OPTHEA

OPT-302:
VEGF-C/D ‘trap’ for Eye Diseases

Corporate Presentation, January 2018

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Opthea Limited

Opthea Overview	• Opthea is a Melbourne-based biotechnology company with novel IP and therapy for eye diseases • Publicly-traded, listed on ASX (ASX:OPT) • Developing OPT-302, a new approach for the treatment of wet AMD and DME
OPT-302 is a novel approach therapy addressing unmet needs for wet AMD and DME	• OPT-302 (sVEGFR-3) is a biologic that targets VEGF-C and VEGF-D, blocking the same, as well as independent pathways, to VEGF-A • Combination therapy with approved VEGF-A therapies to more completely shut-down VEGF/VEGFR pathway • Targets mechanisms of resistance and sub-optimal clinical response to existing therapies
Strong and growing commercial potential	• Current & growing market opportunity of $10B+ worldwide • Broad development opportunity in wet AMD, Diabetic Macular Edema (DME) and Retinal Vein Occlusion (RVO)
Phase 1/2A data in wet AMD	• OPT-302 well tolerated in 51 patients (>150 IVT injections) • Evidence of improved vision and reduction in retinal fluid • Differentiation of target mechanism to anti-VEGF-A, PDGF and Ang2 agents
Advancing to late stage development	• Currently enrolling patients in two randomized, controlled clinical trials • Phase 2b wet AMD and Phase 1b/2a DME studies • Trials will recruit patients in US, EU and Australia
Robust and broad intellectual property	• Granted Composition of Matter patents (2022-2026); Composition of Matter and ‘Use’ Patents (2023 & 2034); Additional patent term extensions

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Financial Position (Unaudited)

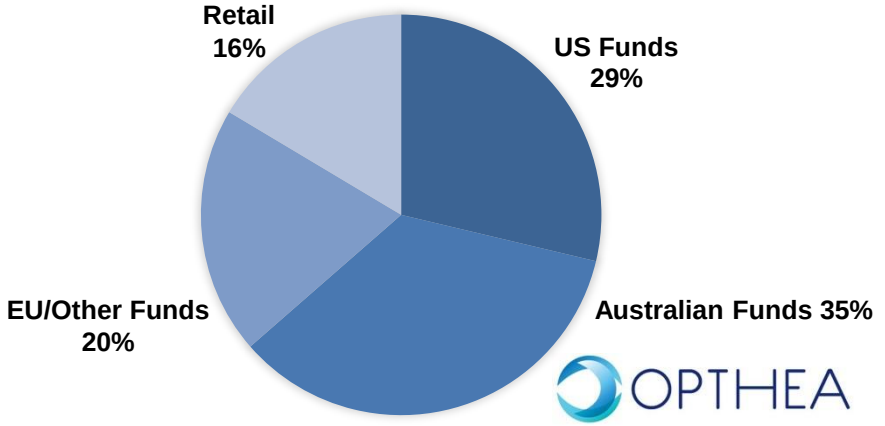
Key Financial Details	ASX: OPT
Ticker Symbol	ASX:OPT
Share Price (Jan 5 2018)	~A$0.71
Total Ordinary Shares on Issue	201,656,670
Options on Issue	48,054,542
Market Capitalisation (Jan 5 2018)	~A$143m (~USD112m)
Trading Range (last 12 months)	A$0.66 – 1.20
Cash Balance (Dec 31 2017)	~A$42m*
Forecast Net Operating Cash Burn (CY 2018)	~$18m
Top 20 Shareholders Own	69%
Institutional Holders	84%

Details

- Cash positive until end 2020
- Fully-funded through
  - 351 pt Ph2b wAMD trial (randomised, statistically powered)
  - ~117 pt Ph1b/2a DME trial (randomised, statistically powered)
  - Additional Ph 2a trial (eg. Prior-Tx Patients)

Share Price Performance (Dec 2015 - Dec 2017)

Shareholders by Region



** Does not include R&D Tax Credit of A$2.7m received Jan 8 2018 for R&D expenditure FY 2016-17*

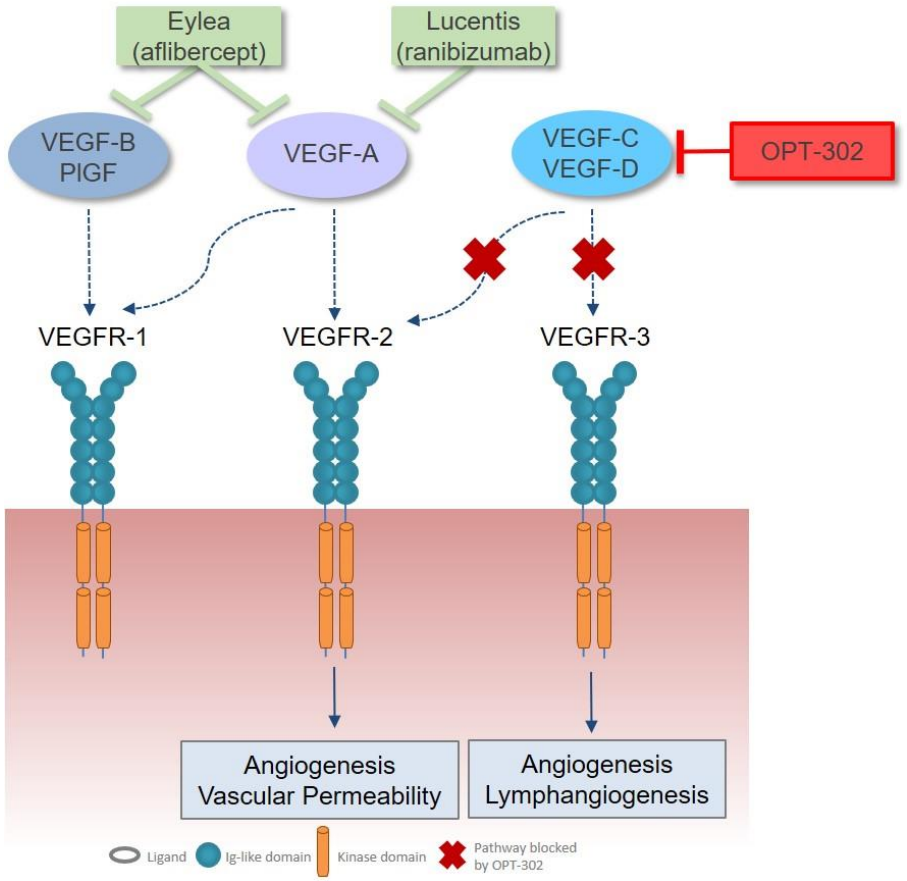
OPT-302 Overview & Scientific Background

By targeting parts of the pathway that established VEGF-A players don't block, OPT-302 aims to improve on the current treatment paradigm's long-term efficacy

OPT-302 for Wet AMD & DME

- **OPT-302: A Soluble Form of VEGFR-3**
  - Targets a validated pathway involved in wet AMD and DME progression and a mechanism of escape from existing therapies that is differentiated to anti-VEGF-A therapies
  - Comprises the extracellular domains 1-3 of VEGFR-3 and the Fc fragment of human IgG1
  - Potent inhibitor of VEGF-C (~5pM) and VEGF-D (~0.5 nM)
  - A 'trap' that binds and neutralises the activity of VEGF-C and VEGF-D, blocking binding to the receptors VEGFR-2 and VEGFR-3
    - Inhibits blood vessel growth
    - Inhibits vascular leakage
- **Strategy**
  - To develop OPT-302 for use in combination with existing VEGF-A inhibitors for the treatment of wet AMD & DME
  - Achieve complete blockade of the VEGF pathway
  - Blocks mechanisms of 'escape' from existing therapies
- **Rationale**
  - Long-term single-agent therapy with VEGF-A inhibitors is associated with sub-optimal responses
    - Sub-optimal improvements in visual acuity (<15-letter gain)
    - Persistent retinal fluid
  - Resistance to VEGF-A monotherapy may be related to other VEGF family members
  - VEGF-C/D are elevated when VEGF-A is inhibited
  - OPT-302 combination therapy achieves a more complete suppression of the VEGF/VEGFR pathway
  - OPT-302 targets incomplete response to VEGF-A inhibition

OPT-302 inhibits VEGF-C/D



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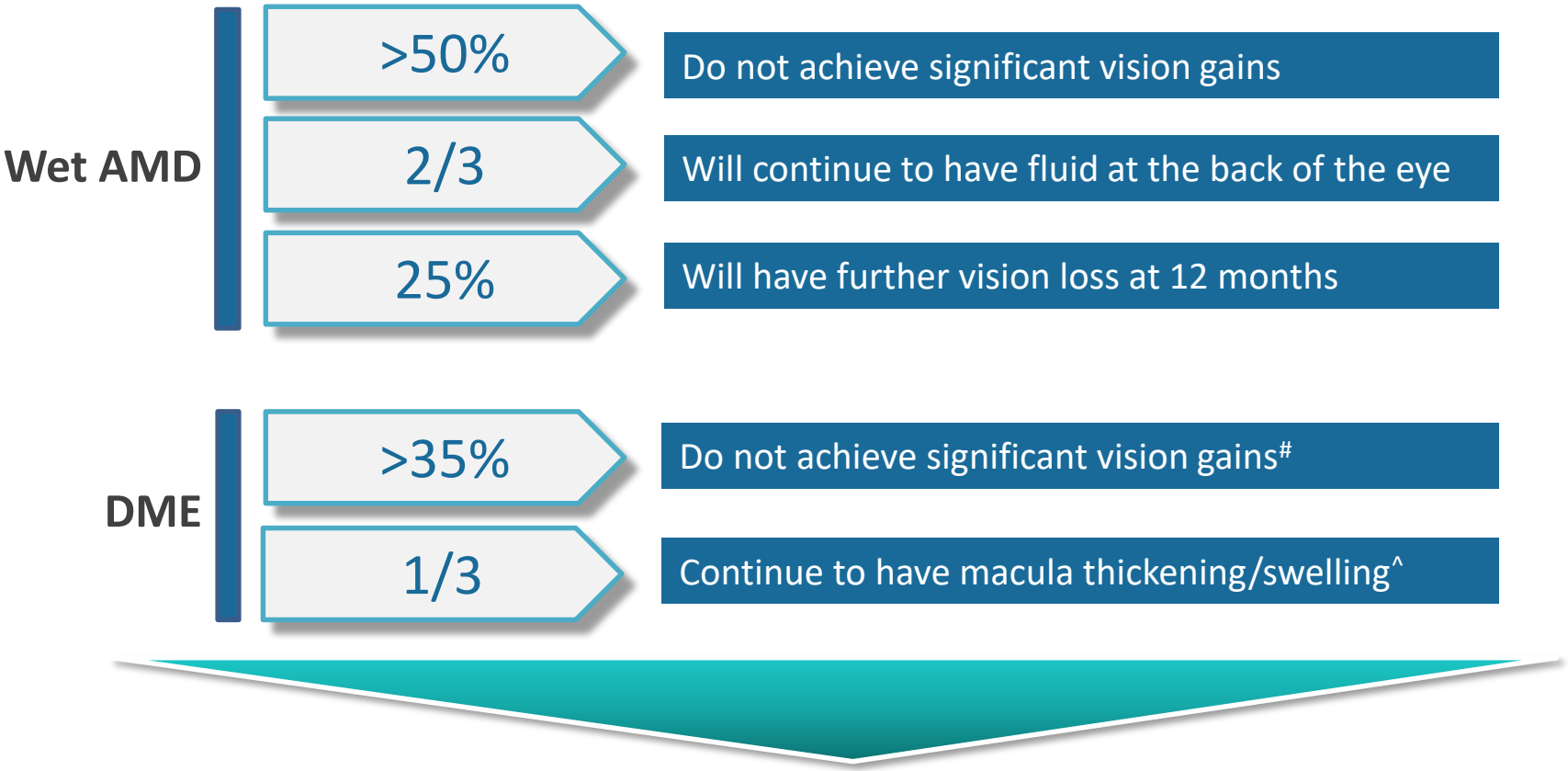
An Unmet Medical Need for Wet AMD and DME

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



Opportunity: New Products that Improve Efficacy and Durability

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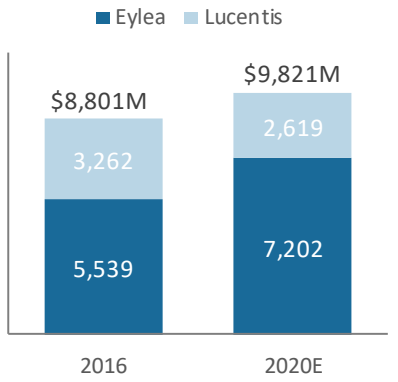
** Based on randomised, controlled clinical trial data; # Fail to achieve ≥ 2 lines improvement in BCVA; ^ SD-OCT CST ≥ 300 µM or Time-Domain OCT CST ≥ 250 µM*

Very Few Novel Combination Therapies in Development

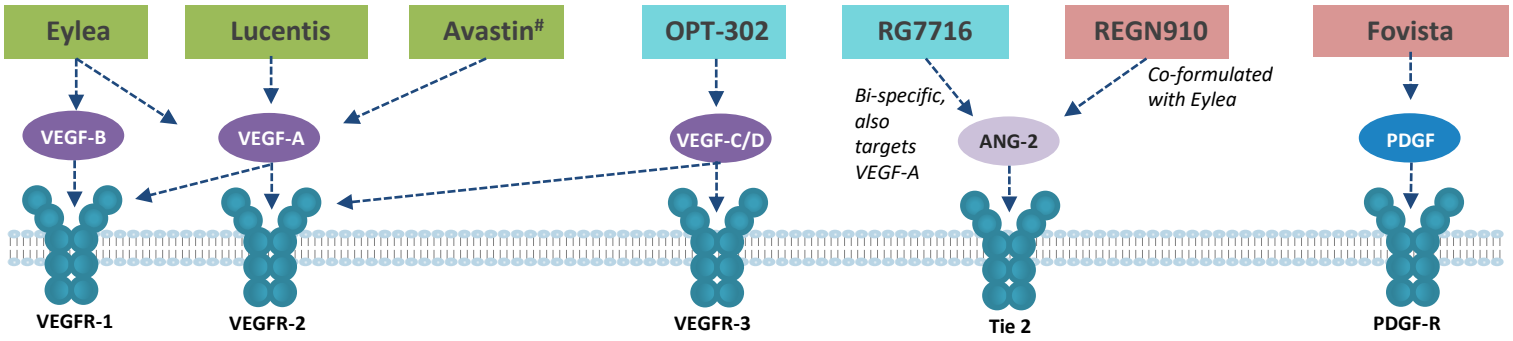
Large & Growing Market Opportunity

- Wet AMD and DME prevalence is increasing due to the growing aging and diabetic populations respectively
- In 2016, Lucentis and Eylea generated revenues >$8.5B
- Existing therapies targeting VEGF-A are sub-optimally clinically effective in the majority of patients – a major unmet medical need

Eylea & Lucentis Aggregate Worldwide Sales



Mechanism Comparison Of IVT Administered Wet AMD Agents



= In Clinical Development
= Failed to meet primary endpoint or not advancing to Phase 3
= Approved therapies

Opthea is the Only Company Working on VEGF-C/D

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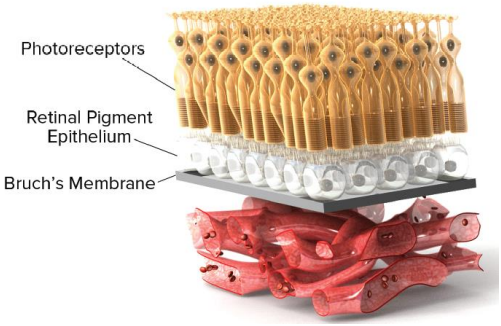
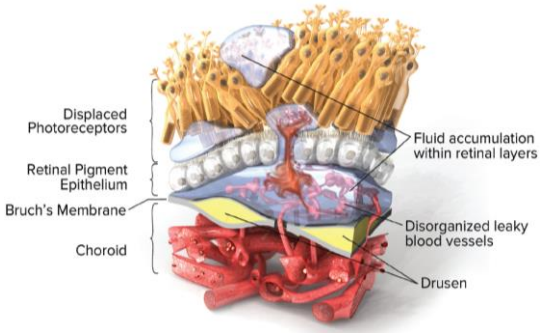
** Small molecule TKIs such as X-82 (Tyrogenix) and Squalamine (Ohr Pharmaceuticals) are not represented here. Other biologics in development that selectively target VEGF-A include Abicipar Pegol (DARPin, Allergan), RTH258 (Novartis), and anti-VEGF-A biosimilars*
 # Avastin is used off-label for the treatment of wet AMD

OPT-302 Targets Mechanisms Involved in Wet AMD & DME Progression



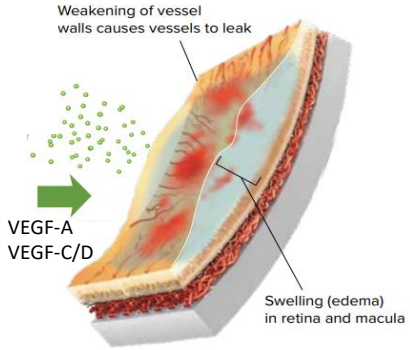
Normal Retina

- Light-sensitive tissue at the back-of-the-eye required for vision
- The macula is the central-region of the retina required for highly detailed, focused vision
- Choroidal vessels functional, non-leaky



Wet (Neovascular) AMD

- Leading cause of blindness in people >55 years
- Loss of vision in central visual field
- Abnormal growth of blood vessels and fluid/protein leakage from vessels leads to retinal degeneration
- Untreated, leads to chronic and rapid decline in visual acuity and increase in retinal fluid

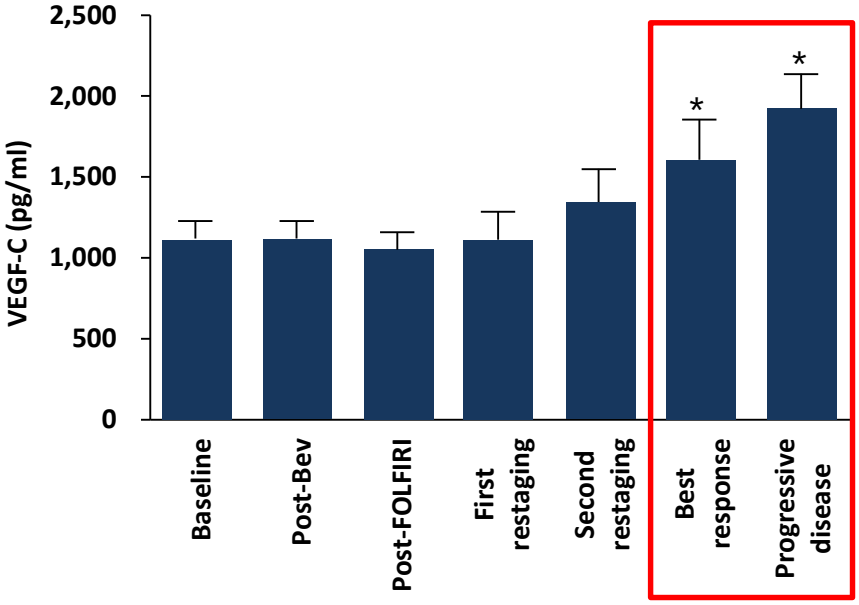


Central-Involved Diabetic Macular Edema

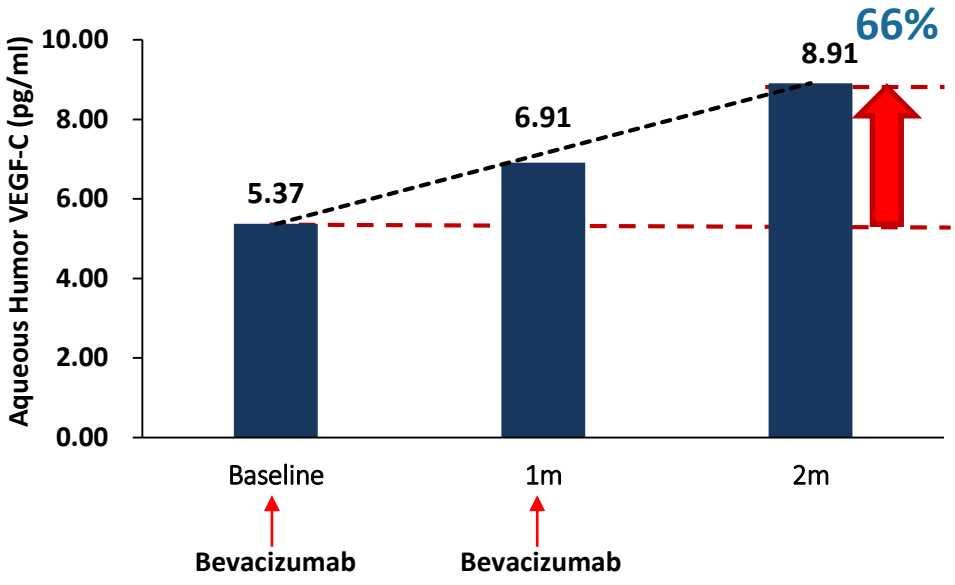
- Leading complication and cause of blindness in diabetics
- Elevated glucose levels in diabetics can lead to inflammation, vascular dysfunction, hypoxia & breakdown of blood-retinal barrier
- Members of VEGF family upregulated, inducing vascular leakage
- Fluid accumulation leads to macular swelling and vision loss

VEGF-A Inhibition Upregulates VEGF-C/D

Metastatic Colorectal Cancer [1]



Neovascular AMD [2]

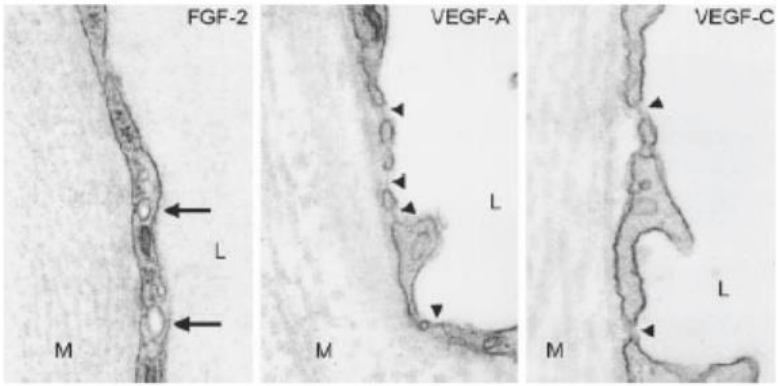


1 *"The association of alternate VEGF ligands with resistance to anti-VEGF therapy in metastatic colorectal cancer" - Lieu et al., 2013.*

2 *"Bevacizumab injection in patients with neovascular age-related macular degeneration increases angiogenic biomarkers." Cabral T, Lima LH, Mello LGM, et al., Ophthalmology Retina 2018;2:1:31-7.*

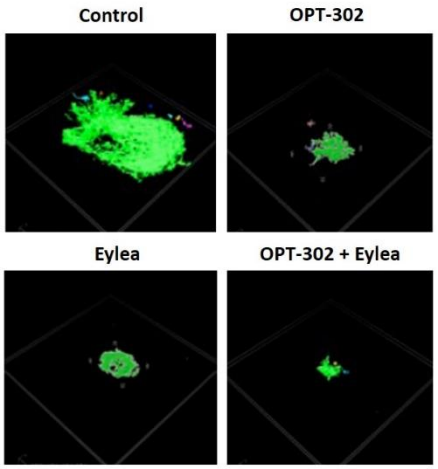
OPT-302 Targets Factors that Induce Vascular Leakage & Is Active in a Mouse Model of Wet AMD

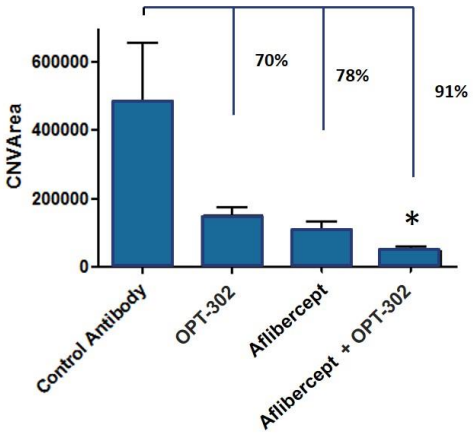
VEGF-C Induces Vascular Permeability – Contribution to Retinal Edema



Cao et al,. Circ Res., 2004

OPT-302 Activity in Mouse Wet AMD Model





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

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

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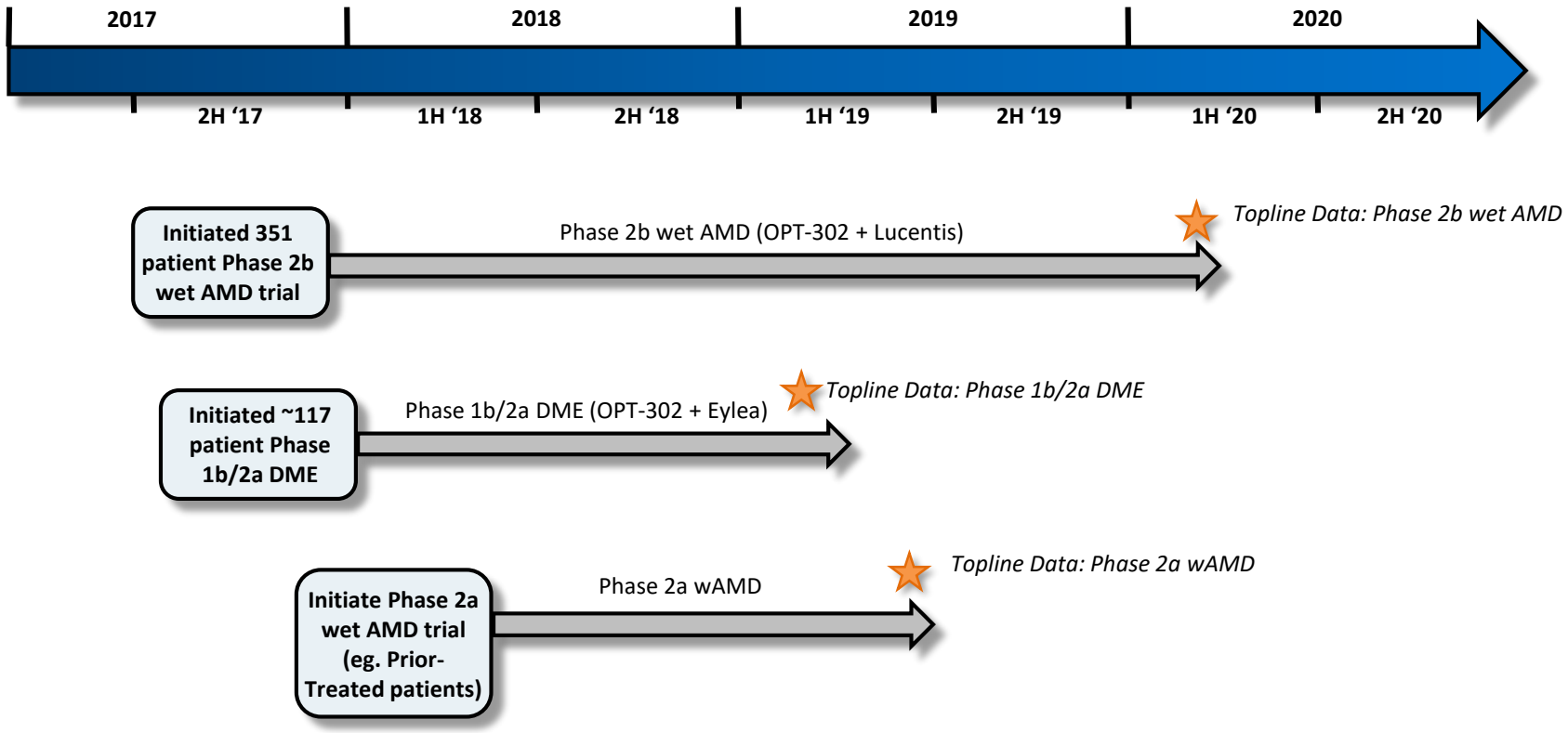
OPT-302: Fully Funded Through a Diversified Clinical Development Program

Opthea fully funded through clinical development program with multiple clinical inflection points including:

- A randomised Phase 2b clinical trial of OPT-302 + Lucentis compared to Lucentis alone in 351 wet AMD (tx-naïve) patients
- A randomised Phase 1b/2a clinical trial of OPT-302 + Eylea compared to Eylea alone in ~117 DME patients
- An additional Phase 2a clinical trial of OPT-302 + α-VEGF-A in wet AMD patients



Note: Dates provided in timelines are estimates, and indicative only, and subject to change as a result of a number of factors outside of Opthea's control

Milestones

OPT-302 Wet AMD Program:

- ✓ Phase 1/2a Data Analysis
  $45m Cap. Raise
  April '17
- ✓ Phase 2b wAMD
  First Patient Dosed (USA)
  4Q'17
- Publication Ph1/2a trial results
  in peer-reviewed journal
  2Q'18
- Additional Phase 2a wAMD Design
  Finalised/Initiation
  1H'18
- Phase 2b wAMD
  Primary Data Analysis
  1H'20

OPT-302 DME Program:

- ✓ Phase 1b/2a DME Trial
  Initiation
  4Q'17
- Phase 1b/2a DME Trial
  Primary Data Analysis
  1H'19

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OPT-302:
Phase 1/2a Trial Results

A Phase 1/2A dose escalation study evaluating the safety, pharmacokinetics and pharmacodynamics of OPT-302 in combination with ranibizumab (Lucentis®) in subjects with wet AMD

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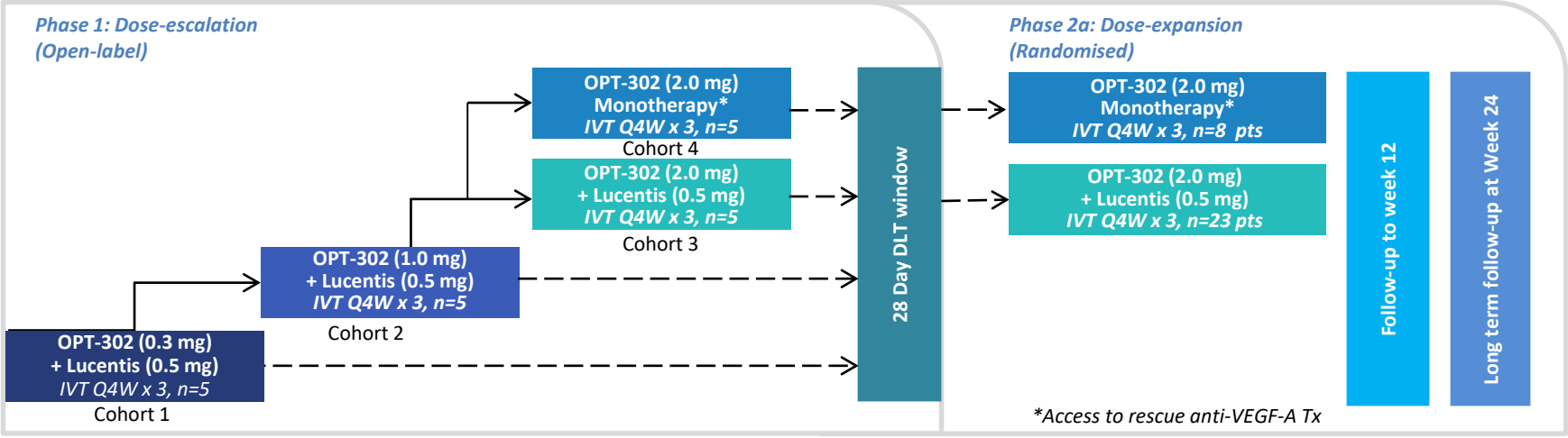
OPT-302 Phase 1/2a Trial Design & Objectives (n=51)

Dose-escalation & dose-expansion of repeated IVT injections



Primary Objectives:

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

Secondary Objectives:

- Mean change in BCVA (visual acuity) (ETDRS) from baseline
- Mean change in central retinal thickness from baseline (SD-OCT)
- Mean change in CNV lesion area from baseline (FA)
- Mean time to, and number of, retreatment injections of anti-VEGF-A therapy during long-term follow-up (week 12 to week 24)
- Need for 'rescue therapy' with Lucentis 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

Phase 1/2A Evaluated OPT-302 as a Monotherapy and in Combination with Lucentis

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OPT-302 Phase 1/2a Safety Summary

- **OPT-302 ± Lucentis administered by repeat IVT injection (Baseline, Week 4, Week 8)**
  - No missed doses, safety experience with ~150 intravitreal (ocular) injections of OPT-302
- **OPT-302 at ocular doses up to 2 mg ± Lucentis (0.5 mg):**
  - No dose limiting toxicities (MTD was not reached)
  - No drug-related serious adverse events or systemic adverse events
- **2 / 51 patients (3.9%) had ocular adverse events related to OPT-302 study drug**
  - Adverse events were Grade 1 / Mild inflammation consistent with anterior uveitis in the low- and mid-dose combination groups*
  - No OPT-302 related AEs observed in the high dose (2mg) combination or monotherapy treated patients (n=41)
- **Majority of ocular emergent adverse events primarily related to IVT injection procedure**
  - (31 / 51 patients; 59%); majority were Grade 1 / Mild or Grade 2 / Moderate and Manageable
  - No signs of infection (endophthalmitis)
- **There were 2 patient deaths due to underlying disease, not considered to be related to OPT-302 or Lucentis treatment**
  - One patient at study day 69 with metastatic ovarian cancer & pulmonary embolism
  - One patient at study day 77 with myocardial infarction#

OPT-302 has consistently demonstrated a clean safety profile

** Lucentis incidence of 1+ ocular inflammation in previous trials ranges from 3.3 – 5.9% (Rosenfeld et al., NEJM, 355;14, pp 1419-1431, 2006, MARINA trial)*
 # Patient had extensive history of cardiovascular disease and risk factors for MI including prior MI, aortic stenosis, coronary artery disease, diabetes mellitus, hyperlipidemia and hypertension. Unrelated to study drugs.

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OPT-302 Phase 1/2a Study

- 51 patients, 32 (63%) females, 19 (37%) males, mean age 77 years
- 37 /51 (73%) occult, 12/51 (23%) min classic, 2/51 (4%) predominantly classic
- Mean min classic component 5.9%
- 49% treatment-naïve
- **51% difficult to treat patients sub-responsive to anti-VEGF-A therapy**
  - Mean number prior anti-VEGF-A injections: 17 (~2 years[#])

Cohort	Treatment	# Naïve Patients	# Prior-Treated Patients
1	OPT-302 (0.3 mg) + Lucentis (0.5 mg)	2	3
2	OPT-302 (1.0 mg) + Lucentis (0.5 mg)	0	5
3 & 5	OPT-302 (2.0 mg) + Lucentis (0.5 mg)	16	12[a]
	Total Combination Tx	***18***	***20***
4 & 6	OPT-302 (2.0 mg)	7[b]	6
	51 Total Patients	**25**	**26**

a. One patient with metastatic ovarian cancer/pulmonary embolism died prior to the week 12 (day 69) visit due to intercurrent illness unrelated to study drugs
b. One patient with a myocardial infarction died prior to the week 12 (day 77) visit (unrelated to study drugs)
#. Assuming treatments every 6 weeks, 1.3 years assuming treatment every 4 weeks.

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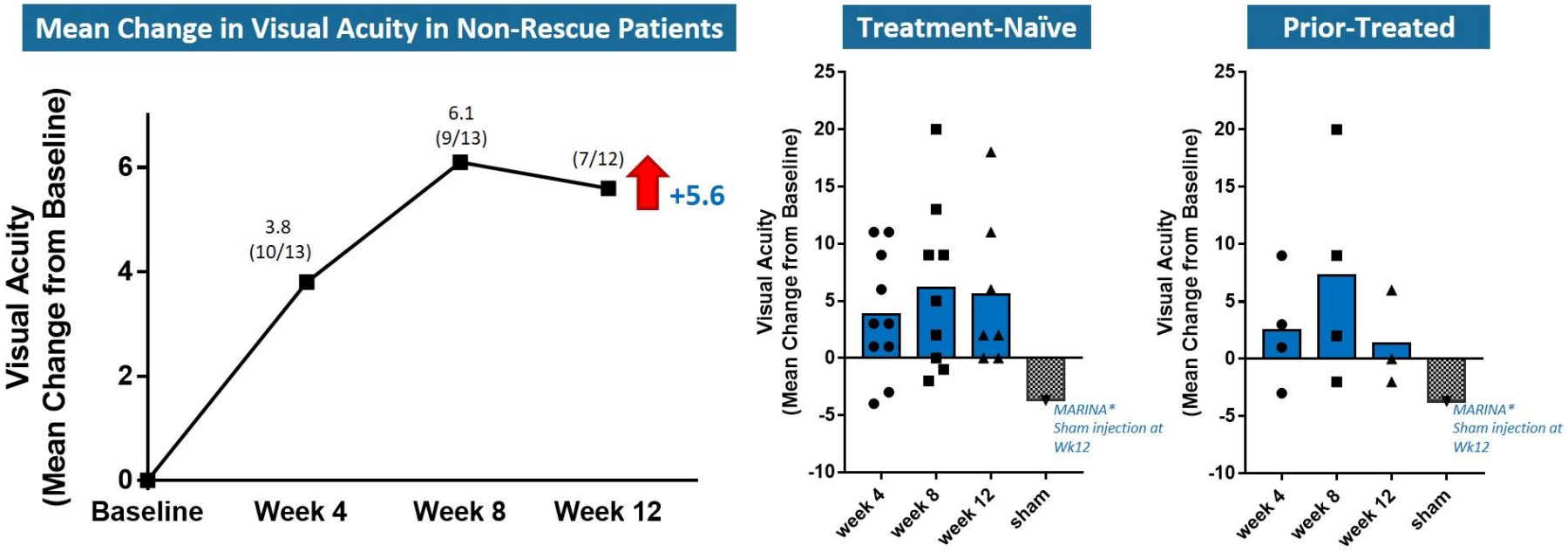
Phase 1/2a Monotherapy Patients



Gains in Visual Acuity in Patients Treated with OPT-302 Monotherapy

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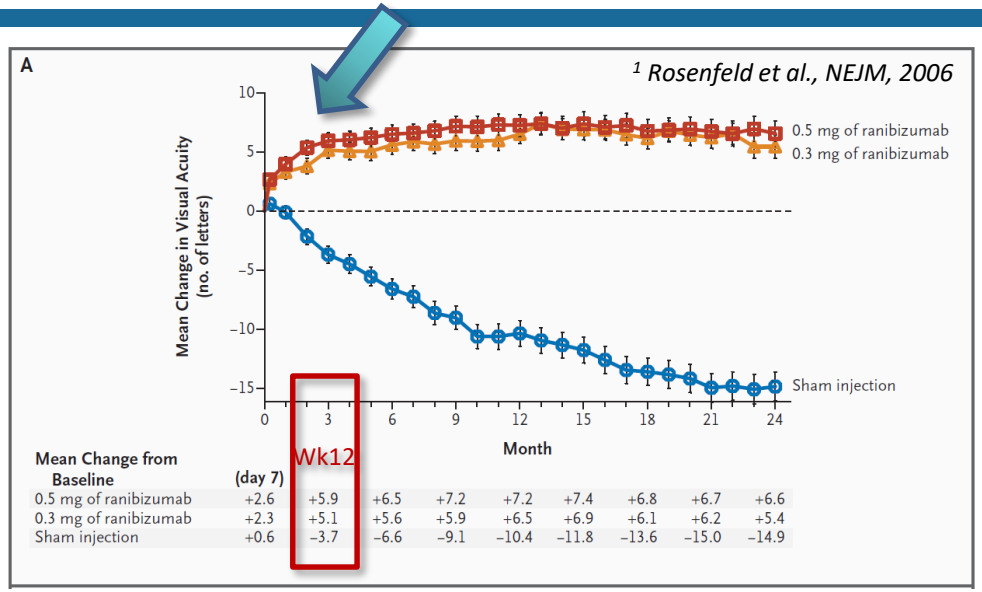
One treatment-naïve patient in the monotherapy cohort with myocardial infarction died (on day 77) prior to the week 12 visit (unrelated to study drugs)

Historical Clinical Activity: Lucentis® Trials



In MARINA trial (Phase 3 registrational):
~6 letters gain in vision compared to baseline at Week 12 in patients with minimally classic/occult wet AMD lesions treated with Lucentis® (ranibizumab)

Opthea's Phase 1/2a trial recruited patients with wet AMD lesion types similar to those patients recruited into the MARINA study

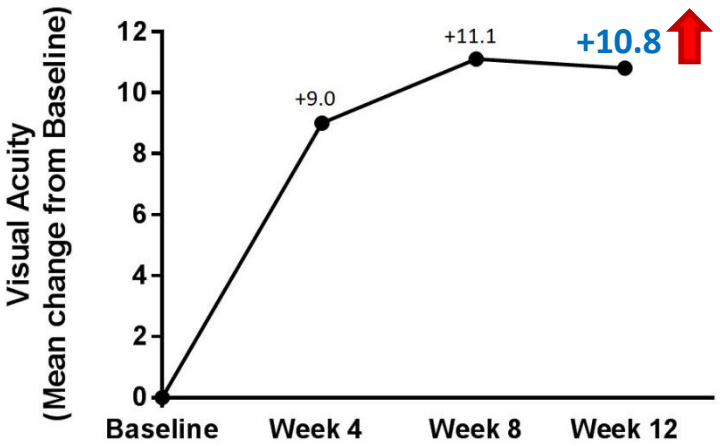
Study	VA gain at 12 Weeks [ETDRS letters]	Prior-Treatment[a]	% Lesion Type Classic (C); Predominantly Classic (PC); Minimally Classic (MC); Occult (Oc)
OPT-302-1001	+10.8	Naïve	PC (8%); MC (36%); Oc/other (56%)
OPT-302-1001	+4.9	Prior-Treated	PC (0%); MC (11%); Oc/other (89%)
Ranibizumab (Lucentis)			
MARINA [1]	+5.9	Naïve	PC (0%); MC (38%); Oc/other (62%)
ANCHOR [2]	+8.4	Naïve	PC (96%); MC (4%); Oc/other (0%)
VIEW 1 [3]	+7.3	Naïve	PC (27%); MC (33%); Oc/other (40%)
VIEW 2 [3]	+7.6	Naïve	PC (24%); MC (36%); Oc/other (40%)
CATT [4]	+6.1	Naïve	PC or MC (39%); Oc/other (61%) *

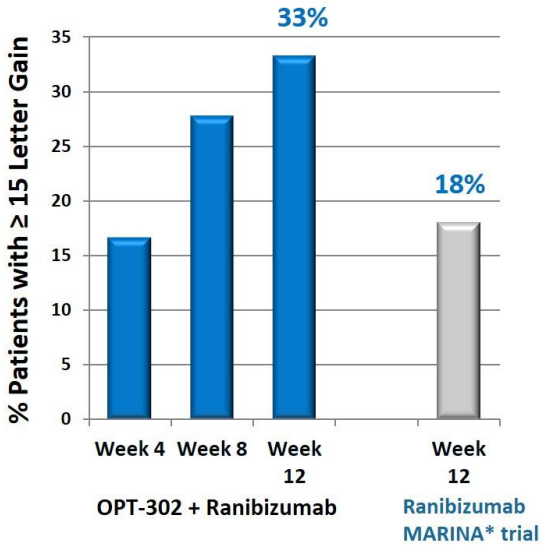
** Ranibizumab and bevacizumab groups combined; [1] Rosenfeld et al. N Engl J Med 2006; [2] Brown et al. N Engl J Med 2006*
[3] Heier et al. Ophthalmology 2012; [4] Martin et al. N Engl J Med 2011; Ying et al. Ophthalmology 2013

OPT-302 Phase 1/2a Treatment-Naïve Patients

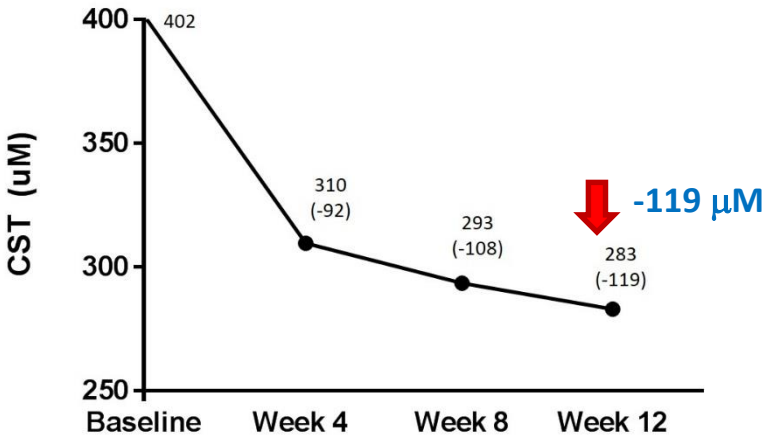
Visual Acuity Gains and Reductions in Retinal Fluid

Mean Change in Visual Acuity from Baseline (letters)

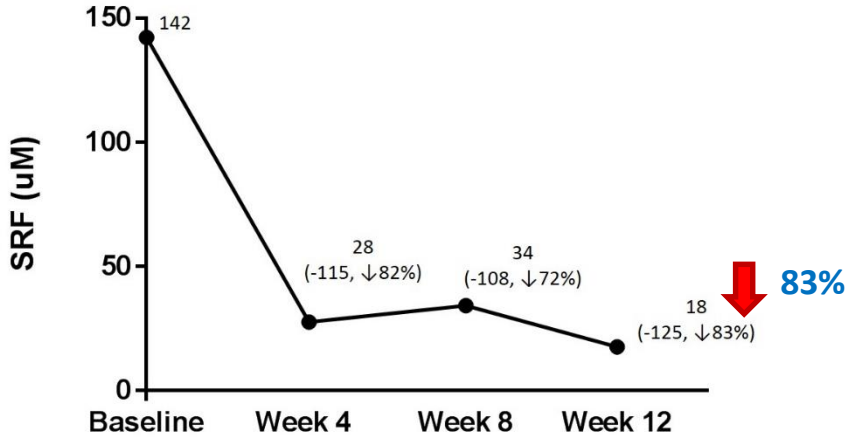




Mean Central Subfield Thickness (CST) (μM)



Mean Sub-Retinal Fluid (SRF) (μM)

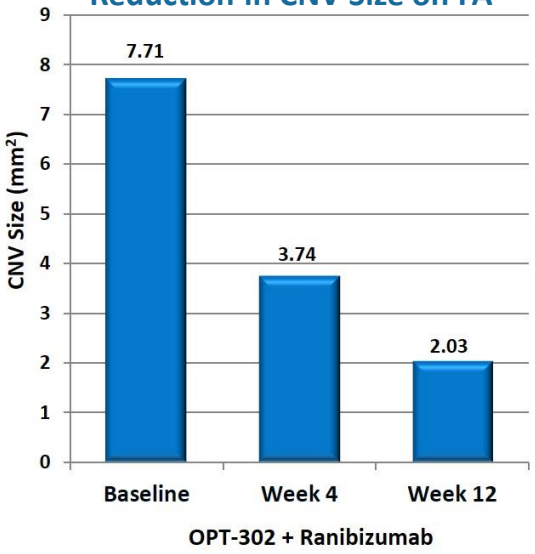


Patients administered OPT-302 + Ranibizumab Q4Wx3. Number of Patients: 18; Mean Baseline VA = 56.5 Letters ; MARINA: Mean Baseline VA = 53.7 letters
**Rosenfeld et al., NEJM, 355(14), pp 1419-1431, 2006; # Martin et al., NEJM, 364(20), pp 1897-1908*

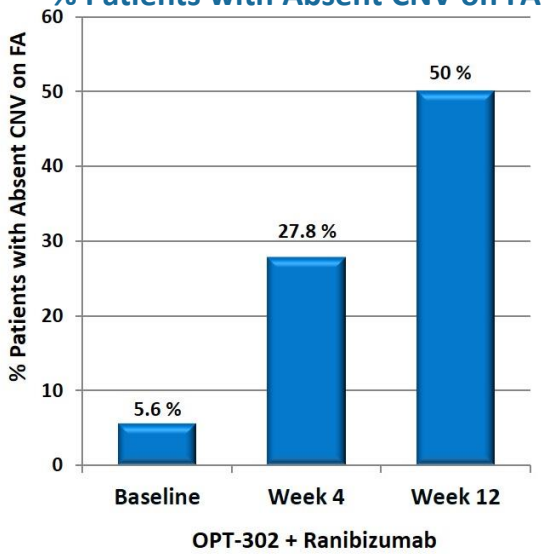
OPT-302 Phase 1/2a Treatment-Naïve Patients

Reductions in Choroidal Neovascularisation (CNV) and SHRM

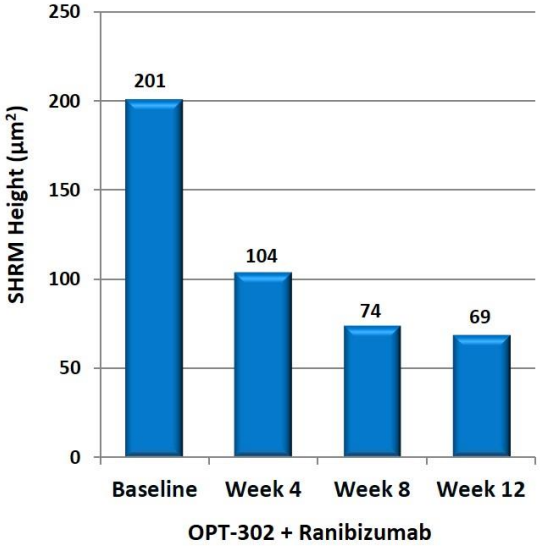
Reduction in CNV Size on FA



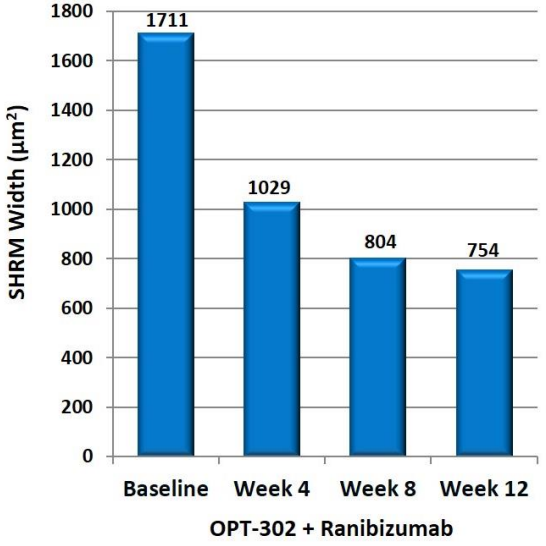
% Patients with Absent CNV on FA



Reduction in SHRM Height



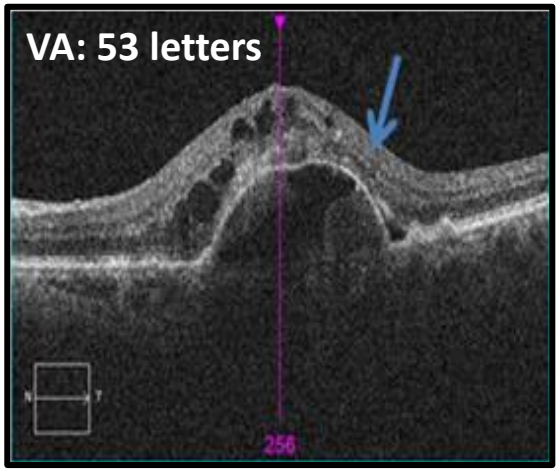
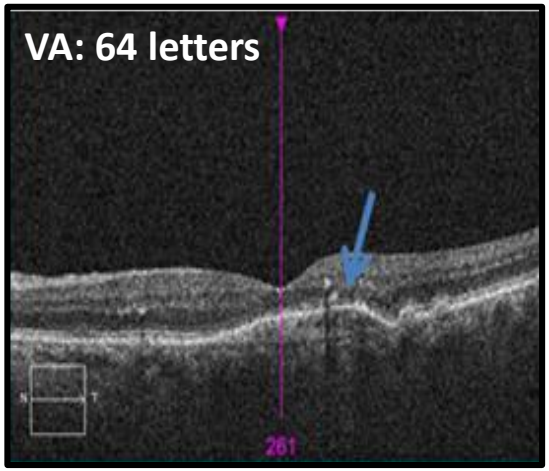
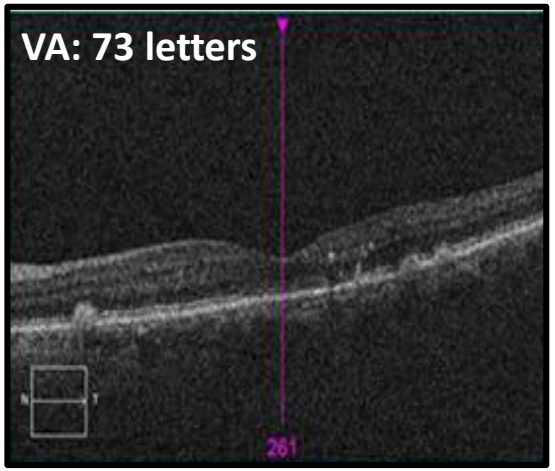
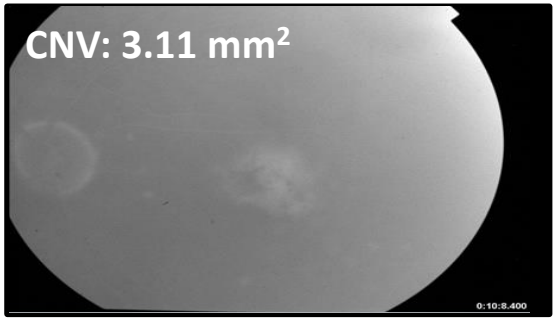
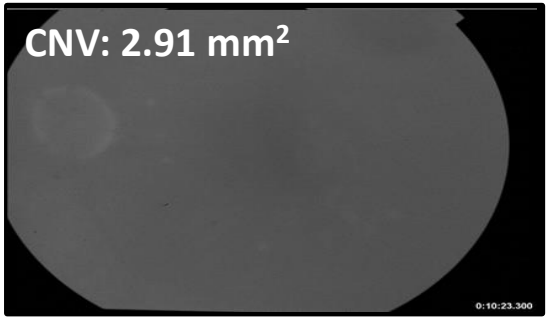
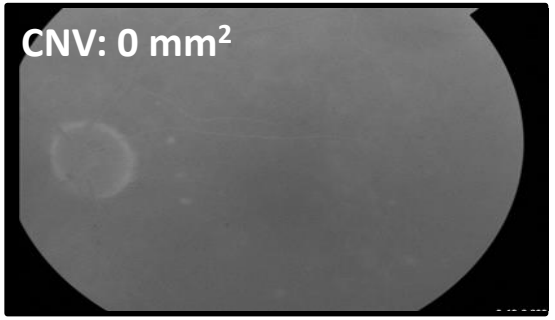
Reduction in SHRM Width



SHRM: Sub-Retinal Hyper-Reflective Material;
Treatment Naïve Patients: n = 18

Case-Study: Treatment-Naïve Patient (Occult)

OPT-302 (2 mg) + Lucentis (0.5 mg)

Baseline	Week 4	Week 12
		
		
CST: **279 µM** SRF: **192 µM** SHRMw: **1053 µM** SHRMh: **194 µM**	CST: **217 µM** SRF: **0 µM** SHRMw: **0 µM** SHRMh: **0 µM**	CST: **233 µM** SRF: **0 µM** SHRMw: **0 µM** SHRMh: **0 µM**

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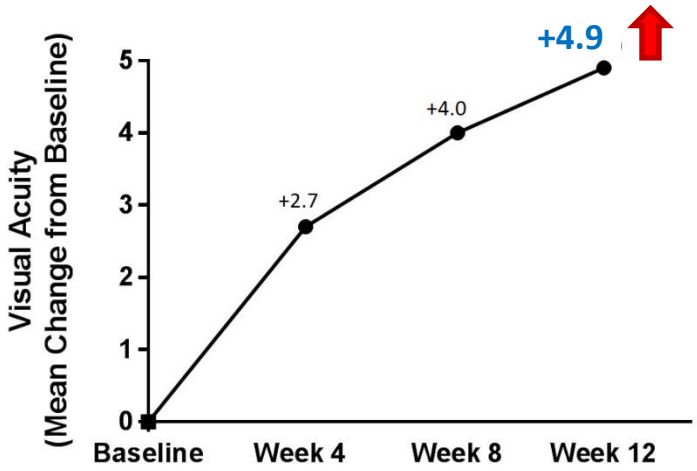
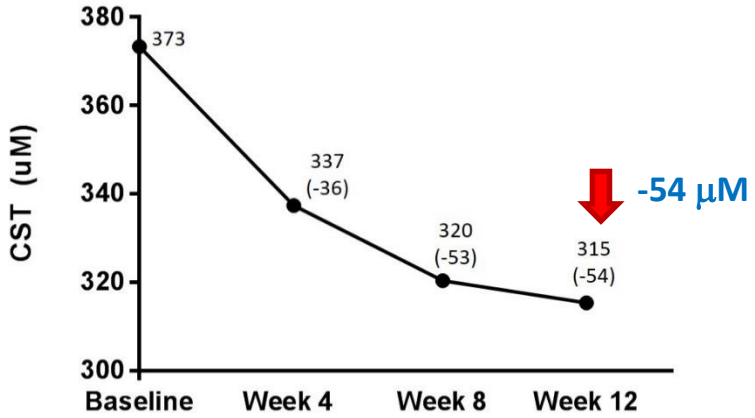
OPT-302 Phase 1/2a Prior-Treated Patients

Visual Acuity Gains and Reductions in Retinal Fluid

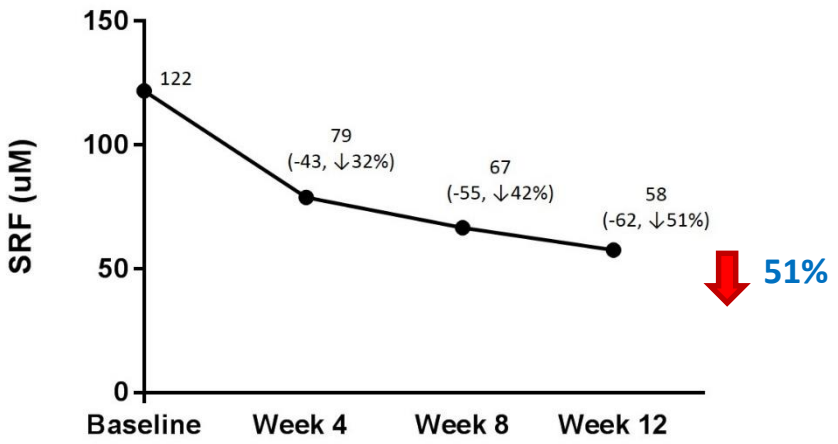
Mean Change in Visual Acuity from Baseline (letters)



Mean Central Subfield Thickness (CST) (μM)



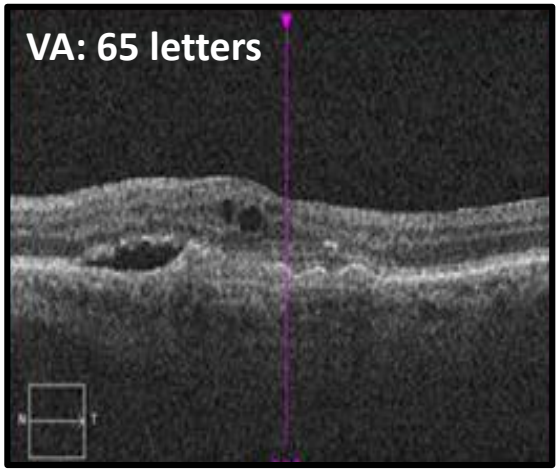
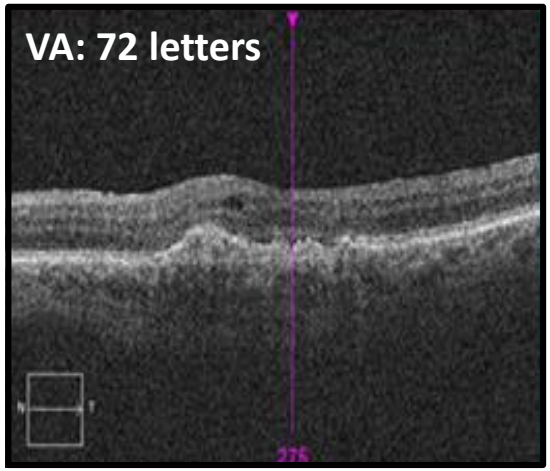
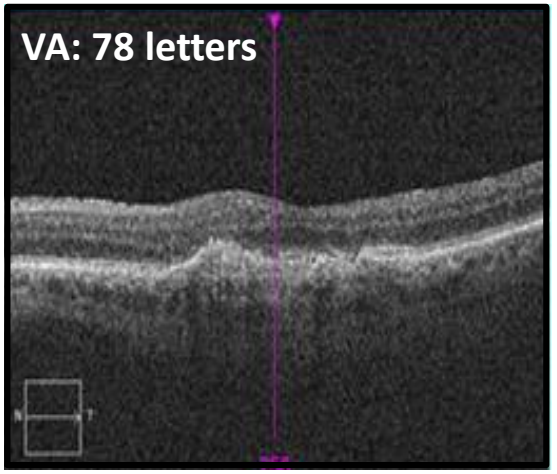
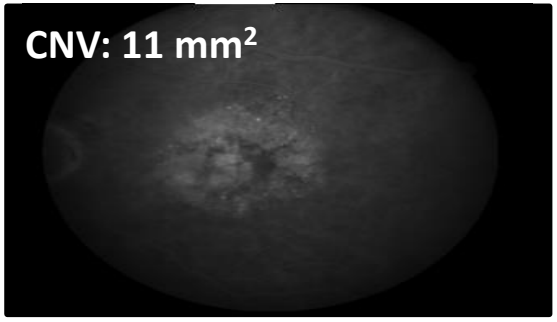
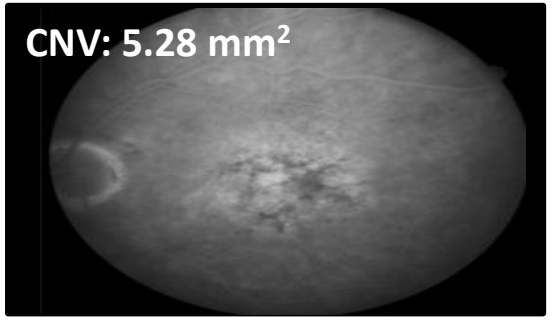
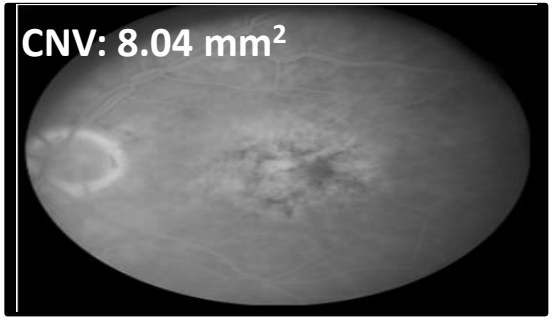
Mean Sub-Retinal Fluid (SRF) (μM)



Number of Patients: 20 pts (BL, Wk 4, Wk 8), 19 pts (Wk 12)

Case-Study: Prior-Treated Patient (Occult)

OPT-302 (2 mg) + Lucentis (0.5 mg) | **Prior-treatment: Lucentis (0.5 mg) x28**

Baseline	Week 4	Week 12
		
		
CST: **303 µM** SRF: **140 µM** SHRMw: **1042 µM** SHRMh: **133 µM**	CST: **249 µM** SRF: **41 µM** SHRMw: **0 µM** SHRMh: **0 µM**	CST: **248 µM** SRF: **0 µM** SHRMw: **0 µM** SHRMh: **0 µM**

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OPT-302 Phase 1/2a Key Take-Aways

- OPT-302 met the primary safety objective of its Phase 1/2A study (well tolerated)
- Evidence of clinical activity of OPT-302 (VEGF-C/D 'trap'), including in treatment naïve (49%) and heavily pre-treated patients (51%), and in a study with a high proportion of patients with occult (73%) wet AMD lesions:
  - **Naïve Patients**:
    - Results suggest OPT-302 + Lucentis may lead to improved outcomes over anti-VEGF-A therapies alone, suggesting additional benefit with more complete suppression of VEGF-A + VEGF-C/D
    - Mean gain in visual acuity at week 12 from baseline was +10.8 letters vs. +5.9 letters for Lucentis alone in the MARINA trial and +6.1 letters for each of Avastin and Lucentis alone in the CATT* study
  - **Prior Treated Patients:**
    - Evidence of improved clinical outcomes, including gain in visual acuity and reduction in retinal fluid (CST and SRF), despite long-term prior treatment with anti-VEGF-A (patients had received an average of 17 prior injections, equating to prior treatment over an average ~1.3 years#)
    - Mean gain in visual acuity at week 12 from baseline was +4.9 letters
    - Mean reductions in CST and SRF at week 12 of 54 μM and 62 μM (51%), respectively, from baseline
  - **Monotherapy Patients:**
    - Evidence of clinical activity and visual acuity gains without background standard of care
    - Mean gain in visual acuity at week 12 from baseline of +5.6 letters for patients who did not require "rescue" therapy (7/13, or 54% of patients)
    - Despite rescue with Lucentis, 3 / 5 evaluable "rescue" patients at week 12 had a decrease in vision compared to baseline (-2, -3, -5 letters)
- A consistency of responses in patients:
  - With different treatment histories
  - Across various secondary outcome measures (VA, OCT)

Martin et al. N Engl J Med 2011; Ying et al. Ophthalmology 2013.
 # Assuming treatments every 4 weeks

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Ongoing Clinical Trials

Phase 2b wAMD

A dose-ranging study of intravitreal OPT-302 in combination with ranibizumab, compared with ranibizumab alone, in participants with wet-AMD

Phase 1b/2a DME

Phase 1b/2a study of OPT-302 in combination with aflibercept for persistent central-involved diabetic macular edema

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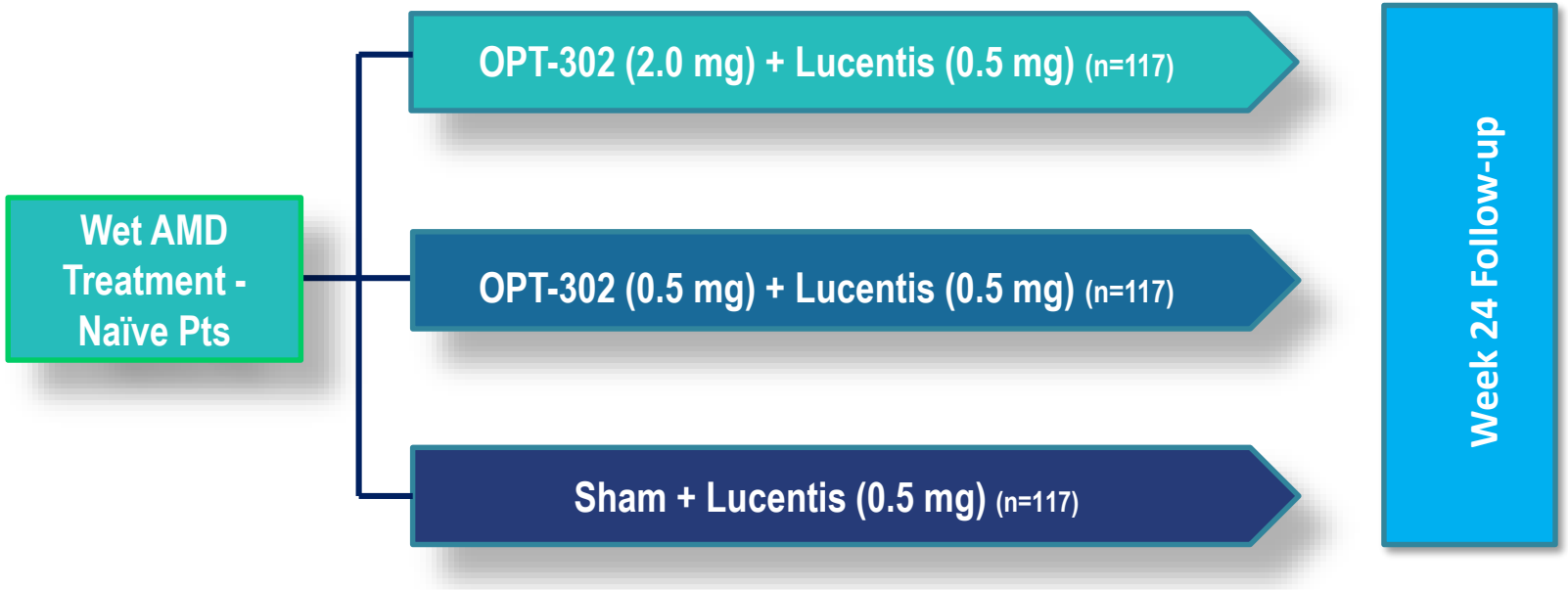
OPT-302 Phase 2b Trial in wet AMD (n=351)

Combination OPT-302 + Lucentis vs Sham + Lucentis



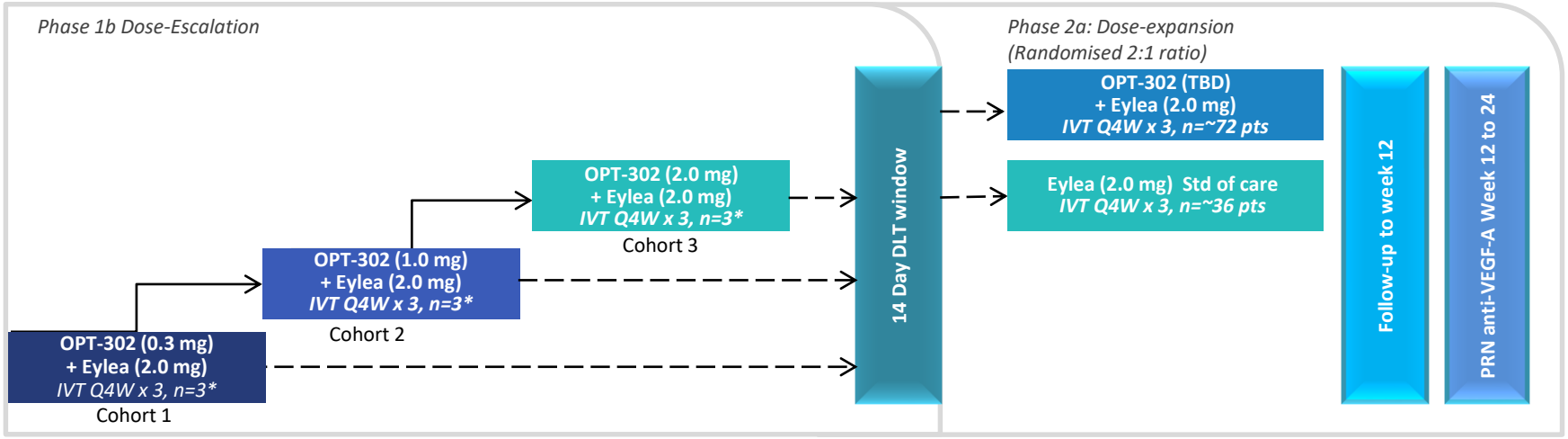
Randomized 1:1:1 to treatment arms : IVT dosing at every 4 weeks (x 6)

- **Primary Objective:**
  - Mean change from baseline in BCVA (visual acuity) (ETDRS) at week 24
- **Secondary Objectives:**
  - The proportion of patients gaining ≥15 or more ETDRS letters from baseline at week 24
  - Area under the BCVA over time curve
  - The proportion of patients losing ≥15 or more ETDRS letters from baseline at week 24
  - Change in central subfield thickness (CST) from baseline at week 24 (SD-OCT)
  - Change in intra-retinal fluid and sub-retinal fluid from baseline to week 24 (SD-OCT)
  - Safety and tolerability

Opthea plans to enrol patients at sites in the US, Europe (United Kingdom, France, Poland, Hungary, Spain, Latvia, Italy and Czech Republic) and Israel

OPT-302 Phase 1b/2a in Diabetic Macular Edema

Combination OPT-302 + Eylea vs Sham + Eylea



- **Primary Objectives:**
  - Response rate as defined by the proportion of participants receiving combination OPT-302 and Eylea achieving at least a 5 letter gain in best corrected visual acuity (BCVA) compared to baseline at week 12
  - Safety and tolerability
- **Secondary Objectives:**
  - Mean change in BCVA (visual acuity) (ETDRS) from baseline to week 12
  - Mean change from baseline in central subfield thickness (CST) and macular volume on SD-OCT
  - Percent of eyes with ≥ 50% reduction in excess foveal thickness from baseline to week 12
  - Percent of eyes with CST < 300 µM on SD-OCT through week 12
  - Percent of participants with a ≥ 2 step improvement from baseline to week 12 in ETDRS Diabetic Retinopathy Severity Score
  - The mean time to, and number of, retreatment injections of Eylea based on protocol specified criteria during week 12 to week 24 follow-up
  - Pharmacokinetics (PK) of OPT-302
  - Incidence of OPT-302 antibody formation

Key Eligibility Criteria

- Males and females ≥18yo
- Diabetes mellitus (type 1 or 2)
- Edema that involves that center of the macula
- Patients with persistent DME despite prior intravitreal anti-VEGF-A therapy with a sub-optimal response
- History of macular edema ≤ 12 months
- ETDRS BCVA letter score ≤ 73 and ≥ 24 (approx. Snellen equiv. 20/40 to 20/320 inclusive in study eye

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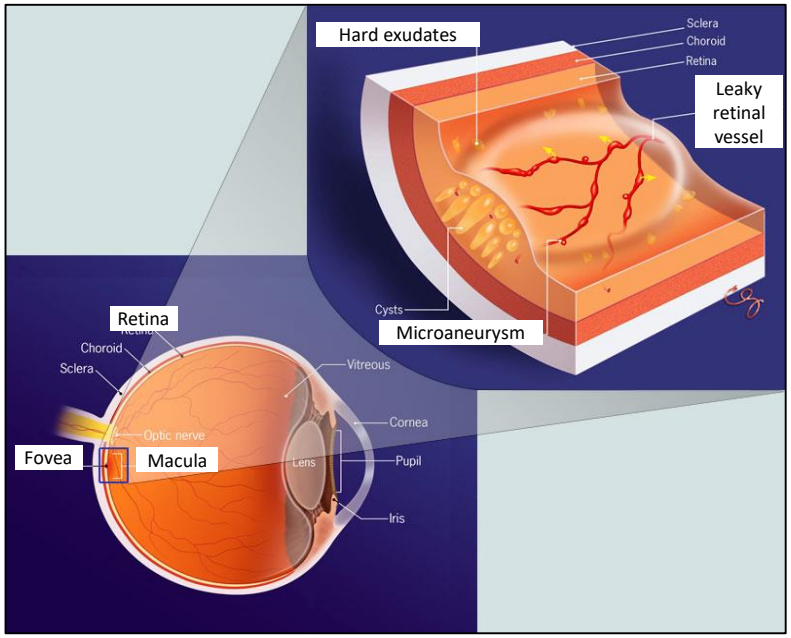
** Should a dose limiting toxicity (DLT) occur, the cohort will be expanded to 6 participants. Ph1b will enrol patients from US sites. Ph2a will enrol patients from US & Australia.*

OPT-302 MOA supports investigation in DME

Published data indicates that VEGF-C and its interaction with VEGFR-2 and VEGFR-3 plays a functional role in pathogenesis of DME



VEGF-C/D signaling pathway is implicated in diabetes

- OPT-302 has shown evidence of activity to resolve retinal fluid [1]
- VEGFR-2 expression is greater in diabetic retina than non-diabetics [2,3,4]
- VEGF-C is elevated in diabetic retinopathy [4]
- Vitreous levels of VEGF-D are elevated in diabetes [5]
- VEGF-C expression is elevated by glucose & pro-inflammatory cytokines [6,7]
- Inhibition of VEGF-C and VEGF-D in adipose tissue of mice improves metabolic parameters and insulin sensitivity [8,9]
- Advanced glycation end products accumulate faster in diabetics and stimulate VEGF-C expression and secretion from the RPE [6]
- Single nucleotide polymorphisms (SNPs) in diabetic patients indicate that genetic variation in the VEGF-C gene is associated with diabetic retinopathy and diabetic macular edema [10]

1. Phase 1/2a OPT-302 trial results: www.opthea.com; 2. Sun et al., 2014; 3. Witmer et al., 2002; 4. Zhao et al., 2007; 5. Kovacs et al., 2015; 6. Puddu et al., 2012; 7. Nagineni et al., 2011; 8. Karaman et al., 2014; 9. Karaman et al., 2016; 10. Kaidonis et al., 2015

OPT-302 Intellectual Property

Summary covering sVEGFR-3 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 • Granted Patent for new specific composition of matter	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)	

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Opthea – Developing OPT-302 for Eye Diseases

- OPT-302 has broad development potential in a range of eye diseases, including wet AMD and DME
- Targets validated pathway involved in wet AMD & DME progression and mechanism of escape from existing therapies that is differentiated to VEGF-A inhibitors
- Wet AMD & DME landscape includes only a limited number of novel combination therapies that may address the sub-optimal clinical responses that many patients experience on anti-VEGF-A therapies
- OPT-302 has a differentiated MOA from VEGF-A inhibitors and other combination agents in development
- OPT-302 met primary safety objective of Phase 1/2A study (well tolerated) and demonstrated evidence of clinical activity in a 51 patient Phase 1/2A clinical trial that enrolled naïve and prior treated patients administered OPT-302 monotherapy and OPT-302 in combination with Lucentis®
- Opthea is fully funded through its clinical development program:
    - A randomised Phase 2b clinical trial of OPT-302 + Lucentis® compared to Lucentis® alone in 351 wet AMD patients
    - A randomised Phase 1b/2a clinical trial of OPT-302 + Eylea® compared to Eylea® alone in ~117 DME patients
    - An additional randomised, controlled Phase 2a clinical trial of OPT-302 + anti-VEGF-A therapy vs anti-VEGF-A therapy alone in wet AMD patients (eg. prior-treated patients)
- Opthea is currently enrolling patients in the Ph 2b wAMD and Ph 1b/2a DME trials
- The OPT-302 program is diversified in two ocular indications and investigates the activity of OPT-302 in combination with two standard of care anti-VEGF-A therapies (Lucentis and Eylea respectively)

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