



ATSENA
THERAPEUTICS



An Update on ATSN-201, a Laterally Spreading Gene Therapy for XLRS

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Retinal Therapeutics Innovation Summit
May 1st, 2026

ATSN-201: Potential First-in-Class Clinical-Stage Program in X-Linked Retinoschisis

Disease / Biology

- Monogenic X-linked disease caused by mutations in *RS1* gene which encodes retinoschisin
- Retinoschisin is a protein secreted by photoreceptors which localizes to the surface of photoreceptors and bipolar cells

Symptoms / Progression

- Patients present with progressive vision loss in early childhood
- Straightforward clinical diagnosis
- Most XLRs patients **ultimately become legally blind**
- Retinal 'separations' (aka schisis cavities) in central retina
- Loss of photoreceptors in later stage disease (large treatment window)

IP & Competitive Landscape

- Potential **First-in-Class** – only clinical stage program in major markets
- Atsena's AAV.SPR subretinal administration potentially provides **greater potency, efficacy, & safety** (even at low doses) than previous AAV approaches
- Exclusive IP licenses from UF, 2041 expiration

Prevalence & Market Size

- ~30,000 in U.S./CA/EU
- **>\$1B peak sales**, cumulative market opportunity **>\$11B in major markets**
- **Eligible for rare pediatric priority review voucher**
- **RPD designation granted**



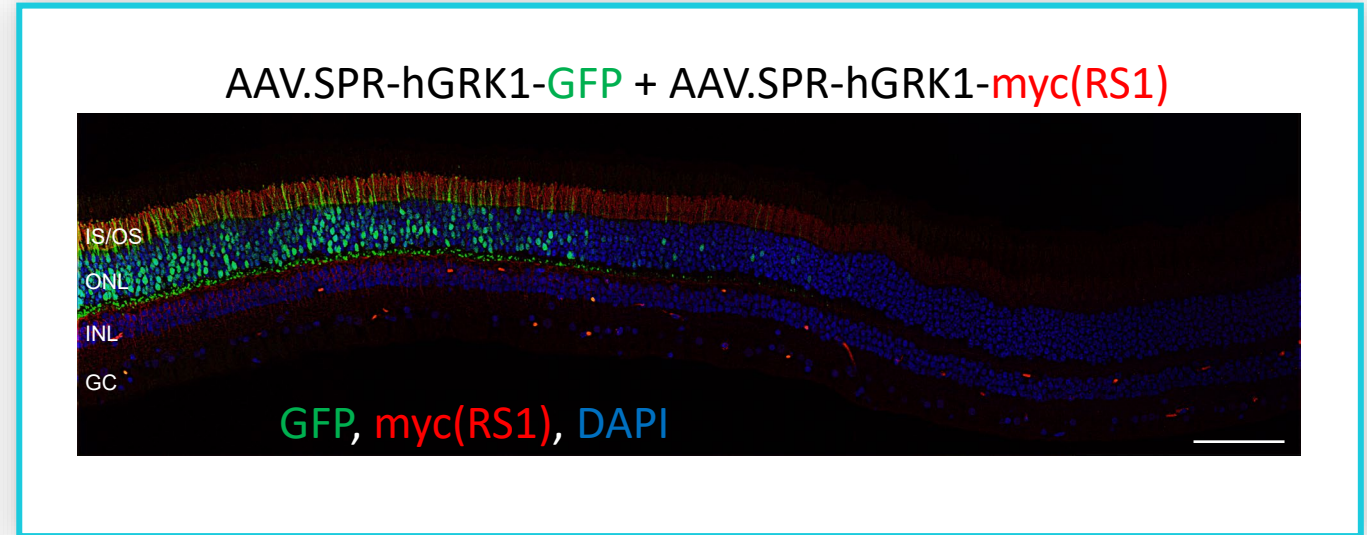
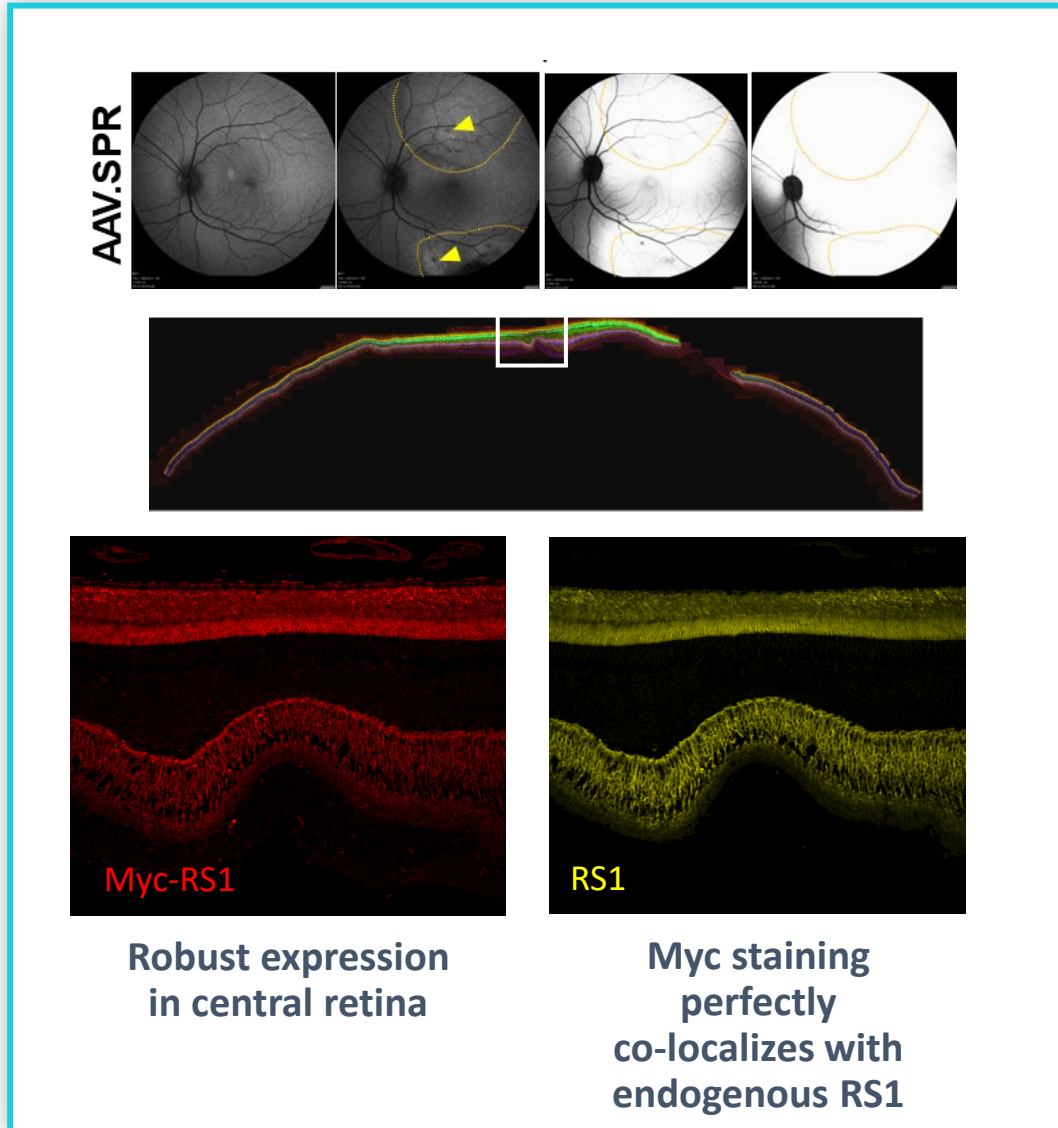
ATSENA'S DIFFERENTIATED APPROACH

Laterally spreading AAV.SPR potentially allows for **safe and efficient delivery** of *RS1* to photoreceptors in the central retina/fovea



AAV.SPR enables safe and efficient delivery of RS1 to the primate fovea following peripheral subretinal injection

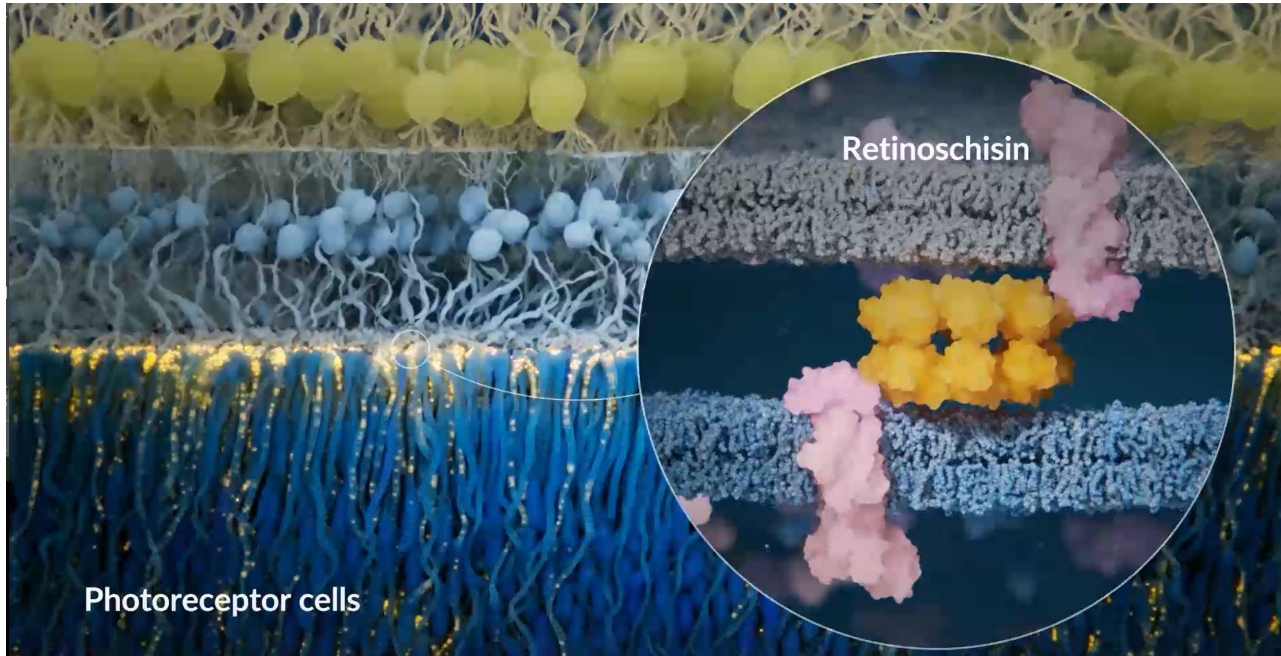
NHP images



- AAV.SPR promotes RS1 expression well beyond the borders of the original subretinal injection bleb
- AAV.SPR transduces foveal cones without the need for submacular injection
- AAV.SPR transduces much larger areas of the retina
- Even though RS1 is a secreted protein, it is only **LOCALLY** secreted. It's ability to get to the fovea depends on the spreading AAV.SPR capsid



We expect structural improvements to precede functional improvements



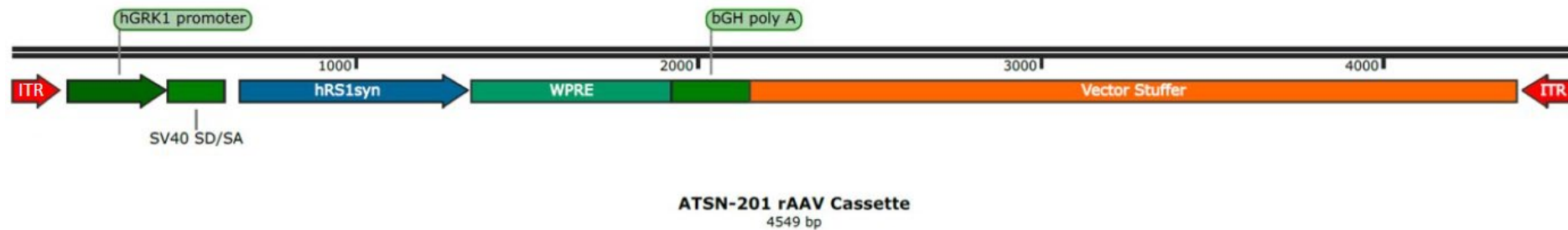
MoA animation by [Visual Science](#), 2025

- ATSN-201 must efficiently transduce photoreceptors
- RS1 must efficiently be secreted
- RS1 must efficiently localize to its sites of function (i.e. photoreceptor-bipolar synapse)
- Synapse must be repaired
- Schisis cavities must improve/resolve
- Retinal function must be improved
- The brain must accommodate to those improvements in retinal function



ATSN-201 subretinal gene therapy for XLRS

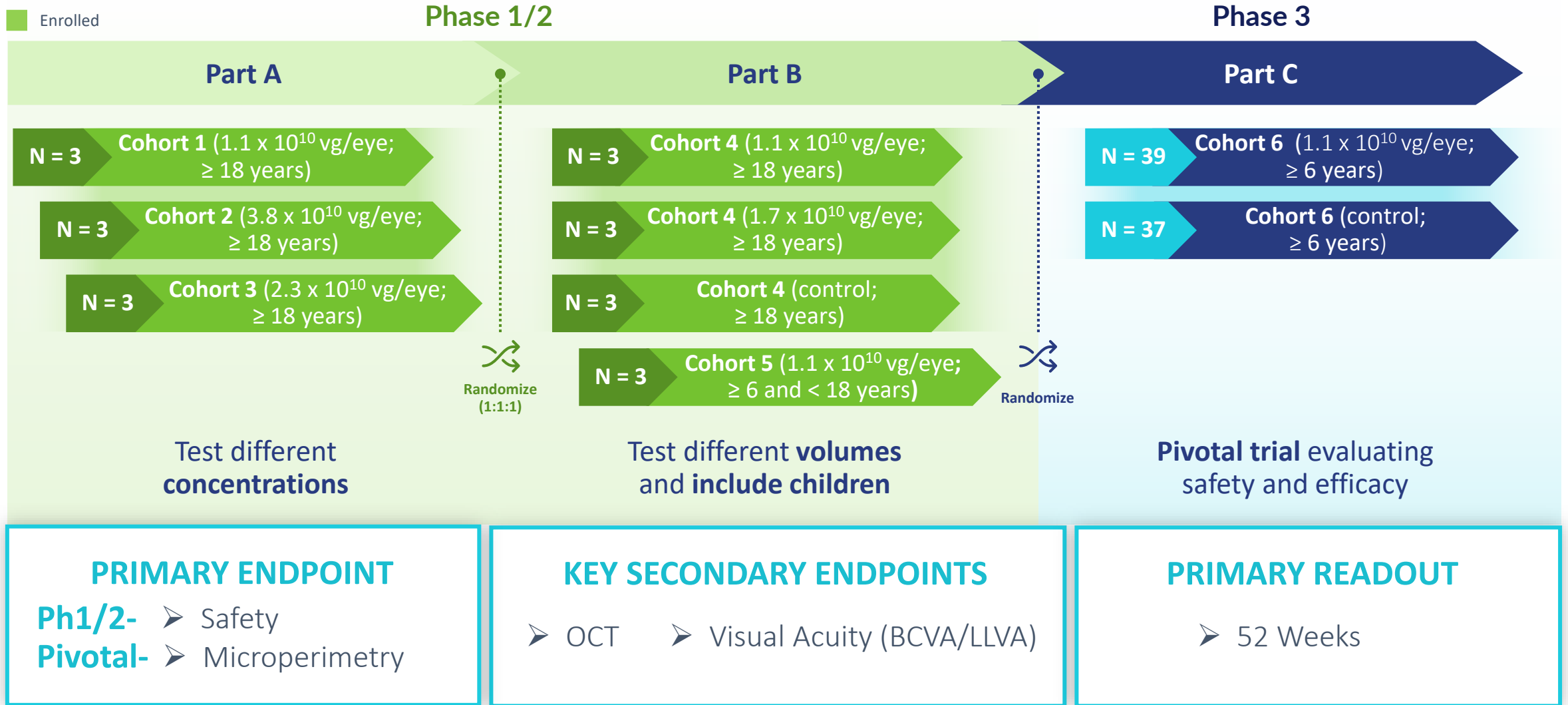
- ATSN-201 (rAAV.SPR-hGRK1-*hRS1syn*) is a subretinal gene therapy product being developed to introduce the functional human retinoschisin (*hRS1*) gene to photoreceptors
- AAV.SPR capsid
- Human rhodopsin kinase promoter
- Synthetic human *RS1* transgene (*hRS1syn*)
- Poly-adenylation signal derived from bovine growth hormone, all flanked by inverted terminal repeats



bGH = bovine growth hormone; hGRK1 = human rhodopsin kinase;
hRS1syn = synthetic human retinoschisin with synonymous point mutations;
ITR = inverted terminal repeat;
poly A = polyadenylation;
rAAV = recombinant adeno-associated virus;
SV40 SD/SA = simian virus 40 splice donor/splice acceptor
WPRE = woodchuck hepatitis virus post-transcriptional regulatory element



LIGHTHOUSE Phase 1/2/3 Clinical Trial Design and Current Status



Demographics and Baseline Characteristics



	Cohort 1 (N=3)	Cohort 2 (N=3)	Cohort 3 (N=3)	Cohort 4-Control (N=3)	Cohort 4-Low (N=3)	Cohort 4-High (N=3)	Cohort 5 (N=3)
Age (Years)							
Median	21	24	26	29	31	43	12
Range (Min, Max)	(18, 26)	(18, 60)	(24, 31)	(23, 41)	(23, 49)	(19, 46)	(8, 12)
Gender, N							
Female	0	0	0	0	0	0	0
Male	3	3	3	3	3	3	3
Race, N							
White	2	3	2	2	3	2	3
Multiple	0	0	1	1	0	1	0
Unknown	1	0	0	0	0	0	0
Study Eye BCVA, Snellen							
Median	20/50	20/100	20/100	20/100	20/80	20/80	20/100
Range (Min, Max)	(20/50, 20/160)	(20/50, 20/100)	(20/40, 20/125)	(20/80, 20/200)	(20/40, 20/100)	(20/40, 20/80)	(20/63, 20/100)

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Summary of Results from Subjects in Cohorts 1-3

Part A

N = 3 Cohort 1 (1.1×10^{10} vg/eye;
 ≥ 18 years)

N = 3 Cohort 2 (3.8×10^{10} vg/eye;
 ≥ 18 years)

N = 3 Cohort 3 (2.3×10^{10} vg/eye;
 ≥ 18 years)

Test different
concentrations

PRIMARY ENDPOINT

- Safety and Tolerability

KEY SECONDARY ENDPOINTS

- Microperimetry
- Visual Acuity (BCVA/LLVA)
- Optical Coherence Tomography (OCT)

PRIMARY READOUT

- 52 Weeks



Cohorts 1-3 Safety



Data cutoff: 22 July 2025

- **Total of 85 TEAEs reported**
 - 82 Grade 1-2 in severity
 - 46 related to surgical procedure
- **No treatment-related SAEs**
 - 1 SAE of fever of unknown origin with negative workup (7 months after treatment)
- **Subretinal deposits at high (N=3) and mid doses (N=1) improved with transient reintroduction of topical or oral corticosteroid treatment**
- **No DLTs and no instances of macular hole formation or retinal detachment**
- **No subjects have discontinued** from the study

Data include: Cohorts 1 through 18 months, Cohort 2 through 12 months and Cohort 3 through 9 months

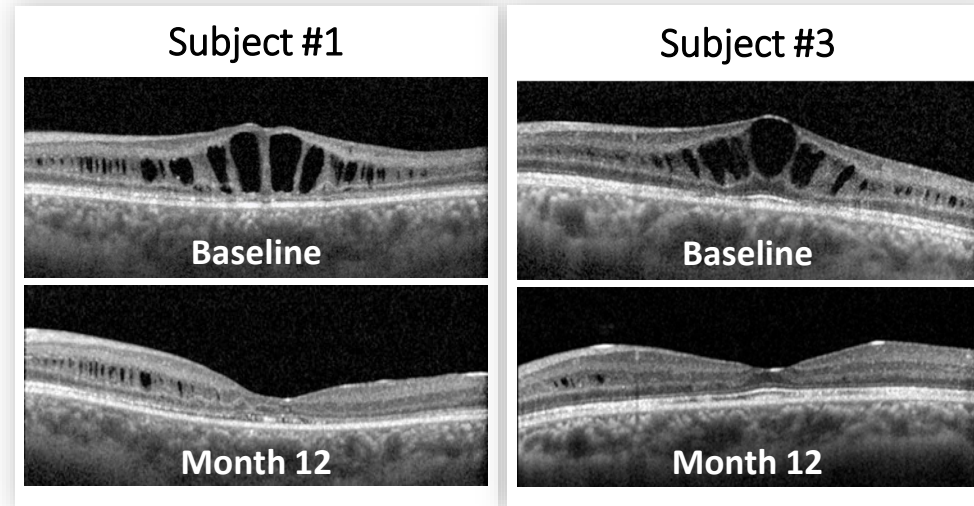
	Cohort 1 N=3	Cohort 2 N=3	Cohort 3 N=3	Total N=9
# of Events				
Any TEAE	29	30	26	85
Any Serious TEAE	1	0	0	1
Any Severe TEAE	1	2	0	3
Severity				
Grade 1	21	15	19	55
Grade 2	7	13	7	27
Grade 3	1	2	0	3
Grade 4 or 5	0	0	0	0
Related to ATSN-201				
Possibly / Probably / Definitely Related	3	9	6	18
Not Related / Unlikely to be Related	26	21	20	67
Related to Surgical Procedure				
Possibly / Probably / Definitely Related	20	17	9	46
Not Related / Unlikely to be Related	9	13	17	39



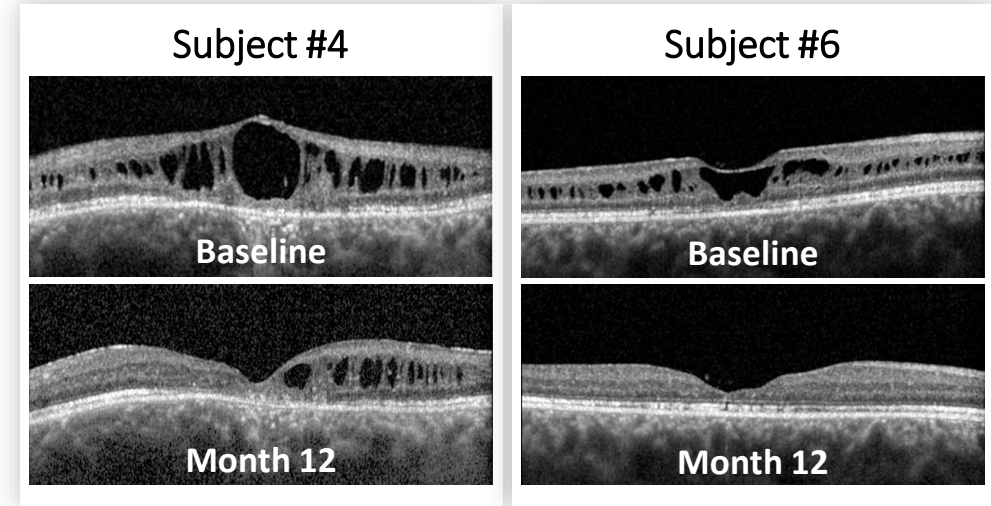
Cohorts 1-3: Foveal schisis closure in 7/9 treated eyes



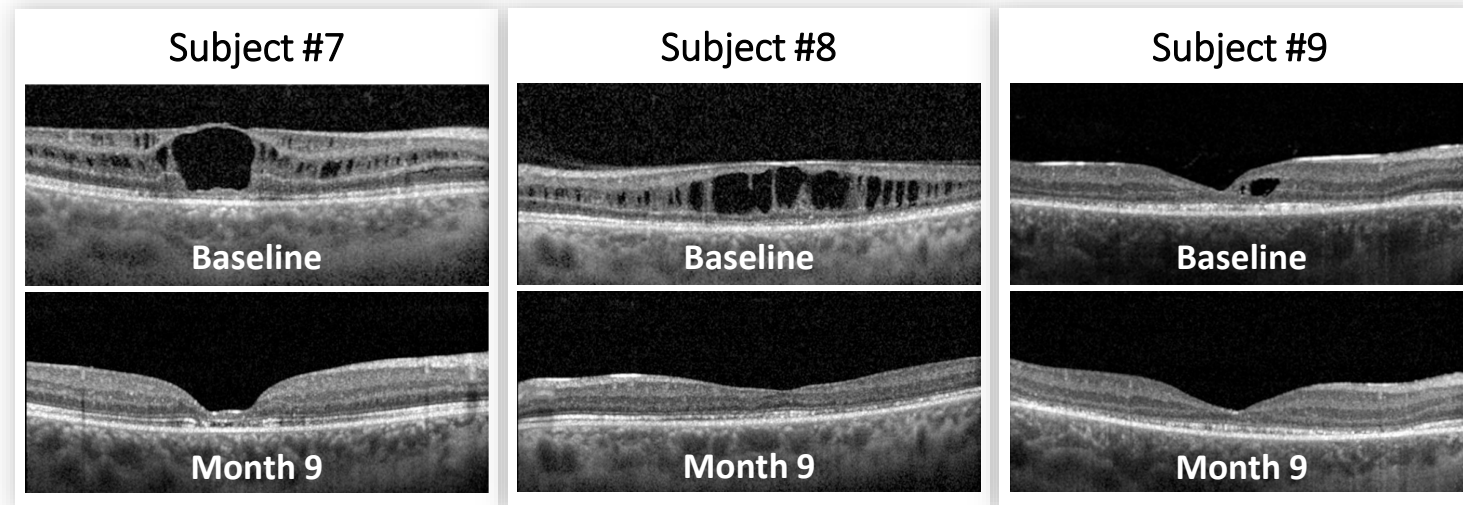
Cohort 1 (Low Dose)



Cohort 2 (High Dose)



Cohort 3 (Mid Dose)



For the 2 treated eyes without foveal schisis closure:

- 1 had blebs placed further in the **periphery**
- 1 developed **ERM** following intra-operative laser



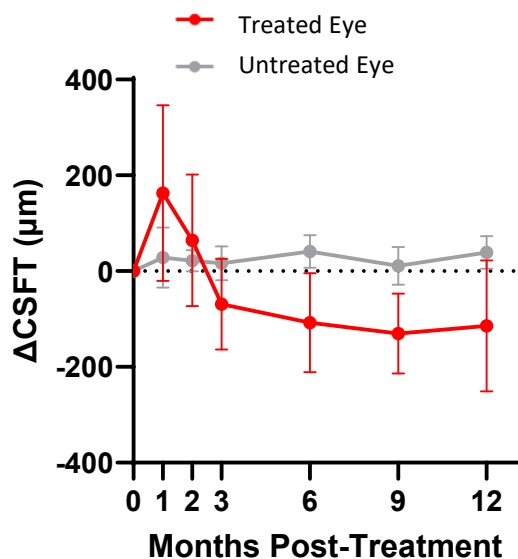
Cohorts 1-3: Treated eyes show greater improvements in visual function



All data include: Cohorts 1 and 2 through 12 months and Cohort 3 through 9 months

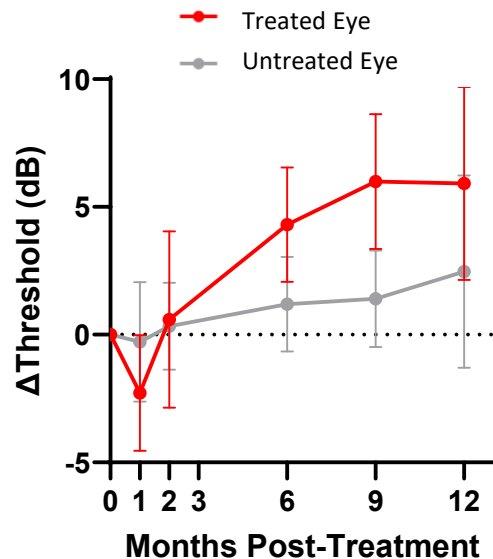
OCT

Change in retinal thickness over time (all cohorts)



Microperimetry*

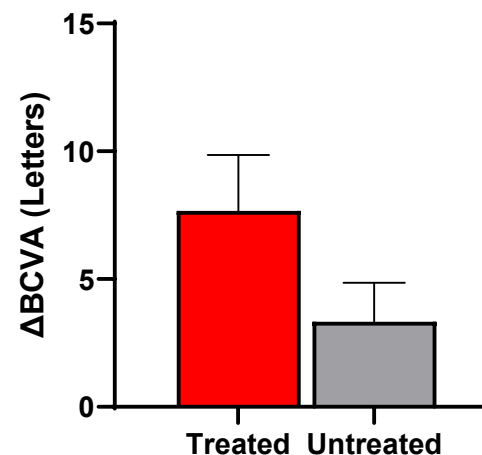
Change in retinal sensitivity over time (all cohorts)



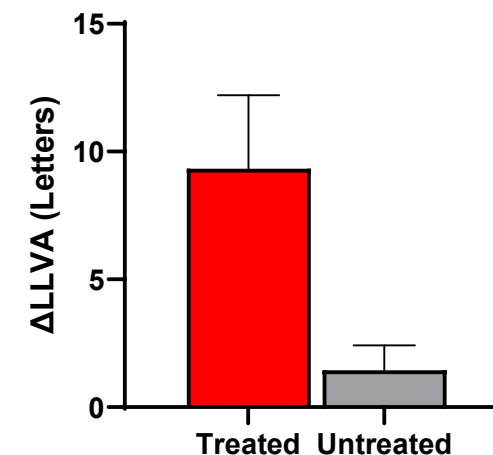
*MP threshold calculated as the mean sensitivity across the subset of central 16 loci with baseline > 0 dB and ≤ 19 dB

Visual Acuity

Change in BCVA for all cohorts combined

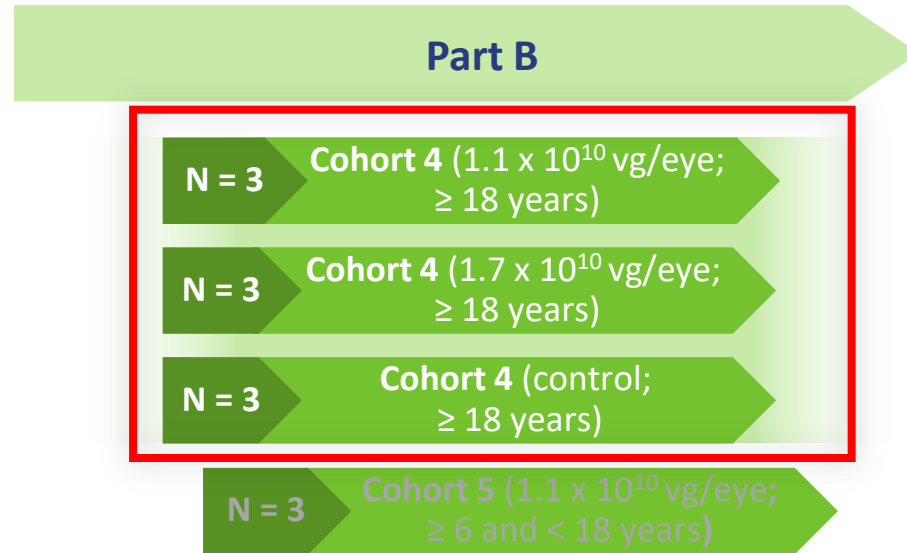


Change in LLVA for all cohorts combined





Update on Safety and Efficacy from Subjects in Cohort 4



Test different **volumes in adults**

PRIMARY ENDPOINT

- Safety and Tolerability

KEY SECONDARY ENDPOINTS

- Microperimetry
- Visual Acuity (BCVA/LLVA)
- Optical Coherence Tomography (OCT)

PRIMARY READOUT

- 52 Weeks

➤ The following is an interim data cut



Cohort 4: Safety



Data cutoff: 13 February 2026

- **Total of 35 TEAEs reported**
 - All Grade 1 or 2 in severity
 - 17 related to surgical procedure
- **No SAEs**
- **Subretinal deposits in high volume (N=3) and low volume (N=1) subjects**
 - 3 instances started on Day 1
 - 1 instance (high volume) started on Day 12 and improved with extended steroid treatment
- No instances of macular hole formation or retinal detachment
- **No subjects have discontinued** from the study

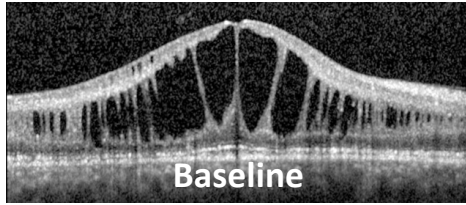
	High Volume N=3	Low Volume N=3	Control N=3	Total N=9
# of Events				
Any TEAE	22	11	2	35
Any Serious TEAE	0	0	0	0
Any Severe TEAE	0	0	0	0
Severity				
Grade 1	12	9	2	23
Grade 2	10	2	0	12
Grade 3	0	0	0	0
Grade 4 or 5	0	0	0	0
Related to ATSN-201				
Possibly / Probably / Definitely Related	5	2	0	7
Not Related / Unlikely to be Related	17	9	2	28
Related to Surgical Procedure				
Possibly / Probably / Definitely Related	14	3	0	17
Not Related / Unlikely to be Related	8	8	2	18

Cohort 4: Foveal schisis closure in 4/6 treated subjects at Month 6

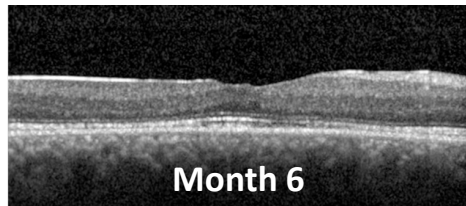


Low Volume (150 μ L, 1.1E10 vg/eye)

Subject L1

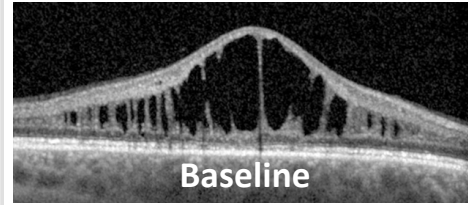


Baseline

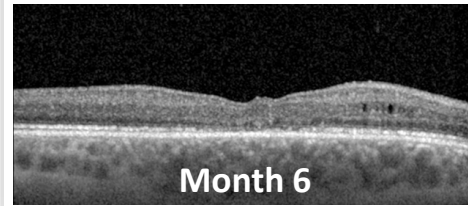


Month 6

Subject L2

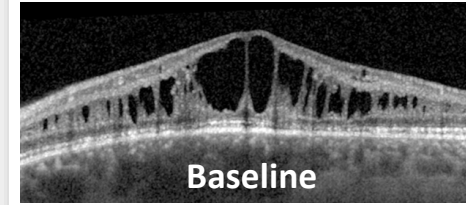


Baseline

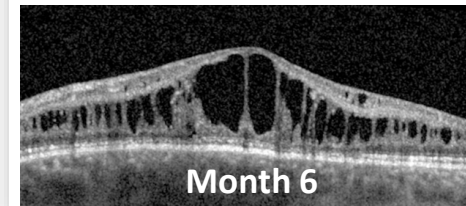


Month 6

Subject L3



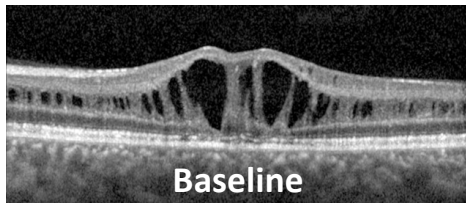
Baseline



Month 6

High Volume (225 μ L, 1.7E10 vg/eye)

Subject H1

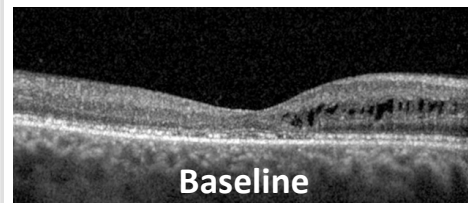


Baseline

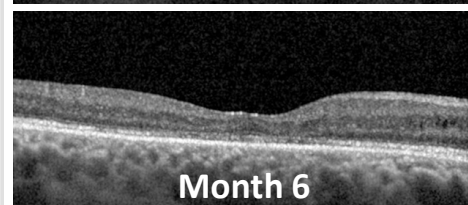


Month 6

Subject H2

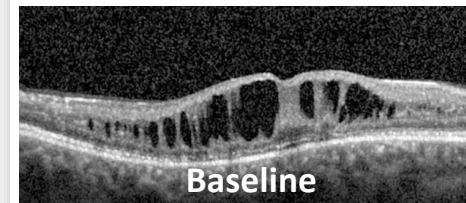


Baseline

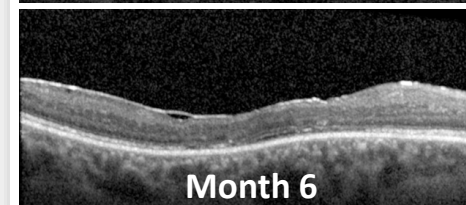


Month 6

Subject H3



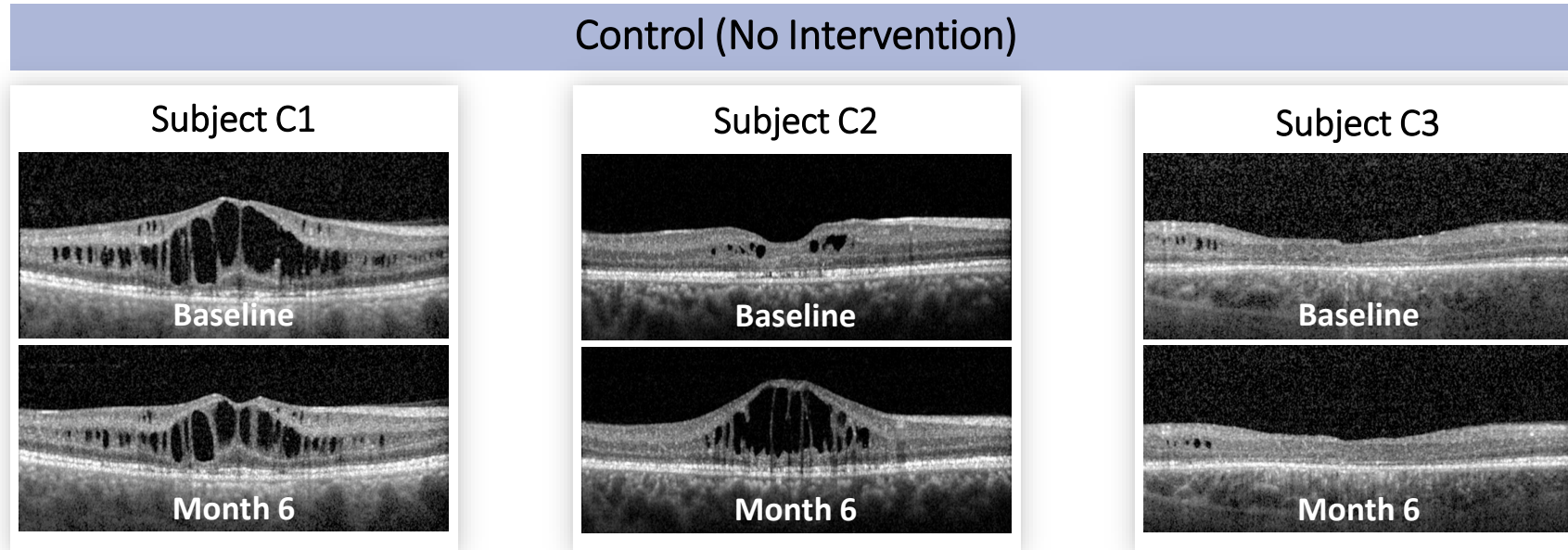
Baseline



Month 6



Cohort 4: Control subjects did not demonstrate foveal schisis closure

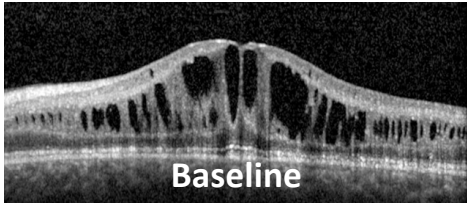


Cohort 4: Untreated eyes did not demonstrate foveal schisis closure

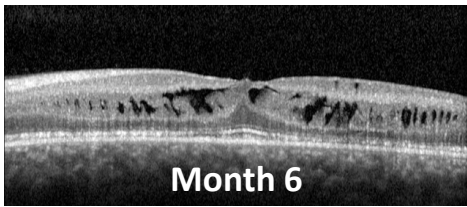


Low Volume (Untreated Eye)

Subject L1

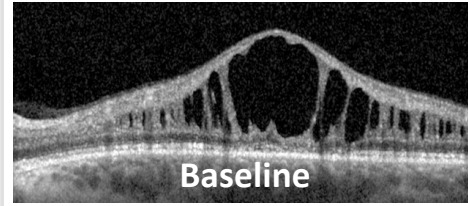


Baseline

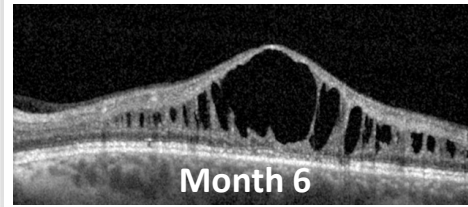


Month 6

Subject L2

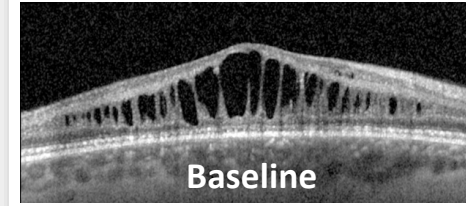


Baseline

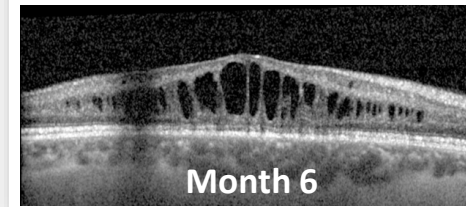


Month 6

Subject L3



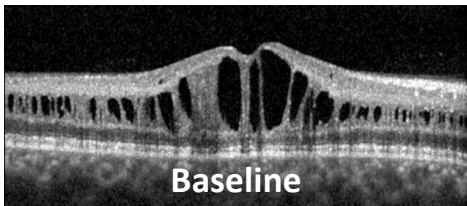
Baseline



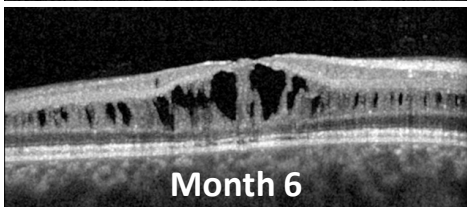
Month 6

High Volume (Untreated Eye)

Subject H1

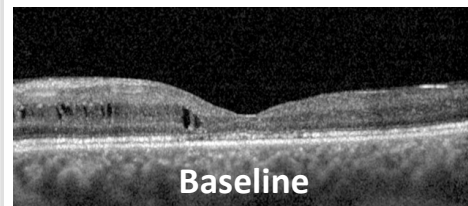


Baseline

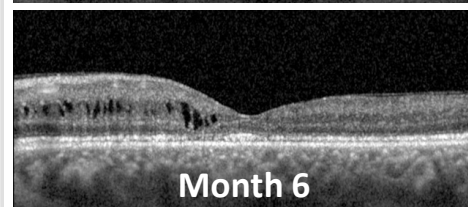


Month 6

Subject H2

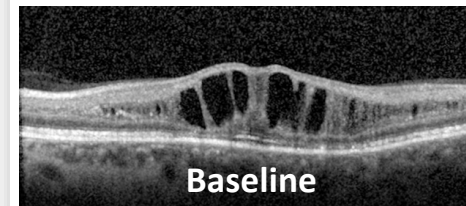


Baseline

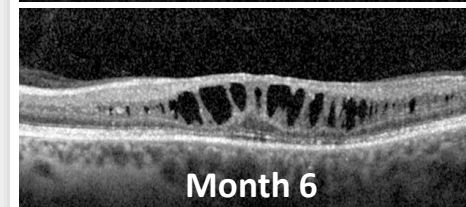


Month 6

Subject H3



Baseline



Month 6



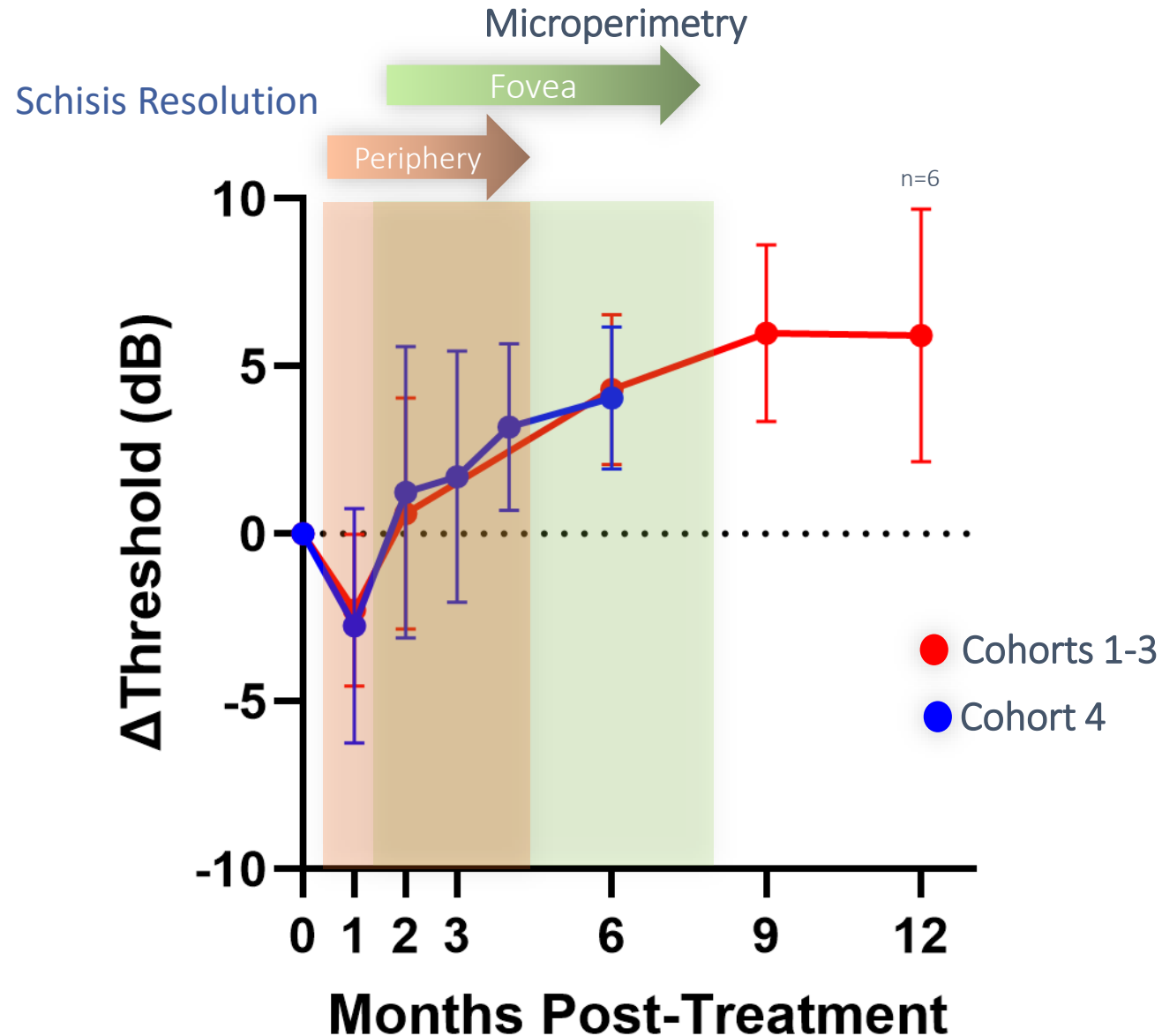
Closure of foveal schisis corresponds with functional improvements



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Kinetics of therapy are remarkably similar across cohorts

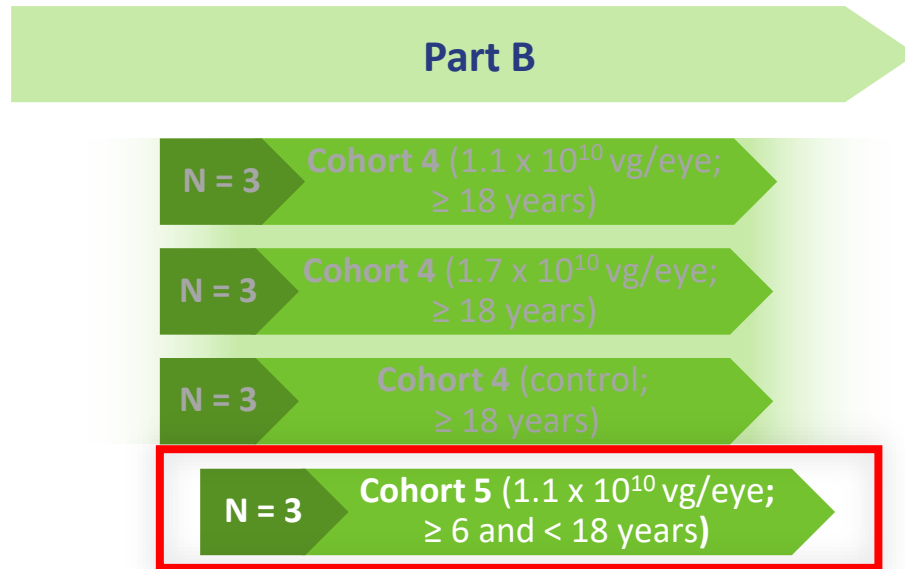


- Data cut @ 9 months for Cohort 3.
 - Cohorts 1 - 3 had 4 / 9 subjects meet MP endpoint at 9 months
 - ARVO Talk: Thursday, May 7, 12:00-12:15 p.m. Lesley Everett, M.D., Ph.D.
- Structural improvements from ATSN-201 precede functional gains
- Schisis closure within peripheral blebs precedes foveal schisis closure
- Functional improvements continue beyond foveal schisis closure
- Results in line with RS1 biology

Data include: Cohorts 1 and 2 through 12 months, Cohort 3 through 9 months, and Cohort 4 through 6 months



Update on Safety from Pediatric Subjects in Cohort 5



Test optimal volume/dose in **children**

PRIMARY ENDPOINT

- Safety and Tolerability

KEY SECONDARY ENDPOINTS

- Microperimetry
- Visual Acuity (BCVA/LLVA)
- Optical Coherence Tomography (OCT)

PRIMARY READOUT

- 52 Weeks



Cohort 5: Safety



Data cutoff: 13 February 2026

- **Total of 8 TEAEs reported**
 - All Grade 1 or 2 in severity
 - 7 related to surgical procedure
- **No SAEs**
- **Minimal inflammation** (transient, mild post-surgical vitreous cells) has resolved
- No instances of subretinal deposits, macular hole formation, or retinal detachment
- **No subjects have discontinued** from the study

**Cohort 5
N=3**

# of Events	
Any TEAE	8
Any Serious TEAE	0
Any Severe TEAE	0
Severity	
Grade 1	7
Grade 2	1
Grade 3	0
Grade 4 or 5	0
Related to ATSN-201	
Possibly / Probably / Definitely Related	2
Not Related / Unlikely to be Related	6
Related to Surgical Procedure	
Possibly / Probably / Definitely Related	7
Not Related / Unlikely to be Related	1



Testimonials from LIGHTHOUSE PIs



“

He told me that he was assigned to sit at the back of the classroom last week (normally doesn't sit there) and he was able to see up front and things in the class he's never seen from that position before

“

He took up rock climbing in the past year and shared that participating in this study was a positive event for him in terms of hope for the future, new goals, and outlook on his life

“

Starting a few months after surgery, he reported that the vision in the surgical eye was 'like looking through an HD-TV' and that colors were more vivid and images more crisp.

“

Driving at night (or even the idea) was previously a source of great anxiety. Now, it's no big deal and he can do so easily

