CLINUVEL

MEDIA RELEASE

CLINUVEL expands DNA Repair Program

SCENESSE® (afamelanotide 16mg) to be evaluated in xeroderma pigmentosum variant (XP-V)

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CLINUVEL has expanded its clinical program to evaluate the DNA reparative potential of afamelanotide in skin cells which have been damaged by ultraviolet (UV) and sun exposure. The program now includes patients with the rare disorders XP-V and XP-C. Having reached agreement with clinical and academic experts, CLINUVEL will generate clinical data on the safety and efficacy of SCENESSE® (afamelanotide 16mg).

"XP patients are at extreme risk of skin cancer – up to 10,000 times that of the general population – due to their inability to repair damage caused by UV and sunlight, known as photodamage," CLINUVEL's Chief Scientific Officer, Dr Dennis Wright said. "Afamelanotide has been shown to protect skin from UV and light, and repair photodamage. We are now working to confirm this concept in clinical trials with both XP patients and healthy volunteers."

UV radiation penetrates into 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, including melanoma.

Human biology contains complex mechanisms to protect itself from UV damage and restore cellular DNA to its original state. 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.

Afamelanotide, the active ingredient in SCENESSE®, improves the function of skin cells which have incurred photodamage and assists these cells to repair DNA through several mechanisms, including nucleotide excision repair (NER). CLINUVEL is conducting clinical trials in XP-C and XP-V patients, as well as healthy volunteers, to evaluate the safety and efficacy of afamelanotide as a DNA regenerative therapy.

"Up to two billion individuals of fair-skinned complexion are known to have defects in UV protective and DNA repair processes, including NER, increasing their long-term risk of skin cancer," Dr Wright said. "XP patients are at the most extreme risk and serve as a model for what happens if UV-induced damage is left unrepaired.

"I am pleased that we have been able to reach agreement with global XP experts to expand the DNA Repair Program and evaluate SCENESSE® in XP-V patients and look forward to first results – pending the COVID-19 pandemic – in 2021," Dr Wright said.

– End –

ABOUT XERODERMA PIGMENTOSUM

XP is a group of eight rare disorders causing extreme UV sensitivity leading to skin cancers, defects in development and neural 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(s).

XP-C results from a defect in one of the genes (chromosome 3p25.1) responsible for replicating proteins involved in a DNA repair process known as nucleotide excision repair (NER). Inefficient NER causes the accumulation and replication of UV-induced DNA lesions (photoproducts) in skin, leading to aggressive and recurrent skin cancers. Due to the frequency and spread of skin cancers during adulthood, XP-C patients have a median survival of 30 years. A small subset of XP-C patients develop neurological disorders, leading to developmental delay and sensory loss.

XP-V is caused by a defect of the POLH gene (chromosome 6p21.1-6p12) causing a disturbance in DNA translesion synthesis of UV-induced pyrimidine dimers (photoproducts). Pyrimidine dimers are molecular lesions formed within the DNA strands. The disease is autosomal recessive in nature (the patient carrying two copies of the affected gene). XP-V patients typically develop skin cancer(s) during late adolescence and adulthood. In this variant, patients have a dysfunction or malfunction of polymerase (pol)eta, an enzyme required to ensure DNA translesion synthesis of skin cells, a process required after sun exposures and sunburns.

Further resources – DNA Damage and Repair

CLINUVEL has published an in-depth video on DNA damage and repair and the eight XP complementation groups. For more details see: https://www.youtube.com/watch?v=9kZgZ0_Ip-M.

CLINUVEL's Scientific Communiqué Series provides an extensive overview of DNA damage and repair, with Communiqué VIII focused on DNA Repair Mechanisms and Communiqué IX looking at the role of the Melanocortin-1 Receptor (MC1R) in DNA Repair.

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

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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 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 2020 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.

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