Corporate Presentation
July 2015

Circadian Technologies
(ASX:CIR, OTCQX:CKDXY)

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Corporate Summary

- Extensive worldwide intellectual property platform in respect of VEGF-C, VEGF-D and VEGFR-3
- Lead compound OPT-302 blocks VEGF-C and VEGF-D
- OPT-302 in development for treatment of wet AMD
- Potential in a range of eye diseases as a monotherapy or in combination with approved anti-VEGF-A therapies
- Phase 1 clinical trial initiated under FDA approved IND
- Potential to move directly into Phase 2A trial following dose-escalation cohorts
- 5 leading US clinical sites
- Funded through end of 2017 and completion of Phase 1 and 2 clinical studies
- Pipeline includes Phase 2 ready oncology asset (VGX-100) and Eli Lilly partnered compound IMC-3C5
- Management team with substantial experience in developing drugs targeting the VEGF pathway

OPT-302 Wet AMD Program: Milestones

IND Approval for OPT-302
June 2015 ✓

Initiated Phase 1 clinical trial:
June 2015 ✓

Ph 1 Primary Data Analysis:
1Q16

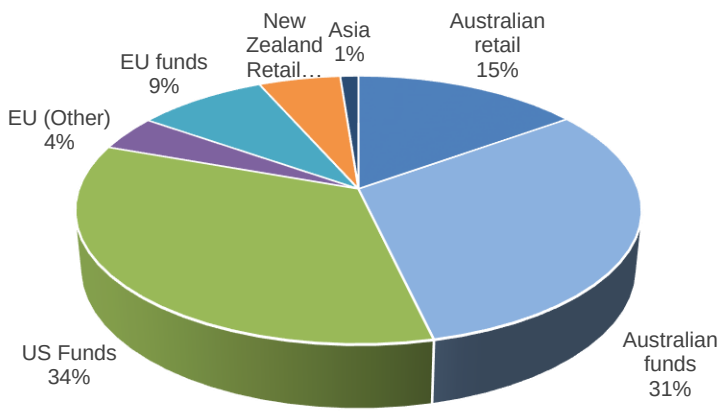
Ph 2B Primary Data Analysis:
2017

Financial Position (Unaudited)

Key Financial Details	ASX: CIR
Ticker Symbol	ASX:CIR
Share Price *(as at July 8 2015)*	A$0.195
Total Ordinary Shares on Issue	150,190,303
Options on Issue	49,722,697
Market Capitalisation *(as at July 8 2015)*	A$29m
Trading Range *(last 12 months)*	A$0.135 – 0.215
Cash Balance *(at 30 June 2015)*	~A$18.2m
Listed Investments	~A$2m
Top 10 Shareholders Own	69%

Substantial Shareholders	% Holding
Biotechnology Value Fund (BVF)*	17.7%
Baker Bros (NY, USA)	9%
Packer & Co.	8.5%

Shareholders by Region

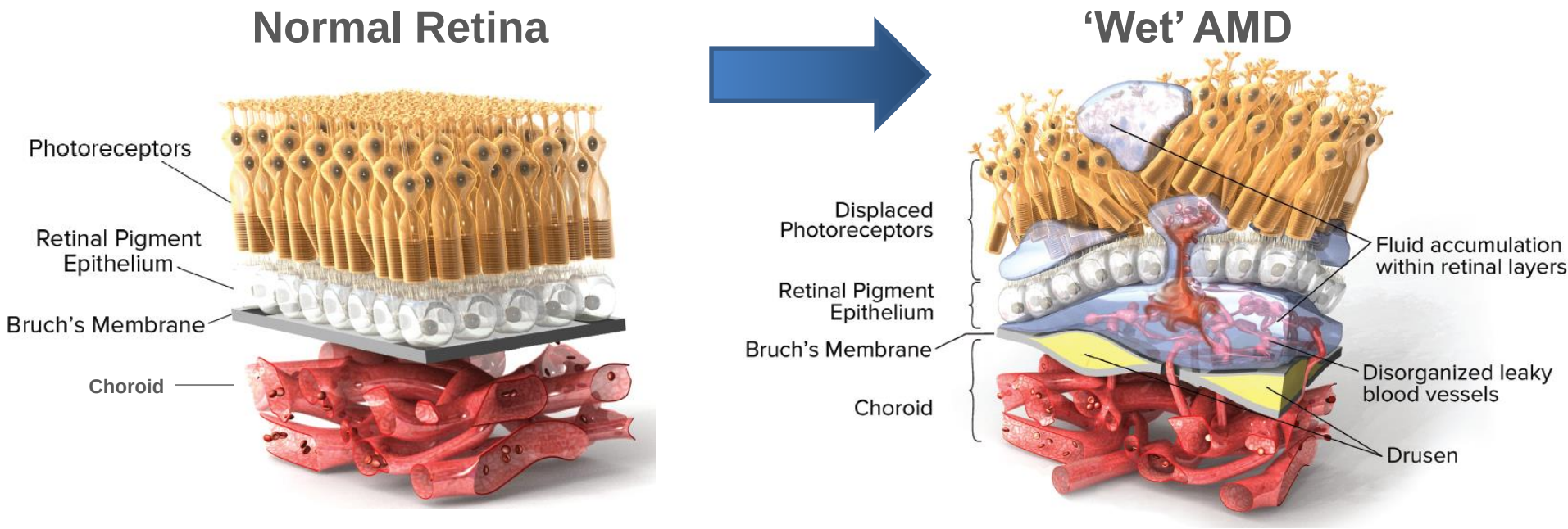


** Increased substantial holding 13% to 17.7% on June 25 2015*

Lead Program: OPT-302 for Wet AMD

- **Lead molecule:**
  - OPT-302 (soluble VEGFR-3, VEGF-C/-D 'Trap')
- **Mechanism:**
  - Blocks VEGF-C and VEGF-D:
    - Inhibits blood vessel growth
    - Inhibits vessel leak
- **Strategy:**
  - To investigate activity as a monotherapy
  - To develop OPT-302 for use in combination with existing VEGF-A inhibitors for the treatment of wet AMD
  - Achieve complete blockade of the VEGF pathway

The disease process of ‘wet’ (neovascular) AMD



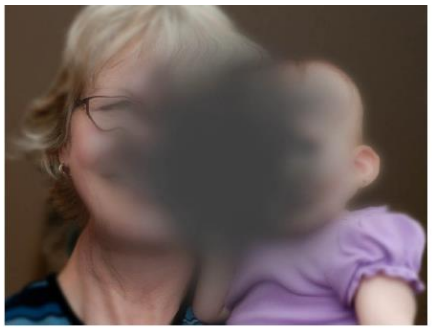
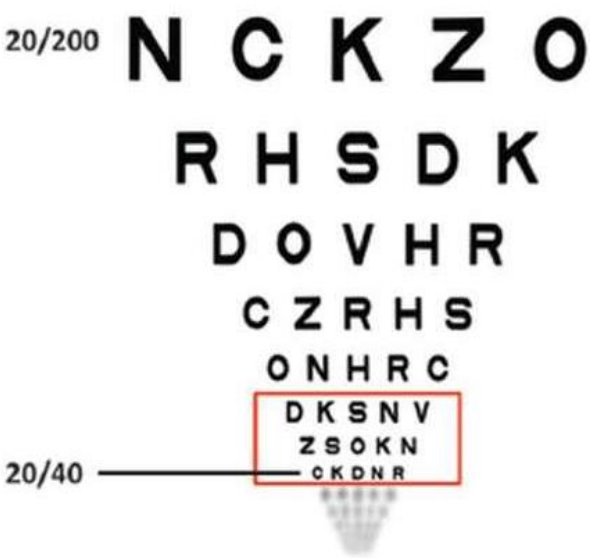


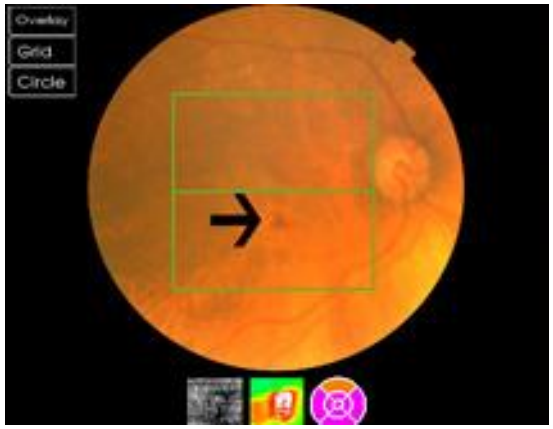
Figure: The Angiogenesis Foundation

Routine Non-Invasive Monitoring Procedures for Disease and Treatment Efficacy

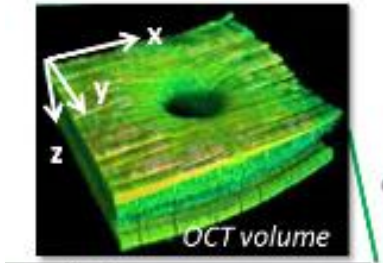
Eye Chart *(Visual Acuity)*

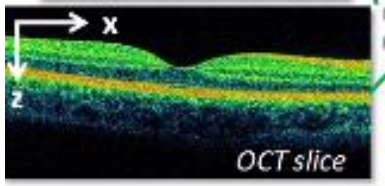


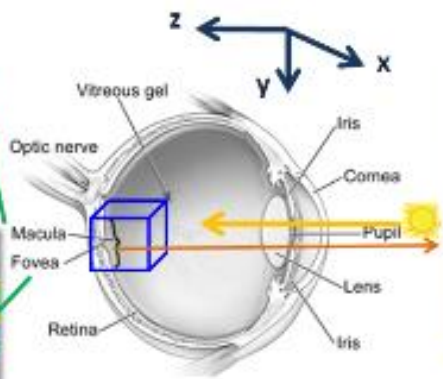
Retinal Image



OCT*(Optical Coherence* Tomography)
(Fluid, hemorrhage, retinal thickness, retinal detachment)



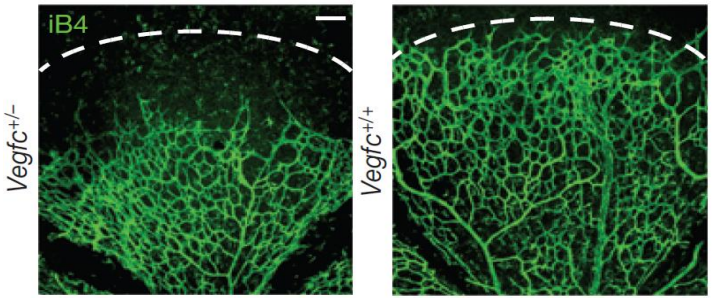




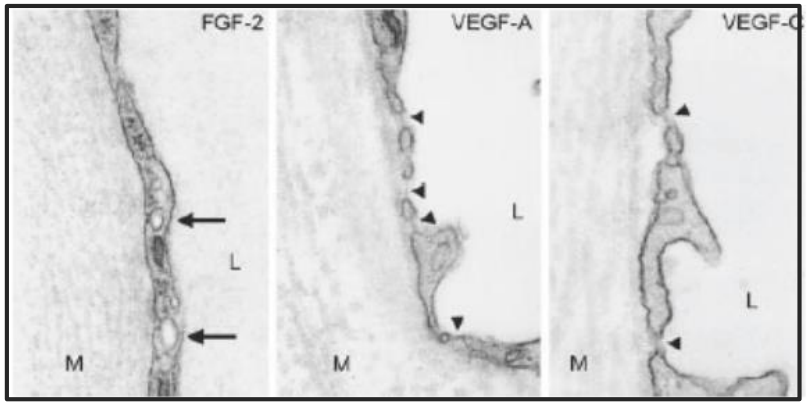
OCT machine

VEGF-C Causes Blood Vessels to Grow & Leak

VEGF-C is required for the development of retinal blood vessels



VEGF-C is a potent inducer of vessel leakage



- Persistent angiogenesis and retinal vascular leakage are observed in patients that are 'sub-responsive' to Lucentis®/Eylea® (VEGF-A inhibitors)

Tammela et al., Nature Cell Biology, 2011; Cao et al,. Circ Res., 2004

OPTHEA circadian

The opportunity for OPT-302:
An unmet medical need remains despite anti-VEGF-A therapy

- Wet AMD is the leading cause of blindness in the western world
- Estimated >$US5BN p.a. market opportunity in wet AMD in US alone and world-wide $US10BN* , increasing with ageing population
- Only two targeted therapies approved for wet AMD (Lucentis® & Eylea®, off-label Avastin®)
- Both target VEGF-A, but not VEGF-C or VEGF-D

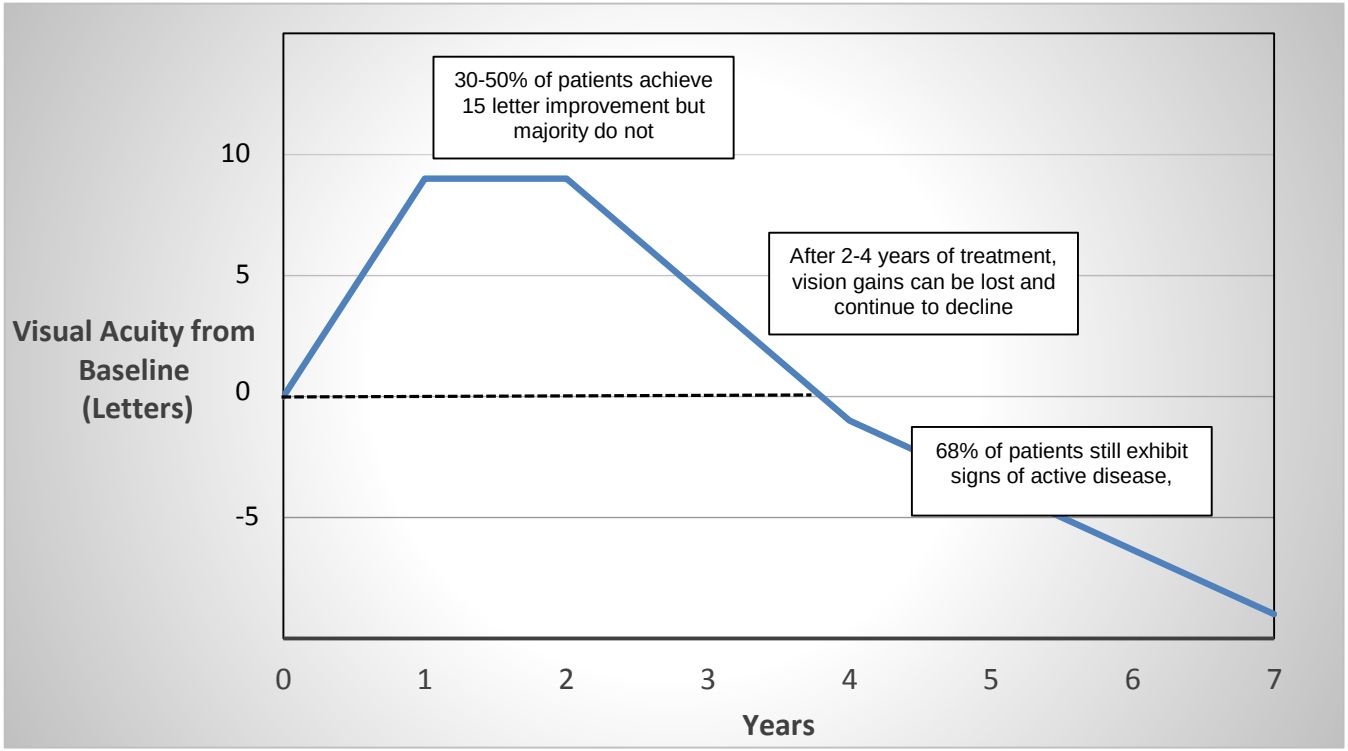
Long term single-agent therapy with VEGF-A inhibitors is associated with sub-optimal response:

- **>50% patients do not achieve a significant gain in vision**
- **Phase 3 trial results indicate that between 50-70% patients have retinal fluid despite anti-VEGF-A therapy**

- VEGF-C & VEGF-D are implicated in mediating resistance to anti-VEGF-A therapy
- VEGF-A, VEGF-C & VEGF-D share signalling through VEGFR-2, a validated pathway involved in wet AMD progression
- VEGF-C & VEGF-D also activate VEGFR-3
- Complete receptor blockade requires blockade of all ligands

**Cowen Analyst Report: Ophthotech July 7 2015*

The opportunity for OPT-302:
An unmet medical need remains despite anti-VEGF-A therapy



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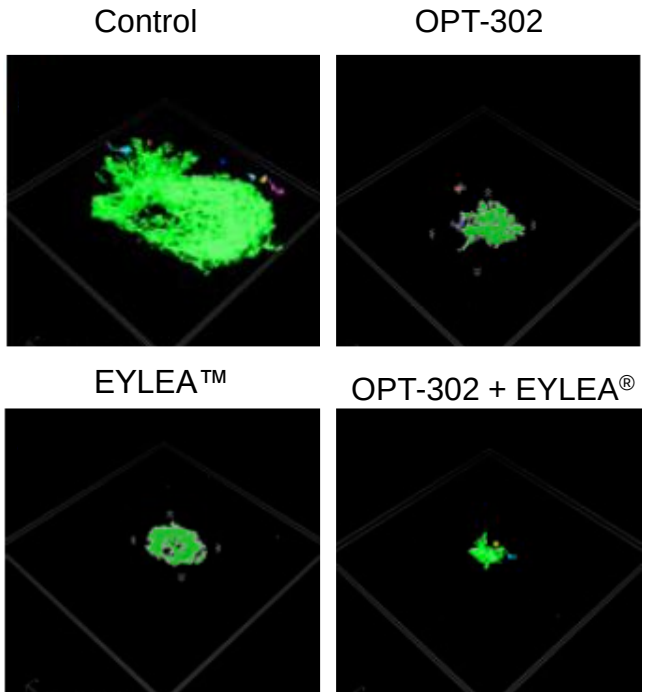
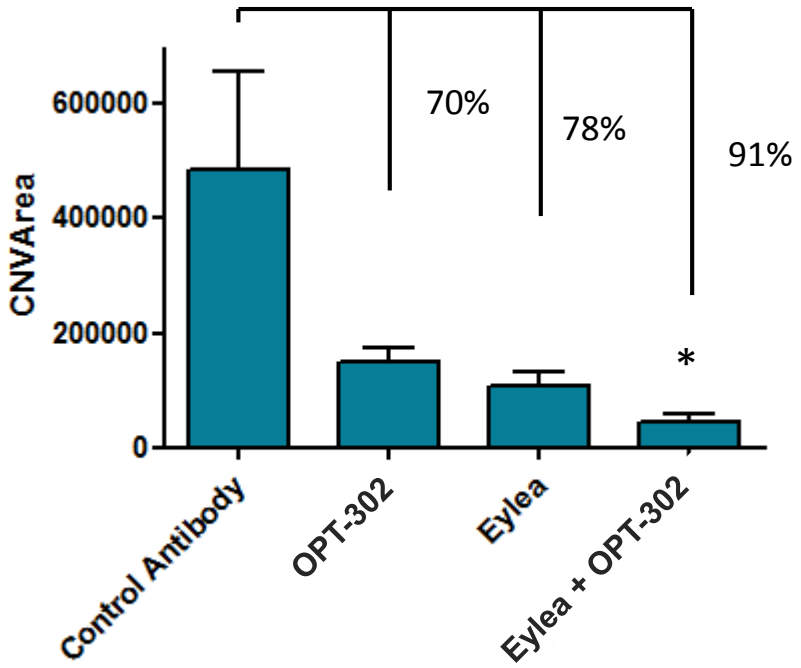
OPT-302 has comparable single-agent and additive activity with Eylea® in mouse AMD

Combined inhibition of VEGF-A (Eylea®), VEGF-C and VEGF-D (OPT-302) is more effective than inhibition of VEGF-A alone





** Pairwise comparison: OPT-302 vs Eylea + OPT-302 (p<0.02)*
Eylea vs Eylea + OPT-302 (p<0.05)

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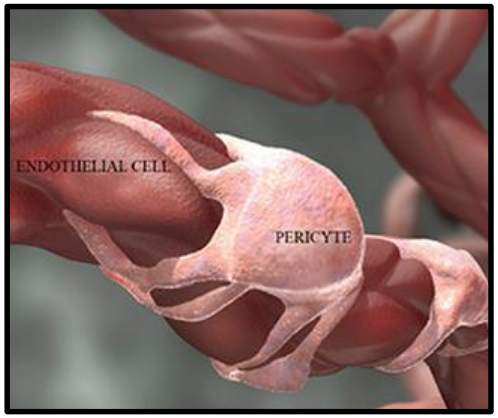
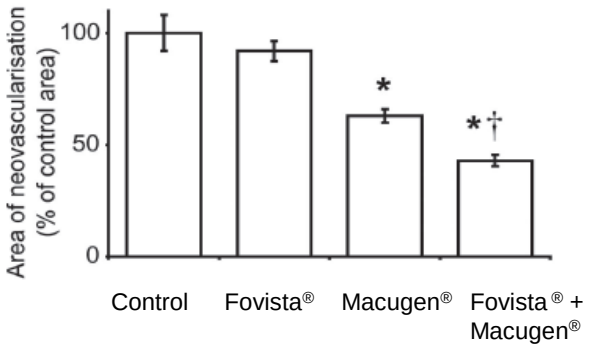
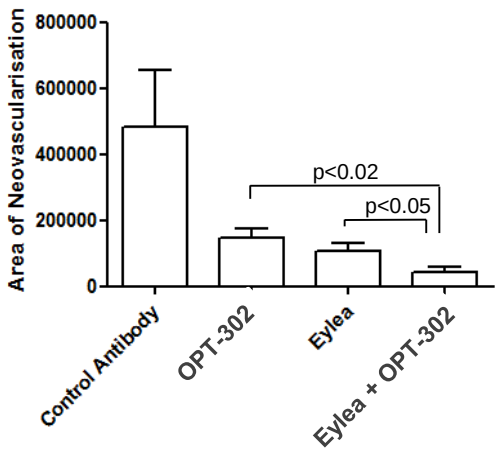
Ophthotech and Opthea:
Distinct approaches for wet AMD combination therapy



Activity in in mouse wet AMD model





	FOVISTA™	OPT-302
Preclinical: Activity as Monotherapy?	NO	YES
Preclinical: Activity in Combination?	YES	YES
Potential Use in DME?	Unlikely	YES
Drug Class	Aptamer	Protein
Mechanism	Strips pericytes (supportive cells for vessel wall) which may enhance a-VEGF-A delivery/activity	Directly targets vessel wall (endothelium, through same and independent pathway to Lucentis/Eylea). Blocks a mechanism of resistance to existing a-VEGF therapies.
Valuation at NASDAQ listing	US$662 m (At end Phase 2)	N/A
Current Market Cap.	**AUD$1.8 bn (Phase 3)**	**AUD$28 m (Phase 1)**

"Macugen®" – targets VEGF-A_{165} isoform; "Fovista®" – aptamer targeting PDGF-b; Jo et al., Am.J.Pathol., 168(6), 2036-2053, 2006.

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OPT-302 Clinical Trials in Wet AMD Patients

Clinical trial protocol covers a Phase 1/2A study in wet AMD patients:

- Phase 1:
  - Dose escalation – Open label
  - Safety & preliminary indicators of clinical activity
  - Data anticipated 1Q'16
- Phase 2A:
  - Dose expansion – Randomised
  - Monotherapy & combination OPT-302 + Lucentis®
- Phase 2B:
  - Randomised, controlled study
  - Design to be finalised following Ph 1/2A
  - OPT-302 + Lucentis® vs Lucentis ® only in previously untreated (naïve) patients
  - OPT-302 as 'rescue' therapy in Lucentis® 'sub-responders'

OPT-302 Wet AMD Program: Milestones

IND Approval for OPT-302 June 2015 ✓

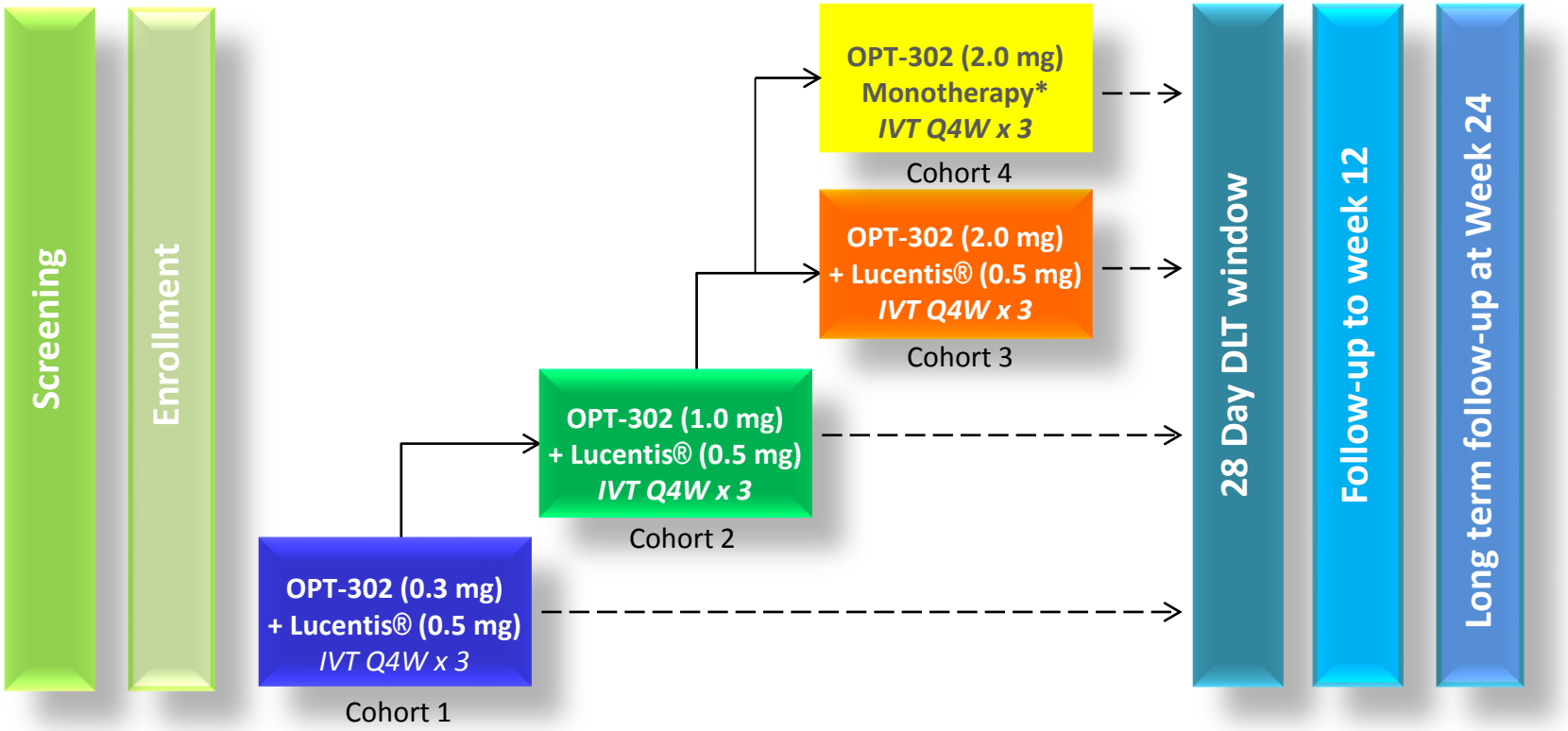
Initiated Phase 1 clinical trial: 30 June 2015 ✓

Ph 1 Primary Data Analysis: 1Q16

Ph 2B Primary Data Analysis: 2017

OPT-302 Phase 1: Protocol: OPT-302-1001

Dose escalation of repeated IVT injections

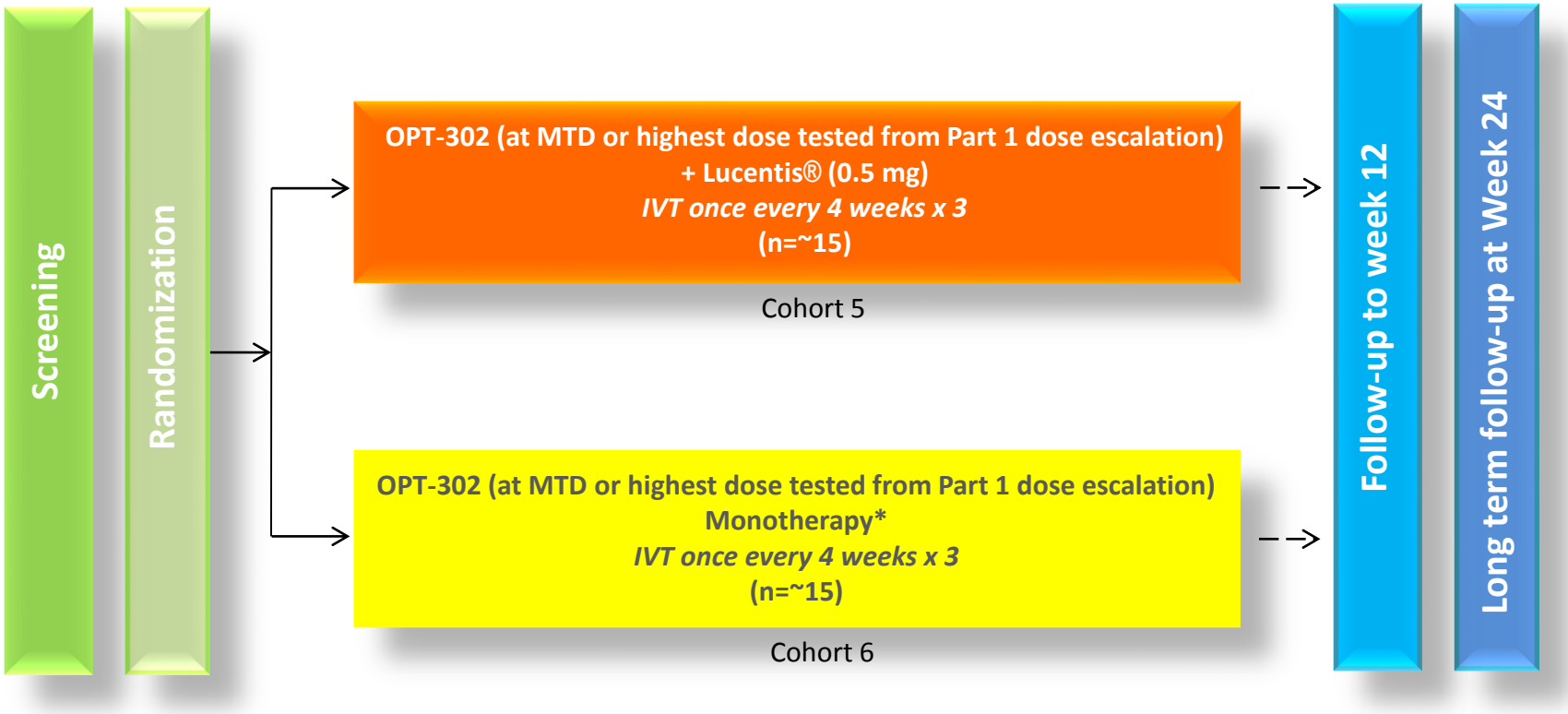


**Access to rescue anti-VEGF-A Tx*

- *Comprises of 4 treatment cohorts of 5 subjects each*
- *Should a dose limiting toxicity (DLT) occur, 3 additional subjects will be enrolled in that cohort*
- *OPT-302 and ranibizumab given as separate IVT injections (each 0.05 mL) once every 4 weeks at day 1, 29 and 57*
- *When used in combination, the ranibizumab IVT injection will be given 30 mins prior to sequential IVT OPT-302*

OPT-302 Phase 1/2A: Protocol: OPT-302-1001

Dose expansion of repeated IVT injections



*Access to rescue anti-VEGF-A Tx

- *Part 2 Dose expansion - Dependent on successful completion of Part 1 Dose Escalation*
- *OPT-302 and ranibizumab given as separate IVT injections (each 0.05 mL) every 4 weeks at day 1, 29 and 57.*
- *When used in combination, the ranibizumab IVT injection will be given 30 mins prior to sequential IVT OPT-302.*

Clinical Advisory Board & Advisors

- Clinical Advisory Board of internationally recognised and experienced key opinion leaders from Australia and US
- Extensive experience in development of novel and FDA approved therapeutics for wet AMD, including Macugen®, Fovista®, Eylea® and Lucentis®

Pravin Dugel MD
Retinal Consultants Arizona
Keck School of Medicine USC

Mark Gillies MD
Save Sight Institute
Sydney Univ.

Peter Campochiaro MD
John Hopkins
Wilmer Eye Institute

Kameran Lashkari MD
Schepens Eye Res.Inst.
Harvard Med.School
Mass Eye & Ear

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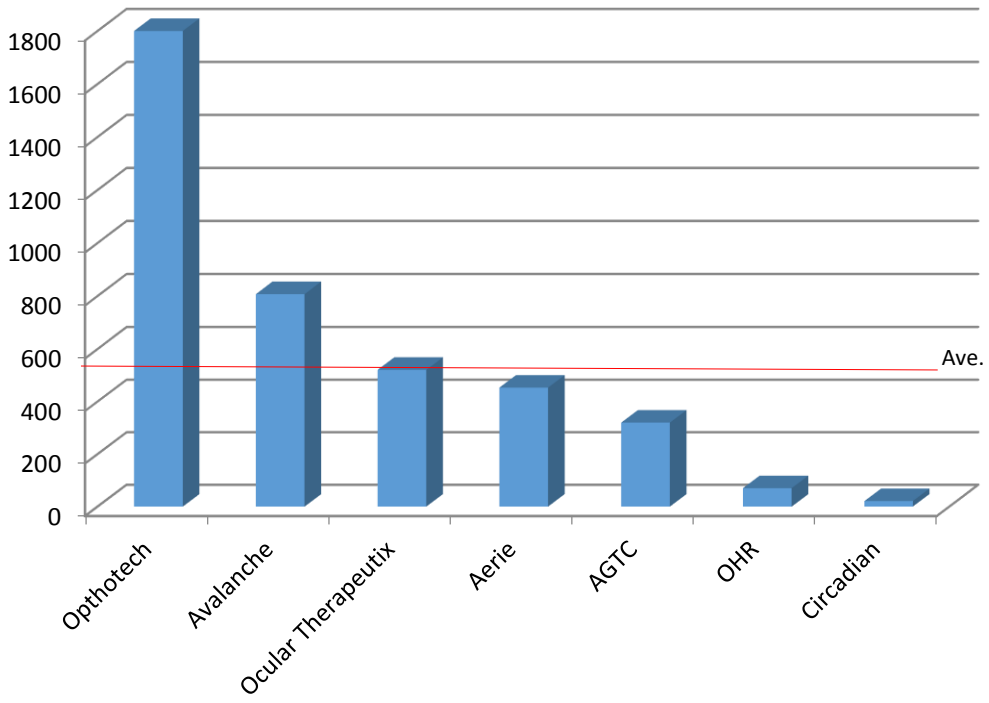
Listed Ophthalmology Companies in Phase 1-3

OPHTHOTECH PDGF-B aptamer Wet AMD		$1.8BN (Phase 3)
AVALANCHE BIOTECH a-VEGF-A gene therapy Wet AMD		$807M (Phase 1/2)
Ocular Therapeutix™	Sustained delivery Wet AMD	$521M (Phase 3)
aerie pharmaceuticals, inc.	ROCK inhib., small mol. Glaucoma	$453M (Phase 3)
agtc	Gene therapy Eye diseases	$320M (Phase 1/2)
OHR Pharmaceutical Inc.	Squalamine Wet AMD	$70M (Phase 2)
circadian	OPT-302 Wet AMD	~$29M (Phase 1 June 15)

Market Cap (AUD $m) Listed Ophthalmology Companies Ph1-3



a At July 7 2015, in USD

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OPT-302: Intellectual Property

Summary covering sVEGFR-3 IP for Eye Disease

COMPOSITION OF MATTER	TERM
Covering sVEGFR-3 (inc. OPT-302) • Granted Patents: Europe, Japan, Canada, Australia • Granted Patent: USA	 2022 2026
Covering OPT-302 • Recently filed new specific composition of matter PCT international patent application	~2034
'USE' PATENT	
• US Patent granted covering generic use of sVEGFR-3 capable of binding VEGF-C to inhibit blood vessels in mammal having disease characterised by expression of VEGFR-3 in blood vessels	2023
PATENT TERM EXTENSION/EXCLUSIVITY	
+5 years under patent term extension **OPT-302 entitled to data exclusivity (DE) and market exclusivity (ME) in many jurisdictions, eg.** • US (12 years DE for biologics • Europe (10 years made up of 8 years DE + 2 years ME) • Japan (up to 8 years de facto DE) • South Korea (5 years DE) • Canada (up to 8 years incl. up to 6 years DE + 2 years ME) • Australia (5 years DE)	

Wet AMD Program Summary

- OPT-302 is a fully owned asset with development potential for a range of eye diseases
- Potent blockade of two members of VEGF family
- Ocular PK and biodistribution similar to Eylea® in rabbit studies
- Monotherapy and additive activity with VEGF-A inhibitors in preclinical models
- IND-enabling preclinical safety toxicology studies completed
  - Well tolerated in preclinical GLP safety toxicology studies
  - Multiple monthly doses via ocular administration alone or in combination with Lucentis®
- Phase 1 clinical trial initiated under FDA approved IND
  - 5 US clinical sites
  - Primary endpoint: safety
  - Secondary endpoints to identify preliminary evidence of clinical activity (eye charts and imaging techniques)
  - Patients receive once monthly injection for 3 months (28 day DLT window)
- Phase 1 data anticipated 1Q'16
- Potential to move directly into Phase 2A randomised dose expansion following Phase 1

Investment Highlights

- Leader in VEGF-C/D and VEGFR-3 targeting compounds in ophthalmology and oncology
- Fully funded through 2017 and Phase 1/2A and Phase 2B clinical studies in wet AMD patients
- Near-term clinical milestones
  - Phase 1 clinical trial for wet AMD initiated under FDA IND June ‘15
  - Primary analysis Phase 1 data 1Q’16
  - Primary analysis Phase 2B data 2017
- Differentiated MOA & strong IP position
- World class CAB & advisors
- Pipeline includes Phase 2 ready oncology asset (VGX-100) and Eli Lilly partnered compound IMC-3C5

Thank-you

Megan Baldwin , PhD

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