CLINUVEL

COMPANY ANNOUNCEMENT

Afamelanotide significantly reduces UV skin damage in a healthy population

First spectrophotometric results positive (CUV151), analyses of DNA repair to follow

Melbourne, Australia, 2 February 2023	ASX:	CUV
	Börse Frankfurt:	UR9
	ADR Level 1:	CLVLY

***A technical explanation to this announcement has been released separately**: technical note*

Executive summary

Afamelanotide in study CUV151:

1. reduces skin damage in healthy skin (n=9)
2. statistically decreases UV-erythema dose response ($p = 0.018$)
3. increases Minimal Erythemal Dose (threshold to sunburn)
4. increases skin pigmentation ($p<0.05$)
5. results from skin biopsies to follow (DNA-repair)
6. supports XP DNA-repair results (CUV156 study first results, 16 January 2023)

CLINUVEL today announced the first positive results from a study evaluating the protective effects of afamelanotide on skin exposed to ultraviolet (UV) radiation (CUV151). The study, conducted at Salford Royal Hospital, Manchester, showed that systemic treatment with afamelanotide decreased the UV-erythema dose-response following ultraviolet radiation (UVR), indicative of reducing the first signs of UV-induced DNA damage. Analyses of biopsies that were taken during the study, assessing the drug's influence on DNA repair capacity, are pending.

Study design CUV151

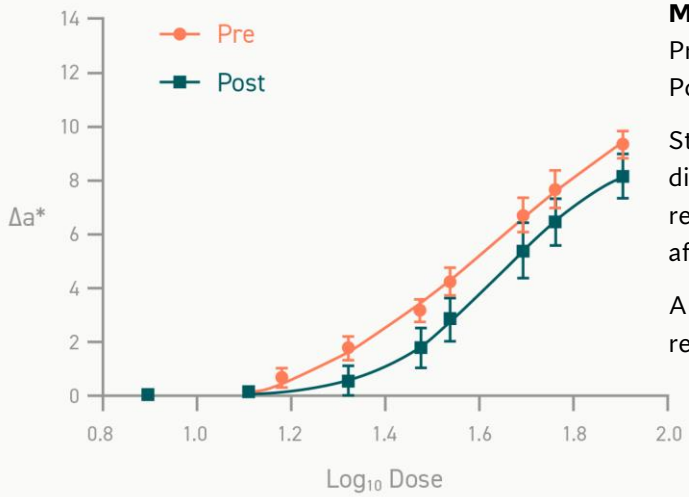
The objective of the study was to assess the impact of afamelanotide on UV-induced DNA-damage and repair capacity in healthy volunteers with fair skin types (Fitzpatrick I-III)[1] by measuring:

- changes in UVR erythema dose response following treatment with afamelanotide
- changes in minimal erythema dose (MED) following treatment with afamelanotide - an increased MED indicates a greater resistance to the mutagenic effects of UVR
- the amount of DNA damage, and DNA damage repair following exposure to controlled doses of UVR.

Manchester University is a renowned specialist centre which undertakes advanced clinical research in skin cancer, and its affiliate hospital (Salford Royal) was chosen for the study. Nine healthy adult volunteers were administered UVR by a solar simulator under controlled clinical conditions. Evaluation of the skin occurred before and after UVR.

Results CUV151

From a safety perspective, afamelanotide was well tolerated with two patients reporting mild headache and one patient experiencing mild nausea.



Mean area under curve [AUC]:
Pre-afamelanotide: 3.55;
Post-afamelanotide: 2.74.

Statistical evaluation of a difference between skin response without and with afamelanotide: p=0.018.

A higher a* value indicates redder skin.

It was found that following UV irradiation, the UV-erythema ("provoked sunburn damage") dose response was reduced (p=0.018). The observed decrease of the UV dose-response indicates the reduction of DNA damage incurred following afamelanotide treatment.

Consistent with earlier studies, skin melanin density increased following treatment with SCENESSE® (p<0.05).

Relevance of the results

Scientific research has long focused on the identification of principal skin cancer risk factors, among which are DNA damage defects incurred due to solar radiation. Short exposure to UVR, and evidently a first sunburn, causes loss of DNA integrity through the formation of helical breaks, and the formation of single-strand dimers (cyclobutane pyrimidine dimers, CPDs), thereby increasing the risk of skin cancer(s).

The scope of this study is limited to erythemal UVR and direct DNA damage. Following the use of solar-simulated UVR, reduction of UV dose-response, and increased melanisation shows the potential of systemically[2] used afamelanotide to significantly reduce solar skin damage, erythema, and therefore first DNA lesions. These results in healthy subjects confirm the earlier results of study CUV156 in xeroderma pigmentosum (XP) patients, who suffer from the highest risk of developing skin cancers due to a defect in DNA-repair mechanisms ("Afamelanotide Reduces DNA Photodamage in Xeroderma Pigmentosum", 16 January 2023). The results in CUV156 showed a reduction in CPDs following dosing of afamelanotide.

As seen in previous studies, in CUV151 it was confirmed that afamelanotide increases human skin pigmentation, which is strongly associated with photoprotection against systemic oxidative stress caused by solar radiation, and which may further reflect the drug's and melanin's antioxidative properties.

Commentary

"The overall goal of our comprehensive DNA Repair Program is to examine the impact of afamelanotide on DNA repair mechanisms in human skin," CLINUVEL's Head of Clinical Operations, Dr Pilar Bilbao said. *"For this, we examine the most extreme conditions leading to skin cancer such as XP, as well as healthy human volunteer studies to analyse DNA repair mechanisms provoked by our lead drug. In January, first results showed that afamelanotide assists XPC patients in reducing UV-provoked skin damage, and now we received the analyses from healthy humans indicating the peptide's beneficial effects in reducing UV-erythema dose response, an objective sign of DNA-damage caused by solar exposure.*

"As our clinical research progresses, it seems that the use of the hormone generates data showing its ability to consistently reduce the odds of forming photodamage, expressed as DNA photoproducts, the most prominent skin cancer risk factor." Dr Bilbao said.

– END –

[1] Fitzpatrick is a numerical classification of human skin colour, with type I skin that always burns, and VI, dark skin that never burns.
[2] Affecting the total body.

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. SCENESSE®, PRÉNUMBRA®, and NEURACTHEL® are registered trademarks of CLINUVEL.

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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