Supporting Information

Discovery of Nanomolar Melanocortin-3 Receptor (MC3R) Selective Small Molecule Pyrrolidine Bis-Cyclic Guanidine Agonist Compounds Via a High Throughput "Unbiased" Screening Campaign

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Pyrrolidine Bis-Cyclic Guanidine Compound Characterization:

1: (R)-1-((S)-3-(adamantan-1-ylmethyl)-1-((R)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-2-iminoimidazolidin-4-yl)ethanol. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-4 was synthesized using the following reagents: Boc-D-Leucine-OH·H2O (R1), Boc-D-Cyclohexylalanine-OH (R2), Boc-D-Threonine(Bzl)-OH (R3), 1-Adamantanecarboxylic acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 10.11 (br. s., 1 H) 8.83 (br. s., 1 H) 8.60 (br. s., 2 H) 4.33 (br. s., 2 H) 4.08 (br. s., 2 H) 3.98 (br. s., 1 H) 3.79 (br. s., 1 H) 3.56 - 3.73 (m, 2 H) 3.49 (br. s., 3 H) 3.29 (br. s., 2 H) 3.14 (br. s., 1 H) 2.91 (d, *J*=14.79 Hz, 1 H) 2.82 (br. s., 1 H) 2.65 (br. s., 1 H) 2.21 - 2.40 (m, 2 H) 1.99 (br. s., 4 H) 1.84 (br. s., 1 H) 1.71 (br. s., 6 H) 1.53 - 1.68 (m, 11 H) 1.41 - 1.53 (m, 3 H) 1.35 (br. s., 1 H) 1.19 (br. s., 6 H) 0.98 (br. s., 4 H) 0.93 (br. s., 4 H); **m/z** calcd $C_{37}H_{65}N_7O$ $[M+H]^+$ 624.54, found (MS ESI) 624.5. **Purity** LCMS: 96.45% (TIC), 98% (214 nm, peak area); **RT** = 4.30 min

2: (R)-1-((S)-3-((4-(tert-butyl)cyclohexyl)methyl)-1-((R)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-2-iminoimidazolidin-4-yl)ethanol. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-5 was synthesized using the following reagents: Boc-D-Leucine-OH·H2O (R1), Boc-D-Cyclohexylalanine-OH (R2), Boc-D-Threonine(Bzl)-OH (R3), 4-tert-butyl-cyclohexancecarboxylic acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 10.21 (br. s., 1 H) 8.60 (br. s., 2 H) 4.35 (br. s., 1 H) 3.84 - 4.06 (m, 3 H) 3.78 (br. s., 2 H) 3.67 (br. s., 2 H) 3.40 - 3.59 (m, 3 H) 3.27 (d, *J*=14.18 Hz, 2 H) 3.01 - 3.21 (m, 2 H) 2.83 (br. s., 1 H) 2.63 (br. s., 1 H) 2.24 - 2.38 (m, 2 H) 2.19 (br. s., 1 H) 1.95 (d, *J*=11.86 Hz, 1 H) 1.83 (br. s., 1 H) 1.70 (br. s., 3 H) 1.52 - 1.67 (m, 8 H) 1.40 - 1.52 (m, 4 H) 1.34 (br. s., 1 H) 1.24 (br. s., 3 H) 1.16 (br. s., 5 H) 0.99 (br. s., 5 H) 0.93 (br. s., 4 H) 0.85 (br. s., 8 H); **m/z** calcd $C_{37}H_{69}N_7O$ $[M+H]^+$ 628.56, found (MS ESI) 628.55. **Purity** LCMS: 98.41% (TIC), 99% (214 nm, peak area); **RT** = 4.52 min

3: (R)-1-((S)-1-((R)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-2-imino-3-(4-methylpentyl)imidazolidin-4-yl)ethanol. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-6 was synthesized using the following reagents: Boc-D-Leucine-OH·H2O (R1), Boc-D-Cyclohexylalanine-OH (R2), Boc-D-Threonine(Bzl)-OH (R3), 4-Methylvaleric acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 10.06 (br. s., 1 H) 8.59 (br. s., 2 H) 4.24 (br. s., 2 H) 3.96 (br. s., 2 H) 3.84 (br. s., 1 H) 3.78 (br. s., 1 H) 3.71 (d, *J*=9.78 Hz, 2 H) 3.44 - 3.58 (m, 1 H) 3.42 (br. s., 1 H) 3.28 - 3.38 (m, 2 H) 3.23 (d, *J*=15.53 Hz, 2 H) 2.81 (br. s., 1 H) 2.72 (br. s., 1 H) 2.35 (d, *J*=13.20 Hz, 2 H) 1.81 - 1.93 (m, 2 H) 1.73 (br. s., 3 H) 1.63 (br. s., 3 H) 1.50 - 1.60 (m, 4 H) 1.45 (br. s., 2 H) 1.36 (br. s., 1 H) 1.17 (s, 3 H) 1.21 (s, 5 H) 0.98 (br. s., 4 H) 0.79 - 0.95 (m, 9 H); **m/z** calcd $C_{32}H_{61}N_7O$ $[M+H]^+$ 560.49, found (MS ESI) 560.45. **Purity** LCMS: 96.78% (TIC), 99% (214 nm, peak area); **RT** = 4.08 min

4: (R)-3-(adamantan-1-ylmethyl)-1-((R)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-4-propylimidazolidin-2-imine. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-7 was synthesized using the following reagents: Boc-D-Leucine-OH·H2O (R1), Boc-D-

Cyclohexylalanine-OH (R2), Boc-D-Norvaline-OH (R3), 1-Adamantanecarboxylic acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 10.75 (br. s., 1 H) 9.24 (br. s., 1 H) 8.64 (br. s., 2 H) 4.20 (br. s., 1 H) 3.95 (br. s., 1 H) 3.74 (br. s., 2 H) 3.46 - 3.65 (m, 2 H) 3.24 - 3.43 (m, 3 H) 3.07 - 3.24 (m, 2 H) 2.93 (br. s., 1 H) 2.82 (br. s., 1 H) 2.73 (d, *J*=15.77 Hz, 1 H) 2.51 - 2.61 (m, 1 H) 2.46 (d, *J*=13.33 Hz, 1 H) 1.99 (br. s., 3 H) 1.86 - 1.97 (m, 2 H) 1.80 (br. s., 3 H) 1.71 (br. s., 5 H) 1.62 (s, 3 H) 1.65 (s, 4 H) 1.56 (br. s., 5 H) 1.44 (br. s., 4 H) 1.31 (br. s., 2 H) 1.07 - 1.23 (m, 4 H) 0.87 - 1.06 (m, 10 H); **m/z** calcd $C_{38}H_{67}N_7$ $[M+H]^+$ 622.55, found (MS ESI) 622.5. **Purity** LCMS: 95.96% (TIC), 99% (214 nm, peak area); **RT** = 4.73min

5: (R)-3-((4-(tert-butyl)cyclohexyl)methyl)-1-((R)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-4-propylimidazolidin-2-imine. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-8 was synthesized using the following reagents: Boc-D-Leucine-OH·H2O (R1), Boc-D-Cyclohexylalanine-OH (R2), Boc-D-Norvaline-OH (R3), 4-tert-butyl-cyclohexancecarboxylic acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 8.62 (br. s., 2 H) 4.19 (br. s., 1 H) 3.90 (br. s., 1 H) 3.84 (br. s., 1 H) 3.74 (br. s., 2 H) 3.59 (br. s., 1 H) 3.39 (d, *J*=14.79 Hz, 1 H) 3.29 (br. s., 2 H) 3.19 (br. s., 2 H) 3.05 (d, *J*=14.67 Hz, 1 H) 2.92 (br. s., 1 H) 2.83 (br. s., 1 H) 2.54 (br. s., 1 H) 2.47 (d, *J*=13.33 Hz, 1 H) 2.09 (br. s., 1 H) 1.83 - 1.96 (m, 2 H) 1.81 (br. s., 2 H) 1.73 (br. s., 3 H) 1.49 - 1.66 (m, 9 H) 1.43 (br. s., 4 H) 1.35 (br. s., 2 H) 1.16 (br. s., 6 H) 0.89 - 1.04 (m, 11 H) 0.86 (br. s., 9 H); **m/z** calcd $C_{38}H_{71}N_7$ $[M+H]^+$ 626.58, found (MS ESI) 626.55. **Purity** LCMS: 97.36% (TIC), 99% (214 nm, peak area); **RT** = 4.92 min

6: (R)-1-((R)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-3-(4-methylpentyl)-4-propylimidazolidin-2-imine. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-9 was synthesized using the following reagents: Boc-D-Leucine-OH·H2O (R1), Boc-D-Cyclohexylalanine-OH (R2), Boc-D-Norvaline-OH (R3), 4-Methylvaleric acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 8.59 (br. s., 2 H) 4.11 (br. s., 1 H) 3.79 (br. s., 1 H) 3.63 - 3.75 (m, 3 H) 3.55 (br. s., 1 H) 3.38 (d, *J*=14.79 Hz, 1 H) 3.25 (br. s., 2 H) 3.02 - 3.19 (m, 3 H) 2.88 (br. s., 1 H) 2.80 (br. s., 1 H) 2.37 - 2.52 (m, 2 H) 1.72 - 1.88 (m, 4 H) 1.64 (d, *J*=18.46 Hz, 4 H) 1.52 (br. s., 5 H) 1.24 - 1.46 (m, 6 H) 1.14 (br. s., 6 H) 0.81 - 1.01 (m, 17 H); **m/z** calcd $C_{33}H_{63}N_7$ $[M+H]^+$ 558.51, found (MS ESI) 558.45. **Purity** LCMS: 97.89% (TIC), 99% (214 nm, peak area); **RT** = 4.48 min

7: (R)-3-(adamantan-1-ylmethyl)-1-((R)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-4-isopropylimidazolidin-2-imine. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-10 was synthesized using the following reagents: Boc-D-Leucine-OH·H2O (R1), Boc-D-Cyclohexylalanine-OH (R2), Boc-D-Valine-OH (R3), 1-Adamantanecarboxylic acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 25/45. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 10.51 (br. s., 1 H) 9.25 (br. s., 1 H) 8.63 (br. s., 2 H) 4.13 (br. s., 1 H) 4.00 (br. s., 1 H) 3.73 (br. s., 2 H) 3.60 (d, *J*=15.28 Hz, 1 H) 3.35 - 3.52 (m, 2 H) 3.26 (br. s., 3 H) 3.15 (d, *J*=14.79 Hz, 1 H) 2.94 (br. s., 1 H) 2.79 - 2.89 (m, 1 H) 2.71 (d, *J*=15.41 Hz, 1 H) 2.47 (d, *J*=10.76 Hz, 2 H) 2.25 (br. s., 1 H) 1.99 (br. s., 3 H) 1.85 - 1.95 (m, 2 H) 1.80 (br. s., 2 H) 1.60 - 1.75 (m, 12 H) 1.57 (br. s., 4 H) 1.49 (br. s., 3 H)

1.29 - 1.45 (m, 1 H) 1.08 - 1.25 (m, 4 H) 1.02 (br. s., 1 H) 0.88 - 0.99 (m, 9 H) 0.80 (br. s., 3 H); **m/z** calcd $C_{38}H_{67}N_7$ $[M+H]^+$ 622.55, found (MS ESI) 622.5. **Purity** LCMS: 97.72% (TIC), 99% (214 nm, peak area); **RT** = 4.72 min

8: (R)-3-((4-(tert-butyl)cyclohexyl)methyl)-1-((R)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-4-isopropylimidazolidin-2-imine. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-11 was synthesized using the following reagents: Boc-D-Leucine-OH·H2O (R1), Boc-D-Cyclohexylalanine-OH (R2), Boc-D-Valine-OH (R3), 4-tert-butyl-cyclohexancecarboxylic acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 8.63 (br. s., 2 H) 4.15 (br. s., 1 H) 3.97 (br. s., 1 H) 3.86 (br. s., 1 H) 3.73 (br. s., 3 H) 3.36 - 3.58 (m, 2 H) 3.28 (br. s., 3 H) 3.17 (d, *J*=14.79 Hz, 1 H) 3.01 (br. s., 1 H) 2.92 (d, *J*=18.46 Hz, 2 H) 2.39 - 2.59 (m, 2 H) 2.14 (br. s., 2 H) 1.76 - 1.92 (m, 5 H) 1.71 (br. s., 2 H) 1.66 (br. s., 3 H) 1.52 - 1.62 (m, 5 H) 1.48 (br. s., 2 H) 1.43 (br. s., 2 H) 0.95 - 1.22 (m, 14 H) 0.92 (br. s., 4 H) 0.84 (br. s., 11 H); **m/z** calcd $C_{38}H_{71}N_7$ $[M+H]^+$ 626.58, found (MS ESI) 626.55. **Purity** LCMS: 98.51% (TIC), 99% (214 nm, peak area); **RT** = 4.92 min

9: (R)-1-((R)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-4-isopropyl-3-(4-methylpentyl)imidazolidin-2-imine. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-12 was synthesized using the following reagents: Boc-D-Leucine-OH·H2O (R1), Boc-D-Cyclohexylalanine-OH (R2), Boc-D-Valine-OH (R3), 4-Methylvaleric acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 25/45 **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 8.62 (br. s., 2 H) 4.09 (br. s., 1 H) 3.87 (br. s., 1 H) 3.73 (br. s., 3 H) 3.35 - 3.59 (m, 2 H) 3.26 (br. s., 3 H) 3.14 (d, *J*=14.43 Hz, 1 H) 3.06 (br. s., 1 H) 2.81 - 2.98 (m, 2 H) 2.40 - 2.52 (m, 2 H) 2.16 (br. s., 1 H) 1.87 (br. s., 1 H) 1.82 (br. s., 2 H) 1.68 (d, *J*=17.61 Hz, 4 H) 1.57 (br. s., 4 H) 1.35 - 1.53 (m, 5 H) 1.18 (br. s., 6 H) 0.97 (br. s., 7 H) 0.75 - 0.93 (m, 12 H); **m/z** calcd $C_{33}H_{63}N_7$ $[M+H]^+$ 558.51, found (MS ESI) 558.45. **Purity** LCMS: 96.02% (TIC), 98% (214 nm, peak area); **RT** = 4.49 min

10: (R)-1-((S)-3-(adamantan-1-ylmethyl)-2-imino-1-((R)-1-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)imidazolidin-4-yl)ethanol. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-13 was synthesized using the following reagents: Boc-D-Leucine-OH·H2O (R1), Boc-D-Phenylalanine-OH (R2), Boc-D-Threonine(Bzl)-OH (R3), 1-Adamantanecarboxylic acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 25/45. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 10.14 (br. s., 1 H) 8.94 (br. s., 1 H) 8.63 (br. s., 2 H) 8.38 (br. s., 1 H) 7.35 (br. s., 2 H) 7.21 (br. s., 2 H) 4.74 (br. s., 1 H) 4.04 (br. s., 3 H) 3.84 (br. s., 2 H) 3.67 (br. s., 1 H) 3.58 (br. s., 1 H) 3.51 (br. s., 1 H) 3.42 (br. s., 1 H) 3.36 (br. s., 1 H) 3.21 - 3.33 (m, 2 H) 2.92 - 3.19 (m, 3 H) 2.70 (d, *J*=16.63 Hz, 3 H) 2.47 (d, *J*=11.13 Hz, 1 H) 2.33 (br. s., 1 H) 1.78 - 1.93 (m, 3 H) 1.64 (s, 3 H) 1.67 (s, 2 H) 1.50 - 1.60 (m, 5 H) 1.41 - 1.50 (m, 1 H) 1.30 - 1.41 (m, 3 H) 1.16 - 1.27 (m, 3 H) 1.11 (br. s., 3 H) 1.00 (br. s., 3 H) 0.94 (br. s., 3 H); **m/z** calcd $C_{37}H_{59}N_7O$ $[M+H]^+$ 618.48, found (MS ESI) 618.45. **Purity** LCMS: 98.23% (TIC), 99% (214 nm, peak area); **RT** = 4.12 min

11: (R)-1-((S)-3-((4-(tert-butyl)cyclohexyl)methyl)-2-imino-1-((R)-1-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)imidazolidin-4-

yl)ethanol. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-14 was synthesized using the following reagents: Boc-D-Leucine-OH·H2O (R1), Boc-D-Phenylalanine-OH (R2), Boc-D-Threonine(Bzl)-OH (R3), 4-tert-butyl-cyclohexancecarboxylic acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 25/40. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 8.62 (br. s., 2 H) 7.23 (br. s., 2 H) 4.69 (br. s., 1 H) 3.94 (br. s., 3 H) 3.79 (br. s., 1 H) 3.74 (br. s., 1 H) 3.68 (br. s., 1 H) 3.60 (br. s., 2 H) 3.39 - 3.55 (m, 2 H) 3.30 (br. s., 2 H) 3.11 (br. s., 1 H) 2.99 (d, *J*=13.20 Hz, 3 H) 2.61 - 2.85 (m, 2 H) 2.46 (d, *J*=11.49 Hz, 1 H) 2.34 (br. s., 1 H) 1.79 - 1.99 (m, 2 H) 1.69 (br. s., 2 H) 1.36 - 1.63 (m, 7 H) 1.26 (br. s., 2 H) 1.15 (br. s., 3 H) 1.00 (br. s., 4 H) 0.86 - 0.97 (m, 5 H) 0.83 (br. s., 9 H); **m/z** calcd $C_{37}H_{63}N_7O$ $[M+H]^+$ 622.51, found (MS ESI) 622.5. **Purity** LCMS: 98.73% (TIC), 99% (214 nm, peak area); **RT** = 4.33 min

12: (R)-1-((S)-2-imino-1-((R)-1-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)-3-(4-methylpentyl)imidazolidin-4-yl)ethanol. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-15 was synthesized using the following reagents: Boc-D-Leucine-OH·H2O (R1), Boc-D-Phenylalanine-OH (R2), Boc-D-Threonine(Bzl)-OH (R3), 4-Methylvaleric acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 25/45. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 10.01 (br. s., 1 H) 9.01 (br. s., 1 H) 8.59 (br. s., 2 H) 7.29 (br. s., 2 H) 7.23 (br. s., 2 H) 4.61 (br. s., 1 H) 4.14 (br. s., 2 H) 3.90 (br. s., 2 H) 3.78 (br. s., 1 H) 3.60 - 3.75 (m, 2 H) 3.38 - 3.59 (m, 3 H) 3.27 (br. s., 2 H) 3.12 (br. s., 2 H) 2.97 (br. s., 2 H) 2.74 (d, *J*=12.96 Hz, 2 H) 2.46 (d, *J*=12.35 Hz, 1 H) 2.40 (br. s., 1 H) 1.87 (br. s., 1 H) 1.72 (br. s., 2 H) 1.54 (d, *J*=11.74 Hz, 3 H) 1.40 - 1.50 (m, 2 H) 1.35 (br. s., 1 H) 1.24 (br. s., 1 H) 1.13 (br. s., 3 H) 0.99 (br. s., 4 H) 0.93 (br. s., 3 H) 0.86 (br. s., 5 H); **m/z** calcd $C_{32}H_{55}N_7O$ $[M+H]^+$ 554.45, found (MS ESI) 554.4. **Purity** LCMS: 98.87% (TIC), 99% (214 nm, peak area); **RT** = 3.86 min

13: (R)-3-(adamantan-1-ylmethyl)-1-((R)-1-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)-4-propylimidazolidin-2-imine. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-16 was synthesized using the following reagents: Boc-D-Leucine-OH·H2O (R1), Boc-D-Phenylalanine-OH (R2), Boc-D-Norvaline-OH (R3), 1-Adamantanecarboxylic acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/35. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 10.74 (br. s., 1 H) 9.43 (br. s., 1 H) 8.66 (br. s., 2 H) 7.40 (br. s., 2 H) 7.29 (br. s., 2 H) 7.21 (br. s., 1 H) 4.75 (br. s., 1 H) 3.73 (br. s., 4 H) 3.58 (br. s., 2 H) 3.27 (br. s., 4 H) 3.20 (br. s., 1 H) 3.10 (d, *J*=13.94 Hz, 1 H) 2.99 (br. s., 2 H) 2.77 (t, *J*=11.80 Hz, 1 H) 2.47 - 2.70 (m, 3 H) 2.00 (br. s., 1 H) 1.90 (br. s., 3 H) 1.74 - 1.86 (m, 2 H) 1.66 (d, *J*=11.62 Hz, 4 H) 1.49 - 1.60 (m, 5 H) 1.28 - 1.46 (m, 4 H) 1.22 (br. s., 5 H) 0.88 - 1.07 (m, 8 H); **m/z** calcd $C_{38}H_{61}N_7$ $[M+H]^+$ 616.50, found (MS ESI) 616.5. **Purity** LCMS: 98.41% (TIC), 99% (214 nm, peak area); **RT** = 4.50 min

14: (R)-3-((4-(tert-butyl)cyclohexyl)methyl)-1-((R)-1-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)-4-propylimidazolidin-2-imine. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-17 was synthesized using the following reagents: Boc-D-Leucine-OH·H2O (R1), Boc-D-Phenylalanine-OH (R2), Boc-D-Norvaline-OH (R3), 4-tert-butyl-cyclohexancecarboxylic acid (R4). The final crude product was purified using HPLC as

described above, with a gradient of (B). **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 8.65 (br. s., 2 H) 7.35 (br. s., 3 H) 7.22 (br. s., 1 H) 4.70 (br. s., 1 H) 3.73 (br. s., 3 H) 3.48 - 3.68 (m, 3 H) 3.25 - 3.45 (m, 3 H) 3.16 - 3.25 (m, 1 H) 3.01 - 3.15 (m, 2 H) 2.98 (br. s., 1 H) 2.89 (d, *J*=14.79 Hz, 1 H) 2.73 - 2.85 (m, 1 H) 2.62 (d, *J*=11.37 Hz, 2 H) 1.86 - 1.99 (m, 1 H) 1.81 (br. s., 3 H) 1.66 (br. s., 1 H) 1.48 - 1.62 (m, 4 H) 1.33 - 1.47 (m, 3 H) 1.24 (br. s., 3 H) 1.05 - 1.19 (m, 1 H) 0.88 - 1.02 (m, 11 H) 0.84 (br. s., 9 H); **m/z** calcd $C_{38}H_{65}N_7$ $[M+H]^+$ 620.53, found (MS ESI) 620.5. **Purity** LCMS: 98.68% (TIC), 99% (214 nm, peak area); **RT** = 4.69 min

15: (R)-1-((R)-1-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)-3-(4-methylpentyl)-4-propylimidazolidin-2-imine. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-18 was synthesized using the following reagents: Boc-D-Leucine-OH·H2O (R1), Boc-D-Phenylalanine-OH (R2), Boc-D-Norvaline-OH (R3), 4-Methylvaleric acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/30. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 10.53 (br. s., 1 H) 9.34 (br. s., 1 H) 8.61 (br. s., 2 H) 7.30 (br. s., 2 H) 7.20 (br. s., 2 H) 4.54 (br. s., 1 H) 4.08 (br. s., 1 H) 3.72 (br. s., 2 H) 3.56 (br. s., 2 H) 3.45 (br. s., 1 H) 3.14 - 3.39 (m, 4 H) 2.89 - 3.09 (m, 4 H) 2.72 - 2.89 (m, 1 H) 2.60 (d, *J*=14.06 Hz, 2 H) 1.90 (br. s., 1 H) 1.78 (br. s., 2 H) 1.65 (br. s., 1 H) 1.33 - 1.60 (m, 5 H) 1.22 (br. s., 4 H) 0.91 (s, 5 H) 0.95 (s, 5 H) 0.83 (br. s., 5 H); **m/z** calcd $C_{33}H_{57}N_7$ $[M+H]^+$ 552.47, found (MS ESI) 552.4. **Purity** LCMS: 98.02% (TIC), 99% (214 nm, peak area); **RT** = 4.29 min

16: (R)-3-(adamantan-1-ylmethyl)-1-((R)-1-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)-4-isopropylimidazolidin-2-imine. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-19 was synthesized using the following reagents: Boc-D-Leucine-OH·H2O (R1), Boc-D-Phenylalanine-OH (R2), Boc-D-Valine-OH (R3), 1-Adamantanecarboxylic acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/30, 35/35. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 10.00 (br. s., 1 H) 9.13 (br. s., 1 H) 8.64 (br. s., 1 H) 7.42 (br. s., 2 H) 7.29 (br. s., 1 H) 7.20 (br. s., 2 H) 4.71 (br. s., 1 H) 3.75 (br. s., 2 H) 3.70 (br. s., 1 H) 3.50 (br. s., 2 H) 3.32 - 3.45 (m, 3 H) 3.27 (br. s., 3 H) 3.13 (d, *J*=14.18 Hz, 1 H) 3.02 (br. s., 2 H) 2.77 - 2.95 (m, 1 H) 2.48 - 2.74 (m, 3 H) 2.15 (br. s., 1 H) 2.01 (br. s., 1 H) 1.89 (br. s., 3 H) 1.79 (br. s., 2 H) 1.63 (br. s., 3 H) 1.55 (br. s., 5 H) 1.37 (d, *J*=11.00 Hz, 4 H) 1.10 - 1.30 (m, 3 H) 0.83 - 1.04 (m, 8 H) 0.74 (br. s., 3 H); **m/z** calcd $C_{38}H_{61}N_7$ $[M+H]^+$ 616.50, found (MS ESI) 616.45. **Purity** LCMS: 98.05% (TIC), 98% (214 nm, peak area); **RT** = 4.51 min

17: (R)-3-((4-(tert-butyl)cyclohexyl)methyl)-1-((R)-1-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)-4-isopropylimidazolidin-2-imine. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-20 was synthesized using the following reagents: Boc-D-Leucine-OH·H2O (R1), Boc-D-Phenylalanine-OH (R2), Boc-D-Valine-OH (R3), 4-tert-butyl-cyclohexancecarboxylic acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/30. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 8.64 (br. s., 2 H) 7.32 (br. s., 2 H) 7.20 (br. s., 2 H) 4.63 (br. s., 1 H) 3.69 (d, *J*=9.90 Hz, 3 H) 3.56 (br. s., 1 H) 3.41 (br. s., 1 H) 3.27 - 3.37 (m, 1 H) 3.23 (br. s., 3 H) 3.07 (d, *J*=13.69 Hz, 1 H) 2.94 (br. s., 2 H) 2.71 - 2.90 (m, 2 H) 2.46 - 2.69 (m, 2 H) 2.00 (br. s., 1 H) 1.90 (br. s., 1 H) 1.78 (br. s., 3 H) 1.44 - 1.65 (m, 4 H) 1.37 (d, *J*=15.65 Hz, 3 H) 1.23 (br. s., 1 H) 1.03 - 1.17 (m, 1 H) 0.96 (br. s., 4 H) 0.90 (br. s., 7 H) 0.82 (br. s., 9 H) 0.75 (br. s., 4 H);

m/z calcd $C_{38}H_{65}N_7$ $[M+H]^+$ 620.53, found (MS ESI) 620.5. **Purity** LCMS: 98.57% (TIC), 99% (214 nm, peak area); **RT** = 4.71 min

18: (R)-1-((R)-1-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)-4-isopropyl-3-(4-methylpentyl)imidazolidin-2-imine. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-21 was synthesized using the following reagents: Boc-D-Leucine-OH·H2O (R1), Boc-D-Phenylalanine-OH (R2), Boc-D-Valine-OH (R3), 4-Methylvaleric acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/30. **1H NMR** (400 MHz, DMSO-d_6): δ 8.5 (br. s., 2 H) 7.4 (d, J=7.1 Hz, 4 H) 7.2-7.3 (m, 17 H) 7.2 (d, J=7.2 Hz, 6 H) 3.7-3.9 (m, 5 H) 3.7 (d, J=9.4 Hz, 2 H) 3.5 (d, J=12.7 Hz, 3 H) 3.3 (d, J=12.6 Hz, 4 H) 3.1 (d, J=12.8 Hz, 2 H) 2.9-3.0 (m, 7 H) 2.7-2.9 (m, 11 H) 2.6 (br. s., 4 H) 2.0-2.2 (m, 4 H) 1.9 (d, J=11.74 Hz, 4 H) 1.5-1.7 (m, 12 H) 1.2 (br. s., 5 H) 1.2 (br. s., 6 H) 0.8-1.1 (m, 4 H) **^{13}C NMR** (100 MHz, DMSO-d_6) δ 158.0, 157.8, 157.3, 156.8, 139.2, 137.9, 137.7, 129.8, 129.4, 129.1, 129.0, 128.8, 127.3, 127.1, 126.8, 62.8, 58.5, 55.6, 53.8, 51.2, 48.4, 40.7, 40.5, 37.9, 37.8, 37.5, 34.5, 33.6, 33.5, 32.8, 29.6, 26.6, 26.3, 26.1, 22.8; **m/z** calcd $C_{33}H_{57}N_7$ $[M+H]^+$ 552.47, found (MS ESI) 552.45. **Purity** LCMS: 97.09% (TIC), 99% (214 nm, peak area); **RT** = 4.26 min

19: (R)-1-((S)-3-(adamantan-1-ylmethyl)-1-((R)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isopropylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-2-iminoimidazolidin-4-yl)ethanol. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-22 was synthesized using the following reagents: Boc-D-Valine-OH (R1), Boc-D-Cyclohexylalanine-OH (R2), Boc-D-Threonine(Bzl)-OH (R3), 1-Adamantanecarboxylic acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/30. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 10.01 (br. s., 1 H) 8.74 - 9.01 (m, 1 H) 8.58 (br. s., 2 H) 4.27 (br. s., 2 H) 4.06 (br. s., 2 H) 3.92 (br. s., 1 H) 3.79 (br. s., 1 H) 3.59 (d, *J*=15.04 Hz, 1 H) 3.42 - 3.54 (m, 3 H) 3.38 (br. s., 1 H) 3.18 (d, *J*=16.63 Hz, 2 H) 2.95 (d, *J*=14.79 Hz, 1 H) 2.78 (br. s., 1 H) 2.69 (br. s., 1 H) 2.30 (br. s., 2 H) 2.06 (br. s., 1 H) 1.97 (br. s., 3 H) 1.82 (br. s., 1 H) 1.69 (br. s., 6 H) 1.43 - 1.65 (m, 11 H) 1.33 (br. s., 1 H) 1.15 (br. s., 6 H) 0.98 (d, *J*=11.74 Hz, 2 H) 0.90 (br. s., 3 H) 0.84 (br. s., 3 H); **m/z** calcd $C_{36}H_{63}N_7O$ $[M+H]^+$ 610.51, found (MS ESI) 610.5. **Purity** LCMS: 97.44% (TIC), 99% (214 nm, peak area); **RT** = 4.11 min

20: (R)-1-((S)-3-((4-(tert-butyl)cyclohexyl)methyl)-1-((R)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isopropylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-2-iminoimidazolidin-4-yl)ethanol. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-23 was synthesized using the following reagents: Boc-D-Valine-OH (R1), Boc-D-Cyclohexylalanine-OH (R2), Boc-D-Threonine(Bzl)-OH (R3), 4-tert-butyl-cyclohexancecarboxylic acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/30. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 8.58 (br. s., 2 H) 4.05 - 4.34 (m, 3 H) 3.98 (br. s., 2 H) 3.88 (br. s., 1 H) 3.80 (br. s., 2 H) 3.42 - 3.65 (m, 3 H) 3.40 (br. s., 1 H) 3.31 (br. s., 1 H) 3.18 (br. s., 2 H) 2.69 - 2.87 (m, 2 H) 2.34 (d, *J*=13.08 Hz, 2 H) 2.19 (br. s., 1 H) 2.08 (br. s., 1 H) 1.78 - 1.97 (m, 2 H) 1.71 (br. s., 4 H) 1.48 - 1.67 (m, 6 H) 1.42 (br. s., 1 H) 1.34 (br. s., 1 H) 1.05 - 1.23 (m, 8 H) 0.96 (br. s., 3 H) 0.90 (br. s., 4 H) 0.83 (br. s., 11 H); **m/z** calcd $C_{36}H_{67}N_7O$ $[M+H]^+$ 614.54, found (MS ESI) 614.55. **Purity** LCMS: 98.01% (TIC), 99% (214 nm, peak area); **RT** = 4.35 min

21: (R)-1-((S)-1-((R)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isopropylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-2-imino-3-(4-methylpentyl)imidazolidin-4-yl)ethanol. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-24 was synthesized using the following reagents: Boc-D-Valine-OH (R1), Boc-D-Cyclohexylalanine-OH (R2), Boc-D-Threonine(Bzl)-OH (R3), 4-Methylvaleric acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/30. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 9.05 (br. s., 1 H) 8.59 (br. s., 2 H) 4.21 (br. s., 3 H) 3.95 (br. s., 2 H) 3.80 (br. s., 3 H) 3.55 (br. s., 1 H) 3.48 (br. s., 1 H) 3.30 - 3.44 (m, 3 H) 3.20 (br. s., 2 H) 2.77 (br. s., 2 H) 2.26 - 2.48 (m, 2 H) 2.07 (br. s., 1 H) 1.87 (br. s., 2 H) 1.72 (br. s., 3 H) 1.63 (br. s., 3 H) 1.49 - 1.59 (m, 3 H) 1.42 (br. s., 1 H) 1.36 (br. s., 1 H) 1.17 (br. s., 8 H) 0.99 (br. s., 1 H) 0.76 - 0.95 (m, 12 H); **m/z** calcd $C_{31}H_{59}N_7O$ $[M+H]^+$ 546.48, found (MS ESI) 546.45. **Purity** LCMS: 97.57% (TIC), 99% (214 nm, peak area); **RT** = 3.88 min

22: (R)-3-(adamantan-1-ylmethyl)-1-((R)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isopropylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-4-propylimidazolidin-2-imine. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-25 was synthesized using the following reagents: Boc-D-Valine-OH (R1), Boc-D-Cyclohexylalanine-OH (R2), Boc-D-Norvaline-OH (R3), 1-Adamantanecarboxylic acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/30. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 10.54 (br. s., 1 H) 9.28 (br. s., 1 H) 8.61 (br. s., 2 H) 4.16 (br. s., 1 H) 3.93 (br. s., 1 H) 3.75 (br. s., 1 H) 3.48 - 3.60 (m, 3 H) 3.33 - 3.46 (m, 2 H) 3.25 (br. s., 1 H) 3.06 - 3.22 (m, 2 H) 2.92 (br. s., 1 H) 2.80 (br. s., 1 H) 2.71 (d, *J*=15.28 Hz, 1 H) 2.48 - 2.55 (m, 1 H) 2.44 (d, *J*=13.08 Hz, 1 H) 2.06 (br. s., 1 H) 1.97 (br. s., 3 H) 1.83 - 1.93 (m, 2 H) 1.78 (br. s., 3 H) 1.68 (br. s., 5 H) 1.59 (s, 3 H) 1.63 (s, 4 H) 1.54 (br. s., 4 H) 1.40 (br. s., 3 H) 1.24 - 1.34 (m, 2 H) 1.07 - 1.23 (m, 4 H) 0.92 - 1.06 (m, 4 H) 0.89 (br. s., 3 H) 0.81 (br. s., 3 H); **m/z** calcd $C_{37}H_{65}N_7$ $[M+H]^+$ 608.53, found (MS ESI) 608.5. **Purity** LCMS: 96.94% (TIC), 98% (214 nm, peak area); **RT** = 4.55 min

23: (R)-3-((4-(tert-butyl)cyclohexyl)methyl)-1-((R)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isopropylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-4-propylimidazolidin-2-imine. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-26 was synthesized using the following reagents: Boc-D-Valine-OH (R1), Boc-D-Cyclohexylalanine-OH (R2), Boc-D-Norvaline-OH (R3), 4-tert-butyl-cyclohexancecarboxylic acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/30. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 8.60 (br. s., 2 H) 4.16 (br. s., 1 H) 3.87 (br. s., 1 H) 3.76 (br. s., 2 H) 3.58 (br. s., 2 H) 3.33 - 3.49 (m, 2 H) 3.27 (br. s., 1 H) 3.10 - 3.21 (m, 2 H) 3.03 (d, *J*=13.82 Hz, 1 H) 2.91 (br. s., 1 H) 2.81 (br. s., 1 H) 2.53 (br. s., 1 H) 2.44 (d, *J*=12.84 Hz, 1 H) 2.07 (br. s., 2 H) 1.86 (br. s., 2 H) 1.78 (br. s., 3 H) 1.71 (br. s., 2 H) 1.62 (br. s., 2 H) 1.46 - 1.59 (m, 5 H) 1.40 (br. s., 3 H) 1.31 (br. s., 2 H) 1.06 - 1.22 (m, 5 H) 0.96 (br. s., 5 H) 0.90 (br. s., 4 H) 0.83 (br. s., 12 H); **m/z** calcd $C_{37}H_{69}N_7$ $[M+H]^+$ 612.56, found (MS ESI) 612.55. **Purity** LCMS: 97.60% (TIC), 98% (214 nm, peak area); **RT** = 4.78 min

24: (R)-1-((R)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isopropylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-3-(4-methylpentyl)-4-propylimidazolidin-2-imine. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-27 was synthesized using the following reagents: Boc-D-Valine-OH (R1), Boc-D-

Cyclohexylalanine-OH (R2), Boc-D-Norvaline-OH (R3), 4-Methylvaleric acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/30. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 10.43 (br. s., 1 H) 8.59 (br. s., 2 H) 4.14 (br. s., 2 H) 3.79 (br. s., 2 H) 3.69 (br. s., 1 H) 3.59 (br. s., 2 H) 3.35 - 3.52 (m, 2 H) 3.26 (br. s., 1 H) 3.06 - 3.22 (m, 3 H) 2.94 (br. s., 1 H) 2.84 (br. s., 1 H) 2.53 (br. s., 1 H) 2.45 (d, *J*=13.08 Hz, 1 H) 2.09 (br. s., 1 H) 1.80 (br. s., 4 H) 1.70 (br. s., 2 H) 1.64 (br. s., 2 H) 1.38 - 1.60 (m, 6 H) 1.32 (br. s., 2 H) 1.17 (br. s., 6 H) 0.93 - 1.05 (m, 5 H) 0.73 - 0.93 (m, 12 H); **m/z** calcd $C_{32}H_{61}N_7$ $[M+H]^+$ 544.50, found (MS ESI) 544.45. **Purity** LCMS: 98.63% (TIC), 99% (214 nm, peak area); **RT** = 4.34 min

25: (R)-3-(adamantan-1-ylmethyl)-1-((R)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isopropylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-4-isopropylimidazolidin-2-imine. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-28 was synthesized using the following reagents: Boc-D-Valine-OH (R1), Boc-D-Cyclohexylalanine-OH (R2), Boc-D-Valine-OH (R3), 1-Adamantanecarboxylic acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/30 **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 10.42 (br. s., 1 H) 9.18 (br. s., 1 H) 8.62 (br. s., 2 H) 4.08 (br. s., 1 H) 3.99 (br. s., 1 H) 3.77 (br. s., 1 H) 3.55 - 3.68 (m, 1 H) 3.53 (br. s., 1 H) 3.47 (br. s., 1 H) 3.36 (br. s., 1 H) 3.26 (br. s., 2 H) 3.12 (d, *J*=14.67 Hz, 1 H) 2.92 (br. s., 1 H) 2.81 (br. s., 1 H) 2.71 (d, *J*=15.77 Hz, 1 H) 2.37 - 2.53 (m, 2 H) 2.25 (br. s., 1 H) 2.05 (br. s., 1 H) 1.98 (br. s., 3 H) 1.88 (br. s., 2 H) 1.80 (br. s., 2 H) 1.59 - 1.75 (m, 11 H) 1.36 - 1.59 (m, 6 H) 1.08 - 1.29 (m, 4 H) 1.02 (br. s., 1 H) 0.89 (s, 3 H) 0.93 (s, 3 H) 0.80 (br. s., 5 H); **m/z** calcd $C_{37}H_{65}N_7$ $[M+H]^+$ 608.53, found (MS ESI) 608.55. **Purity** LCMS: 96.79% (TIC), 99% (214 nm, peak area); **RT** = 4.55 min

26: (R)-3-((4-(tert-butyl)cyclohexyl)methyl)-1-((R)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isopropylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-4-isopropylimidazolidin-2-imine. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-29 was synthesized using the following reagents: Boc-D-Valine-OH (R1), Boc-D-Cyclohexylalanine-OH (R2), Boc-D-Valine-OH (R3), 4-tert-butyl-cyclohexancecarboxylic acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/30. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 8.61 (br. s., 2 H) 4.06 (br. s., 1 H) 3.86 - 3.99 (m, 1 H) 3.82 (br. s., 1 H) 3.75 (br. s., 1 H) 3.53 (d, *J*=12.47 Hz, 2 H) 3.38 - 3.49 (m, 1 H) 3.36 (br. s., 1 H) 3.25 (br. s., 2 H) 3.12 (d, *J*=14.43 Hz, 1 H) 2.97 (d, *J*=14.43 Hz, 1 H) 2.90 (br. s., 1 H) 2.81 (br. s., 1 H) 2.40 - 2.50 (m, 2 H) 2.08 (br. s., 2 H) 1.75 - 1.93 (m, 4 H) 1.66 - 1.75 (m, 2 H) 1.63 (br. s., 2 H) 1.48 - 1.59 (m, 5 H) 1.44 (br. s., 2 H) 1.13 (br. s., 5 H) 0.94 (br. s., 6 H) 0.88 (br. s., 4 H) 0.83 (br. s., 14 H); **m/z** calcd $C_{37}H_{69}N_7$ $[M+H]^+$ 612.56, found (MS ESI) 612.55. **Purity** LCMS: 98.26% (TIC), 99% (214 nm, peak area); **RT** = 4.79 min

27: (R)-1-((R)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isopropylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-4-isopropyl-3-(4-methylpentyl)imidazolidin-2-imine. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-30 was synthesized using the following reagents: Boc-D-Valine-OH (R1), Boc-D-Cyclohexylalanine-OH (R2), Boc-D-Valine-OH (R3), 4-Methylvaleric acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/30. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 8.59 (br. s., 2 H) 4.05 (br. s., 2 H) 3.84 (br. s., 1 H) 3.75 (br. s., 2 H) 3.32 - 3.60 (m, 4 H) 3.19 - 3.30 (m, 2 H) 3.12 (d, *J*=14.67 Hz,

1 H) 3.03 (br. s., 1 H) 2.77 - 2.97 (m, 2 H) 2.38 - 2.50 (m, 2 H) 2.13 (br. s., 1 H) 2.05 (br. s., 1 H) 1.80 (br. s., 4 H) 1.66 (d, *J*=17.85 Hz, 4 H) 1.54 (br. s., 3 H) 1.45 (br. s., 2 H) 1.15 (br. s., 6 H) 0.94 (br. s., 4 H) 0.86 (br. s., 10 H) 0.80 (br. s., 5 H); **m/z** calcd $C_{32}H_{61}N_7$ $[M+H]^+$ 544.50, found (MS ESI) 544.5. **Purity** LCMS: 98.73% (TIC), 99% (214 nm, peak area); **RT** = 4.33 min

28: (R)-1-((S)-3-(adamantan-1-ylmethyl)-2-imino-1-((R)-1-((S)-2-(((R)-2-imino-5-isopropylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)imidazolidin-4-yl)ethanol. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-31 was synthesized using the following reagents: Boc-D-Valine-OH (R1), Boc-D-Phenylalanine-OH (R2), Boc-D-Threonine(Bzl)-OH (R3), 1-Adamantanecarboxylic acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/30. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 8.96 (br. s., 1 H) 8.63 (br. s., 2 H) 8.32 (br. s., 1 H) 7.39 (br. s., 2 H) 7.29 (br. s., 1 H) 7.21 (br. s., 1 H) 4.79 (br. s., 1 H) 4.02 (br. s., 2 H) 3.81 (br. s., 3 H) 3.46 - 3.66 (m, 3 H) 3.29 - 3.46 (m, 2 H) 3.22 (d, *J*=12.72 Hz, 1 H) 3.13 (br. s., 1 H) 3.05 (d, *J*=13.20 Hz, 1 H) 2.95 (br. s., 1 H) 2.81 (br. s., 1 H) 2.73 (br. s., 2 H) 2.52 (d, *J*=10.64 Hz, 1 H) 2.38 (br. s., 1 H) 2.10 (br. s., 1 H) 1.88 (br. s., 3 H) 1.59 - 1.76 (m, 4 H) 1.55 (br. s., 4 H) 1.32 (br. s., 3 H) 1.06 - 1.23 (m, 5 H) 1.01 (br. s., 1 H) 0.94 (br. s., 2 H) 0.88 (br. s., 3 H); **m/z** calcd $C_{36}H_{57}N_7O$ $[M+H]^+$ 604.46, found (MS ESI) 614.45. **Purity** LCMS: 97.03% (TIC), 99% (214 nm, peak area); **RT** = 3.92 min

29: (R)-1-((S)-3-((4-(tert-butyl)cyclohexyl)methyl)-2-imino-1-((R)-1-((S)-2-(((R)-2-imino-5-isopropylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)imidazolidin-4-yl)ethanol. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-32 was synthesized using the following reagents: Boc-D-Valine-OH (R1), Boc-D-Phenylalanine-OH (R2), Boc-D-Threonine(Bzl)-OH (R3), 4-tert-butyl-cyclohexancecarboxylic acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/30. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 10.00 (br. s., 1 H) 8.59 (br. s., 2 H) 7.31 (br. s., 2 H) 7.21 (br. s., 2 H) 4.68 (br. s., 1 H) 4.20 (br. s., 2 H) 3.92 (br. s., 1 H) 3.81 (br. s., 1 H) 3.66 (br. s., 1 H) 3.44 - 3.62 (m, 4 H) 3.40 (br. s., 1 H) 3.20 (d, *J*=13.33 Hz, 1 H) 3.12 (br. s., 1 H) 2.87 - 3.07 (m, 2 H) 2.62 - 2.83 (m, 2 H) 2.50 (d, *J*=11.37 Hz, 1 H) 2.40 (br. s., 1 H) 2.09 (br. s., 1 H) 1.86 (br. s., 1 H) 1.70 (br. s., 2 H) 1.51 (br. s., 2 H) 1.36 (br. s., 2 H) 1.07 - 1.27 (m, 4 H) 1.00 (br. s., 1 H) 0.92 (br. s., 3 H) 0.77 - 0.89 (m, 13 H) 0.66 (br. s., 1 H); **m/z** calcd $C_{36}H_{61}N_7O$ $[M+H]^+$ 608.49, found (MS ESI) 608.45. **Purity** LCMS: 98.13% (TIC), 99% (214 nm, peak area); **RT** = 4.18 min

30: (R)-1-((S)-2-imino-1-((R)-1-((S)-2-(((R)-2-imino-5-isopropylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)-3-(4-methylpentyl)imidazolidin-4-yl)ethanol. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-33 was synthesized using the following reagents: Boc-D-Valine-OH (R1), Boc-D-Phenylalanine-OH (R2), Boc-D-Threonine(Bzl)-OH (R3), 4-Methylvaleric acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/15, 30/25, 35/30. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 9.90 (br. s., 1 H) 9.00 (br. s., 1 H) 8.59 (br. s., 2 H) 7.29 (br. s., 2 H) 7.21 (br. s., 2 H) 4.59 (br. s., 2 H) 4.27 (br. s., 2 H) 3.89 (br. s., 1 H) 3.79 (br. s., 1 H) 3.66 (br. s., 1 H) 3.54 (br. s., 1 H) 3.34 - 3.51 (m, 4 H) 3.21 (d, *J*=13.94 Hz, 1 H) 3.13 (br. s., 1 H) 2.86 - 3.06 (m, 2 H) 2.77 (br. s., 2 H) 2.36 - 2.63 (m, 2 H) 2.07 (br. s., 1 H) 1.86 (br. s., 1 H) 1.72 (br. s., 2 H) 1.39 - 1.60 (m, 2 H) 1.30 (br. s., 1 H) 1.04 - 1.22 (m, 3 H) 0.97 (br. s., 2 H) 0.91 (br. s., 3 H) 0.84 (br. s., 7 H); **m/z** calcd $C_{31}H_{53}N_7O$

$[M+H]^+$ 540.43, found (MS ESI) 540.4. **Purity** LCMS: 96.78% (TIC), 99% (214 nm, peak area); **RT** = 3.63 min

31: (R)-3-(adamantan-1-ylmethyl)-1-((R)-1-((S)-2-(((R)-2-imino-5-isopropylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)-4-propylimidazolidin-2-imine. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-34 was synthesized using the following reagents: Boc-D-Valine-OH (R1), Boc-D-Phenylalanine-OH (R2), Boc-D-Norvaline-OH (R3), 1-Adamantanecarboxylic acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/30. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 10.47 (br. s., 1 H) 9.33 (br. s., 1 H) 8.63 (br. s., 2 H) 7.37 (br. s., 2 H) 7.18 (br. s., 2 H) 4.68 (br. s., 1 H) 4.01 (br. s., 2 H) 3.76 (br. s., 1 H) 3.68 (br. s., 1 H) 3.58 (br. s., 2 H) 3.30 - 3.48 (m, 2 H) 3.16 - 3.30 (m, 3 H) 3.07 (d, *J*=14.06 Hz, 1 H) 2.98 (br. s., 2 H) 2.74 (t, *J*=11.55 Hz, 1 H) 2.45 - 2.67 (m, 3 H) 2.08 (br. s., 1 H) 1.87 (br. s., 4 H) 1.71 - 1.82 (m, 2 H) 1.63 (d, *J*=11.49 Hz, 4 H) 1.53 (br. s., 3 H) 1.27 - 1.41 (m, 3 H) 1.24 (br. s., 1 H) 1.05 - 1.21 (m, 3 H) 0.90 (br. s., 5 H) 0.82 (br. s., 3 H); **m/z** calcd $C_{37}H_{59}N_7$ $[M+H]^+$ 602.48, found (MS ESI) 602.45. **Purity** LCMS: 96.95% (TIC), 99% (214 nm, peak area); **RT** = 4.36 min

32: (R)-3-((4-(tert-butyl)cyclohexyl)methyl)-1-((R)-1-((S)-2-(((R)-2-imino-5-isopropylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)-4-propylimidazolidin-2-imine. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-35 was synthesized using the following reagents: Boc-D-Valine-OH (R1), Boc-D-Phenylalanine-OH (R2), Boc-D-Norvaline-OH (R3), 4-tert-butyl-cyclohexancecarboxylic acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/28. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 8.64 (br. s., 2 H) 7.33 (br. s., 2 H) 7.20 (br. s., 2 H) 4.65 (br. s., 1 H) 3.75 (br. s., 2 H) 3.57 (br. s., 4 H) 3.30 - 3.49 (m, 3 H) 3.17 - 3.30 (m, 2 H) 3.12 (br. s., 1 H) 3.04 (d, *J*=14.06 Hz, 1 H) 2.96 (br. s., 1 H) 2.88 (d, *J*=15.53 Hz, 1 H) 2.69 - 2.82 (m, 1 H) 2.61 (d, *J*=10.39 Hz, 2 H) 2.09 (br. s., 1 H) 1.90 (br. s., 1 H) 1.79 (br. s., 2 H) 1.65 (br. s., 1 H) 1.43 - 1.59 (m, 2 H) 1.36 (d, *J*=12.10 Hz, 3 H) 1.23 (br. s., 3 H) 1.07 (d, *J*=12.72 Hz, 2 H) 0.86 - 1.00 (m, 8 H) 0.82 (br. s., 11 H); **m/z** calcd $C_{37}H_{63}N_7$ $[M+H]^+$ 606.51, found (MS ESI) 606.5. **Purity** LCMS: 97.57% (TIC), 99% (214 nm, peak area); **RT** = 4.57 min

33: (R)-1-((R)-1-((S)-2-(((R)-2-imino-5-isopropylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)-3-(4-methylpentyl)-4-propylimidazolidin-2-imine. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-36 was synthesized using the following reagents: Boc-D-Valine-OH (R1), Boc-D-Phenylalanine-OH (R2), Boc-D-Norvaline-OH (R3), 4-Methylvaleric acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/30. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 8.60 (br. s., 2 H) 7.29 - 7.33 (m, 2 H) 7.23 - 7.27 (m, 2 H) 7.19 (br. s., 1 H) 4.55 (br. s., 1 H) 3.74 (br. s., 1 H) 3.32 - 3.60 (m, 6 H) 3.21 (br. s., 2 H) 2.90 - 3.10 (m, 4 H) 2.80 (d, *J*=10.27 Hz, 2 H) 2.47 - 2.68 (m, 2 H) 2.07 (br. s., 1 H) 1.81 - 1.93 (m, 1 H) 1.76 (br. s., 2 H) 1.64 (br. s., 1 H) 1.53 (br. s., 1 H) 1.39 - 1.49 (m, 1 H) 1.20 (br. s., 5 H) 0.96 (br. s., 2 H) 0.88 (br. s., 6 H) 0.81 (br. s., 10 H); **m/z** calcd $C_{32}H_{55}N_7$ $[M+H]^+$ 538.45, found (MS ESI) 538.4. **Purity** LCMS: 96.73% (TIC), 99% (214 nm, peak area); **RT** = 4.11 min

34: (R)-3-(adamantan-1-ylmethyl)-1-((R)-1-((S)-2-(((R)-2-imino-5-isopropylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)-4-isopropylimidazolidin-2-imine. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-37 was synthesized using the following reagents: Boc-D-Valine-OH (R1), Boc-D-Phenylalanine-OH (R2), Boc-D-Valine-OH (R3), 1-Adamantanecarboxylic acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/30. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 10.45 (br. s., 1 H) 9.29 (br. s., 1 H) 8.65 (br. s., 2 H) 7.36 (br. s., 2 H) 7.29 - 7.33 (m, 2 H) 7.21 (br. s., 1 H) 4.63 (br. s., 1 H) 4.03 (br. s., 2 H) 3.75 (br. s., 2 H) 3.56 (br. s., 1 H) 3.46 (br. s., 1 H) 3.37 (t, *J*=14.12 Hz, 3 H) 3.27 (br. s., 1 H) 3.06 - 3.24 (m, 2 H) 2.90 - 3.03 (m, 2 H) 2.72 - 2.89 (m, 1 H) 2.62 (d, *J*=15.53 Hz, 1 H) 2.55 (br. s., 1 H) 2.16 (br. s., 1 H) 2.07 (br. s., 1 H) 1.89 (br. s., 3 H) 1.78 (br. s., 2 H) 1.60 - 1.71 (m, 3 H) 1.56 (br. s., 3 H) 1.37 (d, *J*=10.88 Hz, 3 H) 1.22 (d, *J*=11.25 Hz, 3 H) 0.86 - 0.99 (m, 5 H) 0.82 (br. s., 3 H) 0.73 (br. s., 3 H); **m/z** calcd C37H59N7 $[M+H]^+$ 602.48, found (MS ESI) 602.45. **Purity** LCMS: 95.20% (TIC), 99% (214 nm, peak area); **RT** = 4.36 min

35: (R)-3-((4-(tert-butyl)cyclohexyl)methyl)-1-((R)-1-((S)-2-(((R)-2-imino-5-isopropylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)-4-isopropylimidazolidin-2-imine. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-38 was synthesized using the following reagents: Boc-D-Valine-OH (R1), Boc-D-Phenylalanine-OH (R2), Boc-D-Valine-OH (R3), 4-tert-butyl-cyclohexancecarboxylic acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/30. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 8.65 (br. s., 2 H) 7.36 (br. s., 2 H) 7.29 (br. s., 2 H) 7.22 (br. s., 1 H) 4.65 (br. s., 1 H) 3.65 - 3.90 (m, 2 H) 3.58 (br. s., 2 H) 3.35 - 3.52 (m, 4 H) 3.23 - 3.33 (m, 2 H) 3.20 (br. s., 1 H) 3.09 (d, *J*=12.84 Hz, 1 H) 3.01 (br. s., 2 H) 2.71 - 2.92 (m, 2 H) 2.45 - 2.69 (m, 2 H) 2.09 (br. s., 1 H) 2.04 (br. s., 1 H) 1.92 (br. s., 1 H) 1.80 (br. s., 2 H) 1.62 - 1.74 (m, 1 H) 1.57 (br. s., 1 H) 1.39 - 1.53 (m, 2 H) 1.29 - 1.39 (m, 1 H) 1.23 (d, *J*=11.74 Hz, 1 H) 1.06 - 1.18 (m, 1 H) 0.99 (br. s., 2 H) 0.91 (br. s., 7 H) 0.84 (br. s., 10 H) 0.77 (br. s., 3 H); **m/z** calcd C37H63N7 $[M+H]^+$ 606.51, found (MS ESI) 606.5. **Purity** LCMS: 97.88% (TIC), 99% (214 nm, peak area); **RT** = 4.58 min

36: (R)-1-((R)-1-((S)-2-(((R)-2-imino-5-isopropylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)-4-isopropyl-3-(4-methylpentyl)imidazolidin-2-imine. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-39 was synthesized using the following reagents: Boc-D-Valine-OH (R1), Boc-D-Phenylalanine-OH (R2), Boc-D-Valine-OH (R3), 4-Methylvaleric acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/28. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 9.10 (br. s., 1 H) 8.38 (br. s., 2 H) 7.00 - 7.09 (m, 4 H) 6.95 (br. s., 1 H) 4.28 (br. s., 1 H) 3.50 (br. s., 1 H) 3.22 - 3.37 (m, 3 H) 3.13 (d, *J*=11.00 Hz, 3 H) 2.96 (br. s., 3 H) 2.74 (d, *J*=14.79 Hz, 3 H) 2.59 (d, *J*=10.27 Hz, 2 H) 2.34 (d, *J*=12.96 Hz, 1 H) 2.17 - 2.29 (m, 1 H) 1.83 (br. s., 1 H) 1.59 - 1.79 (m, 2 H) 1.52 (br. s., 2 H) 1.30 (br. s., 1 H) 1.16 - 1.26 (m, 1 H) 1.02 (br. s., 1 H) 0.92 (br. s., 1 H) 0.75 (br. s., 2 H) 0.63 (br. s., 5 H) 0.57 (br. s., 8 H) 0.47 (br. s., 4 H); **m/z** calcd C32H55N7 $[M+H]^+$ 538.45, found (MS ESI) 538.4. **Purity** LCMS: 96.55% (TIC), 99% (214 nm, peak area); **RT** = 4.11 min

37: 4-((1-((R)-1-((S)-2-(((R)-5-((S)-sec-butyl)-2-iminoimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)-3-((4-(tert-butyl)cyclohexyl)methyl)-2-

iminoimidazolidin-4-yl)methyl)phenol. Using General Scheme (scheme 1) for the synthesis of bis-cyclic guanidines compound 2509-40 was synthesized using the following reagents: Boc-D-Isoleucine-OH (R1), Boc-D-Phenylalanine-OH (R2), Boc-D-Tyrosine(2-Br-Z)-OH (R3), 4-tert-butyl-cyclohexancecarboxylic acid (R4). The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 30/28. **1H NMR** (400 MHz, CHLOROFORM-*d*) d ppm 9.26 (br. s., 1 H) 8.66 (br. s., 2 H) 7.22 (br. s., 2 H) 6.88 (br. s., 3 H) 4.38 (br. s., 1 H) 3.94 (br. s., 2 H) 3.85 (br. s., 2 H) 3.64 (br. s., 2 H) 3.48 - 3.58 (m, 2 H) 3.45 (br. s., 1 H) 3.38 (br. s., 1 H) 3.23 (br. s., 1 H) 2.98 - 3.18 (m, 3 H) 2.92 (br. s., 1 H) 2.69 (br. s., 2 H) 2.53 (br. s., 2 H) 2.44 (br. s., 1 H) 1.95 (br. s., 1 H) 1.82 (br. s., 3 H) 1.52 (br. s., 2 H) 1.39 (br. s., 1 H) 1.33 (br. s., 1 H) 1.22 (d, *J*=13.45 Hz, 3 H) 0.95 (br. s., 4 H) 0.69 - 0.90 (m, 10 H); **m/z** calcd C42H65N7O $[M+H]^+$ 684.54, found (MS ESI) 684.5. **Purity** LCMS: 98.23 % (TIC), 99% (214 nm, peak area); **RT** = 4.47 min

Penta-amine Compound Characterization

2494-1: (3S)-4-((R)-2-((((2R,3S)-1-amino-3-methylpentan-2-yl)amino)methyl)pyrrolidin-1-yl)-3-(((S)-2-((4-ethoxyphenethyl)amino)-3-phenylpropyl)amino)butan-2-ol. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-1 was synthesized using the following reagents: (R1) Boc-D-Ile-OH, (R2) Boc-D-Thr(Bzl)-OH, (R3) Boc-Phe-OH, (R4) 4-ethoxyphenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/10, 35/40. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.52 (br. s., 1 H) 7.29 (br. s., 1 H) 7.26 (br. s., 1 H) 7.14 (d, *J*=8.93 Hz, 3 H) 6.98 (br. s., 1 H) 6.73 - 6.89 (m, 3 H) 6.64 (br. s., 3 H) 4.01 (br. s., 2 H) 3.92 (br. s., 2 H) 3.61 (br. s., 1 H) 3.49 (br. s., 1 H) 3.32 (br. s., 1 H) 3.18 (br. s., 2 H) 2.97 - 3.14 (m, 5 H) 2.85 (br. s., 4 H) 2.19 (br. s., 1 H) 2.08 (br. s., 1 H) 2.02 (br. s., 2 H) 1.89 (br. s., 1 H) 1.76 (br. s., 1 H) 1.42 (br. s., 3 H) 1.31 (br. s., 1 H) 1.02 - 1.25 (m, 3 H) 0.92 (br. s., 3 H) 0.83 (br. s., 2 H) **m/z** calcd $C_{34}H_{57}N_5O_2$ $[M+H]^+$ 567.45, found (MS ESI) 568.20. **Purity** LCMS: 97.51% (TIC), 100% (214 nm, peak area); **RT** = 3.2 min

2494-2: (2R,3S)-4-((R)-2-((((2R,3S)-1-amino-3-methylpentan-2-yl)amino)methyl)pyrrolidin-1-yl)-3-(((S)-2-(((4-(tert-butyl)cyclohexyl)methyl)amino)-3-phenylpropyl)amino)butan-2-ol. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-2 was synthesized using the following reagents: (R1) Boc-D-Ile-OH, (R2) Boc-D-Thr(Bzl)-OH, (R3) Boc-Phe-OH, 4-tert-butyl-cyclohexancecarboxylic acid (R4) 4-tert-butyl-cyclohexancecarboxylic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/15, 35/45. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.51 (br. s., 1 H) 7.33 (br. s., 2 H) 7.26 (br. s., 3 H) 6.81 (br. s., 5 H) 3.74 - 4.02 (m, 2 H) 3.60 (br. s., 1 H) 3.47 (br. s., 1 H) 3.07 - 3.32 (m, 3 H) 3.02 (br. s., 3 H) 2.94 (br. s., 2 H) 2.80 (d, *J*=15.77 Hz, 3 H) 2.31 (br. s., 1 H) 2.18 (br. s., 1 H) 2.03 (br. s., 4 H) 1.97 (br. s., 1 H) 1.85 - 1.94 (m, 1 H) 1.65 - 1.85 (m, 3 H) 1.42 - 1.64 (m, 3 H) 1.32 (br. s., 1 H) 1.17 (br. s., 1 H) 1.02 - 1.14 (m, 2 H) 0.95 (br. s., 5 H) 0.84 (br. s., 9 H) **m/z** calcd $C_{35}H_{65}N_5O$ $[M+H]^+$ 571.52, found (MS ESI) 572.20. **Purity** LCMS: 98.89% (TIC), 93.02% (214 nm, peak area); **RT** = 3.6 min

2494-3: (3S)-4-((R)-2-((((2R,3S)-1-amino-3-methylpentan-2-yl)amino)methyl)pyrrolidin-1-yl)-3-(((S)-2-((3,5-bis(trifluoromethyl)phenethyl)amino)-3-phenylpropyl)amino)butan-2-ol. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-3 was synthesized using the following reagents: (R1) Boc-D-Ile-OH, (R2) Boc-D-Thr(Bzl)-OH, (R3) Boc-Phe-OH, (R4) 3,5-Bis(Trifluoromethyl)-Phenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/15, 35/45. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.48 (br. s., 1 H) 7.75 (br. s., 1 H) 7.66 (br. s., 1 H) 7.31 (br. s., 2 H) 7.24 (br. s., 2 H) 7.18 (br. s., 1 H) 6.62 (br. s., 4 H) 3.98 (br. s., 1 H) 3.89 (br. s., 1 H) 3.54 (br. s., 1 H) 3.35 (br. s., 1 H) 3.15 - 3.30 (m, 3 H) 2.99 - 3.15 (m, 4 H) 2.87 - 2.99 (m, 3 H) 2.81 (br. s., 1 H) 2.68 (br. s., 1 H) 2.22 (br. s., 1 H) 2.10 (br. s., 1 H) 2.02 (br. s., 2 H) 1.90 (br. s., 1 H) 1.78 (br. s., 1 H) 1.51 (br. s., 1 H) 1.31 (br. s., 1 H) 1.18 (br. s., 1 H) 1.12 (br. s., 2 H) 0.93 (br. s., 3 H) 0.83 (br. s., 3 H) **m/z** calcd $C_{34}H_{51}F_6N_5O$ $[M+H]^+$ 659.4, found (MS ESI) 660.00. **Purity** LCMS: 92.73% (TIC), 91.69% (214 nm, peak area); **RT** = 3.62 min

2494-4: (3S)-4-((R)-2-((((2R,3S)-1-amino-3-methylpentan-2-yl)amino)methyl)pyrrolidin-1-yl)-3-(((R)-3-cyclohexyl-2-((4-ethoxyphenethyl)amino)propyl)amino)butan-2-ol. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-4 was synthesized using the following reagents: (R1) Boc-D-Ile-OH, (R2) Boc-D-Thr(Bzl)-OH, (R3) Boc-D-Cha-OH, (R4) 4-ethoxyphenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/10, 35/40. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.51 (br. s., 2 H) 7.29 (br. s., 1 H) 7.01 - 7.26 (m, 2 H) 6.74 - 7.00 (m, 3 H) 6.65 (br. s., 3 H) 4.01 (br. s., 4 H) 3.65 (br. s., 1 H) 3.28 (br. s., 1 H) 3.18 (br. s., 3 H) 2.98 - 3.14 (m, 5 H) 2.94 (br. s., 1 H) 2.66 - 2.89 (m, 1 H) 2.21 (br. s., 1 H) 2.09 (br. s., 1 H) 2.03 (br. s., 2 H) 1.90 (br. s., 1 H) 1.63 - 1.79 (m, 5 H) 1.47 - 1.63 (m, 2 H) 1.41 (br. s., 3 H) 1.09 - 1.33 (m, 7 H) 0.88 - 1.05 (m, 4 H) 0.84 (br. s., 3 H) **m/z** calcd $C_{34}H_{63}N_5O_2$ $[M+H]^+$ 573.5, found (MS ESI) 574.20. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.40 min

2494-5: N/A

2494-6: (3S)-4-((R)-2-((((2R,3S)-1-amino-3-methylpentan-2-yl)amino)methyl)pyrrolidin-1-yl)-3-(((R)-2-((3,5-bis(trifluoromethyl)phenethyl)amino)-3-cyclohexylpropyl)amino)butan-2-ol. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-6 was synthesized using the following reagents: (R1) Boc-D-Ile-OH, (R2) Boc-D-Thr(Bzl)-OH, (R3) Boc-D-Cha-OH, (R4) 3,5-Bis(Trifluoromethyl)-Phenylacetic acid. The final crude product was purified using HPLC as described above a gradient of (B) 2, 0/2, 2/2, 6/15, 35/45. **1H NMR** (400 MHz, CHLOROFORM, with -*d*) δ ppm 8.54 (br. s., 1 H) 7.79 (d, *J*=9.54 Hz, 3 H) 6.77 (br. s., 3 H) 4.06 (br. s., 1 H) 3.97 (br. s., 1 H) 3.63 (br. s., 1 H) 3.51 (d, *J*=12.23 Hz, 1 H) 3.28 - 3.45 (m, 2 H) 3.21 (d, *J*=11.74 Hz, 4 H) 2.91 - 3.15 (m, 5 H) 2.77 - 2.89 (m, 1 H) 2.72 (d, *J*=9.66 Hz, 1 H) 2.23 (br. s., 1 H) 2.11 (br. s., 1 H) 2.03 (br. s., 3 H) 1.92 (br. s., 1 H) 1.78 (br. s., 1 H) 1.65 - 1.74 (m, 4 H) 1.60 (br. s., 1 H) 1.55 (br. s., 1 H) 1.27 (br. s., 5 H) 1.19 (br. s., 3 H) 0.95 (br. s., 4 H) 0.84 (br. s., 3 H) **m/z** calcd $C_{34}H_{57}F_6N_5O$ $[M+H]^+$ 665.45, found (MS ESI) 666.25. **Purity** LCMS: 98.78% (TIC), 100% (214 nm, peak area); **RT** = 3.76 min

2494-7: 4-((2S)-3-(((2S)-1-((R)-2-((((2R,3S)-1-amino-3-methylpentan-2-yl)amino)methyl)pyrrolidin-1-yl)-3-hydroxybutan-2-yl)amino)-2-((4-ethoxyphenethyl)amino)propyl)phenol. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-7 was synthesized using the following reagents: (R1) Boc-D-Ile-OH, (R2) Boc-D-Thr(Bzl)-OH, (R3) Boc-D-Tyr(2-Br-Z)-OH, (R4) 4-ethoxyphenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/10, 35/40. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.38 (br. s., 1 H) 7.14 (br. s., 1 H) 6.99 (br. s., 2 H) 6.82 (br. s., 3 H) 6.65 (br. s., 4 H) 3.84 (br. s., 2 H) 3.63 (br. s., 2 H) 3.44 (br. s., 1 H) 3.29 (br. s., 1 H) 3.11 (br. s., 2 H) 2.95 (br. s., 3 H) 2.83 (br. s., 4 H) 2.60 (br. s., 3 H) 2.00 (br. s., 1 H) 1.87 (br. s., 5 H) 1.71 (br. s., 1 H) 1.57 (br. s., 2 H) 1.24 (br. s., 3 H) 1.13 (br. s., 1 H) 0.96 (d, *J*=19.44 Hz, 1 H) 0.85 (br. s., 2 H) 0.74 (br. s., 3 H) 0.63 (br. s., 2 H) **m/z** calcd $C_{34}H_{57}N_5O_3$ $[M+H]^+$ 583.45, found (MS ESI) 584.25. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 2.96 min

2494-8: 4-((2S)-3-(((2S)-1-((R)-2-((((2R,3S)-1-amino-3-methylpentan-2-yl)amino)methyl)pyrrolidin-1-yl)-3-hydroxybutan-2-yl)amino)-2-(((4-(tert-butyl)cyclohexyl)methyl)amino)propyl)phenol. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-8 was synthesized using the following reagents: (R1) Boc-D-Ile-OH, (R2) Boc-D-Thr(Bzl)-OH, (R3) Boc-D-Tyr(2-Br-Z)-OH, (R4) 4-tert-butyl-cyclohexancecarboxylic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/10, 35/40. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.52 (br. s., 1 H) 7.29 (br. s., 1 H) 7.02 (br. s., 3 H) 6.82 (br. s., 5 H) 3.78 (br. s., 2 H) 3.63 (br. s., 1 H) 3.31 (br. s., 2 H) 3.10 (br. s., 3 H) 2.96 (br. s., 4 H) 2.76 (br. s., 3 H) 2.33 (br. s., 1 H) 2.18 (br. s., 1 H) 2.03 (br. s., 5 H) 1.85 - 1.97 (m, 2 H) 1.82 (br. s., 1 H) 1.73 (br. s., 1 H) 1.58 (br. s., 3 H) 1.29 (br. s., 1 H) 1.16 (br. s., 2 H) 1.02 (br. s., 4 H) 0.93 (br. s., 3 H) 0.68 - 0.89 (m, 9 H) **m/z** calcd $C_{35}H_{65}N_5O_2$ $[M+H]^+$ 587.51, found (MS ESI) 588.20. **Purity** LCMS: 99.12% (TIC), 100% (214 nm, peak area); **RT** = 3.95 min

2494-9: 4-((2S)-3-(((2S)-1-((R)-2-((((2R,3S)-1-amino-3-methylpentan-2-yl)amino)methyl)pyrrolidin-1-yl)-3-hydroxybutan-2-yl)amino)-2-((3,5-bis(trifluoromethyl)phenethyl)amino)propyl)phenol. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-9 was synthesized using the following reagents: (R1) Boc-D-Ile-OH, (R2) Boc-D-Thr(Bzl)-OH, (R3) Boc-D-Tyr(2-Br-Z)-OH, (R4) 3,5-Bis(Trifluoromethyl)-Phenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/10, 35/40. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.52 (br. s., 1 H) 7.77 (br. s., 2 H) 7.00 (br. s., 2 H) 6.84 - 6.96 (m, 2 H) 6.78 (br. s., 5 H) 3.79 (br. s., 2 H) 3.60 (br. s., 1 H) 3.26 - 3.50 (m, 3 H) 3.21 (br. s., 2 H) 2.95 - 3.14 (m, 4 H) 2.92 (br. s., 2 H) 2.57 - 2.85 (m, 2 H) 2.18 (br. s., 1 H) 2.02 (br. s., 5 H) 1.86 (br. s., 1 H) 1.75 (br. s., 2 H) 1.28 (br. s., 1 H) 1.13 (br. s., 1 H) 1.02 (br. s., 2 H) 0.92 (br. s., 2 H) 0.80 (br. s., 2 H) **m/z** calcd $C_{34}H_{51}F_6N_5O_2$ $[M+H]^+$ 675.39, found (MS ESI) 676.15. **Purity** LCMS: 96.45% (TIC), 98% (214 nm, peak area); **RT** = 4.30 min

2494-10: (2R,3S)-N2-(((R)-1-((S)-3-cyclohexyl-2-(((R)-2-((4-ethoxyphenethyl)amino)-3-phenylpropyl)amino)propyl)pyrrolidin-2-yl)methyl)-3-methylpentane-1,2-diamine. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-10 was synthesized using the following reagents: (R1) Boc-D-Ile-OH, (R2) Boc-Cha-OH, (R3) Boc-Phe-OH, (R4) 4-ethoxyphenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/15, 35/45. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.53 (br. s., 1 H) 7.29 - 7.38 (m, 2 H) 7.20 - 7.27 (m, 2 H) 7.00 - 7.19 (m, 3 H) 6.83 (d, *J*=6.60 Hz, 5 H) 4.01 (br. s., 2 H) 3.87 (br. s., 1 H) 3.69 (br. s., 1 H) 3.47 (br. s., 1 H) 3.36 (br. s., 2 H) 3.09 - 3.29 (m, 5 H) 3.03 (d, *J*=13.08 Hz, 2 H) 2.70 - 2.98 (m, 6 H) 2.20 (br. s., 1 H) 2.10 (br. s., 1 H) 2.01 (br. s., 2 H) 1.77 (br. s., 2 H) 1.63 (br. s., 4 H) 1.50 (d, *J*=11.98 Hz, 2 H) 1.41 (br. s., 3 H) 1.33 (br. s., 1 H) 1.27 (br. s., 2 H) 1.13 (d, *J*=11.98 Hz, 4 H) 0.93 (br. s., 4 H) 0.84 (br. s., 3 H) 0.70 (d, *J*=10.39 Hz, 1 H) **m/z** calcd $C_{39}H_{65}N_5O$ $[M+H]^+$ 619.52, found 620.20 (MS ESI) . **Purity** LCMS: 99.25% (TIC), 98.65% (214 nm, peak area); **RT** = 3.70 min

2494-11: (2R,3S)-N2-(((R)-1-((S)-2-(((R)-2-(((4-(tert-butyl)cyclohexyl)methyl)amino)-3-phenylpropyl)amino)-3-cyclohexylpropyl)pyrrolidin-2-yl)methyl)-3-methylpentane-1,2-diamine. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-11 was synthesized using the following reagents: (R1) Boc-D-Ile-OH, (R2) Boc-Cha-OH, (R3)

Boc-Phe-OH, (R4) 4-tert-butyl-cyclohexancecarboxylic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 35/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.52 (br. s., 1 H) 7.33 (br. s., 2 H) 6.57 (br. s., 5 H) 3.83 (br. s., 1 H) 3.67 (br. s., 1 H) 3.32 (br. s., 2 H) 3.21 (br. s., 1 H) 3.07 (d, *J*=10.51 Hz, 2 H) 2.84 - 3.03 (m, 5 H) 2.60 - 2.83 (m, 2 H) 2.30 (br. s., 1 H) 2.18 (br. s., 1 H) 2.07 (br. s., 1 H) 1.88 - 2.04 (m, 4 H) 1.73 - 1.87 (m, 3 H) 1.46 - 1.73 (m, 8 H) 1.33 (br. s., 2 H) 1.27 (br. s., 2 H) 1.06 - 1.21 (m, 4 H) 0.89 - 1.04 (m, 7 H) 0.68 - 0.89 (m, 12 H) **m/z** calcd $C_{40}H_{73}N_5$ $[M+H]^+$ 623.59, found (MS ESI) 624.20. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.98 min

2494-12: (2R,3S)-N2-(((R)-1-((S)-2-(((R)-2-((3,5-bis(trifluoromethyl)phenethyl)amino)-3-phenylpropyl)amino)-3-cyclohexylpropyl)pyrrolidin-2-yl)methyl)-3-methylpentane-1,2-diamine. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-12 was synthesized using the following reagents: (R1) Boc-D-Ile-OH, (R2) Boc-Cha-OH, (R3) Boc-Phe-OH, (R4) 3,5-Bis(Trifluoromethyl)-Phenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 35/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.50 (br. s., 1 H) 7.75 (br. s., 1 H) 7.68 (br. s., 2 H) 7.32 (br. s., 2 H) 7.20 (br. s., 3 H) 6.76 (br. s., 3 H) 3.80 (br. s., 1 H) 3.64 (br. s., 1 H) 3.35 (br. s., 3 H) 3.29 (br. s., 1 H) 2.97 - 3.25 (m, 7 H) 2.85 - 2.97 (m, 2 H) 2.77 (t, *J*=11.86 Hz, 2 H) 2.23 (br. s., 1 H) 2.12 (br. s., 1 H) 2.01 (br. s., 2 H) 1.79 (br. s., 2 H) 1.64 (br. s., 3 H) 1.54 (d, *J*=13.20 Hz, 2 H) 1.36 (br. s., 1 H) 1.31 (br. s., 1 H) 1.15 (d, *J*=12.10 Hz, 4 H) 0.89 - 1.05 (m, 4 H) 0.85 (br. s., 3 H) 0.75 (br. s., 1 H) **m/z** calcd $C_{39}H_{59}F_6N_5$ $[M+H]^+$ 711.47, found (MS ESI) 712.20. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.99 min

2494-13: (2R,3S)-N2-(((R)-1-((S)-3-cyclohexyl-2-(((R)-3-cyclohexyl-2-((4-ethoxyphenethyl)amino)propyl)amino)propyl)pyrrolidin-2-yl)methyl)-3-methylpentane-1,2-diamine. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-13 was synthesized using the following reagents: (R1) Boc-D-Ile-OH, (R2) Boc-Cha-OH, (R3) Boc-D-Cha-OH, (R4) 4-ethoxyphenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 35/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.53 (br. s., 2 H) 7.29 (br. s., 1 H) 7.18 (d, *J*=7.21 Hz, 3 H) 6.84 (d, *J*=6.85 Hz, 4 H) 3.98 - 4.25 (m, 2 H) 3.96 (br. s., 1 H) 3.68 (br. s., 1 H) 3.33 - 3.49 (m, 2 H) 3.26 (d, *J*=12.84 Hz, 2 H) 3.17 (br. s., 2 H) 2.93 - 3.13 (m, 4 H) 2.84 - 2.93 (m, 1 H) 2.57 - 2.83 (m, 2 H) 2.16 - 2.43 (m, 1 H) 2.12 (br. s., 1 H) 2.03 (br. s., 3 H) 1.63 - 1.87 (m, 10 H) 1.55 (br. s., 3 H) 1.41 (br. s., 3 H) 1.32 (br. s., 2 H) 1.09 - 1.29 (m, 7 H) 0.93 (br. s., 6 H) 0.69 - 0.89 (m, 3 H) **m/z** calcd $C_{39}H_{71}N_5O$ $[M+H]^+$ 625.57, found (MS ESI) 626.20. **Purity** LCMS: 99.16% (TIC), 100% (214 nm, peak area); **RT** = 3.87 min

2494-14: N/A

2494-15: (2R,3S)-N2-(((R)-1-((S)-2-(((R)-2-((3,5-bis(trifluoromethyl)phenethyl)amino)-3-cyclohexylpropyl)amino)-3-cyclohexylpropyl)pyrrolidin-2-yl)methyl)-3-methylpentane-1,2-diamine. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-15 was synthesized using the following reagents: (R1) Boc-D-Ile-OH, (R2) Boc-Cha-OH, (R3) Boc-D-Cha-OH, (R4) 3,5-Bis(Trifluoromethyl)-Phenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 35/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.51 (br. s., 2 H) 7.73 - 7.99 (m, 3 H) 6.63 (br. s., 3

H) 3.91 (br. s., 1 H) 3.75 (br. s., 1 H) 3.37 - 3.61 (m, 3 H) 3.11 - 3.36 (m, 5 H) 3.04 (d, *J*=14.31 Hz, 2 H) 2.91 (d, *J*=10.64 Hz, 1 H) 2.63 - 2.85 (m, 2 H) 2.26 (br. s., 1 H) 2.13 (br. s., 1 H) 2.03 (br. s., 3 H) 1.84 (br. s., 1 H) 1.65 - 1.77 (m, 9 H) 1.58 (br. s., 3 H) 1.34 (br. s., 3 H) 1.21 (br. s., 7 H) 0.89 - 1.07 (m, 6 H) 0.64 - 0.89 (m, 4 H) **m/z** calcd $C_{39}H_{65}F_6N_5$ $[M+H]^+$ 717.51, found (MS ESI) 718.10. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 4.15 min

2494-16: 4-((R)-3-(((S)-1-((R)-2-((((2R,3S)-1-amino-3-methylpentan-2-yl)amino)methyl)pyrrolidin-1-yl)-3-cyclohexylpropan-2-yl)amino)-2-((4-ethoxyphenethyl)amino)propyl)phenol. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-16 was synthesized using the following reagents: (R1) Boc-D-Ile-OH, (R2) Boc-Cha-OH, (R3) Boc-D-Tyr(2-Br-Z)-OH, (R4) 4-ethoxyphenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/10, 35/40. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.57 (br. s., 2 H) 7.30 (br. s., 1 H) 7.14 (d, *J*=6.85 Hz, 3 H) 6.90 - 7.02 (m, 2 H) 6.79 - 6.89 (m, 4 H) 6.08 (br. s., 2 H) 4.00 (br. s., 2 H) 3.77 (br. s., 1 H) 3.68 (br. s., 1 H) 3.30 (br. s., 2 H) 3.21 (br. s., 2 H) 3.07 (br. s., 4 H) 3.01 (br. s., 3 H) 2.89 (br. s., 1 H) 2.73 (d, *J*=9.78 Hz, 2 H) 2.63 (br. s., 1 H) 2.19 (br. s., 1 H) 1.90 - 2.11 (m, 2 H) 1.75 (br. s., 2 H) 1.63 (br. s., 5 H) 1.40 (br. s., 5 H) 1.04 - 1.28 (m, 6 H) 0.90 (br. s., 4 H) 0.81 (br. s., 4 H) **m/z** calcd $C_{39}H_{65}N_5O_2$ $[M+H]^+$ 635.51, found (MS ESI) 636.25. **Purity** LCMS: 99.48% (TIC), 100% (214 nm, peak area); **RT** = 3.47 min

2494-17: 4-((R)-3-(((S)-1-((R)-2-((((2R,3S)-1-amino-3-methylpentan-2-yl)amino)methyl)pyrrolidin-1-yl)-3-cyclohexylpropan-2-yl)amino)-2-(((4-(tert-butyl)cyclohexyl)methyl)amino)propyl)phenol. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-17 was synthesized using the following reagents: (R1) Boc-D-Ile-OH, (R2) Boc-Cha-OH, (R3) Boc-D-Tyr(2-Br-Z)-OH, (R4) 4-tert-butyl-cyclohexancecarboxylic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 35/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.52 (br. s., 1 H) 7.01 (br. s., 7 H) 6.90 (br. s., 1 H) 6.84 (br. s., 2 H) 3.80 (br. s., 1 H) 3.65 (br. s., 1 H) 3.36 (br. s., 2 H) 3.23 (d, *J*=11.49 Hz, 1 H) 2.97 - 3.17 (m, 4 H) 2.85 - 2.96 (m, 2 H) 2.81 (br. s., 1 H) 2.73 (d, *J*=11.74 Hz, 2 H) 2.28 (br. s., 1 H) 2.19 (br. s., 1 H) 1.83 - 2.09 (m, 8 H) 1.78 (br. s., 2 H) 1.48 - 1.72 (m, 7 H) 1.35 (br. s., 2 H) 1.15 (br. s., 5 H) 0.89 - 1.05 (m, 6 H) 0.84 (br. s., 10 H) **m/z** calcd $C_{40}H_{73}N_5O$ $[M+H]^+$ 639.58, found (MS ESI) 640.25. **Purity** LCMS: 99.31% (TIC), 100% (214 nm, peak area); **RT** = 3.81 min

2494-18: 4-((R)-3-(((S)-1-((R)-2-((((2R,3S)-1-amino-3-methylpentan-2-yl)amino)methyl)pyrrolidin-1-yl)-3-cyclohexylpropan-2-yl)amino)-2-((3,5-bis(trifluoromethyl)phenethyl)amino)propyl)phenol. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-18 was synthesized using the following reagents: (R1) Boc-D-Ile-OH, (R2) Boc-Cha-OH, (R3) Boc-D-Tyr(2-Br-Z)-OH, (R4) 3,5-Bis(Trifluoromethyl)-Phenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 35/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.53 (br. s., 1 H) 7.73 (br. s., 2 H) 7.29 (br. s., 1 H) 6.83 - 7.12 (m, 6 H) 6.57 - 6.83 (m, 3 H) 3.78 (br. s., 1 H) 3.46 (br. s., 1 H) 3.22 - 3.39 (m, 3 H) 3.10 (d, *J*=13.82 Hz, 3 H) 3.03 (br. s., 2 H) 2.65 - 2.92 (m, 4 H) 2.21 (d, *J*=16.99 Hz, 1 H) 2.09 (br. s., 1 H) 2.02 (br. s., 6 H) 1.86 (br. s., 1 H) 1.54 - 1.82 (m, 5 H) 1.34 (d, *J*=18.46 Hz, 2 H) 1.14 (d, *J*=11.86 Hz,

4 H) 0.92 (br. s., 3 H) 0.83 (br. s., 3 H) **m/z** calcd $C_{39}H_{59}F_6N_5O$ $[M+H]^+$ 727.46, found (MS ESI) 728.20. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.79 min

2494-19: (2R,3S)-N2-(((R)-1-((R)-2-(((S)-2-((4-ethoxyphenethyl)amino)-3-phenylpropyl)amino)-3-phenylpropyl)pyrrolidin-2-yl)methyl)-3-methylpentane-1,2-diamine. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-19 was synthesized using the following reagents: (R1) Boc-D-Ile-OH, (R2) Boc-D-Phe-OH, (R3) Boc-Phe-OH, (R4) 4-ethoxyphenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 35/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.51 (br. s., 2 H) 7.35 (d, *J*=6.24 Hz, 3 H) 7.19 - 7.27 (m, 3 H) 7.15 (d, *J*=7.95 Hz, 3 H) 6.93 - 7.11 (m, 4 H) 6.83 (d, *J*=6.97 Hz, 4 H) 3.98 - 4.15 (m, 2 H) 3.90 - 3.98 (m, 1 H) 3.51 (br. s., 1 H) 3.40 (d, *J*=13.69 Hz, 1 H) 3.26 (br. s., 2 H) 2.96 - 3.23 (m, 7 H) 2.79 - 2.95 (m, 3 H) 2.60 - 2.78 (m, 2 H) 2.55 (d, *J*=11.74 Hz, 1 H) 2.38 (t, *J*=10.82 Hz, 1 H) 2.19 (br. s., 1 H) 2.03 (br. s., 2 H) 1.94 (br. s., 1 H) 1.74 (br. s., 2 H) 1.42 (br. s., 3 H) 1.35 (br. s., 1 H) 1.19 (br. s., 1 H) 0.94 (br. s., 3 H) 0.69 - 0.90 (m, 2 H) **m/z** calcd $C_{39}H_{59}N_5O$ $[M+H]^+$ 613.47, found (MS ESI) 614.15. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.55 min

2494-20: (2R,3S)-N2-(((R)-1-((R)-2-(((S)-2-(((4-(tert-butyl)cyclohexyl)methyl)amino)-3-phenylpropyl)amino)-3-phenylpropyl)pyrrolidin-2-yl)methyl)-3-methylpentane-1,2-diamine. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-20 was synthesized using the following reagents: (R1) Boc-D-Ile-OH, (R2) Boc-D-Phe-OH, (R3) Boc-Phe-OH, (R4) 4-tert-butyl-cyclohexancecarboxylic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 35/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.54 (br. s., 1 H) 7.29 - 7.55 (m, 4 H) 7.20 - 7.27 (m, 3 H) 6.98 - 7.19 (m, 4 H) 6.91 (br. s., 3 H) 3.99 (br. s., 1 H) 3.92 (br. s., 1 H) 3.52 (br. s., 2 H) 3.28 (d, *J*=10.51 Hz, 2 H) 3.20 (br. s., 1 H) 3.10 (d, *J*=12.84 Hz, 1 H) 3.00 (d, *J*=11.98 Hz, 3 H) 2.81 - 2.96 (m, 3 H) 2.75 (br. s., 1 H) 2.65 (d, *J*=13.57 Hz, 1 H) 2.58 (br. s., 1 H) 2.38 (br. s., 1 H) 2.14 (br. s., 1 H) 1.93 - 2.07 (m, 6 H) 1.90 (br. s., 1 H) 1.81 (br. s., 1 H) 1.72 (br. s., 2 H) 1.58 (d, *J*=12.35 Hz, 2 H) 1.33 (br. s., 1 H) 1.17 (br. s., 1 H) 0.89 - 1.06 (m, 6 H) 0.84 (br. s., 9 H) **m/z** calcd $C_{40}H_{67}N_5O$ $[M+H]^+$ 617.54, found (MS ESI) 618.15. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.83 min

2494-21: (2R,3S)-N2-(((R)-1-((R)-2-(((S)-2-((3,5-bis(trifluoromethyl)phenethyl)amino)-3-phenylpropyl)amino)-3-phenylpropyl)pyrrolidin-2-yl)methyl)-3-methylpentane-1,2-diamine Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-21 was synthesized using the following reagents: (R1) Boc-D-Ile-OH, (R2) Boc-D-Phe-OH, (R3) Boc-Phe-OH, (R4) 3,5-Bis(Trifluoromethyl)-Phenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 35/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.47 (br. s., 2 H) 8.20 (br. s., 1 H) 7.76 (br. s., 2 H) 7.68 (br. s., 2 H) 7.59 (br. s., 1 H) 7.29 - 7.47 (m, 6 H) 7.18 (br. s., 3 H) 7.12 (br. s., 1 H) 7.05 (br. s., 2 H) 3.99 (t, *J*=11.07 Hz, 1 H) 3.56 (br. s., 1 H) 3.50 (br. s., 1 H) 3.30 - 3.44 (m, 2 H) 3.00 - 3.29 (m, 7 H) 2.93 (d, *J*=12.72 Hz, 3 H) 2.66 (d, *J*=11.62 Hz, 1 H) 2.28 - 2.51 (m, 1 H) 2.20 (br. s., 1 H) 2.03 (br. s., 2 H) 1.96 (br. s., 1 H) 1.75 (br. s., 2 H) 1.36 (br. s., 1 H) 1.21 (br. s., 1 H) 0.95 (br. s., 3 H) 0.86 (br. s., 2 H) **m/z** calcd $C_{39}H_{53}F_6N_5$ $[M+H]^+$ 705.42, found (MS ESI) 706.10. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.89 min

2494-22: (2R,3S)-N2-(((R)-1-((R)-2-(((R)-3-cyclohexyl-2-((4-ethoxyphenethyl)amino)propyl)amino)-3-phenylpropyl)pyrrolidin-2-yl)methyl)-3-methylpentane-1,2-diamine Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-22 was synthesized using the following reagents: (R1) Boc-D-Ile-OH, (R2) Boc-D-Phe-OH, (R3) Boc-D-Cha-OH, (R4) 4-ethoxyphenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 35/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.52 (br. s., 2 H) 7.33 (br. s., 4 H) 7.26 (br. s., 1 H) 7.18 (br. s., 3 H) 6.78 - 7.02 (m, 3 H) 6.70 (br. s., 1 H) 3.92 - 4.08 (m, 3 H) 3.52 (br. s., 1 H) 3.16 - 3.36 (m, 4 H) 3.12 (d, *J*=14.67 Hz, 4 H) 3.01 (br. s., 1 H) 2.75 - 2.96 (m, 2 H) 2.70 (d, *J*=12.35 Hz, 1 H) 2.59 (br. s., 1 H) 2.48 (t, *J*=11.62 Hz, 1 H) 2.14 (br. s., 1 H) 2.05 (br. s., 3 H) 1.88 (br. s., 1 H) 1.71 (br. s., 5 H) 1.50 - 1.66 (m, 2 H) 1.41 (br. s., 3 H) 1.10 - 1.37 (m, 5 H) 0.89 - 1.06 (m, 4 H) 0.86 (br. s., 3 H) **m/z** calcd $C_{39}H_{65}N_5O$ $[M+H]^+$ 619.52, found (MS ESI) 620.15. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.77 min

2494-23: (2R,3S)-N2-(((R)-1-((R)-2-(((R)-2-(((4-(tert-butyl)cyclohexyl)methyl)amino)-3-cyclohexylpropyl)amino)-3-phenylpropyl)pyrrolidin-2-yl)methyl)-3-methylpentane-1,2-diamine. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-23 was synthesized using the following reagents: (R1) Boc-D-Ile-OH, (R2) Boc-D-Phe-OH, (R3) Boc-D-Cha-OH, (R4) 4-tert-butyl-cyclohexancecarboxylic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 35/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.57 (br. s., 1 H) 7.33 (br. s., 2 H) 7.26 (br. s., 1 H) 7.19 (br. s., 2 H) 6.44 (br. s., 3 H) 3.69 - 3.97 (m, 1 H) 3.47 (br. s., 1 H) 3.25 (br. s., 1 H) 2.96 - 3.21 (m, 5 H) 2.83 - 2.96 (m, 2 H) 2.78 (br. s., 1 H) 2.68 (d, *J*=12.84 Hz, 1 H) 2.40 - 2.58 (m, 2 H) 2.35 (br. s., 1 H) 2.18 (br. s., 1 H) 2.02 (br. s., 4 H) 1.77 - 1.98 (m, 5 H) 1.73 (br. s., 4 H) 1.45 - 1.67 (m, 5 H) 1.11 - 1.40 (m, 6 H) 1.02 (br. s., 4 H) 0.93 (br. s., 4 H) 0.85 (br. s., 9 H) **m/z** calcd $C_{40}H_{73}N_5$ $[M+H]^+$ 623.59, found (MS ESI) 624.30. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 4.05 min

2494-24: (2R,3S)-N2-(((R)-1-((R)-2-(((R)-2-((3,5-bis(trifluoromethyl)phenethyl)amino)-3-cyclohexylpropyl)amino)-3-phenylpropyl)pyrrolidin-2-yl)methyl)-3-methylpentane-1,2-diamine. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-24 was synthesized using the following reagents: (R1) Boc-D-Ile-OH, (R2) Boc-D-Phe-OH, (R3) Boc-D-Cha-OH, (R4) 3,5-Bis(Trifluoromethyl)-Phenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 35/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.60 (br. s., 2 H) 7.72 - 7.92 (m, 3 H) 7.34 (br. s., 3 H) 7.26 (br. s., 1 H) 7.19 (br. s., 2 H) 6.55 (br. s., 2 H) 4.00 (br. s., 1 H) 3.95 (br. s., 1 H) 3.58 (br. s., 1 H) 3.46 (br. s., 1 H) 3.29 - 3.41 (m, 1 H) 3.15 - 3.29 (m, 4 H) 3.10 (br. s., 3 H) 3.02 (br. s., 1 H) 2.94 (d, *J*=12.35 Hz, 1 H) 2.77 - 2.90 (m, 1 H) 2.70 (d, *J*=13.08 Hz, 1 H) 2.46 - 2.62 (m, 2 H) 2.13 (br. s., 1 H) 2.03 (br. s., 2 H) 1.87 (br. s., 1 H) 1.73 (br. s., 5 H) 1.59 (br. s., 2 H) 1.50 (br. s., 1 H) 1.36 (br. s., 1 H) 1.11 - 1.33 (m, 4 H) 1.01 (br. s., 1 H) 0.94 (br. s., 3 H) 0.70 - 0.91 (m, 3 H) **m/z** calcd $C_{39}H_{59}F_6N_5$ $[M+H]^+$ 711.47, found (MS ESI) 712.15. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 4.05 min

2494-25: 4-((R)-3-(((R)-1-((R)-2-((((2R,3S)-1-amino-3-methylpentan-2-yl)amino)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)amino)-2-((4-ethoxyphenethyl)amino)propyl)phenol. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-25 was synthesized using the following reagents: (R1) Boc-D-Ile-OH, (R2) Boc-D-Phe-OH, (R3) Boc-D-Tyr(2-Br-Z)-OH, (R4) 4-ethoxyphenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 35/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.48 (br. s., 2 H) 7.23 (br. s., 2 H) 7.13 - 7.20 (m, 3 H) 7.09 (br. s., 1 H) 6.86 - 7.04 (m, 4 H) 6.83 (br. s., 6 H) 3.99 (br. s., 2 H) 3.84 (br. s., 1 H) 3.44 (br. s., 1 H) 3.21 (d, *J*=15.53 Hz, 2 H) 3.14 (br. s., 2 H) 2.95 - 3.10 (m, 4 H) 2.78 - 2.94 (m, 4 H) 2.55 - 2.78 (m, 3 H) 2.48 (br. s., 1 H) 2.33 (d, *J*=11.00 Hz, 1 H) 2.03 (br. s., 2 H) 1.84 (br. s., 1 H) 1.69 (br. s., 2 H) 1.40 (br. s., 3 H) 1.28 (br. s., 1 H) 1.15 (br. s., 1 H) 0.91 (br. s., 3 H) 0.81 (br. s., 3 H) **m/z** calcd $C_{39}H_{59}N_5O_2$ $[M+H]^+$ 629.47, found (MS ESI) 630.15. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.32 min

2494-26: 4-((R)-3-(((R)-1-((R)-2-((((2R,3S)-1-amino-3-methylpentan-2-yl)amino)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)amino)-2-(((4-(tert-butyl)cyclohexyl)methyl)amino)propyl)phenol. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-26 was synthesized using the following reagents: (R1) Boc-D-Ile-OH, (R2) Boc-D-Phe-OH, (R3) Boc-D-Tyr(2-Br-Z)-OH, (R4) 4-tert-butyl-cyclohexancecarboxylic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 35/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.54 (br. s., 1 H) 7.29 (br. s., 2 H) 7.26 (br. s., 1 H) 7.19 (br. s., 1 H) 7.02 (s, 2 H) 7.06 (s, 2 H) 6.88 (br. s., 3 H) 6.69 (br. s., 3 H) 3.87 (br. s., 1 H) 3.47 (br. s., 1 H) 3.29 (br. s., 1 H) 3.05 (br. s., 5 H) 2.70 - 2.96 (m, 4 H) 2.63 (d, *J*=11.37 Hz, 2 H) 2.37 (d, *J*=12.96 Hz, 1 H) 2.05 (br. s., 6 H) 1.94 (d, *J*=11.49 Hz, 2 H) 1.83 (br. s., 2 H) 1.68 (br. s., 2 H) 1.57 (br. s., 2 H) 1.28 (br. s., 1 H) 1.16 (br. s., 1 H) 1.00 (br. s., 2 H) 0.92 (br. s., 3 H) 0.84 (br. s., 11 H) **m/z** calcd $C_{40}H_{67}N_5O$ $[M+H]^+$ 633.53, found (MS ESI) 634.30. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.64 min

2494-27: N/A

2494-28: (3S)-4-((R)-2-((((S)-1-amino-3-methylbutan-2-yl)amino)methyl)pyrrolidin-1-yl)-3-(((S)-2-((4-ethoxyphenethyl)amino)-3-phenylpropyl)amino)butan-2-ol. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-28 was synthesized using the following reagents: (R1) Boc-Val-OH, (R2) Boc-D-Thr(Bzl)-OH, (R3) Boc-Phe-OH, (R4) 4-ethoxyphenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 4/10, 40/38. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.53 (br. s., 1 H) 7.29 (br. s., 1 H) 7.25 (br. s., 1 H) 7.00 - 7.21 (m, 3 H) 6.83 (br. s., 2 H) 6.00 (br. s., 6 H) 4.02 (br. s., 2 H) 3.87 (br. s., 1 H) 3.56 (br. s., 1 H) 3.49 (br. s., 1 H) 3.27 - 3.42 (m, 1 H) 3.10 - 3.26 (m, 3 H) 3.05 (br. s., 2 H) 2.92 - 3.01 (m, 2 H) 2.86 (d, *J*=13.33 Hz, 4 H) 2.69 (br. s., 1 H) 2.13 (br. s., 1 H) 2.00 (br. s., 4 H) 1.79 (br. s., 1 H) 1.41 (br. s., 2 H) 1.12 (br. s., 2 H) 1.01 (br. s., 1 H) 0.95 (br. s., 2 H) 0.87 (br. s., 3 H) **m/z** calcd $C_{33}H_{55}N_5O_2$ $[M+H]^+$553.44, found (MS ESI) 554.20. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.07 min

2494-29: (2R,3S)-4-((R)-2-((((S)-1-amino-3-methylbutan-2-yl)amino)methyl)pyrrolidin-1-yl)-3-(((S)-2-(((4-(tert-butyl)cyclohexyl)methyl)amino)-3-

phenylpropyl)amino)butan-2-ol. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-29 was synthesized using the following reagents: (R1) Boc-Val-OH, (R2) Boc-D-Thr(Bzl)-OH, (R3) Boc-Phe-OH, (R4) 4-tert-butyl-cyclohexancecarboxylic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 35/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.50 (br. s., 2 H) 7.33 (br. s., 2 H) 7.27 (br. s., 2 H) 6.09 (br. s., 6 H) 3.87 (br. s., 2 H) 3.54 - 3.72 (m, 1 H) 3.51 (br. s., 1 H) 3.29 - 3.45 (m, 1 H) 3.21 (br. s., 2 H) 2.95 - 3.14 (m, 3 H) 2.75 - 2.95 (m, 5 H) 2.70 (br. s., 1 H) 2.25 (br. s., 1 H) 2.14 (br. s., 1 H) 1.86 - 2.08 (m, 5 H) 1.77 (d, *J*=15.16 Hz, 2 H) 1.55 (d, *J*=13.08 Hz, 3 H) 1.14 (br. s., 3 H) 1.04 (br. s., 1 H) 0.97 (br. s., 4 H) 0.72 - 0.92 (m, 10 H) **m/z** calcd $C_{34}H_{63}N_5O$ $[M+H]^+$ 557.50, found (MS ESI) 558.20. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.52min

2494-30: (3S)-4-((R)-2-((((S)-1-amino-3-methylbutan-2-yl)amino)methyl)pyrrolidin-1-yl)-3-(((S)-2-((3,5-bis(trifluoromethyl)phenethyl)amino)-3-phenylpropyl)amino)butan-2-ol. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-30 was synthesized using the following reagents: (R1) Boc-Val-OH, (R2) Boc-D-Thr(Bzl)-OH, (R3) Boc-Phe-OH, (R4) 3,5-Bis(Trifluoromethyl)-Phenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 35/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.48 (br. s., 2 H) 7.68 - 7.88 (m, 1 H) 7.64 (br. s., 1 H) 7.31 (br. s., 2 H) 7.25 (br. s., 2 H) 6.06 (br. s., 6 H) 3.91 (br. s., 1 H) 3.65 (t, *J*=11.07 Hz, 1 H) 3.54 (br. s., 1 H) 3.38 (br. s., 1 H) 3.15 - 3.33 (m, 4 H) 3.09 (d, *J*=10.27 Hz, 2 H) 3.00 (d, *J*=11.74 Hz, 2 H) 2.92 (br. s., 2 H) 2.76 - 2.88 (m, 2 H) 2.17 (br. s., 1 H) 2.07 (br. s., 1 H) 2.01 (br. s., 2 H) 1.76 (br. s., 1 H) 1.10 - 1.23 (m, 2 H) 1.04 (br. s., 1 H) 0.97 (br. s., 2 H) 0.88 (br. s., 2 H) **m/z** calcd $C_{33}H_{49}F_6N_5O$ $[M+H]^+$ 645.38, found (MS ESI) 646.05. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.54 min

2494-31: (3S)-4-((R)-2-((((S)-1-amino-3-methylbutan-2-yl)amino)methyl)pyrrolidin-1-yl)-3-(((R)-3-cyclohexyl-2-((4-ethoxyphenethyl)amino)propyl)amino)butan-2-ol. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-31 was synthesized using the following reagents: (R1) Boc-Val-OH, (R2) Boc-D-Thr(Bzl)-OH, (R3) Boc-D-Cha-OH, (R4) 4-ethoxyphenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/15, 35/40. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.51 (br. s., 2 H) 7.04 - 7.27 (m, 2 H) 6.80 - 6.96 (m, 2 H) 6.04 (br. s., 4 H) 3.91 - 4.13 (m, 3 H) 3.68 (t, *J*=11.74 Hz, 1 H) 3.56 (br. s., 1 H) 3.39 (d, *J*=13.08 Hz, 1 H) 3.15 - 3.32 (m, 3 H) 2.88 - 3.15 (m, 7 H) 2.81 (t, *J*=11.98 Hz, 1 H) 1.95 - 2.23 (m, 5 H) 1.82 (br. s., 1 H) 1.68 (br. s., 5 H) 1.47 - 1.61 (m, 1 H) 1.41 (br. s., 3 H) 1.27 (br. s., 4 H) 1.09 - 1.22 (m, 2 H) 1.04 (br. s., 1 H) 0.97 (br. s., 3 H) 0.69 - 0.92 (m, 3 H) **m/z** calcd $C_{33}H_{61}N_5O_2$ $[M+H]^+$ 559.48, found (MS ESI) 560.20. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.32 min

2494-32: (3S)-4-((R)-2-((((S)-1-amino-3-methylbutan-2-yl)amino)methyl)pyrrolidin-1-yl)-3-(((R)-2-(((4-(tert-butyl)cyclohexyl)methyl)amino)-3-cyclohexylpropyl)amino)butan-2-ol. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-32 was synthesized using the following reagents: (R1) Boc-Val-OH, (R2) Boc-D-Thr(Bzl)-OH, (R3) Boc-D-Cha-OH, (R4) 4-tert-butyl-cyclohexancecarboxylic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 35/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.24 (br. s., 2 H) 5.58 (br. s., 5 H) 3.71 (br. s., 2 H)

3.39 (br. s., 1 H) 3.34 (br. s., 1 H) 3.12 (br. s., 1 H) 2.88 - 3.04 (m, 2 H) 2.74 - 2.86 (m, 3 H) 2.58 - 2.72 (m, 3 H) 2.37 - 2.58 (m, 1 H) 2.05 (br. s., 1 H) 1.91 (br. s., 1 H) 1.69 - 1.86 (m, 3 H) 1.63 (br. s., 2 H) 1.42 - 1.58 (m, 5 H) 1.36 (d, *J*=12.72 Hz, 3 H) 1.29 (br. s., 2 H) 0.92 - 1.13 (m, 6 H) 0.67 - 0.90 (m, 8 H) 0.60 (br. s., 11 H) **m/z** calcd $C_{34}H_{69}N_5O$ $[M+H]^+$ 563.55, found (MS ESI) 564.25. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.70 min

2494-33: (3S)-4-((R)-2-((((S)-1-amino-3-methylbutan-2-yl)amino)methyl)pyrrolidin-1-yl)-3-(((R)-2-((3,5-bis(trifluoromethyl)phenethyl)amino)-3-cyclohexylpropyl)amino)butan-2-ol. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-33 was synthesized using the following reagents: (R1) Boc-Val-OH, (R2) Boc-D-Thr(Bzl)-OH, (R3) Boc-D-Cha-OH, (R4) 3,5-Bis(Trifluoromethyl)-Phenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 35/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.50 (br. s., 2 H) 7.79 (br. s., 3 H) 6.09 (br. s., 5 H) 3.99 (br. s., 1 H) 3.63 - 3.84 (m, 1 H) 3.55 (br. s., 1 H) 3.45 (d, *J*=12.59 Hz, 1 H) 3.34 (br. s., 2 H) 3.22 (br. s., 3 H) 3.02 - 3.16 (m, 2 H) 2.98 (br. s., 2 H) 2.91 (br. s., 1 H) 2.62 - 2.88 (m, 1 H) 2.25 (br. s., 1 H) 1.95 - 2.20 (m, 4 H) 1.86 (br. s., 1 H) 1.68 (br. s., 5 H) 1.54 (br. s., 1 H) 1.28 (br. s., 3 H) 1.21 (d, *J*=13.82 Hz, 3 H) 1.04 (br. s., 1 H) 0.98 (br. s., 3 H) 0.89 (br. s., 4 H) **m/z** calcd $C_{33}H_{55}F_6N_5O$ $[M+H]^+$ 651.43, found (MS ESI) 652.20. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.70 min

2494-34: 4-((2S)-3-(((2S)-1-((R)-2-((((S)-1-amino-3-methylbutan-2-yl)amino)methyl)pyrrolidin-1-yl)-3-hydroxybutan-2-yl)amino)-2-((4-ethoxyphenethyl)amino)propyl)phenol. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-34 was synthesized using the following reagents: (R1) Boc-Val-OH, (R2) Boc-D-Thr(Bzl)-OH, (R3) Boc-D-Tyr(2-Br-Z)-OH, (R4) 4-ethoxyphenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/8, 35/35. **1H NMR** (400 MHz, DMSO-*d6*) δ ppm 8.35 (br. s., 1 H) 7.02 - 7.29 (m, 3 H) 6.97 (br. s., 2 H) 6.76 - 6.90 (m, 3 H) 6.47 - 6.75 (m, 3 H) 6.17 (br. s., 1 H) 3.99 (br. s., 2 H) 3.71 (br. s., 1 H) 3.13 (br. s., 1 H) 2.93 (br. s., 2 H) 2.73 - 2.90 (m, 4 H) 2.69 (br. s., 3 H) 2.58 (br. s., 3 H) 2.33 - 2.48 (m, 2 H) 2.19 (br. s., 1 H) 1.82 - 2.03 (m, 2 H) 1.77 (br. s., 1 H) 1.65 (br. s., 3 H) 1.32 (br. s., 3 H) 1.06 (br. s., 2 H) 0.71 - 0.97 (m, 5 H) **m/z** calcd $C_{33}H_{55}N_5O_3$ $[M+H]^+$ 569.43 found (MS ESI) 570.20. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 2.83 min

2494-35: 4-((2S)-3-(((2S)-1-((R)-2-((((S)-1-amino-3-methylbutan-2-yl)amino)methyl)pyrrolidin-1-yl)-3-hydroxybutan-2-yl)amino)-2-(((4-(tert-butyl)cyclohexyl)methyl)amino)propyl)phenol. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-35 was synthesized using the following reagents: (R1) Boc-Val-OH, (R2) Boc-D-Thr(Bzl)-OH, (R3) Boc-D-Tyr(2-Br-Z)-OH, (R4) 4-tert-butyl-cyclohexancecarboxylic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/15, 35/40. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.14 (br. s., 2 H) 7.29 (br. s., 1 H) 7.16 (br. s., 1 H) 6.86 (d, *J*=12.72 Hz, 1 H) 4.29 (br. s., 1 H) 4.02 (br. s., 2 H) 3.90 (br. s., 4 H) 3.39 (br. s., 7 H) 3.29 (br. s., 3 H) 3.18 (br. s., 7 H) 2.47 (br. s., 1 H) 2.38 (br. s., 1 H) 2.12 (br. s., 4 H) 1.90 (br. s., 2 H) 1.71 (br. s., 1 H) 1.60 (br. s., 2 H) 1.43 (br. s., 2 H) 1.28 (br. s., 2 H) 1.15 (br. s., 3 H) 1.01 (br. s., 4 H) 0.85 (br. s., 6 H) 0.40 (br. s.,

1 H) **m/z** calcd $C_{34}H_{63}N_5O_2$ $[M+H]^+$ 573.50, found (MS ESI) 574.20. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.26 min

2494-36: 4-((2S)-3-(((2S)-1-((R)-2-((((S)-1-amino-3-methylbutan-2-yl)amino)methyl)pyrrolidin-1-yl)-3-hydroxybutan-2-yl)amino)-2-((3,5-bis(trifluoromethyl)phenethyl)amino)propyl)phenol. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-36 was synthesized using the following reagents: (R1) Boc-Val-OH, (R2) Boc-D-Thr(Bzl)-OH, (R3) Boc-D-Tyr(2-Br-Z)-OH, (R4) 3,5-Bis(Trifluoromethyl)-Phenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/10, 35/40. **1H NMR** (400 MHz, DMSO-*d*6) δ ppm 8.36 (br. s., 1 H) 8.13 (d, *J*=19.81 Hz, 1 H) 7.95 (br. s., 2 H) 7.16 (br. s., 1 H) 6.97 (d, *J*=6.85 Hz, 2 H) 6.62 - 6.81 (m, 2 H) 3.69 (br. s., 1 H) 3.07 (br. s., 2 H) 2.94 (br. s., 3 H) 2.75 - 2.89 (m, 4 H) 2.66 (br. s., 2 H) 2.60 (br. s., 3 H) 2.43 (br. s., 1 H) 2.34 (d, *J*=12.23 Hz, 1 H) 2.12 (br. s., 1 H) 1.91 (br. s., 3 H) 1.82 (br. s., 1 H) 1.75 (br. s., 1 H) 1.45 - 1.69 (m, 3 H) 1.03 (br. s., 2 H) 0.83 (s, 3 H) 0.87 (s, 2 H) 0.74 (br. s., 1 H) **m/z** calcd $C_{33}H_{49}F_6N_5O_2$ $[M+H]^+$ 661.38, found (MS ESI) 662.05. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.29 min

2494-37: (S)-N2-(((R)-1-((S)-3-cyclohexyl-2-(((R)-2-((4-ethoxyphenethyl)amino)-3-phenylpropyl)amino)propyl)pyrrolidin-2-yl)methyl)-3-methylbutane-1,2-diamine. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-37 was synthesized using the following reagents: (R1) Boc-Val-OH, (R2) Boc-Cha-OH, (R3) Boc-Phe-OH, (R4) 4-ethoxyphenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/10, 35/40. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.43 (br. s., 2 H) 7.14 (br. s., 2 H) 7.09 (br. s., 2 H) 6.86 - 7.06 (m, 3 H) 6.62 - 6.74 (m, 2 H) 6.18 (br. s., 2 H) 3.87 (br. s., 2 H) 3.76 (br. s., 1 H) 3.18 - 3.33 (m, 2 H) 3.13 (br. s., 1 H) 2.88 - 3.05 (m, 4 H) 2.86 (br. s., 1 H) 2.78 (d, *J*=19.93 Hz, 4 H) 2.45 - 2.72 (m, 4 H) 1.81 - 1.98 (m, 3 H) 1.77 (br. s., 1 H) 1.35 - 1.61 (m, 6 H) 1.27 (br. s., 4 H) 1.13 (br. s., 1 H) 0.95 - 1.08 (m, 3 H) 0.93 (br. s., 1 H) 0.83 (br. s., 3 H) 0.71 (br. s., 3 H) 0.40 - 0.67 (m, 2 H) **m/z** calcd $C_{38}H_{63}N_5O$ $[M+H]^+$ 605.50, found (MS ESI) 606.15. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.64 min

2494-38: (S)-N2-(((R)-1-((S)-2-(((R)-2-(((4-(tert-butyl)cyclohexyl)methyl)amino)-3-phenylpropyl)amino)-3-cyclohexylpropyl)pyrrolidin-2-yl)methyl)-3-methylbutane-1,2-diamine. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-38 was synthesized using the following reagents: (R1) Boc-Val-OH, (R2) Boc-Cha-OH, (R3) Boc-Phe-OH, (R4) 4-tert-butyl-cyclohexancecarboxylic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/15, 35/45. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.58 (br. s., 1 H) 7.29 (s, 1 H) 7.31 (s, 2 H) 6.03 (br. s., 4 H) 3.69 (br. s., 1 H) 3.35 (br. s., 2 H) 3.01 - 3.20 (m, 3 H) 2.90 - 3.01 (m, 4 H) 2.86 (br. s., 2 H) 2.79 (d, *J*=14.31 Hz, 4 H) 2.24 (br. s., 1 H) 1.98 (br. s., 4 H) 1.89 (d, *J*=13.08 Hz, 1 H) 1.72 - 1.84 (m, 2 H) 1.48 - 1.72 (m, 8 H) 1.38 (br. s., 2 H) 1.27 (br. s., 1 H) 1.10 - 1.22 (m, 3 H) 1.04 (br. s., 2 H) 0.98 (br. s., 5 H) 0.84 (br. s., 13 H) **m/z** calcd $C_{39}H_{71}N_5$ $[M+H]^+$ 609.57, found (MS ESI) 610.25. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.94 min

2494-39: (S)-N2-(((R)-1-((S)-2-(((R)-2-((3,5-bis(trifluoromethyl)phenethyl)amino)-3-phenylpropyl)amino)-3-cyclohexylpropyl)pyrrolidin-2-yl)methyl)-3-methylbutane-1,2-

diamine. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-39 was synthesized using the following reagents: (R1) Boc-Val-OH, (R2) Boc-Cha-OH, (R3) Boc-Phe-OH, (R4) 3,5-Bis(Trifluoromethyl)-Phenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/15, 35/45. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.55 (br. s., 1 H) 7.76 (br. s., 1 H) 7.69 (br. s., 2 H) 7.49 (br. s., 2 H) 7.16 (br. s., 2 H) 6.35 (br. s., 3 H) 3.89 (br. s., 1 H) 3.49 (br. s., 2 H) 3.32 (br. s., 3 H) 3.11 (br. s., 4 H) 2.98 (br. s., 5 H) 2.79 (d, *J*=15.89 Hz, 4 H) 2.06 (br. s., 2 H) 1.98 (br. s., 1 H) 1.83 (br. s., 1 H) 1.66 (br. s., 3 H) 1.59 (br. s., 2 H) 1.45 (br. s., 1 H) 1.24 - 1.38 (m, 1 H) 1.07 - 1.23 (m, 4 H) 0.98 (br. s., 3 H) 0.86 (br. s., 3 H) 0.76 (d, *J*=11.13 Hz, 1 H) **m/z** calcd $C_{38}H_{57}F_6N_5$ $[M+H]^+$ 697.45, found (MS ESI) 698.15. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.95 min

2494-40: (S)-N2-(((R)-1-((S)-3-cyclohexyl-2-(((R)-3-cyclohexyl-2-((4-ethoxyphenethyl)amino)propyl)amino)propyl)pyrrolidin-2-yl)methyl)-3-methylbutane-1,2-diamine. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-40y was synthesized using the following reagents: (R1) Boc-Val-OH, (R2) Boc-Cha-OH, (R3) Boc-D-Cha-OH, (R4) 4-ethoxyphenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/15, 35/45. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.39 (br. s., 2 H) 7.03 (d, *J*=7.09 Hz, 2 H) 6.69 (d, *J*=6.11 Hz, 2 H) 5.86 (br. s., 2 H) 3.86 (br. s., 3 H) 3.43 (br. s., 1 H) 3.27 (d, *J*=8.68 Hz, 2 H) 3.08 (d, *J*=10.88 Hz, 2 H) 2.89 - 3.03 (m, 4 H) 2.79 - 2.89 (m, 3 H) 2.74 (br. s., 1 H) 2.66 (d, *J*=11.37 Hz, 2 H) 2.50 (br. s., 1 H) 1.97 (br. s., 2 H) 1.86 (br. s., 3 H) 1.37 - 1.64 (m, 12 H) 1.26 (br. s., 3 H) 0.96 - 1.20 (m, 8 H) 0.82 (br. s., 6 H) 0.71 (br. s., 4 H) **m/z** calcd $C_{38}H_{69}N_5O$ $[M+H]^+$ 611.55, found (MS ESI) 612.25. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.84 min

2494-41: (S)-N2-(((R)-1-((S)-2-(((R)-2-(((4-(tert-butyl)cyclohexyl)methyl)amino)-3-cyclohexylpropyl)amino)-3-cyclohexylpropyl)pyrrolidin-2-yl)methyl)-3-methylbutane-1,2-diamine. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-41 was synthesized using the following reagents: (R1) Boc-Val-OH, (R2) Boc-Cha-OH, (R3) Boc-D-Cha-OH, (R4) 4-tert-butyl-cyclohexancecarboxylic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 35/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.54 (br. s., 1 H) 6.60 (br. s., 4 H) 3.98 (br. s., 1 H) 3.55 (br. s., 1 H) 3.35 (d, *J*=9.41 Hz, 1 H) 3.27 (br. s., 1 H) 3.20 (d, *J*=10.15 Hz, 1 H) 3.04 (br. s., 2 H) 2.88 - 3.01 (m, 3 H) 2.85 (br. s., 1 H) 2.74 - 2.82 (m, 1 H) 2.71 (br. s., 1 H) 2.46 - 2.68 (m, 1 H) 2.27 (br. s., 1 H) 2.09 (br. s., 2 H) 2.01 (br. s., 5 H) 1.87 (br. s., 2 H) 1.66 - 1.82 (m, 10 H) 1.60 (br. s., 3 H) 1.55 (br. s., 3 H) 1.11 - 1.38 (m, 8 H) 0.97 (s, 5 H) 1.01 (s, 4 H) 0.85 (br. s., 11 H) **m/z** calcd $C_{39}H_{77}N_5$ $[M+H]^+$ 615.62, found (MS ESI) 616.25. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 4.09 min

2494-42: (S)-N2-(((R)-1-((S)-2-(((R)-2-((3,5-bis(trifluoromethyl)phenethyl)amino)-3-cyclohexylpropyl)amino)-3-cyclohexylpropyl)pyrrolidin-2-yl)methyl)-3-methylbutane-1,2-diamine. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-42 was synthesized using the following reagents: (R1) Boc-Val-OH, (R2) Boc-Cha-OH, (R3) Boc-D-Cha-OH, (R4) 3,5-Bis(Trifluoromethyl)-Phenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 35/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.55 (br. s., 1 H) 7.77 (s, 1 H) 7.80 (s, 1 H) 6.13

(br. s., 3 H) 5.73 (br. s., 1 H) 3.96 (br. s., 1 H) 3.57 (br. s., 1 H) 3.37 - 3.49 (m, 2 H) 3.32 (br. s., 1 H) 3.23 (br. s., 2 H) 3.07 (d, *J*=11.13 Hz, 3 H) 2.89 - 3.03 (m, 2 H) 2.80 (br. s., 2 H) 2.68 (br. s., 1 H) 2.12 (br. s., 2 H) 2.01 (br. s., 4 H) 1.64 - 1.83 (m, 10 H) 1.57 (br. s., 3 H) 1.12 - 1.38 (m, 8 H) 1.04 (br. s., 1 H) 0.90 - 1.01 (m, 5 H) 0.86 (br. s., 4 H) **m/z** calcd $C_{38}H_{63F6}N_5$ $[M+H]^+$ 703.50, found (MS ESI) 704.20. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 4.11 min

2494-43: 4-((R)-3-(((S)-1-((R)-2-((((S)-1-amino-3-methylbutan-2-yl)amino)methyl)pyrrolidin-1-yl)-3-cyclohexylpropan-2-yl)amino)-2-((4-ethoxyphenethyl)amino)propyl)phenol. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-43 was synthesized using the following reagents: (R1) Boc-Val-OH, (R2) Boc-Cha-OH, (R3) Boc-D-Tyr(2-Br-Z)-OH, (R4) 4-ethoxyphenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/10, 35/40. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.51 (br. s., 2 H) 7.29 (br. s., 1 H) 7.13 (d, *J*=6.72 Hz, 2 H) 7.07 (br. s., 1 H) 6.94 (br. s., 2 H) 6.82 (br. s., 4 H) 6.55 (br. s., 3 H) 4.00 (br. s., 2 H) 3.88 (br. s., 1 H) 3.47 (br. s., 2 H) 3.38 (br. s., 1 H) 3.19 (br. s., 2 H) 3.07 (br. s., 5 H) 2.78 - 2.99 (m, 3 H) 2.56 - 2.77 (m, 2 H) 2.23 (br. s., 1 H) 2.01 (br. s., 4 H) 1.52 - 1.80 (m, 5 H) 1.40 (br. s., 3 H) 1.27 (br. s., 1 H) 1.14 (br. s., 3 H) 1.03 (br. s., 1 H) 0.93 (br. s., 2 H) 0.81 (br. s., 3 H) **m/z** calcd $C_{38}H_{63}N_5O_2$ $[M+H]^+$ 621.50, found (MS ESI) 622.20. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.39 min

2494-44: 4-((R)-3-(((S)-1-((R)-2-((((S)-1-amino-3-methylbutan-2-yl)amino)methyl)pyrrolidin-1-yl)-3-cyclohexylpropan-2-yl)amino)-2-(((4-(tert-butyl)cyclohexyl)methyl)amino)propyl)phenol. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-44 was synthesized using the following reagents: (R1) Boc-Val-OH, (R2) Boc-Cha-OH, (R3) Boc-D-Tyr(2-Br-Z)-OH, (R4) 4-tert-butyl-cyclohexancecarboxylic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/15, 35/45. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.53 (br. s., 1 H) 7.01 (br. s., 2 H) 6.75 - 6.92 (m, 3 H) 6.68 (br. s., 5 H) 3.82 (br. s., 1 H) 3.40 (br. s., 2 H) 3.14 - 3.31 (m, 1 H) 3.07 (d, *J*=10.27 Hz, 3 H) 2.96 (br. s., 2 H) 2.64 - 2.91 (m, 5 H) 2.27 (br. s., 1 H) 2.03 (br. s., 7 H) 1.89 (d, *J*=14.67 Hz, 2 H) 1.80 (br. s., 2 H) 1.66 (br. s., 3 H) 1.59 (br. s., 4 H) 1.41 (br. s., 1 H) 1.08 - 1.35 (m, 5 H) 0.96 (s, 3 H) 0.99 (s, 3 H) 0.85 (br. s., 10 H) **m/z** calcd $C_{39}H_{71}N_5O$ $[M+H]^+$ 625.57, found (MS ESI) 626.25. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.73 min

2494-45: 4-((R)-3-(((S)-1-((R)-2-((((S)-1-amino-3-methylbutan-2-yl)amino)methyl)pyrrolidin-1-yl)-3-cyclohexylpropan-2-yl)amino)-2-((3,5-bis(trifluoromethyl)phenethyl)amino)propyl)phenol. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-45 was synthesized using the following reagents: (R1) Boc-Val-OH, (R2) Boc-Cha-OH, (R3) Boc-D-Tyr(2-Br-Z)-OH, (R4) 3,5-Bis(Trifluoromethyl)-Phenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/15, 35/45. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.54 (br. s., 1 H) 7.74 (br. s., 2 H) 6.95 (br. s., 2 H) 6.61 - 6.87 (m, 3 H) 6.42 (br. s., 5 H) 3.85 (br. s., 1 H) 3.47 (br. s., 2 H) 3.33 (br. s., 2 H) 3.26 (br. s., 2 H) 3.06 (br. s., 4 H) 2.91 (d, *J*=14.31 Hz, 2 H) 2.80 (br. s., 1 H) 2.52 - 2.77 (m, 3 H) 2.01 (br. s., 6 H) 1.85 (br. s., 1 H) 1.54 - 1.75 (m, 4 H) 1.45 (br. s., 1 H) 1.14 (br. s., 4 H) 1.05 (br. s., 1 H) 0.96

(br. s., 2 H) 0.90 (br. s., 1 H) 0.83 (br. s., 3 H) **m/z** calcd $C_{38}H_{57}F_6N_5O$ $[M+H]^+$ 713.45, found (MS ESI) 714.15. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.72 min

2494-46: (S)-N2-(((R)-1-((R)-2-(((S)-2-((4-ethoxyphenethyl)amino)-3-phenylpropyl)amino)-3-phenylpropyl)pyrrolidin-2-yl)methyl)-3-methylbutane-1,2-diamine. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-46 was synthesized using the following reagents: (R1) Boc-Val-OH, (R2) Boc-D-Phe-OH, (R3) Boc-Phe-OH, (R4) 4-ethoxyphenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/15, 35/45. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.53 (br. s., 2 H) 7.29 - 7.54 (m, 3 H) 7.21 (br. s., 3 H) 7.03 - 7.17 (m, 4 H) 6.84 (d, *J*=6.36 Hz, 2 H) 5.90 (br. s., 4 H) 4.02 (br. s., 2 H) 3.81 (t, *J*=11.25 Hz, 1 H) 3.57 (br. s., 1 H) 3.43 (br. s., 1 H) 3.25 (br. s., 3 H) 3.11 (br. s., 5 H) 2.95 (d, *J*=12.35 Hz, 2 H) 2.69 - 2.88 (m, 3 H) 2.62 (br. s., 1 H) 2.52 (br. s., 2 H) 2.22 (br. s., 1 H) 1.79 - 2.07 (m, 4 H) 1.42 (br. s., 2 H) 0.97 (br. s., 2 H) 0.88 (br. s., 3 H) **m/z** calcd $C_{38}H_{57}N_5O$ $[M+H]^+$ 599.46, found (MS ESI) 600.20. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.49 min

2494-47: (S)-N2-(((R)-1-((R)-2-(((S)-2-(((4-(tert-butyl)cyclohexyl)methyl)amino)-3-phenylpropyl)amino)-3-phenylpropyl)pyrrolidin-2-yl)methyl)-3-methylbutane-1,2-diamine. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-47 was synthesized using the following reagents: (R1) Boc-Val-OH, (R2) Boc-D-Phe-OH, (R3) Boc-Phe-OH, (R4) 4-tert-butyl-cyclohexancecarboxylic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/15, 35/45. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.51 (br. s., 2 H) 7.35 (br. s., 4 H) 7.09 (br. s., 5 H) 6.04 (br. s., 4 H) 3.85 (t, *J*=11.19 Hz, 1 H) 3.61 (br. s., 1 H) 3.43 (br. s., 1 H) 3.26 (br. s., 3 H) 3.00 - 3.18 (m, 3 H) 2.97 (br. s., 2 H) 2.67 - 2.93 (m, 4 H) 2.53 (br. s., 2 H) 2.34 (br. s., 1 H) 2.19 (br. s., 1 H) 2.03 (br. s., 3 H) 1.92 (d, *J*=13.33 Hz, 2 H) 1.84 (d, *J*=15.53 Hz, 2 H) 1.58 (d, *J*=14.31 Hz, 3 H) 0.97 (br. s., 6 H) 0.85 (br. s., 11 H) **m/z** calcd $C_{39}H_{65}N_5$ $[M+H]^+$ 603.52, found (MS ESI) 604.25. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.78 min

2494-48: (S)-N2-(((R)-1-((R)-2-(((S)-2-((3,5-bis(trifluoromethyl)phenethyl)amino)-3-phenylpropyl)amino)-3-phenylpropyl)pyrrolidin-2-yl)methyl)-3-methylbutane-1,2-diamine. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-48 was synthesized using the following reagents: (R1) Boc-Val-OH, (R2) Boc-D-Phe-OH, (R3) Boc-Phe-OH, (R4) 3,5-Bis(Trifluoromethyl)-Phenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/15, 35/45. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.57 (br. s., 2 H) 7.75 (br. s., 1 H) 7.63 - 7.72 (m, 2 H) 7.31 - 7.44 (m, 2 H) 7.29 (br. s., 1 H) 7.18 - 7.27 (m, 3 H) 7.10 (br. s., 2 H) 5.89 (br. s., 5 H) 4.06 (br. s., 1 H) 3.83 (t, *J*=11.31 Hz, 1 H) 3.58 (br. s., 1 H) 3.22 - 3.43 (m, 4 H) 3.09 - 3.21 (m, 4 H) 3.05 (br. s., 1 H) 2.75 - 3.01 (m, 4 H) 2.43 - 2.71 (m, 3 H) 2.26 (br. s., 1 H) 2.15 (br. s., 1 H) 1.91 - 2.07 (m, 3 H) 1.85 (br. s., 1 H) 1.73 (br. s., 1 H) 0.98 (br. s., 2 H) 0.88 (br. s., 3 H) **m/z** calcd $C_{38}H_{51}F_6N_5$ $[M+H]^+$ 691.40, found (MS ESI) 692.15. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.79 min

2494-49: (S)-N2-(((R)-1-((R)-2-(((R)-3-cyclohexyl-2-((4-ethoxyphenethyl)amino)propyl)amino)-3-phenylpropyl)pyrrolidin-2-yl)methyl)-3-methylbutane-1,2-diamine. Using General Scheme (scheme 1) for the synthesis of penta-

amines compound 2494-49 was synthesized using the following reagents: (R1) Boc-Val-OH, (R2) Boc-D-Phe-OH, (R3) Boc-D-Cha-OH, (R4) 4-ethoxyphenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/15, 35/45. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.43 (br. s., 2 H) 7.18 (br. s., 2 H) 7.10 (br. s., 1 H) 6.91 - 7.07 (m, 3 H) 6.70 (d, *J*=6.36 Hz, 2 H) 5.85 (br. s., 4 H) 3.82 - 4.00 (m, 2 H) 3.74 (t, *J*=11.49 Hz, 1 H) 3.05 - 3.24 (m, 4 H) 2.89 - 3.05 (m, 6 H) 2.82 (d, *J*=12.10 Hz, 2 H) 2.66 (t, *J*=12.29 Hz, 1 H) 2.25 - 2.52 (m, 2 H) 2.05 (br. s., 1 H) 1.73 - 1.94 (m, 6 H) 1.48 - 1.72 (m, 5 H) 1.42 (br. s., 2 H) 1.27 (br. s., 3 H) 0.94 - 1.21 (m, 4 H) 0.63 - 0.89 (m, 7 H) **m/z** calcd $C_{38}H_{63}N_5O$ $[M+H]^+$ 605.50, found (MS ESI) 606.15. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.69 min

2494-50: (S)-N2-(((R)-1-((R)-2-(((R)-2-(((4-(tert-butyl)cyclohexyl)methyl)amino)-3-cyclohexylpropyl)amino)-3-phenylpropyl)pyrrolidin-2-yl)methyl)-3-methylbutane-1,2-diamine. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-50 was synthesized using the following reagents: (R1) Boc-Val-OH, (R2) Boc-D-Phe-OH, (R3) Boc-D-Cha-OH, (R4) 4-tert-butyl-cyclohexancecarboxylic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 35/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.58 (br. s., 1 H) 7.33 (br. s., 2 H) 7.01 - 7.27 (m, 3 H) 6.31 (br. s., 4 H) 4.01 (br. s., 1 H) 3.82 (d, *J*=10.51 Hz, 1 H) 3.05 - 3.32 (m, 6 H) 2.88 - 3.05 (m, 2 H) 2.70 - 2.87 (m, 2 H) 2.60 (t, *J*=11.55 Hz, 1 H) 2.49 (d, *J*=11.86 Hz, 1 H) 2.30 (br. s., 1 H) 2.14 (br. s., 1 H) 1.95 - 2.07 (m, 5 H) 1.67 - 1.95 (m, 8 H) 1.58 (br. s., 4 H) 1.24 - 1.46 (m, 3 H) 1.22 (br. s., 2 H) 1.02 (br. s., 3 H) 0.97 (br. s., 4 H) 0.86 (br. s., 10 H) **m/z** calcd $C_{39}H_{71}N_5$ $[M+H]^+$ 609.57, found (MS ESI) 610.35. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.99 min

2494-51: (S)-N2-(((R)-1-((R)-2-(((R)-2-((3,5-bis(trifluoromethyl)phenethyl)amino)-3-cyclohexylpropyl)amino)-3-phenylpropyl)pyrrolidin-2-yl)methyl)-3-methylbutane-1,2-diamine. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-51 was synthesized using the following reagents: (R1) Boc-Val-OH, (R2) Boc-D-Phe-OH, (R3) Boc-D-Cha-OH, (R4) 3,5-Bis(Trifluoromethyl)-Phenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/20, 35/50. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.58 (br. s., 1 H) 7.79 (br. s., 3 H) 7.29 - 7.51 (m, 2 H) 7.04 - 7.27 (m, 3 H) 5.96 (br. s., 3 H) 4.09 (br. s., 1 H) 3.92 (t, *J*=10.94 Hz, 1 H) 3.49 (d, *J*=12.23 Hz, 1 H) 3.07 - 3.33 (m, 8 H) 3.00 (d, *J*=12.72 Hz, 2 H) 2.73 - 2.85 (m, 1 H) 2.48 - 2.67 (m, 2 H) 2.24 (d, *J*=18.95 Hz, 1 H) 2.16 (br. s., 1 H) 1.90 - 2.08 (m, 4 H) 1.79 (br. s., 1 H) 1.72 (d, *J*=13.08 Hz, 4 H) 1.60 (br. s., 2 H) 1.51 (br. s., 1 H) 1.38 (br. s., 1 H) 1.10 - 1.35 (m, 4 H) 0.98 (br. s., 4 H) 0.88 (br. s., 4 H) **m/z** calcd $C_{38}H_{57F6}N_5$ $[M+H]^+$ 697.45, found (MS ESI) 698.20. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.98 min

2494-52: 4-((R)-3-(((R)-1-((R)-2-((((S)-1-amino-3-methylbutan-2-yl)amino)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)amino)-2-((4-ethoxyphenethyl)amino)propyl)phenol. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-52 was synthesized using the following reagents: (R1) Boc-Val-OH, (R2) Boc-D-Phe-OH, (R3) Boc-D-Tyr(2-Br-Z)-OH, (R4) 4-ethoxyphenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/10, 35/40. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.59 (br. s., 1 H) 7.22 (br. s., 2

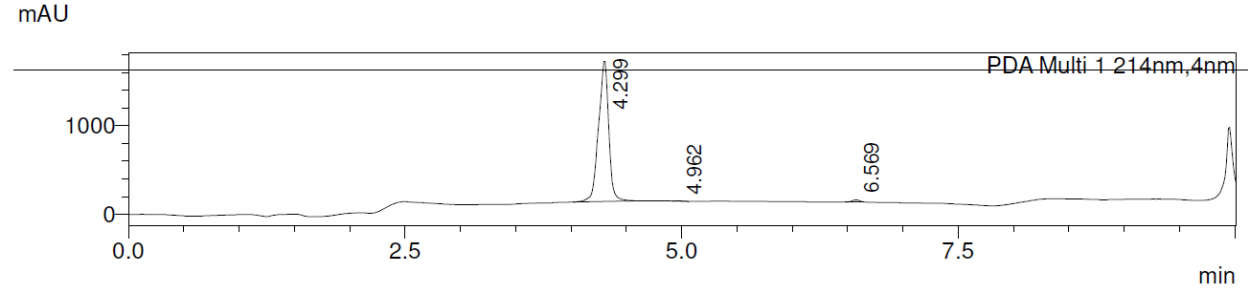
H) 7.08 - 7.19 (m, 2 H) 6.99 (br. s., 3 H) 6.83 (br. s., 5 H) 6.40 (br. s., 4 H) 3.96 - 4.04 (m, 1 H) 3.94 (br. s., 1 H) 3.64 - 3.88 (m, 1 H) 3.05 - 3.32 (m, 6 H) 2.78 - 3.05 (m, 6 H) 2.68 (d, *J*=11.49 Hz, 1 H) 2.52 (br. s., 1 H) 2.43 (br. s., 1 H) 2.13 (br. s., 1 H) 1.81 - 2.08 (m, 7 H) 1.40 (br. s., 3 H) 0.98 (br. s., 1 H) 0.92 (br. s., 2 H) 0.83 (br. s., 3 H) **m/z** calcd $C_{38}H_{57}N_5O_2$ $[M+H]^+$ 615.45, found (MS ESI) 616.20. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.23 min

2494-53: 4-((R)-3-(((R)-1-((R)-2-((((S)-1-amino-3-methylbutan-2-yl)amino)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)amino)-2-(((4-(tert-butyl)cyclohexyl)methyl)amino)propyl)phenol. Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-53 was synthesized using the following reagents: (R1) Boc-Val-OH, (R2) Boc-D-Phe-OH, (R3) Boc-D-Tyr(2-Br-Z)-OH, (R4) 4-tert-butyl-cyclohexancecarboxylic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/15, 35/45. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.56 (br. s., 1 H) 7.26 (br. s., 1 H) 7.19 (br. s., 1 H) 6.98 - 7.12 (m, 3 H) 6.93 (br. s., 1 H) 6.86 (br. s., 3 H) 6.37 (br. s., 4 H) 3.96 (br. s., 1 H) 3.66 - 3.83 (m, 1 H) 3.31 (br. s., 1 H) 3.12 - 3.28 (m, 2 H) 3.06 (br. s., 3 H) 2.91 - 3.04 (m, 3 H) 2.88 (br. s., 1 H) 2.63 - 2.84 (m, 2 H) 2.54 (br. s., 1 H) 2.46 (br. s., 1 H) 2.31 (br. s., 1 H) 2.11 (br. s., 1 H) 2.03 (br. s., 4 H) 1.89 (d, *J*=13.08 Hz, 3 H) 1.81 (br. s., 2 H) 1.57 (br. s., 3 H) 1.00 (br. s., 4 H) 0.93 (br. s., 3 H) 0.85 (br. s., 10 H) **m/z** calcd $C_{39}H_{65}N_5O$ $[M+H]^+$ 619.52, found (MS ESI) 620.25. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.59 min

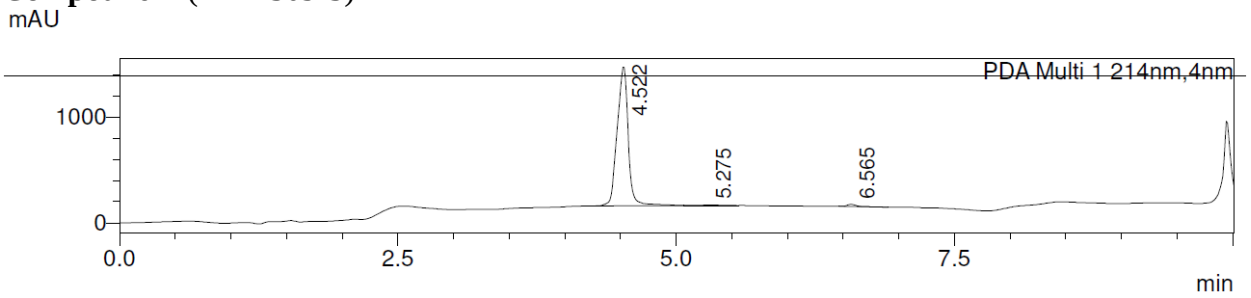
2494-54:
4-((R)-3-(((R)-1-((R)-2-((((S)-1-amino-3-methylbutan-2-yl)amino)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)amino)-2-((3,5-bis(trifluoromethyl)phenethyl)amino)propyl)phenol.
Using General Scheme (scheme 1) for the synthesis of penta-amines compound 2494-54 was synthesized using the following reagents: (R1) Boc-Val-OH, (R2) Boc-D-Phe-OH, (R3) Boc-D-Tyr(2-Br-Z)-OH, (R4) 3,5-Bis(Trifluoromethyl)-Phenylacetic acid. The final crude product was purified using HPLC as described above, with a gradient of (B) 2, 0/2, 2/2, 6/15, 35/45. **1H NMR** (400 MHz, CHLOROFORM-*d*) δ ppm 8.58 (br. s., 2 H) 7.78 (br. s., 2 H) 7.29 (br. s., 1 H) 7.22 (br. s., 2 H) 7.16 (br. s., 1 H) 7.05 (br. s., 2 H) 6.99 (br. s., 2 H) 6.85 (br. s., 3 H) 6.40 (br. s., 3 H) 3.28 - 3.54 (m, 2 H) 3.23 (d, *J*=15.28 Hz, 2 H) 3.07 - 3.17 (m, 2 H) 3.03 (br. s., 2 H) 2.93 (d, *J*=18.83 Hz, 3 H) 2.62 - 2.86 (m, 3 H) 2.53 (br. s., 1 H) 2.43 (br. s., 1 H) 2.21 (br. s., 1 H) 2.03 (br. s., 6 H) 1.61 (br. s., 1 H) 0.94 (br. s., 2 H) 0.84 (br. s., 3 H) **m/z** calcd $C_{38}H_{51}F_6N_5O$ $[M+H]^+$ 707.40, found (MS ESI) 708.15. **Purity** LCMS: 100% (TIC), 100% (214 nm, peak area); **RT** = 3.62 min

HPLC Characterization of Key Compounds

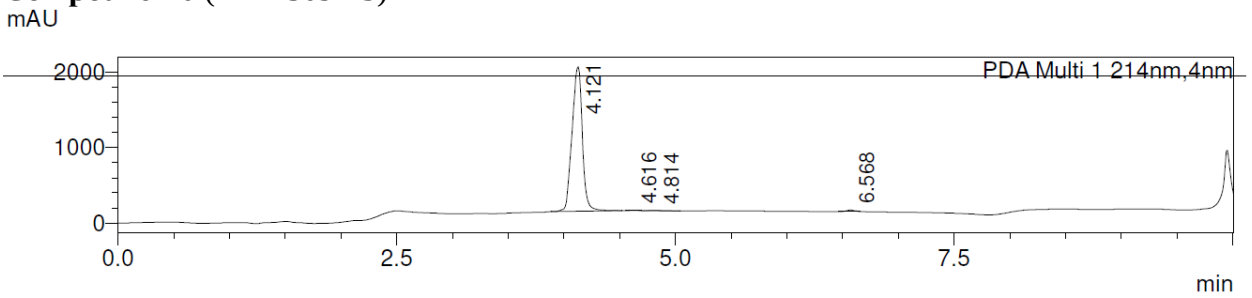
Compound 1 (TPI 2509-4)



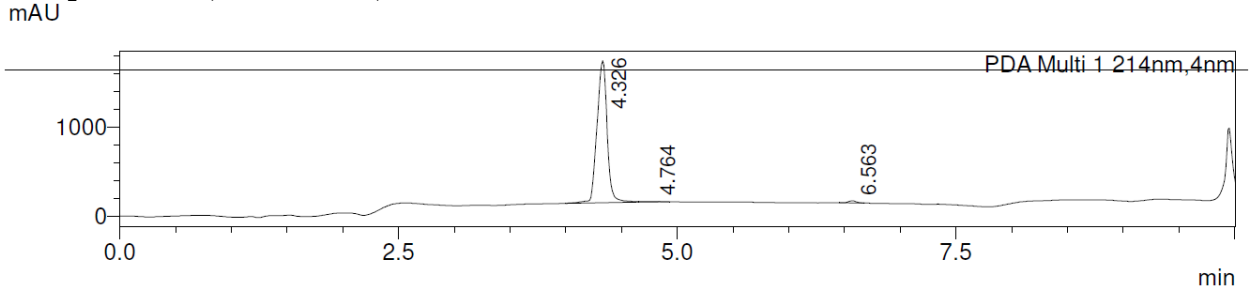
Compound 2 (TPI 2509-5)



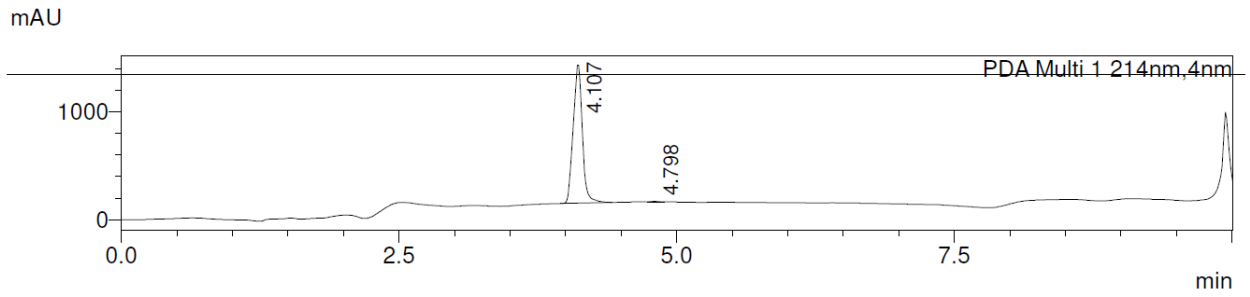
Compound 10 (TPI 2509-13)



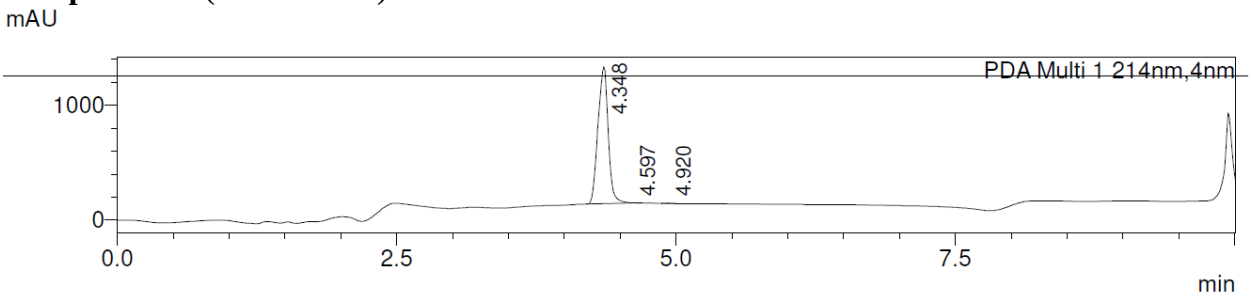
Compound 11 (TPI 2509-14)



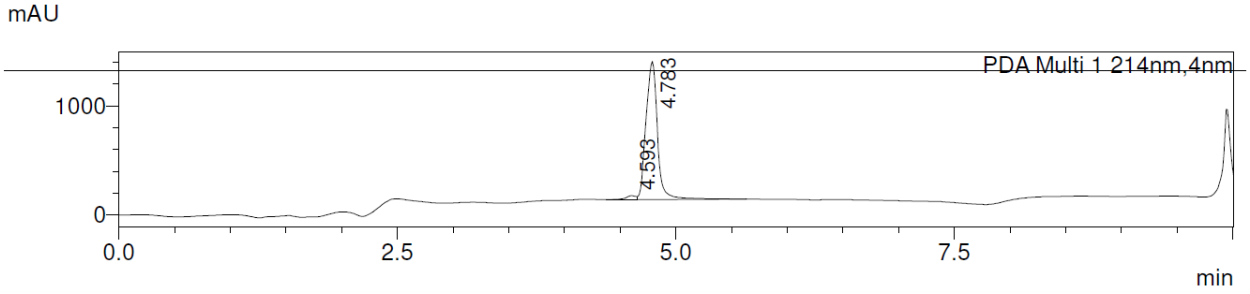
Compound 19 (TPI 2509-22)



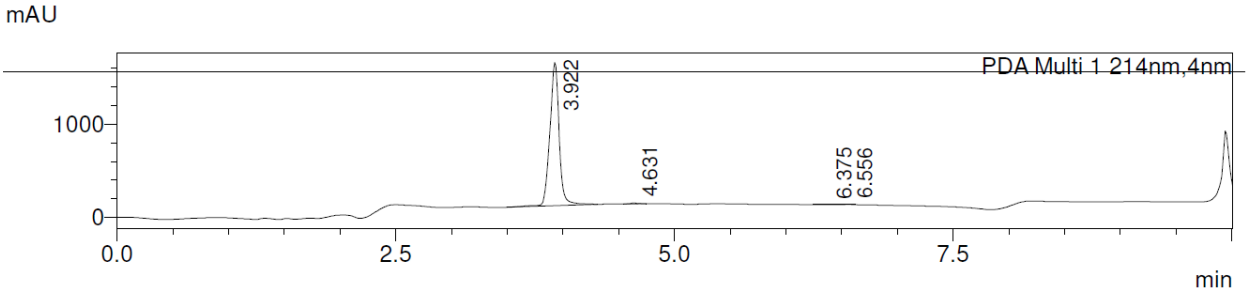
Compound 20 (TPI 2509-23)



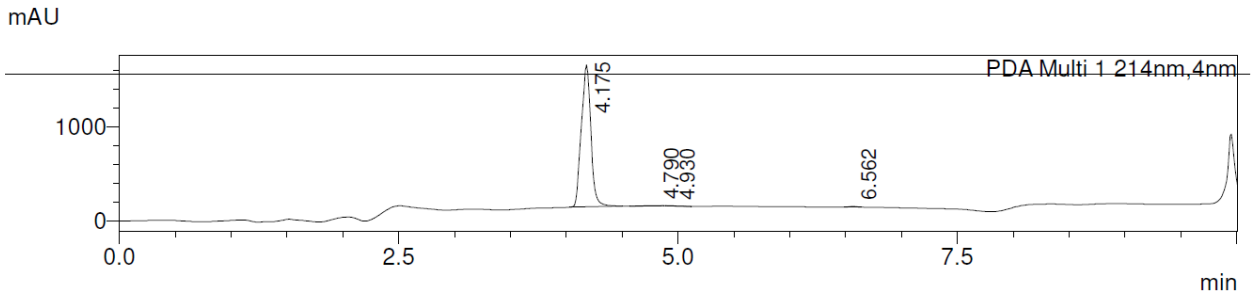
Compound 23 (TPI 2509-26)



Compound 28 (TPI 2509-31)



Compound 29 (TPI 2509-32)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4.790
4.930
6.562
0.0
2.5
5.0
7.5
min

SI Table 1: Building Block to Functionality Table. Mixture-based positional scan library, building blocks, and corresponding functionalities for the pyrrolidine bis-cyclic guanidine and penta-amine libraries

R_1	R_2	R_3	R_4	Building Block	Functionality
1	27	53		Boc-L-Ala	S-methyl
2	28	54		Boc-L-Phe	S-benzyl
3	29	55		Boc-Gly	hydrogen
4	30	56		Boc-L-Ile	S-2-butyl
5	31	57		Boc-L-Leu	S-isobutyl
6	32	58		Boc-L-Ser(Bzl)	R-hydroxymethyl
7	33	59		Boc-L-Thr(Bzl)	(R,R)-1-hydroxyethyl
8	34	60		Boc-L-Val	S-isopropyl
9	35	61		Boc-L-Tyr(BrZ)	S-4-hydroxybenzyl
10	36	62		Boc-D-Ala	R-methyl
11	37	63		Boc-D-Phe	R-benzyl
12	38	64		Boc-D-Ile	R-2-butyl
13	39	65		Boc-D-Leu	R-isobutyl
14	40	66		Boc-D-Ser(Bzl)	S-hydroxymethyl
15	41	67		Boc-D-Thr(Bzl)	(S,R)-1-hydroxyethyl
16	42	68		Boc-D-Val	R-isopropyl
17	43	69		Boc-D-Tyr(BrZ)	R-4-hydroxybenzyl
18	44	70		Boc-L-Phenylglycine	S-phenyl
19	45	71		Boc-L-Norvaline	S-propyl
20	46	72		Boc-D-Norvaline	R-propyl
21	47	73		Boc-L-Norleucine	S-butyl
22	48	74		Boc-D-Norleucine	R-butyl
23	49	75		Boc-L-Naphthylalanine	S-2-naphthylmethyl
24	50	76		Boc-D-Naphthylalanine	R-2-naphthylmethyl
25	51	77		Boc-L-Cyclohexylalanine	S-cyclohexyl
26	52	78		Boc-D-Cyclohexylalanine	R-cyclohexyl
			79	1-phenyl-1-cyclopropanecarboxylic acid	(1-phenyl-cyclopropyl)-methyl
			80	2-phenylbutyric acid	2-phenylbutyl
			81	3-phenylbutyric acid	3-phenylbutyl
			82	m-tolylacetic acid	m-tolylethyl
			83	3-fluorophenylacetic acid	2-(3-fluoro-phenyl)-ethyl
			84	3-bromophenylacetic acid	2-(3-bromo-phenyl)-ethyl
			85	(α-α-α-Trifluoro-m-tolyl) acetic acid	2-(3-trifluoromethyl-phenyl)-ethyl
			86	p-tolylacetic acid	p-tolylethyl
			87	4-fluorophenylacetic acid	2-(4-fluoro-phenyl)-ethyl
			88	3-methoxyphenylacetic acid	2-(3-methoxy-phenyl)-ethyl
			89	4-bromophenylacetic acid	2-(4-bromo-phenyl)-ethyl

90	4-methoxyphenylacetic acid	2-(4-methoxy-phenyl)-ethyl
91	4-ethoxyphenylacetic acid	2-(4-ethoxy-phenyl)-ethyl
92	4-isobutyl-α-methylphenylacetic acid	2-(4-isobutyl-phenyl)-propyl
93	3,4-dichlorophenylacetic acid	3,4-dichlorophenethyl
94	3,5-bis(trifluoromethyl)-phenylacetic acid	2-(3,5-bis-trifluoromethyl-phenyl)-ethyl
95	3-(3,4-dimethoxyphenyl)-propionic acid	3-(3,4-dimethoxy-phenyl)-propyl
96	phenylacetic acid	phenyl-ethyl
97	3,4,5-trimethoxybenzoic acid	3,4,5-trimethoxy-benzyl
98	butyric acid	butyl
99	heptanoic acid	heptyl
100	isobutyric acid	isobutyl
101	2-methylbutyric acid	2-methylbutyl
102	isovaleric acid	3-methylbutyl
103	3-methylvaleric acid	3-methylpentyl
104	4-methylvaleric acid	4-methylpentyl
105	p-toluic acid	4-methyl-benzyl
106	cyclopentanecarboxylic acid	cyclopentyl-methyl
107	cyclohexanecarboxylic acid	cyclohexyl-methyl
108	cyclohexylacetic acid	cyclohexyl-ethyl
109	cyclohexanebutyric acid	cyclohexyl-butyl
110	cycloheptanecarboxylic acid	cycloheptyl-methyl
111	2-methylcyclopropanecarboxylic acid	(2-methyl-cyclopropyl)-methyl
112	cyclobutanecarboxylic acid	cyclobutyl-methyl
113	3-cyclopentylpropionic acid	3-cyclopentyl-propyl
115	4-methyl-1-cyclohexanecarboxylic acid	4-methyl-1-cyclohexyl-methyl
116	4-tert-butyl-cyclohexanecarboxylic acid	4-tert-butyl-cyclohexyl-methyl
117	4-biphenylacetic acid	2-biphenyl-4-yl-ethyl
118	1-adamantanecarboxylic acid	adamantan-1-yl-methyl
119	1-adamantaneacetic acid	2-adamantan-1-yl-ethyl
120	2-norbornaneacetic acid	2-bicyclo[2,2,1]hept-2-yl-ethyl

The pyrrolidine bis-cyclic guanidine scaffold (TPI1955) was accessed through a tetrapeptide, Xaa^4-Xaa^3-Xaa^2-Pro-Xaa^1-NH_2, which was reduced to the corresponding polyamine and subsequently cyclized with cyanogen bromide. The amino acid and carboxylic acid building

blocks maintained their chirality, if there was any, and the side chain functionality after the transformation. Above tabulates the correct nomenclature to describe the substitutions around the template in addition to the building block it was derived from. For example, the amino acid building block Boc-L-Leu was transformed into an *S*-isobutyl sidechain. Also included is the well number for each of the mixtures scanned in the mixture-based positional scan library.

SI Table 2: Pyrrolidine Bis-Cyclic Guanidine Compound SMILES.

ID	SMILES
1	N=C1N(C[C@@H]([C@](C)([H])O)N1CC23CC4CC(C3)CC(C4)C2)[C@H](CC5CCCCC5)CN6[C@@H](CCC6)CN7[C@H](CC(C)C)CNC7=N
2	N=C1N(C[C@@H]([C@](C)([H])O)N1CC2CCC(C(C)(C)C)CC2)[C@H](CC3CCCCC3)CN4[C@@H](CCC4)CN5[C@H](CC(C)C)CNC5=N
3	N=C1N(C[C@@H]([C@](C)([H])O)N1CCCC(C)C)[C@H](CC2CCCCC2)CN3[C@@H](CCC3)CN4[C@H](CC(C)C)CNC4=N
4	N=C1N(C[C@@H](CCC)N1CC23CC4CC(C3)CC(C4)C2)[C@H](CC5CCCCC5)CN6[C@@H](CCC6)CN7[C@H](CC(C)C)CNC7=N
5	N=C1N(C[C@@H](CCC)N1CC2CCC(C(C)(C)C)CC2)[C@H](CC3CCCCC3)CN4[C@@H](CCC4)CN5[C@H](CC(C)C)CNC5=N
6	N=C1N(C[C@@H](CCC)N1CCCC(C)C)[C@H](CC2CCCCC2)CN3[C@@H](CCC3)CN4[C@H](CC(C)C)CNC4=N
7	N=C1N(C[C@@H](C(C)C)N1CC23CC4CC(C3)CC(C4)C2)[C@H](CC5CCCCC5)CN6[C@@H](CCC6)CN7[C@H](CC(C)C)CNC7=N
8	N=C1N(C[C@@H](C(C)C)N1CC2CCC(C(C)(C)C)CC2)[C@H](CC3CCCCC3)CN4[C@@H](CCC4)CN5[C@H](CC(C)C)CNC5=N
9	N=C1N(C[C@@H](C(C)C)N1CCCC(C)C)[C@H](CC2CCCCC2)CN3[C@@H](CCC3)CN4[C@H](CC(C)C)CNC4=N
10	N=C1N(C[C@@H]([C@](C)([H])O)N1CC23CC4CC(C3)CC(C4)C2)[C@H](CC5=CC=CC=C5)CN6[C@@H](CCC6)CN7[C@H](CC(C)C)CNC7=N
11	N=C1N(C[C@@H]([C@](C)([H])O)N1CC2CCC(C(C)(C)C)CC2)[C@H](CC3=CC=CC=C3)CN4[C@@H](CCC4)CN5[C@H](CC(C)C)CNC5=N
12	N=C1N(C[C@@H]([C@](C)([H])O)N1CCCC(C)C)[C@H](CC2=CC=CC=C2)CN3[C@@H](CCC3)CN4[C@H](CC(C)C)CNC4=N
13	N=C1N(C[C@@H](CCC)N1CC23CC4CC(C3)CC(C4)C2)[C@H](CC5=CC=CC=C5)CN6[C@@H](CCC6)CN7[C@H](CC(C)C)CNC7=N
14	N=C1N(C[C@@H](CCC)N1CC2CCC(C(C)(C)C)CC2)[C@H](CC3=CC=CC=C3)CN4[C@@H](CCC4)CN5[C@H](CC(C)C)CNC5=N
15	N=C1N(C[C@@H](CCC)N1CCCC(C)C)[C@H](CC2=CC=CC=C2)CN3[C@@H](CCC3)CN4[C@H](CC(C)C)CNC4=N
16	N=C1N(C[C@@H](C(C)C)N1CC23CC4CC(C3)CC(C4)C2)[C@H](CC5=CC=CC=C5)CN6[C@@H](CCC6)CN7[C@H](CC(C)C)CNC7=N
17	N=C1N(C[C@@H](C(C)C)N1CC2CCC(C(C)(C)C)CC2)[C@H](CC3=CC=CC=C3)CN4[C@@H](CCC4)CN5[C@H](CC(C)C)CNC5=N
18	N=C1N(C[C@@H](C(C)C)N1CCCC(C)C)[C@H](CC2=CC=CC=C2)CN3[C@@H](CCC3)CN4[C@H](CC(C)C)CNC4=N
19	N=C1N(C[C@@H]([C@](C)([H])O)N1CC23CC4CC(C3)CC(C4)C2)[C@H](CC5CCCCC5)CN6[C@@H](CCC6)CN7[C@H](C(C)C)CNC7=N
20	N=C1N(C[C@@H]([C@](C)([H])O)N1CC2CCC(C(C)(C)C)CC2)[C@H](CC3CCCCC3)CN4[C@@H](CCC4)CN5[C@H](C(C)C)CNC5=N
21	N=C1N(C[C@@H]([C@](C)([H])O)N1CCCC(C)C)[C@H](CC2CCCCC2)CN3[C@@H](CCC3)CN4[C@H](C(C)C)CNC4=N
22	N=C1N(C[C@@H](CCC)N1CC23CC4CC(C3)CC(C4)C2)[C@H](CC5CCCCC5)CN6[C@@H](CCC6)CN7[C@H](C(C)C)CNC7=N
23	N=C1N(C[C@@H](CCC)N1CC2CCC(C(C)(C)C)CC2)[C@H](CC3CCCCC3)CN4[C@@H](CCC4)CN5[C@H](C(C)C)CNC5=N
24	N=C1N(C[C@@H](CCC)N1CCCC(C)C)[C@H](CC2CCCCC2)CN3[C@@H](CCC3)CN4[C@H](C(C)C)CNC4=N
25	N=C1N(C[C@@H](C(C)C)N1CC23CC4CC(C3)CC(C4)C2)[C@H](CC5CCCCC5)CN6[C@@H](CCC6)CN7[C@H](C(C)C)CNC7=N
26	N=C1N(C[C@@H](C(C)C)N1CC2CCC(C(C)(C)C)CC2)[C@H](CC3CCCCC3)CN4[C@@H](CCC4)CN5[C@H](C(C)C)CNC5=N
27	N=C1N(C[C@@H](C(C)C)N1CCCC(C)C)[C@H](CC2CCCCC2)CN3[C@@H](CCC3)CN4[C@H](C(C)C)CNC4=N
28	N=C1N(C[C@@H]([C@](C)([H])O)N1CC23CC4CC(C3)CC(C4)C2)[C@H](CC5=CC=CC=C5)CN6[C@@H](CCC6)CN7[C@H](C(C)C)CNC7=N
29	N=C1N(C[C@@H]([C@](C)([H])O)N1CC2CCC(C(C)(C)C)CC2)[C@H](CC3=CC=CC=C3)CN4[C@@H](CCC4)CN5[C@H](C(C)C)CNC5=N
30	N=C1N(C[C@@H]([C@](C)([H])O)N1CCCC(C)C)[C@H](CC2=CC=CC=C2)CN3[C@@H](CCC3)CN4[C@H](C(C)C)CNC4=N

31	N=C1N(C[C@@H](CCC)N1CC23CC4CC(C3)CC(C4)C2)[C@H](CC5=CC=CC=C5)CN6[C@@H](CCC6)CN7[C@H](C(C)C)CNC7=N
32	N=C1N(C[C@@H](CCC)N1CC2CCC(C(C)(C)C)CC2)[C@H](CC3=CC=CC=C3)CN4[C@@H](CCC4)CN5[C@H](C(C)C)CNC5=N
33	N=C1N(C[C@@H](CCC)N1CCCC(C)C)[C@H](CC2=CC=CC=C2)CN3[C@@H](CCC3)CN4[C@H](C(C)C)CNC4=N
34	N=C1N(C[C@@H](C(C)C)N1CC23CC4CC(C3)CC(C4)C2)[C@H](CC5=CC=CC=C5)CN6[C@@H](CCC6)CN7[C@H](C(C)C)CNC7=N
35	N=C1N(C[C@@H](C(C)C)N1CC2CCC(C(C)(C)C)CC2)[C@H](CC3=CC=CC=C3)CN4[C@@H](CCC4)CN5[C@H](C(C)C)CNC5=N
36	N=C1N(C[C@@H](C(C)C)N1CCCC(C)C)[C@H](CC2=CC=CC=C2)CN3[C@@H](CCC3)CN4[C@H](C(C)C)CNC4=N
37	N=C1N(CCN1CC2CCC(C(C)(C)C)CC2)[C@H](CC3=CC=CC=C3)CN4[C@@H](CCC4)CN5[C@H]([C@@H](C)CC)CNC5=N

SI Table 3: Penta-amine Compound SMILES.

ID	SMILES
2494-1	NC[C@@H]([C@@](CC)([H])C)NC[C@@H](CCC1)N1C[C@@H](C(C)([H])O)NC[C@H](CC2=CC=CC=C2)NCCC3=CC=C(OCC)C=C3
2494-2	NC[C@@H]([C@@](CC)([H])C)NC[C@@H](CCC1)N1C[C@@H]([C@](C)([H])O)NC[C@H](CC2=CC=CC=C2)NCC3CCC(C(C)(C)C)CC3
2494-3	NC[C@@H]([C@@](CC)([H])C)NC[C@@H](CCC1)N1C[C@@H](C(C)([H])O)NC[C@H](CC2=CC=CC=C2)NCCC3=CC(C(F)(F)F)=CC(C(F)(F)F)=C3
2494-4	NC[C@@H]([C@@](CC)([H])C)NC[C@@H](CCC1)N1C[C@@H](C(C)([H])O)NC[C@@H](CC2CCCCC2)NCCC3=CC=C(OCC)C=C3
2494-5	NC[C@@H]([C@@](CC)([H])C)NC[C@@H](CCC1)N1C[C@@H](C(C)([H])O)NC[C@@H](CC2CCCCC2)NCC3CCC(C(C)(C)C)CC3
2494-6	NC[C@@H]([C@@](CC)([H])C)NC[C@@H](CCC1)N1C[C@@H](C(C)([H])O)NC[C@@H](CC2CCCCC2)NCCC3=CC(C(F)(F)F)=CC(C(F)(F)F)=C3
2494-7	NC[C@@H]([C@@](CC)([H])C)NC[C@@H](CCC1)N1C[C@@H](C(C)([H])O)NC[C@H](CC2=CC=C(O)C=C2)NCCC3=CC=C(OCC)C=C3
2494-8	NC[C@@H]([C@@](CC)([H])C)NC[C@@H](CCC1)N1C[C@@H](C(C)([H])O)NC[C@H](CC2=CC=C(O)C=C2)NCC3CCC(C(C)(C)C)CC3
2494-9	NC[C@@H]([C@@](CC)([H])C)NC[C@@H](CCC1)N1C[C@@H](C(C)([H])O)NC[C@H](CC2=CC=C(O)C=C2)NCCC3=CC(C(F)(F)F)=CC(C(F)(F)F)=C3
2494-10	NC[C@@H]([C@@](CC)([H])C)NC[C@@H](CCC1)N1C[C@H](CC2CCCCC2)NC[C@@H](CC3=CC=CC=C3)NCCC4=CC=C(OCC)C=C4
2494-11	NC[C@@H]([C@@](CC)([H])C)NC[C@@H](CCC1)N1C[C@H](CC2CCCCC2)NC[C@@H](CC3=CC=CC=C3)NCC4CCC(C(C)(C)C)CC4
2494-12	NC[C@@H]([C@@](CC)([H])C)NC[C@@H](CCC1)N1C[C@H](CC2CCCCC2)NC[C@@H](CC3=CC=CC=C3)NCCC4=CC(C(F)(F)F)=CC(C(F)(F)F)=C4
2494-13	NC[C@@H]([C@@](CC)([H])C)NC[C@@H](CCC1)N1C[C@H](CC2CCCCC2)NC[C@@H](CC3CCCCC3)NCCC4=CC=C(OCC)C=C4
2494-14	NC[C@@H]([C@@](CC)([H])C)NC[C@@H](CCC1)N1C[C@H](CC2CCCCC2)NC[C@@H](CC3CCCCC3)NCC4CCC(C(C)(C)C)CC4
2494-15	NC[C@@H]([C@@](CC)([H])C)NC[C@@H](CCC1)N1C[C@H](CC2CCCCC2)NC[C@@H](CC3CCCCC3)NCCC4=CC(C(F)(F)F)=CC(C(F)(F)F)=C4
2494-16	NC[C@@H]([C@@](CC)([H])C)NC[C@@H](CCC1)N1C[C@H](CC2CCCCC2)NC[C@@H](CC3=CC=C(O)C=C3)NCCC4=CC=C(OCC)C=C4
2494-17	NC[C@@H]([C@@](CC)([H])C)NC[C@@H](CCC1)N1C[C@H](CC2CCCCC2)NC[C@@H](CC3=CC=C(O)C=C3)NCC4CCC(C(C)(C)C)CC4
2494-18	NC[C@@H]([C@@](CC)([H])C)NC[C@@H](CCC1)N1C[C@H](CC2CCCCC2)NC[C@@H](CC3=CC=C(O)C=C3)NCCC4=CC(C(F)(F)F)=CC(C(F)(F)F)=C4
2494-19	NC[C@@H]([C@@](CC)([H])C)NC[C@@H](CCC1)N1C[C@@H](CC2=CC=CC=C2)NC[C@H](CC3=CC=CC=C3)NCCC4=CC=C(OCC)C=C4
2494-20	NC[C@@H]([C@@](CC)([H])C)NC[C@@H](CCC1)N1C[C@@H](CC2=CC=CC=C2)NC[C@H](CC3=CC=CC=C3)NCC4CCC(C(C)(C)C)CC4
2494-21	NC[C@@H]([C@@](CC)([H])C)NC[C@@H](CCC1)N1C[C@@H](CC2=CC=CC=C2)NC[C@H](CC3=CC=CC=C3)NCCC4=CC(C(F)(F)F)=CC(C(F)(F)F)=C4
2494-22	NC[C@@H]([C@@](CC)([H])C)NC[C@@H](CCC1)N1C[C@@H](CC2=CC=CC=C2)NC[C@@H](CC3CCCCC3)NCCC4=CC=C(OCC)C=C4
2494-23	NC[C@@H]([C@@](CC)([H])C)NC[C@@H](CCC1)N1C[C@@H](CC2=CC=CC=C2)NC[C@@H](CC3CCCCC3)NCC4CCC(C(C)(C)C)CC4
2494-24	NC[C@@H]([C@@](CC)([H])C)NC[C@@H](CCC1)N1C[C@@H](CC2=CC=CC=C2)NC[C@@H](CC3CCCCC3)NCCC4=CC(C(F)(F)F)=CC(C(F)(F)F)=C4
2494-25	NC[C@@H]([C@@](CC)([H])C)NC[C@@H](CCC1)N1C[C@@H](CC2=CC=CC=C2)NC[C@@H](CC3=CC=C(O)C=C3)NCCC4=CC=C(OCC)C=C4
2494-26	NC[C@@H]([C@@](CC)([H])C)NC[C@@H](CCC1)N1C[C@@H](CC2=CC=CC=C2)NC[C@@H](CC3=CC=C(O)C=C3)NCC4CCC(C(C)(C)C)CC4
2494-27	NC[C@@H]([C@@](CC)([H])C)NC[C@@H](CCC1)N1C[C@@H](CC2=CC=CC=C2)NC[C@@H](CC3=CC=C(O)C=C3)NCCC4=CC(C(F)(F)F)=CC(C(F)(F)F)=C4
2494-28	NC[C@H](C(C)([H])C)NC[C@@H](CCC1)N1C[C@@H](C(C)([H])O)NC[C@H](CC2=CC=CC=C2)NCCC3=CC=C(OCC)C=C3
2494-29	NC[C@H](C(C)([H])C)NC[C@@H](CCC1)N1C[C@@H]([C@](C)([H])O)NC[C@H](CC2=CC=CC=C2)NCC3CCC(C(C)(C)C)CC3
2494-30	NC[C@H](C(C)([H])C)NC[C@@H](CCC1)N1C[C@@H](C(C)([H])O)NC[C@H](CC2=CC=CC=C2)NCCC3=CC(C(F)(F)F)=CC(C(F)(F)F)=C3
2494-31	NC[C@H](C(C)([H])C)NC[C@@H](CCC1)N1C[C@@H](C(C)([H])O)NC[C@@H](CC2CCCCC2)NCCC3=CC=C(OCC)C=C3
2494-32	NC[C@H](C(C)([H])C)NC[C@@H](CCC1)N1C[C@@H](C(C)([H])O)NC[C@@H](CC2CCCCC2)NCC3CCC(C(C)(C)C)CC3

2494-33	NC[C@H](C(C)([H])C)NC[C@@H](CCC1)N1C[C@@H](C(C)([H])O)NC[C@@H](CC2CCCCC2)NCCC3=CC(C(F)(F)F)=CC(C(F)(F)F)=C3
2494-34	NC[C@H](C(C)([H])C)NC[C@@H](CCC1)N1C[C@@H](C(C)([H])O)NC[C@H](CC2=CC=C(O)C=C2)NCCC3=CC=C(OCC)C=C3
2494-35	NC[C@H](C(C)([H])C)NC[C@@H](CCC1)N1C[C@@H](C(C)([H])O)NC[C@H](CC2=CC=C(O)C=C2)NCC3CCC(C(C)(C)C)CC3
2494-36	NC[C@H](C(C)([H])C)NC[C@@H](CCC1)N1C[C@@H](C(C)([H])O)NC[C@H](CC2=CC=C(O)C=C2)NCCC3=CC(C(F)(F)F)=CC(C(F)(F)F)=C3
2494-37	NC[C@H](C(C)([H])C)NC[C@@H](CCC1)N1C[C@H](CC2CCCCC2)NC[C@@H](CC3=CC=CC=C3)NCCC4=CC=C(OCC)C=C4
2494-38	NC[C@H](C(C)([H])C)NC[C@@H](CCC1)N1C[C@H](CC2CCCCC2)NC[C@@H](CC3=CC=CC=C3)NCC4CCC(C(C)(C)C)CC4
2494-39	NC[C@H](C(C)([H])C)NC[C@@H](CCC1)N1C[C@H](CC2CCCCC2)NC[C@@H](CC3=CC=CC=C3)NCCC4=CC(C(F)(F)F)=CC(C(F)(F)F)=C4
2494-40	NC[C@H](C(C)([H])C)NC[C@@H](CCC1)N1C[C@H](CC2CCCCC2)NC[C@@H](CC3CCCCC3)NCCC4=CC=C(OCC)C=C4
2494-41	NC[C@H](C(C)([H])C)NC[C@@H](CCC1)N1C[C@H](CC2CCCCC2)NC[C@@H](CC3CCCCC3)NCC4CCC(C(C)(C)C)CC4
2494-42	NC[C@H](C(C)([H])C)NC[C@@H](CCC1)N1C[C@H](CC2CCCCC2)NC[C@@H](CC3CCCCC3)NCCC4=CC(C(F)(F)F)=CC(C(F)(F)F)=C4
2494-43	NC[C@H](C(C)([H])C)NC[C@@H](CCC1)N1C[C@H](CC2CCCCC2)NC[C@@H](CC3=CC=C(O)C=C3)NCCC4=CC=C(OCC)C=C4
2494-44	NC[C@H](C(C)([H])C)NC[C@@H](CCC1)N1C[C@H](CC2CCCCC2)NC[C@@H](CC3=CC=C(O)C=C3)NCC4CCC(C(C)(C)C)CC4
2494-45	NC[C@H](C(C)([H])C)NC[C@@H](CCC1)N1C[C@H](CC2CCCCC2)NC[C@@H](CC3=CC=C(O)C=C3)NCCC4=CC(C(F)(F)F)=CC(C(F)(F)F)=C4
2494-46	NC[C@H](C(C)([H])C)NC[C@@H](CCC1)N1C[C@@H](CC2=CC=CC=C2)NC[C@H](CC3=CC=CC=C3)NCCC4=CC=C(OCC)C=C4
2494-47	NC[C@H](C(C)([H])C)NC[C@@H](CCC1)N1C[C@@H](CC2=CC=CC=C2)NC[C@H](CC3=CC=CC=C3)NCC4CCC(C(C)(C)C)CC4
2494-48	NC[C@H](C(C)([H])C)NC[C@@H](CCC1)N1C[C@@H](CC2=CC=CC=C2)NC[C@H](CC3=CC=CC=C3)NCCC4=CC(C(F)(F)F)=CC(C(F)(F)F)=C4
2494-49	NC[C@H](C(C)([H])C)NC[C@@H](CCC1)N1C[C@@H](CC2=CC=CC=C2)NC[C@@H](CC3CCCCC3)NCCC4=CC=C(OCC)C=C4
2494-50	NC[C@H](C(C)([H])C)NC[C@@H](CCC1)N1C[C@@H](CC2=CC=CC=C2)NC[C@@H](CC3CCCCC3)NCC4CCC(C(C)(C)C)CC4
2494-51	NC[C@H](C(C)([H])C)NC[C@@H](CCC1)N1C[C@@H](CC2=CC=CC=C2)NC[C@@H](CC3CCCCC3)NCCC4=CC(C(F)(F)F)=CC(C(F)(F)F)=C4
2494-52	NC[C@H](C(C)([H])C)NC[C@@H](CCC1)N1C[C@@H](CC2=CC=CC=C2)NC[C@@H](CC3=CC=C(O)C=C3)NCCC4=CC=C(OCC)C=C4
2494-53	NC[C@H](C(C)([H])C)NC[C@@H](CCC1)N1C[C@@H](CC2=CC=CC=C2)NC[C@@H](CC3=CC=C(O)C=C3)NCC4CCC(C(C)(C)C)CC4
2494-54	NC[C@H](C(C)([H])C)NC[C@@H](CCC1)N1C[C@@H](CC2=CC=CC=C2)NC[C@@H](CC3=CC=C(O)C=C3)NCCC4=CC(C(F)(F)F)=CC(C(F)(F)F)=C4