

1/46

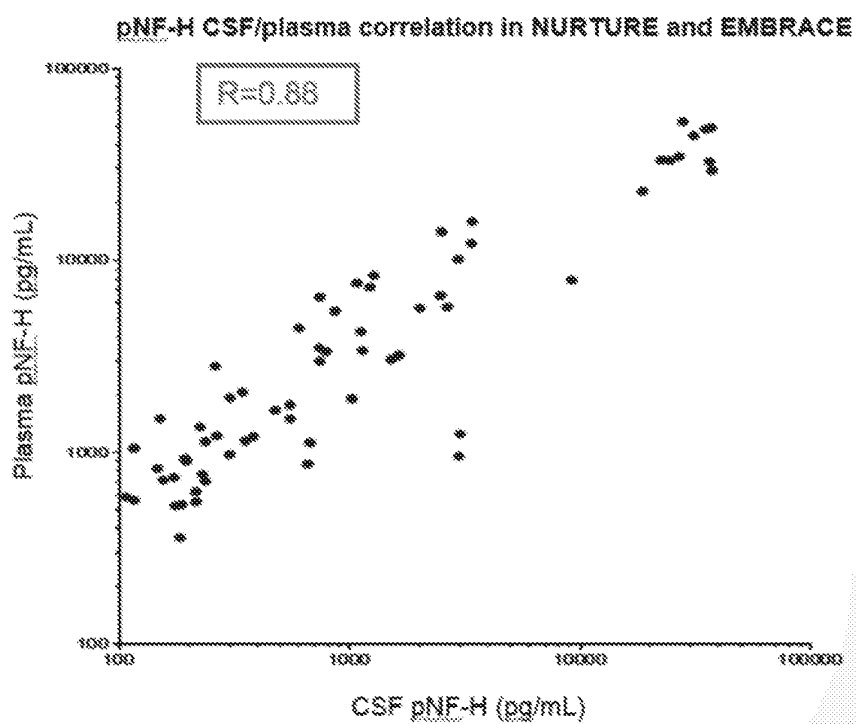


FIG. 1

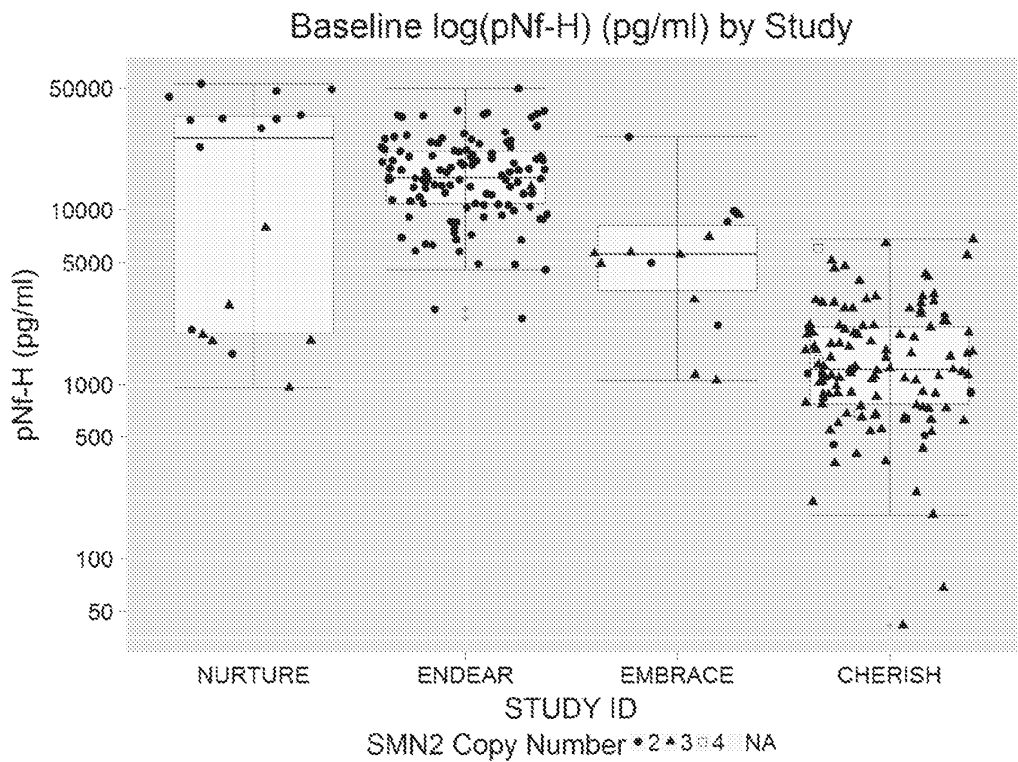


FIG. 2

3/46

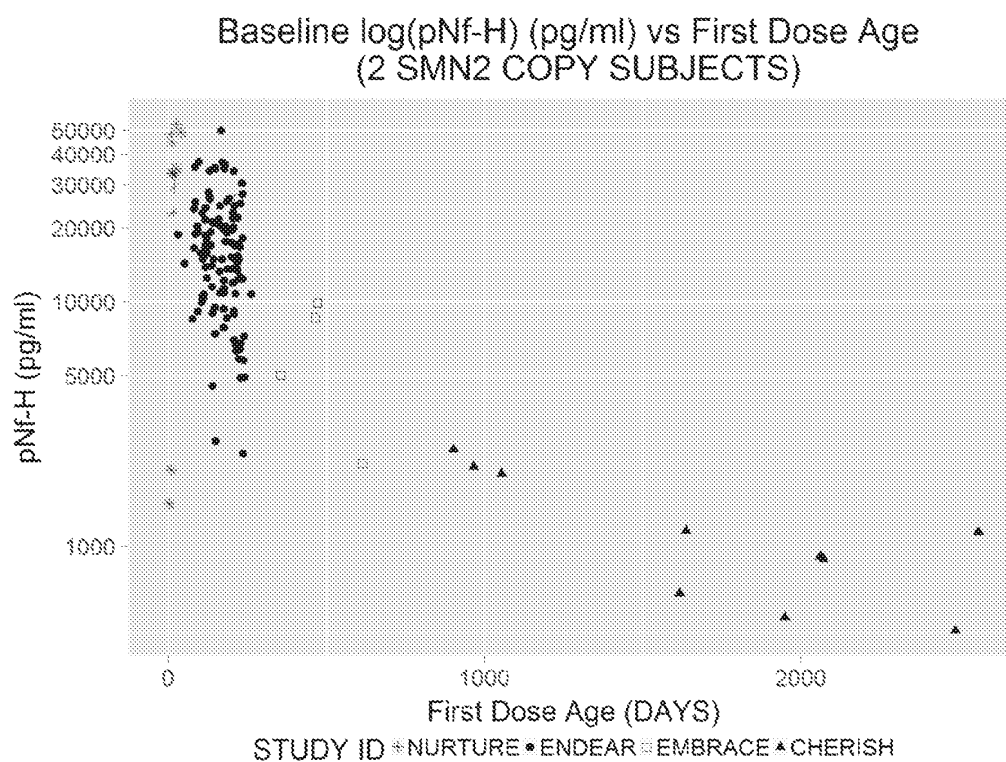


FIG. 3

4/46

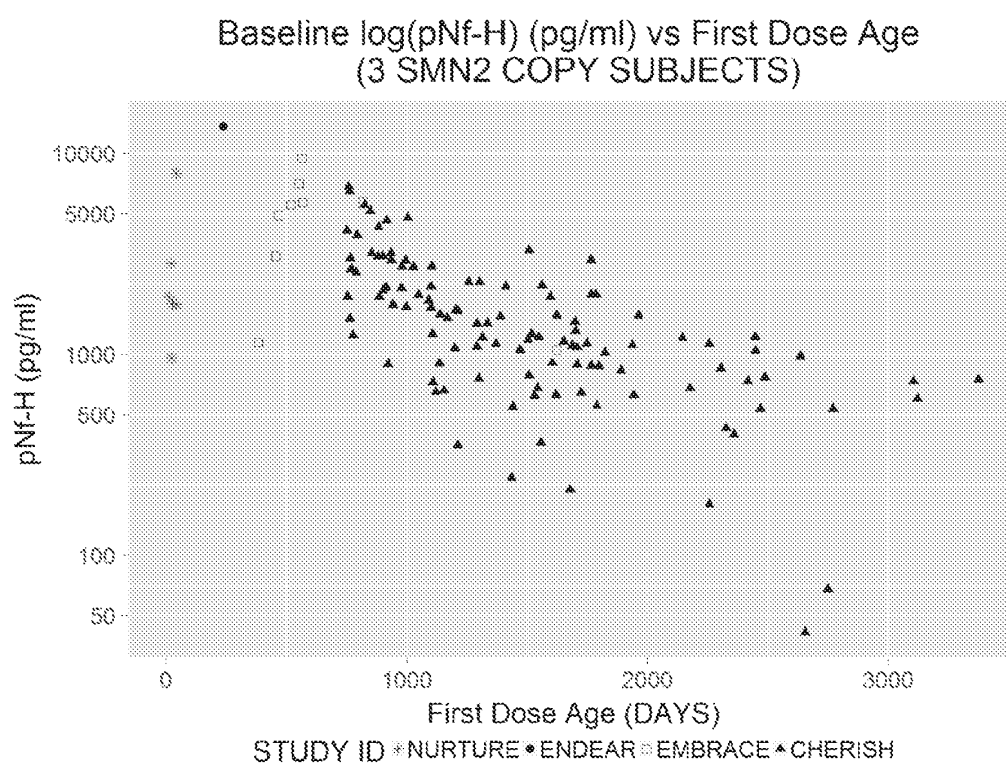


FIG. 4

5/46

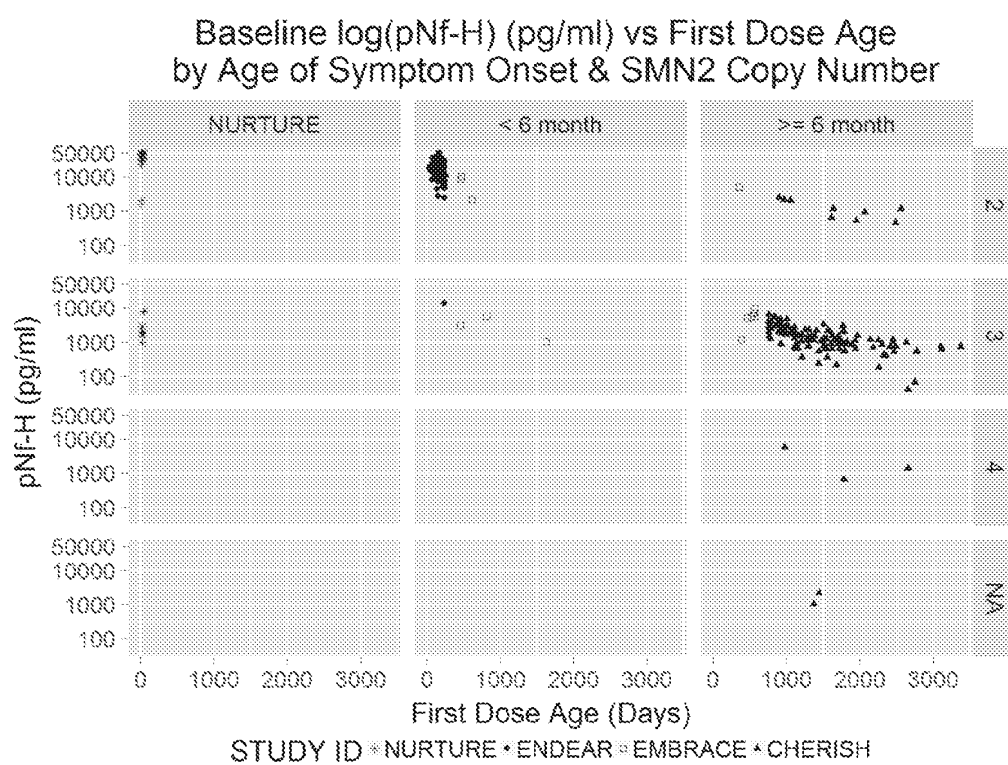


FIG. 5

6/46

Summary of baseline characteristics and HRH history by baseline pHH-R concentrations (pg/ml) quartiles				
Page 1 of 3				
Quartiles of Baseline pHH-R				
	1st Quartile (2890 - 10800)	2nd Quartile (10800 - 18450)	3rd Quartile (18450 - 21800)	4th Quartile (21800 - 55100)
Number of subjects	28	28	29	30
Female sex n (%)	18 (64%)	13 (46%)	16 (55%)	17 (57%)
Age at first dose (Days) mean (min,max)	181.4 (77, 382)	177.8 (52, 337)	184.2 (30, 235)	181.9 (81, 330)
Age of symptom onset at baseline (weeks) mean (min,max)	6.8 (4, 20)	8.1 (5, 18)	6.8 (5, 12)	7.8 (2, 19)
Age at OGA diagnosis (weeks) mean (min,max)	16.73 (6, 28)	18.19 (8, 26)	17.34 (8, 25)	18.00 (2, 30)
Disease duration at screening (weeks) mean (min,max)	11.4 (5, 21.1)	14.1 (5.6, 25.8)	13.1 (8, 22)	13.5 (8, 23.1)
Notes: (a) Number of subjects in the table refers to subjects who have non-missing baseline value in each quartile				
(b) SD=Standard Deviation				
SOURCE: 13T5186443/BIOGRAPHY/CSSB-R080C/T-SUN-BASCHER-000-PATQUINX.SAS				
DATE: 08NOV2017				

FIG. 6

7/46

Summary of baseline Characteristics and SMA History by baseline
pNF-H concentrations (pg/ml) quartiles
Page 2 of 3

	Quartiles of Baseline pNf-H			
	1st Quartile (2390 - 10900)	2nd Quartile (10900 - 15400)	3rd Quartile (15400 - 21600)	4th Quartile (21600 - 50100)
Symptoms of SMA				
Hyptonia	29 (100%)	29 (100%)	29 (100%)	30 (100%)
Dev Delay of Motor Funtion	28 (97%)	28 (97%)	24 (83%)	26 (87%)
Paradoxical Breathing	23 (79%)	23 (79%)	24 (83%)	25 (83%)
Pneumonia/Resp. Symptoms	8 (28%)	10 (34%)	12 (41%)	6 (20%)
Limb weakness	29 (100%)	29 (100%)	29 (100%)	29 (97%)
Swallowing Abnormalities	15 (52%)	11 (38%)	14 (48%)	12 (40%)
Other	8 (28%)	4 (14%)	9 (31%)	13 (43%)
Use of ventilator support n (%)	7 (24%)	7 (24%)	8 (28%)	5 (17%)

Note: (a) Number of subjects in the table refers to subjects who have non-missing baseline value in each quartile (b) SD=Standard Deviation

SOURCE: ISIS396443/BIOMARKER/CS3B-ADHOC/T-SUM-BASCHAR-SMA-PNFHQART.SAS

DATE: 09NOV2017

FIG. 7**SUBSTITUTE SHEET (RULE 26)**

8/46

Summary of baseline Characteristics and SMA History by baseline
pNF-H concentrations (pg/ml) quartiles
Page 3 of 3

	Quartiles of Baseline pNf-H			
	1st Quartile (2390 - 10900)	2nd Quartile (10900 - 15400)	3rd Quartile (15400 - 21600)	4th Quartile (21600 - 50100)
Total HINE-2 score mean +/- SD (b)	1.7 +/- 1.41	1.4 +/- 1.18	1.0 +/- 0.85	1.4 +/- 1.00
CHOP INTEND score mean +/- SD	30.90 +/- 6.607	28.09 +/- 7.456	24.36 +/- 7.295	25.83 +/- 8.412
Peroneal mean +/- SD	0.39 +/- 0.311	0.41 +/- 0.348	0.27 +/- 0.199	0.29 +/- 0.283
Ulnar mean +/- SD	0.24 +/- 0.150	0.19 +/- 0.171	0.29 +/- 0.202	0.17 +/- 0.089

Note: (a) Number of subjects in the table refers to subjects who have non-missing baseline value in each quartile (b) SD=Standard Deviation

SOURCE: ISIS396443/BIOMARKER/CS3B-ADHOC/T-SUM-BASCHAR-SMA-PNFHQUART.SAS

DATE: 09NOV2017

FIG. 8

9/46

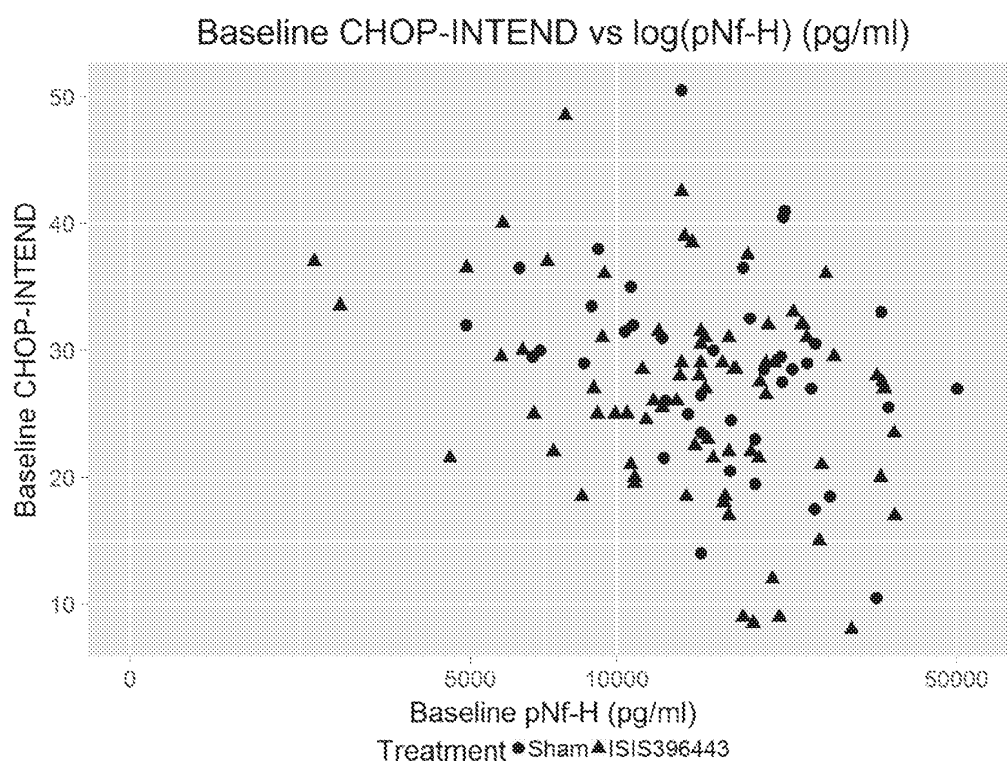


FIG. 9

10/46

Variables in the initial model:

- Baseline log(pNF-H)
- Treatment group
- Disease duration (weeks)
- Sex
- Age of first dose (days)
- Age of SMA symptom onset (weeks)
- Age of SMA diagnosis (weeks)
- Gestational age (weeks)
- Baseline weight (kg)
- (Gestational age + age of first dose [weeks]) x (Gestational age + age of SMA symptom onset [weeks])
- Gestational age + age of SMA diagnosis (weeks)

Variables in the Final Model	P-value
Intercept	<0.0001
Baseline log(pNF-H)	0.0062
Age of SMA diagnosis (weeks)	0.0016
Baseline weight (kg)	0.0075

FIG. 10

11/46

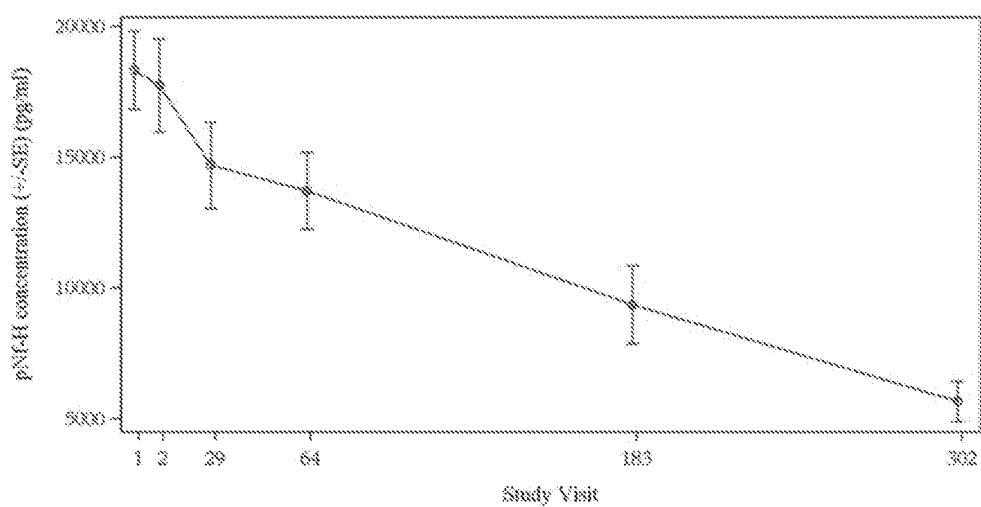


FIG. 11

12/46

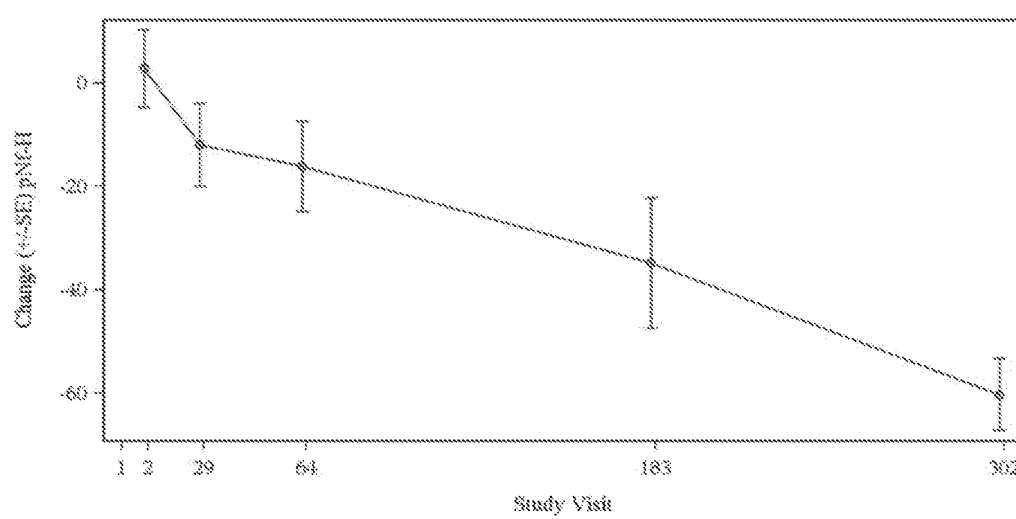


FIG. 12

13/46

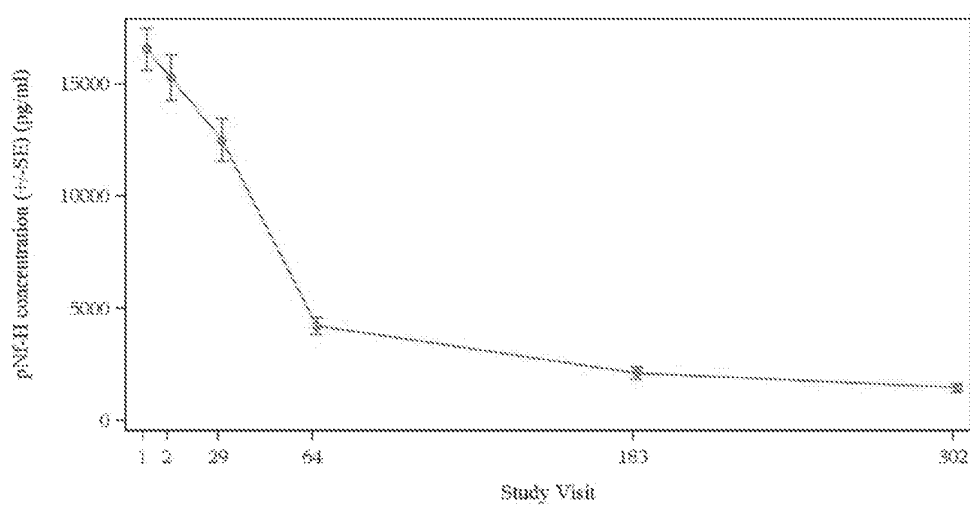


FIG. 13

14/46

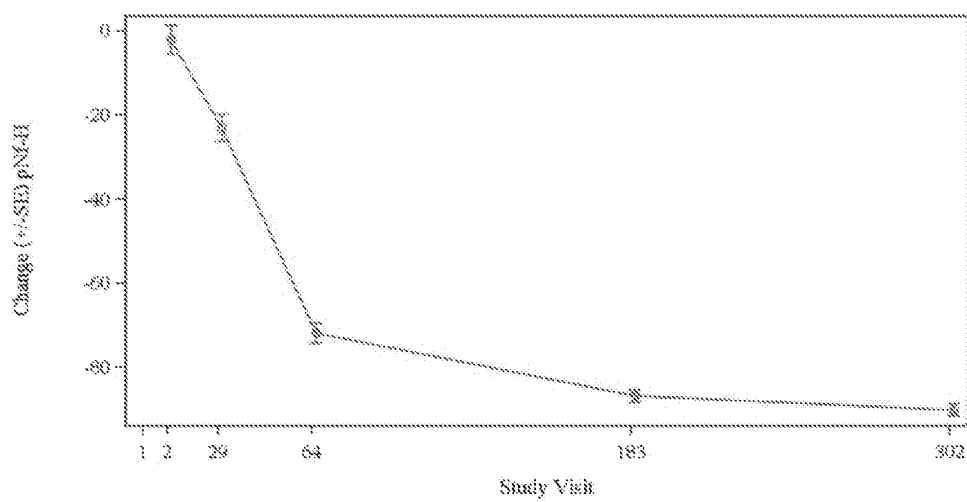


FIG. 14

15/46

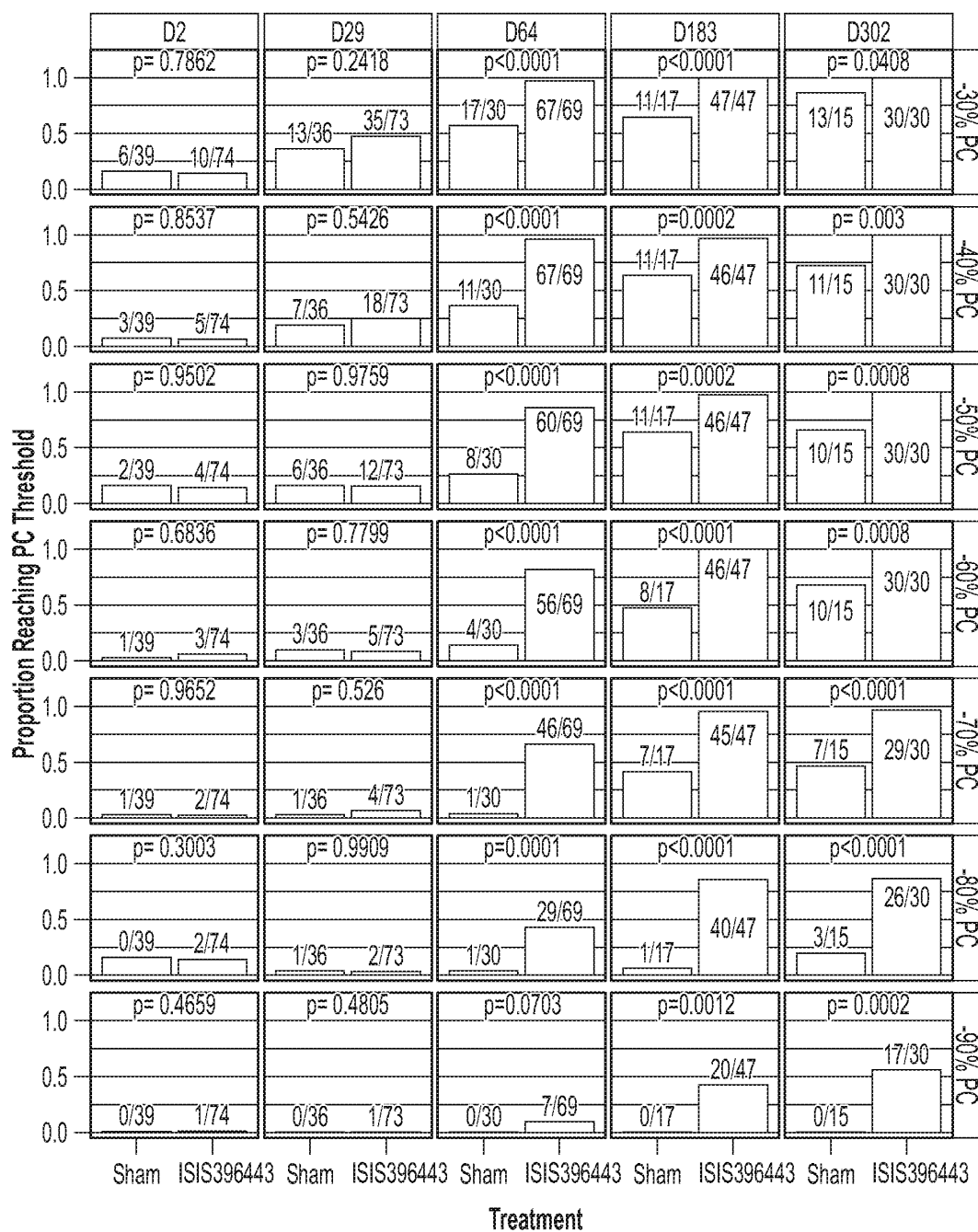


FIG. 15

16/46

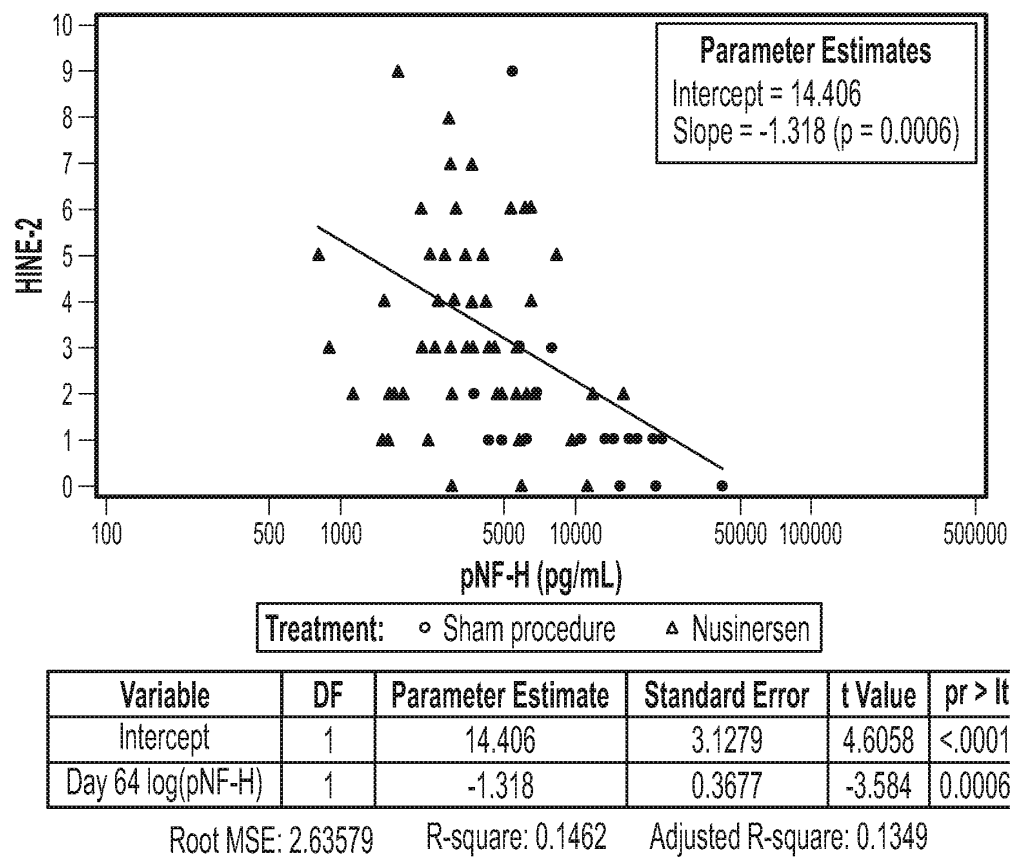


FIG. 16

17/46

Variables in the initial model:

- Day 64 log(pNF-H)
- Treatment group
- Disease duration (weeks)
- Sex
- Age of first dose (days)
- Age of SMA symptom onset (weeks)
- Age of SMA diagnosis (weeks)
- Gestational age (weeks)
- Baseline weight (kg)
- (Gestational age + age of first dose [weeks]) x (Gestational age + age of SMA symptom onset [weeks])
- Gestational age + age of SMA diagnosis (weeks)

Variables in the Final Model	P-value
Intercept	<0.0001
Day 64 log(pNF-H)	<0.0001
Disease duration	0.0029

FIG. 17

18/46

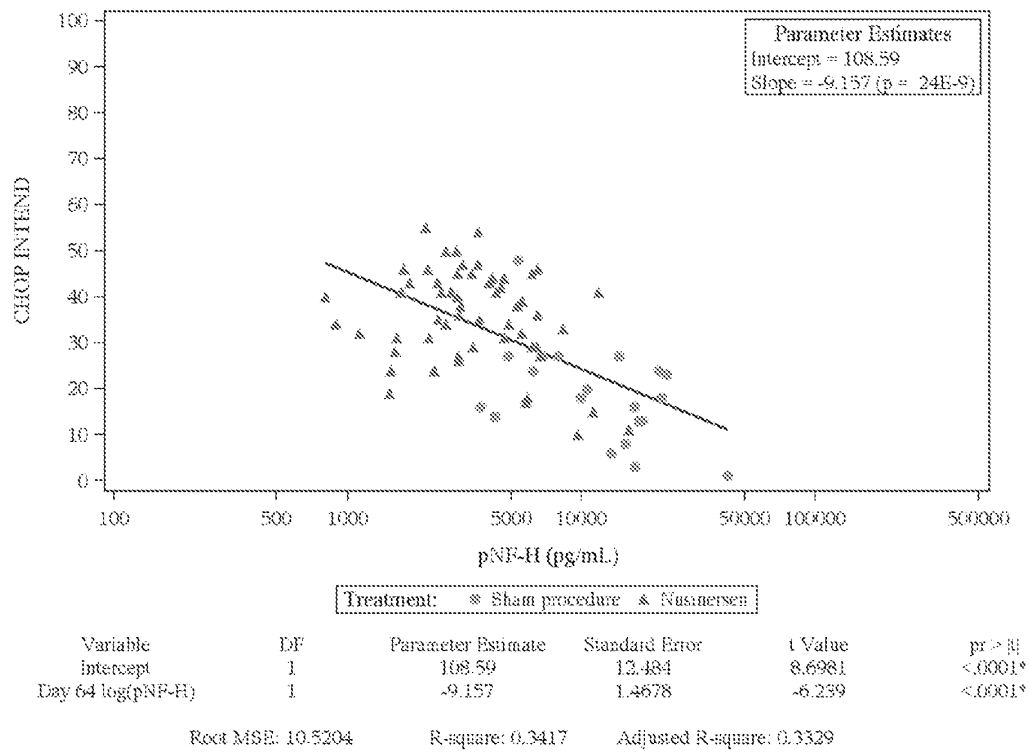


FIG. 18

19/46

Variables in the initial model:

- Day 64 log(pNF-H)
- Treatment group
- Disease duration (weeks)
- Sex
- Age of first dose (days)
- Age of SMA symptom onset (weeks)
- Age of SMA diagnosis (weeks)
- Gestational age (weeks)
- Baseline weight (kg)
- (Gestational age + age of first dose [weeks]) x (Gestational age + age of SMA symptom onset [weeks])
- Gestational age + age of SMA diagnosis (weeks)

Variables in the Final Model	P-value
Intercept	<0.0001
Day 64 log(pNF-H)	0.0001
Treatment group: nusinersen	0.0050
Disease duration	0.0003

FIG. 19

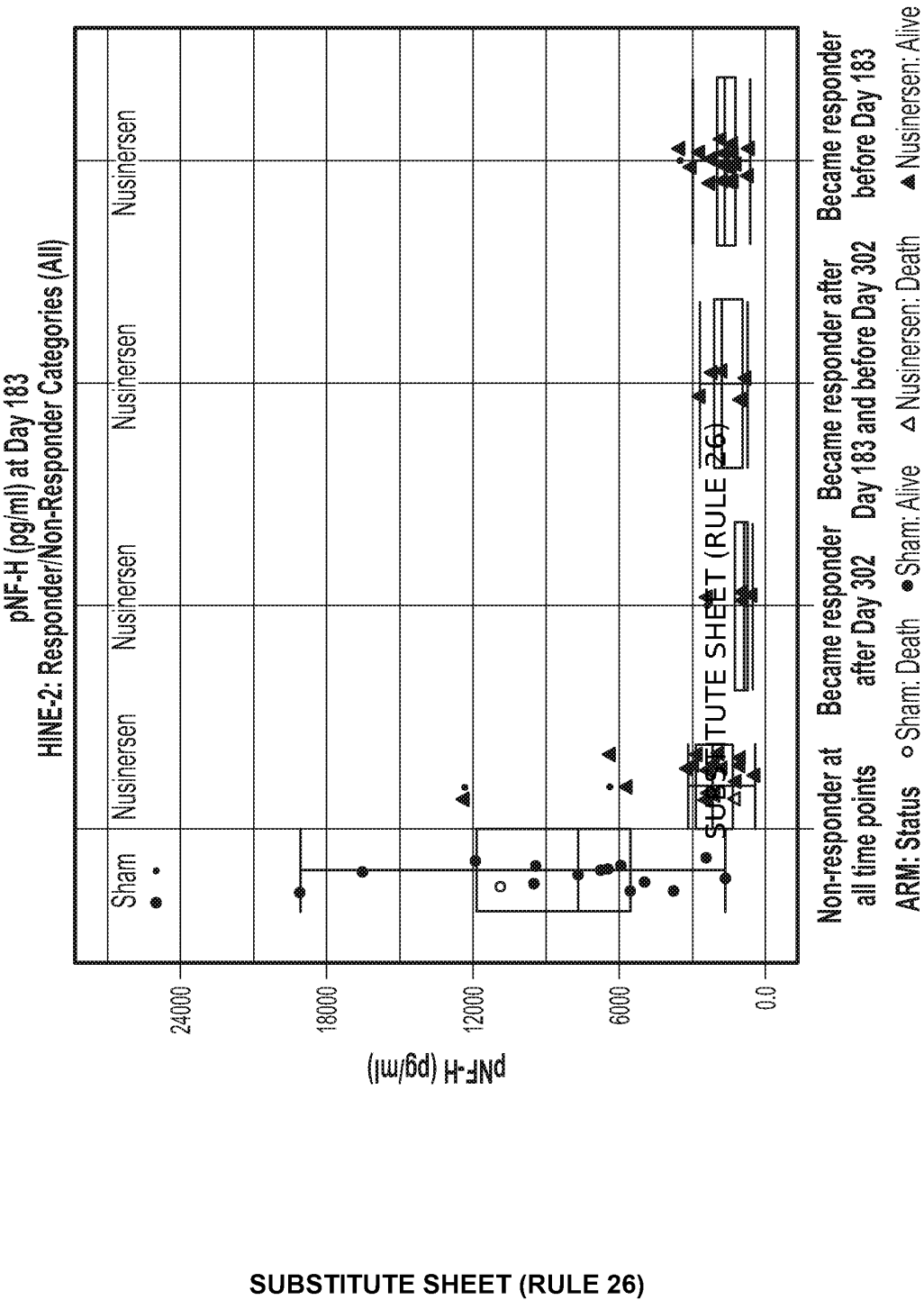


FIG. 20

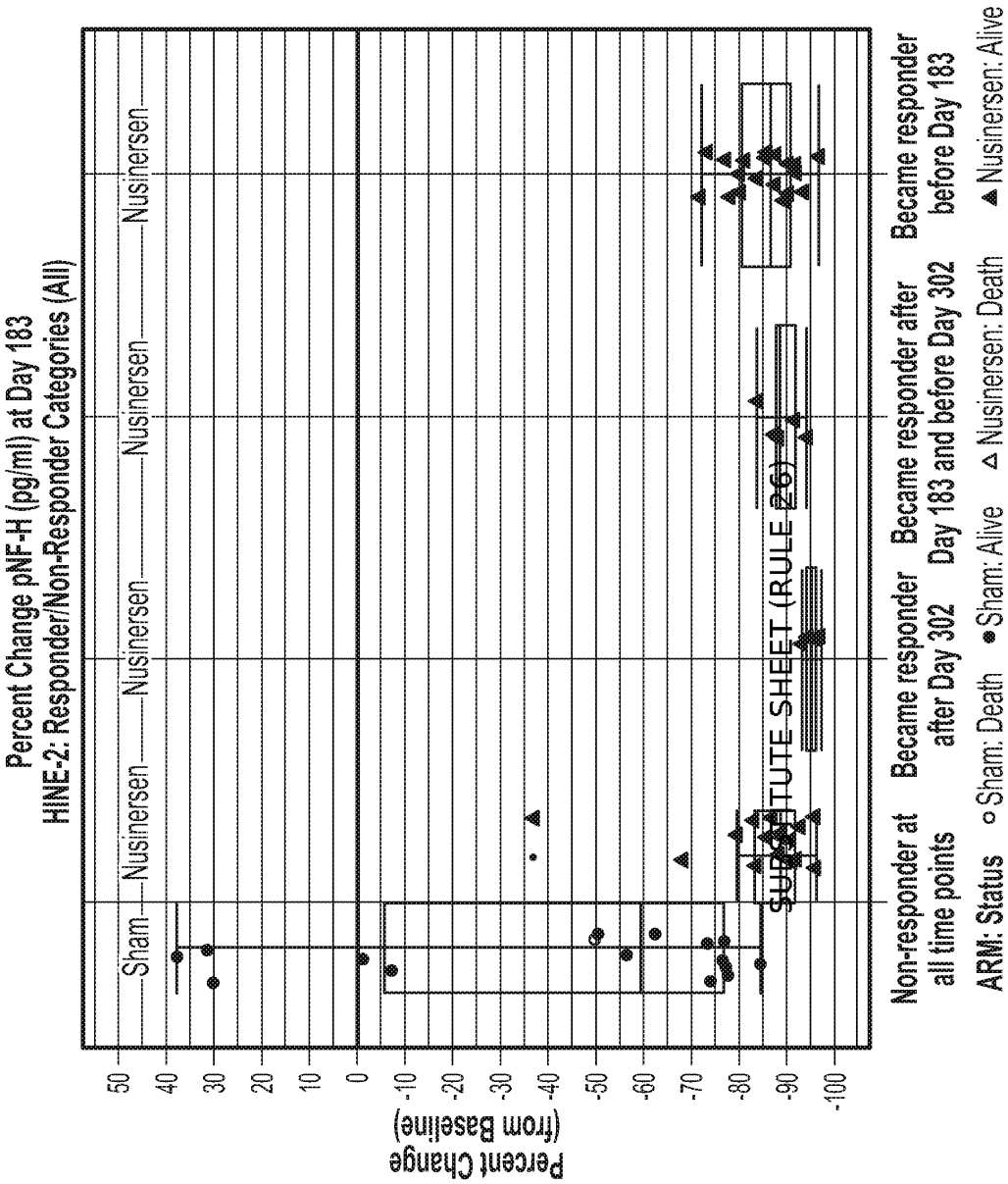


FIG. 21

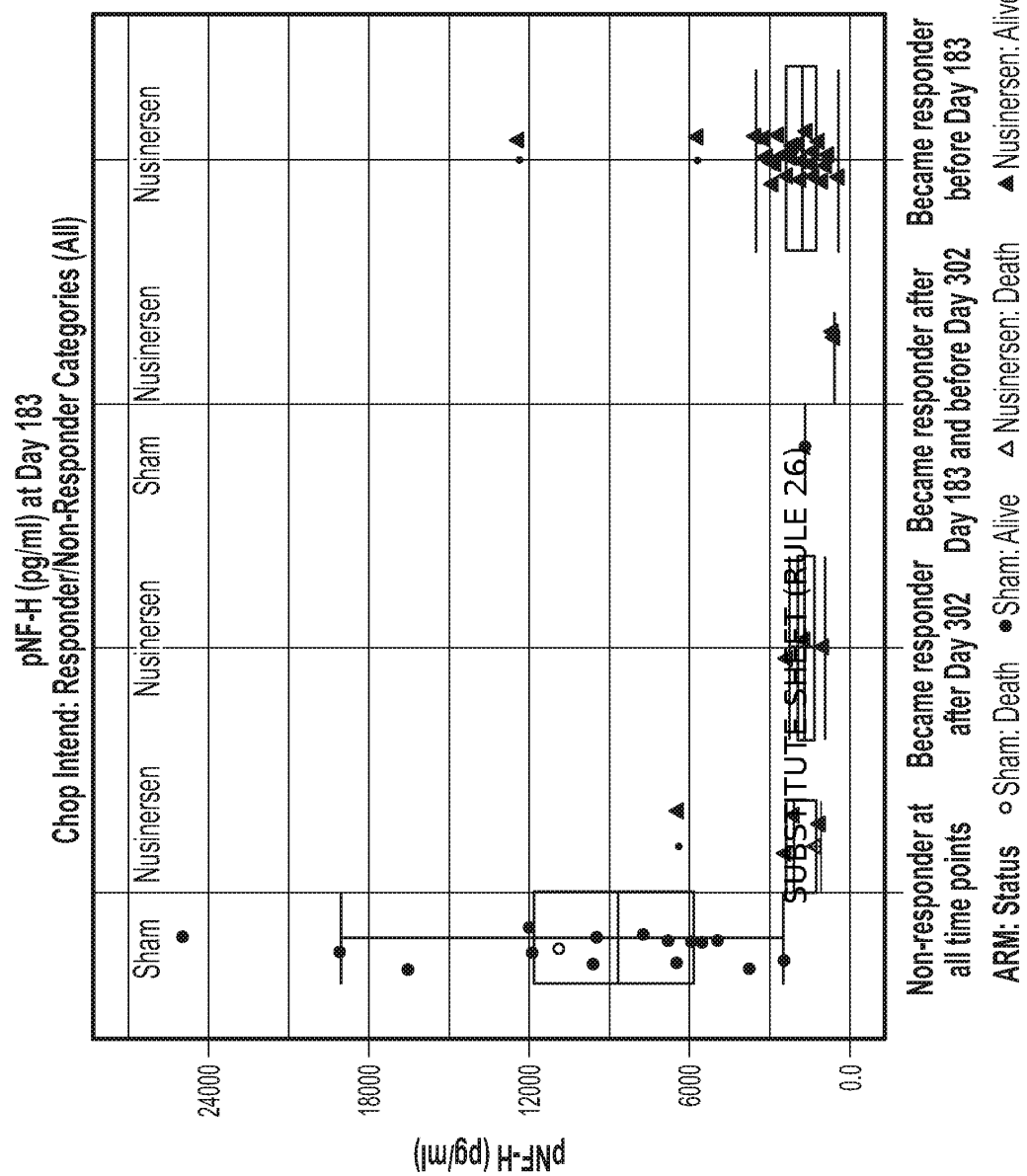


FIG. 22

SUBSTITUTE SHEET (RULE 26)

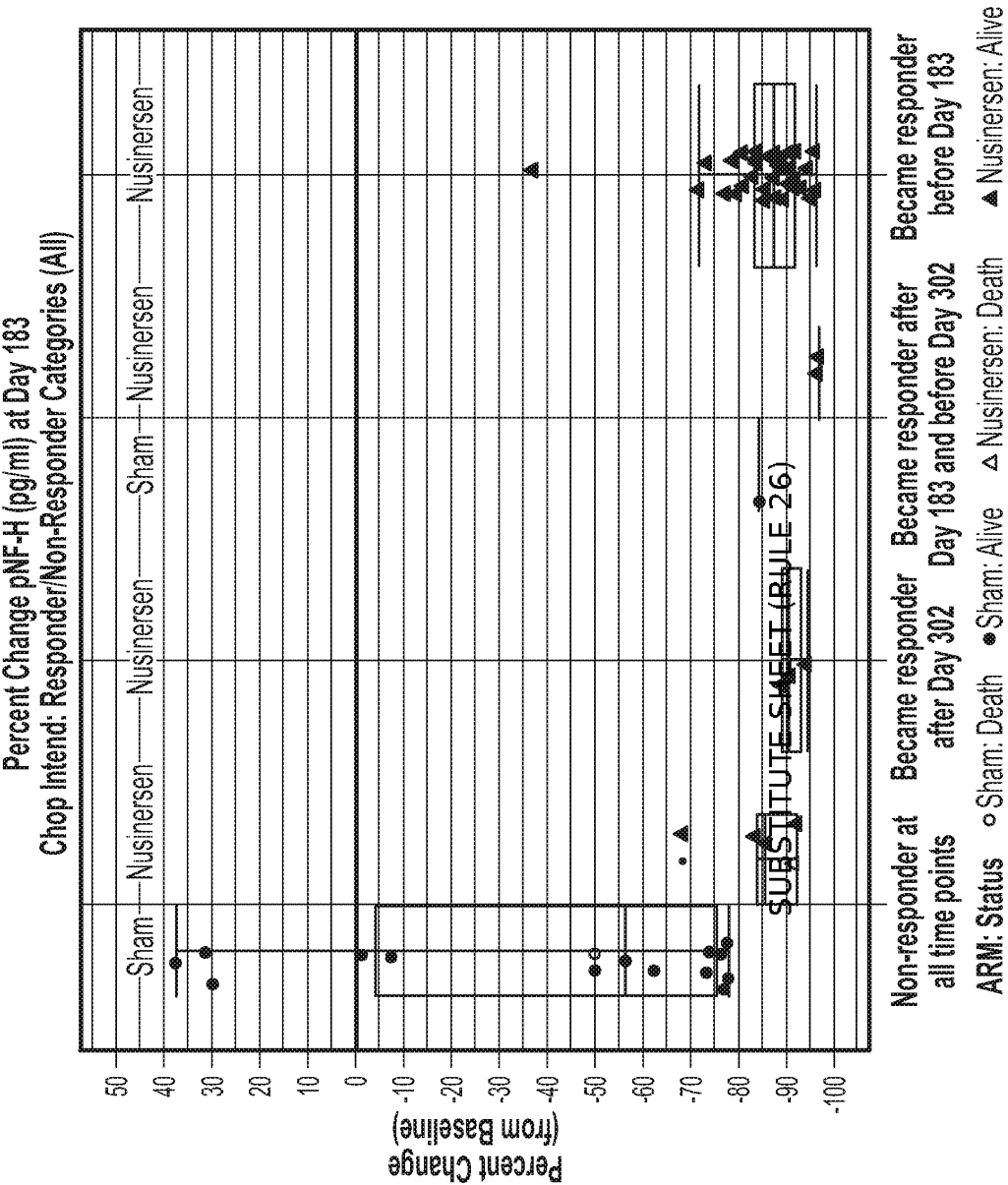


FIG. 23

24/46

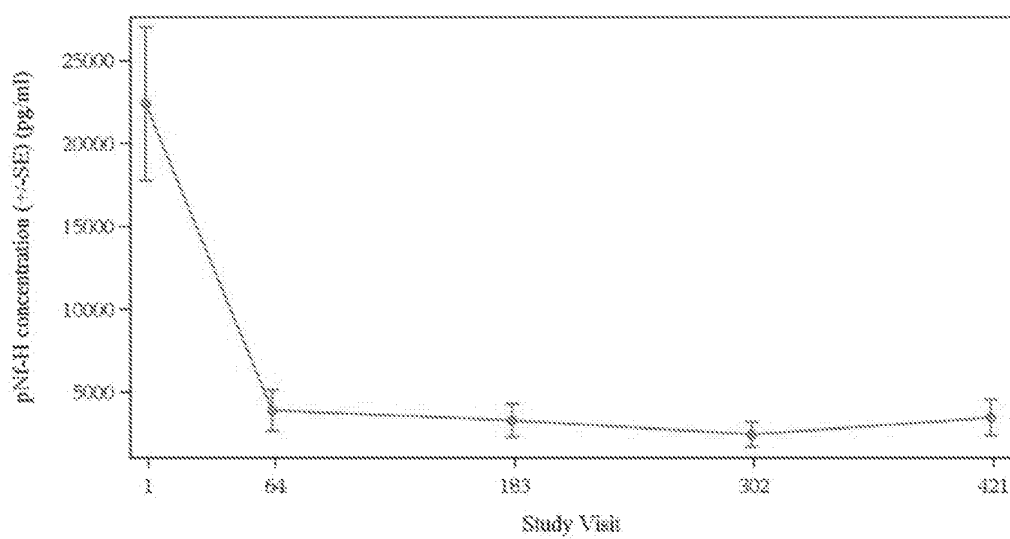


FIG. 24

25/46

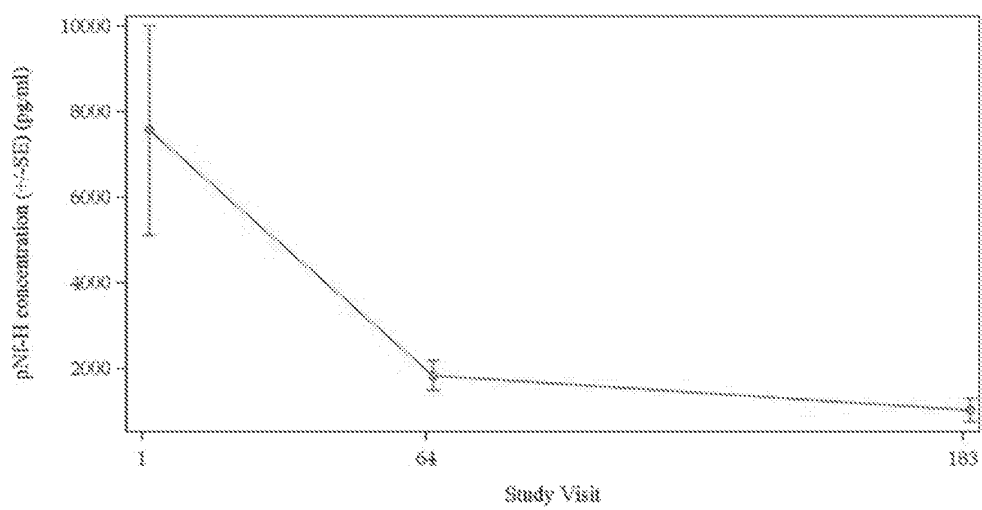


FIG. 25

26/46

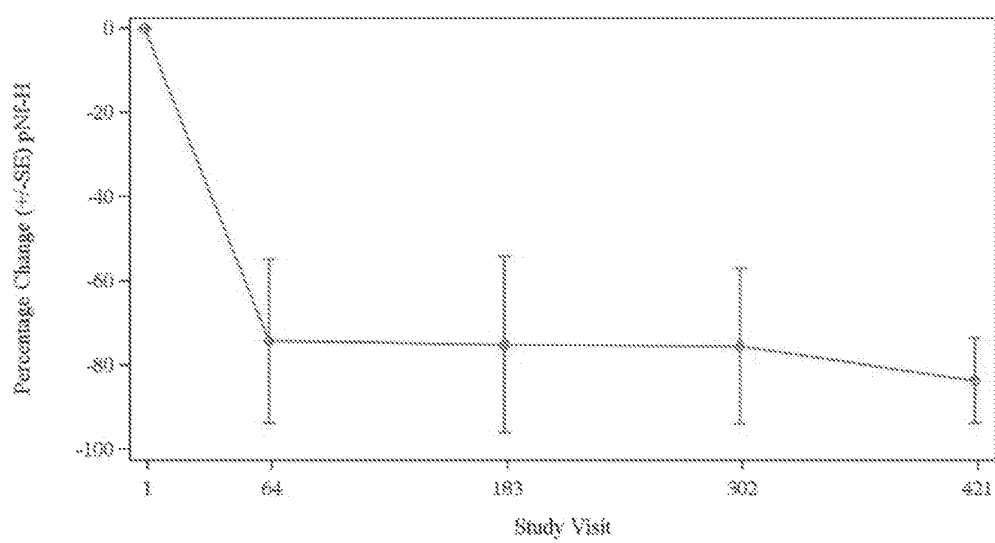


FIG. 26

27/46

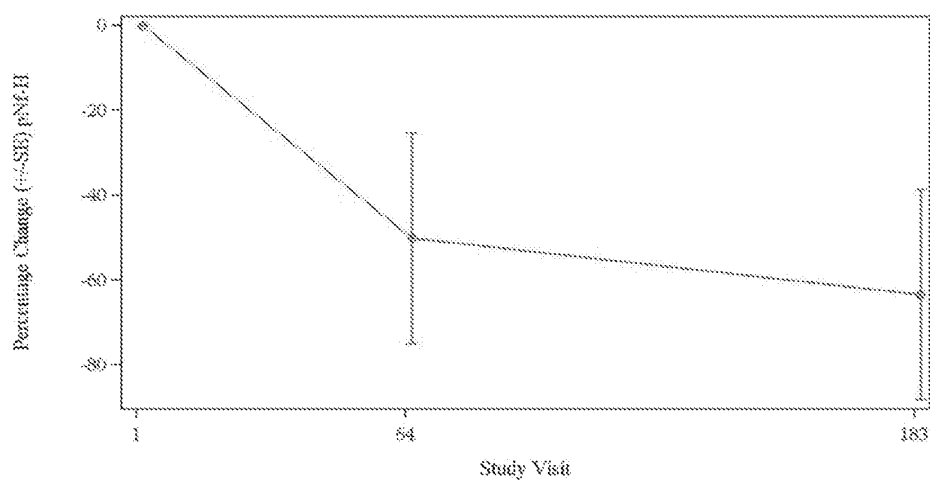


FIG. 27

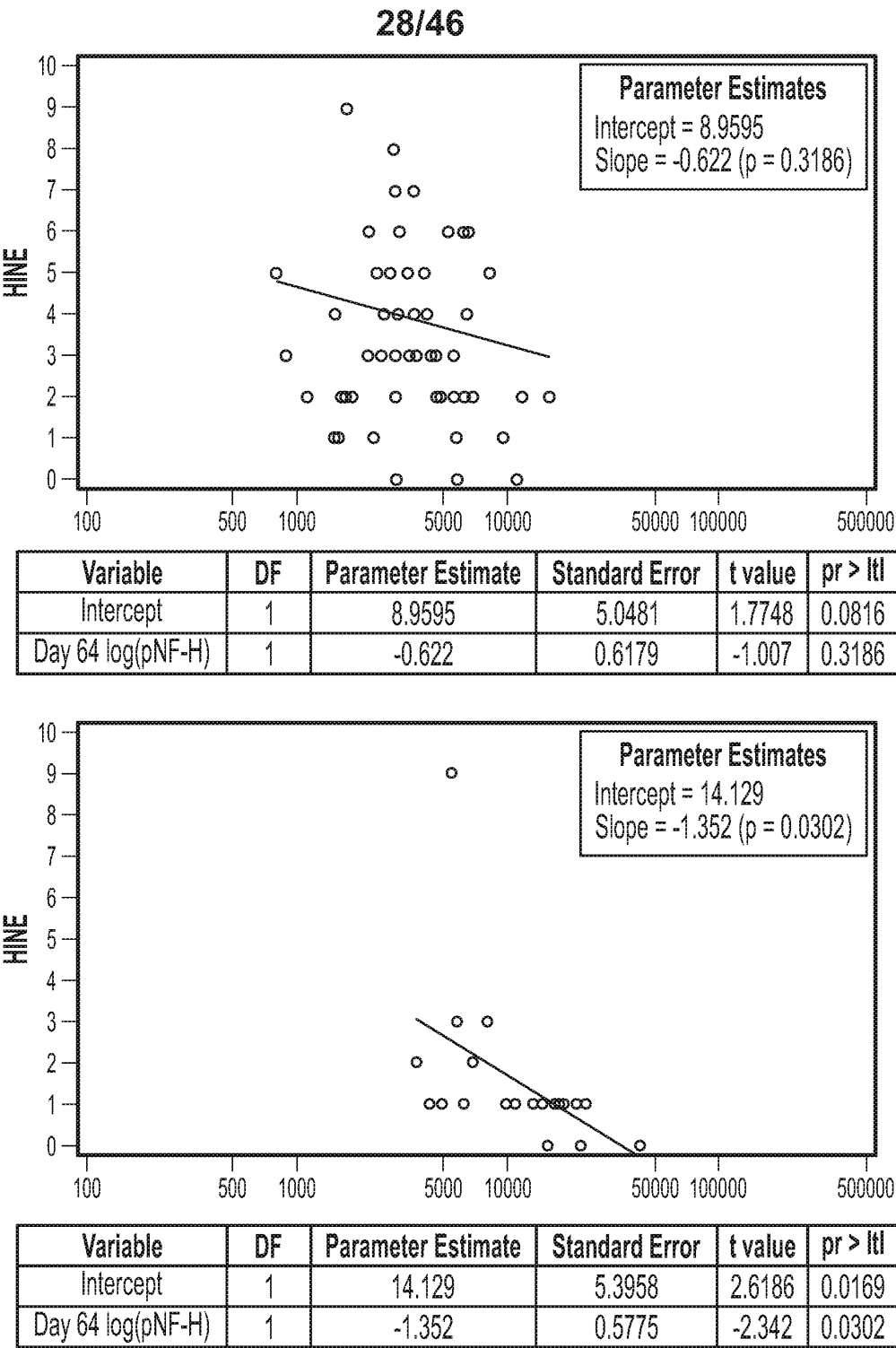


FIG. 28

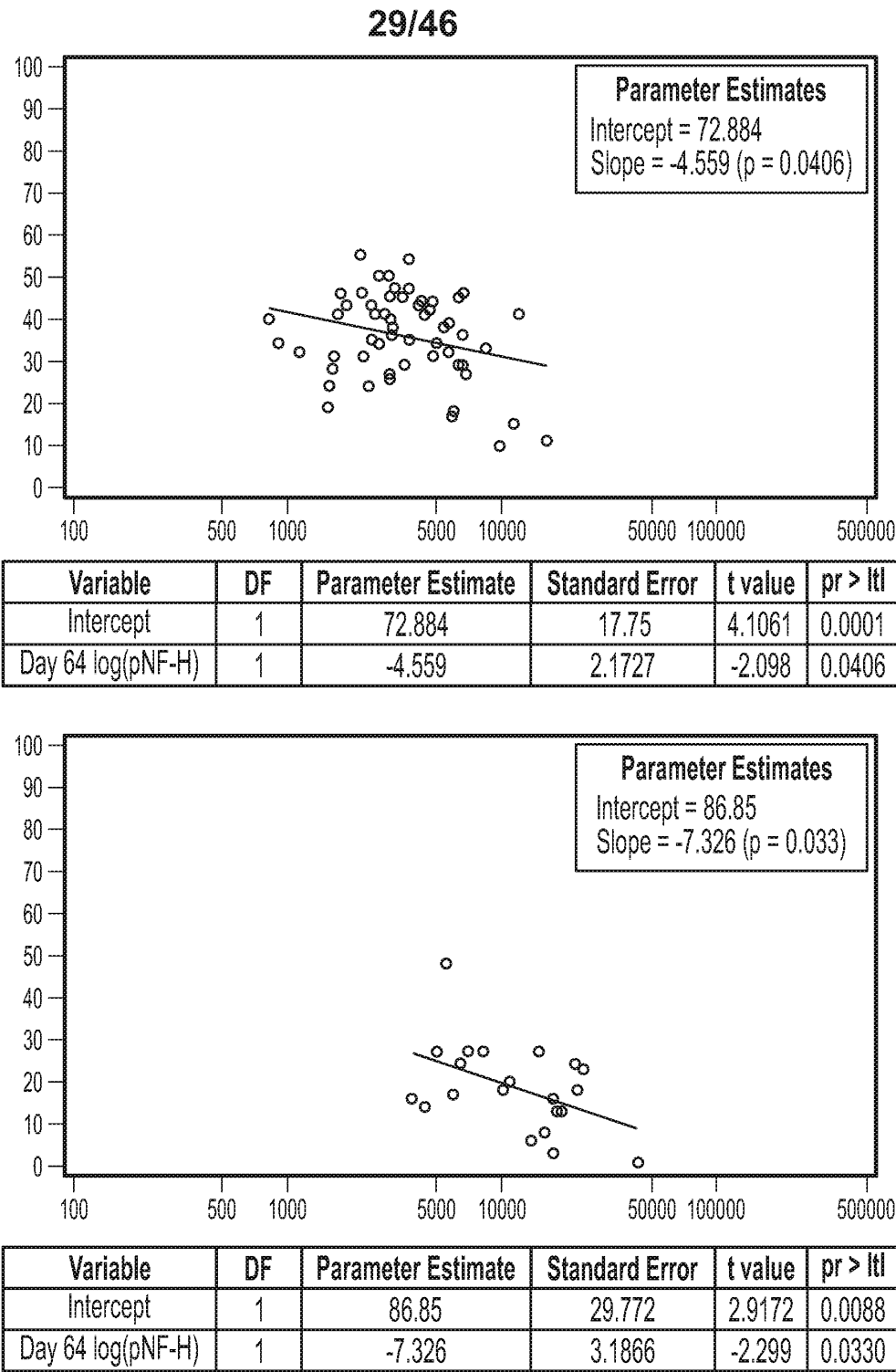


FIG. 29

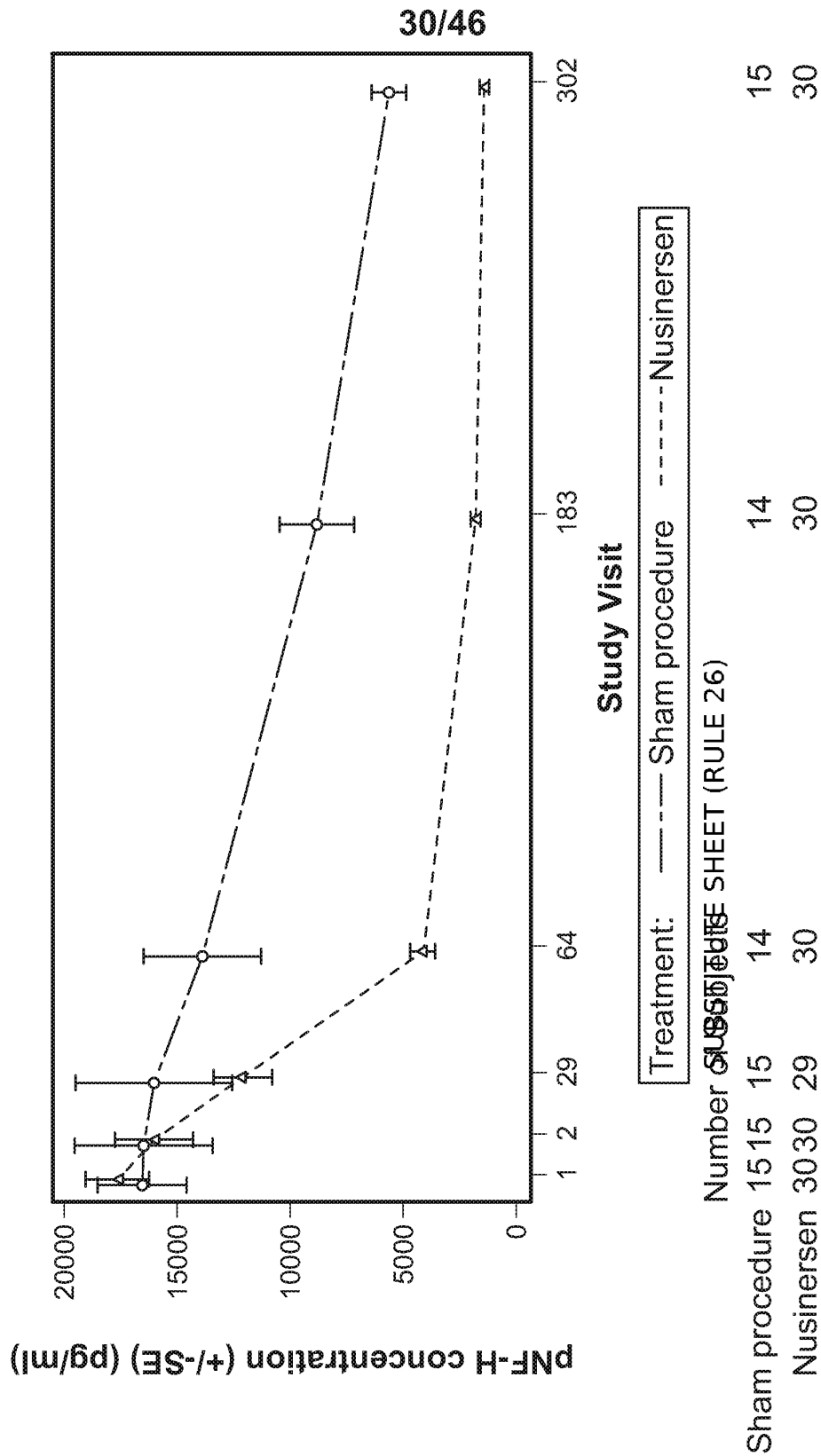


FIG. 30

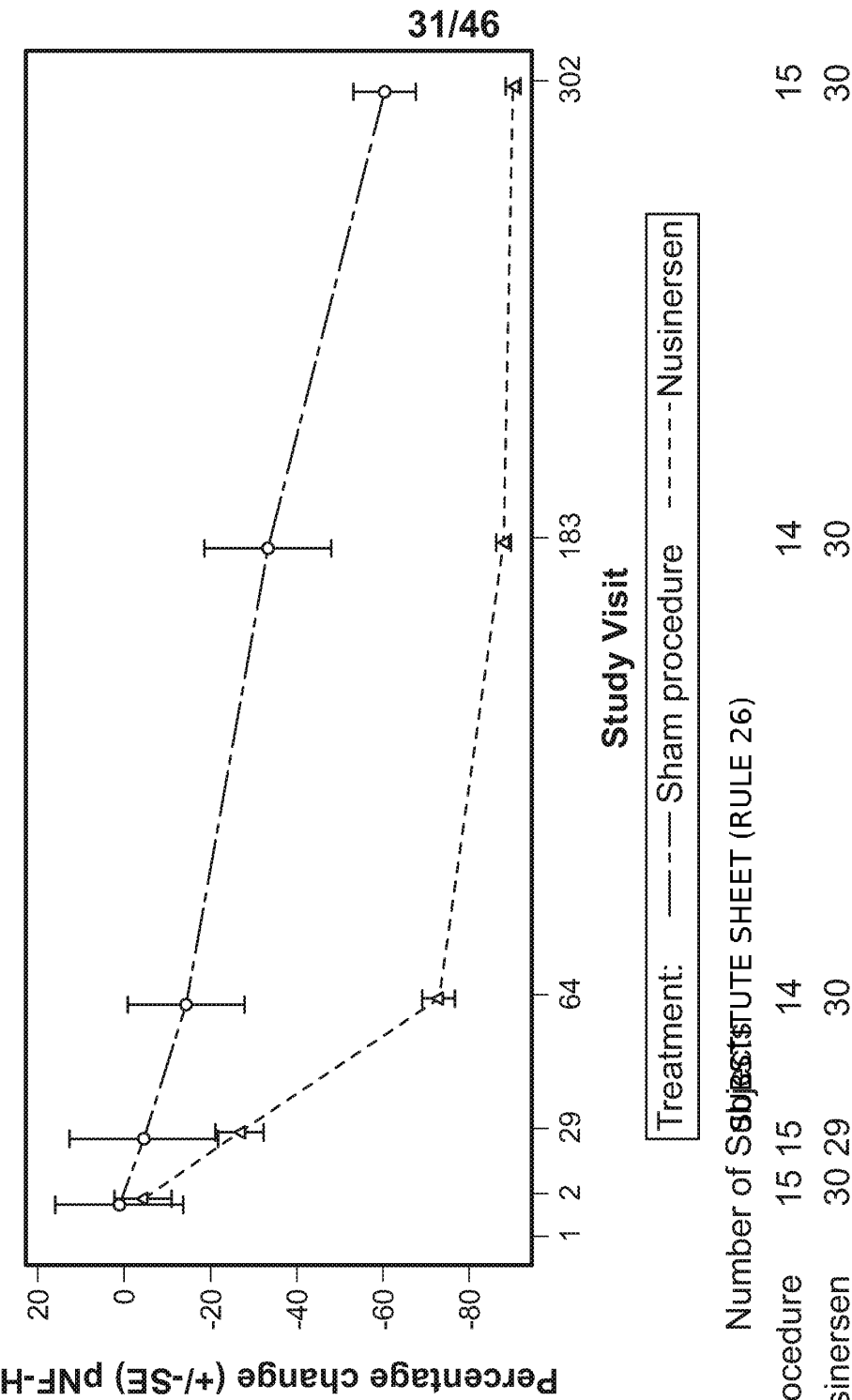


FIG. 31

32/46

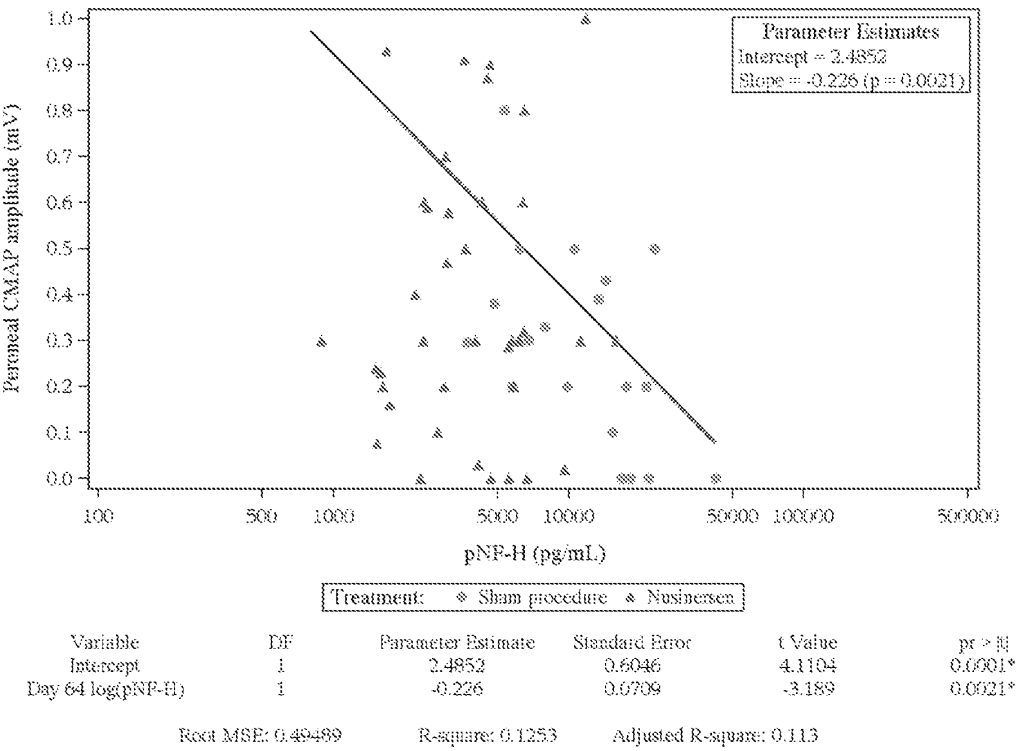


FIG. 32

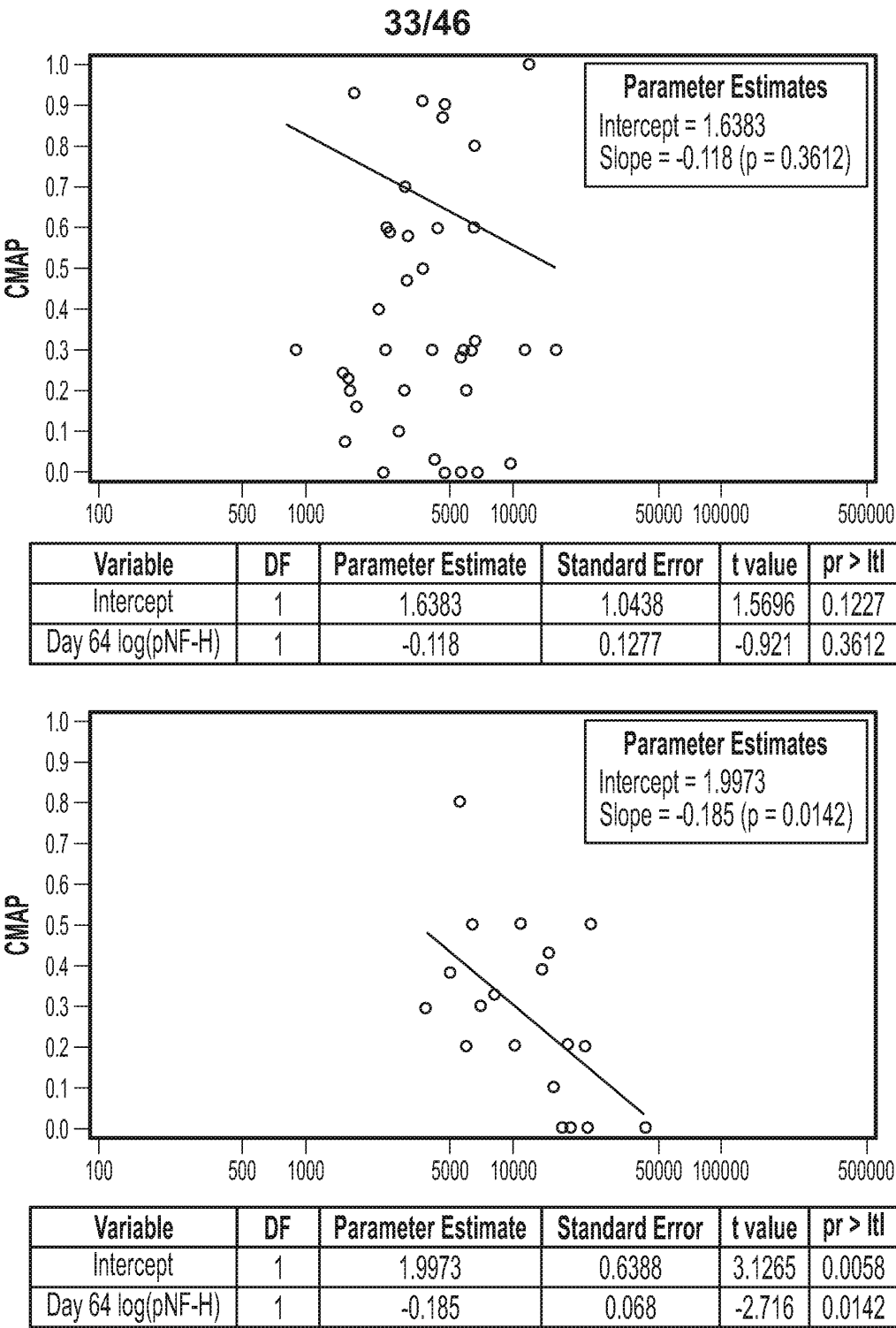


FIG. 33

34/46

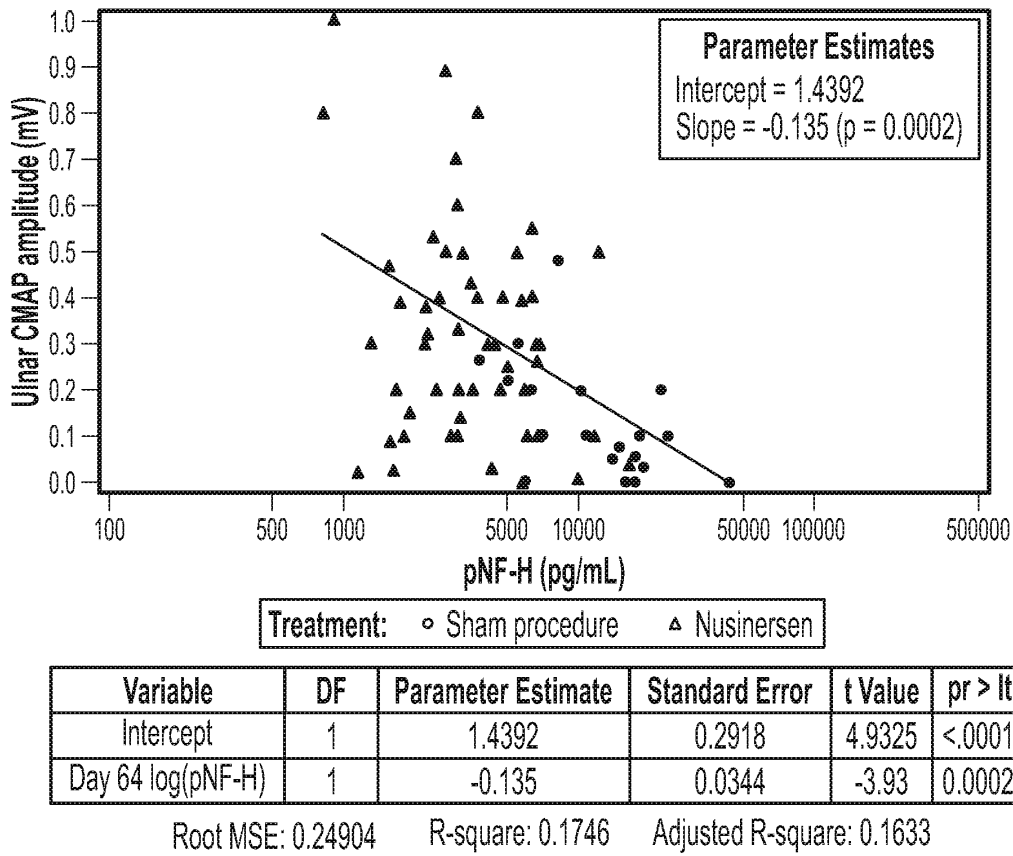


FIG. 34

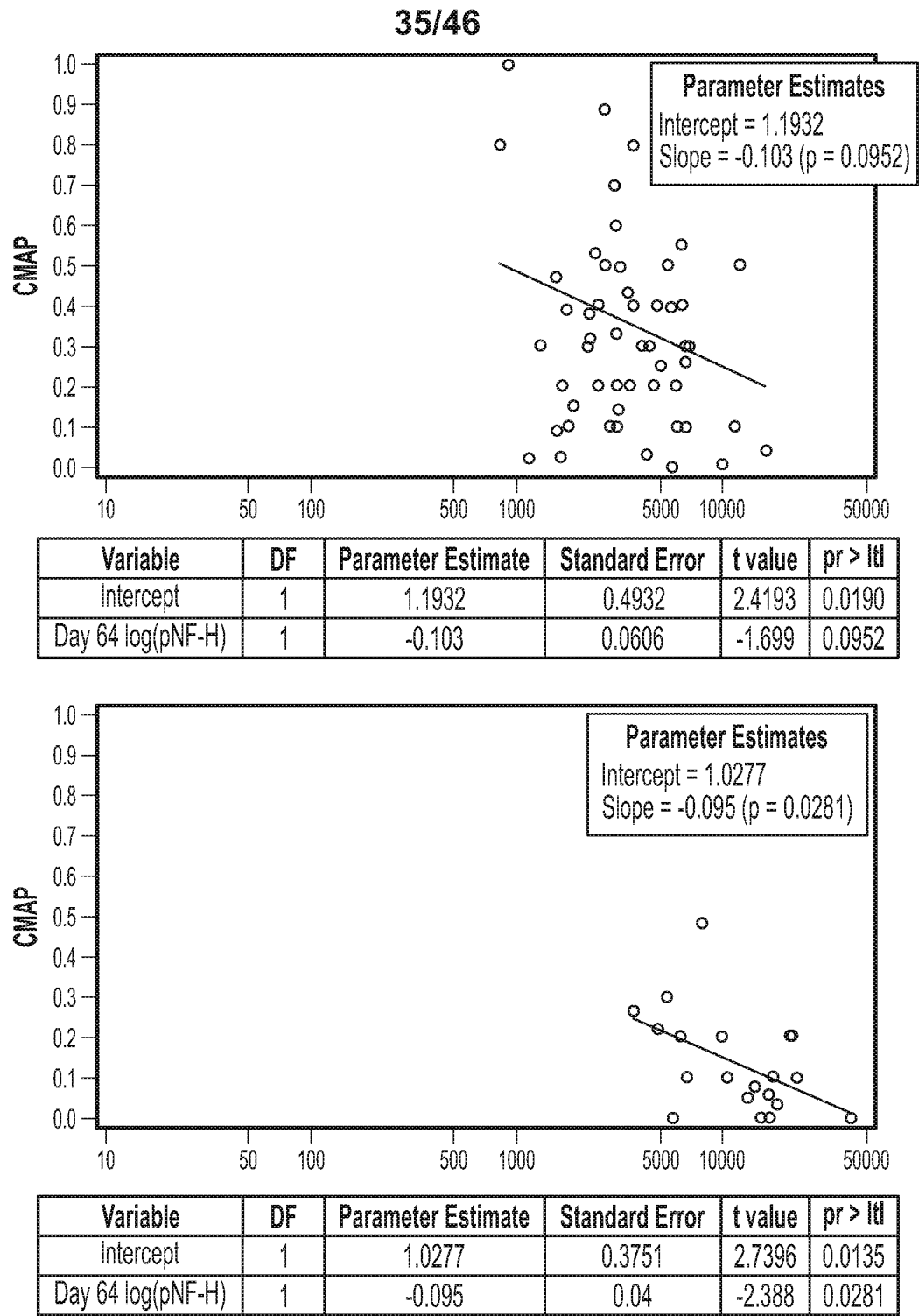


FIG. 35

36/46

Day 29
AUC = 60.1%

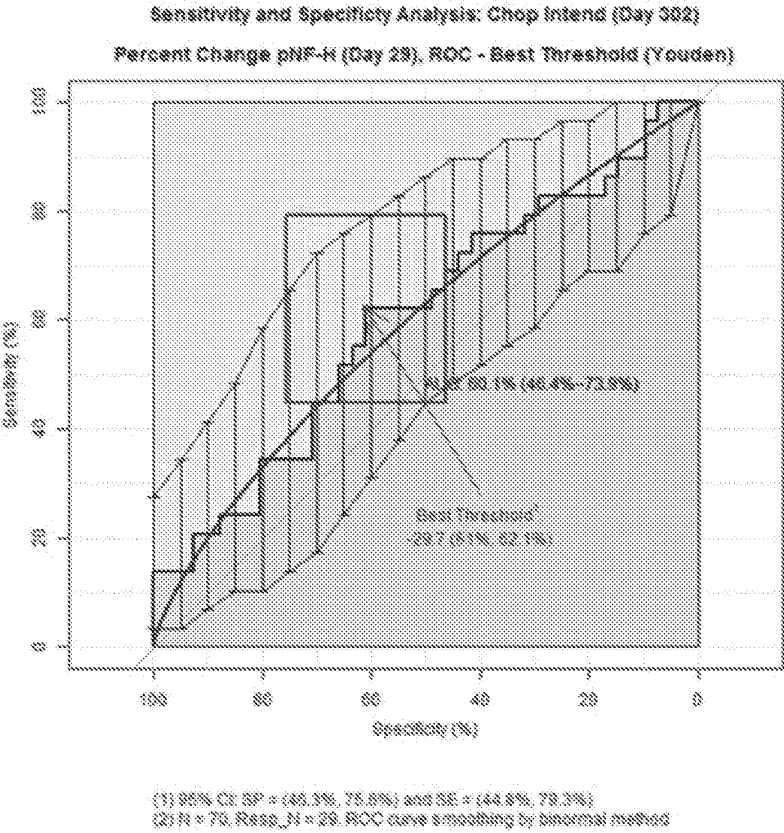
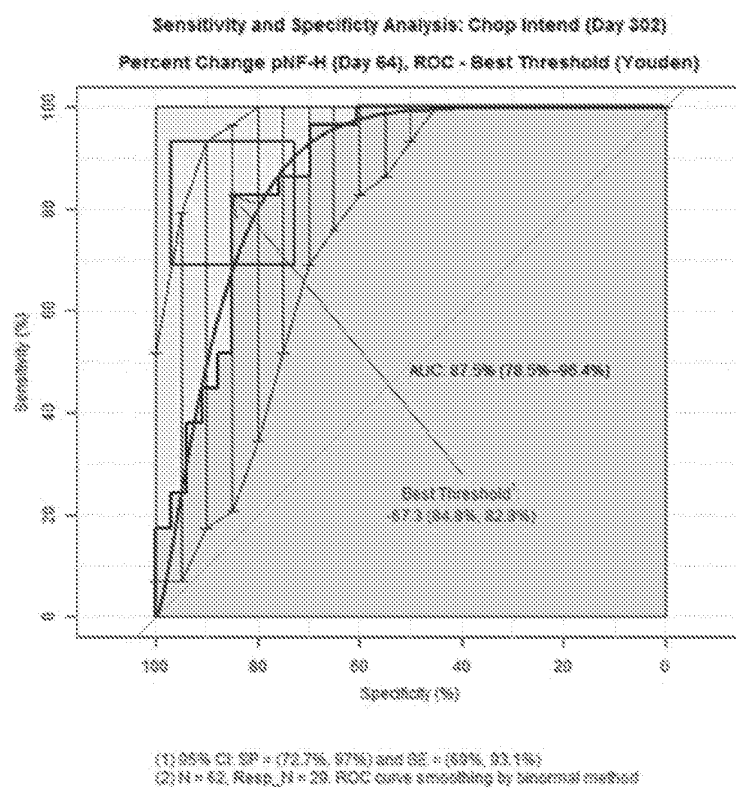


FIG. 36A

37/46

Day 64
AUC = 87.5%

**FIG. 36B**

38/46

Day 183
AUC = 81.5%

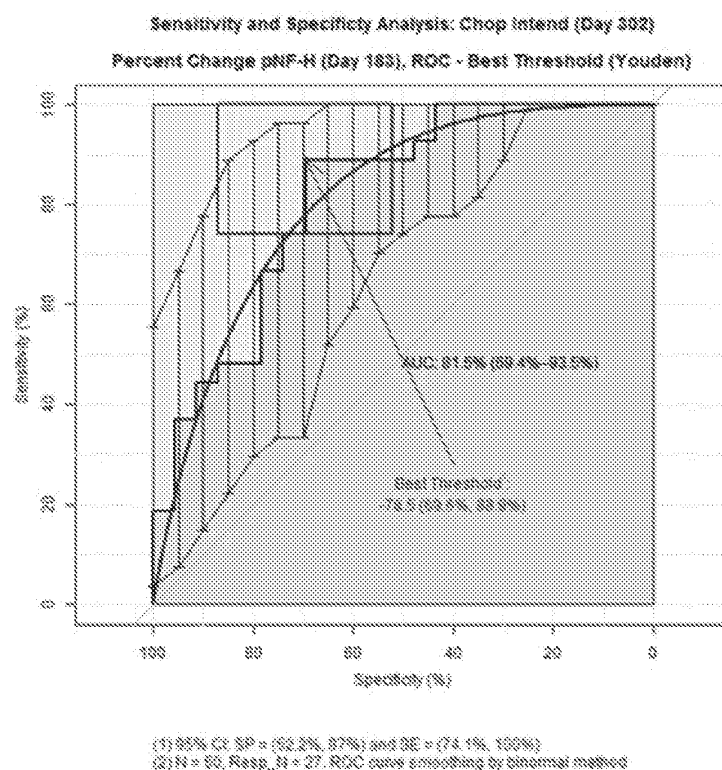
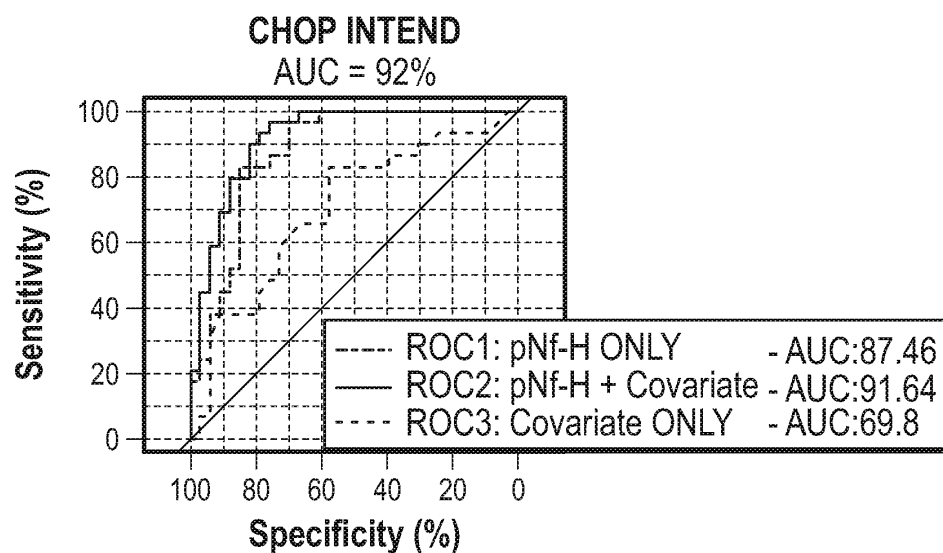


FIG. 36C

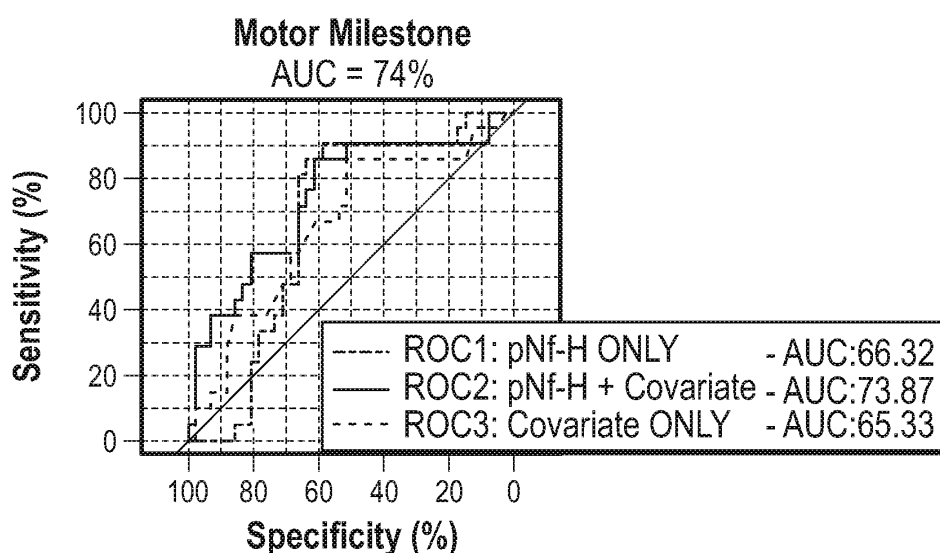
SUBSTITUTE SHEET (RULE 26)

39/46



Notes: (1) Significance, ROC1 vs ROC2: p-value = 0.15124
 (2) Significance, ROC3 vs ROC2: p-value = 0.00096
 (3) N = 62; Resp_N = 29

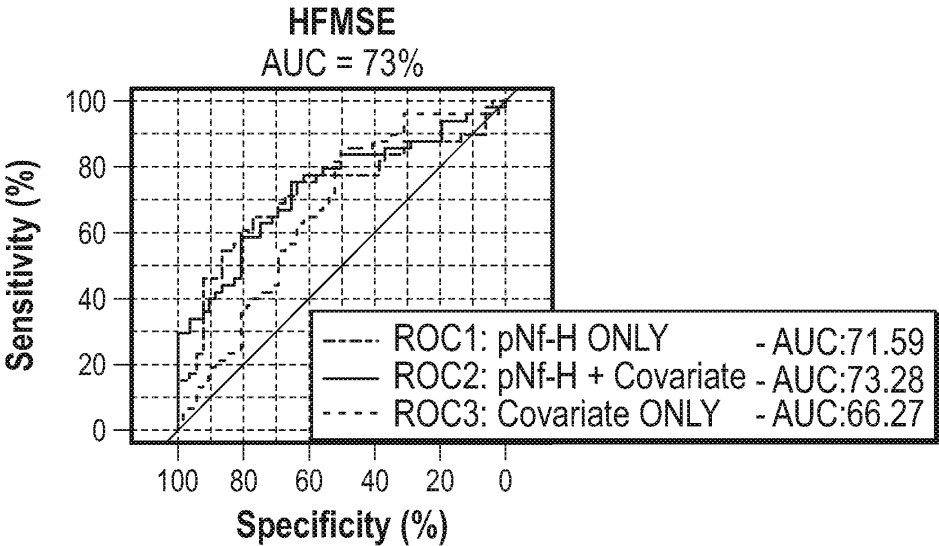
FIG. 37A



Notes: (1) Significance, ROC1 vs ROC2: p-value = 0.20867
 (2) Significance, ROC3 vs ROC2: p-value = 0.05903
 (3) N = 62; Resp_N = 21

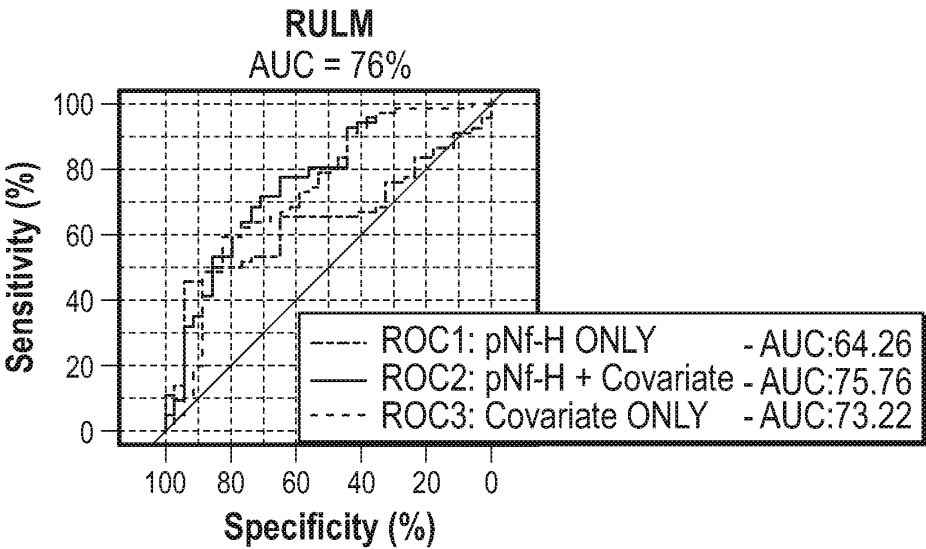
FIG. 37B

40/46



Notes: (1) Significance, ROC1 vs ROC2: p-value = 0.68253
(2) Significance, ROC3 vs ROC2: p-value = 0.09021
(3) N = 100; Resp_N = 48

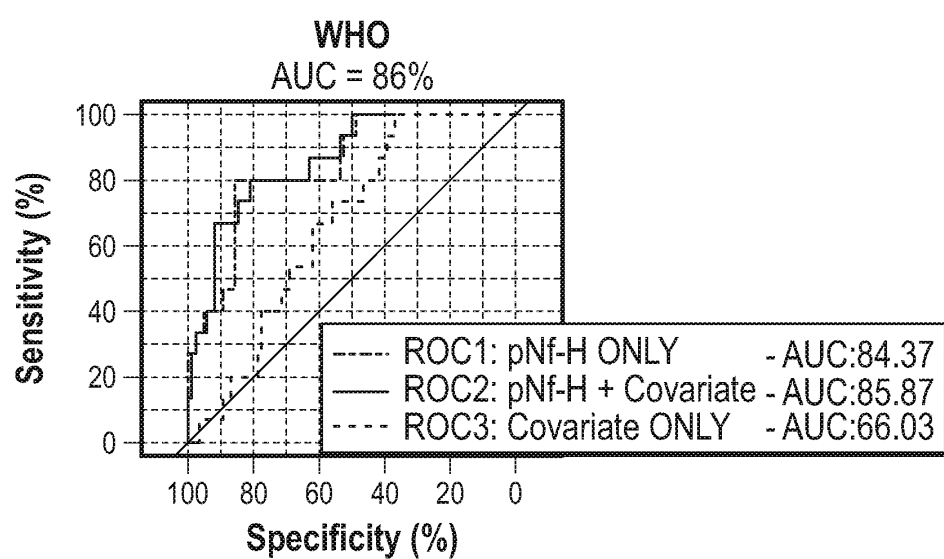
FIG. 38A



Notes: (1) Significance, ROC1 vs ROC2: p-value = 0.09997
(2) Significance, ROC3 vs ROC2: p-value = 0.08413
(3) N = 100; Resp_N = 66

FIG. 38B

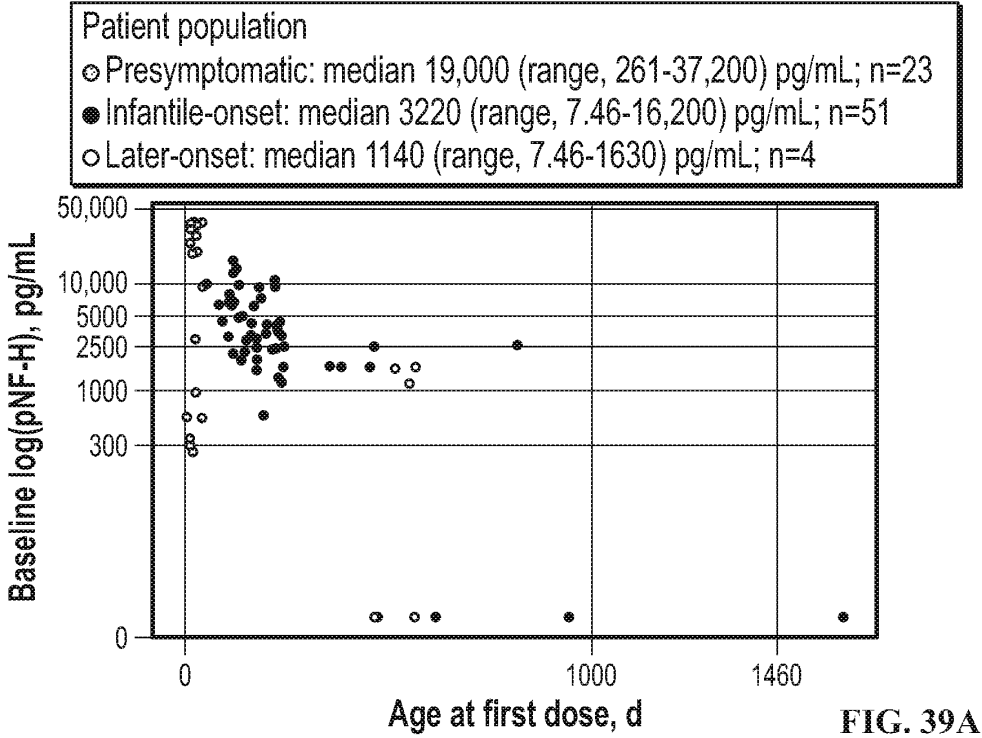
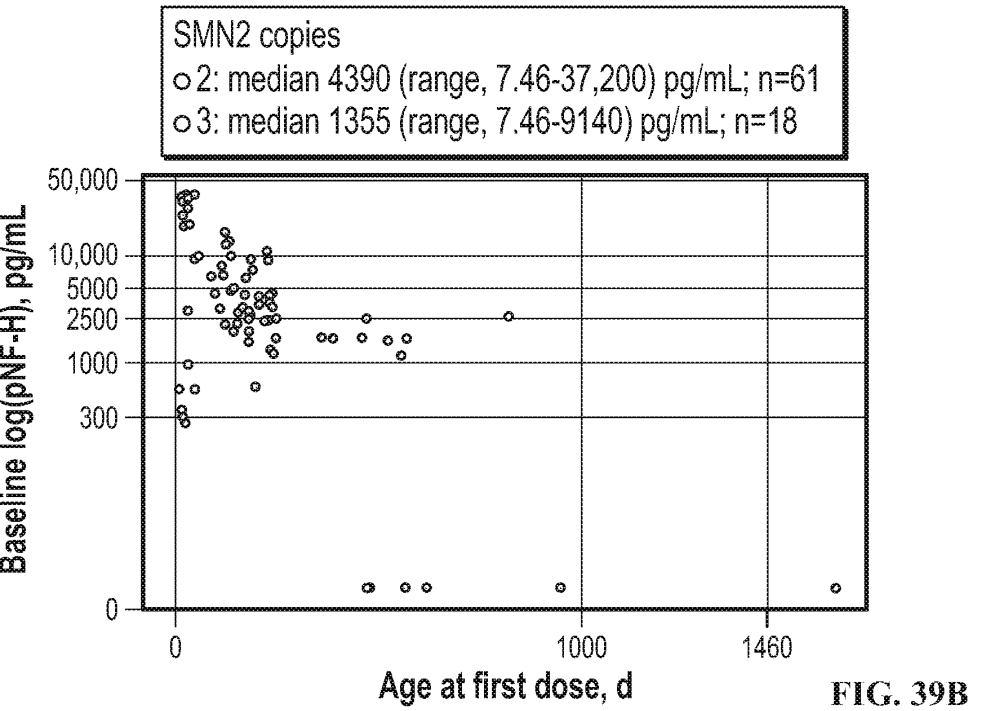
41/46



Notes: (1) Significance, ROC1 vs ROC2: p-value = 0.30269
(2) Significance, ROC3 vs ROC2: p-value = 0.00032
(3) N = 99; Resp_N = 15

FIG. 38C

42/46



43/46

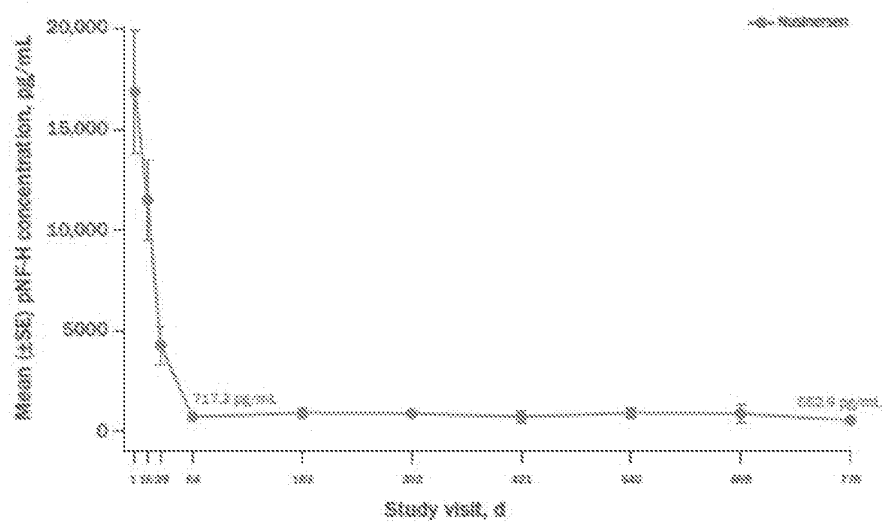


FIG. 40

44/46

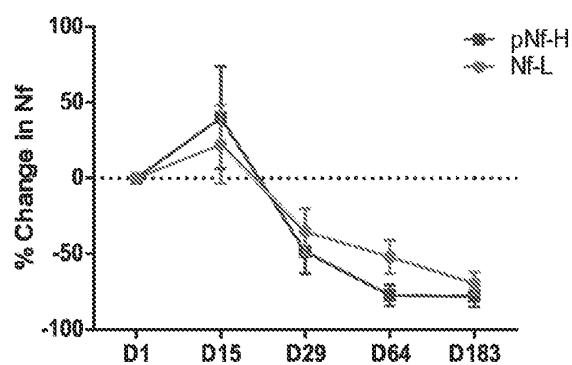


FIG. 41A

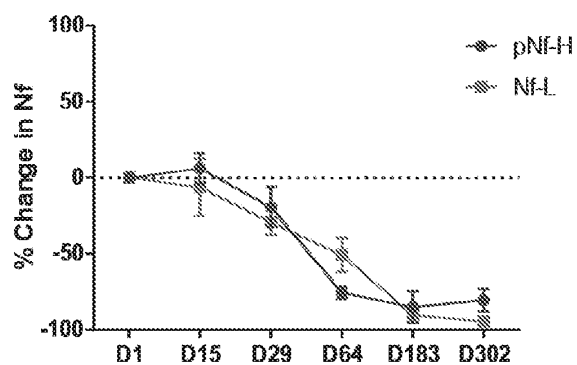


FIG. 41B

45/46

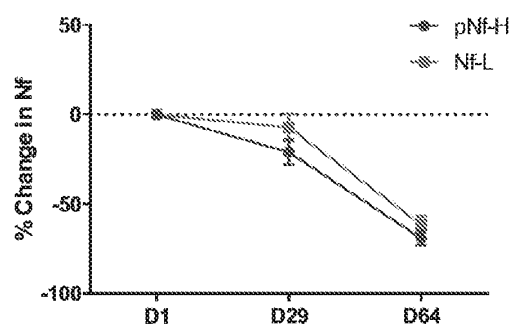


FIG. 41C

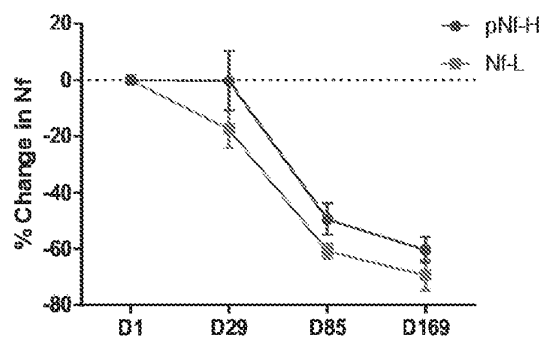


FIG. 41D

46/46

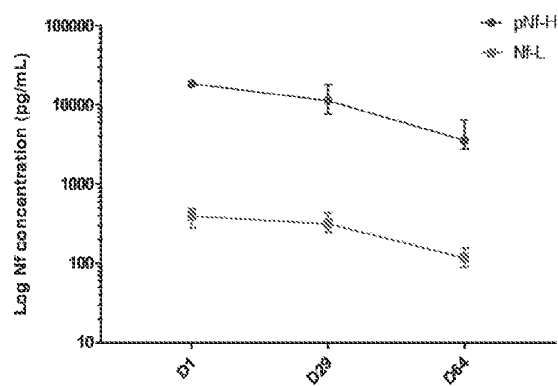


FIG. 41E

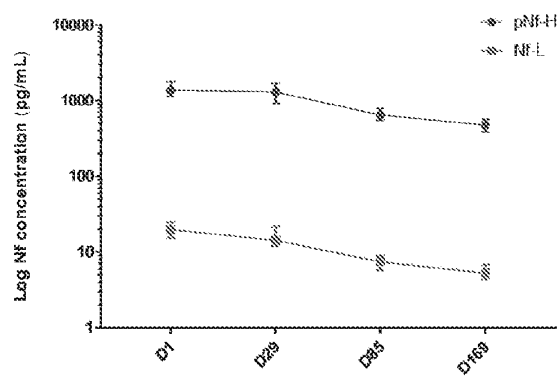


FIG. 41F