OPT-302: Phase 1/2A wet AMD Trial Update

Corporate Update, April 3 2017

Megan Baldwin, CEO & Managing Director

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Corporate Summary

- OPT-302 is in development for the treatment of wet Age-related Macular Degeneration ('wet AMD'), a progressive eye disease that is the leading cause of blindness in people over the age of 50 years
- OPT-302 blocks VEGF-C and VEGF-D that cause vessels to grow and leak and are hallmarks of wet AMD disease progression
- Approved therapies for wet AMD block VEGF-A and include blockbuster drugs Lucentis® and Eylea®. In 2016, Lucentis® and Eylea® generated revenues > USD 8.5 billion
- Existing therapies targeting VEGF-A are sub-optimally clinically effective in the majority of patients – major unmet medical need

Strategy:

- To develop OPT-302 for use in combination with existing VEGF-A inhibitors for the treatment of eye diseases
  - Achieves more complete blockade of the VEGF pathway involved in disease progression
  - Blocks mechanisms of clinical 'resistance' to existing therapies

Clinical Development:

- Phase 1/2A wet AMD clinical trial run under FDA approved IND at 14 US clinical sites
- Plans to expand OPT-302 clinical development program with a larger Phase 2B wet AMD clinical trial and Phase 2A clinical trials for diabetic macular edema ('DME') and in prior-treated wet AMD patients
  - Phase 2B and Phase 2A DME and prior-treated patient trials to initiate in 2H 2017
  - Diversifies clinical development strategy in multiple eye diseases
  - Multiple upcoming clinical development milestones

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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

Trial Results

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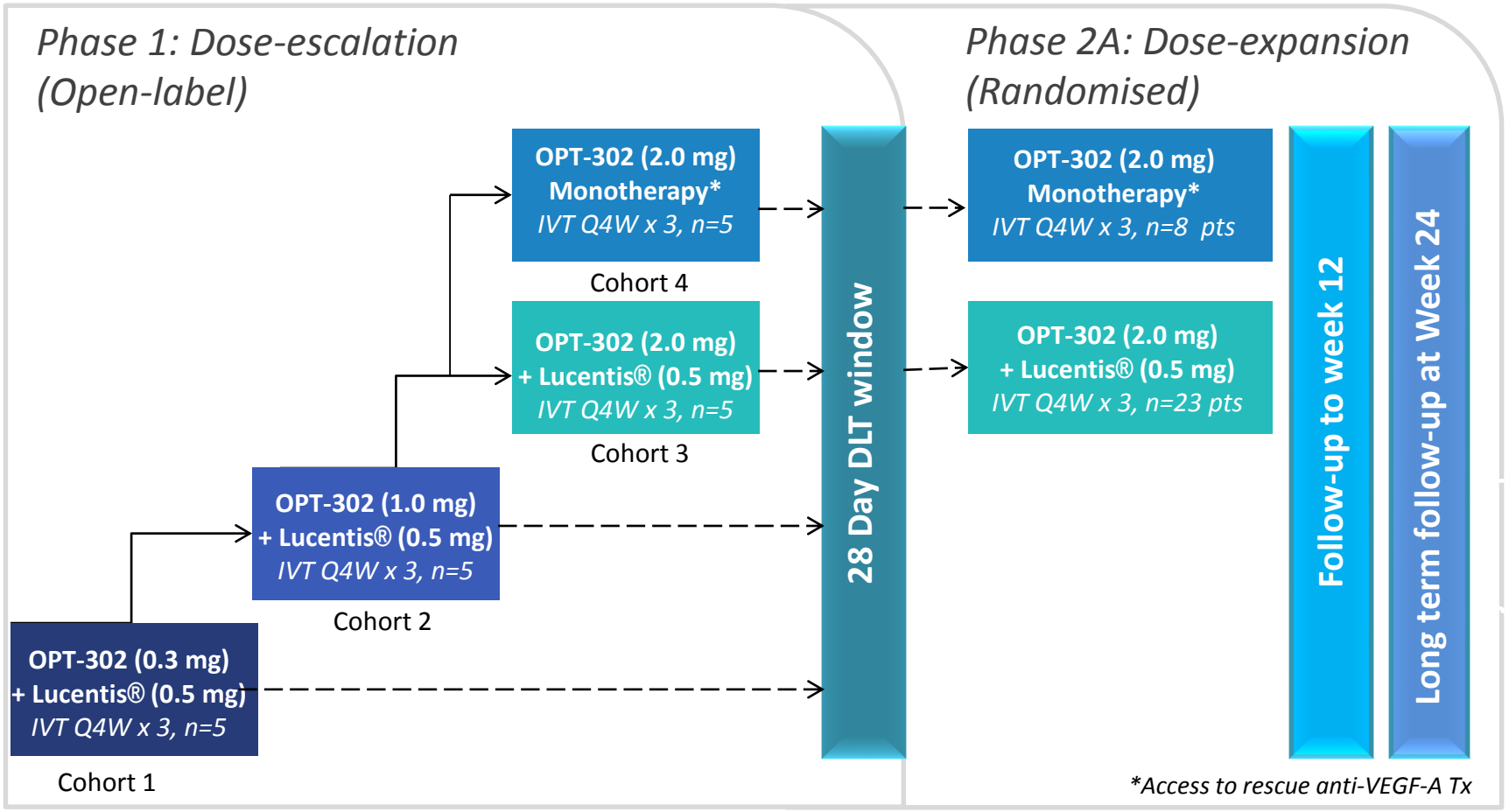
OPT-302 Phase 1/2A

ClinTrials.gov ID#: NCT02543229

Dose-escalation & dose-expansion of repeated IVT injections



- Each patient dosed on a monthly basis for 3 months
- Primary data analysis at week 12

OPT-302 Phase 1/2A: Patient Cohorts

Phase 1/2A

- 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

Cohort	Treatment	# Naïve Pts	# Prior Treated Pts
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

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)

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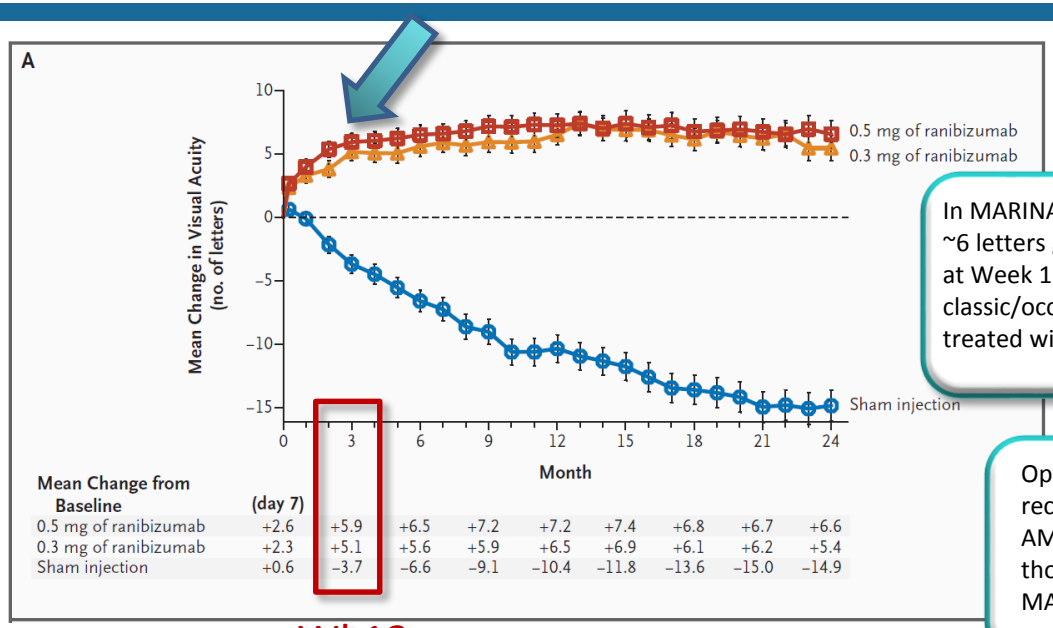
Phase 1/2A Visual Acuity Outcomes



Mean Change from Baseline	(day 7)								
0.5 mg of ranibizumab	+2.6	+5.9	+6.5	+7.2	+7.2	+7.4	+6.8	+6.7	+6.6
0.3 mg of ranibizumab	+2.3	+5.1	+5.6	+5.9	+6.5	+6.9	+6.1	+6.2	+5.4
Sham injection	+0.6	−3.7	−6.6	−9.1	−10.4	−11.8	−13.6	−15.0	−14.9

Wk12

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

Treatment	OPT-302: Phase 1/2A
Overall % Patients Gained/Maintained Vision to Wk 12	**44/49** (90%)
% Patients Non-Rescued in OPT-302 Monotherapy	**54%** (n=7/13)
Mean Change Visual Acuity at Wk 12 (letters)	
Combo OPT-302 + Lucentis® in **Naïve** pts	**+10.8** (n=18)
Combo OPT-302 + Lucentis® in **Prior Tx** pts	**+4.9** (n=19)
Combo OPT-302 + Lucentis® in both **Naïve & Prior Tx** pts	**+7.8** (n=37)
OPT-302 **Monotherapy** in Non-Rescue pts	**+5.6** (n=7)

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** Rosenfeld et al., NEJM, 355;14, pp 1419-1431, 2006. In MARINA, occult lesions (62% pts), min.classic (38% pts)*

Phase 1/2A: Patients Gaining or Maintaining Vision @ Wk12

- 51 patients enrolled
- 49 patients evaluable at the week 12 endpoint

Cohort	Treatment	# patients	# pts Gained or Maintained	# pts Gained	# pts Maintained	# pts lost less than 5 letters	# pts lost b/w >5 = <10 letters
1 -6	**ALL: OPT-302 (0.3/1.0/2.0 mg) +/- Lucentis®**	**49**	**44 (90%)**	**37 (76%)**	**7 (14%)**	**3**	**2**
1,3,5	**Naïve: OPT-302 (0.3/2.0 mg) + Lucentis®**	**18**	**16 (89%)**	**14 (78%)**	**2 (11%)**	**1** (-3 letters)	**1** (-8 letters)*
1-3,5	**Prior Tx: OPT-302 (0.3/2.0 mg) + Lucentis®**	**19**	**19 (100%)**	**16 (84%)**	**3 (16%)**	**0**	**0**
4,6	**Monotherapy: All**	**12**	**9 (75%)**	**7 (58%)**	**2 (16%)**	**2**	**1**
	Monotherapy: Non-Rescue	7	7	5	2	0	0
	Monotherapy: Rescue	5	2	2	0	2 (-3,-2 letters)	1 (-5 letters)

- 44/49 (90%) patients enrolled in the study gained or maintained vision at week 12
- 5/49 (10%)* patients lost between -2 and -8 letters
- All of the patients that had a decrease in vision received Lucentis® therapy

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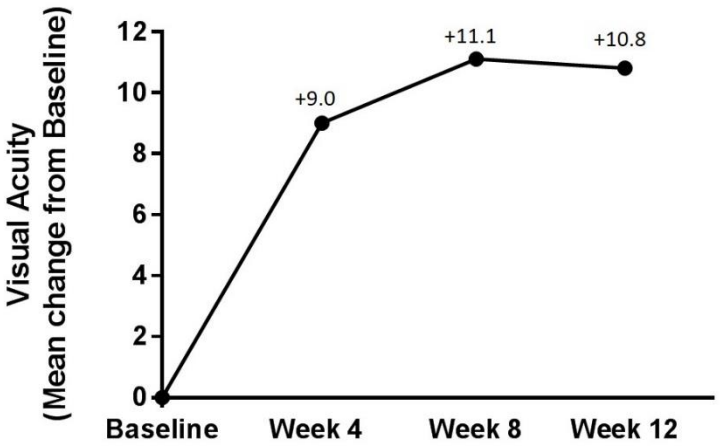
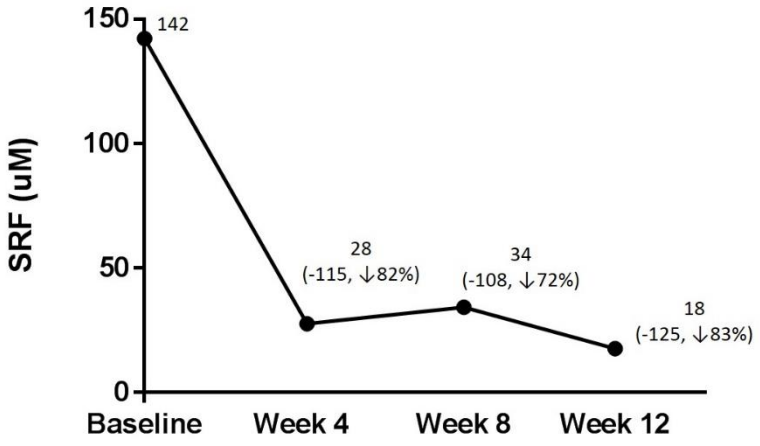
** In the MARINA study, 13% of patients that received Lucentis® therapy had lost ≥6 letters at week 12 (Hariprasad et al., J Ophthal., 2012)*

Phase 1/2A: Naïve Patients OPT-302 (0.3 & 2mg) + Lucentis® (0.5mg)

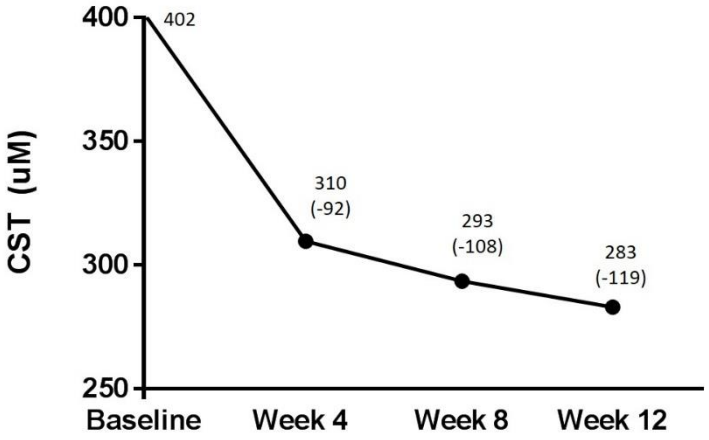
Mean Change in Visual Acuity from Baseline (letters)



Mean Sub-Retinal Fluid (SRF) (uM)



Mean Central Subfield Thickness (CST) (uM)



Naïve patients:

- Mean gain in visual acuity at week 12 from baseline was +10.8 letters
  - *In the MARINA* trial, ~+6 letters gain in vision compared to baseline at Week 12 in patients treated with monthly Lucentis®*
- CST was reduced by 119 uM to 283 uM , approaching normal retinal thickness
- SRF reduced by 83% by Week 12
- At week 12, 72% (13/18) patients had complete (100%) resolution of SRF

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*

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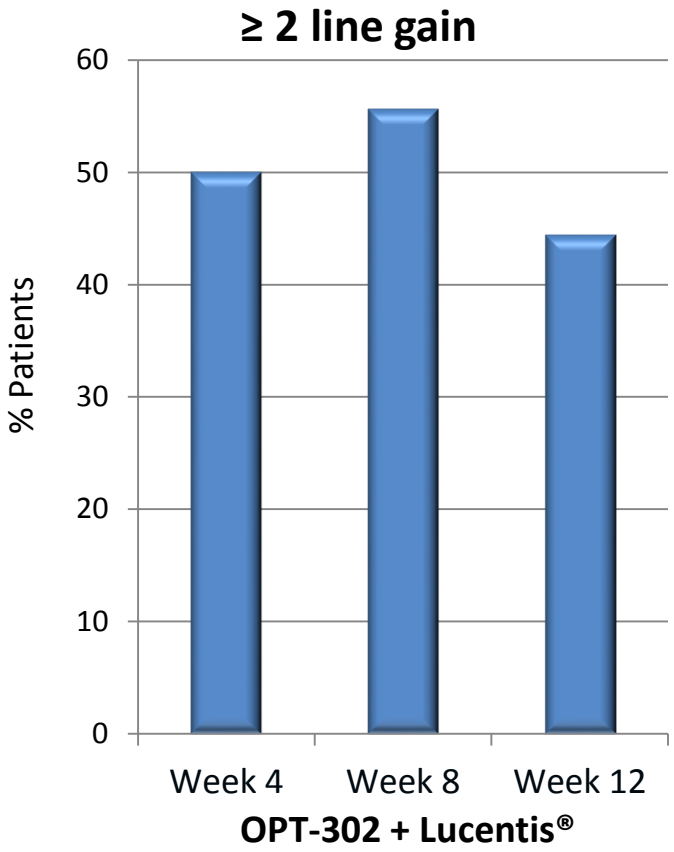
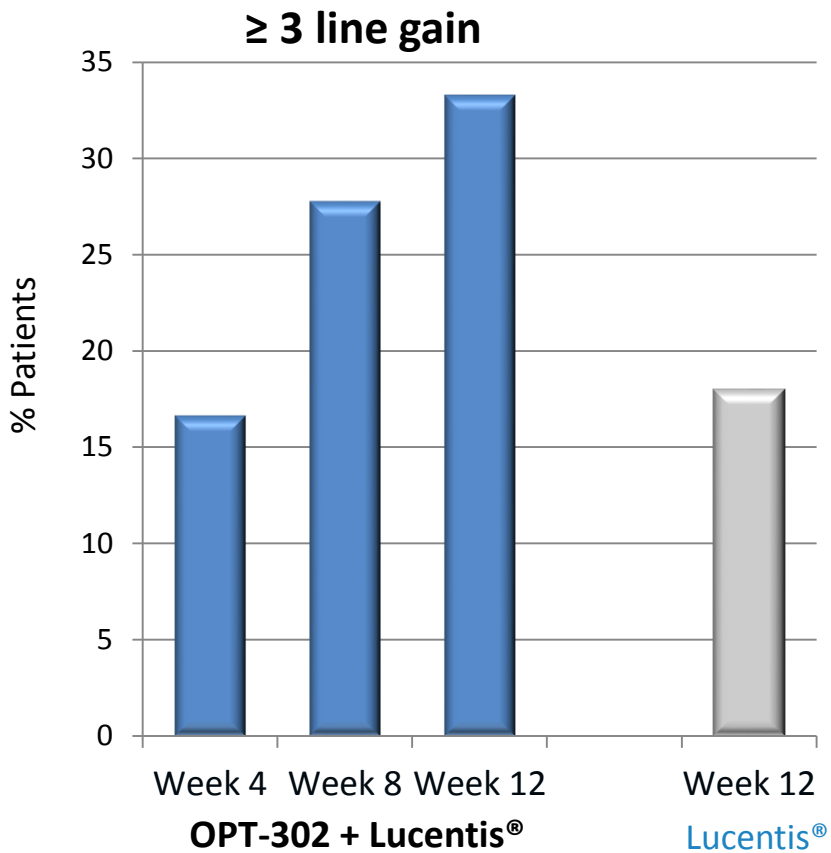
Phase 1/2A: Naïve Patients OPT-302 (0.3 & 2mg) + Lucentis® (0.5mg)

Improved Visual Outcome through week 12





Number of Patients: 18
Mean Baseline VA = 56.5 Letters
MARINA: Mean Baseline VA = 53.7 letters

**Mean ranibizumab data (0.3 & 0.5 mg) from MARINA trial:*
Hariprasad et al J Opht 2012 p1-8;
Rosenfeld et al NEJM 2006, Vol 355, No. 14, pp. 1419-1431

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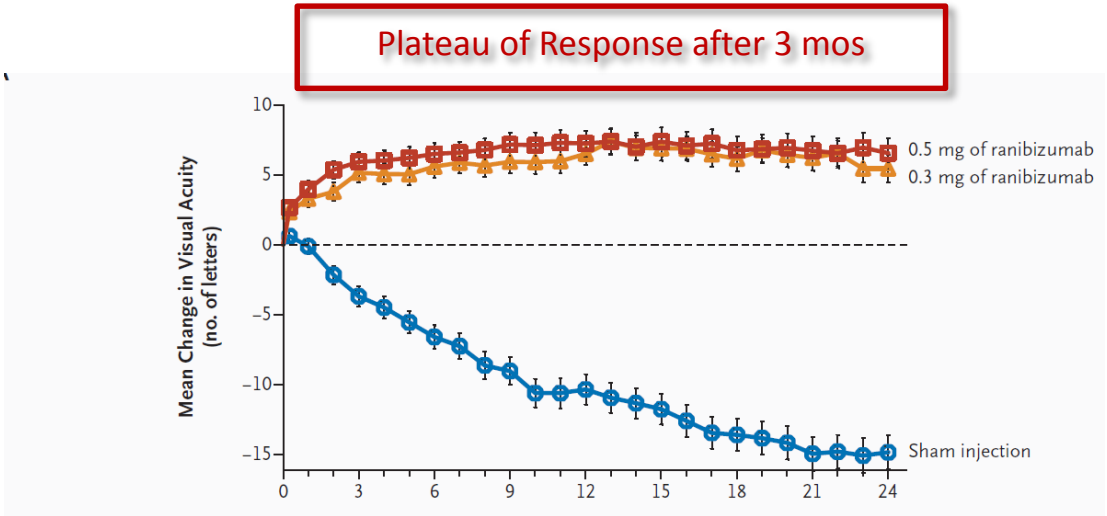
Prior-Treated Patients: Visual Acuity

- Majority of vision gain in Lucentis® treated patients occurs within 3 months
- Plateau "ceiling effect" of response with no other treatment options
- Difficult to treat patient population, very large market opportunity



Mean Change from Baseline	(day 7)								
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0.3 mg of ranibizumab	+2.3	+5.1	+5.6	+5.9	+6.5	+6.9	+6.1	+6.2	+5.4
Sham injection	+0.6	−3.7	−6.6	−9.1	−10.4	−11.8	−13.6	−15.0	−14.9

MARINA Phase 3 in wet AMD. Rosenfeld et al., NEJM, 355;14, pp 1419-1431, 2006

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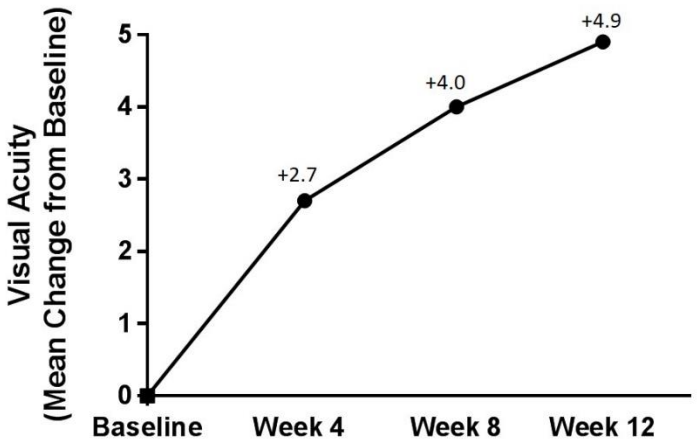
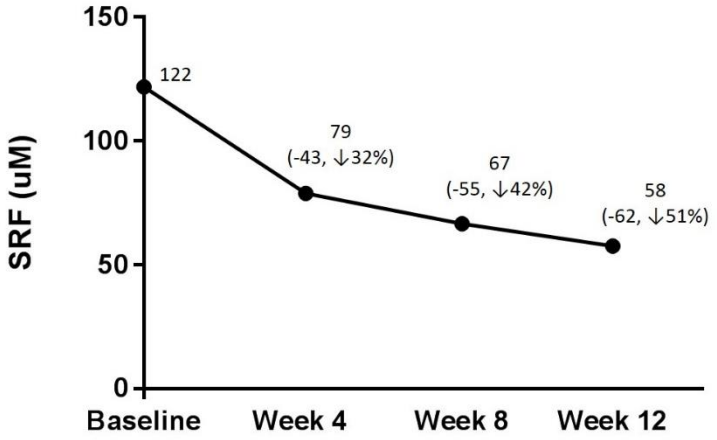
Phase 1/2A: Prior-Treated Patients OPT-302 (0.3, 1 & 2mg) + Lucentis® (0.5mg)

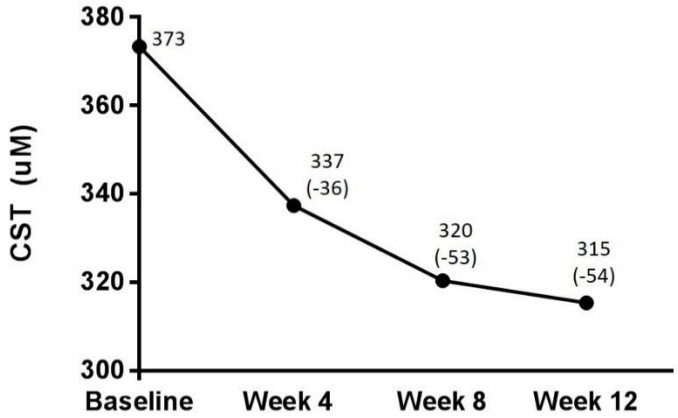
Mean Change in Visual Acuity from Baseline (letters)



Mean Sub-Retinal Fluid (SRF) (uM)



Mean Central Subfield Thickness (CST) (uM)



Prior-Treated patients:

- Mean number prior anti-VEGF-A injections per patient: 17
- 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 uM and 62 uM (51%) respectively from baseline
- 3/19 (16%) patients had complete (100%) resolution of SRF
- 9/19 (47%) had > 50% resolution of SRF at week 12 compared to baseline

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

OPT-302 Monotherapy

- OPT-302 monotherapy included to identify clinical activity without a background standard of care
- Natural history of wet AMD: without treatment, often chronic, rapid decline in visual acuity and increase in retinal fluid
- α-VEGF-A rescue therapy offered to patients at physician discretion or if patient met criteria of progression according to defined criteria

Treatment	# patients	# Naïve pts	# Prior Tx pts
OPT-302, 2 mg	**13[a]**	**7 (54%)**	**6 (46%)**
No rescue	7 (54%)	4 (57%)	3 (50%)
Rescue	6 (46%)	3 (43%)	3 (50%)

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

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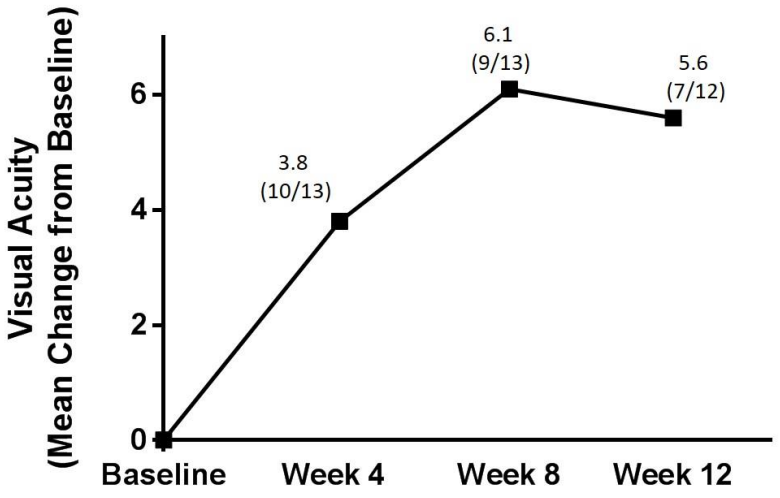
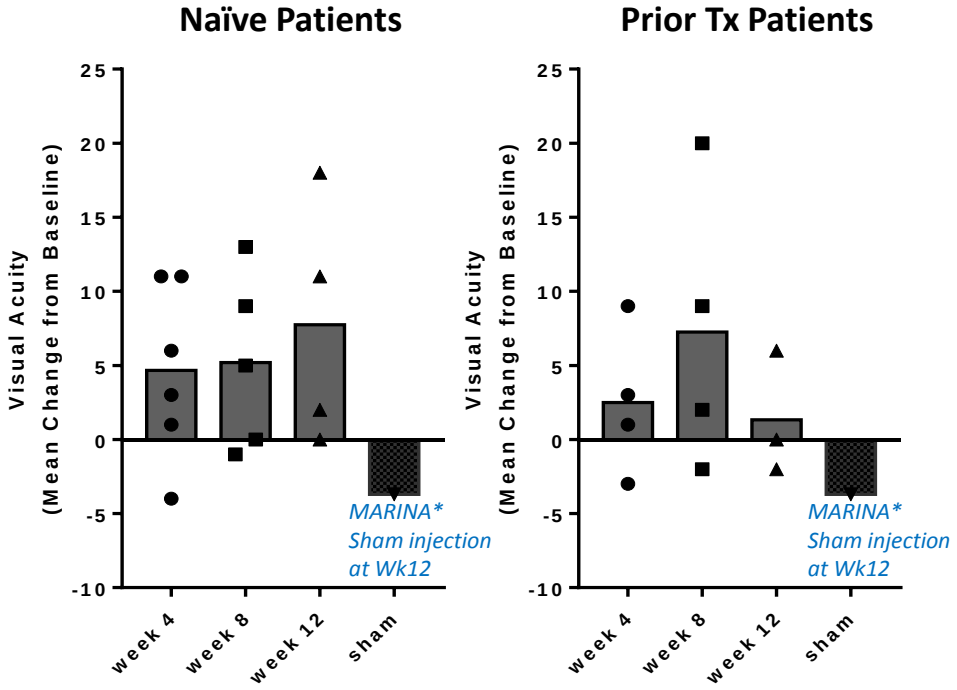
Phase 1/2A: Monotherapy Patients OPT-302 (2mg) (Naïve & Prior-Treated)

Mean Change in Visual Acuity in Non-Rescue Patients at Each Time Point



Visual Acuity in Non-Rescue Patients at Each Time Point



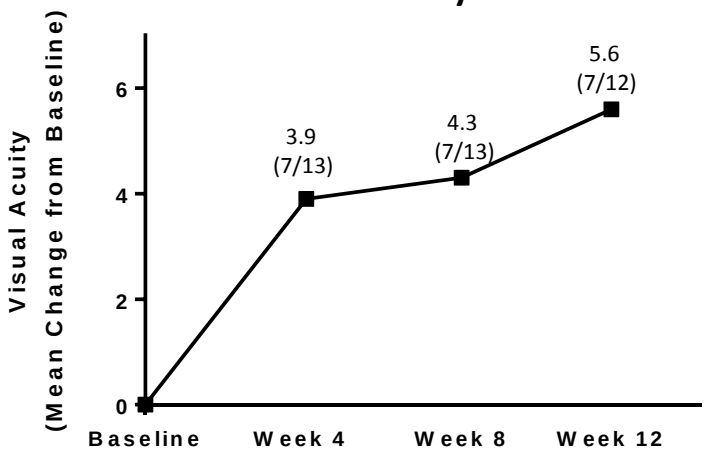
One naïve patient in the monotherapy cohort with myocardial infarction died (on day 77) prior to the week 12 visit (unrelated to study drugs)

** Rosenfeld et al., NEJM, 355;14, pp 1419-1431, 2006*

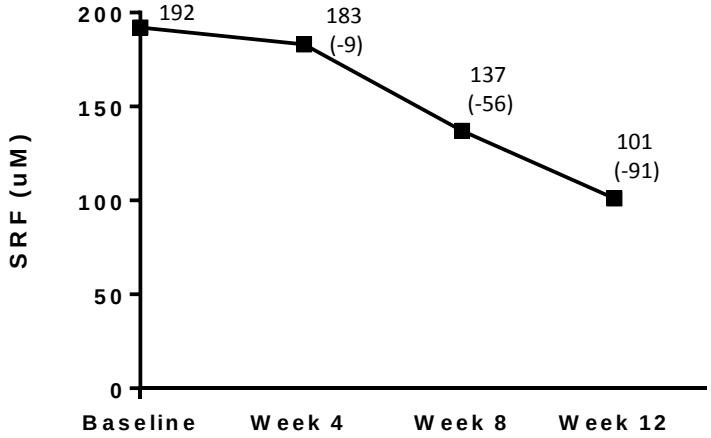
Phase 1/2A: Monotherapy Patients OPT-302 (2mg) (Naïve & Prior-Treated)

- 7/13 (54%) patients did not require 'rescue' therapy

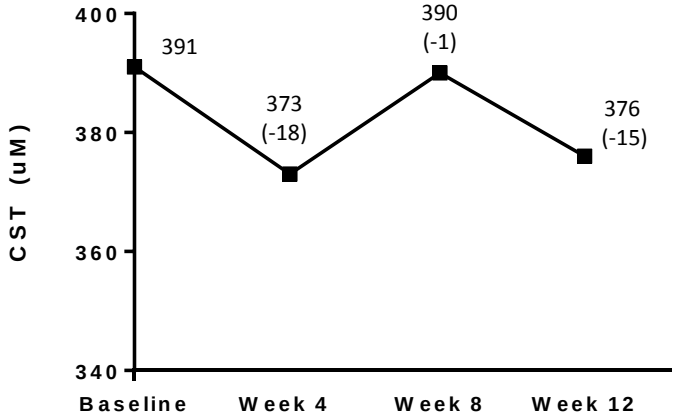
Visual Acuity in Patients who were not rescued by Week 12



Sub-Retinal Fluid in Patients who were not rescued by Week 12



Central Sub-Field Thickness in Patients who were not rescued by Week 12



Monotherapy Patients, at week 12:

- 7/13 (54%) patients did not require 'rescue' therapy
- Patients that did not require rescue therapy had:
  - a mean visual acuity gain of 5.6 letters from baseline (range 0 to 18 letters)
  - a mean decrease in CST of -15 uM (baseline CST non-rescue pts: 390 uM) and
  - a 91 uM reduction in SRF
- 6/13 (46%) patients were rescued with α-VEGF-A therapy
- Despite rescue with Lucentis®, 3/5 evaluable patients at week 12 had a decrease in vision compared to baseline (-2, -3, -5 letters)

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 (4%) had ocular adverse events related to OPT-302 study drug
  - Adverse events were Grade 1/Mild in the low and mid-dose combination groups
- 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 related to study treatment
  - One patient at study day 69 with metastatic ovarian cancer & pulmonary embolism
  - One patient at study day 77 with myocardial infarction

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OPT-302 Phase 1/2A: Key Take-Aways

- OPT-302 met primary safety objective of Phase 1/2A study (well tolerated)
- Evidence of clinical activity of OPT-302 (anti-VEGF-C/D) in patients including heavily pre-treated patients (51%) and a high proportion of occult (73%) wet AMD lesions:
  - **Naïve Patients**:
    - Results suggest OPT-302 + Lucentis® may lead to improved outcomes over Lucentis® alone, suggesting additional benefit with more complete suppression of VEGF-A + VEGF-C/D
  - **Prior Treated Patients:**
    - Evidence of improved clinical outcomes, including gain in visual acuity and reduction in CST and SRF, despite long-term prior treatment with anti-VEGF-A
  - **Monotherapy Patients:**
    - Evidence of clinical activity and visual acuity gains without background standard of care
- A consistency of responses in patients:
  - With different treatment histories
  - Across various secondary outcome measures (VA, OCT)

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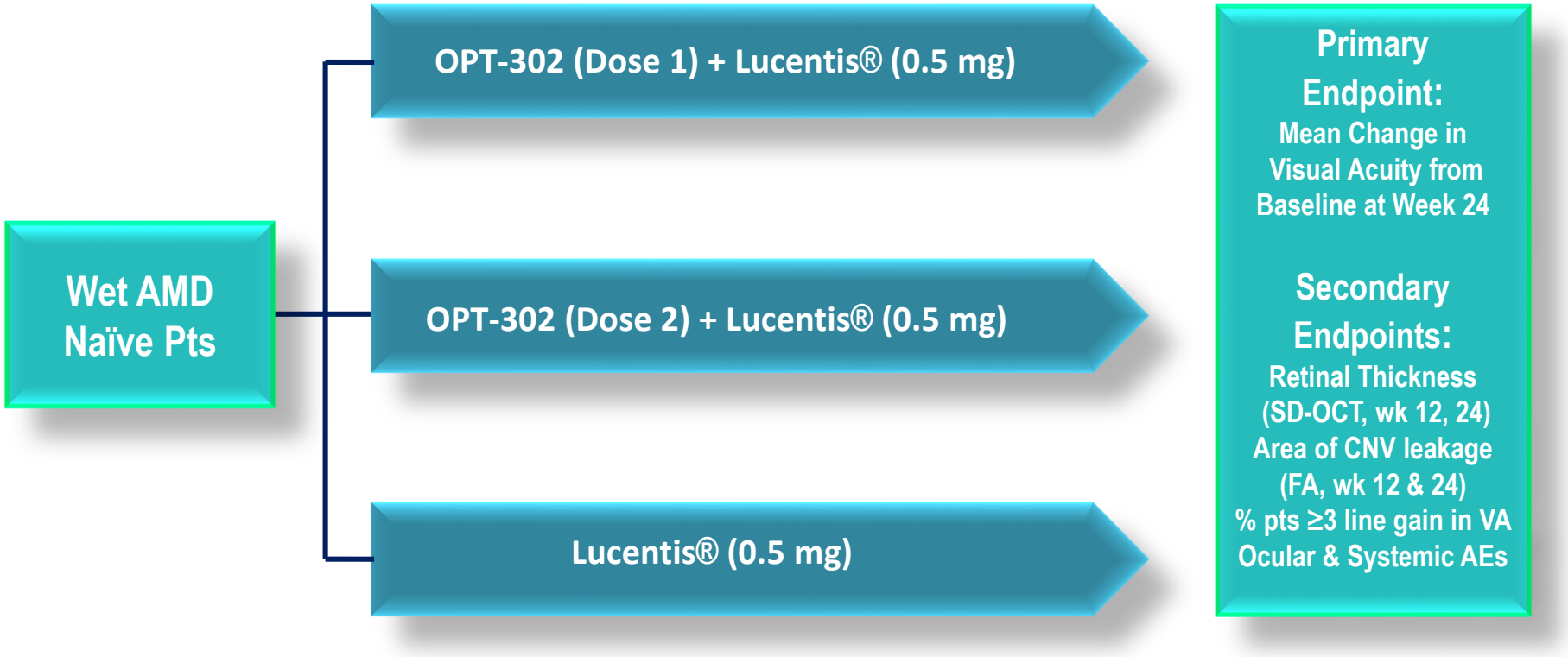
OPT-302 Proposed Phase 2B in Wet AMD

Combination OPT-302 + Lucentis® vs Lucentis®



All treatment arms : IVT dosing at every 4 weeks (x 6)

- *Phase 2b Prospective, randomized, controlled trial*
- *3 arms (randomized 1:1:1)*
- *Primary Analysis at 6 months*

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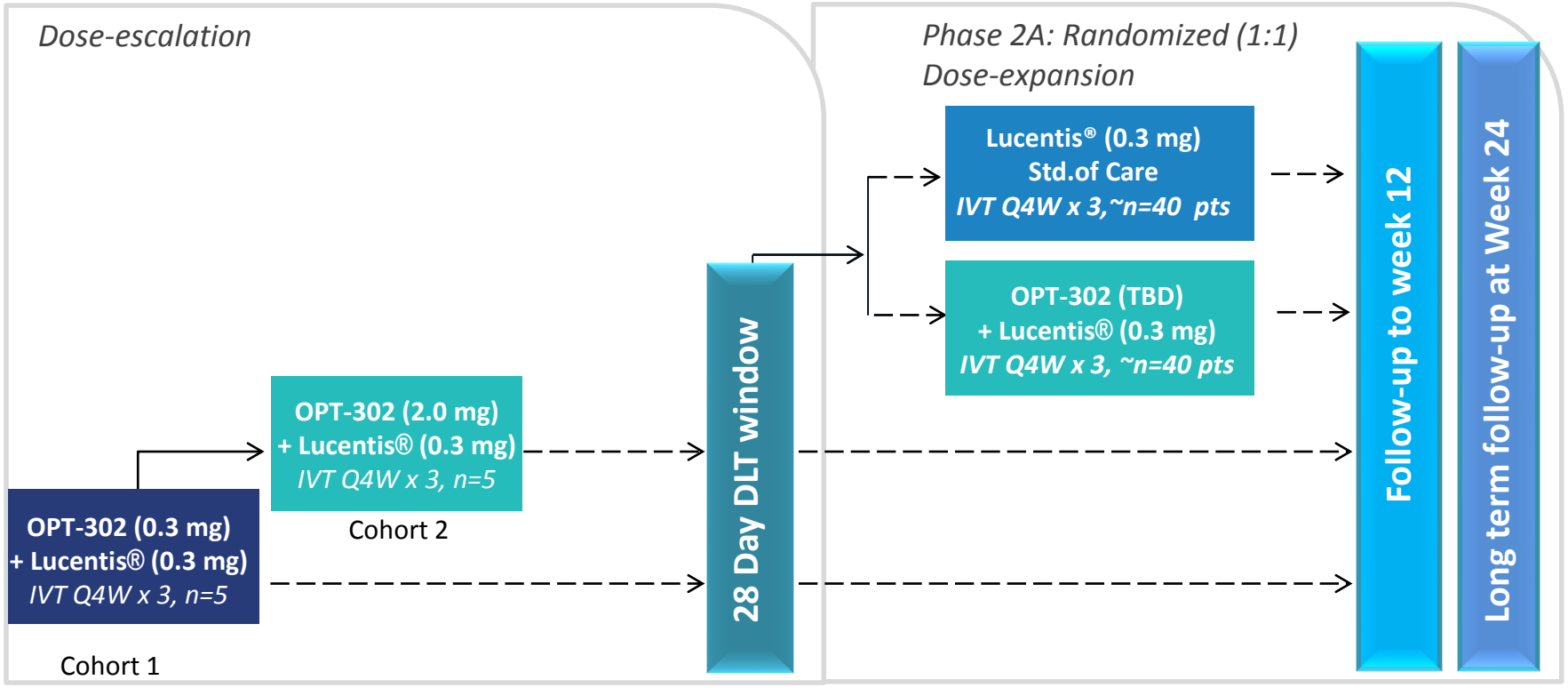
OPT-302 Proposed Phase 2A in Diabetic Macular Edema

Combination OPT-302 + Lucentis® vs Lucentis®



Primary endpoint:

- *Dose-escalation: Systemic & Ocular AEs;*
- *Phase 2A: Mean change from baseline in CST at week 12 (SD-OCT)*

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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 progression and mechanism of escape from existing therapies that is differentiated to a-VEGF-A therapies
- Large unmet medical need for wet AMD, current treatments only target VEGF-A
- Wet AMD landscape of products in development 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 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 plans to expand its clinical development program by conducting:
  - A randomised Phase 2B clinical trial of OPT-302 + Lucentis® compared to Lucentis® alone in ~350 wet AMD patients
  - A randomised Phase 2A clinical trial of OPT-302 + Lucentis® compared to Lucentis® alone in ~90 DME patients
  - A Phase 2A clinical trial of OPT-302 + Lucentis® compared to Lucentis® alone in prior-treated wet AMD patients
- The expanded program establishes and diversifies a robust OPT-302 clinical development strategy, whilst increasing the potential value accretion points for the program

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Suite 0403, Level 4,
650 Chapel Street,
South Yarra 3141 Victoria Australia

T +61 (3) 9826 0399
E megan.baldwin@opthea.com

www.opthea.com