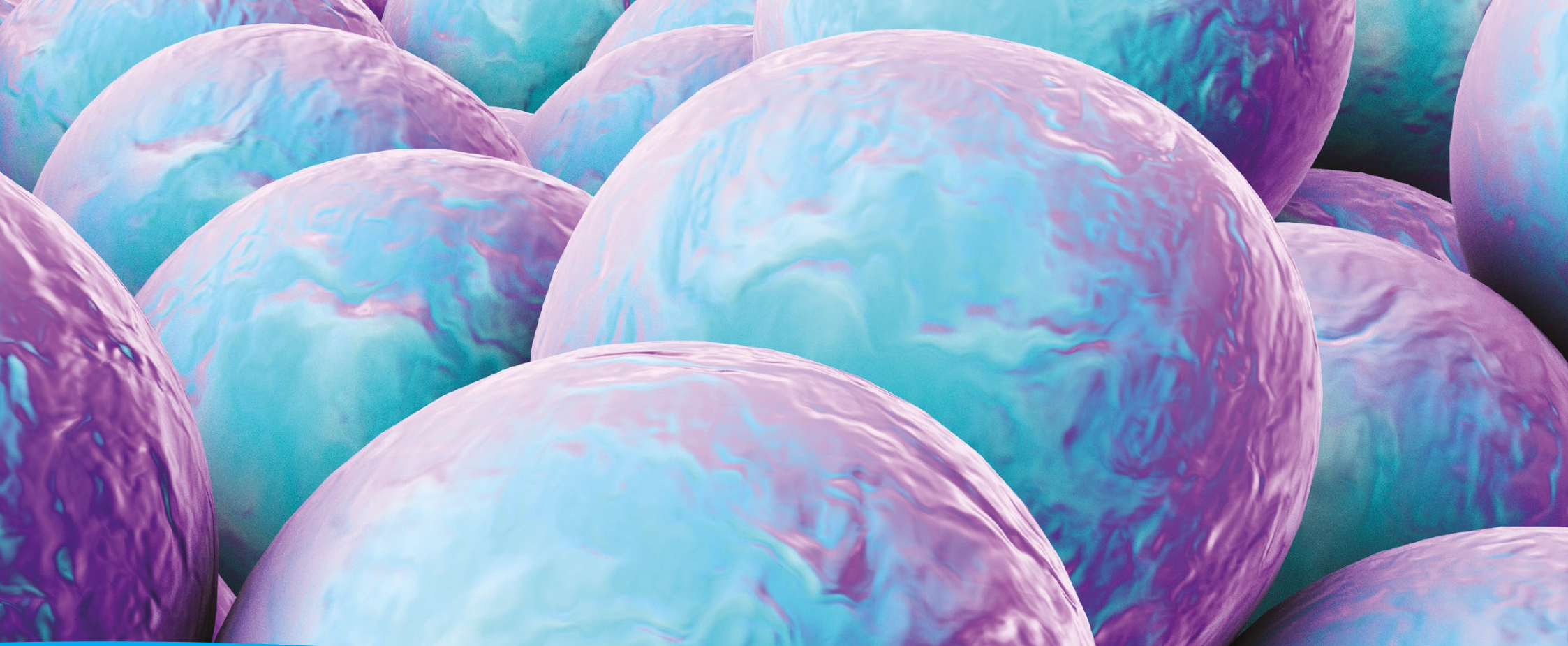


Emerging Antimicrobials and Diagnostics in AMR

20th November 2019

Developing novel products that prevent serious infections

Destiny Pharma

AMR INSIGHTS®

TOWARDS A WORLD FREE FROM AMR

Tackling Antimicrobial Resistance

A Global Imperative

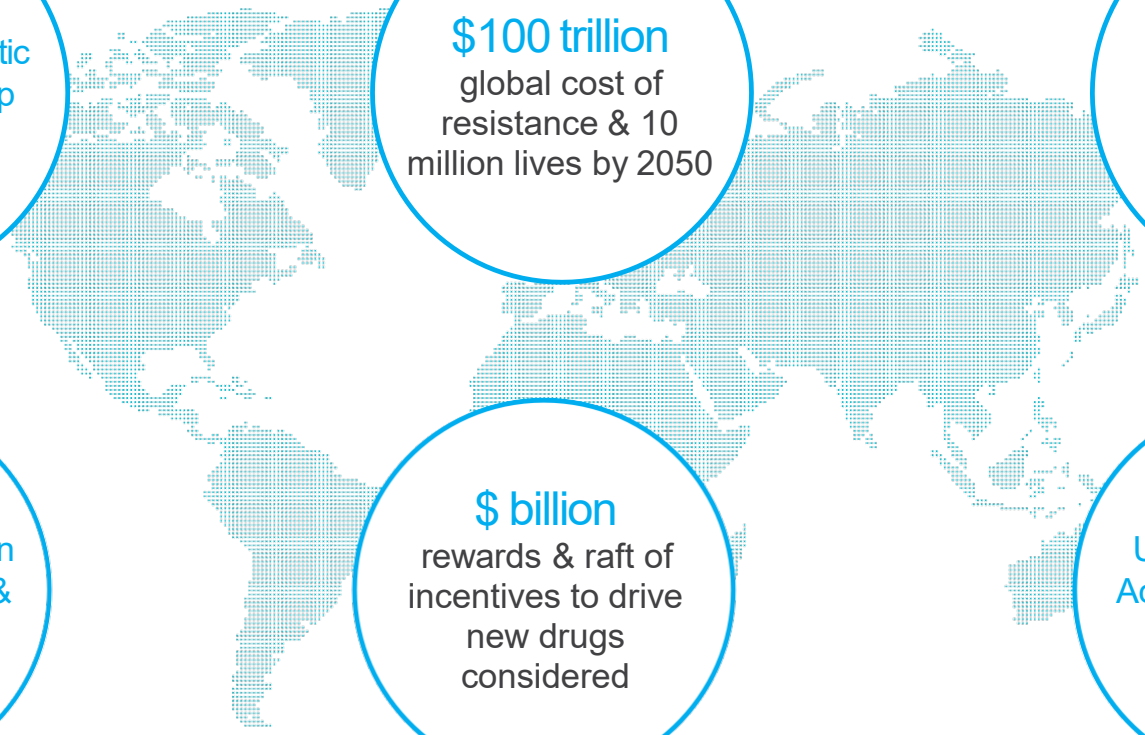
Destiny Pharma

WHO name antibiotic resistance as a top global concern

$100 trillion global cost of resistance & 10 million lives by 2050

"Threatens the end of modern medicine"

Dr Margaret Chan
President, WHO



Tackling resistance on United Nations, G7 & G20 main agenda

$ billion rewards & raft of incentives to drive new drugs considered

US GAIN & Cures Acts lower regulatory hurdles

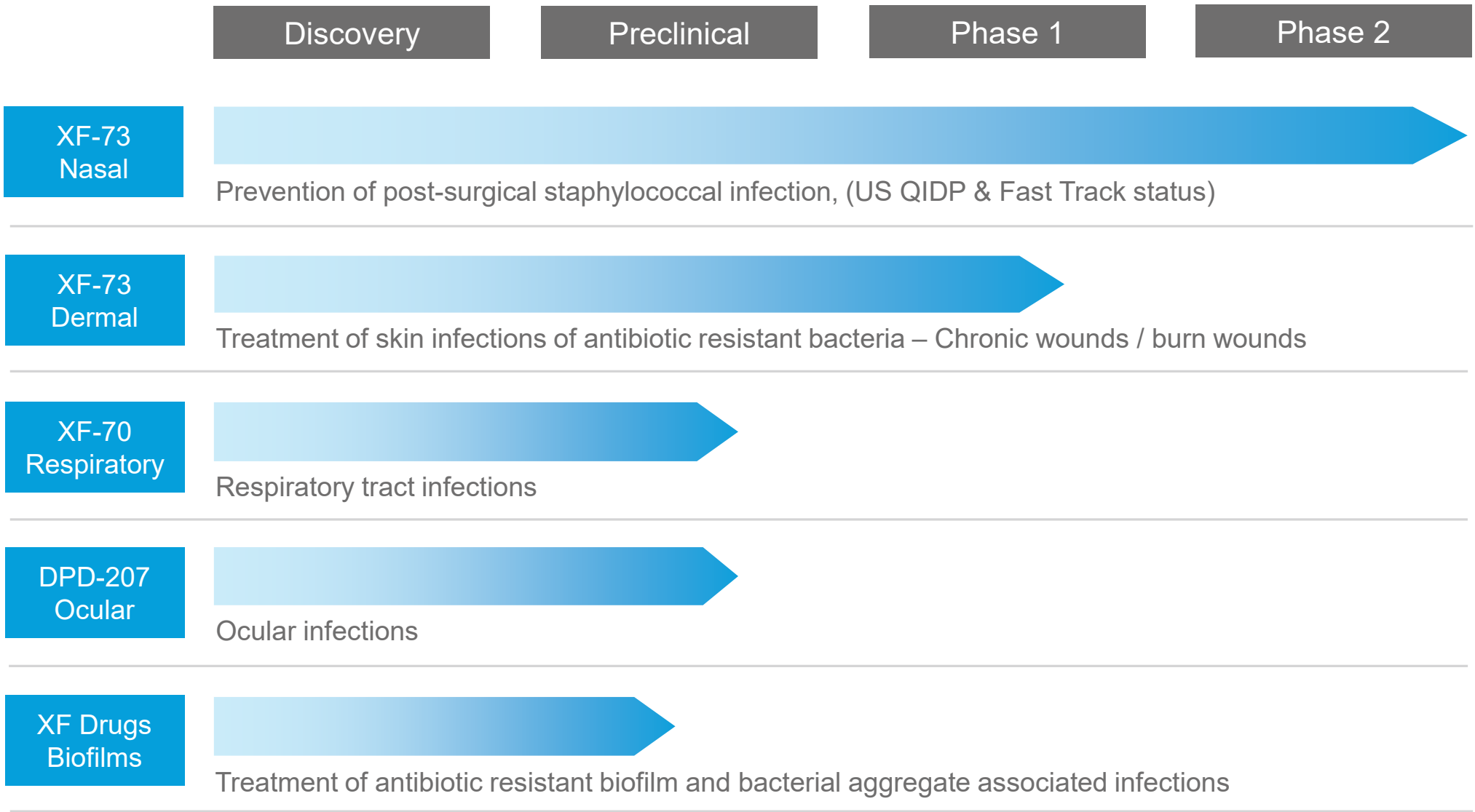
XF Drugs address resistance and opens new preventative markets

(Tackling Drug-Resistant Infections Globally: Final Report and Recommendations. The Review on Antimicrobial Resistance. Jim O'Neil. May 2016)

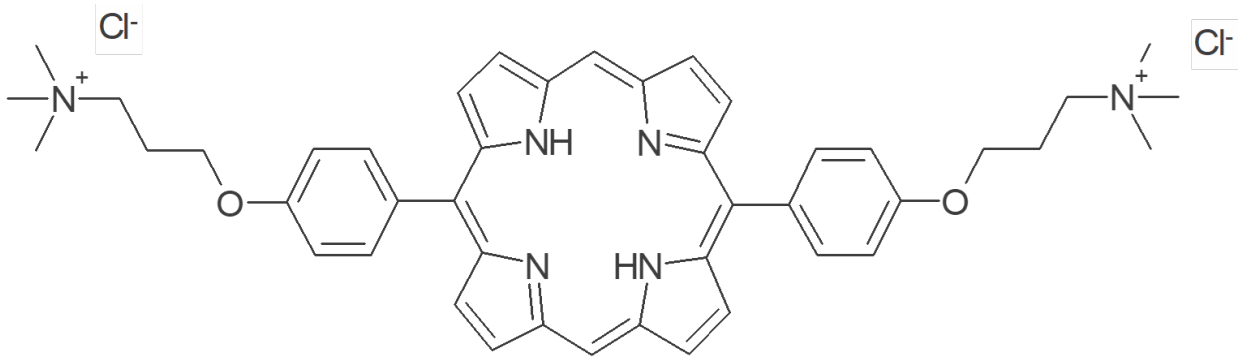
Prevention is better than cure

- Significant value inflection Phase 2b read-out in mid-2020 from lead asset, XF-73, is a novel hospital-use antimicrobial drug to prevent post-surgical infections
- XF-73 is uniquely differentiated from current antibiotics – target profile is compelling, with a strong IP position protecting product franchise into 2030s
- XF-73 has favourable pharmaco-economics that support the pricing strategy and strong cost benefit argument, particularly in US
- Strong pipeline potential – opportunities for line extensions for XF-73 and other XF drugs from proprietary platform
- Destiny Pharma is well-funded to late 2020 – cash comfortably extends past XF-73 Phase 2b trial read out

XF Drug Product Pipeline: Targeting clear, clinical unmet need



XF Drugs: Providing a solution to AMR



Molecular formula : $C_{44}H_{50}Cl_2N_6O_2$
Relative molecular mass : 765.83

- XF-73
- INN Exeporfinium chloride
- Novel drug structure
- Patent protected
- Platform of XF Drugs
- Topical antibacterial drugs

'XF Drug' Platform based on a unique, bacteria kill mechanisms of action

- Intrinsic targeting of the Gram positive bacterial membrane
- Ultra-rapid, bacterial kill (within minutes)
- Kills any stage of bacterial growth – including within biofilms
- Kills all antibiotic resistant Gram positive bacteria tested
- MRSA shown no ability to become resistant to XF Drug action
- Potency against Gram negative bacteria can be achieved by an additional photodynamic mechanism of action.

XF-73

Potent against all MSSA & MRSA strains tested

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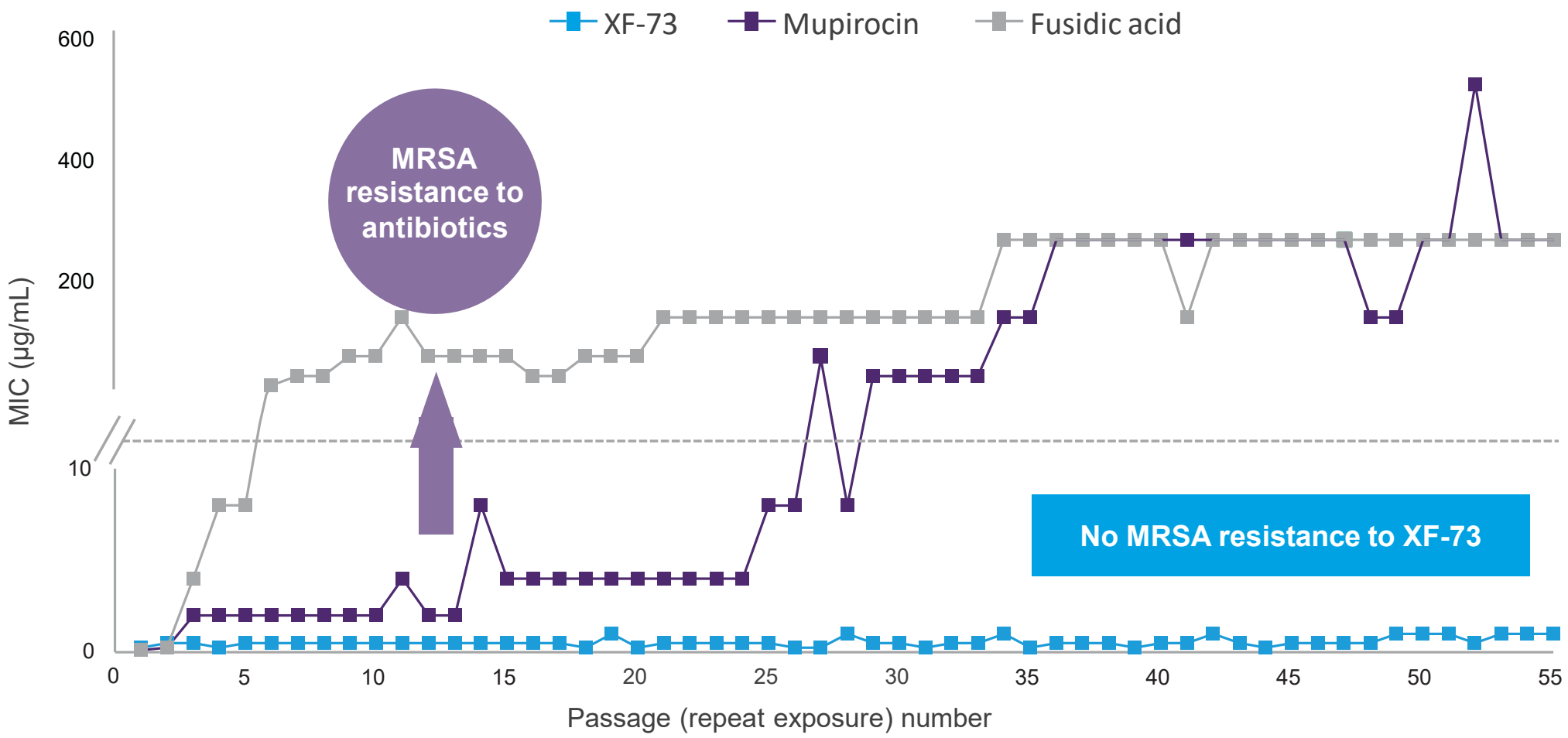
***S. aureus* Strain Description**	**XF-73 MIC (µg/mL)**
MSSA CLSI control strains (ATCC 29213 & ATCC 25923)	**0.5**
Methicillin-resistant clinical isolate & multi-drug resistant clinical isolate MRSAs	**1**
SSCmec type 1 - EMRSA3 & SSCmec type 2 - EMRSA16	**0.5**
SSCmec type 3 - EMRSA1 & SSCmec type 4 - EMRSA15	**1**
Linezolid-resistant, E-MRSA 15 clone	**1**
High level mupirocin resistance (>256 mg/L) clinical isolate	**1**
Daptomycin non susceptible (2mg/L) MRSA clinical isolate	**1**
Daptomycin MIC of 32 mg/L USA300 MRSA laboratory isolate	**0.5**
Mupirocin MIC of 256 mg/L USA300 MRSA laboratory isolate	**0.25**
Fusidic acid MIC of 128 mg/L USA300 MRSA laboratory isolate	**0.25**
Japan/NY MRSA clone - USA100	**0.25**
(MRSA) - PVL positive - HT2001254	**1**
Community-Associated MRSA - USA400	**0.5**
Community-Associated MRSA - USA300	**0.25**
Paediatric MRSA clone - USA800	**0.5**
VISA type strain - MU50	**1**

XF-73
No MRSA Resistance to XF-73 – Unlike Mupirocin & Fusidic Acid



Farrell, *et al*.; 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. *Antimicrobial Agents & Chemotherapy* **(2011)**; 55; (3) 1177-1181

XF-73

Focus on 'Prevention of post-surgical *S. aureus* infections'

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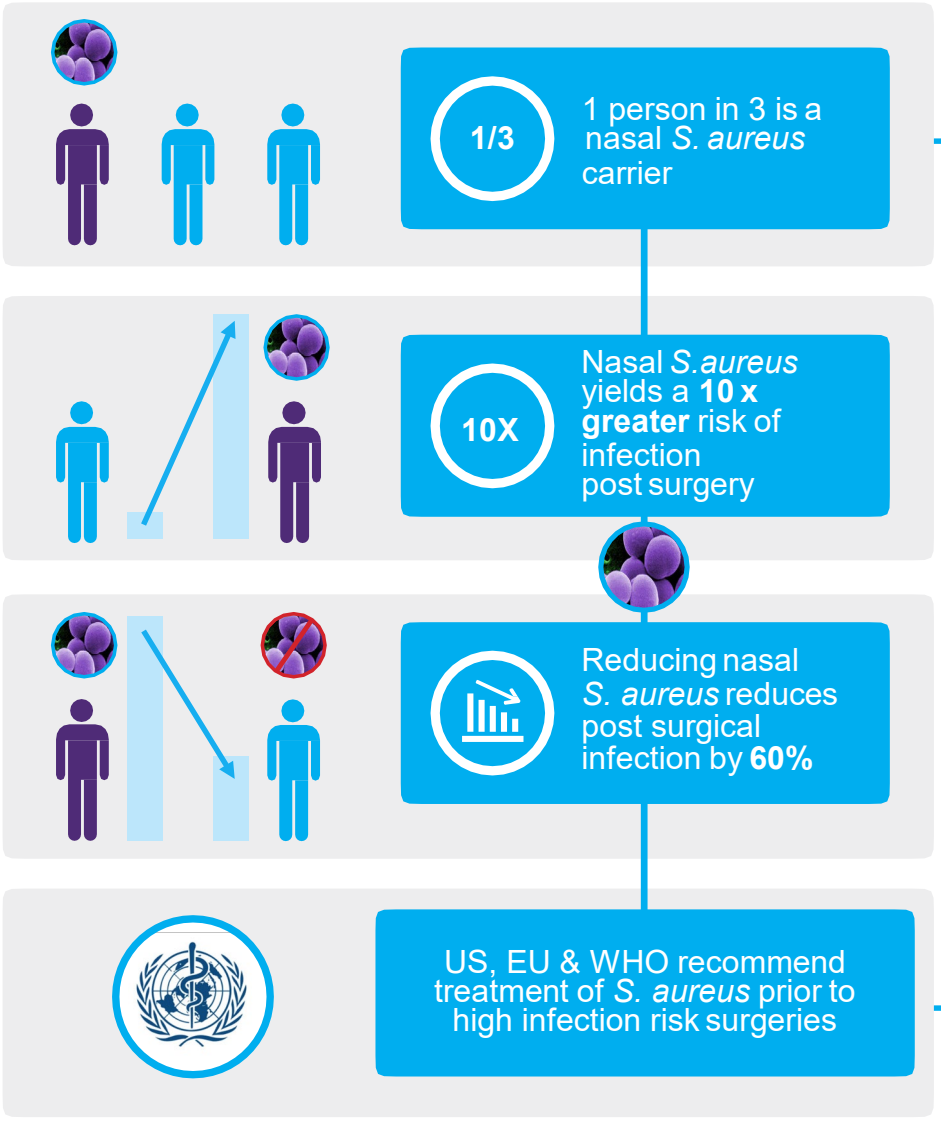
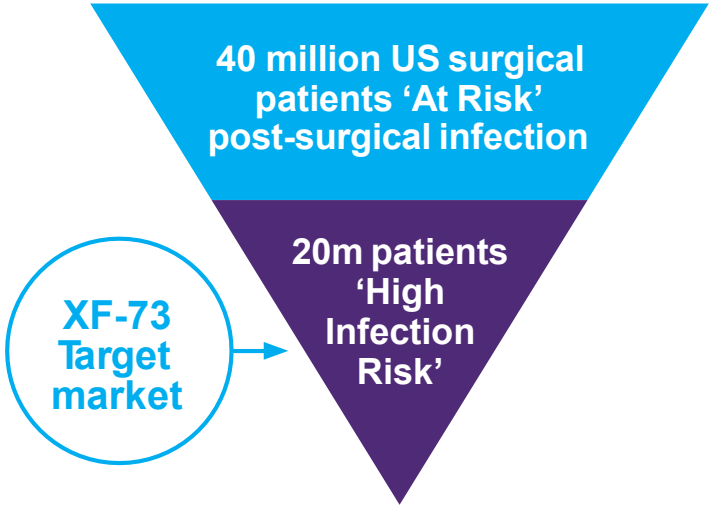


Current US practice:

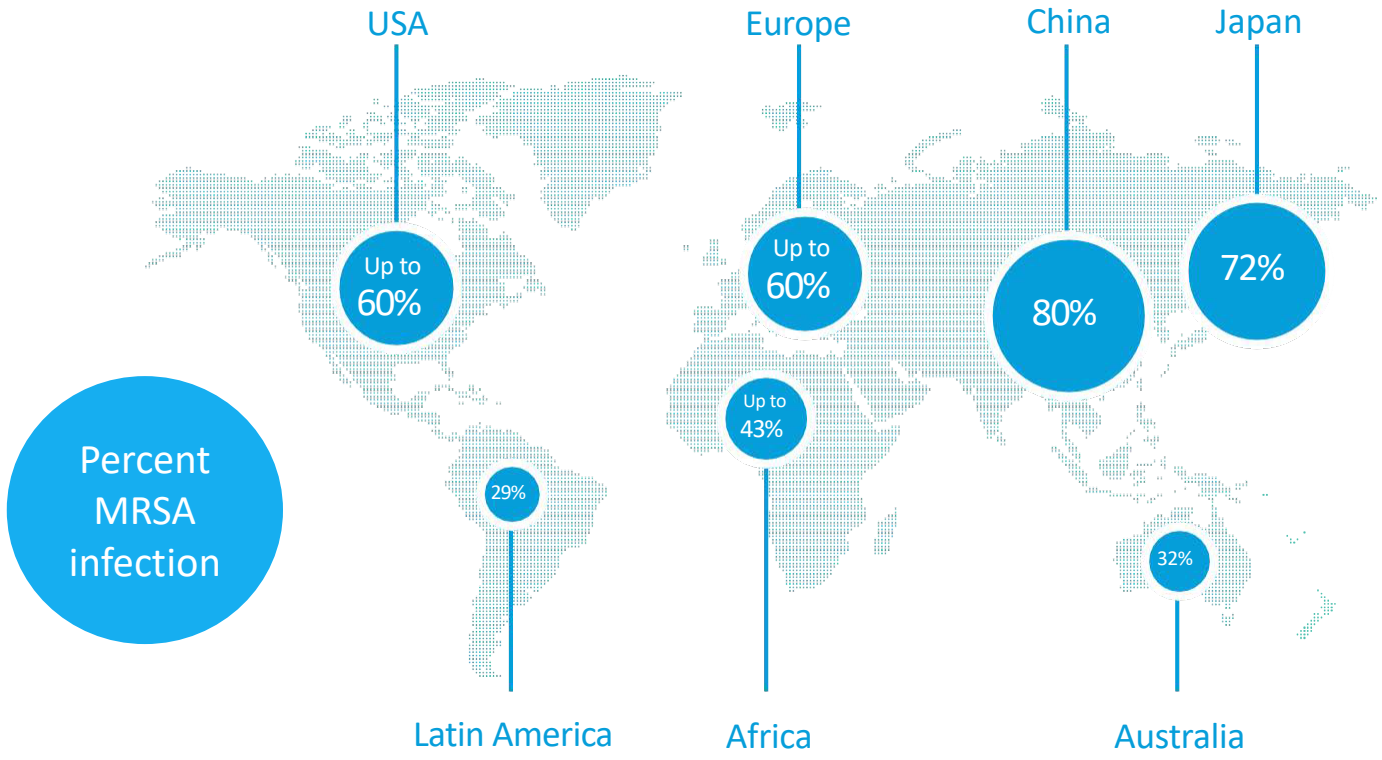
1. No treatment or,
2. High risk patient, pre-surgical use of the nasal antibiotic, mupirocin, (off label)

BUT

- Widespread & prolonged use has led to **rapid emergence of *S. aureus* mupirocin resistance**
- Resistance rates of up to 95% reported
- Some US hospitals have halted use due to 400% increase in rate of mupirocin resistance



Methicillin Resistant Staphylococcus aureus (MRSA)
Major Cause of Global Hospital Infection



S.aureus (incl. MRSA) hospital infections cost US economy alone up to $10 billion p.a.

40 million US surgical patients p.a. 'at risk' of *S.aureus*/MRSA infection

XF-73 aims to address this global unmet medical need

Decolonisation Strategies for the Prevention of post-surgical *Staphylococcus aureus* infections

Destiny Pharma

- Center for Disease Control (Surgical site infection (SSI) prevention practices)

  For all patients undergoing high risk surgeries (e.g. cardiothoracic (CT), orthopedic, and neurosurgery), **unless known to be S. aureus negative**, use an intranasal antistaphyloccal antibiotic/antiseptic (e.g. mupirocin or iodophor) and chlorhexidine wash or wipes prior to surgery (SHEA and IDSA).

- Hospital Corp of America

  The **Universal ICU Decolonization** protocol in adult intensive care units (ICUs) (AHRQ).

- NHS (Surgical site infections: prevention and treatment)

  Consider nasal mupirocin in combination with a chlorhexidine body wash before procedures in which Staphylococcus aureus is a likely cause of a surgical site infection. This should be locally determined and take into account:

  - the type of procedure
  - individual patient risk factors
  - the increased risk of side effects in preterm infants
  - the potential impact of infection.

REDUCE MRSA Trial: Targeted versus Universal Decolonization to Prevent ICU Infection
Susan S. Huang 2013

"*Universal decolonization of patients in the ICU was the most effective strategy, significantly reducing MRSA-positive clinical cultures by 37% and bloodstream infections from any pathogen by 44%*."

XF-73 addresses pre-surgical nasal eradication, a significant unmet clinical need

No approved drug in US market – current practice:

- Either, no treatment (despite "best practice" recommending decolonisation)
- Or, pre-surgical use of the old GSK nasal antibiotic, mupirocin, as unapproved drug

Significant unmet medical need:

- Widespread and prolonged use of mupirocin leads to rapid emergence of *S. aureus* mupirocin resistance and some hospitals have halted mupirocin use

XF-73 addresses this unmet clinical need

- Hospitals are incentivised to prevent post-surgical infections and reimbursement is simplified

"The use of an effective agent, should be the incentive since it would lower [the cost of] post-operative infections"
- Medical Director, California hospital

XF 73 nasal US clinical development plan

Stage	Status
• Phase 2b 200 patient efficacy study in US/Europe	• Results mid-2020 - ongoing
• Easy to use single dose presentation for Phase 3 study (see below)	• Ongoing development with Swiss contractor
• Phase 3 study	• Discuss design with FDA in 2020 • Complete study in 2022 • US / EU / International sites included
• US registration	• Submission in 2023
• EMA marketing authorisation application	• Options to be discussed with regulators
• China FDA registration	• Strategy led by partner CMS

Un-dispensed

Dispensed

XF-73 nasal gel product applicator:

- Easy use for self or nurse administration
- Dispenses single clinical nasal dose
- Convenient & encourages compliance
- Efficient and accurate dosing
- Minimises product wastage

XF Preclinical and discovery programmes

Research collaborations/grant funding validate XF platform potential

- Grant funded biofilm research projects signed with Aston, Southampton and Sheffield Universities targeting dermal, ocular and respiratory infections
  - Biofilms are a key component in serious infections associated with cystic fibrosis, medical devices, implants and catheters

- Research into mechanisms of action and resistance potential being conducted at Universities of Oxford and Sheffield

- Awarded up to £1.6m under UK-China AMR fund
  - Research projects addressing infections (including ocular) and AMR in collaboration with Cardiff University, Tianjin University and Chinese partners

- Partnered with China Medical Systems in Indo-China territories, other major global territories available for licence

<u>Seeking to enter further collaborations/grants to extend XF drug platform projects</u>

XF Drug Product Pipeline: Targeting clear, clinical unmet need

Destiny Pharma

	Discovery	Preclinical	Phase 1	Phase 2
XF-73 Nasal				

Prevention of post-surgical staphylococcal infection, (US QIDP & Fast Track status)

	Discovery	Preclinical	Phase 1	Phase 2
XF-73 Dermal				

Innovate UK · Tianjin University

Treatment of skin infections of antibiotic resistant bacteria – Diabetic Foot Ulcers / burn wounds

	Discovery	Preclinical	Phase 1	Phase 2
XF-70 Respiratory				

University of Southampton

Ventilator Associated Pneumonia / Cystic Fibrosis / Bronchiectasis

	Discovery	Preclinical	Phase 1	Phase 2
DPD-207 Ocular				

Innovate UK · Tianjin University · The University Of Sheffield.

Eye infections caused by bacteria & fungi

	Discovery	Preclinical	Phase 1	Phase 2
XF Drugs Biofilms				

National Biofilms Innovation Centre · The University Of Sheffield. · University of Southampton · Aston University Birmingham UK · Cardiff University Prifysgol Caerdydd

Treatment of antibiotic resistant biofilm and bacterial aggregate associated infections

CMS

Partnered with China Medical Systems in Indo-China territories, other major global territories available for licence

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TOWARDS A WORLD FREE FROM AMR

Thank you

Destiny Pharma

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