

Supplementary Information

Discovery of Novel Class of Histone Deacetylase Inhibitors as Anticancer Agents

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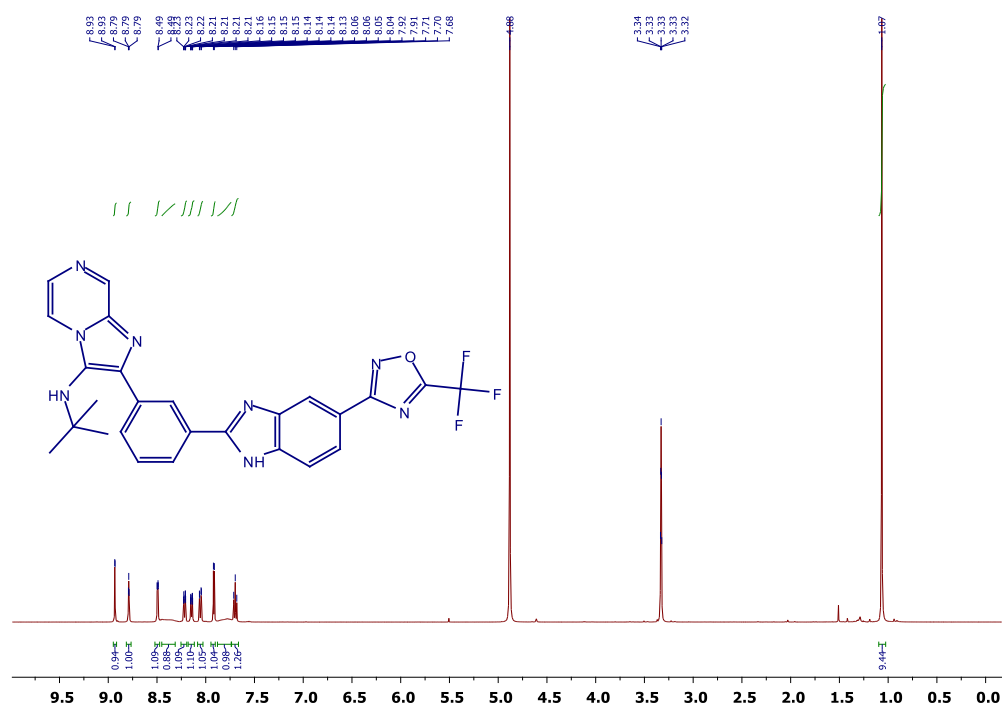


Figure S1: ¹H NMR (500 MHz, CD₃OD) spectra of N-(tert-butyl)-2-(3-(5-(5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl)-1H-benzo[d]imidazol-2-yl)phenyl)imidazo[1,2-a]pyrazin-3-amine (**14**)

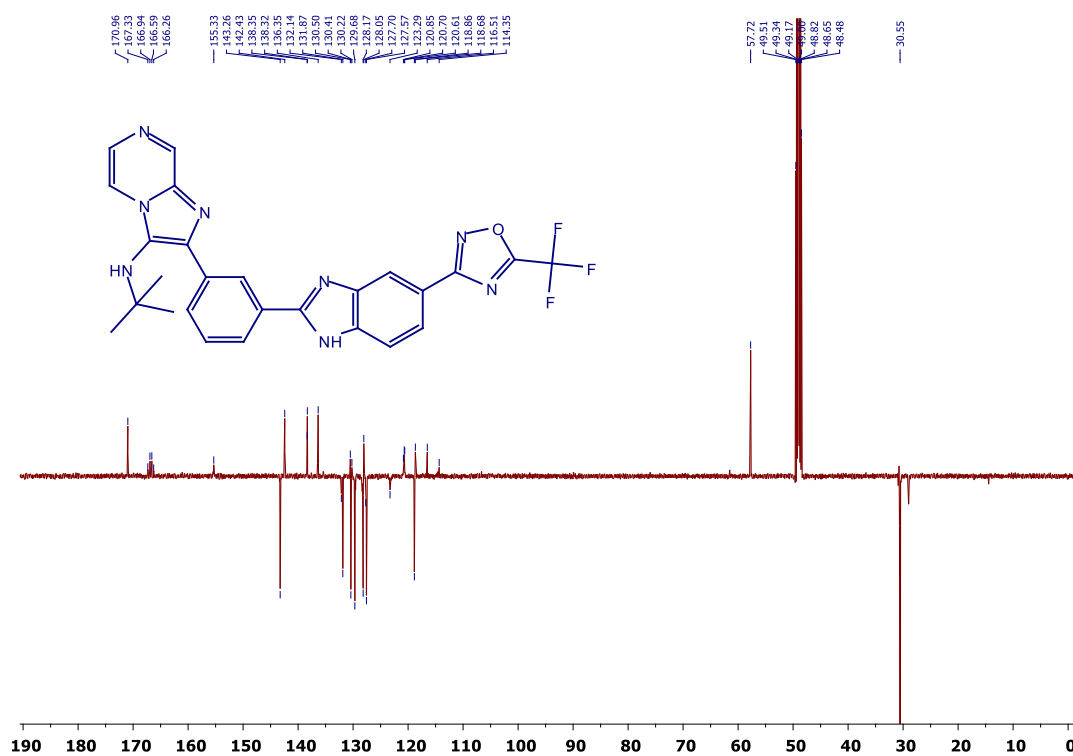
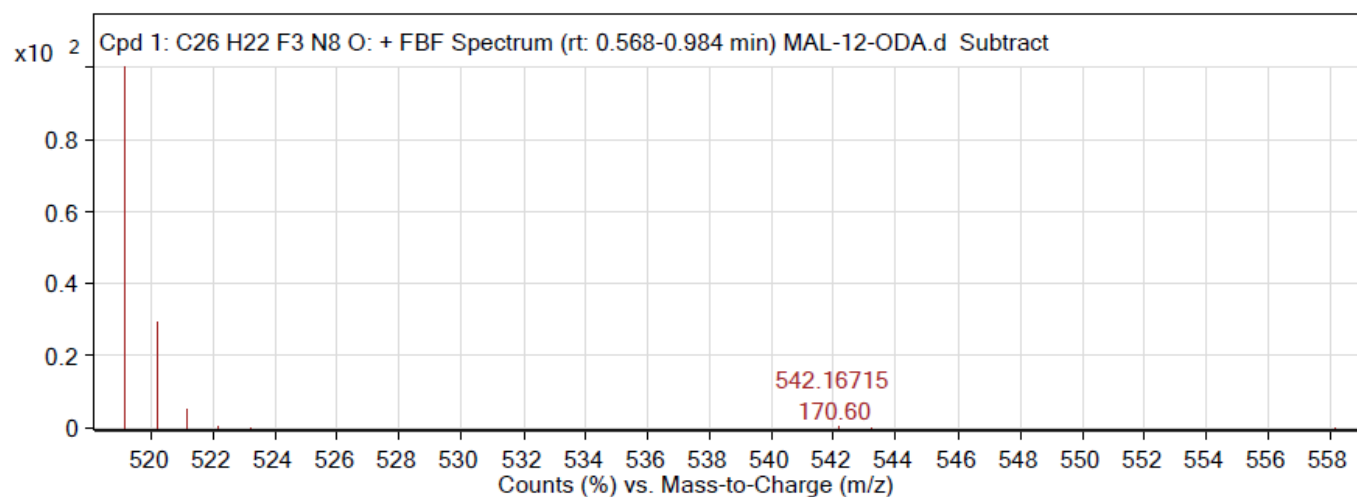


Figure S2: ¹³C NMR (125 MHz, CD₃OD) spectra of N-(tert-butyl)-2-(3-(5-(5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl)-1H-benzo[d]imidazol-2-yl)phenyl)imidazo[1,2-a]pyrazin-3-amine (**14**)



Peak List

m/z	z	Abund	Formula	Ion
519.18549	1	47287.17	C ₂₆ H ₂₂ F ₃ N ₈ O	M ⁺
520.18821	1	13966.45	C ₂₆ H ₂₂ F ₃ N ₈ O	M ⁺
521.19084	1	2339.03	C ₂₆ H ₂₂ F ₃ N ₈ O	M ⁺
522.19134	1	315.91	C ₂₆ H ₂₂ F ₃ N ₈ O	M ⁺
523.18926	1	47.42	C ₂₆ H ₂₂ F ₃ N ₈ O	M ⁺
542.16715	1	170.6	C ₂₆ H ₂₂ F ₃ N ₈ NaO	(M+Na) ⁺
543.17326	1	24.65	C ₂₆ H ₂₂ F ₃ N ₈ NaO	(M+Na) ⁺
558.14291	1	89.63	C ₂₆ H ₂₂ F ₃ KN ₈ O	(M+K) ⁺

Figure S3: HRMS spectra of N-(tert-butyl)-2-(3-(5-(5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl)-1H-benzo[d]imidazol-2-yl)phenyl)imidazo[1,2-a]pyrazin-3-amine (**14**)

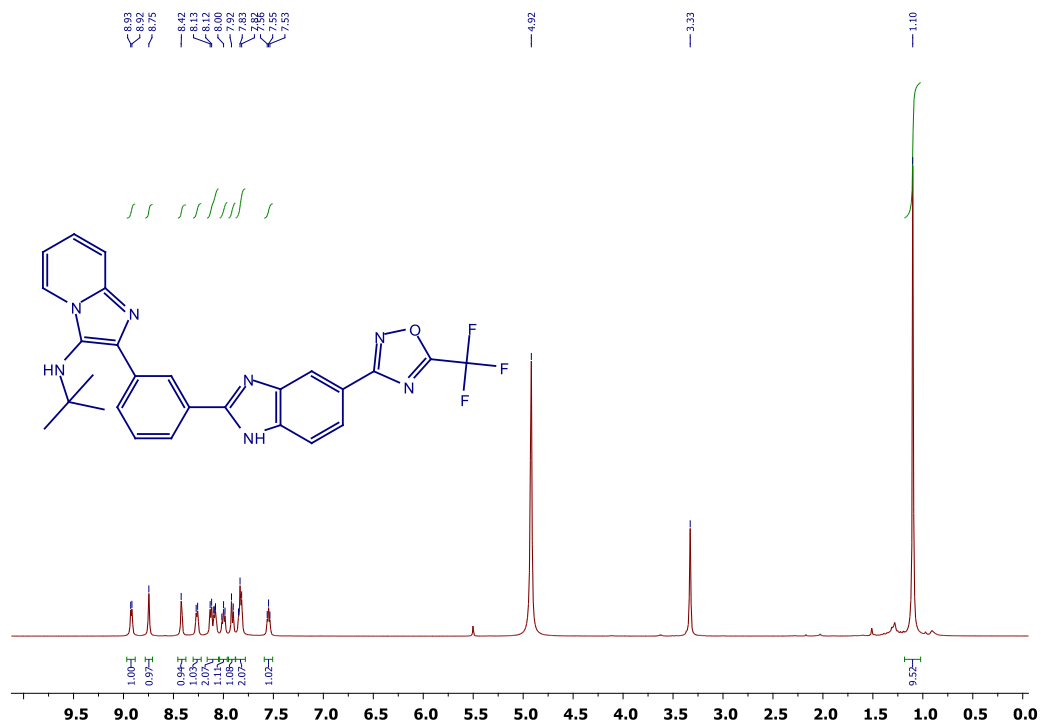


Figure S4: ¹H NMR (500 MHz, CD₃OD) spectra of N-(tert-butyl)-2-(3-(5-(5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl)-1H-benzo[d]imidazol-2-yl)phenyl)imidazo[1,2-a]pyridin-3-amine (**15**)

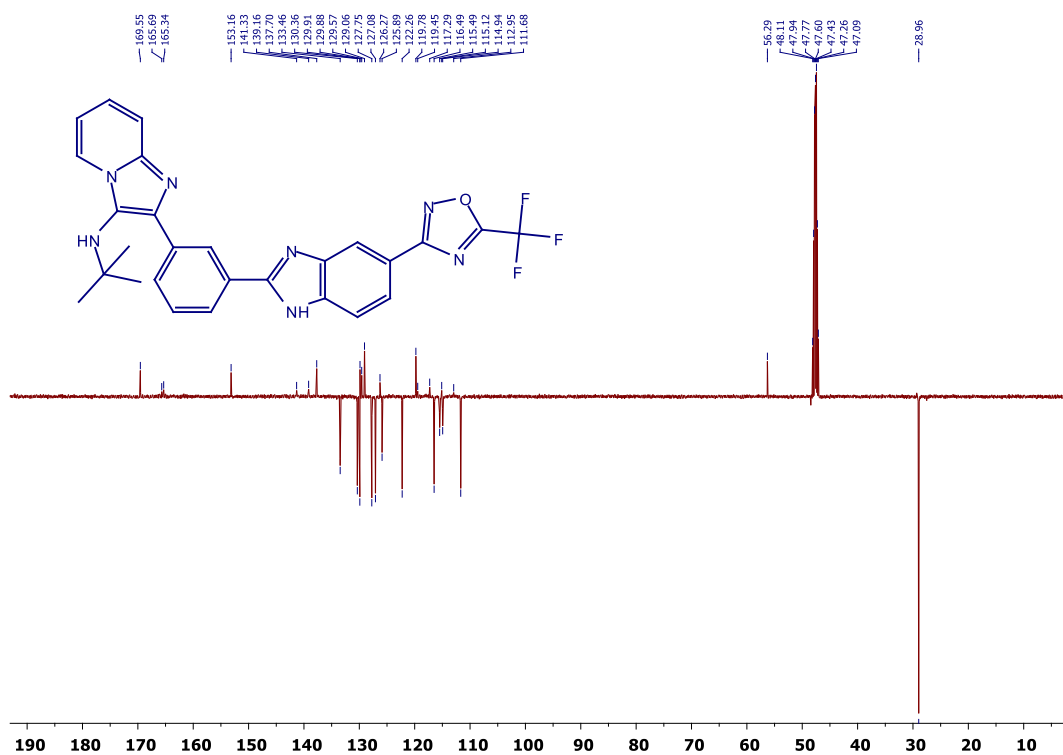
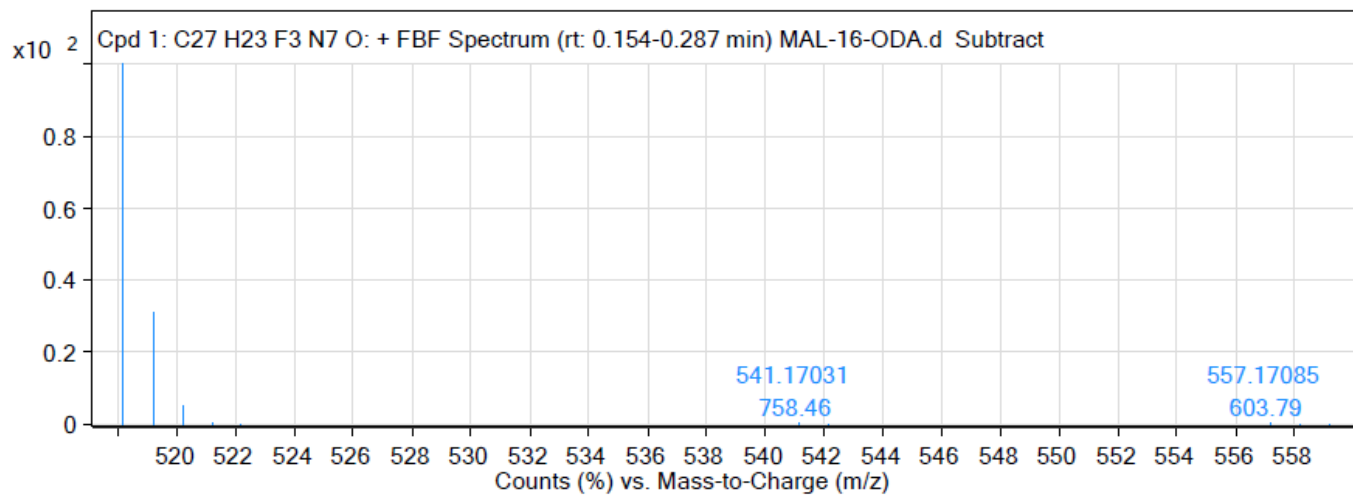


Figure S5: APT NMR (125 MHz, CD₃OD) spectra of N-(tert-butyl)-2-(3-(5-(5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl)-1H-benzo[d]imidazol-2-yl)phenyl)imidazo[1,2-a]pyridin-3-amine (**15**)



Peak List

m/z	z	Abund	Formula	Ion
518.1904	1	119608.36	C ₂₇ H ₂₃ F ₃ N ₇ O	M ⁺
519.19334	1	37309.67	C ₂₇ H ₂₃ F ₃ N ₇ O	M ⁺
520.19622	1	5993.9	C ₂₇ H ₂₃ F ₃ N ₇ O	M ⁺
521.19658	1	875.65	C ₂₇ H ₂₃ F ₃ N ₇ O	M ⁺
522.19626	1	164.39	C ₂₇ H ₂₃ F ₃ N ₇ O	M ⁺
541.17031	1	758.46	C ₂₇ H ₂₃ F ₃ N ₇ NaO	(M+Na) ⁺
542.16941	1	89.12	C ₂₇ H ₂₃ F ₃ N ₇ NaO	(M+Na) ⁺
557.17085	1	603.79	C ₂₇ H ₂₃ F ₃ KN ₇ O	(M+K) ⁺
558.17143	1	333.25	C ₂₇ H ₂₃ F ₃ KN ₇ O	(M+K) ⁺
559.19185	1	47.09	C ₂₇ H ₂₃ F ₃ KN ₇ O	(M+K) ⁺

Figure S6: HRMS spectra of N-(tert-butyl)-2-(3-(5-(5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl)-1H-benzo[d]imidazol-2-yl)phenyl)imidazo[1,2-a]pyridin-3-amine (**15**)

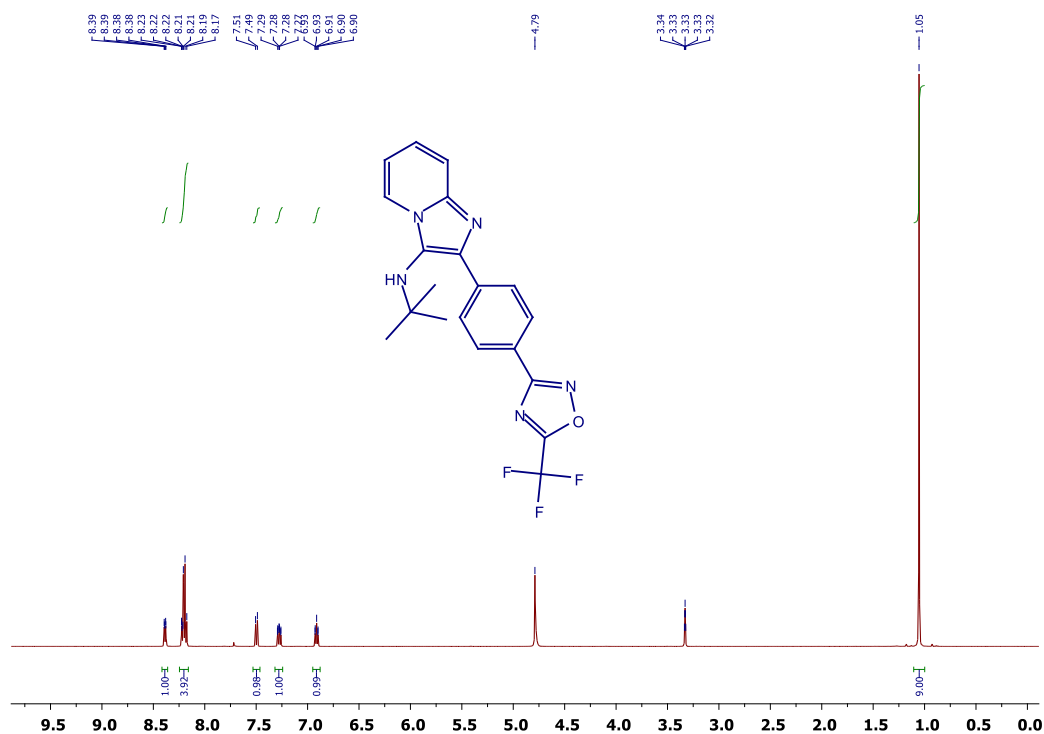


Figure S7: ¹H NMR (500 MHz, CD₃OD+CDCl₃) spectra of N-(tert-butyl)-2-(4-(5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl)phenyl)imidazo[1,2-a]pyridin-3-amine (**19**)

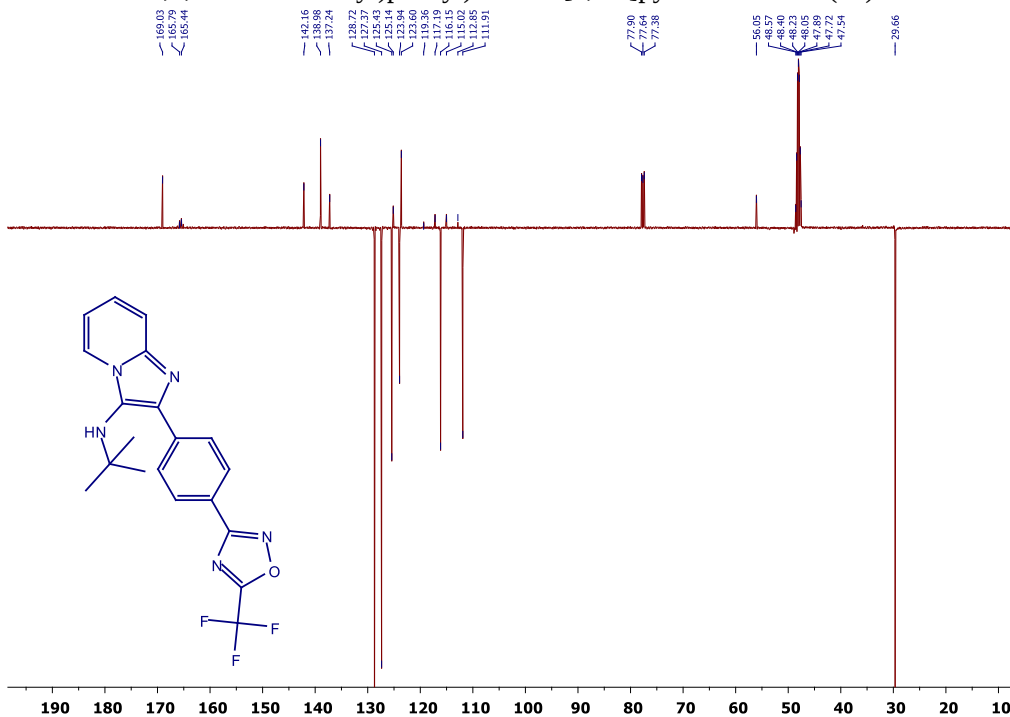
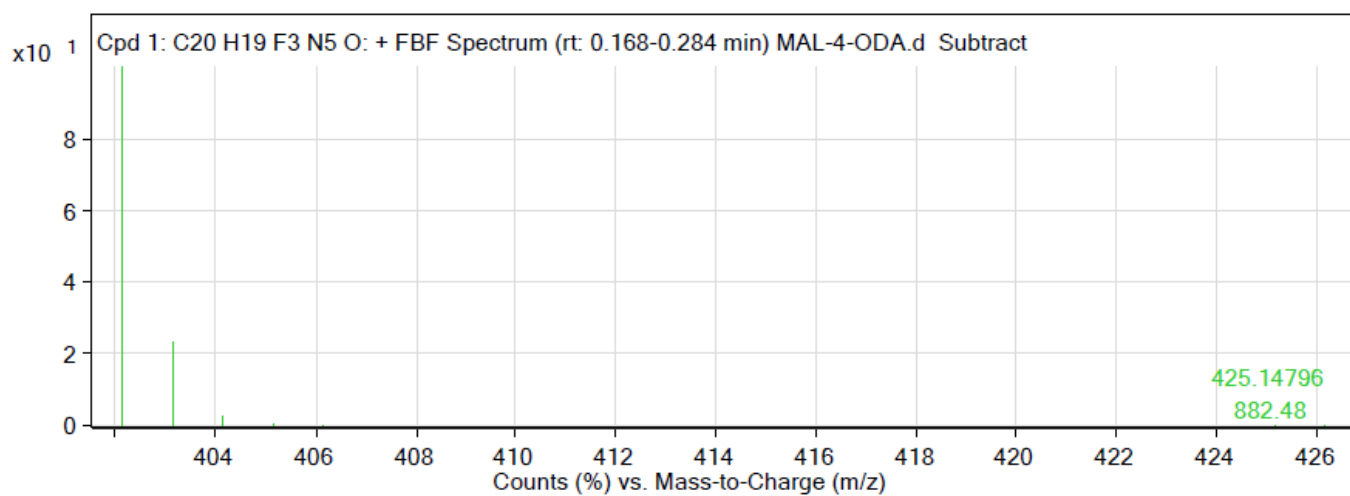


Figure S8: APT NMR (125 MHz, CD₃OD+CDCl₃) spectra of N-(tert-butyl)-2-(4-(5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl)phenyl)imidazo[1,2-a]pyridin-3-amine (**19**)



Peak List

m/z	z	Abund	Formula	Ion
402.15307	1	380393.94	C ₂₀ H ₁₉ F ₃ N ₅ O	M ⁺ +
403.15592	1	88149.09	C ₂₀ H ₁₉ F ₃ N ₅ O	M ⁺ +
404.15886	1	10653.47	C ₂₀ H ₁₉ F ₃ N ₅ O	M ⁺ +
405.16366	1	1277.46	C ₂₀ H ₁₉ F ₃ N ₅ O	M ⁺ +
406.17329	1	247.98	C ₂₀ H ₁₉ F ₃ N ₅ O	M ⁺ +
425.14796	1	882.48	C ₂₀ H ₁₉ F ₃ N ₅ NaO	(M+Na) ⁺
426.14404	1	375.48	C ₂₀ H ₁₉ F ₃ N ₅ NaO	(M+Na) ⁺

Figure S9: HRMS spectra of N-(tert-butyl)-2-(4-(5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl)phenyl)imidazo [1,2-a]pyridin-3-amine (**19**)

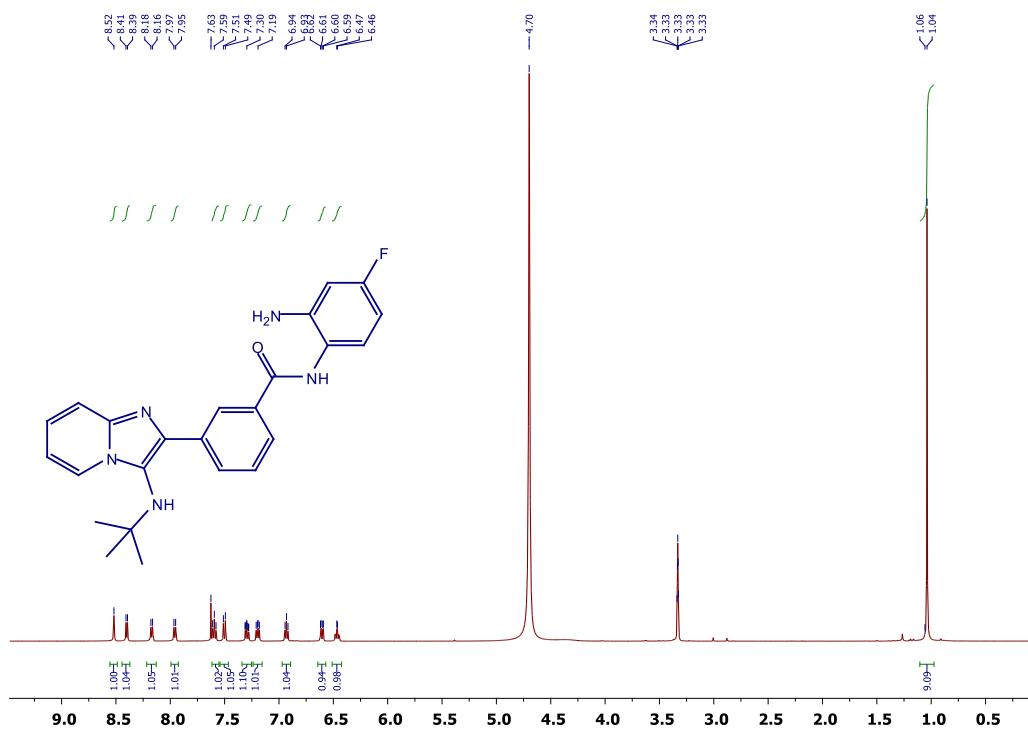


Figure S10: ¹H NMR (500 MHz, CD₃OD+CDCl₃) spectra of N-(2-amino-4-fluorophenyl)-3-(3-(tert-butylamino)imidazo[1,2-a]pyridin-2-yl)benzamide (22)

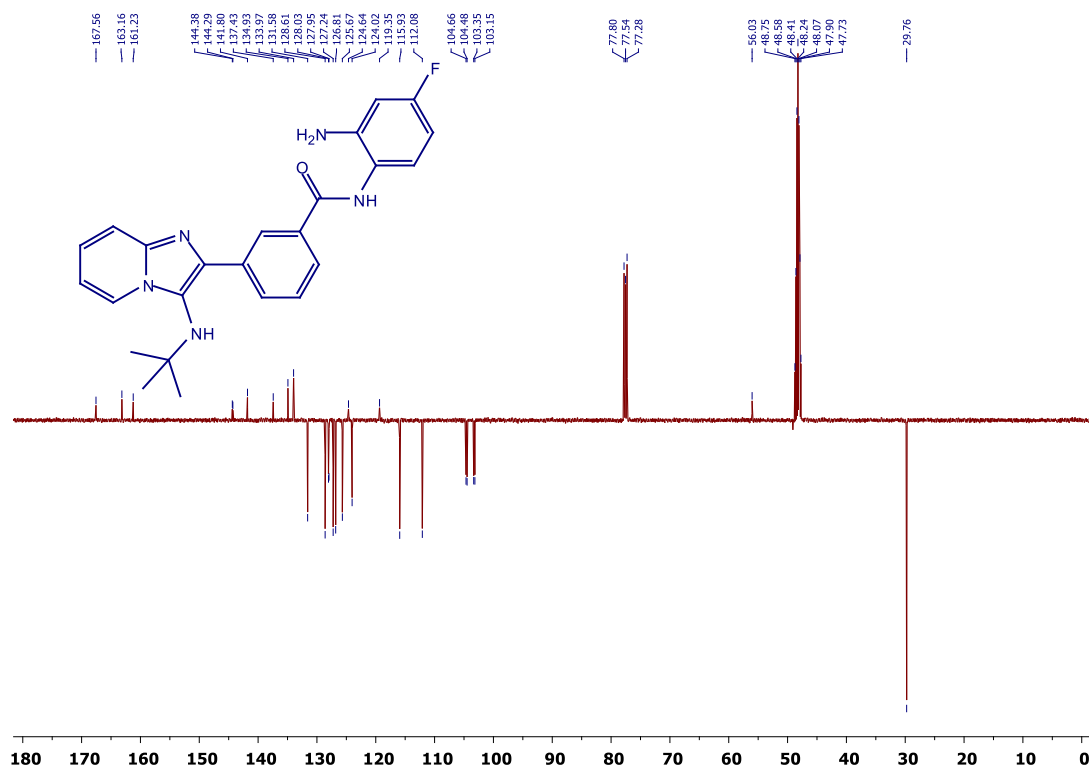
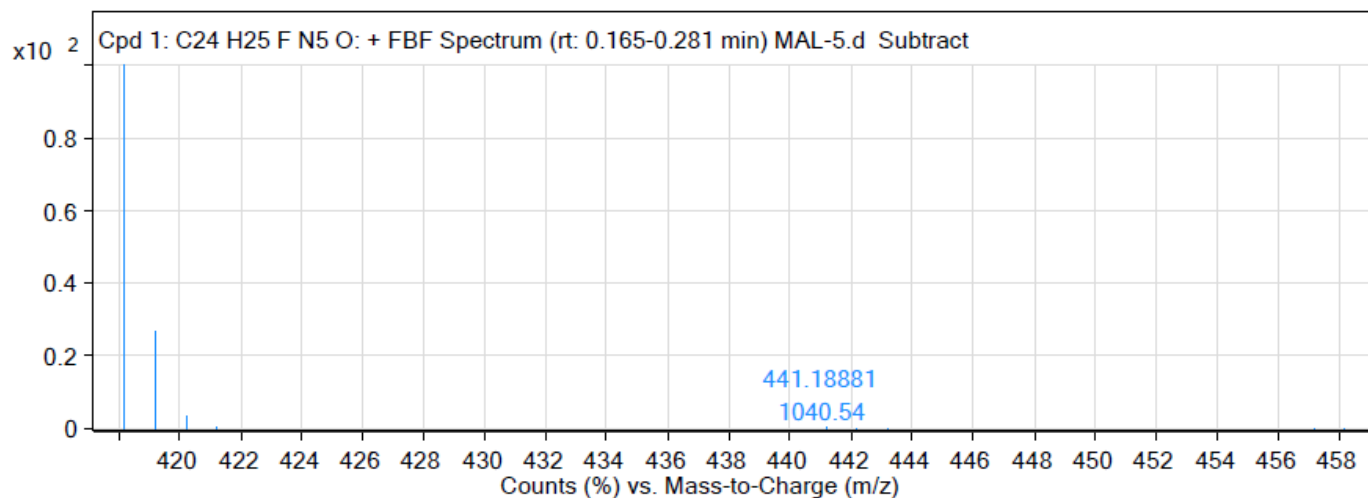


Figure S11: ¹³C NMR (125 MHz, CD₃OD+CDCl₃) spectra of N-(2-amino-4-fluorophenyl)-3-(3-(tert-butylamino)imidazo[1,2-a]pyridin-2-yl)benzamide (22)



Peak List

m/z	z	Abund	Formula	Ion
418.20337	1	186790.25	C ₂₄ H ₂₅ FN ₅ O	M ⁺
419.2064	1	49943.92	C ₂₄ H ₂₅ FN ₅ O	M ⁺
420.20925	1	7101.9	C ₂₄ H ₂₅ FN ₅ O	M ⁺
421.21494	1	1428.46	C ₂₄ H ₂₅ FN ₅ O	M ⁺
441.18881	1	1040.54	C ₂₄ H ₂₅ FN ₅ NaO	(M+Na) ⁺
442.18695	1	296.36	C ₂₄ H ₂₅ FN ₅ NaO	(M+Na) ⁺
443.18484	1	199.11	C ₂₄ H ₂₅ FN ₅ NaO	(M+Na) ⁺
457.16638	1	262.15	C ₂₄ H ₂₅ FKN ₅ O	(M+K) ⁺
458.15605	1	143.27	C ₂₄ H ₂₅ FKN ₅ O	(M+K) ⁺

Figure

S12: HRMS spectra of N-(2-amino-4-fluorophenyl)-3-(3-(tert-butylamino)imidazo[1,2-a]pyridin-2-yl)benzamide (22)

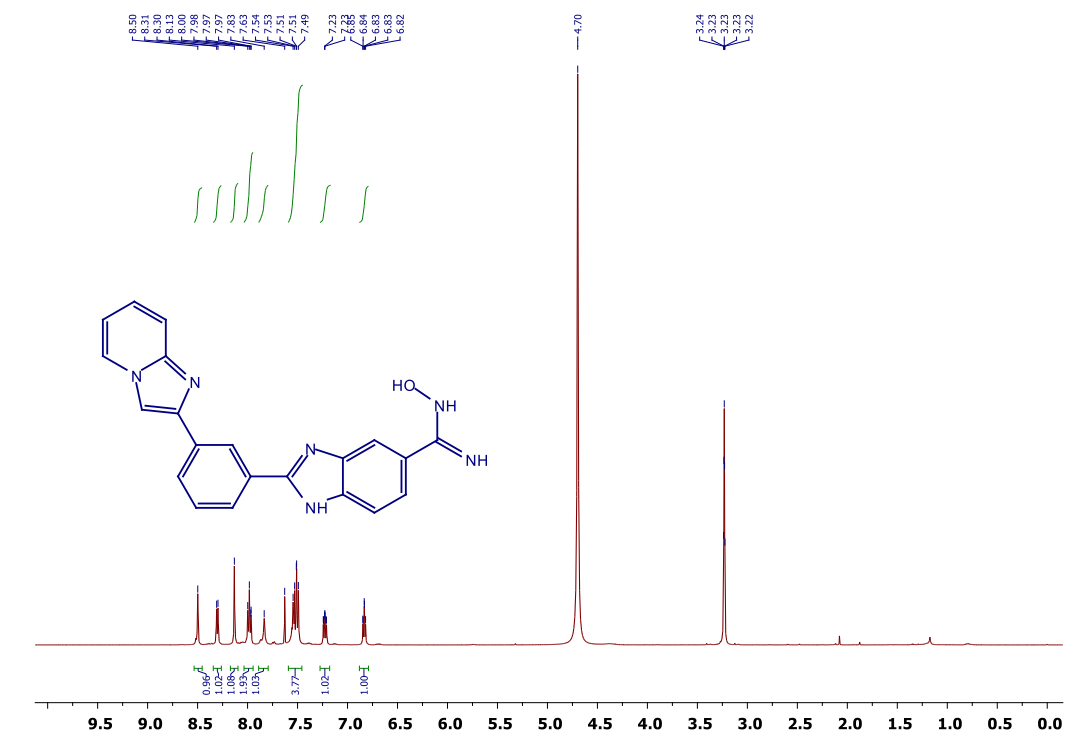


Figure S13: ¹H NMR (500 MHz, CD₃OD) spectra of N-hydroxy-2-(3-(imidazo[1,2-a]pyridin-2-yl)phenyl)-1H-benzo[d]imidazole-5-carboximidamide (**28**)

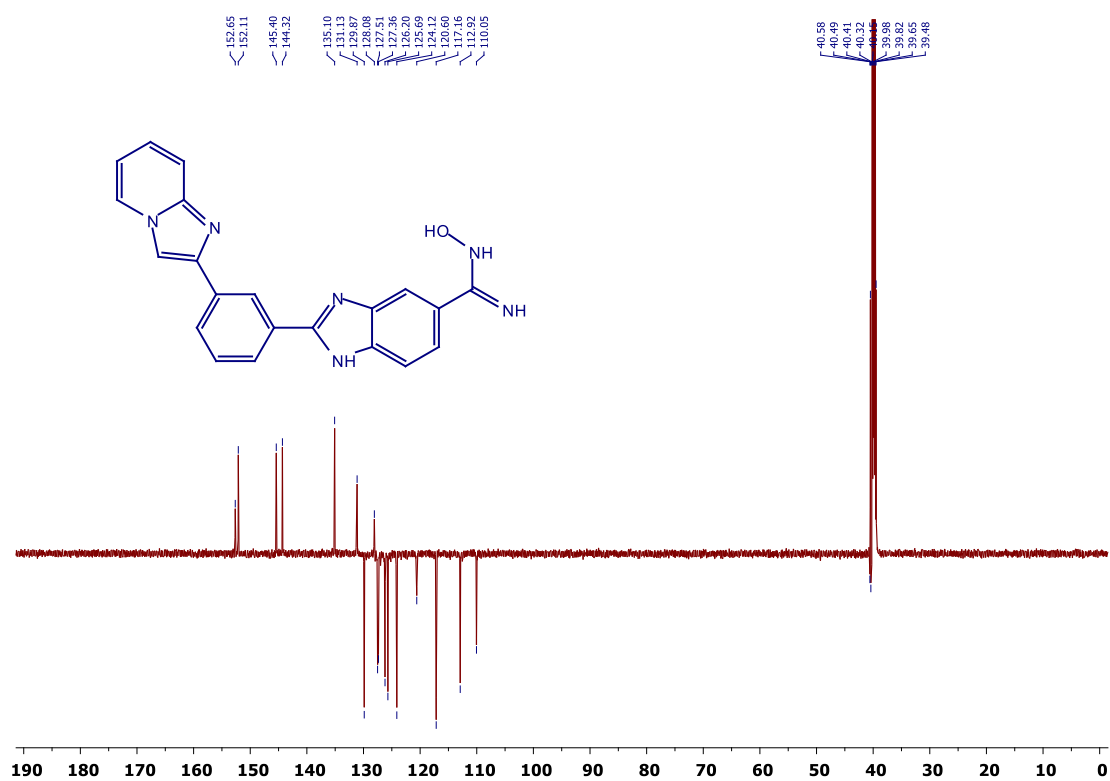
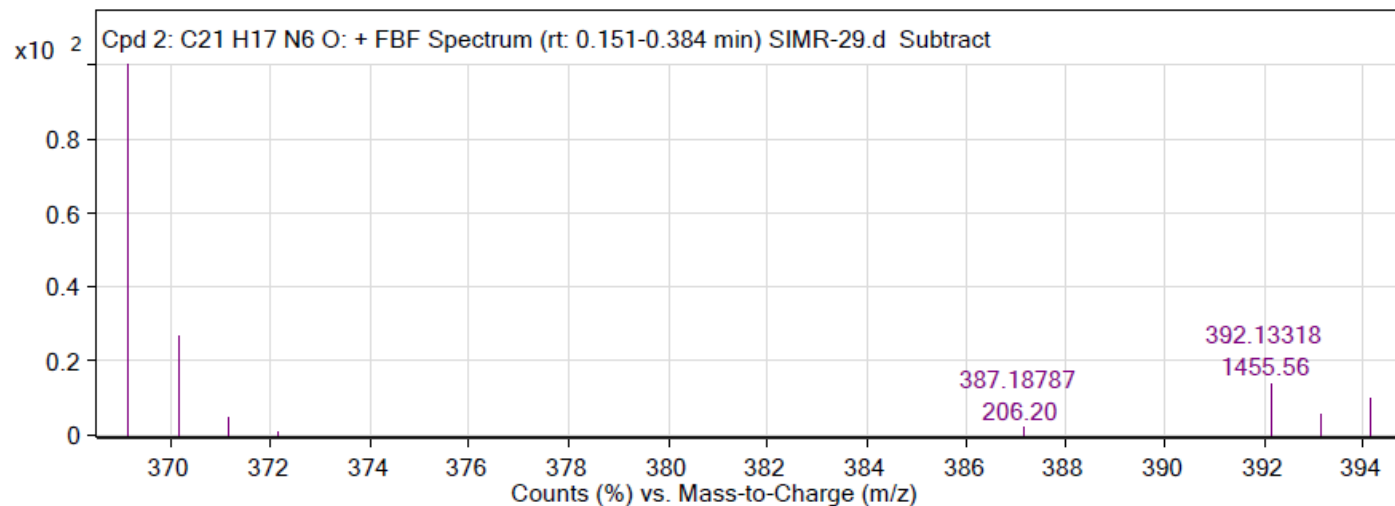


Figure S14: ¹³C NMR (500 MHz, CD₃OD) spectra of N-hydroxy-2-(3-(imidazo[1,2-a]pyridin-2-yl)phenyl)-1H-benzo[d]imidazole-5-carboximidamide (**28**)

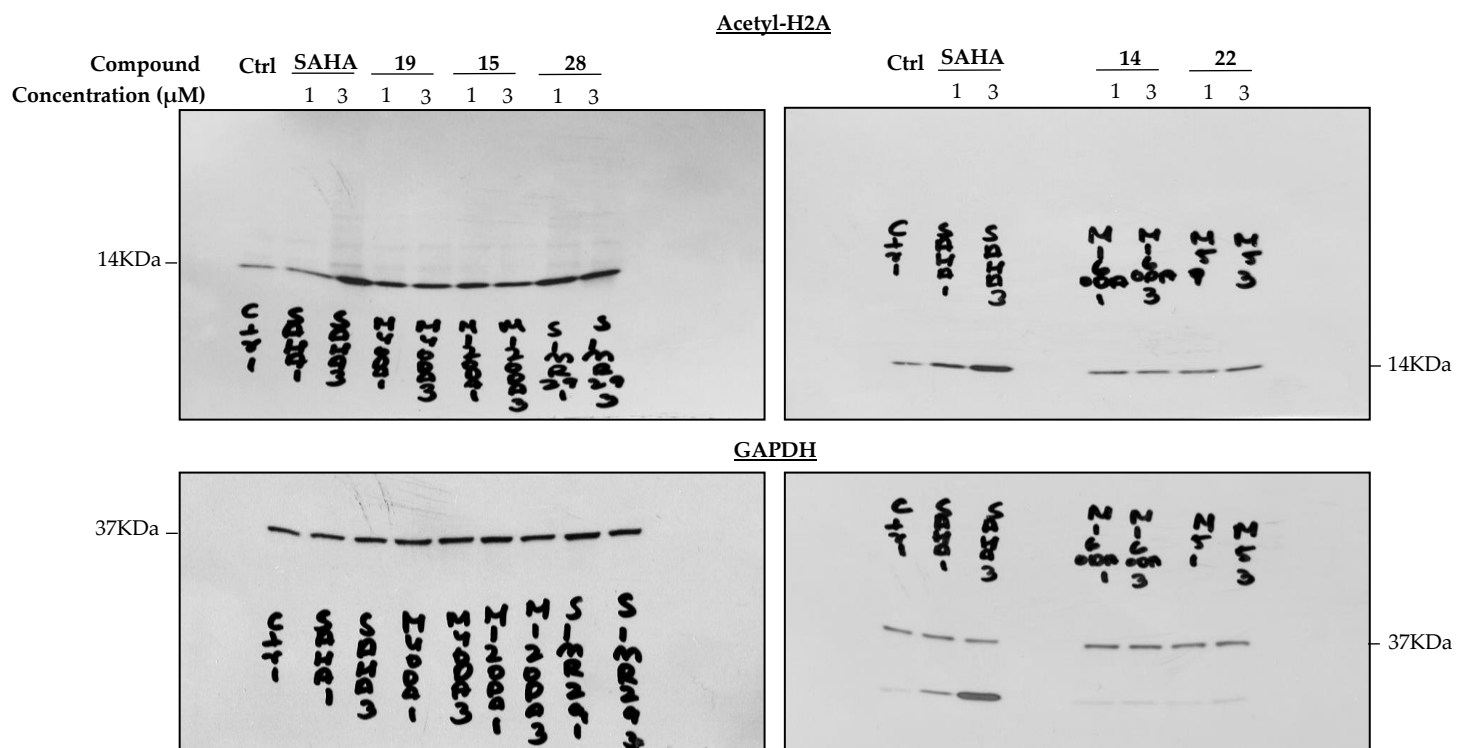


Peak List

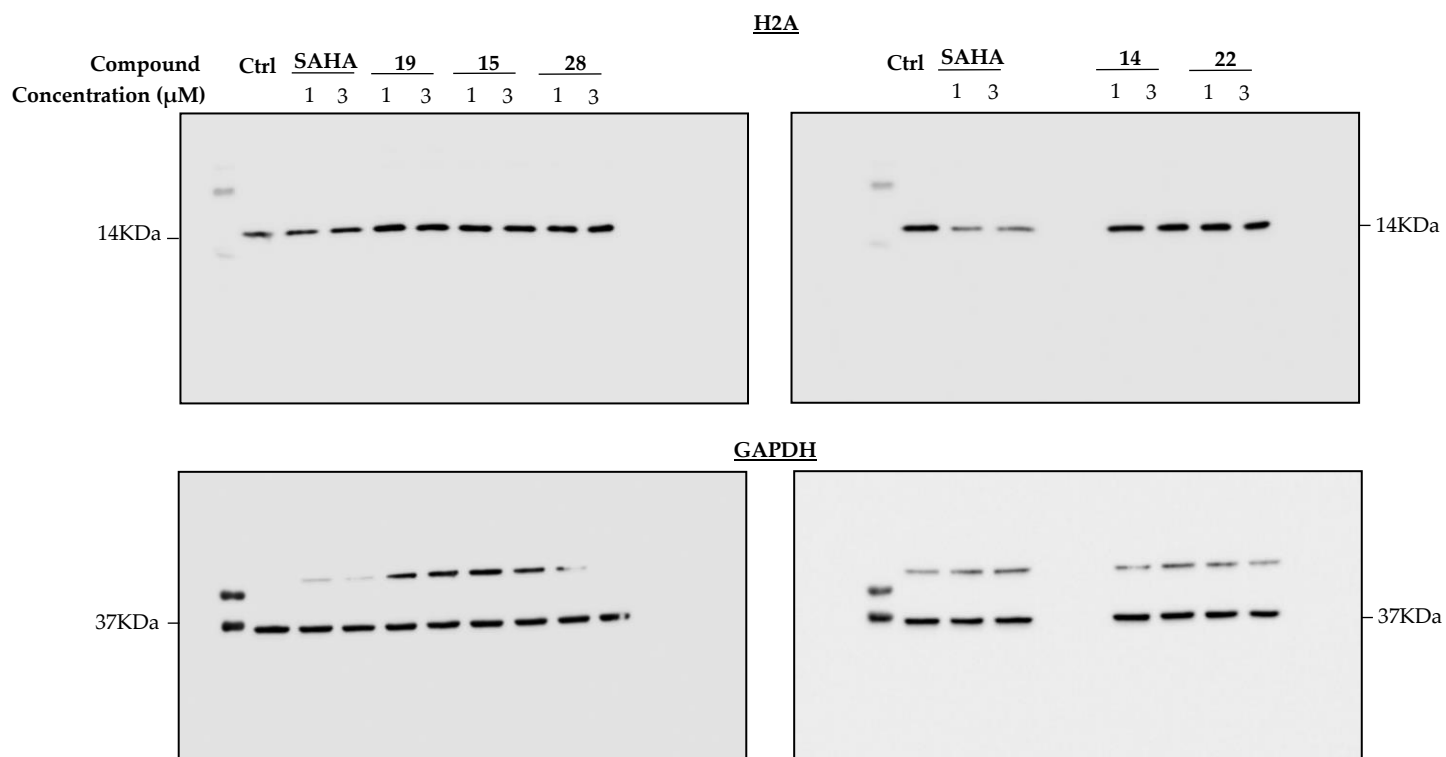
m/z	z	Abund	Formula	Ion
369.14555	1	10428.36	C ₂₁ H ₁₇ N ₆ O	M ⁺ +
370.14857	1	2806.28	C ₂₁ H ₁₇ N ₆ O	M ⁺ +
371.15348	1	474.62	C ₂₁ H ₁₇ N ₆ O	M ⁺ +
372.17112	1	100.38	C ₂₁ H ₁₇ N ₆ O	M ⁺ +
387.18787	1	206.2	C ₂₁ H ₂₁ N ₇ O	(M+NH ₄) ⁺
392.13318	1	1455.56	C ₂₁ H ₁₇ N ₆ NaO	(M+Na) ⁺
393.14131	1	606.31	C ₂₁ H ₁₇ N ₆ NaO	(M+Na) ⁺
394.13551	1	1013.02	C ₂₁ H ₁₇ N ₆ NaO	(M+Na) ⁺

Figure S15: HRMS spectra of N-hydroxy-2-(3-(imidazo[1,2-a]pyridin-2-yl)phenyl)-1H-benzo[d]imidazole-5-carboximidamide (**28**)

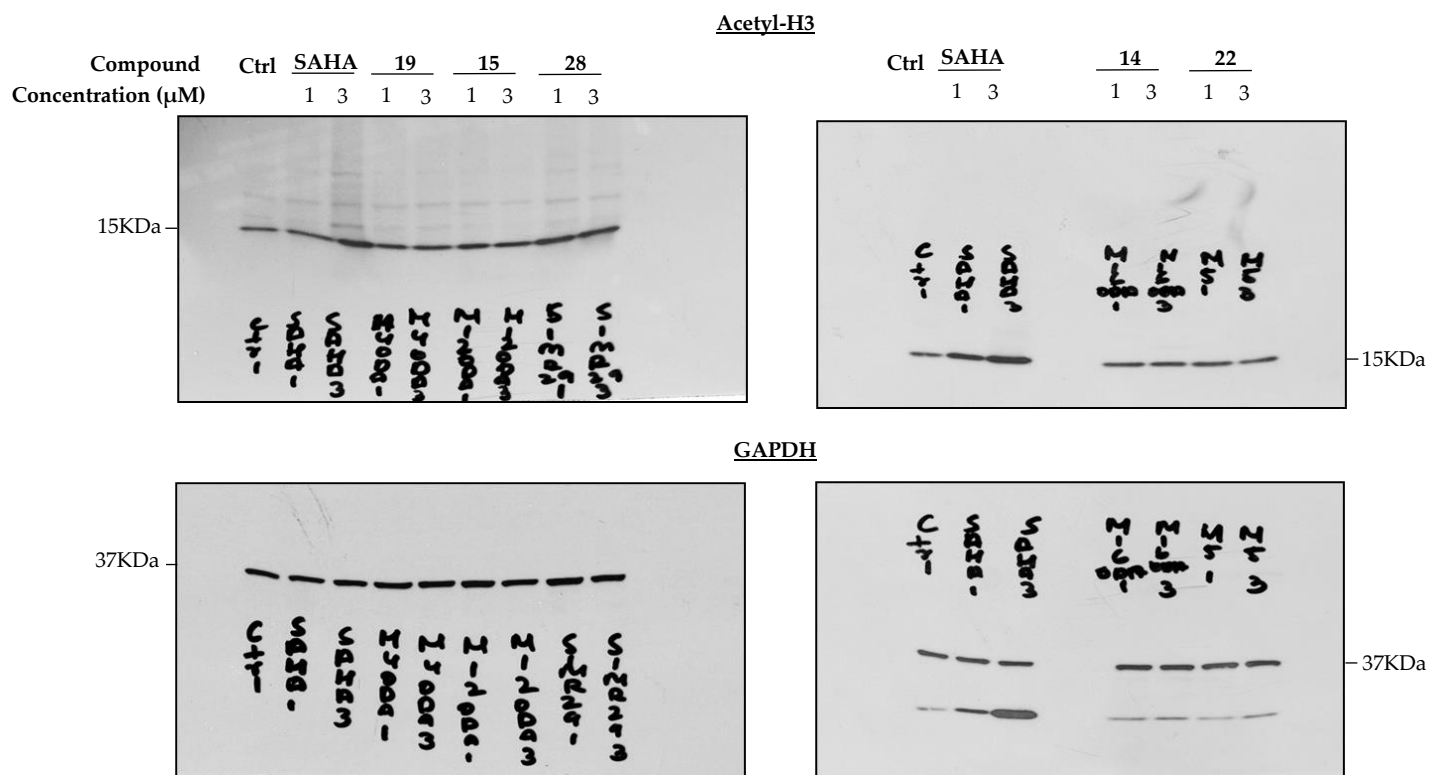
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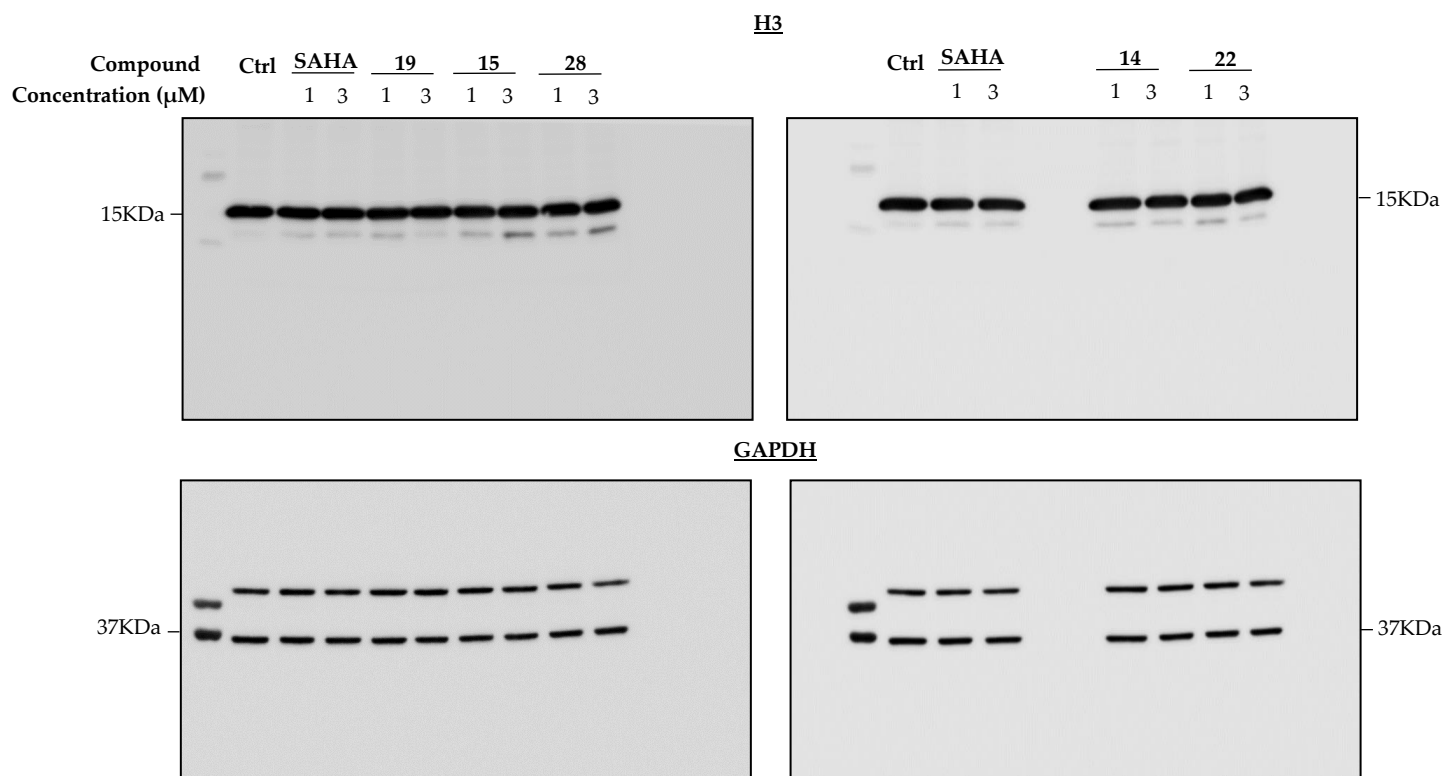
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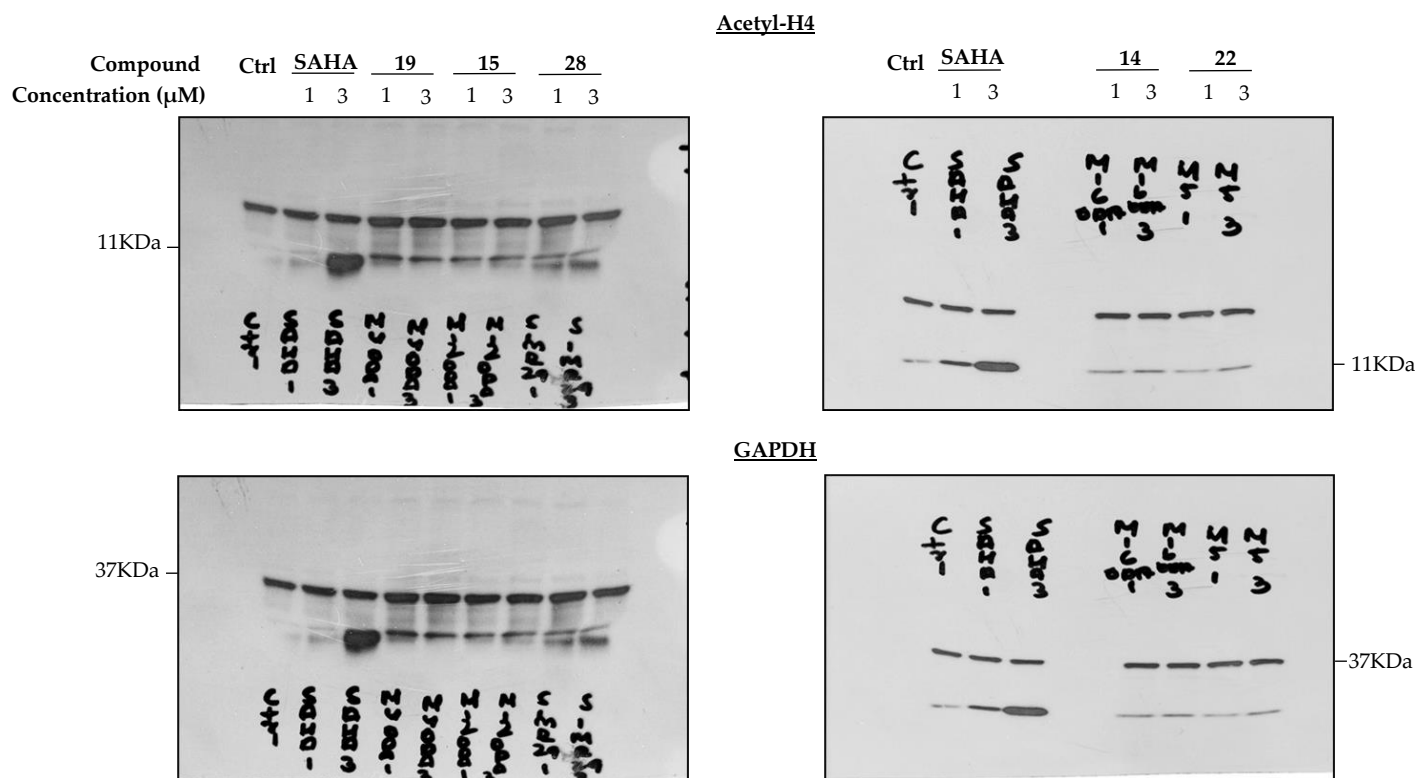
C



D



E



F

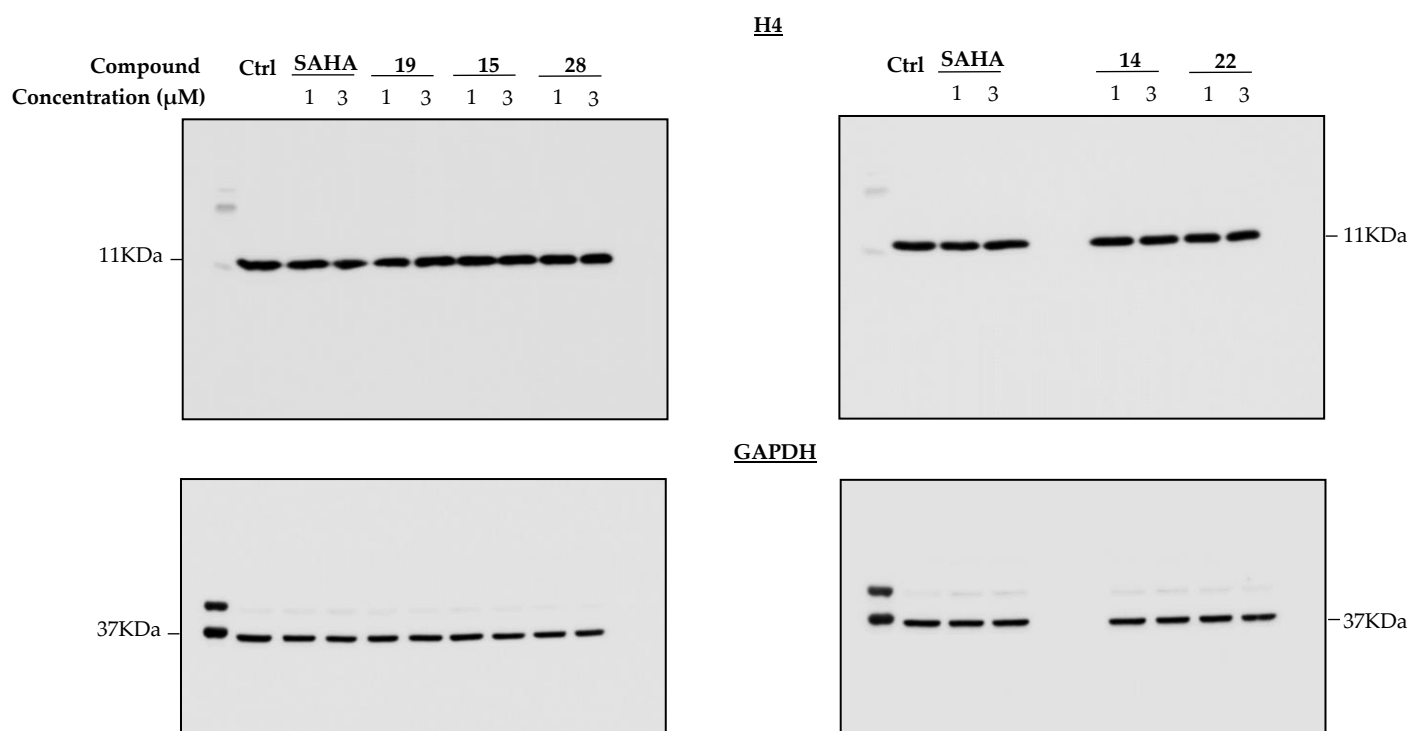


Figure S16: Full length blots of western photos of acetylated and total histones