



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

ANIMAL	DURATION	PUMPS REPLACED	REFERENCE
Mouse	32 weeks	Not stated	P7341 Zhou Y, Chen R, Catanzaro SE, Hu LF, Dansky HM, Catanzaro DF. Differential effects of angiotensin II on atherogenesis at the aortic sinus and descending aorta of apolipoprotein-E-deficient mice. <i>Am J Hypertens</i> 2005; 18(4):486-492
*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	8 weeks	After 28 days	P9771 Roche JR, Sheahan AJ, Chagas LM, Blache D, Berry DP, Kay JK. Long-Term Infusions of Ghrelin and Obestatin in Early Lactation Dairy Cows. <i>J Dairy Sci</i> 2008; 91(12):4728-4740
*Guinea-pig	8 weeks	Every 13 days	P4742 Tang W, Seidman MD, Henig JP, Shulman A, Stracher A. The effects of leupeptin on cochlear blood flow, auditory sensitivity, and histology. <i>International Tinnitus Journal</i> 2001; 7(1):4-12
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.

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@durect.com.



Recent References (2017-2020) on the Long Term Administration of Agents Using ALZET® Osmotic Pumps

- 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; **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. *Neurobiol Dis* 2020;146(105089)
Agents: Metoprolol **Vehicle:** Not stated; **Route:** SC; **Species:** Mice; **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. *Eur J Pharmacol* 2020;873(172979)
Agents: Vasoactive intestinal peptide **Vehicle:** Hartmann's Solution; **Route:** IV (iliac); **Species:** Rat; **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; **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;
- 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; **Pump:** 2ML4; **Duration:** 56 days;
ALZET Comments: Dose (15 mg/kg/day); animal info (male Sprague-Dawley 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; **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 SD 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; **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 SHR and Wistar Kyoto 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; **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, ApoE(-/-)Fbni(C1039G+/-)); 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; **Pump:** 1004; **Duration:** 16 weeks;

ALZET Comments: Dose (10 or 30 µg/kg/day); Controls received mp w/ vehicle; animal info (female APOE3Leiden.CETP transgenic 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; **Pump:** Not stated; **Duration:** 12 weeks;

ALZET Comments: Dose (75 mg/kg/day); Controls received mp w/ vehicle; animal info (12 weeks old, Male, C57BL/6N); 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; **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; **Pump:** 2ML4; **Duration:** 12 weeks;

ALZET Comments: Dose (36 mg/ml); 0.9% Saline used; Controls received mp w/ vehicle; animal info (Sprague Dawley, 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; **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;

Q7961: Y. Birnbaum, *et al.* DPP-4 inhibition by linagliptin prevents cardiac dysfunction and inflammation by targeting the Nlrp3/ASC inflammasome. *Basic Res Cardiol* 2019;114(5):35

Agents: Exendin-4 **Vehicle:** Not stated; **Route:** SC; **Species:** Mice; **Pump:** Not stated; **Duration:** 2 weeks;

ALZET Comments: Dose (24 nmol/kg/day); Controls received sham surgery; animal info (10 weeks, male, C57BL/6J and db/db); ischemia (coronary artery occlusion); cardiovascular; diabetes; "As there has been no published protocol for long-term EX administration in mice, we followed the initial EX injection with prolonged Exendin-4 administration via osmotic pump for 2 weeks" p.35-36;



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; **Pump:** 2006; **Duration:** 58 weeks;

ALZET Comments: Dose (1 mM #56-40 or 3 mM #56-59); Controls received mp w/ vehicle; animal info (22 weeks, male, C57BL/6); 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; **Pump:** 2004; **Duration:** 1 or 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; **Pump:** 1004; **Duration:** 20 weeks;

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; **Pump:** Not Stated; **Duration:** 18 weeks;

ALZET Comments: Dose (3.2 mg/kg/day); animal info (10–12 week old Sprague Dawley 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; **Pump:** Not Stated; **Duration:** 10 weeks;

ALZET Comments: Dose (100 ug/day); Controls received mp w/ vehicle; animal info (C57BL6 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; **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 R6/2 HD and wild-type 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; **Pump:** 28 day pump; **Duration:** 60 days;

ALZET Comments: Dose (3 mg/kg/day); animal info (4–6 weeks old AdultB6SJL Tg (SOD1G93A) 1 Gur/J 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; **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 mice); 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; **Pump:** 1004; **Duration:** 8 weeks;

ALZET Comments: Dose (1 mg/kg/day); Controls received mp w/ vehicle; animal info (CD86-/- non-obese diabetic (NOD) 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. *Sci Rep* 2018;8(1):4337

Agents: Thyroxine, 3,5,3'-triiodothyronine **Vehicle:** NaOH, propylenglycol, PBS; **Route:** SC; **Species:** Rat (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 (Ansell's mole 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:** Mouse; **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;

R0392: P. R. O. de Montellano. 1-Aminobenzotriazole: A Mechanism-Based Cytochrome P450 Inhibitor and Probe of Cytochrome P450 Biology. *Med Chem (Los Angeles)* 2018;8(3):

Agents: Aminobenzotriazole, 1- **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice; **Pump:** Not Stated; **Duration:** 6, 16 days;

ALZET Comments: 1-ABT is a pan-specific, mechanism-based inactivator of the xenobiotic metabolizing forms of cytochrome P450; "Osmotic pumps can be used to maintain maximum blood concentrations of 1-ABT for at least 6 days. Indeed, ALZET osmotic pumps were able to maintain the 1-ABT plasma concentration above 4.1 mg/ml over 336 hours without overt toxicity." p.40. "Furthermore, administration of 1-ABT to mice via an ALZET osmotic pump for 16 days caused no overt toxicity" pg. 41; studies referenced include "Stringer RA, Ferreira S, Rose J, Ronseaux S (2016) Application of osmotic pumps for sustained release of 1-aminobenzotriazole and inhibition of cytochrome P450 enzymes in mice: model comparison with the hepatic P450 reductase null mouse. *Drug Metab Dispos* 44:1213-1216." and "Watanabe A, Mayumi K, Nishimura K, Osaki H (2016) In vivo use of the CYP inhibitor 1-aminobenzotriazole to increase long-term exposure in mice. *Biopharm Drug Disp* 37: 373-378.";

Q7746: I. Cote, *et al.* Activation of the central melanocortin system in rats persistently reduces body and fat mass independently of caloric reduction. *Canadian Journal of Physiology and Pharmacology* 2018;96(3):308-312

Agents: Melanotan II **Vehicle:** CSF, Artificial; **Route:** CSF/CNS (lateral ventricle); **Species:** Rat; **Pump:** Not Stated; **Duration:** 28 days;

ALZET Comments: Dose (2 µg/day); Controls received mp w/ vehicle; animal info (10 months, male, F344BN, 360-480g); MTII is a synthetic analog of alpha-MSH; Brain coordinates (1.3 mm posterior to bregma, 1.9 mm lateral to midsagittal



suture, depth of 3.5 mm); Cannula placement verified via a stereotaxic device; Original mini-pumps were replaced after recovery from the surgery through a small incision (1 cm); Therapeutic indication (long-term reduction of body mass independent of caloric reduction);

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; **Pump:** Not Stated; **Duration:** 6 months;

ALZET Comments: Dose (0.5 mg/d); animal info (Cynomolgus); 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; **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, Sprague-Dawley, 240–250 g); pumps replaced every 4 weeks; long-term study; dependence;

Q5727: Y. Zhu, *et al.* Protective Effect of 17beta-Estradiol Upon Hippocampal Spine Density and Cognitive Function in an Animal Model of Vascular Dementia. *Sci Rep* 2017;7(42660

Agents: Estradiol, 17b- **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2006; **Duration:** Not Stated;

ALZET Comments: Controls received mp w/ 20% cyclodextrin; animal info (male, Sprague Dawley, 250-300g, adult); functionality of mp verified by serum levels; behavioral testing (Morris water maze); replacement therapy (estradiol infusion); long-term study; cardiovascular; Dose (0.05 ug/h); “exogenous E2 replacement produced E2 levels of 25-33pg/ml” (pg 2);

Q5933: S. Yonekubo, *et al.* Alpha1A-adrenoceptor antagonist improves underactive bladder associated with diabetic cystopathy via bladder blood flow in rats. *BMC Women's Health* 2017;17(1):64

Agents: Silodosin **Vehicle:** Hartmann's solution; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 8 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (female, Sprague Dawley, 6 weeks old); long-term study; diabetes; Dose (0.3 or 1 mg/kg/day);

Q5956: J. Tam, *et al.* Peripheral cannabinoid-1 receptor blockade restores hypothalamic leptin signaling. *Mol Metab* 2017;6(10):1113-1125

Agents: Leptin; SHU-9119 **Vehicle:** PBS; **Route:** SC; CSF/CNS; **Species:** Mice; **Pump:** 2004; **Duration:** 12 weeks, 7 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (leptin-deficient ob/ob mice); long-term study; pumps replaced every 28 days; SHU-9119 is a MC4R antagonist; Leptin dissolved in PBS and delivered SC for 12 weeks; SHU-9119 dissolved in saline and delivered ICV for 7 days; Pumps model incorrectly listed as Model 2001D. It should be Model 2004 based on description.

Q6183: M. Sudo, *et al.* Inhibition of plaque progression and promotion of plaque stability by glucagon-like peptide-1 receptor agonist: Serial in vivo findings from iMap-IVUS in Watanabe heritable hyperlipidemic rabbits. *Atherosclerosis* 2017;265(283-291

Agents: Lixisenatide **Vehicle:** Saline; **Route:** SC; **Species:** Rabbits; **Pump:** 2ML4; **Duration:** 12 weeks;

ALZET Comments: Dose (30 nmoL/kg/day); Controls received mp w/ vehicle; animal info (Watanabe heritable hyperlipidemic); pumps replaced every 4 weeks; long-term study (12 weeks); Lixisenatide is a GLP-1 receptor agonist;

Q6180: A. Sike, *et al.* Improved method for cannula fixation for long-term intracerebral brain infusion. *J Neurosci Methods* 2017;290(145-150

Agents: Black Ink **Vehicle:** PBS; **Route:** CSF/CNS (ventricle); **Species:** Mice; **Pump:** 2006; **Duration:** 50 days;



ALZET Comments: Dose (PBS with 1:100 black ink); animal info (50-day old male C57BL/6J mice); functionality of mp verified by in vitro priming visualization; ALZET brain infusion kit 3 used; cyanoacrylate adhesive; no stress: The implanted pump and the cannula caused minimal discomfort to the animals and it had no effect on the moving ability (see pg.5); good methods; This report describes an improved method for better fixation of cannula during long-term brain infusion experiments using a non-toxic, soft and elastic silicone spacer.

Q5742: M. P. Serrano, *et al.* The proof-of-concept of ASS234: Peripherally administered ASS234 enters the central nervous system and reduces pathology in a male mouse model of Alzheimer disease. *J Psychiatry Neurosci* 2017;42(1):59-69

Agents: ASS234 **Vehicle:** PBS, DMSO; **Route:** SC; **Species:** Mice (transgenic); **Pump:** 2004; **Duration:** 4 months;

ALZET Comments: Controls received mp w/ vehicle; animal info (10 weeks old, APP^{swe}/PS1^{ΔE9}); long-term study; pumps replaced every 28 days for 4 months; 3.6% DMSO; neurodegenerative (Alzheimer's disease); behavioral testing (Object recognition task); enzyme inhibitor (AChE/MAO inhibitor); Therapeutic indication (Alzheimer's disease, AD); Dose (0.62 mg/kg/day);

Q6708: Y. J. Oh, *et al.* Role of tissue transglutaminase in age-associated ventricular stiffness. *Amino Acids* 2017;49(3):695-704

Agents: Cystamine **Vehicle:** Saline; **Route:** Not Stated; **Species:** Mice; **Pump:** 2ML4; **Duration:** 12 weeks;

ALZET Comments: Dose (60 mg/kg/day); animal info (Male Fisher 344 rats aged 6 and 18 months); pumps replaced every 4 weeks; long-term study; enzyme inhibitor (transglutaminase);

Q6195: H. Noh, *et al.* Beta 2-adrenergic receptor agonists are novel regulators of macrophage activation in diabetic renal and cardiovascular complications. *Kidney Int* 2017;92(1):101-113

Agents: Salbutamol **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Rat; **Pump:** Not Stated; **Duration:** 12 weeks; 5 weeks;

ALZET Comments: Dose (0.5 mg/kg/day); Controls received mp w/ vehicle; animal info (Male 8-week-old ZDF rats); long-term study; Salbutamol is a beta2AR agonist; diabetes;

Q6701: P. Mota, *et al.* Mp17-14 Depletion of Peripheral Serotonin Synthesis Induces Benign Prostatic Growth in Mice: More Evidence for the New "Neuroendocrine Theory" in Bph Etiology. *The Journal of Urology* 2017;197(4):e216-e217

Agents: Leptin **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 24 weeks;

ALZET Comments: Dose (5 mg/day; 10 mg/day); Controls received mp w/ vehicle; animal info (10-week-old male ObOb and strain-matched control mice); pumps replaced every 12 weeks; Multiple pumps per animal (2); long-term study;

Q6363: J. Lukas, *et al.* Glucosylsphingosine Causes Hematological and Visceral Changes in Mice-Evidence for a Pathophysiological Role in Gaucher Disease. *Int J Mol Sci* 2017;18(10):

Agents: Glucosylsphingosine **Vehicle:** DMSO; Propylene glycol; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 12 weeks;

ALZET Comments: Dose (10 mg/kg/day); 50% DMSO:50% propylene glycol used; Controls received mp w/ vehicle; animal info (Male C57BL/6JRj mice); functionality of mp verified by plasma levels; pumps replaced every 4 weeks; long-term study (12 weeks); Resultant plasma level (between 700 and 900 ng/mL); no stress: The pumps were well tolerated and no mortalities were observed (see pg. 11); good methods (p.10); Lyso-Gb1 levels were strongly elevated after four, eight and 12 weeks (levels ranging between 700 and 900 ng/mL). This represented a >500-fold increase compared with vehicle-treated mice

Q6324: K. Fujiu, *et al.* A heart-brain-kidney network controls adaptation to cardiac stress through tissue macrophage activation. *Nat Med* 2017;23(5):611-622

Agents: Antibody, anti-mouse-GM-CSF, Antibody, rat isotype (IgG2a) **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 8 weeks;

ALZET Comments: Dose (2.5 µg/d); Controls received mp w/ vehicle; pumps replaced every 4 weeks; long-term study;

Q6222: E. C. El Hajj, *et al.* Detrimental role of lysyl oxidase in cardiac remodeling. *J Mol Cell Cardiol* 2017;109(17-26

Agents: Aminopropionitrile, beta **Vehicle:** Saline; **Route:** Not Stated; **Species:** Rat; **Pump:** Not Stated; **Duration:** 12 weeks;

ALZET Comments: Dose (100 mg/kg/day); Controls received mp w/ vehicle; animal info (8 week old male Sprague Dawley); post op. care (analgesia by buprenorphine HCl (1 mg/kg); long-term study; enzyme inhibitor (lysyl oxidase);