24-week Cohort 1 Data From the OPTIC Trial – Intravitreal Gene Therapy With ADVM-022 (AAV.7m8-aflibercept) for Neovascular Age-related Macular Degeneration

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– On behalf of the OPTIC investigators –

OPTIC
Gene Therapy in nAMD

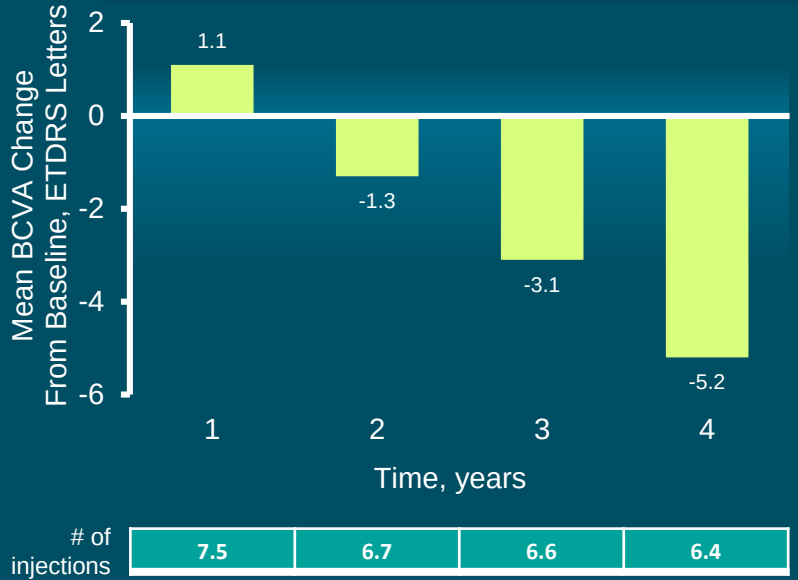
Disclosures

- Adverum Biotechnologies – Consultant/Advisor, Equity
- Regenxbio – Consultant/Advisor, Equity
- Genentech/Roche – Consultant/Advisor
- Fortress Bio – Consultant/Advisor, Equity
- Optos – Consultant/Advisor, Research grant support
- Novartis – Consultant/Advisor
- Intellectual Property related to gene and cellular therapy – assigned to Weill Cornell/Cornell University

Real-world Anti-VEGF Patient Outcomes

Undertreatment Leads to Vision Loss

98,821 Eyes From 79,885 US Patients
Receiving Routine Intravitreal Anti-VEGF Therapy



Development Approaches to Deliver Long-term Efficacy

Surgical

- Subretinal gene therapy
- Implantable reservoir

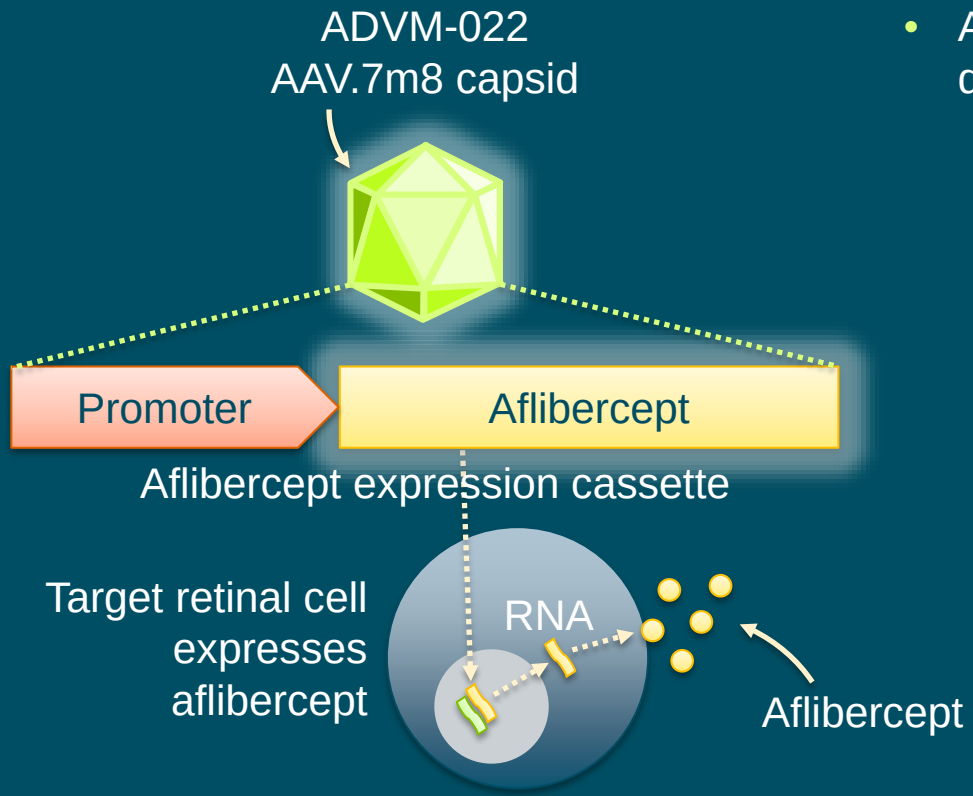
Intravitreal

- Depot formulations
- IVT gene therapy

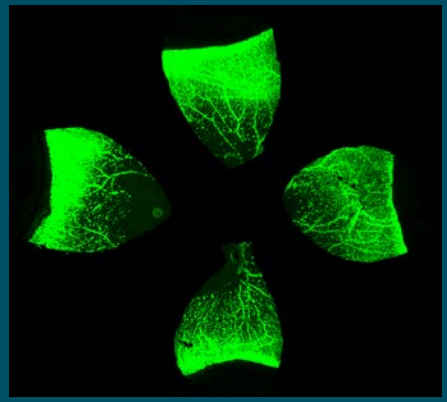
BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study
IVT, intravitreal therapy; VEGF, vascular endothelial growth factor

Khanani AM, et al. Submitted.

ADVM-022 is Specifically Designed for Long-term Intraocular VEGF Suppression With a Single Intravitreal Injection



- Advanced AAV.7m8 vector developed using directed evolution to:
  - Enable efficient intravitreal delivery
  - Increase transduction of retinal cells
  - Increase protein expression



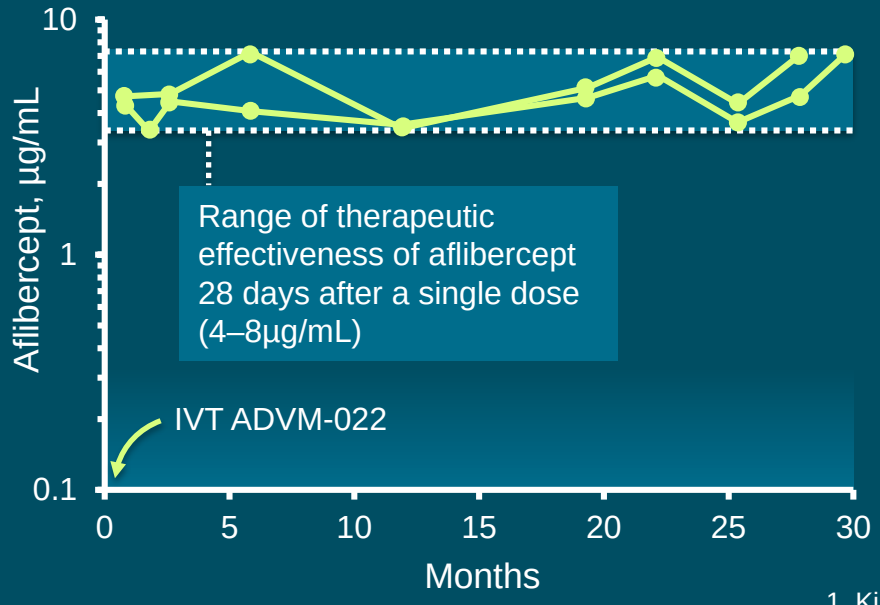
Green fluorescent protein expression in non-human primate retina

VEGF, vascular endothelial growth factor

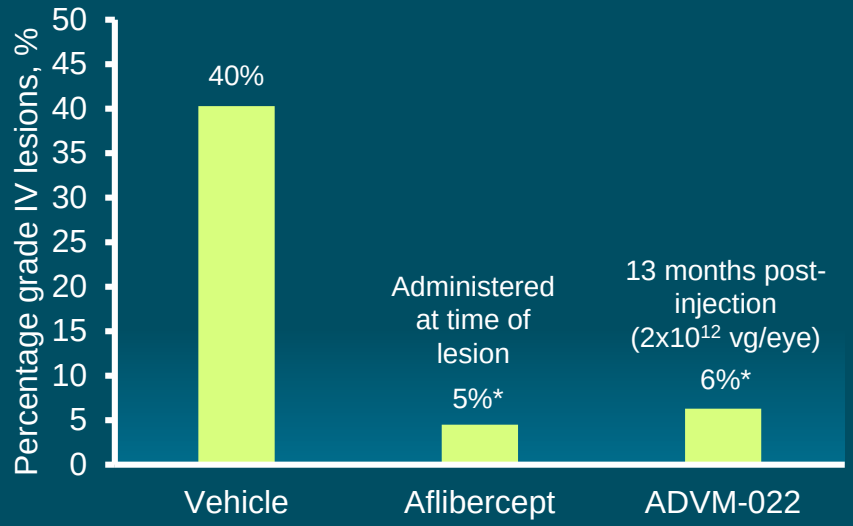
Grishanin, R. et al. Mol. Ther. 2019;27:118–29

Preclinical Data Demonstrate the Potential for Long-term Efficacy With a Single Intravitreal Injection of ADVM-022

ADVM-022 results in aflibercept protein expression for 30 months within the therapeutic range for single-dose aflibercept[1,2]



ADVM-022 given 13 months prior to laser CNV is as effective as aflibercept at the time of laser[3]

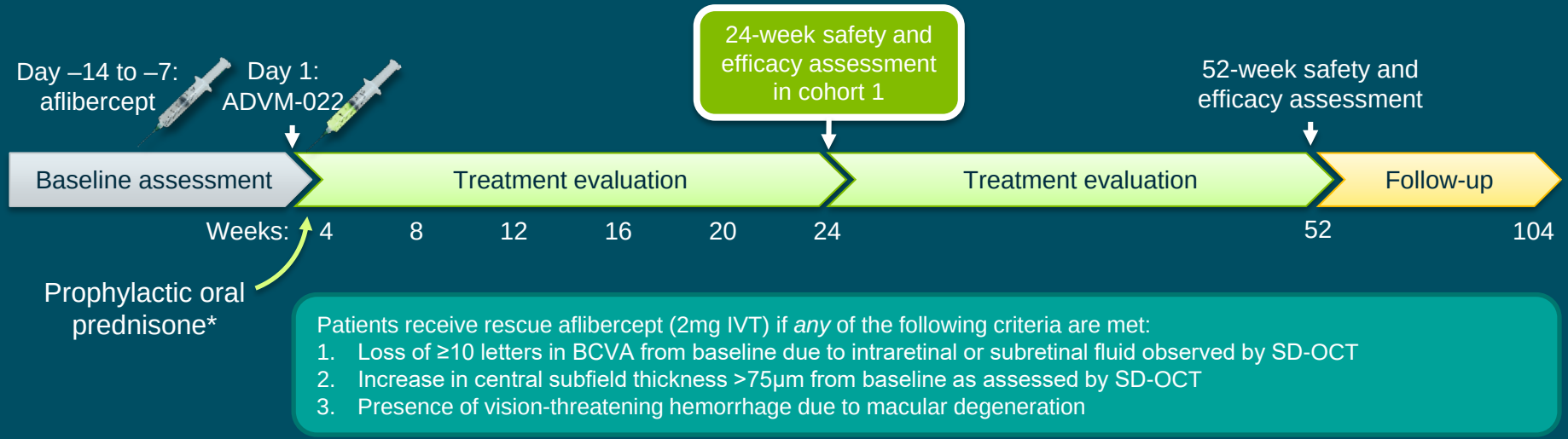


*p<0.0001
CNV, choroidal neovascularization

1. Kiss, S. Ann Meeting of the Am Soc Gene Cell Ther; May 2019, Washington, DC
2. Kiss S. Ann Meeting Am Assoc Ophtha; October 2018, Chicago, IL
3. Grishanin, R. et al. Mol. Ther. 2019;27:118–29

OPTIC: Phase 1, Two-year Multicenter Study of ADVM-022 in Neovascular AMD

- Primary objective
  - Assess the safety and tolerability of a single IVT injection of ADVM-022
- Secondary objectives
  - Evaluate vision (BCVA)
  - Evaluate anatomy (SD-OCT)
  - Assess the need for rescue therapy



*All subjects received 60mg of oral prednisone for 6 days starting at Day –3 followed by 7-day taper
BCVA, best-corrected visual acuity; IVT, intravitreal therapy; SD-OCT, scanning domain optical coherence tomography

NCT03748784

Study Population Previously Required Frequent Injections to Maintain Vision

Baseline Characteristic	Value
Mean age, years	79.0
Mean time since nAMD diagnosis, years	3.3
Mean number anti-VEGF injections since initial diagnosis (range), n	35.3 (7–109)
Mean number anti-VEGF injections in 8 months prior to screening, n	6.2
Average annualized injection frequency, n	9.3
Mean BCVA study eye, ETDRS letters Approximate Snellen equivalent	65.8 20/50
Mean CST study eye, µm	369.2

BCVA, best corrected visual acuity: CST, central subfield thickness; ETDRS, Early Diabetic Retinopathy Study
nAMD, neovascular age-related macular degeneration; VEGF, vascular endothelial growth factor

Cohort 1 Safety Results Through Week 24

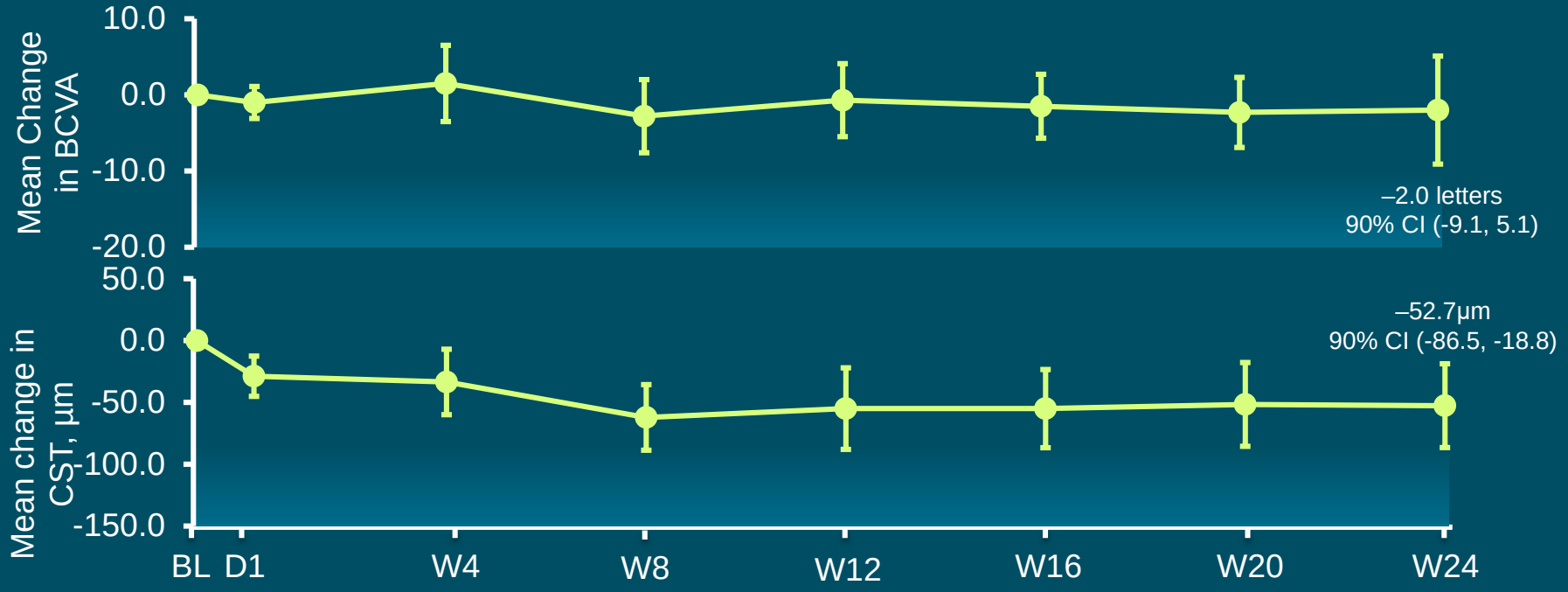
- No serious adverse events
- No adverse events met criteria for dose-limiting toxicity
- No drug-related non-ocular adverse events
- 19 ocular AEs potentially related to ADVM-022:
  - 14 mild AEs, 5 moderate adverse events[§]

- No early clinically significant inflammation observed post ADVM-022
- No vasculitis, no retinitis, no choroiditis
- No worsening or new events observed when receiving steroid eye drops
- Anterior chamber cellular inflammation resolved or improving by Week 24

ADVM-022-related Ocular AEs[†]	Patients, n	Number of Events, n
Anterior chamber cells	3	4**
Anterior chamber flare	3	4
Vitreous cells	3	3*
Intermediate uveitis	2	2**
Keratic precipitates	1	2
Poor pupil dilation	1	1
Ocular floaters	1	1
Vitreous debris	1	1
Vitreous haze	1	1
Total	6	19

[†]Treatment emergent adverse events related to ADVM-022; *1 moderate event; **2 moderate events; [§]CTCAE v5.0, General guidelines;

Cohort 1: Mean BCVA Stable and Mean CST Improved Through 24 Weeks



Aflibercept 2mg IVT administered at baseline. ADVM-022 IVT administered 7-14 days later at Day 1

BCVA, best corrected visual acuity; CST, central retinal thickness BL, baseline; D, day; W, week; Day 1 visit is 7–15 days after baseline visit

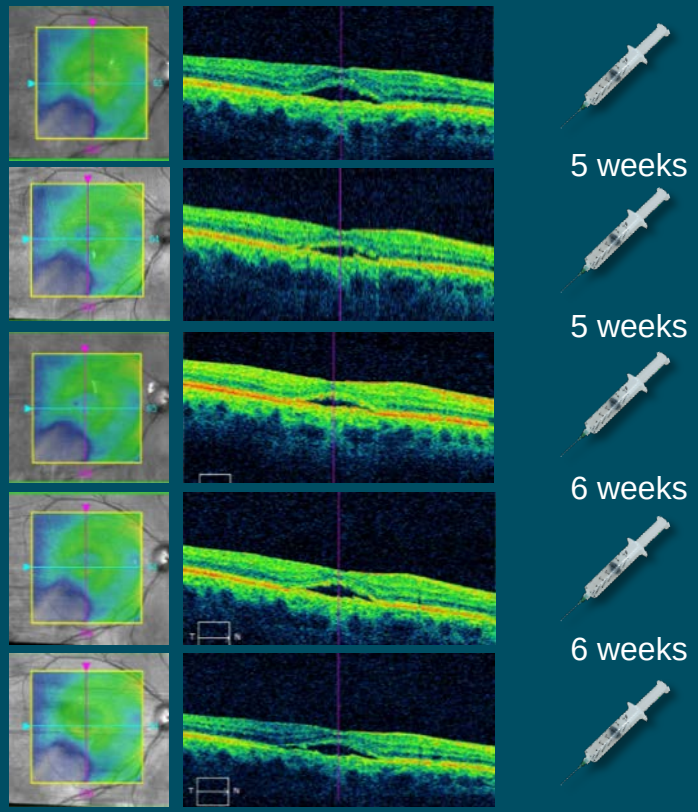
90% CIs on mean change in BCVA and CST were calculated using the T-distribution.

Case Study: Anti-VEGF Centurion (>100 Injections)

62 year-old male	
Previous IVT, n	109
IVT in last 8 months, n	6

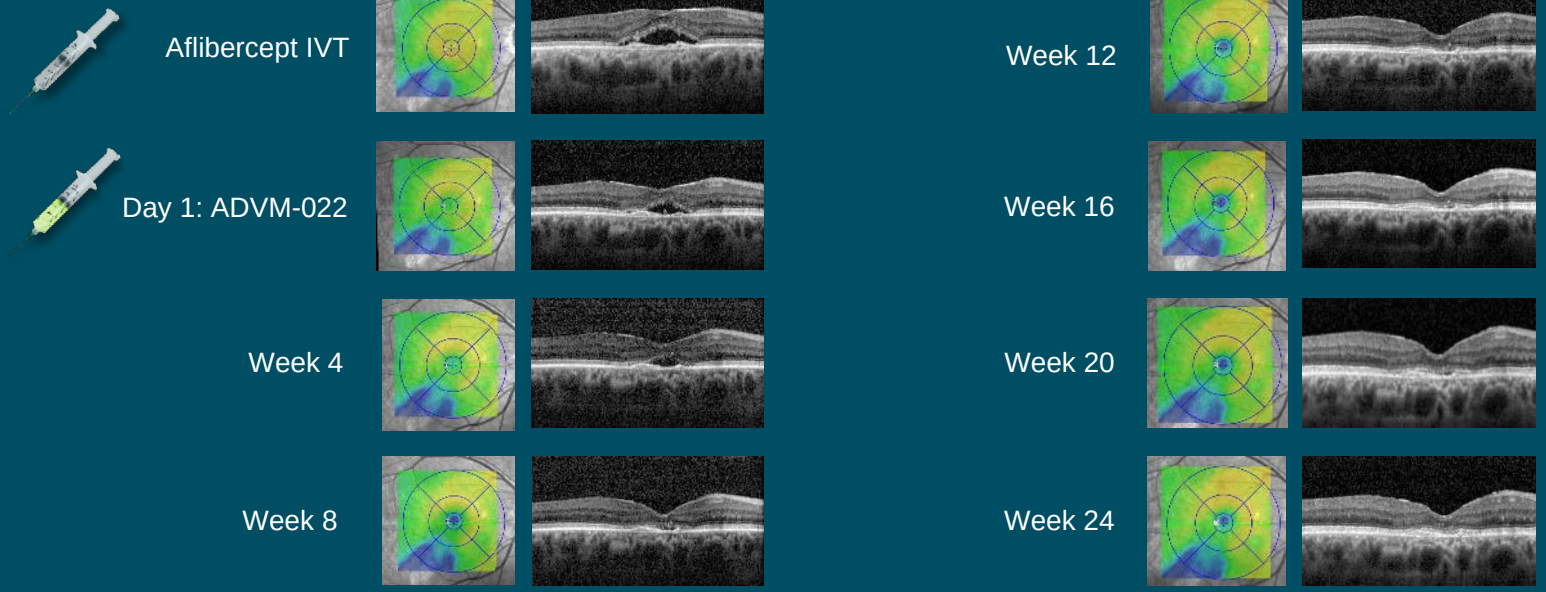
OCT scans and treatment intervals from most recent 5 anti-VEGF injections visits prior to OPTIC

OCTs graded by independent central reading center



IVT, intravitreal therapy; OCT, optical coherence tomography
VEGF, vascular endothelial growth factor

After ADMV-022, Fluid Resolved on OCT, No Requirements for Rescue Anti-VEGF Injections



No rescue injection received over 24 weeks

IVT, intravitreal therapy; OCT, optical coherence tomography
VEGF, vascular endothelial growth factor

Cohort 1 Update: Additional follow-up data

Outcomes Through October 1, 2019	Value
Median follow-up, weeks	34.0
Follow-up (min, max), weeks	28, 44
Grade 3* adverse events, n	0
Serious adverse events, n	0
Dose-limiting toxicities, n	0
Mean BCVA change from baseline, ETDRS letters	–1.5
BCVA change from baseline (min, max), ETDRS letters	–9, +5
Total number of rescue injections, n	0

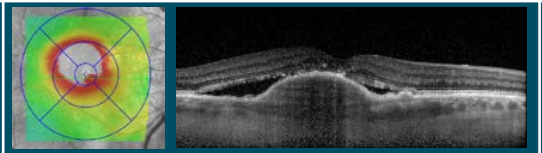
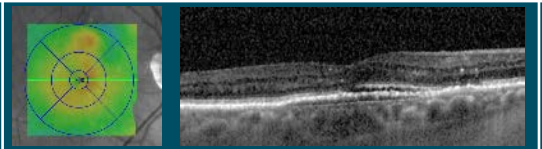
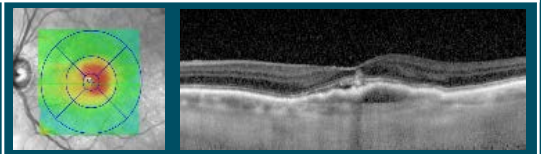
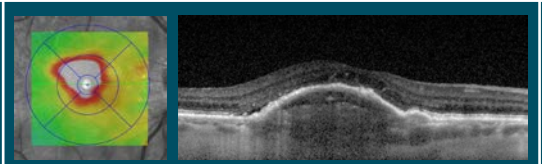
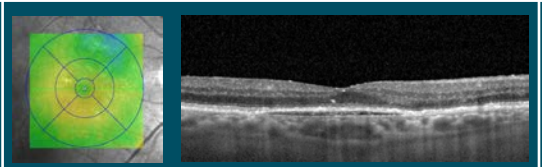
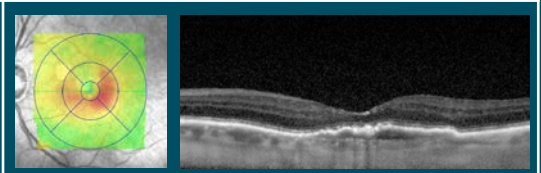
No new safety concerns identified, BCVA maintained, no rescue injections required

*Severe or medically significant per CTCAE v5.0, General Guidelines

BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study

Anatomic Improvements and BCVA Maintained

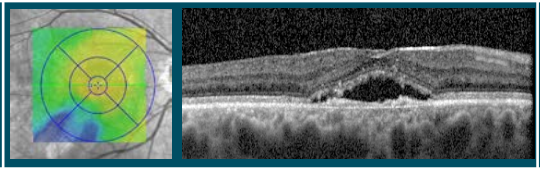
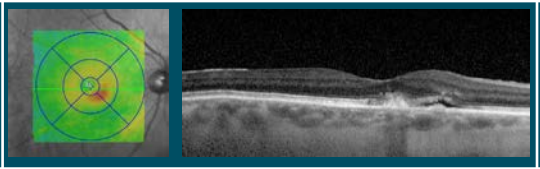
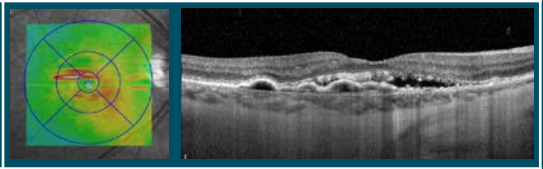
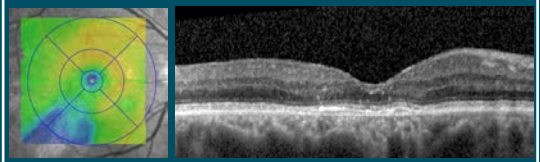
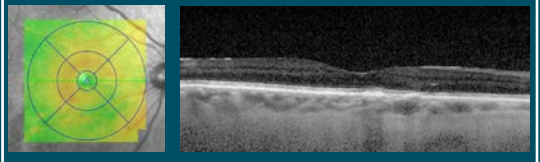
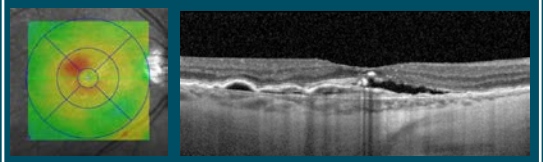
Additional Follow-up Beyond 24 Weeks Through October 1, 2019

	Patient 1: 44 Weeks Post-ADVM-022	Patient 2: 40 Weeks Post-ADVM-022	Patient 3: 36 Weeks Post-ADVM-022
Baseline OCT			
Latest OCT			
BCVA Change from Baseline, ETDRS letters	+3	–9	–6
IVT in 8 months Prior to OPTIC, n	5	6	6
Rescue IVT in OPTIC, n	0	0	0

BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study
IVT, intravitreal therapy; OCT, optical coherence tomography

Anatomic Improvements and BCVA Maintained

Additional Follow-up Beyond 24 Weeks Through October 1, 2019

	Patient 4: 32 Weeks Post-ADVM-022	Patient 5: 28 Weeks Post-ADVM-022	Patient 6: 28 Weeks Post-ADVM-022
Baseline OCT			
Latest OCT			
BCVA Change from Baseline, ETDRS letters	+5	+1	–3
IVT in 8 months Prior to OPTIC, n	6	6	8
Rescue IVT in OPTIC, n	0	0	0

BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study
IVT, intravitreal therapy; OCT, optical coherence tomography

OPTIC Cohort 1 Conclusions

Through Latest Follow-up Visit (Median of 34 Weeks)

- ADVM-022 was safe and well tolerated
- Inflammation generally mild and manageable with steroid eye drops
- Consistent and sustained anatomical improvements on OCT
- Patients maintained vision
- Zero rescue injections required for any subject

ADVM-022 offers transformative potential to greatly reduce treatment burden and improve retinal anatomy with a single intravitreal injection in nAMD

nAMD, neovascular age-related macular degeneration; OCT, optical coherence tomography

ADVM-022 Outlook

- OPTIC (nAMD)
  - Cohort 2 completed enrollment
  - Cohort 3 enrollment open
    - ADVM-022 ($2x10^{11}$vg/eye) with steroid eye drops prophylaxis
  - Cohort 4 enrollment Q1 2020
    - ADVM-022 ($6x10^{11}$vg/eye) with steroid eye drops prophylaxis
  - Cohort 1 52-week data H1 2020
  - Cohort 2 24-week data H1 2020

- IND in diabetic retinopathy planned for submission H1 2020

H, half of year; IND, investigational new drug program; nAMD, neovascular age-related macular degeneration

ADVM-022 Acknowledgments

Investigators, study teams and participants

- David Boyer MD, Beverly Hills, CA
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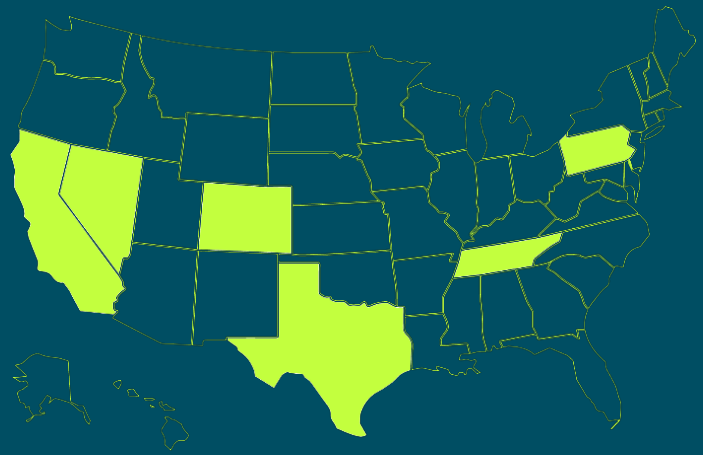
- Dante Pieramici MD, Bakersfield, CA
- Carl Regillo MD, Philadelphia, PA
- Charles Wykoff MD, PhD, Woodlands, TX



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