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USFDA Approval Process for Technegas™ Enters Final Six-Month Review Cycle

Cyclopharm Limited (ASX: CYC) is pleased to announce the submission today of the formal reply to the US Food and Drug Administration ("USFDA") Complete Response Letter ("CRL") for its proprietary functional lung ventilation imaging agent Technegas.

This submission initiates the USFDA's stated six-month review process, which is the final major approval hurdle for Technegas in the USA. Cyclopharm expects that USFDA approval and the commencement of Technegas sales in the US will create an initial addressable market of US$180 million per annum for the product in the diagnosis of Pulmonary Embolism (PE). This estimate does not include the exponentially larger potential for Technegas' application for *Beyond PE* indications, including the diagnosis and management of Chronic Obstructive Pulmonary Disease, lung cancer, asthma and Long COVID.

Highlights:

- **USFDA Complete Response Letter Reply submitted**
- **Six-month review process commences**
- **Cyclopharm well progressed in building initial inventory of Technegas generators required for US launch**
- **Support for the use of Technegas remains strong with a growing list of registered expressions of interest from end users throughout the USA**
- **Medical journals and respiratory professionals continue to highlight the superiority of Technegas compared with existing products**
- **Technegas' introduction will likely improve clinical practice in the USA in the similar ways seen in the more than 60 countries in which it is already approved**
- **Strong Balance Sheet to fully fund growth strategy - $20.3 million net cash as at 31 December 2022**

USFDA Approval Process

Cyclopharm has entered the final review process for attaining USFDA approval to commence commercial sales of Technegas in the US market in 2023, consistent with previous expectations.

This submission initiates the USFDA's stated six-month timetable to review and respond to the Company's CRL reply. Cyclopharm expects to maintain an active dialogue with the

USFDA throughout this review period. Given this timetable, sales of Technegas in the US are expected to commence in late 2023.

The CRL is a substantial document, containing over 145 supporting attachments, which comprehensively addresses the definitive list of items and recommendations requested by the USFDA on 25 June 2021. The majority and more complex elements of the response pertains to the manufacturing and product characteristics related to the components that make up the unique Technegas system.

Technegas is unique amongst lung imaging agents and unique in the way it is viewed by the USFDA. Firstly, the USFDA has deemed Technegas as a drug-device Combination Product[1], meaning both the Technegas particle for inhalation along with the components that are required in its manufacture and administration are evaluated together as a drug. Secondly, given the bespoke nature of the equipment required to manufacture the elements making up the Technegas system, full outsourced contract manufacturing is not possible. Lastly, and most importantly, the Technegas radioactive particle for inhalation is manufactured at point of care within a nuclear medicine department and administrated to the patient within 10 minutes.

During the six-month review process, it is expected that Cyclopharm will continue to provide the USFDA with updated data and access to information upon request. During the period the USFDA may also require a follow up from its April 2021 inspection of the Company's manufacturing facilities in Sydney. Since the April 2021 inspection, Cyclopharm has provided the USFDA with bi-monthly updates, totaling thirteen to the end of March 2023, documenting the actions taken in response to their assessment.

US Market Development

To date the Company has received hundreds of expressions of interest from locations across the US requesting access to the Technegas technology as soon as it is approved. The company is targeting the rollout of 200 sites within the first twelve months post approval.

In preparation for the USFDA approval, Cyclopharm is building its inventory of Technegas generators to support a rapid roll out in the US. These generators remain at the sub-assembly stage while we await the final labelling agreement from the USFDA.

Like its roll out across other jurisdictions including Canada, the proposed rapid US deployment incorporates three key pillars of Cyclopharm's growth strategy for Technegas;

1. Replace existing technology for the diagnosis of Pulmonary Embolism ("PE"),
2. Convert a portion of the CT Pulmonary Angiogram (CTPA) market back to nuclear medicine (using Technegas), and
3. Leverage Technegas' true functional ventilation imaging in relation to much larger indications such as Asthma, COPD, and Long Covid, our Beyond PE initiative.

[1] https://www.fda.gov/combination-products

A recent article published in the US Journal of Nuclear Medicine and Technology[2], highlights the opportunity and superiority of Technegas compared with other products in the USA and how the introduction of Technegas will likely change clinical practice in relation to diagnostic lung imaging.

In addition, the upcoming Society of Nuclear Medicine meeting held in Chicago Illinois this June will be attended by representatives of Cyclopharm and will provide an important conduit to communicate to the broader US nuclear medicine community of the impending approval for Technegas.

'Beyond PE'

In addition to actively progressing USFDA approval, Cyclopharm remains committed to expanding the use of Technegas™ in new applications, such as the diagnosis and monitoring of COPD, asthma, Long-COVID, lung cancer and other respiratory disease states, as part of our 'Beyond PE' initiatives.

The recently published Canadian Association of Nuclear Medicine Guidelines[3] and the updated 2019 European Association of Nuclear Medicine Guidelines[4] identify Technegas as the recognised functional ventilation imaging agent for diagnosing Pulmonary Embolism and reinforce the superior use of Technegas, particularly in patients with COPD.

Cyclopharm estimates the global COPD market is approximately 30 times the size of the PE market and that over 500 million patients suffering with COPD and a similar number with Asthma, could benefit from the use of Technegas. These markets represent significant opportunities to expand sales of Technegas, drive shareholder value over the medium term and ultimately improve patient outcomes.

Cyclopharm also continues to sponsor several clinical trials that investigate new applications for Technegas. While these Beyond PE trials were impacted by a reduction in the rate of patient recruitment because of COVID-19, this impact eased during the course of 2022 as patient recruitment recommenced. The Company expects the flow of publications from sponsored trials to commence mid-2023.

Cyclopharm Managing Director and Chief Executive Officer James McBrayer said, "Entering the final stage in gaining USFDA approval for the use of Technegas in the US market is a significant and exciting milestone for our organisation as our key near-term growth driver.

"Of similar importance is the work that we are doing to access even larger growth drivers through our Beyond PE initiatives. Beyond PE has the potential to open huge additional markets for us, such as COPD, Asthma and Long COVID. "

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[2] Bailey, Bailey. Journal of Nuclear Medicine Technology March 2023, 51 (1) 9-15; DOI: https://doi.org/10.2967/jnmt.122.264880

[3] Leblanc et. Al. CANM Guidelines for Ventilation/Perfusion (V/P SPECT) In Pulmonary Embolism. November 2018

[4] Bajc et. Al. EANM guideline for ventilation/perfusion single-photon emission computed tomography (SPECT) for diagnosis of pulmonary embolism and beyond. European Journal of Nuclear Medicine and Molecular Imaging. July 2019. https://doi.org/10.1007/s00259-019-04450-0

"It is also pleasing to be progressing these growth opportunities from a position of strength, underpinned by record FY22 sales revenues, an expanding operational foot-print, robust sales of Technegas and continuing strong growth in Third Party sales."

"Cyclopharm is a well-established, profitable company, with sales across 64 different countries, and a strong pipeline of future growth opportunities."

[ENDS]

This ASX announcement was approved and authorised for release by James McBrayer, Managing Director and CEO

For more information, please refer to our website at www.cyclopharm.com or contact:

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Cyclopharm Limited

Cyclopharm is an ASX Listed radiopharmaceutical company servicing the global medical community. The Company's mission is to provide nuclear medicine and other clinicians with the ability to improve patient care outcomes. Cyclopharm achieves this objective primarily through the provision of its core radiopharmaceutical product, Technegas used in functional lung ventilation imaging.

Technegas

The Technegas technology is a structured ultra-fine dispersion of radioactive labelled carbon, produced by using dried Technetium-99m in a carbon crucible, micro furnaced for a few seconds at around 2,700^{o} C. The resultant gas like substance is inhaled by the patient (lung ventilation) via a breathing apparatus, which then allows multiple views and tomography imaging under a gamma or single photon emission computed tomography (SPECT) camera for evaluating functional ventilation imaging. Historically used in the diagnosis of pulmonary embolism, Technegas, together with advancements in complementary technology to multimodality imaging and analytical software, is being used in other disease states to include COPD, asthma, pulmonary hypertension and certain interventional applications to include lobectomies in lung cancer and lung volume reduction surgery.