OPT-302: A novel therapy for Wet AMD

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Opthea: Developing OPT-302 for Wet AMD

- Opthea Limited is a public ASX listed company (ASX: OPT)
- Exclusive worldwide rights to extensive IP portfolio around members of the Vascular Endothelial Growth Factor family
  - VEGF-C
  - VEGF-D
  - VEGFR-3

Key Financial Details	ASX: OPT
Ticker Symbol	ASX:OPT
Share Price (as at Aug 5 2016)	~A$0.64
Total Ordinary Shares on Issue	150,205,903
Options on Issue	49,707,097
Market Capitalisation (as at Aug 5 2016)	~USD 70m (AUD 96m)

- Lead compound OPT-302: a VEGF-C/-D 'Trap'
  - Neovascular effects (eg. inhibitor of angiogenesis & vascular permeability)
  - Non-neovascular effects (eg. inflammation)
- Wet AMD program with potential in a range of eye diseases
- Combination therapy OPT-302 with an anti-VEGF-A inhibitor targets mechanisms of incomplete response to VEGF-A inhibition
- Complementary to α-VEGF-A and other agents in development
- Phase 1/2a trial ongoing under IND at 14 clinical sites in US

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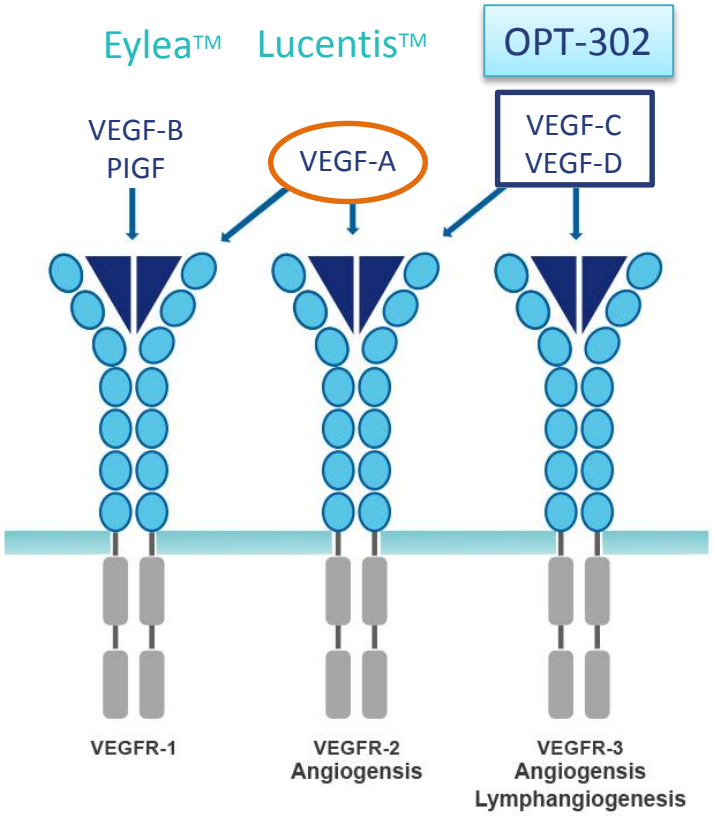
Resistance to anti-VEGF-A Monotherapy

- Long-term single-agent therapy with VEGF-A inhibitors is associated with sub-optimal response
  - Sub-optimal improvements in visual acuity (<15-letter gain)
  - Persistent retinal fluid
- Resistance to VEGF-A inhibitors may be related to other VEGF family members

- **OPT-302 combination therapy achieves more complete suppression of the VEGF/VEGFR pathway**
- **Targets incomplete response to VEGF-A inhibition**



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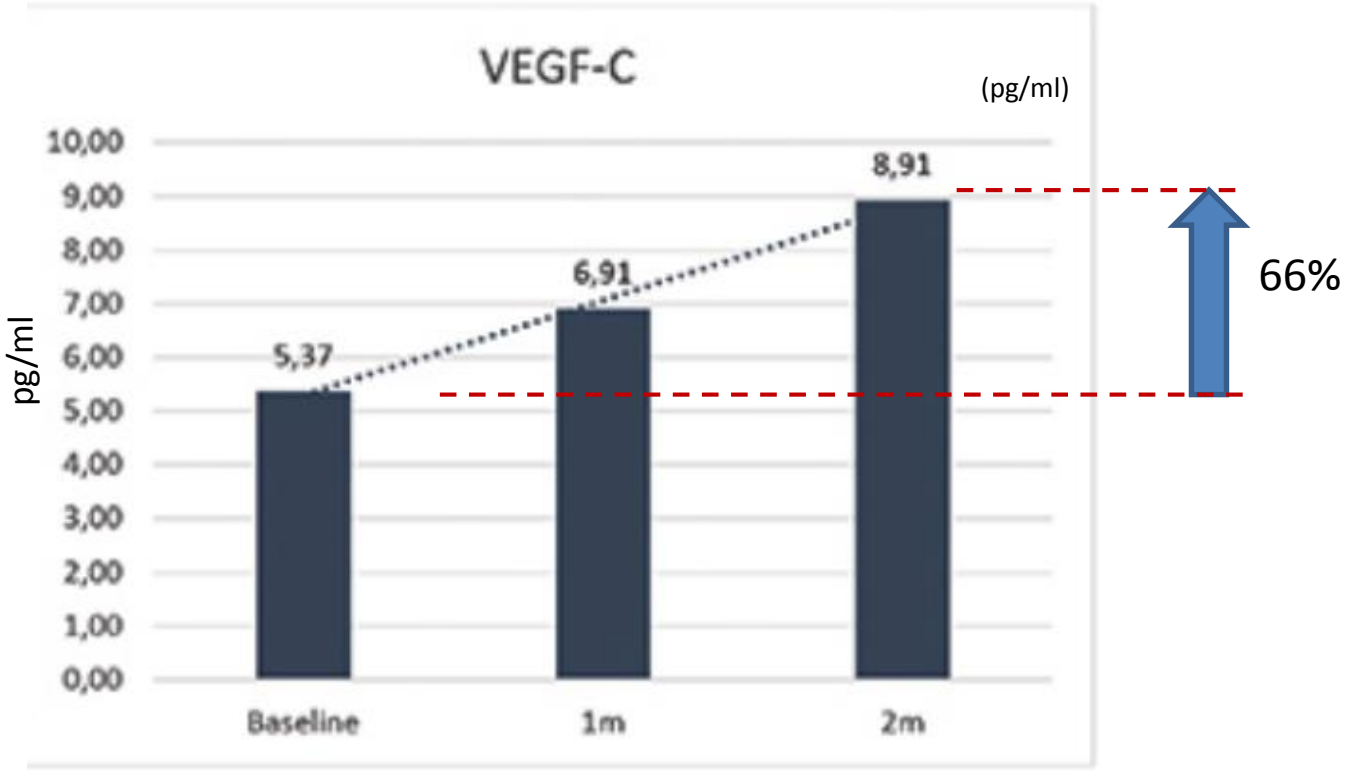
Elevated VEGF-C in Wet AMD Patients

- VEGF-C levels in the retina increase with disease severity
- Aqueous levels of VEGF-C are significantly increased at 1 and 2 months following IVT injection of Avastin® (a-VEGF-A mAb) to wet AMD pts*



* *ARVO (Association for Research in Vision & Ophthalmology) Annual Meeting 2016, Cabral et al., Program 3341, Poster D0144*

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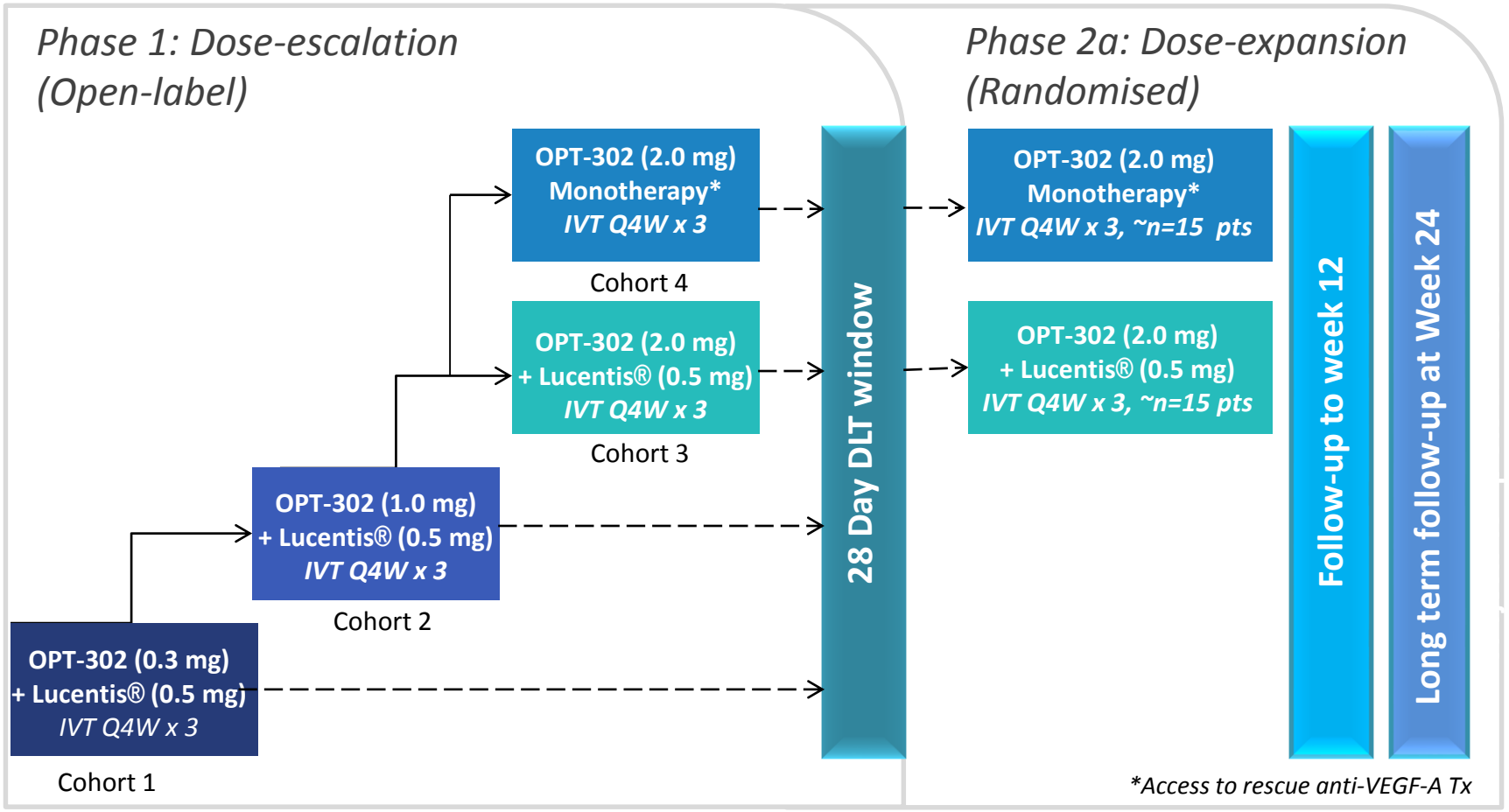
OPT-302 Phase 1/2a

ClinTrials.gov ID#: NCT02543229

Dose-escalation & dose-expansion of repeated IVT injections



- *Comprises of 4 treatment cohorts of 5 subjects each*

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OPT-302 Phase 1: Patient Demographics

- Run under FDA IND at 14 clinical sites in the US
- 20 pts (mean age 74.8)
- 14/20 females, 6/20 males
- 17/20 occult, 2/20 min classic, 1/20 predominantly classic
- Each patient received 3 intravitreal injections of OPT-302 either alone or in combination with Lucentis ® every 4 weeks, with a week 12 follow-up one month after the third dose.
- 70% difficult to treat patients sub-responsive to anti-VEGF-A therapy
- 30% treatment-naïve

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	OPT-302 (2.0 mg) + Lucentis® (0.5 mg)	2	3*
4	OPT-302 (2.0 mg)	2	3

**One pt with metastatic ovarian cancer died prior to the week 12 (day 78) visit due to intercurrent illness unrelated to study drugs.*

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OPT-302 Safe & Well Tolerated in Phase 1 Study

- OPT-302 successfully met primary safety objective in Phase 1 dose escalation study
- No dose limiting toxicities (and MTD not reached) through week 12 in:
  - OPT-302 monotherapy (2.0 mg), and
  - Cohorts of OPT-302 (0.3, 1, 2 mg) in combination with Lucentis® (0.5 mg)
- No signs of infection (endophthalmitis)
- No clinically significant changes in:
  - Intraocular pressure
  - ECGs
  - Blood pressure
  - Blood chemistry or other vital signs
- No evidence of drug-related immunogenicity

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Phase 1 Secondary Endpoints

- Overall, 16/19 evaluable pts maintained or gained vision from baseline to week 12
- No patient lost more than 3 letters. All of the patients that lost VA from baseline received combination OPT-302 + Lucentis® therapy.

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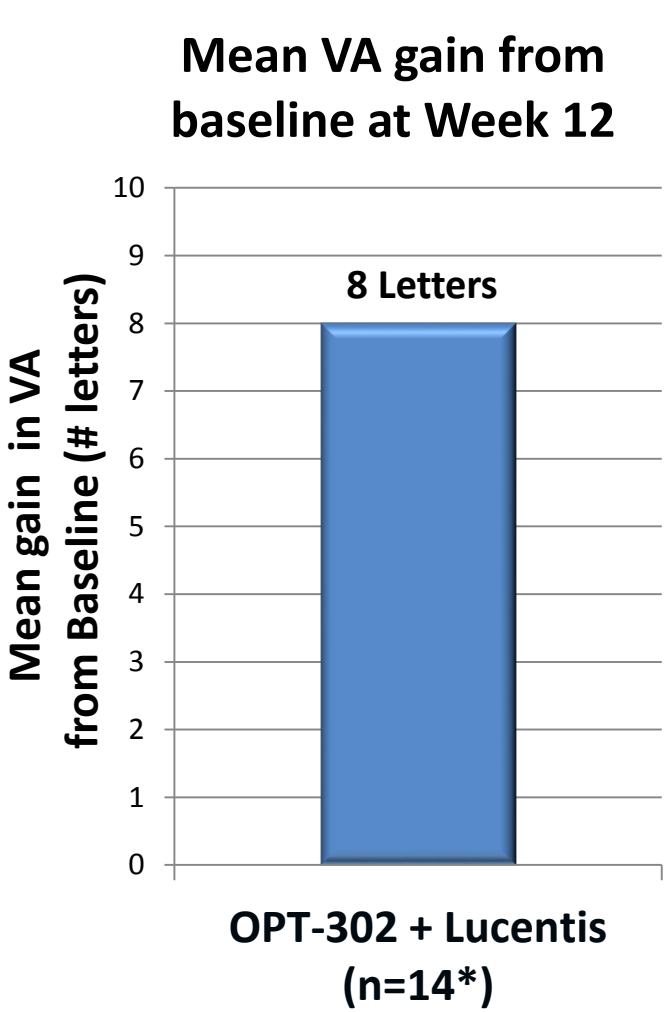
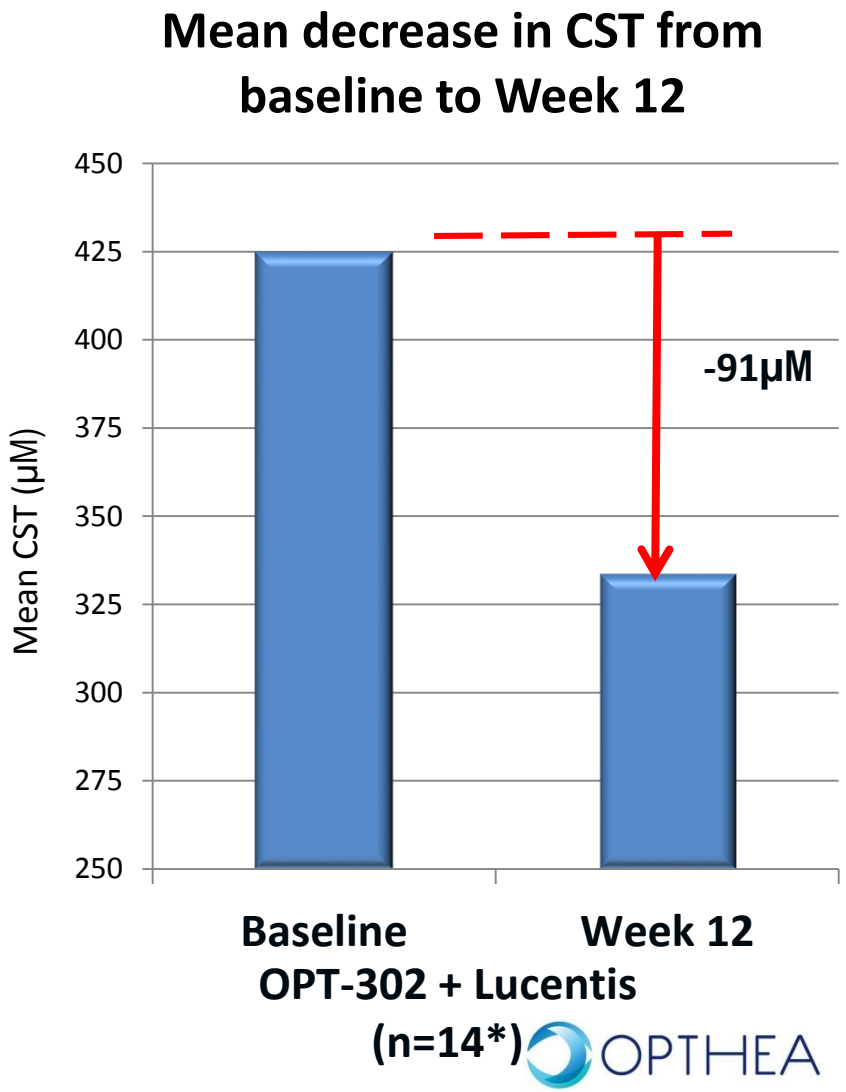
Combination Therapy: All Patients (Full cohort) (Naïve & Prior-Tx)

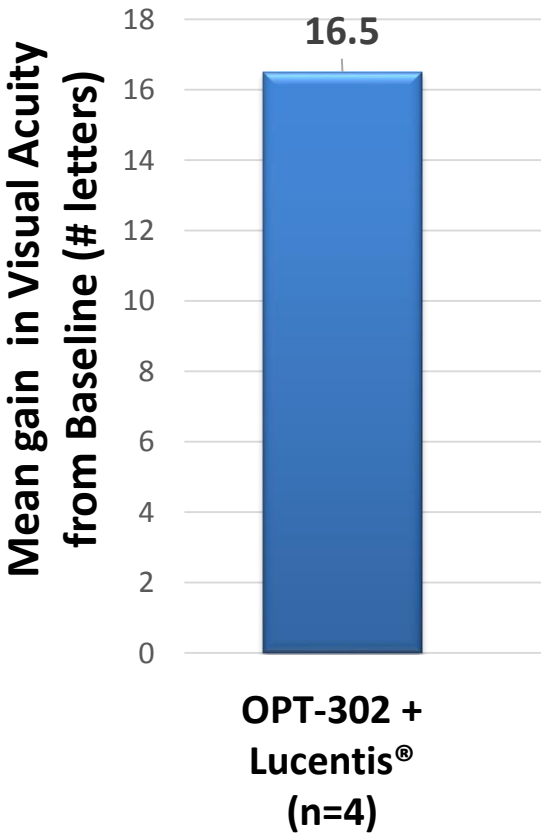




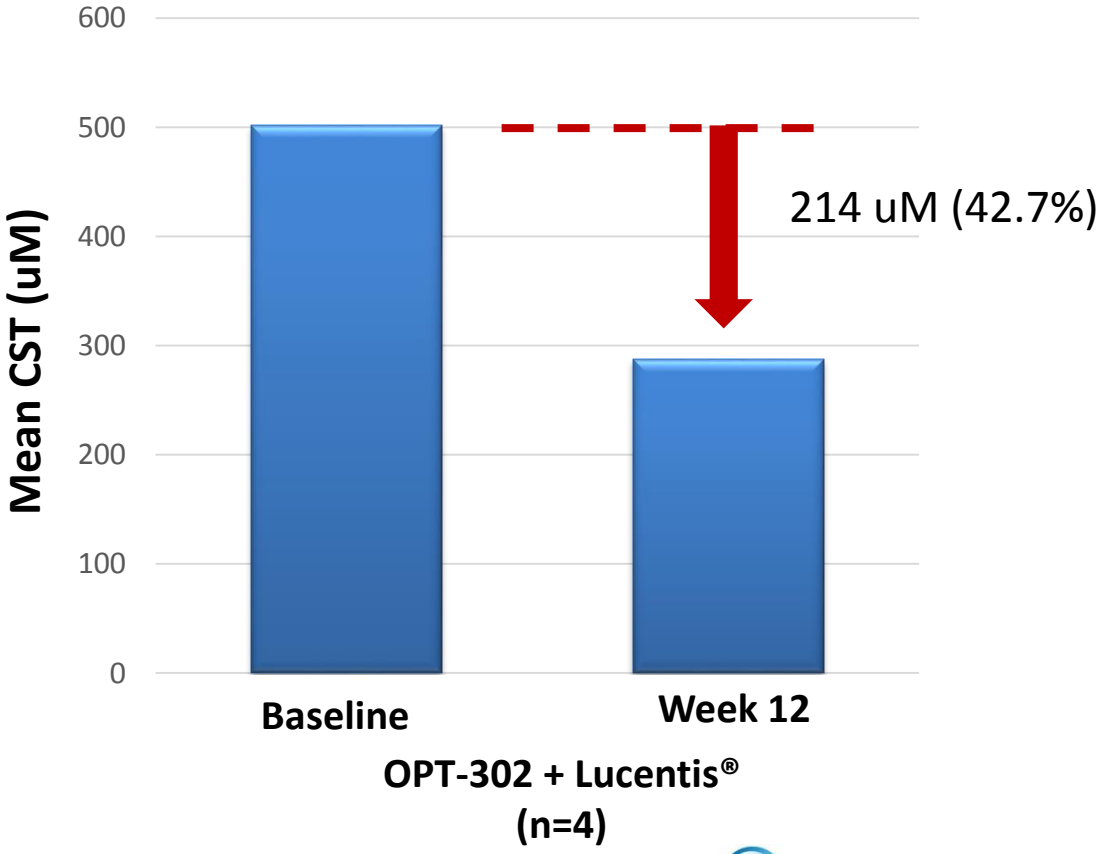
** 1 pt not evaluable at W12*

Combination Therapy: Treatment-Naïve Patients

Mean Gain VA from Baseline



Mean Central Subfield Thickness



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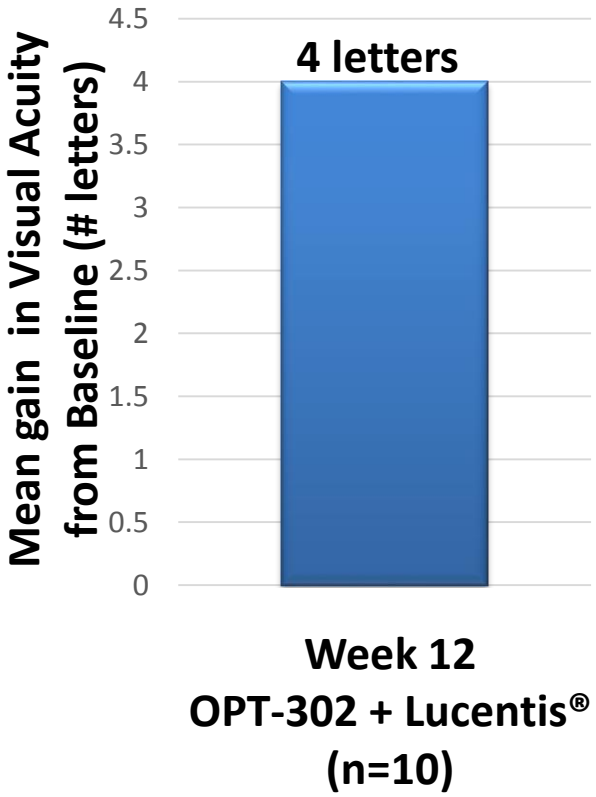
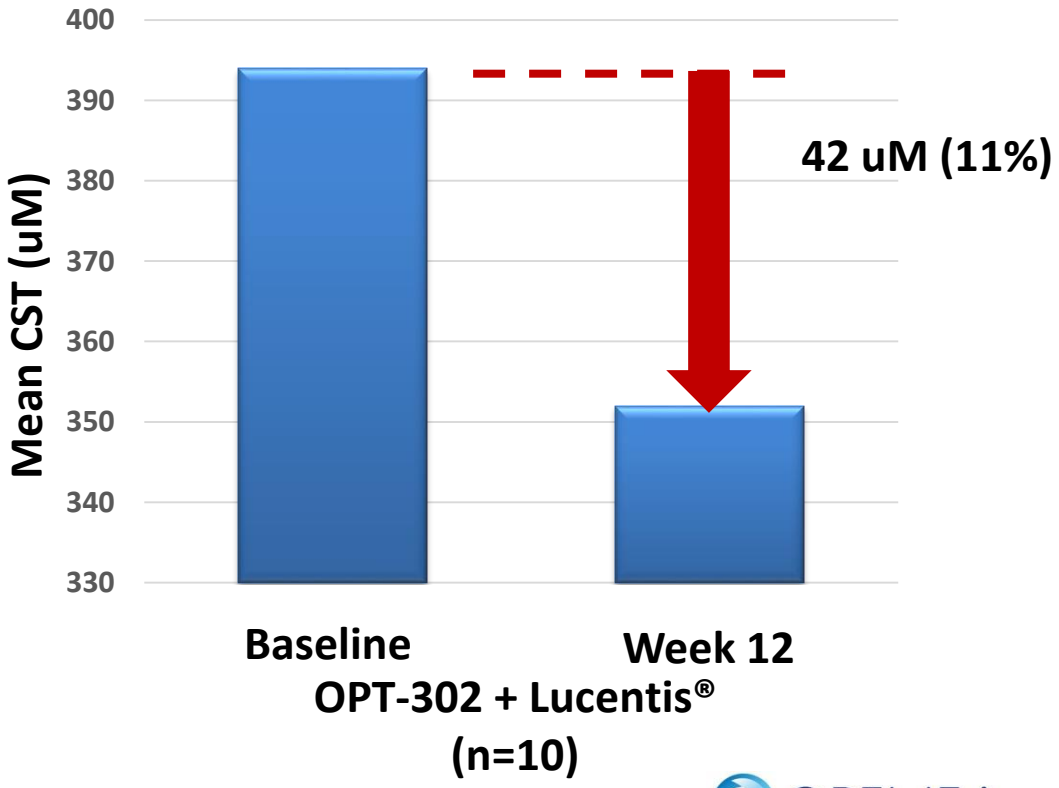
Combination Therapy: Prior-Treated Patients

- Mean number prior treatment injections: 10.5 (range 3 – 55)

Mean Change VA from Baseline

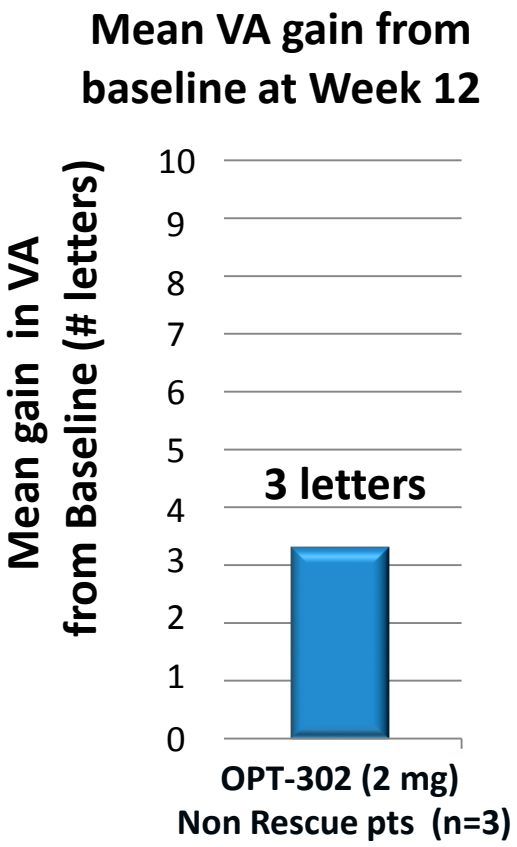


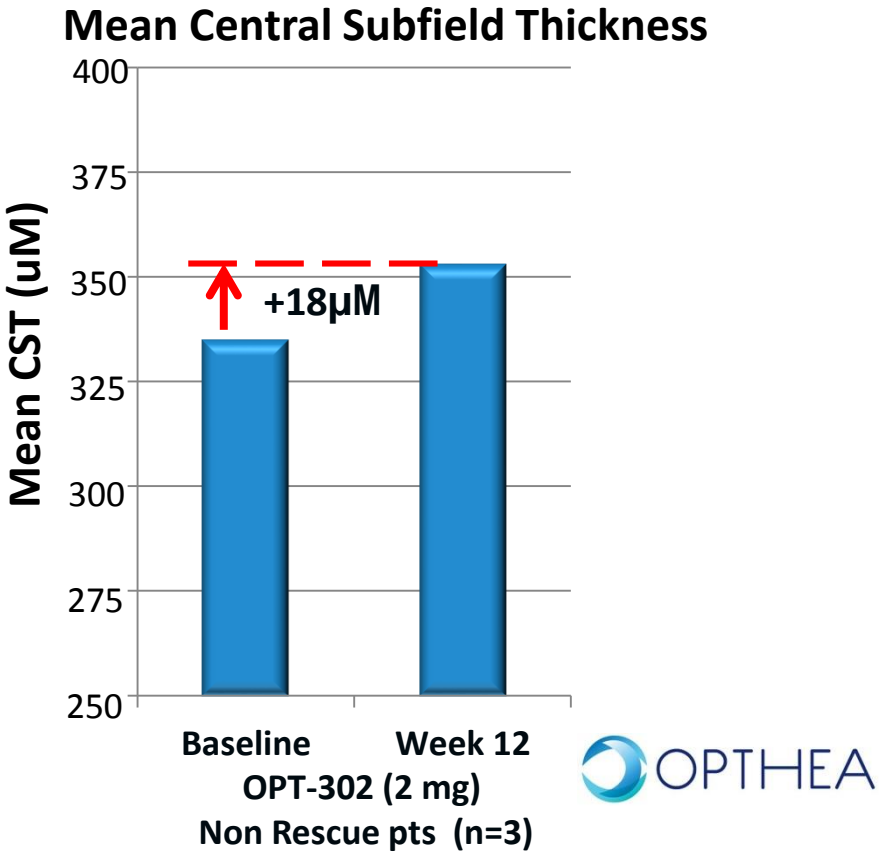
Mean Central Subfield Thickness



OPT-302 Monotherapy

- 3/5 patients did not require ‘rescue’ therapy
- 2 patients were rescued (at d25 and d29). At week 12, both had lost vision compared to baseline.
- At week 12, in patients that did not require rescue therapy, mean VA gain of 3.3 letters from baseline (range 2 to 6 letters) and mean increase in CST of 18 uM





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OPT-302 Program Highlights

- Large unmet medical need for wet AMD, current treatments only target VEGF-A
- OPT-302 targets VEGF-C and VEGF-D that are associated with incomplete response to VEGF-A inhibition
- OPT-302 met primary objective of Phase 1 study: OPT-302 safe & well tolerated
- Evidence of clinical activity:
  - Patients treated with combination OPT-302 + Lucentis® therapy showed mean vision gains and retinal thickness improvements equal to or superior to historic, 12 week anti-VEGF-A (Lucentis®) alone, despite including heavily pre-treated, sub-responsive patients with a high proportion of occult lesions
  - Naïve pts: data suggests meaningful additional VA gain and reduction in CST with OPT-302 + Lucentis® compared to historic data with Lucentis® alone
  - Prior Tx pts: improved outcomes in difficult to treat, sub-responsive pts suggest additional benefit of VEGF-A, VEGF-C and VEGF-D inhibition
  - OPT-302 monotherapy maintained mean VA and CST
- Totality of data warrants advancing OPT-302 + Lucentis® to a Phase 2B randomised, controlled trial
- Actively accruing into Phase 2A , planning for Phase 2B in 2017

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