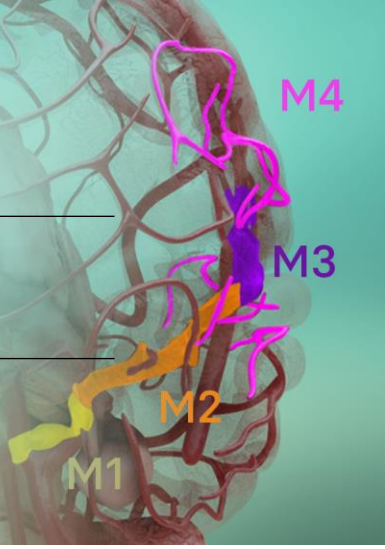
CLINUVEL

COMPANY ANNOUNCEMENT

PRÉNUMBRA® for stroke

Flexible PRÉNUMBRA® Instant formulation
to be evaluated in first clinical indication



Melbourne, Australia, 28 July 2022	ASX: XETRA-DAX: Level 1 ADR:	CUV UR9 CLVLY

Watch CLINUVEL's Head of Clinical Operations, Dr Pilar Bilbao, discuss the Company's stroke program and the upcoming CUV803 study here.

EXECUTIVE SUMMARY

- PRÉNUMBRA® Instant to be evaluated in arterial ischaemic stroke, first clinical indication
- Flexible dosing option
- CUV803 study to commence in H2 2022

CLINUVEL today announced that it intends to evaluate its drug candidate PRÉNUMBRA® Instant (afamelanotide) as a treatment for patients diagnosed with arterial ischaemic stroke (AIS) in its next clinical trial (CUV803). AIS is the first clinical target for CLINUVEL's flexible PRÉNUMBRA® formulations.

PRÉNUMBRA® Instant – fast-acting, flexible afamelanotide dose for stroke

PRÉNUMBRA® Instant is the second pharmaceutical product developed by CLINUVEL. The product is designed to allow physicians to administer a fast-acting, flexible dosage formulation of the active ingredient afamelanotide in acute care. Afamelanotide, a melanocortin drug, is shown to provide anti-oxidative, anti-oncotic and vaso-active effects.

Stroke was selected as the first clinical target for PRÉNUMBRA® Instant, enabling physicians to personalise treatment in acute care. CLINUVEL's recent stroke study (CUV801) showed afamelanotide to be well tolerated in a standard dose, with the majority of patients experiencing a strong functional recovery.

The CUV803 study will generate further data of afamelanotide at higher and more frequent dosing to understand the safety and clinical benefit of the new dosage form. CUV803 is expected to commence during the second half of 2022, pending regulatory and ethics approvals. Further clinical targets for PRÉNUMBRA® Instant are under evaluation, including other disorders of the central nervous system (CNS).

Working under an exclusive agreement the PRÉNUMBRA® Instant presentation is manufactured according to current Good Manufacturing Practice (cGMP) guidelines for use in clinical trials.

PRÉNUMBRA® Instant contains the same active pharmaceutical ingredient as CLINUVEL's commercially available SCENESSE® (afamelanotide 16mg) product.[1]

Commentary

"After six years of post-marketing experience with SCENESSE®, both authorities and our team have gained confidence in the longer-term safety of afamelanotide. Logically, it was now the time to accelerate our clinical

program with a more flexible dosage form of afamelanotide," CLINUVEL's Head of Clinical Operations, Dr Pilar Bilbao said.

"In having defined the potential benefit-risk profile of flexible afamelanotide dosing, we identified those patient groups for whom this product would be of greatest value. Based on extensive analyses, acute vascular injuries would be a potential target, although we recognise there may be other neurological conditions which could benefit from PRÉNUMBRA® Instant.

"Our teams have an acute awareness that the history of developing pharmaceutical treatments for stroke has not been successful, with many companies having abandoned a program. But by focusing on clinical safety and the therapeutic window in AIS, we made an important first clinical development step, as seen from the first results from the CUV801 study. We are now adding to this body of knowledge with a view to being able to offer a range of treatment options for stroke physicians and their patients in future," Dr Bilbao said.

Addressing unmet medical need in stroke

Ischaemic strokes account for around 85% of the estimated 15 million suffered worldwide each year. Stroke is the leading cause of serious, long-term disability in the United States. Estimates vary, but approximately 80% of stroke patients who report to hospitals are ineligible for either intravenous thrombolysis (IVT; drug therapy to dissolve a brain clot) or endovascular thrombectomy (EVT; interventional surgery to physically remove a brain clot). Considering the staggering prevalence of stroke, the burden of post-stroke recovery and ongoing disability is of primary public health importance.

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[1] SCENESSE® (afamelanotide 16mg) is approved in the European Union and Australia 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.

Afamelanotide in stroke

Scientific progress has demonstrated melanocortins, including afamelanotide, provide a positive effect on 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 thought to improve blood flow and increase the delivery of oxygen and nutrients to deprived brain tissue.

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, systemic, and life-threatening, acute 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 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), 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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