

Figure 1

Non-Human Primate (NHP) Study design

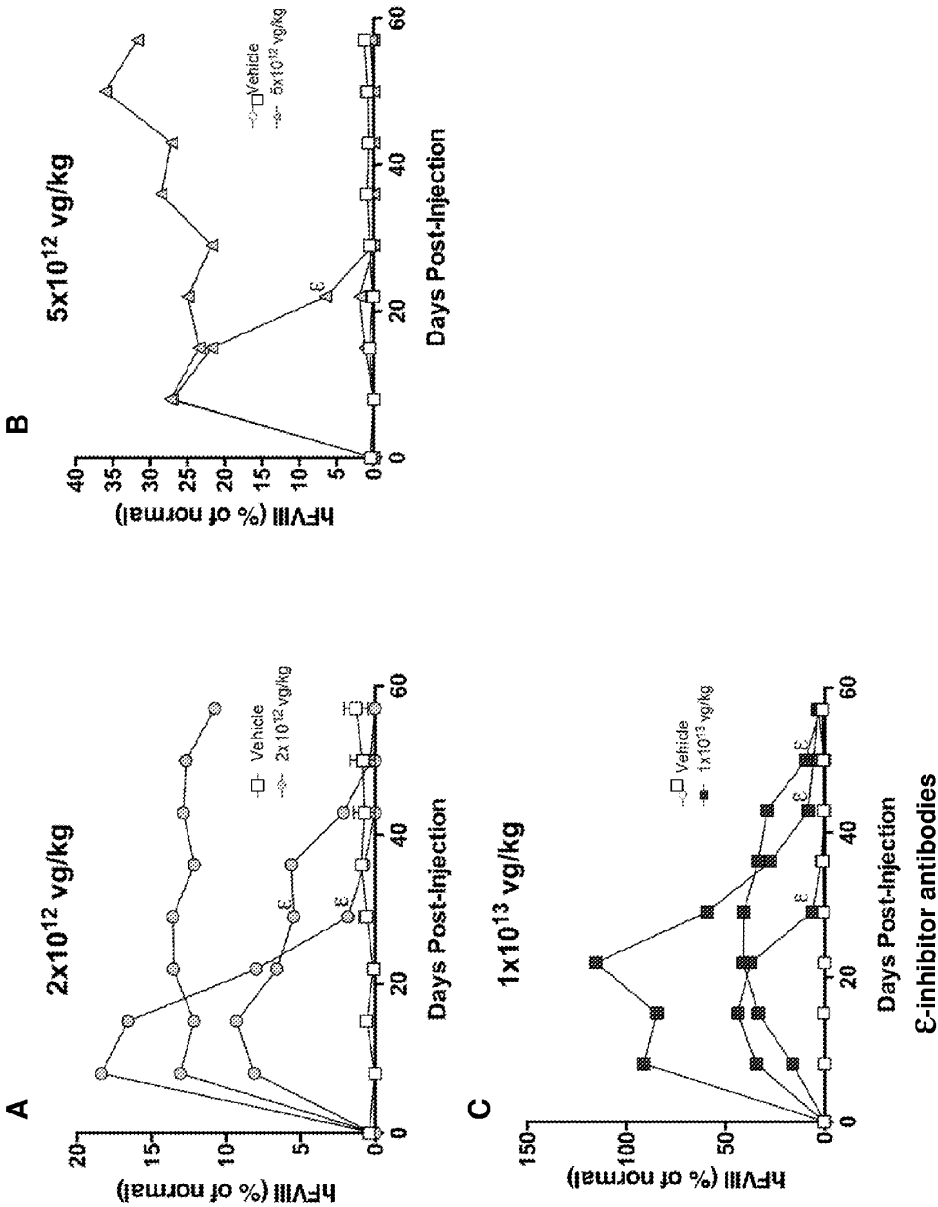
Species	Cynomolgus monkeys (<i>Macaca fascicularis</i>)
Test article	SPK-8005 or SPK-8011 (LK03 capsid)
Age	2 to 3 years
Weight	2 to 4 kg
Duration	8 weeks

AAV-SPK-8005			
GROUP	# of NHPs	DOSE LEVEL	
	Male	vg/kg	
1 (Control)	2	0	
2 (Low)	3	2x10 ¹²	
3 (Medium)	3	5x10 ¹²	
4 (High)	3	1x10 ¹³	

AAV-SPK-8011 (LK03 capsid)			
GROUP	# of NHPs	DOSE LEVEL	
	Male	vg/kg	
1 (Control)	2	0	
2 (Low)	3	2x10 ¹²	
3 (Medium)	3	6x10 ¹²	
4 (High)	3	2x10 ¹³	

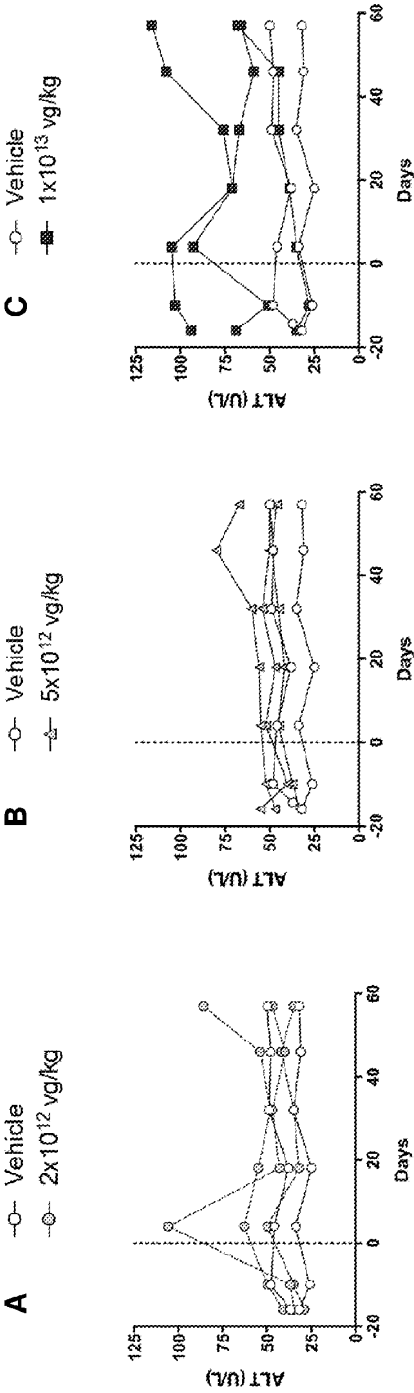
Figures 2A-2C

hFVIII antigen levels in NHPs



Figures 3A-3C

ALT levels in NHPs



Figures 4A-4C

D-Dimer levels in NHPs

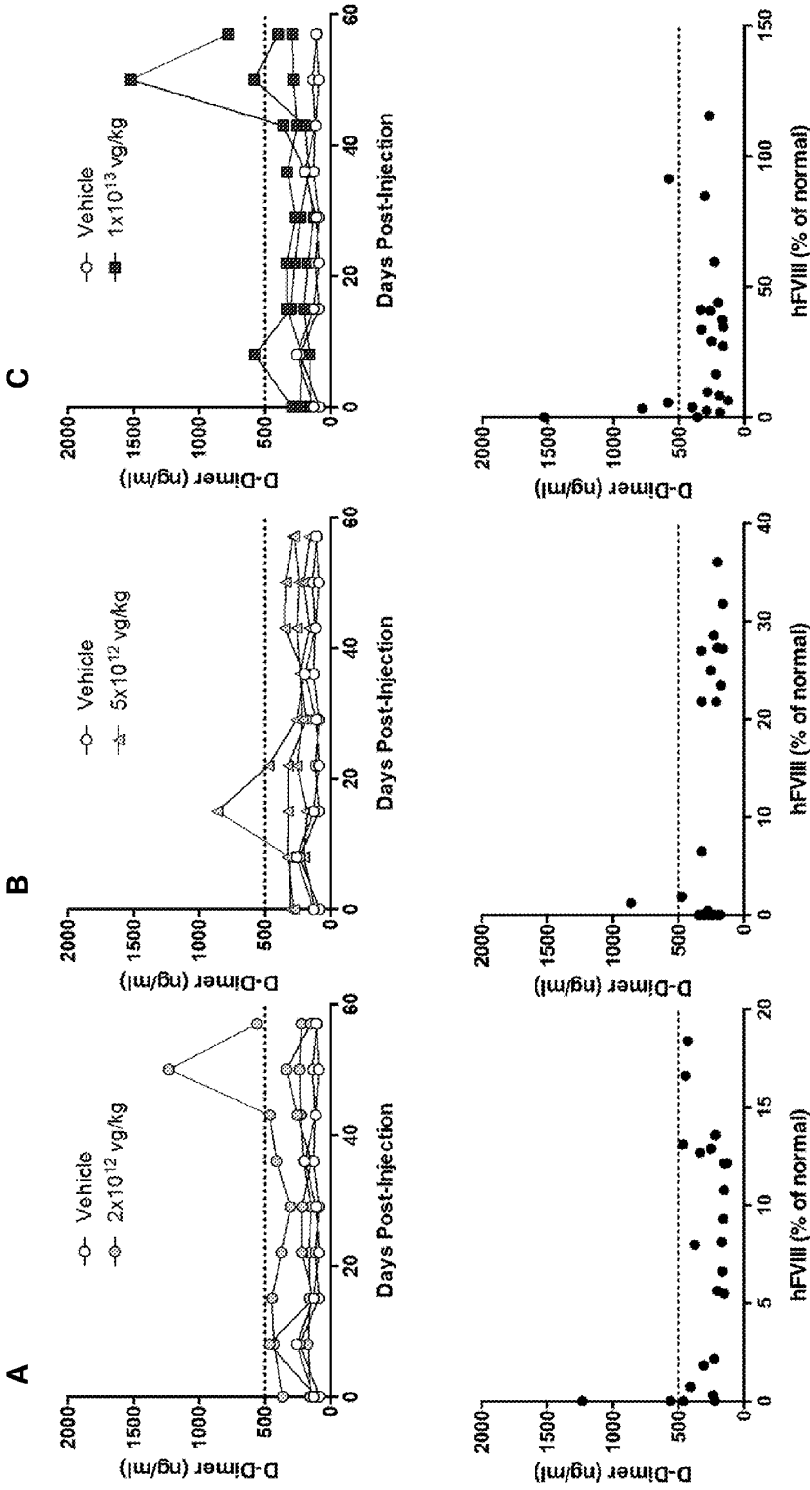


Figure 5

Summary

- Therapeutic levels of hFVIII achieved in all three doses of SPK-8005

Dose	Average peak hFVIII in ALL animals (% of normal)	Average “stable” hFVIII in NHPs w/o Inh. (% of normal)
2x10 ¹² vg/kg	13.2	10.8
5x10 ¹² vg/kg	27.1	31.8
1x10 ¹³ vg/kg	54.1	N/A

- Neutralizing Abs against human FVIII observed in 6/8 animals, as expected
- No safety issues

Figure 6A-6D

AAV-SPK-8011 (LK03): hFVIII antigen levels in cynomolgus macaques

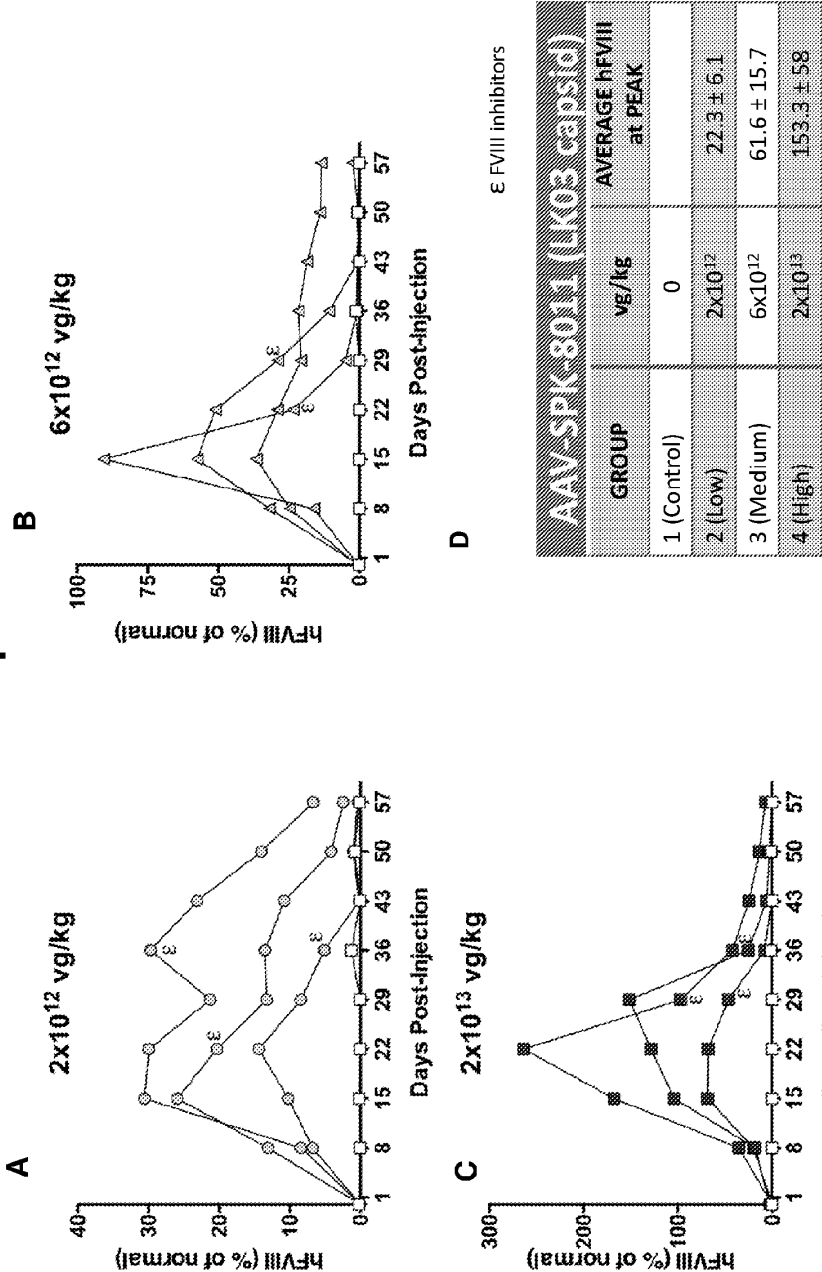


Figure 7

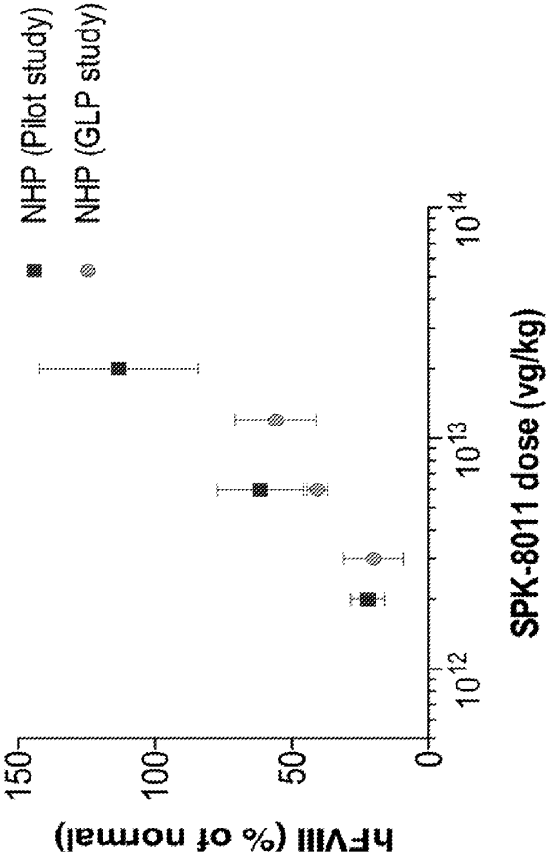
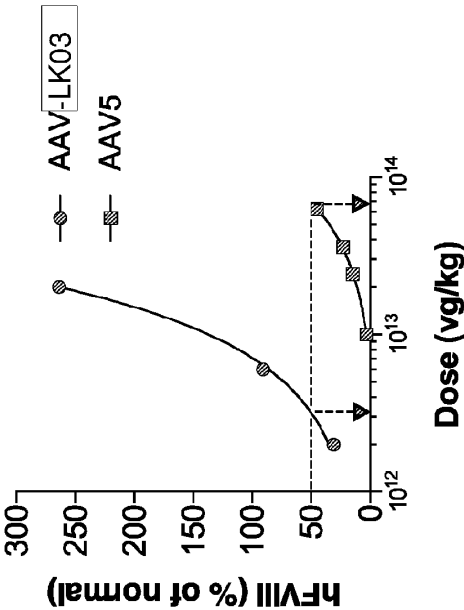


Figure 8

AAV-SPK-8011 (LK03 capsid) vs AAV5 vs AAV8:
hFVIII antigen levels in macaques

vg/kg	AAV-SPK-8011 (LK03)	AAV5	AAV8
	MAXIMUM hFVIII at PEAK (% of normal)		
2x10 ¹²	31		
6x10 ¹²	91		
1x10 ¹³		~3	
2x10 ¹³	264		~120
2.4x10 ¹³		~15	
3.6x10 ¹³		~23	
6.3x10 ¹³		~45	



AAV-SPK-8011 (LK03 capsid)	AAV5
Predicted dose to achieve 50% of normal hFVIII	
3.2x10 ¹² vg/kg	69.5x10 ¹² vg/kg

Figure 9

AAV-LK03 tissue bio-distribution in non-human primates

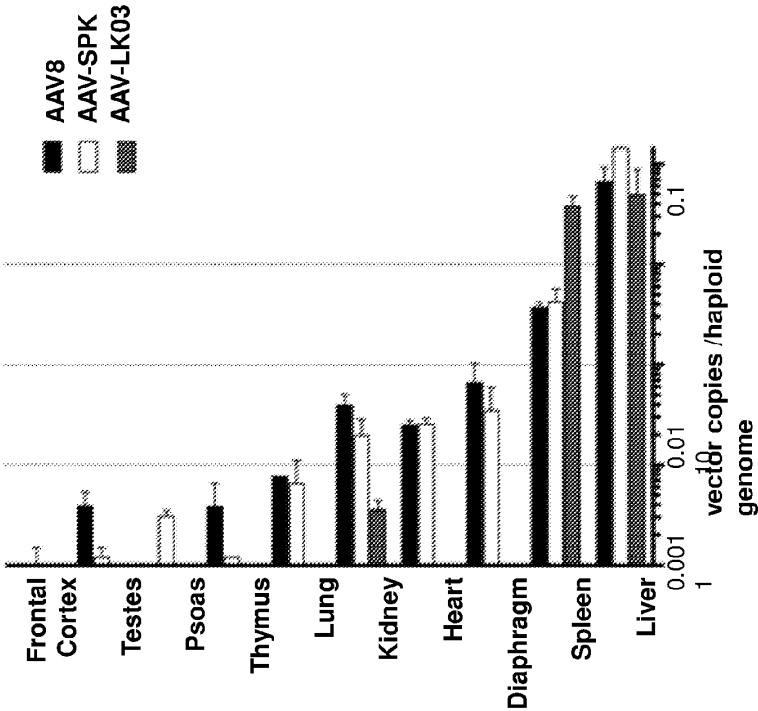


Figure 10

Hepatic and splenic FVIII expression after systemic administration of AAV-hFVIII (SPK-8005) into mice

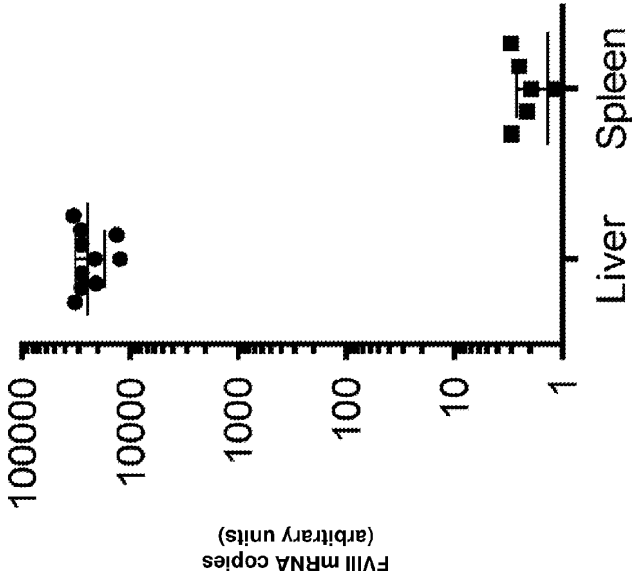


Figure 11

Transduction Efficiency of AAV-LK03 Capsid

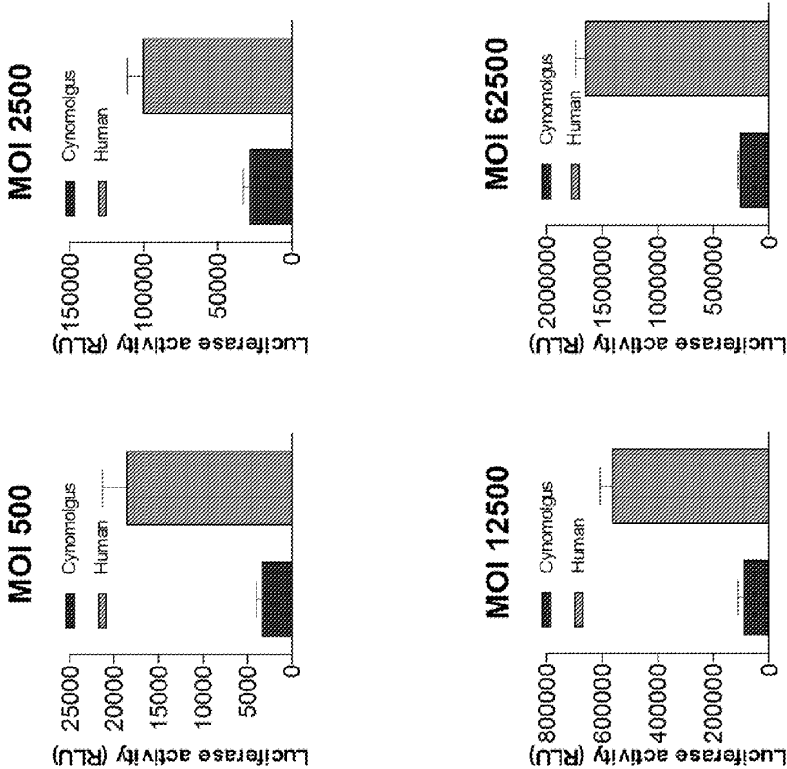


Figure 12

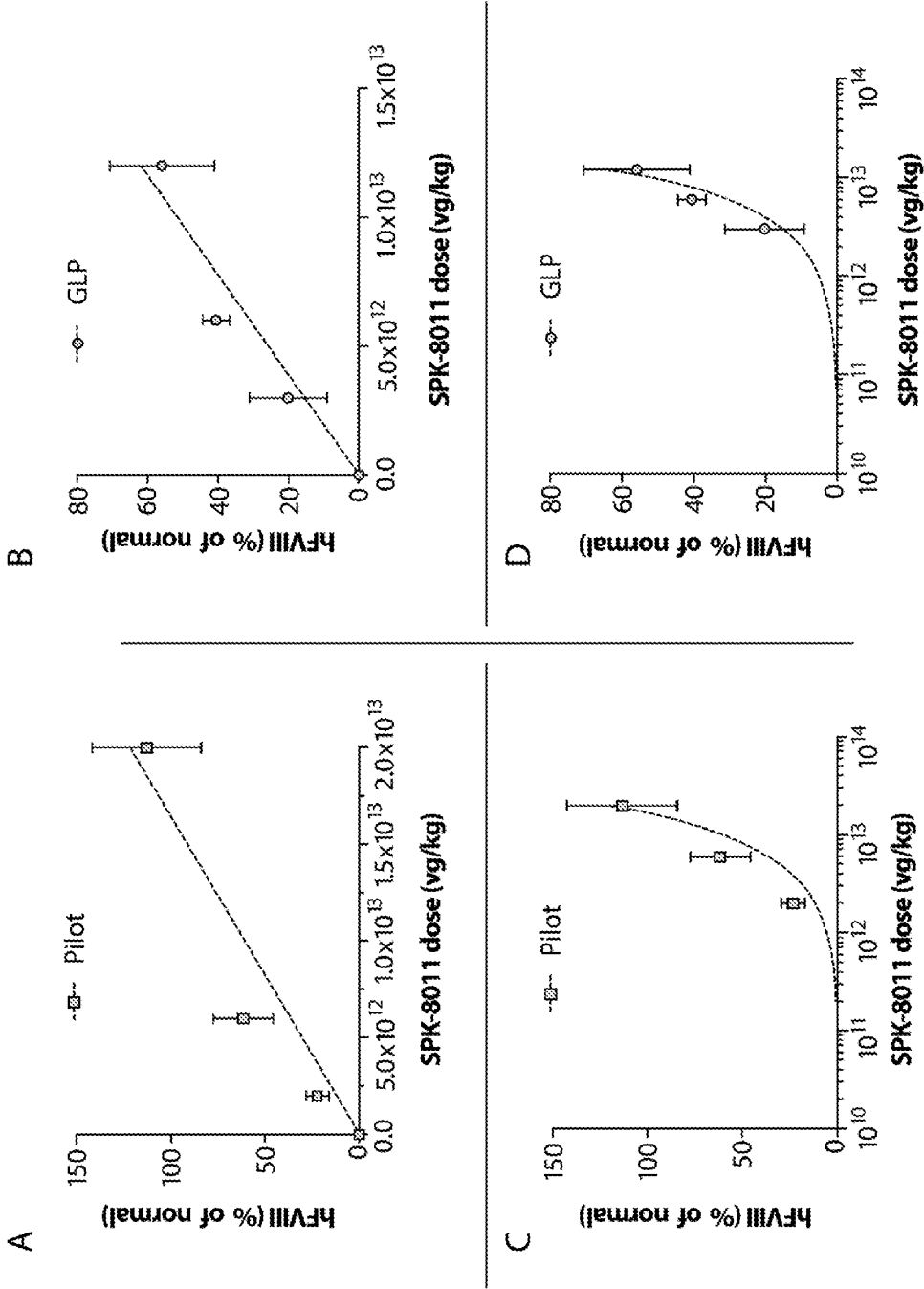


Figure 13

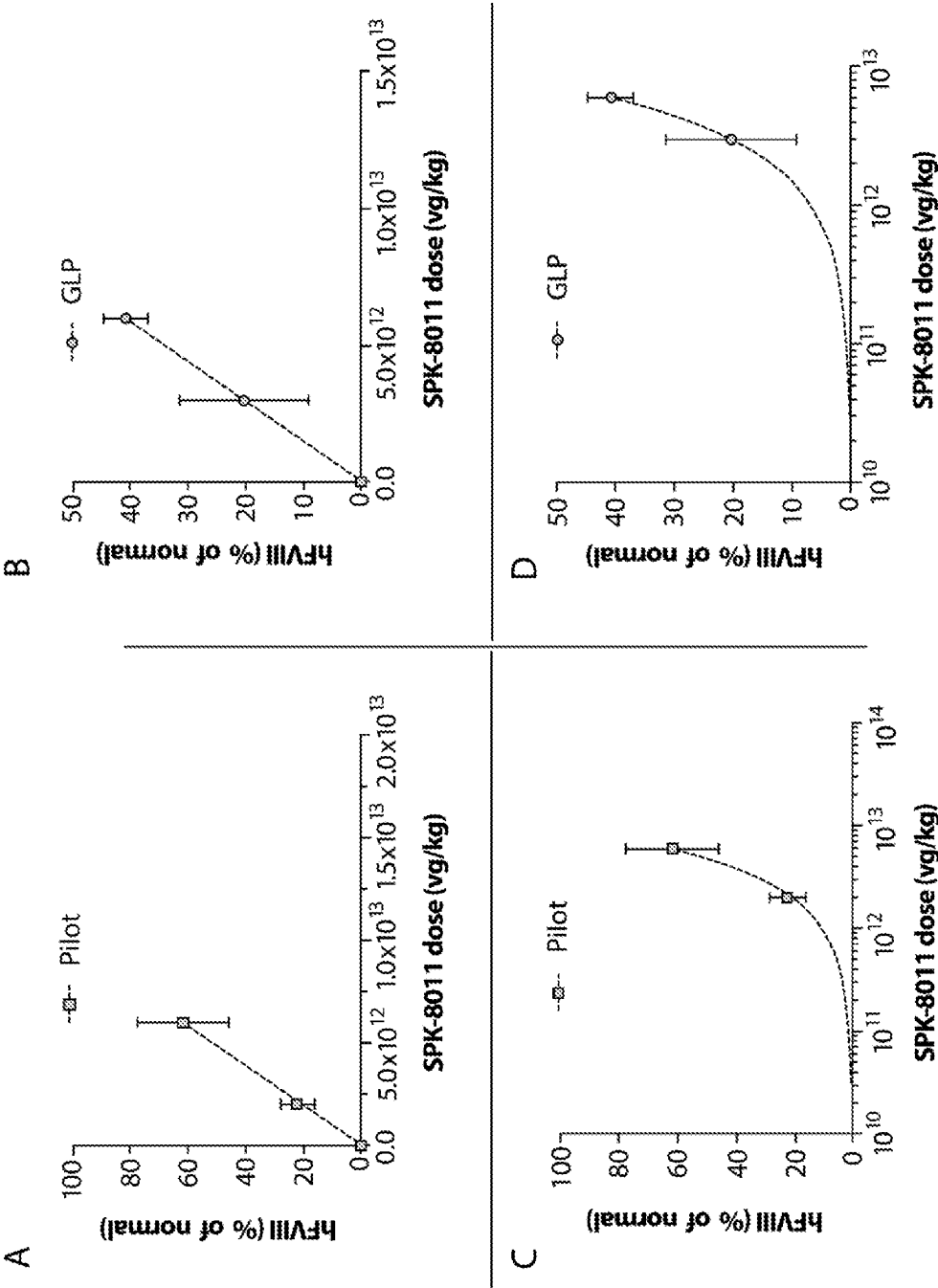


Figure 14

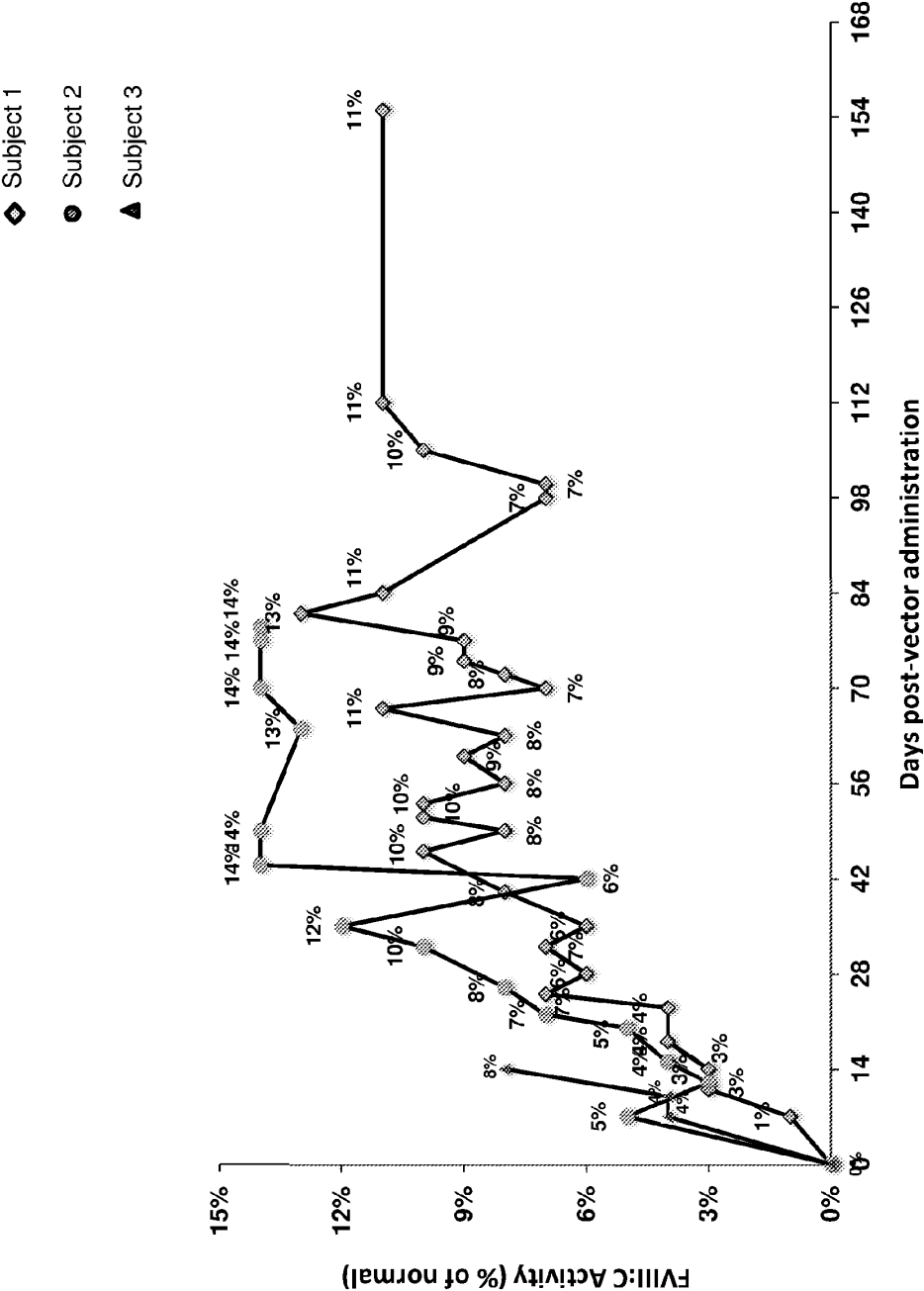


Figure 15

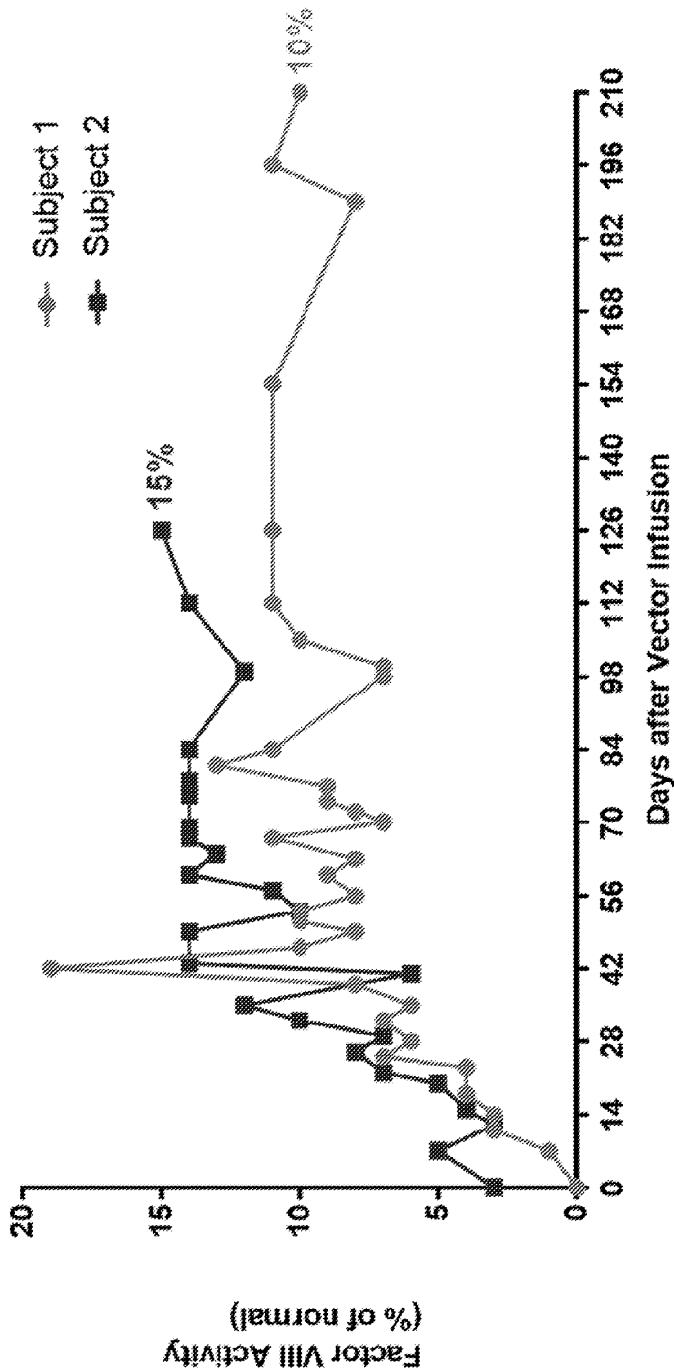


Figure 16

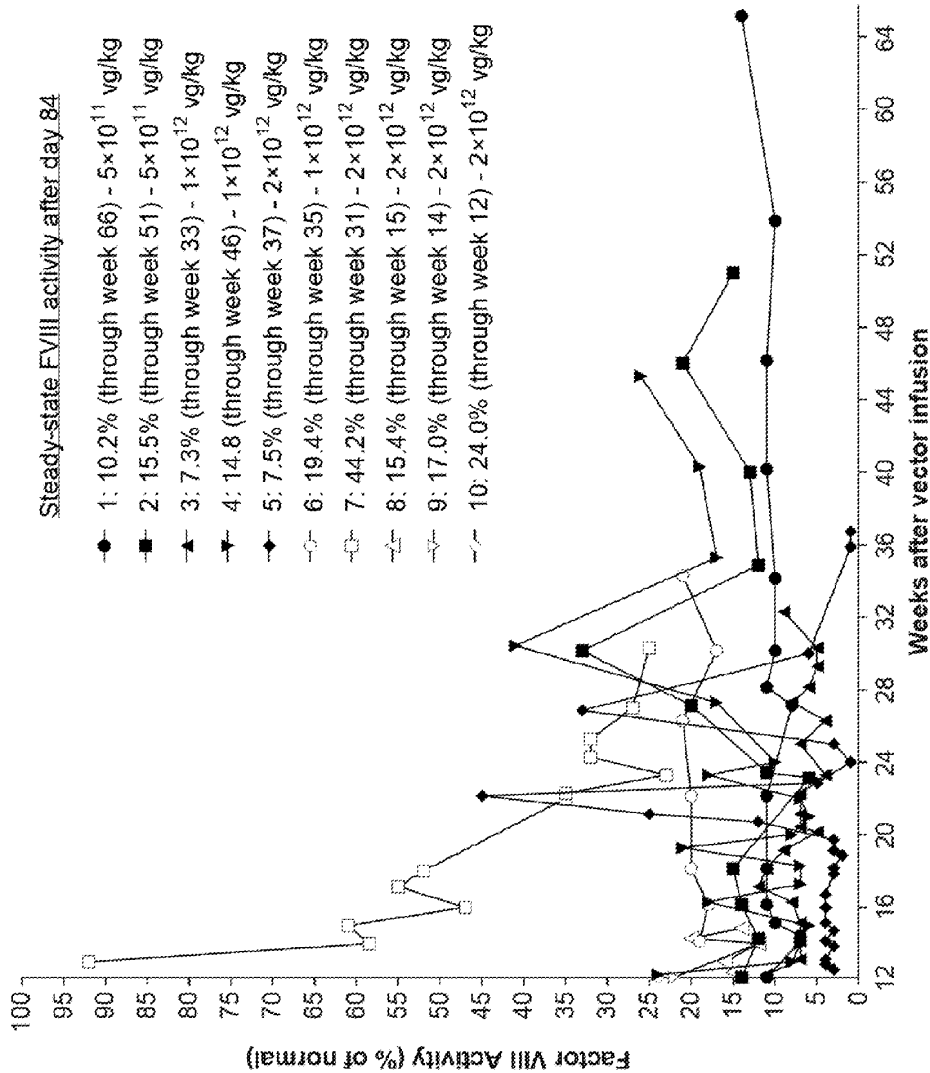


Figure 17

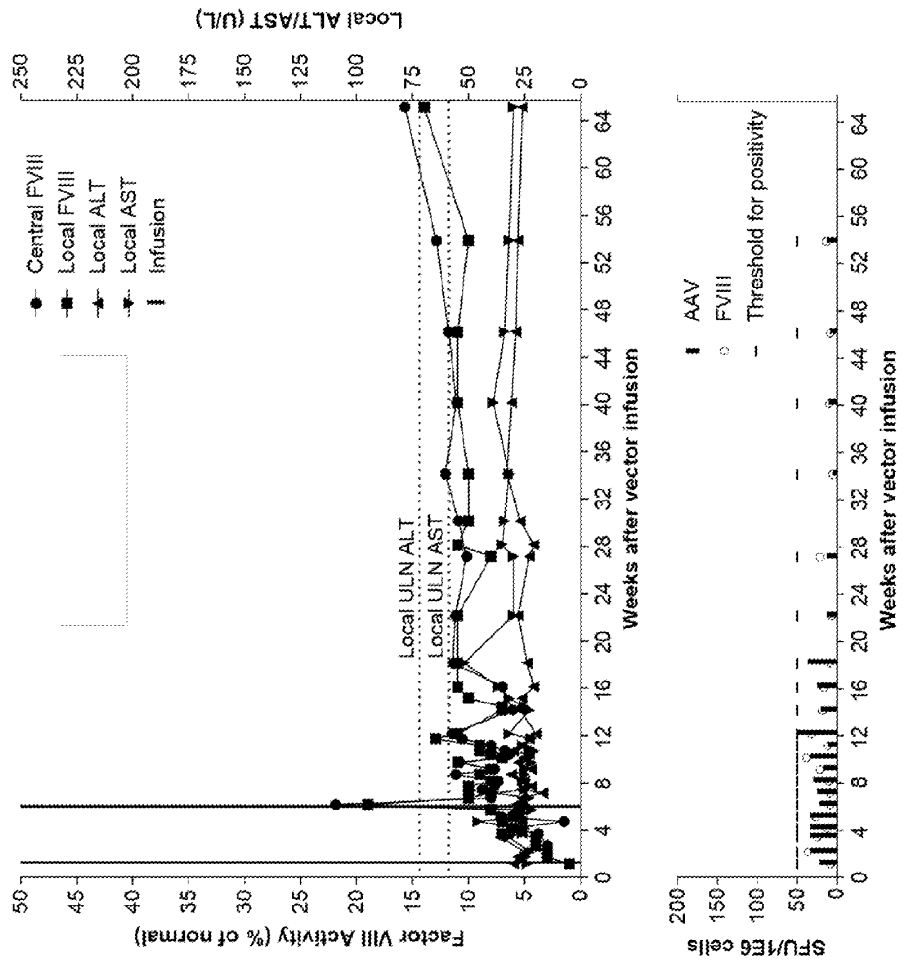


Figure 18

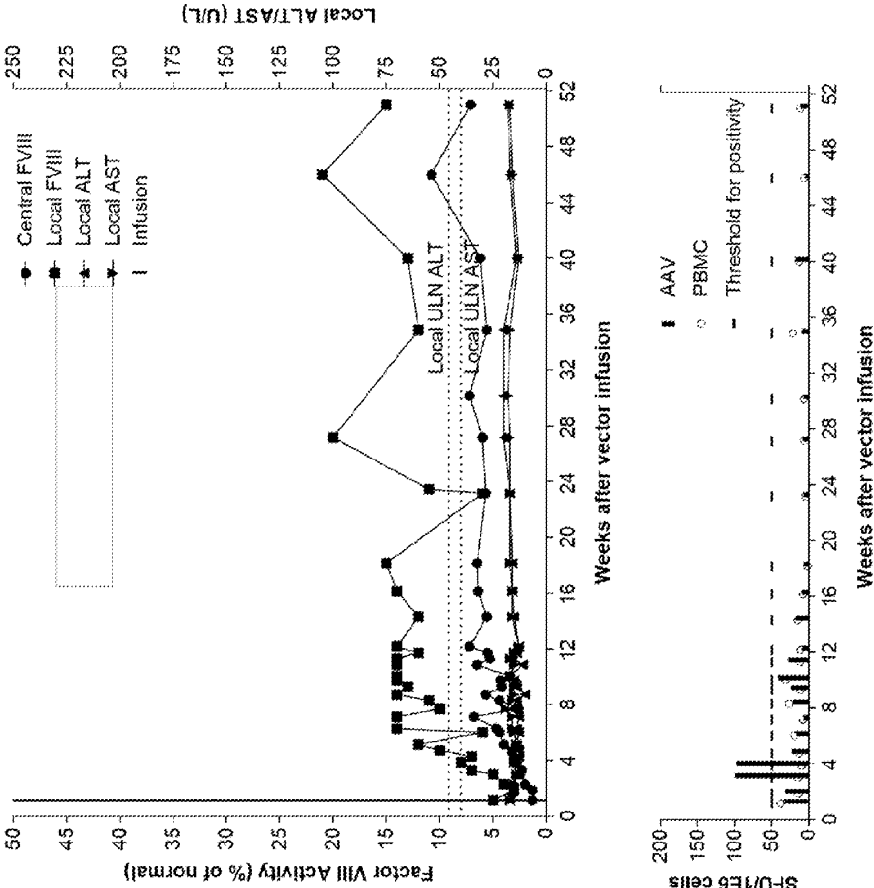


Figure 19

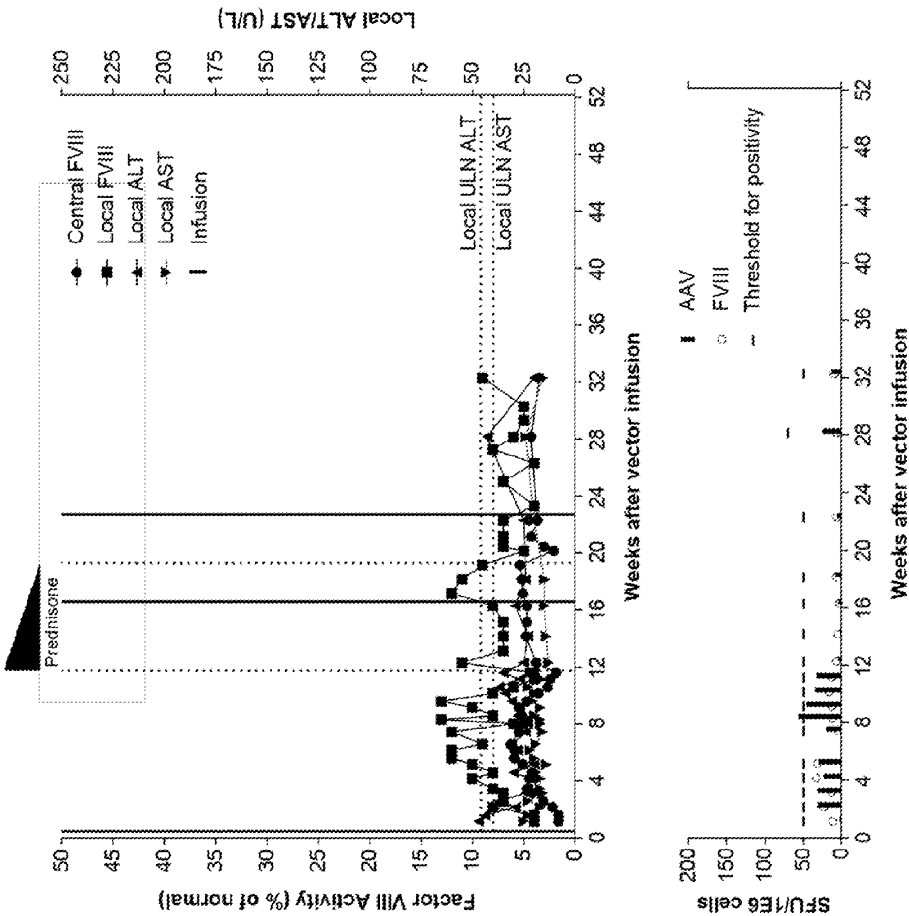


Figure 20

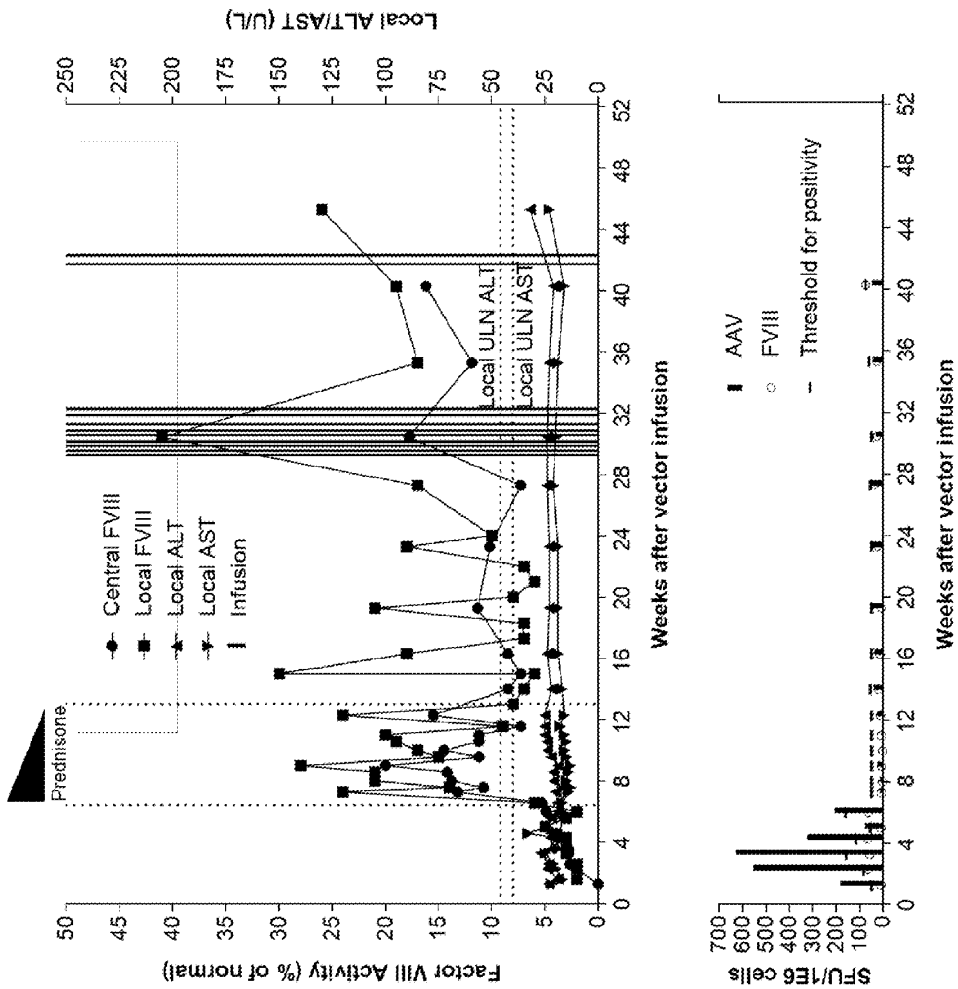


Figure 21

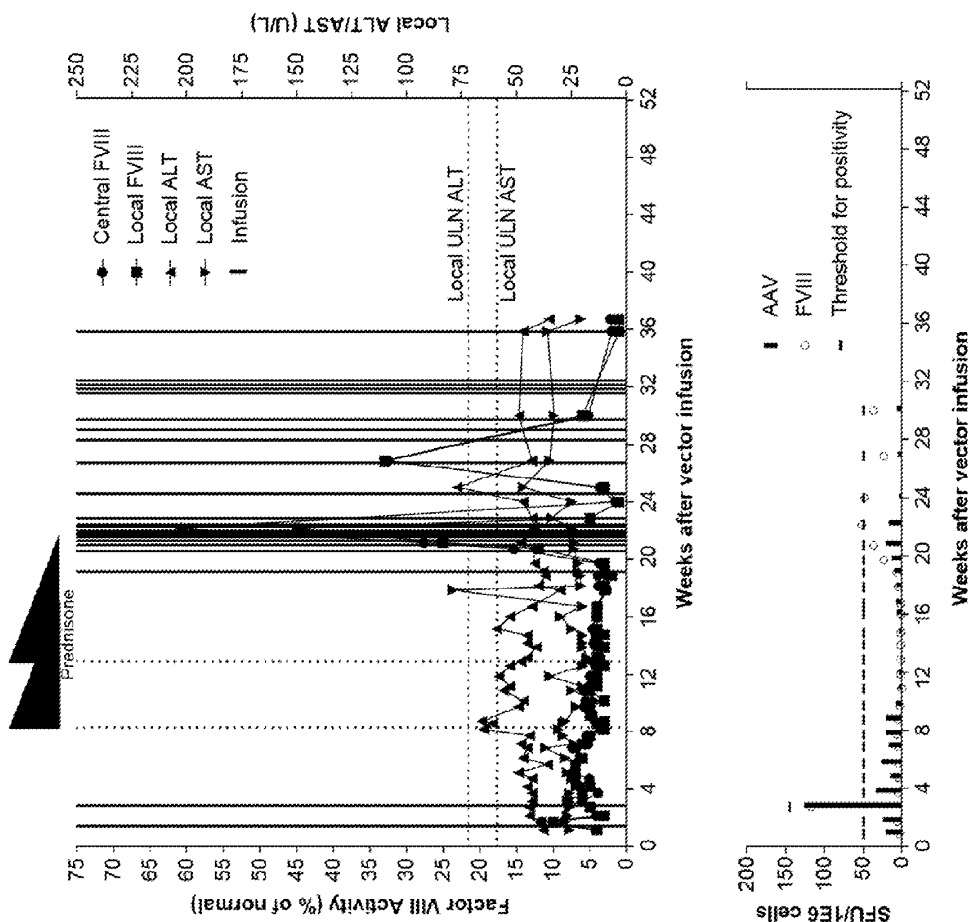


Figure 22

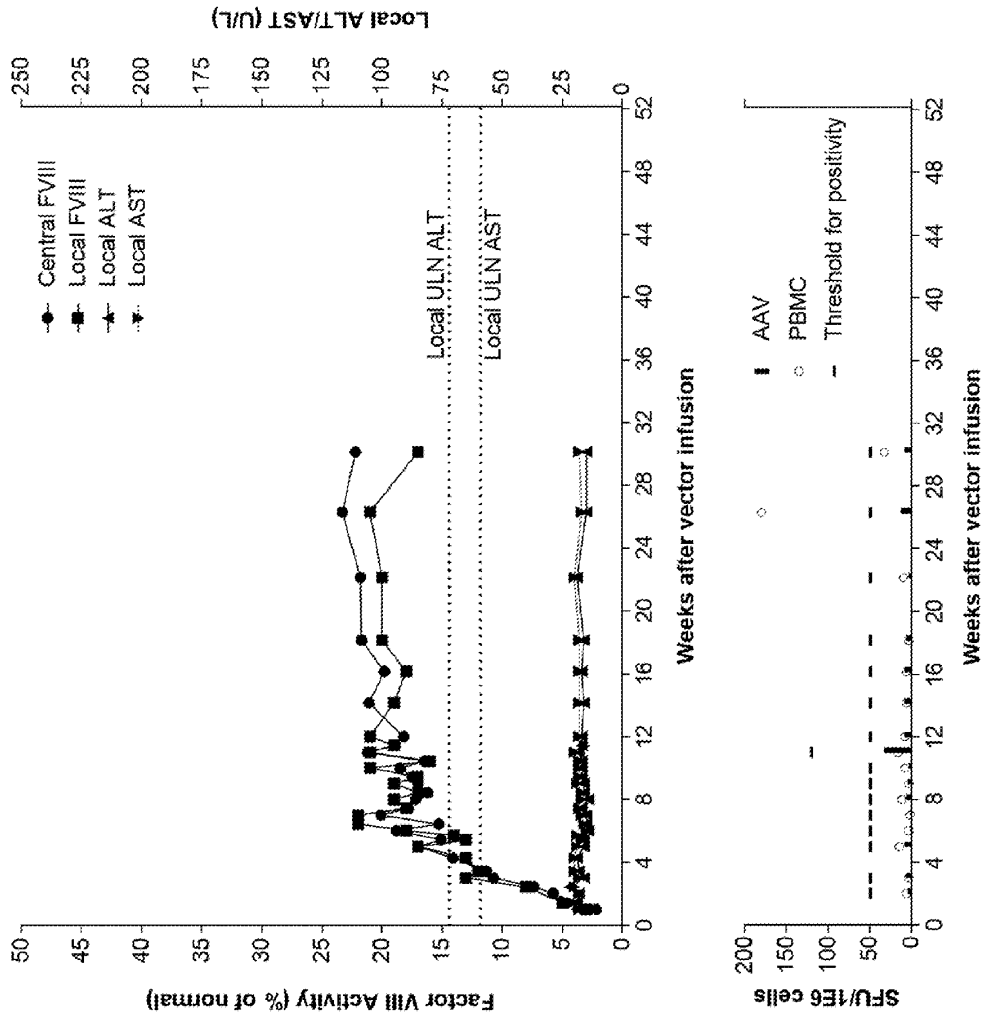


Figure 23

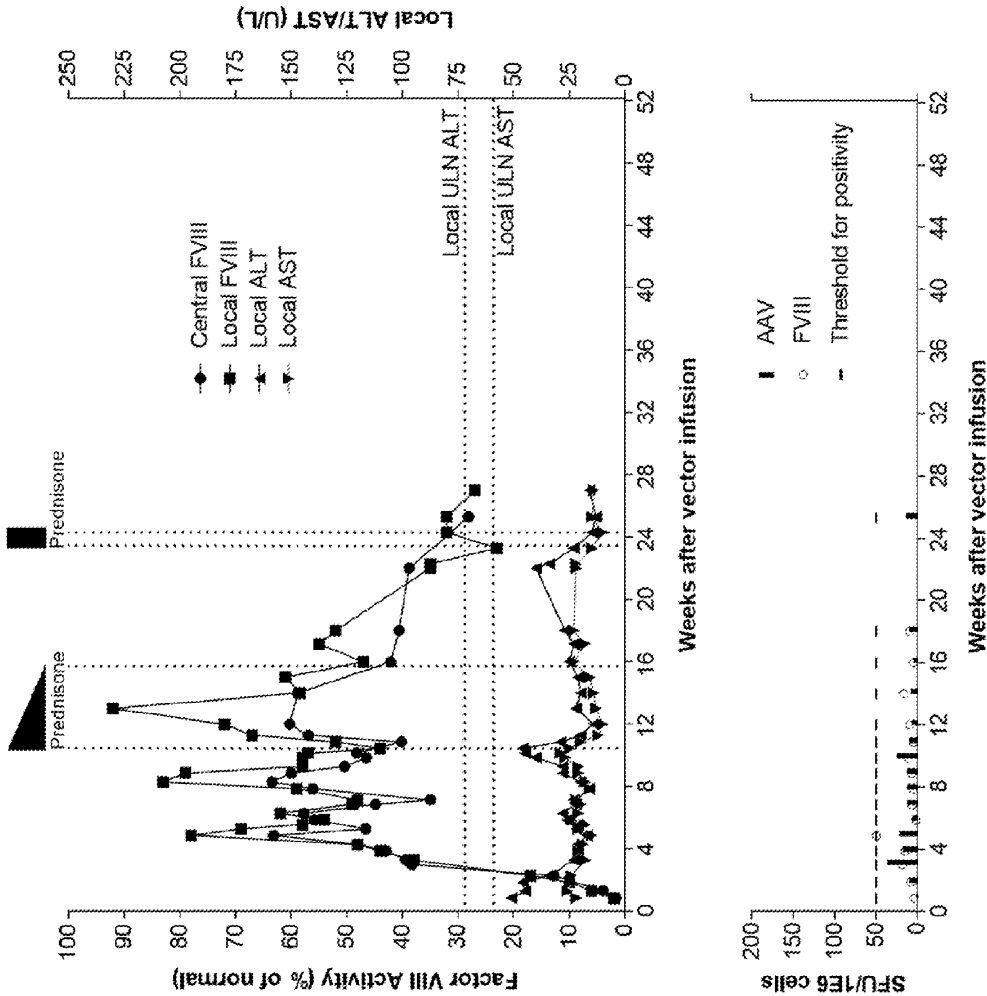


Figure 24

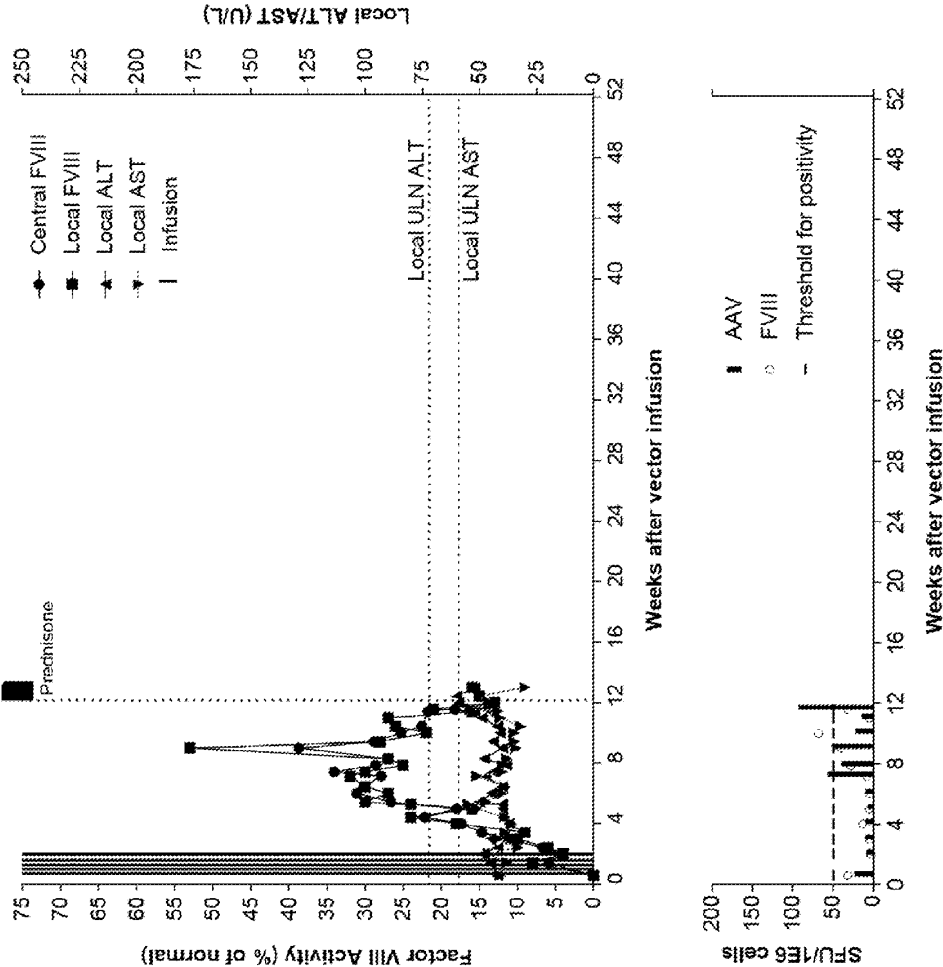


Figure 25

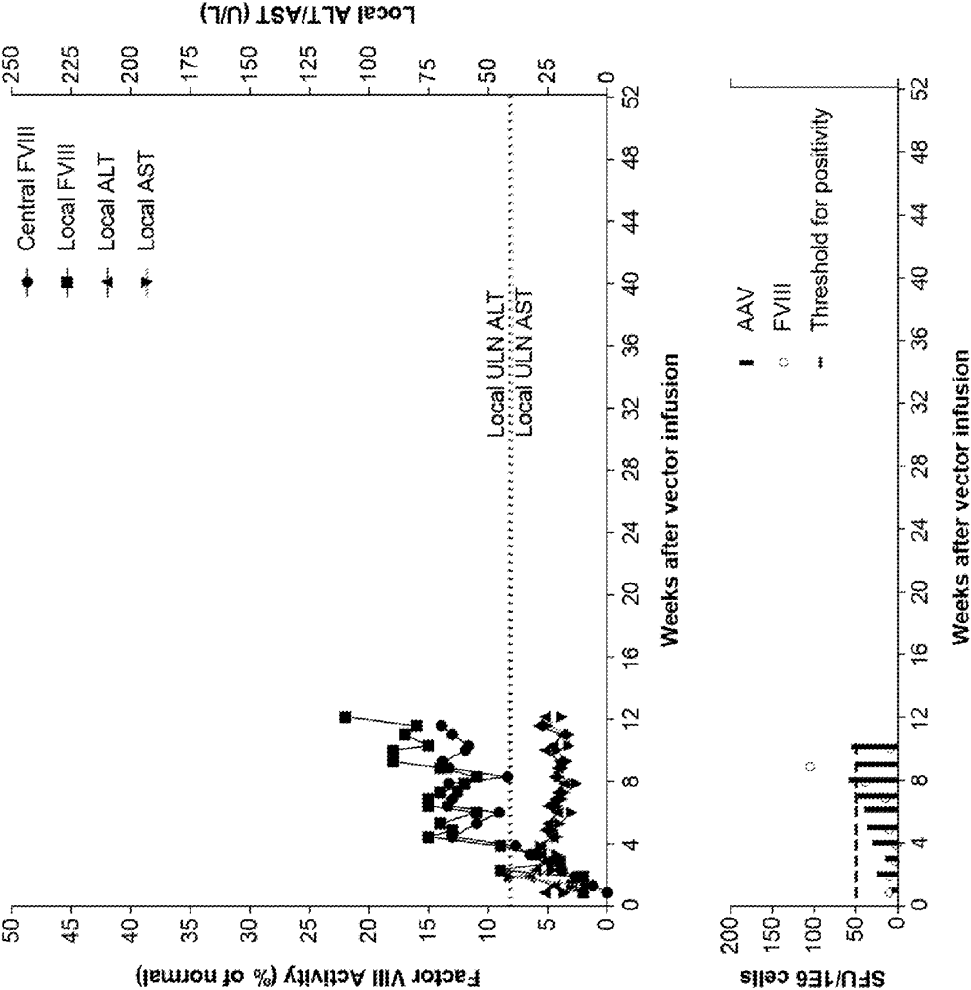


Figure 26

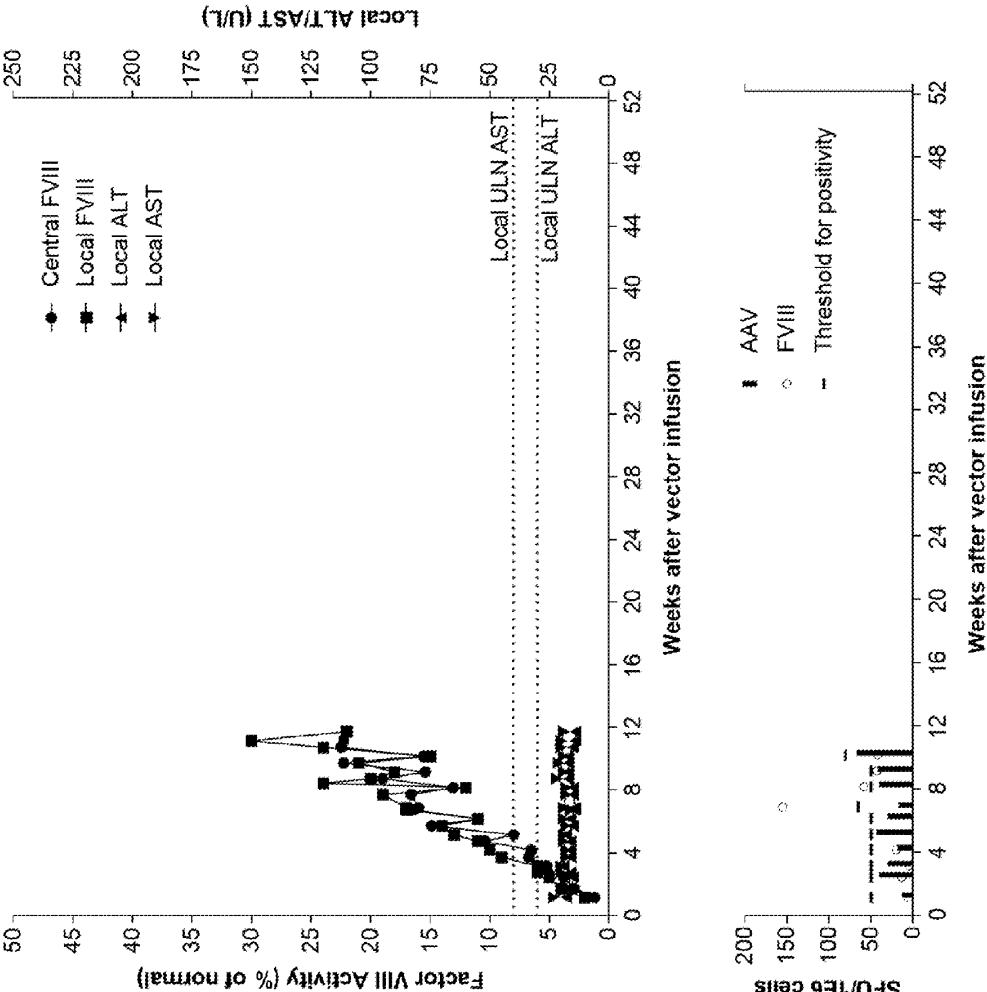


Figure 27

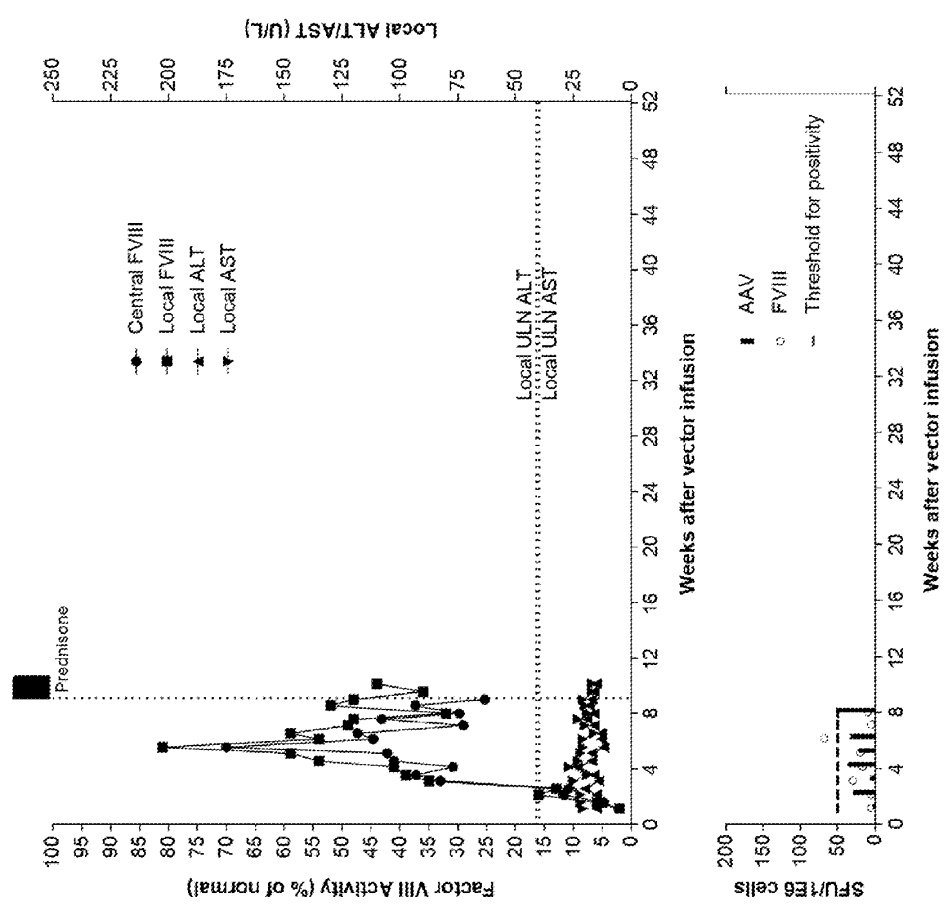


Figure 28

