Clinical trial results:
A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study in Cat-Allergic Patients with Asthma to Evaluate the Efficacy of a Single Dose of REGN1908-1909 to Reduce Bronchoconstriction Upon Cat Allergen Challenge

Summary

EudraCT number	2018-002477-22
Trial protocol	FR
Global end of trial date	06 April 2020

Results information

Result version number	v2 (current)
This version publication date	16 September 2021
First version publication date	17 April 2021
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	R1908-1909-ALG-1703

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03838731
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Regeneron Pharnaceuticals, Inc.
Sponsor organisation address	777 Old Saw Mill River Rd., Tarrytown, NY, United States, 10591
Public contact	Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 844-734-6643, clinicaltrials@regeneron.com
Scientific contact	Clinical Trials Administrator, Regeneron Pharnaceuticals, Inc., 001 844-734-6643, clinicaltrials@regeneron.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
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	06 April 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 April 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the prophylactic efficacy of REGN1908-1909 (anti-Fel d 1) administered as a single dose on day 1 in cat-allergic asthmatic subjects not living with a cat in the prevention of a Controlled Cat Allergen Challenge-induced early asthmatic response (EAR) assessed by measures of lung function (forced expiratory volume in 1 second [FEV1]) compared to placebo-treated subjects on day 8.

Protection of trial subjects:

This clinical study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with the International Council for Harmonisation (ICH) guidelines for Good Clinical Practice (GCP) and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 February 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 56
Worldwide total number of subjects	56
EEA total number of subjects	56

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)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	56
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 130 subjects were screened for study eligibility. Screen failures were mostly attributed to eligibility criteria not being met. The study was conducted at one site in France.

Pre-assignment

Screening details:

A total of 56 subjects were randomized in a 1:1 ratio to receive a single dose of either 600 milligrams (mg) of REGN1908-1909 or matching placebo.

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, Monitor, Data analyst, Assessor, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received a single dose of matching placebo

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single subcutaneous (SC) dose of matching placebo

Arm title	REGN1908-1909 600 mg

Arm description:

Subjects received a single 600 mg dose of REGN1908-1909

Arm type	Experimental
Investigational medicinal product name	REGN1908-1909
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single subcutaneous (SC) dose of REGN1908 and REGN1909

Number of subjects in period 1	Placebo	REGN1908-1909 600 mg
Started	27	29
Completed	26	28
Not completed	1	1
Pregnancy	-	1
Withdrawal of consent	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received a single dose of matching placebo	
Reporting group title	REGN1908-1909 600 mg
Reporting group description:	
Subjects received a single 600 mg dose of REGN1908-1909	

Reporting group values	Placebo	REGN1908-1909 600 mg	Total
Number of subjects	27	29	56
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational 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)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	27	29	56
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	30.2	28.4	
standard deviation	± 8.8	± 7.1	-
Sex: Female, Male Units: Subjects			
Female	17	18	35
Male	10	11	21
Race, Customized Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	1	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	3	0	3
White	24	27	51
Other	0	1	1
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	1	2
Not Hispanic or Latino	26	28	54
Unknown or Not Reported	0	0	0

End points

End points reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received a single dose of matching placebo	
Reporting group title	REGN1908-1909 600 mg
Reporting group description:	
Subjects received a single 600 mg dose of REGN1908-1909	

Primary: Time to Early Asthmatic Response (EAR) upon Controlled Cat Allergen Challenge in an Environmental Exposure Unit (EEU) on Day 8	
End point title	Time to Early Asthmatic Response (EAR) upon Controlled Cat Allergen Challenge in an Environmental Exposure Unit (EEU) on Day 8
End point description:	
Time to EAR was defined as the time to a ≥20% reduction in FEV1 or when the subject voluntarily departed the EEU due to clinically significant allergic and/or asthmatic symptoms.	
End point type	Primary
End point timeframe:	
Day 8	

End point values	Placebo	REGN1908-1909 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	29		
Units: Minutes				
median (confidence interval 95%)	51 (33.92 to 70.70)	99999 (130.87 to 99999)		

Statistical analyses

Statistical analysis title	Placebo vs. REGN1908-1909 600 mg
Comparison groups	Placebo v REGN1908-1909 600 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0083
Method	Cox Hazard Proportional
Parameter estimate	Hazard ratio (HR)
Point estimate	0.36

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.17
upper limit	0.77

Secondary: Time to EAR upon Controlled Cat Allergen Challenge in an EEU on Days 29, 57, and 85

End point title	Time to EAR upon Controlled Cat Allergen Challenge in an EEU on Days 29, 57, and 85

End point description:

Time to EAR was defined as the time to a ≥20% reduction in FEV1 or when the subject voluntarily departed the EEU due to clinically significant allergic and/or asthmatic symptoms

End point type	Secondary

End point timeframe:

Days 29, 57 and 85

End point values	Placebo	REGN1908-1909 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	29		
Units: Minutes				
median (confidence interval 95%)				
Day 29	41 (31.38 to 61.13)	99999 (131.22 to 99999)		
Day 57	56 (40.52 to 80.63)	232 (81.05 to 99999)		
Day 85	41 (31.03 to 60.93)	99999 (90.97 to 99999)		

Statistical analyses

Statistical analysis title	Placebo, REGN1908-1909 600 mg
Comparison groups	Placebo v REGN1908-1909 600 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.0001
Method	Cox Hazard Model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.12
upper limit	0.48

Notes:
[1] - Day 29

Statistical analysis title	Placebo, REGN1908-1909 600 mg
Statistical analysis description:	
Day 85	
Comparison groups	Placebo v REGN1908-1909 600 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0003
Method	Cox Hazard Model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.13
upper limit	0.56

Statistical analysis title	Placebo, REGN1908-1909 600 mg
Statistical analysis description:	
Day 57	
Comparison groups	Placebo v REGN1908-1909 600 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0222
Method	Cox Hazard Model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.22
upper limit	0.89

Secondary: Percent Change in Normalized Area Under the Curve (AUC) of the Forced Expiratory Volume in 1 Second (FEV1) Induced by a Controlled Cat Allergen Challenge over Exposure Interval from Baseline to Controlled Cat Allergen Challenge on Days 8, 29, 57, and 85

End point title	Percent Change in Normalized Area Under the Curve (AUC) of the Forced Expiratory Volume in 1 Second (FEV1) Induced by a Controlled Cat Allergen Challenge over Exposure Interval from Baseline to Controlled Cat Allergen Challenge on Days 8, 29, 57, and 85

End point description:

The AUC was analyzed by mixed-effect model repeated measures (MMRM) with the treatment, time, treatment-by-time interaction, and day of challenge as factors and baseline FEV1 as a continuous covariate. Full analysis set; Here 'n' = number of evaluable participants analyzed at each time point. For each participant at each controlled cat allergen challenge, AUC was calculated over the time period of 0 to 2 hours, with last observation carried forward used to impute values out to 2 hours if the patients remained in EEU for less than 2 hours. The AUCs were calculated using the trapezoidal rule and were normalized by dividing by the length of time (2 hours).

End point type	Secondary

End point timeframe:

Days 8, 29, 57, and 85

End point values	Placebo	REGN1908-1909 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	29		
Units: Percentage of change				
least squares mean (standard error)				
Day 8	1.59 (± 2.58)	15.15 (± 2.50)		
Day 29	0.46 (± 3.60)	16.67 (± 3.43)		
Day 57	1.77 (± 3.55)	14.07 (± 3.43)		
Day 85	0.20 (± 3.28)	12.73 (± 3.14)		

Statistical analyses

Statistical analysis title	Placebo, REGN1908-1909 600 mg
Comparison groups	Placebo v REGN1908-1909 600 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	< 0.001
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	13.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.35
upper limit	20.77
Variability estimate	Standard error of the mean
Dispersion value	3.59

Notes:

[2] - Day 8

Statistical analysis title	Placebo, REGN1908-1909 600 mg
Comparison groups	Placebo v REGN1908-1909 600 mg

Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.002
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	16.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.18
upper limit	26.24
Variability estimate	Standard error of the mean
Dispersion value	4.97

Notes:

[3] - Day 29

Statistical analysis title	Placebo, REGN1908-1909 600 mg
Comparison groups	Placebo v REGN1908-1909 600 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	= 0.016
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	12.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.4
upper limit	22.2
Variability estimate	Standard error of the mean
Dispersion value	4.94

Notes:

[4] - Day 57

Statistical analysis title	Placebo, REGN1908-1909 600 mg
Comparison groups	Placebo v REGN1908-1909 600 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.008
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	12.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.43
upper limit	21.65

Variability estimate	Standard error of the mean
Dispersion value	4.54

Notes:

[5] - Day 85

Secondary: Change in Normalized Area Under the Curve (AUC) of the Forced Expiratory Volume in 1 Second (FEV1) Induced by a Controlled Cat Allergen Challenge over Exposure Interval from Baseline to Controlled Cat Allergen Challenge on Days 8, 29, 57, and 85

End point title	Change in Normalized Area Under the Curve (AUC) of the Forced Expiratory Volume in 1 Second (FEV1) Induced by a Controlled Cat Allergen Challenge over Exposure Interval from Baseline to Controlled Cat Allergen Challenge on Days 8, 29, 57, and 85

End point description:

The AUC was analyzed by mixed-effect model repeated measures (MMRM) with the treatment, time, treatment-by-time interaction, and day of challenge as factors and baseline FEV1 as a continuous covariate. Full analysis set; Here "n" = number of evaluable participants analyzed at each time point. For each participant at each controlled cat allergen challenge, AUC was calculated over the time period of 0 to 2 hours, with last observation carried forward used to impute values out to 2 hours if the patients remained in EEU for less than 2 hours. The AUCs were calculated using the trapezoidal rule and were normalized by dividing by the length of time (2 hours).

End point type	Secondary

End point timeframe:

Days 8, 29, 57 and 85

End point values	Placebo	REGN1908-1909 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	29		
Units: Liters (L)				
least squares mean (standard error)				
Day 8	0.01 (± 0.06)	0.38 (± 0.06)		
Day 29	-0.03 (± 0.08)	0.43 (± 0.08)		
Day 57	0.00 (± 0.08)	0.34 (± 0.07)		
Day 85	-0.05 (± 0.08)	0.32 (± 0.08)		

Statistical analyses

Statistical analysis title	Placebo, REGN1908-1909 600 mg

Statistical analysis description:

Day 8

Comparison groups	Placebo v REGN1908-1909 600 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	0.37

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.21
upper limit	0.53
Variability estimate	Standard error of the mean
Dispersion value	0.08

Statistical analysis title	Placebo, REGN1908-1909 600 mg
Statistical analysis description:	
Day 29	
Comparison groups	Placebo v REGN1908-1909 600 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.23
upper limit	0.68
Variability estimate	Standard error of the mean
Dispersion value	0.11

Statistical analysis title	Placebo, REGN1908-1909 600 mg
Statistical analysis description:	
Day 57	
Comparison groups	Placebo v REGN1908-1909 600 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.13
upper limit	0.55
Variability estimate	Standard error of the mean
Dispersion value	0.11

Statistical analysis title	Placebo, REGN1908-1909 600 mg
Statistical analysis description: Day 85	
Comparison groups	Placebo v REGN1908-1909 600 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.15
upper limit	0.47
Variability estimate	Standard error of the mean
Dispersion value	0.11

Secondary: Change from Baseline in the Normalized AUC of Patient-Assessed Nasal Symptoms Induced by a Controlled Cat Allergen Challenge over the Exposure Interval to the Controlled Cat Allergen Challenge on Days 8, 29, 57, and 85

End point title	Change from Baseline in the Normalized AUC of Patient-Assessed Nasal Symptoms Induced by a Controlled Cat Allergen Challenge over the Exposure Interval to the Controlled Cat Allergen Challenge on Days 8, 29, 57, and 85

End point description:

Individual nasal symptoms, including rhinorrhea, nasal congestion, nasal itching, and sneezing were evaluated on a 4-point Likert scale (0, none; 1, mild; 2, moderate; and 3, severe) and combined to give the Total Nasal Symptom Score (TNSS) with a maximum score of 12. Scale range is 0-12. The higher the total, the more severe the symptoms. Full analysis set; Here 'n' = number of evaluable participants analyzed at each time point. For each participant at each controlled cat allergen challenge, AUC was calculated over the time period of 0 to 2 hours, with last observation carried forward used to impute values out to 2 hours if participants remained in EEU for less than 2 hours. AUCs were calculated using trapezoidal rule and were normalized by dividing by the length of time (2 hours).

End point type	Secondary

End point timeframe:

Days 8, 29, 57 and 85

End point values	Placebo	REGN1908-1909 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	29		
Units: Scores on a scale				
least squares mean (standard error)				
Day 8	-0.71 (± 0.38)	-0.49 (± 0.38)		

Day 29	-0.70 (± 0.37)	-1.39 (± 0.34)		
Day 57	-0.93 (± 0.43)	-0.83 (± 0.43)		
Day 85	-0.49 (± 0.43)	-1.37 (± 0.41)		

Statistical analyses

Statistical analysis title	Placebo, REGN1908-1909 600 mg
Statistical analysis description: Day 8	
Comparison groups	Placebo v REGN1908-1909 600 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.675
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.85
upper limit	1.29
Variability estimate	Standard error of the mean
Dispersion value	0.53

Statistical analysis title	Placebo, REGN1908-1909 600 mg
Statistical analysis description: Day 29	
Comparison groups	Placebo v REGN1908-1909 600 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.182
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	0.33
Variability estimate	Standard error of the mean
Dispersion value	0.51

Statistical analysis title	Placebo, REGN1908-1909 600 mg
Statistical analysis description: Day 57	
Comparison groups	Placebo v REGN1908-1909 600 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.866
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.12
upper limit	1.32
Variability estimate	Standard error of the mean
Dispersion value	0.61

Statistical analysis title	Placebo, REGN1908-1909 600 mg
Statistical analysis description: Day 85	
Comparison groups	Placebo v REGN1908-1909 600 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.146
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.08
upper limit	0.32
Variability estimate	Standard error of the mean
Dispersion value	0.6

Secondary: Change from Baseline in the Normalized AUC in Patient-Assessed Ocular Symptoms Induced by a Controlled Cat Allergen Challenge over the Exposure Interval to the Controlled Cat Allergen Challenge on Days 8, 29, 57, and 85

End point title	Change from Baseline in the Normalized AUC in Patient-Assessed Ocular Symptoms Induced by a Controlled Cat Allergen Challenge over the Exposure Interval to the Controlled Cat Allergen Challenge on Days 8, 29, 57, and 85

End point description:

Individual ocular symptoms for itching/burning, redness, swelling/puffiness, and tearing/watery eyes were evaluated on a 4-point Likert scale (0, none; 1, mild; 2, moderate; and 3, severe) and combined

to give the TOSS, with a maximum score of 12. Scale range is 0-12. The higher the score, the more severe the symptoms. Full analysis set; Here 'n' = number of evaluable participants analyzed at each time point. For each participant at each controlled cat allergen challenge, AUC was calculated over the time period of 0 to 2 hours, with last observation carried forward used to impute values out to 2 hours if participants remained in EEU for less than 2 hours. AUCs were calculated using trapezoidal rule and were normalized by dividing by the length of time (2 hours).

End point type	Secondary

End point timeframe:

Days 8, 29, 57 and 85

End point values	Placebo	REGN1908-1909 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	29		
Units: Scores on a scale				
least squares mean (standard error)				
Day 8	-0.37 (± 0.17)	-0.23 (± 0.17)		
Day 29	-0.43 (± 0.15)	-0.43 (± 0.14)		
Day 57	-0.40 (± 0.15)	-0.34 (± 0.15)		
Day 85	-0.36 (± 0.11)	-0.51 (± 0.10)		

Statistical analyses

Statistical analysis title	Placebo, REGN1908-1909 600 mg

Statistical analysis description:

Day 8

Comparison groups	Placebo v REGN1908-1909 600 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.572
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.35
upper limit	0.63
Variability estimate	Standard error of the mean
Dispersion value	0.24

Statistical analysis title	Placebo, REGN1908-1909 600 mg

Statistical analysis description:

Day 29

Comparison groups	Placebo v REGN1908-1909 600 mg

Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.997
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.41
upper limit	0.41
Variability estimate	Standard error of the mean
Dispersion value	0.2

Statistical analysis title	Placebo, REGN1908-1909 600 mg
Statistical analysis description:	
Day 57	
Comparison groups	Placebo v REGN1908-1909 600 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.756
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.36
upper limit	0.49
Variability estimate	Standard error of the mean
Dispersion value	0.21

Statistical analysis title	Placebo, REGN1908-1909 600 mg
Statistical analysis description:	
Day 85	
Comparison groups	Placebo v REGN1908-1909 600 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.333
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.15

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.46
upper limit	0.16
Variability estimate	Standard error of the mean
Dispersion value	0.15

Secondary: Mean Change from Baseline in Cat Allergen Quantity as Experienced by Subjects During Exposure on Days 8, 29, 57, and 85

End point title	Mean Change from Baseline in Cat Allergen Quantity as Experienced by Subjects During Exposure on Days 8, 29, 57, and 85

End point description:

Cat Allergen Exposure Tolerated in ng = Minute Ventilation (L/min) x Allergen Concentration (ng/m3) x Time in EEU (minutes), where 1 L/min = 0.001 m3/min. The change in cat allergen quantity (tolerated exposure) from the baseline Cat Allergen Challenge, will be analyzed using a similar MMRM model with treatment, visit and treatment by-visit interaction as factors and the cat allergen quantity tolerated in the baseline Controlled Cat Allergen Challenge as a covariate.
Full analysis set: included all randomized participants who received any investigational product and had completed the Day 8 Cat Allergen Challenge; Here 'n' = number of evaluable participants analyzed at each time point

End point type	Secondary

End point timeframe:

Days 8, 29, 57 and 85

End point values	Placebo	REGN1908-1909 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	29		
Units: Nanograms (ng)				
least squares mean (standard error)				
Day 8	19.55 (± 8.93)	59.05 (± 8.70)		
Day 29	14.14 (± 8.67)	68.21 (± 8.21)		
Day 57	21.94 (± 10.23)	55.38 (± 9.93)		
Day 85	12.93 (± 9.29)	54.03 (± 8.94)		

Statistical analyses

Statistical analysis title	Placebo, REGN1908-1909 600 mg

Statistical analysis description:

Day 8

Comparison groups	Placebo v REGN1908-1909 600 mg

Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	39.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.36
upper limit	64.65
Variability estimate	Standard error of the mean
Dispersion value	12.5

Statistical analysis title	Placebo, REGN1908-1909 600 mg
Statistical analysis description:	
Day 29	
Comparison groups	Placebo v REGN1908-1909 600 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	39.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.36
upper limit	64.65
Variability estimate	Standard error of the mean
Dispersion value	12.5

Statistical analysis title	Placebo, REGN1908-1909 600 mg
Statistical analysis description:	
Day 57	
Comparison groups	Placebo v REGN1908-1909 600 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.023
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	33.44

Confidence interval	
level	95 %
sides	2-sided
lower limit	4.79
upper limit	62.08
Variability estimate	Standard error of the mean
Dispersion value	14.28

Statistical analysis title	Placebo, REGN1908-1909 600 mg
Statistical analysis description:	
Day 85	
Comparison groups	Placebo v REGN1908-1909 600 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	41.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	15.1
upper limit	67.09
Variability estimate	Standard error of the mean
Dispersion value	12.92

Secondary: Percent Change in Cat Allergen Quantity as Experienced by Subjects During Exposure on Days 8, 29, 57, and 85

End point title	Percent Change in Cat Allergen Quantity as Experienced by Subjects During Exposure on Days 8, 29, 57, and 85

End point description:

Cat Allergen Exposure Tolerated in ng = Minute Ventilation (L/min) x Allergen Concentration (ng/m3) x Time in EEU (minutes), where 1 L/min = 0.001 m3/min. The change in cat allergen quantity (tolerated exposure) from the baseline Cat Allergen Challenge, will be analyzed using a similar MMRM model with treatment, visit and treatment by-visit interaction as factors and the cat allergen quantity tolerated in the baseline Controlled Cat Allergen Challenge as a covariate.
Full analysis set: included all randomized participants who received any investigational product and had completed the Day 8 Cat Allergen Challenge; Here 'n' = number of evaluable participants analyzed at each time point

End point type	Secondary

End point timeframe:

Days 8, 29, 57 and 85

End point values	Placebo	REGN1908-1909 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	29		
Units: Percentage of change				
least squares mean (standard error)				
Day 8	119.86 (± 73.22)	325.29 (± 70.79)		
Day 29	93.62 (± 71.48)	338.22 (± 68.26)		
Day 57	118.08 (± 69.58)	301.11 (± 67.11)		
Day 85	76.75 (± 82.08)	317.76 (± 78.84)		

Statistical analyses

Statistical analysis title	Placebo, REGN1908-1909 600 mg
Statistical analysis description:	
Day 8	
Comparison groups	Placebo v REGN1908-1909 600 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.049
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	205.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	410.17
Variability estimate	Standard error of the mean
Dispersion value	102.09

Statistical analysis title	Placebo, REGN1908-1909 600 mg
Statistical analysis description:	
Day 29	
Comparison groups	Placebo v REGN1908-1909 600 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.017
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	244.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	45.6
upper limit	443.59
Variability estimate	Standard error of the mean
Dispersion value	99.05

Statistical analysis title	Placebo, REGN1908-1909 600 mg
Statistical analysis description:	
Day 57	
Comparison groups	Placebo v REGN1908-1909 600 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.064
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	183.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.29
upper limit	377.35
Variability estimate	Standard error of the mean
Dispersion value	96.91

Statistical analysis title	Placebo, REGN1908-1909 600 mg
Statistical analysis description:	
Day 85	
Comparison groups	Placebo v REGN1908-1909 600 mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.039
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	241.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.44
upper limit	469.57
Variability estimate	Standard error of the mean
Dispersion value	114

Secondary: Number of Non-Serious and Serious Treatment-Emergent Adverse Events (TEAEs) through End of Study

End point title	Number of Non-Serious and Serious Treatment-Emergent Adverse Events (TEAEs) through End of Study

End point description:

Adverse events and serious adverse events were collected from the time of informed consent signature and then at each visit until the end of the study with the exception of symptoms that occurred in response to the EEU within 24 hours following the EEU. Safety Analysis Set (SAF): included all subjects who received any investigational product and were analyzed as treated.

End point type	Secondary

End point timeframe:

Baseline to 16 weeks

End point values	Placebo	REGN1908-1909 600 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	29		
Units: Events				
number (not applicable)				
Non-serious TEAEs	66	76		
Serious TEAEs	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline (day 1) to the end of study (week 16)	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	22
Reporting groups	
Reporting group title	REGN1908-1909 600mg
Reporting group description:	
Subjects received single 600 mg dose of REGN1908-1909	
Reporting group title	Placebo
Reporting group description:	
Subjects received a single dose of matching placebo	

Serious adverse events	REGN1908-1909 600mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 29 (0.00%)	0 / 27 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	REGN1908-1909 600mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 29 (75.86%)	19 / 27 (70.37%)	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 29 (6.90%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 29 (17.24%)	2 / 27 (7.41%)	
occurrences (all)	5	2	
General disorders and administration site conditions			

Influenza like illness			
subjects affected / exposed	3 / 29 (10.34%)	4 / 27 (14.81%)	
occurrences (all)	3	4	
Injection site pain			
subjects affected / exposed	2 / 29 (6.90%)	1 / 27 (3.70%)	
occurrences (all)	2	1	
Eye disorders			
Conjunctivitis allergic			
subjects affected / exposed	3 / 29 (10.34%)	0 / 27 (0.00%)	
occurrences (all)	3	0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 29 (6.90%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	11 / 29 (37.93%)	16 / 27 (59.26%)	
occurrences (all)	19	35	
Asthma exercise induced			
subjects affected / exposed	1 / 29 (3.45%)	3 / 27 (11.11%)	
occurrences (all)	1	3	
Rhinitis allergic			
subjects affected / exposed	5 / 29 (17.24%)	2 / 27 (7.41%)	
occurrences (all)	5	2	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 29 (3.45%)	2 / 27 (7.41%)	
occurrences (all)	1	2	
Nasopharyngitis			
subjects affected / exposed	2 / 29 (6.90%)	2 / 27 (7.41%)	
occurrences (all)	2	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 December 2018	Added exploratory objective information; clarification of several sections and study exit parameters, addition of Independent Data Monitoring Committee (IDMC) section; updates to inclusion and exclusion criteria; editorial changes
20 May 2019	Clarified language in adverse events; clarified inclusion and exclusion criteria information; clarified timing of analysis; procedural clarifications of timing of events, tests and measurements; added clarification on concomitant medications; other administrative updates

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported