Title: A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate the Efficacy and Safety of Lumacaftor in Combination With Ivacaftor in Subjects Aged 12 Years and Older With Cystic Fibrosis, Homozygous for the *F508del-CFTR* Mutation – Protocol Number VX-809-104

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Sponsor: Vertex Pharmaceuticals Incorporated (Vertex)

Purpose of Research
The purpose of this study is to evaluate the efficacy and safety of lumacaftor in combination with ivacaftor in persons 12 years and older with Cystic Fibrosis who are homozygous for the F508del mutation.This study is being done to learn more about the safety and effects of taking lumacaftor with ivacaftor.

Lumacaftor given with ivacaftor is experimental; "experimental" means it is not approved by the United States (US) Food and Drug Administration (FDA).

Ivacaftor, at a different dose, is approved in the US and the European Union (EU) for patients aged 6 and older who have the *G551D-CFTR* mutation. Ivacaftor is marketed in the US and EU under the trade name Kalydeco. Ivacaftor is experimental in patients with CF that are homozygous for the *F508del-CFTR* mutation.

Inclusion Criteria

1. Males and females, aged 12 years or older on the date of informed consent or, where appropriate, date of assent
2. Confirmed diagnosis of CF
3. Homozygous for the F508del CFTR mutation
4. FEV1 ≥40% and ≤90% of predicted normal for age, sex, and height
5. Willing to remain on a stable CF medication regimen through Week 24 or, if applicable, the Safety Follow up Visit

Exclusion Criteria

1. An acute upper or lower respiratory infection, pulmonary exacerbation, or changes in therapy (including antibiotics) for pulmonary disease within 4 weeks before first dose of study drug
2. History of solid organ or hematological transplantation
3. History of alcohol or drug abuse in the past year
4. Ongoing or prior participation in an investigational drug study (including studies investigating lumacaftor and/or ivacaftor) within 30 days of screening.
5. Use of moderate to strong inhibitors or inducers of CYP3A, including consumption of certain herbal medications (e.g., St. John's Wort) and certain fruit and fruit juices within 14 days before Day 1 of dosing