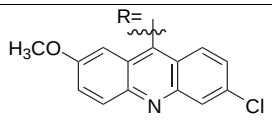
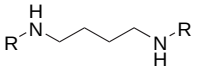
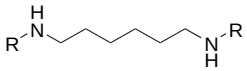
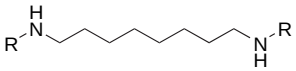
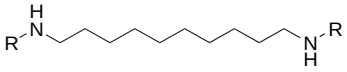
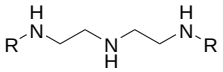
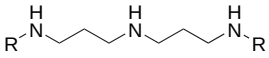
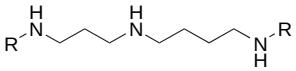
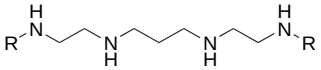
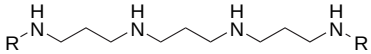
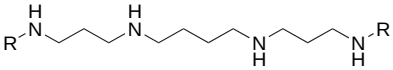
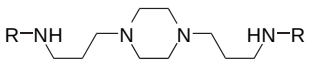
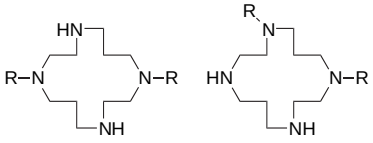
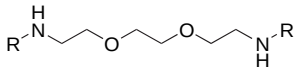
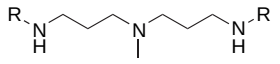
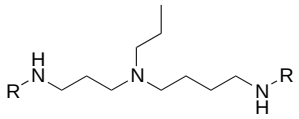
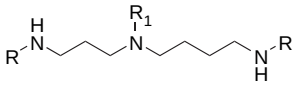
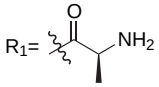
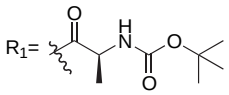
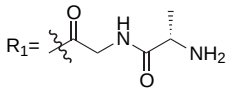
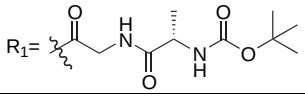
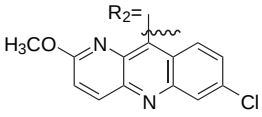
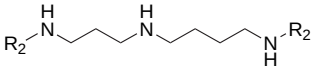
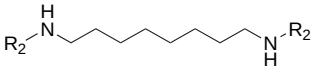
Table 2. Efficacy and cellular toxicity screen of bis-acridine compounds, a potent class of PrP^{Sc} inhibitors in ScN2a

		% PrP^{Sc} (±SEM), nM			% Cell viability (±SEM), nM		
Compound*		**50**	**200**	**400**	**50**	**200**	**500**
Alkyl							
1		72 (±1)	65 (±2)	54 (±1)	100 (±9)	100 (±9)	100 (±6)
2		84 (±6)	50 (±7)	41 (±3)	90 (±3)	96 (±3)	82 (±3)
3		93 (±7)	71 (±3)	78 (±2)	100 (±4)	100 (±2)	97 (±6)
4		100 (±2)	58 (±4)	20 (±1)	99 (±21)	95 (±21)	90 (±17)
Polyamine							
5		90 (±7)	58 (±1)	44 (±10)	100 (±20)	100 (±9)	100 (±18)
6		98 (±5)	59 (±6)	46 (±8)	98 (±5)	33 (±1)	1 (±1)
7		61 (±3)	26 (±2)	13 (±3)	26 (±1)	8 (±1)	1 (±1)
8		72 (±6)	19 (±3)	9 (±4)	100 (±13)	23 (±10)	1 (±1)
9		85 (±1)	32 (±3)	13 (±5)	92 (±7)	16 (±7)	10 (±2)
10		72 (±3)	71 (±5)	31 (±6)	100 (±4)	43 (±5)	1 (±1)
Heterocyclic							
11		61 (±3)	19 (±5)	4 (±2)	94 (±11)	89 (±9)	79 (±1)
12[†]		80 (±2)	75 (±6)	67 (±1)	100 (±10)	100 (±6)	100 (±11)

Alkyl ether							
13		41 (±8)	29 (±8)	15 (±7)	97 (±8)	90 (±9)	98 (±11)
***N*-alkylated polyamine**							
14		78 (±9)	49 (±8)	38 (±9)	73 (±2)	59 (±8)	1 (±1)
15		88 (±2)	41 (±6)	11 (±1)	100 (±5)	77 (±4)	0 (±1)
***N*-acylated polyamine**							
16		100 (±6)	80 (±12)	‡	100 (±22)	59 (±13)	0 (±1)
17		84 (±10)	36 (±1)	7 (±1)	98 (±12)	85 (±6)	84 (±3)
18		90 (±5)	83 (±5)	79 (±3)	96 (±4)	93 (±1)	0 (±1)
19		97 (±2)	84 (±6)	72 (±10)	88 (±18)	78 (±13)	70 (±12)
Bis-aza-acridines							
20		88 (±3)	82 (±8)	65 (±1)	100 (±15)	100 (±9)	88 (±8)
21		100 (±6)	88 (±8)	77 (±3)	95 (±3)	100 (±6)	96 (±5)

*Structure-activity data reveal both efficacy and cytotoxicity of bis-acridine compounds depend on the structure of the acridine linker. Compounds are grouped according to the structure of the bis-acridine linker. Individual compounds were incubated with ScN2a cells at 50, 200, and 400 nM concentrations for 3 d. ScN2a cell lysates were PK-digested prior to immunoblot (Fab D13). PK-resistant PrP was quantified by immunoblot densitometry. Activity is expressed as the average percent of PK-resistant PrP remaining after incubation with compound at the given concentration, versus control cells incubated with no compound (standard errors from at least three independent immunoblots are given). N2a cells were incubated with individual compounds at 50, 200, and 500 nM concentrations for 7 d. Cell viability was determined by the thiazolyl blue (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyl tetrazolium bromide) cytotoxicity assay and is expressed as an average percent of viable cells versus control cells treated with no compound (standard error from two experiments are given).

†Assayed as a 1:1 mixture of regioisomers.

‡Toxic at 400 nM concentration.