



**Supplemental Figure 1.** Polymorphism plot of three each for high- (HABs) and mixed- (MABs) affinity binders and two low-affinity binders (LABs) to determine a population average of nondisplaceable distribution volume ( $V_{ND}$ ) (A) or  $V_{ND}$  corrected for plasma free fraction ( $V_{ND}/f_P$ ) (B) of  $^{11}\text{C}$ -ER176 in brain. The combination of HABs and MABs (HAB-MAB) showed a poor linear fitting.

**Supplemental Table 1.** Administered doses for 20 scans in 17 healthy subjects injected with  $^{11}\text{C}$ -ER176.

Whole-body scans

	All (n = 9 batches)	HABs (n = 3)	MABs (n = 3)	LABs (n = 3)
Injected mass dose (pmol/kg)	107 ± 54 (34 – 193)	66 ± 48	116 ± 56	140 ± 46
Injected activity (MBq)	646 ± 127 (371 – 735)	536 ± 184	691 ± 55	712 ± 24

Brain scans

	All (n = 11 batches)	HABs (n = 3)		MABs (n = 3)	LABs (n = 2)
		Baseline	Blocked*	Baseline	Baseline
Injected mass dose (pmol/kg)	91 ± 52 (33 – 198)	89 ± 94	102 ± 49	66 ± 12	113 ± 27
Injected activity (MBq)	700 ± 25 (656 – 725)	672 ± 23	696 ± 21	720 ± 4	718 ± 9

HABs = high-affinity binders, MABs = mixed-affinity binders, LABs = low-affinity binders. Data are mean ± SD (above) and range (below). \*Preblocking dose with XBD173 was 90 mg.

**Supplemental Table 2.** Residence times of source organs determined from whole-body imaging of nine healthy subjects injected with  $^{11}\text{C}$ -ER176.

Organ	Residence time (hours)
Brain	0.0116 ± 0.0031
Thyroid	0.0004 ± 0.0002
Lung	0.0363 ± 0.0100
Heart	0.0049 ± 0.0016
Liver	0.0270 ± 0.0086
Spleen	0.0081 ± 0.0033
Kidney	0.0145 ± 0.0036
Remainder of Body	0.3869 ± 0.0206

Values are mean ± SD.

**Supplemental Table 3.** Radiation dosimetry estimates for  $^{11}\text{C}$ -ER176 determined from nine healthy subjects.

Organ	Radiation dose ( $\mu\text{Sv}/\text{MBq}$ )
Adrenals	3.4 $\pm$ 0.1
Brain	3.1 $\pm$ 0.7
Breasts	2.2 $\pm$ 0.4
Gallbladder Wall	4.4 $\pm$ 1.9
Lower Large Intestine Wall	2.8 $\pm$ 0.1
Small Intestine	2.9 $\pm$ 0.1
Stomach Wall	3.0 $\pm$ 0.0
Upper Large Intestine Wall	2.9 $\pm$ 0.1
Heart Wall	5.7 $\pm$ 1.3
Kidneys	14.3 $\pm$ 3.2
Liver	5.7 $\pm$ 1.4
Lungs	10.4 $\pm$ 2.5
Muscle	2.5 $\pm$ 0.1
Ovaries	2.9 $\pm$ 0.1
Pancreas	3.5 $\pm$ 0.1
Red Marrow	2.4 $\pm$ 0.0
Osteogenic Cells	3.6 $\pm$ 0.1
Skin	2.0 $\pm$ 0.1
Spleen	13.5 $\pm$ 4.8
Testes	2.3 $\pm$ 0.1
Thymus	2.8 $\pm$ 0.1
Thyroid	6.0 $\pm$ 2.5
Urinary Bladder Wall*	2.7 $\pm$ 0.1
Uterus	2.9 $\pm$ 0.1
Total Body	2.9 $\pm$ 0.0
Effective Dose	4.1 $\pm$ 0.4

\* Dynamic urinary bladder model was not used.

Values are expressed as mean  $\pm$  SD.