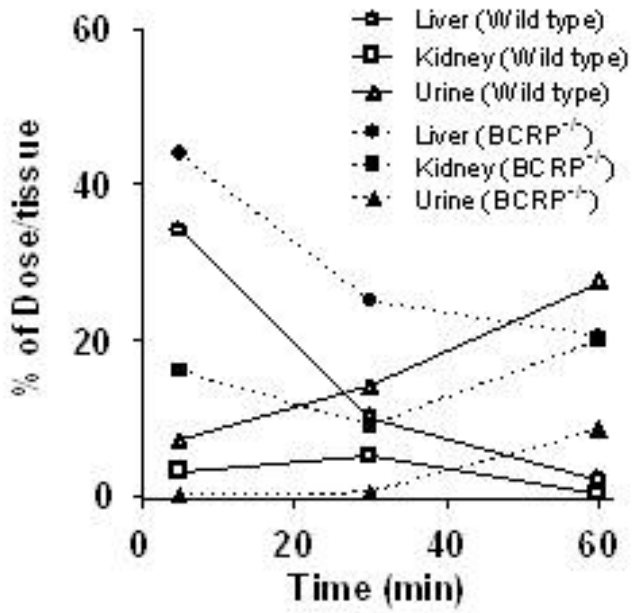
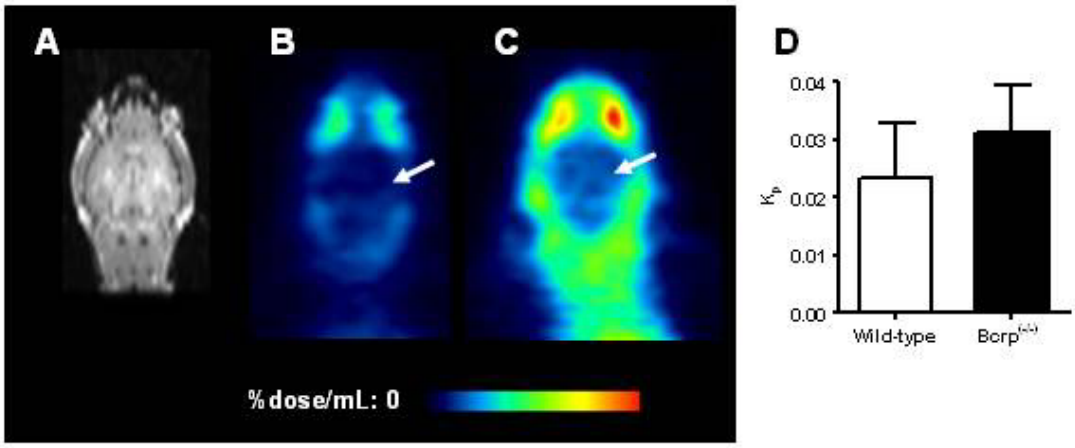


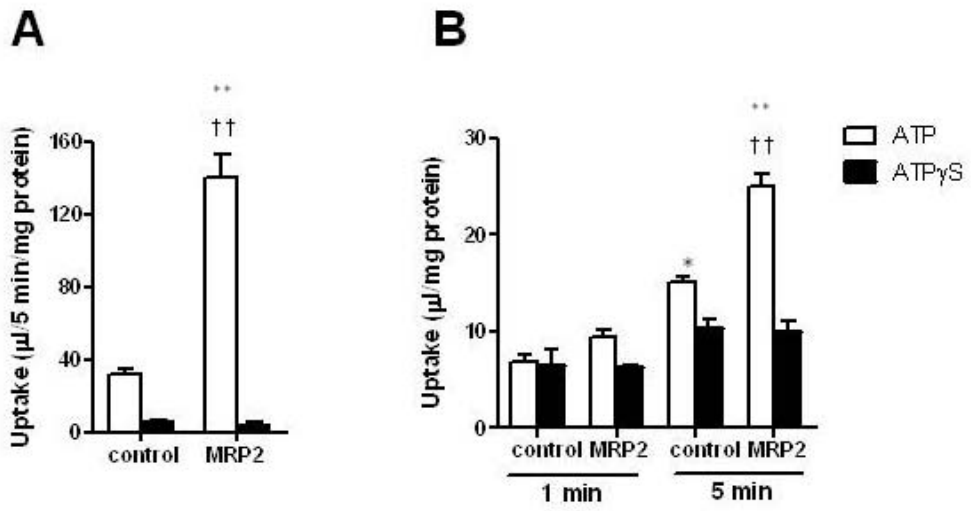
Supplemental Figure 1. Liver, kidney, and urine biodistribution after administration of [^{11}C]SC–62807 to wild-type and *Bcrp*$^{-/-}$ mice.

Each animal received 2.2-5.5 MBq of [^{11}C]SC-62807 via IV bolus administration. Urine was sampled via the urinary bladder at designated times (5, 30, 60 min) after administration. Following urine sampling, blood flow was terminated by exsanguination via aortic puncture and the liver and kidney were quickly removed, weighed, and assayed for regional radioactivity using a 1470 WIZARD® automatic gamma counter. The radioactivity measured in each sample was decay-corrected to the injection time and expressed as %-dose/tissue or %-dose/mL blood, normalized to the injected radioactivity.



Supplemental Figure 2. Typical MRI template and PET images, and brain-to-blood radioactivity concentration ratio following administration of [^{11}C]SC–62807 to wild-type and *Bcrp*$^{-/-}$ mice.

Horizontal slices of the representative brain MRI template (A) and corresponding summation of PET images (B and C, from 5 to 30 min) of cerebral ^{11}C-radioactivity uptake in wild-type and *Bcrp*$^{-/-}$ mice. (D) The brain-to-blood radioactivity ratio (K_p value) in wild-type and *Bcrp*$^{-/-}$ mice determined 60 min after administration of [^{11}C]SC–62807. Each bar represents the mean ± SD (n=3).



Supplemental Figure 3. ATP-dependent uptake of $E_2$17βG and SC–62807 by control and MRP2-expressing membrane vesicles.

Recombinant adenoviruses containing human MRP2 or tetracycline-responsive transcriptional activator (tTA) (Ad-MRP2 and Ad-tTA, respectively) were constructed as described previously (*27*). HEK293 cells were infected with Ad-MRP2 (50 multiplicity of infection (MOI)) or Ad-tTA (50 MOI). As a negative control, cells were infected with Ad-tTA (100 MOI). Control and MRP2-expressing membrane vesicles (5 μg protein) were incubated at 37°C for the designated time with (A) [^{3}H]estradiol 17β-glucuronide ($E_2$17βG) (36 nM) or (B) SC–62807 (1 μM) in the presence of either ATP or ATPγS. A Prominence UFLC LC-20 system (Shimadzu, Tokyo, Japan) coupled to an Applied Biosystems SciexQtrap™ 5500 mass spectrometer (Concord, Ontario, Canada) via an electrospray ionization (ESI) source was used for analysis. The separation was performed on a CAPCELL PAK C18 column (MGII, 3 μm, 2.0 mm ID, 50 mm; Shiseido, Tokyo, Japan) maintained at 40°C. The isocratic mobile phase consisted of a mixture of methanol and 10 mM ammonium acetate (60:40, v/v) at a flow rate of 0.2 mL/min. The eluate

was introduced into the MS via an electrospray interface. The mass spectrometer was operated in the negative ESI and multiple reaction monitoring (MRM) modes. Precursor-to-production transitions were monitored at *m/z* 409.8→365.9 for SC–62807. Uptake was determined as the amount of test compound associated with the vesicle specimens divided by the concentration in the transport buffer. Bars represent the mean ± SE of 3 or 4 determinations. $^{*}P<0.05$ and $^{**}P<0.01$ for ATP vs. ATPγS $^{\dagger\dagger}P<0.01$ for control vesicles vs. MRP2-expressing vesicles.