HEXIMA LIMITED

ASX ANNOUNCEMENT

5 April 2022

INVESTOR WEBINAR ON TODAY

Hosted by Hexima Managing Director and CEO, Mr Michael Aldridge and Chief Operating Officer, Dr Nicole van der Weerden

MELBOURNE, AUSTRALIA (5 April 2022): Hexima Limited (ASX:HXL), wishes to remind investors of its webinar scheduled for today, 5 April 2022 at 9:00 AM AEST. The webinar follows the presentation by Chief Operating Officer Dr Nicole van der Weerden of pezadeftide's novel fungicidal mode of action at the annual meeting of the American Academy of Dermatology (AAD) on March 25th 2022 in Boston, MA. A copy of the presentation to be delivered in the webinar is attached.

Hexima's CEO and COO will host the webinar to discuss recent progress, upcoming milestones and the mechanism of action of pezadeftide against fungal pathogens.

Investor Webinar: 5 April 2022, 9AM AEST
Registration link: https://bit.ly/3CTn5fP

This announcement is authorised for release to ASX by Michael Aldridge, Managing Director & CEO

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ABOUT HEXIMA

Hexima (ASX:HXL) is a clinical stage, anti-infectives focused biotechnology company engaged in the research and development of defensin peptides for applications as human therapeutics. Our lead product candidate, pezadeftide (HXP124) applied in a topical formulation, is a potential new prescription treatment for toenail fungal infections (or onychomycosis). Hexima is currently conducting an Australian phase IIb clinical trial testing pezadeftide for the treatment of onychomycosis. Hexima holds granted, long-life patents protecting pezadeftide in major markets globally. For additional information please visit www.hexima.com.au. You can also find us on Twitter and LinkedIn or email us at info@hexima.com.au.

ABOUT ONYCHOMYCOSIS

Onychomycosis is a common fungal nail infection in the nail plate and nail bed. Prevalence of onychomycosis has been estimated at 10% (Japan) and 13.8% (USA).[1] Onychomycosis is an infectious disease and is difficult to treat with a significant healthcare burden. It causes pain in approximately 50% of patients and in the US results in close to four doctor's visits annually for treatment.[2] Onychomycosis impacts a patient's quality of life with 51% unable to wear the shoes they would prefer and 66% distressed by the appearance of their nail.[3] It is important to treat onychomycosis as the fungi in the nail

can be a source of secondary infection in other areas of the body or infect family members and spread to the environment.

Onychomycosis is the most common nail disorder accounting for 50% of all nail diseases. It is particularly prevalent in older, diabetic and immune compromised populations.[2] The global market for treatments for onychomycosis was approximately US$3.7 billion in 2018.[4]

TREATMENT OF ONYCHOMYCOSIS

Approved prescription therapies for onychomycosis comprise either oral or topical medications. Oral medications are associated with adverse effects such as nausea, taste disturbance, and flatulence. They can also severely impact liver function and so often require liver function monitoring. The clinical and commercial success of topical medications has been constrained by an inability of anti-fungal agents to effectively penetrate the human nail and the lack of sufficient anti-fungal activity when in contact with the target pathogen.[5]

HEXIMA'S APPROACH

Hexima embraces the significant challenge of new product development for onychomycosis. Hexima has taken a very different approach, building on its many years of ground-breaking research into the evolutionary tools that plants use naturally to fight fungal infections. The result is pezadeftide, a new topical treatment for onychomycosis, with a novel and powerful fungicidal mode of action.

Historically, therapies for onychomycosis have generally focused on new forms of the traditional classes of antifungal agents or improving the topical delivery of systemic antifungal agents. Hexima's technology is a completely novel approach with fundamental differences that address the well-documented limitations of these traditional technologies.

Pezadeftide penetrates the nail more effectively than existing topical treatments and so can more readily target the fungal cells which proliferate in the nail bed. It is also more effective at rapidly killing fungal cells on contact. Together, these properties mean that pezadeftide has the potential to resolve the fungal infection more quickly, leading to faster and more complete clearing of the infected nail area. Consequently, pezadeftide offers the promise to capture significant value in a large and poorly served market.

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[1] Tatchibana et al., Journal of Fungi, 2017
[2] Joseph et al, Supplement to Podiatry Today, 2013
[3] Milobratovic et al., Mycoses, 2013
[4] Persistence Market Research 2018
[5] Wang et al., Onychomycosis: Diagnosis and Effective Management, 2018

APRIL 2022

HEXIMA LIMITED (ASX:HXL)

A game-changing treatment for onychomycosis

hexima

DISCLAIMER

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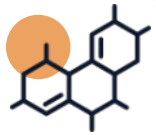
HEXIMA LIMITED (ASX:HXL)

DEVELOPING A NOVEL TOPICAL PRODUCT ADDRESSING A CLEAR UNMET NEED IN A LARGE AND GROWING MARKET



CLINICAL-STAGE, INFECTIOUS DISEASE-FOCUSED BIOTECHNOLOGY COMPANY

Lead program is pezadeftide (HXP124), a **potential new topical treatment** for onychomycosis (fungal nail infections)

Exploring other applications for its anti-fungal peptide platform

LARGE AND GROWING MARKET WITH **SUBSTANTIAL UNMET NEED**

Onychomycosis **affects ~14% of the US population.** Global market for treatments for onychomycosis **US$3.7 bn**

Current treatments do not meet patient needs

- Topical drugs - long course of treatment, limited efficacy
- Oral drugs - more effective but risk of toxic side effects

Patients and clinicians have a **clear preference for a safe topical product** with a more convenient **shorter course of therapy and better efficacy**

NOVEL, PROPRIETARY MOLECULE WITH UNIQUE MOA

Pezadeftide is a patented biologic with a **novel fungicidal mode of action**

Rapidly penetrates the human nail to target the site of infection

PEZADEFTIDE ADDRESSES AN UNMET NEED. GOAL TO BE THE **TREATMENT OF CHOICE**

Demonstrated in a phase I/IIa clinical trial to have a favourable safety profile and deliver effective and rapid anti-fungal treatment

Safe and well tolerated

High efficacy via consumer-friendly topical application

Short, convenient course of therapy, delivers rapid resolution of disease

WELL-DEFINED DEVELOPMENT PATH

Currently in Australian phase II clinical trial – results Q2 2022

Phase III 2022

EXPERIENCED MANAGEMENT TEAM

PROVEN TRACK RECORD OF DELIVERING VALUE

MICHAEL ALDRIDGE

Chief Executive Officer

- CEO Peplin, sold to Leo Pharma in 2009 for $300M
- SVP Corporate Strategy Questcor, sold to Mallinckrodt in 2014 for $5.6B
- SVP Corporate & Strategic Development Codexis, $357M partnership with Nestle in PKU in 2017

DR. NICOLE VAN DER WEERDEN

Chief Operating Officer

- Inventor on all Hexima's key patents
- Led discovery and development program for pezadeftide
- CEO of Hexima 2015-2020

PROF. MARILYN ANDERSON

Chief Science Officer

- Founding scientist of Hexima
- Fellow of the Australian Academy of Science and Australian Academy of Technological Sciences
- Member of Hexima board of directors since 2010

DR NANCY SACCO

Chief Development Officer

- Over 20 years leadership in the pharmaceutical industry.
- VP & Head of Clinical Development roles at Xentria, Inc. & AnaptysBio, Inc.
- Initiated and completed pivotal studies evaluating safety and efficacy of innovative products.

PHILLIP ROSE

Chief Commercial Officer

- Registered Pharmacist
- Specializes in market analysis, preparation & full strategy development to maximize commercial potential.
- Consulted at Alza (now J&J), Reliant Pharmaceuticals (now GSK) and Peplin Inc. (now LEO).

PEZADEFTIDE IN ACTION

Click to play animation

ACHIEVEMENTS AND MILESTONES

PHASE II CLINICAL TRIAL – A CRITICAL MILESTONE

Achieved to date in 2022

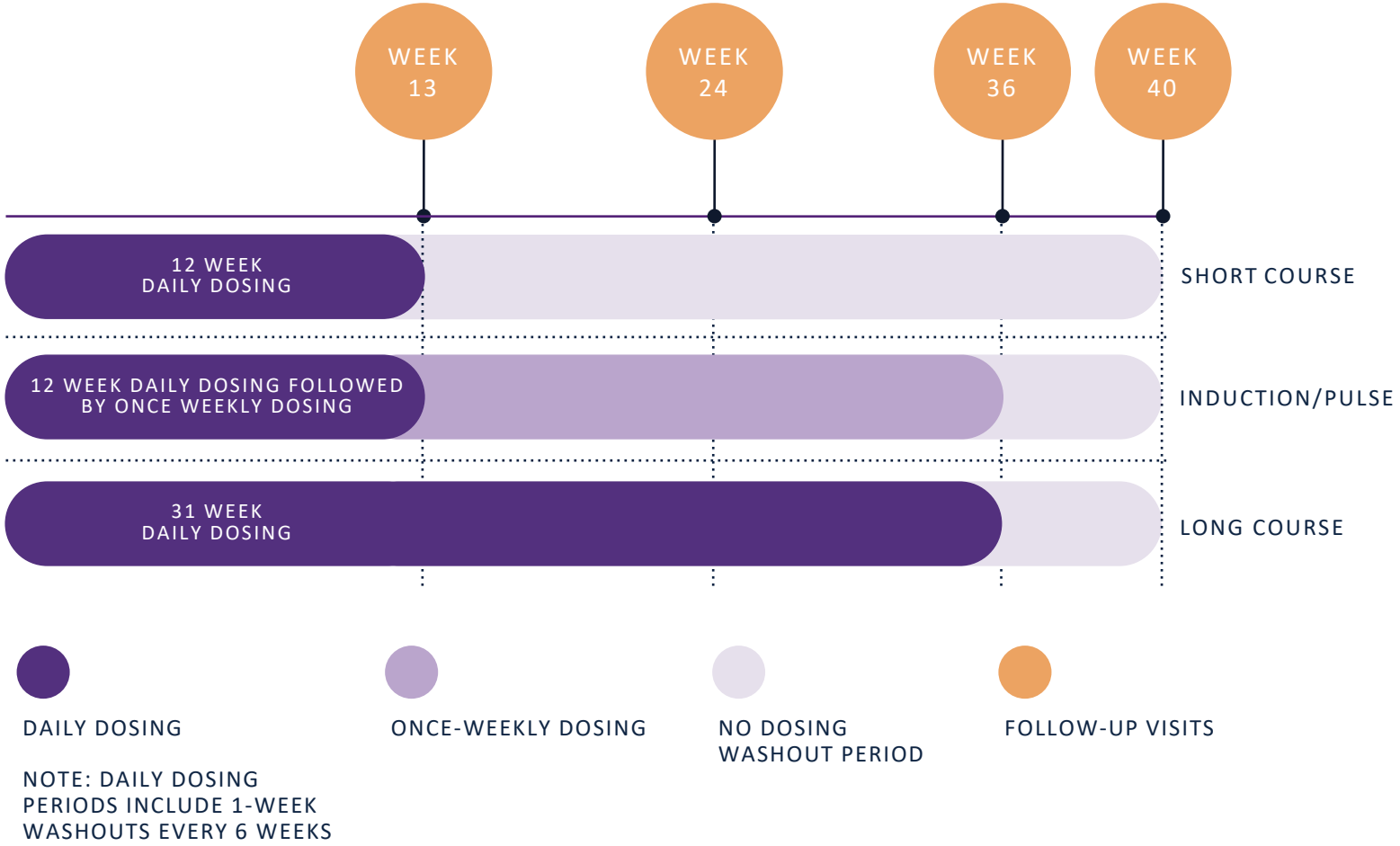
- ✓ Key US hires
- ✓ GMP manufacturing
- ✓ CompliancePak
- ✓ MoA at AAD

Milestones looking forward

- → Initiate US safety study – mid 2022
- → Results of phase II – Q2 2022
- → Japan partnership
- → Phase III

PHASE II CLINICAL TRIAL

HXP124-ONY-002



Results Q2 2022

- Multi-center, randomised, double blind, vehicle-controlled study
- Primary endpoint safety and tolerability, secondary endpoints Mycological Cure and Clinical Efficacy
- Three active (2% pezadeftide) versus vehicle arms to test optimal dosing strategy
- Safety & efficacy assessed at 13, 24, 36 and 40 weeks

HXP124-ONY-002 ANZCTR REGISTRATION NUMBER: ACTRN12620000697987

NOVEL MECHANISM OF ACTION

A WORLD FIRST AND WHY THAT MATTERS

- Onychomycosis is a very common and difficult to treat infection
    1. New topical treatments have been only modestly successful
    2. Oral medications are impacted by negative side effects
- Pezadeftide is highly differentiated and a world first
    1. Very different biophysical properties; and
    2. A completely new mechanism of action
- The promise of a game changer in onychomycosis; and
- A new tool in the constantly evolving battle against drug resistance in infectious disease

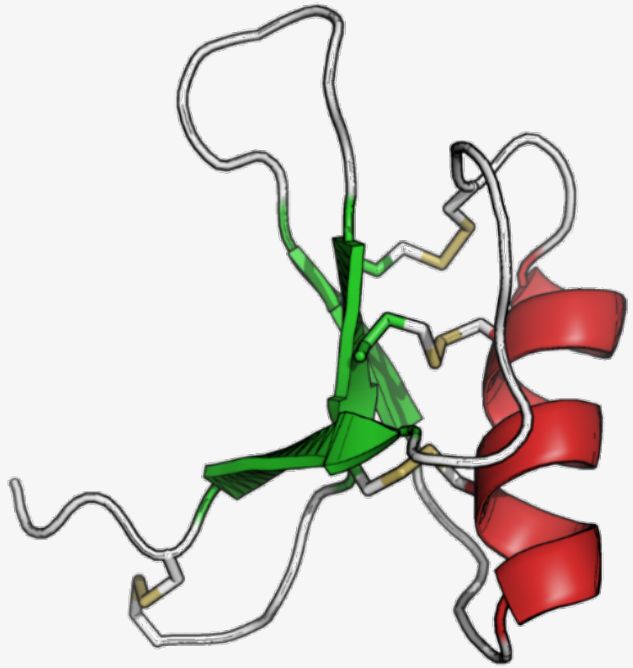
OUR SOLUTION: PEZADEFTIDE IS A NATURALLY OCCURRING PEPTIDE

ITS UNIQUE PROPERTIES ENABLE RAPID NAIL PENETRATION AND FUNGAL KILLING

Pezadeftide is a potent broad-spectrum antifungal peptide that has evolved to kill fungal pathogens

- Hydrophilic & highly soluble – drives nail penetration
- Resistant to proteases & extremely stable
- Regulated as a biologic
- Excellent safety profile
- Does not pass through human skin

PEZADEFTIDE MOLECULE



PEZADEFTIDE HAS POTENT BROAD SPECTRUM ANTIFUNGAL ACTIVITY

ACTIVE AGAINST DERMATOPHYTES, YEASTS, AND NON-DERMATOPHYTIC MOULDS

Pezadeftide is active against a range of fungal pathogens that cause infections of skin, hair and nails

- Specific for fungal cells and does not impact the viability of human cells

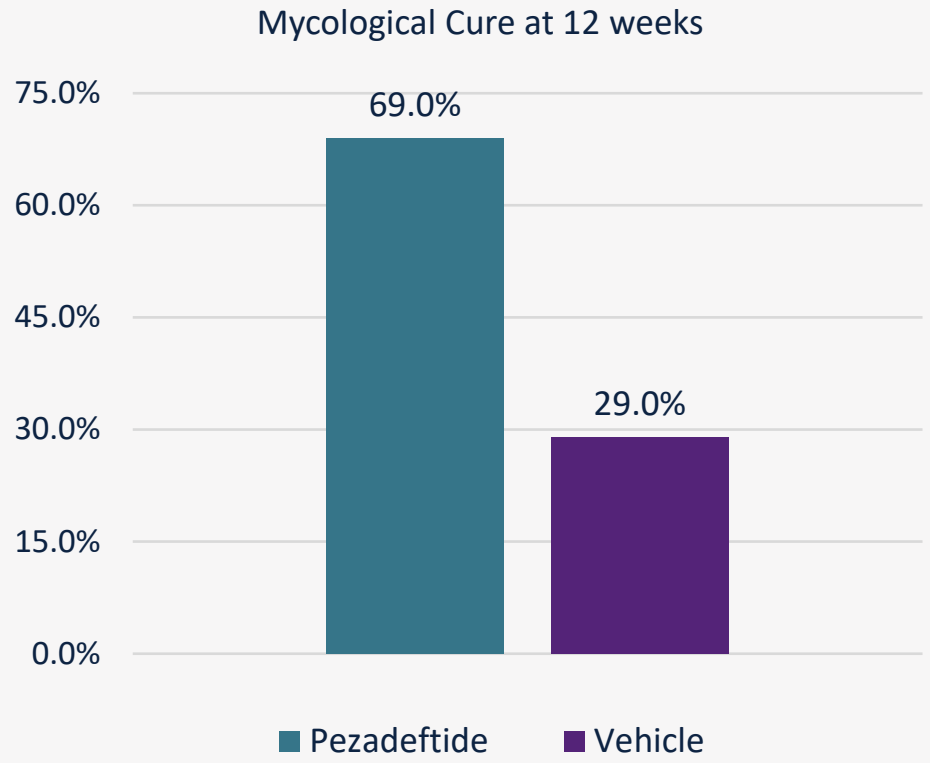
	PEZADEFTIDE	
FUNGAL PATHOGEN	IC50 (µg/ml)	MIC (µg/ml)
Microsporum canis 10214	6.3	32
Microsporum gypseum 13994	6.2	32
Trichophyton interdigitale	8.4	16
Trichophyton rubrum 41041	2.6	32
Trichophyton tonsurans 5724	2.7	8
Candida albicans	3.7	32
Candida tropicalis	1.5	4

EFFECTIVE AND RAPID ANTI-FUNGAL ACTIVITY

HXP124-ONY-001 – MYCOLOGICAL CURE RATE FOR COHORT 4
30 PATIENTS TREATED AT HIGH DOSE (2%) FOR 6 WEEKS

Mycological cure* was achieved in 69% of pezadeftide-treated nails in Cohort 4 within 12 weeks (vehicle 29%)

- **Mycological Cure* rate at 12 weeks**, >2-fold higher than current treatments, after only 6 weeks of daily treatment



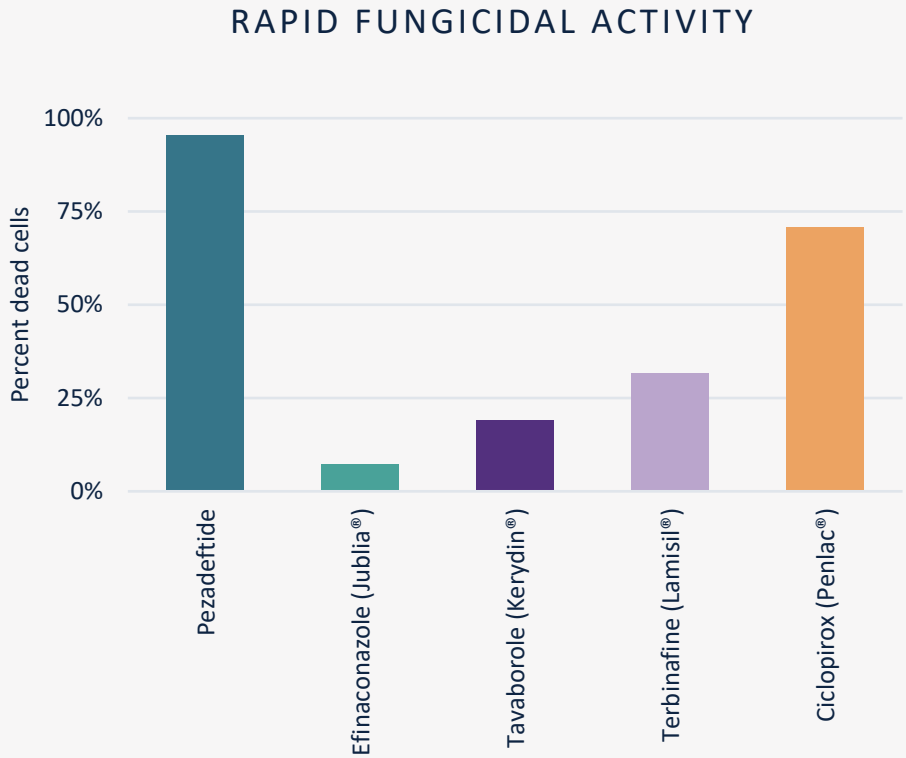
*Mycological cure: KOH stain negative and culture negative

SPECIFIC AND RAPID FUNGICIDAL ACTIVITY

NOVEL FUNGICIDAL MODE OF ACTION ALLOWS RAPID RESOLUTION OF THE INFECTION

Pezadeftide kills fungal cells in less than 30 minutes via a novel mode of action

- Pezadeftide is specific for fungal cells and does not impact the viability of human cells
- Ineffective killing by drugs currently on the market means the fungus often regrows when treatment is stopped



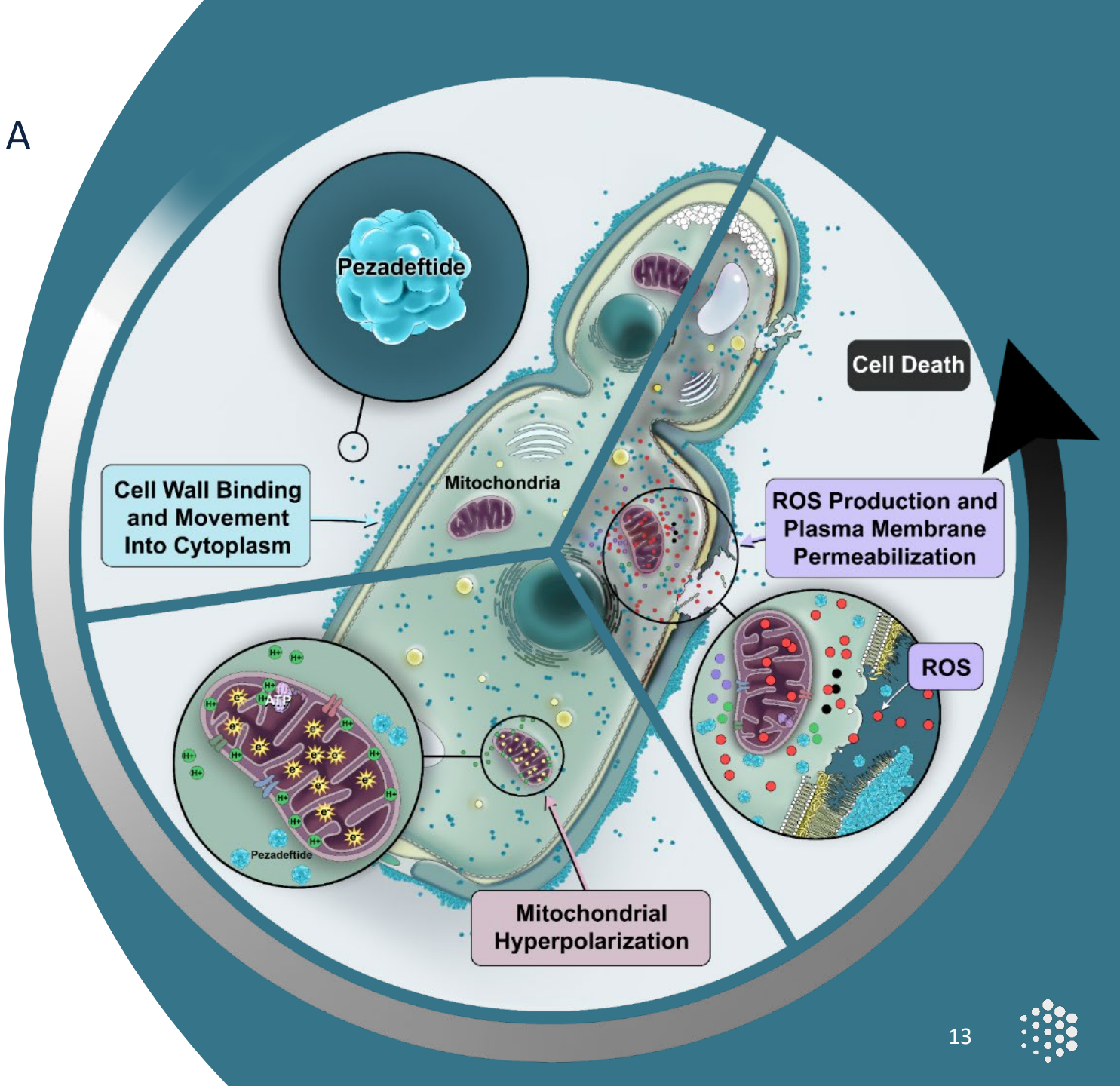
FLUORESCENCE ASSOCIATED CELL SORTING (FACS) OF PROPIDIUM IODIDE STAINED CELLS WAS USED TO IDENTIFY LIVING AND DEAD CANDIDA ALBICANS CELLS AFTER 30 MIN TREATMENT WITH ANTIFUNGAL AGENTS

Note: Internal study

PEZADEFTIDE DISRUPTS FUNGAL CELL MEMBRANE INTEGRITY VIA A NOVEL MECHANISM

- **Pezadeftide has a novel fungicidal mechanism of action distinct from triazole-based drugs**
- **The direct antifungal mechanism of action of pezadeftide reflects 3 key events**

1. Accumulation of pezadeftide at the cell surface as the result of cell wall binding followed by movement into the cytoplasm
2. Induction of mitochondrial membrane hyperpolarization
3. Production of ROS and permeabilization of the fungal cell plasma membrane



ROS, reactive oxygen species.

PEZADEFTIDE BINDS TO THE CELL WALL AND ENTERS THE CELL

PEZADEFTIDE KILLS FUNGAL CELLS VIA A NOVEL MODE OF ACTION

Fungal cells treated with **FAM**-labelled pezadeftide in the presence of **PI** (stains dead cells).

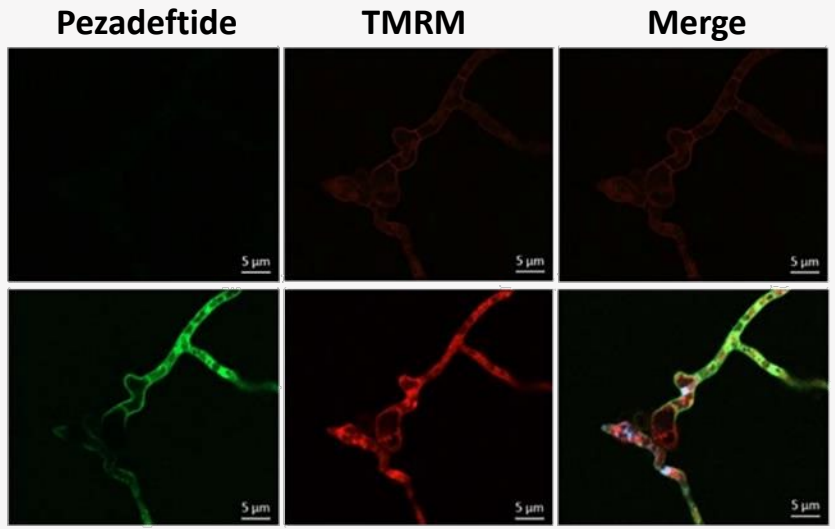
- **Pezadeftide** binds to the fungal cell surface…
- …then enters the cell…
- …and causes membrane disruption leading to **cell death**.

PEZADEFTIDE HYPERPOLARIZES THE MITOCHONDRIAL MEMBRANE

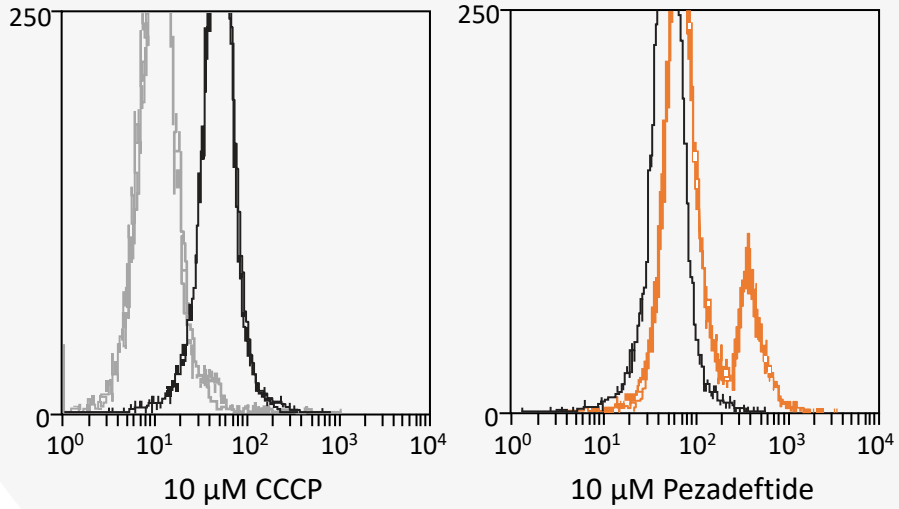
INCREASES THE NEGATIVE CHARGE OF THE MITOCHONDRIAL MATRIX WHICH DRIVES ENERGY PRODUCTION IN THE CELL

Pezadeftide increases the negative charge in the mitochondrial matrix

- Hyperpolarization of the mitochondrial membrane increases the activity of the electron transport chain, effectively putting the cells energy generation into ‘overdrive’
- Hyperpolarisation of mitochondria has not previously been reported for antifungal molecules



In *T. rubrum*, mitochondrial membrane potential was monitored using the indicator dye TMRM (red). Pezadeftide increased the membrane potential within 17 min.



Increase in TMRM fluorescence was monitored by flow cytometry. In contrast to the depolarizing drug, CCCP, pezadeftide increased TMRM fluorescence in *C. albicans*.

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TMRM = tetramethylrhodamine; CCCP = carbonyl cyanide m-chlorophenyl hydrazone

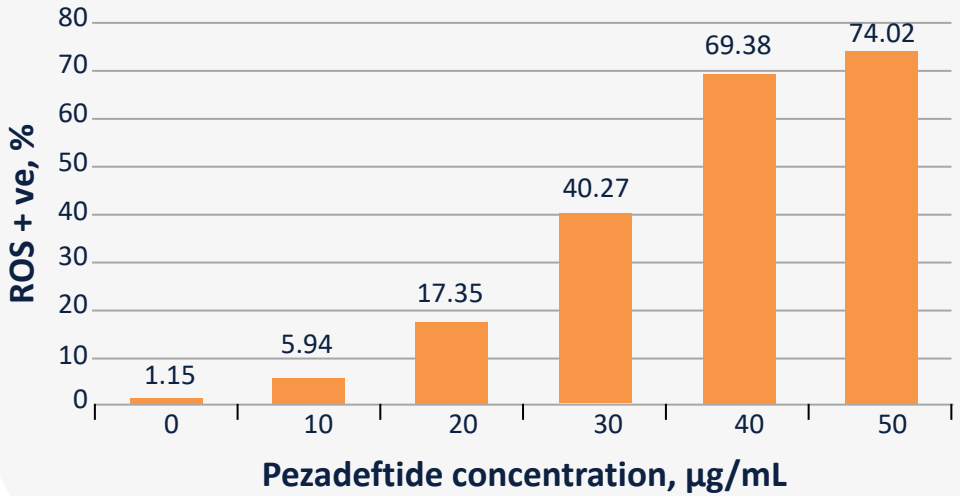
PEZADEFTIDE INCREASES REACTIVE OXYGEN SPECIES PRODUCTION

REACTIVE OXYGEN SPECIES (ROS) ARE DAMAGING TO CELL COMPONENTS INCLUDING THE PLASMA MEMBRANE

Pezadeftide causes accumulation of ROS in a dose-dependant manner

- Mitochondrial membrane hyperpolarization is known to increase ROS production[1]
- Pezadeftide induces excess ROS production, eventually leading to cell death

In *T. rubrum*, ROS accumulation was monitored using a fluorescent dye (DHR123, green). ROS accumulated in cells treated with pezadeftide (red)



The proportion of treated *C. albicans* cells that were positive for ROS was quantified using flow cytometry

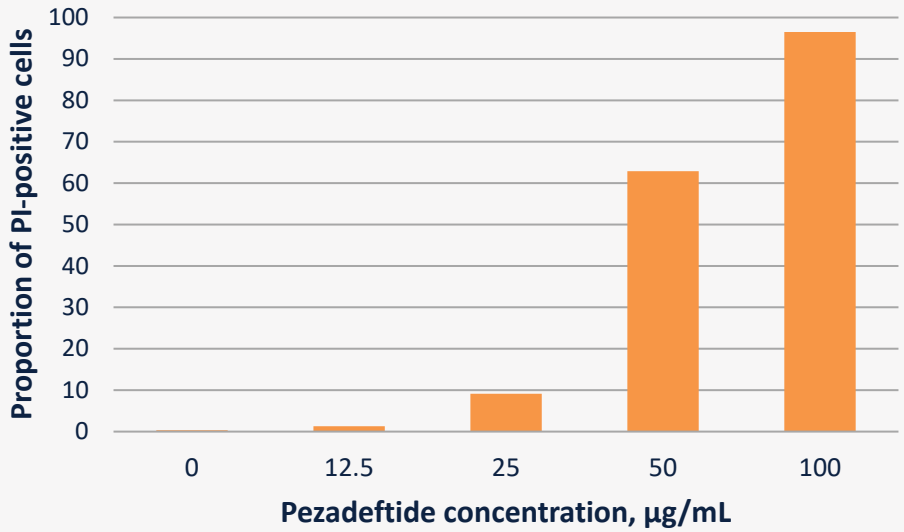
1. Perl A, et al. *Trends Immunol*. 2004;25(7):360-367; DHR123 = Dihydrorhodamine 123

PEZADEFTIDE CAUSES MEMBRANE DISRUPTION AND CELL DEATH

Pezadeftide disrupts the fungal plasma membrane in a dose-dependant manner

- Once the plasma membrane is disrupted the fungal cell is no longer viable

In *T. rubrum*, membrane disruption was monitored using fluorescent dyes that cannot pass through the intact plasma membrane (SYTOX/PI)



The proportion of *C. albicans* cells that were positive for fluorescence was quantified using flow cytometry

PHASE II RESULTS Q2 2022

A CRITICAL MILESTONE

- Onychomycosis is a very common and difficult to treat infection
    1. New topical treatments have been only modestly successful
    2. Oral medications are impacted by negative side effects
- Pezadeftide is a highly differentiated world first
    1. Very different biophysical properties; and
    2. A completely new mechanism of action
- Reported powerful phase I clinical results
- Critical phase II results in Q2 2022
- Positioned to move forward into phase III

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A game-changing treatment for onychomycosis

hexima