INTRODUCTION

This Strategic Update IV needs to be read as an addition to SU I (29 October 2020), SU II (12 April 2021) and SU III (8 November 2021).

The Company's progress is simultaneously discussed during a Swiss investors' meeting in Basel on 12 May, organised by CLINUVEL and Bank J Safra Sarasin for its Swiss clientele and for current Swiss shareholders.

Given the high failure rate of biopharmaceutical companies, CLINUVEL has chosen an approach of **expanding whilst consolidating** its activities. It is not a contradiction, but a conscious choice to manage with a view to establish a sustainable group of companies, centred around a few themes.

Failures in the development of pharmaceuticals occur either as new molecules and treatments no longer pass long-term safety requirements, as regulatory authorities cannot arrive at a positive benefit versus risk decision, or when insurers and decision makers in public healthcare decide to reject reimbursement of the newly approved drugs.

CLINUVEL analysed its commercial opportunities, navigated these challenges, and its current position is wholly owed to the team's ability to plan ahead and to find solutions amid changing environments. While melanocortins hold a great promise for use in medicine, as shown by a number of pharmaceutical companies with melanocortin products in their portfolio, not all of the available melanocortins have proven a resounding success on market, as challenges have shown too great to overcome.

At CLINUVEL, we plan for the longer term as we believe that bull markets and exuberance will not be able to continue without periodic corrections. Management of operations, finances and expansion of our pipeline are geared towards establishing a company able to withstand economic headwinds.

The current financial position of the Company precisely reflects our long-term strategy.

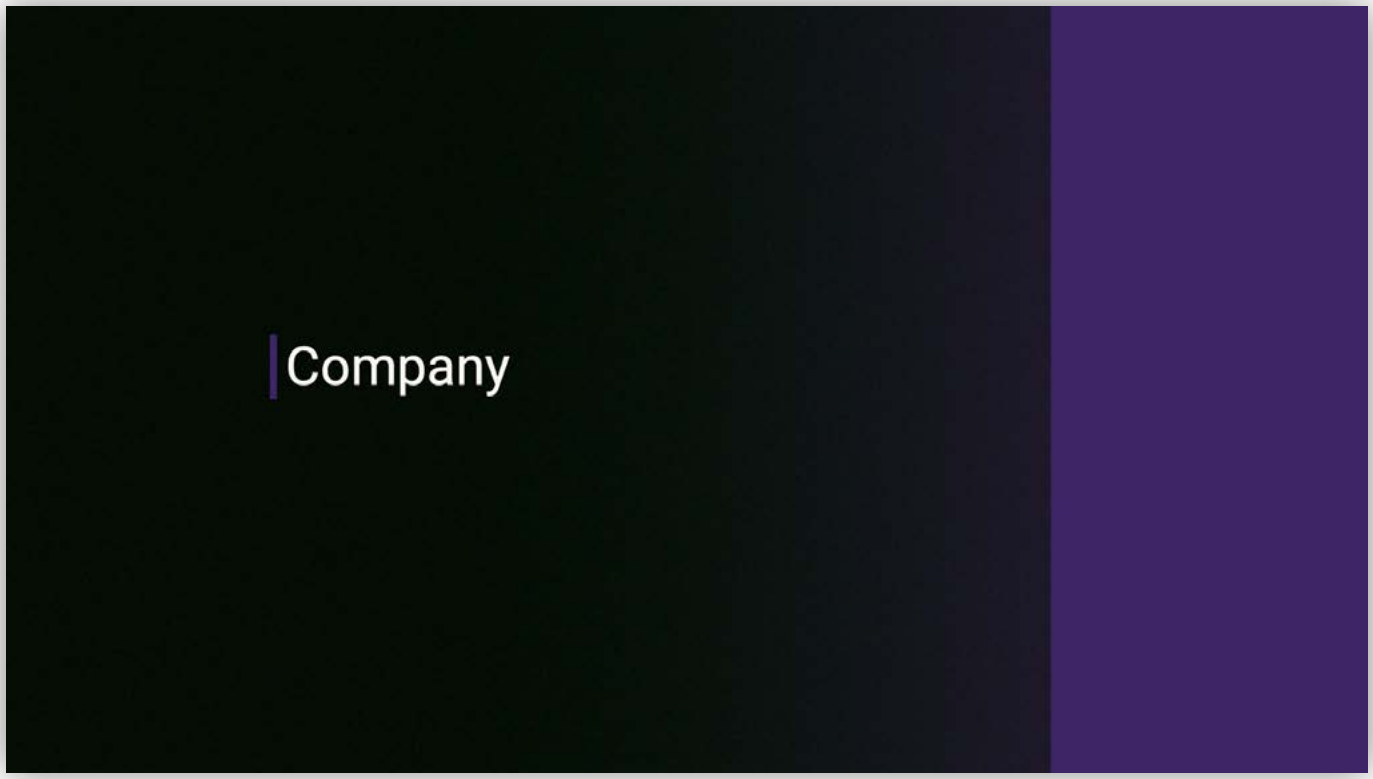
SAFE HARBOUR STATEMENT

The reader is advised to take note of the risks which can affect CLINUVEL, and within the industry it operates.

INDEX

Today we review the:
- Company
- Populations
- Pharmaceuticals
- OTCs
- Performance

of CLINUVEL.


Company

COMPANY'S STRUCTURE

As discussed previously, the starting point of CLINUVEL is to manage risks, be it those found in R&D, commercial, financial, or business domains. The attention to risk has been maintained during two decades, and while past performance cannot be a guarantee for future success, it offers an understanding of the team's approach to this particular business.

The Group consist of eight subsidiaries, four divisions spread over four continents, as our commercial affairs take place in Europe, United States, Switzerland and Israel.

We established **a Pharmaceutical Division (PD) consisting of**

- Research & development
- Regulatory affairs
- Clinical operations
- Commercial affairs & distribution
- Quality
- Pharmacovigilance

A division of Healthcare Solutions (HS) with its activities in

- Research & development
- Regulatory affairs
- Commercial affairs
- Quality
- Marketing

Communications, Branding & Marketing (CBM) consisting of main activities

- Planning, communications
- Creative, branding
- Digital
- Marketing

Manufacturing (MA)

- Quality
- Planning
- Engineering

Our finance team plays an essential role in seeing that controls are in place, planning adhered to, and variances to budgets are considered. The managers in charge of investor relations are working together with the CBM team to ensure communication remain consistent.

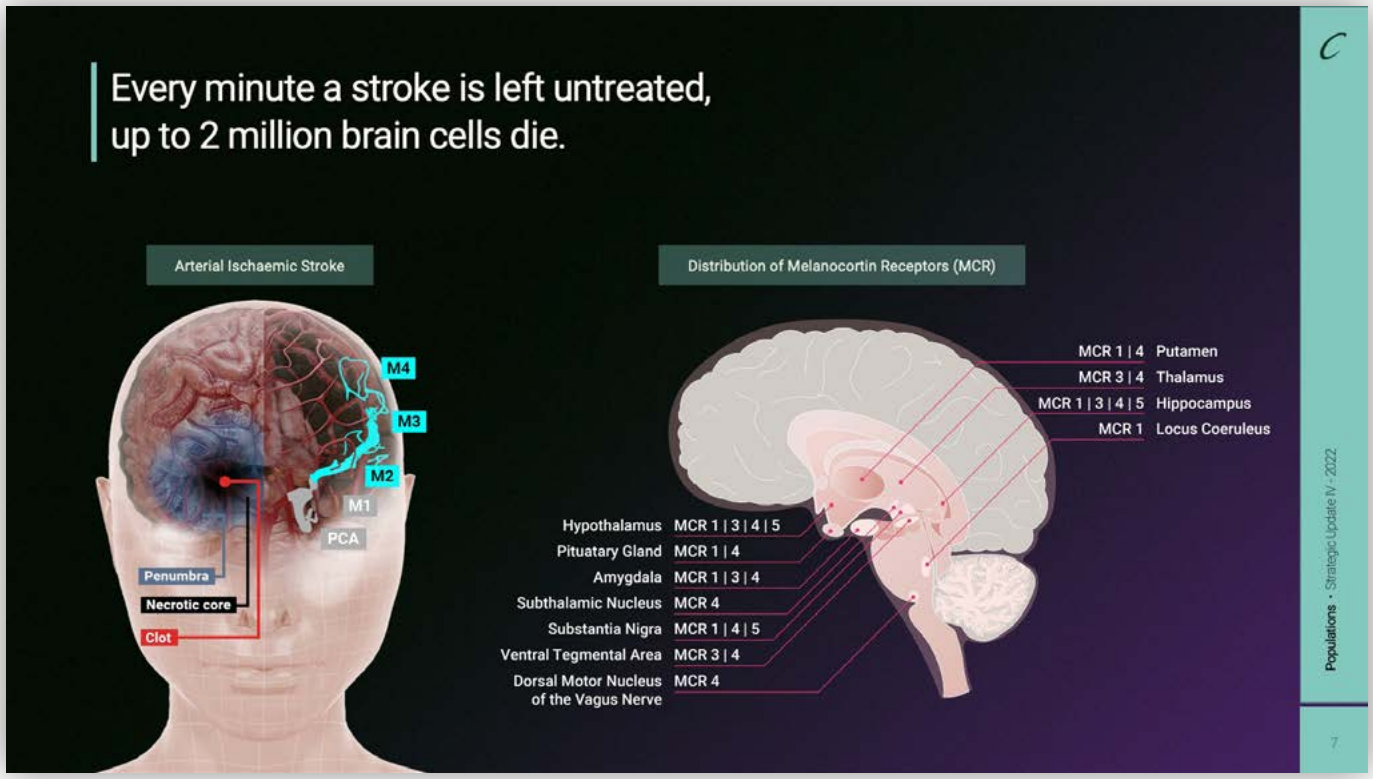
The Group focuses on 'Specialty Drugs', which require special handling, aiming to treat complex diseases.

Our pharmaceutical R&D efforts are based on incremental innovation, whereby we reinvest in research and development. Pharmaceutical technology and knowhow are being translated into non-prescriptive products for wider markets, we refer to this as Targeted Technology Translation (TTT).

The target remains to render CLINUVEL profitable, demonstrate growth, and offer its owners a sustainable and self-sufficient entity for next generations.

The red line running through the Company is to look after, care for and serve populations who have not yet been addressed or attended to. This is a social purpose we believe in.

Populations



ARTERIAL ISCHAEMIC STROKE

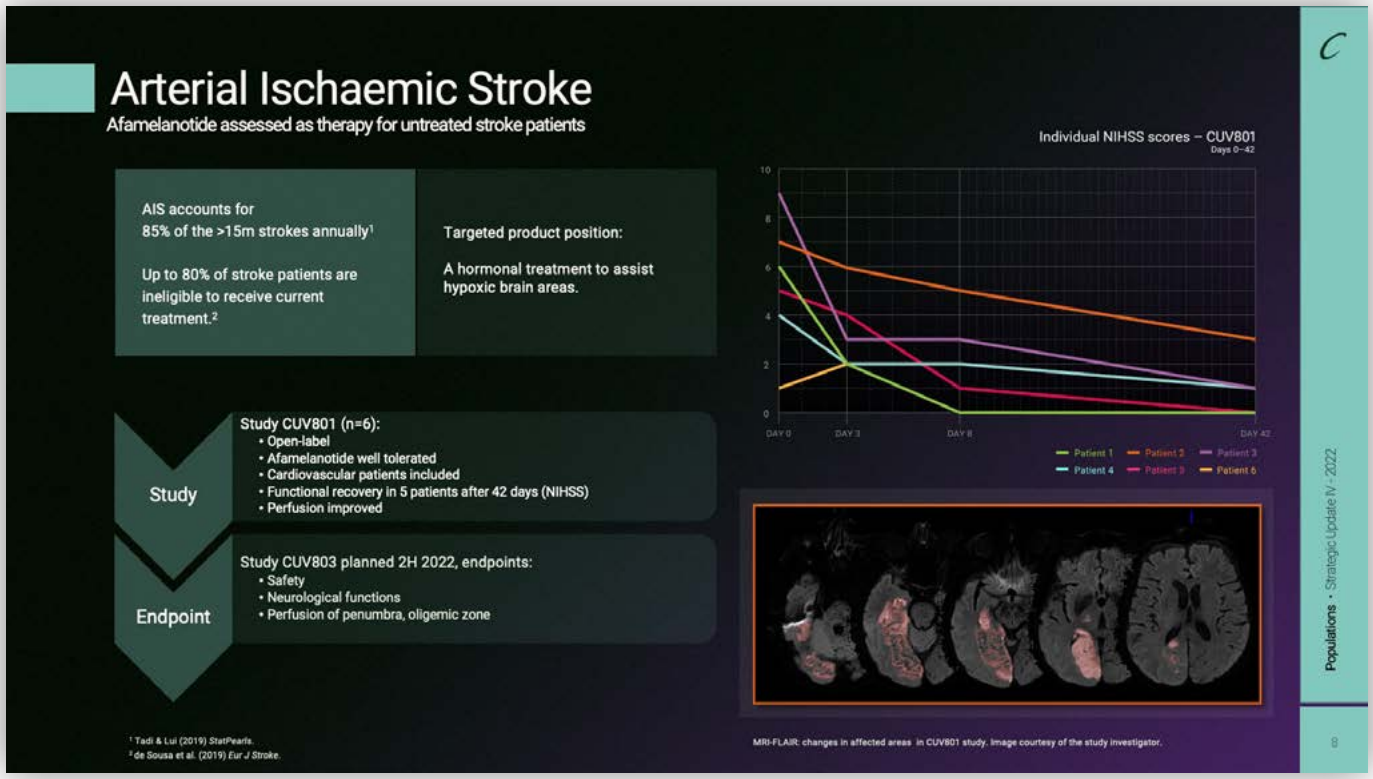
It is well accepted that during the acute phase of vascular brain injury, the critical defence mechanism of the brain, the blood brain barrier (BBB) loses its integrity (endothelial barrier). This implies that, for a short period of time, leakage occurs of proteins and body own's chemical substances. The permeability of the BBB also facilitates the passage of pharmaceutical agents, as the brain vessels require time to recover.

In acute brain injury, here specifically arterial ischaemic stroke (AIS), the affected tissue shows three zones:

- oligemic
- penumbra
- core.

In our program, we aim to assess whether afamelanotide has a therapeutic effect on the size of the brain injury by influencing the blood flow to the brain. In AIS, the brain is deprived of oxygen as a clot blocks essential blood flow.

In reviewing the potential efficacy of afamelanotide based on its pharmacological activity, we illustrate the distribution of target receptors MC1R and MC4R throughout the brain; these are viewed as the docking stations for melanocortins to latch on and to pharmacologically activate cells.



ARTERIAL ISCHAEMIC STROKE II

We designed protocols to address untreated patients, those who suffer a life threatening vascular injury in the higher regions of the brain. In these patients, due to the location of the clot, the standard of care (clot dissolution and mechanical removal) is not possible, and thus a large percentage of stroke patients remain untreated. We summarise this group as those AIS patients who suffer a clot formed at, or beyond, the second branch of the main brain arteries (anterior-middle-posterior cerebral artery).

In our clinical study known as CUV801, we assessed the safety of afamelanotide in patients who suffered mild to moderate stroke. As a secondary objective we assessed the functional recovery of patients following treatment, as well as the status of blood flow (perfusion) of the brain, analysed by using magnetic resonance images (MRI-FLAIR). As a measure of blood flow, we investigated the relative changes in cerebral blood flow.

We looked at functional changes using the National Institutes of Health Stroke Scale (NIHSS), as well as comparisons of the MRI at days 3 and 9 post-stroke.

The MRI images give an impression of the changes we try to discern at various intervals.

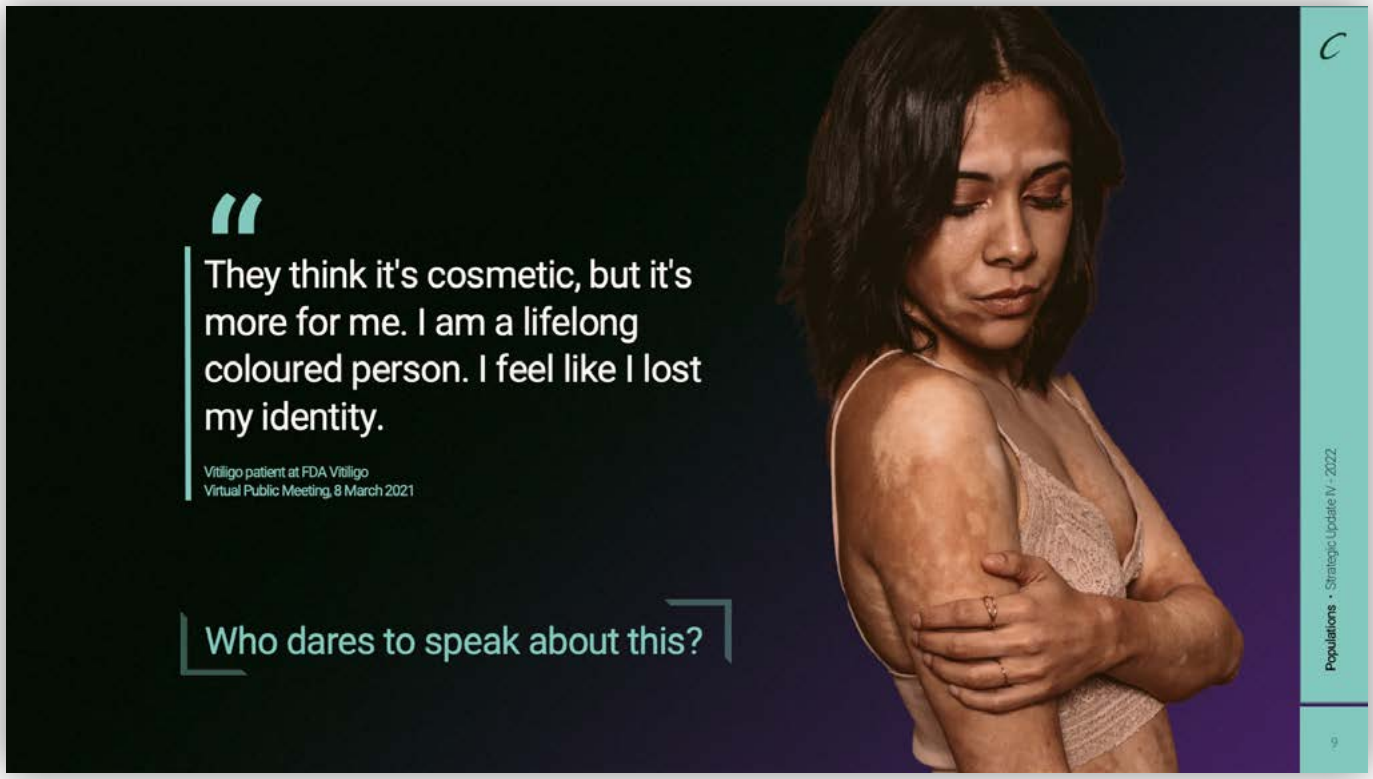
The results of this first uncontrolled study were encouraging, and provide the impetus to refine plans for the next study in stroke patients, to be known as CUV803.

A big gain from CUV801, and perhaps not fully communicated, is that **for the first time afamelanotide has been administered to patients with a complex cardiovascular history**, such as heart valve insufficiency, hypertension due to hardening of the arteries (atherosclerosis), and diabetes. In this study, it was found that the drug did not affect or worsen the underlying disease, or interfere with current medication used by the patients.

These data add substantially to the safety profile of afamelanotide, benefiting other clinical programs we have planned.

The stroke program will continue with CUV803, where the intention is to dose at higher drug levels and at different intervals, enabling us to compare these clinical findings and neuroimaging with those obtained from the CUV801 study. Here, again we work with academic experts in neurology and neuro imaging.

The timelines are illustrated.



VITILIGO I

The eighth of March 2021 marked a different direction for the US Food and Drug Administration (FDA), as it had invited vitiligo patients of **different ethnic backgrounds** to express their struggle owing to the visibility of the disease (depigmentation disorder) for the first time.

Vitiligo has often been described in popular press and by insurers as a cosmetic disease, however further studies in the disease have shown that vitiligo is debilitating, stigmatising, and psychologically distressing.

Although people of all skin types may suffer from vitiligo, the burden of disease seems higher in darker skin populations, as:

- the visible contrast of losing pigmentation is more pronounced than in lighter skin types,
- progressive disease often leads to full loss of pigmentation and therefore of racial and cultural identity, and
- it restricts social interaction and intimacy.

Naturally, the FDA operates on the basis of a non-discrimination policy enabling treatment for all patient populations; the FDA judiciously limits approval of race-specific drugs. However, it also recognises that specific populations can be more sensitive or prone to disease expressions, such as in vitiligo.

CLINUVEL wishes to be the first company to focus on patients of a darker skin type and who have not been adequately addressed. Our technology has been shown to be more effective in repigmentation of patients of darker skin colour, as seen from the follicular melanogenesis in our earlier clinical studies known as CUV102 and CUV103.

We will now proceed with a study using **afamelanotide as a monotherapy** in this specific vitiligo patient population (for further details, see Strategic Update I and II).

VITILIGO II

Our earlier studies, CUV102 and CUV103, assessed the effects of afamelanotide in combination with narrow band ultraviolet B (NB-UVB) phototherapy, showing good results (Lim et al., 2015; Toh et al., 2020).

From CUV102, we learned that mean scores from validated vitiligo tools VASI and VETF decreased significantly from baseline, whereby the mean and median decrease was higher for the afamelanotide/NB-UVB group (p = 0.025; VASI, p = 0.023; VETF extent).

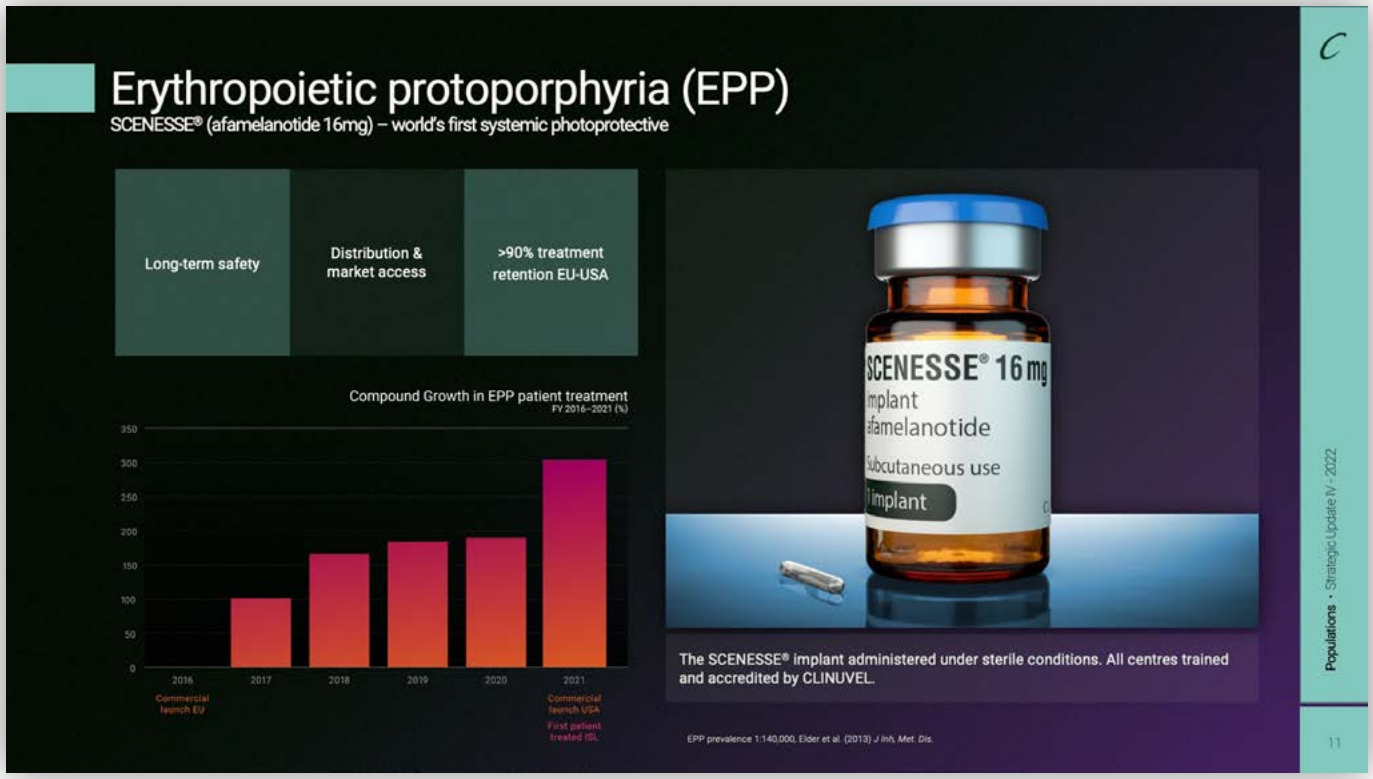
On further analyses, it was found that patients of different ethnic origin and different Fitzpatrick skin types had shown significantly greater improvements in the combination group compared to the NB-UVB group.

From CUV103 we learned important lessons from a small patient sample in Singapore, which had never been reported before by expert centres, and which surprised the medical community and our clinical team. Patients of darker skin types did respond well to the drug, but within their community the darkening of surrounding skin was perceived as socially unacceptable, since fair skin is associated with a higher social status as opposed to darker skin.

The protocol design of CUV104 aims to replicate the **commercial use of the product under real life conditions**, that is when afamelanotide becomes commercially available for prescription. For the first time we are evaluating the degree **of repigmentation of patients of dark skin only**. A beneficial response to afamelanotide as a monotherapy would be a medical breakthrough for these patients.

CUV104 is a three-month study (treatment phase), with a three-month follow-up period (maintenance phase), including patients with a documented history of vitiligo on the face. The study is to be conducted by a prominent North American expert centre during the summer months.

We expect the results of CUV104 in the first half of 2023, depending on the rate of patient recruitment.

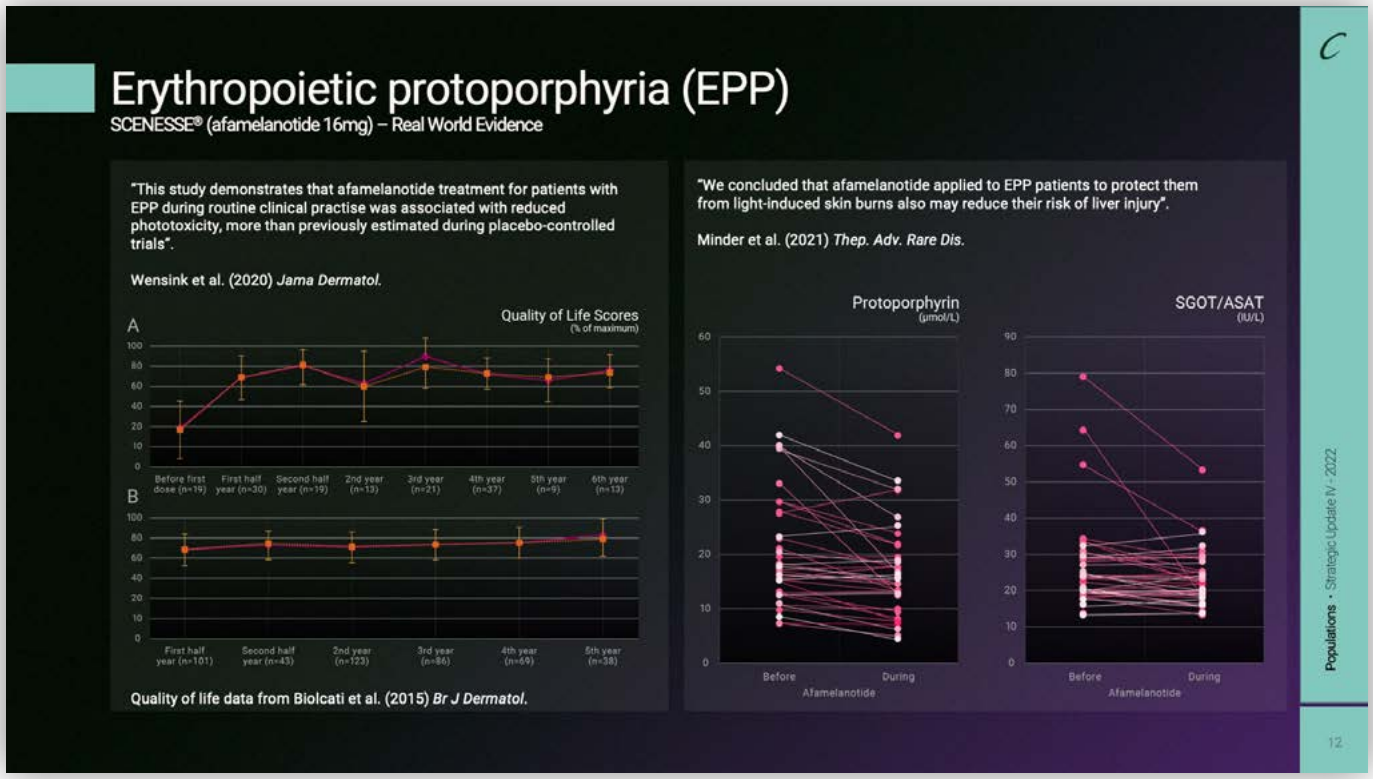


Erythropoietic Protoporphyria (EPP)

The progress in commercially distributing SCENESSE® (afamelanotide 16mg) continues as we have entered the seventh year of supply in Europe, and the second full year in the United States.

Retention rates in Europe have remained above 94% year on year, seen from the demand for the drug by the same patients, while new ones are being introduced to the treatment.

In the US, the retention rate is 98% as we entered the second full season. Feedback from American patients is excellent, as our teams have trained and accredited more than 45 centres across the country. The wide distribution of centres allows patients access to treatment.

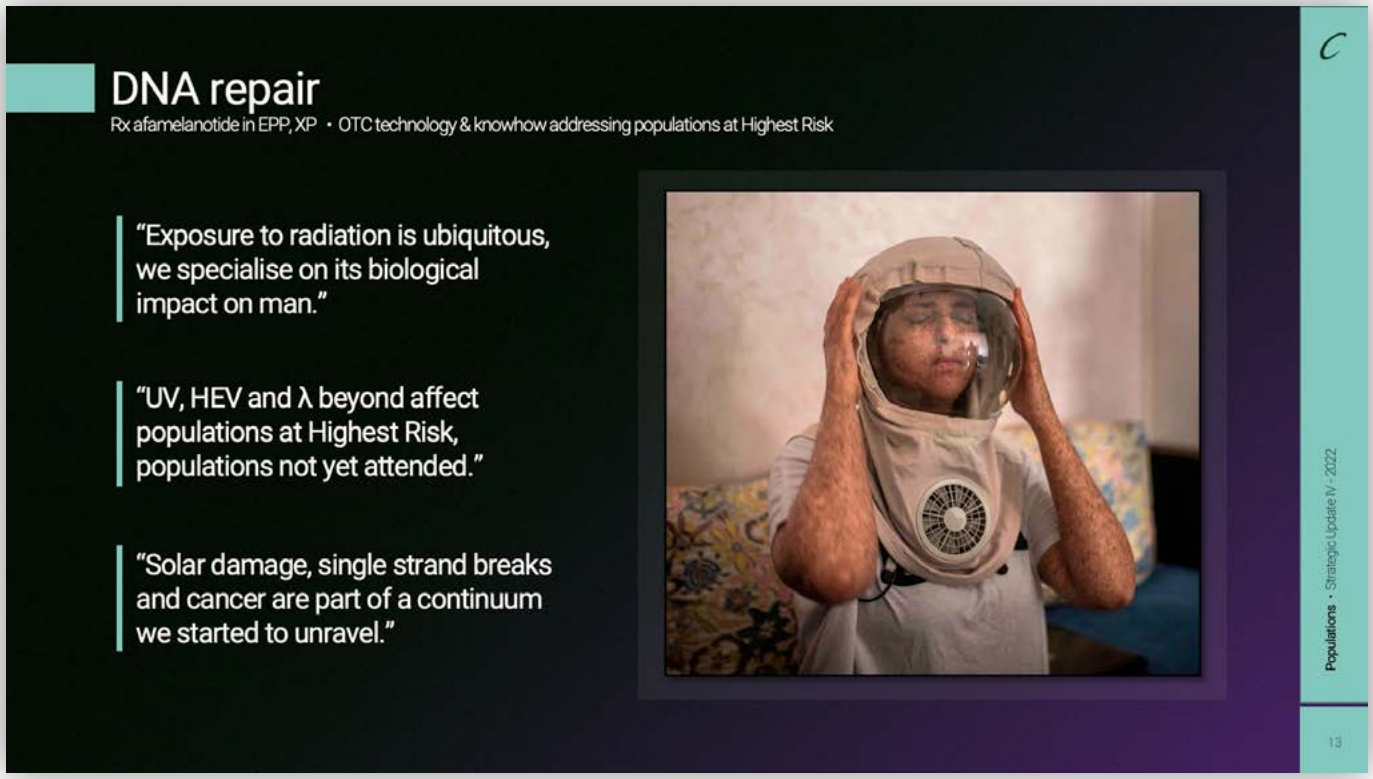


Erythropoietic Protoporphyria (EPP)

Data on the use of SCENESSE® in EPP continue to be generated under **real world conditions**. Longitudinal analyses in Europe show a consistent improvement in quality of life reported by EPP patients under expert care (Biolcati et al., 2015) and overall reduction in phototoxic episodes (Wensink et al., 2020).

Recently, we have seen a first publication on the drug's ability to protect the liver of EPP patients, nearly 20% of whom experience some liver injury (Minder et al., 2021). Laboratory analyses of EPP patients' levels of the porphyrin protoporphyrin IX and enzyme aspartate aminotransferase by the Swiss group showed long-term treatment with SCENESSE® led to reductions of both, and the conclusion that treatment may confer a hepatoprotective effect.

The use of a physiologic (biological) solution – in the form of melanocortins – to treat erythropoietic protoporphyria is preferred as the entire cellular pathway of targeted cells is activated. The safety profile of afamelanotide has been a strong emphasis of CLINUVEL's scientific and pharmacovigilance teams over the decades, and no concerns have been raised from reported adverse (drug) reactions.



DNA REPAIR I

Exposure to non-ionising radiation occurs everywhere, at any place, and during all seasons. Traditionally, medical sciences – but also the pharmaceutical and healthcare industry – have focussed mainly on the effects of ultraviolet B and A (wavelengths of 280-315 nm and 315-400 nanometres, respectively).

However, CLINUVEL's teams have held that the monochromatic (one wavelength) approach is only part of the story to find solutions for patients at risk of solar damage and skin cancer(s).

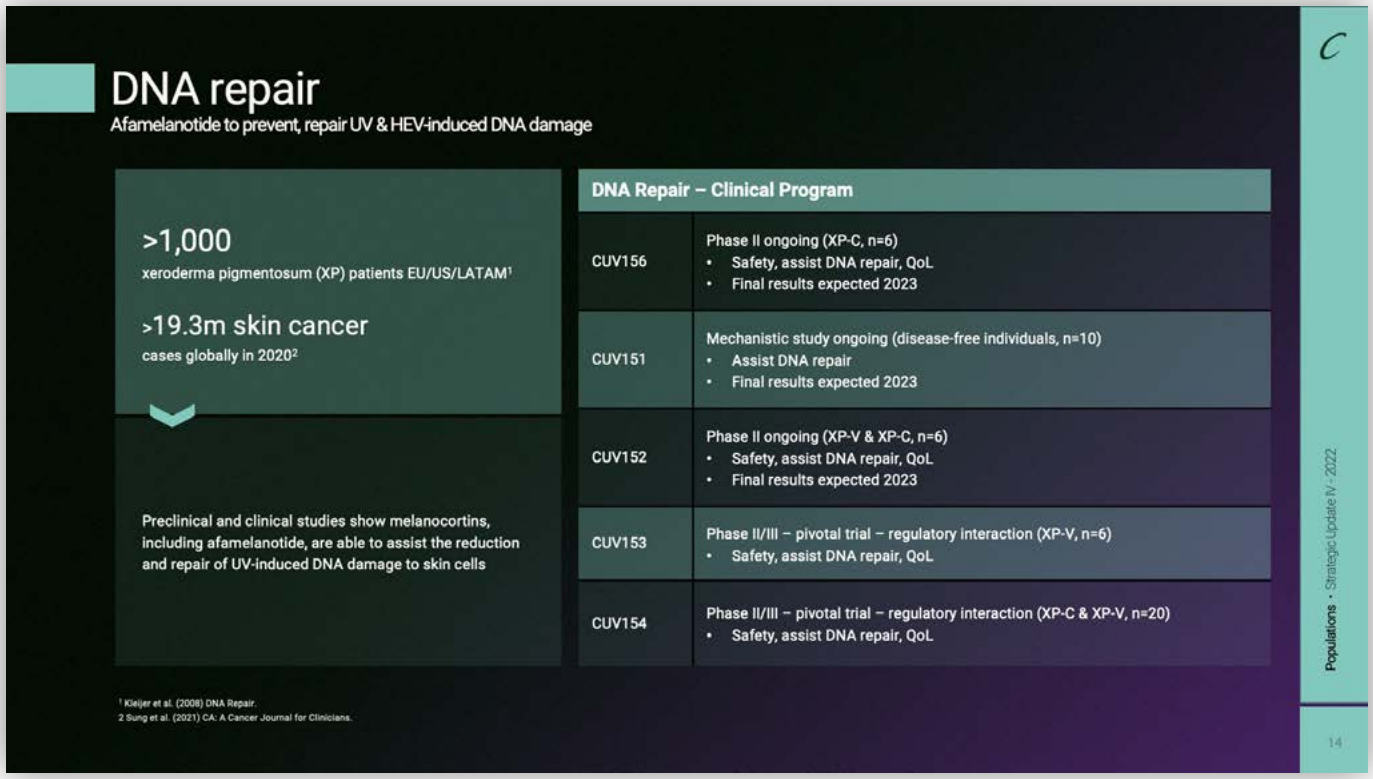
We use a **polychromatic approach** to distinguish the effects of solar radiation, to provide systemic or localised photoprotection to populations at 'Highest Risk'. When light insults our skin, it comes in multiple wavelengths, in multiple colours invisible and visible to the human eye.

In general, when talking about exposure to solar radiation, there is a continuum of: sunburn; solar or photodamage, primary signs of chronic tissue changes (photoaging); and skin cancer(s). For EPP patients, we developed a disruptive pharmaceutical treatment to address the visible portion part of the light spectrum, 'the blue' emission between 400 and 700 nanometres in wavelength.

From EPP, we traversed to pay attention to xeroderma pigmentosum (XP), a disorder whereby patients are known to develop multiple skin cancers yearly due to a genetic deficiency in cellular DNA repair mechanisms (nucleotide excision repair, NER). Upon polychromatic light exposure, these patients rapidly incur skin damage and develop the first signs of skin cancer (actinic damage). Often these skin cancers are lethal to this group.

Part of CLINUVEL's scientific teams have focussed on optics, physics and the interaction of light and human tissues, such as the skin.

The unmet yet addressable problem is immense, and we are steadfast to develop a suite of products, both prescriptive and non-prescriptive to attend 'forgotten' populations.



DNA REPAIR II

We discuss our DNA Repair program conducted in **XP-C and XP-V** patients, whereby non-diseased fair-skinned individuals serve as a control group.

Depending on the strength of the data, our teams intend to file the entire data set of up to 38 XP patients – and 10 controls – to the regulatory authorities to obtain market authorisation, that is if and when results prove to show effectiveness of afamelanotide. Multiple discussions with the authorities are being held prior to filing in this ultra-orphan indication.

Among various others, the main objectives (endpoints) of the XP studies are defined as assessment of

- minimal erythemal dose
- photoproducts
- oxidative damage
- quality of life

With this program, CLINUVEL is the first company to conduct trials using a systemic therapy (targeting the entire body) to assess the benefit to XP patients.

The addressable market for systemic photoprotection in XP is difficult to assess, since many countries do not yet have a patients' registry. However, we are aware of ~1,000 patients worldwide who are affected by this most severe condition. XP-C and XP-V patients have a limited life expectancy in most countries as they succumb to multiple skin cancers.

Illustrated are the clinical studies with anticipated patient numbers

- CUV156, 6 XP-C patients
- CUV151, 10 disease-free individuals
- CUV152, 6 XP-C and XP-V patients
- CUV153, 6 XP-C and XP-V patients
- CUV154, 20 XP-C and XP-V patients.

These studies form our comprehensive program in XP, in which our teams are endeavouring to set new standards and introduce a medication which assists DNA repair.

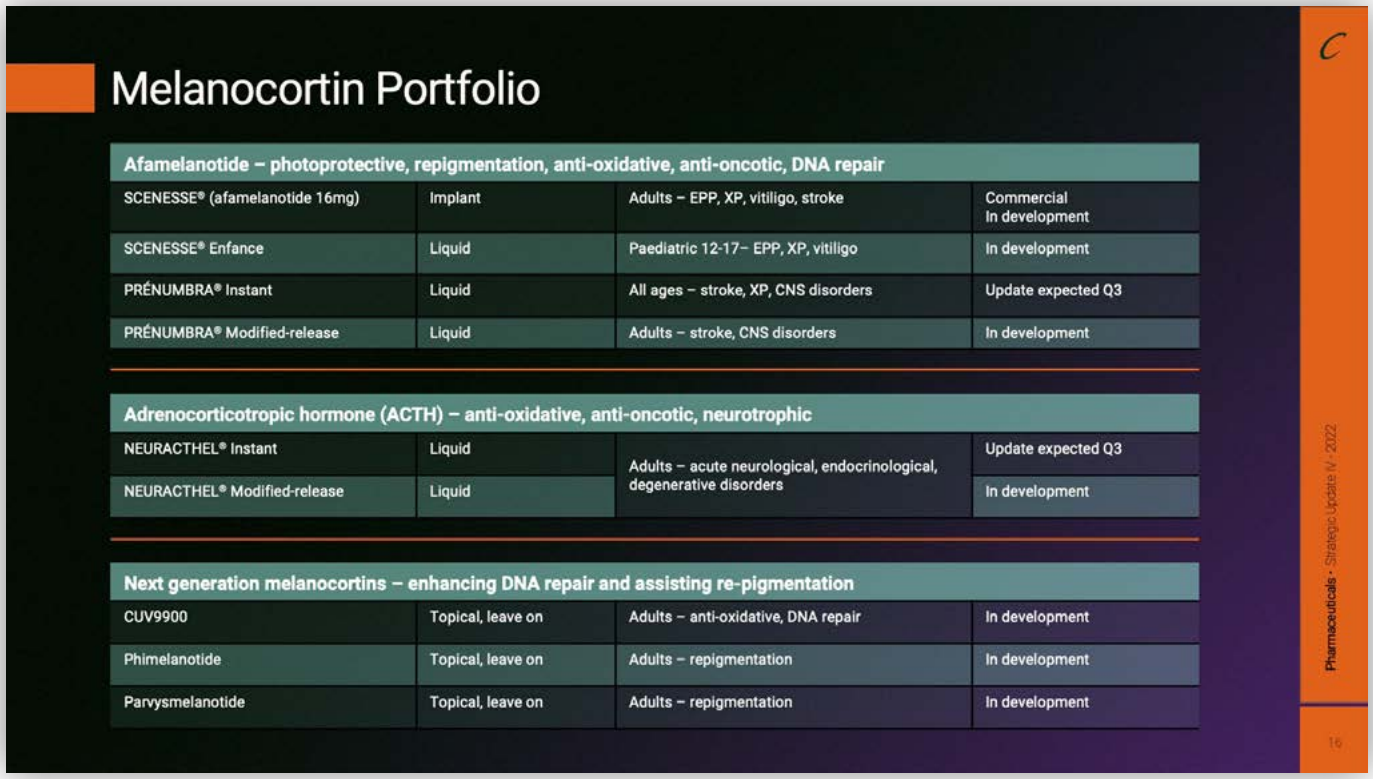
However, the relevance of providing systemic therapy in XP to lower the risk of solar damage is much broader. Swathes of fair skinned populations worldwide are affected by polychromatic radiation from solar exposure, causing damage of the skin and increasing the risk of skin cancer(s). In 2020 alone, over 19 million cases of skin cancer were diagnosed worldwide.

Strengthening CLINUVEL's DNA Repair program, various research groups have already reported and confirmed the beneficial effects of using melanocortins as skin cancer preventives, while CLINUVEL's clinical work has shown the beneficial effects of afamelanotide on UV-irradiated skin cells (keratinocytes).

Three trials (CUV156, CUV151, CUV152) are currently being conducted in expert centres, which have long cared for XP patients without actually ever having had an effective therapy or medication to offer.

In total, five centres are participating in the trials with another two having agreed to be involved in future assessments.

Pharmaceuticals



MELANOCORTIN FAMILY

The table shows the current suite of melanocortins in development, while we intend to add more to our pharmaceutical portfolio.

NEURACTHEL® (adrenocorticotropic hormone) has been the latest addition, and a manufacturing update is expected later this year.

PHARMACEUTICAL TRANSLATION TO HEALTHCARE SOLUTIONS

To understand the expansion to Healthcare Solutions, we walk through a number of steps in following a logical reasoning.

STEP 1 PHOTOMEDICINE

CLINUVEL's scientific teams deepened their knowledge in photomedicine at a time when other pharmaceutical companies were disinterested or had abandoned the investment in either melanocortins or light-induced diseases.

The afamelanotide molecule was developed to prevent and mitigate phototoxicity in patients diagnosed with **EPP.** It was discovered that these patients were uniquely toxic to light emitted along wavelengths higher than 400 nanometres, the blue, green and orange (visible light) segments of the electromagnetic spectrum. The development of a drug that would work throughout the circulation to photoprotect these patients has been entirely novel. **SCENESSE®** became **the first systemic photoprotective drug** in the world.

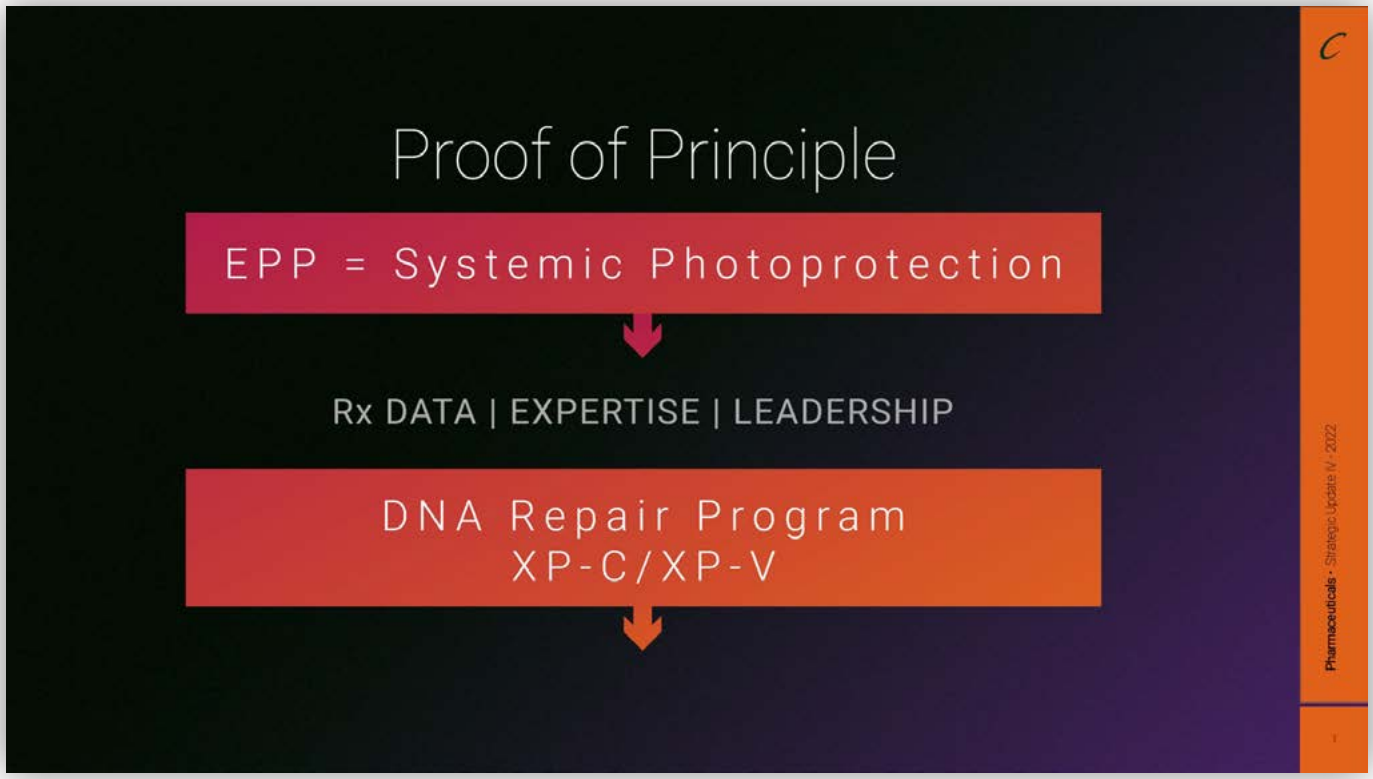
From here onwards, the scientific teams learned how to maximise the delivery of afamelanotide in the human body to arrive at an optimum blood concentration. This work took years, resulting in a thorough understanding of pharmacology, kinetics and therapeutic targets. In simpler words, the delivery of the drug mattered, and our teams arrived at an implant which would dissolve in the body. Although implants had been known in medicine, this method of delivery was equally novel, a first.

Thus, the scientific managers started from a deep understanding of **peptide and proteins**, enlarged their knowledge to **drug formulations** and experimented with various dosage forms. As the specialty in melanocortins had grown, and in parallel their use in targeted diseases, our clinical teams were generating data in diverse patient populations to satisfy our questions but also to enhance regulatory discussions on safety of the long-term use of afamelanotide.

Within the sub-specialty of photodermatology, our scientific talent focussed on action and inhibition spectra, on absorption capacity of chromophores, and the interaction of light and human tissues. Accordingly, CLINUVEL conducted numerous phototesting studies and photoprovocation trials involving varying dose of emitted polychromatic (multiple wavelength) light.

Armed with an increasing pool of safety data obtained from many different patient populations, a consistent profile of afamelanotide was seen, albeit our teams had still not answered the question of drug-drug interaction: how afamelanotide would possibly interfere with the effectiveness of drug administered to patients, who suffered from other diseases.

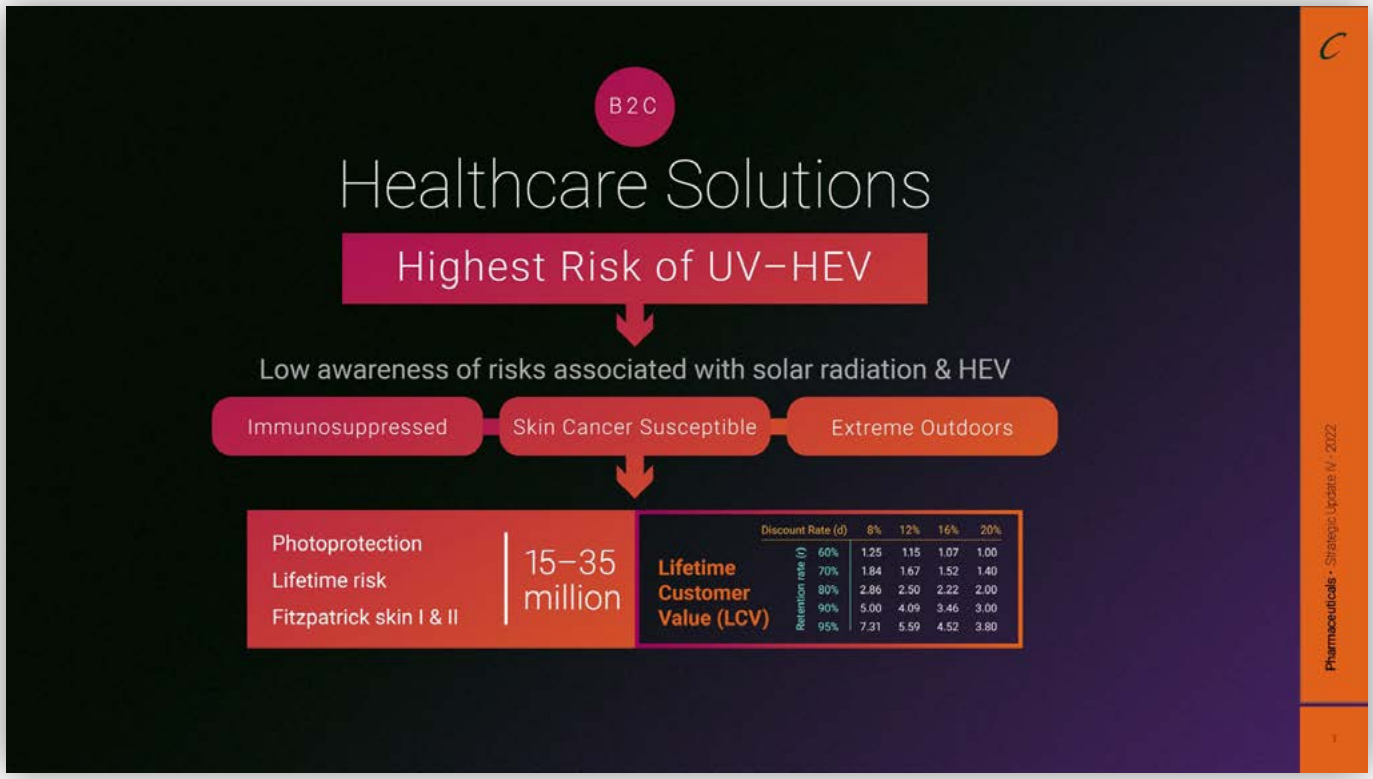
The marketing authorisation of SCENESSE® granted by EMA, FDA, and TGA, and market access in Israel, served as a proof of principle demonstrating the safe use of afamelanotide under real world conditions.



STEP 2

From the severe disorder EPP, our objective had been from the onset to make SCENESSE® available to patients suffering from **XP**, a life-threatening disorder and most disfiguring condition imaginable. It is known that these patients have a short life expectancy, and since no other injectable therapy had been developed for them, we have accepted the challenge to commercialise a **photoprotective** treatment for this "forgotten group".

Thus, departing from EPP the Company transcended to XP, two severe photodermatoses, and invested in scientific technology to lead the pharmaceutical sector by developing "systemic photoprotection" (targeting the entire body) for these patient populations.



STEP 3

It had become increasingly clear that patients suffering from photodermatoses would benefit from being prescribed SCENESSE®, but would also stay with their habit to use sunscreens. As to our experience, many dermatologists in the world recommend using sunscreens to provide a physical barrier to ultraviolet (UV) radiation.

Our teams contemplated that the patients already served, the medical community and other Highest Risk categories would benefit from our photoprotective products, not only the prescriptive injectables based on melanocortins, but also over the counter as a leave-on products.

Hence, CLINUVEL started to develop next generation leave-on products for skin care to accompany and complement SCENESSE® for Highest Risk populations. This strategy is of course risk-laden, as we now enter into a B2C business model compared to our existing pharmaceutical business B2B model.

Nevertheless, the demand for novel products, for **polychromatic photoprotection** and **assisted DNA** repair led us to proceed with the concepts and developments.

For this we established a team around Healthcare Solutions, comprising teams of scientific, regulatory and marketing disciplines.

We found that **the addressable markets for the Highest Risk at solar radiation** are vast, but we equally discovered that three populations have not been attended by the industry:

- immune suppressed patients,
- those with a history or family predisposition to skin cancers, and
- those who expose extensively and chronically outdoors.

Based on available data from secondary market research, prevalence data and medical procedures, **the estimated market consisting of populations at Highest Risk of solar damage and skin cancer(s)** lies between 15 and 35 million.

Since the skin cancer prevention market for products is not well defined, and the only data existing originates from the dermatocosmetic sector,[1],[2],[3] further research was needed to retrieve more accurate data. Repetitively, the expert academic centres and our teams arrived at estimates exceeding 35 million people affected by skin cancer along the three categories.

It is known from primary research that the **Lifetime Customer Value (LCV)** in specialised cosmetics is higher when an awareness of explicit need for care is raised with consumers. In analysing available data and making conservative assumptions, our commercial teams arrive at a margin multiple value table as illustrated on the table on the slide.

At 60% user adherence rate, call it repetitive use and product loyalty, and using a discount rate or cost of capital in the range of 8% to 20%, the multiples can be found in the table.

Among the Highest Risk categories, the LCV of an annual user of CLINUVEL's products is then found by using the factor in the table multiplied with the value of the gross revenue per annum. As with many models, a number of underlying assumptions are made, but here the most conservative base is used.

[1] Mintel (2020), IMARCH (2020), Mayo Clinics (2021)
[2] WCRF (2021), AAD (2022)
[3] Dataintelo Report (2022)

STEP 4

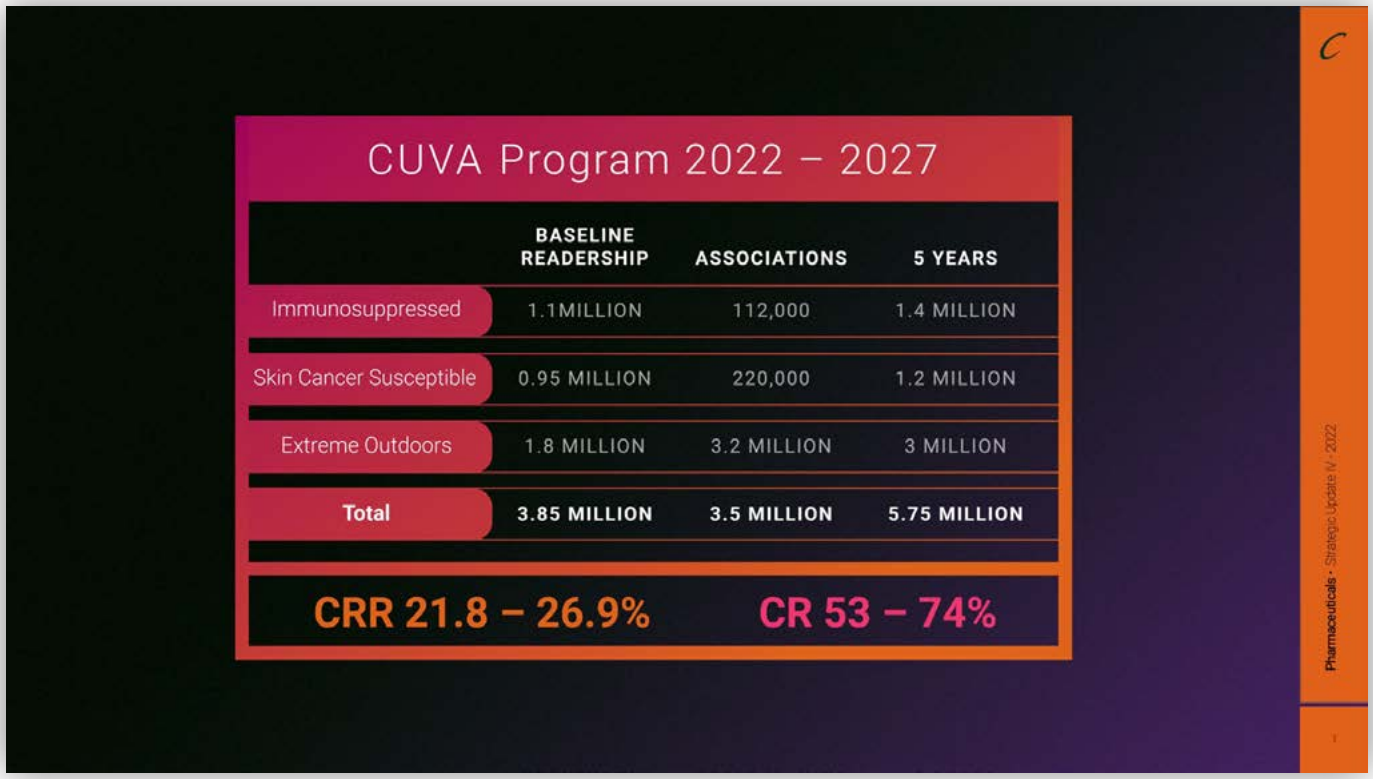
We established a communications, branding and marketing (CBM) team to incorporate skills the Company did not have, essentially bringing in-house professionals with a proven record of marketing, distributing, and using online channels to reach new audiences.

Following the gradual formation of the CBM team, we established a global program, which would satisfy our corporate objectives, three in total to achieve:

- Connectivity
- Dissemination
- Conversion.

Those familiar with targeted digital marketing will recognise the objectives we had formulated to arrive at success.

Our target is to reach 25 million in readership, impressions, leading to engagement and eventually conversions.



STEP 5

We analysed data from the dermatocosmetic industry, other industries and retail sectors – B2C businesses – and gained much intelligence from working closely with agencies, consultants and digital marketing companies.

Eventually, we arrived at **a model differentiating CLINUVEL** from others, but still keeping within the current trends of online marketing. We established a concept authenticating online content, mainly generated by **Ambassadors**, being key **representatives of the three Highest Risk categories**.

We formed **the CUVA team**, being a group of **CUV Ambassadors,** connecting with the fragmented communities of people worldwide who share the same concern, the same risk and being part of unattended clusters. As representatives of the three HR categories listed in Step 3, the objective is to connect with micro communities and disseminate relevant information on solar radiation, DNA damage and skin cancer risks.

The Company committed to **a five year program**, thereby budgeting for a global team executing clear objectives forming online communities. The table on the slide demonstrates the planned program, where numbers indicate the third stage of our CUVA (CUV Ambassadors) program.

The start of the first of three test campaigns - spanning three times every three months in total (nine months) - serve to test and evaluate content generation, adherence and subscription rates. During these campaigns the CUVAs will follow a weekly program connecting and disseminating relevant content to their followers, associations, organisations and professional bodies to raise awareness of CLINUVEL's mission.

OTCs

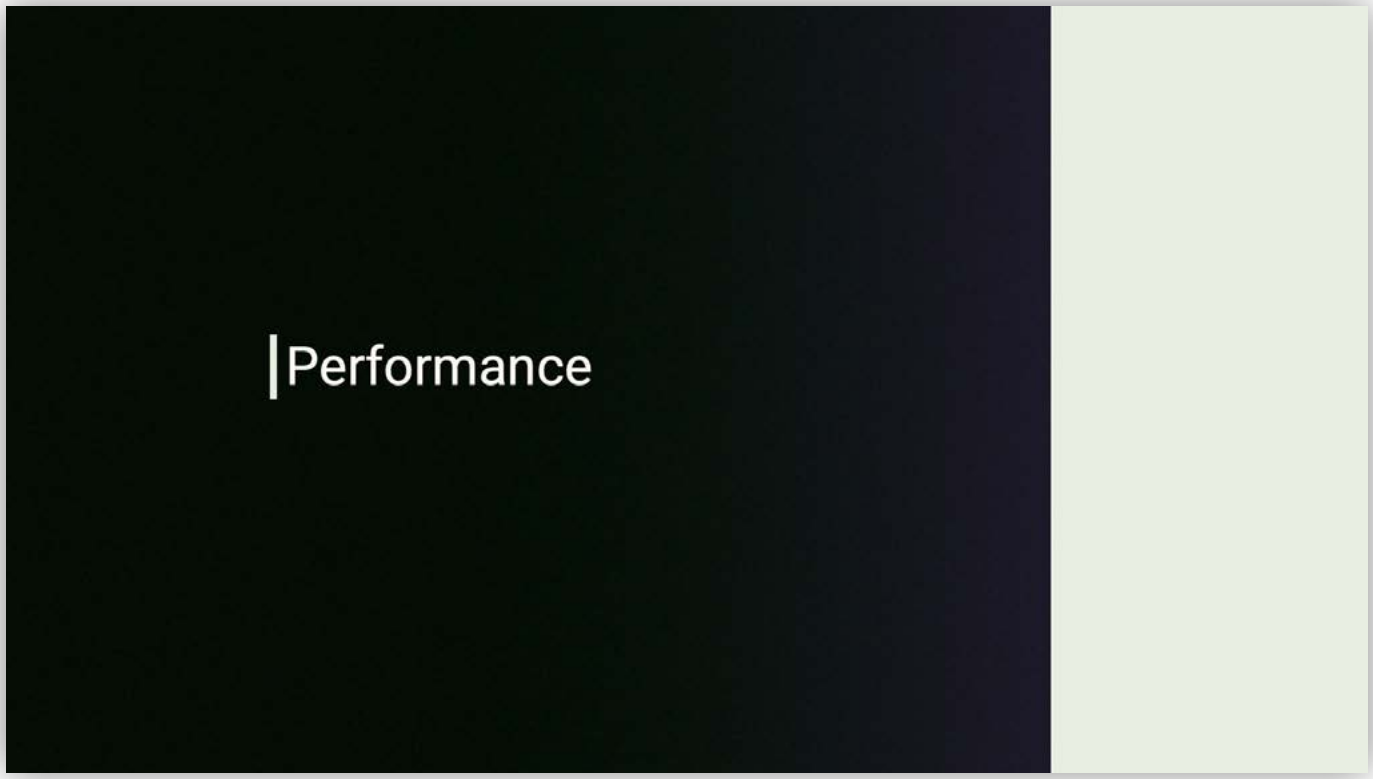
HEALTHCARE SOLUTIONS

The three non-prescriptive over the counter (OTC) product lines aim to serve various populations, such as those users at Highest Risk, those who require cellular repair in assisting cellular DNA fragility, and those who require maintenance of melanogenesis (pigment stability).

With these non-prescriptive products, CLINUVEL extends its care for patient populations served with the prescriptive hormonal treatments, while new populations at Highest Risk are being addressed.

There is an obvious relationship between CLINUVEL's progress in its clinical programs and the timing of release of e.g. the first polychromatic photoprotective product line. Simultaneously, the CUVA Campaigns will be under way to ensure HR populations are being communicated to, are being connected and are provided information on relevant topics.

CLINUVEL's teams are always aware of the risk of entering new markets, and a deliberately timed as well as a staged, approach provides the highest chance of reaching specific audiences in dermatocosmetic care.


Performance

PERFORMANCE

CLINUVEL's share price, but also those of other pharmaceutical mid-size companies, has been a recent talking point among shareholders.

It is thus relevant to share our views on CLINUVEL's public market valuation, which has come under pressure of late.

The discussion is started by looking more closely at the calendar year **2019**. In this year, we witnessed an increase of trading volume in CUV starting in April to last until January 2020. Over a course of 50 trading days, 30% of the Company's outstanding share capital was traded, whereby the price reached an all-time high of A$44.91 to retreat to the same level in January as it had been in September. This increase in volume was seen leading up to the FDA approval of SCENESSE®, which decreased after a positive outcome. The Company had not yet started distributing its lead product in the US, its receipts were increasing due to EU sales, and the balance sheet was not as strong as it is currently in May 2022.

In **CY 2020**, one sees an increase in volume traded in CUV around quarterly results in March, while the share price had reached a low of A$13.59 and year-high of A$29.25 at closing of the markets. During this year, the Company posted continuous increase in receipts and profits, while US receipts had just started.

In **CY 2021**, one observes a year-low of A$19.79 and high of A$43.58, the latter most likely a response to the FY 2021 results.

CUV's share price has retreated ever since while, its profitability has grown, reserves increased, and progress has been made.

CLINUVEL's Board and management do not encourage financial speculation on the basis of its observations, but these are shared for all to consider.

In making objective comparisons with the US and Australian public markets, some analogies are perhaps opportune.

On the Australian Securities Exchange (ASX), 91 listed companies are categorised as biotechs and pharmaceuticals. Closer analyses show that the basket of 91 companies is actually not homogenous, since diagnostic companies are included. However, of these 91, only 10 are profit generating, that is 10.9%.

However, a better analysis is to look at our view of 'pure' pharmaceutical and biotech companies, it then is seen that only three are profit generating (3.3%): CSL (a large, specialised company on blood products), CLINUVEL and AFT Pharmaceuticals (generics). The sobering news is that down-under these companies, 96.7%, are still dependent on finance of some sort.

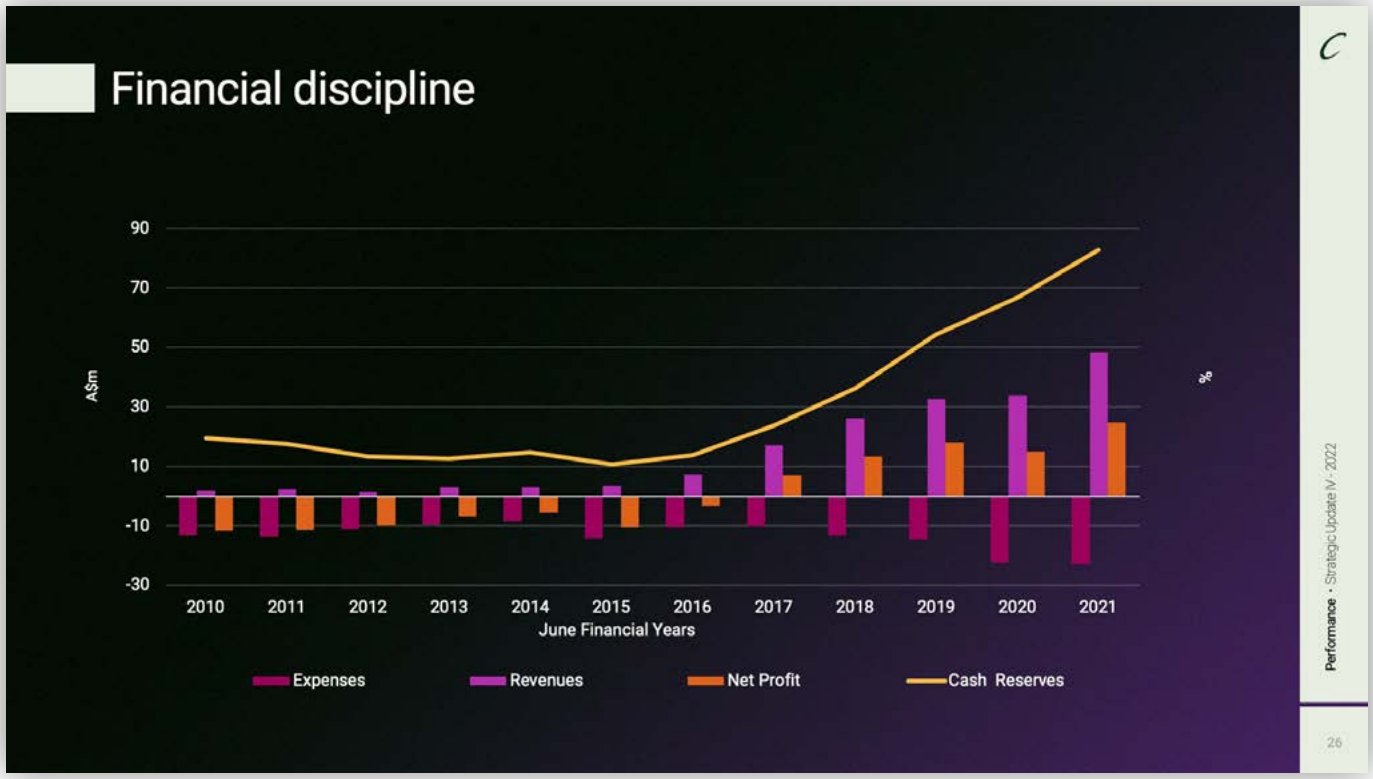
In the US the percentage of profit generating companies is higher, but still low in relative percentages.

Of the companies included in the Nasdaq Biotech Index (NBI), at the end of the December quarter 2021, and beginning of quarter 1, 2022, 62 out of 370 (16.8%) of the biotechs/pharmaceutical companies were posting positive earnings. From the Nasdaq equities team and FactSet, one learns that out of the 798 pharmaceutical and biotech companies on Nasdaq, 68 (8.5%) had posted positive earnings to the SEC in Q1 2022.

Firstly, earnings matter when markets bounce back, and when investors seek sustainable companies with real earnings in the sector. Secondly, being part of a select group of profitable and growing companies within this exclusive subsector is a privilege which allows prominence when investors re-position their focus towards growth companies in an upturn.

Further, in CLINUVEL's recent history – 2019 and 2021 – the valuation reached A$2.1 billion, at moments when its balance sheet was not nearly as strong as it is at present, and when its pipeline was thinner than it currently is. When markets return, when investors seek value, there is ample reason to believe that profitable companies will be noticed and researched by longer term investors.

Of course, management is concerned about an unexpected downturn to CUV's share price – and equally of rising trends in CUV's price – but ultimately management's task is to steer the Company clear of risks and establish a profitable entity, controlling those factors which are within its power.



FINANCIAL DISCIPLINE

Unconventionally, and perhaps contrary to many biotechs and pharmaceutical SMEs, we have managed to impose a fiscal discipline over the years. As publicly reported, we have been able to vary our cost base and limit equity raisings.

Directors and the management team deliberated their wish to see the Company withstand economic downturns, while not being dependent on external funding. Having experienced the GFC, flash crashes, and recessionary environments throughout the pandemic, CLINUVEL viewed a further market correction as likely and prepared the Company accordingly.

The fiscal discipline of the Company has been imposed across all divisions as a deliberate strategy to circumnavigate a possible recession without needing to curtail expansion.

We operate a lower cost of capital than larger pharmaceutical groups, yet the R&D intensity remains high to provide for future products and markets. Another factor influencing our calculated cost of capital is the reported risk of the Company compared to market benchmark index (beta).

CONCLUSION

CLINUVEL operates continuously in a field of tension between the attempt to better the lives of unattended patients and **affected but unaddressed populations**, and the strive for making the Group profitable. This challenge is shared with many biotechs, but our chosen approach differs in many aspects.

The public valuation of the Company has suffered greatly since 23 September 2021 (52 week high - A$43.48), while its strength has been reported in its recent financial results. With an increase of receipts and profits year on year since 2017, a CGAR of 35%, one has witnessed little investor response in public markets across our sector.

We continue to build the Company, and based on our past decades, we must believe for the sake of shareholders that markets will come back. And when investors start looking for equity investments, there is a usual pattern for the first period post-recession, criteria will be on companies with:

- sustainable business model
- profitability
- an absence of financial overhang and debt
- proven ability to deliver
- cash at hand
- pipeline value

With these six criteria in mind, we prolong our development, however we express our regret for the paper losses incurred by our long-term shareholders.

As the markets continue to suffer pressure, we will manage the company in a fiscally prudent and consistent manner. In November 2021, we shared CLINUVEL's five year expenditure projections: up to a total of A$175 million to realise our ambitions. We are tracking well on these projections.

Today, we have given you an update on the programs, expected timelines, projected expenditures and the preparation of global campaigns to establish new audiences. We are certainly excited by the prospects, and intend to deliver on much in the coming period. We wish you good health as we continue the expansion and consolidation of CLINUVEL.