

Supporting Information

DESIGN, SYNTHESIS, AND BIOLOGICAL ACTIVITY ANALYSIS OF NOVEL QUINAZOLINYL ETHER DERIVATIVES CONTAINING PIPERIDINAMIDE STRUCTURE

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***N*-(2-hydroxyphenyl)-1-(quinazolin-4-yl)piperidine-4-carboxamide (II)**: red solid, Yield: 47%, mp 256–257 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 9.80 (s, 1H), 9.29 (s, 1H), 8.63 (s, 1H), 8.00 (d, *J* = 8.4 Hz, 1H), 7.81–7.80 (m, 2H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.58–7.51 (m, 1H), 6.95–6.92 (m, 1H), 6.86 (d, *J* = 8.1 Hz, 1H), 6.78–6.74 (m, 1H), 4.34 (d, *J* = 14.3 Hz, 2H), 3.20 (t, *J* = 12.8 Hz, 2H), 2.95–2.86 (m, 1H), 1.95 (d, *J* = 12.1 Hz, 2H), 1.91–1.81 (m, 2H). ¹³C NMR (100 MHz, DMSO-*d*₆) δ: 173.6, 164.0, 153.8, 151.4, 148.0, 132.8, 128.1, 126.4, 125.7, 125.5, 124.7, 122.4, 119.1, 116.0, 115.8, 49.1, 42.3, 28.6. ESI-HRMS *m/z*: [M – H][–] calcd for C₂₀H₁₉N₄O₂: 347.1503; found: 347.1514.

***N*-[2-[(2-cyanobenzyl)oxy]phenyl]-1-(quinazolin-4-yl)piperidine-4-carboxamide (III-1)**: White solid, mp 219–220 °C, yield: 43.6%. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 9.07 (s, 1H), 8.63 (s, 1H), 7.97 (d, *J* = 8.2 Hz, 1H), 7.90 (d, *J* = 6.5 Hz, 1H), 7.86 (d, *J* = 6.2 Hz, 1H), 7.81–7.79 (m, 2H), 7.78 (s, 1H), 7.76–7.72 (m, 1H), 7.57–7.52 (m, 2H), 7.17–7.07 (m, 2H), 6.98–6.94 (m, 1H), 5.35 (s, 2H), 4.30 (d, *J* = 13.3 Hz, 2H), 3.20 (t, *J* = 11.1 Hz, 2H), 2.91–2.79 (m, 1H), 1.94 (d, *J* = 9.4 Hz, 2H), 1.91–1.79 (m, 2H). ¹³C NMR (100 MHz, DMSO) δ: 173.1, 163.9, 153.6, 151.2, 148.9, 140.1, 133.5, 133.3, 132.8, 129.5, 129.1, 127.9, 127.8, 125.7, 125.4, 124.7, 123.3, 121.2, 117.5, 115.9, 113.1, 110.9, 68.1, 48.9, 42.3, 28.4. ESI-HRMS *m/z*: [M + H]⁺ calcd for: C₂₈H₂₆O₂N₅: 464.2081; found: 464.2079.

***N*-[2-[(3-cyanobenzyl)oxy]phenyl]-1-(quinazolin-4-yl)piperidine-4-carboxamide (III-2)**: White solid, mp 268–269 °C, yield: 39.1%. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 9.30 (s, 1H), 8.63 (s, 1H), 8.02 (s, 1H), 7.98 (d, *J* = 8.2 Hz, 1H), 7.84–7.82 (m, 2H), 7.80–7.78 (m, 2H), 7.72 (d, *J* = 7.2 Hz, 1H), 7.61 (t, *J* = 7.8 Hz, 1H), 7.59–7.51 (m, 1H), 7.14–7.05 (m, 2H), 6.99–6.88 (m, 1H), 5.25 (s, 2H), 4.33 (d, *J* = 13.2 Hz, 2H), 3.21 (t, *J* = 10.6 Hz, 2H), 2.93–2.83 (m, 1H), 1.97 (d, *J* = 9.6 Hz, 2H), 1.92–1.84 (m, 2H). ¹³C NMR (100 MHz, DMSO) δ: 173.1, 164.0, 153.7, 151.3, 149.6, 139.0, 132.8, 132.1, 131.6, 130.9, 129.7, 128.0, 127.4, 125.7, 125.4, 125.2, 124.2, 120.8, 118.8, 116.0, 113.0, 111.4, 68.4, 49.1, 42.2, 28.5. ESI-HRMS *m/z*: [M + H]⁺

calcd for: C₂₈H₂₆O₂N₅: 464.2081; found: 464.2075.

***N*-[2-[(4-cyanobenzyl)oxy]phenyl]-1-(quinazolin-4-yl)piperidine-4-carboxamide**

(III-3): White solid, mp 257–258 °C, yield: 49.4%. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 9.27 (s, 1H), 8.63 (s, 1H), 7.98 (d, *J* = 8.2 Hz, 1H), 7.92 (s, 1H), 7.83–7.80 (m, 3H), 7.75 (d, *J* = 7.1 Hz, 1H), 7.69–7.61 (m, 2H), 7.57–7.53 (m, 1H), 7.12–7.10 (m, 2H), 6.96–6.92 (m, 1H), 5.29 (s, 2H), 4.31 (d, *J* = 13.3 Hz, 2H), 3.19 (t, *J* = 11.6 Hz, 2H), 2.88–2.83 (m, 1H), 1.95 (d, *J* = 9.8 Hz, 2H), 1.89–1.82 (m, 2H). ¹³C NMR (100 MHz, DMSO) δ: 173.1, 164.0, 153.7, 151.3, 149.7, 138.8, 132.8, 131.4, 129.5, 128.0, 127.4, 125.6, 125.4, 125.2, 124.5, 124.1, 123.9, 120.8, 116.0, 113.0, 68.8, 55.0, 49.0, 42.2, 28.5. ESI-HRMS *m/z*: [M – H][–] calcd for: C₂₈H₂₄O₂N₅: 462.1925; found: 462.1918.

***N*-[2-[(2-methylbenzyl)oxy]phenyl]-1-(quinazolin-4-yl)piperidine-4-carboxamide**

(III-4): White solid, mp 116–117 °C, yield: 29.3%. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 9.12 (s, 1H), 8.63 (s, 1H), 7.97 (d, *J* = 8.3 Hz, 1H), 7.83–7.78 (m, 2H), 7.74 (d, *J* = 6.2 Hz, 1H), 7.58–7.54 (m, 1H), 7.46 (d, *J* = 5.5 Hz, 1H), 7.21–7.18 (m, 3H), 7.13–7.08 (m, 2H), 6.94–6.90 (m, 1H), 5.15 (s, 2H), 4.28 (d, *J* = 13.4 Hz, 2H), 3.20 (t, *J* = 10.9 Hz, 2H), 2.88–2.78 (m, 1H), 2.34 (s, 3H), 1.89 (d, *J* = 7.9 Hz, 2H), 1.85–1.78 (m, 2H). ¹³C NMR (100 MHz, DMSO) δ: 173.1, 163.9, 153.7, 151.3, 150.0, 136.3, 134.9, 132.7, 130.1, 128.2, 128.0, 127.9, 127.4, 125.7, 125.6, 125.3, 125.1, 124.0, 120.5, 115.9, 112.9, 68.4, 48.9, 42.1, 28.4, 18.5. ESI-HRMS *m/z*: [M – H][–] calcd for: C₂₈H₂₇O₂N₄: 451.2129; found: 453.2143.

***N*-[2-[(3-methylbenzyl)oxy]phenyl]-1-(quinazolin-4-yl)piperidine-4-carboxamide**

(III-5): White solid, mp 107–108 °C, yield: 31.4%. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 9.11 (s, 1H), 8.63 (s, 1H), 7.98 (d, *J* = 8.2 Hz, 1H), 7.83–7.80 (m, 3H), 7.58–7.54 (m, 1H), 7.45 (d, *J* = 7.5 Hz, 1H), 7.32–7.28 (m, 1H), 7.06–7.04 (m, 3H), 6.94–6.90 (m, 2H), 5.15 (s, 2H), 4.31 (d, *J* = 12.9 Hz, 2H), 3.84 (s, 3H), 3.21 (t, *J* = 11.2 Hz, 2H), 2.90–2.80 (m, 1H), 1.94 (d, *J* = 9.6 Hz, 2H), 1.91–1.80 (m, 2H). ¹³C NMR (100

MHz, DMSO- D_6) δ : 173.1, 164.0, 153.7, 151.3, 149.8, 137.6, 137.1, 132.8, 128.4, 128.3, 128.0, 127.9, 127.5, 125.7, 125.4, 125.0, 124.5, 123.7, 120.5, 116.0, 113.0, 69.7, 49.0, 42.2, 39.6, 28.5, 21.0. ESI-HRMS m/z : $[M + H]^+$ calcd for: $C_{28}H_{29}O_2N_4$: 453.2285; found: 453.2280.

***N*-[2-[(4-methylbenzyl)oxy]phenyl]-1-(quinazolin-4-yl)piperidine-4-carboxamide (III-6)**: White solid, mp 179–180 °C, yield: 31.1%. 1H NMR (400 MHz, DMSO- d_6) δ : 9.15 (s, 1H), 8.63 (s, 1H), 7.98 (d, $J = 8.5$ Hz, 1H), 7.82–7.78 (m, 3H), 7.57–7.54 (m, 1H), 7.37 (d, $J = 7.9$ Hz, 2H), 7.17 (d, $J = 7.7$ Hz, 2H), 7.05–7.02 (m, 2H), 6.90–6.87 (m, 1H), 5.14 (s, 2H), 4.31 (d, $J = 14.0$ Hz, 2H), 3.22 (t, $J = 11.4$ Hz, 2H), 2.91–2.82 (m, 1H), 2.26 (s, 3H), 1.94 (d, $J = 9.9$ Hz, 2H), 1.91–1.79 (m, 2H). ^{13}C NMR (100 MHz, DMSO- D_6) δ : 173.1, 164.0, 153.8, 151.4, 149.5, 137.1, 134.1, 132.8, 129.0, 128.1, 127.6, 127.5, 125.7, 125.4, 124.9, 123.4, 120.5, 116.0, 113.1, 69.6, 49.0, 42.2, 28.5, 20.8. ESI-HRMS m/z : $[M + H]^+$ calcd for: $C_{28}H_{29}O_2N_4$: 453.2285; found: 453.2286.

***N*-[2-[(2-fluorobenzyl)oxy]phenyl]-1-(quinazolin-4-yl)piperidine-4-carboxamide (III-7)**: White solid, mp 185–186 °C, yield: 44.2%. 1H NMR (400 MHz, DMSO- d_6) δ : 9.13 (s, 1H), 8.63 (s, 1H), 7.98 (d, $J = 8.3$ Hz, 1H), 7.83–7.79 (m, 3H), 7.63–7.60 (m, 1H), 7.58–7.54 (m, 1H), 7.41–7.36 (m, 1H), 7.26–7.20 (m, 2H), 7.15–7.07 (m, 2H), 6.93 (t, $J = 7.6$ Hz, 1H), 5.23 (s, 2H), 4.29 (d, $J = 13.4$ Hz, 2H), 3.20 (t, $J = 11.2$ Hz, 2H), 2.89–2.80 (m, 1H), 1.92 (d, $J = 9.6$ Hz, 2H), 1.89–1.77 (m, 2H). ^{13}C NMR (100 MHz, DMSO) δ : 173.1, 163.9, 160.2 (d, $^1J_{C-F} = 245.7$ Hz), 153.7, 151.3, 149.5, 132.8, 130.4, 130.3, 130.2 (d, $^3J_{C-F} = 8.3$ Hz), 128.0, 127.6, 125.5 (d, $^2J_{C-F} = 28.7$ Hz), 125.0, 124.5 (d, $^4J_{C-F} = 3.3$ Hz), 123.9 (d, $^3J_{C-F} = 14.3$ Hz), 123.7, 120.9, 115.9, 115.4 (d, $^2J_{C-F} = 20.9$ Hz), 113.1, 64.2, 64.1, 49.0, 42.2, 28.4. ESI-HRMS m/z : $[M + H]^+$ calcd for: $C_{27}H_{26}O_2N_4F$: 457.2034; found: 457.2034.

***N*-[2-[(3-fluorobenzyl)oxy]phenyl]-1-(quinazolin-4-yl)piperidine-4-carboxamide (III-8)**: White solid, mp 221–222 °C, yield: 39.7%. 1H NMR (400 MHz, DMSO- d_6)

δ : 9.21 (s, 1H), 8.62 (s, 1H), 7.98 (d, $J = 8.3$ Hz, 1H), 7.81–7.79 (m, 2H), 7.74 (d, $J = 7.3$ Hz, 1H), 7.61 (s, 1H), 7.56–7.52 (m, 1H), 7.49–7.40 (m, 1H), 7.39 (t, $J = 7.5$ Hz, 1H), 7.35 (d, $J = 7.7$ Hz, 1H), 7.10–7.05 (m, 2H), 6.96–6.86 (m, 1H), 5.20 (s, 2H), 4.33 (d, $J = 13.3$ Hz, 2H), 3.23 (t, $J = 11.2$ Hz, 2H), 2.94–2.79 (m, 1H), 1.97 (d, $J = 9.3$ Hz, 2H), 1.92–1.80 (m, 2H). ^{13}C NMR (100 MHz, DMSO) δ : 172.9, 164.0, 161.6 (d, $^1J_{\text{C-F}} = 249.4$ Hz), 153.6, 151.1, 140.3, 136.4 (d, $^3J_{\text{C-F}} = 7.3$ Hz), 132.8, 132.2 (d, $^3J_{\text{C-F}} = 8.1$ Hz), 131.1, 127.8, 127.7, 125.7, 125.4, 125.1, 124.9, 124.8 (d, $^4J_{\text{C-F}} = 3.3$ Hz), 123.0, 122.5 (d, $^2J_{\text{C-F}} = 20.9$ Hz), 115.9, 115.4 (d, $^2J_{\text{C-F}} = 24.9$ Hz), 49.0, 41.9, 28.3. ESI-HRMS m/z : $[\text{M} - \text{H}]^-$ calcd for: $\text{C}_{27}\text{H}_{24}\text{O}_2\text{N}_4\text{F}$: 455.1878; found: 455.1868.

***N*-[2-[(4-fluorobenzyl)oxy]phenyl]-1-(quinazolin-4-yl)piperidine-4-carboxamide (III-9)**: White solid, mp 238–239 °C, yield: 23.7%. ^1H NMR (400 MHz, DMSO- d_6) δ : 9.19 (s, 1H), 8.63 (s, 1H), 7.98 (d, $J = 8.5$ Hz, 1H), 7.82–7.80 (m, 2H), 7.78 (d, $J = 7.2$ Hz, 1H), 7.56–7.53 (m, 3H), 7.21 (t, $J = 8.8$ Hz, 2H), 7.08–7.04 (m, 2H), 6.92–6.88 (m, 1H), 5.17 (s, 2H), 4.31 (d, $J = 13.0$ Hz, 2H), 3.21 (t, $J = 11.2$ Hz, 2H), 2.91–2.83 (m, 1H), 1.94 (d, $J = 10.0$ Hz, 2H), 1.89–1.83 (m, 2H). ^{13}C NMR (100 MHz, DMSO) δ : 173.0, 163.9, 161.7 (d, $^1J_{\text{C-F}} = 243.6$ Hz), 153.7, 151.3, 149.4, 133.3 (d, $^4J_{\text{C-F}} = 2.9$ Hz), 132.7, 129.7 (d, $^3J_{\text{C-F}} = 8.1$ Hz), 128.0, 127.5, 125.6, 125.3, 124.8, 123.5, 120.6, 115.2 (d, $^2J_{\text{C-F}} = 21.3$ Hz), 115.1, 113.0, 69.0, 48.9, 42.2, 28.4. ESI-HRMS m/z : $[\text{M} + \text{H}]^+$ calcd for: $\text{C}_{27}\text{H}_{26}\text{O}_2\text{N}_4\text{F}$: 457.2034; found: 457.2026.

***N*-[2-[(2-chlorobenzyl)oxy]phenyl]-1-(quinazolin-4-yl)piperidine-4-carboxamide (III-10)**: White solid, mp 220–221 °C, yield: 35.2%. ^1H NMR (400 MHz, DMSO- d_6) δ : 9.19 (s, 1H), 8.63 (s, 1H), 7.98 (d, $J = 8.3$ Hz, 1H), 7.81–7.79 (m, 3H), 7.67–7.64 (m, 1H), 7.58–7.53 (m, 1H), 7.51–7.49 (m, 1H), 7.38–7.35 (m, 2H), 7.09 (d, $J = 4.0$ Hz, 2H), 6.96–6.92 (m, 1H), 5.25 (s, 2H), 4.30 (d, $J = 13.4$ Hz, 2H), 3.21 (t, $J = 11.2$ Hz, 2H), 2.91–2.81 (m, 1H), 1.94 (d, $J = 9.6$ Hz, 2H), 1.90–1.81 (m, 2H). ^{13}C NMR (100 MHz, DMSO) δ : 173.1, 163.9, 153.7, 151.3, 149.4, 134.4, 132.7, 132.1, 129.7, 129.4, 128.0, 127.6, 127.3, 125.7, 125.4, 125.0, 123.7, 120.9, 116.0, 113.1, 67.4, 49.0, 42.2, 28.4. ESI-HRMS m/z : $[\text{M} + \text{H}]^+$ calcd for: $\text{C}_{27}\text{H}_{26}\text{O}_2\text{N}_4\text{Cl}$: 473.1739; found:

473.1733.

***N*-[2-[(3-chlorobenzyl)oxy]phenyl]-1-(quinazolin-4-yl)piperidine-4-carboxamide (III-11)**: White solid, mp 222–223 °C, yield: 31.2%. ¹H NMR (400 MHz, DMSO-*d*₆) δ : 9.27 (s, 1H), 8.63 (s, 1H), 7.98 (d, *J* = 8.3 Hz, 1H), 7.82–7.81 (m, 2H), 7.73 (d, *J* = 7.2 Hz, 1H), 7.62 (s, 1H), 7.57–7.53 (m, 1H), 7.46–7.42 (m, 1H), 7.40 (d, *J* = 7.5 Hz, 1H), 7.37 (t, *J* = 1.9 Hz, 1H), 7.08–7.06 (m, 2H), 6.94–6.90 (m, 1H), 5.20 (s, 2H), 4.33 (d, *J* = 13.4 Hz, 2H), 3.22 (t, *J* = 11.2 Hz, 2H), 2.93–2.82 (m, 1H), 1.97 (d, *J* = 9.7 Hz, 2H), 1.93–1.85 (m, 2H). ¹³C NMR (10 MHz, DMSO) δ : 173.1, 164.0, 153.7, 151.3, 149.7, 139.8, 133.2, 132.7, 130.3, 128.0, 127.7, 127.4, 127.1, 125.9, 125.6, 125.4, 125.1, 124.0, 120.7, 116.0, 112.9, 68.7, 49.0, 42.0, 28.5. ESI-HRMS *m/z*: [M + H]⁺ calcd for: C₂₇H₂₆O₂N₄Cl: 473.1739; found: 473.1737.

***N*-[2-[(4-chlorobenzyl)oxy]phenyl]-1-(quinazolin-4-yl)piperidine-4-carboxamide (III-12)**: White solid, mp 232–233 °C, yield: 31.4%. ¹H NMR (400 MHz, DMSO-*d*₆) δ : 9.21 (s, 1H), 8.63 (s, 1H), 7.99 (d, *J* = 8.3 Hz, 1H), 7.82–7.78 (m, 3H), 7.57–7.52 (m, 3H), 7.46 (s, 1H), 7.44 (s, 1H), 7.06 (d, *J* = 3.6 Hz, 2H), 6.93–6.88 (m, 1H), 5.20 (s, 2H), 4.32 (d, *J* = 13.5 Hz, 2H), 3.22 (t, *J* = 12.2 Hz, 2H), 2.93–2.83 (m, 1H), 1.95 (d, *J* = 9.9 Hz, 2H), 1.90–1.81 (m, 2H). ¹³C NMR (100 MHz, DMSO) δ : 173.1, 164.0, 153.7, 151.3, 149.3, 136.2, 132.7, 132.4, 129.3, 128.4, 128.0, 127.5, 125.7, 125.4, 124.9, 123.6, 120.6, 116.0, 113.0, 68.8, 49.0, 42.2, 28.5. ESI-HRMS *m/z*: [M – H][–] calcd for: C₂₇H₂₄O₂N₄Cl: 471.1582; found: 471.1599.

1-(quinazolin-4-yl)-*N*-[2-[[2-(trifluoromethyl)benzyl]oxy]phenyl]piperidine-4-carboxamide (III-13): White solid, mp 218–219 °C, yield: 34.4%. ¹H NMR (400 MHz, DMSO-*d*₆) δ : 9.14 (s, 1H), 8.62 (s, 1H), 7.97 (d, *J* = 8.3 Hz, 1H), 7.84 (d, *J* = 7.8 Hz, 1H), 7.82–7.80 (m, 3H), 7.79–7.77 (m, 1H), 7.71 (t, *J* = 7.6 Hz, 1H), 7.57–7.53 (m, 2H), 7.11–7.06 (m, 1H), 7.04–7.02 (m, 1H), 6.97–6.93 (m, 1H), 5.32 (s, 2H), 4.30 (d, *J* = 13.3 Hz, 2H), 3.20 (t, *J* = 11.1 Hz, 2H), 2.91–2.76 (m, 1H), 1.93 (d, *J* = 9.3 Hz, 2H), 1.87–1.77 (m, 2H). ¹³C NMR (100 MHz, DMSO) δ : 173.0, 163.9, 153.6,

151.3, 149.4, 135.1, 132.8, 132.6, 129.6, 128.5, 128.0, 127.5, 126.3 (d, $^2J_{\text{C-F}} = 31.2$ Hz), 126.0 (d, $^3J_{\text{C-F}} = 5.4$ Hz), 125.4 (d, $^2J_{\text{C-F}} = 28.3$ Hz), 125.3, 125.0, 124.3 (d, $^1J_{\text{C-F}} = 274.3$ Hz), 123.8, 121.0, 115.9, 112.8, 66.5, 48.9, 42.2, 28.3. ESI-HRMS m/z : $[\text{M} + \text{H}]^+$ calcd for: $\text{C}_{28}\text{H}_{26}\text{O}_2\text{N}_4\text{F}_3$: 507.2002; found: 507.1998.

1-(quinazolin-4-yl)-N-[2-[[2-(trifluoromethoxy)benzyl]oxy]phenyl]piperidine-4-carboxamide (III-14): White solid, mp 248–249 °C, yield: 45.0%. ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ : 9.21 (s, 1H), 8.63 (s, 1H), 7.98 (d, $J = 8.3$ Hz, 1H), 7.84 (d, $J = 7.8$ Hz, 1H), 7.82–7.78 (m, 4H), 7.72 (t, $J = 7.6$ Hz, 1H), 7.57–7.53 (m, 2H), 7.11–7.07 (m, 1H), 7.03–7.01 (m, 1H), 6.95 (t, $J = 6.9$ Hz, 1H), 5.33 (s, 2H), 4.30 (d, $J = 13.2$ Hz, 2H), 3.20 (t, $J = 11.8$ Hz, 2H), 2.88–2.81 (m, 1H), 1.92 (d, $J = 3.7$ Hz, 2H), 1.86–1.81 (m, 2H). ^{13}C NMR (100 MHz, DMSO) δ : 173.1, 163.9, 153.7, 151.3, 149.4, 135.2, 132.9, 132.7, 129.6, 128.6, 128.0, 127.5, 126.4, 126.1 (q, $^4J_{\text{C-F}} = 5.6$ Hz), 125.7, 125.4, 125.1, 123.9, 123.0, 121.0, 116.0, 112.7, 66.5, 49.0, 42.2, 28.4. ESI-HRMS m/z : $[\text{M} + \text{H}]^+$ calcd for: $\text{C}_{28}\text{H}_{26}\text{O}_3\text{N}_4\text{F}_3$: 523.1952; found: 523.1944.

1-(quinazolin-4-yl)-N-[2-[[4-(trifluoromethoxy)benzyl]oxy]phenyl]piperidine-4-carboxamide (III-15): White solid, mp 217–218 °C, yield: 45.2%. ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ : 9.26 (s, 1H), 8.63 (s, 1H), 7.99 (d, $J = 8.3$ Hz, 1H), 7.88 (d, $J = 8.3$ Hz, 2H), 7.82–7.77 (m, 3H), 7.71 (d, $J = 8.3$ Hz, 2H), 7.58–7.54 (m, 1H), 7.07–7.05 (m, 2H), 6.94–6.90 (m, 1H), 5.31 (s, 2H), 4.33 (d, $J = 13.3$ Hz, 2H), 3.25 (t, $J = 11.5$ Hz, 2H), 2.94–2.83 (m, 1H), 1.96 (d, $J = 9.7$ Hz, 2H), 1.92–1.84 (m, 2H). ^{13}C NMR (100 MHz, DMSO) δ : 173.0, 163.9, 159.0, 153.7, 151.3, 149.4, 132.7, 129.8, 129.2, 128.9, 127.8, 127.6, 125.5 (q, $^4J_{\text{C-F}} = 26.0$ Hz), 124.7, 123.2, 120.4, 115.9, 113.9, 113.8, 113.1, 69.5, 55.1, 48.9, 42.1, 28.4. ESI-HRMS m/z : $[\text{M} + \text{H}]^+$ calcd for: $\text{C}_{28}\text{H}_{26}\text{O}_3\text{N}_4\text{F}_3$: 523.1952; found: 523.1952.

N-[2-[[4-(tert-butyl)benzyl]oxy]phenyl]-1-(quinazolin-4-yl)piperidine-4-carboxamide (III-16): White solid, mp 89–90 °C, yield: 44.5%. ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ : 9.09 (s, 1H), 8.62 (s, 1H), 7.99 (d, $J = 8.8$ Hz, 1H), 7.81 (s, 3H), 7.57–

7.53 (m, 1H), 7.42–7.36 (m, 4H), 7.11–7.04 (m, 2H), 6.90 (t, $J = 7.5$ Hz, 1H), 5.15 (s, 2H), 4.31 (d, $J = 13.0$ Hz, 2H), 3.22 (t, $J = 12.3$ Hz, 2H), 2.93–2.76 (m, 1H), 1.94 (d, $J = 11.6$ Hz, 2H), 1.89–1.78 (m, 2H), 1.24 (s, 9H). ^{13}C NMR (100 MHz, DMSO) δ : 173.0, 163.9, 153.6, 151.3, 150.2, 134.1, 132.6, 128.0, 127.7, 127.6, 127.3, 125.5, 125.3, 125.1, 124.8, 123.2, 120.4, 115.9, 112.9, 69.6, 48.9, 42.1, 34.2, 31.1, 28.4. ESI-HRMS m/z : $[\text{M} + \text{H}]^+$ calcd for: $\text{C}_{31}\text{H}_{35}\text{O}_2\text{N}_4$: 495.2755; found: 495.2746.

***N*-[2-[(2,6-dichlorobenzyl)oxy]phenyl]-1-(quinazolin-4-yl)piperidine-4-carboxamide (III-17)**: White solid, mp 77–78 °C, yield: 42.4%. ^1H NMR (400 MHz, DMSO- d_6) δ : 8.87 (s, 1H), 8.62 (s, 1H), 7.94 (d, $J = 8.1$ Hz, 1H), 7.84–7.78 (m, 3H), 7.58–7.55 (m, 1H), 7.53 (d, $J = 7.9$ Hz, 2H), 7.43–7.39 (m, 1H), 7.27 (d, $J = 8.3$ Hz, 1H), 7.14 (t, $J = 7.8$ Hz, 1H), 6.98 (t, $J = 7.7$ Hz, 1H), 5.29 (s, 2H), 4.22 (d, $J = 13.3$ Hz, 2H), 3.18 (t, $J = 10.6$ Hz, 2H), 2.83–2.70 (m, 1H), 1.81 (d, $J = 3.8$ Hz, 2H), 1.81–1.71 (m, 2H). ^{13}C NMR (100 MHz, DMSO) δ : 173.0, 163.9, 153.6, 151.1, 149.7, 136.3, 132.8, 131.7, 131.6, 128.8, 127.9, 125.7, 125.4, 125.0, 123.6, 121.3, 115.9, 113.7, 66.2, 48.8, 42.0, 28.3. ESI-HRMS m/z : $[\text{M} + \text{H}]^+$ calcd for: $\text{C}_{27}\text{H}_{25}\text{O}_2\text{N}_4\text{Cl}_2$: 507.1349; found: 507.1343.

***N*-[2-(benzyloxy)phenyl]-1-(quinazolin-4-yl)piperidine-4-carboxamide (III-18)**: White solid, mp 231–232 °C yield: 20.4%. ^1H NMR (400 MHz, DMSO- d_6) δ : 9.18 (s, 1H), 8.63 (s, 1H), 7.98 (d, $J = 8.0$ Hz, 1H), 7.82–7.79 (m, 3H), 7.57–7.54 (m, 1H), 7.50 (d, $J = 7.4$ Hz, 2H), 7.38 (t, $J = 7.7$ Hz, 2H), 7.30 (t, $J = 7.2$ Hz, 1H), 7.09–7.05 (m, 2H), 6.91–6.88 (m, 1H), 5.20 (s, 2H), 4.31 (d, $J = 13.2$ Hz, 2H), 3.21 (t, $J = 11.1$ Hz, 2H), 2.89–2.85 (m, 1H), 1.95 (d, $J = 9.7$ Hz, 2H), 1.87–1.82 (m, 2H). ^{13}C NMR (100 MHz, DMSO) δ : 173.1, 164.0, 153.7, 151.3, 149.5, 137.2, 132.8, 128.4, 128.0, 127.8, 127.5, 127.4, 125.7, 125.4, 124.9, 123.5, 120.5, 116.0, 113.0, 69.7, 49.0, 42.2, 28.5. ESI-HRMS m/z : $[\text{M} + \text{H}]^+$ calcd for: $\text{C}_{27}\text{H}_{27}\text{O}_2\text{N}_4$: 439.2129; found: 439.2124.

***N*-[2-[(2-methoxybenzyl)oxy]phenyl]-1-(quinazolin-4-yl)piperidine-4-carboxamide (III-19)**: White solid, mp 174–175 °C, yield: 54.3%. ^1H NMR (400 MHz,

DMSO-*d*₆) δ : 9.11 (s, 1H), 8.63 (s, 1H), 7.98 (d, *J* = 8.2 Hz, 1H), 7.83–7.81 (m, 3H), 7.58–7.54 (m, 1H), 7.46–7.43 (m, 1H), 7.32–7.27 (m, 1H), 7.06–7.01 (m, 3H), 6.96–6.90 (m, 2H), 5.15 (s, 2H), 4.31 (d, *J* = 12.9 Hz, 2H), 3.84 (s, 3H), 3.21 (t, *J* = 11.2 Hz, 2H), 2.91–2.79 (m, 1H), 1.94 (d, *J* = 9.6 Hz, 2H), 1.91–1.77 (m, 2H). ¹³C NMR (100 MHz, DMSO) δ : 173.0, 163.9, 156.7, 153.7, 151.3, 149.5, 132.8, 129.3, 128.7, 128.0, 127.7, 125.7, 125.4, 124.9, 124.6, 123.2, 120.6, 120.3, 116.0, 113.0, 110.8, 65.3, 55.5, 49.0, 42.3, 28.5. ESI-HRMS *m/z*: [M + H]⁺ calcd for: C₂₈H₂₉O₃N₄: 469.2234; found: 469.2229.

***N*-(2-methoxyphenyl)-1-(quinazolin-4-yl)piperidine-4-carboxamide (III-20):**

White solid, mp 201–202 °C, yield: 14.8%. ¹H NMR (400 MHz, DMSO-*d*₆) δ : 9.17 (s, 1H), 8.63 (s, 1H), 8.00–7.94 (m, 2H), 7.82–7.79 (m, 2H), 7.56–7.52 (m, 1H), 7.06–7.02 (m, 2H), 6.90–6.87 (m, 1H), 4.34 (d, *J* = 13.4 Hz, 2H), 3.84 (s, 3H), 3.20 (t, *J* = 11.1 Hz, 2H), 2.95–2.90 (m, 1H), 1.94 (d, *J* = 13.1 Hz, 2H), 1.90–1.80 (m, 2H). ¹³C NMR (100 MHz, DMSO-*D*₆) δ : 173.2, 164.0, 153.7, 151.3, 149.7, 132.8, 128.0, 127.3, 125.7, 125.4, 124.4, 122.1, 120.2, 116.0, 111.1, 55.7, 49.0, 42.3, 28.5. ESI-HRMS *m/z*: [M + H]⁺ calcd for: C₂₁H₂₃O₂N₄: 363.1816; found: 363.1810.

***N*-(2-ethoxyphenyl)-1-(quinazolin-4-yl)piperidine-4-carboxamide (III-21):**

White solid, mp 172–173 °C, yield: 26.6%. ¹H NMR (400 MHz, DMSO-*d*₆) δ : 9.02 (s, 1H), 8.63 (s, 1H), 8.00 (d, *J* = 8.3 Hz, 1H), 7.89 (d, *J* = 6.4 Hz, 1H), 7.82–7.80 (m, 2H), 7.57–7.53 (m, 1H), 7.07–7.03 (m, 2H), 6.91–6.87 (m, 1H), 4.34 (d, *J* = 13.3 Hz, 2H), 4.11–4.06 (m, 2H), 3.21 (t, *J* = 9.4 Hz, 2H), 2.97–2.85 (m, 1H), 1.95 (d, *J* = 9.5 Hz, 2H), 1.91–1.79 (m, 2H), 1.37 (t, *J* = 7.0 Hz, 3H). ¹³C NMR (100 MHz, DMSO) δ : 173.0, 163.9, 153.7, 151.3, 149.2, 132.7, 128.0, 127.5, 125.6, 125.4, 124.5, 122.5, 120.2, 116.0, 112.3, 63.9, 49.0, 42.3, 28.4, 14.7. ESI-HRMS *m/z*: [M + H]⁺ calcd for: C₂₂H₂₅O₂N₄: 377.1972; found: 377.1967.

***N*-(2-propoxyphenyl)-1-(quinazolin-4-yl)piperidine-4-carboxamide (III-22):**

White solid, mp 173–174 °C, yield: 29.3%. ¹H NMR (400 MHz, DMSO-*d*₆) δ : 8.94

(s, 1H), 8.62 (s, 1H), 7.99 (d, $J = 8.3$ Hz, 1H), 7.85–7.80 (m, 3H), 7.56–7.52 (m, 1H), 7.08–7.01 (m, 2H), 6.90–6.84 (m, 1H), 4.34 (d, $J = 13.3$ Hz, 2H), 3.98 (t, $J = 6.5$ Hz, 2H), 3.23 (t, $J = 11.1$ Hz, 2H), 2.94–2.84 (m, 1H), 1.96 (d, $J = 12.8$ Hz, 2H), 1.92–1.84 (m, 2H), 1.83–1.73 (m, 2H), 1.00 (t, $J = 7.4$ Hz, 3H). ^{13}C NMR (100 MHz, DMSO) δ : 172.9, 163.9, 153.6, 151.3, 150.0, 132.7, 128.0, 127.1, 125.6, 125.3, 125.0, 123.3, 120.1, 115.9, 112.2, 74.4, 48.9, 42.2, 28.4, 27.7, 19.1. ESI-HRMS m/z : $[\text{M} + \text{H}]^+$ calcd for: $\text{C}_{23}\text{H}_{27}\text{O}_2\text{N}_4$: 391.2129; found: 391.2127.

***N*-(2-butoxyphenyl)-1-(quinazolin-4-yl)piperidine-4-carboxamide (III-23)**: White solid, mp 139–140 °C, yield: 37.8%. ^1H NMR (400 MHz, DMSO- d_6) δ : 8.93 (s, 1H), 8.62 (s, 1H), 7.99 (d, $J = 8.3$ Hz, 1H), 7.83 (d, $J = 2.3$ Hz, 1H), 7.81–7.80 (m, 2H), 7.56–7.52 (m, 1H), 7.08–7.00 (m, 2H), 6.91–6.86 (m, 1H), 4.33 (d, $J = 13.2$ Hz, 2H), 4.01 (t, $J = 6.6$ Hz, 2H), 3.23 (t, $J = 11.2$ Hz, 2H), 2.93–2.82 (m, 1H), 1.96 (d, $J = 13.3$ Hz, 2H), 1.93–1.82 (m, 2H), 1.79–1.68 (m, 2H), 1.54–1.40 (m, 2H), 0.93 (t, $J = 7.4$ Hz, 3H). ^{13}C NMR (100 MHz, DMSO) δ : 172.9, 163.9, 153.6, 151.3, 149.6, 132.6, 128.0, 127.3, 125.5, 125.3, 124.7, 122.8, 120.1, 116.0, 112.2, 67.9, 48.9, 42.2, 30.7, 28.4, 18.7, 13.7. ESI-HRMS m/z : $[\text{M} + \text{H}]^+$ calcd for: $\text{C}_{24}\text{H}_{29}\text{O}_2\text{N}_4$: 405.2285; found: 405.2280.

***N*-[2-(*sec*-butoxy)phenyl]-1-(quinazolin-4-yl)piperidine-4-carboxamide (III-24)**: White solid, mp 156–157 °C, yield: 42.9%. ^1H NMR (400 MHz, DMSO- d_6) δ : 8.87 (s, 1H), 8.63 (s, 1H), 7.98 (d, $J = 8.4$ Hz, 1H), 7.89 (d, $J = 7.6$ Hz, 1H), 7.80 (d, $J = 3.8$ Hz, 2H), 7.55–7.51 (m, 1H), 7.04–7.00 (m, 2H), 6.89–6.86 (m, 1H), 4.39–4.32 (m, 4H), 3.23 (t, $J = 10.8$ Hz, 2H), 2.94–2.86 (m, 1H), 1.96 (d, $J = 9.5$ Hz, 2H), 1.88–1.82 (m, 2H), 1.63–1.56 (m, 1H), 1.24 (d, $J = 6.1$ Hz, 3H), 0.92 (t, $J = 7.4$ Hz, 3H). ^{13}C NMR (100 MHz, DMSO) δ : 172.9, 163.9, 153.6, 151.3, 148.5, 132.6, 128.3, 128.0, 125.6, 125.3, 124.6, 122.8, 120.1, 116.0, 113.9, 75.7, 48.9, 42.3, 28.6, 28.4, 19.1, 9.6. ESI-HRMS m/z : $[\text{M} + \text{H}]^+$ calcd for: $\text{C}_{24}\text{H}_{29}\text{O}_2\text{N}_4$: 405.2285; found: 405.2279.

***N*-(2-isobutoxyphenyl)-1-(quinazolin-4-yl)piperidine-4-carboxamide (III-25)**:

White solid, mp 139–140 °C, yield: 32.0%. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 8.95 (s, 1H), 8.62 (s, 1H), 7.99 (d, *J* = 8.4 Hz, 1H), 7.83–7.79 (m, 2H), 7.76 (d, *J* = 7.8 Hz, 1H), 7.57–7.53 (m, 1H), 7.09–7.05 (m, 1H), 7.02–7.00 (m, 1H), 6.89 (t, *J* = 7.6 Hz, 1H), 4.34 (d, *J* = 13.4 Hz, 2H), 3.78 (d, *J* = 6.5 Hz, 2H), 3.24 (t, *J* = 11.4 Hz, 2H), 2.93–2.81 (m, 1H), 2.15–1.99 (m, 1H), 1.97 (d, *J* = 9.5 Hz, 2H), 1.89–1.83 (m 2H), 1.01 (s, 3H), 0.99 (s, 3H). ¹³C NMR (100 MHz, DMSO) δ: 172.9, 163.9, 153.6, 151.2, 150.0, 132.7, 127.9, 127.1, 125.7, 125.4, 125.0, 123.3, 120.1, 115.9, 112.2, 74.4, 48.9, 42.2, 28.5, 27.7, 19.2. ESI-HRMS *m/z*: [M + H]⁺ calcd for: C₂₄H₂₉O₂N₄: 405.2285; found: 405.2285.

methyl 2-[[2-[1-(quinazolin-4-yl)piperidine-4-carboxamide]phenoxy]sulfonyl]acetate (III-26): White solid, mp 178–179 °C, yield: 26.1%. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 9.17 (s, 1H), 8.63 (s, 1H), 8.02–7.96 (m, 2H), 7.82–7.80 (m, 2H), 7.57–7.53 (m, 1H), 7.06–7.02 (m, 1H), 6.99–6.93 (m, 2H), 4.87 (s, 2H), 4.35 (d, *J* = 13.3 Hz, 2H), 3.72 (s, 3H), 3.23 (t, *J* = 11.3 Hz, 2H), 2.96–2.85 (m, 1H), 1.96 (d, *J* = 3.3 Hz, 2H), 1.94–1.82 (m, 2H). ¹³C NMR (100 MHz, DMSO) δ: 173.0, 169.5, 163.9, 153.6, 151.2, 148.3, 132.7, 128.0, 127.9, 125.6, 125.4, 124.2, 122.2, 121.4, 115.9, 113.1, 65.8, 52.0, 49.0, 42.4, 28.4. ESI-HRMS *m/z*: [M + H]⁺ calcd for: C₂₃H₂₅O₄N₄: 421.1870; found: 421.1871.

ethyl 2-[[2-[1-(quinazolin-4-yl)piperidine-4-carboxamide]phenoxy]sulfonyl]acetate (III-27): White solid, mp 109–110 °C, yield: 28.0%. ¹H NMR (400 MHz, DMSO-*d*₆) δ: 9.19 (s, 1H), 8.63 (s, 1H), 8.01–7.97 (m, 2H), 7.82–7.80 (m, 2H), 7.57–7.53 (m, 1H), 7.06–7.02 (m, 1H), 6.98–6.93 (m, 2H), 4.85 (s, 2H), 4.34 (d, *J* = 13.6 Hz, 2H), 4.20–4.16 (m, 2H), 3.22 (t, *J* = 11.6 Hz, 2H), 2.93–2.87 (m, 1H), 1.97 (d, *J* = 10.1 Hz, 2H), 1.91–1.81 (m, 2H), 1.21 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (100 MHz, DMSO-*D*₆) δ: 173.1, 169.0, 164.0, 153.7, 151.3, 148.3, 132.8, 128.0, 125.7, 125.4, 124.3, 122.2, 121.4, 116.0, 113.1, 65.9, 60.9, 49.0, 42.5, 28.5, 14.1. ESI-HRMS *m/z*: [M + H]⁺ calcd for: C₂₄H₂₇O₄N₄: 435.2027; found: 435.2022.

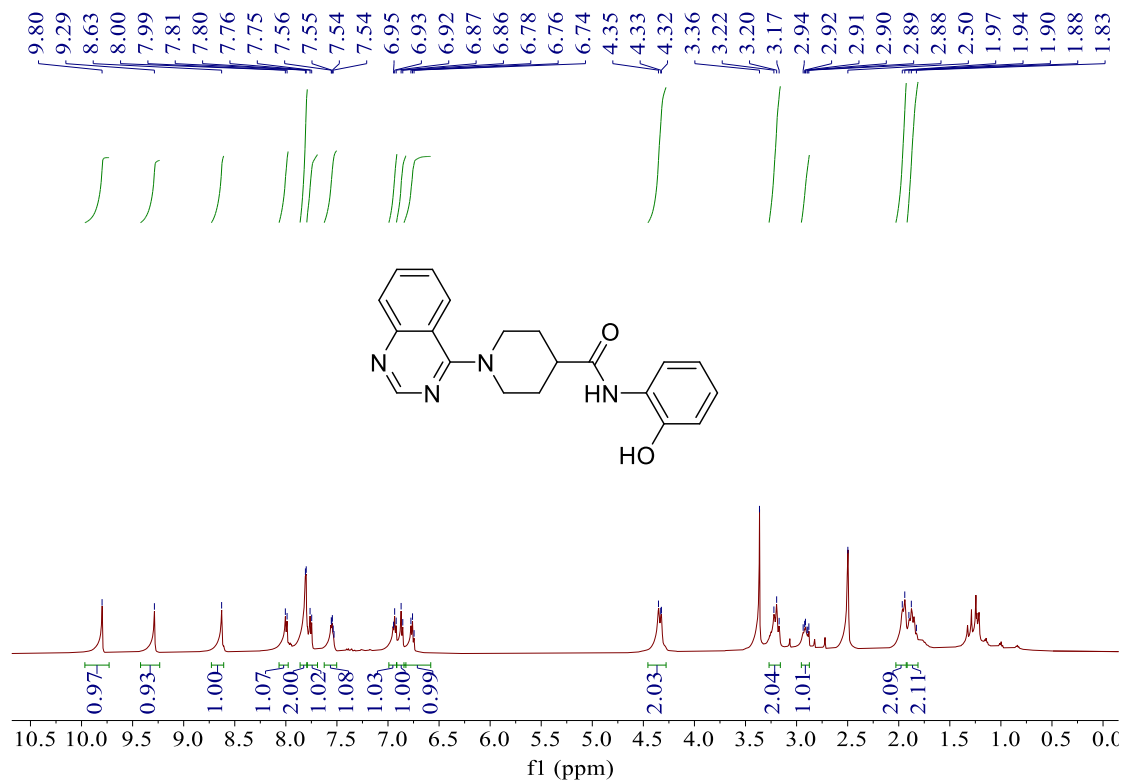


Figure S1. ¹H NMR spectrum of intermediate II (DMSO-*d*₆)

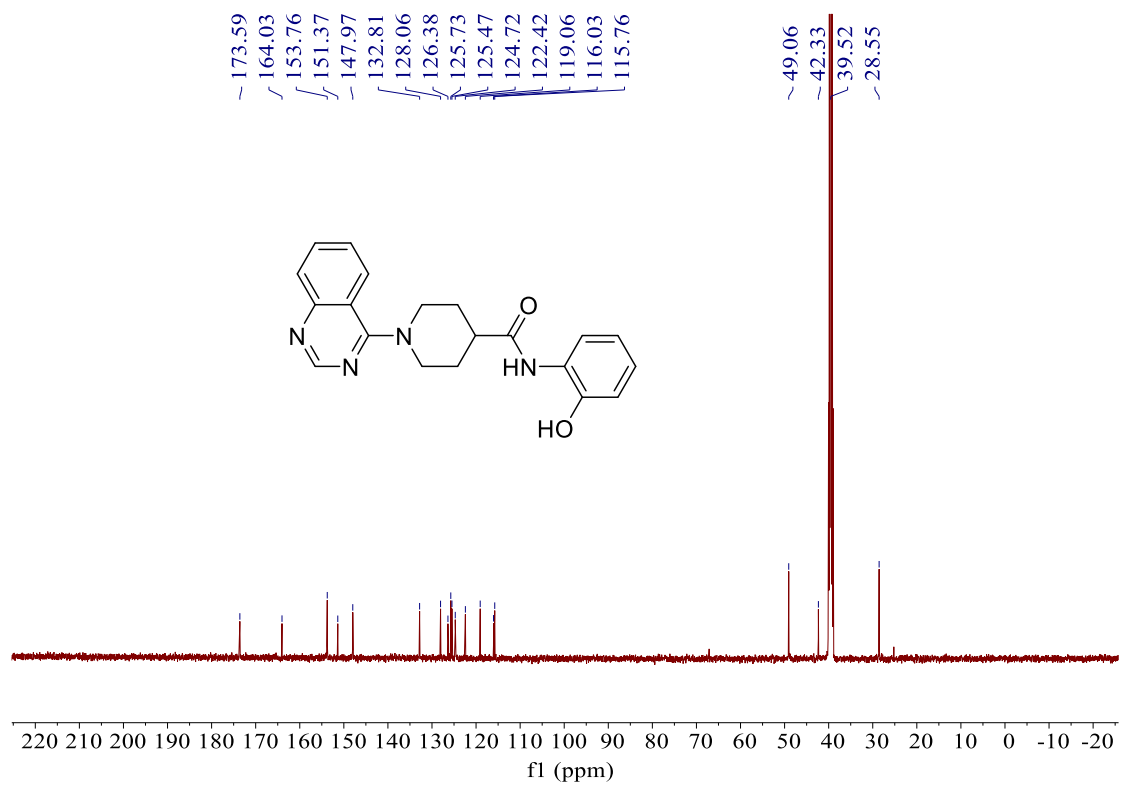


Figure S2. ¹³C NMR spectrum of intermediate II (DMSO-*d*₆)

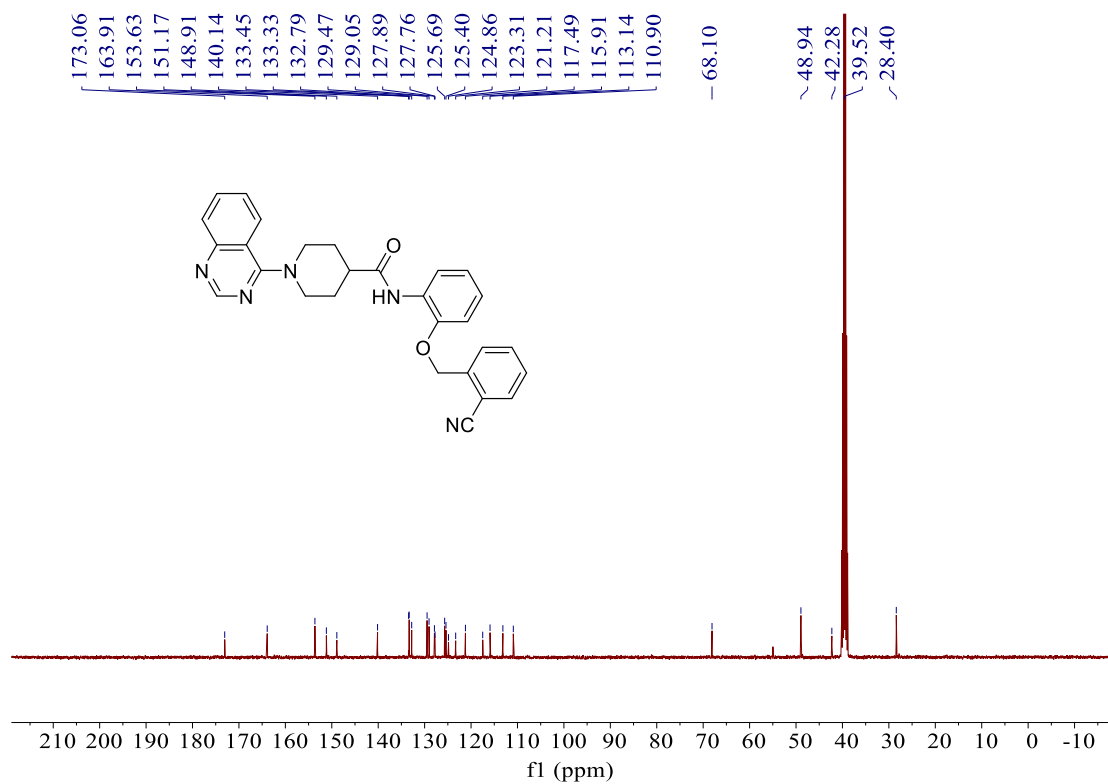


Figure S5. ^{13}C NMR spectrum of compound **III-1** ($\text{DMSO}-d_6$)

116 #37 RT: 0.37 AV: 1 NL: 7.75E7
T: FTMS + p ESI Full ms [150.0000-2200.0000]

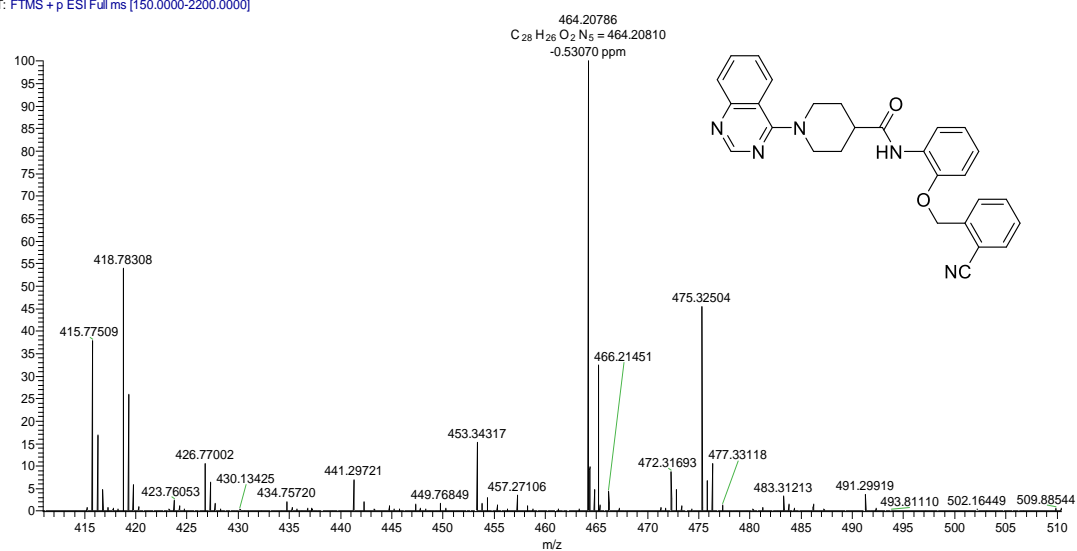


Figure S6. HRMS spectrum of compound **III-1**

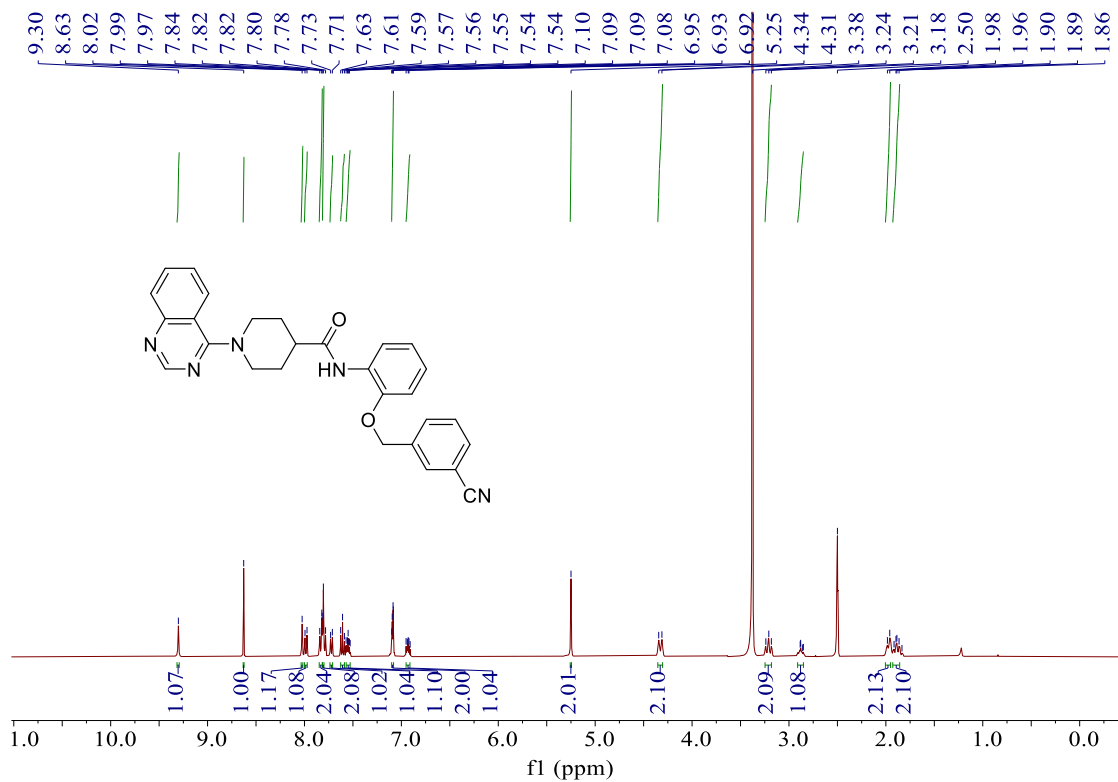


Figure S7. ^1H NMR spectrum of compound **III-2** ($\text{DMSO-}d_6$)

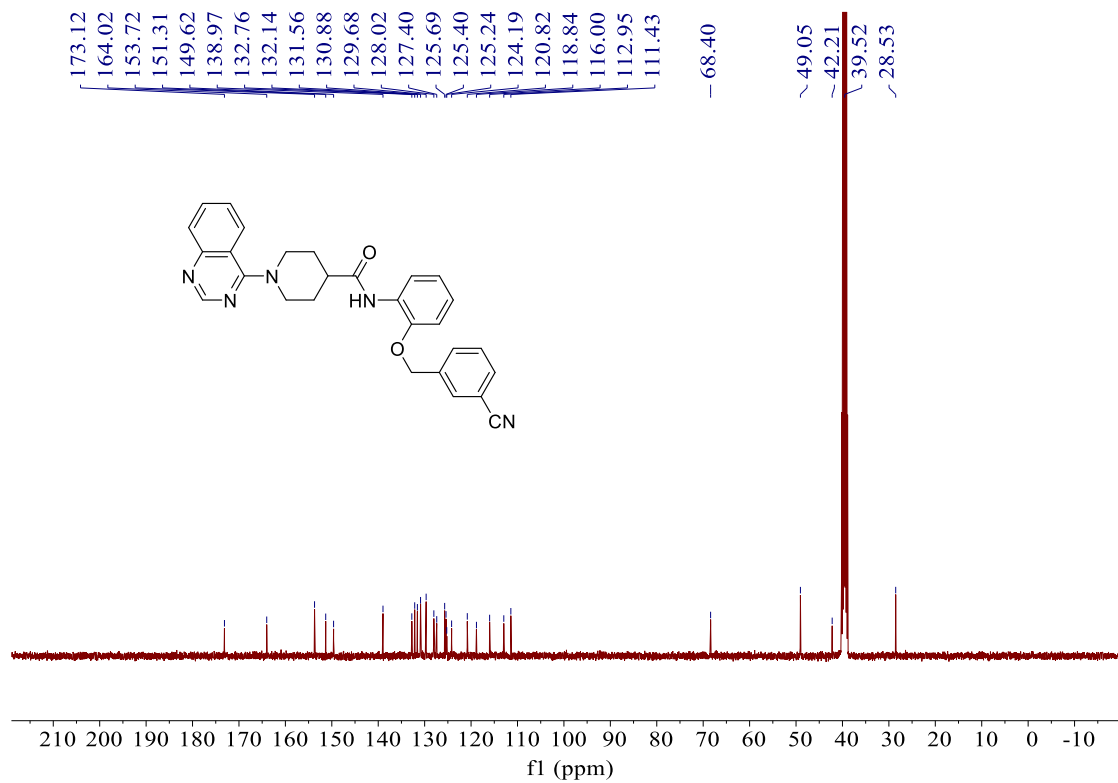


Figure S8. ^{13}C NMR spectrum of compound **III-2** ($\text{DMSO-}d_6$)

177 #33 RT: 0.33 AV: 1 NL: 5.00E7
T: FTMS + p ESI Full ms [100.0000-1000.0000]

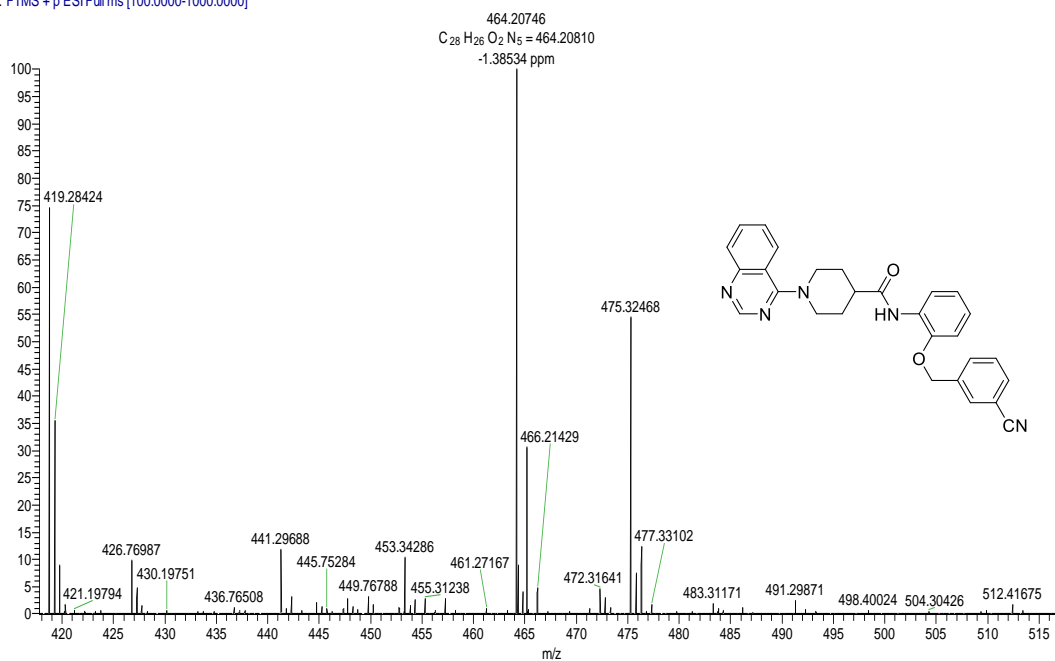


Figure S9. HRMS spectrum of compound III-2

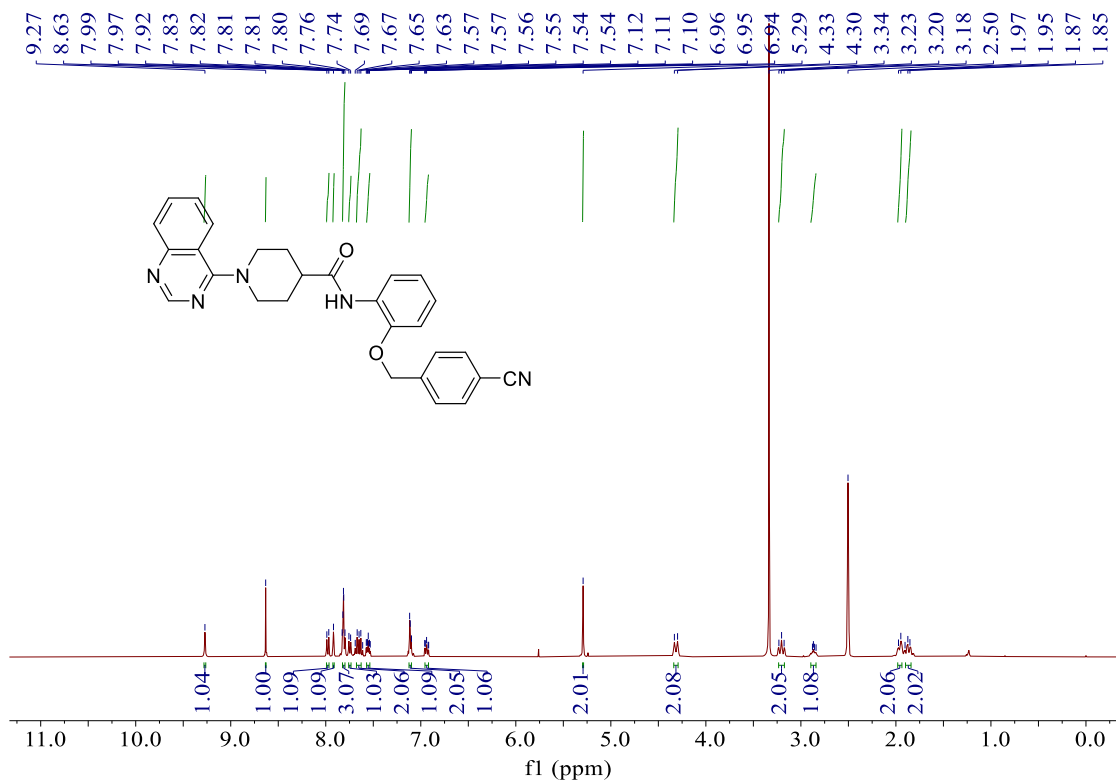


Figure S10. ¹H NMR spectrum of compound III-3 (DMSO-*d*₆)

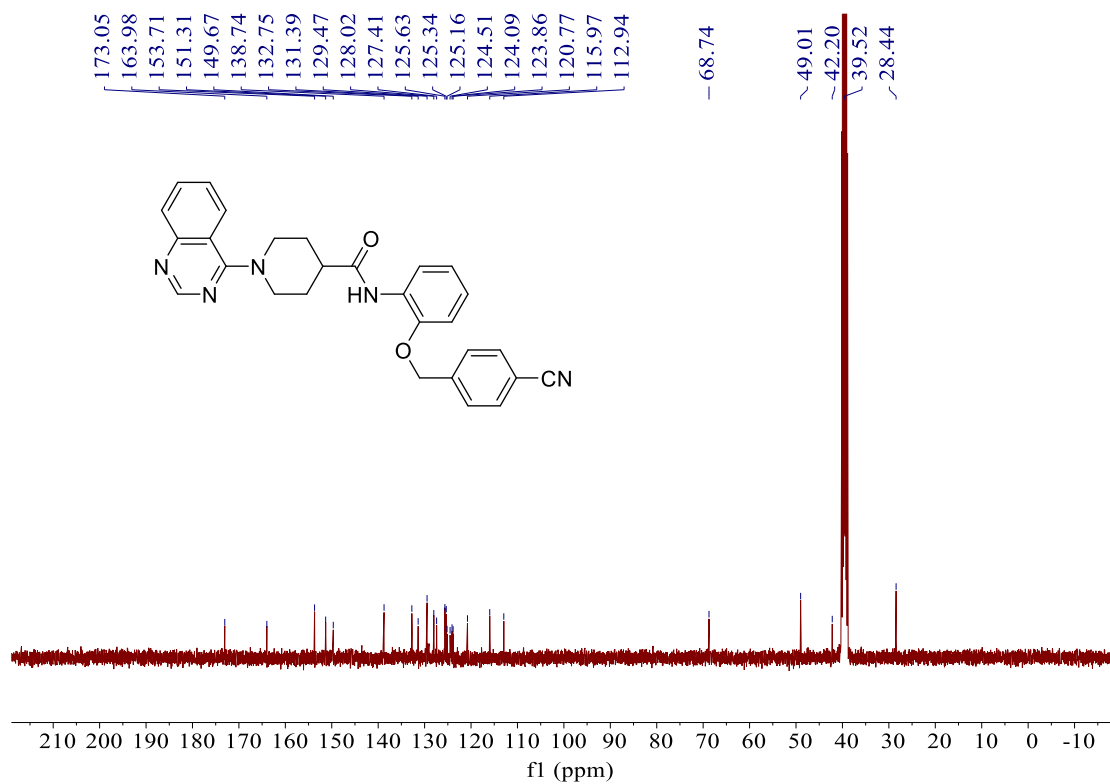


Figure S11. ^{13}C NMR spectrum of compound **III-3** ($\text{DMSO}-d_6$)

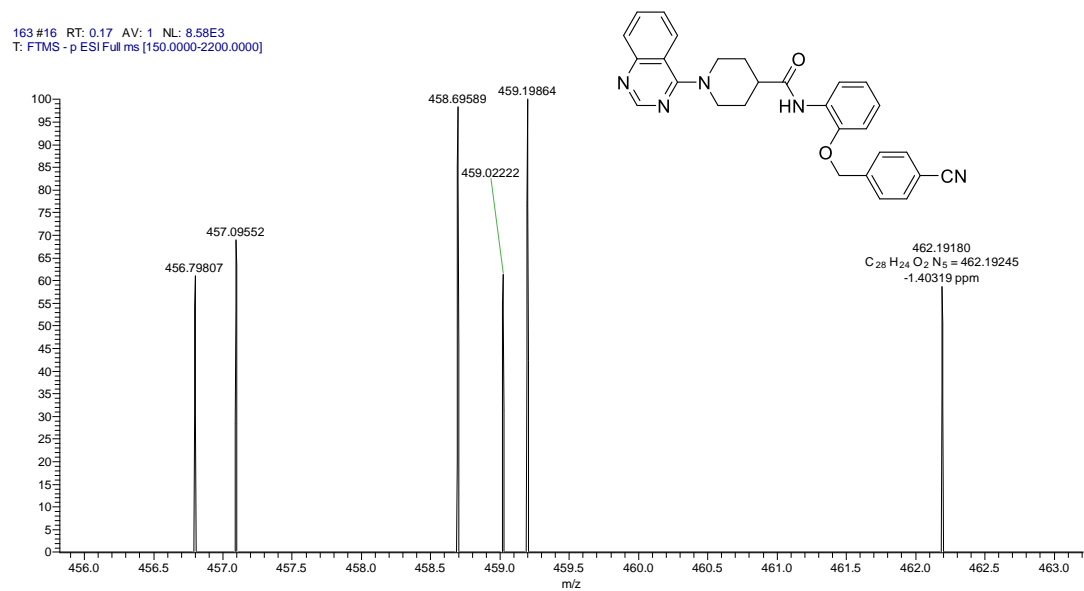


Figure S12. HRMS spectrum of compound **III-3**

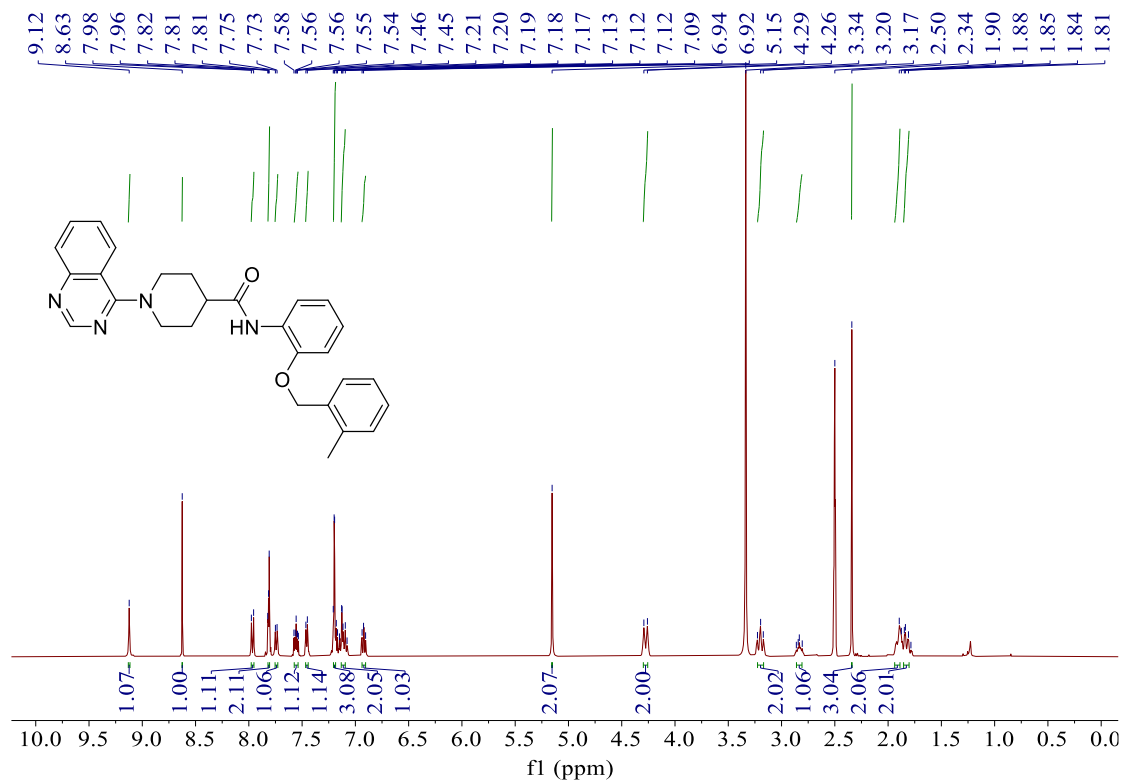


Figure S13. ^1H NMR spectrum of compound III-4 (DMSO- d_6)

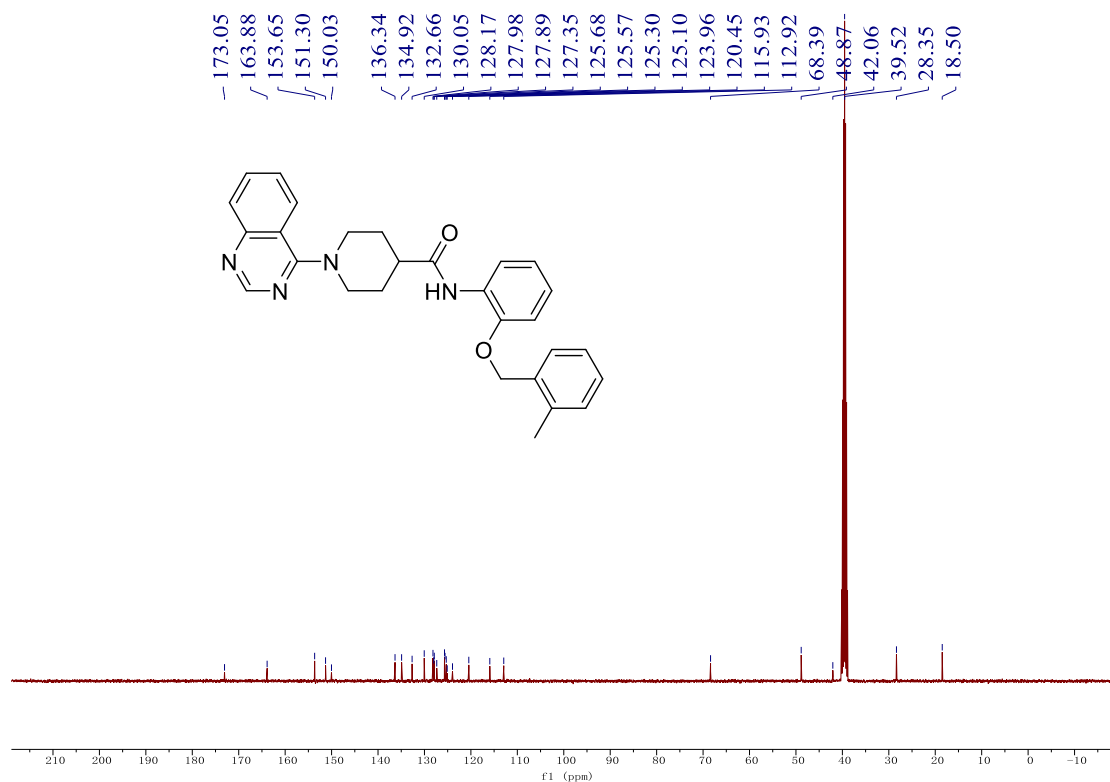


Figure S14. ^{13}C NMR spectrum of compound III-4 (DMSO- d_6)

144 #50 RT: 0.50 AV: 1 NL: 4.46E5
T: FTMS - p ESI Full ms [150.0000-2200.0000]

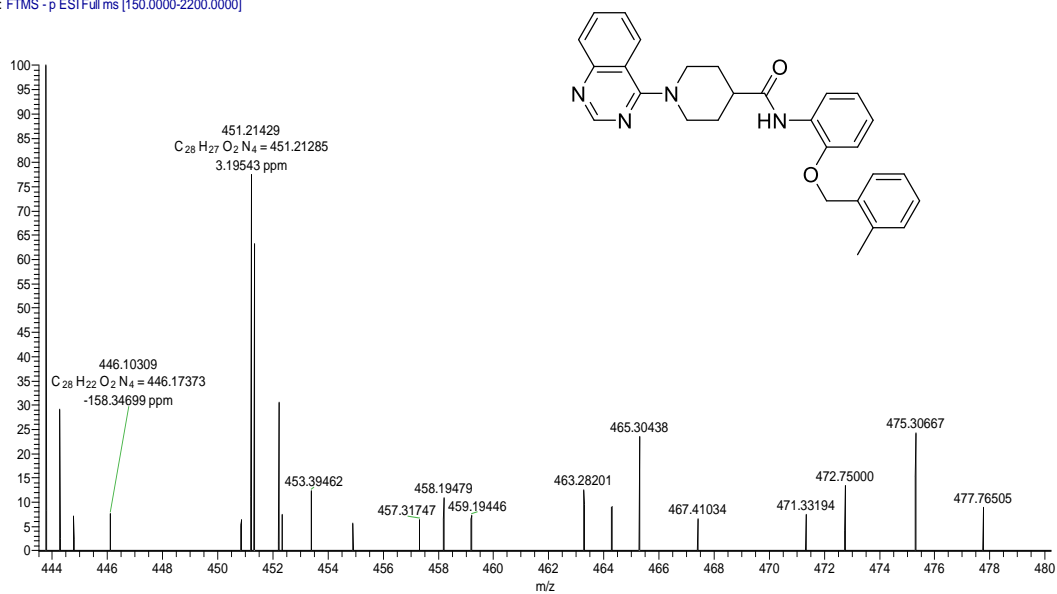


Figure S15. HRMS spectrum of compound III-4

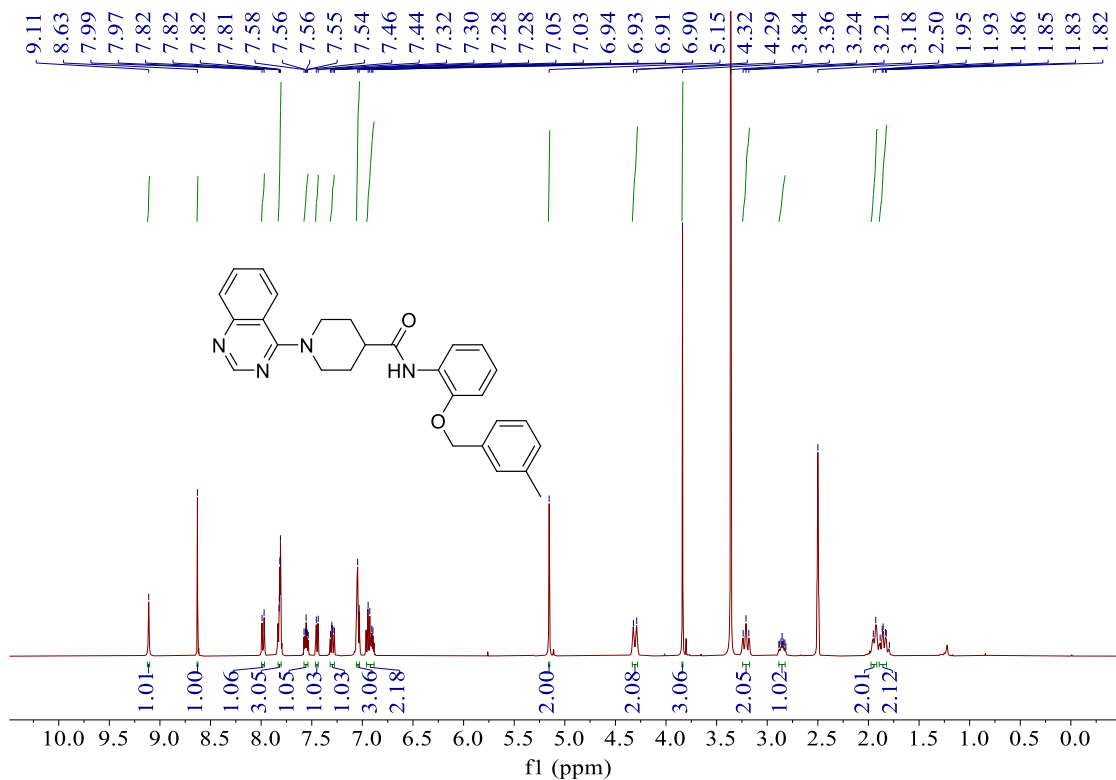


Figure S16. ¹H NMR spectrum of compound III-5 (DMSO-d₆)

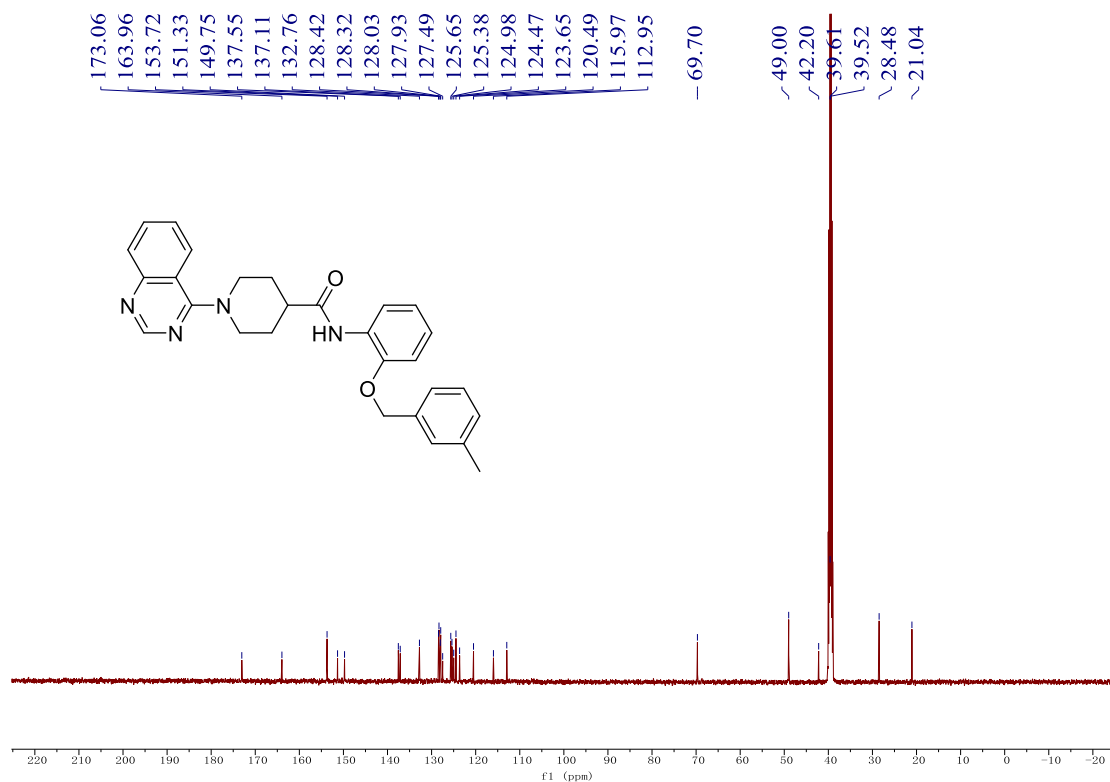


Figure S17. ¹³C NMR spectrum of compound III-5 (DMSO-*d*₆)

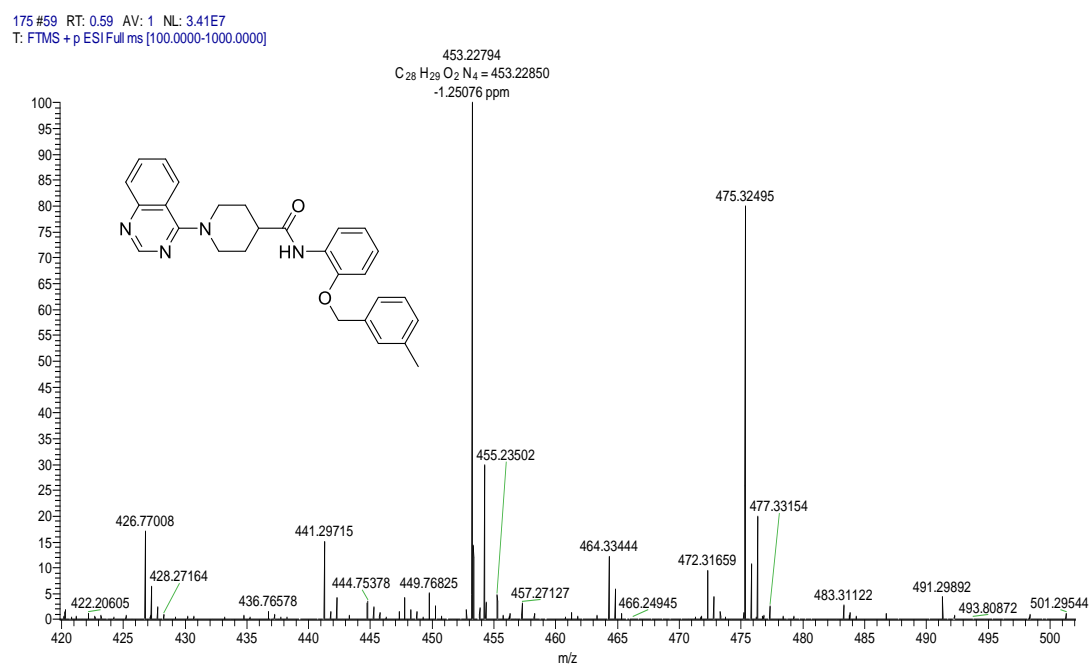


Figure S18. HRMS spectrum of compound III-5

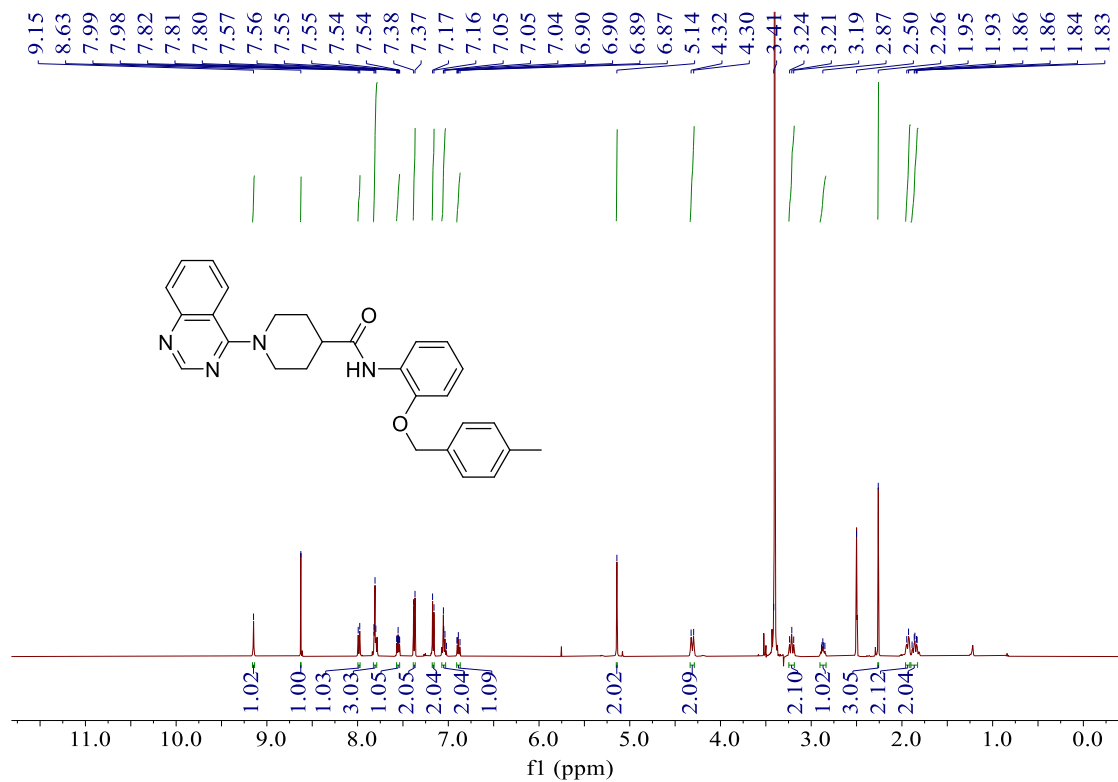


Figure S19. ^1H NMR spectrum of compound III-6 (DMSO- d_6)

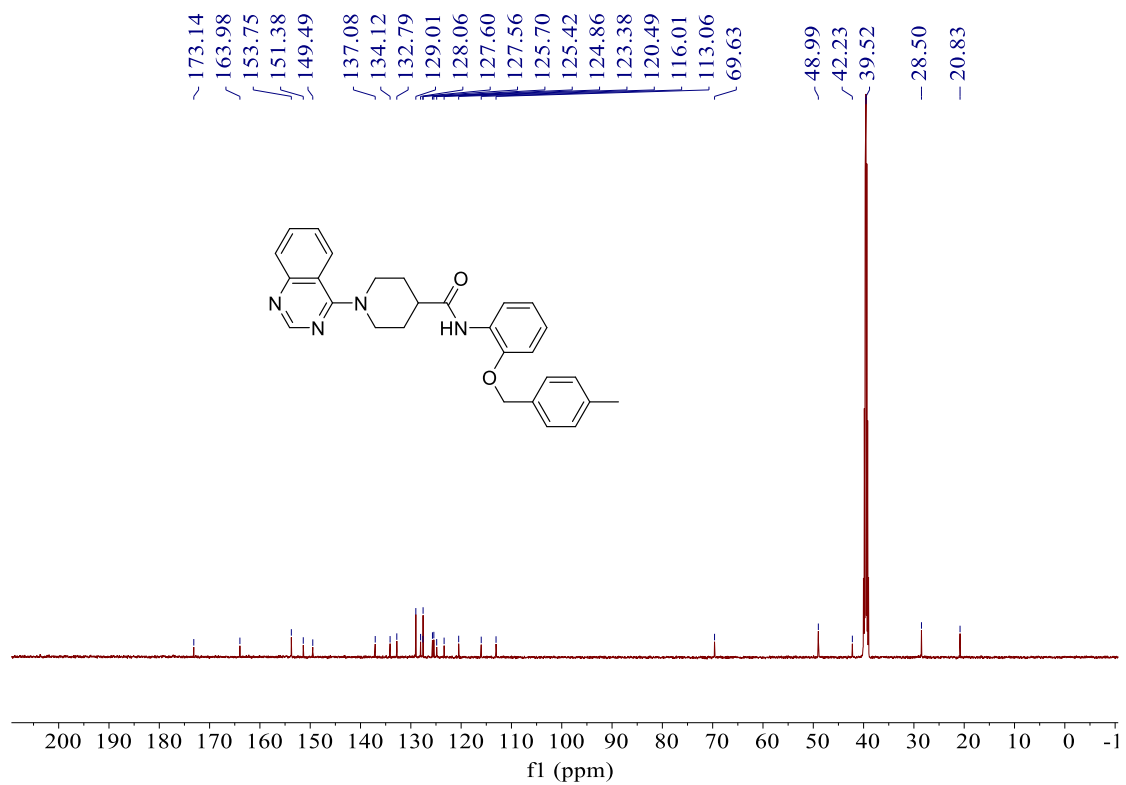


Figure S20. ^{13}C NMR spectrum of compound III-6 (DMSO- d_6)

117 #43 RT: 0.44 AV: 1 NL: 6.51E7
T: FTMS + p ESI Full ms [150.0000-2200.0000]

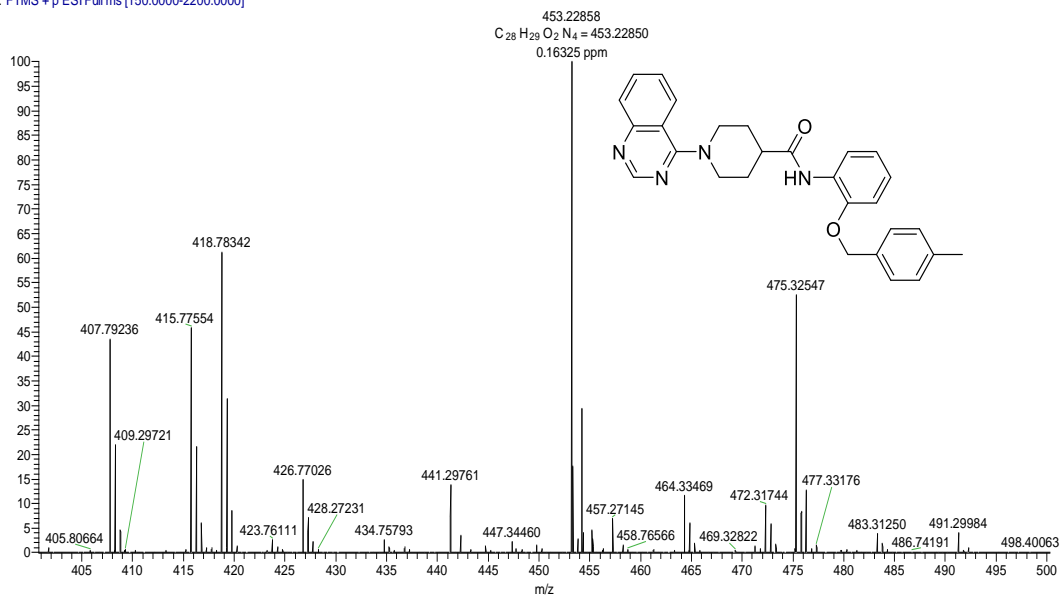


Figure S21. HRMS spectrum of compound III-6

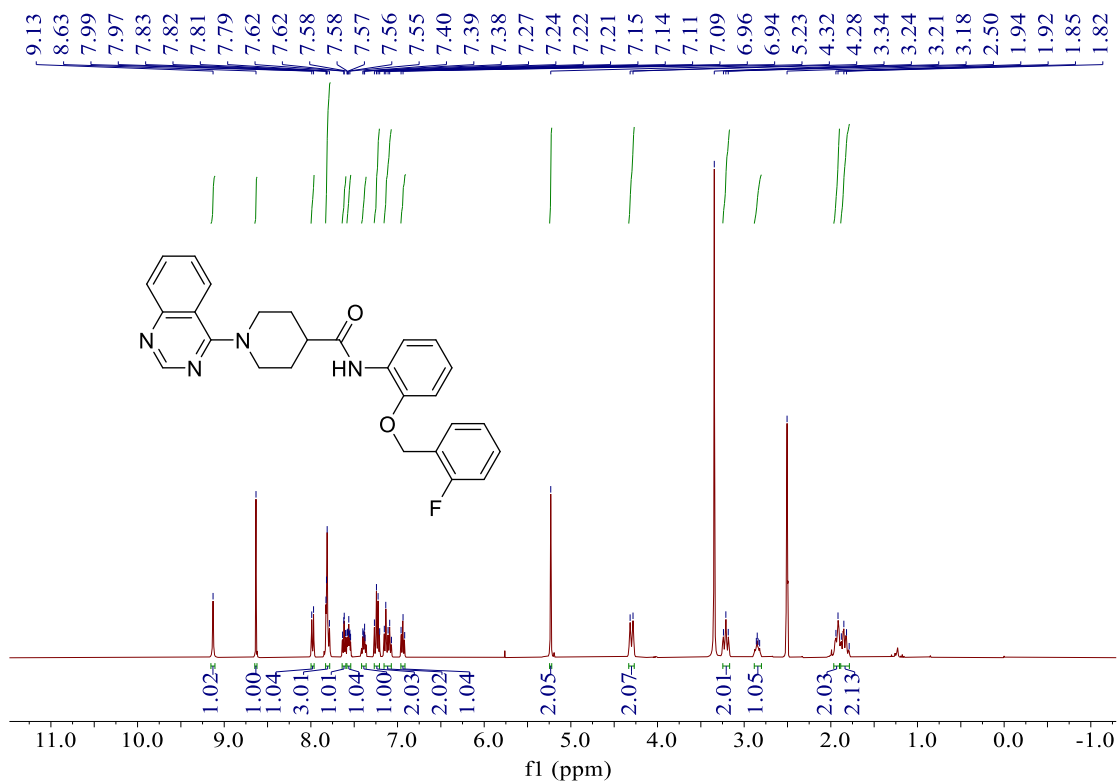


Figure S22. ¹H NMR spectrum of compound III-7 (DMSO-d₆)

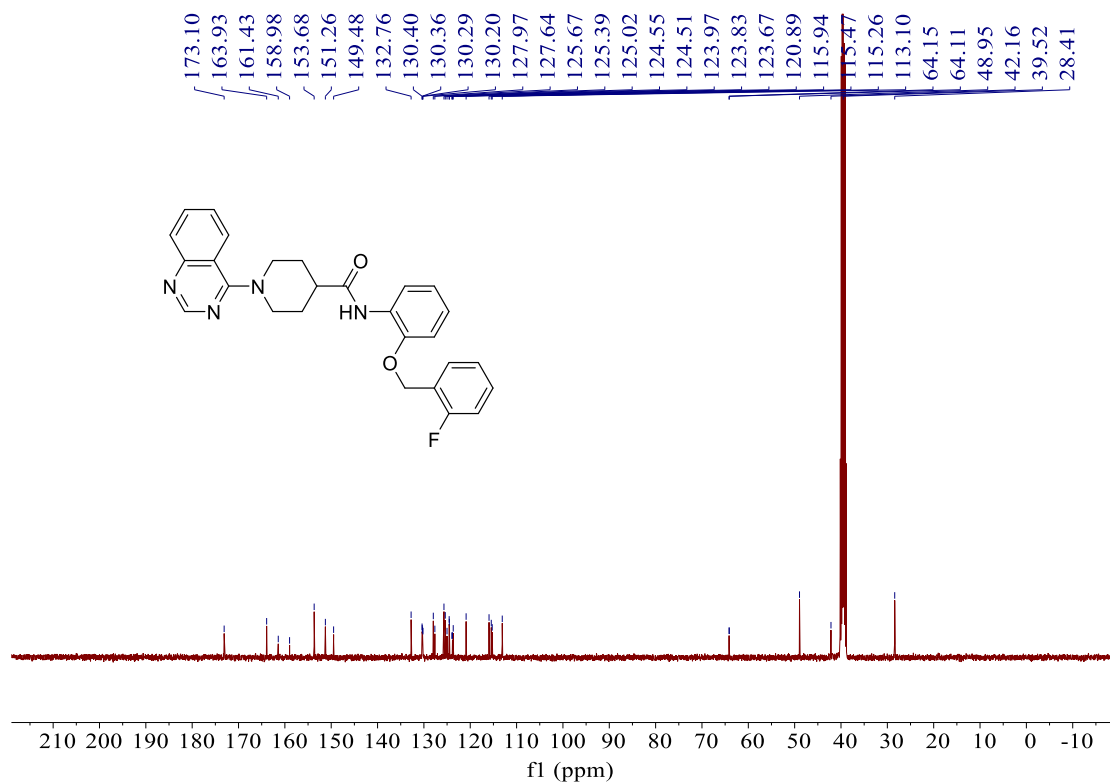


Figure S23. ^{13}C NMR spectrum of compound **III-7** ($\text{DMSO}-d_6$)

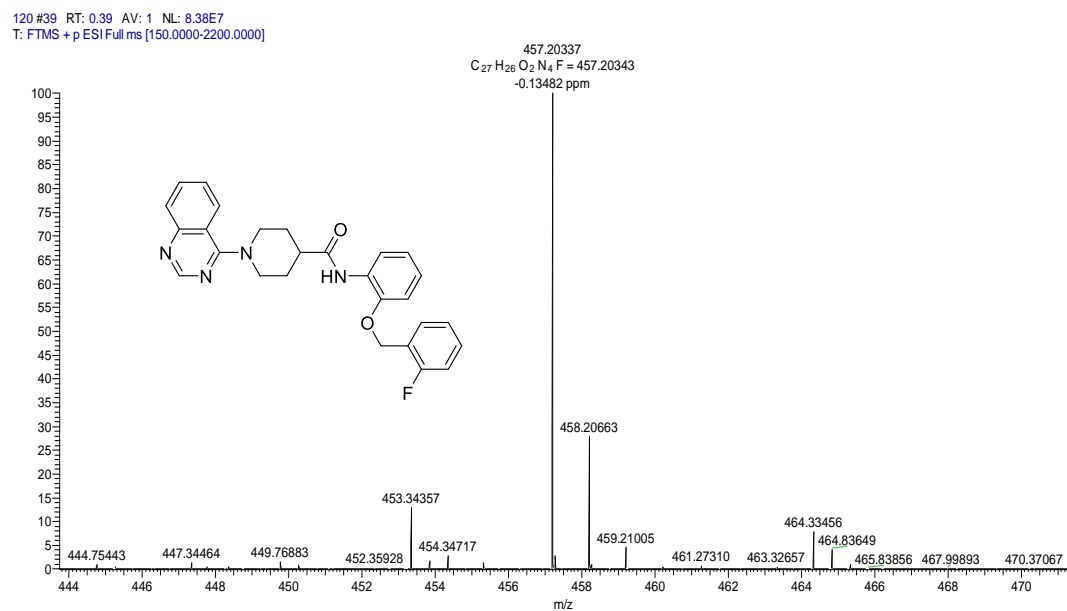


Figure S24. HRMS spectrum of compound **III-7**

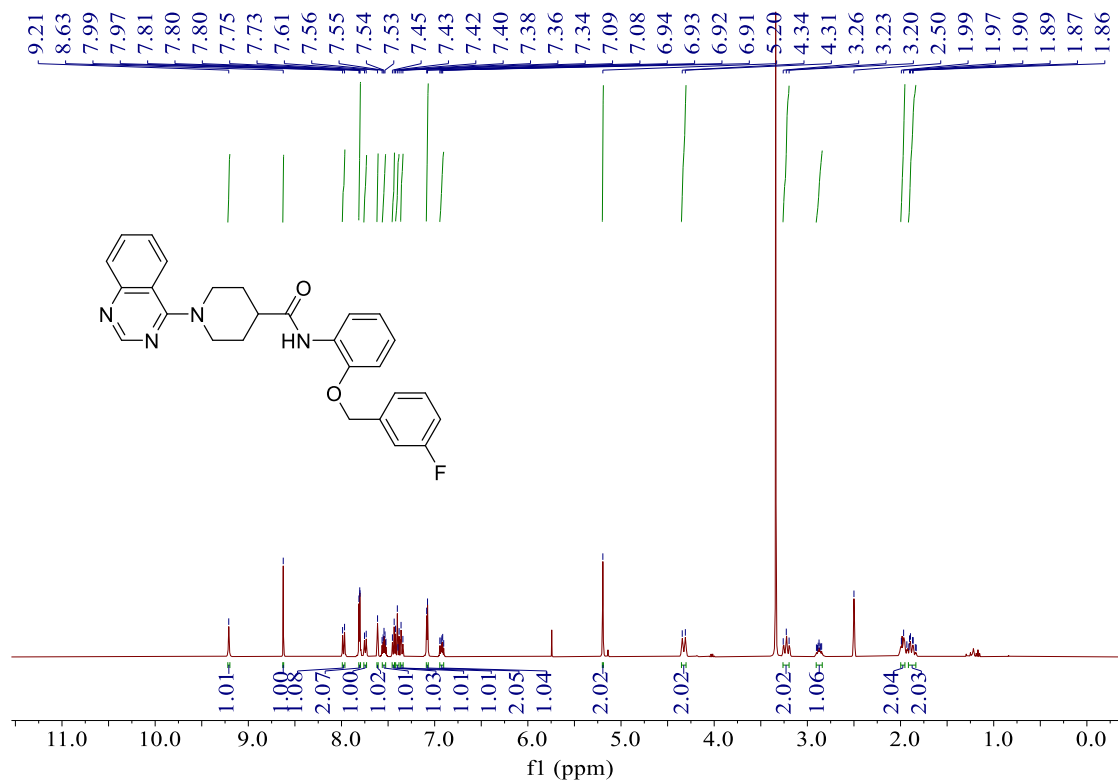


Figure S25. ^1H NMR spectrum of compound **III-8** ($\text{DMSO-}d_6$)

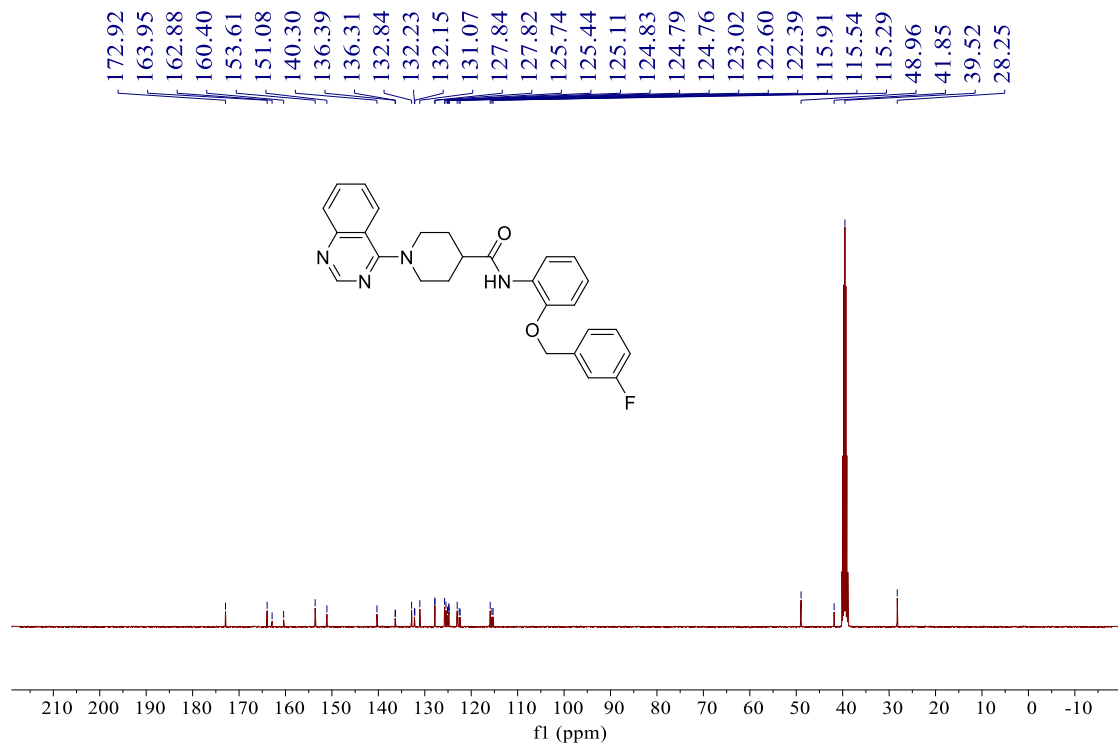


Figure S26. ^{13}C NMR spectrum of compound **III-8** ($\text{DMSO-}d_6$)

180 #62 RT: 0.62 AV: 1 NL: 6.09E4
T: FTMS - p ESI Full ms [100.0000-1000.0000]

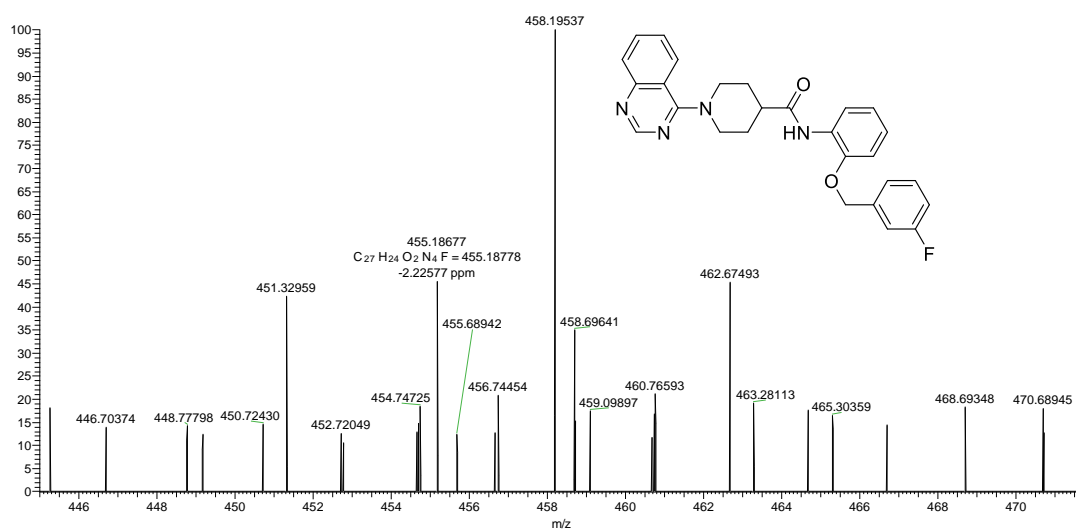


Figure S27. HRMS spectrum of compound **III-8**

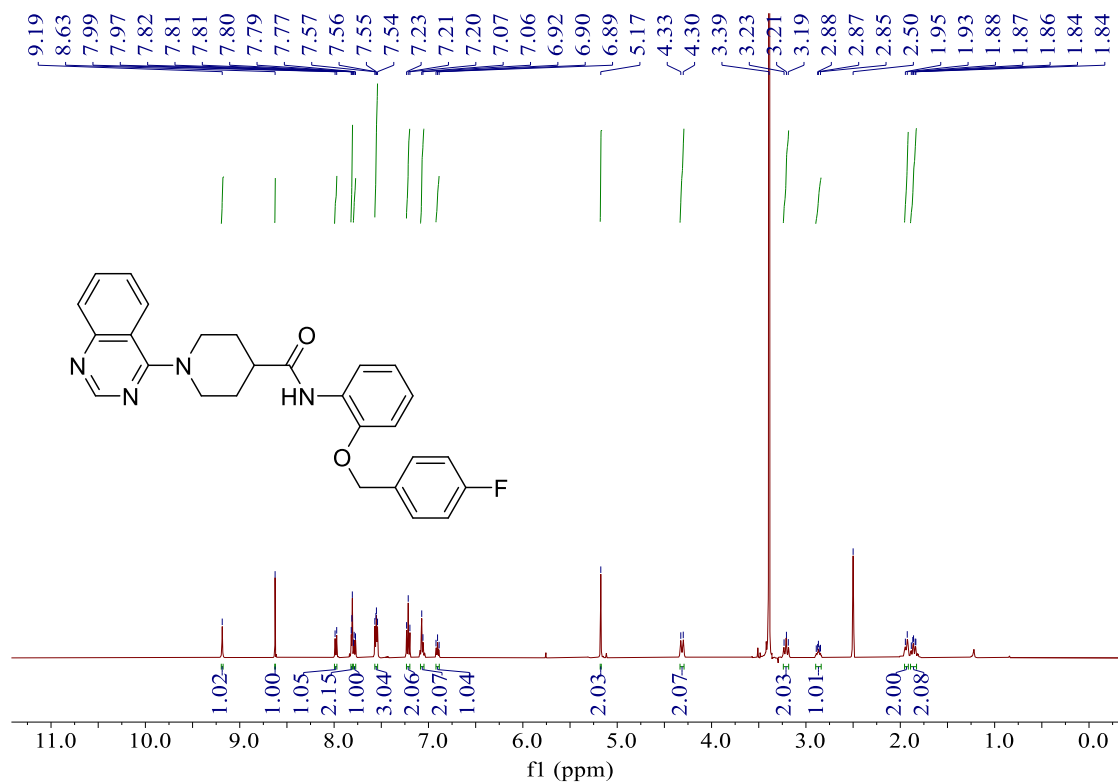


Figure S28. ¹H NMR spectrum of compound **III-9** (DMSO-*d*₆)

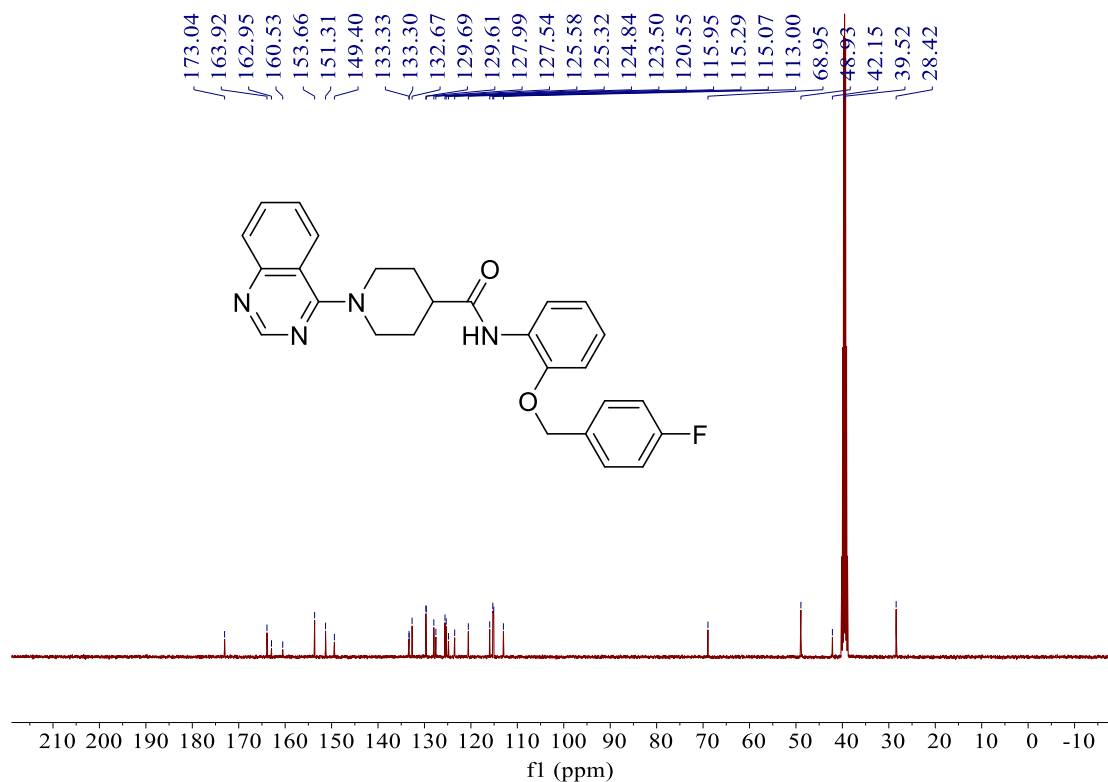


Figure S29. ¹³C NMR spectrum of compound III-9 (DMSO-*d*₆)

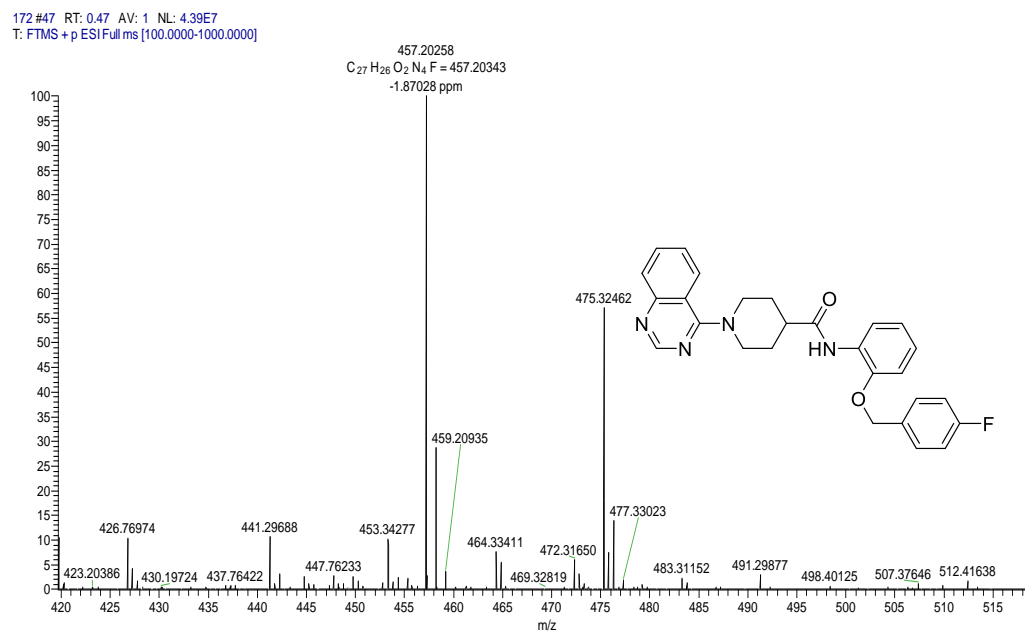
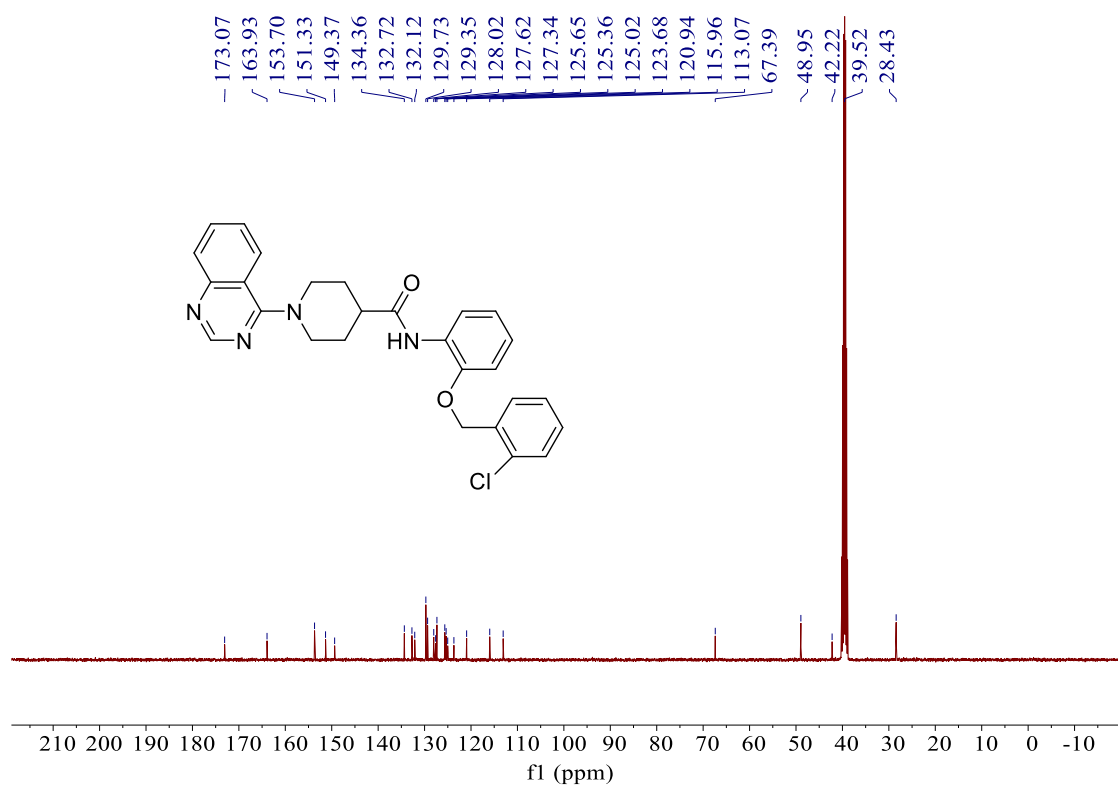
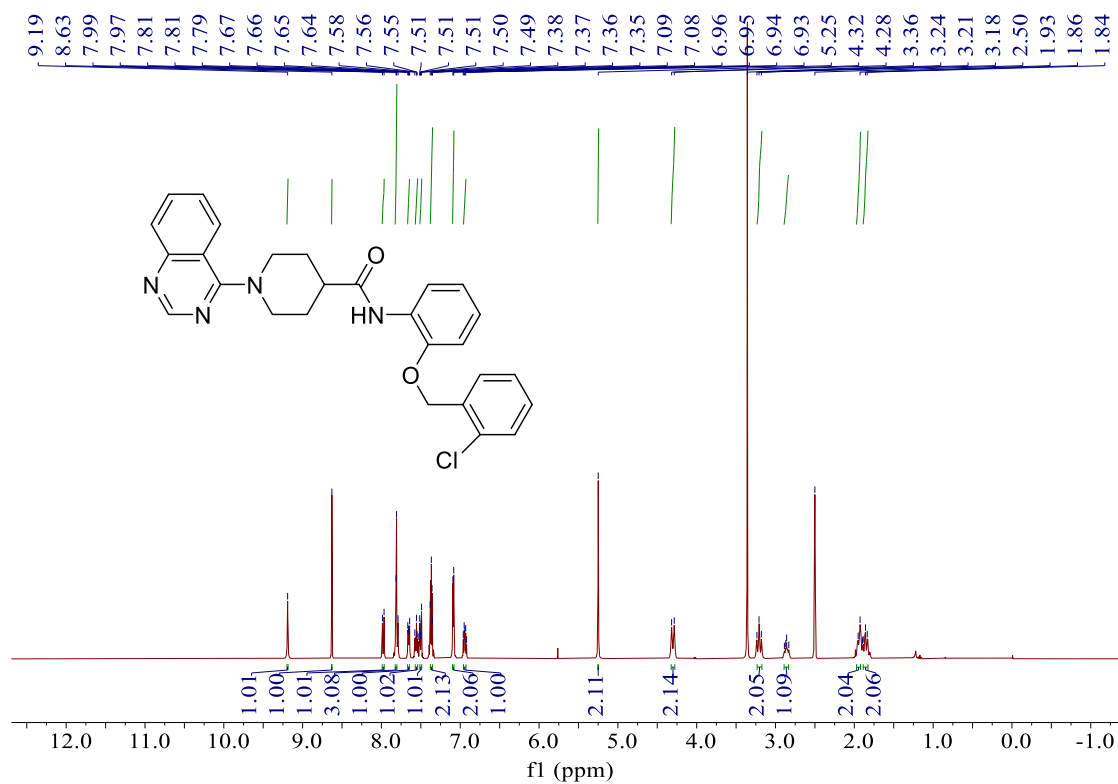


Figure S30. HRMS spectrum of compound III-9



T: FTMS + p ESI Full ms [100.0000-1000.0000]

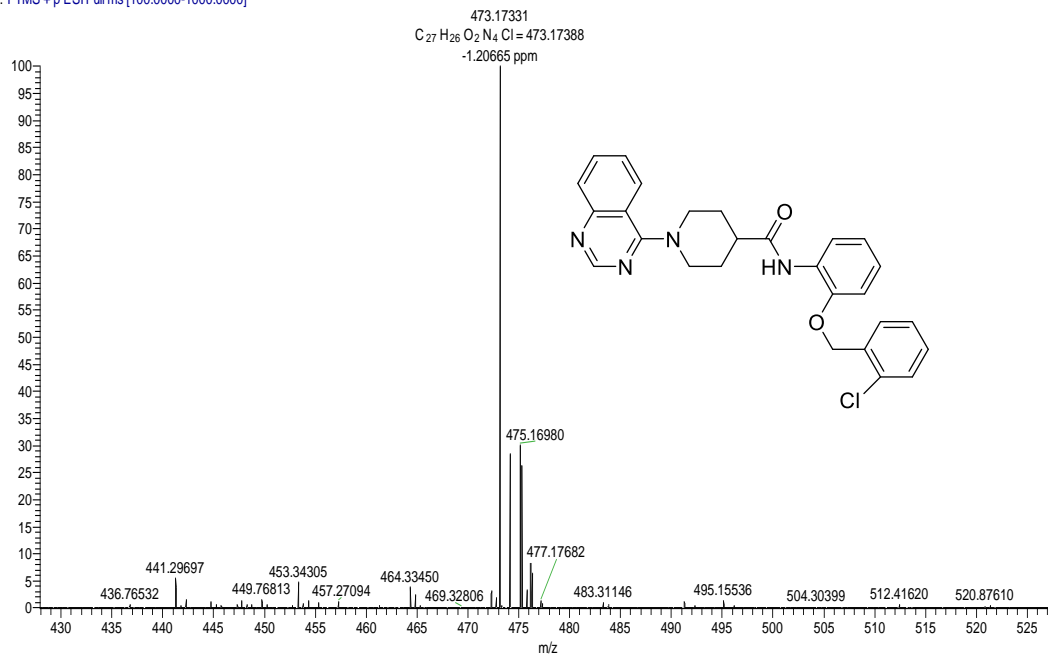


Figure S33. HRMS spectrum of compound III-10

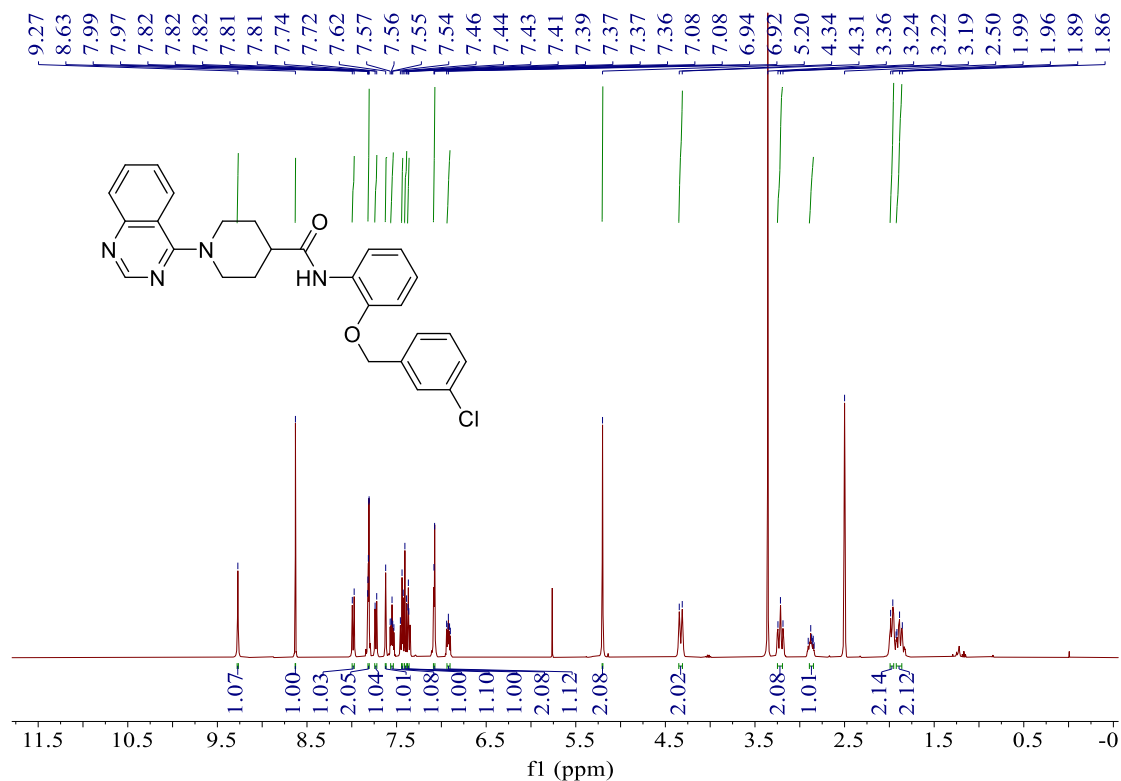
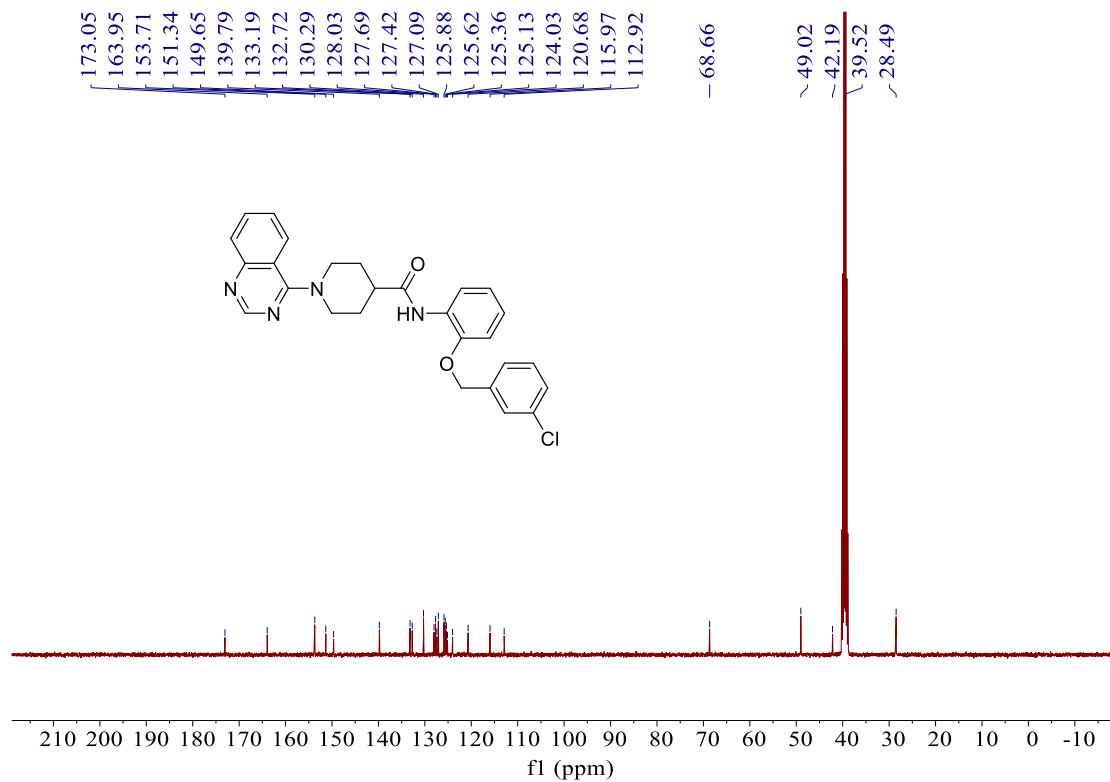
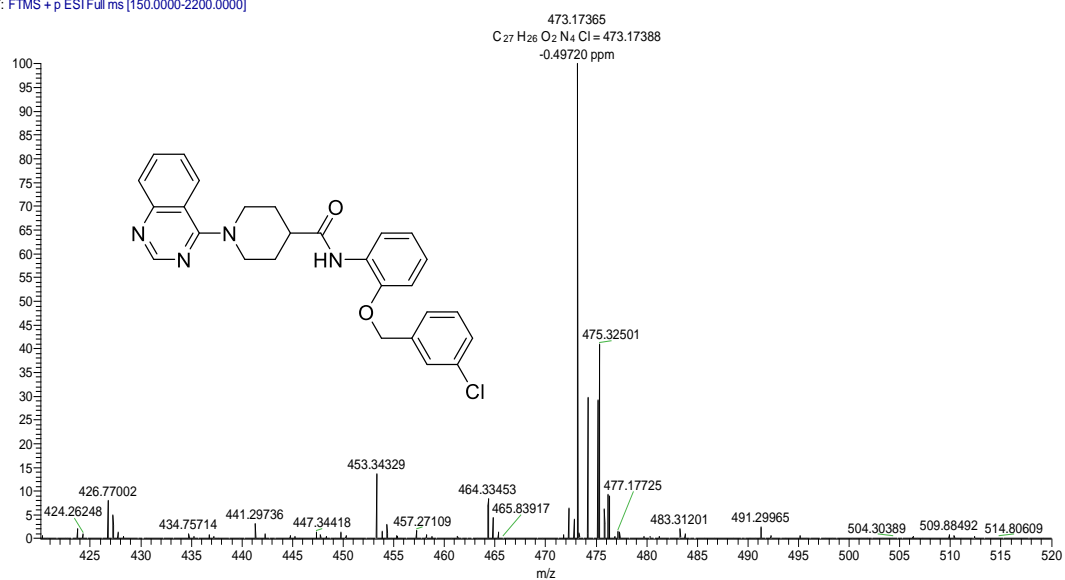
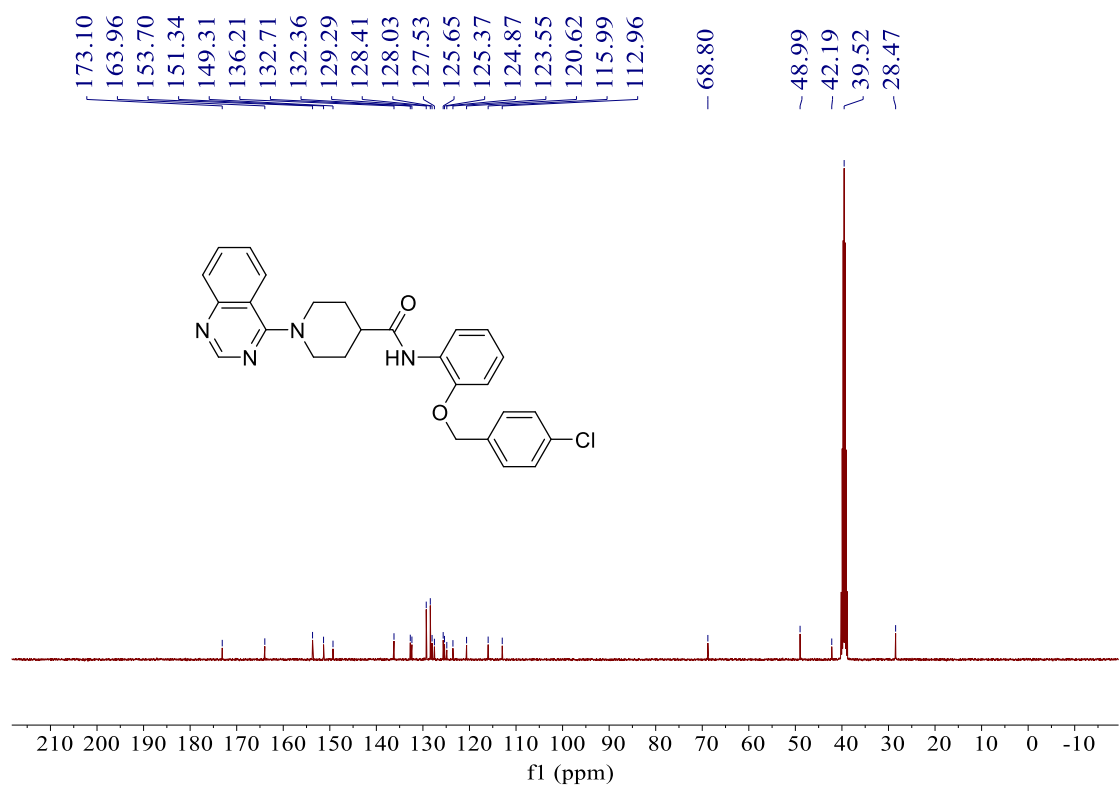
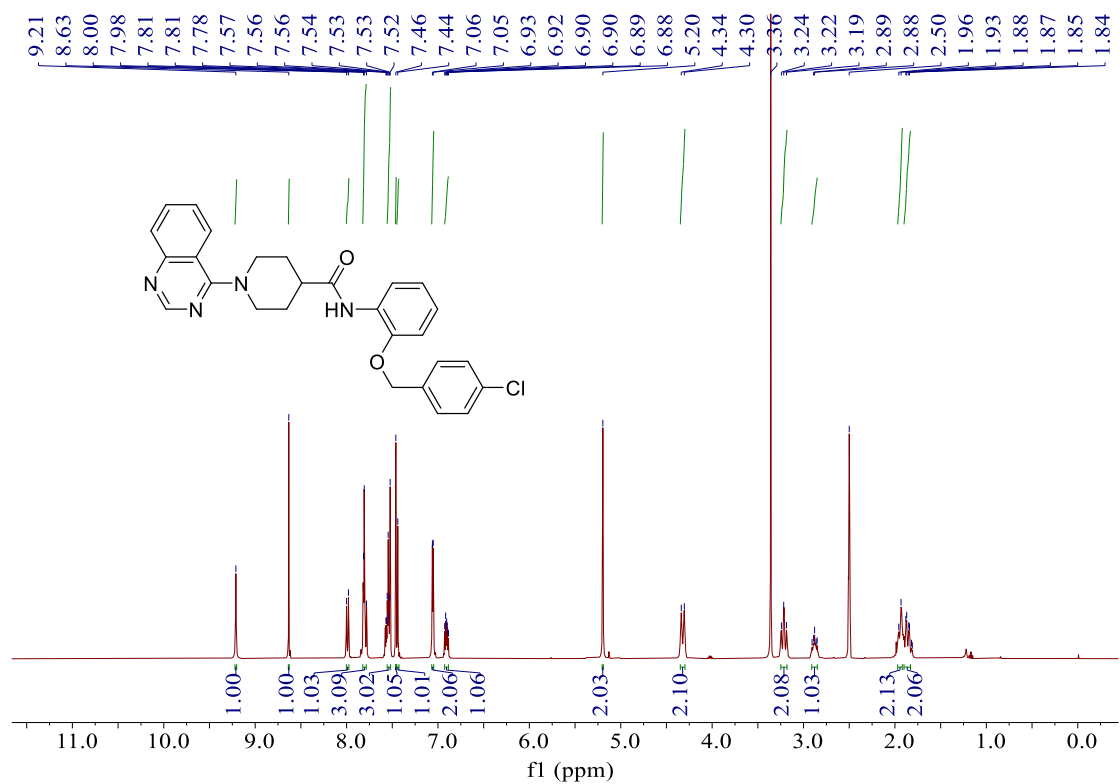


Figure S34. ¹H NMR spectrum of compound III-11 (DMSO-d₆)



119#43 RT: 0.43 AV: 1 NL: 7.81E7
T: FTMS + p ESI Full ms [150.0000-2200.0000]





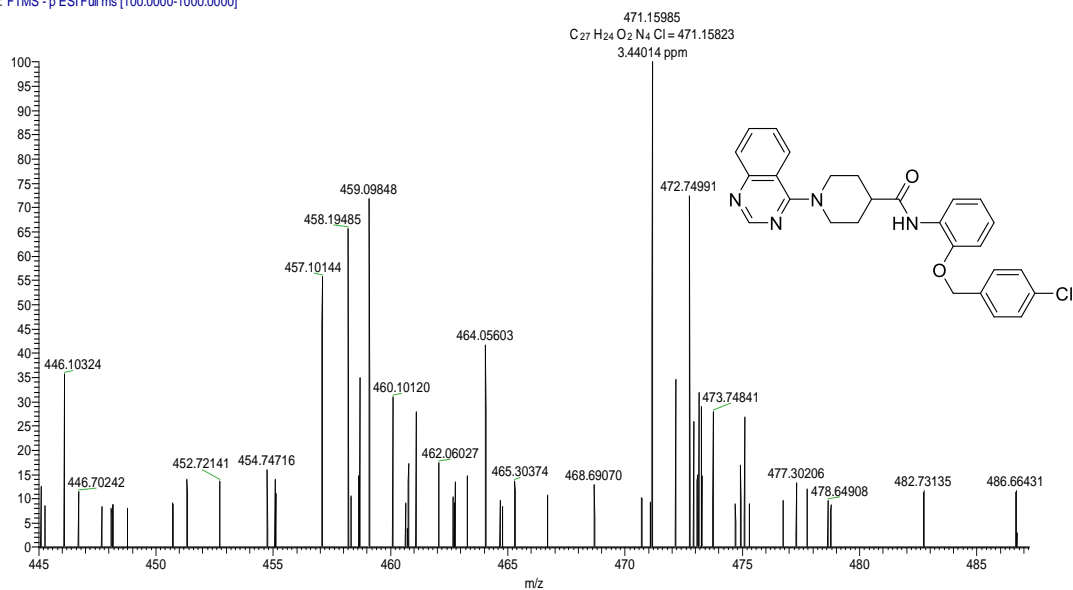


Figure S39. HRMS spectrum of compound III-12

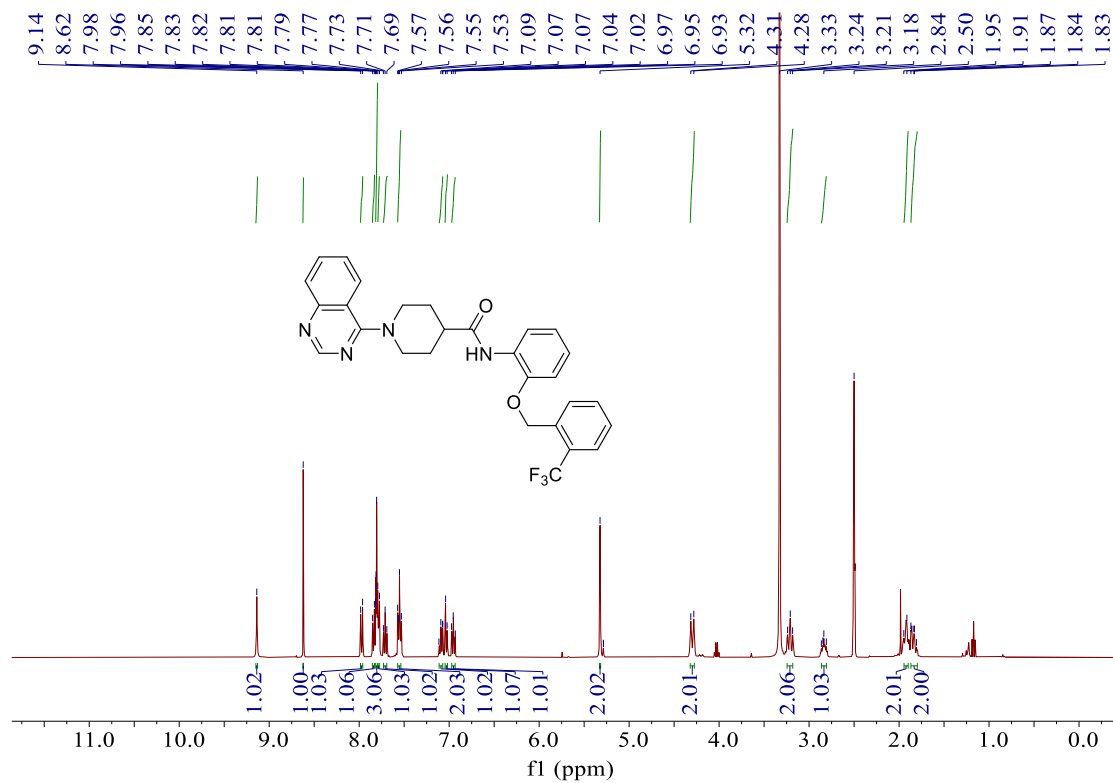


Figure S40. ¹H NMR spectrum of compound III-13 (DMSO-d₆)

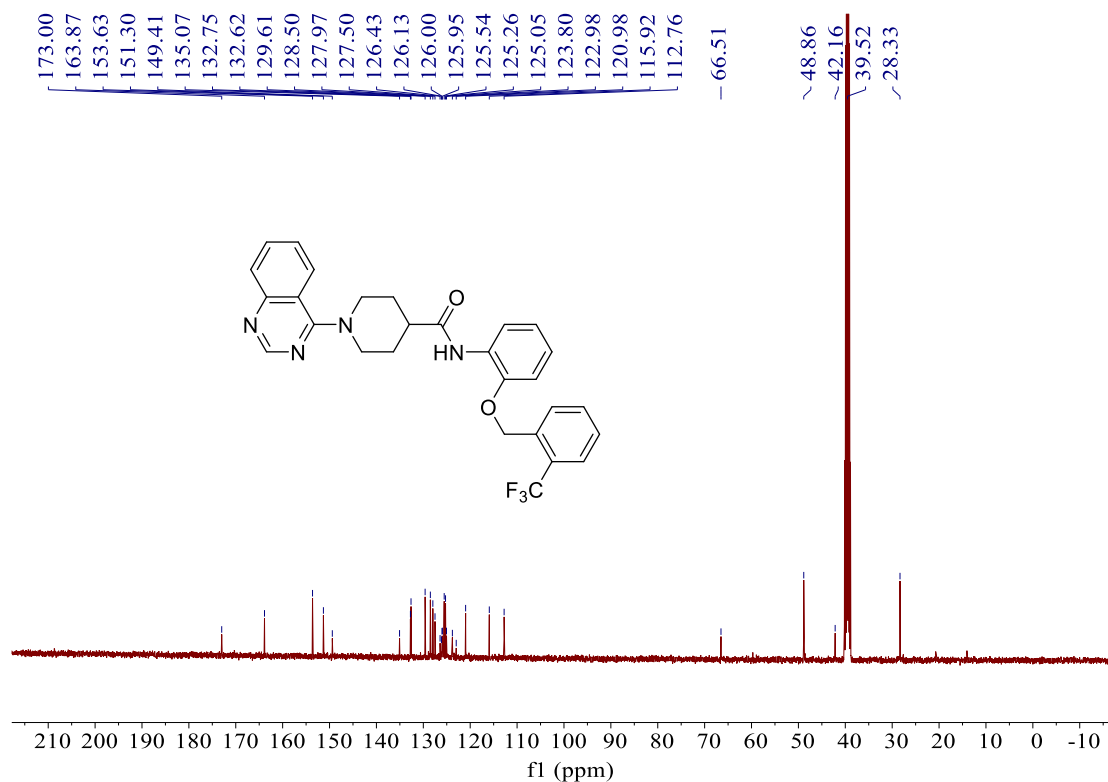


Figure S41. ^{13}C NMR spectrum of compound III-13 (DMSO- d_6)

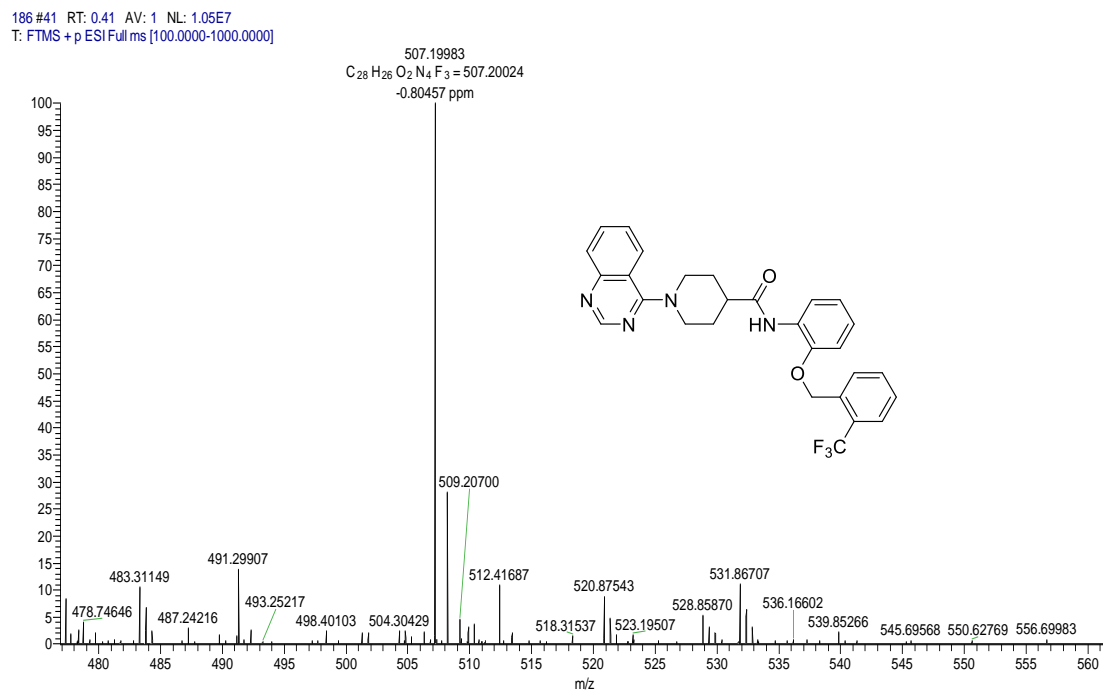
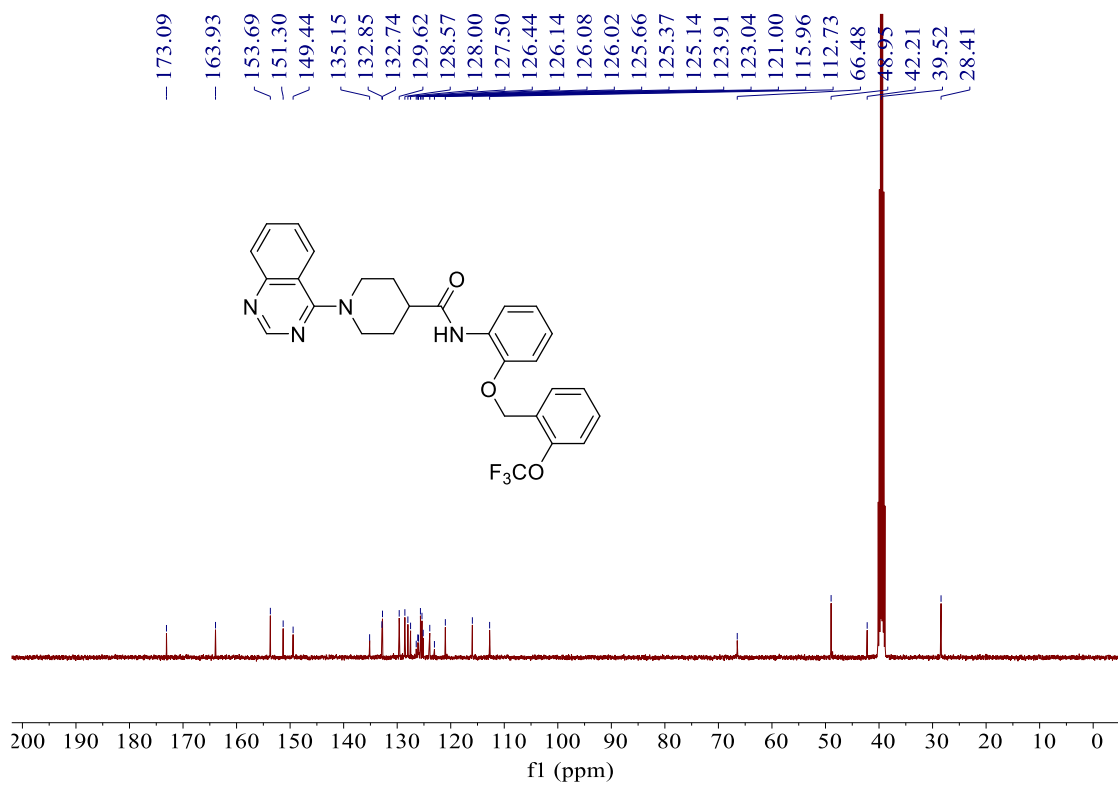
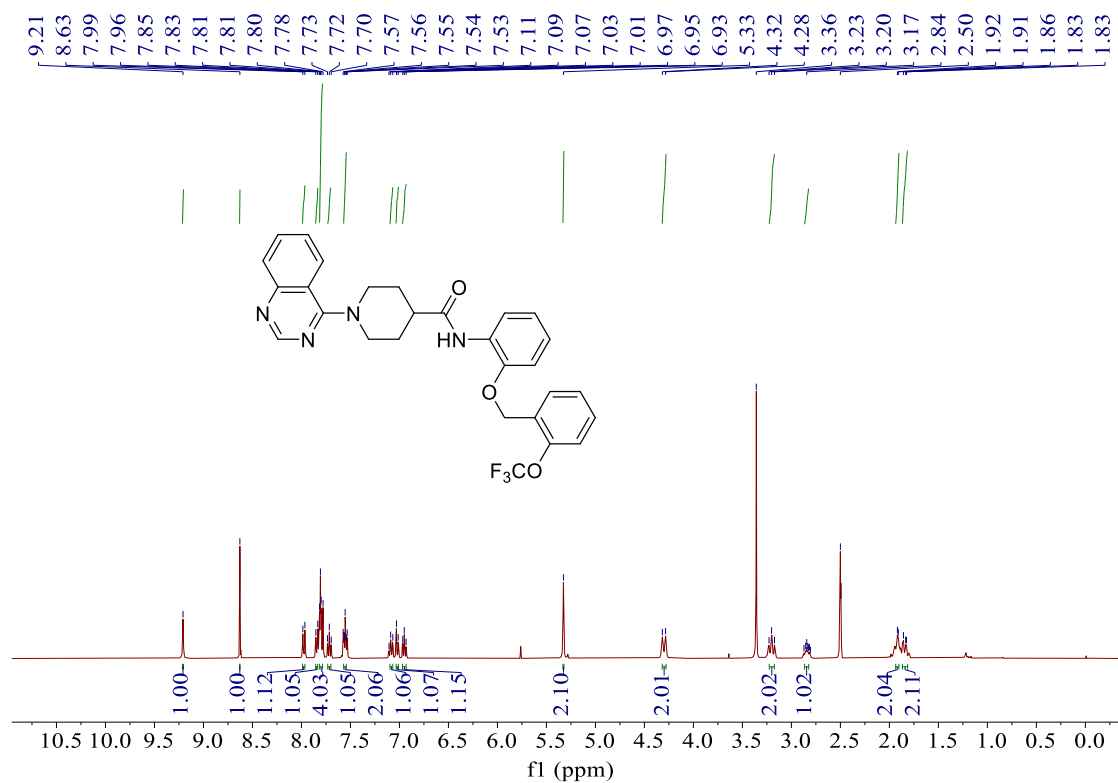


Figure S42. HRMS spectrum of compound III-13



113 #43 RT: 0.43 AV: 1 NL: 1.74E5
T: FTMS + p ESI Full ms [150.0000-2200.0000]

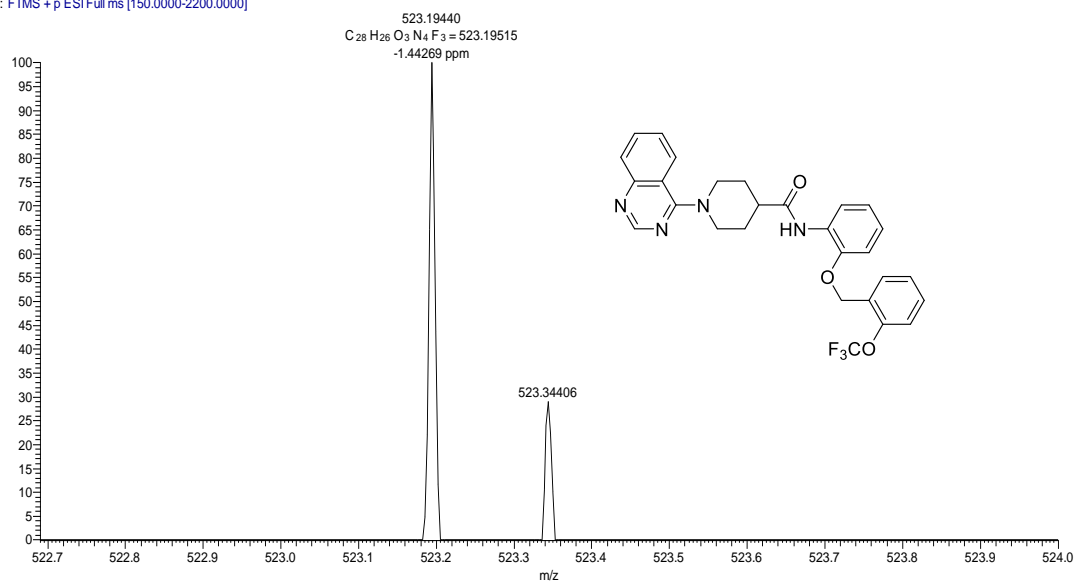


Figure S45. HRMS spectrum of compound III-14

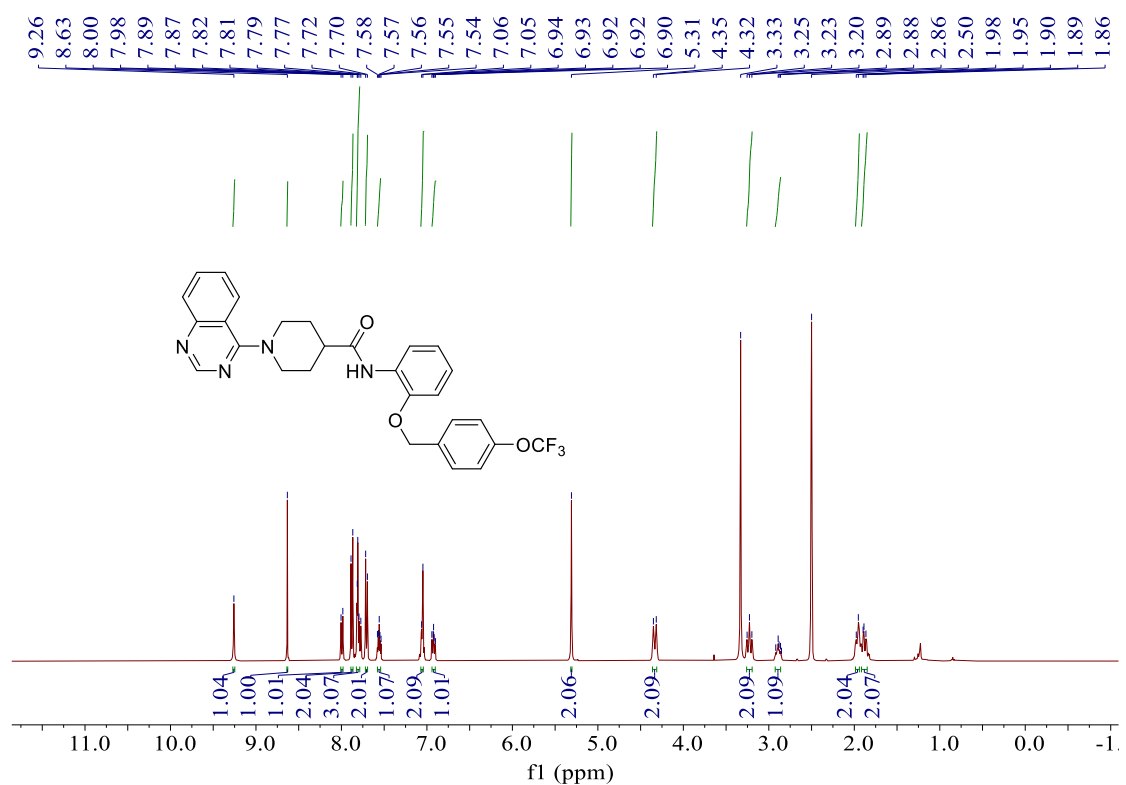


Figure S46. ¹H NMR spectrum of compound III-15 (DMSO-*d*₆)

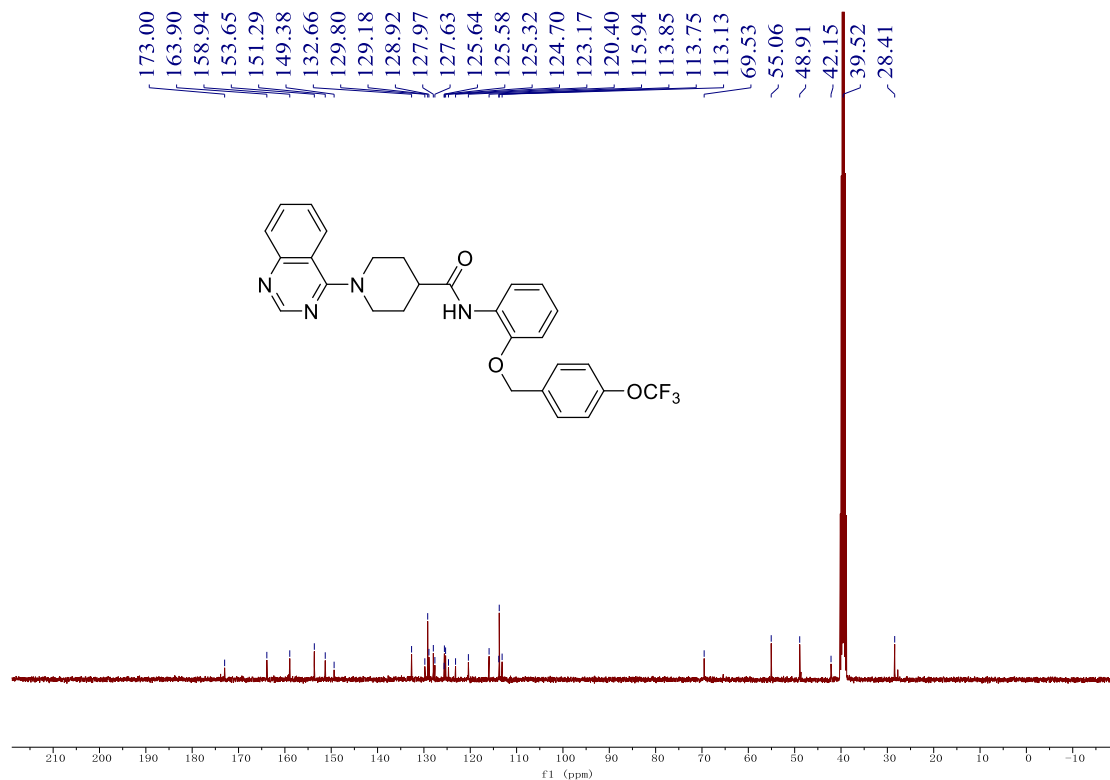


Figure S47. ¹³C NMR spectrum of compound III-15 (DMSO-*d*₆)

115#39 RT: 0.39 AV: 1 NL: 2.68E7
T: FTMS + p ESI Full ms [150.0000-2200.0000]

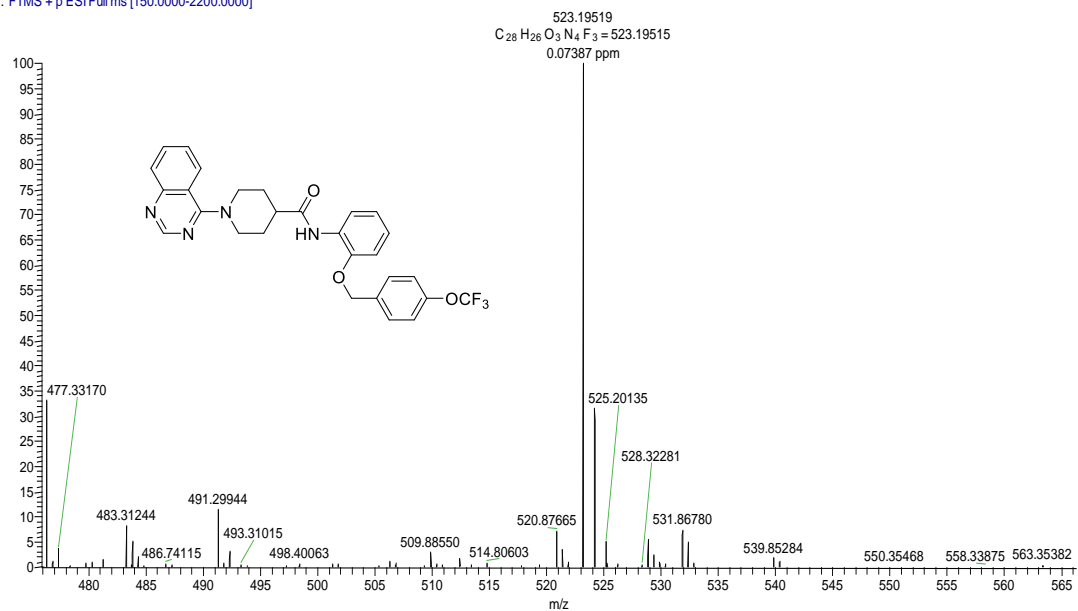
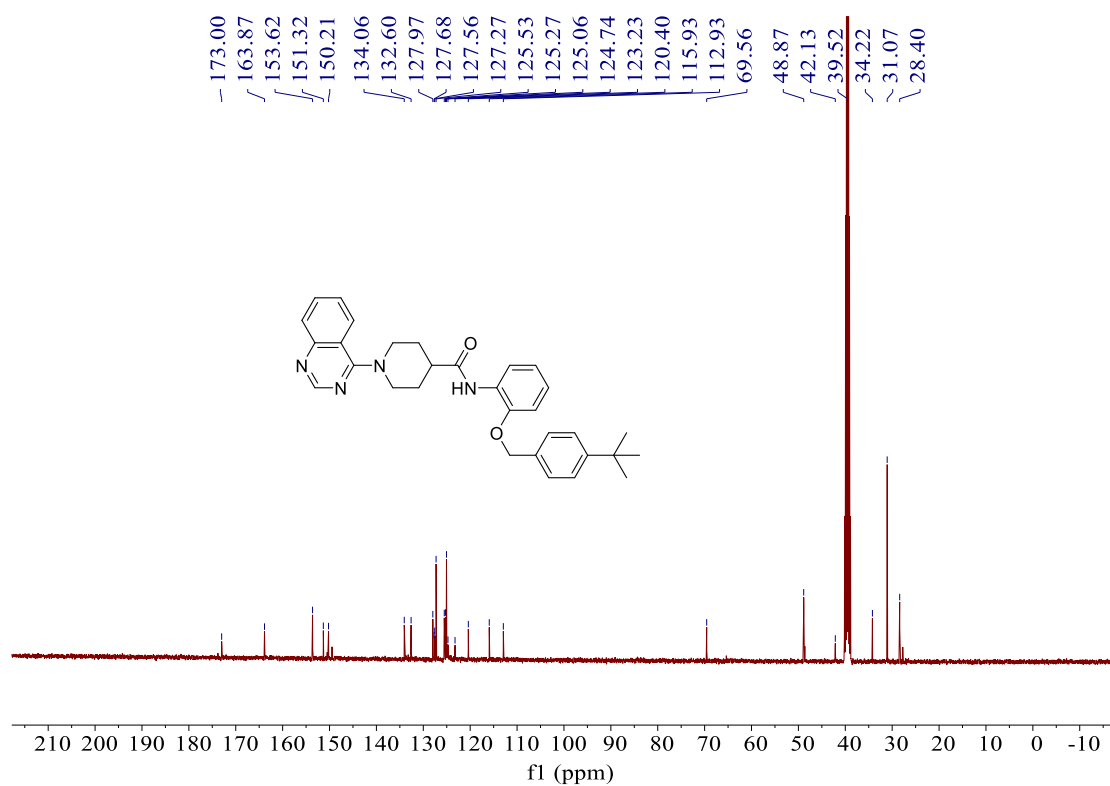
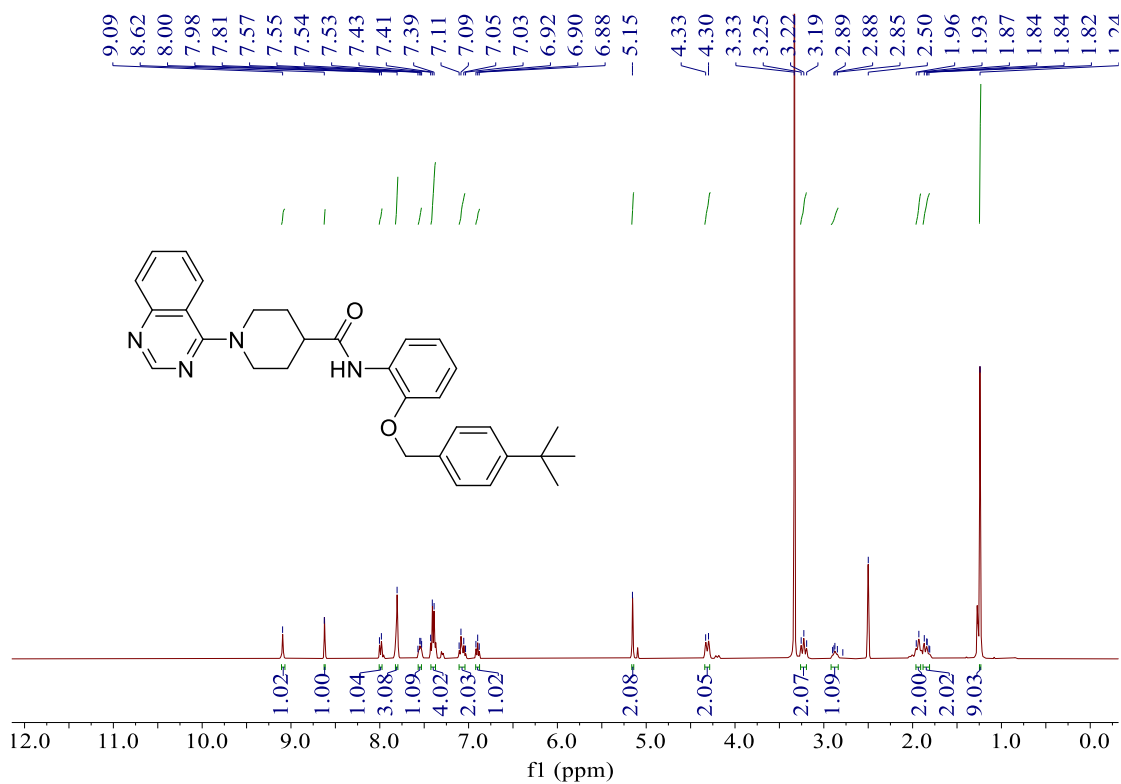


Figure S48. HRMS spectrum of compound III-15



190 #63 RT: 0.63 AV: 1 NL: 2.27E7
T: FTMS + p ESI Full ms [100.0000-1000.0000]

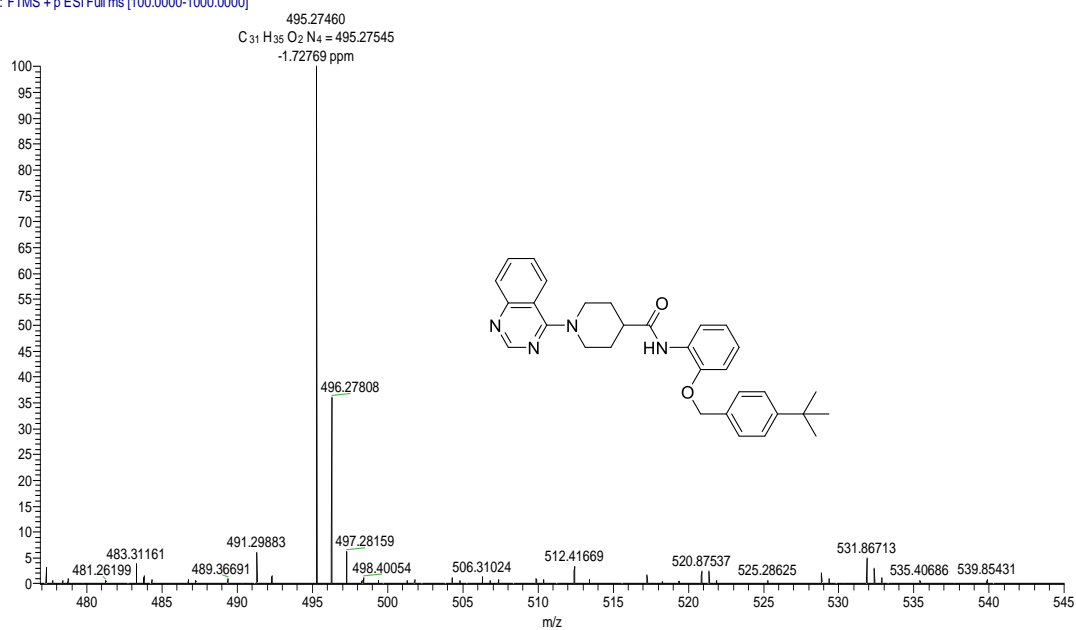


Figure S51. HRMS spectrum of compound III-16

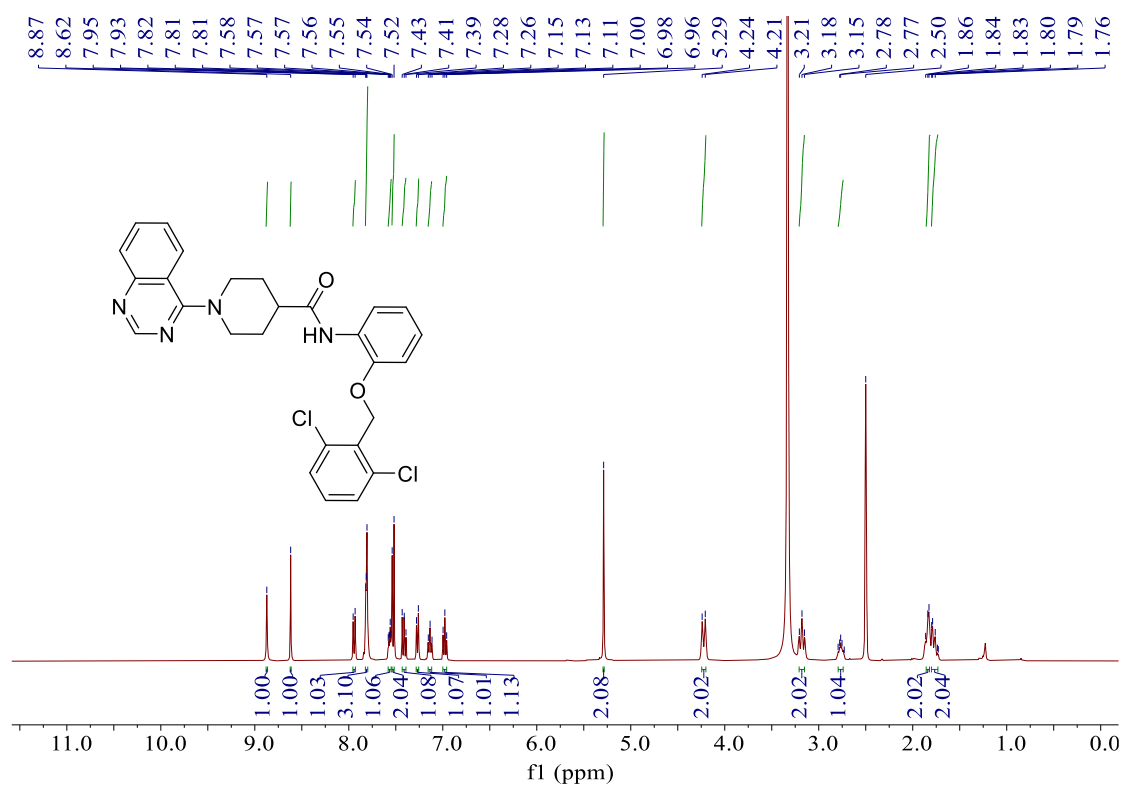


Figure S52. ¹H NMR spectrum of compound III-17 (DMSO-*d*₆)

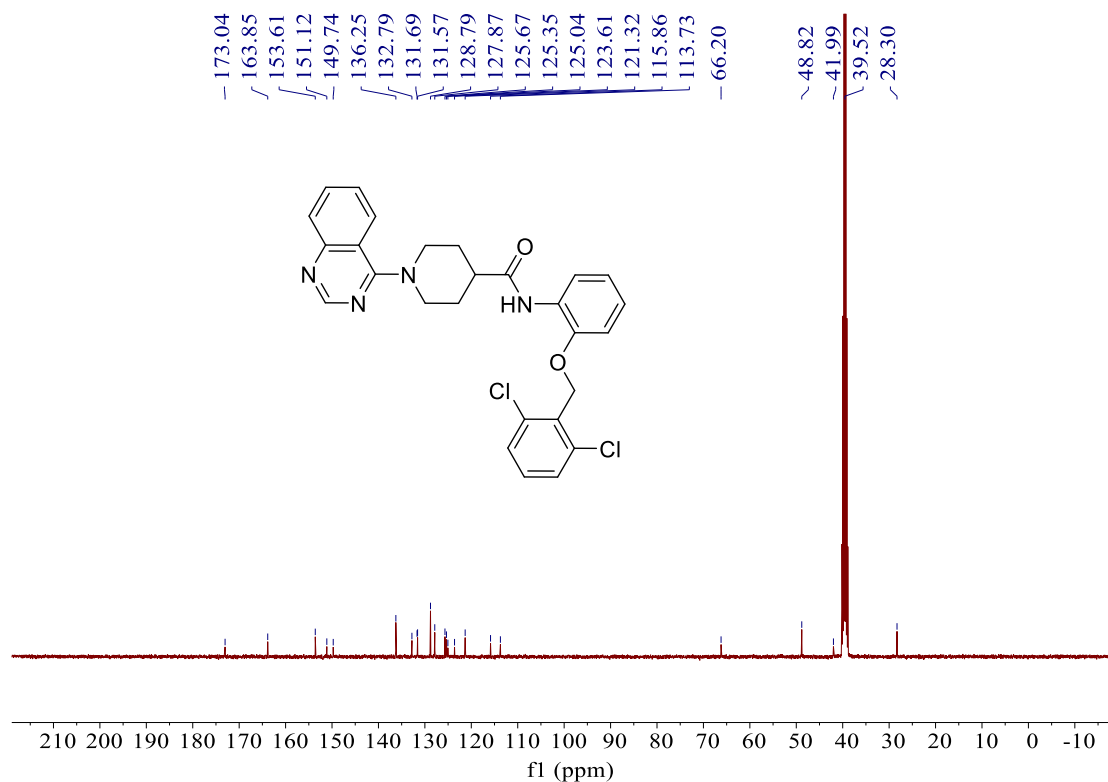


Figure S53. ¹³C NMR spectrum of compound III-17 (DMSO-*d*₆)

176 #47 RT: 0.47 AV: 1 NL: 8.85E6
T: FTMS + p ESI Full ms [100.0000-1000.0000]

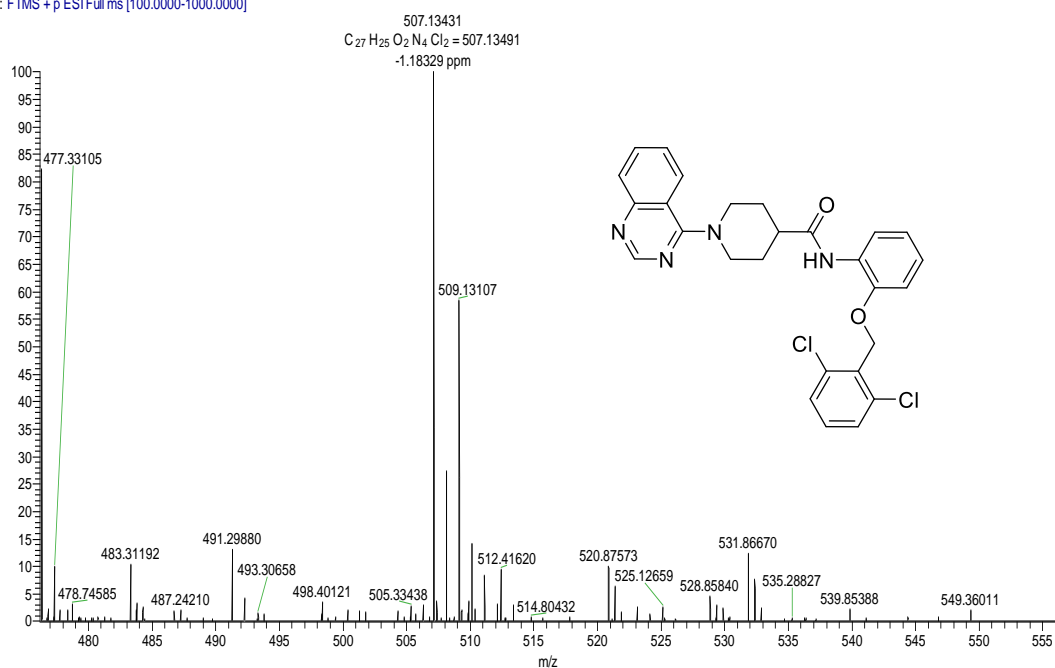


Figure S54. HRMS spectrum of compound III-17

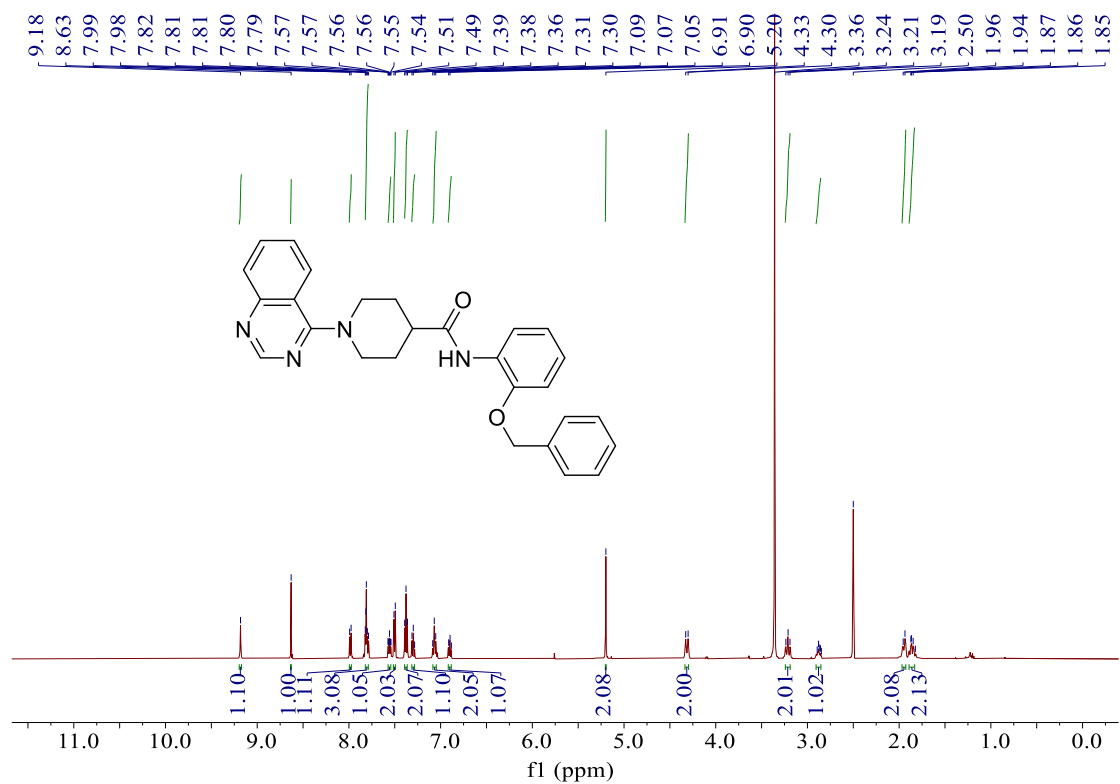


Figure S55. ^1H NMR spectrum of compound III-18 ($\text{DMSO}-d_6$)

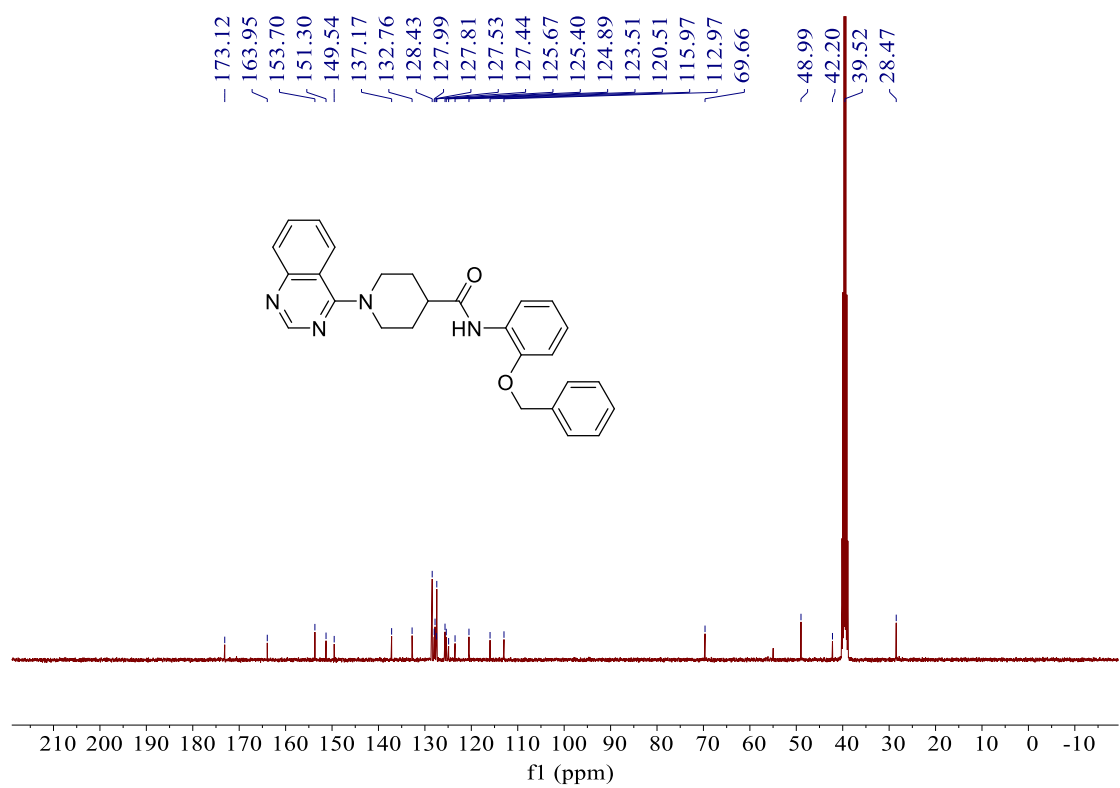


Figure S56. ^{13}C NMR spectrum of compound III-18 ($\text{DMSO}-d_6$)

178 #45 RT: 0.45 AV: 1 NL: 5.25E7
T: FTMS + p ESI Full ms [100.0000-1000.0000]

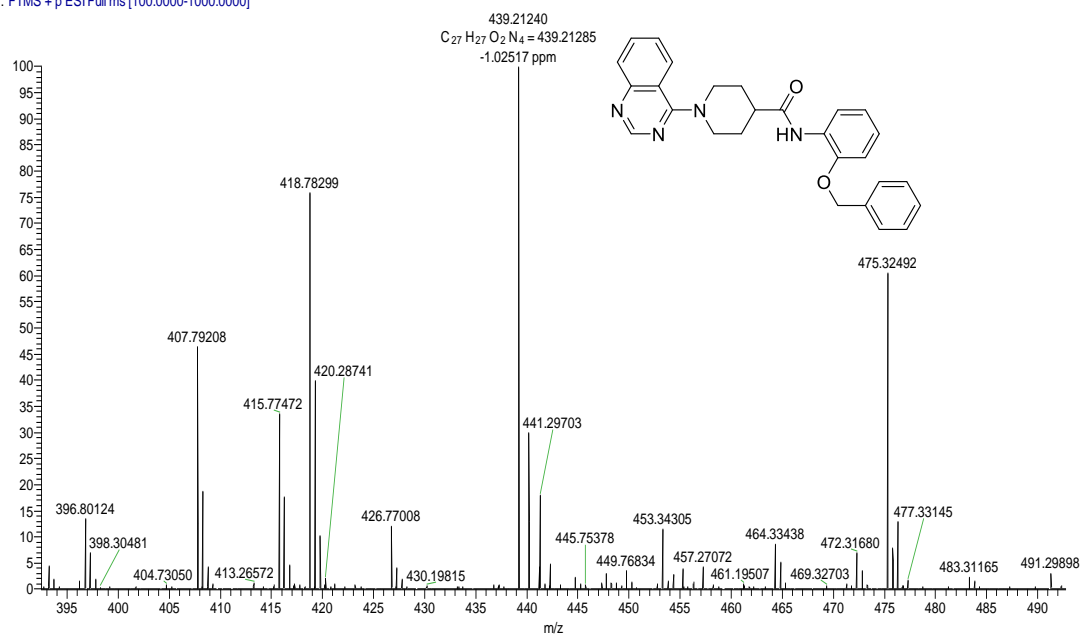


Figure S57. HRMS spectrum of compound III-18

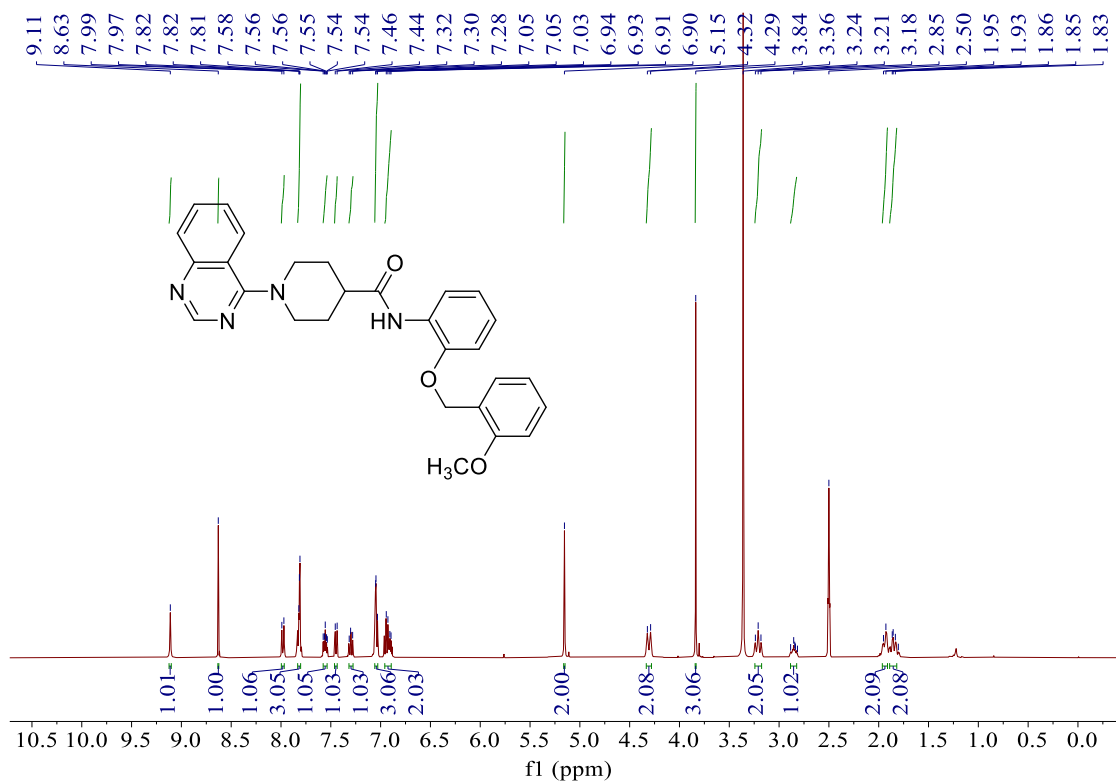


Figure S58. ¹H NMR spectrum of compound III-19 (DMSO-*d*₆)

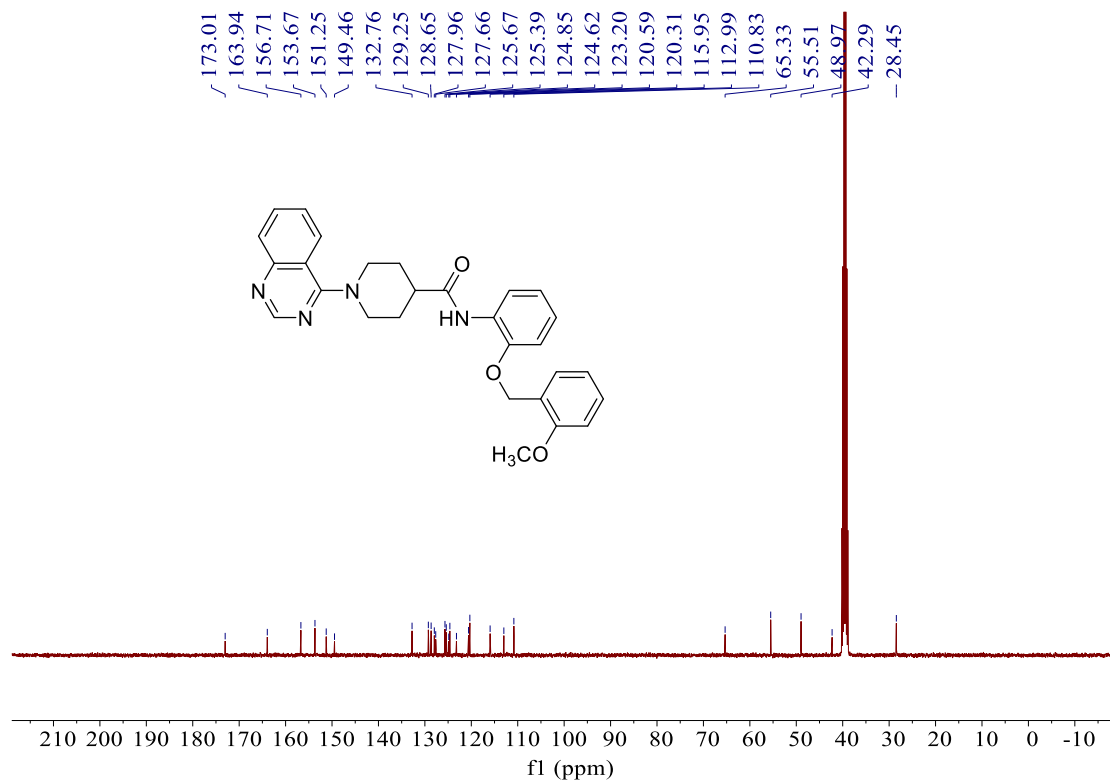


Figure S59. ¹³C NMR spectrum of compound III-19 (DMSO-*d*₆)

173 #47 RT: 0.47 AV: 1 NL: 2.51E7
T: FTMS + p ESI Full ms [100.0000-1000.0000]

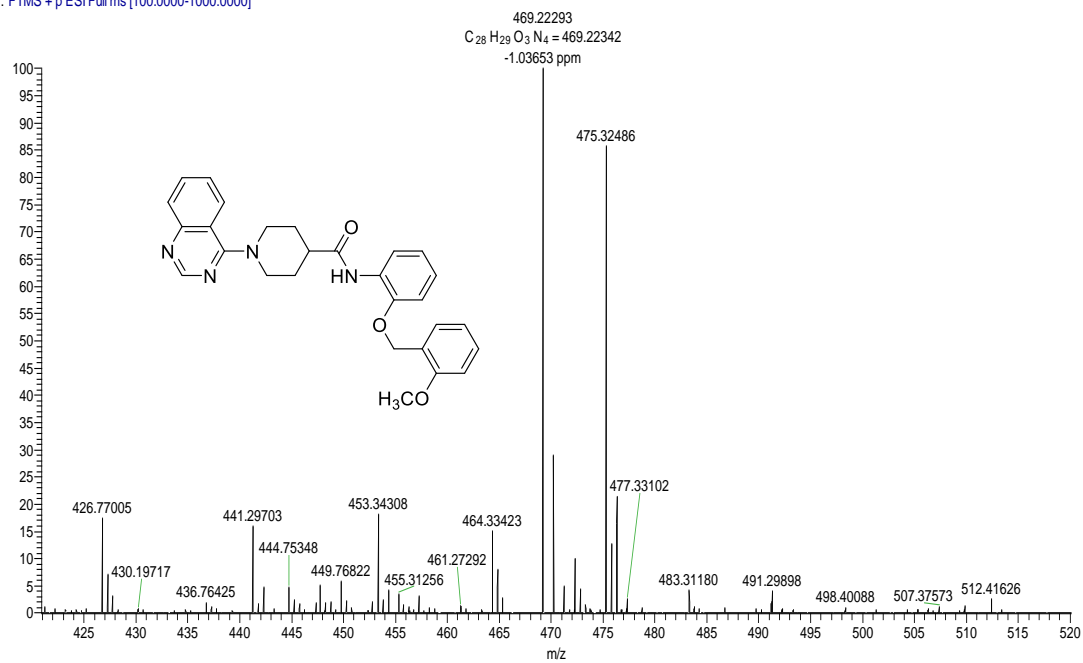


Figure S60. HRMS spectrum of compound III-19

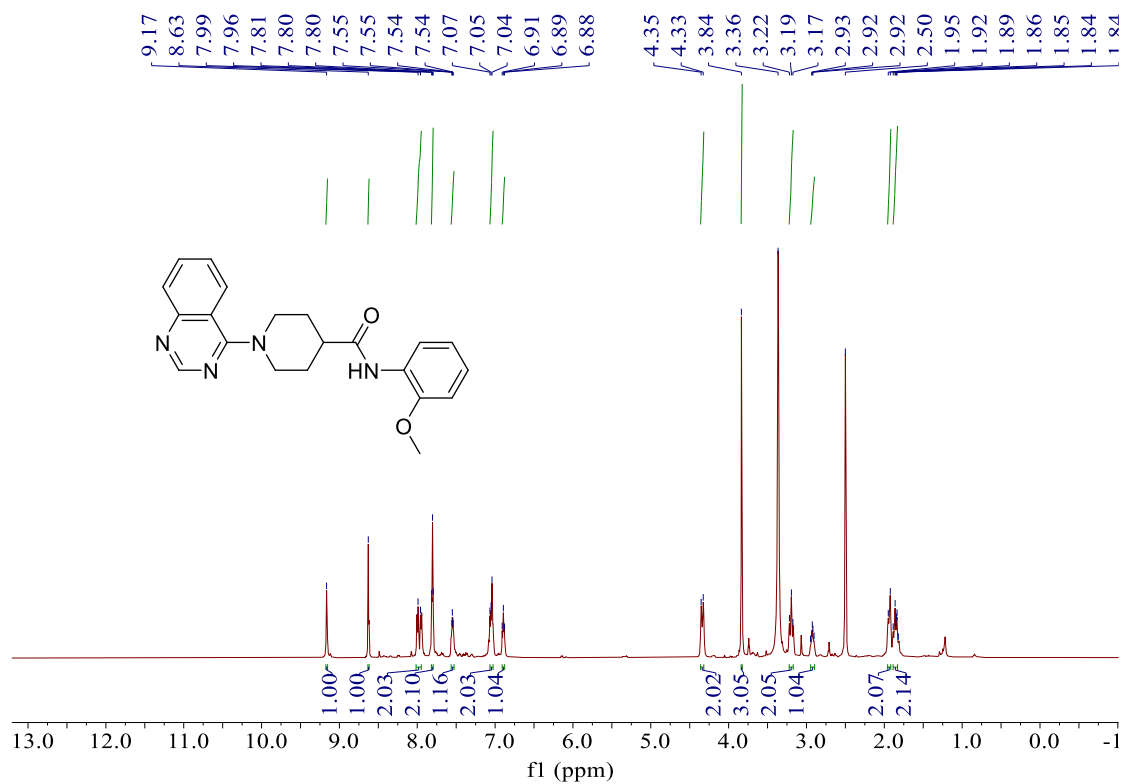


Figure S61. ¹H NMR spectrum of compound III-20 (DMSO-*d*₆)

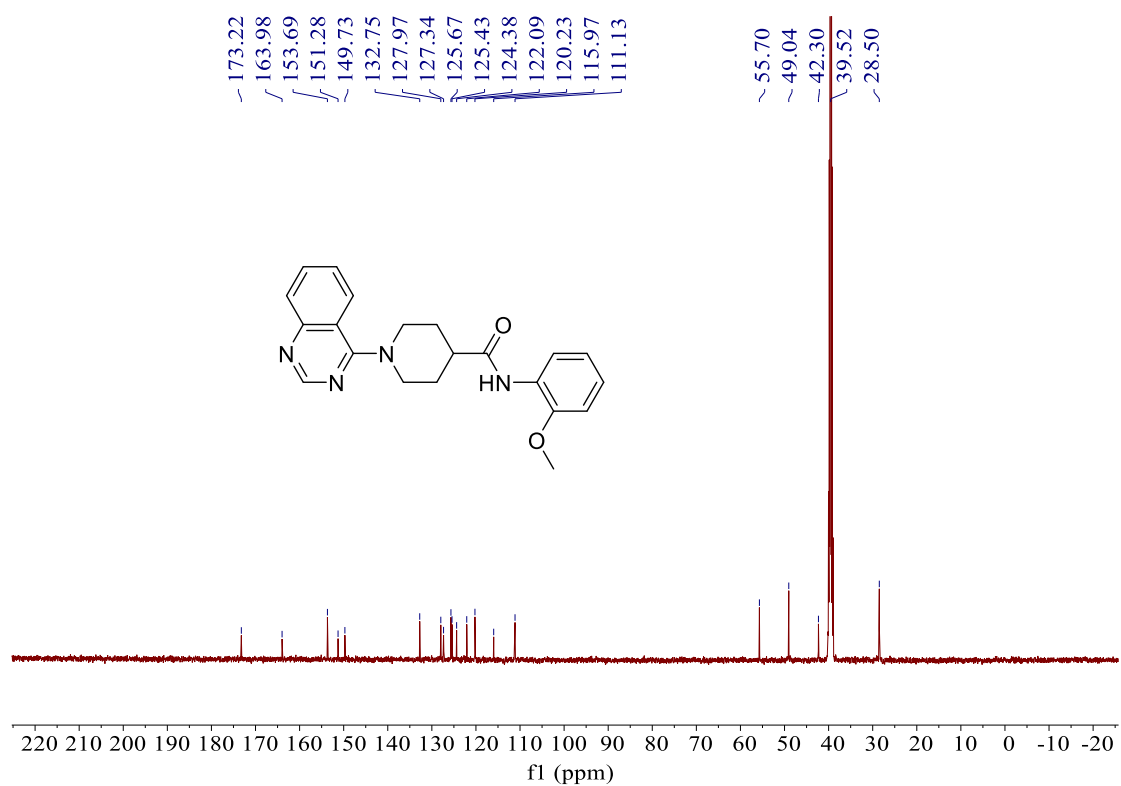


Figure S62. ¹³C NMR spectrum of compound III-20 (DMSO-*d*₆)

184 #39 RT: 0.39 AV: 1 NL: 1.29E8
T: FTMS + p ESI Fullms [100.0000-1000.0000]

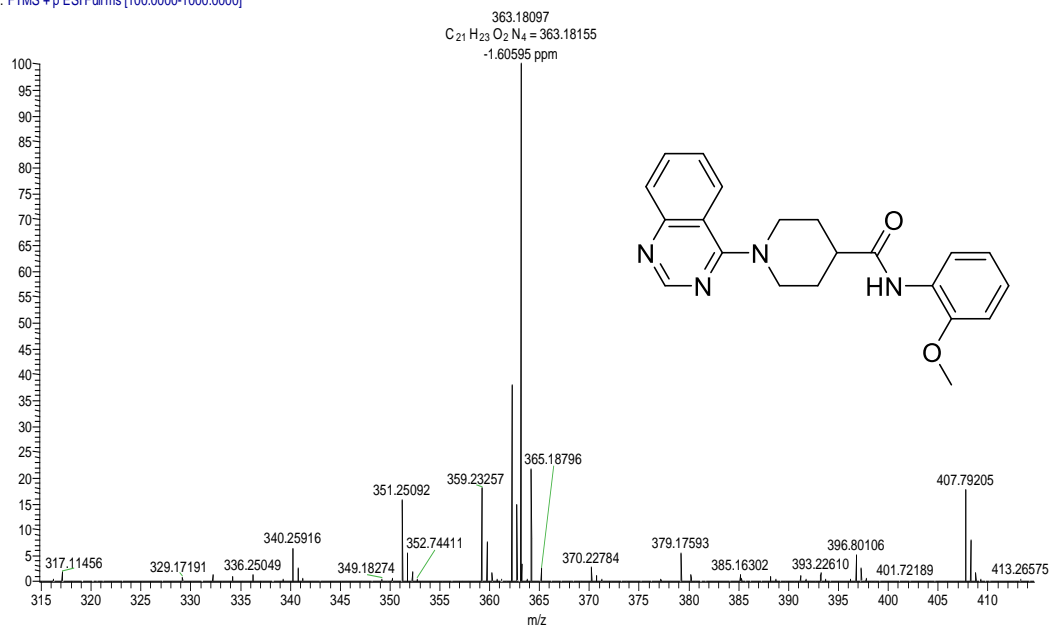


Figure S63. HRMS spectrum of compound III-20

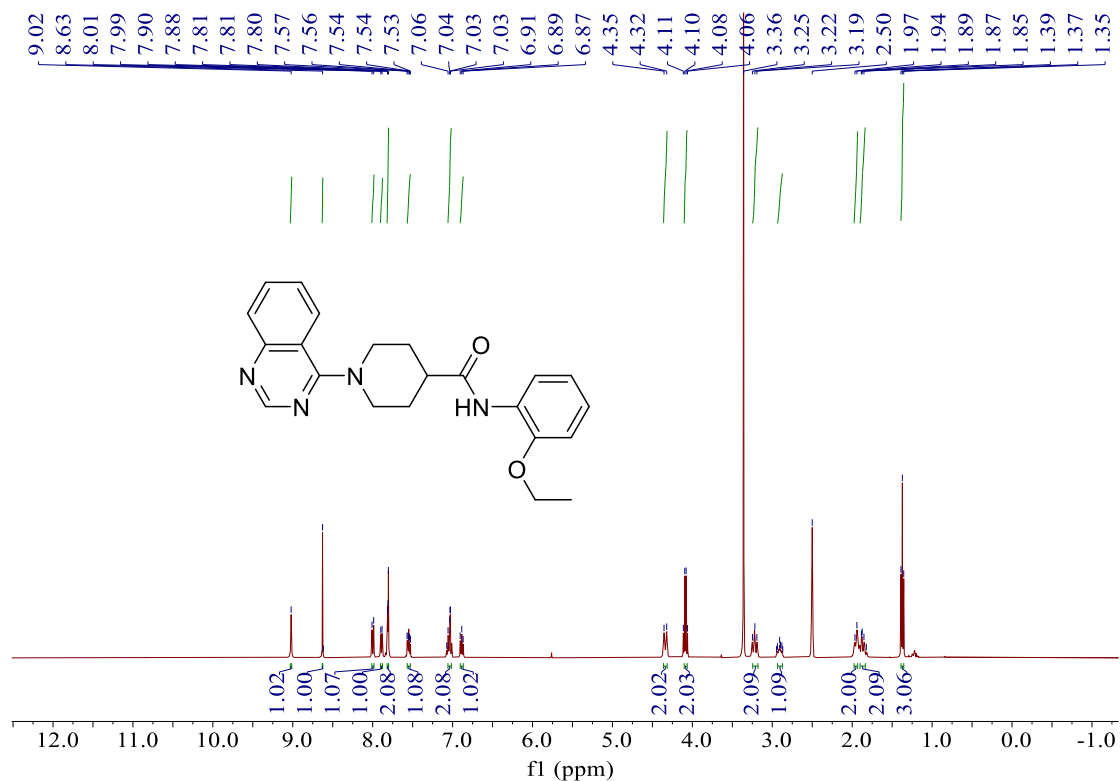


Figure S64. ¹H NMR spectrum of compound III-21 (DMSO-*d*₆)

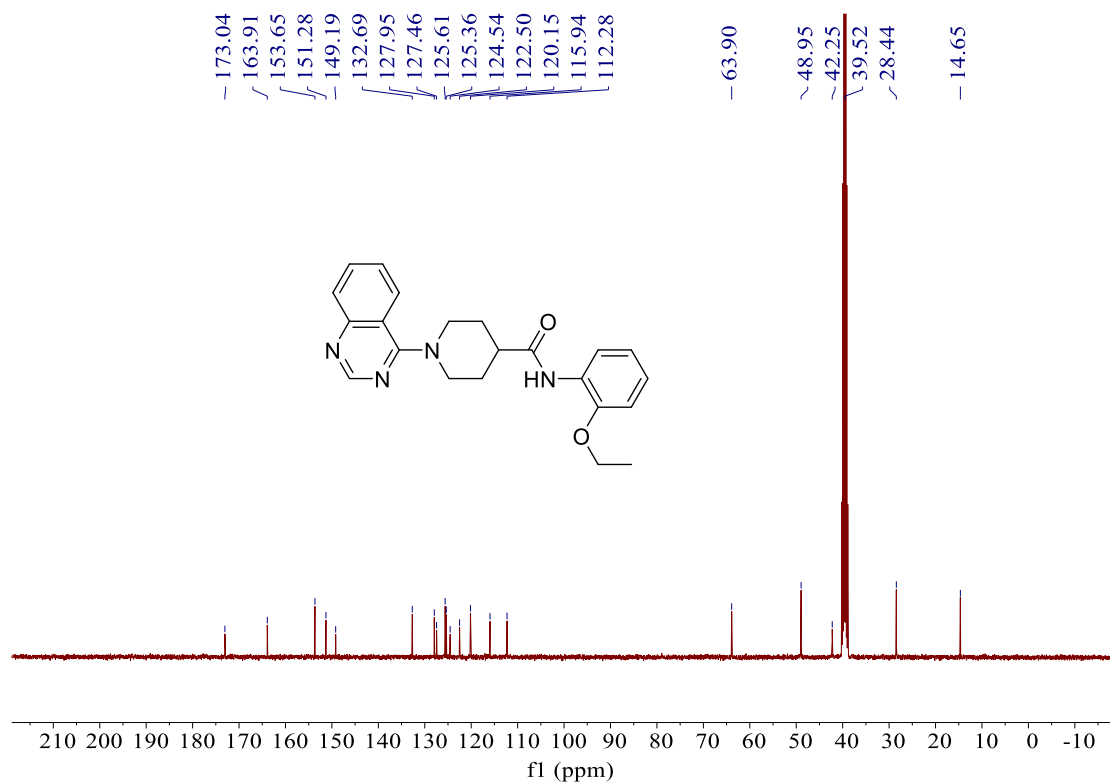


Figure S65. ¹³C NMR spectrum of compound III-21 (DMSO-*d*₆)

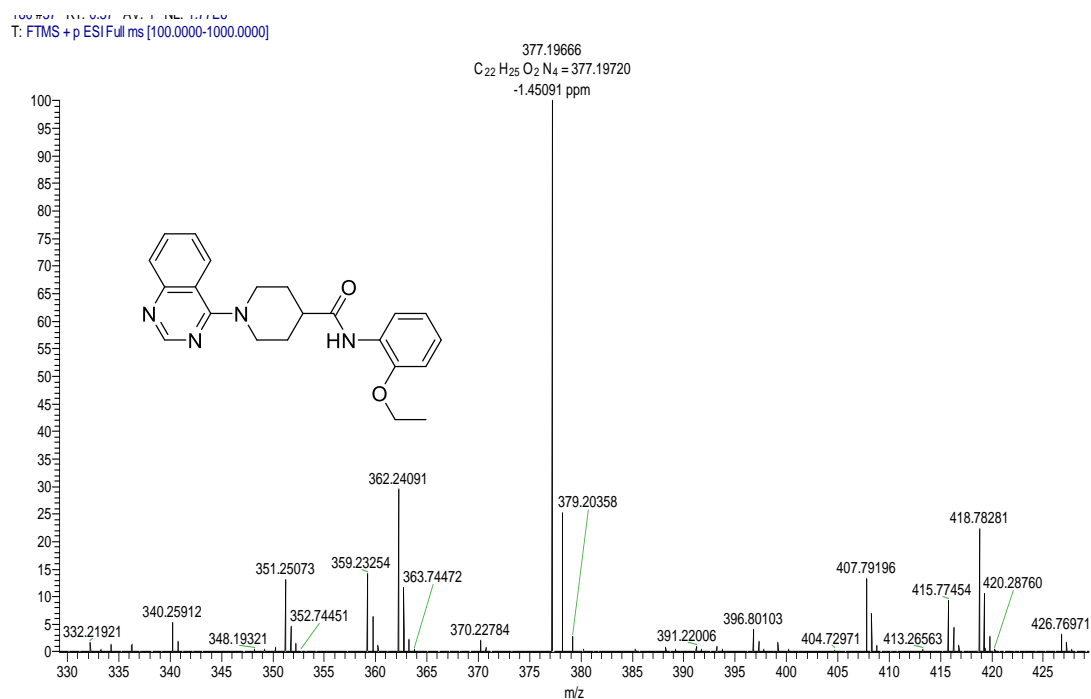


Figure S66. HRMS spectrum of compound III-21

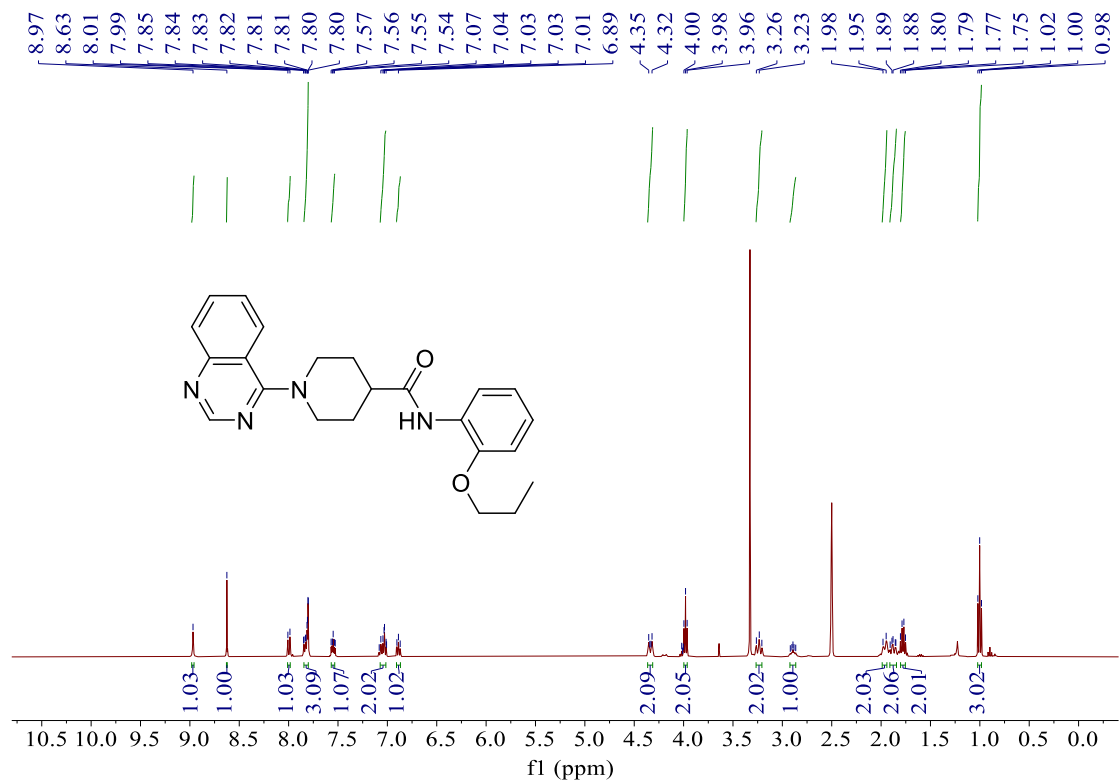


Figure S67. ^1H NMR spectrum of compound III-22 ($\text{DMSO-}d_6$)

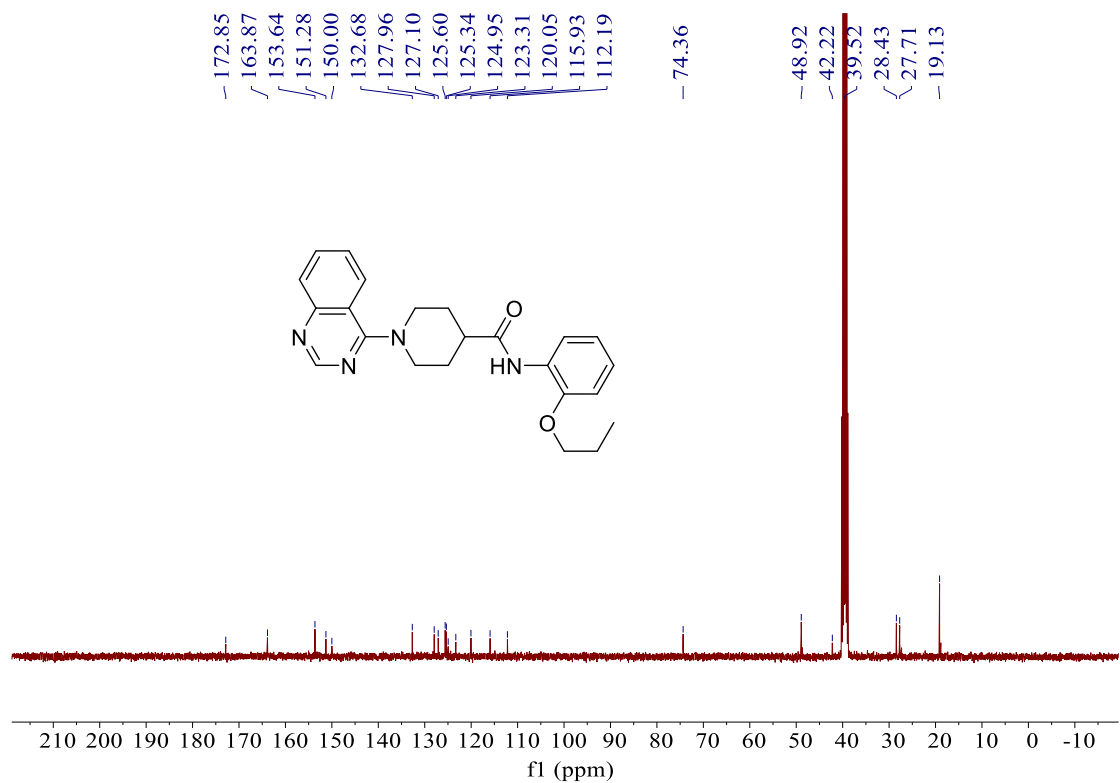


Figure S68. ^{13}C NMR spectrum of compound III-22 ($\text{DMSO-}d_6$)

118 #37 RT: 0.38 AV: 1 NL: 8.38E7
T: FTMS + p ESI Full ms [150.0000-2200.0000]

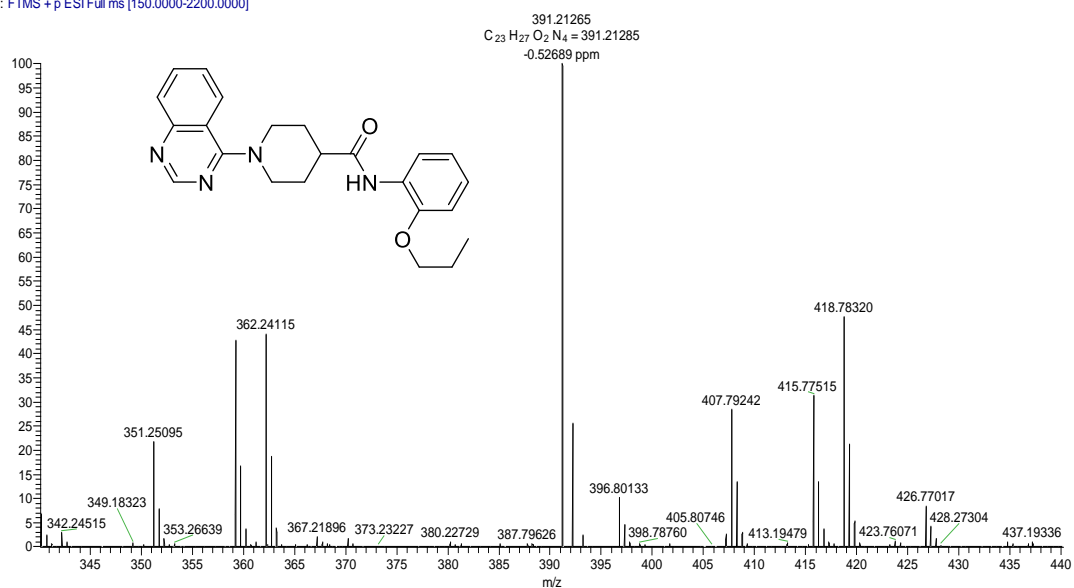


Figure S69. HRMS spectrum of compound III-22

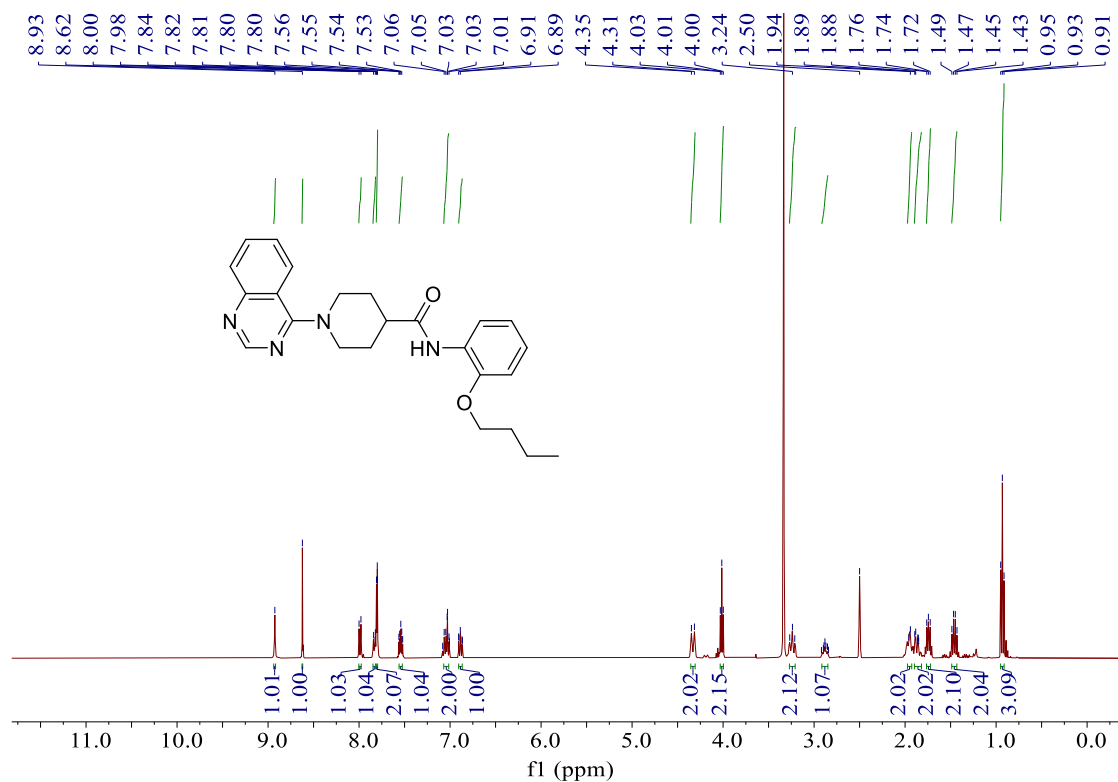


Figure S70. ¹H NMR spectrum of compound III-23 (DMSO-*d*₆)

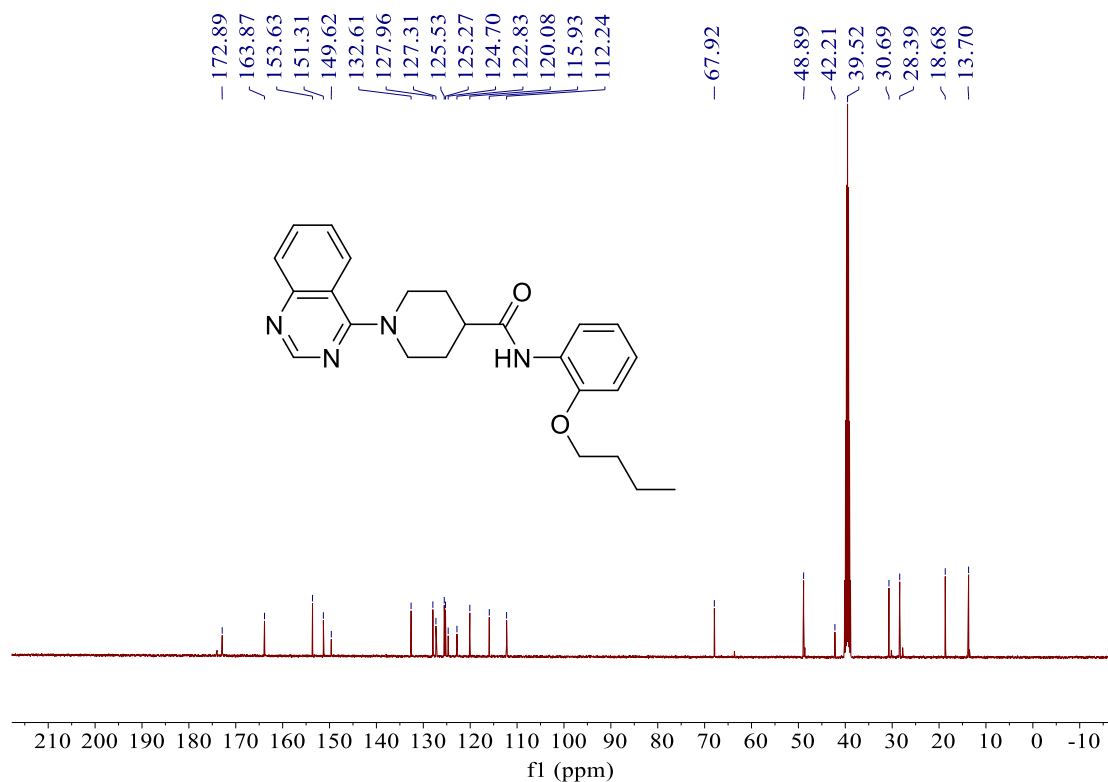


Figure S71. ¹³C NMR spectrum of compound III-23 (DMSO-*d*₆)

191 #45 RT: 0.45 AV: 1 NL: 6.95E7
T: FTMS + p ESI Full ms [100.0000-1000.0000]

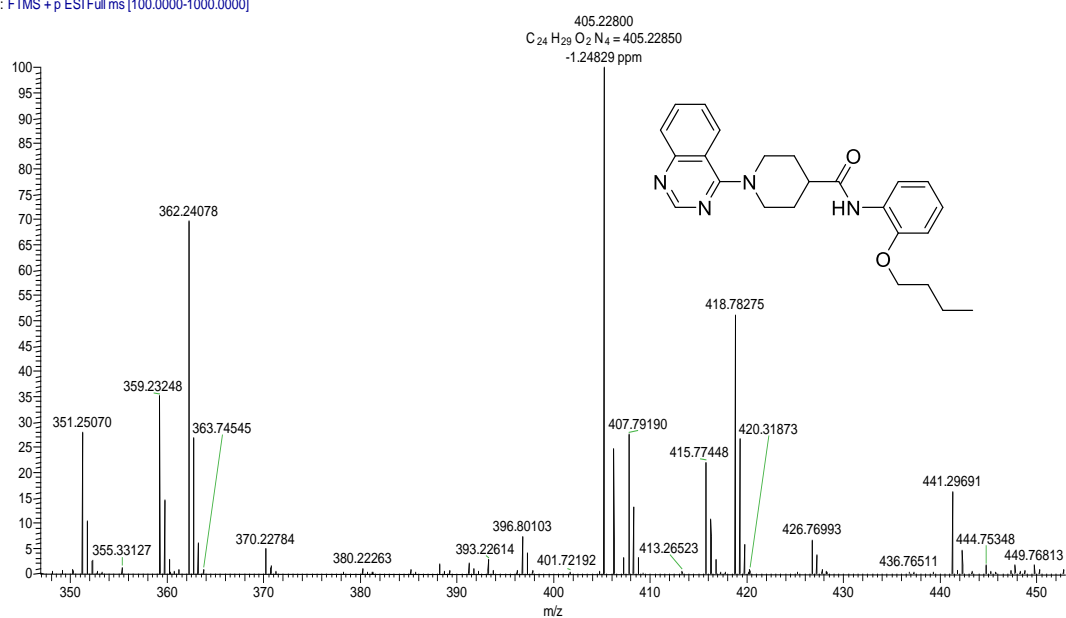


Figure S72. HRMS spectrum of compound III-23

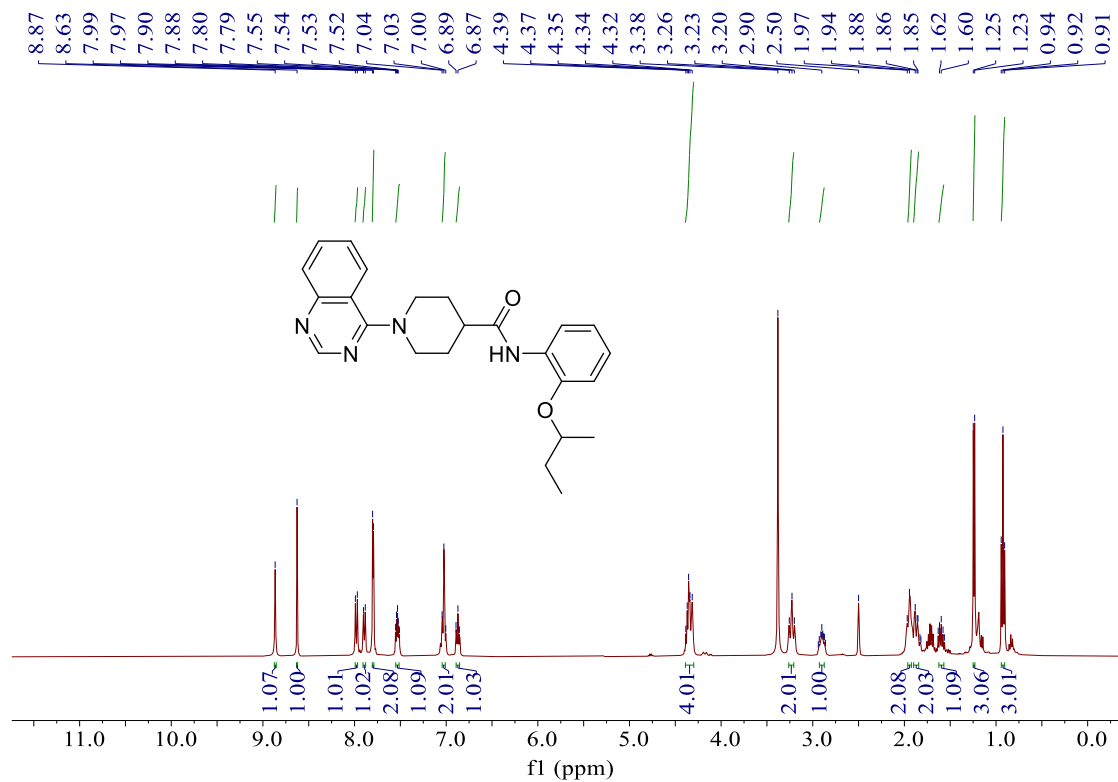


Figure S73. ¹H NMR spectrum of compound **III-24** (DMSO-*d*₆)

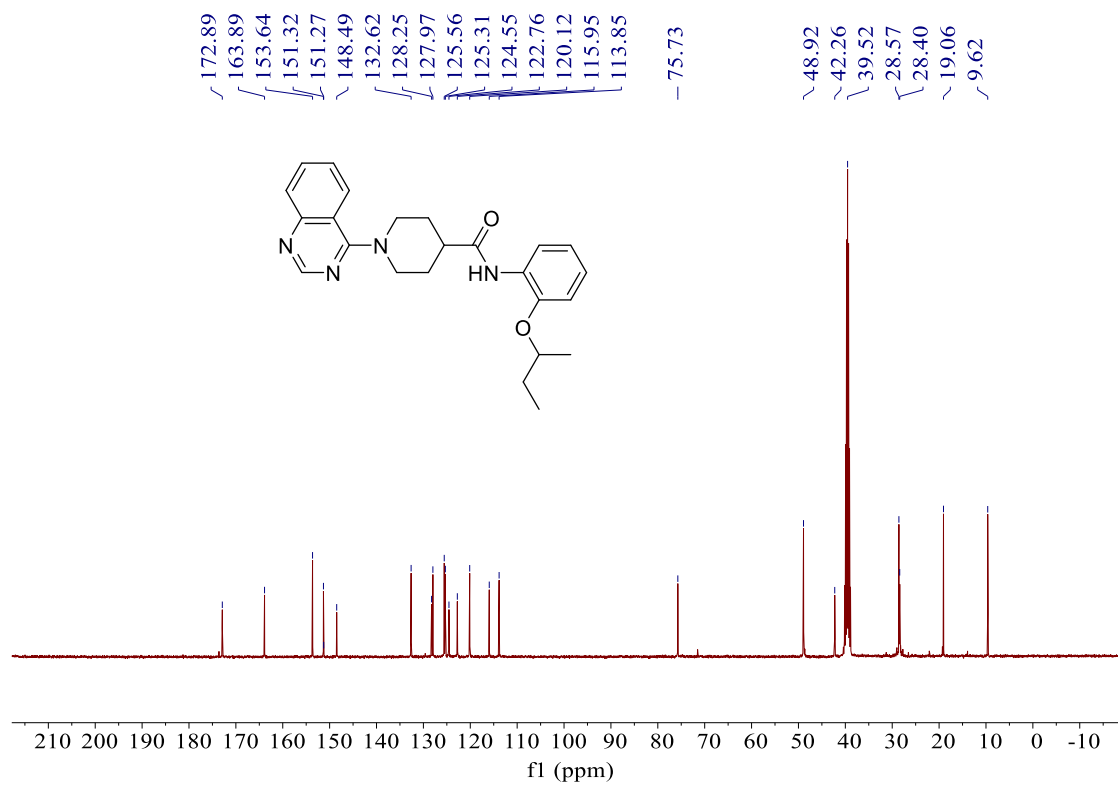


Figure S74. ¹³C NMR spectrum of compound **III-24** (DMSO-*d*₆)

192 #43 RT: 0.43 AV: 1 NL: 1.27E8
T: FIMS + p ESI Full ms [100.0000-1000.0000]

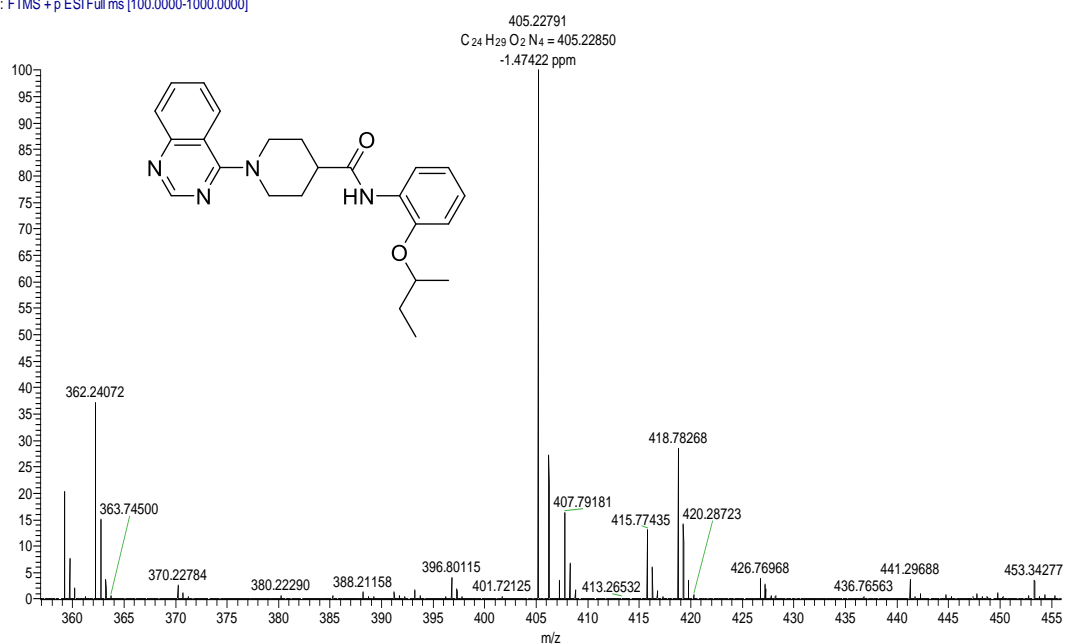


Figure S75. HRMS spectrum of compound III-24

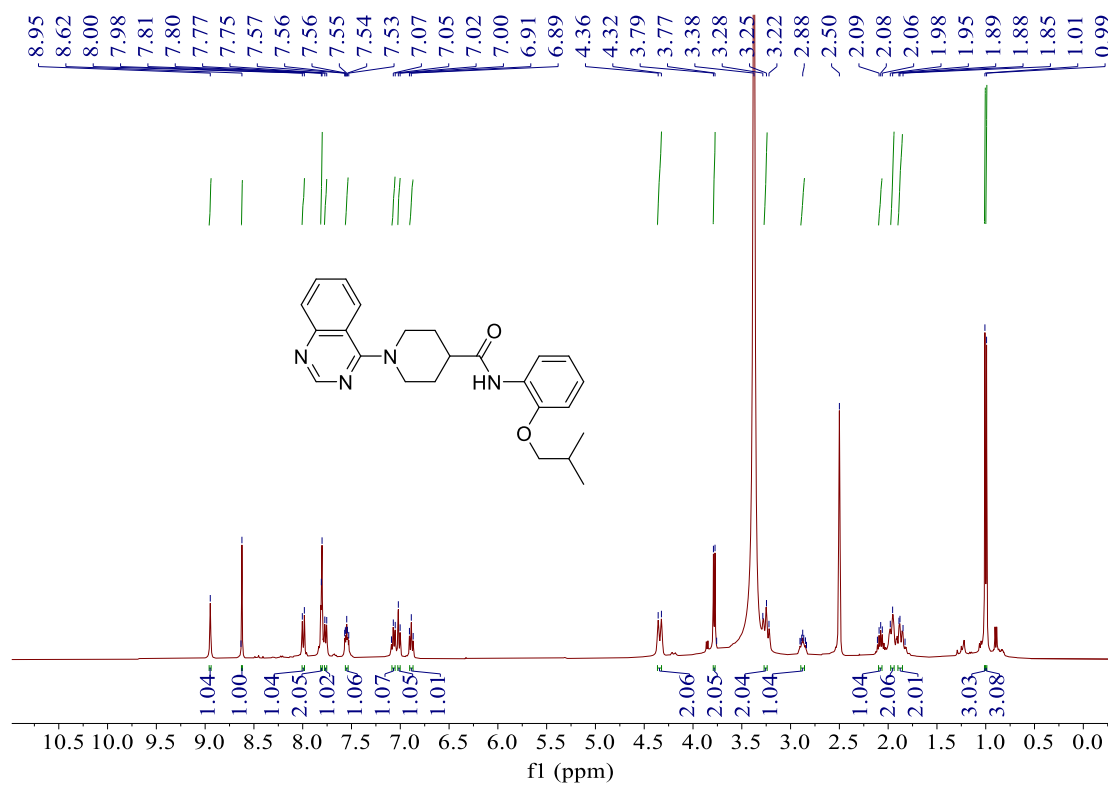


Figure S76. ¹H NMR spectrum of compound III-25 (DMSO-*d*₆)

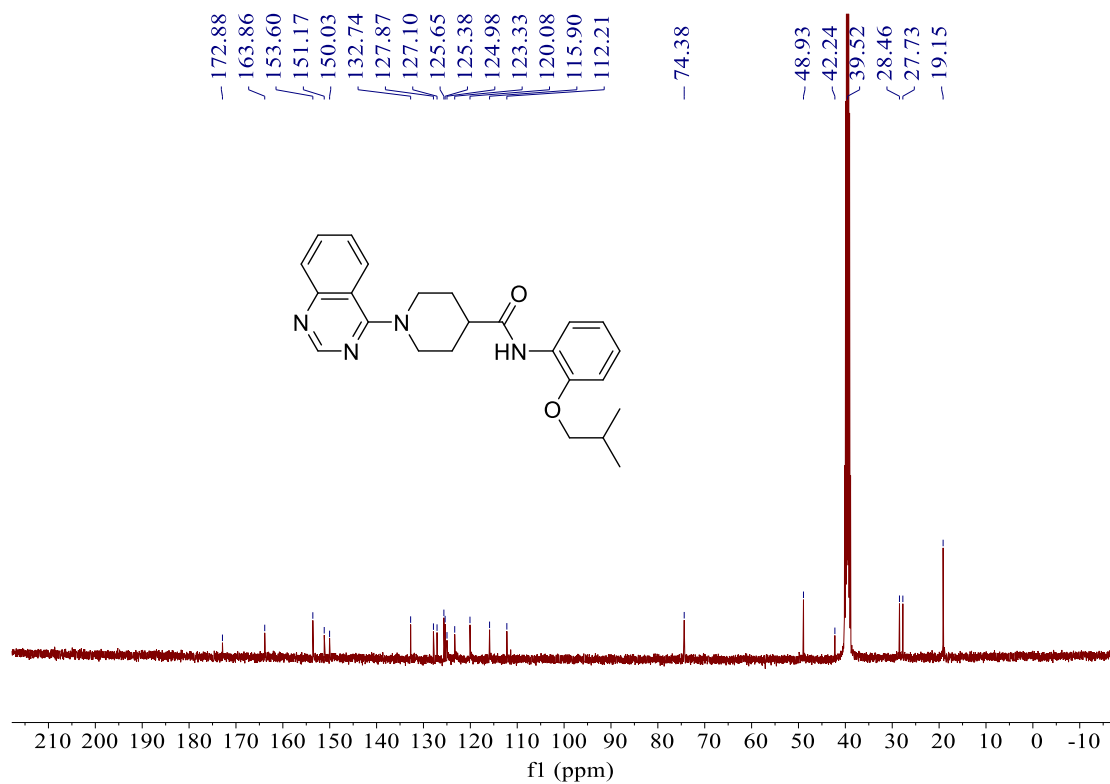


Figure S77. ¹³C NMR spectrum of compound III-25 (DMSO-*d*₆)

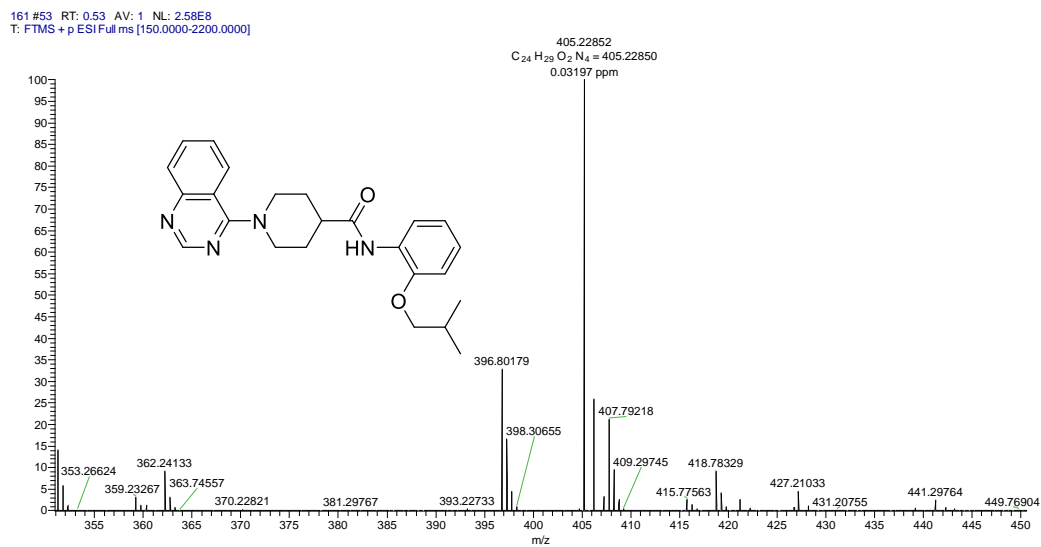


Figure S78. HRMS spectrum of compound III-25

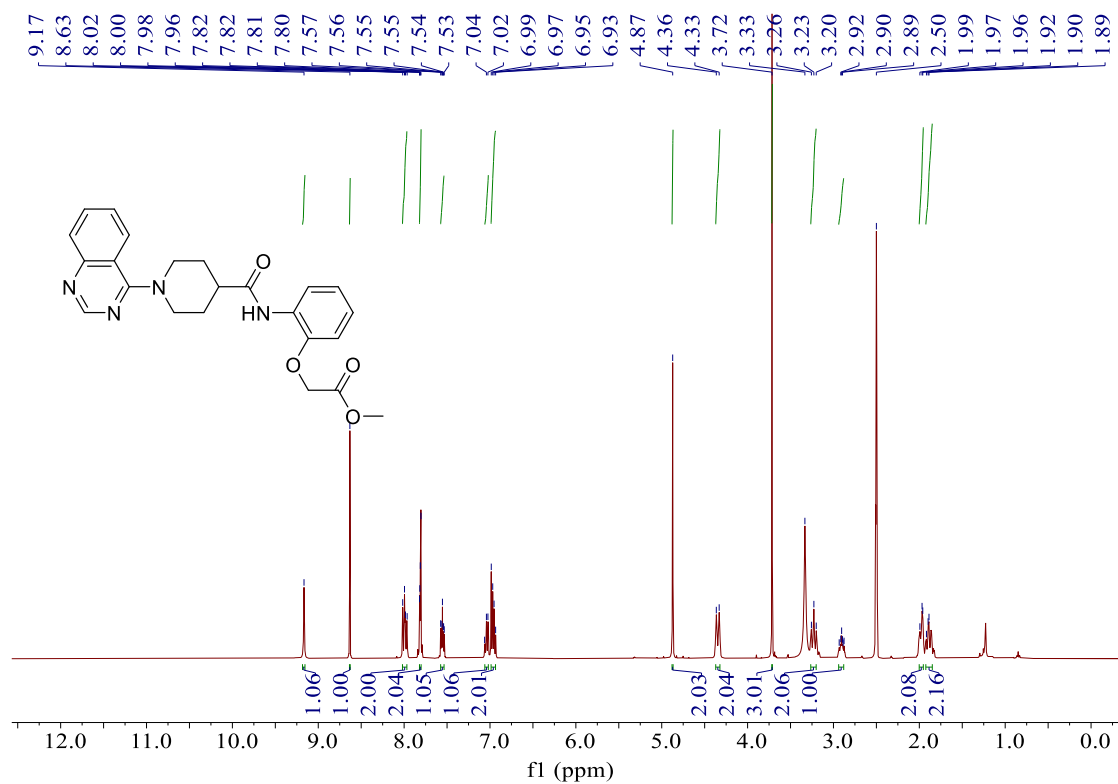


Figure S79. ^1H NMR spectrum of compound III-26 ($\text{DMSO}-d_6$)

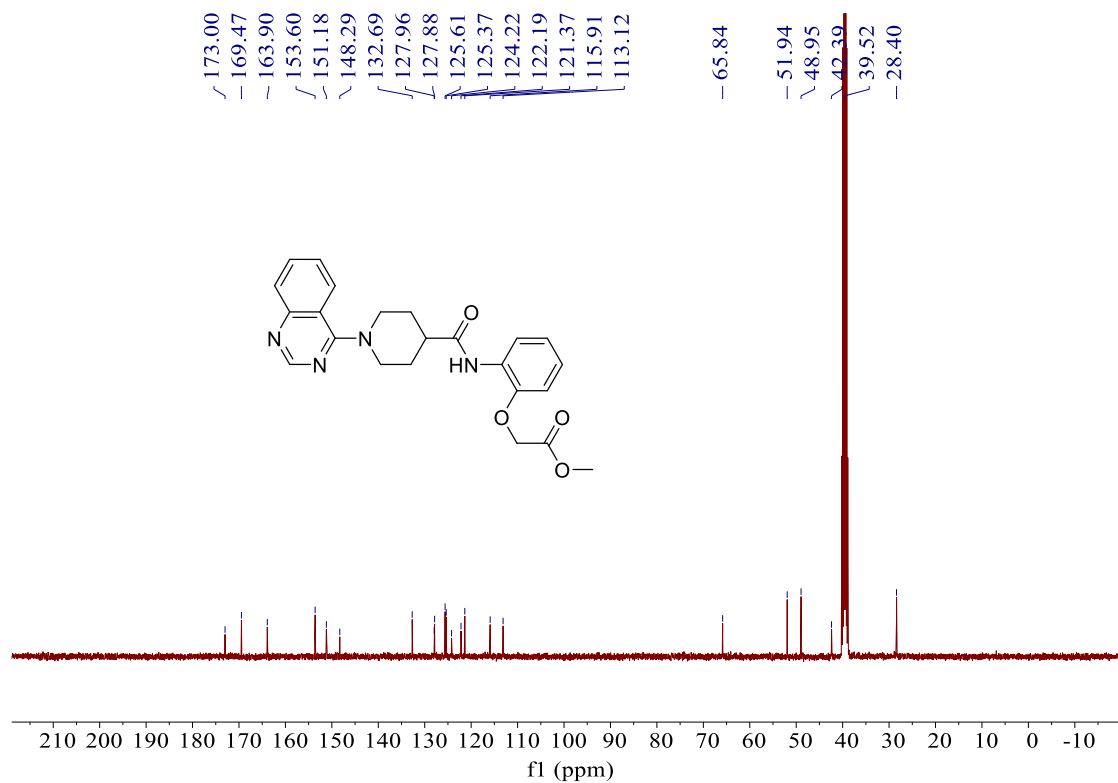


Figure S80. ^{13}C NMR spectrum of compound III-26 ($\text{DMSO}-d_6$)

114 #31 RT: 0.32 AV: 1 NL: 6.20E7
T: FTMS + p ESI Full ms [150.0000-2200.0000]

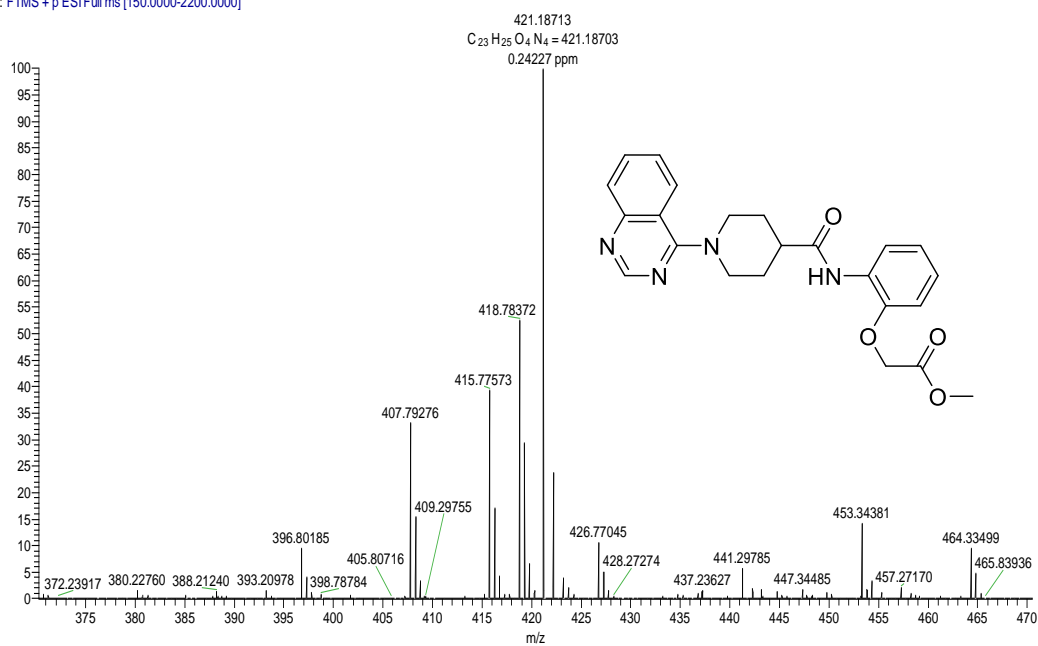


Figure S81. HRMS spectrum of compound III-26

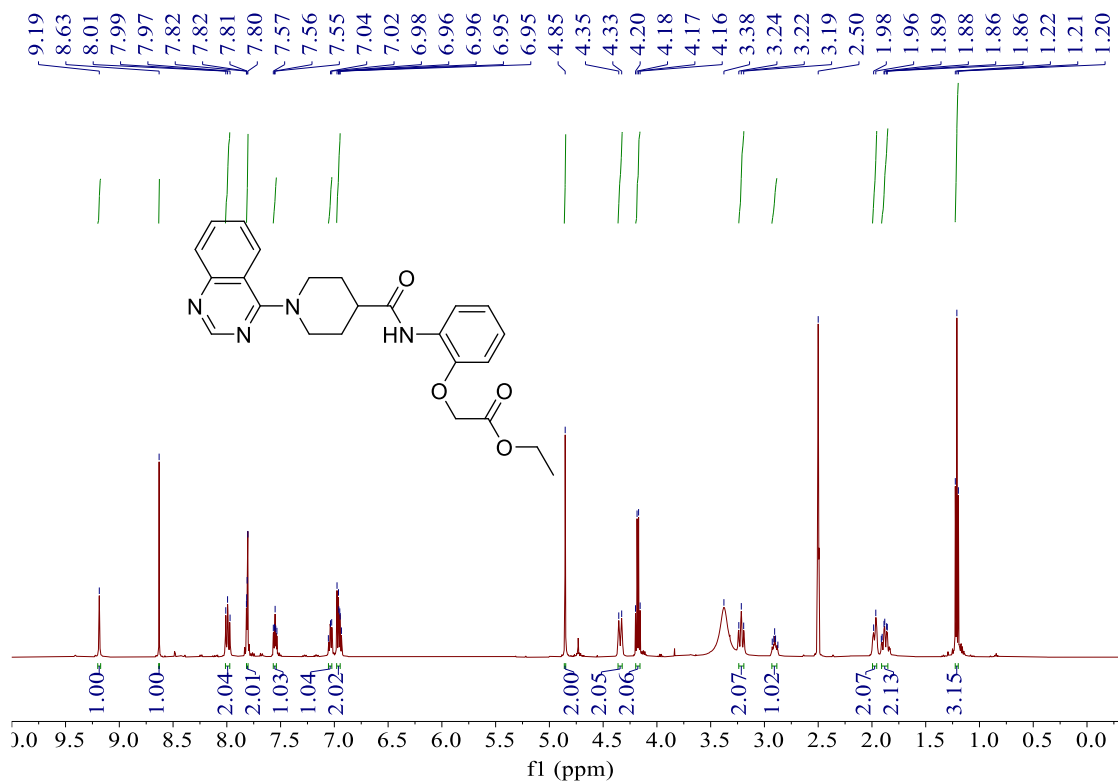


Figure S82. ¹H NMR spectrum of compound III-27 (DMSO-*d*₆)

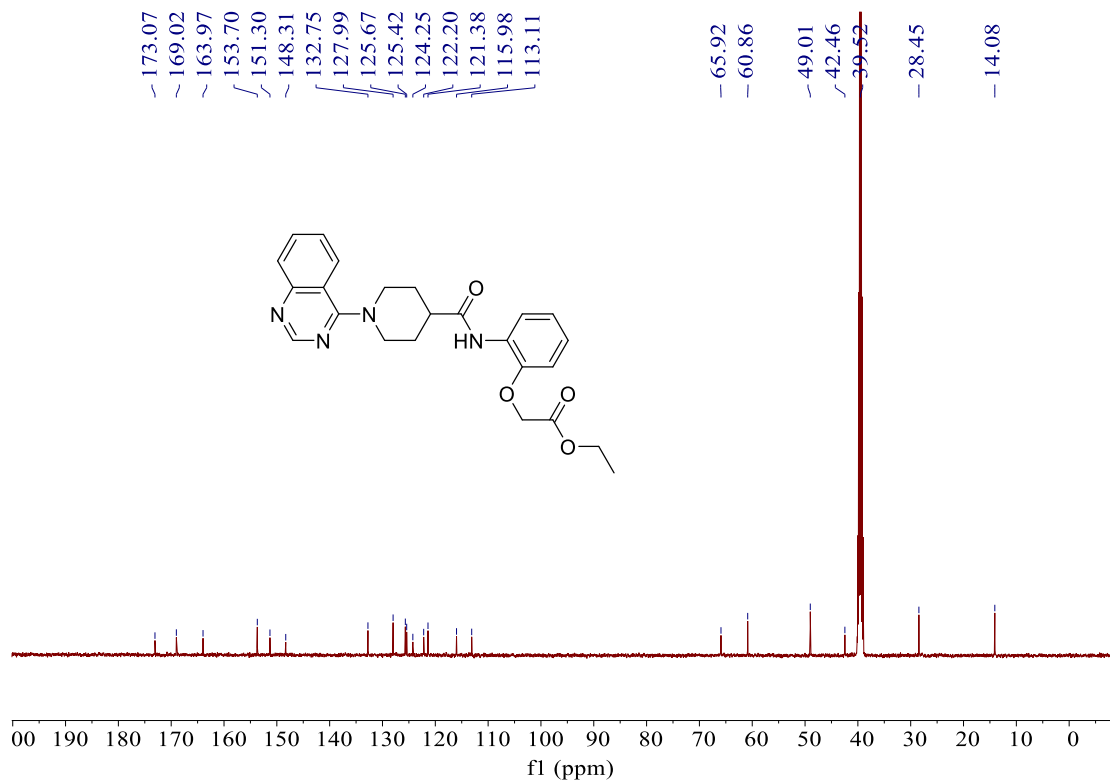


Figure S83. ¹³C NMR spectrum of compound III-27 (DMSO-*d*₆)

185 #35 RT: 0.35 AV: 1 NL: 6.29E7
T: FTMS + p ESI Full ms [100.0000-1000.0000]

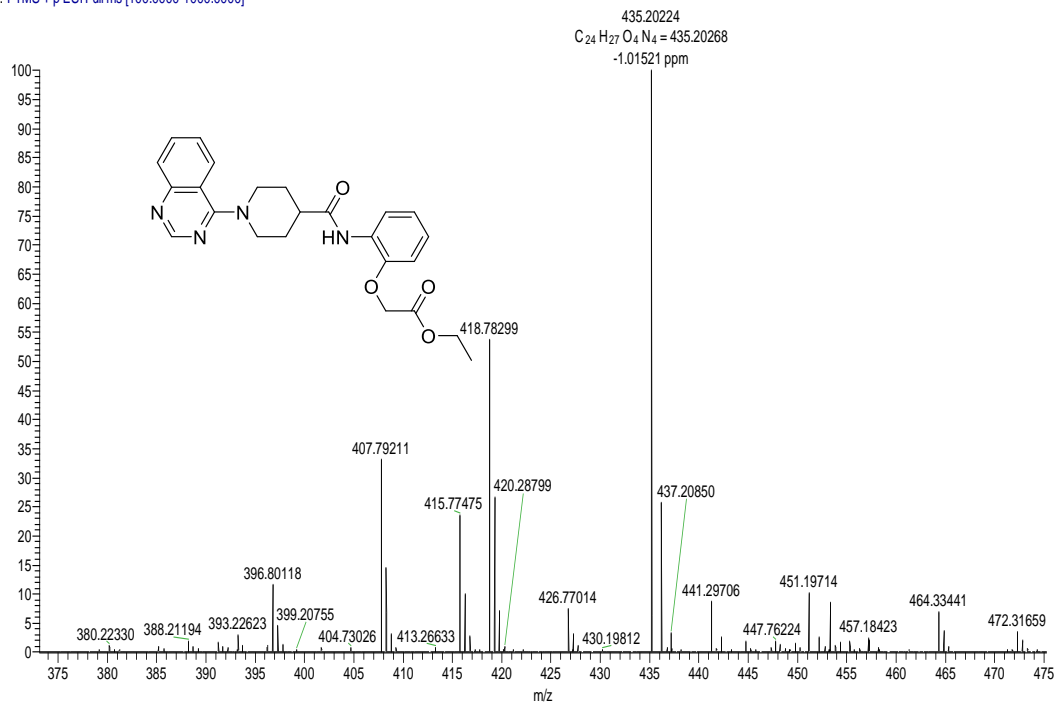


Figure S84. HRMS spectrum of compound III-27