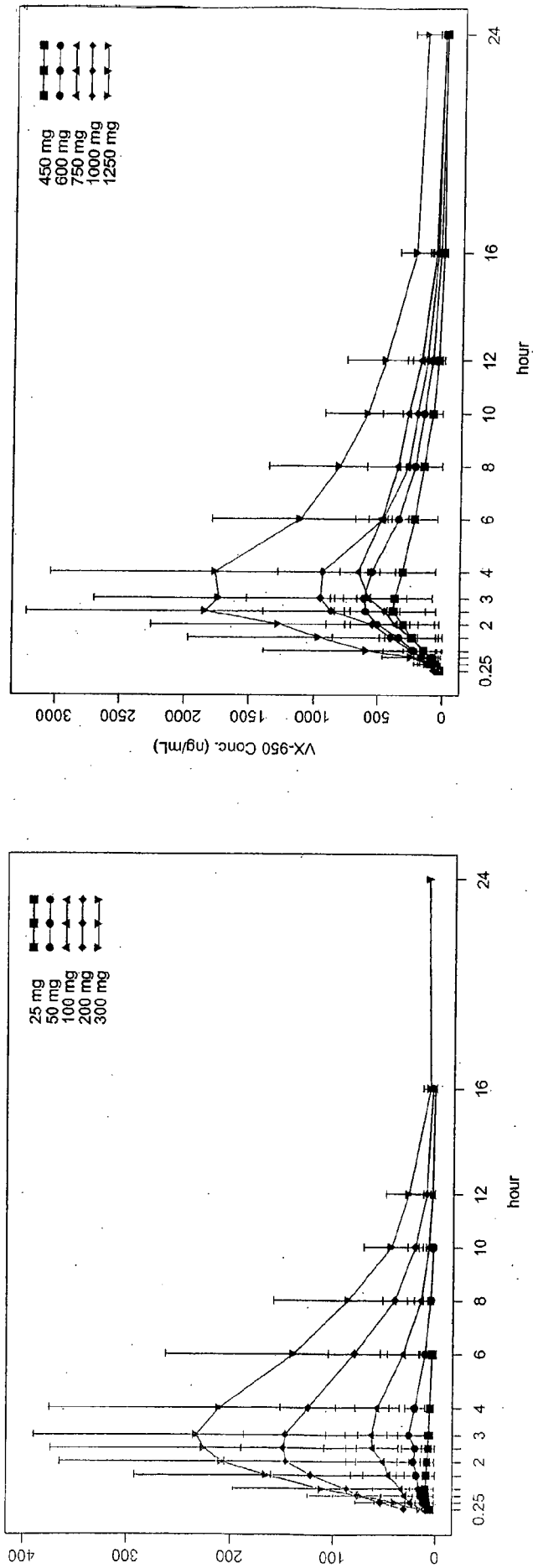
Mean Concentration Time Profiles by Dose Levels

FIG. 1A & FIG.1B



PK Parameters for Single Dose Escalation (Part A)
FIGS. 2A-D

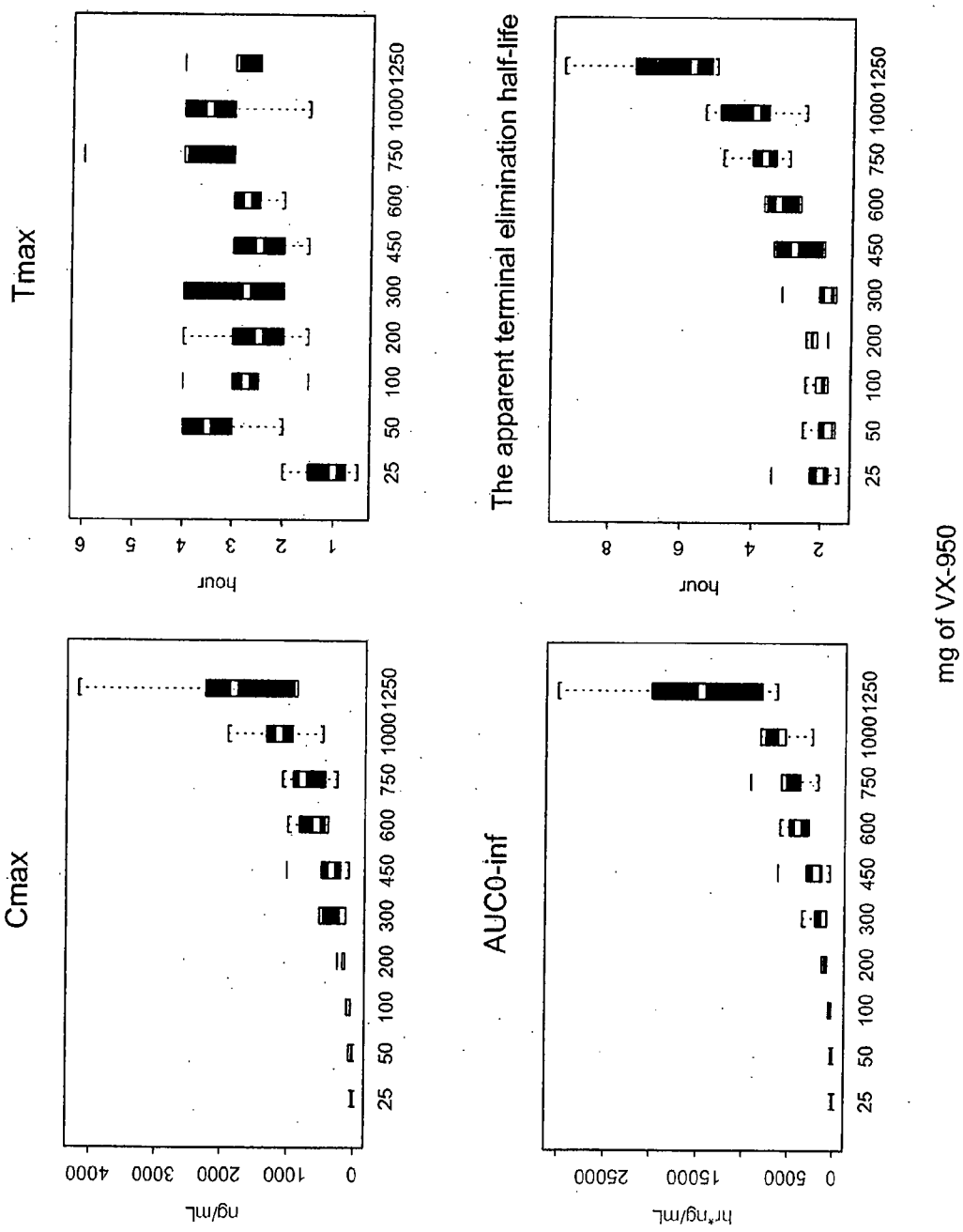


Fig. 3

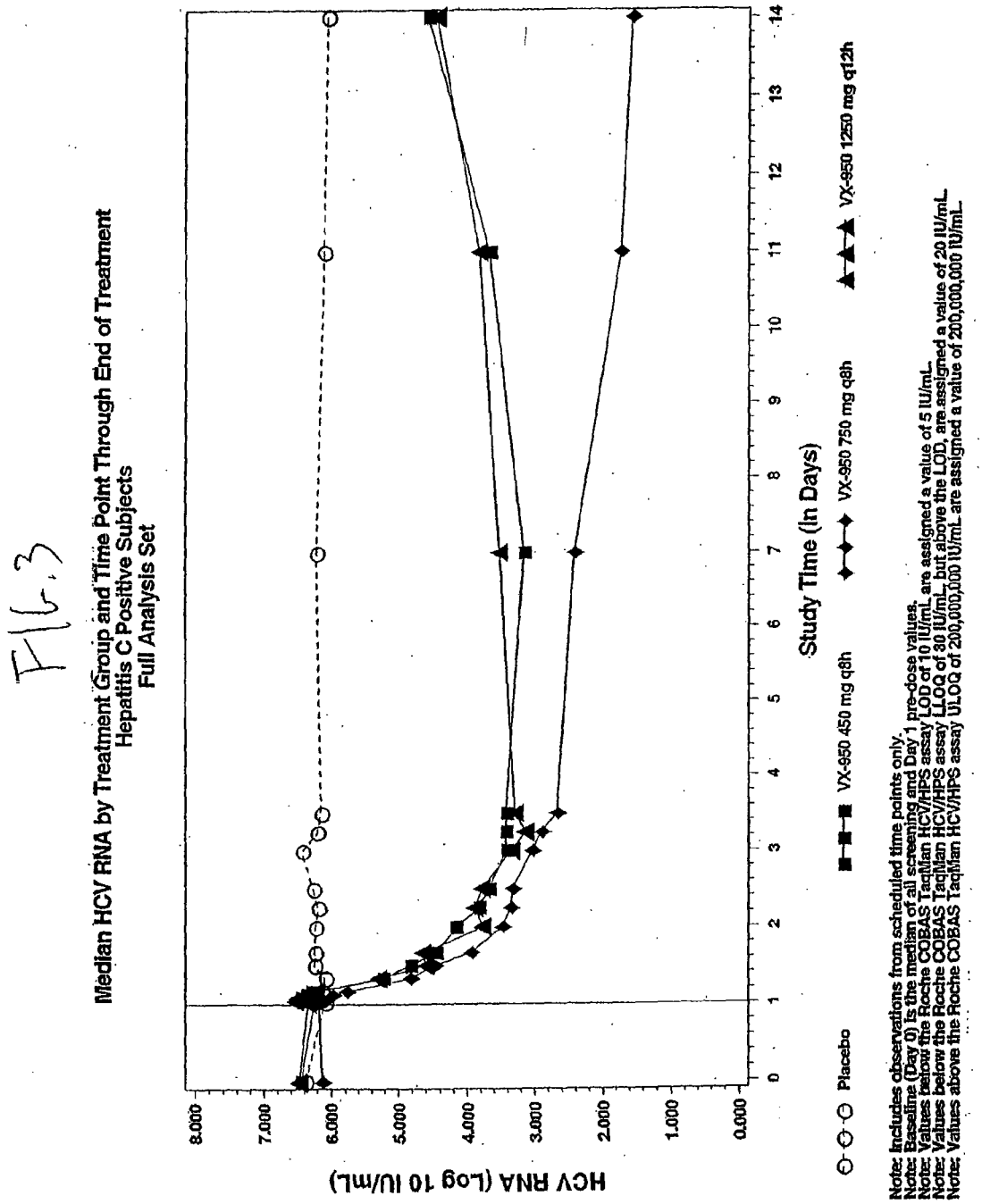

Median HCV RNA by Treatment Group and Time Point Through End of Treatment
Hepatitis C Positive Subjects
Full Analysis Set
HCV RNA (Log 10 IU/mL)
8.000
7.000
6.000
5.000
4.000
3.000
2.000
1.000
0.000
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
Study Time (In Days)
Placebo
VX-950 450 mg q8h
VX-950 750 mg q8h
VX-950 1250 mg q12h
Note: Includes observations from scheduled time points only.
Note: Baseline (Day 0) is the median of all screening and Day 1 pre-dose values.
Note: Values below the Roche COBAS TaqMan HCV/HPS assay LOD of 10 IU/mL are assigned a value of 5 IU/mL.
Note: Values below the Roche COBAS TaqMan HCV/HPS assay LLOQ of 30 IU/mL, but above the LOD, are assigned a value of 20 IU/mL.
Note: Values above the Roche COBAS TaqMan HCV/HPS assay ULOQ of 200,000,000 IU/mL are assigned a value of 200,000,000 IU/mL.

FIG 4

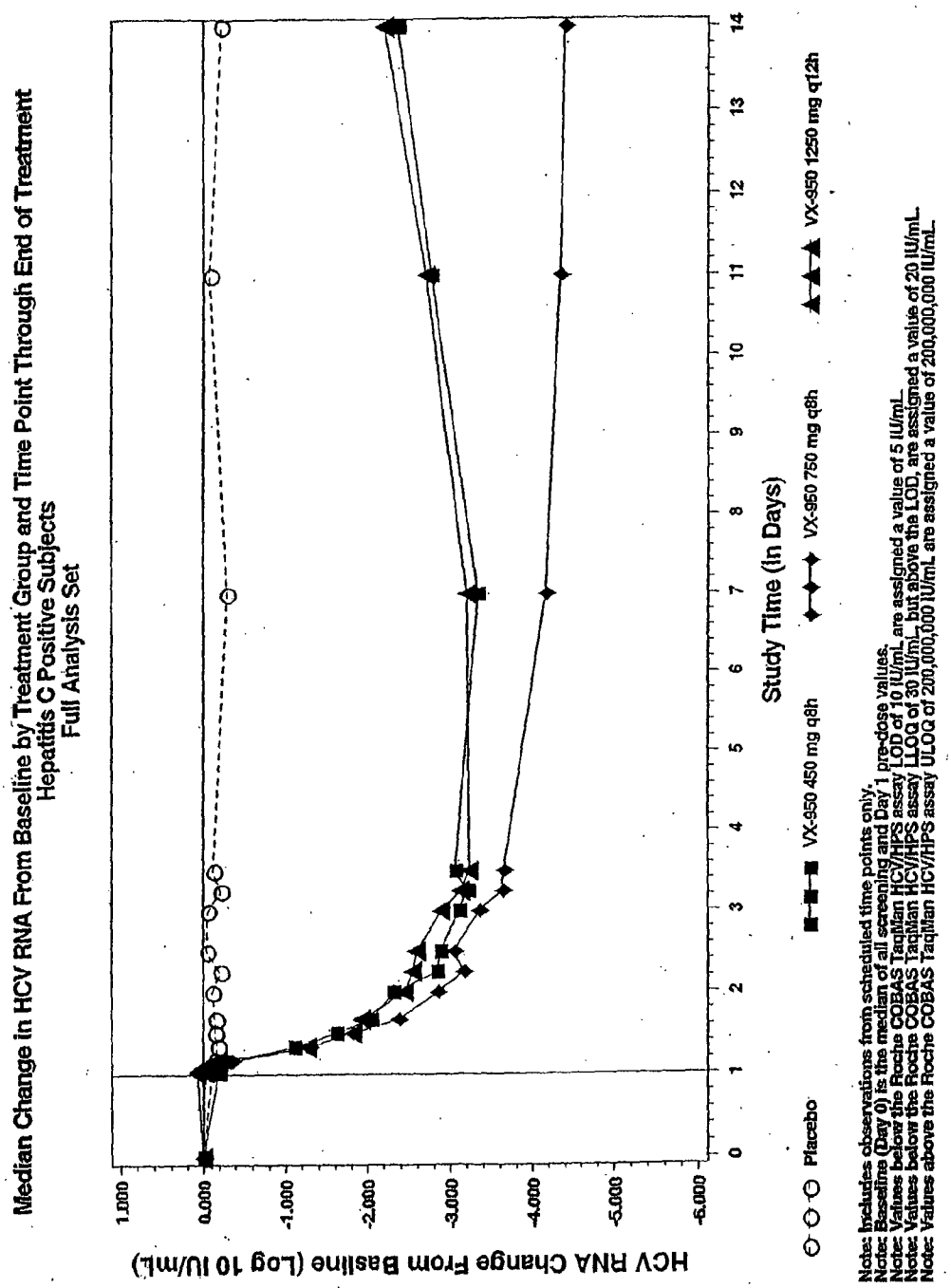

Median Change in HCV RNA From Baseline by Treatment Group and Time Point Through End of Treatment
Hepatitis C Positive Subjects
Full Analysis Set
HCV RNA Change From Baseline (Log 10 IU/mL)
1.000
0.000
-1.000
-2.000
-3.000
-4.000
-5.000
-6.000
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
Study Time (in Days)
Placebo
VX-950 450 mg q8h
VX-950 750 mg q8h
VX-950 1250 mg q12h
Note: Includes observations from scheduled time points only.
Note: Baseline (Day 0) is the median of all screening and Day 1 pre-dose values.
Note: Values below the Roche COBAS TaqMan HCV/HPS assay LOD of 10 IU/mL are assigned a value of 5 IU/mL.
Note: Values below the Roche COBAS TaqMan HCV/HPS assay LLOQ of 30 IU/mL, but above the LOD, are assigned a value of 20 IU/mL.
Note: Values above the Roche COBAS TaqMan HCV/HPS assay ULOQ of 200,000,000 IU/mL are assigned a value of 200,000,000 IU/mL.

FIG. 5

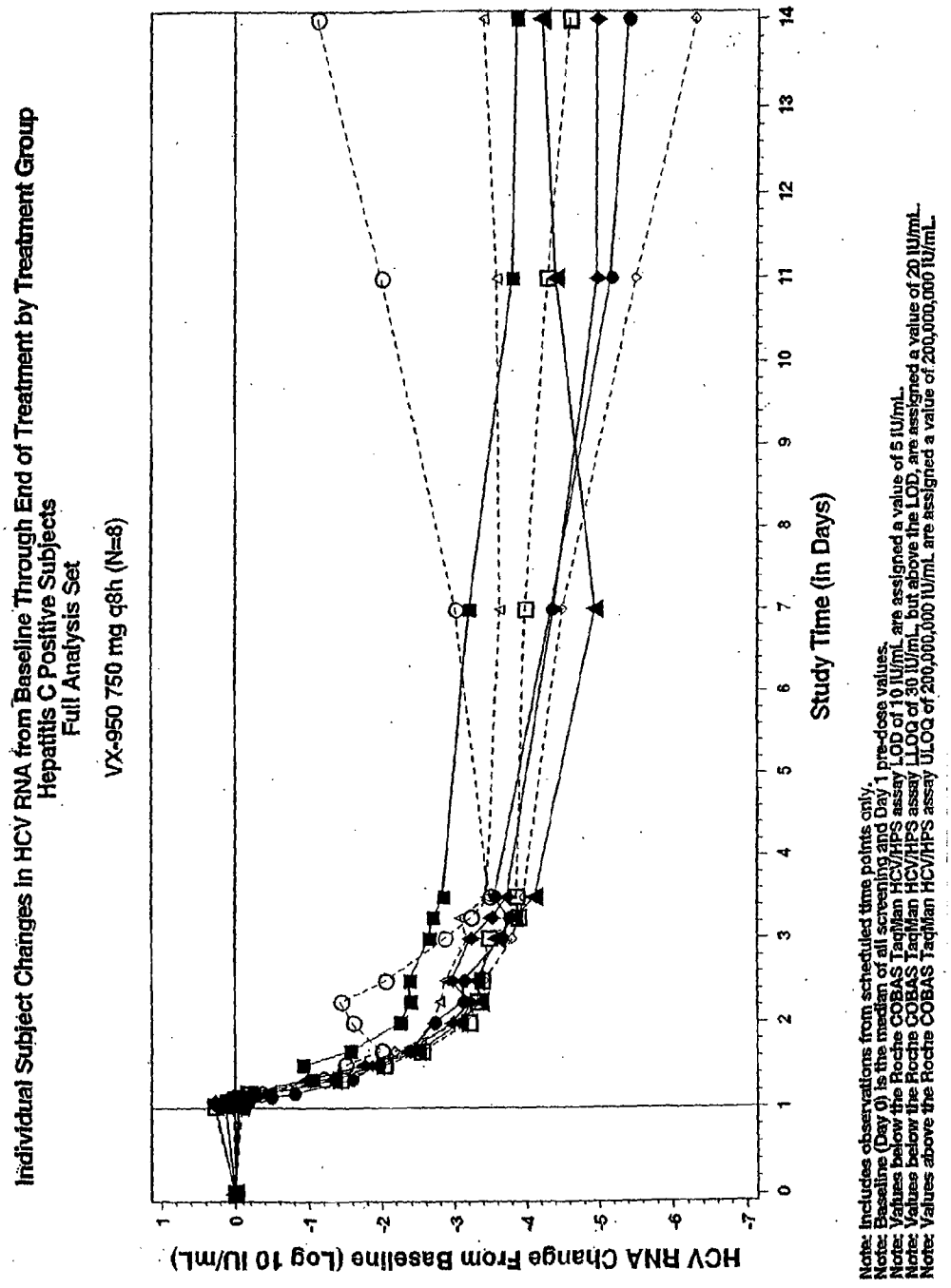

Individual Subject Changes in HCV RNA from Baseline Through End of Treatment by Treatment Group
Hepatitis C Positive Subjects
Full Analysis Set
VX-950 750 mg q8h (N=8)
HCV RNA Change From Baseline (Log 10 IU/mL)
Study Time (in Days)
1
0
-1
-2
-3
-4
-5
-6
-7
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
Note: Includes observations from scheduled time points only.
Note: Baseline (Day 0) is the median of all screening and Day 1 pre-dose values.
Note: Values below the Roche COBAS TaqMan HCV/HPS assay LOD of 10 IU/mL are assigned a value of 5 IU/mL.
Note: Values below the Roche COBAS TaqMan HCV/HPS assay LLOQ of 30 IU/mL, but above the LOD, are assigned a value of 20 IU/mL.
Note: Values above the Roche COBAS TaqMan HCV/HPS assay ULOQ of 200,000,000 IU/mL are assigned a value of 200,000,000 IU/mL.

Figure 6

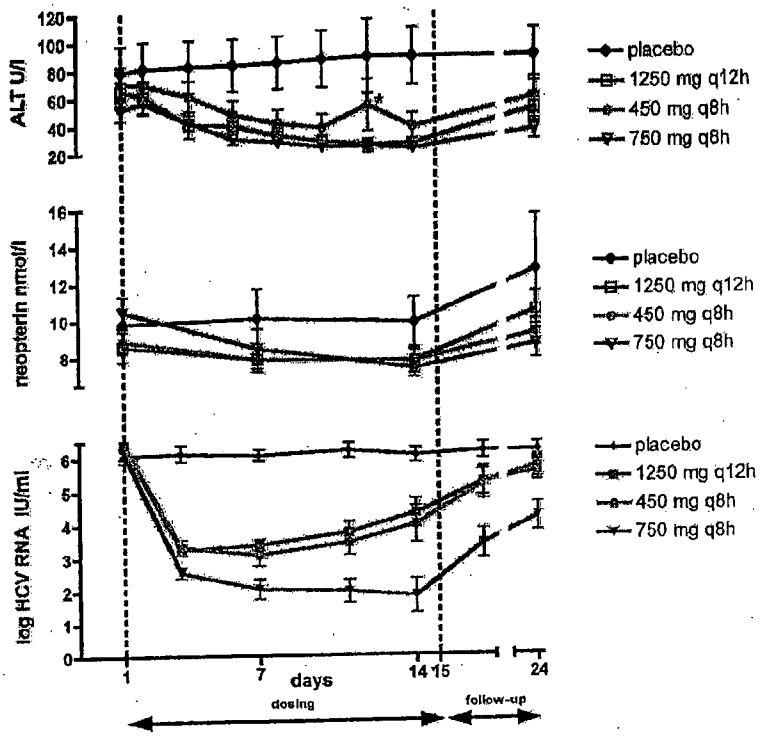


Figure 7

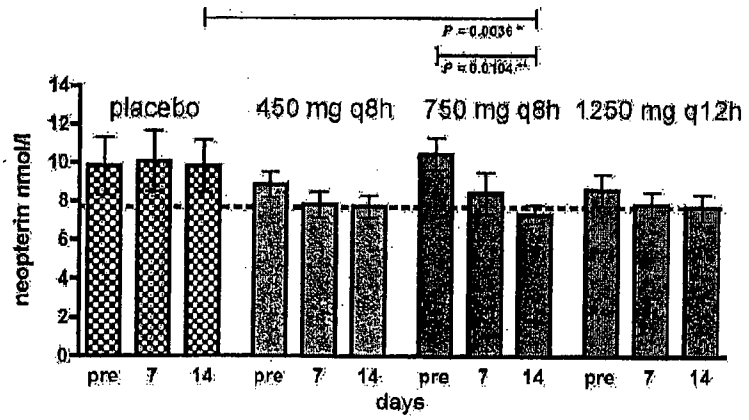


Figure 8

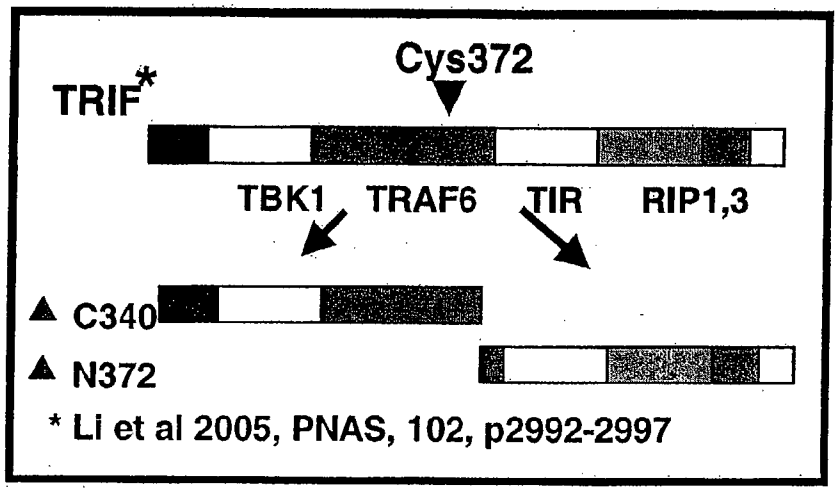


Figure 9

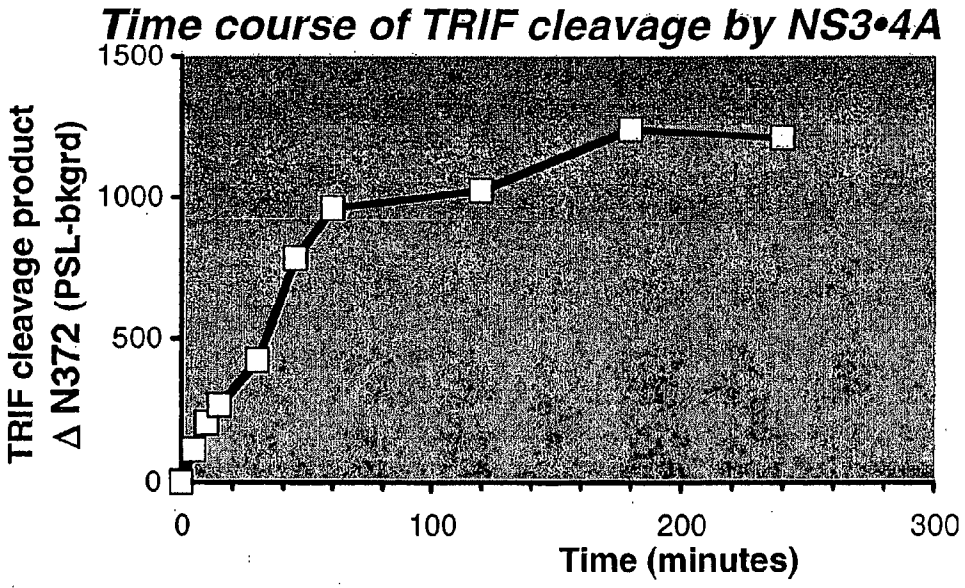


Figure 10

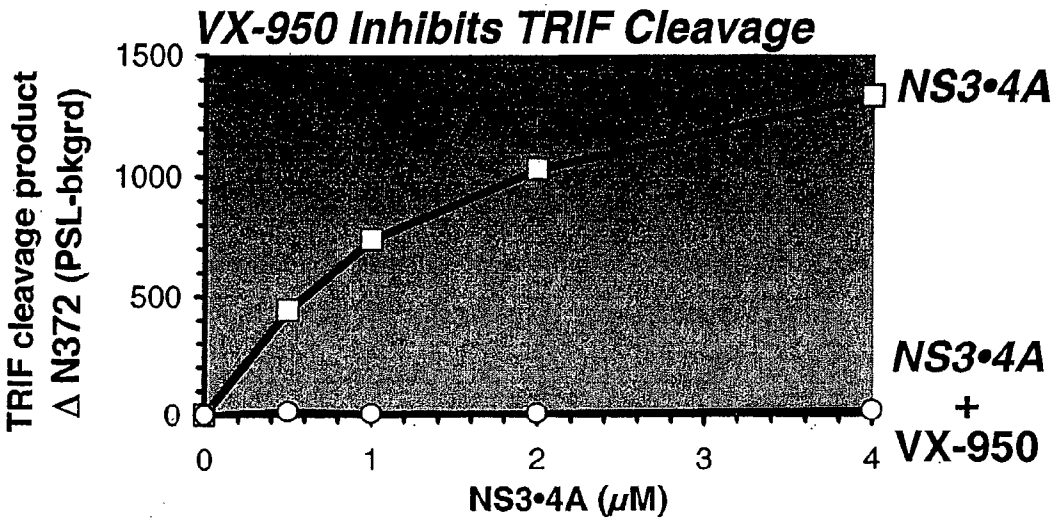


Figure 11

Fold increase over WT	VX-950		Protease Kcat/km
	K_i	IC_{50}	
A156V	330	>75	0.25
A156T	99	>75	0.1

Figure 12

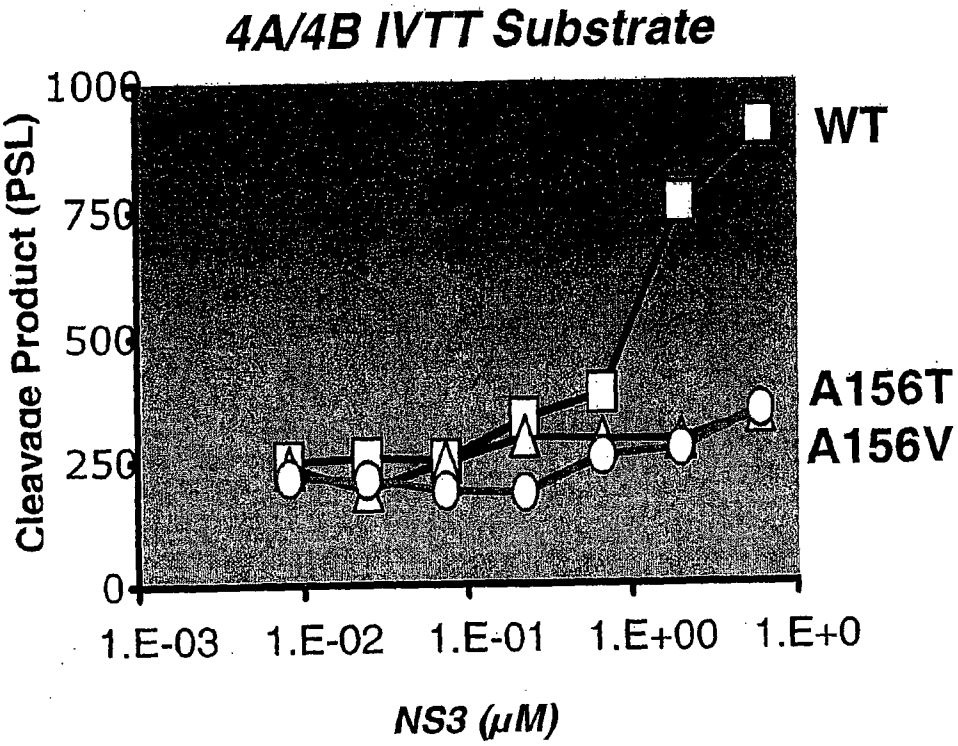


Figure 13

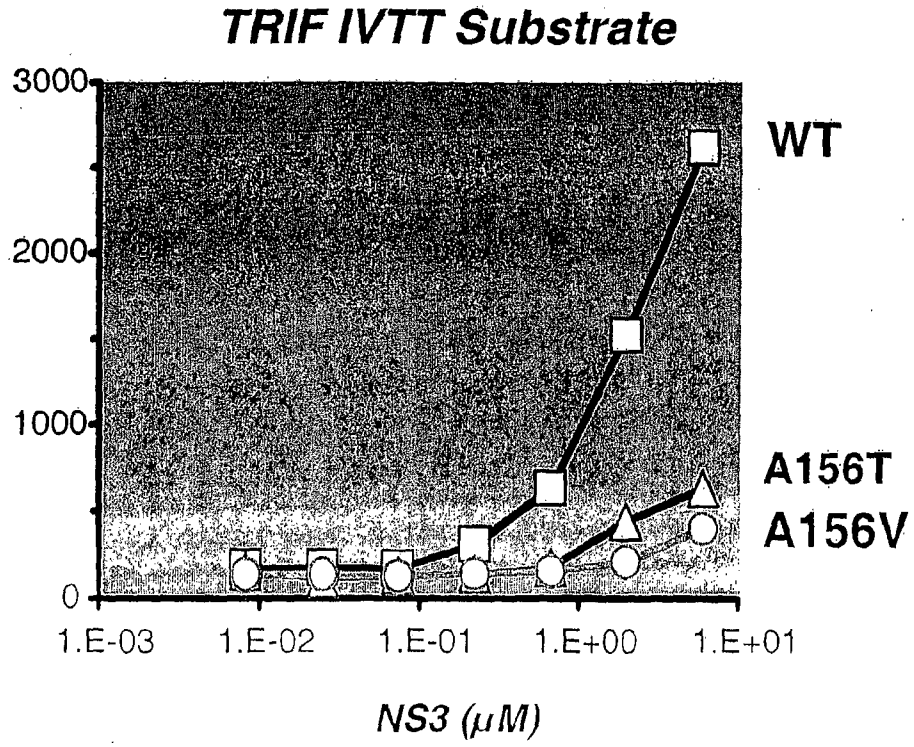


Figure 14

	VX-950 450 mg q8h (1350 mg daily) n = 10	VX-950 750 mg q8h (2250 mg daily) n = 8	VX-950 1250 mg q12h (2500 mg daily) n = 10
Mean baseline log HCV RNA	6.42	6.14	6.41
Mean log HCV RNA – IU/ml at day 7 (decline from baseline)	3.08 (-3.33)	2.04 (-4.10)	3.38 (-3.03)
Mean log HCV RNA – IU/ml at day 14 (decline from baseline)	3.98 (-2.43)	1.81 (-4.33)	4.32 (-2.09)
Mean baseline neopterin	8.88	10.48	8.59
Mean neopterin – nmol/l at day 7 (decline from baseline)	7.84 (-1.05)	8.43 (-2.04)	7.85 (-0.74)
Mean neopterin – nmol/l at day 14 (decline from baseline)	7.74 (-1.14)	7.32* (-3.16)	7.72 (-0.88)
Mean baseline ALT U/l	71	52	66
Mean ALT U/l at day 8 (decline from baseline)	41 (-30)	28 (-24)	33 (-33)
Mean ALT U/l at day 14 (decline from baseline)	38 (-33)	23 (-29)	26 (-41)

* Decrease in the 750 mg q8h dose group is significant vs baseline value in the same group (Mann Whitney test, $P = 0.0104$) and vs the placebo group at day 14 (unpaired two-tailed T test, $P = 0.0036$)

FIG. 15

Huh7 cells with IFNβ-Luc and NS3•4A

IFNβ induction after Sendai virus stimulation

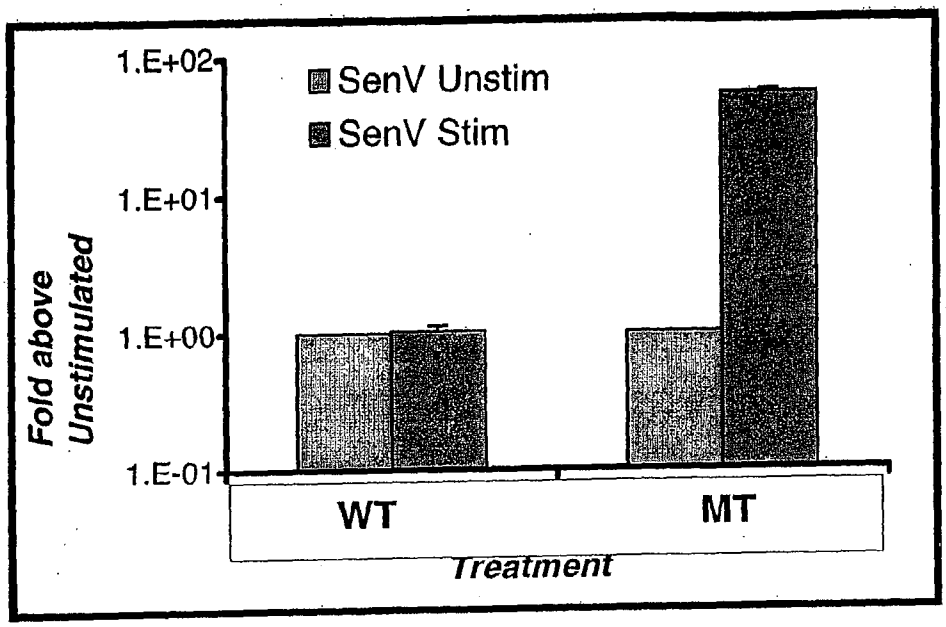


FIG. 16

Addition of VX-950

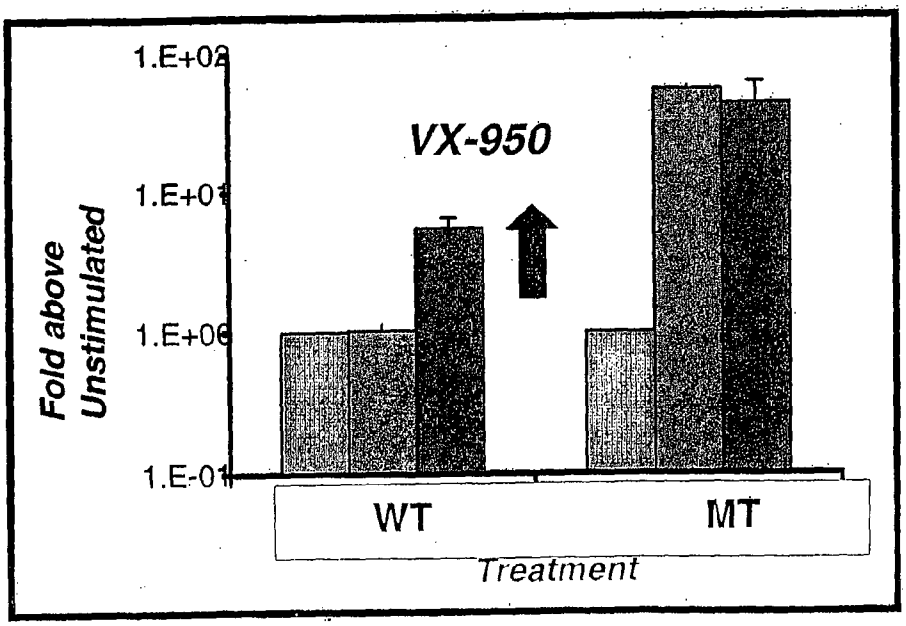


FIG. 17A

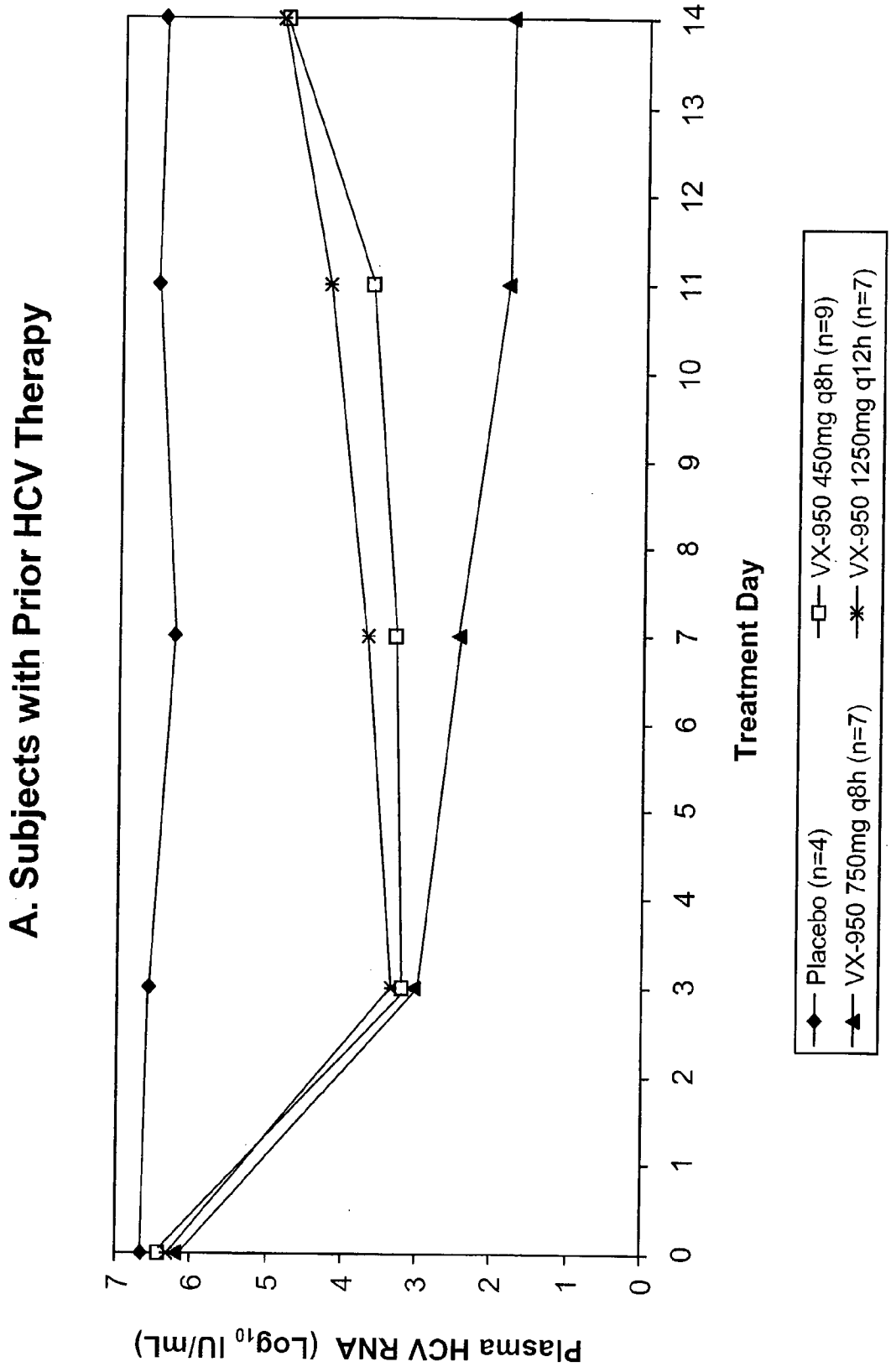
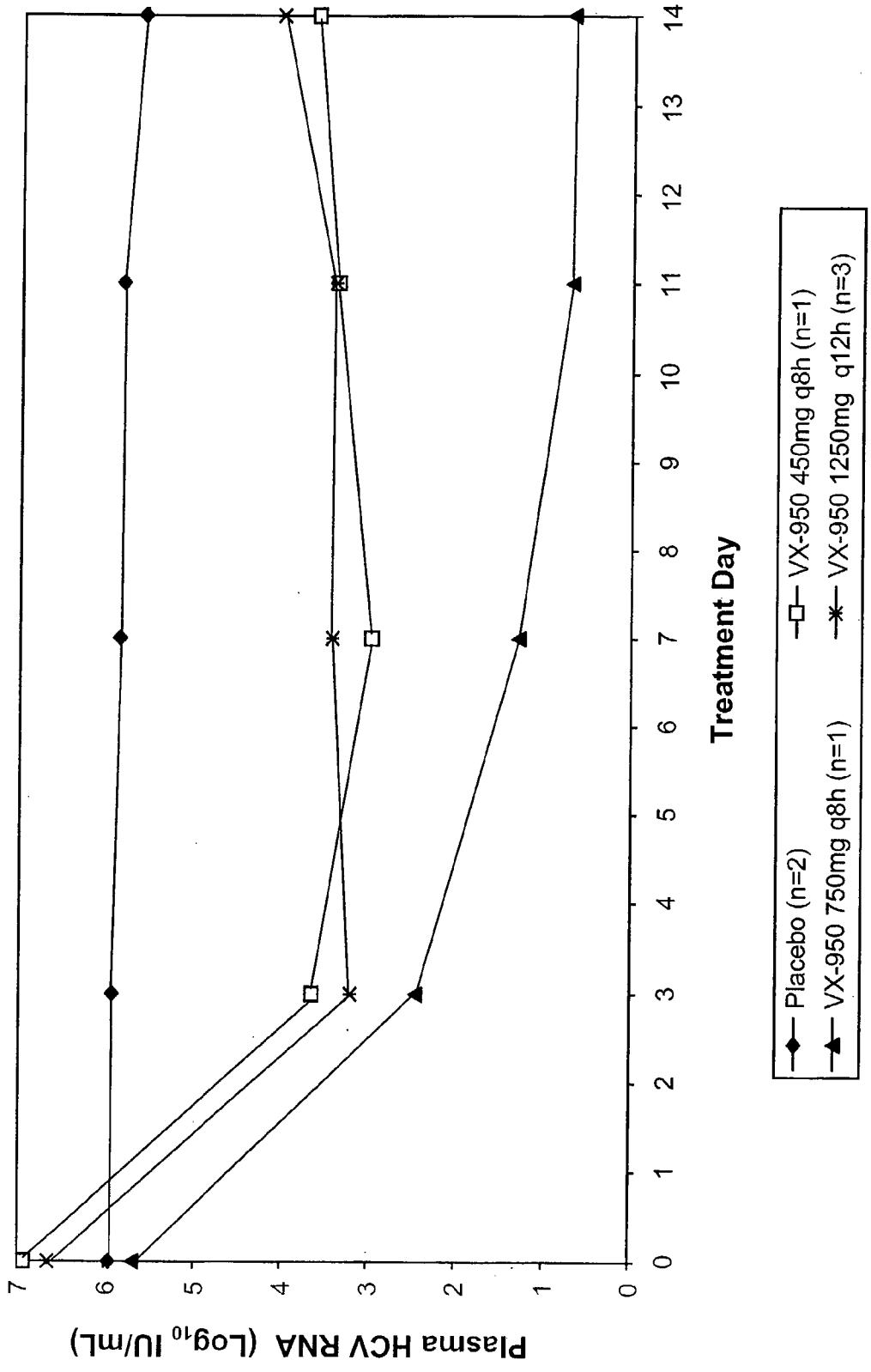

A. Subjects with Prior HCV Therapy
Plasma HCV RNA (Log10 IU/mL)
Treatment Day
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
Placebo (n=4)
VX-950 450mg q8h (n=9)
VX-950 750mg q8h (n=7)
VX-950 1250mg q12h (n=7)

FIG. 17B


B. Subjects without Prior HCV Therapy
Plasma HCV RNA (Log10 IU/mL)
Treatment Day
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
Placebo (n=2)
VX-950 450mg q8h (n=1)
VX-950 750mg q8h (n=1)
VX-950 1250mg q12h (n=3)