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UNITED STATES FDA GRANTS APPROVAL FOR TECHNEGAS®

Highlights

- **USFDA grants approval for the use of Technegas® in the United States**
- **Approval opens an anticipated US$180 million+ addressable Pulmonary Embolism market**
- **Strong pre-existing demand expected to drive sales momentum for an immediate US wide rollout**
- **Approval allows for broad use of Technegas®, supporting wider future indications across other respiratory disease states including Chronic Obstructive Pulmonary Disease (COPD), Asthma, Long COVID and lung cancer**

Cyclopharm Limited (ASX: CYC) announces the company has received United States Food and Drug Administration (USFDA) approval to commence commercial sales of Technegas in the US market. The approval opens for Cyclopharm the single largest market for Technegas globally, and one which the company estimates to be initially worth approximately US$180 million annually for the diagnosis and management of Pulmonary Embolism (PE).

Commercial rollout can commence immediately and Cyclopharm will now complete final assembly of its first wave of 200 generators, with plans for the first air shipments to arrive in the US by early November. Cyclopharm will also execute its planned marketing strategy which will leverage the company's sales and operational expertise across 64 countries globally in which the product is already approved and established. Under the US sales model, based on anticipated high volumes, Cyclopharm will provide and install Technegas generators to nuclear medicine departments to increase adoption and use of the single patient consumables which generate recurring annuity style revenue. Already in place are agreements for third-party distribution, generator service, installation, and administrative support for Technegas in the US.

Cyclopharm notes significant pre-existing demand for Technegas in the US healthcare market. US clinicians and their representative bodies have lobbied heavily for Technegas' approval, and the company has to date received 420 formal expressions of interest in the product.

Technegas is most commonly used in the diagnosis and management of Pulmonary Embolism (PE). Over the past three decades Technegas has been successfully used in 64 countries worldwide, amassing 4.7 million patient studies. In each of these countries, the technology has become accepted

as the preferred nuclear medicine lung ventilation imaging agent, referenced, for example, in the Canadian and European nuclear medicine guidelines[1&2].

The innovative clinical driven approach of combining Technegas with advanced multimodality imaging and analytical software continues to rapidly increase its clinical relevance in all its current markets - and is expected to also leverage the product's appeal in the US.

In its approval letter dated 29 September, 2023 (received 30 September AEST), the USFDA approved the use of Technegas in the diagnosis of Pulmonary Embolism as well as for the wider "Visualization of Pulmonary Ventilation". This broad indication underpins Cyclopharm's *Beyond PE* growth strategy for the use of the technology in other respiratory disease states including COPD, asthma, Long COVID and Pulmonary Hypertension. Backed by a growing body of clinical research around the world, this strategy creates an exponentially larger eventual addressable US market for Technegas.

USFDA Approval

The USFDA approval covers the complete Technegas product, including its manufacture in and distribution from Australia. The USFDA deems Technegas as a drug-device Combination Product[3], an uncommon USFDA evaluation category, collectively covering the Technegas Generator, the single use Technegas Crucible and Patient Administration Set (PAS) as interdependent elements.

Maximising the US opportunity

To rapidly penetrate the US market, Cyclopharm will use its experience from the successful introduction of Techengas into markets globally including its largest country market, Canada. In Canada, the company has displaced the same competitive products currently being used in the US to a level where close to 100% of Canada's nuclear medicine ventilation procedures are imaged using Technegas.

In the US, there are approximately 4 million procedures conducted annually to rule out the presence of PE. Of those procedures, 85% are imaged through Computed Tomography Pulmonary Angiography (commonly known as CT or CTPA). The remaining 15% of the market (or 600,000 procedures) which utilise nuclear medicine rather than CT to diagnose PE, comprises patients with contraindications including those who are pregnant, have renal impairment, allergies to CT contrast media, or radiation concerns.

Cyclopharm is initially targeting the 600,000 nuclear medicine imaging procedures for PE, a market which it estimates to be approximately US$90 million per annum. Based on Cyclopharm's experience in the Canadian market and globally, the company reiterates expectations it can achieve a 50% share of this market over the next 2 to 3 years, rising to in excess of an 80% share over a 3 to 5-year period.

The second stage involves increasing the total US PE diagnostic market which is imaged through nuclear medicine from 15% to 30%. This target, which equates to a total PE market for Technegas of

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

[2] 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

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

US$180 million annually, is based on the company's extensive and successful global track record, the unique properties of Technegas including its ability to enhance 3-D imaging technology and create superior outcomes to CT.

Underpinning these projections is the key fact that US reimbursement codes are based on established nuclear medicine procedures. Technegas can therefore be immediately utilised under existing bundled procedural codes.

As an indication of the larger *Beyond PE* markets in the US which Cyclopharm intends to access, the company estimates the global COPD market to be approximately 30 times the size of the PE market. Clinical studies have supported the potential for the use of Technegas for over 500 million patients suffering with COPD and a similar number with asthma. These markets, the largest being the US, represent significant opportunities to expand sales of Technegas, drive shareholder value over the medium term and ultimately improve patient outcomes.

Approval process

Technegas is designated in the United States as a Combination Product meaning its approval is based on meeting the regulatory frameworks of both a drug and device. With this uncommon US classification, a higher burden of regulatory compliance is required for both the use and the manufacture of Technegas, resulting in a highly complex regulatory pathway for Cyclopharm which has culminated in today's approval.

Importantly, the USFDA's regulatory framework has created a high barrier to entry for potential competitors in the US market. Specifically:

- The way in which the final drug product, the crucible, and the generator should be assessed is novel. Even during the review process the FDA acknowledged the challenge of point-of-care manufacturing of advanced novel drug products in a 2022 discussion paper entitled, "Distributed Manufacturing and Point-of-Care Manufacturing of Drugs"

- The FDA's navigation of its own drug requirements for current Good Manufacturing Practices (cGMPs) in relation to the administered product required adaptability. Although the GMP processes and controls for Technegas Aerosol have been approved in Canada, throughout the European Union (EU), in Australia, and multiple other geographies, the Technegas Aerosol was a novel drug for GMP assessment by the USFDA. In April 2021, the FDA conducted a site inspection of Cyclopharm's manufacturing facilities in Sydney, the findings of which supported the upgrade of our manufacturing rooms to include the implementation of additional process controls and monitoring.

- The requirement for Cyclopharm to conduct extensive product characterization studies to further validate the reproducibility of the product manufacture which included studies which the FDA required to be performed in testing centers in the United States. This comprehensive analysis reinforced the reliability and efficacy of Technegas to an even higher standard than had previously been demonstrated.

Cyclopharm Managing Director James McBrayer said, “USFDA approval for Technegas has been achieved through the persistence and the hard work of our highly skilled global team along with the unwavering support of our Board and shareholders. Importantly, USFDA approval has also established a platform for maximising the clinical use of Technegas across a wide range of respiratory applications going forward”.

“While FDA approval for Technegas is a major milestone for Cyclopharm, our ability to now make this technology available to US clinicians and to the patients they serve, is where the key significance lies. I look forward to providing you with regular updates on the US rollout of Technegas as we proceed with this exciting new phase for the company.”

- ENDS -

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

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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, Long COVID and certain interventional applications to include lobectomies in lung cancer and lung volume reduction surgery.