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

Dasatinib

Q10346: Q. Su, *et al.* Inhibition of Maternal c-Src Ameliorates the Male Offspring Hypertension by Suppressing Inflammation and Neurotransmitters in the Paraventricular Nucleus. Cardiovascular Toxicology 2021;21(10):820-834
Agents: Dasatinib **Vehicle:** Not Stated; **Route:** CSF/CNS (paraventricular nucleus); **Species:** Rat; **Pump:** 2006; **Duration:** 6 weeks;
ALZET Comments: Dose: (0.15 µl/h,200 µl); Controls received mp w/ vehicle; animal info: Female Sprague–Dawley rats weighing 250–300 g; Blood pressure measured via:tail-cuff; Blood pressure measurement results (see pg 4); Dasatinib (DAS); cardiovascular;

Q9966: V. Tsvankin, *et al.* ABC Transporter Inhibition Plus Dexamethasone Enhances the Efficacy of Convection Enhanced Delivery in H3.3K27M Mutant Diffuse Intrinsic Pontine Glioma. Neurosurgery 2020;86(5):742-751
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); cancer

Q7794: R. W. D'Amico, *et al.* Saracatinib and Dasatinib Fail To Prevent Heritable Pulmonary Arterial Hypertension. bioRxiv 2018;345447
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;

Q3781: S. L. Ho, *et al.* Toxicity evaluation of prolonged convection-enhanced delivery of small-molecule kinase inhibitors in naive rat brainstem. Child's Nervous System 2015;31(221-226
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" pg 221; enzyme inhibitor (receptor tyrosine kinase)

Q4317: S. Balasubramanian, *et al.* Dasatinib Attenuates Pressure Overload Induced Cardiac Fibrosis in a Murine Transverse Aortic Constriction Model. PLoS One 2015;10(U407-U425
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

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)

Q2100: G. Dhawan, *et al.* Inhibition of Src kinase activity attenuates amyloid associated microgliosis in a murine model of Alzheimer's disease. Journal of Neuroinflammation 2012;9(;):U1-U17
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);

Q1444: P. M. Reeves*, et al.* Variola and Monkeypox Viruses Utilize Conserved Mechanisms of Virion Motility and Release That Depend on Abl and Src Family Tyrosine Kinases. JOURNAL OF VIROLOGY 2011;85(1):21-31
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)

Erlotinib

Q2576: S. Agarwal*, et al.* Function of the Blood-Brain Barrier and Restriction of Drug Delivery to Invasive Glioma Cells: Findings in an Orthotopic Rat Xenograft Model of Glioma. Drug Metabolism and Disposition 2013;41(1):33-39
Agents: Erlotinib **Vehicle:** DMSO; **Route:** IP; **Species:** Mice; **Pump:** 1003D; **Duration:** 48 hours;
ALZET Comments: Animal info (Mdr1ab -/-, Bcrp1 -/-, 8-10 wks old); wound clips used; half-life ("approximately 1 hour") pg 34; cancer (glioma); "Erlotinib half-life in mice has been reported to be approximately 1 hour (Marchetti et al., 2008), so an infusion lasting 48 hours was considered to be sufficient to attain steady state in both the brain and plasma." pg 34; chemotherapeutic; enzyme inhibitor (tyrosine kinase);

Imatinib (Gleevec)

Q10274: S. Hegde*, et al.* Inhibition of the RacGEF VAV3 by the small molecule IODVA1 impedes RAC signaling and overcomes resistance to tyrosine kinase inhibition in acute lymphoblastic leukemia. Leukemia 2022;36(3):637-647
Agents: IODVA1; Imatinib **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 28 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (Vav3-deficient mice and Rac1Δ/Δ+Rac2-deficient mice; C57Bl/10 (females, 8–16 weeks old) and NSG (NOD/SCID/IL2RG-/- males and females, 8–14 weeks old); IODVA1 aka 2-guanidinobenzimidazole derivative with anti-tumorigenic properties; cancer (leukemia)

Q10054: L. Pandolfi*, et al.* Loading Imatinib inside targeted nanoparticles to prevent Bronchiolitis Obliterans Syndrome. Scientific Reports 2020;10(1):20726
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;

Q6168: R. C. Nayak*, et al.* The signaling axis atypical protein kinase C lambda/iota-Satb2 mediates leukemic transformation of B-cell progenitors. Nat Commun 2019;10(1):1-16
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 week old transgenic mice); enzyme inhibitor (Protein Kinase C);

Q10082: H. K. Ananthula*, et al.* Preclinical pharmacokinetic evaluation to facilitate repurposing of tyrosine kinase inhibitors nilotinib and imatinib as antiviral agents. BMC Pharmacology and Toxicology 2018;19(1):80
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;

Q6491: Tucheng Sun, *et al.* Imatinib inhibits angiotensin II-induced aortic dissection through the c-Abl signaling pathway. International Journal for Clinical Experimental Pathology 2017;10(5):5316-5324
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); enzyme inhibitor (tyrosine kinase, c-Abl); cardiovascular; Pump incorrectly noted as model #1014D

Q5735: R. Callahan, *et al.* Original Research: Featured Article: Imatinib mesylate (Gleevec) inhibits Notch and c-Myc signaling: Five-day treatment permanently rescues mammary development. Experimental Biology and Medicine 2017;242(1):53-67
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); Imatinib mesylate a.k.a Gleevec ; Therapeutic indication (Mammary gland development, Breast cancer); Dose (21 mg/mouse/week); enzyme inhibitor (tyrosine kinase);

Q4546: R. J. Napier, *et al.* Low Doses of Imatinib Induce Myelopoiesis and Enhance Host Anti-microbial Immunity. PLoS Pathogens 2015;11(U1651-U1677
Agents: Imatinib mesylate **Vehicle:** Water; **Route:** SC; **Species:** Mice; **Pump:** 1007D; 2002; **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);

Q3443: J. Chu, *et al.* Pharmacological Modulation of GSAP Reduces Amyloid-beta Levels and Tau Phosphorylation in a Mouse Model of Alzheimer's Disease with Plaques and Tangles. Journal of Alzheimers Disease 2014;41(729-737
Agents: Imatinib **Vehicle:** CSF, artificial; **Route:** CSF/CNS (intrathecal); **Species:** Mice (transgenic); **Pump:** 1007D; **Duration:** 1 week;
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; Imatinib aka STI571 akd Gleevec; used dental cement; enzyme inhibitor (tyrosine kinase);

Q1933: J. M. Launay, *et al.* Serotonin 5-HT(2B) receptors are required for bone-marrow contribution to pulmonary arterial hypertension. Blood 2012;119(7):1772-1780
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);

Q1444: P. M. Reeves, *et al.* Variola and Monkeypox Viruses Utilize Conserved Mechanisms of Virion Motility and Release That Depend on Abl and Src Family Tyrosine Kinases. JOURNAL OF VIROLOGY 2011;85(1):21-31
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; one group contained a mixture of dasatinib and imatinib mesylate in a single pump; enzyme inhibitor (tyrosine kinase, Src Abl)

Q2221: R. J. Napier, *et al.* Imatinib-Sensitive Tyrosine Kinases Regulate Mycobacterial Pathogenesis and Represent Therapeutic Targets against Tuberculosis. Cell Host & Microbe 2011;10(5):475-485
Agents: Imatinib **Vehicle:** Water; **Route:** SC; **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, C57BL/6, 6 wks old); enzyme inhibitor (tyrosine kinase);

Q0111: M. Demestre, *et al.* Imatinib mesylate (Glivec) inhibits Schwann cell viability and reduces the size of human plexiform neurofibroma in a xenograft model. Journal of Neuro-oncology 2010;98(1):11-19
Agents: Imatinib mesylate **Vehicle:** PBS; **Route:** SC; **Species:** Mice (nude); **Pump:** 2004; **Duration:** 28 days;
ALZET Comments: Controls received mp w/ vehicle; cancer (Plexiform neurofibromas); enzyme inhibitor (receptor tyrosine kinase); stress/adverse reaction: (see pg 13) "because of inflammation at the ALZET pump site, four mice of the treatment group had to be discontinued"; animal info (female, athymic nu/nu Balb/c); agent also known as Glivec or Gleevec;

R0265: D. F. Smee. Progress in the discovery of compounds inhibiting orthopoxviruses in animal models. Antiviral Chemistry and Chemotherapy 2008;19(3):115-124
Agents: Gleevec **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** Not Stated;
ALZET Comments: Enzyme inhibitor (tyrosine kinase); Review, pg. 121, ref #21; compound also known as ST-571

P8330: A. Raafat, *et al.* Kit and PDGFR-alpha activities are necessary for Notch4/Int3-induced tumorigenesis. Oncogene 2007;26(5):662-672
Agents: Imatinib mesylate **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice (transgenic); **Pump:** 2001; **Duration:** 1,3,4,5,7 days;
ALZET Comments: Controls received mp w/ water; dose-response (fig 2); no stress (see pg. 663); cancer (mammary); animal info (female, FVB/N, 10 wks old); antiangiogenic; "Continuous release of Gleevec for a week resulted in 33% inhibition of tumor growth by day 2 and 66% by day 4." (p. 668); enzyme inhibitor (tyrosine kinase);

P8159: S. Bihorel, *et al.* Influence of hydroxyurea on imatinib mesylate (gleevec) transport at the mouse blood-brain barrier. Drug Metabolism and Disposition 2006;34(12):1945-1949
Agents: Imatinib mesylate; Hydroxyurea **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 7, 14 days;
ALZET Comments: Half-life (p. 1948) hydroxyurea <1 hour in rats; enzyme inhibitor (ribonucleotide reductase, tyrosine kinase); cancer (glioblastoma); animal info (Hanover Wistar, 270-310 grams);

P7552: P. M. Reeves, *et al.* Disabling poxvirus pathogenesis by inhibition of Abl-family tyrosine kinases. Nature Medicine 2005;11(7):731-739
Agents: Imatinib mesylate **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** 1007D; 1002; **Duration:** 5, 8,15 days;
ALZET Comments: Controls received mp w/ vehicle; no stress (see pg. 738); enzyme inhibitor (Abl-family kinase, tyrosine kinase); animal info (female, C57/BL, 6 wk. old); agent formerly known as STI571; virology; Gleevec

P6097: W. J. Netzer, *et al.* Gleevec inhibits beta-amyloid production but not Notch cleavage. Proceedings of the National Academy of Sciences of the United States of America 2003;100(21):12444-12449
Agents: Imatinib mesylate; Inhibitor 2 **Vehicle:** Saline; DMSO; **Route:** CSF/CNS (Intrathecal); **Species:** Guinea pig (albino);
Pump: 2001; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ vehicle; inhibitor 2 was dissolved in DMSO; "it has been shown that STI571 does not penetrate the blood-brain barrier efficiently, we therefore delivered (p. 12447) each inhibitor intrathecally over 7 days by means of implanted osmotic minipumps."; neurodegenerative (Alzheimer's disease)

PD153035

Q2985: M. Mizuno, *et al.* ErbB inhibitors ameliorate behavioral impairments of an animal model for schizophrenia: implication of their dopamine-modulatory actions. TRANSLATIONAL PSYCHIATRY 2013;3(;):U74-U84
Agents: PD153035; ZD1839 **Vehicle:** DMSO; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: Animal info (male Sprague-Dawley rats); post op. care (topical antiseptic (50mg/day)); behavioral testing (7 days after mp implantation); 10-20% DMSO used; enzyme inhibitor (EGF receptor tyrosine kinase);

Q1665: F. Watanabe, *et al.* Signaling through erbB receptors is a critical functional regulator in the mature cochlea. European Journal of Neuroscience 2010;32(5):717-724
Agents: PD153035; 4557W **Vehicle:** DMSO; artificial perilymph; **Route:** Ear (cochlea); **Species:** Guinea pig; **Pump:** 2002;
ALZET Comments: Controls received mp w/ artificial perilymph; animal info (female, pigmented, 250-500 g); functionality of mp verified by residual volume; tissue perfusion (intracochlear); 0.1% DMSO used; enzyme inhibitor (tyrosine kinase)

Q0890: M. Mizuno, *et al.* Antipsychotic Potential of Quinazoline ErbB1 Inhibitors in a Schizophrenia Model Established With Neonatal Hippocampal Lesioning. Journal of Pharmacological Sciences 2010;114(3):320-331
Agents: PD153035; ZD1839; OSI-774 **Vehicle:** DMSO; Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague-Dawley); behavioral testing (locomotor activity test, acoustic startle test, contextual conditioning); 10% DMSO used; PD153035, OSI-774, and ZD1839 is an epidermal growth factor receptor family (ErbB1) inhibitor; enzyme inhibitor (tyrosine kinase);

PP2

P8118: H. Katsura*, et al.* Activation of Src-family kinases in spinal microglia contributes to mechanical hypersensitivity after nerve injury. Journal of Neuroscience 2006;26(34):8680-8690
Agents: PP2; PP3 **Vehicle:** DMSO; Saline; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ normal saline; dose-response (fig.8); enzyme inhibitor (Src-Family tyrosine kinase); animal info (male, Sprague-Dawley, 200-250g., spinal nerve ligation); 50% DMSO; enzyme inhibitor (tyrosine kinase);

P6195: M. Mizuno*, et al.* Involvement of BDNF receptor TrkB in spatial memory formation. Learning & Memory 2003;10(2):108-115
Agents: PP2 **Vehicle:** Not Stated; **Route:** CSF/CNS; **Species:** Rat; **Pump:** Not Stated; **Duration:** 11 days;
ALZET Comments: Enzyme inhibitor (tyrosine kinase); PP2 is 4-amino-5-(4-chlorophenyl)-7-(t-butyl) pyrazolo [3,4-d] pyrimidine

Sorafenib

Q2916: A. Z. Dudek*, et al.* Brain Metastases from Renal Cell Carcinoma in the Era of Tyrosine Kinase Inhibitors. Clinical Genitourinary Cancer 2013;11(2):155-160
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

Q1442: S. Agarwal*, et al.* The Role of the Breast Cancer Resistance Protein (ABCG2) in the Distribution of Sorafenib to the Brain. Journal of Pharmacology and Experimental Therapeutics 2011;336(1):223-233
Agents: Sorafenib **Vehicle:** DMSO; **Route:** IP; **Species:** Mice; **Pump:** 1003D; **Duration:** 48 hours;
ALZET Comments: Animal info (FVB wild-type, Mdr1a/b -/-, Bcrp1 -/-, Mdr1a/b -/-, Bcrp1 -/-); half-life pg 226 "Sorafenib half-life in plasma and brain after an intravenous dose was determined to be 1.6 and 0.9 h, respectively. Therefore an infusion lasting 48 h was considered to be sufficiently long to attain steady state in both plasma and brain."; good methods, pg 226 "In the intraperitoneal infusion studies, the apparent plasma clearance (CLapp) was calculated by using the equation, *CL*app = *k*0/*Css,* where, *k*(*0*) is the rate of infusion into the peritoneal cavity normalized to body weight (ng/h/kg), and *Css* is the plasma concentration at steady state (ng/ml)."; enzyme inhibitor (biaryl-urea RAF kinase, tyrosine kinase); cancer (glioma); chemotherapeutic

Sunitinib

Q4264: Y. Zhu*, et al.* Hematogenous macrophage depletion reduces the fibrotic scar and increases axonal growth after spinal cord injury. NEUROBIOLOGY OF DISEASE 2015;74(114-125
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;

Q6739: R. K. Oberoi*, et al.* Pharmacokinetic assessment of efflux transport in sunitinib distribution to the brain. J Pharmacol Exp Ther 2013;347(3):755-64
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);

Q2916: A. Z. Dudek*, et al.* Brain Metastases from Renal Cell Carcinoma in the Era of Tyrosine Kinase Inhibitors. Clinical Genitourinary Cancer 2013;11(2):155-160
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

Other TK Inhibitors

Q7320: P. J. Wermuth, *et al.* Abrogation of transforming growth factor-beta-induced tissue fibrosis in TBRIcaCol1a2Cre transgenic mice by the second generation tyrosine kinase inhibitor SKI-606 (Bosutinib). PLoS One 2018;13(5):e0196559
Agents: Bosutinib **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2006; **Duration:** 42 days;
ALZET Comments: Dose (2.5, 5.0, or 10.0 mg/kg/day); Controls received mp w/ vehicle; Bosutinib aka SKI-606; Enzyme inhibitor (tyrosine kinase); dependence;

Q7232: T. Miladinovic, *et al.* Functional effects of TrkA inhibition on system xC(-)-mediated glutamate release and cancer-induced bone pain. Mol Pain 2018;14(1744806918776467
Agents: AG879 **Vehicle:** DMSO; **Route:** IP; **Species:** Mice; **Pump:** 1002; **Duration:** Not Stated;
ALZET Comments: Dose (5 mg/kg/day); animal info (immunocompetent female BALB/c mice, 4 to 6 weeks old, 20g); AG879 is a TrkA inhibitor; enzyme inhibitor (Tyrosine kinase A); cancer (Breast cancer);

Q5054: K. M. Henkels, *et al.* Phospholipase D (PLD) drives cell invasion, tumor growth and metastasis in a human breast cancer xenograph model. Oncogene 2013;32(49):5551-62
Agents: Apigenin, FIPI, NOPT **Vehicle:** DMSO; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 4, 5 weeks;
ALZET Comments: animal info: SCID; cancer (breast); dose-response: Fig. 5; enzyme inhibitor (tyrosine kinase); half-life: >12 hrs. in humans; mp were used to study the effect of apigenin on tumor cell metastasis. Paper does not mention ALZET pump model; dose: 1.8 mg/kg/day

Q1928: T. L. Wang, *et al.* Brain Distribution of Cediranib Is Limited by Active Efflux at the Blood-Brain Barrier. Journal of Pharmacology and Experimental Therapeutics 2012;341(2):386-395
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); enzyme inhibitor (tyrosine kinase); chemotherapeutic

P6894: M. Tejeda, *et al.* Growth Inhibitory Effect of the Somatostatin Structural Derivative (TT-232) on Leukemia Models. Anticancer Research 2005;25(325-330
Agents: TT-232 **Vehicle:** Acetic acid; sodium acetate; water; mannitol; **Route:** IV; SC; **Species:** Mice; **Pump:** 2002; **Duration:** 14, 28 days;
ALZET Comments: Dose-response (p. 328, fig 1); comparison of IP/SC injections vs. SC/IV mp; pumps replaced at day 14 for 28 day group; stability verified, 37 degrees Celsius for over 3 weeks; cancer (leukemia); TT-232 is a novel somatostatin analog; "The IV infusion for 28 days resulted in 82% growth inhibition." (p. 328); "The infusion of TT-232 by ALZET osmotic minipump resulted in 70-80% tumor growth inhibition and 20% tumor free survival." (p. 329); "...serial injections represent significant stress to the animals..." "To reduce and eliminate the above mentioned problem [stress] we used an ALZET osmotic minipump..." "Infusion from inserted ALZET minipumps maintains a constant drug level, resulting in a well defined, consistent pattern of drug exposure throughout the period of drug administration." "These studies suggest that TT-232 is a potent inhibitor of leukemia tumor in vitro and in vivo and suggest infusion treatment as a beneficial application in clinical practice." (p. 330); oligopeptide; enzyme inhibitor (tyrosine kinase); animal info (CBA/ca, immunosuppressed, female)

P6629: J. E. Davies, *et al.* Decorin Suppresses Neurocan, Brevican, Phosphacan and NG2 Expression and Promotes Axon Growth Across Adult Rat Spinal Cord Injuries. European Journal of Neuroscience 2004;19(1226-1242
Agents: Decorin, recomb. human **Vehicle:** PBS; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2001; **Duration:** 8 days;
ALZET Comments: Controls received mp w/ vehicle; tissue perfusion (spinal lesion); enzyme inhibitor (tyrosine kinase); decorin is known to inhibit TGF beta and is an antagonist to EGF receptor tyrosine kinase

P6396: I. F. Benter, *et al.* Inhibition of Ras-GTPase, but not tyrosine kinases or Ca^{2+}/calmodulin-dependent protein kinase II, improves recovery of cardiac function in the globally ischemic heart. MOLECULAR AND CELLULAR BIOCHEMISTRY 2004;259(1-2):35-42
Agents: FPT III; KN-93; Genistein **Vehicle:** Saline; **Route:** IP; **Species:** Rat; **Pump:** 2ML1; **Duration:** 6 days;
ALZET Comments: Controls received mp w/ vehicle; enzyme inhibitor (tyrosine kinase, CaMKII); cardiovascular; ischemia (cardiac)

P6010: S. Q. Liu, *et al.* Pattern formation of vascular smooth muscle cells subject to nonuniform fluid shear stress: role of PDGF-β receptor and Src. American Journal of Physiology Heart and Circulatory Physiology 2003;285(3):H1081-H1090
Agents: AG-1296; PP1 **Vehicle:** Not Stated; **Route:** IV (vena cava); **Species:** Rat; **Pump:** 2001D; **Duration:** 10 days;
ALZET Comments: AG-1296 and PP1 are selective PDGF-B receptor tyrosine kinase and SRC inhibitors; enzyme inhibitor (tyrosine kinase)

P6530: T. Grunberger, *et al.* Inhibition of acute lymphoblastic and myeloid leukemias by a novel kinase inhibitor. Blood 2003;102(12):4153-4158
Agents: CR4 **Vehicle:** DMSO; medium; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 14,21 days;
ALZET Comments: Controls received mp w/ vehicle; pumps replaced every 7 days; CR4 was dissolved in 50% DMSO/medium and is a novel enzyme inhibitor (tyrosine kinase)

P5764: F.-Q. Liang, *et al.* Role of brain-derived neurotrophic factor in the circadian regulation of the suprachiasmatic pacemaker by light. J Neurosci 2000;20(8):2978-2987
Agents: Brain-derived neurotrophic factor; K252a **Vehicle:** CSF, artificial; BSA; DMSO; **Route:** CSF/CNS (suprachiasmatic nucleus); **Species:** Rat; **Pump:** 2004; **Duration:** 28 days;
ALZET Comments: Controls received mp w/ vehicle; comparison of acute injections vs. mp p.2979; enzyme inhibitor (tyrosine kinase); BDNF was recombinant human; dissolved in a CSF & 0.1% BSA; K252a was dissolved in DMSO; guide cannula used with a stylet; 3-day recovery period before pump implantation