CLINUVEL

From Orphan to Large

CAPITAL MARKETS BRIEFING

Strategic Update VIII | Sydney, 01 May 2024

ASX: CUV | **Börse Frankfurt**: UR9 | **ADR Level 1**: CLVLY

Forward-looking statement

CLINUVEL GROUP

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), CYACÊLLE, 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®, CYACÊLLE, 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 2023 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.

Introduction

Malcolm Bull

From Orphan to Large

09:00	**Introduction**
09:05	**Chairman**
09:10	**Commercial Update**
09:35	**R&D Pipeline**
10:00	*Break*
10:20	**Focus on Vitiligo, Stroke & DNA Repair**
11:10	**Diversification Strategy and Decision-Making**
12:00	**Q&A**
12:45	*Buffet Lunch*
14:00	*Close*

Chairman

Prof Jeffrey Rosenfeld

Longevity

Board
(5)
median tenure 4.4 yrs

Executive Management
(9)
median tenure 14.9 yrs

Management
(10)
median tenure 4.5 yrs

Integrated skill set	
Accountancy, bookkeeping, legal, investor relations	12
Medicine, pharma. sciences, chemistry, engineering	52
Gen mgmt., comms, back office	21
Creative, branding	13
	98

Commercial Update

Lachlan Hay

SCENESSE® (afamelanotide) for EPP

MILESTONES

2006	Ph II CUV010 commences
2007	Ph III CUV017 commences
2009	CUV010 published *NEJM*
2010	Italian 648/96 – first reimbursement
2011	Ph III CUV029 completed
2012	Swiss Special Access (reimbursed) launched
2013	Ph III CUV039 completed
2014	EMA approval
2015	CUV029/039 published *NEJM*
	Long-term observational study *BJD*

R&D '06-'15

2016	EU launch
2017	GKV pricing agreement (DE)
2019	FDA approval
2020	US launch
	TGA approval
	Long-term post-authorisation data *JAMA*
2021	Israeli National Health Basket
2022	First adolescent patients treated
2023	First Canadian patients treated
	First US Medicare-Medicaid-VA treatments

COMMERCIAL '16-'24

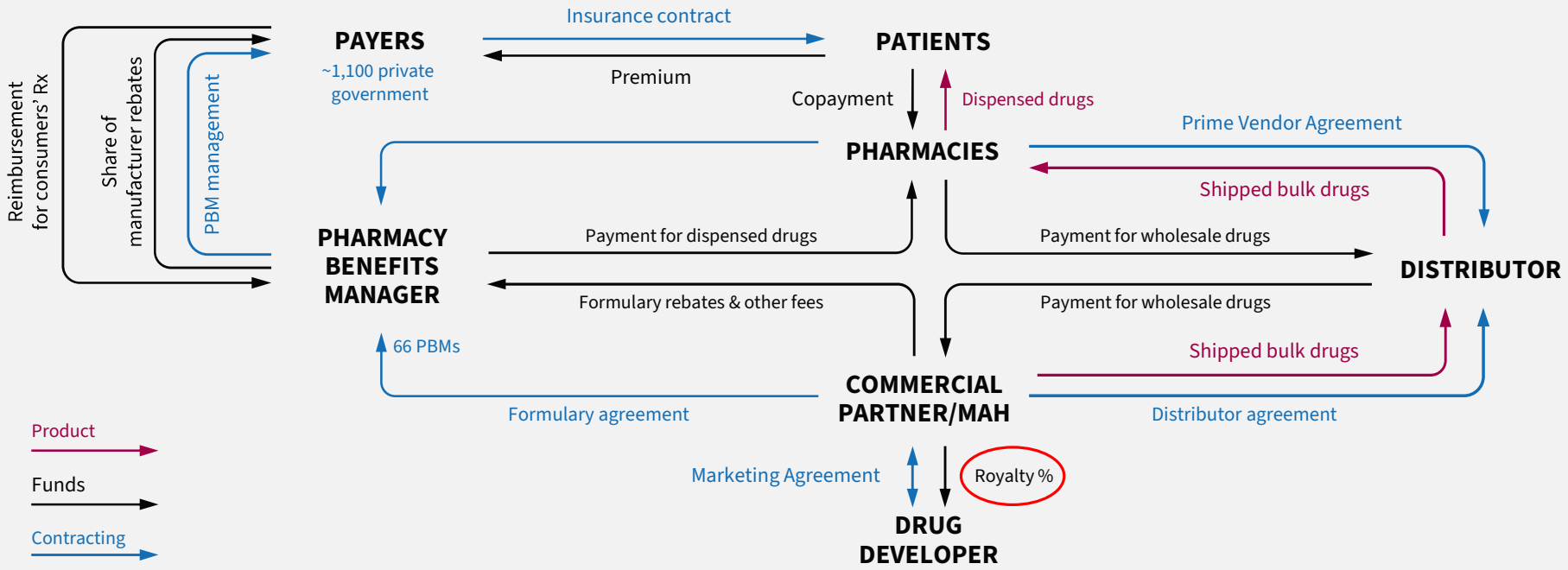
SCENESSE® first-in-class (EMA-FDA)

18 years of clinical experience

- **>30** publications
- **>14,500** doses
- **>300 EPP patients, ≥15 doses**

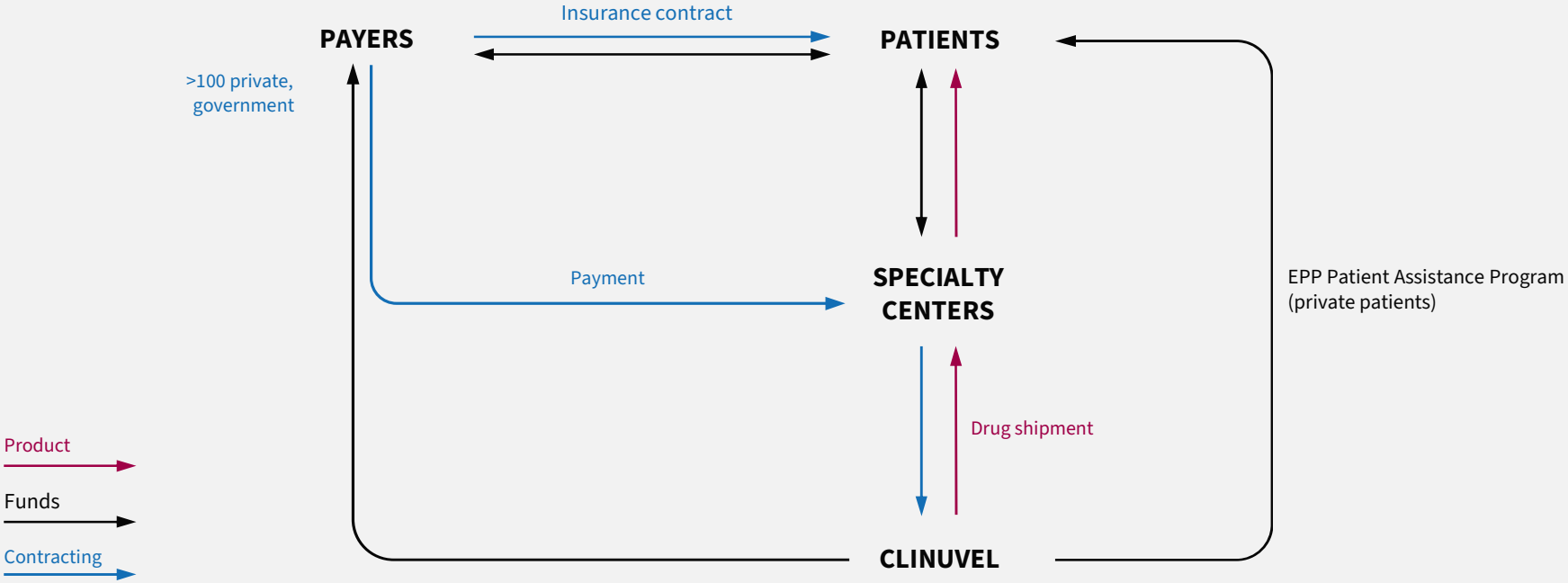
longitudinal use is foundation for expansion

Traditional US commercial model



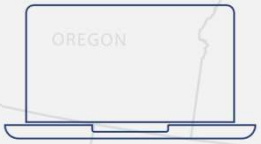
Source: adapted from US Assistant Secretary for Planning and Evaluation (ASPE) / Fein (2016).

CLINUVEL's US commercial model



US Commercial Infrastructure

Direct Distribution 2019–2024



In-house commercial team

Director, Nth American Operations
Financial specialists
VA-Medicare-Medicaid
Patient liaison
Executive support
Finance support
Pharmacovigilance
Quality Assurance / distribution

Logistics

DC – cold storage
labelling / packaging
QA
product release

Shipping

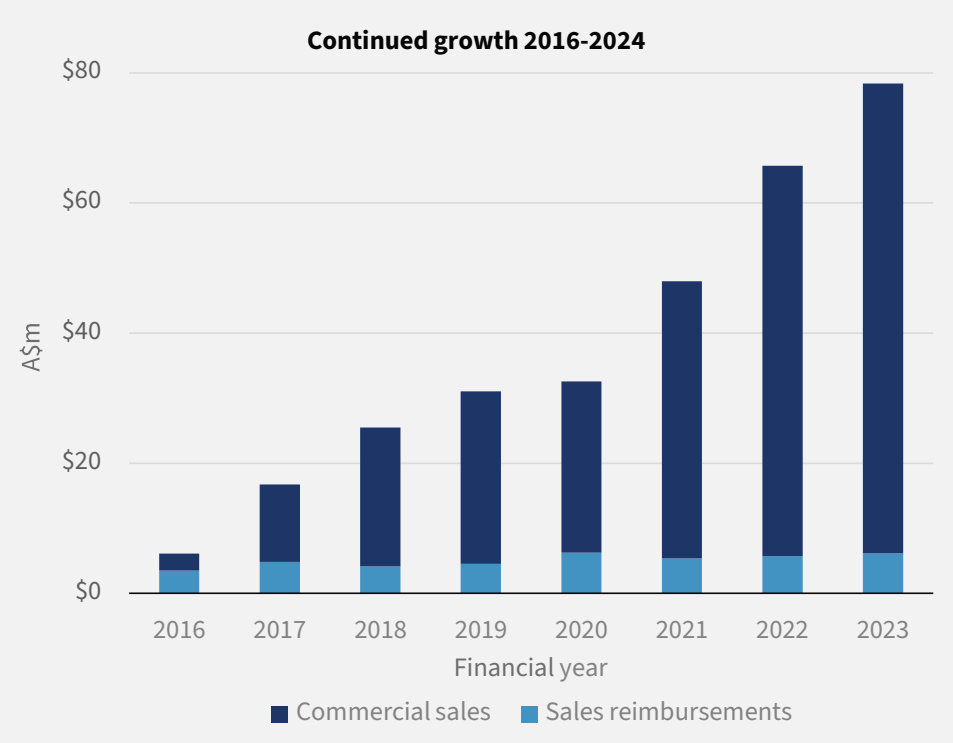
cold transportation
direct supply
US medical centers

Medical centers

orders
pharmacy storage
Rx filled
direct contact

<$5m p/a

SCENESSE® (Rx) for EPP



CLINUVEL self-distributing EU-USA-ISL

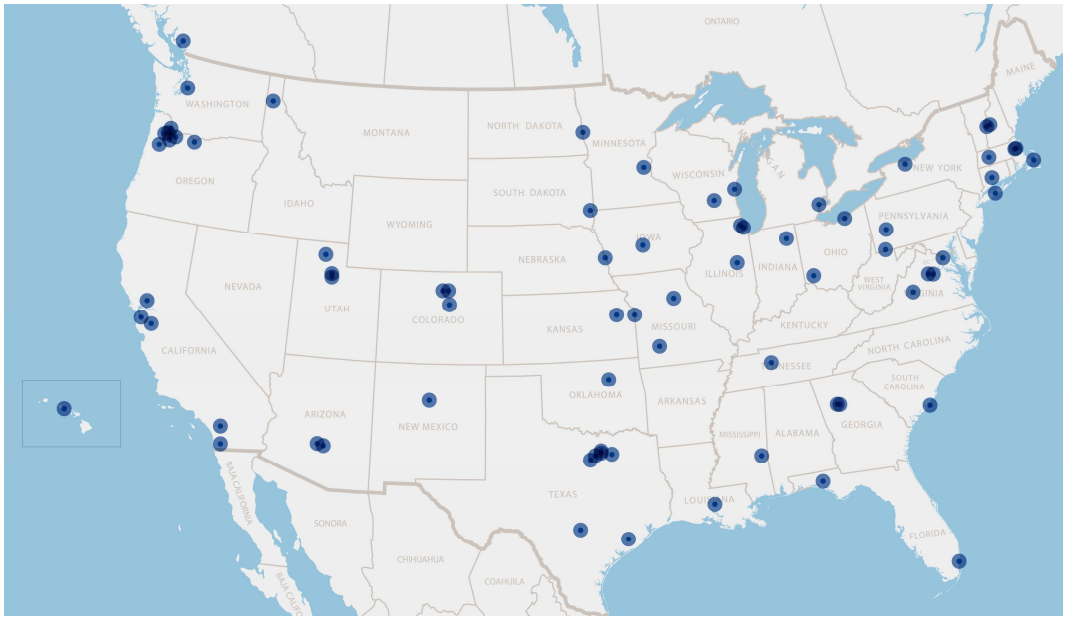
- 7% increase filled prescriptions (CY23 vs CY22)
- 4% volume growth (1H FY24 vs 1H FY23)

Distribution agreement in new region negotiated

Revenues >A$330m since launch (June 2016)

North American distribution 2020-2024

Patient centricity



Objective: 3–4hrs access (cluster distribution)

95% access for patients (pursued PA process)
80 Specialty Centers (trained and accredited)
30 States
100+ private insurers
CMS, VA
CPT® code (11981) & J-Code (J7352) established

- AMA CPT® 12 months
- CMS J-Code 18-24 months

Canada special access
'24/'25 Health Canada filing

Target 120 Specialty Centers

European distribution 2016-2024

CY23 highest number of patients treated
95% treatment continuation (2022-23)*

FY24 5 new European EPP Expert Centres
EMA submission label expansion

Future claims

Hepatoprotective effect published**, research ongoing

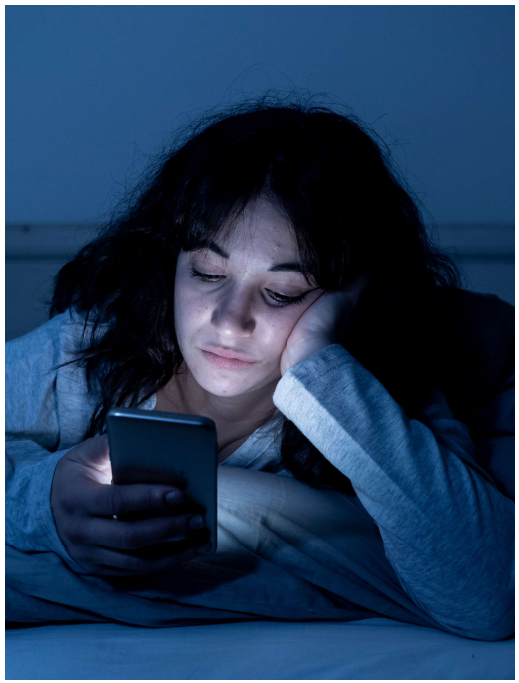
*In our clinical experience afamelanotide treatment is **much more effective** in clinical practice than demonstrated in clinical trials and **should be made available for all EPP patients** meeting inclusion-criteria.*

Wensink et al, 2021 – Rotterdam (NL)

CLINUVEL

* Data from European EPP Disease Registry
** Minder et al (2023) . Afamelanotide Is Associated with Dose-Dependent Protective Effect from Liver Damage Related to Erythropoietic Protoporphyria. *Life.* 13(4):1066.

SCENESSE® for adolescent EPP



EU+US regulatory pathway

7 adolescents (15-17 yrs) off-label treatment

- ≥4 implants
- fully reimbursed

Estimated 60 patients (15-17 yrs) FR-DE-NL-IT

CUV052 pharmacokinetic study underway

- (n=28), 9 patients treated
- first results in 2024

Attempts to date

Experimental therapies	Target, endpoint focus	Status
Beta carotene	Anti-oxidant, no RCT	Use largely discontinued, deployed in absence of therapy access (i.e. paediatric)
Cimetidine, H_2-receptor antagonist	Inhibit ALAS, reduce PPIX	Lack of clinical, academic support for use, lack of evidence of safety-efficacy
Dersimelagon, MC1R agonist	Activate melanin, time to prodrome	Phase III (2 doses) failed to meet primary endpoint, compassionate use discontinued, new Phase III recruiting treatment naïve patients
Bitopertin, GlyT1 inhibitor	Limit glycine, reduce PPIX	Phase II failed to meet time in sunlight endpoint, program “pending regulatory feedback”

PPIX: Protoporphyrin IX
RCT: Randomised Controlled Trial

R&D Pipeline

Dennis Wright

Melanocortin peptides for skin and brain

Afamelanotide (α-MSH analogue)
SCENESSE® & PRÉNUMBRA®

Photoprotective

Anti-oxidative

Assist DNA repair

Anti-oncotic

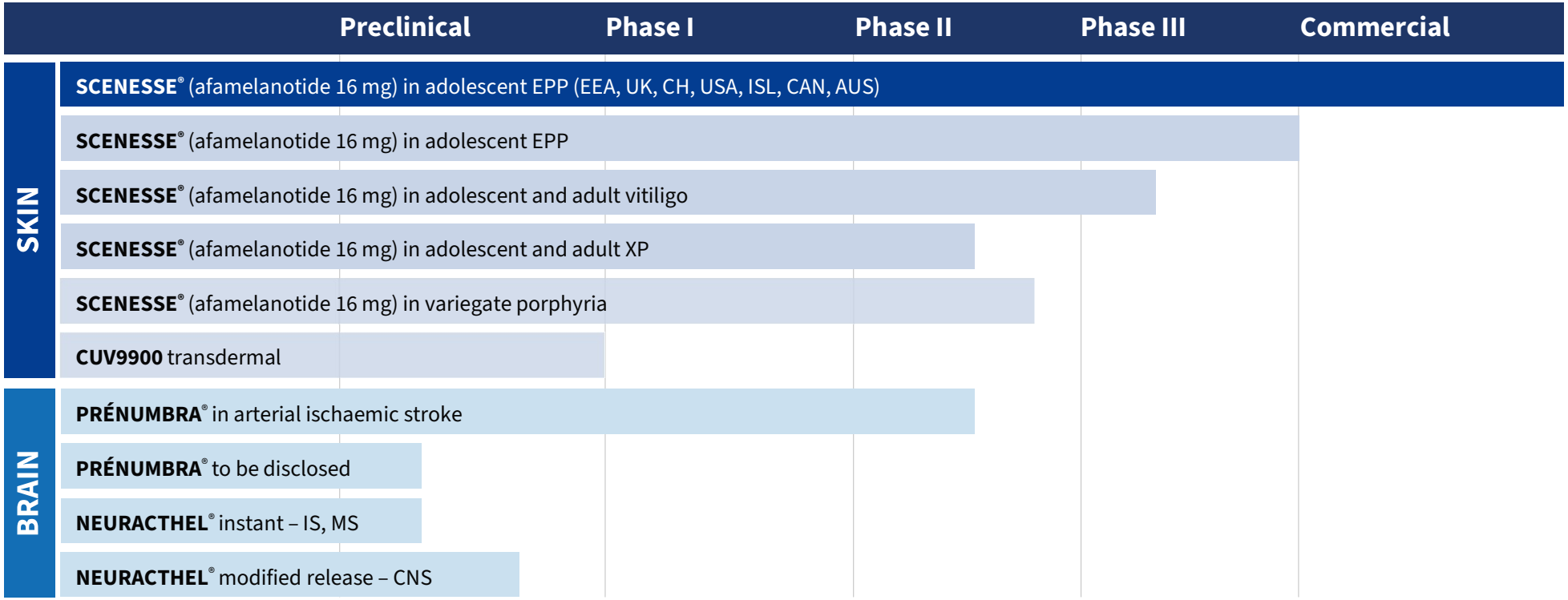
Melanogenesis
(bronzing, repigmentation)

Adrenocorticotropic hormone (ACTH)
NEURACTHEL®

Anti-inflammatory

Immune modulation

Pharmaceutical Pipeline



NEURACTHEL®

Unmet needs with adrenocorticotropic hormone (ACTH)

Manufacturing agreements (2, exclusive)

Analytical methods advanced

DMF in development

Generic (Instant), Branded (Modified-release) in development

sNDA submission 2026

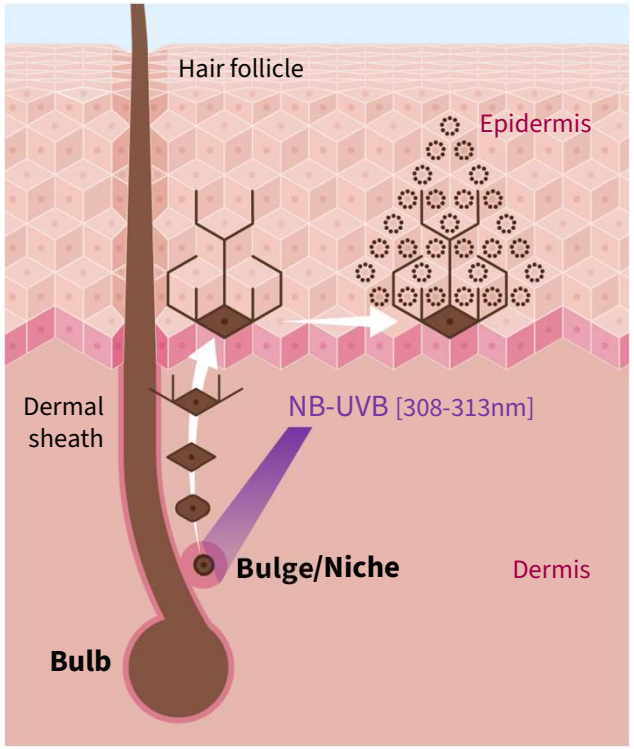
Clinical program planned for

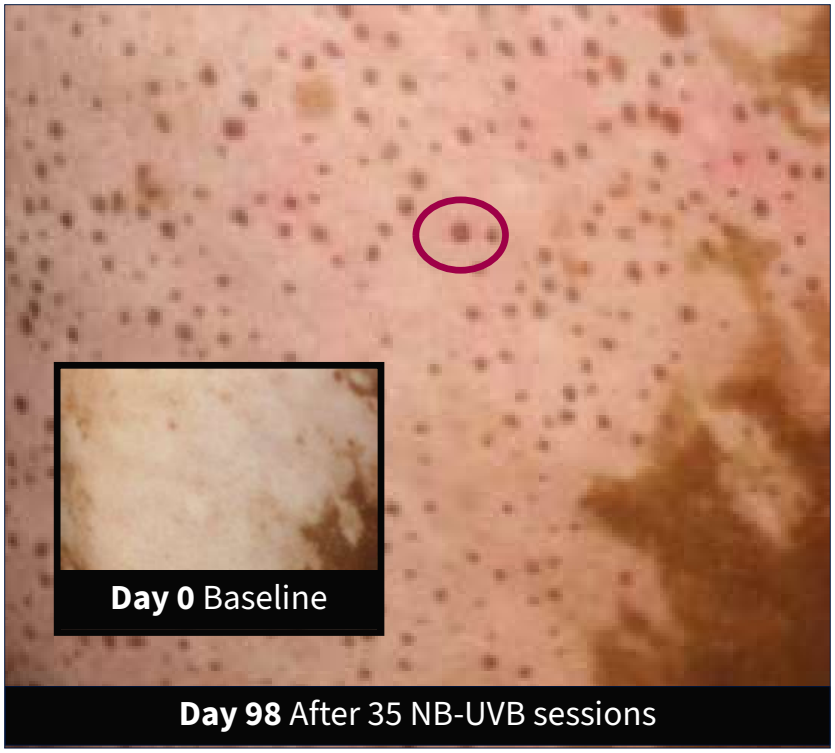
1. West Syndrome
2. Relapsing MS

Vitiligo

Dennis Wright

NB-UVB – follicular repigmentation





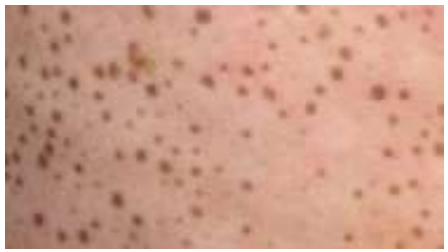
NB-UVB differentiating follicular stem cells

Melanoblasts migrating, become fully functioning melanocytes

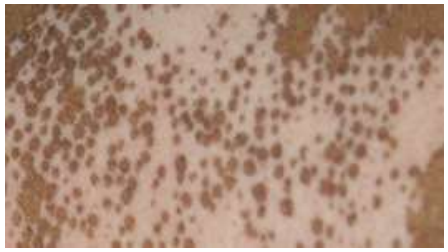
Afamelanotide acting as agonist to MC1R expressed

Vitiligo

Path to market



NB-UVB treatment



NB-UVB treatment + afamelanotide

CUV102 +NB-UVB n = 56

↓

CUV103 +NB-UVB n = 21

↓

CUV104 monotherapy n = 6

↓

CUV105 +NB-UVB n = 200 **2024**

CUV107 +NB-UVB n = 200 **2024**

FDA submission[1] 2026

Step 1	>15,600 doses afamelanotide administered • Safety profile accepted
Step 2	NB-UVB combination • program planning resulted in savings $75 – 145M
Step 3	**2022** FDA – precedent for NB-UVB as combination therapy
Step 4	**2022** Insurers providing reimbursement codes
Step 5	Project finance - clinical trials A$77m
Step 6	**2023** Vitiligo Expert Panel
Step 7	**Train & accredit 120 US centres pre-marketing**

Total addressable market USA: US$4.5bn

9% penetration of patients likely to seek treatment, years 1-2: US$490-570m

[1] Regulatory timelines are dictating timings and progress of filings | [2] All indications | Clinical images courtesy of CUV102 investigatorsz

Vitiligo

Global Phase III study (CUV105)

	CLINUVEL CUV105 Phase III	Pfizer pivotal Phase III oral JAK inhibitor*
Study population	N=200, adults and adolescents (≥12 years) highest unmet need: darker skin (Fitzpatrick IV-VI)	
Inclusion	≥0.3% body surface area with facial vitiligo: T-VASI ≥0.3 & F-VASI ≥0.3	
Primary endpoint	repigmentation of total body surface (T-VASI50)	proportion of participants achieving F-VASI75
Secondary endpoint/s	evaluate repigmentation of the face, maintenance of repigmentation	proportion of participants achieving T-VASI50
Randomisation	1:1 to SCENESSE® + NB-UVB vs NB-UVB monotherapy	
Treatment duration	20-week treatment phase, six-month follow up	
Sites	expert treatment centres globally	
Status	12-month recruitment (to October 2024)	

"Once on the market, SCENESSE® will clinically become the pigment booster for every dermatologist in North America"

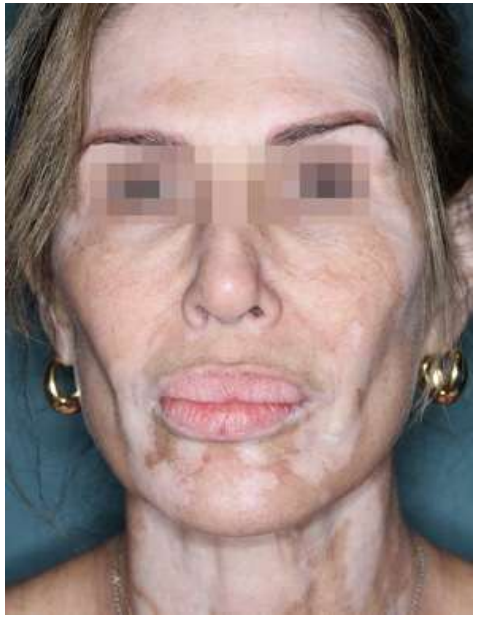
Vitiligo Expert Panel member

CLINUVEL

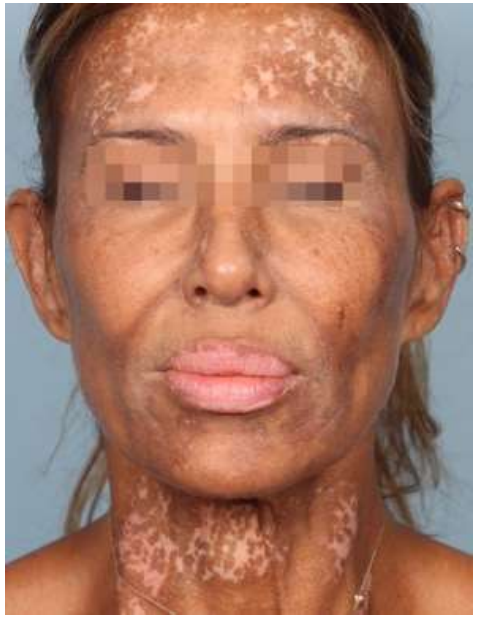
* Source: ClinicalTrials.gov

SCENESSE® (afamelanotide) for vitiligo

Case study presented to 2024 American Academy of Dermatology (FST IV)



Day 0
baseline



Day 134
7 implants, 39 NB-UVB sessions

CLINUVEL

Images have been amended/cropped and pixelated to protect the patient's privacy but are otherwise unaltered.
Images courtesy of the investigator.

SCENESSE® (afamelanotide) for vitiligo

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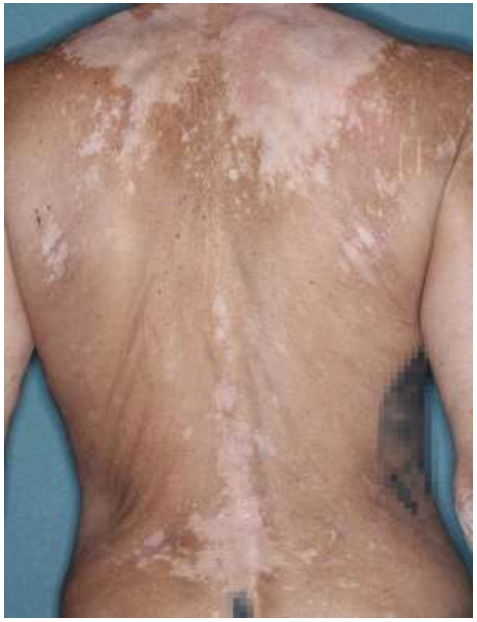

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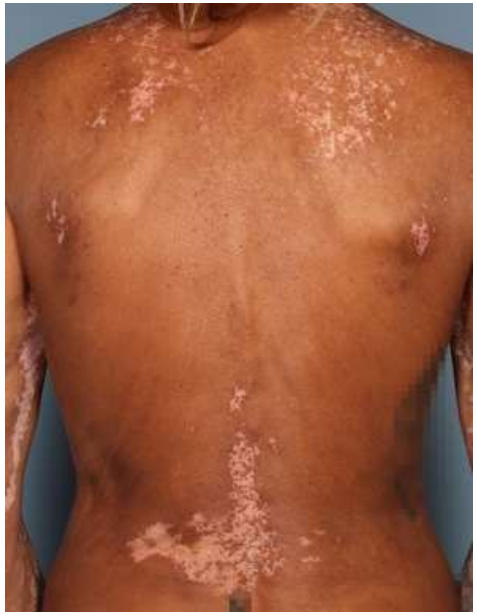
baseline



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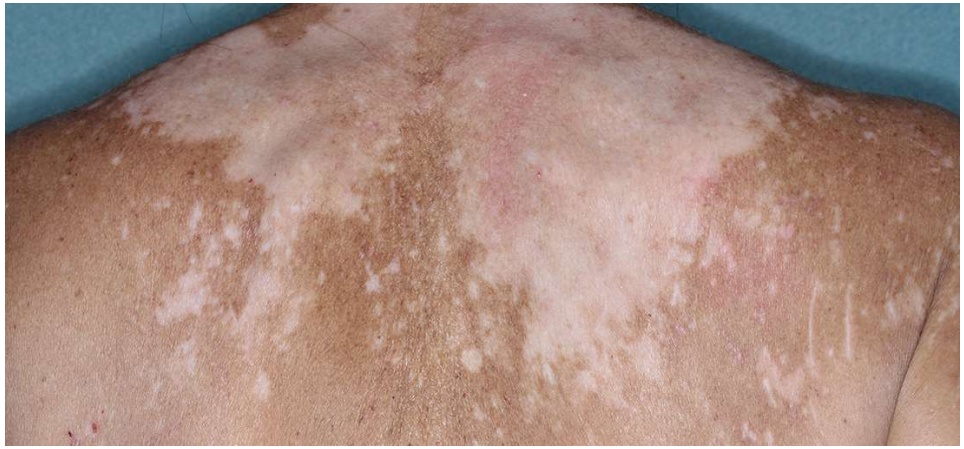

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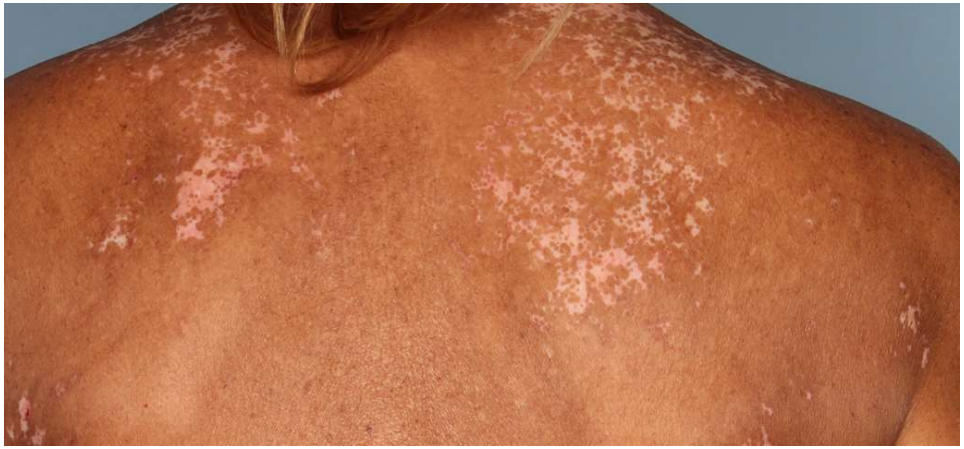

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Images courtesy of the investigator.

CNS

Philippe Wolgen

Arterial Ischaemic Stroke

Targeted product position

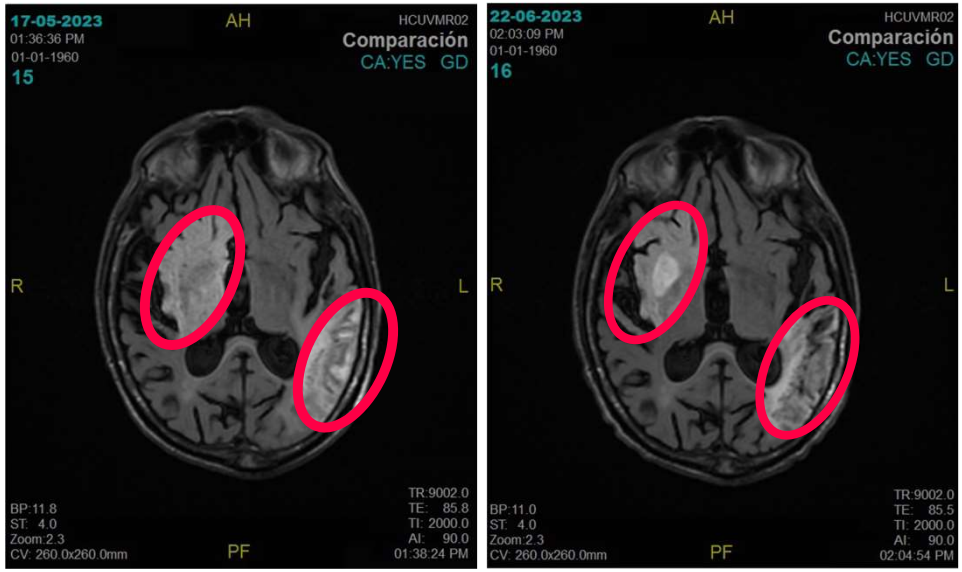
A hormonal treatment to assist hypoxic brain

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: > M1
- functional recovery in 5 patients; NIHSS ≥ 4 (4/6)
- cerebral perfusion improved per MRI-FLAIR (CBF, Tmax)

Study CUV803 (n = 12) 9 patients on treatment

- moderate & severe patients
- occlusion higher regions: > M2/A2/P2
- higher, more frequent dosing, PRÉNUMBRA®
- safety
- neurological functionality (NIHSS)
- perfusion of penumbra, oligemic zone



Total addressable market: US$31B

Penetration US$1.98-2.23B

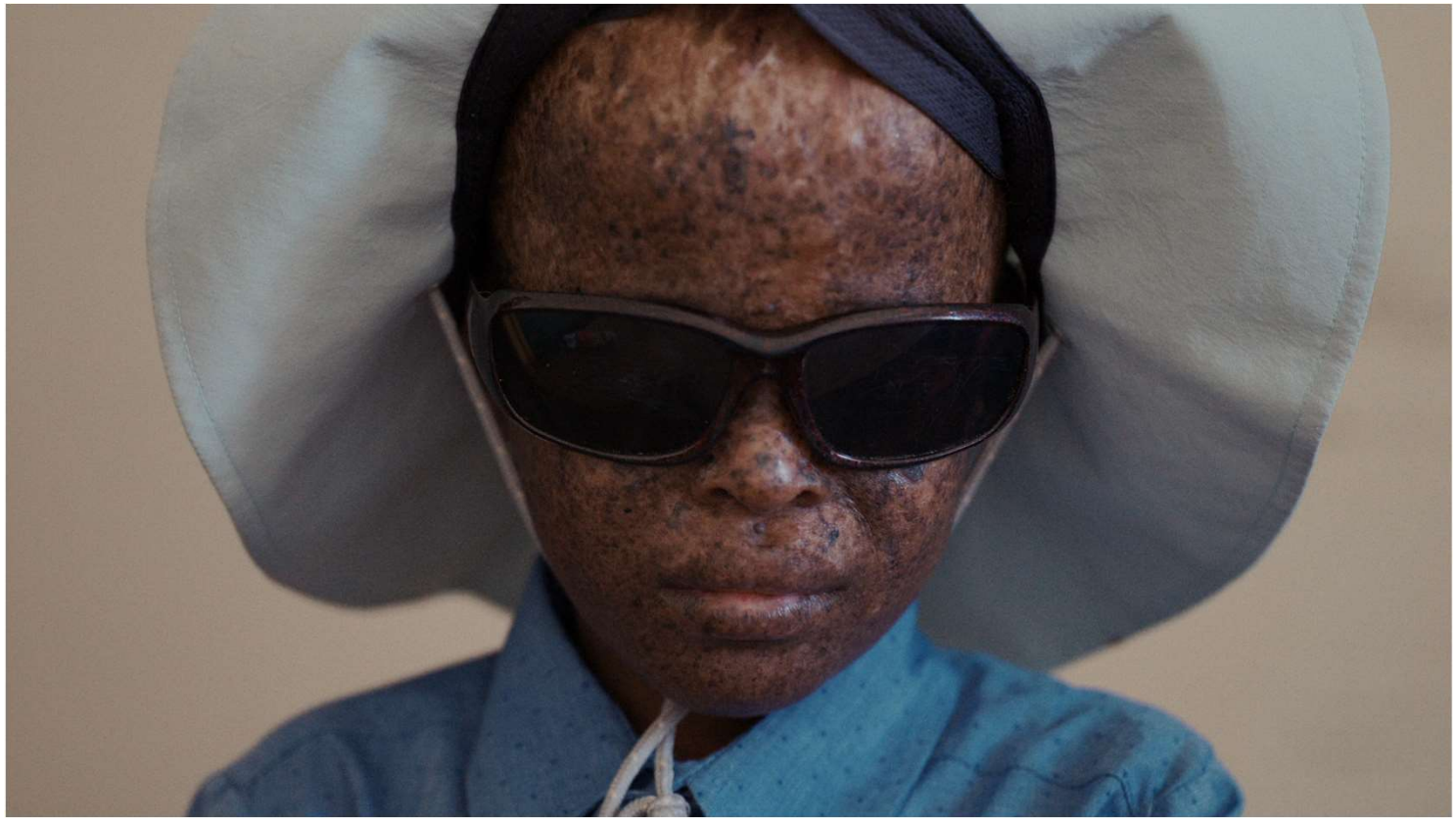
- USA + EU + AU

NIHSS: National Institutes of Health Stroke Scale | CBF: cerebral blood flow

DNA Repair

Philippe Wolgen

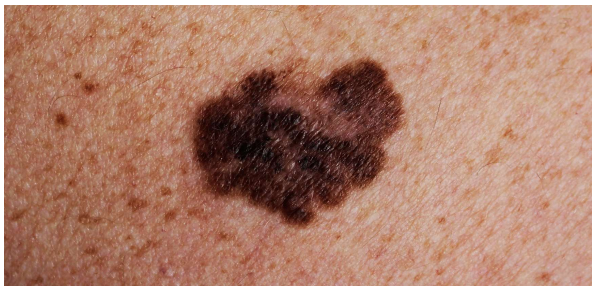
The Photomedicine Foundation



Evaluating XP – DNA Repair – objectives

Reducing DNA damage

Decreasing photodamage



Reducing the risk of skin cancer

29 April 2024

Afamelanotide granted ODD in Europe

- first clinical data on efficacy
- lack of therapy,
- high unmet need,
- medical plausibility of treatment

→

- potential to “extend” label
- reduction in fees
- 10 years market exclusivity

Evaluating XP – DNA Repair – clinical endpoints

		CUV156	CUV151
DNA repair markers	• 'photoproducts' (CPDs) • γ-H2AX • P53 • Ki67	- reduction - increase - variable, increase	- reduction at 15 mins (p=0.0039) - reduction at 24 hours (p=0.0078) - no change - no change
Quality of life	validated questionnaires	pending	
Safety	treatment-emergent adverse events clinical & laboratory evaluations	safety profile maintained	no SADRs
Erythema response **Severity** **Melanin density**	minimal Erythemal Dose (MED) patient & physician assessments spectrophotometry	- variable - pending - increase	- reduction (p=0.018) - increase (p<0.05)

Total addressable market: <US$100m

Europe | USA | Africa | Middle East | S&C America

~1,300 XP patients worldwide

Decision Model & Diversification Strategy

Philippe Wolgen

CUV Construct

2005 – 2024

1. focus resources	<A$140M equity
2. platform technology	“MC peptides”
3. specialists inhouse	train & retain
4. profits accruing	A$175M

MELANOCORTIN HOUSE

2016–2023 CAGR 30%

Porphyria	XP	Stroke
Vitiligo	ACTH	PhotoCosmetics

M&A

CUV Differentiated Decision Model

NEUROPEPTIDES

→ no alternative or significant improvement | life threatening or severe | academic/clinical belief | reimbursable

TECHNOLOGY → **PROOF OF PRINCIPLE** —$$→ **Ph III** → **COMMERCIALISATION**

↓

1. SEVERE/LIFE-THREATENING – Brain

2. EXTREME CONDITIONS – Skin

			TRANSLATION	**PHOTOCOSMETICS**
I	EPP	– absolute intolerance to UV + HEV λ	→	CYACÊLLE (UV–HEV)
II	XP-DNA repair	– photodamage from UV	→	DNA assisted repair, DECREASE photodamage
III	Vitiligo	– loss of pigmentation	→	Risk-free-sunless bronzing

Pharmaceuticals – Core | **Cosmetics** – Complementary

Risk Management

Global Biopharmaceutical Market US$1.7 trillion*

New compounds 1:5,000–10,000 | 9,000 products in clinical development | 21,000 compounds** (406,000 centres)

13.8% success rate: Meeting objectives (endpoints)

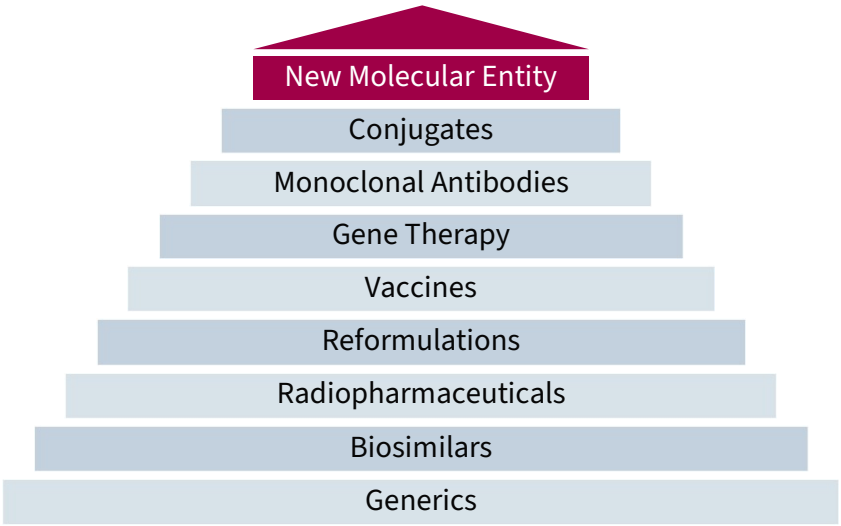
Objectives

1. **reduce risk**
2. **curtail costs**

Approach

1. **proof of concept (POC):** small Ph II trials, more datapoints
2. **early financial POC**
3. **integrate skills, focus**

Risk & Complexity



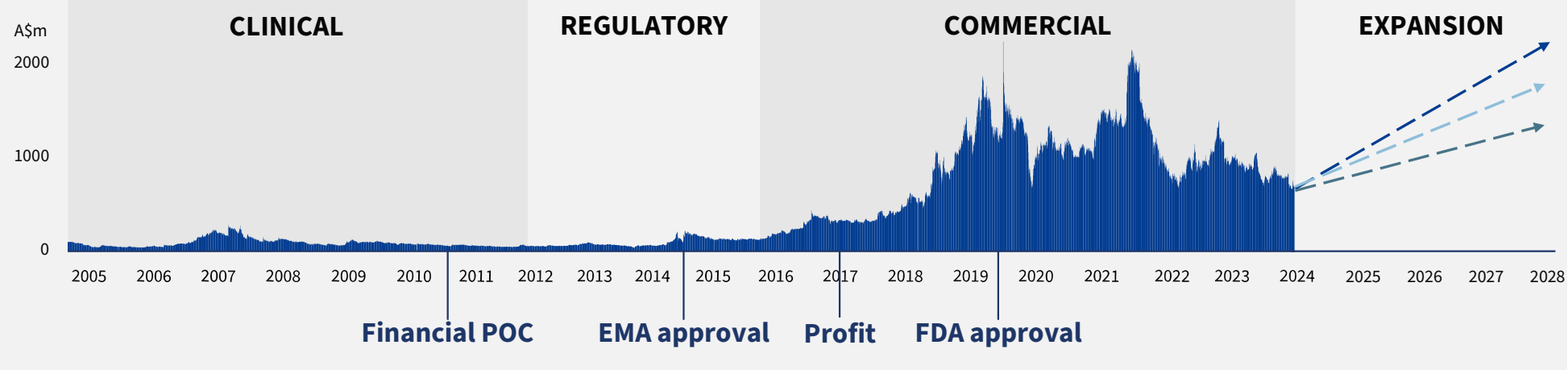
Cost Comparison

Production stage	US$
med, cost P/P***	42K
med R&D P/drug P/OD	1B 700M
CUV (EPP)	**~105M**
POC, Ph II–III vitiligo#	**~140M**

CLINUVEL

*… **J Bioslat iq Wong, Siah ***IQVIA Institute for Human Data Science, BMS #PhIII $75–90m

Longitudinal Valuation CUV

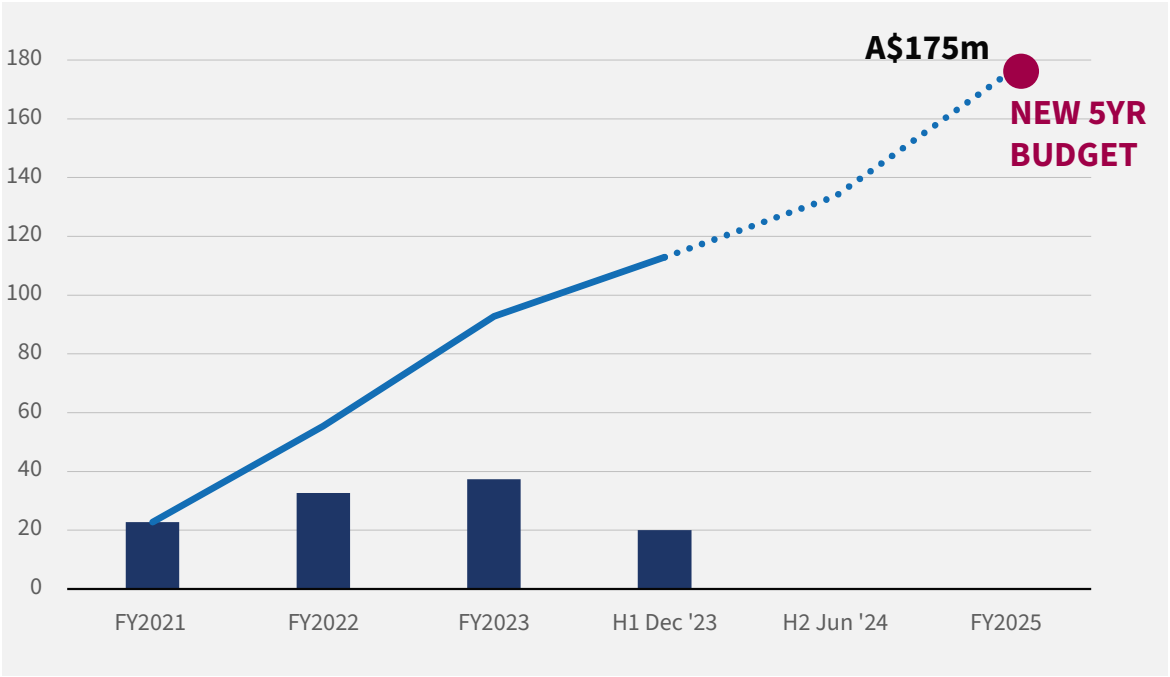


FINANCIAL STRENGTH

1. Phase III vitiligo – commercial
2. DNA repair
3. Neurodegenerative Disease
4. PhotoCosmetics
5. Manufacturing

Controlled Expenses

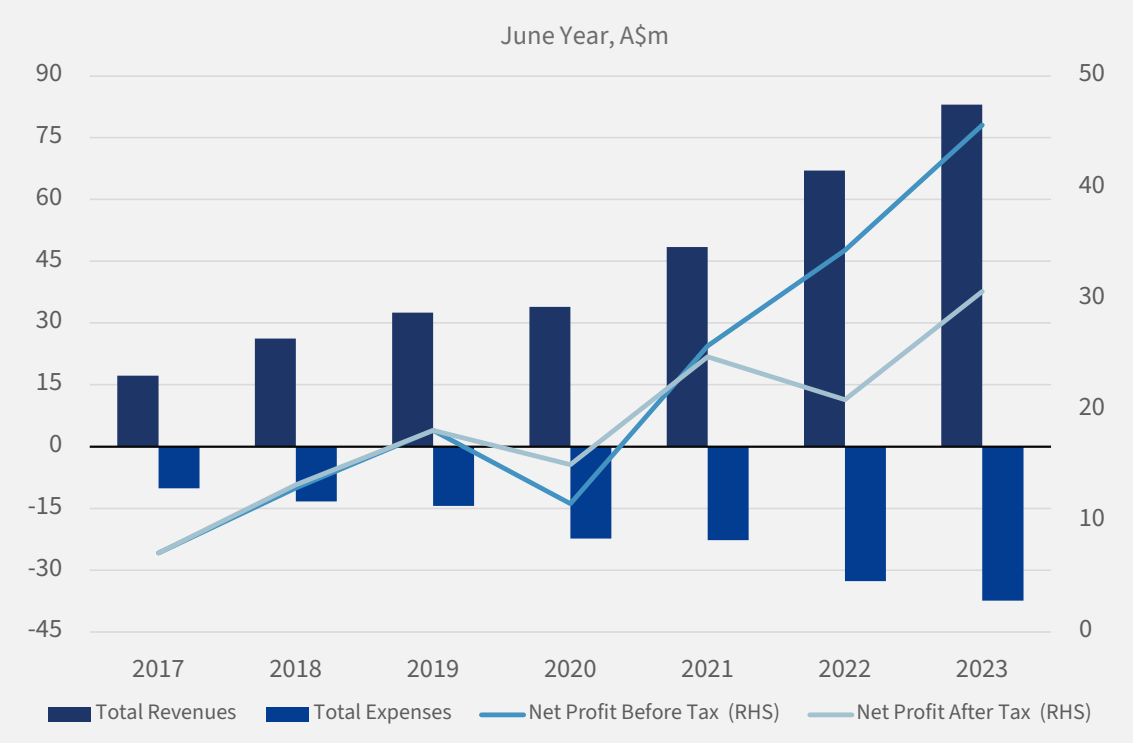
Tracking 5-year expense projections 2021–2025



- **A$175 million expenses** (5-yrs to Jun ’25)
- cumulative expenses on track (65% of plan: 18 months remaining)
- expenses rose 28% - half year ‘23 cf. ‘22)
- excludes capital expenditures and marketing for PhotoCosmetics

1. **possible label extensions**
2. **manufactured, DMF for ACTH**
3. **translation into PhotoCosmetics**
4. **integrated house complete**

Earnings Growth



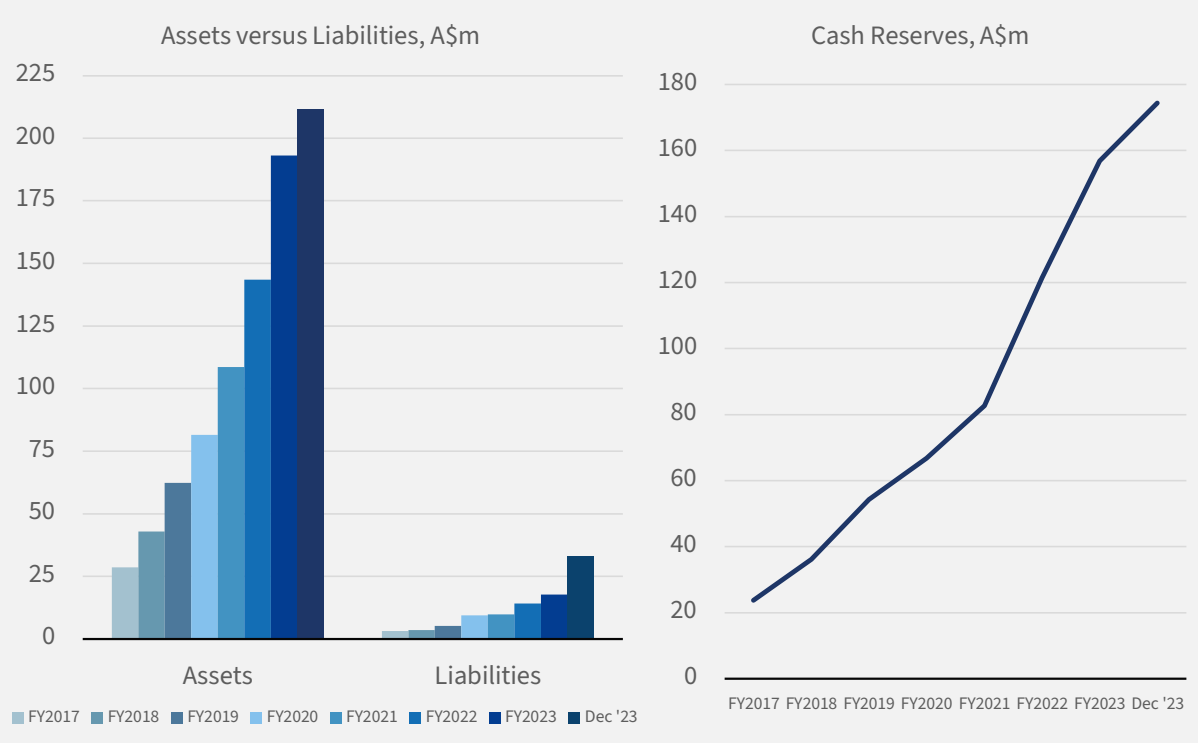
30 June 2023

- 7 yrs annual growth - revenues, profits, net cashflow
- 6 yrs annual dividends (< 5% of NPAT)
- cash reserves financing expansion
- earnings per share A$0.62
- return on equity 19%

Half Year to December 2023

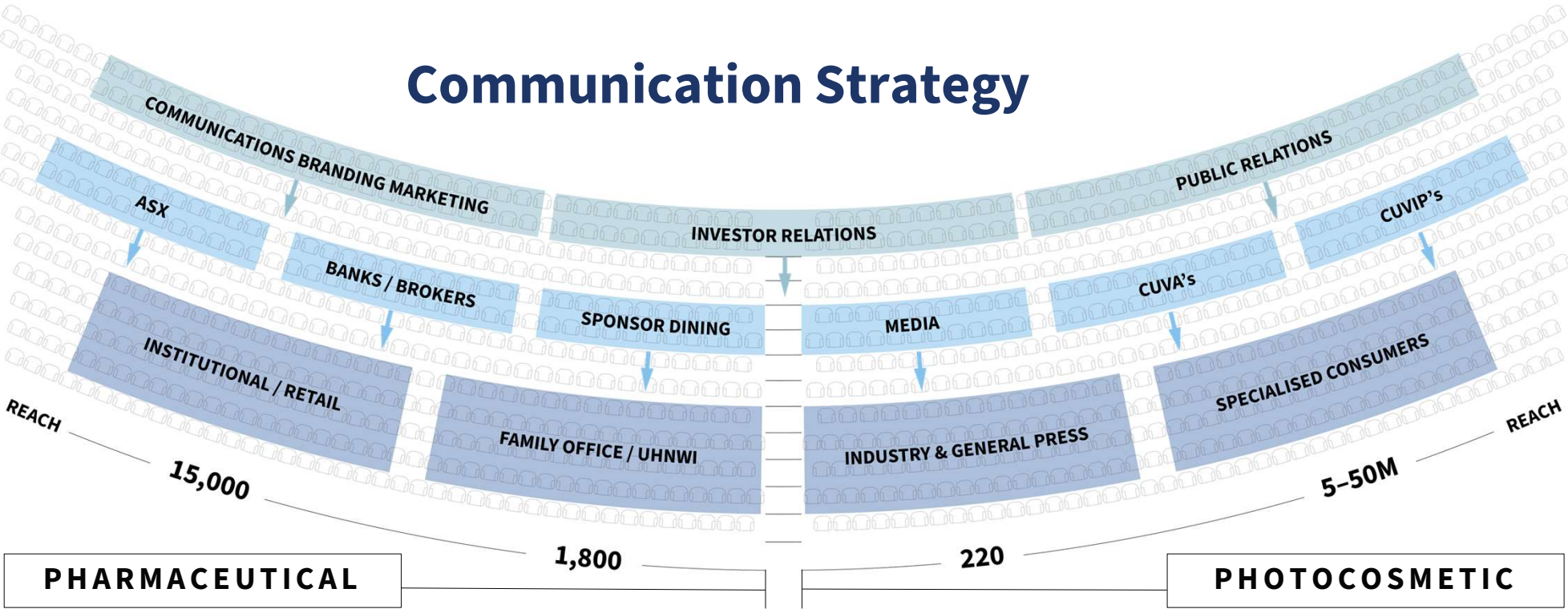
- revenues up 10% (cf. half yr Dec '22)
- expenses up 28% supporting growth
- NPBT up 1% to A$14.8 M
- NPAT down 4% to A$10.9 M
  [due to increased tax expenses]
- earnings per share A$0.22

Strong Balance Sheet



AS OF	30 Jun ’23	31 Dec ‘23
Total Assets	**$193.7m**	**$211.7m**
Total Liabilities	**$29.1m**	**$33.0m**
• no debt		
Net Assets	**$164.6m**	**$178.7m**
Cash Reserves	**$156.8m**	**$174.5m**
• cyclical buffer		
• financing organic growth		
• **share buy-back** (12 months 28/03/25)		**$20m**
• acquisition (opportunistic)		

Communication Strategy



TARGETS OVER 3 YEARS	
Impressions	~110M
Followers	~1M
Institutional / Retail	~30%
Family Office / UHNWI	~25%

Conversion Per Campaign	0.9%
Active Database	~5M

A BRAND

CLINUVEL

Establishing a Brand

PHARMACEUTICAL

CORE TECHNOLOGY — melanocortins

INNOVATION — chemistry formulations

DATA — safety efficacy

Medical Community

Analysts

ASX

News Communiqués / Bulletins

Patient experience

Malibu Event

3.4m Instagram

8,300 CUV Instagram

1,000% traffic increase

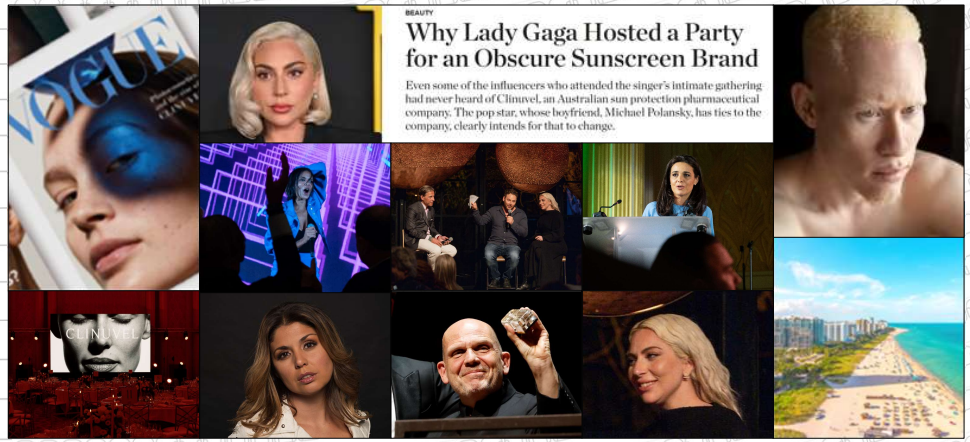
Target 5m CUV database

PHOTOCOSMETIC

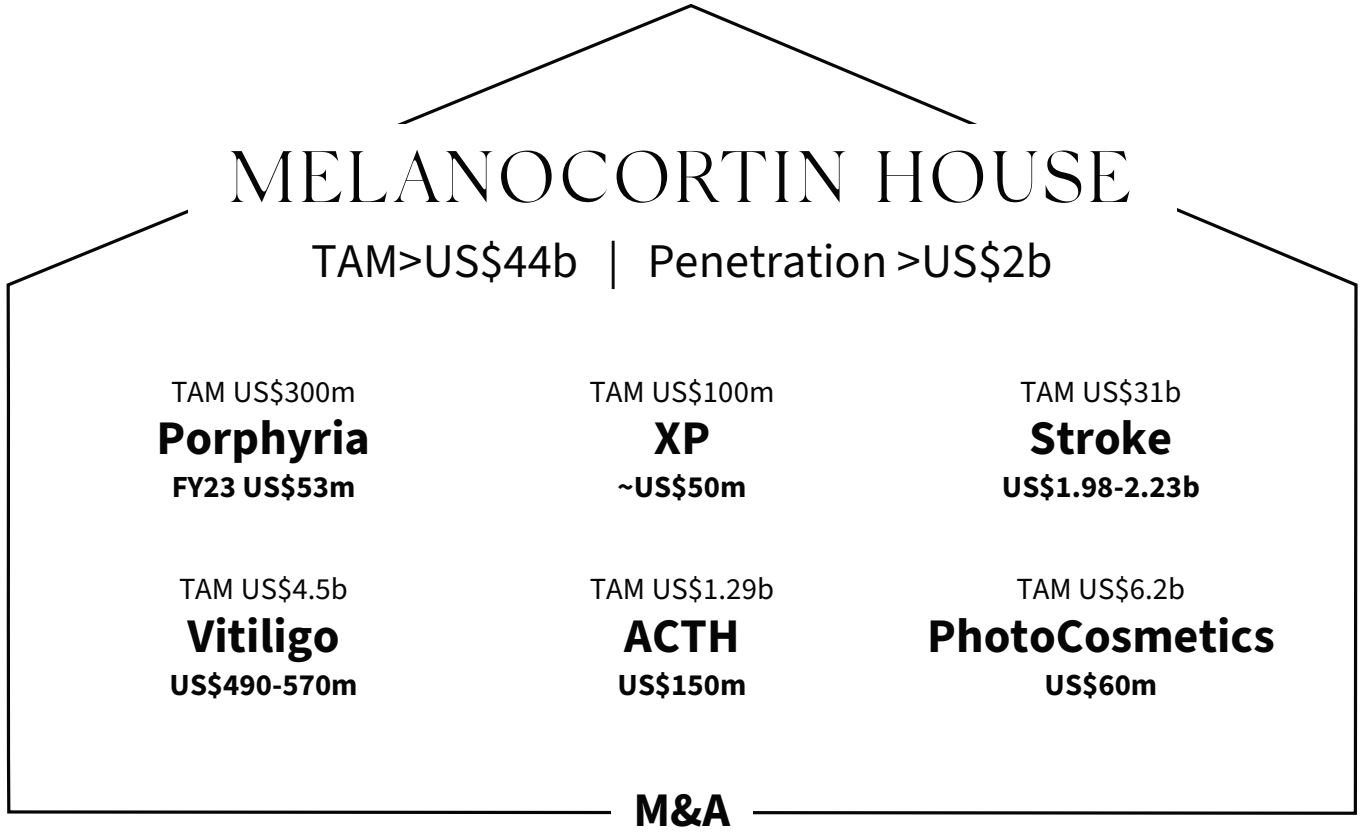
PHOTOPROTECTION

DNA ASSISTED REPAIR

SELF-BRONZING



The Future


MELANOCORTIN HOUSE
TAM>US$44b | Penetration >US$2b
TAM US$300m
Porphyria
FY23 US$53m
TAM US$100m
XP
~US$50m
TAM US$31b
Stroke
US$1.98-2.23b
TAM US$4.5b
Vitiligo
US$490-570m
TAM US$1.29b
ACTH
US$150m
TAM US$6.2b
PhotoCosmetics
US$60m
M&A

Objectives CY 2024

1	SCENESSE® adolescent outcome EMA
2	SCENESSE® Canada Health submission
3	Vitiligo CUV105 completion recruitment
4	Vitiligo CUV107 start recruitment
5	XP-DNA Repair CUV151 read out complete (selected markers)
6	CUV156 read out complete (selected markers)
7	CUV154 start
8 ✓	Paediatric PK study CUV052 start – March 2024

9 ✓	VP CUV040 complete results – March 2024
10	CNS CUV803 completed with final results
11	CNS and/or New Indication
12	NEURACTHEL® manufacturing progress
13 ✓	Website launch
14	PhotoCosmetics E-shop launched
15	CYACÊLLE global launch
16 ✓	Financial growth earnings: half year (Feb 2024), final year end

Q&A

with the audience

CLINUVEL Chair and Executives

CLINUVEL

Thank you for your attendance

Authorised for ASX release by the Board of Directors of CLINUVEL PHARMACEUTICALS LTD
Head of Investor Relations: Mr Malcolm Bull, CLINUVEL PHARMACEUTICALS LTD
Investor Enquiries: https://www.clinuvel.com/investors/contact-us
Level 22, 535 Bourke Street, Melbourne – Victoria, Australia, 3000 | T +61 3 9660 4900 | F +61 3 9660 4909
www.clinuvel.com

ASX: CUV | **Börse Frankfurt**: UR9 | **ADR Level 1**: CLVLY