

HXP124: an onychomycosis therapeutic opportunity



hexima

Forward looking statements



Certain statements in this presentation relate to the future, including forward looking statements relating to Hexima's future expectations, beliefs, goals, plans, prospects, financial position and strategy. These forward looking statements involve known and unknown risks, uncertainties, assumptions and other important factors that could cause the actual results, performance or achievements of Hexima to be materially different from future results, performance or achievements expressed or implied by such statements. Neither Hexima nor any other person gives any representation, assurance or guarantee that the occurrence expressed or implied in any forward looking statements in this document will actually occur and you are cautioned not to place undue reliance on such forward looking statements.

Subject to any continuing obligations under applicable law, Hexima disclaims any obligation or undertaking to disseminate any updates or revisions to any forward looking statements in this document to reflect any change in expectations in relation thereto or any change in events, conditions or circumstances on which any such statement is based.

Hexima Limited

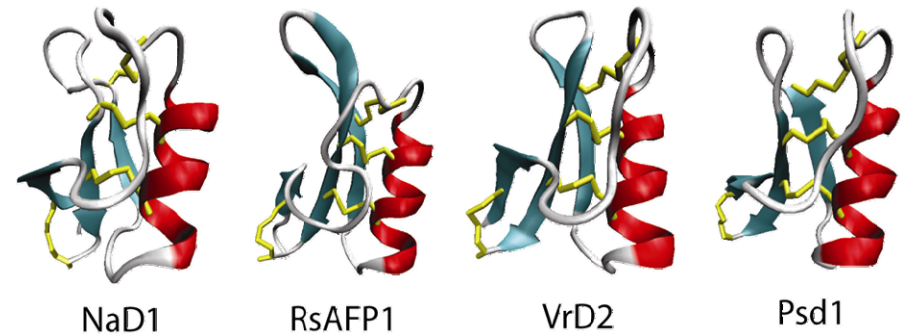


- A 16 year old company based in Melbourne focused on agricultural and pharmaceutical applications of plant defensins.
- Hexima is developing a novel therapeutic (HXP124) for the onychomycosis (fungal nail infection) market.
- HXP124 will be superior to current therapies.
 - Potent, broad-spectrum antifungal molecule
 - Readily penetrates nails
 - Rapidly kills fungal cells

Plant defensins



- **Source of potent, broad spectrum antifungal agents.**
 - Small, stable peptides abundant in plants
 - Hydrophilic and highly soluble
 - Stable at extremes of pH (<2) and temperature (>95°C)
 - Resistant to proteases and stable in serum
 - Manufacturable using yeast fermentation



Hexima antifungal peptides



- **Hexima has built the world's leading competency in plant defensins and a broad IP portfolio.**
 1. Plant-derived molecules and genetic sequences encoding same and uses thereof (2001) – US granted
Claims to the plant defensin NaD1 (mature domain, CTPP, mature domain & CTPP).
 2. Modified plant defensin useful as anti-pathogenic agents (2011)
Claims to cover modified solanaceous class II defensins with improved antifungal activity.
 3. Antipathogenic methods (defensin-defensin synergy) (2013)
Claims to combinations of plant defensins that act synergistically.
 4. Agents and methods for treatment & treatment of pathogens (April 2015)
Claims to cover the use of plant defensins in combination with fungicides, proteinase inhibitors and other antimicrobial peptides that act synergistically.
 5. A method of treatment (May 2015)
Claims to cover the use of Hexima's lead onychomycosis defensin (HXP124) plus additional active defensins (and any defensin with >80% sequence identity) to treat fungal infections of skin, hair and nails.
 6. A method of *in vivo* treatment (May 2015)
Claims to cover the use of 10 defensins (plus any defensin with >80% sequence identity) to treat systemic fungal infections (Candidiasis, Aspergillosis, Cryptococcal meningitis etc).

Global onychomycosis market



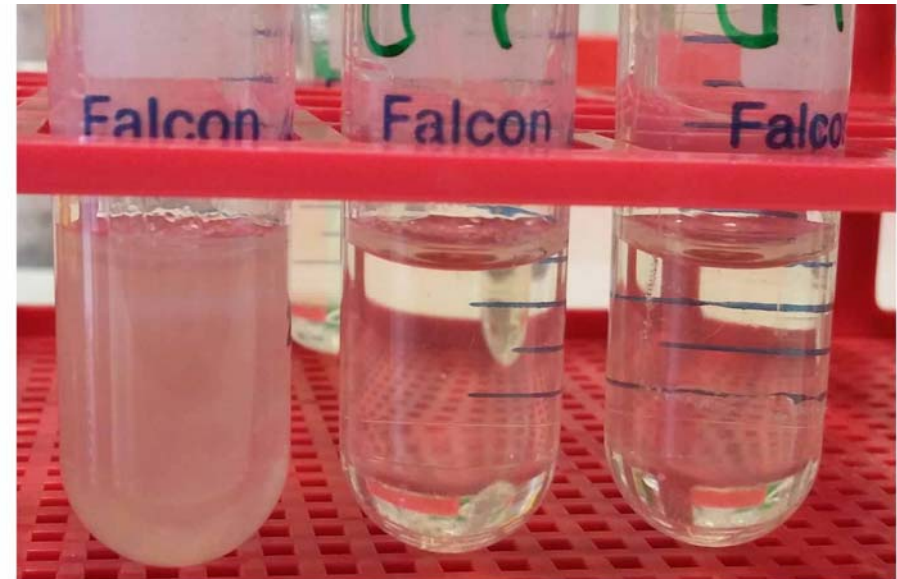
- **US\$2.34 billion** in 2012 and projected to reach **US\$3.1 billion** by 2016.
- Deficiencies in current available therapies.
 - Poor efficacy rates
 - Long treatment times
 - Toxicity associated with oral therapies
 - Expensive
 - Between 50 and 90% of individuals with fungal nail infections are not receiving treatment.
- Large potential for rapid growth in the market with an effective product.



HXP124: a broad-spectrum antifungal peptide specific for fungal cells



- Active against a range of human fungal pathogens including *Candida* and the causative agents of onychomycosis.
- Kills fungal cells within 30 min.
 - no activity against mammalian cells
 - no activity against bacterial cells



No treatment

Low dose

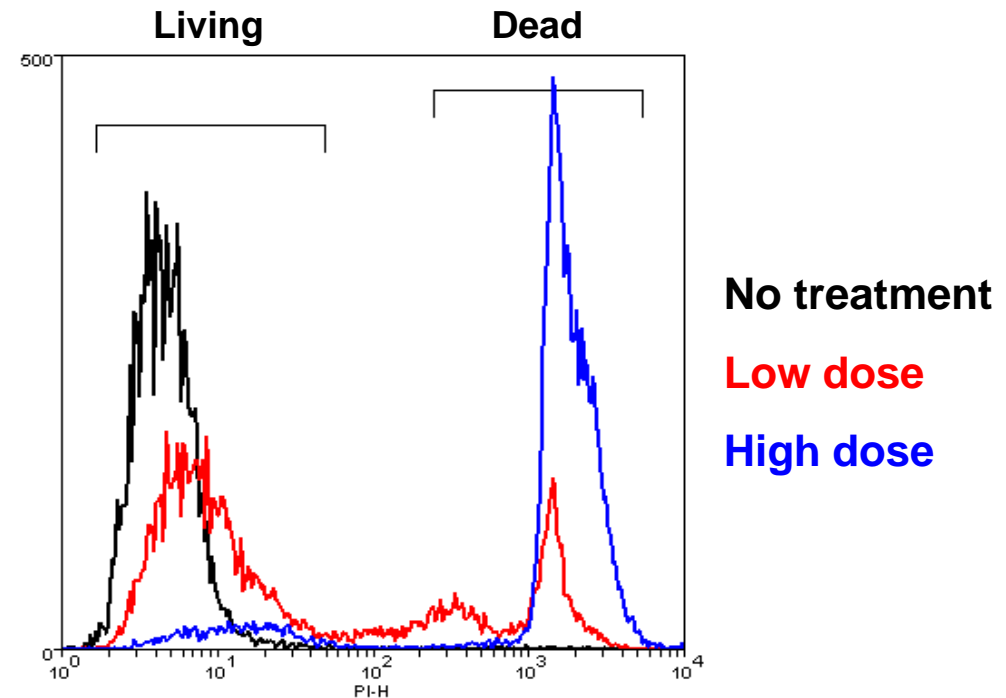
High dose

Growth of *Trichophyton rubrum* (causative agent of ~90% of onychomycosis cases) in the presence and absence of HXP124.

HXP124: a broad-spectrum antifungal peptide specific for fungal cells



- Active against a range of human fungal pathogens including *Candida* and the causative agents of onychomycosis.
- Kills fungal cells within 30 min.
 - no activity against mammalian cells
 - no activity against bacterial cells

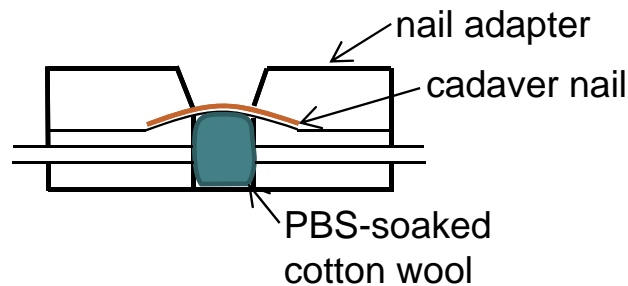
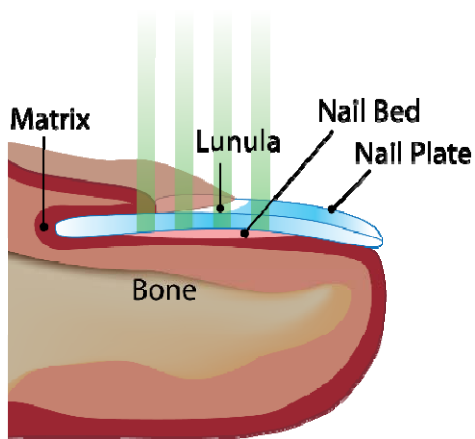


Fluorescence Associated Cell Sorting (FACS) of *Candida albicans* to identify living and dead cells after 30 min treatment with HXP124.

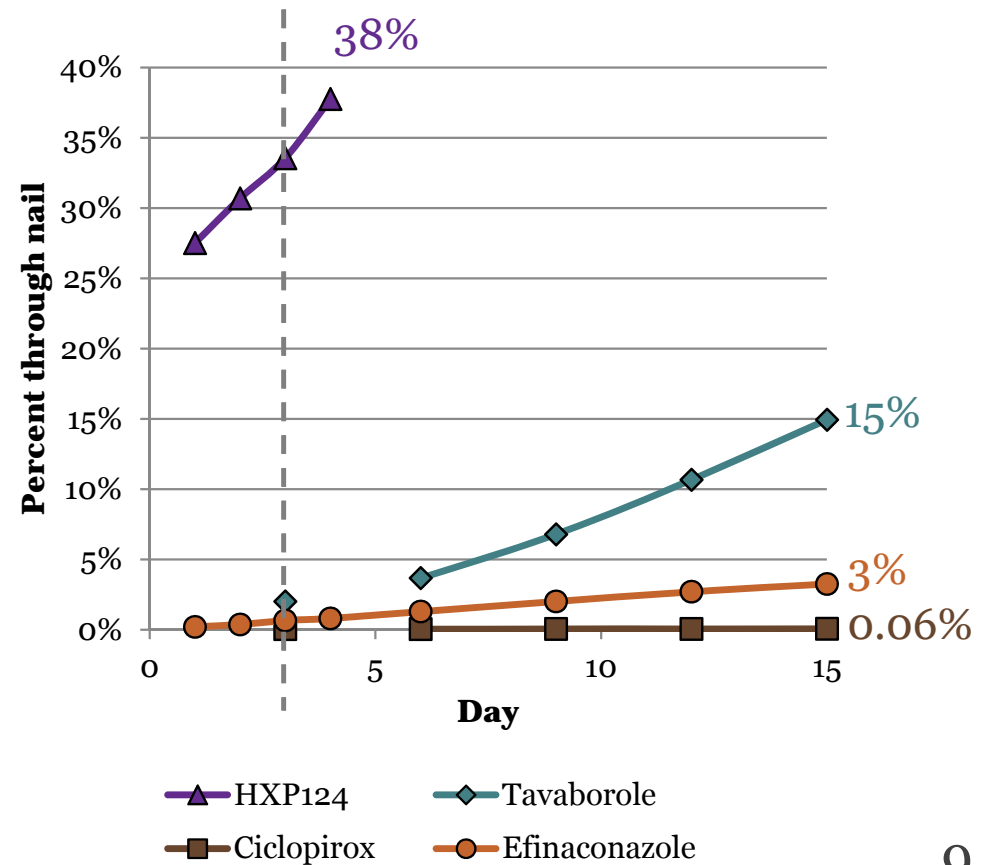
HXP124 penetrates nails faster and more efficiently than current marketed products



- Topical treatments for onychomycosis must penetrate human nails.
- An *in vitro* nail adapter assay can be used to assess nail penetration.



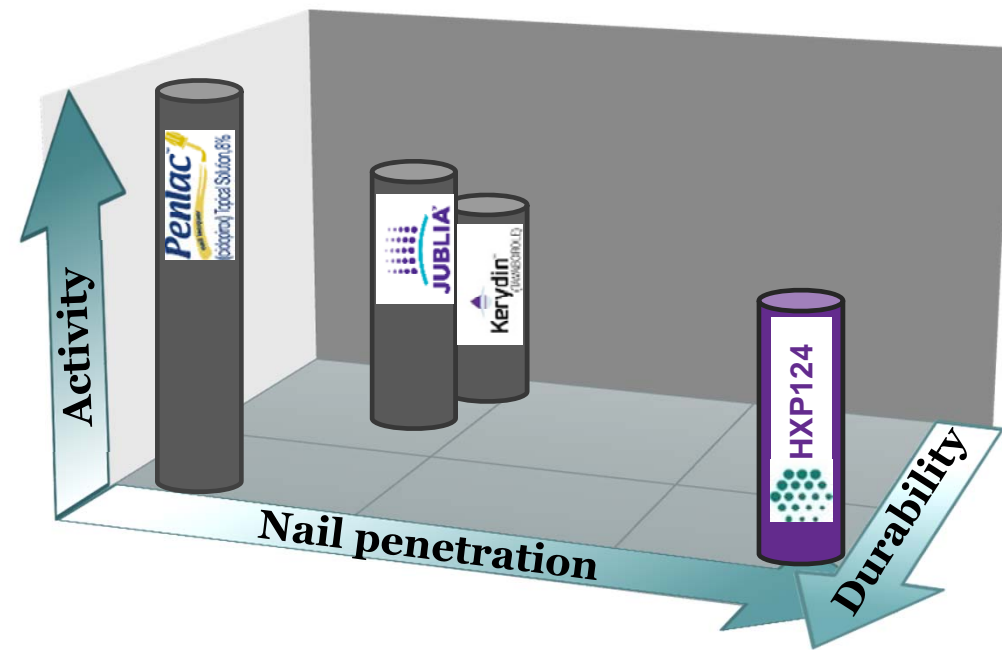
Permeation model based on method developed by Dr Howard Maibach. (UCSF Medical Centre, Hui et al., 2006)



HXP124 is superior to current onychomycosis topical products



	Activity (IC ₅₀)	Mode-of-action	Nail penetration
HXP124	3 µg/mL	Fungicidal Kills cells within 30 min No resistance after 20 cycles of sub-MIC treatment.	>30% , 24 h
Tavaborole (Kerydin™)	6 µg/mL	Only fungicidal at very high concentrations Resistance develops easily.	2% after 72 h (24 h not reported)
Efinaconazole (Jublia®)	2.5 µg/mL	Fungicidal Fungi readily develop resistance to azoles.	0.7% after 72 h (0.2% at 24 h)
Ciclopirox (Penlac™)	0.5 µg/mL	Fungistatic and fungicidal	0.03% after 72 h (24 h not reported)



- Better nail penetration
- More durable mod-of-action

HXP124 can be produced rapidly and economically



- Produced in off-patent *P. pastoris* expression system.
- Two-step purification process.
 - Highly pure protein (>99.99%)
- GMP manufacture completed by Pharmasynth.



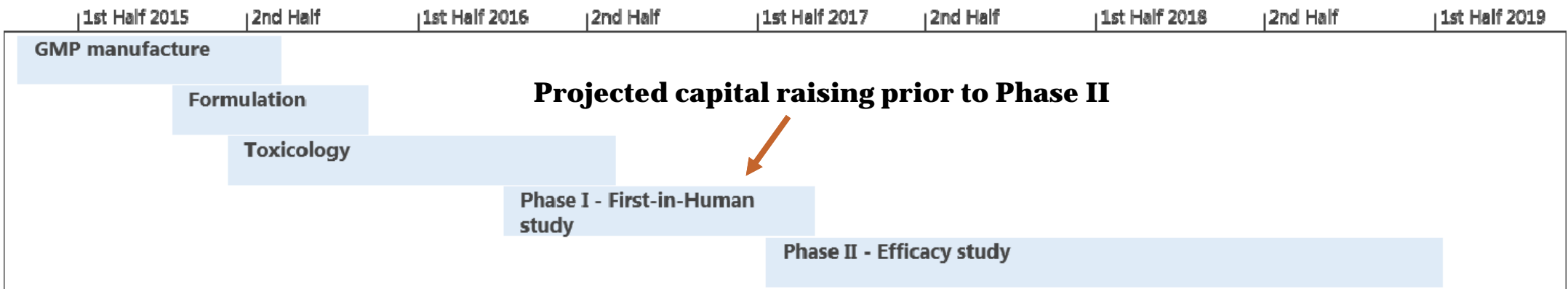
PharmaSynth 

500 L fermentor in Pharmasynth's GMP facility (Brisbane, AUS).

HXP124 Development Plan



- Hexima will complete formulation work by November 2015 and begin pivotal toxicology studies.
- Hexima intends to begin a Phase I, First-In-Human (FIH) clinical trial in March 2016.
- Capital raising expected mid-late 2016.



Hexima's defensin platform is applicable to a broad range of indications



- Vulvovaginal candidiasis (thrush)
 - HXP124 and other lead candidates are active against *Candida spp*
 - Stability in a topical formulation is a significant advantage for this indication
 - Molecules retain activity at low pH
- Fungal infections of traumatic injuries/wounds
 - HXP124 and other lead candidates are active against non-dermatophyte moulds
- Fungal skin infections and dandruff
- Plant fungal diseases
 - Transgenic and topical applications
- Veterinary applications

Summary



- Hexima has developed a defensin platform applicable to a range of applications.
- Hexima is developing HXP124 as a superior therapeutic for onychomycosis.
 - Better nail penetration.
 - Rapidly kills fungal cells.
 - Shorter treatment regimen.
- Hexima expects to begin Phase I trials in Q1, 2016.

