CLINUVEL

CLINUVEL.COM SPRING 2024

THE ART OF PHOTOMEDICINE

Meet the biopharmaceutical company whose revolutionary treatments and science-based skincare herald a new era for the treatment of light-related conditions

1

MELANOCORTIN HOUSE

1

BIOPHARMACEUTICAL PRODUCT - SCENESSE®

14,200+

DOSES OF SCENESSE® ADMINISTERED

2

PRODUCTS IN DEVELOPMENT

5+

DISEASES OF THE SKIN AND BRAIN

1

PHOTOCOSMETIC BRAND

7

YEARS OF CONSISTENT GROWTH

UNVEILING THE ART OF PHOTOMEDICINE

It was the era of Michael Jackson, Princess Diana and Grace Jones. In the 1980s hair was big—and shoulder pads were even bigger. Subtlety was passé. Along with the lamé catsuits and blingy earrings, being tanned was in vogue. Sun-kissed skin was seen as glamorous and aspirational; planes packed with pale-skinned punters looking to bronze were landing in Mediterranean beach resorts.

All this sun-worshipping was at odds with doctors' advice, however. Experts knew that prolonged exposure to ultraviolet (UV) rays could lead to skin cancer, ageing and other health concerns. As this knowledge trickled down to the public, the market for self-tanning products boomed. People began lathering on bronzing creams and hopping onto sunbeds to top up their glow; one home solarium was even advertised as "The Safety Tan". It was not until decades later that the carcinogenic effects of indoor-tanning devices became widely known.

In the early 1980s researchers at the University of Arizona began to experiment with the idea of "sunless tanning". What if, they wondered, it was possible to recreate the sun's effect on the skin without exposing it to harmful UV radiation? Their hypothesis hinged on a member of the melanocortin family called alpha-melanocyte-stimulating hormone (α-MSH) which plays a role in the production of melanin, the skin-darkening pigment. The scientists set about trying to synthesise molecules, or analogues, of α-MSH. The idea for artificially-induced melanogenesis—bronzing inspired by the body's natural mechanism—was born.

Their forward-thinking science would not be realised until years later, however. In 1999 the founders of CLINUVEL recognised the potential of this "sunless tanner" and bought the patent for the α-MSH analogue, known as afamelanotide. Yet their aspirations went far beyond the cosmetic industry. Melanocortin hormones regulate processes throughout the body, including skin pigmentation, inflammation, appetite, sexual response and energy levels. CLINUVEL's scientists therefore believed that α-MSH could treat a spectrum of light-related diseases that affect the skin and brain. In 2005, the CLINUVEL Group began the journey to turn α-MSH's therapeutic potential into reality.

Since then, the company's pioneering research has pushed the frontiers of photomedicine. CLINUVEL's scientists have illuminated the complex interactions between UV light and human biology, and pinpointed how melanocortins fit in. Over the last 25 years, CLINUVEL's work has furthered scientific knowledge, delivered breakthroughs in medical technology and transformed patients' lives.

ADDRESSING UNMET MEDICAL NEEDS IS IN CLINUVEL'S DNA

CLINUVEL adopted a novel approach to building a biopharmaceutical company — one that has paid off. Instead of seeking solutions to prevalent diseases, the company focused on treating small groups of patients with seemingly incurable conditions, whose needs had been overlooked by other pharmaceutical brands. For almost two decades, CLINUVEL has developed cutting-edge melanocortin therapies that target three rare, life-threatening skin disorders.

The company developed and commercialised the only approved treatment in the world for erythropoietic protoporphyria (EPP), a genetic condition which affects 10,000 people globally. Patients with EPP experience severe and potentially life-threatening reactions when exposed to light. Regular sun cream fails them, meaning they must avoid sunlight at all costs. This makes SCENESSE® a therapy with the potential to change people's lives.

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The European Medicines Agency approved SCENESSE® in 2014, followed by America's Food and Drug Administration in 2019. The treatment is now licensed on four continents: Asia, Australasia, Europe and North America. SCENESSE® protects the body from wavelengths of light that can prompt DNA to mutate, therefore reducing a patient's chances of developing skin cancer. Following treatment, EPP patients need no longer live in the shadows. "I didn't know the sun was warm", said Chris De Mase, one of CLINUVEL's EPP patients in New Jersey.

In addition to creating the world's first systemic photoprotective treatment, CLINUVEL is striving to develop the first melanocortin drug that can correct mutations in the genetic code. In healthy people, the skin continuously renews itself. Yet a genetic defect in patients with xeroderma pigmentosum (XP) hampers this ability. XP is a severe inherited disorder which afflicts only 1,300 people worldwide. As a result, they are 10,000 times more likely to develop skin cancers than most people; less than 40% of XP patients live past the age of 20.

CLINUVEL is investigating whether SCENESSE® can repair this UV-damaged DNA in four clinical trials. The technology works by installing a temporary repair centre inside XP patients' skin cells; cutting out damaged nucleotides which could trigger harmful mutations and stitching together healthy DNA bases. The treatment would be the first, long-term solution for this rare, debilitating condition.

The Group's research into vitiligo is equally promising. Vitiligo causes colourless patches to develop on the skin and the lack of melanin leaves the patient vulnerable to UV damage. Treatment for the condition is relatively new: the FDA only approved the first at-home drug in July 2022. CLINUVEL's proposed treatment offers hope.

Early studies show that their melanocortin therapy accelerates the process of repigmentation, restoring colour to bleached skin and strengthening the body's barrier against the sun. This is a groundbreaking result, not least because it would lighten the mental toll that vitiligo can inflict on patients. A trial with up to 200 vitiligo patients will evaluate the effects of combining afamelanotide with exposure to narrowband UVB. As CLINUVEL makes headway with this programme, it will enter a market estimated to be worth $5.4bn.

WHAT DOES THE FUTURE OF PHOTOMEDICINE LOOK LIKE?

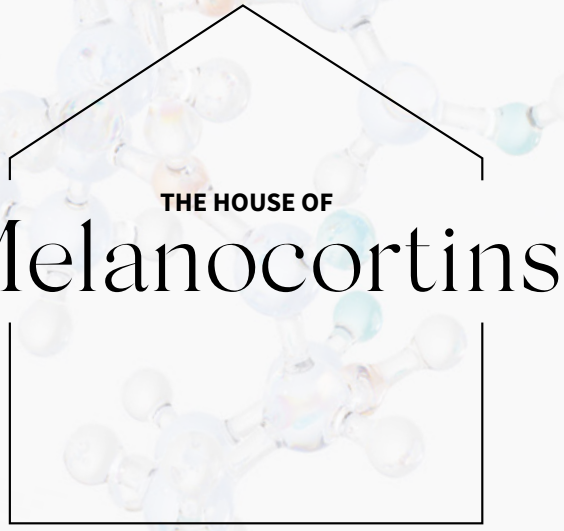
CLINUVEL is defined by firsts. It is the only pharmaceutical company in the world to unite melanocortin research, drug development and manufacturing under one roof. By bringing everything in-house, the firm will control the entire pipeline, from research, to marketing and distribution of the melanocortin products. This will give CLINUVEL a monopolistic position in biopharmaceuticals, particularly for SCENESSE®, where it remains years ahead of its competitors.

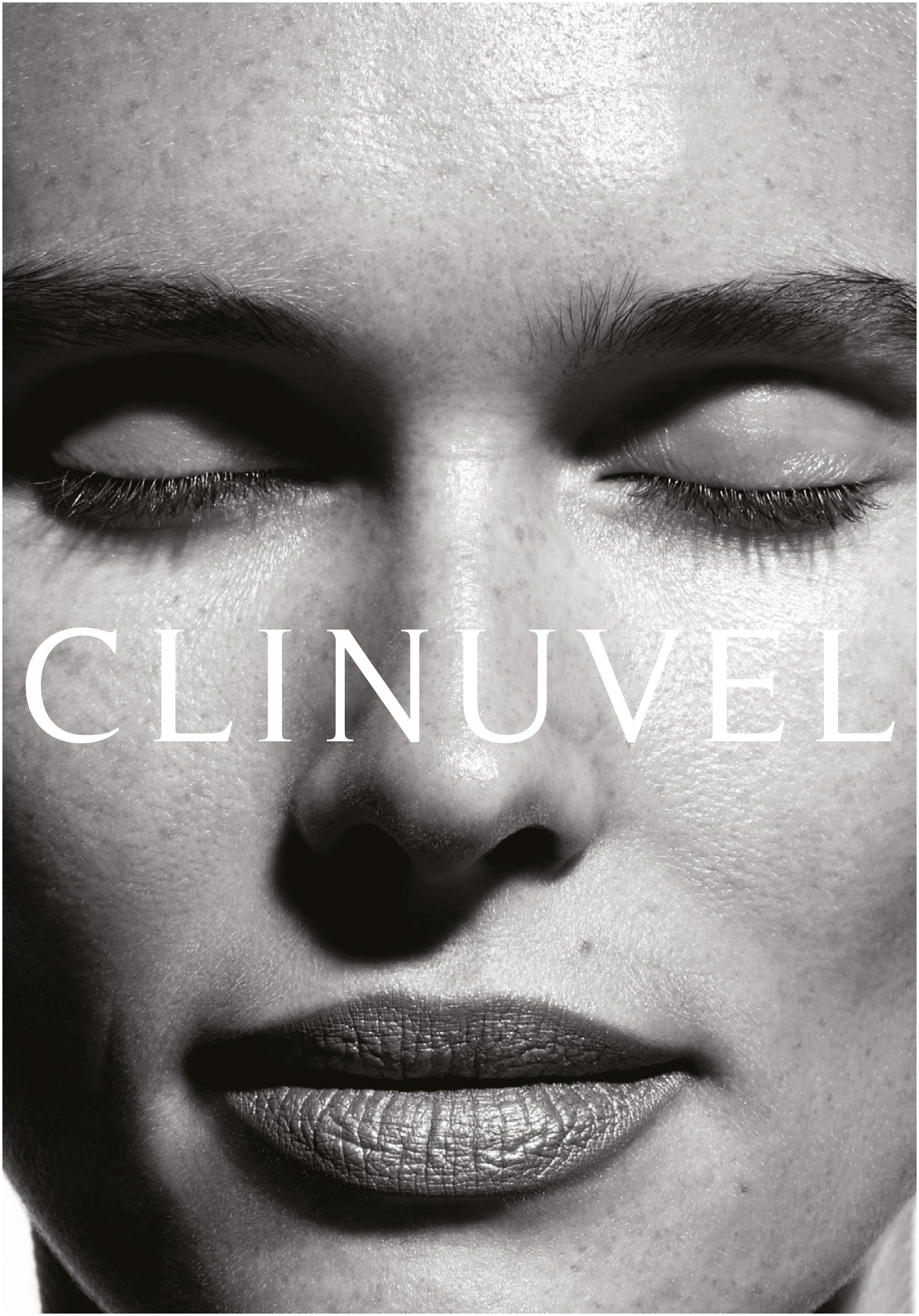
CLINUVEL's managers are broadening the Group's clinical ambitions too. While the focus was initially on treating small numbers of patients; now the firm is exploring how their medicine can target widespread health conditions. The potential of their melanocortin technology is vast —and lucrative. CLINUVEL estimates the total addressable market to be US$44bn. As the Group scales up, its experts will dig deeper into the mysteries of melanocortins to unlock new therapeutic areas.

The company is already studying the efficacy of SCENESSE® on patients with variegate porphyria (VP), a genetic metabolic disorder that results in fragile skin. Melanocortins may also help conditions of the brain. In 2020 CLINUVEL developed a fast-acting, liquid formula of afamelanotide called PRÉNUMBRA®. This can aid patients whose blood vessels are damaged, as happens during a stroke. CLINUVEL is testing PRÉNUMBRA® on people who have experienced an ischaemic arterial stroke. If found to be effective, this would have a significant impact on public health: strokes are the leading cause of serious, long-term disability in America, yet historically efforts to develop treatments have largely been unsuccessful, despite the lure of a total addressable market size worth US$31bn.

The house of melanocortins continues to grow. The newest addition to CLINUVEL's melanocortin family is the adrenocorticotropic hormone (ACTH) product NEURACTHEL®. The ACTH analogue—a linear chain of 39 peptides—could help people struggling with inflammatory and central nervous system disorders. Regulators can expect a dossier for approval on their desks soon.

As CLINUVEL moves towards realising its long term vision, scientific rigour and an unwavering commitment to patient safety remain the company's lodestars. Its aim is to revolutionise the treatment of light-related disorders, strengthen skin health and improve people's relationship with the sun. The road to developing and commercialising life-changing therapies is not a short one, but a brilliant journey lies ahead.




CLINUVEL

PhotoCosmetics
LUXURY SKINCARE, POWERED BY PHOTOMEDICINE

Everyone stands to benefit from CLINUVEL's expertise in photoprotection. Rates of skin cancer are on the rise globally: the World Health Organisation predicts a 25% increase in the number of cases by 2030. The sun also causes 90% of the visible signs of aging. As consumers become more conscious of the dangers of UV and deeper-penetrating, high-energy visible light (HEV), they are subsequently adapting their skincare habits.

CLINUVEL is uniquely positioned to respond to these health and beauty needs. The company is harnessing its specialist knowledge to formulate PhotoCosmetics: luxury skincare, backed by 43 years of photomedicine. CLINUVEL will be the first company in the world to launch a line of cosmetics based on melanocortin technology.

The PhotoCosmetics range incorporates their science in three revolutionary lines. The first, Protect, will deliver the most advanced photoprotection on the market, shielding the skin against UVA, UVB and HEV light. No other suncream provides a near-total barrier against this deeper-penetrating, blue light.

The second, Preserve, will nurture the skin by accelerating the body's natural mechanism of DNA repair. This breakthrough serum, powered by CLINUVEL's melanocortin peptide, will prevent premature ageing caused by photodamage and preserve the skin's youthful appearance.

Bronze will complete the trio. The science behind it originates from the blue-sky thinking of melanocortin researchers in the 1980s—the same technology that is delivering breakthroughs in CLINUVEL's vitiligo research. When people apply Melanogenesis, it will stimulate the pigment-producing cells in their skin, safely enhancing its natural process of bronzing. Launching in 2026, this next-generation product will be the first of its kind to enter a market forecast to be worth almost US$25bn by 2031.

PhotoCosmetics unites CLINUVEL's spirit of innovation with their authority in photomedicine. This trinity of brilliant products will protect, strengthen and enhance the body's natural armour, empowering people to enjoy the benefits of sunlight. CLINUVEL is well positioned to carve a niche within a competitive market. Within the next three years, the brand will become a name on the lips of tastemakers, beauty editors and luxury consumers. This is a company on a meteoric rise.

PHOTOMEDICINE	TO	PhotoCosmetics
ERYTHROPOIETIC PROTOPORPHYRIA Intolerance to all types of light	1	**POLYCHROMATIC PHOTOPROTECTION** Advanced solar shield
XERODERMA PIGMENTOSUM Severe photodamage and skin cancer	2	**DNA REPAIR** Preserves and repairs the skin's DNA
VITILIGO Loss of pigmentation in the skin	3	**MELANOGENESIS** Activates pigmentation

1 PROTECT

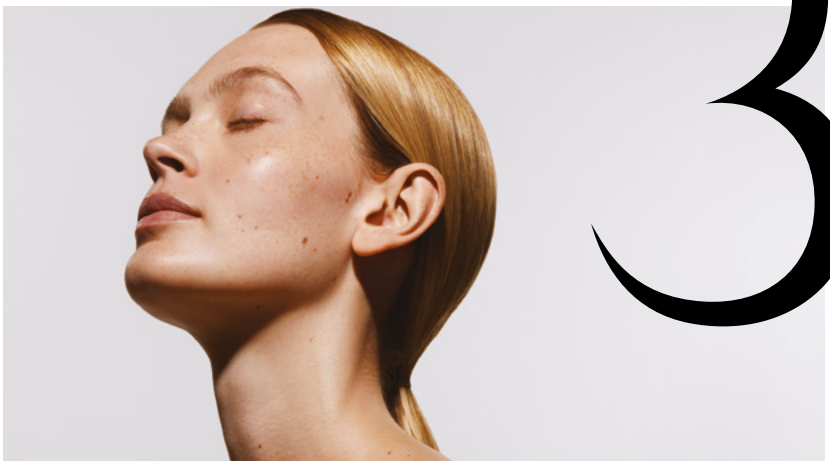
POLYCHROMATIC PHOTOPROTECTION

Shields the skin against UVA, UVB and deeper-penetrating HEV light, with mineral filters that provide the highest level of solar protection

2 PRESERVE

DNA REPAIR

Designed to accelerate the skin's natural mechanism of renewal, this serum reduces signs of sun damage and preserves a youthful appearance



3 BRONZE

MELANOGENESIS

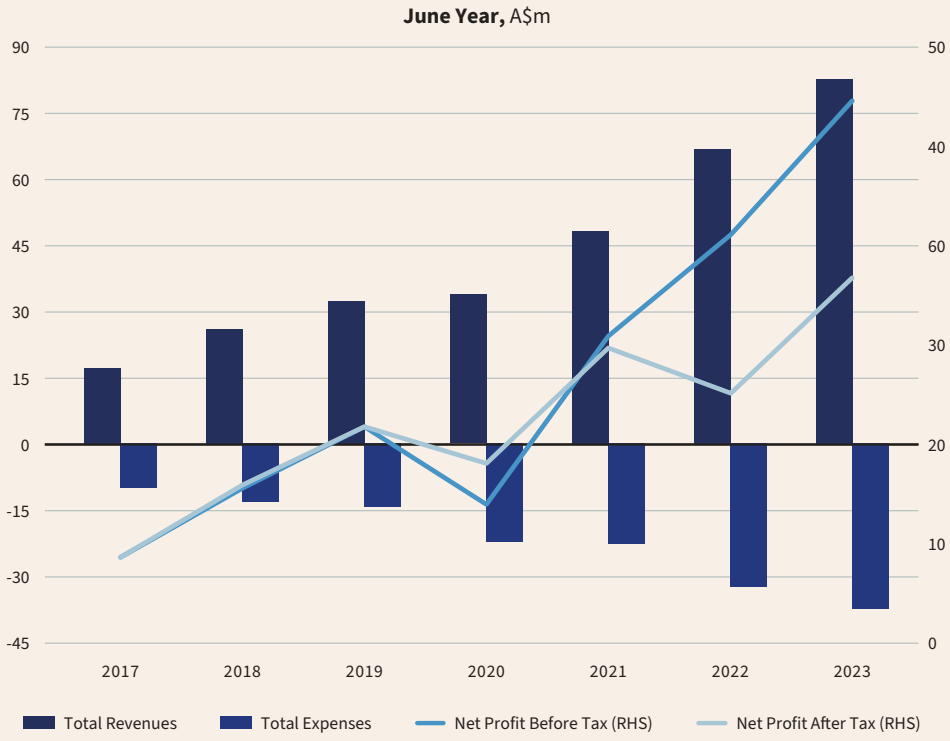
Bronze without absorbing UV rays. This product will enhance the skin's natural process of bronzing, strengthening the body's protective barrier. Powered by CLINUVEL's pioneering technology that safely activates melanin production in the skin

STRONG FOUNDATIONS ARE SUPPORTING CLINUVEL'S GROWTH

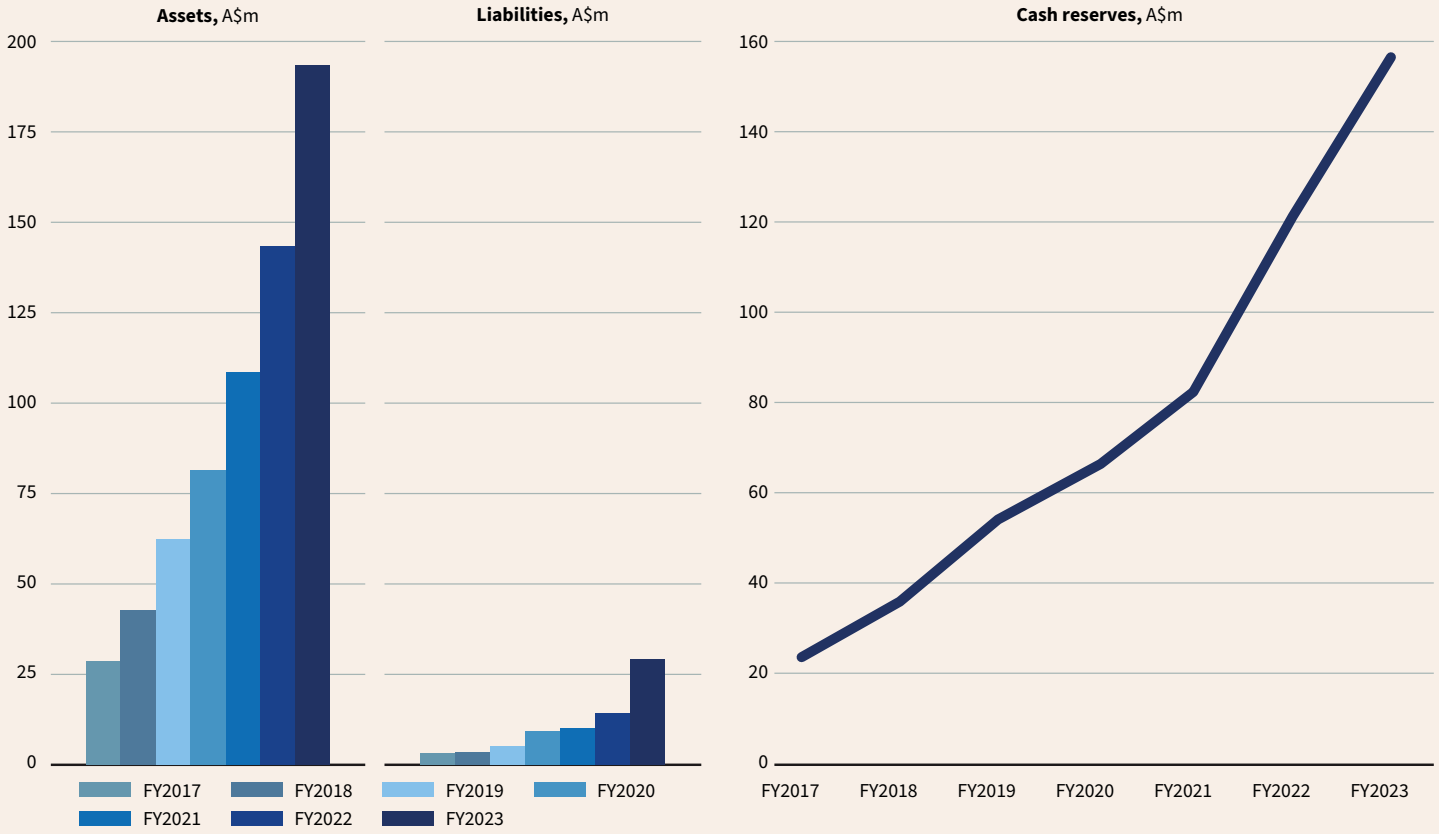
Dynamic. Evolving. Profitable. These words summarise CLINUVEL's story so far. As the firm implements its ambitious plan to become a diversified, self-sustaining and truly global biopharmaceutical company, it remains focused on delivering real value for investors and shareholders. A strong financial foundation powers their engine of growth. CLINUVEL's robust finances support their forays into new markets, with the ambition to create new revenue streams.

The last financial year was the strongest in CLINUVEL's 25-year history. The company weathered the significant macro-economic factors hindering the world economy—from the wars in Ukraine and the Middle East to stubbornly high inflation—to achieve a 24% increase in global revenues year-on-year. It marked the seventh consecutive year of annual growth in revenues, profit and cash reserves. Shareholders received an annual dividend for the sixth year running. Since 2017—when the company first turned a profit—total income has leapt by 383%, from AU$17.2m to AU$83m in 2023.

CLINUVEL is part of a small, select group of biotech firms that make money. The pool narrows even further in Australia, where the Group is listed. Of the 100 life-science companies on the Australian Stock Exchange (ASX), only three are profitable. CLINUVEL has also achieved extraordinary growth. Net profits before tax have climbed by 542% in six years, reaching AU$45.6m in 2023 (see chart). All this is good news for investors, who received a 19% return on equity in 2023, against an industry average of 12% in Australia.



WHY FINANCIAL RESILIENCE WILL DELIVER LONG-TERM VALUE

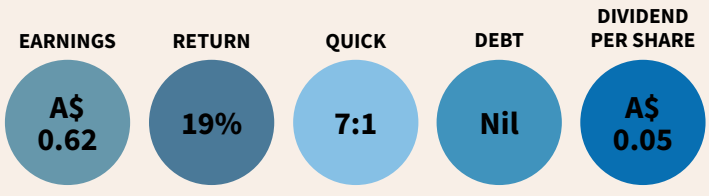


CLINUVEL's dynamism is buttressed by a strong balance sheet. As of June 2023, its total assets were worth AU$193.7m against liabilities of AU$29.1m, a working-capital ratio of 6.7. Its asset growth was largely powered by a hefty vault of cash, worth AU$156.8m in 2023 (see chart). That is the biggest sum in CLINUVEL's history and represents a jump of 29% year-on-year.

Why does CLINUVEL want this cash reserve? First, it serves a bulwark against future economic shocks. Second, it reinforces the Group's ability to self-finance its growth plan. Being highly solvent also distinguishes CLINUVEL from competitors. According to Bioshares, an Australian biotech report, as of last December 60 life-science firms on the ASX had less than one year of cash left. Only nine were cash-flow positive. By contrast, CLINUVEL has enough to cover its expenses—which totalled AU$37.4m in 2023—for more than four years. Nor is the company hampered by any bank debt. As it scales up, a lengthy cash runway indicates a strong position to provide long-term value for shareholders.

ON THE UP

By diversifying revenue streams, CLINUVEL will generate significant incremental value in future. Their innovations in both pharmaceuticals and cosmetics will positively impact market sentiment, coinciding with strengthening markets as inflation eases. In turn, the company's stock will become more desirable. Expect the share price to tick upwards in the years ahead.



Key indicators of high performance

OUT OF THE SHADOWS

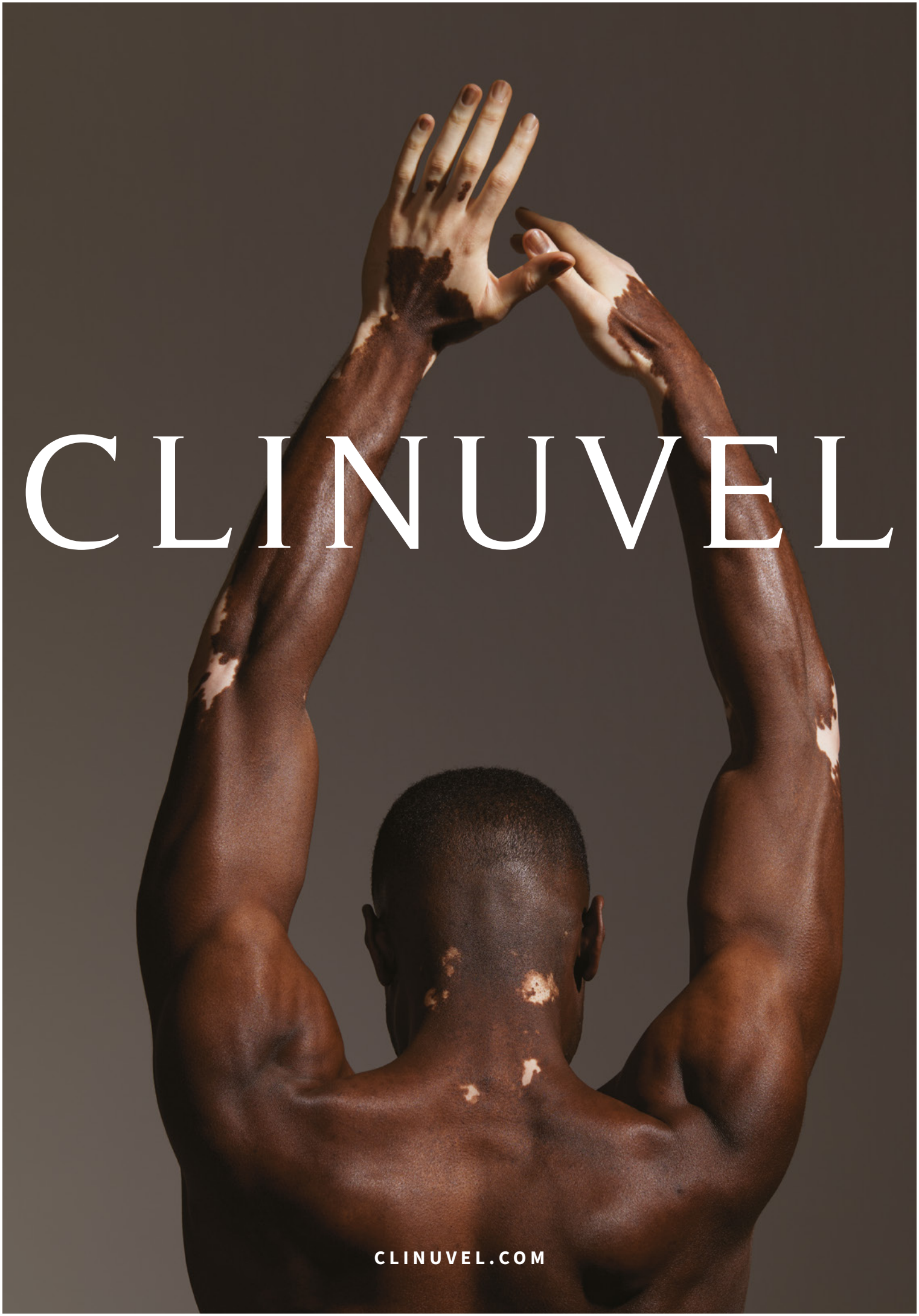
HOW CLINUVEL IS BRIGHTENING PATIENTS' FUTURES

CLINUVEL prides itself on bringing groundbreaking therapies to small groups of patients with unmet medical needs. Now the company is taking its world-leading expertise directly to communities who cannot afford care or treatment. The Photomedicine Foundation has been set up to help those who are most affected by debilitating conditions related to the sun.

The foundation's mission is to support vulnerable patients at extreme risk of photodamage and skin cancer. The initiative will initially focus on two diseases: XP and albinism. XP is a rare inherited disease which inhibits the body's ability to repair damaged DNA in skin cells. Albinism is a genetic pigmentation disorder characterised by partial or complete absence of melanin. This strips the patient of the skin's natural barrier against the damaging effects of UV light, eventually causing skin cells to mutate into cancer cells. The foundation's objective is to prevent malignant cancers, provide access to life-changing treatments, equip physicians with specialist knowledge and radically improve patients' wellbeing.

CLINUVEL is running photoprotective programmes in partnership with clinics in America, Brazil, Europe, Tanzania, Tunisia and Saudi Arabia. In addition, the foundation is establishing accessible teledermatology clinics for these disorders and creating global patient registries. CLINUVEL will fund this foundation through Vallaurix, its subsidiary in Singapore. The company will also provide in-kind resourcing for projects, in addition to donating 5% of net profits from the sale of PhotoCosmetics products.

Furthermore, the foundation is appointing five trustees – Michael Polansky – to oversee its activities, each of whom care deeply about the health of patients affected by UV and skin cancers.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