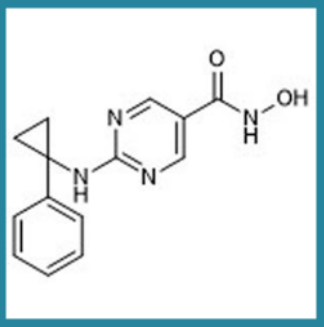
Supplementary Materials

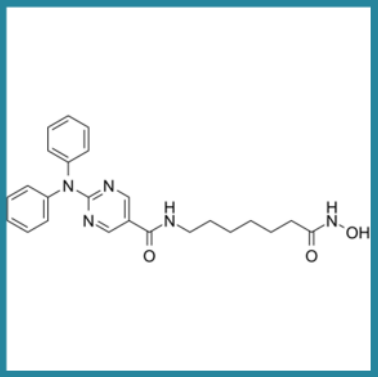
ACY-738



Acetylon Pharmaceuticals

IC_{50} (HDAC1) = 94 nM *(HDAC1/6) 55-fold*
IC_{50} (HDAC2) = 128 nM *(HDAC2/6) 75-fold*
IC_{50} (HDAC3) = 218 nM *(HDAC3/6) 128-fold*
IC_{50} (HDAC6) = 1.7 nM

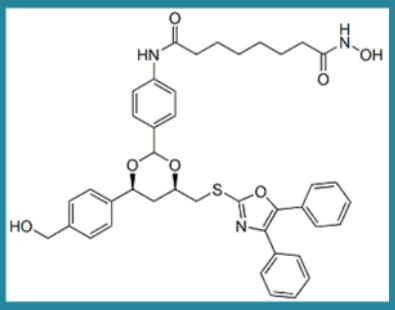
Ricolinostat (ACY-1215)



Acetylon Pharmaceuticals

IC_{50} (HDAC1) = 58 nM *(HDAC1/6) 12-fold*
IC_{50} (HDAC2) = 48 nM *(HDAC2/6) 10-fold*
IC_{50} (HDAC3) = 51 nM *(HDAC3/6) 11-fold*
IC_{50} (HDAC6) = 4.7 nM

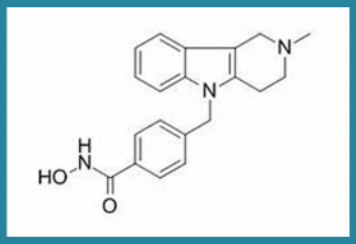
Tubacin



IC_{50} (HDAC1) = 1,400 nM *(HDAC1/6) 350-fold*
IC_{50} (HDAC2) = 6,270 nM *(HDAC2/6) >1000-fold*
IC_{50} (HDAC3) = 1,270 nM *(HDAC3/6) 318-fold*
IC_{50} (HDAC6) = 4 nM

Dr. Stuart L. Schreiber

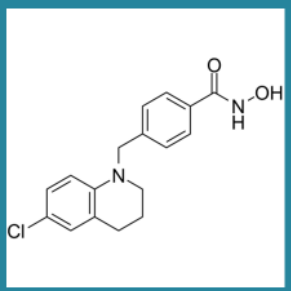
Tubastatin A



IC_{50} (HDAC1) = 8,100 nM *(HDAC1/6) > 1000-fold*
IC_{50} (HDAC2) = 18,600 nM *(HDAC2/6) > 1000-fold*
IC_{50} (HDAC3) = 7,6000 nM *(HDAC3/6) > 1000fold*
IC_{50} (HDAC6) = 4.4 nM

Dr. Alan P. Kozikowski group

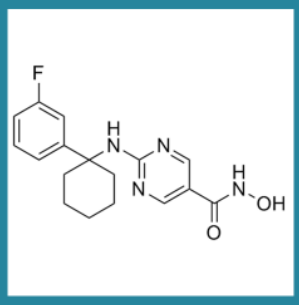
SW-100



IC_{50} (HDAC1) = 5,230 nM *(HDAC1/6) >1000-fold*
IC_{50} (HDAC2) = 32,800 nM *(HDAC2/6) >1000-fold*
IC_{50} (HDAC3) = 29,500 nM *(HDAC3/6) >1000fold*
IC_{50} (HDAC6) = 2.3 nM

Dr. Alan P. Kozikowski group

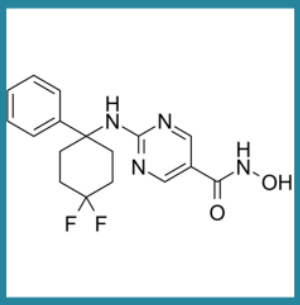
ACY-775



Acetylon Pharmaceuticals

IC_{50} (HDAC1) = 2,123 nM *(HDAC1/6) 283-fold*
IC_{50} (HDAC2) = 2,570 nM *(HDAC2/6) 343-fold*
IC_{50} (HDAC3) = 11,223 nM *(HDAC3/6) >1000-fold*
IC_{50} (HDAC6) = 7.5 nM.

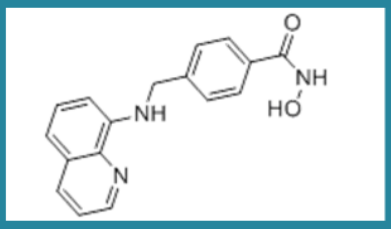
ACY-1083



Acetylon Pharmaceuticals

HDAC1/6 > 260-fold
HDAC2/6 >260-fold
HDAC3/6 > 260-fold
IC_{50} (HDAC6) = 3 nM

MPTOG211



Dr. Jing-Ping Liou group

IC_{50} (HDAC1) = 9,550 nM*(HDAC1/6) >1,000-fold*
IC_{50} (HDAC2) = 12,500 nM *(HDAC2/6) >1,000-fold*
IC_{50} (HDAC3) = 7,750 nM *(HDAC3/6) >1,000-fold*
IC_{50} (HDAC6) = 0.29 nM

Legend. HDAC6 inhibitors and selectivity over HDAC 1, 2, and 3. The half maximal inhibitory concentration (IC50) is indicated for each HDAC6 inhibitor. The selectivity over HDAC 1, 2, and 3 is indicated for each drug.

Additional HDAC6 inhibitors

HDAC6 inhibitor W-2 from Dr. Alan P. Kozikowski group, IC50 21 nM.

HDAC1/6 153 fold, HDAC2/6 59.5 fold, HDAC3/6 62.9 fold.

HDAC6 inhibitor 5-Aroylindole 6 from Dr. Jing-Ping Liou group, IC50 3.92 nM.

HDAC1/6 558.7 fold, HDAC2/6 144.9 fold, HDAC3/6 > 1000 fold.

References

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3. Pulya, S.; Amin, S.A.; Adhikari, N.; Biswas, S.; Jha, T.; Ghosh, B. HDAC6 as privileged target in drug discovery: A perspective. *Pharmacol. Res.* **2020**, *105274*, 105274, doi:10.1016/j.phrs.2020.105274.
4. Shen, S.; Kozikowski, A.P. A patent review of histone deacetylase 6 inhibitors in neurodegenerative diseases (2014-2019). *Expert Opin. Ther. Patents* **2019**, *30*, 121–136, doi:10.1080/13543776.2019.1708901.
5. Nikolian, V.C.; Dennahy, I.S.; Weykamp, M.; Williams, A.M.; Bhatti, U.F.; Eidy, H.; Ghandour, M.H.; Chtraklin, K.; Li, Y.; Alam, H.B. Isoform 6–selective histone deacetylase inhibition reduces lesion size and brain swelling following traumatic brain injury and hemorrhagic shock. *J. Trauma Acute Care Surg.* **2019**, *86*, 232–239, doi:10.1097/ta.0000000000002119.