

MOLECULAR PHARMACOLOGY

Supplemental Data

POTENTIATORS OF DEFECTIVE $\Delta F508$ -CFTR CHANNEL GATING THAT DO NOT INTERFERE WITH CORRECTOR ACTION

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Supplemental Table 1. EC₅₀ and percentage VX-809 correction of indicated potentiators

Supplemental Table 2. Structure-activity analysis of class A analogs.

Supplemental Table 3. Structure-activity analysis of class H analogs.

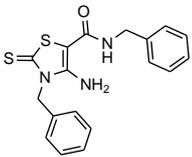
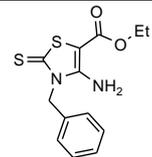
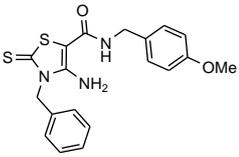
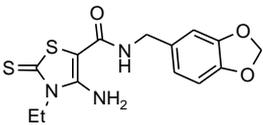
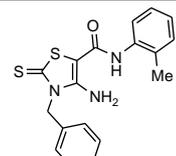
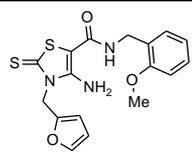
Supplemental Table 4. Structure-activity analysis of P5 analogs.

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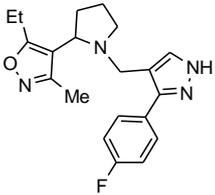
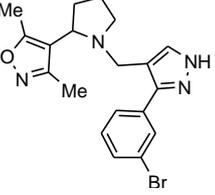
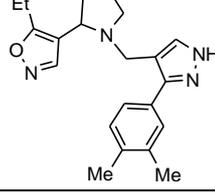
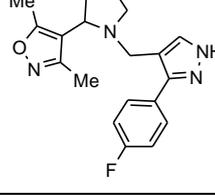
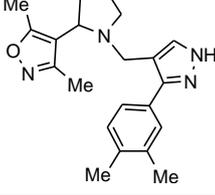
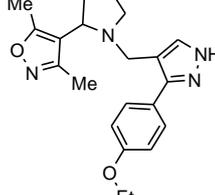
Class	EC ₅₀ (μM)	VX-809 % correction
A01	0.05	87 ± 5
A02	0.03	90 ± 8
B01	0.6	108 ± 7
C01	0.7	86 ± 5
D01	0.5	105 ± 10
E01	0.9	107 ± 6
F01	0.7	86 ± 5
G01	0.9	105 ± 5
H01	0.4	95 ± 6
H02	0.2	85 ± 5
H03	1.1	80 ± 5
I01	0.5	85 ± 5

EC₅₀ as determined from plate-reader fluorescence assay using FRT-ΔF508-YFP cells. 100% VX-809 correction is defined as background-subtracted luminescence signal of VX-809-corrected ΔF508-HRP CFBE cells.

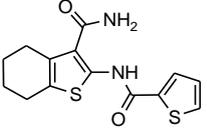
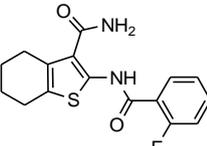
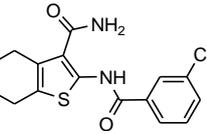
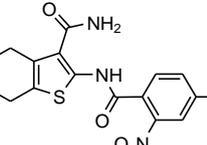
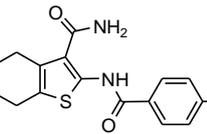
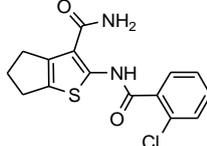
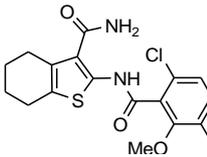
Supplemental Table 2. Structure-activity analysis of class A analogs.

Class A	Structure	EC ₅₀ (nM)	VX-809 % Correction
A03		25	95 ± 6
A04		18	83 ± 7
A05		35	101 ± 8
A06		760	88 ± 5
A07		37	94 ± 6
A08		910	90 ± 4
A09		940	105 ± 5

Supplemental Table 3. Structure-activity analysis of class H analogs.

Class H	Structure	EC ₅₀ (μM)	VX-809 % Correction
H04		0.6	87 ± 8
H05		0.4	93 ± 5
H06		2.0	82 ± 6
H08		0.6	91 ± 5
H09		1.1	84 ± 5
H10		1.0	84 ± 6

Supplemental Table 4. Structure-activity analysis of P5 analogs.

P5 analogs	Structure	EC ₅₀ (nM)	VX-809 % Correction
P11		58	107 ± 4
P12		42	108 ± 2
P14		250	106 ± 7
P16		64	101 ± 5
P17		210	86 ± 3
P18		220	96 ± 4
P20		130	94 ± 5