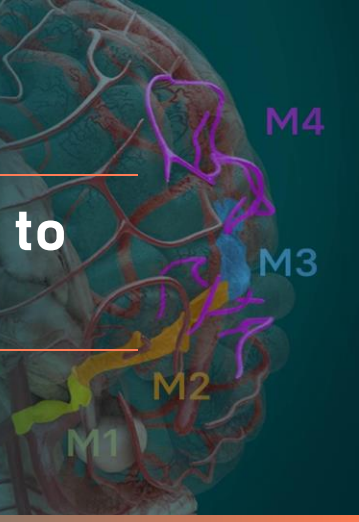
CLINUVEL

COMPANY ANNOUNCEMENT

CLINUVEL escalates PRÉNUMBRA® to moderate/severe stroke patients

First three patients with mild stroke tolerate drug in CUV803 study



Melbourne, Australia, 9 May 2023	ASX:	CUV
	Börse Frankfurt:	UR9
	ADR Level 1:	CLVLY

Executive Summary

- Escalation of PRÉNUMBRA® Instant to moderate-to-severe and severe stroke (NIHSS 16-42)
- Dosing well tolerated in three mild ischemic stroke patients (NIHSS 1-15)
- Preliminary reports of functional improvement in all three patients

The first three patients diagnosed with arterial ischaemic stroke (AIS) have been treated with PRÉNUMBRA® Instant (afamelanotide), as part of CLINUVEL's ongoing CUV803 clinical study.

All three patients were admitted to specialist stroke centres with mild to moderate strokes (measured by the National Institutes of Health Stroke Scale[1], scores 1-15) and showed functional improvement following PRÉNUMBRA® dosing, with the drug well tolerated. The CUV803 study will now be expanded to include patients who have suffered moderate to severe and severe strokes (NIHSS 16-42).

NIHSS Scores	
Mild	1-4
Moderate	5-15
Moderate to severe	16-20
Severe	21-42

The CUV803 study marks the first time that afamelanotide has been administered to stroke patients at a flexible and escalating dose, who are at risk of suffering recurrent life-threatening vascular accidents.

"*We have arrived at an important landmark as we learned that the flexible PRÉNUMBRA® dosing was well tolerated by the first three patients with mild or moderate ischemic strokes,*" CLINUVEL's Head of Clinical Operations, Dr Pilar Bilbao said. "*From our flow of news, it may be clearer that – over the years – we have gradually widened the envelope of afamelanotide, providing data on its safety profile which have remained remarkably constant. This chosen strategy allows us to use the molecule for a wide range of metabolic and neurological conditions with different formulations and dosing frequencies.*"

Afamelanotide in stroke

Ischaemic stroke is caused by a clot blocking blood supply to the brain, leading to immediate permanent brain damage and the risk of further tissue death in the surrounding area due to fluid formation and inflammation. Afamelanotide, an analogue of a naturally occurring hormone, is understood to protect brain tissue and increase blood flow following

a stroke, as well as acting as an anti-oxidant and anti-oncotic (anti-swelling) agent, which could ultimately limit the extent of brain damage and disability incurred.

CLINUVEL's first clinical trial (CUV801) of afamelanotide in AIS patients used a controlled-release implant formulation, with the drug well tolerated and five of six AIS patients diagnosed with mild to moderate stroke showing improved neurological function following treatment. The PRÉNUMBRA® Instant formulation is expected to provide a faster clinical response and provide clinicians the ability to personalise treatment.

First efficacy results from CUV803 are expected in late 2023.

– END –

[1] The National Institutes of Health Stroke Scale (NIHSS) consists of 15 tests to evaluate neurologic functioning and impairment caused by a 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. The scale categorises severity according to mild (score 1-4), moderate (5-15), moderate-severe (16-20) and severe (≥21).

About CLINUVEL PHARMACEUTICALS LIMITED

CLINUVEL (ASX: CUV; ADR LEVEL 1: CLVLY; Frankfurt Börse: 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 specialized 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

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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), CYACÊLLE®, 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®, CYACÊLLE®, 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 2022 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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