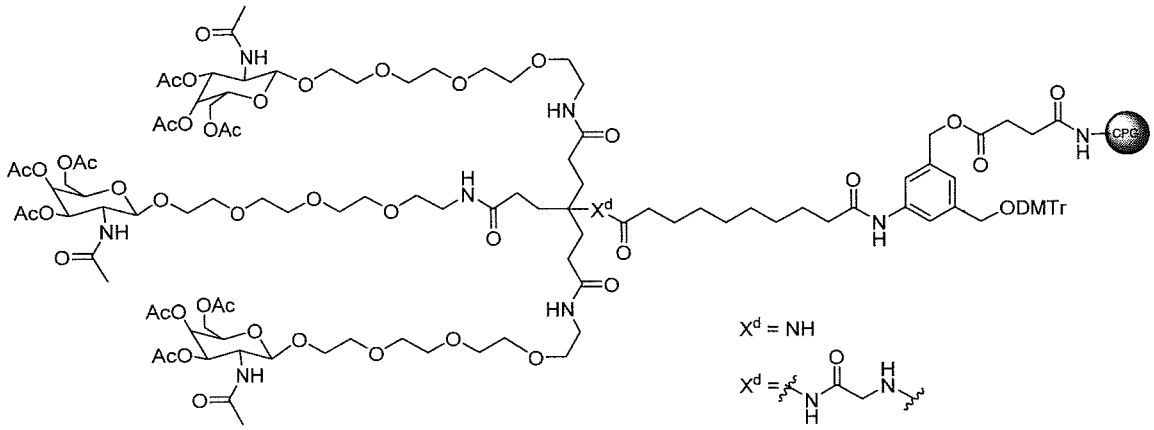


Figure 1

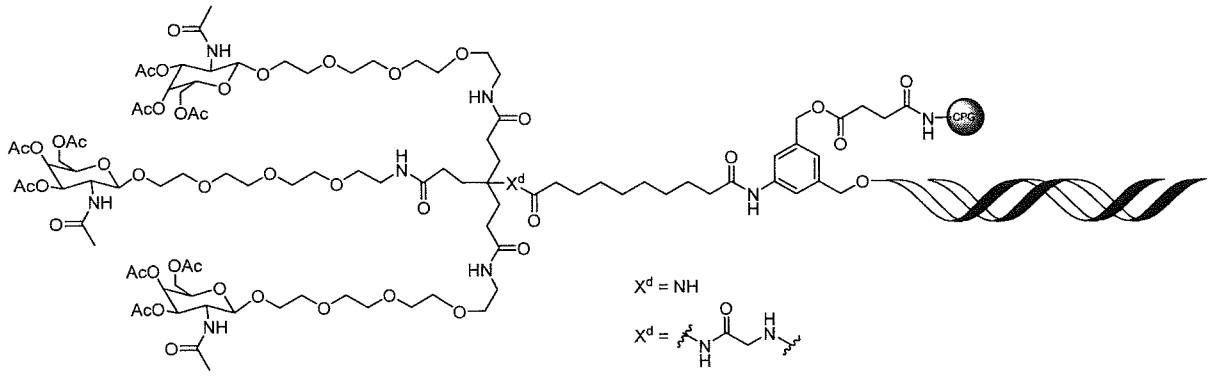


Figure 2

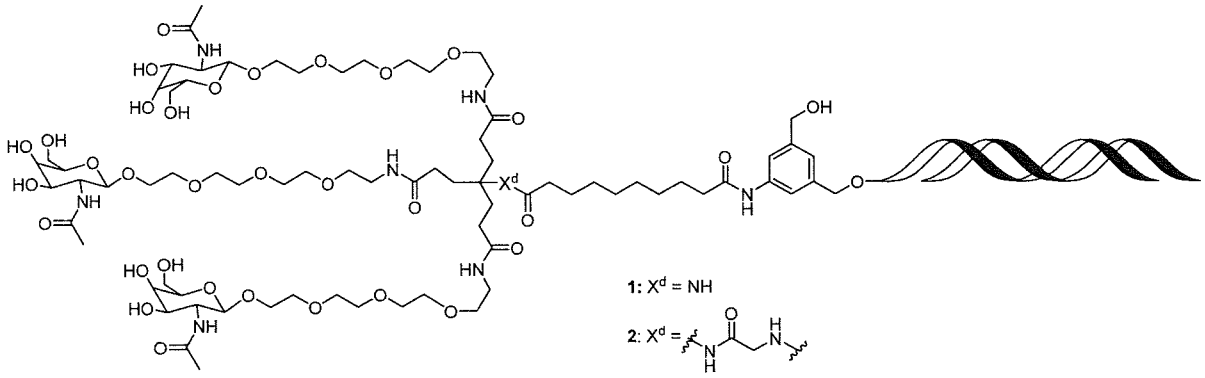


Figure 3

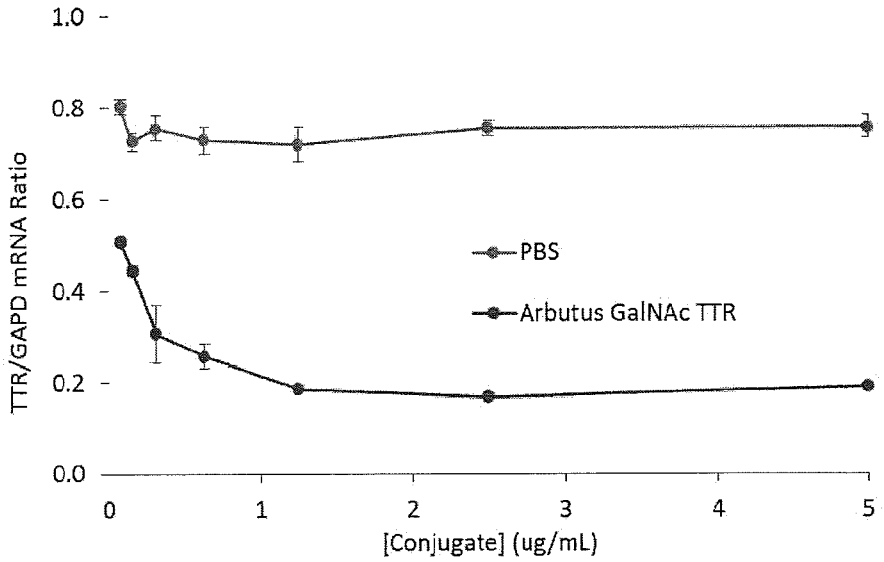

1.0
0.8
0.6
0.4
0.2
0.0
TTR/GAPD mRNA Ratio
PBS
Arbutus GalNAc TTR
0
1
2
3
4
5
[Conjugate] (ug/mL)

Figure 4

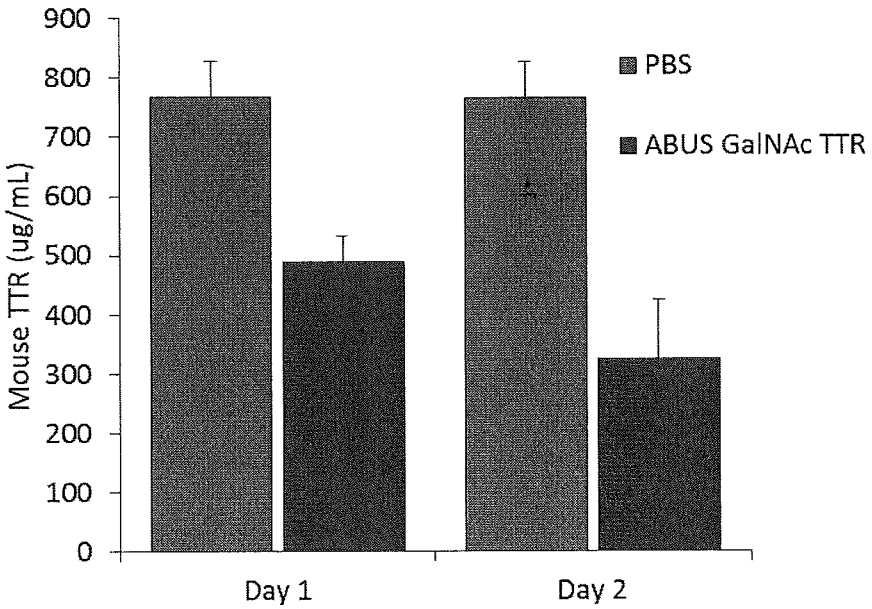

900
800
700
600
500
400
300
200
100
0
Mouse TTR (ug/mL)
PBS
ABUS GalNAc TTR
Day 1
Day 2

Figure 5

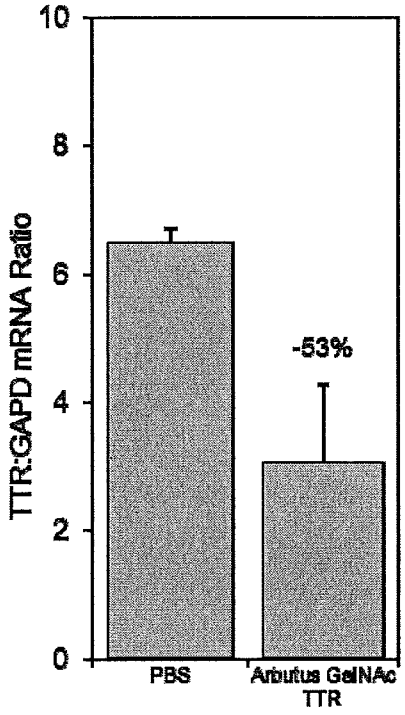


Figure 6

Figure 7

Table 1: Efficacy of subcutaneously administered siRNA (TTR) – Conjugates (1mg/kg). (% of Plasma TTR Relative to PBS Control)

Conjugates #	Day 2	Day 4	Day 5	Day 7	Day 8	Day 9	Day 11	Day 14	Day 21	Day 28
1	37.7	37.2	ND	45.6	ND	ND	55.0	75.4	76.5	ND
34	58.1	56.5	ND	84.5	ND	ND	90.2	ND	ND	ND
36	55.1	54.1	ND	69.9	ND	ND	97.8	104.3	95.6	ND
42	100.9	112.8	ND	119.1	ND	ND	118.8	ND	ND	ND
43	63.3	68.5	ND	83.8	ND	ND	98.4	94.8	112.8	ND
142	61.6	ND	65.1	64.9	ND	73.5	ND	88.6	99.3	ND
145	34.1	ND	16.9	19.8	ND	25.2	ND	45.1	74.3	ND
153	42.0	ND	26.3	25.3	ND	31.2	ND	50.3	70.7	ND
158	43.4	ND	41.6	53.5	50.1	ND	ND	82.6	103.2	ND
168	56.6	ND	50.7	63.8	60.0	ND	ND	92.7	104.9	ND
173	48.5	ND	56.9	55.4	56.6	ND	ND	87.4	84.2	ND
176	29.6	ND	12.3	14.5	ND	20.5	ND	ND	ND	ND
179	56.9	63.9	ND	72.9	ND	ND	75.1	ND	91.3	100.9
182	61.8	ND	57.2	64.9	ND	65.4	ND	89.0	100.1	ND
185	64.1	ND	67.7	67.7	ND	68.9	ND	89.6	83.3	ND
191	35.8	ND	ND	26.4	ND	32.0	ND	44.9	73.1	ND
194	40.6	ND	17.6	18.6	ND	20.3	ND	ND	ND	ND
197	41.6	ND	24.4	27.1	ND	31.9	ND	ND	ND	ND
200	41.5	ND	24.4	31.0	ND	33.5	ND	ND	ND	ND
203	53.6	ND	34.1	46.0	ND	47.3	ND	ND	ND	ND
206	41.6	ND	41.7	50.8	ND	50.9	ND	67.8	84.3	ND
212	44.6	ND	23.3	29.7	ND	28.2	ND	ND	ND	ND
215	42.1	ND	22.3	27.7	ND	29.5	ND	ND	ND	ND
231	42.9	ND	ND	37.6	ND	46.5	ND	53.0	76.1	ND

Figure 8

Table 2: Efficacy of subcutaneously administered siRNA (TTR) – Conjugates (2mg/kg). (% of Plasma TTR Relative to PBS Control)

Compound #	Day 2	Day 4	Day 5	Day 7	Day 8	Day 9	Day 11	Day 14	Day 21	Day 28
1	21.2	13.9	ND	24.5	ND	ND	36.5	54.3	71.5	ND
34	48.9	45.3	ND	59.2	ND	ND	87.9	ND	ND	ND
36	34.4	33.3	ND	40.2	ND	ND	66.4	78.0	84.4	ND
42	103.9	106.5	ND	131.6	ND	ND	130.9	ND	ND	ND
43	31.6	32.2	ND	40.6	ND	ND	65.3	69.6	98.3	ND
142	41.1	ND	39.1	43.0	ND	53.3	ND	84.5	95.6	ND
145	13.5	ND	4.7	5.7	ND	6.2	ND	14.7	42.2	ND
153	22.5	ND	8.7	8.7	ND	11.1	ND	23.2	46.8	ND
158	29.1	ND	21.4	27.5	27.8	ND	ND	56.5	79.4	ND
168	32.4	ND	22.6	33.6	28.7	ND	ND	56.3	83.7	ND
173	28.7	ND	22.6	23.5	22.8	ND	ND	54.8	82.2	ND
176	17.0	ND	4.4	5.3	ND	6.2	ND	ND	ND	ND
179	48.0	34.9	ND	39.7	ND	ND	58.9	ND	89.1	101.6
182	40.4	ND	36.7	38.5	ND	47.7	ND	64.9	87.7	ND
185	38.4	ND	46.3	51.1	ND	52.1	ND	69.4	85.8	90.5
191	19.2	ND	ND	10.2	ND	11.8	ND	21.4	45.3	ND
194	20.3	ND	5.9	6.5	ND	6.2	ND	ND	ND	ND
197	24.6	ND	9.3	8.6	ND	10.1	ND	ND	ND	ND
200	31.6	ND	10.9	14.2	ND	12.6	ND	ND	ND	ND
203	28.7	ND	17.6	21.3	ND	26.3	ND	ND	ND	ND
206	24.0	ND	21.3	19.0	ND	21.1	ND	45.1	65.2	90.6
212	30.5	ND	10.4	10.8	ND	11.0	ND	ND	ND	ND
215	24.2	ND	9.5	10.9	ND	10.4	ND	ND	ND	ND