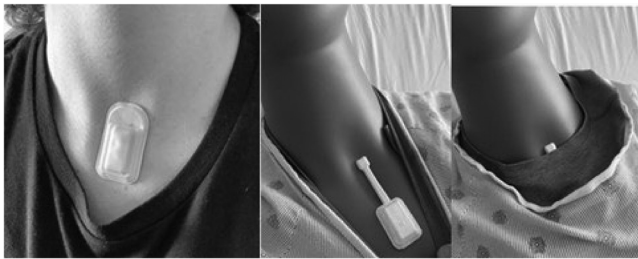


were asked to fill out the Acceptability and Usability Questionnaire, which consisted of six questions ranked on a 4-point Likert scale.

**Results:** Cohort 1 included 21 children aged 3 to 18 (mean age  $9.25 \pm 4.85$ ), and Cohort 2 included 12 children aged 7 to 18 (mean age  $12.15 \pm 4.42$ ). On 31 (94%) questionnaires returned, 35.5% of participants strongly agreed and 61.3% agreed with the statement "I [or my child] like(s) wearing the cough sensor." Similarly, most participants found the cough sensor easy to use (74.2% strongly agreed, 25.8% agreed) and comfortable to wear (64.5% strongly agreed, 29.0% agreed), although they found the adhesive sticker difficult to take off and the device too obvious or large.

**Conclusions:** Although qualitative and quantitative acceptability and usability data were overall positive, we have redesigned the cough sensor for comfort and are continuing enrollment. The new sensor,  $3.5 \times 1.6 \times 0.8$  cm, is smaller and sits lower on the neck so participants can better conceal it underneath clothing (Figure 1). We are providing universal adhesive remover wipes to all participants. Future work includes long-term monitoring (1–2 weeks) of pulmonary exacerbations using the new devices and further assessing usability and acceptability from participants.



**Figure 1.** New cough sensor design with a longer neck and a smaller body, allowing it to be better concealed underneath a shirt

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#### Long-term safety and efficacy of elexacaftor/tezacaftor/ivacaftor in children 6 years and older with cystic fibrosis and at least one *F508del* alleles: 96-week interim results from an open-label extension study

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**Background:** A 24-week, Phase 3 open-label study showed that elexacaftor/tezacaftor/ivacaftor (ELX/TEZ/IVA) was safe and efficacious in children 6 through 11 years of age with cystic fibrosis (CF) and at least one *F508del*-CFTR allele. All children who completed this trial entered a 192-week, Phase 3, open-label extension study to assess long-term safety and efficacy. Here, we report results of the 96-week interim analysis (IA).

**Methods:** Dosing in the study is based on weight. Children who weigh less than 30 kg receive ELX 100 mg once daily (qd)/TEZ 50 mg qd/IVA 75 mg every 12 hours (q12h), while children weighing 30 kg or more receive ELX 200 mg qd/TEZ 100 mg qd/IVA 150 mg q12h (adult dose). The primary endpoint is safety and tolerability; secondary endpoints include absolute changes from parent study baseline in percent predicted FEV<sub>1</sub> (ppFEV<sub>1</sub>), sweat chloride, Cystic Fibrosis Questionnaire-Revised (CFQ-R) respiratory domain score, body mass index, body mass index z-score, lung clearance index<sub>2.5</sub> (LCI<sub>2.5</sub>), weight and weight-for-age z score, and height and height-for-age z-score and number of pulmonary exacerbations (PEX) and

CF-related hospitalizations. Data collection for the 96-week IA was based on the date the last participant completed the Week 96 study visit.

**Results:** 64 children (*F508del*/minimal function [*F*/*MF*] genotypes, n = 36; *F508del*/*F508del* [*F*/*F*] genotype, n = 28) were enrolled and dosed. At the 96-week IA, mean (SD) exposure to ELX/TEZ/IVA was 93.9 (11.1) weeks. Adverse events (AEs) and serious AEs (SAEs) were consistent with common manifestations of CF disease. The overall exposure-adjusted rates of AEs and SAEs (407.74 and 4.72 events per 100 patient years) were lower compared with the 24-week parent study (987.04 and 8.68 events per 100 patient years). One child (1.6%) discontinued due to an AE of aggression, which was moderate in severity and considered unlikely to be related to the study drug. From parent study baseline to Week 96, mean ppFEV<sub>1</sub> increased (11.2 [95% CI, 8.3, 14.2] percentage points), sweat chloride concentration decreased (-62.3 [95% CI, -65.9, -58.8] mmol/L), CFQ-R respiratory domain score increased (13.3 [95% CI, 11.4, 15.1] points), and LCI<sub>2.5</sub> decreased (-2.00 [95% CI, -2.45, -1.55] units). Improvements were also seen in growth parameters. The estimated PEX rate per 48 weeks was 0.04. The annualized rate of change (95% CI) in ppFEV<sub>1</sub> and LCI<sub>2.5</sub> was 0.51 (-0.73, 1.75) percentage points and -0.06 (-0.17, 0.05) units, respectively.

**Conclusions:** ELX/TEZ/IVA continued to be generally safe and well tolerated in children 6 through 11 years of age through an additional 96 weeks of treatment, with no new safety findings. Improvements in lung function, respiratory symptoms, and CFTR function reported in the parent study were maintained through the interim analysis of this extension study. These results demonstrate the favorable safety profile and durable clinical benefits of ELX/TEZ/IVA treatment in this pediatric population.

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#### Tolerance of ETD001, a long-acting inhaled epithelial sodium channel blocker, in humans

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**Background:** To assess the safety, tolerability, and pharmacokinetic (PK) profile in humans of the novel inhaled epithelial sodium channel blocker ETD001.

**Methods:** Inhaled ETD001 or placebo, delivered via nebulizer, have been administered in a 3:1 ratio to 96 healthy subjects in a blinded, first-in-human clinical trial (ClinicalTrials.gov Identifier: NCT04926701). The study consisted of two parts. Part A evaluated single ascending doses (SADs) up to 10.8 mg, and Part B evaluated multiple ascending doses (MADs) up to 3.1 mg once daily (QD) for 7 days and 4.65 mg twice daily (BID) for 14 days. Safety was assessed by monitoring for adverse events (AEs), laboratory safety tests (including blood potassium monitoring), vital signs, 12-lead electrocardiogram (ECG), and spirometry. Systemic exposure was assessed using serial pharmacokinetic blood draws.

**Results:** There were no serious AEs. Twenty-four subjects reported 38 AEs, all of mild to moderate intensity and all resolved. There were no clinically relevant changes in laboratory safety tests, vital signs, ECGs, or spirometry measurements. All blood potassium assessments were within normal range at all doses. Three subjects withdrew in Part B; all withdrawals were considered unrelated to study drug; one on day 6 from the 3.1-mg QD cohort for personal reasons, one after the first dose of the 3.1-mg BID cohort because of vasovagal syncope at time of venipuncture triggering atrial fibrillation that spontaneously resolved, and one on Day 4 of the 3.1-mg BID cohort because of a positive COVID-19 test. Pharmacokinetic parameters were approximately dose proportional in Part A, with peak concentrations 1 to 2 hours after dose and exposure out to 12 to 24 hours at all doses, indicating good lung retention. Part B plasma concentrations displayed dose-independent kinetics and showed minimal accumulation, with a mean of 1.11-fold observed over 14 days.

**Conclusions:** ETD001 was well tolerated at single doses up to 10.8 mg and multiple doses of 3.1 mg QD for 7 days and 4.65 mg BID for 14 days. The wide safety margin is predicted to enable doses capable of durable target engagement in the lung, which are expected to enhance mucociliary clearance in people with cystic fibrosis.