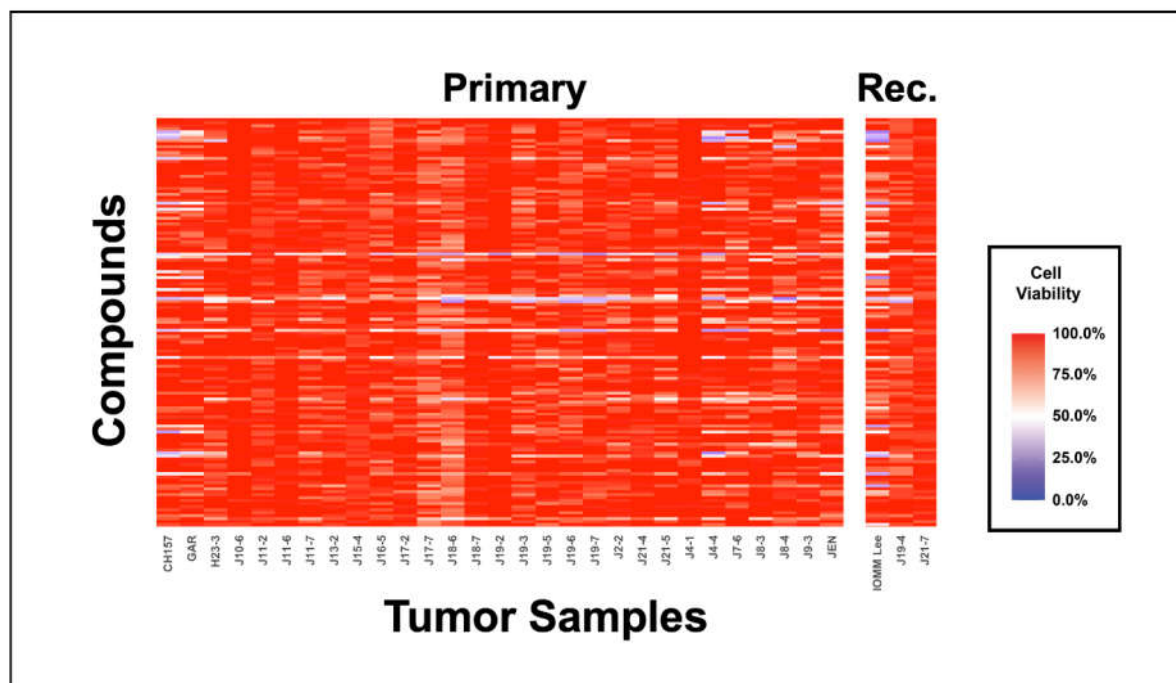
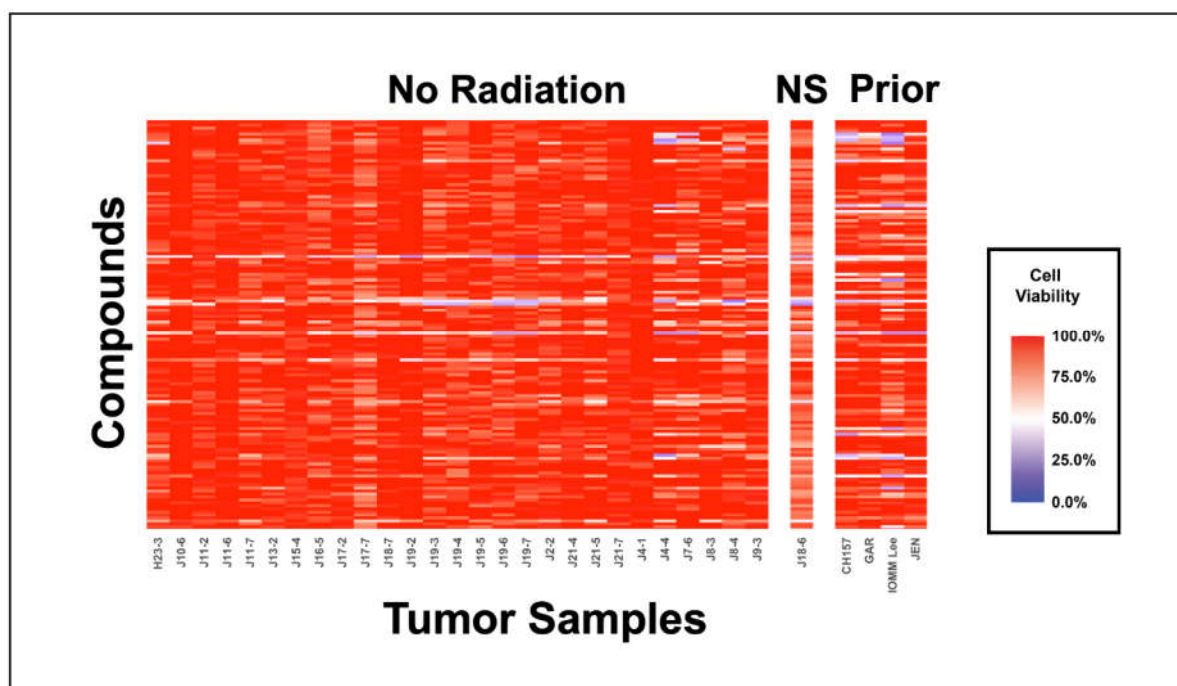


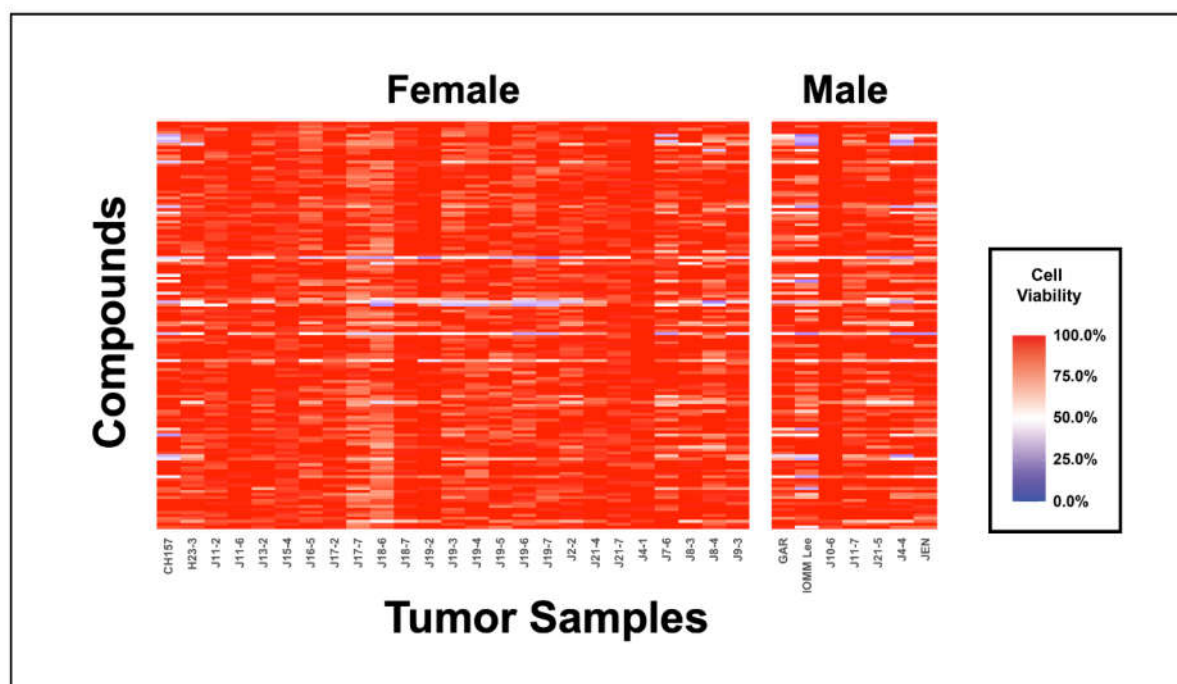
Supplementary Figure S1. Meningioma cohort sensitivity to epigenetic compounds separated by tumor grade. Heat map of meningiomas screened against the epigenetic compound panel, separated by grade 1, grade 2, and grade 3 (denoted as “G3”) tumors.



Supplementary Figure S2. Meningioma cohort sensitivity to epigenetic compounds separated by primary and recurrent tumors. Heat map of meningiomas screened against the epigenetic compound panel, separated by primary and recurrent (denoted as “Rec.”) tumors.



Supplementary Figure S3. Meningioma cohort sensitivity to epigenetic compounds separated by history of radiation. Heat map of meningiomas screened against the epigenetic compound panel, separated by tumors with no radiation, non-specified radiation (denoted as “NS”), and tumor with a prior history of radiation (denoted as “Prior”).



Supplementary Figure S4. Meningioma cohort sensitivity to epigenetic compounds separated by patient gender. Heat map of meningiomas screened against the epigenetic compound panel, separated by tumors with derived from female and male patients.

Supplementary Table S3. Average cell viability for each epigenetic compound. Table of the 139 epigenetic compounds screened, ranked by broad effectiveness. Average cell viability is reported as a percentage normalized to the untreated tumor control cohort and reported with standard deviation. p values are calculated with the Student's t test (confidence level of 0.95) between the group treated with the epigenetic compound and the untreated control group.

| Compound | Avg. Cell Viability | Std. Deviation | p Value |
|--|---------------------|----------------|----------|
| Pandobinostat | 51.9% | 23.9 | 1.08E-40 |
| LAQ824 | 56.1% | 24.0 | 2.16E-36 |
| HC Toxin | 59.4% | 24.7 | 3.16E-32 |
| Gemcitabine | 71.4% | 22.3 | 6.59E-25 |
| JIB-64 | 77.3% | 28.9 | 4.60E-13 |
| SB939 | 79.6% | 23.7 | 9.30E-15 |
| Apicidin | 80.1% | 22.9 | 4.99E-15 |
| UNC0631 | 81.0% | 27.7 | 4.51E-10 |
| Trichostatin A | 81.7% | 21.3 | 8.22E-15 |
| 6-Thioguanine | 82.8% | 21.0 | 6.78E-14 |
| CPI-203 | 83.1% | 20.6 | 7.14E-14 |
| UNC0646 | 83.4% | 26.5 | 2.03E-09 |
| CAY10398 | 83.5% | 20.3 | 1.77E-13 |
| (+)-JQ1 | 84.3% | 19.5 | 2.13E-13 |
| Lestauritinib | 84.6% | 18.3 | 5.49E-14 |
| Mi-nc (hydrochloride) | 85.8% | 21.2 | 2.53E-10 |
| UNC0638 | 86.4% | 26.9 | 7.58E-07 |
| CAY10603 | 86.6% | 19.7 | 2.49E-10 |
| BIX01294 (hydrochloride hydrate) | 86.7% | 26.2 | 9.70E-07 |
| I-BET762 | 87.3% | 16.9 | 1.05E-15 |
| M 344 | 88.1% | 18.1 | 6.11E-10 |
| 4-Iodo-SAHA | 88.1% | 18.9 | 2.75E-09 |
| OTX015 | 88.8% | 18.7 | 1.21E-08 |
| SAHA | 89.1% | 19.6 | 6.53E-10 |
| Oxamflatin | 89.6% | 16.0 | 1.23E-09 |
| I-BET151 | 90.4% | 15.8 | 6.46E-09 |
| coumarin-SAHA | 90.6% | 15.8 | 1.74E-08 |
| ITF 2357 | 91.5% | 18.6 | 7.91E-06 |
| CUDC-101 | 92.1% | 17.4 | 1.41E-05 |
| UNC0642 | 92.4% | 22.1 | 6.10E-04 |
| MS-275 | 92.5% | 17.3 | 2.19E-05 |
| CPH2 (hydrochloride) | 92.6% | 12.8 | 4.86E-08 |
| 3-Deazaneplanocin A | 92.8% | 14.7 | 2.57E-06 |
| CI-894 | 93.1% | 12.7 | 2.34E-07 |
| Bromosporine | 93.3% | 17.8 | 2.30E-04 |
| Scriptaid | 93.5% | 14.2 | 7.54E-06 |
| UNC0224 | 93.8% | 18.7 | 1.10E-03 |
| PF-1 | 94.0% | 15.0 | 7.67E-05 |
| 3-Deazaneplanocin A (hydrochloride) | 94.4% | 15.2 | 2.25E-04 |
| Pyroxamide | 94.6% | 13.8 | 1.60E-04 |
| Sodium Butyrate | 95.2% | 15.7 | 2.07E-03 |
| CBHA | 95.2% | 11.4 | 4.88E-05 |
| Rucaparib (phosphate) | 95.4% | 13.8 | 8.70E-04 |
| Pimelic Diphenylamide 106 | 95.6% | 15.5 | 4.97E-03 |
| Phthalazinone pyrazole | 95.6% | 17.7 | 1.32E-02 |
| (-)-Neplanocin A | 95.8% | 14.6 | 4.35E-03 |
| Tenovin-6 | 96.1% | 14.7 | 7.80E-03 |
| S-Adenosylhomocysteine | 96.1% | 14.7 | 6.55E-03 |
| Spilomicin | 96.1% | 12.2 | 1.70E-03 |
| GSK-J2 (sodium salt) | 96.5% | 10.9 | 1.71E-03 |
| RVK-208 | 96.5% | 11.2 | 2.51E-03 |
| Methylstat (hydrate) | 96.9% | 13.3 | 1.96E-02 |
| Decitabine | 96.9% | 12.1 | 3.28E-03 |
| GSK126 | 96.9% | 13.3 | 2.11E-02 |
| Lomeguatrib | 97.0% | 11.5 | 9.64E-03 |
| Ellagic Acid | 97.0% | 11.4 | 9.29E-03 |
| IOX1 | 97.0% | 10.7 | 6.67E-03 |
| Etoposide | 97.1% | 13.3 | 2.89E-02 |
| Tenovin-1 | 97.1% | 10.3 | 6.56E-03 |
| (R)-PF1-2 (hydrochloride) | 97.3% | 16.7 | 1.05E-01 |
| Garcinol | 97.4% | 10.5 | 1.42E-02 |
| UNC1999 | 97.4% | 10.8 | 2.03E-02 |
| DMOG | 97.6% | 12.8 | 6.15E-02 |
| C646 | 97.6% | 10.4 | 9.77E-03 |
| Salsarimide | 97.6% | 10.5 | 2.86E-02 |
| SGI-1027 | 97.7% | 14.0 | 9.87E-02 |
| Valproic Acid (sodium salt) | 97.7% | 9.9 | 2.46E-02 |
| SGC0946 | 97.7% | 12.2 | 6.90E-02 |
| Chidamide | 97.8% | 11.6 | 6.86E-02 |
| Tubacin | 97.8% | 11.9 | 7.07E-02 |
| Mirin | 97.9% | 11.7 | 7.52E-02 |
| EX-527 | 98.0% | 10.7 | 6.81E-02 |
| BRD73954 | 98.0% | 9.1 | 3.51E-02 |
| GSK4112 | 98.1% | 10.4 | 7.37E-02 |
| 3,3'-Dioxodimethane | 98.1% | 11.0 | 6.53E-02 |
| Butyrolactone 3 | 98.1% | 9.7 | 6.72E-02 |
| Sinefungin | 98.2% | 13.8 | 1.79E-01 |
| 5-Azacytidine | 98.3% | 9.3 | 7.55E-02 |
| 2',3',5'-triacetyl-5-Azacytidine | 98.3% | 8.8 | 6.60E-02 |
| Tubastatin A (trifluoroacetate salt) | 98.4% | 8.7 | 7.07E-02 |
| Mi-2 (hydrochloride) | 98.4% | 10.4 | 1.27E-01 |
| Zabularine | 98.4% | 11.8 | 1.92E-01 |
| Sirtinol | 98.4% | 10.6 | 1.45E-01 |
| (+)-Abiscisic Acid | 98.5% | 11.1 | 1.85E-01 |
| RSC-133 | 98.6% | 9.4 | 1.65E-01 |
| AK-7 | 98.7% | 12.2 | 2.77E-01 |
| Sodium 4-Phenylbutyrate | 98.7% | 11.7 | 2.66E-01 |
| 3-amino Benzamide | 98.7% | 10.6 | 2.21E-01 |
| Anacardic Acid | 98.7% | 9.0 | 1.57E-01 |
| HNHA | 98.7% | 9.3 | 1.77E-01 |
| PCI34051 | 98.8% | 9.9 | 2.18E-01 |
| S-(5'-Adenosyl)-L-methionine (tosylate) | 98.8% | 15.6 | 4.25E-01 |
| trans-Resveratrol | 98.9% | 9.6 | 2.76E-01 |
| I-CBP112 (hydrochloride) | 99.0% | 10.9 | 3.74E-01 |
| Tubastatin A | 99.0% | 10.8 | 3.69E-01 |
| Delphinidin (chloride) | 99.1% | 9.5 | 3.59E-01 |
| RG-108 | 99.2% | 8.0 | 3.52E-01 |
| Octyl- α -ketoglutarate | 99.3% | 11.8 | 5.67E-01 |
| BSh-201 | 99.4% | 11.4 | 5.87E-01 |
| GSK343 | 99.4% | 10.8 | 5.73E-01 |
| GSK-J1 (sodium salt) | 99.4% | 11.4 | 6.22E-01 |
| SGC-CBP30 | 99.5% | 10.0 | 5.77E-01 |
| AGK2 | 99.5% | 11.0 | 6.77E-01 |
| CAY10591 | 99.6% | 14.1 | 7.62E-01 |
| 2,4-Pyridinedicarboxylic Acid | 99.6% | 11.9 | 7.94E-01 |
| CCG-100602 | 99.6% | 11.1 | 7.35E-01 |
| Picestanol | 99.6% | 10.3 | 7.17E-01 |
| α -Hydroxyglutaric Acid (sodium salt) | 99.6% | 10.2 | 7.23E-01 |
| UNC0321 (trifluoroacetate salt) | 99.7% | 10.7 | 7.72E-01 |
| Cl-Amidine (hydrochloride) | 99.7% | 8.4 | 7.47E-01 |
| BML-216 | 99.8% | 10.7 | 8.76E-01 |
| N-Oxalylglycine | 99.8% | 10.2 | 8.81E-01 |
| UNC1215 | 99.9% | 12.5 | 9.19E-01 |
| GSK-J4 (hydrochloride) | 99.9% | 9.6 | 9.00E-01 |
| CAY10669 | 99.9% | 11.7 | 9.25E-01 |
| (-)-JQ1 | 99.9% | 11.9 | 9.37E-01 |
| MC 1568 | 99.9% | 8.0 | 9.27E-01 |
| GSK2401 | 100.0% | 9.7 | 9.65E-01 |
| JGB1741 | 100.1% | 9.0 | 9.13E-01 |
| 1-Naphthoic Acid | 100.3% | 11.9 | 7.97E-01 |
| CAY10683 | 100.3% | 9.2 | 7.19E-01 |
| Isoliquiritigenin | 100.4% | 10.8 | 7.06E-01 |
| EPZ005687 | 100.4% | 7.8 | 5.92E-01 |
| 5-Methyl-2'-deoxycytidine | 100.5% | 10.1 | 6.25E-01 |
| WDK5-0183 | 100.5% | 7.5 | 5.07E-01 |
| Nicotinamide | 100.5% | 12.3 | 6.58E-01 |
| RGFP966 | 100.5% | 10.9 | 6.18E-01 |
| F-Amidine (trifluoroacetate salt) | 100.7% | 9.1 | 4.81E-01 |
| HPOB | 100.7% | 10.5 | 4.84E-01 |
| Daminozide | 100.8% | 11.5 | 4.93E-01 |
| 2-PCPA (hydrochloride) | 100.8% | 9.1 | 3.14E-01 |
| EPZ04761 | 101.0% | 9.4 | 2.87E-01 |
| PF1-3 | 101.2% | 11.7 | 3.05E-01 |
| Suramin (sodium salt) | 101.3% | 11.5 | 2.81E-01 |
| 2-hexyl-4-Pentynoic Acid | 101.4% | 10.9 | 1.98E-01 |
| SIRT12 Inhibitor IV | 101.6% | 9.8 | 1.02E-01 |
| GSK-LSD1 (hydrochloride) | 102.1% | 10.5 | 4.70E-02 |
| AGK7 | 102.3% | 10.8 | 3.96E-02 |
| 5-Methylcytidine | 103.5% | 11.3 | 2.48E-03 |

Supplementary Table S4. The most effective compound for each tumor sample. Table of the most effective compound for each of the 32 tumors screened. The most effective compound is determined as the compound that reduces the cell viability the most and has a p value less than 0.05. For the single sample (GAR) that did not have any compound which significantly reduced cell viability, the compound that reduced cell viability to the greatest extent is reported. Cell viability is reported as a percentage normalized to the untreated tumor control cohort and p values are calculated using the Mann-Whitney-U test (confidence level of 0.95).

| Sample | Cell Viability | p Value | Compound |
|------------------|-----------------------|----------------|----------------------------------|
| CH157* | 28.6% | 3.81E-03 | CAY10398 |
| GAR* | 38.7% | 1.17E-01 | LAQ824 |
| H23-3 | 40.4% | 2.96E-03 | UNC0631 |
| IOMM Lee* | 22.1% | 8.15E-04 | UNC0631 |
| J10-6 | 46.6% | 3.81E-03 | Panobinostat |
| J11-2 | 53.0% | 3.81E-03 | JIB-04 |
| J11-6 | 48.1% | 3.81E-03 | Panobinostat |
| J11-7 | 53.9% | 3.81E-03 | Panobinostat |
| J13-2 | 46.0% | 3.72E-05 | LAQ824 |
| J15-4 | 82.2% | 4.94E-05 | JIB-04 |
| J16-5 | 40.0% | 3.81E-03 | Panobinostat |
| J17-2 | 59.1% | 3.81E-03 | Panobinostat |
| J17-7 | 32.9% | 3.81E-03 | Panobinostat |
| J18-6 | 25.7% | 3.70E-03 | JIB-04 |
| J18-7 | 47.8% | 3.70E-03 | Panobinostat |
| J19-2 | 28.5% | 3.70E-03 | Panobinostat |
| J19-3 | 35.7% | 3.70E-03 | JIB-04 |
| J19-4 | 32.8% | 3.70E-03 | JIB-04 |
| J19-5 | 37.4% | 3.70E-03 | Panobinostat |
| J19-6 | 30.5% | 3.70E-03 | JIB-04 |
| J19-7 | 25.5% | 3.70E-03 | Panobinostat |
| J2-2 | 38.5% | 3.53E-03 | LAQ824 |
| J21-4 | 50.0% | 5.04E-05 | Panobinostat |
| J21-5 | 36.0% | 3.70E-03 | Panobinostat |
| J21-7 | 52.7% | 3.70E-03 | Panobinostat |
| J4-1 | 88.8% | 2.10E-02 | OTX015 |
| J4-4 | 24.0% | 7.93E-04 | BIX01294 (hydrochloride hydrate) |
| J7-6 | 28.7% | 3.81E-03 | HC Toxin |
| J8-3 | 51.1% | 3.81E-03 | OTX015 |
| J8-4 | 21.4% | 3.81E-03 | LAQ824 |
| J9-3 | 42.2% | 3.68E-03 | Panobinostat |
| JEN* | 27.7% | 1.81E-02 | HC Toxin |

Supplementary Table S5. Broadly effective epigenetic compounds separated by tumor grade. Epigenetic compounds that were broadly effective in (a) grade 1, (b) grade 2, and (c) grade 3 meningiomas. Broadly effective compounds for each grade are identified as compounds that reduce the average cell viability of the group by 80% or less and have a p value less than 0.05.

a) Grade 1 Broadly Effective Compounds

| Compound | Avg. Cell Viability | Std. Deviation | p Value | Category |
|--------------|---------------------|----------------|----------|----------|
| Panobinostat | 51.9% | 24.8 | 1.05E-30 | Grade1 |
| HC Toxin | 59.3% | 24.5 | 1.16E-25 | Grade1 |
| LAQ824 | 60.0% | 24.0 | 1.89E-25 | Grade1 |
| Gemcitabine | 73.9% | 21.4 | 2.04E-18 | Grade1 |
| JIB-04 | 79.0% | 27.8 | 1.10E-09 | Grade1 |
| CPI-203 | 79.6% | 20.9 | 7.61E-14 | Grade1 |

b) Grade 2 Broadly Effective Compounds

| Compound | Avg. Cell Viability | Std. Deviation | p Value | Category |
|----------------|---------------------|----------------|----------|----------|
| LAQ824 | 44.8% | 16.8 | 1.67E-12 | Grade2 |
| Panobinostat | 52.7% | 19.1 | 3.04E-10 | Grade2 |
| HC Toxin | 64.3% | 24.5 | 1.69E-06 | Grade2 |
| Gemcitabine | 65.6% | 16.9 | 8.39E-09 | Grade2 |
| JIB-04 | 71.2% | 31.4 | 4.50E-04 | Grade2 |
| SB939 | 77.0% | 19.0 | 1.98E-05 | Grade2 |
| Apicidin | 77.6% | 22.4 | 1.81E-04 | Grade2 |
| Trichostatin A | 78.6% | 27.0 | 1.65E-03 | Grade2 |
| CAY10398 | 79.2% | 24.8 | 1.01E-03 | Grade2 |

c) Grade 3 Broadly Effective Compounds

| Compound | Avg. Cell Viability | Std. Deviation | p Value | Category |
|-------------------------------------|---------------------|----------------|----------|----------|
| UNC0631 | 22.1% | 1.2 | 1.82E-35 | Grade3 |
| UNC0646 | 22.4% | 2.9 | 1.39E-08 | Grade3 |
| MI-nc (hydrochloride) | 24.2% | 7.4 | 1.33E-04 | Grade3 |
| HC Toxin | 27.6% | 1.0 | 1.09E-27 | Grade3 |
| SB939 | 28.9% | 4.2 | 3.50E-06 | Grade3 |
| CAY10603 | 30.2% | 10.4 | 6.85E-04 | Grade3 |
| 4-iodo-SAHA | 31.5% | 4.1 | 4.02E-06 | Grade3 |
| 6-Thioguanine | 31.7% | 6.3 | 8.24E-05 | Grade3 |
| UNC0638 | 31.9% | 19.6 | 5.86E-03 | Grade3 |
| Apicidin | 32.1% | 4.6 | 1.12E-05 | Grade3 |
| UNC0642 | 34.6% | 25.4 | 1.40E-02 | Grade3 |
| LAQ824 | 39.1% | 31.7 | 1.25E-02 | Grade3 |
| Panobinostat | 46.6% | 33.5 | 4.96E-02 | Grade3 |
| (-)-Neplanocin A | 47.7% | 11.4 | 2.35E-03 | Grade3 |
| CAY10398 | 50.1% | 18.1 | 1.13E-02 | Grade3 |
| MS-275 | 50.3% | 15.7 | 7.55E-03 | Grade3 |
| SAHA | 53.3% | 27.9 | 1.99E-02 | Grade3 |
| UNC0224 | 55.9% | 24.1 | 1.47E-02 | Grade3 |
| CI-994 | 59.3% | 22.8 | 3.72E-02 | Grade3 |
| 3-Deazaneplanocin A (hydrochloride) | 63.8% | 12.4 | 9.14E-03 | Grade3 |
| 3-Deazaneplanocin A | 70.8% | 15.9 | 1.43E-02 | Grade3 |

Supplementary Table S6. Comparison of compound effectiveness across tumor grade. p values for the comparison of cell viabilities for broadly effective compounds across grade 1, 2, and 3 meningiomas. Comparisons were conducted with an ANOVA followed by a Tukey HSD post-hoc test (confidence level of 0.95) by comparing compound sensitivity across tumor grade.

| Compound | p Value | | |
|-----------------------|----------------------|----------------------|----------------------|
| | Grade2-Grade1 | Grade3-Grade1 | Grade3-Grade2 |
| (-)-Neplanocin A | 3.10E-01 | 1.11E-13 | 3.54E-11 |
| 4-iodo-SAHA | 3.09E-02 | 7.67E-12 | 2.29E-08 |
| 6-Thioguanine | 9.81E-01 | 5.21E-07 | 3.40E-06 |
| Apicidin | 5.46E-01 | 1.89E-05 | 3.61E-04 |
| CAY10398 | 3.02E-01 | 1.15E-03 | 1.82E-02 |
| CAY10603 | 5.11E-02 | 1.24E-10 | 1.67E-07 |
| CPI-203 | 1.86E-03 | 7.56E-01 | 6.42E-01 |
| Gemcitabine | 2.67E-01 | 8.76E-02 | 3.96E-01 |
| HC Toxin | 6.74E-01 | 7.15E-02 | 4.13E-02 |
| JIB-04 | 5.15E-01 | 8.84E-01 | 9.94E-01 |
| LAQ824 | 2.28E-02 | 1.28E-01 | 8.75E-01 |
| MI-nc (hydrochloride) | 4.12E-01 | 1.75E-10 | 2.44E-08 |
| Panobinostat | 9.90E-01 | 9.05E-01 | 8.89E-01 |
| SB939 | 5.25E-01 | 1.18E-05 | 2.57E-04 |
| Trichostatin A | 5.43E-01 | 6.47E-03 | 4.11E-02 |
| UNC0631 | 6.29E-01 | 2.43E-05 | 1.47E-05 |
| UNC0638 | 6.52E-01 | 4.58E-05 | 5.78E-04 |
| UNC0642 | 3.74E-01 | 2.04E-08 | 1.80E-06 |
| UNC0646 | 4.99E-01 | 1.70E-06 | 5.38E-05 |

Supplementary Table S7. Broadly effective epigenetic compounds separated by primary and recurrent tumors. Epigenetic compounds that were broadly effective in (a) primary and (b) recurrent meningiomas. Broadly effective compounds for each grade are identified as compounds that reduce the average cell viability of the group to 80% or less and have a p value less than 0.05.

| a) Primary Tumor Broadly Effective Compounds | | | | |
|---|----------------------------|-----------------------|----------------|-----------------|
| Compound | Avg. Cell Viability | Std. Deviation | p Value | Category |
| Panobinostat | 52.1% | 24.321 | 2.34E-36 | Primary |
| LAQ824 | 56.2% | 23.206 | 6.62E-34 | Primary |
| HC Toxin | 59.2% | 24.333 | 2.88E-30 | Primary |
| Gemcitabine | 71.5% | 20.976 | 2.11E-24 | Primary |
| JIB-04 | 78.2% | 28.116 | 1.09E-11 | Primary |

| b) Recurrent Tumor Broadly Effective Compounds | | | | |
|---|----------------------------|-----------------------|----------------|-----------------|
| Compound | Avg. Cell Viability | Std. Deviation | p Value | Category |
| Panobinostat | 49.0% | 20.404 | 2.28E-05 | Recurrent |
| LAQ824 | 55.0% | 31.534 | 7.91E-04 | Recurrent |
| HC Toxin | 60.9% | 30.229 | 4.64E-03 | Recurrent |
| Apicidin | 61.9% | 28.895 | 2.41E-03 | Recurrent |
| SB939 | 62.7% | 29.897 | 3.37E-03 | Recurrent |
| UNC0631 | 63.9% | 36.444 | 1.21E-02 | Recurrent |
| MI-nc (hydrochloride) | 65.8% | 36.403 | 1.57E-02 | Recurrent |
| CAY10603 | 66.3% | 33.007 | 1.04E-02 | Recurrent |
| UNC0646 | 67.0% | 39.477 | 2.68E-02 | Recurrent |
| 6-Thioguanine | 67.1% | 32.388 | 1.06E-02 | Recurrent |
| 4-iodo-SAHA | 67.2% | 31.897 | 1.00E-02 | Recurrent |
| JIB-04 | 69.2% | 35.850 | 1.74E-02 | Recurrent |
| UNC0638 | 69.5% | 34.401 | 2.06E-02 | Recurrent |
| Gemcitabine | 70.2% | 34.427 | 2.31E-02 | Recurrent |
| Trichostatin A | 70.5% | 29.663 | 1.18E-02 | Recurrent |
| BIX01294 (hydrochloride hydrate) | 74.3% | 35.547 | 4.83E-02 | Recurrent |
| CAY10398 | 76.6% | 25.232 | 1.67E-02 | Recurrent |
| UNC0224 | 77.3% | 27.308 | 2.02E-02 | Recurrent |
| (-)-Neplanocin A | 77.4% | 27.013 | 2.65E-02 | Recurrent |
| M 344 | 78.9% | 29.500 | 4.98E-02 | Recurrent |
| CI-994 | 80.0% | 22.717 | 2.12E-02 | Recurrent |

Supplementary Table S8. Comparison of compound effectiveness across primary and recurrent tumors. p values for the comparison of cell viabilities for broadly effective compounds across primary and recurrent meningiomas. Comparisons were conducted with the Student's t test (confidence level of 0.95) by comparing compound sensitivity between primary and recurrent tumors.

| Compound | p Value |
|-----------------------|--------------------------|
| | Primary-Recurrent |
| 4-iodo-SAHA | 4.93E-02 |
| 6-Thioguanine | 1.29E-01 |
| Apicidin | 5.91E-02 |
| CAY10603 | 6.22E-02 |
| Gemcitabine | 9.08E-01 |
| HC Toxin | 8.79E-01 |
| JIB-04 | 4.40E-01 |
| LAQ824 | 9.02E-01 |
| MI-nc (hydrochloride) | 8.98E-02 |
| Panobinostat | 6.56E-01 |
| SB939 | 8.42E-02 |
| Trichostatin A | 2.29E-01 |
| UNC0631 | 1.31E-01 |
| UNC0638 | 1.27E-01 |
| UNC0646 | 1.88E-01 |

Supplementary Table S9. Broadly effective epigenetic compounds separated by tumor radiation history. Epigenetic compounds that were broadly effective in (a) tumors with no prior history of radiation, (b) tumors with a prior history of radiation and (c) tumors with a non-specified history of radiation. Broadly effective compounds for each grade are identified as compounds that reduce the average cell viability of the group to 80% or less and have a p value less than 0.05.

a) Tumors with No History of Radiation Broadly Effective Compounds

| Compound | Avg. Cell Viability | Std. Deviation | p Value | Category |
|--------------|---------------------|----------------|----------|--------------|
| Panobinostat | 52.5% | 23.1 | 7.82E-35 | No Radiation |
| LAQ824 | 59.0% | 23.0 | 6.51E-30 | No Radiation |
| HC Toxin | 62.7% | 24.6 | 9.51E-26 | No Radiation |
| Gemcitabine | 73.8% | 18.7 | 1.38E-23 | No Radiation |
| JIB-04 | 77.7% | 28.6 | 4.57E-11 | No Radiation |

b) Tumors with a Prior History of Radiation Broadly Effective Compounds

| Compound | Avg. Cell Viability | Std. Deviation | p Value | Category |
|-------------------------------------|---------------------|----------------|----------|-----------------|
| JIB-04 | 25.7% | 9.6 | 4.29E-03 | Prior Radiation |
| Panobinostat | 31.8% | 1.4 | 2.81E-16 | Prior Radiation |
| LAQ824 | 35.8% | 8.5 | 4.18E-03 | Prior Radiation |
| HC Toxin | 42.2% | 8.4 | 5.22E-03 | Prior Radiation |
| CPI-203 | 43.5% | 1.3 | 7.50E-18 | Prior Radiation |
| (+)-JQ1 | 48.3% | 17.3 | 3.43E-02 | Prior Radiation |
| Gemcitabine | 53.2% | 2.5 | 3.08E-06 | Prior Radiation |
| Lestaurtinib | 55.0% | 4.5 | 8.91E-04 | Prior Radiation |
| Apicidin | 60.2% | 10.9 | 2.17E-02 | Prior Radiation |
| I-BET762 | 64.0% | 18.3 | 4.46E-03 | Prior Radiation |
| Bromosporine | 68.6% | 11.8 | 4.15E-02 | Prior Radiation |
| 6-Thioguanine | 71.1% | 4.6 | 3.23E-03 | Prior Radiation |
| BSI-201 | 73.0% | 7.2 | 1.77E-02 | Prior Radiation |
| Phthalazinone pyrazole | 73.0% | 5.8 | 9.51E-03 | Prior Radiation |
| 3-Deazaneplanocin A (hydrochloride) | 75.4% | 6.9 | 1.92E-02 | Prior Radiation |
| 2,4-Pyridinedicarboxylic Acid | 76.7% | 8.4 | 3.53E-02 | Prior Radiation |
| UNC0631 | 77.6% | 4.5 | 5.89E-03 | Prior Radiation |
| (-)-JQ1 | 78.9% | 8.7 | 4.62E-02 | Prior Radiation |
| Trichostatin A | 79.4% | 4.8 | 8.99E-03 | Prior Radiation |

c) Tumors with a Non-Specified History of Radiation Broadly Effective Compounds

| Compound | Avg. Cell Viability | Std. Deviation | p Value | Category |
|----------------------------------|---------------------|----------------|----------|---------------|
| HC Toxin | 35.7% | 9.2 | 3.07E-13 | Not Specified |
| SB939 | 39.0% | 11.3 | 6.21E-14 | Not Specified |
| UNC0646 | 40.5% | 27.1 | 1.22E-06 | Not Specified |
| LAQ824 | 41.5% | 26.0 | 8.74E-07 | Not Specified |
| 6-Thioguanine | 45.4% | 21.6 | 5.88E-08 | Not Specified |
| MI-nc (hydrochloride) | 50.0% | 25.7 | 2.00E-06 | Not Specified |
| CAY10398 | 50.6% | 23.6 | 1.92E-06 | Not Specified |
| Apicidin | 51.1% | 21.3 | 5.81E-07 | Not Specified |
| Panobinostat | 52.2% | 30.1 | 2.20E-05 | Not Specified |
| SAHA | 53.9% | 22.3 | 2.18E-06 | Not Specified |
| CAY10603 | 55.7% | 28.4 | 2.70E-05 | Not Specified |
| Trichostatin A | 56.9% | 24.8 | 7.82E-06 | Not Specified |
| BIX01294 (hydrochloride hydrate) | 57.4% | 33.4 | 3.58E-04 | Not Specified |
| UNC0642 | 59.3% | 30.3 | 1.29E-04 | Not Specified |
| Gemcitabine | 59.5% | 37.7 | 1.47E-03 | Not Specified |
| UNC0638 | 59.7% | 35.6 | 9.72E-04 | Not Specified |
| M 344 | 62.2% | 24.4 | 5.35E-05 | Not Specified |
| UNC0631 | 63.1% | 38.2 | 2.19E-03 | Not Specified |
| Oxamflatin | 64.1% | 21.0 | 1.86E-05 | Not Specified |
| MS-275 | 67.2% | 23.1 | 6.99E-05 | Not Specified |
| 4-iodo-SAHA | 71.8% | 29.2 | 3.18E-03 | Not Specified |
| 3-Deazaneplanocin A | 78.6% | 13.6 | 1.85E-05 | Not Specified |
| CI-994 | 78.6% | 20.1 | 2.38E-03 | Not Specified |
| UNC0224 | 78.7% | 24.0 | 4.14E-03 | Not Specified |
| ITF 2357 | 79.2% | 26.9 | 1.68E-02 | Not Specified |
| (-)-Neplanocin A | 79.3% | 23.4 | 5.92E-03 | Not Specified |

Supplementary Table S10. Broadly effective epigenetic compounds separated by patient gender. Epigenetic compounds that were broadly effective in tumors originating from (a) female and (b) male patients. Broadly effective compounds for each grade are identified as compounds that reduce the average cell viability of the group to 80% or less and have a p value less than 0.05.

| a) Female-Derived Patient Tumors Broadly Effective Compounds | | | | |
|---|----------------------------|-----------------------|----------------|-----------------|
| Compound | Avg. Cell Viability | Std. Deviation | p Value | Category |
| Panobinostat | 53.1% | 23.7 | 4.10E-31 | Female |
| LAQ824 | 58.4% | 23.9 | 3.75E-27 | Female |
| HC Toxin | 62.8% | 24.8 | 1.10E-23 | Female |
| Gemcitabine | 73.5% | 19.0 | 7.98E-22 | Female |
| JIB-04 | 74.5% | 30.2 | 1.69E-11 | Female |

| b) Male-Derived Patient Tumors Broadly Effective Compounds | | | | |
|---|----------------------------|-----------------------|----------------|-----------------|
| Compound | Avg. Cell Viability | Std. Deviation | p Value | Category |
| HC Toxin | 45.3% | 19.3 | 1.14E-11 | Male |
| Panobinostat | 47.6% | 24.8 | 9.62E-11 | Male |
| LAQ824 | 48.1% | 23.2 | 7.08E-11 | Male |
| SB939 | 55.2% | 25.1 | 6.71E-09 | Male |
| 6-Thioguanine | 61.2% | 25.0 | 4.29E-08 | Male |
| UNC0646 | 63.9% | 36.6 | 7.28E-05 | Male |
| Gemcitabine | 63.9% | 30.8 | 7.70E-06 | Male |
| Apicidin | 64.9% | 24.6 | 3.53E-07 | Male |
| BIX01294 (hydrochloride hydrate) | 66.0% | 34.1 | 6.40E-05 | Male |
| UNC0631 | 66.9% | 35.1 | 8.78E-05 | Male |
| CAY10398 | 69.8% | 25.6 | 6.61E-06 | Male |
| Trichostatin A | 70.6% | 24.4 | 3.04E-06 | Male |
| UNC0638 | 70.9% | 37.5 | 9.62E-04 | Male |
| MI-nc (hydrochloride) | 71.0% | 31.5 | 1.18E-04 | Male |
| CAY10603 | 72.5% | 28.8 | 7.67E-05 | Male |
| SAHA | 72.5% | 28.6 | 3.68E-05 | Male |
| M 344 | 74.9% | 22.2 | 1.30E-05 | Male |
| CPI-203 | 75.9% | 19.9 | 3.08E-06 | Male |
| UNC0642 | 76.2% | 33.2 | 1.95E-03 | Male |
| Oxamflatin | 78.1% | 20.4 | 2.55E-05 | Male |
| 4-iodo-SAHA | 79.7% | 24.3 | 4.75E-04 | Male |
| MS-275 | 79.9% | 18.6 | 1.69E-05 | Male |

Supplementary Table S11. Comparison of compound effectiveness between female and male-derived patient tumors. p values for the comparison of cell viabilities for broadly effective compounds between meningiomas originated from female and male patients. Comparisons were conducted with the Student's t test (confidence level of 0.95) by comparing compound sensitivity between tumors derived from female and male patients.

| Compound | p Value Male-Female |
|----------------------------------|--------------------------------|
| 6-Thioguanine | 9.56E-06 |
| Apicidin | 1.25E-03 |
| BIX01294 (hydrochloride hydrate) | 1.05E-03 |
| CAY10398 | 3.49E-03 |
| CAY10603 | 4.56E-03 |
| Gemcitabine | 1.60E-01 |
| HC Toxin | 1.19E-03 |
| JIB-04 | 2.79E-02 |
| LAQ824 | 6.40E-02 |
| MI-nc (hydrochloride) | 6.38E-03 |
| Panobinostat | 3.34E-01 |
| SB939 | 3.20E-06 |
| Trichostatin A | 1.06E-02 |
| UNC0631 | 1.57E-02 |
| UNC0638 | 1.98E-02 |
| UNC0646 | 3.48E-03 |

Supplementary Table S12. Compounds used in this study. The 139-compound library utilized in this study, including the primary targets for each of these compounds.

| Compound | Target |
|---|--|
| (-)-JQ1 | BET proteins, no specific affinity as (+)-JQ1 does. |
| (+)-Naphthol A | SAH hydrolase, IC50 39nM |
| (+)-Abacisic Acid | Ubiquitous signaling molecule, in humans is known for anti-inflammatory and cellular metabolic reprogramming |
| (+)-JQ1 | BET proteins, notably BRD4 |
| (R)-PFH-2 (hydrochloride) | BET/BR, IC50 2nM |
| 1-Naphthol Acid | Precursor molecule |
| 2-Nethyl-4-Pentynoic Acid | HDACs |
| 2-PCPA (hydrochloride) | LSO1, IC50 20.7uM |
| 2,4-Hydroxydicarboxylic Acid | Chelator of Zinc and involved in JMJ protein pathways |
| 2'-3'-5'-thioethyl-5-Azacythidine | Inhibitor of DNA methyltransferase |
| 3-Amino Benzamide | Poly(ADP-Ribose) polymerases, Ki = 1.8uM |
| 3-Deazaneplanon A | S-adenosyl-L-homocysteine hydrolase inhibitor |
| 3-Deazaneplanon A (hydrochloride) | Inhibits trimethylation of lysine on histone H3 |
| 3,3'-Oindolylethene | NQ inhibitor |
| 4-iodo-SAHA | HDAC1, 40% inhibition at 1uM |
| 5-Azacythidine | DNA methyltransferase inhibitor |
| 5-Methyl-2'-deoxycytidine | Incorporates into single strand DNA |
| 5-Methylcytosine | Incorporates into RNA, 1 to 2 per 1,000 residues |
| 6-Thioguanine | DNA methyltransferase inhibitor |
| a-Hydroxyglutamic Acid (sodium salt) | L-2-dehydrogenases inhibitor |
| AGK2 | SIRT2 inhibitor |
| AGK7 | SIRT2 inhibitor, IC50 3.5uM |
| AK-7 | SIRT2 inhibitor, IC50 15.5uM |
| Anacardic Acid | Inhibitor of HATs p300 and p300/CREB |
| Apicidin | HDACs, IC50 = 0.7 nM |
| BIO-1294 (hydrochloride hydrate) | G9a HMTase, IC50 1.7uM |
| BML-219 | HDAC, IC50 30uM |
| BRD73954 | HDACs, IC50 36nM |
| Bromopropion | Non-specific bromodomain inhibitor |
| B5A-201 | PARP1 inhibitor |
| Butyrolactone 3 | Histone acetyltransferase Gcn5, IC50 100uM |
| C646 | Histone acetyltransferase p300, IC50 = 1.6uM, Ki = 400 nM |
| CAY10398 | HDAC1, IC50 15uM |
| CAY10591 | SIRT1 |
| CAY10603 | HDACs, other HDACs to lower extent |
| CAY10669 | Histone acetyltransferase PCAF |
| CAY10683 | HDAC2, IC50 0.119nM |
| CB4A | HDACs |
| CGG-100602 | Inhibitor Rho pathway-mediated signaling |
| Chilamide | Increases histone H3 acetylation levels |
| CS-994 | HDACs 1,2,3,8 |
| Ci-Ararsine (hydrochloride) | Protein arginine deiminases (PAD1, PAD3, PAD4) |
| Coarasin-SAHA | Class I and II HDACs. Coarasin is a fluorescent tag for SAHA |
| CPL-203 | BRD4 |
| CPTC2 (hydrochloride) | Inhibitor of HAT activity of Gcn5 |
| CUDC-107 | HEMT, HDAC, IC50 2.4nM, 18 nM |
| Daninodide | 200uM KDM2A, PHF8, KDM7A |
| Oscabine | DNA methyltransferases |
| Delphinidin (chloride) | ER-alpha, ultimately EGFR |
| DMG | H3F-1alpha |
| Ellagic Acid | Blocks methylation of arginine 12 on histone 3 through CA/M1 |
| EP2005687 | EZH2 |
| EP20676 | DOT1L histone methyltransferase, Ki 80pM |
| Etoposide | Nuclear receptor coactivator |
| EX-527 | SIRT1, IC50 98nM |
| F-Ararsine (trifluoroacetate salt) | PAD1, PAD4 |
| Genistein | Histone acetyltransferases (HAT) p300, IC50 = 7uM |
| Gercitabine | DNA damage inducible protein 45a |
| GSK-J1 (sodium salt) | Inhibitor of HDK27 histone demethylases, JMJD3, UTX |
| GSK-J2 (sodium salt) | Negative control for above GSK-J1, poorly inhibits JMJD3 |
| GSK-J4 (hydrochloride) | Inhibits JMJD3, less effective than GSK-J1, but more permeable to cells |
| GSK-LSD1 (hydrochloride) | LSO1, IC50 16nM |
| GSK126 | EZH2 methyltransferase, IC50 9.9nM |
| GSP-201 | BAZA |
| GSK343 | EZH2, ultimately acts on HDK27 |
| GSK4112 | REV-ERB-alpha, ultimately impacting circadian target gene transcription |
| HC-Tsien | HDACs |
| HNH4A | HDACs |
| HPD8 | HDACs, IC50 56nM |
| I-BET1151 | BRD2, BRD3, BRD4 |
| I-BET782 | BET proteins, including BRD2, BRD3, BRD4 |
| I-CBP112 (hydrochloride) | CBP |
| IKK1 | 20S oxygenases, PHF8, PHD2, FIH |
| Indigotin | Estrogen receptor alpha and beta antagonist |
| ITF 2357 | Class I and II HDACs |
| JGR1741 | SIRT1, IC50 15uM |
| JIB-64 | Jumonji histone demethylases |
| LAQ824 | HDAC, IC50 30uM |
| Levamisole | JAK2, IC50 1nM |
| Longguanin | HDACs |
| M 344 | HDACs, esp HDAC8, then HDAC1 |
| MC 1568 | Class Ia HDAC |
| Methylster (hydrate) | JMJD2A, JMJD2C, JMJD2G, JMJD2E, JMJD3 |
| M-2 (hydrochloride) | Blocks to menin, blocking menin-MLL fusion protein interaction |
| Minic (hydrochloride) | Weaker version of above M-2, worse blocker of menin-MLL |
| Minic | MRN, thus inhibiting MRN dependent phosphorylation of histone H2AX and prevents ATM activation |
| MS-275 | HDACs, HDAC3 |
| N-Oxalylglycine | JMJD2A, HMD2C, JMJD2E, IC50 250, 500, 24 uM |
| Nicotinamide | SIRT1 |
| Octyl-a-ketoglutarate | Stimulates PHD activity, increasing H3F-1alpha turnover |
| OTX015 | BRD2, BRD3, BRD4, IC50 levels 10-19nM |
| Oxamflatin | HDACs |
| Panobinostat | Broad-spectrum HDAC inhibitor |
| PCI 34051 | HDACs, IC50 = 0.01 uM |
| PP1-1 | BRD2, BRD4, other bromodomain things |
| PT-3 | SMARCA4 |
| Phthalazine pyrazole | Aurora A Kinase, IC50 31nM |
| Phosteinol | ER-alpha |
| Pinnic Diphenylamide 108 | Class I HDACs |
| Pyroxamide | HDAC1 |
| RG-108 | DNA methyltransferase, IC50 115nM |
| RG-PP966 | HDAC3, IC50 0.8uM |
| RSC-133 | DNA methyltransferase |
| Rucaparib (phosphate) | PARP1 |
| RVK-208 | BD2, IC50 0.04-0.29uM |
| S-(5'-Adenosyl)-L-methionine (broylate) | Ubiquitous methyl donor |
| S-Adenosylhomocysteine | Controls levels of AdoMet, which is an inhibitor of some methyltransferases |
| SAHA | HDAC1 100-200nM |
| Salemite | SIRT1 |
| SBR39 | HDAC isozymes, Ki = 16-26 nM |
| Sulaglad | HDAC |
| SOC-CBP30 | CREBBP, IC50 21-60nM |
| SOC9946 | DOT1L, IC50 0.3nM |
| SG-1027 | DNMT1, DNMT3A, DNMT3B |
| Sirtinungin | SIRT1 domain containing methyltransferases |
| SIRT1/2 inhibitor IV | SIRT1, IC50 56uM |
| Sirtinol | Sirtinol NAD+-dependent deacetylases, IC50 = 65uM |
| Sodium 4-Phenylbutyrate | Weak inhibitor of HDACs |
| Sodium Butyrate | HDACs |
| Splitomicin | Surp |
| Suramin (sodium salt) | Pyrimidine receptor-1 |
| Tenovin-1 | SIRT1 |
| Tenovin-6 | SIRT2, IC50 10uM |
| Trans-Resveratrol | COK-1 |
| Trichostatin A | HDAC1, 70nM |
| Tubacin | HDACs, IC50 4nM |
| Tubastatin A | HDACs, IC50 15nM |
| Tubastatin A (trifluoroacetate salt) | HDACs, IC50 = 15 nM |
| UNC0224 | G9a HMTase, IC50 150nM |
| UNC0321 (trifluoroacetate salt) | G9a HMTase |
| UNC0631 | G9a |
| UNC0638 | G9a HMTase inhibitor |
| UNC0642 | G9a, GLP, ultimately H3K9 |
| UNC0648 | G9a-GLP |
| UNC1215 | Kine reading function of L3MBTL3, IC50 60nM |
| UNC1998 | EZH2, IC50 2nM |
| Valproic Acid (sodium salt) | Class I HDACs |
| VDRO-0123 | HDACs |
| Zebularine | DNMT3A |