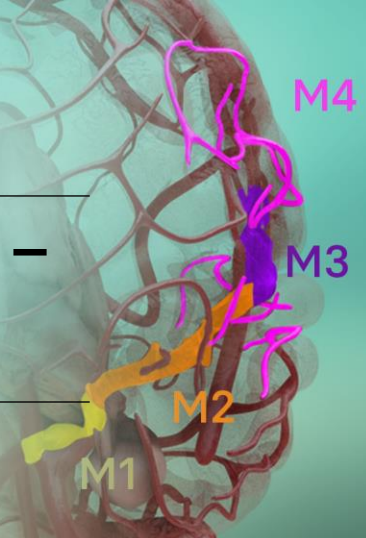


Afamelanotide in stroke (AIS) – positive preliminary results

Neurological impairment evaluated up to day 8 following acute stroke



Melbourne, Australia, 15 March 2022

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EXECUTIVE SUMMARY

- First use of afamelanotide in arterial ischaemic stroke (AIS) patients
- Drug well tolerated
- Five of six patients showed improved neurological functions (NIHSS¹ scores)
- Final results on day 42 of the trial to follow.

CLINUVEL today released positive preliminary results from its pilot study (CUV801) in arterial ischaemic stroke (AIS), evaluating afamelanotide in six adult patients. The trial focused on the safety of multiple afamelanotide doses and patient recovery over 42 days, using the National Institutes of Health Stroke Scale (NIHSS¹) and brain imaging (CTP and MRI²).

“This is the first time that a melanocortin has been administered to stroke patients. No adverse drug reactions were reported, and a meaningful improvement was seen in five of the six patients’ health by day 8,” CLINUVEL’s Head of Clinical Operations, Dr Pilar Bilbao said. *“We are awaiting the results from the final evaluation of the patients at day 42, which will give us further data on afamelanotide as a possible treatment for this life-threatening disease.”*

STUDY DESIGN CUV801

The CUV801 study was conducted by the Stroke Unit of The Alfred Hospital in Melbourne, Australia. Patients with an arterial blockage, who were ineligible to receive standard treatment (consisting of clot removal and/or dissolution³), were administered afamelanotide as a single therapy.

The six adult patients had suffered mild to moderate strokes (NIHSS scores 1-15) due to a clot lodged within the second branch of one of the three major brain arteries – beyond A1/M1/P1.⁴ Upon hospital admission, the patients received routine brain scanning (CTP), with follow up brain imaging not involving further radiation (MRI) on day 3 and day 9, and their disability assessed through neurological tests (NIHSS) throughout the study period.

Patients were treated with up to four doses of afamelanotide on days 0 (admission), 1, 7, and 8.

The primary objective of the study was to determine the safety of afamelanotide, with clinical assessment as a secondary measure.

PRELIMINARY NEUROLOGICAL RESULTS

All six patients suffered a stroke of the left half of the brain and carried an increased risk of stroke due to a history of cardiovascular disease, elevated blood pressure, or diabetes type II.

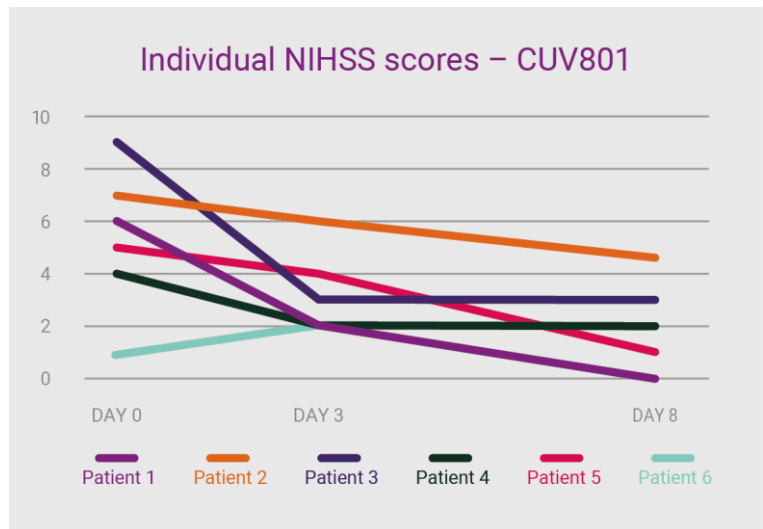
The brain scans were performed to quantify changes in blood flow to the ischaemic penumbra (salvageable brain cells), with further evaluation made of neurological function as an indication of recovery from the brain injury.

Four patients were administered only two doses of afamelanotide, one each on days 0 and 1, since the treating physicians judged that these patients had already recovered well. Two of the six patients received the total four doses.

Five patients were discharged from hospital by day 9. One patient with a complex medical history passed away following a second stroke, suffered on day 5 while hospitalised. This fatal event was assessed by the specialist treating neurologists and the study safety committee as unrelated to the administration of afamelanotide.

Analyses of the NIHSS scores up to day 8 indicated that five of the six stroke patients showed neurological improvement and strong degree of functional recovery. A reduction in NIHSS score translates to an improvement in neurological function (including language, and facial and limb weakness).

Five of six patients showed a clinically meaningful improvement (decrease) at day 8, expressed as a change equal or greater to four points on the NIHSS. The median NIHSS score for the five patients was 6 upon admission, and overall improvement with a median score of 2 on day 8, and five out of six patients were assessed - according to NIHSS - as mild to symptom-free by day 8.



The graphic above shows the NIHSS preliminary scores of all six patients, assessed at days 0, 3, and 8.

Five patients are being followed up for six weeks (day 42), after which a final evaluation of the neurological functions and brain injury will be made, while long-term disability is being assessed through the modified Rankin Scale (mRS).

- END -

¹ the National Institutes of Health Stroke Scale (NIHSS) consists of 15 tests to evaluate neurologic functioning and impairment caused by acute cerebral infarction (stroke). A clinical assessment is made on the basis of consciousness, language, neglect, visual-field loss, extraocular movement, motor strength, muscle control, speech, and sensory loss. A trained clinician assesses the patient's ability to answer questions and perform specific activities. In general, the evaluation is made in less than 10 minutes.

² computed tomography perfusion, magnetic resonance imaging

³ endovascular thrombectomy, intravenous recombinant tissue plasminogen activator

⁴ anterior cerebral artery, middle cerebral artery, posterior cerebral artery

MODE OF ACTION AFAMELANOTIDE IN STROKE

Scientific progress has demonstrated melanocortins, including afamelanotide, provide a positive effect on diseases of the central nervous system (CNS). Afamelanotide is known to offer neuroprotection and act as a potent anti-oxidative hormone. The drug possesses further therapeutic benefits, activating vessels, reducing fluid formation, protecting critical nerve and brain tissue, and restoring the blood brain barrier (BBB: a critical defence mechanism protecting the brain). The drug therapy is expected to improve the blood flow and increase the delivery of oxygen and nutrients to deprived brain tissue.

About CLINUVEL PHARMACEUTICALS LIMITED

CLINUVEL (ASX: CUV; ADR LEVEL 1: CLVLY; XETRA-DAX: 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 the general population. 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, DNA repair, repigmentation and acute or life-threatening conditions who lack alternatives.

COMPANY ANNOUNCEMENT

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>.

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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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