CLINUVEL

COMPANY ANNOUNCEMENT

AFAMELANOTIDE SIGNIFICANTLY REDUCES DNA DAMAGE IN A HEALTHY POPULATION

First positive DNA repair results from human biopsy (study CUV151)

Melbourne, Australia, 15 August 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, skin biopsy results:

1. reduces cyclobutane pyrimidine dimers (CPDs) in ultraviolet (UV) irradiated skin (n=9)
2. statistically decreases CPD formation ($p < 0.01$)
3. supports first UV-erythema dose-response (CUV151 preliminary results, 2 February 2023)
4. supports DNA repair results in XP patients (CUV156 study first results, 16 January 2023)

CLINUVEL today announced the second set of results from a study (CUV151) evaluating the DNA repair capacity of afamelanotide on skin exposed to ultraviolet (UV) radiation. The study was conducted at Salford Royal Hospital, Manchester, a leading centre in assessing the effects of UV-induced skin damage.

CUV151 STUDY SHOWS REDUCTION OF DNA DAMAGE IN FAIR SKIN TYPES

The CUV151 study enrolled ten healthy volunteers with fair skin type (Fitzpatrick I-III[1]), nine of whom received afamelanotide treatment and were included in the analyses. The volunteers were administered SCENESSE® (afamelanotide 16mg) and exposed to controlled UV irradiation, both before and after treatment.

Biopsies of irradiated skin showed that DNA photodamage, expressed as bulky DNA adducts (cyclobutane pyrimidine dimers or CPDs), was significantly reduced at several time points following afamelanotide treatment, compared to baseline. Following afamelanotide, the percentage of cells presenting CPDs was reduced significantly at 15 minutes, 24 hours, and 48 hours following UV irradiation ($p<0.01$).

These results complement those obtained in February, when it was found that damage – characterised by the UV-erythema ("provoked sunburn damage") dose response – had been reduced ($p=0.018$).

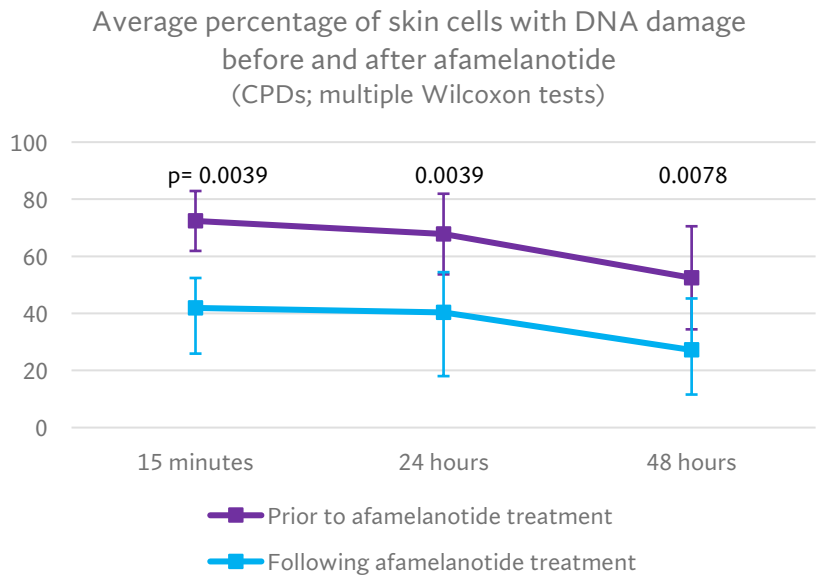
Consistent with earlier studies, melanin density (skin pigmentation) significantly increased following treatment with SCENESSE® ($p<0.05$).

These results will be presented at the European Association of Dermatology and Venereology in Berlin in October 2023. A further set of skin biopsy analyses assessing DNA markers (such as p53 and gamma-H2AX) are to follow.

RELEVANCE OF THE CUV151 RESULTS

Following the use of controlled UV radiation, a demonstrated reduction of CPDs indicates the potential of systemically[2] administered afamelanotide to significantly reduce DNA skin damage caused by solar radiation and, ultimately, skin cancer. The results also show – for the first time – that afamelanotide treatment results in a significant reduction in DNA damage both shortly after irradiation (15 minutes) and over a subsequently longer time point (48 hours). Results from CUV151 released earlier this year found that individuals who received afamelanotide showed a reduced UV dose-response, and increased melanisation. Both sets of results from CUV151 strongly point to the photoprotective and DNA reparative effects of afamelanotide.

The CUV151 analyses from healthy subjects also confirm the 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 biopsies in three XP patients (CUV156) showed a significant reduction in CPDs following afamelanotide administration.



Compared total DNA damage (skin cells presenting CPDs) in healthy volunteers incurred from controlled UV irradiation prior to, and following, SCENESSE® treatment, with a significant reduction 15 minutes, 24 hours, and 48 hours after a single SCENESSE® dose.

COMMENTARY

"These results add to a momentum, when all the pieces of the puzzle and data come together from our DNA Repair Program," CLINUVEL's Head of Clinical Operations, Dr Pilar Bilbao said. "It is widely accepted that decreasing DNA photoproducts leads to a reduced risk and development of skin cancers, and we are working to evaluate these effects in high-risk populations.

"We are the first company to run a comprehensive program using a human hormone analogue to show its effects on lessening DNA photodamage caused by UV, both in fair skinned individuals and XP patients, who are at highest risk of developing skin cancers following UV irradiation. It is very exciting for our team to further this program with more patients, and more centres now prepared to join.

"These data not only support our clinical work to pursue a marketing authorisation for the use of afamelanotide in XP patients – who are at high risk of developing multiple skin cancers per year and are left to lead an isolated life – but also for our photocosmetic product lines," Dr Bilbao 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] 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.
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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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