

Supporting information

Nanomolar-potency aminophenyl-1,3,5-triazine activators of the cystic fibrosis transmembrane conductance regulator (CFTR) chloride channel activators for pro-secretory therapy of dry eye diseases

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EXPERIMENTAL SECTION

All final analogs (**6a-6g**, **7a-7k**, and **11**) were prepared by same method described for **1** with various substituted anilines and precursors.

3-({4-(Diethylamino)-6-[(1,1,1,3,3,3-hexafluoropropan-2-yl)oxy]-1,3,5-triazin-2-yl}amino)benzoic acid (**6a**) : Purified by flash chromatography (1:6 EtOAc/Hex) to afford **6a** as a white powder (56%).

¹H NMR (300 MHz, acetone-*d*6): δ = 9.0 (brs, 1H), 8.79 (brs, 1H), 7.90 (d, 1H, *J* = 8.1 Hz), 7.76 (dt, 1H, *J* = 1.3, 7.9 Hz), 7.48 (t, 1H, *J* = 7.9 Hz), 6.79 (quint, 1H, *J* = 6.4 Hz), 3.78-3.66 (m, 4H), 1.29-1.20 (m, 6H); ¹³C NMR (75 MHz, acetone-*d*6): δ = 168.6, 166.8, 165.3, 139.6, 131.1, 128.7, 124.2, 123.9, 123.1, 121.2, 119.3, 68.9, 68.5, 68.0, 67.6, 67.1 (quint, 34 Hz), 42.1, 41.6, 12.35, 12.32; HRMS (ESI): *m/z* calculated for C₁₇H₁₈F₆N₅O₃ [M + H⁺]: 454.1309. Found: 454.1311.

N,N-Diethyl-*N'*-(3-fluorophenyl)-6-[(1,1,1,3,3,3-hexafluoropropan-2-yl)oxy]-1,3,5-triazine-2,4-diamine (**6b**) : Purified by flash chromatography (1:10 EtOAc/Hex) to afford **6b** as a white powder (70%).

¹H NMR (300 MHz, CDCl₃): δ = 7.69 (m, 1H), 7.48 (brs, 1H), 7.26 (m, 1H), 7.11 (d, 1H, *J* = 7.9 Hz), 6.79 (td, 1H, *J* = 8.2, 2.5 Hz), 6.31 (dt, 1H, *J* = 12.4, 6.3 Hz), 3.64 (m, 4H), 1.25 (m, 6H); ¹³C NMR (75 MHz, CDCl₃): δ = 168.5, 165.1, 164.8, 164.6, 161.3, 140.1, 139.9, 129.8, 129.7, 122.7, 118.9, 115.1, 110.0, 109.7, 107.6, 107.2, 68.8, 68.4, 67.9 (t, 34 Hz), 42.6, 42.2, 12.8, 12.7; HRMS (ESI): *m/z* calculated for C₁₆H₁₇F₇N₅O [M + H⁺]: 428.1316. Found: 428.1316.

N,N-Diethyl-*N'*-(3-chlorophenyl)-6-[(1,1,1,3,3,3-hexafluoropropan-2-yl)oxy]-1,3,5-triazine-2,4-diamine (**6c**) : Purified by flash chromatography (1:10 EtOAc/Hex) to afford **6c** as a white powder (47%).

¹H NMR (300 MHz, CDCl₃): δ = 7.98 (brs, 1H), 7.28-7.05 (m, 4H), 6.31 (quint, 1H, *J* = 6.3 Hz), 3.64 (sex, 4H, *J* = 7.0 Hz), 1.30 (t, 3H, *J* = 7.1 Hz), 1.23 (t, 3H, *J* = 7.1 Hz); ¹³C NMR (75 MHz, CDCl₃): δ = 168.5, 165.1, 164.7, 139.5, 134.5, 129.7, 123.2, 122.6, 120.1, 118.9, 117.6, 68.9, 68.4, 68.0 (t, 32 Hz), 42.6, 42.2, 12.9, 12.8; HRMS (ESI): *m/z* calculated for C₁₆H₁₇ClF₆N₅O [M + H⁺]: 444.1021. Found: 444.1021.

N,N-Diethyl-6-[(1,1,1,3,3,3-hexafluoropropan-2-yl)oxy]-*N'*-(3-nitrophenyl)-1,3,5-triazine-2,4-diamine (**6d**)

: Yellowish powder, 49% yield. ¹H NMR (300 MHz, CDCl₃): δ = 9.15 (brs, 1H), 8.23-7.74 (m, 2H), 7.70-7.34 (1m, 2H), 6.31 (quint, 1H, *J* = 6.2 Hz), 3.74 (q, 2H, *J* = 6.9 Hz), 3.63 (q, 2H, *J* = 7.0 Hz), 1.89 (brs, 1H), 1.33 (t, 3H, *J* = 7.1 Hz), 1.24 (t, 4H, *J* = 7.1 Hz); ¹³C NMR (75 MHz, CDCl₃): δ = 168.4, 164.79, 164.75, 148.6, 139.7, 129.3, 124.9, 124.1, 121.8, 119.6, 117.3 (q, 168 Hz), 117.8, 114.8, 69.0, 68.7, 68.5, 68.2, 67.9 (quint, 20 Hz), 42.9, 42.4, 12.8, 12.7; HRMS (ESI): *m/z* calculated for C₁₆H₁₇F₆N₆O₃ [M + H⁺]: 455.1261. Found: 455.1263.

4-({4-(Diethylamino)-6-[(1,1,1,3,3,3-hexafluoropropan-2-yl)oxy]-1,3,5-triazin-2-yl}amino)benzoic acid (**6e**) : Purified by flash chromatography (1:10 EtOAc/Hex) to afford **6e** as a white powder (56%).

¹H NMR (300 MHz, acetone-*d*6): δ = 9.12 (brs, 1H), 8.05-7.89 (m, 4H), 6.80 (quint, 1H, *J* = 6.4 Hz), 3.72 (quint, 4H, *J* = 7.2 Hz), 1.31-1.18 (m, 6H); ¹³C NMR (75 MHz, acetone-*d*6): δ = 168.7, 166.7, 165.3, 143.6, 143.5, 130.5, 124.8, 119.1, 119.0, 68.6, 67.7, 42.1, 41.7, 12.3, 12.2; HRMS (ESI): *m/z* calculated for C₁₇H₁₈F₆N₅O₃ [M + H⁺]: 454.1309. Found: 454.1308.

N,N-Diethyl-*N'*-(4-fluorophenyl)-6-[(1,1,1,3,3,3-hexafluoropropan-2-yl)oxy]-1,3,5-triazine-2,4-diamine (**6f**)
: Purified by flash chromatography (1:10 EtOAc/Hex) to afford **6f** as a white powder (62%).

¹H NMR (300 MHz, CDCl₃): δ = 7.55-7.50 (m, 2H), 7.25 (brs, 1H), 7.08-7.01 (m, 2H), 6.32 (quint, 1H, *J* = 6.3 Hz), 3.61 (dq, 4H, *J* = 3.1, 7.9 Hz), 1.23 (q, 6H, *J* = 7.2 Hz); ¹³C NMR (75 MHz, CDCl₃): δ = 168.5, 165.1, 160.6, 134.2, 122.7, 122.2, 122.1, 118.9, 115.5, 115.2, 68.8, 68.3, 67.9 (t, 34 Hz), 42.3, 42.0, 12.9, 12.8; HRMS (ESI): *m/z* calculated for C₁₆H₁₇F₇N₅O [M + H⁺]: 428.1316. Found: 428.1319.

N,N-Diethyl-6-[(1,1,1,3,3,3-hexafluoropropan-2-yl)oxy]-*N'*-(4-nitrophenyl)-1,3,5-triazine-2,4-diamine (**6g**)
: Purified by flash chromatography (1:10 EtOAc/Hex) to afford **6g** as a yellowish powder (55%).

¹H NMR (300 MHz, CDCl₃): δ = 8.37 (brs, 1H), 8.24-8.19 (m, 2H), 7.84-7.79 (m, 2H), 6.33 (quint, 1H, *J* = 6.2 Hz), 3.71-3.60 (m, 4H), 1.30 (t, 3H, *J* = 7.1 Hz), 1.23 (t, 3H, *J* = 7.1 Hz); ¹³C NMR (75 MHz, CDCl₃): δ = 168.5, 164.9, 164.8, 144.7, 142.7, 124.8, 119.2, 126.3, 122.6, 118.8, 115.1 (q, 281 Hz), 69.4, 69.0, 68.5, 68.0, 67.6 (quint, 34 Hz), 42.7, 42.4, 12.79, 12.76; HRMS (ESI): *m/z* calculated for C₁₆H₁₇F₆N₆O₃ [M + H⁺]: 455.1261. Found: 455.1264.

N,N-Diethyl-6-[(1,1,1,3,3,3-hexafluoropropan-2-yl)oxy]-*N'*-(1*H*-indazol-6-yl)-1,3,5-triazine-2,4-diamine (**6h**)
: Purified by flash chromatography (1:6 EtOAc/Hex) to afford **6h** as a white powder (28%).

¹H NMR (300 MHz, acetone-*d*₆): δ = 8.96 (brs, 1H), 8.38 (brs, 1H), 7.97 (d, 1H, *J* = 1.05 Hz), 7.71 (dd, 1H, *J* = 0.7, 8.7 Hz), 7.34 (dd, 1H, *J* = 1.8, 8.7 Hz), 6.79 (quint, 1H, *J* = 6.5 Hz), 3.79 (m, 4H), 1.32-1.21 (m, 6H); ¹³C NMR (75 MHz, acetone-*d*₆): δ = 168.6, 165.3, 162.8, 140.9, 137.7, 133.5, 126.9, 123.1, 120.4, 119.5, 115.3, 68.0, 42.1, 41.6, 12.4, 12.2; HRMS (ESI): *m/z* calculated for C₁₇H₁₈F₆N₇O [M + H⁺]: 450.1472. Found: 450.1475.

N,N-Diethyl-6-[(1,1,1,3,3,3-hexafluoropropan-2-yl)oxy]-*N'*-(1*H*-indazol-5-yl)-1,3,5-triazine-2,4-diamine (**6i**)
: Purified by flash chromatography (1:6 EtOAc/Hex) to afford **6i** as a white powder (28%).

¹H NMR (300 MHz, acetone-*d*₆): δ = 12.22 (brs, 1H), 8.85 (brs, 1H), 8.29 (brs, 1H), 8.03 (d, 1H, *J* = 1.0 Hz), 7.67 (d, 1H, *J* = 8.9 Hz), 7.57 (d, 1H, *J* = 8.9 Hz), 6.79 (quint, 1H, *J* = 6.5 Hz), 3.68 (q, 4H, *J* = 7.0 Hz), 1.28-1.17 (m, 6H); ¹³C NMR (75 MHz, acetone-*d*₆): δ = 168.6, 165.4, 165.3, 137.5, 133.6, 132.3, 131.5, 123.4, 121.8, 126.9, 123.2, 123.1, 119.46, 119.43, 115.6 (q, 281 Hz), 113.3, 111.1, 109.8, 68.4, 68.0, 67.5 (t, 34 Hz), 42.0, 41.5, 12.4, 12.3; HRMS (ESI): *m/z* calculated for C₁₇H₁₈F₆N₇O [M + H⁺]: 450.1472. Found: 450.1472.

N'-(1,3-Benzoxazol-6-yl)-*N,N*-diethyl-6-[(1,1,1,3,3,3-hexafluoropropan-2-yl)oxy]-1,3,5-triazine-2,4-diamine (**6j**)
: Purified by flash chromatography (1:8 EtOAc/Hex) to afford **6j** as a purple powder (25%).

¹H NMR (300 MHz, acetone-*d*₆): δ = 9.08 (brs, 1H), 8.46 (brs, 1H), 8.39 (s, 1H), 7.70 (d, 1H, *J* = 8.6 Hz), 7.63 (dd, 1H, *J* = 1.9, 8.6 Hz), 6.80 (quint, 1H, *J* = 6.8 Hz), 3.76-3.67 (m, 4H), 1.31-1.18 (m, 6H); ¹³C NMR (75 MHz, CDCl₃): δ = 168.6, 165.3, 153.0, 150.2, 137.5, 135.7, 119.7, 117.6, 105.6, 102.6, 68.1, 42.1, 41.7, 12.3, 12.2; HRMS (ESI): *m/z* calculated for C₁₇H₁₇F₆N₆O₂ [M + H⁺]: 451.1312. Found: 451.1313.

N'-(1,3-Benzothiazol-6-yl)-*N,N*-diethyl-6-[(1,1,1,3,3,3-hexafluoropropan-2-yl)oxy]-1,3,5-triazine-2,4-diamine (**6k**)

: Purified by flash chromatography (1:7 EtOAc/Hex) to afford **6k** as a white powder (40%).

¹H NMR (300 MHz, CDCl₃): δ = 8.93 (brs, 1H), 8.47 (brs, 1H), 8.02 (d, 1H, *J* = 8.5 Hz), 7.52 (dd, 2H, *J* = 8.8, 2.2 Hz), 6.30 (m, 1H), 3.66 (m, 4H), 1.27 (m, 6H); ¹³C NMR (75 MHz, CDCl₃): δ = 168.5, 164.5, 152.9, 149.6, 136.0, 134.7, 123.5, 121.9, 119.8, 119.6, 112.7, 97.3, 68.9, 68.7, 68.4, 42.7, 42.3, 12.9, 12.8; HRMS (ESI): *m/z* calculated for C₁₇H₁₇F₆N₆OS [M + H⁺]: 467.1083. Found: 467.1089.

N,N-Diethyl-*N'*-phenyl-6-(2,2,3,3-tetrafluoropropoxy)-1,3,5-triazine-2,4-diamine (**7a**)

: Purified by flash chromatography (1:10 EtOAc/Hex) to afford **7a** as a white powder (38%).

¹H NMR (300 MHz, CDCl₃): δ = 7.60 (d, 2H, *J* = 8.4 Hz), 7.34 (t, 2H, *J* = 7.4 Hz), 7.08 (t, 1H, *J* = 7.3 Hz), 6.06 (tt, 1H, *J* = 4.9, 53.0 Hz), 3.68-3.59 (m, 2H), 4.78-4.70 (m, 4H), 1.28-1.20 (m, 6H); ¹³C NMR (75 MHz, CDCl₃): δ = 169.2, 165.2, 164.8, 138.6, 128.7, 123.1, 120.0, 114.4 (t, 26 Hz), 112.3 (t, 34 Hz), 109.0 (t, 34 Hz), 105.7 (t, 34 Hz), 62.1 (t, 30 Hz), 42.1, 41.7, 13.1, 12.9; HRMS (ESI): *m/z* calculated for C₁₆H₂₀F₄N₅O [M + H⁺]: 374.1599. Found: 374.1597.

3-{[4-(Diethylamino)-6-(2,2,3,3-tetrafluoropropoxy)-1,3,5-triazin-2-yl]amino}benzoic acid (**7b**)

: Purified by flash chromatography (1:5 EtOAc/Hex) to afford **7b** as a white powder (60%).

¹H NMR (300 MHz, acetone-*d*₆): δ = 8.68 (brs, 1H), 7.92 (m, 1H), 7.74-7.71 (m, 1H), 7.46 (t, 1H, *J* = 7.8 Hz), 6.45 (tt, 1H, *J* = 4.9, 53 Hz), 4.91-4.82 (m, 2H), 3.74-3.65 (m, 4H), 1.28-1.18 (m, 6H); ¹³C NMR (75 MHz, acetone-*d*₆): δ = 169.6, 166.9, 165.5, 140.1, 138.1, 131.2, 128.5, 123.8, 123.5, 120.9, 110.0, 61.7, 41.8, 41.4, 12.4; HRMS (ESI): *m/z* calculated for C₁₇H₂₀F₄N₅O₃ [M + H⁺]: 418.1497. Found: 418.1501.

N,N-Diethyl-*N'*-(3-fluorophenyl)-6-(2,2,3,3-tetrafluoropropoxy)-1,3,5-triazine-2,4-diamine (**7c**)

: Purified by flash chromatography (1:10 EtOAc/Hex) to afford **7c** as a white powder (40%).

¹H NMR (300 MHz, CDCl₃): δ = 7.73 (dt, 1H, *J* = 2.1, 7.7 Hz), 7.37 (brs, 1H), 7.26 (td, 1H, *J* = 6.3, 8.2 Hz), 7.12 (ddd, 1H, *J* = 0.9, 2.0, 8.2 Hz), 6.76 (ddt, 1H, *J* = 0.9, 2.5, 8.2 Hz), 6.02 (tt, 1H, *J* = 4.9, 53 Hz), 4.74 (tt, 2H, *J* = 1.6, 12.4 Hz), 3.64 (sex, 4H, *J* = 7.0 Hz), 1.23 (m, 6H); ¹³C NMR (75 MHz, CDCl₃): δ = 169.2, 165.2, 164.8, 164.6, 161.4, 140.4, 140.3, 129.8, 129.7, 114.9, 114.9, 114.7, 114.3, 114.0, 112.7, 112.3, 111.0, 109.7, 109.47, 109.42, 109.0, 108.5, 107.3, 107.0, 105.7, 62.5, 62.1, 61.7, 42.3, 41.9, 13.0, 12.8; HRMS (ESI): *m/z* calculated for C₁₆H₁₉F₅N₅O [M + H⁺]: 392.1505. Found: 392.1505.

N'-(3-Chlorophenyl)-*N,N*-diethyl-6-(2,2,3,3-tetrafluoropropoxy)-1,3,5-triazine-2,4-diamine (**7d**)

: Purified by flash chromatography (1:10 EtOAc/Hex) to afford **7d** as a white powder (81%).

¹H NMR (300 MHz, CDCl₃): δ = 7.99 (brs, 1H), 7.25 (m, 3H), 7.04 (dt, 1H, *J* = 7.0, 2.0 Hz), 6.02 (t, 1H, *J* = 4.9 Hz), 4.73 (t, 2H, *J* = 12.3 Hz), 3.64 (m, 4H), 1.84 (brs, 1H), 1.25 (m, 6H); ¹³C NMR (75 MHz, CDCl₃): δ = 169.2, 165.2, 164.7, 139.9, 134.5, 129.6, 122.9, 120.0, 117.6, 114.5, 114.3, 114.1, 112.3, 111.3, 111.0, 110.7, 109.3, 109.0, 108.8, 107.3, 107.0, 106.8, 62.4, 62.1, 61.9, 42.4, 42.0, 13.0, 12.9; HRMS (ESI): *m/z* calculated for C₁₆H₁₉ClF₄N₄O [M + H⁺]: 408.1209. Found: 408.1210.

N,N-Diethyl-*N'*-(3-nitrophenyl)-6-(2,2,3,3-tetrafluoropropoxy)-1,3,5-triazine-2,4-diamine (**7e**)

: Purified by flash chromatography (1:10 EtOAc/Hex) to afford **7e** as a yellowish powder (61%).

¹H NMR (300 MHz, CDCl₃): δ = 9.12 (brs, 1H), 8.15 (brs, 1H), 7.90 (dd, 1H, *J* = 8.2, 1.6 Hz), 7.57 (d, 1H, *J* = 7.6 Hz), 7.44 (t, 1H, *J* = 8.0 Hz), 5.96 (m, 1H), 4.75 (t, 2H, *J* = 12.6 Hz), 3.72 (q, 2H, *J* = 6.9 Hz), 3.65 (q, 2H, *J* = 6.9 Hz), 2.12 (brs, 1H), 1.31 (t, 3H, *J* = 7.1 Hz), 1.24 (t, 3H, *J* = 7.1 Hz); ¹³C NMR (75 MHz, CDCl₃): δ =

169.1, 164.9, 164.7, 148.6, 140.1, 129.2, 124.8, 117.4, 116.2, 114.6, 114.5, 114.2, 114.0, 112.3, 111.3, 111.0, 110.7, 109.3, 109.0, 108.7, 107.3, 107.0, 106.7, 62.3, 62.1, 61.8, 42.6, 42.1, 12.9, 12.8; HRMS (ESI): m/z calculated for $C_{16}H_{19}F_4N_6O_3$ [$M + H^+$]: 419.1450. Found: 419.1449.

4-({4-(Diethylamino)-6-[(2,2,3,3-tetrafluoropropoxy]-1,3,5-triazin-2-yl)amino}benzoic acid (**7f**)

: Purified by flash chromatography (1:10 EtOAc/Hex) to afford **7f** as a white powder (37%).

1H NMR (300 MHz, acetone-*d*6): δ = 8.97 (brs, 1H), 8.04-7.96 (m, 4H), 6.45 (tt, 1H, J = 5.1, 52 Hz), 4.88 (t, 2H, J = 13.5 Hz), 3.74-3.64 (m, 4H), 1.29-1.19 (m, 6H); ^{13}C NMR (75 MHz, acetone-*d*6): δ = 169.7, 166.4, 165.5, 165.4, 144.2, 130.5, 124.0, 118.8, 109.6, 109.1, 62.1, 61.7, 61.4, 41.8, 41.5, 12.4, 12.3; HRMS (ESI): m/z calculated for $C_{17}H_{20}F_4N_5O_3$ [$M + H^+$]: 418.1497. Found: 418.1499.

N,N-Diethyl-*N'*-(4-fluorophenyl)-6-(2,2,3,3-tetrafluoropropoxy)-1,3,5-triazine-2,4-diamine (**7g**)

: Purified by flash chromatography (1:10 EtOAc/Hex) to afford **7g** as a white powder (72%).

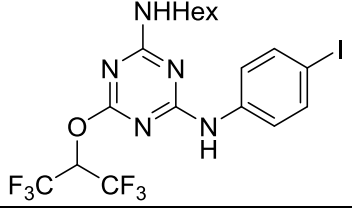
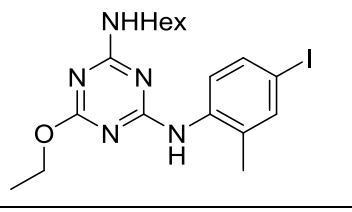
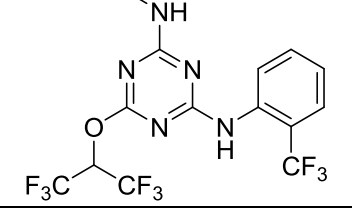
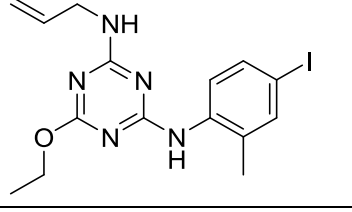
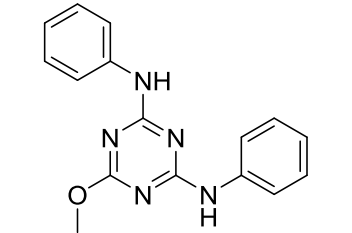
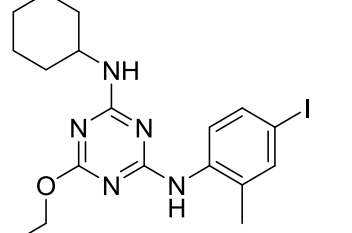
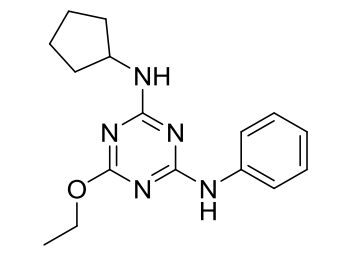
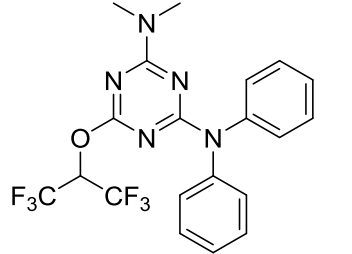
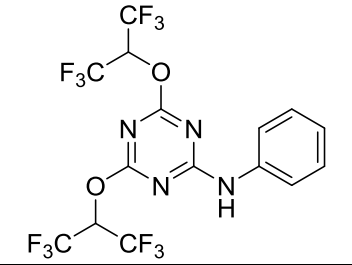
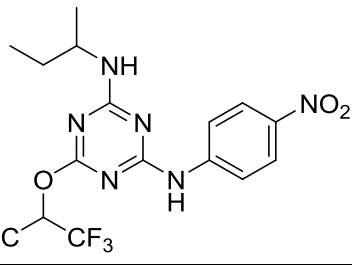
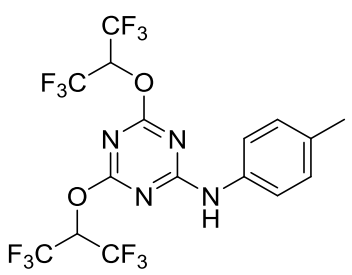
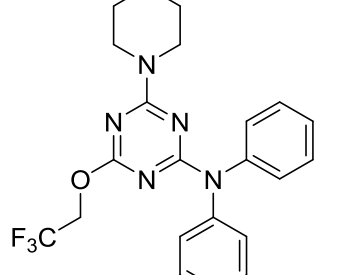
1H NMR (300 MHz, $CDCl_3$): δ = 7.53 (m, 2H), 7.36 (brs, 1H), 7.02 (m, 2H), 6.03 (m, 1H), 4.73 (m, 2H), 3.61 (m, 4H), 1.24 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.1, 164.6, 159.8, 157.9, 142.3, 134.5, 131.2, 125.5, 121.9, 118.7, 115.4, 115.2, 114.3, 112.3, 111.2, 111.0, 110.7, 110.07, 109.2, 109.0, 108.7, 107.3, 107.0, 106.7, 62.7, 62.3, 62.1, 61.8, 42.1, 41.8, 29.6, 13.0, 12.8, 12.7; HRMS (ESI): m/z calculated for $C_{16}H_{19}F_5N_5O$ [$M + H^+$]: 392.1505. Found: 392.1503.

N-Methyl-*N'*-phenyl-6-[(1,1,1,3,3,3-hexafluoropropan-2-yl)oxy]-1,3,5-triazine-2,4-diamine **11**

To a solution of **9** (80 mg, 0.26 mmol) in THF (3 ml) was added diisopropylethylamine (0.09 ml, 0.51 mmol) and aniline (0.03 ml, 0.31 mmol). The mixture was refluxed for 16 h. After cooling to room temperature the reaction mixture was extracted with EtOAc, washed with brine and dried over $MgSO_4$. Solvent was removed under reduced pressure and purified by flash chromatography (1:2 EtOAc/Hex) to afford **11** as a white powder (63 mg, 74%). 1H NMR (300 MHz, $CDCl_3$): δ = 7.61 (brs, 1H), 7.53 (d, 1H, J = 7.8 Hz), 7.38 (t, 2H, J = 7.5 Hz), 7.17-7.08 (m, 2H), 6.37 (sep, 1H, J = 6.0 Hz), 5.77 (brs, 0.6 H), 5.51 (brs, 0.4 H) 3.06 (m, 3H); HRMS (ESI): m/z calculated for $C_{13}H_{11}F_6N_5O$ [$M + H^+$]: 368.0942. Found: 368.0941.

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

Code	structure	% Activation (EC ₅₀ , nM)	code	Structure	% Activation (EC ₅₀ , nM)
K001		32	K047		17
K002		63	K048		46
K003		16	K049		28
K004		16	K050		66
K005		29	K051		45

K006		16	K052		15
K007		21	K053		24
K008		32	K054		14
K009		57	K055		42
K010		21	K056		38
K011		20	K057		28

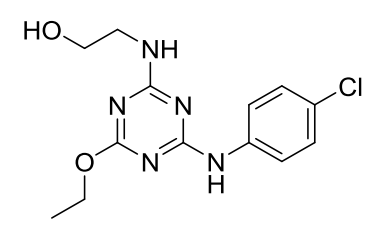
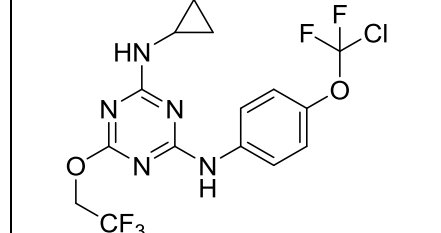
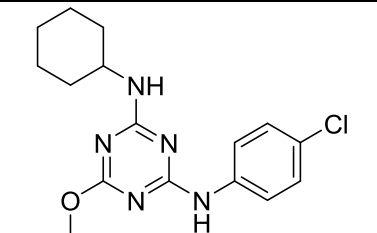
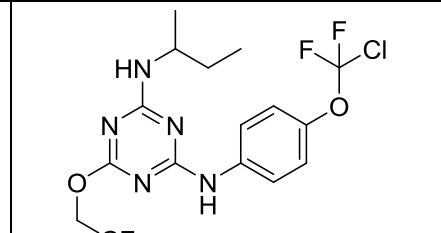
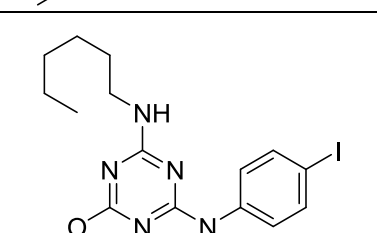
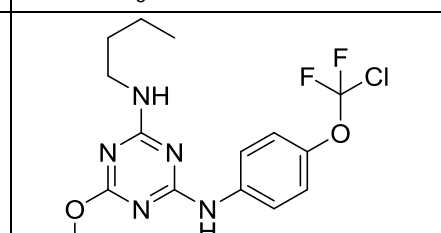
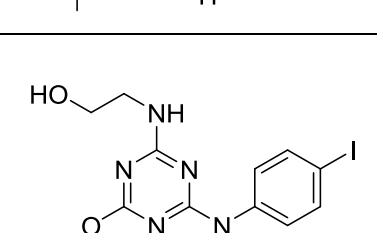
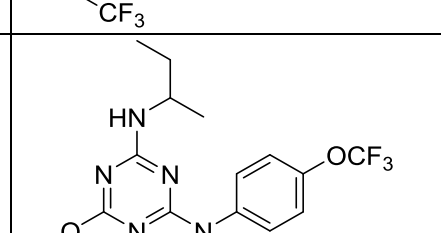
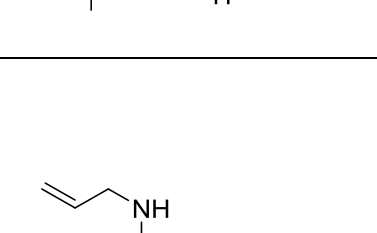
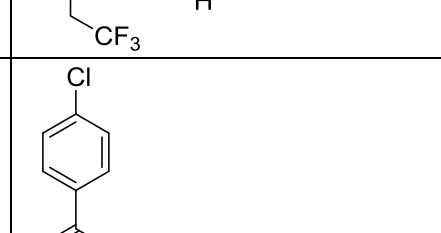
K012		19	K058		37
K013		15	K059		90 (750)
K014		18	K060		38
K015		6	K061		31
K016		19	K062		49

K017		16	K063		41
K018		60	K064		40
K019		28	K065		38
K020		37	K066		87 (2900)
K021		16	K067		49

K022		53	K068		84 (4100)
K023		41	K069		37
K024		64	K070		28
K025		19	K071		25
K026		16	K072		31

K027		20	K073		19
K028		23	K074		25
K029		9	K075		32
K030		16	K076		46
K031		61	K077		29

K032		105 (70)	K078		28
K033		22	K079		40
K034		73	K080		26
K035		55	K081		24
K036		46	K082		28

K037		36	K083		54
K038		53	K084		22
K039		27	K085		25
K040		17	K086		20
K041		35	K087		47

K042		15	K088		33
K043		19	K089		111 (250)
K044		55	K090		52
K045		15	K091		43
K046		16			

% Activation of commercial analogs at 10 μ M.

Compounds with >80% activation efficacy in plate reader assays were also assayed by short-circuit analysis to determine EC₅₀ values (in nM).