SUPPLEMENTARY FILE 1

Direct protein target hyptolide

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| **Target** | **Common name** | **Target Class** | **Probability\*** |
| Programmed cell death protein 4 | PDCD4 | Unclassified protein | 1.0934E+11 |
| Phosphodiesterase 4D | PDE4D | Phosphodiesterase | 1.0934E+11 |
| Cyclooxygenase-2 | PTGS2 | Oxidoreductase | 1.0934E+11 |
| Protein kinase C alpha | PRKCA | Kinase | 1.0934E+11 |
| Interleukin-8 receptor A | CXCR1 | Family A G protein-coupled receptor | 1.0934E+11 |
| Protein kinase C delta | PRKCD | Kinase | 1.0934E+11 |
| Poly [ADP-ribose] polymerase-1 | PARP1 | Enzyme | 1.0934E+11 |
| Phosphodiesterase 3 | PDE3A | Phosphodiesterase | 1.0934E+11 |
| Phosphodiesterase 3B | PDE3B | Phosphodiesterase | 1.0934E+11 |
| Neuropeptide Y receptor type 5 | NPY5R | Family A G protein-coupled receptor | 1.0934E+11 |
| Protein kinase C epsilon | PRKCE | Kinase | 1.0934E+11 |
| Translocator protein (by homology) | TSPO | Membrane receptor | 1.0934E+11 |
| Phosphodiesterase 10A | PDE10A | Phosphodiesterase | 1.0934E+11 |
| Cyclin-dependent kinase 5/CDK5 activator 1 | CDK5R1 CDK5 | Kinase | 1.0934E+11 |
| HERG | KCNH2 | Voltage-gated ion channel | 1.0934E+11 |
| Cathepsin S | CTSS | Protease | 1.0934E+11 |
| Voltage-gated potassium channel subunit Kv7.1 | KCNQ1 | Voltage-gated ion channel | 1.0934E+11 |
| Complement factor D | CFD | Protease | 1.0934E+11 |
| Serine/threonine-protein kinase Chk1 | CHEK1 | Kinase | 1.0934E+11 |
| Sorbitol dehydrogenase | SORD | Enzyme | 1.0934E+11 |
| Thrombin and coagulation factor X | F10 | Protease | 1.0934E+11 |
| Proteasome Macropain subunit MB1 | PSMB5 | Protease | 1.0934E+11 |
| Serine/threonine-protein kinase PLK1 | PLK1 | Kinase | 1.0934E+11 |
| Serine/threonine-protein kinase PLK2 | PLK2 | Kinase | 1.0934E+11 |
| Androgen Receptor | AR | Nuclear receptor | 1.0934E+11 |
| MAP kinase signal-integrating kinase 2 | MKNK2 | Kinase | 1.0934E+11 |
| Dopamine D4 receptor | DRD4 | Family A G protein-coupled receptor | 1.0934E+11 |
| Hepatocyte growth factor receptor | MET | Kinase | 1.0934E+11 |
| Adenosine A1 receptor | ADORA1 | Family A G protein-coupled receptor | 1.0934E+11 |
| Chymotrypsin C | CTRC | Protease | 1.0934E+11 |
| Cyclin-dependent kinase 9 | CDK9 | Kinase | 1.0934E+11 |
| Leukocyte elastase | ELANE | Protease | 1.0934E+11 |
| MAP kinase p38 alpha | MAPK14 | Kinase | 1.0934E+11 |
| Ribosomal protein S6 kinase alpha 3 | RPS6KA3 | Kinase | 1.0934E+11 |
| Fibroblast activation protein alpha (by homology) | FAP | Protease | 1.0934E+11 |
| Protein-tyrosine phosphatase 1B | PTPN1 | Phosphatase | 1.0934E+11 |
| Protein kinase C theta | PRKCQ | Kinase | 1.0934E+11 |
| Aldose reductase | AKR1B1 | Enzyme | 1.0934E+11 |
| PI3-kinase p110-delta subunit | PIK3CD | Enzyme | 1.0934E+11 |
| Tyrosine-protein kinase TYK2 | TYK2 | Kinase | 1.0934E+11 |
| Tyrosine-protein kinase ABL | ABL1 | Kinase | 1.0934E+11 |
| Epidermal growth factor receptor erbB1 | EGFR | Kinase | 1.0934E+11 |
| Serine/threonine-protein kinase Aurora-B | AURKB | Kinase | 1.0934E+11 |
| Tyrosine-protein kinase SRC | SRC | Kinase | 1.0934E+11 |
| Vascular endothelial growth factor receptor 2 | KDR | Kinase | 1.0934E+11 |
| Cathepsin L | CTSL | Protease | 1.0934E+11 |
| Adenosine A3 receptor | ADORA3 | Family A G protein-coupled receptor | 1.0934E+11 |
| Chymase | CMA1 | Protease | 1.0934E+11 |
| Neuronal acetylcholine receptor protein alpha-7 subunit | CHRNA7 | Ligand-gated ion channel | 1.0934E+11 |
| Focal adhesion kinase 1 | PTK2 | Kinase | 1.0934E+11 |
| Matrix metalloproteinase 9 | MMP9 | Protease | 1.0934E+11 |
| Matrix metalloproteinase 1 | MMP1 | Protease | 1.0934E+11 |
| Induced myeloid leukemia cell differentiation protein Mcl-1 | MCL1 | Other cytosolic protein | 1.0934E+11 |
| Matrix metalloproteinase 8 | MMP8 | Protease | 1.0934E+11 |
| CREB-binding protein/p53 | CREBBP | Writer | 1.0934E+11 |
| Serine/threonine-protein kinase 17B | STK17B | Kinase | 1.0934E+11 |
| MAP kinase ERK2 | MAPK1 | Kinase | 1.0934E+11 |
| Smoothened homolog (by homology) | SMO | Frizzled family G protein-coupled receptor | 1.0934E+11 |
| Protein kinase C beta | PRKCB | Kinase | 1.0934E+11 |
| Tyrosine-protein kinase receptor FLT3 | FLT3 | Kinase | 1.0934E+11 |
| Isocitrate dehydrogenase [NADP] cytoplasmic | IDH1 | Enzyme | 1.0934E+11 |
| Thyrotropin-releasing hormone receptor | TRHR | Family A G protein-coupled receptor | 1.0934E+11 |
| Macrophage colony stimulating factor receptor | CSF1R | Kinase | 1.0934E+11 |
| Cyclin-dependent kinase 2/cyclin A | CDK2 CCNA1 CCNA2 | Other cytosolic protein | 1.0934E+11 |
| Serine/threonine-protein kinase 17A | STK17A | Kinase | 1.0934E+11 |
| Orexin receptor 2 | HCRTR2 | Family A G protein-coupled receptor | 1.0934E+11 |
| Orexin receptor 1 | HCRTR1 | Family A G protein-coupled receptor | 1.0934E+11 |
| Trace amine-associated receptor 1 (by homology) | TAAR1 | Family A G protein-coupled receptor | 1.0934E+11 |
| Estrogen receptor beta | ESR2 | Nuclear receptor | 1.0934E+11 |
| Cyclin-dependent kinase 2 | CDK2 | Kinase | 1.0934E+11 |
| dUTP pyrophosphatase | DUT | Enzyme | 1.0934E+11 |
| Beta secretase 2 (by homology) | BACE2 | Protease | 1.0934E+11 |
| Histone deacetylase 8 | HDAC8 | Eraser | 1.0934E+11 |
| Serine/threonine-protein kinase Aurora-A | AURKA | Kinase | 1.0934E+11 |
| Beta-secretase 1 (by homology) | BACE1 | Protease | 1.0934E+11 |
| Lysine-specific histone demethylase 1 | KDM1A | Eraser | 1.0934E+11 |
| GABA-A receptor; alpha-5/beta-3/gamma-2 | GABRB3 GABRG2 GABRA5 | Ligand-gated ion channel | 1.0934E+11 |
| Adenosine A2a receptor | ADORA2A | Family A G protein-coupled receptor | 1.0934E+11 |
| Adenosine A2b receptor | ADORA2B | Family A G protein-coupled receptor | 1.0934E+11 |
| PI3-kinase p110-gamma subunit | PIK3CG | Enzyme | 1.0934E+11 |
| ADAM17 | ADAM17 | Protease | 1.0934E+11 |
| Carnitine O-palmitoyltransferase 1, liver isoform | CPT1A | Enzyme | 1.0934E+11 |
| Protein farnesyltransferase | FNTA FNTB | Enzyme | 1.0934E+11 |
| GABA-A receptor; alpha-3/beta-3/gamma-2 | GABRB3 GABRA3 GABRG2 | Ligand-gated ion channel | 1.0934E+11 |
| GABA-A receptor; alpha-1/beta-3/gamma-2 | GABRB3 GABRG2 GABRA1 | Ligand-gated ion channel | 1.0934E+11 |
| GABA-A receptor; alpha-2/beta-3/gamma-2 | GABRA2 GABRB3 GABRG2 | Ligand-gated ion channel | 1.0934E+11 |
| Integrin alpha-4/beta-7 | ITGB7 ITGA4 | Membrane receptor | 1.0934E+11 |
| 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 3 | PFKFB3 | Enzyme | 1.0934E+11 |
| Interleukin-8 receptor B | CXCR2 | Family A G protein-coupled receptor | 1.0934E+11 |
| Beta amyloid A4 protein | APP | Membrane receptor | 1.0934E+11 |
| Metabotropic glutamate receptor 4 | GRM4 | Family C G protein-coupled receptor | 1.0934E+11 |
| Cyclin-dependent kinase 1 | CDK1 | Kinase | 1.0934E+11 |
| Aldehyde dehydrogenase dimeric NADP-preferring | ALDH3A1 | Enzyme | 1.0934E+11 |
| Protein cereblon | CRBN | Unclassified protein | 1.0934E+11 |
| Hexokinase type IV | GCK | Enzyme | 1.0934E+11 |
| Calpain 2 | CAPN2 | Protease | 1.0934E+11 |
| Metabotropic glutamate receptor 5 (by homology) | GRM5 | Family C G protein-coupled receptor | 1.0934E+11 |
| Calpain 1 | CAPN1 | Protease | 1.0934E+11 |
| Cathepsin (B and K) | CTSB | Protease | 1.0934E+11 |
| P2X purinoceptor 7 | P2RX7 | Ligand-gated ion channel | 1.0934E+11 |