Supporting Information

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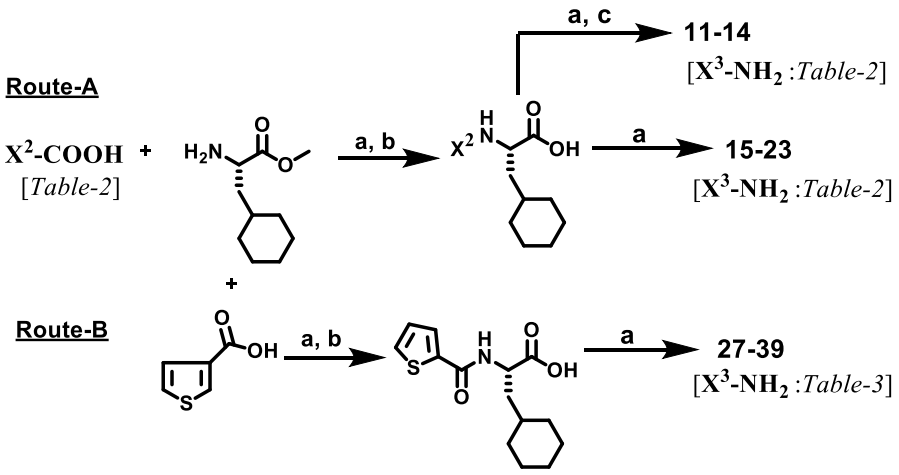
1. Experimental outline for Synthesis of Compound 11–39:

All compounds **11–39** were synthesized using solution phase synthesis except for phosphoserine (pSer) containing compounds **24–26**. Compounds **11-23** and **27-39** were synthesized according to route-A and route-B respectively as shown below.



General synthesis protocol: *Reagents and Conditions*: (a) **X^2–CO_2H**, EDC, HOBt, NMM, DMF, RT overnight, or **X^3–NH_2**, EDC, HOBt, NMM, RT, overnight; (b) LiOH, MeOH: H_2O (4:1), 6 h; (c) 4N HCl/dioxane, RT, 1 h.

Compounds **11-23** and **27-39** were synthesized by coupling corresponding amine and carboxy acid using EDC, HOBt and NMM in DMF whereas methyl ester hydrolysis was performed under basic condition using lithium hydroxide as shown in general synthesis protocol. Boc-deprotection of a amine was carried out by using 4N HCl in dioxane.

Synthesis of compounds **24–26**: These compounds were synthesized using solid phase peptide synthesis (SPPS) by assembling on NovaPEG Rink amide resin with appropriate amino acids. All the amino acids were coupled by using HOBt/HBTU coupling reagent and DIPEA (N,N-Diisopropylethylamine). A phosphorylated Serine was incorporated as Fmoc-Ser[PO(OBzl)OH]. For compound **24** and **25** final *N*-terminal capping was performed with acetic anhydride/DIPEA whereas in case of compound **26** it was capped with 3-hydroxybenzoic acid. All synthesized peptides using this method was cleavage from resin with a cocktail of Reagent K [(TFA/Thioanisole/Water/Phenol/EDT:82.5:5:5:5:2.5 *v/v*)] + 1% *Triisopropylsilane* (TIPS) for 3 h at room temperature.

After the resin had been removed by filtration, the filtrate was concentrated by flushing with nitrogen gas and were precipitated with diethyl ether. Crude peptides were purified using reversed-phase high-performance liquid chromatography (RP-HPLC) on a preparative C4 column (BioAdvantage Pro 300, Thomson Liquid Chromatography) with 0.05% trifluoroacetic acid/water/acetonitrile mixtures as a solvent system. The purity of the peptides was found to be >98% and were characterized by matrix-associated laser desorption ionization time-of-flight mass spectrometry (MALDI microMX, Waters).

2. Spectral data for selected compounds:

All compounds were synthesized according to Scheme **1** and **Route-A-B** using **General Experimental Procedures** described in an **Experimental Section**.

Spectral characterization data for the selected compounds **1, 2, 9, 11, 12, 14, 18, 27, 28, 35–39** is as shown below:

2.1. Compound–1:

Compound **1** was synthesized starting from thiophene-2-carboxylic acid according to *Route-A*. Purity: >98%. MALDI-TOF Mass (*m/z*): calcd. for $C_{28}H_{37}N_3O_6S$ 543.24 found 545.1 for $[M+2H]^+$, 567.1 for $[M+Na]^+$, 583.1 for $[M+K]^+$. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.56 (d, J = 7.3 Hz, 1H), 8.41 (dd, J = 3.8, 8.3 Hz, 1H), 7.98 (t, J = 5.7 Hz, 1H), 7.89 (dd, J = 1.1, 3.7 Hz, 1H), 7.73 (dd, J = 1.1, 5.0 Hz, 1H), 7.33–7.19 (m, 3H), 7.12 (dd, J = 3.7, 5.0 Hz, 1H), 6.90 (ddd, J = 1.1, 2.5, 7.9 Hz, 1H), 4.46–4.28 (m, 2H), 3.61 (s, 3H), 3.13–2.98 (m, 2H), 1.78–1.73 (m, 2H), 1.68 – 1.46 (m, 7H), 1.44 – 1.21 (m, 5H), 1.08 (m, 3H), 0.90–0.78 (m, 2H).

2.2. Compound–2:

Compound **2** was prepared starting from thiophene-2-carboxylic acid according to *Route-A*. Purity: >95%. MALDI-TOF Mass: calcd. for $C_{25}H_{33}N_3O_6S$ 503.21, found 505.0 for $[M+2H]^+$, 527.0 $[M+Na]^+$, 543.0 $[M+K]^+$. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.62 (s, 1H), 8.56 (d, J = 7.3 Hz, 1H), 8.42 (dd, J = 3.6, 8.3 Hz, 1H), 7.99 (t, J = 5.7 Hz, 1H), 7.89 (dd, J = 1.2, 3.7 Hz, 1H), 7.73 (dd, J = 1.1, 5.0 Hz, 1H), 7.30–7.16 (m, 3H), 7.12 (dd, J = 3.7, 5.0 Hz, 1H), 6.90 (ddd, J = 1.2, 2.5, 7.9 Hz, 1H), 4.44 – 4.30 (m, 2H), 3.61 (s, 3H), 3.10 – 2.95 (m, 2H), 1.81–1.29 (m, 9H), 0.86 (d, J = 6.4 Hz, 3H), 0.82 (d, J = 6.4 Hz, 3H).

2.3. Compound–9:

Compound **9** was prepared starting from 4-hydroxy-phenylacetic acid according to *Route-A*. Purity: >98%. MALDI-TOF mass: calcd. for $C_{29}H_{37}N_3O_7$ 539.26 found 540.78 $[M+1H]^+$, 562.76 $[M+Na]^+$, 578.76 $[M+K]^+$. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.53 (d, J = 7.3 Hz, 1H), 7.53 (s, 1H), 7.31–7.17 (m, 4H), 7.08–7.00 (m, 2H), 6.90 (ddd, J = 1.1, 2.6, 8.0 Hz, 1H), 6.69 – 6.60 (m, 2H), 4.31 (q, J = 7.2 Hz, 1H), 3.62 (s, 3H), 3.33 (s, 2H), 2.98 (q, J = 6.3 Hz, 2H), 1.90 (m, 2H), 1.73 (d, J = 6.5 Hz, 2H), 1.49 (dt, J = 12.3, 25.1 Hz, 3H), 1.36–1.26 (m, 8H), 1.07 (d, J = 11.7 Hz, 1H).

2.4. Compound–11:

Compound **11** was prepared starting from 3-((tert-butoxycarbonyl)amino)benzoic acid according to *Route-A*. Purity: >98%. MALDI-TOF Mass: calcd. for $C_{26}H_{33}ClN_4O_3$ 484.22, found 485.9 $[M+2H]^+$, 507.9 $[M+Na]^+$, 523.9 $[M+K]^+$. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.06 (s, 1H), 8.29 (d, J = 8.2 Hz, 1H), 7.98 (t, J = 5.7 Hz, 1H), 7.79 (t, J = 2.1 Hz, 1H), 7.45–7.35 (m, 3H), 7.29 (t, J = 8.1 Hz, 2H), 7.09–6.99 (m, 2H), 4.45 (ddd, J = 4.8, 8.1, 10.2 Hz, 1H), 3.16 – 3.01 (m, 2H), 2.30 (t, J = 7.4 Hz, 2H), 1.73 – 1.46 (m, 9H), 1.30 (d, J = 11.1 Hz, 1H), 1.09 (m, 3H), 0.96–0.77 (m, 2H).

2.5. Compound–12:

Compound **12** was prepared starting from 3-((tert-butoxycarbonyl)amino)benzoic acid according to *Route-A*. Purity: >95%. MALDI-TOF Mass: calcd. for $C_{23}H_{29}N_3O_4$ 411.22, found 412.9

$[M+2H]^+$, 434.9 $[M+Na]^+$, 450.9 $[M+K]^+$. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.72 (s, 1H), 8.31–8.22 (m, 2H), 7.42–7.23 (m, 3H), 7.00 (d, J = 8.0 Hz, 1H), 6.62 (dd, J = 2.9, 5.1 Hz, 2H), 6.47 (dd, J = 2.1, 8.1 Hz, 1H), 4.51 (ddd, J = 4.9, 8.2, 10.3 Hz, 1H), 4.12–4.01 (m, 2H), 1.74–1.48 (m, 7H), 1.34–1.25 (m, 1H), 1.18–1.03 (m, 3H), 0.97–0.77 (m, 2H).

2.6. Compound–14: (*mixture of two diastereomers*)
Compound **14** was prepared starting from 3-((tert-butoxycarbonyl)amino)benzoic acid according to *Route-A*. Purity: >94%. MALDI-TOF Mass: calcd. for $C_{25}H_{30}ClN_3O_4$ 471.19, found 472.49 $[M+H]^+$, 494.21 $[M+Na]^+$, 510.9 $[M+K]^+$. ^{1}H NMR (400 MHz, DMSO-d_6) δ ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.85 (dd, J = 7.2, 36.3 Hz, o1H), 8.29 (dd, J = 8.3, 12.2 Hz, 1H), 7.49–7.35 (m, 4H), 7.27–7.16 (m, 3H), 6.90 (d, J = 7.6 Hz, 1H), 5.44 (dd, J = 7.2, 17.2 Hz, 1H), 4.62 (ddt, J = 5.4, 8.1, 18.9 Hz, 1H), 3.60 (d, J = 4.0 Hz, 3H), 1.69–1.53 (m, 7H), 1.42–1.04 (m, 4H), 0.94–0.81 (m, 2H).

2.7. Compound–17:
Compound **17** was prepared starting from 4-hydroxy-phenylacetic acid according to *Route-A*. Purity: >98%. MALDI-TOF Mass: calcd. for $C_{34}H_{39}ClN_4O_5$ 618.26 found 620.2 $[M+2H]^+$, 642.2 $[M+Na]^+$, 658.2 $[M+K]^+$. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.18 (s, 1H), 10.05 (s, 1H), 8.32 (d, J = 8.1 Hz, 1H), 8.02 – 7.93 (m, 2H), 7.82 – 7.74 (m, 2H), 7.55 (dt, J = 1.3, 7.8 Hz, 1H), 7.44 – 7.24 (m, 3H), 7.14 – 7.01 (m, 3H), 6.72 – 6.64 (m, 2H), 4.46 (ddd, J = 4.9, 8.2, 10.2 Hz, 1H), 3.18 – 2.99 (m, J = 6.5 Hz, 2H), 2.30 (t, J = 7.4 Hz, 2H), 1.76 – 1.46 (m, 10H), 1.09 (q, J = 10.3, 10.7 Hz, 3H), 0.87 (dt, J = 11.5, 21.7 Hz, 2H).

2.8. Compound–18:
Compound **18** was prepared starting from 2-nitrobenzylsulfonyl chloride according to *Route-A*. Purity: >98%. MALDI-TOF Mass: calcd. for $C_{30}H_{32}ClN_5O_7S$ 641.17 found 665.2 $[M+Na]^+$, 681.2 $[M+K]^+$. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.88 (s, 1H), 9.95 (s, 1H), 8.56 (d, J = 7.5 Hz, 1H), 8.36 (t, J = 5.9 Hz, 1H), 7.95 (ddd, J = 1.5, 5.6, 7.4 Hz, 2H), 7.86–7.72 (m, 3H), 7.70–7.61 (m, 2H), 7.46 (dt, J = 1.1, 8.4 Hz, 1H), 7.40–7.24 (m, 3H), 7.09 (ddd, J = 1.2, 2.4, 8.0 Hz, 1H), 4.46 (ddd, J = 4.8, 7.5, 10.3 Hz, 1H), 1.73–1.55 (m, 7H), 1.38–1.28 (m, 1H), 1.22–1.07 (m, 3H), 0.88 (dq, J = 10.7, 11.2, 22.7 Hz, 2H).

2.9. Compound–27:
Compound **27** was prepared starting from thiophene-2-carboxylic acid according to *Route-B*. Purity: >94%. MALDI-TOF Mass: calcd. for $C_{22}H_{33}N_3O_5S$ 451.21 found 452.9 $[M+2H]^{2+}$, 475.0 $[M+Na]^+$, 491.0 $[M+K]^+$. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.41 (dd, J = 3.2, 8.3 Hz, 1H), 8.03 (d, J = 8.0 Hz, 1H), 7.96 (t, J = 5.6 Hz, 1H), 7.73 (dd, J = 1.2, 5.2 Hz, 1H), 7.12 (dd, J = 3.7, 5.0 Hz, 1H), 4.41 (ddd, J = 5.3, 8.2, 10.0 Hz, 1H), 4.09 (ddd, J = 4.8, 7.6, 9.2 Hz, 1H), 3.01 (ddt, J = 6.5, 13.0, 31.7 Hz, 2H), 1.82 (s, 3H), 1.67–1.46 (m, 10H), 1.38–1.20 (m, 5H), 1.16–1.05 (m, 3H), 0.89 (dt, J = 11.5, 22.2 Hz, 2H).

2.10. Compound–28:
Compound **28** was prepared starting from thiophene-2-carboxylic acid according to *Route-B*. Purity: >96%. MALDI-TOF Mass: calcd. for $C_{23}H_{35}N_3O_5S$ 465.23 found 467.0 $[M+2H]^+$, 489.0 $[M+Na]^+$, 505.0 $[M+K]^+$. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.42 (dd, J = 3.4, 8.3 Hz, 1H), 8.18 (d, J = 7.4 Hz, 1H), 7.96 (t, J = 5.6 Hz, 1H), 7.89 (d, J = 3.6 Hz, 1H), 7.73 (dd, J = 0.8, 5.2 Hz,

1H), 7.13 (dd, *J* = 3.7, 5.0 Hz, 1H), 4.47–4.36 (m, 1H), 4.19–4.07 (m, 1H), 3.59 (s, 3H), 3.00 (ddq, *J* = 6.4, 12.8, 31.3 Hz, 2H), 1.82 (s, 3H), 1.70–1.45 (m, 10H), 1.38–1.22 (m, 5H), 1.16–1.05 (m, 3H), 0.89 (dt, *J* = 10.6, 20.5 Hz, 2H).

2.11. Compound–35:

Compound **35** was prepared starting from thiophene-2-carboxylic acid according to *Route-B*. Purity: >94%. MALDI-TOF Mass: calcd. for $C_{27}H_{35}N_3O_6S$ 529.22 found 531.0 $[M+2H]^+$, 553.0 $[M+Na]^+$, 569.0 $[M+K]^+$. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.60 (s, 1H), 8.45 – 8.36 (m, 2H), 7.98 (t, *J* = 5.7 Hz, 1H), 7.89 (dd, *J* = 1.2, 3.7 Hz, 1H), 7.73 (dd, *J* = 1.2, 4.8 Hz, 1H), 7.33–7.18 (m, 3H), 7.12 (dd, *J* = 3.7, 5.0 Hz, 1H), 6.89 (ddd, *J* = 1.1, 2.6, 8.0 Hz, 1H), 4.41 (ddd, *J* = 5.3, 8.2, 9.8 Hz, 1H), 4.28 (td, *J* = 5.8, 8.1 Hz, 1H), 3.12–2.91 (m, 2H), 1.81–1.72 (m, 2H), 1.71–1.44 (m, 8H), 1.43–1.36 (m, 3H), 1.28 (td, *J* = 4.5, 8.2, 8.8 Hz, 2H), 1.08 (q, *J* = 9.1, 10.7 Hz, 3H), 0.89–0.78 (m, 2H).

2.12. Compound–36:

Compound **36** was prepared starting from thiophene-2-carboxylic acid according to *Route-B*. Purity: >96%. MALDI-TOF Mass: calcd. for $C_{26}H_{33}N_3O_5S$ 499.21 found 500.9 $[M+2H]^+$, 522.9 $[M+Na]^+$, 538.9 $[M+K]^+$. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.09 (d, *J* = 18.3 Hz, 1H), 8.44 (d, *J* = 8.2 Hz, 1H), 8.25 (s, 1H), 8.04 (t, *J* = 5.7 Hz, 1H), 7.90 (dd, *J* = 1.2, 3.7 Hz, 1H), 7.84–7.70 (m, 2H), 7.60 (td, *J* = 1.2, 7.6 Hz, 1H), 7.42 (t, *J* = 7.9 Hz, 1H), 7.13 (dd, *J* = 3.7, 5.0 Hz, 1H), 4.43 (ddd, *J* = 5.1, 8.2, 10.1 Hz, 1H), 3.83 (s, 3H), 3.09 (qq, *J* = 6.8, 13.0 Hz, 2H), 2.31 (t, *J* = 7.4 Hz, 2H), 1.77 – 1.47 (m, 9H), 1.33–1.24 (m, 1H), 1.16–1.02 (m, 3H), 0.87 (dt, *J* = 11.0, 21.1 Hz, 2H).

2.13. Compound–37:

Compound **37** was prepared starting from thiophene-2-carboxylic acid according to *Route-B*. Purity: >94%. MALDI-TOF Mass: calcd. for $C_{26}H_{35}N_3O_4S$ 485.23 found 487.0 $[M+2H]^+$, 509.0 $[M+Na]^+$, 525.0 $[M+K]^+$. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.41 (d, *J* = 8.3 Hz, 1H), 8.28 (t, *J* = 5.6 Hz, 1H), 7.95 (t, *J* = 5.6 Hz, 1H), 7.89 (dd, *J* = 1.2, 3.6 Hz, 1H), 7.73 (dd, *J* = 1.2, 4.8 Hz, 1H), 7.28 – 7.09 (m, 4H), 6.86 (dt, *J* = 2.4, 6.6 Hz, 1H), 4.42 (ddd, *J* = 5.4, 8.2, 9.8 Hz, 1H), 3.18 (q, *J* = 6.7 Hz, 2H), 3.13–2.92 (m, 2H), 1.72–1.35 (m, 12H), 1.30–1.22 (m, 3H), 1.16–1.05 (m, 3H), 0.92–0.79 (m, 2H).

2.14. Compound–38:

Compound **38** was prepared starting from thiophene-2-carboxylic acid according to *Route-B*. Purity: >99%. MALDI-TOF Mass: calcd. for $C_{24}H_{30}N_3O_3$ 475.17 found 476.9 $[M+2H]^+$, 498.9 $[M+Na]^+$, 515.0 $[M+K]^+$. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.05 (s, 1H), 8.44 (d, *J* = 8.2 Hz, 1H), 8.03 (t, *J* = 5.7 Hz, 1H), 7.90 (dd, *J* = 1.2, 3.8 Hz, 1H), 7.82–7.70 (m, 2H), 7.41 (ddd, *J* = 1.0, 2.0, 8.3 Hz, 1H), 7.29 (t, *J* = 8.1 Hz, 1H), 7.16–7.02 (m, 2H), 4.42 (ddd, *J* = 5.1, 8.1, 10.1 Hz, 1H), 3.08 (dp, *J* = 6.3, 19.0 Hz, 2H), 2.30 (t, *J* = 7.4 Hz, 2H), 1.76–1.46 (m, 10H), 1.34–1.24 (m, 1H), 1.16–1.05 (m, 3H), 0.93–0.82 (m, 2H).

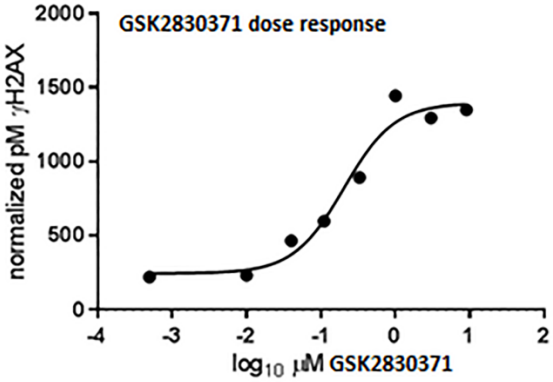
2.15. Compound–39:

Compound **39** was prepared starting from thiophene-2-carboxylic acid according to *Route-B*. Purity: >98%. MALDI-TOF Mass: calcd. for $C_{22}H_{26}ClN_3O_3S$ 447.14 found 470.8 $[M+Na]^+$,

486.8 $[M+K]^+$.^{1}H NMR (400 MHz, DMSO-d_6) δ 9.87 (s, 1H), 8.64 (d, J = 7.3 Hz, 1H), 8.46 (t, J = 5.9 Hz, 1H), 7.93 (dd, J = 1.2, 3.8 Hz, 1H), 7.86–7.74 (m, 2H), 7.53 (dt, J = 1.1, 8.4 Hz, 1H), 7.33 (t, J = 8.1 Hz, 1H), 7.19–7.06 (m, 2H), 4.44 (ddd, J = 5.1, 7.3, 10.0 Hz, 1H), 3.86 (t, J = 5.4 Hz, 2H), 1.76–1.54 (m, 7H), 1.41–1.33 (m, 1H), 1.14 (p, J = 10.2, 11.5 Hz, 3H), 1.00–0.82 (m, 2H).

3. Supporting Figures:

3.1. Figure S1: Wip1 inhibition with GSK2830371 results in an increase in IR-induced H2AX phosphorylation levels.



3.2. Figure S2: Pre-treatment of MCF7 cells with GSK2830371, Compound **39**, or compound **1** resulted in a dose-dependent increase in γH2AX levels 75′ min after exposure to 10 Gy IR.