CLINUVEL

Welcome to the Sydney Soirée

PRESENTERS

Malcolm Bull – Head of Australian Operations & Investors Relations

Lachlan Hay – Director of Global Operations

Philippe Wolgen – Chief Executive Officer

ASX:	CUV
XETRA-DAX:	UR9
Level 1 ADR:	CLVLY

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Forward-Looking Statement

This release contains forward-looking statements, which reflect the current beliefs and expectations of CLINUVEL's management. Statements may involve a number of known and unknown risks that could cause our future results, performance or achievements to differ significantly from those expressed or implied by such forward-looking statements. Important factors that could cause or contribute to such differences include risks relating to: our ability to develop and commercialise pharmaceutical products; the COVID-19 pandemic and/or other world, regional or national events affecting the supply chain for a protracted period of time, including our ability to develop, manufacture, market and sell biopharmaceutical products; competition for our products, especially SCENESSE® (afamelanotide 16mg), PRÉNUMBRA® or NEURACTHEL®; our ability to achieve expected safety and efficacy results in a timely manner through our innovative R&D efforts; the effectiveness of our patents and other protections for innovative products, particularly in view of national and regional variations in patent laws; our potential exposure to product liability claims to the extent not covered by insurance; increased government scrutiny in either Australia, the U.S., Europe, Israel, China and Japan of our agreements with third parties and suppliers; our exposure to currency fluctuations and restrictions as well as credit risks; the effects of reforms in healthcare regulation and pharmaceutical pricing and reimbursement; that the Company may incur unexpected delays in the outsourced manufacturing of SCENESSE®, PRÉNUMBRA® or NEURACTHEL® which may lead to it being unable to supply its commercial markets and/or clinical trial programs; any failures to comply with any government payment system (i.e. Medicare) reporting and payment obligations; uncertainties surrounding the legislative and regulatory pathways for the registration and approval of biotechnology and consumer based products; decisions by regulatory authorities regarding approval of our products as well as their decisions regarding label claims; our ability to retain or attract key personnel and managerial talent; the impact of broader change within the pharmaceutical industry and related industries; potential changes to tax liabilities or legislation; environmental risks; and other factors that have been discussed in our 2022 Annual Report. Forward-looking statements speak only as of the date on which they are made, and the Company undertakes no obligation, outside of those required under applicable laws or relevant listing rules of the Australian Securities Exchange, to update or revise any forward-looking statement, whether as a result of new information, future events or otherwise. More information on preliminary and uncertain forecasts and estimates is available on request, whereby it is stated that past performance is not an indicator of future performance.

Business Evolution

Date	Cumulative spend	Key activities	Addressable markets
1980–2005	AUS **$70m**	Invention aimed at lifestyle	US **$5bn**
2006–2016	AUS **$150m**	Restructure | Reformulation | Regulatory approvals | Market entry	
2017–2022	AUS **$320m**	Commercialisation | Profitability | Liquidity ratio ↑	US **$300m**
2023–2024	AUS **$495m**	Expansion | Scalability | **Targeted Technology Translation**	US **$12bn**

Core pharmaceutical business – 3 drugs

PHOTOMEDICINE
SCENESSE® – **EPP | vitiligo | XP**

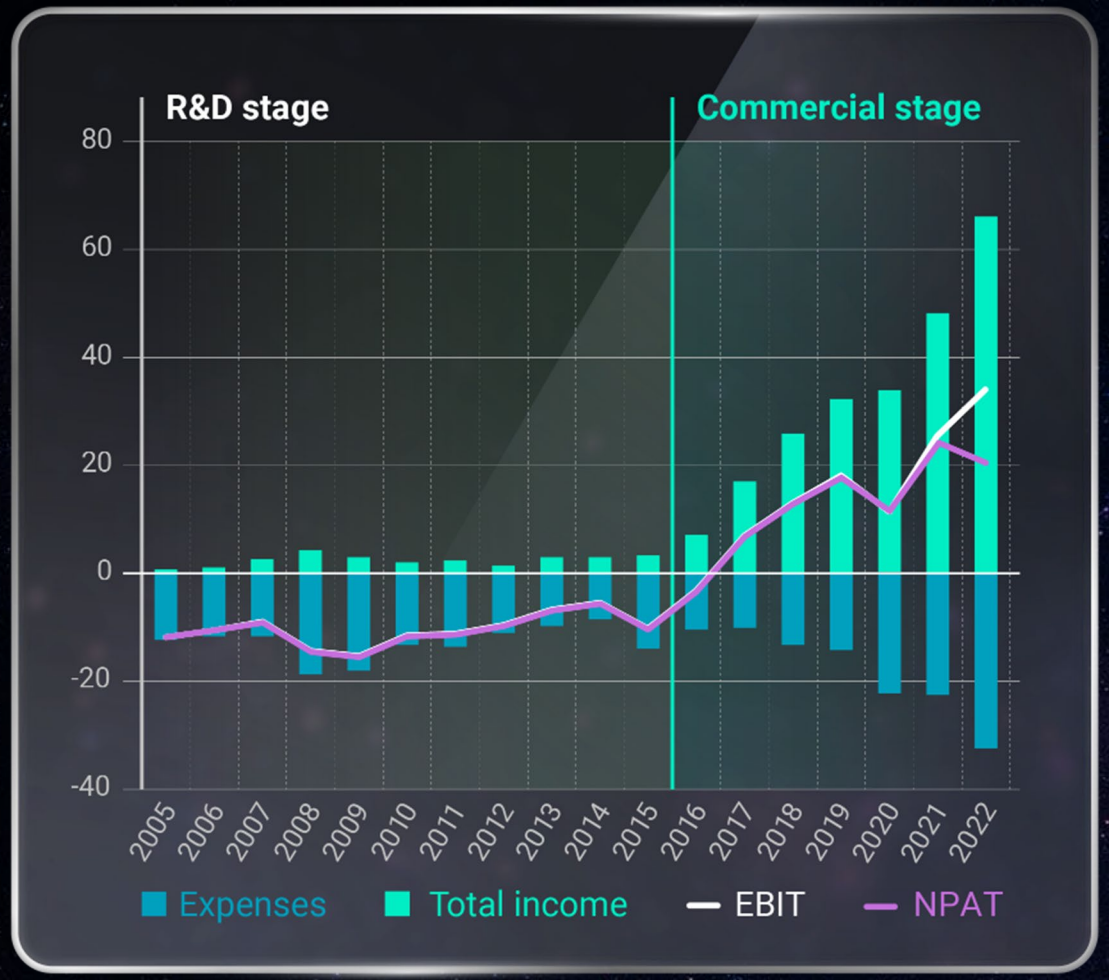
PRÉNUMBRA® – Stroke | Vascular disorders

NEURACTHEL® – Infantile spasms | Relapsing multiple sclerosis

Consumer healthcare – 4 products

Highest risk skin cancer

Financials 2005 – 2022



FY'22 dividend:	**10% of net profit**
<300% dilution	
ROCE 27%	(6yrs)
Cash reserves:	AUS **$121m** (30 June '22)
Expenses:	AUS **$175m** (FY '21-25)
	AUS **$55.5m** (FY '21-22)

Nasdaq '22*	Bio-pharmaceuticals	Profitable
Main board	798	67 (8.4%)
NBI	274	25 (9.1%)
ASX	91	3 (3.2%)

Beneficial Ownership by Region

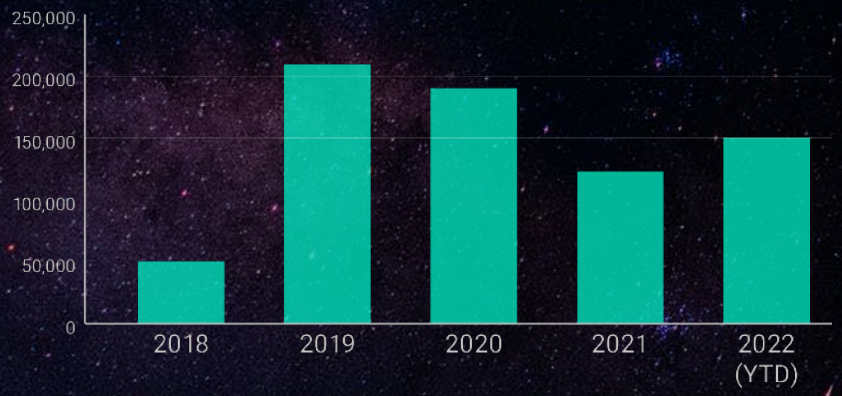
Global distribution

- 2/3rd – held EU / US / AS
- 1/3rd – held Aust / NZ

Aust / NZ share increased, ’18 – ’22

- institutions from 2.9% to 14%

ADTV has increased



Vitiligo Classifications

I Non-inflammatory — leucomelanosis

VITILIGO = 'hypomelanosis = hypopigmentation = leukoderma'

- acrofacial, mixed

II Inflammatory

- pruritus (itching)
- erythematosous lesions (redness)
- elevated lesions

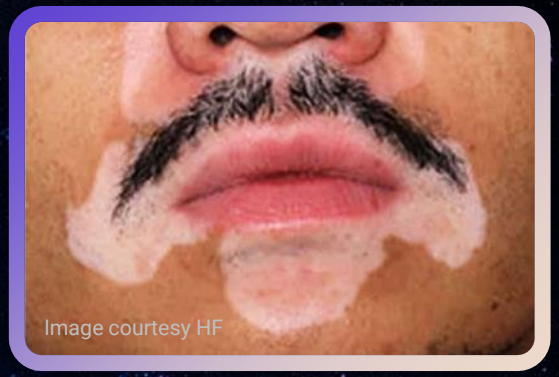
III Koebner effect — localized

IV Piebaldism — leucoderma, leucotrichia

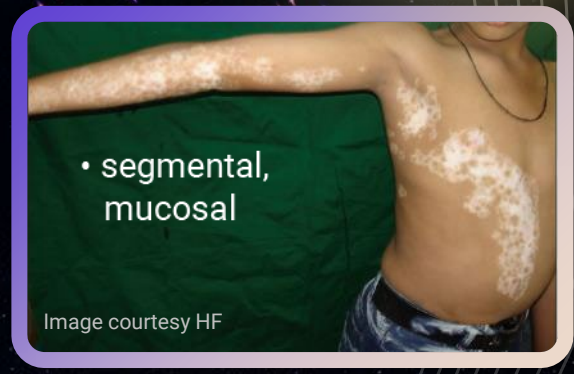
Waardenburg Syndrome
Woolf Syndrome
Fisch Syndrome

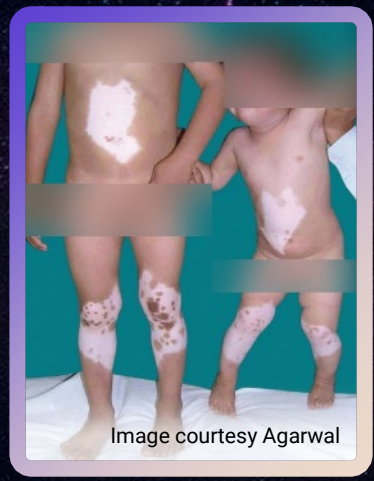
- partial albinism (rhomboidism)
- retarded development
- deafness
- musculoskeletal

GV (generalized) leucotrichia



FV (focal) acquired





Differential diagnosis

- post-traumatic hypopigmentation
- tinea versicolor
- tuberosclerosis
- hypomelanocytosis
- guttate hypomelanosis
- nevus depigmentosus
- pitriasis alba

Pathogenesis Vitiligo – Hypotheses ‘22

Mechanism	Impact of melanocyte	Markers
Neural ‘59	sympathetic neuronal system	↓ NPY, VIP, CGRP, PGP, NGF
Intrinsic	deficiency in melanocytes	↓ bFGF, c-kit
Biochemical, cellular, molecular	apoptosis, accelerated senescence	↑ Bcl-2, FLIP, GF, SCF, ET-1 ↑ BAX, p53, caspase-3, 8, TNF-α, IL-6
Viral	destruction of melanocytes	↑ HCV, HBV, CMV, EBV, HIV
ROS	imbalanced redox state	↓ H2o2, SOD, MDA, GPx
ZAG	loss of epidermal adhesion	↓ ZAG
Auto-immune	destruction melanocytes	↑ antibodies: MCHR-1, TH, antithyroglobulin, antithyroid, anti-peroxidase, Ig-M, -G, -A
	T-cells	IL-2R, CD8:CD4 shift, macrophages (CD36)
	cytokines	↑ TNF-α, IF, IL-10, IL-17, IL-6, IL-1
	genetics	AIS 1-2-3, CTLA4, SLEV1

Vitiligo Treatments – Unmet Need

	Categories	Clinical status	CUV's views
A	**Non-pharmaceutical**		
I	narrowband UVB (308nm)	standard of care, 12–18 m, 200 mJ/cm²	remains adjuvant for GV >10%, non-face BSA
II	PUVA	experimental, 0.6 mg/kg + 2 J/cm²	less used
III	XTRAC LASER (308nm)	in practice, 100–200 mJ/cm²	small lesions, head/neck/scalp
IV	Erbium-YAG LASER (2940 nm)	60 J/cm² fluence	small lesions, not often used
V	CO2 LASER	1–2 Hz, 0.9W	small, lesions, hardly used
B	**Topical**		
VI	steroids	0.05–0.1mg/kg	cheap solutions, low compliance, ineffective
VII	calcineurin inhibitors	0.03–0.1% (tacrol), 3mg/kg/day(cyclspor)	100–200 treatments BID, mixed results
VIII	pseudocatalase '95	100 mg	hardly used
IX	methoxsalen	0.4 mg/kg or 1%	before PUVA
X	5-fuorouracil	5%	not often used, side effects
XI	apremilast	30 mg BID	little effect
XII	ruxolitinib Rx 2022 (FDA)	1–5% BID	except head and neck, will become Tx of last resort
C	**Surgical**		
XIII	auto-grafting	melanocyte transfer	only in specialized hands, burdensome
XIV	extra-corporal cell culture	abrasion, spray-on	hardly effective, burdensome
XV	microneedling	⌀ 200μ – active agents and HA	using various agents, local lesions
D	**Systemic**		
XVI	ritlecitinib	10–30–50 mg (po)	immune suppression
XVII	afamelanotide	physiological MC1R agonist	non-immune-suppressive, >15% on head/neck, extremities, torso/back

CLINUVEL's Innovation – Proof of Concept

Biomimicry as a therapeutic approach

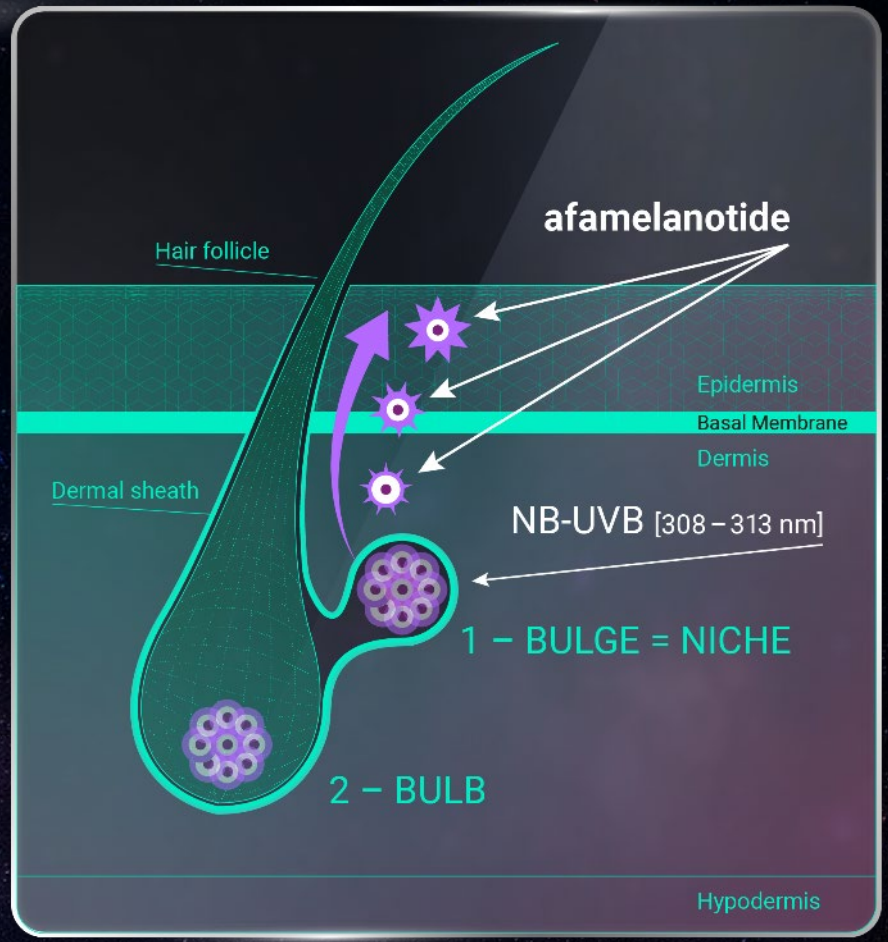
CUV102 (2012-2013) n=58 Afa 16mg + NB-UVB

• FST Type III vs IV-VI	20 vs 35
• FST IV-VI: VASI day 56 + 84	p<0.05
• D-spreading: day 56	p<0.001
• Time-to-onset: face	p=0.0001
• Extremities	p=0.003

[1]non-parametric testing means between 2 ITT arms
FST: Fitzpatrick Skin Type

CUV104 (2013-2014) n=18 Afa 16 mg + NB-UVB

- Repigment > day 140, face/upper extremities p=0.001/.004
- Ethnic origin and culture determines perception "melanogenesis"



CLINUVEL – Vitiligo Clinical Objectives

Afamelanotide repigmentation

- systemic treatment, 16 mg
- generalised vitiligo, adults
- type IV-V-VI (darker skin)
- head & neck
- >0.5% depigmentation total body
- 28 weeks study
- double-blind randomised, 2 arms

→ Primary Endpoint: F-VASI75

→ Secondary Endpoint: F-VASI50
T to repigment
VitiQoL

**Palmar Method: head & neck = 8% BSA*
***Browder & Lund: head & neck = 9% BSA*

Ruxilitinib FDA approved 2022

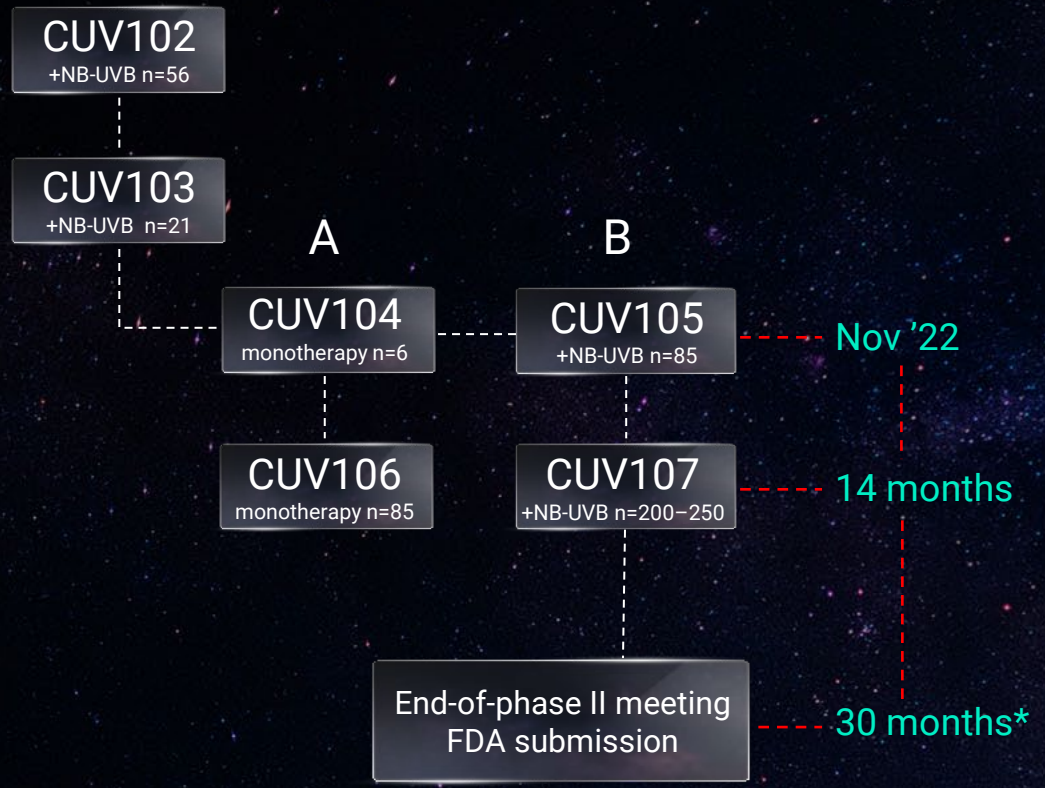
- 1.5% cream (topical, BID)
- children >12 yr
- Ph II (n=157): double-blind randomized
- 24 weeks study, crossover + 28 weeks

→ Primary Endpoint: F-VASI75:
33% repigmented >75% of face at 6 months
51% >75% at 12 months

→ Secondary Endpoint: F-VASI50
51% achieved >75%

Ph III (n = 2*300): TRUE-V1 and TRUE-V2
29.9% achieved >75% at week 24
~50% achieved >75% at week 52

CLINUVEL's Regulatory Pathway – Vitiligo



2022: >12,000 doses FDA accepts safety profile afamelanotide

NB-UVB combination

- 2012 – 2022 FDA-CUV misaligned
- Delay resulted in savings $75 – 145m

2022: FDA sets precedent for NB-UVB as combination therapy

Regulatory pathways are either A+B or B

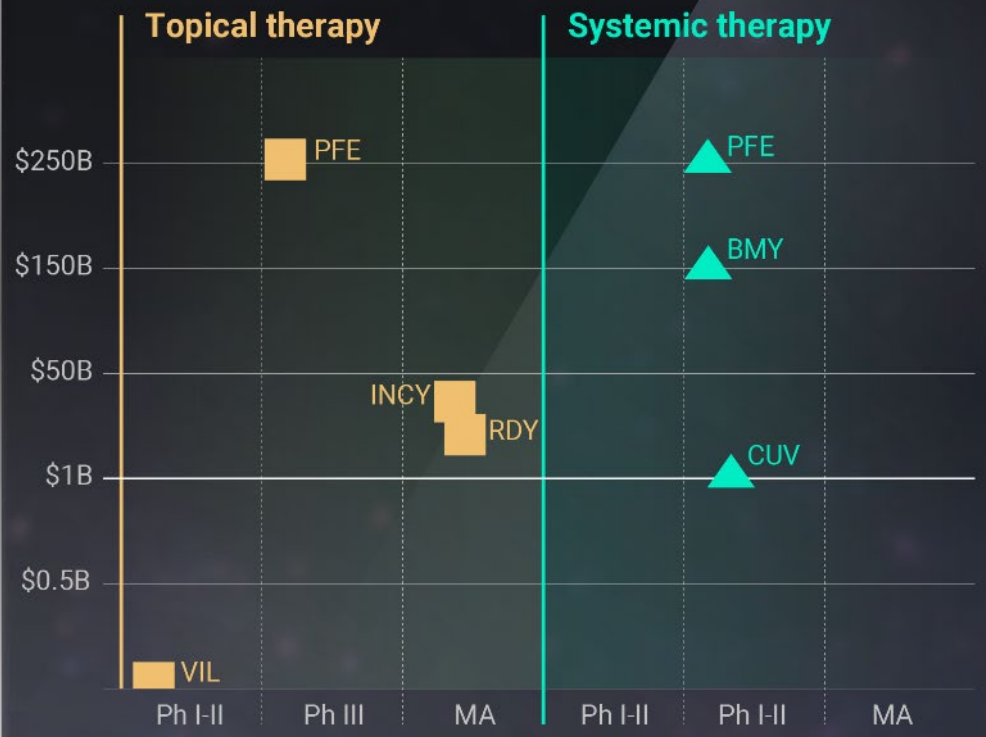
1. A+B: projected expenditures $96m
2. B: projected expenditures $77m

Regulatory timelines are dictating timings and progress of filings

Vitiligo Market Segmentation

Main clinical research – Oct 2022

1. BMS: NB-UVB + apremilast 30 mg p/o	Ph II, n=23
2. Pfizer: crisaborole (PDE4i) + NB-UVB 2% topical	Ph II, n=64
3. U Bordeaux: baricitinib + NB-UVB 4mg/d p/o	Ph II, n=48
4. U Sth Car: rapamycin 01%-0.001% topical	Ph II, n=20
5. Villaris/NIAID: AMG714, 300mg s.c.	Ph IIa, n=57
6. Pfizer: PF06651600/06700841, oral	Ph II, n=366
7. CLINUVEL: afamelanotide monotherapy	Ph II, n=6



*Surgical treatments such as needling, autografts and cell spray have been omitted since these are only viable case by case.

**XTRAC, Erbium-YAG, CO2 and NB-UVB are not separately discussed here.

**Growth Plus Report '21*
***MarketResearchFuture '21*
****FortuneBusinessInsights'18*
*****Pfizer, Incyte pres JPM 2019*

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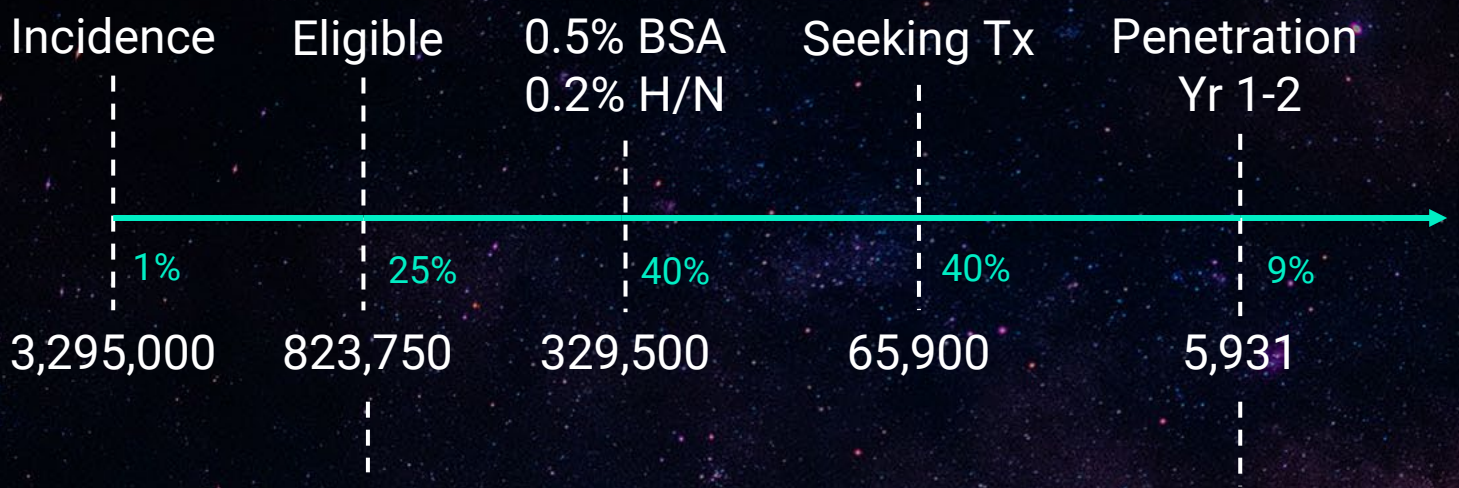
Afamelanotide Addressable Vitiligo Market

North America

Global market 2027
$4.5B*



Market
$490-570M*

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Summary

Pharmaceuticals		
1	Xeroderma pigmentosum – assisted DNA repair	(3 trials ongoing)
2	Vitiligo - afamelanotide monotherapy + combination therapy	(2 trials)
3	Stroke – reduction in penumbra, NIHSS	(1 trial)
	I. SCENESSE®	commercial US-EU-CH-IS
	II. PRÉNUMBRA®	in manufacturing
	III. NEURACTHEL®	in manufacturing
Healthcare Solutions		
A	R&D: 4 OTC product lines	CYACÊLLE (1st product)
Communications Program		
1	IR, traditional roadshows, conferences	meeting cycles p/a
2	targeted events	global events, soirées
3	CBM team established	increased social media
Finance		
	stability, counter cyclical buffer	financial discipline

CATALYSTS 2022-2023
XP/DNA repair read out Ph II
Start Ph II trial Vitiligo
Start Ph II stroke high/freq dosing
I. SCENESSE® expansion adolescents
II. PRÉNUMBRA® to be used in stroke
III. NEURACTHEL® manufacturing
HEALTHCARE SOLUTIONS
Launch CYACÊLLE
COMMUNICATIONS
6 – 8 cycles next 12 months
13 events in 16 months
Increased social media CUVA/CUVIPs
FINANCE
Growth

Authorised for ASX release by the Board of Directors of CLINUVEL PHARMACEUTICALS LTD

Head of Investor Relations

Mr Malcolm Bull, CLINUVEL PHARMACEUTICALS LTD

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