CLINUVEL

News Communiqué II

05 April 2023

Objectives 2023

The Managing Director set the tone for the Group for 2023 in the first Communiqué of the year:

> *"You may have gleaned that I have difficulty in containing my enthusiasm for 2023, my expectations are high, the only prerequisite for all the deliverables to see light is for staff and Board to remain in full spiritual and physical health. If so, barring unforeseen calamities, the rest of the puzzle will need to come together throughout the year."*

From my recent interactions with personnel across our global operations, CLINUVEL's teams have been and are motivated to deliver on the aggressive objectives set for this year and beyond. At the end of quarter one of 2023, we had met all our internal objectives, as seen by the 22 announcements made so far in 2023.

Much of the work expected this year is intended to lay the foundation for the Company to advance its promising pipeline and successfully transition to multiple product offerings across pharmaceuticals and dermatocosmetics.

This combination of treating medically compromised patients and attending specialised consumer populations is not often seen but makes a lot of sense given the hormone technologies we have developed. In both markets, we remain focused on unaddressed audiences to make a difference to the quality of people's lives.

In this communiqué II we will cover:

- the launch of CYACÊLLE, our first dermatocosmetic product;
- progress of the DNA Repair program;
- the commencement of CUV803 for Stroke with the first clinical use of PRÉNUMBRA® Instant;
- the ongoing development of NEURACTHEL®;
- a recap of the half year results;
- recent and planned investor relations activities; and
- the recent recognition of CLINUVEL as one of the fastest growth companies in the Asia-Pacific region.

...CLINUVEL's teams have been and are motivated to deliver on the aggressive objectives set for this year and beyond.

Dermatocosmetic Products

CYACÊLLE – λ3 Next Generation Solar Protection

On 01 March, we achieved the first milestone in the evolution of the Group from pure pharmaceutical products to a specialised cosmetic product range, with the test launch of CYACÊLLE, a polychromatic screen, as our first dermatocosmetic product.

Translating our expertise in photomedicine, this advanced cream is formulated for skin at highest risk of damage from harmful ultraviolet (UV) and high energy visible (HEV) light, risks increased by environmental changes.

CYACÊLLE is being distributed 1) to hospitals for use in treatment of patients with erythropoietic protoporphyria (EPP) and xeroderma pigmentosum (XP) as an adjuvant (not a substitution) to the systemic treatment provided by SCENESSE® (afamelanotide) and 2) through a dedicated e-commerce platform www.CLINUVELDNA.com, initially to European audiences, with plans to expand to the US and Australia later this year. The Company has been deliberate in its approach to roll out the first dermatocosmetic product, CYACÊLLE, taking key learnings from late 2022. We are advancing plans to distribute at larger scale supported by similarly scaled marketing campaigns in more countries.

We will set a new standard in the global approach to manage the risks of solar damage...

Digital outreach

Last year, the Company launched its first CLINUVEL Ambassador (CUVA) campaigns, engaging leaders from three identified groups at higher risk of photodamage and skin cancer. The CUVA programs seek to engage with high-risk groups over the long-term and be a central part of our conversation on solutions to photodamage and skin cancer, rather than focus on a single interaction. The initial campaign reached over 600,000 individuals, introducing novel concepts and the Company to entirely new audiences. Our second wave of CUVA campaigns is now underway, with the objective of growing the CUVA group to 60 and expanding conversations on photoprotection, DNA repair and skin cancer globally.

In parallel, the Company announced its first CLINUVEL Intriguing Personality (CUVIP) partnership, with Dutch Maestro Jaap van Zweden, the musical director of the New York and Hong Kong Philharmonic Orchestras. You can read Maestro van Zweden's first News Communiqué here. Through further CUVIP partnerships, CLINUVEL seeks to introduce the Company's messages, story, and mission in a unique way, using digital platforms and events to build longitudinal relationships with common audiences.

The goal of the digital-first approach is for CUVAs and CUVIPs to ensure that CLINUVEL's overall mission be known to larger parts of the population.

We will need to be a company found at the center of all matters relating to photodamage, skin cancer and prevention. Our objective is bold and aims to set a new standard in the global approach to manage the risks of solar damage and personalised skin care.

Next steps

We are spurred to advance our dermatocosmetic product ranges with enhancements to the first products in the product line, while new products provide regenerative benefits to people at Highest Risk to exposure to UV and HEV light. A summary of the product lines being released is provided below:

Product Line	Global Description
P1	Polychromatic solar screen, CYACÊLLE, 3rd generation (λ3)
P2	Polychromatic anti-oxidative emulsions with strong reflective and refractive properties
M1	Melanocortin assisted DNA skin repair
M2	Melanocortin assisted stabilisation of melanogenesis (self-tanning of the skin)

We will provide updates on the development of new products as each line nears release and global campaigns take place. Importantly, the progress in our branding, marketing and global events will be reported by our new Creative and Brand Director, Mrs Marga Arrom Bibiloni, intended through three Bulletins per annum ("CBM Bulletins"). Through this channel, we aim to give interested parties greater insight on our planned approach worldwide, and how we seek to differentiate CLINUVEL's product offerings, drawing on the success of the pharmaceutical business over the past decades.

DNA Repair Program

Exposure to UV and HEV light – predominantly from solar radiation – causes damage to DNA of skin cells which, if left unrepaired, leads to replication of damaged DNA in cells, and an increased risk of skin cancer. The stage before irreversible cell damage turns to permanent defects is one known as photodamage, or solar damage. People living in Australia and New Zealand, as well as Florida, California, and Texas, are familiar with the phenomenon of sunspots, actinic keratosis, and chronic sun damage of exposed skin.

While this poses a health risk for a large segment of society, we identified individuals amongst us who are even at higher risk due to genetic disorders or necessary medical interventions. It is for these groups that CLINUVEL is first seeking to evaluate afamelanotide as a protective and reparative treatment, before making the products available in a second stage to larger populations. Our expertise in photomedicine stems from the decades of testing and use of our technologies across melanocortin peptides. We are best placed to report on systemic photoprotective properties of melanocortins, knowledge on our products which can protect skin from light and UV, HEV, and how melanocortins play a role in UV-DNA damaged repair processes.

Our deep knowledge stems from the decades of testing and use of our technologies, melanocortin peptides....

CLINUVEL's initial clinical focus is on patients with the rare genetic disorder XP, a life-threatening disorder caused by an inability to repair UV-provoked DNA skin damage, called nucleotide excision repair (NER).

CLINUVEL's current clinical program involves three studies:

- CUV156 – ongoing, first results published; six patients with the XPC complementation;
- CUV151 – treatment protocol complete, first results published; nine healthy volunteers with fair skin types (Fitzpatrick I-III), as a control group; and
- CUV152 – ongoing; six patients with the either the XPC or XPV complementation.

First results CUV156 and CUV151

The first results reported from our DNA Repair Program studies are encouraging and start to shed light on some of the key questions our scientific teams want to see answered, and specifically the potential of afamelanotide to prevent and repair DNA skin damage caused by UV.

Initial data from the Phase II CUV156 study showed afamelanotide was well tolerated and that a decrease in UV-induced skin damage was seen in three adult XPC patients following treatment. Results showed a reduction in cyclobutene pyrimidine dimers (CPDs) which are characteristic of DNA damage, and an increase in yH2AX, a DNA marker, indicating activation of cellular repair mechanisms of the skin. In two patients, there was an increase in p53 expression, a marker for tumour suppression. The overall clinical assessment of these results was positive but with a degree of variability in some measures. These results were presented last month at the Photodermatology Society Meeting at the American Academy of Dermatology in New Orleans, the first global exposure at an expert meeting. The commentary from the medical experts in photomedicine was very good, and the studies provoked further interest.

The CUV151 mechanistic study reported that afamelanotide reduced the UV-erythema dose-response, indicative of reducing the first signs of UV-induced DNA damage, and increased Minimal Erythemal Dose, the threshold to sunburn, in the nine volunteers recruited.

Together, this first evidence is supportive of the hypotheses proposed for the program and indicates the first melanocortin drug is acting as a modulating agent in DNA repair processes, both for XPC patients and healthy volunteers.

To read more on the results announcements, go to: CUV156 first results, technical note to CUV156 results, CUV151 first results, technical note to CUV151 results.

A new video featuring Dr Pilar Bilbao discussing the DNA Repair Program can be viewed on CLINUVELNews.com.

Next steps

Further results from the DNA Repair Program can be expected during 2023. Subject to the results of the initial studies, two additional studies – CUV153 and CUV154 – are planned, taking the number of XP patients involved in the studies to 38 with a total study population of 48. Regulatory interaction is foreseen since this program is the first ever conducted worldwide.

PRÉNUMBRA® for Stroke

The Company has been developing a liquid formulation of afamelanotide, PRÉNUMBRA®, in Instant and Modified-release forms, to provide flexible treatment options in a range of indications. In January 2023, we announced PRÉNUMBRA® Instant is intended for first clinical use in a second study in arterial ischaemic stroke (AIS) patients (CUV803).

Despite the prevalence of stroke – on a global scale, some 15 million are suffered annually – most patients are ineligible for the standard of care, being either pharmaceutical treatment with Intravenous Thrombolysis (IVT), or mechanical removal of the clot with Endovascular Thrombectomy (EVT). This is, in part, due to the restricted therapeutic window of time for both treatments after stroke onset during which IVT or EVT are considered effective and not harmful to the patient (generally 4.5-6 hours for IVT and up to 24 hours for EVT). This leads to a limited use of these interventions: even in specialty stroke units, the highest rates of IVT or EVT use in Europe and the USA are around 20% and 5% respectively, with much lower rates expected at generalist emergency departments. As a result, there is a clear need for new treatments which can be easily administered and may provide clinical benefits beyond the existing therapeutic window.

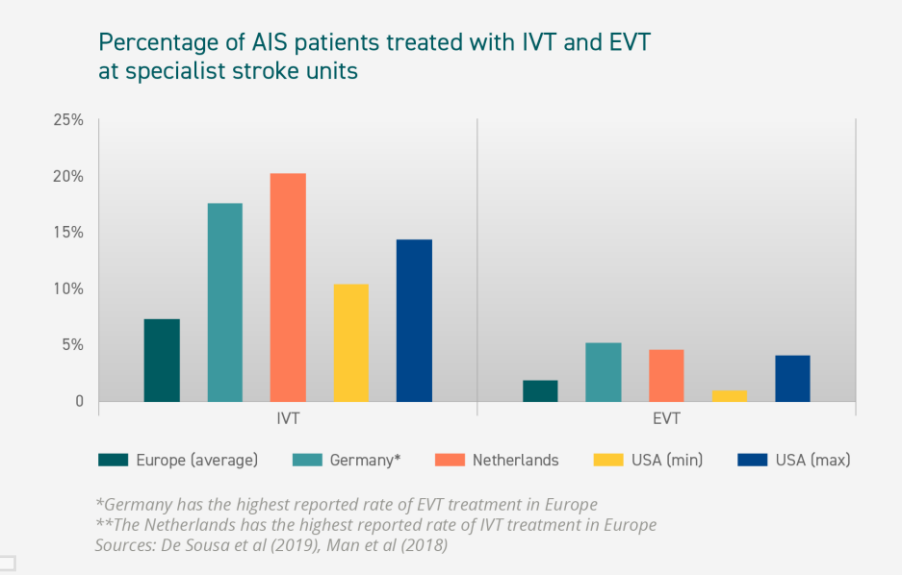


Figure 1: *despite more than 15 million strokes per year, many patients remain ineligible for standard of care treatment, IVT or EVT. Data from specialist stroke units in the USA and Europe show that use of these two therapies remains restricted with many patients ineligible, indicating a clear need for new interventions.*

CLINUVEL has identified a number of mechanisms by which afamelanotide may provide therapeutic benefit to stroke patients

CLINUVEL has identified a number of mechanisms by which afamelanotide may provide therapeutic benefit to stroke patients. In the initial CUV801 study, it was shown that five of six patients with a mild to moderate stroke had improved neurological function following administration of drug.

In stroke, the speed of intervention is associated with an improved chance of recovery. The flexible PRÉNUMBRA® Instant formulation allows physicians to make faster dosing decisions, administering the drug within hours, taking into account each individual patient's clinical status and need. The new formulation of afamelanotide is expected to provide a faster clinical response in order to prevent further brain damage and, ultimately, physical disability.

The first patient was treated in the CUV803 study in a European specialist stroke centre in March, with first results expected later in the year. Alongside

the formal announcement, the Company issued a technical note, delving into the science behind the use of afamelanotide in stroke.

Development NEURACTHEL®

In November 2021, we announced the addition of a new line of pharmaceutical products containing the melanocortin adrenocorticotropic hormone (ACTH), developed as NEURACTHEL®, to our portfolio. NEURACTHEL® Instant and NEURACTHEL® Modified-release, are intended for patients with neurological, endocrinological and degenerative disorders. During the first half of FY2023, work on the manufacturing process and analytical method development was completed and this was announced in January 2023.

The next steps are to:

- manufacture validation baches under current Good Manufacturing Processes; and
- compile a regulatory drug master file (DMF) for ACTH.

The DMF for ACTH is expected to be filed in the second half of 2023. The clinical intention is to first treat children with infantile spasms and patients with multiple sclerosis, with other indications to be disclosed.

Recap: Half Year Results

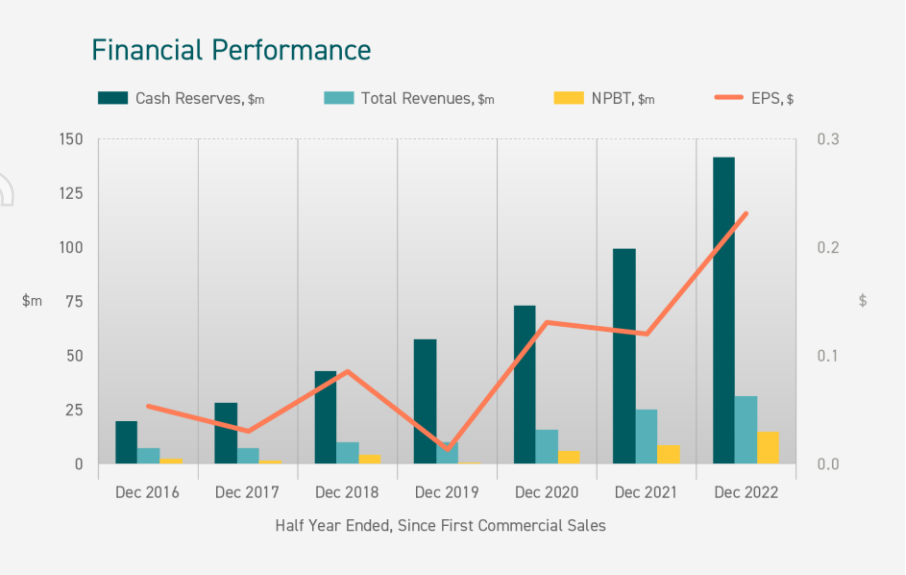
Highlights

The half year to 31 December 2022 marked the fourteenth consecutive half year profit of the Group, since the commencement of commercial operations in June 2016. The highlights are summarised below:

Variable	Outcome and Comment
Total Revenues	$29.355 million, an increase of 19.2% compared to the December 2021 half year, driven by growth in commercial distribution programs
Total Expenses	$16.377 million, an increase of 1.1%, well controlled in this inflationary environment
NPAT	11.388 million, up 94% compared to the December 2021 half year
Total Net Assets	Rose by 11% from 30 June 2022 to 31 December 2022
Cash	Rose by 16% from 30 June 2022 to 31 December 2022
Basic Earnings per Share	23 Australian cents, growth of 93% compared to the outcome for the December 2021half year
Net Tangible Asset Backing per share	$2.778, up 29.6% compared to the December 2021 half year

All figures are in Australian dollars (A$)

The December 2022 half year marks the halfway point of the five-year expenditure plan of A$175.0 million for FY2021-2025. Fifty-nine percent of the A$175.0 million plan is still to be expended to support the growth and expansion initiatives of the Group. Importantly, we hold sufficient cash reserves to self-finance our programs as published in 2021, and part of our five-year projections, and importantly to weather the current inflationary environment.



Market reaction

As we distributed the half year results on 24 February, we received positive feedback on the achievement from a range of stakeholders. Despite the strong December half year profit, the share price declined by 20% between 24 February and 01 March, levelling around $A20.00 in following days, very much owing to wider market dynamics. The commercial update on SCENESSE® issued on 09 March provided more colour on the robust commercial performance in 2022, reporting increases in:

- treatment demand (27%), prescriptions (32%), and Specialty Centers (17%) in the USA; and
- prescriptions (15%) in Europe, with the largest ever number of patients treated annually.

We note that key independent analysts have target prices of CUV above the current share price, ranging from A$23.21 to A$37.30.

Investor Relations Activities

Focus of activities

It is important during these volatile times to look at the larger picture and understand the Company's longer-term strategy and trajectory. Investor Relations works across a wide range of activities to support the Company's objectives, among many we collaborate in:

- presenting to new investors;
- engaging with independent analysts, looking to cover the Company's story; and
- representing the Company during life science conferences.

In recent years, we have increased independent analyst coverage and achieved higher institutional ownership, particularly in Australia. We have also maintained the diversity of shareholdings across geographical regions – Europe, Australia/New Zealand, and the USA – and this has provided stability to share ownership, which is important in the current environment.

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Recent company announcements

The Company's announcements in 2023 to date are listed below:

Date	Announcement
10 January	News Communiqué I
16 January	Afamelanotide Reduces DNA Photodamage in XP
16 January	Technical Note – Xeroderma Pigmentosum
23 January	NEURACTHEL® Manufacturing Processes Advance
31 January	Quarterly Activities / Appendix 4C Cash Flow Report
02 February	Afamelanotide Reduces UV Skin Damage in a Healthy Population
02 February	Technical Note – CUV151 Results
09 February	Chair's Letter
15 February	PRÉNUMBRA® Formulation Competed for Clinical Trial Use
24 February	CUV Appendix 4D Half Year Report
24 February	Global SCENESSE® Demand Drives Increased Revenues, Earnings
28 February	Proposed Issue of Securities – CUV
01 March	CLINUVEL Launches First Dermatocosmetic Product
02 March	Relief from Quarterly Reporting
09 March	Commercial Update SCENESSE®
10 March	Proposed Issue of Securities – CUV
13 March	Statement on Silicon Valley Bank (SVB)
17 March	DNA Repair data presented at American Academy of Dermatology Meeting
20 March	First Stroke Patient Treated with PRÉNUMBRA® Instant Technical Note – CUV803 Study and AIS
30 March	Investor Presentation – NYC Nasdaq Event
05 April	News Communiqué II

The new initiative of the Company to provide additional technical notes to complement announcements of progress in drug development and clinical programs has received positive commentary from stakeholders and we will continue this practice which sets us apart from peers.

All of CLINUVEL's announcements are available on the CLINUVEL website and CLINUVEL News. More specifically, announcements to the Australian Securities Exchange are available on the investor pages of the CLINUVEL website. The website will undergo a total rebuild this year to bring it in line with our wishes to see more simplified and clearer presentation of the Company, distinguishing our pharmaceutical arm from the cosmetic one.

Roadshow on half year results

Following the release of the half year results, meetings were held with a wide range of stakeholders. In particular, the Executive team conducted a roadshow in Melbourne and Sydney; a variety of individual meetings as well as discussions with analysts were held. We thank those firms who hosted meetings, which provided valuable feedback on the Company's performance. In general, we

received high interest in the clinical programs and the ongoing performance of the business.

Update on Soirées and conferences

The re-opening of the world to travel and face-to-face meetings due to control of COVID enabled us to commence a series of shareholder gatherings, called Soirées, in 2022. Soirées were held in Basel (May), Monaco (September) and Sydney (October). The Soirées have been well-received and attended by stakeholders. These gatherings complement our traditional investor relations program based on regular communications through announcements and media releases, webinars and webcasts, presentations to investor conferences and meetings with investors.

The schedule of Soirées set out in News Communique II – 2022 has changed to accommodate venue, shareholder, and executive availability. The first Soirée for 2023 was held in New York on 29 March. It was well attended by existing and potential institutional shareholders, investment banks and key stakeholders. For those who have not received social media, our CEO was invited to speak to Nasdaq's "TradeTalk", which can be viewed here.

The presentation to the Soirée was well received, as was its announcement to the ASX on 30 March 2023.

The key events planned for 2023, covering Soirées and conferences, is summarised below:

Month	Planned Event
March	New York Soirée – Held
May	Wilsons Rapid Insights Conference, Sydney Frankfurt Soirée
June	Jefferies Healthcare Conference, New York
August	Los Angeles Soirée
September	H C Wainwright Annual Global Investment Conference, New York Monaco Soirée
October	Goldman Healthcare Day, Sydney Sydney Soirée
November	Morgans Value in the Vines Conference, NSW Melbourne Investor Briefing Singapore Soirée Jefferies London Healthcare Conference

Note that the timing of Soirées and conferences in the second half of 2023 are indicative and may change.

The Soirées and conferences are important occasions for CLINUVEL to tell its broadening story, particularly the evolution from a company with one pharmaceutical drug for the treatment of one indication to a diverse and integrated pharmaceutical group with both pharmaceutical and dermatocosmetic products to address multiple populations. The complementary Pharmaceuticals and Healthcare Solutions Divisions are being increasingly and favourably recognised by stakeholders. At a time, when the Company is transforming, it is exciting to lead the Investor Relations effort to tell this dynamic, unusual, and positive story to existing and new audiences.

CLINUVEL ranked amongst the fastest growing companies in Asia-Pacific

CLINUVEL was included in the 5th edition of High-Growth Companies Asia-Pacific 2023, published on 15 March by The Financial Times and Statista. CLINUVEL ranked 380th out of 500 companies from 13 countries of the Asia-Pacific region in terms of revenues growth between 2018 and 2021, achieving a CAGR of 28.4%. Sixty-three Australian companies are recognised, with only 12 pharmaceutical companies from across the region. CLINUVEL is one of only two pharmaceutical companies from Australia listed.

Summary and Conclusion

The first quarter of this year marks a concerted advance on the Group's objectives, with a high frequency of public announcements. The drug development path is fraught with fallen trees, ditches, sharp rocks, and other barriers to progress, but the tenacity of CLINUVEL, which is becoming well known, will see us through to achieve our objectives. We continue to focus on our mission to offer innovative solutions for individuals who lack alternatives and, in doing so, achieve positive financial outcomes for investors. This spurs us to recharge each night with pride, and do it again and again, day after day. The market will ultimately assign appropriate value and reward long-term investors.

We hope all stakeholders have had a positive start to 2023 and maintain good health and focus to meet their objectives for year.

Malcolm Bull

Head of Australian Operations & Investor Relations

– END –

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

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 and/or other world, regional or national events 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), PRÉNUMBRA® or NEURACTHEL®; our ability to achieve expected safety and efficacy results in a timely manner 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, Israel, 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®, PRÉNUMBRA® or NEURACTHEL® 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 and consumer based products; decisions by regulatory authorities regarding approval of our products as well as their decisions regarding label claims; our ability 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 2022 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 preliminary and uncertain forecasts and estimates is available on request, whereby it is stated that past performance is not an indicator of future performance.

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