SUPPLEMENTARY INFORMATION

Supplementary Table 1: Baseline Participant Characteristics (individual)

Code	Sex	2nd *CEP290* Allele #	Age/Grp ~	Baseline VA [log MAR] +	Treated Eye @	Dose [ug] &	Num. of Inj. ^	Length of f/u [mon]$
P1	M	c.2506_2507delGA	19 / A	LP / LP	RE	160 / 80	4	9.0
P2	M	c.4723A>T	41 / A	LP / LP	RE	160 / 80	3	7.0
P3	M	c.5668G>T	44 / A	2.3 / 2.4	LE	160 / 80	2	3.0
P4	F	c.4438-3delC	16 / P	2.5 / 2.5	RE	160 / 80	3	6.0
P5	M	c.6277delG	8 / P	1.9 / 2.1	LE	160 / 80	2	5.0
P6	F	c.3167_3168insA	21 / A	LP / LP	RE	320 / 160	3	6.5
P7	F	c.4723A>T	27 / A	1.1 / 0.7	RE	320 / 160	2	5.0
P9	F	c.4393C>T	24 / A	LP / LP	RE	320 / 160	1	1.0
P8	M	c.6277delG	10 / P	1.9 / 1.4	RE	320 / 160	2	3.0
P10	F	c.547_550delTACC	15 / P	LP / LP	RE	320 / 160	1	1.0

all patients had c.2991+1655A>G/p.(Cys998*) allele in common; nucleotide change of the additional allele shown

~ Age in years at the time of enrollment; A=adult; P=pediatric

+ Visual acuity in right / left eyes in logarithm of minimum angle of resolution (MAR); 0 log MAR corresponds to Snellen acuity of 20/20, 2 log MAR corresponds to 20/2000; LP=Light perception

@ RE=right eye, LE=left eye

& Loading / maintenance dose of QR110 injected intravitreally in a 50 uL volume

^ Intravitreal injections every 3 months

$ Length of followup in months after the first injection

Supplementary Table 2: Baseline Participant Characteristics

			QR-110 160/80 µg ^ (n = 5) (A = 3, P = 2)	QR-110 320/160 µg ^ (n = 5) (A = 3, P = 2)	QR-110 combined (n = 10) (A = 6, P = 4)
Sex	Male		4 (80.0)	1 (20.0)	5 (50.0)
	Female		1 (20.0)	4 (80.0)	5 (50.0)
Race	White		5 (100.0)	5 (100.0)	10 (100.0)
Age (years)			25.60 [15.98]	19.40 [6.88]	22.50 [12.05]
Adults weight (kg)			87.0 [20.95]	56.00 [6.08]	71.50 [21.88]
Pediatrics weight (kg)			41.5 [16.26]	43.50 [12.02]	42.50 [11.73]
Adults heart rate (beats/min)			70.0 [28.16]	76.67 [11.02]	73.33 [19.47]
Pediatrics heart rate (beats/min)			91.0 [4.24]	72.00 [2.83]	81.50 [11.36]
Adults blood pressure		(systolic, mmHg)	140.3 [8.50]	116.00 [13.45]	128.17 [16.70]
		(diastolic, mmHg)	84.0 [4.36]	78.00 [16.09]	81.00 [11.05]
Pediatrics blood pressure		(systolic, mmHg)	118.0 [5.66]	94.50 [0.71]	106.25 [13.96]
		(diastolic, mmHg)	73.0 [1.41]	57.50 [12.02]	65.25 [11.35]
Creatinine ~ (µmol/L)			71.42 [25.50]	56.40 [9.85]	63.91 [19.87]
Adults glomerular filtration rate ~ (mL/min/SSA)			96.33 [17.04]	117.67 [5.13]	107.00 [16.22]
Pediatrics glomerular filtration rate ~ (mL/min/SSA)			> 75	> 75	> 75
Alanine aminotransferase ~ (U/L)			21.20 [10.64]	16.00 [9.00]	18.60 [9.69]
Aspartate aminotransferase ~ (U/L)			17.20 [5.12]	15.80 [1.92]	16.50 [3.72]

Values represent number of patients (percent) or means [SD]

* 160/80 µg n = 5 (3 adults and 2 pediatrics), 320/160 µg n = 5 (3 adults and 2 pediatric), Combined n = 10 (6 adults and 4 pediatrics)

^ Loading / maintenance dose of QR-110 injected intravitreally in a 50 µL volume

~ Laboratory parameters measured at screening

Supplementary Table 3: Treatment effect at 3 months

		Mean change from BL* [log_{10}]	P-value +
All patients (n=8)			
VA	Treated eyes	**-0.67**	**0.022**
	Untreated eyes	0.02	
Red FST ~	Treated eyes	**-0.62**	**1E-06**
	Untreated eyes	-0.09	
Blue FST ~	Treated eyes	**-0.81**	**< 2E-16**
	Untreated eyes	-0.01	
Withholding data from P2 (n=7)			
VA	Treated eyes	**-0.38**	**0.018**
	Untreated eyes	0.02	
Red FST ~	Treated eyes	**-0.63**	**3E-04**
	Untreated eyes	-0.16	
Blue FST ~	Treated eyes	**-0.76**	**2E-13**
	Untreated eyes	-0.04	

* Negative values correspond to improvement of function compared to baseline (BL).
+ Linear mixed-effects models were used for the statistical analysis of all efficacy outcomes to account for the correlation structure and repeated measures within each data set. P-values for the significance of treatment-by-visit interactions
~ Sessions with an intravisit sd greater than 1.01 have been censored; conclusions are unchanged when censoring is not used

Additional safety-related findings

There were no adverse events leading to treatment discontinuation or interruption. Regarding general and systemic parameters, there were no changes in hepatic and renal functions, assessed by liver enzymes and glomerular filtration rate, respectively. Two subjects presented a transitory and moderate elevation of the Prothrombin International Normalized Ratio (INR); this elevation was unrelated to the study drug and spontaneously returned to normal. Hematology evaluations of these two subjects were normal. Finally, pharmacokinetic measures showed the serum level of the study drug to be below the level of quantification (1.02 ng/ml) supporting negligible systemic exposure for all patients. Listing of all non-ocular treatment-emergent AEs are provided (Supplementary Table 4).

No intra-ocular inflammation occurred for all subjects, who received up to 4 injections at 160/80 µg or 320/160 µg dose levels. Following IVT injection, five subjects had a subconjunctival hemorrhage at the site of injection and three subjects had a transitory elevation of the intraocular pressure, rapidly resolving without treatment or intervention. Mild lens modifications (vacuoles/lenticular opacities/posterior capsule opacification) and an air bubble in the superior peripheral vitreous were observed for one subject; mild vitreous opacities were detected for another subject. One subject developed symptoms that we describe as diplopia and metamorphopsia; diplopia was likely related to the improvement of visual function in the treated eye according to investigator judgement. Finally, one subject presented mild parafoveal intraretinal cysts at OCT detected at 4 months after the first injection. Listing of all ocular treatment-emergent AEs are provided (Supplementary Table 5).

Supplementary Table 4: Summary of Adverse Events

Event *	QR-110 160/80 µg ^ (n = 5) (A = 3, P = 2)	QR-110 320/160 µg ^ (n = 5) (A = 3, P = 2)	QR-110 combined (n = 10) (A = 6, P = 4)
	Number of patients (percent)		
Adverse event leading to treatment discontinuation	0	0	0
Adverse event leading to dose interruption	0	0	0
Adverse event leading to dose reduction	0	0	0
Allergy to arthropod bite	0	1 (20.0)	1 (10.0)
Cough	0	1 (20.0)	1 (10.0)
Dizziness	0	1 (20.0)	1 (10.0)
Ear infection	1 (20.0)	0	1 (10.0)
Ear lobe infection	1 (20.0)	0	1 (10.0)
Gastroenteritis viral	1 (20.0)	0	1 (10.0)
Gout	1 (20.0)	0	1 (10.0)
Headache	1 (20.0)	0	1 (10.0)
Impetigo	1 (20.0)	0	1 (10.0)
Influenza like illness	0	1 (20.0)	1 (10.0)
Nausea	0	1 (20.0)	1 (10.0)
Otitis externa	1 (20.0)	0	1 (10.0)
Pain	1 (20.0)	0	1 (10.0)
Pain in extremity	1 (20.0)	0	1 (10.0)
Rash	1 (20.0)	0	1 (10.0)
Seasonal allergy	0	1 (20.0)	1 (10.0)
Sinus congestion	1 (20.0)	0	1 (10.0)
Solar dermatitis	0	1 (20.0)	1 (10.0)
Viral upper respiratory tract infection	1 (20.0)	2 (40.0)	3 (30.0)

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^ Loading / maintenance dose of QR-110 injected intravitreally in a 50 µL volume

Supplementary Table 5: Summary of Ocular Adverse Events

Event *	QR-110 160/80 µg ^ (n = 5) (A = 3, P = 2)	QR-110 320/160 µg ^ (n = 5) (A = 3, P = 2)	QR-110 combined (n = 10) (A = 6, P = 4)
	Number of patients (percent)		
Adverse event leading to treatment discontinuation	0	0	0
Adverse event leading to dose interruption	0	0	0
Adverse event leading to dose reduction	0	0	0
Subconjunctival haemorrhage	2 (40.0)	3 (60.0)	5 (50.0)
Conjunctival hyperaemia	1 (20.0)	1 (20.0)	2 (20.0)
Conjunctival oedema	0	1 (20.0)	1 (10.0)
Diplopia	0	1 (20.0)	1 (10.0)
Dry eye	1 (20.0)	0	1 (10.0)
Eyelid oedema	0	1 (20.0)	1 (10.0)
Lens disorder @	0	1 (20.0)	1 (10.0)
Lenticular opacities	0	1 (20.0)	1 (10.0)
Metamorphopsia	0	1 (20.0)	1 (10.0)
Post procedural complication $	0	1 (20.0)	1 (10.0)
Posterior capsule opacification	0	1 (20.0)	1 (10.0)
Retinal cyst	0	1 (20.0)	1 (10.0)
Small subconjunctival hemorrhage	0	1 (20.0)	1 (10.0)
Vitreous opacities	0	1 (20.0)	1 (10.0)

* 160/80 µg n = 5 (3 adults and 2 pediatrics), 320/160 µg n = 5 (3 adults and 2 pediatric), Combined n = 10 (6 adults and 4 pediatrics)

^ Loading / maintenance dose of QR-110 injected intravitreally in a 50 µL volume

@ Lens disorder: <10 small round vacuoles in lens nucleus

$ Post procedural complication: Air bubble in superior periphery of vitreous, post injection