INTRAVITREAL INJECTION OF ALLOGENEIC HUMAN RETINAL PROGENITOR CELLS (jCELL) FOR TREATMENT OF RETINITIS PIGMENTOSA: *RESULTS FROM THE PHASE 2B TRIAL*

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- CLINICAL RESEARCH
  - Alcon, Allegro, Allergan, Apellis, Clearside, Genentech, GSK, Ionis, IVERIC bio, jCyte, Novartis, Regeneron
- CONSULTANT
  - Allegro, Allergan, Aprea, Cell Care, Dose, Eyedaptic, Galimedix, Genentech, Glaukos, Interface Biologics, IVERIC bio/Ophthotech, jCyte, Novartis, Oculis, Regeneron, Revana, Ripple Therapeutics, Theravance Biopharma

Summary

- **Single Intravitreal injection of jCell** (allogeneic Human Retinal Progenitor Cells) demonstrated promising results in visual acuity improvement in the per protocol population with the 6M dose (+7.4 letters) compared to sham (+2.8 letters) at Month 12 in a Phase 2b study
- Identified **target population** showed clinically significant improvement in visual acuity in the 6M dose (+16.3 letters) as compared to sham (+1.9 letters) at Month 12
  - All **functional endpoints** showed similar trends
- Intravitreal administration of jCell was **well tolerated with a good safety profile**
- These results support development of
  - **Phase 2 study**: subjects from this study will be re-dosed
  - **Phase 3 study**
- FDA granted Regenerative Medicine Advance Therapy **(RMAT) designation** for jCell

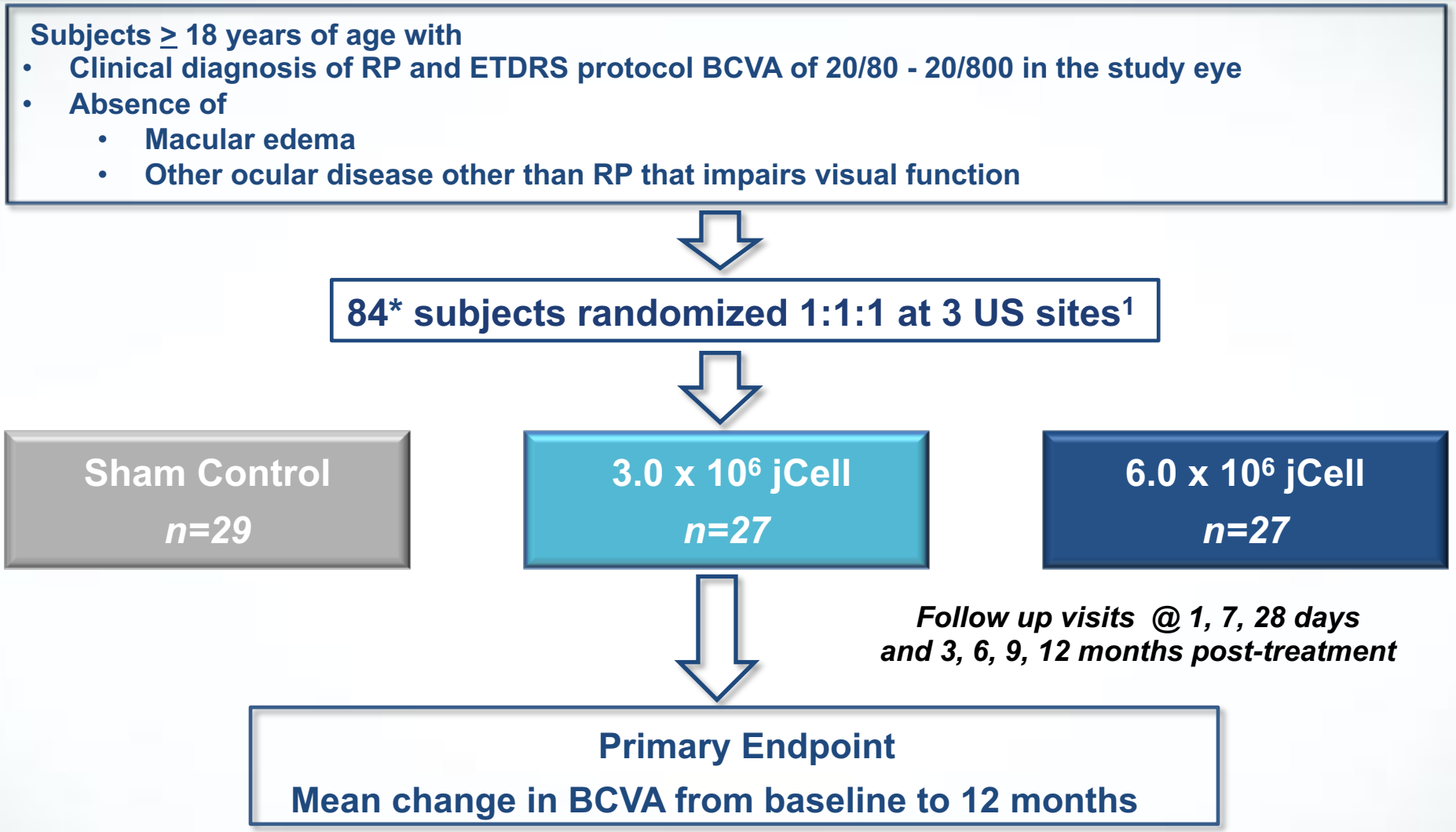
Retinitis Pigmentosa

- Diseases caused by genetic mutations resulting in progressive loss of photoreceptor cells (rods then cones), pathological migration of retinal pigment epithelial cells and other degenerative changes in the retina
- Rare diseases that affect 1:4000 individuals (≈ 1.9MM worldwide)
- Often diagnosed in childhood or adolescence with most patients rendered legally blind by middle age
- Beyond for a small subset of patients with RPE65 mutations, there is no current treatment for retinitis pigmentosa
    - Gene therapy (voretigene neparvovec-rzyl) targets this specific mutation

Human Retinal Progenitor Cells (hRPC): *jCell*

- **Intravitreal injection of *allogeneic hRPC (jCell)*** is a novel approach for treatment of RP
- RPCs provide **sustained expression** of **neurotrophic factors** that are mediators of neuronal survival
  - Transplanted RPCs modulate the ocular microenvironment via neurotrophic factors to **reduce photoreceptor death** and **promote function of surviving photoreceptors**
- jCell's **paracrine mechanism** may result in significant slowing of host photoreceptor loss, **agnostic to genetic subtype**
  - Phase 1/2a dose escalation 12-month trial demonstrated a favorable safety profile and suggestion of treatment benefit

Study Design Phase 2b



*1 subject received 4.0 x 10^6 dose per the original study design; protocol amendment changed high dose group from 4.0 x 10^6 to 6.0 x 10^6

[1] UCI /Gavin Herbert Eye Institute, Irvine, CA; Retina Vitreous Associates Medical Group, Los Angeles, CA; Ophthalmic Consultants of Boston, Boston, MA

Per Protocol Population

Randomized Population (n=83)	**Sham** *(n=29)*	**3.0 x 10^6 jCell** *(n=27)*	**6.0 x 10^6 jCell** *(n=27)*
Lost to follow-up, n	1	1	1
Pre-existing ophthalmic conditions meeting pre-specified exclusionary criteria, n	1	2*	1
Medical event unrelated to study treatment precluding Month 12 assessments, n	0	0	1
Different treatment than assignment, n	1	0	1
Per Protocol Population (n=74)	**26 (89.7%)**	**25 (92.6%)**	**23 (85.2%)**

*1 subject that was lost to follow up also had pre-existing ophthalmic conditions meeting pre-specified exclusion criteria

Study Endpoints

Primary Endpoint:

Mean change in ETDRS protocol BCVA from baseline to 12 months

Secondary Endpoints:

- **Low Light Mobility:** Identify the lowest light level at which the patient can functionally navigate the maze – Critical Illumination Level (CIL)
- **Kinetic Visual Field:** Map patient's "islands" of remaining vision to capture total area of field
- **Contrast Sensitivity:** Innovative test that utilizes computer technology to display gratings of various size and contrast
- **Vision Related Quality of Life Questionnaire (VA LV VFQ-48):** Measure visually impaired persons' difficulty in performing daily activities

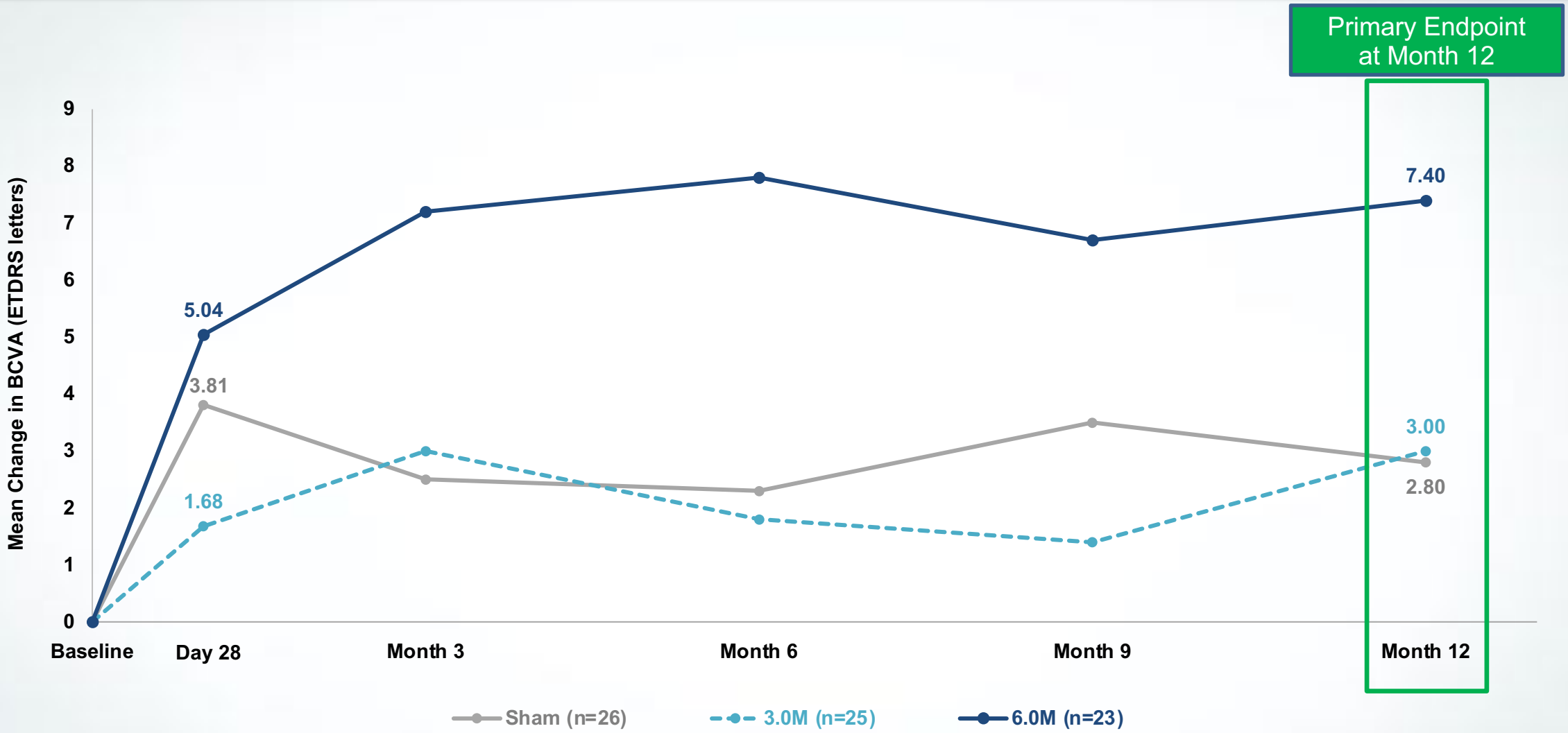
Baseline Characteristics

	Sham *(n=26)*	3.0 x 10^6 jCell *(n=25)*	6.0 x 10^6 jCell *(n=23)*
Age, mean (SD), years	52.3 (12.0)	46.4 (14.8)	41.3 (12.4)
Sex, n (%), female	6 (23.1)	13 (52.0)	10 (43.5)
Race, n (%), White	20 (76.9)	21 (84.0)	17 (73.9)
BCVA, ETDRS letters			
Mean (SD) *Snellen Equivalent*	27.3 (18.4) *~20/320*	29.8 (17.6) *~20/250*	32.5 (16.4) *~20/250*
Range *Snellen Equivalent*	58.0 – 1.0 *~ 20/80 - <20/800*	56.0 – 3.0 *~ 20/80 - <20/800*	54.0 – 2.0 *~ 20/80 - <20/800*

Per Protocol Population (n=74)

Mean Change in Best-Corrected Visual Acuity (*Per Protocol Population*)

Baseline to 12 Months

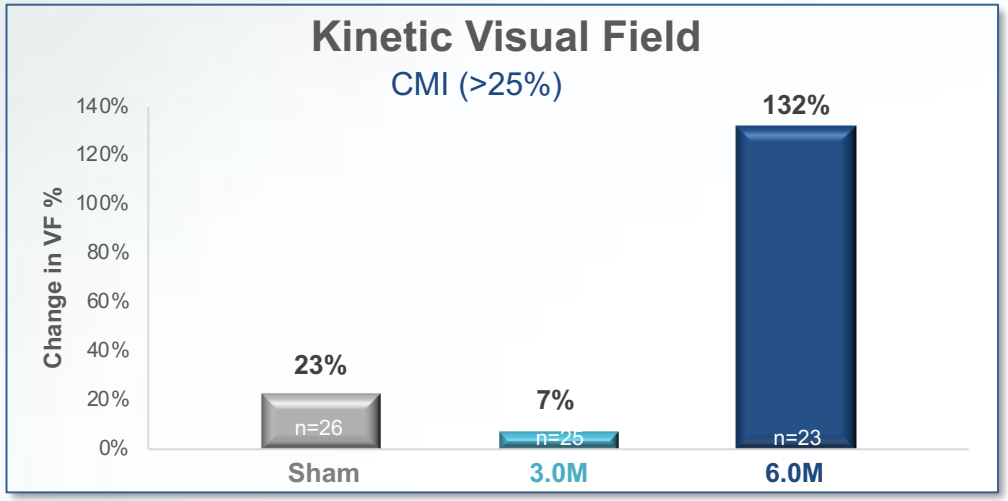


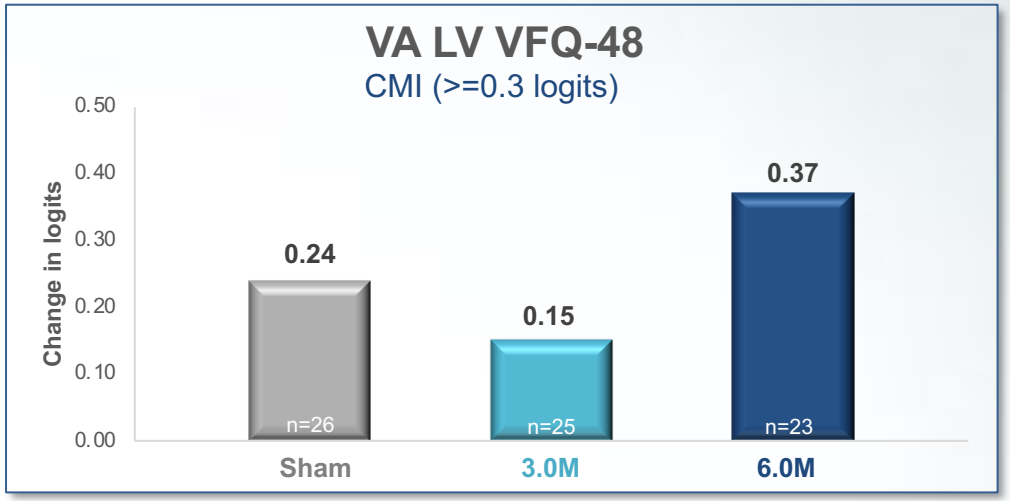
Per Protocol Population (n=74)

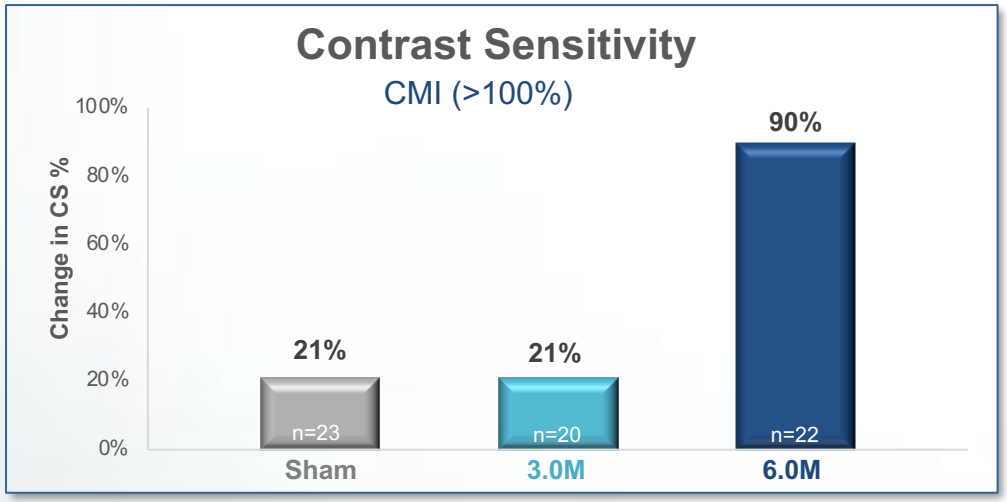
p = 0.10 (6.0M vs sham at month 12)

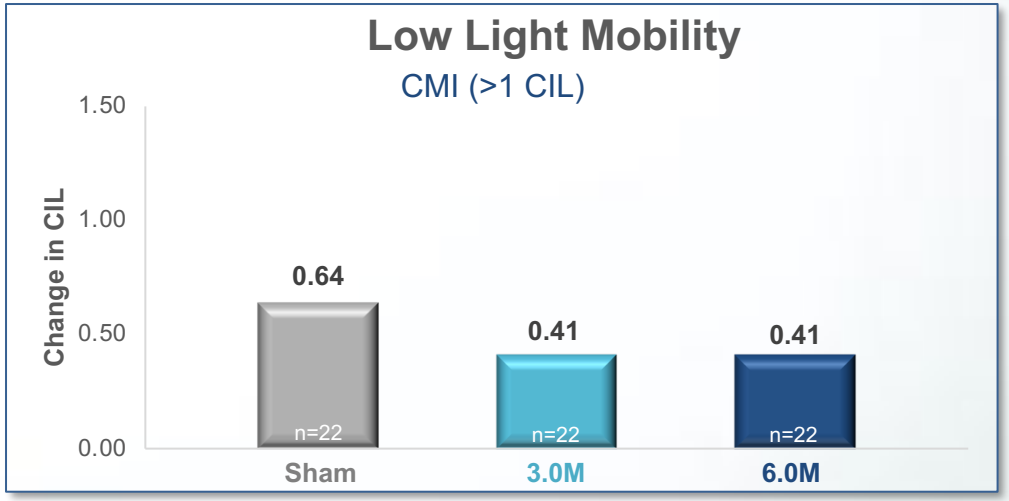
Secondary Outcomes: Mean Change in Visual Function (*Per Protocol Population*)

Baseline to 12 Months





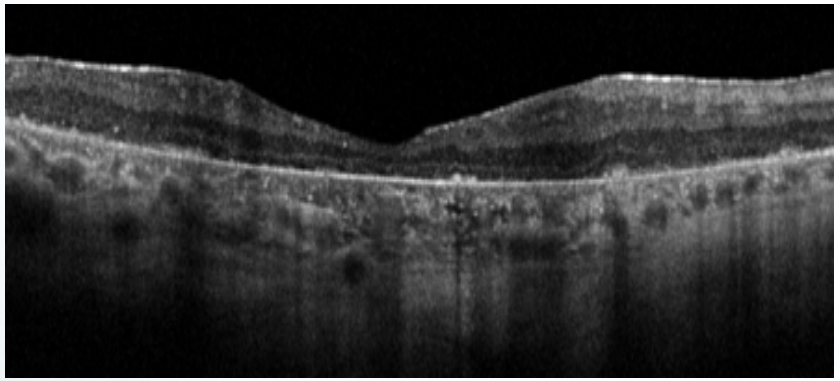


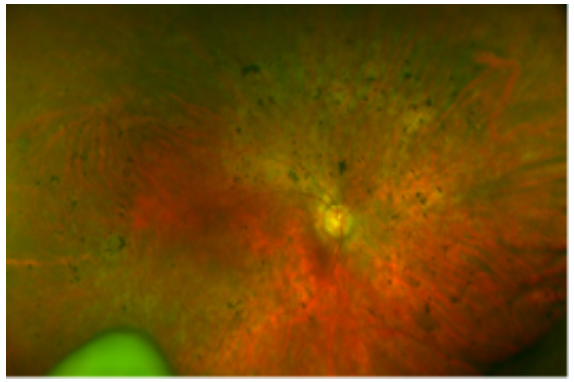


Per Protocol Population (n=74): *Subjects must post a Baseline and Month 12 value to be included in an analysis*
CMI: Clinically Meaningful Improvement based on literature and validation studies (data on file)
None were statistically significant

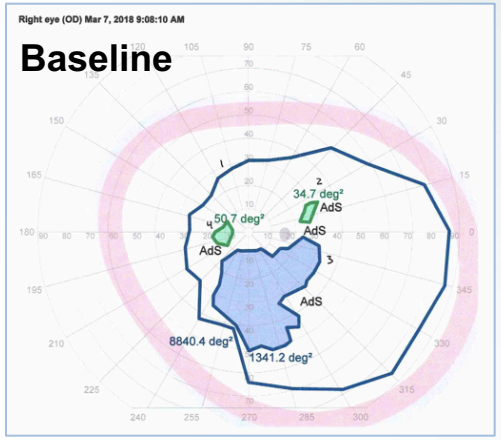
Subject 1: 6.0M, Age 41
Study Eye: OD

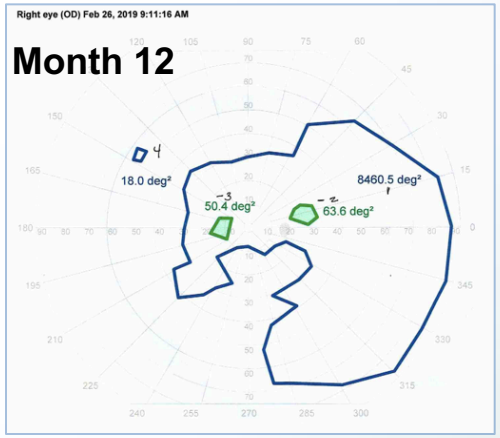
	Baseline	Month 12	Change
BCVA, ETDRS letters *Snellen Equivalent*	36 *~20/200*	54 *~20/80*	+18
Critical Illumination Level, lux	125	63	1 level
Visual Field, area	7414	8365	12.82 %
Contrast Sensitivity, peak	1.9	2.3	18.30 %
VFQ, logit	0.24	0.45	0.2





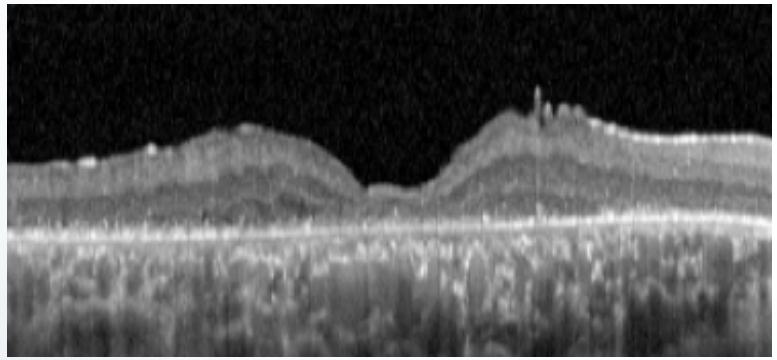
Visual Field

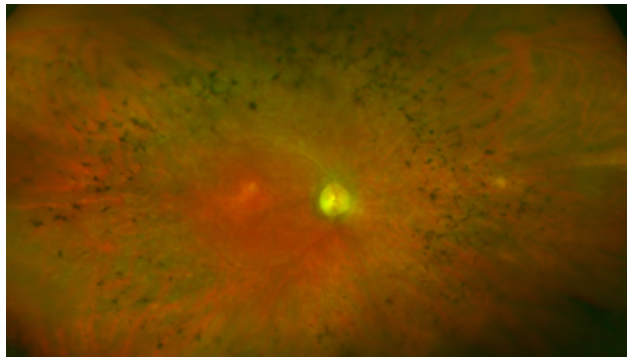




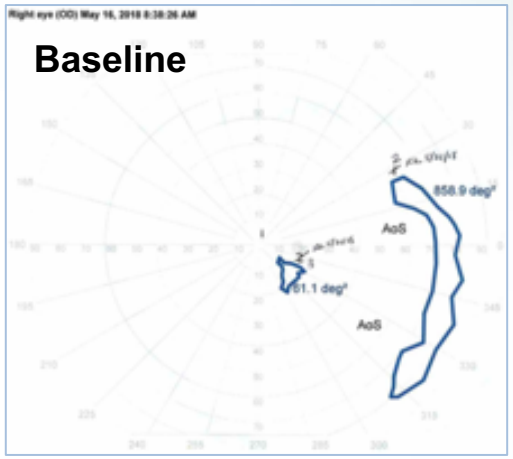
Subject 2: 6.0M group, Age 44
Study Eye: OD

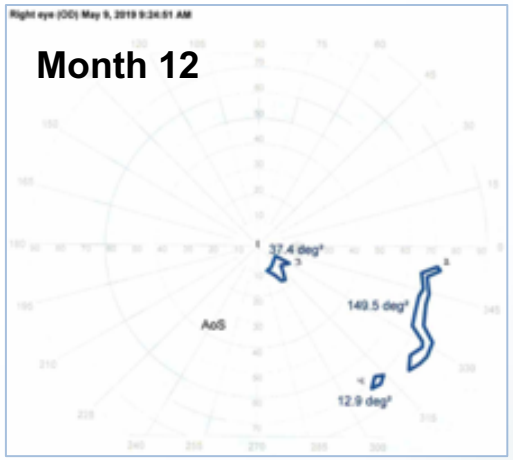
	Baseline	Month 12	Change
BCVA, ETDRS letters *Snellen Equivalent*	13 *~20/640*	8 *~20/800*	*-5*
Critical Illumination Level, lux	Unable (no pass)	Unable (no pass)	n/a
Visual Field, area	920	200	-78.28%
Contrast Sensitivity, peak	1.5	1.3	-12.78%
VFQ, logit	-0.456	-0.498	-0.043





Visual Field



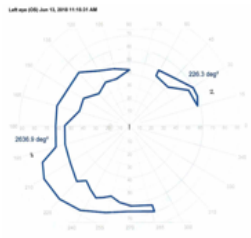


Identification of Target Population

Criteria established for subjects that can't be reliably measured based on literature and validation study*

Inability to maintain fixation

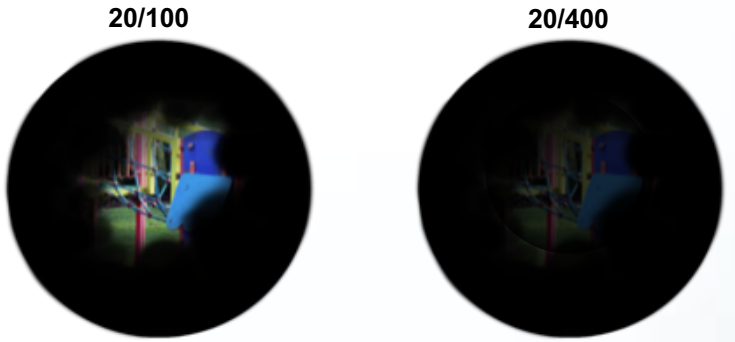
- **No central vision**
  - Peripheral islands or unsteady fixation scotoma/nystagmus unreliable



- **Constricted field <12 degrees**
  - VF Variability, same visit test-retest[1]
    - 19.2% for VF >14 degrees,
    - 32.8% when include subjects with <14 degrees
  - Validation study* (n=20)
    - Mobility test variability in 5 subjects with VF<12 degrees

Study eye significantly worse than fellow eye

- **>3 lines difference**
  - Worse eye is variable and can improve in function when it has been suppressed from disuse[2,3,4,5,6]



>15 letters difference between eyes

[1]Bittner et al 2011; [2]Kong et al, 2017; [3]Sunness et al 2000; [4]Sunness et al 2014; [5]Kim et al, 1996; [6]Cotter et al, 2006

*Data on file

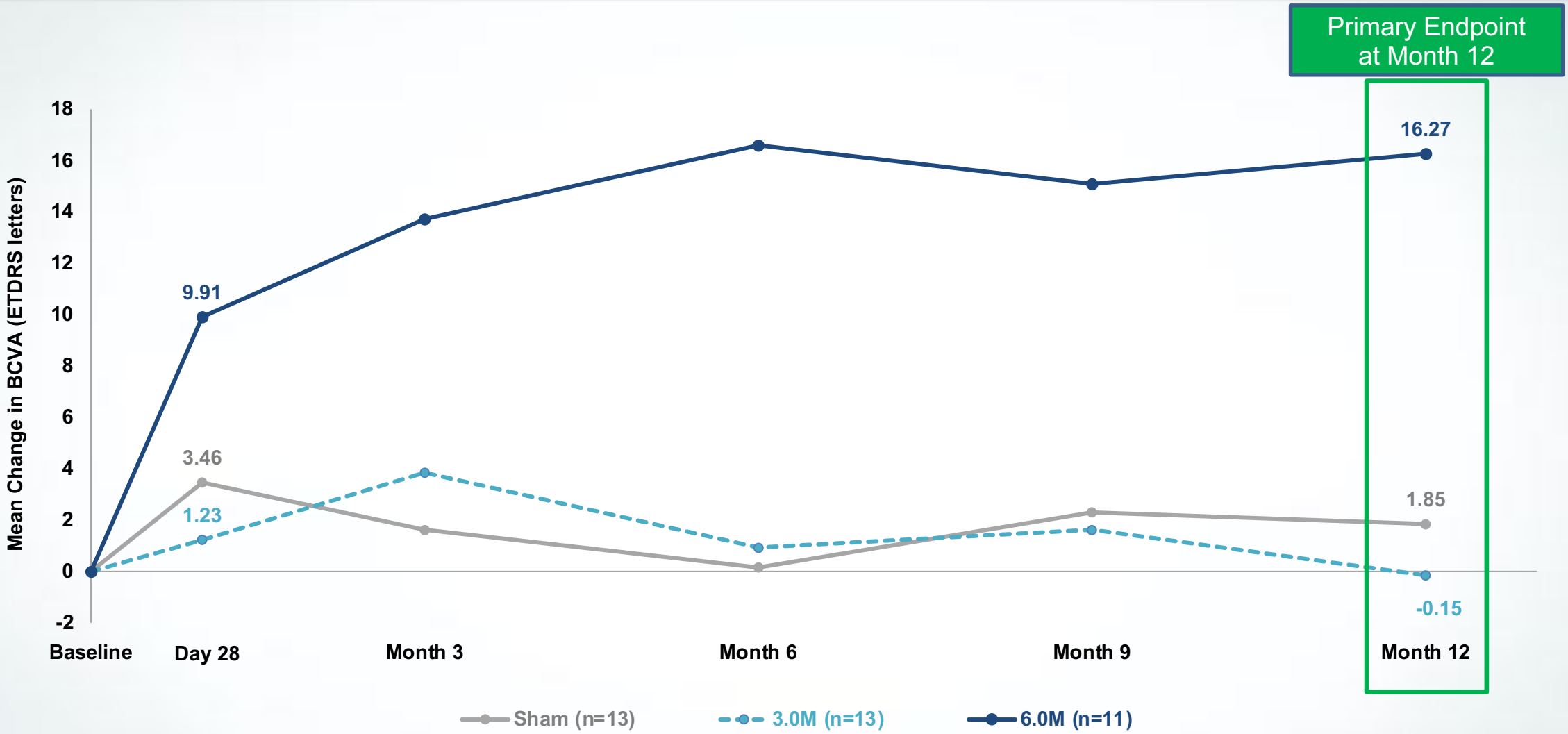
Target Population

Per protocol population (n=74)	**Sham** *(n=26)*	**3.0 x 10^6 jCell** *(n=25)*	**6.0 x 10^6 jCell** *(n=23)*
No central vision, n	7	3	3
Constricted field <12 degrees, n	4	1	4
>3 lines difference between fellow eye and study eye, n	5	8	7
Target Population (n=37)	**13 (50.0%)**	**13 (52.0%)**	**11 (47.8%)**

Subjects meeting multiple criteria: 3 subjects in sham group; 2 subjects in 6M group

Mean Change in Best-Corrected Visual Acuity (Target Population)

Baseline to 12 Months

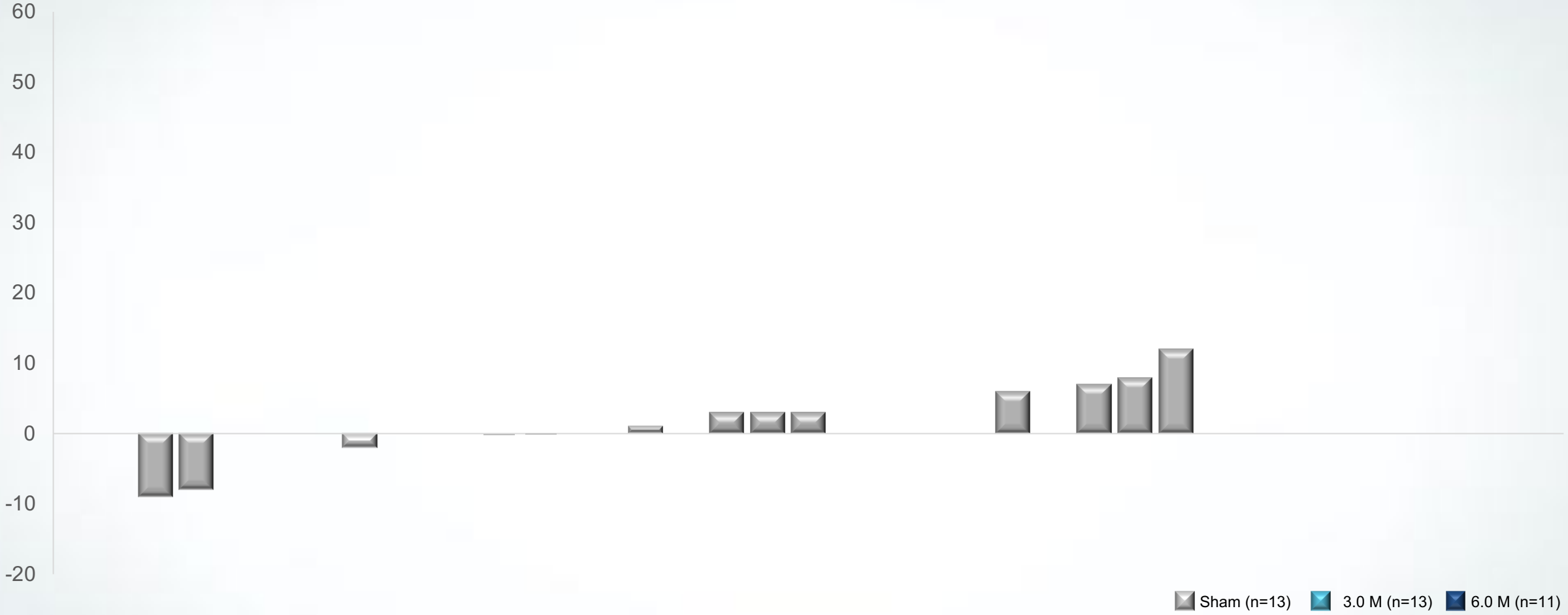


Target Population (n=37)

p < 0.01 (6.0M vs sham at month 12)

Change in Best-Corrected Visual Acuity *(Target Population)*

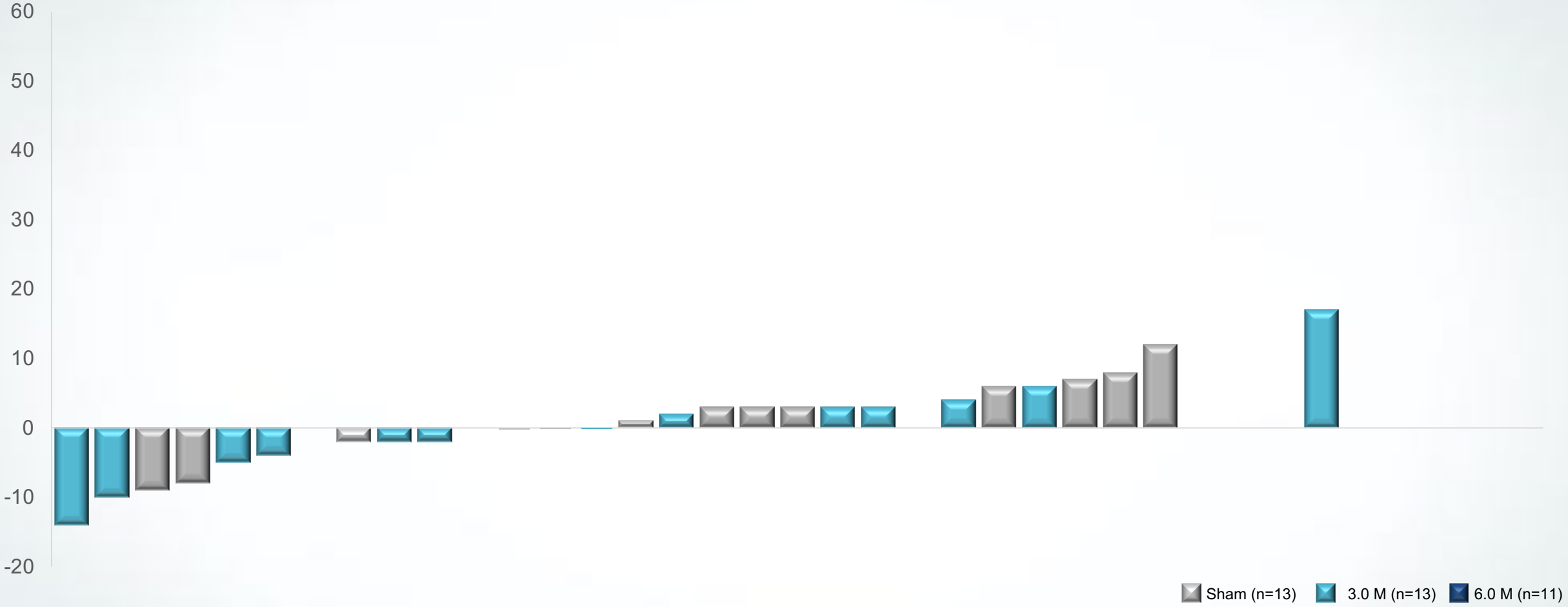
Baseline to 12 Months



Target Population (n=37)

Change in Best-Corrected Visual Acuity *(Target Population)*

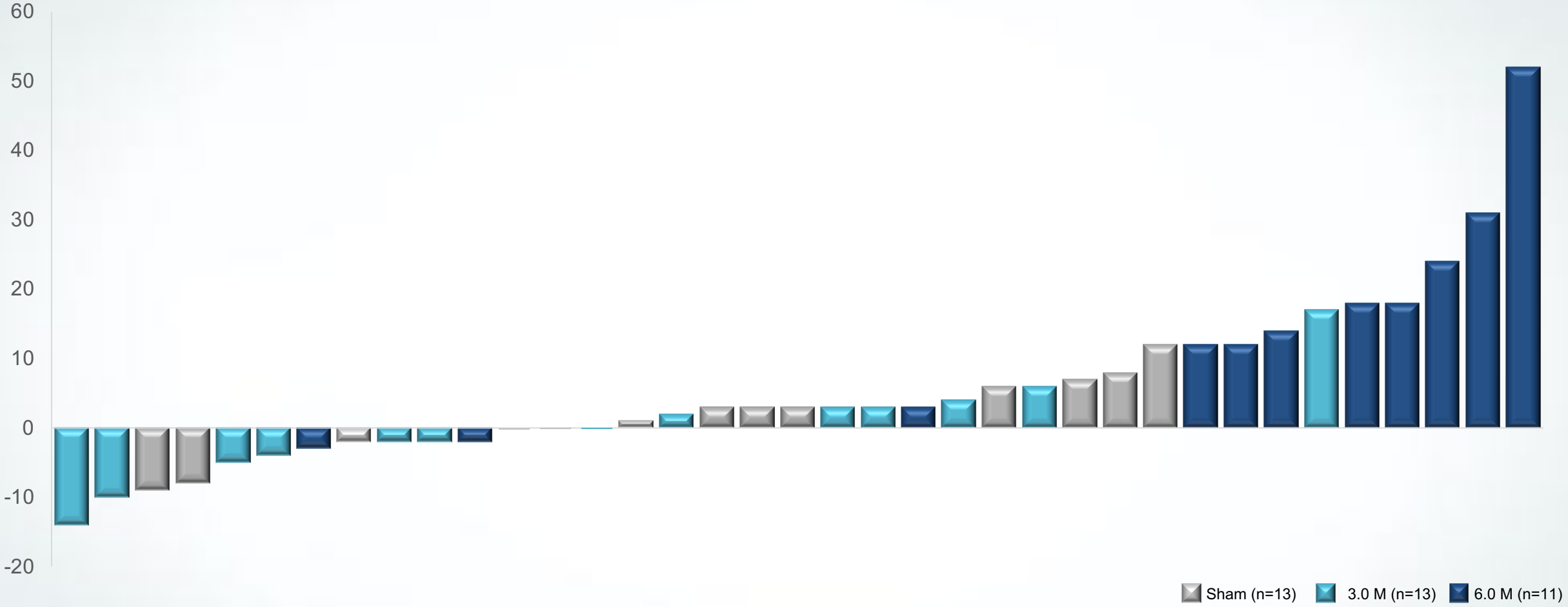
Baseline to 12 Months



Target Population (n=37)

Change in Best-Corrected Visual Acuity *(Target Population)*

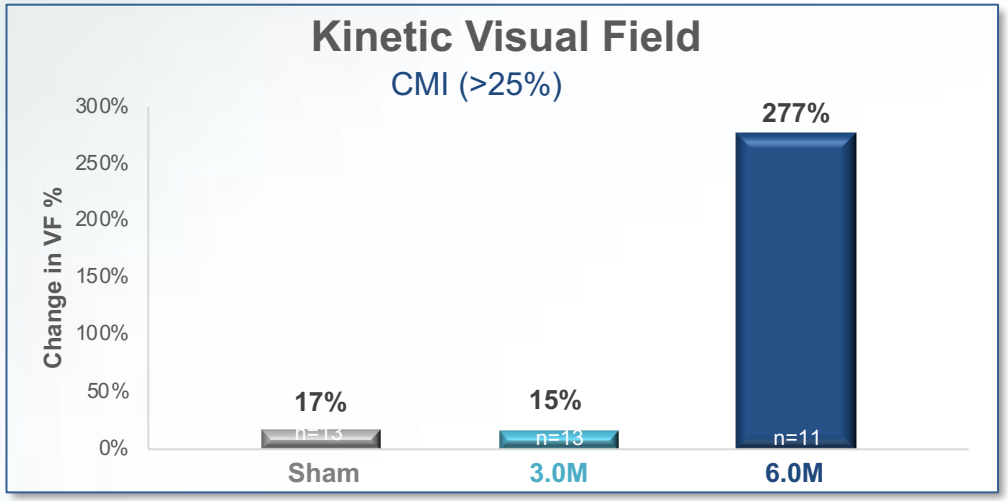
Baseline to 12 Months

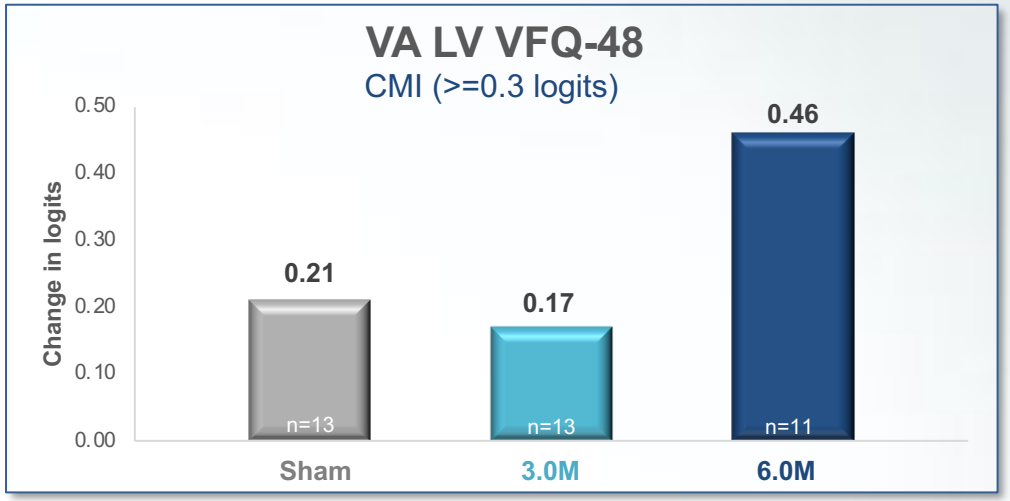


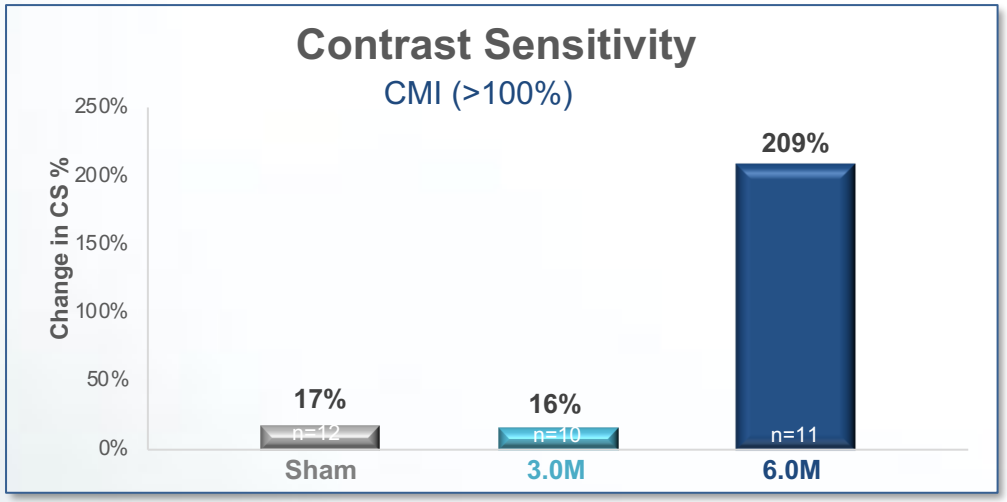
Target Population (n=37)

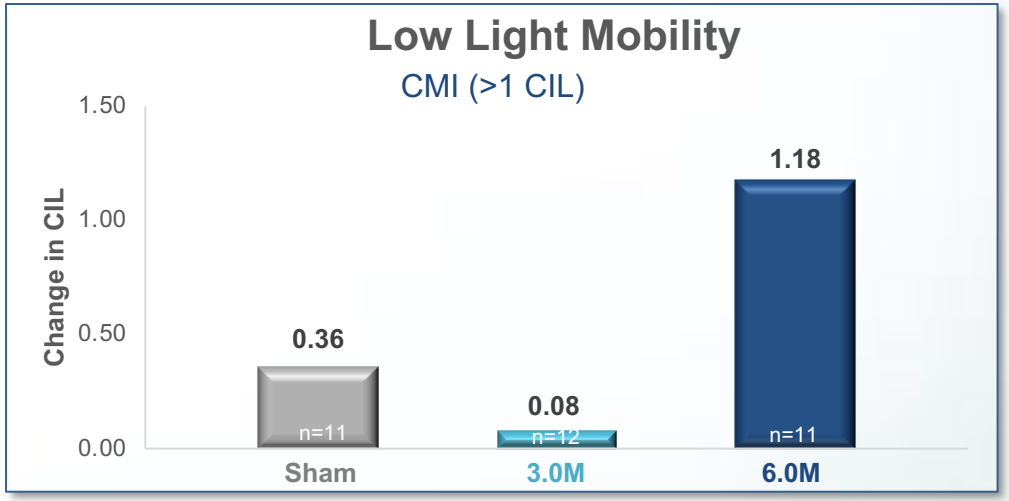
Mean Change in Visual Function *(Target Population)*

Baseline to 12 Months









Target Population (n=37)

Subjects must post a Baseline and Month 12 value to be included in an analysis

CMI: Clinically Meaningful Improvement based on literature and validation studies (data on file)

None were statistically significant

Safety:
Treatment Emergent Adverse Events Related To Study Drug Through Month 12

	Sham *(N=29)*	3.0 x 10^6 jCell *(N= 27)*	6.0 x 10^6 jCell *(N= 27)*
Subjects with at least one drug-related TEAE, n (%)	**7 (24.1%)**	**14 (51.9%)**	**13 (48.1%)**
Preferred Term			
Altered visual depth perception	0	0	1 (3.7 %)
Anterior chamber flare	0	0	3 (11.1 %)
Anterior chamber inflammation	0	0	1 (3.7 %)
Conjunctival hemorrhage	5 (17.2 %)	8 (29.6 %)	6 (22.2 %)
Cystoid macular edema	0	1 (3.7 %)	0
Eye irritation	0	0	2 (7.4 %)
Eye pain	0	3 (11.1 %)	1 (3.7 %)
Intraocular Pressure Increased	1 (3.4 %)	1 (3.7 %)	1 (3.7 %)
Iridocyclitis	0	1 (3.7 %)	0
Iris adhesions	0	1 (3.7 %)	1 (3.7 %)
Iris disorder	0	0	1 (3.7 %)
Lenticular opacities	0	1 (3.7 %)	0
Nystagmus	0	1 (3.7 %)	0
Ocular hyperaemia	0	0	1 (3.7 %)
Ocular hypertension	0	1 (3.7 %)	0
Post procedural discomfort	0	2 (7.4%)	1 (3.7 %)
Pruritus	0	1 (3.7 %)	0
Punctate keratitis	0	1 (3.7 %)	0
Retinal detachment	0	1 (3.7 %)	0
Uveitis	0	1 (3.7 %)	0
Visual acuity reduced	1 (3.4 %)	1 (3.7 %)	0
Vitreous adhesions	0	1 (3.7 %)	0
Vitreous fibrin	0	0	1 (3.7 %)
Vitreous floaters	0	1 (3.7 %)	0
Vitritis	0	1 (3.7 %)	0

Subject treated with 4M is not included; subject reported a few mild TEAEs including eye pain, photophobia, vision blurred, iris adhesions and iridocyclitis

Safety:
Intraocular Inflammation Through Month 12 Visit

	Sham *(N=29)*	3.0 x 10^6 jCell *(N= 27)*	6.0 x 10^6 jCell *(N= 27)*
Number of subjects with Intraocular Inflammation, n (%)			
Anterior chamber flare	0	0	3 (11.1 %)
Anterior chamber inflammation	0	0	1 (3.7 %)
Iridocyclitis	0	1 (3.7 %)	0
Uveitis	0	1 (3.7 %)	0

Safety Population (n=83)

Safety:
Serious Adverse Events Through Month 12

	Sham *(N=29)*	**3.0 x 10^6 jCell** *(N= 27)*	**6.0 x 10^6 jCell** *(N= 27)*
Subjects with at least one SAE, n (%)	**0**	**1 (3.7%)***	**0**
Ocular hypertension*	0	1 (3.7%)*	0
Systemic	0	0	0

**Reported as related to study drug and was resolved with treatment*

Subject treated with 4M is not included; subject reported a few mild TEAEs including eye pain, photophobia, vision blurred, iris adhesions and iridocyclitis

Conclusion

- **Single Intravitreal injection of jCell** (allogeneic Human Retinal Progenitor Cells) demonstrated promising results in visual acuity improvement in the per protocol population with the 6M dose (+7.4 letters) compared to sham (+2.8 letters) at Month 12 in a Phase 2b study
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  - All **functional endpoints** showed similar trends
- Intravitreal administration of jCell was **well tolerated with a good safety profile**
- These results support development of
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Acknowledgements

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- Anthony Joseph, MD
- David Liao, MD
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- David Boyer, MD
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jCell Scientific Team

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Thank you!