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Title: Effects of the CFTR potentiator, ivacaftor, in two phase 3 trials in subjects with CF who have the G551D-CFTR mutation

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Body: Rationale: Two Phase 3 studies were conducted to assess the effect of ivacaftor in subjects with CF who have the G551D-CFTR mutation. Methods: These were randomized, double-blind, placebo-controlled, multicenter studies. Subjects received placebo or ivacaftor (150 mg q12h) for 48 weeks in addition to their prescribed therapies. STRIVE enrolled 161 subjects with CF who were ≥12 years and had % predicted FEV_1 at screening of 40%-90%. ENVISION enrolled 52 subjects who were 6-11 years and had % predicted FEV_1 at screening of 40%-105%. ResultsAnalysis of the primary endpoint (absolute change in % predicted FEV_1 through Week 24) showed a significant treatment effect in both studies. The treatment difference was 10.6 percentage points in STRIVE (P<0.0001) and 12.5 percentage points in ENVISION (P<0.0001) when compared to placebo. In both studies, the improvements were rapid in onset. In STRIVE, there was a 55% reduction in pulmonary exacerbation risk for subjects in the ivacaftor group vs. subjects in the placebo group through Week 48 (P=0.0012). In ENVISION, too few subjects experienced pulmonary exacerbations to make meaningful comparisons. In both studies, most adverse events were respiratory in nature and similar to placebo. In STRIVE, 10 placebo (12.8%) and 6 ivacaftor (7.2%) subjects discontinued treatment. In ENVISION, 4 placebo (15.4%) subjects discontinued treatment while no ivacaftor-treated subjects discontinued. Conclusions: In subjects with CF 6 years and older with the G551D mutation, ivacaftor was highly effective in the treatment of CF, as evidenced by improvement in clinical outcomes. Safety of ivacaftor was comparable to placebo. Sponsored by Vertex.