CLINUVEL

COMPANY ANNOUNCEMENT

FIRST PATIENT TREATED IN CLINUVEL DNA REPAIR STUDY

Xeroderma pigmentosum (XP) patient dosed with afamelanotide in CUV156

Melbourne, Australia, 22 October 2021	ASX: XETRA-DAX: NASDAQ INTERNATIONAL DESIGNATION:	CUV UR9 CLVLY

EXECUTIVE SUMMARY:

- Afamelanotide evaluated as DNA repair therapy, photoprotective, in rare disorder XP
- First XP patient receives afamelanotide in innovative CUV156 study
- CUV156 focus on safety, reduction and repair of DNA damage

CLINUVEL PHARMACEUTICALS LTD today announced that the first xeroderma pigmentosum (XP) patient has received afamelanotide treatment in the CUV156 study, part of the Company's DNA Repair Program.

The adult XP patient – diagnosed with the XP-C complementation variant and treated at a European XP expert centre – will receive up to six doses of afamelanotide during the pilot study. CLINUVEL and XP expert physicians will evaluate the safety and effect of afamelanotide treatment on reducing and repairing ultraviolet (UV) provoked DNA damage.

"XP patients belong to the group at highest risk of skin cancer due to UV light exposure, which damages their DNA," CLINUVEL's Head of Clinical Operations, Dr Pilar Bilbao said. "Tragically, this genetic disease severely limits their lives and life expectancy, and there are no protective or effective treatments available.

"We know afamelanotide is capable of assisting the repair of UV induced DNA damage, and are now trying to evaluate the drug's potential in clinical trials, starting with CUV156. While waiting for COVID-19 restrictions to lift and safely allow patients into a hospital environment, we have been working together with expert XP physicians to add to the trial design and ensure we could capture more indicative data.

"We are the first to administer a systemic drug in a DNA Repair Program, and have designed innovative studies which provide an opportunity for translation of knowledge and technologies to broader patient populations," Dr Bilbao said.

DNA Damage and Repair

UV radiation penetrates the nucleus of skin cells and causes defects of the DNA helix known as photoproducts. If left unrepaired, these chemical changes to DNA may replicate as mutations, leading to irreversible damage (photoaging) and may further progress to skin cancer.

Under optimal conditions, the human body is able to repair photoproducts. Processes such as Nucleotide Excision Repair (NER) and Base Excision Repair (BER) can restore DNA to its prelesional state by removing and replacing defects in the DNA helix. Both genetic and environmental factors, however, can lead to deficiencies in these mechanisms and an accumulation of DNA damage.

Due to genetic defects, XP patients have impaired DNA repair processes, leading to an extreme risk of skin cancer from an early age and a life expectancy of around 30 years. Globally, it is estimated that over two billion individuals have defects in their DNA repair processes, placing them at an increased risk of skin cancer.

CLINUVEL's DNA Repair Program

CLINUVEL is conducting clinical trials of afamelanotide in both healthy volunteers and XP patients as part of its DNA Repair Program to confirm the drug's ability to repair UV provoked DNA damage and protect skin from light (photoprotection).

Clinically, afamelanotide has been confirmed to show reduction of photoproducts (oxidative damage and pyrimidine dimers) caused by UV radiation and visible light. Further research has shown the ability of afamelanotide and other melanocortin molecules to assist skin cells in DNA repair mechanisms (NER and BER) as well as protecting skin from UV damage through the induction of eumelanin, the dark pigment, in skin. Eumelanin also provides antioxidative defence and has a neutralising effect on skin damage.

The CUV156 study focuses on the safety profile of afamelanotide in XP patients and seeks to quantify whether treatment can increase protection from UV, reduce DNA photoproducts, and increase the cellular signalling levels which lead to increased levels of DNA repair. Up to six XP-C patients will be enrolled for treatment with skin samples (biopsies) of exposed skin areas taken for laboratory analyses of DNA damage before and after drug administration. CLINUVEL has also collaborated with expert physicians to develop global assessment tools and patient reported outcomes for its use in the study, in order to evaluate disease severity in this population.

Further studies in the DNA Repair Program are planned in patients with both the XP-C and XP-V complementation groups, with healthy volunteers of fair skin complexion serving as a control group.

Potential therapy for XP patients

XP is a group of eight rare disorders (XP-A through XP-G and XP-V) causing extreme UV burning and defects leading to skin cancers, slow-down of development, and neurological disease. Compared to the general population, XP patients have been shown to have a 1,000- to 10,000-fold increased risk of developing skin cancer.

Few clinical trials have been conducted in XP patients and no disease specific treatments exist to date. Current therapies focus on managing skin cancers and total avoidance of UV exposure, requiring specialised clothing (such as visor hats and gloves), sunscreens and UV blocking films in the windows of homes, schools, and workplaces.

"A proven therapy, which offers both photoprotection and assists DNA repair, would reduce the overall burden of the disease for XP patients and their families and could dramatically improve quality of life and life expectancy. Since, afamelanotide seems to be the only proposed XP therapy currently subject to clinical trials, the start of this study is a major event for the XP community and we all look forward to results in 2022," Dr Bilbao said.

– End –

Further reading & resources

- What is Xeroderma Pigmentosum? September 2020
- CLINUVEL Scientific Communique VI: Ultraviolet Radiation Damage and Oxidative Stress in Skin Cancer, October 2020
- CLINUVEL Scientific Communique VIII: DNA Repair Mechanisms, December 2020
- CLINUVEL Scientific Communique IX: Beyond Pigment, the Melanocortin 1 Receptor (MC1R) in DNA Repair, March 2021

About CLINUVEL PHARMACEUTICALS LIMITED

CLINUVEL PHARMACEUTICALS LTD (ASX: CUV; NASDAQ INTERNATIONAL DESIGNATION ADR: CLVLY; XETRA-DAX: UR9) is a global and diversified biopharmaceutical company focused on developing and commercialising treatments for patients with genetic, metabolic, and life-threatening disorders, as well as healthcare solutions for the general population.

As pioneers in photomedicine and understanding the interaction of light and human biology, CLINUVEL's research and development has led to innovative treatments for patient populations with a clinical need for systemic photoprotection, DNA repair and acute or life-threatening conditions. These patient groups range in size from 5,000 to 45 million worldwide. CLINUVEL's lead compound, SCENESSE® (afamelanotide 16mg), was approved by the European Commission in 2014, the US Food and Drug Administration in 2019 and the Australian Therapeutic Goods Administration in 2020 for the prevention of phototoxicity (anaphylactoid reactions and burns) in adult patients with erythropoietic protoporphyria (EPP). More information on EPP can be found at http://www.epp.care. Headquartered in Melbourne, Australia, CLINUVEL has operations in Europe, Singapore, and the USA. For more information, please go to http://www.clinuvel.com.

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

Head of Investor Relations
Mr Malcolm Bull, CLINUVEL PHARMACEUTICALS LTD

Investor Enquiries
https://www.clinuvel.com/investors/contact-us

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 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); our ability to achieve expected safety and efficacy results 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, 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® 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 based products; decisions by regulatory authorities regarding approval of our products as well as their decisions regarding label claims; any failure 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 the forecasts and estimates is available on request. Past performance is not an indicator of future performance.

www.clinuvel.com

Level 11
535 Bourke Street
Melbourne - Victoria, Australia, 3000

T +61 3 9660 4900 F +61 3 9660 4909