CLINUVEL

ASX ANNOUNCEMENT

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Commercial update on vitiligo

Assessing clinical benchmarks for SCENESSE®

Executive Summary

1. standard of care and efficacy for extensive vitiligo – narrowband UVB dosing schedule
2. topical JAK Inhibitor, ruxolitinib – efficacy in Phase II and Phase III
3. systemic JAK Inhibitors – efficacy in Phase II and Phase III
4. afamelanotide & adjunct NB-UVB – comparison to JAK Inhibitors

Melbourne / San Francisco – 30 July 2026 – CLINUVEL PHARMACEUTICALS LTD (ASX: CUV | Nasdaq: CUVL) today shared a commercial update on the emerging vitiligo market with current standard of care of narrowband ultraviolet B (NB-UVB) phototherapy, and Janus kinase (JAK) inhibitors under development for vitiligo. With the completion of CLINUVEL's advanced trial CUV105 comparing SCENESSE® (afamelanotide) and the adjunct NB-UVB therapy to the monotherapy NB-UVB, CLINUVEL's commercial review addresses recently posed questions while providing objective peer reviewed benchmarks.

To date, extensive vitiligo of total body surface (≥10% affected by depigmentation) lacks an effective therapy, whereby NB-UVB remains the preferred first-line and most widely used whole-body phototherapy for patients with extensive vitiligo to provide some therapeutic results (repigmentation).

Narrowband UVB: standard of care for extensive depigmentation

Narrowband UVB requires frequent brief exposure – two to three times per week – to specific wavelengths of light (308-311nm), generally for 12-18 months. This long-term use has been reported to provide limited efficacy in vitiligo populations.

In 2025, in a study of 176 patients, 45% achieved clinically significant repigmentation, with the highest success rates observed on the face and neck region (53%). Among responders, 95% maintained their response for six or more months post-treatment discontinuation, and 59% retained repigmentation for more than 72 months.[1] In another study in 32 patients, 42.2% achieved at least 50% repigmentation of limbs and 37.5% of total body.[2]

In an analysis of 1,428 patients reviewing 35 studies, a marked response was found in 19% after six months and 36% after 12 months of NB-UVB treatment.[3]

A clinically significant response to NB-UVB phototherapy is associated with longer treatment duration (>18 months) and higher cumulative radiation dose (>356 J/cm^2).[4]

JAK inhibitor (topical ruxolitinib)

The first pharmaceutical product to have been approved in vitiligo is ruxolitinib 1.5% cream. The topical formulation is applied twice daily for vitiligo affecting less than 10% of body surface area. It is noted in the U.S. prescribing information that satisfactory patient response may require more than 24 weeks of treatment.[5]

Results of a phase II of ruxolitinib (n=157) showed achievement of ≥50% improvement from baseline in facial Vitiligo Area Scoring Index (F-VASI50) at week 24, and 45% (1.5% twice daily) and 50% (1.5% once daily), versus 3% for the placebo vehicle.[6]

Phase III results (TRuE-V1 and TRuE-V2, n=674) demonstrated that at week 52, F-VASI75 was achieved by 50.3% (176/350) of patients who applied ruxolitinib cream throughout, and 28.2% (46/163) who crossed over from vehicle after week 24.[7]

Oral JAK inhibitors in development

A number of systemic JAK inhibitors, administered as oral tablets, are in development for vitiligo. Some are already approved for other clinical indications, while others are subject to regulatory review for the first time. Three late-stage programs have reported results from larger clinical trials.

Upadacitinib – Phase III results from two replicate studies (n=614) demonstrated achievement of co-primary endpoints of T-VASI50 and F-VASI75 at week 48 versus placebo. T-VASI50 was achieved by 19.4% (Study 1) and 21.5% (Study 2) of upadacitinib-treated patients versus 5.9% for placebo. F-VASI75 was achieved by 25.2% (Study 1) and 23.4% (Study 2) versus 5.9–6.9% for placebo.[8]

Povorcitinib – Phase II results demonstrated substantial total body and facial repigmentation in adult patients with extensive nonsegmental vitiligo through 52 weeks of treatment. At week 24, T-VASI improvement from baseline was 15.7–19.1% across doses versus a 2.3% worsening on placebo.[9] Top-line phase III results (n=917) demonstrated that 18.9% of patients achieved F-VASI75 after 52 weeks of therapy as opposed to 3.1-6.8% of placebo patients.[10]

Ritlecitinib – Phase IIb results showed three doses (200/50 mg, 100/50 mg, and 50 mg) were all statistically significant versus placebo on F-VASI at week 24. Phase III (Tranquillo program) is ongoing with primary endpoint of F-VASI75 at week 52 to be evaluated.[11]

Ruxolitinib, along with other JAK inhibitor drugs, carries a boxed warning regarding serious infections, malignancy, major adverse cardiovascular events (MACE), mortality, and thrombosis associated with JAK inhibition. Therefore, careful patient selection and risk–benefit assessment are required, particularly in individuals with increased infection risk, immunosuppression, a history of malignancy, cardiovascular risk factors, or prior thromboembolic disease.

Afamelanotide and adjunct NB-UVB

SCENESSE® is being developed as the first systemic (total body) repigmentation therapy for vitiligo. Unlike JAK inhibitors which suppress the immune system, afamelanotide, the peptide in SCENESSE®, targets melanocortin receptors to stimulate melanin synthesis following melanocyte stem cell differentiation and proliferation induced by adjunct narrowband UVB to activate repigmentation.

Early clinical data from the CUV105 study have demonstrated visible and lasting repigmentation. In 12 case reports, SCENESSE® implant injections and adjunct NB-UVB (up to 40 NB-UVB sessions), physicians observed progressive repigmentation of facial and body regions, with skin tone returning towards baseline over time.

Prior studies (CUV102, CUV103) have shown that SCENESSE® in combination with NB-UVB significantly improves repigmentation compared to NB-UVB as a monotherapy. A pilot study confirmed that SCENESSE® as monotherapy is unable to provoke repigmentation, illustrating the need for adjunctive NB-UVB.[10]

Commercial preparation – North American vitiligo market

CLINUVEL is completing its first late-stage study of SCENESSE® in vitiligo (CUV105). It is anticipated that the topline results of the CUV105 study will be ready for release in December 2026 (see ASX announcement 28 July 2026).

CLINUVEL has reinforced its supply chain for expansion, scaled up North American infrastructure, and engaged more than 100 potential new Specialty Centers at the American Academy of Dermatology meeting in 2026. The anticipated start of the pivotal CUV107 study is November 2026.

Commentary

“It is relevant to all of CLINUVEL’s stakeholders that we provide benchmarks in vitiligo, given the frequent questions from analysts and the medical community on what to expect from the clinical trials of afamelanotide and adjunct NB-UVB,” said Dr Dennis Wright, CLINUVEL's Chief Scientific Officer.

“The medical community understands that NB-UVB as monotherapy provides irregular repigmentation in about 40% to 50% of the patients after 12 months of administration. On analyses, the response to the first JAK inhibitor as a cream to treat facial vitiligo was approximately 45% after 24 weeks, and for a systemic JAK3 inhibitor treating full body vitiligo response ranges from 15.7% to 19.1%. These numbers provide a good reference for the evaluation of afamelanotide and adjunct NB-UVB in the future.

“These data show that while JAK inhibitors offer meaningful repigmentation in patients with limited body surface area involvement (<10%), there remains a significant unmet need for patients with more extensive vitiligo. The CUV105 topline results in December 2026 will be a welcome moment to evaluate afamelanotide in the treatment challenge posed by extensive vitiligo.”

– END –

References and notes

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About CLINUVEL PHARMACEUTICALS LIMITED

CLINUVEL is a global biopharmaceutical company focused on developing and delivering innovative therapies for patients with genetic, metabolic, and dermatological disorders. The Company's portfolio is centred around melanocortin peptides, with programs advancing in photomedicine and vitiligo. CLINUVEL is listed on the Australian Securities Exchange (ASX: CUV) and the Nasdaq Stock Market (Nasdaq: CUVL).

CLINUVEL's lead therapy, SCENESSE® (afamelanotide 16mg), is approved for commercial distribution in Europe, the USA, Canada, 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). For further information, visit 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. All statements other than statements of historical or current facts made in this document are forward-looking. We identify forward-looking statements in this document by using words or phrases such as "anticipate," "believe," "consider," "continue," "could," "estimate," "expect," "foresee," "intend," "likely," "may," "objective," "potential," "plan," "predict," "project," "seek," "should," "will" and similar words or phrases and their negatives. Forward-looking statements reflect our current expectations and are inherently uncertain. Actual outcomes or results could differ materially for a variety of reasons. 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 but are not limited to risks relating to: our ability to develop and commercialise pharmaceutical products; pandemics, epidemics, public health emergencies, geopolitical conflicts, trade restrictions, natural disasters and other disruptions affecting global supply chains, 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 including the risk factors described in the Company's Annual Report on Form 20-F and other filings with the U.S. Securities and Exchange Commission, together with the Company's announcements lodged with the Australian Securities Exchange. Forward-looking statements speak only as of the date on which they are made, and the Company undertakes no obligation except as required by applicable law, the rules of the Australian Securities Exchange, the U.S. Securities and Exchange Commission, Nasdaq, or other applicable regulatory requirements, 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.

Contact:
Tel: +61 3 9660 4900
Fax: +61 3 9660 4909
Email: mail@clinuvel.com

Australia (Head Office), Level 22, 535 Bourke Street, Melbourne, Victoria, 3000, Australia