Annual General Meeting

November 30 2015

Megan Baldwin , PhD

CEO & Managing Director

Circadian Technologies (ASX:CIR, OTCQX:CKDXY)

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Financial Position (Unaudited)

Key Financial Details	ASX: CIR
Ticker Symbol	ASX:CIR
Share Price *(as at Nov 23 2015)*	A$0.31
Total Ordinary Shares on Issue	150,190,303
Options on Issue	49,722,697
Market Capitalisation *(as at Nov 1 2015)*	A$46.5m
Trading Range *(last 12 months)*	A$0.135 – 0.33
Cash Balance *(at 31 Oct 2015)* *(R&D Tax Credit not yet rec'd)*	~A$15.8m
Listed Investments	~A$1.3m
Top 10 Shareholders Own	69%

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

Share Price Performance (Jun '14 – Nov '15)

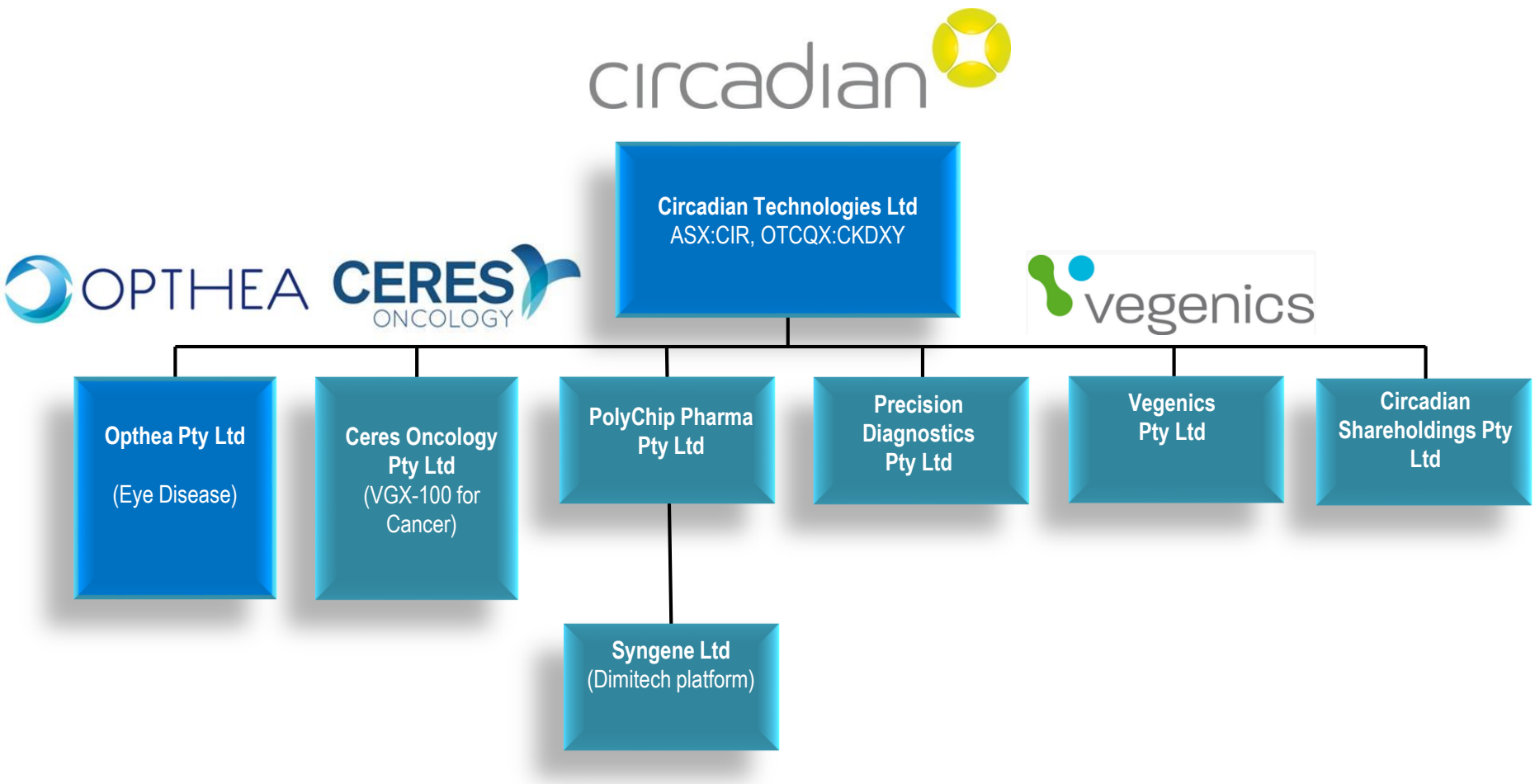
** Increased substantial holding 13% to 17.7% on June 25 2015*

Corporate Achievements

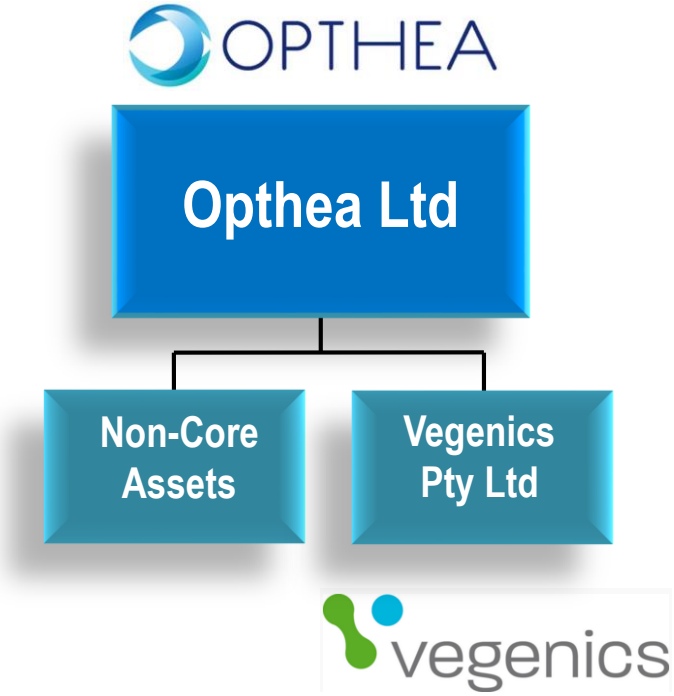
Corporate

- ✓ Continued execution of strategy to focus on ophthalmology
- ✓ Prudent financial management post A$17.4m capital raising Nov ‘14
- ✓ Anticipated ~A$3m R&D tax rebate (2014-15) on local & international R&D expenditure
- ✓ Regained VEGFR-3 intellectual property licensed to Eli Lilly
- ✓ Simplification of Circadian Group by initiation of deregistration of subsidiaries
  - ✓ Including solvent members’ voluntary liquidation of Syngene Ltd
  - ✓ Pro-rata allocation of remaining capital to Syngene shareholders
- ✓ Shareholder approval to change company name to Opthea Ltd

Corporate Re-Structure



Simplification of Corporate Structure*



** Anticipated corporate structure following simplification which may be subject to changes.*
Contingent on shareholder approval of Circadian Technologies Limited name change to Opthea Limited.

Program Achievements

Opthea

- ✓ Completed IND-enabling GLP safety/toxicology studies to support Ph 1/2A trial
- ✓ Completed preclinical pharmacokinetic studies to support Ph 1/2A
- ✓ Produced clinical grade OPT-302 to US FDA specifications required for Ph 1/2A
- ✓ US FDA approval of IND
- ✓ Initiation of Phase 1/2A clinical trial for OPT-302 in wet AMD patients
- ✓ Continued patient recruitment
- ✓ Presented OPT-302 data at international conferences (ARVO, ASCRS and World Congress on Angiogenesis) and Ophthalmology Innovation Summit (OIS/AAO)
- ✓ Established world recognised Clinical Advisory Board

Program Update
OPT-302 for Wet AMD

Overview

- Extensive worldwide intellectual property platform in respect of VEGF-C, VEGF-D and VEGFR-3
- Lead compound OPT-302 blocks VEGF-C & VEGF-D
- US FDA approved IND, open US clinical trial sites
- Actively recruiting patients in Phase 1/2A clinical trial in wet AMD patients
- Strong management team with experience in developing drugs targeting the VEGF pathway, wet AMD and oncology

OPT-302 Wet AMD Program: Milestones

IND Approval & Ph1/2A Initiated June 2015 ✓

Ph 1 Primary Data Analysis: 1Q16

Ph 2A Primary Data Analysis: 2H16

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
  - Blocks a mechanism of 'escape' from existing therapies

The disease process of ‘wet’ (neovascular) AMD

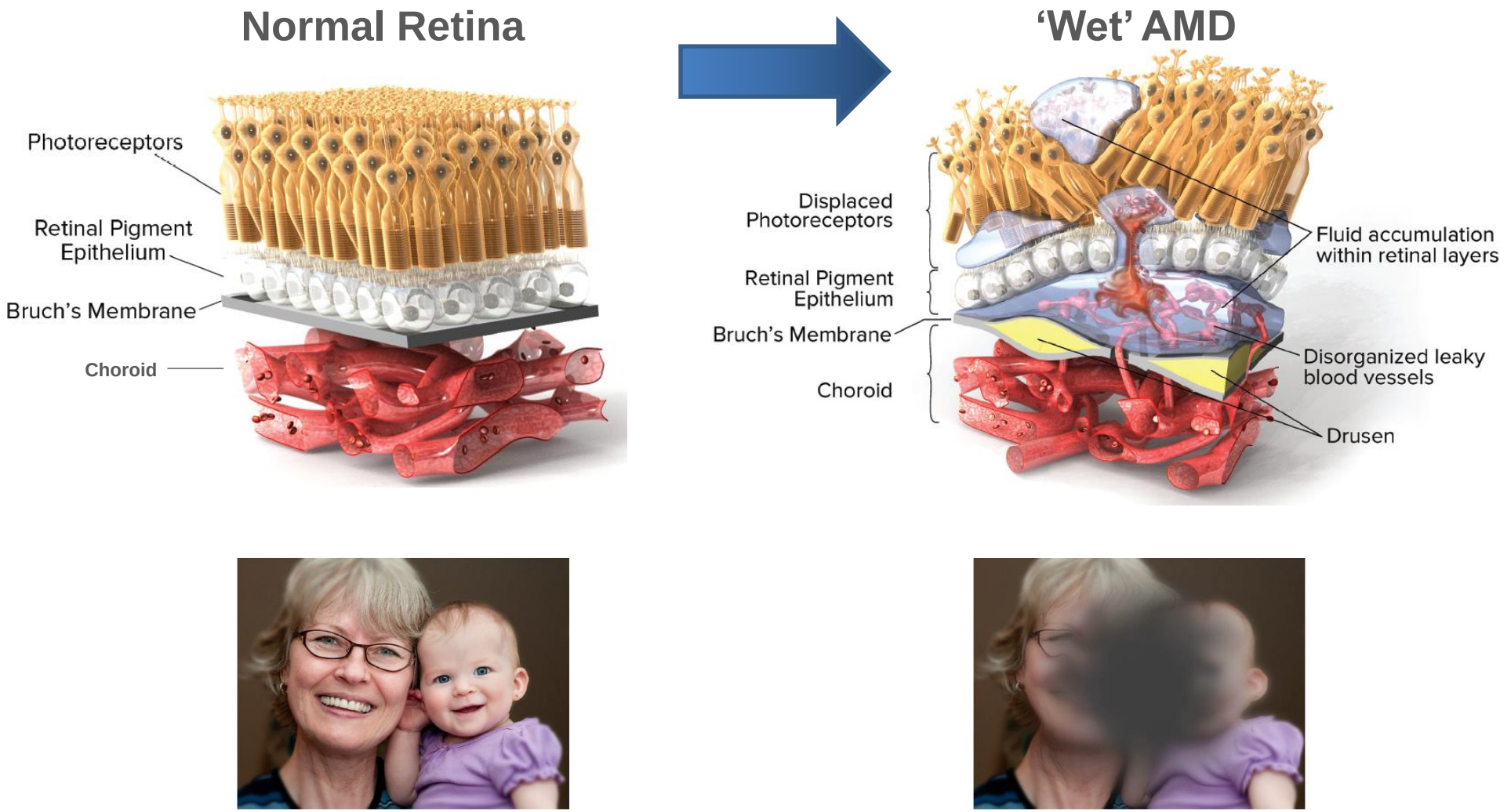


Figure: The Angiogenesis Foundation

Large Market Opportunity & Unmet Medical Need

- Wet AMD is the leading cause of blindness in the western world
- Market Opportunity: world-wide $US10BN*
- Only two targeted therapies approved for wet AMD (Lucentis™ & Eylea™, off-label Avastin®)
- All target VEGF-A, but not VEGF-C or VEGF-D

VEGF-A Inhibitors

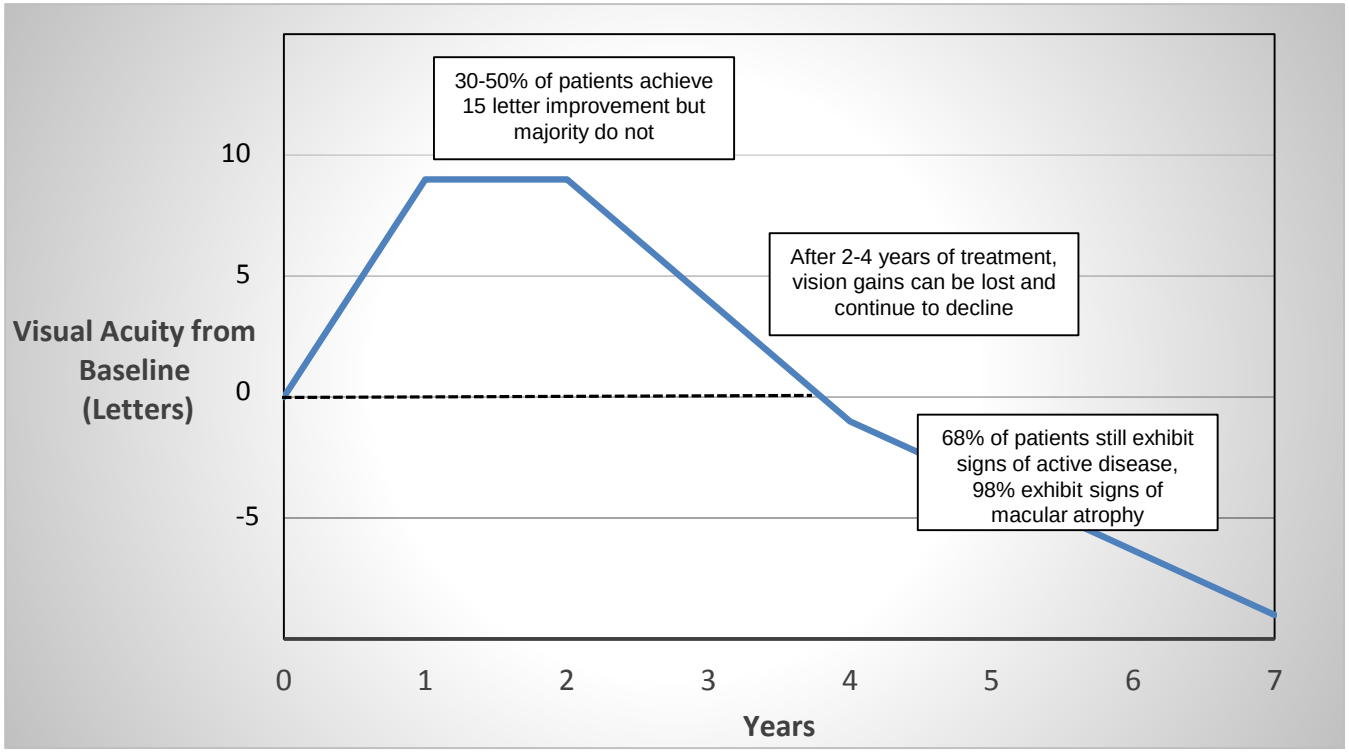
Long term therapy with Lucentis™ or Eylea™ is associated with sub-optimal response:

- **>50% patients do not achieve a significant gain in vision**
- **50-70% patients have retinal fluid despite anti-VEGF-A therapy**

**Cowen Analyst Report: Ophthotech July 7 2015*

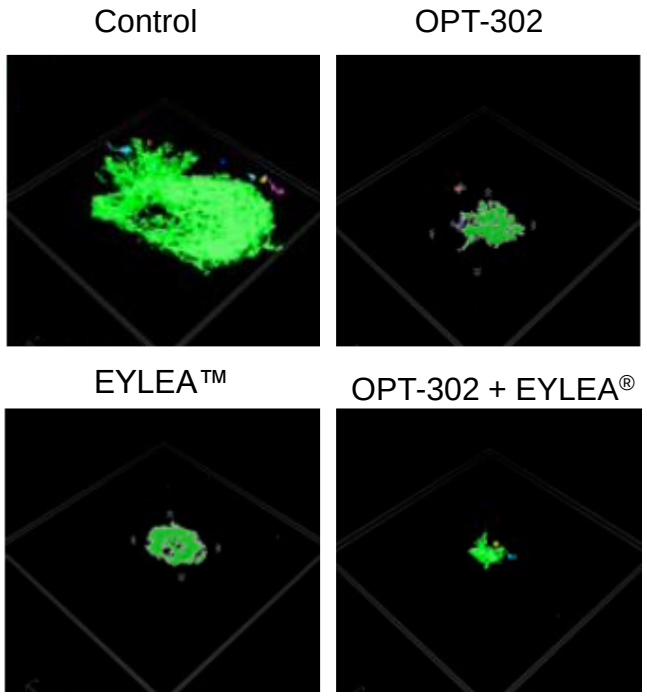
The opportunity for OPT-302:
An unmet medical need remains despite anti-VEGF-A therapy

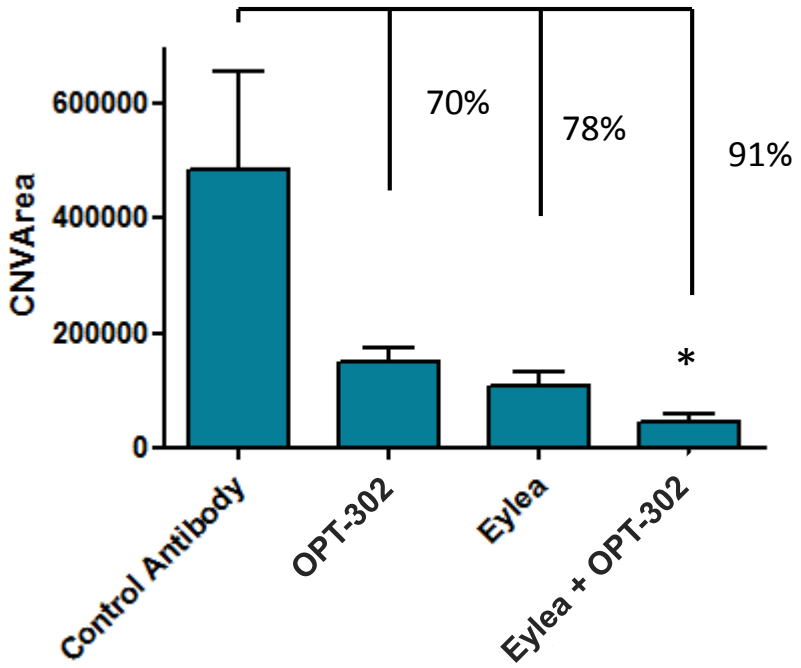
- To increase the **number** of patients who experience a significant gain in vision
- To increase the **magnitude** of the vision gain
- To **prolong response** to therapy and prevent visual decline
- Potential to **reduce** dosing frequency



Significant additive activity of OPT-302 & 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)

OPTHEA circadian

Protocol OPT-302-1001: Phase 1/2A study in wet AMD

A Phase 1/2A Dose Escalation Study Evaluating the Safety, Pharmacokinetics and Pharmacodynamics of OPT-302 in combination with Ranibizumab in subjects with wet AMD

Two stage Design

Part 1 Dose escalation – Open Label

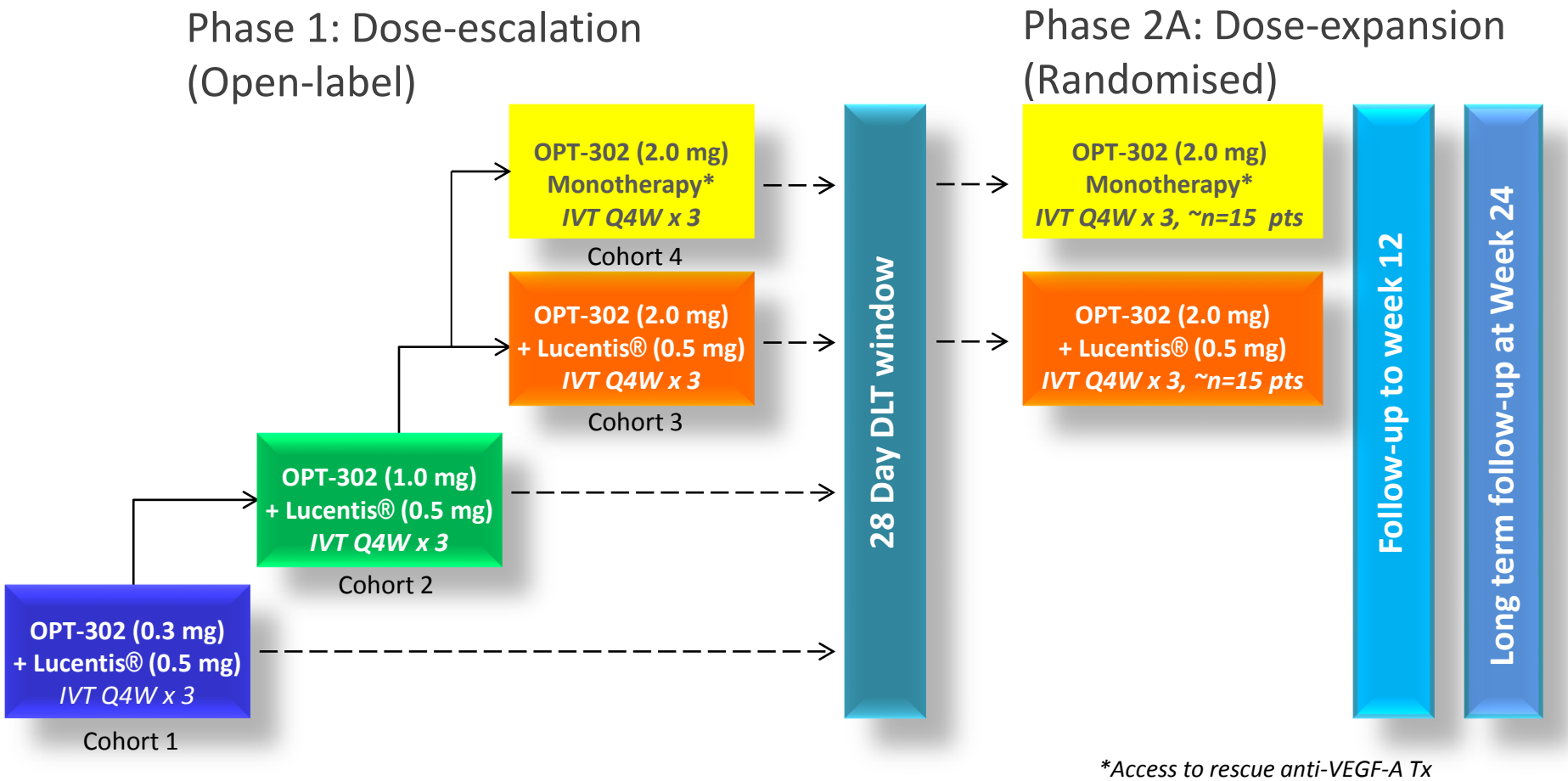
Part 2 Dose expansion - Randomized

Subjects with active CNV associated with wet AMD including those that are either treatment naive or have received prior therapy will be eligible for the study.

IND #: 122162
Sterling IRB study #: 5123 (*Approved*)
ClinTrials.gov ID#: NCT02543229

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

Dose-escalation & dose-expansion 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 study objectives

Primary Objectives:

- To evaluate the safety and establish the dose of OPT-302 administered by intravitreal (IVT) injection in combination with IVT ranibizumab in subjects with wet AMD

Secondary Objectives:

- mean change in central retinal thickness from baseline (SD-OCT)
- mean change in CNV lesion area from baseline (FA)
- mean change in BCVA (ETDRS) from baseline
- mean time to, and number of, retreatment injections of anti-VEGF-A therapy during long term follow-up (week 12 to 24)
- need for 'rescue therapy' with ranibizumab in subjects receiving OPT-302 monotherapy
- pharmacokinetics (PK) of OPT-302
- incidence of anti-OPT-302 antibody formation

Exploratory Objective(s):

- To evaluate changes in systemic levels of angiogenesis-related biomarkers

Clinical Advisory Board & Investigators
Near-term Clinical Milestones

- 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 Uni.)
  - Peter Campochiaro MD (Johns Hopkins, Wilmer Eye Institute)
  - Kameran Lashkari MD (Schepens Eye Research Inst., Mass.Eye & Ear)
- Actively recruiting
- ClinTrials.gov ID#: NCT02543229

OPT-302 Wet AMD Program: Milestones

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In combination with a VEGF-A inhibitor, OPT-302 achieves more effective VEGF suppression

- OPT-302 is a novel ‘trap’ that blocks the alternative VEGF-C/VEGF-D pathway
- Used in combination, OPT-302 can achieve more effective VEGF suppression and target a key mechanism of sub-responsiveness to existing therapies
- Combination OPT-302 + a-VEGF-A therapy may improve visual acuity outcomes, reduce retreatment rates and lead to larger treatment free intervals for patients
  - Potential for:
    - Improved patient responses
    - Reduced treatment burden

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Thank-you

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