CLINUVEL

ASX ANNOUNCEMENT

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

Vitiligo and Operational Update

CUV105 protocol extension, inclusion criteria relaxed

SUMMARY

Phase III vitiligo study (CUV105) amended following expert clinician feedback

- Extension treatment with SCENESSE® offered to patients assigned NB-UVB monotherapy (20 weeks)
- Inclusion criteria relaxed
- Primary and secondary study endpoints unchanged
- Changes extend CUV105 recruitment window to 30 June 2025

Clinical Affairs team restructured to deliver on larger, more complex global programs

CLINUVEL today announced updates on its clinical program assessing the safety and efficacy of its drug SCENESSE® (afamelanotide 16mg) as a systemic repigmentation therapy for vitiligo. SCENESSE® is being evaluated as a combination therapy with narrowband ultraviolet B (NB-UVB) versus treatment with NB-UVB monotherapy in both adult and adolescent (12 years and above) vitiligo patients with darker skin complexions (Fitzpatrick Skin Types IV-VI).[1]

Phase III CUV105 study amendments

CLINUVEL is updating its ongoing Phase III vitiligo study (CUV105) protocol in response to expert clinicians' feedback on study enrolment and patient retention. The CUV105 study aims to demonstrate that the combination therapy provides faster, deeper repigmentation than NB-UVB monotherapy, which is currently the only systemic (full body) vitiligo therapy, yet provides unsatisfactory results.[2]

The Company has identified that patients assigned the NB-UVB monotherapy appear less motivated to start or complete the 20-week study and follow up period (24 weeks). Given the visible effects and improvement of pigmentation of the combination therapy, patients receiving monotherapy are less willing to adhere to the study protocol.

In response to clinical expert requests, CLINUVEL has agreed an extension to the protocol, providing all patients receiving monotherapy and completing the study with access to subsequent SCENESSE® combination therapy. This implies that all study patients will be eligible to receive the 20-week combination therapy, increasing retention rates. The extension will capture further safety and efficacy data on the use of SCENESSE® in generalised vitiligo.

In addition, the CUV105 recruitment inclusion criteria are being relaxed to allow enrolment of patients with vitiliginous lesions (depigmentation) on the face including the scalp and neck, broadening the potential eligible population. It has been widely recognised that lesions on visible areas of the body can have the greatest impact on patient quality of life. The primary and secondary endpoints, including those evaluating depigmentation of the total body and face (T-VASI and F-VASI), remain unchanged.[3]

CLINUVEL anticipates that changes to the protocol will result in the last patients being enrolled in the CUV105 study by 30 June 2025. Further updates on the vitiligo program will be provided.

Clinical Affairs team restructure

Following her appointment in April 2024 as Director, Global Clinical Affairs, Dr Emilie Rodenburger has led a restructure of the Company's Clinical Affairs team, focusing on streamlining operations to accommodate larger and more complex programs, and new products. The new Clinical Affairs structure has integrated clinical operations, medical monitoring, and data sciences across two continents.

Commentary

"We have worked closely with study sites during setup and initial recruitment to understand where we can enable patient inclusion, as well as encouraging study continuation for those patients who may be disappointed to be enrolled in the monotherapy arm," Dr Rodenburger said. *"Some of these solutions have been elegant in their simplicity, while others have led to the conclusion that protocol amendments are necessary to enable us to reach the core objectives of fully recruiting CUV105 and commencing the upcoming CUV107 study.*

"I see it as my task to straddle several objectives at once and, after evaluation, it has proven possible to set up the clinical team in three streams. First, we would like to activate study sites capable of prescribing the drug down the line to larger populations of vitiligo patients. Second, we established infrastructure to assist these centres with the additional administrative burden of conducting the study. Third, we are pragmatically amending protocols such that more patients are potentially eligible, willing to adhere to the monotherapy protocol, and ultimately complete the study. It is both challenging and exciting to be one of the very few globally to scale the infrastructure necessary to treat 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.

[2] Bae, J. M., et al. (2017). Phototherapy for Vitiligo: A Systematic Review and Meta-analysis. JAMA Dermatology, 153(7), 666.

[3] The Vitiligo Area Scoring Index (VASI) is a validated clinical tool for evaluating repigmentation in vitiligo. See Hamzavi, I., et al. (2004). Parametric modeling of narrowband UV-B phototherapy for vitiligo using a novel quantitative tool: The Vitiligo Area Scoring Index. Archives of Dermatology, 140(6), 677–683.

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.

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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 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.

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