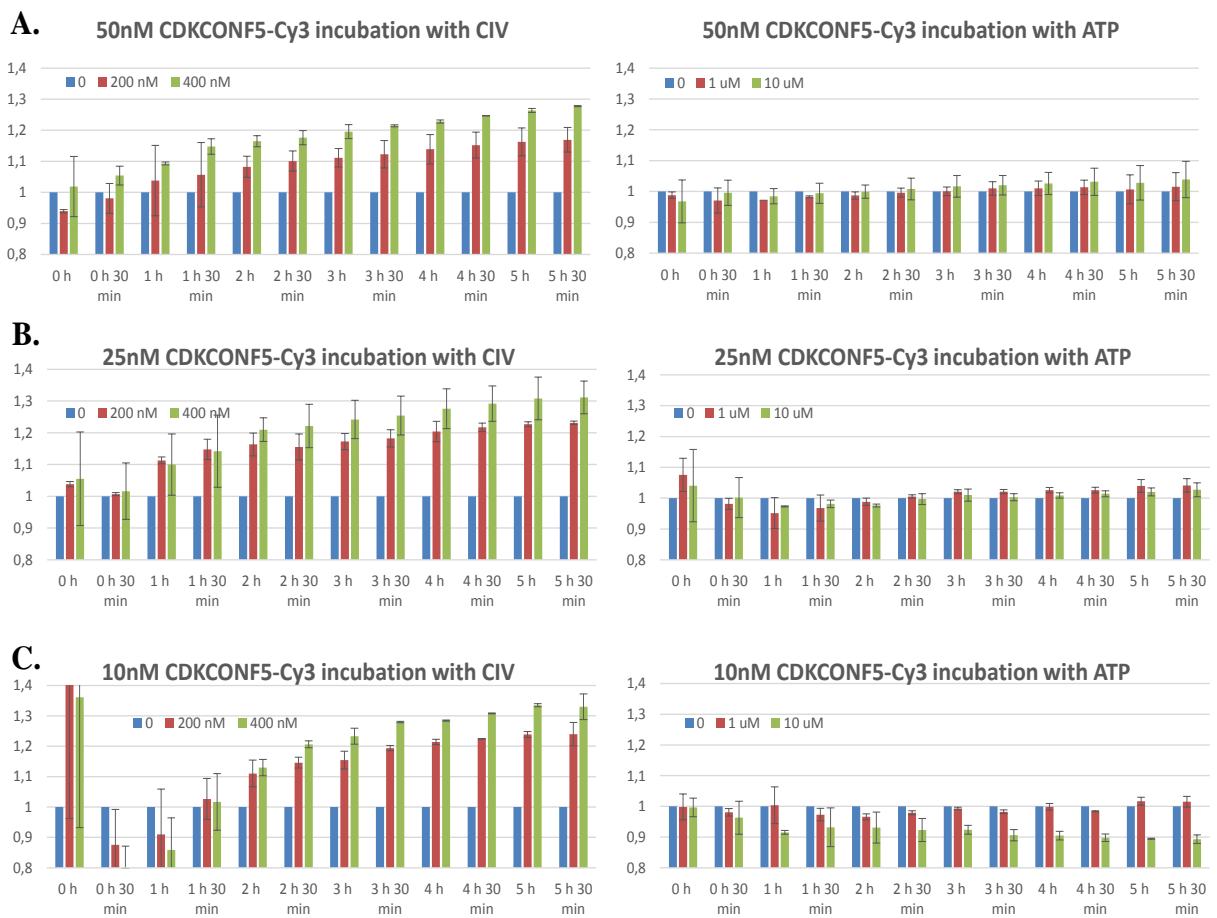


Supplementary Material

Supplementary Figures

Supplementary Figure 1 - Fluorescence response of CDKCONF5-Cy3 biosensor to CIV (200 nM and 400 nM) and ATP (1 μ M and 10 μ M) in PBS / 1% DMSO) at 30 °C in a ClariostarTM fluorimeter. A : 50 nM CDKCONF5-Cy3; B. 25 nM CDKCONF5-Cy3; C. 10 nM CDKCONF5-Cy3

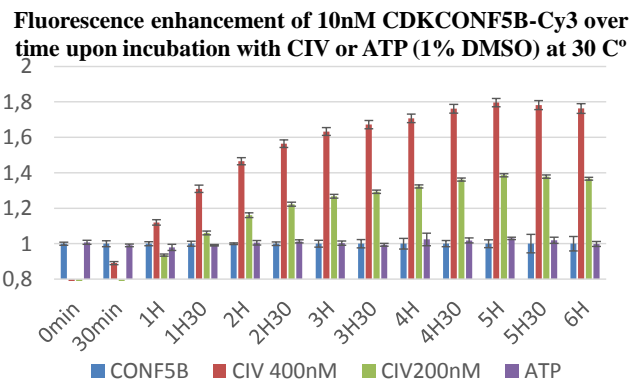
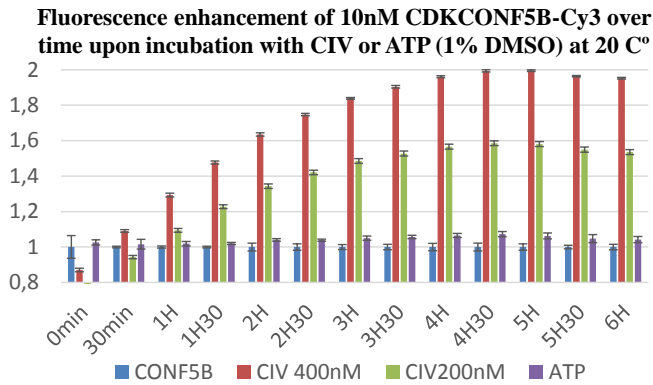
SUPPLEMENTARY FIGURE 1



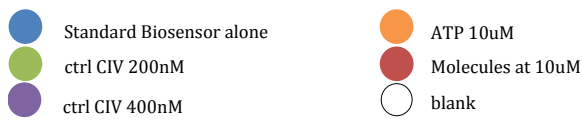
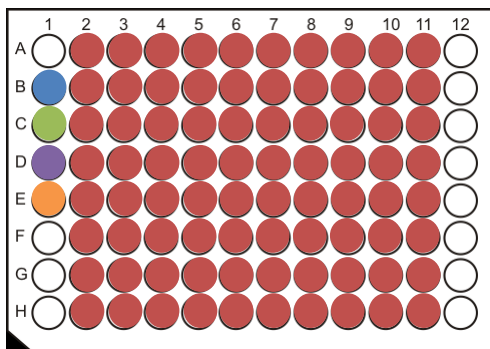
Supplementary Figure 2 – A. Fluorescence response of 10 nM CDKCONF5B-Cy3 to CIV (200 nM and 400 nM) and ATP (10 μ M) in PBS / 1% DMSO) at 20 and 30 $^{\circ}$ C in a TecanTM fluorimeter used for the screen B. Layout of biosensor, positive and negative controls in the plates for the screen.

SUPPLEMENTARY FIGURE 2

A.

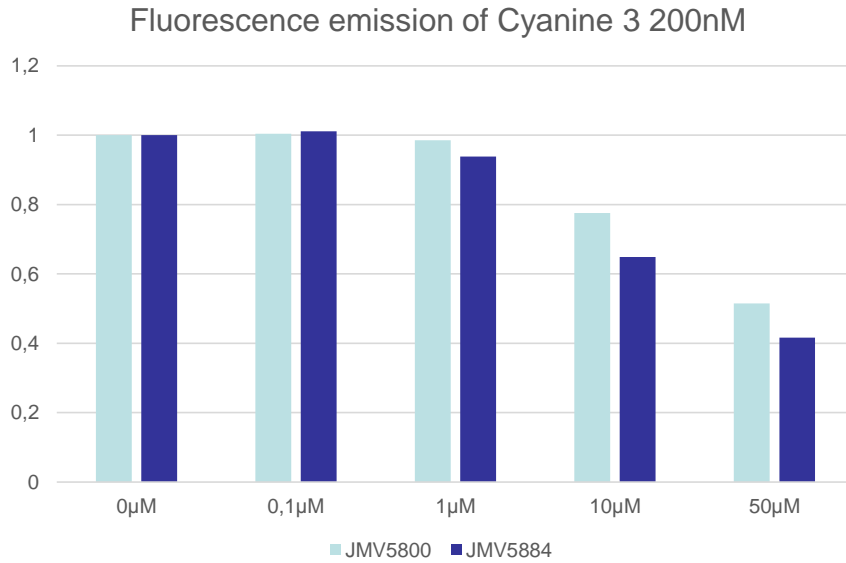


B.

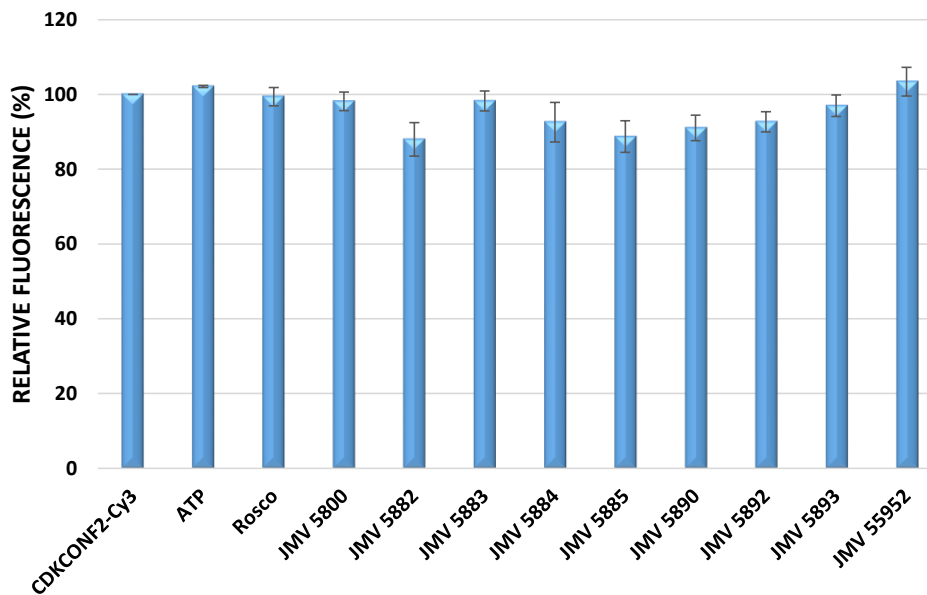


Supplementary Figure 3 – A. Fluorescence titration of 200 nM Cy3 with increasing concentrations of JMV5800 and JMV5884. **B.** Fluorescence titration of CDKCONF2-Cy3 with the 10 μ M quinazolines identified in the primary screen with CDKCONF5-Cy3 and in the same conditions, following 5h incubation at 25°C.

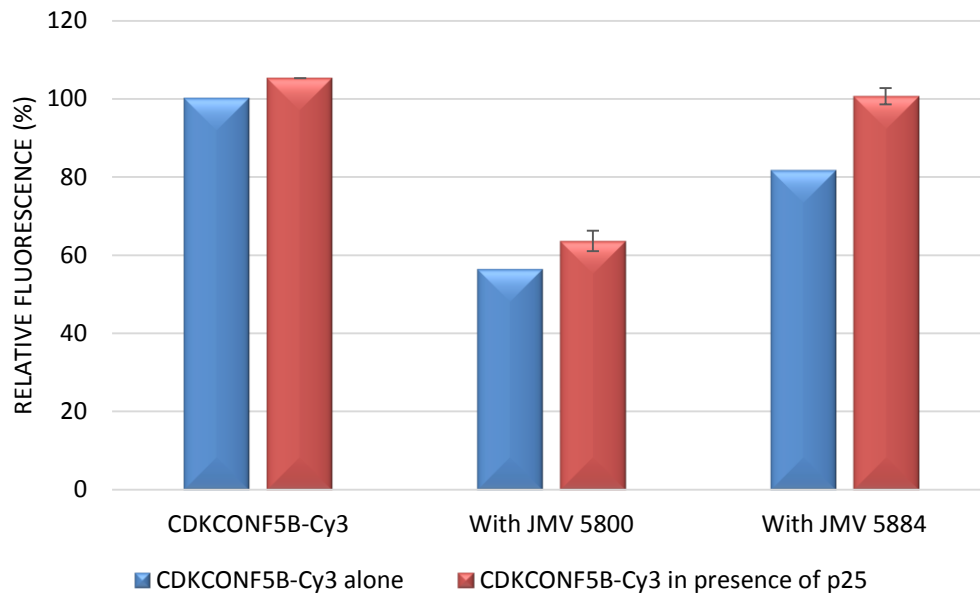
A.



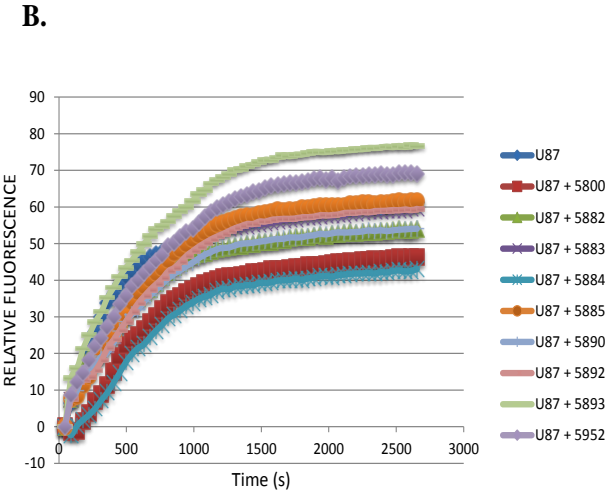
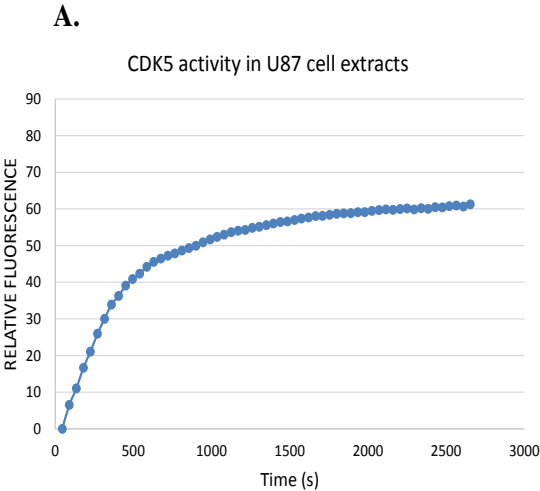
B.



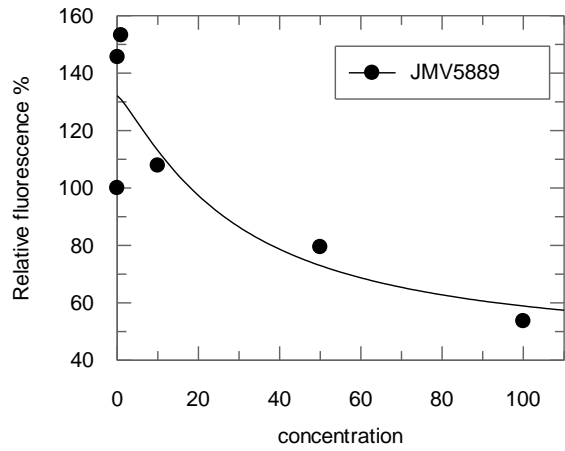
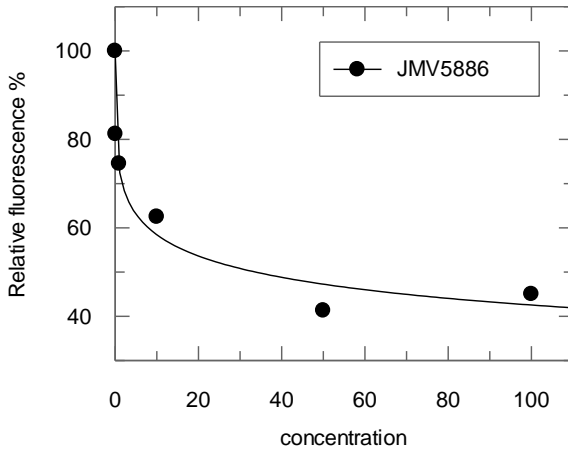
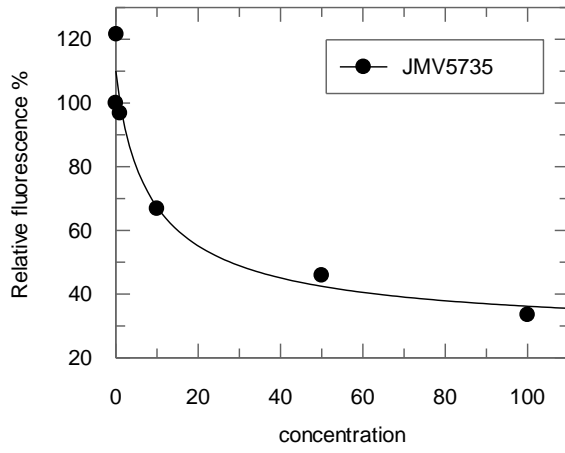
Supplementary Figure 4 –Fluorescence titration of CDKCONF5-Cy3 with p25 and JMV5800 or JMV5884.



Supplementary Figure 5 – A. CDK5 activity in U87 cell extracts – fluorescence based assay with the CDKACT5-Cy5 activity biosensor B. Evaluation of 10 μ M quinazolinones on CDK5 activity in U87 cell extracts



Supplementary Figure 6 - A. Dose-dependent inhibition curves of CDK5 activity in U87 cell extracts for determination of IC50



Supplementary methods

Commercially available reagents and solvents were used without further purification. Reactions were monitored by HPLC using an analytical Chromolith Speed Rod RP-C18 185 Pm column (50x4.6 mm, 5 mm), at a flow rate of 3.0 mL/min, and gradients of 100/0 to 0/100 eluents A/B for 5 min (eluent A = H₂O/0.1% TFA and B = CH₃CN/0.1% TFA). Detection was performed at 214 nm using a photodiode array detector. Retention times (Tr) are reported in min. ¹H and ¹³C NMR spectra were recorded at room temperature in deuterated solvents. Chemical shifts (δ) are expressed in parts per million (ppm), relative to the resonance of CDCl₃ = 7.26 ppm for ¹H (77.16 ppm for ¹³C), CD₃OD = 3.31 ppm for ¹H (49.00 ppm for ¹³C) or DMSO *d*₆ = 2.50 ppm for ¹H (39.52 ppm for ¹³C). The following abbreviations were used: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad). Analytical thin-layer chromatography (TLC) was performed using 60 F254 aluminium-backed silica gel plates coated with a 0.2 mm thickness of neutral aluminium oxide. LC-MS spectra (ESI) were recorded using an analytical Chromolith Speed Rod RP-C18 185 Pm column (50 x 4.6 mm, 5 mm); solvent A, H₂O/HCOOH 0.1%; solvent B, CH₃CN/HCOOH 0.1%; gradient, 0% solvent B to 100% solvent B in solvent A in 3 min; flow rate, 3.0 mL/min. High-resolution mass spectrometry analyses were performed with a time-of-flight mass spectrometer fitted with an electrospray ionisation source. All measurements were performed in the positive ion mode. Melting points (Mp) are uncorrected and were recorded on a capillary melting point apparatus.

Synthesis of compounds 2 :

To a solution of 2 g of anthranilic acid **1a** or **1b** in 20 mL of dichloromethane was added one equivalent of triethylamine. The reaction was stirred and cooled at 0°C. One equivalent of chloroacetyl chloride was then added dropwise during 15 min. The mixture was then stirred at room temperature (r.t.) for 6 h. After completion of the reaction, the precipitate was filtered and washed with water and then dried under vacuum to offer compounds **2** as white powders.

2-(2-chloroacetamido)benzoic acid **2a**: white powder (2.68 g; 90% yield); mp: 183°C (litt.^[1]:183-185°C); ¹H NMR (CDCl₃, 300 MHz): δ ppm 4.22 (s, 2H), 7.18 (t, 1H, *J* = 9.0 Hz), 7.60 (t, 1H, *J* = 9.0 Hz), 8.15 (dd, 1H, *J* = 9.0, 3.0 Hz), 8.71 (d, 1H, *J* = 9.0 Hz), 11.95 (bs, 1H) ; ¹³C NMR (CDCl₃, 75 MHz): δ ppm 43.4, 120.6, 123.8, 127.8, 132.0, 135.2, 140.9, 164.3, 165.4; HPLC, Tr = 2.20 min ; MS (ESI⁺): calc. for C₉H₉NO₃Cl: 214.0, found 214.1 [M+H]⁺.

2-(2-chloroacetamido)-4-methylbenzoic acid **2b**: white powder (2.08 g, 71% yield); mp: 208°C (litt.^[2]: 208-209°C); ¹H NMR (CDCl₃, 300 MHz): δ ppm 2.35 (s, 3H), 4.42 (s, 2H), 7.00 (d, 1H, *J* = 8.1 Hz), 7.88 (d, 1H, *J* = 8.1 Hz), 8.31 (s, 1H); ¹³C NMR (CDCl₃, 75 MHz): δ ppm 22.4, 43.4, 112.4, 121.1, 124.8, 132.0, 140.7, 147.2, 165.3 171.4; HPLC, Tr = 2.75 min; MS (ESI⁺): calc. for C₁₀H₁₁NO₃Cl: 228.0, found 228.2 [M+H]⁺.

Synthesis of quinazolines 3 and 3'

To a solution of 1.4 mmol of compound **2a** or **2b** in 10 mL of toluene, were added 7 mmol of PCl₃ (5 equiv.) and 2.1 mmol of the suitable aniline (1.5 equiv.). The mixture was stirred at reflux for 6-10 h (monitoring by HPLC). After completion of the reaction and cooling to r.t., the mixture was evaporated to dryness and 10 mL of water were added. The reaction mixture was neutralized with the addition of sodium bicarbonate and extracted with chloroform (4 x 25 mL). The organic layers were combined, dried over Na₂SO₄, filtered and evaporated under vacuum to offer a mixture of **3** + **3'** which was used without further purification in the next step.

Synthesis of substituted quinazolines 4 :

To a solution of 1 mmol of quinazoline **3+3'** in 10 mL of ethanol, were added 1 mmol of 2-mercapto-5-nitrobenzimidazole (195 mg, 1 equiv.) and 0.2 mL of a 5N NaOH aqueous solution. The mixture was stirred at r.t. for 2 h. After reaction completion, the precipitate was filtered and washed with diethyl ether to offer compounds **4**.

2-(((5-nitro-1H-benzo[*d*]imidazol-2-yl)thio)methyl)-3-(3-(trifluoromethyl)-phenyl)quinazolin-4(3H)-one **4a**: yellow solid (0.159 g, 32% yield); ¹H NMR (CDCl₃, 400 MHz) : δ ppm 4.45 (dd, 2H, *J* = 20.0, 16.0 Hz), 7.53 (d, 1H, *J* = 8.0 Hz), 7.57 (t, 1H, *J* = 8.0 Hz), 7.71 (d, 1H, *J* = 8.0 Hz), 7.76-7.83 (m, 2H), 7.89 (t, 1H, *J* = 8.0 Hz), 7.95 (d, 1H, *J* = 8.0 Hz), 8.02 (d, 1H, *J* = 8.0 Hz), 8.10 (s, 1H), 8.14 (d, 1H, *J* = 8.0 Hz), 8.23 (s, 1H), 13.28 (s, 1H); ¹³C NMR (CDCl₃, 100 MHz): δ ppm 35.9, 106.7, 110.6, 113.0, 117.6, 120.6, 122.3, 125.3, 126.3, 126.5, 127.0, 127.4, 130.0, 130.4, 130.8, 133.5, 135.0, 137.2, 140.2, 146.6, 151.9, 154.4, 161.2; HPLC, Tr = 3.07 min; MS (ESI⁺): calc. for C₂₃H₁₅F₃N₅O₃S: 498.1, found 498.2 [M+H]⁺.

2-(((5-nitro-1H-benzo[*d*]imidazol-2-yl)thio)methyl)-3-(2-(trifluoromethyl)-phenyl)quinazolin-4(3H)-one **4b**: yellow solid (0.407g; 82% yield); ¹H NMR (DMSO-*d*₆, 400 MHz) : δ ppm 4.44 (ABX, 2H), 7.55 (d, 1H, *J* = 8.0 Hz), 7.61 (t, 1H, *J* = 8.0 Hz), 7.72 (d, 1H, *J* = 8.0 Hz), 7.76 (t, 1H, *J* = 8.0 Hz), 7.80-7.93 (m, 3H), 8.01-8.06 (m, 2H), 8.15 (dd, 1H, *J* = 8.0, 4.0 Hz), 8.24 (d, 1H, *J* = 4.0 Hz), 13.30 (bs, 1H) ; ¹³C NMR (DMSO-*d*₆, 100 MHz) : δ ppm 35.6, 117.5, 119.0, 120.2, 121.7, 124.5, 126.0, 126.3, 126.6, 126.9, 127.1, 127.8, 127.9, 130.8, 131.9, 133.8, 134.5, 135.4, 142.2, 144.6, 146.4, 151.7, 161.0; HPLC, Tr = 3.35 min; MS (ESI⁺): calc for C₂₃H₁₅F₃N₅O₃S: 498.1, found 497.9 [M+H]⁺.

2-(((5-nitro-1H-benzo[*d*]imidazol-2-yl)thio)methyl)-3-(4-(trifluoromethyl)-phenyl)quinazolin-4(3H)-one **4c**: yellow solid (0.273 mg; 55% yield); ¹H NMR (DMSO-*d*₆, 400 MHz): δ ppm 4.45 (s, 2H), 7.53 (d, 1H, *J* = 12.0 Hz), 7.58 (t, 1H, *J* = 8.0 Hz), 7.72 (d, 1H, *J* = 8.0 Hz), 7.85-7.93 (m, 6H), 8.02 (dd, 1H, *J* = 8.0, 4.0 Hz), 8.13 (d, 1H, *J* = 4.0 Hz), 8.23 (s, 1H) ; ¹³C NMR (DMSO-*d*₆, 100 MHz) : δ ppm 36.0, 117.4, 120.6, 125.2, 126.5, 126.7 (2C), 127.0, 127.4, 127.9, 129.2, 129.6, 129.9, 130.3 (2C), 133.5, 135.1, 140.2, 142.1, 146.6, 151.7, 155.3, 161.1; HPLC, Tr = 3.38 min; MS (ESI⁺): calc for C₂₃H₁₅F₃N₅O₃S: 498.1, found 498.0 [M+H]⁺.

2-(((5-nitro-1H-benzo[*d*]imidazol-2-yl)thio)methyl)-3-phenylquinazolin-4(3H)-one **4d**: yellow solid (0.356 g, 83% yield); ^1H NMR (DMSO- d_6 , 400 MHz) : δ ppm 4.4 (s, 2H), 7.50-7.59 (m, 7H), 7.69 (d, 1H, $J = 8.0$ Hz), 7.85 (t, 1H, $J = 12.0$ Hz), 8.03 (d, 1H, $J = 12.0$ Hz), 8.13 (d, 1H, $J = 12.0$ Hz), 8.25 (s, 1H), 13.25 (s, 1H) ; ^{13}C NMR (DMSO- d_6 , 100 MHz) : δ ppm 36.1, 110.3, 113.4, 117.2, 120.7, 126.5, 126.9, 127.2, 128.8 (2C), 129.4, 129.6 (2C), 134.8, 136.5, 139.6, 141.9, 144.0, 146.6, 152.1, 155.9, 161.1; HPLC, Tr = 3,07 min; MS (ESI $^+$): calc for C₂₂H₁₇N₅O₃S 430.1, found 430.1 [M+H] $^+$.

2-(((5-nitro-1H-benzo[*d*]imidazol-2-yl)thio)methyl)-3-(*m*-tolyl)quinazolin-4(3H)-one **4f**: beige solid (0.354 g, 80% yield); ^1H NMR (DMSO- d_6 , 300 MHz) : δ ppm 2.34 (s, 3H), 4.44 (ABX, 2H), 7.28 (d, 1H, $J = 9.0$ Hz), 7.36-7.48 (m, 3H), 7.57 (t, 2H, $J = 9.0$ Hz), 7.69 (d, 1H, $J = 9.0$ Hz), 7.86 (td, 1H, $J = 9.0, 3.0$ Hz), 8.02 (dd, 1H, $J = 9.0, 3.0$ Hz), 8.12 (dd, 1H, $J = 9.0, 3.0$ Hz), 8.24 (s, 1H) ; ^{13}C NMR (DMSO- d_6 , 75 MHz) : δ ppm 20.8, 36.0, 98.4, 117.4, 120.6, 125.8, 126.4, 126.9, 127.2, 129.2, 129.5, 130.0, 130.5, 131.9, 134.8, 135.5, 136.1, 136.3, 139.1, 142.1, 146.6, 152.2, 161.0; HPLC, Tr = 3.19 min; MS (ESI $^+$): calc. for C₂₃H₁₉N₅O₃S 444.1, found 444.0 [M+H] $^+$.

3-(2-methoxyphenyl)-2-(((5-nitro-1H-benzo[*d*]imidazol-2-yl)thio)methyl)-quinazolin-4(3H)-one **4g**: beige solid (0.418 g, 91% yield); ^1H NMR (DMSO- d_6 , 400 MHz): δ ppm 3.78 (s, 3H), 4.44 (ABX, 2H), 7.12 (td, 1H, $J = 8.0, 4.0$ Hz), 7.26 (dd, 1H, $J = 8.0, 4.0$ Hz), 7.47-7.60 (m, 4H), 7.70 (d, 1H, $J = 4.0$ Hz), 7.88 (td, 1H, $J = 8.0, 4.0$ Hz), 8.03 (dd, 1H, $J = 8.0, 4.0$ Hz), 8.12 (dd, 1H, $J = 8.0, 4.0$ Hz), 8.25 (d, 1H, $J = 4.0$ Hz), 13.66 (bs, 1H) ; ^{13}C NMR (DMSO- d_6 , 100 MHz): δ ppm 35.5, 55.9, 112.7, 113.0, 117.5, 120.5, 121.0, 124.4, 126.5, 127.0, 127.4, 129.0, 129.4, 130.1, 131.3, 132.8, 135.0, 142.1, 146.6, 147.0, 152.7, 154.4, 160.6; HPLC, Tr = 3,08 min; MS (ESI $^+$): calc. for C₂₃H₁₉N₅O₄S 460.1, found 460.0 [M+H] $^+$.

3-(3-methoxyphenyl)-2-(((5-nitro-1H-benzo[*d*]imidazol-2-yl)thio)methyl)-quinazolin-4(3H)-one **4h**: beige solid (0.298 g, 65% yield); ^1H NMR (DMSO- d_6 , 400 MHz) : δ ppm 3.77 (s, 3H), 4.47 (s, 2H), 7.05 (ddd, 1H, $J = 8.0, 4.0, 0.8$ Hz), 7.14 (ddd, 1H, $J = 8.0, 4.0, 0.8$ Hz), 7.20 (t, 1H, $J = 4.0$ Hz), 7.48 (t, 1H, $J = 8.0$ Hz), 7.57 (td, 2H, $J = 8.0, 4.0$ Hz), 7.69 (d, 1H, $J = 8.0$ Hz), 7.86 (td, 1H, $J = 8.0, 4.0$ Hz), 8.03 (dd, 1H, $J = 8.0, 4.0$ Hz), 8.13 (dd, 1H, $J = 8.0, 4.0$ Hz), 8.25 (d, 1H, $J = 4.0$ Hz), 13.66 (bs, 1H) ; ^{13}C NMR (DMSO- d_6 , 100 MHz) : δ ppm 36.0, 55.4, 114.6, 115.1, 117.5, 119.4, 120.7, 120.9, 126.5, 126.9, 127.3, 129.4, 130.4, 134.9, 137.5, 140.9, 142.1, 143.9, 146.6, 152.2, 155.6, 160.1,

161.0; HPLC, Tr = 3.04 min; MS (ESI+): MS (ESI+): calc. for C₂₃H₁₉N₅O₄S 460.1, found 460.0 [M+H]⁺.

3-(4-methoxyphenyl)-2-(((5-nitro-1H-benzo[d]imidazol-2-yl)thio)methyl)-quinazolin-4(3H)-one **4i**: beige solid (0.330 g, 72% yield); ¹H NMR (DMSO-*d*₆, 400 MHz) : δ ppm 3.76 (s, 3H), 4.45 (s, 2H), 7.05 (dd, 2H, *J* = 8.0, 4.0 Hz), 7.45-7.49 (m, 2H), 7.56 (td, 2H, *J* = 8.0, 4.0 Hz), 7.69 (d, 1H, *J* = 8.0 Hz), 7.86 (td, 1H, *J* = 8.0, 4.0 Hz), 8.03 (d, 1H, *J* = 8.0, 4.0 Hz), 8.12 (dd, 1H, *J* = 8.0, 4.0 Hz), 8.26 (bs, 1H), 13.64 (bs, 1H) ; ¹³C NMR (DMSO-*d*₆, 100 MHz) : δ ppm 36.2, 55.3, 110.7, 112.9, 114.7 (2C), 117.5, 119.7, 120.7, 120.9, 126.5, 126.9, 127.2, 128.8, 130.0 (2C), 134.8, 140.3, 142.2, 146.6, 152.7, 159.6, 161.4; HPLC, Tr = 3.03 min; MS (ESI+): calc. for C₂₃H₁₉N₅O₄S 460.1, found 460.0 [M+H]⁺.

3-(2-bromophenyl)-2-(((5-nitro-1H-benzo[d]imidazol-2-yl)thio)methyl)-quinazolin-4(3H)-one **3j**: yellow solid (0.198 g, 39% yield); ¹H NMR (DMSO-*d*₆, 400 MHz): δ ppm 4.44 (ABX, 2H), 7.46 (td, 1H, *J* = 9.0, 3.0 Hz), 7.55 (d, 1H, *J* = 9.0 Hz), 7.58-7.64 (m, 2H), 7.73 (d, 1H, *J* = 9.0 Hz), 7.82 (dd, 1H, *J* = 6.0, 3.0 Hz), 7.87-7.95 (m, 2H), 8.03 (dd, 1H, *J* = 9.0, 3.0 Hz), 8.17 (dd, 1H, *J* = 9.0, 3.0 Hz), 8.25 (d, 1H, *J* = 3.0 Hz), 13.25 (s, 1H); ¹³C NMR (DMSO-*d*₆, 100 MHz) : δ ppm 36.1, 97.3, 117.5, 120.4, 122.5, 126.6, 127.1, 127.7, 129.0, 129.3, 131.2, 131.7, 133.5, 135.3, 135.4, 141.6, 142.2, 146.5, 151.5, 155.0, 160.3, 162.3; HPLC, Tr = 3.31 min; MS (ESI+): calc. for C₂₂H₁₅N₅O₃S 508.0, found 508.0 [M+H]⁺, 510.0 [M+2+H]⁺.

3-(3-bromophenyl)-2-(((5-nitro-1H-benzo[d]imidazol-2-yl)thio)methyl)-quinazolin-4(3H)-one **4k**: yellow solid (0.229 g, 45% yield); ¹H NMR (DMSO-*d*₆, 400 MHz) : δ ppm 4.45 (ABX, 2H), 7.49-7.71 (m, 7H), 7.85-7.90 (m, 2H), 8.03 (dd, 1H, *J* = 9.0, 3.0 Hz), 8.12 (d, 1H, *J* = 9.0 Hz), 8.27 (bs, 1H) ; ¹³C NMR (DMSO-*d*₆, 100 MHz) : δ ppm 36.0, 117.5, 119.0, 120.6, 121.9, 122.6, 126.5, 127.0, 127.4, 128.3, 128.6, 129.0, 131.4, 132.0, 132.4, 135.0, 137.8, 142.2, 146.6, 151.8, 155.3, 161.1; HPLC, Tr = 3.32 min; MS (ESI+): calc. for C₂₂H₁₅N₅O₃S 508.0, found 508.0 [M+H]⁺, 510.0 [M+2+H]⁺.

3-(4-bromophenyl)-2-(((5-nitro-1H-benzo[d]imidazol-2-yl)thio)methyl)-quinazolin-4(3H)-one **4l**: brown solid (0.153 g, 30% yield); ¹H NMR (DMSO-*d*₆, 400 MHz) : δ ppm 4.45 (s, 2H), 7.54-7.60 (m, 4H), 7.55 (d, 1H, *J* = 9.0 Hz), 7.69-7.74 (m, 3H), 7.88 (td, 1H, *J* = 8.0, 4.0 Hz), 8.03 (dd, 1H, *J* = 8.0, 4.0 Hz), 8.14 (dd, 1H, *J* = 8.0, 4.0 Hz), 8.28 (d, 1H, *J* = 4.0 Hz); ¹³C NMR (DMSO-*d*₆, 100 MHz) : δ ppm 36.5, 109.9, 117.2, 120.6, 126.5, 127.0 (2C), 127.3, 128.0 (2C), 129.2, 129.5, 131.1,

131.7, 133.6, 135.0, 137.8, 143.2, 146.7, 152.3, 161.1, 165.9; HPLC, Tr = 3,30 min; MS (ESI+): calc. for C₂₂H₁₅N₅O₃S 508.0, found 508.0 [M+H]⁺, 510.0 [M+2+H]⁺.

3-(3-chlorophenyl)-2-(((5-nitro-1H-benzo[*d*]imidazol-2-yl)thio)methyl)-quinazolin-4(3H)-one **4m**: yellow solid (0.158 g, 34% yield); ¹H NMR (DMSO-*d*₆, 400 MHz) : δ ppm 4.46 (ABX, 2H), 7.52-7.60 (m, 5H), 7.70 (d, 1H, *J* = 8.0 Hz), 7.77-7.78 (m, 1H), 7.88 (td, 1H, *J* = 8.0, 4.0 Hz), 8.03 (d, 1H, *J* = 8.0 Hz), 8.13 (dd, 1H, *J* = 8.0, 4.0 Hz), 8.27 (bs, 1H), 13.29 (bs, 1H) ; ¹³C NMR (DMSO-*d*₆, 100 MHz) : δ ppm 36.0, 106.8, 110.7, 113.1, 117.2, 117.7, 120.6, 126.5, 127.0, 127.4, 128.0, 129.2, 129.8, 131.1, 133.6, 135.0, 137.8, 140.1, 142.7, 146.6, 151.8, 161.1; HPLC, Tr = 3.34 min; MS (ESI+): calc. for C₂₂H₁₅N₅O₃SCl 464.1, found 464,0 [M+H]⁺, 465,0 [M+2+H]⁺.

3-(4-methyl-3-nitrophenyl)-2-(((5-nitro-1H-benzo[*d*]imidazol-2-yl)thio)methyl)quinazolin-4(3H)-one **4n**: beige solid (0.332 g, 68% yield); ¹H NMR (DMSO-*d*₆, 300 MHz) : δ ppm 2.37 (s, 3H), 4.52 (s, 2H), 7.51-7.61 (m, 3H), 7.71 (d, 1H, *J* = 9.0 Hz), 7.84-7.92 (m, 2H), 8.03 (d, 1H, *J* = 9.0, 3.0 Hz), 8.14 (d, 1H, *J* = 6.0 Hz), 8.23 (d, 1H, *J* = 3.0 Hz), 8.31 (d, 1H, *J* = 6.0 Hz) ; ¹³C NMR (DMSO-*d*₆, 75 MHz) : δ ppm 19.1, 35.7, 117.4, 119.7, 120.6, 125.4, 126.4, 127.0 (2C), 127.4, 133.7, 134.0, 134.2, 134.9 (2C), 135.0, 142.1, 146.6, 148.9, 151.9 (2C), 155.0, 161.2 ; HPLC, Tr = 3,25 min; MS (ESI+): calc. for C₂₃H₁₈N₆O₅S 4689.1, found 489.0 [M+H]⁺.

7-methyl-2-(((5-nitro-1H-benzo[*d*]imidazol-2-yl)thio)methyl)-3-(3-(trifluoromethyl)phenyl)quinazolin-4(3H)-one **4o**: beige solid (0.312 g, 61%); ¹H NMR (DMSO-*d*₆, 300 MHz) : δ ppm 2.48 (bs, 3H), 7.42 (d, 1H, *J* = 6.0 Hz), 7.53 (bs, 1H), 7.54 (d, 1H, *J* = 9.0 Hz), 7.79 (d, 3H, *J* = 6.0 Hz), 7.91 (d, 2H, *J* = 9.0 Hz), 8.01-8.07 (m, 4H), 8.23 (d, 1H, *J* = 3.0 Hz); ¹³C NMR (DMSO-*d*₆, 75 MHz) : δ ppm 19.1, 35.7, 106.7, 110.6, 113.0, 117.6, 120.6, 122.3, 125.3, 126.3, 126.5, 127.0, 127.4, 130.0, 130.4, 130.8, 133.5, 135.0, 137.2, 140.2, 146.6, 151.9, 154.4, 161.2; HPLC, Tr = 3,25 min; MS (ESI+): calc. for C₂₄H₁₇F₃N₅O₃S 512.1, found 512.0 [M+H]⁺.

7-methyl-2-(((5-nitro-1H-benzo[*d*]imidazol-2-yl)thio)methyl)-3-phenyl-quinazolin-4(3H)-one **4p**: yellow solid (0.345g, 78%); ¹H NMR (DMSO-*d*₆, 300 MHz) : δ ppm 2.48 (bs, 3H), 4.40 (bs, 2H), 7.39 (d, 1H, *J* = 9.0 Hz), 7.45-7.64 (m, 7H), 8.02 (d, 2H, *J* = 9.0 Hz), 8.24 (d, 1H, *J* = 3.0 Hz); ¹³C NMR (DMSO-*d*₆, 75 MHz) : δ ppm 21.3, 36.1, 117.7, 118.2, 119.4, 124.6, 126.3, 126.5, 126.6,

127.8, 128.5, 128.8 (2C), 129.2, 129.3, 129.6 (2C), 136.5, 145.4, 146.7, 152.1, 155.8, 160.9; HPLC, Tr = 3,22 min; MS (ESI+): calc. for C₂₃H₁₈N₅O₃S 444.1, found 444.1 [M+H]⁺.

Synthesis of quinazolines 5 :

A solution of compound **4** (0.3 mmol) and SnCl₂.H₂O (1.5 mmol, 5 equiv.) in MeOH (40 mL) was refluxed for 2 h. After completion of the reaction (HPLC monitoring), the mixture was evaporated to dryness. 20 mL of dichloromethane and 20 mL of saturated aqueous NaHCO₃ were added and the mixture was stirred for 16 h at room temperature. The mixture was then filtered through a pad of Celite and the organic layer separated. The aqueous layer was extracted with CH₂Cl₂ and the combined organic layer were washed with water, dried (Na₂SO₄), and evaporated in vacuo to give **5**.

2-(((5-amino-1H-benzo[*d*]imidazol-2-yl)thio)methyl)-3-(3-(trifluoromethyl)-phenyl)quinazolin-4(3H)-one **5a**: yellow solid (0.127 g, 91% yield); mp: 135.0-140.0°C; ¹H NMR (CDCl₃, 300 MHz) : δ ppm 3.98 (m, 2H), 6.58 (dd, 1H, J = 6.0, 3.0 Hz), 6.75 (bs, 1H), 7.27 (d, 1H, J = 12.0 Hz), 7.52-7.68 (m, 5H), 7.72 (t, 3H, J = 12.0 Hz), 7.81 (t, 1H, J = 8.0 Hz), 8.26 (d, 1H, J = 8.0 Hz); ¹³C NMR (CDCl₃, 100 MHz) : δ ppm 35.9, 112.5, 119.3, 121.0, 122.0, 124.7, 126.0, 126.8, 127.7, 128.3, 131.1, 132.5, 132.7, 133.0, 135.5 (2C), 136.7, 142.7, 146.3, 146.7, 153.7, 157.7, 161.8; FT-IR: γ_{max} (cm⁻¹): 3067, 2917, 1680, 1634, 1602, 1589, 1568, 1472, 1443, 1328, 1268, 1166, 1124, 1069, 805, 771, 698; HPLC, Tr = 2,44 min; MS (ESI+): m/z 468,2 [M+H]⁺; HRMS calc. for C₂₃H₁₇F₃N₅O₃S 468.1106, found 468,1104.

2-(((5-amino-1H-benzo[*d*]imidazol-2-yl)thio)méthyl)-3-(2-(trifluorométhyl)-phényl)quinazolin-4(3H)-one **5b**: brown solid (0.074g, 53% yield); ¹H NMR (DMSO-*d*₆, 400 MHz) : δ ppm 4.17 (bs, 2H), 4.85 (bs, 2H), 6.42 (m, 2H), 7.07 (m, 1H), 7.60 (t, 1H, J = 8.0 Hz), 7.70 (d, 1H, J = 8.0 Hz), 7.75-7.80 (m, 1H), 7.87-7.93 (m, 3H), 8.00 (d, 1H, J = 8.0 Hz), 8,13 (dd, 1H, J = 8.0, 1.2 Hz); ¹³C NMR (DMSO-*d*₆, 100 MHz) : δ ppm 36.1, 94.0, 110.5, 117.5, 120.0, 121.6, 124.3, 126.1, 126.4, 127.0, 127.5, 127.6, 127.7 (2C), 130.7, 131.9, 133.8, 134.2, 135.2, 144.5, 146.4, 152.1, 161.0; FT-IR: γ_{max} (cm⁻¹): 3349, 3047, 2917, 1683, 1632, 1598, 1473, 1453, 1408, 1350, 1314, 1286, 1214, 1173, 1108, 1059, 1035, 806, 769, 696; HPLC, Tr = 2,26 min; MS (ESI+): m/z 468,0 [M+H]⁺; HRMS calc. for C₂₃H₁₇N₅OS 468.1106, found 468,1104.

2-(((5-amino-1H-benzo[*d*]imidazol-2-yl)thio)methyl)-3-(4-(trifluoromethyl)-phenyl)quinazolin-4(3H)-one **5c**: pink solid (0.074g, 53% yield); mp: 205.8 – 208.2°C; ¹H NMR (DMSO-*d*₆, 400 MHz): δ ppm 4.26 (s, 2H), 6.46 (dd, 1H, *J* = 8.5, 1.8 Hz), 6.54 (bs, 1H), 7.06 (d, 1H, *J* = 8.5 Hz), 7.55 (t, 1H, *J* = 8.0 Hz), 7.67 (d, 1H, *J* = 8.1 Hz), 7.68-8.0 (m, 5H), 8.13 (d, 1H, *J* = 8.0 Hz); ¹³C NMR (DMSO-*d*₆, 100 MHz): δ ppm 36.5, 96.2, 110.9, 120.5, 122.4, 125.1, 126.4, 126.5, 126.6, 126.9 (2C), 127.2, 129.5, 129.8, 130.2 (2C), 134.9, 140.2, 143.7, 144.5, 146.6, 152.0, 161.1; FT-IR : γ_{max} (cm⁻¹) : 3369, 3067, 2789, 1683, 1633, 1591, 1470, 1413, 1324, 1283, 1165, 1126, 1104, 1065, 1020, 831, 696; HPLC, Tr = 2.38 min ; MS (ESI+): m/z 468.0 [M+H]⁺; HRMS calc. for C₂₃H₁₇F₃N₅OS 468.1106, found 468.1103.

2-(((5-amino-1H-benzo[*d*]imidazol-2-yl)thio)methyl)-3-phenylquinazolin-4(3H)-one **5d**: beige solid (0.098 g, 82% yield), mp: 132,0-134,3°C; ¹H NMR (CDCl₃, 300 MHz): δ ppm 4.00 (s, 2H), 6.60 (dd, 1H, *J* = 8.4, 2.1 Hz), 6.79 (s, 1H), 7.31-7.34 (m, 3H), 7.51-7.58 (m, 4H), 7.73 (d, 1H, *J* = 7.5 Hz), 7.83 (td, 1H, *J* = 8.4, 1.5 Hz), 8.29 (dd, 1H, *J* = 7.8, 1.2 Hz); ¹³C NMR (CDCl₃, 75 MHz): δ ppm 36.1, 110.3, 113.4, 117.2, 120.7, 126.5, 126.9, 127.2, 128.8 (2C), 129.4, 129.6 (2C), 134.8, 136.5, 139.6, 141.9, 144.1, 146.6, 152.2, 155.9, 161.1; FT-IR: γ_{max} (cm⁻¹): 3345, 3063, 2920, 1680, 1634, 1606, 1588, 1568, 1490, 1472, 1447, 1407, 1352, 1329, 1276, 1211, 1169, 1118, 1024, 994, 806, 768, 696 ; HPLC, Tr = 1,95 min; MS (ESI+) : m/z 400,1 [M+H]⁺; HRMS calc. for C₂₂H₁₈N₅OS 400.1232, found 400.1231.

2-(((5-amino-1H-benzo[*d*]imidazol-2-yl)thio)methyl)-3-cyclohexylquinazolin-4(3H)-one **5e**: beige solid (0.091 g, 75% yield); mp: 131.9- 136.6°C; ¹H NMR (DMSO-*d*₆, 400 MHz) : δ ppm 1.11-1.82 (m, 8H), 2.56 (m, 2H), 4.23 (bs, 1H), 4.84 (bs, 3H), 6.47 (d, 1H, *J* = 8.4, 1.6 Hz), 6.59 (bs, 1H), 7.16 (d, 1H, *J* = 8.4 Hz), 7.48 (td, 1H, *J* = 8.0, 1.2 Hz), 7.55 (d, 1H, *J* = 8.0 Hz), 7.77 (td, 1H, *J* = 8.4, 1.6 Hz), 8.10 (dd, 1H, *J* = 8.0, 1.2 Hz) ; ¹³C NMR (DMSO-*d*₆, 100 MHz) : δ ppm 24.8, 25.3 (2C), 28.0 (2C), 37.1, 59.8, 110.9, 121.5, 125.9, 126.4 (2C), 126.9, 128.3, 128.7, 134.2, 136.7, 144.4, 146.0, 153.5, 161.5; FT-IR : γ_{max} (cm⁻¹): 3341, 3194, 2928, 2853, 1667, 1633, 1607, 1589, 1567, 1475, 1443, 1408, 1353, 1318, 1214, 1167, 1143, 1009, 895, 806, 770, 696; HPLC, Tr = 2.42 min; MS (ESI+): m/z 406.1 [M+H]⁺; HRMS calc. for C₂₂H₂₄N₅OS 406.1702, found 406.1699.

2-(((5-amino-1H-benzo[*d*]imidazol-2-yl)thio)methyl)-3-(*m*-tolyl)quinazolin-4(3H)-one **5f**: brown solid (0.067 g, 54% yield); ¹H NMR (DMSO-*d*₆, 400 MHz) : δ ppm 2.34 (s, 3H), 4.23 (ABX, 2H), 6.42 (dd, 1H, *J* = 8.4, 2.0 Hz), 6.52 (bs, 1H), 7.07 (d, 1H, *J* = 8.4 Hz), 7.29-7.32 (m, 3H), 7.43 (t, 1H,

$J = 8.4$ Hz), 7.56 (td, 1H, $J = 8.0, 1.2$ Hz), 7.66 (d, 1H, $J = 8.0$ Hz), 7.86 (td, 1H, $J = 8.4, 1.6$ Hz), 8.12 (dd, 1H, $J = 8.0, 1.2$ Hz) ; ^{13}C NMR (DMSO- d_6 , 100 MHz) : δ ppm 20.7, 36.5, 96.7, 110.7, 120.6, 125.7, 126.3, 126.8 (2C), 127.0, 128.3, 129.1 (2C), 129.2, 129.9, 133.5, 134.7, 136.3, 139.0, 144.2, 146.6, 152.7, 161.1; FT-IR: γ_{max} (cm^{-1}) : 3349, 3210, 3059, 2918, 1674, 1633, 1598, 1583, 1567, 1472, 1407, 1350, 1285, 1213, 1163, 1110, 806, 771, 694; HPLC, Tr = 2.11 min; MS (ESI+): m/z 414.0 $[\text{M}+\text{H}]^+$; HRMS calc. for $\text{C}_{23}\text{H}_{20}\text{N}_5\text{O}_2\text{S}$ 414.1389, found 414.1388.

2-(((5-amino-1H-benzo[*d*]imidazol-2-yl)thio)methyl)-3-(2-methoxyphenyl)-quinazolin-4(3H)-one **5g**: beige solid (0.080 g, 62% yield); mp: 143.6-145.6°C; ^1H NMR (DMSO- d_6 , 400 MHz) : δ ppm 3.77 (s, 3H), 4.22 (ABX, 2H), 6.42 (d, 1H, $J = 8.0$ Hz), 6.52 (bs, 1H), 7.11 (dd, 2H, $J = 15.0, 9.0$ Hz), 7.24 (d, 1H, $J = 8.0$ Hz), 7.48-7.69 (m, 4H), 7.86 (t, 1H, $J = 15.0, 9.0$ Hz), 8.12 (d, 1H, $J = 9.0$ Hz); ^{13}C NMR (DMSO- d_6 , 100 MHz): δ ppm 36.0, 54.8, 55.8, 110.7, 112.5 (2C), 116.3, 119.4, 120.4, 120.8, 124.4, 126.4 (2C), 126.9, 127.1, 130.0, 131.1, 134.8, 144.0, 146.6, 153.0, 154.3, 160.5 ; FT-IR: γ_{max} (cm^{-1}) : 3349, 3063, 2920, 2853, 1678, 1632, 1606, 1569, 1498, 1472, 1438, 1408, 1353, 1332, 1278, 1251, 1212, 1162, 1125, 1110, 1044, 1021, 806, 771, 753, 697; HPLC, Tr = 2.02 min; MS (ESI+): m/z 430.1 $[\text{M}+\text{H}]^+$; HRMS calc. for $\text{C}_{23}\text{H}_{20}\text{N}_5\text{O}_2\text{S}$ 430.1338, found 430.1339.

2-(((5-amino-1H-benzo[*d*]imidazol-2-yl)thio)methyl)-3-(3-methoxyphenyl)-quinazolin-4(3H)-one **5h**: brown solid (0.082 g, 64% yield); mp: 142.3-144.9°C; ^1H NMR (DMSO d_6 , 400 MHz): δ ppm 3.78 (s, 3H), 4.28 (s, 2H), 6.42 (d, 1H, $J = 8.4$ Hz), 6.52 (bs, 1H), 7.06 - 7.11 (td, 3H, $J = 7.6, 2.4$ Hz), 7.18 (bs, 1H), 7.46 (t, 1H, $J = 8.0$ Hz), 7.56 (t, 1H, $J = 8.0$ Hz), 7.66 (d, 1H, $J = 8.0$ Hz), 7.86 (t, 1H, $J = 8.4$ Hz), 8.14 (d, 1H, $J = 8.0$ Hz); ^{13}C NMR (DMSO d_6 , 100 MHz): δ ppm 36.4, 55.3, 110.7, 114.5, 115.0, 120.6, 120.8, 126.3, 126.8 (2C), 127.0, 130.2, 132.0, 134.7 (2C), 137.5, 144.2, 146.6 (2C), 152.6, 159.9, 161.0 (2C); FT-IR: γ_{max} (cm^{-1}): 3341, 3198, 2922, 1674, 1587, 1566, 1489, 1440, 1409, 1352, 1328, 1290, 1214, 1167, 1127, 1028, 803, 770, 694; HPLC, Tr = 2.08 min; MS (ESI+): m/z 430.1 $[\text{M}+\text{H}]^+$; HRMS calc. for $\text{C}_{23}\text{H}_{20}\text{N}_5\text{O}_2\text{S}$ 430,1338, found 430.1338.

2-(((5-amino-1H-benzo[*d*]imidazol-2-yl)thio)methyl)-3-(4-methoxyphényl)-quinazolin-4(3H)-one **5i**: beige solid (0,117 g, 91% yield); mp: 144.4-148.8°C; ^1H NMR (DMSO- d_6 , 400 MHz): δ ppm 3.79 (s, 3H), 4.24 (bs, 2H), 6.42-6.53 (m, 2H), 7.05-7.10 (m, 3H), 7.42 (d, 2H, $J = 8.8$ Hz), 7.55 (t, 1H, $J = 8.0$ Hz), 7.65 (d, 1H, $J = 7.6$ Hz), 7.85 (t, 1H, $J = 8.0$ Hz), 8.11 (d, 1H, $J = 8.0$ Hz); ^{13}C NMR (DMSO- d_6 , 100 MHz): δ ppm 36.7, 55.2, 94.0, 110.5, 114.4, 114.5, 117.6, 120.6, 126.2 (2C), 126.4, 126.5, 126.8, 127.0, 128.8 (2C), 129.4, 129.9, 134.6, 146.6, 153.1, 159.4, 161.3; FT-IR: γ_{max} (cm^{-1}):

3357, 3067, 3000, 2915, 1679, 1633, 1608, 1592, 1469, 1411, 1353, 1299, 1278, 1248, 1167, 1106, 1029, 829, 784, 696; HPLC, Tr = 1,98 min; MS (ESI+): m/z 430,1 [M+H]⁺; HRMS calc. for C₂₃H₂₀N₅OS 430.1338, found 430.1330.

2-(((5-amino-1H-benzo[d]imidazol-2-yl)thio)methyl)-3-(2-bromophenyl)-quinazolin-4(3H)-one **5j**: beige solid (0.071 g, 50% yield); mp: 230,5-231,6°C; ¹H NMR (DMSO-*d*₆, 400 MHz): δ ppm 2.08 (s, 2H), 4.19 (bs, 2H), 6.41-6.49 (m, 2H), 7.07 (bs, 1H), 7.47 (td, 1H, *J* = 7.6, 1.6 Hz), 7.58 (dd, 1H, *J* = 8.4, 1.2 Hz), 7.71 (d, 1H, *J* = 8.0 Hz), 7.76 (dd, 1H, *J* = 8.0, 1.6 Hz), 7.88-7.93 (m, 2H), 8.16 (dd, 1H, *J* = 8.0, 1.2 Hz); ¹³C NMR (DMSO-*d*₆, 100 MHz): δ ppm 54.9, 94.0, 110.5, 117.6, 120.3, 122.4, 126.5, 127.0, 127.4, 129.1, 131.1, 131.5, 133.3, 135.1, 135.4, 135.7, 136.5, 143.8, 144.5, 146.5, 151.8, 160.2 ; FT-IR : γ_{max} (cm⁻¹) : 3459, 3369, 2575, 1689, 1635, 1607, 1572, 1458, 1418, 1406, 1350, 1330, 1287, 1276, 1240, 1210, 1186, 1024, 995, 900, 825, 798, 767, 757, 718, 693; HPLC, Tr = 2.20 min; MS (ESI+) : m/z 478.0 [M+H]⁺; HRMS calc. for C₂₂H₁₇N₅OSBr 478.0337, found 478.0335.

2-(((5-amino-1H-benzo[d]imidazol-2-yl)thio)methyl)-3-(3-bromophenyl)-quinazolin-4(3H)-one **5k**: beige solid (0.110 g, 77% yield); mp: 148.7-150.1°C; ¹H NMR (DMSO-*d*₆, 400 MHz): δ ppm 4.25 (s, 2H), 6.43 (dd, 1H, *J* = 8.4, 2.0 Hz), 6.53 (bs, 1H), 7.08 (d, 1H, *J* = 8.4 Hz), 7.50-7.72 (m, 5H), 7.85-7.90 (m, 2H), 8.12 (dd, 1H, *J* = 8.0, 1.2 Hz); ¹³C NMR (DMSO-*d*₆, 100 MHz): δ ppm 36.4, 96.1, 110.7, 119.5, 120.5, 121.7, 126.3 (2C), 126.9, 127.1, 128.2, 131.2, 131.9 (2C), 132.3, 134.8, 137.8, 143.9, 146.6, 152.2, 158.9, 161.0; FT-IR : γ_{max} (cm⁻¹): 3357, 2916, 1685, 1633, 1607, 1584, 1472, 1414, 1350, 1329, 1278, 1241, 1178, 1161, 998, 880, 799, 770, 730, 696; HPLC, Tr = 2,25 min; MS (ESI+): m/z 478.0 [M+H]⁺; HRMS calc. for C₂₂H₁₇N₅OSBr 478.0337, found 478.0336.

2-(((5-amino-1H-benzo[d]imidazol-2-yl)thio)methyl)-3-(4-bromophenyl)-quinazolin-4(3H)-one **5l**: white solid (0.084 g, 59% yield); mp: 140,3-141,2°C; ¹H NMR (DMSO-*d*₆, 400 MHz): δ ppm 4.23 (s, 2H), 6.43 (dd, 1H, *J* = 12.0, 4.0 Hz), 6,53 (bs, 1H), 7,09 (d, 1H, *J* = 8.0 Hz), 7,48-7,60 (m, 3H), 7,66 (d, 1H, *J* = 7.8 Hz), 7,73-7,79 (m, 2H), 7,86 (td, 1H, *J* = 8.0, 2.0 Hz), 8,13 (dd, 1H, *J* = 8.0, 4.0 Hz); ¹³C NMR (DMSO-*d*₆, 100 MHz): δ ppm 36.7, 96.9, 110.8, 117.1, 120.6, 122.7, 126.5, 127.0, 127.2, 127.9, 131.2 (2C), 132.6 (2C), 134.9, 135.9, 144.2, 146.7, 149.3, 152.4, 159.2, 161.1; FT-IR: γ_{max} (cm⁻¹): 3656, 3349, 2917, 1682, 1633, 1595, 1469, 1412, 1350, 1334, 1279, 1148, 1065, 1010, 984, 818, 789, 695 ; HPLC, Tr = 2.21 min; MS (ESI+): m/z 477.9 [M+H]⁺; HRMS calc. for C₂₂H₁₇BrN₅OS 478.0337, found 478.0340.

2-(((5-amino-1H-benzo[d]imidazol-2-yl)thio)methyl)-3-(3-chlorophenyl)-quinazolin-4(3H)-one **5m**: beige solid (0.096 g, 74% yield), mp: 133,7-134,5°C; ¹H NMR (DMSO-*d*₆, 400 MHz): δ ppm 4.26 (s, 2H), 6.46 (dd, 1H, *J* = 8.0, 4.0 Hz), 6.57 (bs, 1H), 7.09 (d, 1H, *J* = 8.0 Hz), 7.54-7.59 (m, 5H), 7.66 (t, 1H, *J* = 8.0 Hz), 7.75 (bs, 1H), 7.87 (td, 1H, *J* = 8.0, 4.0 Hz), 8.12 (d, 1H, *J* = 8.0 Hz); ¹³C NMR (DMSO-*d*₆, 100 MHz) : δ ppm 36.5, 94.5, 99.5, 109.8, 109.9, 111.1, 120.6, 126.5, 127.0, 127.3, 127.9, 129.2, 131.0, 131.1, 133.4, 133.6, 137.8, 137.9, 143.3, 146.7, 152.3, 161.1; FT-IR : γ_{\max} (cm⁻¹): 3357, 3057, 2922, 1679, 1633, 1607, 1585, 1472, 1414, 1354, 1330, 1282, 1212, 1175, 993, 775, 746, 696; HPLC, Tr = 2.17 min; MS (ESI+): *m/z* 434.1 [M+H]⁺; HRMS calc. for C₂₂H₁₇N₅O₂Cl 434.0842, found 434.0843.

2-(((5-amino-1H-benzo[d]imidazol-2-yl)thio)methyl)-3-(3-amino-4-methyl-phenyl)quinazolin-4(3H)-one **5n**: brown solid (0.081 g, 63% yield); mp: 164,9-165,9°C; ¹H NMR (CD₃OD, 400 MHz): δ ppm 2.07 (s, 3H), 2.17-2.30 (m, 1H), 4.21 (s, 2H), 6.52 (d, 1H, *J* = 8.0 Hz), 6.65 (s, 1H), 6.72 (d, 1H, *J* = 8.4 Hz), 6.80 (s, 1H), 6.98 (d, 1H, *J* = 8.0 Hz), 7.21 (d, 1H, *J* = 8.4 Hz), 7.48-7.54 (m, 2H), 7.77 (t, 1H, *J* = 8.4 Hz), 8.17 (d, 1H, *J* = 8.0 Hz) ; ¹³C NMR (CD₃OD, 100 MHz): δ ppm 17.4, 54.9, 100.2, 114.7, 115.4, 116.7, 118.2, 122.1, 125.3, 128.2 (2C), 129.4 (2C), 135.6 (2C), 140.3, 144.4, 147.3 (2C), 148.5, 155.1, 164.1; FT-IR : γ_{\max} (cm⁻¹): 3338, 3206, 2922, 2853, 1670, 1629, 1588, 1566, 1503, 1472, 1407, 1352, 1296, 1210, 1113, 994, 800, 770, 694; HPLC, Tr = 1.76 min; MS (ESI+): *m/z* 429.1 [M+H]⁺; HRMS calc. for C₂₃H₂₁N₆O₂S 429.1498, found 429.1500.

2-(((5-amino-1H-benzo[d]imidazol-2-yl)thio)methyl)-7-methyl-3-(3-(trifluorométhyl)phenyl)quinazolin-4(3H)-one **5o**: beige solid (0.093 g, 64.5% yield); mp: 143.7- 144.9°C; ¹H NMR (CDCl₃, 300 MHz): δ ppm 2.52 (s, 3H), 4.03 (s, 2H), 6.56 (d, 1H, *J* = 9.0 Hz), 6.74 (s, 1H), 7.24-7.72 (m, 9H), 8.10 (d, 1H, *J* = 9.0 Hz) ; ¹³C NMR (CDCl₃, 100 MHz): δ ppm 22.3, 36.0, 112.5, 118.5, 122.1, 124.8, 126.1, 126.1, 126.6, 127.0, 127,1, 127,5, 129.8, 131.1, 132.6, 132.7, 133.1, 136.8, 142.7, 146.5, 146.8 (2CH), 153.8, 161.8; FT-IR : γ_{\max} (cm⁻¹) : 3345, 3067, 2919, 2849, 1680, 1631, 1606, 1590, 1567, 1497, 1441, 1409, 1353, 1328, 1290, 1165, 1125, 1069, 1022, 828, 803, 784, 755, 698; HPLC, Tr = 2,59 min; MS (ESI+): *m/z* 482.0 [M+H]⁺; HRMS calc. for C₂₄H₁₉F₃N₅O₂S 482.1262, found 482.1261.

2-(((5-amino-1H-benzo[d]imidazol-2-yl)thio)methyl)-7-methyl-3-phenylquinazolin-4(3H)-one **5p**: beige solid (0.102 g, 82% yield); mp: 156.7-157.5°C; ¹H NMR (CDCl₃, 300 MHz): δ ppm 2.55 (s, 3H), 3.98 (s, 2H), 6.58 (d, 1H, *J* = 9.0 Hz), 6.80 (s, 1H), 7.30-7.54 (m, 8H), 8.16 (d, 1H, *J* = 9.0 Hz);

Supplementary Material

^{13}C NMR (CDCl_3 , 100 MHz) : δ ppm 22.1, 36.0, 112.5, 118.5, 118.8, 126.3, 127.3, 127.6, 128.7, 129.4, 129.6, 129.9, 130.2, 130.5, 136.3, 142.6, 146.5, 147.7, 154.8, 155.2, 161.9; FT-IR: γ_{max} (cm^{-1}): 3218, 3035, 2918, 1676, 1615, 1589, 1562, 1509, 1454, 1335, 1252, 1233, 1175, 1141, 1020, 810, 761, 729, 695; HPLC, Tr = 2.75 min; MS (ESI+): m/z 414.2 $[\text{M}+\text{H}]^+$; HRMS calc. for $\text{C}_{23}\text{H}_{20}\text{N}_5\text{OS}$ 414.1310, found 414.1312.