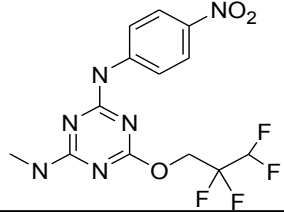
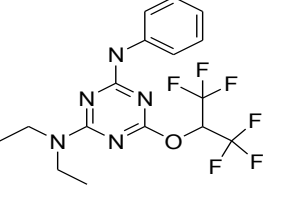
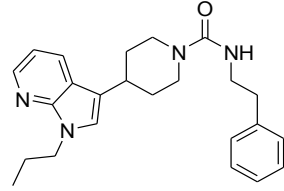
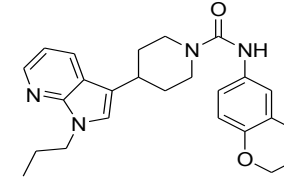
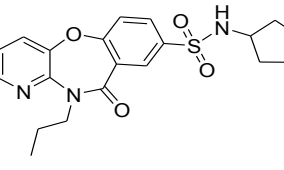
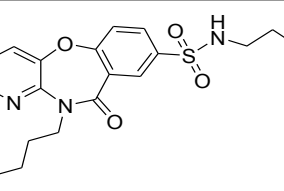
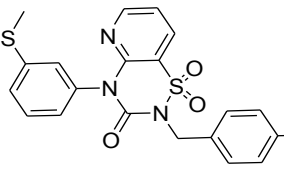
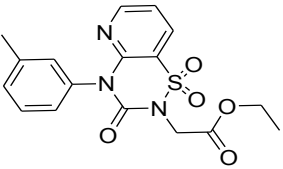
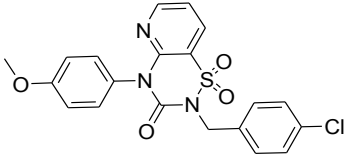
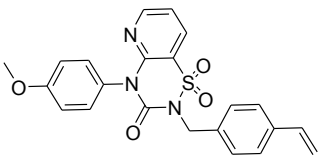
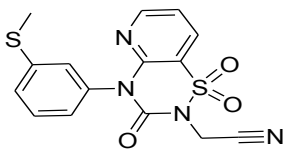
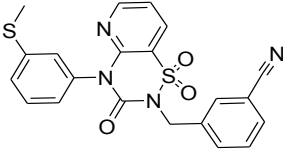
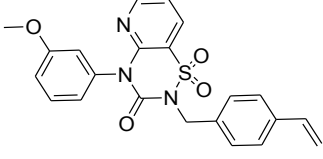
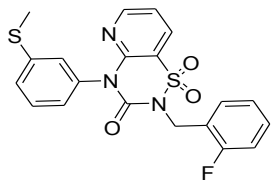
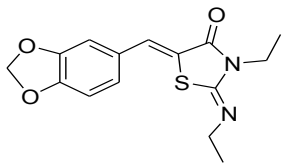
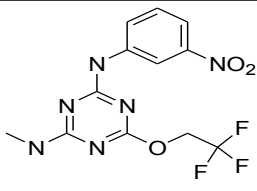
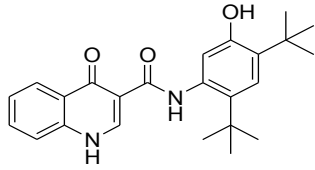


Supplementary Table 1. Chemical structures and data for CFTR activators.

Class	Compound	Structure	EC50 (nM)	Vmax	ΔPD (mV)
A	CFTR _{act} -A043		332	89%	-8.6 ± 0.49
B	CFTR _{act} -B018		685	86%	-2.5 ± 0.43
B	CFTR _{act} -B074		340	93%	-9.9 ± 0.99
B	CFTR _{act} -B089		377	91%	-3.4 ± 0.53
B	CFTR _{act} -B156		571	93%	-3.1 ± 1.1
E	CFTR _{act} -E053		385	94%	-4.1 ± 1.0
J	CFTR _{act} -J027		138	90%	-9.1 ± 0.39

K	CFTR _{act} -K032		70	97%	-10 ± 1.1
K	CFTR _{act} -K089		251	93%	-8.5 ± 0.81
O	CFTR _{act} -O018		752	93%	-5.7 ± 1.8
O	CFTR _{act} -O037		513	82%	
Q	CFTR _{act} -Q022		802	90%	
Q	CFTR _{act} -Q86		640	93%	
R	CFTR _{act} -R014		21	100%	-14 ± 0.42

R	CFTR _{act} -R053		399	98%	
R	CFTR _{act} -R088		379	95%	
R	CFTR _{act} -R101		174	94%	
R	CFTR _{act} -R103		126	100%	
R	CFTR _{act} -R142		31	100%	
R	CFTR _{act} -R176		36	100%	
R	CFTR _{act} -R185		35	94%	

	ref. 27		2000	65%	-2.5 ± 0.38
	ref. 27		400	49%	-7.4 ± 0.90
	VX-770		Variable	39%	-1.8 ± 0.29

Compounds identified in primary and analog screening were grouped into 8 chemical classes. EC_{50} and V_{max} against human CFTR were determined from I_{sc} measurement on FRT-CFTR cells. 100% CFTR activation was defined as that produced by 20 mM forskolin. Measurements of ocular surface PD were performed in wild-type CD1 mice. Summary of ΔPD produced by 1mM test compound (low Cl^- perfusate containing amiloride; mean \pm SE, $n \geq 3$ independent experiments per activator).