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# CLINUVEL PHARMACEUTICALS

## SCENESSE® OPTICAL PHYSICS IN EPP

### "DIFFERENTIATION & SYMMETRY"

ANNUAL GENERAL MEETING 2016

MELBOURNE

28 NOVEMBER

CLINUVEL MANAGEMENT

# CLINUVEL

Good morning and welcome to CLINUVEL's Annual General Meeting.

The challenges ahead for 2017 are to reconcile the asymmetry in knowledge with regulators, governmental advisory bodies, payors, medical community and press on CLINUVEL's innovative technology SCENESSE® (afamelanotide 16mg)<sup>1</sup> and to differentiate CLINUVEL from other companies in our sector.

We aim to reach full symmetry with third parties on knowhow of technology and disease.

Owing to the novelty of the field of **optical physics and photomedicine** there is still considerable lack of understanding about the medical need to treat patients who are lifelong deprived of light, and suffer from anaphylactoid reactions upon light exposure.

Gradual knowledge is being gained by the outside world on the disease symptomatology of erythropoietic protoporphyria (EPP) and the novel medical solution offered by SCENESSE®.

<sup>1</sup> SCENESSE® (afamelanotide 16mg) is approved in Europe as an orphan medicinal product for the prevention of phototoxicity (anaphylactoid reactions and second degree burns) in adult patients with EPP. The innovative nature of the therapy in an orphan disorder, the lack of available scientific instruments to adequately measure the therapy, ethical considerations and the drug's positive safety profile were some of the factors which led to the European marketing authorisation of SCENESSE®. Information on the product can be found on CLINUVEL's website at [www.clinuvel.com](http://www.clinuvel.com).

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## SAFE HARBOUR STATEMENT

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, 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. and Europe 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; 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 2016 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.

**CLINUVEL**

CLINUVEL forewarns against any speculative comments, suggestions or perceived guidance provided during this session and dissuades any member of the public to speculate, trade and act on the information obtained.

The audience is advised to read the Safe Harbour Statement provided herewith and all disclaimers in CLINUVEL's public announcements. A copy of this statement is made available on CLINUVEL's website at [www.clinuvel.com](http://www.clinuvel.com).

## ANNUAL GENERAL MEETING 2016

**CLINUVEL SHAREHOLDERS OWNING >70% SEEM TO HAVE IN COMMON A NUMBER OF INVESTMENT MOTIVES:**

1. "Wish to be part of a company which enters new frontiers, business domains where no competition exists"
2. Wish to be one of the first investors to have discovered a new equity story
3. Doing good for patients requiring treatment
4. Expect multiple returns on investment while being patient"

**CLINUVEL**

CLINUVEL's major active investors have made their investment motives known, why they invested and remain invested in CLINUVEL over sometimes more than five years, some even more than 11 years.

We share the four broad categories of how shareholders have consistently expressed their motives to remain invested or further invest in CLINUVEL.

## ANNUAL GENERAL MEETING 2016

### CLINUVEL SETS ITS CORPORATE OBJECTIVES IN A SPECIFIC SEQUENCE:

3. Establish a company which pioneers in photomedicine
4. Deliver on a colourful equity story
1. Doing the maximum for underserved patients requiring treatment
2. Aim to provide returns on investment for patient shareholders

**CLINUVEL**

In the four investment motives expressed, CLINUVEL and its shareholders seem aligned, we just have taken the liberty to adhere to a sequence of priorities for the sake of our primary stakeholders: patients, physicians, and ultimately those who funded the Company the past 12 years.

## 2016 AGM

- I 'POWDER SNOW'
- II SCENESSE® IN EUROPE
- III NDA FILING (FDA) SCENESSE® IN EPP
- IV DIFFERENTIATE CLINUVEL GROUP

CLINUVEL

The calendar year 2017 is marked by a focused number of topics providing an indication of CLINUVEL's current thinking and direction of the CLINUVEL GROUP:

**I Ensuring continuation of the POWDER SNOW strategy**

**II Expansion of the distribution of SCENESSE® in the European Economic Area**

2016 saw the start of distribution of the product for EPP patients in Europe, whereby we intended to introduce the product sequentially in a number of countries.

Discussions with national authorities and European insurance groups are being conducted in individual countries to ensure that EPP patients have access to SCENESSE®.

**III FDA filing of the SCENESSE® modules on a rolling basis**

The FDA provided the filing pathway through a Fast Track designation and assessed CLINUVEL to be ready for filing its dossier for EPP, that is 12 years after CLINUVEL first started the dialogue with the agency. While the Company obtained orphan drug designation for SCENESSE® in 2008, it has taken eight years to convince the FDA of the need to treat EPP patients, the novelty of the concept and the innovative drug to be prescribed.

It is expected that the asymmetry of knowledge between CLINUVEL's acquired expertise in optical physics and the FDA will be reconciled during the filings in 2017 and continuous discussions with the FDA and review process of the dossier.

**IV Differentiating CLINUVEL from other pharmaceutical companies and ensuring all stakeholders learn the Company's mission and vision**

Global popular press is influencing public opinion on pharmaceutical companies as has been seen during 2015 and continuing in 2016. Four US companies the past 12 months have managed to attract negative attention from press, politicians and public for their marketing and pricing practices for pharmaceutical products and healthcare technologies.

Global press has not yet differentiated between R&D companies purely focused on medical innovation and those which “re-bottle existing drugs” with little or no differentiation nor innovation to be introduced at higher cost.

In contrast, CLINUVEL has spent 12 consecutive years on R&D of one drug in one disorder and will continue to make the funds available for further research on SCENESSE® for paediatric patients and follow on products.

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## I. POWDER SNOW STRATEGY

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### **How to view SCENESSE® in current medicine and what is the relevance to all stakeholders of CLINUVEL?**

Whereas breakthrough technology transforms a sector or the way we dramatically apply knowledge or suddenly change the way we undertake things, disruptive strategies and technology - first described by Clayton Christensen in 1995 - zooms in on the topic of moving up technology to commoditised and general use of specific technology, but not necessarily new.

Blue Ocean strategy was first described by Kim & Mauborgne in 2005 to illustrate organisations seeking an uncontested market or an environment where no competition yet exists. This concept is certainly applicable to CLINUVEL, however it does not fully capture the challenges the Company had to overcome. These challenges have prepared our teams to discern patterns and learn how to overcome the future ones, a corporate resilience to accept that each component of the business

**CLINUVEL believes it has been required to adopt a POWDER SNOW approach**, very much like a lover of skiing/snowboarding is excited when new snow overnight has hit the slopes.

Taking on powder snow is for those who want to create one's own tracks and who want to find a way up or down untrodden paths of a mountain. The analogy is presented to describe how the CLINUVEL team needed, for more than a decade, to lead by introducing novel technology in medicine where no tracks were yet developed:

### **Optical physics in a genetic metabolic disease to provide patients with protection against the visible spectrum of light.**

It is anticipated that the challenge of thoroughly explaining the *why-what-how-when* of EPP

and SCENESSE® will continue in 2017, both in Europe and the US.

In the future we expect that the same approach will be adopted when introducing the technology to a wider audience for the treatment of vitiligo.

Clearly there is a cost to entering an 'untouched domain' however it also provides a maiden medical field of medicine to treat underserved patients.



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**ERYTHROPOIETIC PROTOPORPHYRIA**  
PEAK ABSORPTION AT 'BLUE-GREEN' SPECTRUM,  
 $\lambda$  408, 550, 650 nm



**CLINUVEL**

From isolation to visible handicap.

Patients have lost the courage to participate in social activities and can only do so when fully covered and remain stigmatised in life.

The shared patients' experiences have become more prominent through online communities.

## II. SCENESSE® IN EUROPE

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SCENESSE® is the first pharmaceutical treatment approved for EPP patients, with a centralised European Medicines Agency marketing authorisation.

A gradual roll out per country is being pursued while patients await the treatment.

Discussions with each National Competent Authority and payment institution is being held to ensure market access for SCENESSE®.

Payors have been unaware of the need to treat EPP patients due to the rarity of the disease, and unfamiliarity of the phenomenon of anaphylactoid reactions following light exposure.

## EUROPEAN MARKET ACCESS



**CLINUVEL (UK) LTD DISTRIBUTION PLAN**

- AIMED AT 15-17 COUNTRIES
- EXCLUSIVELY EXPERT CENTRES
- ONE NATIONAL REFERENCE CENTRE FOR PORPHYRIA PER COUNTRY
- FEW SATELLITE CENTRES
- IDENTIFIED 42 CENTRES
- PHARMACOVIGILANCE, DISEASE REGISTRY
- CONTROLLED DISTRIBUTION

**SCENESSE® REIMBURSEMENT**

- SPECIALISED TECHNOLOGY
- HOSPITAL PRODUCT ONLY
- OUTPATIENT TREATMENT
- AGREEMENT PER EC COUNTRY
- CODING OFTEN LACKING
- UNIFORM PRICING
- CUV BEARS FOREIGN EXCHANGE

Patients currently treated in

- Netherlands
- Austria
- Germany
- Italy
- Switzerland

# CLINUVEL

In each country there is typically one National Reference Centre for porphyria or rare metabolic disorders. Sometimes there are satellite centres acting as a supporting treatment hub. These centres require training and accreditation according to strict protocol and requiring retraining and frequent monitoring by CLINUVEL teams.

EPP is typically treated in an university hospital, where various medical specialties look after the patients.

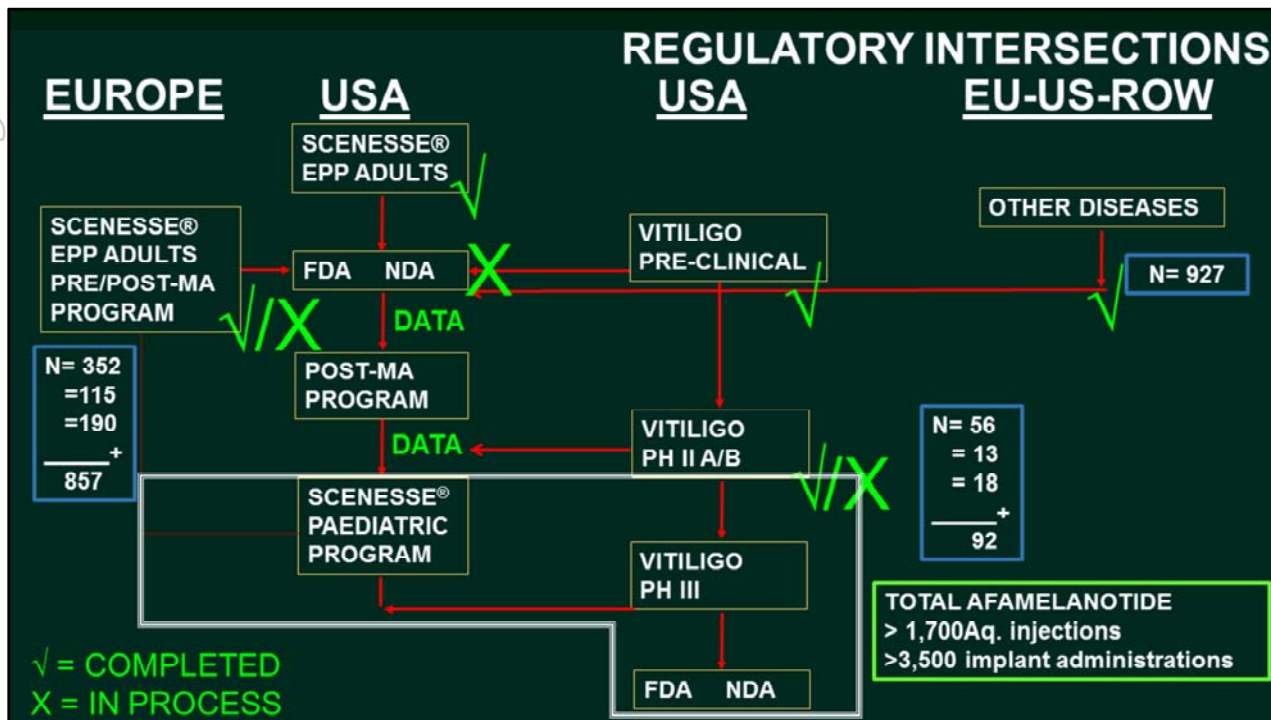
CLINUVEL is required to ensure that all these specialties are coordinated to look after the EPP patients on the days that they attend the outpatient clinics.

Pricing will be announced when the European reference countries have published the uniform European price.

### III. NDA FILING (FDA) SCENESSE® IN EPP

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In CLINUVEL's programs of EPP and vitiligo it is imperative to gain knowledge on the common features which influence the regulatory strategies and filings.



The FDA strategy to reintroduce the to US has been planned for years, safety dictated CLINUVEL’s program.

CLINUVEL had identified that SCENESSE® would pose a new concept for regulatory agencies in EU and US. The one drug would be used as a systemic injectable as a periodic solution as a photoprotective in EPP patients, who would return annually for treatment, lifelong.

However, in vitiligo patients, it would be foreseen that SCENESSE® would be a curative or definitive treatment, whereby patients would suffice with one course of treatments estimated between 6-10 injections depending on the severity and extent of depigmentation. EPP and vitiligo have different dose regimens however; in vitiligo one would add the use of narrowband UVB concomitantly (drug-device interaction).

The regulatory pathways were long foreseen to be intersecting, whereby both programs would contribute to the safety data for the US regulators (FDA). Timing was important as well as progress in the US regulatory review and assessments.

Since July and October 2016, there is clarity on FDA’s position on SCENESSE® for the treatment of US EPP patients; the US submission was long awaited.

As part of the safety data package and number of patients exposed to the drug, CLINUVEL presents the FDA data on other (photo)dermatoses in combination with the pre-clinical and clinical vitiligo data generated the past years. The ultimate objective is for FDA to gain total comfort in the clinical safety of the novel product, a first-in-class pharmaceutical which will always be subject to a higher level of scrutiny.

CLINUVEL viewed that EPP and vitiligo would both present ‘clinical novelty’ to US regulators in terms of mode of action, use of the proposed therapies, dose frequency and expected effectiveness.

#### IV. SEPARATE THE WHEAT FROM THE CHAFF

**CLINUVEL**

In current economic turmoil in the EU and US differentiation of CLINUVEL is desired to make all stakeholders understand that this unique company has focused all its resources on one innovative technology in one rare disorder at considerably lower expenditures than its peers. Popular press is currently painting a grim picture of all innovative companies and pricing policies, and do not differentiate the good from the bad.

## CLINUVEL SHAREHOLDER STRUCTURE

### SHARE PRICE

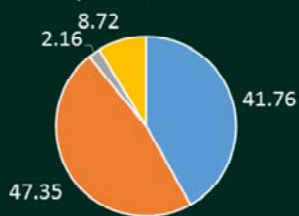


ASX: CUV	
MCAP	A\$375m
Shares on issue	47,725,227
Cash at hand	A\$17.3m (30/9/16)
Debt	--
Equity issuance	A\$8.3m (15/3/16)

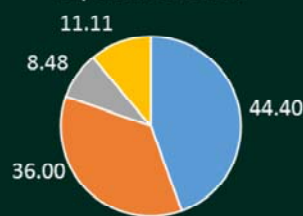
### CUV ownership structure

- Institutions
- Brokers, other
- Related parties
- American Depositary Receipts

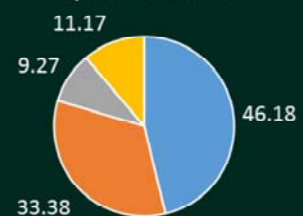
#### September 2013



#### September 2015

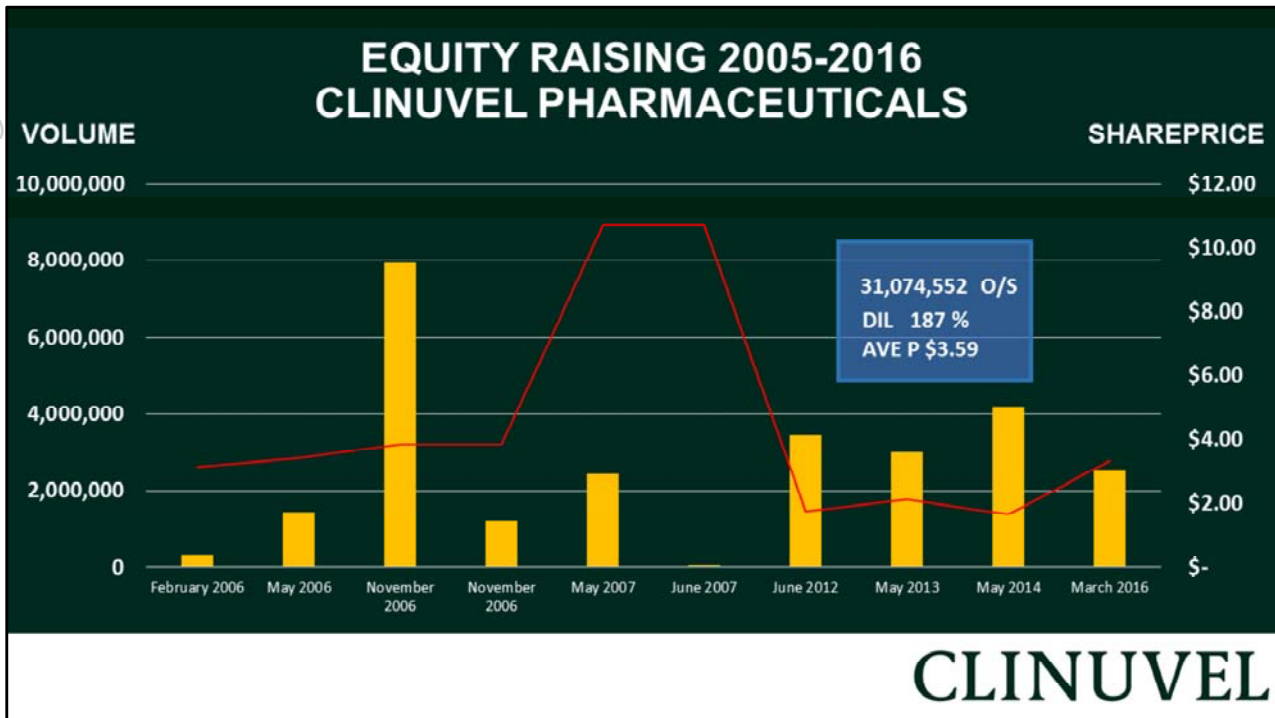


#### September 2016



CLINUVEL's share price has outperformed most indices and Australian peers. This follows the positive news flow from the Company during 2016.

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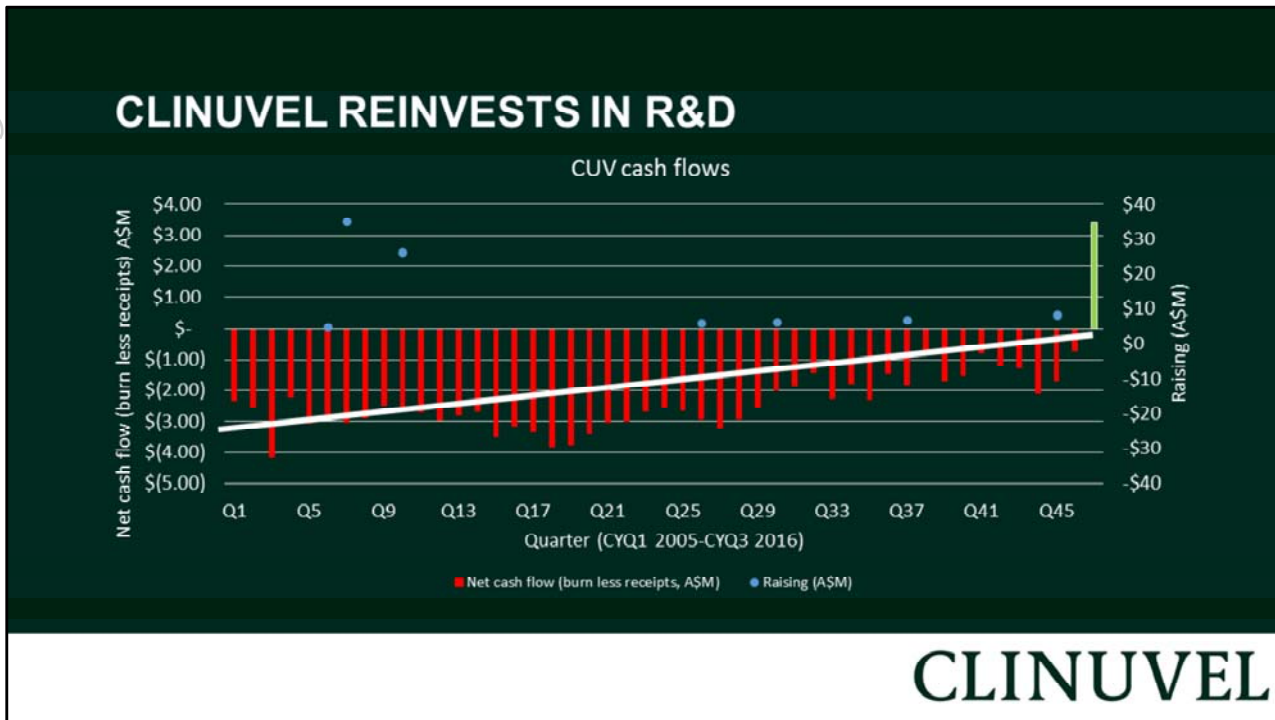
CLINUVEL has consistently aimed to minimise costs to arrive at a finished product for distribution to EU-US EPP patients.

At an average price of AUD\$3.59 per share shareholders would have been able to calculate their returns over the years, that is if their equity holdings could be realised all at once in the market. Hence the theoretical returns point in the right direction when one views the investments for a novel pharmaceutical product.

At minimal equity dilution of 186.6% CLINUVEL's management stayed ahead of all its Australian peers during 12 years of R&D.

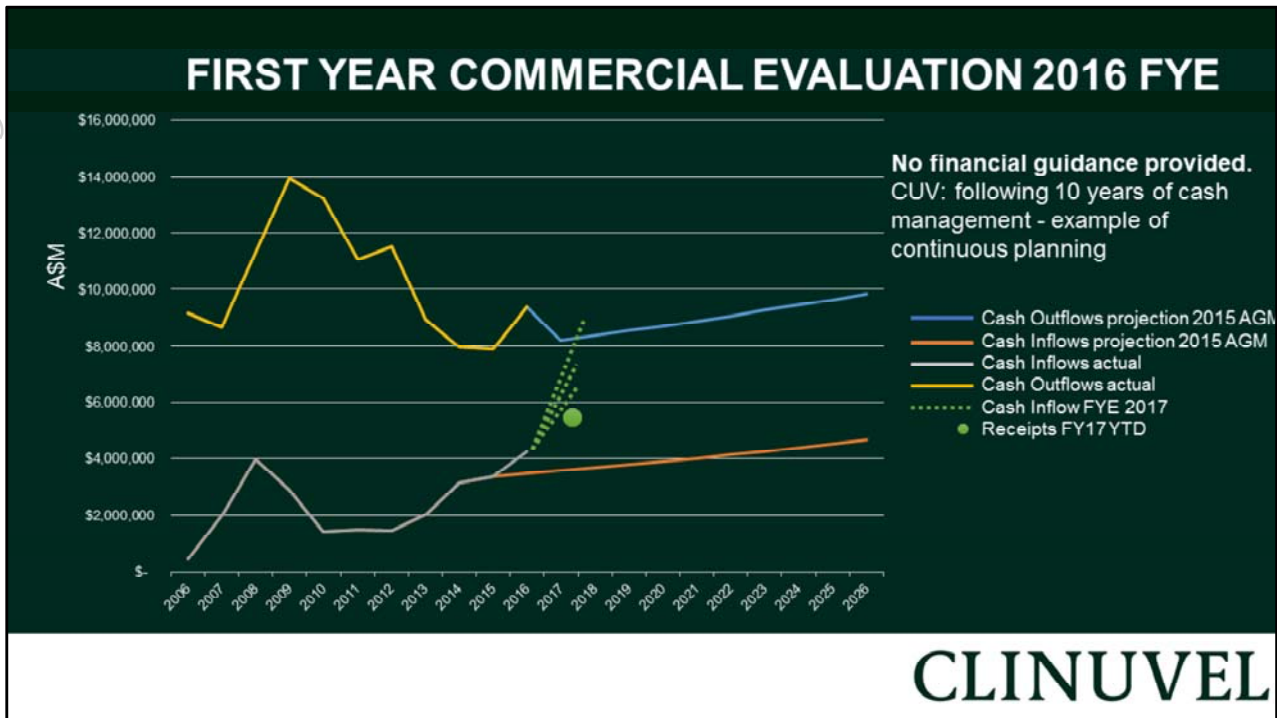
These metrics are essential when estimating the expected rate of returns on investment in years to come as well as the required future investments required for the CLINUVEL GROUP.





Contrary to other pharmaceutical companies mentioned in US & EU press, CLINUVEL does genuinely invest in research and development to grow the Company.

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This slide **does not intend to provide financial guidance**, but merely shows how CLINUVEL is tracking commercially against three hypothetical scenarios discussed at the 2015 AGM (reference is made to 2015 AGM presentation). The graph here shows financial year data (July 1-June 30).

Comparing the base case for calendar year 2016, the Company has recorded \$7,784,000 in receipts from the final period of special access schemes and the beginning of the commercial distribution of SCENESSE®.

In a hypothetical base case, the Company would incur cash inflows from its EU sales of SCENESSE®. However in the hypothetical SCENARIO 1, a slow uptake of the product would allow cash (in)flows to take longer and funding would be needed to bridge the gap. In more hypothetical bullish scenarios cash inflows would be faster and higher.



Traditionally the company summarises the number of publications on drug, disease and CLINUVEL over the past calendar year: 94 to date, a relatively large reach for a small size pharmaceutical entity with one product.



A summary of TV broadcast in Switzerland, Netherlands and UK is shown.

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## CLINUVEL PLATFORM TECHNOLOGY

N- ● ● ● ● NLE ● ● DPH ● ● ● ● ● -C

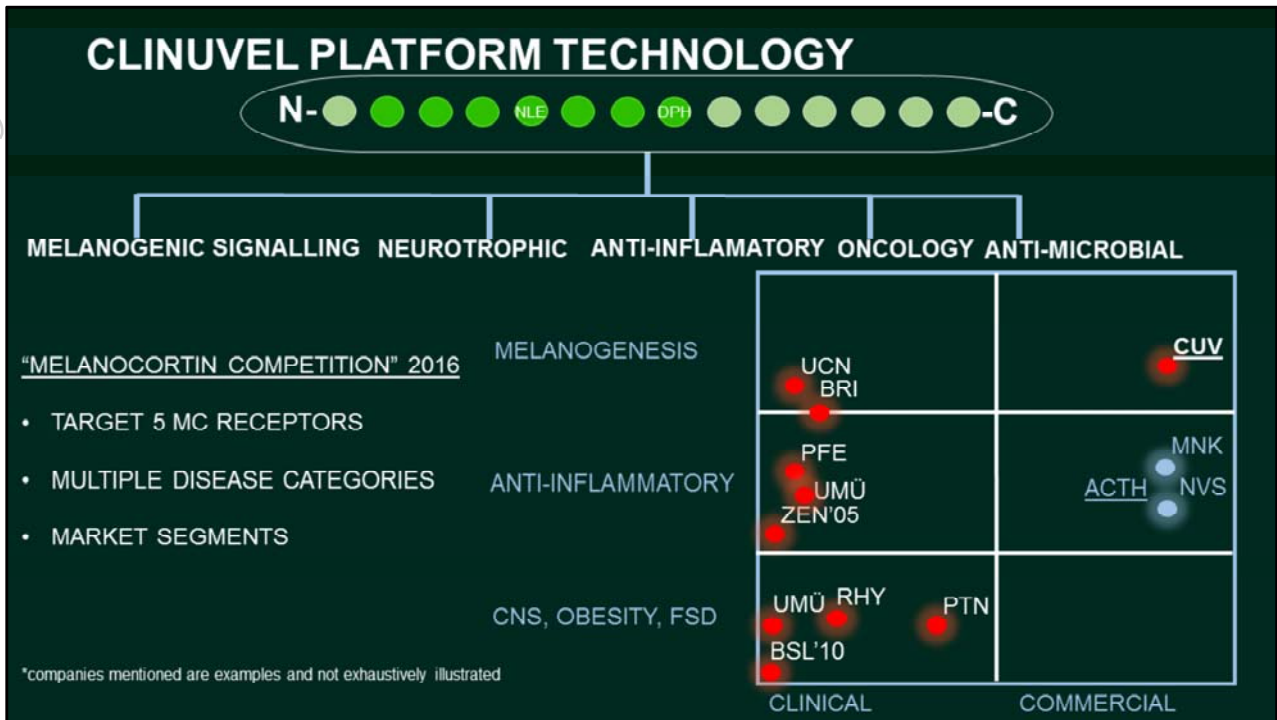
MELANOGENIC SIGNALLING NEUROTROPHIC ANTI-INFLAMMATORY ONCOLOGY ANTI-MICROBIAL

- alpha-MSH wide array of applications
- > 6,000 publications
- linear versus cyclic compounds high risk
- biological activity on N- and/or C- terminal end
- 5 target receptors Mc1R – MC5R
- dose, frequency determine effectiveness
- toxicology serves as guide for clinical use (SAFETY)
- UNFINISHED BUSINESS: FIRST MELANOGENIC DOMAIN THEN CNS AND OTHERS

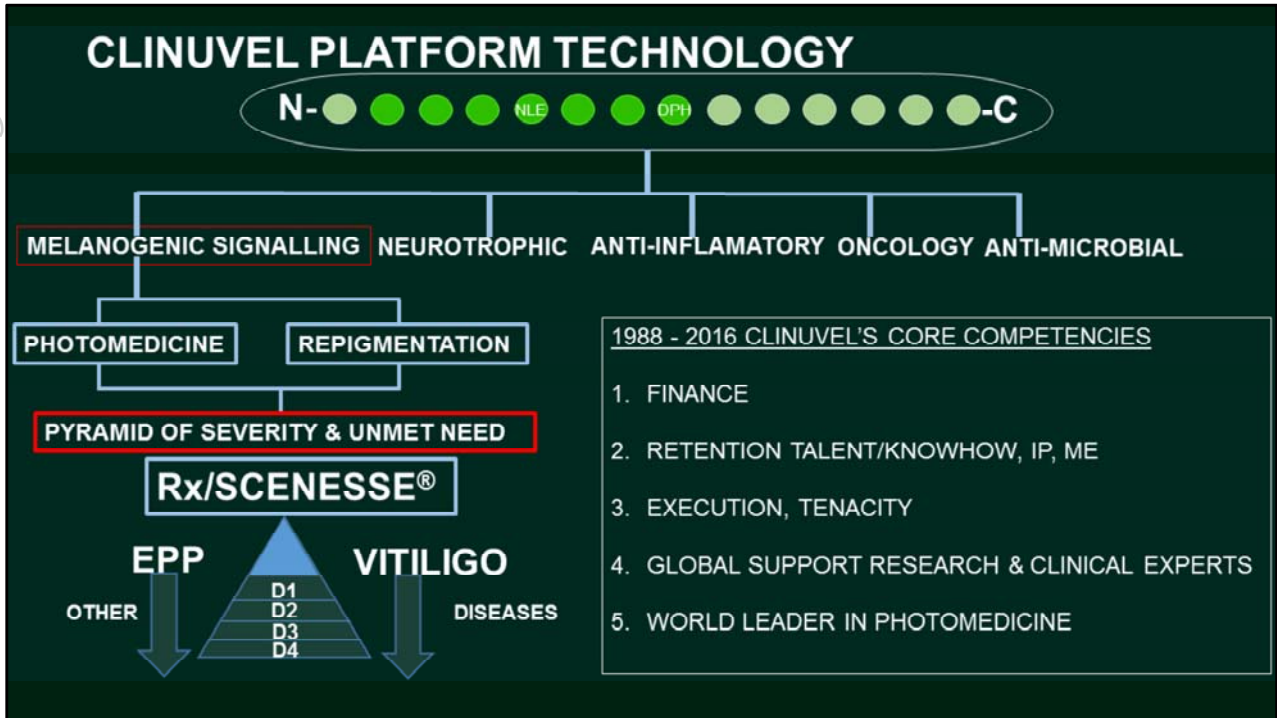
CLINUVEL

Physiologic alpha MSH has attracted much scientific attention resulting in more than 6,000 articles.  
CLINUVEL opts to work with compounds of linear structure given its relatively benign safety profile.  
Toxicology and safety drives our objectives.

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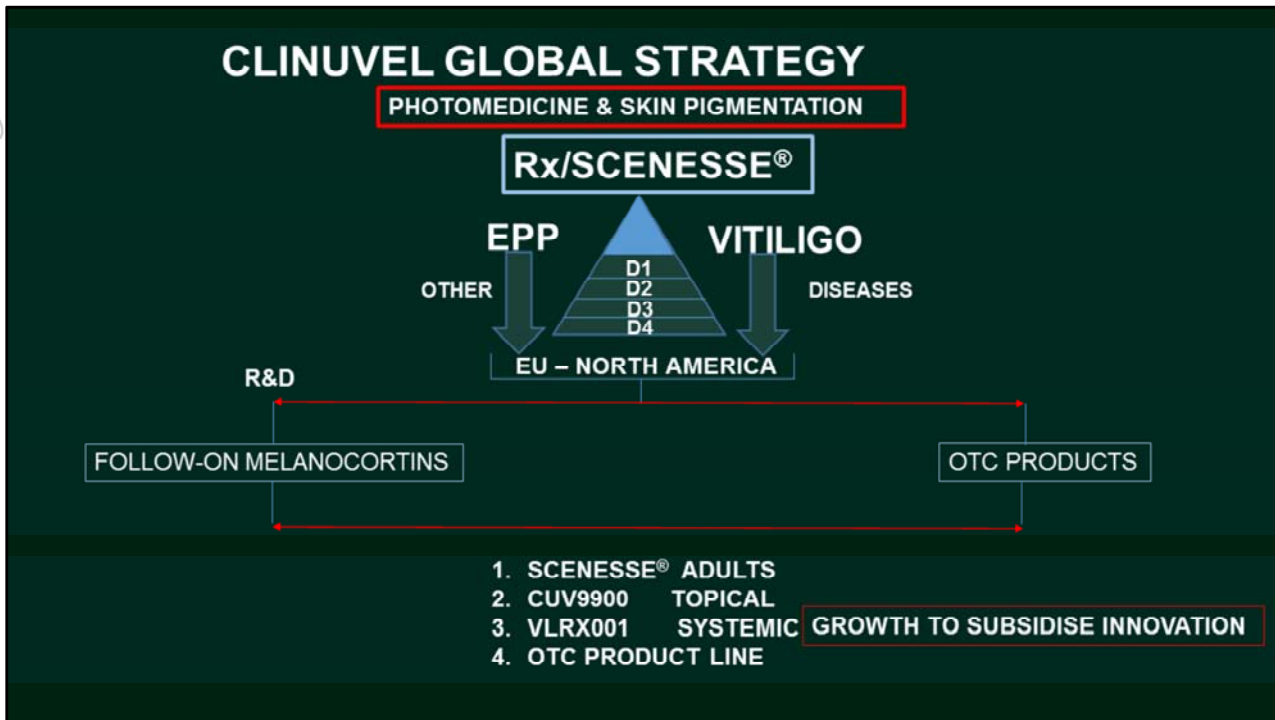


A competitive breakdown of research groups and companies active in melanocortins is discussed.  
 In using alpha-MSH analogues in melanogenesis CLINUVEL is the furthest down the development path compared to competitors.



CLINUVEL focuses on unmet diseases with high severity, EPP and vitiligo fit this criterion. Five core strengths have characterised CLINUVEL over the years.

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CLINUVEL will expand its position as leader in photomedicine and melanogenesis and also will enter the market of non-prescriptive products to add to its portfolio.



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## CLINUVEL GLOBAL STRATEGY

PHOTOMEDICINE & SKIN PIGMENTATION

Rx/SCENESSE®



### SOCIAL RESPONSIBILITY AS FIRST PHARMACEUTICAL COMPANY

1. 'PROVIDING LIGHT' TO EPP PATIENTS LIVING IN THE DARK AND NEGLECTED BY SOCIETY
2. SERVING 'VITILIGO PATIENTS OF COLOUR' WHO HAVE LOST THEIR IDENTITY

# CLINUVEL

A strong social mandate has emerged, CLINUVEL being the first company to treat patients of Caucasian skin (EPP) and patients of darker skin colour (vitiligo). The conscious direction to treat patients of colour fulfils a social objective of the CLINUVEL GROUP to do good for patients who have been neglected, misunderstood and ignored by society, medical community and other stakeholders.

Patients of colour not only lose their skin colour but also their identity, and it is a privilege for CLINUVEL to do something about this stigmatising medical problem.

## AGM 2016 SUMMARY

- Further differentiation & symmetry in EU & US
- Commercial success is driven by patients' and physicians' demand
- Expand successful EU distribution **SCENESSE®** in 2017
- Uniform global pricing 2017
- Expansion CUV portfolio

**CLINUVEL**

There is much work ahead, but we look with much optimism and energy to 2017.

## TESTIMONIES FOLLOWING PRESS ON EPP

***“no longer forgotten and ignored”***

*“As I discovered more sources about the disease, including the NBC Dateline episode “Out of the Shadows” and the website of the American Porphyria Foundation, I grew more convinced that I had EPP. I look forward to the day when Scenesse® (afamelanotide) is available as a treatment for adult patients of EPP in the United States, and for testing to begin on children so that they can gain access to this treatment.” J.*

*“Since last January, I have been diagnosed with erythropoietic protoporphyria (EPP), an extremely rare genetic disease that explains the symptoms I have had since a very young child, symptoms without any visible manifestations. Symptoms that only I can feel. Symptoms that everyone had already doubted were real, including my very self. I finally have a justification for my symptoms and a simple way to explain them to others without being judged in any way. As a future physician, I will do the very best I can to be aware of these rare and afflictive diseases.” J.*

*“I never heard of anyone else who had the same symptoms as I, NEVER. And believe me, I asked everyone I could if they heard of anyone with burning hands, feet and face. I'm in tears even as I write this, it's not that I have EPP, it's that I am not alone, & other people know & understand what I had lived for 45 years, (at that time). Tears of relief, I am not crazy! This isn't in my head, I didn't deserve to be beat for this!” A.*

**CLINUVEL**

As a function of CLINUVEL's continuous R&D investments as well as the patient associations' long term efforts to aggregate patients with common disease have resulted in a number of unintended phenomenon.

During the past year many reports have emerged from the exposure by media, press and TV broadcast on EPP. Many individuals who had been suffering since childhood from intense burns following light exposure and who had been characterised as hysteric, mad and exaggerating had now seen, for the first time, kindred EPP patients described and shown by popular press and TV. Not only has the media exposure prompted many patients to seek diagnostic confirmation of EPP, all of these patients have found solace and relief in that they are now acknowledged and recognised by society and other EPP patients, their new community.

Without the continuous support of CLINUVEL's investors and shareholders we collectively would never have been able to create a platform for those who have been forgotten, ignored and labelled as mad by their immediate environment. These patients are literally now “coming out” after decades of suffering a misunderstood, misdiagnosed and neglected disease.

CLINUVEL thanks the investment community for persevering and remaining interested in the Company and its principal cause to develop SCENESSE® for adult EPP patients.

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# CLINUVEL PHARMACEUTICALS

SCENESSE®  
OPTICAL PHYSICS IN EPP

## APPRECIATION FOR SHAREHOLDERS, PATIENTS & CUV STAFF

ANNUAL GENERAL MEETING 2016  
MELBOURNE  
28 NOVEMBER

CLINUVEL MANAGEMENT

# CLINUVEL

On behalf of patients, physicians and staff we thank all shareholders for their continuous support. Without the belief in the Company, SCENESSE® would not have reached EPP patients. The gratitude of patients is at times overwhelming and makes our team realise that the fundamental human right to live free of fear, and have the ability to have the choice to go outdoors and live a normal life or not.

CLINUVEL's shareholders have enabled EPP patients receiving drug to obtain a life they never had.

Gratitude is expressed herewith.