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1H 2020 BUSINESS UPDATE

Cyclopharm Limited (ASX: CYC) is pleased to provide the following update on its business performance during the first half of financial year 2020, including progress towards gaining United States Food and Drug Administration ("USFDA") approval to begin sales of Technegas® into the US and other operational matters.

Highlights

- **1H 2020 total revenue, ex France, increased 10% on the prior corresponding period (PCP), COVID-19 caused delays to order of consumables – resuming in 2H**
- **European 3rd party distribution strategy delivers new revenue stream**
- **Technegas being used in COVID-19 patients**
- **Technegas® FDA approval process progressing well –product marketing expected in early 2021**
- **New Cyclotek NSW Joint Venture makes profit contribution**
- **CYC continues to progress litigation actions to protect its IP**
- **Beyond PE Strategy advancing with first publication expected and new trial commencing**

Business Update

Following a review of Cyclopharm's unaudited management accounts for the six months' period ending 30 June 2020, the Company anticipates sales revenue for that period will be approximately $5.6 million (vs $6.5 million in 1H 2019). Revenue for the period was impacted by factors relating to the COVID-19 pandemic and a consequential deferral of Patient Administration Set (PAS) consumable orders from predominantly a delay in the scheduled late 2Q France order and generally lower PAS volumes in most markets. The Company anticipates sales orders from France will resume in the second half of this financial year along with rebound in volumes to the rest of the world.

Excluding sales to France, total revenue for the group increased by approximately 10% on the prior corresponding period. New revenue streams from the distribution of third-party products in Europe, contributing approximately $0.6 million in revenue, combined with favourable sales mix to more profitable regions more than offset the impact of lower volumes, ex France.

Because of these factors, the Company anticipates reporting Gross Margin for the period of approximately $4.4 million (vs $5.4 million in 1H 2019).

As at 30 June 2020 cash balances equal $7.9 million. Cyclopharm remains well funded to begin our launch of Technegas® in the US market. The Company's balance sheet remains strong following the completion of a $9.8 million capital raising in December 2019, and ongoing positive cash flows from its core operations. This balance sheet strength also continues to support delivery of Cyclopharm's other strategic priorities, including expanding the use of Technegas® beyond pulmonary embolism (Beyond PE) and product and system enhancements.

Impact of COVID-19

Globally, diagnostic imaging has been impacted as part of broader strategies to contain the spread of COVID-19[A]. Faced with the rapidly emerging crisis, decisions were universally made to prioritise the delivery of healthcare services toward the pandemic. That decision, combined with the initial sparsity of personal protection equipment (PPE) and the implementation of an unprecedented level of infection control procedures, left large number of the hospital wards and departments at a virtual standstill.

With more known about COVID-19 containment, we are starting to see a return to a pre-pandemic standard of care, albeit modified to cater to the potential threat of transmission, in most healthcare sectors. This renewal includes diagnostic imaging broadly and more specifically, in relation to CYC, nuclear medicine.

With each month, more evidence of the utility of Technegas® in understanding COVID-19 emerges. Cyclopharm's expectation is for sales of PAS kits to rebound as COVID-19 restrictions ease. The Company believes that there will be an increase in the use of Technegas® both in ascertaining the extent of pulmonary embolism in infected patients and in managing the long-term implications associated with COVID-19 lung injury.

USFDA Progress

Cyclopharm continues to make progress towards USFDA approval to commence marketing of Technegas® in the United States by early 2021. In the first half of 2020, through its wholly owned subsidiary Cyclomedica Australia, the company lodged a New Drug Application (NDA) submission; received a full application fee waiver; received approval to file an NDA and the USFDA initiated a 10-month NDA review process.

Since receiving the Approval to File status in late May, the Company has been actively responding to questions and requests for additional or clarifying information relating to our NDA from the USFDA.

In the United States, infectious control concerns relating to the risks associated with the provision of nuclear medicine ventilation imaging procedures using competitive products have dramatically impacted the utilisation of this important study in that market. In response to this concern, the company has been made aware that 77 United States Nuclear Medicine Clinicians in late June 2020 co-signed a letter to the USFDA requesting an expedited evaluation of Technegas. [B]

The positive response from US physicians gives the Board of Cyclopharm great confidence to initiate an increase in Technegas® inventory in the 3rd Quarter of 2020, with a target of manufacturing 200 Generators to ensure the company is operationally ready for rapid market entry upon USFDA approval.

The market prior to the COVID-19 pandemic for nuclear medicine ventilation imaging in the USA is estimated to be approximately US$90 million annually, representing approximately 600,000 individual procedures. Based on Cyclopharm's experience in the Canadian market, it remains confident that Technegas® can achieve a 50% share of the USA market over 2 to 3 years, post US market entry, with an 80% share representing around 480,000 procedures per annum achievable over a 5 to 7-year period.

[A] COVID-19 is diagnosed either by using a Nucleic Acid Amplification Test (NAAT) or serological tests. Diagnostic imaging is not considered to be first choice to diagnose the presence of COVID-19.

[B] Cyclopharm confirms that none of the signatories have any professional or financial relationship with the Company or any of its affiliates.

Cyclotek NSW Business Venture Collaboration

Further to the Company's ASX announcement of 19 December 2019, Cyclopharm confirms during the first half of 2020 Cyclotek NSW PTY ltd made a small positive contribution to the company's profitability. Cyclotek NSW PTY ltd is a collaboration between Cyclopharm, Cyclotek (Aust) Pty Ltd and the Australian Nuclear Science and Technical Organisation ('ANSTO') set up, in part, to realise the inherent value of Cyclopharm's legacy Cyclotron assets both to generate profits and contribute to enhanced health outcomes for the Australian community.

Under the terms of the joint venture Cyclopharm is to contribute $40,000 per annum, over a period of 9 years, to fund the ongoing research activities of Cyclotek NSW and gains an entitlement to receive a 15% share of any profits of the business venture collaboration.

European Third-party Distribution Update

Cyclopharm's strategy to leverage our core global regulatory strengths and well-developed expertise in nuclear medicine by seeing out complementary technology is beginning to gain traction. Revenue from third-party distribution agreements with TEMA and ROTOP totalled approximately $0.6 million during the first half of 2020. We expect second half 2020 revenues from third-party products will exceed first half revenues as we continue to grow this new revenue stream.

Litigation Update

Cyclopharm continues to defend its valuable Intellectual Property vigorously and successfully. In 2019, the company successfully brought an initial civil case against its former employee in the German market, Mr Bjorn Altmann and Almedis Altmann GmbH ("Almedis"), resulting in Cyclopharm's subsidiary Cyclomedica, being awarded and receiving a payment of approximately A$339,000, which represents 100% of this claim. A bad debt provision of A$540k was raised in 2017 to cover this and other claims. The company is continuing with its efforts to recover the remainder of this bad debt provision.

Further actions have been subsequently launched in both German and Australian courts with favourable progress being made. Last month the company successfully attained an injunction against a company related to Altmann pertaining to misleading conduct relating to servicing aspects on TechnegasPlus Generators in Germany.

The company expect decisions to be handed down in two additional actions in Germany in the coming weeks. Whilst it is difficult to predict a timeframe for these separate Australian proceedings to be concluded, we are confident that we will achieve a successful outcome from these actions.

BEYOND PE – New Growth Opportunities

The company's Beyond PE initiatives are linked to significant Research and Development activities, which are being impacted by COVID-19 as the rate of patient recruitment for trials slowed during the first half of 2020 and in some cases has been put on hold.

Study	Indication	Status	Reference(s)
CYC-009	Ventilation comparison of Technegas vs Xe133	On- hold 204 of 240 patients completed	https://clinicaltrials.gov/ct2/show/NCT03054870
HMRI	Asthma/COPD	Fully Recruited 100 patients First publication pending	https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=373490 https://hmri.org.au/news-article/nuclear-imaging-clear-airway-diagnosis
McMasters University	Lung Resection Surgery	On-hold 12 of 115 Patients Recruited	https://clinicaltrials.gov/ct2/show/NCT04191174
CHUM	COPD	On-hold 5 of 30 Patients Recruited	https://clinicaltrials.gov/ct2/show/NCT03728712
Woolcock Institute	Asthma/COPD	1st Patient Imaged 23/06/2020 1 of 100 Patients Recruited	http://investor.cyclopharm.com/site/PDF/1561_0/BetterDefiningAirwaysDiseasewithTechnegas
Dalhousie University	Lung Transplant complications	On-hold 9 of 30 Patients Recruited	https://canm-acmn.wildapricot.org/resources/Documents/Documents%20-%20Web%20pages/Édition%20spéciale%202019.pdf

The implication in advancing these initiatives could expand the use of Technegas® by improving the diagnosis and management of patients with COPD and other small airways diseases. Cyclopharm estimates the global COPD market is 30 times the size of the PE market and over 500 million patients suffering with COPD and Asthma could benefit from the use of Technegas® in diagnosis and ongoing patient monitoring/management. These markets represent significant opportunities to expand sales of Technegas® and drive shareholder value over the medium term.

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° 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.

Appendix
Additional information on Technegas'® evolving role in combatting COVID-19

Despite the general slowdown for diagnostic imaging services, clinicians are using imaging to assist in assessing the severity or related complications associated with COVID-19 or rule out other disease states that present with similar symptoms. The decision to use imaging is dependent on diagnostic algorithms to include the severity of the symptoms.

One of the life-threatening complications seen in COVID-19 is the presence of pulmonary embolism. Despite the overall decrease in Technegas consumables, we are seeing evidence that Technegas is playing a part in combating COVID-19. Technegas is the recognised ventilation imaging agent of choice in diagnosing pulmonary embolism. Further to its clinical advantages, Technegas'® unique technical properties in production, administration and risk mitigation has seen our innovative product referenced by name in COVID-19 practice guidelines in France, Belgium, Britain and Canada.

In addition to the inflammatory issues arising in COVID-19 patients, according to an article published by the American Heart Association, early estimates show that 20% of ICU patients are presenting PE.[1] These preliminary reports were confirmed by others investigators; *Klok et al* reported a 31% incidence of thrombotic events in critically ill patients admitted to the ICU despite the use of at least prophylactic anticoagulation.[2]

In the past few weeks, an emerging trend in VTE linked to COVID-19 in young adults has been observed. Indeed, Mount Sinai Hospital experts have recorded a handful of cases in which young coronavirus patients have VTE issues.[3] Other investigators published a few cases of acute PE in young patients associated with COVID-19 infection, even in the absence of other underlying risk factors.[4]

Nuclear Medicine Associations from countries in Europe have also provided guidance on V/Q imaging in the context of COVID-19. In France, the fifth highest COVID-19 mortality rate per capita seen globally[5], the French Society of Nuclear Medicine (SFMN) have provided guidelines stating that a "CT scan as an alternative to ventilation scans is not recommended. Both scans, ventilation and perfusion, should be performed. Current COVID-19 precautionary measures should be taken and adapted to the clinical setting and local organizational constraints".[6] Furthermore, the French guidelines go on to state specifically that "*Technegas™ and Krypton 81m have been used worldwide for several decades. No events of viral cross-contamination or other illness associated with the inhalation system have been reported to date. The risk of cross-contamination of COVID-19 associated with the use of the inhalation system therefore appears to be extremely low".*

In Belgium the highest COVID-19 mortality per capita seen globally[13] the Belgian Nuclear Medicine Society (BELNUC) reflects the position of the SFMN also citing Technegas in its recommendation by stating that "*Both ventilation and perfusion studies should be performed to rule out pulmonary embolism as substituting ventilation scintigraphy by CT as part of a stand-alone perfusion SPECT/CT is not ideal, as this reduces the specificity of the study".*[7] *In another publication by BELNUC '*Recommendations For the Organization of Care in Nuclear Medicine', BELNUC cite that "*examinations with impact on patient management or risk of loss of treatment opportunities, including pulmonary scan, should be performed*".[8]

An 15 April 2020 publication in the European Journal of Nuclear Medicine by Dr Geoff Currie[9] comments on the impact of COVID-19 on Nuclear Medicine from an Australian perspective by stating "*There are concerns that the ventilation scan requires staff to spend more time close to the patient during a ventilation scan that is known to be a high risk of area contamination from patients breaking the apparatus seal or coughing. Furthermore, aerosol units are difficult to decontaminate. Departments performing SPECT/CT (common in Australia) may forgo the ventilation scan in favour of using the CT scan to represent airways and potential mismatch for pulmonary embolism diagnosis. Technegas is in widespread use in Australia and offers a number of clear advantages in the COVID-19 patient. The ventilation procedure is faster, reducing time and improving compliance which in turn decreases the risk of room and staff contamination. The apparatus is single use*

without recirculation and so poses no risk between patients. In either case, subject to PPE availability, staff should wear a N95 mask, gown and gloves with all equipment being sanitised afterward".

In the April 2020 edition of the European Journal of Nuclear Medicine the "Image of the Month" features Technegas SPECT CT images with the authors citing "*present observation suggests that signs of a tracheobronchitis may be detected by lung scintigraphy* (using Technegas®) *in the course of COVID-19 infection. Although the mechanism is presumably not specific to the SARS-CoV2 virus, such signs might have diagnostic and therapeutic applications, especially in the absence of any previous history of pulmonary disease*".[10]

As an initiative from the United States Society of Nuclear Medicine and Molecular Imaging (SNMMI) COVID-19 Industry Partners Satellite Symposium series, the authors of the above paper from the Hospital Center University of Nancy presented on 28 May 2020 a webinar entitled "How Nuclear Medicine may help in (or serve for) the diagnostic and monitoring of COVID-19 patients"[11]. The speakers commented that vascular and endothelial dysfunctions observed in severe COVID-19 patients may be explained by the involvement of the receptor of the angiotensin-2 converting enzyme (ACE) that lead to thrombosis and to capillary leakage.[12] The invited speakers described that V/Q SPECT with Technegas could be particularly indicated in COVID-19 patients as PE is a common complication of the disease. The authors have showed that V/Q defects observed in COVID-19 patients closely matched to a focal ground-glass opacity on CT which is typical of COVID-19. They reveal also that foci of high uptake of Technegas on ventilation scans are present in 30% of dyspneic COVID-19 patients referred to V/Q imaging and could have a diagnostic value, especially in the absence of any history of pulmonary disease. The authors confirmed also that V/Q imaging can be performed in COVID-19 patients in safe conditions for patients and staff. The main potential benefit for COVID-19 patients seems to be provided by V/Q SPECT/CT, with Technegas as ventilation agent, to identify causes of onset or aggravation of dyspnea in the inflammatory phase as it allows for identification of PE, tracheobronchitis and parenchymal lesions.

In the June 2020 edition of the European Journal of Nuclear Medicine Cobes[13] et al state that "*V/Q SPECT/CT (using Technegas in 3 out of the 5 patients evaluated) not only is a tool allowing the diagnosis of pulmonary embolism in a single modality, but it can also, with the associated CT scanner, assess the degree of pulmonary involvement of COVID-19 while avoiding the risk of renal failure linked to the injection of iodinated contrast medium particularly to patients at risk*". The authors then go on to comment on the safety of the ventilation procedure by commenting *"….. to date, no case of cross contamination has been described with the use of Krypton and Technegas®. The French Society of Nuclear Medicine (SFMN) recommends maintaining V/Q scan with the ventilation to search for PE. According to its recommendations, the risk of contamination is extremely low. "*

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