

ASX Announcement

ASX: CUV  
Nasdaq International Designation: CLVLY  
XETRA-DAX: UR9

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## CLINUVEL STRATEGIC UPDATE

*Dual strategy for melanocortins*

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Melbourne, Australia, 29 October 2020

CLINUVEL PHARMACEUTICALS LTD today released a strategic update on its business. An extensive version (31 slide illustrations) and executive summary (13 slide illustrations) have both been lodged with the ASX.

CLINUVEL is focussing on the commercialisation of the medicinal product SCENESSE® (afamelanotide controlled-release) for the treatment of erythropoietic protoporphyria (EPP) in the European Union, United States and – since 26 October – Australia.

The Update reveals CLINUVEL's strategic intentions are described as dual: ongoing work to scientifically translate melanocortins as prescription medicines for further life-threatening disorders as well as making the technology available for healthcare solutions as non-prescription products. The focus of the latter product category is to provide DNA protection and repair of the skin in individuals at highest risk of solar skin damage from UV exposure.

– End –

### Media enquiries

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### Notes to editors:

CLINUVEL's Strategic Update has been issued to the Australian Securities Exchange and is available on CLINUVEL's website [www.clinuvel.com](http://www.clinuvel.com).

<sup>1</sup> SCENESSE® (afamelanotide 16mg) is approved in the European Union and Australia as an orphan medicinal product and the world's first systemic photoprotective pharmaceutical for the prevention of phototoxicity in adult patients with erythropoietic protoporphyria (EPP). SCENESSE® is approved in the USA to increase "pain-free" light exposure in adult EPP patients with a history of phototoxicity. Information on the product can be found on CLINUVEL's website at [www.clinuvel.com](http://www.clinuvel.com).

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

### About CLINUVEL PHARMACEUTICALS LIMITED

CLINUVEL PHARMACEUTICALS LTD (ASX: CUV; NASDAQ INTERNATIONAL DESIGNATION ADR: CLVLY; XETRA-DAX: UR9) is a global and diversified biopharmaceutical company focused on developing and commercialising treatments for patients with genetic, metabolic, and life-threatening disorders, as well as healthcare solutions for the general population. As pioneers in photomedicine and understanding the interaction of light and human biology, CLINUVEL's research and development has led to innovative treatments for patient populations with a clinical need for systemic photoprotection, DNA repair and acute or life threatening conditions. These patient groups range in size from 5,000 to 45 million worldwide. CLINUVEL's lead compound, SCENESSE® (afamelanotide 16mg), was approved by the European Commission in 2014, the US Food and Drug Administration in 2019 and the Australian Therapeutic Goods Administration in 2020 for the prevention of phototoxicity (anaphylactoid

reactions and burns) in adult patients with erythropoietic protoporphyria (EPP). More information on EPP can be found at <http://www.epp.care>. Headquartered in Melbourne, Australia, CLINUVEL has operations in Europe, Singapore and the USA. For more information please go to <http://www.clinuvel.com>.

SCENESSE® and PRÉNUMBRA® are two of several registered trademarks 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 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); our ability to achieve expected safety and efficacy results 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, 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® 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 based products; decisions by regulatory authorities regarding approval of our products as well as their decisions regarding label claims; any failure 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 2020 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 the forecasts and estimates is available on request. Past performance is not an indicator of future performance.

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# Strategic Update

## Targeted Technology Translation

CLINUVEL Group  
29 October 2020

ASX:  
Level 1 ADR (Nasdaq International Designation):  
XETRA-DAX:

CUV  
CLVLY  
UR9

[www.clinuvel.com](http://www.clinuvel.com)

Today we share CLINUVEL's strategy, its planning and execution which started in November 2005 and which concluded in June 2006.

In order to communicate to all readers coming from varying backgrounds, the language and definitions used in these illustrations are balanced with a mix of technical and simple expressions so that a non-technical audience is able to understand the concepts and thought processes underlying the successfully executed strategy, while an executive summary is also announced and published on CLINUVEL's website ([clinuvel.com](http://clinuvel.com)) provided for faster reading.

While any navigating crew needs to adjust continuously to unexpected events, adverse conditions, and unforeseen hazards, nearly all objectives set in 2006 have been realised.

The time it took to overturn regulatory objections, scepticism and adversities has been long and has required much patience and incalculable persistence from the same CLINUVEL team which had started the journey exactly 15 years ago.

Now today, the next chapter in the use of melanocortins is unveiled as data, scientific progress, safety and an environment of acceptance of the technology has been established. The strategy is unfolding as had been designed and desired a long time ago with some variations allowing for changes to the business plan when needed; flexibility is imperative when executing complexities.

At these uncertain times of global viral threat, one is required to look ahead and imagine how the world will look, a new world order, new international economic relationships, a digital era and a high level of individualism, requiring one to take responsibility for one's own life.

All of the Group's staff, employees and Board share one common trait:

*At CLINUVEL, we realise each day that it is a privilege to work for our common causes and to build a company from its ashes to its current remarkable success, while staying humble to the fact that success can vanish overnight when one becomes complacent. Too big to fail does not exist in our minds nor too small to succeed where others ceased, we manage uncertainty and build in contingency scenarios where we can.*

Today, will focus on the expansion of the Pharmaceutical Division as well as the revelation of the Healthcare

[www.clinuvel.com](http://www.clinuvel.com)

Solutions Division, making CLINUVEL a unique hybrid among its peers, but with good reason.

Whereas it has taken decades of innovation, research and development to bring to market(s) a truly unique pharmaceutical product - SCENESSE® (afamelanotide 16mg) - the derivatives and further application should be finding its way to the markets in significantly less time; and that anticipation is owing to the fact that knowledge, IP, data and scientific observations are all transportable to CLINUVEL's downstream applications, products and target markets.

Whereas in pharmaceuticals and medicine one frequently speaks of *translational science*, when using one technology for wider medicinal use, in contrast it is rare to find highly specialised medical technology which can be rendered into a *non-medical application for universal use*. At CLINUVEL we had identified this differential pathway in 2006, but were required – for the protection of patients and our own – *to prove safety of the melanocortin beyond any reasonable doubt*.

The Group has have arrived at a point where the scientific breakthrough of melanocortins will be made available for wider societal utility, benefit for all at risk, all of us who self-identify a need.

*With considerable humility, the CLINUVEL staff summarises the execution of this strategy as the completion of a trilogy, the third chapter of a planned CLINUVEL journey, Targeted Technology Translation.*

The reader will come away with answers to the questions, WHAT – WHY – HOW – WHERE – and WHEN.

# Vitiligo Program

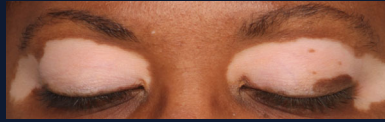
## SCENESSE® in combination with NB-UVB:

1. acceleration of repigmentation
2. darker skin most responsive to treatment
3. North-America first target market

Strategic Update – 29/10/20

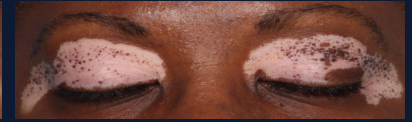
## Day 0

At start of the study  
CUV102



## Day 35

After 1 implant – 15 NB-UVB  
CUV102



## Day 66

After 2 implants – 29 NB-UVB  
CUV102



## Day 171

After 4 implants – 62 NB-UVB  
CUV102



SCENESSE® in combination with NB-UVB provided  
80% repigmentation of head & neck [CUV102] in darker skin



/ 02

The vitiligo program is aimed at using SCENESSE® in combination with narrow-band UVB (NB-UVB) in darker skin patients since they are most responsive to the hormone.

CLINUVEL intends to first market SCENESSE® in generalised vitiligo in North-America.



# Vitiligo Addressable Market

SCENESSE® in combination with NB-UVB

The phototherapy market in the US is growing at a CGAR of 6% per year

Phototherapy is used mainly for psoriasis, acne and vitiligo (NB-UVB).

For generalised vitiligo there is no standard of care, but NB-UVB is the best alternative for treatment [range 6 – 18 months].

Highest need: dark skin patients suffer from the strongest contrast between pigmented and depigmented skin.

USA addressable market for vitiligo skin type IV-V-VI: est. 2,749 to 5,498 patients (depigmentation of ≥40% body surface area).

UNITED STATES	POPULATION 328,239,523 <sup>1</sup>	
Dark skin, African-Americans (IV-V-VI)	13.4% <sup>1</sup>	43,984,096
Vitiligo prevalence	1% <sup>2</sup>	439,840
≥40% depigmentation	10-20%	10,996–21,992
Seeking initial treatment	25%	2,749–5,498
Compounded Annual Growth Rate	5%	137–274

PHOTOTHERAPY EQUIPMENT (USA)	% OF TOTAL CARE FACILITIES	
Hospitals	>5,000	81.3%
Dermatology clinics	3,900	50%

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CLINUVEL's focus in vitiligo is on patients with the highest unmet medical need and most likely to respond to the combination therapy of afamelanotide with NB-UVB.

With a lack of standard of care in vitiligo, treatment approaches vary. NB-UVB is considered the best alternative treatment. It is widely adopted in clinical practice within the USA as a treatment for vitiligo, but also other dermatological disorders (such as psoriasis and acne), with use of phototherapy growing at a CGAR of 6% per annum.

Vitiligo often affects the face, chest and extremities and may gradually spread to the limbs and other body surfaces. Patients are most affected psychologically when exposed parts of the body show extensive loss of pigmentation, quantified as greater or equal to 40% of total body surface area, as US expert physicians state. It is not the case that patients with smaller body surface do not suffer equally or more, however in patients of dark skin

Although vitiligo is seen in all skin types (Fitzpatrick types I-VI), the highest psychological and societal impact is reported in darker skin complexions (types IV-VI). Based on the prevalence of vitiligo in the USA, it is estimated that 10,996-21,992 individuals (all ages) meet the definition of widespread depigmentation in skin type IV-VI. The estimated addressable market is 25% of these patients, reflecting the broader vitiligo population who seek treatment for their condition.

<sup>1</sup> US population 2019, United States Census Bureau.

<sup>2</sup> Ezzedine et. al., (2015). Vitiligo. *Lancet*. 386(9988):74-84.

# EPP Program

## SCENESSE® systemic photoprotection 2005 -2020

1. Erythropoietic protoporphyria patients request continuous treatment >94% [data 2019].
2. CLINUVEL first entrant, growing market YOY.
3. 5,000 to 10,000 patients worldwide.
4. Dramatic treatment effect: able to engage in normal daily activities exposing to HEV light and UV.



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CLINUVEL is marketing afamelanotide (SCENESSE®) in the European Union and United States for the treatment of patients suffering from erythropoietic protoporphyria (EPP) and it has recently received the same status to distribute the product in Australia (26 October 2020).

In summarising the symptoms of EPP patients, they are absolute intolerant to light to due to their lifelong risk to incur phototoxicity, that is the severe burning reactions caused by HEV and UV light, triggering a chemical reaction within the skin of these patients. EPP is a genetic disorder rendering these patients at high risk since birth.

The illustration shows the immediate reaction leading to swelling (fluid accumulation) in skin and underlying tissues, which makes patients ill for weeks. As a reaction, patients are forced to live indoors and shield from light. Many of the EPP patients lead a nocturnal existence and sleep during day, depriving them of normal social activities and contacts.

SCENESSE® is approved for the prevention of phototoxicity in adult erythropoietic protoporphyria (EPP) patients in Europe, the USA and Australia. CLINUVEL has developed and commercialised the drug for EPP, pioneering the concept of systemic photoprotection. There are no alternative treatments which have proven safe and effective in a completed clinical trial program, or subject to regulatory review.

EPP is a poorly characterised rare metabolic disorder causing lifelong absolute light intolerance. Due to a genetic defect, EPP patients suffer debilitating acute phototoxic reactions (anaphylactoid reactions and second-degree burns) after just a few minutes of exposure to visible light (including sun and artificial light). Burns and reactions may last days to weeks. Without treatment patients must withdraw from light exposure to prevent phototoxicity, leading to lifelong social isolation. SCENESSE® has been shown to reduce the incidence and severity of phototoxic reactions and increase the amount of time patients can expose to light without incurring phototoxicity. Most satisfying for the CLINUVEL team, patients report being able to expose to light and sun for the first time without phototoxicity or the fear of incapacitating burns following SCENESSE® treatment.

Data from the real-world use of the drug in Europe since launch in 2016 shows strong patient demand year on year, with over 94% of patients returning for treatment (2019 post-authorisation safety study data). Treatment access continues to grow year on year, with the drug launched in the USA in April 2020.

Over 7,500 doses of SCENESSE® have been administered to over 1,000 EPP patients globally since the first clinical trials in 2006. A growing cohort of patients have received continuous treatment for five years, with a number of Swiss and Italian patients treated continuously for more than ten years.

Image courtesy of the K family.



# Arterial Ischaemic Stroke Program (AIS)

*Afamelanotide in patients with stroke of large vessels at M2 level and higher*

Stroke occurs most frequently (>50%) in the middle cerebral artery (MCA).

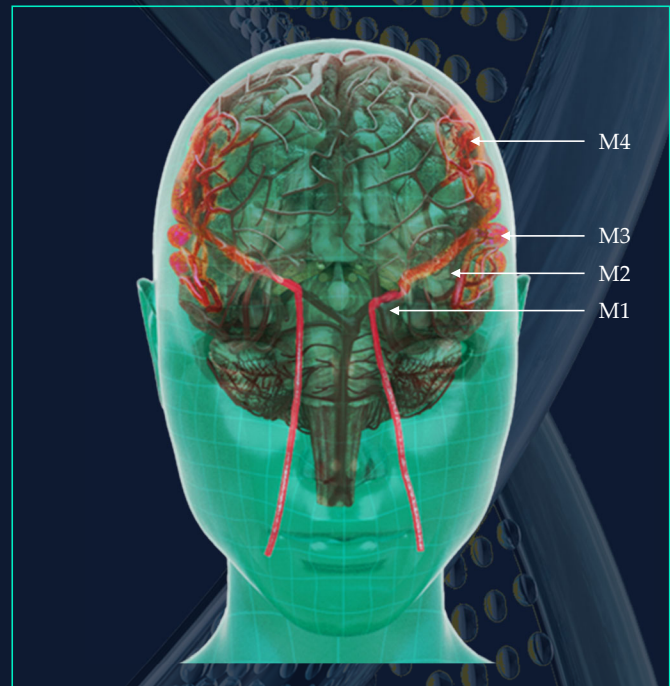
Blockages (clots) occur at various segments (levels), M1-M2-M3-M4.

High unmet need: minimal to no chance of treating stroke at M2 and higher.

Afamelanotide to

- improve blood flow,
- reduce oxidative damage, and
- reduce fluid formation in brain.

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∞ / 05

Ischaemic stroke is characterised by either a bleeding or clot formed inside the brain artery. CLINUVEL focuses on the ischaemic strokes, which forms the lion's share of all strokes (85%).

CLINUVEL focuses on those patients who do not receive any therapy, those with blockages at M2 levels and higher.

Scientific progress has shown melanocortins to exert a positive effect on the central nervous system, including the brain.

# AIS Addressable Market

*Afamelanotide in occlusion of brain artery at M2 level and higher*

Addressable market of stroke M2 and higher, not receiving IVT or EVT.

Acute arterial ischaemic stroke (AIS)

- arterial clot accounts for 85% of all acute strokes (ischaemic)
- 15% of acute strokes are caused by an acute bleeding (haemorrhage).

ISCHEMIC STROKE	UK	USA
Annual stroke incidence	113,000	795,000
Haemorrhagic stroke : Ischaemic Stroke	15% : 85%	
Arterial ischaemic stroke (LVO) <sup>1</sup>	46%	
AIS eligible for IVT	<20%	<20%
AIS contra-indications for IVT <sup>2</sup>	38.3%	
AIS eligible for EVT <sup>2</sup>	12%	11%
AIS patients untreated,	>35%–60%	

Strokes occur frequently in western societies: in the England there are more than 113,000 cases per year and close to 800,000 in the USA.

The majority of strokes are those caused by blockage of a brain artery, whereby the middle cerebral artery (MCA) is the most frequently affected.

The table illustrates that most patients are not receiving IVT or EVT due to underlying diseases, delay in time of hospital admission and location of the clot within the brain.

The range in percentage of untreated AIS patients remains alarmingly high, and the condition poses a true unmet medical need.

<sup>1</sup> Large vessel occlusion.

<sup>2</sup> See illustration on slide 17.

# DNA Repair Program

*Afamelanotide repairs DNA skin damage caused by UV radiation*

Drug safely used in humans since 1996.

Afamelanotide to confirm DNA-damage response following UV skin damage in three studies.

Afamelanotide in genetic disease XP serves as model for assisting DNA repair in all populations affected and at risk of solar damage.



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DNA repair is relevant to every human, since all of us expose to High Energy Visible light and UV radiation. Among the general population, there is a hierarchy of most susceptible groups to least susceptible individuals to photoaging and premature ageing due to UV exposure.

CLINUVEL has frequently reported on its scientific and clinical work to evaluate melanocortin(s) in various populations susceptible to various forms of photodamage.

Short studies were conducted in a number of diseases either initiated by CLINUVEL or individual clinical centres evaluating the effect of afamelanotide in polymorphous light eruption (PLE), Solar Urticaria (SU), Hailey-Hailey Disease (HHD), Erythropoietic Protoporphyrria (EPP), Congenital Porphyria (CEP).

In all these diseases, patients are still able to respond and recover in some manner from DNA damage, but they express severe reactions to light. These patients have a sufficient DNA damage response.

However, various groups carry genetic traits or lack the efficient mechanisms of DNA skin repair and are at high or highest risk of developing skin cancers.

Some examples of patent populations who deserve CLINUVEL's highest attention are to people of Anglo-Saxon origin with blue eyes, ginger colour hair, tendency to develop freckles and sunspots fast (RHC type). Typically, these individuals burn fast under solar radiation, and are prone to develop first signs of sun damage and precancerous (before mature cancer stage) wounds of the skin. Chronic exposure to sun is not recommended for these patients since the DNA reparative process in these patients is shown to be suboptimal.

Another example of individuals in society at high risk of photodamage, are those patients who receive immune-suppressive therapy for longer time due to chronic disease. These patients are known to develop a higher rate of skin cancers, among other.

In summary, DNA regeneration of skin damage caused by solar exposure is a topic which affects us all, and the interest to address and find healthcare solutions for photodamage or solar damage is growing. The older we become, the more our DNA repair systems of the skin risk failure, and following previous periods of long exposure to sun we become prone to skin cancers - as the global statistics show.

With the scientific progress and understanding of the role of afamelanotide and other melanocortin molecules (drugs in development), the use of molecules to prevent and restore DNA damage of the skin can be expected

and follows a trail of evidence.

CLINUVEL's attention is owed to these highly susceptible individuals mentioned above.

The recently announced clinical program of afamelanotide in xeroderma pigmentosum (XP) serves as a clinical model to demonstrate the drug's ability to positively affect patients who suffer greatly from a genetic disease, which leads to the highest frequency of skin cancers and melanoma due to a defective DNA repair system.

In parallel, the Company is collecting final data confirming the ability of melanocortins to assist DNA-regeneration in randomly selected (non-diseased) individuals.

Naturally, various formulations and products have been planned to address DNA-restoration since the need remains high.

# Xeroderma Pigmentosum [XP]

*Afamelanotide in genetic disease XP: deficiency DNA Repair of skin*

In XP, UV causes damage to DNA of skin/eyes since patients lack sufficient NER<sup>1</sup> repair capacity.

Lack of sufficient DNA repair capacity leads to skin cancers in XP.

XP patients have up to 10,000-fold risk of developing skin cancers, all are treated for multiple skin cancers and melanoma.

Afamelanotide has been shown to repair DNA in healthy patients, now it is evaluated in XP and repeat studies.



A young girl diagnosed with XP-C showing poikiloderma (disintegration of skin), leathery appearance, several wounds below the eyes and around the nose, persistent fluid of lower lip.

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Eight variants of XP are known, CLINUVEL's initial focus is on patients diagnosed with XP-C. The C variant is expressed in patients who have an extreme high rate of skin cancer development and melanoma since they are deficient in the DNA repair process known as nucleotide excision repair (NER)<sup>1</sup>. The changes of the skin in these patients occur at infancy, when the skin starts to change in texture becoming leathery and easily develops wounds upon any solar exposure. As time passes, in early childhood their skin starts to break, disintegrate (poikiloderma) and first superficial skin cancers are reported. Needless to state how painful, distressing and traumatic this is for a growing child and their parents.

While there are three main causes of skin cancers (basal cell and squamous cell carcinoma, and melanoma), in XP patients the consequences are grave and mutilating; frequent surgeries leave scars on all exposed areas, while wound healing is compromised.

In XP-C, patients frequently live to the third decade while eventually passing away due to spread of the cancers (metastases).

The quality of life in these patients is unfortunately – despite advances in modern medicine – very low.

CLINUVEL had planned to treat these patients 15 years ago at the start of the scientific work on afamelanotide, but needed to generate sufficient data to be able and allowed to treat these patients, due to the high risk of disease and death in these patients.

It is most gratifying and somewhat emotional after more than a decade for the CLINUVEL team to seek a treatment for this forgotten group of affected patients, being able to contribute is a force which bonds all staff at CLINUVEL.



# Foundation for Branding DNA-Repair

PUBLICATIONS ON AFAMELANOTIDE – MELANOCORTINS 2005 - 2020

PUBLICATIONS	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	TOTAL
ASX announcements	73	55	54	43	45	56	47	38	39	59	36	52	32	54	72	54	17,289
Media	198	80	80	66	305	242	132	109	66	119	124	98	121	113	439	408	
Publications – melanocortins	994	1073	1026	954	969	987	891	884	947	813	854	777	782	667	619	307	
Publications – Afamelanotide	1	5	0	4	9	12	5	3	9	5	15	6	15	36	43	68	
Total	1266	1213	1160	1067	1328	1297	1075	1034	1061	996	1029	933	950	870	1173	837	17,289

**Afamelanotide: Heightened awareness global medical community**



*essential step to ensure first adoption of technology*

**Global regulatory recognition & validation: EMA - FDA - TGA**



*essential step to ensure first adoption of technology*

**Long term clinical value to patients at risk<sup>1</sup>**



*essential step to ensure first adoption of technology*

**Translation into DNA Repair products – universal care for all**

## STAGE 1: MEDICAL COMMUNITY

- AWARENESS: ESTABLISHED
- RELEVANCE MELANOCORTINS: LOW- SPECIFIC TO PATIENTS

## STAGE 2: GENERAL PUBLIC AT RISK

- AWARENESS: VERY HIGH
- RELEVANCE: HIGH TO ALL

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/ 09

*Longevity and consistency* in communicating a theme, a product and service generally leads to raised awareness among a target audience.

In thinking about CLINUVEL's main focus on the validity of claims of safely using melanocortins for medical purposes, an audience consisting of a targeted medical community had been established over two decades. The table illustrates the number of announcements to the Australian Securities Exchange, media releases and peer review publications on melanocortins and afamelanotide over the past decennia confirming frequent and systematic communication around the technology.

From here onwards, a heightened awareness has been seen among the medical community, expert physicians, researchers, target medical specialists, patient associations and patients as end users. A desired halo effect was being created during this time as wider audiences consisting of patients' families, national authorities, insurers and stakeholders in general became aware of the innovation in melanocortin technology as it became more widely used by hospitals globally.

Industry and general press heeded the relevance of the technology with more attentiveness, once the European Medicines Agency (EMA) and US Food and Drug Administration (FDA) formally acknowledged the technology in 2014 and 2019, respectively. To put the position of CLINUVEL's branding, relative to the timetable, in the innovation curve one finds itself just at the beginning of adoption of a DNA-reparative technology.

Awareness of a fledgling product brand in pharmaceuticals is heightened once the safety of a product becomes widely known among its users and medical community validating the status of the drug for a much larger group of users.

<sup>1</sup>For instance, among others, the peer review publications by Biolcati et al (2015) in the *British Journal of Dermatology*, Langendonk et al (2015) in the *New England Journal of Medicine*, Barman-Aksoezen et al (2020) in *Orphanet Journal of Rare Diseases* and Wensink et al (2020) in *JAMA Dermatology*, confirmed the safety of the melanocortin product long term. These are landmark events in the life cycle of new technology and underpin the initiation of broader awareness surrounding the themes relating to DNA-restoration, systemic photoprotection and risk of skin cancers over time. Effectively linking these themes along a path of evidence will be one of CLINUVEL's objectives the coming years.



In a staged manner, a final trajectory in confirming the utility of the melanocortin technology, in casu SCENESSE® (afamelanotide controlled-release formulation), is found in its use as a DNA-reparative agent, its benefits derived from scientific data in vitro, ex vivo and from human use.

*Thus the preceding journey spanning decades took CLINUVEL along pharmaceutical branding markers such as consistent communication, safety, acceptance in peer reviews, wide acceptance by the medical community, validation by the two main global regulators and long term safety under real-world-conditions. In essence, the foundation was laid to be in the position **to brand the concept of DNA repair by melanocortins for patients and universal use.***

# DNA Repair Addressable Market

	Europe	USA	Australia
Actinic keratoses – prevalence in adult patients <sup>1</sup>	6-29%	10-27%	37-55%
Skin cancer (SCC-BCC) incidence <sup>2</sup>	119-145/100,000	5.3m per annum	2,448/100,000 patient years

Global anti-aging services market (2018) <sup>3</sup>	US\$23.45bn
Global facial rejuvenation market (2019) <sup>4</sup>	US\$19bn
Projected DNA-based skin care products market, 2025 <sup>5</sup>	US\$11.7bn

This table gives a broad impression of the market of solar damage, anti-ageing and rejuvenation without a specific subdomain for DNA repair of the skin. The latter is a relatively new field of attention under the premise that it is better to focus on prevention of photodamage and skin cancer.

With CLINUVEL's upcoming products this new subsegment of users will need to grow as awareness will increase.

<sup>1</sup> News Medical – Actinic Keratosis Epidemiology, online at <https://www.news-medical.net/health/Actinic-Keratosis-Epidemiology.aspx>; Ferrandiz et. al., (2016). Prevalence of actinic keratosis among dermatology outpatients in Spain. *Actas Dermo-Sifiliographicas*. 107(8):674-680.

<sup>2</sup> Skin Cancer Foundation – Skin Cancer Facts & Statistics, online at <https://www.skincancer.org/skin-cancer-information/skin-cancer-facts/>; Perera et. al., (2015) Incidence and prevalence of non-melanoma skin cancer in Australia: A systematic review. *Australas J Dermatol*. 56(4):258-67, Eisemann et. al., (2014). Non-Melanoma Skin Cancer Incidence and Impact of Skin Cancer Screening on Incidence. *J Inv Dermatol*. 134(1):43-50.

<sup>3</sup> Grand View Research - Anti-aging Services Market Size, Share & Trends Analysis Report By Demographics, By Type (Chemical Peel, BOTOX, Microdermabrasion, Breast Augmentation, Liposuction), And Segment Forecasts, 2019 – 2026, abstract online at <https://www.grandviewresearch.com/industry-analysis/anti-aging-market>.

<sup>4</sup> InsightSlice - Facial Rejuvenation Market size was estimated to be US\$ 19 billion in 2019, online at <https://www.globenewswire.com/fr/news-release/2020/09/22/2097541/0/en/Facial-Rejuvenation-Market-size-was-estimated-to-be-US-19-billion-in-2019-insightSLICE.html>.

<sup>5</sup> Grand View Research - DNA-based Skin Care Products Market Size Worth \$11.7 Billion By 2025, abstract online at <https://www.grandviewresearch.com/press-release/global-dna-based-skin-care-products-market>.

# Technology Translation of DNA Repair



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*Two cardinal questions will stand out in time:*

What makes CLINUVEL special compared to its peers and competitors? And why are CLINUVEL's products relevant to larger audiences beyond a limited patient population it serves now? The company's consistent communication onwards will provide answers to both questions and will attract larger interested readers and users.

In the illustration, one sees – on the top row – that the five medicinal melanocortin products SCENESSE® - SCENESSE® ENFANCE - PRÉNUMBRA® - and phimelanotide and CUV9900 aim to serve *prescription only demand*. The pharmaceuticals are being developed and marketed to provide systemic repigmentation, systemic photoprotection, neurotrophic properties and DNA repair. The awareness of melanocortins among the wider medical community has been significantly raised the past years due to innovation and medical need for these hormones.

On the bottom row, one sees how the attributes of the medicinal product parvysmelanotide from the top row are translated to *non-prescription products* (pharmaceumables) for universal care aiming to provide healthcare solutions to wider audiences.

The first product line to be released is a product line offering polychromatic protection under extreme conditions and targeting populations at risk of HEV and solar damage. Awareness of the new products will be raised before and during the initial launch of the product line, while larger campaigns are being prepared for the global distribution.

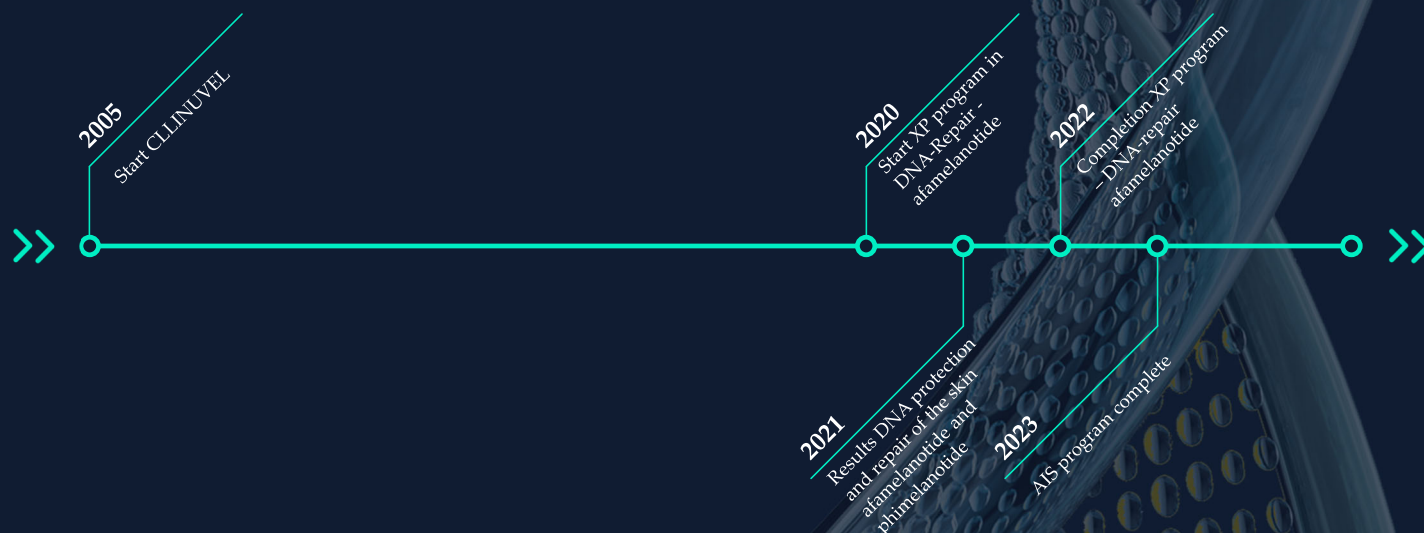
The second product line aims to provide DNA protection and repair of the skin in individuals at risk of solar damage and specific high-risk populations. Awareness of the healthcare risk is relatively high among the users, and modern marketing will assist in raising attributes of the product line and awareness of value proposed.

In launching new products (pharmaceumables) originating from pharmaceutical product(s) and relevant to all future users, consistency is required in communicating to larger audiences. The consistency will be found in messages, approach, technology, healthcare solutions and all broadcasts.

**The translation of technology and knowhow from medicinal use to healthcare solutions stems from one of the core attributes of melanocortins lending themselves uniquely to universal care benefiting all.**

# Timeline

## PRODUCTS VERSUS BRANDING



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The CLINUVEL team is on a trajectory to complete the majority of the DNA-repair program. This projection much depends on regulatory timelines, turnaround and ability to generate data under current global restrictions.

The first launch of the non-prescription polychromatic protective is foreseen in 2021, from here on further product extensions are being prepared.

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# Thank You

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For your support & trust

CLINUVEL Group  
29 October 2020

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Level 1 ADR (Nasdaq International Designation):  
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