

SUPPORTING INFORMATION

Indole Compounds with *N*-Ethyl Morpholine Moieties as CB2 Receptor Agonist for Anti-Inflammatory Management of Pain: Synthesis and Biological Evaluation

Jiaojiao Li ^{1,#}, Jing Ji ^{1,2,#}, Ruibo Xu ^{1,*} and Zhengfu Li ^{3,*}

¹ Pharmacy School, Jiangsu Ocean University, Lianyungang 222005, China

² Jiangsu Key Laboratory of Marine Pharmaceutical Compound Screening, Jiangsu Ocean University, Lianyungang 222005, China

³ School of Computer Engineering, Jiangsu Ocean University, Lianyungang 222005, China

: These authors contributed equally to this work.

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1. Intermediate compounds characterization

Ethyl 2-(5-methoxy-2-methyl-1*H*-indol-3-yl)acetate (2a): Yield: 82%, ¹H NMR (CDCl₃, 400 MHz) δ 7.78 (brs, 1H), 7.13 (d, 1H, *J* = 8.4 Hz), 7.01 (d, 1H, *J* = 2.0 Hz), 6.77 (dd, 1H, *J*₁ = 9.2 Hz, *J*₂ = 2.8 Hz), 4.16-4.10 (m, 2H), 3.86 (s, 3H), 3.64 (s, 2H), 2.38 (s, 3H), 1.25 (t, 3H, *J* = 6.8 Hz); ESI-MS *m/z* 248.2 (M+H)⁺.

Ethyl 2-(5-chloro-2-methyl-1*H*-indol-3-yl)acetate (2b): Yield: 89%, ¹H NMR (CDCl₃, 400 MHz) δ 8.15 (brs, 1H), 7.48 (s, 1H), 7.03-6.09 (m, 2H), 4.19-4.14 (m, 2H), 3.63 (s, 2H), 2.24 (s, 3H), 1.27 (t, 3H, *J* = 7.6 Hz); ESI-MS *m/z* 251.9 (M+H)⁺.

Ethyl 2-(5-fluoro-2-methyl-1*H*-indol-3-yl)acetate (2c): Yield: 67%, ¹H NMR (CDCl₃, 400 MHz) δ 8.18 (brs, 1H), 7.13 (dd, 1H, *J*₁ = 10.0 Hz, *J*₂ = 2.0 Hz), 6.90 (dd, 1H, *J*₁ = 8.8 Hz, *J*₂ = 4.8 Hz), 6.76 (td, 1H, *J*₁ = 9.2 Hz, *J*₂ = 2.4 Hz), 4.14-4.08 (m, 2H), 3.59 (s, 2H), 2.17 (s, 3H), 1.22 (t, 3H, *J* = 7.2 Hz); ESI-MS *m/z* 236.1(M+H)⁺.

Ethyl 2-(5-bromo-2-methyl-1*H*-indol-3-yl)acetate (2d): Yield: 83%, ¹H NMR

(CDCl₃, 400 MHz) δ 8.12 (brs, 1H), 7.63 (s, 1H), 7.14 (dd, 1H, $J_1 = 8.4\text{Hz}$, $J_2 = 1.6\text{ Hz}$), 6.96 (d, 1H, $J = 8.8\text{ Hz}$), 4.18-4.13 (m, 2H), 3.62 (s, 2H), 2.56 (s, 3H), 1.27 (t, 3H, $J = 6.8\text{ Hz}$); ESI-MS m/z 295.9(M+H)⁺.

2-(5-Methoxy-2-methyl-1H-indol-3-yl)acetic acid (3a): Yield: 98%, ¹H NMR (CDCl₃, 400 MHz) δ 7.76 (brs, 1H), 7.15 (d, 1H, $J = 8.4\text{ Hz}$), 6.97 (d, 1H, $J = 2.0\text{ Hz}$), 6.78 (dd, 1H, $J_1 = 8.8\text{Hz}$, $J_2 = 2.8\text{ Hz}$), 3.84 (s, 3H), 3.67 (s, 2H), 2.38 (s, 3H); ESI-MS m/z 220.1(M+H)⁺.

2-(5-Chloro-2-methyl-1H-indol-3-yl)acetic acid (3b): Yield: 99%, ¹H NMR (CDCl₃, 400 MHz) δ 8.39 (brs, 1H), 7.44 (s, 1H), 7.13 (d, 1H, $J = 8.4\text{ Hz}$), 7.02 (d, 1H, $J = 7.6\text{Hz}$), 3.64 (s, 2H), 2.34(s, 3H); ESI-MS m/z 223.9(M+H)⁺.

2-(5-Fluoro-2-methyl-1H-indol-3-yl)acetic acid (3c): Yield: 96%, ¹H NMR (CDCl₃, 400 MHz) δ 7.89 (brs, 1H), 7.35 (s, 1H), 7.18-7.15 (m, 2H), 3.67 (s, 2H), 2.41(s, 3H); ESI-MS m/z 205.9(M-H)⁻.

2-(5-Bromo-2-methyl-1H-indol-3-yl)acetic acid (3d): Yield: 94%, ¹H NMR (CDCl₃, 400 MHz) δ 7.90 (brs, 1H), 7.63 (s, 1H), 7.20(dd, 1H, $J_1 = 8.8\text{Hz}$, $J_2 = 1.6\text{ Hz}$), 7.13 (d, 1H, $J = 8.4\text{ Hz}$), 3.67 (s, 2H), 2.41 (s, 3H); ESI-MS m/z 267.9(M+H)⁺.

2-(5-Methoxy-2-methyl-1H-indol-3-yl)-1-morpholinoethanone (4a): Yield: 70%, ¹H NMR (CDCl₃, 400 MHz) δ 7.80 (brs, 1H), 7.15 (d, 1H, $J = 8.8\text{ Hz}$), 6.98 (d, 1H, $J = 2.4\text{ Hz}$), 6.77 (dd, 1H, $J_1 = 8.8\text{Hz}$, $J_2 = 2.0\text{ Hz}$), 3.84 (s, 3H), 3.72 (s, 2H), 3.63-3.62 (m, 4H), 3.41-3.39 (m, 4H), 2.37(s, 3H); ESI-MS m/z 289.2(M+H)⁺.

2-(5-Chloro-2-methyl-1H-indol-3-yl)-1-morpholinoethanone (4b): Yield: 83%, ¹H NMR (CDCl₃, 400 MHz) δ 8.11 (brs, 1H), 7.43 (s, 1H), 7.12 (d, 1H, $J = 8.0\text{ Hz}$), 7.04 (d, 1H, $J = 8.4\text{ Hz}$), 3.69 (s, 3H), 3.65 (s, 4H), 3.47 (s, 4H), 2.33(s, 3H); ESI-MS m/z 291.0(M-H)⁻.

2-(5-Fluoro-2-methyl-1H-indol-3-yl)-1-morpholinoethanone (4c): Yield: 61%, ¹H NMR (CDCl₃, 400 MHz) δ 8.50 (brs, 1H), 7.11 (dd, 1H, $J_1 = 9.6\text{Hz}$, $J_2 = 2.0\text{ Hz}$), 7.05 (dd, 1H, $J_1 = 8.8\text{Hz}$, $J_2 = 4.4\text{ Hz}$), 6.79 (td, 1H, $J_1 = 9.2\text{Hz}$, $J_2 = 2.0\text{ Hz}$), 3.67 (s, 2H), 3.63 (d, 4H, $J = 2.8\text{ Hz}$), 3.45 (s, 4H), 2.24(s, 3H); ESI-MS m/z 299.2(M+Na).

2-(5-Bromo-2-methyl-1H-indol-3-yl)-1-morpholinoethanone (4d): Yield: 89%, ¹H NMR (CDCl₃, 400 MHz) δ 7.93 (brs, 1H), 7.60 (s, 1H), 7.20 (dd, 1H, $J_1 = 8.4\text{Hz}$,

$J_2 = 1.2$ Hz), 7.13 (d, 1H, $J = 8.4$ Hz), 3.69 (s, 3H), 3.65 (s, 4H), 3.47 (s, 4H), 2.39 (s, 3H); ESI-MS m/z 237.1(M+H)⁺.

5-Methoxy-2-methyl-3-(2-morpholinoethyl)-1H-indole (5a): Yield: 99%, ¹H NMR (CDCl₃, 400 MHz) δ 7.65 (brs, 1H), 7.15 (d, 1H, $J = 8.8$ Hz), 6.97 (d, 1H, $J = 2.0$ Hz), 6.77 (dd, 1H, $J_1 = 8.8$ Hz, $J_2 = 2.8$ Hz), 3.85 (s, 3H), 3.78 (t, 4H, $J = 4.4$ Hz), 2.88-2.84 (m, 2H), 2.57-2.53 (m, 6H), 2.36 (s, 3H); ESI-MS m/z 275.2(M+H)⁺.

5-Chloro-2-methyl-3-(2-morpholinoethyl)-1H-indole (5b): Yield: 94%, ¹H NMR (CDCl₃, 400 MHz) δ 7.81 (brs, 1H), 7.45 (s, 1H), 7.16 (d, 1H, $J = 8.8$ Hz), 7.05 (d, 1H, $J = 8.8$ Hz), 3.78 (t, 4H, $J = 4.8$ Hz), 2.84 (t, 2H, $J = 8.0$ Hz), 2.57-2.51 (m, 6H), 2.37 (s, 3H); ESI-MS m/z 279.1(M+H)⁺.

5-Fluoro-2-methyl-3-(2-morpholinoethyl)-1H-indole (5c): Yield: 88%, ¹H NMR (CDCl₃, 400 MHz) δ 7.96 (brs, 1H), 7.15-7.17 (m, 2H), 6.84 (td, 1H, $J_1 = 9.2$ Hz, $J_2 = 2.4$ Hz), 3.79 (t, 4H, $J = 4.4$ Hz), 2.84 (t, 2H, $J = 7.6$ Hz), 2.57-2.52 (m, 6H), 2.35 (s, 3H); ESI-MS m/z 263.2(M+H)⁺.

5-Bromo-2-methyl-3-(2-morpholinoethyl)-1H-indole (5d): Yield: 90%, ¹H NMR (CDCl₃, 400 MHz) δ 7.79 (brs, 1H), 7.61 (s, 1H), 7.18 (dd, 1H, $J_1 = 8.8$ Hz, $J_2 = 2.0$ Hz), 7.13 (d, 1H, $J = 8.0$ Hz), 3.78 (t, 4H, $J = 4.4$ Hz), 2.84 (t, 2H, $J = 7.6$ Hz), 2.57-2.51 (m, 6H), 2.38 (s, 3H); ESI-MS m/z 323.1(M+H)⁺.

tert-Butyl-2-(5-methoxy-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)acetate (6a): Yield: 61%, ¹H NMR (CDCl₃, 400 MHz) δ 7.05 (d, 1H, $J = 8.8$ Hz), 6.98 (t, 1H, $J = 2.0$ Hz), 6.79 (dd, 1H, $J_1 = 8.8$ Hz, $J_2 = 2.4$ Hz), 4.61 (s, 2H), 3.84 (s, 3H), 3.79 (t, 4H, $J = 4.8$ Hz), 2.90-2.87 (m, 2H), 2.60-2.54 (m, 6H), 2.30 (s, 3H), 1.42 (s, 9H); ESI-MS m/z 389.3 (M+H)⁺.

tert-Butyl-2-(5-chloro-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)acetate (6b): Yield: 99%, ¹H NMR (CDCl₃, 400 MHz) δ 7.40 (s, 1H), 7.09-7.05 (m, 2H), 4.63 (s, 2H), 3.78 (t, 4H, $J = 4.0$ Hz), 2.90-2.86 (m, 2H), 2.58-2.51 (m, 6H), 2.31 (s, 3H), 1.42 (s, 9H); ESI-MS m/z 393.1(M+H)⁺.

tert-Butyl-2-(5-fluoro-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)acetate (6c): Yield: 97%, ¹H NMR (CDCl₃, 400 MHz) δ 7.15 (d, 1H, $J = 9.2$ Hz), 7.06-7.03 (m, 1H), 6.86 (t, 1H, $J = 8.4$ Hz), 4.62 (s, 2H), 3.77 (s, 4H), 2.88-2.85 (m, 2H),

2.56-2.50 (m, 6H), 2.30 (s, 3H), 1.42 (s, 9H); ESI-MS m/z 377.3(M+H)⁺.

***tert*-Butyl-2-(5-bromo-2-methyl-3-(2-morpholinoethyl)-1*H*-indol-1-yl)acetate**

(6d): Yield: 99%, ¹H NMR (CDCl₃, 400 MHz) δ 7.61 (d, 1H, J = 1.6 Hz), 7.20 (dd, 1H, J_1 = 8.4 Hz, J_2 = 2.0 Hz), 7.01 (d, 1H, J = 8.8 Hz), 4.61 (s, 2H), 3.77 ((t, 4H, J = 4.4 Hz), 2.86 ((t, 2H, J = 7.6 Hz), 2.56-2.49 (m, 6H), 2.30 (s, 3H), 1.42 (s, 9H); ESI-MS m/z 437.0(M+H)⁺.

2-(5-Methoxy-2-methyl-3-(2-morpholinoethyl)-1*H*-indol-1-yl)acetic acid (7a):

Yield: 97%, ¹H NMR (CDCl₃, 400 MHz) δ 10.86 (brs, 1H), 7.03 (d, 1H, J = 8.8 Hz), 6.83 (s, 1H), 6.77 (d, 1H, J = 8.8 Hz), 4.68 (s, 2H), 3.91-3.84 (m, 4H), 3.81 (s, 3H), 3.03-2.92 (m, 6H), 2.73-2.71 (m, 2H), 2.07 (s, 3H); ESI-MS m/z 333.2 (M+H)⁺.

2-(5-Chloro-2-methyl-3-(2-morpholinoethyl)-1*H*-indol-1-yl)acetic acid (7b):

Yield: 91%, ¹H NMR (CDCl₃, 400 MHz) δ 7.22 (s, 1H), 7.07-7.01 (m, 2H), 4.63 (s, 2H), 3.87 (s, 4H), 2.91 (s, 2H), 2.84 (s, 6H), 2.06 (s, 3H); ESI-MS m/z 337.1(M+H)⁺.

2-(5-Fluoro-2-methyl-3-(2-morpholinoethyl)-1*H*-indol-1-yl)acetic acid (7c):

Yield: 99%, ¹H NMR ((CD₃)₂SO, 400 MHz) δ 10.06 (brs, 1H), 7.40 (dd, 1H, J_1 = 8.8 Hz, J_2 = 4.4 Hz), 7.35 (dd, 1H, J_1 = 10.4 Hz, J_2 = 2.4 Hz), 6.93 (td, 1H, J_1 = 9.2 Hz, J_2 = 2.4 Hz), 4.98 (s, 2H), 4.03 (s, 2H), 3.76-3.60 (m, 4H), 3.29-3.21 (m, 4H), 3.07-3.03 (m, 2H), 2.31 (s, 3H); ESI-MS m/z 321.2(M+H)⁺.

2-(5-Bromo-2-methyl-3-(2-morpholinoethyl)-1*H*-indol-1-yl)acetic acid (7d):

Yield: 90%, ¹H NMR ((CD₃)₂SO, 400 MHz) δ 13.07 (brs, 1H), 7.74 (s, 1H), 7.38 (d, 1H, J = 8.8 Hz), 7.20 (d, 1H, J = 8.4 Hz), 4.98 (s, 2H), 4.03 (s, 2H), 3.70-3.57 (m, 4H), 3.19 (s, 4H), 3.06-3.02 (m, 2H), 2.31 (s, 3H); ESI-MS m/z 321.2(M+H)⁺.

Ethyl 2-(5-methoxy-2-methyl-1-(2-morpholinoethyl)-1*H*-indol-3-yl)acetate (8a):

Yield: 89%, ¹H NMR (CDCl₃, 400 MHz) δ 7.15 (d, 1H, J = 8.8 Hz), 7.02 (d, 1H, J = 2.0 Hz), 6.81 (dd, 1H, J_1 = 8.8 Hz, J_2 = 2.4 Hz), 4.18-4.09 (m, 4H), 3.86 (s, 3H), 3.71 (t, 4H, J = 4.8 Hz), 3.66 (s, 2H), 2.61 (t, 2H, J = 7.2 Hz), 2.49 (t, 4H, J = 4.0 Hz), 2.41 (s, 3H), 1.24 (t, 3H, J = 6.8 Hz); ESI-MS m/z 361.6 (M+H)⁺

Ethyl 2-(5-chloro-2-methyl-1-(2-morpholinoethyl)-1*H*-indol-3-yl)acetate (8b):

Yield: 96%, ¹H NMR (CDCl₃, 400 MHz) δ 7.50 (s, 1H), 7.17 (d, 1H, J = 8.8 Hz), 7.09 (d, 1H, J = 8.8 Hz), 4.19-4.10 (m, 4H), 3.70 (s, 4H), 3.64 (s, 2H), 2.61 (t, 2H, J = 7.2

Hz), 2.48 (s, 4H), 2.41 (s, 3H), 1.24 (t, 3H, $J = 7.2$ Hz); ESI-MS m/z 365.2 (M+H)⁺.

Ethyl 2-(5-fluoro-2-methyl-1-(2-morpholinoethyl)-1H-indol-3-yl)acetate (8c):

Yield: 85%, ¹H NMR (CDCl₃, 400 MHz) δ 7.19-7.12 (m, 2H), 6.85 (dd, 1H, $J_1 = 8.8$ Hz, $J_2 = 2.0$ Hz), 4.16-4.08 (m, 4H), 3.68 (t, 4H, $J = 4.4$ Hz), 3.62 (s, 2H), 2.59 (t, 2H, $J = 7.6$ Hz), 2.46 (t, 4H, $J = 4.0$ Hz), 2.39 (s, 3H), 1.22 (t, 3H, $J = 7.6$ Hz); ESI-MS m/z 349.4 (M+H)⁺.

2-(5-Methoxy-2-methyl-1-(2-morpholinoethyl)-1H-indol-3-yl)acetic acid (9a):

Yield: 83%, ¹H NMR ((CD₃)₂SO, 400 MHz) δ 7.25 (d, 1H, $J = 8.8$ Hz), 6.92 (d, 1H, $J = 2.4$ Hz), 6.70 (dd, 1H, $J_1 = 8.8$ Hz, $J_2 = 2.4$ Hz), 4.17 (t, 2H, $J = 6.8$ Hz), 3.73 (s, 3H), 3.56-3.54 (m, 6H), 3.36 (s, 3H) (overlaps with the water peak), 2.40 (s, 4H), 2.34 (s, 3H); ESI-MS m/z 333.1(M+H)⁺.

2-(5-Chloro-2-methyl-1-(2-morpholinoethyl)-1H-indol-3-yl)acetic acid (9b):

Yield: 79%, ¹H NMR ((CD₃)₂SO, 400 MHz) δ 11.25 (brs, 1H), 7.58 (d, 1H, $J = 6.8$ Hz), 7.49 (s, 1H), 7.13 (d, 1H, $J = 8.8$ Hz), 4.59 (s, 2H), 4.02 (m, 2H), 3.81-3.76 (m, 2H), 3.62 (s, 2H), 3.55 (d, 2H, $J = 12.4$ Hz), 3.42 (s, 3H), 3.19-3.15 (s, 2H), 2.40 (s, 3H); ESI-MS m/z 337.1(M+H)⁺.

2-(5-Fluoro-2-methyl-1-(2-morpholinoethyl)-1H-indol-3-yl)acetic acid (9c):

Yield: 91%, ¹H NMR ((CD₃)₂SO, 400 MHz) δ 11.94 (s, 1H), 7.60 (dd, 1H, $J_1 = 8.8$ Hz, $J_2 = 4.4$ Hz), 7.20 (dd, 1H, $J_1 = 10.0$ Hz, $J_2 = 2.4$ Hz), 6.95 (td, 1H, $J_1 = 8.8$ Hz, $J_2 = 2.0$ Hz), 4.63 (t, 2H, $J = 7.2$ Hz), 4.00 (d, 2H, $J = 12.0$ Hz), 3.84 (t, 2H, $J = 11.6$ Hz), 3.60 (s, 2H), 3.53 (d, 2H, $J = 12.0$ Hz), 3.36 (s, 3H) (overlaps with the water peak), 3.20-3.15 (m, 2H), 2.40 (s, 3H); ESI-MS m/z 321.4(M+H)⁺.

2. Target compounds characterization

(5-Chloro-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)(2,3-dichlorophenyl)methanone (1): Yield: 89%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.63-7.61 (m, 1H), 7.41 (s, 1H), 7.38-7.32 (m, 3H), 7.07 (d, 1H, $J = 8.4$ Hz), 3.73 (s, 4H), 2.79-2.76 (m, 2H), 2.53-2.47 (m, 6H), 2.12 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz) 165.62, 138.21, 134.38, 134.33, 134.12, 132.72, 131.94, 130.14, 129.40, 128.30, 127.27, 124.19, 118.55, 117.89, 115.96, 66.93 (2C), 58.34, 53.74 (2C), 21.66, 13.41; ESI-MS m/z

451.1 (M+H)⁺; HRMS (ESI) calcd for C₂₂H₂₂Cl₃N₂O₂ (M+H)⁺ 451.0747, found 451.0741.

(2,3-Dichlorophenyl)(5-fluoro-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)methanone (2): Yield: 97%., white solid, ¹H NMR (CDCl₃, 400 MHz) 7.60 (d, 1H, J = 5.2 Hz), 7.46 (s, 1H), 7.34-7.33 (m, 2H), 7.09 (d, 1H, J = 7.6 Hz), 6.83 (t, 1H, J = 8.0 Hz), 2.72 (s, 3H), 2.77-2.75 (m, 2H), 2.52 (s, 6H), 2.09 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz) 165.48, 159.83 (d, 1C, J = 238.9 Hz), 138.22, 134.26, 134.22, 132.55, 132.23, 131.79 (d, 1C, J = 9.9 Hz), 130.04, 128.24, 127.15, 118.87, 116.10 (d, 1C, J = 8.7 Hz), 111.51 (d, 1C, J = 23.7 Hz), 103.98 (d, 1C, J = 23.3 Hz), 66.86 (2C), 58.22, 53.68 (2C), 21.66, 13.41; ESI-MS m/z 435.2 (M+H)⁺; HRMS (ESI) calcd for C₂₂H₂₂Cl₂FN₂O₂ (M+H)⁺ 435.1042, found 435.1037.

(5-Bromo-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)(2,3-dichlorophenyl)methanone (3): Yield: 100%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.64 (dd, 1H, J₁ = 6.4 Hz, J₂ = 3.2 Hz), 7.58 (s, 1H), 7.37-7.35 (m, 2H), 7.33-7.30 (m, 1H), 7.24-7.21 (m, 1H), 3.74 (t, 4H, J = 4.0 Hz), 2.79 (t, 2H, J = 7.6 Hz), 2.54-2.48 (m, 6H), 2.13 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz) 165.69, 138.23, 134.75, 134.45, 134.06, 132.79, 132.43, 130.20, 128.34, 127.30, 126.96, 120.97, 118.44, 117.17, 116.35, 66.94 (2C), 58.37, 53.76 (2C), 21.66, 13.43; ESI-MS m/z 497.0 (M+H)⁺; HRMS (ESI) calcd for C₂₂H₂₂BrCl₂N₂O₂ (M+H)⁺ 495.0242, found 495.0236.

(5-Methoxy-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)(pyrrolidin-1-yl)methanone (4): Yield: 63%, yellow solid, ¹H NMR (CDCl₃, 400 MHz) 7.09 (d, 1H, J = 8.8 Hz), 6.95 (d, 1H, J = 1.2 Hz), 6.80 (dd, 1H, J₁ = 8.4 Hz, J₂ = 1.2 Hz), 3.85 (s, 3H), 3.78 (t, 4H, J = 4.4 Hz), 3.85 (brs, 4H), 2.85 (t, 2H, J = 7.6 Hz), 2.58-2.52 (m, 6H), 2.39 (s, 3H), 1.94 (s, 4H); ¹³C NMR (CDCl₃, 100 MHz) 154.85, 153.02, 132.85, 129.53, 129.39, 112.61, 111.85, 111.12, 101.18, 67.02 (2C), 59.18, 56.01, 53.84 (2C), 47.77, 47.69, 25.46, 25.42, 21.73, 11.49; ESI-MS m/z 372.4 (M+H)⁺; HRMS (ESI) calcd for C₂₁H₃₀N₃O₃ (M+H)⁺ 272.2209, found 272.2281.

(5-Chloro-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)(pyrrolidin-1-yl)methanone (5): Yield: 84%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.44 (s, 1H), 7.09 (s, 2H), 3.75 (s, 4H), 3.49 (brs, 4H), 2.81 (t, 2H, J = 7.2 Hz), 2.54-2.50 (m, 6H), 2.38 (s, 3H), 1.93 (s, 4H); ¹³C NMR (CDCl₃, 100 MHz) 152.33, 133.45, 132.64, 130.00, 126.29, 122.23, 118.02, 112.49, 111.91, 67.05 (2C), 59.17, 53.84 (2C), 47.75, 47.55, 25.43, 25.35, 21.72, 11.05; ESI-MS m/z 376.3 (M+H)⁺; HRMS (ESI) calcd for C₂₀H₂₇ClN₃O₂ (M+H)⁺ 376.1792, found 376.1786.

(5-Fluoro-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)(pyrrolidin-1-yl)methanone (6): Yield: 66%, colorless oil, ^1H NMR (CDCl_3 , 400 MHz) 7.11-7.05 (m, 2H), 6.84 (t, 1H, $J = 7.2$ Hz), 3.72 (s, 4H), 3.44 (brs, 4H), 2.80 (t, 2H, $J = 7.6$ Hz), 2.53-2.47 (m, 6H), 2.36 (s, 3H), 1.90 (s, 4H); ^{13}C NMR (CDCl_3 , 100 MHz) 158.30 (d, 1C, $J = 235.2$ Hz), 152.43, 133.70, 130.63, 129.34 (d, 1C, $J = 9.2$ Hz), 112.64, 111.49 (d, 1C, $J = 8.7$ Hz), 109.83 (d, 1C, $J = 25.2$ Hz), 103.60 (d, 1C, $J = 23.9$ Hz), 66.81 (2C), 58.93, 53.65 (2C), 47.46 (2C), 25.23 (2C), 21.56, 10.99; ESI-MS m/z 360.2 ($\text{M}+\text{H}$) $^+$; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{27}\text{FN}_3\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 360.2087, found 360.2082.

(5-Bromo-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)(pyrrolidin-1-yl)methanone (7): Yield: 78%, white solid, ^1H NMR (CDCl_3 , 400 MHz) 7.60 (s, 1H), 7.22 (dd, 1H, $J_1 = 8.4$ Hz, $J_2 = 1.6$ Hz), 7.05 (d, 1H, $J = 8.8$ Hz), 3.76 (t, 4H, $J = 3.2$ Hz), 3.48 (brs, 4H), 2.83 (t, 2H, $J = 7.6$ Hz), 2.58-2.51 (m, 6H), 2.38 (s, 3H), 1.93 (s, 4H); ^{13}C NMR (CDCl_3 , 100 MHz) 152.22, 132.38, 132.96, 130.52, 124.88, 121.05, 113.88, 112.35, 112.14, 66.82 (2C), 59.04, 53.69 (2C), 47.68 (2C), 25.33 (2C), 21.51, 11.01; ESI-MS m/z 420.3 ($\text{M}+\text{H}$) $^+$; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{27}\text{BrN}_3\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 420.1287, found 420.1281.

N-Cyclopropyl-2-(5-methoxy-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)acetamide (8): Yield: 73%, white solid, ^1H NMR (CDCl_3 , 400 MHz) 7.05 (d, 1H, $J = 8.8$ Hz), 6.99 (d, 1H, $J = 1.6$ Hz), 6.83 (dd, 1H, $J_1 = 8.8$ Hz, $J_2 = 2.0$ Hz), 5.36 (s, 1H), 4.62 (s, 2H), 3.85 (s, 3H), 3.77 (t, 4H, $J = 4.0$ Hz), 2.88 (t, 2H, $J = 7.6$ Hz), 2.63-2.51 (m, 7H), 2.27 (s, 3H), 0.71-0.67 (m, 2H), 0.31-0.27 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) 170.16, 154.68, 133.25, 131.47, 128.79, 111.20, 110.79, 109.39, 101.15, 67.04 (2C), 59.62, 56.11, 53.92 (2C), 47.28, 22.49, 22.08, 10.25, 6.75 (2C); ESI-MS m/z 372.2 ($\text{M}+\text{H}$) $^+$; HRMS (ESI) calcd for $\text{C}_{21}\text{H}_{30}\text{N}_3\text{O}_3$ ($\text{M}+\text{H}$) $^+$ 372.2209, found 372.2282.

2-(5-Chloro-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)-N-cyclopropylacetamide (9): Yield: 69%, white solid, ^1H NMR (CDCl_3 , 400 MHz) 7.36 (s, 1H), 6.97 (d, 2H, $J = 9.2$ Hz), 5.99 (s, 1H), 4.39 (s, 2H), 3.69 (s, 4H), 2.70 (s, 2H), 2.55-2.48 (m, 7H), 2.18 (s, 3H), 0.63 (d, 2H, $J = 4.8$ Hz), 0.30 (s, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) 169.41, 134.56, 134.32, 129.08, 125.39, 121.48, 117.66, 110.09, 109.51, 66.66 (2C), 59.23, 53.53 (2C), 46.47, 22.42, 21.58, 10.04, 6.43 (2C); ESI-MS m/z 376.1 ($\text{M}+\text{H}$) $^+$; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{27}\text{ClN}_3\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 376.1792, found 376.1786.

N-Cyclopropyl-2-(5-fluoro-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)acetamide (10): Yield: 58%, white solid, ^1H NMR (CDCl_3 , 400 MHz) 7.13 (dd, 1H, $J_1 = 9.2$ Hz, $J_2 = 2.0$ Hz), 7.04-7.01 (m, 1H), 6.88-6.84 (m, 1H), 5.49 (s, 1H), 4.58 (s, 2H),

3.72 (t, 4H, J = 4.4 Hz), 2.82 (t, 2H, J = 7.2 Hz), 2.60-2.46 (m, 7H), 2.25 (s, 3H), 0.69-0.64 (m, 2H), 0.30-0.27 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) 169.63, 158.16 (d, 1C, J = 233.8 Hz), 134.34, 132.70, 128.61 (d, 1C, J = 9.6 Hz), 111.03 (d, 1C, J = 3.9 Hz), 109.70 (d, 1C, J = 26.8 Hz), 109.17 (d, 1C, J = 9.7 Hz), 103.56 (d, 1C, J = 23.4 Hz), 66.88 (2C), 59.39, 53.74 (2C), 47.07, 22.44, 21.93, 10.21, 6.62 (2C); ESI-MS m/z 360.1 ($\text{M}+\text{H}$) $^+$; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{27}\text{FN}_3\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 360.2087, found 360.2082.

2-(5-Bromo-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)-N-cyclopropylacetamide (11): Yield: 60%, white solid, ^1H NMR (CDCl_3 , 400 MHz) 7.59 (s, 1H), 7.18 (d, 1H, J = 8.4 Hz), 6.97 (d, 1H, J = 8.4 Hz), 5.59 (s, 2H), 4.53 (s, 2H), 3.70 (t, 4H, J = 4.8 Hz), 2.79 (t, 2H, J = 7.6 Hz), 2.60-2.56 (m, 1H), 2.51-2.45 (m, 6H), 2.24 (s, 3H), 0.68-0.63 (m, 2H), 0.31-0.27 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) 169.38, 134.88, 133.97, 129.89, 124.35, 120.95, 113.22, 110.60, 110.00, 66.84 (2C), 59.39, 53.71 (2C), 46.86, 22.47, 21.81, 10.13, 6.58 (2C); ESI-MS m/z 420.3 ($\text{M}+\text{H}$) $^+$; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{27}\text{BrN}_3\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 420.1287, found 420.1281.

N-Cyclohexyl-2-(5-methoxy-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)acetamide (12): Yield: 51%, white solid, ^1H NMR (CDCl_3 , 400 MHz) 7.08 (d, 1H, J = 8.8 Hz), 7.01 (s, 1H), 6.83 (d, 1H, J = 8.8 Hz), 5.05 (d, 1H, J = 8.4 Hz), 4.63 (s, 2H), 3.87 (s, 3H), 3.79-3.75 (m, 5H), 2.91 (brs, 2H), 2.59 (brs, 6H), 2.29 (s, 3H), 1.70 (d, 2H, J = 11.6 Hz), 1.49 (d, 3H, J = 10.0 Hz), 1.29-1.23 (m, 2H), 1.05-0.98 (m, 1H), 0.91-0.83 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) 167.66, 154.64, 133.34, 131.58, 128.76, 111.18, 110.71, 109.52, 101.09, 67.01 (2C), 59.67, 56.10, 53.89 (2C), 48.02, 47.39, 37.76 (2C), 25.34, 24.52 (2C), 22.05, 10.23; ESI-MS m/z 414.4 ($\text{M}+\text{H}$) $^+$; HRMS (ESI) calcd for $\text{C}_{24}\text{H}_{36}\text{N}_3\text{O}_3$ ($\text{M}+\text{H}$) $^+$ 414.2757, found 414.2751.

2-(5-Chloro-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)-N-cyclohexylacetamide (13): Yield: 43%, white solid, ^1H NMR (CDCl_3 , 400 MHz) 7.49 (s, 1H), 7.11-7.06 (m, 2H), 5.00 (d, 1H, J = 8.0 Hz), 4.62 (s, 2H), 3.74 (s, 5H), 2.85 (t, 2H, J = 7.6 Hz), 2.54-2.47 (m, 6H), 2.29 (s, 3H), 1.70 (t, 2H, J = 10 Hz), 1.48 (t, 2H, J = 10 Hz), 1.27-1.23 (m, 2H), 1.01-0.99 (m, 1H), 0.90-0.82 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) 167.00, 134.67, 134.06, 129.31, 125.84, 121.98, 118.03, 110.98, 109.71, 67.03 (2C), 59.62, 53.85 (2C), 48.07, 47.24, 32.72 (2C), 25.25, 24.49 (2C), 21.99, 10.21; ESI-MS m/z 418.2 ($\text{M}+\text{H}$) $^+$; HRMS (ESI) calcd for $\text{C}_{23}\text{H}_{33}\text{ClN}_3\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 418.2261, found 418.2256.

N-Cyclohexyl-2-(5-fluoro-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)acetamide (14): Yield: 56%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.16 (dd, 1H, J₁ = 9.6 Hz, J₂ = 2.0 Hz), 7.06 (dd, 1H, J₁ = 8.8 Hz, J₂ = 3.6 Hz), 6.91-6.86 (m, 1H), 5.03 (d, 2H, J = 8.0 Hz), 4.62 (s, 2H), 3.74 (t, 5H, J = 4.4 Hz), 2.86 (t, 2H, J = 7.6 Hz), 2.55-2.49 (m, 6H), 2.29 (s, 3H), 1.70-1.67 (m, 2H), 1.48-1.46 (m, 3H), 1.29-1.20 (m, 2H), 1.04-0.95 (m, 1H), 0.91-0.83 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) 167.18, 158.25 (d, 1C, J = 233.8 Hz), 134.39, 132.80, 128.65 (d, 1C, J = 9.6 Hz), 111.18 (d, 1C, J = 3.6 Hz), 109.84 (d, 1C, J = 26.2 Hz), 109.35 (d, 1C, J = 9.2 Hz), 103.63 (d, 1C, J = 23.4 Hz), 66.95 (2C), 59.53, 53.81 (2C), 47.99, 47.32, 32.68 (2C), 25.25, 24.43 (2C), 21.99, 10.24; ESI-MS m/z 402.3 (M+H)⁺; HRMS (ESI) calcd for C₂₃H₃₃FN₃O₂ (M+H)⁺ 402.2557, found 402.2551.

2-(5-Bromo-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)-N-cyclohexylacetamide (15): Yield: 47%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.62 (s, 1H), 7.20 (dd, 1H, J₁ = 8.4 Hz, J₂ = 1.6 Hz), 7.00 (d, 1H, J = 8.4 Hz), 5.09 (d, 1H, J = 8.0 Hz), 4.58 (s, 2H), 3.72 (t, 5H, J = 4.4 Hz), 2.83 (t, 2H, J = 7.2 Hz), 2.52-2.46 (m, 6H), 2.27 (s, 3H), 1.68 (d, 2H, J = 9.6 Hz), 1.47 (d, 3H, J = 10.4 Hz), 1.28-1.19 (m, 2H), 1.03-0.95 (m, 1H), 0.90-0.82 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) 166.88, 134.94, 133.94, 129.89, 124.43, 120.98, 113.29, 110.74, 110.09, 66.88 (2C), 59.47, 53.74 (2C), 48.06, 47.11, 32.65 (2C), 25.20, 24.45 (2C), 21.84, 10.10; ESI-MS m/z 462.3 (M+H)⁺; HRMS (ESI) calcd for C₂₃H₃₃BrN₃O₂ (M+H)⁺ 462.1756, found 462.1751.

N-(Benzo[d][1,3]dioxol-5-ylmethyl)-2-(5-methoxy-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)acetamide (16): Yield: 53%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.09 (d, 1H, J = 8.8 Hz), 6.99 (s, 1H), 6.84 (d, 1H, J = 8.4 Hz), 6.66 (d, 1H, J = 8.0 Hz), 6.54-6.49 (m, 2H), 5.91 (s, 2H), 5.53 (brs, 1H), 4.71 (s, 2H), 4.24 (d, 2H, J = 6.0 Hz), 3.85 (s, 3H), 3.76 (s, 4H), 2.87 (t, 2H, J = 7.2 Hz), 2.55-2.50 (m, 6H), 2.27 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz) 168.73, 154.76, 148.01, 147.09, 133.29, 131.62, 131.54, 128.85, 120.71 (2C), 111.28, 109.52, 108.34, 107.97, 101.20 (2C), 67.03 (2C), 59.59, 56.15, 53.91 (2C), 47.31, 43.05, 22.07, 10.31; ESI-MS m/z 466.5 (M+H)⁺; HRMS (ESI) calcd for C₂₆H₃₂N₃O₅ (M+H)⁺ 466.2342, found 466.2337.

N-(Benzo[d][1,3]dioxol-5-ylmethyl)-2-(5-chloro-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)acetamide (17): Yield: 49%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.46 (s, 1H), 7.09-7.06 (m, 2H), 6.46 (d, 1H, J = 8.0 Hz), 6.53-6.48 (m, 2H), 5.88 (s, 2H), 5.64 (brs, 1H), 4.67 (s, 2H), 4.22 (d, 2H, J = 5.2 Hz), 3.73 (s, 4H), 2.84 (t, 2H, J = 6.8 Hz), 2.54-2.48 (m, 6H), 2.27 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz) 168.07,

147.95, 147.05, 134.68, 134.16, 131.44, 129.35, 125.92, 121.98, 120.66, 118.01, 110.84, 109.73, 108.29, 107.90, 101.15, 66.81 (2C), 59.40, 53.71 (2C), 47.10, 43.05, 21.81, 10.25; ESI-MS m/z 470.3 (M+H)⁺; HRMS (ESI) calcd for C₂₅H₂₉ClN₃O₄ (M+H)⁺ 470.1847, found 470.1841.

N-(Benzo[d][1,3]dioxol-5-ylmethyl)-2-(5-fluoro-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)acetamide (18): Yield: 64%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.14 (dd, 1H, J₁ = 9.6 Hz, J₂ = 2.0 Hz), 7.07 (dd, 1H, J₁ = 8.8 Hz, J₂ = 4.4 Hz), 6.90-6.85 (m, 1H), 6.63 (d, 1H, J = 8.0 Hz), 6.52-6.48 (m, 2H), 5.87 (s, 2H), 5.70 (t, 1H, J = 5.2 Hz), 4.67 (s, 2H), 4.22 (d, 2H, J = 6.0 Hz), 3.71 (t, 4H, J = 4.4 Hz), 2.82 (t, 2H, J = 7.6 Hz), 2.50-2.45 (m, 6H), 2.27 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz) 168.24, 158.20 (d, 1C, J = 238.0 Hz), 147.90, 146.99, 134.36, 132.78, 131.47, 128.68 (d, 1C, J = 9.5 Hz), 120.58, 111.18 (d, 1C, J = 4.8 Hz), 109.12 (d, 1C, J = 25.8 Hz), 109.31 (d, 1C, J = 9.9 Hz), 108.23, 107.84, 103.62 (d, 1C, J = 23.4 Hz), 101.10, 66.85 (2C), 59.38, 53.73 (2C), 47.13, 42.98, 21.91, 10.26; ESI-MS m/z 454.3 (M+H)⁺; HRMS (ESI) calcd for C₂₅H₂₉FN₃O₄ (M+H)⁺ 454.2142, found 454.2137.

N-(Benzo[d][1,3]dioxol-5-ylmethyl)-2-(5-bromo-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)acetamide (19): Yield: 62%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.64 (s, 1H), 7.25 (d, 1H, J = 8.4 Hz), 7.06-7.04 (m, 1H), 6.67-6.65 (m, 2H), 6.55-6.50 (m, 2H), 5.91 (s, 2H), 5.59 (s, 1H), 4.70 (s, 2H), 4.24 (s, 2H), 3.73 (s, 4H), 2.84 (s, 2H), 2.53-2.49 (m, 6H), 2.29 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz) 168.08, 148.01, 147.14, 135.02, 133.97, 131.47, 130.07, 124.66, 120.98, 121.17, 120.74, 113.53, 111.04, 110.20, 108.35, 107.97, 101.22, 66.97 (2C), 59.50, 53.84 (2C), 47.18, 43.12, 21.95, 10.27; ESI-MS m/z 514.4 (M+H)⁺; HRMS (ESI) calcd for C₂₅H₂₉BrN₃O₄ (M+H)⁺ 514.1341, found 514.1336.

2-(5-Methoxy-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)-1-(piperidin-1-yl)ethanone (20): Yield: 64%, colorless oil, ¹H NMR (CDCl₃, 400 MHz) 6.98-6.94 (m, 2H), 6.73 (dd, 1H, J₁ = 8.8 Hz, J₂ = 2.0 Hz), 4.63 (s, 2H), 3.81-3.78 (m, 7H), 3.49 (m, 2H), 3.36 (m, 2H), 2.91 (t, 2H, J = 7.6 Hz), 2.61-2.57 (m, 6H), 2.27 (s, 3H), 1.63-1.61 (m, 2H), 1.51 (brs, 4H); ¹³C NMR (CDCl₃, 100 MHz) 165.61, 153.95, 134.27, 131.97, 128.22, 110.22, 108.92, 108.26, 100.76, 66.31 (2C), 59.21, 56.08, 53.36 (2C), 45.88, 44.61, 43.33, 26.43, 25.49, 24.35, 21.48, 10.24; ESI-MS m/z 400.3 (M+H)⁺; HRMS (ESI) calcd for C₂₃H₃₄N₃O₃ (M+H)⁺ 400.2600, found 400.2595.

2-(5-Chloro-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)-1-(piperidin-1-yl)ethanone (21): Yield: 53%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.45 (s, 1H),

7.04-6.99 (m, 2H), 4.75 (s, 2H), 3.81 (s, 4H), 3.45 (s, 2H), 2.91 (s, 2H), 2.61 (s, 6H), 2.28 (s, 3H), 1.67 (s, 2H), 1.57 (s, 4H); ^{13}C NMR (CDCl_3 , 100 MHz) 165.25, 135.23, 135.16, 129.15, 124.91, 121.05, 117.57, 109.00, 66.74 (2C), 59.53, 53.68 (2C), 46.04, 44.68, 43.51, 26.59, 25.58, 24.44, 21.80, 10.37; ESI-MS m/z 404.2 ($\text{M}+\text{H}$) $^+$; HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{31}\text{ClN}_3\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 404.2105, found 404.2099.

2-(5-Fluoro-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)-1-(piperidin-1-yl)ethanone (22): Yield: 40%, white solid, ^1H NMR (CDCl_3 , 400 MHz) 7.13 (dd, 1H, $J_1 = 9.6$ Hz, $J_2 = 2.0$ Hz), 6.97 (dd, 1H, $J_1 = 8.8$ Hz, $J_2 = 4.4$ Hz), 6.84-6.79 (m, 1H), 4.70 (s, 2H), 3.77 (t, 4H, $J = 4.4$ Hz), 3.52 (t, 2H, $J = 5.2$ Hz), 3.42-3.41 (m, 2H), 2.87 (t, 2H, $J = 8.0$ Hz), 2.58-2.52 (m, 6H), 2.25 (s, 3H), 1.66-1.65 (m, 2H), 1.56-1.55 (m, 4H); ^{13}C NMR (CDCl_3 , 100 MHz) 165.38, 157.86 (d, 1C, $J = 232.3$ Hz), 135.35, 133.30, 128.33 (d, 1C, $J = 9.5$ Hz), 109.25, 108.87, 108.70 (d, 1C, $J = 17.5$ Hz), 103.10 (d, 1C, $J = 23.4$ Hz), 66.71 (2C), 59.46, 53.62 (2C), 45.97, 44.67, 43.43, 26.51, 25.54, 24.39, 21.83, 10.36; ESI-MS m/z 388.6 ($\text{M}+\text{H}$) $^+$; HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{31}\text{FN}_3\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 388.2400, found 388.2395.

2-(5-Bromo-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)-1-(piperidin-1-yl)ethanone (23): Yield: 55%, white solid, ^1H NMR (CDCl_3 , 400 MHz) 7.60 (d, 1H, $J = 1.6$ Hz), 7.15 (dd, 1H, $J_1 = 8.8$ Hz, $J_2 = 1.6$ Hz), 6.92 (d, 1H, $J = 8.4$ Hz), 4.66 (s, 2H), 3.76 (t, 4H, $J = 4.4$ Hz), 3.52 (t, 2H, $J = 5.2$ Hz), 3.42-3.40 (m, 2H), 2.84 (t, 2H, $J = 8.0$ Hz), 2.55-2.49 (m, 6H), 2.25 (s, 3H), 1.66-1.65 (m, 2H), 1.56-1.55 (m, 4H); ^{13}C NMR (CDCl_3 , 100 MHz) 165.23, 135.48, 134.87, 129.87, 123.54, 120.65, 112.44, 109.81, 109.26, 66.97 (2C), 59.66, 53.81 (2C), 46.03, 44.62, 26.57, 25.56, 24.42, 21.99, 10.30; ESI-MS m/z 448.3 ($\text{M}+\text{H}$) $^+$; HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{31}\text{BrN}_3\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 448.1600, found 448.1594.

2-(5-Methoxy-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)-1-(pyrrolidin-1-yl)ethanone (24): Yield: 49%, yellow oil, ^1H NMR (CDCl_3 , 400 MHz) 7.02 (d, 1H, $J = 8.4$ Hz), 6.98 (s, 1H), 6.76 (d, 1H, $J = 8.4$ Hz), 4.67 (s, 2H), 3.83 (s, 3H), 3.77 (s, 4H), 3.48 (t, 2H, $J = 6.4$ Hz), 3.32 (t, 2H, $J = 6.0$ Hz), 2.88 (t, 2H, $J = 7.2$ Hz), 2.56 (m, 6H), 2.29 (s, 3H), 1.97-1.94 (m, 2H), 1.84-1.81 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) 166.19, 154.02, 134.08, 131.97, 128.42, 110.32, 109.17, 109.04, 100.91, 66.99 (2C), 59.74, 56.12, 53.85 (2C), 46.41, 46.06, 45.69, 26.42, 23.92, 22.08, 10.41; ESI-MS m/z 386.2 ($\text{M}+\text{H}$) $^+$; HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{32}\text{N}_3\text{O}_3$ ($\text{M}+\text{H}$) $^+$ 386.2444, found 386.2438.

2-(5-Chloro-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)-1-(pyrrolidin-1-yl)ethanone (25): Yield: 60%, white solid, ^1H NMR (CDCl_3 , 400 MHz) 7.43 (s, 1H),

6.99 (s, 2H), 4.59 (s, 2H), 3.75 (s, 4H), 3.44 (s, 2H), 3.35 (s, 2H), 2.82 (s, 2H), 2.53 (s, 6H), 2.25 (s, 3H), 1.97 (s, 2H), 1.82 (s, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) 165.54, 135.06, 134.99, 129.10, 124.74, 120.83, 117.46, 109.41, 109.18, 66.90 (2C), 59.57, 53.72 (2C), 46.28, 45.66, 45.59, 26.30, 23.90, 21.90, 10.30; ESI-MS m/z 390.2 ($\text{M}+\text{H}$) $^+$; HRMS (ESI) calcd for $\text{C}_{21}\text{H}_{29}\text{ClN}_3\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 390.1948, found 390.1943.

2-(5-Fluoro-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)-1-(pyrrolidin-1-yl)ethanone (26): Yield: 57%, white solid, ^1H NMR (CDCl_3 , 400 MHz) 7.13 (d, 1H, $J = 9.2$ Hz), 7.00 (dd, 1H, $J_1 = 8.4$ Hz, $J_2 = 3.6$ Hz), 6.82 (t, 1H, $J = 8.8$ Hz), 4.67 (s, 2H), 3.76 (s, 4H), 3.48 (t, 2H, $J = 6.4$ Hz), 3.38 (t, 2H, $J = 6.4$ Hz), 2.86 (t, 2H, $J = 7.6$ Hz), 2.55-2.51 (m, 6H), 2.28 (s, 3H), 2.00-1.97 (m, 2H), 1.87-1.82 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) 165.79, 157.89 (d, 1C, $J = 231.5$ Hz), 135.29, 133.24, 128.38 (d, 1C, $J = 9.5$ Hz), 109.48 (d, 1C, $J = 3.7$ Hz), 108.93 (d, 1C, $J = 8.0$ Hz), 108.77 (d, 1C, $J = 25.4$ Hz), 103.14 (d, 1C, $J = 23.1$ Hz), 66.85 (2C), 59.54, 53.72 (2C), 46.36, 45.82, 45.73, 26.37, 23.94, 21.95, 10.44; ESI-MS m/z 374.3 ($\text{M}+\text{H}$) $^+$; HRMS (ESI) calcd for $\text{C}_{21}\text{H}_{29}\text{FN}_3\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 374.2244, found 374.2238.

2-(5-Bromo-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)-1-(pyrrolidin-1-yl)ethanone (27): Yield: 57%, white solid, ^1H NMR (CDCl_3 , 400 MHz) 7.60 (d, 1H, $J = 1.6$ Hz), 7.16 (dd, 1H, $J_1 = 8.4$ Hz, $J_2 = 1.6$ Hz), 6.96 (d, 1H, $J = 8.8$ Hz), 4.65 (s, 2H), 3.76 (t, 4H, $J = 4.8$ Hz), 3.48 (t, 2H, $J = 6.8$ Hz), 3.37 (t, 2H, $J = 6.8$ Hz), 2.84 (t, 2H, $J = 8.0$ Hz), 2.55-2.49 (m, 6H), 2.29 (s, 3H), 2.03-1.96 (m, 2H), 1.88-1.81 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) 165.64, 135.43, 134.86, 129.87, 123.60, 120.70, 112.52, 109.92, 109.39, 67.03 (2C), 59.69, 53.85 (2C), 46.43, 45.80 (2C), 26.42, 23.98, 22.03, 10.40; ESI-MS m/z 434.3 ($\text{M}+\text{H}$) $^+$; HRMS (ESI) calcd for $\text{C}_{21}\text{H}_{29}\text{BrN}_3\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 434.1443, found 434.1438.

N-(Cyclopropylmethyl)-2-(5-methoxy-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)acetamide (28): Yield: 55%, white solid, ^1H NMR (CDCl_3 , 400 MHz) 7.10 (d, 1H, $J = 8.8$ Hz), 7.02 (d, 1H, $J = 2.0$ Hz), 6.84 (dd, 1H, $J_1 = 8.8$ Hz, $J_2 = 2.0$ Hz), 5.37-5.34 (m, 1H), 4.66 (s, 2H), 3.86 (s, 3H), 3.78 (t, 4H, $J = 4.4$ Hz), 3.03 (t, 2H, $J = 6.8$ Hz), 2.91 (t, 2H, $J = 7.6$ Hz), 2.58-2.53 (m, 6H), 2.31 (s, 3H), 0.80-0.72 (m, 1H), 0.38-0.34 (m, 2H), 0.05-0.01 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) 168.68, 154.69, 133.39, 131.59, 128.82, 111.20, 110.83, 109.56, 101.12, 67.08 (2C), 59.73, 56.15, 53.96 (2C), 47.32, 43.87, 22.12, 10.77, 10.25, 3.24 (2C); ESI-MS m/z 385.5 ($\text{M}+\text{H}$) $^+$; HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{32}\text{N}_3\text{O}_3$ ($\text{M}+\text{H}$) $^+$ 386.2444, found 386.2438.

2-(5-Chloro-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)-N-(cyclopropylmethyl)acetamide (29): Yield: 38%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.49 (s, 1H), 7.10 (s, 2H), 5.32 (s, 1H), 4.66 (s, 2H), 3.76 (s, 4H), 3.02 (t, 2H, J = 6.0 Hz), 2.88 (t, 2H, J = 7.2 Hz), 2.57 (m, 6H), 2.32 (s, 3H), 0.76 (m, 1H), 0.36 (d, 2H, J = 7.2 Hz), 0.03 (d, 2H, J = 4.0 Hz); ¹³C NMR (CDCl₃, 100 MHz) 167.98, 134.72, 134.23, 129.37, 125.90, 122.00, 118.00, 110.80, 109.79, 66.91 (2C), 59.56, 53.79 (2C), 47.18, 43.92, 21.90, 10.71, 10.22, 3.22 (2C); ESI-MS m/z 390.2 (M+H)⁺; HRMS (ESI) calcd for C₂₁H₂₉ClN₃O₂ (M+H)⁺ 390.1948, found 390.1943.

N-(Cyclopropylmethyl)-2-(5-fluoro-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)acetamide (30): Yield: 57%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.15 (dd, 1H, J₁ = 9.6 Hz, J₂ = 2.4 Hz), 7.07 (dd, 1H, J₁ = 8.8 Hz, J₂ = 4.4 Hz), 6.89-6.84 (m, 1H), 5.39 (m, 1H), 4.63 (s, 2H), 3.72 (t, 4H, J = 4.0 Hz), 3.01 (t, 2H, J = 6.4 Hz), 2.85 (t, 2H, J = 7.6 Hz), 2.53-2.48 (m, 6H), 2.30 (s, 3H), 0.80-0.70 (m, 1H), 0.36-0.31 (m, 2H), 0.03-0.01 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) 168.11, 158.18 (d, 1C, J = 234.4 Hz), 134.42, 132.77, 128.64 (d, 1C, J = 9.4 Hz), 111.06 (d, 1C, J = 4.4 Hz), 109.70 (d, 1C, J = 25.1 Hz), 109.32 (d, 1C, J = 9.9 Hz), 103.53 (d, 1C, J = 23.2 Hz), 66.89 (2C), 59.49, 53.75 (2C), 47.13, 43.77, 26.37, 21.94, 10.64, 10.19, 3.11 (2C); ESI-MS m/z 374.2 (M+H)⁺; HRMS (ESI) calcd for C₂₁H₂₉FN₃O₂ (M+H)⁺ 374.2244, found 374.2238.

2-(5-Bromo-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)-N-(cyclopropylmethyl)acetamide (31): Yield: 61%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.63 (s, 1H), 7.21 (d, 1H, J = 8.4 Hz), 7.03 (d, 1H, J = 8.8 Hz), 5.37 (s, 1H), 4.62 (s, 2H), 3.72 (t, 4H, J = 4.4 Hz), 3.01 (t, 2H, J = 6.4 Hz), 2.86 (t, 2H, J = 7.6 Hz), 2.53-2.48 (m, 6H), 2.30 (s, 3H), 0.78-0.72 (m, 1H), 0.37-0.32 (m, 2H), 0.03-0.00 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) 167.86, 134.96, 134.01, 129.96, 124.43, 121.00, 113.32, 110.75, 110.15, 66.89 (2C), 59.51, 53.76 (2C), 47.04, 43.85, 21.88, 10.65, 10.12, 3.17 (2C); ESI-MS m/z 434.3 (M+H)⁺; HRMS (ESI) calcd for C₂₁H₂₉BrN₃O₂ (M+H)⁺ 434.1443, found 434.1438.

N-Cyclopentyl-2-(5-methoxy-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)acetamide (32): Yield: 52%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.07 (d, 1H, J = 8.8 Hz), 7.00 (d, 1H, J = 1.2 Hz), 6.83 (dd, 1H, J₁ = 8.8 Hz, J₂ = 1.6 Hz), 5.09 (d, 1H, J = 7.6 Hz), 4.62 (s, 2H), 4.20-4.11 (m, 1H), 3.86 (s, 3H), 3.77 (t, 4H, J = 4.4 Hz), 2.89 (t, 2H, J = 7.6 Hz), 2.57-2.51 (m, 6H), 2.28 (s, 3H), 1.87-1.80 (m, 3H), 1.49-1.37 (m, 3H), 1.11-1.05 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) 168.22, 154.65, 133.33, 131.54, 128.79, 111.19, 110.85, 109.51, 101.12, 67.07 (2C), 59.71, 56.11, 53.94 (2C), 51.16,

47.38, 32.93 (2C), 23.47 (2C), 22.09, 10.25; ESI-MS m/z 400.3 (M+H)⁺; HRMS (ESI) calcd for C₂₃H₃₄N₃O₃ (M+H)⁺ 400.2600, found 400.2595.

2-(5-Chloro-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)-N-cyclopentylacetamide (33): Yield: 50%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.48 (s, 1H), 7.12-7.06 (m, 2H), 5.09 (d, 1H, J = 6.8 Hz), 4.62 (s, 2H), 4.18-4.09 (m, 1H), 3.77 (s, 4H), 2.89 (t, 2H, J = 7.6 Hz), 2.59-2.52 (m, 6H), 2.29 (s, 3H), 1.86-1.81 (m, 2H), 1.47-1.40 (m, 4H), 1.11-1.06 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) 167.51, 134.71, 134.25, 129.27, 125.89, 122.02, 117.98, 110.62, 109.74, 66.77 (2C), 59.45, 53.70 (2C), 47.22, 32.89 (2C), 23.44 (2C), 21.75, 10.23; ESI-MS m/z 404.3 (M+H)⁺; HRMS (ESI) calcd for C₂₂H₃₁ClN₃O₂ (M+H)⁺ 404.2105, found 404.2099.

N-Cyclopentyl-2-(5-fluoro-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)acetamide (34): Yield: 52%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.16 (dd, 1H, J₁ = 9.2 Hz, J₂ = 2.0 Hz), 7.06 (dd, 1H, J₁ = 8.4 Hz, J₂ = 4.0 Hz), 6.91-6.86 (m, 1H), 5.08 (d, 1H, J = 7.2 Hz), 4.61 (s, 2H), 4.18-4.09 (m, 1H), 3.74 (t, 4H, J = 4.4 Hz), 2.86 (t, 2H, J = 8.0 Hz), 2.55-2.48 (m, 6H), 2.28 (s, 3H), 1.84-1.80 (m, 2H), 1.50-1.34 (m, 4H), 1.10-1.06 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) 167.70, 158.24 (d, 1C, J = 233.9 Hz), 134.41, 132.80, 128.64 (d, 1C, J = 9.4 Hz), 111.13 (d, 1C, J = 3.8 Hz), 109.83 (d, 1C, J = 26.6 Hz), 109.33 (d, 1C, J = 9.3 Hz), 103.62 (d, 1C, J = 23.2 Hz), 66.92 (2C), 59.50, 53.78 (2C), 51.14, 47.27, 32.86 (2C), 23.38 (2C), 21.96, 10.25; ESI-MS m/z 388.2 (M+H)⁺; HRMS (ESI) calcd for C₂₂H₃₁FN₃O₂ (M+H)⁺ 388.2400, found 388.2395.

2-(5-Bromo-2-methyl-3-(2-morpholinoethyl)-1H-indol-1-yl)-N-cyclopentylacetamide (35): Yield: 54%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.63 (d, 1H, J = 1.6 Hz), 7.22 (dd, 1H, J₁ = 8.4 Hz, J₂ = 1.6 Hz), 7.02 (d, 1H, J = 8.4 Hz), 5.09 (d, 1H, J = 7.6 Hz), 4.60 (s, 2H), 4.17-4.09 (m, 1H), 3.73 (t, 4H, J = 4.8 Hz), 2.84 (t, 2H, J = 7.6 Hz), 2.54-2.47 (m, 6H), 2.28 (s, 3H), 1.85-1.81 (m, 2H), 1.47-1.38 (m, 4H), 1.10-1.06 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) 167.48, 134.98, 133.97, 129.95, 124.54, 121.07, 113.39, 110.85, 110.12, 66.95 (2C), 59.55, 53.81 (2C), 47.15, 32.84 (2C), 23.43 (2C), 21.91, 10.17; ESI-MS m/z 448.4 (M+H)⁺; HRMS (ESI) calcd for C₂₂H₃₁BrN₃O₂ (M+H)⁺ 448.1600, found 448.1594.

N-Cyclohexyl-2-(5-methoxy-2-methyl-1-(2-morpholinoethyl)-1H-indol-3-yl)acetamide (36): Yield: 47%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.18 (d, 1H, J = 8.8 Hz), 6.88 (s, 1H), 6.83 (d, 1H, J = 8.8 Hz), 5.52 (d, 1H, J = 8.4 Hz), 4.18 (t, 2H, J = 7.2 Hz), 3.81 (s, 3H), 3.76-3.73 (m, 1H), 3.69 (t, 4H, J = 4.4 Hz), 3.61 (s, 2H), 2.62 (t, 2H, J = 7.2 Hz), 2.48 (s, 4H), 2.35 (s, 3H), 1.77-1.74 (m, 2H), 1.55-1.52 (m, 3H),

1.33-1.23 (m, 2H), 1.05-0.96 (m, 1H), 0.93-0.84 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) 170.46, 154.44, 135.16, 131.26, 120.03, 111.41, 109.81, 104.36, 99.97, 66.98 (2C), 58.14, 55.99, 54.22 (2C), 48.00, 41.46, 33.04 (2C), 32.88, 25.47, 24.78 (2C), 10.46; ESI-MS m/z 414.3 ($\text{M}+\text{H}$) $^+$; HRMS (ESI) calcd for $\text{C}_{24}\text{H}_{36}\text{N}_3\text{O}_3$ ($\text{M}+\text{H}$) $^+$ 414.2757, found 414.2751.

2-(5-Chloro-2-methyl-1-(2-morpholinoethyl)-1H-indol-3-yl)-N-cyclohexylacetamide (37); Yield: 76%, white solid, ^1H NMR (CDCl_3 , 400 MHz) 7.40 (s, 1H), 7.18 (d, 1H, $J = 8.4$ Hz), 7.09 (d, 1H, $J = 8.4$ Hz), 5.47 (d, 1H, $J = 7.6$ Hz), 4.16 (t, 2H, $J = 7.2$ Hz), 3.74-3.72 (m, 1H), 3.66 (s, 4H), 3.56 (s, 2H), 2.60 (t, 2H, $J = 6.8$ Hz), 2.46 (s, 4H), 2.36 (s, 3H), 1.77 (d, 2H, $J = 11.2$ Hz), 1.56-1.53 (m, 3H), 1.32-1.23 (m, 2H), 1.02-1.00 (m, 1H), 0.95-0.86 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) 169.97, 136.18, 134.46, 128.72, 125.46, 121.48, 117.52, 110.04, 104.55, 66.93 (2C), 57.97, 54.17 (2C), 48.08, 41.55, 32.98 (2C), 32.66, 25.44, 24.74 (2C), 10.50; ESI-MS m/z 418.2 ($\text{M}+\text{H}$) $^+$; HRMS (ESI) calcd for $\text{C}_{23}\text{H}_{33}\text{ClN}_3\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 418.2261, found 418.2256.

N-Cyclohexyl-2-(5-fluoro-2-methyl-1-(2-morpholinoethyl)-1H-indol-3-yl)acetamide (38); Yield: 81%, white solid, ^1H NMR (CDCl_3 , 400 MHz) 7.16 (dd, 1H, $J_1 = 8.8$ Hz, $J_2 = 4.0$ Hz), 7.06 (dd, 1H, $J_1 = 9.2$ Hz, $J_2 = 1.6$ Hz), 6.88-6.83 (m, 1H), 5.55 (d, 1H, $J = 8.4$ Hz), 4.16 (t, 2H, $J = 6.4$ Hz), 3.70-3.65 (m, 5H), 3.53 (s, 2H), 2.59 (t, 2H, $J = 6.8$ Hz), 2.45 (s, 4H), 2.34 (s, 3H), 1.74 (d, 2H, $J = 10.4$ Hz), 1.54-1.50 (m, 3H), 1.29-1.23 (m, 2H), 1.02-0.85 (m, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) 170.01, 157.96 (d, 1C, $J = 233.1$ Hz), 136.32, 132.50, 127.94 (d, 1C, $J = 10.2$ Hz), 109.54 (d, 1C, $J = 9.6$ Hz), 109.24 (d, 1C, $J = 26.4$ Hz), 104.80 (d, 1C, $J = 3.5$ Hz), 102.96 (d, 1C, $J = 23.6$ Hz), 66.78 (2C), 57.86, 54.04 (2C), 47.98, 41.40, 32.88 (2C), 32.65, 25.36, 24.66 (2C), 10.43; ESI-MS m/z 402.6 ($\text{M}+\text{H}$) $^+$; HRMS (ESI) calcd for $\text{C}_{23}\text{H}_{33}\text{FN}_3\text{O}_2$ ($\text{M}+\text{H}$) $^+$ 402.2557, found 402.2551.

2-(5-Methoxy-2-methyl-1-(2-morpholinoethyl)-1H-indol-3-yl)-1-(piperidin-1-yl)ethanone (39); Yield: 42%, colorless oil, ^1H NMR (CDCl_3 , 400 MHz) 7.13 (d, 1H, $J = 8.8$ Hz), 7.01 (d, 1H, $J = 2.0$ Hz), 6.78 (dd, 1H, $J_1 = 8.4$ Hz, $J_2 = 2.0$ Hz), 4.14 (t, 2H, $J = 6.8$ Hz), 3.83 (s, 3H), 3.71 (s, 2H), 3.68 (t, 4H, $J = 4.0$ Hz), 3.54 (t, 2H, $J = 5.2$ Hz), 3.36 (t, 2H, $J = 5.2$ Hz), 2.58 (t, 2H, $J = 7.6$ Hz), 2.47 (t, 4H, $J = 4.4$ Hz), 2.38 (s, 3H), 1.52-1.46 (m, 4H), 1.24-1.22 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) 169.94, 154.06, 134.01, 131.10, 128.04, 110.53, 109.35, 104.74, 100.59, 66.97 (2C), 58.12, 56.03, 54.17 (2C), 47.14, 43.08, 41.22 31.24, 26.16, 25.75, 24.53, 10.64; ESI-MS m/z 400.3 ($\text{M}+\text{H}$) $^+$; HRMS (ESI) calcd for $\text{C}_{23}\text{H}_{34}\text{N}_3\text{O}_3$ ($\text{M}+\text{H}$) $^+$ 400.2600, found 400.2595.

2-(5-Chloro-2-methyl-1-(2-morpholinoethyl)-1H-indol-3-yl)-1-(piperidin-1-yl)ethanone (40): Yield: 37%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.46 (s, 1H), 7.14 (d, 1H, J = 8.0 Hz), 7.04 (d, 1H, J = 8.0 Hz), 4.13 (s, 2H), 3.67 (s, 6H), 3.54 (s, 2H), 3.38 (s, 2H), 2.57 (s, 2H), 2.45 (s, 4H), 1.54 (s, 2H), 1.48 (s, 2H), 1.29 (s, 2H); ¹³C NMR (CDCl₃, 100 MHz) 169.36, 135.19, 134.23, 128.79, 124.95, 120.90, 117.58, 109.70, 104.90, 66.90 (2C), 57.94, 54.11 (2C), 47.06, 43.06, 41.29, 30.48, 26.02, 25.65, 24.48, 10.65; ESI-MS m/z 404.1 (M+H)⁺; HRMS (ESI) calcd for C₂₂H₃₁ClN₃O₂ (M+H)⁺ 404.2105, found 404.2099

2-(5-Fluoro-2-methyl-1-(2-morpholinoethyl)-1H-indol-3-yl)-1-(piperidin-1-yl)ethanone (41): Yield: 91%, yellow oil, ¹H NMR (CDCl₃, 400 MHz) 7.17-7.11(m, 2H), 6.85-6.80 (m, 1H), 4.13 (t, 2H, J = 7.2 Hz), 3.67-3.65 (m, 6H), 3.52 (t, 2H, J = 5.2 Hz), 3.36 (t, 2H, J = 5.2 Hz), 2.57 (t, 2H, J = 6.8 Hz), 2.45 (s, 4H), 2.37 (s, 3H), 1.52-1.48 (m, 4H), 1.25 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) 169.41, 157.78 (d, 1C, J = 231.9 Hz), 135.28, 132.32, 127.67 (d, 1C, J = 9.7 Hz), 109.16 (d, 1C, J = 9.4 Hz), 108.69 (d, 1C, J = 26.3 Hz), 105.13 (d, 1C, J = 4.4 Hz), 103.21 (d, 1C, J = 23.8 Hz), 66.81 (2C), 57.87, 54.03 (2C), 47.00, 42.99, 41.20, 30.67, 26.11, 25.62, 24.41, 10.61; ESI-MS m/z 388.2 (M+H)⁺; HRMS (ESI) calcd for C₂₂H₃₁FN₃O₂ (M+H)⁺ 388.2400, found 388.2395.

N-Cyclopropyl-2-(5-methoxy-2-methyl-1-(2-morpholinoethyl)-1H-indol-3-yl)acetamide (42): Yield: 49%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.13 (d, 1H, J = 8.8 Hz), 6.82 (s, 1H), 6.76 (d, 1H, J = 8.4 Hz), 5.85 (s, 1H), 4.11 (t, 2H, J = 6.4 Hz), 3.76 (s, 3H), 3.63 (s, 4H), 3.55 (s, 2H), 2.58-2.54 (m, 3H), 2.42 (s, 4H), 2.30 (s, 3H), 0.62 (d, 2H, J = 6.0 Hz), 0.27 (s, 2H); ¹³C NMR (CDCl₃, 100 MHz) 172.84, 154.20, 135.00, 131.01, 127.76, 110.99, 109.60, 103.97, 99.76, 66.73 (2C), 57.87, 55.74, 53.96 (2C), 41.20, 32.43, 22.39, 10.46, 6.42 (2C); ESI-MS m/z 372.2 (M+H)⁺; HRMS (ESI) calcd for C₂₁H₂₉N₃NaO₃ (M+Na)⁺ 394.2107, found 394.2101.

2-(5-Chloro-2-methyl-1-(2-morpholinoethyl)-1H-indol-3-yl)-N-cyclopropylacetamide (43): Yield: 74%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.34 (s, 1H), 7.12 (d, 1H, J = 8.0 Hz), 7.01 (d, 1H, J = 7.6 Hz), 5.98 (s, 1H), 4.09 (s, 2H), 3.62 (s, 4H), 3.48 (s, 2H), 2.55 (s, 3H), 2.41 (s, 4H), 2.31 (s, 3H), 0.61 (d, 2H, J = 5.6 Hz), 0.30 (s, 2H); ¹³C NMR (CDCl₃, 100 MHz) 172.49, 136.08, 134.25, 128.56, 125.14, 121.18, 117.22, 109.88, 104.31, 66.69 (2C), 57.71, 53.93 (2C), 41.25, 32.17, 22.50, 10.65, 6.39 (2C); ESI-MS m/z 376.2 (M+H)⁺; HRMS (ESI) calcd for C₂₀H₂₇ClN₃O₂ (M+H)⁺ 379.1792, found 376.1786

N-Cyclopropyl-2-(5-fluoro-2-methyl-1-(2-morpholinoethyl)-1H-indol-3-yl)acetamide (44): Yield: 83%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.17 (dd, 1H, J₁ = 8.8 Hz, J₂ = 4.0 Hz), 7.04 (dd, 1H, J₁ = 9.2 Hz, J₂ = 2.4 Hz), 6.89-6.84 (m, 1H), 5.80 (s, 1H), 4.16 (t, 2H, J = 7.2 Hz), 3.66 (t, 4H, J = 4.4 Hz), 3.53 (s, 2H), 2.60 (t, 3H, J = 7.2 Hz), 2.46 (s, 4H), 2.34 (s, 3H), 0.67-0.62 (m, 2H), 0.32-0.28 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) 172.67, 158.02 (d, 1C, J = 234.4 Hz), 136.41, 132.52, 127.90 (d, 1C, J = 10.3 Hz), 109.60 (d, 1C, J = 9.4 Hz), 109.35 (d, 1C, J = 26.5 Hz), 104.64 (d, 1C, J = 4.3 Hz), 102.92 (d, 1C, J = 23.6 Hz), 66.82 (2C), 57.88, 54.08 (2C), 41.42, 32.45, 22.57, 10.48, 6.54 (2C); ESI-MS m/z 360.2 (M+H)⁺; HRMS (ESI) calcd for C₂₀H₂₇FN₃O₂ (M+H)⁺ 360.2087, found 360.2082.

N-(Cyclopropylmethyl)-2-(5-methoxy-2-methyl-1-(2-morpholinoethyl)-1H-indol-3-yl)acetamide (45): Yield: 73%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.14 (d, 1H, J = 8.8 Hz), 6.87 (s, 1H), 6.77 (d, 1H, J = 8.4 Hz), 5.83 (s, 1H), 4.13 (t, 2H, J = 6.4 Hz), 3.76 (s, 3H), 3.63 (s, 4H), 3.58 (s, 2H), 0.77 (brs, 1H), 0.31 (d, 2H, J = 7.2 Hz), 0.01 (d, 2H, J = 3.6 Hz); ¹³C NMR (CDCl₃, 100 MHz) 171.19, 154.18, 135.00, 131.06, 127.85, 111.03, 109.57, 104.09, 99.82, 66.72 (2C), 57.89, 55.69, 53.96 (2C), 43.65, 41.19, 32.44, 10.61, 10.21, 2.97 (2C); ESI-MS m/z 386.3 (M+H)⁺; HRMS (ESI) calcd for C₂₂H₃₂N₃O₃ (M+H)⁺ 386.2444, found 386.2438.

2-(5-Chloro-2-methyl-1-(2-morpholinoethyl)-1H-indol-3-yl)-N-(cyclopropylmethyl)acetamide (46): Yield: 43%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.42 (s, 1H), 7.19 (d, 1H, J = 8.0 Hz), 7.09 (d, 1H, J = 7.6 Hz), 5.74 (s, 1H), 4.18 (s, 2H), 3.67 (s, 4H), 3.59 (s, 2H), 3.03 (s, 2H), 2.61 (s, 2H), 2.47 (s, 4H), 2.38 (s, 3H), 0.81 (s, 1H), 0.37 (d, 2H, J = 6.8 Hz), 0.05 (s, 2H); ¹³C NMR (CDCl₃, 100 MHz) 170.92, 136.21, 134.49, 128.73, 125.47, 121.51, 117.58, 110.04, 104.53, 66.89 (2C), 57.94, 54.14 (2C), 44.08, 41.49, 32.50, 10.77, 10.48, 3.21 (2C); ESI-MS m/z 390.3 (M+H)⁺; HRMS (ESI) calcd for C₂₁H₂₉ClN₃O₂ (M+H)⁺ 390.1948, found 390.1943.

N-(Cyclopropylmethyl)-2-(5-fluoro-2-methyl-1-(2-morpholinoethyl)-1H-indol-3-yl)acetamide (47): Yield: 82%, yellow oil, ¹H NMR (CDCl₃, 400 MHz) 7.17 (dd, 1H, J₁ = 9.2 Hz, J₂ = 4.4 Hz), 7.08 (dd, 1H, J₁ = 9.2 Hz, J₂ = 2.0 Hz), 6.88-6.83 (m, 1H), 5.83 (m, 1H), 4.16 (t, 2H, J = 7.2 Hz), 3.65 (t, 4H, J = 4.4 Hz), 3.56 (s, 2H), 3.00 (t, 2H, J = 6.4 Hz), 2.60 (t, 2H, J = 7.2 Hz), 2.46 (s, 4H), 2.36 (s, 3H), 0.83-0.74 (m, 1H), 0.35-0.32 (m, 2H), 0.05-0.01 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) 170.99, 157.95 (d, 1C, J = 233.1 Hz), 136.36, 132.52, 127.94 (d, 1C, J = 9.7 Hz), 109.54 (d, 1C, J = 9.6 Hz), 109.24 (d, 1C, J = 26.6 Hz), 104.74 (d, 1C, J = 4.3 Hz), 103.02 (d, 1C, J = 24.2 Hz),

66.77 (2C), 57.85, 54.03 (2C), 43.94, 41.37, 32.47, 10.67, 10.48, 3.10 (2C); ESI-MS m/z 374.2 (M+H)⁺; HRMS (ESI) calcd for C₂₁H₂₉FN₃O₂ (M+H)⁺ 374.2244, found 374.2238.

2-(5-Methoxy-2-methyl-1-(2-morpholinoethyl)-1H-indol-3-yl)-1-(pyrrolidin-1-yl)ethanone (48): Yield: 44%, yellow oil, ¹H NMR (CDCl₃, 400 MHz) 7.14 (d, 1H, J = 8.8 Hz), 7.06 (d, 1H, J = 2.4 Hz), 6.79 (dd, 1H, J₁ = 8.8 Hz, J₂ = 2.0 Hz), 4.15 (t, 2H, J = 7.2 Hz), 3.84 (s, 3H), 3.69 (t, 4H, J = 6.4 Hz), 3.67 (s, 2H), 3.47 (t, 2H, J = 6.8 Hz), 3.40 (t, 2H, J = 6.4 Hz), 2.60 (t, 2H, J = 7.2 Hz), 2.48 (t, 4H, J = 4.4 Hz), 2.40 (s, 3H), 1.91-1.85 (m, 2H), 1.82-1.76 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) 170.12, 154.06, 134.49, 131.11, 128.35, 110.53, 109.32, 104.27, 100.90, 66.99 (2C), 58.09, 56.06, 54.19 (2C), 46.77, 46.06, 41.28, 32.27, 26.38, 24.33, 10.78; ESI-MS m/z 386.2 (M+H)⁺; HRMS (ESI) calcd for C₂₂H₃₂N₃O₃ (M+H)⁺ 386.2444, found 386.2438.

2-(5-Chloro-2-methyl-1-(2-morpholinoethyl)-1H-indol-3-yl)-1-(pyrrolidin-1-yl)ethanone (49): Yield: 54%, yellow solid, ¹H NMR (CDCl₃, 400 MHz) 7.48 (s, 1H), 7.17 (d, 1H, J = 8.4 Hz), 7.07 (d, 1H, J = 8.0 Hz), 4.19 (brs, 2H), 3.67 (s, 4H), 3.71 (s, 4H), 3.64 (s, 2H), 3.49-3.44 (m, 4H), 2.63 (brs, 2H), 2.50 (brs, 4H), 2.42 (s, 3H), 1.97-1.91 (m, 2H), 1.86-1.80 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) 169.31, 135.44, 134.08, 128.91, 124.59, 120.57, 117.58, 109.57, 104.34, 66.67 (2C), 57.65, 53.88 (2C), 46.56, 45.79, 41.12, 31.36, 26.10, 24.09, 10.52; ESI-MS m/z 390.3 (M+H)⁺; HRMS (ESI) calcd for C₂₁H₂₉ClN₃O₂ (M+H)⁺ 390.1948, found 390.1943.

2-(5-Fluoro-2-methyl-1-(2-morpholinoethyl)-1H-indol-3-yl)-1-(pyrrolidin-1-yl)ethanone (50): Yield: 84%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.17 (dd, 1H, J₁ = 10.0 Hz, J₂ = 2.0 Hz), 7.12 (dd, 1H, J₁ = 8.8 Hz, J₂ = 4.4 Hz), 6.84-6.79 (m, 1H), 4.12 (t, 2H, J = 6.8 Hz), 3.65 (t, 4H, J = 4.0 Hz), 3.60 (s, 2H), 3.45-3.38 (m, 4H), 2.57 (t, 2H, J = 6.8 Hz), 2.44 (s, 4H), 2.38 (s, 3H), 1.91-1.84 (m, 2H), 1.80-1.74 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) 169.55, 157.73 (d, 1C, J = 232.2 Hz), 135.68, 132.28, 128.20 (d, 1C, J = 9.5 Hz), 109.08 (d, 1C, J = 10.0 Hz), 108.58 (d, 1C, J = 25.1 Hz), 104.69 (d, 1C, J = 4.3 Hz), 103.31 (d, 1C, J = 23.7 Hz), 66.76 (2C), 57.78, 53.98 (2C), 46.65, 45.87, 41.20, 31.64, 26.19, 24.17, 10.68; ESI-MS m/z 374.2 (M+H)⁺; HRMS (ESI) calcd for C₂₁H₂₉FN₃O₂ (M+H)⁺ 374.2244, found 374.2238.

N-Cyclopentyl-2-(5-methoxy-2-methyl-1-(2-morpholinoethyl)-1H-indol-3-yl)acetamide (51): Yield: 62%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.17 (d, 1H, J = 8.8 Hz), 6.86 (s, 1H), 6.80 (d, 1H, J = 8.4 Hz), 5.59 (d, 1H, J = 7.2 Hz), 4.20-4.11 (m, 3H), 3.79 (s, 3H), 3.66 (t, 4H, J = 4.4 Hz), 3.58 (s, 2H), 2.59 (t, 2H, J = 7.2 Hz), 2.54 (s,

4H), 2.33 (s, 3H), 1.87-1.83 (m, 2H), 1.44 (d, 4H, J = 5.2 Hz), 1.14-1.09 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) 170.93, 154.34, 135.06, 131.17, 127.90, 111.28, 109.74, 104.24, 99.83, 66.88 (2C), 58.05, 55.87, 54.12 (2C), 51.00, 41.38, 32.89 (2C), 32.73, 23.50 (2C), 10.37; ESI-MS m/z 400.3 (M+H)⁺; HRMS (ESI) calcd for C₂₃H₃₄N₃O₃ (M+H)⁺ 400.2600, found 400.2595.

2-(5-Chloro-2-methyl-1-(2-morpholinoethyl)-1H-indol-3-yl)-N-cyclopentylacetamide (52): Yield: 70%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.38 (s, 1H), 7.16 (d, 1H, J = 8.4 Hz), 7.05 (d, 1H, J = 8.4 Hz), 5.16 (d, 1H, J = 7.2 Hz), 4.14 (t, 3H, J = 6.8 Hz), 3.64 (s, 4H), 3.53 (s, 2H), 2.58 (t, 2H, J = 6.4 Hz), 2.34 (s, 3H), 1.87-1.82 (m, 2H), 1.46 (s, 4H), 1.17-1.13 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) 170.48, 136.10, 134.39, 128.64, 125.31, 121.34, 117.39, 109.99, 104.50, 66.81 (2C), 57.87, 54.07 (2C), 51.11, 41.41, 32.85 (2C), 32.50, 23.49 (2C), 10.42; ESI-MS m/z 404.1 (M+H)⁺; HRMS (ESI) calcd for C₂₂H₃₁ClN₃O₂ (M+H)⁺ 404.2105, found 404.2099.

N-Cyclopentyl-2-(5-fluoro-2-methyl-1-(2-morpholinoethyl)-1H-indol-3-yl)acetamide (53): Yield: 76%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.16 (dd, 1H, J₁ = 8.8 Hz, J₂ = 4.4 Hz), 7.06 (dd, 1H, J₁ = 9.2 Hz, J₂ = 2.0 Hz), 6.88-6.83 (m, 1H), 5.64 (d, 1H, J = 7.2 Hz), 4.17-4.08 (m, 3H), 3.65-3.64 (m, 4H), 3.53 (s, 2H), 2.59 (t, 2H, J = 6.8 Hz), 2.45 (s, 4H), 2.34 (s, 3H), 1.86-1.82 (m, 2H), 1.45 (m, 4H), 1.16-1.11 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) 170.95, 157.95 (d, 1C, J = 233.2 Hz), 136.31, 132.50, 127.91 (d, 1C, J = 9.4 Hz), 109.55 (d, 1C, J = 9.5 Hz), 109.23 (d, 1C, J = 25.2 Hz), 104.83 (d, 1C, J = 4.4 Hz), 102.92 (d, 1C, J = 23.7 Hz), 66.76 (2C), 57.85, 54.03 (2C), 51.06, 41.39, 32.84 (2C), 32.56, 23.47 (2C), 10.42; ESI-MS m/z 388.6 (M+H)⁺; HRMS (ESI) calcd for C₂₂H₃₁FN₃O₂ (M+H)⁺ 388.2400, found 388.2395.

N-(Benzo[d][1,3]dioxol-5-ylmethyl)-2-(5-methoxy-2-methyl-1-(2-morpholinoethyl)-1H-indol-3-yl)acetamide (54): Yield: 59%, white solid, ¹H NMR (CDCl₃, 400 MHz) 7.15 (d, 1H, J = 8.8 Hz), 6.87 (d, 1H, J = 2.0 Hz), 6.79 (dd, 1H, J₁ = 8.8 Hz, J₂ = 2.0 Hz), 6.62 (d, 1H, J = 7.6 Hz), 6.58 (s, 1H), 6.53 (d, 1H, J = 7.6 Hz), 6.05 (t, 1H, J = 5.6 Hz), 5.83 (s, 3H), 4.23 (d, 2H, J = 6.0 Hz), 4.12 (t, 2H, J = 7.2 Hz), 3.77 (s, 2H), 3.63 (t, 4H, J = 4.0 Hz), 2.56 (t, 2H, J = 7.2 Hz), 2.43 (t, 4H, J = 4.4 Hz), 2.33 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz) 171.39, 154.34, 147.71, 146.65, 135.15, 132.28, 131.09, 127.85, 120.41, 111.26, 109.71, 108.01, 107.77, 103.90, 100.90, 66.76 (2C), 57.92, 55.75, 54.00 (2C), 42.93, 41.23, 32.48, 10.32; ESI-MS m/z 466.4 (M+H)⁺; HRMS (ESI) calcd for C₂₆H₃₂N₃O₅ (M+H)⁺ 466.2342, found 466.2337.

N-(Benzo[d][1,3]dioxol-5-ylmethyl)-2-(5-chloro-2-methyl-1-(2-morpholinoethyl)-1H-indol-3-yl)acetamide (55): Yield: 79%, white solid, ^1H NMR (CDCl_3 , 400 MHz) 7.39 (s, 1H), 7.14 (d, 1H, $J = 8.0$ Hz), 7.05 (d, 1H, $J = 8.0$ Hz), 6.63 (d, 1H, $J = 8.0$ Hz), 6.57-6.53 (m, 2H), 6.12 (s, 1H), 5.85 (s, 2H), 4.21 (d, 4H, $J = 5.2$ Hz), 4.12 (s, 2H), 3.62-3.60 (m, 6H), 2.56 (s, 2H), 2.42 (s, 4H), 2.31 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) 170.96, 147.71, 146.69, 136.19, 134.33, 132.13, 128.59, 125.30, 121.35, 120.50, 117.38, 109.97, 108.08, 107.88, 104.22, 100.92, 66.70 (2C), 57.74, 53.95 (2C), 43.06, 41.28, 32.27, 10.39; ESI-MS m/z 470.2 ($\text{M}+\text{H}$) $^+$; HRMS (ESI) calcd for $\text{C}_{25}\text{H}_{29}\text{ClN}_3\text{O}_4$ ($\text{M}+\text{H}$) $^+$ 470.1847, found 470.1841.

N-(Benzo[d][1,3]dioxol-5-ylmethyl)-2-(5-fluoro-2-methyl-1-(2-morpholinoethyl)-1H-indol-3-yl)acetamide (56): Yield: 91%, white solid, NMR (CDCl_3 , 400 MHz) 7.16 (dd, 1H, $J_1 = 8.8$ Hz, $J_2 = 4.8$ Hz), 7.08 (dd, 1H, $J_1 = 9.6$ Hz, $J_2 = 2.4$ Hz), 6.88-6.83 (m, 1H), 6.62 (d, 1H, $J = 8.0$ Hz), 6.57 (s, 1H), 6.53 (d, 1H, $J = 8.0$ Hz), 6.10 (t, 1H, $J = 5.6$ Hz), 5.82 (s, 2H), 4.21 (d, 2H, $J = 6.0$ Hz), 4.13 (t, 2H, $J = 7.2$ Hz), 3.63-3.60 (m, 6H), 2.57 (t, 2H, $J = 6.8$ Hz), 2.43 (s, 4H), 2.43 (s, 4H), 2.34 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) 171.09, 157.96 (d, 1C, $J = 234.1$ Hz), 147.73, 146.71, 136.42, 132.49, 132.17, 127.89 (d, 1C, $J = 9.4$ Hz), 120.50, 109.56 (d, 1C, $J = 9.5$ Hz), 109.27 (d, 1C, $J = 25.0$ Hz), 108.06, 107.88, 104.52 (d, 1C, $J = 4.7$ Hz), 102.96 (d, 1C, $J = 23.0$ Hz), 100.92, 66.72 (2C), 57.79, 53.98 (2C), 43.06, 41.32, 32.38, 10.43; ESI-MS m/z 454.2 ($\text{M}+\text{H}$) $^+$; HRMS (ESI) calcd for $\text{C}_{25}\text{H}_{28}\text{FN}_3\text{NaO}_4$ ($\text{M}+\text{H}$) $^+$ 476.1962, found 476.1956.

3. Supplementary Figure1. EC50 values for Compounds













