4DMT

Harnessing the Power of Directed Evolution for Targeted, Next-Generation Genetic Medicines

Corporate Presentation | January 2025

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This Presentation discusses our product candidates that are under preclinical study and in clinical trials, and which have not yet been approved for marketing by the U.S. Food and Drug Administration. No representation is made as to the safety or effectiveness of our product candidates for the therapeutic use for which they are being studied.

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Boldly Innovating to Unlock the Full Potential of Genetic Medicines for Millions of Patients

PROVEN Platform

DIRECTED EVOLUTION PLATFORM
Customized & Differentiated Clinical-Stage Vectors

MODULAR
Discovery and Product Development Platform

STRONG Clinical Data & Development Plan

4D-150
Robust Phase 1/2 data validates potential to be **multi-year backbone therapy** in wet AMD and DME

Potential best-in-class safety

Robust global pivotal development program in Wet AMD underway

Streamlined U.S. registration path in DME

4D-710
Promising Transduction & Early Clinical Signals

LATE-STAGE Capabilities

WORLD CLASS SENIOR RETINA TEAM
Six Approvals & Five Launches of Major Products

GMP MFG EXPERTISE
Hybrid & De-Risked

COMMERCIAL
Development Strategy for Transformational Products in Large Markets

$506M cash* as of December 31, 2024; Runway into 2028

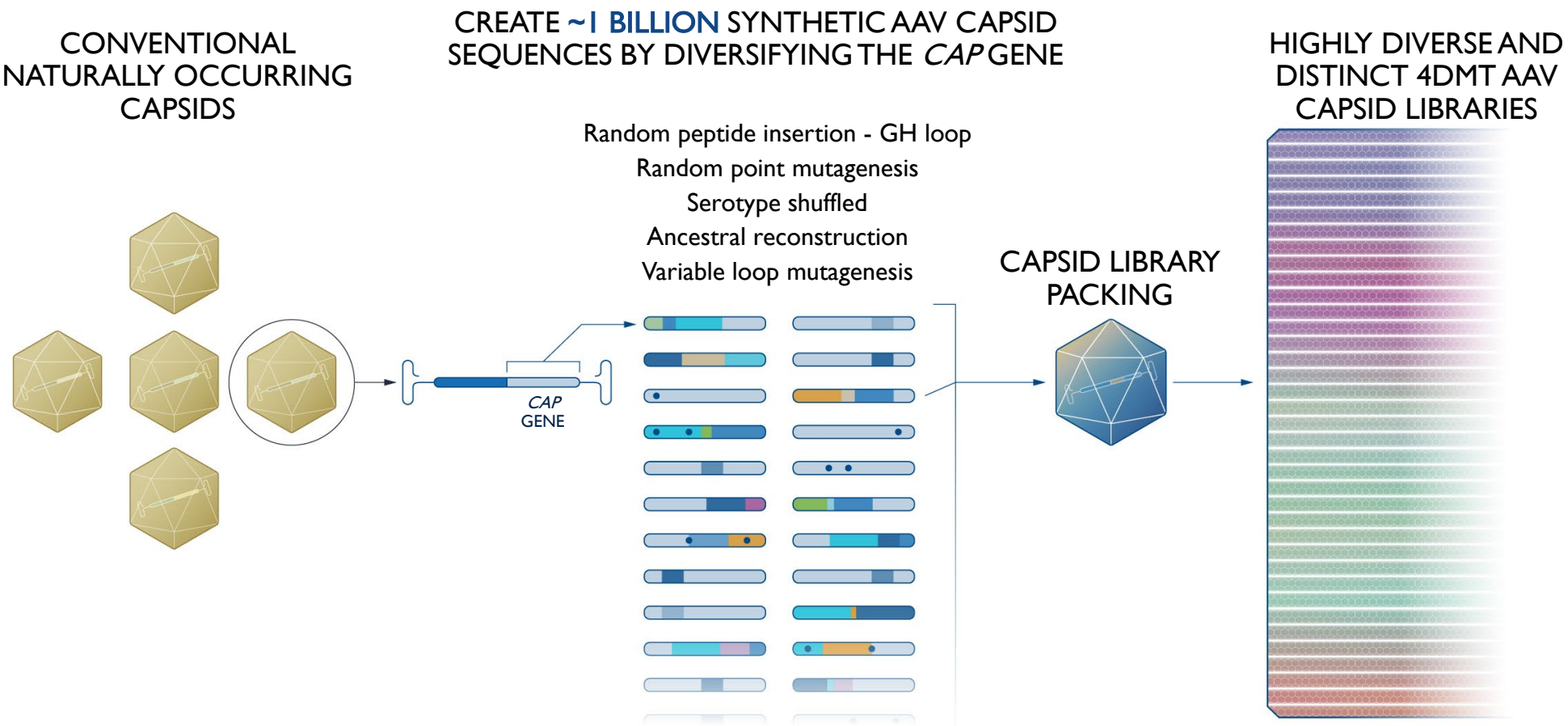
*Includes cash equivalents and marketable securities (unaudited)

4D-150 Designed to be **the First Widely Adopted Genetic Medicine** in a Large Market Disease (Wet AMD & Beyond)

Characteristics:	Barriers for Conventional Genetic Medicines	Target Profile of 4DMT Medicines
Diseases(s) Targeted	Rare diseases: Low Prevalence & Incidence	**Large market diseases:** **Sustainable** commercial markets
Route of Delivery & Safety Risk	Complex (Surgical, Systemic) Challenging safety management	**Simple** delivery and **best-in-class safety**
Pivotal Trial	Highly negotiated & Non-standard regulatory pathways	**Regulatory alignment** in major markets
Manufacturing	High doses & COGM	**Low** COGM
Commercial Potential	High payor barriers & Limited global potential	**Low** payor barriers & broad global potential

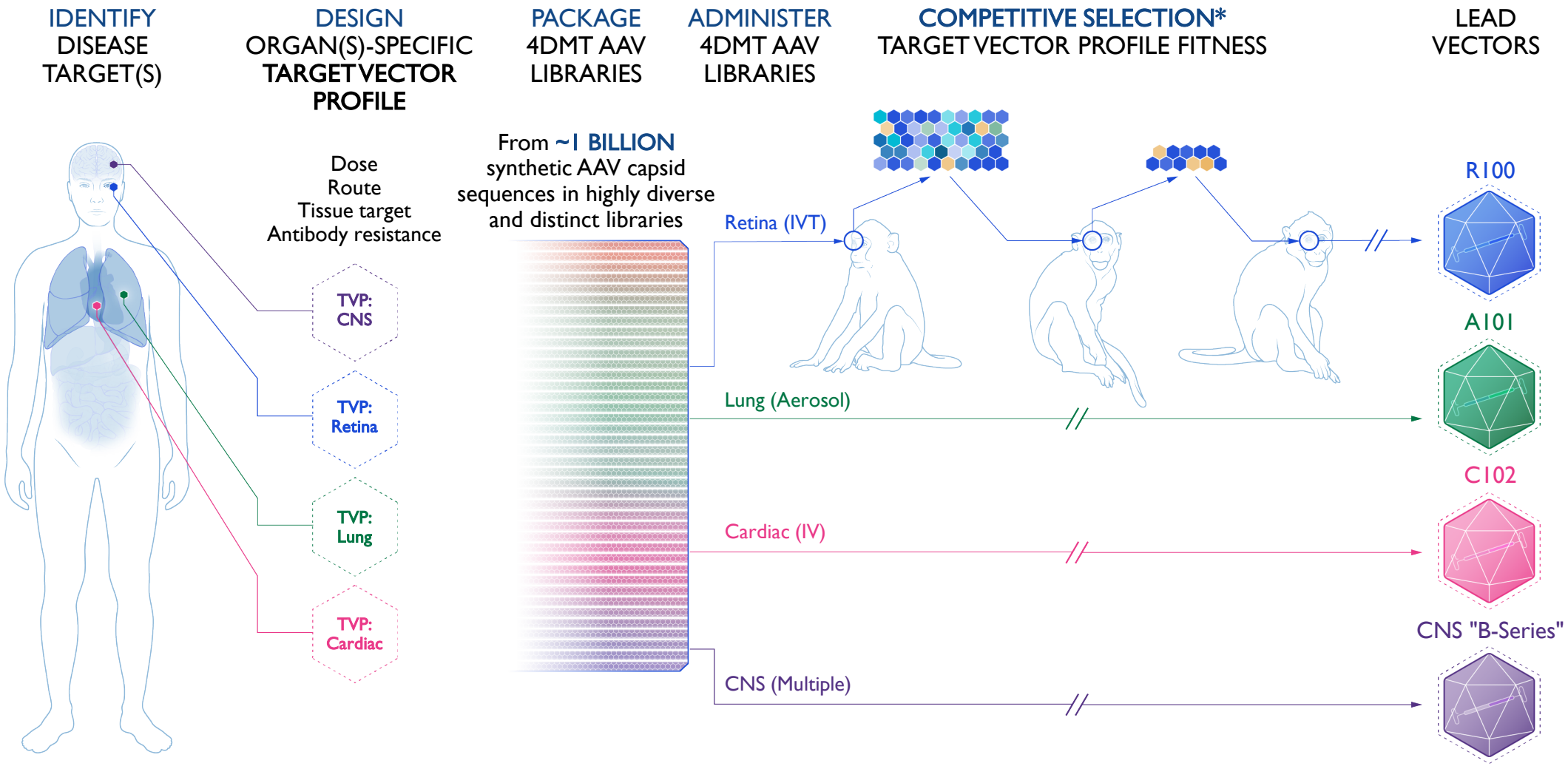
Platform Solution: ~1 Billion Synthetic Capsid Sequences

Step 1: Create Massive Diversity in Highly Diverse and Distinct Libraries



Platform Solution: Target Vector Profile Fitness Competition

Steps 2 & 3: Therapeutic Vector Evolution



*Capsid library placed under varying selective pressures // Actual number of selection rounds varies by target

Focused Pipeline on Large Market, High Unmet Need Indications

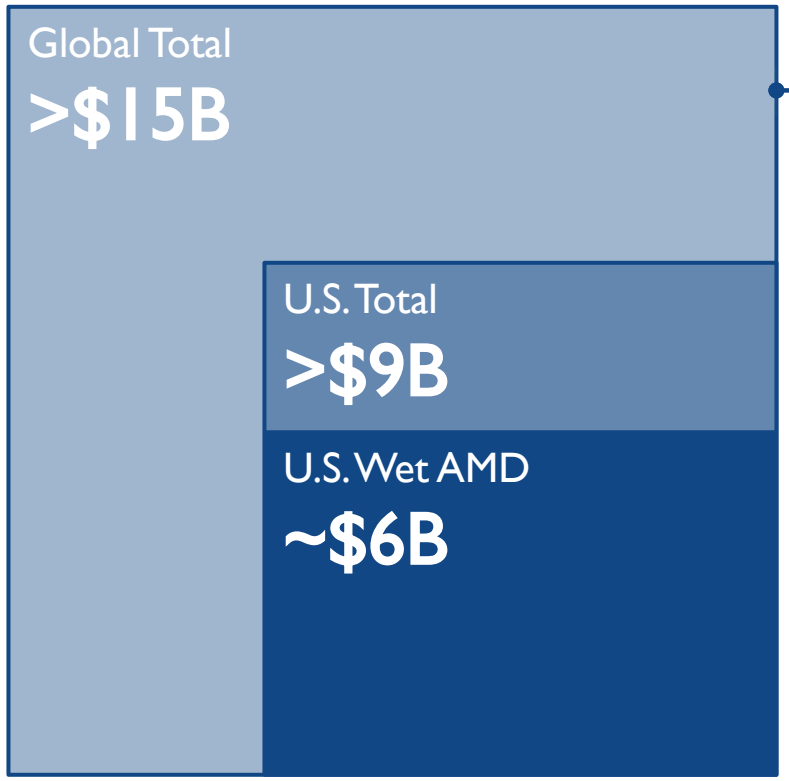
THERAPEUTIC AREA VECTOR ROUTE OF ADMIN	PRODUCT CANDIDATE	INDICATION	ESTIMATED PREVALENCE	PHASE 1	PHASE 2	PIVOTAL	STATUS
LARGE MARKET OPHTHALMOLOGY **R100** Intravitreal	4D-150	Wet AMD	*~3M U.S./EUMM*				▪ PRISM Ph2b 52-week interim data: **Feb 10, 2025** ▪ 4FRONT-1 Initiation: **Q1 2025** ▪ 4FRONT-2 Initiation: **Q3 2025** ▪ 4FRONT-1 & -2 topline data: **H2 2027**
		DME	*~5M U.S./EUMM*				Part 1: ✓ 32-week interim data ▪ 52-week interim data: **Mid-2025**
PULMONOLOGY **A101** Aerosol	4D-710	CF lung disease (mod. ineligible/ intolerant)	*~15K WW*				▪ Interim data: **Mid-2025**

- **Other Pipeline**: 4D-175 for Geographic Atrophy, 4D-725 for A1AT, 4D-310 for Fabry Disease
- **Partnership**: R100 out-licensed to Astellas for Rare IRDs

4D-150 in Wet Age-related Macular Degeneration (wet AMD)

Global Branded Anti-VEGF Market is ~$16B Today

2024 Branded Ocular Anti-VEGF Market*



Global Addressable Population Estimates (2024)

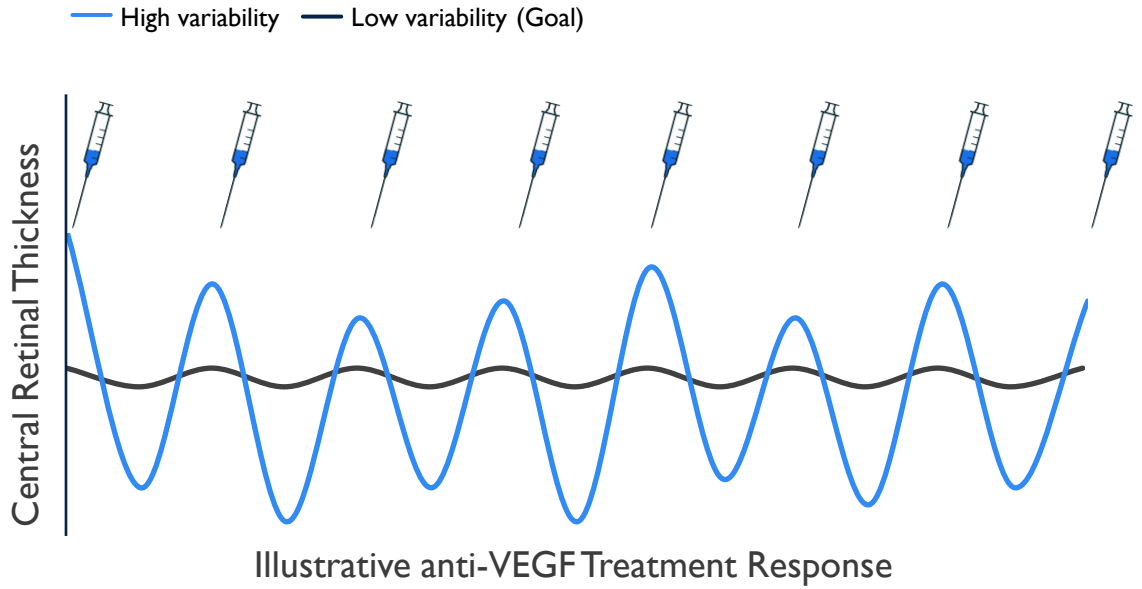
~25M Prevalence

~2.5% Pop. Growth (65+)

Sources: For anti-VEGF market - GlobalData, GrandView Research.
Annual incidence derived from analysis of key publications (Vanderbeek 2011, Rudnicka 2015, Klein 2011 and Fisher 2016), triangulated with IQVIA claims data; population growth calculated from U.S. census projections for ages 65+ in the U.S.
Prevalence sourced from Marketscope Retina Market Report 2023; *Forecast for 2024.

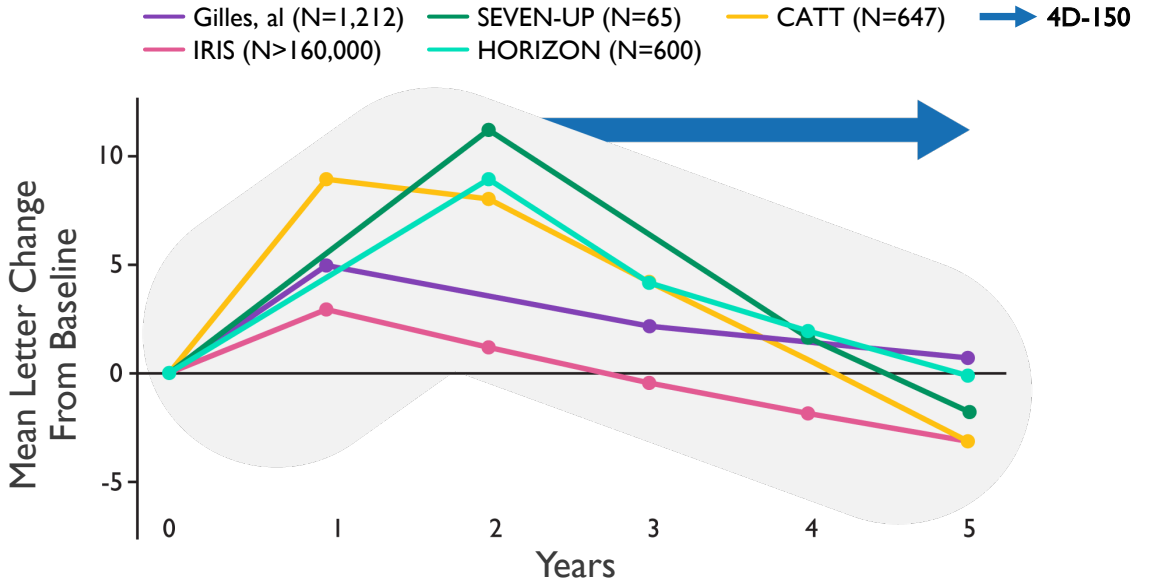
Unmet Clinical Need: Bolus Treatments, Fluctuating Disease Control Results in Loss of Vision Gains

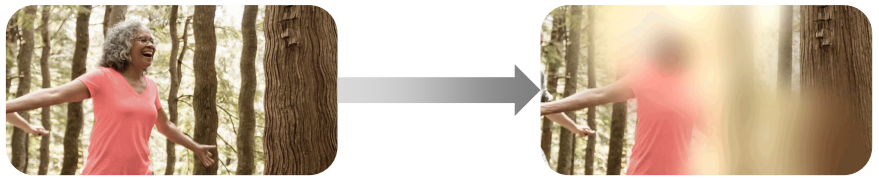
Chronic Bolus Therapy Leads to Variability in CST



Higher CRT variability during the first year of treatment is associated with greater vision loss[1] & fibrosis[2]

Visual Acuity



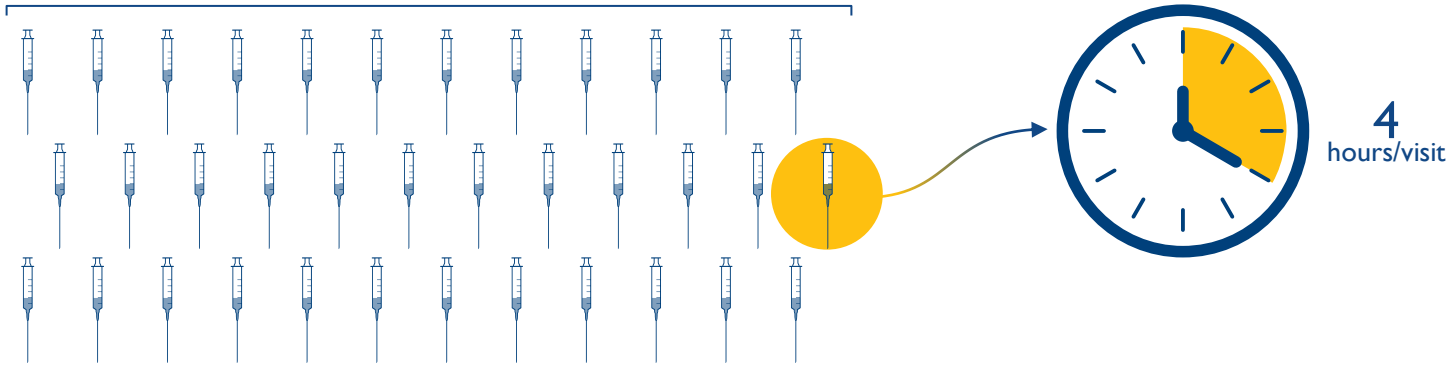


[1]Guo et al. *Ophthal Res* 2023; 66:406-12. [2]Evans et al. *JAMA Ophtalmol* 2020;138:1043-51. High variability: coefficient ≥20% in first year. Overall visual preservation rate: time from first injection to legal blindness (≤35 ETDRS letters). CRT, central retinal thickness.
Abbreviations: BCVA, best corrected visual acuity; BL, baseline; CRT, central retinal thickness; CST, central subfield thickness; SoC, standard of care; VEGF, vascular endothelial growth factor; Y, year.

Patient Need: Burden & Lifestyle Disruption Extends Beyond the Injection

Standard of Care Bolus Therapy: High burden on patients and caregivers

Injection regimen over 5 years[1]



4 hours/visit

Current & future therapies

AVASTIN bevacizumab

LUCENTIS RANIBIZUMAB INJECTION

EYLEA (aflibercept) Injection For Intravitreal Injection

VABYSMO faricimab-svoa injection 6 mg

EYLEA HD (aflibercept) Injection 8 mg

Byooviz ranibizumab-nuna

CIMERLI (ranibizumab-eqrn) injection

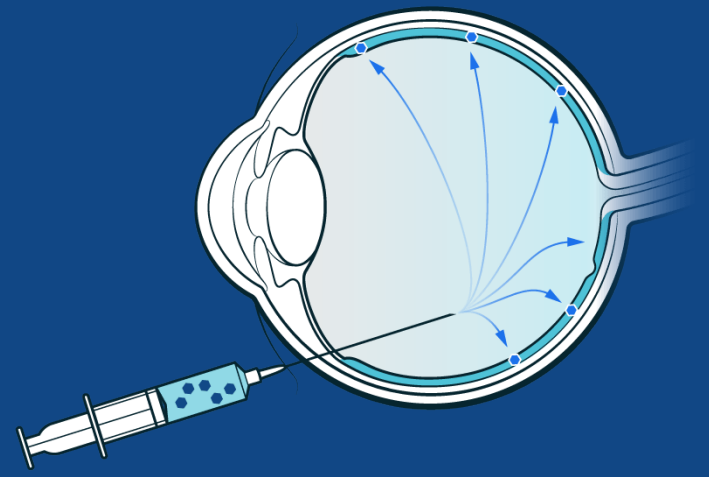
PAVBLU (aflibercept-ayyh) Injection 2mg

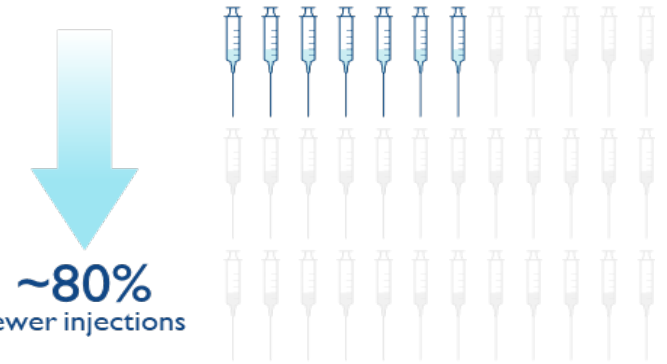
TKI Inserts

Burden of injections

- Caregiver commitment
- Missed life events
- Conflict with care for comorbidities
- Needle anxiety

New Paradigm: 4D-150





~80% fewer injections

1. Ciulla, et al, 2022. *Ophthalmology. Retina,* 6(9), 796–806.

Ideal Therapy to Address Key Unmet Needs

1 Favorable Safety Profile

Comparable
to approved anti-VEGF agents

LUCENTIS® RANIBIZUMAB INJECTION

EYLEA® (aflibercept) Injection For Intravitreal Injection

EYLEA® HD (aflibercept) Injection 8 mg

VABYSMO™ faricimab-svoa injection 6 mg

2 Maximize Visual Outcomes as a Potential Backbone Therapy

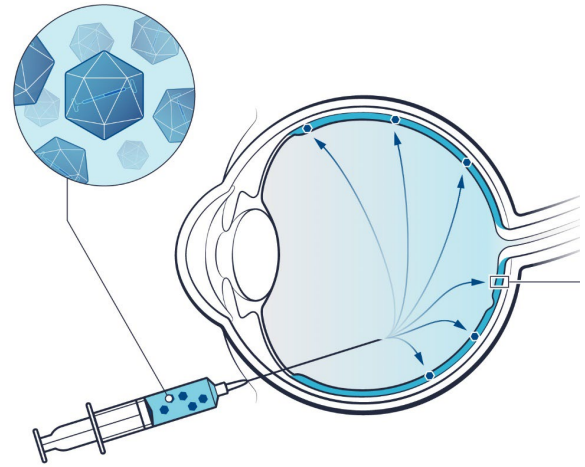
Robust reduction of overall treatment burden

Long-term durability

Potential for
extended vision preservation

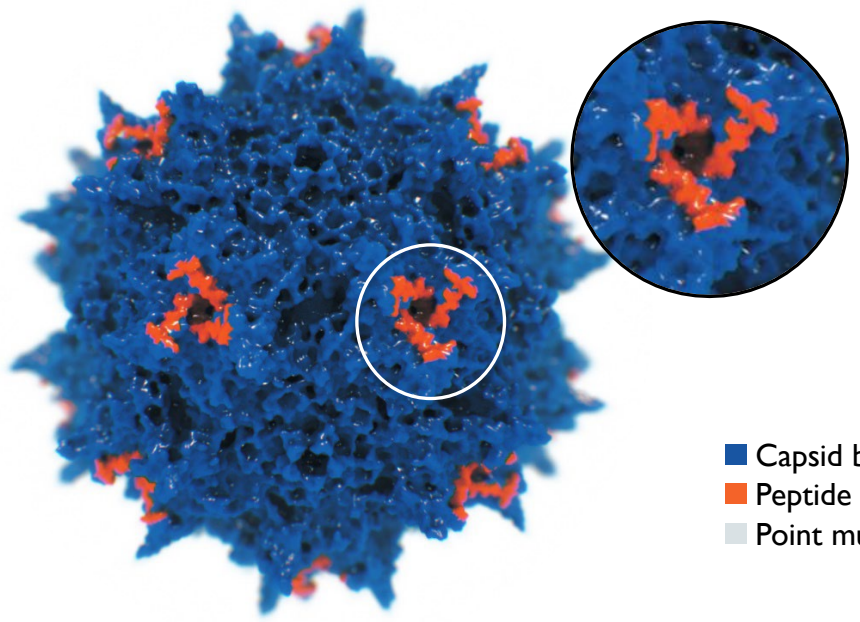
3 Route of Administration

Routine
intravitreal injection



4D-150 Designed for Sustained Intraretinal Expression of Anti-VEGF & Blockade of VEGF-C Production to Address Key Unmet Needs

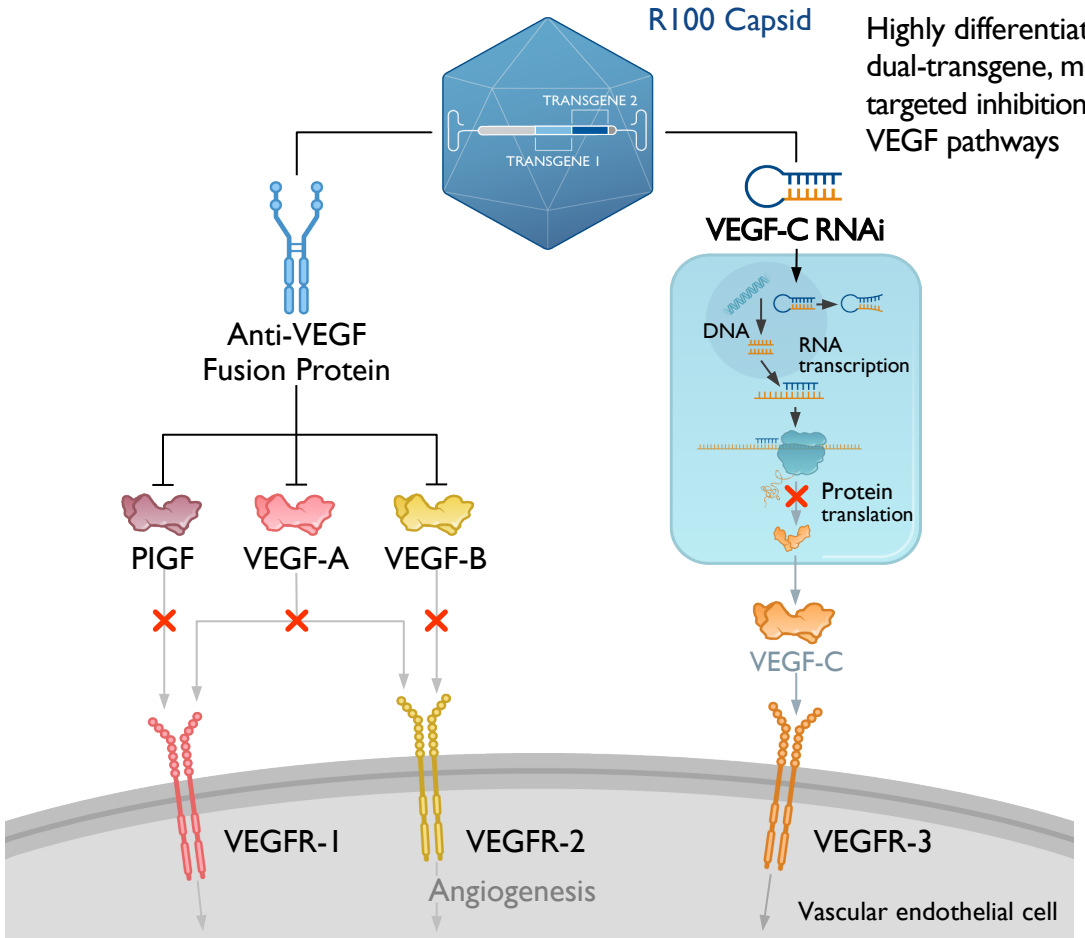
R100 Capsid



- Capsid base
- Peptide insertions
- Point mutations (internal)

- ✓ Minimal inflammation potential based on clinical data to date
- ✓ Robust delivery to multiple retinal layers
- ✓ Durable expression of transgenes

4D-150



Abbreviations: ILM, inner limiting membrane; NHP, nonhuman primate; RPE, retinal pigment epithelium.

Key 4D-150 Takeaways in Wet AMD

1. **Robust & Durable Clinical Activity:** Across all populations studied, including recently diagnosed patients

2. **Tolerability:** Well-tolerated with profile comparable to approved anti-VEGF agents

3. **4FRONT Phase 3 Design:** Maximizes probabilities of clinical, regulatory & commercial success

Data cutoff (clinical activity data), September 3, 2024.
Data cutoff (safety data), August 23, 2024.

PRISM Population Compared to Recent Phase 3 IVT Wet AMD Studies

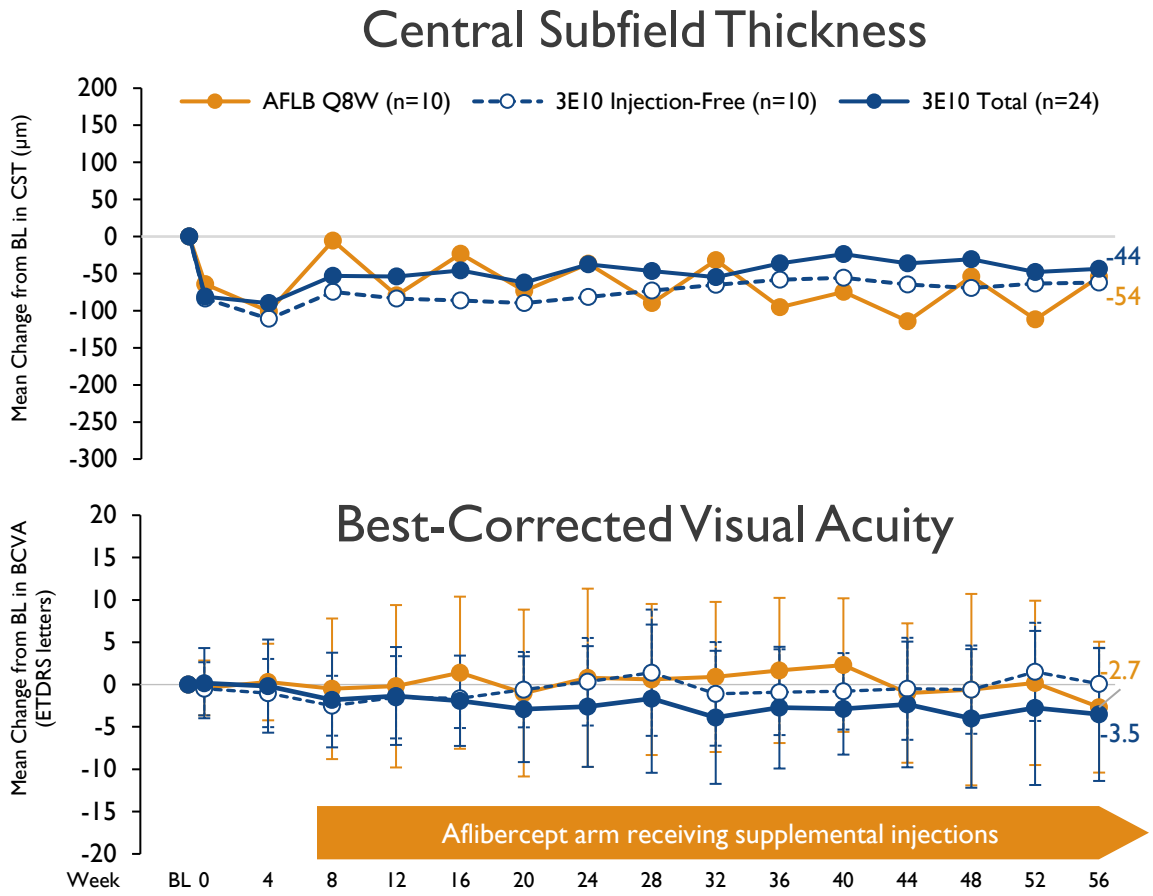
Asset	Study	Population	Mean time since Dx	Mean CST	Mean number of injections in previous year	Number of Loading Doses
EYLEA	VIEW1/2	**Treatment Naïve**	NA	313-342 µm	0	3
BEOVU	HAWK/HARRIER	**Treatment Naïve**	NA	360-370 µm	0	3
VABYSMO	TENAYA/LUCERNE	**Treatment Naïve**	67-74% within 1 month	350-360 µm	0	4
EYLEA HD	PULSAR	**Treatment Naïve**	NA	370 µm	0	3
SUSVIMO	Archway	**Previously Treated**	5.6 months	177 µm (CPT)	5	0*
4D-150 Ph1/2a (3E10)	**PRISM**	**Previously Treated**	**3.7 years**	**425 µm**	**10.2**	**1**
4D-150 Ph1/2a (AFLB)	**PRISM**	**Previously Treated**	**2.1 years**	**419 µm**	**9.3**	**1**
4D-150 Ph2b (3E10)	**PRISM**	**Previously Treated**	**1.8 years**	**336 µm**	**4.4**	**2**

1. Heier JS et al. *Ophthalmol* 2012; 119(12):2537-48 (VIEW 1 & 2) 2. Dugel PU et al. *Ophthalmol* 2020; 127:72-84 (HAWK & HARRIER) 3. Khanani A et al. *Ophthalmol* 2024; 131(8):914-26 (TENAYA & LUCERNE) 4. Lanzetta P et al. *Lancet* 2024; 403:1141–52 (PULSAR) 5. Holekamp NM et al. *Ophthalmol* 2022; 129(3):295-307 (ARCHWAY)

4D-150 vs. Aflibercept in Severe Patients (Phase 1/2a)

Visual Acuity & Anatomy Comparable to Q8W AFLB 2mg with Robust Reduction in Treatment Burden

Anatomy & Visual Acuity 4D-150 vs. Aflibercept

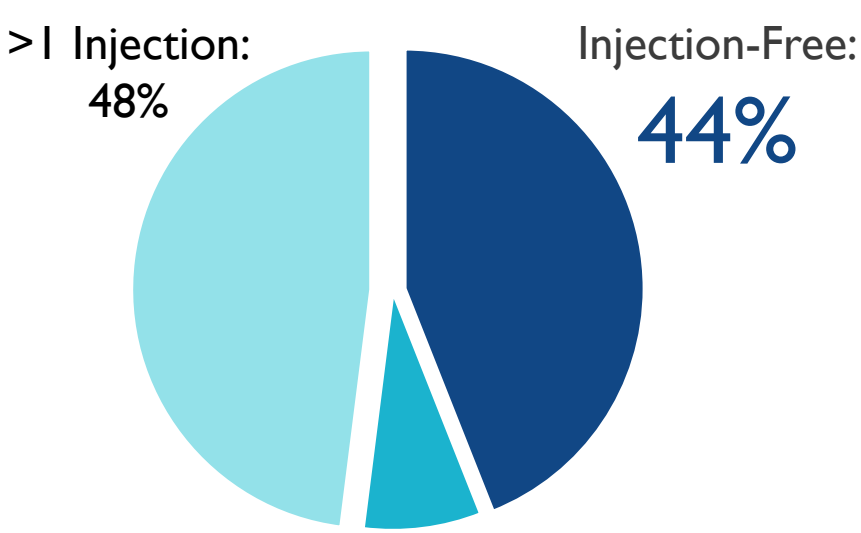


Treatment Burden Post-4D-150 Through Year 1 (KM Est.)

4D-150
3E10 vg/eye

~10 injections in 12 mos. prior to study entry

>400 µm mean CST



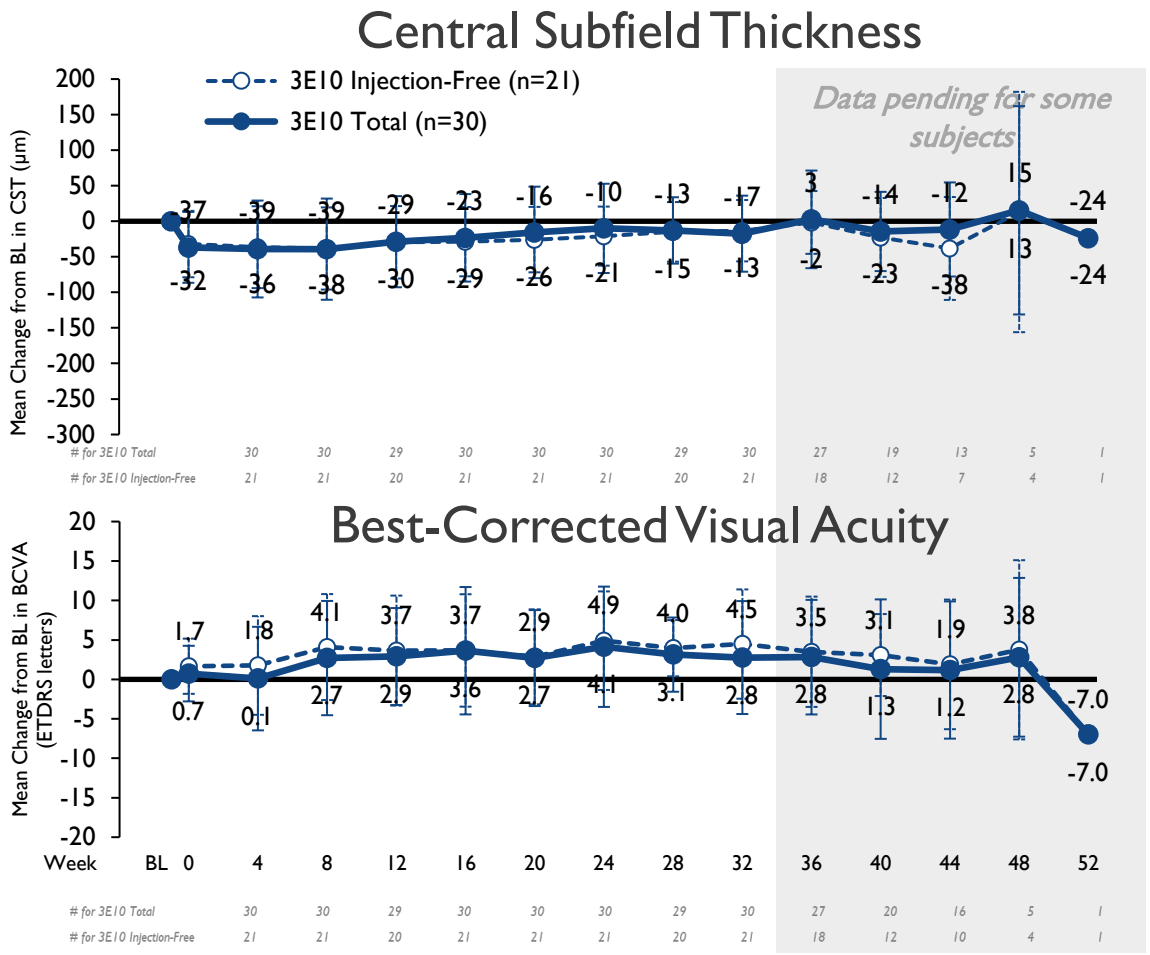
Overall Treatment Burden Reduction:

83%

4D-150 in Broad Population (Phase 2b)

Visual Acuity & Anatomy Stable with Robust Reduction in Treatment Burden

Anatomy & Visual Acuity 4D-150

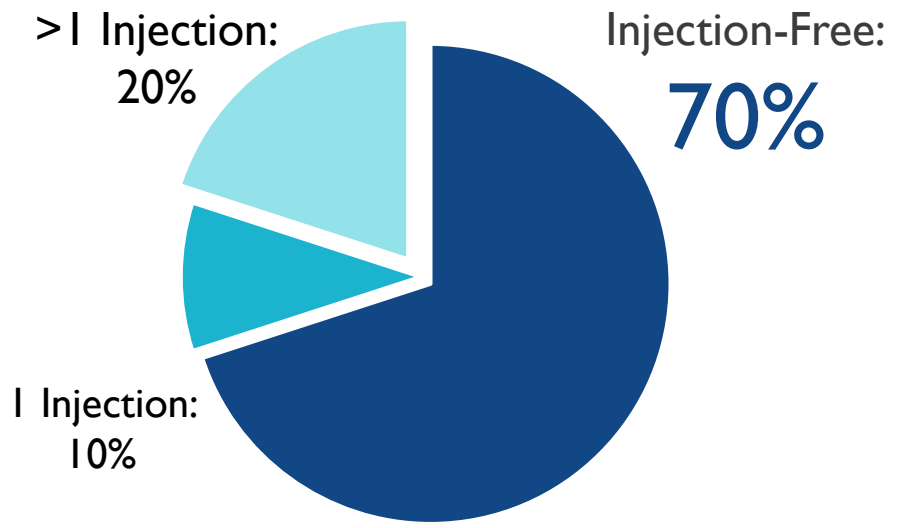


Treatment Burden Post-4D-150 Through Year 1 (KM Est.)

4D-150
3E10vg/eye

~4-5 injections in 12 mos. prior to study entry

<350 µm mean CST



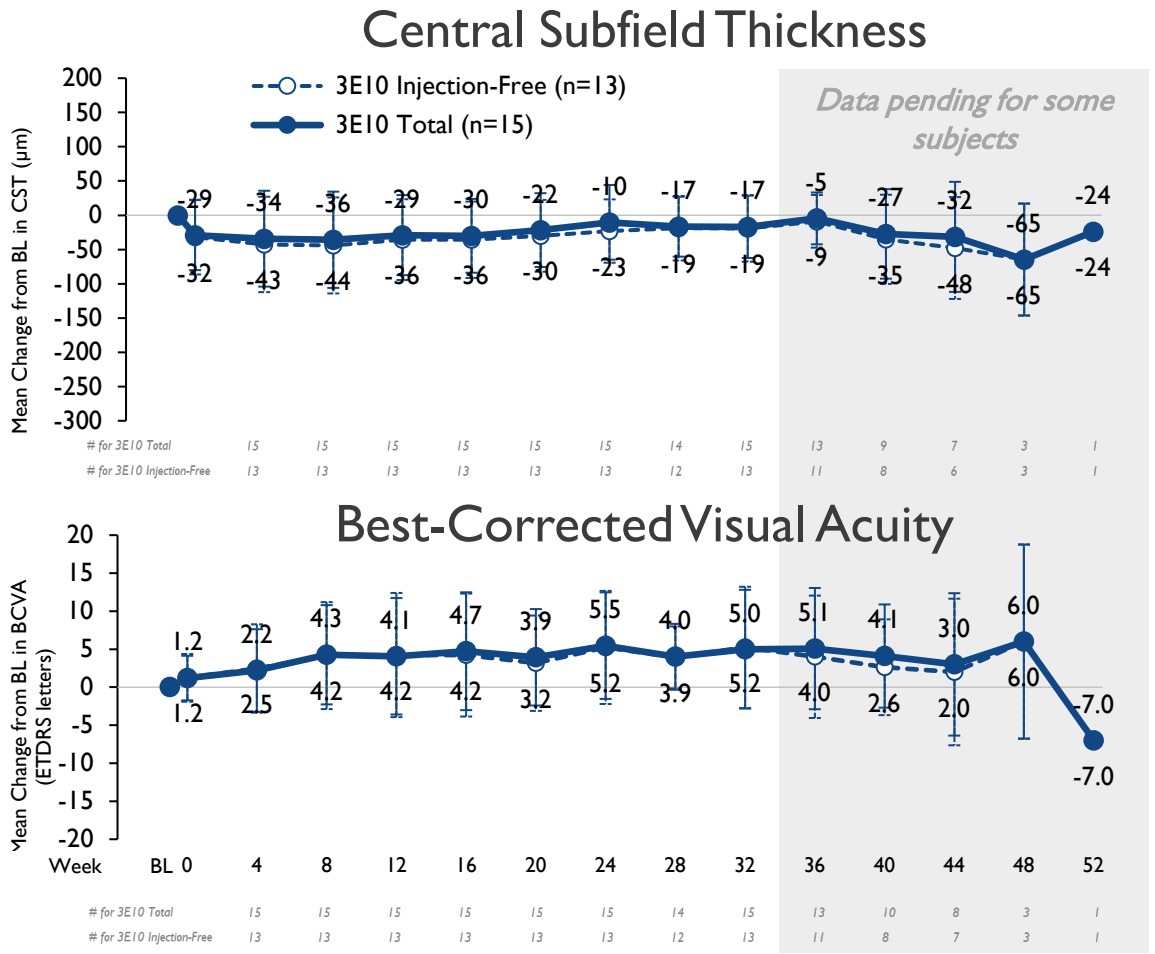
Overall Treatment Burden Reduction:

89%

4D-150 in Recently Diagnosed (≤6 Months) Population from Phase 2b

Visual Acuity & Anatomy Stable With Robust Reduction in Treatment Burden

Anatomy & Visual Acuity 4D-150

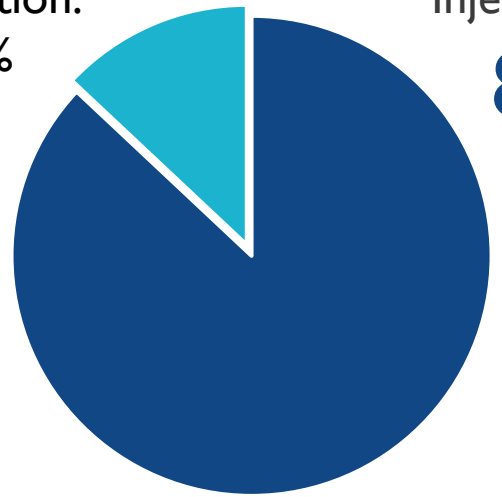


Treatment Burden Post-4D-150 Through Year 1 (KM Est.)

4D-150
3E10vg/eye

~3 injections in 12 mos. prior to study entry

~300 µm mean CST



Overall Treatment Burden Reduction:

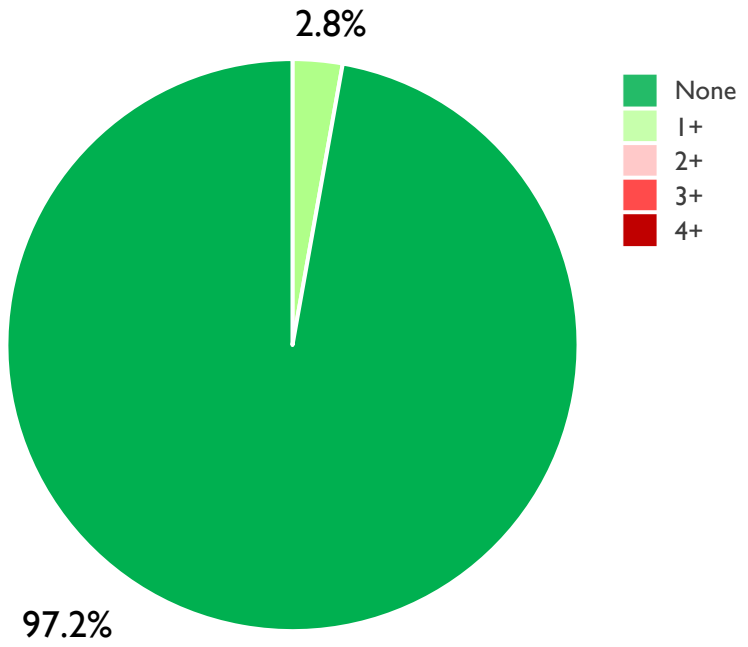
98%

4D-150 Continues to be Well Tolerated

- No 4D-150–related serious adverse events
- Rate of 3E10 dose 4D-150–related intraocular inflammation
  - **2.8%** (2 of 71) had transient 1+VC at any timepoint
  - **99%** (70 of 71) completed steroid prophylaxis taper on schedule
- No 4D-150–related hypotony, endophthalmitis, vasculitis, choroidal effusions or retinal artery occlusions observed to date

All 4D-150 3E10 vg/eye-Treated Wet AMD Patients (N=71)

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



Data cutoff, August 23, 2024.
*Duration of follow up, ≤2.5 years. NEI, National Eye Institute; SUN, Standardization of Uveitis Nomenclature.

4FRONT Phase 3 Wet AMD Study Design

Primary Endpoint: BCVA Noninferiority of 4D-150 3E10 vg/eye to Aflibercept 2mg Q8 weeks

Key Inclusion Criteria

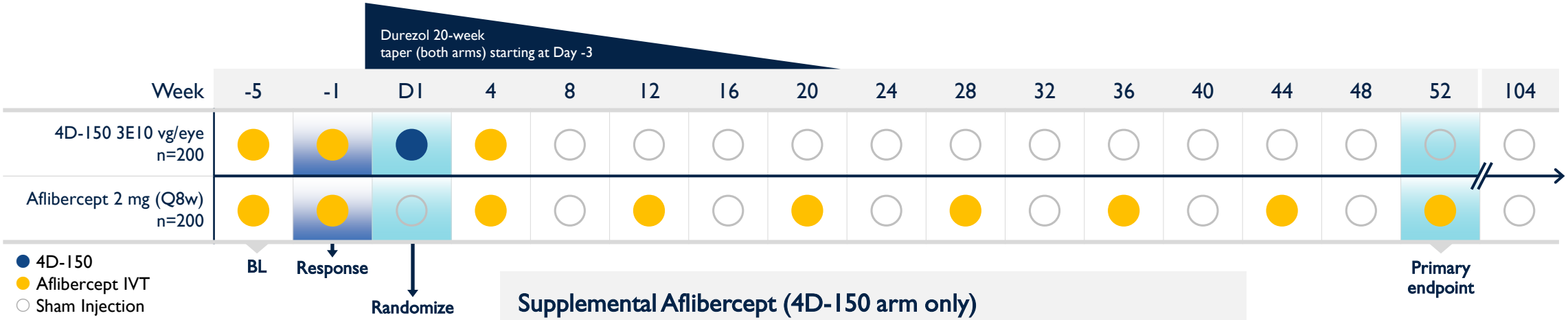
BCVA:
25-78 letters

Anti-VEGF responsive:
After Week -5 loading dose

Patient Population

4FRONT-1
Treatment naïve

4FRONT-2
Treatment naïve & previously treated (diagnosed within 6 months)



Supplemental Aflibercept (4D-150 arm only)

Reference Point:
After 3 loading doses

Pre-specified criteria for BCVA & CST worsening to maintain BCVA and **protect primary endpoint**

Designed to Drive Clinical, Regulatory & Commercial Success

4D-150 in Diabetic Macular Edema (DME)

Key 4D-150 Takeaways in DME

1

Well Tolerated: No intraocular inflammation; all patients completed topical steroid taper on schedule and remained completely off

2

3E10 vg/eye Efficacy Results: Sustained gain in BCVA & reduction in CST

86% reduction in injection burden vs. projected on-label aflibercept, dose response vs. 1E10 vg/eye

3

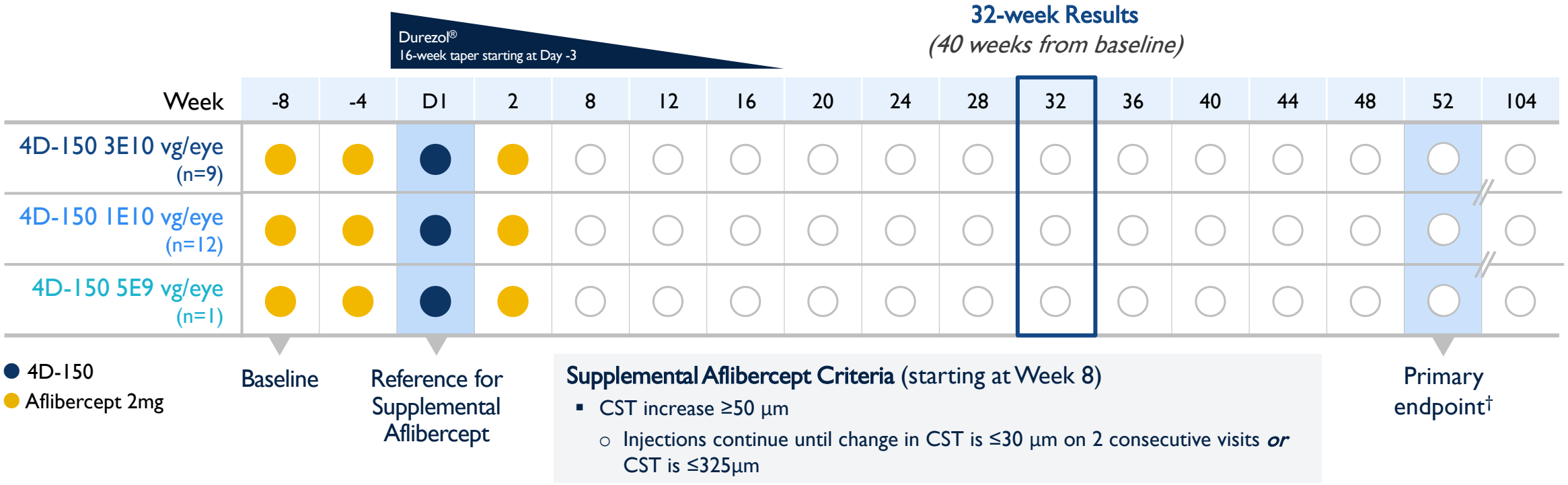
FDA Alignment: Single Phase 3 clinical trial acceptable for BLA submission in DME

May proceed to Phase 3 per FDA feedback, SPECTRA Part 2 no longer needed

Data cutoff, December 13, 2024.

Part 1: Designed to Enroll Patients with High CST and Employed Stringent Supplemental Criteria, with Focus on Safety & Dose Selection

Key Objectives	Evaluate **safety & tolerability** Identify dose level for further evaluation
Key Eligibility Criteria	Diagnosis within 2 years, CST ≥350 µm (includes treatment naïve) Confirmed anti-VEGF response (CST decrease ≥40 µm at Week –1 versus Week –8)*



Supplemental Aflibercept Criteria (starting at Week 8)

- CST increase ≥50 µm
  - Injections continue until change in CST is ≤30 µm on 2 consecutive visits ***or*** CST is ≤325µm

*Assessed by SD-OCT and confirmed by independent reading center.
†Safety and tolerability (frequency and severity of treatment emergent adverse events). CST, central subfield thickness: defined as thickness of 1mm area from ILM to BM.

Study Population: Baseline CST, BCVA, and Prior Treatment Status Balanced Across Dose Arms

	3E10 vg/eye (n=9)	1E10 vg/eye (n=12)	5E9 vg/eye (n=1)	Total (N=22)
Central subfield thickness, µm				
Mean	**513**	**488**	**515**	**499**
(range)	(382–671)	(356–669)		(356–671)
BCVA, ETDRS letters				
Mean	63	62	68	63
(range)	(41–79)	(32–84)		(32–84)
Treatment Experienced, n (%)	7 (78)	9 (75)	0	16 (73)

- 1 patient in 1E10 vg/eye arm terminated the study due to death unrelated to 4D-150 prior to completion of a post-baseline assessment

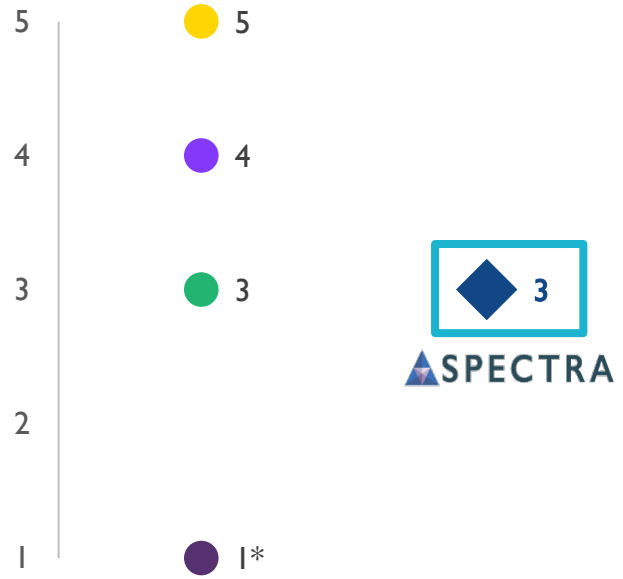
BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study.

SPECTRA Designed With Fewer Loading Doses and Enrolled Population With High CST and Majority Treatment Experienced

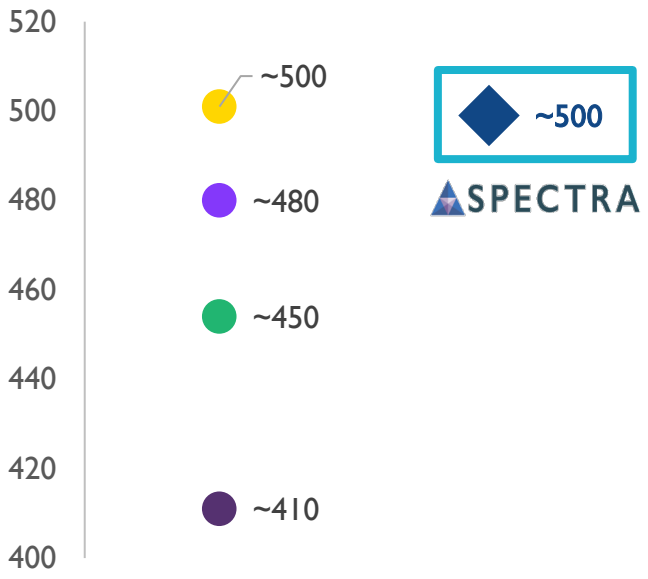
Selected Studies:

Phase 3			Phase 1/2	
EYLEA (aflibercept) Injection For Intravitreal Injection	EYLEA HD (aflibercept) Injection 8 mg	VABYSMO faricimab-svoa injection 6 mg	DURAVYU	4D-150
VIVID/VISTA[1]	PHOTON[2]	YOSEMITE/RHINE[3]	VERONA[4]	SPECTRA

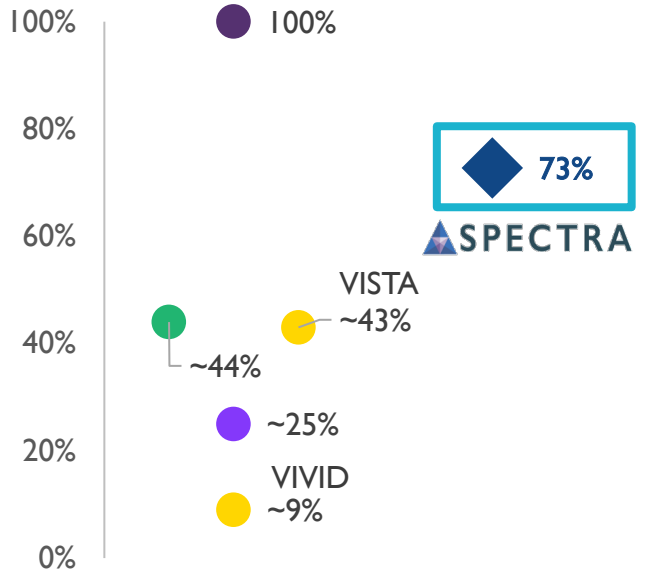
Anti-VEGF Loading Doses



Mean CST at Baseline (µm)



Treatment Experienced at Baseline (%)

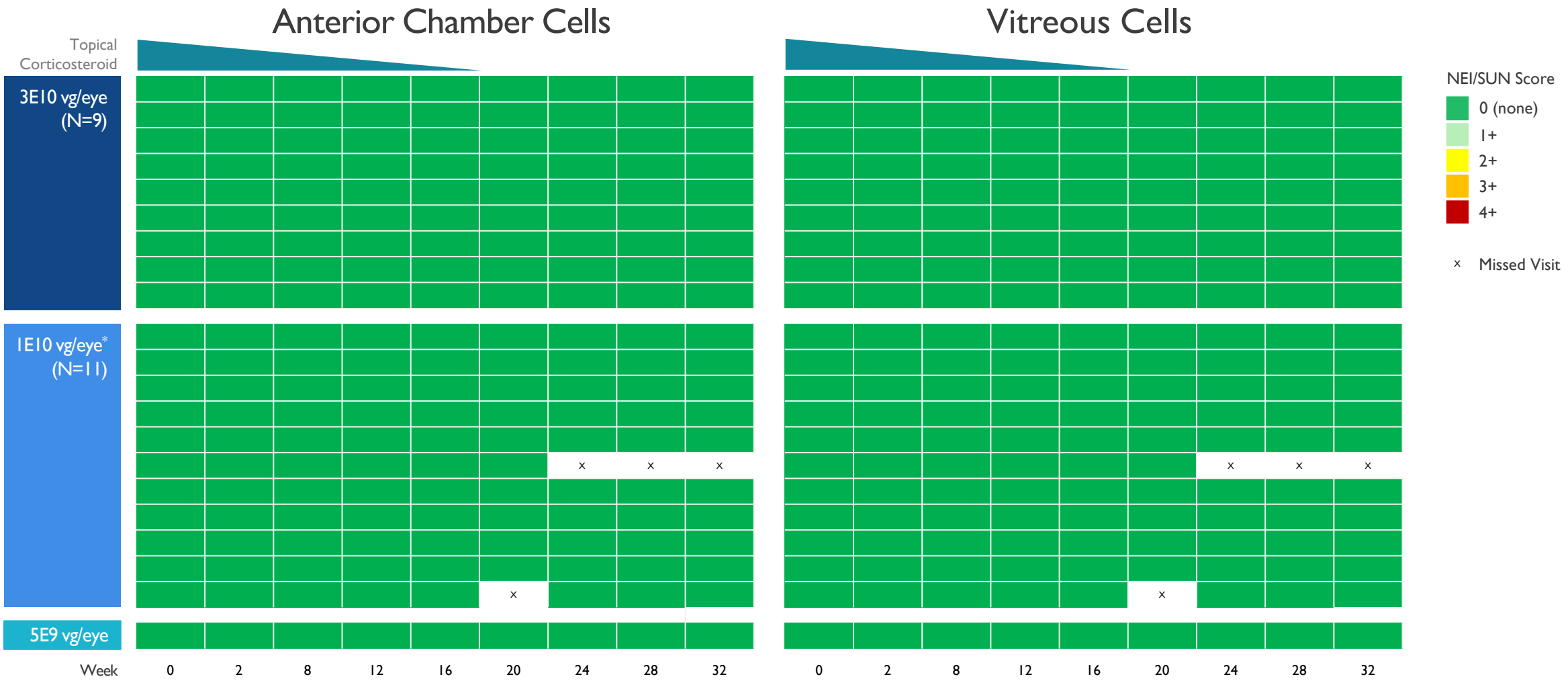


CST, central subfield thickness; BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study.

Sources: 1. Korobelnik et al. *Ophthalmology* 2014;121:2247–54. 2. Brown et al. *Lancet* 2024;403:1153–63. 3. Wykoff et al. *Lancet* 2022;399:741–55. 4. EyePoint Corporate Presentation, October 2024.

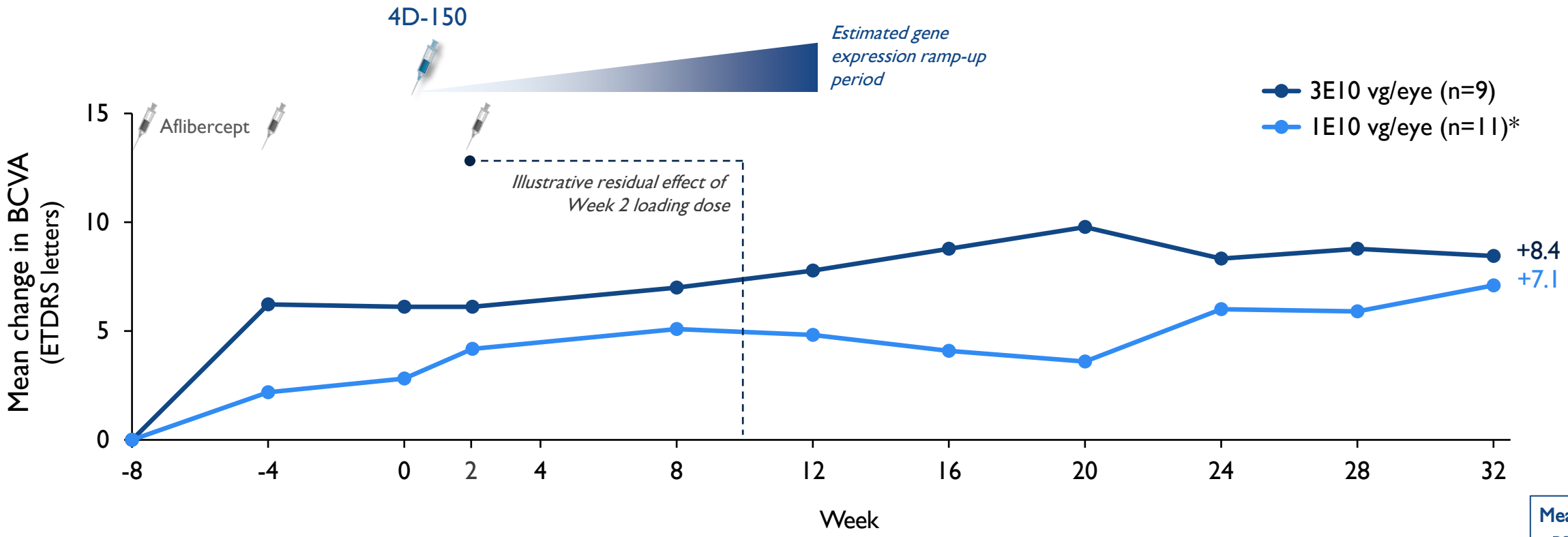
*Given concurrently with DURAVYU.

No Intraocular Inflammation and All Patients Completed Prophylactic Topical Steroids on Schedule and Remained Completely Off Steroids



Data cutoff date, December 13, 2024. *Excludes patient with early termination due to death (unrelated to 4D-150) prior to completion of a post-baseline assessment. NEI, National Eye Institute; SUN, Standardization of Uveitis Nomenclature; TR, trace (not observed); PC, pigmented cells (not observed); X, missed visit.

4D-150 3E10 vg/eye: Sustained Improvement in Visual Acuity Through 32 Weeks (+8.4 Letters vs Baseline)

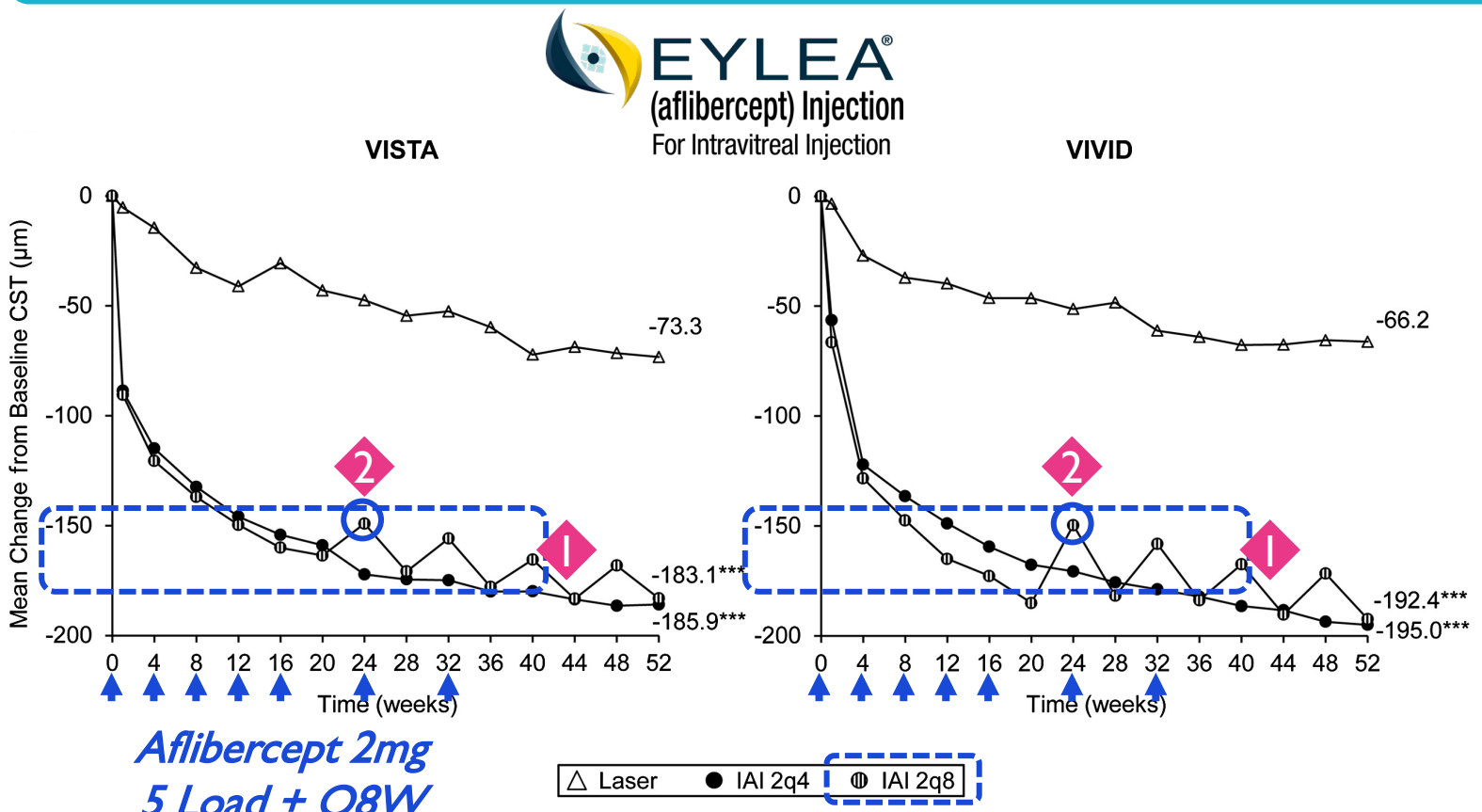


Supplemental Injections**, n									Mean per patient
	3E10 vg/eye (n=9)	0	0	2	0	2	1	0	0.6
	1E10 vg/eye (n=11)	1	2	2	4	2	1	3	1.4

Data cutoff date, December 13, 2024.
*Excludes patient with early termination due to death (unrelated to 4D-150) prior to completion of a post-baseline assessment. **No patient in 3E10 or 1E10 vg/eye arm would have received a supplemental injection based on disease activity measurement at time of first supplemental injection based on disease activity worsening criteria in VIVID/VISTA or PHOTON.
BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study.

On-label Eylea Improves CST ~165 µm But Requires High Treatment Burden

Eylea Phase 3 Studies in DME[1] Compared 5 Loading Doses + Q4W or Q8W vs. Laser

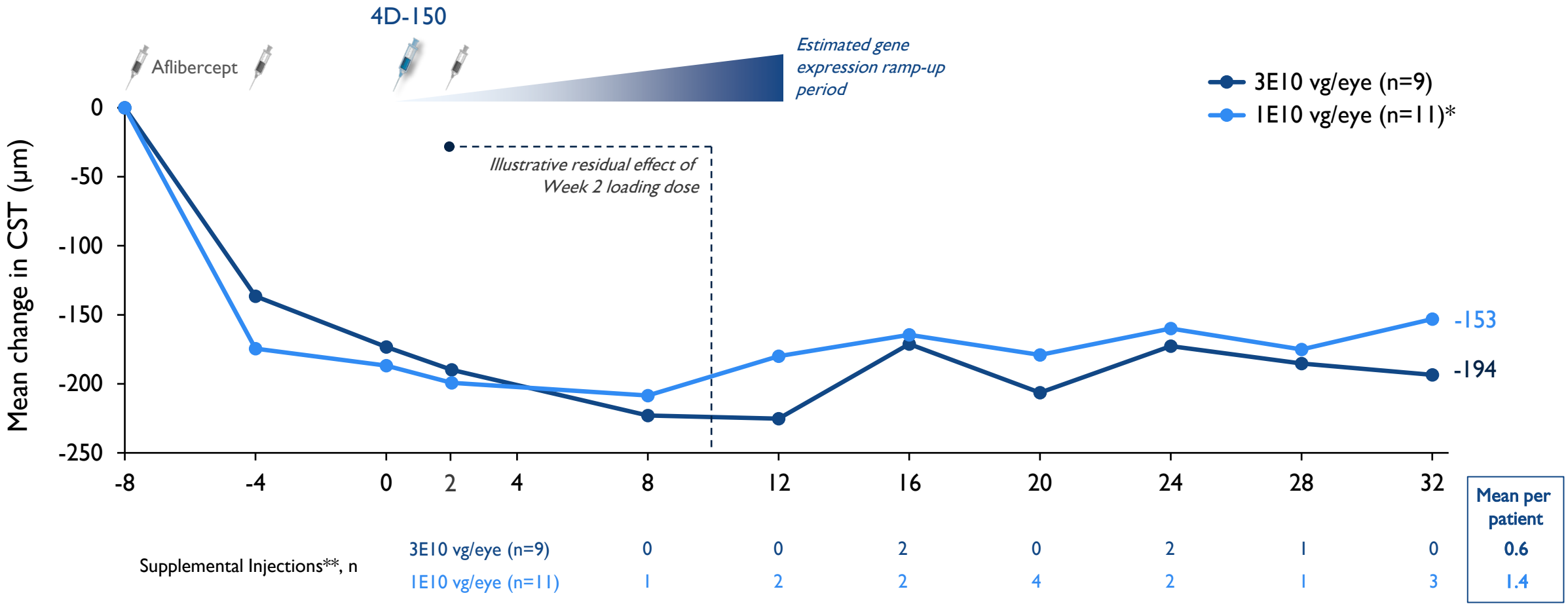


1 Eylea consistently achieved CST improvements of ~165 µm in DME patients

2 Eylea saw CST rebounds ~8 weeks after last dose of the loading dose regimen, rebounds continue in Q8W arms

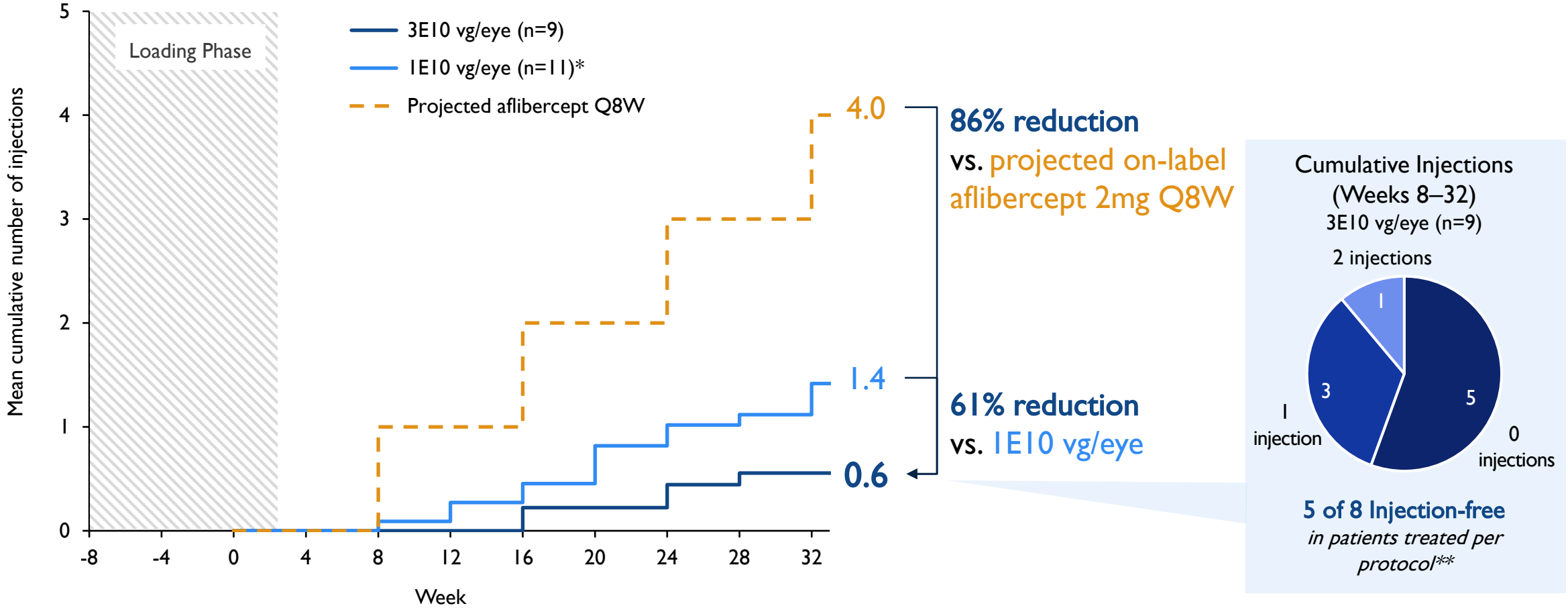
1. Korobelnik et al. *Ophthalmology* 2014;121:2247–54.

4D-150 3E10 vg/eye: Sustained Improvement in Anatomic Control Through 32 Weeks (–194 µm vs Baseline)



Data cutoff date, December 13, 2024.
*Excludes patient with early termination due to death (unrelated to 4D-150) prior to completion of a post-baseline assessment. **No patient in 3E10 or 1E10 vg/eye arm would have received a supplemental injection based on disease activity measurement at time of first supplemental injection based on disease activity worsening criteria in VIVID/VISTA or PHOTON,
CST, central subfield thickness.

3E10 vg/eye Post-loading Phase: 86% Reduction in Treatment Burden vs. Projected On-label Aflibercept 2mg Q8W; Dose Response in Favor of 3E10



Data cutoff date, December 13, 2024.

*Excludes patient with early termination due to death (unrelated to 4D-150) prior to completion of a post-baseline assessment. **Excludes n=1 patient who did not receive the Week 2 aflibercept. This patient received 1 supplemental injection through 32 weeks. Mean cumulative function from Cox proportional hazard regression model for recurrent events was used to estimate the mean cumulative number of supplemental aflibercept injections.

Rapidly Advancing Development of 4D-150

VECTOR DELIVERY	PRODUCT CANDIDATE	INDICATION	EPIDEMIOLOGY (PREVALENCE)	PHASE 1	PHASE 2	PHASE 3	MILESTONES
LARGE MARKET OPHTHALMOLOGY **R100** Intravitreal 	**4D-150** Aflibercept + VEGF-C RNAi	**Wet AMD**	*~3M U.S./EUMM*	4FRONT-1 4FRONT-2 PRISM			▪ PRISM Ph2b 52-week interim data: **Feb 10, 2025** ▪ 4FRONT-1 Initiation: **Q1 2025** ▪ 4FRONT-2 Initiation: **Q3 2025** ▪ 4FRONT-1 & -2 topline data: **H2 2027**
		Diabetic Macular Edema	*~5M U.S./EUMM*	SPECTRA			✓ **Jan 2025** 32-week interim data ▪ **Mid-2025** 52-week interim data

4DMT

4D-710 for Cystic Fibrosis

A101: Next-Gen Aerosolized Genetic Medicine Vector for Pulmonology

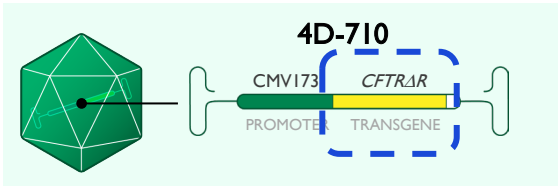
Prior aerosol gene therapy trials failed to achieve transgene expression in lung[1,2]; potential limitations:

- ✕ Poor mucus penetration
- ✕ Inefficient airway cell transduction
- ✕ Suboptimal tissue tropism
- ✕ Susceptibility to clearance by human AAV immunity

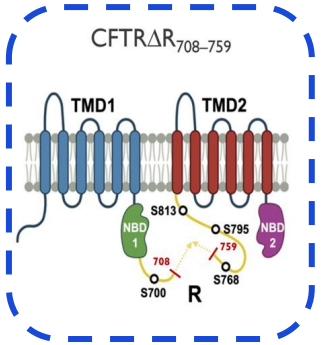
A101 invented at 4DMT to overcome these limitations:

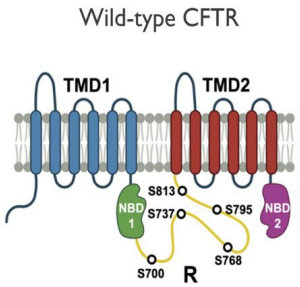
- ✓ Mucus penetration efficient
- ✓ Transgene expression efficient
- ✓ Transduction of multiple airway cell types
- ✓ Specificity for lung (>99.9%)
- ✓ Resistance to pre-existing human AAV immunity

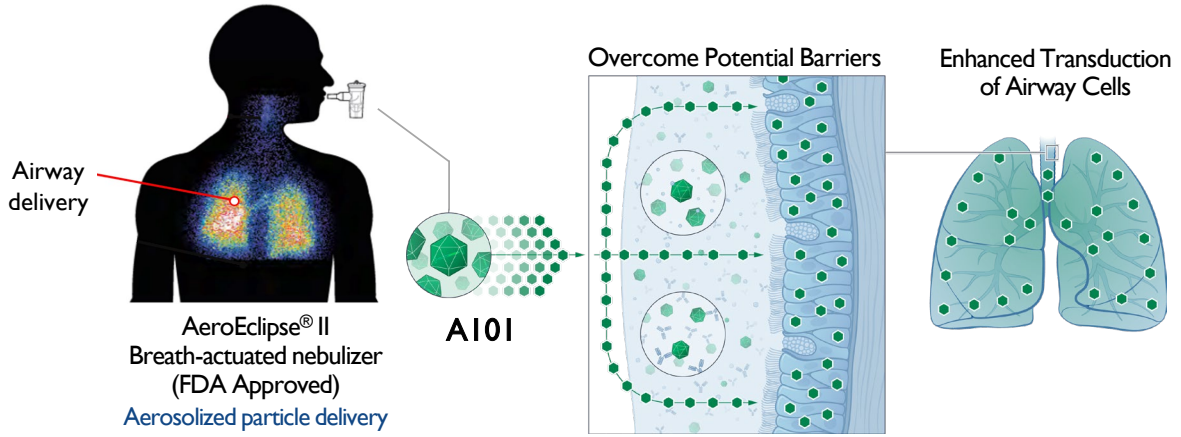
Aerosolized 4D-710-Based Genetic Medicines



1. Novel, clinically validated vector
2. Highly functional transgene
3. Efficient nebulizer





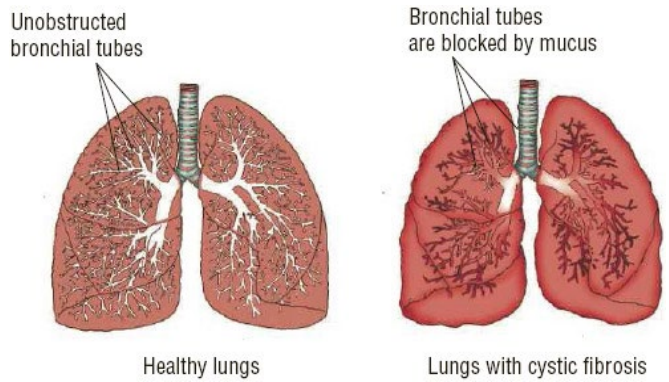


1. Aitken ML et al. Hum Gene Ther 2001; 12:1907–16. 2. Moss RB et al. Chest 2004;125:509–21.

CF Lung Disease Has High Unmet Medical Need Despite Modulators

Disease Burden

- **Dysfunctional cystic fibrosis transmembrane conductance regulator (CFTR) protein** → inability to transport chloride at the apical membrane → thickened mucus
- **Lung disease:** inflammation, infections, respiratory failure
- **Lung function** ($ppFEV_1$) **annual decline:** –1 to –2.3%[1*,2]
- **Median survival (Pre-modulators):** ~40 years[3]



Epidemiology

- **~105,000[4,5] prevalence worldwide:**
  - ~40,000 prevalence in U.S. alone
  - ~1,000 incidence in U.S. alone

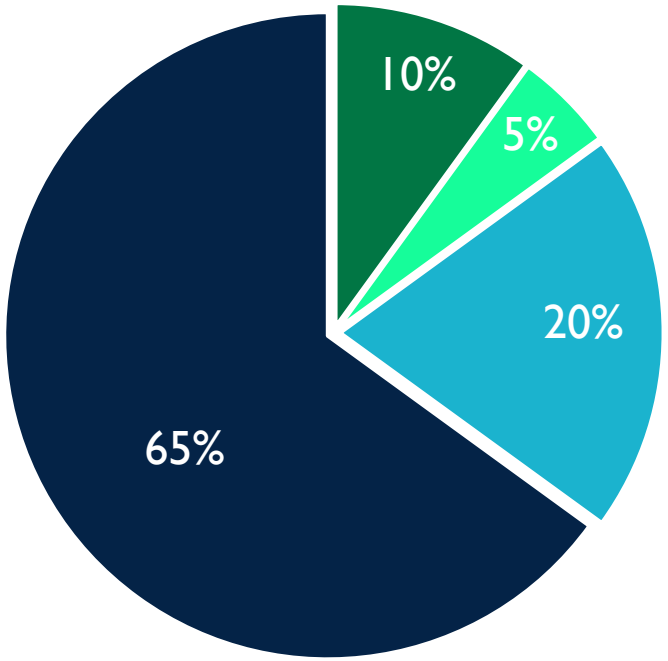
Standard of Care

- **Daily Supportive Care:**
  - Airway clearance (~100 mins)
  - Inhaled antibiotics & bronchodilators
- **Disease modifying CFTR modulators:**
  - **$9.9 billion** annually (2023)[6]

Illustration by Frank Forney. © 2016 Cengage Learning *Estimate based on *DF508* homozygous population, which appears to have a similar rate of decline as Class I (null) variant population. 1. Konstan MW et al. *Lancet Respir Med* 2017; 5:107–18. 2. Caley et al. Journal of Cystic Fibrosis 2021;20:86–90. 3. Ramsey & Welsh. *Am J Respir Crit Care Med* 2017;195(9):1092–9. 4. Guo J et al. *Journal of Cystic Fibrosis* 2022; 21:456-62. 5. Cystic Fibrosis Foundation. 6. Vertex Pharmaceuticals FY 2023 financial results.
ppFEV1, percent predicted forced expiratory volume in 1 second.

Highest Unmet Need in ~35K People with Cystic Fibrosis

4D-710 has the Potential to Treat Cystic Fibrosis Lung Disease Regardless of Genetic Variant

Cystic Fibrosis Population WW	Population Segment	Estimated People	
	■ **Ineligible** for CFTR modulators	~10k	AEROW study population evaluating 4D-710 as **monotherapy**
	■ **Intolerant** to CFTR modulators	~5k	
	■ **Suboptimal response** to CFTR modulators[1]	~20k	Potential future 4D-710 study population
	■ Responsive to CFTR modulators	~70k	*Upside if superior dosing, efficacy, and/or safety is demonstrated*
~105k			~35k

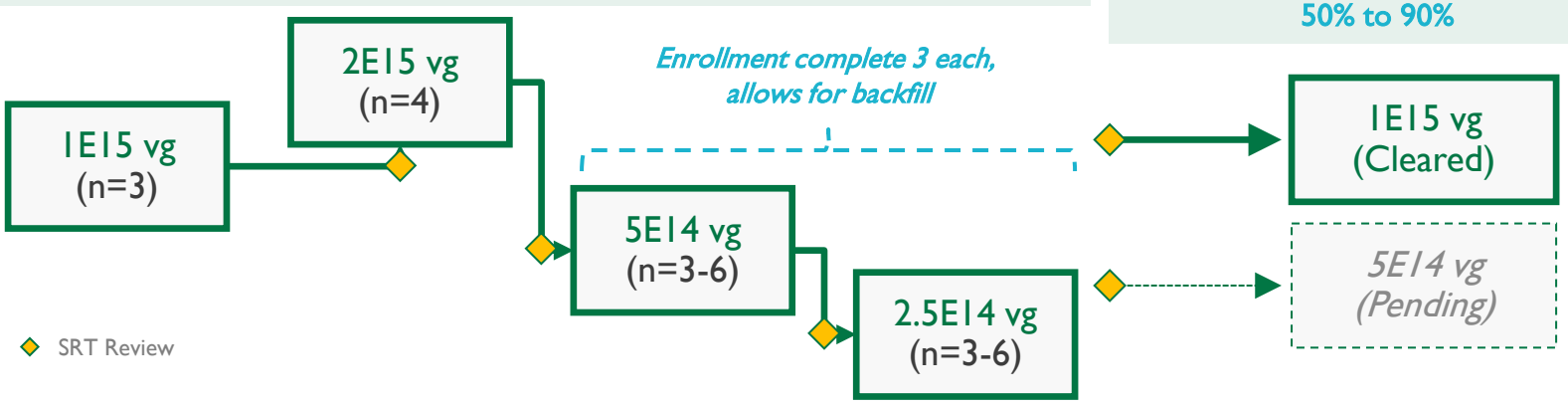
CFTR, cystic fibrosis transmembrane conductance regulator. 1. Based on assumptions derived from Middleton, 2019 and CFF registry analysis.

Phase 1/2 Designed to Identify Doses for Late-Stage Development

Generate Safety, Biomarker & Clinical Activity Data to Inform Selection of Phase 2 & 3 Dose

Phase 1 (Dose Exploration)

$ppFEV_1$ Eligibility Criteria: 50% to 100%



Phase 2 (Dose Expansion)

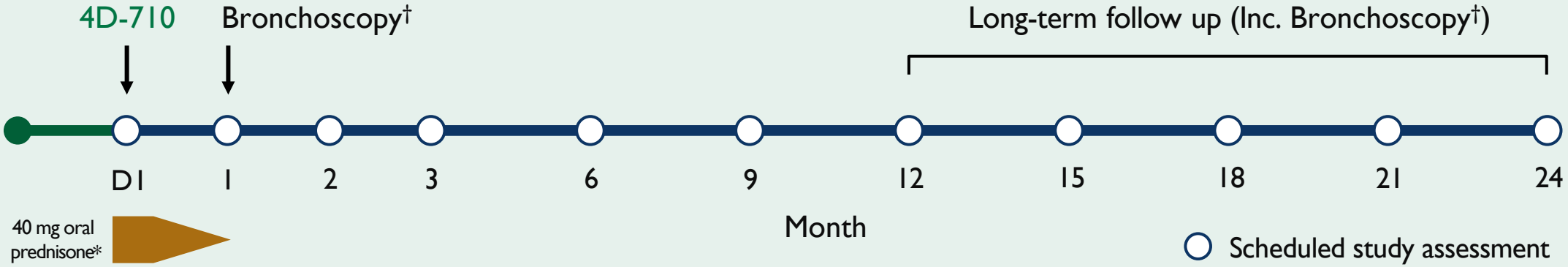
$ppFEV_1$ Eligibility Criteria: 50% to 90%

Primary Objectives:

- **Phase 1:** Dose ranging to characterize safety & biomarkers
- **Phase 2:** Expand in selected dose to confirm clinical activity for Phase 3

Key Endpoints:

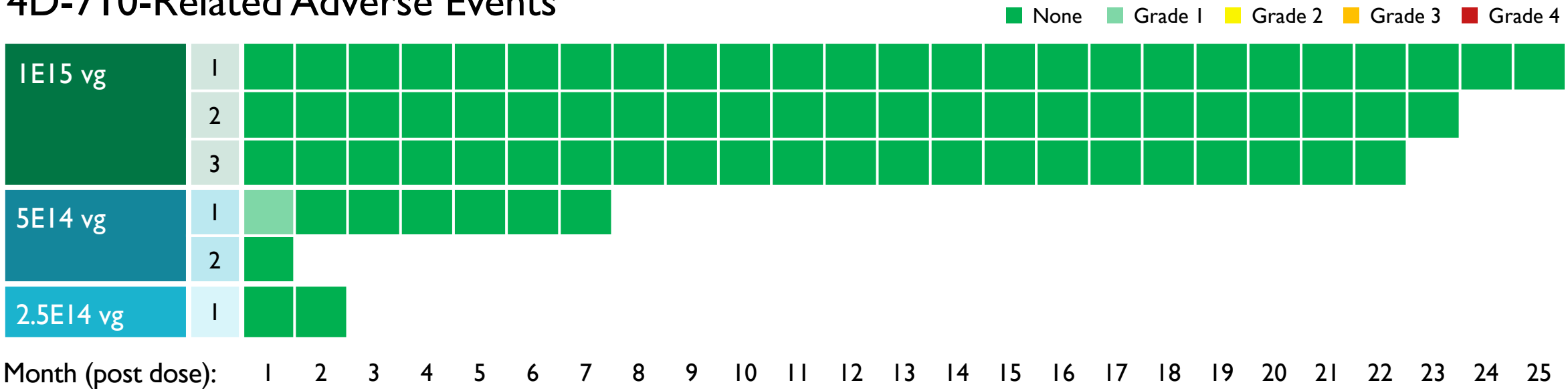
- Safety & tolerability
- Lung biomarkers
- Clinical activity



*28-day taper. †Endobronchial biopsy (4D-710 transgene and protein expression), 2nd biopsy allowed beyond 12 months. ppFEV1, percent predicted forced expiratory volume in 1 second; SRT, Safety Review Team.

Aerosolized 4D-710 (Up to 1E15 vg) Was Well Tolerated

4D-710-Related Adverse Events

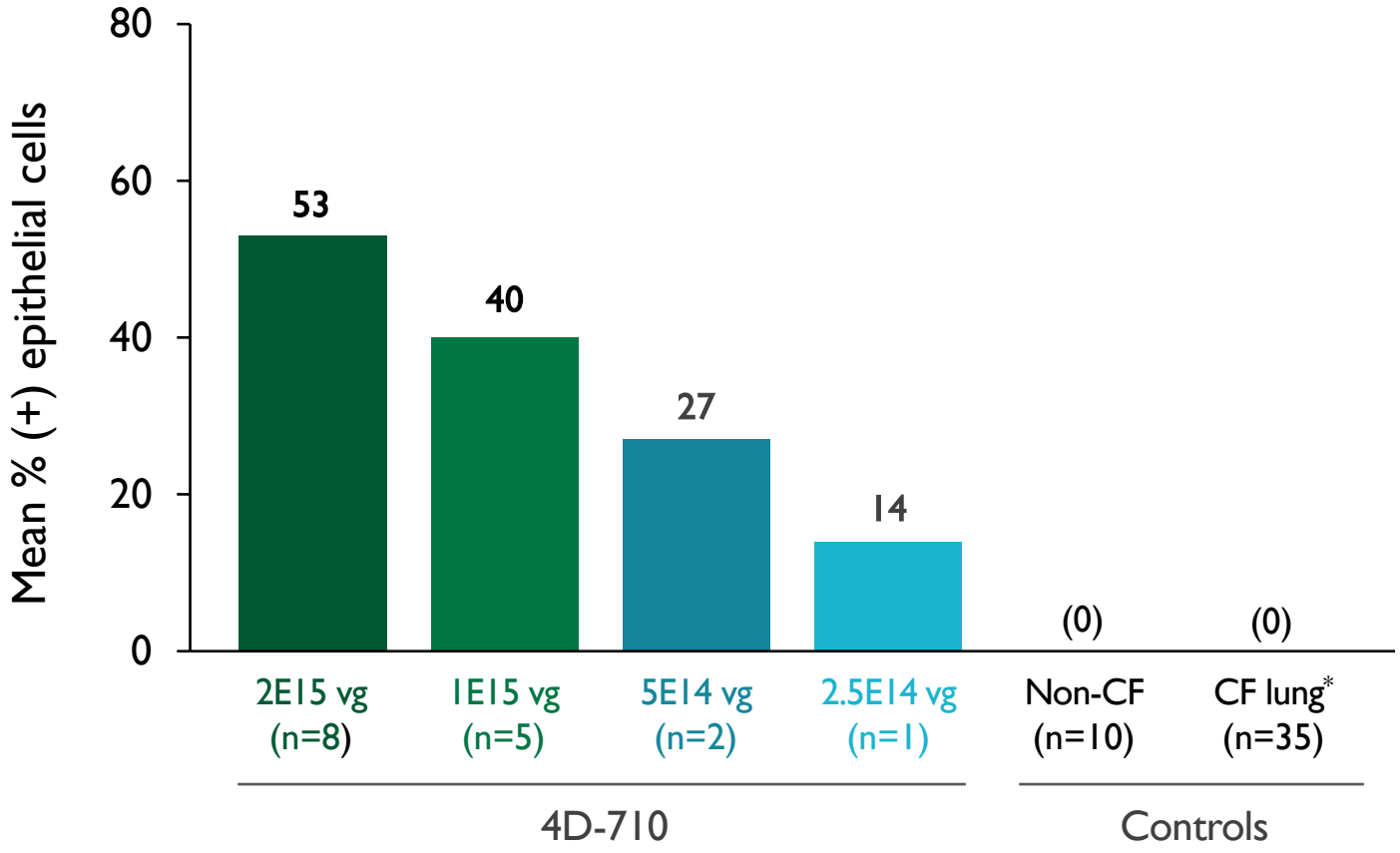


- Administration of aerosolized 4D-710 well tolerated
  - No dose-limiting toxicities
  - No 4D-710–related SAEs
  - No clinically significant 4D-710-related adverse events after administration
- No inflammation or toxicity in lung biopsies samples

Best available data as of May 24, 2024.

Dose-dependent *CFTRΔR* RNA Expression Following 4D-710 Administration

CFTRΔR RNA (ISH): mean % (+) airway epithelial cells

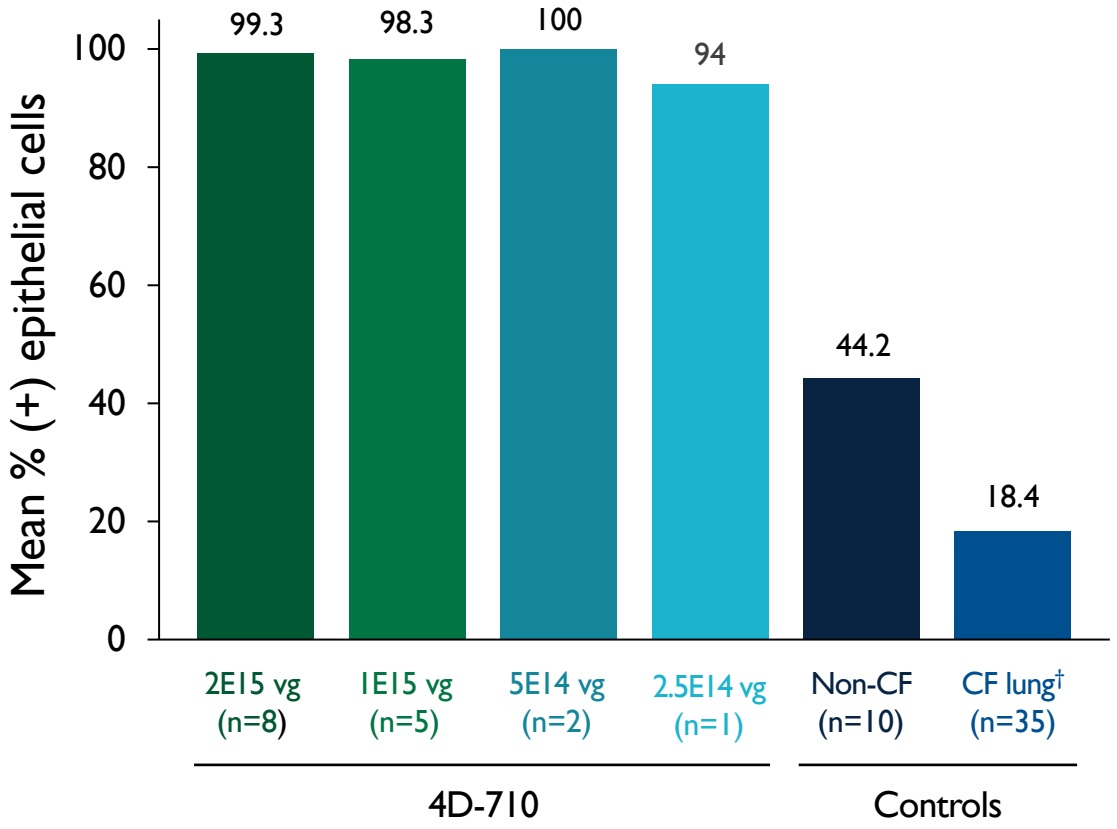


- Dose-dependent *CFTRΔR* mRNA expression in bronchial epithelial cells
- No *CFTRΔR* mRNA expression observed in commercial non-CF and CF lung samples
- Commercial non-CF samples positive for endogenous *CFTR* mRNA expression

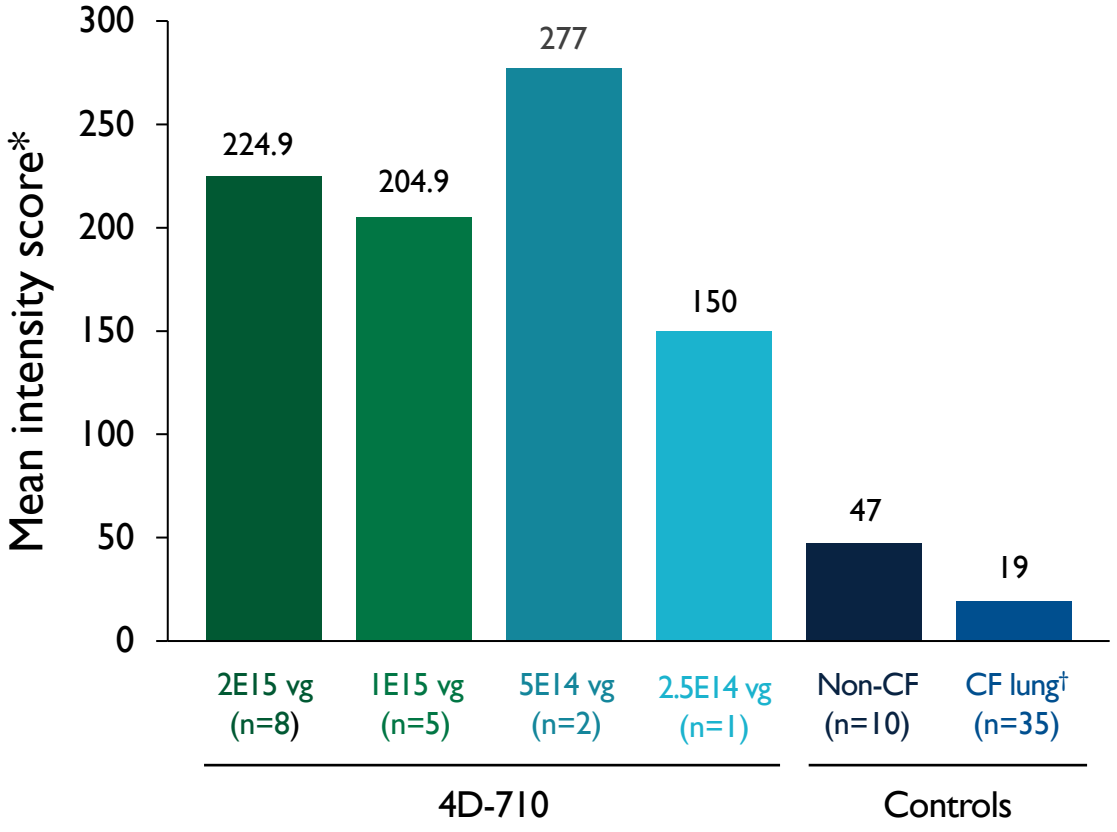
Best available data as of May 24, 2024. Quantification by Visiopharm® AI Machine Learning Analysis. Number shown below each group indicates the number of lung samples. *Attempts to genotype commercial CF samples yielded results for 13/35 samples; of these, a majority were ΔF508 homozygous mutations. CFTR, cystic fibrosis transmembrane conductance regulator; ISH, in situ hybridization.

Widespread 4D-710–Mediated CFTR Protein Expression at All Doses and in All Participants

CFTR (+) Epithelial Cells (IHC)



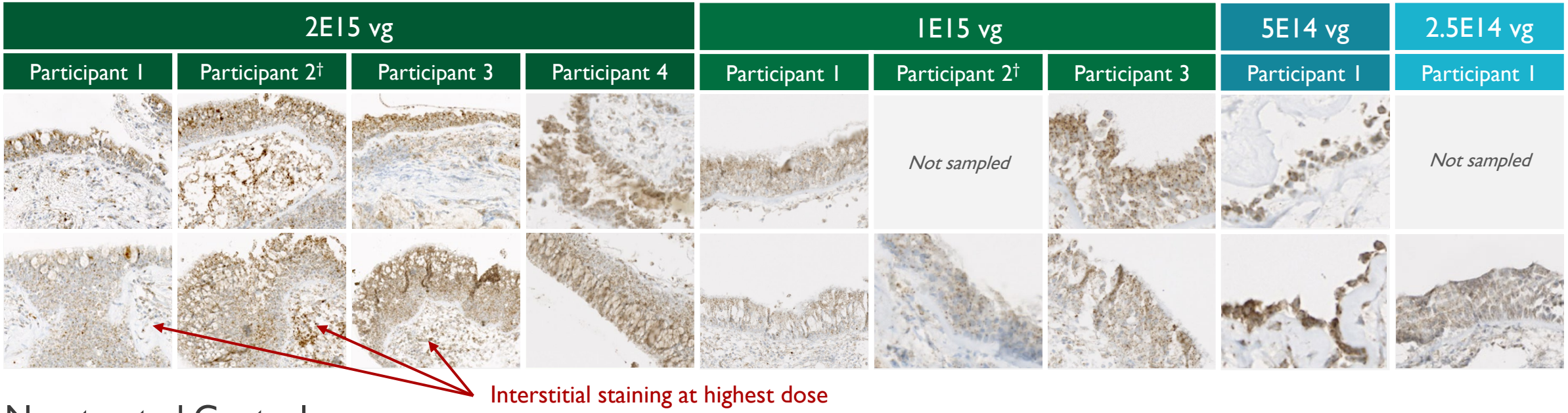
CFTR Staining Intensity (IHC)*



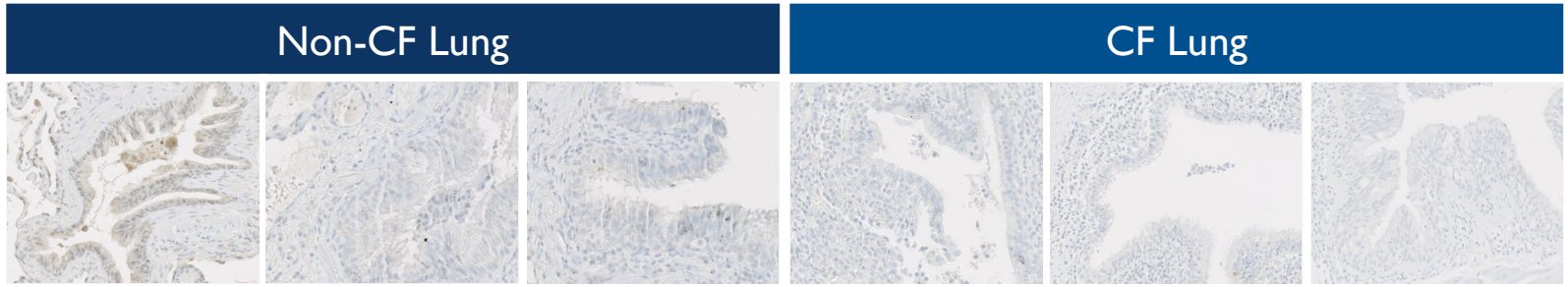
Best available data as of May 24, 2024. Quantification by Visiopharm AI Machine Learning Analysis. Number shown below each group indicates the number of lung samples. *H-score. †Attempts to genotype commercial CF samples yielded results for 13/35 samples; of these, a majority were ΔF508 homozygous mutations. IHC, immunohistochemistry.

Widespread & Consistent CFTR Protein Expression: 100% of Samples

4D-710 Treated



Non-treated Controls

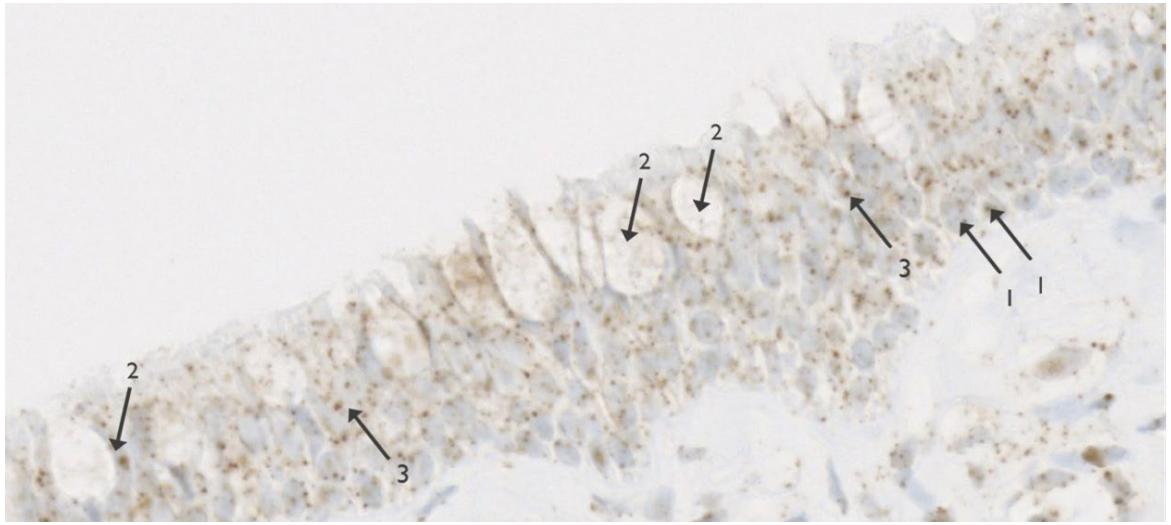


Best available data as of May 24, 2024. *Representative images, endobronchial biopsy samples obtained from the left secondary carina (row 1) and right middle lobe (row 2). †Endobronchial biopsy performed at Week 8.

CFTR Protein Expression Observed in Multiple Airway Cell Types

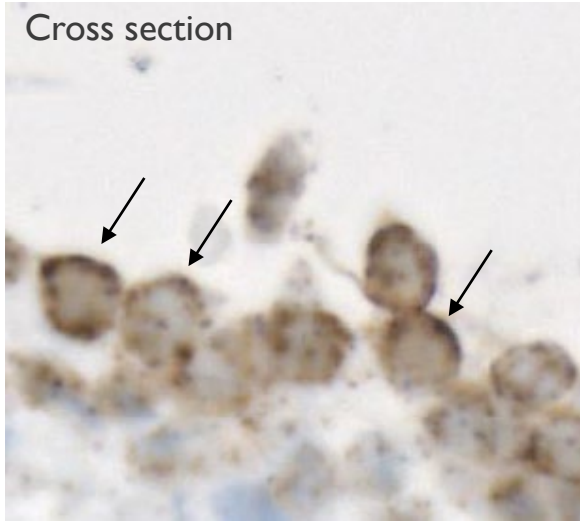
CFTR Protein Expression (IHC) Following Administration of 4D-710: Secretory, Ciliated & Basal Cells

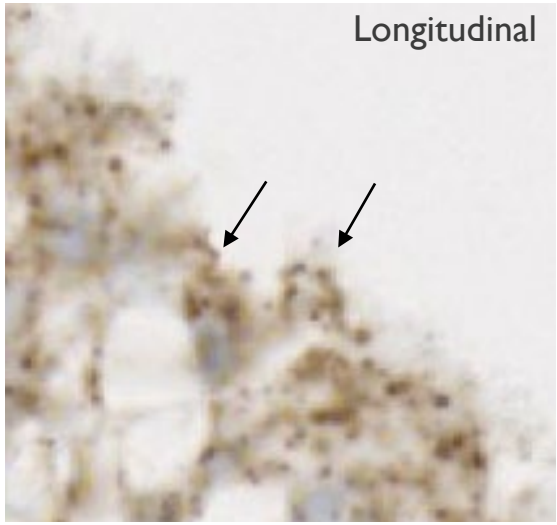
CFTR Protein Expressed in Multiple Cell Types*



(1) Basal cells (2) Goblet cells (3) Columnar ciliated cells

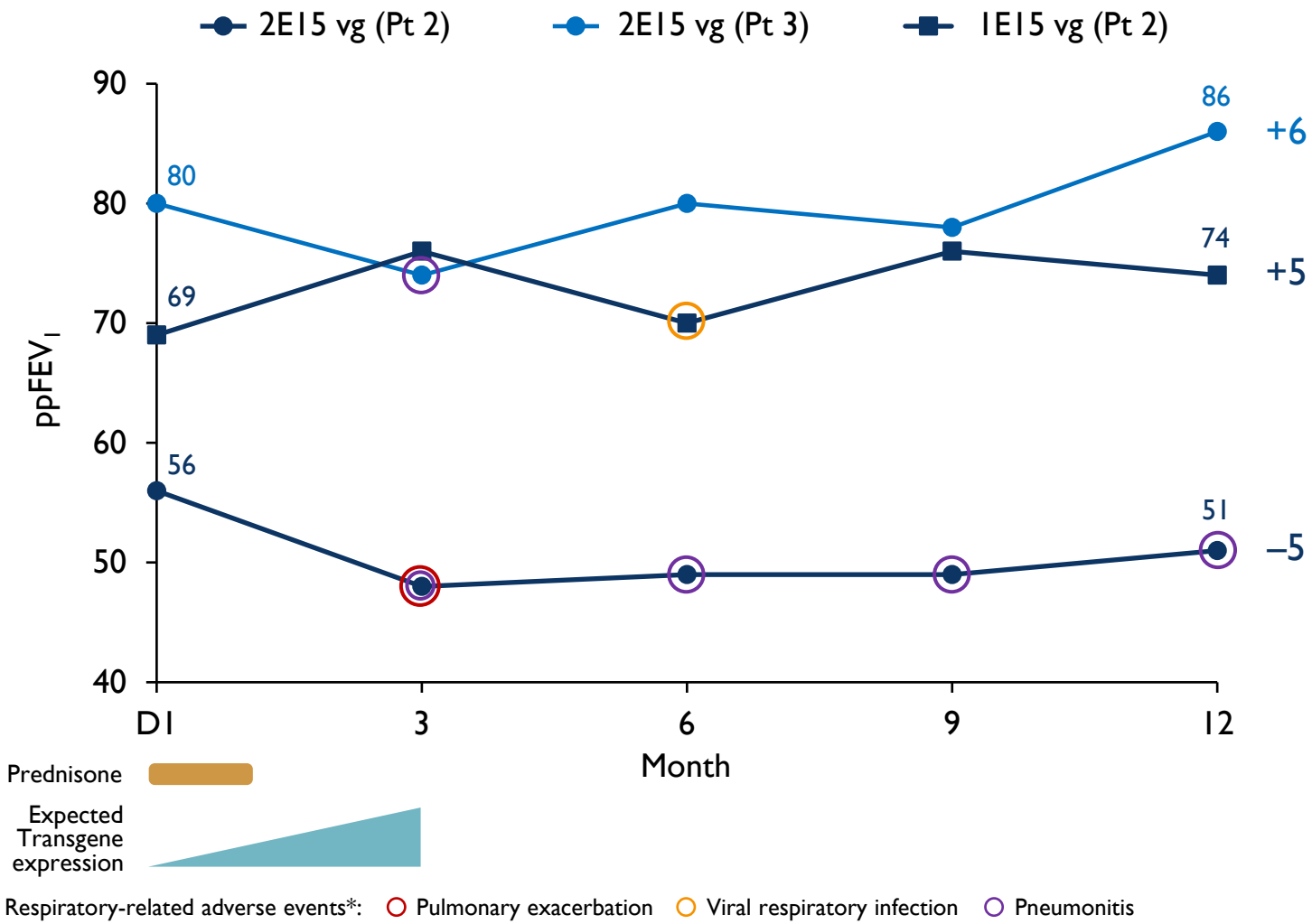
Localization to Apical Region†





Best available data as of May 24, 2024. *Image from 1E15 vg participant. †Images from 2E15 vg participants. CFTR, cystic fibrosis transmembrane conductance regulator. IHC, immunohistochemistry.

Two of Three Participants with Mild to Moderate ppFEV$_1$ Impairment at Baseline Showed Improvement at 12 Months

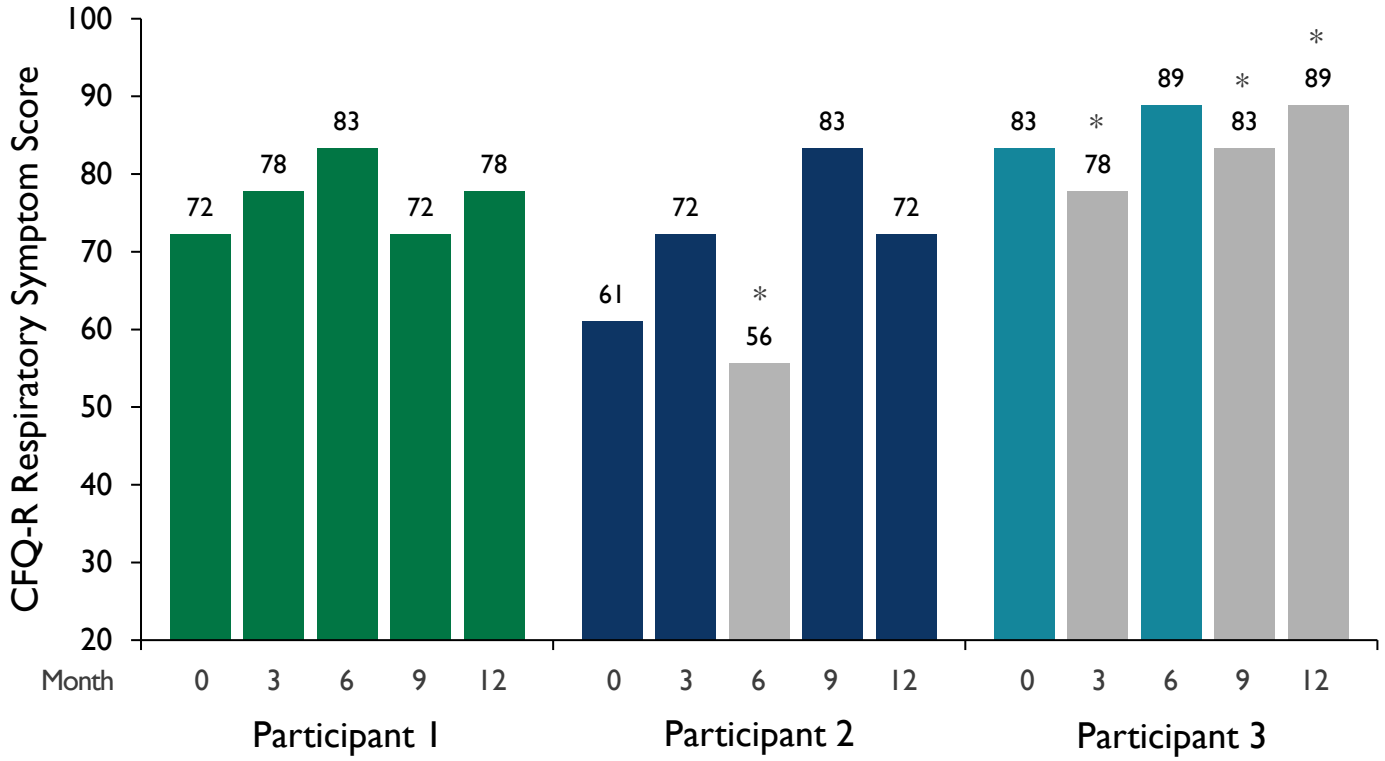


- Three participants had a baseline ppFEV$_1$ ≤80% and >6 months of follow up
- Two showed improvement in ppFEV$_1$ at 12 months
  - 2E15 vg (n=1): +6%
  - 1E15 vg (n=1): +5%

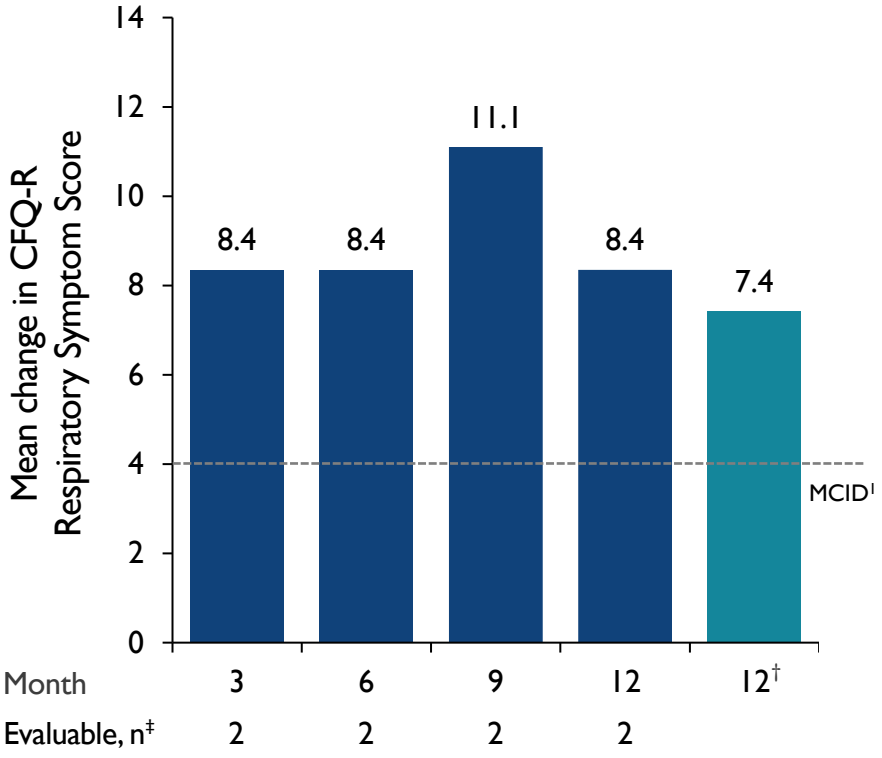
Best available data as of May 24, 2024.

4D-710 (1E15 vg): Durable Improvement in CFQ-R-R Score

CFQ-R Respiratory Symptom Score



Mean Change in CFQ-R-R Score



Best available data as of May 24, 2024. *Respiratory-related adverse event within 21 days of assessment. †All enrolled participants (n=3). ‡Excludes participants with a respiratory-related event within 21 days of assessment. CFQ-R-R, Cystic Fibrosis Questionnaire-Revised (respiratory symptoms scale). Scores range from 0 to 100, with higher scores indicating better health. MCID=4 points [1]. 1. Quittner AL et al. Chest 2009;135:1610–18.

Totality of Clinical & Biomarker Data To-date Supports **1E15 vg** as Intended Phase 2 Expansion Dose, 5E14 vg Dose Pending Additional Follow-Up

Dose Selection Criteria:		Target Profile	2E15 vg (n=4)	1E15 vg (n=3)	5E14 vg (n=1)	2.5E14 vg (n=1)
Expression	*CFTRΔR* RNA expression (ISH)	≥15% cells[1,2]	✓	✓	✓	✗
	CFTR protein expression (IHC)	≥15% cells[1,2]	✓	✓	✓	✓
	Cell types transduced	Basal cells & secretory cells	✓	✓	✓	✓
		No/limited expression in interstitial cells	✗	✓	✓	✓
	Pre-existing A101 Immunity	No effect on expression	✓	✓	✓	*Pending*
Safety & Tolerability	Safety & tolerability	No ≥Grade 3 related AEs, No related SAEs	✗	✓	✓	✓
Clinical Activity	$ppFEV_1$ (at 6-12 months)	>4.5% change from baseline	✓	✓	*Pending*	*Pending*
	CFQ-R-R (at 6-12 months)	>4 points change from baseline	*Not interpretable*	✓	*Pending*	*Pending*
				Cleared	***Pending***	

Best available data as of May 24, 2024.
*Both events reported by one study participant (Participant 2) 1. Dannhoffer L et al. Am J Respir Cell Mol Biol 2009; 40:717–23. 2. Bell S et al. Lancet Resp Med 2020; 8:65–124.

Program Expectations & Cash Position

Strong Cash Balance to Execute Through Key Near-Term Expected Milestones

Large Market Ophthalmology		Corporate webcast to discuss Ph2b cohort of PRISM in wAMD and SPECTRA in DME: **Feb 10, 2025**
	4D-150 Wet AMD	Initiation of Phase 3 4FRONT-1 and -2 pivotal trials: **Q1 2025** (4FRONT-1) and **Q3 2025** (4FRONT-2)
		Primary endpoint 52-week topline data for both 4FRONT-1 and -2: **H2 2027**
	4D-150 DME	✓ SPECTRA clinical trial 32-week interim data & program update: **January 2025**
		52-week interim data update expected at a scientific conference: **Mid-2025**
Pulmonology	4D-710 CF	Interim data & program update from AEROW clinical trial: **Mid-2025**
Cash Balance		**$506M cash as of December 31, 2024** (Unaudited); **Runway into 2028**

THANK YOU

5858 Horton Street, Suite 455 | Emeryville, California 94608

(510) 505-2680 | Investor.Relations@4DMT.com

IR.4DMT.com | LinkedIn