

# Annual General Meeting 2018



*KPMG*

*Level 36, 727 Collins St  
Melbourne*

*Tuesday 20 November 2018  
11.00am*

# Forward looking statements



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# AGM 2018

Dr Nicole van der Weerden – Chief Executive Officer



# Key achievements for 2018



Ø Fully enrolled a 48-patient phase I/IIa clinical trial for HXP124 as a treatment for onychomycosis

- Part 1 completed – results announced October 2018
  - No treatment-related adverse events, HXP124 substantially reduced the area of infected nail
- Part 2 data available January 2019

Ø Achieved >4.5-fold improvement in yield of HXP124 with new production strain

- Reduces cost of manufacture

Ø Demonstrated that HXP124 is stable in the clinical formulation at 25°C for at least 1 year

Ø Further defined the mechanism of action for HXP124

- Required for marketing approval

Ø Key patent for HXP124 granted in the USA

- Valid until 2035

Ø Appointed key consultants with expertise in drug development and licencing of pharmaceutical products



# Key achievements for 2018



- Ø Demonstrated that HXP124 and other proprietary defensins are active against the new superbug, *Candida auris*.
- Ø Partner in the \$5 million **Industry Transformation Research Hub for Medicinal Agriculture** grant to La Trobe University
  - Provides funding for screening Hexima's natural products library for novel antifungal molecules



ØHexima is developing a novel therapeutic (HXP124) for the treatment of fungal nail infections (onychomycosis).

ØHXP124 has the potential to be superior to current therapies.

- Potent, broad-spectrum antifungal molecule
  - Member of the Plant Defensin class of molecules
- Readily penetrates nails
- Rapidly kills the fungus





# Global onychomycosis market

Ø US\$3.06 billion in 2015 and projected to reach US\$4.7 billion by 2021.

Ø Major deficiencies in current therapies.

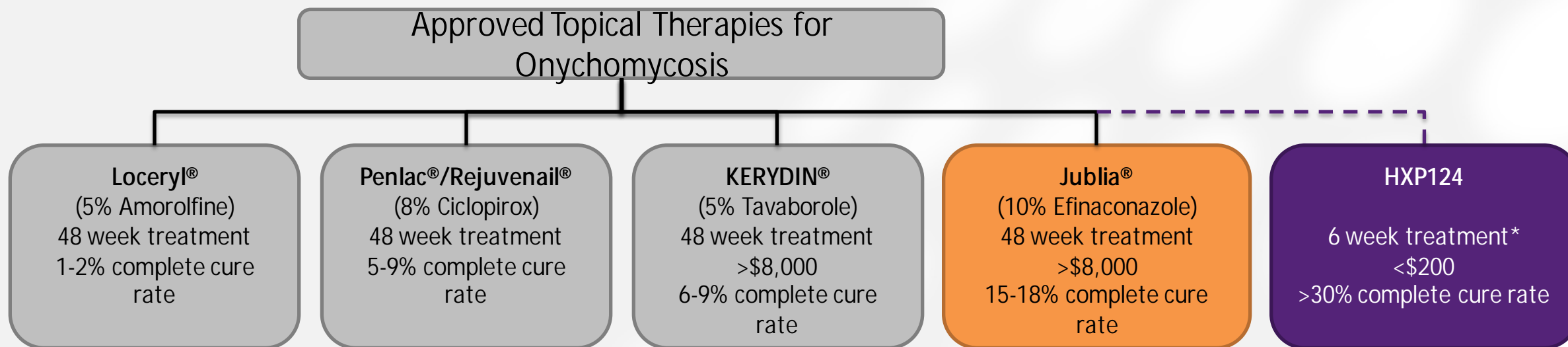
- Poor efficacy rates
- Long treatment times
- Oral therapies can be toxic
- Expensive

— Estimated that between 50 and 90% of individuals with fungal nail infections are not receiving treatment.

Ø Large potential for rapid growth in the market with an effective product.



# Global onychomycosis products



Ø Jublia® is the number 1 selling topical product (by revenue) in the USA

- US\$330 million sales in 2015 (Launched by Valeant in 2014)
- Japanese version of product sold US\$190 million in FY 2015 (Clenafin, Kaken Pharmaceuticals)

Ø HXP124 is likely to be superior to current products

- Shorter treatment time - 6 weeks vs 48 weeks (treatment may be repeated periodically to avoid reinfection)
- Superior efficacy (>2-fold higher cure rates)
- Substantially lower cost per course of treatment

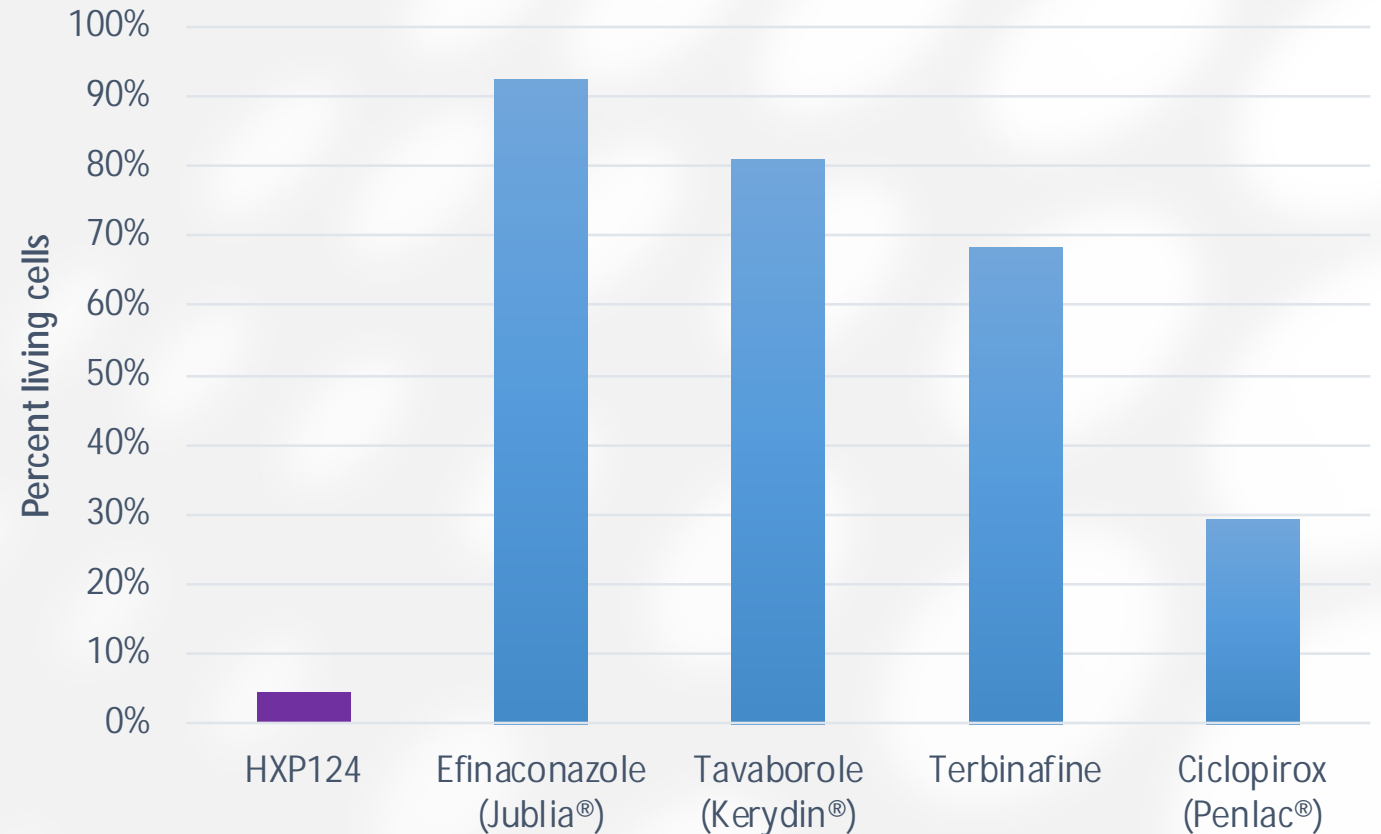


# HXP124 kills fungi better than current treatments for nail infections



Ø Kills fungal cells within 30 min.

- Inefficient killing by the drugs currently on the market means the fungus is likely to become resistant during long treatment times and may regrow when treatment is stopped.



**Fluorescence Associated Cell Sorting (FACS) of Propidium Iodide stained cells was used to identify living and dead *Candida albicans* cells after 30 min treatment with various antifungal molecules.**

# HXP124 is as effective as efinaconazole in an infected nail model

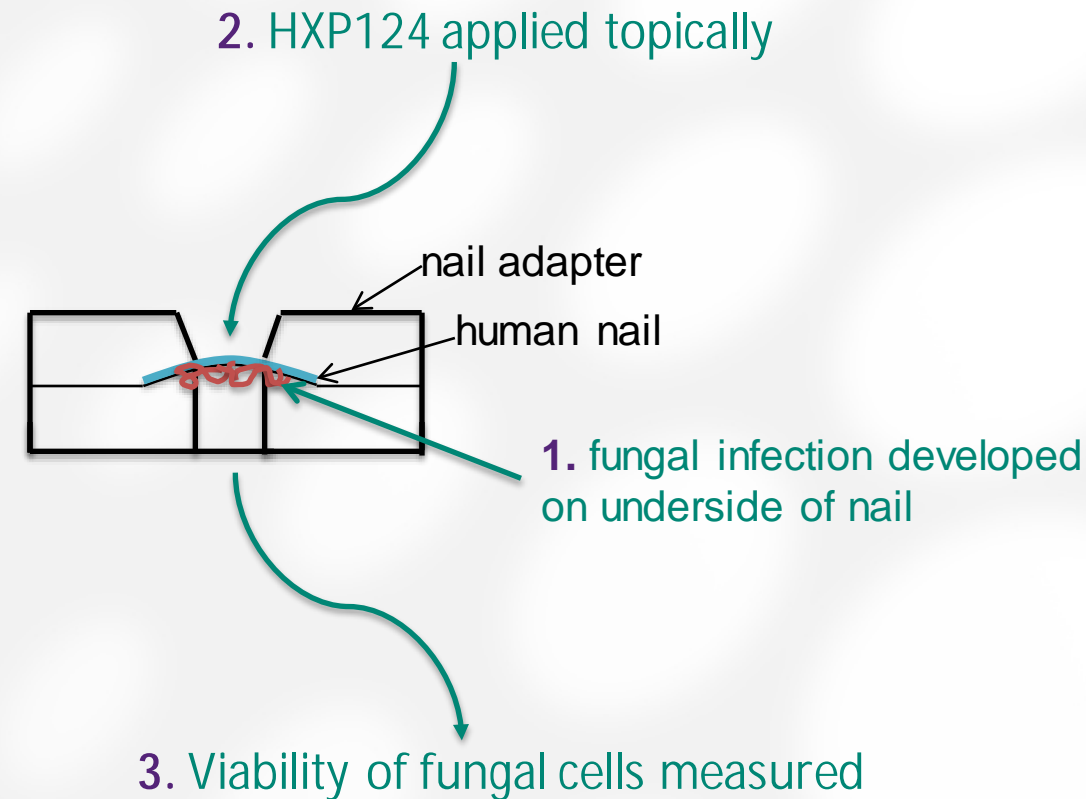


ØMedPharm (UK) tested HXP124 in an “infected nail model” to provide additional confidence that HXP124 passes through nails and kills fungal cells.

- Industry standard assay.
- Nail and fungal growth conditions more representative of clinical condition.

ØJublia<sup>®</sup> and Penlac<sup>®</sup> were used as comparator products in this study.

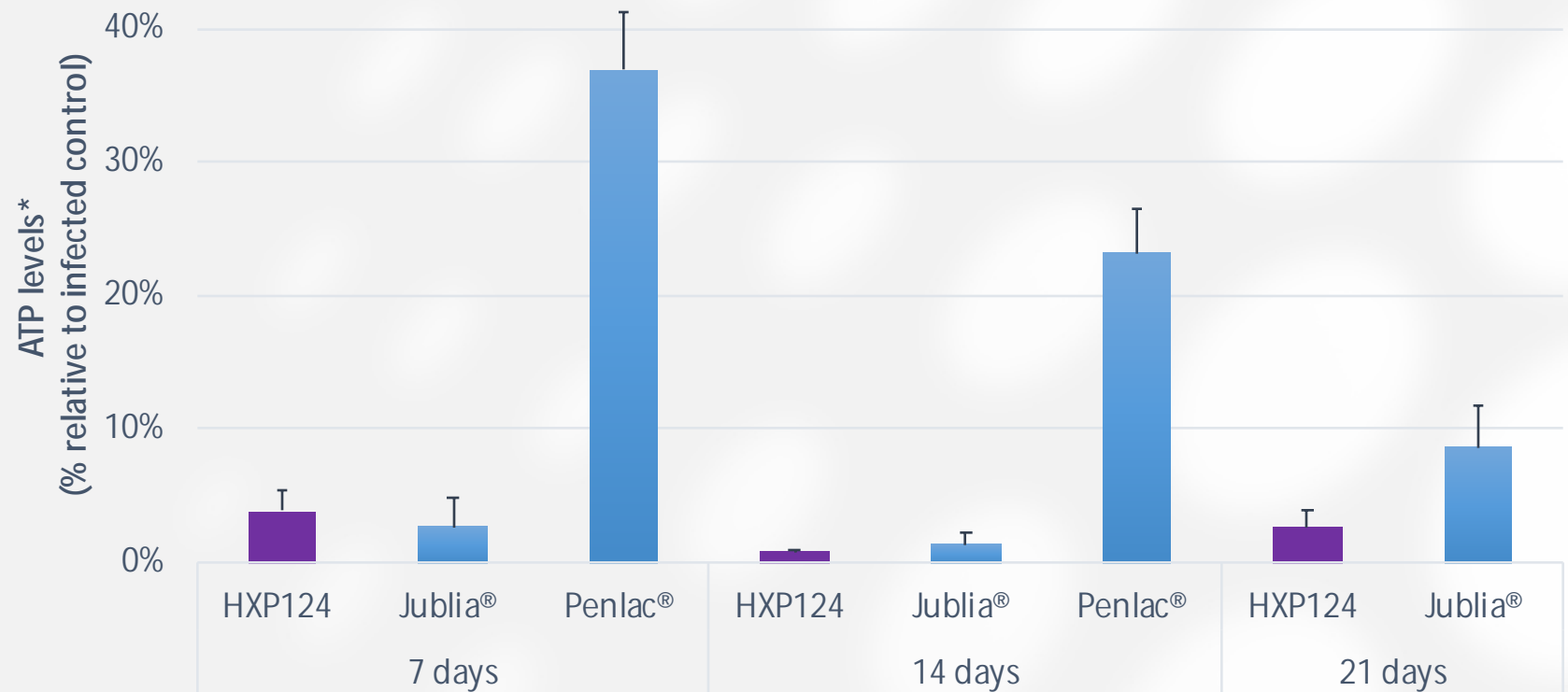
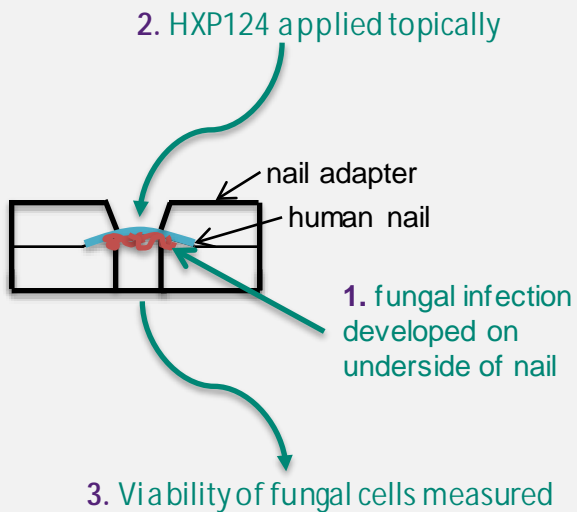
- Jublia<sup>®</sup> is the current industry ‘gold standard’.



# HXP124 is as effective as efinaconazole in an infected nail model



ØHXP124 killed over 95% of fungal cells within 7 days and was as efficient as Jublia® in this model.



\*ATP levels are used as a measure of cell survival

# Phase I/IIa clinical trial fully enrolled



Ø Randomised, Double-Blind, Vehicle-Controlled Multiple Ascending Dose Study in Healthy Volunteers with Mild to Moderate Onychomycosis.

- Patients treat nails daily with HXP124 (or placebo) for 42 days
- Follow-up at 1, 2, 6, 9 and 12 weeks

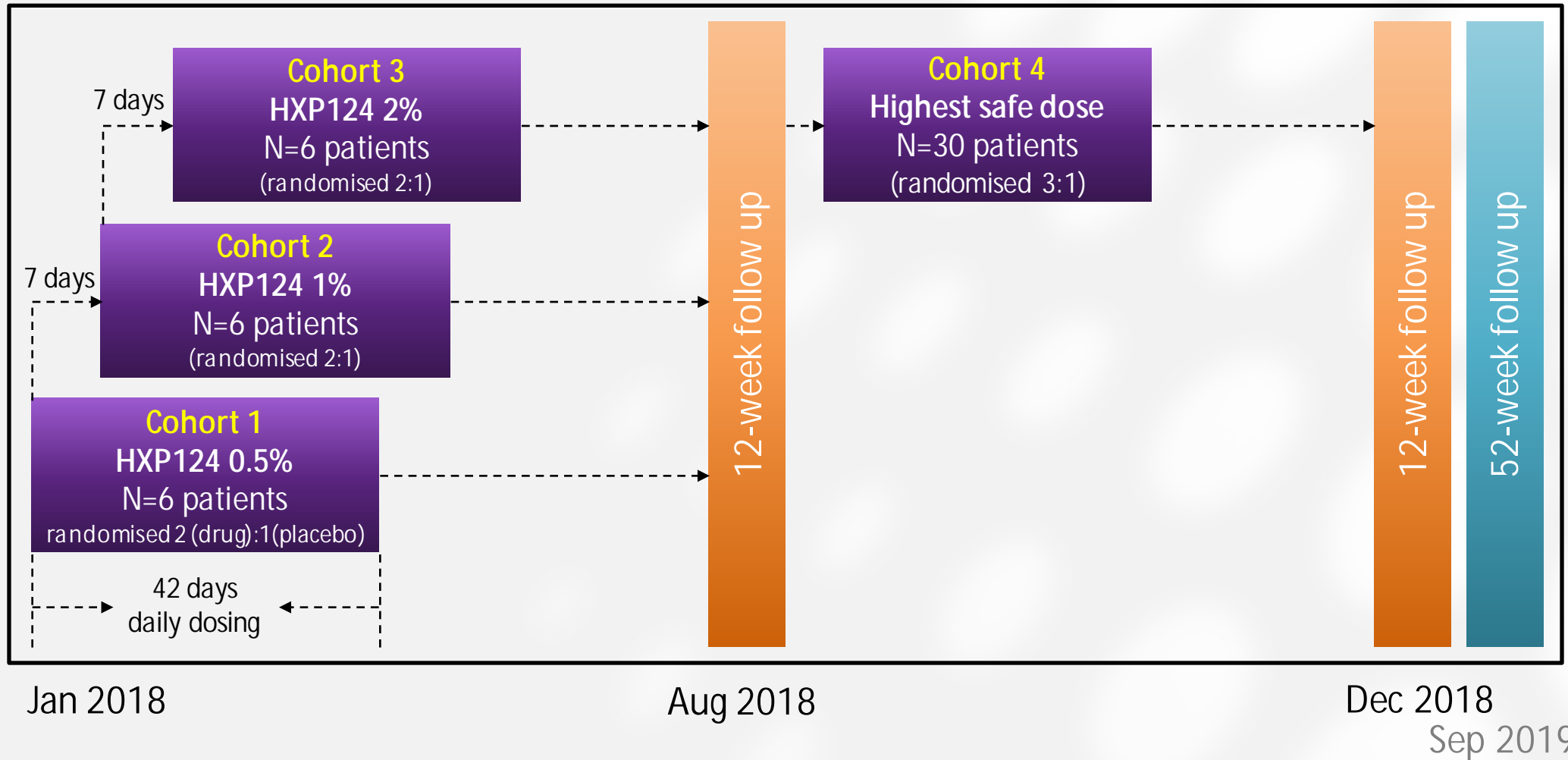
Ø Part 1 data announced Oct 2018

Ø Part 2 data available end-Jan 2019





# Clinical trial design



# Phase I/Ia clinical trial endpoints



ØThe trial was designed to address 3 questions:

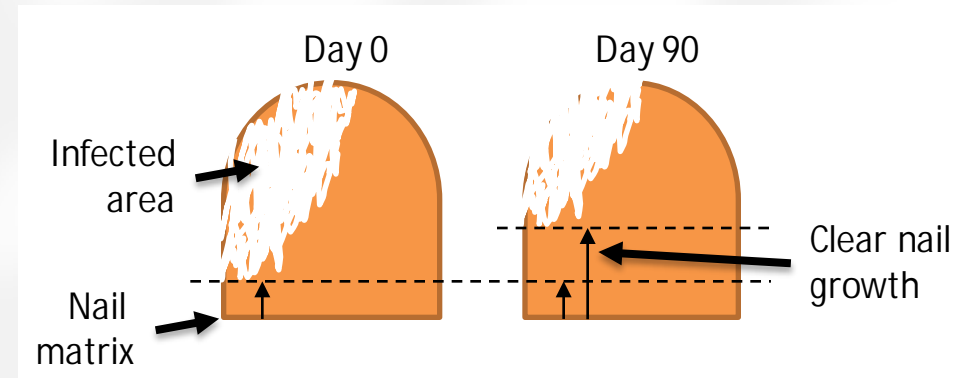
- Is HXP124:
1. safe when applied topically?
  2. effective in treating onychomycosis?
  3. likely to be superior to current best therapies for onychomycosis?

ØPrimary endpoint

- Safety and tolerability

ØSecondary endpoints

- Preliminary efficacy data
  - Partial cure (clear nail growth)
  - Mycological cure (clearance of fungi from the nail)
  - Complete cure (mycological cure and clear nail growth at 12 months – Part 2 only)



Schematic representation of method to assess clear nail growth.

# Phase I/IIa - Part 1 results



Ø Follow-up period for Part 1 was 12 weeks.

- Due to the slow rate of toenail growth, only partial clearing of the infected nail area could be expected over this time.

Ø Part 1 was not intended to include sufficient patients to provide statistically-significant results.

- 3 cohorts, each consisting of 6 patients randomised 2:1 (4 active, 2 vehicle).
- Due to the relatively small numbers in each cohort, the results have been analysed together (12 active, 6 vehicle).

Ø Vehicle-controlled study

- Placebo group received an intended formulation for HXP124 but without any active drug. The vehicle contains substances known to control the growth of fungi *in vitro* and had some activity in the Infected Nail Model conducted by MedPharm.

# Q1. Is HXP124 safe when applied topically?

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ØHXP124 is safe when applied topically over the period of the study.

- No drug-related adverse events.
- HXP124 did not cause pain or irritation.
- HXP124 was not detected in the bloodstream.



# Q2. Is HXP124 an effective treatment for onychomycosis?

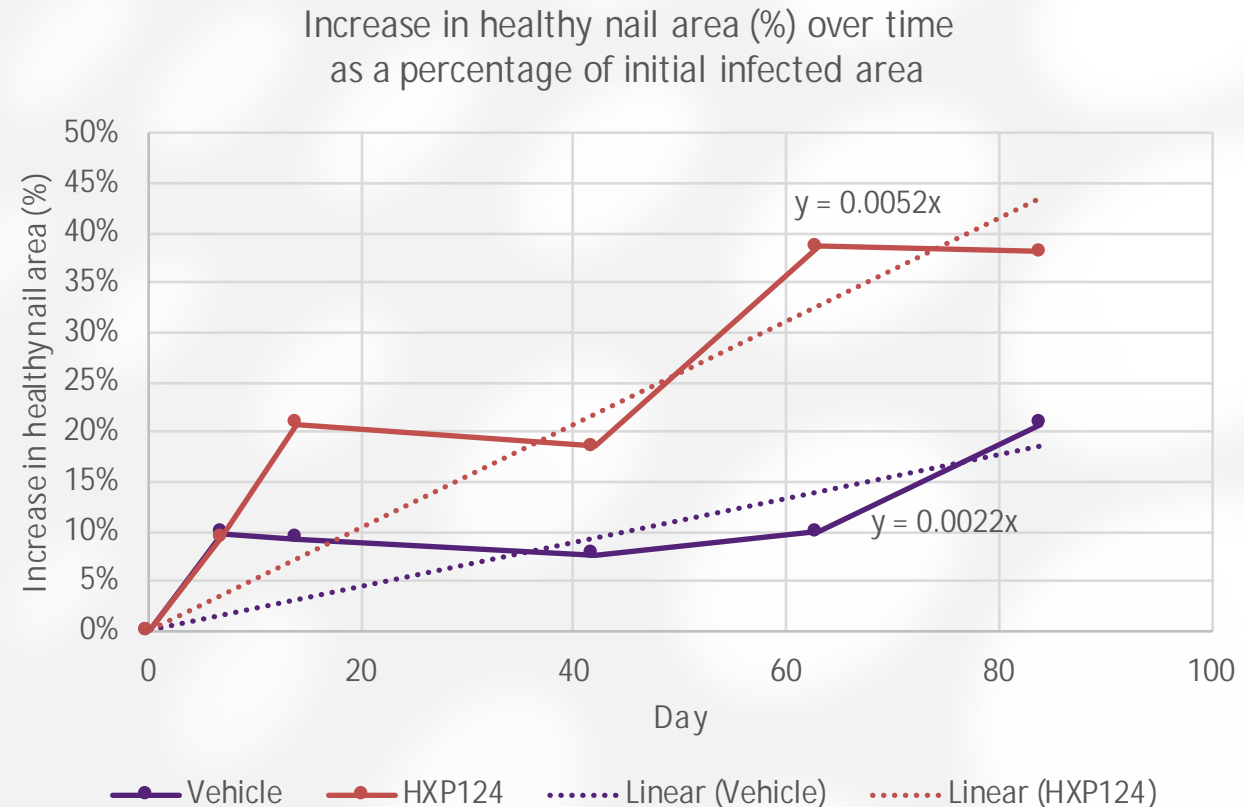


Ø The data indicate that HXP124 is an effective therapy for onychomycosis.

Ø 12 of 13 treated nails showed a clear response.

- The single patient not showing an apparent response had a suspected dermatophytoma. These are known to be difficult to treat with topical products.

Ø The area of infected nail in the HXP124-treated patients decreased by almost twice as much as the vehicle-treated patients (39% vs 21%).

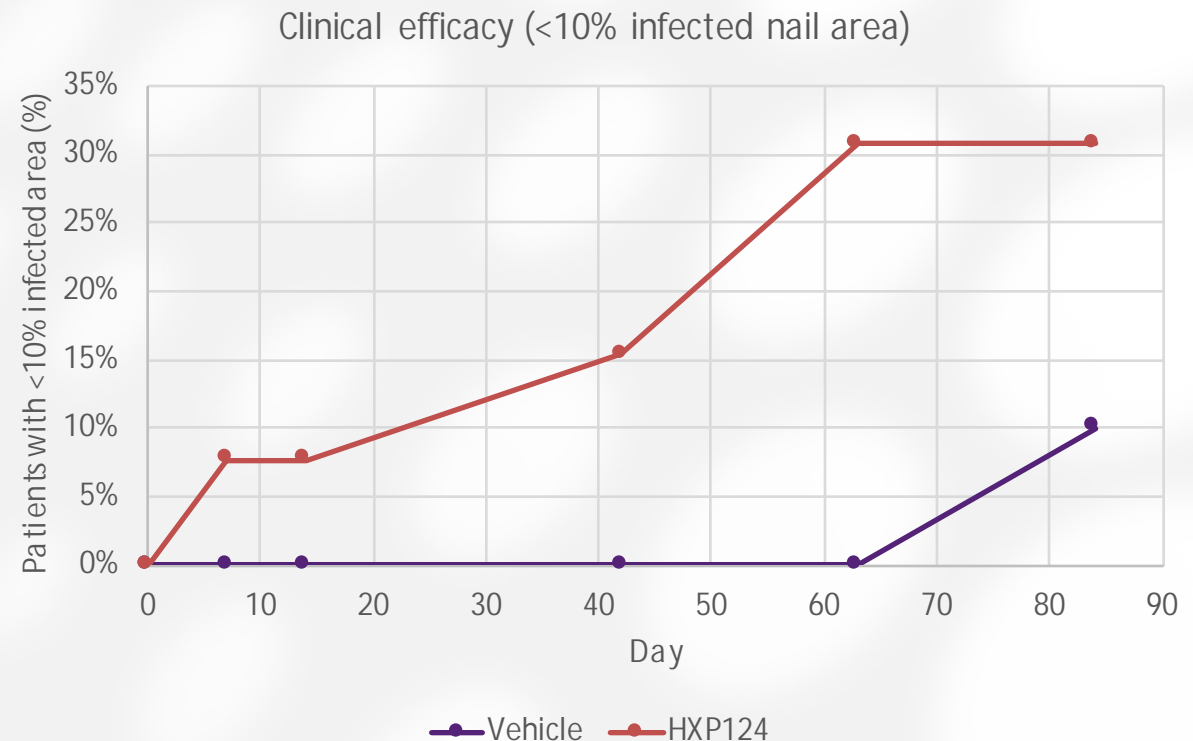


# Q3. Is HXP124 likely to be superior to current therapies?



Ø31% of HXP124-treated patients achieved clinical efficacy (defined as <10% of the nail area infected) within 12 weeks.

- It takes 48-weeks of treatment with Jublia® to produce clinical efficacy in 31-36% of patients.

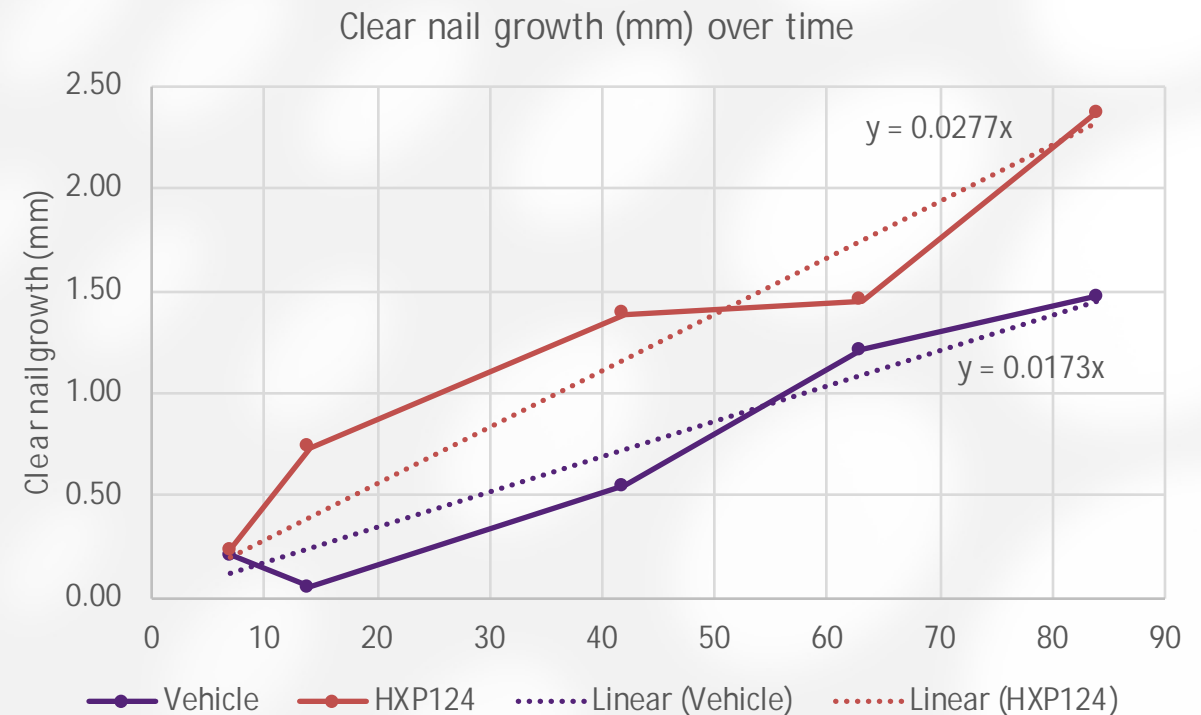


# Q3. Is HXP124 likely to be superior to current therapies?



ØRate of clear nail growth suggests a path of superior efficacy to efinaconazole (Jublia®).

- HXP124-treated patients averaged 2.4 mm of clear nail growth in 12 weeks.
  - Extrapolating these data suggests ~10 mm of clear nail growth in 12 months, twice that of Jublia®.
- Treatment with Jublia® for 48-weeks produces clear nail growth of 3.8 – 5 mm.



# Selected images of HXP124-treated patients

Baseline



Week 12



Baseline



Week 12



Baseline



Week 12



Baseline



Week 12





# Recruitment strategy

ØFacebook recruitment very effective.

- 1.7 million impressions
- 20,000 link clicks
- 3,000 leads passed pre-screen

ØHexima achieved recruitment rate of 10 patients/month.

- Typical recruitment rates for onychomycosis trials are 3.5 patients/month

ØSignificant learnings for phase II/III trials.



The image shows a Facebook post from the page 'Clinical Trial Seeker'. The post is sponsored and features a 'Like Page' button. The text of the post reads: 'New study now available for toenail problems. Eligible participants are paid for their time!'. Below the text is a photograph showing several people's feet, some of which are being examined or treated. The post includes a call to action: 'Signup For the Toenail Study Today' with a checkmark icon, followed by the text 'Study is open now. Hurry, spaces are limited!'. At the bottom of the post is the website 'WWW.CLINICALTRIALSEEKER.COM' and a 'Learn More' button. The Facebook interaction bar at the bottom shows 'Like', 'Comment', and 'Share' options.

**Clinical Trial Seeker**  
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Like Page

New study now available for toenail problems. Eligible participants are paid for their time! 🇺🇸 🇬🇧



**Signup For the Toenail Study Today ✓**  
Study is open now. Hurry, spaces are limited!

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Learn More

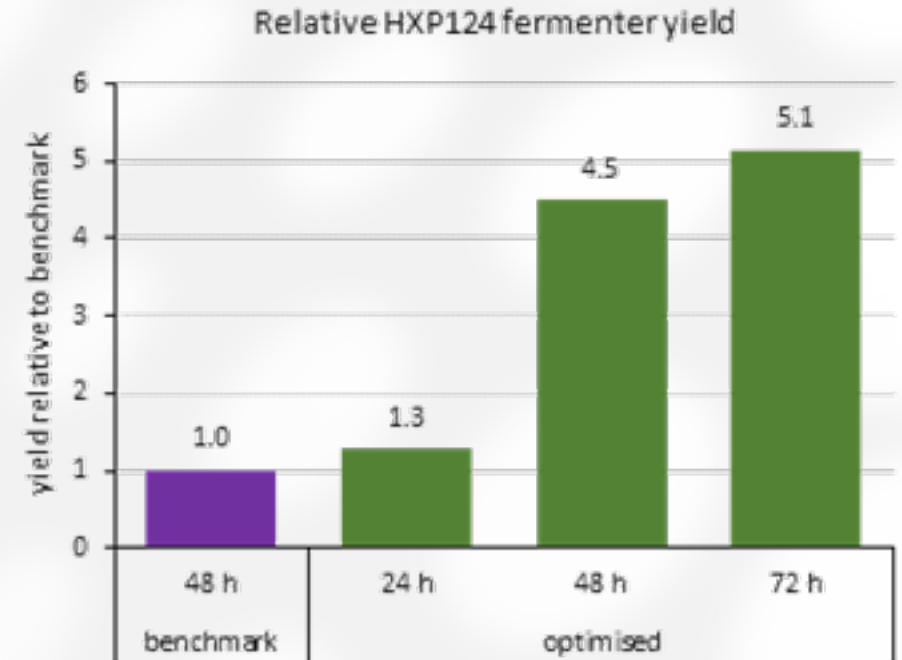
Like Comment Share

# Decrease in cost of production

Ø HXP124 is produced in an off-patent yeast expression system.

Ø Construct optimisation during 2018 achieved a >4.5-fold increase in yield of HXP124.

- Substantial reduction in cost of production
- Strain ready for transfer to Good Manufacture Practice (GMP)-accredited manufacturer



# Patent portfolio



Ø United States patent for use of HXP124 to treat fungal nail infections has been allowed.

- Expiry 2035 (17 years patent life remaining)
- Patent pending in several other jurisdictions including
  - Australia, Brazil, Canada, China, Europe, India, Japan, Malaysia, Mexico, New Zealand, Singapore and South Korea

Ø HXP124 is a biologic drug.

- 12 years marketing exclusivity in USA

# HXP124 commercialisation plan



- Ø Proof-of-concept clinical efficacy data is a major value creation step during drug development.
- Ø Hexima is engaged in discussions with several pharmaceutical companies regarding licencing of HXP124.
  - USA and Japan are highest priority
  - Europe, China and Australia additional key markets
- Ø During licencing discussions, Hexima will raise additional capital and continue development of HXP124.
  - Strengthens negotiating position
  - Minimises time to market



# Business development expertise



Mr Scott Robertson

- Former Business Development Director for DuPont Pioneer.
- Extensive venture investment experience (MPM Capital, Merrill Lynch & Co, Thomas Weisel Partners)
- Chief Financial Officer for DiCE Molecules, which recently closed a US\$40 mil funding round.



Dr John Bedbrook

- Experienced biotechnology founder and chief executive
- Former Vice President of Research and Development at DuPont Agriculture & Nutrition



Dr Michael Rabson

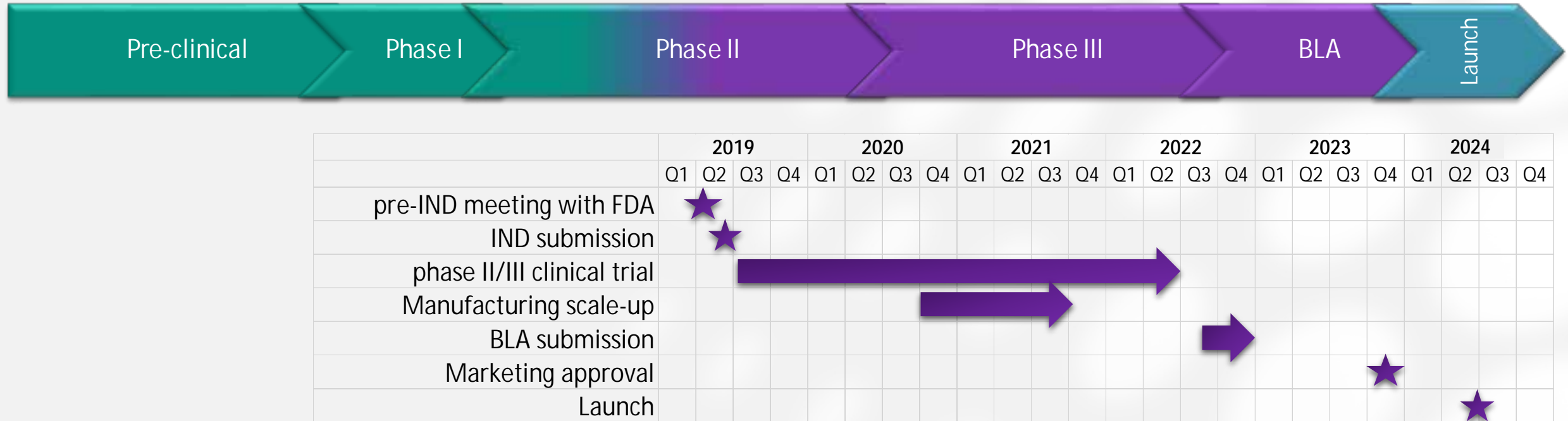
- Lawyer with >20 years of experience providing advice to life sciences companies, both as external counsel and in-house counsel, on negotiation and structuring of complex technology transactions, intellectual property, and corporate matters, including mergers and acquisitions, both in the U.S. and abroad.



Dr Kevin Judice

- Experienced drug development entrepreneur.
- Co-founder and former Chief Science Officer of Cidara Therapeutics, an antifungal company.
- Founder and former CEO of Achaogen, an antibacterial company.
- Co-founder and CEO of DiCE Molecules.

# Development timeline for HXP124



ØPre-IND meeting April 2019

ØPhase IIb/III clinical trial to begin mid-2019

ØTargeting Biological Licence Application (BLA) submission with FDA by mid-2022

# Capital raising 2019



Ø Seeking \$25 million to fund clinical and non-clinical development through to a BLA.

Ø Key dates

- Dec 2018 – Appoint US investment bank
- Jan 2019 – 12-week clinical data from Part 2 available
- Apr 2019 – pre-IND meeting with FDA
- May-Jun 2019 – close funding round

# Focus for 2019

- Ø Business development activities for HXP124
  - Licencing discussions with preferred partners
- Ø Raise additional capital (\$25 million) to progress development of HXP124
- Ø Pre-Investigational New Drug (IND) meeting with FDA to discuss key requirements for marketing approval
  - Design of phase IIb/III clinical trials
  - Bioanalytical methods
  - Data required to support extended dosing
- Ø HXP124 phase IIb/III clinical trial
  - Anticipate start mid-2019
  - Conducted in USA and Australia
  - IND application filed with FDA
  - Protocol design pending feedback from FDA
- Ø Begin production with new, higher yielding strain of HXP124





# AGM 2018

Prof Marilyn Anderson — Chief Science Officer







# Hexima's defensin platform is applicable to other fungal diseases



## ØVulvovaginal candidiasis (thrush)

- HXP124 and other Hexima lead candidates rapidly kill *Candida spp*
- HXP124 is stable in a topical formulation which is a significant advantage for this application

## ØSystemic candidiasis

- SIEF STEM+ Fellowship for Dr James McKenna (La Trobe University) to conduct preliminary research
- Plant defensins are active against a range of *Candida* species, including the new superbug *C. auris*.
- Plant defensins enhance the activity of current best-in-class treatments.

## ØFungal skin infections and dandruff

- HXP124 kills *Malessezia spp.*, a fungal pathogen that causes dandruff

## ØFungal sinusitis

# Defensins are active in a rat model of vaginal thrush



- Ø Topical treatment with defensin reduced the number of *C. albicans* cells in vaginal fluid by 70-87% within 3 days
- Less effective than miconazole after 5 days
    - BUT - Miconazole is fungistatic and yeast cells re-emerge after 9-12 days
  - Need to assess lead defensin over longer period to ensure cell number continues to decrease

# *Candida auris* is an emerging pathogen

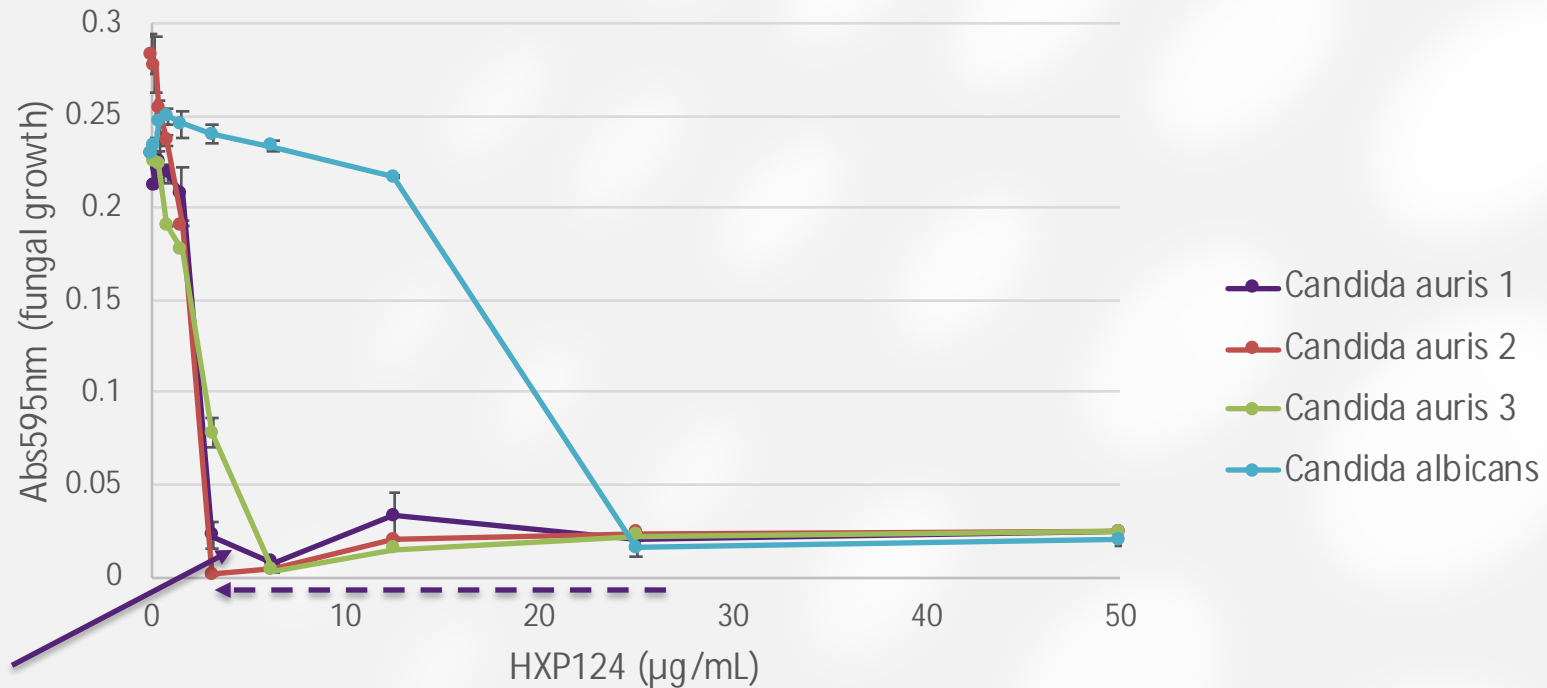
- Ø Causes serious infections
  - 30% mortality rate
- Ø Often resistant to current drugs
  - 90% of strains resistant to fluconazole
  - 50% of strains resistant to multiple classes of antifungals
  - ~5% resistant to all current antifungal drugs
- Ø Spreads through hospitals and nursing homes
  - Outbreaks reported in USA and UK
  - Recently identified in Victoria



# HXP124 has excellent activity against the emerging pathogen *Candida auris*



Ø8-fold lower MIC against *C. auris* relative to *C. albicans*



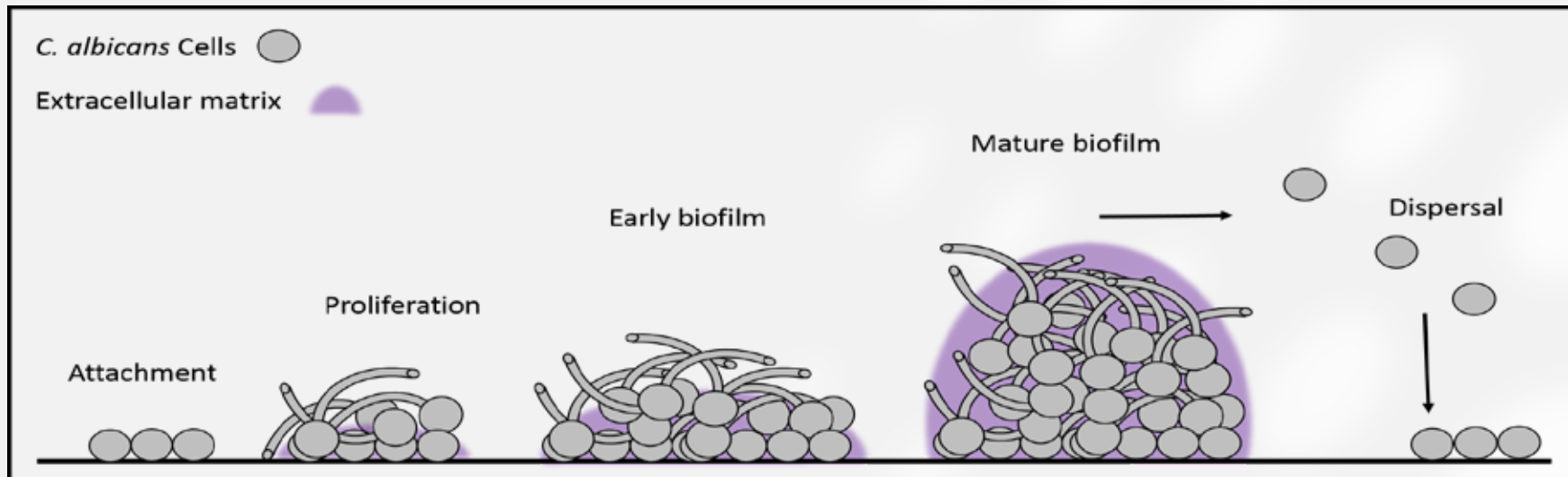
*C. auris* #1 has increased resistance to caspofungin

# *C. albicans* biofilm development

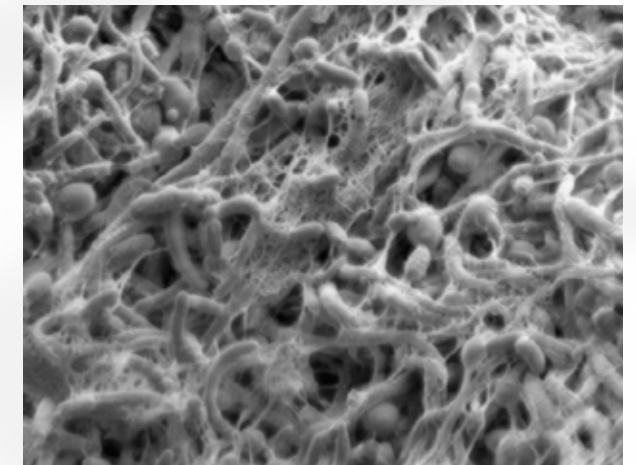
Ø *Candida* biofilms on medical device implants are a major cause of systemic infections

- Help protect the fungus from antifungal drugs

Ø Hexima's defensins kill established *Candida* biofilms



Growth and development of a *C. albicans* based biofilms schematic illustrating the stages of *C. albicans* biofilm development. **Attachment**: yeast cells adhere to a substrate forming a basal layer of cells. **Proliferation**: cells reproduce and form germ tubes. **Mature biofilm**: hyphae are formed and extracellular matrix accumulates. **Dispersal**: the mature biofilm releases cells to seed new locations. Modified from Tsui et al 2016.



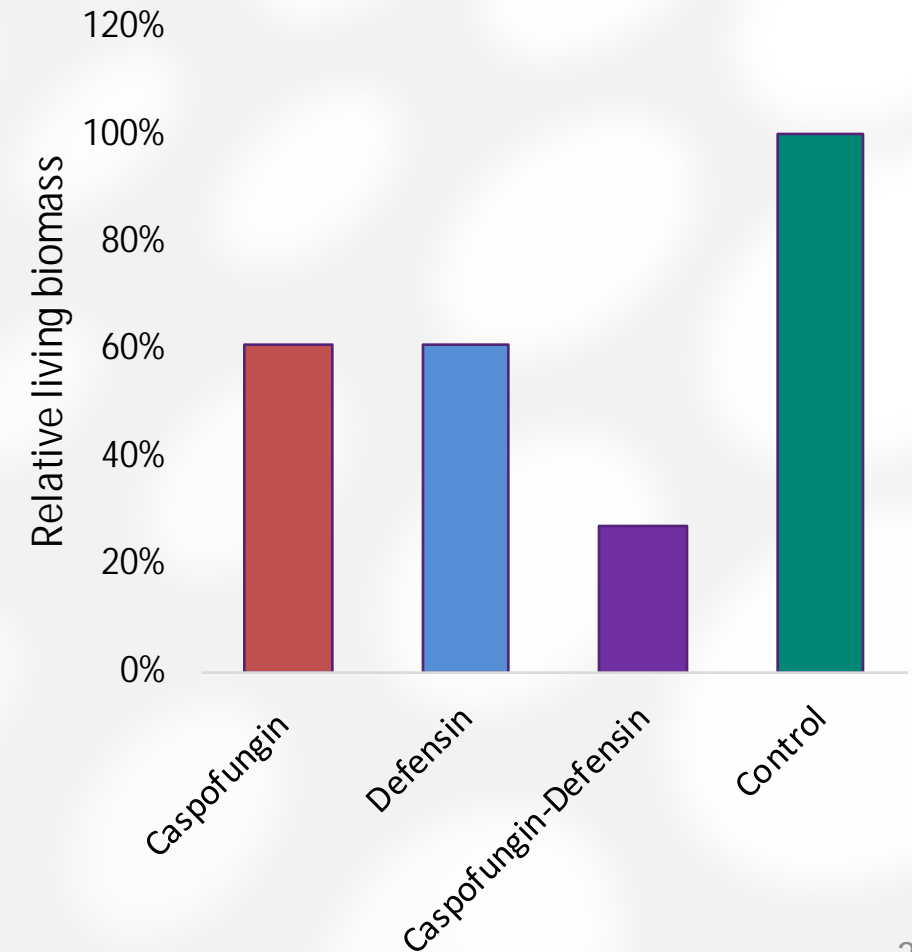
SEM of *C. albicans* in a biofilm.  
Modified from Tsui et al 2016



# Defensins enhance the activity of 'gold standard' antifungal drugs

Ø Caspofungin is a best-in-class therapy for systemic fungal infections

Ø Defensins enhance the activity of caspofungin against *C. albicans* biofilms



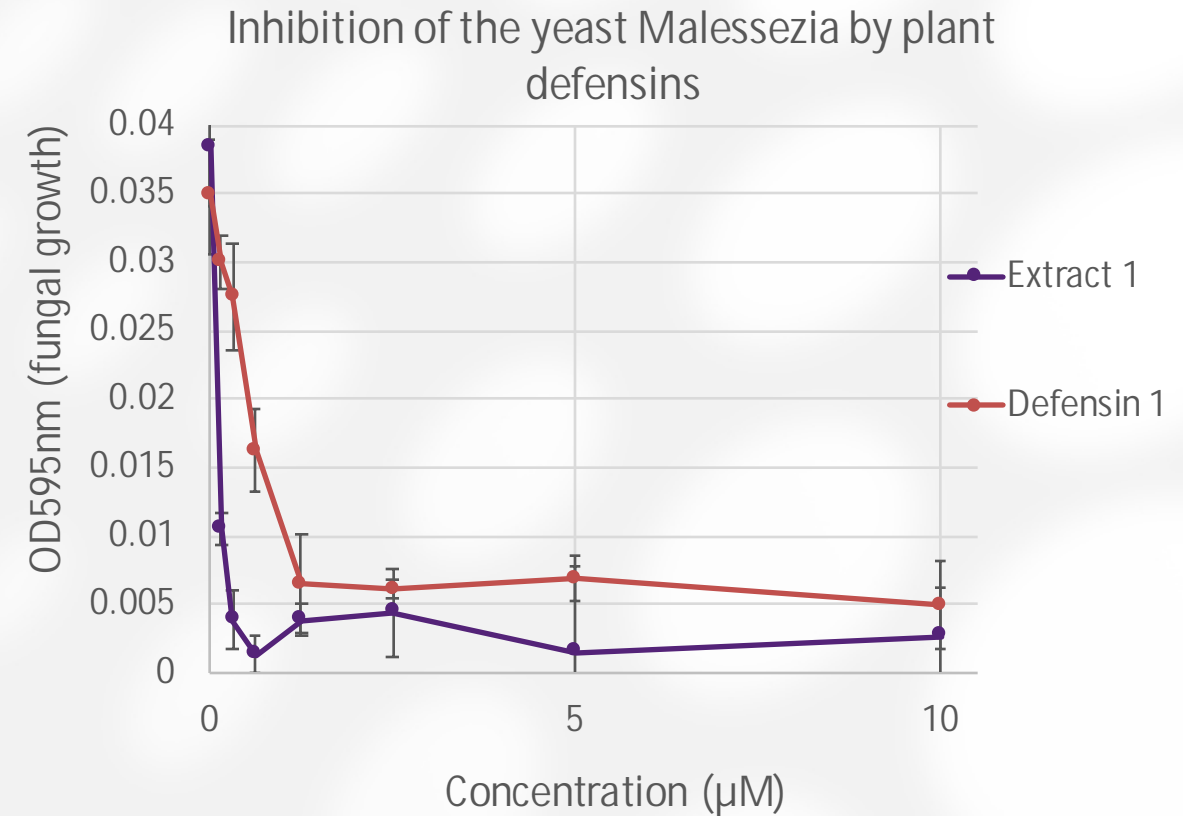
# Plant defensins and plant extracts are active against *Malessezia*



Ø *Malessezia* is a yeast (fungus) that causes dandruff

- Hexima proprietary plant defensins and plant extracts kill *Malessezia* spp.

Ø The global anti-dandruff shampoo market is expected to exceed US\$ 6 billion by 2020



# Pioneer project and natural products library



ØA natural products library of >10,000 diverse plant samples and 57,500 bacteria has been collected.

ØHexima is screening this library for novel antimicrobial molecules

- Funding received through La Trobe ARC ITRH for Medicinal Plants.

ØNovel insect-active leads continue to progress through the development pipeline at Dow-DuPont

- Hexima entitled to royalties from commercial products