CLINUVEL

COMPANY ANNOUNCEMENT

First vitiligo patient enrolled in afamelanotide monotherapy study

CUV104 study to evaluate the role of afamelanotide as monotherapy in patients with darker skin

Melbourne, Australia, 20 October 2022	ASX: XETRA-DAX: Level 1 ADR:	CUV UR9 CLVLY

EXECUTIVE SUMMARY

- First vitiligo patient enrolled in CUV104 study
- Afamelanotide evaluated as first systemic monotherapy in vitiligo
- Study to enrol up to six patients with darker skin complexions (Fitzpatrick IV-VI)
- Endpoint: facial repigmentation

CLINUVEL today announced that the first patient has been enrolled in a new clinical study (CUV104), evaluating the safety and efficacy of afamelanotide as a monotherapy in vitiligo patients with darker skin complexions (Fitzpatrick Skin Types IV-VI).

"Vitiligo patients lose skin pigment, creating irregular white patches across the body surface and the disease often has the most severe impact on patients with darker skin types, who report a loss of identity as the skin visibly changes," CLINUVEL's Director of North American Operations, Dr Linda Teng said. *"Afamelanotide, which is based on a natural hormone, is shown to improve the pigmentary response in vitiligo. It is generally thought that afamelanotide will serve as a pigmentary booster to vitiligo patients, improving their overall response without the need for immunomodulation. Afamelanotide is a systemic treatment being evaluated in vitiligo."*

"We expect to enrol all patients and complete the treatment phase of this study by mid-2023, with results later in the year," Dr Teng said.

AFAMELANOTIDE AS VITILIGO THERAPY

Vitiligo is a depigmentation disorder characterised by chronic and progressive loss of functional epidermal melanocytes (the melanin producing skin cells), which can lead to disfiguration and psychosocial distress. The precise cause of vitiligo remains unknown.

There is no effective systemic treatment to date, however phototherapy is uniformly used by dermatologists worldwide. In July 2022, an immune modulating topical drug was approved by the FDA as the first commercial therapy in vitiligo.

Afamelanotide has been shown to repigment skin faster and more extensively as combination with narrowband UVB (NB-UVB) phototherapy, and is now being evaluated for its ability to boost the pigmentary response as monotherapy. A successful approach will eliminate or reduce the need for concomitant therapies that require prolonged exposure to ultraviolet light and/or long-term local or systemic immunotherapies.

CLINUVEL has announced an adaptive regulatory pathway for developing afamelanotide as the first systemic therapy for vitiligo patients, with late-stage studies to be conducted over the next 30 months. Pending regulatory discussions and clinical results, the use of afamelanotide as both a monotherapy and combination therapy with NB-UVB will be pursued.

"Following an evolution in regulatory thinking, afamelanotide is well positioned to revolutionise the approach to vitiligo therapy," Dr Teng said. *"Most dermatologists already deploy escalation approaches and we expect that afamelanotide will become the first-line treatment for a great percentage of patients, either as a monotherapy or combination therapy."*

CUV104 STUDY

The CUV104 study will enrol up to six adult vitiligo patients with darker skin complexions (Fitzpatrick skin types IV-VI) and vitiligo lesions present on their face. Patients will be treated with SCENESSE® every two weeks for three months, with a three-month follow-up, in expert vitiligo centres in North America. In earlier studies of afamelanotide, patients with darker skin complexions experienced a significantly greater pigmentary response to treatment.

Due to their prominence, facial lesions are recognised as having the greatest impact on many patients' quality of life, with successful repigmentation of these lesions widely recognised as providing considerable clinical benefit to patients.

Results from the CUV104 study will be discussed with regulatory authorities and help determine the next steps in CLINUVEL's vitiligo program.

– End –

CLINUVEL released details on its vitiligo development pathway in a recent corporate presentation, available on the Company's website.

References

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.

Silvan, M. (2004). The psychological aspects of vitiligo. *Cutis*, 73(3), 163–167.

US Food and Drug Administration (2021). Public Meeting on Patient-Focused Drug Development for Vitiligo: Remote Proceeding Transcript. Available online at https://www.fda.gov/media/146995/download.

Annex I: Following ASX Best Practice

Name of trial
An Open Label, Phase II Study to Assess the Changes in Pigmentation and Safety of Subcutaneous, Bioresorbable Afamelanotide Implants in the Treatment of Vitiligo on the Face.

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

Secondary endpoints
- To determine the short-term safety of SCENESSE® administered every 14 days in patients with vitiligo.
- To evaluate the efficacy of SCENESSE® in repigmentation of vitiligo on the body.
- To assess the maintenance of pigmentation in patients with vitiligo treated with SCENESSE®.

Blinding status
Open label.

Product development status
Good Manufacturing Practice (GMP) Standard.

Treatment method and dose levels
SCENESSE® (afamelanotide) implants, total of 96mg of afamelanotide.

Number of trial subjects
Up to six vitiligo patients.

Subject selection criteria
- Male and female patients with a confirmed diagnosis of vitiligo on the face
- Stable face vitiligo

- Aged 18-75
- Stable or slowly progressive vitiligo over a 3-month period
- Fitzpatrick skin types IV-VI
- Previous treatment with NB-UVB light three times per week during the last four weeks preceding the first implant.

Further safety related exclusion criteria apply.

Trial location
Specialist vitiligo treatment centres in the USA.

Duration of trial
Three-month treatment phase with three-month follow up.

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

About CLINUVEL PHARMACEUTICALS LIMITED
CLINUVEL (ASX: CUV; ADR LEVEL 1: CLVLY; XETRA-DAX: 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 the general population. 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, 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.

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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 2022 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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