Polarean Imaging plc

(AIM:POLX)

Breathtaking Images:
A Novel, Commercial Stage, Differentiated Pulmonary Functional Imaging Technology

Investor Presentation

January 2021

POLAREAN
BREATHTAKING IMAGES

Today's Presenting Team

Richard Hullihen
CEO
E-mail: rhullihen@polarean.com

- 30+ years of experience in medical imaging
- Previous experience with GEC-Picker International, and Marconi Medical systems
- Founded m2m Imaging with Amphion Innovations

Chuck Osborne
CFO
E-mail: cosborne@polarean.com

- 25+ years of experience in executive roles, including as CFO
- Previous experience with Innocrin Pharmaceuticals, Scynexis and Nobex Corporation

Management Team & Board Of Directors

Richard Hullihen
CEO and Executive Director
GE PICKER

Chuck Osborne
CFO
innocrin precision therapeutics

Bastiaan Driehuys, Ph.D.
Founder and CTO, Executive Director
Duke

Jonathan Allis, Ph.D.
Non-Executive Chairman
BLUE EARTH DIAGNOSTICS
A Bracco Company

Kenneth West
Non-Executive Director
EMBREX

Juergen Laucht
Non-Executive Director
NUKEM Isotopes

Cyrille Petit
Non-Executive Director
BRACCO IMAGING

Polarean Imaging: A Novel, Commercial Stage, Differentiated Pulmonary Imaging Technology Company Targeting Areas of High Unmet Medical Need

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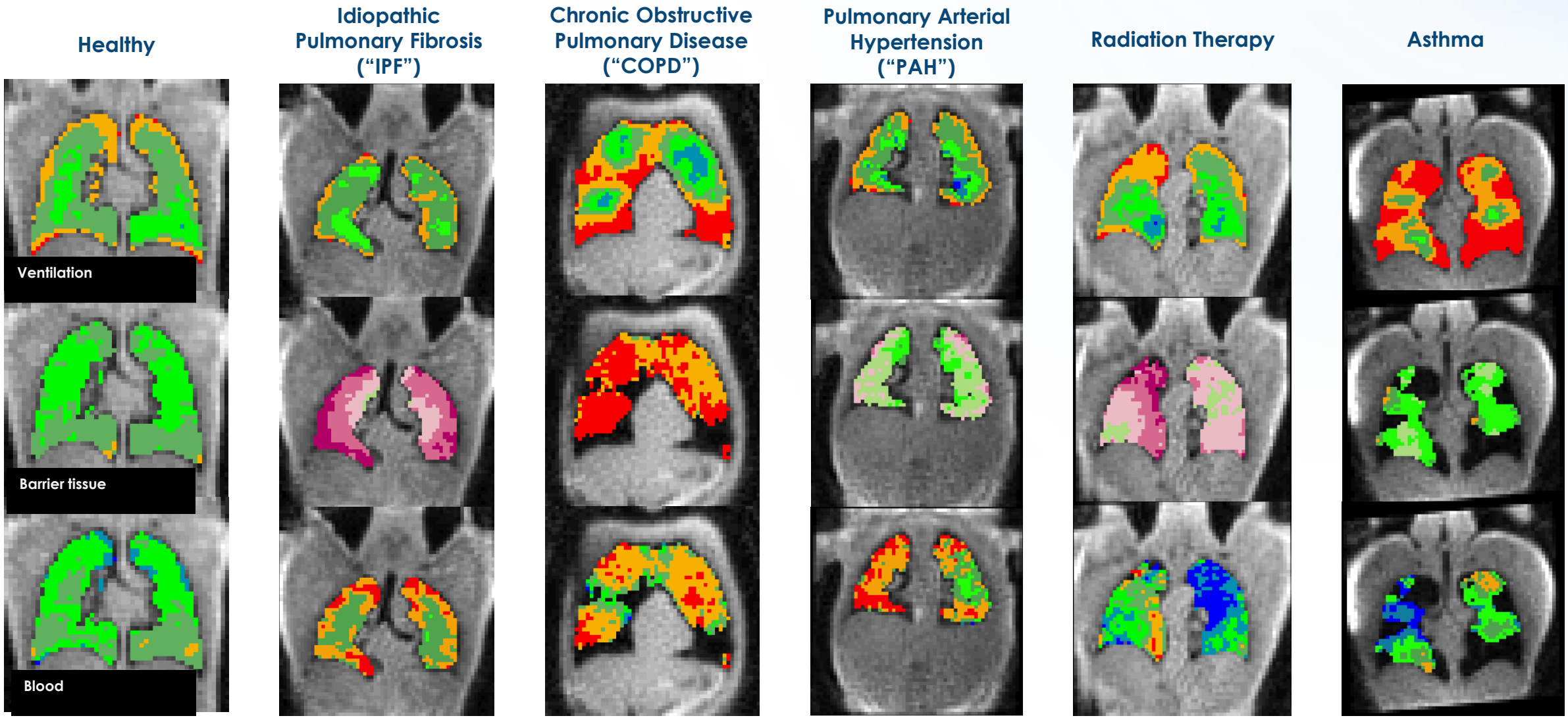
1. Highly innovative drug-device combination using hyperpolarised ^{129}Xe to enhance Magnetic Resonance Imaging (MRI) of the lung, validated by positive Phase III clinical trial results
2. Highly attractive near term commercial opportunity: large total addressable market in multiple indications with high unmet need
3. Impressive hyperpolariser sales traction to the research market; Linde relationship offers end-to-end solution, both xenon supply and distribution infrastructure to healthcare facilities
4. Significant regulatory progress achieved with NDA submission in Q4 2020 and US FDA confirmed target PDUFA action date of October 5th for the first indications
5. Potential development of ^{129}Xe as companion diagnostic as well, e.g. Pulmonx's Zephyr® valve system for the treatment of emphysema
6. Highly experienced management team and board with strong track record of execution of the company strategy, including on the commercial and regulatory fronts

Polarean's Technology is Broadly Applicable Across Multiple Pulmonary Diseases…



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Polarean Imaging: A Commercial-stage, Differentiated Pulmonary Imaging Technology

Company Overview

- Formed in May 2017 after securing all of GE Healthcare's assets in the field of hyperpolarized gas Magnetic Resonance Imaging (MRI)
- Incorporated in UK; Head office in Durham, USA
- Listed on AIM (LSE): POLX
- Market cap: £104m

Key Shareholders

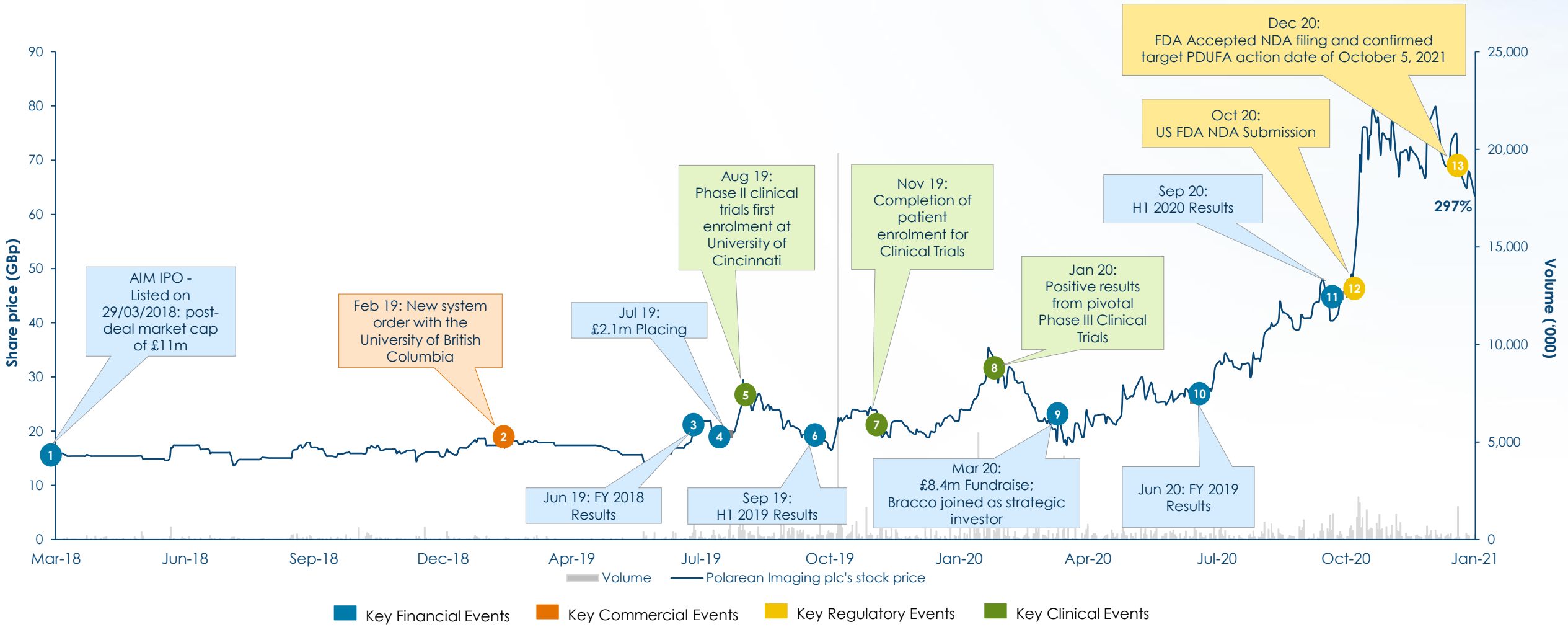
#	Investor Name	% of Capital	Type	Country
1	Amati Global Investors	14.6%	Institutional	
2	Bracco Imaging	7.6%	Strategic	
3	NUKEM Isotopes Imaging	7.0%	Strategic	
4	Chelverton Asset Management	4.8%	Institutional	
5	Tyndall Investment Management	4.1%	Institutional	
6	Canaccord Genuity WM	3.4%	Institutional	

Source: Company Information, Thomson Reuters as of January 4th, 2021

Pulmonary Imaging Technology with a Large TAM

- The Company operates in pulmonary disease diagnostics and monitoring, an area of significant unmet medical need
- **Pulmonary disease affects nearly 40 million people in the US and costs approximately US$150bn**
- **Polarean's drug-device combination product** enables the visualisation of hyperpolarised ^{129}Xe using MRI technology, to help diagnose lung disease earlier, identify the type of intervention likely to benefit a patient, and to monitor the efficacy of treatment
- Hyperpolarised ^{129}Xe MRI is a differentiated pulmonary imaging technology:
  - **Non-invasive and radiation-free functional imaging platform**
  - **More accurate and less harmful** to the patient than current methods
- **New Drug Application (NDA) was filed with the US FDA in October 2020, requesting Hatch Waxman protection, with confirmed target PDUFA action date of 5 October 2021**
- Oxford University Covid-19 Study ongoing: Regional Lung Imaging Using ^{129}Xe of patients with respiratory issues three months after being diagnosed with Covid-19

Consistent Operational Delivery Since IPO Driving Share Price Rerating



Source: Press releases; Thomson Reuters as of January 4th, 2021

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The Scale of the Problem

The Problem

- Pulmonary disease is widespread and growing, affects 40 million Americans
- Heavy US economic burden : US$150 billion/year, similar in EU
- Higher prevalence in countries with poor air quality and smoking use

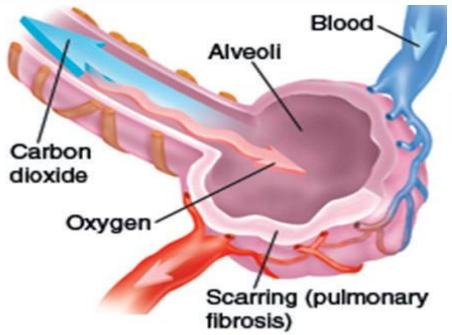
Prevalence of Pulmonary Disease in the US

Disease	Estimated US Population
Asthma	25,000,000
Chronic obstructive pulmonary disease	16,000,000
Pulmonary hypertension	500,000
Interstitial lung disease	225,000
Idiopathic pulmonary fibrosis	100,000
Cystic Fibrosis	30,000

Ventilation, Gas Exchange & Microvascular Bloodflow

Pulmonary disease is characterised by specific patterns of impaired:

1. Ventilation (airflow into and out of the alveoli)
2. Gas exchange (through barrier tissue into and out of bloodstream)
3. Microvascular hemodynamics (bloodflow through capillary bed)



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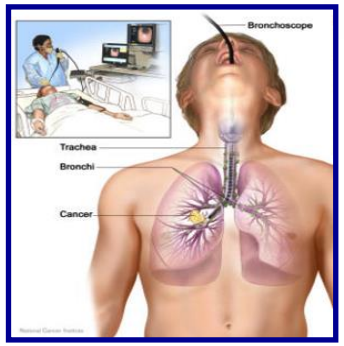
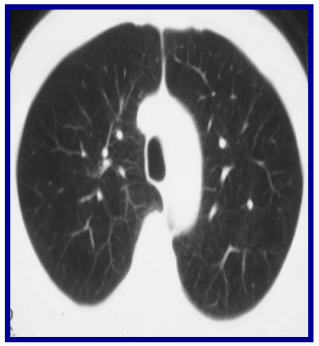
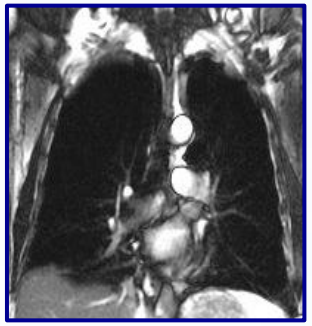
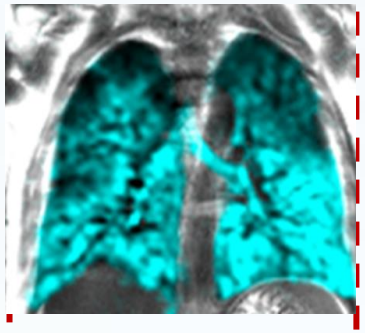
Current Methods to Diagnose and Monitor Lung Disease are Suboptimal

Polarean's Technology is Superior: Quantitative, MRI-based, and Cost-Effective

Methods	Spirometry	Bronchoscopy	Scintigraphy	X-ray, CT	Proton MRI	^{129}Xe MRI
						
Pros	✓ Low Cost ✓ Assesses lung function ✓ No ionizing radiation	✓ Assesses regional lung structure ✓ No ionizing radiation	✓ Regional lung function	✓ Airflow, lung volumes, gas exchange, ✓ Assesses regional lung structure	✓ Assesses regional lung structure ✓ No ionizing radiation	✓ Assesses regional structure and lung function ✓ No ionizing radiation ✓ Visualises effects
Cons	× Effort dependent × No regional information × No information on lung structure	× Invasive procedure × Risk of complications if airways inflamed or damaged by disease	× Poor resolution × Insensitive to disease progression × Ionizing radiation	× Ionizing radiation × Unable to visualise past 6th lung branch	× Poor visualisation of lung associated structure	× Awaiting regulatory approval: Target PDUFA Action Date of October 5th, 2021

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Polarean Imaging's Unique Solution: Hyperpolarised ^{129}Xe MRI

A drug-device combination product that enables the visualisation of hyperpolarised ^{129}Xe using MRI technology in order to help diagnose lung disease earlier, and identify the type of intervention likely required

Process Overview

Drug → **Device (3 components)** → **Administration** → **Outcome**

^{129}Xe Gas Blend

Hyperpolarizer w/ Manifold

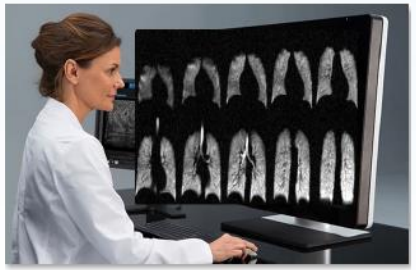
Dose Delivery Bag

Measurement Station, QA

Administer Dose

- ✓ Brief exam requiring <15s breath-hold
- ✓ Easy to administer, not effort-dependent
- ✓ Noninvasive, no radiation, repeatable

A Faster, Simpler, Safer Test



Outcome

- ✓ Quantifiable 3D maps of ventilation and gas exchange
- ✓ Quantitative measures of cardiopulmonary dynamics

Comprehensive Information

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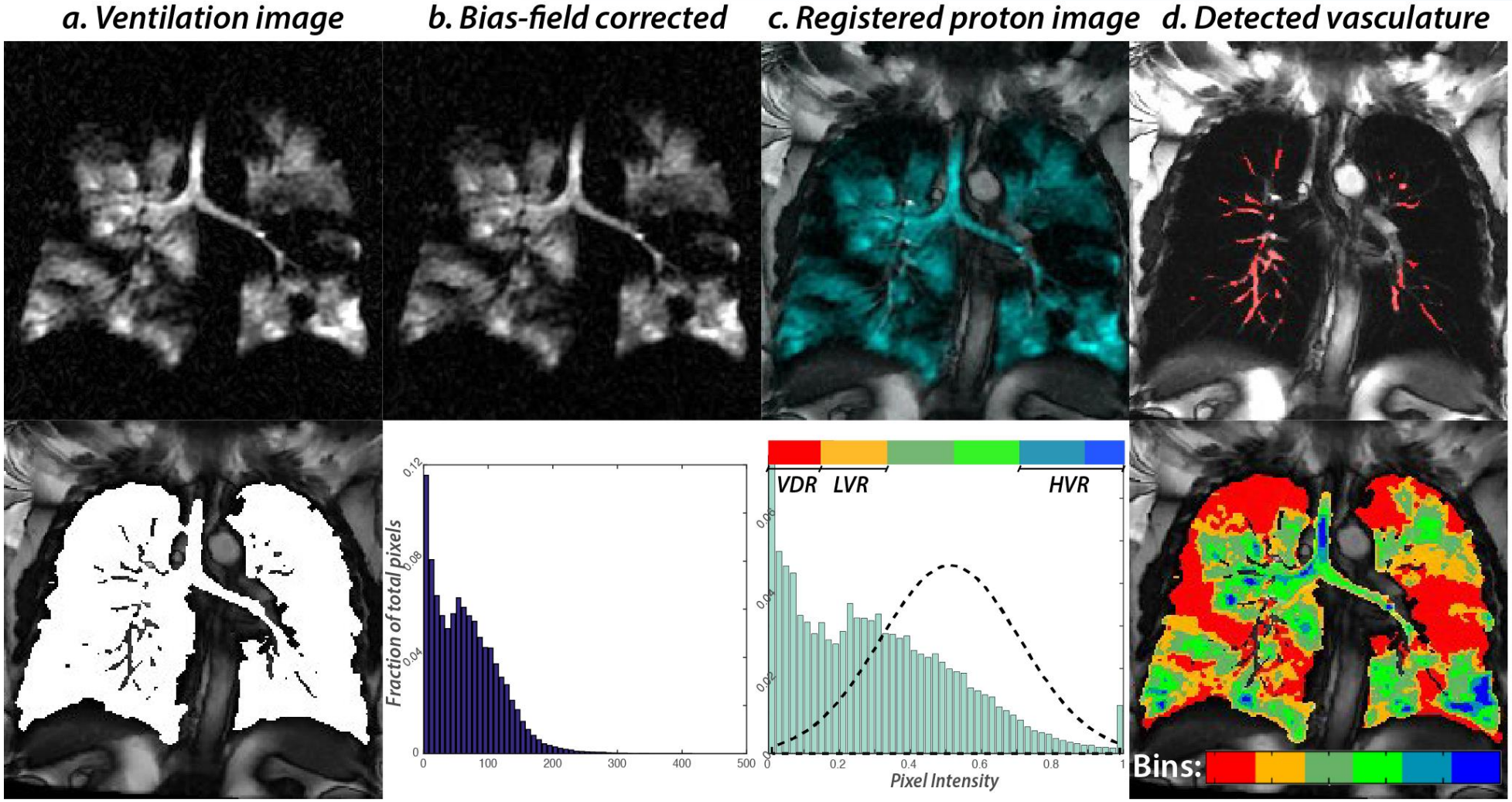
From Qualitative to Quantitative: ^{129}Xe Ventilation MRI



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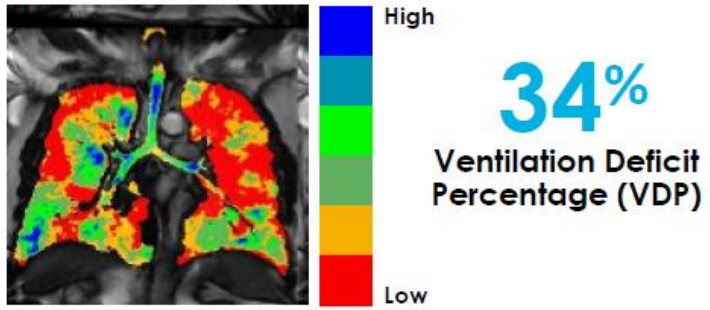
Example of Ventilation Clinical Applications

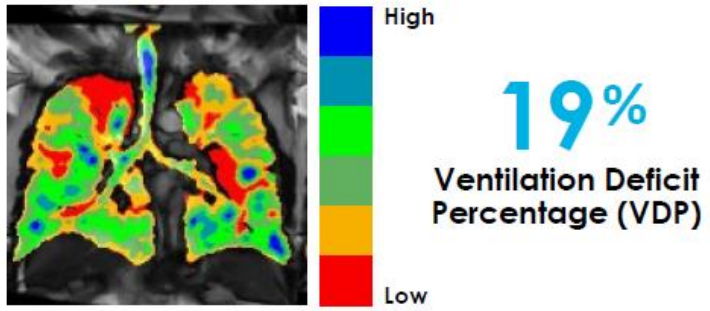
Quantitatively monitor asthma treatment response

Pre-treatment



34%
Ventilation Deficit Percentage (VDP)

Post-treatment



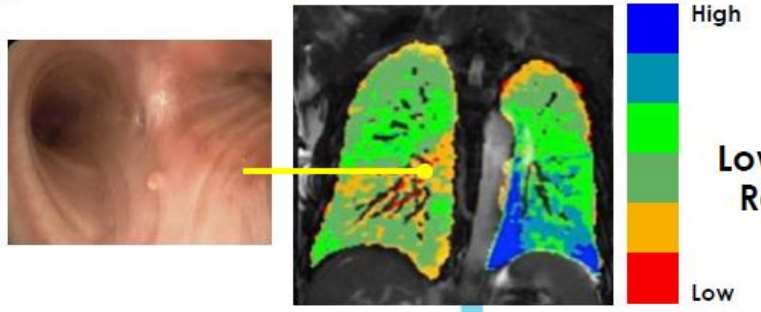
19%
Ventilation Deficit Percentage (VDP)

Research publications in additional lung diseases

- Asthma
- COPD
- Cystic Fibrosis

Regional interventional pulmonology procedure

Pre-Stent Placement



21%
Low Ventilation Region (LVR)

Post-Stent Placement

Stent Placement

9%
Low Ventilation Region (LVR)

Research publications in additional lung diseases

- Stent Placement
- Bronchial Thermoplasty
- Resection
- Radiation Therapy
- Transplant Rejection
- Valve Placement

He M, Driehuys B, Que LG, Huang YCT. Using hyperpolarized Xe-129 MRI to quantify the pulmonary ventilation distribution. *Acad Radiol*. 2016;23(12):1521-1531.
Mahmood K, Ebner L, He M, et al. Novel magnetic resonance imaging for assessment of bronchial stenosis in lung transplant recipients. *Am J Transplant*. 2017;17(7):1895-1904.

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Covid-19: Oxford University Study Using ^{129}Xe MRI Lung Imaging

C-MORE-POST: Post COVID-19 disease follow up imaging using hyperpolarised xenon MRI and CT (POST)

- **Regional Lung Imaging Using Hyperpolarised Xenon Gas of [10] patients aged between 19 and 69, with respiratory issues three months after being diagnosed with Covid-19**
- Eight of the patients had persistent shortness of breath and tiredness three months after being diagnosed with coronavirus, even though none of them had been admitted to intensive care or required ventilation
- No lung dysfunction identified with conventional CT scans had found no problems in their lungs

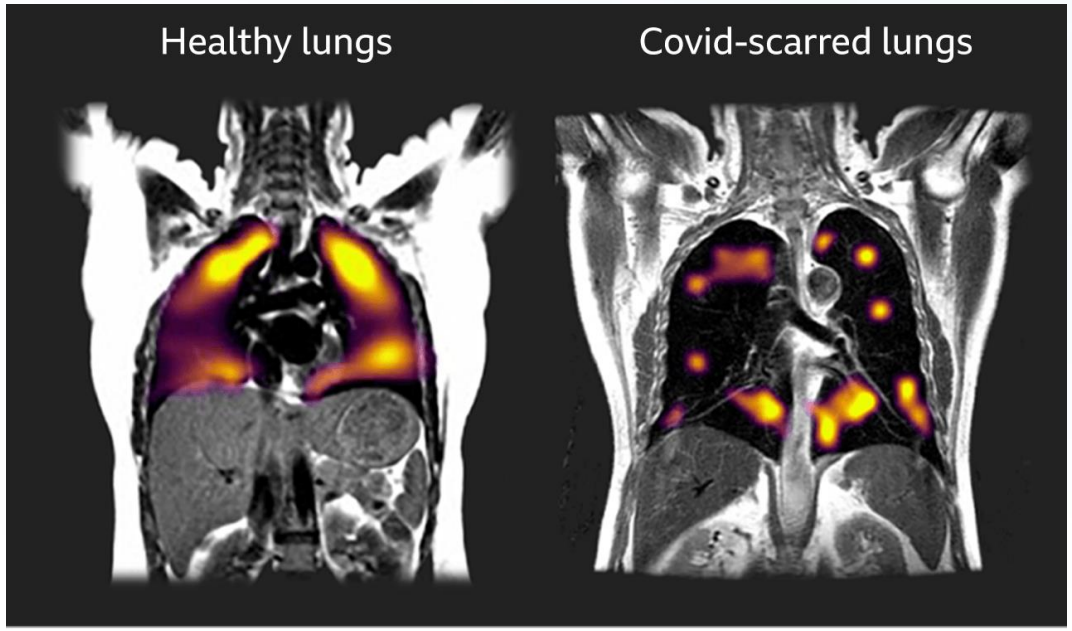
Early findings

- So far, the hyperpolarised xenon MRI technique has identified weakened lung function in all patients who have taken part in the study
- Early data suggests that the ability to transfer oxygen from the lungs into the bloodstream when breathing is visibly impaired for some time
- The damage to lungs from Covid-19 identified with hyperpolarised ^{129}Xe is not visible on a standard MRI or CT scan

Next steps

- The university is now planning a trial of up to 100 people confirm the findings of the study

Lung Imaging Using Hyperpolarised ^{129}Xe MRI: Healthy vs Covid-scarred lungs



Source: Oxford University

In the scarred lungs, on the right, areas of darkness represent parts of the lungs that are having difficulty transporting oxygen into the bloodstream

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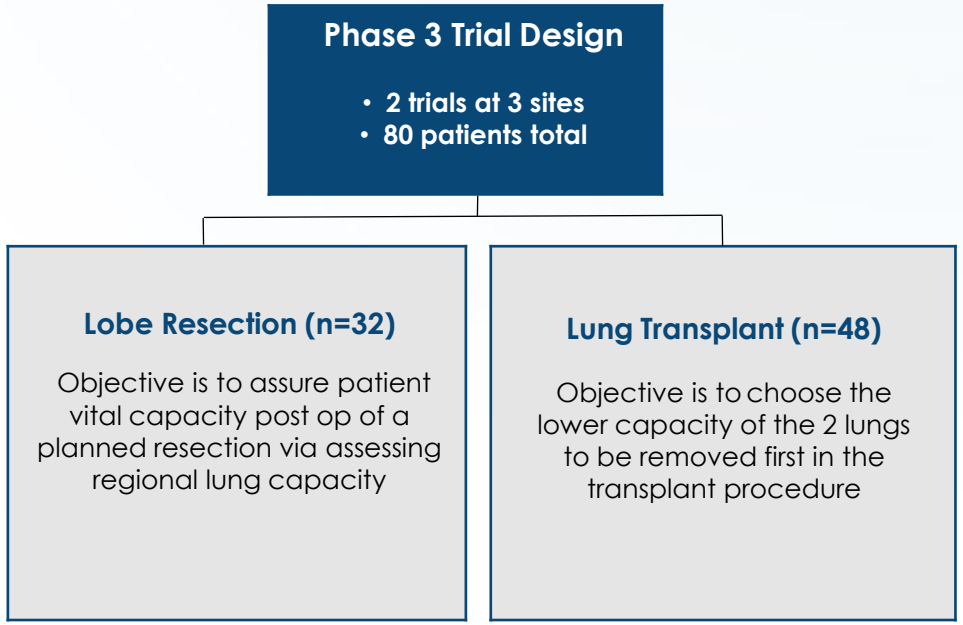
Phase III Clinical Trial Design

FDA Agreed Trial Design: Head to Head Equivalence Trial

- Multi-center, randomised, open-label studies comparing Xenon^{129} gas to Xenon^{133} scintigraphy (an approved technique)
- Measure regional pulmonary function in patients being evaluated for possible lung resection surgery and possible lung transplant surgery
- Primary endpoints were the prospectively defined equivalence (+/- 14.7% margin) when compared to Xenon^{133} scintigraphy imaging of the same patient



Each patient imaged twice (once with Xe^{133} and once with Xe^{129}) and then quantitatively compared

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Phase III Clinical Trial Results

Results Overview

- **Met primary endpoints in both trials**
  - Lung Resection Trial: Intrapatient mean difference of 1.4% with a 95% confidence interval of (-0.75%, 3.60%)
  - Lung Transplant Trial: Intrapatient mean difference of -1.59% with a 95% confidence interval of (-3.69%, 0.50%)
- **Met all requirements for drug safety**
- **Minimal adverse events, no Significant Adverse Events, attributed to 129Xe**

Regulatory Strategy Overview and Key Milestones

Regulatory Strategy

- **Regulated by the FDA as a drug/device combination product**
- **Seek US approval first, and obtain a broad claim that allows our technology to be used in all diseases for clinical diagnosis and monitoring therapy**
- Expand indications into gas exchange and red blood cell transfer, perhaps using COVID 19 as vehicle
- Expand into cardiology and pulmonary vascular disease
- Explore ex-US approval pathways

Milestones

Positive results from Phase 3 clinical trials to support approval for 1st indication, assessment of ventilation in lung transplant and lung resection	**Q1 20** ✓
New Drug Application (NDA) filed and Accepted by US FDA	**Q4 20** ✓
FDA Feedback on Potential Label and Hatch Waxman grant	**Q1-Q3 2021**
Reimbursement: CPT code, coverage, and pricing confirmation	**Q1-Q3 2021**
FDA Approval: Target PDUFA Action Date	**October 5**

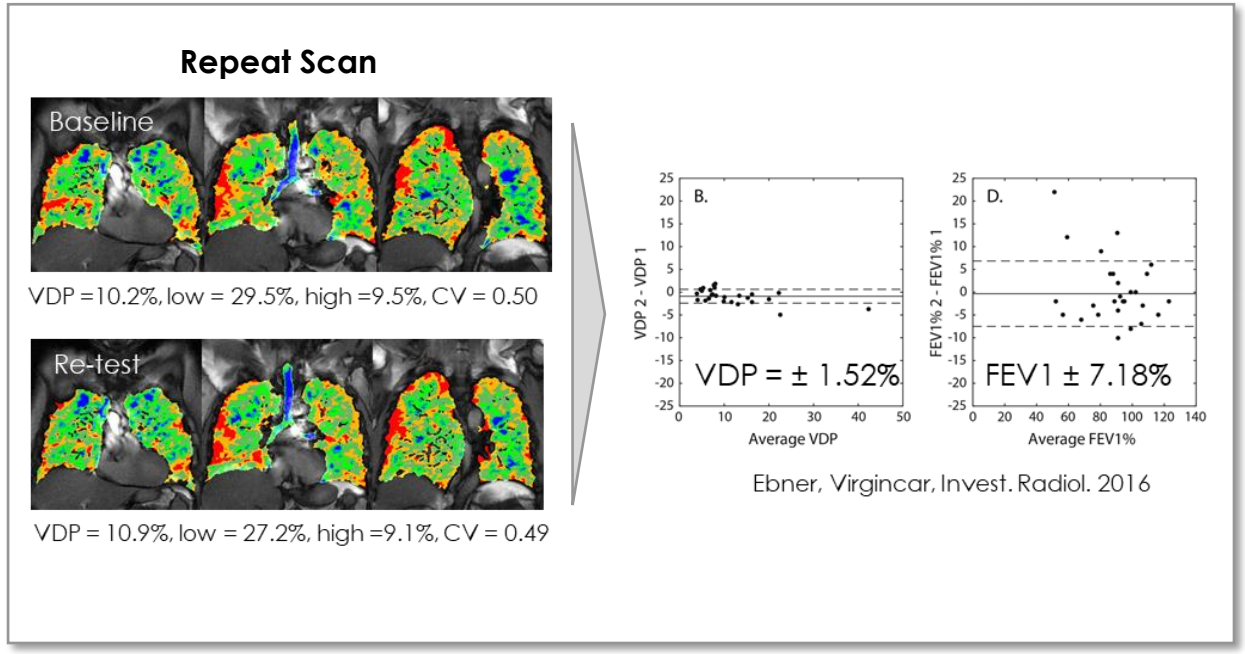
Significant Interest From Researchers and Drug Companies

Cost Reduction Opportunity for Research	Commercial Partnership Opportunities
Sale of polarisers for research use: 24 polarisers are either installed or on order from medical research institutions ✓	In process of investigating corporate partnering opportunities to facilitate drug development and product differentiation
^{129}Xe currently being investigated in 42 clinical trials in the US, with >10 drugs in IPF, PAH, Asthma, and COPD ✓	Potential development as true biomarker
Significant opportunities to reduce cost of clinical trials (sample size, length of trial)	Potential development as a "companion diagnostic" in, for example, pulmonary stents for emphysema

Pharma Partnerships: Potential to Facilitate Drug Development and Product Differentiation and Reduce costs

The Use of ^{129}Xe MRI could simplify clinical trials design, increase precision and lower costs, representing an attractive partnership opportunity for pharma companies

The use of ^{129}Xe MRI can reduce inter-test variability and therefore reduce standard deviation…



… Leading to a reduction of the patient sample size, time required and therefore costs of clinical trials

- Increases power to detect difference (when holding sample size constant)
- Decreases sample size required to show result (when holding power to detect constant), as per below

Diagnostic	Minimum Treatment Difference to Detect	Alpha	Power	Standard Deviation	Numbers of subjects needed
Xe MRI VDP	2%	.05	90%	1.52	24
Spirometry FEV-1	2%	.05	90%	7.18	542

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Overview of Commercial Strategy

	2020	2021			
	4Q	1Q	2Q	3Q	4Q
Regulatory	NDA Submitted and Accepted by FDA ✓				Target PDUFA Action date: 5 October
Commercial		Initial US launch, *direct*, to high end Academic Centers of Excellence, including captive leasing (Same as CT and MRI)			
Reimbursement		Reimbursement Discussions with CMS/Private Payors indicate current assumptions likely conservative, 3yr "New Tech" window on drug pricing			

Centers of Excellence Map: Top Tier (Centers matching all 5 criteria) will be key; total with any COE (n=344)

★ = Site currently with Polarean system (n=9):

1) Duke
2) UNC
3) U Virginia
4) UC Children's
5) UI Chicago
6) U Missouri
7) U Wisconsin
8) U Iowa
9) UKMC
10) MD Anderson

COE Criteria:

1) CF Care Center
2) IPF Care Center
3) PAH Care center
4) Lung Transplant Program
5) Asthma/COPD: Pulmonary and Critical Care Medicine Fellowship Training Programs

- Tier 1 (5 of 5 criteria; n=20)
- Tier 2 (4 of 5 criteria; n=20)
- Tier 3 (3 of 5 criteria; n=32)
- Tier 4 (2 of 3 criteria; n=60)
- Tier 5 (1 of 5 criteria; n=212)

Source: Protean COE Database – Draft, May 15, 2020.

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Broad IP Portfolio and Data Exclusivity Post US Launch

The Group's competitive protections strategy includes:

- Patents including those covering: imaging methods, hyperpolarization methods, RF coil designs that proceed from current time to 2035 and potentially beyond.
- A Submission requesting Hatch Waxman protection for our new drug that in conjunction with our Orange Book may lead to 5-7 years of regulatory exclusivity.
- Additional developments underway in process.

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Appendix

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Overview of Products and Workflow

Polarean's products are compatible with existing MRI systems, directly integrate into existing clinical workflow

Our Drug
Proprietary Xenon^{129} blend

Polariser
Uses laser technology, cryogenics, and magnetic fields to excite Xenon spins

Dispense
Polarised Xenon^{129} into inhalation bag

Quality Assessment (QA) Station
Used to certify and document the polarisation process, per patient batch

Inhale & Image

Torso Xenon RF Coil
Multi-element array RF coil worn by the patient for thoracic imaging in MR

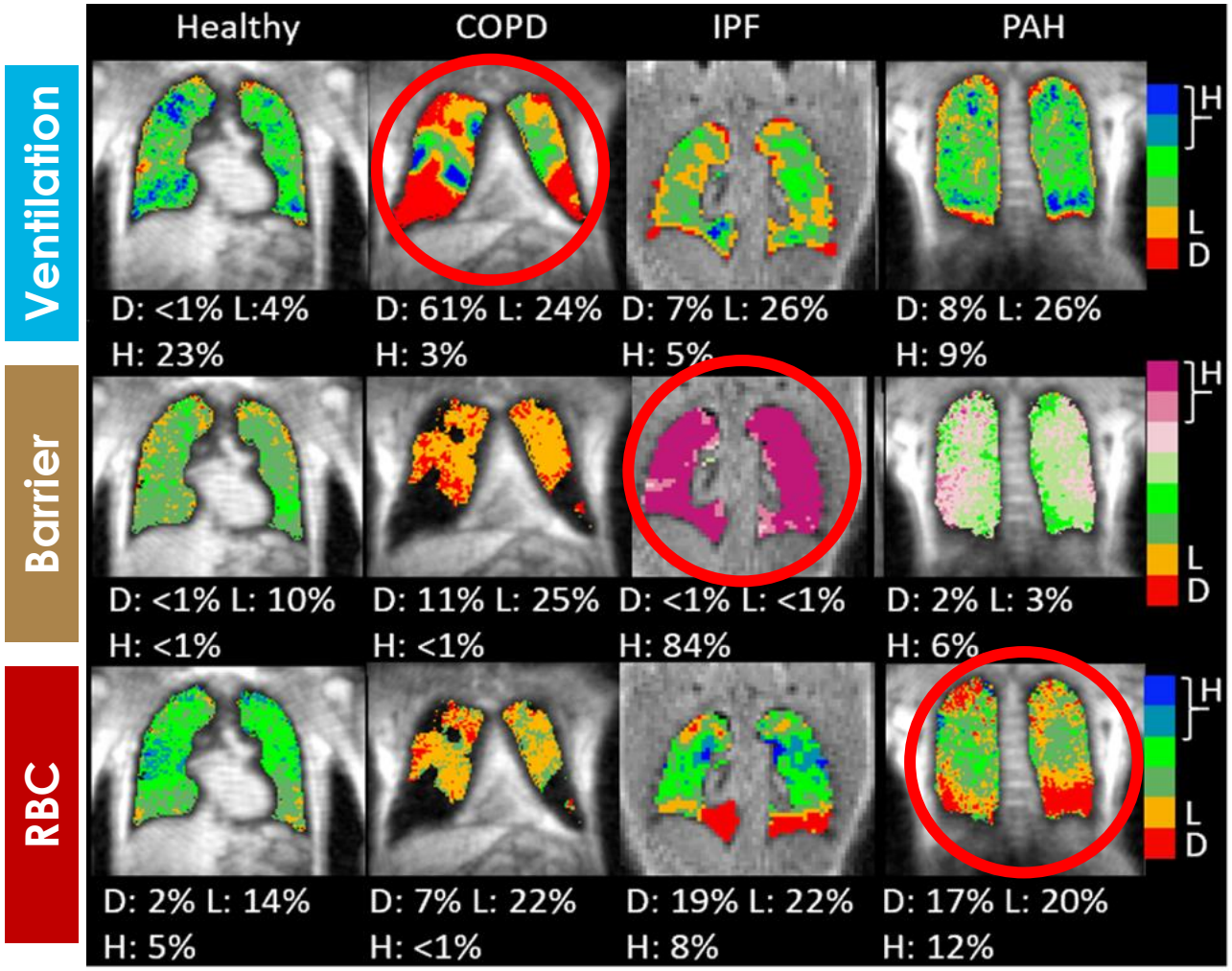
In **10 SECONDS**, we get:

- ✓ 3D multi-slice data
- ✓ Direct ventilation image
- ✓ Barrier tissue signal
- ✓ Arterial blood signal

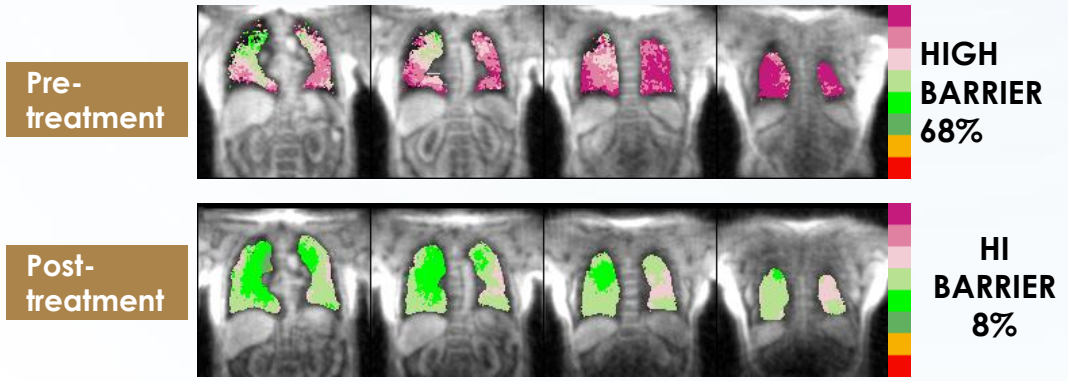
Installed and operating with Siemens, GE and Philips systems…

Example Gas Exchange Clinical Applications

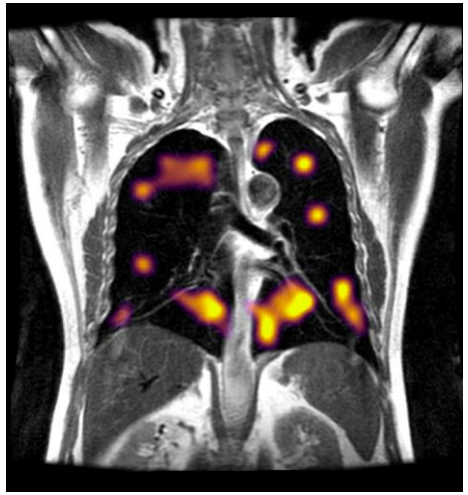
Example 1:
Phenotyping Difficult Cases



Example 2:
Assessing Antifibrotic Treatment Response



Example 3:
COVID-19 Visualizing Chronic Defects



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Phase III Clinical Trial Results (Cont'd)

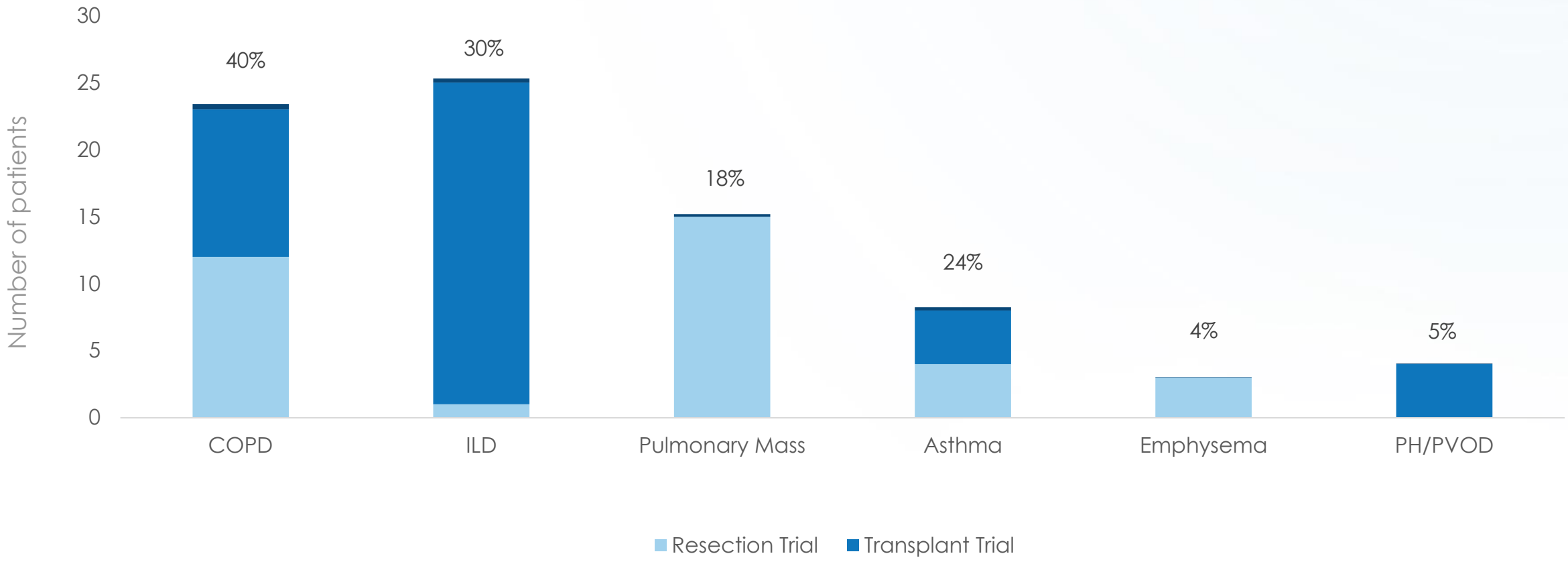
Secondary analyses included:

- By-zone comparison for each lung zone (from the 6-zone analysis) – both studies
- Comparison of predicted versus measured post-operative FEV1 – POL-Xe-001 only
- Secondary analyses results are discussed in 2.7.3 Summary of Clinical Efficacy and each clinical study report

Exploratory analyses for both studies included:

- Patient-level evaluation to determine number of patients exceeding the equivalence margin
- Within-subject difference between ^{129}Xe MRI and ^{133}Xe scintigraphy for the primary endpoint, standardized to the ^{133}Xe scintigraphy measure (e.g. [^{129}Xe-^{133}Xe]/^{133}Xe)
- Exploratory analyses are presented in the individual clinical study reports

Phase III Clinical Trials: Breadth of Respiratory Disorders



Notes: COPD: Chronic obstructive pulmonary disease; ILD: Interstitial lung disease; PH: Pulmonary Hypertension; PVOD: Pulmonary veno-occlusive disease

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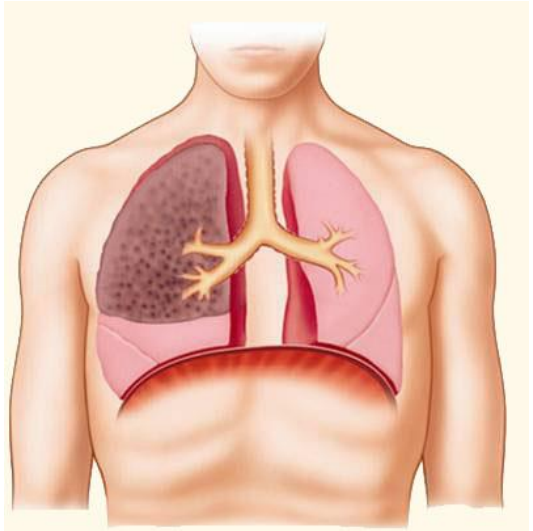
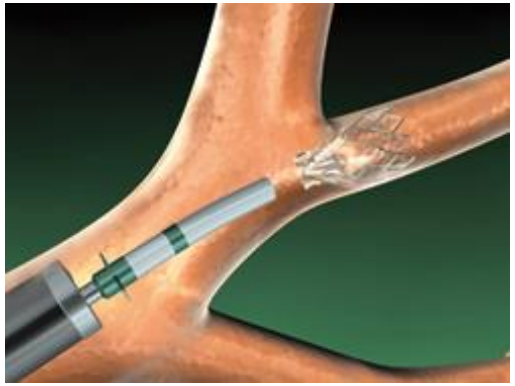
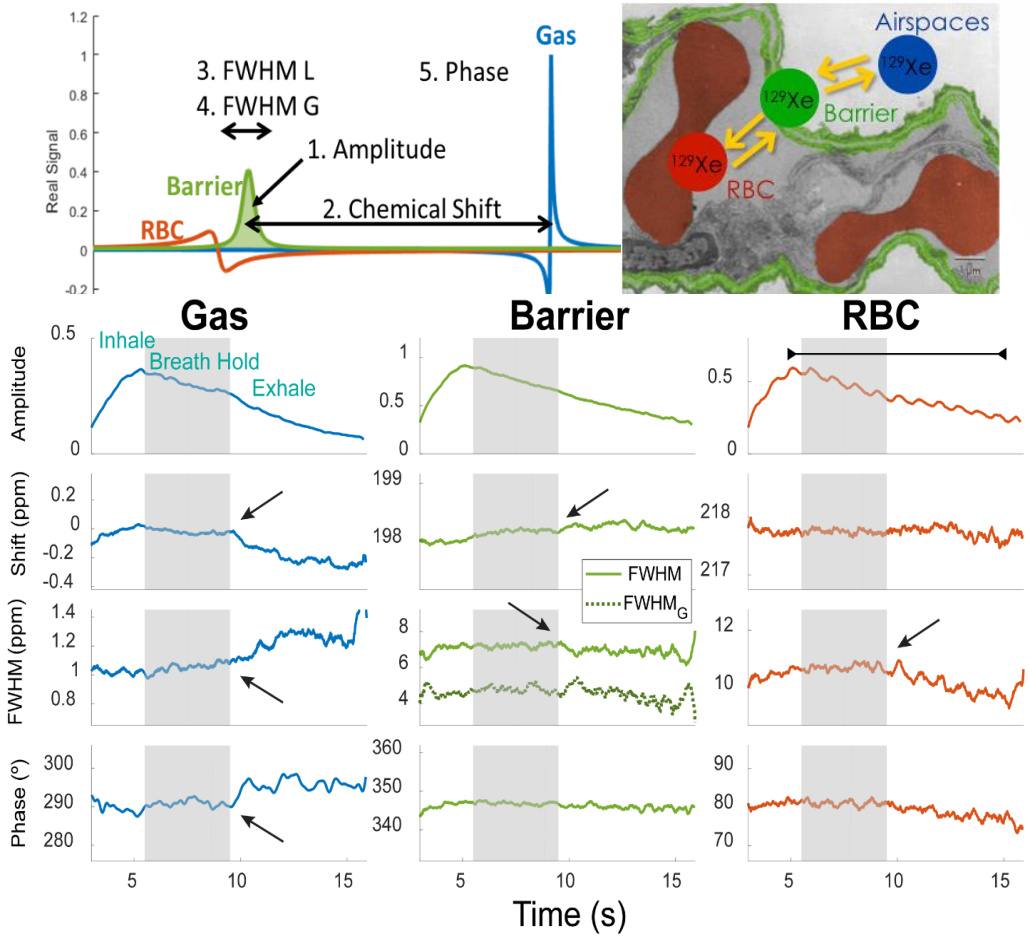
Case Study: ^{129}Xe as Potential Companion Diagnostic for Endobronchial Valves to Treat COPD

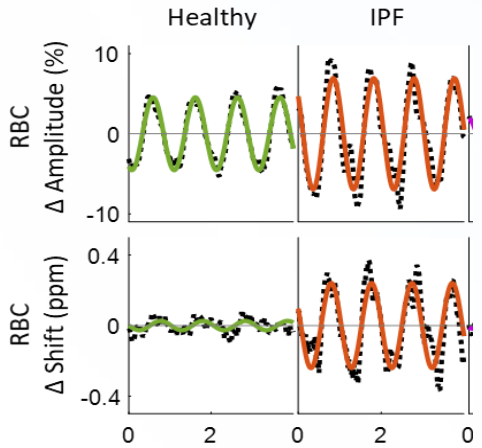
- Potential relief for 3 to 4 million COPD patients with emphysema
- Pulmonx, Spiration Valve System – FDA approved in 2018
- US $10,000 in disposables cost, operating room time, 3- to 5-day hospital stay
- Paid for under major chest DRG

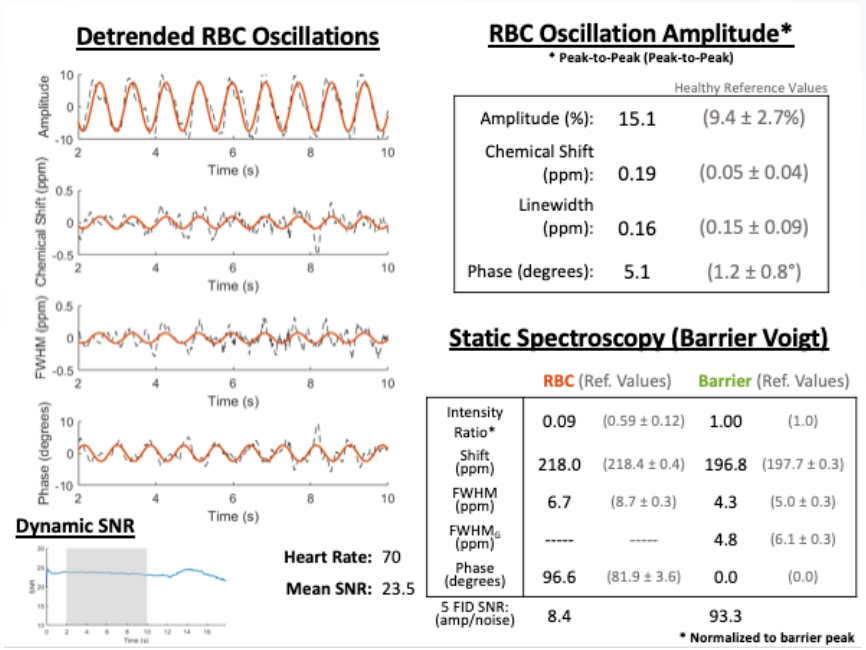




^{129}Xe Spectroscopy adds Hemodynamics & Oxygenation in PVD







Bier et al., NMR in Biomed 2018

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Overview of Hatch-Waxman Act Protection

- **The Hatch-Waxman Act also provides periods of regulatory exclusivity for certain pioneer products** during which FDA review or approval of an Abbreviated New Drug Application ("ANDA")[1] or 505(b)(2)[2] application is precluded
- **If the pioneer product is a New Chemical Entity ("NCE"), the FDA is precluded for a period of 5 years from accepting for review an ANDA or 505(b)(2) application for the same chemical entity**
- Under NCE exclusivity, the FDA may accept an ANDA or 505(b)(2) application for review after 4 years, however, if that application contains a certification that a listed patent is invalid or will not be infringed by the marketing of the applicant's product ("Paragraph IV certification")
- If an ANDA or 505(b)(2) application containing a Paragraph IV certification is accepted for filing by the FDA, the NDA holder or patent owner may then file suit for patent infringement and benefit from a potential 30-month extension of regulatory exclusivity

Source: FDA

(1) An ANDA is submitted for review and potential approval by the FDA of a generic drug

(2) Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act provides a reduced burden of demonstrating safety and effectiveness for an NDA for a product that is similar, but not identical, to an approved product