Table S1: Statistical analysis of prion infectivity shown in Fig. 2A, B and C. Mantel-Haenszel common odds ratio (c.o.r.) estimate is given with a 95% confidence interval comparing number of negative wells at each dilution (10^{-4} to 10^{-8}) of a sample in the SCEPA. P-values indicate statistical difference to control. Statistical analysis of the differences of efficiency between drugs was only performed for PTAA, pHTAA and pFTAA. Analysis of all molecules would require a Bonferroni correction that would decrease statistical significance.

Fig. 2A	µg ml^{-1}	p-values	conf. interval for c.o.r.
Control to PTAA	300	p < 0.001	
Control to pHTAA	300	p < 0.001	
Control to pFTAA	300	p < 0.001	
Control to PBAT	300	p < 0.001	
Control to POMT	300	p < 0.001	
Control to POWT	300	p < 0.001	
pHTAA vs PTAA	300	p = 0.450	1.69(0.61-4.67)
pFTAA vs PTAA	300	p = 0.005	0.13(0.03-0.50)
pFTAA vs pHTAA	300	p = 0.001	10(2.66-37.64)

Fig. 2B	µg ml^{-1}	p-values	conf. interval for c.o.r.
Control to pFTAA	900	p < 0.0001	
	300	p = 0.002	0.07(0.01-0.36)
	150	p = 0.004	0.15(0.04-0.52)
	75	p = 0.047	0.32(0.12-0.87)

Fig. 2C	µg ml^{-1}	p-values	conf. interval for c.o.r.
Control to PTAA	5000	p < 0.0001	
	900	p < 0.0001	

	300	$p < 0.0001$	
	150	$p < 0.0001$	
	100	$p < 0.0003$	0.16(0.06-0.43)
	10	$p = 0.081$	0.34(0.12-0.99)

Table S2: Comparison of infectivities of samples described in Fig. S7A. Differences were computed by using a Mantel-Haenszel Chi-square test for comparing number of negative wells at each dilution (10^{-4} to 10^{-8}) of a sample in the SCEPA.

Plate n°:	1	2	3	4
Infectivity (log TCI_{50} g^{-1}):	7.91	6.83	8.05	7.80
1		p < 0.001	p = 0.398 1.89(0.62-5.79)	p = 0.826 0.78(0.29-2.15)
2			p < 0.001	p < 0.001
3				p = 0.178 0.39(0.13-1.24)

Table S3: Infectivity of samples described in Fig. S7B.

Plate n°:	1	2
PTAA (µg ml^{-1}l):	0	10
Infectivity (log TCI_{50} g^{-1}):	8.05	7.78

The difference between the non- and PTAA-treated samples was computed by using a Mantel-Haenszel Chi-square test for comparing the number of negative wells at each dilution (10^{-4} to 10^{-8}) of a sample in the SCEPA: p = 0.551 (n.s.) and conf. interval for c.o.r.: 0.58(0.17-1.92).

Table S4: Summary of end-point titrations of RML6 inoculums in tga20 mice

Dilution of brain homogenate[a]	(Clinical TSE/total inoculated)	Mean incubation period (days)
10^{-3}	4/4	77.8 ± 1.3
10^{-4}	5/5	56.4 ± 23.5
10^{-5}	4/4	95 ± 5.8
10^{-6}	4/4	105.8 ± 8.4
10^{-7}	3/4	96, 107, 247, >249
10^{-8}	0/4	>253
10^{-9}	0/4	>253
10^{-10}	1/4	70, >253

[a] Dilutions were started from a 10% brain homogenate.

Table S5: Statistical analysis of the data presented in Fig. 2D.

	µg ml^{-1}	p-values	conf. interval for mean ratio
mock + H_2O to mock + PTAA[1]	0 to 300	p = 0.001	1.21(1.12-1.30)
Control to PTAA[1]	300	p < 0.001	8.95(6.57-12.20)
	100	p < 0.001	6.50(4.89-8.65)
	10	p = 0.004	1.97(1.37-2.82)
	1	p = 0.348	1.23(0.74-2.04)
Control to POMT[1]	300	p < 0.001	9.80(7.21-13.33)
	100	p < 0.001	3.27(2.30-4.67)
	10	p = 0.015	1.75(1.17-2.63)
	1	p = 0.374	1.15(0.81-1.62)
Control to pHTAA[1]	300	p < 0.001	3.14(2.25-4.38)
	100	p = 0.007	2.21(1.37-3.55)
	10	p = 0.057	1.49(0.86-2.25)
	1	p = 0.737	0.95(0.69-1.32)
Control to pFTAA[1]	300	p < 0.001	3.79(2.66-5.41)
	100	p < 0.001	3.86(2.57-5.80)
	10	p = 0.003	2.39(1.56-3.68)
	1	p = 0.028	1.55(1.07-2.25)

PTAA to POMT[2]	All conc.	p = 0.078	1.20(0.66-1.01)
PTAA to pHTAA[2]	All conc.	p < 0.001	0.51(0.42-0.63)
PTAA to pFTAA[2]	All conc.	p = 0.017	0.79(0.64-0.97)
POMT to pHTAA[2]	All conc.	p < 0.001	0.62(0.51-0.77)
POMT to pFTAA[2]	All conc.	p = 1.000	1.04(0.78-0.85)

pHTAA to pFTAA[2]	All conc.	$p < 0.001$	1.53(1.24-1.89)

[1] P-values represent the statistical difference between non- (control) and LCP-treated RML6 samples. The first lane of the table describes the difference between non-treated (mock) and PTAA-treated non-infected brain homogenate from CD1 mice. Differences were computed by using a T- test comparing the $\log_{10}$ RLU signals in the MPA.

[2] P-values represent statistical difference between groups of four concentrations of each LCP compared as groups by using a two-tailed independent sample T-test (equal variances assumed) comparing $\log_{10}$ RLU signal in the MPA.

Table S6: Statistical analysis of the data shown in Fig. S10. The difference between MPA signals for untreated CD1 brain homogenate (mock) and PTAA-treated CD1 brain homogenate and for untreated RML6 (control) and PTAA-treated RML6 were computed by using a T- test comparing $\log_{10}$ RLU signal in the MPA.

	bead treatment	p-values	conf. interval for mean ratio
CD1+H_2O to CD1+PTAA	No	p = 0.339	1.08(0.90-1.31)
CD1+H_2O to CD1+H_2O	Yes	p = 0.004	1.29(1.12-1.49)
CD1+PTAA to CD1+PTAA	Yes	p = 0.024	1.24(1.04-1.48)
RML+PTAA to RML+PTAA	Yes	p = 0.992	1.00(0.69-1.45)
Control to RML+H_2O	Yes	P = 0.274	1.10(0.91-1.32)

Table S7: Statistical analysis shown in Fig. 4.

Fig. 4B[1]	p-values	Conf. interval for c. o. r.
Non-treated (21 DIV)	p = 0.007	-1.71(-2.35 to -1.07)
PPS 0.3 μg ml^{-1}	p = 0.012	1.99(-2.96 to -1.03)
PTAA 60 μg ml^{-1}	p < 0.001	-3.32(-3.62 to -3.01)
PTAA 6 μg ml^{-1}	p = 0.001	-2(-2.19 to -1.81)
PTAA 1 μg ml^{-1}	p = 0.106	-0.66(-1.66 to 0.34)
PTAA 0.1 μg ml^{-1}	p = 0.695	-0.13(-1.36 to 1.10)
PTAA 0.01 μg ml^{-1}	n/a	n/a

Fig. 4C[2]	p-values	95% c.i. of difference
Untreated (21 DIV)	p < 0.0001	-228.7(-309.8 to -147.6)
PPS 0.3 μg ml^{-1}	p < 0.0001	216.9(135.8 to 298.0)
PTAA 60 μg/ml	p < 0.0001	236.1(155.0 to 317.1)
PTAA 6 μg/ml	p < 0.0001	233.9(152.8 to 315.0)
PTAA 1 μg/ml	p < 0.0001	229.0(147.9 to 310.1)
PTAA 0.1 μg/ml	p < 0.0001	199.4(118.4 to 280.5)
PTAA 0.01 μg/ml	n/s	-46.9(-128.0 to 34.18)

Fig. 4D[3]	p-values	95% c.i. of difference
Untreated (21 DIV)	p < 0.001	-41.79(-66.96 to -16.62)
PPS 0.3 μg ml^{-1}	p < 0.001	37.56(12.39 to 62.73)
PTAA 60 μg ml^{-1}	p < 0.001	42.94(17.77 to 68.11)
PTAA 6 μg ml^{-1}	p < 0.001	40.57(15.40 to 65.74)
PTAA 1 μg ml^{-1}	p < 0.001	35.09(9.917 to 60.26)

PTAA 0.1 µg ml^{-1}	$p < 0.001$	26.51(1.36 to 51.70)
PTAA 0.01 µg ml^{-1}	$p = 0.450$	12.11(-13.06 to 37.28)

[1] Statistical analysis of prion infectivity using a Mantel-Haenszel Chi-square test with Bonferroni correction comparing TCI_{50} difference to control (COCS homogenates from untreated cultures harvested after 42 dpi).

[2, 3] Statistical analysis using a one-way ANOVA with Tukey's multiple comparison test.

Table S8: Statistical analysis of data shown in Fig. 4D using a one-way ANOVA with Tukey's multiple comparison test.

Fig. 4D	p-value	95% c.i. of difference
PTAA 60 μg/ml	$p < 0.05$	47.70(0.65 to 94.75)

Table S9: Statistical analysis shown in Fig. 5 using a one-way ANOVA with Tukey's multiple comparison test.

Fig. 5A	p-values	95% c.i. of difference
7 DIV	ns	-9(-108.8 to 90.80)
19 DIV	ns	-13.86(-113.7 to 85.94)
21 DIV	ns	-23.77(-123.6 to 76.03)
28 DIV	ns	-60.36(-160.2 to 39.44)
35 DIV	p < 0.001	-205.5(-305.3 to -105.7)
42 DIV	p < 0.001	-252.8(-352.6 to 153.0)
From 7 DIV	ns	-2.11(-101.9 to 97.68)
From 19 DIV	ns	-1.26(-101.1 to 98.54)
From 21 DIV	ns	0(-99.80 to 99.80)
From 28 DIV	ns	-0.49(-100.3 to 99.30)
From 35 DIV	ns	-0.04(-99.84 to 99.75)

Fig. 5B	p-values	95% c.i. of difference
7 DIV	n/s	0(-38 to 38)
19 DIV	n/s	-0.09(-38 to 38)
21 DIV	n/s	-0.95(-39 to 37)
28 DIV	n/s	-6.2(-44 to 32)
35 DIV	n/s	-16(-54 to 21)
42 DIV	p < 0.001	-54(-92 to -17)
45 DIV	p < 0.001	-113(-151 to -76)
49 DIV	p < 0.001	-114(-152 to -76)
56 DIV	p < 0.001	-114(-152 to -77)
From 7 DIV	n/s	-0.43(-38 to 37)

From 19 DIV	n/s	0(-38 to 38)
From 21 DIV	n/s	0(-38 to 38)
From 28 DIV	n/s	-4.6(-42 to 33)
From 35 DIV	n/s	-21(-59 to 17)
42 DIV vs. from 7 DIV	$p < 0.001$	54(16 to 92)
42 DIV vs. from 19 DIV	$p < 0.001$	54(17 to 92)
42 DIV vs. from 21 DIV	$p < 0.001$	54(17 to 92)
42 DIV vs. from 28 DIV	$p < 0.01$	50(12 to 87)
42 DIV vs. from 35 DIV	n/s	33(-4.5 to 71)

Fig. 5C	p-values	95% c.i. of difference
7 DIV	ns	44(-174 to 261)
19 DIV	ns	71(-146 to 289)
21 DIV	ns	67(-151 to 284)
28 DIV	ns	52(-165 to 270)
35 DIV	ns	162(-55 to 380)
42 DIV	ns	53(-165 to 270)
45 DIV	ns	107(-110 to 325)
49 DIV	ns	14(-203 to 232)
56 DIV	ns	88(-130 to 305)
From 7 DIV	ns	211(-6.6 to 428)
From 19 DIV	ns	196(-22 to 413)
From 21 DIV	$p < 0.05$	223(5.7 to 441)
From 28 DIV	ns	189(-28 to 407)
From 35 DIV	$p < 0.05$	236(18 to 453)
42 DIV vs. from 7 DIV	ns	158(59 to 376)

42 DIV vs. from 19 DIV	ns	143(-74 to 361)
42 DIV vs. from 21 DIV	ns	170(-47 to 388)
42 DIV vs. from 28 DIV	ns	136(-81 to 354)
42 DIV vs. from 35 DIV	ns	183(-34 to 400)

Statistical analysis using a one-way ANOVA with Tukey's multiple comparison test. Unless stated otherwise, time points are compared to the non-infected COCS. For 42 DIV vs. from 7 DIV, for instance, the value obtained for COCS harvested at 42 DIV is compared to the value obtained for COCS harvested at 42 DIV with treatment from 7 DIV.