



H.C. Wainwright Virtual Ophthalmology Day: Discussion on Recent 4D-150 Data and Upcoming 4D-150 Development Day

August 15, 2024

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Leading Clinical Stage Next Generation AAV Company

Mission: Become a Fully Integrated Biopharma Company Boldly Innovating to Unlock the Full Potential of Genetic Medicines for Millions of Patients

<p>PLATFORM</p>	<p>DIRECTED EVOLUTION Nobel Prize-Winning Technology</p>	<p>~1 BILLION Proprietary Capsid Sequences</p>	<p>MODULAR Customized & Evolved Vectors + Optimized Payloads</p>
<p>PRODUCT ENGINE</p>	<p>CLINICAL PROOF-OF-CONCEPT</p>	<p>4 THERAPEUTIC AREAS</p> 	<p>3 ROUTES OF ADMIN Intravitreal Aerosol Intravenous</p>
<p>PIPELINE</p>		<p>5 CLINICAL CANDIDATES 7 PATIENT POPULATIONS 4 Large Market Opportunities 2 IND CANDIDATES</p>	<p>FDA RMAT & EMA PRIME DESIGNATION 4D-I50 for Wet AMD</p>
<p>CAPABILITIES</p>	<p>IN-HOUSE GMP Manufacturing</p>	<p>NEXT GENERATION Vector Discovery & Payload Design</p>	<p>STRONG BALANCE SHEET \$578M cash as of June 30, 2024 Runway through H1 2027</p>

Recent Announcements & Highlights in Ophthalmology

- **Strengthened ophthalmology senior leadership team & assembled World Class Ophthalmology Advisory Board**
- 4D-150 continues to be **safe and well tolerated in 139 patients** (wet AMD and DME)
- **Strong clinical activity for 4D-150** demonstrated in **Broad wet AMD Population (includes patients representative of the planned Phase 3 study population)**
- **4D-150 Development Day** (September, date ~EURETINA TBD) :
 - 1 Interim data (**longest available follow-up, up to 2.5 years**) from PRISM Phase 1/2 in wet AMD, that will be presented at 24th EURETINA Congress on **September 19**
 - 2 Final Phase 3 design for **Global Registration in wet AMD**

Data cutoff: June 24, 2024

Senior Leadership Team: Added 65+ Years of Large Market Ophthalmology Experience with 4 Approvals of Major Products



Dhaval Desai, PharmD
Chief Development Officer
20+ years

Late-stage Product Development, Medical Affairs, Scientific Communications, Regulatory and Quality operations



Christopher Simms
Chief Commercial Officer
25+ years

Pre-commercial and Commercial organizations, pre-launch preparations and development



Carlos Quezada-Ruiz, M.D., FASRS
SVP, Therapeutic Area Head, Ophthalmology
20+ years

Lead Ophthalmology franchise and oversee early- and late-stage clinical development



4D-I50 has Potential Multi-billion Annual Revenue Opportunity for the Broad Wet AMD Patient Population in the U.S., if Approved

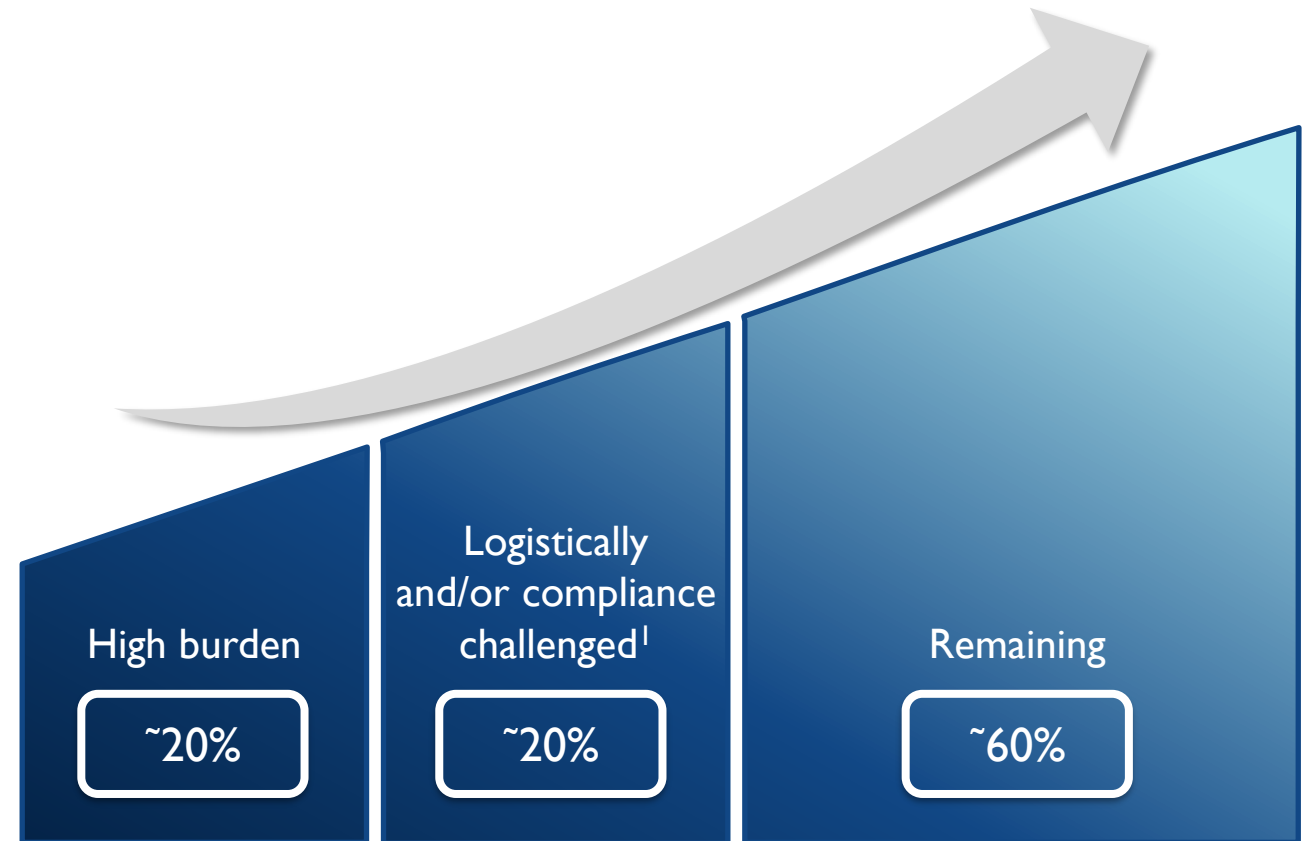
Wet AMD U.S. Opportunity

Estimated in 2035



1% share
translates to **\$300M to \$500M**
(assumes 3-5 years of benefit)

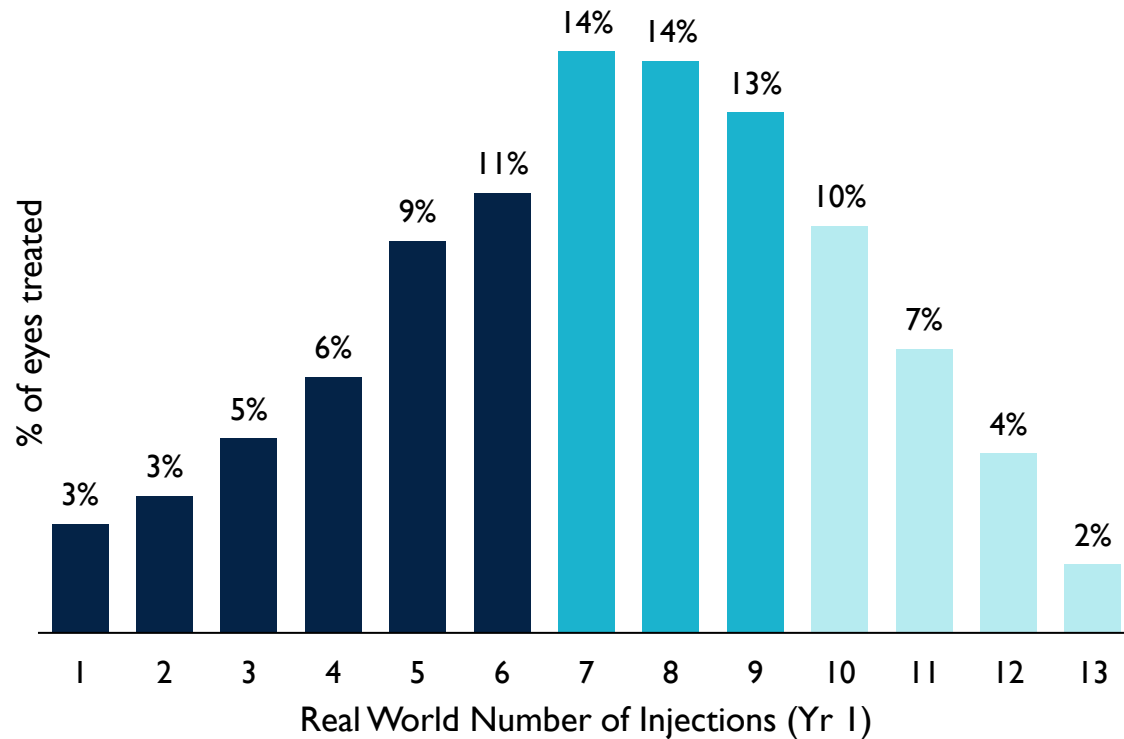
4D-I50 Being Developed to Treat All Wet AMD Patients



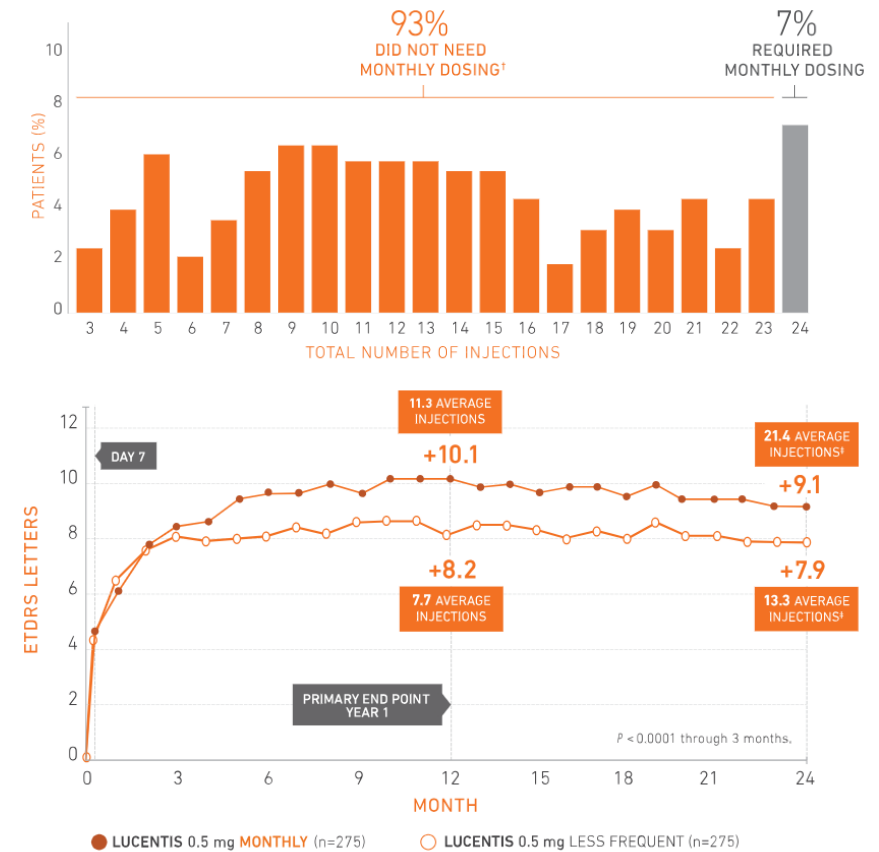
*Company estimates. 1. Patients receiving less than or equal to 4 injections from Ciulla et al: Ophthalmol Retina. 2020 Jan;4(1):19-30.

Wet AMD Patients is a Heterogenous Patient Population with Varying Anti-VEGF Needs

Real World Injection Frequency¹



Lucentis HARBOR Study (lucentis.com)



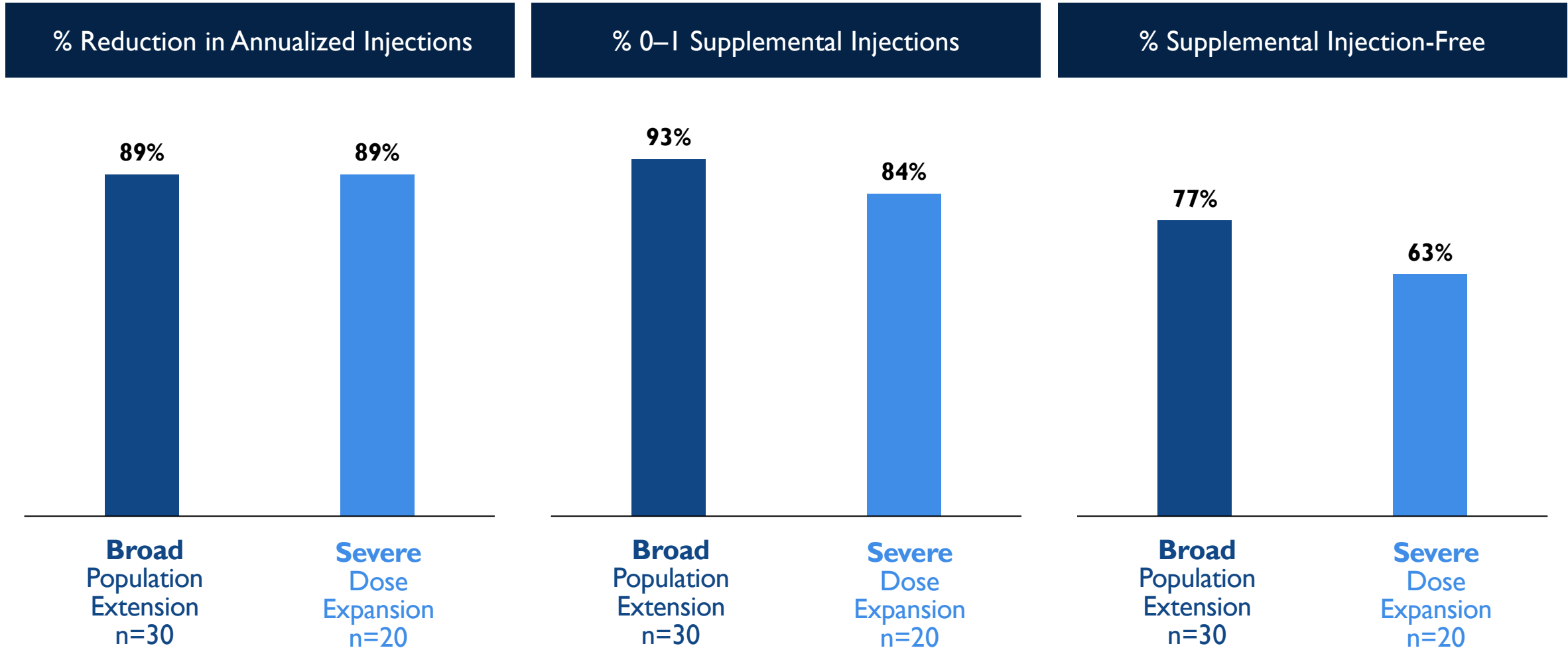
1. Adapted from Ciulla et al: Ophthalmol Retina. 2020 Jan;4(1):19-30.; n = 49,485 eye.

Population Extension Enrolled Broad Wet AMD Population with Earlier Disease & Lower Prior Anti-VEGF Exposure

	Population Extension ("Broad") 3E10 vg/eye (N=30)	Dose Expansion ("Severe") 3E10 vg/eye (N=21)
Age, years (Mean ±SD)	77 ±7.7	77 ±8.0
BCVA, ETDRS letters (Mean ±SD)	71 ±9.9	68 ±11.3
CST (central subfield thickness), μm (Mean ±SD)	336 ±135.0	429 ±89.3
Time since diagnosis, years (Mean ±SD)	1.8 ±3.5	4.0 ±3.0
N= (%) Recently Diagnosed (<u>1-2</u> prior injections)	12 (40%)	0 (0%)
Actual anti-VEGF injections in prior 12 months* (Mean ±SD)	4.4 ±2.0	9.9 ±2.4
Mean <i>annualized</i> injection rate, prior 12 months*	8.3	10.0

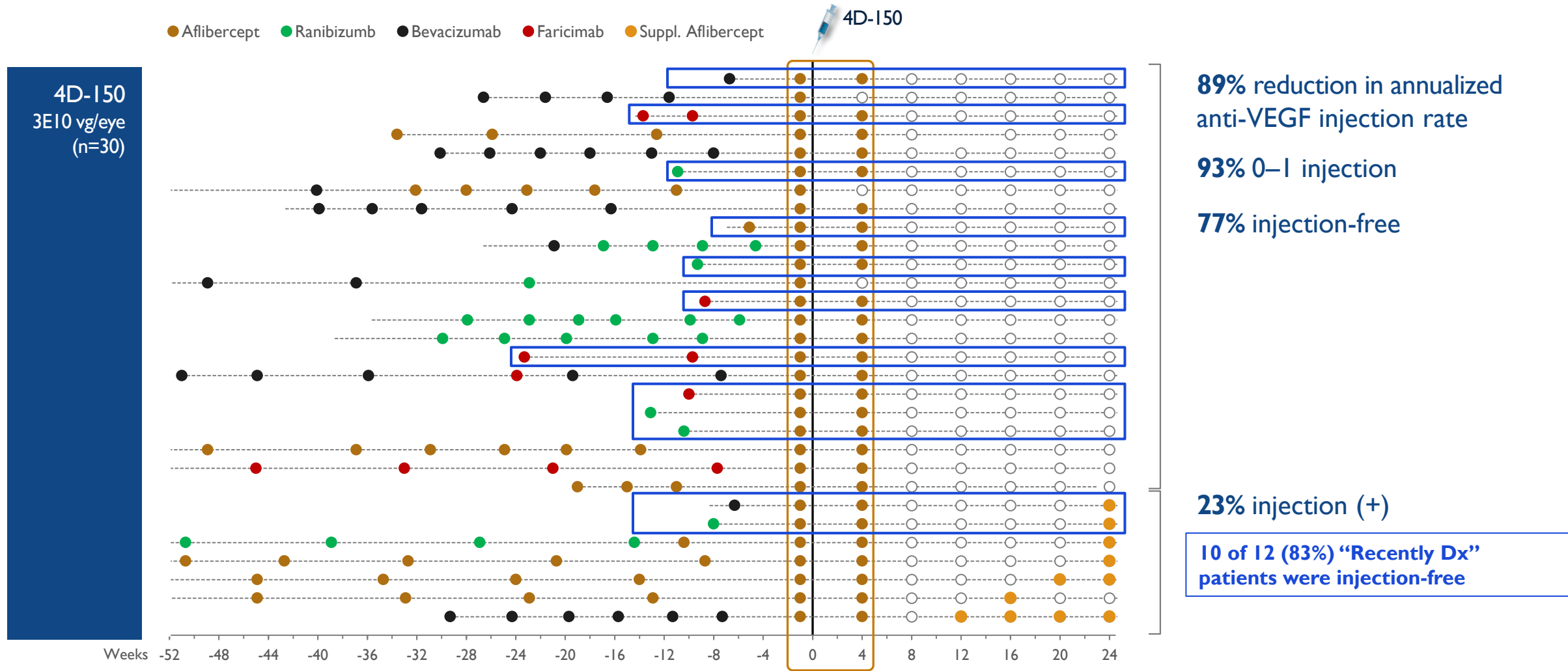
*Includes Day -7 aflibercept injection. BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; SD, standard deviation; VEGF, vascular endothelial growth factor.

Robust & Consistent Reduction in Treatment Burden Through 24 Weeks Across **All Wet AMD Populations** Studied at the 3E10 vg/eye Dose



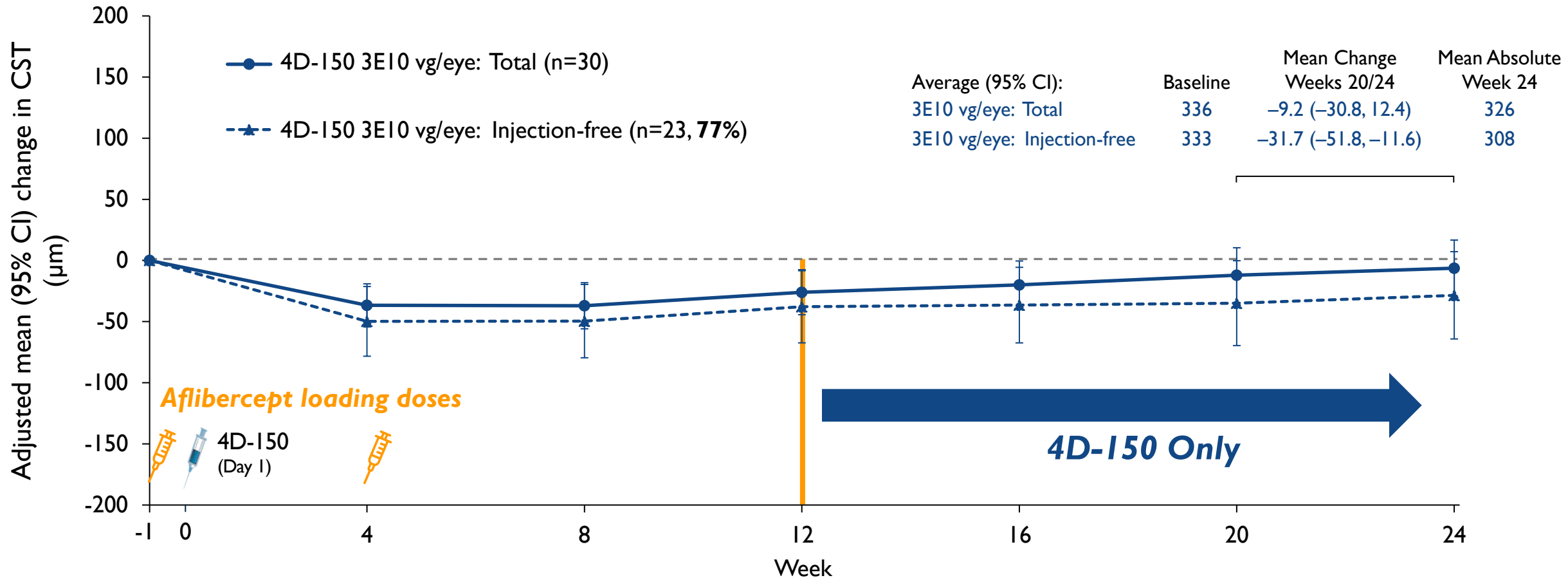
Data cutoff dates: Dose Expansion, January 19, 2024; Population Extension, June 24, 2024.

Broad Disease Activity Patients: Robust Anti-VEGF Treatment Burden Reduction with 4D-I50



Data cutoff date, June 24, 2024. *Scheduled on-study aflibercept injection administered at Weeks -1 and 4; post-4D-I50 annualized anti-VEGF injection rate calculated from Week 4 onward (time of last loading aflibercept dose)

Broad Disease Activity Patients: Sustained & Greater Anatomic Control Without Fluctuations with 4D-150



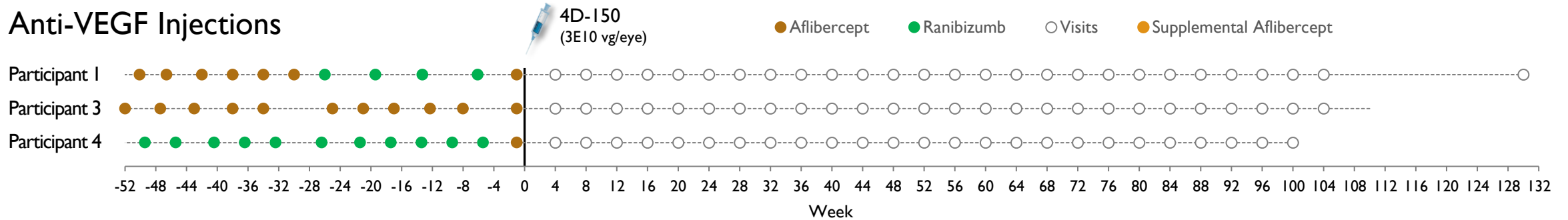
Data cutoff date, June 24, 2024.

Adjusted mean and 95% CI estimated from a mixed-effect model for repeated measures (MMRM) including observed data (weeks 4-24) without imputing missing values.

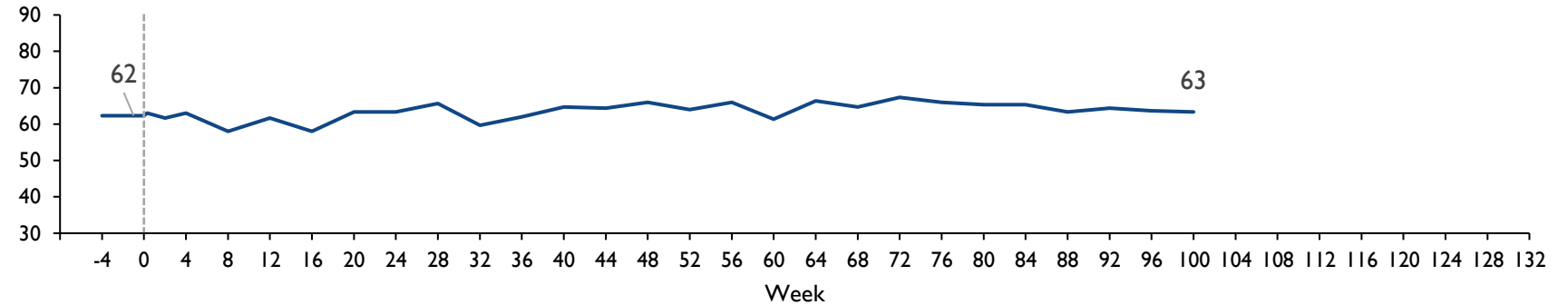
CI, confidence interval; CST, central subfield thickness.

3 Severe Patients from Phase I Treated with a Single Dose of 4D-150 Remain Injection-free Through ~2 to 2.5 Years with Strong Disease Control

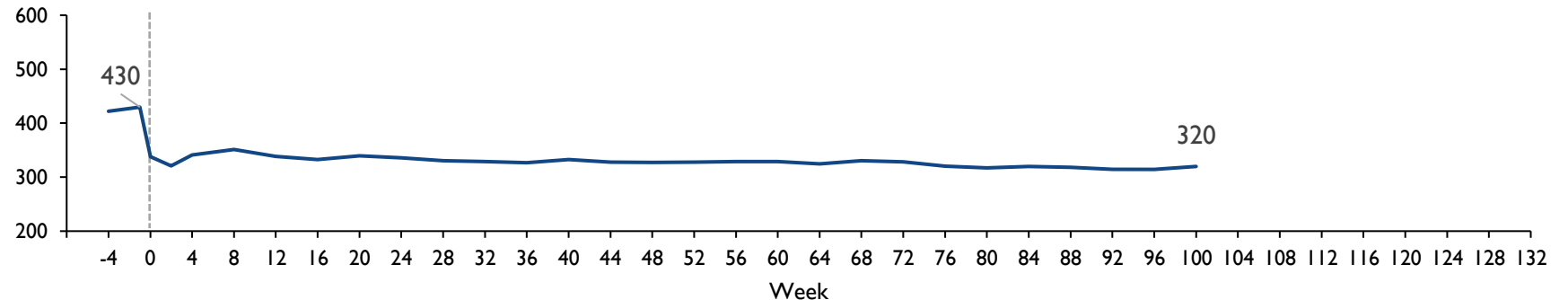
Anti-VEGF Injections



Mean BCVA (ETDRS letters)



Mean CST (μm)



Data cutoff: June 24, 2024.

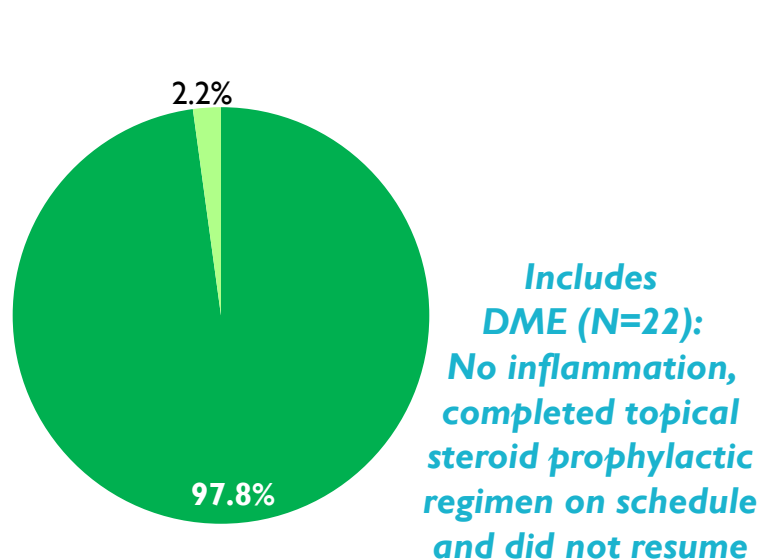
Baseline = Week -1. BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; CST, central subfield thickness.

4D-150 Continues to be Safe and Well Tolerated in Wet AMD & DME (N=139)

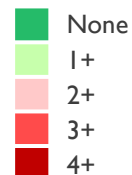
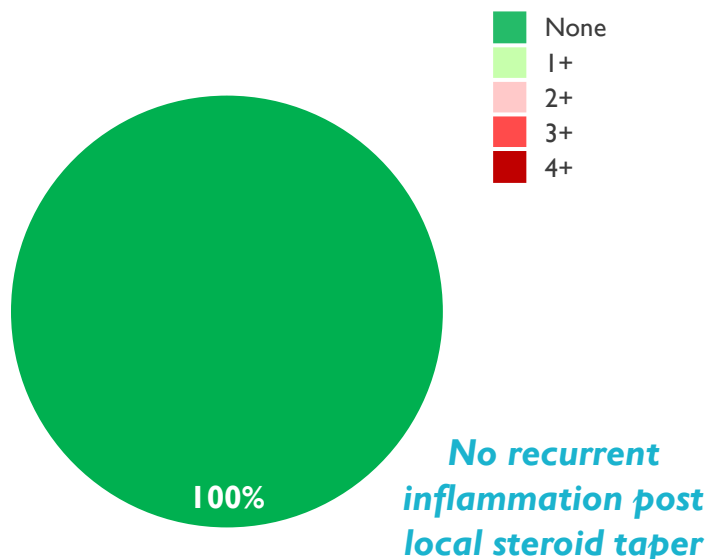
No Significant Inflammation in Patients Treated with Planned Phase 3 Dose & Durezol Regimen

Highest SUN/NEI Score Observed (4D-150-Related)*

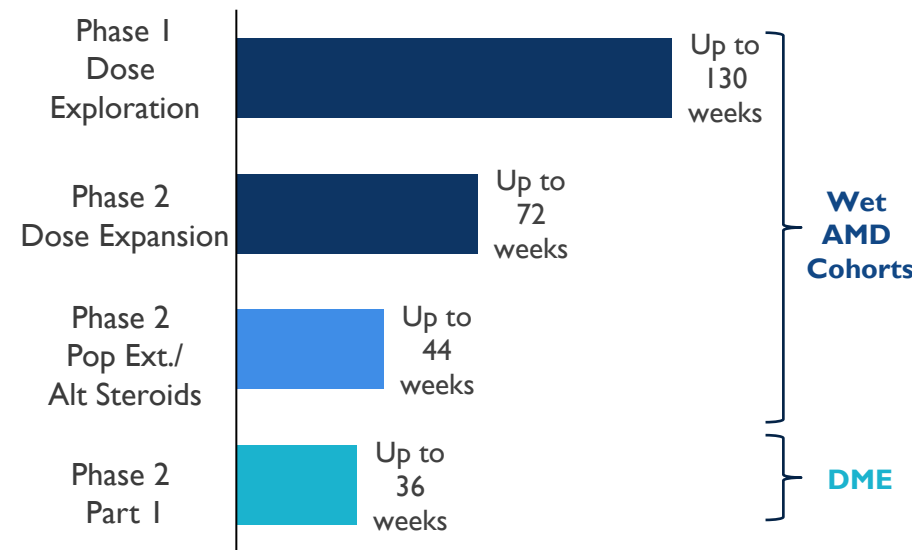
All Doses & Steroid Regimens Tested†
(5E9 to 3E10 vg/eye, N=139)



Planned Phase 3 Dose & Durezol Regimen
(3E10 vg/eye, N=51)



Range of Maximum Follow-up†
(5E9 to 3E10 vg/eye, N=139)



No 4D-150-related hypotony, endophthalmitis, vasculitis, choroidal effusions or retinal artery occlusions observed to date

Data cutoff date, June 24, 2024. Additional follow-up beyond data cutoff confirmed previously reported 2+ inflammation not related to 4D-150.

*Duration of follow up, ≤2.5 years. NEI, National Eye Institute; SUN, Standardization of Uveitis Nomenclature. †N=29 3E10 vg/eye patients received one of the following: (a) triamcinolone acetonide with prednisolone taper or (b) dexamethasone.

Key Highlights from 4D-I50 Interim Data Presented at To-Date

- 1 STRONG CLINICAL ACTIVITY DEMONSTRATED IN BROAD WET AMD DISEASE ACTIVITY POPULATION:**
Includes Patients Representative of the Planned Phase 3 Study Population
- 2 DEMONSTRATED DURABLE CLINICAL ACTIVITY UP TO 2.5 YEARS**
- 3 CONTINUES TO BE SAFE & WELL-TOLERATED (WET AMD & DME):**
IOI Profile Similar to Eylea: ~2% Mild, 0% Moderate
- 4 PROVIDES FURTHER SUPPORT FOR PLANNED WET AMD PHASE 3**

Data cutoff date, June 24, 2024. Additional follow-up beyond data cutoff confirmed previously reported 2+ inflammation not related to 4D-I50.

4D-150 Development Day / EURETINA Data Disclosure Expectations

Prior Efficacy Disclosures (Landmarks):

N=3 injection-free
2-2.5 Years

36-week



24-week



Up to 40 weeks



MAXIMUM FOLLOW-UP
as of
June 24, 2024
Data Cutoff
(ASRS)

Severe:
Phase I Dose
Exploration
& Phase 2 Dose
Expansion (N=66,
including control arm)

Broad:
Population Extension
(N=45)

**4D-150 Development Day /
EURETINA Disclosure**
(~September 19):





**ALL available
follow-up**
(“Waterfall vs. Landmark”)
with an August 2024 Cutoff

Key Data Analyses Expected with “Longest Available” Follow-up:

- **Safety & tolerability**
- **Δ in BCVA**
- **Δ in CST**
- **Anti-VEGF supplemental injections:**
 - Overall reduction in annualized injection rate
 - % receiving 0-1 injections
 - % injection-free

Data cutoff date, June 24, 2024

Rapidly Advancing Development in Large Market Ophthalmology

VECTOR DELIVERY	PRODUCT CANDIDATE	INDICATION	EPIDEMIOLOGY (PREVALENCE)	PHASE 1	PHASE 2	PHASE 3	MILESTONES
LARGE MARKET OPTHALMOLOGY RI00 Intravitreal 	4D-I50 Aflibercept + VEGF-C RNAi	Wet AMD	~3M U.S./EUMM				<ul style="list-style-type: none"> ✓ 24-week Ph 2 Dose Expansion (N=51) ✓ 24-week Ph 2 Pop. Extension (N=45) <ul style="list-style-type: none"> ▪ Sep 24 4D-I50 Development Day: Interim longest available follow up through up to 2.5 years from severe (Dose Exploration & Expansion) & broad (Pop. Extension) cohorts, final Ph 3 trial design update ▪ Feb 25 52-week Ph 2 update from both cohorts ▪ Q1:25 Initiate 1st Ph 3 study
		Diabetic Macular Edema	~5M U.S./EUMM				<ul style="list-style-type: none"> ▪ Q4:24 Initial interim data from Phase 2 Part 1 Dose Confirmation (N=22)
	4D-I75 Short Form Complement Factor H	Geographic Atrophy	~2.5M U.S./EUMM				<ul style="list-style-type: none"> ✓ IND Cleared June 2024 ▪ H2:24 Begin Phase I enrollment



THANK YOU

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