

ASX Announcement

12 June 2026

Revised Webinar Details and Investor Presentation

Opthea Limited (ASX:OPT) (“Opthea” or the “Company”), will provide a corporate update to the market today, Friday 12 June 2026, with Executive Chair Dr Jeremy Levin and Chief Financial Officer Hamish George to host an online webinar for analysts and investors from 11:00am (AEST).

The attached presentation will be discussed on the webinar.

Participants are requested to register for the webinar using the following **updated** link:
https://us04web.zoom.us/webinar/register/WN_PevXmllqSfy5VexelKAfOg

ENDS

This announcement was authorised for release by the Board of Directors.

Enquires

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OPTHEA

OPTHEA REIMAGINED

Unlocking VEGF biology for unmet medical needs

Investor presentation

12 June 2026

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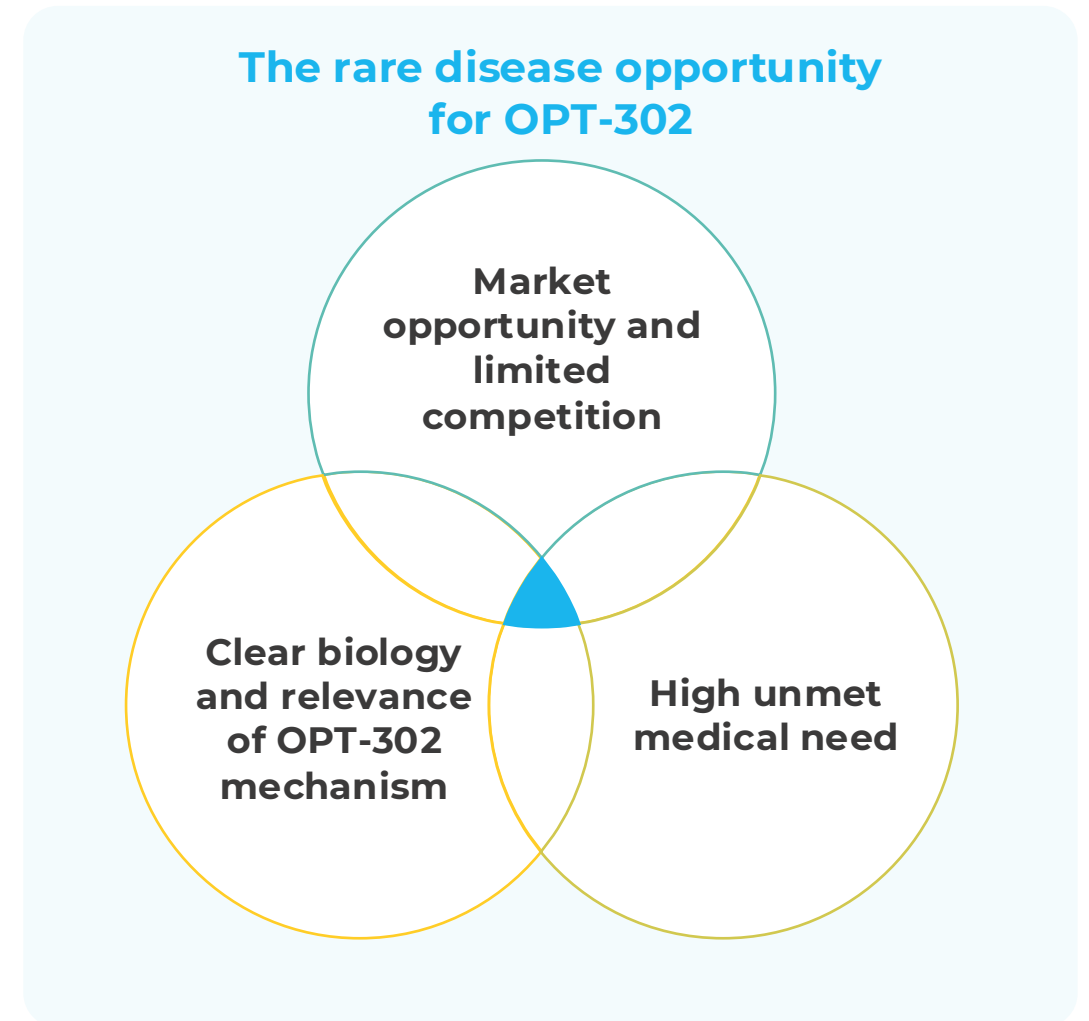
Agenda

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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



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

Lymphangiomyomatosis (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
population³**

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.

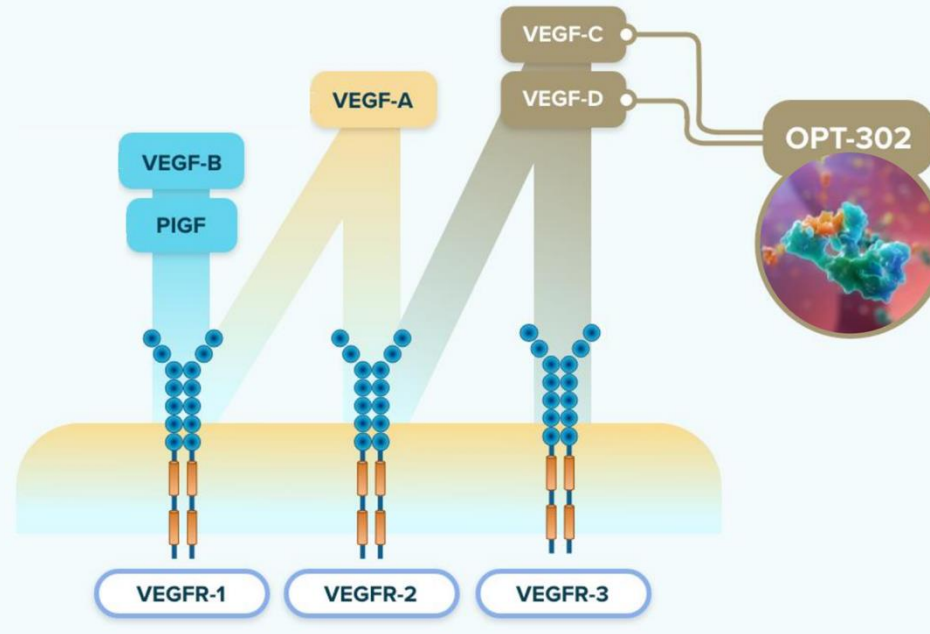


When VEGF-C or VEGF-D bind to VEGFR-3, the lymphatic system gets a strong “expand and remodel” message. In LAM, this leads to abnormal, dilated, and leaky lymphatic vessels.



The problem¹

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

- 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



Why it fits LAM

- 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



What happens next

- Goal is to build a differentiated rare disease program through rigorous staged development.

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

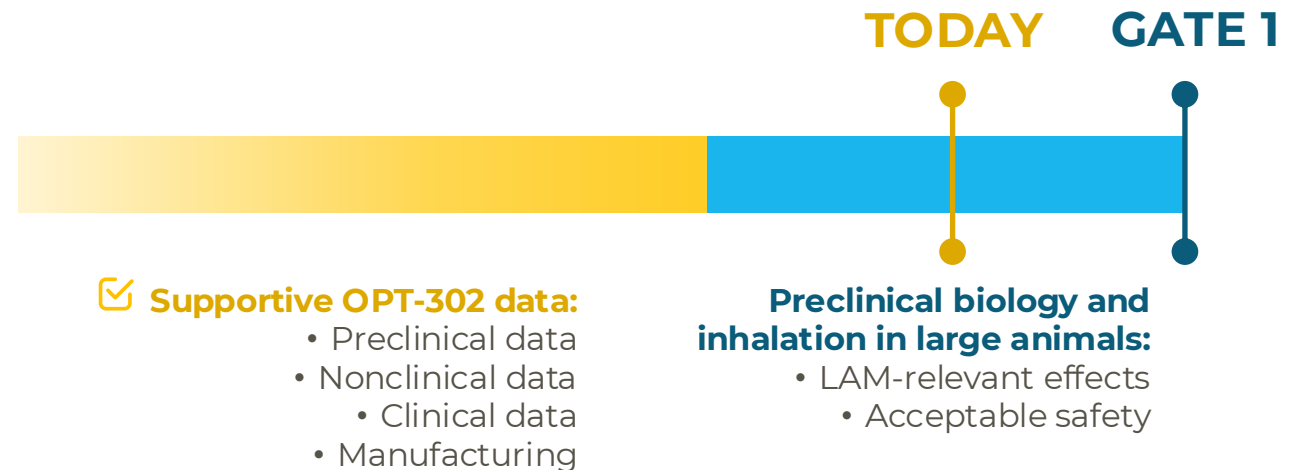
Status Update

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

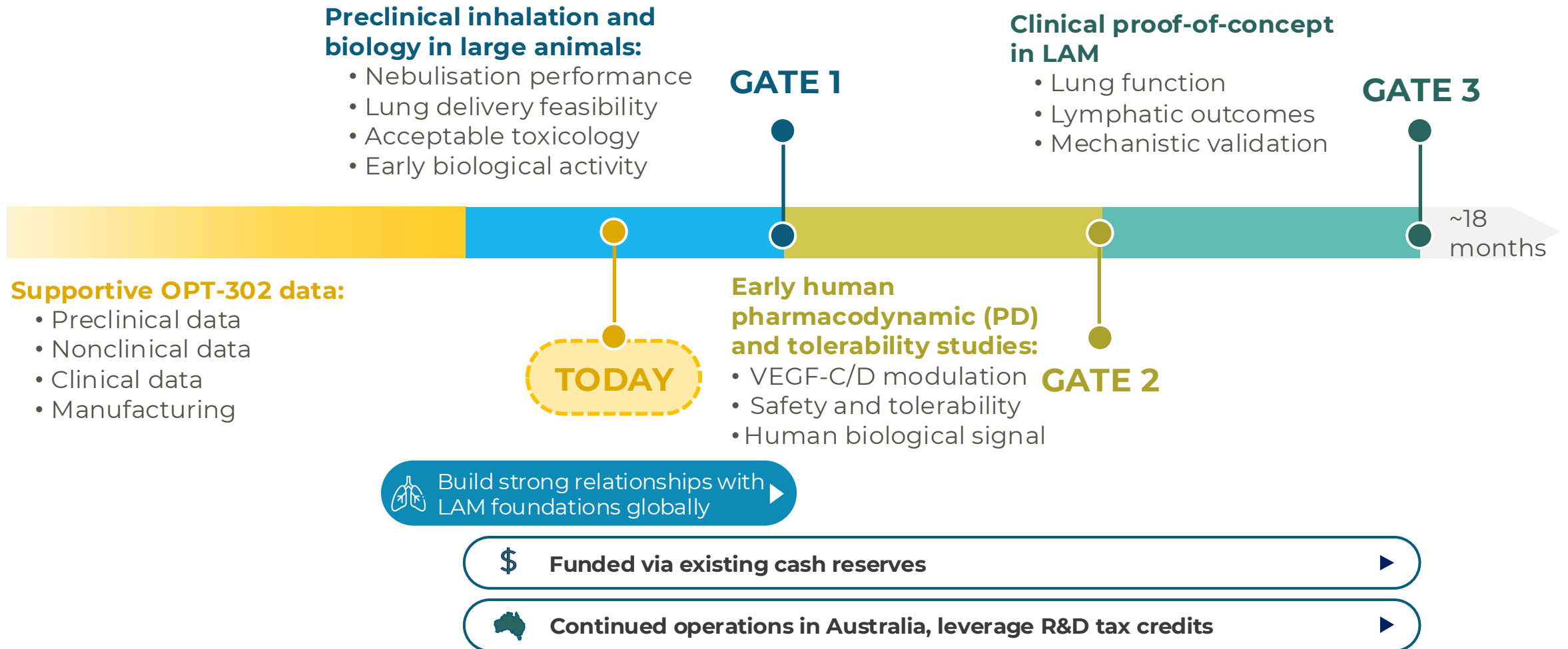
PRE-CLINICAL PROGRESS

- 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

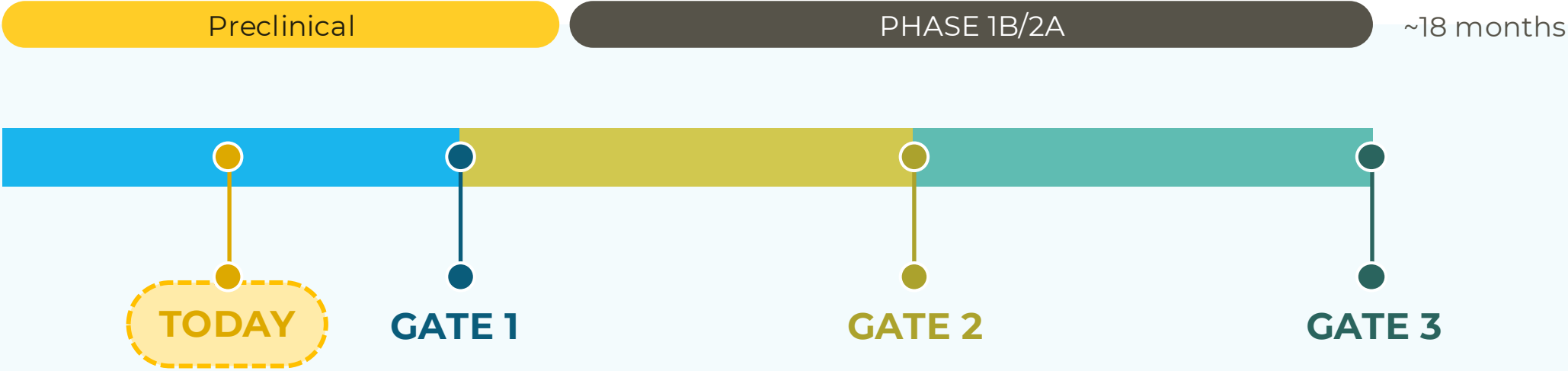


Stage-gated plan

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

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 Daugherty
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

Corporate and financial overview

Company name¹

Opthea Limited

ASX ticker¹

OPT

Total ordinary shares on issue

1,367,978,173

Share price²

A\$0.014

Market capitalisation²

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



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 Lymphangiomiomatosis 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: Lymphangiomiomatosis 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 Lymphangiomiomatosis*, *The New England Journal Of Medicine* Vol 364 No 17.: [Efficacy and Safety of Sirolimus in Lymphangiomiomatosis | 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



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



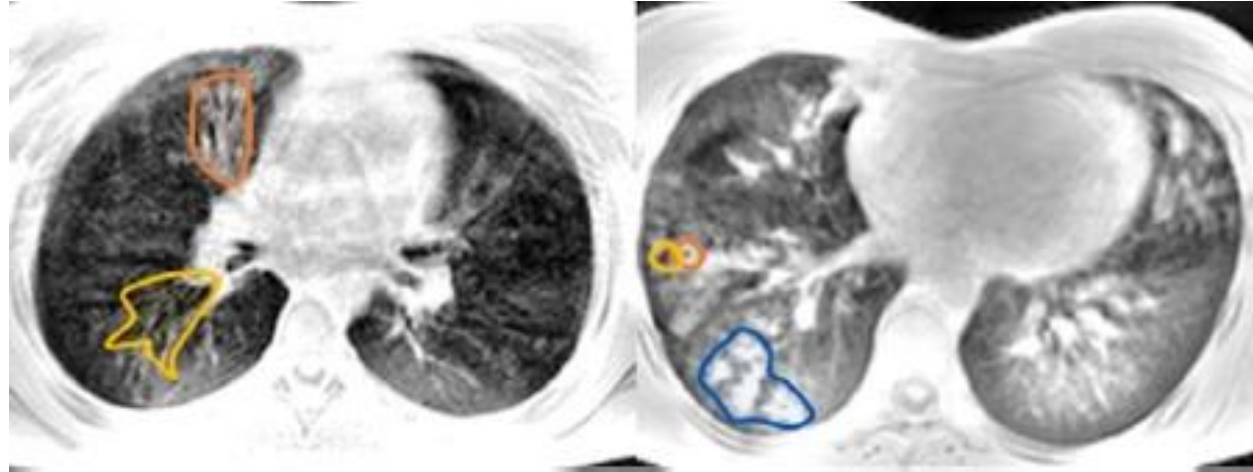
...and more

Estimated patient populations in select rare diseases

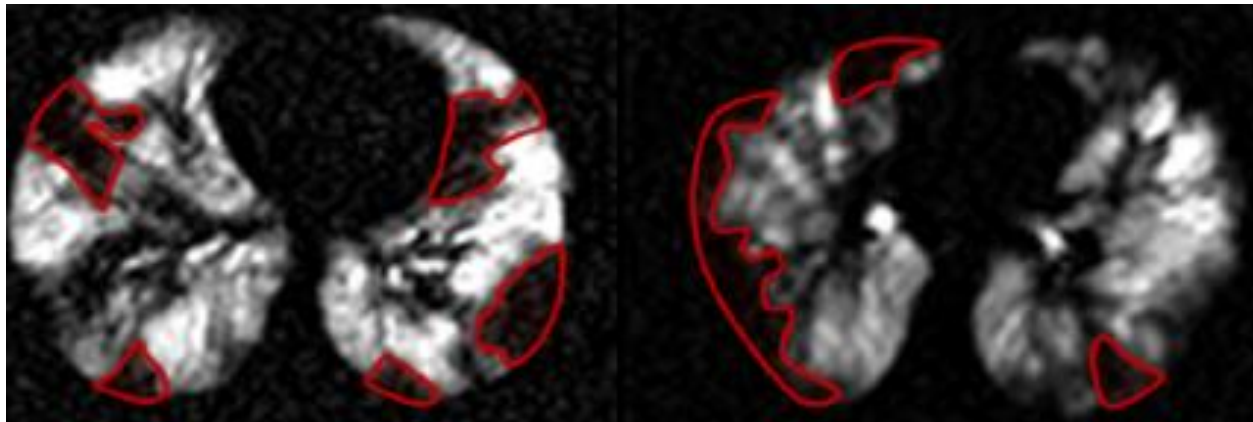
Indication	Lymphangi leiomyomatosis (LAM)	Rett syndrome	Paediatric SR-aGvHD	Erythropoietic protoporphyria (EPP)
Description	Rare progressive lung disease predominantly affecting women	Rare neurodevelopmental disorder predominantly affecting girls and women	Severe complication of allogeneic stem cell 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)



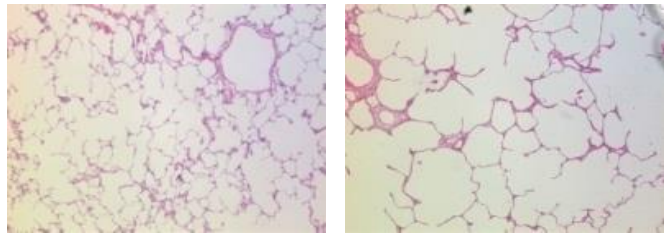
Function (by Xenon MRI)



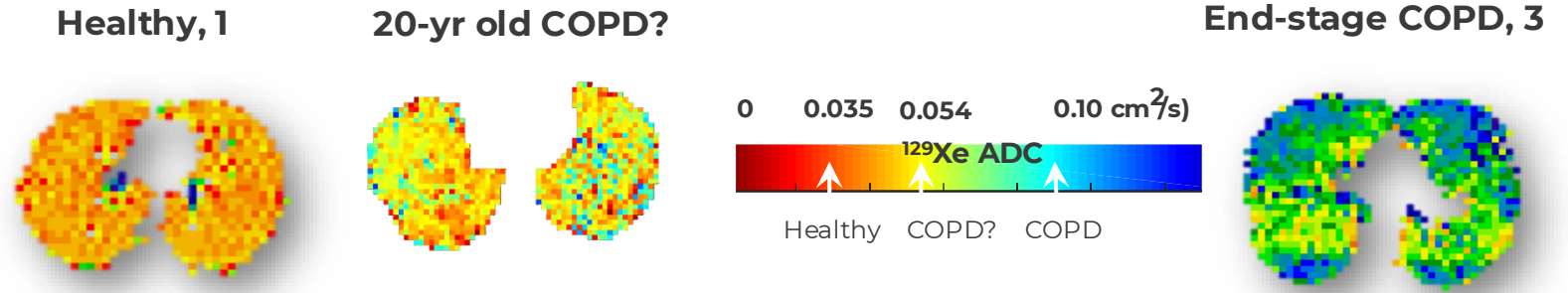
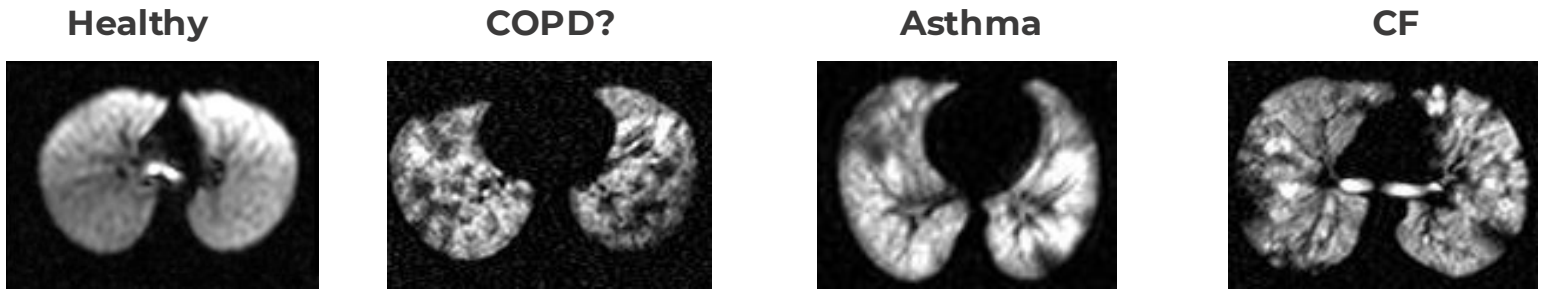
Hyperpolarized ^{129}Xe MRI: 3 measures

Ventilation

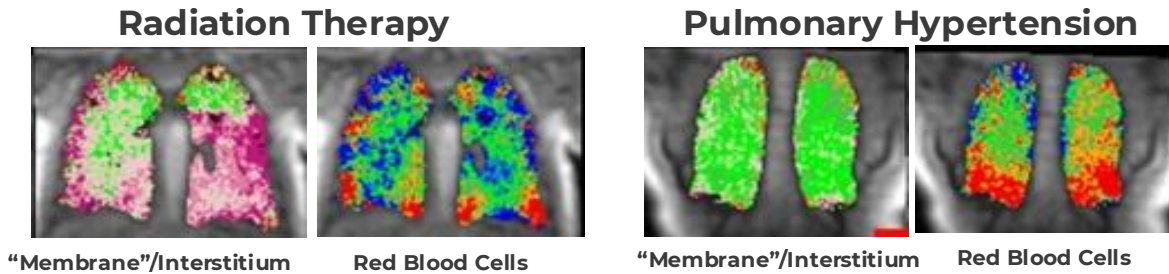
Alveolar size



with histologic validation



Gas-exchange abnormalities (Xenon dissolved phase)



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

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

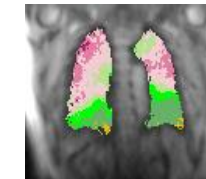
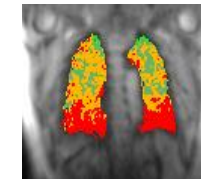
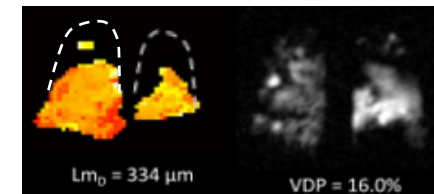
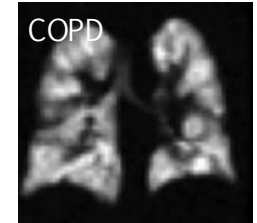
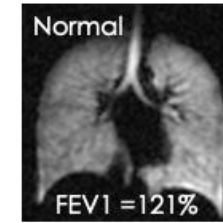
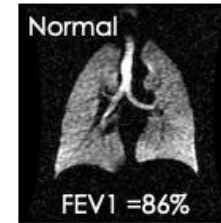
- Can quantify alveolar-airspaces with exquisite accuracy and precision

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



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Thank you

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