CLINUVEL

COMPANY ANNOUNCEMENT

PROGRESS OF CLINUVEL'S DNA REPAIR PROGRAM

Xeroderma pigmentosum (XP) patients dosed with afamelanotide in CUV156

Melbourne, Australia, 23 December 2021	ASX:	CUV
	XETRA-DAX:	UR9
	NASDAQ INTERNATIONAL DESIGNATION:	CLVLY

EXECUTIVE SUMMARY:

- First systemic therapy globally in genetic disorder XP
- Afamelanotide expanded from systemic photoprotection to DNA repair therapy of the skin
- Two XP-C patients have received afamelanotide in study CUV156
- No safety issues have been observed to date

CLINUVEL PHARMACEUTICALS LTD today announced that two xeroderma pigmentosum (XP) patients have received afamelanotide treatments in the CUV156 study, part of the Company's DNA Repair Program. The patients have been diagnosed with the XP-C complementation variant, a genetic defect which causes insufficient repair of ultraviolet (UV) provoked DNA damage of the skin. As a consequence of a specific genetic defect, XP-C patients belong to the group at highest risk of skin cancer following UV light exposure, necessitating multiple surgical interventions and often having a relatively short life span.

AFAMELANOTIDE DNA REPAIR PROGRAM IN XP

It is believed that afamelanotide is able to assist the DNA damage repair process, known as nucleotide excision repair (NER), in XP patients. A first European XP expert centre has been trained to administer afamelanotide implants as part of the Phase II CUV156 study. The main objective of this first DNA Repair study is to evaluate the safety of afamelanotide in XP patients. To date, no safety issues have been observed.

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.

The CUV156 study focuses on the safety profile of afamelanotide in XP patients and seeks to

1. quantify whether treatment can increase protection from UV,
2. reduce DNA photoproducts, and
3. 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 collaborated with expert physicians to develop global assessment tools and patient reported outcomes for use in the study, in order to evaluate disease severity in this population.

In 2022, further studies in the DNA Repair Program are planned to evaluate patients with both the XP-C and XP-V complementation variants, and healthy volunteers of fair skin complexion serving as a control group.

COMMENTARY

"As no other attempt has ever been made to treat XP patients systemically, the significance of conducting this study with afamelanotide is regarded as a breakthrough by the medical community and regulatory authorities," CLINUVEL's Head of Clinical Operations, Dr Pilar Bilbao said.

"Since XP-C patients have a relatively short life span, and given the high frequency of skin cancers, our aim is to evaluate the safety of the proposed afamelanotide therapy in the first six patients as part of CUV156 study.

"CLINUVEL's overall aim is distinct and clear: we expand from systemic photoprotection to DNA repair therapy. All our systemic and topical products in the DNA Repair Program will address patients and individuals at highest risk of solar damage", Dr Bilbao concluded.

– 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, systemic, and life-threatening, acute 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 as the world's first systemic photoprotective drug for the prevention of phototoxicity (anaphylactoid reactions and burns) in adult patients with erythropoietic protoporphyria (EPP). More information on EPP can be found at https://www.epp.care. Headquartered in Melbourne, Australia, CLINUVEL has operations in Europe, Singapore and the USA. For more information, please go to https://www.clinuvel.com.

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 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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