CLINUVEL

ASX ANNOUNCEMENT

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# Pilot study confirms adjunct NB-UVB needed to activate repigmentation in vitiligo

## Results of CUV104 study demonstrate afamelanotide monotherapy ineffective in pigment loss disorder

CLINUVEL today announced final results from its Phase II pilot study evaluating SCENESSE® (afamelanotide) as a monotherapy in patients with the depigmentation disorder vitiligo. The single arm open label study failed to demonstrate repigmentation in the skin of three adult vitiligo patients treated with SCENESSE® as monotherapy for up to three months. SCENESSE® was well tolerated at a high dose of six implants administered at 14-day intervals.

The lack of repigmentation seen in patients in CUV104 illustrates the utility of adjunct narrowband ultraviolet B (NB-UVB) phototherapy for treating vitiligo patients with afamelanotide.

“We now have clinical evidence supporting our scientific hypothesis that afamelanotide requires concomitant activation of pigment producing cells by NB-UVB to effectively repigment vitiligo patients,” CLINUVEL’s Director, Global Clinical Affairs, Dr Emilie Rodenburger said. “These data confirm the Company’s decision to pursue afamelanotide and adjunct NB-UVB as part of its pivotal study designs, while at the same time addressing regulatory questions as to the effects of afamelanotide as monotherapy.”

### Focus on SCENESSE® and adjunct NB-UVB phototherapy

NB-UVB is known to trigger the differentiation of stem cells adjacent to the hair follicle to become fully functioning pigment producing cells (melanocytes). Real time results of NB-UVB therapy vary, but twice- or thrice-weekly clinical treatment over six to 12 months is generally required to achieve some degree of repigmentation. NB-UVB adjunct to afamelanotide has been shown in earlier trials to provide faster and more widespread repigmentation than NB-UVB alone.

No further studies are planned to evaluate afamelanotide as monotherapy for vitiligo patients. The ongoing CUV105 Phase III study and planned CUV107 pivotal Phase III study are evaluating SCENESSE® as a systemic repigmentation therapy with adjunct NB-UVB.

### Monotherapy results add to regulatory dossier

Following suggestions from global regulators in early program discussions to assess the safety and efficacy of afamelanotide as a monotherapy in patients with darker skin types (Fitzpatrick IV–VI)[1], CLINUVEL conducted the CUV104 study.

The study designs of CUV105 and CUV107 have both incorporated learnings from CUV104, and clinical data will be included in the dossier to be submitted for marketing authorisation for afamelanotide in vitiligo.

“The CUV104 results have once and for all confirmed our thinking and expertise that vitiligo cannot be treated with a single modality. We are making clinically meaningful steps towards offering vitiligo patients with darker skin complexions a treatment derived from our natural pigmentation hormone,” Dr Rodenburger said.

## CUV104 study design and outcomes

The CUV104 study was set up to enrol up to six adult vitiligo patients of darker skin complexion, treating them with up to six SCENESSE® implants over three months after priming with NB-UVB. The study sought to determine whether afamelanotide monotherapy, following NB-UVB, would repigment the skin. The Vitiligo Area Scoring Index (VASI) was used to evaluate repigmentation.

Of the three patients enrolled, one completed the full treatment regimen, with the other two withdrawing early due to the darkening of unaffected skin showing a contrast with vitiligo affected skin. At the conclusion of up to three months of therapy, none of the three patients achieved repigmentation as measured with the VASI. Afamelanotide treatment was well tolerated, with no serious or severe adverse reactions.

"We can now answer the regulatory suggestion to use monotherapy afamelanotide in vitiligo. With these data in hand, we inch towards a robust set of data to be part of a future submission of SCENESSE® for vitiligo patients," Dr Rodenburger said.

**– END –**

[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.

**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, assisted DNA repair, 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 and PhotoCosmetic products; competition for our products, especially SCENESSE® (afamelanotide 16mg), CYACÊLLE, PRÉNUMBRA®, NEURACTHEL® or products developed and characterised by us as PhotoCosmetics; 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, the UK, Israel, China, Japan, and/or LATAM regions 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®, NEURACTHEL® or products developed as PhotoCosmetics which may lead to the Company being unable to launch, supply or serve its commercial markets, special access programs and/or clinical trial programs; any failures to comply with any government payment system (i.e. Medicare, Medicaid, and U.S. Department of Veteran's Affairs) reporting and payment obligations; uncertainties surrounding the legislative and regulatory pathways for the registration and approval of biotechnology, cosmetic 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, cosmetic 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.

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