ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: August 1, 2015

ClinicalTrials.gov ID: NCT00865904

## Study Identification

| | |
|---|---|
| Unique Protocol ID: | VX08-809-101 |
| Brief Title: | Study of VX-809 in Cystic Fibrosis Subjects With the ΔF508-CFTR Gene Mutation |
| Official Title: | A Randomized, Double-Blind, Placebo-Controlled, Multiple Dose Study of VX-809 to Evaluate Safety, Pharmacokinetics, and Pharmacodynamics of VX-809 in Cystic Fibrosis Subjects Homozygous for the ΔF508-CFTR Gene Mutation |
| Secondary IDs: | |

## Study Status

| | |
|---|---|
| Record Verification: | June 2015 |
| Overall Status: | Completed |
| Study Start: | March 2009 |
| Primary Completion: | December 2009 [Actual] |
| Study Completion: | December 2009 [Actual] |

## Sponsor/Collaborators

| | |
|---|---|
| Sponsor: | Vertex Pharmaceuticals Incorporated |
| Responsible Party: | Sponsor |
| Collaborators: | |

## Oversight

| | |
|---|---|
| FDA Regulated?: | Yes |
| Applicable Trial?: | Section 801 Clinical Trial? Yes |

| | |
|---|---|
| | Delayed Posting? No |
| IND/IDE Protocol?: | Yes |
| IND/IDE Information: | Grantor: CDER<br>IND/IDE Number: 79,521<br>Serial Number: 0019<br>Has Expanded Access? No |
| Review Board: | Approval Status: Approved<br>Approval Number: 02/03/2009<br>Board Name: Administrative Panel on Human Subjects in Medical Research<br>Board Affiliation: Stanford University<br>Phone: 650-736-4390<br>Email: |
| Data Monitoring?: | Yes |
| Plan to Share IPD?: | |
| Oversight Authorities: | United States: Food and Drug Administration<br>Canada: Health Canada<br>Germany: Federal Institute for Drugs and Medical Devices<br>Belgium: Federal Agency for Medicinal Products and Health Products<br>Netherlands: The Central Committee on Research Involving Human Subjects (CCMO) |

## Study Description

| | |
|---|---|
| Brief Summary: | The primary objective of the study was to evaluate the safety and tolerability of VX-809 in participants with cystic fibrosis (CF) who are homozygous for the F508del mutation on the CF transmembrane conductance regulator (CFTR) gene. |
| Detailed Description: | This was a Phase 2, randomized, double-blind, placebo-controlled, multiple-dose study of orally-administered VX-809 in participants with CF who are homozygous for the specific CFTR mutation known as ΔF508 or F508del. Enrollment was planned for 90 participants at approximately 20 centers. Participants were planned to be randomized in a 4:1 ratio to receive 1 of 4 doses of VX-809 or placebo once a day for 28 days in a parallel design. Participants were outpatients during the study, except for overnight stays on Day 1 and 28. |

## Conditions

| | |
|---|---|
| Conditions: | Cystic Fibrosis |
| Keywords: | ΔF508<br>F508del<br>Cystic Fibrosis Transmembrane Conductance Regulator<br>CFTR<br>Pancreatic diseases<br>Lung diseases |

Genetic disease, inborn
Infant, newborn, diseases

## Study Design

| | |
|---|---|
| Study Type: | Interventional |
| Primary Purpose: | Treatment |
| Study Phase: | Phase 2 |
| Intervention Model: | Parallel Assignment |
| Number of Arms: | 5 |
| Masking: | Double Blind (Subject, Caregiver, Investigator) |
| Allocation: | Randomized |
| Endpoint Classification: | Safety Study |
| Enrollment: | 93 [Actual] |

## Arms and Interventions

| Arms | Assigned Interventions |
|---|---|
| Placebo Comparator: Placebo<br>Placebo matched to VX-809 capsule orally once daily for 28 days. | Drug: Placebo<br>Placebo matched to VX-809 capsules. |
| Experimental: VX-809, 25 mg<br>VX-809, 25 milligram (mg) capsule orally once daily for 28 days. | Drug: VX-809<br>Capsules |
| Experimental: VX-809, 50 mg<br>VX-809, 50 mg capsule orally once daily for 28 days. | Drug: VX-809<br>Capsules |
| Experimental: VX-809, 100 mg<br>VX-809, 100 mg capsule orally once daily for 28 days. | Drug: VX-809<br>Capsules |
| Experimental: VX-809, 200 mg<br>VX-809, 200 mg capsule orally once daily for 28 days. | Drug: VX-809<br>Capsules |

## Outcome Measures

[See Results Section.]

## Eligibility

| | |
|---|---|
| Minimum Age: | 18 Years |
| Maximum Age: | |

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Confirmed diagnosis of CF with ΔF508-CFTR mutation in both alleles
- Forced expiratory volume in 1 second (FEV1) greater than or equal to (>=) 40 percent (%) of predicted normal for age, gender, and height
- Weight >=40 kilograms (kg) and body mass index greater than or equal to 18.5 kilogram per square meter (kg/m^2)
- Screening laboratory values, tests, and physical examination within acceptable ranges
- Negative pregnancy test (for women of child-bearing potential)
- Able and willing to follow contraceptive requirements
- Willing to remain on a stable medication regimen for the duration of study participation

Exclusion Criteria:

- History of any illness, or any ongoing acute illness, that could impact the safety of the study participant or may confound results of study
- Pulmonary exacerbation or changes in therapy for pulmonary disease within 14 days before receiving the first dose of study drug
- Impaired hepatic or renal function
- History of organ or hematological transplant

## Contacts/Locations

Study Officials: Medical Monitor
Study Director
Vertex Pharmaceuticals Incorporated

Locations: United States, Colorado
Aurora, Colorado, United States

United States, Alabama
Birmingham, Alabama, United States

United States, Maryland
Baltimore, Maryland, United States

United States, Iowa
Iowa City, Iowa, United States

United States, Ohio
Cincinnati, Ohio, United States

Columbus, Ohio, United States

United States, Washington
Seattle, Washington, United States

United States, North Carolina
Chapel Hill, North Carolina, United States

United States, Ohio
Cleveland, Ohio, United States

United States, Pennsylvania
Pittsburgh, Pennsylvania, United States

United States, Minnesota
Minneapolis, Minnesota, United States

United States, California
Palo Alto, California, United States

San Diego, California, United States

United States, Pennsylvania
Philadelphia, Pennsylvania, United States

United States, Missouri
St. Louis, Missouri, United States

United States, Georgia
Atlanta, Georgia, United States

Canada, Ontario
Toronto, Ontario, Canada

Germany
Hannover, Germany

Belgium
Leuven, Belgium

Netherlands
Rotterdam, Netherlands

Utrecht, Netherlands

Belgium
Brussels, Belgium

United States, Illinois
Chicago, Illinois, United States

United States, Massachusetts
Boston, Massachusetts, United States

Germany
Cologne, Germany

## References

Citations:

Links:

Study Data/Documents:

## Delayed Results

| | |
|---|---|
| Delay Type | Certify Initial Approval |
| Intervention Name(s) | VX-809 |

# Study Results

## Participant Flow

Reporting Groups

| | Description |
|---|---|
| Placebo | Placebo matched to VX-809 capsule orally once daily for 28 days. |
| VX-809, 25 mg | VX-809, 25 milligram (mg) capsule orally once daily for 28 days. |
| VX-809, 50 mg | VX-809, 50 mg capsule orally once daily for 28 days. |
| VX-809, 100 mg | VX-809, 100 mg capsule orally once daily for 28 days. |
| VX-809, 200 mg | VX-809, 200 mg capsule orally once daily for 28 days. |

Overall Study

| | Placebo | VX-809, 25 mg | VX-809, 50 mg | VX-809, 100 mg | VX-809, 200 mg |
|---|---|---|---|---|---|
| Started | 19 [1] | 18 [1] | 18 [1] | 18 [1] | 20 [1] |
| Completed | 17 [2] | 18 [2] | 18 [2] | 17 [2] | 19 [2] |
| Not Completed | 2 | 0 | 0 | 1 | 1 |
| Randomized but not Treated | 2 | 0 | 0 | 1 | 1 |

[1] Randomized.
[2] Completed 14-day follow-up.

## Baseline Characteristics

Baseline Analysis Population Description

Full Analysis Set (FAS) included all randomized participants who received at least 1 dose of study drug.

Reporting Groups

| | Description |
|---|---|
| Placebo | Placebo matched to VX-809 capsule orally once daily for 28 days. |
| VX-809, 25 mg | VX-809, 25 mg capsule orally once daily for 28 days. |
| VX-809, 50 mg | VX-809, 50 mg capsule orally once daily for 28 days. |
| VX-809, 100 mg | VX-809, 100 mg capsule orally once daily for 28 days. |
| VX-809, 200 mg | VX-809, 200 mg capsule orally once daily for 28 days. |

Baseline Measures

| | | Placebo | VX-809, 25 mg | VX-809, 50 mg | VX-809, 100 mg | VX-809, 200 mg | Total |
|---|---|---|---|---|---|---|---|
| Overall Number of Participants | | 17 | 18 | 18 | 17 | 19 | 89 |
| Age, Continuous<br>Mean (Standard Deviation)<br>Unit of measure: years | Number Analyzed | 17 participants | 18 participants | 18 participants | 17 participants | 19 participants | 89 participants |
| | | 31.5 (9.35) | 27.7 (8.98) | 27.1 (8.20) | 30.1 (11.55) | 26.7 (6.82) | 28.6 (9.1) |

| | | Placebo | VX-809, 25 mg | VX-809, 50 mg | VX-809, 100 mg | VX-809, 200 mg | Total |
|---|---|---|---|---|---|---|---|
| Gender, Male/ Female<br>Measure Type: Count of Participants<br>Unit of measure: participants | Number Analyzed | 17 participants | 18 participants | 18 participants | 17 participants | 19 participants | 89 participants |
| | Female | 6 35.29% | 9 50% | 9 50% | 5 29.41% | 7 36.84% | 36 40.45% |
| | Male | 11 64.71% | 9 50% | 9 50% | 12 70.59% | 12 63.16% | 53 59.55% |

## Outcome Measures

1. Primary Outcome Measure:

| | |
|---|---|
| Measure Title | Safety and Tolerability Based on Adverse Events (AEs) |
| Measure Description | AE: any untoward medical occurrence in a participant during the study; the event does not necessarily have a causal relationship with the treatment. This includes any newly occurring event or previous condition that has increased in severity or frequency after the informed consent form is signed. AE includes serious as well as Non-serious AEs. Serious adverse event (SAE) (subset of AE): medical event or condition, which falls into any of the following categories, regardless of its relationship to the study drug: death, life threatening adverse experience, in-patient hospitalization/ prolongation of hospitalization, persistent/significant disability or incapacity, congenital anomaly/birth defect, important medical event. Number of participants with AEs and SAEs are reported. An AE that started at or after initial dosing of study drug, or increased in severity after initial dosing of study drug visit is considered treatment-emergent. |
| Time Frame | Up to 14 days after last dose (last dose = Day 28) |
| Safety Issue? | Yes |

Analysis Population Description

Safety set included all participants who received at least 1 dose of study drug.

Reporting Groups

| | Description |
|---|---|
| Placebo | Placebo matched to VX-809 capsule orally once daily for 28 days. |
| VX-809, 25 mg | VX-809, 25 mg capsule orally once daily for 28 days. |
| VX-809, 50 mg | VX-809, 50 mg capsule orally once daily for 28 days. |
| VX-809, 100 mg | VX-809, 100 mg capsule orally once daily for 28 days. |
| VX-809, 200 mg | VX-809, 200 mg capsule orally once daily for 28 days. |

Measured Values

| | Placebo | VX-809, 25 mg | VX-809, 50 mg | VX-809, 100 mg | VX-809, 200 mg |
|---|---|---|---|---|---|
| Number of Participants Analyzed | 17 | 18 | 18 | 17 | 19 |
| Safety and Tolerability Based on Adverse Events (AEs)<br>Measure Type: Number<br>Unit of measure: participants | | | | | |
| Participants With Any AE | 17 | 16 | 15 | 16 | 18 |
| Participants With SAE | 1 | 5 | 1 | 0 | 3 |

2. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Change From Baseline in Forced Expiratory Volume in 1 Second (FEV1) at Day 28 |
| Measure Description | FEV1 is the volume of air that can forcibly be blown out in one second, after full inspiration. |
| Time Frame | Baseline, Day 28 |
| Safety Issue? | No |

Analysis Population Description

Full Analysis Set (FAS) included all randomized participants who received at least 1 dose of study drug. Number of participants analyzed signifies participants evaluable for this outcome.

Reporting Groups

| | Description |
|---|---|
| Placebo | Placebo matched to VX-809 capsule orally once daily for 28 days. |
| VX-809, 25 mg | VX-809, 25 mg capsule orally once daily for 28 days. |
| VX-809, 50 mg | VX-809, 50 mg capsule orally once daily for 28 days. |
| VX-809, 100 mg | VX-809, 100 mg capsule orally once daily for 28 days. |
| VX-809, 200 mg | VX-809, 200 mg capsule orally once daily for 28 days. |

Measured Values

| | Placebo | VX-809, 25 mg | VX-809, 50 mg | VX-809, 100 mg | VX-809, 200 mg |
|---|---|---|---|---|---|
| Number of Participants Analyzed | 17 | 17 | 17 | 16 | 18 |

| | Placebo | VX-809, 25 mg | VX-809, 50 mg | VX-809, 100 mg | VX-809, 200 mg |
|---|---|---|---|---|---|
| Change From Baseline in Forced Expiratory Volume in 1 Second (FEV1) at Day 28<br>Least Squares Mean (95% Confidence Interval)<br>Unit of measure: liters | 0.029 (-0.0823 to 0.1398) | -0.049 (-0.1578 to 0.0588) | -0.031 (-0.1401 to 0.0787) | 0.015 (-0.0972 to 0.1263) | -0.009 (-0.1146 to 0.0970) |

3. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Change From Baseline in Percent Predicted FEV1 at Day 28 |
| Measure Description | FEV1 is the volume of air that can forcibly be blown out in one second, after full inspiration. Predicted FEV1 (for age, gender, and height) was calculated using the Knudson method. |
| Time Frame | Baseline, Day 28 |
| Safety Issue? | No |

Analysis Population Description

FAS. Number of participants analyzed signifies participants evaluable for this outcome.

Reporting Groups

| | Description |
|---|---|
| Placebo | Placebo matched to VX-809 capsule orally once daily for 28 days. |
| VX-809, 25 mg | VX-809, 25 mg capsule orally once daily for 28 days. |
| VX-809, 50 mg | VX-809, 50 mg capsule orally once daily for 28 days. |
| VX-809, 100 mg | VX-809, 100 mg capsule orally once daily for 28 days. |
| VX-809, 200 mg | VX-809, 200 mg capsule orally once daily for 28 days. |

Measured Values

| | Placebo | VX-809, 25 mg | VX-809, 50 mg | VX-809, 100 mg | VX-809, 200 mg |
|---|---|---|---|---|---|
| Number of Participants Analyzed | 17 | 17 | 17 | 16 | 18 |

| | Placebo | VX-809, 25 mg | VX-809, 50 mg | VX-809, 100 mg | VX-809, 200 mg |
|---|---|---|---|---|---|
| Change From Baseline in Percent Predicted FEV1 at Day 28<br>Least Squares Mean (95% Confidence Interval)<br>Unit of measure: Percent predicted of FEV1 | 0.285 (-2.8268 to 3.3973) | -1.637 (-4.6836 to 1.4089) | -0.375 (-3.4540 to 2.7046) | 0.168 (-2.9653 to 3.3011) | -0.165 (-3.1346 to 2.8044) |

4. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Change From Baseline in Forced Vital Capacity (FVC) at Day 28 |
| Measure Description | FVC is the volume of air that can be forcibly exhaled from the lungs after taking the deepest breath possible. |
| Time Frame | Baseline, Day 28 |
| Safety Issue? | No |

Analysis Population Description

FAS. Number of participants analyzed signifies participants evaluable for this outcome.

Reporting Groups

| | Description |
|---|---|
| Placebo | Placebo matched to VX-809 capsule orally once daily for 28 days. |
| VX-809, 25 mg | VX-809, 25 mg capsule orally once daily for 28 days. |
| VX-809, 50 mg | VX-809, 50 mg capsule orally once daily for 28 days. |
| VX-809, 100 mg | VX-809, 100 mg capsule orally once daily for 28 days. |
| VX-809, 200 mg | VX-809, 200 mg capsule orally once daily for 28 days. |

Measured Values

| | Placebo | VX-809, 25 mg | VX-809, 50 mg | VX-809, 100 mg | VX-809, 200 mg |
|---|---|---|---|---|---|
| Number of Participants Analyzed | 17 | 17 | 17 | 16 | 18 |
| Change From Baseline in Forced Vital Capacity (FVC) at Day 28<br>Mean (Standard Deviation)<br>Unit of measure: liters | 0.085 (0.2857) | -0.055 (0.2331) | -0.020 (0.3494) | -0.004 (0.1916) | -0.023 (0.3668) |

5. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Change From Baseline in Forced Expiratory Flow Over the Middle Half of the FVC (FEF25-75) at Day 28 |
| Measure Description | FEF25-75 is total volume of air exhaled from the lungs over the middle half of the FVC test, expressed as liters per second (L/sec). |
| Time Frame | Baseline, Day 28 |
| Safety Issue? | No |

Analysis Population Description

FAS. Number of participants analyzed signifies participants evaluable for this outcome.

Reporting Groups

| | Description |
|---|---|
| Placebo | Placebo matched to VX-809 capsule orally once daily for 28 days. |
| VX-809, 25 mg | VX-809, 25 mg capsule orally once daily for 28 days. |
| VX-809, 50 mg | VX-809, 50 mg capsule orally once daily for 28 days. |
| VX-809, 100 mg | VX-809, 100 mg capsule orally once daily for 28 days. |
| VX-809, 200 mg | VX-809, 200 mg capsule orally once daily for 28 days. |

Measured Values

| | Placebo | VX-809, 25 mg | VX-809, 50 mg | VX-809, 100 mg | VX-809, 200 mg |
|---|---|---|---|---|---|
| Number of Participants Analyzed | 17 | 17 | 17 | 16 | 18 |
| Change From Baseline in Forced Expiratory Flow Over the Middle Half of the FVC (FEF25-75) at Day 28<br>Mean (Standard Deviation)<br>Unit of measure: liters per second (L/sec) | -0.030 (0.1730) | -0.011 (0.3231) | -0.029 (0.4373) | 0.045 (0.2702) | -0.052 (0.3558) |

6. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Change From Baseline in Sweat Chloride at Day 28 |
| Measure Description | Sweat samples were collected using an approved Macroduct (Wescor) collection device. A volume of greater than or equal to (>=) 15 microliter was required for determination of sweat chloride. |

| | |
|---|---|
| Time Frame | Baseline, Day 28 |
| Safety Issue? | No |

Analysis Population Description

FAS. Number of participants analyzed signifies participants evaluable for this outcome.

Reporting Groups

| | Description |
|---|---|
| Placebo | Placebo matched to VX-809 capsule orally once daily for 28 days. |
| VX-809, 25 mg | VX-809, 25 mg capsule orally once daily for 28 days. |
| VX-809, 50 mg | VX-809, 50 mg capsule orally once daily for 28 days. |
| VX-809, 100 mg | VX-809, 100 mg capsule orally once daily for 28 days. |
| VX-809, 200 mg | VX-809, 200 mg capsule orally once daily for 28 days. |

Measured Values

| | Placebo | VX-809, 25 mg | VX-809, 50 mg | VX-809, 100 mg | VX-809, 200 mg |
|---|---|---|---|---|---|
| Number of Participants Analyzed | 16 | 16 | 16 | 15 | 16 |
| Change From Baseline in Sweat Chloride at Day 28<br>Least Squares Mean (95% Confidence Interval)<br>Unit of measure: millimole per liter (mmol/L) | 0.84 (-3.493 to 5.166) | 0.93 (-3.308 to 5.173) | -3.77 (-7.966 to 0.416) | -5.29 (-9.618 to -0.963) | -7.38 (-11.590 to -3.166) |

7. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Change From Baseline in Nasal Potential Difference (NPD) of Zero Chloride Plus Isoproterenol Response at Day 28 |
| Measure Description | Nasal potential difference (NPD) provides a direct and sensitive evaluation of sodium and chloride transport in secretory epithelial cells via assessment of transepithelial bioelectric properties. NPD under conditions of zero chloride concentration perfusion solution in the presence of isoproterenol is reported.<br><br>NPDs were performed according to Cystic Fibrosis Foundation Therapeutics Development Network (CFFT TDN) Standard Operating Procedure (SOP) 528.00 “Standardization of Measurement of Nasal Membrane Transepithelial Potential Difference (NPD) – electronic data capture (EDC) and Perfusion or Perfusion-Free Probe”. |
| Time Frame | Baseline, Day 28 |
| Safety Issue? | No |

Analysis Population Description

FAS. Number of participants analyzed signifies participants evaluable for this outcome.

Reporting Groups

| | Description |
|---|---|
| Placebo | Placebo matched to VX-809 capsule orally once daily for 28 days. |
| VX-809, 25 mg | VX-809, 25 mg capsule orally once daily for 28 days. |
| VX-809, 50 mg | VX-809, 50 mg capsule orally once daily for 28 days. |
| VX-809, 100 mg | VX-809, 100 mg capsule orally once daily for 28 days. |
| VX-809, 200 mg | VX-809, 200 mg capsule orally once daily for 28 days. |

Measured Values

| | Placebo | VX-809, 25 mg | VX-809, 50 mg | VX-809, 100 mg | VX-809, 200 mg |
|---|---|---|---|---|---|
| Number of Participants Analyzed | 12 | 16 | 13 | 11 | 12 |
| Change From Baseline in Nasal Potential Difference (NPD) of Zero Chloride Plus Isoproterenol Response at Day 28<br>Least Squares Mean (95% Confidence Interval)<br>Unit of measure: millivolts (mV) | -1.017 (-3.2979 to 1.2637) | 0.832 (-1.1302 to 2.7943) | 0.142 (-2.0369 to 2.3208) | 1.382 (-0.9853 to 3.7491) | 1.583 (-0.6952 to 3.8612) |

8. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Change From Baseline in Cystic Fibrosis Questionnaire-Revised (CFQ-R) Domain Scores at Day 28 |
| Measure Description | The CFQ-R is a validated participant-reported outcome measuring health-related quality of life for participants with cystic fibrosis. CFQ-R domains include: Body, Digestion, Eat, Emotion, Health Perceptions, Physical, Respiratory, Role, Social, Treatment Burden, Vitality, and Weight. Individual domain score range: 0-100; higher scores indicating fewer symptoms and better health-related quality of life. |
| Time Frame | Baseline, Day 28 |
| Safety Issue? | No |

Analysis Population Description

FAS. Number of participants analyzed signifies participants evaluable for this outcome.

Reporting Groups

| | Description |
|---|---|
| Placebo | Placebo matched to VX-809 capsule orally once daily for 28 days. |
| VX-809, 25 mg | VX-809, 25 mg capsule orally once daily for 28 days. |
| VX-809, 50 mg | VX-809, 50 mg capsule orally once daily for 28 days. |
| VX-809, 100 mg | VX-809, 100 mg capsule orally once daily for 28 days. |
| VX-809, 200 mg | VX-809, 200 mg capsule orally once daily for 28 days. |

Measured Values

| | Placebo | VX-809, 25 mg | VX-809, 50 mg | VX-809, 100 mg | VX-809, 200 mg |
|---|---|---|---|---|---|
| Number of Participants Analyzed | 17 | 17 | 17 | 16 | 18 |
| Change From Baseline in Cystic Fibrosis Questionnaire-Revised (CFQ-R) Domain Scores at Day 28<br>Least Squares Mean (95% Confidence Interval)<br>Unit of measure: units on a scale | | | | | |
| Body | -1.341 (-6.4183 to 3.7370) | -0.206 (-5.2276 to 4.8151) | -1.626 (-6.6796 to 3.4276) | 2.611 (-2.5525 to 7.7746) | 0.058 (-4.8954 to 5.0123) |
| Digestion | 4.620 (-0.2530 to 9.4935) | 2.284 (-2.4928 to 7.0605) | -0.719 (-5.5599 to 4.1216) | 0.251 (-4.6794 to 5.1810) | 2.578 (-2.1027 to 7.2580) |
| Eat | 2.110 (-3.9925 to 8.2128) | -3.662 (-9.6704 to 2.3463) | -7.269 (-13.3216 to -1.2161) | 3.242 (-3.0242 to 9.5087) | -2.576 (-8.4313 to 3.2793) |
| Emotion | 4.859 (-0.4200 to 10.1372) | -3.222 (-8.4312 to 1.9866) | -1.358 (-6.5817 to 3.8666) | 3.489 (-1.9312 to 8.9087) | -2.624 (-7.7058 to 2.4585) |
| Health Perceptions | 5.034 (-1.6041 to 11.6713) | -2.839 (-9.2912 to 3.6131) | -6.967 (-13.4203 to -0.5137) | -0.435 (-7.0778 to 6.2074) | -1.896 (-8.3524 to 4.5604) |
| Physical | 1.225 (-5.3271 to 7.7764) | -5.968 (-12.3586 to 0.4217) | -7.384 (-13.8167 to -0.9508) | -3.464 (-10.0613 to 3.1335) | -0.976 (-7.2596 to 5.3067) |
| Respiratory | 4.534 (-1.6158 to 10.6842) | -5.223 (-11.2414 to 0.7956) | -6.324 (-12.3453 to -0.3026) | -1.290 (-7.5407 to 4.9598) | 2.215 (-3.6610 to 8.0901) |
| Role | 2.210 (-3.2279 to 7.6481) | -5.941 (-11.3247 to -0.5577) | -4.599 (-9.9912 to 0.7925) | 1.097 (-4.4579 to 6.6510) | -6.533 (-11.7858 to -1.2803) |

| | Placebo | VX-809, 25 mg | VX-809, 50 mg | VX-809, 100 mg | VX-809, 200 mg |
|---|---|---|---|---|---|
| Social | -0.554 (-4.8235 to 3.7152) | -0.001 (-4.2221 to 4.2200) | -1.013 (-5.2372 to 3.2122) | 0.469 (-3.8898 to 4.8273) | -2.640 (-6.7802 to 1.5008) |
| Treatment Burden | 2.463 (-3.1916 to 8.1169) | 4.185 (-1.4220 to 9.7914) | -5.962 (-11.5712 to -0.3530) | 1.421 (-4.3528 to 7.1954) | -0.676 (-6.1363 to 4.7843) |
| Vitality | -2.178 (-8.8193 to 4.4629) | -4.645 (-11.1048 to 1.8139) | -7.227 (-13.6961 to -0.7589) | -1.516 (-8.1800 to 5.1472) | 0.730 (-5.5932 to 7.0522) |
| Weight | 0.304 (-9.4460 to 10.0543) | 5.410 (-4.2393 to 15.0600) | 2.175 (-7.5500 to 11.8997) | 8.827 (-1.1524 to 18.8063) | -4.186 (-13.5956 to 5.2233) |

9. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Maximum Plasma Concentration (Cmax) of VX-809 |
| Measure Description | Only participants who received VX-809 were analyzed for this outcome measure. |
| Time Frame | Day 1 (pre dose, 0.75, 1.5, 3, 4, 6, 9, 12, and 24 hours post-dose), Day 28 (pre dose, 0.75, 1.5, 3, 4, 6, 9, 12, 24, and 30-60 hours post dose) |
| Safety Issue? | No |

Analysis Population Description

FAS. Here, n = participants evaluable for specified category for each arm, respectively.

Reporting Groups

| | Description |
|---|---|
| VX-809, 25 mg | VX-809, 25 mg capsule orally once daily for 28 days. |
| VX-809, 50 mg | VX-809, 50 mg capsule orally once daily for 28 days. |
| VX-809, 100 mg | VX-809, 100 mg capsule orally once daily for 28 days. |
| VX-809, 200 mg | VX-809, 200 mg capsule orally once daily for 28 days. |

Measured Values

| | VX-809, 25 mg | VX-809, 50 mg | VX-809, 100 mg | VX-809, 200 mg |
|---|---|---|---|---|
| Number of Participants Analyzed | 18 | 18 | 17 | 19 |

| | VX-809, 25 mg | VX-809, 50 mg | VX-809, 100 mg | VX-809, 200 mg |
|---|---|---|---|---|
| Maximum Plasma Concentration (Cmax) of VX-809<br>Mean (Standard Deviation)<br>Unit of measure: nanogram per milliliter (ng/mL) | | | | |
| Day 1 (n= 18, 18, 17, 19) | 760 (280) | 1850 (697) | 2930 (916) | 6410 (2550) |
| Day 28 (n= 17, 17, 16, 18) | 1100 (443) | 2660 (1010) | 4620 (1840) | 10300 (4490) |

10. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Area Under the Concentration Versus Time Curve From Time 0 to 24 Hours (AUC0-24) of VX-809 |
| Measure Description | Only participants who received VX-809 were analyzed for this outcome measure. |
| Time Frame | Day 1 (pre dose, 0.75, 1.5, 3, 4, 6, 9, 12, and 24 hours post-dose), Day 28 (pre dose, 0.75, 1.5, 3, 4, 6, 9, 12, and 24 hours post dose) |
| Safety Issue? | No |

Analysis Population Description

FAS. Here, n = participants evaluable for specified category for each arm, respectively.

Reporting Groups

| | Description |
|---|---|
| VX-809, 25 mg | VX-809, 25 mg capsule orally once daily for 28 days. |
| VX-809, 50 mg | VX-809, 50 mg capsule orally once daily for 28 days. |
| VX-809, 100 mg | VX-809, 100 mg capsule orally once daily for 28 days. |
| VX-809, 200 mg | VX-809, 200 mg capsule orally once daily for 28 days. |

Measured Values

| | VX-809, 25 mg | VX-809, 50 mg | VX-809, 100 mg | VX-809, 200 mg |
|---|---|---|---|---|
| Number of Participants Analyzed | 18 | 18 | 17 | 19 |
| Area Under the Concentration Versus Time Curve From Time 0 to 24 Hours (AUC0-24) of VX-809<br>Mean (Standard Deviation)<br>Unit of measure: hour*nanogram per milliliter (hr*ng/mL) | | | | |

| | VX-809, 25 mg | VX-809, 50 mg | VX-809, 100 mg | VX-809, 200 mg |
|---|---|---|---|---|
| Day 1 (n= 18, 18, 17, 19) | 7190 (2190) | 16600 (6290) | 29000 (11400) | 59500 (26400) |
| Day 28 (n= 17, 17, 16, 18) | 12900 (4920) | 28800 (13100) | 54100 (31600) | 119000 (73700) |

## Reported Adverse Events

| | |
|---|---|
| Time Frame | Up to 14 days after last dose (last dose = Day 28) |
| Additional Description | [Not specified] |

Reporting Groups

| | Description |
|---|---|
| Placebo | Placebo matched to VX-809 capsule orally once daily for 28 days. |
| VX-809, 25 mg | VX-809, 25 mg capsule orally once daily for 28 days. |
| VX-809, 50 mg | VX-809, 50 mg capsule orally once daily for 28 days. |
| VX-809, 100 mg | VX-809, 100 mg capsule orally once daily for 28 days. |
| VX-809, 200 mg | VX-809, 200 mg capsule orally once daily for 28 days. |

Serious Adverse Events

| | Placebo | VX-809, 25 mg | VX-809, 50 mg | VX-809, 100 mg | VX-809, 200 mg |
|---|---|---|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) |
| Total | 1/17 (5.88%) | 5/18 (27.78%) | 1/18 (5.56%) | 0/17 (0%) | 3/19 (15.79%) |

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 0%

| | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) |
|---|---|---|---|---|---|
| Total | 17/17 (100%) | 16/18 (88.89%) | 15/18 (83.33%) | 16/17 (94.12%) | 18/19 (94.74%) |

## More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to

discuss or publish trial results after the trial is completed.

PI is free to publish results of the study after (1) the first multi-center publication, (2) if the sponsor elects not to publish the results, or (3) 18 months
after close of the study, whichever occurs first. Proposed publications are to be submitted to the sponsor for review and comment for a period of at least
45 days (which may be extended under certain circumstances related to protection of intellectual property); the sponsor cannot require changes to the
proposed publications.

---

Results Point of Contact:

Name/Official Title: Medical Monitor
Organization: Vertex Pharmaceuticals Incorporated
Phone: 617-341-6777

Email: medicalinfo@vrtx.com