CLINUVEL

ASX ANNOUNCEMENT

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

Positive preliminary results for PRÉNUMBRA® Instant in stroke patients

Nine arterial ischaemic stroke (AIS) patients completed second afamelanotide study

EXECUTIVE SUMMARY

- CUV803 study complete
- Nine patients with mild (3), moderate (3) and moderate-to-severe (3) stroke treated with PRÉNUMBRA® Instant
- Treatment well tolerated, with mild and transient treatment related adverse events reported
- Functional improvement in 8 out of 9 (88.9%) patients at day 42
- Radiological improvement or stability in 6 out of 9 (66.7%) patients
- Results consistent with reports from earlier CUV801 study evaluating afamelanotide implant formulation in AIS patients

CLINUVEL today released preliminary results from its second clinical study investigating its drug afamelanotide as a treatment for arterial ischaemic stroke (AIS). The CUV803 study enrolled nine adult patients with mild (n=3), moderate (n=3) and moderate-to-severe (n=3) AIS (as measured by NIHSS[1]) at two European specialist stroke treatment units. All patients – who were not eligible for standard of care intravenous thrombolysis (IVT) or endovascular thrombectomy (EVT) – were administered PRÉNUMBRA® Instant (afamelanotide) daily for up to five days.

Preliminary results CUV803

The primary endpoint of the CUV803 study was to evaluate the safety of afamelanotide in stroke patients. The drug was shown to be well tolerated in all nine participants. All treatment-related adverse events were mild, transient, and consistent with the established safety profile for afamelanotide. Two of the three patients with moderate-to-severe stroke (NIHSS scores 17 and 19) passed away due to complications unrelated to afamelanotide treatment. One of these patients died two months after study completion.

Secondary endpoints sought to evaluate the impact of afamelanotide on neurological functions. By day 42, eight out of nine patients (88.9%) demonstrated an improvement in initial stroke symptoms and neurological disability[2] following treatment with afamelanotide, as measured by reduced NIHSS and functional disability[2] scores. Analysis of brain imaging (MRI) showed that the infarct size – the total volume of dead brain tissue due to the stroke – had decreased or stabilised in six of nine patients up to 42 days after treatment.

Global data: treating stroke patients with afamelanotide

Fifteen AIS patients have now been evaluated as part of CLINUVEL's program, either receiving afamelanotide as a subcutaneous injectable implant (CUV801[3], n=6) or liquid (CUV803, n=9).

Review of the data globally suggest the safety profile of afamelanotide in AIS is consistent with that seen in other patient groups. Thirteen of the AIS patients treated with afamelanotide (86.7%) demonstrated functional improvement, while ten (66.7%) showed a reduction or stabilisation of infarct size up to 42 days after treatment.

Commentary

“While considerable progress has been made in treating stroke with approved therapies, a large number of patients remain ineligible for existing therapies,” CLINUVEL’s Chair, Prof Jeffrey Rosenfeld said. “Afamelanotide represents an innovative approach, taking a drug with a long-standing safety profile and evaluating whether a known mechanism of action may provide a therapeutic option for these previously untreated patients.

“With the CUV801 and CUV803 studies we have generated a small, but encouraging, data set that demonstrates the drug’s safety profile in patients with strokes of varying degrees of severity, as well as first indications that patients may benefit from treatment. While the stroke program is not an immediate focus for the business, I expect our teams will be able to use these data to support future decision making that may result in positive outcomes for patients,” Prof Rosenfeld said.

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 antioxidant and anti-oncotic (anti-swelling) agent, which could ultimately limit the extent of brain damage and disability incurred. Following a review of its clinical programs in 2024, CLINUVEL decided to suspend further work in its stroke program to focus on the development of afamelanotide for vitiligo and porphyrias, as well as the development of adrenocorticotropic hormone (ACTH) and PhotoCosmetic product lines.

– 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).

[2] As measured by the modified Rankin scale (mRS).

[3] In CUV801, afamelanotide was administered as 16mg implants up to four times within the first eight days of randomisation, to minor and moderate stroke patients only.

Annex 1: CUV803 STUDY DESIGN AND ENDPOINTS

Name of trial

A Phase IIa, Open Label, Proof of Concept Study to Evaluate the Safety of Aqueous Afamelanotide Solution in Patients with acute Arterial Ischaemic Stroke (AIS) who are ineligible for Intravenous Thrombolysis (IVT) or Endovascular Thrombectomy (EVT)

Primary endpoint

To evaluate the safety of afamelanotide in AIS patients.

Secondary endpoints

Evaluate the impact of afamelanotide on neurological functions in patients with AIS

Identify changes in reperfusion of the ischaemic penumbra in AIS patients, specifically the ischaemic core and/ or the penumbral ischaemic zone (salvageable tissue).

Assess cognitive functions and activities of daily living in AIS patients.

Blinding status

Open label.

Product development status

Good Manufacturing Practice (GMP) Standard.

Treatment method and dose levels

PRÉNUMBRA® Instant Number of trial subjects Up to twelve AIS patients.

Subject selection criteria

To be eligible to enter the study, patients must meet the following inclusion criteria:

- Male or female subjects with a diagnosis of Arterial Ischaemic Stroke (AIS)
- No severe disability prior to stroke
- Written informed consent obtained from patient and or immediate family or carer(s) prior to study-start.

Further safety related exclusion criteria apply.

Trial location

Specialist stroke centres in Europe.

Duration of trial

42 days

Trial standard

In compliance with Good Clinical Practice (GCP) and ICH guidelines.

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.

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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 and PhotoCosmetic products; competition for our products, especially SCENESSE® (afamelanotide 16mg), CYACÊLLE, PRÉNUMBRA®, NEURACTHEL® or products developed and characterised by us as PhotoCosmetics; 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, the UK, Israel, China, Japan, and/or LATAM regions 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®, NEURACTHEL® or products developed as PhotoCosmetics which may lead to the Company being unable to launch, supply or serve its commercial markets, special access programs and/or clinical trial programs; any failures to comply with any government payment system (i.e. Medicare, Medicaid, and U.S. Department of Veteran's Affairs) reporting and payment obligations; uncertainties surrounding the legislative and regulatory pathways for the registration and approval of biotechnology, cosmetic 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, cosmetic industry and related industries; potential changes to tax liabilities or legislation; environmental risks; and other factors that have been discussed in our 2024 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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