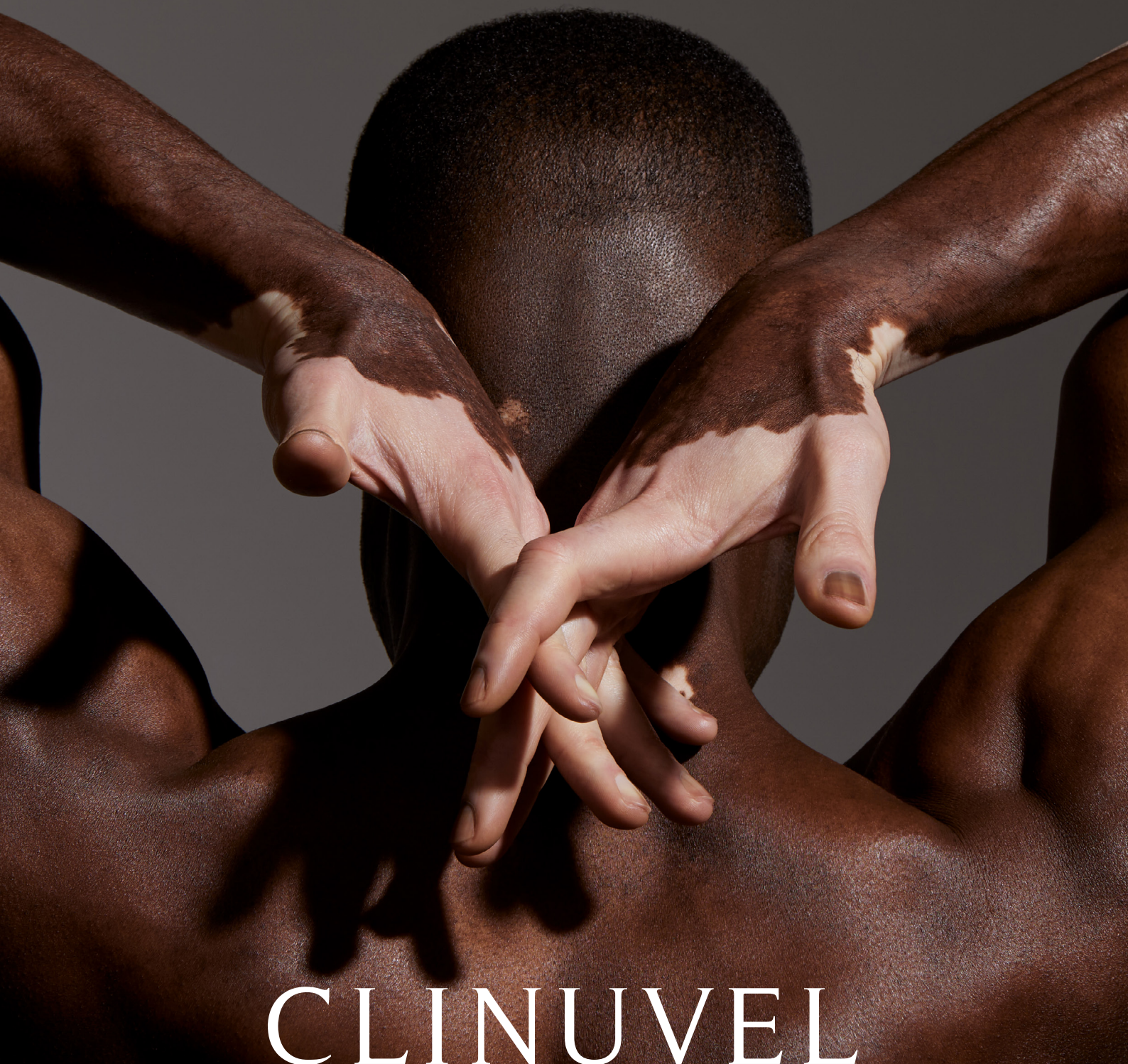
SCENESSE®
IN VITILIGO

A GLOBAL UPDATE

Melbourne, Australia, 04 June 2025



CLINUVEL

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FOREWORD
COMMERCIALISING THE FIRST SYSTEMIC REPIGMENTATION TREATMENT

EXECUTIVE SUMMARY

- SCENESSE® – first systemic treatment to restore pigmentation in vitiligo
- Phase III CUV105 study recruitment complete (n=210)
- active regulatory discussions on CUV107 protocol and pathways to market
- supply chain reinforced for expansion
- scaling up North American infrastructure
- >100 potential new Specialty Centers engaged at AAD 2025

Dear Shareholders, friends, patients,

One of the many gains from the American Academy of Dermatology Meeting (6–11 March) has been the response from the medical community regarding the current and future use of SCENESSE® (afamelanotide). I don't overestimate if I state that the role of the emerging treatment in vitiligo is now acknowledged by experts, and the question is now posed in medical conferences by dermatologists as to which place and position the drug will obtain in dermatology offices in the future. So it is no longer if, but when and how?

Why am I so pertinent in my views? Well, most competitors developing drugs for vitiligo are aiming to silence the immune system. CLINUVEL is unique in that it focuses on stem cell stimulation of pluripotent cells near the hair follicle and on activating pigmentation through the use of its drug with adjuvant narrowband UVB (NB-UVB). While all other therapeutic attempts usually take one year or more to achieve some results in select patients, through the use of body's own hormone analogue, a visible response is seen within months.

In simpler terms, over decades we have seen visible repigmentation in vitiligo owing to the use of SCENESSE® in adjunct to NB-UVB. This has proven a safe and faster way to restore pigmentation.

In this extended update, we provide an overview of some of the considerations and plans for our vitiligo program (chapter I–III) covering the clinical program, as well as next steps in regulatory and commercial affairs.

As a final note, I wish to thank patients and physicians for whom we continue to work.

Lachlan Hay
Acting Chief Executive Officer, CLINUVEL

I) VITILIGO MILESTONES (clinical-regulatory, commercial)*

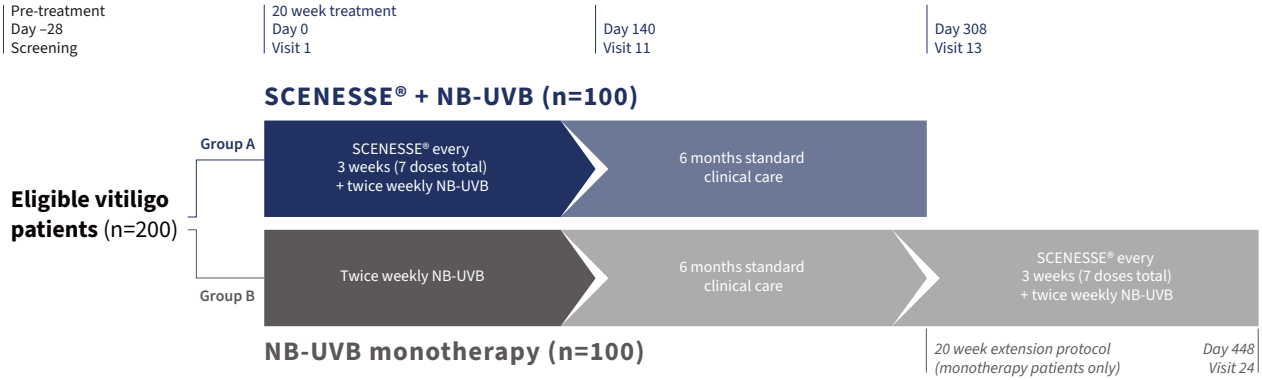
2025	May	CUV105 complete recruitment (NB-UVB adjunct)
	Mid	CUV104 final results (afamelanotide monotherapy)
	17–20 September	EADV Congress, Paris
	Ongoing, complete 2H	Regulatory discussions CUV107 (pivotal Phase III)
	2H	Commence CUV107 study
	Q4	Last patient, last visit CUV105 treatment protocol
	31 December	Train and accredit 120 Specialty Centers
2026	27–31 March	American Academy of Dermatology meeting, Denver, Colorado
	2H	CUV105 first results
	2H	CUV107 complete recruitment

**Clinical and regulatory milestones are subject to ongoing regulatory discussions.*

II) DEVELOPMENT PATH IN VITILIGO

"The treatment modalities in vitiligo have mostly been nonspecific and generalised like topical immuno-suppressants, phototherapy, surgical methods with modest efficacy and potential adverse effects." **KARAGAIAH ET AL 2022**

CUV105 STUDY DESIGN



The extension of CUV105 with six months became necessary, as the patients who were assigned to the NB-UVB arm only did not seem motivated to finish the study, since they already could see after start that they had not received the implant treatment. The promise to these patients that they would receive the drug treatment after the trial made a big difference to their willingness to stay in the study.

First clinical observations CUV105
CUV105 is the first advanced study of SCENESSE® in vitiligo, involving 37 clinical sites across the USA, Europe and Africa. The study has concluded recruitment, with 5% more patients enrolled than planned (n=210).

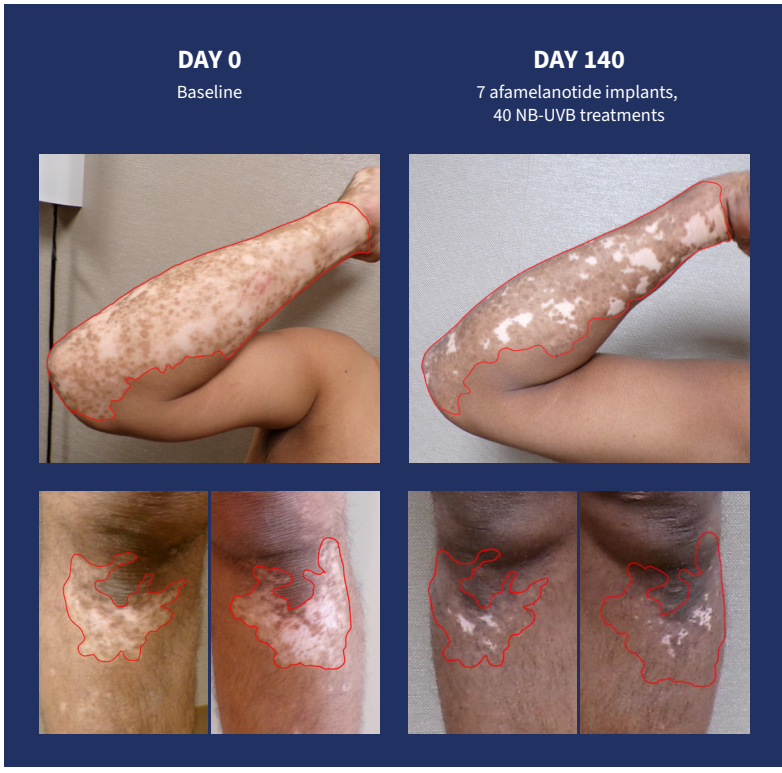
The primary endpoint in CUV105 is the percentage of participants achieving a 50% improvement in total body (excluding hands and feet) repigmentation or T-VASI 50 on Day 140. Secondary endpoints include F-VASI (facial) measures along with a range of patient-reported outcomes, including VitiQoL, a validated questionnaire to assess the impact of disease on quality of life.

First clinical observations released from CUV105 to date show repigmentation of vitiliginous lesions on the face, back, arms or legs following treatment with afamelanotide. Some patients also experienced spontaneous repigmentation following the conclusion of the treatment protocol, that is an entirely new learning. All case study patients reported satisfaction with the treatment results and high tolerance to afamelanotide with adjunct NB-UVB.

Among the key takeaways is that one needs to aim to achieve a few shades darker than usual pigmentary complexion to achieve the best results in the vitiligo areas. In other words, in the beginning a contrast between normal pigmented skin and vitiligo will be expected while after weeks the affected vitiligo skin will start to "catch up" in production and intensity thereby the contrast will start to diminish and fade. In short, transient melanogenesis (darkening) is necessary to rev up the pigment producing cells in the vitiligo lesions.

Further details and images from the five case studies can be found here and here.

CUV105 CASE STUDY RELEASED IN MAY 2025



The forearm shows reduction in vitiligo surface, while darkening of the unaffected skin is expected during treatment.

The knees show a regeneration of melanocytes and consequently repigmentation of the skin.

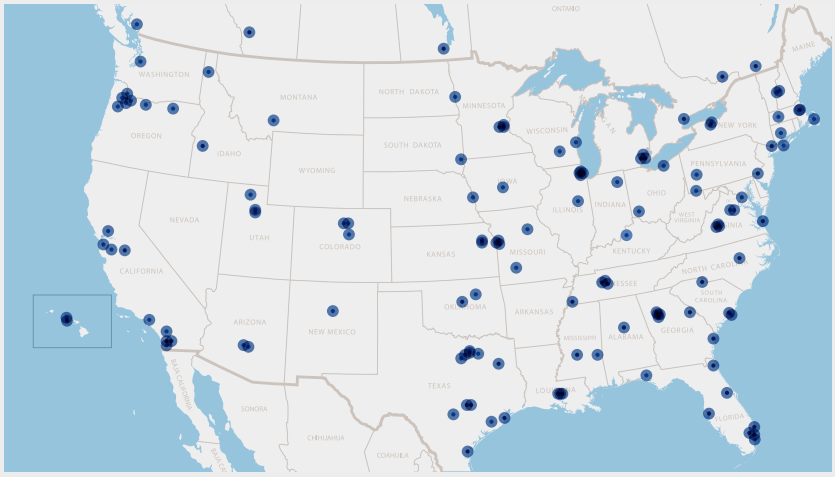
1. The Fitzpatrick Skin Type is a numerical classification of human skin colour, from type I skin that always burns, to type VI, dark skin that never burns.

III) COMMERCIAL PATHWAY VITILIGO

In anticipation of demand for SCENESSE® to treat vitiligo patients, CLINUVEL is expanding its North American commercial infrastructure.

Specialty Center Network: on track for 120 Centers in 2025
SCENESSE® was launched in the USA for EPP patients in 2020. The drug has been available in Canada through a special access program since 2023.

CLINUVEL has built a network of 104 trained and accredited Specialty Centers across North America to treat EPP patients, with plans to expand this network to 120 Centers by the end of 2025. Since a large percentage of clinicians are also caring for vitiligo patients, we expect our network to be able to facilitate treatment of up to 6,000 vitiligo patients annually within the first two years of commercial roll out. The infrastructure, systems and processes we establish cater for much larger distribution.



CLINUVEL has established 104 Specialty Centers across North America

Engagement with the broader dermatological community is essential. The recent American Academy of Dermatology meeting in Orlando established a new standard for the Group, with over 100 new potential centres identified across three days, while our broader story was introduced to some 20,000 attendees. Further global conferences are planned, with both a physical presence from the Company as well as supporting the presentation of data and observations.

Market access and reimbursement
CLINUVEL's Financial Specialist team supports Centers and patients with reimbursement and insurance claims, including facilitating access to the SCENESSE® Patient Assistance Program for eligible patients.

SCENESSE® is available for the treatment of EPP through prior authorization (PA) and a similar approach is expected for vitiligo, with patients to receive treatment through the Specialty Center network. This anticipates and reflects the changing payor landscape in the USA, where insurance firms are increasingly focused on patients receiving the most appropriate – and cost-effective – treatment. CPT® and J-Codes (*see breakout box*) have been established to standardise the SCENESSE® treatment procedure and reduce the administrative work required to treat patients in the USA. These codes can also be used to cover future FDA-approved indications of SCENESSE® for patients, with either private or government insurance.

CLINUVEL has completed pricing surveys in North America as part of its commercial planning for vitiligo, improving its understanding of payors' opinions and views. These exercises help us to shape our approach to pricing and reimbursement for SCENESSE® in vitiligo.

CODES SMOOTH PATIENT TREATMENT PROCESS

Procedure codes enable US health insurance companies to more easily determine appropriate reimbursement for treatments and procedures.

Current Procedural Terminology (CPT®) codes are standard codes developed and maintained by the American Medical Association (AMA) for health insurance companies, hospitals, and other healthcare organisations to: 1) describe medical, surgical, and diagnostic services and procedures performed; 2) determine appropriate reimbursement for the service; and 3) process and track medical claims.

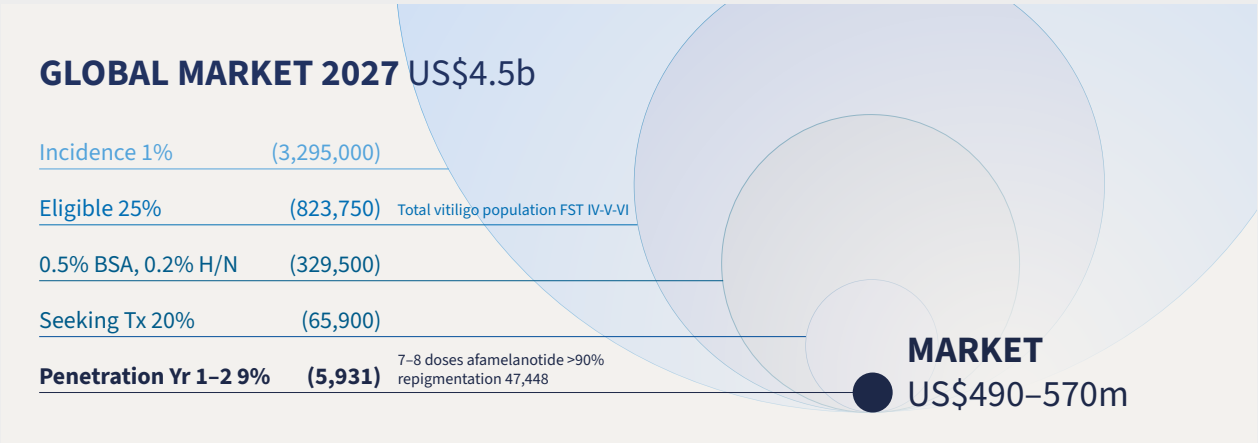
HCPCS (Healthcare Common Procedure Coding System) codes or J-codes are developed and maintained by the Centers for Medicare & Medicaid Services (CMS) for Medicare and health insurance companies to describe drugs, supplies, and other medical products that are not described by CPT® codes. The code is based on the type of device or product, its cost, and the manufacturer.

Supply chain
CLINUVEL has expanded its US commercial team and worked to reinforce its supply chain for SCENESSE®. This has included relocation of select manufacturing and distribution operations. Part of the goal has been to shorten the supply chain for SCENESSE®, refining upstream operations and building in optionality, while ensuring continuity of supply for commercial and clinical use. This has also involved implementing new digital systems within the business to better monitor and forecast product supply in a scale-up scenario.

A potential market for SCENESSE® in vitiligo
The total addressable market for vitligo is estimated at US$4.5bn per annum by 2027. A personalised treatment intervention is based on a range of factors:

- Location, extent and duration of disease
- Skin type
- Whether depigmentation is stable (i.e. dormant) or progressive
- Concomitant disorders of a systemic or autoimmune nature
- The psychosocial impact of depigmentation and possible treatment interventions
- Attempted and failed or relapsed response to previous treatment

Across each of these categories, CLINUVEL aims to first focus on those patients who are at highest burden of disease and thus have the greatest unmet clinical need, in particular those with widespread depigmentation on visible or sensitive areas (face, head, neck and/or genitals), extensive depigmentation (≥5% of total body surface area) and darker skin types (Fitzpatrick III-VI). Based on these criteria, and others within our internal decision models, there is a logic to the Company's approach to commercialise first in North America, where an estimated 6,000 patients per annum would be targeted for treatment within the first two years of commercialisation, of a total potential eligible population of 330,000 individuals.



CLINUVEL anticipates a potential annual market for SCENESSE® in vitiligo of $490-570m within the first two years of launch

ABOUT CLINUVEL PHARMACEUTICALS LIMITED

CLINUVEL (ASX: CUV; ADR LEVEL 1: CLVLY; Börse Frankfurt: UR9) is a global specialty pharmaceutical group focused on developing and commercialising treatments for patients with genetic, metabolic, systemic, and life-threatening, acute disorders, as well as healthcare solutions for specialised populations. As pioneers in photomedicine and the family of melanocortin peptides, CLINUVEL's research and development has led to innovative treatments for patient populations with a clinical need for systemic photoprotection, repigmentation and acute or life-threatening conditions who lack alternatives.

CLINUVEL's lead therapy, SCENESSE® (afamelanotide 16mg), is approved for commercial distribution in Europe, the USA, Israel, and Australia as the world's first systemic photoprotective drug for the prevention of phototoxicity (anaphylactoid reactions and burns) in adult patients with erythropoietic protoporphyria (EPP). Headquartered in Melbourne, Australia, CLINUVEL has operations in Europe, Singapore, and the USA. For more information, please go to https://www.CLINUVEL.com.

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

Forward-Looking Statements
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 2024 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.

Contact:
Tel: +61 3 9660 4900
Fax: +61 3 9660 4909
Email: mail@clinuvel.com
Australia (Head Office), Level 22, 535 Bourke Street, Melbourne, Victoria, 3000, Australia

References and further reading

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