CLINUVEL

ASX ANNOUNCEMENT

Melbourne, Australia, 5 July 2024

ASX: CUV | **Börse Frankfurt**: UR9 | **ADR Level 1**: CLVLY

Afamelanotide Assists DNA Repair Response Following UV Radiation

Results presented at the British Association of Dermatologists Meeting in Manchester

EXECUTIVE SUMMARY

Afamelanotide in study CUV151, skin biopsy results:

- differentially expressed genes (DEGs) in skin reduced by a factor of 3.4 (from 625 to 183)
- afamelanotide assists DNA repair after UV damage (UV-irradiated skin)
- results support reduction in UV-erythema dose-response, photoproducts (CUV151 previously released results: 2 February and 15 August 2023)
- results first presented at British Association of Dermatology Meeting, 4 July 2024

CLINUVEL today announced the final set of results from a study (CUV151) evaluating the DNA-repair capacity of afamelanotide on skin of healthy volunteers exposed to ultraviolet (UV) radiation. The study was conducted at Salford Royal Hospital, Manchester, a centre globally acknowledged for its expertise in assessing the effects of UV-induced skin damage.

Afamelanotide leads to reduction of differentially expressed genes (DEGs) in skin

Analysing biopsies from seven patients with fair skin types (Fitzpatrick I-III[1]) – taken prior to, and six days after, afamelanotide treatment – RNA sequencing[2] illustrated that, without afamelanotide, UV-irradiation resulted in 625 differentially expressed genes (DEGs) in comparison to non-irradiated skin. With afamelanotide, the DEGs between irradiated versus non-irradiated skin reduced to 183, a factor 3.4 less DEGs ($p<0.05$). The genes evaluated are found as being crucial in the regulation of DNA repair and inflammatory reactions following solar and UV exposure.

These results complement those analysed in 2023, illustrating that skin damage – characterised by the UV-erythema ("provoked sunburn damage") dose response – had been reduced ($p=0.018$), and that DNA-damage markers such as γH2AX and cyclobutane pyrimidine dimers[3] had been significantly reduced ($p<0.01$).

The latest results from CUV151 were presented overnight at the British Association of Dermatologists meeting in Manchester.[4]

Relevance of the CUV151 results

For the overall XP-DNA Repair Program, the RNA sequencing results indicate that critical genes expressed after UV-damage can be positively affected with afamelanotide treatment.

For the general population, and specifically individuals with a fair skin type who easily sun burn, the results indicate that afamelanotide can reduce oxidative damage and inflammatory reactions after sun exposure and skin damage.

Commentary

"The results from RNA sequencing complement the earlier results we saw from immunohistochemistry, in that afamelanotide consistently seems to assist repair of UV-damaged DNA in the skin," CLINUVEL's Chief Scientific Officer, Dr Dennis Wright said.

"The significance of these results evaluating the use of afamelanotide in reducing oxidative and inflammatory damage caused by UV is high for those at high risk of solar damage, sunburn and skin cancers, hence we will repeat and confirm these results in a final study," Dr Wright concluded.

– END –

[1] The Fitzpatrick Skin Type is a numerical classification of human skin colour, from type I skin that always burns, to type VI, dark skin that never burns.

[2] RNA sequencing evaluates gene expression of cells and transcription taking place.

[3] Cyclobutane pyrimidine dimers (CPDs) are defined as photoproducts, or single-strand DNA defects of skin cells, incurred after solar exposure.

[4] Peak, M., et al., (2024, July 4). The effects of afamelanotide on ultraviolet radiation-induced acute inflammatory and DNA repair responses in healthy human skin. British Association of Dermatologists 104th Annual Meeting, Manchester.

About CLINUVEL PHARMACEUTICALS LIMITED

CLINUVEL (ASX: CUV; ADR LEVEL 1: CLVLY; Börse Frankfurt: UR9) is a global specialty pharmaceutical group focused on developing and commercialising treatments for patients with genetic, metabolic, systemic, and life-threatening, acute disorders, as well as healthcare solutions for specialised populations. As pioneers in photomedicine and the family of melanocortin peptides, CLINUVEL's research and development has led to innovative treatments for patient populations with a clinical need for systemic photoprotection, assisted DNA repair, repigmentation and acute or life-threatening conditions who lack alternatives.

CLINUVEL's lead therapy, SCENESSE® (afamelanotide 16mg), is approved for commercial distribution in Europe, the USA, Israel, and Australia as the world's first systemic photoprotective drug for the prevention of phototoxicity (anaphylactoid reactions and burns) in adult patients with erythropoietic protoporphyria (EPP). 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.

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 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 2023 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.

Contact:

Tel: +61 3 9660 4900
Fax: +61 3 9660 4909
Email: mail@clinuvel.com
Australia (Head Office), Level 22, 535 Bourke Street, Melbourne, Victoria, 3000, Australia