Compound	Cas number	well: row	well: column	Target/MoA/Pathway	Selected References
DMSO		A	1	control	
JG-231	1627126-59-3	B	1	Hsp70s, allosteric inhibitor that disrupts the Hsp70-BAG3 interaction	Analogs of the Heat Shock Protein 70 Inhibitor MKT-077 Suppress Medullary Thyroid Carcinoma Cells (Hong et al.„ 2022). Exploration of Benzothiazole Rhodacyanines as Allosteric Inhibitors of Protein-Protein Interactions with Heat Shock Protein 70 (Hsp70) (Shao et al.„ 2018). Mortalin/HSPA9 targeting selectively induces KRAS tumor cell death by perturbing mitochondrial membrane permeability (Wu et al.„ 2020).
VER-155008	1134156-31-2	C	1	Hsp70s, competetitve	Filamentous Aggregates Are Fragmented by the Proteasome Holoenzyme (Cliffe et al., 2019). The heat shock protein 70 inhibitor VER155008 suppresses the expression of HSP27, HOP and HSP90beta and the androgen receptor, induces apoptosis, and attenuates prostate cancer cell growth (Brunnert et al., 2019). A biosensor-based framework to measure latent proteostasis capacity (Wood et al., 2018). Targeting Heat Shock Protein 70 as an antiviral strategy against grass carp reovirus infection (Shan et al., 2018). Dual targeting of HSP70 does not induce the heat shock response and synergistically reduces cell viability in muscle invasive bladder cancer (Prince et al., 2018). Acute HSF1 depletion induces cellular senescence through the MDM2-p53-p21 pathway in human diploid fibroblasts (Oda et al., 2018). PRDM14 directly interacts with heat shock proteins HSP90alpha and glucose-regulated protein 78 (Moriya et al., 2018). Development of a microarray-based assay for efficient testing of new HSP70/DnaK inhibitors (Mohammadi-Ostad-Kalayeh et al., 2017). The nuclear factor erythroid 2-like 2 activator, tert-butylhydroquinone, improves cognitive performance in mice after mild traumatic brain injury (Saykally et al., 2012). HSC70 Inhibitor Reduces Memory Deficits and Axonal Degeneration in a Mouse Model of AD (Yang X et al., 2018). Potent anti-cancer activity on lung cancer cell lines (Wen et al., 2014). Heat Shock Cognate 70 Inhibitor, VER-155008, Reduces Memory Deficits and Axonal Degeneration in a Mouse Model of Alzheimer's Disease (Yang and Tohda 2018). Hsp70 Isoforms Are Essential for the Formation of Kaposi's Sarcoma-Associated Herpesvirus Replication and Transcription Compartments (Baquero-Perez and Whitehouse 2015). VER-155008, a small molecule inhibitor of HSP70 with potent anti-cancer activity on lung cancer cell lines (Wen et al., 2014). Functional analysis of Hsp70 inhibitors (Schlecht et al., 2013). A novel, small molecule inhibitor of Hsc70/Hsp70 potentiates Hsp90 inhibitor induced apoptosis in HCT116 colon carcinoma cells (Massey et al., 2010). Heat Shock Cognate 70 Inhibitor, VER-155008, Reduces Memory Deficits and Axonal Degeneration in a Mouse Model of Alzheimer's Disease (Yang and Tohda 2018). Maslinic acid induces autophagy by down-regulating HSPA8 in pancreatic cancer cells (Tian et al., 2018). Hsp70 Isoforms Are Essential for the Formation of Kaposi's Sarcoma-Associated Herpesvirus Replication and Transcription Compartments (Baquero-Perez and Whitehouse 2015). VER-155008, a small molecule inhibitor of HSP70 with potent anti-cancer activity on lung cancer cell lines (Wen et al., 2014). Functional analysis of Hsp70 inhibitors (Schlecht et al., 2013). A novel, small molecule inhibitor of Hsc70/Hsp70 potentiates Hsp90 inhibitor induced apoptosis in HCT116 colon carcinoma cells (Massey et al., 2010).
MAL3-101	831217-40-4	D	1	Hsp70s, allosteric JDPs	Dual targeting of HSP70 does not induce the heat shock response and synergistically reduces cell viability in muscle invasive bladder cancer (Prince et al., 2018). Hsp70 plays an important role in high-fat diet induced gestational hyperglycemia in mice (Xing et al., 2015). MARCKS and HSP70 interactions regulate mucin secretion by human airway epithelial cells in vitro (Fang et al., 2013). Chemical methodology as a source of small-molecule checkpoint inhibitors and heat shock protein 70 (Hsp70) modulators (Huryn et al., 2011). Antimyeloma Effects of the Heat Shock Protein 70 Molecular Chaperone Inhibitor MAL3-101 (Braunstein et al., 2011).
JG-258	not listed?	E	1	Hsp70s, allosteric JDPs	Hsp70:CHIP Ubiquitinates Dysfunctional but Not Native Neuronal NO Synthase (Davis et al.„ 2020). Inhibitors and chemical probes for molecular chaperone networks (Gestwicki and Shao, 2019). Zika Virus Dependence on Host Hsp70 Provides a Protective Strategy against Infection and Disease (Taguwa et al.„ 2019).
NVP-AUY922 (Luminespib)	747412-49-3	F	1	Hsp90, N-terminus	Approaches to develop therapeutics to treat frontotemporal dementia (Elia et al.„ 2020). Genetic Regulation of Neuronal Progranulin Reveals a Critical Role for the Autophagy-Lysosome Pathway (Elia et al.„ 2019). HSP90 Inhibitor, NVP-AUY922, Improves Myelination in Vitro and Supports the Maintenance of Myelinated Axons in Neuropathic Mice (Chittoor-Vinod et al.„ 2019). Methods to validate Hsp90 inhibitor specificity, to identify off-target effects, and to rethink approaches for further clinical development (Neckers et al.„ 2018). Potent antitumor activity of the novel HSP90 inhibitors AUY922 and HSP990 in neuroendocrine carcinoid cells (Zitzmann et al.„ 2013). A screen for enhancers of clearance identifies huntingtin as a heat shock protein 90 (Hsp90) client protein (Baldo et al.„ 2012).
NVP-BEP800	847559-80-2	G	1	Hsp90, N terminus	Anti-myeloma activity of the novel 2-aminothienopyrimidine Hsp90 inhibitor NVP-BEP800 (Stuhmer et al.„ 2009). Novel HSP90 inhibitors, NVP-AUY922 and NVP-BEP800, radiosensitise tumour cells through cell-cycle impairment, increased DNA damage and repair protraction (Stingl et al.„ 2010). Preclinical antitumor activity of the orally available heat shock protein 90 inhibitor NVP-BEP800 (Massey et al.„ 2010).
KU-32	956498-70-7	H	1	HSP90, C-terminus	C-terminal modulators of heat shock protein of 90kDa (HSP90): State of development and modes of action (Bickel and Gohlke, 2019). Development of noviomimetics that modulate molecular chaperones and manifest neuroprotective effects (Forsberg et al.„ 2018). Heat shock protein 70 is necessary to improve mitochondrial bioenergetics and reverse diabetic sensory neuropathy following KU-32 therapy (Ma et al.„ 2014). Heat shock protein 90 inhibitors block the antinociceptive effects of opioids in mouse chemotherapy-induced neuropathy and cancer bone pain models (Stine et al.„ 2020). Hsp90 Inhibition: A Promising Therapeutic Approach for ARSACS (Nethisinghe et al.„ 2021). Inhibiting heat-shock protein 90 reverses sensory hypoalgesia in diabetic mice (Urban et al.„ 2010). KU32 prevents 5-fluorouracil induced cognitive impairment (Sofis et al.„ 2017). Stimulation of heat shock protein 90 chaperone function through binding of a novobiocin analog KU-32 (Chatterjee et al.„ 2019).
4-Br-Bnim	1654775-71-9	A	2	GRP94	Exploiting the interaction between Grp94 and aggregated myocilin to treat glaucoma (Stothert et al.„ 2014). Isoform-selective Hsp90 inhibition rescues model of hereditary open-angle glaucoma (Stothert et al.„ 2017).
17-DMAG	467214-21-7	B	2	Hsp90, N-terminus	17-DMAG ameliorates polyglutamine-mediated motor neuron degeneration through well-preserved proteasome function in an SBMA model mouse (Tokui et al.„ 2009). Combined pharmacological induction of Hsp70 suppresses prion protein neurotoxicity in Drosophila (Zhang et al.„ 2014). Heat Shock Protein 70 (HSP70) Induction: Chaperonotherapy for Neuroprotection after Brain Injury (Kim et al.„ 2020). Heat shock protein 90 inhibition by 17-Dimethylaminoethylamino-17-demethoxygeldanamycin protects blood-brain barrier integrity in cerebral ischemic stroke (Qi et al.„ 2015). The Hsp90 Inhibitor 17-DMAG Attenuates Hyperglycemia-Enhanced Hemorrhagic Transformation in Experimental Stroke (Zhang et al.„ 2021). A quantitative high throughput screen identifies compounds that lower expression of the SCA2- and ALS-associated gene ATXN2 (Scoles et al.„ 2022). Translational Shift of HSP90 as a Novel Therapeutic Target from Cancer to Neurodegenerative Disorders: An Emerging Trend in the Cure of Alzheimer's and Parkinson's Diseases (Alam et al.„ 2017).
Pu-H71	873436-91-0	C	2	Hsp90, C-terminus	Extracellular vesicles and anti-cancer drug resistance (Namee and O'Driscoll, 2018). The Hsp70/Hsp90 Chaperone Machinery in Neurodegenerative Diseases (Lackie et al.„ 2017). Methods to validate Hsp90 inhibitor specificity, to identify off-target effects, and to rethink approaches for further clinical development (Neckers et al.„ 2018). Molecular chaperones and regulation of tau quality control: strategies for drug discovery in tauopathies (Miyata et al.„ 2011). The penalty of stress - Epichaperomes negatively reshaping the brain in neurodegenerative disorders (Ginsberg et al.„ 2021).
IU1-47	670270-31-2	D	2	USP14	Compensatory increase in USP14 activity accompanies impaired proteasomal proteolysis during aging (Ponnappan et al.„ 2013). Discovery of new promising USP14 inhibitors: computational evaluation of the thumb-palm pocket (Adelakun et al.„ 2022). An inhibitor of the proteasomal deubiquitinating enzyme USP14 induces tau elimination in cultured neurons (Boselli et al.„ 2017). Post-endocytotic Deubiquitination and Degradation of the Metabotropic gamma-Aminobutyric Acid Receptor by the Ubiquitin-specific Protease 14 (Lahaie et al.„ 2016). USP14 deubiquitinates proteasome-bound substrates that are ubiquitinated at multiple sites (Lee et al.„ 2016). USP14 inhibitor attenuates cerebral ischemia/reperfusion-induced neuronal injury in mice (Min et al.„ 2017).
bortezomib	179324-69-7	E	2	20S proteasome	The Autophagy Lysosomal Pathway and Neurodegeneration (Finkbeiner, 2019). Bortezomib induces neuropathic pain through protein kinase C-mediated activation of presynaptic NMDA receptors in the spinal cord (Xie et al.„ 2017). Methods for measuring misfolded protein clearance in the budding yeast Saccharomyces cerevisiae (Samant and Frydman, 2019). Rapid induction of p62 and GABARAPL1 upon proteasome inhibition promotes survival before autophagy activation (Sha et al.„ 2018). Targeted degradation of aberrant tau in frontotemporal dementia patient-derived neuronal cell models (Silva et al.„ 2019). Vincristine- and bortezomib-induced neuropathies - from bedside to bench and back (Geisler, 2021). ZFAND1 Recruits p97 and the 26S Proteasome to Promote the Clearance of Arsenite-Induced Stress Granules (Turakhiya et al.„ 2018).
KZR-616	1629677-75-3	F	2	immuno-proteasome	Clinical trials and novel therapeutics in dermatomyositis (Chandra and Aggarwal, 2020). Immunoproteasome-selective inhibitors: An overview of recent developments as potential drugs for hematologic malignancies and autoimmune diseases (Xi et al.„ 2019). A patent review of immunoproteasome inhibitors (Ogorevc et al.„ 2018). Proteasome Inhibitors: Harnessing Proteostasis to Combat Disease (Sherman and Li, 2020). Required Immunoproteasome Subunit Inhibition Profile for Anti-Inflammatory Efficacy and Clinical Candidate KZR-616 ((2 S,3 R)- N-((S)-3-(Cyclopent-1-en-1-yl)-1-((R)-2-methyloxiran-2-yl)-1-oxopropan-2-yl)-3-hydroxy-3-(4-methoxyphenyl)-2-((S)-2-(2-morpholinoacetamido)propanamido)propenamide) (Johnson et al.„ 2018). Role of Epoxide Hydrolases and Cytochrome P450s on Metabolism of KZR-616, a First-in-Class Selective Inhibitor of the Immunoproteasome (Fang et al.„ 2021).

Spautin-1	1262888-28-7	G	2	USP10	The Autophagy Inhibitor Spautin-1 Antagonizes Rescue of Mutant CFTR Through an Autophagy-Independent and USP13-Mediated Mechanism (Pesce et al.„ 2018). Beclin1 controls the levels of p53 by regulating the deubiquitination activity of USP10 and USP13 (Liu et al.„ 2011). Effect of Autophagy Modulators on Vascular, Glial, and Neuronal Alterations in the Oxygen-Induced Retinopathy Mouse Model (Subirada et al.„ 2019). Induction of autophagy by a novel small molecule improves abeta pathology and ameliorates cognitive deficits (Chu et al.„ 2013). Novel Ubiquitin Specific Protease-13 Inhibitors Alleviate Neurodegenerative Pathology (Liu et al.„ 2021). SQSTM1/p62 and PPARGC1A/PGC-1alpha at the interface of autophagy and vascular senescence (Salazar et al.„ 2019).
MLN4924/Pevonedistat	905579-51-3	H	2	NEDDylation (NAE)	Autophagy and senescence: A new insight in selected human diseases (Rajendran et al.„ 2019). Transient inhibition of neddylation at neonatal stage evokes reversible cardiomyopathy and predisposes the heart to isoproterenol-induced heart failure (Zou et al.„ 2019).Autophagy and senescence: A new insight in selected human diseases (Rajendran et al.„ 2019). MLN4924 Exerts a Neuroprotective Effect against Oxidative Stress via Sirt1 in Spinal Cord Ischemia-Reperfusion Injury (Yu et al.„ 2019). Synaptic structure and function are altered by the neddylation inhibitor MLN4924 (Scudder and Patrick, 2015). Systemic inhibition of neddylation by 3-day MLN4924 treatment regime does not impair autophagic flux in mouse hearts and brains (Reihe et al.„ 2017). Targeted degradation of aberrant tau in frontotemporal dementia patient-derived neuronal cell models (Silva et al.„ 2019).
TAK981/Subasumstat	1858276-04-6	A	3	SUMOylation inhibitor	Discovery of TAK-981, a First-in-Class Inhibitor of SUMO-Activating Enzyme for the Treatment of Cancer (Langston et al.„ 2021). A small-molecule SUMOylation inhibitor activates antitumor immune responses and potentiates immune therapies in preclinical models (Lightcap et al.„ 2021). Targeting pancreatic cancer by TAK-981: a SUMOylation inhibitor that activates the immune system and blocks cancer cell cycle progression in a preclinical model (Kumar et al.„ 2022).
nutlin-3	1858276-04-6	B	3	mdm-p53	Decreased p53 is associated with a decline in asymmetric stem cell self-renewal in aged human epidermis (Charruyer et al.„ 2021). Autophagy promotes mammalian survival by suppressing oxidative stress and p53 (Yang et al.„ 2020). Autophagy suppresses TRP53/p53 and oxidative stress to enable mammalian survival (Yang and White, 2020). P53/NRF2 mediates SIRT1's protective effect on diabetic nephropathy (Ma et al.„ 2019). Small-molecule MDM2 antagonists attenuate the senescence-associated secretory phenotype (Wiley et al.„ 2018).
ubistatin-a	759437-26-8	C	3	ubiquitin binder	The ubiquitin proteasomal system: a potential target for the management of Alzheimer's disease (Gadhave et al.„ 2016). Cell biology. Chemical genetics hits (Bellows and Tyers, 2004). Hydrophobic Patch of Ubiquitin is Important for its Optimal Activation by Ubiquitin Activating Enzyme E1 (Singh et al.„ 2017). A role for ubiquitin in the spliceosome assembly pathway (Bellare et al.„ 2008). Ubistatins inhibit proteasome-dependent degradation by binding the ubiquitin chain (Verma et al.„ 2004).
CB-5083	1542705-92-9	D	3	p97 competitive	AAA+ ATPase p97/VCP mutants and inhibitor binding disrupt inter-domain coupling and subsequent allosteric activation (Caffrey et al.„ 2021). A p97/Valosin-Containing Protein Inhibitor Drug CB-5083 Has a Potent but Reversible Off-Target Effect on Phosphodiesterase-6 (Leinonen et al.„ 2021). P97/VCP ATPase inhibitors can rescue p97 mutation-linked motor neuron degeneration (Wang et al.„ 2022).
NMS873	1418013-75-8	E	3	p97 competitive	Filamentous Aggregates Are Fragmented by the Proteasome Holoenzyme (Cliffe et al.„ 2019). P97/VCP ATPase inhibitors can rescue p97 mutation-linked motor neuron degeneration (Wang et al.„ 2022). Spironolactone-induced XPB degradation requires TFIIH integrity and ubiquitin-selective segregase VCP/p97 (Chauhan et al.„ 2021). Specific inhibition of p97/VCP ATPase and kinetic analysis demonstrate interaction between D1 and D2 ATPase domains (Chou et al.„ 2014). VCP/p97 cooperates with YOD1, UBXD1 and PLAA to drive clearance of ruptured lysosomes by autophagy (Papadopoulos et al.„ 2017).
cotransin/Apratoxin S4	not listed?	F	3	Sec61A	An allosteric Sec61 inhibitor traps nascent transmembrane helices at the lateral gate (Mackinnon et al.„ 2014). Apratoxin Kills Cells by Direct Blockade of the Sec61 Protein Translocation Channel (Paatero et al.„ 2016). Cotransin induces accumulation of a cytotoxic clusterin variant that cotranslationally rerouted to the cytosol (Choi et al.„ 2013). Targeting of HER/ErbB family proteins using broad spectrum Sec61 inhibitors coibamide A and apratoxin A (Kazemi et al.„ 2021).
Omacetaxine mepesuccinate (Homoharringtonine)	26833-87-4	G	3	translation elongation	Homoharringtonine Inhibits Alzheimer's Disease Progression by Reducing Neuroinflammation via STAT3 Signaling in APP/PS1 Mice (Jiang et al.„ 2021).
IOX2	931398-72-0	H	3	PHD inhib., HIF1a activ.	Fracture repair by IOX2: Regulation of the hypoxia inducible factor-1α signaling pathway and BMSCs (Chen et al.„ 2022). Liposomal PHD2 Inhibitors and the Enhanced Efficacy in Stabilizing HIF-1α (Jian et al.„ 2022). Metabolic studies of hypoxia-inducible factor stabilisers IOX2, IOX3 and IOX4 (in vitro) for doping control (Philip et al.„ 2021). RNA-seq analysis of PHD and VHL inhibitors reveals differences and similarities to the hypoxia response (Frost et al.„ 2019). UPLC-MS-Based Procedures to Detect Prolyl-Hydroxylase Inhibitors of HIF in Urine (Mazzarino et al.„ 2021). Von Hippel-Lindau (VHL) small-molecule inhibitor binding increases stability and intracellular levels of VHL protein (Frost et al.„ 2021).
PF429242	2248666-66-0	A	4	S1P/ATF6 inhibitor	Membrane-Bound Transcription Factor Site-1 Protease in PF429242 Bound State: Computational Kinetics and Dynamics of Reversible Binding (Olaposi et al.„ 2019). Site-1 protease is required for the generation of soluble (pro)renin receptor (Nakagawa et al.„ 2017). Sterol regulatory element-binding protein 1 inhibitors decrease pancreatic cancer cell viability and proliferation (Siqingaowa et al.„ 2017).
Ceapin-A7	2323027-38-7	B	4	ATF6 inhibitor	ATF6 aggravates angiogenesis-osteogenesis coupling during ankylosing spondylitis by mediating FGF2 expression in chondrocytes (Ma et al.„ 2021). Coordinated signaling of activating transcription factor 6α and inositol-requiring enzyme 1α regulates hepatic stellate cell-mediated fibrogenesis in mice (Xue et al.„ 2021). Zika Virus Induces an Atypical Tripartite Unfolded Protein Response with Sustained Sensor and Transient Effector Activation and a Blunted BiP Response (Mufrrih et al.„ 2021). Ceapins are a new class of unfolded protein response inhibitors, selectively targeting the ATF6alpha branch (Gallagher et al.„ 2016). Ceapins block the unfolded protein response sensor ATF6alpha by inducing a neomorphic inter-organelle tether (Torres et al.„ 2019). Ceapins inhibit ATF6alpha signaling by selectively preventing transport of ATF6alpha to the Golgi apparatus during ER stress (Gallagher and Walter, 2016). The UPR Activator ATF6 Responds to Proteotoxic and Lipotoxic Stress by Distinct Mechanisms (Tam et al.„ 2018).
BIX	101714-41-4	C	4	BiP/ATF6 activator	BiP Inducer X: An ER Stress Inhibitor for Enhancing Recombinant Antibody Production in CHO Cell Culture (Ha et al.„ 2019). Effect of an inducer of BiP, a molecular chaperone, on endoplasmic reticulum (ER) stress-induced retinal cell death (Inokuchi et al.„ 2009). Induction of BiP, an ER-resident protein, prevents the neuronal death induced by transient forebrain ischemia in gerbil (Oida et al.„ 2008). Mn(II) coordination polymers based on bi-, tri-, and tetranuclear and polymeric chain building units: crystal structures and magnetic properties (Ma et al.„ 2012). The Molecular Chaperone GRP78/BiP as a Therapeutic Target for Neurodegenerative Disorders: A Mini Review (Gorbatyuk and Gorbatyuk, 2013). [A molecular chaperone inducer as potential therapeutic agent for neurodegenerative disease] (Kudo et al.„ 2007). A molecular chaperone inducer protects neurons from ER stress (Kudo et al.„ 2008). The protective effect of a newly developed molecular chaperone-inducer against mouse ischemic acute kidney injury (Prachasilchai et al.„ 2009). Protective effects of BiP inducer X (BIX) against diabetic cardiomyopathy in rats (Idari et al.„ 2021). Remodeling the endoplasmic reticulum proteostasis network restores proteostasis of pathogenic GABAA receptors (Fu et al.„ 2018). Role of endoplasmic reticulum stress in light-induced photoreceptor degeneration in mice (Nakanishi et al.„ 2013).
ISRIB	1597403-47-8	D	4	eIF2alpha-P inhibitor	Binding of ISRIB reveals a regulatory site in the nucleotide exchange factor eIF2B (Zyryanova et al.„ 2018). Binding of ISRIB reveals a regulatory site in the nucleotide exchange factor eIF2B (Zyryanova et al.„ 2018). Fine tuning of the unfolded protein response by ISRIB improves neuronal survival in a model of amyotrophic lateral sclerosis (Bugallo et al.„ 2020). Impaired Restoration of Global Protein Synthesis Contributes to Increased Vulnerability to Acute ER Stress Recovery in Huntington's Disease (Xu et al.„ 2021). ISRIB Blunts the Integrated Stress Response by Allosterically Antagonising the Inhibitory Effect of Phosphorylated eIF2 on eIF2B (Zyryanova et al.„ 2021). Long-Term Depression-Inducing Low Frequency Stimulation Enhances p-Tau181 and p-Tau217 in an Age-Dependent Manner in Live Rats (Zhang et al.„ 2022). Small molecule cognitive enhancer reverses age-related memory decline in mice (Krukowski et al.„ 2020). Inhibition of the SEC61 translocon by mycolactone induces a protective autophagic response controlled by EIF2S1-dependent translation that does not require ULK1 activity (Hall et al.„ 2022). Integrated stress response inhibition provides sex-dependent protection against noise-induced cochlear synaptopathy (Rouse et al.„ 2020). Role of Endoplasmic Reticulum Stress in Learning and Memory Impairment and Alzheimer's Disease-Like Neuropathology in the PS19 and APP(Swe) Mouse Models of Tauopathy and Amyloidosis (Briggs et al.„ 2017). Role of Endoplasmic Reticulum Stress in Learning and Memory Impairment and Alzheimer's Disease-Like Neuropathology in the PS19 and APP(Swe) Mouse Models of Tauopathy and Amyloidosis (Briggs et al.„ 2017).
4μ8c	14003-96-4	E	4	IRE1 kinase inhibitor	The inositol-requiring enzyme 1 (IRE1α) RNAse inhibitor, 4μ8C, is also a potent cellular antioxidant (Chan et al.„ 2018). Phenotypic assays identify azoramide as a small-molecule modulator of the unfolded protein response with antidiabetic activity (Fu et al.„ 2015). Targeting the unfolded protein response in disease (Hetz et al.„ 2013). The inositol-requiring enzyme 1 (IRE1α) RNAse inhibitor, 4μ8C, is also a potent cellular antioxidant (Chan et al.„ 2018). The molecular basis for selective inhibition of unconventional mRNA splicing by an IRE1-binding small molecule (Cross et al.„ 2012). Targeting IRE1 with small molecules counteracts progression of atherosclerosis (Tufanli et al.„ 2017). Toll-like receptor 2 (TLR2) engages endoplasmic reticulum stress sensor IRE1α to regulate retinal innate responses in Staphylococcus aureus endophthalmitis (Kumar et al.„ 2020).
Kira8 (AMG-18)	1630086-20-2	F	4	IRE1 kinase inhibitor	IRE1α drives lung epithelial progenitor dysfunction to establish a niche for pulmonary fibrosis (Auyeung et al.„ 2022). Small molecule inhibition of IRE1α kinase/RNase has anti-fibrotic effects in the lung (Thamsen et al.„ 2019). Targeting ABL-IRE1α Signaling Spares ER-Stressed Pancreatic β Cells to Reverse Autoimmune Diabetes (Morita et al.„ 2017). Targeting Adaptive IRE1α Signaling and PLK2 in Multiple Myeloma: Possible Anti-Tumor Mechanisms of KIRA8 and Nilotinib (Yamashita et al.„ 2020).

APY29	1216665-49-4	G	4	IRE1 kinase inhibitor	ER stress signaling has an activating transcription factor 6α (ATF6)-dependent "off-switch" (Walter et al.„ 2018).
GSK2606414	1337531-36-8	H	4	PERK/RIPK inhibitor	Activation of the Protein Kinase R-Like Endoplasmic Reticulum Kinase (PERK) Pathway of the Unfolded Protein Response after Experimental Traumatic Brain Injury and Treatment with a PERK Inhibitor (Brady et al.„ 2021). Attenuation of PKR-like ER Kinase (PERK) Signaling Selectively Controls Endoplasmic Reticulum Stress-induced Inflammation Without Compromising Immunological Responses (Guthrie et al.„ 2016). Endoplasmic Reticulum Stress Contributes to the Loss of Newborn Hippocampal Neurons after Traumatic Brain Injury (Hood et al.„ 2018). Endoplasmic Reticulum Stress Is Involved in Stress-Induced Hypothalamic Neuronal Injury in Rats via the PERK-ATF4-CHOP and IRE1-ASK1-JNK Pathways (Yi et al.„ 2019). Fine tuning of the unfolded protein response by ISRIB improves neuronal survival in a model of amyotrophic lateral sclerosis (Bugallo et al.„ 2020). GSK2606414 attenuates PERK/p-eIF2α/ATF4/CHOP axis and augments mitochondrial function to mitigate high glucose induced neurotoxicity in N2A cells (Gundu et al.„ 2022). Hes1 Knockdown Exacerbates Ischemic Stroke Following tMCAO by Increasing ER Stress-Dependent Apoptosis via the PERK/eIF2α/ATF4/CHOP Signaling Pathway (Li et al.„ 2020). Inhibition of PERK-dependent pro-adaptive signaling pathway as a promising approach for cancer treatment (Rozpedek et al.„ 2017). Neurite atrophy and apoptosis mediated by PERK signaling after accumulation of GM2-ganglioside (Virgolini et al.„ 2019). [Niskocząsteczkowe inhibitory szlaku adaptacyjnej odpowiedzi na stres zależnego od kinazy PERK jako nowatorska strategia terapeutyczna w leczeniu choroby Alzheimera] (Rozpędek et al.„ 2019). Partial restoration of protein synthesis rates by the small molecule ISRIB prevents neurodegeneration without pancreatic toxicity (Halliday et al.„ 2015). PERK inhibition prevents tau-mediated neurodegeneration in a mouse model of frontotemporal dementia (Radford et al.„ 2015). PERK Pathway Activation Promotes Intracerebral Hemorrhage Induced Secondary Brain Injury by Inducing Neuronal Apoptosis Both in Vivo and in Vitro (Meng et al.„ 2018). The PERK Pathway Plays a Neuroprotective Role During the Early Phase of Secondary Brain Injury Induced by Experimental Intracerebral Hemorrhage (Zhang et al.„ 2020). Pharmacological inhibition of UPR sensor PERK attenuates HIV Tat-induced inflammatory M1 phenotype in microglial cells (Silveira et al.„ 2022). Possible mechanisms of the PERK pathway on neuronal apoptosis in a rat model of surgical brain injury (Wu et al.„ 2021). Suppression of CHOP Reduces Neuronal Apoptosis and Rescues Cognitive Impairment Induced by Intermittent Hypoxia by Inhibiting Bax and Bak Activation (Xu et al.„ 2021). Targeting PERK signaling with the small molecule GSK2606414 prevents neurodegeneration in a model of Parkinson's disease (Mercado et al.„ 2018). Zika Virus Induces an Atypical Tripartite Unfolded Protein Response with Sustained Sensor and Transient Effector Activation and a Blunted BiP Response (Mufrrih et al.„ 2021).
IXA4	1185329-96-7	A	5	IRE1alpha/XBP1 activator	Pharmacologic IRE1/XBP1s activation promotes systemic adaptive remodeling in obesity (Madhavan et al.„ 2022). Small molecule strategies to harness the unfolded protein response: where do we go from here? (Grandjean and Wiseman, 2020).
AA147	393121-74-9	B	5	ATF6 activator	ARF6 is an important host factor for SARS-CoV-2 infection in vitro (Mirabelli et al.„ 2022). Metabolically Activated Proteostasis Regulators Protect against Glutamate Toxicity by Activating NRF2 (Rosarda et al.„ 2021). Pharmacological Activating Transcription Factor 6 Activation Is Beneficial for Liver Retrieval With ex vivo Normothermic Mechanical Perfusion From Cardiac Dead Donor Rats (Cheng et al.„ 2021). Pharmacological activation of ATF6 remodels the proteostasis network to rescue pathogenic GABA(A) receptors (Wang et al.„ 2022). Small molecule strategies to harness the unfolded protein response: where do we go from here? (Grandjean and Wiseman, 2020). Pharmacologic ATF6 activating compounds are metabolically activated to selectively modify endoplasmic reticulum proteins (Paxman et al.„ 2018). Pharmacological activation of ATF6 remodels the proteostasis network to rescue pathogenic GABA(A) receptors (Wang et al.„ 2022). Small molecule proteostasis regulators that reprogram the ER to reduce extracellular protein aggregation (Plate et al.„ 2016). The unfolded protein response regulator ATF6 promotes mesodermal differentiation (Kroeger et al.„ 2018).
MK-28	864388-65-8	C	5	PERK activator	A novel specific PERK activator reduces toxicity and extends survival in Huntington's disease models (Ganz et al.„ 2020).
HSF1A	1196723-93-9	D	5	TRiC inhib./HSF1 act.	A direct regulatory interaction between chaperonin TRiC and stress-responsive transcription factor HSF1 (Neef et al.„ 2014). Modulation of heat shock transcription factor 1 as a therapeutic target for small molecule intervention in neurodegenerative disease (Neef et al.„ 2010).
RTA 408/ Omaveloxolone	1474034-05-3	E	5	Nrf2 act.	The Effects of Two Nrf2 Activators, Bardoxolone Methyl and Omaveloxolone, on Retinal Ganglion Cell Survival during Ischemic Optic Neuropathy (Chien et al.„ 2021). KEAP1 inhibition is neuroprotective and suppresses the development of epilepsy (Shekh-Ahmad et al.„ 2018). Mechanisms and therapeutic implications of RTA 408, an activator of Nrf2, in subarachnoid hemorrhage-induced delayed cerebral vasospasm and secondary brain injury (Tsai et al.„ 2020). A novel Nrf2 activator from microbial transformation inhibits radiation-induced dermatitis in mice (Nakagami and Masuda, 2016). The novel triterpenoid RTA 408 protects human retinal pigment epithelial cells against H2O2-induced cell injury via NF-E2-related factor 2 (Nrf2) activation (Liu et al.„ 2016). RTA 408, A Novel Synthetic Triterpenoid with Broad Anticancer and Anti-Inflammatory Activity (Probst et al.„ 2015). Targeted Nrf2 activation therapy with RTA 408 enhances regenerative capacity of diabetic wounds (Rabbani et al.„ 2018). Topical application of RTA 408 lotion activates Nrf2 in human skin and is well-tolerated by healthy human volunteers (Reisman et al.„ 2015). Topical application of the synthetic triterpenoid RTA 408 activates Nrf2 and induces cytoprotective genes in rat skin (Reisman et al.„ 2014).
CBR-470-1	2416095-06-0	F	5	PGK1 inh./Nrf2 act.	Discovery and SAR studies of 3-amino-4-(phenylsulfonyl)tetrahydrothiophene 1,1-dioxides as non-electrophilic antioxidant response element (ARE) activators (Jo et al.„ 2021). PGK1 inhibitor CBR-470-1 protects neuronal cells from MPP+ (Zheng et al.„ 2020).
Sulforaphane	4478-93-7	G	5	Nrf2 activator	Sulforaphane Activates a lysosome-dependent transcriptional program to mitigate oxidative stress (Li et al.„ 2021). Melatonin-sulforaphane hybrid ITH12674 attenuates glial response in vivo by blocking LPS binding to MD2 and receptor oligomerization (Michalska et al.„ 2020). Role of increased expression of the proteasome in the protective effects of sulforaphane against hydrogen peroxide-mediated cytotoxicity in murine neuroblastoma cells (Kwak et al.„ 2007). Sulforaphane as a potential protective phytochemical against neurodegenerative diseases (Tarozzi et al.„ 2013). Sulforaphane as a potential protective phytochemical against neurodegenerative diseases (Tarozzi et al.„ 2013). Therapeutic approaches to mitochondrial dysfunction in Parkinson's disease (Beal, 2009). Up-Regulation Thioredoxin Inhibits Advanced Glycation End Products-Induced Neurodegeneration (Ren et al.„ 2018).
KI696	1799974-70-1	H	5	Nrf2 activator	Monoacidic Inhibitors of the Kelch-like ECH-Associated Protein 1: Nuclear Factor Erythroid 2-Related Factor 2 (KEAP1:NRF2) Protein-Protein Interaction with High Cell Potency Identified by Fragment-Based Discovery (Davies et al.„ 2016).
Torin 1	1222998-36-8	A	6	mTor inhibitor	Dual mTORC1/C2 inhibitors suppress cellular geroconversion (a senescence program) (Leontieva et al.„ 2015). Dual mTORC1/C2 inhibitors: gerosuppressors with potential anti-aging effect (Sousa-Victor et al.„ 2015). Gerosuppression by pan-mTOR inhibitors (Leontieva and Blagosklonny, 2016). A system to identify inhibitors of mTOR signaling using high-resolution growth analysis in Saccharomyces cerevisiae (Lee et al.„ 2017). Lysosome size, motility and stress response regulated by fronto-temporal dementia modifier TMEM106B (Stagi et al.„ 2014). Two mTOR inhibitors, rapamycin and Torin 1, differentially regulate iron-induced generation of mitochondrial ROS (Huang et al.„ 2017).
PP242 (Torkinib)	1092351-67-1	B	6	mTor inhibitor	Phenotypic Screening Using High-Content Imaging to Identify Lysosomal pH Modulators in a Neuronal Cell Model (Chin et al.„ 2022). Prolyl oligopeptidase inhibition activates autophagy via protein phosphatase 2A (Svarcbahs et al.„ 2020). TNF compromises lysosome acidification and reduces α-synuclein degradation via autophagy in dopaminergic cells (Wang et al.„ 2015).
Rapamycin	53123-88-9	C	6	mTor inhibitor	Long term rapamycin treatment improves mitochondrial DNA quality in aging mice (Bielas et al.„ 2018). Rapamycin Confers Neuroprotection Against Aging-Induced Oxidative Stress, Mitochondrial Dysfunction, and Neurodegeneration in Old Rats Through Activation of Autophagy (Singh et al.„ 2019). Rapamycin modulates tissue aging and lifespan independently of the gut microbiota in Drosophila (Schinaman et al.„ 2019). Rapamycin and fasting sustain autophagy response activated by ischemia/reperfusion injury and promote retinal ganglion cell survival (Russo et al.„ 2018). Rapamycin Confers Neuroprotection Against Aging-Induced Oxidative Stress, Mitochondrial Dysfunction, and Neurodegeneration in Old Rats Through Activation of Autophagy (Singh et al.„ 2019). Rapamycin directly activates lysosomal mucolipin TRP channels independent of mTOR (Zhang et al.„ 2019). Rapamycin improves motor function, reduces 4-hydroxynonenal adducted protein in brain, and attenuates synaptic injury in a mouse model of synucleinopathy (Bai et al.„ 2015). Rapamycin pre-treatment protects against apoptosis (Ravikumar et al.„ 2006). Two mTOR inhibitors, rapamycin and Torin 1, differentially regulate iron-induced generation of mitochondrial ROS (Huang et al.„ 2017).

AZD8055	1009298-09-2	D	6	mTor inhibitor	Acute mTOR inhibition induces insulin resistance and alters substrate utilization in vivo (Kleinert et al.„ 2014). Gerosuppression by pan-mTOR inhibitors (Leontieva and Blagosklonny, 2016). mTORC Inhibitors as Broad-Spectrum Therapeutics for Age-Related Diseases (Walters and Cox, 2018). Pan-mTOR inhibitors sensitize the senolytic activity of navitoclax via mTORC2 inhibition-mediated apoptotic signaling (Xu et al.„ 2022). Prevention of BMS-777607-induced polyploidy/senescence by mTOR inhibitor AZD8055 sensitizes breast cancer cells to cytotoxic chemotherapeutics (Sharma et al.„ 2014). Reversal of phenotypes of cellular senescence by pan-mTOR inhibition (Walters et al.„ 2016).
PI-103	371935-74-9	E	6	control mTor/PI3K inhibitor	Multiple molecular pathways stimulating macroautophagy protect from alpha-synuclein-induced toxicity in human neurons (Höllerhage et al.„ 2019). Akt and autophagy cooperate to promote survival of drug-resistant glioma (Fan et al.„ 2010). Autophagy and Akt promote survival in glioma (Fan and Weiss, 2011). Control of proliferation in astrocytoma cells by the receptor tyrosine kinase/PI3K/AKT signaling axis and the use of PI-103 and TCN as potential anti-astrocytoma therapies (Gürsel et al.„ 2011). A dual phosphoinositide-3-kinase alpha/mTOR inhibitor cooperates with blockade of epidermal growth factor receptor in PTEN-mutant glioma (Fan et al.„ 2007). A dual PI3 kinase/mTOR inhibitor reveals emergent efficacy in glioma (Fan et al.„ 2006). Inhibition of PI3K-Akt-mTOR signaling in glioblastoma by mTORC1/2 inhibitors (Fan and Weiss, 2012).
SMER28	307538-42-7	F	6	autophagy enhancer	Autophagy modulates articular cartilage vesicle formation in primary articular chondrocytes (Rosenthal et al.„ 2015). Compounds activating VCP D1 ATPase enhance both autophagic and proteasomal neurotoxic protein clearance (Wrobel et al.„ 2022). The convergence of endosomal and autophagosomal pathways: implications for APP-CTF degradation (Tian et al.„ 2014). Human Cytomegalovirus Replication Is Inhibited by the Autophagy-Inducing Compounds Trehalose and SMER28 through Distinctively Different Mechanisms (Clark et al.„ 2018). Important role of autophagy in endothelial cell response to ionizing radiation (Kalamida et al.„ 2014). Novel cell- and tissue-based assays for detecting misfolded and aggregated protein accumulation within aggresomes and inclusion bodies (Shen et al.„ 2011). Regulatory role of DEPTOR-mediated cellular autophagy and mitochondrial reactive oxygen species in angiogenesis in multiple myeloma (Wang et al.„ 2021). SMER28 Attenuates Dopaminergic Toxicity Mediated by 6-Hydroxydopamine in the Rats via Modulating Oxidative Burdens and Autophagy-Related Parameters (Darabi et al.„ 2018). SMER28 Attenuates PI3K/mTOR Signaling by Direct Inhibition of PI3K p110 Delta (Kirchenwitz et al.„ 2022). SMER28 is a mTOR-independent small molecule enhancer of autophagy that protects mouse bone marrow and liver against radiotherapy (Koukourakis et al.„ 2018). Uncoupling of ER/Mitochondrial Oxidative Stress in mTORC1 Hyperactivation-Associated Skin Hypopigmentation (Yang et al.„ 2018).
ML-SA1	332382-54-4	G	6	TRPML1 agonist	Differential mechanisms of action of the mucolipin synthetic agonist, ML-SA1, on insect TRPML and mammalian TRPML1 (Feng et al.„ 2014). Effects of silica nanoparticles on endolysosome function in primary cultured neurons (1) (Ye et al.„ 2019). Lysosomal calcium is modulated by STIM1/TRPML1 interaction which participates to neuronal survival during ischemic preconditioning (Tedeschi et al.„ 2021). Reactivation of Lysosomal Ca2+ Efflux Rescues Abnormal Lysosomal Storage in FIG4-Deficient Cells (Zou et al.„ 2015). Sulforaphane Activates a lysosome-dependent transcriptional program to mitigate oxidative stress (Li et al.„ 2021).
KYP-2047	796874-99-2	H	6	prolyl-oligopeptidase (POP) inhibitor,	In situ prolyl oligopeptidase activity assay in neural cell cultures (Klimaviciusa et al.„ 2012). KYP-2047 penetrates mouse brain and effectively inhibits mouse prolyl oligopeptidase (Jalkanen et al.„ 2014). Prolyl oligopeptidase acts as a link between chaperone-mediated autophagy and macroautophagy (Cui et al.„ 2022). Prolyl oligopeptidase inhibition activates autophagy via protein phosphatase 2A (Svarcbahs et al.„ 2020). Prolyl oligopeptidase inhibition by KYP-2407 increases alpha-synuclein fibril degradation in neuron-like cells (Rostami et al.„ 2020). Prolyl oligopeptidase inhibition reduces alpha-synuclein aggregation in a cellular model of multiple system atrophy (Cui et al.„ 2021). Prolyl oligopeptidase inhibition reduces oxidative stress via reducing NADPH oxidase activity by activating protein phosphatase 2A (Eteläinen et al.„ 2021). Prolyl oligopeptidase inhibition reduces PolyQ aggregation and improves cell viability in cellular model of Huntington's disease (Norrbacka et al.„ 2019).
Verapamil	52-53-9	A	7	Ca++ channel blocker	An Autophagy Modifier Screen Identifies Small Molecules Capable of Reducing Autophagosome Accumulation in a Model of CLN3-Mediated Neurodegeneration (Petcherski et al.„ 2019). Verapamil Ameliorates Motor Neuron Degeneration and Improves Lifespan in the SOD1(G93A) Mouse Model of ALS by Enhancing Autophagic Flux (Zhang et al.„ 2019). Verapamil extends lifespan in Caenorhabditis elegans by inhibiting calcineurin activity and promoting autophagy (Liu et al.„ 2020).
Felodipine	72509-76-3	B	7	Ca++ channel blocker decr. Inos. & IP3	[The effect and mechanism of felodipine and valsartan on a novel salt-sensitive hypertensive rat induced by sensory denervation] (Han et al.„ 2005). Felodipine induces autophagy in mouse brains with pharmacokinetics amenable to repurposing (Siddiqi et al.„ 2019).
Fluspiriline	1841-19-6	C	7	antipsychotic 20S, atg act.	An Autophagy Modifier Screen Identifies Small Molecules Capable of Reducing Autophagosome Accumulation in a Model of CLN3-Mediated Neurodegeneration (Petcherski et al.„ 2019). Control of basal autophagy by calpain1 mediated cleavage of ATG5 (Xia et al.„ 2010). Psychotropic Drugs Show Anticancer Activity by Disrupting Mitochondrial and Lysosomal Function (Varalda et al.„ 2020). Small molecule regulators of autophagy identified by an image-based high-throughput screen (Zhang et al.„ 2007).
Pimozide	2062-78-4	D	7	antipsychotic AMPK/ULK1 act.	Automated high-content live animal drug screening using C. elegans expressing the aggregation prone serpin α1-antitrypsin Z (Gosai et al.„ 2010). Neuroleptics as therapeutic compounds stabilizing neuromuscular transmission in amyotrophic lateral sclerosis (Patten et al.„ 2017). The Novel Small Molecule TRVA242 Stabilizes Neuromuscular Junction Defects in Multiple Animal Models of Amyotrophic Lateral Sclerosis (Bose et al.„ 2019). Off-target effects of psychoactive drugs revealed by genome-wide assays in yeast (Ericson et al.„ 2008). Psychotropic Drugs Show Anticancer Activity by Disrupting Mitochondrial and Lysosomal Function (Varalda et al.„ 2020).
Fluphenazine	69-23-8	E	7	antipsychotic (mTor-dep?)	Aging-related Repositioned Drugs, Donepezil and Sildenafil Citrate, Increase Apoptosis of Anti-mitotic Drug-resistant KBV20C Cells Through Different Molecular Mechanisms (Kim et al.„ 2018). Autophagy induction enhances TDP43 turnover and survival in neuronal ALS models (Barmada et al.„ 2014). A cell-based quantitative high-throughput image screening identified novel autophagy modulators (Li et al.„ 2016). Enhancement in Phospholipase D Activity as a New Proposed Molecular Mechanism of Haloperidol-Induced Neurotoxicity (Krzystanek et al.„ 2020).
EN6	1808714-73-9	F	7	vATPase activator lysosomal pH decrease	Covalent targeting of the vacuolar H(+)-ATPase activates autophagy via mTORC1 inhibition (Chung et al., 2019).
SRT2104	1093403-33-8	G	7	sirtuin activator	Axonal protection by a small molecule SIRT1 activator, SRT2104, with alteration of autophagy in TNF-induced optic nerve degeneration (Kitaoka et al.„ 2020). Aβ-Induced Damage Memory in hCMEC/D3 Cells Mediated by Sirtuin-1 (Liu et al.„ 2020). Deacetylation of ZKSCAN3 by SIRT1 induces autophagy and protects SN4741 cells against MPP(+)-induced oxidative stress (Wu et al.„ 2022). Hippocampal insulin resistance and the Sirtuin 1 signaling pathway in diabetes-induced cognitive dysfunction (Yang et al.„ 2021). Molecular and Cellular Characterization of SIRT1 Allosteric Activators (Schultz et al., 2019). P53/NRF2 mediates SIRT1's protective effect on diabetic nephropathy (Ma et al.„ 2019). Pharmacokinetics and tolerability of SRT2104, a first-in-class small molecule activator of SIRT1, after single and repeated oral administration in man (Hoffmann et al.„ 2013). A pilot randomized, placebo controlled, double blind phase I trial of the novel SIRT1 activator SRT2104 in elderly volunteers (Libri et al.„ 2012). Sirt1 activator SRT2104 protects against oxygen-glucose deprivation/reoxygenation-induced injury via regulating microglia polarization by modulating Sirt1/NF-κB pathway (Fu et al.„ 2021). Sirtuin 1 activator SRT2104 protects Huntington's disease mice (Jiang et al.„ 2014). SRT2104 attenuates chronic unpredictable mild stress-induced depressive-like behaviors and imbalance between microglial M1 and M2 phenotypes in the mice (Duan et al.„ 2020).
Selisistat (EX-527)	49843-98-3	H	7	SIRT1 inhibitor	Sirtuin inhibitors, EX527 and AGK2, suppress cellmigration by inhibiting HSF1 protein stability (Kim et al., 2016). Induction of Autophagy and Activation of SIRT-1 Deacetylation Mechanisms Mediate Neuroprotection by the Pomegranate Metabolite Urolithin A in BV2 Microglia and Differentiated 3D Human Neural Progenitor Cells (Velagapudi et al., 2019). Resveratrol protects against doxorubicin-induced cardiotoxicity in aged hearts through the SIRT1-USP7 axis (Sin et al., 2015)

adiporon HCl	1781835-20-8	A	8	PPARα activatorTFEB activator	Mechanisms of Adiponectin Action: Implication of Adiponectin Receptor Agonism in Diabetic Kidney Disease (Kim and Park, 2019). Design, synthesis chalcone derivatives as AdipoR agonist for type 2 diabetes (Zhu et al., 2018). Restoring diabetes-induced autophagic flux arrest in ischemic/reperfused heart by ADIPOR (adiponectin receptor) activation involves both AMPK-dependent and AMPK-independent signaling (Wang et al., 2017). Adiponectin receptor agonist AdipoRon suppresses adipogenesis in C3H10T1/2 cells through the adenosine monophosphateactivated protein kinase signaling pathway (Wang et al., 2017). Activation of Adiponectin Receptor Regulates Proprotein Convertase Subtilisin/Kexin Type 9 Expression and Inhibits Lesions in ApoE-Deficient Mice (Sun et al., 2017). AdipoRon may be benefit for atherosclerosis prevention (Esfahani et al., 2017). Hepatoprotective effects of AdipoRon against d-galactosamine-induced liver injury in mice (Wang et al., 2016). A small-molecule AdipoR agonist for type 2 diabetes and short life in obesity (Okada-Iwabu et al., 2013).
Gemfibrozil	25812-30-0	B	8	PPARα activator TFEB activator	Master Autophagy Regulator Transcription Factor EB Regulates Cigarette Smoke-Induced Autophagy Impairment and Chronic Obstructive Pulmonary Disease-Emphysema Pathogenesis (Bodas et al., 2017). Autophagy augmentation alleviates cigarette smoke-induced CFTR-dysfunction, ceramide-accumulation and COPD-emphysema pathogenesis (Bodas et al., 2019). Activation of peroxisome proliferator-activated receptor alpha induces lysosomal biogenesis in brain cells: implications for lysosomal storage disorders (Ghosh et al., 2015). Fibrates inhibit the apoptosis of Batten disease lymphoblast cells via autophagy recovery and regulation of mitochondrial membrane potential (Hong et al., 2016). Activation of PPARA-mediated autophagy reduces Alzheimer disease-like pathology and cognitive decline in a murine model (Luo et al., 2019).Safety and potential efficacy of gemfibrozil as a supportive treatment for children with late infantile neuronal ceroid lipofuscinosis and other lipid storage disorders (Kim et al., 2017). Gemfibrozil, food and drug administration-approved lipid-lowering drug, increases longevity in mouse model of late infantile neuronal ceroid lipofuscinosis (Ghosh et al., 2017). Gemfibrozil and fenofibrate, Food and Drug Administration-approved lipid-lowering drugs, up-regulate tripeptidyl-peptidase 1 in brain cells via peroxisome proliferator-activated receptor alpha: implications for late infantile Batten disease therapy (Ghosh et al., 2012).
Pirinixic acid /WY14643	50892-23-4	C	8	PPARα/TFEB activ.	Effect of the peroxisome proliferator-activated receptor beta activator GW0742 in rat cultured cerebellar granule neurons (Smith et al.,, 2004). Peroxisomal proliferation protects from beta-amyloid neurodegeneration (Santos et al.,, 2005). PPARα activation attenuates amyloid-β-dependent neurodegeneration by modulating Endo G and AIF translocation (Cheng et al.,, 2015). Therapeutic applications of the versatile fatty acid mimetic WY14643 (Pollinger and Merk, 2017). Tuning Nuclear Receptor Selectivity of Wy14,643 towards Selective Retinoid X Receptor Modulation (Pollinger et al.,, 2019).
Tubastatin A HCl	1310693-92-5	D	8	HDAC6 inhibitor	HDAC6 Inhibition Promotes Transcription Factor EB Activation and Is Protective in Experimental Kidney Disease (Brijmohan et al., 2018). Histone deacetylases and their inhibitors in cancer, neurological diseases and immune disorders (Falkenberg and Johnstone 2014). Advances in Patient-Specific Induced Pluripotent Stem Cells Shed Light on Drug Discovery for Amyotrophic Lateral Sclerosis (Lee et al., 2018). Targeting the proteostasis network in Huntington's disease (Soares et al., 2019). Inhibition of HDAC6 modifies tau inclusion body formation and impairs autophagic clearance (Leyk et al., 2015). Inhibition of HDAC6 increases acetylation of peroxiredoxin1/2 and ameliorates 6-OHDA induced dopaminergic injury (Jian et al., 2017). Bicyclic-Capped Histone Deacetylase 6 Inhibitors with Improved Activity in a Model of Axonal Charcot-Marie-Tooth Disease (Shen et al., 2016). Inhibition of HDAC6 modifies tau inclusion body formation and impairs autophagic clearance (Leyk et al., 2015). Tubastatin A/ACY-1215 improves cognition in Alzheimer's disease transgenic mice (Zhang et al., 2014) Histone deacetylase 6 inhibition improves memory and reduces total tau levels in a mouse model of tau deposition (Selenica et al., 2014). HDAC6 inhibition results in tau acetylation and modulates tau phosphorylation and degradation in oligodendrocytes (Noack et al., 2014).
PRE-084 HCl	75136-54-8	E	8	S1R activator	Neuroprotective effects of the Sigma-1 receptor (S1R) agonist PRE-084, in a mouse model of motor neuron disease not linked to SOD1 mutation (Peviani et al., 2014). Lack of synergistic effect of resveratrol and sigma-1 receptor agonist (PRE-084) in SOD1G(9)(3)A ALS mice: overlapping effects or limited therapeutic opportunity? (Mancuso et al., 2014). Mitochondrial protection by the mixed muscarinic/sigma1 ligand ANAVEX2-73, a tetrahydrofuran derivative, in Abeta25-35 peptide-injected mice, a nontransgenic Alzheimer's disease model (Lahmy et al., 2014). Pharmacological stimulation of sigma-1 receptors has neurorestorative effects in experimental parkinsonism (Francardo et al., 2014). Blockade of Tau hyperphosphorylation and Abeta(1)(-)(4)(2) generation by the aminotetrahydrofuran derivative ANAVEX2-73, a mixed muscarinic and sigma(1) receptor agonist, in a nontransgenic mouse model of Alzheimer's disease (Lahmy et al., 2013). Sigma-1 Receptor Agonists Induce Oxidative Stress in Mitochondria and Enhance Complex I Activity in Physiological Condition but Protect Against Pathological Oxidative Stress (Goguadze et al., 2019). Glial Activation and Central Synapse Loss, but Not Motoneuron Degeneration, Are Prevented by the Sigma-1 Receptor Agonist PRE-084 in the Smn2B/- Mouse Model of Spinal Muscular Atrophy (Cervero et al., 2018). Dipentylammonium Binds to the Sigma-1 Receptor and Protects Against Glutamate Toxicity, Attenuates Dopamine Toxicity and Potentiates Neurite Outgrowth in Various Cultured Cell Lines (Brimson et al., 2018). Sigma 1 receptor activation modifies intracellular calcium exchange in the G93A(hSOD1) ALS model (Tadic et al., 2017). Sigma-1 receptor activation inhibits osmotic swelling of rat retinal glial (Muller) cells by transactivation of glutamatergic and purinergic receptors (Vogler et al., 2016). Protection by sigma-1 receptor agonists is synergic with donepezil, but not with memantine, in a mouse model of amyloid-induced memory impairments (Maurice 2016). Toward the identification of neuroprotective agents: g-scale synthesis, pharmacokinetic evaluation and CNS distribution of (R)-RC-33, a promising SIGMA1 receptor agonist (Marra et al., 2016). Neuro2A cells in 1% serum treated with the sigma-1 receptor agonist PRE-084 (10 μM) PC6.3 neuronal cells expressing mHtt: DRG explants: 10uM increased neurite length; improved survival of MNs Cerebellar Granule neurons: 10uM promoted neurite outgrowth. MDA-MB-468, T47D breast adenocarcinomas: 50uM did not stimulate atg formation or autophagic flux. SOD1(G93A) mice were daily administration 0.25 mg/kg, 8-16 weeks of age. Improved MN function, locomotor behavior, extended survival, reduced microglial activation Reduced NMDAR-mediated excitotoxic brain injury in grey matter if administered 1 hour after injury. The low dose of 0.1μg/g body weight was as effective as the high dose of 10μg/g bw compared to PBS. 0.25 mg/kg/day attenuated reactive gliosis, mitigated M1/M2 imbalance, and prevented MN deafferentation in Smn2B/- SMA mice. Experimental parkinsonism intrastriatal 6-OH-dopamine lesions: daily treatments, 5 wks with 0.3mg/kg/day--improved spontaneous forelimb use, increased dopaminergic fibers in denervated striatal regions, improved dopamine levels, upregulated BDNF and GDNF.
6-Bio (GSK3 Inhibitor IX)	667463-62-9	F	8	ATP-competitive inhibitor of GSK-3α and GSK-3β.	Anti-fibrotic effect of 6-bromo-indirubin-3'-oxime (6-BIO) via regulation of activator protein-1 (AP-1) and specificity protein-1 (SP-1) transcription factors in kidney cells (Park et al.,, 2022). 6-Bromoindirubin-3'-Oxime (6BIO) Suppresses the mTOR Pathway, Promotes Autophagy, and Exerts Anti-aging Effects in Rodent Liver (Guo et al.,, 2019). A novel autophagy modulator 6-Bio ameliorates SNCA/alpha-synuclein toxicity (Suresh et al.,, 2017). Inhibition of glycogen synthase kinase-3beta downregulates total tau proteins in cultured neurons and its reversal by the blockade of protein phosphatase-2A (Martin et al.,, 2009).
Cilostazol	73963-72-1	G	8	PDE3A inhibitor	Cilostazol protects against myocardial ischemia and reperfusion injury by activating transcription factor EB (TFEB) (Li et al., 2019). Cilostazol protects hepatocytes against alcohol-induced apoptosis via activation of AMPK pathway (Lee et al., 2019). Cilostazol Mediated Nurr1 and Autophagy Enhancement: Neuroprotective Activity in Rat Rotenone PD Model (Hedya et al., 2018). Cilostazol Modulates Autophagic Degradation of beta-Amyloid Peptide via SIRT1-Coupled LKB1/AMPKalpha Signaling in Neuronal Cells (Park et al., 2016). Cilostazol Upregulates Autophagy via SIRT1 Activation: Reducing Amyloid-beta Peptide and APP-CTFbeta Levels in Neuronal Cells (Lee et al., 2015).
Carbamazepine	298-46-4	H	8		The autophagy-enhancing drug carbamazepine improves neuropathology and motor impairment in mouse models of Machado-Joseph disease. Vasconcelos-Ferreira A, Carmo-Silva S, Codêsso JM, Silva P, Martinez ARM, França MC Jr, Nóbrega C, Pereira de Almeida L. Neuropathol Appl Neurobiol. 2022 Feb;48(1):e12763. doi: 10.1111/nan.12763. Epub 2021 Oct 13. PMID: 34432315 Kim JS, Wang JH, Biel TG et al: Carbamazepine suppresses calpain-mediated autophagy impairment after ischemia/reperfusion in mouse livers. Toxicol Appl Pharmacol, 2013; Sarkar S, Ravikumar B, Floto RA, Rubinsztein DC: Rapamycin and mTOR-independent autophagy inducers ameliorate toxicity of polyglutamine-expanded huntingtin and related proteinopathies. Cell Death Differ, 2009). Li L, Zhang S, Zhang X et al: Autophagy enhancer carbamazepine alleviates memory deficits and cerebral amyloid-beta pathology in a mouse model of Alzheimer's disease. Curr Alzheimer Res, 2013; 10: 433–41. Hidvegi T, Ewing M, Hale P et al: An autophagy-enhancing drug promotes degradation of mutant alpha1-antitrypsin Z and reduces hepatic fibrosis. Science, 2010; 329: 229–32
Bafilomycin-A1	88899-55-2	A	9	vATPase inhibitor	Amyloid beta peptide promotes lysosomal degradation of clusterin via sortilin in hippocampal primary neurons (Wang et al.,, 2017). Rescue of progranulin deficiency associated with frontotemporal lobar degeneration by alkalizing reagents and inhibition of vacuolar ATPase (Capell et al.,, 2011). Sulforaphane Activates a lysosome-dependent transcriptional program to mitigate oxidative stress (Li et al.,, 2021). TNF compromises lysosome acidification and reduces α-synuclein degradation via autophagy in dopaminergic cells (Wang et al.,, 2015).
MRT68921	2080306-21-2	B	9	ULK1/2 inhibitor	STAT3 suppresses the AMPKα/ULK1-dependent induction of autophagy in glioblastoma cells (Bhattacharya et al.,, 2022). AMPK activation does not enhance autophagy in neurons in contrast to MTORC1 inhibition: different impact on β-amyloid clearance (Benito-Cuesta et al.,, 2021). Assessing Autophagy in Microglia: A Two-Step Model to Determine Autophagosome Formation, Degradation, and Net Turnover (Plaza-Zabala et al.,, 2020). Dual targeting of NUAK1 and ULK1 using the multitargeted inhibitor MRT68921 exerts potent antitumor activities (Chen et al.,, 2020). Pharmacological inhibition of ULK1 kinase blocks mammalian target of rapamycin (mTOR)-dependent autophagy (Petherick et al.,, 2015).

SAR405	1523406-39-4	C	9	vps34 autophagy inhibitor	The neurosteroid allopregnanolone protects retinal neurons by effects on autophagy and GABRs/GABA(A) receptors in rat glaucoma models (Ishikawa et al.,, 2021). Reduction of Autophagosome Overload Attenuates Neuronal Cell Death After Traumatic Brain Injury (Quan et al.,, 2021). SAR405, a Highly Specific VPS34 Inhibitor, Disrupts Auditory Fear Memory Consolidation of Mice via Facilitation of Inhibitory Neurotransmission in Basolateral Amygdala (Li et al.,, 2019). A highly potent and selective Vps34 inhibitor alters vesicle trafficking and autophagy (Ronan et al.,, 2014). SAR405, a PIK3C3/Vps34 inhibitor that prevents autophagy and synergizes with MTOR inhibition in tumor cells (Pasquier, 2015).
C381	not listed	D	9	vATPase activator lysosomal pH decrease	Small molecule C381 targets the lysosome to reduce inflammation and ameliorate disease in models of neurodegeneration (Vest et al.,, 2022).
3-Methyladenine	5142-23-4	E	9	autophagy inhibitor	17-AAG induces cytoplasmic alpha-synuclein aggregate clearance by induction of autophagy (Riedel et al.,, 2010). Dysregulated autophagy in the RPE is associated with increased susceptibility to oxidative stress and AMD (Mitter et al.,, 2014). Effects of Cellular Pathway Disturbances on Misfolded Superoxide Dismutase-1 in Fibroblasts Derived from ALS Patients (Keskin et al.,, 2016). Small molecule-driven NLRP3 inflammation inhibition via interplay between ubiquitination and autophagy: implications for Parkinson disease (Han et al.,, 2019).
YM201636	371942-69-7	F	9	PIKfyve inhibitor	Inhibition of PIKfyve by YM-201636 dysregulates autophagy and leads to apoptosis-independent neuronal cell death (Martin et al.,, 2013). Inhibition of PIKfyve using YM201636 suppresses the growth of liver cancer via the induction of autophagy (Hou et al.,, 2019). PIKfyve inhibition interferes with phagosome and endosome maturation in macrophages (Kim et al.,, 2014). Vacuolin-1 inhibits autophagy by impairing lysosomal maturation via PIKfyve inhibition (Sano et al.,, 2016).
EACC	864941-31-1	G	9	inhibits SNARE Stx17 translocation	A reversible autophagy inhibitor blocks autophagosome-lysosome fusion by preventing Stx17 loading onto autophagosomes (Vats and Manjithaya, 2019).
Apilimod	541550-19-0	H	9	PIKfyve inhibitor	ELAVL4, splicing, and glutamatergic dysfunction precede neuron loss in MAPT mutation cerebral organoids (Bowles et al.,, 2021). PIKfyve inhibition increases exosome release and induces secretory autophagy (Hessvik et al.,, 2016).
ZLN005	49671-76-3	A	10	PGC-1α Activator	PGC-1α activator ZLN005 promotes maturation of cardiomyocytes derived from human embryonic stem cells (Liu et al.,, 2020). PGC-1α alleviates mitochondrial dysfunction via TFEB-mediated autophagy in cisplatin-induced acute kidney injury (Yuan et al.,, 2021). Novel small-molecule PGC-1α transcriptional regulator with beneficial effects on diabetic db/db mice (Zhang et al.,, 2013). The PGC-1α Activator ZLN005 Ameliorates Ischemia-Induced Neuronal Injury In Vitro and In Vivo (Xu et al.,, 2018). Pharmaceutical Induction of PGC-1α Promotes Retinal Pigment Epithelial Cell Metabolism and Protects against Oxidative Damage (Satish et al.,, 2018). ZLN005 protects cardiomyocytes against high glucose-induced cytotoxicity by promoting SIRT1 expression and autophagy (Li et al.,, 2016).
CA77.1	2412270-22-3	B	10	(QX77/AR7 analog) CMA activator	Chaperone-Mediated Autophagy Upregulation Rescues Megalin Expression and Localization in Cystinotic Proximal Tubule Cells (Zhang et al.,, 2019). Analysis of Chaperone-Mediated Autophagy (Juste and Cuervo, 2019). Chemical modulation of chaperone-mediated autophagy by retinoic acid derivatives (Anguiano et al.,, 2013). Cystinosin, the small GTPase Rab11, and the Rab7 effector RILP regulate intracellular trafficking of the chaperone-mediated autophagy receptor LAMP2A (Zhang et al.,, 2017).
MF-094	2241025-68-1	C	10	USP30 inhibitor mitophagy activator	MF-094, a potent and selective USP30 inhibitor, accelerates diabetic wound healing by inhibiting the NLRP3 inflammasome (Li et al.,, 2022). Novel highly selective inhibitors of ubiquitin specific protease 30 (USP30) accelerate mitophagy (Kluge et al.,, 2018).
FT385 (FT3967385)	No CAS number	D	10	USP30 inhibitor mitophagy activator	USP30 sets a trigger threshold for PINK1-PARKIN amplification of mitochondrial ubiquitylation (Rusilowicz-Jones et al.,, 2020).
JQ1	1268524-70-4	E	10	Inhibitor of BRD2, BRD4, BRD3, BRDT bromodomain proteins	BRD4 contributes to LPS-induced macrophage senescence and promotes progression of atherosclerosis-associated lipid uptake (Wang et al.,, 2020). Brd4-p300 inhibition downregulates Nox4 and accelerates lung fibrosis resolution in aged mice (Sanders et al.,, 2020). Degradation and inhibition of epigenetic regulatory protein BRD4 exacerbate Alzheimer's disease-related neuropathology in cell models (Zhang et al.,, 2022). Neuroprotective effects of targeting BET proteins for degradation with dBET1 in aged mice subjected to ischemic stroke (DeMars et al.,, 2019). The Senolytic Drug JQ1 Removes Senescent Cells via Ferroptosis (Go et al.,, 2021). Sequential targeting of YAP1 and p21 enhances the elimination of senescent cells induced by the BET inhibitor JQ1 (Zhang et al.,, 2021). Photoreceptor protection via blockade of BET epigenetic readers in a murine model of inherited retinal degeneration (Zhao et al.,, 2017).
SB202190 HCl	350228-36-3	F	10	p38 MAPK Inhibitor	A stress response p38 MAP kinase inhibitor SB202190 promoted TFEB/TFE3-dependent autophagy and lysosomal biogenesis independent of p38 (Yang et al.,, 2020). Role of p38/MAPKs in Alzheimer's disease: implications for amyloid beta toxicity targeted therapy (Kheiri et al.,, 2018). Activation of p38MAPK contributes to expanded polyglutamine-induced cytotoxicity (Tsirigotis et al.,, 2008). Mitogen-activated protein kinase regulates neurofilament axonal transport (Chan et al.,, 2004). p38 MAP kinase is involved in lipopolysaccharide-induced dopaminergic neuronal cell death in rat mesencephalic neuron-glia cultures (Jeohn et al.,, 2002).
NSC697923	343351-67-7	G	10	UBE2N inhibitor	Dynamic regulation of dynein localization revealed by small molecule inhibitors of ubiquitination enzymes (Monda and Cheeseman, 2018). A small-molecule inhibitor of UBE2N induces neuroblastoma cell death via activation of p53 and JNK pathways (Cheng et al.,, 2014).
PD169316	152121-53-4	H	10	proteasome activator/p38 inhibitor	Proteasome Activation by Small Molecules (Leestemaker et al.,, 2017). Role of p38/MAPKs in Alzheimer's disease: implications for amyloid beta toxicity targeted therapy (Kheiri et al.,, 2018). Small molecules for fat combustion: targeting obesity (Liu et al.,, 2019). Suramin and NF449 are IP5K inhibitors that disrupt IP6-mediated regulation of cullin RING ligase and sensitize cancer cells to MLN4924/pevonedistat (Zhang et al.,, 2020).
Sildenafil	171599-83-0	A	11	PDE5 inhibitor, Protein Kinase G activation	Verplank et al., 2022; Ranek et al., 2013 26S Proteasomes are rapidly activated by diverse hormones and physiological states that raise cAMP and cause Rpn6 phosphorylation (VerPlank et al.,, 2019). Exploring the Regulation of Proteasome Function by Subunit Phosphorylation (VerPlank and Goldberg, 2018). Impairment of protein degradation and proteasome function in hereditary neuropathies (VerPlank et al.,, 2018). Regulating protein breakdown through proteasome phosphorylation (VerPlank and Goldberg, 2017). cAMP-induced phosphorylation of 26S proteasomes on Rpn6/PSMD11 enhances their activity and the degradation of misfolded proteins (Lokireddy et al.,, 2015).
Forskolin	66575-29-9	B	11	adenylyl cyclase activator	Phenotypic transition of microglia into astrocyte-like cells associated with disease onset in a model of inherited ALS (Trias et al.,, 2013). AMPA silencing is a prerequisite for developmental long-term potentiation in the hippocampal CA1 region (Abrahamsson et al.,, 2008). The cAMP/PKA Pathway Inhibits Beta-amyloid Peptide Release from Human Platelets (Sepúlveda et al.,, 2019). Enhancing the GLP-1 receptor signaling pathway leads to proliferation and neuroprotection in human neuroblastoma cells (Li et al.,, 2010).
Rolipram	61413-54-5	C	11	PDE4 inhibitor	Amyloid beta -peptide inhibition of the PKA/CREB pathway and long-term potentiation: reversibility by drugs that enhance cAMP signaling (Vitolo et al.,, 2002). Phosphodiesterase 4 inhibitor activates AMPK-SIRT6 pathway to prevent aging-related adipose deposition induced by metabolic disorder (Wang et al.,, 2018). Potent PDE4 inhibitor activates AMPK and Sirt1 to induce mitochondrial biogenesis (Park et al.,, 2021). Evaluation of longevity enhancing compounds against transactive response DNA-binding protein-43 neuronal toxicity (Tauffenberger et al.,, 2013). The phosphodiesterase-4 inhibitor rolipram protects from ischemic stroke in mice by reducing blood-brain-barrier damage, inflammation and thrombosis (Kraft et al.,, 2013). Reversal of long-term dendritic spine alterations in Alzheimer disease models (Smith et al.,, 2009).
Bay11-7082	19542-67-7	D	11	IκBα phosphorylation and NF-κB inhibitor.	Age sensitivity of NFκB abundance and programmed cell death in erythrocytes induced by NFκB inhibitors (Ghashghaeinia et al.,, 2013). BAY 11-7082 inhibits the secretion of interleukin-6 by senescent human microglia (Cook et al.,, 2022). Kainic acid hyperphosphorylates tau via inflammasome activation in MAPT transgenic mice (Zheng et al.,, 2019). Kainic acid Induces production and aggregation of amyloid β-protein and memory deficits by activating inflammasomes in NLRP3- and NF-κB-stimulated pathways (Ruan et al.,, 2019). Nuclear factor-kappaB-dependent reversal of aging-induced alterations in T cell cytokines (Huang et al.,, 2008). Poly(ADP-ribose)polymerase 1 inhibition protects against age-dependent endothelial dysfunction (Zhang et al.,, 2015).
SEW04784	not listed	E	11	aha1 cochaperone:HSP90 PPI inhibitor	Management of Hsp90-Dependent Protein Folding by Small Molecules Targeting the Aha1 Co-Chaperone (Singh et al.,, 2020).

A3	496011-51-9	F	11	HSF1 activator	Heat shock response activation exacerbates inclusion body formation in a cellular model of Huntington disease (Bersuker et al.„ 2013). Calamini et al., (2010). ML346: A Novel Modulator of Proteostasis for Protein Conformational Diseases. In Probe Reports from the NIH Molecular Libraries Program (Bethesda (MD): National Center for Biotechnology Information (US)). Small-molecule proteostasis regulators for protein conformational diseases (Calamini et al.„ 2011).
F1	100872-83- 1	G	11	HSF1 activator	Heat shock response activation exacerbates inclusion body formation in a cellular model of Huntington disease (Bersuker et al.„ 2013). Calamini et al., (2010). ML346: A Novel Modulator of Proteostasis for Protein Conformational Diseases. In Probe Reports from the NIH Molecular Libraries Program (Bethesda (MD): National Center for Biotechnology Information (US)). Small-molecule proteostasis regulators for protein conformational diseases (Calamini et al.„ 2011).
NSC363998	not listed yet	H	11	Neddylation inhibitor	Neddylation activity modulates the neurodegeneration associated with fragile X associated tremor/ataxia syndrome (FXTAS) through regulating Sima (Lin et al.„ 2020).
SRT1720	1001645-58-4	A	12	sirtuin activator	Catalysis and mechanistic insights into sirtuin activation (Dittenhafer-Reed et al.„ 2011). Oral resveratrol reduces neuronal damage in a model of multiple sclerosis (Shindler et al.„ 2010). Sirtuin1 over-expression does not impact retinal vascular and neuronal degeneration in a mouse model of oxygen-induced retinopathy (Michan et al.„ 2014). Sirtuin functions and modulation: from chemistry to the clinic (Carafa et al.„ 2016).
EN460	496807-64-8	B	12	ERO1-alpha inhibitor	CYT997(Lexibulin) induces apoptosis and autophagy through the activation of mutually reinforced ER stress and ROS in osteosarcoma (Wang et al.„ 2019). High-content screen using zebrafish (Danio rerio) embryos identifies a novel kinase activator and inhibitor (Geldenhuys et al.„ 2017). A small molecule inhibitor of endoplasmic reticulum oxidation 1 (ERO1) with selectively reversible thiol reactivity (Blais et al.„ 2010).
A-485	1889279-16-6	**C**	**12**	Acetylase activator inhibitor	Domain-Independent Inhibition of CBP/p300 Attenuates α-Synuclein Aggregation (Hlushchuk et al.„ 2021). Discovery of a selective catalytic p300/CBP inhibitor that targets lineage-specific tumours (Lasko et al.„ 2017). Targeting Lineage-specific MITF Pathway in Human Melanoma Cell Lines by A-485, the Selective Small-molecule Inhibitor of p300/CBP (Wang et al.„ 2018).
WP1066	857064-38-1	**D**	**12**	JAK2/STAT3 inhibitor	Effect of the STAT3 inhibitor STX-0119 on the proliferation of cancer stem-like cells derived from recurrent glioblastoma (Ashizawa et al.„ 2013). The role of STAT3 in autophagy (You et al.„ 2015). Chemokine CCL2-CCR2 Signaling Induces Neuronal Cell Death via STAT3 Activation and IL-1β Production after Status Epilepticus (Tian et al.„ 2017).
HA15	1609402-14-3	**E**	**12**	GRP78 inhibitor	Compounds Triggering ER Stress Exert Anti-Melanoma Effects and Overcome BRAF Inhibitor Resistance (Cerezo et al.„ 2016). GRP78 blockade overcomes intrinsic resistance to UBA1 inhibitor TAK-243 in glioblastoma (Zhang et al.„ 2022). HA15 alleviates bone loss in ovariectomy-induced osteoporosis by targeting HSPA5 (Han et al.„ 2021). New anti-cancer molecules targeting HSPA5/BIP to induce endoplasmic reticulum stress, autophagy and apoptosis (Cerezo and Rocchi, 2017). Proteomic Discovery of VEEV E2-Host Partner Interactions Identifies GRP78 Inhibitor HA15 as a Potential Therapeutic for Alphavirus Infections (Barrera et al.„ 2021). Targeted inhibition of GRP78 by HA15 promotes apoptosis of lung cancer cells accompanied by ER stress and autophagy (Wu et al.„ 2020).
MS.001	53619-67-3	**F**	**12**	CHIP inhibitor	Chemical Regulation of the Protein Quality Control E3 Ubiquitin Ligase C-Terminus of Hsc70 Interacting Protein (CHIP) (Kanack et al.„ 2022).
VH298	2097381-85-4	**G**	**12**	potent inhibitor of the VHL:HIF-α interaction	Potent and selective chemical probe of hypoxic signalling downstream of HIF-α hydroxylation via VHL inhibition (Frost et al.„ 2016). Rapid and Reversible Knockdown of Endogenously Tagged Endosomal Proteins via an Optimized HaloPROTAC Degrader (Tovell et al.„ 2019). Von Hippel-Lindau (VHL) small-molecule inhibitor binding increases stability and intracellular levels of VHL protein (Frost et al.„ 2021).
IOX2	931398-72-0	**H**	**12**	PHD domain inhibitor, HIF1a activator	Direct Peritoneal Resuscitation with Pyruvate Protects the Spinal Cord and Induces Autophagy via Regulating PHD2 in a Rat Model of Spinal Cord Ischemia-Reperfusion Injury (Xiong et al.„ 2020). RNA-seq analysis of PHD and VHL inhibitors reveals differences and similarities to the hypoxia response (Frost et al.„ 2019). Von Hippel-Lindau (VHL) small-molecule inhibitor binding increases stability and intracellular levels of VHL protein (Frost et al.„ 2021).