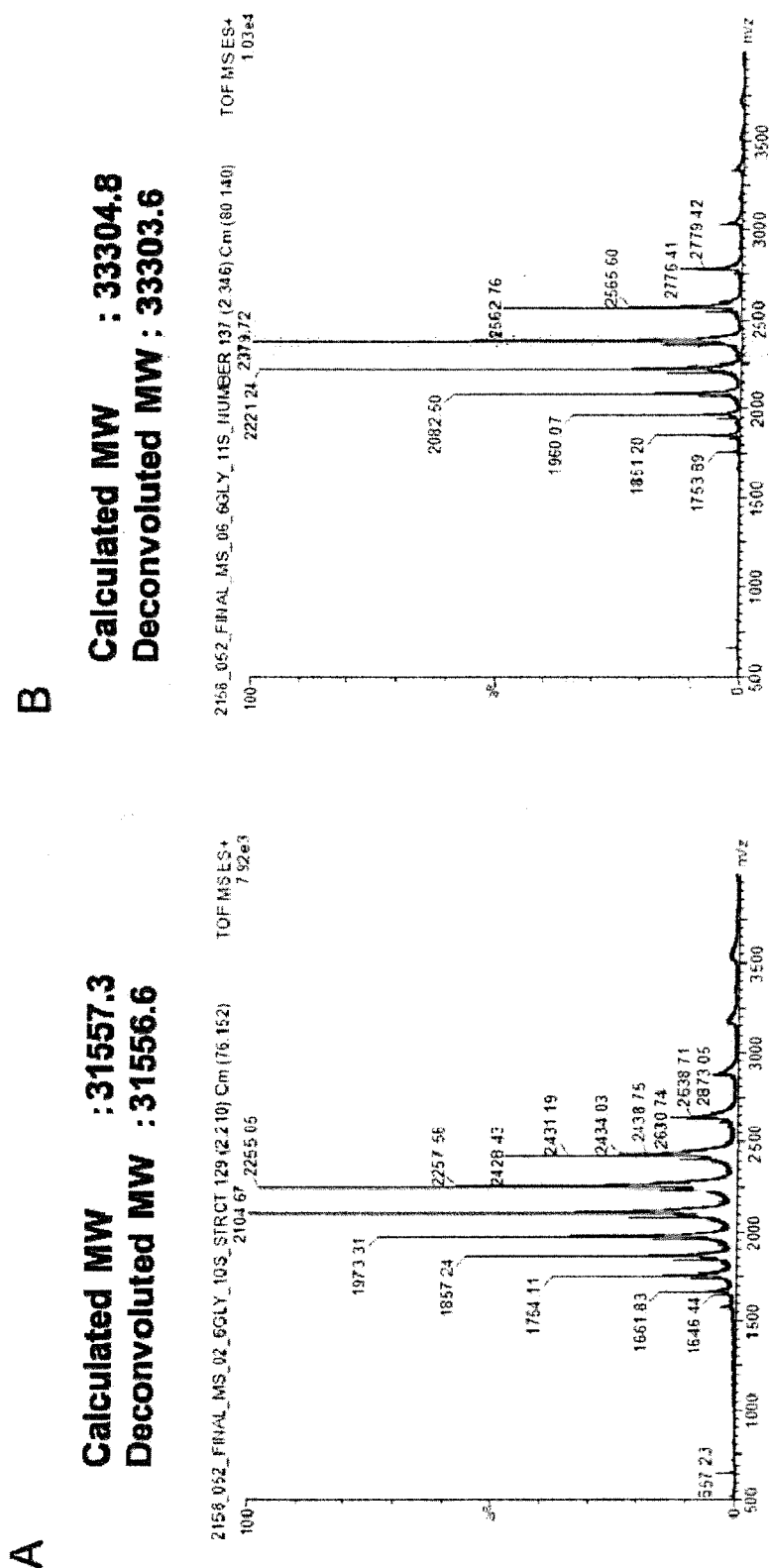


FIGURES

[Figure 1]



A: monoSialo (S1C-Q48C-N79C-K107C-R112C-R123C)

B: diSialo (S1C-Q48C-N79C-K107C-R112C-R123C)

[Figure 2]

Lane 1 2

kDa

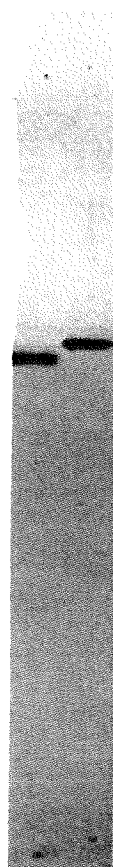
60 -

50 -

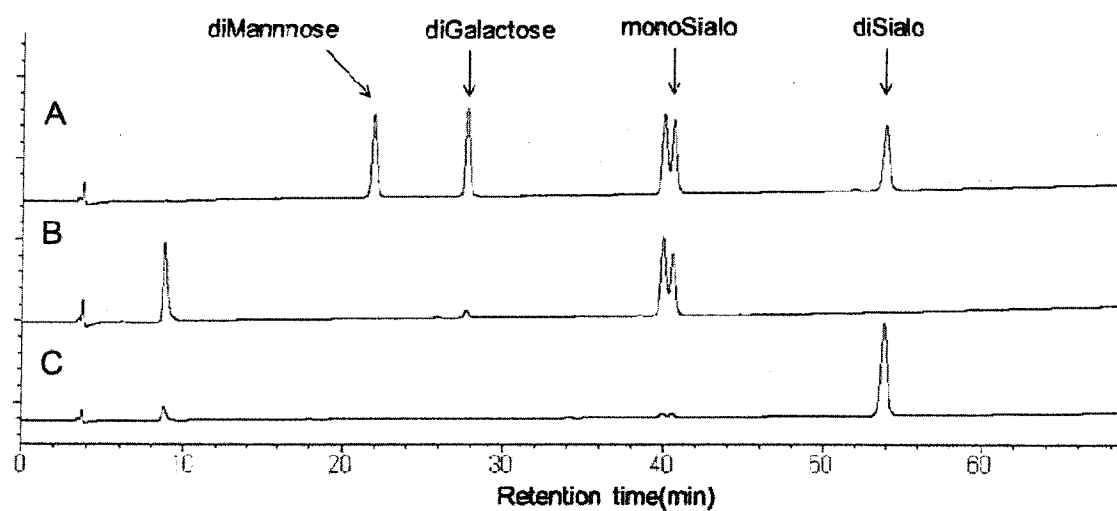
40 -

30 -

20 -

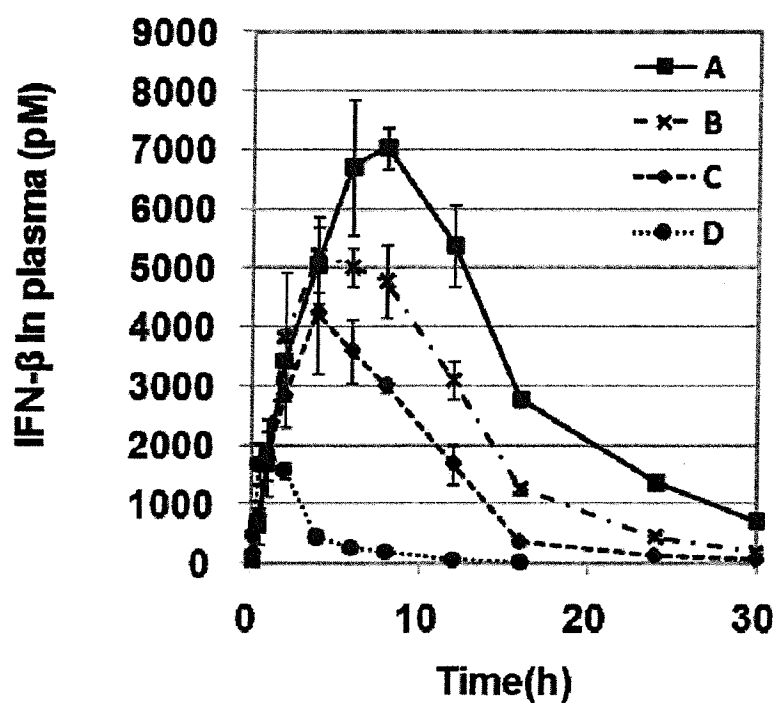
**lane1: monoSialo (S1C-Q48C-N79C-K107C-R112C-R123C)****lane2: diSialo (S1C-Q48C-N79C-K107C-R112C-R123C)**

[Figure 3]



A: standard sugars
 B: monoSialo (S1C-Q48C-N79C-K107C-R112C-R123C)
 C: diSialo (S1C-Q48C-N79C-K107C-R112C-R123C)

[Figure 4]



A: 2-6 diSialo (S1C-Q48C-N79C-K107C-R112C-R123C)
 B: 2-6 diSialo (S1C-Q48C-N79C-K107C-R112C)
 C: 2-6 diSialo (S1C-Q48C-N79C-K107C)
 D: Avonex

[Figure 5]

Multiply Sugar Chain-Modified Form	S.C.				
	$t_{1/2}$ (h)	AUC_{∞} (h·pM)	MRT (h)	C_{max} (pM)	T_{max} (h)
A	7.1	108351.3	13.0	7033.5	8.0
B	5.0	67000.1	9.5	5226.0	4.0
C	3.9	40608.2	7.5	4229.1	4.0
D	2.7	6876.8	3.3	1858.3	1.0

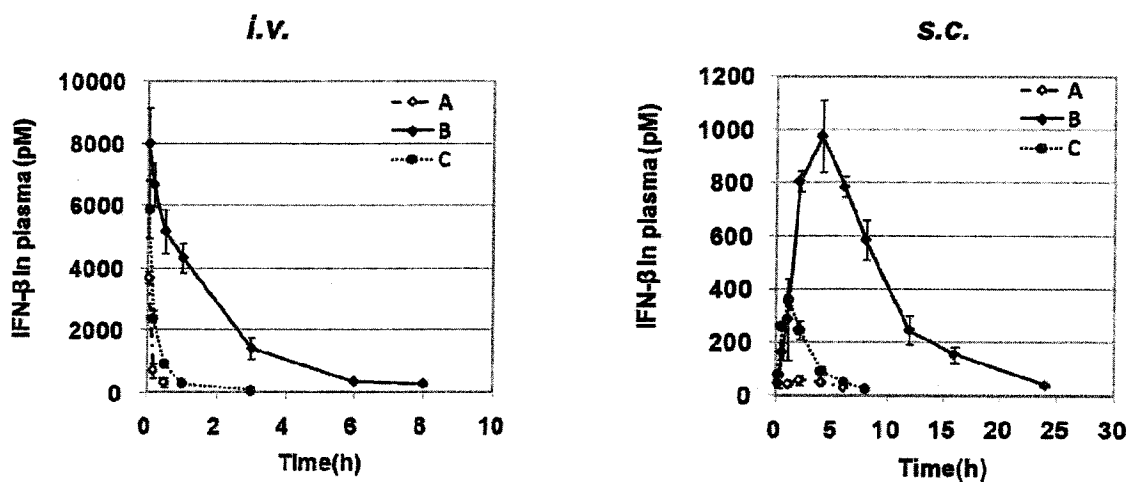
A: 2-6 diSialo (S1C-Q48C-N79C-K107C-R112C-R123C)

B: 2-6 diSialo (S1C-Q48C-N79C-K107C-R112C)

C: 2-6 diSialo (S1C-Q48C-N79C-K107C)

D: Avonex

[Figure 6]



A: 2-6 monoSialo (S1C-Q48C-N79C-K107C)

B: 2-6 diSialo (S1C-Q48C-N79C-K107C)

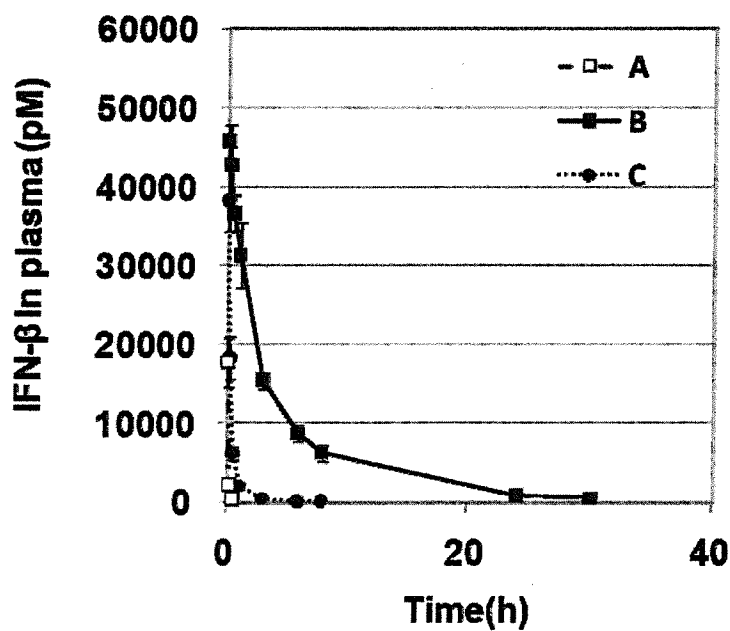
C: Avonex

[Figure 7]

4-gly Sugar Substituted IFN β	i.v.				s.c.					Bio- availability
	$t_{1/2}$ (h)	AUC_{∞} (h·pM)	MRT (h)	C_0 (pM)	$t_{1/2}$ (h)	AUC_{∞} (h·pM)	MRT (h)	C_{max} (pM)	T_{max} (h)	
A	0.11	458.0	0.13	4245.8	ND	458.9	ND	57.7	2	1
B	2.56	11998.9	2.33	7454.4	4.2	9066.9	7.9	975.0	4	0.76
C	1.07	1569.3	0.71	5111.8	2.19	1155.5	3.03	361.2	1	0.74

A: 2-6 monoSialo (S1C-Q48C-N79C-K107C)
 B: 2-6 diSialo (S1C-Q48C-N79C-K107C)
 C: Avonex

[Figure 8]



A: 2-6 monoSialo (S1C-Q48C-N79C-K107C-R112C-R123C)
 B: 2-6 diSialo (S1C-Q48C-N79C-K107C-R112C-R123C)
 C: Avonex

[Figure 9]

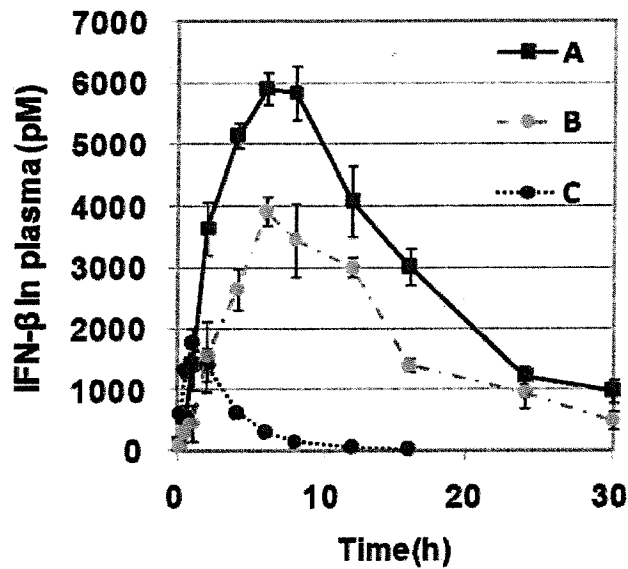
6-gly Sugar Substituted IFN β	<i>i.v.</i>			
	$t_{1/2}$ (h)	AUC^∞ (h·pM)	MRT (h)	C_0 (pM)
A	0.1	2092.3	0.1	29773.9
B	5.7	199219.3	5.8	46547.0
C	2.1	14536.2	1.0	46049.0

A: 2-6 monoSialo (S1C-Q48C-N79C-K107C-R112C-R123C)

B: 2-6 diSialo (S1C-Q48C-N79C-K107C-R112C-R123C)

C: Avonex

[Figure 10]



A: 2-6 diSialo (S1C-Q48C-N79C-K107C-R112C-R123C)

B: PEG20K (N terminus)

C: Avonex

[Figure 11]

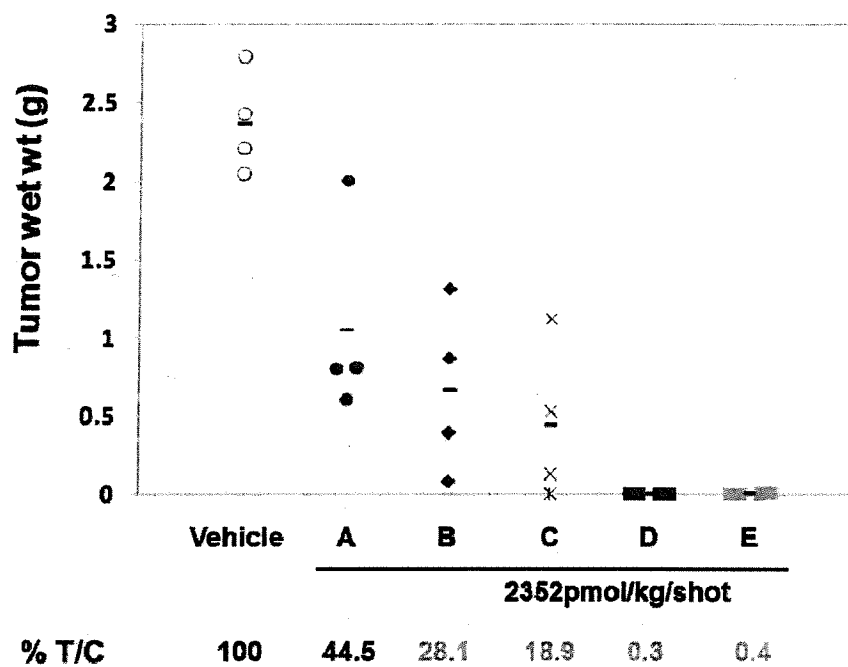
IFN β	S.C.			
	$t_{1/2}$ (h)	AUC_{∞} (h·pM)	MRT (h)	C_0 (pM)
A	8.1	102479.3	14.3	5902.2
B	7.8	60421.7	14.4	3919.5
C	3.2	6816.8	3.5	1766.4

A: 2-6 diSialo (S1C-Q48C-N79C-K107C-R112C-R123C)

B: PEG20K (N terminus)

C: Avonex

[Figure 12]



A: Avonex

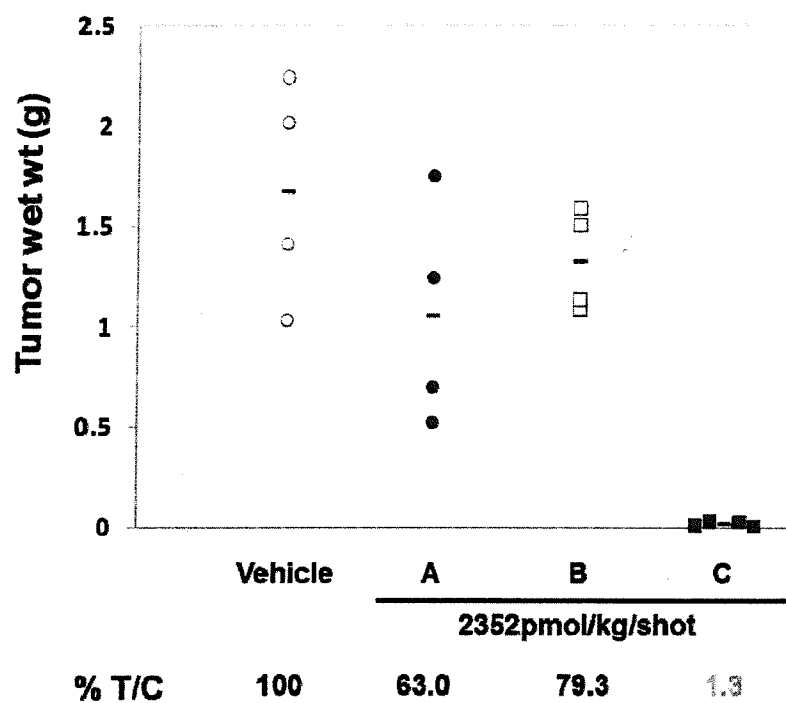
B: 2-6 diSialo (S1C-Q48C-N79C-K107C)

C: 2-6 diSialo (S1C-Q48C-N79C-K107C-R112C)

D: 2-6 diSialo (S1C-Q48C-N79C-K107C-R112C-R123C)

E: 2-6 diSialo (S1C-N3C-Q48C-N79C-K107C-R112C)

[Figure 13]

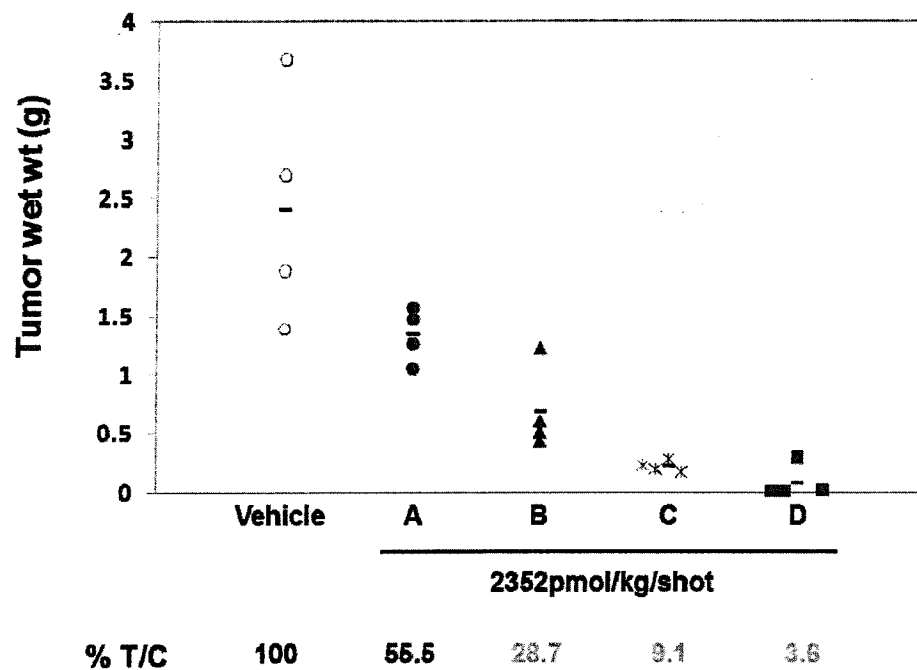
Day 22

A: Avonex

B: 2-6 monoSialo (S1C-Q48C-N79C-K107C-R112C-R123C)

C: 2-6 diSialo (S1C-Q48C-N79C-K107C-R112C-R123C)

[Figure 14]

Day 21

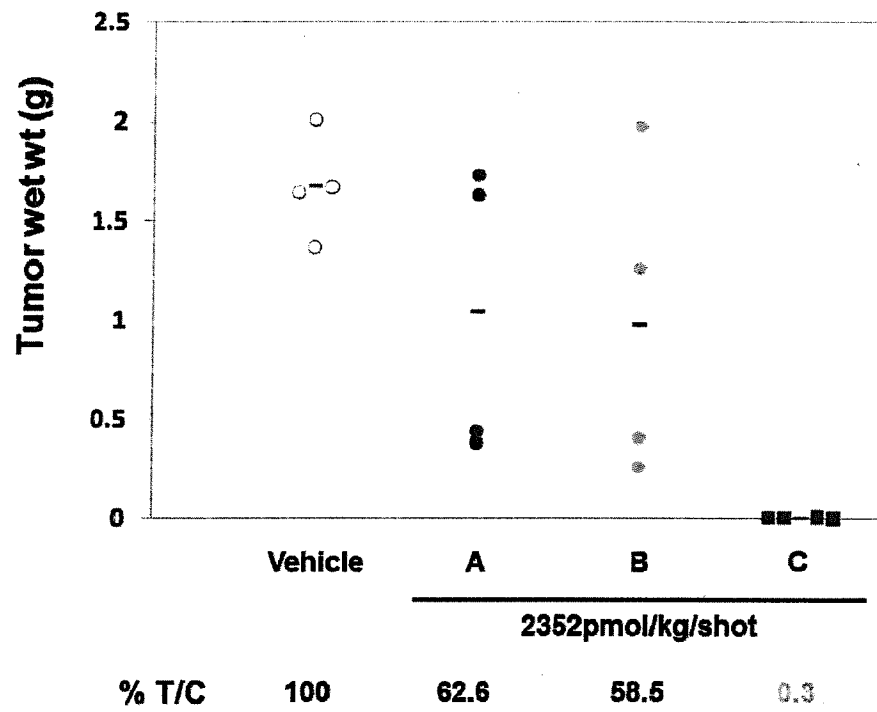
A: Avonex

B: 2-6 triSialo (S1C-Q48C-N79C-K107C-R112C-R123C)

C: 2-6 tetraSialo (S1C-Q48C-N79C-K107C-R112C-R123C)

D: 2-6 diSialo (S1C-Q48C-N79C-K107C-R112C-R123C)

[Figure 15]

Day 21

A: Avonex

B: PEG20K (N terminus)

C: 2-6 diSialo (S1C-Q48C-N79C-K107C-R112C-R123C)

[Figure 16]

(SEQ ID NO. 1)

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
 Ser-Tyr-Asn-Leu-Leu-Gly-Phe-Leu-Gln-Arg-Ser-Ser-Asn-Phe-Gln-Ser-Gln-Lys-Leu-Leu-

21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40
 Trp-Gln-Leu-Asn-Gly-Arg-Leu-Glu-Tyr-Cys-Leu-Lys-Asp-Arg-Met-Asn-Phe-Asp-Ile-Pro-

41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60
 Glu-Glu-Ile-Lys-Gln-Leu-Gln-Gln-Phe-Gln-Lys-Glu-Asp-Ala-Ala-Leu-Thr-Ile-Tyr-Glu-

61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80
 Met-Leu-Gln-Asn-Ile-Phe-Ala-Ile-Phe-Arg-Gln-Asp-Ser-Ser-Ser-Thr-Gly-Trp-Asn-Glu-

81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100
 Thr-Ile-Val-Glu-Asn-Leu-Leu-Ala-Asn-Val-Tyr-His-Gln-Ile-Asn-His-Leu-Lys-Thr-Val-

101 102 103 104 105 106 107 108 109 110 111 112 113 114 115 116 117 118 119 120
 Leu-Glu-Glu-Lys-Leu-Glu-Lys-Glu-Asp-Phe-Thr-Arg-Gly-Lys-Leu-Met-Ser-Ser-Leu-His-

121 122 123 124 125 126 127 128 129 130 131 132 133 134 135 136 137 138 139 140
 Leu-Lys-Arg-Tyr-Tyr-Gly-Arg-Ile-Leu-His-Tyr-Leu-Lys-Ala-Lys-Glu-Tyr-Ser-His-Cys-

141 142 143 144 145 146 147 148 149 150 151 152 153 154 155 156 157 158 159 160
 Ala-Trp-Thr-Ile-Val-Arg-Val-Glu-Ile-Leu-Arg-Asn-Phe-Tyr-Phe-Ile-Asn-Arg-Leu-Thr-

161 162 163 164 165
 Gly-Tyr-Leu-Arg-Asn