FOUNDATION FOR GROWTH 2021

A predisposition to long-termism

CLINUVEL PHARMACEUTICALS LTD
Annual General Meeting
21 November 2018
Melbourne

ASX:	CUV
Nasdaq Int'l:	CLVLY
Xetra-Dax:	UR9

CLINUVEL

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., Europe 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 2018 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.

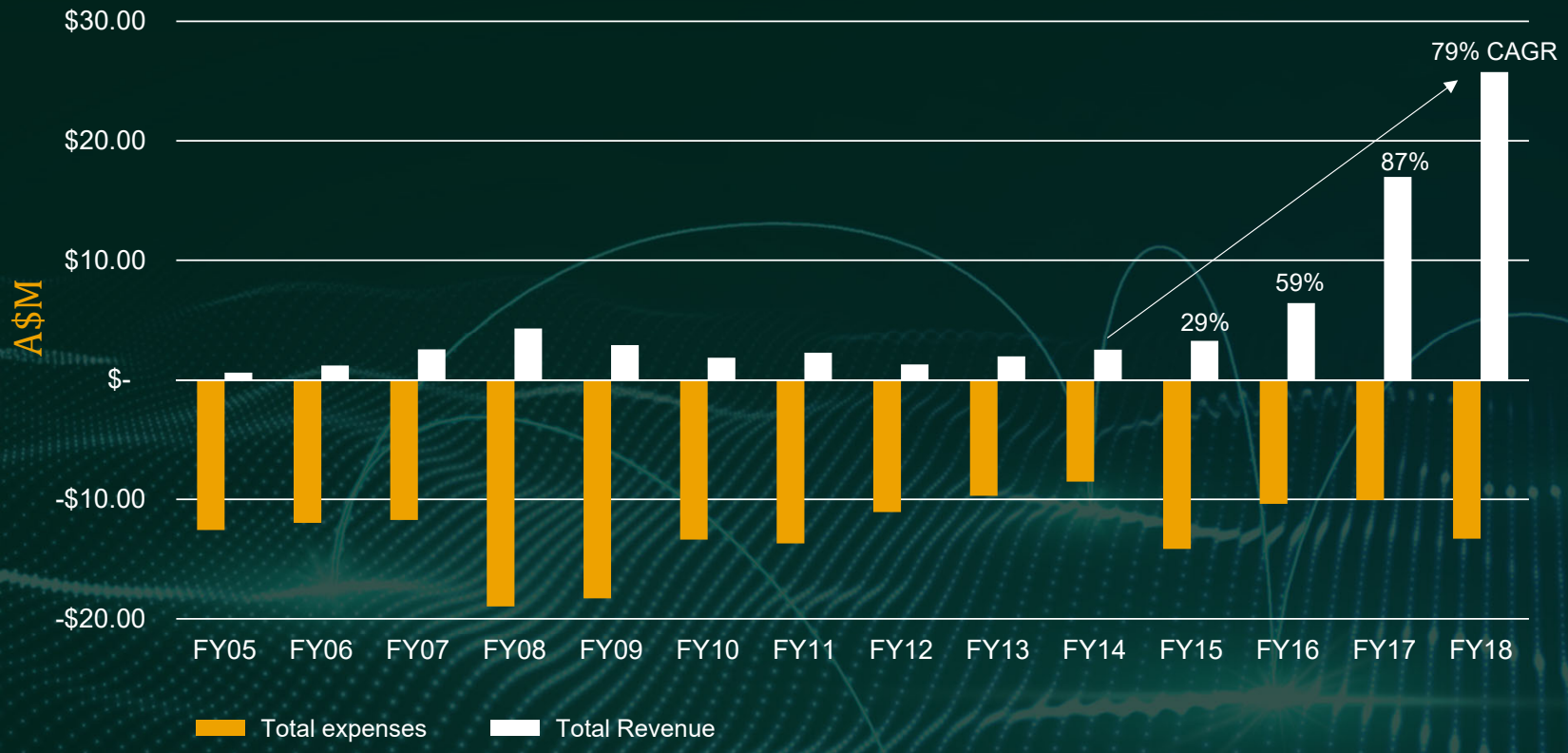
Sections

1. Financial Management
2. EU & US Update
3. Pipeline CUV
4. Growth 2020
5. Conclusions

1

Financial management

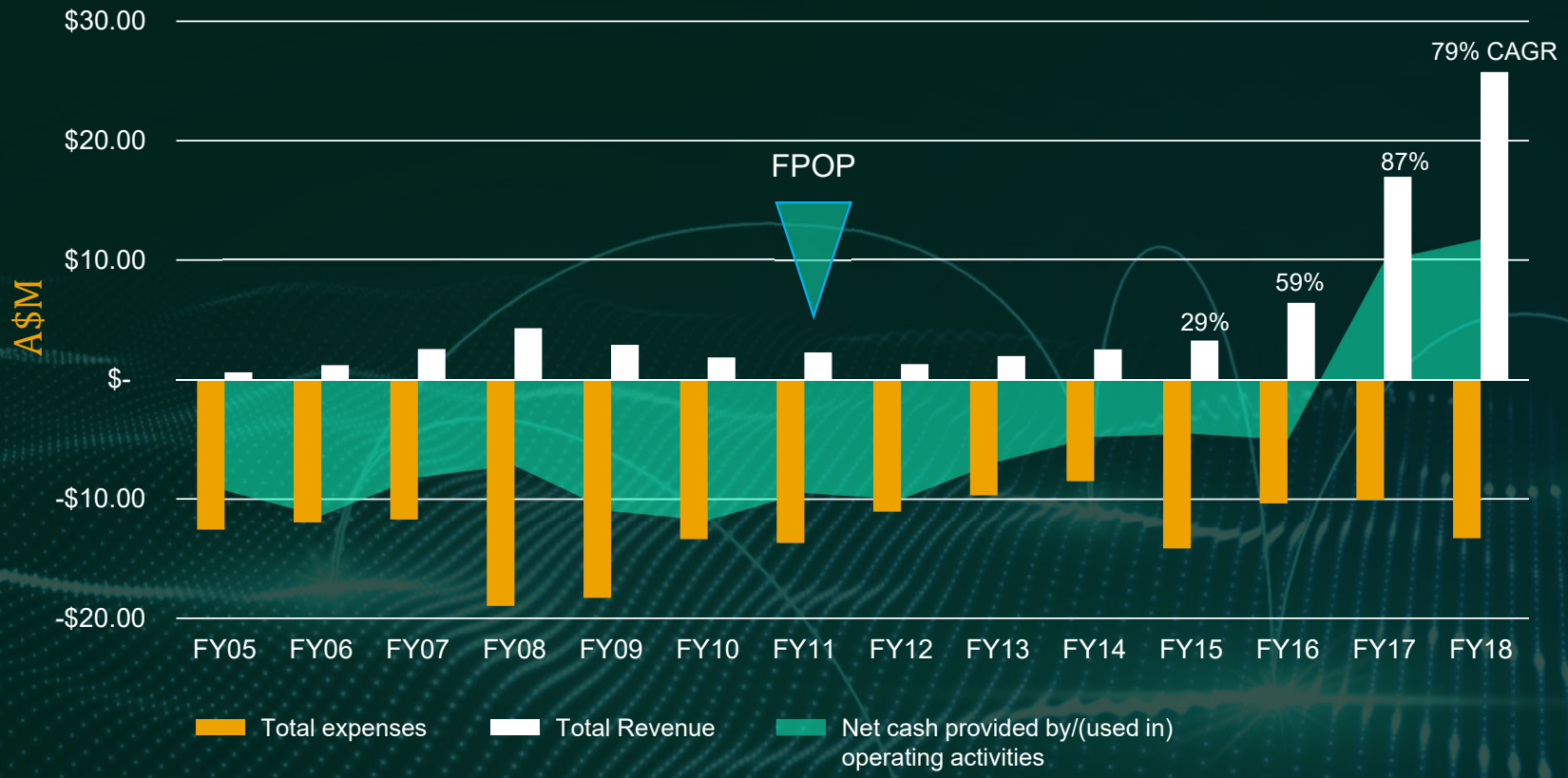
Financials I



CUV continues quarterly reporting

Cash flow statement will reflect seasonal fluctuations due to cyclical treatment period

Financials I



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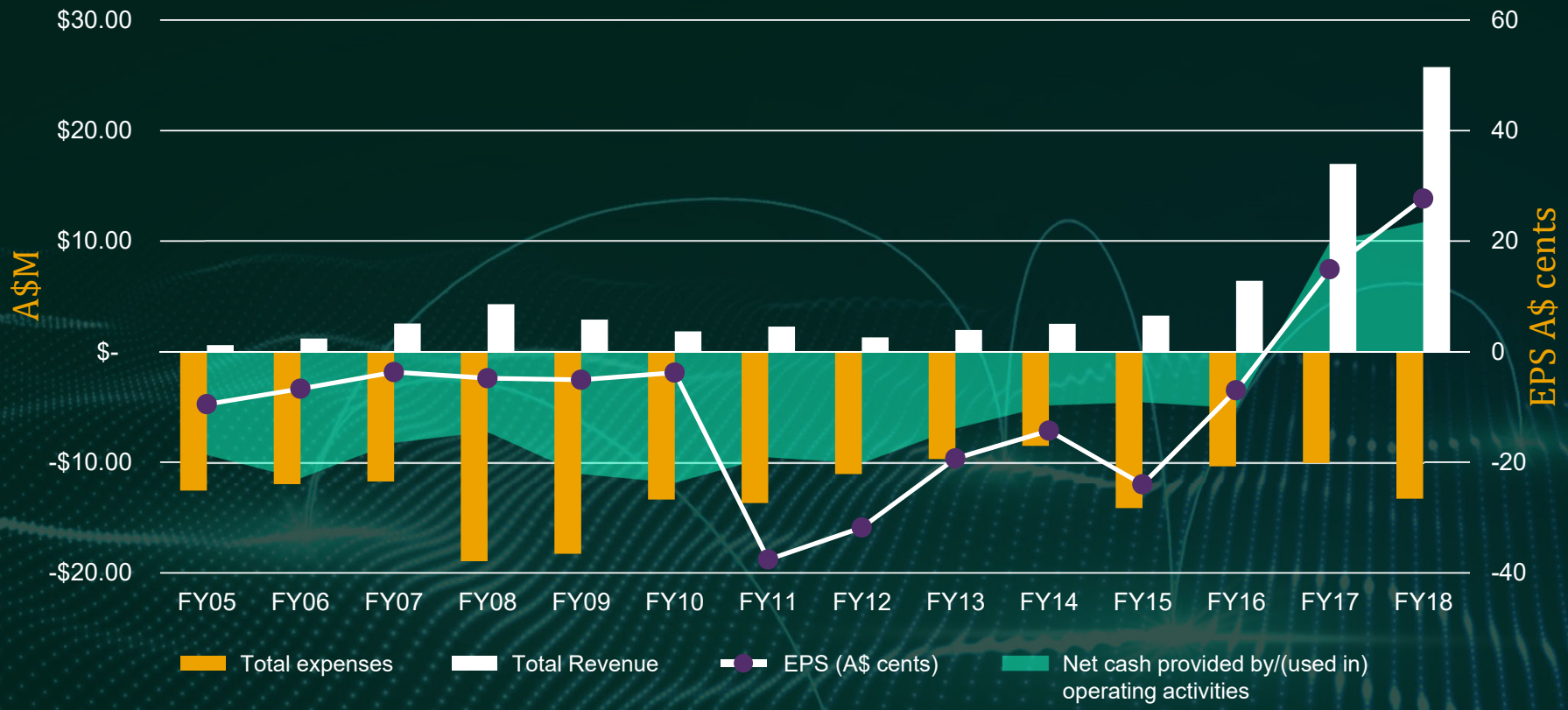
Financials I

PRE-REVENUE 2005-2016

- cost-management
- share capital
- financial proof of principle
- minimum cash reserves

POST-REVENUE 2016 ONWARDS

- cost-management
- cash positivity
- profitability
- growth



CUV continues quarterly reporting

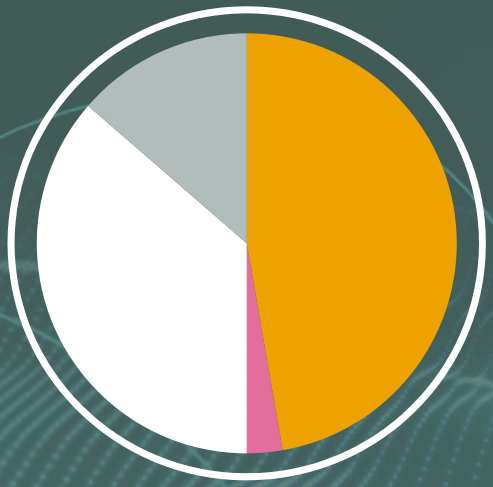
Cash flow statement will reflect seasonal fluctuations due to cyclical treatment period

Financials II

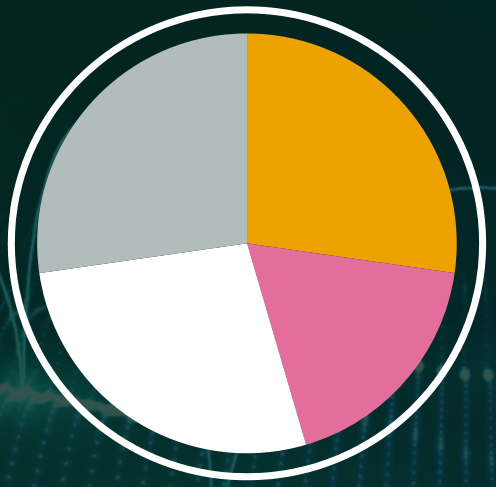
Ownership by region

- Australia
- Asia-pacific
- EU/Switzerland
- North America

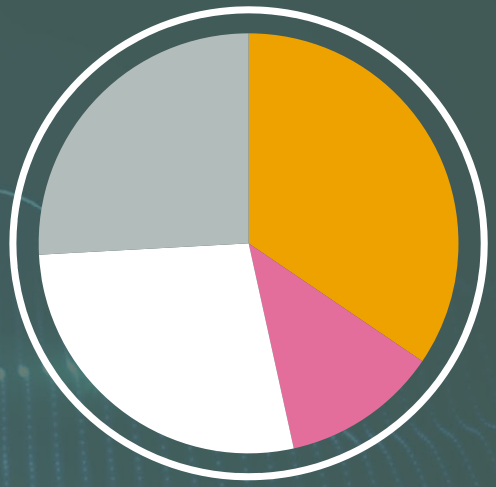
2010



2015



2018



2

EU & US Update

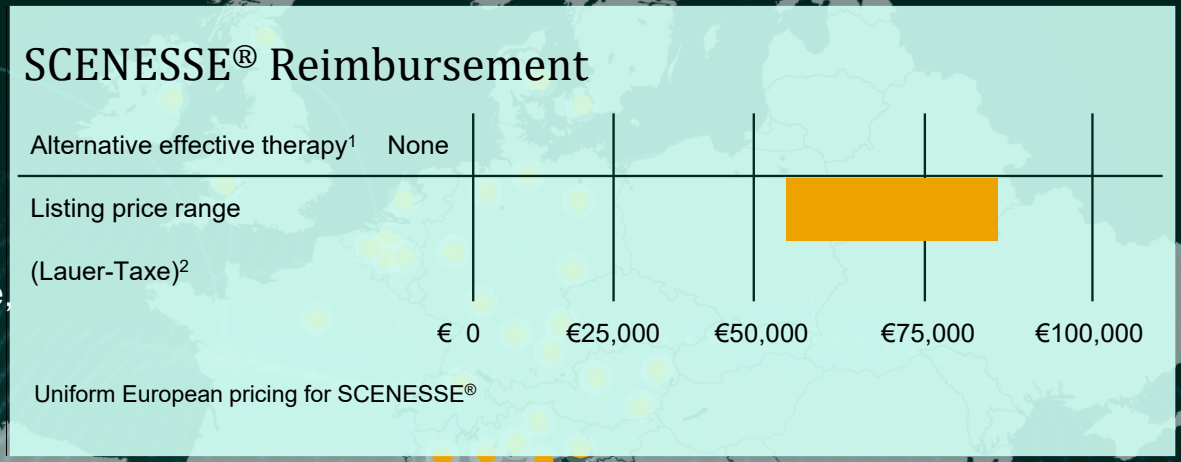
EU distribution

SCENESSE® approved for adult patients with EPP in 2014, first post-MA use June 2016

Brexit, 29 March 2019
Transfer of marketing authorisation

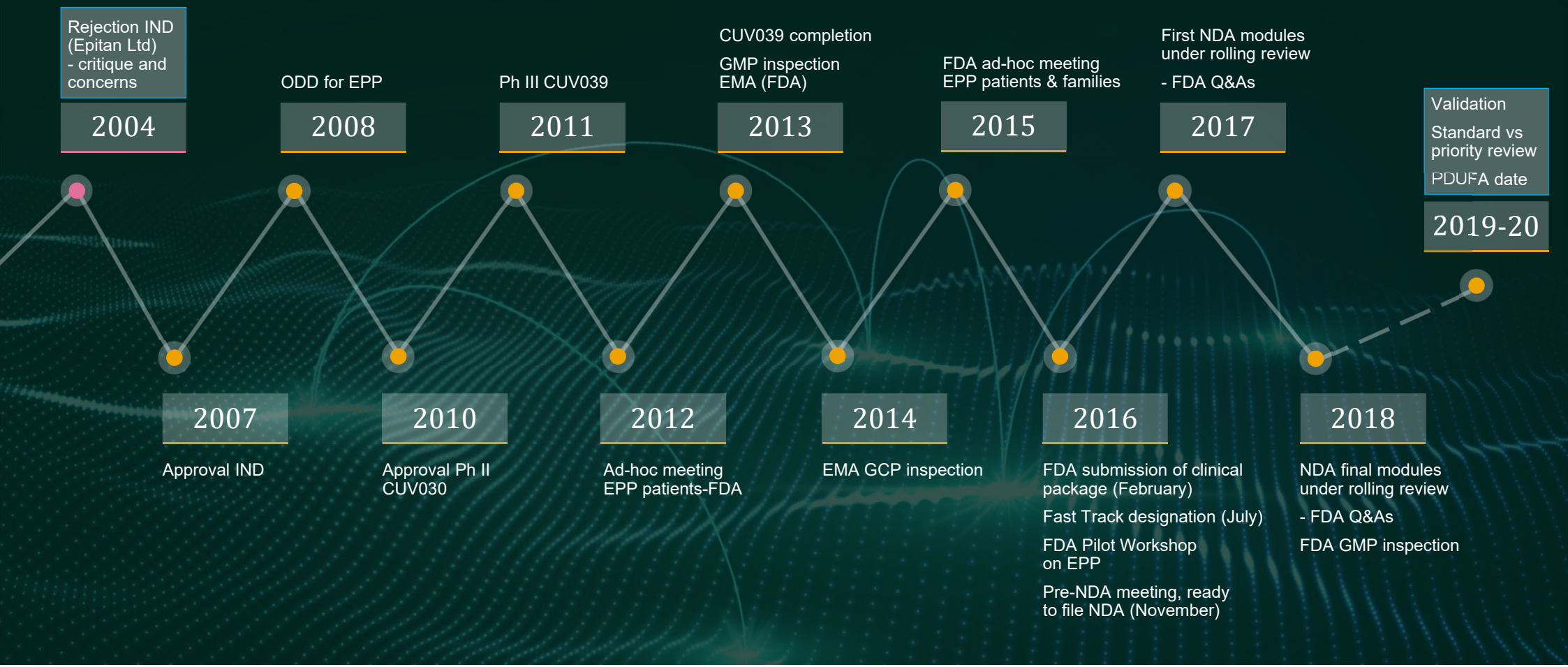
PASS
100% prescriber continuation (CY2016-2018)
>95% continuation on treatment
Most common AEs: headache, nausea, fatigue, flushing, somnolence, asthenia
PSUR #7, Annual Report #3
2019, first reduction in reporting obligations (PSUR)

Pricing & reimbursement ongoing
Implant administrations growth FY17-FY18 +52%
Increase in prescribers, patients, use
NICE/NHS England Appeal upheld



SCENESSE® featured internationally in 2018

US regulatory progress



Risk-balance assessment SCENESSE®

RISK VS BENEFIT

SYSTEMIC PHOTOPROTECTION

↓

New Molecular Entity (NME)

↓

Novel mode of action

↓

Emphasis on safety

Risk-balance assessment SCENESSE®

RISK VS BENEFIT

SYSTEMIC PHOTOPROTECTION

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Emphasis on safety

RISK - SAFETY

Known risks of NME (afamelanotide):

- during clinical trials
- Real World Experience (RWE) = EU PASS

Most frequent ADRs: nausea-flushing-gastrointestinal-injection site discolouration

>1,200 patients exposed, ~8,200 doses

suspected unexpected risks (theoretical)

no off-label use (non-medicinal)

EFFECTIVENESS

- increase in exposure time (“clinical benefit” p=0.107)
- reduction of phototoxicity (“pain free days” p<0.001)

“ability to overcome anxiety of light sources”

EMA:

“ability to expose to light/sun”

“no adequate scientific instruments to quantify effect”

- RWE “dramatic” clinical benefit
- high continuation rate

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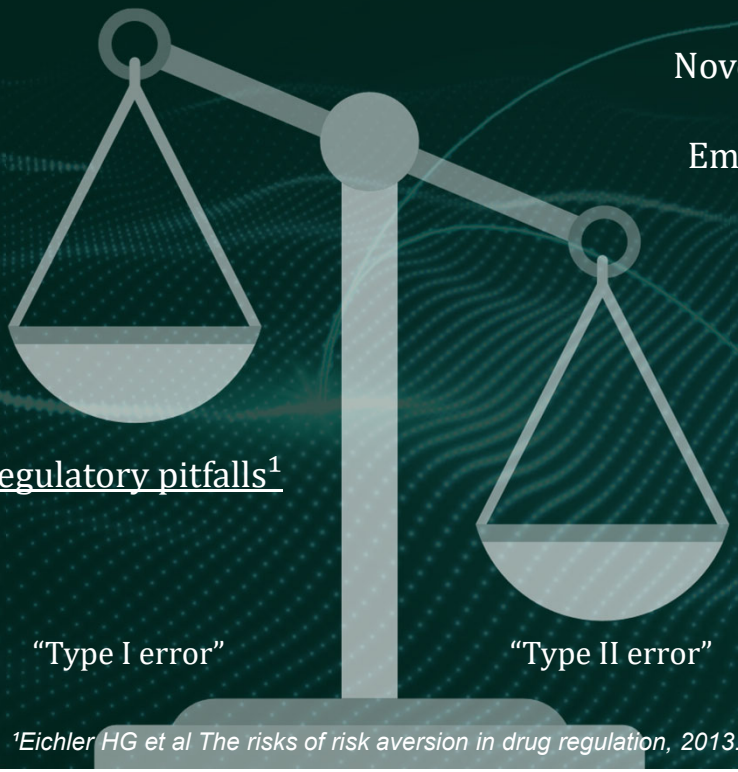

Regulatory pitfalls[1]

"Type I error"

"Type II error"

[1]Eichler HG et al The risks of risk aversion in drug regulation, 2013.

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Prof E Minder – Triemli Hospital Zürich:

Clinical experience in EPP 2005-2018

Long-term observation (up to 12 years) on the treatment of EPP patients with SCENESSE®

Signs of effectiveness under routine clinical condition:

1. Triemli Hospital experience with 1,384 implant administrations
2. High adherence rate >90%
2. Patients permanently acknowledge life changing effects of treatment, they
   - undertake activities they thought to be never able to do in their lives
   - tell that they start to forget suffering from EPP
   - sacrifice time and money in getting SCENESSE® treatment
   - state that they never want to lose this treatment again (mental state)

CLINUVEL does not edit or moderate physicians' declarations or patient testimonies

Long-term observation on the treatment of EPP patients with SCENESSE®

Adverse effects:

- 1 day nausea (0.5-3) immediately after implantation in 10-20% of applications, mild, no treatment required. Most frequently observed after first dose, frequency decreases with following doses.
- Flushing 15-30 min immediately after application, no treatment required
- Increased pigmentation at injection site, especially on irritated skin (patch reaction), reversible, Especially visible in dark complexion such as skin type IV-V
- Pruritus and redness (delayed allergic reaction) – anti-histamines locally
- Increased pigmentation of naevi (no growth), freckles, no skin malignancies
- Mild tiredness, dizziness, no treatment required (better, prolonged sleep)
- Headache, migraine often without temporal relationship to implantation

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Long-term observation on the treatment of EPP patients with SCENESSE®

Benefit/risk judgement:

Patients: "treatment worthwhile, adverse effects minor with respect to effectiveness of treatment"

Medical judgment and observations:

- change in behaviour, more self esteem (adolescents)
- change in clothing, less or no protective clothing
- less fear of EPP symptoms (forget to take protective clothing with them)
- no serious or severe adverse effects, only few moderately severe adverse effects
- positive benefit / risk ratio

THANK YOU FOR YOUR ATTENTION

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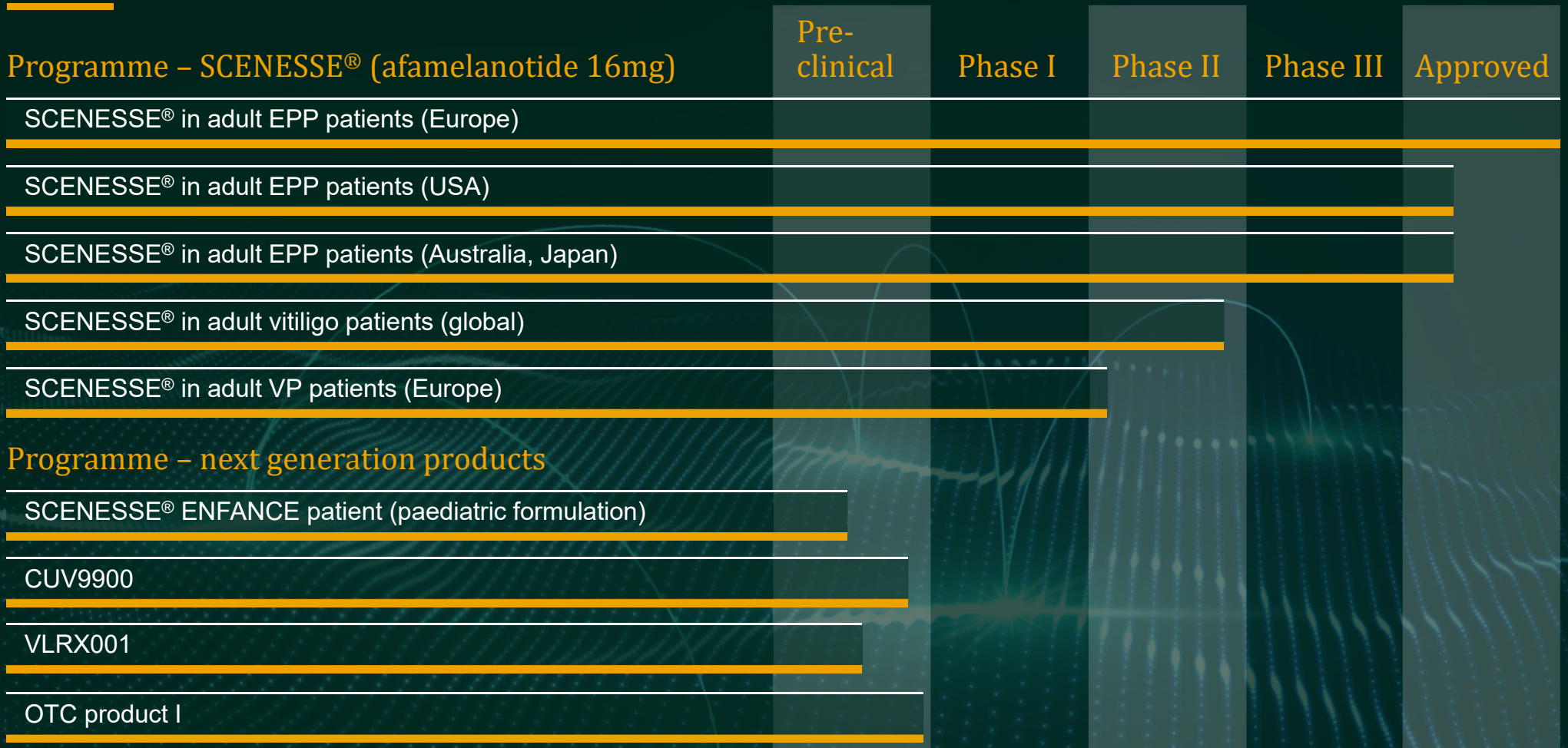
Pipeline CUV

Pipeline


Programme – SCENESSE® (afamelanotide 16mg)
Pre-clinical
Phase I
Phase II
Phase III
Approved
SCENESSE® in adult EPP patients (Europe)
SCENESSE® in adult EPP patients (USA)
SCENESSE® in adult EPP patients (Australia, Japan)
SCENESSE® in adult vitiligo patients (global)
SCENESSE® in adult VP patients (Europe)
Programme – next generation products
SCENESSE® ENFANCE patient (paediatric formulation)
CUV9900
VLRX001
OTC product I

SCENESSE® in vitiligo

FACTS

- prevalence ~1%[1]
  - addressable market 20-30%
- expression
  - generalised vs non-segmental
- pathophysiology
  - auto immune response
- standard of care
  - NB-UVB,, mc transplants
  - steroids, mTOR-inhib.
- poor response rates[2]
  = unmet medical need

EFFECTIVENESS

CUV103 analyses in progress

CUV102 [2013]

- extent or repigmentation VASI ($p<0.025$)
- face: time to repigmentation ($p=0.01$)
- anatomical locations

- Clinical Objectives
  1. repigmentation face/H&N
  2. follicular response

MODE OF ACTION

Hypothesis 1

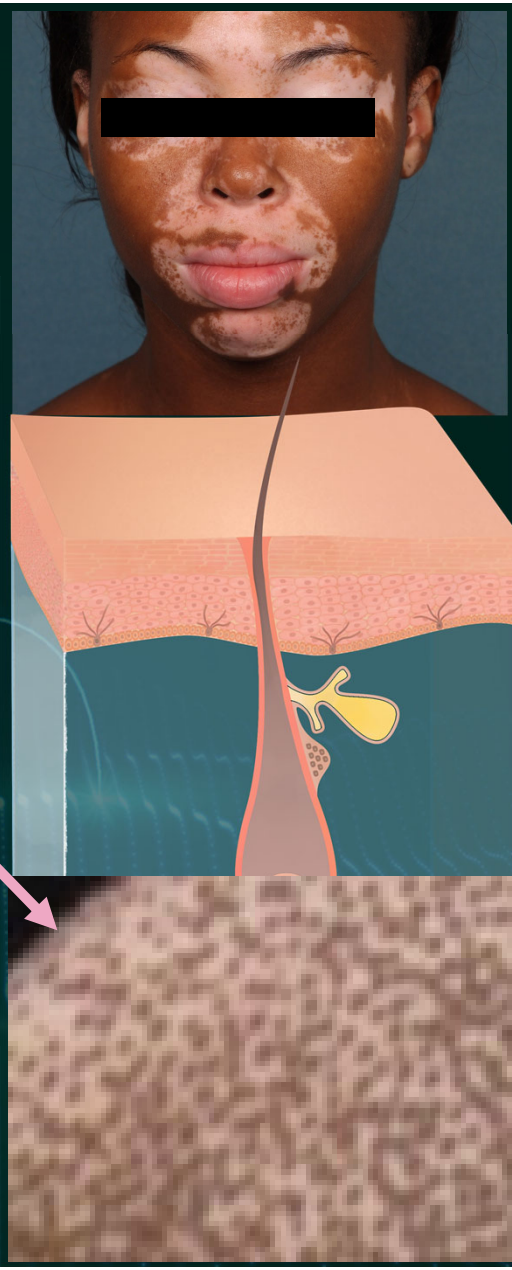
SCENESSE® + NB-UVB activates

- differentiated stem cells
- melanoblasts to migrate
- **follicular repigmentation**

Hypothesis 2

SCENESSE®

- monotherapy is effective



[1]*Ezzedine et al. Vitiligo. The Lancet, 2015.*

[2]*Rodrigues et al. Current and emerging treatments for vitiligo. JAAD, 2017.*

Patient images courtesy of Phase II vitiligo study medical specialists

4

Growth CUV

SCENESSE® *NME world's first systemic photoprotective*

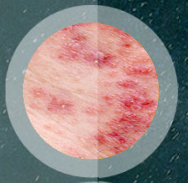
EFFECTIVENESS

EPP

Vitiligo

- Human volunteers: melanogenesis, reduction in apoptotic epidermal cells
- EPP: reduction in phototoxicity
  reduction in anxiety, increased freedom
- Solar Urticaria: reduction in wheal formation
- AK/SCC in OTRs: no malignancies
- Vitiligo: repigmentation

VP



Paediatric

>1,200 patients exposed, ~8,200 doses

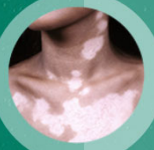
DNA REPAIR → PHOTOPROTECTION

1988-2018

SCENESSE® *NME world's first systemic photoprotective*

EFFECTIVENESS

EPP



Vitiligo

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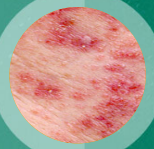


Paediatric

- **TOXICOLOGY**
- **CLINICAL SAFETY**
- **LONG-TERM USE**
- **LONG-TERM MONITORING**

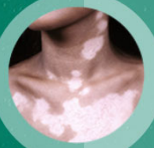
DNA REPAIR → PHOTOPROTECTION

1988-2018

SCENESSE® *NME world's first systemic photoprotective*

EFFECTIVENESS

EPP



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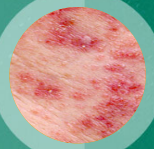

Paediatric

- **TOXICOLOGY**
- **CLINICAL SAFETY**
- **LONG-TERM USE**
- **LONG-TERM MONITORING**

DNA REPAIR → PHOTOPROTECTION

SAFETY

World's first locoregional photoprotective

TOPICAL MELANOGENESIS

CUV9900
VLRX001

FIRST-IN-MAN

5

Conclusions

Conclusions & thank you to CUV team & Board

FY14-18	CAGR 79%
FY18	first dividend to shareholders of >15 years
	increase in patients, prescribers of SCENESSE®
	>94% treatment continuation (3 years)
CY18	EU PASS: no safety signals from SCENESSE®
CY18	*vitiligo results CUV103 pending*
	announcement of new indication, subject to ethics agreements
CY19	*first relaxation of reporting requirements (PSUR)*
	US FDA awaiting decision on validation & priority review
CY19	*From world's first systemic photoprotective to topical melanogenic products*

Patient testimonies – PASS Disease Registry

"

"With SCENESSE® my life has become so positive! I am now capable of doing the every day stuff (driving my car, outings, meeting friends and family, cleaning the windows, gardening, basically enjoying myself) without having to think about it. Not looking for shadows in the subway, driving the car by myself, bicycle tours with my husband all possible without any trouble. Just now I realize how limited I've been without SCENESSE®!"

"These summer and fall were very special. As a family, but also personally, I have experienced a life without worries and full of freedom, which I did not really realized. SCENESSE® has made my life bigger very much. I'm experiencing this as a great gift for me and for my surroundings as well."

"SCENESSE® really changed my life! I am almost completely symptom free. This summer I even went on a holiday to India and I was able to walk around with almost no protection. I never have to worry about where to sit in the train. I can now get my groceries in the daytime instead of sending someone else. It is amazing!"

CLINUVEL does not edit or moderate patient testimonies

Company Announcement

CLINUVEL

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

CEO's presentation to the Annual General Meeting

Melbourne, Australia 21 November 2018

GOOD MORNING LADIES, GENTLEMEN, MEMBERS OF CLINUVEL,

And welcome to Melbourne. It is exciting to see new shareholders attending, and I specifically greet the international visitors who have taken long flights to attend CLINUVEL's AGM. It is a privilege to see you all in good health and spirit, enabling you to see the unfolding of this fascinating journey.

The transcript of this AGM is simultaneously released to the ASX for all audiences worldwide to obtain the same information on CLINUVEL. No recordings or photographs are permitted, while our teams will be posting selected photographs and text of this meeting on Twitter this morning.

For those shareholders who recently took a position in CLINUVEL, we presume prior knowledge of the Company's legacy. Today I will only refer to relevant parts of our history; I invite you to read more on our website to better understand the context of management's decisions. The specific business context makes CUV unique and different from any other biopharmaceutical company on this planet.

Let us start, since there is much discussion ahead of us.

FOUNDATION FOR GROWTH 2021

We have enjoyed the longest bull run in equities since the end of WWII, which started on 9 March 2009. In the wake of the surge of global market indices CLINUVEL has enjoyed an appreciation in enterprise value from A$8.64 on 11 November 2017 to A$20.98 on 9 November 2018; this provided CUV a market value of over A$1B on that day. Reaching the threshold of A$1B valuation is a momentous occasion not only for the Australian biopharmaceutical sector, but for all of us to pause and reflect on a trajectory which was deemed by most European hedge funds, journalists, analysts, scientists, brokers and regulators as impossible in 2005, given the long history of the Company and its lead drug afamelanotide.

From CLINUVEL's perspective, the sole conclusion to be drawn thus far is that a focussed mindset, a never-let-go attitude and a bespoke business approach executed by a small team can lead to success in the pharmaceutical business, also when initiated and executed down under.

My task is to guard that CLINUVEL's DNA is replicated within the organisation which, by now, is specialised in overcoming resistance, first rejections and naysayers as part of our usual business under circumstances where others have walked away.

At this AGM 2018, we are discussing the overall performance of the Company as well as our objectives for 2021 and beyond.

SAFE HARBOUR STATEMENT

I start off by exhorting the audience today to take note of the **Safe Harbour Statement** and not to use any of the prospective information presented today as representative of certain activities to take place and facts to unfold in the future, and to respect the risks involved in this pharmaceutical venture. Please read the Safe Harbour Statement carefully.

FINANCIALS I

As you can see from the bar chart, CLINUVEL enjoyed **significant growth in revenues** over the past three financial years due to the increase in demand for SCENESSE® both within the European Union and Switzerland.[1] Our compounded annual growth rate has been 59%, 87% and 79% over the past three years. In executing the European distribution program, a number of business models were open to us. In order to maximise value in the changing economic environment we opted to directly distribute the medical product to hospitals by disintermediating distributors and possible licensees. This allows us to retain control over our product and pricing, and maintain the critical relationships forged over a decade with our prescribers and, indirectly, 'our' patients. Our financial management is skewed towards long-termism as to the preservation of capital, retention of specific knowledge, and expansion of IP.

We completed the financial turnaround of the Company at the first quarter of FY2017, becoming cash flow positive while maintaining a relatively low fixed cost base. Operating on a fixed ratio of low fixed costs versus variable expenditures seems at first sight a contradiction in pharmaceutical R&D, but by tracking on **a financial dashboard** we have achieved our objectives thus far.

In the green translucent areas under and above the curve you see **the net operating cash flows** over the years, while the green triangle indicates our first revenues from SCENESSE®. This milestone in 2011 served as **a financial proof of principle [FPOP]**, reflecting the first supply of the drug to Italian patients, subsidised at 23% by the Italian government and 77% by CLINUVEL, and – exceptionally – three years ahead of European marketing authorisation. Without this essential financial proof of principle, it is unsure whether we would have persisted with the technology and stand here today. The members of this Board believe that a company needs to have an *indication of commercial feasibility* early on in the R&D cycle, rather than relying solely on scientific and commercial hope.

In navigating the Company and in all our development decisions, we religiously keep in sight a **financial dashboard**, to be divided in a *pre-commercialisation and post-commercialisation* stage. During the R&D of a novel technology and at the pre-revenue stage we rely on the following 'instruments':

1. cost-management (ratio of fixed versus variable costs)
2. share capital
3. a financial proof of principle
4. a minimum of cash reserves

During the post-revenue stage and from here onwards our financial management has not changed much, but our main 'dials' are:

- cost management
- cash positivity
- profitability
- growth

In nursing *financial consistency,* Mr Keamy and his team have ensured solvency of the Company in the early stages, enabling a foundation for growth in the mature stage and turning CLINUVEL into **an investment grade life science entity**.

From the financial risk scenarios played out it is apparent that without this specific approach which were necessitated by contextual factors**,** CLINUVEL would conventionally have had to incur dilution of more than 800%, resorted to debt financing by taking advantage of cheap money in the markets, or have urged our team to license out its technology at an early stage. Under these scenarios and at a weighted average cost of capital between 12% and 17%, it is highly unlikely that the Company would have commanded the same market position on the ASX and the range in enterprise values as it has recently attained.

Importantly, we see cash in hand serving as a cyclical capital buffer during economic retreat, market corrections, or unexpected operational set-backs.

Although CLINUVEL is *not providing financial guidance at this stage* given ongoing and incomplete discussions on reimbursement in Europe, management *will continue to report its quarterly financial cash flow receipts through the ASX*. We stress that the seasonality of the symptomatology of erythropoietic protoporphyria (EPP) will be reflected in the cash flow receipts.

CLINUVEL's recent and first distribution of capital back to shareholders in the form of unfranked dividend is a first demonstration that we had not taken those who had supported the Company and its mission since 2005 for granted.

FINANCIALS II

When looking at the ownership structure of CLINUVEL we have seen remarkable and unexpected changes the past year, certainly in comparison to the shareholder base of 2010 and 2015.
We have seen that Australian holdings have increased to almost 34%, approaching – but just short of – the total positions in 2010, held mainly by retail shareholders.
The increase in Australian institutional holdings is to the detriment of US and Asian institutions; we may expect that more Australian investors will show interest in CLINUVEL should financial results continue in FY2019.
In meeting the new and prospective shareholders in Australia and abroad, a number of factors have been highlighted as being decisive in the open-market purchases of CUV:

- revenue growth
- profitability
- dividend
- ASX-300
- Director purchasing 3.2% of the Company
- consistency of management
- financial discipline

All these investment criteria coincide with our own views on long-termism in progressing CUV.

EU DISTRIBUTION

Since obtaining approval in 2014, the Company has had to address pricing and reimbursement for SCENESSE® in each eligible European country, each with its own set of pricing policies and assessments of the product.

In our teams navigating and overcoming the national health systems, we have unexpectedly seen 100% continuation in physicians' decisions to prescribe the drug, and more than 94% of patients seeking treatment in second and third years of drug access.

While these rates are strong and meaningful, we stress the importance of safety data coming out of Europe and the absence of off-label use. These two factors are – as we will discuss later – of critical importance to continue to provide value for patients and shareholders, in that particular order.

I conclude by reiterating our commitment to make SCENESSE® available in the United Kingdom, and the recent appeals upheld by the NICE Appeal Panel are a first step towards this objective. Undoubtedly more information will come from NICE/NHS in 2019, and shareholders are directed to recent ASX announcements for more on this matter.

As to the pricing in Europe, for those new shareholders, the range in price per patient per annum varies from approximately €56K to €84K per annum, whereby the Company is treating each nation and its hospitals equitably and not providing discounts or rebates to make CLINUVEL's books as transparent as possible. It is of note that the price of SCENESSE® has remained unchanged since March 2017.

Significant in 2019 will be the first reduction and relaxation of reporting obligations under the post-authorisation commitments as agreed with the European Medicines Agency (EMA). Instead of safety analyses being performed every six months to populate periodic safety update reports (PSURs), CLINUVEL will now be allowed to supply the EMA with these reports once per annum, together with an Annual Report. Our teams are working to reduce the burden to physicians and patients who literally spend hours recording diaries and transferring these data in the European EPP Disease Registry with very little added value.

At the bottom of the slide, the viewer can see that the last year 52% more implant administrations were provided through direct distribution to trained and accredited centres.

SCENESSE® FEATURED INTERNATIONALLY IN 2018
As per tradition we provide a compilation of media coverage on CLINUVEL the past year, whereby the main theme has been the introduction of SCENESSE®.

Please start the film reel.

US REGULATORY PROCESS
On the screen you see an illustration of some of the many and continuous interactions our regulatory, clinical and technical teams have had with the FDA over the years.

We needed a bespoke approach to CLINUVEL simply due to the legacy left by Epitan in 2004. Although, we have optimised the synthesis, reformulated, and identified the appropriate indication for SCENESSE®, the FDA has had prior exposure to the molecule in 1999 and 2004, when it rejected the notion of the use of afamelanotide for cosmetic and lifestyle use and issued its early concerns on unknown long-term safety and future potential off-label use.

Overcoming historic regulatory objections and expressed doubt – based on human assessment while data were lacking in these early days – takes much more than starting from a blanco sheet. At CLINUVEL we have always been aware of this phenomenon and have "*overcompensated*" on generation of safety data. This has received much of our emphasis during the 13-year development program. We are growing in confidence since data have not shown any safety concerns or new "signals" (pharmacovigilance term) thus far.

We do not have the time today to go through each regulatory highlight in this diagram but leave you to read this in your own time. However, I call your attention to two separate events worth mentioning and perhaps indicating the gradual progress **CLINUVEL made vis-à-vis the FDA**.

In 2016, our teams were asked once again to provide the FDA – ahead of any pre-NDA meeting and Rolling Review – with all individual clinical studies, as well as and pooled data, to assess and familiarise itself with the status of the development program. Following this assessment, **in October 2016** the FDA called – in an agency first – an EPP Workshop in Silver Spring, Maryland, where 150 families and porphyria experts attended for a full day session.

In November 2016, thus six months after our informal submission initiated by the FDA, CLINUVEL held its pre-New Drug Application (NDA) meeting with the FDA and the outcome was that our teams *were ready to file* a NDA on the basis of the available information.

The sequence of these events would logically lead to progressive FDA review and allaying of possible existing anxiety on the side of the FDA towards safety concerns with afamelanotide.

One should always keep in mind that other divisions of the FDA – while it is using a centrally accessible intranet and database – may be familiar with cyclic melanocortins which exert central effects (central nervous system and systemic circulation), and that the submission of a dossier on a linear configured molecule is totally novel to the agency. An advantage of SCENESSE® is that afamelanotide does not cross the blood brain barrier (99.6%) and therefore yields the safety profile seen thus far. We suggest that the caution observed by the FDA is well within expectations.

Our regulatory team are now awaiting reactions from the FDA on CLINUVEL's latest responses on product and manufacturing. Due to strict confidentiality between sponsor and FDA, nothing further may be disclosed at this time.

Logically, the next steps would ordinarily be the formal conclusion of the validation period and issuance of a PDUFA date under Standard or Priority Review. CLINUVEL applied for Priority Review in July 2017.

Given the interest in the ongoing FDA review, we will walk you *factually* through the risk–benefit assessment to be made by the regulator.

RISK-BALANCE ASSESSMENT SCENESSE®
In proposing a novel molecule, novel mode of action and novel formulation to be used in a poorly characterised disorder which has never known a standard of care, one can easily understand that the burden of proof rests heavily on the pharmaceutical company. Novelty in the hands of pioneers comes at a risk but also provides one a head start over possible competitors. Once one breaks through cordon, one receives reward as a first mover. In the case of orphan drugs, this is most prominent with market exclusivity of seven years in the US and ten in Europe, extended once a paediatric formulation is available.

One sees on this presentation the risk – balance assessment to be made by the Division of Dental and Dermatology Products (DDDP) of the FDA with regard to SCENESSE®. This is the world's first systemic photoprotective – a New Molecular Entity – and scrutiny is expectedly high due to its novelty, and a lack of reference standard.

On the risk side, we have the known risks ("side effects") from the use of afamelanotide 16mg. These stem from 12 years of use in clinical trials and importantly – very much following the suggestions of the new FDA Commissioner and Head of CDER – from Real World Experience (RWE). Real World Experience consists of patient data and structural observations captured in disease registries under pharmacovigilance programs, in our case data coming out of Europe as we speak. The FDA can assess these data as part of its assessment of risk.

The most frequent adverse reactions, "side effects", seen in post-authorisation use are listed here.

Whereas we treat an orphan indication, the CUV team has facilitated drug exposure for more than 1,200 individuals to SCENESSE®, and the administration of more than 8,200 doses in various drug presentations of afamelanotide. These are, in reference to other orphan drugs, relatively high numbers.

As I stated before, given the legacy of the chemistry we chose to "*overcompensate" and overdeliver – if there is such a thing – on safety.*

I share with you my experience and view on drug development: "*a pharmaceutical company may come back from a US regulatory and NDA rejection on the basis of uncertain efficacy, but one may never be able to overcome concerns on safety, these will always dominate the regulators' and company's decisions*".

With this adage, CLINUVEL set out and never compromised.

Lastly, **on the risk side**, it is apparent that regulators – US and EU – have been concerned about *the potential for off-label use* of SCENESSE® which provides a pharmacodynamic effect or visible effect of the skin. To address this concern CLINUVEL has:

- never allowed off-label use (other than one patient who was terminally ill with congenital erythropoietic porphyria, CEP);
- controlled the distribution;
- provided consistency of 13 years in its communication and development and commercial plans;
- laid out a set of corporate values.

Only two factors can allay concerns or fears and convince regulators: **time and consistency**. A change in strategy would jeopardise all the work and credibility our teams have established for such a long time; CLINUVEL cannot allow this to occur now or in the future.

On the benefit side, the EPP trials showed a consistent increase in exposure time and an increase in number of days without phototoxicity. The question thus arises: what does this mean for patients? Since we are the first team globally endeavouring to capture the impact of light on human biology, and there is no reference to our work, we are gradually discovering – and without bias - what SCENESSE® means for EPP patients:

> "*an ability to overcome a lifelong anxiety for light/sun and light sources*"

And as the EMA has ruled:

> *"EPP patients are unwilling to expose to light sources or sunlight"*
>
> *"Under normal conditions of use, the status of current scientific knowledge, tools and instruments, does not allow for sufficient precise measurements of impact of disease and 'visible light' to exposed skin"*

Our teams specialise in physics and optics, a domain of medicine which has not found a solution to quantify light exposure in the blue and green spectrum.

Nevertheless, the Real World Experience allude to a meaningful clinical effect. EPP patients return year on year for their two-monthly injection. This is reflected in the aforementioned high continuation rate, despite distances travelled and time taken off work.

The risk-benefit assessment deserves various perspectives.
Eichler and Rasi have described this for the first time from a regulatory perspective: "the risk of risk aversion" really was ground breaking in that withholding the option of treatment for EPP patients – where there is no alternative therapy available – needs to be put in context of the overall risk of the product in a limited and controlled setting.

In our case, I have already explained a few minutes ago the known and expected risk ("side effects") of SCENESSE® used in a confined environment (university hospitals) and in limited hands (trained, accredited physicians) only. By not allowing off-label use in larger populations, the risk of unexpected side effects is further minimised.

Rationally, the probability of significant adverse reactions to SCENESSE® is sufficiently limited for regulators to lower their possible anxiety for unexpected health risks to the public. In this model and along these thoughts, the "type I" regulatory risk of making a drug available, which has shown under real world experience and clinical trials, is low or minimal, while the "type II" regulatory risk of withholding a seemingly effective product from EPP patients – who have no other options – is substantial.

The aim of CLINUVEL has therefore been to decrease the "type I" regulatory risk and increase the "type II" regulatory risk such that the regulatory authority acknowledges our decade long strategy.

We will leave the audience to reflect on this. We discussed a complex issue in short space of time; there is much to think about here.

PROF E MINDER – TRIEMLI HOSPITAL ZÜRICH
This is an appropriate moment and a privilege to introduce to you in Melbourne a well-known expert in genetic metabolic diseases and porphyria from Zürich, Switzerland, Professor Elisabeth Minder. Professor Minder has administered more than 1,379 implants during her professional life and has devoted her ambition to porphyrias. Professor Minder has published 94 publications, 41 on EPP, and 14 on afamelanotide with 284 cross-references to date.

Without censure or editing, Professor Minder will speak about her experiences with SCENESSE® in EPP.
In accordance to it policy, CLINUVEL does not induce reimburse or pay Professor Minder or any other physician and aims to keep prescribers independent for them to take decisions without bias. Professor Minder was reimbursed for her flight and accommodation to Melbourne.

PIPELINE
We now turn to the pipeline of the Company, the next generation products in R&D.

I will spend limited time on this, and allow you to read in your own time.

CLINUVEL publicly stated that it seeks to advance the next drug candidates in the clinic.

Further value will need to come from the adult use of SCENESSE® in EPP, vitiligo and possibly VP – depending on the results of the exploratory study, as well as the new chosen indication.

Once the paediatric indication is approved by regulators, value will be added by treating children with EPP. As we will discuss later, we are in pursuit of other follow-on products which are part of the melanocortin family.

SCENESSE® IN VITILIGO
Analogous with EPP, CLINUVEL's team believes the physicians and patients are the ultimate stakeholders to demand a treatment, and are thus important protagonists in our development decisions.

At present, vitiligo offers an opportunity of unmet medical need, in other words where no other therapy has proven sufficiently effective to speak about standard of care. The current best available treatment – but deemed ineffective by the global experts in vitiligo – is narrowband UVB (NB-UVB) irradiation of vitiligo, of depigmented patients.

On the left hand column one can see the facts about vitiligo.

The centre-left column shows CLINUVEL's results seen in 54 North American patients. The results of 18 patients in Singapore are expected before year end as our teams have recently refocused their attention away from the FDA work.

For the new shareholders, the mode of action of SCENESSE® is slightly different to that targeted in EPP, in that by using the drug in combination therapy with NB-UVB we seek to repopulate new pigment cells (melanocytes) by stimulating these to grow and migrate from the hair follicles back to function in the skin. This is hailed by the medical community, experts in vitiligo as one of the most exciting domains of dermatology and medicine.

On the right hand column one sees the effect provoked by the drug and NB-UVB, generating follicular repigmentation. Perfect concentric islands of repigmentation in the skin of African-American patients.

We are excited about progressing this indication in North America.

SCENESSE® NME WORLD'S FIRST SYSTEMIC PHOTOPROTECTIVE
Last year we unveiled our growth strategy for CLINUVEL to be implemented by 2020.

While a team is of utmost importance in executing a plan, the scientific technology and chemistry at hand ultimately provides the direction of the development.

In the diagram one sees the various learnings gained from SCENESSE®, the first systemic linear molecule to provide protection from light sources, and it has been evaluated in human volunteers and a number of patient populations.

For a long time we have held a scientific focus serving the medical population and pursued the commercial ambition to grow the Company. But to realise these ambitions, we needed to start systemically and work our way downstream.

We gained the understanding of how linear molecules of the melanocortin family were able to act biologically, and their limitations in certain formulations.

However, we arrived at providing photoprotection to a range of patients, and we chose the patient population with highest medical need.

SCENESSE® NME WORLD'S FIRST SYSTEMIC PHOTOPROTECTIVE
In total 1,200 patients and human volunteers have been exposed to 8,200 afamelanotide doses during close to 20 years. The significance is found in that safety data have been collected. As we illustrated on earlier slides, the emphasis on safety has significance for regulatory scrutiny, but for us inhouse too.

CLINUVEL analysed and used the safety profile to make decisions on follow-on molecules and products.
Most of all, our teams looked at:

- Toxicology
- Clinical safety of patients short- and long-term
- Long-term use of afamelanotide, and
- Long-term monitoring

The summation of these factors gave us the confidence to assess risk versus benefit and develop further, downstream translations and derivatives of our lead technology.

In 1988 scientists around the world and pharmaceutical companies were striving to develop various drug presentations to achieve one outcome; the ambition had been expressed in Arizona but never saw the light.

In discussing biomimicry, we need light to provoke the locoregional response, melanogenesis demarcated by exposure versus covered skin surface. Following the administration of SCENESSE® we observe pandermal melanogenesis, darkening occurring without light and without incurring photoproducts as a warning signal.

Now, following the second Annual Report to EMA, 8,200 doses onwards, we are closer than ever to the quest for the locoregional melanogenic response, veritable biomimicry, melanogenesis where we need it as a photoprotective measure.

SCENESSE® NME WORLD'S FIRST SYSTEMIC PHOTOPROTECTIVE
Without safety data from long-term use of afamelanotide our teams could not have arrived there, downstream use of upstream information to formulate the first topical presentations of melanocortins.

These products aim to protect skin while activating pigmentation locoregionally, where we need protection most and where we seek to prevent.

In CUV9900 and VLRX001 we hope that we will again be pioneers and lead the way.

We will report from the first-in-man study, which depends on regulatory and ethics approvals.

The effectiveness would complete a quest which started more than 30 years ago; we are all eager to be the first complementing our portfolio of products in development. CLINUVEL believes there is clinical value and therefore also value for shareholders in this avenue, I trust you are as excited about this prospect as our teams are.

CONCLUSIONS & THANK YOU TO CUV TEAM & BOARD
We have discussed today with you a rationale, an approach and business model which is bespoke to CLINUVEL and aims at long-termism.

In choosing to manage this asset class, we seek a commonality between stakeholders while we recognise that there are different perspectives and interests. Most of you present today share that you invest or remain invested in CLINUVEL because the equity provides direct benefit to patients and their carers.

We are privileged in that it may well be the ideal function of capital markets in fulfilling a social mandate by developing and making accessible effective medical solutions for those who live with ill health while providing returns for those who fund medical care. In that sense the stakes are high, but we are all conscious to contribute to the creation of economic value.

In that sequence we pursue, and in my view if one would change the order of objectives one is prone to commit errors and stray towards failure.

Thank you for your ongoing support and to our team and Board.

– End –

[1] SCENESSE® (afamelanotide16mg) is approved in Europe as an orphan medicinal product for the prevention of phototoxicity in adult patients with EPP. Information on the product can be found on CLINUVEL's website at www.clinuvel.com.

About CLINUVEL PHARMACEUTICALS LIMITED
CLINUVEL PHARMACEUTICALS LTD (ASX: CUV; NASDAQ INTERNATIONAL DESIGNATION ADR: CLVLY; XETRA-DAX: UR9) is a global biopharmaceutical company focused on developing and delivering treatments for patients with a range of severe genetic and skin disorders. 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 photoprotection and repigmentation. 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 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, Switzerland, the US and Singapore, with the UK acting as the EU distribution centre.
For more information go to http://www.clinuvel.com.

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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, 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 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 2018 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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