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

Ophthalmology Innovation Summit @ ASRS, August 10 2017

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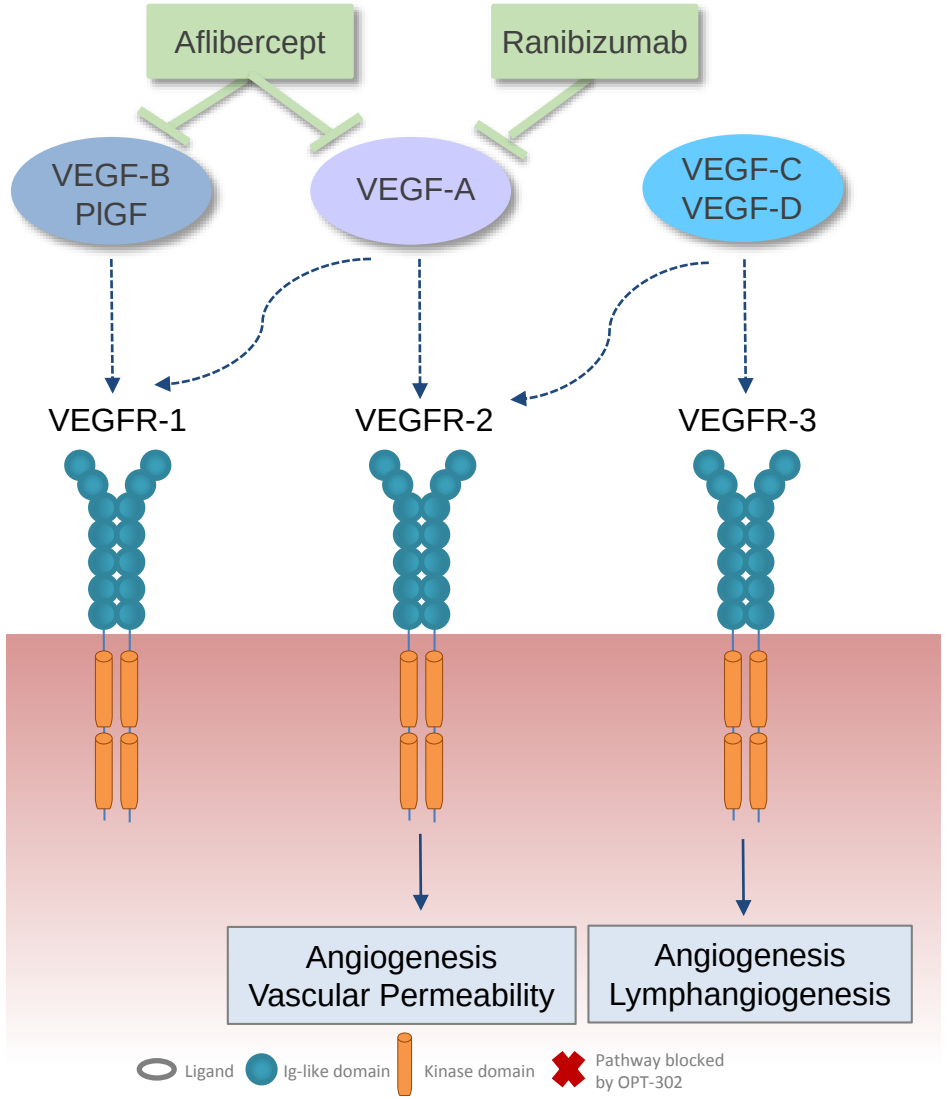
Current Treatment Strategies Primarily Target VEGF-A



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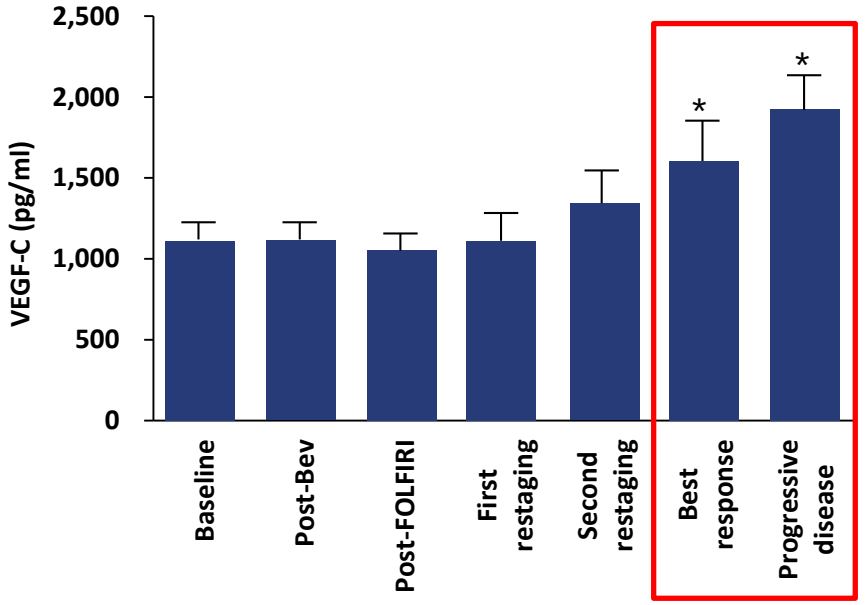
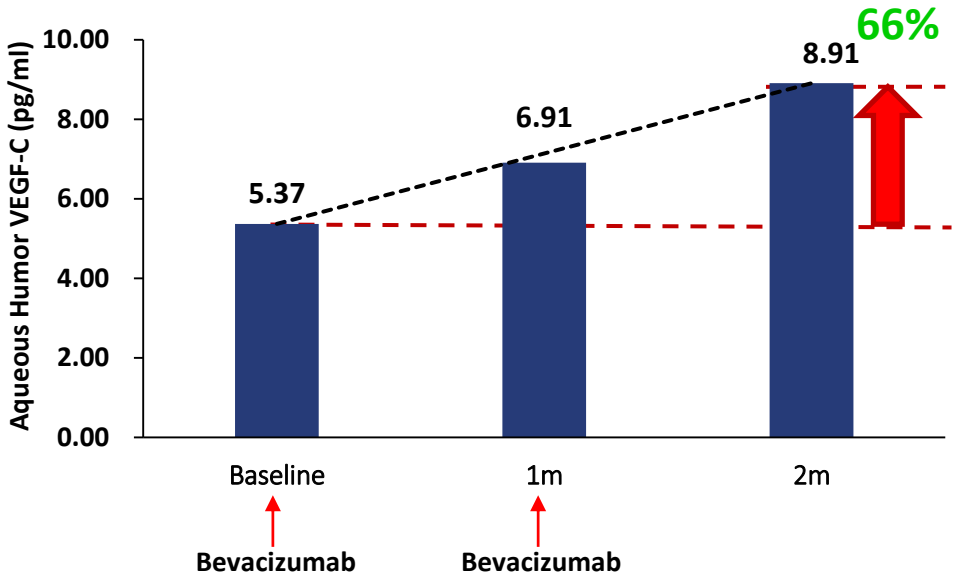
VEGF-A Inhibition Upregulates VEGF-C/D

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

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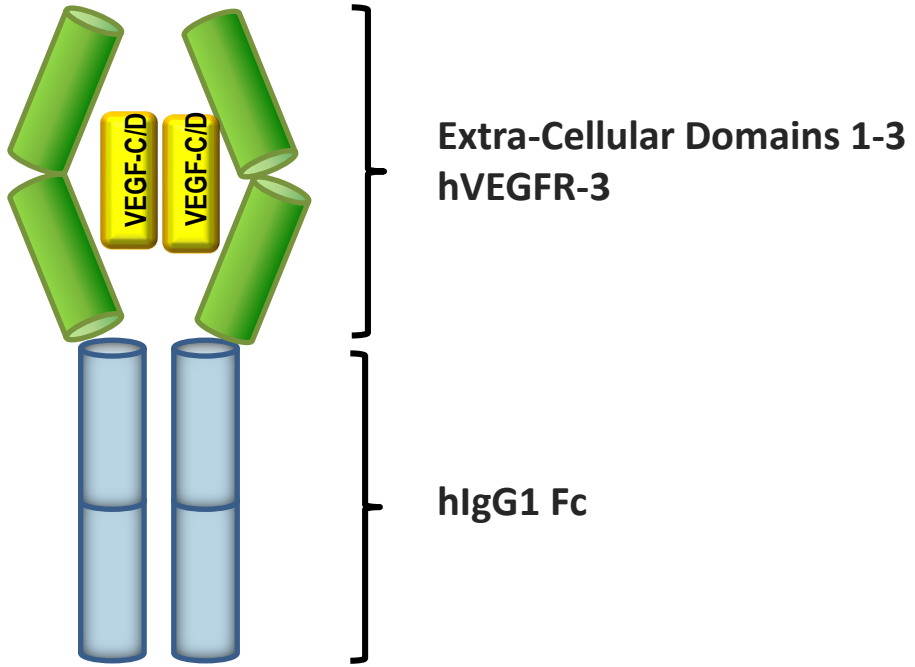
OPT-302

- Potent inhibitor of VEGF-C (~5pM) and VEGF-D (~0.5 nM)
- A ‘trap’ that blocks VEGF-C and VEGF-D binding to the receptors VEGFR-2 and VEGFR-3



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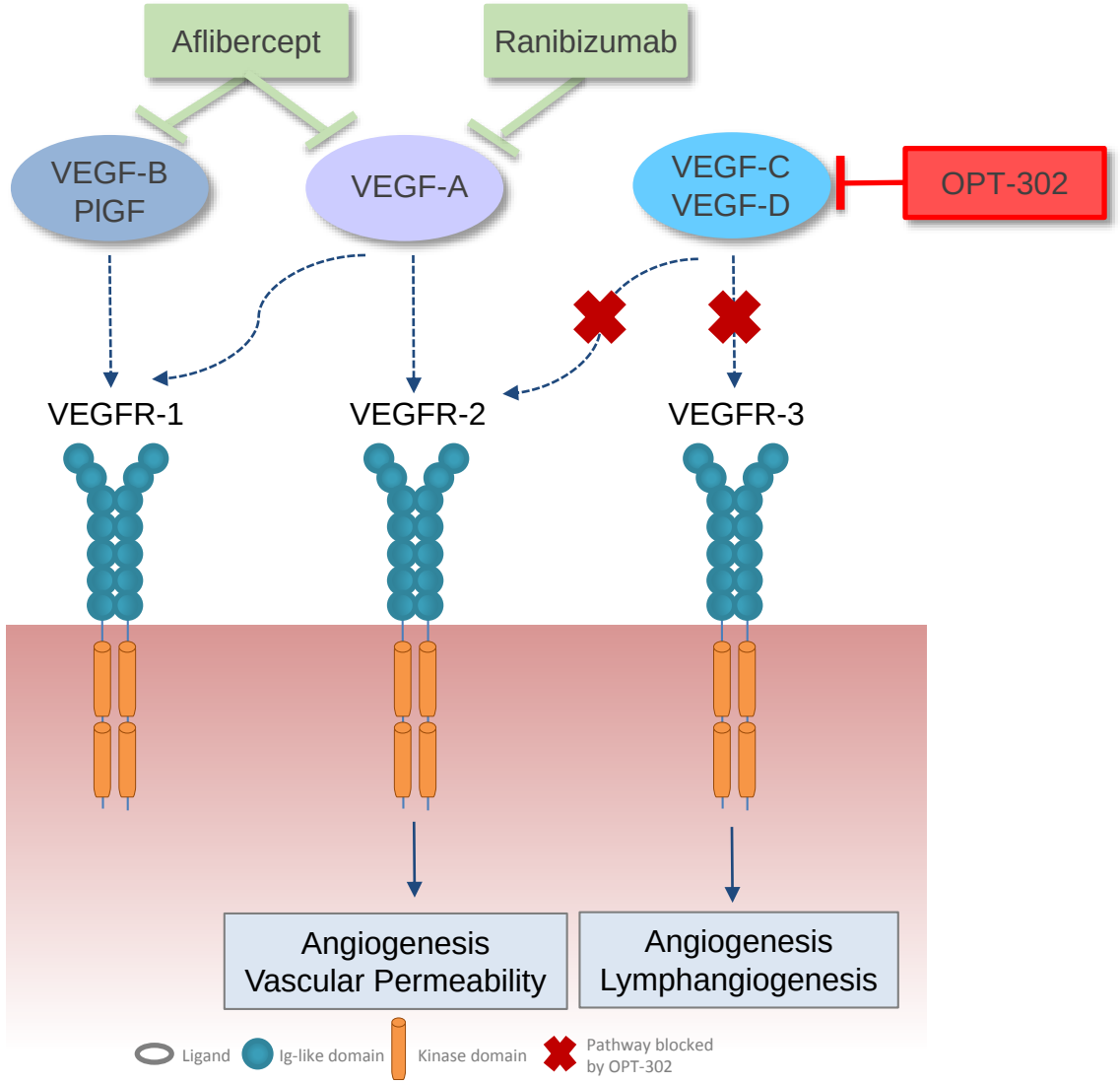
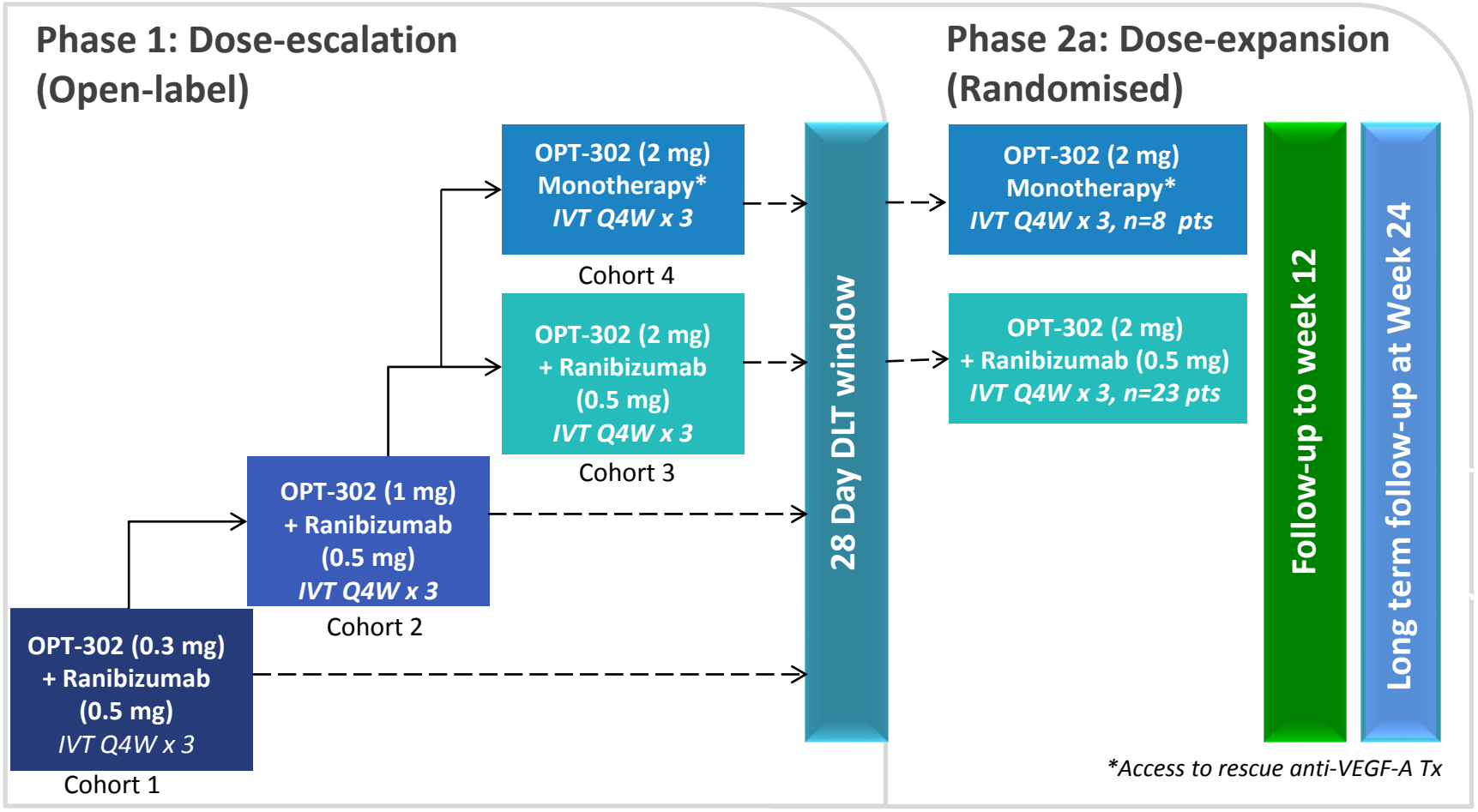
OPT-302 Inhibits VEGF-C and VEGF-D



OPT-302 Phase 1/2a Study



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

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Investigators

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Michael Tolentino *Center for Retina & Macular Disease* Winter Haven, FL	**Lawrence Singerman** *Retina Associates of Cleveland* Cleveland, OH	**Nathan Steinle** *California Retina Consultants* Santa Maria, CA	**Michael Varenhorst** *Vitreo-Retinal Consultants & Surgeons* Wichita, KS
	Joseph P. Walker *National Ophthalmic Research Institute* Fort Myers, FL	**John Wells III** *Palmetto Retina Center* West Columbia, SC	

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OPT-302 Phase 1/2a Study Enrolled 51 Patients with Neovascular AMD

OPT-302 Monotherapy

n=13 patients
Administered OPT-302 alone, both naïve and prior-treated patients

OPT-302 + Lucentis® Naïve Patients

n=18 patients
Administered combination therapy to patients who had not previously received nAMD therapy

OPT-302 + Lucentis® Prior-Treated Patients

n=20 patients
Administered combination therapy to patients who had previously received nAMD therapy and shown a sub-response

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OPT-302 Phase 1/2a Safety Summary

OPT-302 ± Ranibizumab (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 ± Ranibizumab (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 inflammation indicative of 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 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 Ranibizumab 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

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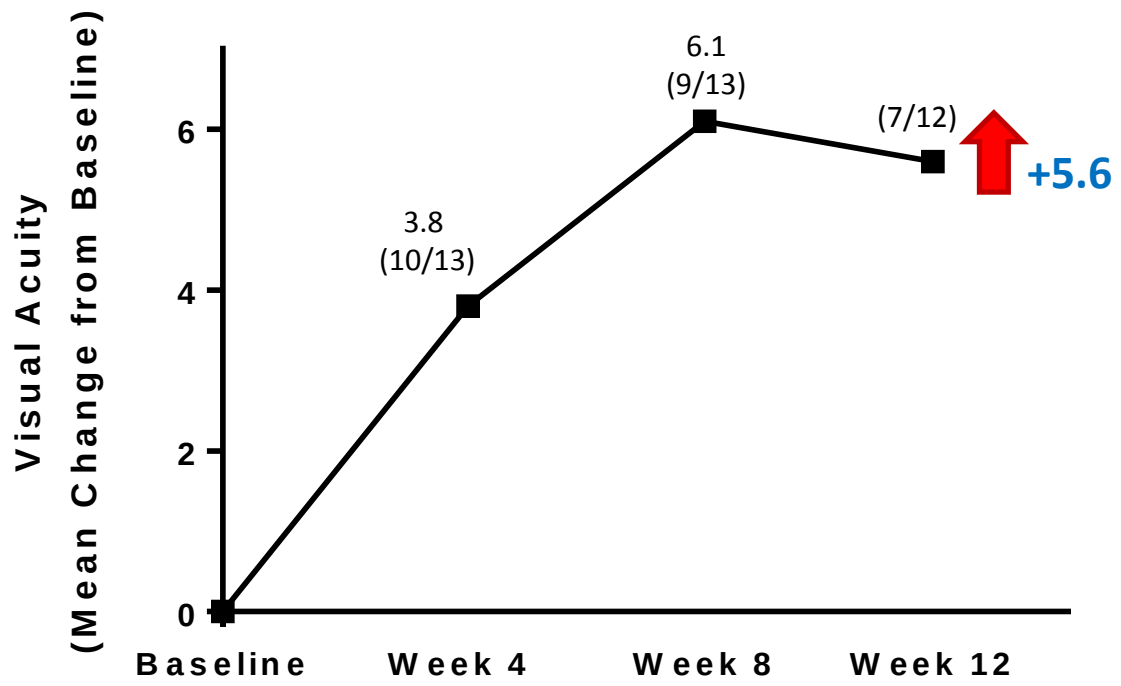
Phase 1/2a: Monotherapy Patients

Mean Change in Visual Acuity in Non-Rescue Patients



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)

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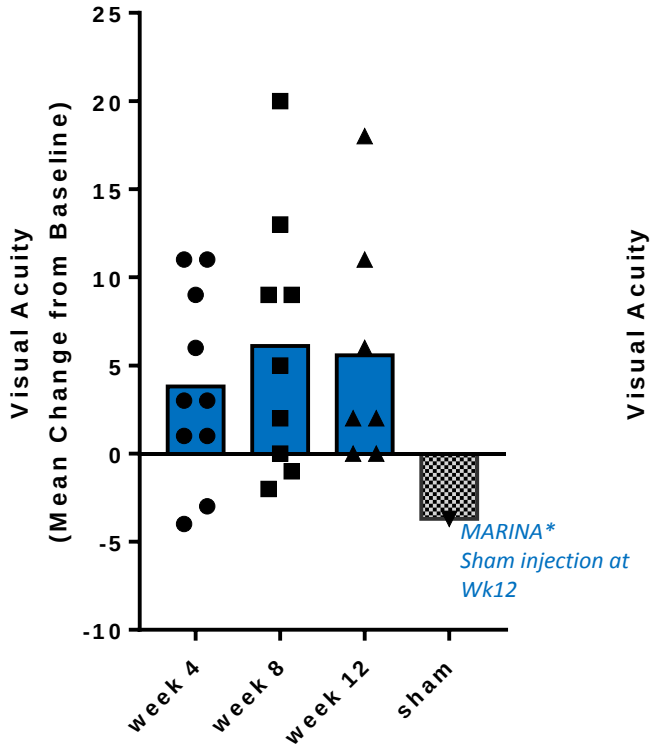
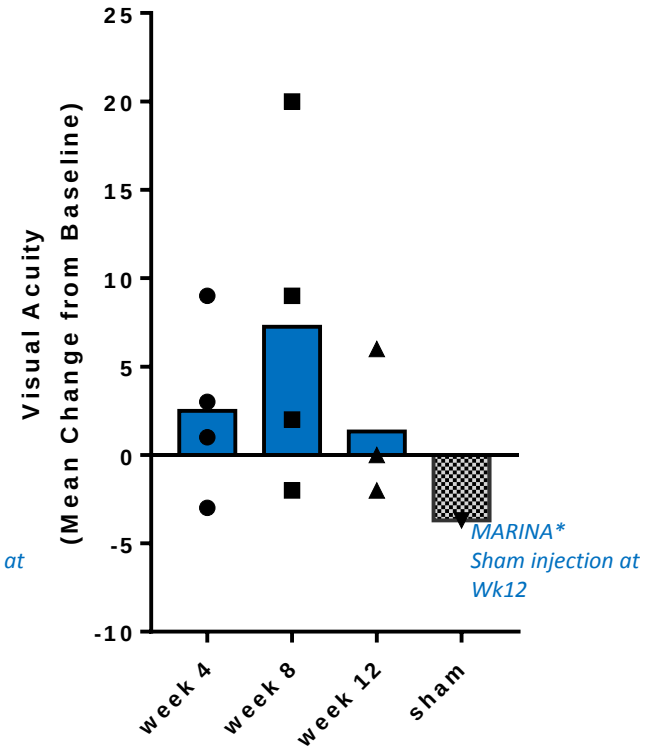
Phase 1/2a: Monotherapy Patients

Treatment-Naïve



Prior-Treated



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

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

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OPT-302 Phase 1/2a: Patient Demographics

- **51% difficult to treat patients sub-responsive to anti-VEGF-A therapy**
  - Mean number prior anti-VEGF-A injections: 17
- 73% Occult, 23% Min. Classic, 4% Predominantly Classic

Study	Visual Acuity gain at 12 Weeks (letters)	Prior-Treatment[a]	% Lesion Type Classic (C); Predominantly Classic (PC); Minimally Classic (MC); Occult (Oc)
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%) *
FOVISTA PHASE 2b [5]	+5.1	Naïve	PC or MC (100%)

[1] Rosenfeld et al., NEJM, 355;14, pp 1419-1431, 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; [5] Jaffe et al. Ophthalmology 2017

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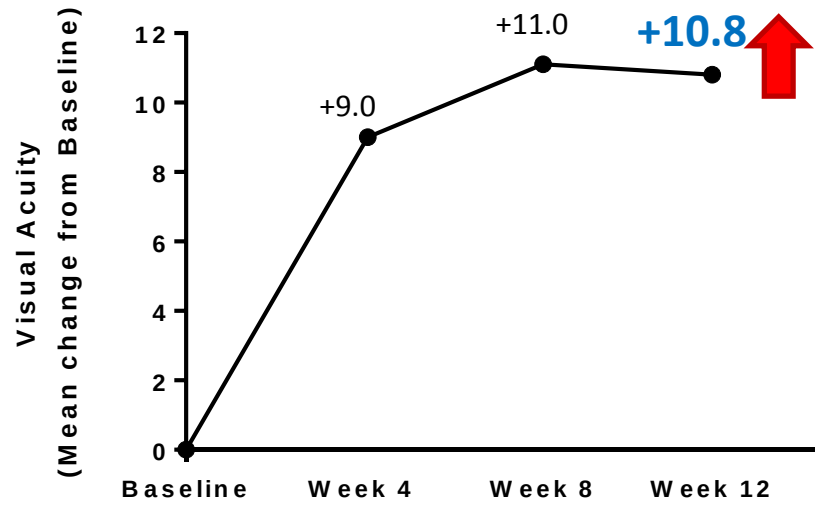
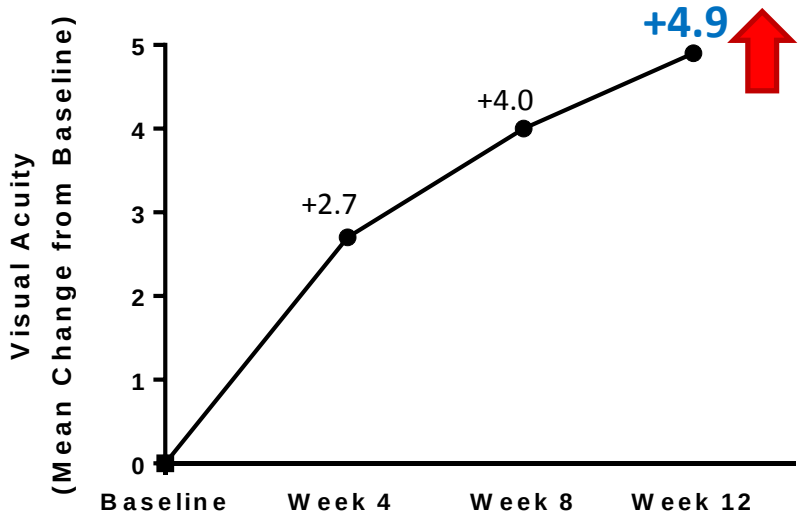
Gains in Visual Acuity in Patients with OPT-302 Combination Therapy

Treatment-Naïve



Prior-Treated



Improved Visual Acuity in both Treatment-Naïve and Prior-Treated Patients Treated with OPT-302 + Ranibizumab Combination Therapy

Treatment Naïve Patients:
n = 18; OPT-302 (0.3, 2.0 mg) + ranibizumab (0.5 mg)
Mean Baseline VA = 56.5 Letters

Prior-Treated Patients:
n = 20 (wk 4, 8), 19 (wk 12); OPT-302 (0.3-2.0 mg) + ranbizumab (0.5 mg)
Mean Baseline VA = 64.5 Letters

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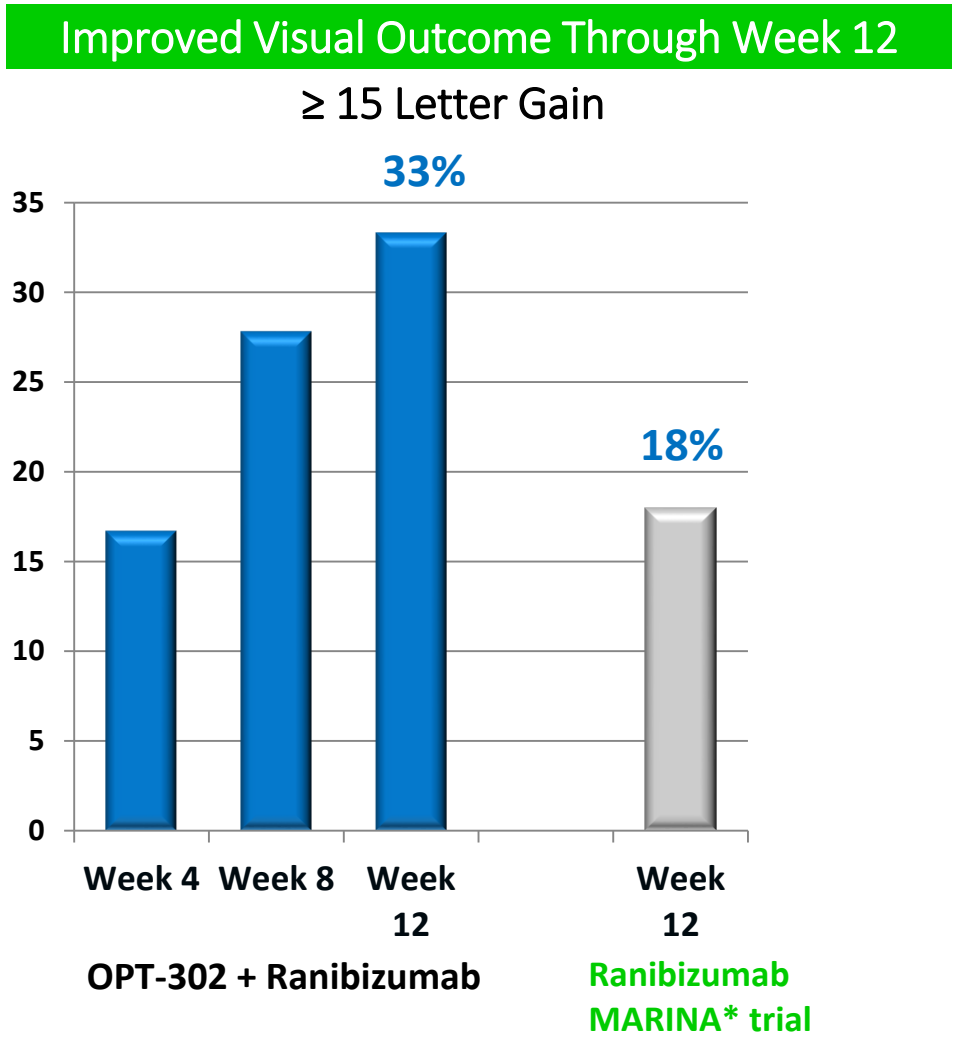
OPT-302 Phase 1/2a: Treatment-Naïve Patients



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Mean Baseline VA = 56.5 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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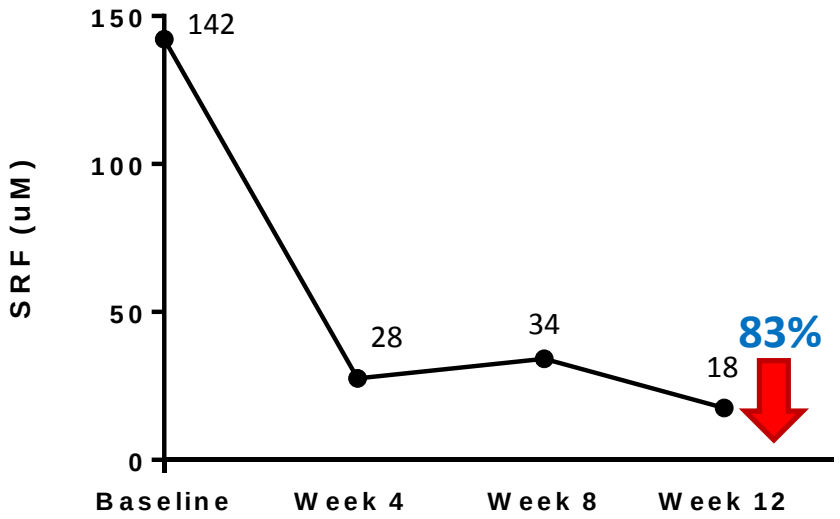
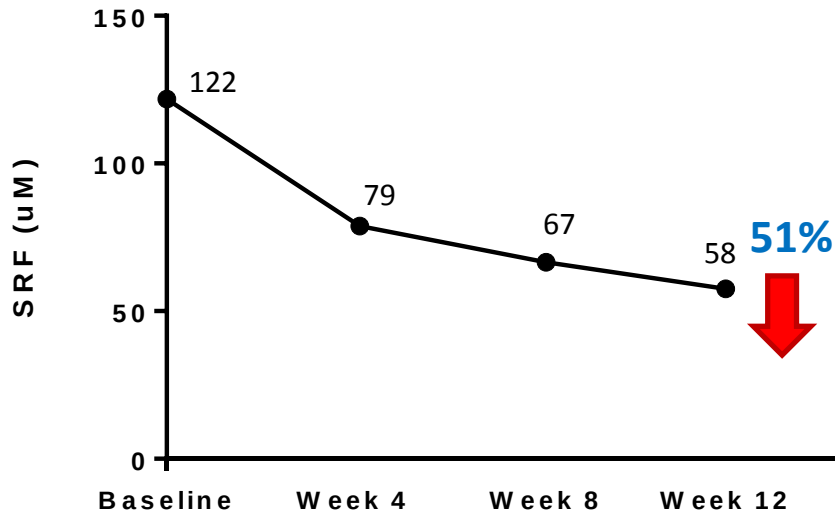
Reductions in Retinal Fluid in Patients with OPT-302 Combination Therapy

Treatment Naïve



Prior Treated



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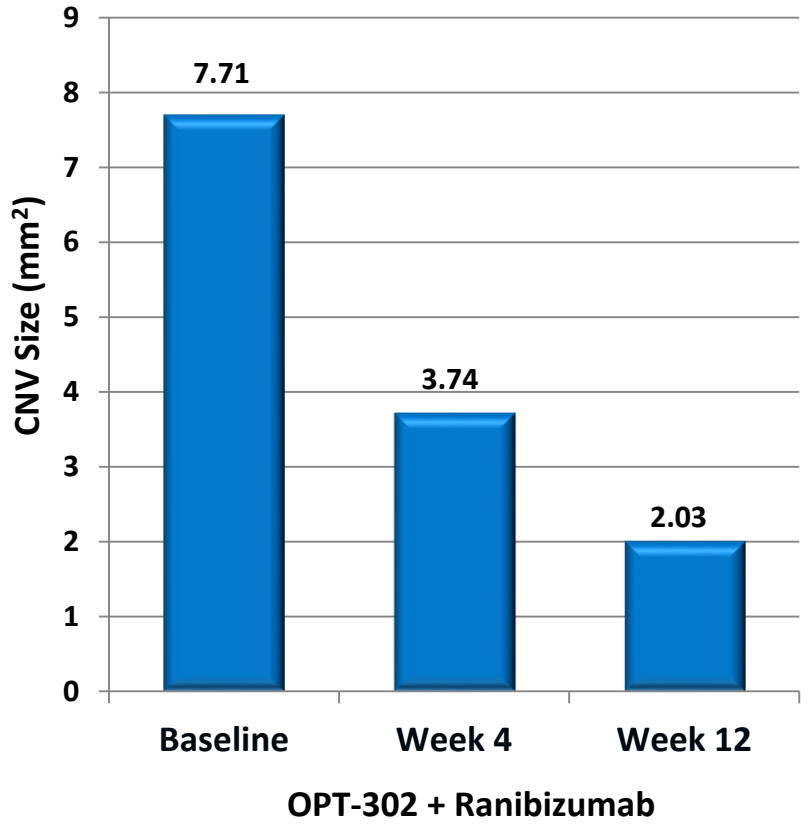
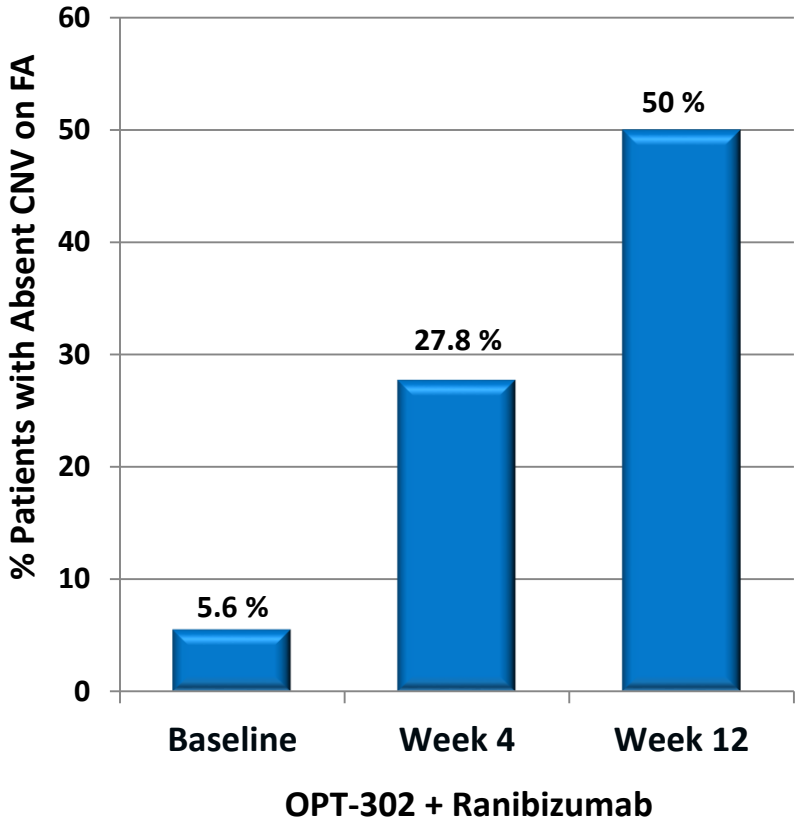
Treatment-Naïve Patients: Reductions in CNV

Reduction in CNV Size on FA



% Patients with Absent CNV on FA



CNV: Choroidal Neovascularisation
Treatment Naïve Patients:
n = 18; OPT-302 (0.3, 2.0 mg) + ranibizumab (0.5 mg)

50% of Treatment-Naïve Patients had no detectable CNV after 12 weeks

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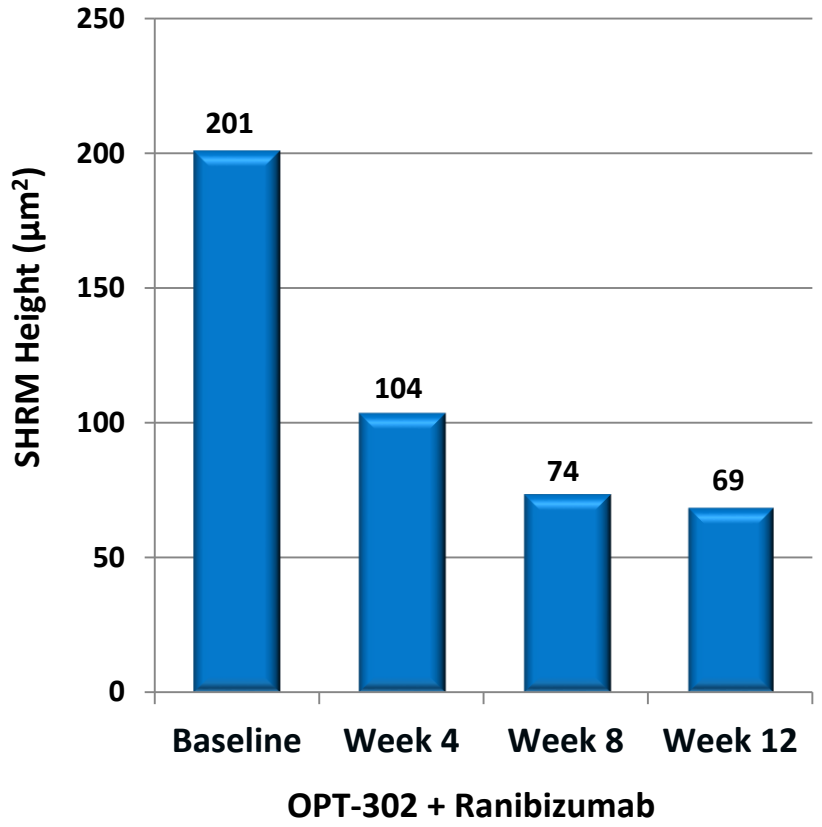
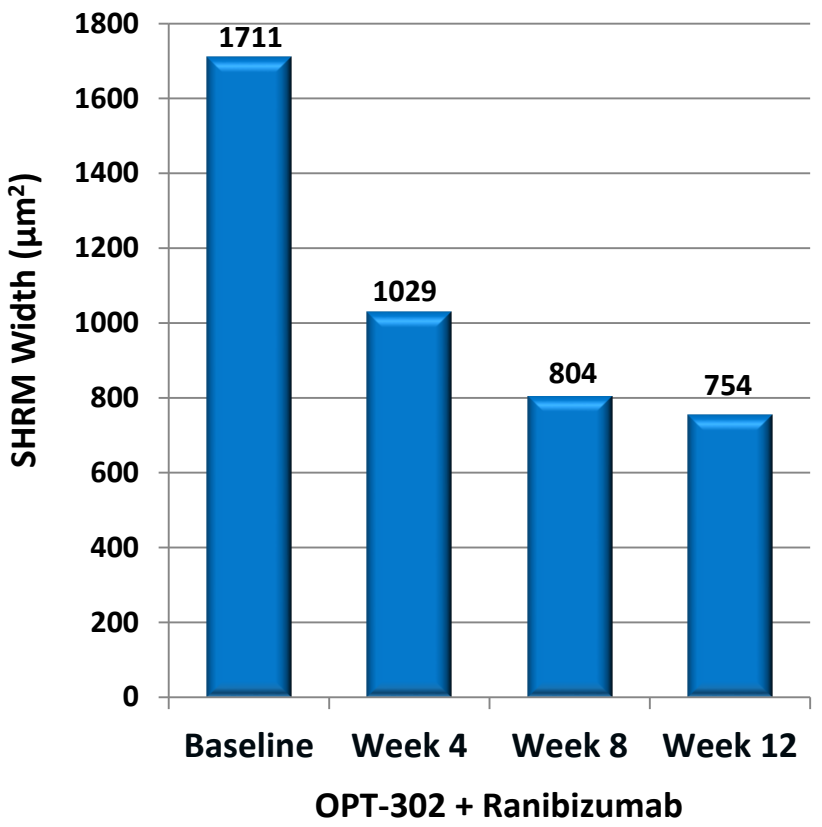
Treatment-Naïve Patients: Reductions in SHRM

Reduction in SHRM Height



Reduction in SHRM Width



SHRM: Subretinal Hyper-Reflective Material
Treatment Naïve Patients:
n = 18; OPT-302 (0.3, 2.0 mg) + ranibizumab (0.5 mg)

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Conclusion

- Current treatments target primarily VEGF-A
- OPT-302 inhibits VEGF-C and VEGF-D
- OPT-302 met the primary objectives of Phase 1/2A study:
  - Excellent safety profile and positive biological signal
- Evidence across multiple endpoints that Pan-VEGF (A, C and D) inhibition is more effective than VEGF-A alone
- Potential for additive efficacy and improved durability

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