MDM2-recruiting PROTAC Offers Superior, Synergistic Anti-proliferative Activity via Simultaneous Degradation of BRD4 and Stabilization of p53

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Supplementary Data File – Table S1

| compound concentration (µM) | mean % inhibition by JQ1 | EJ | mean % inhibition by idasanutlin | E _N | mean % inhibition by A1874 | EA | CI |
|-----------------------------------|--------------------------------|-------|---|----------------|----------------------------------|-------|------|
| 0.01 | 0.4 % | 0.004 | 12.2 % | 0.122 | 2.4 % | 0.024 | 5.20 |
| 0.025 | 0.0 % | 0.000 | 16.2 % | 0.162 | 0.7 % | 0.007 | 23.1 |
| 0.10 | 7.9 % | 0.079 | 37.7 % | 0.377 | 9.2 % | 0.092 | 4.60 |
| 0.25 | 3.6 % | 0.036 | 47.7 % | 0.477 | 53.7 % | 0.537 | 0.92 |
| 1.00 | 7.2 % | 0.072 | 59.1 % | 0.591 | 96.5 % | 0.965 | 0.64 |
| 2.50 | 9.0 % | 0.090 | 60.6 % | 0.606 | 98.6 % | 0.986 | 0.65 |
| 10.0 | 15.1 % | 0.151 | 64.4 % | 0.644 | 96.8 % | 0.968 | 0.72 |

Supplementary Table S1: Bliss Independence analysis of A1874 activities in A375 cells

The percentage cell inhibition (compared to vehicle-treated control cells) for each compound at each concentration from Figure 3B was converted to their decimal equivalents (E_J for JQ1; E_N for idasanutlin; E_A for A1874) and the Combination Index (CI) value was derived as explained in the Experimental Methods. CI values <1 indicate synergy.