CLINUVEL

COMPANY ANNOUNCEMENT

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

DNA Repair Program expanded to patients diagnosed with XP-V

Melbourne, Australia, 24 March 2021	ASX: XETRA-DAX: NASDAQ INTERNATIONAL DESIGNATION:	CUV UR9 CLVLY

CLINUVEL today announced that it has reached agreement with clinical and academic experts to expand its DNA Repair Program to patients diagnosed with xeroderma pigmentosum-variant (XP-V). The Program commenced in 2020, evaluating SCENESSE® (afamelanotide 16mg) in XP-C patients.

"The progression of making afamelanotide available to a further group of XP patients, who are extremely affected by ultraviolet (UV) and sun damage, is logical," CLINUVEL's Clinical Operations Manager, Dr Pilar Bilbao said. "We had identified that both XP-C and XP-V patients are most likely to benefit from the hormonal therapy we have developed.

"The drug's benefit will be analysed by observing these patients' skin reactions to UV light and by analysing markers in skin samples such as pyrimidine dimers, which really are indicators of the inability to repair damaged strands of DNA. Given our pioneering work on providing systemic photoprotection, we are in the best position to make a positive impact on XP patients' lives," Dr Bilbao said.

XP-V VERSUS XP-C

Clinically, it is apparent that both XP-V and XP-C populations are extremely prone to developing skin cancers. In XP-C patients a defect in a DNA repair mechanism (nucleotide excision repair or NER) directly leads to skin cancers. XP-V patients have a genetic defect (POLH gene) leading to an increase of mutations, giving rise to phototoxicity and increased risk of skin carcinogenesis.

XP-V and XP-C comprise an estimated 20% and 40%, respectively, of the global XP patient population. The prevalence of XP-V ranges from 1:450,000 to 1:1,000,000 worldwide.

CLINICAL TRIAL PROGRAM (CUV150 TO CUV153), DNA REPAIR

CLINUVEL's current DNA Repair Program aims to confirm the clinical effect of SCENESSE® in assisting the protection and regeneration of DNA in XP patients, with healthy volunteers of fair skin complexion serving as a control group. Treated groups will receive afamelanotide either every one, two, or three weeks for a duration of up to four months. Skin samples (biopsies) of exposed skin areas will be taken for laboratory analyses of DNA damage before and after drug administration. Patients will be frequently monitored,

including complete skin examinations before and during treatment. Quality of life questionnaires will assist in evaluating the possible impact of the treatment on patients' wellbeing.

The first XP-C patient was treated with SCENESSE® under a Special Access Program in 2020. No significant or notable adverse events were observed or reported by the expert clinical centre responsible for medical care.

Clinical trial	Phase	Target population	Participants
CUV150	Phase IIb	XP-C	n = 6
CUV151	Phase II	Healthy volunteers	n = 10
CUV152	Phase IIb	XP-C and XP-V	n = 6
CUV153	Phase II	XP-V	n = 6

Table 1: Clinical trials forming CLINUVEL's current DNA Repair Program. The Program has been expanded to evaluate afamelanotide in XP-V patients.

Depending on ongoing COVID restrictions in leading university hospitals, the Ethics Committees and hospital administrations are expected to allow the start of the XP studies once the risk of infection is assessed as acceptable.

A limited number of clinical trials have been conducted with XP patients, and there is currently no efficacious therapy available for them.

Authorities carefully evaluate the requests of a pharmaceutical company seeking permission to subject these high-risk patients to a possible drug therapy, and it is especially important in these patients, given the high mortality and morbidity of XP patients. Various clinical centres and authorities have responded positively to CLINUVEL's XP program.

SCENESSE® MODE OF ACTION

Afamelanotide's clinical mode of action provides anti-oxidation, vascular activity, reduction of tissue fluid, and improvement of inflammatory signs. To provide its pharmacological activity, the drug binds to a number of human cells, predominantly to the melanocortin-1 and melanocortin-4 receptors (MC1R and MC4R).

Importantly, afamelanotide offers systemic photoprotection by preventing photodamage and improving the regeneration of skin cells. Clinically, afamelanotide has been confirmed to show reduction of DNA damage caused by UV radiation and visible light (oxidative damage and pyrimidine dimers). Further research has shown the ability of afamelanotide and other melanocortin molecules to assist skin cells in DNA repair mechanisms (NER).

– 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.
XP-C results from a defect in one of the genes (chromosome 3p25.2) 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 eta, an enzyme required to ensure DNA translesion synthesis of skin cells, a regenerative 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

Media enquiries
Monsoon Communications
Mr Rudi Michelson, 61 411 402 737, rudim@monsoon.com.au

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 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.

www.clinuvel.com

Level 11
535 Bourke Street
Melbourne - Victoria, Australia, 3000
T +61 3 9660 4900
F +61 3 9660 4999