OPTHEA

OPTHEA REIMAGINED

Unlocking VEGF biology for unmet medical needs

Investor presentation

12 June 2026

Important notice and disclaimer

This presentation has been prepared by Opthea Limited (ABN 32 006 340 567) ("Opthea" or "Company") to provide summary information about Opthea and its affiliates and subsidiaries (the "Opthea Group") and their activities. The information contained in this presentation is of general background, does not purport to be complete, is provided as at the date of this presentation and remains subject to change without notice. Except as otherwise required by law, Opthea has no obligation to update or correct this presentation. This presentation should be read in conjunction with Opthea's other periodic and continuous disclosure announcements lodged with the Australian Securities Exchange ("ASX"), which are available at www.asx.com.au.

The information contained in this presentation does not constitute investment or financial product advice (nor taxation or legal advice) for investors or potential investors, who should consider seeking independent professional advice depending upon their specific investment objectives, financial situation or particular needs. Nothing in this presentation constitutes or forms part of any offer, invitation, solicitation or recommendation to buy or sell securities.

All references to dollar amounts are references to Australian dollars ("A$" or "$") unless otherwise stated. This presentation is unaudited.

This presentation contains certain forward-looking statements. Forward looking statements can generally be identified by the use of words such as "project", "foresee", "forecast", "plan", "expect", "aim", "ambition", "aspiration", "potential", "goal", "objective", "target", "intend", "see", "anticipate", "expect", "believe", "trend", "estimate", "may", "could", "should", "would", "need", "will", "must", "commit", "guidance" or similar expressions. Indications of, and guidance on, future earnings and financial position and performance are also forward-looking statements. Forward-looking statements may also be made, verbally or in writing, by members of Opthea Group's management or Opthea's board in connection with this presentation. Such statements are subject to the same limitations, uncertainties, assumptions and disclaimers set out in this presentation. Forward looking statements, opinions, and estimates provided in this presentation involve a number of risks, assumptions and contingencies, many of which are beyond Opthea's control and which are subject to change without notice. It is believed that the expectations reflected in these forward-looking statements, opinions and estimates are reasonable at this time, but there can be no assurance that actual outcomes will not differ materially from these statements. Such forward looking statements, opinions and estimates are provided as a general guide only, should not be relied on as an indication or guarantee of future performance. You should not place undue reliance on forward looking statements. An investment in Opthea securities is subject to investment and other known and unknown risks, some of which are beyond the control of the Opthea Group including risks inherent in the regulatory processes, delays in clinical trials, results of clinical trials, contractual risks, risks associated with patent protection, future capital needs or other general risks or factors, along with those factors outlined in the most recent Opthea Annual Report. Opthea does not guarantee any particular rate of return or the performance of the Opthea Group nor does it guarantee the repayment of capital from Opthea or any particular tax treatment.

This presentation may include statistical and other industry and market data obtained from industry publications and research, surveys and studies conducted by third parties as well as our own estimates of potential market opportunities. Such data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. Industry publications and third party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our estimates of the potential market opportunities include several key assumptions based on our industry knowledge, industry publications, third party research and other surveys, which may be based on a small sample size and may fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions.

No representation or warranty, express or implied, is made as to the accuracy, completeness or reliability of the information. To the fullest extent permitted by law, neither Opthea nor any other member of the Opthea Group nor any of their or its directors, officers, employees and advisers accept any liability for any loss arising from reliance on this presentation or its contents.
This presentation may contain trademarks and other trade names of third parties, which are the property of their respective owners. Third party trademarks and trade names used in this presentation belong to the relevant owners and use is not intended to represent sponsorship, approval or association by or with any of the Opthea Group.

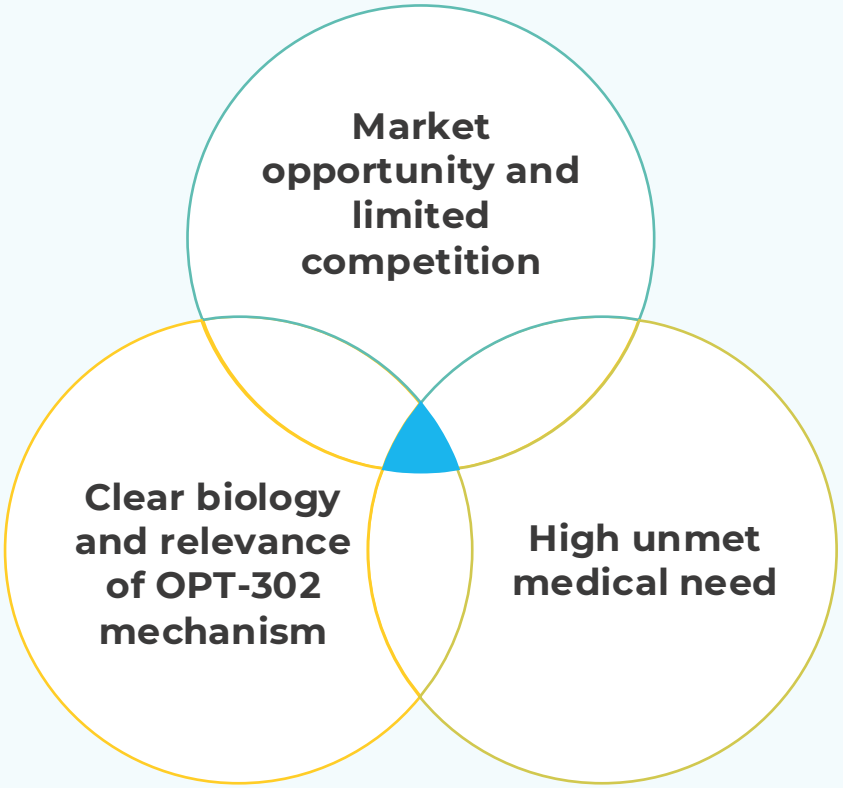
Agenda

Rebuilding Opthea

Building a focused rare disease company around VEGFR-3 biology

- Existing clinical-stage biologic with extensive prior human experience
- Strategic transition toward rare pulmonary and lymphatic disease
- Targeting VEGF-C and VEGF-D signalling through VEGFR-3 modulation
- Focused rare disease strategy built around disciplined execution and capital efficiency
- Reinstatement and operational rebuilding underway

The rare disease opportunity for OPT-302



What we learned from the OPT-302 review

- Comprehensive review confirmed a high-quality clinical, manufacturing, and development package
- No significant safety, CMC, or data integrity concerns identified
- Wet AMD outcome appears driven largely by unexpectedly strong control-arm performance rather than an identifiable development failure
- VEGF-C/VEGF-D biology remains scientifically compelling and clinically validated
- Greatest opportunity may lie in diseases where VEGFR-3 signalling is a primary driver of pathology
- Company strategy focused on disciplined capital deployment and rapid evaluation of high-probability rare disease opportunities
- Company has selected LAM as greatest potential in near term

LAM: A focused path to clinical proof-of-concept

- Mechanism-driven indication with strong biological rationale
- Rare disease population with significant unmet need
- Established specialist network and efficient recruitment model
- Biomarkers and imaging endpoints support early decision-making
- Potential inhaled delivery directly to the site of disease
- Capital-efficient development strategy
- Opportunity to create value through rapid biological validation

Why LAM

Lymphangioleiomyomatosis (LAM), a rare progressive disease predominantly affecting women's lungs

- VEGF-C and VEGF-D biology strongly implicated in lymphatic dysfunction in LAM
- Existing therapies are not curative and disease progression often resumes off treatment
- Specialist global clinic network and defined patient populations support efficient rare disease development
- Strong biomarker framework including VEGF-D
- Opportunity for focused studies with meaningful mechanistic endpoints and defined patient populations
- Approximately ~70 specialist LAM centres globally support concentrated patient management

No existing cure

3-8 per 1M

Adult women impacted by LAM

More recent studies suggest ~20–26 per 1m[1,2]

5-7K

Estimated diagnosed and addressable US patient population

15-30K

Estimated global patient population[3]

OPTHEA

1. Prevalence is reported as 3.4-7.8 cases per million women but newer Northern Europe data suggest 20.9–26.04 per million adult women, consistent with underdiagnosis.
2. Issaka, R. B., et al. (2009). See Appendix for full citation.
3. Based on low estimates

Scientific rationale

Targeting VEGF-C/D pathway in LAM

“Lock and key” system

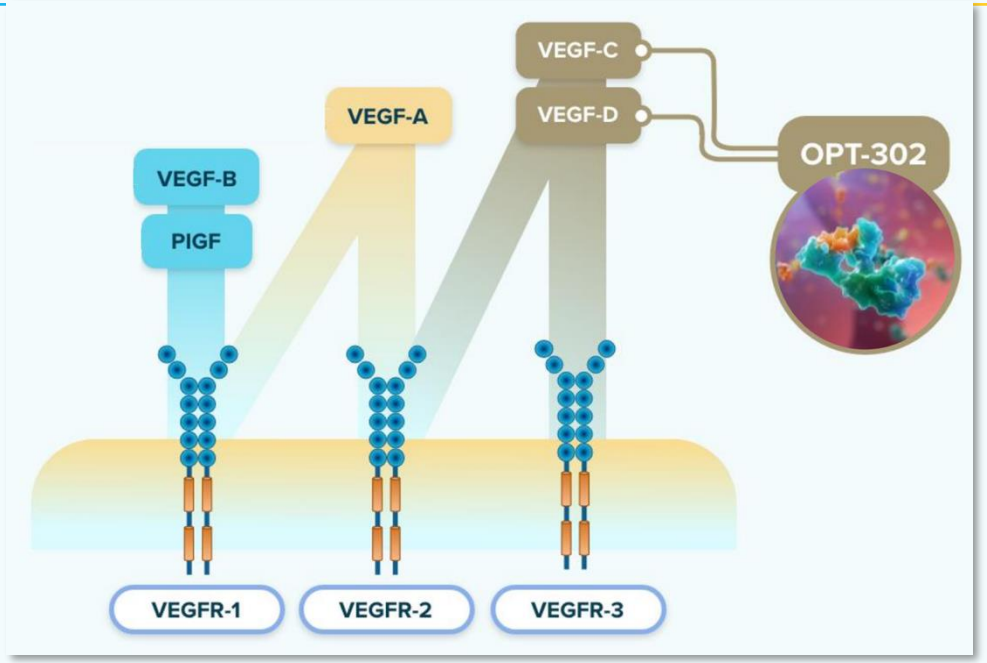
VEGF-C and VEGF-D are growth signals that tell lymphatic vessels to grow and become more permeable.

VEGFR-3 is the receptor on lymphatic cells that receives these signals.

When VEGF-C or VEGF-D bind to VEGFR-3, the lymphatic system gets a strong “expand and remodel” message. In LAM, this leads to abnormal, dilated, and leaky lymphatic vessels.

The problem[1]

In LAM, excess VEGF-D (and VEGF-C) activates VEGFR-3 on lymphatic vessels, driving abnormal, leaky lymphatics in the lungs and accelerating disease progression.



The mechanism

By trapping VEGF-C/D with OPT-302 before they activate VEGFR-3, we aim to dampen the lymphatic signaling that fuels LAM, aiming to stabilise lung function and slow disease progression.

1. Issaka, R. B., et al. (2009). See Appendix for full citation.

OPT-302

A VEGF-C/D “trap” suited to LAM[1, 2]

Fitting the Mechanism of Action with the underlying pathology

OPT-302 a VEGF-C/D “trap” protein designed to bind and sequester VEGF-C and VEGF-D, preventing activation of VEGFR-3–mediated lymphatic signaling

What is de-risked	Why it fits LAM	What happens next
• Target biology and mechanism are well characterised in lymphatic biology. • OPT-302 has an established molecular mechanism and data informing manufacturability and safety monitoring. • US$120m already invested in commercial manufacturing of OPT-302	• Mechanism directly aligned with abnormal lymphatic signaling observed in LAM • Existing molecule already supported by extensive manufacturing and clinical experience • Potential to complement rather than replace current mTOR-based therapy	• Goal is to build a differentiated rare disease program through rigorous staged development.

OPTHEA

1. Jackson TL. (2023), See Appendix for full citation.
2. McCormack FX (2016). See Appendix for full citation.

Building a capital efficient rare disease company

Focused execution to unlock value for patients and shareholders

Existing clinical-stage molecule with substantial historical investment already completed

Leveraging prior toxicology and clinical experience and $US120m already invested in commercial manufacturing of OPT-302

Streamlined operational structure and outsourced development model

Australian R&D tax incentives support efficient capital deployment

Focused rare disease development designed around defined decision points and stop criteria

Objective is disciplined value creation through focused execution and measured risk-taking

Status Update

OPERATIONAL PROGRESS

- Reinstatement on ASX effective 3 June 2026
- Extraordinary General Meeting scheduled for 3 July 2026 to consider a resolution to change Company name to Ceryvyn Therapeutics (ASX:CYV)
- Engagement underway with specialist rare disease clinical and preclinical partners
- Scientific Advisory Board (SAB) established with internationally recognized pulmonary and LAM experts
- A$31.2 million in cash and cash equivalents (as at 31 March 2026)
- No debt following settlement of Development Funding Agreement in August 2025

PRE-CLINICAL PROGRESS

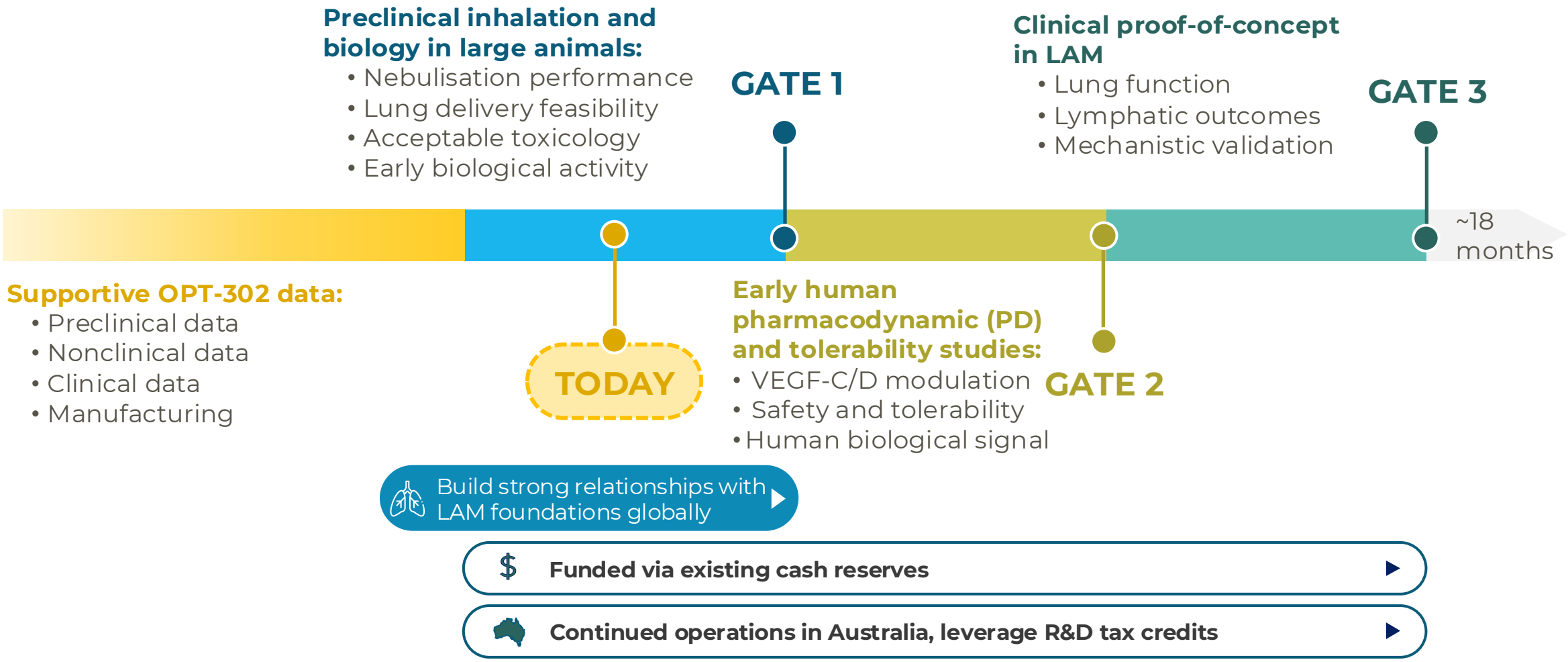
- Excellent existing tox package
- On track in development of nebulised OPT-302
- Third parties contracted for preclinical and nonclinical development plan
- Intellectual property development ongoing

Supportive OPT-302 data:
- Preclinical data
- Nonclinical data
- Clinical data
- Manufacturing

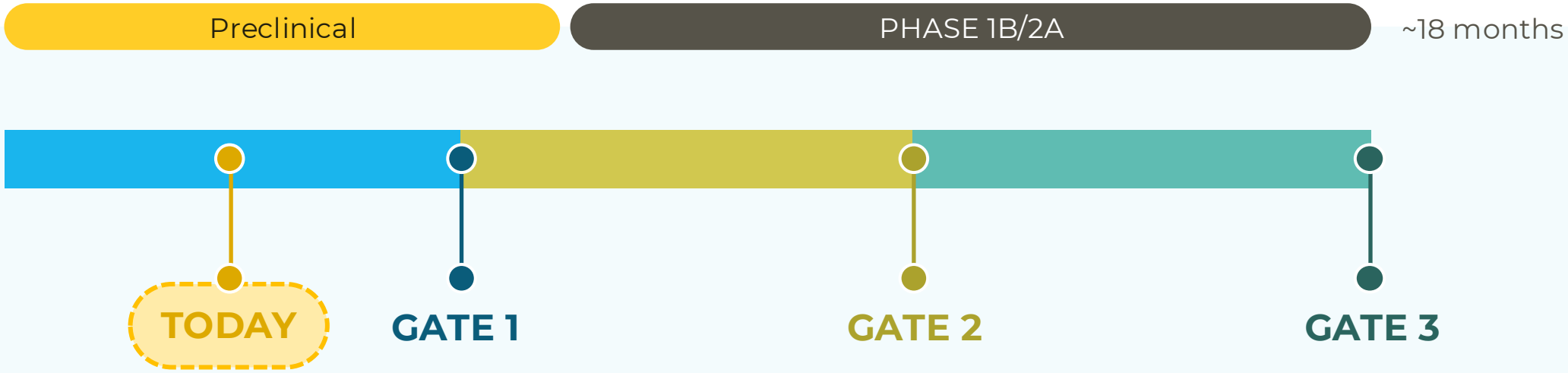
Preclinical biology and inhalation in large animals:
- LAM-relevant effects
- Acceptable safety

Stage-gated plan

Rigorous data-driven milestones and pre-defined stop criteria at each gate



Potential clinical development program



Proposed 6-month Phase 1b/2a study of OPT-302 in LAM*

OBJECTIVE — Test whether OPT-302 adds biological and clinical benefit in LAM patients

PRIMARY FOCUS

- Safety and tolerability
- Pharmacokinetics
- Immunogenicity
- VEGF-C / VEGF-D target engagement

KEY 3- and 6- MONTH MEASURE

- Hyperpolarised ^{129}Xe MRI
- FEV1
- DLCO (Carbon Monoxide Diffusing Capacity of the Lungs)
- 6-minute walk distance
- Oxygen desaturation
- Serum biomarkers (e.g. VEGF-D)

EXPLORATORY MEASURE

- Quantitative CT cyst burden
- Quality of life / dyspnoea
- Pneumothorax, chylous events, oxygen use

GOAL — **Show early safety, target engagement, and a signal of improved ventilation or gas exchange by three months, with confirmation at six months**

* Final details will be subject to review by full clinical and scientific board

Scientific and operational leadership

Strong executional capability and expertise supporting program development

- Streamlined Board and operating structure focused on execution, led by Executive Chair Dr Jeremy Levin, with non-executive directors Mr Lawrence Gozlan and Ms Kathy Connell
- Deep experience across biotechnology, rare disease development and capital allocation
- Scientific Advisory Board includes globally recognised pulmonary and LAM experts
- Strong patient and physician engagement strategy
- Commitment to external scientific challenge and data-driven decision-making
- Focus on rebuilding credibility through disciplined execution and transparency

Scientific Advisory Board

We have brought together global thought leaders in LAM with decades of clinical experience and patient collaboration to inform our development efforts.

Frank McCormack
Professor of Pulmonary Medicine
SAB Co-Chair

Deborah Yates
Respiratory Physician
SAB Co-Chair

Beth Daugherity
Patient-Scientist

Building a unique rare diseases company[1,2,3]

Rare diseases support focused development pathways and concentrated specialist care

Existing diagnostic framework and biomarker use support patient identification

Potential orphan-drug advantages across major jurisdictions

Smaller patient populations may support efficient clinical development

Commercial opportunity driven by unmet need, chronic disease burden and specialist treatment networks

1. Estimating the clinical cost of drug development for orphan versus non-orphan drugs
2. FDA approval, clinical trial evidence, efficacy, epidemiology, and price for non-orphan and ultra-rare, rare, and common orphan cancer drug indications: cross sectional analysis | The BMJ
3. Disentangling the Cost of Orphan Drugs Marketed in the United States, Hana Althobaiti et al.

Corporate and financial overview

Company name[1]
Opthea Limited

ASX ticker[1]
OPT

Total ordinary shares on issue
1,367,978,173

Share price[2]
A$0.014

Market capitalisation[2]
A$19.15 million

Financial position

A$31.2 million cash and cash equivalents (as at 31 March 2026)

No debt following settlement of Development Funding Agreement in August 2025

Cash is sufficient to support the three-stage LAM development program

1. Extraordinary General Meeting scheduled for 3 July 2026 to consider a resolution to change Company name to Ceryvyn Therapeutics (ASX:CYV)
2. As at 11 June 2026

Conclusion

- Existing clinical-stage biologic with differentiated VEGF-C/D mechanism
- Building a focused rare disease company centred on VEGFR-3 biology
- Encouraging early operational progress supporting inhaled delivery evaluation
- Disciplined, stage-gated framework with predefined milestones and stop criteria
- Strong scientific, operational and governance capabilities in place
- Rebuilding the company on focused, stage-gated rare disease development

Q&A

Appendix

Citations

- Baldwin M. *OPT-302: A novel therapy for Wet AMD*. Corporate Presentation (Opthea Limited; ASX PDF). January 2017. p. 11 (slide 11) (states "OPT-302 (soluble VEGFR-3, VEGF-C/-D 'Trap')").
- Issaka, R. B., et al. (2009). Vascular Endothelial Growth Factors C and D Induce Proliferation of Lymphangioleiomyomatosis Cells through Autocrine Crosstalk with Endothelium. *The American Journal of Pathology, 175*(4), 1410–1420. https://doi.org/10.2353/ajpath.2009.080830
- Jackson TL et al. *A Randomized Controlled Trial of OPT-302, a VEGF-C/D Inhibitor for Neovascular Age-Related Macular Degeneration*. Ophthalmology. 2023 Jun; 130(6):588–597. Epub 2023 Feb 6.
- Launch Price and Access Report: Drug Approvals from 2022–2024 (Final Report). Institute for Clinical and Economic Review (ICER). Report. 2025 Oct 23. p. 11 (Table 3.2: inflation-adjusted median annual list and net launch prices for 2022–2024 approvals).
- Lynn E et al . *Am J Respir Crit Care Med*. 2024 Feb 15;209(4):456–459. doi:10.1164/rccm.202310-1736LE.
- McCormack FX et al . *Official American Thoracic Society/Japanese Respiratory Society Clinical Practice Guidelines: Lymphangioleiomyomatosis Diagnosis and Management*. Am J Respir Crit Care Med. 2016 Sep 15;194(6):748–761.
- McCormack FX. et al (2011) *Efficacy and Safety of Sirolimus in Lymphangioleiomyomatosis*, The New England Journal Of Medicine Vol 364 No 17.: Efficacy and Safety of Sirolimus in Lymphangioleiomyomatosis | New England Journal of Medicine

LAM organisations

A family of networks and resources for individuals with LAM across the globe

Opthea will build on the substantial work completed and ongoing with the global LAM foundations, clinics and communities, establishing long-term partnerships

THE LAM FOUNDATION
A BREATH OF HOPE

Living with LAM
www.livingwithlam.org

Foundation for Women's Health

Lung Foundation Australia

~70 global LAM clinics, patient data bases, biospecimen repository, focused International LAM research conference & LAMposium

ATS

TSC Alliance®

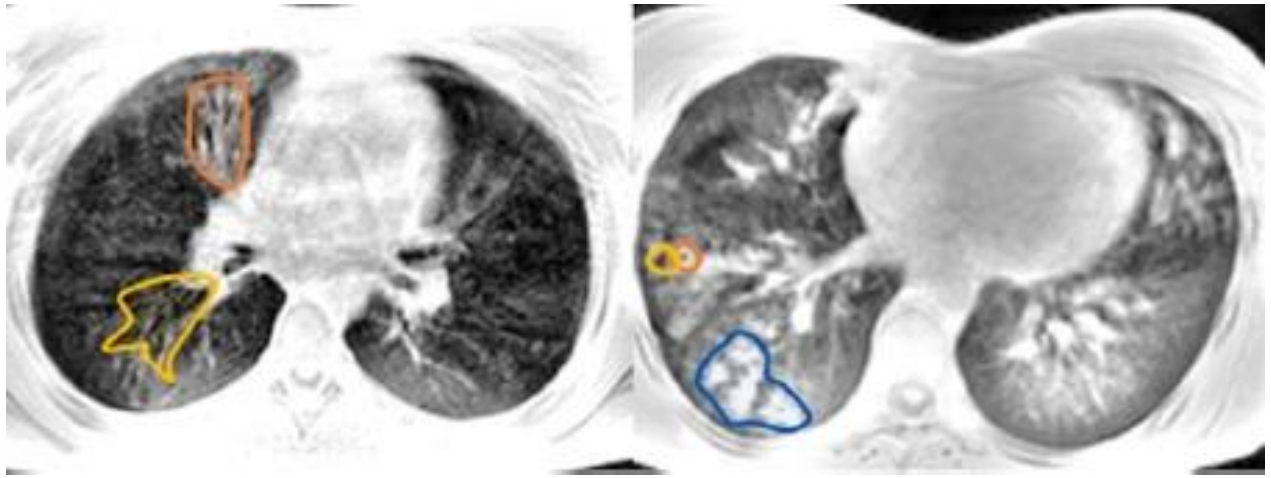
...and more

Estimated patient populations in select rare diseases

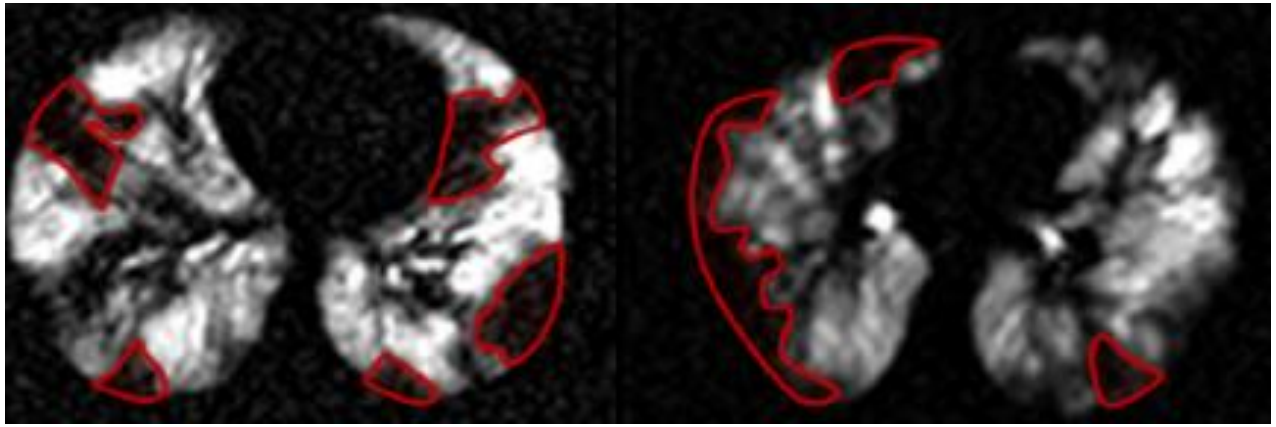
Indication	Lymphangioleiomyomatosis (LAM)	Rett syndrome	Paediatric SR-aGvHD	Erythropoietic protoporphyria (EPP)
Description	Rare progressive lung disease predominantly affecting women	Rare neurodevelopmental disorder predominantly affecting girls and women	Severe complication of allogeneic stem cell transplants	Rare inherited metabolic disease
Drug	OPT-302®	DAYBUE® (trofinetide)	Ryoncil® (remestemcel-L)	SCENESSE® (afamelanotide)
Manufacturer	Opthea	Neuren	Mesoblast	Clinuvel
Status	Pre-clinical / early development	FDA approved March 2023	FDA approved December 2024	EU 2014; FDA 2019
Orphan designation	Ultra orphan-eligible	Yes (US and EU)	Yes	Yes (US and EU)
Estimated US patient population	~5,000-7,000	~6,000-10,000	~500-600 new cases per year	~4,000
Estimated global patient population	~15,000-30,000	~15,000-20,000	Small absolute patient numbers but very high unmet medical need and treatment intensity	~10,000
Management	Approximately ~70 specialist LAM centres globally support concentrated patient management	Managed through concentrated paediatric neurology and specialist care centres	Ultra-rare acute treatment setting concentrated in major transplant centres	Managed through specialist dermatology and metabolic centres

Lung MRI for LAM[1,2]

Structure (by MRI or CT)



Function (by Xenon MRI)



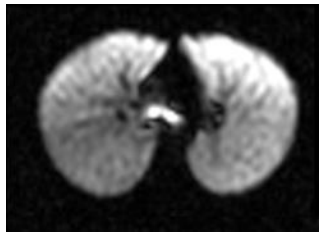
OPTHEA

1. Prof. Jason Woods. 2026
2. Images courtesy of University of Cincinnati

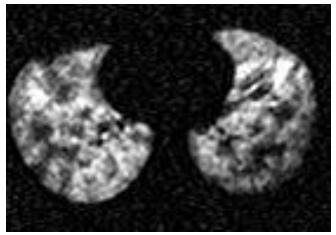
Hyperpolarized ^{129}Xe MRI: 3 measures

Ventilation

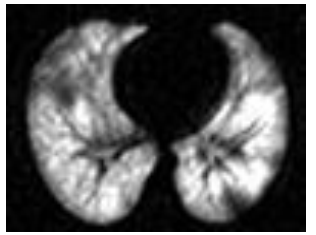
Healthy



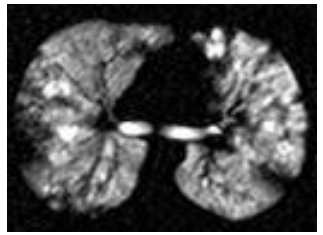
COPD?



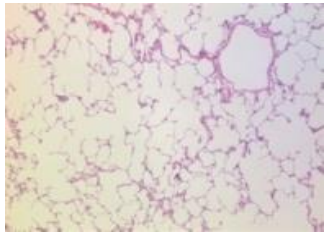
Asthma

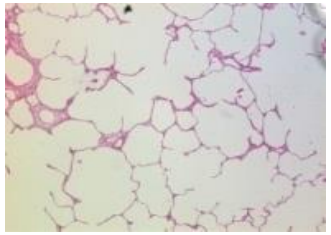


CF



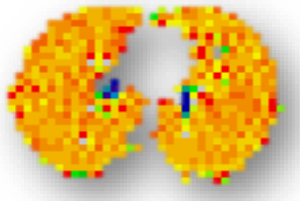
Alveolar size



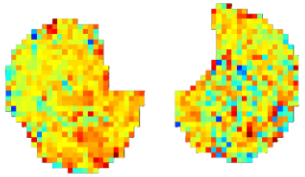


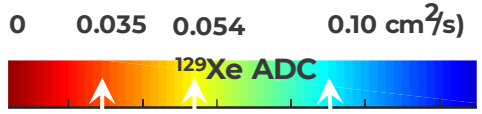
with histologic validation

Healthy, 1

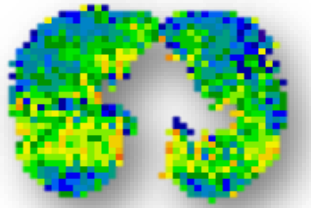


20-yr old COPD?



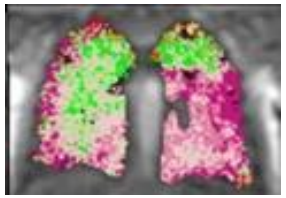


End-stage COPD, 3

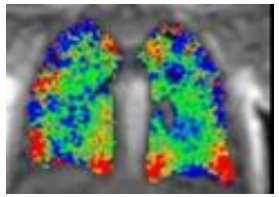


Gas-exchange abnormalities (Xenon dissolved phase)

Radiation Therapy

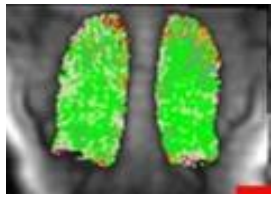


“Membrane”/Interstitium

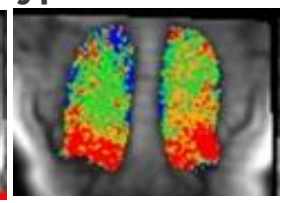


Red Blood Cells

Pulmonary Hypertension



“Membrane”/Interstitium



Red Blood Cells

1. Thomen, et al., J Cyst Fibros 2017; 46: 992
2. Ratjen, et al., Annals ATS 2025; in press.
3. Thomen, et al, Magn Reson Med, 2017; 77: 265
4. Plummer, et al. Magn Reson Med 2023; 89 1117

OPTHEA

Xe MRI: Full Lung Function Assessment

Xe Ventilation MRI

- Can quantify lung function near-perfectly, with regional specificity
- Validated sensitivity and treatment-effect in multi-site trials

Xe ADC MRI

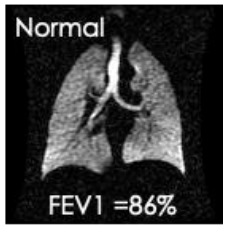
- Can quantify alveolar-airspaces with exquisite accuracy and precision

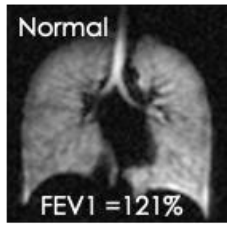
Gas Exchange MRI (like regional DLco)

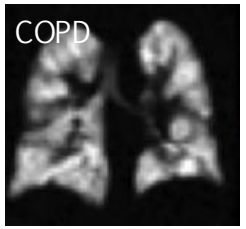
- Xenon RBC reveals direct capillary gas exchange
- Xenon Membrane reveals average thickness of interstitium

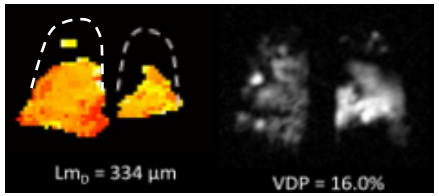
Combine with UTE MRI for structure-function

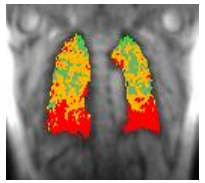
- Provides new & unprecedented precision & phenotyping

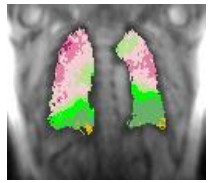












OPTHEA

Thank you

Investor contacts

Ryan Thompson
+61 (0)423 151 378
ryan.thompson@sodali.com

Alexandra Abeyratne
+61 (0)438 380 057
alexandra.abeyratne@sodali.com