CLINUVEL

ASX ANNOUNCEMENT

CLINUVEL starts global Phase III vitiligo study

First vitiligo patient treated in Phase III combination therapy study following regulatory, ethics approvals

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	Börse Frankfurt:	UR9
	ADR Level 1:	CLVLY

EXECUTIVE SUMMARY: VITILIGO PHASE III

- Open-label randomised Phase III study
- SCENESSE® as combination therapy with narrowband UVB (NB-UVB) in vitiligo (depigmentation disorder)
- Primary end point: T-VASI50 (50% body surface repigmented)
- Up to 200 patients to be recruited: adults and adolescents (12 years and older)
- Vitiligo patients with darker skin types (Fitzpatrick IV-V-VI)
- First patient treated (12-month recruitment)
- First systemic therapy, no immune system suppression

CLINUVEL today announced that SCENESSE® (afamelanotide 16mg) has been administered as a systemic treatment to the first vitiligo patient in a company-sponsored Phase III study, CUV105. Up to 200 adolescent and adult vitiligo patients with darker skin types (Fitpatrick Types IV-VI)[1] will be enrolled in the study, comparing the use of SCENESSE® in combination with narrowband UVB (NB-UVB) light therapy to NB-UVB as a monotherapy.

"Our clear goal is to bring the first systemic vitiligo therapy to market," CLINUVEL's Director of North American Operations, Dr Linda Teng said. *"Physicians specialised in depigmentation disorders expect that afamelanotide will be an important tool in the treatment of severe vitiligo in patients with darker skin, since it is the only drug on the horizon which does not suppress the immune system."*

CUV105 STUDY

The study evaluates whether afamelanotide in combination with NB-UVB provides faster, deeper, and longer-lasting repigmentation of total body surface compared to NB-UVB alone (T-VASI50). A number of patient reported outcomes, including quality of life surveys, will provide data for secondary objectives.

Vitiligo impacts patients' identity

"Vitiligo forced me into self-isolation, extreme introversion and at times fully closed me off from the world."

"I don't want to go outside. I don't want to see my face in the mirror."

"They think it's cosmetic, but it's more for me. I am a lifelong colored person. I feel like I lost my identity. I'm sorry. It's very difficult to not be so emotional."

Patient testimony from FDA vitiligo workshop, March 2021

Uniquely, up to 200 vitiligo patients with darker skin complexions (Fitzpatrick skin types IV-VI) will be enrolled. For the first time, adolescent patients of 12 years of age and older are also included.

All patients will receive NB-UVB twice weekly for the duration of twenty weeks, with half receiving SCENESSE® every three weeks. Patients will be followed up for six months.

Full recruitment of patients is estimated to be 12 months, depending on the centres' ability to identify suitable patients.

"We possess data on the efficacy of the drug-UVB combination from 58 patients who participated in the CUV102 trial, now we look forward to evaluating the effects of the drug in a larger randomised study, since vitiligo patients deserve a systemic solution," Dr Teng said.

ADDRESSING UNMET NEED IN VITILIGO

Vitiligo causes progressive loss of functional epidermal melanocytes (melanin producing skin cells), which lead to disfiguration and psychosocial distress.

While the disease can have an impact on all patients, it is recognised that those with darker skin types are most severely affected. In North America, an estimated 820,000 individuals of darker skin types are affected by vitiligo. The precise cause of the sudden start of this disorder remains unknown.

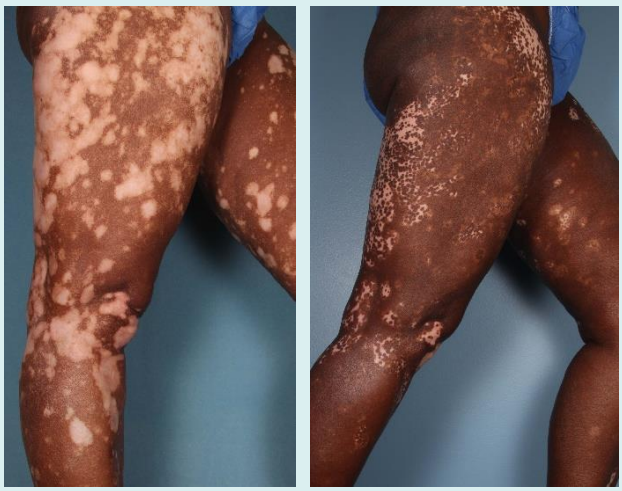

Figure 1 *Repigmentation of a vitiligo patient's legs in CLINUVEL's CUV102 study.*

The patient received 55 NB-UVB treatments and four SCENESSE® implants over six months.

Left at the start, right after afamelanotide treatment.

Images courtesy of the investigators.

The mainstay of vitiligo treatment in dermatology offices remains the use of phototherapy, specifically NB-UVB, and transdermal drugs which suppress or modulate the immune system. Treatment remains burdensome providing inconsistent and unsatisfactory results. Phototherapy protocols recommend thrice weekly treatment administered in dermatology offices for up to 18 months.

Transdermal therapies cannot be used for extended periods of time or to treat extensive vitiligo with large body surfaces.

Afamelanotide activates pigment producing cells and is considered to boost a pigmentary response following NB-UVB therapy. In earlier trials, the drug in combination with NB-UVB phototherapy has been shown to repigment skin faster and deeper, with excellent results observed in patients with darker skin types.

– 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.

References

1. Bibeau, K. et al., (2023). Mental Health and Psychosocial Quality-of-Life Burden Among Patients With Vitiligo: Findings From the Global VALIANT Study. JAMA Dermatology, e232787.
2. Grimes, P. E. et al., (2013). The Efficacy of Afamelanotide and Narrowband UV-B Phototherapy for Repigmentation of Vitiligo. JAMA Dermatology, 149(1), 68.

3. Lim, H. W., et al., (2015). Afamelanotide and Narrowband UV-B Phototherapy for the Treatment of Vitiligo: A Randomized Multicenter Trial. JAMA Dermatology, 151(1), 42.

Annex I: Following ASX Best Practice

Name of trial
A Double-Arm, Open Label, Phase III Study to Compare the Efficacy and Safety of SCENESSE® and Narrowband Ultraviolet B (NB-UVB) Light versus NB-UVB Light Alone in the Treatment of Vitiligo

Primary endpoint
To evaluate the efficacy of SCENESSE® in repigmentation of vitiligo on the body.

Secondary endpoints
- To determine the safety of SCENESSE® and NB-UVB light treatment in patients with vitiligo
- To evaluate the efficacy of SCENESSE® and NB-UVB compared to NB-UVB alone in repigmentation of vitiligo on the face
- To compare the maintenance of pigmentation achieved with SCENESSE® and NB-UVB versus NB-UVB alone in patients with vitiligo

Blinding status
Double arm, open label.

Product development status
Current Good Manufacturing Practice (cGMP) Standard.

Treatment method and dose levels
SCENESSE® (afamelanotide) implants, total of 7 implants of afamelanotide.

Number of trial subjects
Up to 200 vitiligo patients.

Subject selection criteria
- Male and female patients with a confirmed diagnosis of vitiligo on the face and body
- Stable or active vitiligo diagnosed for at least three months
- Aged 12 or more
- Fitzpatrick skin types IV-VI
- Further safety related exclusion criteria apply.

Trial location
Expert vitiligo treatment centres worldwide.

Duration of trial
20- week treatment phase with six-month follow up.

Trial standard
In compliance with Good Clinical Practice (GCP) and ICH guidelines.

Appendix II: 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 specialized 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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