# Corporate Update

## Extraordinary General Meeting, March 7 2016

**Opthea Limited**

**(ASX:OPT, OTCQX:CKDXY)**

**Megan Baldwin PhD, CEO & Managing Director**

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# Opthea Limited

- Clinical stage biotechnology company
- Developing a novel therapy for wet AMD
- Wet AMD is the leading cause of blindness in the Western world in older adults
- Technology is based on targeting signals that control blood vessel growth and leakage
- Lead compound OPT-302 blocks VEGF-C and VEGF-D
- Ongoing Phase 1/2A clinical trial being conducted at US sites in wet AMD patients
  - Potential to expand development program in a range of eye diseases
  - Investigating OPT-302 as monotherapy and in combination with existing treatments
  - Combination therapy more completely shuts down pathways involved in disease progression
- Near-term clinical milestones

**OPT-302 Wet AMD Program: Milestones**

IND Approval for OPT-302
June 2015 ✓

Initiated Phase 1/2A clinical trial:
30 June 2015 ✓

Ph 1 Primary Safety Data Analysis:
1Q16 (20 patients)

Ph 2A Primary Data Analysis:
2H16 (~30 patients)



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# Financial Position (Unaudited)

| Key Financial Details | ASX: OPT |
|---|---|
| Ticker Symbol | ASX:OPT |
| Share Price *(as at Mar 5 2016)* | ~A$0.375 |
| Total Ordinary Shares on Issue | 150,190,303 |
| Options on Issue | 49,722,697 |
| Market Capitalisation *(as at Mar 4 2016)* | ~A$56.3m |
| Trading Range *(last 12 months)* | A$0.14 – 0.55 |
| Cash Balance *(at 31 Dec 2015)* | ~A$17.8m |
| Listed Investments | ~A$0.9m |
| Top 10 Shareholders Own | 69% |

| Substantial Shareholders | % Holding |
|---|---|
| Biotechnology Value Fund (BVF)* | 18% |
| Baker Bros (NY, USA) | 9% |
| Packer & Co. | 8.5% |

**Share Price Performance (Feb '15 – Feb '16)**




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

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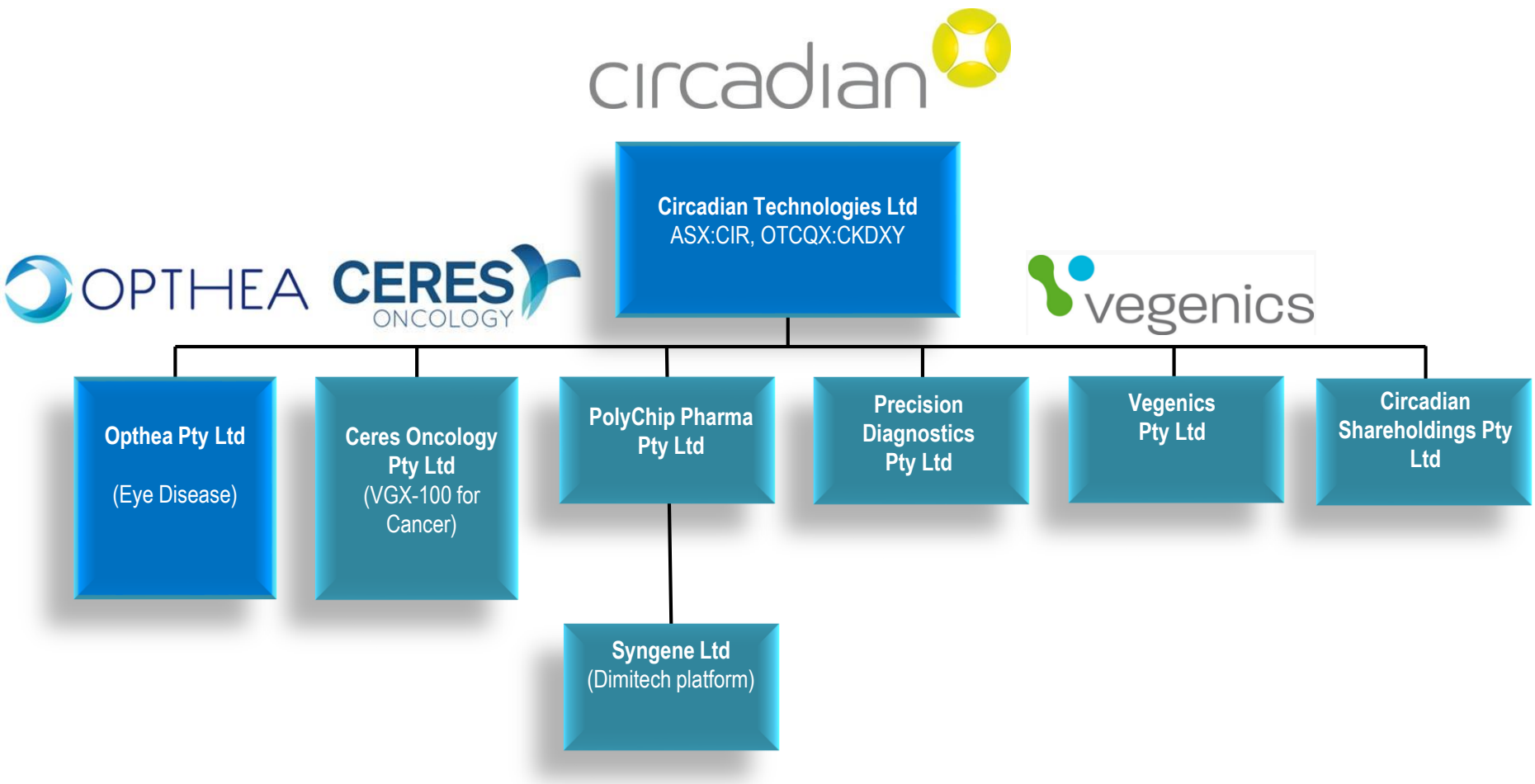
# Corporate Achievements – last 12 months

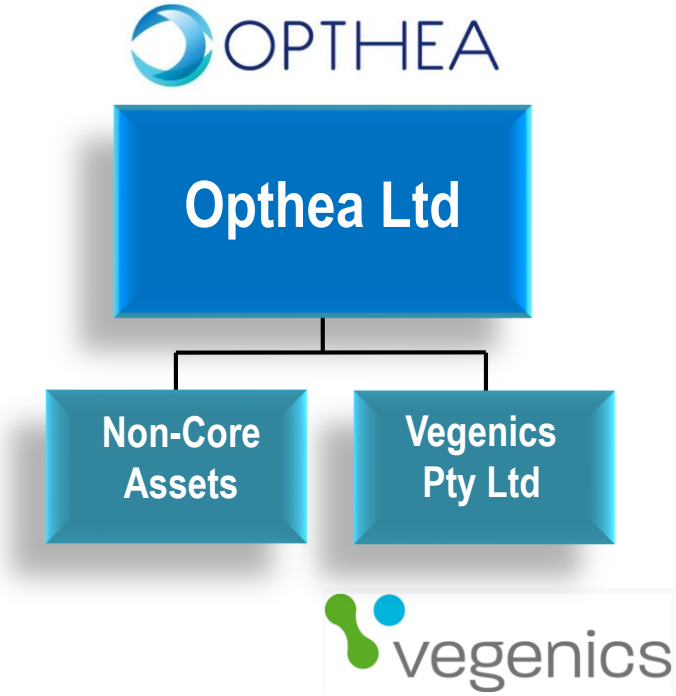
**Corporate**

- ✓ Board renewal
- ✓ Company name change
- ✓ Continued execution of strategy to focus on ophthalmology
- ✓ Prudent financial management post A$17.4m capital raising Nov ‘14
- ✓ ~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 the Group by initiation of deregistration of subsidiaries
  - ✓ Including solvent members’ voluntary liquidation of Syngene Ltd
  - ✓ Pro-rata allocation of remaining capital to Syngene shareholders

# Corporate Re-Structure



# Simplification of Corporate Structure*






** Anticipated corporate structure following simplification which may be subject to changes.*

# 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, 14 trial sites open
- ✓ Grown local & international profile
- ✓ 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

# 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

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# The disease process of ‘wet’ (neovascular) AMD

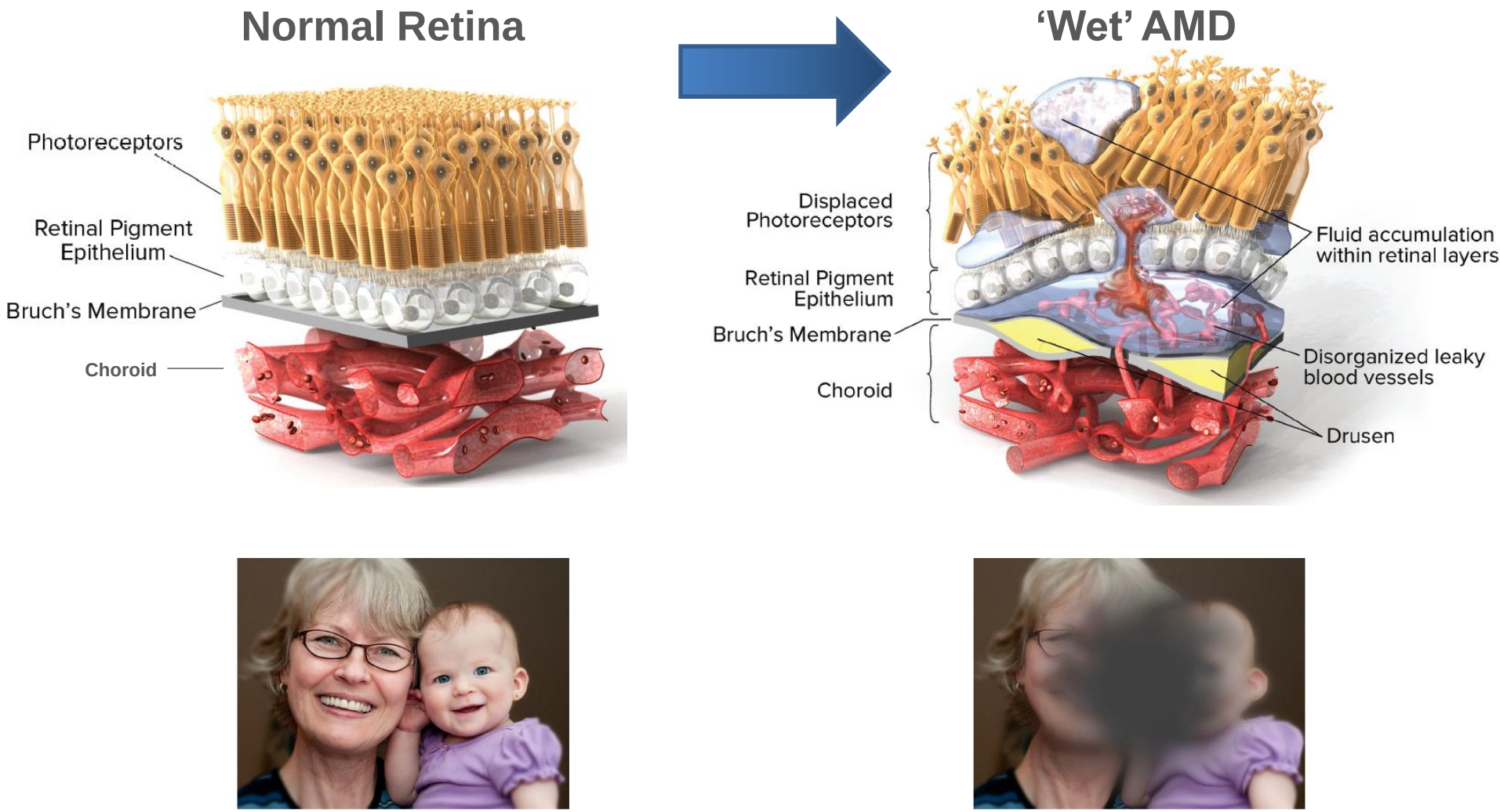






*Figure: The Angiogenesis Foundation*



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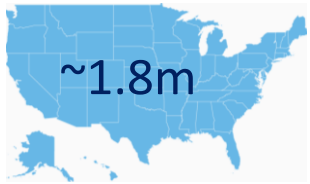
# Large and growing market opportunity

- Wet AMD is the leading cause of blindness in the western world
- Increasing prevalence due to ageing population
- Prevalence expected to double by 2020


- Approved therapies for wet AMD target VEGF-A, but not VEGF-C or VEGF-D

***Our approach is novel and differentiated from the existing therapies, yet targets a validated pathway in wet AMD disease progression***


2015: >$7BN


60% Market Share

Market Opportunity*:

# >$10BN Worldwide



*Cowen Analyst Report: Ophthotech July 7 2015

# An unmet medical need despite availability of VEGF-A inhibitors

Despite receiving a VEGF-A inhibitor (Lucentis®, Eylea® or Avastin®):

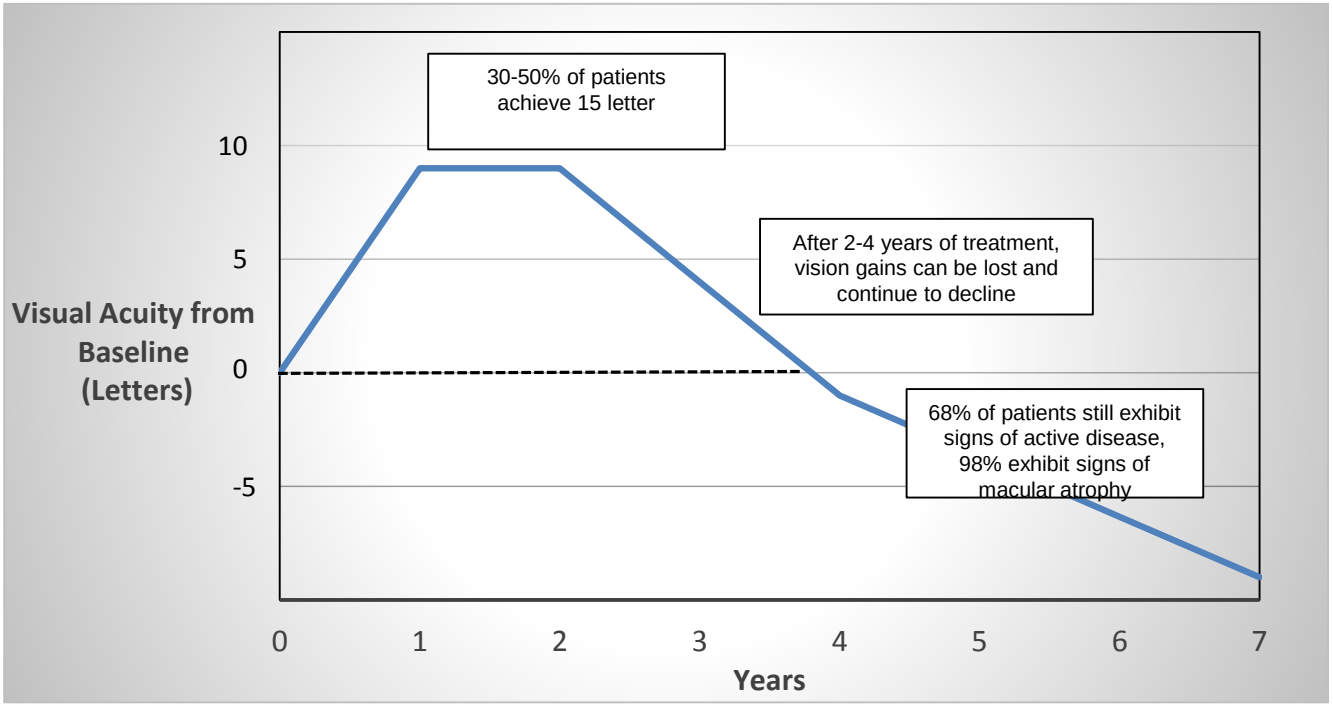
**>50%** do not achieve significant vision gain

**2/3** will continue to have fluid at the back of the eye

**25%** will have further vision loss at 12 mos

# 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



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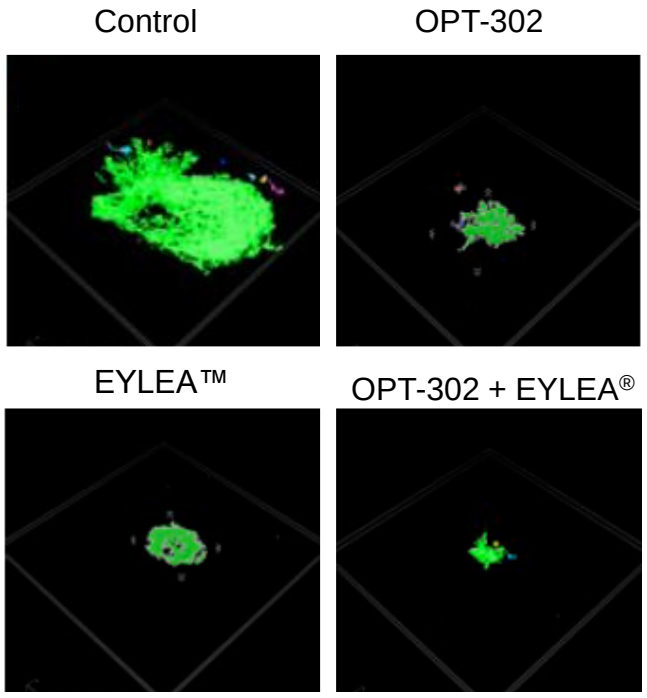
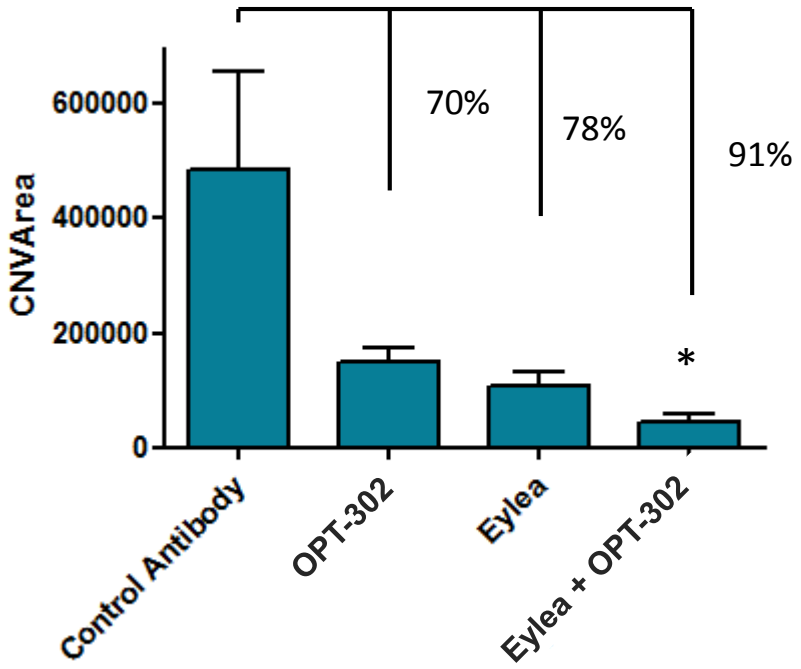
# Significant additive activity of OPT-302 & Eylea® in mouse AMD

**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)*



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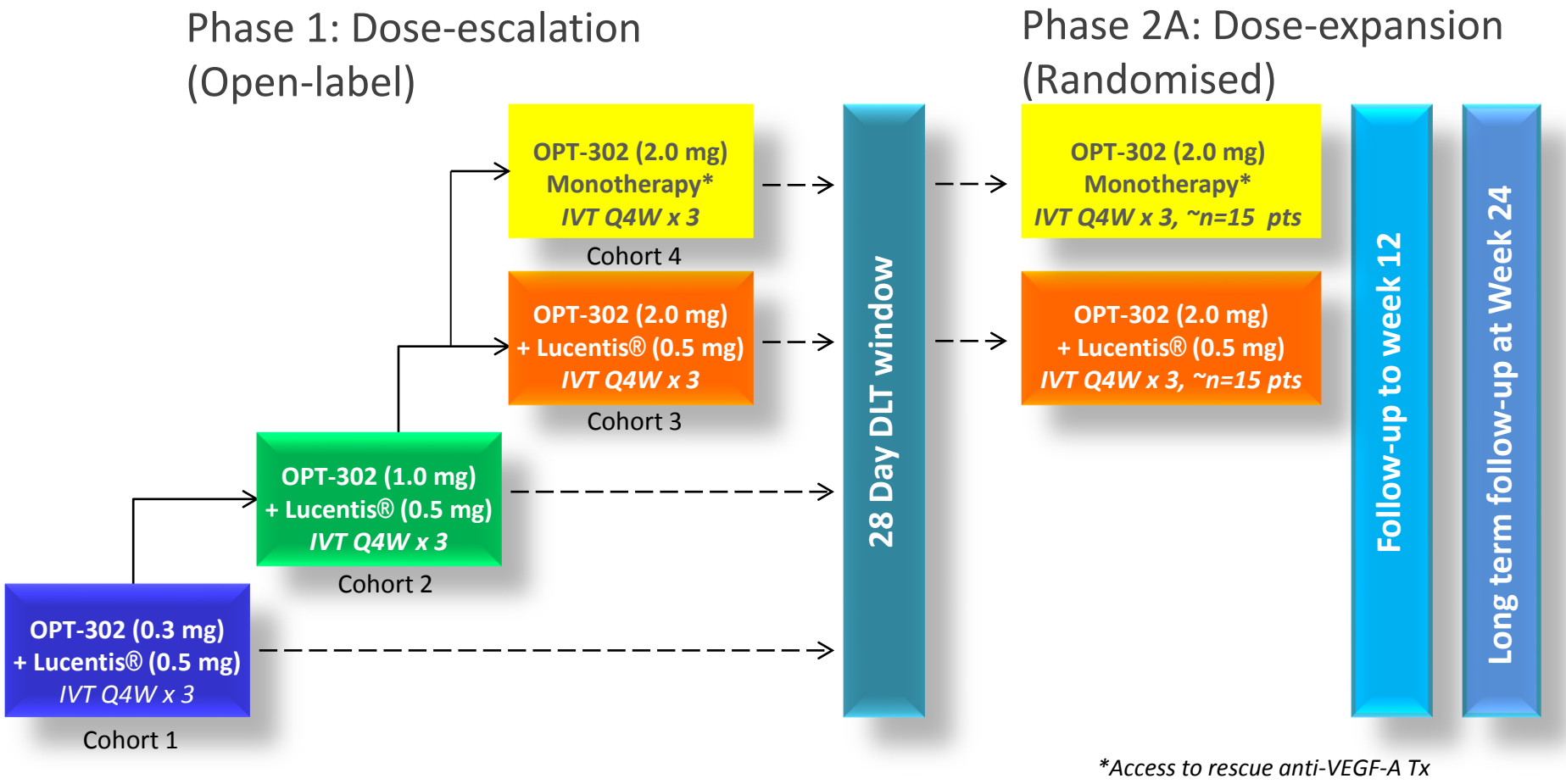
# OPT-302 Phase 1/2A: Protocol: OPT-302-1001

## 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.*

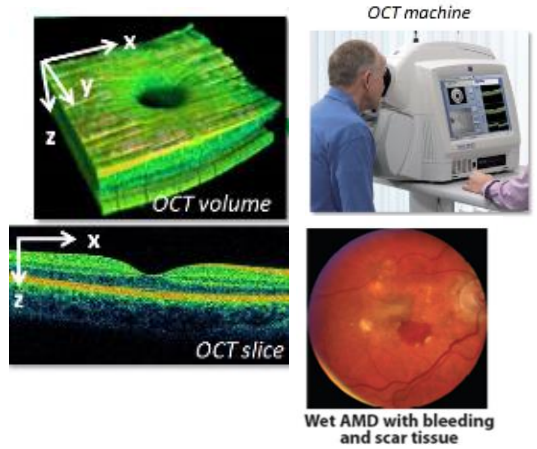
# Phase 1/2A Trial Endpoints

Primary Endpoint of Phase 1/2A trial:

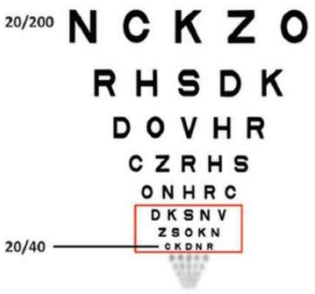
- Safety

Secondary Endpoints:

- Preliminary measures of clinical activity
- Vision (Eye-Chart)
- Size of lesion
- Fluid
- Need for ‘rescue therapy’ in monotherapy cohort
- Need for a-VEGF-A therapy in long-term follow-up




Anatomical Changes by Imaging (OCT,FA)
(Retinal fluid, thickness, area)




Visual Acuity
Eye Chart



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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
  - lead to larger treatment free intervals for patients
- Potential for:
    - Improved patient responses
    - Reduced treatment burden

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