Clinical trial results:
Phase 3 Randomized, Controlled Study of AAV5-hRKp.RPGR for the Treatment of X-linked Retinitis Pigmentosa Associated with Variants in the RPGR gene

Summary

EudraCT number	2020-002873-88
Trial protocol	IE NL BE ES FR DK DE IT Outside EU/EEA
Global end of trial date	30 September 2024

Results information

Result version number	v2 (current)
This version publication date	04 July 2025
First version publication date	13 April 2025
Version creation reason	
Summary attachment (see zip file)	Rationale_extension request_ (Rationale_extension request_MGT021_EudraCT.pdf)

Trial information

Trial identification

Sponsor protocol code	MGT-RPGR-021

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04671433
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development, LLC
Sponsor organisation address	920 Route 202 South, Raritan, New Jersey, United States, 08869
Public contact	Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002827-PIP01-20
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 September 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 September 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of bilateral treatment with an adeno-associated virus vector with a serotype 5 capsid, a human rhodopsin kinase promoter, and the retinitis pigmentosa guanosine triphosphatase regulator gene (AAV5-hRKp.RPGR) on functional vision as measured by vision-guided mobility assessment (VMA).

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 March 2021
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	48 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Switzerland: 10
Country: Number of subjects enrolled	Denmark: 2
Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	United Kingdom: 13
Country: Number of subjects enrolled	Israel: 6
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Netherlands: 9
Country: Number of subjects enrolled	United States: 35
Worldwide total number of subjects	97
EEA total number of subjects	32

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	2
Adolescents (12-17 years)	4
Adults (18-64 years)	91
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Total 97 adult and pediatric subjects were enrolled, out of which 94 subjects completed. Study consisted of Cohort (C) 1, 2 and pediatric cohort. C 1 subjects were randomised to assess safety after treatment up to Week 10. Randomisation for C 2 began after the IDMC completed their review of C 1 safety data and recommended to continue study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Deferred Group (Control Group)

Arm description:

Adults (cohort [C] 1 and 2) and pediatric subjects with X-linked retinitis pigmentosa (XLRP) caused by mutations in the human retinitis pigmentosa guanosine triphosphatase regulator (RPGR) gene (RPGR-XLRP) were randomised in the Deferred Group and did not receive any treatment in the study. Subjects were followed up for safety from Day 1 up to Week 52.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Immediate Treatment Group: RPGR2e11

Arm description:

Adults (cohort 1 and 2) and pediatric subjects with RPGR-XLRP were randomised to receive an adeno-associated virus vector with a serotype 5 capsid, a human rhodopsin kinase promoter, and the retinitis pigmentosa guanosine triphosphatase regulator gene (AAV5-hRKp.RPGR) therapy as a subretinal injection on the day of first eye surgery (Day 1) and second eye surgery (any time between Day 8 to Day 22) with 2.0*10^11 viral genome per millilitre (vg/mL) (RPGR2e11) dose (300 microlitres [mcL] to 800 mcL in each eye). Subjects were followed up for safety up to Week 52 after first dose of study drug on Day 1.

Arm type	Experimental
Investigational medicinal product name	RPGR2e11
Investigational medicinal product code	
Other name	Botaretigene sparoparvovec
Pharmaceutical forms	Solution for injection
Routes of administration	Subretinal use

Dosage and administration details:

Subjects received AAV5-hRKp.RPGR gene therapy with (RPGR2e11) at a dose of 300 mcL to 800 mcL in each eye on the day of first eye surgery on Day 1 and on the day of second eye surgery between Day 8 to Day 22.

Arm title	Immediate Treatment Group: RPGR4e11

Arm description:

Adults (cohort 1 and 2) and pediatric subjects with RPGR-XLRP were randomised to receive AAV5-hRKp.RPGR gene therapy as a subretinal injection on the day of first eye surgery (Day 1) and second eye surgery (any time between Day 8 to Day 22) with 4.0*10^11 vg/mL (RPGR4e11) dose (300 mcL to 800 mcL in each eye). Subjects were followed up for safety up to Week 52 after first dose of study drug on Day 1.

Arm type	Experimental

Investigational medicinal product name	RPGR4e11
Investigational medicinal product code	
Other name	Botaretigene sparoparvovec
Pharmaceutical forms	Solution for injection
Routes of administration	Subretinal use

Dosage and administration details:

Subjects received AAV5-hRKp.RPGR gene therapy with (RPGR4e11) at a dose of 300 mcL to 800 mcL in each eye on the day of first eye surgery on Day 1 and on the day of second eye surgery between Day 8 to Day 22.

Number of subjects in period 1	Deferred Group (Control Group)	Immediate Treatment Group: RPGR2e11	Immediate Treatment Group: RPGR4e11
Started	33	33	31
Treated	0 [1]	32	30
Completed	33	32	29
Not completed	0	1	2
Consent withdrawn by subject	-	1	-
Subject did not meet inclusion criteria	-	-	1
Lost to follow-up	-	-	1

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Only reported subjects were planned to be included in this milestone.

Baseline characteristics

Reporting groups	
Reporting group title	Deferred Group (Control Group)
Reporting group description:	
Adults (cohort [C] 1 and 2) and pediatric subjects with X-linked retinitis pigmentosa (XLRP) caused by mutations in the human retinitis pigmentosa guanosine triphosphatase regulator (RPGR) gene (RPGR-XLRP) were randomised in the Deferred Group and did not receive any treatment in the study. Subjects were followed up for safety from Day 1 up to Week 52.	
Reporting group title	Immediate Treatment Group: RPGR2e11
Reporting group description:	
Adults (cohort 1 and 2) and pediatric subjects with RPGR-XLRP were randomised to receive an adeno-associated virus vector with a serotype 5 capsid, a human rhodopsin kinase promoter, and the retinitis pigmentosa guanosine triphosphatase regulator gene (AAV5-hRKp.RPGR) therapy as a subretinal injection on the day of first eye surgery (Day 1) and second eye surgery (any time between Day 8 to Day 22) with 2.0*10^11 viral genome per millilitre (vg/mL) (RPGR2e11) dose (300 microlitres [mcL] to 800 mcL in each eye). Subjects were followed up for safety up to Week 52 after first dose of study drug on Day 1.	
Reporting group title	Immediate Treatment Group: RPGR4e11
Reporting group description:	
Adults (cohort 1 and 2) and pediatric subjects with RPGR-XLRP were randomised to receive AAV5-hRKp.RPGR gene therapy as a subretinal injection on the day of first eye surgery (Day 1) and second eye surgery (any time between Day 8 to Day 22) with 4.0*10^11 vg/mL (RPGR4e11) dose (300 mcL to 800 mcL in each eye). Subjects were followed up for safety up to Week 52 after first dose of study drug on Day 1.	

Reporting group values	Deferred Group (Control Group)	Immediate Treatment Group: RPGR2e11	Immediate Treatment Group: RPGR4e11
Number of subjects	33	33	31
Age categorical Units: Subjects			
In Utero	0	0	0
Preterm newborn infants (gestional age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days - 23 months)	0	0	0
Children (2 - 11 years)	1	0	1
12 - 17 years	1	2	1
Adults (18 - 64 years)	31	31	29
From 65 - 84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	24.9	27.0	28.0
standard deviation	± 7.47	± 9.36	± 7.54
Gender categorical Units: Subjects			
Male	32	31	31
Female	1	2	0

Reporting group values	Total		
Number of subjects	97		

Age categorical Units: Subjects			
In Utero	0		
Preterm newborn infants (gestional age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days - 23 months)	0		
Children (2 - 11 years)	2		
12 - 17 years	4		
Adults (18 - 64 years)	91		
From 65 - 84 years	0		
85 years and over	0		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Male	94		
Female	3		

End points

End points reporting groups

Reporting group title	Deferred Group (Control Group)

Reporting group description:

Adults (cohort [C] 1 and 2) and pediatric subjects with X-linked retinitis pigmentosa (XLRP) caused by mutations in the human retinitis pigmentosa guanosine triphosphatase regulator (RPGR) gene (RPGR-XLRP) were randomised in the Deferred Group and did not receive any treatment in the study. Subjects were followed up for safety from Day 1 up to Week 52.

Reporting group title	Immediate Treatment Group: RPGR2e11

Reporting group description:

Adults (cohort 1 and 2) and pediatric subjects with RPGR-XLRP were randomised to receive an adeno-associated virus vector with a serotype 5 capsid, a human rhodopsin kinase promoter, and the retinitis pigmentosa guanosine triphosphatase regulator gene (AAV5-hRKp.RPGR) therapy as a subretinal injection on the day of first eye surgery (Day 1) and second eye surgery (any time between Day 8 to Day 22) with 2.0*10^11 viral genome per millilitre (vg/mL) (RPGR2e11) dose (300 microlitres [mcL] to 800 mcL in each eye). Subjects were followed up for safety up to Week 52 after first dose of study drug on Day 1.

Reporting group title	Immediate Treatment Group: RPGR4e11

Reporting group description:

Adults (cohort 1 and 2) and pediatric subjects with RPGR-XLRP were randomised to receive AAV5-hRKp.RPGR gene therapy as a subretinal injection on the day of first eye surgery (Day 1) and second eye surgery (any time between Day 8 to Day 22) with 4.0*10^11 vg/mL (RPGR4e11) dose (300 mcL to 800 mcL in each eye). Subjects were followed up for safety up to Week 52 after first dose of study drug on Day 1.

Subject analysis set title	C 2: Pooled Immediate Treatment Group: RPGR2e11 & RPGR4e11
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The pooled immediate treatment group included cohort 2 subjects of RPGR2e11 and RPGR4e11 dose groups combined.

Subject analysis set title	C 2: Control Group
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Cohort 2 subjects with RPGR-XLRP were randomised and did not receive any treatment in the study. Subjects were followed up for safety from Day 1 up to Week 52.

Primary: Cohort 2: Percentage of Subjects With Vision-guided Mobility Assessment (VMA) Response in Binocular Assessment at Week 52

End point title	Cohort 2: Percentage of Subjects With Vision-guided Mobility Assessment (VMA) Response in Binocular Assessment at Week 52

End point description:

Percentage of subjects with VMA response in binocular assessment at Week 52 was reported. The VMA tests the ability of a subject to navigate through a maze at various illumination (lux) levels and presents an environment with obstacles that was meant to simulate real-life conditions at varying light levels. VMA responder was defined as a subject who passes a lux level at least 2 levels lower at Week 52 compared to the lowest lux level the subject passed at baseline. Intent-to-treat (ITT) analysis set included all adult subjects who were randomly assigned to a treatment group (treated or control group) in Cohort 2. In this endpoint pooled data for immediate treatment groups RPGR2e11 and RPGR4e11 was planned to be reported.

End point type	Primary

End point timeframe:

At Week 52

End point values	C 2: Pooled Immediate Treatment Group: RPGR2e11 & RPGR4e11	C 2: Control Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	55	30		
Units: Percentage of responders				
number (not applicable)	27.3	13.3		

Statistical analyses

Statistical analysis title	Statistical Analysis-1
Comparison groups	C 2: Pooled Immediate Treatment Group: RPGR2e11 & RPGR4e11 v C 2: Control Group
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.247
Method	Fisher exact
Parameter estimate	Difference in percentage of responders
Point estimate	13.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.6
upper limit	30.5

Secondary: Cohort 2: Change From Baseline in Mean Retinal Sensitivity (MRS) Within the Central 10 Degrees Excluding Scotoma in Static Perimetry (MRS10) at Week 52

End point title	Cohort 2: Change From Baseline in Mean Retinal Sensitivity (MRS) Within the Central 10 Degrees Excluding Scotoma in Static Perimetry (MRS10) at Week 52

End point description:

Change from baseline in MRS10 at Week 52 were reported. ITT analysis set included all adult subjects who were randomly assigned to a treatment group (treated or control group) in Cohort 2. In this endpoint pooled data for immediate treatment groups RPGR2e11 and RPGR4e11 was planned to be reported.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	C 2: Pooled Immediate Treatment Group: RPGR2e11 & RPGR4e11	C 2: Control Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	55	30		
Units: Decibels (dB)				
least squares mean (standard error)	0.88 (± 0.22)	-0.36 (± 0.29)		

Statistical analyses

Statistical analysis title	Statistical Analysis-2
Comparison groups	C 2: Pooled Immediate Treatment Group: RPGR2e11 & RPGR4e11 v C 2: Control Group
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least square (LS) mean difference
Point estimate	1.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	1.94

Secondary: Cohort 2: Percentage of Subjects With VMA Response in Binocular Assessment at Week 52 Comparing RPGR2e11 Group with Control Group

End point title	Cohort 2: Percentage of Subjects With VMA Response in Binocular Assessment at Week 52 Comparing RPGR2e11 Group with Control Group[1]

End point description:

Percentage of subjects with VMA response in binocular assessment at Week 52 comparing RPGR2e11 group with control group was reported. The VMA tests the ability of a subject to navigate through a maze at various illumination (lux) levels and presents an environment with obstacles that was meant to simulate real-life conditions at varying light levels. VMA responder was defined as a subject who passes a lux level at least 2 levels lower at Week 52 compared to the lowest lux level the subject passed at baseline. ITT analysis set included all adult subjects who were randomly assigned to a treatment group (treated or control group) in Cohort 2. In this endpoint data for immediate treatment groups RPGR2e11 and deferred treatment was planned to be reported.

End point type	Secondary

End point timeframe:

At Week 52

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be reported for specified arms only.

End point values	Deferred Group (Control Group)	Immediate Treatment Group: RPGR2e11		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: Percentage of responders				
number (not applicable)	13.3	24.1		

Statistical analyses

Statistical analysis title	Statistical Analysis-3
Comparison groups	Deferred Group (Control Group) v Immediate Treatment Group: RPGR2e11
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage of responders
Point estimate	10
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.7
upper limit	29.7

Secondary: Cohort 2: Percentage of Subjects With VMA Response in Binocular Assessment at Week 52 Comparing RPGR4e11 Group with Control Group

End point title	Cohort 2: Percentage of Subjects With VMA Response in Binocular Assessment at Week 52 Comparing RPGR4e11 Group with Control Group [2]

End point description:

Percentage of subjects with VMA response in binocular assessment at Week 52 comparing RPGR4e11 group with control group was reported. The VMA tests the ability of a subject to navigate through a maze at various illumination (lux) levels and presents an environment with obstacles that was meant to simulate real-life conditions at varying light levels. VMA responder was defined as a subject who passes a lux level at least 2 levels lower at Week 52 compared to the lowest lux level the subject passed at baseline. ITT analysis set included all adult subjects who were randomly assigned to a treatment group (treated or control group) in Cohort 2. In this endpoint data for immediate treatment groups RPGR4e11 and deferred treatment was planned to be reported.

End point type	Secondary

End point timeframe:

At Week 52

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be reported for specified arms only.

End point values	Deferred Group (Control Group)	Immediate Treatment Group: RPGR4e11		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	26		
Units: Percentage of responders				
number (not applicable)	13.3	30.8		

Statistical analyses

Statistical analysis title	Statistical Analysis-4
Comparison groups	Deferred Group (Control Group) v Immediate Treatment Group: RPGR4e11
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage of responders
Point estimate	16.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	38.7

Secondary: Cohort 2: Percentage of Pointwise Responders in Full Visual Field at Week 52

End point title	Cohort 2: Percentage of Pointwise Responders in Full Visual Field at Week 52

End point description:

Percentage of pointwise responders in full visual field at Week 52 were reported. A responder at Week 52 was defined as a subject with at least 1 treated eye with greater than or equal to (>=)7 dB increase from baseline in >=5 loci repeated at Week 52 and 1 or more other time points prior to Week 52. ITT analysis set included all adult subjects who were randomly assigned to a treatment group (treated or control group) in Cohort 2. In this endpoint pooled data for immediate treatment groups RPGR2e11 and RPGR4e11 was planned to be reported.

End point type	Secondary

End point timeframe:

At Week 52

End point values	C 2: Pooled Immediate Treatment Group: RPGR2e11 & RPGR4e11	C 2: Control Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	55	30		

Units: Percentage of responders				
number (not applicable)	58.2	23.3		

Statistical analyses

Statistical analysis title	Statistical Analysis-5
Comparison groups	C 2: Pooled Immediate Treatment Group: RPGR2e11 & RPGR4e11 v C 2: Control Group
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage of responders
Point estimate	36.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.2
upper limit	54.9

Secondary: Cohort 2: Percentage of Pointwise Responders in the Central 30 Degrees Visual Field at Week 52

End point title	Cohort 2: Percentage of Pointwise Responders in the Central 30 Degrees Visual Field at Week 52

End point description:

Percentage of pointwise responders in the central 30 degrees visual field at Week 52 were reported. A responder at Week 52 was defined as a subject with at least 1 treated eye with a >=7 dB increase from baseline in >=5 loci repeated at Week 52 and 1 or more other time points prior to Week 52. ITT analysis set included all adult subjects who were randomly assigned to a treatment group (treated or control group) in Cohort 2. In this endpoint pooled data for immediate treatment groups RPGR2e11 and RPGR4e11 was planned to be reported.

End point type	Secondary

End point timeframe:

At Week 52

End point values	C 2: Pooled Immediate Treatment Group: RPGR2e11 & RPGR4e11	C 2: Control Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	55	30		
Units: Percentage of responders				
number (not applicable)	47.3	10.0		

Statistical analyses

Statistical analysis title	Statistical Analysis-6
Comparison groups	C 2: Pooled Immediate Treatment Group: RPGR2e11 & RPGR4e11 v C 2: Control Group
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage of responders
Point estimate	38.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	21.4
upper limit	54.7

Secondary: Cohort 2: Percentage of VMA Responders in the "Worse-seeing Eye" at Week 52

End point title	Cohort 2: Percentage of VMA Responders in the "Worse-seeing Eye" at Week 52

End point description:

The VMA tests the ability of a subject to navigate through a maze at various illumination (lux) levels and presents an environment with obstacles that was meant to simulate real-life conditions at varying light levels. VMA responder was defined as a subject who passes a lux level at least 2 levels lower at Week 52 compared to the lowest lux level the subject passed at baseline. Worse-seeing Eye was determined by best corrected visual acuity (BCVA). If BCVA was identical in both eyes, static perimetry mean retinal sensitivity (MRS) was used to determine the worse-seeing eye. If both BCVA and MRS were equal in both eyes, the right eye was the first eye receiving treatment (and considered as the worse-seeing eye). ITT analysis set included all adult subjects who were randomly assigned to a treatment group (treated or control group) in Cohort 2. In this endpoint pooled data for immediate treatment groups RPGR2e11 and RPGR4e11 was planned to be reported.

End point type	Secondary

End point timeframe:

At Week 52

End point values	C 2: Pooled Immediate Treatment Group: RPGR2e11 & RPGR4e11	C 2: Control Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	55	30		
Units: Percentage of responders				

number (not applicable)	29.1	23.3		

Statistical analyses

Statistical analysis title	Statistical Analysis-7
Comparison groups	C 2: Pooled Immediate Treatment Group: RPGR2e11 & RPGR4e11 v C 2: Control Group
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in percentage of responders
Point estimate	5.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.4
upper limit	25.3

Secondary: Cohort 2: Change From Baseline in the Modified Low Luminance Questionnaire (mLLQ)- Extreme Lighting Domain Score at Week 52

End point title	Cohort 2: Change From Baseline in the Modified Low Luminance Questionnaire (mLLQ)- Extreme Lighting Domain Score at Week 52

End point description:

The mLLQ was 30-item disease-specific questionnaire for use in eye diseases to assess self reported visual problems under low luminance and at night. The instrument consisted of 6 domains and was scored by each of its 6 domains (extreme lighting, mobility, general dim lighting, peripheral vision, driving, emotional distress). The extreme lighting domain comprised of 7 items (Items 1 to 7) and was used to assess patient-reported functional vision under low light/at night and in extreme (ie, bright light) conditions. Response options included 5- point Likert Scales ranging from 'No difficulty at all' to 'Not able to' and 'None of the time' to 'All of the time'. The mLLQ uses scale from 0 to 100, higher scores reflect a higher level of functioning. A positive change from baseline reflects improvement; negative reflects worsening. ITT analysis set. In this endpoint pooled data for immediate treatment groups RPGR2e11 and RPGR4e11 was planned to be reported.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	C 2: Pooled Immediate Treatment Group: RPGR2e11 & RPGR4e11	C 2: Control Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	55	30		
Units: Score on a scale				

least squares mean (standard error)	1.80 (± 1.50)	-5.49 (± 2.05)		

Statistical analyses

Statistical analysis title	Statistical Analysis-8
Comparison groups	C 2: Pooled Immediate Treatment Group: RPGR2e11 & RPGR4e11 v C 2: Control Group
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	7.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.2
upper limit	12.38

Secondary: Cohort 2: Change From Baseline in Low Luminance Visual Acuity (LLVA) by Early Treatment Diabetic Retinopathy Study (ETDRS) Chart Letter Score in Monocular Assessment at Week 52

End point title	Cohort 2: Change From Baseline in Low Luminance Visual Acuity (LLVA) by Early Treatment Diabetic Retinopathy Study (ETDRS) Chart Letter Score in Monocular Assessment at Week 52

End point description:

Change from baseline in LLVA by ETDRS chart letter score in monocular assessment at Week 52 were reported. The LLVA was determined using the ETDRS chart by counting the number of ETDRS letters read under low light conditions. ETDRS chart letter score ranged from 0 to 100 letters. 20/20 snellen was equivalent to 85 letters on the ETDRS chart or 0 logMAR. The higher ETDRS score indicated the better vision. ITT analysis set included all adult subjects who were randomly assigned to a treatment group (treated or control group) in Cohort 2. In this endpoint pooled data for immediate treatment groups RPGR2e11 and RPGR4e11 was planned to be reported.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	C 2: Pooled Immediate Treatment Group: RPGR2e11 & RPGR4e11	C 2: Control Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	55	30		
Units: Number of ETDRS letters				

least squares mean (standard error)	6.86 (± 0.94)	2.11 (± 1.26)		

Statistical analyses

Statistical analysis title	Statistical Analysis-9
Comparison groups	C 2: Pooled Immediate Treatment Group: RPGR2e11 & RPGR4e11 v C 2: Control Group
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	4.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.64
upper limit	7.86

Secondary: Cohort 2: Change From Baseline in Best Corrected Visual Acuity (BCVA) by ETDRS Chart Letter Score in Monocular Assessment at Week 52

End point title	Cohort 2: Change From Baseline in Best Corrected Visual Acuity (BCVA) by ETDRS Chart Letter Score in Monocular Assessment at Week 52

End point description:

Change from baseline in BCVA by ETDRS chart letter score in monocular assessment at Week 52 were reported. The BCVA was determined using the ETDRS chart by counting the number of ETDRS letters read under normal lighting conditions. ETDRS chart letter score ranged from 0 to 100 letters. 20/20 snellen was equivalent to 85 letters on the ETDRS chart or 0 logMAR. The higher ETDRS score indicated the better vision. ITT analysis set included all adult subjects who were randomly assigned to a treatment group (treated or control group) in Cohort 2. In this endpoint pooled data for immediate treatment groups RPGR2e11 and RPGR4e11 was planned to be reported.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	C 2: Pooled Immediate Treatment Group: RPGR2e11 & RPGR4e11	C 2: Control Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	55	30		
Units: Number of ETDRS letters				
least squares mean (standard error)	1.79 (± 0.54)	0.83 (± 0.73)		

Statistical analyses

Statistical analysis title	Statistical Analysis-10
Comparison groups	C 2: Pooled Immediate Treatment Group: RPGR2e11 & RPGR4e11 v C 2: Control Group
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.84
upper limit	2.76

Secondary: Cohort 2: Change From Baseline in Mean Retinal Sensitivity Within the Full Visual Field Excluding Scotoma in Static Perimetry (MRS90) at Week 52

End point title	Cohort 2: Change From Baseline in Mean Retinal Sensitivity Within the Full Visual Field Excluding Scotoma in Static Perimetry (MRS90) at Week 52

End point description:

Change from baseline in MRS90 at Week 52 were reported. ITT analysis set included all adult subjects who were randomly assigned to a treatment group (treated or control group) in Cohort 2. In this endpoint pooled data for immediate treatment groups RPGR2e11 and RPGR4e11 was planned to be reported.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	C 2: Pooled Immediate Treatment Group: RPGR2e11 & RPGR4e11	C 2: Control Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	55	30		
Units: Decibels (dB)				
least squares mean (standard error)	0.00 (± 0.19)	-0.93 (± 0.26)		

Statistical analyses

Statistical analysis title	Statistical Analysis-11
Comparison groups	C 2: Pooled Immediate Treatment Group: RPGR2e11 & RPGR4e11 v C 2: Control Group
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	LS mean difference
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	1.55

Secondary: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs)

End point title	Number of Subjects With Treatment-Emergent Adverse Events (TEAEs)

End point description:

Adverse event (AE) was any untoward medical occurrence in a clinical study subject administered a medicinal (investigational or non-investigational) product. AE does not necessarily have a causal relationship with intervention. Any AE occurring on or after the initial administration of study drug and on or before the last visit of the study was considered treatment-emergent for immediate treatment group. Any AE occurring on or after the last baseline visit (Day 1) and on or before the last visit of the study was considered treatment-emergent for deferred group. TEAEs included serious and non-serious events. Analysis population included all subjects randomised to immediate treatment and had received AAV5-hRKp.RPGR administration in at least 1 eye, and all subjects randomised to deferred treatment and had completed at least 1 baseline assessment during deferred period.

End point type	Secondary

End point timeframe:

Day 1 up to Week 52

End point values	Deferred Group (Control Group)	Immediate Treatment Group: RPGR2e11	Immediate Treatment Group: RPGR4e11	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	32	30	
Units: Subjects	19	32	30	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Significant Change in Laboratory Parameters

End point title	Number of Subjects With Clinically Significant Change in

	Laboratory Parameters

End point description:

Number of subjects with clinically significant change in laboratory parameters (clinical chemistry and hematology) were reported. Analysis population included all subjects randomised to immediate treatment and had received AAV5-hRKp.RPGR administration in at least 1 eye, and all subjects randomised to deferred treatment and had completed at least 1 baseline assessment during deferred period.

End point type	Secondary

End point timeframe:

Day 1 up to Week 52

End point values	Deferred Group (Control Group)	Immediate Treatment Group: RPGR2e11	Immediate Treatment Group: RPGR4e11	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	32	30	
Units: Subjects	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 up to Week 52

Adverse event reporting additional description:

Analysis population included all subjects randomised to immediate treatment and had received AAV5-hRKp.RPGR administration in at least 1 eye, and all subjects randomised to deferred treatment and had completed at least 1 baseline assessment during deferred period.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Deferred Group (Control Group)

Reporting group description:

Adults (cohort 1 and 2) and pediatric subjects with X-linked retinitis pigmentosa (XLRP) caused by mutations in the human retinitis pigmentosa guanosine triphosphatase regulator (RPGR) gene (RPGR-XLRP) were randomised in the Deferred Group and did not receive any treatment in the study. Subjects were followed up for safety from Day 1 up to Week 52.

Reporting group title	Immediate Treatment Group: RPGR2e11

Reporting group description:

Adults (cohort 1 and 2) and pediatric subjects with RPGR-XLRP were randomised to receive adeno-associated virus vector with a serotype 5 capsid-human rhodopsin kinase promoter retinitis pigmentosa guanosine triphosphatase regulator (AAV5-hRKp.RPGR) gene therapy as a subretinal injection on the day of first eye surgery (Day 1) and second eye surgery (any time between Day 8 to Day 22) with 2.0*10^11 viral genome per millilitre (vg/mL) (RPGR2e11) dose (300 microlitres [mcL] to 800 mcL in each eye). Subjects were followed up for safety up to Week 52 after first dose of study drug (Day 1).

Reporting group title	Immediate Treatment Group: RPGR4e11

Reporting group description:

Adults (cohort 1 and 2) and pediatric subjects with RPGR-XLRP were randomised to receive AAV5-hRKp.RPGR gene therapy as a subretinal injection on the day of first eye surgery (Day 1) and second eye surgery (any time between Day 8 to Day 22) with 4.0*10^11 vg/mL (RPGR4e11) dose (300 mcL to 800 mcL in each eye). Subjects were followed up for safety up to Week 52 after first dose of study drug (Day 1).

Serious adverse events	Deferred Group (Control Group)	Immediate Treatment Group: RPGR2e11	Immediate Treatment Group: RPGR4e11
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 33 (0.00%)	5 / 32 (15.63%)	5 / 30 (16.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Intraocular Pressure Increased			
subjects affected / exposed	0 / 33 (0.00%)	2 / 32 (6.25%)	3 / 30 (10.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural			

complications			
Urinary Retention Postoperative			
subjects affected / exposed	0 / 33 (0.00%)	0 / 32 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Choroidal Haemorrhage			
subjects affected / exposed	0 / 33 (0.00%)	1 / 32 (3.13%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotony of Eye			
subjects affected / exposed	0 / 33 (0.00%)	1 / 32 (3.13%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhegmatogenous Retinal Detachment			
subjects affected / exposed	0 / 33 (0.00%)	1 / 32 (3.13%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Anal Abscess			
subjects affected / exposed	0 / 33 (0.00%)	0 / 32 (0.00%)	1 / 30 (3.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Deferred Group (Control Group)	Immediate Treatment Group: RPGR2e11	Immediate Treatment Group: RPGR4e11
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 33 (39.39%)	32 / 32 (100.00%)	30 / 30 (100.00%)
Investigations			
Blood Bicarbonate Decreased			
subjects affected / exposed	0 / 33 (0.00%)	1 / 32 (3.13%)	2 / 30 (6.67%)
occurrences (all)	0	1	2
Intraocular Pressure Decreased			

subjects affected / exposed	1 / 33 (3.03%)	6 / 32 (18.75%)	8 / 30 (26.67%)
occurrences (all)	1	7	11
Intraocular Pressure Increased			
subjects affected / exposed	0 / 33 (0.00%)	11 / 32 (34.38%)	14 / 30 (46.67%)
occurrences (all)	0	30	35
Injury, poisoning and procedural complications			
Hyphaema			
subjects affected / exposed	0 / 33 (0.00%)	0 / 32 (0.00%)	3 / 30 (10.00%)
occurrences (all)	0	0	4
Lens Feathering			
subjects affected / exposed	0 / 33 (0.00%)	6 / 32 (18.75%)	1 / 30 (3.33%)
occurrences (all)	0	10	2
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 33 (0.00%)	2 / 32 (6.25%)	2 / 30 (6.67%)
occurrences (all)	0	2	9
Eye disorders			
Anterior Chamber Flare			
subjects affected / exposed	0 / 33 (0.00%)	4 / 32 (12.50%)	7 / 30 (23.33%)
occurrences (all)	0	5	9
Anterior Chamber Cell			
subjects affected / exposed	0 / 33 (0.00%)	14 / 32 (43.75%)	15 / 30 (50.00%)
occurrences (all)	0	28	31
Conjunctival Haemorrhage			
subjects affected / exposed	0 / 33 (0.00%)	20 / 32 (62.50%)	21 / 30 (70.00%)
occurrences (all)	0	32	40
Cataract Subcapsular			
subjects affected / exposed	4 / 33 (12.12%)	11 / 32 (34.38%)	8 / 30 (26.67%)
occurrences (all)	4	19	17
Cataract			
subjects affected / exposed	1 / 33 (3.03%)	3 / 32 (9.38%)	5 / 30 (16.67%)
occurrences (all)	2	8	11
Anterior Chamber Inflammation			
subjects affected / exposed	0 / 33 (0.00%)	2 / 32 (6.25%)	2 / 30 (6.67%)
occurrences (all)	0	3	2
Conjunctival Oedema			

subjects affected / exposed	0 / 33 (0.00%)	8 / 32 (25.00%)	6 / 30 (20.00%)
occurrences (all)	0	10	10
Conjunctival Hyperaemia			
subjects affected / exposed	0 / 33 (0.00%)	16 / 32 (50.00%)	15 / 30 (50.00%)
occurrences (all)	0	28	25
Epiretinal Membrane			
subjects affected / exposed	2 / 33 (6.06%)	3 / 32 (9.38%)	4 / 30 (13.33%)
occurrences (all)	3	5	5
Diplopia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 32 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	4
Cystoid Macular Oedema			
subjects affected / exposed	0 / 33 (0.00%)	3 / 32 (9.38%)	3 / 30 (10.00%)
occurrences (all)	0	4	4
Corneal Infiltrates			
subjects affected / exposed	0 / 33 (0.00%)	2 / 32 (6.25%)	0 / 30 (0.00%)
occurrences (all)	0	3	0
Eye Inflammation			
subjects affected / exposed	0 / 33 (0.00%)	2 / 32 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	3	2
Eye Irritation			
subjects affected / exposed	0 / 33 (0.00%)	3 / 32 (9.38%)	1 / 30 (3.33%)
occurrences (all)	0	3	2
Eye Movement Disorder			
subjects affected / exposed	0 / 33 (0.00%)	2 / 32 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	2	1
Iridocyclitis			
subjects affected / exposed	0 / 33 (0.00%)	2 / 32 (6.25%)	0 / 30 (0.00%)
occurrences (all)	0	2	0
Hypotony of Eye			
subjects affected / exposed	0 / 33 (0.00%)	3 / 32 (9.38%)	1 / 30 (3.33%)
occurrences (all)	0	4	1
Flat Anterior Chamber of Eye			
subjects affected / exposed	0 / 33 (0.00%)	1 / 32 (3.13%)	2 / 30 (6.67%)
occurrences (all)	0	1	2
Eye Pain			

subjects affected / exposed	0 / 33 (0.00%)	3 / 32 (9.38%)	7 / 30 (23.33%)
occurrences (all)	0	3	11
Lenticular Opacities			
subjects affected / exposed	0 / 33 (0.00%)	1 / 32 (3.13%)	2 / 30 (6.67%)
occurrences (all)	0	2	3
Posterior Capsule Opacification			
subjects affected / exposed	0 / 33 (0.00%)	0 / 32 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	4
Photophobia			
subjects affected / exposed	0 / 33 (0.00%)	2 / 32 (6.25%)	2 / 30 (6.67%)
occurrences (all)	0	4	3
Papilloedema			
subjects affected / exposed	0 / 33 (0.00%)	0 / 32 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	4
Metamorphopsia			
subjects affected / exposed	0 / 33 (0.00%)	2 / 32 (6.25%)	3 / 30 (10.00%)
occurrences (all)	0	2	4
Macular Oedema			
subjects affected / exposed	0 / 33 (0.00%)	2 / 32 (6.25%)	2 / 30 (6.67%)
occurrences (all)	0	10	3
Macular Degeneration			
subjects affected / exposed	0 / 33 (0.00%)	3 / 32 (9.38%)	0 / 30 (0.00%)
occurrences (all)	0	4	0
Low Luminance Best-Corrected Visual Acuity Decreased			
subjects affected / exposed	4 / 33 (12.12%)	2 / 32 (6.25%)	1 / 30 (3.33%)
occurrences (all)	5	2	1
Loss of Visual Contrast Sensitivity			
subjects affected / exposed	1 / 33 (3.03%)	3 / 32 (9.38%)	5 / 30 (16.67%)
occurrences (all)	1	7	9
Punctate Keratitis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 32 (3.13%)	3 / 30 (10.00%)
occurrences (all)	0	2	5
Retinal Degeneration			
subjects affected / exposed	0 / 33 (0.00%)	4 / 32 (12.50%)	0 / 30 (0.00%)
occurrences (all)	0	8	0

Visual Acuity Reduced			
subjects affected / exposed	1 / 33 (3.03%)	4 / 32 (12.50%)	5 / 30 (16.67%)
occurrences (all)	1	4	6
Vision Blurred			
subjects affected / exposed	0 / 33 (0.00%)	2 / 32 (6.25%)	0 / 30 (0.00%)
occurrences (all)	0	4	0
Subretinal Fluid			
subjects affected / exposed	0 / 33 (0.00%)	1 / 32 (3.13%)	2 / 30 (6.67%)
occurrences (all)	0	1	4
Retinal Oedema			
subjects affected / exposed	1 / 33 (3.03%)	0 / 32 (0.00%)	6 / 30 (20.00%)
occurrences (all)	1	0	12
Retinal Haemorrhage			
subjects affected / exposed	0 / 33 (0.00%)	3 / 32 (9.38%)	4 / 30 (13.33%)
occurrences (all)	0	4	4
Visual Impairment			
subjects affected / exposed	0 / 33 (0.00%)	0 / 32 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	2
Vitreal Cells			
subjects affected / exposed	1 / 33 (3.03%)	8 / 32 (25.00%)	10 / 30 (33.33%)
occurrences (all)	2	18	23
Vitreous Disorder			
subjects affected / exposed	0 / 33 (0.00%)	3 / 32 (9.38%)	1 / 30 (3.33%)
occurrences (all)	0	3	1
Vitritis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 32 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	3
Vitreous Opacities			
subjects affected / exposed	0 / 33 (0.00%)	2 / 32 (6.25%)	3 / 30 (10.00%)
occurrences (all)	0	3	5
Vitreous Haemorrhage			
subjects affected / exposed	0 / 33 (0.00%)	5 / 32 (15.63%)	2 / 30 (6.67%)
occurrences (all)	0	5	2
Vitreous Floaters			
subjects affected / exposed	0 / 33 (0.00%)	0 / 32 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	3

Gastrointestinal disorders			
Abdominal Pain Upper			
subjects affected / exposed	0 / 33 (0.00%)	1 / 32 (3.13%)	2 / 30 (6.67%)
occurrences (all)	0	1	2
Vomiting			
subjects affected / exposed	0 / 33 (0.00%)	0 / 32 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	2
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 33 (0.00%)	0 / 32 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	2
Dermatitis			
subjects affected / exposed	0 / 33 (0.00%)	2 / 32 (6.25%)	0 / 30 (0.00%)
occurrences (all)	0	2	0
Acne			
subjects affected / exposed	0 / 33 (0.00%)	1 / 32 (3.13%)	3 / 30 (10.00%)
occurrences (all)	0	1	3
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 33 (0.00%)	2 / 32 (6.25%)	1 / 30 (3.33%)
occurrences (all)	0	2	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 33 (3.03%)	5 / 32 (15.63%)	5 / 30 (16.67%)
occurrences (all)	1	6	8
Localised Infection			
subjects affected / exposed	0 / 33 (0.00%)	0 / 32 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	0	2
Covid-19			
subjects affected / exposed	1 / 33 (3.03%)	2 / 32 (6.25%)	4 / 30 (13.33%)
occurrences (all)	1	2	4

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 July 2020	The overall reason for this amendment was to add research sample in Schedule of Activities for Deferred Treatment Group, correct the inclusion and exclusion criteria, and correct route of drug administration in Appendix 6.
26 August 2020	The overall reason for this amendment was to update the inclusion criteria to a retinal function assessment instead of a functional vision assessment, address health authority feedback, and to make administrative and operational changes.
04 February 2021	The overall reason for this amendment was to update the screening timeline, respond to regulatory input requiring subjects to consent to the long-term follow up study at the time of consent to MGT-RPGR-021, address safety in the second eye by gating the first 3 treated patients, and make administrative and operational changes.
31 March 2021	The overall reason for this amendment was to update numerous sections of the protocol with new or revised details, to note changes in procedures/methods, and to clarify content.
15 July 2021	The overall reason for this amendment was to update numerous sections of the protocol with new or revised details, to note changes in procedures/methods, and to make and/or clarify administrative and operational changes.
10 November 2021	The overall reason for this amendment was to revise time frames in relation to randomization and Non-Ocular Exclusion Criteria, to update sections of the protocol with new or revised details, and to make and/or clarify administrative and operational changes.
24 December 2021	The overall reason for this amendment was to update sections of the protocol with additional or revised specifics to enable clarity and implement administrative and operational changes. The update also contains changes to the population for efficacy analysis to allow for maze refinement prior to starting of Cohort 2.
06 April 2022	The overall reason for this amendment was to revise the definition of Cohort 1 and add that subjects who discontinue from Cohort 1 prior to Week 10 may be replaced. Additional changes have been made to align the protocol with requests made by Health Authorities following their review and also to provide further clarification to investigators on some aspects of the study.
14 July 2022	The overall reason for this amendment was to revise the objectives and endpoints of the study to align with data from other studies and utilize a more sensitive and appropriate primary endpoint of functional vision. The section on statistical power has been updated based on the change in primary endpoint. Additional time points for assessing viral shedding have been added and the total blood volume to be collected has been updated.
16 October 2023	The overall reason for this amendment was to update sections of the protocol with additional or revised specifics to enable clarity and implement administrative and operational changes including sponsorship transfer from MeiraGTx UK II Ltd to Janssen Research & Development.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported