CYCLOPHARM

SHAREHOLDER UPDATE

James McBrayer, CEO & Managing Director

23 September 2020

SAFE HARBOUR STATEMENT

Certain views expressed here contain information derived from publicly available sources that have not been independently verified.

The presentation includes certain statements, estimates and projections with respect to the anticipated future financial performance of Cyclopharm Limited and as to the markets for the company's products. Such statements, estimates and projections reflect various assumptions made by the directors concerning anticipated results, which assumptions may or may not prove to be correct. Cyclopharm Limited has not sought independent verification of information in this presentation.

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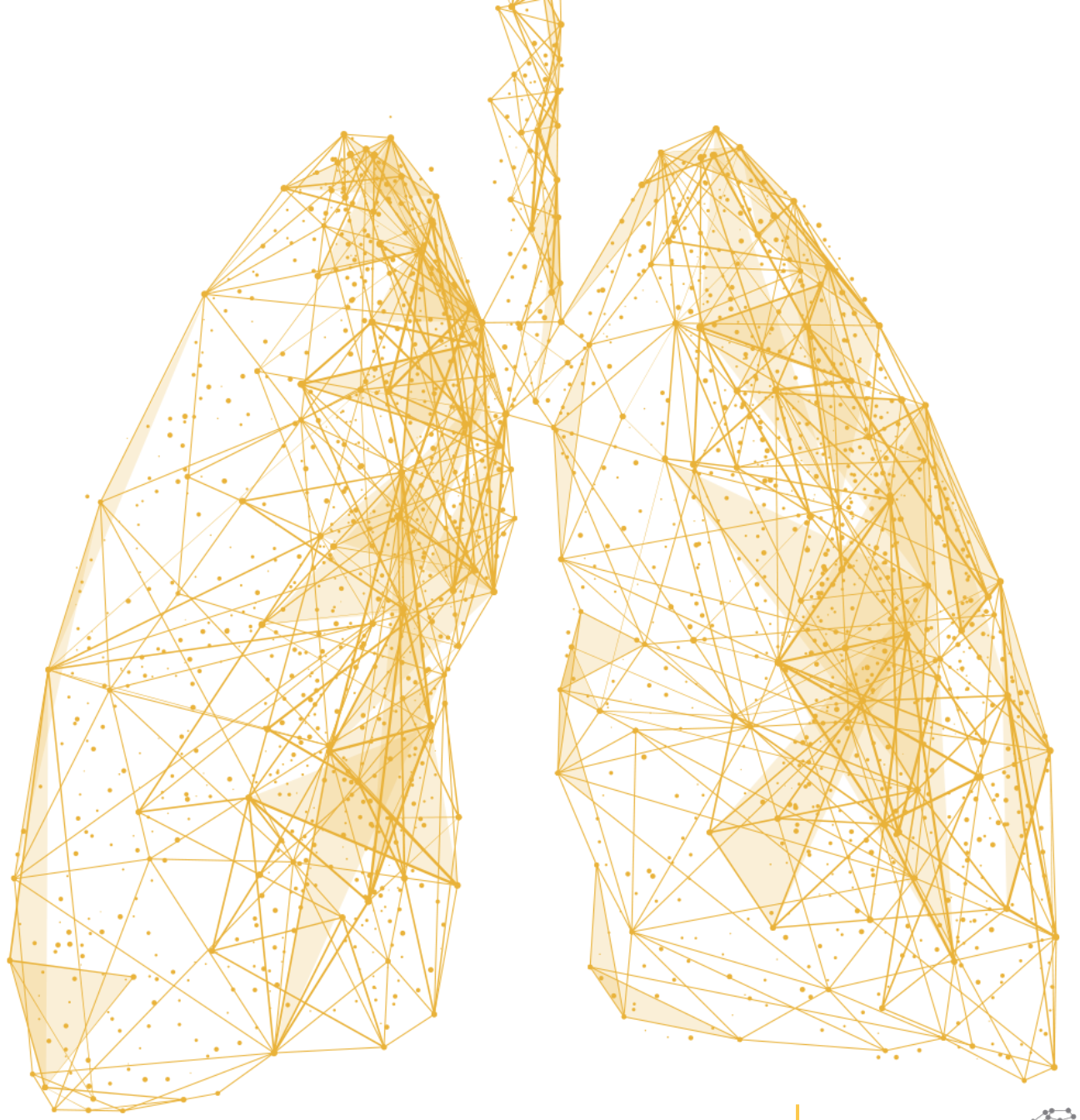
All references to dollars unless otherwise specified are to Australian dollars.

COMPANY OVERVIEW

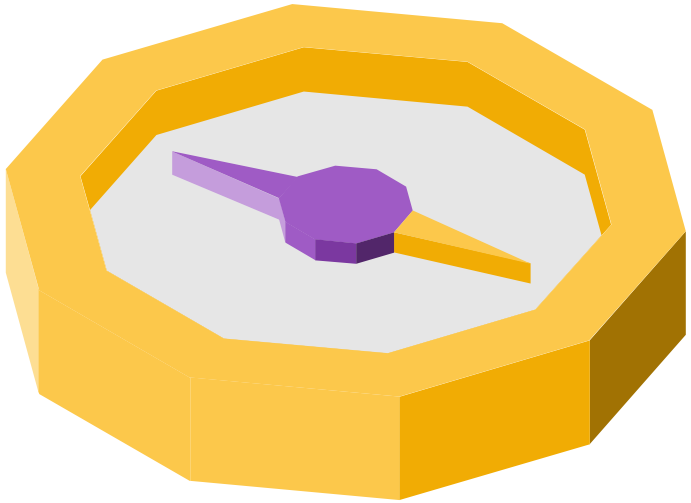
Cyclopharm Limited (CYC) is a leading diagnostic lung imaging company

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



OUR STRATEGIC PRIORITIES

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 **COPD[1] 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

CYCLOPHARM INVESTMENT CASE

TECHNEGAS™

Profitable and Growing MedTech

Underlying business is cash positive and issuing dividends

First in Class

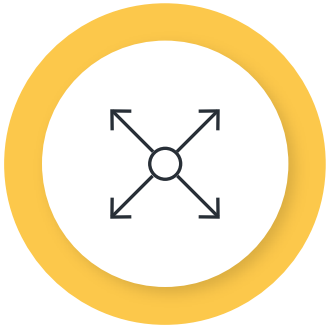
Proprietary product sales to 60 countries with over 4.2 million studies to date

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

TECHNEGAS®

World's Best Functional Lung Ventilation Imaging Agent

Patient inhales extremely small carbon particles labeled with 99mTechnetium[1]

The small size and hydrophobic properties demonstrates gas like-behavior and alveoli deposition into the lungs[2-3]

Clinicians can visualise functional ventilation using Technegas®

PULMONARY EMBOLISM

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

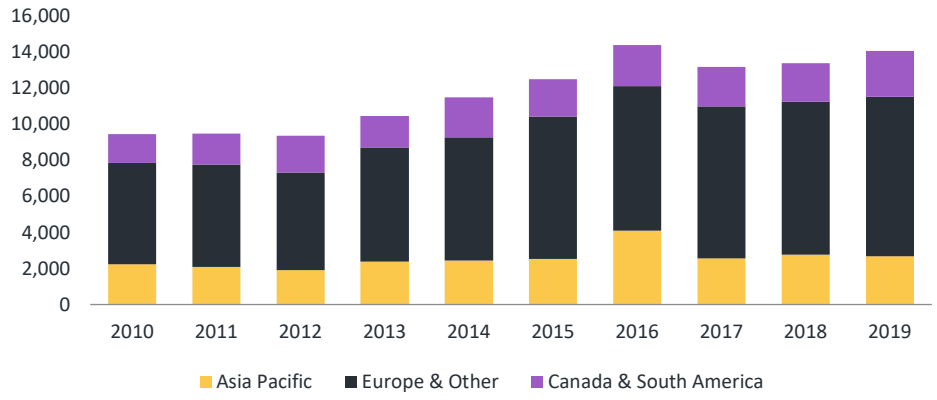
Symptoms
are varied with diagnosis confirmed either through CTPA or a nuclear medicine ventilation-perfusion study

30%
of pulmonary embolisms are fatal if left untreated

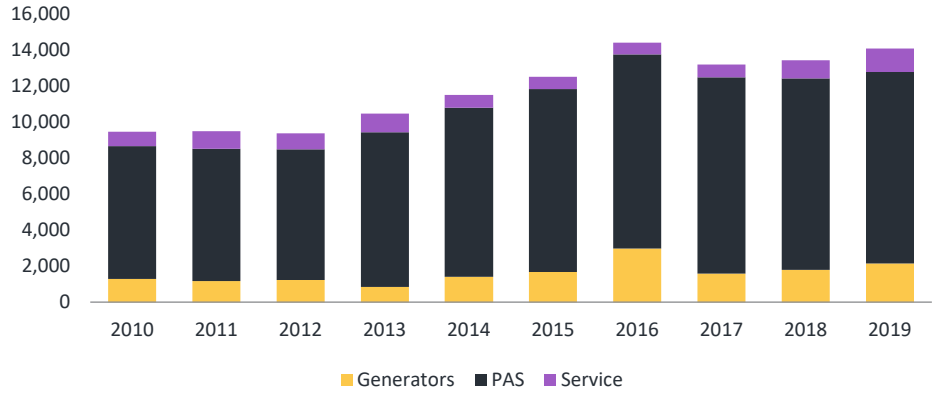
Nuclear Medicine
using 3-D imaging is the most accurate method of diagnosis

BUILDING FOR GROWTH – COMPANY DEVELOPMENT

Technegas® Revenue by Region ($ 000's)



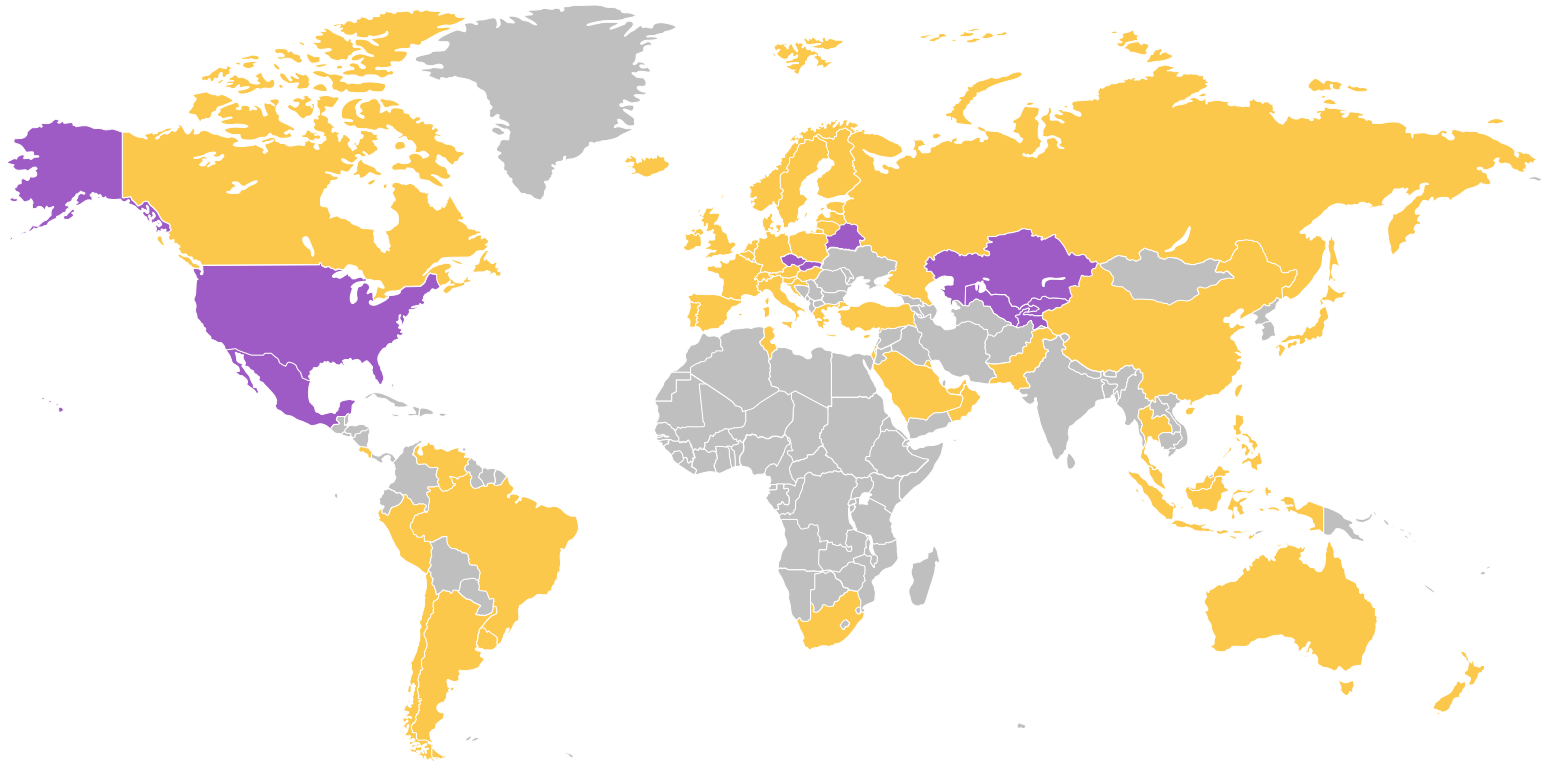
Technegas® Regional Revenue by Category ($ 000's)



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



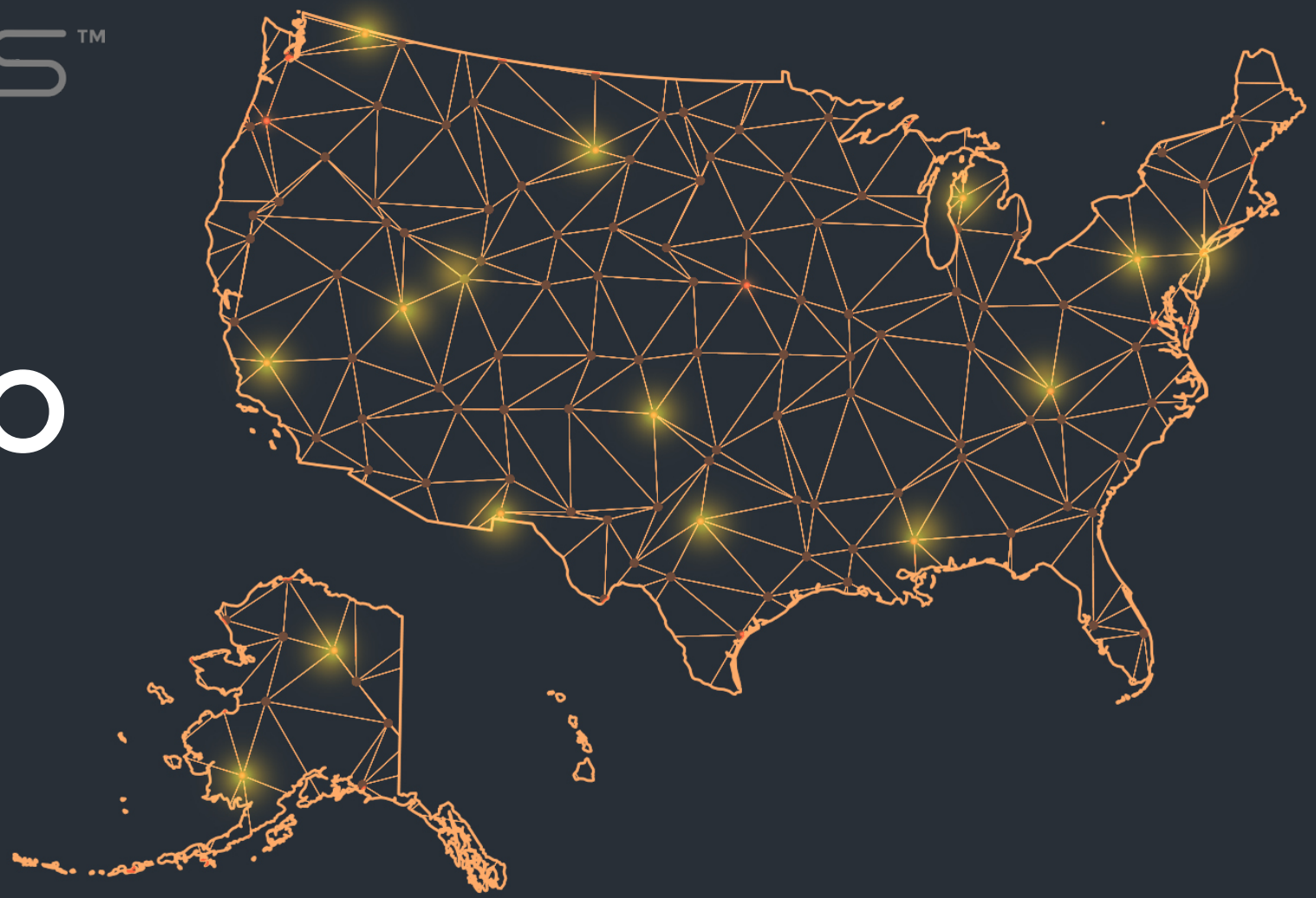
Technegas® was introduced to the medical community **in 1986** [1]

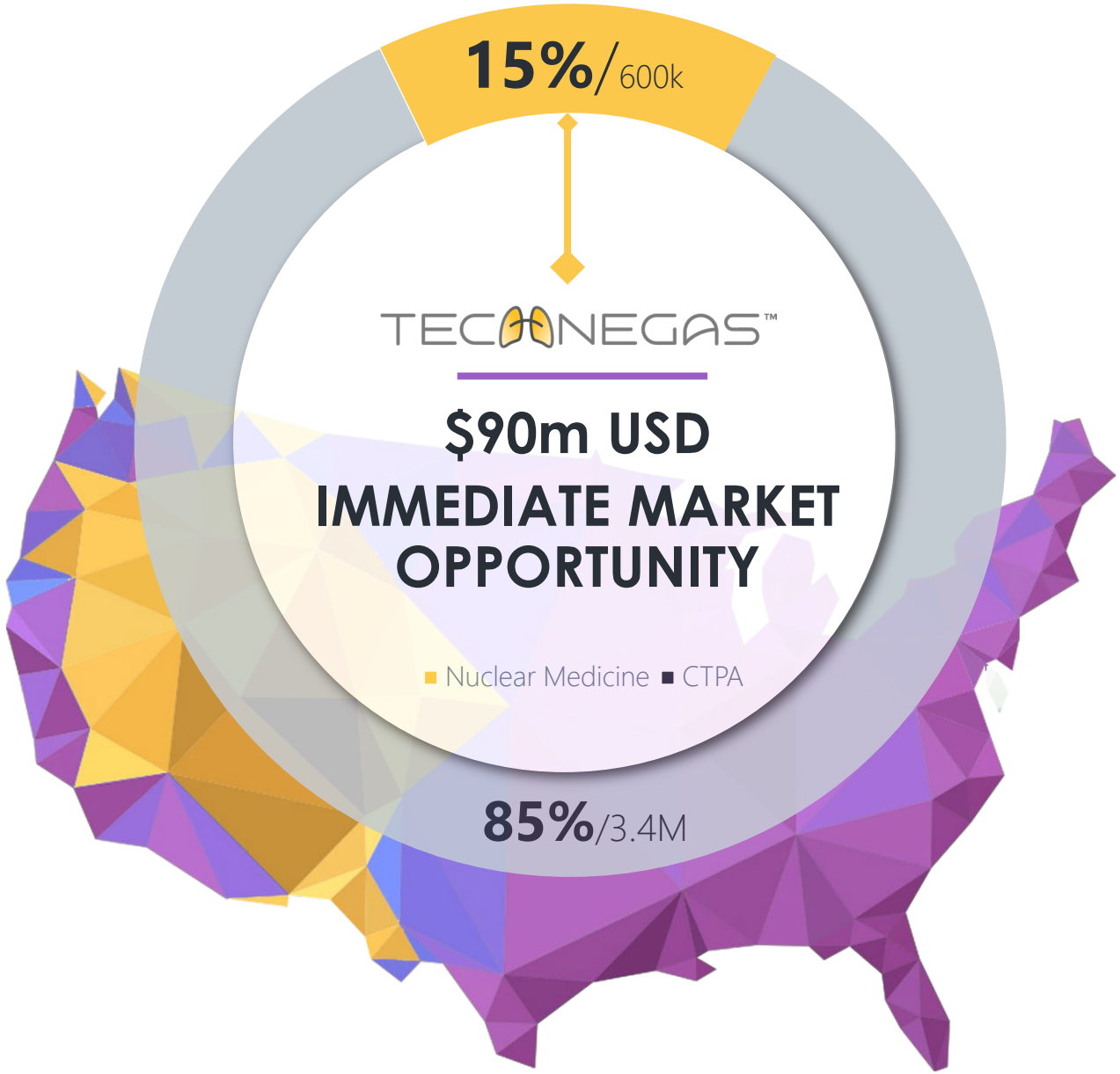
Technegas® revenues are generated in **60 countries** via a combination of direct and distributor sales models

Over **4.2 million** patient procedures to date

TECNEGAS™

COMING TO AMERICA

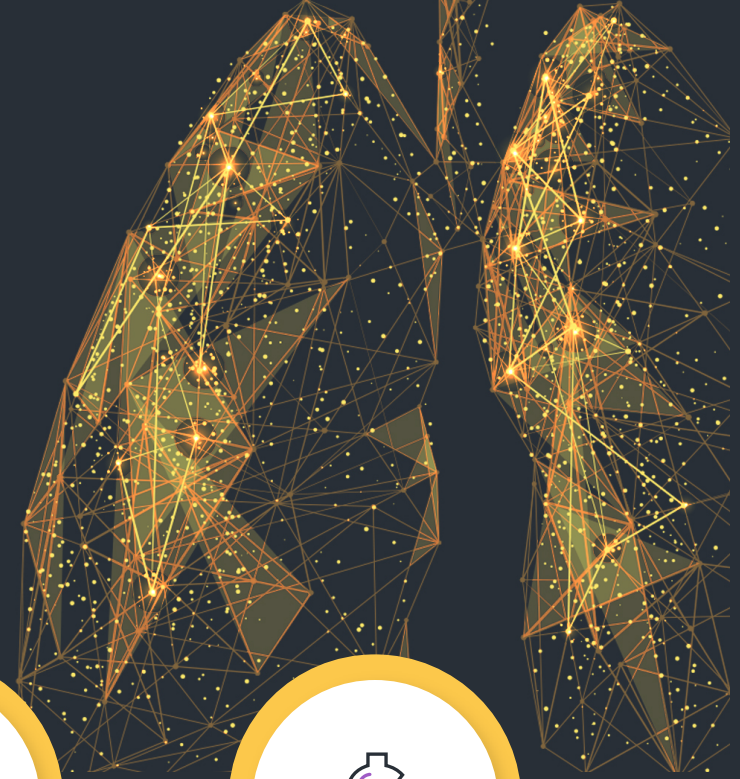




600K Nuclear Medicine Ventilation Procedures p.a.

- 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
- 3 to 4 breaths
- 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 SPECT[1]

Contraindications

CTPA should not be performed with pregnancy[1-2], renal impairment[3], contrast media allergy[3], diabetes[4]

Acute kidney injury (AKI)

AKI occurs in up to 13% of CTPA cases[5]

Lower clinical sensitivity

V/Q planar[6]	= 76%
CTPA[7]	= 82%
V/Q SPECT[7]	= 93%

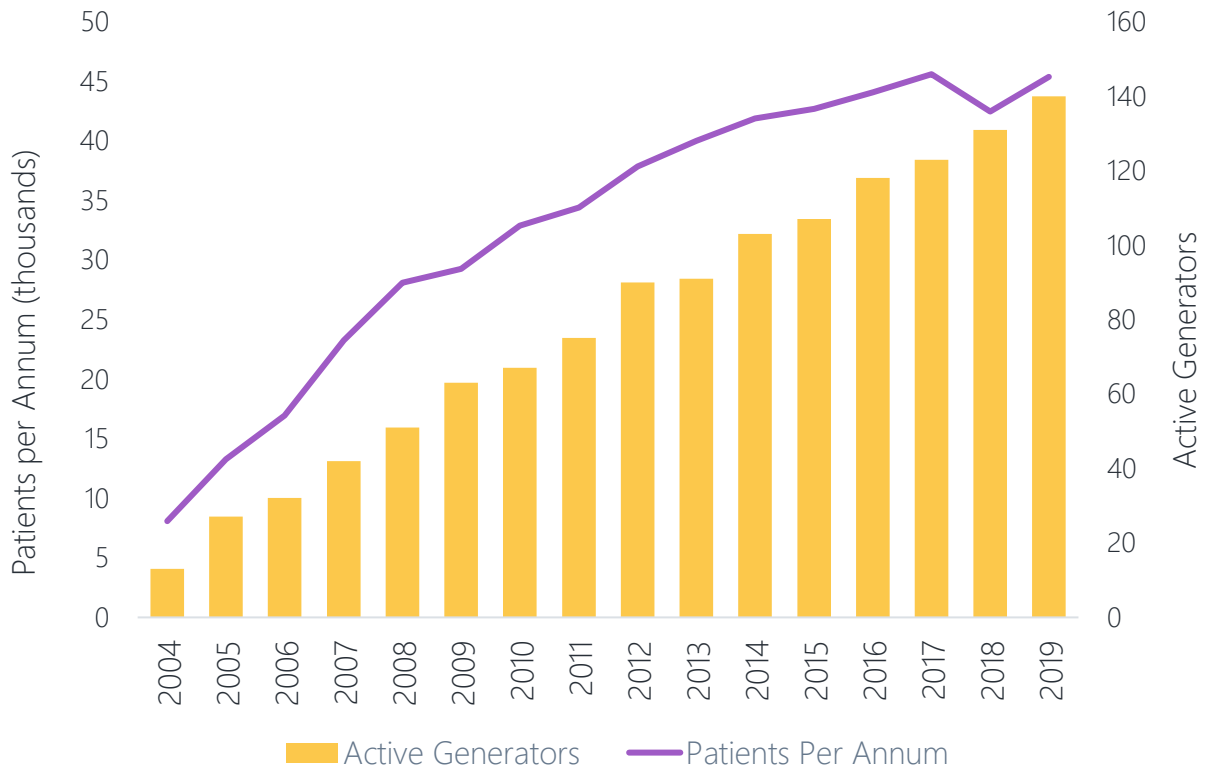
Availability

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

1. Isidoro J, et al. Phys Med 2017; 41: 93-96
2. Bajc M, et al. Eur J Nucl Mol Imaging 2015; 42: 1325-1330
3. Miles S, et al. Chest 2009; 136: 1546-1553
4. Roach PJ, et al. J Nucl Med 2013; 54: 1588-1596
5. Doganay S, et al. Renal Failure 2015; 37(7): 1138-1144
6. Reinartz P, et al. J Nucl Med 2004; 45: 1501-1508
7. Hess S, et al. Semin Thromb Hemost 2016; 42(8): 833-845

TECHNEGAS®

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

USA 2021 COMMERCIALISATION PLAN*

USFDA Regulatory Approval

Submission of 505(b)2 NDA March 2020

Approval to file May 2020

Build Inventory

Materials Resource Planning underway with production targeting 200 Techengas generators roll-out per anum

Secure Customer Commitments

Securing commitments in line with Technegas® Generator lead time

People

Hire Key USA Personnel to include Sales and Service

Service and Distribution

Secure service capabilities and stock 3PL Partners for USA launch

***USA Operational costs estimated to be $5m USD p.a.**

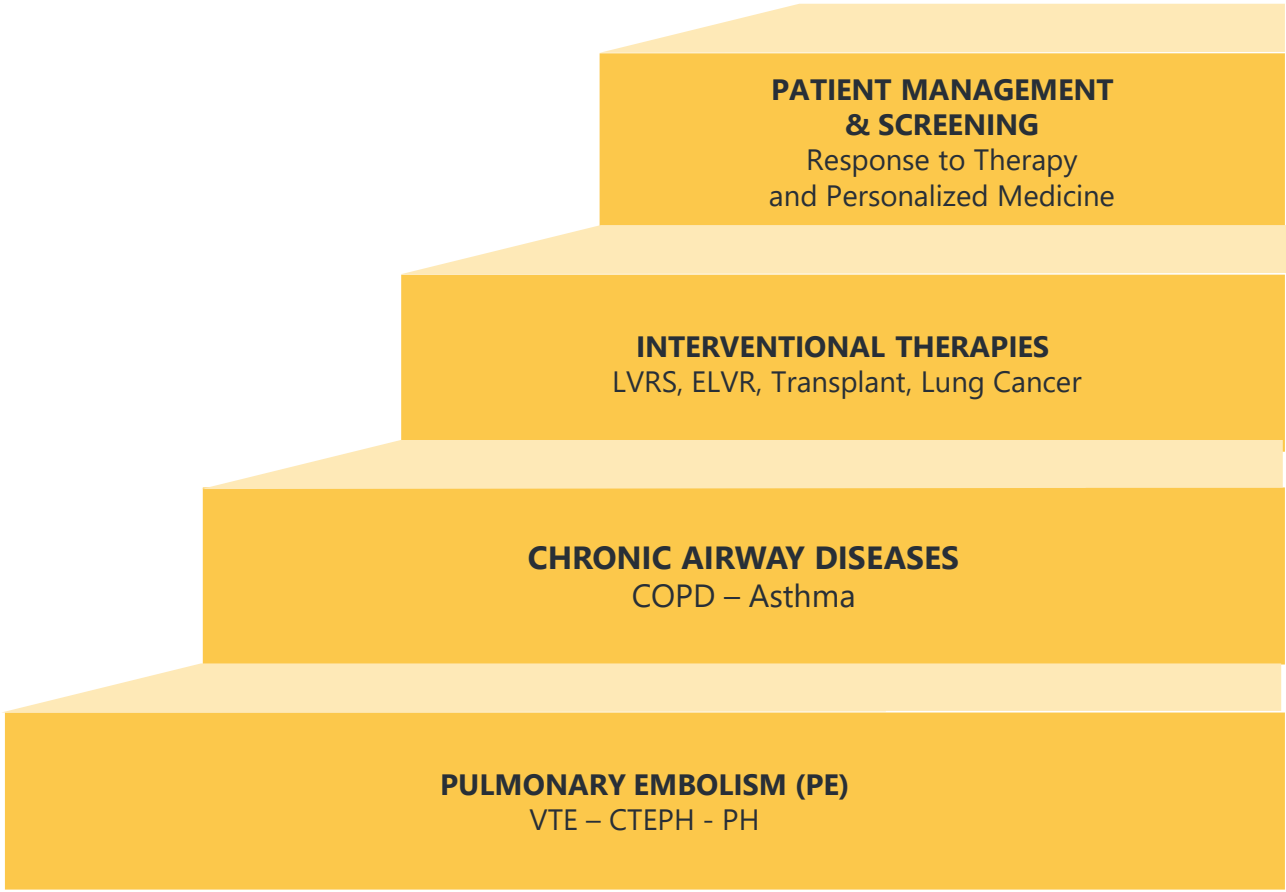
BEYOND PE : clinical initiatives

Clinical Trials Sponsored by Cyclomedica

- **Hunter Medical Research Institute (Newcastle, AU):** Diagnosis and response to therapy in severe asthma and COPD[1]
- **Woolcock Institute (Sydney, AU):** Diagnosis and response therapy in mild to moderate COPD[3]
- **CHUM (Montreal, CA):** Early detection of COPD in asymptomatic smokers[4]
- **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 Injury[5]

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



1. ACTRN12617001275358 - Can functional lung ventilation imaging identify treatable traits in obstructive airway disease?
2. https://clinicaltrials.gov/ct2/show/NCT04191174?term=technegas&draw=2&rank=3
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

CYCLOPHARM:

Helping in the fight against COVID-19

McMaster University

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

1

<u>Primary Endpoint:</u>

To investigate and characterize the extent of COVID-19 infection related ventilation and perfusion injury at ≤4-weeks and 6-months post infection recovery in asthmatic and healthy populations.

2

<u>Secondary Endpoints:</u>

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

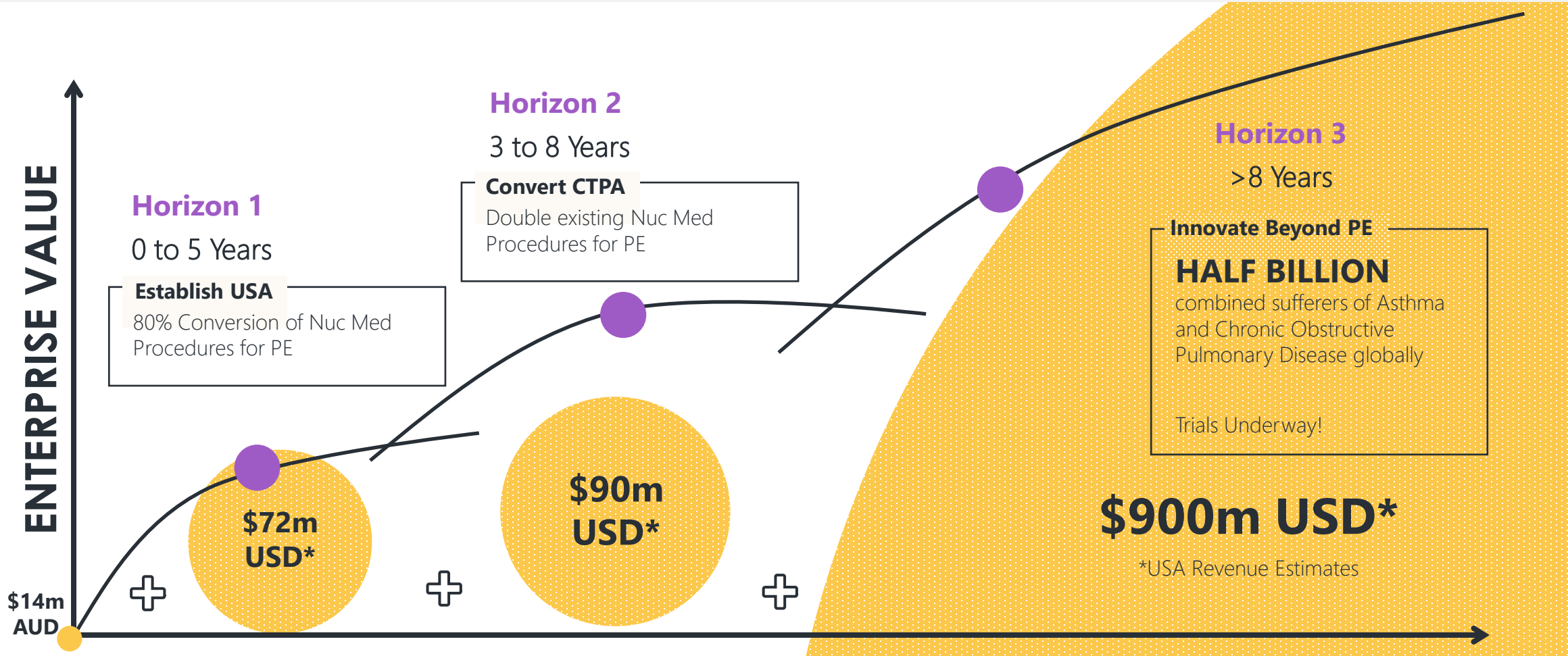
3

<u>Exploratory Objective:</u>

To determine if COVID-19 infection related ventilation and perfusion injury) ≤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.

*https://clinicaltrials.gov/ct2/show/NCT04549636

THREE VALUE HORIZONS



BUILDING FROM A STRONG AND WELL-ESTABLISHED FOUNDATION

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

APPENDIX

2019 FINANCIALS

FY2019 RESULTS HIGHLIGHTS

Group Sales Revenue	$14.08 million - an increase of 5%
Gross Margin	$11.62 million – an increase of 7%
Gross Margin %	82.5%
Net Loss After Tax	($2.91) million including USFDA investment
Dividends	1.0 cents per share
Underlying Technegas® PBT[1]	$0.89 million
FDA Trial expenses	($3.84) million
Strong balance sheet	$12.66 million of cash reserves as @ 31 December 2019
Guidance	The Board expects continuing modest growth in underlying Technegas® revenues from existing markets for FY2020

[1] PBT=Profit Before Tax

FY2019 OPERATIONAL HIGHLIGHTS

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

GROUP UNDERLYING PERFORMANCE

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**.

Solid Underlying Financial Results

YEAR ENDED 31 DECEMBER	2019 $'000	2018 $'000	INC/(DEC) $'000	CHANGE %
SALES REVENUE	**14,079**	**13,404**	**675**	**5%**
GROSS MARGIN	**11,619**	**10,855**	**764**	**7%**
GROSS MARGIN % SALES	82.5%	81.0%	1.5%	
UNDERLYING PROFIT BEFORE TAX TECHNEGAS®	**887**	**1,406**	**(519)**	**(37%)**
ADD BACK NON-OPERATING ACTIVITIES :				
INCOME				
CYCLOPET DIVISION	746*	(335)	1,081	323%
R&D TAX INCENTIVE GRANT	2,934	2,122	812	38%
REVERSAL OF CONTINGENT CONSIDERATION ON ACQUISITION OF SUBSIDIARY	-	314	(314)	(100%)
UNREALISED GAIN ON FORWARD EXCHANGE CONTRACT	-	275	(275)	(100%)
RECOVERY FROM GERMAN LITIGATION	339	-	339	100%
EXPENSES				
FDA EXPENSES	(3,842)	(2,965)	(877)	(30%)
BEYOND PE CLINICAL TRIALS	(351)	(251)	(100)	(40%)
RETIREMENT/SEVERANCE PAYMENTS	(322)	-	(322)	(100%)
QUALITY AND REGULATORY DEPARTMENT EXPANSION	(238)	-	(238)	(100%)
CYC QUALITY SYSTEM INVESTMENT	(827)	-	(827)	(100%)
LITIGATION EXPENSES	(1,064)	(410)	(654)	(160%)
COST OF TERMINATING PUT OPTION	(309)	-	(309)	(100%)
COST OF LTIP PROGRAM	(378)	(38)	(340)	(895%)
REPORTED (LOSS) / PBT	**(2,425)**	**118**	**(2,543)**	**(2,155%)**

*INCLUDES ONE-OFF RENT ABATEMENT OF $1,043K

GROUP BALANCE SHEET

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

Financial Foundation to Leverage Growth Strategy

Year ended 31 December *($000's)*	2019	2018	2017
Cash	12,660	5,855	8,690
Other current assets	6,950	9,600	8,139
Non-current Assets	12,918	8,082	6,548
Total Assets	**32,528**	**23,537**	**23,377**
Current Liabilities	3,480	5,219	5,212
Non-current Liabilities	5,844	1,302	916
Total Liabilities	**9,324**	**6,521**	**6,128**
Net Assets	**23,204**	**17,016**	**17,249**

GROUP CASH POSITION

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**

Cash Position Funding Growth

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

TECNEGAS™

Product Profile

TECHNEGAS

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.1

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.2

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.3

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 SPECT3 ventilation imaging

Particles remain in the lung until they are cleared by ciliary action or phagocytosis4.

1. Wiebe LI, et al. Current Radiopharmaceuticals 2010; 3(1): 49-59
2. Lemb M, et al. Eur J Nucl Med 1993; 20(576-579)
3. Leblanc M, et al. CANM guidelines; Nov 2018: www.canm-acmn,ca/guidelines
4. Möller W, et al. Am J Respir Crit Care Med 2008; 177: 426-432

ADVANTAGES OF TECHNEGAS®

Technegas® provides a safer clinically superior outcomes to its competitors

- Technegas product characteristics, Delivery System and etremely 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

Product	Comparison to Technegas®
Xenon 133	• Patient has to continually re-breathe gas causing patient discomfort / anxiety • Can't provide 3D images • Costly air-handling infrastructure required in order to administer
DTPA	• Inferior images in patients with obstructive lung disease (COPD)

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 European[1-2] and the Canadian[3] 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 "

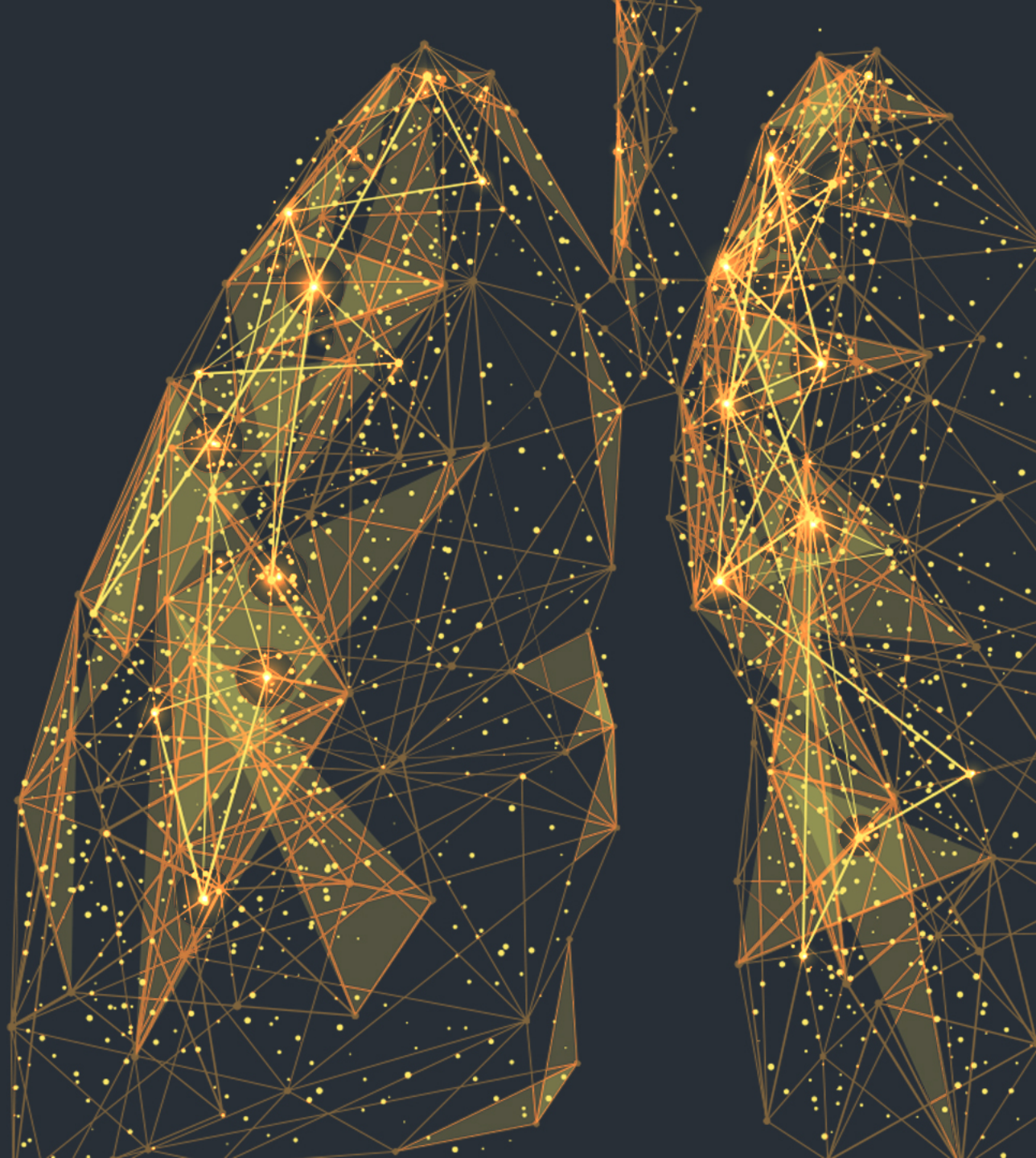
1. 1Bajc M, et al. Eur J Nucl Med Mol Imaging 2019; [Epub ahead of print]: https://link.springer.com/content/pdf/10.1007%2Fs00259-019-04450-0.pdf
2. 2Bajc M, et al. Eur J Nucl Med Mol Imaging 2009; 36(8): 1356-70; https://eanm.org/publications/guidelines/gl_pulm_embolism_part1.pdf
3. 3. Leblanc M, et al. CANM 2018; https://canm-acmn.ca/resources/Documents/Guidelines_Resources/MasterDocument_Final_Nov_21_incl-Exec-Sum_ver3_Dec.%2012_.pdf 2.a

TECHNEGAS®
In recent literature

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

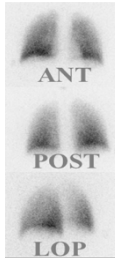
1. King GG, et al. Dismantling the pathophysiology of **asthma** using imaging. Eur Respir Rev 2019; 28(152): pii: 1801111
2. Yang L, et al. Changes in ventilation and perfusion following lower lobe endoscopic lung volume reduction **(ELVR)** with endobronchial valves in severe COPD. Clin Respir J 2019; [Epub ahead of print].
3. Kjellberg M, et al. Ten-year-old children with a history of **bronchopulmonary dysplasia** have regional abnormalities in ventilation perfusion matching. Pediatr Pulmonol 2019; 54(5): 602-609
4. Paludan JPD, et al. Improvement in image quality of Tc-99m-based ventilation/perfusion single-photon emission computed tomography in patients with **chronic obstructive pulmonary disease** through pretest continuous positive airway pressure treatment. World J Nucl Med 2019; 18(2): 185–186
5. Myc LA, et al. Role of medical and molecular imaging in **COPD.** Clin Transl Med 2019; 8(1): 12
6. Ling T, et al. Ventilation/perfusion SPECT/CT in patients with severe and rigid **scoliosis**: An evaluation by relationship to spinal deformity and lung function. Clin Neurol Neurosurg 2019; 176: 97-102
7. Farrow CE, et al. SPECT Ventilation imaging in **asthma**. Semin Nucl Med 2019; 49(1): 11-15
8. Mortensen J, et al. Lung scintigraphy in **COPD**. Semin Nucl Med 2019; 49(1): 16-21
9. Sanchez-Crespo A, et al. Lung VQ SPECT in **infants and children** with nonembolic chronic pulmonary disorders. Semin Nucl Med 2019; 49(1): 37-46
10. Bajc M, et al. Ventilation/Perfusion SPECT Imaging - Diagnosing other **cardiopulmonary diseases** beyond PE. Semin Nucl Med 2019; 49(1): 4-10
11. Sanchez-Crespo A, et al. Lung scintigraphy in the assessment of **aerosol deposition and clearance**. Semin Nucl Med 2019; 49(1): 47-57
12. Bailey DL, et al. V/Q SPECT - Normal Values for **Lobar Function** and Comparison With CT Volumes. Semin Nucl Med 2019; 49(1): 58-61
13. Lawrence NC, et al. Ventilation perfusion single photon emission computed tomography: Referral practices and diagnosis of acute pulmonary embolism in the quaternary clinical setting. J Med Imaging Radiat Oncol 2018; 62(6): 777-780.
14. Leblanc M, et al. CANM Guidelines for Ventilation/Perfusion (V/P SPECT) in pulmonary embolism.www.canm-acnm.ca/guidelines
15. Hsu K, et al. Endoscopic Lung Volume Reduction in **COPD**: Improvements in Gas Transfer Capacity Are Associated With Improvements in Ventilation and Perfusion Matching. J Bronchology Interv Pulmonol. 2018; 25(1): 48-53
16. Dimastromatteo J, et al. Molecular imaging of pulmonary diseases. Respir Res 2018; 19(1): 17
17. Jögi J, et al. Diagnosing and **grading heart failure** with tomographic perfusion lung scintigraphy: validation with right heart catheterization. ESC Heart Fail 2018; 5(5): 902-910
18. Waxman AD, et al. Appropriate use Criteria for Ventilation-Perfusion imaging in Pulmonary embolism : Summary and Excerpts. J Nucl Med 2017; 58(5): 13N-15N
19. Isidoro J, et al. Radiation dose comparison between V/P SPECT and CT-angiography in the diagnosis of pulmonary embolism. Phys Med 2017; 41: 93-96
20. Righini M, et al. Diagnosis of acute pulmonary embolism. J Thromb Haemost. 2017; 15: 1251-1261
21. Le Roux PY, et al. New developments and future challenges of nuclear medicine and molecular imaging for pulmonary embolism. Thromb Res 2018; 163: 236-241
22. Farrow CE, et al. Peripheral ventilation heterogeneity determines the extent of bronchoconstriction in **asthma**. J Appl Physiol (1985). 2017; 123(5): 1188-1194
23. Tulchinsky M, et al. Applications of Ventilation-Perfusion Scintigraphy in Surgical Management of **Chronic Obstructive Lung Disease and Cancer**. Semin Nucl Med. 2017; 47(6): 671-679
24. Cheimariotis GA, et al. Automatic lung segmentation in functional SPECT images using active shape models trained on reference lung shapes from CT. Ann Nucl Med. 2017; 10: 25-30
25. Bajc M et al. Identifying the heterogeneity of **COPD** by V/P SPECT: a new tool for improving the diagnosis of parenchymal defects and grading the severity of small airways disease. Int J Chron Obstruct Pulmon Dis 2017; 12: 1579-1587
26. Nasr A, et al. Ventilation defect typical for **COPD** is frequent among patients suspected for pulmonary embolism but does not prevent the diagnosis of PE by V/P SPECT. EC Pulmonology and Respiratory Medicine. 2017; 4(3): 85-91
27. Provost K, et al. Reproducibility of **lobar perfusion and ventilation quantification** using SPECT/CT segmentation software in lung cancer patients. J Nucl Med Technol 2017; 45(3): 185-192
28. Metter DF, et al. Current status of ventilation-perfusion scintigraphy for suspected pulmonary embolism. AJR Am J Roentgenol 2017; 208(3): 489-494
29. Stubbs M, et al. Incidence of a single subsegmental mismatched perfusion defect in SPECT and planar ventilation/perfusion scans. Nucl Med Commun 2017; 38(2): 135-140
30. El-Barhoun EN, et al. Reproducibility of a **semi-quantitative lobar pulmonary ventilation** and perfusion technique using SPET and CT. Hell J Nucl Med 2017; 20(1): 71-75

PULMONARY IMAGING WITH TECNEGAS™

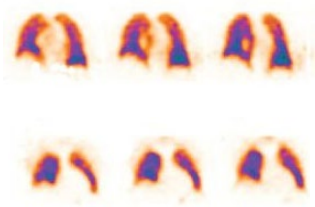


EVOLUTION OF FUNCTIONAL LUNG VENTILATION IMAGING

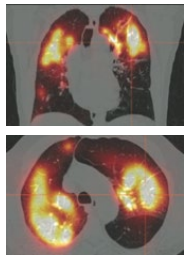
- Improvements in 3D imaging techniques, hybrid imaging and the advent of analytical software have dramatically improved the sensitivity and specificity in functional lung imaging with Technegas®
- Traditionally used in the diagnosis of Pulmonary Embolism, nuclear medicine functional lung ventilation 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:



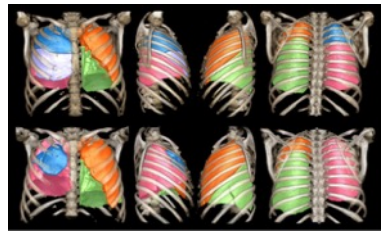
1980s
Planar Imaging



2000
SPECT Imaging



2010
SPECT with Low Dose CT



2015
SPECT withLow Dose CT & Lobular Quantification

NUCLEAR MEDICINE IMAGING TECHNOLOGY HAS EVOLVED BEYOND CTPA IN DIAGNOSING PE

1986 → 2020

Planar

- Inherent limitations of 2-dimensional imaging
- Overlap of anatomical segments
- Shine-through from underlying
- Lung segments
- Difficulty visualizing all the lung segments[1-2]
- PIOPED II recently updated to AUC Trinary interpretation of V/Q findings[3]

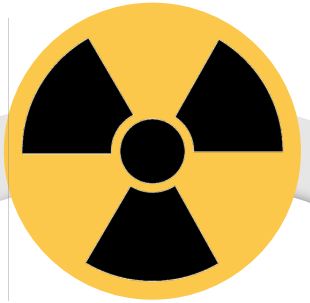
SPECT

- Three-dimensional imaging
- Superior contrast resolution
- Improved anatomical detail
- Higher sensitivity and specificity
- Accurate definition of size and location of the perfusion defects[1-2]

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[4]

1. Gutte H, et al. Nucl Med Commun 2010; 31: 82-86
2. Roach PJ et al. Semin Nucl Med 2010; 40:397-407
3. Waxman AD, et al. J Nucl Med 2017; 58: 13N-15N
4. Roach PJ, et al. J Nucl Med 2013; 54:1588–1596



RADIATION DOSIMETRY

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

Technique	Effective dose (mSv/MBq)	Effective dose (mSv)	Breast absorbed dose (mGy)	Lung absorbed dose (mGy)
Ventilation Technegas (20MBq) [1-3]	0.015	0.30	0.13	2.2
Ventilation ^{99m}Tc-DTPA (20MBq) [1-2]	0.007	0.14	0.04	0.30
Ventilation ^{133}Xe (800MBq) [1]	0.0014	1.12	0.09	0.89
Perfusion MAA (120MBq) [1-3]	0.012	1.44	0.60	7.92
Low dose CT non-contrast [4]	NA	~ 1.00	-	-
CTPA 16 slice [1]	NA	14.4	10-20	10
CTPA 64 slice [1,3]	NA	19.9	22	20

1. Bajc M, et al. Eur J Nucl Med Mol Imaging 2009; 36(8): 1356-1370
2. Schembri GP, et al. Semin Nucl Med 2010; 40: 442-454
3. Isidoro J, et al. Phys Med 2017; 41: 93-96
4. Ling IT, et al. Intern Med J 2012; 42(11): 1257-1261

NUCLEAR MEDICINE PROVIDES BETTER DIAGNOSTIC OUTCOMES IN DIAGNOSING PE

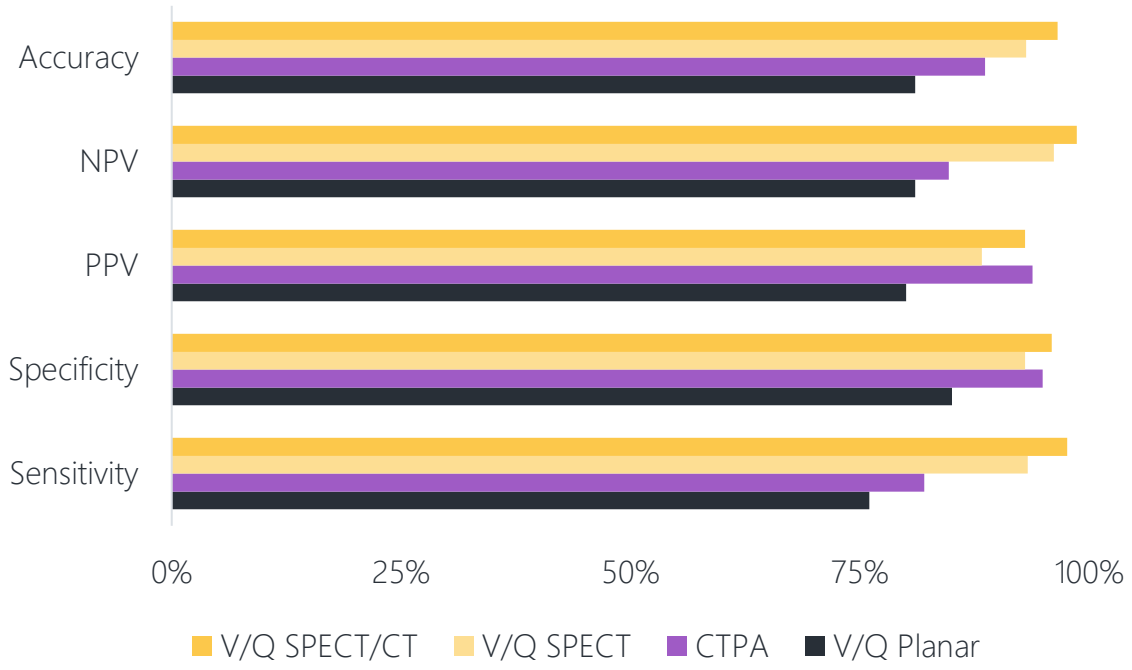


Table: Diagnostic ability of V/Q SPECT/CT[1], V/Q SPECT[1], CTPA[1] and V/Q Planar[2] to detect PE (adapted from Hess and al, 20161 and from Reinartz et al, 20042)

- 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 PE3 due to:

Its low radiation and no adverse reactions[3]

Its higher accuracy, sensitivity and negative predictive value when compared to CTPA[3]

1. Hess S, et al. Semin Thromb Hemost 2016; 42(8): 833-845
2. Reinartz P, et al. J Nucl Med 2004; 45: 1501-1508
3. Leblanc M, et al. CANM guidelines; Nov 2018: www.canm-acmn.ca/guidelines

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

CANM ACMN | The Canadian Association of Nuclear Medicine
Association canadienne de médecine nucléaire

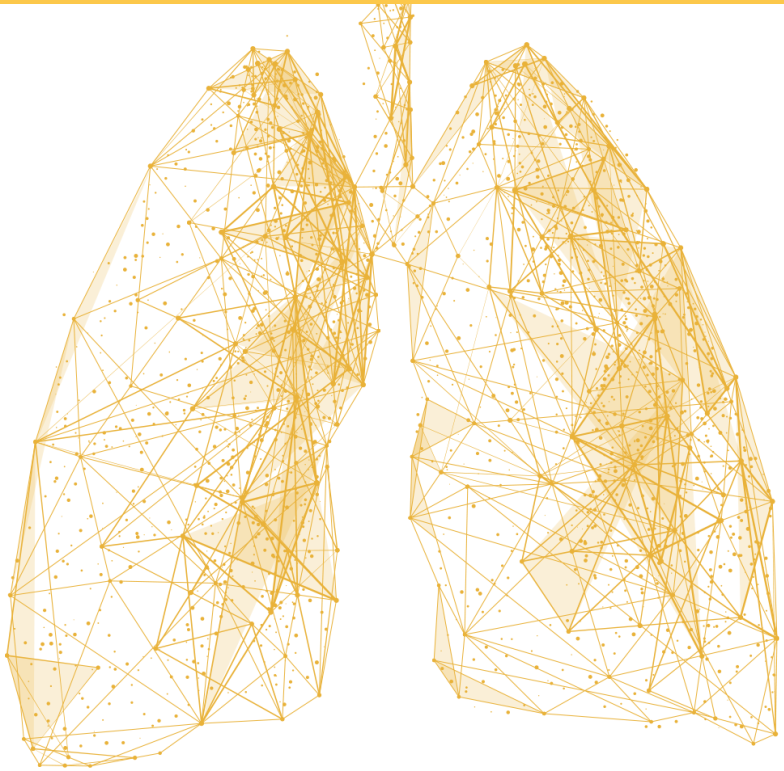
EXPANDING INDICATIONS

TECHNEGAS™

TECHNEGAS

Global Indication Expansion

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

Lung Reduction Intervention

- Application in determining ventilation pre and post lung reduction intervention

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

CTEPH

- Ventilation/Perfusion imaging is recommended
- Up to 40 million patients globally

CLICNICAL CALL FOR ACTION

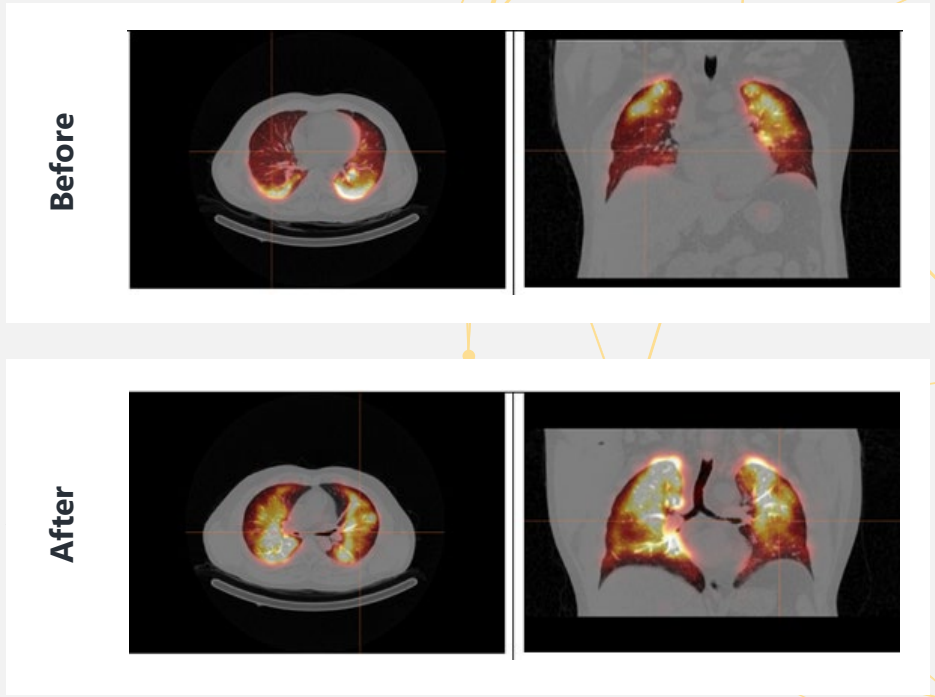
A new way of thinking about respiratory Medicine

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

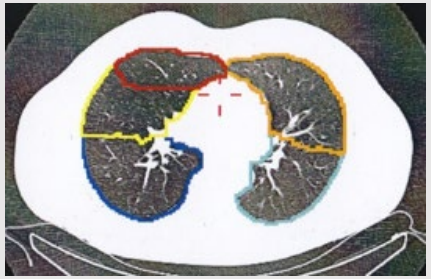
V/Q SPECT provides functional information on ventilation and perfusion of the lungs[1,2]

Low-dose CT provides anatomical information such as fissures delineation[3]

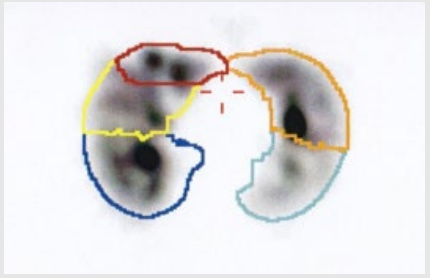
Combination of functional and anatomical information allow for objective results through **quantitative software**[2,3]

VENTILATION SPECT

LOW-DOSE CT



FUSED SPECT/CT



LOBAR DISTRIBUTION OF VENTILATION

		RIGHT				LEFT		
		RUL	RML	RLL	Total	LUL	LLL	Total
Counts	kcts	27% 254	11% 103	28% 261	66% 617	24% 227	10% 95	34% 321
Volume	ml	24% 1256	9% 456	25% 1321	57% 3033	26% 1364	17% 914	43% 2278

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

1. Reinartz P, et al. J Nucl Med 2004; 45: 1501-1508
2. King GG, et al. Semin Nucl Med 2010; 40(6): 467-473
3. Provost K, et al J Nucl Med Technol 2017; 45(3): 185-192

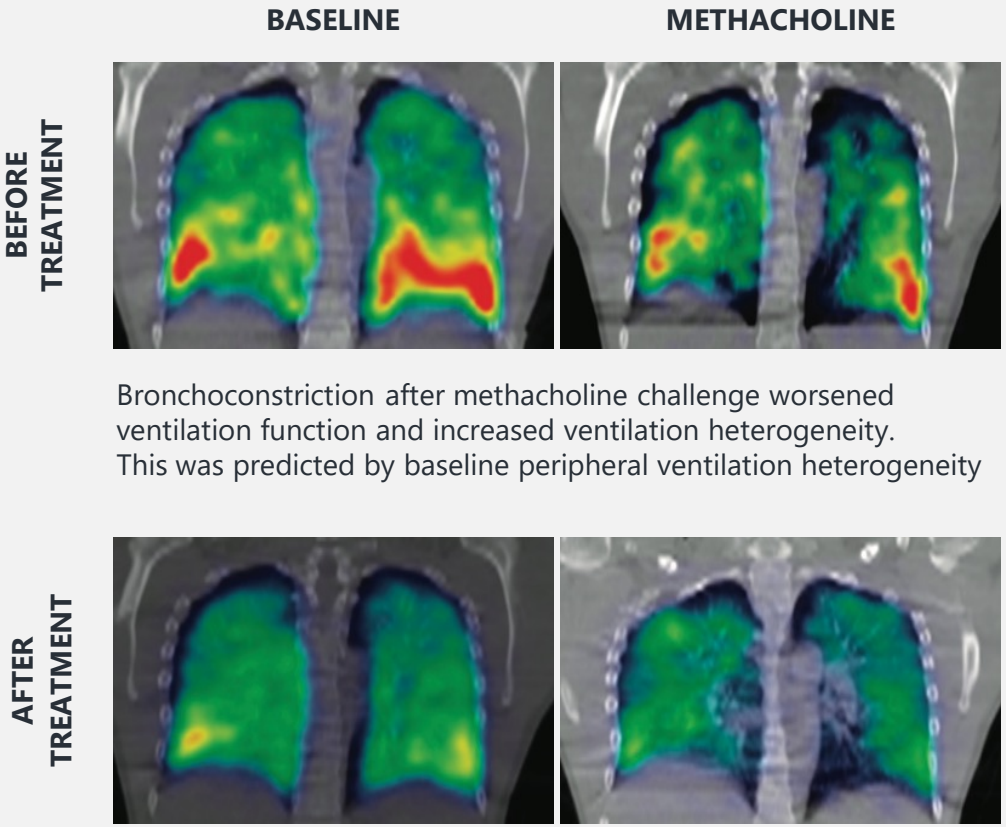
TREATMENT RESPONSE IN ASTHMA PATIENT

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



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

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

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

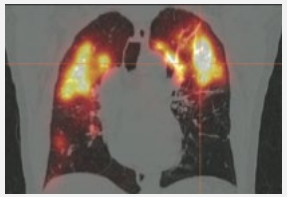
PLANNING LUNG VOLUME REDUCTION SURGERY

Case
#2

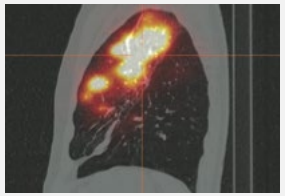
CLINICAL HISTORY
Male patient of 64 years old with emphysema

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

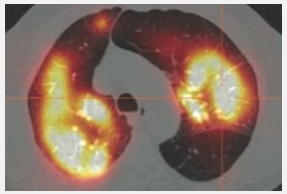
PROTOCOL
VQ SPECT/CT imaging with TECHNEGAS as ventilation agent



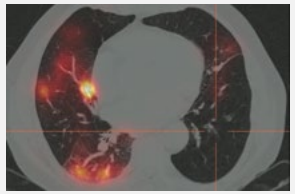
CORONAL FUSION



SAGITTAL FUSION



UPPER LOBES TRANSVERSE FUSION



LOWER LOBES TRANSVERSE FUSION

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 RELATIVE UPTAKE [%]	*Right*	*Left*
UPPER	45 %	36 %
MIDDLE	12 %	N/A
LOWER	**3 %**	**4 %**
TOTAL	60 %	40 %

Lobar 3D quantification provided by Hermes

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

CYCLOPHARM

BUILDING FOR GROWTH