Clinical trial results:
A Phase 3, 2-Part, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate the Pharmacokinetics, Efficacy and Safety of VX-770 in Subjects Aged 6 to 11 Years with Cystic Fibrosis and the G551D Mutation

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2008-007479-26
Trial protocol	IE GB DE FR
Global end of trial date	28 April 2011

Results information

Result version number	v2 (current)
This version publication date	13 July 2016
First version publication date	07 August 2015
Version creation reason	• Correction of full data set Address EudraCT system related issues through full data set Quality check and review prior to final release for publication

Trial information

Trial identification

Sponsor protocol code	VX08-770-103

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00909727
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Vertex Pharmaceuticals Incorporated
Sponsor organisation address	50 Northern Avenue, Boston, Massachusetts, United States, 02210-1862
Public contact	Medical Monitor, Vertex Pharmaceuticals Incorporated, +1 617-444-6777, medicalinfo@vrtx.com
Scientific contact	Medical Monitor, Vertex Pharmaceuticals Incorporated, +1 617-444-6777, medicalinfo@vrtx.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000335-PIP01-08

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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 October 2011
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 April 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Part A: To evaluate the pharmacokinetics (PK) of a single dose of orally-administered VX-770 treatment in subjects 6 to 11 years of age with cystic fibrosis (CF) who have the G551D-cystic fibrosis transmembrane conductance regulator protein (CFTR) mutation on at least 1 allele.

Part B: To evaluate the efficacy of VX-770 after 24 weeks of treatment in subjects 6 to 11 years of age with CF who have the G551D CFTR mutation on at least 1 allele.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and the International Conference on Harmonization (ICH) Guideline for Good Clinical Practice (GCP).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 August 2009
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Ireland: 2
Country: Number of subjects enrolled	United States: 25
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Australia: 14
Worldwide total number of subjects	52
EEA total number of subjects	11

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)	48
Adolescents (12-17 years)	4
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Part A started on 05 August 2009 (signing of first informed consent). Screening evaluations were completed during Day -28 to Day -2. All subjects completing Part A were offered the opportunity to participate in Part B, which started on 12 March 2010. Screening evaluations were completed during Day -35 to Day -15 before the first dose of study drug.

Pre-assignment

Screening details:

Nine subjects were dosed and included in Part A. In Part B, 52 subjects were enrolled and all were randomized to ivacaftor (26 subjects) or placebo (26 subjects). A 2-week run-in period was included to establish the baseline assessments on Day 1 after ensuring that subjects were properly taking their cystic fibrosis (CF) medication regimens.

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, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Oral tablet every 12 hours (q12h) for up to 48 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Oral tablet q12h for up to 48 weeks.

Arm title	150 mg Ivacaftor q12h

Arm description:

Oral tablet of 150 milligram (mg) of ivacaftor q12h for up to 48 weeks.

Arm type	Experimental
Investigational medicinal product name	Ivacaftor
Investigational medicinal product code	VX-770
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Oral tablet of 150 mg of ivacaftor q12h for up to 48 weeks.

Number of subjects in period 1	Placebo	150 mg Ivacaftor q12h
Started	26	26
Completed Treatment Period, Week 24	23	26
Completed	22	26
Not completed	4	0
Withdrawal of Consent	1	-
Adverse event	1	-
Wrong Genotype	1	-
Prohibited Medication	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Oral tablet every 12 hours (q12h) for up to 48 weeks.	
Reporting group title	150 mg Ivacaftor q12h
Reporting group description:	
Oral tablet of 150 milligram (mg) of ivacaftor q12h for up to 48 weeks.	

Reporting group values	Placebo	150 mg Ivacaftor q12h	Total
Number of subjects	26	26	52
Age categorical Units: Subjects			
6 to 8 Years	13	12	25
9 to 11 Years	12	11	23
> 11 Years	1	3	4
Age continuous Units: years			
arithmetic mean	8.9	8.9	
standard deviation	± 1.86	± 2	-
Gender categorical Units: Subjects			
Female	10	17	27
Male	16	9	25
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	0	1	1
Not Hispanic or Latino	24	23	47
Not Allowed to Ask Per Local Regulations	2	2	4
Region of Enrollment Units: Subjects			
North America	15	12	27
Europe	5	6	11
Australia	6	8	14
Percent Predicted Forced Expiratory Volume in 1 Second (FEV1)			
Percent predicted for age, gender, and height.			
Units: Subjects			
< 70%	8	4	12
≥ 70% to ≤ 90%	6	12	18
> 90%	12	10	22
Percent Predicted Forced Expiratory Volume in 1 Second (FEV1)			
Percent predicted for age, gender, and height.			
Units: percentage			
arithmetic mean	83.7	84.7	

standard deviation	± 20.37	± 15.83	-
Weight			
Units: kilograms			
arithmetic mean	30	31.8	
standard deviation	± 7.16	± 9.95	-
Body Mass Index			
Units: kilograms per square meter			
arithmetic mean	16.8	17.1	
standard deviation	± 1.75	± 2.61	-
Sweat Chloride			
Units: millimoles per liter			
arithmetic mean	104.8	104.3	
standard deviation	± 8.87	± 14.54	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Oral tablet every 12 hours (q12h) for up to 48 weeks.	
Reporting group title	150 mg Ivacaftor q12h
Reporting group description:	
Oral tablet of 150 milligram (mg) of ivacaftor q12h for up to 48 weeks.	

Primary: Absolute Change From Baseline in Percent Predicted Forced Expiratory Volume in 1 Second (FEV1) Through Week 24

End point title	Absolute Change From Baseline in Percent Predicted Forced Expiratory Volume in 1 Second (FEV1) Through Week 24
End point description:	
Spirometry (as measured by FEV1) is a standardized assessment to evaluate lung function that is the most widely used endpoint in cystic fibrosis studies. All randomized subjects who received at least 1 dose of study drug (ivacaftor or placebo)and had available assessments during the time frame.	
End point type	Primary
End point timeframe:	
Baseline through 24 weeks	

End point values	Placebo	150 mg Ivacaftor q12h		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	26		
Units: percent of predicted volume (L)				
least squares mean (standard error)	0.1 (± 2.1)	12.6 (± 2.1)		

Statistical analyses

Statistical analysis title	FEV1 Through Week 24
Statistical analysis description:	
Primary analysis for primary efficacy variable was based on MMRM. Model included absolute change from baseline in percent predicted FEV1 as dependent variable, treatment (ivacaftor versus placebo) and visit (Day 15, Week 8, Week 16, and Week 24) as fixed effects, and subject as a random effect, with adjustment for the continuous baseline value of percent predicted FEV1. Denominator degrees of freedom were estimated using the Kenward-Roger approximation. No imputation of missing data was done.	
Comparison groups	Placebo v 150 mg Ivacaftor q12h

Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [1]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	12.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.6
upper limit	18.3
Variability estimate	Standard error of the mean
Dispersion value	2.9

Notes:

[1] - The primary endpoint and key secondary endpoints were tested in sequence. test 1: primary (α=0. 05); test 2: using Hochberg's step-up procedure on weight (Wk 24) and sweat chloride (Wk 24)(α=0. 05); test 3: CFQ-R respiratory domain score (Wk 24).

Secondary: Absolute Change From Baseline in Percent Predicted Forced Expiratory Volume in 1 Second (FEV1) Through Week 48

End point title	Absolute Change From Baseline in Percent Predicted Forced Expiratory Volume in 1 Second (FEV1) Through Week 48

End point description:

Spirometry (as measured by FEV1) is a standardized assessment to evaluate lung function that is the most widely used endpoint in cystic fibrosis studies.

All randomized subjects who received at least 1 dose of study drug (ivacaftor or placebo) and had available assessments during the time frame.

End point type	Secondary

End point timeframe:

Baseline through 48 weeks

End point values	Placebo	150 mg Ivacaftor q12h		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	26		
Units: percent of predicted volume (L)				
least squares mean (standard error)	0.7 (± 2)	10.7 (± 1.9)		

Statistical analyses

Statistical analysis title	FEV1 Through Week 48

Statistical analysis description:

Analysis for this variable was similar to that of the primary analysis of the primary efficacy endpoint, MMRM. Estimates were obtained from MMRM with dependent variable absolute change from baseline, fixed effects for categorical visit & treatment group, & adjustment for the continuous baseline value of percent predicted FEV1, using unstructured covariance matrix. Denominator degrees of freedom were estimated using the Kenward-Roger approximation. No imputation of missing data was done.

Comparison groups	Placebo v 150 mg Ivacaftor q12h

Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0006 [2]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	10
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.5
upper limit	15.5
Variability estimate	Standard error of the mean
Dispersion value	2.7

Notes:

[2] - There was no adjustment for multiple comparisons.

Secondary: Absolute Change From Baseline in Cystic Fibrosis Questionnaire-Revised (CFQ-R) Through Week 24 and Week 48 (Respiratory Domain Score, Children)

End point title	Absolute Change From Baseline in Cystic Fibrosis Questionnaire-Revised (CFQ-R) Through Week 24 and Week 48 (Respiratory Domain Score, Children)

End point description:

The CFQ-R is a health-related quality of life measure for subjects with cystic fibrosis. Each domain is scored from 0 (worst) to 100 (best). A difference of at least 4 points in the respiratory domain score of the CFQ-R is considered a minimal clinically important difference (MCID).

All randomized subjects who received at least 1 dose of study drug (ivacaftor or placebo) and had available assessments during the time frame.

End point type	Secondary

End point timeframe:

Baseline through 24 weeks and 48 weeks

End point values	Placebo	150 mg Ivacaftor q12h		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	26		
Units: score on a scale				
least squares mean (standard error)				
Change from Baseline Through Week 24	0.3 (± 2.6)	6.3 (± 2.5)		
Change from Baseline Through Week 48	1 (± 2.3)	6.1 (± 2.2)		

Statistical analyses

Statistical analysis title	CFQ-R Through Week 24

Statistical analysis description:

Through Week 24: Analysis for this variable was similar to that of the primary analysis of the primary efficacy endpoint, a Mixed-Effects Model for Repeated Measures (MMRM), with the addition of the baseline domain score as a covariate.

Comparison groups	Placebo v 150 mg Ivacaftor q12h
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1092 [3]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	6.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	13.5
Variability estimate	Standard error of the mean
Dispersion value	3.7

Notes:

[3] - The primary endpoint and key secondary endpoints were tested in sequence. test 1: primary (α=0.05); test 2: using Hochberg's step-up procedure on weight (Wk 24) and sweat chloride (Wk 24)(α=0.05); test 3: CFQ-R respiratory domain score (Wk 24).

Statistical analysis title	CFQ-R Through Week 48

Statistical analysis description:

Through Week 48: Analysis for this variable was similar to that of the primary analysis of the primary efficacy endpoint, a Mixed-Effects Model for Repeated Measures (MMRM), with the addition of the baseline domain score as a covariate.

Comparison groups	Placebo v 150 mg Ivacaftor q12h
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1354 [4]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	5.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	11.8
Variability estimate	Standard error of the mean
Dispersion value	3.3

Notes:

[4] - There was no adjustment for multiple comparisons.

Secondary: Absolute Change From Baseline in Sweat Chloride Concentration Through Week 24 and Week 48

End point title	Absolute Change From Baseline in Sweat Chloride Concentration Through Week 24 and Week 48

End point description:

The sweat chloride (quantitative pilocarpine iontophoresis) test is a standard diagnostic tool for CF, serving as an indicator of cystic fibrosis transmembrane conductance regulator (CFTR) activity.

All randomized subjects who received at least 1 dose of study drug (ivacaftor or placebo) and had available assessments during the time frame.

End point type	Secondary

End point timeframe:

Baseline through 24 weeks and 48 weeks

End point values	Placebo	150 mg Ivacaftor q12h		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	23		
Units: millimoles per liter				
least squares mean (standard error)				
Change from Baseline Through Week 24	-1.2 (± 2.6)	-55.5 (± 2.6)		
Change from Baseline Through Week 48	-2.6 (± 2.6)	-56 (± 2.5)		

Statistical analyses

Statistical analysis title	Sweat Chloride Concentration Through Week 24

Statistical analysis description:

Through Week 24: Analysis for this variable was similar to that of the primary analysis of the primary efficacy endpoint. Estimates were from Mixed-Effects Model for Repeated Measures (MMRM) with dependent variable absolute change from baseline, fixed effects for categorical visit and treatment group, and adjustment for continuous baseline value for sweat chloride and percent predicted forced expiratory volume in 1 second (FEV1), using unstructured covariance matrix.

Comparison groups	Placebo v 150 mg Ivacaftor q12h
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [5]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-54.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-61.8
upper limit	-46.8
Variability estimate	Standard error of the mean
Dispersion value	3.7

Notes:

[5] - The primary endpoint and key secondary endpoints were tested in sequence. test 1: primary (α=0.05); test 2: using Hochberg's step-up procedure on weight (Wk 24) and sweat chloride (Wk 24)(α=0.05); test 3: CFQ-R respiratory domain score (Wk 24).

Statistical analysis title	Sweat Chloride Concentration Through Week 48

Statistical analysis description:

Through Week 48: Analysis for this variable was similar to that of the primary analysis of the primary efficacy endpoint. Estimates were from Mixed-Effects Model for Repeated Measures (MMRM) with dependent variable absolute change from baseline, fixed effects for categorical visit and treatment group, and adjustment for continuous baseline value for sweat chloride and percent predicted forced expiratory volume in 1 second (FEV1), using unstructured covariance matrix.

Comparison groups	Placebo v 150 mg Ivacaftor q12h

Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [6]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-53.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-60.9
upper limit	-46
Variability estimate	Standard error of the mean
Dispersion value	3.7

Notes:

[6] - There was no adjustment for multiple comparisons.

Secondary: Absolute Change From Baseline in Weight at Week 24 and Week 48

End point title	Absolute Change From Baseline in Weight at Week 24 and Week 48

End point description:

As malnutrition is common in subjects with CF because of increased energy expenditures due to lung disease and fat malabsorption, body weight is an important clinical measure of nutritional status.

All randomized subjects who received at least 1 dose of study drug (ivacaftor or placebo) and had available assessments during the time frame.

End point type	Secondary

End point timeframe:

Baseline to 24 weeks and 48 weeks

End point values	Placebo	150 mg Ivacaftor q12h		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	26		
Units: kilograms				
least squares mean (standard error)				
At Week 24	1.8 (± 0.4)	3.7 (± 0.4)		
At Week 48	3.1 (± 0.5)	5.9 (± 0.5)		

Statistical analyses

Statistical analysis title	Weight at Week 24

Statistical analysis description:

At Week 24: Analysis for this variable was based on a Linear Mixed Effect (LME) model with dependent variable weight; treatment as a fixed effect; and intercept, visit, and treatment by visit interaction as random effects, with adjustment for baseline percent predicted forced expiratory volume in 1 second (FEV1) severity.

Comparison groups	Placebo v 150 mg Ivacaftor q12h

Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0004 [7]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	2.9
Variability estimate	Standard error of the mean
Dispersion value	0.5

Notes:

[7] - The primary endpoint and key secondary endpoints were tested in sequence. test 1: primary (α=0. 05); test 2: using Hochberg's step-up procedure on weight (Wk 24) and sweat chloride (Wk 24)(α=0. 05); test 3: CFQ-R respiratory domain score (Wk 24).

Statistical analysis title	Weight at Week 48

Statistical analysis description:

At Week 48: Analysis for this variable was based on a Linear Mixed Effect (LME) model with random intercept and random slope, treatment as a fixed effect, and visit (days on study) and treatment by visit interaction as random effects, with adjustment for categorical baseline percent predicted forced expiratory volume in 1 second (FEV1) severity.

Comparison groups	Placebo v 150 mg Ivacaftor q12h
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002 [8]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.3
upper limit	4.2
Variability estimate	Standard error of the mean
Dispersion value	0.7

Notes:

[8] - P-value is for the treatment effect at Week 48 (obtained as a linear contrast of treatment at Day 336). There was no adjustment for multiple comparisons.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

For enrolled subjects, adverse events (AEs) were collected through the follow-up visit in each study part. For subjects who completed 48 weeks of treatment and enrolled in the open-label extension study, AEs were only collected through the Week 48 visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Oral tablet every 12 hours (q12h) for up to 48 weeks.

Reporting group title	150 mg Ivacaftor q12h

Reporting group description:

Oral tablet of 150 mg of ivacaftor q12h for up to 48 weeks.

Serious adverse events	Placebo	150 mg Ivacaftor q12h	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 26 (23.08%)	5 / 26 (19.23%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary function test decreased			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Muscle strain			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic			

disorders			
Cystic fibrosis lung			
subjects affected / exposed	3 / 26 (11.54%)	2 / 26 (7.69%)	
occurrences causally related to treatment / all	0 / 3	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Pseudomonas infection			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Productive cough			
subjects affected / exposed	1 / 26 (3.85%)	1 / 26 (3.85%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung consolidation			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			

Adjustment disorder			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Affective disorder			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conversion disorder			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Placebo	150 mg Ivacaftor q12h	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 26 (96.15%)	26 / 26 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	7 / 26 (26.92%)	6 / 26 (23.08%)	
occurrences (all)	16	6	
Fatigue			
subjects affected / exposed	2 / 26 (7.69%)	1 / 26 (3.85%)	
occurrences (all)	2	1	
Malaise			

subjects affected / exposed	1 / 26 (3.85%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Application site rash			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Chest pain			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Pain			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	2 / 26 (7.69%)	1 / 26 (3.85%)	
occurrences (all)	2	1	
Allergy to animal			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	19 / 26 (73.08%)	13 / 26 (50.00%)	
occurrences (all)	40	21	
Oropharyngeal pain			
subjects affected / exposed	4 / 26 (15.38%)	7 / 26 (26.92%)	
occurrences (all)	9	10	
Nasal congestion			
subjects affected / exposed	4 / 26 (15.38%)	5 / 26 (19.23%)	
occurrences (all)	7	7	
Rhinorrhoea			
subjects affected / exposed	4 / 26 (15.38%)	3 / 26 (11.54%)	
occurrences (all)	8	3	
Wheezing			
subjects affected / exposed	4 / 26 (15.38%)	3 / 26 (11.54%)	
occurrences (all)	4	4	
Productive cough			

subjects affected / exposed	4 / 26 (15.38%)	2 / 26 (7.69%)	
occurrences (all)	5	2	
Rales			
subjects affected / exposed	4 / 26 (15.38%)	2 / 26 (7.69%)	
occurrences (all)	5	2	
Dysphonia			
subjects affected / exposed	1 / 26 (3.85%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Epistaxis			
subjects affected / exposed	1 / 26 (3.85%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Nasal inflammation			
subjects affected / exposed	1 / 26 (3.85%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Pharyngeal erythema			
subjects affected / exposed	0 / 26 (0.00%)	2 / 26 (7.69%)	
occurrences (all)	0	2	
Respiratory tract congestion			
subjects affected / exposed	2 / 26 (7.69%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Rhinitis allergic			
subjects affected / exposed	0 / 26 (0.00%)	2 / 26 (7.69%)	
occurrences (all)	0	2	
Asthma			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	2	
Asthma exercise induced			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Lung hyperinflation			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Nasal mucosal disorder			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Nasal ulcer			

subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
PostNasal Drip			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Prolonged expiration			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Rhonchi			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Sinus congestion			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Sneezing			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Throat irritation			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Tonsillar hypertrophy			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Tonsillar inflammation			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Anger			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Anxiety			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Personality change			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 26 (11.54%)	2 / 26 (7.69%)	
occurrences (all)	6	2	
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 26 (7.69%)	3 / 26 (11.54%)	
occurrences (all)	3	3	
Bacteria Sputum Identified			
subjects affected / exposed	3 / 26 (11.54%)	2 / 26 (7.69%)	
occurrences (all)	3	2	
Eosinophil count increased			
subjects affected / exposed	1 / 26 (3.85%)	3 / 26 (11.54%)	
occurrences (all)	1	5	
Culture throat positive			
subjects affected / exposed	1 / 26 (3.85%)	2 / 26 (7.69%)	
occurrences (all)	1	2	
Breath sounds abnormal			
subjects affected / exposed	2 / 26 (7.69%)	0 / 26 (0.00%)	
occurrences (all)	3	0	
Forced expiratory volume decreased			
subjects affected / exposed	0 / 26 (0.00%)	2 / 26 (7.69%)	
occurrences (all)	0	2	
Neutrophil count decreased			
subjects affected / exposed	0 / 26 (0.00%)	2 / 26 (7.69%)	
occurrences (all)	0	3	
White blood cell count decreased			
subjects affected / exposed	0 / 26 (0.00%)	2 / 26 (7.69%)	
occurrences (all)	0	3	
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Blood pressure increased			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Chest X-ray abnormal			

subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Coagulation test abnormal			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Haematocrit increased			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
International normalised ratio increased			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Intraocular pressure increased			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Liver palpable subcostal			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Lymphocyte count decreased			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Lymphocyte count increased			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Neutrophil count increased			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Neutrophil percentage decreased			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Platelet count decreased			

subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	2	
Prothrombin time prolonged			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Sputum abnormal			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Sputum culture positive			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Urine ketone body present			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Virus Serology Test Positive			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
White blood cell count increased			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
PULMONARY FUNCTION TEST DECREASED			
subjects affected / exposed	3 / 26 (11.54%)	2 / 26 (7.69%)	
occurrences (all)	4	2	
Injury, poisoning and procedural complications			
Excoriation			
subjects affected / exposed	2 / 26 (7.69%)	1 / 26 (3.85%)	
occurrences (all)	3	2	
Skin Laceration			
subjects affected / exposed	1 / 26 (3.85%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Arthropod sting			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	2	
Contusion			

subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Foreign body in eye			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Joint Sprain			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Limb injury			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Lower limb fracture			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Medical device complication			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Post-traumatic pain			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Procedural pain			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Skeletal injury			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Sunburn			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Tooth fracture			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Wrong drug administered			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Congenital, familial and genetic			

disorders Cystic fibrosis lung subjects affected / exposed occurrences (all)	6 / 26 (23.08%) 8	7 / 26 (26.92%) 9	
Nervous system disorders Headache subjects affected / exposed occurrences (all) Lethargy subjects affected / exposed occurrences (all)	4 / 26 (15.38%) 8 1 / 26 (3.85%) 1	7 / 26 (26.92%) 15 0 / 26 (0.00%) 0	
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	2 / 26 (7.69%) 2	1 / 26 (3.85%) 1	
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all) Tympanic membrane hyperaemia subjects affected / exposed occurrences (all)	1 / 26 (3.85%) 1 0 / 26 (0.00%) 0	1 / 26 (3.85%) 2 1 / 26 (3.85%) 1	
Eye disorders Astigmatism subjects affected / exposed occurrences (all) Conjunctivitis subjects affected / exposed occurrences (all) Hypermetropia subjects affected / exposed occurrences (all)	0 / 26 (0.00%) 0 0 / 26 (0.00%) 0 0 / 26 (0.00%) 0	1 / 26 (3.85%) 1 1 / 26 (3.85%) 1 1 / 26 (3.85%) 1	
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all) Vomiting	5 / 26 (19.23%) 5	6 / 26 (23.08%) 9	

subjects affected / exposed	7 / 26 (26.92%)	2 / 26 (7.69%)	
occurrences (all)	11	3	
Abdominal pain			
subjects affected / exposed	3 / 26 (11.54%)	3 / 26 (11.54%)	
occurrences (all)	5	4	
Constipation			
subjects affected / exposed	2 / 26 (7.69%)	2 / 26 (7.69%)	
occurrences (all)	2	2	
Diarrhoea			
subjects affected / exposed	0 / 26 (0.00%)	3 / 26 (11.54%)	
occurrences (all)	0	3	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 26 (0.00%)	2 / 26 (7.69%)	
occurrences (all)	0	2	
Nausea			
subjects affected / exposed	2 / 26 (7.69%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Abdominal discomfort			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Dysphagia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Eosinophilic oesophagitis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Gingival bleeding			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Lip blister			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Loose tooth			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Post-tussive vomiting			

subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Steatorrhoea			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Tooth disorder			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	3 / 26 (11.54%)	2 / 26 (7.69%)	
occurrences (all)	3	3	
Dermatitis contact			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Drug eruption			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Ecchymosis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Nail discolouration			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Onychoclasis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Rash maculo-papular			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Rash vesicular			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	

Swelling face			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Urticaria			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 26 (3.85%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Myalgia			
subjects affected / exposed	0 / 26 (0.00%)	2 / 26 (7.69%)	
occurrences (all)	0	4	
Neck pain			
subjects affected / exposed	0 / 26 (0.00%)	2 / 26 (7.69%)	
occurrences (all)	0	2	
Pain in extremity			
subjects affected / exposed	1 / 26 (3.85%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Joint swelling			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal pain			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal stiffness			

subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 26 (7.69%)	6 / 26 (23.08%)	
occurrences (all)	3	8	
Upper respiratory tract infection			
subjects affected / exposed	2 / 26 (7.69%)	6 / 26 (23.08%)	
occurrences (all)	2	9	
Bronchitis			
subjects affected / exposed	2 / 26 (7.69%)	3 / 26 (11.54%)	
occurrences (all)	2	4	
Otitis media			
subjects affected / exposed	1 / 26 (3.85%)	4 / 26 (15.38%)	
occurrences (all)	2	7	
Sinusitis			
subjects affected / exposed	3 / 26 (11.54%)	2 / 26 (7.69%)	
occurrences (all)	4	3	
Ear infection			
subjects affected / exposed	2 / 26 (7.69%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Pharyngitis streptococcal			
subjects affected / exposed	0 / 26 (0.00%)	2 / 26 (7.69%)	
occurrences (all)	0	2	
Rhinitis			
subjects affected / exposed	0 / 26 (0.00%)	2 / 26 (7.69%)	
occurrences (all)	0	3	
Bacterial disease carrier			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Bronchopulmonary aspergillosis allergic			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Coxsackie viral infection			

subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Eye infection			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Febrile infection			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Laryngitis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Molluscum contagiosum			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Oral candidiasis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Otitis externa			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Pharyngitis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Pseudomonas Infection			
subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Respiratory tract infection			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Respiratory tract infection viral			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Sinobronchitis			

subjects affected / exposed	0 / 26 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	2	
Urinary tract infection			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Diabetes mellitus			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Weight gain poor			
subjects affected / exposed	1 / 26 (3.85%)	0 / 26 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 April 2009	Added a 24-week Extension Period in Part B for a total treatment duration of 48 weeks to obtain further safety data of VX-770. Changed the Part B secondary objective to evaluate the safety of VX-770 after both 24 weeks (original objective) and 48 weeks (newly added) of treatment. Added a Part B secondary objective "To evaluate the efficacy of VX-770 after 48 weeks of treatment in subjects 6 to 11 years of age with CF who have the G551DCFTR mutation on at least 1 allele". Added a Part B secondary efficacy endpoint of "Absolute change from baseline in percent predicted FEV1 through Week 48". Added the analysis of Part B secondary and tertiary efficacy endpoints at Week 48. Added the option for subjects who complete 48 weeks of treatment in Part B to enroll in an open-label safety study of VX-770. Removed exclusion criterion regarding change in antibiotic therapy for pulmonary exacerbation in Part B.
31 August 2009	Increased the upper limit of eligible FEV1 to 105 percent (%) predicted value. Allowed the scheduling of the Day -14 Visit after a subject without verification of the screening clinical laboratory and ECG results to accommodate those subjects who wish to undergo screening on Day -15 and enter the Run-in Period the next day (Day -14). Updated study restrictions, the emergency unblinding process, and clarified the criteria for withdrawal of subjects from the study.
05 February 2010	Based on preliminary results from Part A, changed the dose to be administered from 100 mg to 150 mg in Part B. Updated the description of the number of Part B subjects in the Overall Study Design and Plan to indicate that "at least 20 of the 30 subjects with less than equal to (<=) 90% predicted FEV1" will be included in Part B.
12 April 2010	Changes in study procedures regarding liver function testing and considerations for study drug interruption and discontinuation to ensure the continued safety of subjects in this study. A PK sample collection was added to the Early Termination Visit to assess any potential association between study drug exposure and the reason for discontinuation.
09 July 2010	FEV1 value to be used to stratify randomization in Part B was inadvertently changed from the Screening Visit to the Day -14 Visit to align the stratification on a visit common to all subjects participating in Part B. Changed the definition of treatment emergent adverse events (TEAEs) for clarity and consistency with the adverse event definition.
13 November 2010	Changed the secondary endpoint "Rate of change in weight through Weeks 24 and 48" to "Change from baseline in weight at Weeks 24 and 48".

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported