Recent References on the Administration of Protein Kinase Inhibitors
Using ALZET® Osmotic Pumps

Calphostin C (2002-Present)

Q3801: P. Almela, et al. Crosstalk between G protein-coupled receptors (GPCRs) and tyrosine kinase receptor (TXR) in the heart after morphine withdrawal. FRONTIERS IN PHARMACOLOGY 2013;4(U1547-U1559HA-1004; calphostin c
Agents: HA-1004; calphostin c Vehicle: Water, sterile; DMSO; Route: SC; Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 220-240g); 0.06% DMSO used; dependence; cardiovascular; pumps primed for 5 hours in 37C saline;

Agents: Calphostin C chelerythrine Vehicle: Not Stated; Route: SC; Species: Rat; Pump: Not Stated; Duration: 7 days;
ALZET Comments: Animal info (Sprague Dawley, male, 220-240 g); enzyme inhibitor (PKC, protein kinase C)

Agents: Calphostin C Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: Controls received mp w/ saline; animal info (male, Sprague-Dawley, 220-240 g); enzyme inhibitor (PKC, protein kinase C)

Agents: HA-1004; calphostin C Vehicle: Water; DMSO; Route: SC; Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: Animal info (male, Sprague Dawley, 220-240 g); enzyme inhibitor (PKA, PKC);

Agents: HA-1004; calphostin C Vehicle: DMSO; water; Route: SC; Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: Controls received mp w/ vehicle; no stress (see pg. 378); enzyme inhibitor (PKA, PKC); pumps were primed for 5 hours prior to implantation

Agents: Calphostin C Vehicle: Water, Milli-Q; DMSO; Route: SC; Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: Controls received mp w/ vehicle; no stress (see pg. 378); enzyme inhibitor (protein kinase C, protein kinase A); animal info (male, Sprague-Dawley, 220-240 g); mp primed 5 hours in 37 celsius saline; 0.06% DMSO; “Animals infused with calphostin c showed no untoward effects: their weights were equivalent to those of vehicle injected groups, and the rats showed no behavioural changes.” (pg.378)

Agents: Calphostin C Vehicle: DMSO; water; Route: SC; Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague-Dawley, 220-240 g); enzyme inhibitor (protei

Agents: HA-1004; calphostin C Vehicle: Water, sterile; DMSO; Route: SC; Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: Controls received mp w/ vehicle; enzyme inhibitor (protein kinase A, protein kinase C)
Cediranib
Agents: Cediranib Vehicle: DMSO; Route: IP; Species: Mice; Pump: 1003D; Duration: 72 hours; ALZET Comments: Animal info (wt, Mdr1a/b -/-, Bcrp1 -/-, and Mdr1a/b -/-, Bcrp1 -/-); cancer (glioma);

Cetuximab
Agents: Cetuximab Vehicle: Not Stated; Route: CSF/CNS (intratumoral) Species: Mice (nude) Pump: 2ML4; Duration: 4 weeks; ALZET Comments: Control animals received mp w/ PBS; ALZET brain infusion kit 2 used; convection enhanced delivery (CED); tissue perfusion (intratumoral)

Agents: Cetuximab Vehicle: Not Stated Route: CSF/CNS (intratumor) Species: Mice (nude) Pump: 2004 Duration: Not Stated; ALZET Comments: Controls received mp w/ vehicle; ALZET brain infusion kit 2 used; animal info (NMRI- nu/nu, 6-8 wks old);

Chelerythrine
Agents: Calcitonin gene-related peptide, SP600125, chelerythrine, CGRP8-37 receptor antagonist Vehicle: Saline; DMSO; Route: IP, Kidney (cortical region); Species: Mice; Pump: Not Stated; Duration: Not Stated;
ALZET Comments: Dose (30 ng/kg/d); 10% DMSO used; Controls received mp w/ vehicle; animal info (Male C57BL/6 mice aged 8 to 10 weeks); The catheter was anchored to the obstructed ureter, and osmotic pump placed SC; some mice were given CGRP8-37 (120 μg/kg/d), SP600125 (30 mg/kg/d), chelerythrine (5 mg/kg/d)

Agents: Peptide, zeta-inhibitory; chelerythrine Vehicle: CSF, artificial; PBS; Route: CSF/CNS (third ventricle); Species: Mice; Pump: 1002; Duration: 2 days; 6 days; ALZET Comments: Controls received mp w/ vehicle; animal info (C57BL/6Jx129T2SvEms/J, adult); post op. care (buprenorphine injection); behavioral testing (locomotion, locomotor sensitization); Lynch coil of ZIP administration for 14.5 hours;

Agents: Chelerythrine Vehicle: Saline; Route: CSF/CNS (intrathecal); Species: Rat; Pump: 2001; Duration: 7 days; ALZET Comments: Controls received mp w/ vehicle; animal info (adult, male, Sprague Dawley, 200-300 g);

Agents: Calphostin C; chelerythrine Vehicle: Not Stated; Route: SC; Species: Rat; Pump: Not Stated; Duration: 7 days; ALZET Comments: Animal info (Sprague Dawley, male, 220-240 g); enzyme inhibitor (PKC, protein kinase C)

Agents: Phorbol 12, 13-didecanoate; chelerythrine; apamin; iberiotoxin Route: CSF/CNS (thalamus); Species: Mice; ALZET Comments: Controls received mp w/ vehicle; animal info (male, C57BL/6, 129S4/SvJac, wt, PLCB4 -/-); cannula position confirmed by post mortem histology; behavioral testing (visceral pain test)
Agents: Angiotensin II; Chelerythrine Vehicle: Saline; Route: SC; Species: Rat; Pump: Not Stated; Duration: 7 days;
ALZET Comments: controls received mp w/ vehicle; peptides; cardiovascular; enzyme inhibitor; some animals received ang II and the protein kinase C inhibitor chelerythrine concomitantly

Agents: Rp-8-Cl-cAMPS; Rp-8-Cl-cGMPS; Chelerythrine chloride; Peptide, inhibitory myristolated; Species: Cat;
ALZET Comments: Peptides; Fig. 5 mentions minipump infusion; enzyme inhibitors; protein kinase A, C, and G inhibitors

Dasatinib
Agents: Dasatinib Vehicle: Not Stated; Route: CSF/CNS; Species: Mice; Pump: 2002; Duration: 14 days;
ALZET Comments: Dose (2 uM); Dasatinib aka Tyrosine Kinase Inhibitor; enzyme inhibitor (Tyrosine Kinase Inhibitor);

Agents: Dasatinib, Saracatinib Vehicle: DMSO; 16-OHE; Route: SC; Species: Mice; Pump: 1004; Duration: 4 weeks;
ALZET Comments: Dose (1 mg/kg/day); 50% DMSO/50% 16α-hydroxyestrone (16-OHE) used; Controls received mp w/ vehicle; animal info (10-14 weeks old)cardiovascular;

Agents: Dasatinib; everolimus Vehicle: DMSO; ethanol anhydrous; CSF, artificial; Route: CSF/CNS (brain stem); Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: Control animals received mp w/ aCSF and coomassie blue; animal info (Sprague-Dawley, 188-250 g); convection-enhanced delivery; Plastics One cannula used; “an Elizabethan collar was placed on animals to prevent disturbance of cannula” pg 222; “brainstem targeting using pCED to infuse single and multi-drug therapy was well tolerated in these rats”

Agents: Dasatinib Vehicle: DMSO; saline; Route: IP; Species: Mice; Pump: 1004; Duration: 4 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, C57BL6, 3 months old); 50% DMSO used; no stress (see pg. 4); cardiovascular;

Q2412: G. Dhawan, et al. Amyloid-beta oligomers stimulate microglia through a tyrosine kinase dependent mechanism. NEUROBIOLOGY OF AGING 2012;33(10):2247-2261
Agents: Dasatinib; oligomer, amyloid beta (1-42) Vehicle: HEPES; Route: CSF/CNS; Species: Mice; Pump: 1004; Duration: 14 days;
ALZET Comments: Control animals received mp w/ vehicle; animal info (C57BL/6, female, 12 mo old); ALZET brain infusion kit used; neurodegenerative (Alzheimer’s disease); peptide; enzyme inhibitor (tyrosine kinase)

Agents: Dasatinib Vehicle: DMSO; HEPES; Route: SC; Species: Mice; Pump: 1004; Duration: 28 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (female, APP/PS1, 13 mo old);
Agents: Dasatinib; imatinib mesylate Vehicle: DMSO; water; PBS, Route: SC, Species: Mice, Duration: 4 days; ALZET Comments: Controls received mp w/ vehicle; animal info (6 wks old, female, C57/BL6); 50% DMSO used; dasatinib also known as BMS-354825; one group contained a mixture of dasatinib and imatinib mesylate in a single pump; imatinib mesylate also known as STI-571; enzyme inhibitor (tyrosine kinase, Src Abl)

Fasudil (2010-Present)
Agents: Fasudil Vehicle: Not stated, Route: CNS/CSF, Species: Mice, Pump: 2001, Duration: 7 days; ALZET Comments: Dose (25 gm/kg/day); Controls received mp w/ vehicle; animal info (CD1, Male, 25-30 g)

Agents: Fasudil Vehicle: Saline, Route: CSF/CNS (intrathecal), Species: Rat, Pump: 1007D, Duration: 3 days; 7 days; 14 days; ALZET Comments: Controls received mp w/ vehicle; animal info (male, SD, adult, 260-300g); behavioral testing (BBB behavioral testing); Dose (180 ug/day);

Q4644: M. Wermke, et al. RNAi profiling of primary human AML cells identifies ROCK1 as a therapeutic target and nominates fasudil as an antileukemic drug. Blood 2015;125(3760-3768
Agents: Fasudil Vehicle: Not Stated, Route: SC, Species: Mice (NSG), Pump: Not Stated, Duration: 2 weeks; ALZET Comments: Animal info (female, NSG, 4-6 weeks old); cancer (acute myeloid leukemia); immunology;

Agents: Y-27632; dimethylfasudil Vehicle: DMSO; saline, Route: IP, Species: Mice, Pump: Not Stated, Duration: Not Stated; ALZET Comments: Controls received mp w/ vehicle; animal info (C57BL6J, adult); pumps replaced every 4 weeks; behavioral testing (statici rod test); enzyme inhibitor (Rho-associated protein kinase; ROCK);

Agents: Fasudil Vehicle: Not Stated, Route: Not Stated, Species: Rat, Pump: Not Stated, Duration: 28 days; ALZET Comments: Animal info (EAN); neurodegenerative (Guillain-Barr syndrome);

Agents: Fasudil Vehicle: Saline, sterile, Route: CSF/CNS, Species: Rabbit, Pump: Not Stated, Duration: 4 days; ALZET Comments: Controls received mp w/ vehicle; animal info (New England, white, male, 3.0-4.5 kg); enzyme inhibitor (ROCK II, Rho associated protein kinase)

Agents: L-NAME; fasudil Vehicle: Not Stated, Route: SC, Species: Rat (pregnant), Pump: Not Stated, Duration: Not Stated; ALZET Comments: Controls received mp w/ normal saline; animal info (Wistar Han, 200-250 g, E14, female);

Agents: Fasudil Vehicle: Not Stated, Route: SC, Species: Rat, Pump: Not Stated, Duration: Not Stated; ALZET Comments: Controls received mp w/ PBS; animal info (male, Lewis, 7-8 wks old, 250-300 g);
**Agents:** Fasudil  
**Vehicle:** Water, sterile  
**Route:** SC  
**Species:** Rat  
**Pump:** 2004  
**Duration:** 4 weeks  
**ALZET Comments:** Controls received mp w/ sterile saline; animal info (male, Wistar, 6 wks old, 260-310 g) |
| Q1920 | S. de Frutos, et al. Endothelin-1 contributes to increased NFATc3 activation by chronic hypoxia in pulmonary arteries. American Journal of Physiology Heart and Circulatory Physiology 2010;299(2):U133-U140  
**Agents:** Fasudil  
**Vehicle:** Not Stated  
**Route:** SC  
**Species:** Mice  
**Pump:** Not Stated  
**Duration:** 3 days  
**ALZET Comments:** Animal info (adult, male, 9x-NFAT-luciferase reporter, NFATc3 knockout, BalB/C wild-type, 25-30 g) |
**Agents:** Fasudil  
**Vehicle:** Saline  
**Route:** SC  
**Species:** Rat  
**Pump:** 2ML4  
**Duration:** Not Stated  
**ALZET Comments:** Controls received mp w/ vehicle; animal info (8-10 wks old, Wistar Han, 200-225 g) |
**Agents:** Fasudil  
**Vehicle:** CSF, artificial  
**Route:** CSF/CNS (right lateral ventricle)  
**Species:** Rat  
**Pump:** 1003D  
**Duration:** 24-26 days  
**ALZET Comments:** Animal info (naive, 3-mo old, wt, A-betaPP/PS1); ALZET brain infusion kit 3 used; artificial CSF recipe |
**Agents:** Bisindolylmaleimide; KN-93; H-89; U0126; H-89; U0126; H-89; U0126  
**Vehicle:** Not Stated  
**Route:** CSF/CNS (right lateral ventricle)  
**Species:** Rat  
**Pump:** 1003D  
**Duration:** 3 days  
**ALZET Comments:** Controls received mp w/ vehicle; animal info (male Sprague-Dawley (SD) rats (7 weeks old)); behavioral testing (Morris Water maze test); enzyme inhibitor ALZET brain infusion kit 1 used; Brain coordinates (1 mm posterior; 1.5 mm lateral; 3.5 mm depth to the bregma) |
| Q6203 | S. J. Min, et al. Leptomycin B attenuates neuronal death via PKA- and PP2B-mediated ERK1/2 activation in the rat hippocampus following status epilepticus. Brain Research 2017;1670(14-23  
**Agents:** Cyclosporin A; H-89; Leptomycin B; U0126  
**Vehicle:** Not Stated  
**Route:** CSF/CNS (right lateral ventricle)  
**Species:** Rat  
**Pump:** 1007D  
**Duration:** 3 days  
**ALZET Comments:** Controls received mp w/ vehicle; animal info (Adult male Sprague-Dawley rats weighing 320–370 g); H-89 is a PKA inhibitor; U0126 is an ERK ½ inhibitor; ALZET brain infusion kit 1 used; Brain coordinates (1 mm posterior; 1.5 mm lateral; 3.5 mm depth) Therapeutic indication (seizure) |
| Q4915 | L. Yang, et al. Activation of protein kinase A in the amygdala modulates anxiety-like behaviors in social defeat exposed mice. Mol Brain 2016;9(3  
**Agents:** 8-Br-cAMP; H-89;  
**Route:** CSF/CNS (basolateral amygdala)  
**Species:** Mice  
**Pump:** 1002  
**Duration:** 10 days  
**ALZET Comments:** Controls received mp w/ saline; animal info (male, C57BL6J, 8 weeks old); ALZET brain infusion kit 2 used; behavioral testing (social defeat stress; social interaction; open field; elevated plus maze; rotarod test ); bilateral infusion; pumps removed after 10 days; Dose (8-Br-cAMP 2 ug/day; H-89 0.3 ug/day) |
Agents: H89; U73122; U73343 Vehicle: Saline; DMSO; Route: CSF/CNS (motor cortex); Species: Rat; Pump: 1002; Duration: 5, 9 days
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Long-Evans 8-10 weeks old, 250-350g); post op. care (buprenorphin 0.01 mg/kg IP); behavioral testing (motor skill); Cannula placement verified via Nissl staining; “double-loaded” vehicle and agent solution for vehicle only during recovery;

Agents: 8CPT; H-89 Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 2004; Duration: 28 days;
ALZET Comments: Control animals received mp w/ PBS; animal info (male, athymic, 15-20 g, 4-6 wks old);

Agents: H89 Vehicle: Not Stated; Route: CSF/CNS; Species: Mice; Pump: 1002; Duration: 8 days;
ALZET Comments: Controls received mp w/ saline; animal info (8 wks old, male, AM+/-, C57BL/6 Wt); enzyme inhibitor (PKA, protein kinase A); middle cerebral artery occlusion (MCAO)

Agents: Bortezomib; cyclic AMP; H89 Vehicle: Not Stated; Route: SC; Species: Mice (nude); mice (transgenic); Pump: Not Stated; Duration: 1, 3, 6, 7 days;
ALZET Comments: Controls received no treatment; animal info (nude, PLZF-RARA-RARA-PLZF; PML-RARA5873A Tg);

Agents: H89 Vehicle: Saline; Route: CSF/CNS (intrathecal); Species: Rat; Pump: Not Stated; Duration: 1 week;
ALZET Comments: Controls received mp w/ vehicle; 1 week stability verified (results not shown); enzyme inhibitor;
P8249: P. Almela, et al. Differential involvement of 3', 5'-cyclic adenosine monophosphate-dependent protein kinase in regulation of Fos and tyrosine hydroxylase expression in the heart after naloxyne induced morphine withdrawal. 
NAUNYN-SCHMIEDEBERGS ARCHIVES OF PHARMACOLOGY 2007;374(4):293-303
**Agents:** HA-1004 **Vehicle:** Water, sterile; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 7 days; 
**ALZET Comments:** Controls received mp w/ vehicle; enzyme inhibitor (protein kinase A); animal info (male, SD, 220-240g)


**Imatinib (2011-Present)**


**Agents:** Imatinib **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 28 days; 
**ALZET Comments:** Controls received mp w/ vehicle; animal info (Pathogen-free, male C57BL/6 and Balb/c mice, 20-24 g); Imatinib aka GNP-HClm; toxicology;


**Agents:** Ro-31-8220; imatinib **Vehicle:** PBS; **Route:** SC; **Species:** Mice (transgenic); **Pump:** 2002; **Duration:** 14 days; 
**ALZET Comments:** Dose (Ro-31-8220 (1 mM); imatinib (0.5 mM)); Controls received mp w/ vehicle; animal info (6-12 wk old transgenic mice);


**Agents:** Nilotinib; Imatinib **Vehicle:** Ethanol:PEG300: Cremophor EL, Sterile water; **Route:** IV injection; Gavage; **Species:** Mice; Guinea pigs; Prairie Dogs; Cynomolgus monkeys; Pump: Not Stated; **Duration:** Not Stated; 
**ALZET Comments:** Nilotinib 1.5:4.5:20 (ethanol:PEG300:Cremophor) in 3.7% dextrose solution used; animal info (Mice C57BL/6, 20g both genders; Prairie dogs wild caught male black tailed, 1-2 years; Guinea pigs male hartley 450-650g); half-life (p.1,8); Resultant plasma level (Figure 1 nilotinib, Figure 2 imatinib); enzyme inhibitor (tyrosine kinase (TKI)); good methods (elimination half-lives were quite short (1–2 h). Thus, further testing of these agents in C57BL/6 mice is feasible but may require a continuous delivery system such as an Alzet® mini pump.); didn’t use Alzet pmup, but recommends using it in future studies of these agents in mice or guinea pigs;


**Agents:** Angiotensin II; Imatinib mesylate **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 2 weeks; 
**ALZET Comments:** Dose (Angiotensin II: 3 mg/kg/day; Angiotensin II + Imatinib mesylate: 60 mg/kg per day); 0.9% saline used; Controls received mp w/ vehicle; animal info (12-30 week old C57BL/6 male mice weighing 25-35g);


**Agents:** Imatinib mesylate **Vehicle:** Saline; **Route:** SC; **Species:** Mice (pregnant); **Pump:** 2001; **Duration:** 5 days; 
**ALZET Comments:** Controls received mp w/ vehicle; animal info (10 weeks old); cancer (Breast); Therapeutic indication (Mammary gland development, Breast cancer); Dose (21 mg/mouse/week);
**Agents:** Imatinib mesylate  
**Vehicle:** Water  
**Route:** SC  
**Species:** Mice  
**Pump:** 1007D  
**Duration:** 28 days  
**ALZET Comments:** Controls received mp w/ vehicle; animal info (male, C57BL6, 6 weeks old); functionality of mp verified by serum levels; dose-response (pg.9); immunology; enzyme inhibitor (tyrosine kinase);

**Agents:** Imatinib  
**Vehicle:** CSF, artificial  
**Route:** CSF/CNS (intrathecal)  
**Species:** Mice (transgenic)  
**Pump:** 1007D  
**Duration:** 1 wk  
**ALZET Comments:** Controls received mp w/ vehicle; animal info (triple transgenic ABBP, PS1, P301L); neurodegenerative (Alzheimer’s); “Since it is known that the drug does not penetrate the blood-brain barrier efficiently, it is possible that the contradictory results reflect this property of the drug. For this reason in the current study, we delivered Imatinib by means of implanted osmotic minipumps directly in the brains of the triple transgenic mice” pg 730;

**Agents:** Imatinib mesylate  
**Vehicle:** Not Stated  
**Route:** Not Stated  
**Species:** Mice  
**Pump:** Not Stated  
**Duration:** 5 weeks  
**ALZET Comments:** Controls received mp w/ vehicle; animal info (5HT-2b -/-, adult, 7-9 wks old); imatinib mesylate also known as Gleevec or STI-571; hypoxia; enzyme inhibitor (tyrosine kinase);

**Agents:** Dasatinib; imatinib mesylate  
**Vehicle:** DMSO; water; PBS  
**Route:** SC  
**Species:** Mice  
**Pump:** Not Stated  
**Duration:** 4 days  
**ALZET Comments:** Controls received mp w/ vehicle; animal info (6 wks old, female, C57/BL6); 50% DMSO used; dasatinib also known as BMS-354825; one group contained a mixture of dasatinib and imatinib mesylate in a single pump; imatinib mesylate also known as STI-571; enzyme inhibitor (tyrosine kinase, Src Abl)

KN92 or KN93 (2015-Present)
**Agents:** KN-93  
**Vehicle:** PBS  
**Route:** SC  
**Species:** Mice  
**Pump:** Not Stated  
**Duration:** 28 days  
**ALZET Comments:** Dose (5 umol/kg/day); Controls received mp w/ vehicle; animal info (Ten week old, male C57BL/6 mice);

**Agents:** Bisindolylmaleimide; 3-chloroacetyl-indole; U0126; KN-93; PJ-34; SC79  
**Vehicle:** Not stated  
**Route:** CSF/CNS (lateral ventricle)  
**Species:** Rat  
**Pump:** 1007D  
**Duration:** 3 days  
**ALZET Comments:** Dose (BIM 25uM, KN-93 25uM, H-89 10uM, U0126 25uM, okadaic acid 10uM, cyclosporine A 250uM); animal info (male Sprague-Dawley (SD) rats (7 weeks old)); behavioral testing (Morris Water maze test); ALZET brain infusion kit 1 used; Brain coordinates (1 mm posterior; 1.5 mm lateral; -3.5 mm depth);

**Agents:** Bisindolylmaleimide; KN-93; H-89; U0126; SP600125; okadaic acid; cyclosporin A  
**Vehicle:** Not Stated  
**Route:** CSF/CNS (right lateral ventricle)  
**Species:** Rat  
**Pump:** 1003D  
**Duration:** 3 days  
**ALZET Comments:** Dose (BIM 25uM, KN-93 25uM, H-89 10uM, U0126 25uM, okadaic acid 10uM, cyclosporine A 250uM); animal info (male Sprague-Dawley (SD) rats (7 weeks old)); behavioral testing (Morris Water maze test); ALZET brain infusion kit 1 used; Brain coordinates (1 mm posterior; 1.5 mm lateral; 3.5 mm depth to the bregma);

Agents: KN-92; KN-93
Vehicle: Not Stated
Route: IA (femoral)
Species: Woodchuck
Pump: 2ML1
Duration: 24 hours

ALZET Comments: Dose ((KN-92 125 μg/kg/h), (KN-93 125 μg/kg/h)); Controls received mp w/ KN-92; animal info (1-2 years, male and female, wild-caught, 2-3kg); cardiovascular; Therapeutic indication (inhibition of CaMKII activity by lessening its oxidized and/or phosphorylated levels may mediate its antiarrhythmic effects);

Q4601: K. Tagawa, et al. Comprehensive phosphoproteome analysis unravels the core signaling network that initiates the earliest synapse pathology in preclinical Alzheimer’s disease brain. HUMAN MOLECULAR GENETICS 2015;24(540-558

Agents: Go6976; MLR1023; KN-93
Vehicle: DMSO; PBS
Route: Not Stated
Species: Mice (transgenic)
Pump: 1003D

ALZET Comments: Animal info (male, APP770 human double mutant); 0.1% DMSO used; neurodegenerative (Alzheimer’s); behavioral testing (morris water maze, rotarod test, fear-conditioning, light-dark box, elevated plus maze);


Agents: KN-93; CBO-P11
Vehicle: Saline
Route: SC
Species: Mice
Pump: 1002
Duration: 2 weeks

ALZET Comments: Controls received mp w/ vehicle; animal info (male, Foxn1 nu, 6 weeks old); cancer (osteosarcoma);

Other (2012-Present)


Agents: Pan-PKC inhibitor
Vehicle: Not stated
Route: CSF/CNS (lateral ventricle)
Species: Mice
Pump: 1003D
Duration: 3 days

ALZET Comments: Dose (0.11 ul/hr); animal info (Male, 2 months old, 22-25 g, KM); Pan-PKC inhibitor aka Go6983; enzyme inhibitor (PKC inhibitor); ALZET brain infusion kit 2 used;


Agents: Bisindolylmaleimide I
Vehicle: PBS, sterile; DMSO, buffered
Route: CSF/CNS (cortex)
Species: Mice
Pump: 1004
Duration: 14 days

ALZET Comments: Dose (0.5 μM); PBS with 0.4% DMSO used; Controls received mp w/ vehicle; animal info (2 months, male, CD1); Go-6850 AKA Bisindolylmaleimide I, is a broad-spectrum PKC inhibitor; enzyme inhibitor (protein kinase B); Brain coordinates (~0.2 mm anterior and 1.0 mm lateral relative to bregma and 2.3 mm below the surface of the skull); Cannula placement verified via stereotaxic frame; immunology; mp model 2002 was used for chronic injections and model 1003D for acute injections;


Agents: Gö6976
Vehicle: PBS
Route: CSF/CNS (intrathecal)
Species: Mouse
Pump: 2006
Duration: 2 weeks

ALZET Comments: Dose (0.15 ul/h); animal info (PGRN-KI and C57BL/6J, 10-12 weeks old); behavioral testing (Morris water maze test, Fear-conditioning test, Probe test, Rotarod test, Open-field test, Light-dark box test)
Agents: 8-Br-cAMP; H-89 Vehicle: Not Stated; Route: CSF/CNS (basolateral amygdala); Species: Mice; Pump: 1002; Duration: 10 days;
ALZET Comments: Controls received mp w/ saline; animal info (male, CS7BL6J, 8 weeks old); ALZET brain infusion kit 2 used; behavioral testing (social defeat stress; social interaction; open field; elevated plus maze; rotarod test ); bilateral infusion; pumps removed after 10 days; Dose (8-Br-cAMP 2 ug/day; H-89 0.3 ug/day); brain coordinates;

Agents: Fluoroacetate, Propionamide ditri- Vehicle: PEG 400, PBS; Route: SC; Species: Rat, mice; Pump: 1003D, 1007D; Duration: 1 day, 2 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (Male Sprague-Dawley (SD) rats 10 wks, plasma prekallikrein gene-deficient mice (KLKB1-/-)); functionality of mp verified by enzyme activity assays; 10% PEG 400 used; dose-response (pg 2394, 2398); stability verified by (single bolus subcutaneous injection); Fluoroacetate, Resultant plasma level (pg 2394);

Agents: 8CPT; H-89 Vehicle: Not Stated; Route: SC; Species: Mice; Pump: 2004; Duration: 28 days;
ALZET Comments: Control animals received mp w/ PBS; animal info (male, athymic, 15-20 g, 4-6 wks old); 8CPT also known as 8-pCPT-2’-O-Me-cAMP; enzyme inhibitor (PKA); cancer (prostate)

Agents: PKGi; ODQ Vehicle: Water, distilled, deionized; Route: Kidney (cortex); Species: Rat; Duration: 6 days;
ALZET Comments: Control animals received mp w/ vehicle; animal info (Sprague Dawley, male, 4 wks old); Vetbond used to glue catheter to kidney

Agents: Stauorospine Vehicle: CSF, artificial; ethanol; Route: CSF/CNS; Species: Rat; Pump: 2002; Duration: 2 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (5-6 wks old, male, Dahl S, Wistar); guide cannula used;

PD98059 (2014-Present)
Agents: Dextrose; Fluorocitrate; Minocycline; SB203580; PD98059 Vehicle: DMSO; Route: CSF/CNS (intracerebral); IV (jugular); Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: 1% DMSO used; Controls received mp w/ vehicle; animal info (male, Sprague-Dawley rats (weight, 200–250 g)); behavioral testing (Von Frey filament test, Plantar test); functionality of mp verified by residual volume; Brain coordinates (0.8 mm posterior and 1.3 mm lateral to the bregma, and 4.0 mm ventral to the skull surface); dependence;

Agents: PD98059 Vehicle: DMSO, Saline; Route: Csf/cns (intracisternal); Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: Dose (0.1 μg/μl); 10% DMSO used;Controls received mp w/ vehicle; animal info (Male Sprague-Dawley rats); post op. care (penicillin G potassium); enzyme inhibitor (Mitogen-activated protein kinase kinase 1 inhibitor);
**Agents:** PD-98059  **Vehicle:** CSF, artificial;  **Route:** CSF/CNS;  **Species:** Rat;  **Pump:** 2006;  **Duration:** 6 weeks;
**ALZET Comments:** Controls received mp w/ vehicle; animal info (8 weeks old) ; Controls received mp w/ vehicle; animal info (8 weeks old) ; Therapeutic indication (Oral drug delivery, Pharmacokinetics); Dose (0.025 ug/hr);

Q4903: Y. Y. Shun-Guang Wei, Robert M. Weiss, Robert B. Felder. Inhibition of Brain Mitogen-Activated Protein Kinase Signaling Reduces Central Endoplasmic Reticulum Stress and Inflammation and Sympathetic Nerve Activity in Heart Failure Rats. Hypertension 2016;67(229-236)
**Agents:** PD98059; SB203580; SP600125  **Vehicle:** CSF, artificial; DMSO;  **Route:** CSF/CNS;  **Species:** Rat;  **Pump:** 2004;  **Duration:** 4wk
**ALZET Comments:** Controls received mp w/ vehicle; animal info (male, Sprague Dawley, adult, 275-325g); 5% DMSO used;

**Agents:** PD98059  **Vehicle:** DMSO, Ringer’s solution;  **Route:** SC;  **Species:** Rat;  **Pump:** 2004;  **Duration:** 28 days;
**ALZET Comments:** Controls underwent median nerve CCI or sham operation; functionality of mp verified by residual volume; Dose (2, 2.5, 3.0 mM);

**Agents:** PD98059  **Vehicle:** Not Stated;  **Route:** CSF/CNS (intrathecal);  **Species:** Rat;  **Pump:** 2001;  **Duration:** 7 days;
**ALZET Comments:** Controls received mp w/ saline; animal info (male, Sprague Dawley, 250-450g); functionality of mp verified by residual volume; used PE45 tubing to catheterize IT space;

**Ruxolitinib**

**Agents:** Ruxolitinib  **Vehicle:** Not Stated;  **Route:** Not Stated;  **Species:** Mice;  **Pump:** Not Stated;  **Duration:** 7 days;
**ALZET Comments:** Dose (50 mg/kg/d); cancer (lymphoma);

**Agents:** Ruxolitinib  **Vehicle:** PEG 300;  **Route:** SC;  **Species:** Mice;  **Pump:** Not Stated;  **Duration:** 2 weeks;
**ALZET Comments:** Dose (50 mg/kg/d); Controls received mp w/ vehicle; enzyme inhibitor (JAK1/2 inhibitor);

**Agents:** Ruxolitinib  **Vehicle:** Dimethylacetamide; propylene glycol;  **Route:** SC;  **Species:** Mice;  **Duration:** 4 weeks;
**ALZET Comments:** Control animals received mp w/ vehicle; animal info (BCR-JAK2); 40% DMA; 60% propylene glycol used;

**Agents:** Ruxolitinib  **Vehicle:** Dimethylacetamide; propylene glycol;  **Route:** SC;  **Species:** Mice (NSG);  **Duration:** 3-4 weeks;
**ALZET Comments:** Control animals received mp w/ vehicle; animal info (NOD SCID, nonobese); ruxolitinib also known as INCBO18424; stress/adverse effects “One ruxolitinib-treated mouse... experienced a wound dehiscence at the subcutaneous pump surgical site” pg 3512; cancer (leukemia); chemotherapeutic; 40% DMA used; 60% propylene glycol used;
Sorafenib
Agents: Sorafenib; sunitinib Vehicle: DMSO; saline; Route: IP; Species: Not Stated; Pump: 1003D; Duration: Not Stated;
ALZET Comments: Animal info (Friend virus B-type (FVB) wild type, and Abcb1a/b knockout mice); cancer (renal carcinoma and brain metastases); cancer; enzyme inhibitor (tyrosine kinase); chemotherapeutic

Agents: Sorafenib Vehicle: Not Stated; Route: SC; Species: Mice; Pump: Not Stated; Duration: 17 days;
ALZET Comments: Animal info (AGT KO, 8-10 weeks old); cardiovascular; SU6656 is a selective Src family kinase inhibitor;

SU6656
Agents: SU6656 Vehicle: Not Stated; Route: SC; Species: Mice; Pump: Not Stated; Duration: 17 days;
ALZET Comments: Animal info (AGT KO, 8-10 weeks old); cardiovascular; SU6656 is a selective Src family kinase inhibitor;

Sunitinib
Agents: Sunitinib malate Vehicle: DMSO; Route: CSF/CNS (intrathecal); Species: Mice; Pump: 1002; Duration: 2 weeks;
ALZET Comments: enzyme inhibitor (tyrosine kinase);Animal info (female, 8 weeks old); functionality of mp verified by use of evans blue dye; 2.5% DMSO used; spinal cord injury; immunology; used ALZET mouse IT catheter;

Agents: Sunitinib Vehicle: DMSO; Route: IP; Species: Mice (transgenic); mice (knockout); Pump: 1003D; Duration: 48 hours;
ALZET Comments: Dose (30 µg/h); animal info (8-10 week old wild-type and transgenic mice in which the gene for P-gp [Mdr1a/b(2/2) knockout mice], Bcrp [Bcrp1(2/2) knockout mice], and both P-gp and Bcrp [Mdr1a/b(2/2) Bcrp1(2/2) or “triple knockout” mice] was knocked out); enzyme inhibitor (tyrosine kinase);

Agents: Sorafenib; sunitinib Vehicle: DMSO; saline; Route: IP; Species: Not Stated; Pump: 1003D; Duration: Not Stated;
ALZET Comments: Animal info (Friend virus B-type (FVB) wild type, and Abcb1a/b knockout mice); cancer (renal carcinoma and brain metastases); cancer; enzyme inhibitor (tyrosine kinase); chemotherapeutic

TAT(47-57)
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:
Agents: P110-TAT (47-57)  Vehicle: Not Stated;  Route: SC;  Species: Mice;  Pump: Not Stated;  Duration: 1 week, 8 weeks;
ALZET Comments: Dose (3 mg/Kg/d); Controls received mp w/ vehicle; animal info (5 week old Hemizygous R6/2 HD mice); pumps replaced every 4 weeks; neurodegenerative (Huntington’s);

Agents: TAT 47-57, peptide; beta IV5-3, epsilon V1-2, carrier peptide;  Vehicle: Not Stated;  Route: SC;  Species: Rat;  Pump: Not Stated;  Duration: Not Stated;
ALZET Comments: Controls received mp w/ carrier peptide; animal info (Wistar, normotensive, 12 wks old, male, Dahl, 6 wks old); peptides; pumps replaced every 2 weeks; enzyme inhibitor (protein kinase C, PKC)

Agents: TAT 47-57, peptide; TAT; TAT 47-57, delta conjugated, peptide  Vehicle: Not Stated;  Route: SC;  Species: Rat;  Pump: Not Stated;  Duration: Not Stated;
ALZET Comments: Controls received mp w/ control peptide; animal info (DS, 11-15 wks old, male); peptides

Agents: RACK7, psi epsilon; V1–2,10, epsilon; TAT (47-57)  Vehicle: Not Stated;  Route: SC;  Species: Mice (nude);  Pump: 2001;  Duration: 5 weeks;
ALZET Comments: Controls received mp w/ TAT control peptide; comparison of IP injections vs. mp; pumps replaced every 2 weeks; enzyme inhibitor (PKC betaII, protein kinase C); animal info (6 wks old, male)

Agents: TAT (47-57); IIV5-3, beta-  Vehicle: Saline;  Route: Not Stated;  Species: Mice (nude);  Pump: 2001;  Duration: 5 weeks;
ALZET Comments: Controls received mp w/ vehicle or TAT (47-57); pumps replaced every 2 weeks; half-life (p. 6832) ~ 2 wks; enzyme inhibitor (PKC betaII, protein kinase C); animal info (C57BL/6J (H-2b), 6-8 wks old)

Agents: Peptide, TAT (47-57); Peptide TAT (47-57)-EV1-2  Vehicle: Saline, sterile;  Route: SC;  Species: Mice;  Pump: 1002;  Duration: 4 weeks;
ALZET Comments: Controls received mp w/ TAT control peptide; pumps replaced after 14 days; no stress (see pg. 519); enzyme inhibitor (Epsilon PKC); cardiovascular; peptides; animal info (male, C57BL/6J (H-2b), 6-8 wks old);

Agents: TAT (47-57), dv1-1-; TAT (47-57)  Route: SC;  Species: Rat;  Pump: 2ML2;  Duration: 4.6 weeks, 6.7 days;
ALZET Comments: Controls received mp w/ control peptide TAT; comparison of IP injections vs. mp; pumps replaced every 2 weeks; enzyme inhibitor (Protein kinase C); cardiovascular; peptides; ischemia (cerebral); animal info (11-12 wks old, male)

Trametinib
Agents: Trametinib  Vehicle: DMSO;  Route: SC;  Species: Mice;  Pump: 1002;  Duration: 8 days;
ALZET Comments: Dose (0.1, 1, or 3 mg/kg); Controls received mp w/ vehicle; animal info (C57BL/6, 18-25 g, 8-10 weeks old);

**Agents:** GSK2126458; trametinib, dabrafenib **Vehicle:** DMSO; **Route:** IP; **Species:** Mice; **Pump:** Not Stated; **Duration:** 48 hours; **ALZET Comments:** animal info (WT, Mdr1a/b -/-, Bcrp1 -/-); functionality of mp verified by plasma concentration; pumps primed overnight in 37C saline;

Q4147: S. Vaidhyanathan, et al. Factors Influencing the CNS Distribution of a Novel MEK-1/2 Inhibitor: Implications for Combination Therapy for Melanoma Brain Metastases. Drug Metabolism and Disposition 2014;42(1292-1300

**Agents:** Trametinib **Vehicle:** DMSO; **Route:** IP; **Species:** Mice; **Pump:** Not Stated; **Duration:** 48 hours; **ALZET Comments:** Animal info (WT, Mdr1 a/b -/-, Bcrp1 -/-); functionality of mp verified by plasma levels; cancer (melanoma); post op. care (heating pad for recovery); pumps primed overnight in 37C sterile saline; enzyme inhibitior(mitogen-activated protein kinase kinase-1 (MEK)-1/2 inhibitor); good methods (p. 1294)

**Vemurafenib**


**Agents:** Vemurafenib **Vehicle:** DMSO; propylene glycol; saline **Route:** IP **Species:** Mice **Pump:** Not Stated **Duration:** 48 hours **ALZET Comments:** Animal info (wt, Mdr1a/b -/-, Bcrp1 -/-); infusion rate of 1 ul/hr; wound clips used; brain tissue distribution; cancer (breast); vemurafenib also known as PLX4032; 40% DMSO used; chemotherapeutic