



ALZET® Osmotic Pumps References from 2017-2019: Injection-Infusion Comparison

ALZET pumps allow researchers to understand and optimize the key determinants of drug action. These determinants are the level of drug exposure and its duration, and the spatial distribution of drug relative to the target tissue. By manipulating these variables, drug effects can be optimized early in preclinical development, allowing clinical studies to be conducted at lower cost and with better results.

A drug's therapeutic index is a ratio reflecting the quotient of its therapeutic effects and adverse effects. Varying the schedule of administration can have a major influence on the therapeutic index of some drugs. Relative to bolus dosing, constant infusion can:

- increase efficacy,
- reduce side effects, or
- both increase efficacy and reduce side effects.

All of these changes can increase a drug's therapeutic index, improving its value as a pharmaceutical. One cannot assume, however, that infusion regimens are superior to injections for all drugs. The relationship between dose, regimen, and drug effect must be carefully explored for each drug. Dose-response testing, where the effects of one or more schedules of injections are compared with the effects of constant infusion, helps elucidate schedule-dependent drug effects. This type of testing has been termed the injection-infusion comparison (IIC) protocol. This protocol is an established method for optimizing the effectiveness of anticancer agents, and it is important in the preclinical testing of proteins, peptides, and other recombinant DNA products.

The references which follow explore the schedule or regimen dependence of a drug's therapeutic index. The notes following each reference detail the substance(s) infused, the route of administration, the animal model used, the vehicle for infusion, the pump model used, the duration of infusion, and notable technical achievements or results.

This list does not include references in this category from before 2010. To obtain a complete list of references published since 1975, please contact ALZET Technical Services at (800) 692-2990 (U.S. & Canada), or (408) 367-4036. You may also contact us via e-mail at alzet@direct.com.

A more complete review of the injection-infusion comparison protocol can be found in the following references:

R0050 Fara J, and Urquhart J. *The Value of Infusion and Injection Regimens in Assessing Efficacy and Toxicity of Drugs. Trends Pharmacol Sci* 5 (1): pp. 21-25, 1984.

R0051 Urquhart J, Fara J, and Willis KL. *Rate-controlled Delivery Systems in Drug and Hormone Research. Ann Rev Pharmacol Toxicol* 24: pp. 199-236, 1984.



Recent References (2017-2019) Comparing Injection versus Infusion Using ALZET® Osmotic Pumps

Q7654: I. A. Zhuravin, *et al.* Regulation of Neprilysin Activity and Cognitive Functions in Rats After Prenatal Hypoxia. *Neurochem Res* 2019;44(6):1387-1398

Agents: epigallocatechin-3-gallate **Vehicle:** Saline; **Route:** CSF/CNS (parietal cortex); **Species:** Rat; **Pump:** Not Stated; **Duration:** 4 weeks;

ALZET Comments: Dose (0.25 µL/h of 10⁻³ M); Controls received mp w/ vehicle; animal info (4 months, Wistar); behavioral testing (novel object recognition test); comparison of oral administration vs mp; EGCG is a green tea catechin; Brain coordinates (Bregma=+0.20; L=3; H=1 mm); neurodegenerative (Alzheimer's); organisms used were offspring of rats submitted to prenatal hypoxia. Oral EGCG administration via drinking water was more beneficial than intracranial injection resulting in better cognitive outcome on memory test; Therapeutic indication (protect hippocampal formation and spatial memory in aged rats through an increase in NEP activity in blood plasma, Cx and Hip along with increased number of labile dendritic spines in their hippocampal CA1 area.);

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);

Q7620: N. Kokuho, *et al.* Analyses of alveolar epithelial injury via lipid-related stress in mammalian target of rapamycin inhibitor-induced lung disease. *Lab Invest* 2019;99(6):853-865

Agents: Bleomycin hydrochloride **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 14 days; **ALZET Comments:** Dose (100 mg/kg); Controls received i.p. injection w/ DMSO; animal info (7 weeks, female, C57BL/6); comparison of i.p. temsirolimus injection vs mp; BLM causes marked inflammation and epithelial injury in the lung; immunology; BLM dissolved in saline for pump (injury group) although controls used i.p. injected DMSO;

Q7582: B. Hunter, *et al.* (352) Sex Differences in Sensory Processing: The Role of Stimulus Modality and Psychological Factors. *The Journal of Pain* 2019;20(4):

Agents: fentanyl **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 5 days; **ALZET Comments:** Dose (0.01mg/kg/hr); Controls received mp w/ vehicle; animal info (male, Sprague-Dawley); comparison of oxycodone and morphine injection vs mp; opioids administered 1 hour, 10 days, or 28 days post-CCI (chronic constriction injury) surgery;

Q7586: K. A. Horton, *et al.* Systemic Blockade of the CB1 Receptor Augments Hippocampal Gene Expression Involved in Synaptic Plasticity but Perturbs Hippocampus-Dependent Learning Task. *Cannabis and Cannabinoid Research* 2019;4(1):33-41

Agents: rimonabant **Vehicle:** saline; DMSO; Tween-80 buffer; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 28 days; **ALZET Comments:** Dose (1.0 mg/kg/day); 10% DMSO and 0.1% Tween-80 in sterile saline used; Controls received mp w/ vehicle; animal info (male, Long-Evans); behavioral testing (DNMS cognitive task); comparison of intraperitoneal injection vs mp; rimonabant is a CB1 receptor antagonist; "Moreover, no performance deficits were observed in the current study using the continuous osmotic mini-pump infusion protocol." pg.39; "In three of the rimonabant treatment animals a second osmotic mini-pump was implanted because DNMS training was not successfully completed within the functional lifespan on the initial osmotic mini-pump." p.34;

Q7964: B. K. Chen, *et al.* Prophylactic efficacy of 5-HT4R agonists against stress. *BioRxiv* 2019;

Agents: RS 67333 **Vehicle:** saline; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 3 weeks;



ALZET Comments: Dose (1.5 mg/kg/day); Controls received mp w/ vehicle; animal info (8 weeks, male, C57BL/6NTac); behavioral testing (elevated plus maze, novelty-suppressed feeding, sucrose splash test); comparison of acute injection vs mp; RS-67,333 (aka 1-(4-amino-5-chloro-2-methoxyphenyl)-3-[1(n-butyl)-4-piperidinyl]-1-propanone HCl) is a high-affinity 5-HT4R partial agonist; Osmotic minipumps were rotated under the skin two to three times per week. "RS-67,333 was not performed in C57BL/6NTac mice, as a previous study of our own has shown that female C57BL/6NTac mice are insensitive to chronic CORT" p.20; Therapeutic indication (In C57BL/6NTac mice prophylactic RS-67,333 was effective at decreasing depressive- and anxiety-like behavior. In 129S6/SvEv mice, prophylactic RS-67,333 was effective at attenuating learned fear, but not decreasing depressive-like behavior.);

Q7951: R. Caire, *et al.* Parathyroid Hormone Remodels Bone Transitional Vessels and the Leptin Receptor-Positive Pericyte Network in Mice. *J Bone Miner Res* 2019;34(8):1487-1501

Agents: Parathyroid hormone (1-84) **Vehicle:** saline; **Route:** SC; **Species:** Mice; **Pump:** Not stated; **Duration:** 7, 14, 28 days; **ALZET Comments:** Dose (100 µg/kg/day); Controls received SC injection of vehicle; animal info (4 months, female, C57BL/6J); comparison of SC injection vs mp; mp model not stated;

Q7950: W. Cai, *et al.* Translationally controlled tumor protein (TCTP) plays a pivotal role in cardiomyocyte survival through a Bnip3-dependent mechanism. *Cell Death Dis* 2019;10(8):549

Agents: isoproterenol **Vehicle:** Not stated; **Route:** SC; **Species:** Mice; **Pump:** Not stated; **Duration:** 2, 7 days; **ALZET Comments:** Dose (60 mg/kg/day); animal info (2-3 months, male, C57BL/6); comparison of IP DOX injection and TAC vs mp; cardiovascular; mp used for ISO-induced heart failure model. mp model not stated.;

Q7963: V. M. Breinholt, *et al.* TransCon CNP, a Sustained-Release C-Type Natriuretic Peptide Prodrug, a Potentially Safe and Efficacious New Therapeutic Modality for the Treatment of Comorbidities Associated with Fibroblast Growth Factor Receptor 3-Related Skeletal Dysplasias. *J Pharmacol Exp Ther* 2019;370(3):459-471

Agents: Peptide, C-type natriuretic **Vehicle:** Acetate Buffer; **Route:** SC; **Species:** Mice; **Pump:** 1002; 1004; **Duration:** 5 weeks; **ALZET Comments:** Dose (203 µg/kg/d); 30 mM acetate buffer (pH 4) with 5% sucrose and 1% benzylic alcohol used; Controls received mp w/ vehicle; animal info (3 weeks, male, FVB); pumps exchanged on day 15; comparison of SC injection vs mp; CNP-38 is a C-terminal 38 amino acid peptide structurally identical to endogenous CNP; peptides; "Overall growth effects on femur, tibia and spine were much stronger when CNP-38 was applied as a continuous subcutaneous infusion compared to a daily s.c. bolus injection indicating improved efficacy as a result of continuous exposure." pg.33; mp model 1002 used for days 1-15 and model 1004 for days 15-34;

Q7932: D. A. Vousden, *et al.* Continuous manganese delivery via osmotic pumps for manganese-enhanced mouse MRI does not impair spatial learning but leads to skin ulceration. *Neuroimage* 2018;173(411-420

Agents: manganese chloride **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 15 days; **ALZET Comments:** Dose (25, 50 mg/kg/day); Controls received mp w/ vehicle; animal info (10-12 weeks, male, B6129SF1/Tac); post op. care (2 mg/kg meloxicam for 3 days); behavioral testing (Morris Water Maze); comparison of IP injection vs mp; MRI; stress/adverse reaction: ("mice implanted with pumps swam more slowly on the first 2 days of training than the control animals. By day 3 this difference had normalized, and there was no effect of pumps, MnCl2 treatment, or specific treatment group on swim speed." p.417. "Some mice that received MnCl2 via osmotic pump developed skin ulceration where the solution was being released from the pump. In 4/17 cases, the ulceration was so severe that the mice had to be euthanized." p.417); "when mice are given 50 mg/kg/day MnCl2 via osmotic pump, the useable imaging window is only from day 3 to day 5. The useable imaging window for mice receiving 25 mg/kg/day is approximately 3–14 days." p.419;

Q7929: S. B. Vasamsetti, *et al.* Sympathetic Neuronal Activation Triggers Myeloid Progenitor Proliferation and Differentiation. *Immunity* 2018;49(1):93-106 e7

Agents: ICI-118,551 hydrochloride; Toxin, Diphtheria; reserpine; captopril; norepinephrine **Vehicle:** PBS; **Route:** Intrasplenic; **Species:** Mice; **Pump:** 1002; **Duration:** 1, 2, 3 weeks; **ALZET Comments:** "Dose ((ICI-118,551 12 mg/kg/hr), (Diphtheria Toxin 5 mg/kg/day), (reserpine 5mg/kg/day), (captopril 6mg/kg/day), (norepinephrine 5mg/kg/day)); Controls received mp w/ vehicle; animal info (10-12 weeks, Apoe(-/-));



comparison of intrasplenic injection vs mp; ICI-118,551 hydrochloride is a selective antagonist of the beta2 adrenergic receptor. angiotensin converting enzyme (ACE) inhibitor. Reserpine blocks the uptake of catecholamines into synaptic vesicles; Reserpine is an enzyme inhibitor (vesicular monoamine transporter 2); immunology; Diptheria toxin used to deplete TH+ leukocytes. Splenic nerves were depleted by intrasplenic DT using mp for 7 days; Therapeutic indication (ICI-118,551 reduced splenic GMP proliferation and inflammatory myeloid cell generation); "

Q6549: M. Shimamura, *et al.* Development of a novel RANKL-based peptide, microglial healing peptide1-AcN (MHP1-AcN), for treatment of ischemic stroke. *Sci Rep* 2018;8(1):17770

Agents: Microglial healing peptide1-AcN **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2001D; **Duration:** 24 hours; **ALZET Comments:** Dose (0.5, 1, or 2 mg/ml); Controls received mp w/ vehicle; animal info (C57Bl6/J mice); comparison of intravenous injection vs mp; MHP1-AcN is a novel partial peptide of RANKL with N-terminal acetylation and C-terminal amidation; Therapeutic indication (ischemic stroke);

Q7766: A. R. Johnson, *et al.* Amphetamine maintenance differentially modulates effects of cocaine, methylenedioxypyrovalerone (MDPV), and methamphetamine on intracranial self-stimulation and nucleus accumbens dopamine in rats. *Neuropsychopharmacology* 2018;43(8):1753-1762

Agents: amphetamine **Vehicle:** saline, bacteriostatic; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 7, 13 days; **ALZET Comments:** Dose (0.1 or 0.32 mg/kg/h), (2ML2 pump 0.5 µl/h); Controls received mp w/ vehicle; animal info (male, Sprague-Dawley, 300-350g); behavioral testing (operant chambers); comparison of IP injection vs mp; dependence;

Q7757: K. Iizuka, *et al.* Analysis of the prolonged infusion of DFP-10917, a deoxycytidine analog, as a therapeutic strategy for the treatment of human tumor xenografts in vivo. *Int J Oncol* 2018;52(3):851-860

Agents: DFP-10917 **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 1, 3, 14 days; **ALZET Comments:** Dose (4.5, 8, 30 mg/kg/day); Controls received no treatment; animal info (5 weeks, male, BALB/cA Jcl-nu, 17.2-24.6g); comparison of bolus injection vs mp; DFP-10917 AKA 2'-C-cyano-2'-deoxy-1-beta-D-arabino-pentofranocylcytosine is a 2'-deoxycytidine analog with antitumor activity; cancer (tumor xenografts); Infusion of agent occurred on three regimens: 24 consecutive hours on days 1 and 8, for 3 consecutive days on days 1 and 15, or for 14 consecutive days (p.852); Therapeutic indication ("regression of tumor growth without any toxicities on human solid and hematological tumor xenografts compared to clinically available deoxycytidine analogs." p.858);

Q7919: R. Ichimaru, *et al.* Raloxifene reduces the risk of local alveolar bone destruction in a mouse model of periodontitis combined with systemic postmenopausal osteoporosis. *Archives of Pharmacal Research* 2018;85(98-103

Agents: Raloxifene **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice (ovariectomized); **Pump:** Not Stated; **Duration:** 4 weeks; **ALZET Comments:** Dose (300 µg/kg/day); Controls received sham surgery and mp w/ agent; animal info (4 weeks, female, ddY strain); comparison of local injection vs mp; "However, our study found that the in vivo local injection of raloxifene did not prevent bone resorption in a mouse model of periodontitis, although the systemic treatment of raloxifene using a mini-osmotic pump did prevent the loss of alveolar bone mass induced by LPS injection." pg.102; Therapeutic indication (raloxifene systemically maintain alveolar bone mass in a mouse model of periodontitis with osteoporosis);

Q7909: R. Hill, *et al.* Oxycodone-induced tolerance to respiratory depression: reversal by ethanol, pregabalin and protein kinase C inhibition. *Bulletin of Experimental Biology and Medicine* 2018;175(12):2492-2503

Agents: oxycodone **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 6 days; **ALZET Comments:** Dose (20, 45 or 120 mg/kg/day); Controls received mp w/ vehicle; animal info (male, CD-1, 30g); comparison of IP injection vs mp; Resultant plasma level ((Low 81±8 ng/ml), (Med 284±147 ng/ml), (High 1670 ± 635 ng/ml)); dependence; brain levels of oxycodone include ((Low 248 ± 126ng/g), (Med 426±87 ng/g), (High 1703±665 ng/g));

Q7828: H. Haselmann, *et al.* Human Autoantibodies against the AMPA Receptor Subunit GluA2 Induce Receptor Reorganization and Memory Dysfunction. *Neuron* 2018;100(1):91-105 e9

Agents: Immunoglobulin G, human; antibody, human IgG **Vehicle:** Saline; **Route:** CSF/CNS (lateral ventricle); **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;



ALZET Comments: Dose (10mg/ml at 0.25 µl/h); Controls received mp w/ vehicle; animal info (male, C57BL/6J); behavioral testing (Novel object recognition, locomotor activity box, elevated plus maze, black-and-white test); comparison of stereotactic microinjection vs mp; a-GluA2 IgG are autoantibodies against only the GluA2 subunit of the AMPAR; Brain coordinates (0.2 mm posterior and ± 1.00 mm lateral from bregma, depth 2.2 mm); bilateral cannula used (PlasticsOne, model 3280PD-2.0/SP); neurodegenerative (Autoimmune encephalitis); immunology; purified IgG fraction and antibody sources described on page e2 of paper.;

Q6281: F. Yang, *et al.* Delivery of epirubicin via slow infusion as a strategy to mitigate chemotherapy-induced cardiotoxicity. PLoS One 2017;12(11):e0188025

Agents: Epirubicin **Vehicle:** Not Stated; **Route:** IP; **Species:** Rat; **Pump:** 1003D; **Duration:** 12-72 hours;

ALZET Comments: Dose (8 mg/kg body weight); animal info (6–9 weeks old male Sprague-Dawley rats); comparison of IV injections vs mp; “we found that continuous intravenous infusion of epirubicin using micro-pumps had less cardiotoxicity than intravenous bolus infusion of epirubicin at the same total dose of 70 mg/m²” pg. @;

Q6539: F. Wichern, *et al.* Perinatal nicotine treatment induces transient increases in NACHO protein levels in the rat frontal cortex. Neuroscience 2017;346(278-283

Agents: Nicotine Hydrogen Tartate **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat (pregnant); **Pump:** 2006; **Duration:** 6 weeks;

ALZET Comments: Dose (4 mg/kg/day); animal info (timed-pregnant Sprague Dawley (SD) rats); comparison of injections vs mp;

Q6745: D. S. Poole, *et al.* Continuous infusion of manganese improves contrast and reduces side effects in manganese-enhanced magnetic resonance imaging studies. Neuroimage 2017;147(1-9

Agents: Manganese Chloride **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 8 days;

ALZET Comments: Dose (30 mg/kg and 60 mg/kg); Controls received mp w/ vehicle; animal info (10 week old C57BL/6J mice); comparison of IP injections vs mp; MRI; “Our study demonstrates that the osmotic pump is able to deliver Mn to the brain (and in a suitable amount) with contrast comparable to that achieved via IP injections. Although a higher dose does appear necessary to achieve a similar contrast, this higher dose administered via osmotic pump can be used without giving side effects. Additionally, the constant delivery of manganese ensures a stable blood level and presumably a more timing-independent manganese uptake during activation. Lastly, osmotic pump delivery ensures less animal handling during the experiment, which may be a large advantage for many studies involving behavior, fear or stress, where animal handling may have a large influence on the experimental outcome.” pg.8 ;

Q6237: A. Patnaik, *et al.* Cabozantinib Eradicates Advanced Murine Prostate Cancer by Activating Antitumor Innate Immunity. Cancer Discovery 2017;7(7):750-765

Agents: Plerixafor; AMD3100; cabozantinib **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice; **Pump:** 1007D; **Duration:** 3 days;

ALZET Comments: Dose (90 mg/mL); animal info (male Pb-Cre; Ptenfl/flTrp53fl/fl mice with tumor); comparison of Plerixafor daily injection vs mp; AMD3100 is a CXCR4 inhibitor; cancer (prostate);

Q5357: F. Muller, *et al.* Paclitaxel synergizes with exposure time adjusted CD22-targeting immunotoxins against B-cell malignancies. ONCOTARGET 2017;1-12

Agents: HA22- PE24 recombinant immunotoxin **Vehicle:** Citrate buffer; **Route:** IP; **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (6-8-week-old NSG mice); JeKo-1 xenograft model; Citrate buffer: 32 mM citrate, 0.65% Tween80, 5 mM EDTA; comparison of 3 times IV bolus injections vs mp; cancer (Mantle Cell Lymphoma); half-life: 15 minutes in mice (p. 4); To enable continuous drug delivery in vivo, the rIT-formulation buffer was optimized to ensure protein stability. Stability for 7-days with citrate buffer verified using WST-8 cell proliferation assay; “Continuous infusion substantially increased efficacy of LR compared to bolus dose administration.” pg 4; “a well-tolerated total amount of 84 µg LR given by continuous infusion is substantially more active than the 120 µg LR given as three bolus doses QOD.” (P. 5); Because rITs have a short plasma half-life in mice and men, blood levels fall quickly after a bolus dose;



Dose (1 mg/ml); Immunotoxin plasma concentration was on average 45 ng/ml, correlating with an AUC of 350 ng x day/ml Plasma. This steady state plasma concentration was higher than the IC50 of any of the MCL cell lines tested.

Q6147: D. Leu, *et al.* CNS bioavailability and radiation protection of normal hippocampal neurogenesis by a lipophilic Mn porphyrin-based superoxide dismutase mimic, MnTnBuOE-2-PyP(5). *Redox Biol* 2017;12(864-871

Agents: Porphyrin, Mn **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 2-6 weeks;

ALZET Comments: Dose (3 mg/kg/day); animal info (25g male C57BL/6J mice); Comparison of 2X daily injections vs mp ("Mice received either two daily subcutaneous (sc) injections (2x1.5 mg/kg) for 7–14 days, or continuous infusion for 2–6 weeks using a model 1004 Alzet® osmotic pump loaded with 28.4 mg/ml MnP"); Resultant plasma level (Fig. 1D p.865);

Q6299: P. B. Katare, *et al.* Toll-Like Receptor 4 Inhibition Improves Oxidative Stress and Mitochondrial Health in Isoproterenol-Induced Cardiac Hypertrophy in Rats. *Front Immunol* 2017;8(719

Agents: TLR4 receptor inhibitor RS-LPS; agonist lipopolysaccharide; isoproterenol **Vehicle:** Saline, pyrogen-free; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 14 days;

ALZET Comments: Dose (RS-LPS: 5 µg/day; lipopolysaccharide: 3.12 ug/day); Controls received mp w/ vehicle; animal info (Male Sprague- Dawley rats weighing 200–250 g); comparison of sc injections vs mp; cardiovascular;

Q6254: S. A. Grenald, *et al.* Targeting the S1P/S1PR1 axis mitigates cancer-induced bone pain and neuroinflammation. *Pain* 2017;158(9):1733-1742

Agents: FTY720 **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Dose (1 mg/kg/d); Controls received mp w/ vehicle; animal info (Female BALB/c mice weighing 18-20 g); comparison of single daily injection vs mp; FTY720 aka fingolimod; cancer ();

Q6473: Gravius A, *et al.* Further pharmacological characterization of eltoprazine: focus on its anxiolytic, anorexic, and adverse effect potential. *Acta Neurobiologiae Experimentalis* 2017;77(1):77-85

Agents: Eltoprazine **Vehicle:** Water; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** Not Stated;

ALZET Comments: Dose (8 mg/kg/day); animal info (male Sprague Dawley rats weighing 180–200 g); behavioral testing (elevated plus testing); comparison of twice daily SC injections (1 mg/kg) vs mp; Eltoprazine aka 1 (2,3 dihydro 1,4 benzodioxin 8 yl)piperazine; neurodegenerative (Parkinson's disease);

Q5327: G. Futamura, *et al.* Evaluation of a novel sodium borocaptate-containing unnatural amino acid as a boron delivery agent for neutron capture therapy of the F98 rat glioma. *Radiat Oncol* 2017;12(1):26

Agents: Boron-10 containing sodium borocaptate, ACBC-BSH (Boron-10 derivative) **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2001D; **Duration:** 24 hours;

ALZET Comments: ALZET brain infusion kit used; comparison of IV injections vs mp; cancer (F98 glioma); brain tissue distribution; "we succeeded in achieving a high accumulation of boron in the tumors of rats in which ACBC-BSH was administered by CED, compared with ACBC-BSH administered intravenously" pg. 9 ; ACBC-BSH is a boron-10 containing sodium borocaptate derivative, 1-amino-3-fluorocyclobutane-1-carboxylic acid; Dose (1.2 mg/kg);

Q6414: L. D. BonDurant, *et al.* FGF21 Regulates Metabolism Through Adipose-Dependent and -Independent Mechanisms. *Cell Metabolism* 2017;25(4):935-944 e4

Agents: Fibroblast growth factor-21, recomb. human **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice (knockout); **Pump:** Not Stated; **Duration:** 2 weeks;

ALZET Comments: Dose (1 mg/kg/day); Controls received mp w/ vehicle; animal info (16–18 week old WT and KLB AdipoKO male mice on HFD for 12 weeks); comparison of IP injection vs mp;

Q5942: A. Akopian, *et al.* Targeting neuronal gap junctions in mouse retina offers neuroprotection in glaucoma. *J Clin Invest* 2017;127(7):2647-2661

Agents: meclofenamic acid **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 8 weeks;

ALZET Comments: animal info (3-4 months); pumps replaced every 4 weeks; comparison of injection vs mp; neurodegenerative (glaucoma); stress/adverse reaction: We found that animals in which subcutaneous minipumps were



inserted for MFA delivery had significant problems swimming the water maze, which compromised the ability to assess the visual behavioral tests (page 2659); Therapeutic indication (Glaucoma); Dose ((5, 10, and 20 mg/kg/d));