chinese pharmaceuticals market valued at over $100bn and forecast to grow at up to 20% per annum over the next five years. In Asia, there is a critical need for new ways of tackling the problems of drug-resistant infections.

The collaboration with CMS brings many strategic and financial benefits for DEST. The key elements of the deal are as follows:

- CMS has the rights to develop, manufacture and commercialise all the XF pipeline candidates in a specific set of Asian countries – (the CMS Territory includes China, Macau, HK, Taiwan, Thailand, Malaysia, Indonesia, Philippines and India).
- CMS will be responsible for all research and development in these territories and both parties will share data and collaborate on the overall development plan for XF candidates, by means of a newly appointed Joint Steering Committee.
- Under the agreement, the Company will receive a manufacturing margin on product supplied for commercial sale as well as a milestone payment in relation to sales made by CMS.
- Dr Huaizheng Peng, General Manager of International Operations at CMS, has been appointed to Destiny Pharma's Board of Directors. Dr Peng brings depth of experience in pharmaceutical licensing and business development as well as knowledge of London capital markets through his experience as corporate financier and asset manager.

In our view, **the deal presents a major opportunity for Destiny**, since it enables it to accelerate the development of the XF pipeline.

We see this is an opportunity for Destiny Pharma to benefit from the additional funding to move existing programs forward and to progress the earlier stage programs where there are significant commercial opportunities and unmet need.

It also provides valuable opportunity to coordinate and share clinical data, potentially accelerating the development of the Company's pipeline.

Prevention of pneumonia in hospitalised patients

Moving back to the pipeline, the next most advanced indication for XF-73 is for **prevention of ventilator-associated pneumonia (VAP)**, supported by evidence that *S aureus* carriers are at elevated risk of developing pneumonia and endorsed by the American Thoracic Society. There is high unmet need and significant mortality rate caused by VAP - with c 300,000 new cases of VAP per annum in the US and a mortality rate of up to 36%.

There are two categories of Hospital-acquired or nosocomial pneumonia - with VAP being a subset of Hospital-acquired pneumonia (HAP):

- HAP is defined as occurring in patients after 48 hours of hospitalisation and refers to those who have not been diagnosed as carriers at the time of admission prior to respiratory intubation.
- VAP by contrast, is defined as pneumonia occurring after 48–72 hours of mechanical ventilation and occurs in 30%[11] of ventilator-intubated patients.

The two main bacteria involved are the Gram positive, *S.aureus* including MRSA and the Gram-negative bacteria *Pseudomonas aeruginosa*.

Symptoms general include fever, abnormal chest examination and breathing, infected sputum and impaired oxygenation, confirmed by laboratory tests. A diagnosis of HAP/VAP also requires radiological screening can generally be more easily diagnosed by means of sampling: via a process known as bronchoalveolar lavage, using the existing respiratory line. Therefore, it can usually be more easily treated with specific antibiotics than HAP.

Current standard of care focuses on treatment rather than prevention, using standard broad-spectrum antibiotics to cover Gram-negative and Gram-positive infection, including *S aureus*.

There are clear challenges in the standard approach given that prior use of antibiotics is a major risk factor for resistance and ongoing development of VAP. **According to the IDSA guidelines, the number one risk factor for multi-drug resistant VAP includes prior intravenous antibiotic use within 90 days: emphasising the need to minimise use of antibiotics**.

So, decolonisation can gain additional recognition as a method of preventing MRSA VAP.

There is already of body of evidence to support this, including studies that have shown a link between MRSA colonisation and a higher likelihood of isolation of MRSA from respiratory samples.[12]

[11] Ventilator-associated pneumonia in the ICU: Kalanuria et al in Critical Care 2014

[12] Pneumonia Caused by Methicillin-Resistant *Staphylococcus aureus; Rubinstein et al, Clinical Infectious Disease 2008*

Standard US broad spectrum Intravenous antibiotics used in Pneumonia

Table 2. Empiric Antimicrobial Agents for VAP and HAP

Pseudomonas aeruginosa Coverage	
Beta-Lactam–Based Antibiotics	*Fluoroquinolones*
• Piperacillin-tazobactam 4.5 g IV q6h or via extended infusion[a]	• Ciprofloxacin 400 mg IV q8h • Levofloxacin 750 mg IV q24h[a]
OR	*OR*
• Imipenem 500 mg IV q6h[a] • Meropenem 1 g IV q8h[a]	*Aminoglycosides*[b] • Amikacin 15-20 mg/kg IV q24h • Gentamicin 5-7 mg/kg IV q24h • Tobramycin 5-7 mg/kg IV q24h
OR	*OR*
• Cefepime 2 g IV q8h[a] • Ceftazidime 2 g IV q8h	*Polymyxins*[c] • Colistin 2.5-5 mg/kg/day IV in 2 to 4 divided doses *OR* 5 mg/kg IV × 1 followed by a daily dose of 2.5 × (1.5 × CrCl + 30) IV divided q8h to 12h
OR	
• Aztreonam 2 g IV q8h	
Methicillin-resistant *Staphylococcus aureus* (MRSA) Coverage	
Linezolid 600 mg IV q12h *OR* Vancomycin 15 mg/kg (consider a loading dose of 25-30 mg/kg) IV, with dosing regimen based on pharmacokinetic parameters	

[a] These agents are specifically recommended by the guidelines for VAP and HAP patients who need coverage for methicillin-sensitive Staphylococcus aureus (MSSA) but do not need MRSA coverage, and for HAP patients who are not at a high risk for mortality.
[b] Avoid using aminoglycosides as the sole antipseudomonal agent or if alternative agents are available.
[c] Should be reserved for settings with a high prevalence of multidrug resistance and for those with expertise in using the medication, since close monitoring and adjustment of doses and/or intervals may be required.
HAP: hospital-acquired pneumonia; VAP: ventilator-associated pneumonia. Source: References 1, 6.

Source: US Pharmacist

There are potentially **300,000 new cases of VAP per annum in the US** with a mortality rate of up to 36%, presenting a significant unmet need for additional treatment and/or preventative approaches. Additionally, patients with VAP have prolonged durations of mechanical ventilation, intensive-care unit (ICU) stays, and hospital stays, as well as almost $40,000 in excess mean hospitalization costs as compared with patients without VAP.

Destiny Pharma is currently carrying out pre-clinical studies to evaluate the efficacy of XF-73 in the indication, prior to proceeding with first clinical trial and with potential data by 2019. It is evaluating the utility of a dual-delivery approach in this setting, via the throat and nose to prevent colonisation of the most vulnerable root causes of pneumonia.

Therefore the company is exploring a delivery mode to the throat, which might include a form of spray in tandem with the existing nasal formulation. We await further news before adding this indication into our forecasts, including potential grant of QIDP status in the indication.

XF-70 unmet need in bacterial burn wound infections

The Company is investigating two more preclinical indications from the XF family, the next being for **XF-70**.

The first indication for XF-70 is a topical application to treat bacterial burn wound infection.

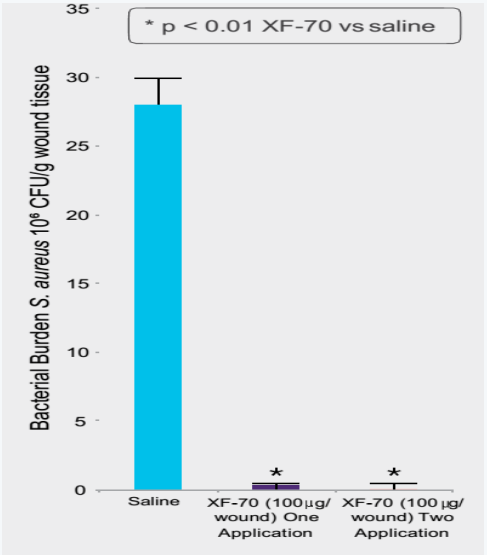
This is a severe, hard-to-treat infection as traditional antibiotics delivered intravenously or orally are largely ineffective due to the breakdown of the circulation surrounding a burn wound.

These are at an earlier stage than with XF-73, although the company has already undertaken preclinical studies and provided early *in vivo* data, illustrated in the following graphic, showing that a single dose of XF-70 reduced bacterial burden by 98.8%.

The mainstay of treatment includes topical antibiotics, such as mafenide, mupirocin and silver sulfadiazine and of early excision and grafting helping to lower mortality from infection. However, Gram-positive and Gram-negative bacterial infection remain one of the most common causes of mortality following burn injury.[13] Acute burns requiring medical treatment affect c 0.5 million Americans each year, with c 40,000 hospitalisations and 3,400 deaths annually (source: Gibran N S et al, American Burn Association consensus statements. J Burn Care Res. 2013).

The next steps include production of formulations, preclinical testing in burn wounds and the creation of a preclinical safety package in the indication. For now, we await further news including the initiation of first human trial before including XF-70 in our forecasts.

The novel antibacterial drug XF-70 is a potent inhibitor of *Staphylococcus aureus* infection of the burn wound



Source: Journal of Burn Care Hurtuk MG et al, 2010

[13] Contribution of bacterial and viral infections to attributable mortality in patients with severe burns: D'Avignon et al in Burns, 2010.

Early promise for treating infection in biofilms

Biofilms, which are formed from a layer of impermeable slime which coats and encloses bacteria, pose an increased risk when treating infection since they are generally highly resistant to treatment. Destiny identified that XF-70 has *in vitro* activity against biofilms – and was **granted a US patent** for using XF drugs in biofilms in 2016.

There are many potential applications for XF drugs if clinical data demonstrate the potency seen *in vitro*, as the formation of a biofilm means that many types of infection can turn into chronic illness. The company is focusing initially on the potential to treat chronic pneumonia in Cystic Fibrosis (CF) sufferers. MRSA is an increasing cause of lung infection in people with CF, with c 25 percent of the c 30,000 sufferers in the US going on to develop pneumonia, according to the US CF Foundation.

This approach would require a new formulation potentially via a nebuliser to reach into the lower respiratory tract and the company is currently exploring reformulation of XF-70. An example of this approach is Gilead Sciences which launched its inhaled antibiotic CAYSTON in 2010, indicated for relief of respiratory symptoms in CF patients with *Pseudomonas aeruginosa* and specifically for use with proprietary Altera nebuliser from PARI Pharma.

We assume that a paediatric indication for XF-70 would be required and that Destiny would look for sources of non-dilutive funding, such as the Swiss biotech company Polyphor achieved. Recently it was awarded €5m by the European - Innovative Medicines Initiative (IMI) - towards the development of an inhaled dosage form of its novel breakthrough antibiotic Murepavadin.

The fact that Cystic Fibrosis is an orphan disease, affecting less than 200,000 people, means that Destiny could attract additional incentives and regulatory status including exclusivity and/or paediatric exclusivity under FDA or European guidelines. Preclinical data demonstrate that **XF-70 required significantly lower concentrations** to eradicate *S aureus* in biofilms compared to standard antibiotics.

Efficacy

Drug	MIC (µg/mL)	MBEC (µg/mL)	Multiple of MIC to kill *S.aureus* in Biofilm (x)
Ciprofloxacin	0.5	>256	>500
Fusidic acid	0.125	>256	>2,000
Tetracycline	0.5	>256	>500
Rifampicin	0.008	128	16,000
XF-70	1	2	2
XF-73	1	2	2

Potential clinical advantage – Biofilms implicated in 80% of infections

Strain: *Staphylococcus aureus* SH1000
Method: Minimum inhibitory concentrations (MIC) and minimum biofilm eradication concentrations (MBEC) determined in the Calgary Biofilm Device

Source: Destiny Pharma

We think that the Company is likely to seek partnerships, or government funding sources to progress further and, as in burn wound infection treatment, we await news that XF-70 has entered clinical trials in humans before including this program in our financial forecasts.

Anti-infective peers - a focus on *S aureus*

Looking at the treatment and prevention landscape, there have been few approvals over the past decade and many notable failures, including many specifically in *S aureus*. The creation of QIDP status by the FDA has helped to spur on a group of companies aiming at the traditional antibiotics approach. First was DALVANCE/dalbavancin, Durata Therapeutics' Intravenous antibiotic for treatment of adult patients with acute bacterial skin and skin structure infections (ABSSSI) caused by Gram-positive microorganisms including *S aureus* and was the first drug to be approved by the FDA under QIDP in 2014. A more recent approval from 2017 is Badexla/delafloxacin also for ABSSSI from NASDAQ-listed Melinta Therapeutics which covers both Gram-positive and Gram-negative infections.

As we have already said, **there are no approved comparators in the prevention of surgical infection caused by *S aureus*,** although looking at pipelines there are products lining up including some products in the categories outlined by Lord O'Neill in his AMR report:

- Antimicrobial peptides; still at the early stages with none approved to our knowledge;
- Microbiome related biological therapies including; probiotics and faecal microbiota an area of emerging and significant interest and supported by FDA framework of regulation is at early stages with further studies needed to establish efficacy;
- Bacteriophages; none approved for human use in US but commonly used to treat infection in the food industry. Bacteriophages are bacterial viruses which can infect and breakdown the bacteria;
- Immune Stimulation; i.e. using monoclonal antibodies (mAbs) or vaccination although there are no approved vaccines and no approved mAbs against MRSA.

A cross-section of clinical programs that are perhaps the most appropriate comparators to XF-73, as they are non-antibiotics which are being or have been studied in the same lead indication, is shown in the following table:

Co/Product/Indications	Status	Data
Helperby Therapeutics/ HY004/HY005/HY006/ Nasal MRSA decolonisation/ Skin & soft tissue MRSA/ Pulmonary Cystic Fibrosis	Phase II/ Phase I/Preclinical/ No data posted	Antibiotic Resistance Breakers (ARBs) combined with approved antibiotics aimed at restoring potency against Gram positive and Gram-negative bacteria. HY005/007 are licensed to Cadila Therapeutics for India. Phase I data in complex urinary tract infection announced 2017 showing to be safe/well-tolerated.
Gangagen/ P128/Nasal MRSA decolonisation	Phase II/No data posted	Preclinical data presented at European Society of Clinical Microbiology and Infectious Diseases ESCMID –Ectolysins, rapidly degrades cell wall, leading to lysis and death of bacterium. Proprietary phage-derived protein active against MRSA, vancomycin-resistant *Staphylococcus aureus* (VRSA) and coagulase-negative Staphylococci.
Lytix Biopharma/ LTX-109/Nasal MRSA/MSSA decolonisation/Diabetic foot infection	Phase I/II No data posted	The company focus is currently immune-oncology. LTX-109 is a synthetic antimicrobial peptide, Phase I/II study started 2010. Diabetic foot infection trial terminated.

Source: Equity Development/Company websites/clinicaltrials.gov

However, there appears to be little data or news flow available for the first two nasal decolonisation programs – while Lytix Biopharma seems to have moved its focus away from bacterial infection definitively.

Looking forward there appears to be a range of earlier stage companies including seven that were beneficiaries of a total of $17.6m grant funding from preclinical company accelerator CARBX in 2017. Many appear to focus on targeting new approaches to multi-drug resistant bacteria and on Gram-negative infection.

Vaccination is an approach thought to offer great promise, but there have been many attempts… but no successes to date. In fact, the CDC states that **'We have no licensed vaccines for any of the bacteria that are considered by the US Centers for Disease Control and Prevention (CDC) to represent our most urgent AMR threats.'**

Notable *S aureus* failures include: StaphVAX NABI Vaccine CP5/CP8, Pentastaph NABI/GSK Vaccine CP5/CP8 and Merck's V710 MERCK Vaccine. The programs all reached Phase III but the issue of identifying suitable surface antigens effective in targeting the bacteria appeared to be the slipping point and could also be a factor in the antibody treatment approach.

Looking forward, there are a range of more vaccines including STEBVax Integrated Biotherapeutics Vaccine Seb at Phase I/II, Pfizer's SA3Ag 3-antigen *S aureus* vaccine, at Phase II and MEDI4893 Medimmune Antibody Hla, Phase II – although the established precedent puts likelihood of approval at a low rate.

Furthermore, it seems that Destiny's XF-73 is better positioned in the prevention of infection given that it has a rapid action against bacteria and more likely to be a convenient modality than vaccination in terms of emergency surgery and in preventing infection in patients with already low immunity.

Sensitivities

While Destiny has already accumulated a broad range of safety and efficacy data on the lead product, the company is subject to the typical risks affecting clinical biotech companies including the risk of delays in recruiting and executing clinical trials or changes in the regulatory rules. On a broader basis, the timely and optimal conditions for taking its products to approval also depend on a favourable economic outlook and the translation of new legislation such as the Cures Act into streamlined approval processes.

We view that while the Company is well-funded now to take XF-73 right through to the end of Phase II studies in the lead indication, the strategy is dependent on achieving a partnership after that stage. If study data show a consistent profile, the probability of attracting a deal appears to be high given the commercial potential of the lead product, and the low propensity for resistance is a key benefit.

For the other products in the pipeline, additional funding or again a partner is needed realistically to get them all off the ground and in the smaller follow on indications, non-dilutive grant funding, collaborations and/or orphan status would help to accelerate development.

As always, adoption of new products can be slow and the pace of acceptance would be affected by buy-in from key opinion leaders. Good safety profile, speed of efficacy and low resistance profile are all factors that could help encourage adoption.

Valuation

We use a SOTP DCF approach to value DESTINY and apply a standard 12.5% drug development discount rate to reach our current valuation of £115m (263p / share).

For now, we consider only the current clinical stage candidate XF-73 which is an advanced Phase II program and due to enter FDA-backed studies in 2018 in Prevention of post-surgical Staph infection.

There is a strong body of supportive clinical data amassed across five different trials and in over 200 subjects, which collectively gives us greater confidence in the established safety profile and evidence of efficacy for XF-73. We also consider that typically drug candidates being developed in infectious disease indications – excluding vaccines – have **twice the likelihood of approval LOA** than an average drug candidate – according to Biomed Tracker. A phase II anti-infective drug has 35% likelihood of approval vs c 16% for all indications.

We only derive this value from the US opportunity at this stage until such times as DEST confirms the timeline and approach for European and other significant global territories. For now, we have included just the clinical stage program for XF-73 underway; allowing future potential to add in the ICU setting once limited pathways defined under the Cures Act are ratified and adding the remaining preclinical indications once human trials start. All providing upside to our current valuation.

Our valuation assumes that Destiny Pharma will look for partnership post Phase II and would subsequently earn royalties on ensuing sales of XF-73. We use a standard Phase II royalty rate of 15%. Our assumptions include five-year ramp to peak, 2022 launch and patent term extension into 2035.

DCF Valuation

	£m	Per share, p
XF-73 prevention of post-surgical infection, S aureus carriers, US	66.9	153.7
XF-73 prevention of post-surgical infection, Universal Decolonisation, US	27.8	63.9
XF-73 Universal Decolonisation in emergency surgery cases, US	5.7	13.0
Corporate expenses	-2.7	-6.2
Estimated net cash (end 2017)	16.8	38.6
Number of shares (43.6m)		
Total	114.5	262.9

Source: Equity Dev. NB rNPVs net of 20% taxation and risk adjusted Phase IIb R&D expenses

The share price has been volatile in the short period since IPO in September, having briefly risen 50% above the 157p admission price in the fortnight following listing. In our view, the current market capitalisation of £70m reflects low likelihood of approval in the lead indication, and fails to fully evaluate the breadth of clinical data and higher than average success rates in infectious disease indications.

Our assumptions

Candidate	LOA*	Royalties	Launch	Peak sales
XF-73 prevention of post-surgical infection, *S aureus* carriers US	35%	16% assuming partnered post Phase II.	2022	$602m, price per patient $200, 50% share of 6m patient pool
XF-73 prevention of post-surgical infection, Universal Decolonisation, US	35%	16% assuming partnered post Phase II	2022	$244, price per patient $200, 10% share of 12.2m patient pool
XF-73 Universal Decolonisation in emergency surgery cases, US	35%	16% assuming partnered post Phase II	2022	$50m, price per patient $200, 50% share of 0.5m patient pool

*Source: Equity Development/BioMed Tracker *Likelihood of Approval, Phase II candidates NB rNPVs of product royalties are net of 20% taxation and risk-adjusted Phase IIb R&D expenses.*

News flow

There should be many developments to watch for, including:

- Initiation of clinical trials for the preclinical candidates, then further data on these programs;
- Policy-led outcomes such as news about accepting revised or expedited approval for urgently needed drugs. For instance, from the 21 C Cures Act or the grant of QIDP status for any other program in the pipeline.
- Further external news on hospital infection penalties, and international initiatives on AMR problem solving.

With the challenges in vaccine development, big pharma attention has turned towards higher profile more lucrative indications like oncology. An exception that stands out is Pfizer's $1.5bn acquisition of Astra Zeneca's antibiotics division in December 2016 motivated by the former's specialism in infectious disease and therefore higher likelihood of maximising commercial potential alongside its existing anti-infectives portfolio.

The relatively low number of new anti-infective drugs in pipelines is reflected in overall partnership deal flow over the period 2012-H116 when anti-infective deals accounted for 10% of volume vs 22% oncology and just 7% of value vs 36% for oncology drugs, according to Medtrack.

Financials

Destiny Pharma is well-funded for existing plans via its recent placing raising £15.3m gross to cover the costs of the Phase IIb program for XF-73 in Prevention of post-surgical *S aureus* infection for the US, plus the follow-on £3m investment by CMS for a further 1.9m shares at the 157p placing price. Our projections include an estimated total R&D spend of £8.6m and £4.7m in FY18/19 to cover both the internal and external costs of the lead program and follow on programs and other projected expenses including IP maintenance.

In parallel, G&A costs are forecast to rise to £1m in FY17 up to £1.9m, £1.7m and £1.3m over 2018, 2019 and 2020 to cover planned investment in regulatory and market research work.

We estimate that the level of R&D tax credits received will rise (from £0.2m estimated in FY17) over the forecast period in line with levels of R&D spend up to £2m, £1.1m and £0.4m over 2018, 2019 and 2020 respectively. We forecast that Destiny will end December 2017 with £16.8m of net cash – including the net proceeds of the fund raising and the £3m additional investment from CMS.

Income statement

Y/e Dec 31 £'000s	2015	2016	2017E	2018E	2019E	2020E
Revenues	0	0	0	0	0	0
Cost of goods sold	0	0	0	0	0	0
Gross Profit	0	0	0	0	0	0
R&D Expenses	-274	-496	-1,647	-8,647	-4,669	-934
G&A Expenses	-646	-753	-1,050	-1,891	-1,701	-1,276
Sales & Marketing	0	0	0	0	0	0
Operating Loss	-921	-1,249	-2,697	-10,537	-6,371	-2,210
Share based payments	-284	-201	-455	-364	-357	-350
Acquisition related amortisation	0	0	0	0	0	0
Exceptionals	0	0	0	0	0	0
Other revenue/expenses	0	0	0	0	0	0
EBITDA	-1,204	-1,448	-3,152	-10,901	-6,727	-2,559
Operating Loss	-1,205	-1,450	-3,153	-10,901	-6,728	-2,560
Interest income	8	0	1	34	16	6
Other financing costs/income	0	0	0	0	0	0
Exceptionals	0	0	0	0	0	0
Loss Before Taxes	-1,197	-1,449	-3,152	-10,868	-6,712	-2,554
Adj. Loss Before Taxes	-913	-1,249	-2,696	-10,504	-6,355	-2,204
Current tax credit	182	192	254	1,956	1,074	307
Deferred tax benefit	0	0	0	0	0	0
Discontinued operations	0	0	0	0	0	0
Net Loss	-1,015	-1,258	-2,897	-8,912	-5,638	-2,248
Loss per share (p)	-3.2	-3.9	-7.7	-20.5	-12.9	-5.2
DPS (p)	0.0	0.0	0.0	0.0	0.0	0.0
Average no. of shares m	31.9	31.9	37.7	43.6	43.6	43.6

Source: Company historic, ED estimates

Balance sheet

Y/e Dec 31 £'000s	2015	2016	2017E	2018E	2019E	2020E
Current assets	1,343	1,698	17,128	8,580	3,298	1,400
Cash and cash equivalents	1,119	1,481	16,806	7,832	2,771	1,065
Assets held for sale	0	0	0	0	0	0
Accounts receivable	201	217	150	150	150	150
Inventories	0	0	0	0	0	0
Other current assets	23	0	172	597	377	185
Non-current assets	3	1	1	2	2	2
Property, plant & equipment	3	1	1	2	2	2
Intangible assets	0	0	0	0	0	0
Other non-current assets	0	0	0	0	0	0
Current liabilities	-94	-155	-93	-93	-93	-93
Short-term debt	0	0	0	0	0	0
Accounts payable & accruals	-94	-155	-94	-94	-94	-94
Liabilities held for sale	0	0	1	1	1	1
Non-current liabilities	0	0	0	0	0	0
Long-term debt	0	0	0	0	0	0
Other non-current liabilities	0	0	0	0	0	0
Equity	1,251	1,544	17,036	8,489	3,208	1,310
Share capital	1	1	18,253	18,253	18,253	18,253
Other	1,250	1,544	-1,217	-9,764	-15,045	-16,943

Source: Company historic, ED estimates

Cash Flow

Y/e Dec 31 £'000s	2015	2016	2017E	2018E	2019E	2020E
Net cash from operating activities	-901	-988	-2,609	-8,972	-5,060	-1,705
Profit/(loss) before tax	-1,197	-1,449	-3,152	-10,868	-6,712	-2,554
Non-cash adjustments	277	202	455	365	358	351
Change in working capital	-163	68	6	0	0	0
Interest paid	0	0	0	0	0	0
Taxes paid	182	192	82	1,531	1,294	498
Investing cash flow	5	0	-1	-1	-1	-1
CAPEX on tangible assets	-3	0	-1	-1	-1	-1
Disposals/Acquisitions/other cash flows	8	0	0	0	0	0
Financing cash flow	10	1,351	17,934	0	0	0
Proceeds from equity	10	1,351	17,934	0	0	0
Increase in loans	0	0	0	0	0	0
Dividends	0	0	0	0	0	0
Other financing cash flow	0	0	0	0	0	0
Net increase in cash	-885	363	15,324	-8,973	-5,061	-1,706
Exchange rate effects	0	0	0	0	0	0
Cash at start of year	2,004	1,119	1,481	16,806	7,832	2,771
Cash at end of year	1,119	1,481	16,806	7,832	2,771	1,065
Net cash at end of year	1,119	1,481	16,806	7,832	2,771	1,065

Source: Company historic, ED estimates

Biographies

Executive team	
Neil Clark FCA - CEO	• An ex Big Four Accountant, Mr Clark was formerly CFO and then CEO at CeNeS Pharma and at then CFO at Ergomed where he was instrumental in floating both companies. • Holds a BSc in Bioscience from Nottingham University. • Appointed to the board of Destiny Pharma in January 2017.
Dr Bill Love PhD - CSO	• Senior Scientist at Ciba Geigy/Novartis focused on novel Drug Delivery technologies and involved in development of the world's leading eye-care pharmaceutical, Visudyne. • Founder of Destiny Pharma and co-inventor of the XF drug platform. Named inventor in more than 70 patents. • A founding member of the BEAM Alliance, an EU group focused on promoting anti-microbial drug development. • Expert Advisory Board member of Global AMR Innovation Fund, appointed in 2016 • Drug R&D experience spans discovery through to Phase I/II clinical development in the UK, EU and US.
Simon Sacerdoti FCA - CFO	• Holder of an MA in Mathematics from Balliol College, Oxford and a qualified Chartered Accountant • Corporate financier at Ernst & Young, BDO and at Dowgate Financial Advisers, a small-cap corporate finance boutique. • In 2009, he became a founding partner of AIM adviser Cairn Financial Advisers and subsequently a co-founder of innovative payments start-up, WeSwap. • Became a consultant to Destiny Pharma in September 2015 and was appointed CFO in April 2016.

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