CLINUVEL
Communiqué VI
December 2021

Dear Shareholders, Friends,

INTRODUCTION

The last month has been a tragic lesson in the challenges posed by a global pandemic and the potential risks of inequality in access to healthcare. While we are prepared for the possible impact of new variants of COVID-19 (and indeed other adverse conditions outside of our control), the team remains focused on ensuring our work can continue and that we make a positive impact to the lives of patients.

We progressed the expansion of the clinical program during the year. As of this week, we have approvals for all four of our announced clinical development programs – DNA Repair, arterial ischaemic stroke, variegate porphyria and vitiligo – to progress, and we are now actively managing studies in various stages across the globe. It has been rewarding for our teams to monitor the treatment of the first patients in new studies and we are pleased to report the patients treated in the xeroderma pigmentosum (CUV156) and stroke (CUV801) studies have tolerated the treatment well. We eagerly await study completion and results, due in 2022. Feedback from some study centres suggests that the pandemic is having an adverse effect on study conduct (in particular, during start up phases), but all are working diligently with our team to minimise this impact.

We continued to receive orders for SCENESSE® (afamelanotide 16mg) throughout the fourth quarter, demonstrating the ongoing demand from erythropoietic protoporphyria (EPP) patients and their physicians to provide year-round treatment. In the US, Dr Teng and her team are focused on expanding access for patients and have taken considerable strides this year to reduce the administrative burden of the Prior Authorization process. In Europe and Israel, Mrs Colucci and team have navigated an ever-shifting set of conditions to ensure continuity of supply and treat more patients than ever before, including many who received the therapy for the first time.

These efforts resulted in the impressive financial results achieved in the year ending 30 June 2021, with the fifth consecutive year of commercial operations crowned by a record revenues and profit outcome. As a profitable company with a consistent track record, including the payment of dividends to shareholders over the last four years, CLINUVEL is well positioned to grow and expand into 2022. Cash reserves are sufficient to self-finance our planned organic growth and manage the adversity of the economic cycle and other events.

Behind the scenes, progress is being made to ensure the Company can reach new audiences and, longer-term, provide improved treatment options for patients. Over the course of the year, we have expanded the Communications, Branding and Marketing Division and begun establishing the infrastructure necessary to engage with more diverse communities worldwide. In particular, CLINUVEL is preparing direct-to-end-user interfaces, allowing us to facilitate long-term dialogue. In Singapore, the RD&I Centre at VALLAURIX has progressed a number of pharmaceutical projects, the most recently announced being the development of NEURACTHEL® (ACTH) formulations for patient use.

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Throughout the course of 2021 we have expanded the global team, consistently adding new talent as our workload expands. Part of the challenge for CLINUVEL has been to ensure we remain a positive and engaging place to work in the face of ever-changing working environments and broader industry pressures. We have largely adapted to a new normal of (at least partial) remote work for the entire team – the exception being in Singapore, where laboratory work necessitates regular time in our facilities – and are constantly looking at ways to ensure our team takes a long-term view to developing their careers at CLINUVEL. It has been rewarding to see many of our early-career professionals take important steps in their development within the business, and we are now working to ensure they can continue to thrive regardless of the pressures of macro trends.

AFAMELANOTIDE FOR VITILIGO: THE IMPORTANCE OF PATIENT REPORTED OUTCOMES (Dr Linda Teng)

In the effort to expedite the development and approval of innovative and new drugs for patients, the 21st Century Cures Act was signed into law by President Obama in December 2016. Known simply as the Cures Act, this legislation aimed to bring "to reality the possibility of new breakthroughs to some of the greatest health challenges of our time" and harken a new era of medical product development, tailoring healthcare to target the right treatments, to the right patients at the right time.

One direct change brought about by the Cures Act has been to broaden the scope of evidence accepted by the US Food and Drug Administration (FDA) when evaluating the clinical benefit of treatments. Historically, clinical trials primarily focused on objective endpoints that are straightforward to measure and interpret. The patient's perspective, however, was often overlooked – secondary to the outcomes obtained from biomarker-led endpoints. With the integration of patient reported outcomes (PROs) into healthcare, both in Europe and the USA a macro trend of improvement can be seen rippling down from regulatory decision making, hospital care, pharmaceutical development, and, most importantly, patient health. Multiple studies have shown how systematic monitoring of patients' symptoms using PROs closes key gaps in healthcare, including improving patient-clinician communication, clinician awareness of symptoms, symptom management, patient satisfaction, quality of life, and overall survival.

Vitiligo is one such condition where distinctions in perspectives of disease between physicians and patients resulted in difficulties in disease characterisation and treatment. For instance, the range of repigmentation differs substantially between patients' and clinicians' viewpoints (Narayan et al. 2020). The design of clinical trials for vitiligo has historically proven to be challenging with limited tools to objectively measure the course of the disease and its treatment. Distinctions in perspectives of disease impact remain visible. Until recently, vitiligo was considered a cosmetic disease, overlooking the psychologically devastating consequences of the disorder – especially within Fitzpatrick Phototypes IV-VI. This important, and often misrepresented, aspect of vitiligo was acknowledged in the FDA Public Meeting on Patient-Focused Drug Development for Vitiligo, discussed in News Communiqué V. A key takeaway from this public meeting was FDA's acknowledgment of the tremendous impact that vitiligo had on the patients' quality of life. Vitiligo patients, particularly those with a darker complexion, experienced a loss of one's identity, feeling of being avoided and bullied, and the challenges in receiving off-label treatments.

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The virtual 2021 Vitiligo International Symposium (VIS) held on 04 - 05 December presented further PROs and anecdotes from vitiligo patients indicating that the greatest burden of vitiligo is its emotional and psychosocial impact. The loss of self-identity, suicidal thoughts and social stigma in vitiligo have been expressed by the patients. Patients feel self-conscious, depressed, and insecure, resulting in the avoidance of social situations, interactions, and romantic relationships.

The emotional and psychosocial implications caused vitiligo patients to suffer from anxiety and depression. Understanding the disease burden in these patients is crucial; therefore, the management and treatment of vitiligo should be a multidisciplinary team approach.

CLINUVEL has paid close attention to developments in vitiligo, its treatment, and the evaluation of clinical benefit of treatment intervention. Our goal is to develop the first safe and effective treatment for vitiligo patients, one which focuses on specific groups of patients who have the greatest clinical need and are most likely to respond to therapy, while avoiding the immunosuppression seen as necessary by other therapeutic approaches.

In the pilot study CUV104, CLINUVEL is focusing on the importance of the psychological impact of vitiligo. A deep appreciation is paid by the team as to how this may differ between phototypes. In assessing SCENESSE® as a monotherapy in patients with darker skin complexions, CLINUVEL aims to provide an innovative solution for patients where the loss of pigmentation has caused significant physical and psychological distress.

INVESTOR RELATIONS (Mr Malcolm Bull)

Key Highlights 2021

A comprehensive overview of recent events was provided in News Communiqué V on 22 November. For this last communiqué of 2021, some specific investor relations highlights for the year are provided below:

- The expansion of independent research coverage of CLINUVEL continued with Wilsons Advisory commencing coverage in the first half of the year. There are now six analysts with an Australian Financial Services Licence covering CLINUVEL (refer to analyst coverage on CLINUVEL's website). From one analyst (*Bioshares,* refer below) at the beginning of 2019, this constitutes a meaningful increase in the conveyance of CLINUVEL's story to the wider investment community;
- The impressive results for the half and full financial year, to December 2020 and June 2021, respectively, with record revenues and profits, and the progressive increase in gross cash receipts and net cash reported quarterly, were well received by investors and other stakeholders;
- We received various feedback that the 2021 Annual Report is the best yet in terms of content and presentation, and is a key reference document that summarises our financial and operational performance and strategy;
- The Annual General Meeting of 10 November, held virtually for the second consecutive year, was well attended with a record number of shares voted. The vote reflected the concerted effort of the CLINUVEL team during the year to reach more shareholders and explain the Company's strategy and approach, particularly to executive remuneration. It was pleasing to witness an increase of 28% in the number of shares voted to adopt the Remuneration Report compared to the average vote in the previous five years. This democratic endorsement of the Board's approach positions the Company well to progress its multi-pronged growth and expansion strategy to accumulate long-term value for all stakeholders;
- Finally, we received broad and positive feedback on the increased frequency and variety of investor relations communications during 2021. We maintained the pace of regular Chair Letters, news and scientific communiqués, and specific announcements on financial and operational outcomes and the progress of the expanded clinical program. In addition to the ongoing translation of the news communiqué to German, we communicated through an increased number of webinars, webcasts, and other presentations. There were three strategic updates, two operations updates and three investor webinars during the year. The Company also participated in nine key conferences, presenting at eight. Multiple meetings were held with existing and potential investors, including conferences hosted by analysts and investment banks. Social media supplemented the distribution of news and updates, reaching an ever-widening audience. This is the way forward, to continue in 2022.

Respects to the Late David Blake

The Company paid its respects to the late David Blake at a memorial service in Melbourne on 15 December. The tributes from family and friends were uplifting and confirmed David's rich and productive life. With business partner, Mark Pachacz, David established *Bioshares* more than two decades ago to cover and report on the biotech sector in Australia, covering

CLINUVEL since 2006. David will be fondly remembered, and amongst many admirable attributes, his discipline and focus is an enduring example to CLINUVEL.

Season's Greetings

As another eventful year concludes, we look to the festive season to rest and enjoy good times with family and friends. The wish of Investor Relations to all stakeholders of CLINUVEL to enjoy a safe and festive season, is expressed in the following lines from a David Blake[1] poem:

> *The warmth of human hands and hearts*
> *the love and company of family and friends*
> *rides over right living.*

2022 AND BEYOND

CLINUVEL's teams have been tasked with delivering more than ever in the coming year. In addition to the four ongoing clinical programs, work continues on a further indication for SCENESSE®, ongoing real-world data collection in EPP, and scientific assessment of new opportunities for our pharmaceutical portfolio. Pending pandemic and market conditions, our Healthcare Solutions Division is poised to launch the first OTC product in the first half of 2022.

The first engagement of Investor Relations in 2022 is to participate in the J P Morgan Healthcare Conference and present at the H.C. Wainwright Bioconnect Conference in the first half of January. More detail on the planned activities of Investor Relations will be provided in the first news communiqué of 2022.

Consistent with our business model to date, much of our work is, and will continue to be, done in-house. This approach gives us control over decisions and timelines and helps us manage resources directly. The structure across four divisions is evolving to ensure this approach can be expanded to meet the Company's ambitions, with a focus on launching new products and engaging new audiences in the near-term, growing our ability to facilitate treatment for EPP patients and assess new opportunities as they arise.

On behalf of the management team, thank you to the patients, physicians, shareholders, and our external partners for your support throughout this year. I also wish to thank our dedicated and growing global team who have progressed our mission and achieved marked success over the past 12 months. Finally, in the spirit expressed above, I wish all our readers a happy and safe holiday period, and good health for the coming year.

Lachlan Hay, Director of Global Operations

1. "Doing Everything Right," David Blake, Drake Street and Other Poems, 2021, Blakeset.

Authorised for ASX release by the Board of Directors of CLINUVEL PHARMACEUTICALS LTD.

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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