ASX Announcement

**ASX: CUV**
**Nasdaq International Designation: CLVLY**
**XETRA-DAX: UR9**

# First patient dosed in SCENESSE® DNA Repair Program

*Xeroderma pigmentosum (XP) patient receives SCENESSE® treatment*

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**Note to editors: CLINUVEL is releasing in-depth infographics and a video explaining the mechanisms of action in XP and the overall DNA repair process. For updates, follow:**
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Melbourne, Australia, 15 September 2020

CLINUVEL PHARMACEUTICALS LTD today announced that the first patient diagnosed with xeroderma pigmentosum (XP-C) has received SCENESSE® (afamelanotide 16mg).[1] The Special Access Program of one patient is part of CLINUVEL's DNA Repair Program.

CLINUVEL is evaluating SCENESSE® in a staged clinical program to confirm the drug's ability to assist repair of ultraviolet (UV)-induced DNA damage of skin. SCENESSE® is currently prescribed as standard of care for erythropoietic protoporphyria (EPP) in the USA and Europe.

**SCENESSE® IN XERODERMA PIGMENTOSUM**

The first XP-C patient serves to confirm the safety of the product. Given the high mortality rate in XP-C, the safety of afamelanotide will be evaluated during 42 days of treatment.

| Program | Objectives |
|---|---|
| Special Access Program<br>XP-C (n=1) | Safety<br>Clinical observations – expert clinician |
| CUV150 (Phase IIa pilot)<br>XP-C (n=6) | Safety<br>DNA repair – biopsies and assays to evaluate photoproducts and repair mechanisms<br>Disease severity and quality of life assessments |
| CUV151 (Phase IIa)<br>Healthy volunteers (n=10) | DNA repair – biopsies and assays to evaluate photoproducts and repair mechanisms |

**Figure 1: SCENESSE® DNA Repair Program – studies 2020/21**

After confirmation of the safety of the drug product, the DNA Repair Program will proceed with an open-label Phase II study involving six XP-C patients (CUV150) and a control study enrolling 10 healthy volunteers (CUV151) whereby clinical and histological (skin biopsies) evaluation of afamelanotide treatment will be undertaken in both groups.

Details of the sponsored studies CUV150 and CUV151 will be released in the following weeks.

**SCENESSE® DNA Repair Program**

Scientific evidence supports the use of afamelanotide, the active ingredient in SCENESSE®, to protect skin from UV and light (systemic photoprotection), and repair UV-induced DNA damage. As part of a staged clinical program, CLINUVEL has worked with global experts to identify and design clinical objectives which focus on clinically meaningful and relevant study endpoints, including assessment of DNA photoproducts (chemical reactions within DNA strands), repair of DNA damage, and evaluation of the treatment impact on patients' quality of life.

**Xeroderma Pigmentosum (XP) patients incur accelerated DNA damage**
Ultraviolet (UVB of wavelengths 290-320 nm and UVA of 320-400 nm) and high energy visible (HEV, 400-600 nm) light penetrate human skin leading to oxidative stress and damage to the DNA helix within the nucleus of skin cells. The photodamage consists of loss of connective tissues and changes to the DNA strands (generation of photoproducts).

XP patients exhibit extreme deficiency in repair of UV-provoked DNA damage, characterised as a model for the most severe form of photodamage. XP has a high rate of mortality with a median survival of 30 years and affects approximately 1:450,000 individuals in the European population.

XP has eight variants (XP-A to G, and V), reflecting eight different genes involved. Each XP gene is involved in nucleotide excision repair (NER), a process of identifying, "snipping", removing and replacing damaged sequences in DNA. If left unrepaired, damaged DNA can replicate and increase the risk of skin cancers, including melanoma.

Due to the inability to initiate or complete the NER process, XP patients are at 10,000- and 2,000-fold risk of non-melanoma and melanoma skin cancers, respectively. Most XP patients will experience the first skin cancer before adolescence, while the leading cause of death remains progressive non-melanoma skin cancers and melanoma in the third decade. Due to the extreme rate of these malignancies, surgical intervention is required frequently, resulting in loss of extremities, facial anatomy such as ears, and eyesight.

**Commentary**
"Having recently announced the scope and aims of the staged DNA Repair Program, it is important to see the first XP patient treated under the Special Access Program," CLINUVEL's Chief Scientific Officer, Dr Dennis Wright said. "We have worked closely with the expert clinic to facilitate this first patient's treatment and we await feedback on the response.

"The use of SCENESSE® in XP, being a model studied for DNA repair originating from UV exposure, is exciting and represents a potential breakthrough for individuals at higher risk of photodamage. Our team has methodically worked towards this one objective and will be the first company to make the final clinical link between afamelanotide and reduction of the risk of skin cancers by addressing DNA damage caused by UV exposure. The thorough work towards the safety profile of SCENESSE® gives us comfort to finally evaluate its use in this group of patients," Dr Wright said.

"We seek to provide meaningful benefit to XP patients, and these results will serve a wider population of fair-skinned individuals at risk of developing skin cancers," CLINUVEL's Clinical Operations Manager, Dr Pilar Bilbao said. "The next 12 months will be exciting for many patients, their families, the clinical experts and our own teams."

**- End -**

[1] SCENESSE® (afamelanotide 16mg) is approved in the European Union as an orphan medicinal product for the prevention of phototoxicity in adult patients with erythropoietic protoporphyria (EPP). SCENESSE® is approved in the USA to increase "pain- free" light exposure in adult EPP patients with a history of phototoxicity. Information on the product can be found on CLINUVEL's website at www.clinuvel.com.

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

**About CLINUVEL PHARMACEUTICALS LIMITED**
CLINUVEL PHARMACEUTICALS LTD (ASX: CUV; NASDAQ INTERNATIONAL DESIGNATION ADR: CLVLY; XETRA-DAX: UR9) is a global biopharmaceutical company focused on developing and delivering treatments for patients with a range of severe genetic, skin, and systemic disorders. As pioneers in photomedicine and understanding the interaction of light and human biology, CLINUVEL's research and development initially has led to innovative treatments for patient populations with a clinical need for photoprotection and repigmentation. 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 and the US Food and Drug Administration in 2019 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. CLINUVEL is advancing its portfolio of melanocortins, among which is PRÉNUMBRA® for the treatment of several critical disorders. Headquartered in Melbourne, Australia, CLINUVEL has operations in Europe, Singapore, and the USA. For more information please go to http://www.clinuvel.com.

SCENESSE® and PRÉNUMBRA® are registered trademarks 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 2019 Annual Report and 2020 Preliminary Final 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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