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All references to dollars unless otherwise specified are to Australian dollars.
COMPANY OVERVIEW

Cyclopharm Limited (CYC) is a leading diagnostic lung imaging company

1. Lead nuclear medicine product Technegas® is currently available in 60 countries with significant opportunity to expand into the USA with sales targeted for 2021 following completion of USFDA New Drug Application review

2. A world leader in functional lung ventilation imaging technology

3. Recurring consumables and capital equipment revenue streams

4. A profitable and growing company with a history of dividend payments

5. Opportunity to broaden Technegas® applications Beyond pulmonary embolism diagnosis into large addressable markets such as COPD and Asthma
CYC has clear strategy to leverage our position as a leading player in the global nuclear medicine imaging market and lung health space to expand the use of our proprietary products and introduce new innovative technology. We will do this by:

1. Attaining approval to distribute Technegas® in the USA

2. Expanding the use of Technegas® beyond the traditional diagnosis of Pulmonary Embolism into significantly larger applications such as COPD¹ and Asthma, Lung Cancer and Pulmonary Hypertension for both diagnosis and patient management.

3. Identifying, developing and commercialising complementary innovative technology such as Ultralute™

4. Leveraging our core global regulatory strengths, fiscal discipline, strong balance sheet and well developed expertise in nuclear medicine and pulmonary healthcare to seek out complementary technologies and businesses

¹ COPD=Chronic Obstructive Pulmonary Disease
Profitable and Growing MedTech
Underlying business is cash positive and issuing dividends

First in Class
Proprietary product sales to 60 countries with over 4.2 million studies to date

Recurring Revenue
From consumables similar to an annuity model

USFDA Approval
Set to quadruple the size of the existing PE business and further leverage penetration into the CTPA market

Optionality
Into indications beyond PE into chronic respiratory disease management could deliver exponential growth
Cyclopharm Update - 23 September 2020

Clinical Trial CYC-009
- Independent Data Efficacy Monitoring Committee (DEMC) determine Primary and Secondary Endpoints have been met
- Clinical trial to be terminated based on success

FDA – NDA Review
- Midcycle review completed by FDA
- Iterative Q&A process continues
- Guidance maintained - Early Q2 2021 target date for USFDA approval for Technegas

Beyond PE Initiatives
- COVID-19 Clinical Trial recruitment commences at McMaster University
- Woolcock Institute COPD trial recruitment recommences
- Other Beyond PE clinical trials are slow to resume recruitment due to the pandemic

USA Commercialisation
- USA Technegas Generator build underway
- Discussions commence with potential USA 3PL Providers and Service Partners

2020 H2 Trading Update & Guidance
- 2020 Revenues trending to exceed FY2019 result of $14.08m
- Signs that Technegas consumables sales are returning to pre-COVID-19 levels
- 400 Box Patient Administration Set order received from France with another 200-box order expected by the end of FY2020
- 140 Box Patient Administration Set order received from China
- Higher than projected Technegas Generator orders (7 in total) from Canada as a result of Technegas’ superior infection control safety profile in comparison with competitive nuclear medicine ventilation imaging products
- Successful tenders for third party products trending to exceed H1 2020 revenues of $700k in H2 2020

Expanding Direct Market Access
- CYC office opened in Brussels, Belgium & Bristol England

Litigation Update
- Civil proceedings progressing in both Australia and Germany against former CYC employees & related parties
- Directors maintain confidence in both jurisdictions of a positive outcome for CYC’s

Systems Improvement
- Global financial accounting system implemented
- Electronic Quality Management System installation project initiated
Patient inhales extremely small carbon particles labeled with 99mTechnetium\(^1\)

The small size and hydrophobic properties demonstrate gas-like behavior and alveoli deposition into the lungs\(^2\,^3\)

Clinicians can visualise functional ventilation using Technegas\(^\circledR\)
PULMONARY EMBOLISM

~3 million cases of PE p.a. but could be much higher

Symptoms are varied with diagnosis confirmed either through CTPA or a nuclear medicine ventilation-perfusion study

30% of pulmonary embolisms are fatal if left untreated

Nuclear Medicine using 3-D imaging is the most accurate method of diagnosis
Building for Growth - Company Development

Technegas® is a substantially de-risked commercial proposition with significant upside in the USA market

- Total global sales of $118 m from 2010
- Technegas® currently available in 60 countries
- Over 4,200,000 patient procedures performed since first approved
- 1,600 Technegas® generators sold globally since first approved
- Approximately 182,100 patient procedures in 2019
- Europe represents 62% of global revenue in 2019
- Canada was the largest single country market by volume (45,400 patients) followed closely by France (42,500 patients) in 2019
- CYC is growing, the underlying business is profitable and the company has a history of paying dividends
- Stable gross margins of greater than 80% - (82% in 2019)
- Around 80% of historical revenue is recurring consumable sales - (75% in 2019)
TECHNEGAS® AROUND THE WORLD

Technegas® was introduced to the medical community in 1986.  

Technegas® revenues are generated in 60 countries via a combination of direct and distributor sales models. 

Over 4.2 million patient procedures to date.
COMING TO AMERICA
15% / 600k

$90m USD
IMMEDIATE MARKET OPPORTUNITY

Nuclear Medicine ■ CTPA

85% / 3.4M

600K Nuclear Medicine Ventilation Procedures p.a.

- 4,000,000 patient procedures conducted in the USA per annum to diagnose pulmonary embolism (15% Nuclear Medicine – 85% CTPA)
- 600,000 Nuclear Medicine Ventilation procedures equals $90m USD
- Target market for Technegas® in the USA equates to ~480,000 patient procedures of the total 600,000 procedures.
- The USA represents the single largest market for Technegas® with half of the world’s nuclear medicine departments
- Subject to a successful FDA approval, the Company is targeting US commercialisation in 2021
- First priority following USFDA approval is to repeat our Canadian experience by first displacing Xe133 followed by DTPA as the standard of care diagnostic product
- 3D SPECT imaging using Technegas® is proven to be clinically superior and safer than CTPA. Once commercialised Cyclopharm will target to double the existing nuclear medicine PE market dominated by CTPA from 15% to 30%.
- Once established in the USA market, the company will seek to expand the use of Technegas® into disease states exponentially larger than the existing markets Beyond PE
BENEFITS OF USING TECHNEGAS®

- Easy to prepare and administer
- Only need 3 to 4 breaths
- 3D images provide functional imaging through to the alveolus
- NO contraindications
- Cost effective
## Superior to Competitive Nuclear Medicine Products

**Technegas®**

- **Easy**
- **3 to 4 breaths**
- **3D images**
- **No contraindications**
- **Cost-effective**

### Xenon - 133
- True radioactive gas inhaled with **full face mask**
- Constant inhale-exhale breathing for 15 mins
- No 3D images limited to planar imaging resulting in inferior clinical outcomes
- Requires special rooms to contain radioactive gas in the event of a release

### DTPA Tc99m
- Wet Aerosol impacts efficacy and clinician interpretations
- Creates hotspots in presence of small airways lung diseases, which is a frequent comorbidity in PE
**SUPERIOR TO COMPETITIVE IMAGING MODALITIES**

Technegas®

- Easy
- 3D images
- No contraindications
- Cost-effective

CTPA

**High radiation burden**
CTPA delivers at least 27 times more radiation to the breast as compared to V/Q SPECT¹

**Contraindications**
CTPA should not be performed with pregnancy¹-², renal impairment³, contrast media allergy³, diabetes⁴

**Acute kidney injury (AKI)**
AKI occurs in up to 13% of CTPA cases⁵

**Lower clinical sensitivity**
V/Q planar⁶ = 76%
CTPA⁷ = 82%
V/Q SPECT⁷ = 93%

**Availability**
Radiology ED services are generally provided 24/7 vs. nuclear medicine after hours on call service

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The Canadian Case Study

Canada is Cyclopharm’s largest single country market

1. Market leader for diagnosing PE
2. 14 consecutive years of PAS growth
3. Represents a strong indicator of USA acceptance
4. Xe-133 rapidly displaced by early adopters
5. Direct correlation with the number of active generators and annual consumable sales
6. Market driven by public healthcare sector
7. Market launch initiated province by province, leveraging off pilot sites

The Generator and Consumable Relationship
Technegas® Growth - Canada

- Patients per Annum (thousands)
- Active Generators

Graph showing the growth of Technegas® in Canada from 2004 to 2019.
USA 2021 COMMERCIALISATION PLAN*

**USFDA Regulatory Approval**
Submission of 505(b)2 NDA March 2020
Approval to file May 2020

**Secure Customer Commitments**
Securing commitments in line with Technegas® Generator lead time

**Build Inventory**
Materials Resource Planning underway with production targeting 200 Techengas generators roll-out per annum

**Service and Distribution**
Secure service capabilities and stock 3PL Partners for USA launch

**People**
Hire Key USA Personnel to include Sales and Service

*USA Operational costs estimated to be $5m USD p.a.
BEYOND PE: Clinical Initiatives

Clinical Trials Sponsored by Cyclomedica

- Hunter Medical Research Institute (Newcastle, AU): Diagnosis and response to therapy in severe asthma and COPD¹
- Woolcock Institute (Sydney, AU): Diagnosis and response therapy in mild to moderate COPD³
- CHUM (Montreal, CA): Early detection of COPD in asymptomatic smokers⁴
- Dalhousie (Halifax, CA): Post-lung transplant patients
- McMaster University Firestone Institute (Hamilton, CA): Prevalence and clinical relevance of ventilation heterogeneity and luminal cellular inflammation in lung cancer patients pre and post lung resection ²
- McMaster University Firestone Institute (Hamilton, CA): COVID-19 Related Lung Ventilation and Perfusion Injury⁵

Other Non-Sponsored Clinical Initiatives

- Macquarie University (Sydney, AU): ELVR with endobronchial valves in severe COPD patients
- Macquarie University (Sydney, AU): Bronchial Thermoplasty procedure in asthma patients

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¹ ACTRN12617001275318 - Can functional lung ventilation imaging identify treatable traits in obstructive airway disease?
³ http://investor.cyclopharm.com/site/PDF/1561_0/BetterDefiningAirwaysDiseasewithTechnegas
⁴ https://ichgcp.net/clinical-trials-registry/NCT03728712
⁵ https://clinicaltrials.gov/ct2/show/NCT04549636
**Primary Endpoint:**
To investigate and characterize the extent of COVID-19 infection related ventilation and perfusion injury at \( \leq 4 \)-weeks and 6-months post infection recovery in asthmatic and healthy populations.

**Secondary Endpoints:**
To investigate if COVID-19 infection related ventilation and perfusion injury \( \leq 4 \)-weeks and 6-months post infection recovery is related to inflammatory markers, symptoms (quality of life, dyspnea, exercise limitation) and clinical measurements (airflow in asthmatic and healthy populations)

To investigate if COVID-19 infection related ventilation and perfusion injury \( \leq 4 \)-weeks post infection recovery is predictive of symptoms and clinical outcomes 6-months post infection recovery in asthmatic and healthy populations

**Exploratory Objective:**
To determine if COVID-19 infection related ventilation and perfusion injury \( \leq 4 \)-weeks and 6-months post SARS-CoV2 infection recovery is less pronounced in asthmatic compared to healthy populations and if this difference can explained by protective mechanisms due to skewing of immune response (Th2/Th1 in asthma) and/or dampening of Th1 cytokine storm due to maintenance corticosteroid therapies.

100-patient clinical trial designed to use ventilation perfusion SPECT-CT with Technegas*:

**Primary Endpoint:**
To investigate and characterize the extent of COVID-19 infection related ventilation and perfusion injury at \( \leq 4 \)-weeks and 6-months post infection recovery in asthmatic and healthy populations.

**Secondary Endpoints:**
To investigate if COVID-19 infection related ventilation and perfusion injury \( \leq 4 \)-weeks and 6-months post infection recovery is related to inflammatory markers, symptoms (quality of life, dyspnea, exercise limitation) and clinical measurements (airflow in asthmatic and healthy populations)

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*https://clinicaltrials.gov/ct2/show/NCT04549636
THREE VALUE HORIZONS

**Horizon 1**
0 to 5 Years
- Establish USA
- 80% Conversion of Nuc Med Procedures for PE

**Horizon 2**
3 to 8 Years
- Convert CTPA
- Double existing Nuc Med Procedures for PE

**Horizon 3**
> 8 Years
- Innovate Beyond PE
- HALF BILLION combined sufferers of Asthma and Chronic Obstructive Pulmonary Disease globally
- Trials Underway!

- $72m USD*
- $90m USD*
- $900m USD*

*USA Revenue Estimates
USA Market nuclear medicine ventilation imaging market to diagnose PE equal to $90m USD with reimbursement already in place

Targeting USA CTPA PE Market opportunity to convert CTPA to nuclear medicine imaging by shifting market to SPECT imaging

Half billion combined sufferers of Asthma and Chronic Obstructive Pulmonary Disease globally. Trials underway
THANK YOU
# FY2019 Results Highlights

<table>
<thead>
<tr>
<th>Category</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group Sales Revenue</strong></td>
<td>$14.08 million - an increase of 5%</td>
</tr>
<tr>
<td><strong>Gross Margin</strong></td>
<td>$11.62 million – an increase of 7%</td>
</tr>
<tr>
<td><strong>Gross Margin %</strong></td>
<td>82.5%</td>
</tr>
<tr>
<td><strong>Net Loss After Tax</strong></td>
<td>($2.91) million including USFDA investment</td>
</tr>
<tr>
<td><strong>Dividends</strong></td>
<td>1.0 cents per share</td>
</tr>
<tr>
<td><strong>Underlying Technegas® PBT¹</strong></td>
<td>$0.89 million</td>
</tr>
<tr>
<td><strong>FDA Trial expenses</strong></td>
<td>($3.84) million</td>
</tr>
<tr>
<td><strong>Strong balance sheet</strong></td>
<td>$12.66 million of cash reserves as @ 31 December 2019</td>
</tr>
<tr>
<td><strong>Guidance</strong></td>
<td>The Board expects continuing modest growth in underlying Technegas® revenues from existing markets for FY2020</td>
</tr>
</tbody>
</table>

¹ PBT=Profit Before Tax
## FY2019 Operational Highlights

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technegas®</td>
<td>Application in determining ventilation pre and post lung reduction intervention</td>
</tr>
<tr>
<td>USFDA</td>
<td>All internal documentation completed with a Q1 2020 USFDA submission</td>
</tr>
<tr>
<td>USA Commercialisation</td>
<td>USA entity established</td>
</tr>
<tr>
<td>Indication Expansion</td>
<td>HMRI completes recruitment – New initiatives commence in Canada and Australia</td>
</tr>
<tr>
<td>R&amp;D Tax Incentive</td>
<td>$2.93 received November 2019</td>
</tr>
<tr>
<td>Strategic Partnerships</td>
<td>Leveraging our infrastructure through Distribution partnerships – Draximage, Tema and Rotop</td>
</tr>
<tr>
<td>Building a Team for the Future</td>
<td>Key resources in place for growth – Sales, Quality, Regulatory and Service</td>
</tr>
<tr>
<td>Guideline Development</td>
<td>CANM and European Guidelines naming TG as the nuclear med ventilation imaging agent of choice for diagnosing PE</td>
</tr>
<tr>
<td>Capital Raising</td>
<td>$9.2m net of costs received in December following a strategic share placement</td>
</tr>
</tbody>
</table>

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**Investor Update**

26
During the year, CYC continued to implement its strategic priorities, which are to:

1. Accelerate the path to regulatory approval to sell Technegas® into the world’s largest and new highly prospective USA market;

2. Pursue sales of Technegas® in new applications: Chronic Obstructive Pulmonary Disease (“COPD”) and Asthma which are significantly larger markets than the Pulmonary Embolism market where CYC traditionally operates;

3. Identifying, developing and commercialising complementary innovative technology such as Ultralute™; and

4. Leveraging our core global regulatory strengths, fiscal discipline, strong balance sheet and well-developed expertise in nuclear medicine and pulmonary healthcare to seek out complementary technologies and businesses.
## Group Balance Sheet

Financial Foundation to Leverage Growth Strategy

<table>
<thead>
<tr>
<th>Financial Statement</th>
<th>2019</th>
<th>2018</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cash</strong></td>
<td>12,660</td>
<td>5,855</td>
<td>8,690</td>
</tr>
<tr>
<td><strong>Other current assets</strong></td>
<td>6,950</td>
<td>9,600</td>
<td>8,139</td>
</tr>
<tr>
<td><strong>Non-current Assets</strong></td>
<td>12,918</td>
<td>8,082</td>
<td>6,548</td>
</tr>
<tr>
<td><strong>Total Assets</strong></td>
<td>32,528</td>
<td>23,537</td>
<td>23,377</td>
</tr>
<tr>
<td><strong>Current Liabilities</strong></td>
<td>3,480</td>
<td>5,219</td>
<td>5,212</td>
</tr>
<tr>
<td><strong>Non-current Liabilities</strong></td>
<td>5,844</td>
<td>1,302</td>
<td>916</td>
</tr>
<tr>
<td><strong>Total Liabilities</strong></td>
<td>9,324</td>
<td>6,521</td>
<td>6,128</td>
</tr>
<tr>
<td><strong>Net Assets</strong></td>
<td>23,204</td>
<td>17,016</td>
<td>17,249</td>
</tr>
</tbody>
</table>

1. **Low debt and cash on hand** – provides balance sheet and funding flexibility.
2. **Funding used toward USFDA clinical trial enrolment and New Drug Application submission**
3. **Strong financial position supports ongoing investment in R&D and expansion into new markets and indications**
## Group Cash Position

### Cash Position Funding Growth

<table>
<thead>
<tr>
<th>Year ended 31 December ($000’s)</th>
<th>2019</th>
<th>2018</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operating Activities</td>
<td>(489)</td>
<td>(1,107)</td>
<td>(682)</td>
</tr>
<tr>
<td>Investing Activities</td>
<td>(821)</td>
<td>(1,403)</td>
<td>(1,136)</td>
</tr>
<tr>
<td>Financing Activities</td>
<td>8,091</td>
<td>(353)</td>
<td>5,828</td>
</tr>
<tr>
<td>Net Increase / (Decrease) in Cash</td>
<td>6,781</td>
<td>(2,863)</td>
<td>4,010</td>
</tr>
<tr>
<td>Opening Cash</td>
<td>5,885</td>
<td>8,690</td>
<td>4,591</td>
</tr>
<tr>
<td>Foreign Exchange</td>
<td>24</td>
<td>28</td>
<td>89</td>
</tr>
<tr>
<td><strong>Closing Cash @ 31 December ($000’s)</strong></td>
<td><strong>12,660</strong></td>
<td><strong>5,855</strong></td>
<td><strong>8,690</strong></td>
</tr>
</tbody>
</table>

1. Institutional share placement of 8.5 million shares in December 2018 resulting in $9.78m at an 11.7% premium

2. Benefited from expanded R&D tax Incentive Program resulting in Other Income of $2.93 million

---

*Institutional share placement of 8.5 million shares in December 2018 resulting in $9.78m at an 11.7% premium

Benefited from expanded R&D tax Incentive Program resulting in Other Income of $2.93 million*
Product Profile
Product Overview

Cyclopharm’s leading product is the Technegas technology system

- The Technegas® proprietary technology provides high quality diagnostic functional lung imaging.

- Predominantly used to diagnose the presence of blood clots in the lung otherwise known as Pulmonary Embolisms (PE). With advances in complementary technology, the potential for use in other indications is rapidly evolving.

- In a clinical setting, the patient inhales, in only a few breaths, an ultrafine dispersion of Technegas® particles. Once inhaled and deposited in the lungs, Technegas® images are then captured by using conventional nuclear medicine scanning equipment.

- The Technegas® images provide the clinician an understanding of how well the patient’s lungs are functioning across a range of disease states.

- CYC sells the Technegas® Generator to hospitals as a one-off capital item. Consumable components are inserted into the Technegas® Generator which then produce the gas like particles that are inhaled by the patient. The consumables which deliver Technegas® are single patient use items.
WHAT IS TECHNegas?

PARTICLE CHARACTERISTICS

Technegas® is composed of Tc-99m cores encapsulated within layers of graphite to form individual hexagonal plate-like particles. These particles agglomerate to reach a dynamic equilibrium with regard to particle size distribution best described as a bell-shaped curve with an average size of 100nm.

MANUFACTURE AND DISTRIBUTION

Technegas® is produced on site at the point of patient administration. Technegas® is manufactured by heating Technetium-99m in a carbon crucible within an argon environment for a few seconds at 2,750 degrees Celsius. Because of the very small particle size, Technegas® is distributed in the lungs almost like a gas and deposited in alveoli by diffusion, providing for SPECT ventilation imaging. Particles remain in the lung until they are cleared by ciliary action or phagocytosis.

Technegas® provides a safer clinically superior outcomes to its competitors

- Technegas product characteristics, Delivery System and extremely short administration time combined significantly reducing risk of viral contamination in comparison to competitive products
- Better clinical results at a fraction of the high radiation doses used in CTPA (angiograms)
- No contraindications
- More accurate and sensitive measurement in diagnosing pulmonary embolism
- Particularly effective when CTPA is contraindicated e.g. renal impairment
- Improved patient comfort and tolerance with only 3-4 breaths required for delivery
- Allows for 3D images and regional quantification
- Named as the preferred ventilation imaging agent of choice in the European Association of Nuclear Medicine Guidelines

IP/Generic protection

- Technegas® is a system - needs the generator, patient administrator set (PAS) and service capability
- R&D on 3rd generator generation underway set to extend IP protection

Competitive Nuclear Medicine Products

<table>
<thead>
<tr>
<th>Product</th>
<th>Comparison to Technegas®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xenon 133</td>
<td>Patient has to continually re-breathe gas causing patient discomfort / anxiety</td>
</tr>
<tr>
<td>DTPA</td>
<td>Can’t provide 3D images</td>
</tr>
<tr>
<td></td>
<td>Costly air-handling infrastructure required in order to administer</td>
</tr>
<tr>
<td></td>
<td>Inferior images in patients with obstructive lung disease (COPD)</td>
</tr>
</tbody>
</table>
EXISTING MARKETING DEVELOPMENT STRATEGY

- Sales and marketing program targeting referring respiratory physicians
- Implemented educational programs for Distributors
- Updating Technegas® distribution contracts to include detailing to respiratory physicians
- Leveraging New Complementary Technologies
- Strengthening relationships with KOL’s and industry bodies
- Guideline Development
- Product Renewal & Enhancements
- Sponsoring pilot clinical trials targeting expanded indications
- Introduction of new products by leveraging off of existing network - Ultralute™
WHAT THE GUIDELINES SAY ABOUT TECHNEGAS®:

Endorsed by the guidelines from the European1-2 and the Canadian3 Associations of Nuclear Medicine (EANM & CANM)


“Using 99m-Tc-Technegas is according to clinical experience better than the best aerosols”
“Technegas® facilitates interpretation, particularly in COPD”
“For ventilation, 99m-Tc Technegas® is the best-aerosol particularly in patients with COPD”
“Liquid aerosols are inferior for SPECT and should not be used unless Technegas® is not available”
“The best widely available agent for ventilation is 99m-Tc-Technegas”
“Because of the very small particle size, this agent is distributed in the lungs almost like a gas and deposited in alveoli by diffusion, where they remain stable, thus providing the best possible images for ventilation SPECT”
“Another advantage is that only a few breaths are sufficient to achieve an adequate amount of activity in the lungs, reducing time and personnel exposure to radiation”
“Technegas® is considered the agent of choice in the COPD population as there is less central airway deposition, better peripheral penetration, and it does not wash out as quickly as traditional aerosols”
In recent literature


66% of references citing Technegas® in the past 24 months are for indications Beyond PE
PULMONARY IMAGING WITH

- Improvements in 3D imaging techniques, hybrid imaging and the advent of analytical software have dramatically improved the sensitivity and specificity in functional lung imaging with Technegas®.
- Traditionally used in the diagnosis of Pulmonary Embolism, nuclear medicine functional lung ventilation imaging utilising improved imaging techniques are expanding the potential clinical utility for Technegas®.
- The following Technegas® images underscore the advancement in complementary technology Cyclopharm is leveraging today:

1980s
Planar Imaging

2000
SPECT Imaging

2010
SPECT with Low Dose CT

2015
SPECT with Low Dose CT & Lobular Quantification
NUCLEAR MEDICINE IMAGING TECHNOLOGY HAS EVOLVED BEYOND CTPA IN DIAGNOSING PE

**Planar**
- Inherent limitations of 2-dimensional imaging
- Overlap of anatomical segments
- Shine-through from underlying lung segments
- Difficulty visualizing all the lung segments
- PIOPED II recently updated to AUC Trinary interpretation of V/Q findings

**SPECT**
- Three-dimensional imaging
- Superior contrast resolution
- Improved anatomical detail
- Higher sensitivity and specificity
- Accurate definition of size and location of the perfusion defects

**SPECT/CT**
- Integration of anatomic information
- Decrease the incidence of false positive PE
- Added benefit to identify various other pulmonary conditions
- Further application in other pulmonary conditions and research

**Radiation Dosimetry**

A nuclear medicine V/Q scan is exponentially lower in dose than CTPA

<table>
<thead>
<tr>
<th>Technique</th>
<th>Effective dose (mSv/MBq)</th>
<th>Effective dose (mSv)</th>
<th>Breast absorbed dose (mGy)</th>
<th>Lung absorbed dose (mGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventilation Tc-Technegas (20MBq)</td>
<td>0.015</td>
<td>0.30</td>
<td>0.13</td>
<td>2.2</td>
</tr>
<tr>
<td>Ventilation $^{99m}$Tc-DTPA (20MBq)</td>
<td>0.007</td>
<td>0.14</td>
<td>0.04</td>
<td>0.30</td>
</tr>
<tr>
<td>Ventilation $^{133}$Xe (800MBq)</td>
<td>0.0014</td>
<td>1.12</td>
<td>0.09</td>
<td>0.89</td>
</tr>
<tr>
<td>Perfusion MAA (120MBq)</td>
<td>0.012</td>
<td>1.44</td>
<td>0.60</td>
<td>7.92</td>
</tr>
<tr>
<td>Low dose CT non-contrast</td>
<td>NA</td>
<td>~ 1.00</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>CTPA 16 slice</td>
<td>NA</td>
<td>14.4</td>
<td>10-20</td>
<td>10</td>
</tr>
<tr>
<td>CTPA 64 slice</td>
<td>NA</td>
<td>19.9</td>
<td>22</td>
<td>20</td>
</tr>
</tbody>
</table>

NUCLEAR MEDICINE PROVIDES BETTER DIAGNOSTIC OUTCOMES IN DIAGNOSING PE

- V/Q SPECT and V/Q SPECT/CT have shown that V/Q SPECT/CT is superior in most clinical settings with better overall diagnostic performance.\(^1\)

- In situation of acute PE, chronic PE pregnancy, paediatrics and the COPD population, V/Q SPECT, with or without low-dose CT, can be considered as a first-line investigation to detect PE due to:
  - Its low radiation and no adverse reactions.\(^3\)
  - Its higher accuracy, sensitivity and negative predictive value when compared to CTPA.\(^3\)

Table: Diagnostic ability of V/Q SPECT/CT\(^1\), V/Q SPECT\(^1\), CTPA\(^1\) and V/Q Planar\(^2\) to detect PE (adapted from Hess and al, 2016\(^1\) and from Reinartz et al, 2004\(^2\))

<table>
<thead>
<tr>
<th></th>
<th>Accuracy</th>
<th>NPV</th>
<th>PPV</th>
<th>Specificity</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>V/Q SPECT/CT</td>
<td>0%</td>
<td>25%</td>
<td>50%</td>
<td>75%</td>
<td>100%</td>
</tr>
<tr>
<td>V/Q SPECT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CTPA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V/Q Planar</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

RECLAIMING AND EXPANDING PULMONARY IMAGING

**Education**
Educating referring physicians to the facts, benefits and capabilities of nuclear medicine will bring back lung imaging to nuclear medicine.

**Utilizing Available Technology**
Leveraging the state of the art techniques to include SPECT, SPECT-CT & Quantification Software.

**CYC Research Strategy Beyond PE**
Exploring new methods and techniques to engage specialists and develop new clinical applications.

**CYC Publication Strategy Beyond PE**
Extending the reach of journal articles beyond the nuclear medicine community... i.e. Respiratory Medicine, Emergency Medicine & Cardiology.
EXPANDING INDICATIONS
Applications in chronic disease has the potential to dwarf the use of Technegas in Pulmonary Embolism. In 2015 Cyclopharm commenced a clinical program targeting Technegas indication expansion to include:

**Chronic Obstructive Pulmonary Disease**
- 30x the size of total PE market
- 1 in 7 Australians over the age of 40
- In 2008, the total economic impact of COPD was estimated to be $98.2 billion of which $8.8 billion was attributed to financial costs and $89.4 billion to the loss of wellbeing
- COPD is a leading cause of death and disease burden after heart disease, stroke and cancer
- Global estimates show that COPD will be the third leading cause of death by 2030

**Asthma**
- 334 million people globally
- 1 in 9 Australians have asthma
- $655 million was spent on asthma in 2008-9; which is 0.9% of all direct health spend on diseases
- 34% of people report that asthma interferes with their daily living, and 21.8% of people aged 15-25 required time off work, school or study due to their asthma

**Lung Reduction Intervention**
- Application in determining ventilation pre and post lung reduction intervention

**CTEPH**
- Ventilation/Perfusion imaging is recommended
- Up to 40 million patients globally
CLINICAL CALL FOR ACTION

A new way of thinking about respiratory Medicine

Lancet Commission - After asthma: redefining airways disease, September 2017

Executive Summary:
Progress in reducing hospital admissions and mortality in people with asthma have stalled in the past 10 years. This Lancet Commission examines where we are in the understanding of this heterogeneous syndrome and where we need to go to kickstart a new era of examining, monitoring, treating, and ultimately preventing airways diseases. The Commissioners recommend to deconstruct airway disease into component parts before planning treatment with a focus on traits that are identifiable and treatable. This approach will require a complete change in how we think about airways diseases with the goal of achieving real precision treatment with better patient outcomes. In addition, primary prevention and disease-modifying interventions need to become a more important ambition. It is unacceptable that people still die from asthma attacks in 2017.

Functional ventilation imaging using Technegas® may provide useful biomarker information in assessing baseline diagnosis and response to therapy in respiratory disease
HYBRID V/Q SPECT/CT

V/Q SPECT provides functional information on ventilation and perfusion of the lungs. Low-dose CT provides anatomical information such as fissures delineation. Combination of functional and anatomical information allow for objective results through quantitative software.

LOBAR DISTRIBUTION OF VENTILATION

Percentages, volumes and counts of individual lobes (Images and 3D quantification provided by MMI)

IMPROVES DIAGNOSTIC CAPABILITIES AND OFFERS ANATOMICALLY-BASED QUANTIFICATION OF LOBAR CONTRIBUTION FOR INTERVENTIONAL THERAPIES

TREATMENT RESPONSE IN ASTHMA PATIENT

Case #1

CLINICAL HISTORY
Male patient of 25 years old with life-long asthma

REFERRAL
Evaluation of asthma treatment efficacy

PROTOCOL
Ventilation SPECT/CT imaging at baseline and after methacholine challenge before and after asthma treatment

VENTILATION SPECT/CT TO MONITOR TREATMENT RESPONSE IN PATIENTS WITH LIFELONG ASTHMA

BASELINE
Bronchoconstriction after methacholine challenge worsened ventilation function and increased ventilation heterogeneity. This was predicted by baseline peripheral ventilation heterogeneity.

METHACHOLINE
After treatment, ventilation improved and is more homogeneous on ventilation SPECT imaging, at baseline and also after methacholine-induced bronchoconstriction.
Case #2

PLANNING LUNG VOLUME REDUCTION SURGERY

CLINICAL HISTORY
Male patient of 64 years old with emphysema

REFERRAL
Assessment of lung ventilation function before planning endoscopic lung volume reduction

PROTOCOL
VQ SPECT/CT imaging with TECHNEGAS as ventilation agent

The ventilation SPECT/CT scan reveals the function of the lower lobes is severely affected. The left oblique fissure is intact so the left lower lobe should be a good target lobe for endobronchial valves insertion.

Assessment for collateral ventilation was confirmed using CHARTIS assessment tool during the procedure.

Decision: 3 valves were inserted into the left lower lobe.

VENTILATION SPECT/CT AS A TOOL TO ASSIST IN PREDICTING FUNCTIONAL LUNG VENTILATION PRIOR TO LUNG VOLUME REDUCTION