



**Long Term Infusion
Using ALZET® Osmotic Pumps**

ALZET pumps range in duration from 24 hours to 6 weeks. Animals can be dosed for periods which exceed the duration of a single pump by serial reimplantation of fresh pumps. This collection of references includes only the most recent citations. However, we do have older references which include infusions of as long as 3 years and in which up to 52 serial implantations have been performed on a single animal. The following table indicates the longest published duration of administration by animal along with a reference.

ANIMAL	DURATION	PUMPS REPLACED	REFERENCE
Mouse	9 months	Every month	Q5858 X. Guo, <i>et al.</i> VCP recruitment to mitochondria causes mitophagy impairment and neurodegeneration in models of Huntington's disease. <i>Nat Commun</i> 2016;7:12646
Rabbit	36 weeks	Every 4 weeks	P8478 Ma T Modulation of allograft incorporation by growth factors over a prolonged continuous infusion of duration in vivo. <i>Bone</i> 2007; 41(3):386-392
Rat	1 year	Not stated	P0818 Murphy WM, Blatnik AF, Shelton TB, Soloway MS. Carcinogenesis in mammalian urothelium: changes induced by non-carcinogenic substances and chronic indwelling catheters. <i>J Urol</i> 1986; 135(4):840-844
Dog	18 months	Every 2-4 weeks	P0752 McRae GI, Roberts BB, Worden AC, Bajka A, Vickery BH. Long-term reversible suppression of oestrus in bitches with nafarelin acetate, a potent LHRH agonist. <i>J Reprod Fertil</i> 1985; 74(2):389-397
Cattle	9 weeks	Every 28 days	Q2176: A. Contri, <i>et al.</i> Successful use of a gonadotropin-releasing hormone (GnRH) analog for the treatment of tertiary hypogonadism (GnRH deficiency) in a 5-year-old Belgian Blue bull. <i>VETERINARY QUARTERLY</i> 2012;32(1):51-54
*Guinea-pig	12 weeks	Every 6 weeks	Q2910 F. Y. Wei, <i>et al.</i> Attenuation of osteoarthritis via blockade of the SDF-1/CXCR4 signaling pathway. <i>Arthritis Research & Therapy</i> 2012;14(4):U233-U243
Monkey	3 years	Every 3 weeks	P2083 Ravindranath N, Ramesh V, Krishnamurthy H, Roa AJ, Moudgal RN. Chronic suppression of testicular function by constant infusion of gonadotropin-releasing hormone agonist and testosterone supplementation in the bonnet monkey (<i>Macaca radiata</i>). <i>Fertil Steril</i> 1992; 57(3):671-676.

**In some cases, more than one study infused for this duration.*

The short abstract following each reference in the attached list details the substance(s) infused, route of administration, animal model studied, solvent(s), model of pump, duration of infusion, and whether stress to the animal was noted.

Note: This list does not contain references in this category from before the years specified. To obtain a complete listing of earlier references, contact ALZET Technical Services at 800-692-2990 (U.S. & Canada) or by email at alzet@duirect.com.



Recent References (2019-Present) on the Long Term Administration of Agents
Using ALZET® Osmotic Pumps

Q11059: K. Momenzadeh, *et al.* Propylene glycol and Kolliphor as solvents for systemic delivery of cannabinoids via intraperitoneal and subcutaneous routes in preclinical studies: a comparative technical note. *Journal of Cannabis Research* 2023;5(1):24

Agents: Tetrahydrocannabinol; cannabinoids **Vehicle:** Propylene glycol; Kolliphor; ethanol; saline; **Route:** SC; **Species:** Rat; **Strain:** Sprague-Dawley; **Pump:** 2ML4; **Duration:** 8 weeks;

ALZET Comments: Dose (20 mg/kg); controls received mp w/ vehicle; animal info (13-week male (approximately 330 g,); post op. care (Enrofloxacin); pumps replaced after 4 weeks; comparison of injection vs mp; stress/adverse reaction: (see pg.3-5); used sterile technique and changed solvent; "We conclude that subcutaneous delivery utilizing osmotic pumps with Kolliphor as a solvent provides viable and consistent route of administration for long-term systemic cannabinoid delivery in the preclinical context."

Q11273: Y. Fu, *et al.* Effects of Leptin and Body Weight on Inflammation and Knee Osteoarthritis Phenotypes in Female Rats. *JBMR Plus* 2023;7(7):e10754

Agents: Leptin, recombinant **Vehicle:** Tris hydrochloride; **Route:** SC; **Species:** Rat; **Strain:** Zucker (F344 BN F1); **Pump:** 2006; **Duration:** 23 weeks;

ALZET Comments: Dose (3.6 ug/day); Controls received mp w/ vehicle; animal info (Female; Obese; 12 months old, hybrid); pumps replaced every 5 weeks; long-term study; functionality of mp verified by plasma levels p. 7

Q10908: D. Zhu, *et al.* Irisin Rescues Diabetic Cardiac Microvascular Injury Via ERK1/2/Nrf2/HO-1 Mediated Inhibition of Oxidative Stress. *Diabetes Research and Clinical Practice* 2022;183(109170)

Agents: Irisin **Vehicle:** Saline; **Route:** IP; **Species:** Mice; **Strain:** T2DM; **Pump:** Not Stated; **Duration:** 12 weeks;

ALZET Comments: Dose (0.5 ug/g body weight/day); controls received mp w/ vehicle; animal info (Male; Fed a high fat diet at 4 weeks old to induce diabetes); long-term study; cardiovascular; diabetes; Therapeutic indication (Diabetes);

Q10651: T. Prasse, *et al.* Bisphenol A-Related Effects on Bone Morphology and Biomechanical Properties in an Animal Model. *Toxics* 2022;10(2):

Agents: Bisphenol A **Vehicle:** DMSO; **Route:** SC; **Species:** Rat; **Strain:** Wistar; **Pump:** 2ML4; **Duration:** 12 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (rats total; 10 weeks old); post op. care (Metamizole); pumps replaced every 4 weeks; long-term study; toxicology;

Q11206: E. Minakova, *et al.* Perinatal oxycodone exposure causes long-term sex-dependent changes in weight trajectory and sensory processing in adult mice. *Psychopharmacology (Berl)* 2022;239(12):3859-3873

Agents: Oxycodone **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Strain:** C57BL/6J; **Duration:** 4 weeks; 6 weeks;

ALZET Comments: Dose-response: 5, 10, 15 mg/kg/day; 0.9% NaCl used; Controls received mp w/ vehicle; animal info: adult male; behavioral testing: (see p.3861) Table 1; dependence; "Specifically, we implemented subcutaneous, continuous infusion of oxycodone (Oxy) at different durations enabling comparison of the long-term consequences of Oxy exposure until birth (short Oxy) to the impact of continued postnatal opioid exposure (long Oxy) spanning gestation through birth and lactation." p. 2

Q11190: C. Liu, *et al.* Mitochondrial HSF1 triggers mitochondrial dysfunction and neurodegeneration in Huntington's disease. *EMBO Molecular Medicine* 2022;14(7):e15851

Agents: DH1 peptide; TAT peptide, control **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Strain:** YAC128 (transgenic); **Pump:** 2006; **Duration:** 3 months;

ALZET Comments: Dose (3 mg/kg/day); Controls received mp w/ vehicle; animal info: Male; Wild-type; 6 months old; behavioral testing (Open-field test; Rotarod test); pumps replaced every 6 weeks; long-term study; peptides; neurodegenerative (Huntington's Disease); "Of note, continuous treatment of DH1 improved motor deficits, as tested by open-field test." p. 10



Q10385: Y. Hasuike, *et al.* CAG repeat-binding small molecule improves motor coordination impairment in a mouse model of Dentatorubral-pallidolusian atrophy. *Neurobiology of Disease* 2022;163(105604

Agents: Naphthyridine-azaquinolone **Vehicle:** PBS; **Route:** CSF/CNS (right lateral ventricle); **Species:** Mice; **Strain:** Not Stated; **Pump:** 2004; **Duration:** 16 weeks;

ALZET Comments: Dose (2 mM); Controls received mp w/ vehicle; animal info (6 weeks old); behavioral testing (Tested motor function with rotarod device; Beam-walking test); pumps replaced every 4 weeks; long-term study; ALZET brain infusion kit used; Brain coordinates (0.4 mm posterior; 1.0 mm right lateral; 2.5 mm ventral); neurodegenerative (Dentatorubral-pallidolusian atrophy); Therapeutic indication (DRPLA);

Q9957: T. Wakamatsu, *et al.* Type I Angiotensin II Receptor Blockade Reduces Uremia-Induced Deterioration of Bone Material Properties. *Journal of Bone & Mineral Research* 2021;36(1):67-79

Agents: Olmesartan, Hydralazine Hydrochloride **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Strain:** Not Stated; **Pump:** 2ML2; **Duration:** 6 weeks;

ALZET Comments: Dose (Olmesartan- 3 mg/kg/day or Hydralazine Hydrochloride- 10 mg/kg/day); Controls received mp w/ vehicle; animal info (); pumps replaced every 2 weeks; long-term study; Blood pressure measured via Tail Cuff Method

Q9538: X. Wang, *et al.* Nogo receptor decoy promotes recovery and corticospinal growth in non-human primate spinal cord injury. *Brain* 2020;143(6):1697-1713

Agents: NgR1(310)-Fc **Vehicle:** Not Stated; **Route:** CSF/CNS (spinal cord); **Species:** Monkey; **Strain:** African green;

Pump: 2ML4; **Duration:** 4 months;

ALZET Comments: Dose (0.10-0.17 mg/kg/day); Controls received mp w/ vehicle; animal info (Adult African green monkeys (vervets, female, baseline body weight 4.2–7.2 kg)); pumps replaced every month; long-term study; NgR1(310)-Fc aka Nogo receptor decoy protein; spinal cord injury;

Q9536: L. Wang, *et al.* Treatment With Treprostinil and Metformin Normalizes Hyperglycemia and Improves Cardiac Function in Pulmonary Hypertension Associated With Heart Failure With Preserved Ejection Fraction. *Arteriosclerosis, Thrombosis, and Vascular Biology* 2020;40(6):1543-1558

Agents: Treprostinil **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat, Mice; **Strain:** ZSF1; **Pump:** 2ML4, 2006; **Duration:** 16 weeks;

ALZET Comments: Dose (40, 300, and 900 ng/kg/min); animal info (8-week old male obese ZSF1 rats; 8-week old male C57BL/6J mice); pumps replaced every 28 or 42 days; long-term study; cardiovascular;

Q9526: G. Wang, *et al.* The study of targeted blocking SDF-1/CXCR4 signaling pathway with three antagonists on MMPs, type II collagen, and aggrecan levels in articular cartilage of guinea pigs. *Journal of Orthopaedic Surgery and Research* 2020;15(1):195

Agents: T140; AMD3100; TN14003 **Vehicle:** PBS; **Route:** SC; **Species:** Guinea Pig; **Strain:** Duncan-Hartley; **Pump:** Not Stated; **Duration:** 12 weeks;

ALZET Comments: Dose (180 ug/ml); Controls received mp w/ vehicle; animal info (male Duncan-Hartley guinea pigs (6-month-old, weight = 600 ± 50g)); pumps replaced every 6 weeks; long-term study; dependence;

Q9469: Y. Shi, *et al.* RIPK3 blockade attenuates tubulointerstitial fibrosis in a mouse model of diabetic nephropathy. *Scientific Reports* 2020;10(1):10458

Agents: Dabrafenib **Vehicle:** DMSO; **Route:** SC; **Species:** Mice; **Strain:** WT; RIPK3^{-/-}; eNOS^{-/-}; C57BL/6; **Pump:** 2006; **Duration:** 24 weeks;

ALZET Comments: Dose (16.7 mg/ml, 0.15 µl/hr); Controls received mp w/ vehicle; animal info (6-8-week-old male mice, weighing 20-25 g); long-term study; diabetes;

Q8612: A. Krishnan, *et al.* Effect of DHT-Induced Hyperandrogenism on the Pro-Inflammatory Cytokines in a Rat Model of Polycystic Ovary Morphology. *Medicina (Kaunas)* 2020;56(3):

Agents: Dihydrotestosterone **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Strain:** Wistar, albino; **Pump:** Not Stated; **Duration:** 90 days;

ALZET Comments: Dose (83 µg/day); Controls received mp w/ vehicle; animal info (female Wistar albino rats, 21 days old); long-term study; Dihydrotestosterone aka DHT; dependence;



Q8463: A. K. Evans, *et al.* Beta-adrenergic receptor antagonism is proinflammatory and exacerbates neuroinflammation in a mouse model of Alzheimer's Disease. *Neurobiology of Disease* 2020;146(105089)

Agents: Metoprolol **Vehicle:** Not stated; **Route:** SC; **Species:** Mice; **Strain:** C57BL/6J; **Adrb1-flox+/+/Cx3cr1-CreER+/-**; **Adrb2-flox+/+/Cx3cr1-CreER+/-**; **Pump:** 1004; **Duration:** 3 months; 2 months;

ALZET Comments: Dose (5 mg/kg/day); Controls received mp w/ vehicle; animal info (male mice, 3.5 months old; female mice, 6 months old); behavioral testing (Morris Water Maze; Fear Conditioning); pumps replaced every 4 weeks; long-term study; neurodegenerative (Alzheimer's);

Q8453: K. A. Duggan, *et al.* Vasoactive intestinal peptide infusion reverses existing renal interstitial fibrosis via a blood pressure independent mechanism in the rat. *European Journal of Pharmacology* 2020;873(172979)

Agents: Vasoactive intestinal peptide **Vehicle:** Hartmann's Solution; **Route:** IV (iliac); **Species:** Rat; **Strain:** SHR; **Pump:** Not stated; **Duration:** 14 weeks;

ALZET Comments: Dose (5 pmol/kg/min); Controls received mp w/ vehicle; animal info (Fourteen week old spontaneous hypertensive rat); long-term study; Blood pressure measured via tail cuff plethysmography; 193 mmHg - 200 mmHg; Vasoactive intestinal peptide aka VIP; peptides; dependence;

Q8439: T. Develi, *et al.* Preventive and therapeutic effects of relaxin on bisphosphonate related osteonecrosis of the jaw: an experimental study in rats. *Brazilian Dental Science* 2020;23(1):

Agents: Relaxin **Vehicle:** Saline; **Route:** IP; **Species:** Rat; **Strain:** Sprague Dawley; **Pump:** Not stated; **Duration:** 12 weeks;

ALZET Comments: Dose (0.17 µg/hr); Controls received mp w/ vehicle; animal info (Sprague Dawley rats); pumps replaced every 4 weeks; long-term study; dependence;

Q8823: C. N. Receno, *et al.* Effects of Prolonged Dietary Curcumin Exposure on Skeletal Muscle Biochemical and Functional Responses of Aged Male Rats. *International Journal of Molecular Sciences* 2019;20(5):

Agents: Curcumin **Vehicle:** DMSO; **Route:** SC; **Species:** Rat; **Strain:** Not Stated; **Pump:** 2ML4; **Duration:** 4 months;

ALZET Comments: Animal info (32 months old, Male); pumps replaced every 4 weeks; long-term study; dependence;

Q6954: S. L. Payne, *et al.* Initial cell maturity changes following transplantation in a hyaluronan-based hydrogel and impacts therapeutic success in the stroke-injured rodent brain. *Biomaterials* 2019;192(309-322)

Agents: Cyclosporine A **Vehicle:** Ethanol, Cremophor; **Route:** SC; **Species:** Rat; **Strain:** Sprague-Dawley; **Pump:** 2ML4; **Duration:** 56 days;

ALZET Comments: Dose (15 mg/kg/day); animal info (male rats, 350 g); post op. care (3 mg/kg- ketoprofen); behavioral testing (Montoya staircase and tapered beam test); long-term study; ischemia (stroke);

Q7377: N. Morozumi, *et al.* ASB20123: A novel C-type natriuretic peptide derivative for treatment of growth failure and dwarfism. *PLoS One* 2019;14(2):e0212680

Agents: ASB20123 **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Strain:** Sprague-Dawley (SD); **Pump:** Not Stated;

Duration: 1 week, 12 weeks;

ALZET Comments: Dose (0.05, 0.15 mg/kg/day); dose-response (fig 5); Controls received mp w/ vehicle; animal info (Seven-week-old male rats); comparison of injections vs mp "We also analyzed whether continuous sc infusion of ASB20123 to rats could accelerate skeletal growth, compared to the effects of multiple sc bolus injections"; long-term study; ASB20123 is a CNP/ghrelin chimeric peptide, composed of CNP(1-22) and human ghrelin (12-28, E17D); peptides; replacement therapy (dwarf);

Q7531: R. M. Lataro, *et al.* Chronic Treatment With Acetylcholinesterase Inhibitors Attenuates Vascular Dysfunction in Spontaneously Hypertensive Rats. *American Journal of Hypertension* 2019;32(6):579-587

Agents: Pyridostigmine Bromide; Donepezil **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Strain:** SHR; Wistar Kyoto; **Pump:** 2004; **Duration:** 16 weeks;

ALZET Comments: Dose (Pyridostigmine bromide at 1.5 mg/kg/day; Donepezil at 1.4 mg/kg/day); animal info (5 week old male rats); pumps replaced every 4 weeks; long-term study; enzyme inhibitor (Pyridostigmine Bromide inhibits plasma acetylcholinesterase activity; Donepezil inhibits brain acetylcholinesterase activity); cardiovascular; Four pump replacements were performed; BP measured via Tail-cuff method;



Q7616: A. Kurdi, *et al.* Everolimus depletes plaque macrophages, abolishes intraplaque neovascularization and improves survival in mice with advanced atherosclerosis. *Vascul Pharmacol* 2019;113(70-76

Agents: Everolimus **Vehicle:** DMSO; Propylene glycol; Ethanol, buffered; **Route:** SC; **Species:** Mice; **Strain:** ApoE(-/-)Fbnl(C1039G+/-; **Pump:** 1004; **Duration:** 12 weeks;

ALZET Comments: "Dose (1.5 mg/kg/day); 50% DMSO, 40% propylene glycol, 10% absolute ethanol supplemented with 0.4 µl/ml Tween 20 used; animal info (6 weeks, female.); pumps replaced every 4 weeks; long-term study; cardiovascular; ""Four out of 12 control animals died abruptly during the experiment, which is a phenomenon that started at 21 weeks of WD (corresponding with 9 weeks of treatment with vehicle solution)."" p.72; Therapeutic indication (stabilizes atherosclerotic plaques and reduce atherosclerosis-driven complications such as cardiac hypertrophy and fibrosis, brain hypoxia and sudden death); "

Q8220: D. V. Keulen, *et al.* Oncostatin M reduces atherosclerosis development in APOE*3Leiden.CETP mice and is associated with increased survival probability in humans. *PLoS One* 2019;14(8):e0221477

Agents: Murine Oncostatin M **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Strain:** APOE3Leiden.CETP transgenic; **Pump:** 1004; **Duration:** 16 weeks;

ALZET Comments: Dose (10 or 30 µg/kg/day); Controls received mp w/ vehicle; animal info (female mice (10–15 weeks of age)); pumps replaced every 5.5 weeks; long-term study; Murine Oncostatin M aka Murine OSM; cardiovascular;

Q8033: E. Heikkila, *et al.* The plant product quinic acid activates Ca(2+) -dependent mitochondrial function and promotes insulin secretion from pancreatic beta cells. *Br J Pharmacol* 2019;176(17):3250-3263

Agents: Quinic acid **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Strain:** C57BL/6N; **Pump:** Not stated; **Duration:** 12 weeks;

ALZET Comments: Dose (75 mg/kg/day); Controls received mp w/ vehicle; animal info (12 weeks old, Male,); pumps replaced every ? weeks; Multiple pumps per animal (); long-term study; Quinic acid aka QA ; dependence;

Q7525: C. Hartmann, *et al.* Angiotensin II-induced hypertension increases the mutant frequency in rat kidney. *Archives of Toxicology* 2019;93(7):2045-2055

Agents: Angiotensin II **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Strain:** Not Stated; **Pump:** 2004, 2006; **Duration:** 20 weeks;

ALZET Comments: Dose (400 µg/kg/day); Controls received mp w/ PBS; animal info (5-8 weeks old, Male); pumps replaced every 7 weeks; long-term study; cardiovascular;

Q8009: D. Gittings, *et al.* Chronic Nicotine Exposure Alters Uninjured Tendon Vascularity and Viscoelasticity. *Foot & Ankle Orthopaedics* 2019;4(2):

Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Strain:** Sprague Dawley; **Pump:** 2ML4; **Duration:** 12 weeks;

ALZET Comments: Dose (36 mg/ml); 0.9% Saline used; Controls received mp w/ vehicle; animal info (, 10-13 weeks old, 367-425 g); long-term study; dependence;

Q7276: P. Y. Chu, *et al.* CXCR4 Antagonism Reduces Cardiac Fibrosis and Improves Cardiac Performance in Dilated Cardiomyopathy. *Front Pharmacol* 2019;10(117

Agents: AMD3100 **Vehicle:** Water; **Route:** Not Stated; **Species:** Mice; **Strain:** Not Stated; **Pump:** 2004; **Duration:** 12 weeks;

ALZET Comments: Dose (6 mg/kg per day.); animal info (male mice age 6 weeks); long-term study; CXCR4 antagonist aka AMD3100; cardiovascular;

Q9006: Y. Zhao, *et al.* Inhibition of Drp1 hyperactivation reduces neuropathology and behavioral deficits in zQ175 knock-in mouse model of Huntington's disease. *Biochemical and Biophysical Research Communications* 2018;507(1-4):319-323

Agents: Peptide, TAT; Peptide, P110 **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Strain:** C57BL/6J; zQ175 knock-in; **Pump:** 2004; **Duration:** 8 months;

ALZET Comments: "Dose ((TAT 3 mg/kg/day), (P110 3 mg/kg/day)); Controls received mp w/ TAT control peptide; animal info (4 months, male,); behavioral testing (open field test); pumps replaced once every month; long-term study; TAT is a control peptide. P110 peptide is a Drp1 inhibitor; P110 peptide is an enzyme inhibitor (Drp1); peptides; (Huntington's); Therapeutic indication (Drp1 hyperactivation by P110 treatment has a neuroprotective effect in zQ175 KI HD mice by attenuating behavioral deficits, striatal neuronal loss and white matter disorganization and also reduces anxiety-like behavior); "



- Q7312:** N. Tsuburaya, *et al.* A small-molecule inhibitor of SOD1-Derlin-1 interaction ameliorates pathology in an ALS mouse model. *Nat Commun* 2018;9(1):2668
Agents: SOD1-Derlin-1 inhibitor #56-40, SOD1-Derlin-1 inhibitor #56-59 **Vehicle:** DMSO; **Route:** CSF/CNS (lateral ventricle); **Species:** Mice; **Strain:** C57BL/6; **Pump:** 2006; **Duration:** 36 weeks;
ALZET Comments: Dose (1 mM #56-40 or 3 mM #56-59); Controls received mp w/ vehicle; animal info (22 weeks, male,); behavioral testing (rotarod performance); behavioral testing (rotarod performance); pumps replaced every 6 weeks until mouse showed paralysis onset; long-term study; stability verified by (in-vitro immunoprecipitation assay); 3-Amino-N-(4-pyridyl)-6-(3-pyridyl)thieno[2,3-b]pyridine-2-carboxamide aka #56-40; N-Allyl-3-amino-N-phenyl-6-(pyridin-3-yl)thieno[2,3-b]pyridine-2-carboxamide aka #56-59; enzyme inhibitor (SOD1-Derlin-1 interaction); ALZET brain infusion kit 3 used; neurodegenerative (Amyotrophic lateral sclerosis);
- Q7154:** S. R. Subramaniam, *et al.* Chronic nicotine improves cognitive and social impairment in mice overexpressing wild type alpha-synuclein. *Neurobiol Dis* 2018;117(170-180)
Agents: Nicotine **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Strain:** Not Stated; **Pump:** 2004; **Duration:** 1 month; 6 months;
ALZET Comments: Dose (0.4 mg/kg/h and 2.0 mg/kg/h); dose-response (); dose-response (); pumps replaced every 4 weeks; long-term study; stress/adverse reaction: Mice treated with the higher nicotine dose (2.0 mg/kg/h) lost weight after surgery and 50% died after one week. This was as a result of combined toxic effects of isoflurane and a higher dose of nicotine. Therefore, pentobarbital was used instead of isoflurane for induction of anesthesia, which reduced the mortality rate and improved weight gain in the higher dose group. (see pg. 172);
- Q7047:** M. Shi, *et al.* Cisplatin nephrotoxicity as a model of chronic kidney disease. *Lab Invest* 2018;98(8):1105-1121
Agents: α Klotho protein, recomb. **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Strain:** Not Stated; **Pump:** 1004; **Duration:** 20 w
ALZET Comments: Dose (0.3 mg/kg/month); Controls received mp w/ vehicle; pumps replaced every 4 weeks; long-term study; Therapeutic indication (Acute kidney injury);
- Q7000:** U. C. Sharma, *et al.* Effects of a novel peptide Ac-SDKP in radiation-induced coronary endothelial damage and resting myocardial blood flow. *Cardio-Oncology* 2018;4(1):
Agents: Ac-SDKP **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Strain:** Sprague Dawley; **Pump:** Not Stated; **Duration:** 18 w
ALZET Comments: Dose (3.2 mg/kg/day); animal info (10–12 week old rats); long-term study; Ac-SDKP aka N-acetyl-Ser-Asp-Lys-Pro;
- Q7053:** K. R. Qurania, *et al.* Systemic inhibition of Janus kinase induces browning of white adipose tissue and ameliorates obesity-related metabolic disorders. *Biochemical and Biophysical Research Communications* 2018;502(1):123-128
Agents: Tofacitinib **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Strain:** C57BL6; **Pump:** Not Stated; **Duration:** 10 weeks;
ALZET Comments: Dose (100 ug/day); Controls received mp w/ vehicle; animal info (mice); pumps replaced every 35 days; long-term study; tofacitinib is a JAK3 inhibitor; enzyme inhibitor (JAK3)
- Q7010:** O. S. Kornfeld, *et al.* Interaction of mitochondrial fission factor with dynamin related protein 1 governs physiological mitochondrial function in vivo. *Sci Rep* 2018;8(1):14034
Agents: P259-TAT **Vehicle:** TAT control peptide; **Route:** SC; **Species:** Mice; **Strain:** R6/2 HD, wild-type; **Pump:** Not Stated; **Duration:** 8 weeks; 12 weeks;
ALZET Comments: Dose (3 mg/Kg/day); Controls received mp w/ vehicle; animal info (5-week old mice); pumps replaced every 4 weeks; long-term study;
- Q7189:** A. U. Joshi, *et al.* Inhibition of Drp1/Fis1 interaction slows progression of amyotrophic lateral sclerosis. *EMBO Molecular Medicine* 2018;10(3):
Agents: P110-TAT (47-57) **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Strain:** B6SJL Tg (SOD1G93A) 1 Gur/J; **Pump:** 28 day pump; **Duration:** 60 days;
ALZET Comments: Dose (3 mg/kg/day); animal info (4–6 weeks old Adult male mice); behavioral testing (Activity chamber); pumps replaced after 30 days; long-term study; P110 is a selective peptide inhibitor of Drp1/Fis1; neurodegenerative (amyotrophic lateral sclerosis); neurodegenerative (amyotrophic lateral sclerosis); stress/adverse reaction: (see pg. 14);



Q7185: S. E. Iismaa, *et al.* Cardiac hypertrophy limits infarct expansion after myocardial infarction in mice. *Sci Rep* 2018;8(1):6114

Agents: Uridine, 5-bromo-2'-deoxy **Vehicle:** DMSO, Water; **Route:** SC; **Species:** Mice; **Strain:** Not Stated; **Pump:** 2002, 2006; **Duration:** 9 days and 12 weeks;

ALZET Comments: Dose (10 mg/kg/day); 50% DMSO/water used; animal info (16 weeks old male); post op. care (bupivacaine, 8 mg/kg, buprenorphine, 0.075 mg/kg); Model 2006 pumps replaced after 6 weeks; long-term study; 5-bromo-2'-deoxyuridine aka BrdU; cardiovascular;

Q7183: P. Huehnchen, *et al.* Fingolimod therapy is not effective in a mouse model of spontaneous autoimmune peripheral polyneuropathy. *Sci Rep* 2018;8(1):5648

Agents: Fingolimod **Vehicle:** Saline; **Route:** IP; **Species:** Mice; **Strain:** CD86-/- non-obese diabetic (NOD); **Pump:** 1004; **Duration:** 8 weeks;

ALZET Comments: Dose (1 mg/kg/day); Controls received mp w/ vehicle; animal info (mice); pumps replaced every 4 weeks; long-term study; Fingolimod is a sphingosine-1-phosphate analogue; neurodegenerative (autoimmune polyneuropathy); stress/adverse reaction: (see pg. 2);

Q7179: Y. Henning, *et al.* Retinal S-opsin dominance in Ansell's mole-rats (*Fukomys anelli*) is a consequence of naturally low serum thyroxine. *Scientific Reports* 2018;8(1):4337

Agents: Thyroxine, 3,5,3'-triiodothyronine **Vehicle:** NaOH, propylene glycol, PBS; **Route:** SC; **Species:** Rat (mole); **Strain:** Ansell's mole; **Pump:** 2006; **Duration:** 12 weeks;

ALZET Comments: Dose (90 ng/g of T4, 2 ng/g of T3); 15 mM NaOH, 50% propylenglycol and PBS containing 5% BSA used; Controls received mp w/ vehicle; animal info (rats, mean age 2.6 ± 0.92 years); post op. care (Carprofen, 5 mg/kg for at least 3 days; animals were isolated for 24–48 h for recovery then housed as family group); pumps replaced every 6 weeks; long-term study; "Osmotic pumps deliver the test agents with a constant flow rate, thus being well-suited for long-term hormone treatments" pg. 9 ;

Q7139: Y. Gao, *et al.* The histone methyltransferase DOT1L inhibits osteoclastogenesis and protects against osteoporosis. *Cell Death & Disease* 2018;9(2):33

Agents: EPZ5676 **Vehicle:** DMSO, Water; **Route:** SC; **Species:** Mice; **Strain:** FVB/N; **Pump:** 2006, 2002; **Duration:** 8 weeks;

ALZET Comments: Dose (1.6 mg/d); 50% DMSO used; Controls received mp w/ vehicle; animal info (Eight-week-old, female, FVB/N); Model 2006 pumps replaced with Model 2002 after six weeks; long-term study; EPZ5676 aka small molecule inhibitor; gene therapy;

Q7744: D. Charvin, *et al.* An mGlu4-Positive Allosteric Modulator Alleviates Parkinsonism in Primates. *Mov Disord* 2018;33(10):1619-1631

Agents: tetrahydropyridine, 1-methyl-4-phenyl-1,2,3,6- **Vehicle:** Not Stated; **Route:** SC; **Species:** Monkey; **Strain:** Cynomolgus; **Pump:** Not Stated; **Duration:** 6 months;

ALZET Comments: Dose (0.5 mg/d); animal info (); long-term study; 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (AKA MPTP) is used to induce Parkinsonism; neurodegenerative (); Pumps were used to induce advanced-stage Parkinsonism in macaques by continuous infusion of MPTP. Agents administered during test were administered orally, not through pump infusion.;

Q7103: A. Calevro, *et al.* Effects of chronic antipsychotic drug exposure on the expression of Translocator Protein and inflammatory markers in rat adipose tissue. *Psychoneuroendocrinology* 2018;95(28-33)

Agents: Haloperidol, olanzapine **Vehicle:** Cyclodextrin, 2-Hydroxypropyl-B-; **Route:** SC; **Species:** Rat; **Strain:** Sprague-Dawley; **Pump:** 2ML4; **Duration:** 8 weeks;

ALZET Comments: Dose (Haloperidol- 2mg/ kg/ day, Olanzapine-10 mg/kg/ day); Controls received mp w/ vehicle; animal info (10-week old, male, , 240–250 g); pumps replaced every 4 weeks; long-term study; dependence;



Q10085: T. Atkinson, *et al.* Assessment of Novel Antioxidant Therapy in Atherosclerosis by Contrast Ultrasound Molecular Imaging. *Journal of the American Society of Echocardiography* 2018;31(11):1252-1259 e1

Agents: EUK-207 **Vehicle:** Mannitol; **Route:** SC; **Species:** Mice; **Strain:** Not Stated; **Pump:** 1004; **Duration:** 8 weeks; 28 weeks; **ALZET Comments:** Dose (9 mg/ml); 5% Mannitol used; Controls received mp w/ vehicle; pumps replaced every 4 weeks; long-term study 40 weeks; cardiovascular; EUK-207 acts to reduce endothelial P-selectin expression and to suppress platelet-endothelial interactions by inhibiting endothelial-associated VWF. The beneficial anti-inflammatory and antiplatelet endothelial effects of EUK-207 occurred with even short duration of therapy, yet meaningful effects on reducing plaque size and content were found only with long-term therapy, indicating a slow cumulative effect of antioxidant therapy.; Therapeutic indication (suppresses high-risk atherosclerotic features);

Q7171: S. Arttamangkul, *et al.* Cellular tolerance at the micro-opioid receptor is phosphorylation dependent. *eLife Journal* 2018;7(**Agents:** Morphine sulfate **Vehicle:** Water; **Route:** SC; **Species:** Rat; **Strain:** Sprague-Dawley; MOR-knock out; **Pump:** 2ML1; **Duration:** 7 days;

ALZET Comments: "Dose (80mg/kg/ml); animal info (Adult 180-300g, 5-6 week male and female rats, Sprague-Dawley rats with ZFN target site (GCTGTCTGCCACCCAgctcaaGCCCTGGATTTC within exon 2) F3 generation); enzyme agonist (mu-opioid receptor aka MOR); dependence; The present work addresses one mechanism that underlies the development of long-term tolerance to morphine. Elimination of phosphorylation sites on the C-terminal rendered MORs resistant to one cellular measure of long-term tolerance induced by morphine. One conclusion is that desensitization and/or internalization of MORs is necessary for the development of this form of cellular tolerance to opioids. Although there were no obvious change in cellular excitability, it could be that continued signaling through the phosphorylation deficient receptors result in downstream homeostatic mechanisms that counteract the lack of cellular tolerance and may well increase signs of withdrawal.;"