CLINUVEL

RENDEZ-VOUS

Nasdaq 29 March 2023

Finance • Pharma • Future

ASX	CUV
Börse Frankfurt	UR9
ADR	CLVLY

Safe Harbor

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.

The Melanocortin Story 1933-2025

ACTH 1-24 / 1-39

↓

α-MSH / Conjugates

↓

Products - Companies

1	Bremelanotide	PTN
2	Setmelanotide	RYTM
3	ACTH	MNK
4	ACTH	ANI
5	ACTH	SYN
6	ACTH	CUV
I	Afamelanotide controlled-release	CUV
II	Afamelanotide instant	CUV
III	Parvys-/Phimelanotide	CUV
IV	CUV9900	CUV

Properties

- Libido ↑
- Anorexic
- › Melanogenesis
- › Anti-oxidative
- › Anti-oncotic
- › Anti-inflammatory
- › Neurotrophic
- › Neuroprotective
- › DNA-reparative
- Anti-pyretic

Environment	
2021	1st FDA workshop - Vitiligo
1999	CLINUVEL acquires afamelanotide
1991	1st in man study of alpha-MSH analogues
1980	1st synthesis Afamelanotide U Arizona
1960	ACTH Klaus Hoffman, U Pitts
1933	Discovery*

NME-Branded	
FDA – SCENESSE® vitiligo	**2025**
Parvysmelanotide	**2025**
EMA – SCENESSE® XP	**24/25**
ACTH – controlled-release	**2024**
FDA – Setmelanotide	2020
FDA – Bremelanotide	2019
EMA – SCENESSE®	**2014**

*Anderson, Collip, Thomson

Chiaroscuro

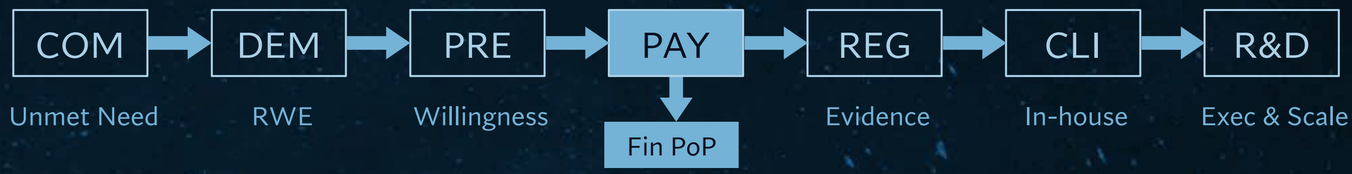
Carvaggio 1608: Fra Antonio Martelli - portrait

Who sees light and who sees shadows?

CLINUVEL's Model – 2 Phases

1. Weighted Investment Thesis

Risk Management



2. Fiscal Discipline

	Period	CAR*	SCA**	HDC
	'05–'10	6m	16–32m	24
Phase 1	'11–'16	12m	39m	31
	'17–'22	18m	49m	<50
Phase 2	'23–'25	36m		<120

R&D

EQ	OPEX
A$110m – A$140m	
US$73m – US$93m	

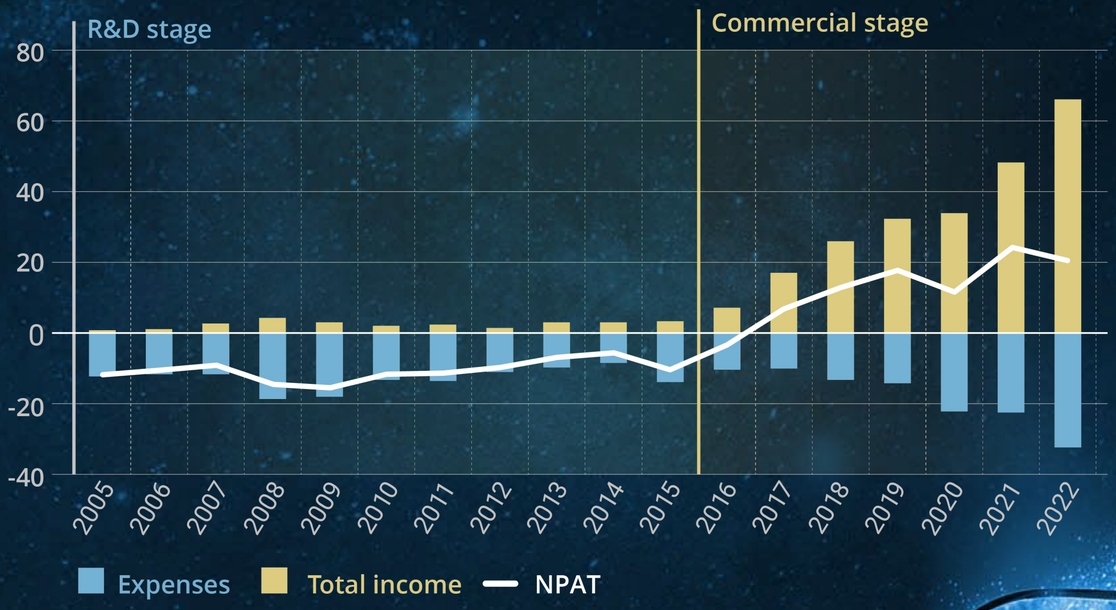
Commercial + R&D: Org/Inorg

3. Profitability

4. Redistribution

Div ~ 9% NPAT

Resourcefulness
Pre-emption
Longitude



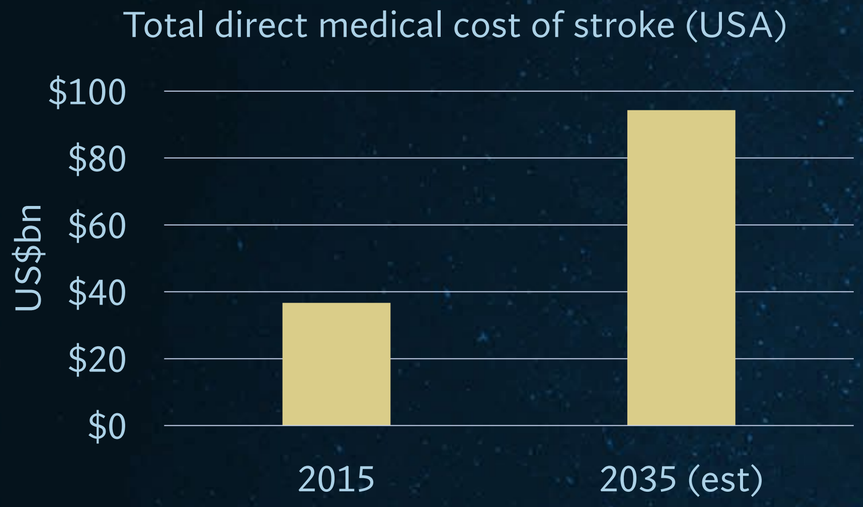
*capital adequacy ratio, **share capital

Targeting Arterial Ischemic Stroke (AIS)

DISEASE BURDEN

US stroke statistics:

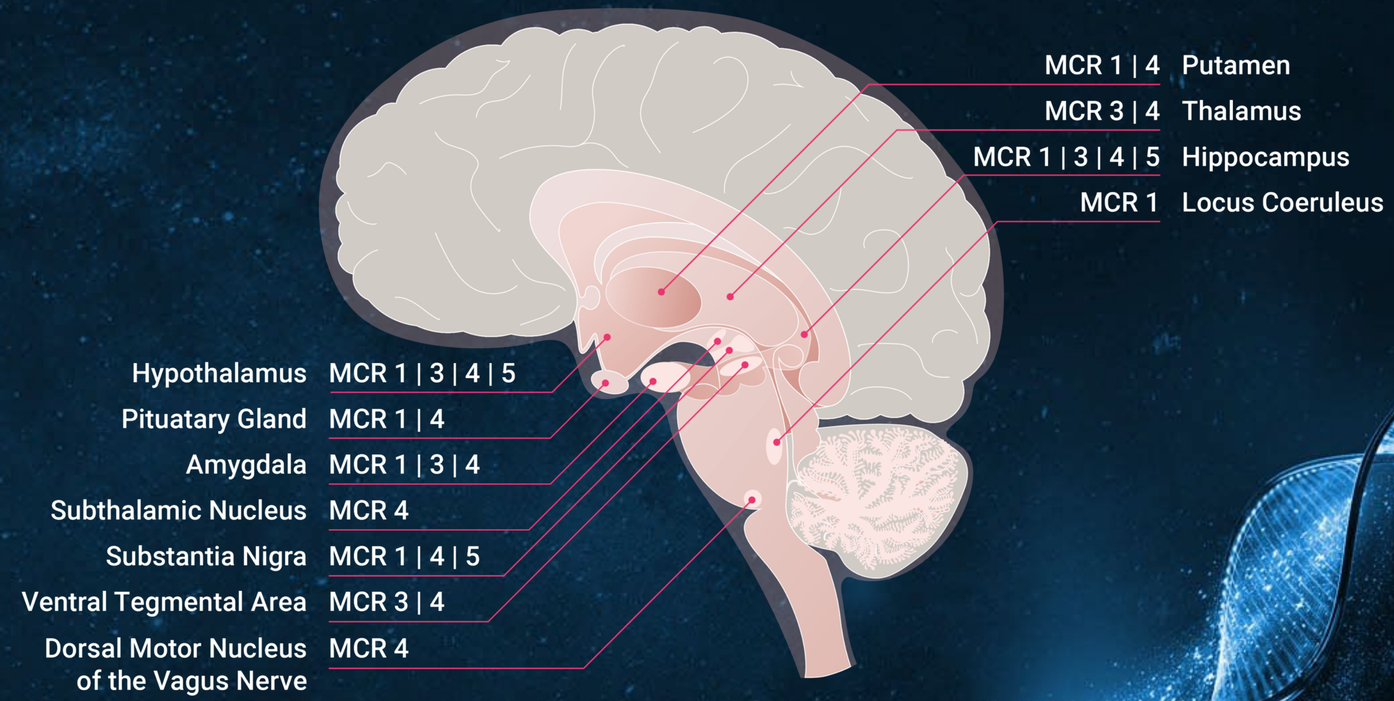
- 795,000 patients suffer an infarct annually
- 150,000 patients succumb
- costs US$52.8bn p/a
- 75% - 80% untreated



Pharmacology afamelanotide

Melanocortin receptors - ubiquitous cerebral location

'The potential for melanocortins and their analogs to address CNS disorders has been widely researched'
(Giuliani et al. 2011; Xu et al. 2020; Wu et al. 2020)



Arterial Ischemic Stroke

Targeted product position

A hormonal treatment to assist hypoxic brain.

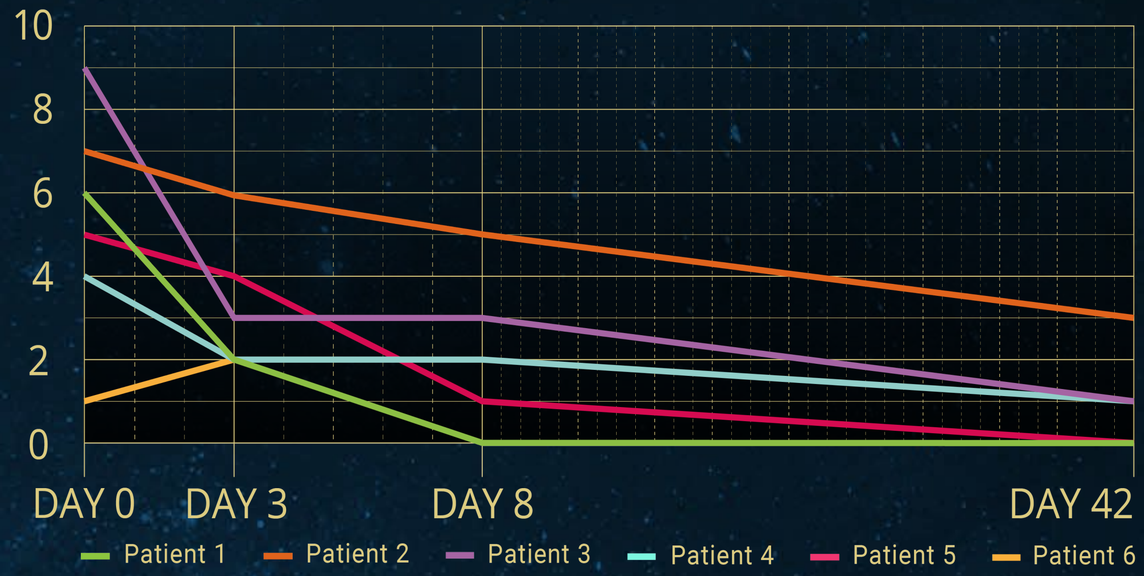
Study CUV801 (n=6): Proof of Concept – afamelanotide

- open-label, up to 4 doses: days 0, 1, 7, 8; evaluation at day 42
- occlusion higher regions: > M2/A2/P2
- functional recovery in 5 patients; NIHSS ≥4 (4/6)
- cerebral perfusion improved per MRI-FLAIR (CBF, Tmax)

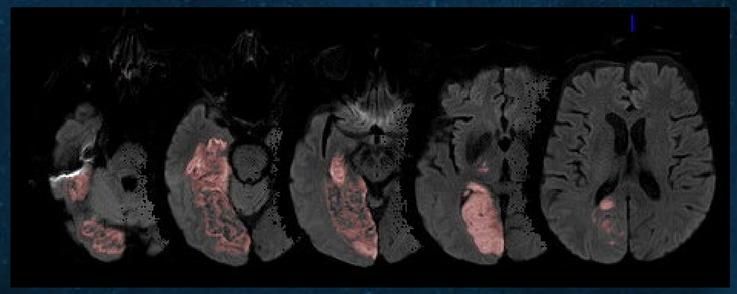
Study CUV803 (n=12): first patient treated March 2023

- occlusion higher regions: > M2/A2/P2
- higher, more frequent dosing of afamelanotide, PRÉNUMBRA®
- safety
- neurological functionality (NIHSS)
- perfusion of penumbra, oligemic zone
- Read out 2023

Individual NIHSS scores – CUV801 Days 0–42

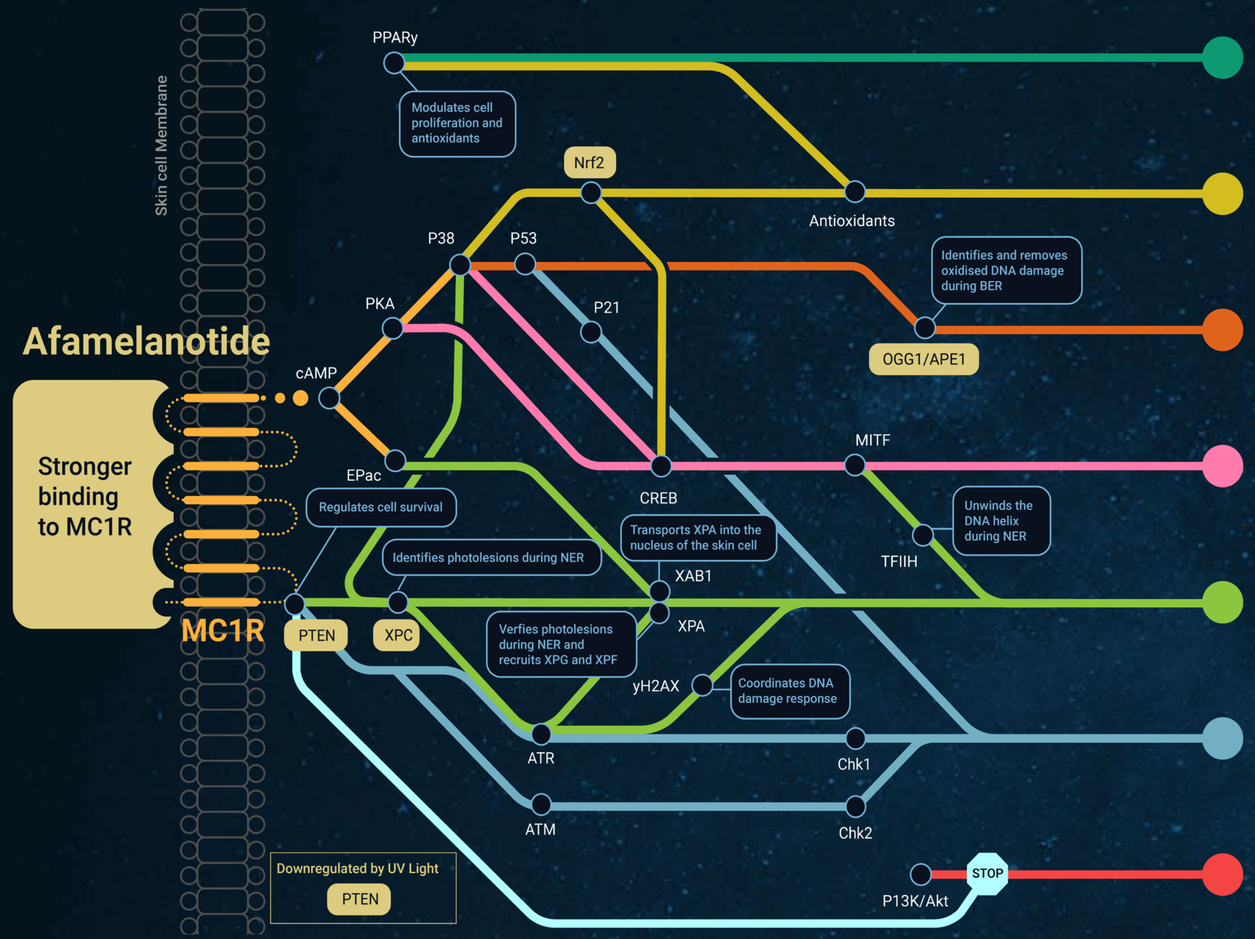


MRI-FLAIR: CUV801 changes in affected areas.
Image courtesy of the study investigator.



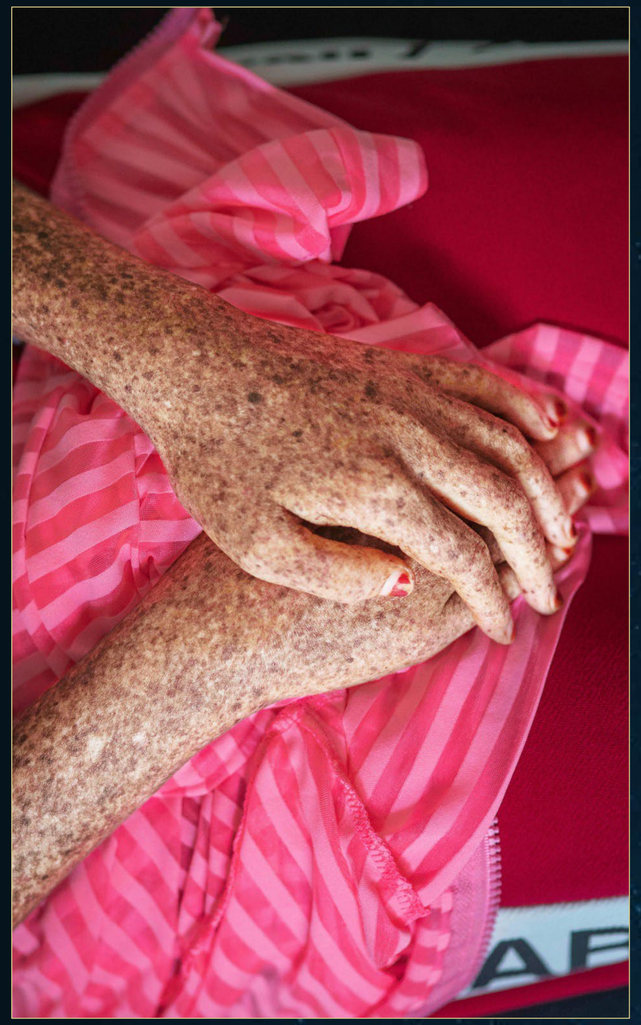
DNA Repair: Xeroderma Pigmentosum (XP)

Afamelanotide – enhancing cellular signalling



- Modulates proliferation
- Reduces DNA Damage
- Base Excision Repair (BER)
- Regulates Melanocyte Function and Survival
- Nucleotide Excision Repair (NER)
- Stalls the Cell Cycle
- Cell Survival

DNA Repair: Xeroderma Pigmentosum (XP)



Clinical profile - XP

Gene defects: 3p25, 6p21

Highest rate of skin cancer(s) – shortened life expectancy

TAM 1,000 EU/US/LATAM/MENA patients

DNA repair program

CUV156: Phase IIa ongoing (XPC, n=6)
- EP: safety, assist DNA repair, QoL
- 1st results: reduction of CPDs, reduced erythema (n=3)
- Read out: expected 2023

CUV151: completed (n=9) - control
- EP: assist DNA repair
- 1st results (n=9): decrease in erythema, increase in MED
- Final read out: expected 2023

CUV152: Phase IIb ongoing (XPV & XPC, n=6)
- EP: safety, assist DNA repair, QoL
- Read out: expected 2023

CUV153: Phase III – pivotal trial – regulatory interaction (XPV, n=6)
- EP: safety, assist DNA repair, QoL

CUV154: Phase III – pivotal trial – regulatory interaction (XPC & XPV, n=20)
- EP: safety, assist DNA repair, QoL

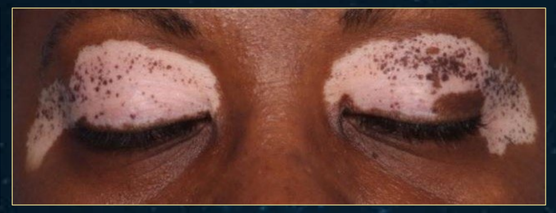
Vitiligo Program

SCENESSE® in combination with NB-UVB

provided >80% repigmentation of head & neck in darker skin [CUV102]

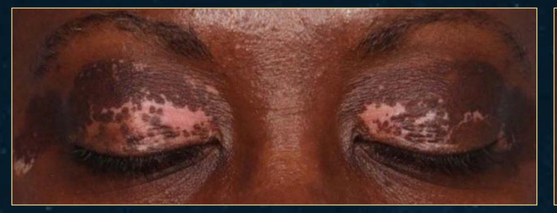
DAY 0

Baseline – At start of study



DAY 35

After 1 implant – 15 NB-UVB

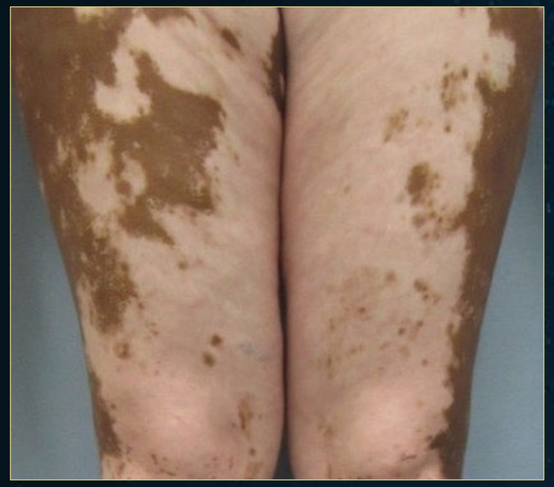


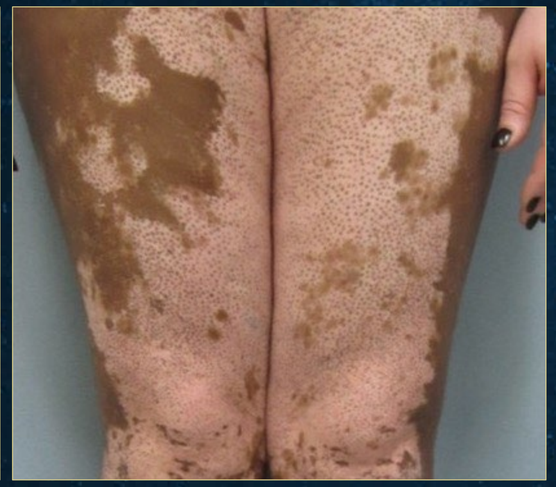
DAY 66

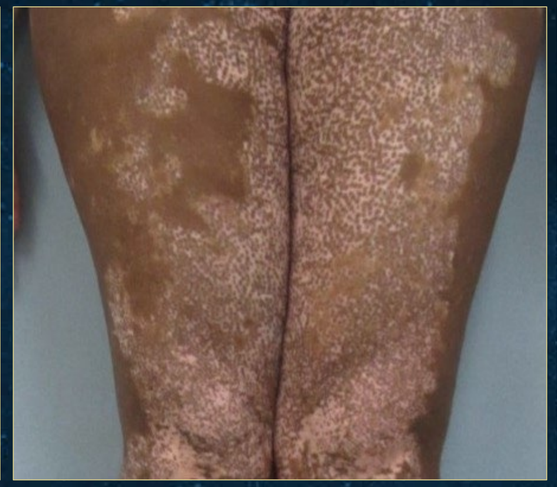
After 2 implants – 29 NB-UVB

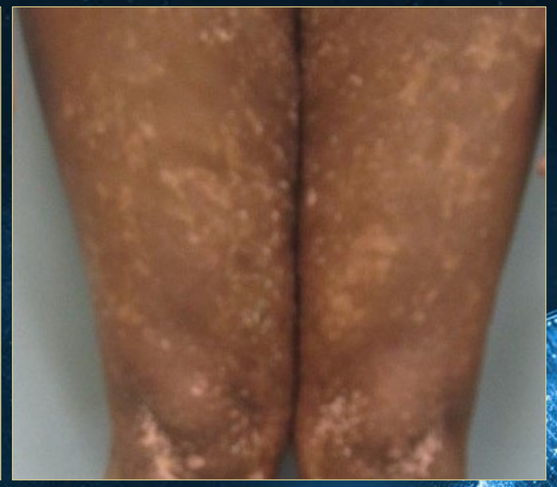
DAY 171

After 4 implants – 62 NB-UVB







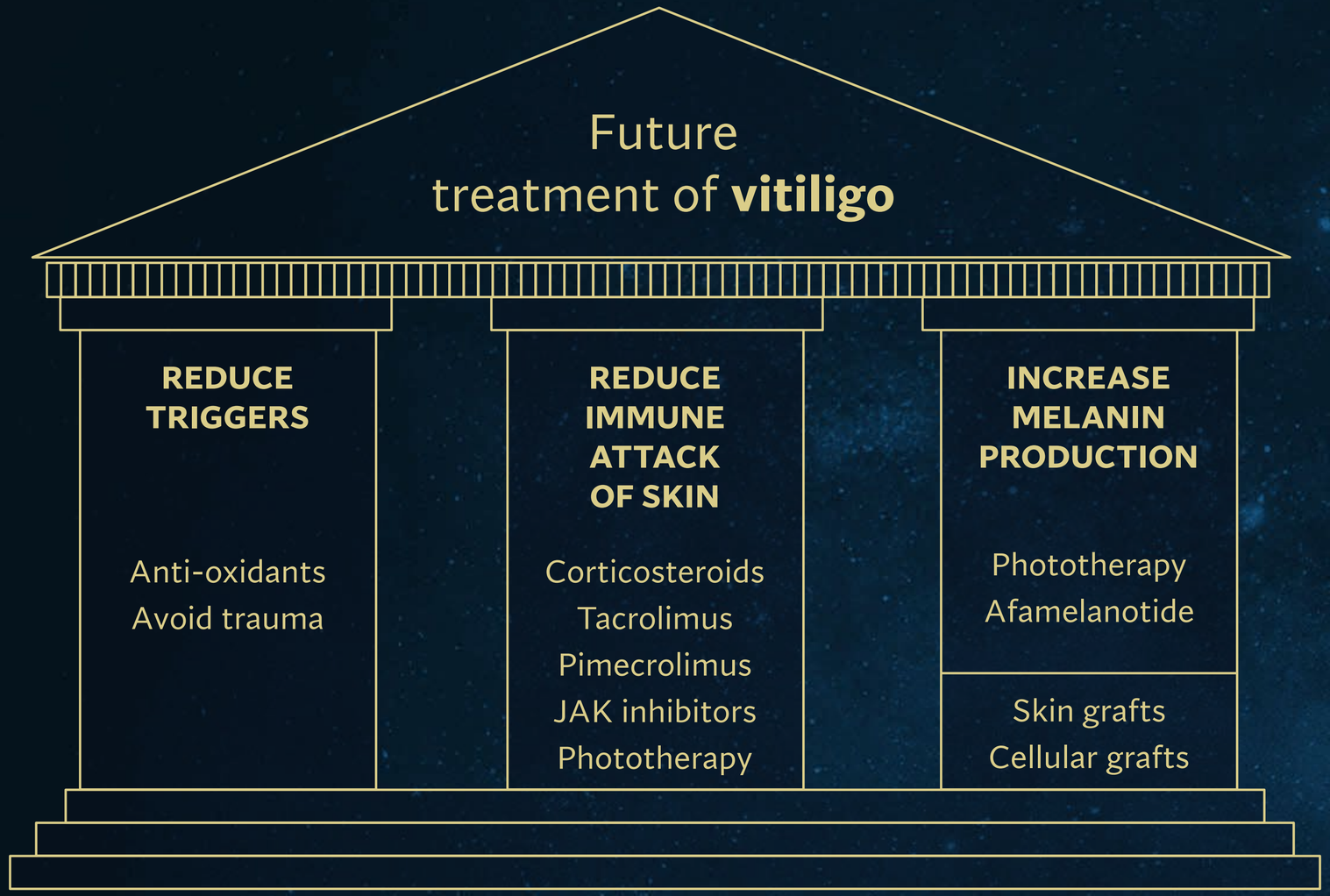


Statistical significance from Day 56 onwards between groups; Mann-Whitney U: $p<0.005$

Images from CUV102 courtesy of the study investigator

Presented at AAD 2023 - Vitiligo Future Treatment

Global Vitiligo Foundation



Afamelanotide

1. non-immune suppressant
2. physiological response
3. activates eumelanin
4. icw NB-UVB differentiates stem cells
5. stabilizes eumelanin
6. < 4 weeks to 1st response
7. systemic = total body

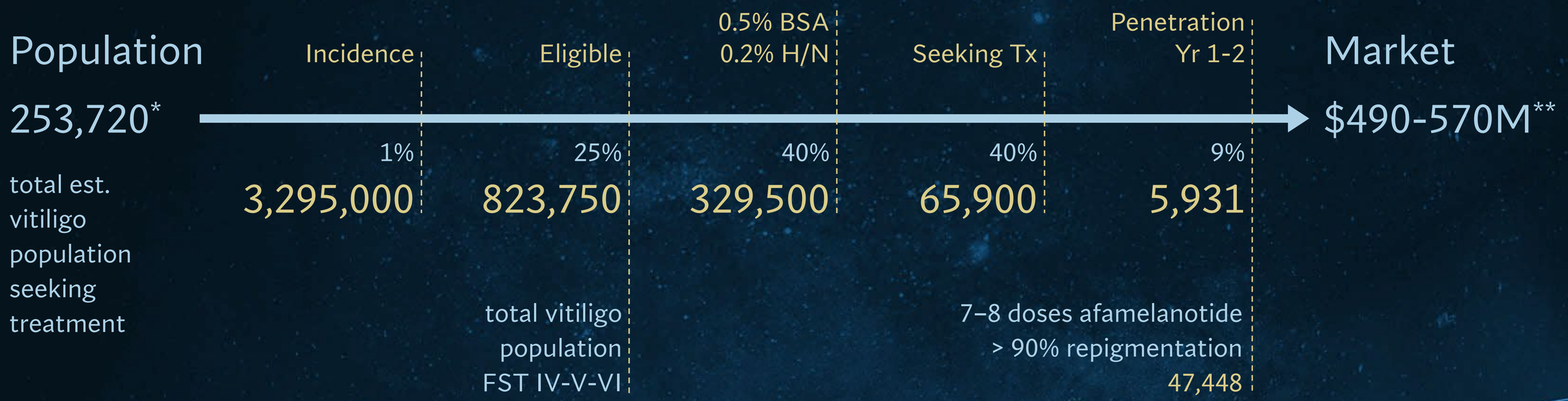
JAK inhibitor(s)

1. immune-suppressant
2. non-physiological
3. not activating eumelanin
4. no effect on stem cells
5. repetitive use
6. long time to response
7. topical = area-specific

Addressable Vitiligo Market

Afamelanotide – North America

Global market 2027
$4.5B**



*Krueger & Schallreuter (2012) Int J Dermatol. **Statcan (2022), Worldbank (2022), ONS (2011), Pew Research Center (2019).; ENAR (2015)

CLINUVEL Strategy part I

Targeted Translational Technology

PHARMACEUTICAL Rx = B2B	DERMATOCOSMETICS = B2C

EPP Rx → POLYCHROMATIC SCREEN 2

Expertise = authority
Data = safety & efficacy

Demand = high unmet need

CLINUVEL Strategy part II

Targeted Translational Technology

PHARMACEUTICAL Rx = B2B	DERMATOCOSMETICS = B2C

XP Phase IIb → DNA REPAIR 3

Expertise = authority
Data = safety & efficacy

Demand = high unmet need

CLINUVEL Strategy part III

Targeted Translational Technology

PHARMACEUTICAL Rx = B2B	DERMATOCOSMETICS = B2C

Vitiligo — Phase II/III → MELANOGENESIS 3

Expertise = authority
Data = safety & efficacy

Demand = high unmet need

CLINUVEL'S STRATEGY IN 3
Targeted Technology Translation - Evidence-based

PHARMACEUTICAL Rx = B2B		DERMATOCOSMETICS = B2C		
	Absolute light intolerance UV–HEV: 320-650nm Systemic photoprotection Rx		POLYCHROMATIC SCREEN	2 — Photoprotection: 390-700nm Reflective & refractive Tinted / non-tinted
	Highest incidence of photodamage Highest frequency of skin cancers Reduce 'UV photoproducts' Lower risk skin cancers Phase IIb		DNA REPAIR	3 — Reduce 'UV photoproducts' Assist DNA-damage repair Increase time of skin repair
	Progressive loss of pigment Highest impact on dark skin Repigment with NB-UVB Fitzpatrick IV/V/VI Phase II/III		MELANOGENESIS	3 — Active pigmentation Stabilize pigmentation Self-tanning to protect

Expertise = authority | Data = safety & efficacy

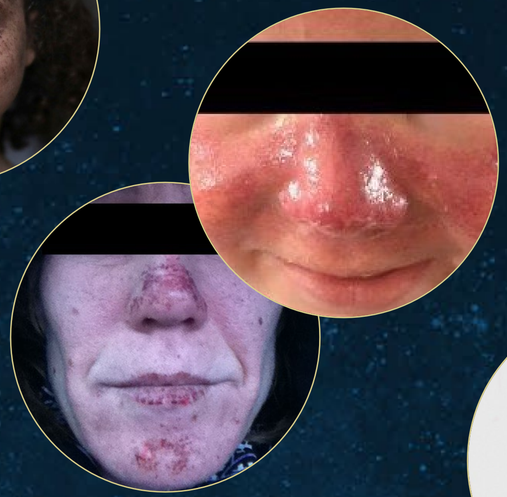
Demand = high unmet need

CLINUVEL's Odyssey 2005 - 2025

Depigmentation

DNA damage

MELANOCORTINS



Phototoxicity

DATA

Photoaging

EXPERTISE

Prevention

EPP images courtesy of the patients and their families

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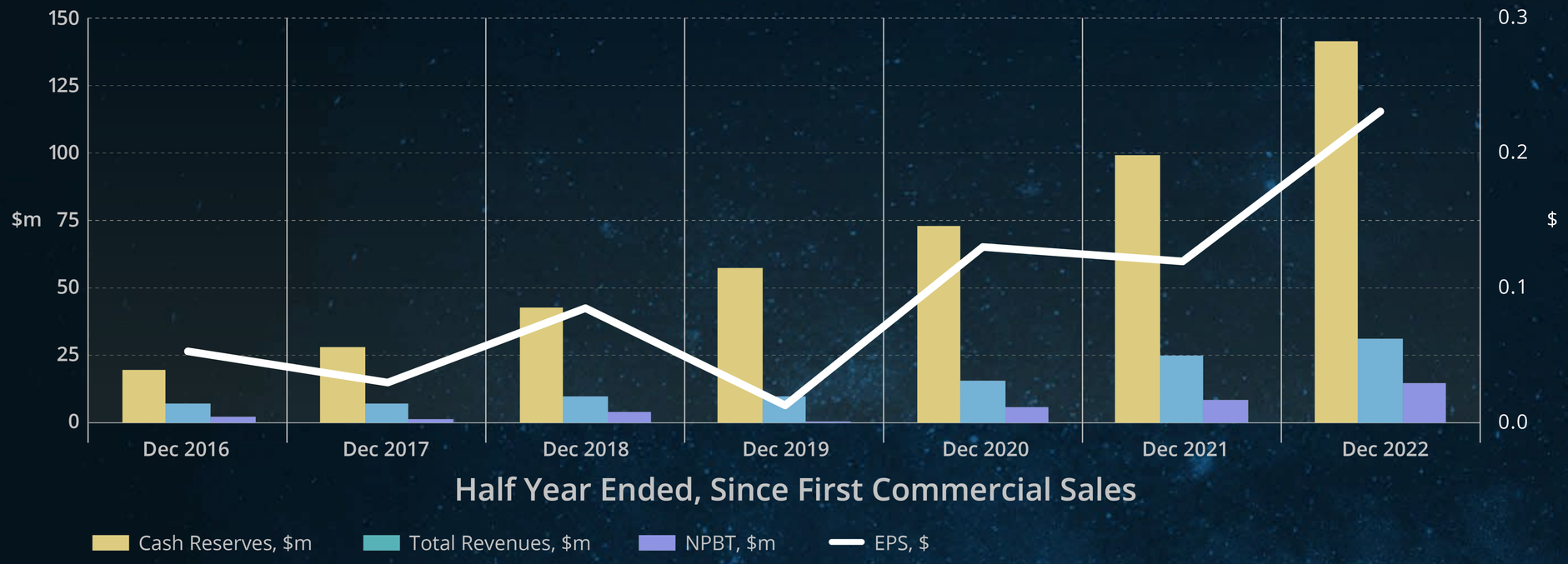
Financial performance 2016 - 2023



Projections ‘21–’25 FYE

	A$175m	US$116m
After 30/60 months 41% of projected expense	A$72m	US$47m
Cash reserves 31-12-’22	A$140m	US$93m

Summary

Pharmaceuticals		
1	Xeroderma pigmentosum – assisted DNA repair	(3 trials ongoing)
2	Vitiligo - afamelanotide monotherapy + combination therapy	(1 trial ongoing, 1 in prep.)
3	Stroke – reduction in penumbra, NIHSS	(1 trial)
	I. SCENESSE®	commercial US-EU-CH-IS
	II. PRÉNUMBRA®	in clinical use
	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	**ongoing**
Start Ph II trial Vitiligo (CUV105)	**in preparation**
PRÉNUMBRA® - Ph II stroke	**started**
I. SCENESSE® expansion adolescents	**awaiting**
II. NEURACTHEL® manufacturing	**ongoing**
HEALTHCARE SOLUTIONS	
Launch CYACÊLLE	**Test phase started**
COMMUNICATIONS	
6 – 8 cycles next 12 months	
13 events in 16 months	**ongoing**
Increased social media CUVA/CUVIPs	**started**
FINANCE	
Growth	**Half year results 31 Dec ’22**

CLINUVEL

Thank you for your interest...

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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