CLINUVEL

News Communiqué III, 11 June 2024

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

Fellow Shareholders,

In this News Communiqué III, we update you on the expanding commercial footing we have built, the erythropoietic protoporphyria (EPP) and DNA Repair programs, activities relating to establishing a PhotoCosmetic venture, and expansion of our Investor Relations.

The Communiqué is to be read with the notion that the Company has well managed operational risks over nearly two decades, giving its present strength.

It is my view that the Group has now reached a stage of maturity when more calculated risks can be taken, we have the infrastructure in place, skills and people in key positions and a balance sheet - enabling further expansion.

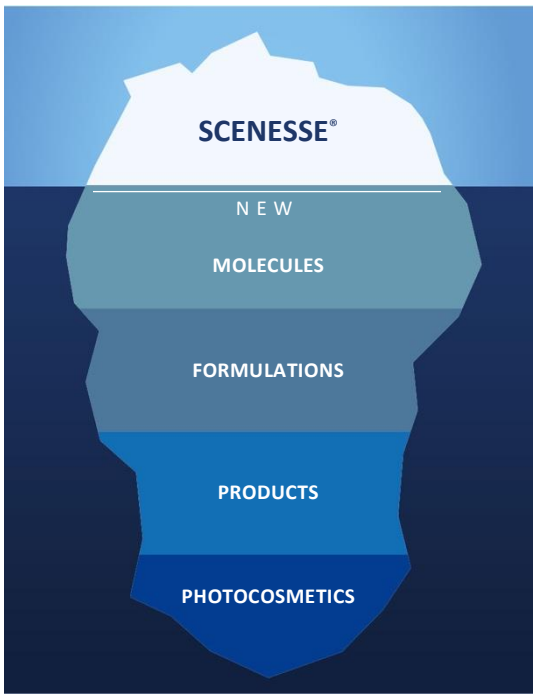
In one of the recent operations meetings, it was apparent that the diversification of the Company has gradually but silently occurred, in development we have:

(i) three melanocortin peptides (including afamelanotide)
(ii) four new formulations
(iii) four new products
(iv) three PhotoCosmetic product lines.

As one of the senior managers stated in the discussion, public markets may only be aware of the tip of the iceberg, while the Group is forming its next generation, kept below the water surface for commercial protection.

Our collective task is to drive these projects and ensure further cost efficiencies to facilitate commercial success. In 2021, we projected A$175M to be spent on our operations over five financial years. With 18 months left on 31 December 2023 we have spent 65% and are just on course to achieve this target. However, we are ahead of our internal forecast with far more cash reserves than originally thought in 2021.

CLINUVEL's Development 2024

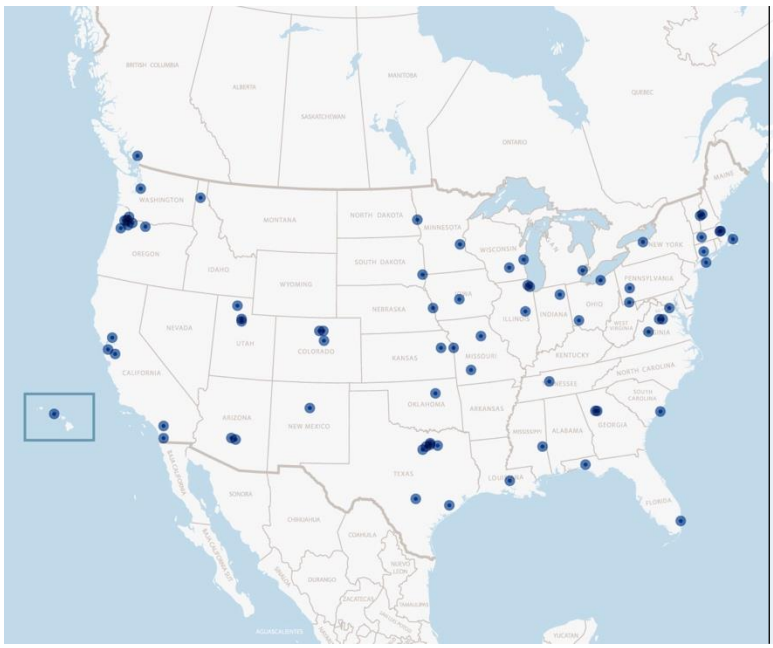


Commercial Update

The rationale building of a melanocortin house was extensively explained during the 2023 Annual General Meeting, and in this construct, we set out to establish a direct distribution system in the US and European Union. Controlling the distribution chain has made much sense to us, as part of a tailored strategy.

To date we have trained and accredited 85 US university and medical centres to prescribe SCENESSE® (afamelanotide). The further ambition is to expand the network to – first – 120, and then go beyond this number in 2025. We are geographically selecting the states where we need to provide current and future access to the drug, understanding the location of known patients. At present we are in 35 states, and we expect to cover 48 states by 2025 subject to patients' needs.

CLINUVEL's US Operations



- 85 Specialty Centers trained & accredited
- target 120 Centers by 2025
- capacity of ~6,000 new vitiligo patients
- establish independent distribution in EPP & vitiligo
- 7-9 implants to revert loss of pigmentation
- optional annual maintenance therapy SCENESSE® in vitiligo

Underlying the strategy was the identification of Board-certified dermatologists and other specialists who have shown to have an expertise and interest in genetic disorders, pigmentary disorders and paediatric populations. At present many of the US Specialty Centers offer their patients phototherapy, UVA and UVB, operating specialised equipment from three lead manufacturers. Since the combination of SCENESSE® and phototherapy seems highly effective, it makes sense to select only those facilities which already operate phototherapy.

The plan is to entrench CLINUVEL as the leader in photomedicine on both continents, whereby the expectation of the medical community is that SCENESSE® will become standard of care in photodermatology and vitiligo. Our ambitious goals are primarily fed by clinical evidence and demand for melanocortins, but also by conviction that patients with pigmentary disorders will want swift and less mercurial options requiring them to bear patience for onerous treatments of 12 to 18 months. Clearly, speed of first visible repigmentation in vitiligo counts, and our solution would obviate the need to travel to the clinics for 12 to 18 months.

Based on experience and research, a US centre generally has the capacity of treating 50 new vitiligo patients per year, around four per month, whereby most patients are required to attend the clinic twice weekly for up to 18 months to see some kind of (re-)pigmentary response. This summarises the current standard of care, however drop-out rates in vitiligo are high given the burden of compliance to such a clinical program. Handheld devices to be used at home are somehow effective, but not providing the desired results due to variability and uncontrolled use.

In sum, the first step to collaborate with 120 US centres will provide treatment access to 6,000 vitiligo patients who have been diagnosed with larger areas of depigmentation. A team of an additional 11 professionals – across patient liaison, compliance, distribution, and finance – is expected to be able to service this initial expansion, following the lean model proven for EPP. The second phase will be to expand the number of trained & accredited centres.

CLINUVEL witnessed in its Phase II study (CUV102) and the first cases published that vitiligo patients obtain faster repigmentation receiving SCENESSE® in combination with twice weekly narrowband UVB, and these initial cases strengthen our belief that the future clinical demand will materialise in drug treatment in combination with existing NB-UVB equipment. Hence our selection of these US centres. It is unique strategy in vitiligo, one not yet followed.

Important is to note that while in EPP we are providing continuous annual treatment of up to six SCENESSE® implants, in vitiligo 85% to 95% repigmentation is anticipated to be offered by a one-off effective treatment cycle of seven to nine doses in combination with narrowband UVB, while as annual maintenance therapy one to two implants may be required. Clearly, our commercial teams are carefully planning the positioning of the treatment as total body repigmentation therapy in vitiligo. However, one well-known clinical disclaimer is that the anatomical surfaces of hands and feet are known to not fully respond to any therapy. The rest of the body surface area seems to be well responding to SCENESSE®.

As part of clinical trials, the industry standard to be met – as determined by regulatory authorities and followed by others – is set at a minimum of 75% repigmentation of lost colour of the head and neck, while 50% for the rest of the total body surface area.

Therefore, an ability to bring back the complexion of vitiligo patients is a long-sought aspiration that seems realistic, whereby the additional goal is to facilitate direct distribution of the product to medical centres.

Expanding Global EPP Program

While the financial year is drawing to a close, and we do not have final data on the global EPP distribution, we have seen robust demand for SCENESSE® in the past months. The testimonies of patients on effectiveness and a new life they are able to lead remains a key driver for all our teams.

We plan for future supply given the strong demand, while we carefully record each experience in databases on the >14,500 doses administered to EPP patients. Recent publications keep emphasising the newly found quality of life for EPP patients receiving afamelanotide.[1] We are also seeing new patient and physician demand following conclusion of experimental therapy clinical and expanded access programs.

There is an emerging trend of requests to treat adolescent patients (aged 12-17), which we continue to answer. Many of these patients are fully reimbursed for their treatment, with payors recognising the high unmet need in adolescent EPP, while the Company will enable compassionate access programs on an individual case basis. Around three percent of the EPP patient population are estimated to fall into the older adolescent (15-17 year) group, with approximately sixty known patients across France, Germany, Italy, and the Netherlands.

Expansion EPP distribution

- EU-US strong demand for SCENESSE®
- Latin America – new access for SCENESSE® through Valentech Collaboration Agreement
- Conclusion of pilot in China – terminating distribution
- Supply to adolescent patients continued, full reimbursement in most cases
- CUV052 – one dose pharmacokinetic study in adolescents

In parallel, the CUV052 study is establishing the pharmacokinetic profile of SCENESSE® in adult and adolescent (12-17 years, ≥50kg) patients. Having sought to establish this protocol for a number of years, clinical support was garnered after initial adolescent patient treatment was well tolerated and three centres identified which could recruit patients. The single dose study will compare the adolescent and adult patient cohorts as well as capturing data on safety and clinical benefit. With 16 patients enrolled to date, and a further 12 to recruit, first data are expected later in 2024. These data – combined with real world evidence captured under conditions of use – will be compiled for further regulatory filings supporting the use of SCENESSE® in adolescent EPP patients.

Despite two years of interactions with the European Medicines Agency (EMA) – and modifying the approach based on feedback to focus on patients for whom there was the strongest clinical evidence and support, older adolescents (aged 15-17) with a minimum bodyweight of 60kg, similar to a large cohort of the adult population – the Agency could not come to a decision on whether the risk-benefit profile of SCENESSE® in adolescents was established. While we don't agree with the opinions expressed, and have withdrawn the formal label extension variation, we continue to seek ways to address all EPP patients.

After considerable diligence and interactions, the Company was pleased to announce the opening of new potential territories by way of a strategic partnership with Valentech Pharma. With extensive experience in Latin America, Valentech have demonstrated to our teams that they understand the challenges of facilitating treatment access for EPP patients and have proven approaches that have helped meet the needs of other rare disease communities. We now enter a period of intensive collaboration with the Valentech team to address the clinical, regulatory and payor audiences that will allow the first EPP patients to receive treatment in Latin America. The program set to be discussed at the upcoming International Symposium of Human Genetics in Colombia this week as part of the introduction to a LATAM audience.

The Company is constantly evaluating regional opportunities that may extend our reach for patients. The first of these, a now terminated pilot program agreement in China, provided insights to a changing regulatory landscape and time to reflect on how best to address the needs of EPP patients in different regions and environments. As the team looks to further expansion, it is with this experience that we evaluate new ventures.

There is much more to come from our EPP program both this year and in the period further ahead. Having established SCENESSE® as the standard of care for adult EPP patients, we are now working exhaustively to expand the program and ensure all patients who demand care can access it.

DNA Repair Program – Orphan Drug Designation

The novel use of melanocortins in the DNA Repair Program seeks to confirm pre-clinical evidence that afamelanotide can repair ultraviolet induced DNA damage, photolesions, in skin cells. The initial focus,

on the genetic disorder xeroderma pigmentosum (XP), has seen the Company initiate two clinical trials in these patients (CUV156 and CUV152), with healthy volunteer studies (CUV151 and the planned CUV158) serving as controls.

The recent orphan drug designation (ODD) for afamelanotide for XP by the EMA was the first positive regulatory review based on data human captured in the program. As part of its review and positive recommendation the EMA's Committee for Orphan Medicinal Products assessed four key criteria: the prevalence of XP (1:450,000 individuals); clinical data on the reduction of DNA skin damage; the unmet need in XP; and the life-threatening nature of the disorder.

The ODD in XP provides a regulatory pathway for SCENESSE®, since a full dossier submission would not be required to see marketing authorisation. Rather, a submission through the Type II variation pathway, providing clinical data to support the application, would be sufficient to expand the label to include XP. The benefit of ODD lies in the provision of formal scientific assistance if required, reduced regulatory fees, and ten years of market exclusivity post-approval.

PhotoCosmetics

A translation of medical technology into consumer markets is rare, however in some cases makes perfect sense when analysing the molecules. With a venture preparing for wider cosmetic markets, CLINUVEL differentiates itself from most pharmaceutical companies. While our core activities will always remain pharmaceuticals, branching out in PhotoCosmetics make our activities synergistic.

We are establishing a team of professionals coming from the luxury retail and marketing sector, collectively the Communications, Branding & Marketing team. The CBM team is tasked to provide global visibility to CLINUVEL through social media and worldwide events, and is working closely with our investor relations team, since communication of our key messages is at the heart of most activities.

We recently re-launched an e-commerce platform – www.cyacelle.com – and introduced the next generation polychromatic screens, CYACÊLLE Radiant Gold and CYACÊLLE Radiant Bronze, as part of an initial soft launch. We see this as a prelaunch phase, a pilot gathering feedback on our first product range CYACÊLLE and CYACÊLLE Radiant.

Formulated by CLINUVEL to protect against UVB, UVA and high energy visible light, with blue light-activated spirulina and reflective mineral filters, the CYACÊLLE Radiant line has been shown to protect against 80% of the blue-light spectrum.

In 2025, we will initiate global product launches of the CYACÊLLE range, in preparation of the M-lines, the melanocortin-containing topical formulations.

The planned Bulletin 2 under the editorial guidance of CBM's head Marga Arrom Bibiloni will provide much more insight on our planned marketing and branding activities.

Investor Relations, Communications

Investor relations spans three professionals full time working on three continents, coordinating with the CBM on the annual news flow coming from the Company. A most recent external review of our communications strategy indicated that the ASX published news flow by CLINUVEL may be too frequent compared to its peers, and that less news posted on the ASX would be more beneficial to shareholders. One of the first measures is to reduce our News Communiqués from six to four (quarterly) editions,

solely published on our website and through social media. To sign up and ensure you don't miss updates, please visit our website.

Reflecting the significant beneficial ownership of CLINUVEL in Europe, a Non-Deal Roadshow (NDR) was held in Germany and Switzerland across Frankfurt, Düsseldorf, and Zurich between 25-28 March. The Düsseldorf Investor Briefing on 27 March provided more than 100 participants with a renewed connection with our teams in person.

Investors were introduced to the clinical benefit of SCENESSE® treatment, the Company's strategy, product development and clinical programs. A highlight was a panel discussion on indications of the skin involving porphyria expert Dr Elizabeth Minder and a Q&A session hosted by ex-UBS banker Helmut Jonen and manager of a German Family Office, Juhani Linde. Feedback of the format was overwhelmingly positive, reinforcing the benefit of face-to-face interaction with our shareholder base.

New recipients were added to the distribution list for the German News Communiqué. If you would like to receive the communique in German, please ask through the Investor Relations Contact Form available on the website.

The Capital Markets Briefing on 1 May addressed an audience of analysts, institutions and representatives of investment banks and brokers in Sydney. Following an address from Chairman Professor Jeffrey Rosenfeld, presentations focused on the:

- distribution of SCENESSE® for EPP with Director of Global Operations, Lachlan Hay; and
- pipeline and vitiligo program with Chief Scientific Officer, Dr Dennis Wright.

Incoming CFO Peter Vaughan also attended to round out a significant contingent of CLINUVEL Executives at the briefing. Thanks to all the attendees and particularly, the analysts that provided input to the briefing content and format. The presentations were announced to the Australian Securities Exchange on the day of the briefing and webcasts of key sessions are being completed to be made available soon on our website.

On 23 May, CLINUVEL presented at the Wilsons Rapid Insights Conference in Melbourne to a range of existing and potential institutional investors in a sequence of round table meetings. Discussions focused on the distribution of SCENESSE® for EPP, product development and the expanded clinical program.

With Mr Myles Clouston recently joining the IR team, and based in New York, in the coming months our Investor Relations activities will see several new US conferences and NDRs to increase awareness of our mission and cause. Mr Clouston has extensive capital markets experience, working with Nasdaq's global leadership team and in investor relations roles in life sciences.

Share Buy-Back

The 12-month Share Buy-Back Program announced on 14 March is intended to support the share price during this current period of market weakness. As of 5 June, 49,490 shares have been purchased under the program. The closing share price at the time of writing is A$15.00 compared to A$13.20 the day prior to the announcement of the buy-back. Notifications of buy-backs are lodged with the ASX the following day and can be monitored by all stakeholders via the Company's website.

Objectives CY2024

The Company continues to focus on 16 key objectives for the calendar year 2024:

	Individual objectives to end of CY2024	
1	SCENESSE® adolescent outcome EMA – May 2024	✓
2	SCENESSE® Canada Health submission	
3	Vitiligo CUV105 completion recruitment	
4	Vitiligo CUV107 start recruitment	
5	XP-DNA Repair CUV151 read out complete (selected markers)	
6	CUV156 read out complete (selected markers)	
7	CUV154 start	

8	Paediatric PK study CUV052 start – March 2024	✓
9	VP CUV040 complete results – March 2024	✓
10	CNS CUV803 completed with final results	
11	CNS and or New Indication	
12	NEURACTHEL® manufacturing progress	
13	Website launch – December 2023	✓
14	PhotoCosmetics E-shop launched – May 2024	✓
15	CYACÊLLE global launch – prelaunch initiated	✓
16	Financial growth earnings: half year (Feb 2024), final year end	✓

Future of CLINUVEL

From a bird's eye view, I see a Company steadily going through development cycles, putting its resources towards a novel class of molecules, melanocortins. These are best described as omnipotent active molecules, restoring pathological imbalances, acting akin corticosteroids without the unfavourable side effects of steroids. Used in the right dose and formulations, these melanocortins have ubiquitous applications. An example is adrenocorticotropic hormone (ACTH), our next molecule in development.

In 2005, we set out to revert misfortune that had befallen the Company, and the past two decades we have managed to derisk the Company across operations, regulatory and finance. Therefore, I view that we have arrived at a mature stage when we can take on new risks, calculated ones without jeopardising the going concern.

We have the financial strength to venture out, qualified and specialised personnel, and processes which forms the basis for new initiatives and expansion. I also believe that these changes will be transformational, while the iceberg keeps growing with developments being progressed and made public. As our audiences are increasing, we will report to you quarterly through Communiqués released on our website, and no longer through the ASX portal.

Late August, we will publish our financial year end results through webcasts and directly via non-deal roadshows to institutional investors. Until then, thank you for your continuous support.

Philippe Wolgen

– END –

Notes

1. See: Leaf R.K., et al. (2024). Afamelanotide for Treatment of the Protoporphyrias: Impact on Quality of Life and Laboratory Parameters in a US Cohort. Life, 14(6), 689. Available online: https://www.mdpi.com/2075-1729/14/6/689.
   O'Reilly, M., et al. (2024). Erythropoietic protoporphyria and afamelanotide: A patient's perspective. Clinical and Experimental Dermatology, 49(2), 186–187.

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.

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