CLINUVEL

COMPANY ANNOUNCEMENT

SCENESSE® as Vitiligo Monotherapy

CLINUVEL study to evaluate afamelanotide as repigmentation monotherapy

Melbourne, Australia, 20 December 2021	ASX: XETRA-DAX: NASDAQ INTERNATIONAL DESIGNATION:	CUV UR9 CLVLY

EXECUTIVE SUMMARY

- FDA agrees to Phase II study CUV104 evaluating SCENESSE® as vitiligo monotherapy
- Patients with darker skin types (Fitzpatrick IV-VI) to be enrolled in study CUV104
- Repigmentation, Quality of Life to be evaluated

CLINUVEL's drug SCENESSE® (afamelanotide 16mg) will be evaluated as a monotherapy in patients with the depigmentation disorder vitiligo, in a six month clinical trial (CUV104). The Company has reached agreement on the clinical protocol and will commence the CUV104 study at a specialist hospital department in the USA.

PROTOCOL DESIGN AND US FDA INPUT

Several meetings have been held with the US Food and Drug Administration (FDA) over the past years, whereby global clinical experts have accompanied CLINUVEL to discuss clinical study protocols in vitiligo. The main discussion point concerned the proposed administration of SCENESSE® in combination with narrowband ultraviolet B (NB-UVB) phototherapy in pivotal studies to support a US New Drug Application.

Vitiligo causes progressive loss of pigmentation in "lesions" across the body and affects around 1% of the population worldwide. Treatment aims to halt the spread of depigmentation and repigment the affected skin. NB-UVB – administered as an off-label (unapproved) treatment in vitiligo – does provoke some skin pigmentary response after 6-18 months of therapy, but seldom does it achieve satisfactory levels of repigmentation in vitiligo patients. In the six-month CUV102 study, the combination of SCENESSE® with NB-UVB led to successful repigmentation in patients with darker skin complexions (Fitzpatrick skin type IV, V, VI).[1]

At the present time, the FDA does acknowledge NB-UVB to be the treatment of choice for vitiligo, and in use by the majority of clinical centres.[2] However, the agency has not evaluated nor approved NB-UVB for the treatment of vitiligo. Further, the FDA stated that the safe use of the NB-UVB as a combination therapy (with any other treatment) had not yet been proven for human use.

Currently, there is no effective or FDA-approved therapy for vitiligo patients. Various drug candidates are being tested at present, with some causing undesired long-term immune suppression.

CUV104 STUDY – REPIGMENTATION, QUALITY OF LIFE

In the pilot study CUV104, for the first time, the response to SCENESSE® as a monotherapy will be assessed in patients with darker skin complexions.The study will focus on the extent and speed of repigmentation seen in patients as measured by the Vitiligo Area Scoring Index (VASI) tool, as well as the impact of the treatment, measured with validated disease-specific quality of life tools.

The study will be conducted under an amendment to CLINUVEL's existing Investigational New Drug (IND) status.

COMMENTARY

"After several discussions with the FDA and clinical experts, we have found a pathway to offer systemic repigmentation treatment with SCENESSE® to vitiligo patients with darker skin," CLINUVEL's Director of North American Operations, Dr Linda Teng said. "It is well acknowledged by the regulatory authorities that the loss of pigmentation in these patients is most dramatic, causing significant psychological distress. If this initial study is successful, we will pursue a larger trial."

– END –

[1] Grimes P et al. (2013). The Efficacy of Afamelanotide and Narrowband UV-B Phototherapy for Repigmentation of Vitiligo. *JAMA Dermatol*. 149(1):68-73

[2] In March 2021 the FDA hosted the first ever Public Meeting on Patient-Focused Drug Development for Vitiligo. For more details go to https://www.fda.gov/drugs/news-events-human-drugs/public-meeting-patient-focused-drug-development-vitiligo-03082021-03082021.

SCENESSE® (afamelanotide 16mg) is approved in the European Union and Australia as an orphan medicinal product for the prevention of phototoxicity in adult patients with erythropoietic protoporphyria (EPP). SCENESSE® is approved in the USA to increase "pain- free" light exposure in adult EPP patients with a history of phototoxicity. Information on the product can be found on CLINUVEL's website at www.clinuvel.com.

Authorised for ASX release by the Board of Directors of CLINUVEL PHARMACEUTICALS LTD

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Investor Enquiries

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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 2021 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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