**Anti-MMP9 Humanized Heavy Chains**

| | | | | | |
|---|---|---|---|---|---|
| AB0041 | QVQLKESGPG | LVAPSQSLSI | TCTVS*GFSLL* | *SYGVHWVRQP* | PGKGLEWLGV |
| VH1 | QVQLQESGPG | LVKPSETLSL | TCTVS*GFSLL* | *SYGVHWVRQP* | PGKGLEWLGV |
| VH2 | QVQLQESGPG | LVKPSETLSL | TCTVS*GFSLL* | *SYGVHWVRQP* | PGKGLEWLGV |
| VH3 | QVQLQESGPG | LVKPSETLSL | TCTVS*GFSLL* | *SYGVHWVRQP* | PGKGLEWLGV |
| VH4 | QVQLQESGPG | LVKPSETLSL | TCTVS*GFSLL* | *SYGVHWVRQP* | PGKGLEWLGV |
| | | | | | |
| AB0041 | *IWTGGTTNYN* | *SALMSR*LSIS | KDDSKSQVFL | KMNSLQTDDT | AIYYCARYYY |
| VH1 | *IWTGGTTNYN* | *SALMSR*LTIS | KDDSKSTVYL | KMNSLKTEDT | AIYYCARYYY |
| VH2 | *IWTGGTTNYN* | *SALMSR*LTIS | KDDSKNTVYL | KMNSLKTEDT | AIYYCARYYY |
| VH3 | *IWTGGTTNYN* | *SALMSR*FTIS | KDDSKNTVYL | KMNSLKTEDT | AIYYCARYYY |
| VH4 | *IWTGGTTNYN* | *SALMSR*FTIS | KDDSKNTLYL | KMNSLKTEDT | AIYYCARYYY |
| | | | | | |
| AB0041 | *GMDYWGQGTS* | VTVSS | (SEQ ID NO:3) | | |
| VH1 | *GMDYWGQGTS* | VTVSS | (SEQ ID NO:5) | | |
| VH2 | *GMDYWGQGTL* | VTVSS | (SEQ ID NO:6) | | |
| VH3 | *GMDYWGQGTL* | VTVSS | (SEQ ID NO:7) | | |
| VH4 | *GMDYWGQGTL* | VTVSS | (SEQ ID NO:8) | | |

FIG. 1

**Anti-MMP9 Humanized Light Chains**

```
AB0041  DIVMTQSHKF MSTSVGDRVS ITCKASQDVR NTVAWYQQKT GQSPKLLIYS
Vk1     DIVMTQSPSF LSASVGDRVT ITCKASQDVR NTVAWYQQKT GKAPKLLIYS
Vk2     DIVMTQSPSS LSASVGDRVT ITCKASQDVR NTVAWYQQKP GKAPKLLIYS
Vk3     DIQMTQSPSS LSASVGDRVT ITCKASQDVR NTVAWYQQKP GKAPKLLIYS
Vk4     DIQMTQSPSS LSASVGDRVT ITCKASQDVR NTVAWYQQKP GKAPKLLIYS

AB0041  SSYRNTGVPD RFTGSGSGTD FTFTISSVQA EDLAVYFCQQ HYITPYTFGG
Vk1     SSYRNTGVPD RFTGSGSGTD FTLTISSLQA EDVAVYFCQQ HYITPYTFGG
Vk2     SSYRNTGVPD RFTGSGSGTD FTLTISSLQA EDVAVYFCQQ HYITPYTFGG
Vk3     SSYRNTGVPD RFSGSGSGTD FTLTISSLQA EDVAVYFCQQ HYITPYTFGG
Vk4     SSYRNTGVPD RFSGSGSGTD FTLTISSLQA EDVAVYYCQQ HYITPYTFGG

AB0041  GTKLEIK (SEQ ID NO:4)
Vk1     GTKVEIK (SEQ ID NO:9)
Vk2     GTKVEIK (SEQ ID NO:10)
Vk3     GTKVEIK (SEQ ID NO:11)
Vk4     GTKVEIK (SEQ ID NO:12)
```

FIG. 2

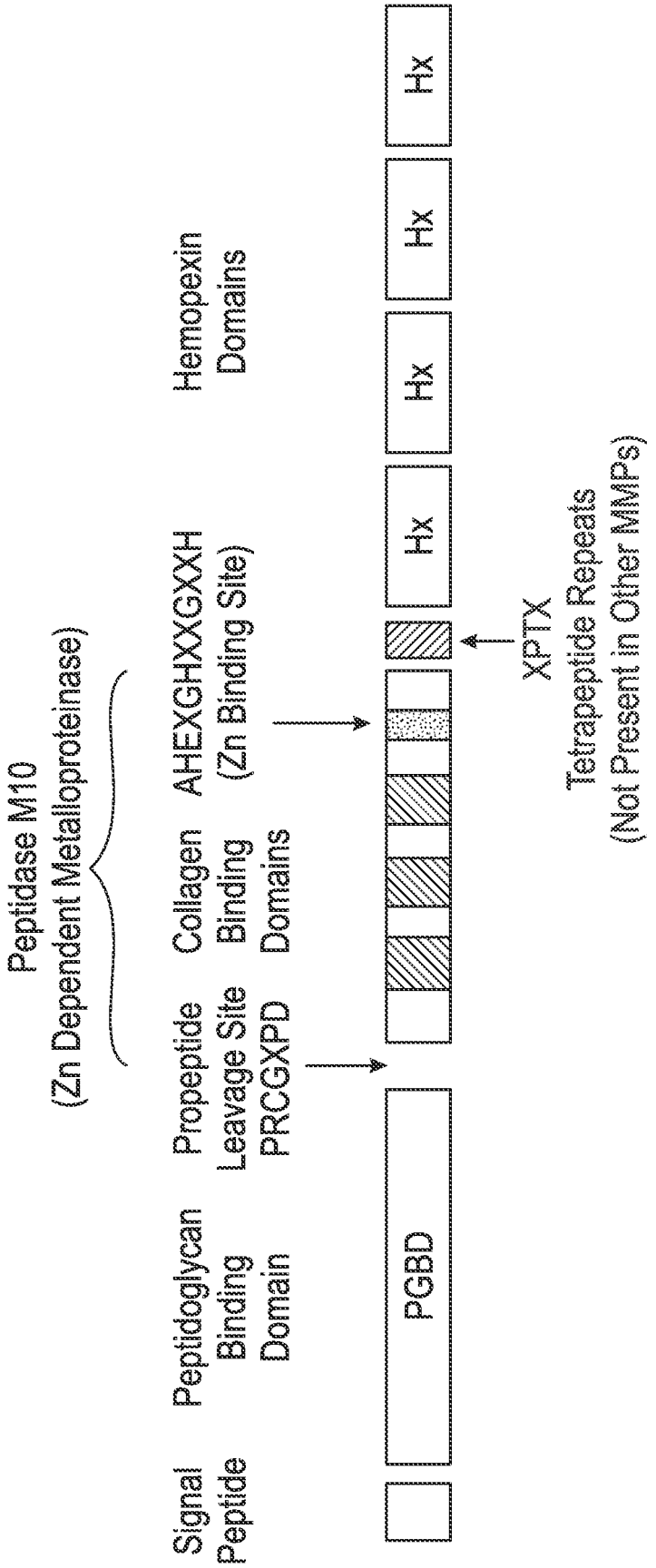

Peptidase M10
(Zn Dependent Metalloproteinase)
Signal Peptide
Peptidoglycan Binding Domain
Propeptide Leavage Site PRCGXPD
Collagen Binding Domains
AHEXGHXXGXXH (Zn Binding Site)
Hemopexin Domains
PGBD
Hx
Hx
Hx
Hx
XPTX
Tetrapeptide Repeats
(Not Present in Other MMPs)

FIG. 3

Comparison Between AB0041, M4, and M12 Heavy and Light Chains
Light Chains
Signal Peptide
CDRL1
CDRL2
M4
AB0041
M12
CDRL3
Kappa Constant
Heavy Chains
Signal Peptide
CDRL1
CDRL2...
CDRL3
IgG2b Constant

FIG. 4

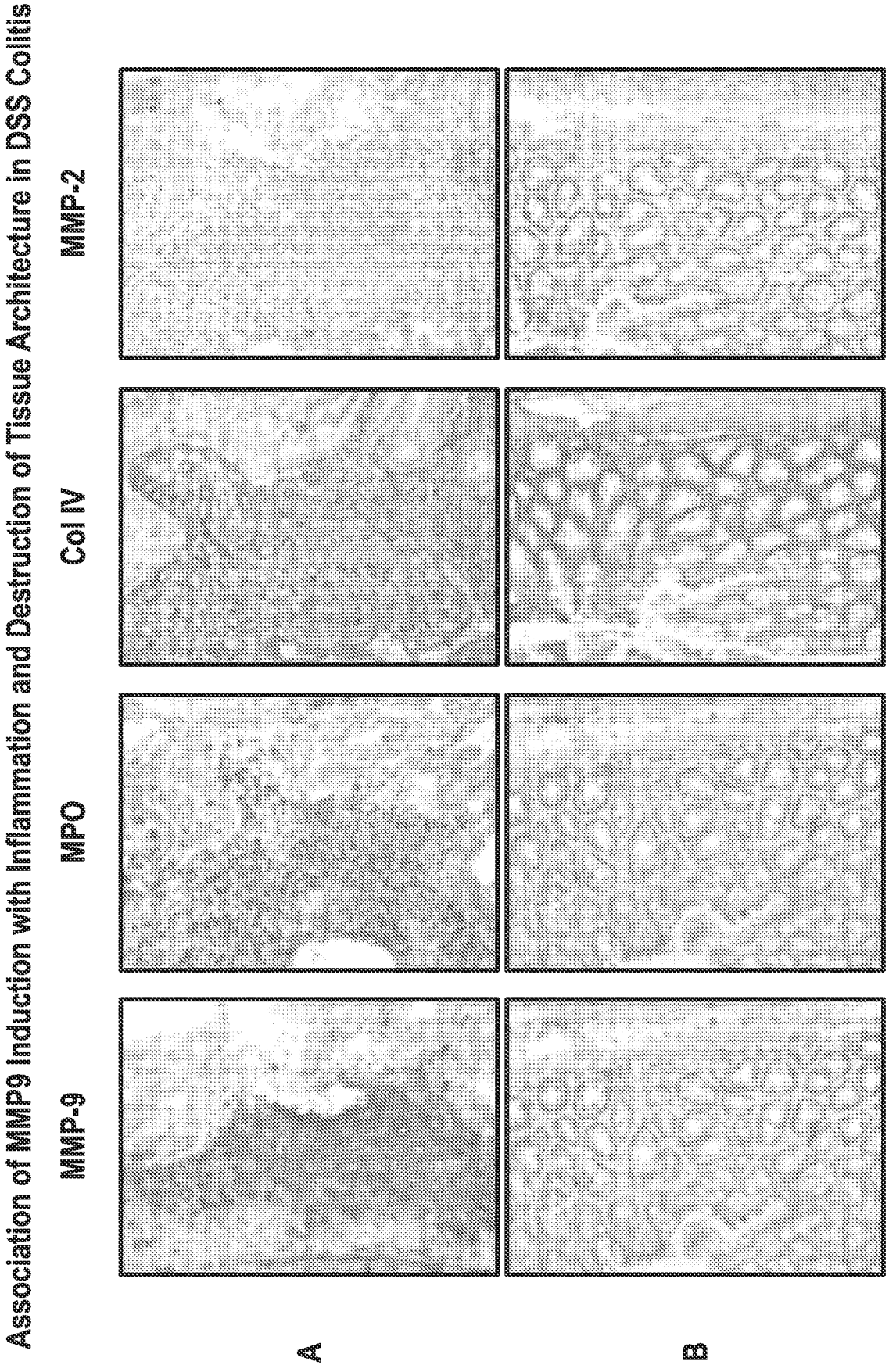

Association of MMP9 Induction with Inflammation and Destruction of Tissue Architecture in DSS Colitis
MMP-9
MPO
Col IV
MMP-2
A
B

FIG. 5

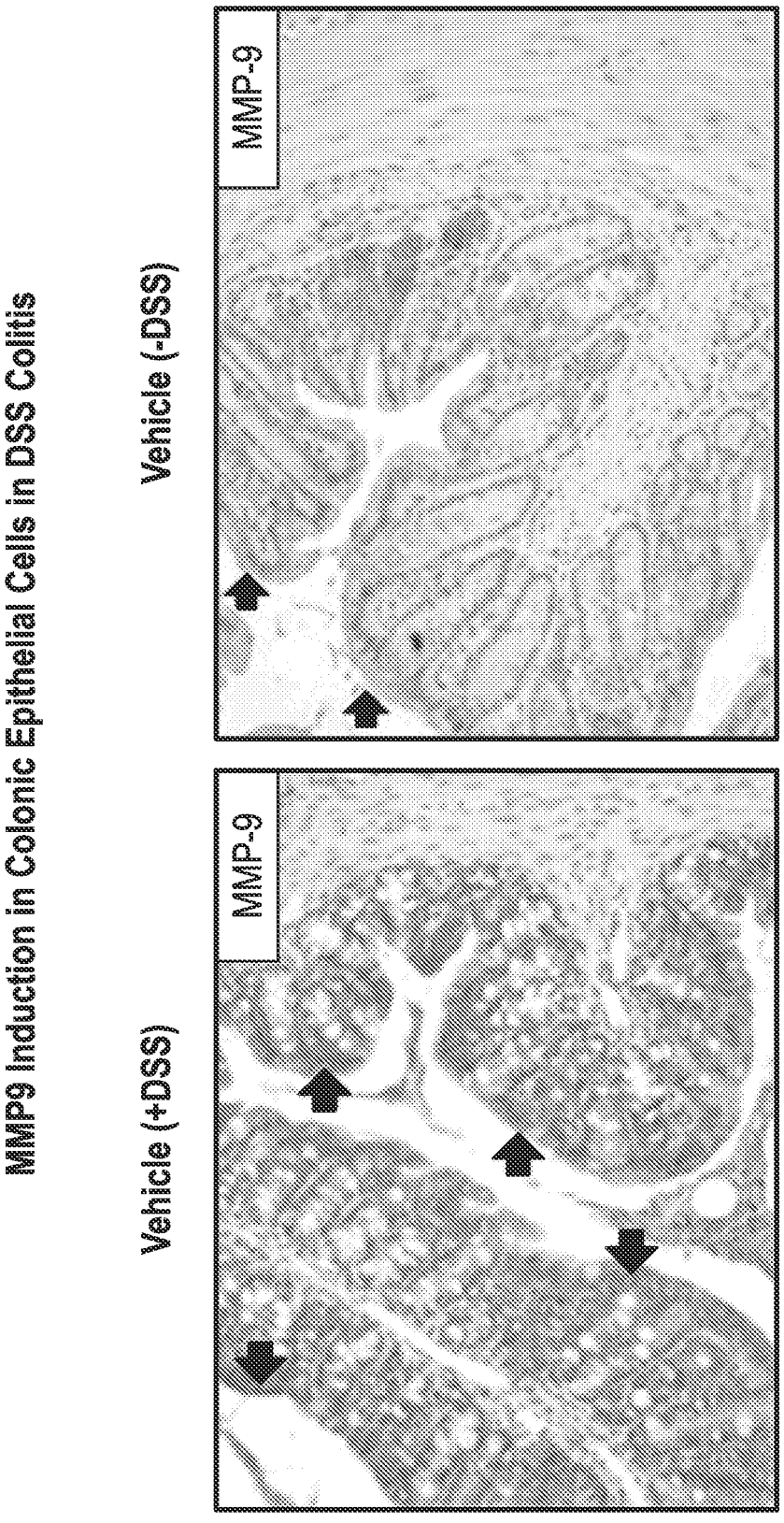

MMP9 Induction in Colonic Epithelial Cells in DSS Colitis
Vehicle (+DSS)
MMP-9
Vehicle (-DSS)
MMP-9

FIG. 6

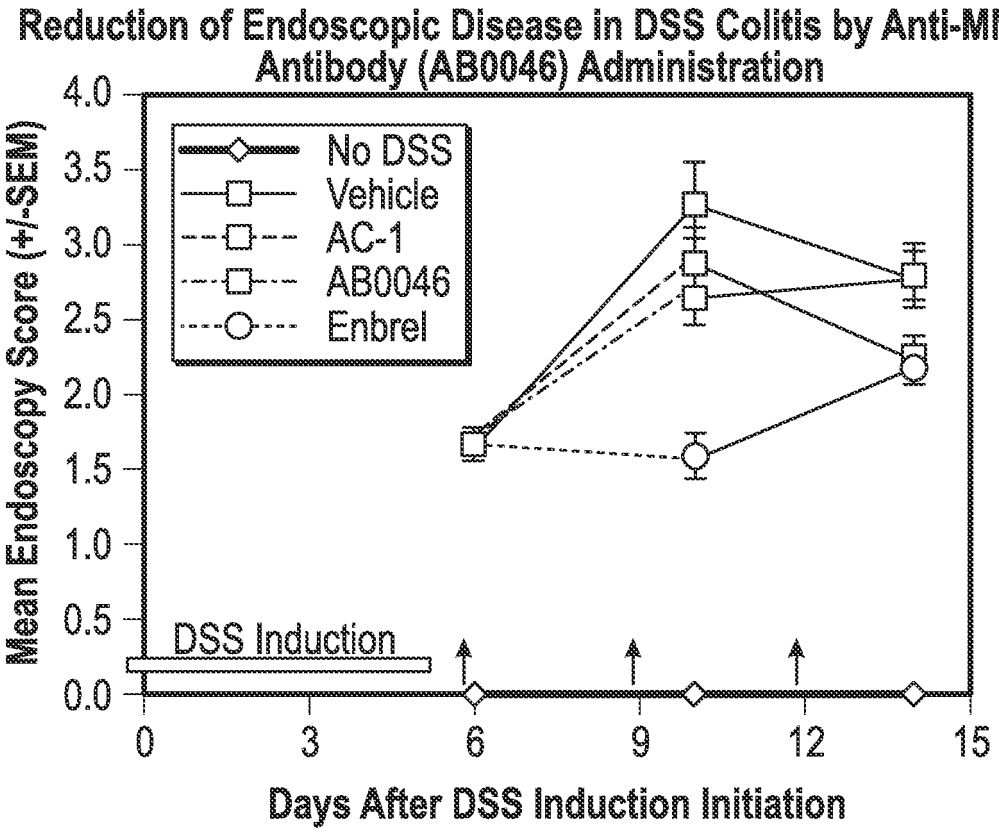

Reduction of Endoscopic Disease in DSS Colitis by Anti-MMP9 Antibody (AB0046) Administration
Mean Endoscopy Score (+/-SEM)
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
No DSS
Vehicle
AC-1
AB0046
Enbrel
DSS Induction
0
3
6
9
12
15
Days After DSS Induction Initiation

FIG. 7A

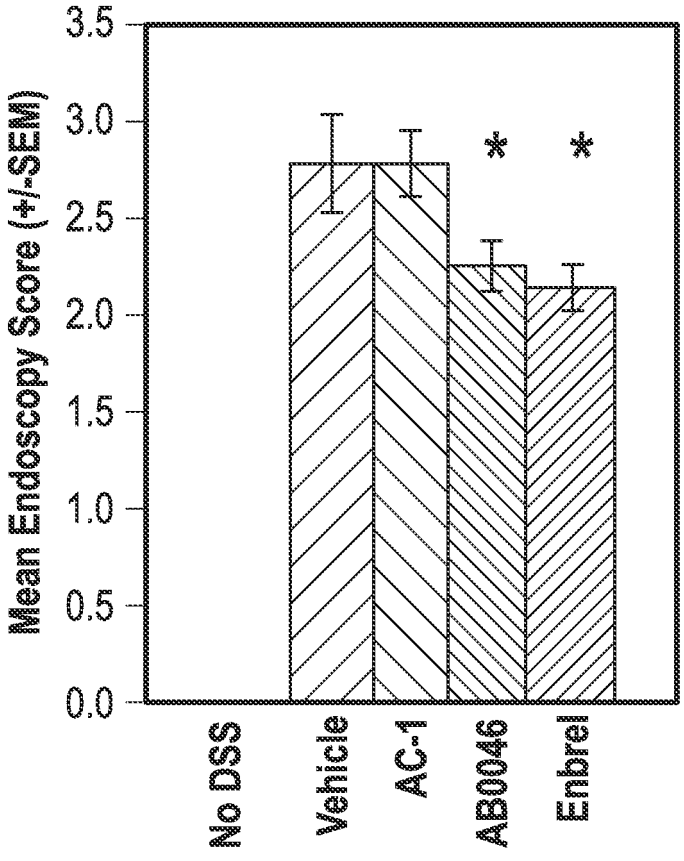

Mean Endoscopy Score (+/-SEM)
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
*
*
No DSS
Vehicle
AC-1
AB0046
Enbrel

FIG. 7B

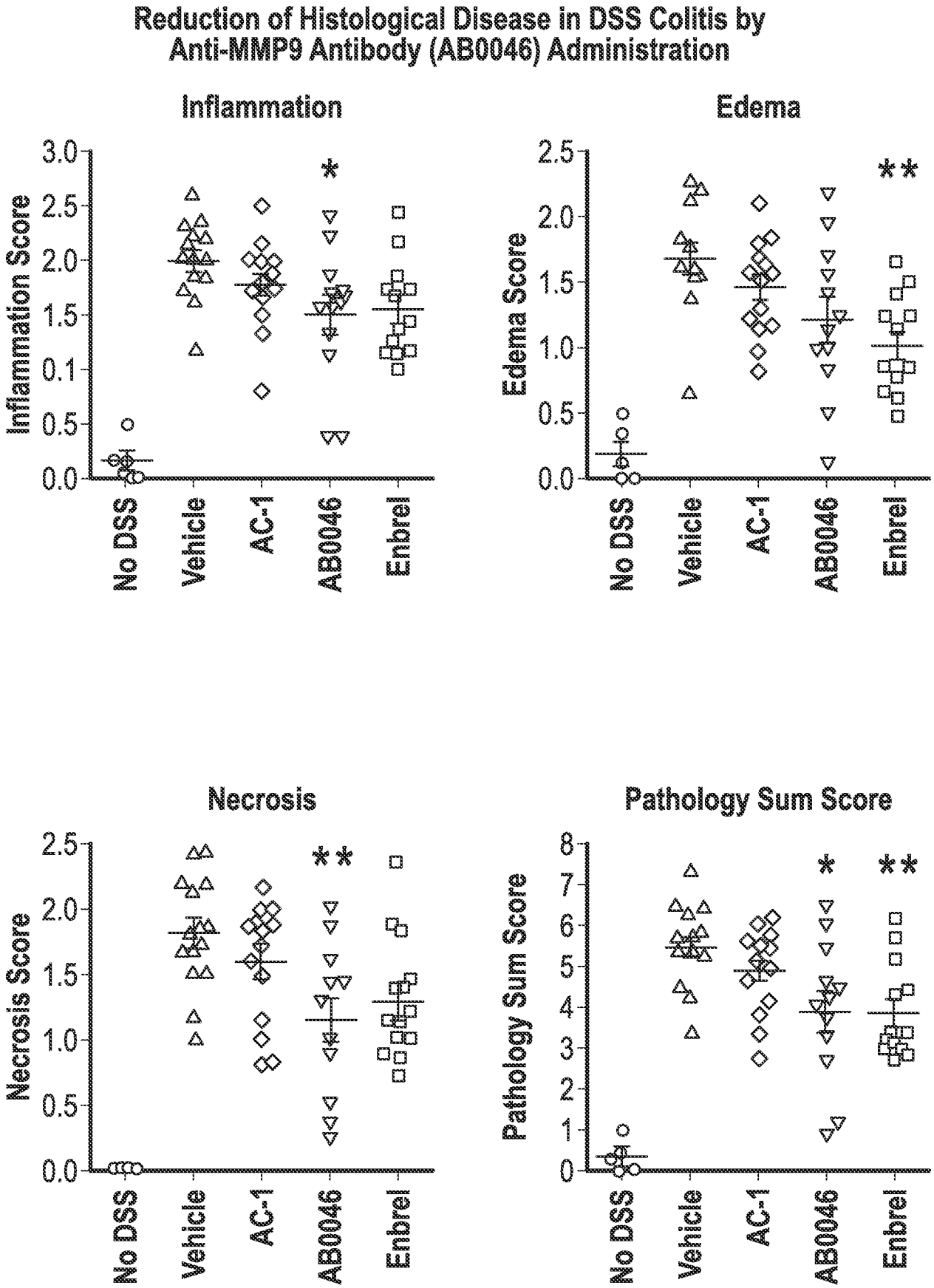

Reduction of Histological Disease in DSS Colitis by Anti-MMP9 Antibody (AB0046) Administration
Inflammation
Inflammation Score
3.0
2.5
2.0
1.5
0.1
0.5
0.0
No DSS
Vehicle
AC-1
AB0046
Enbrel
*
Edema
Edema Score
2.5
2.0
1.5
1.0
0.5
0.0
No DSS
Vehicle
AC-1
AB0046
Enbrel
**
Necrosis
Necrosis Score
2.5
2.0
1.5
1.0
0.5
0.0
No DSS
Vehicle
AC-1
AB0046
Enbrel
**
Pathology Sum Score
Pathology Sum Score
8
7
6
5
4
3
2
1
0
No DSS
Vehicle
AC-1
AB0046
Enbrel
*
**

FIG. 8

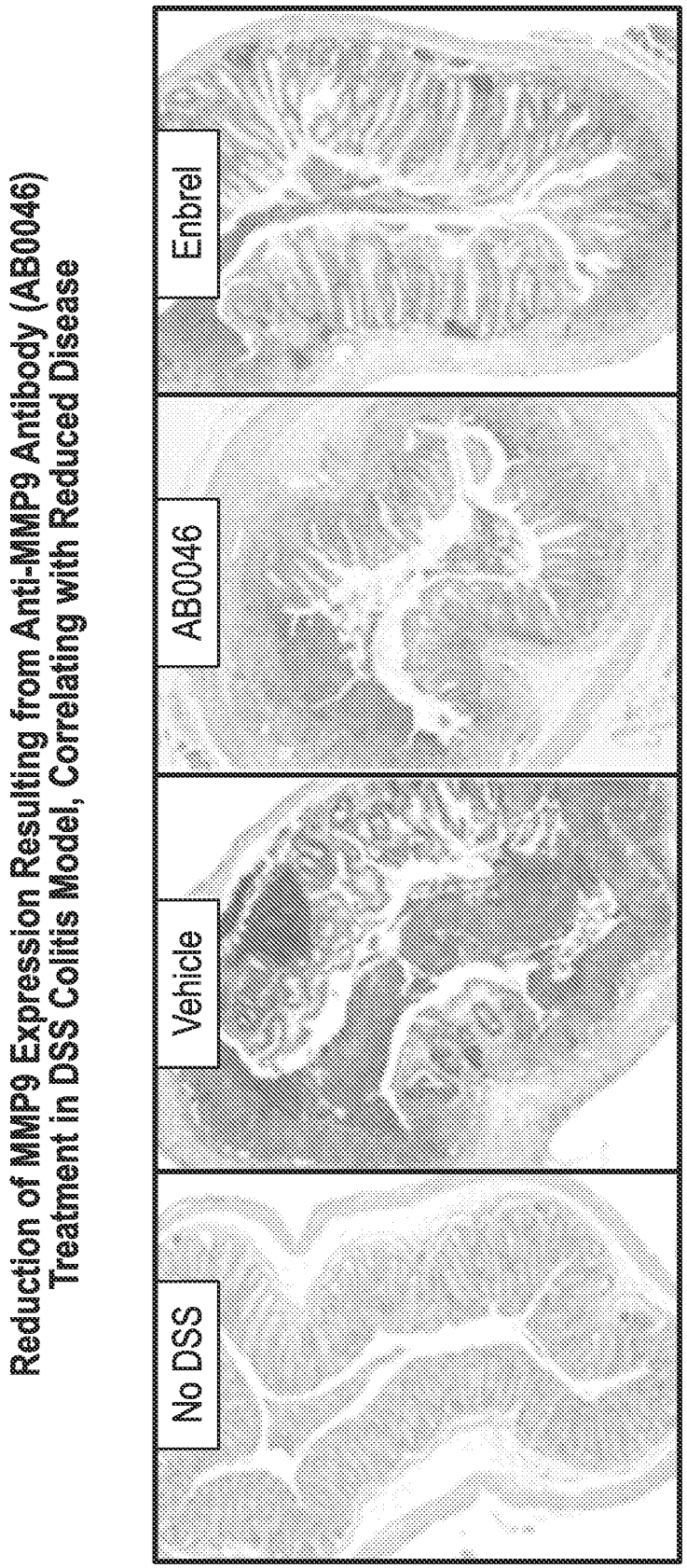

Reduction of MMP9 Expression Resulting from Anti-MMP9 Antibody (AB0046)
Treatment in DSS Colitis Model, Correlating with Reduced Disease
No DSS
Vehicle
AB0046
Enbrel

FIG. 9

Protection Against Body Weight Loss and the Incidence of Diarrhea in DSS Colitis by Anti-MMP9 Antibody (AB0046)

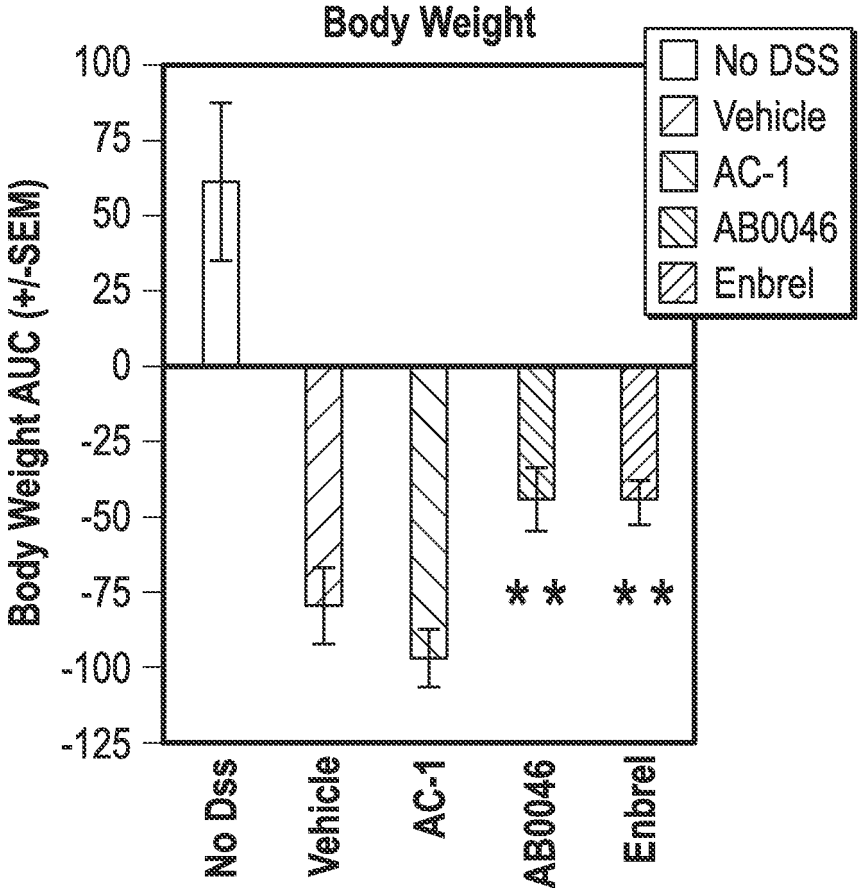



FIG. 10A

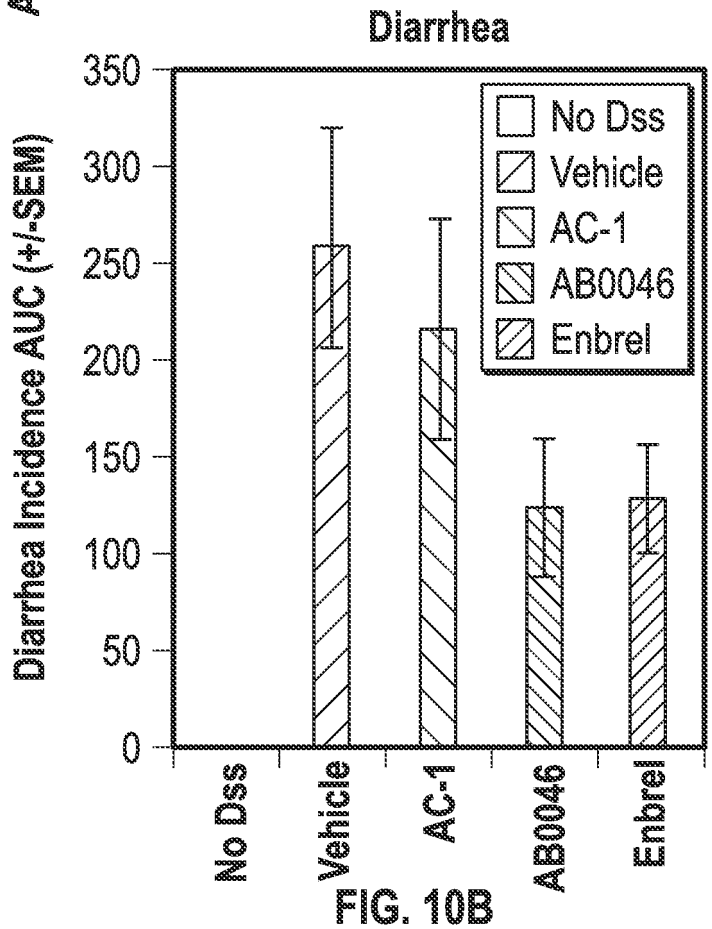



FIG. 10B

Reduction in Systemic Markers of Inflammation in DSS Colitis by Treatment with Anti-MMP9 Antibody AB0046

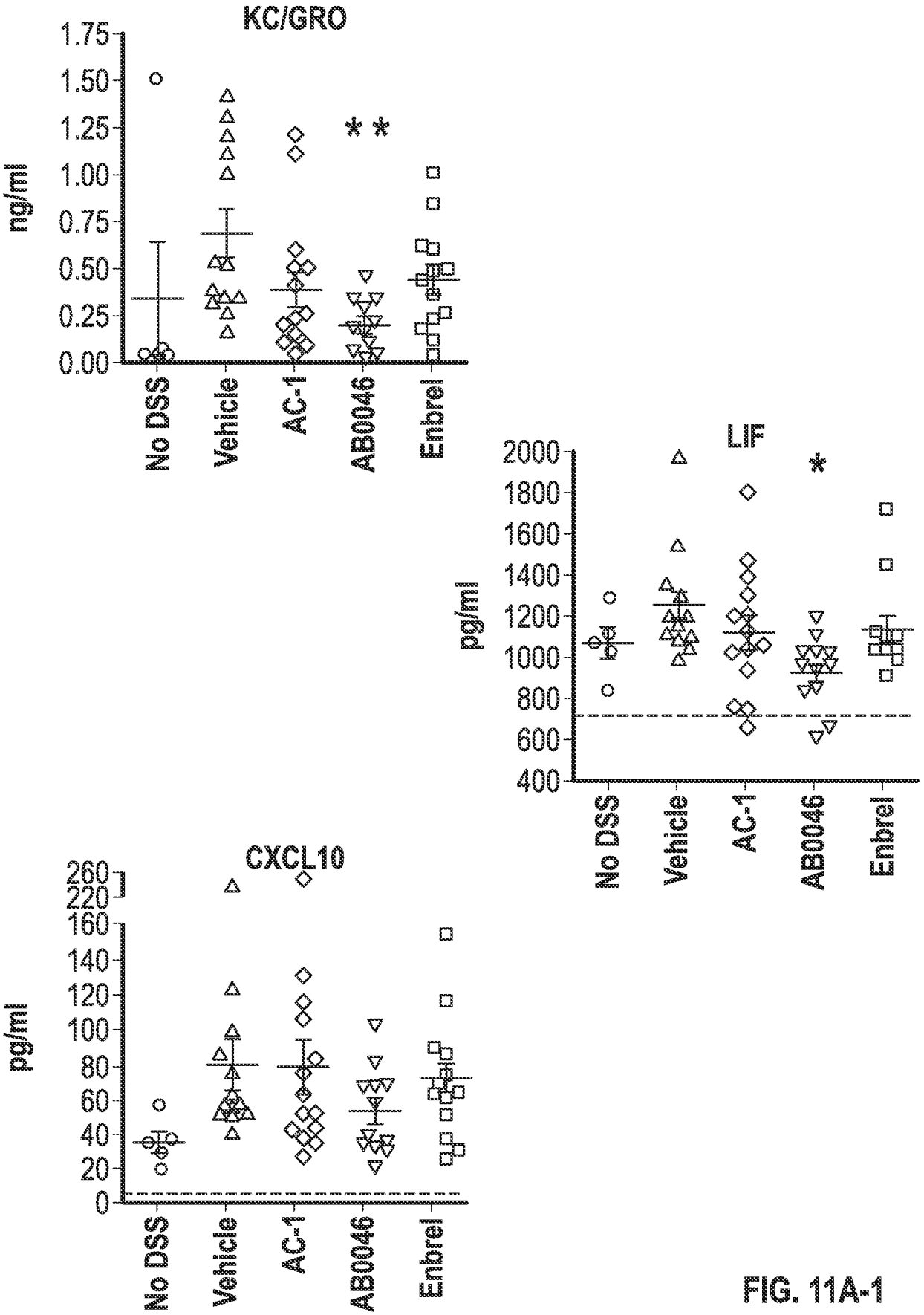



FIG. 11A-1

Reduction in Systemic Markers of Inflammation in DSS Colitis by Treatment with Anti-MMP9 Antibody AB0046

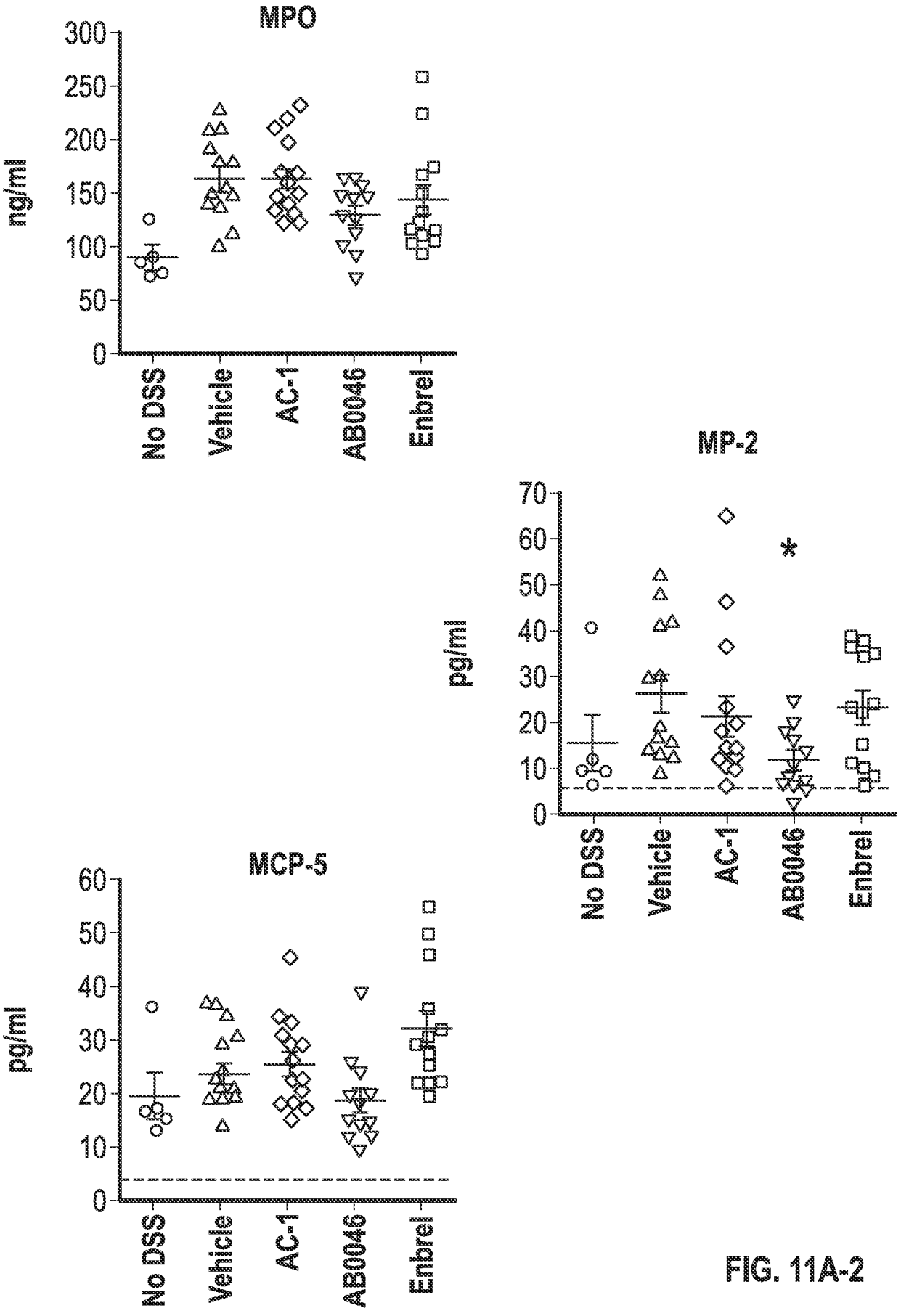



FIG. 11A-2

Additional Serum Marker Data for Murine DSS Colitis Treatment Study

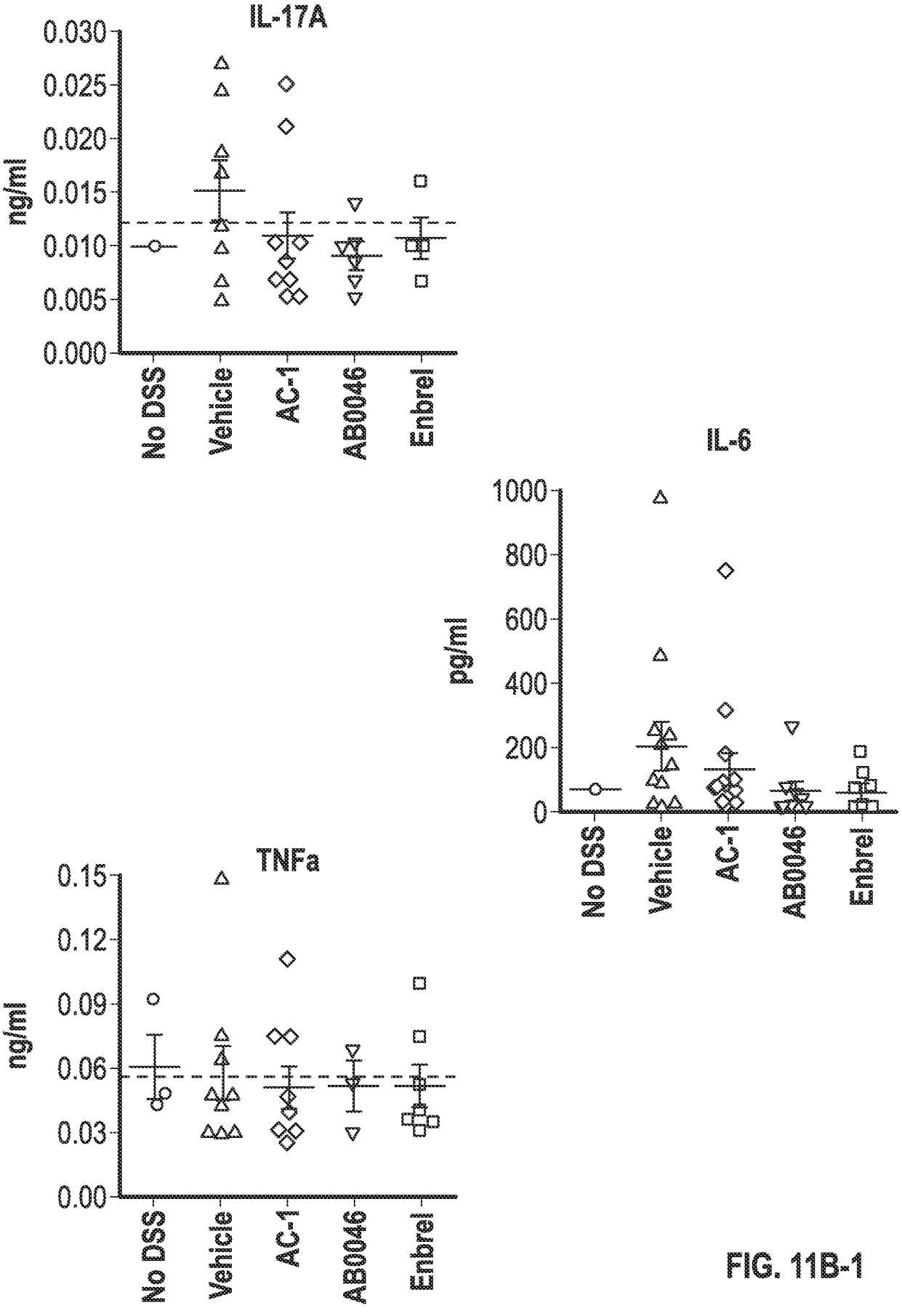



FIG. 11B-1

Additional Serum Marker Data for Murine DSS Colitis Treatment Study

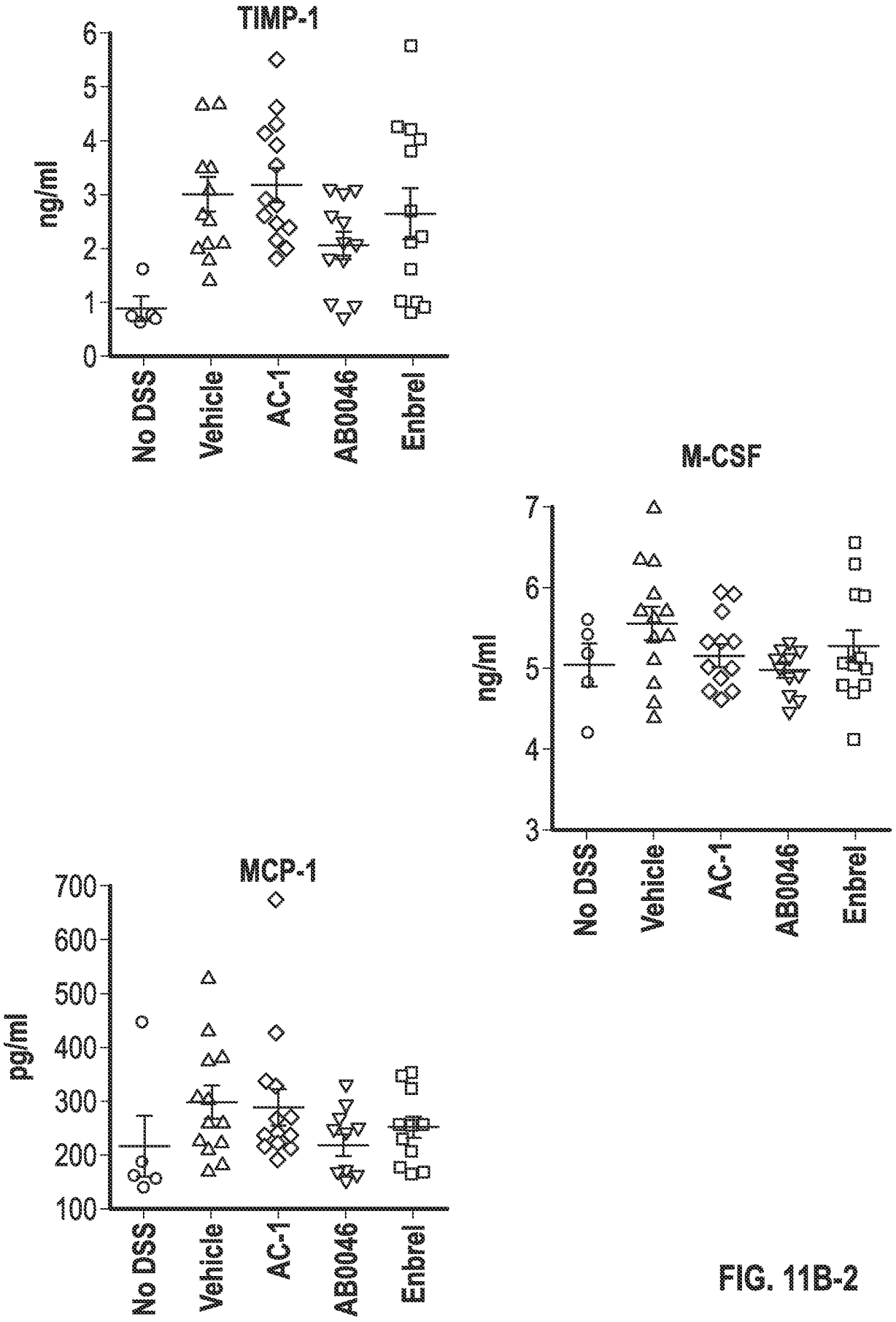



FIG. 11B-2

Additional Serum Marker Data for Murine DSS Colitis Treatment Study

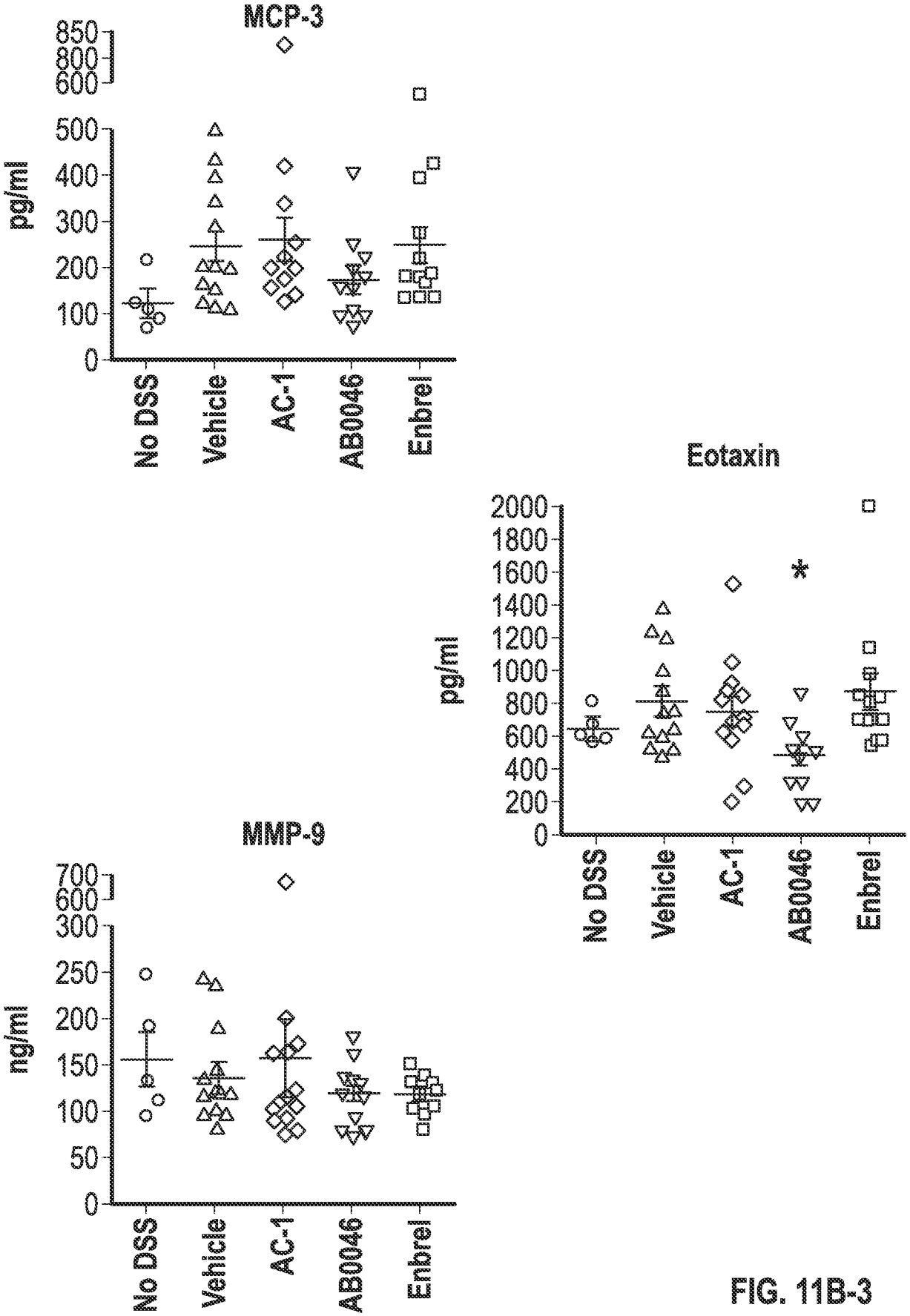
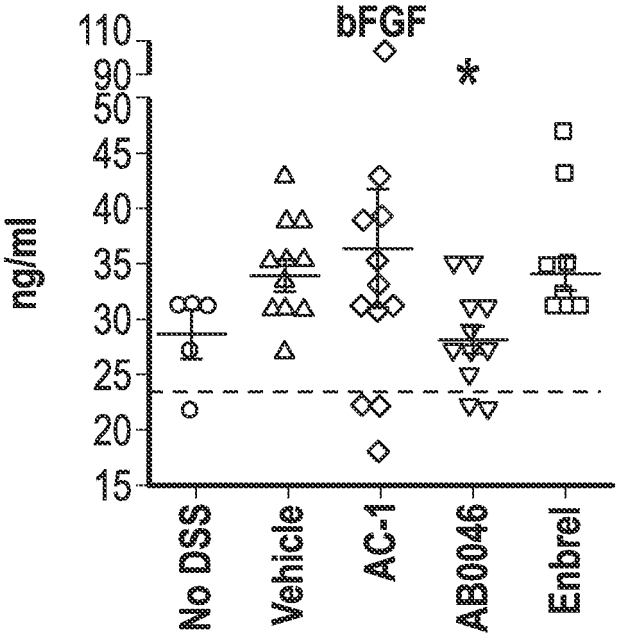



FIG. 11B-3

Additional Serum Marker Data for Murine DSS Colitis Treatment Study



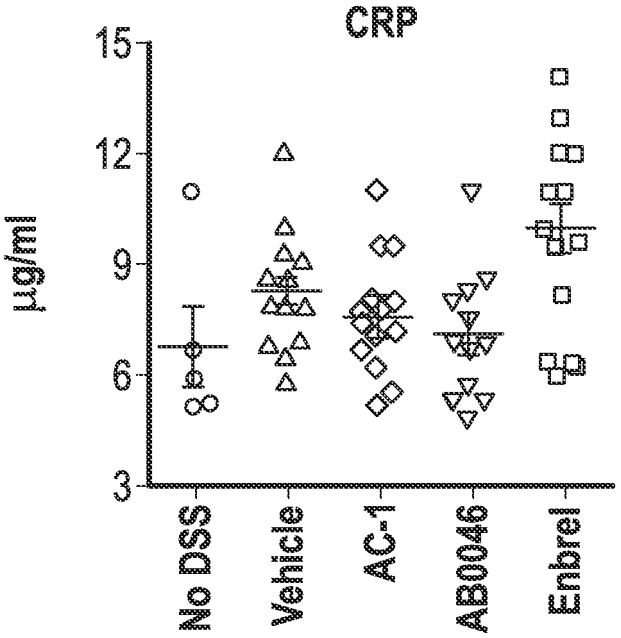




FIG. 11B-4

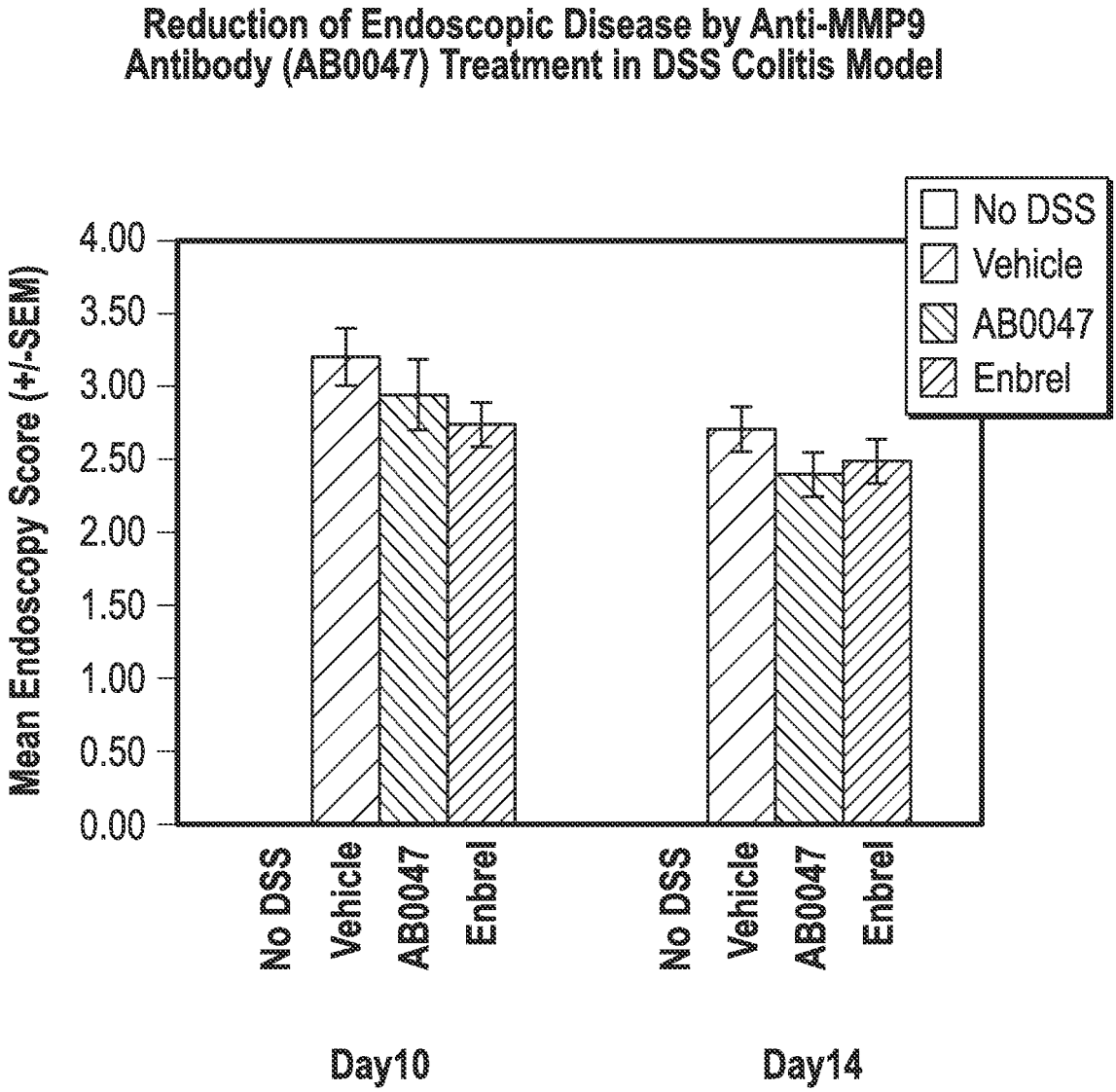

Reduction of Endoscopic Disease by Anti-MMP9 Antibody (AB0047) Treatment in DSS Colitis Model
Mean Endoscopy Score (+/-SEM)
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
No DSS
Vehicle
AB0047
Enbrel
No DSS
Vehicle
AB0047
Enbrel
Day10
Day14

FIG. 12A

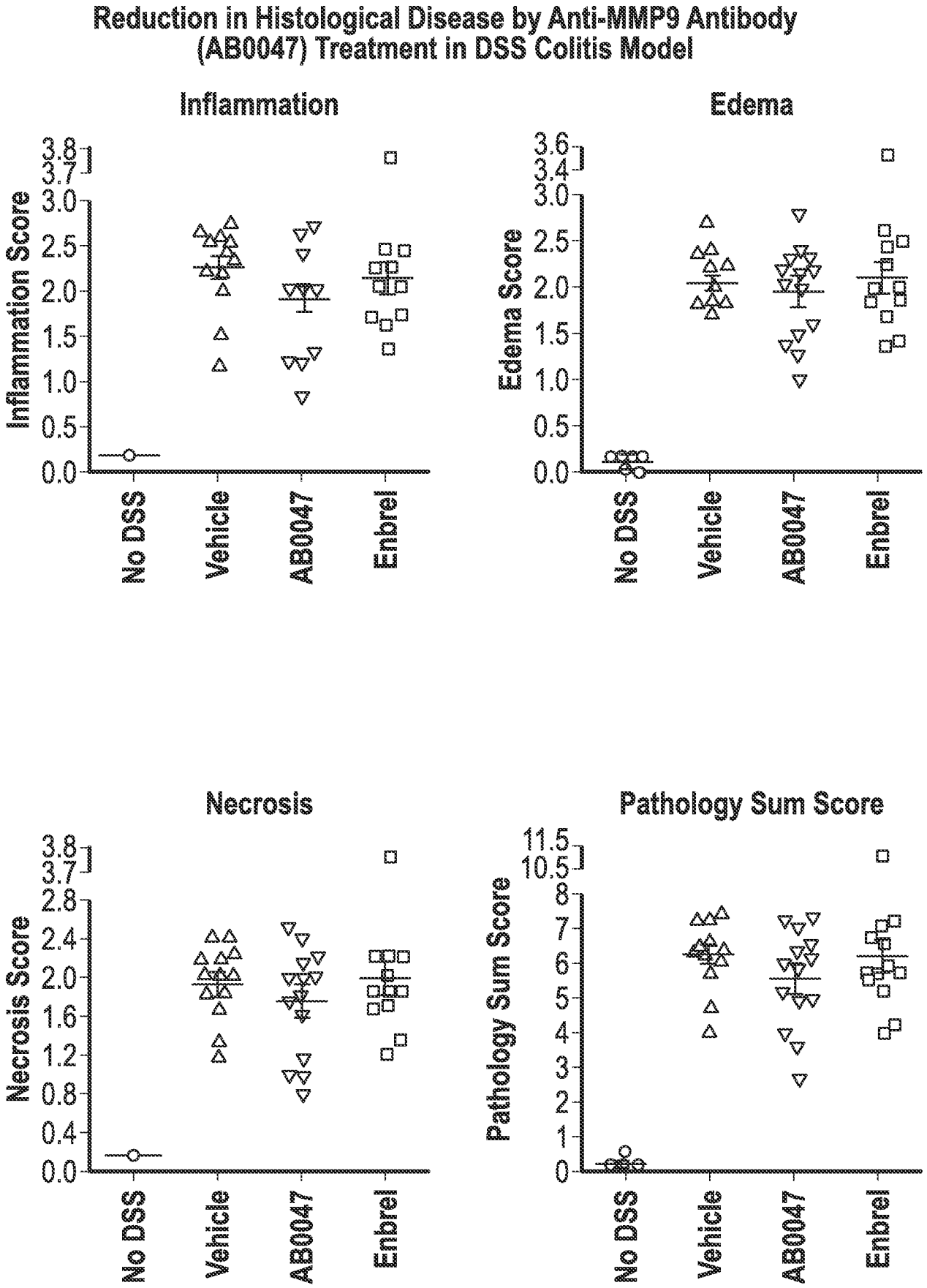

Reduction in Histological Disease by Anti-MMP9 Antibody (AB0047) Treatment in DSS Colitis Model
Inflammation
Inflammation Score
Edema
Edema Score
Necrosis
Necrosis Score
Pathology Sum Score
Pathology Sum Score
No DSS
Vehicle
AB0047
Enbrel

FIG. 12B

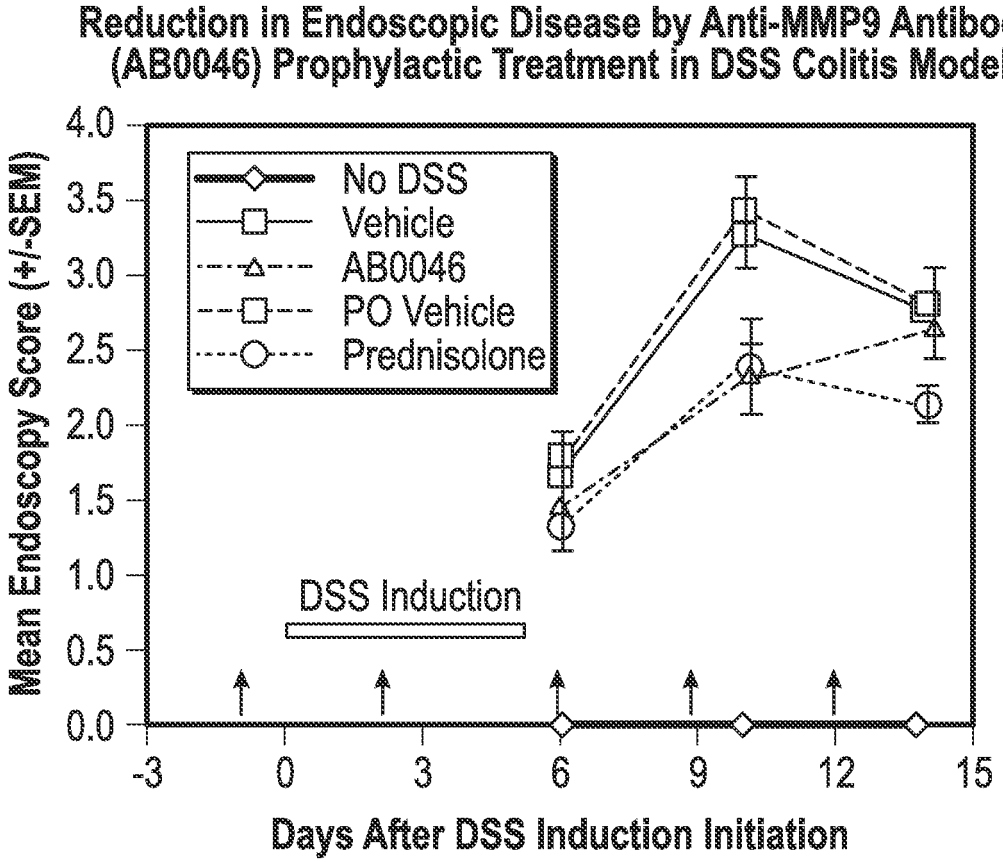



FIG. 13A

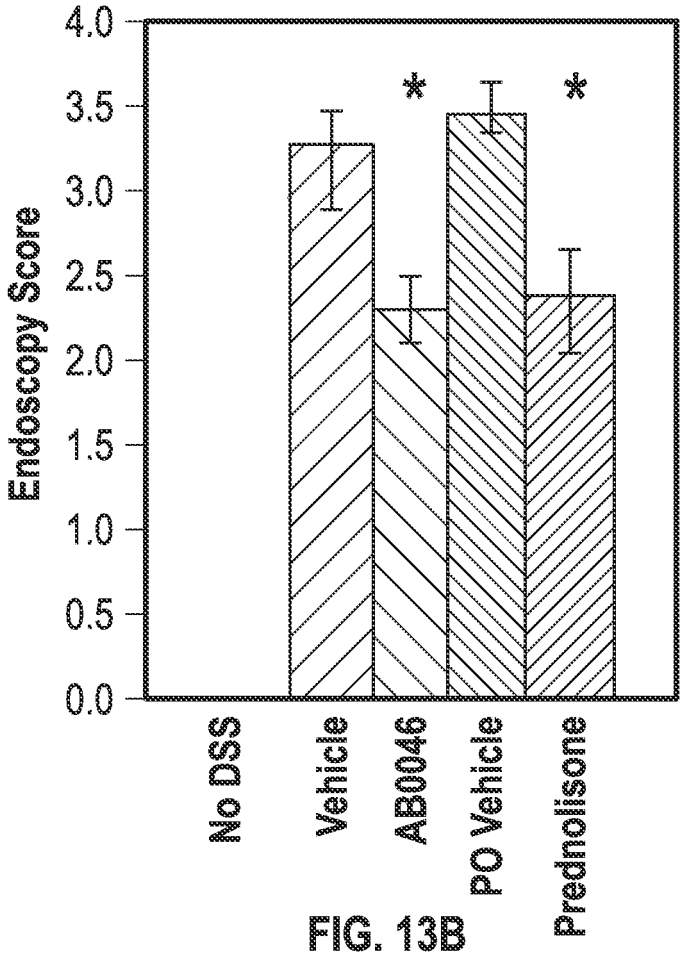



FIG. 13B

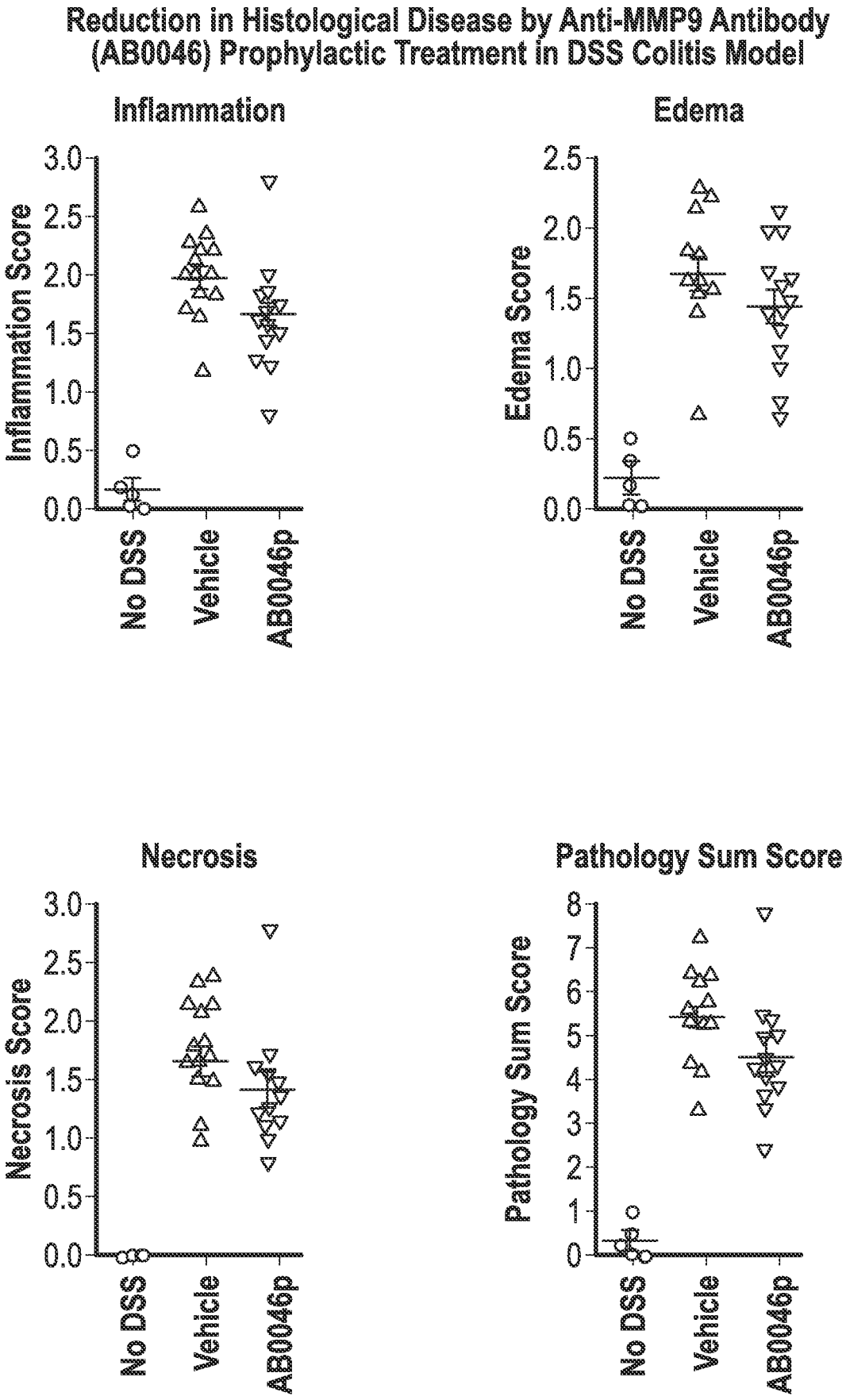

Reduction in Histological Disease by Anti-MMP9 Antibody (AB0046) Prophylactic Treatment in DSS Colitis Model
Inflammation
Inflammation Score
3.0
2.5
2.0
1.5
1.0
0.5
0.0
No DSS
Vehicle
AB0046p
Edema
Edema Score
2.5
2.0
1.5
1.0
0.5
0.0
No DSS
Vehicle
AB0046p
Necrosis
Necrosis Score
3.0
2.5
2.0
1.5
1.0
0.5
0.0
No DSS
Vehicle
AB0046p
Pathology Sum Score
Pathology Sum Score
8
7
6
5
4
3
2
1
0
No DSS
Vehicle
AB0046p

FIG. 14

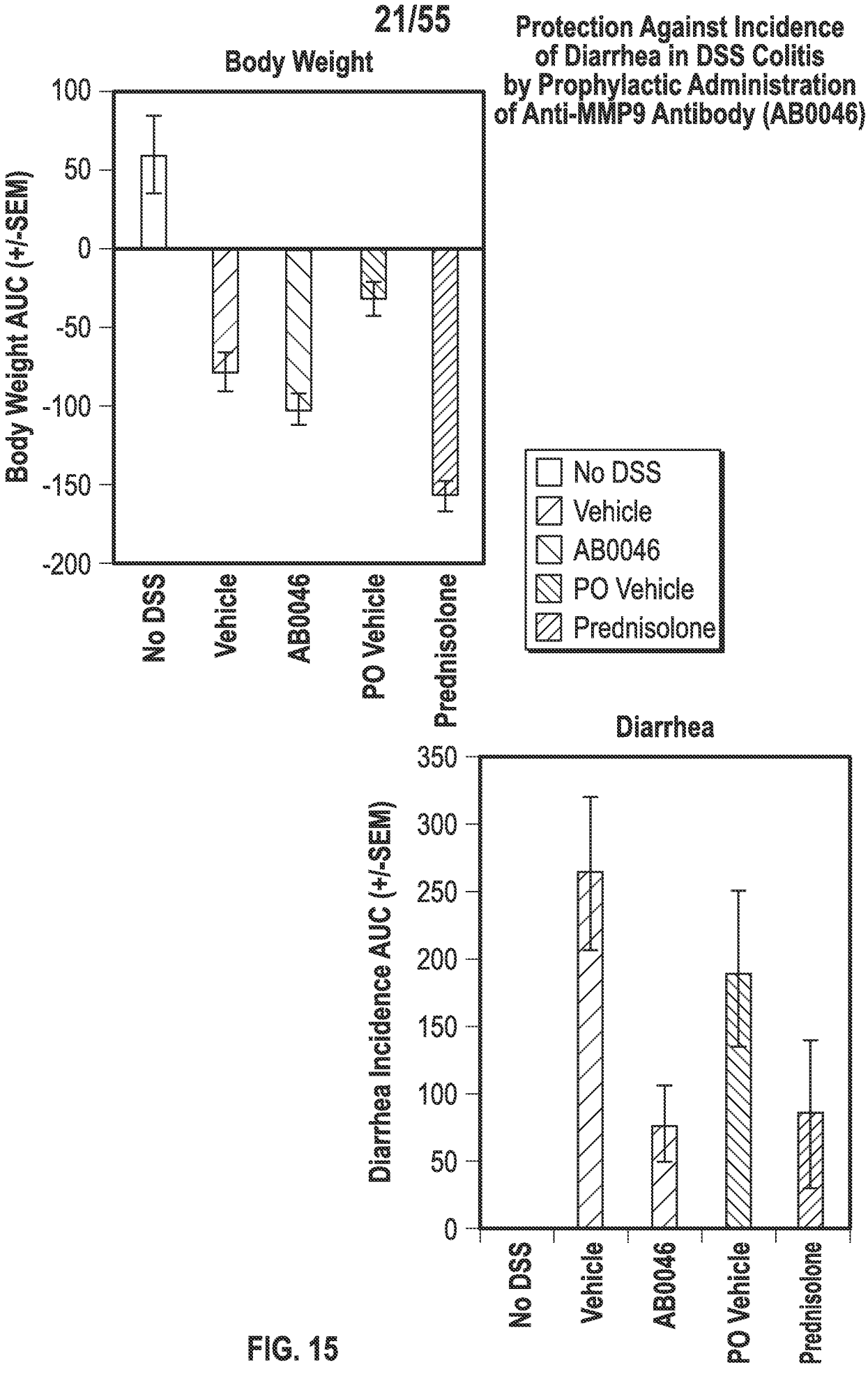
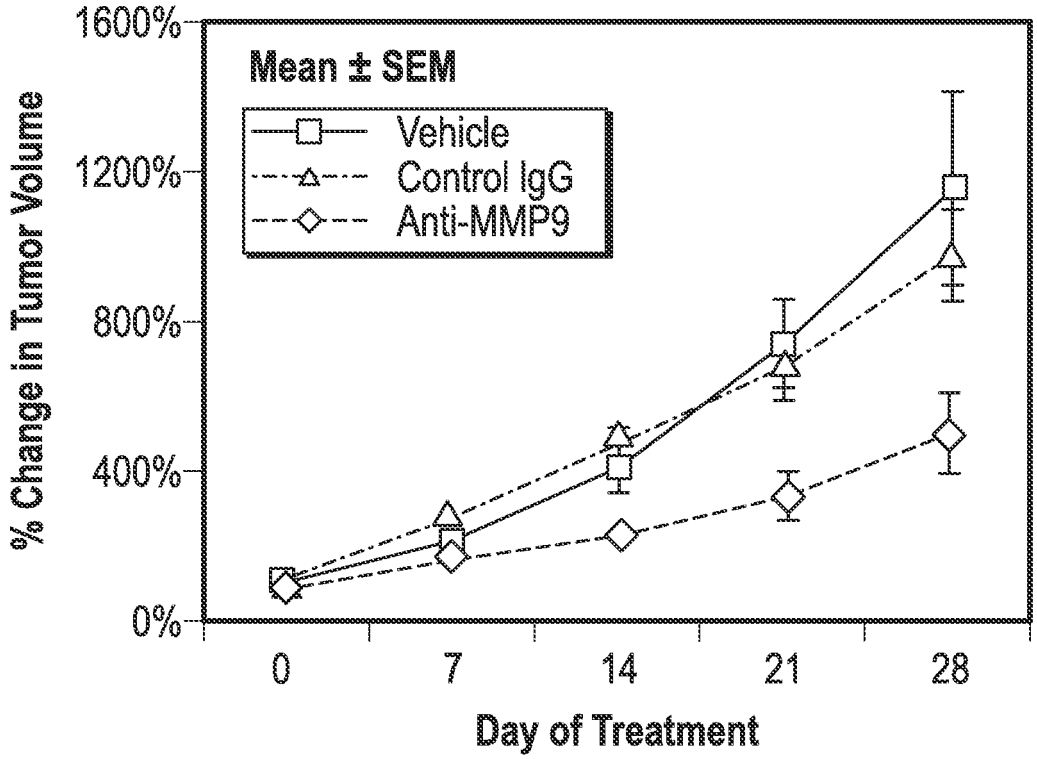

Protection Against Incidence of Diarrhea in DSS Colitis by Prophylactic Administration of Anti-MMP9 Antibody (AB0046)
Body Weight
Body Weight AUC (+/-SEM)
100
50
0
-50
-100
-150
-200
No DSS
Vehicle
AB0046
PO Vehicle
Prednisolone
No DSS
Vehicle
AB0046
PO Vehicle
Prednisolone
Diarrhea
Diarrhea Incidence AUC (+/-SEM)
350
300
250
200
150
100
50
0
No DSS
Vehicle
AB0046
PO Vehicle
Prednisolone

FIG. 15

Decrease in Primary Tumor Growth in Established Colorectal Cancer Tumorigenesis Model with Anti-MMP9 Antibody Treatment



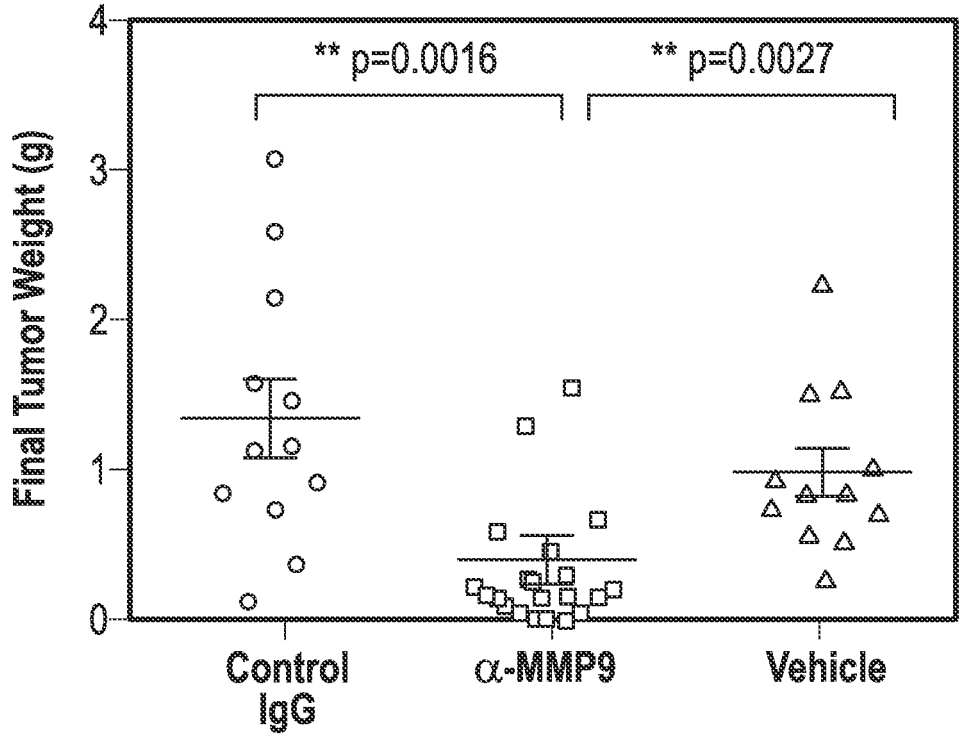
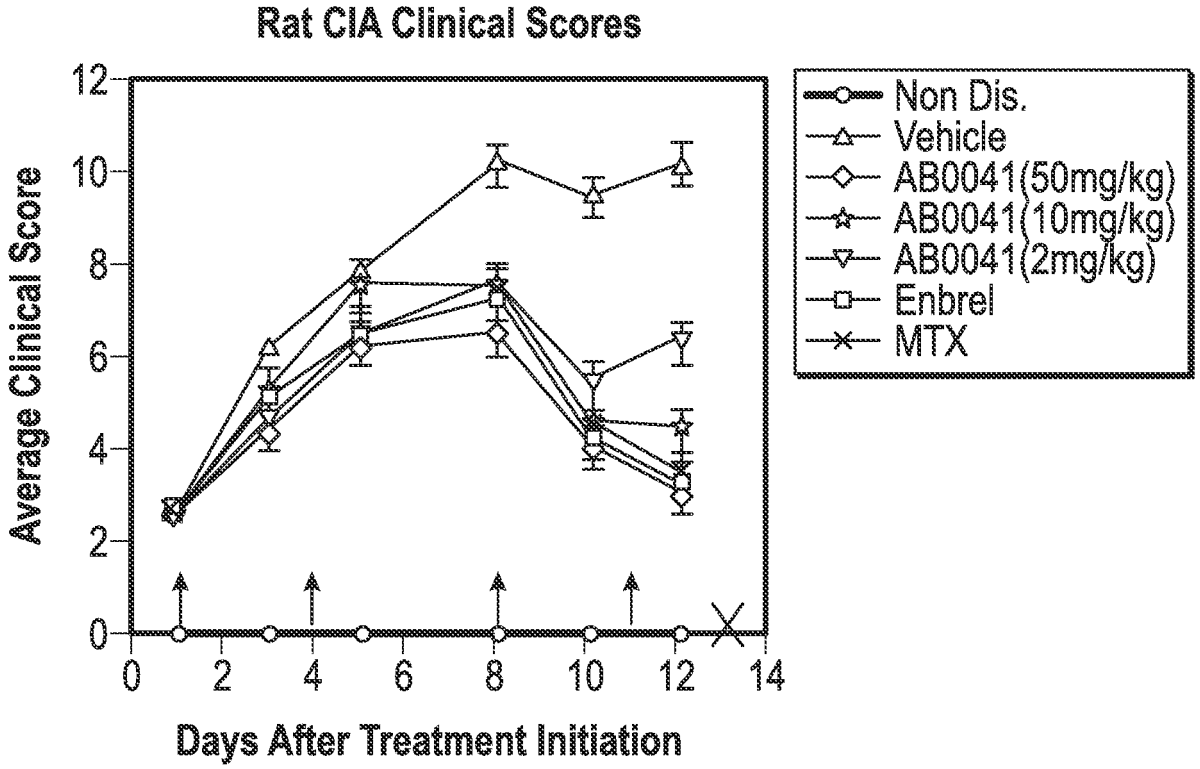




FIG. 16

Efficacy of Murine Surrogate Anti-MMP9 (AB0046) and Anti-human MMP9 (AB0041) Antibodies in Mouse and Rat CIA Models of Rheumatoid Arthritis



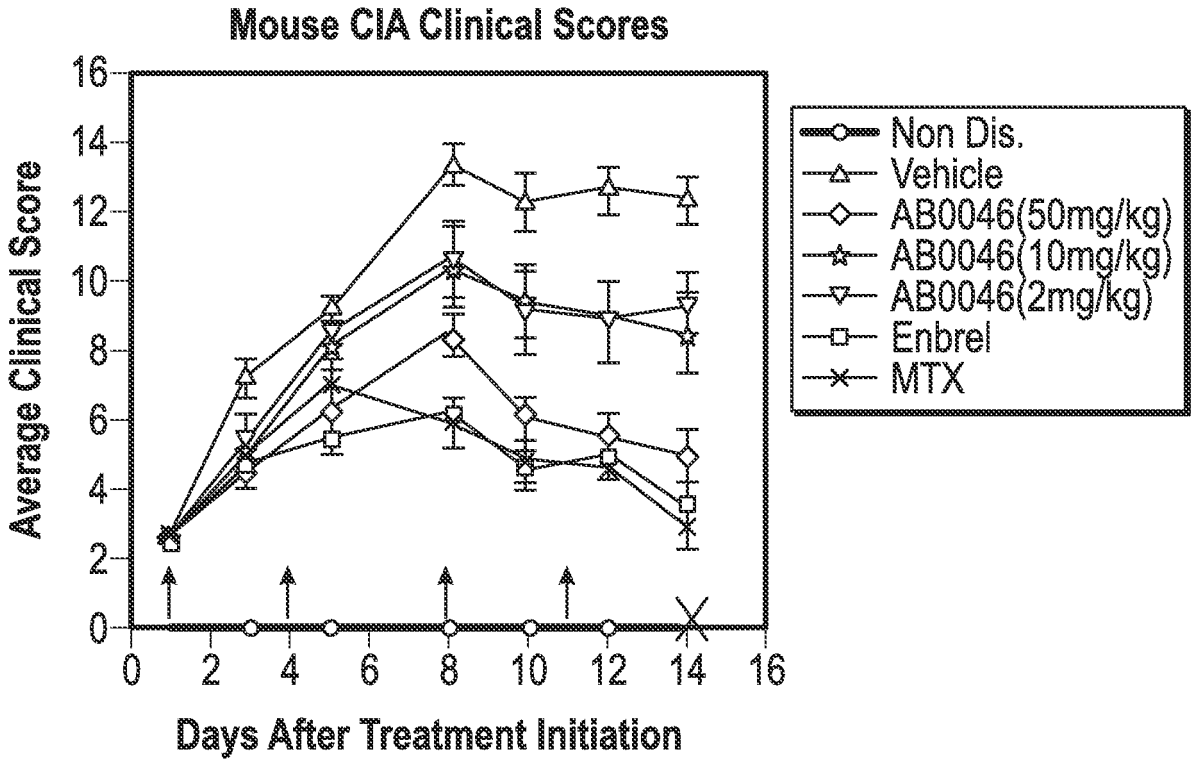




FIG. 17A-1

Efficacy of Murine Surrogate Anti-MMP9 (AB0046) and Anti-human MMP9 (AB0041) Antibodies in Mouse and Rat CIA Models of Rheumatoid Arthritis

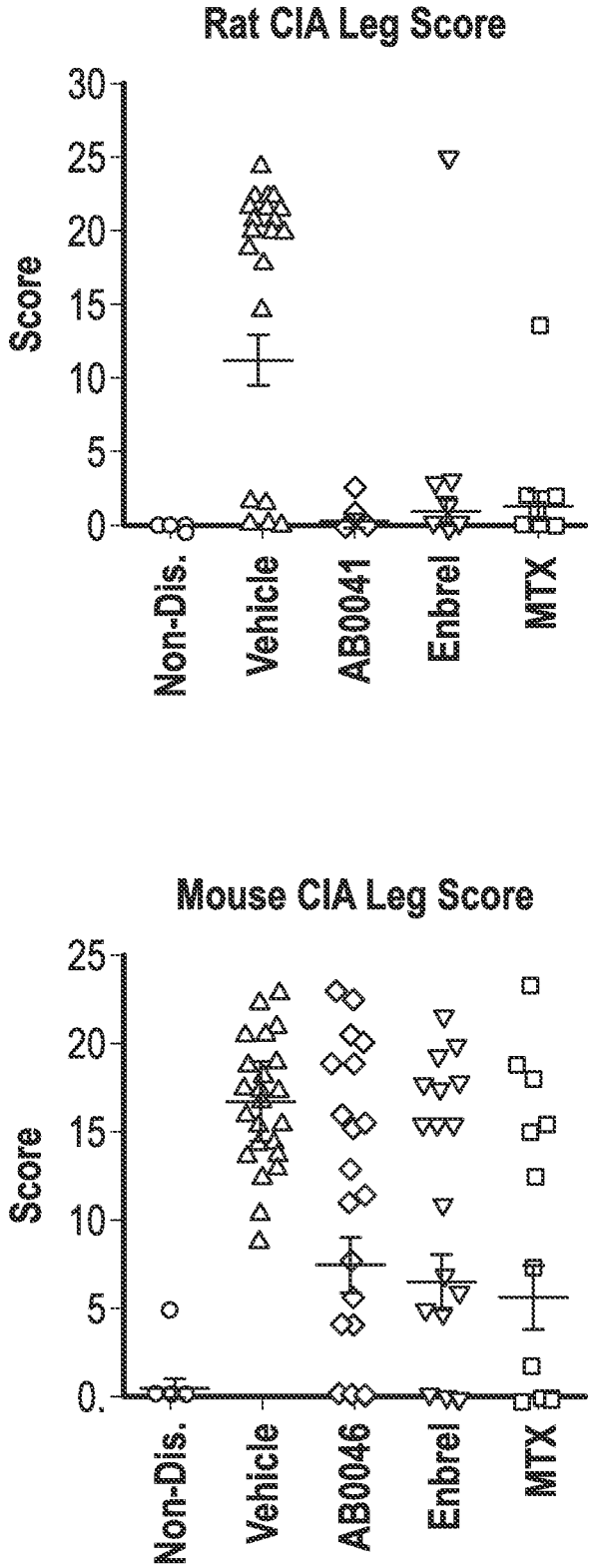
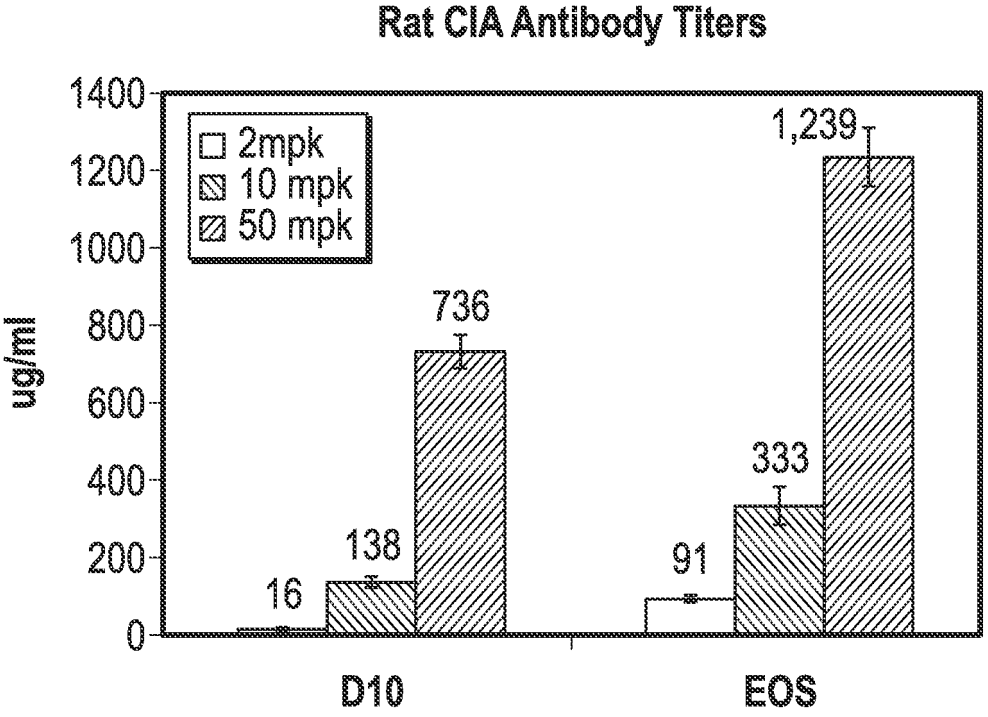



FIG. 17A-2

Titers of Murine Surrogate Anti-MMP9 (AB0046) and Anti-human MMP9 (AB0041) Antibodies in Mouse and Rat CIA Models of Rheumatoid Arthritis



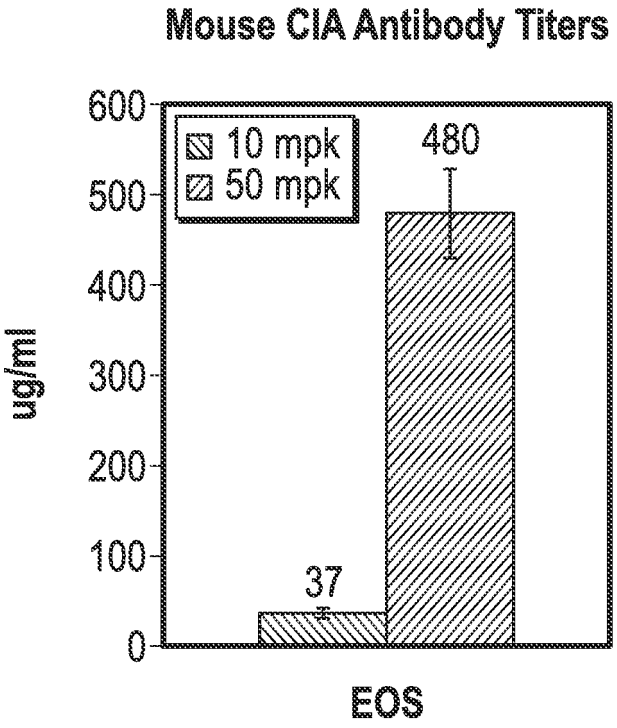




FIG. 17B

End-of-Study Serum Levels of Inflammatory Cytokines in CIA Model of Rheumatoid Arthritis in the Rat

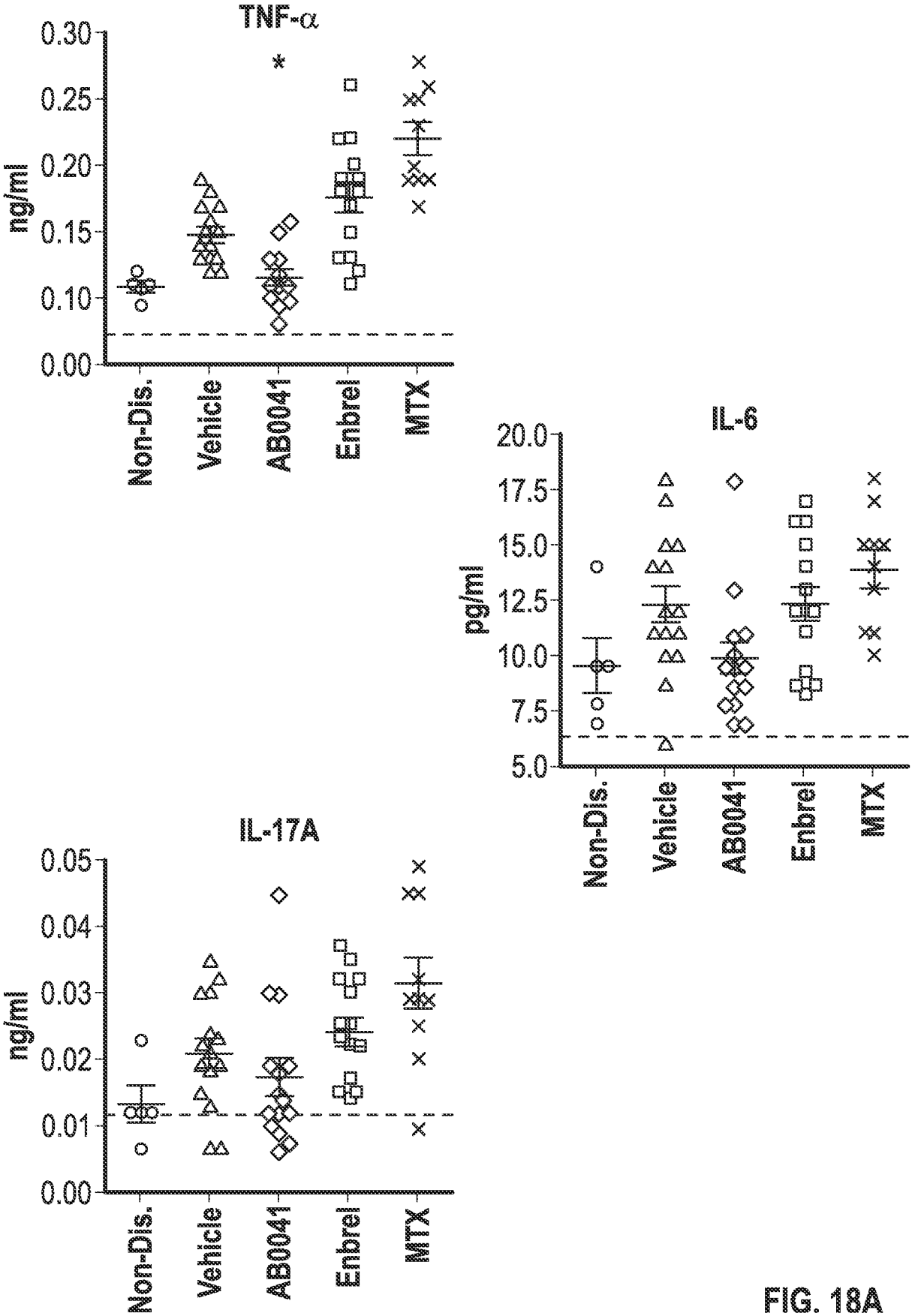



FIG. 18A

End-of-Study Serum Levels of Inflammatory Cytokines in CIA Model of Rheumatoid Arthritis in the Mouse

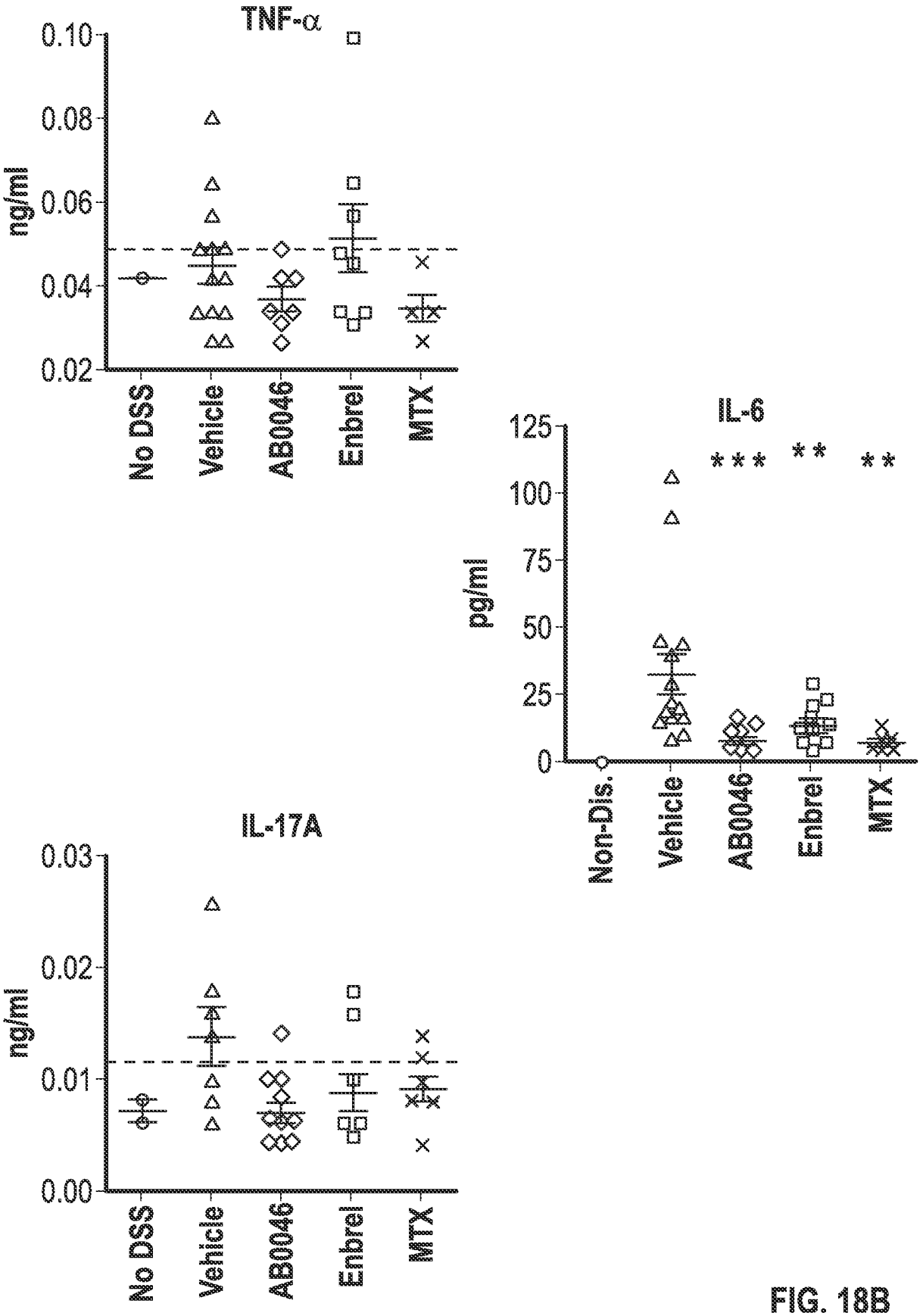



FIG. 18B

## Additional Serum Marker Data for Rat CIA Treatment Study (AB0041)

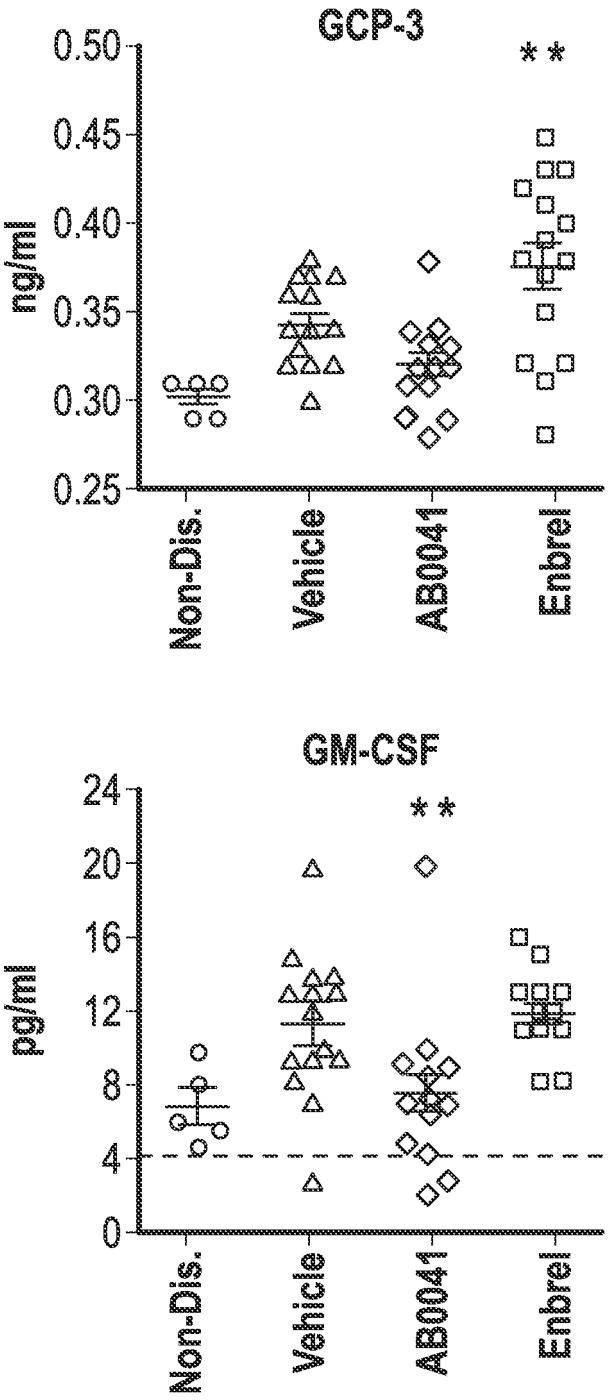



FIG. 19A-1

Additional Serum Marker Data for Rat CIA Treatment Study (AB0041)

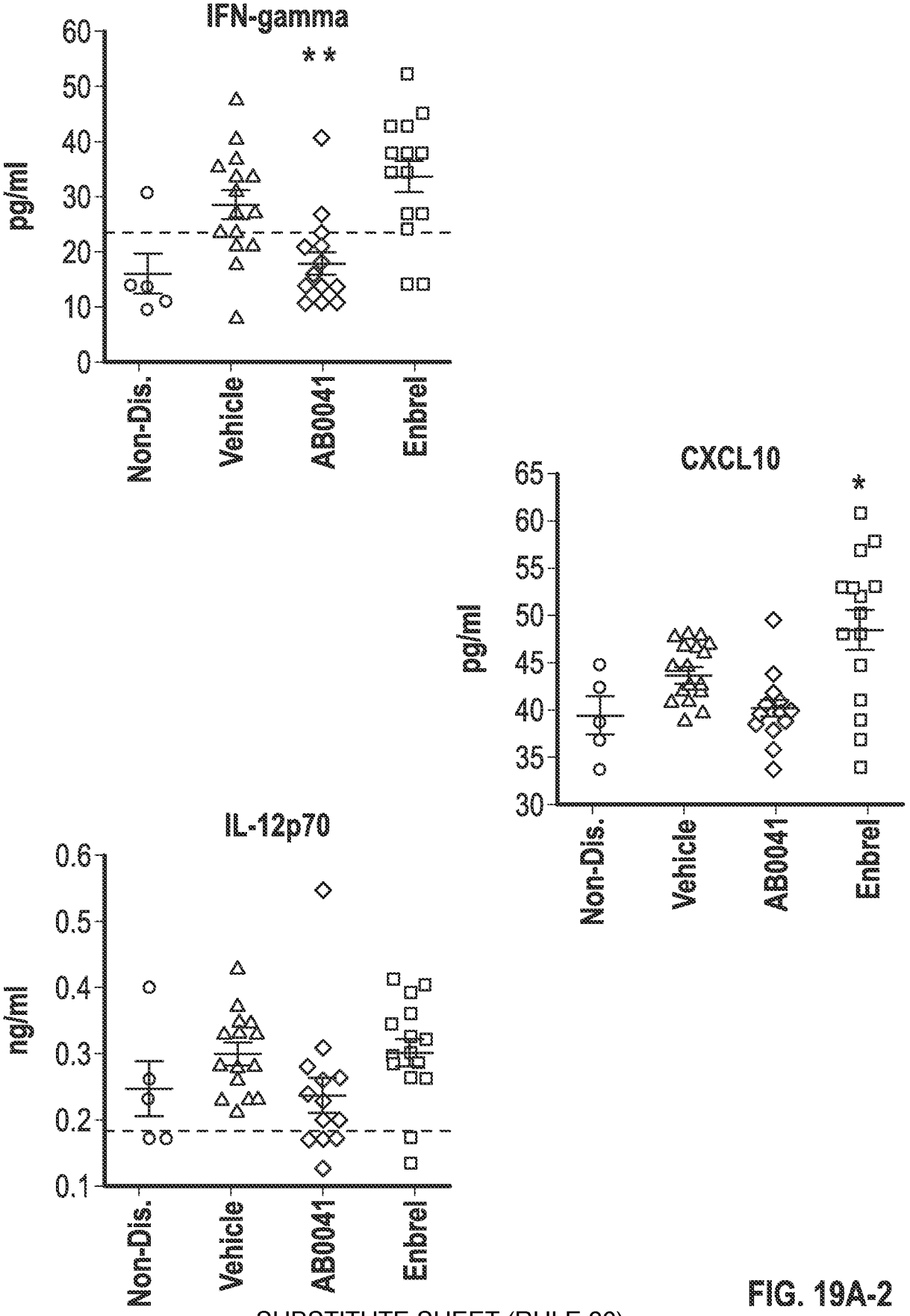



FIG. 19A-2

## Additional Serum Marker Data for Rat CIA Treatment Study (AB0041)

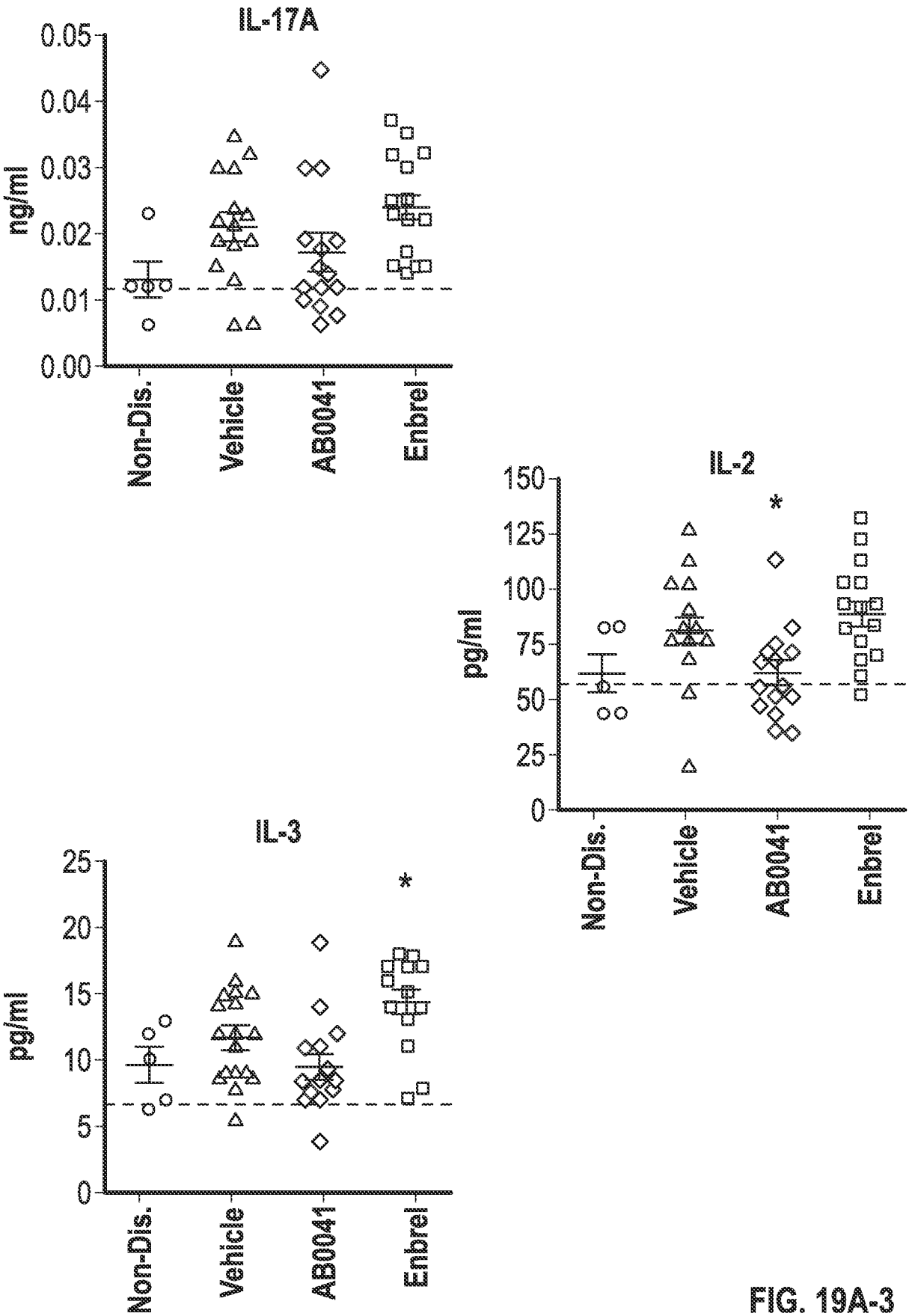



FIG. 19A-3

Additional Serum Marker Data for Rat CIA Treatment Study (AB0041)

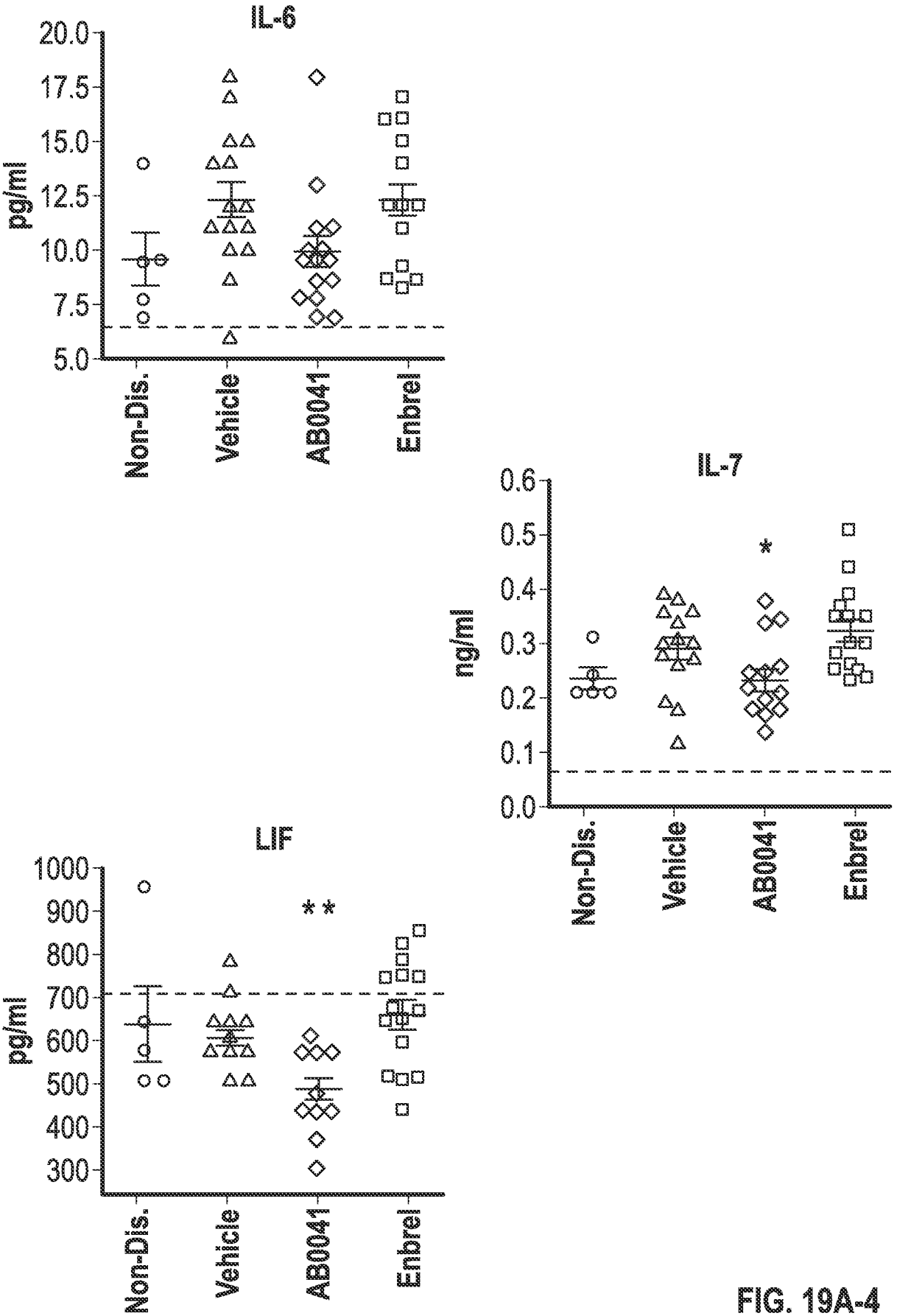



FIG. 19A-4

Additional Serum Marker Data for Rat CIA Treatment Study (AB0041)

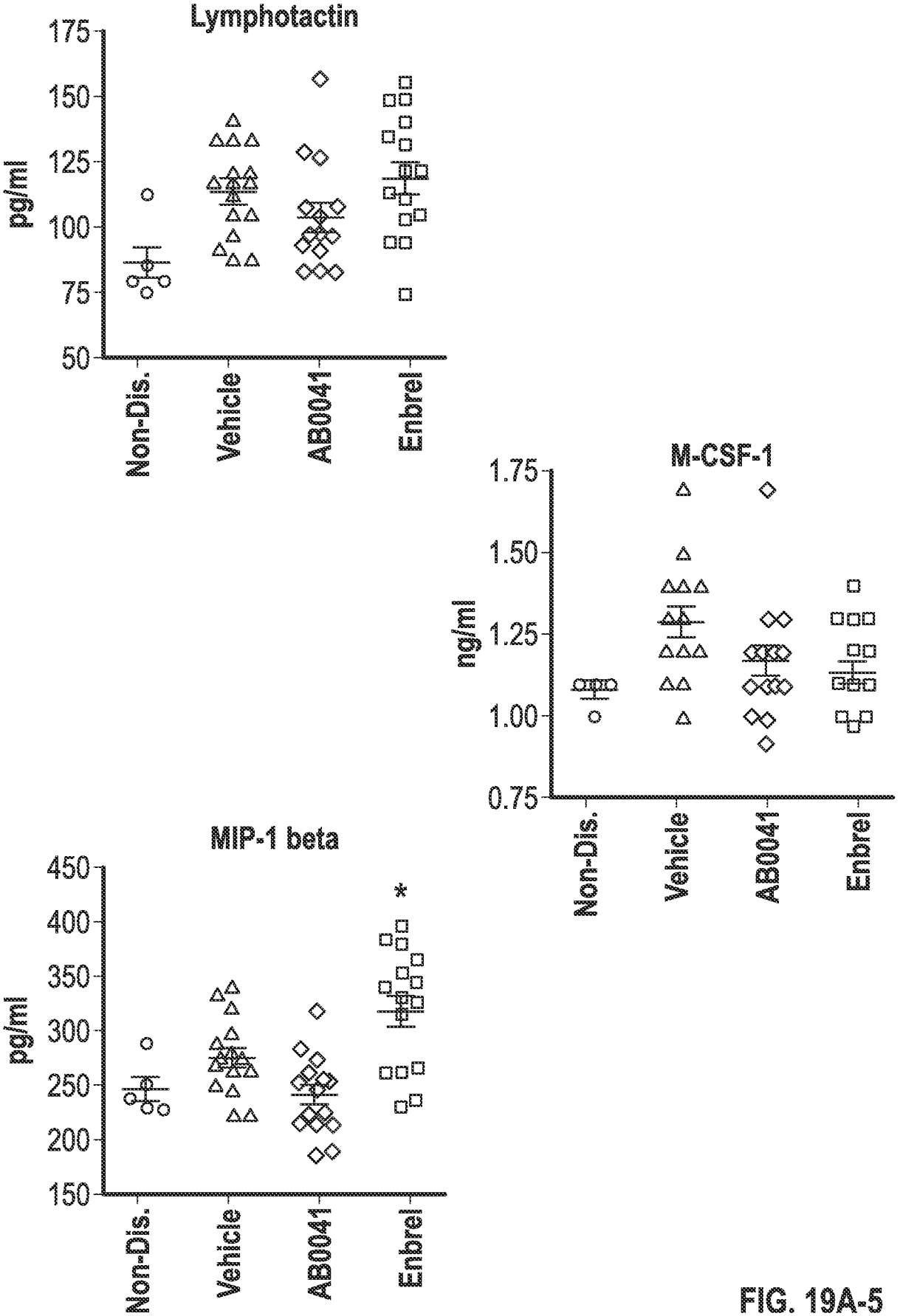



FIG. 19A-5

Additional Serum Marker Data for Rat CIA Treatment Study (AB0041)

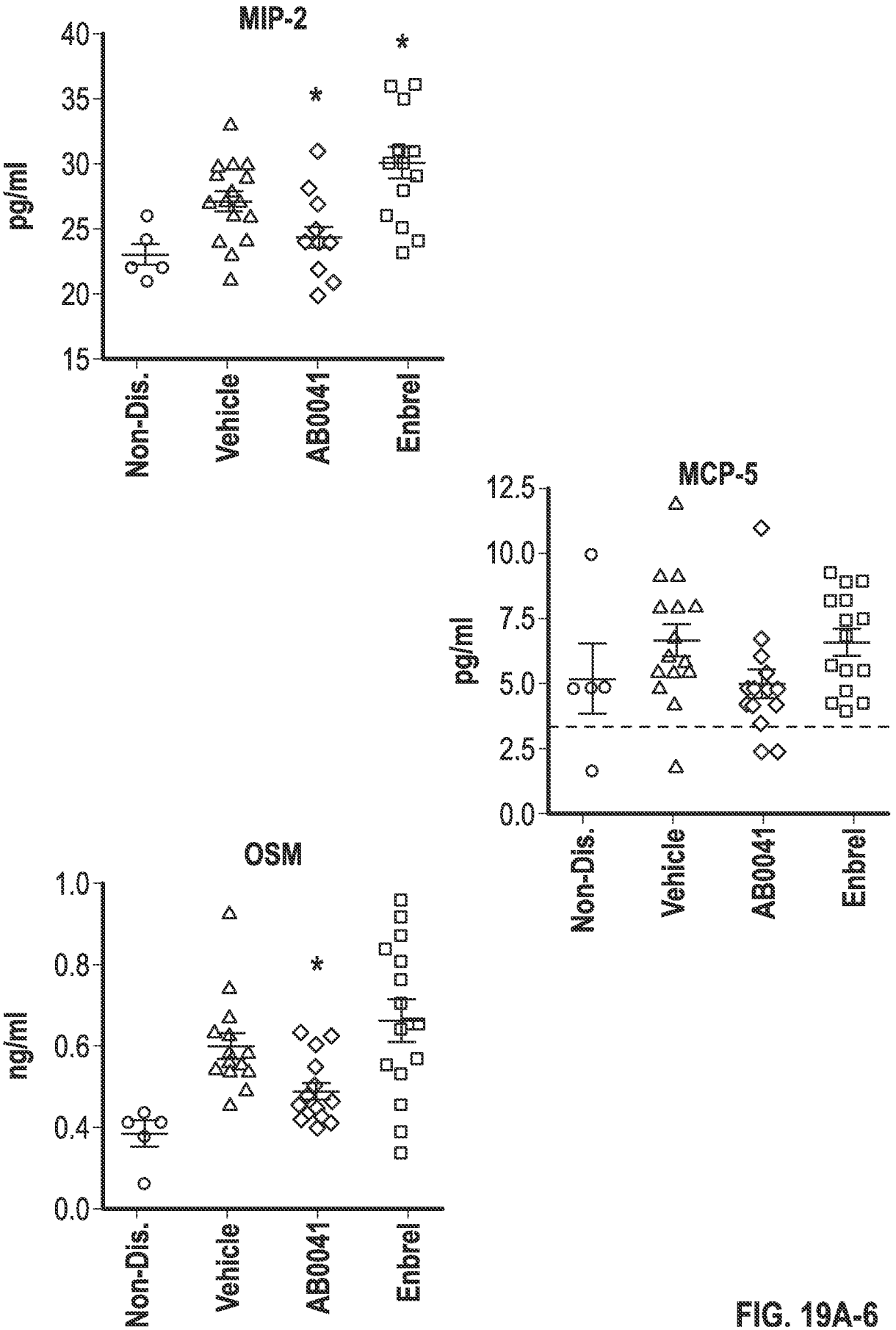



FIG. 19A-6

Additional Serum Marker Data for Rat CIA Treatment Study (AB0041)

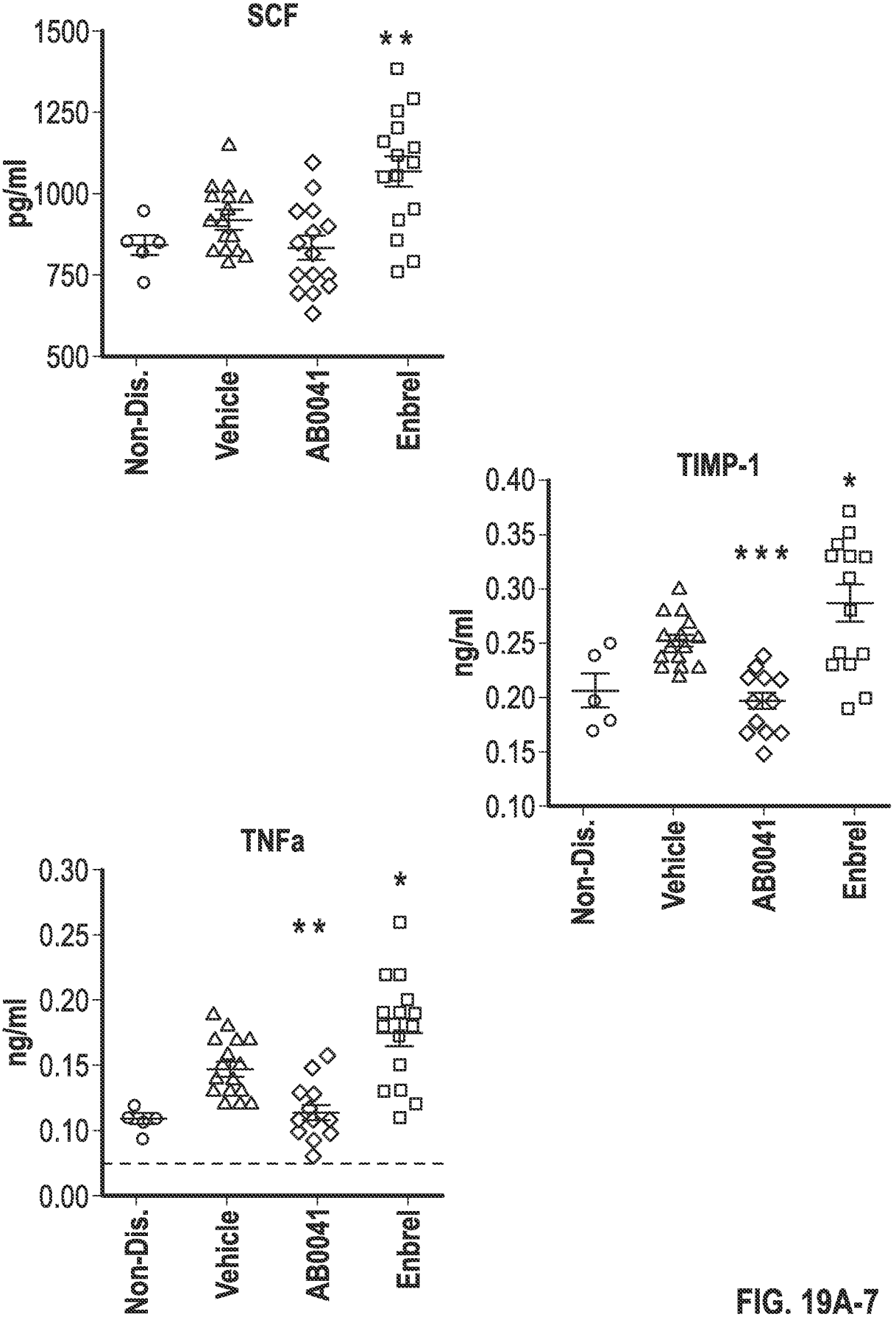



FIG. 19A-7

Additional Serum Marker Data for Mouse CIA Treatment Study (AB0046)

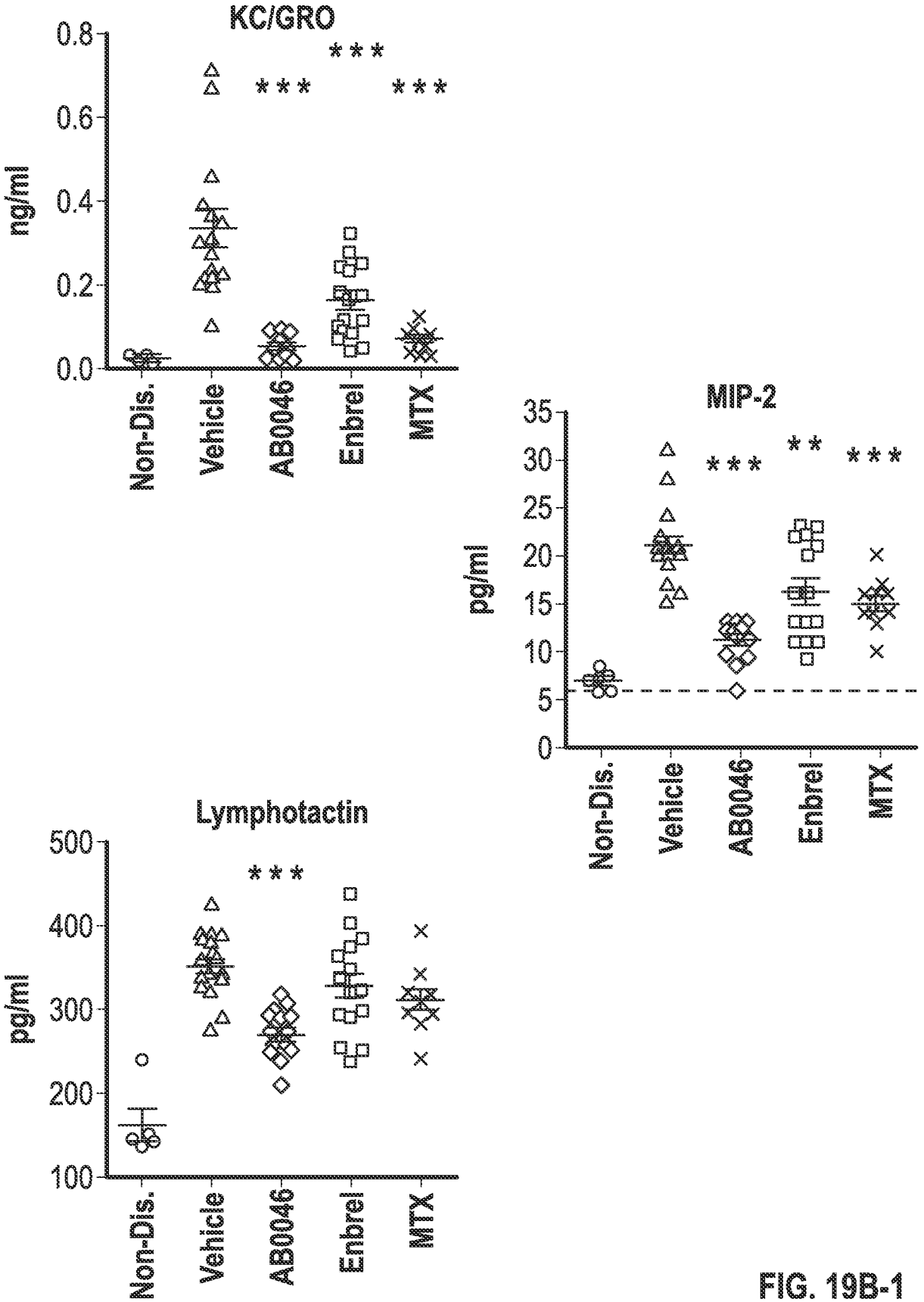



FIG. 19B-1

Additional Serum Marker Data for Mouse CIA Treatment Study (AB0046)

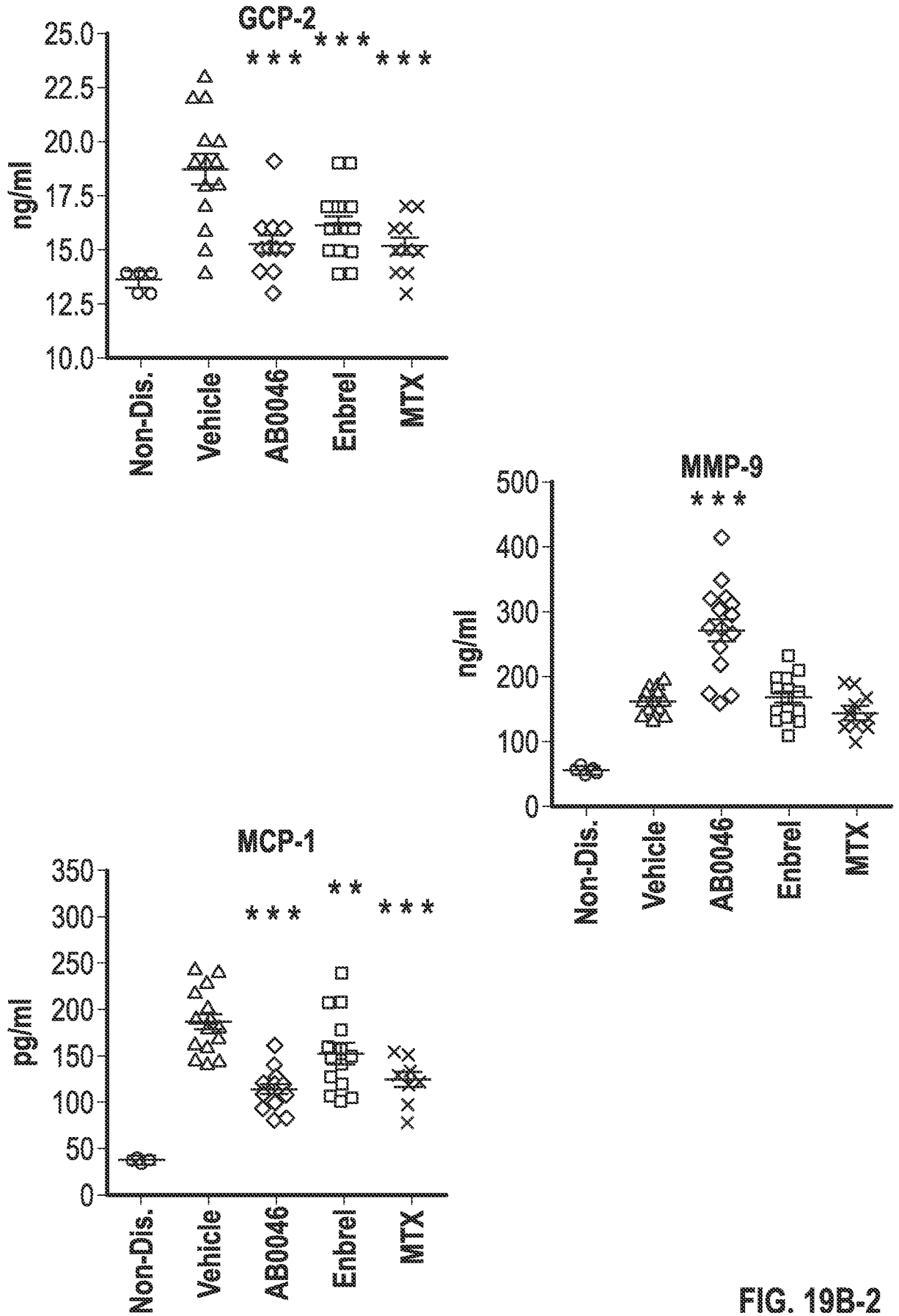



FIG. 19B-2

Additional Serum Marker Data for Mouse CIA Treatment Study (AB0046)

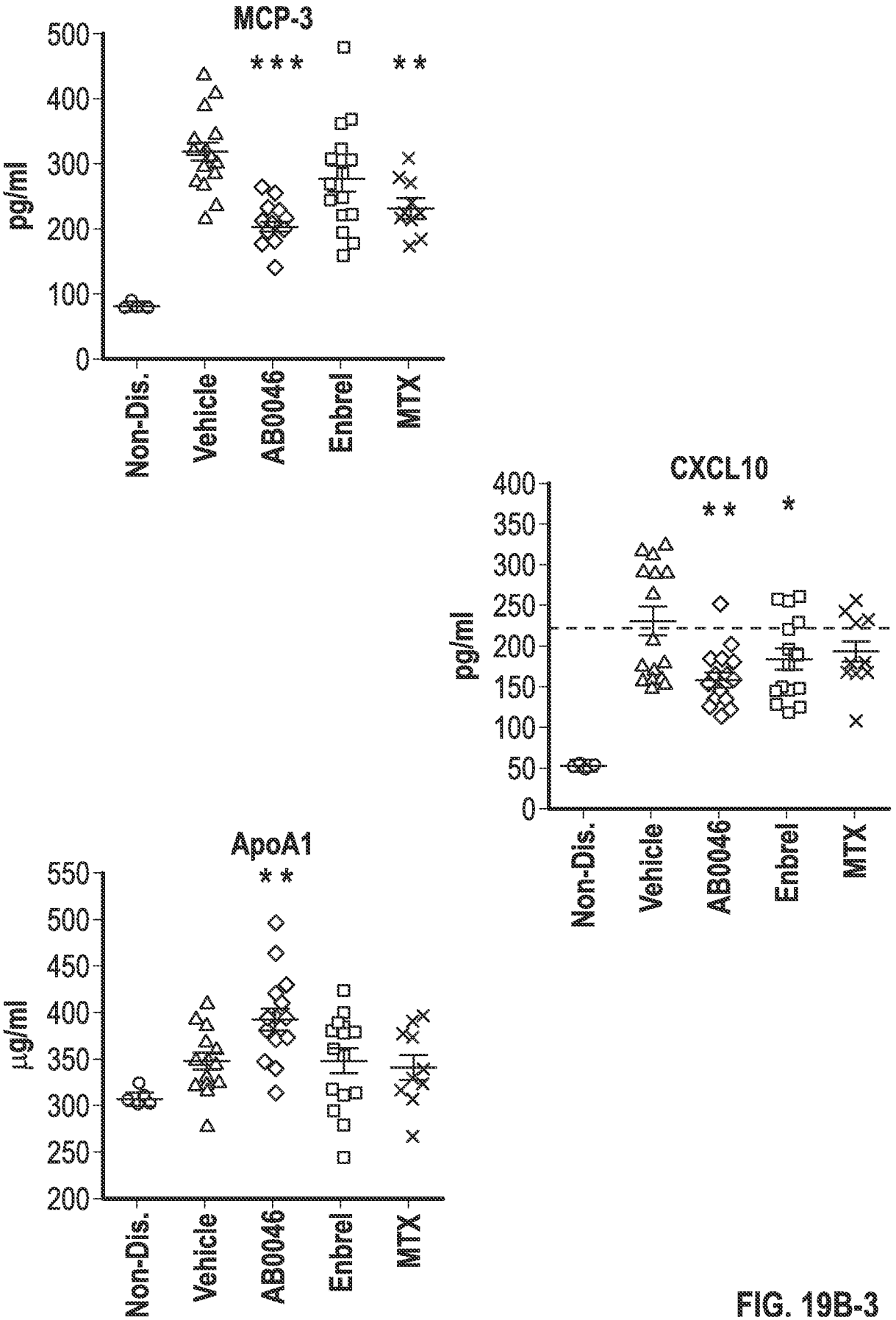



FIG. 19B-3

Additional Serum Marker Data for Mouse CIA Treatment Study (AB0046)

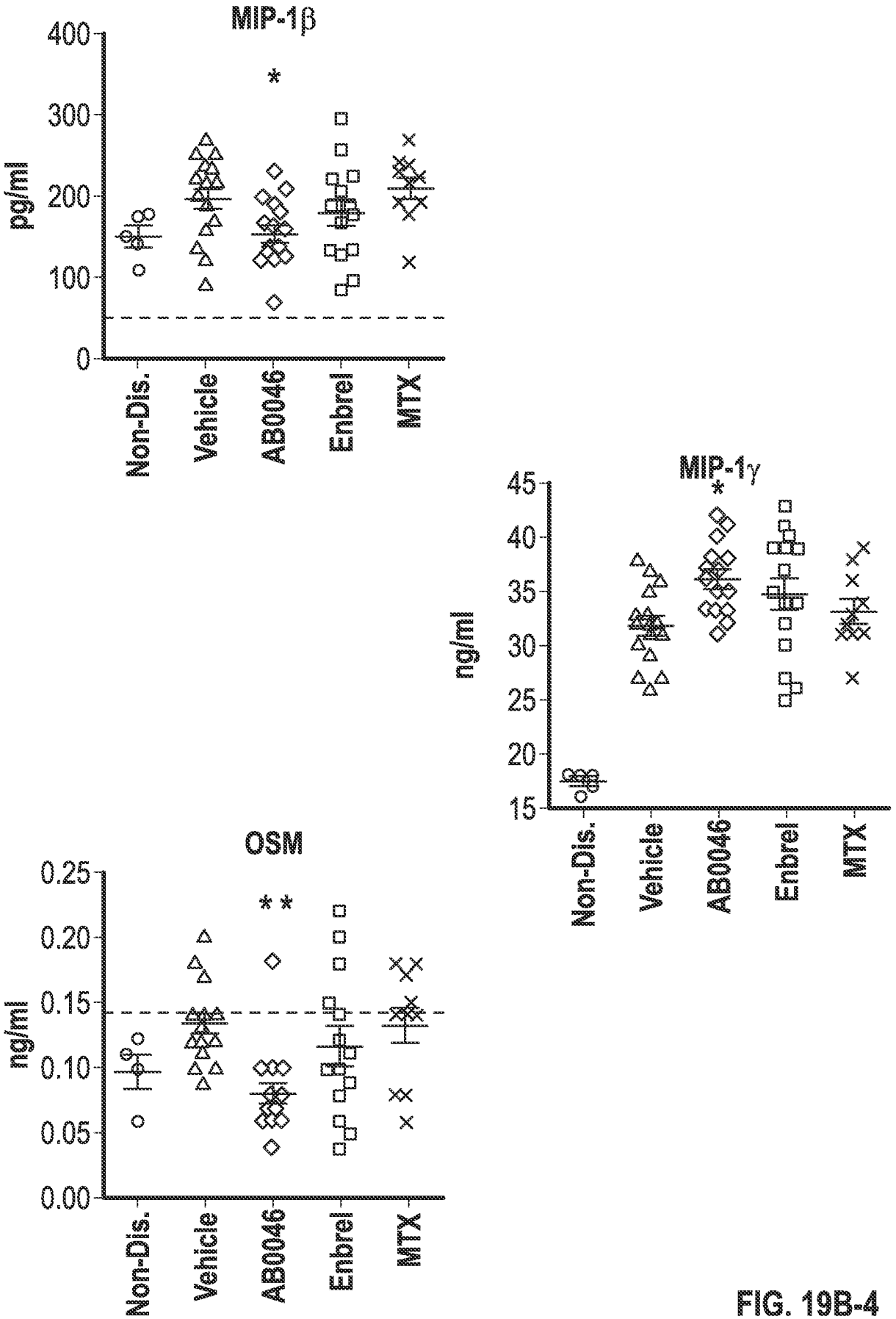



FIG. 19B-4

Additional Serum Marker Data for Mouse CIA Treatment Study (AB0046)

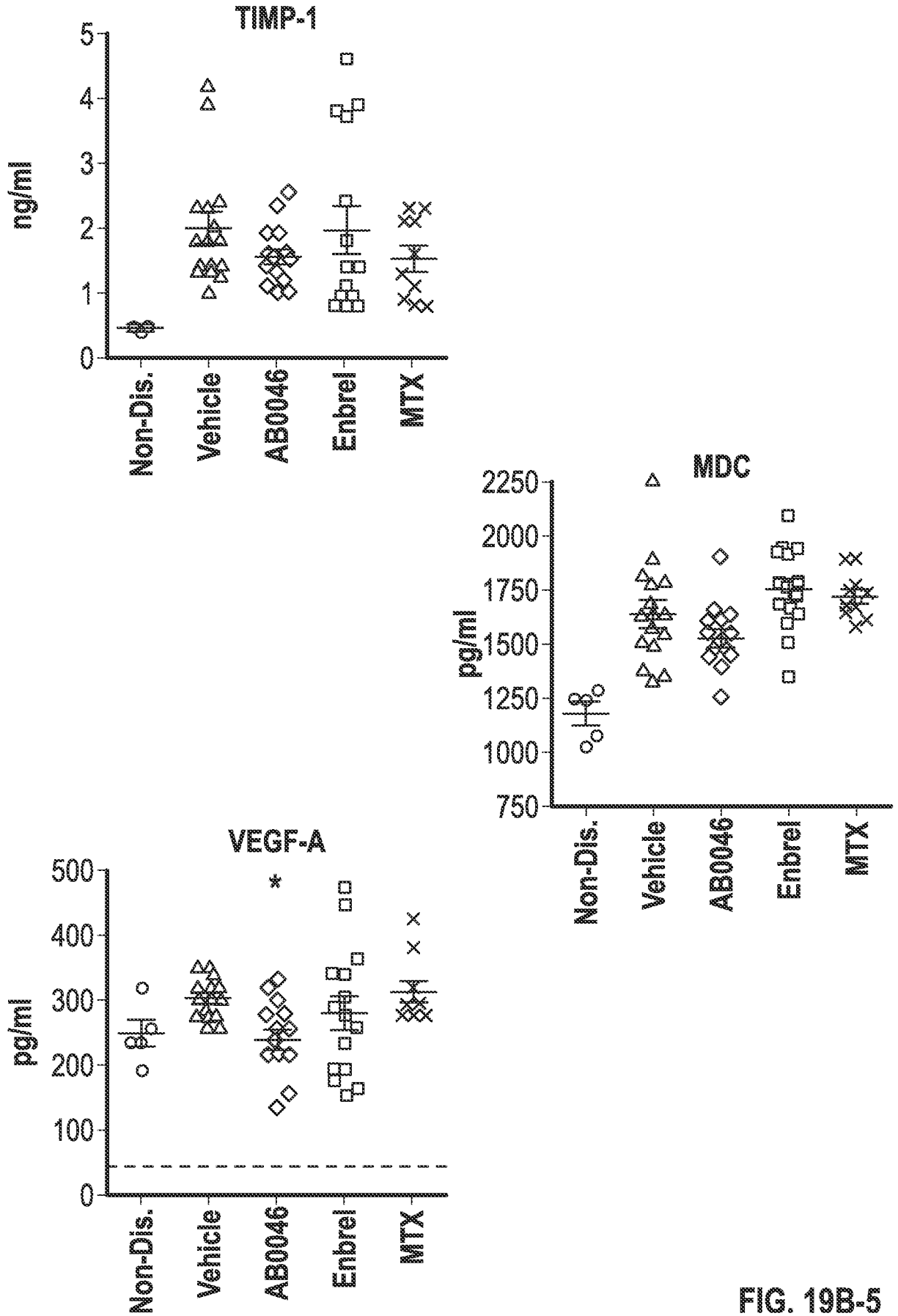
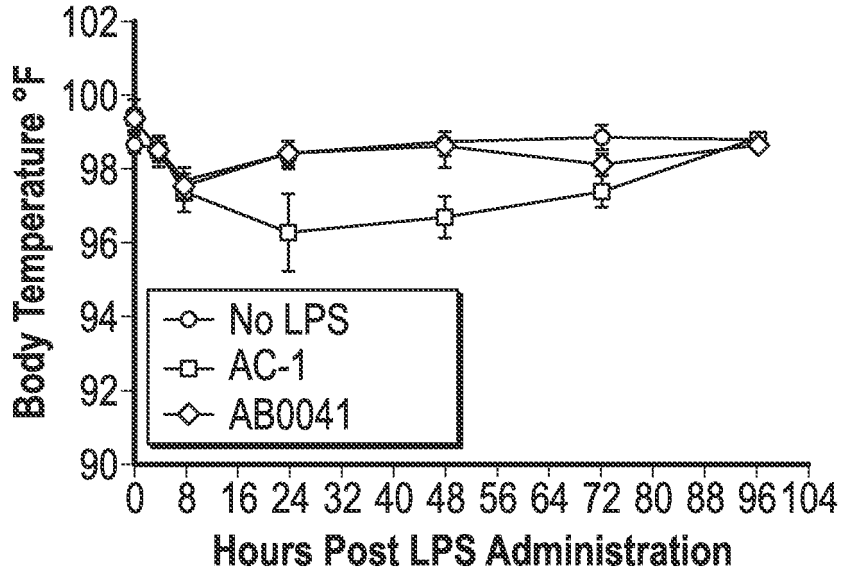



FIG. 19B-5

Anti-MMP9 (AB0041) Administration in an LPS Septicemia Rat Model



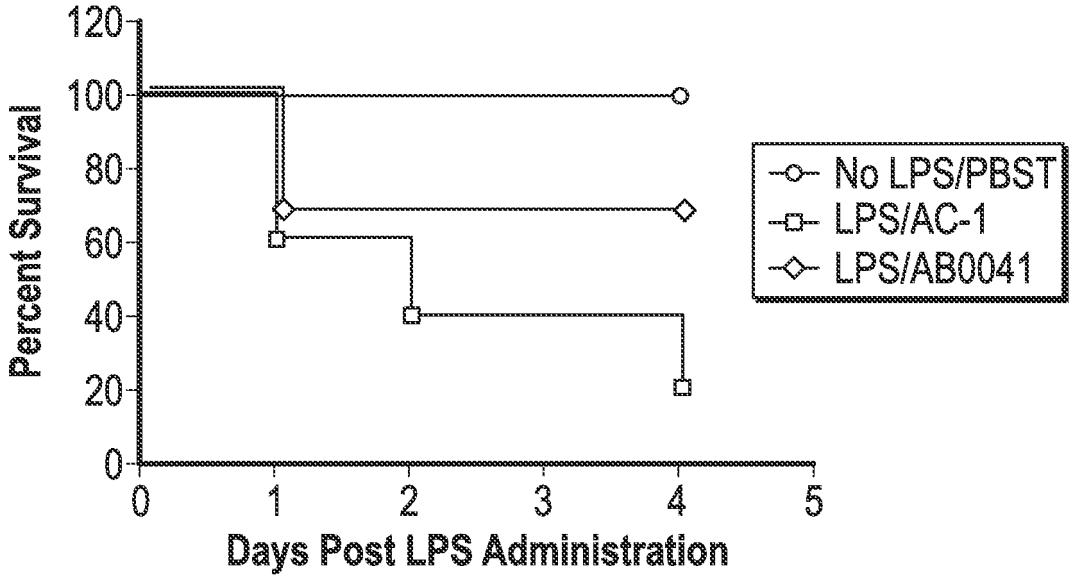




FIG. 20

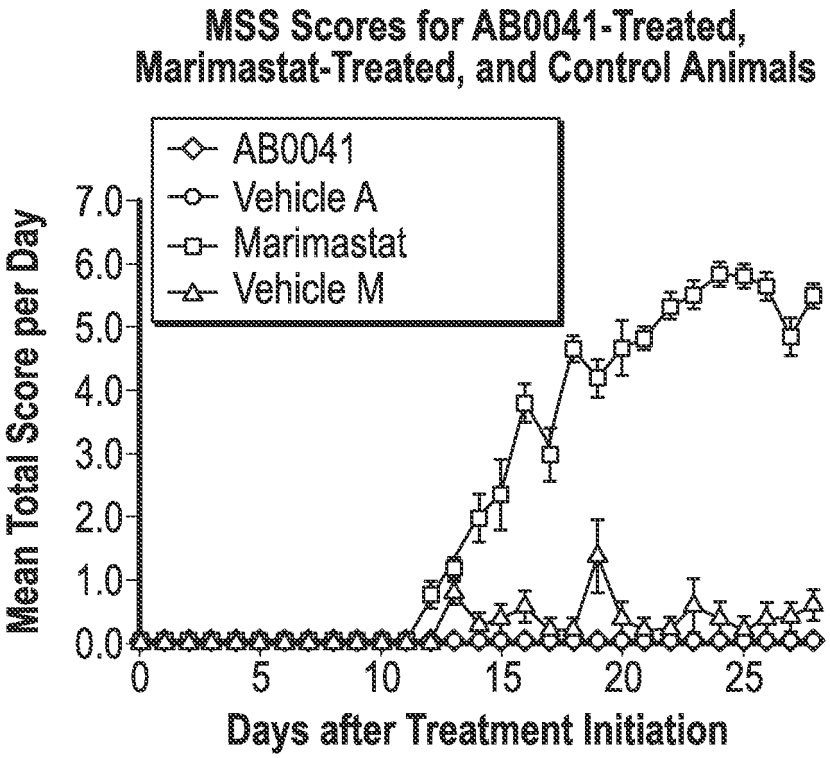

MSS Scores for AB0041-Treated,
Marimastat-Treated, and Control Animals
AB0041
Vehicle A
Marimastat
Vehicle M
Mean Total Score per Day
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
0
5
10
15
20
25
Days after Treatment Initiation

FIG. 21

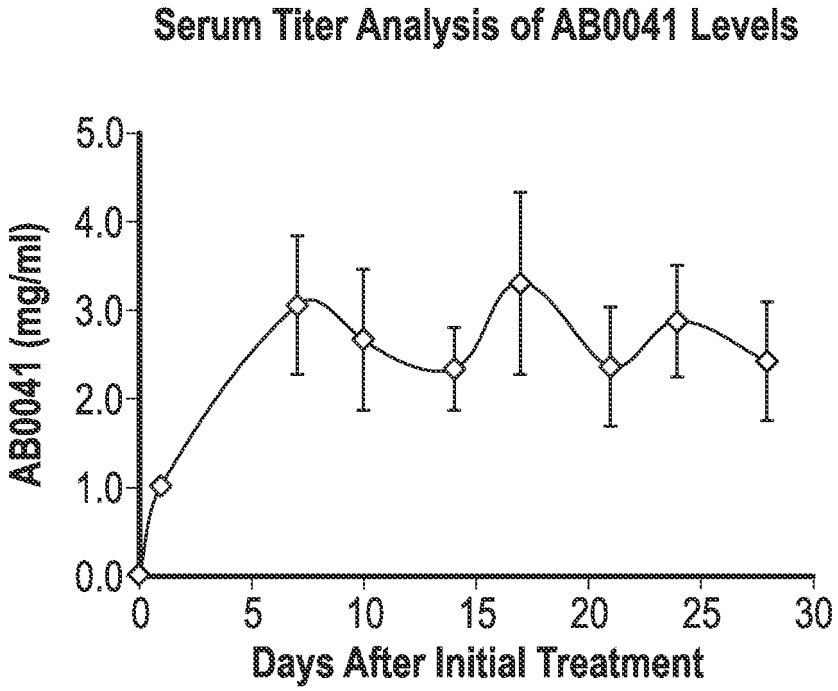

Serum Titer Analysis of AB0041 Levels
AB0041 (mg/ml)
5.0
4.0
3.0
2.0
1.0
0.0
0
5
10
15
20
25
30
Days After Initial Treatment

FIG. 22

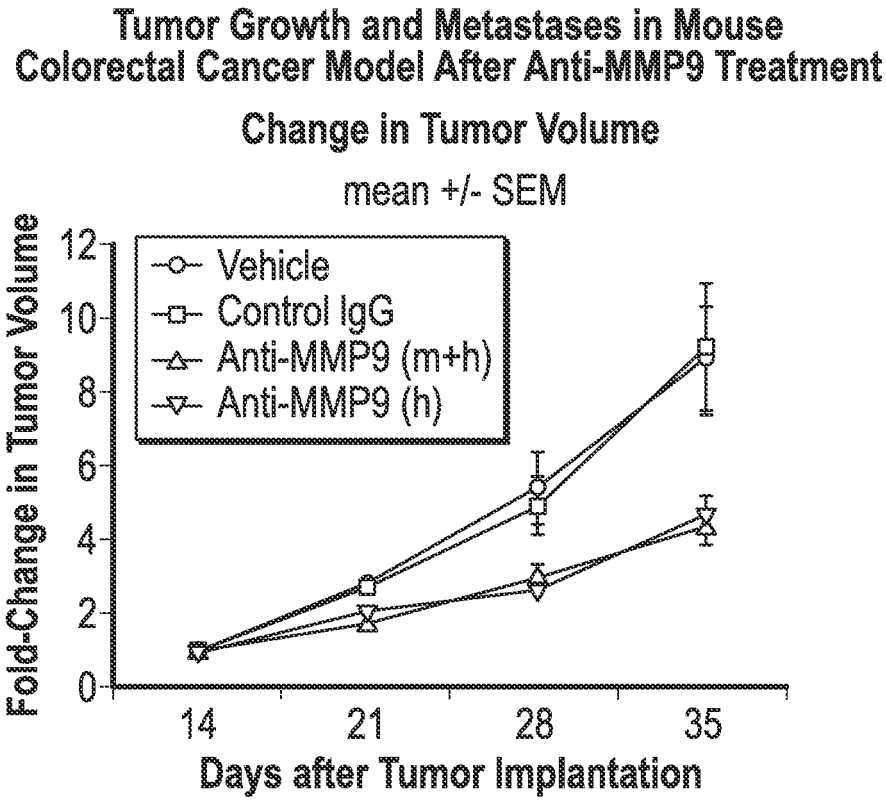



FIG. 23A

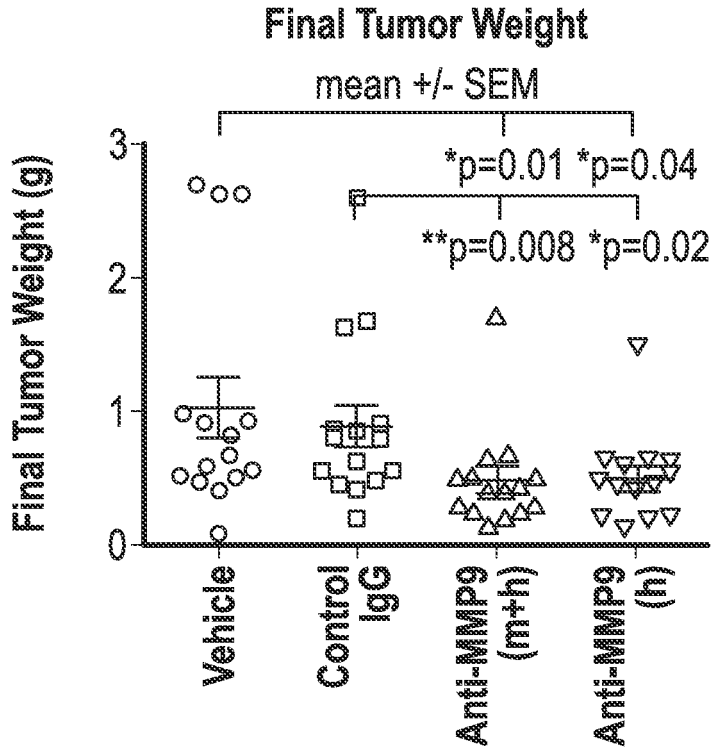



FIG. 23B

**Tumor Growth and Metastases in Mouse Colorectal Cancer Model After Anti-MMP9 Treatment**

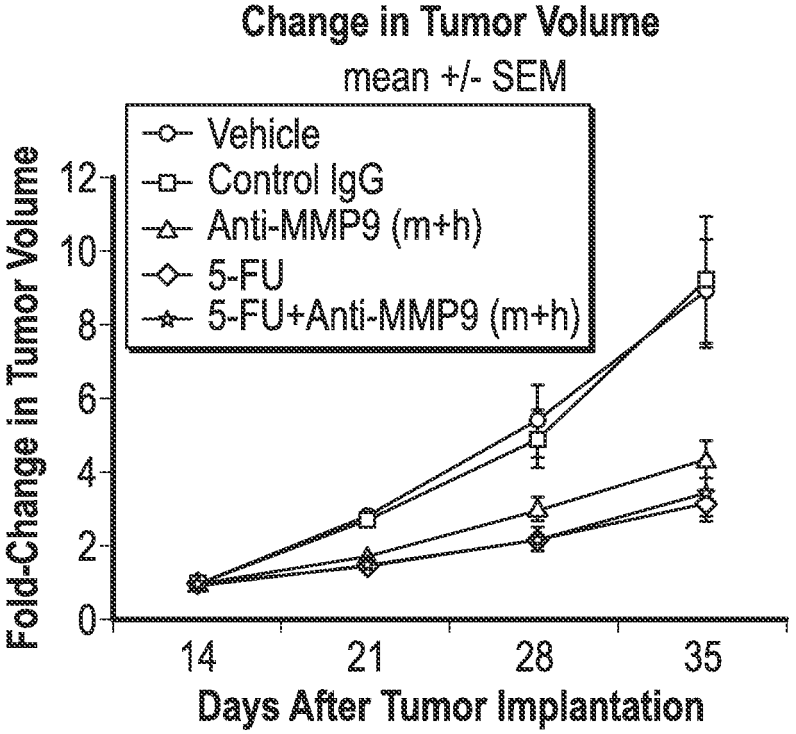



FIG. 23C

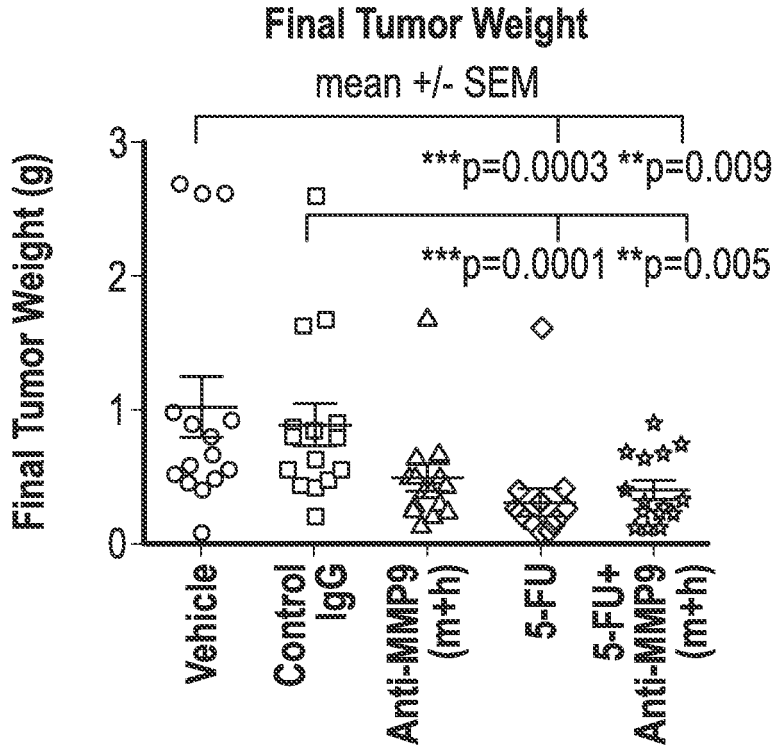



FIG. 23D

Tumor Growth and Metastases in Mouse Colorectal Cancer Model After Anti-MMP9 Treatment

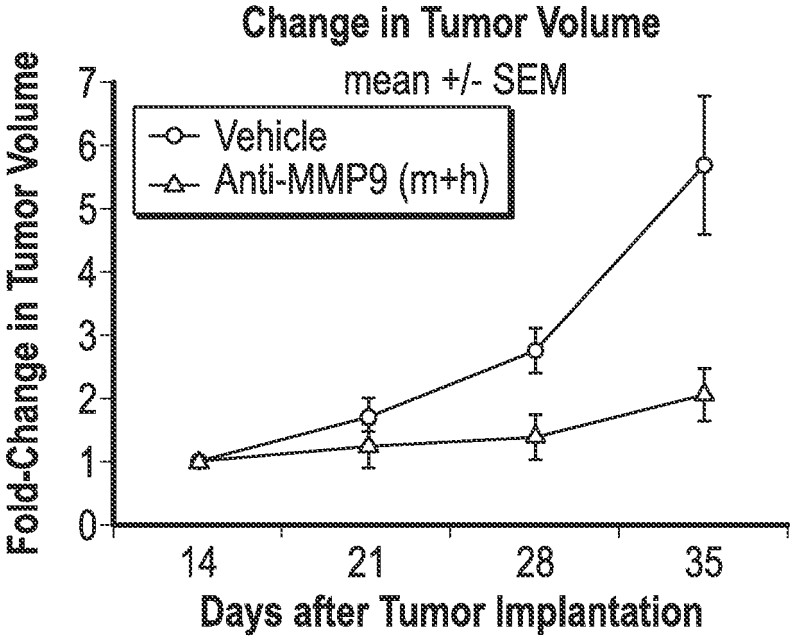



FIG. 23E

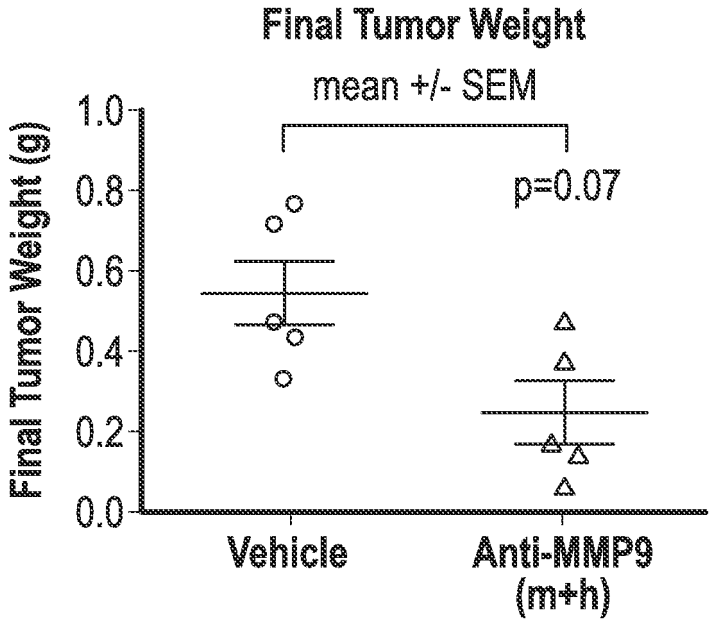



FIG. 23F

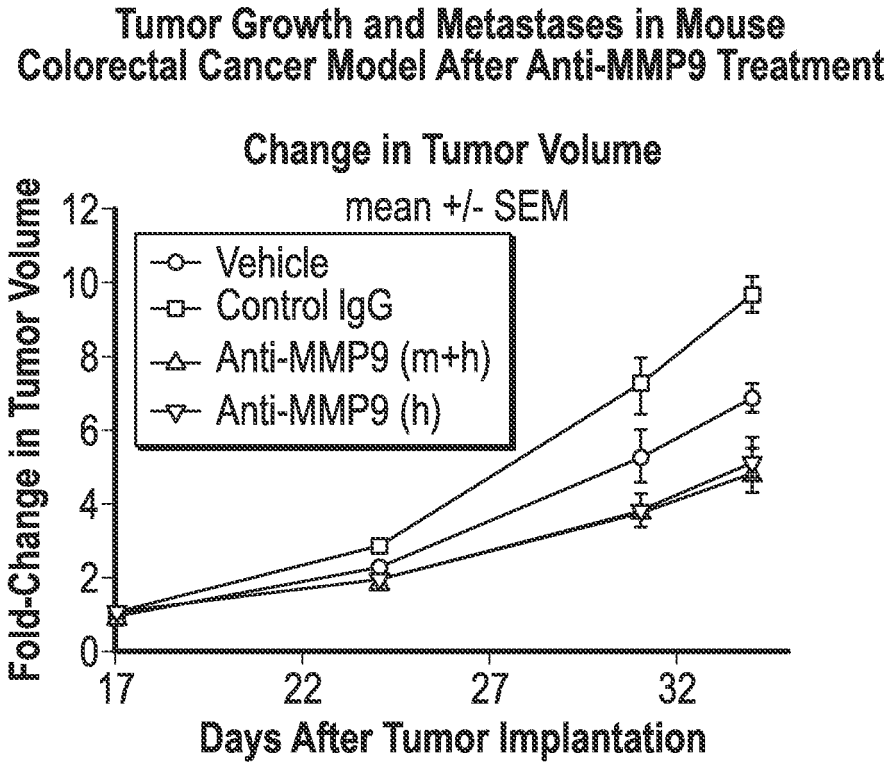



FIG. 24A

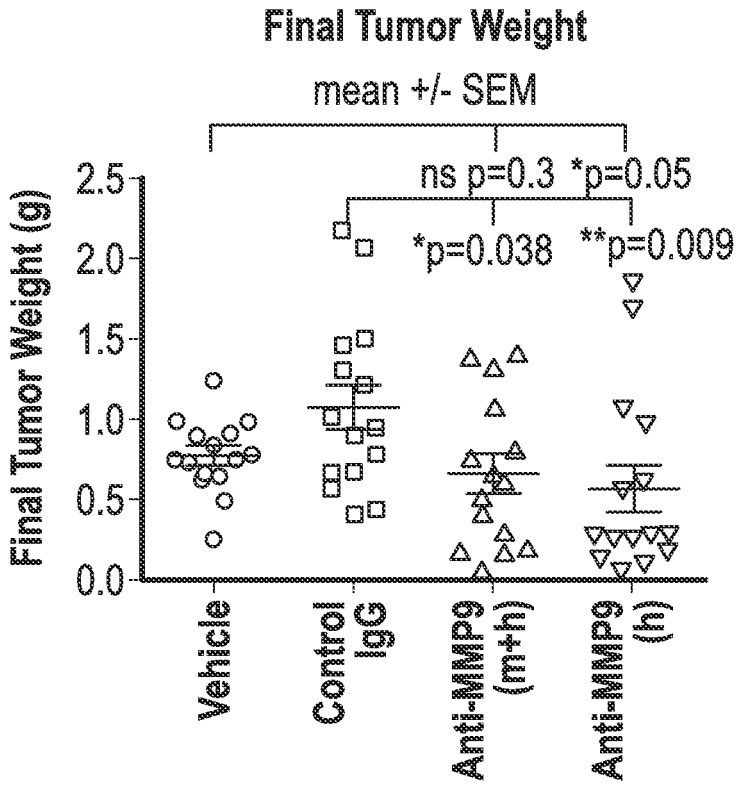



FIG. 24B

Levels of Serum Proteins Following Control and Anti-MMP-9 Treatment

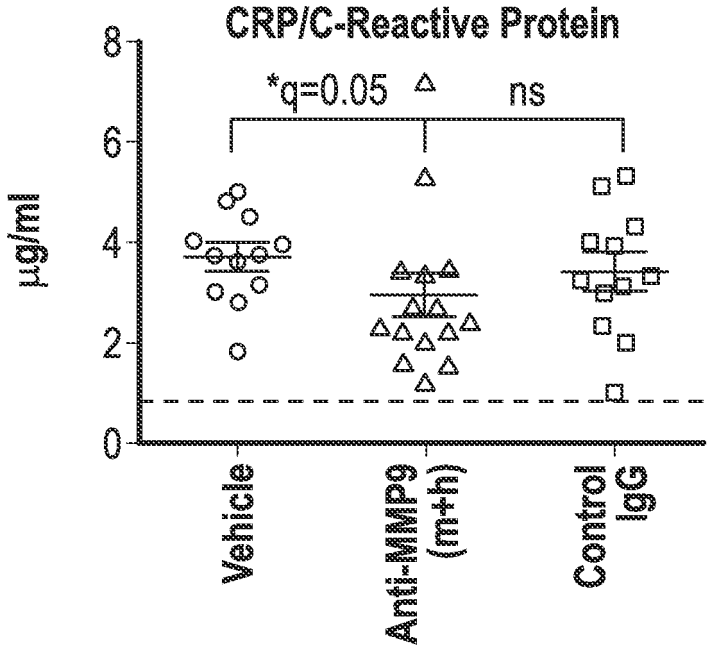



FIG. 25A

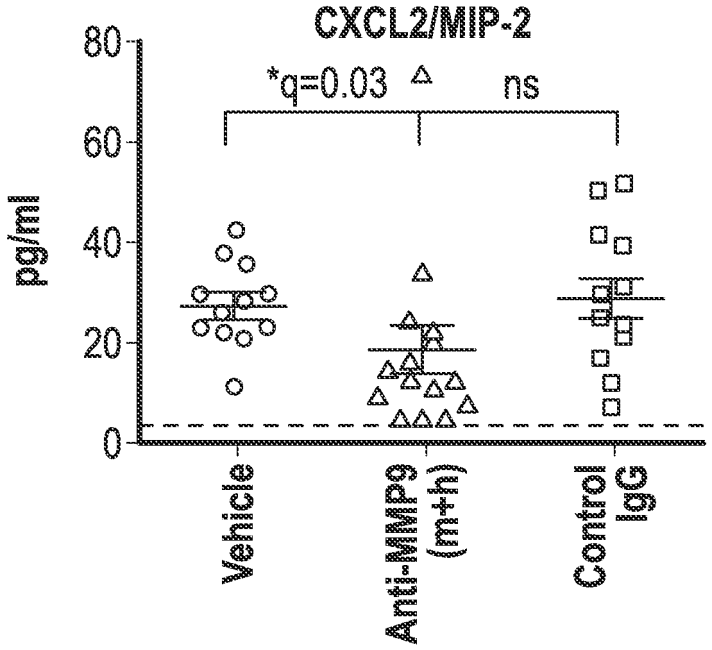



FIG. 25B

Levels of Serum Proteins Following Control and Anti-MMP-9 Treatment

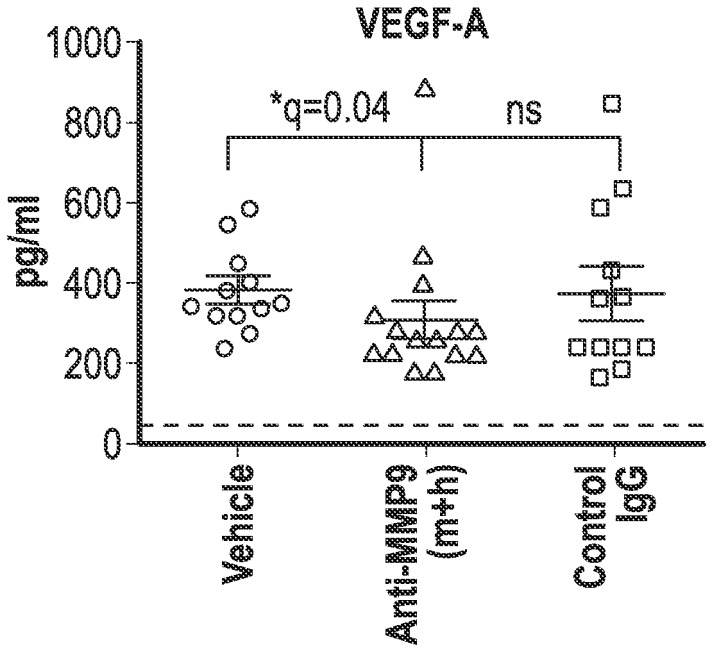



FIG. 25C

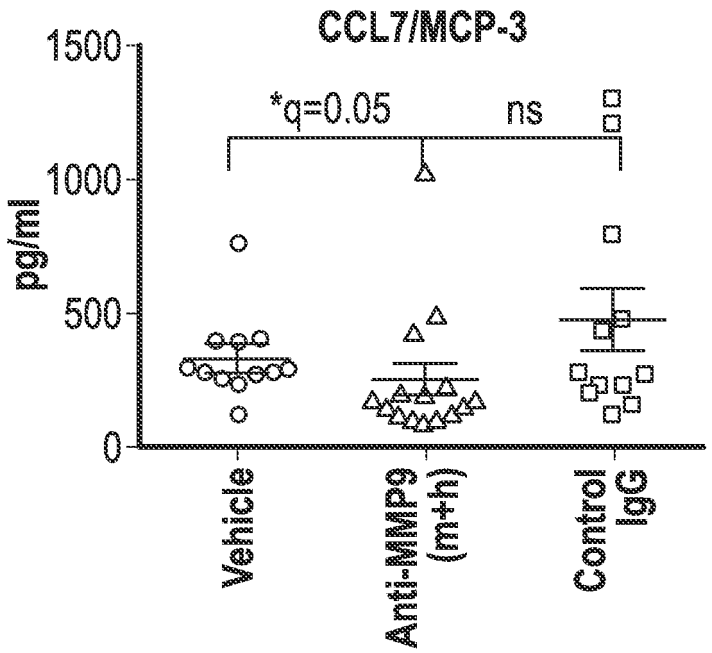



FIG. 25D

## Anti-MMP9 Antibody in Rat CIA Model of Rheumatoid Arthritis

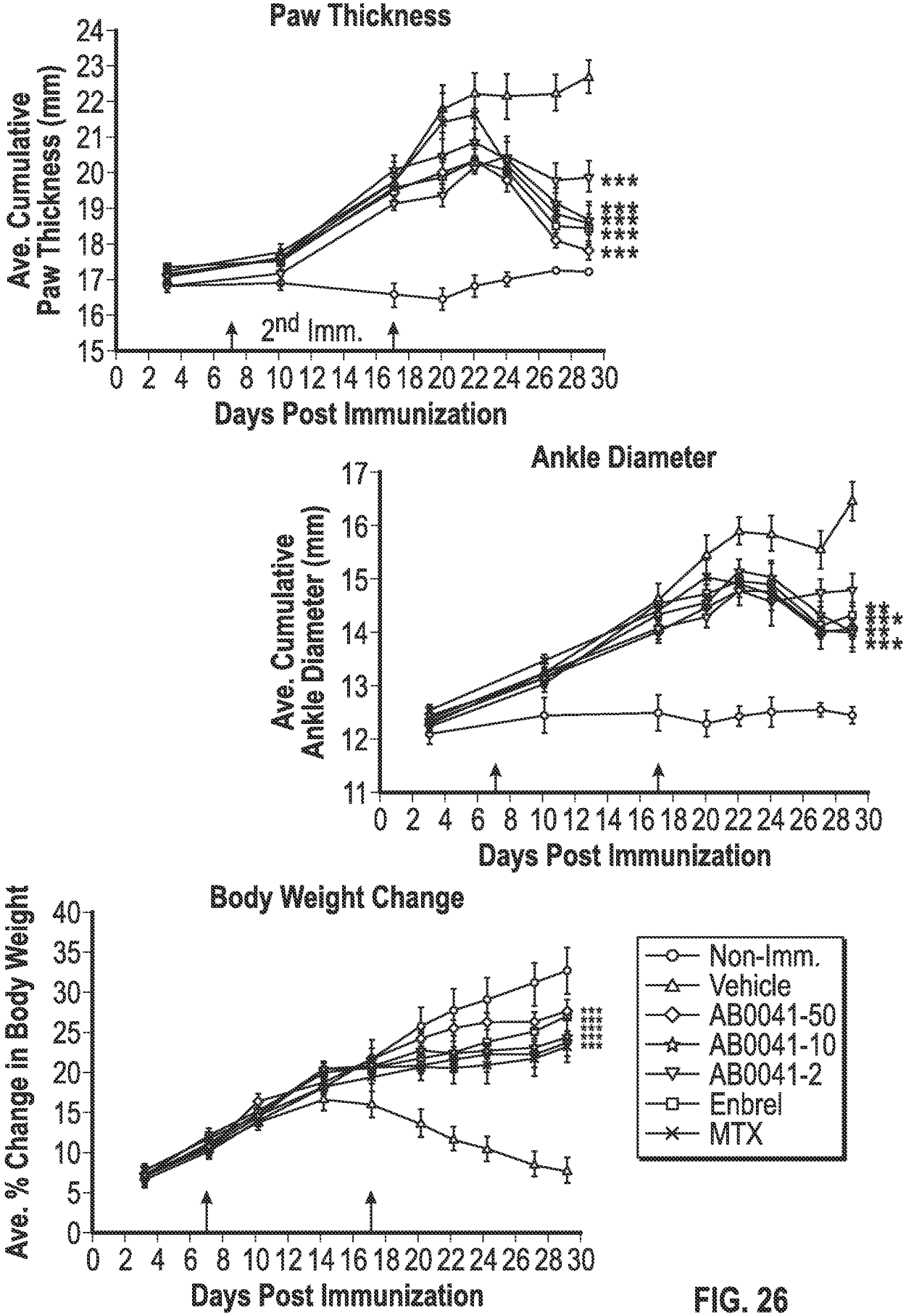



FIG. 26

TNF-Alpha and CD68 Scores Following Anti-MMP9 Treatment in Rat CIA Model of Rheumatoid Arthritis

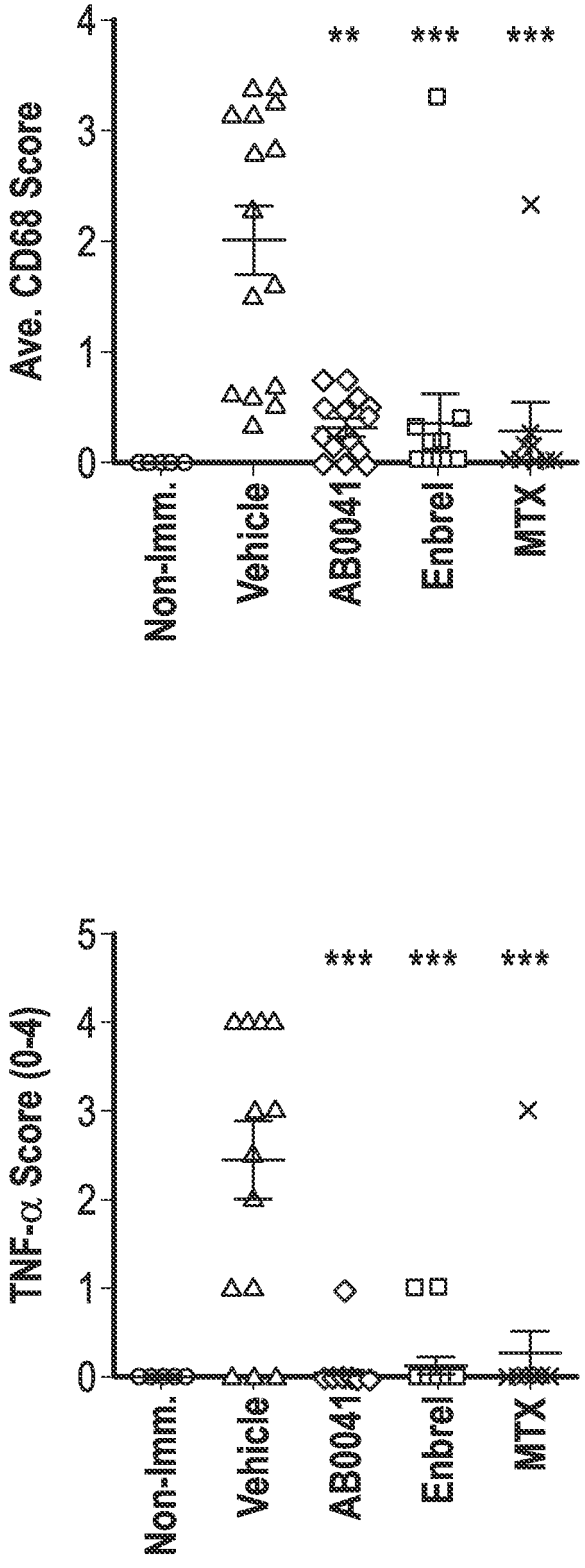



FIG. 27

Serum Markers Following Anti-MMP9
Treatment in Rat CIA Model of Rheumatoid Arthritis

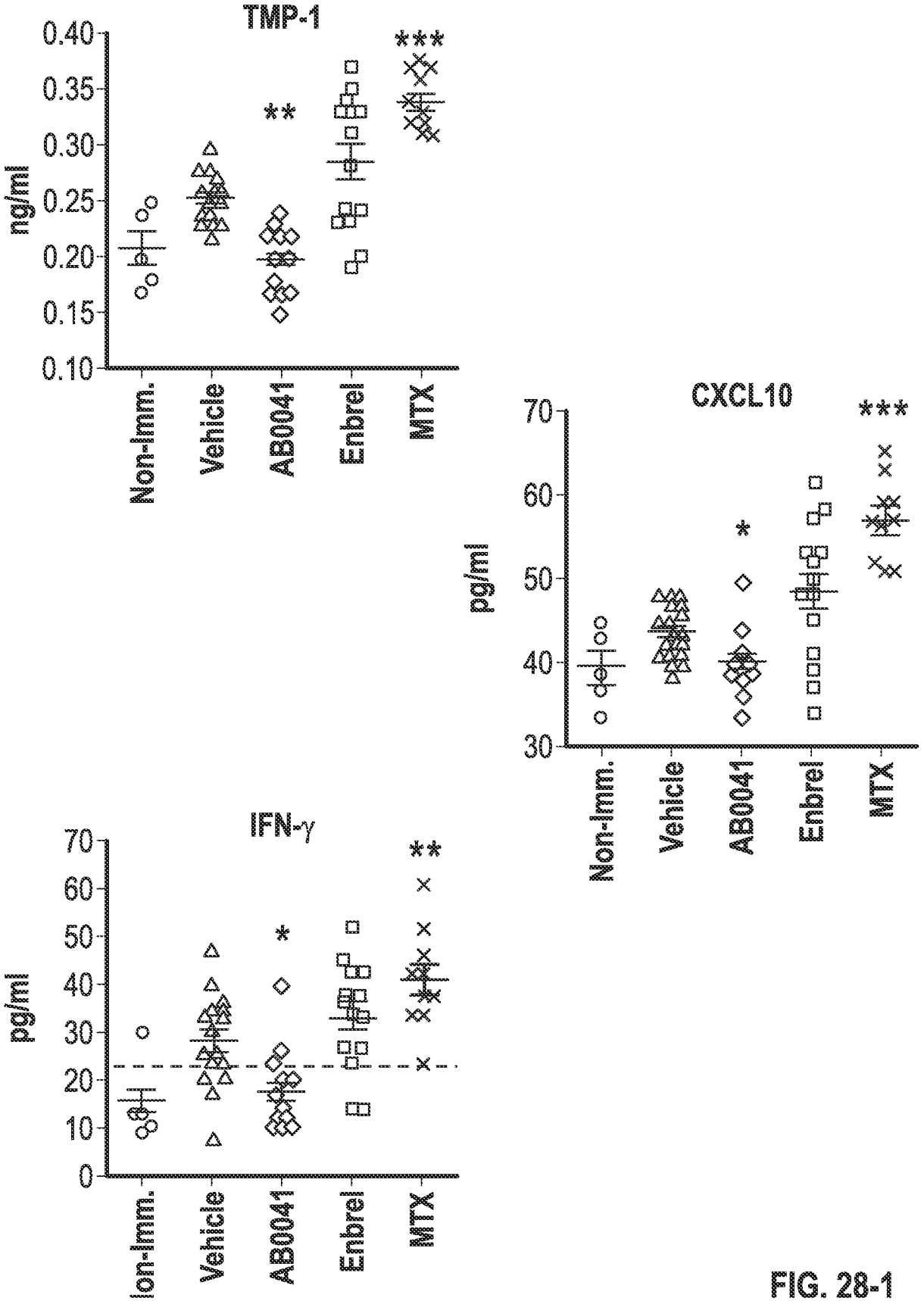



FIG. 28-1

Serum Markers Following Anti-MMP9
Treatment in Rat CIA Model of Rheumatoid Arthritis

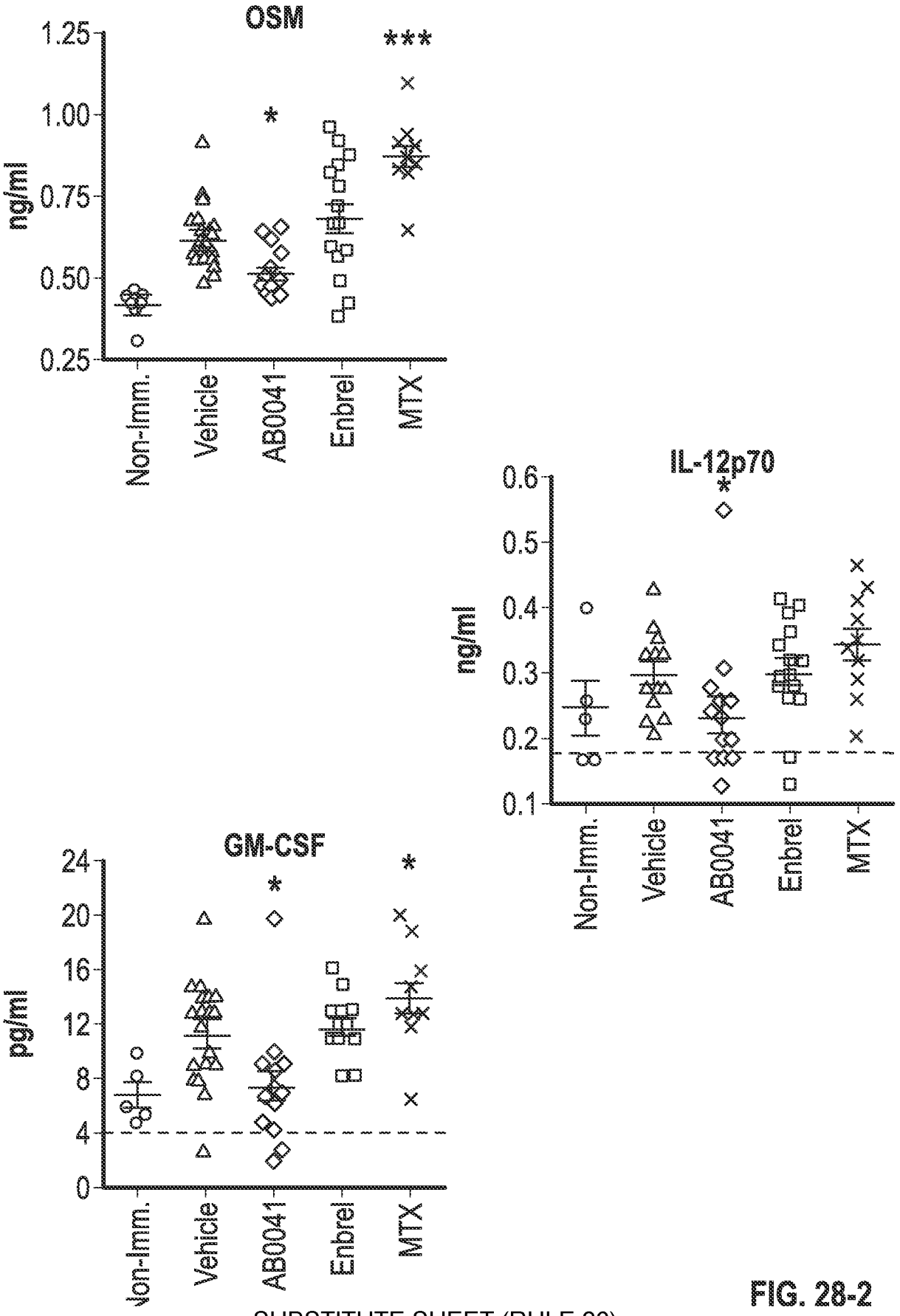



FIG. 28-2

Serum Markers Following Anti-MMP9
Treatment in Rat CIA Model of Rheumatoid Arthritis

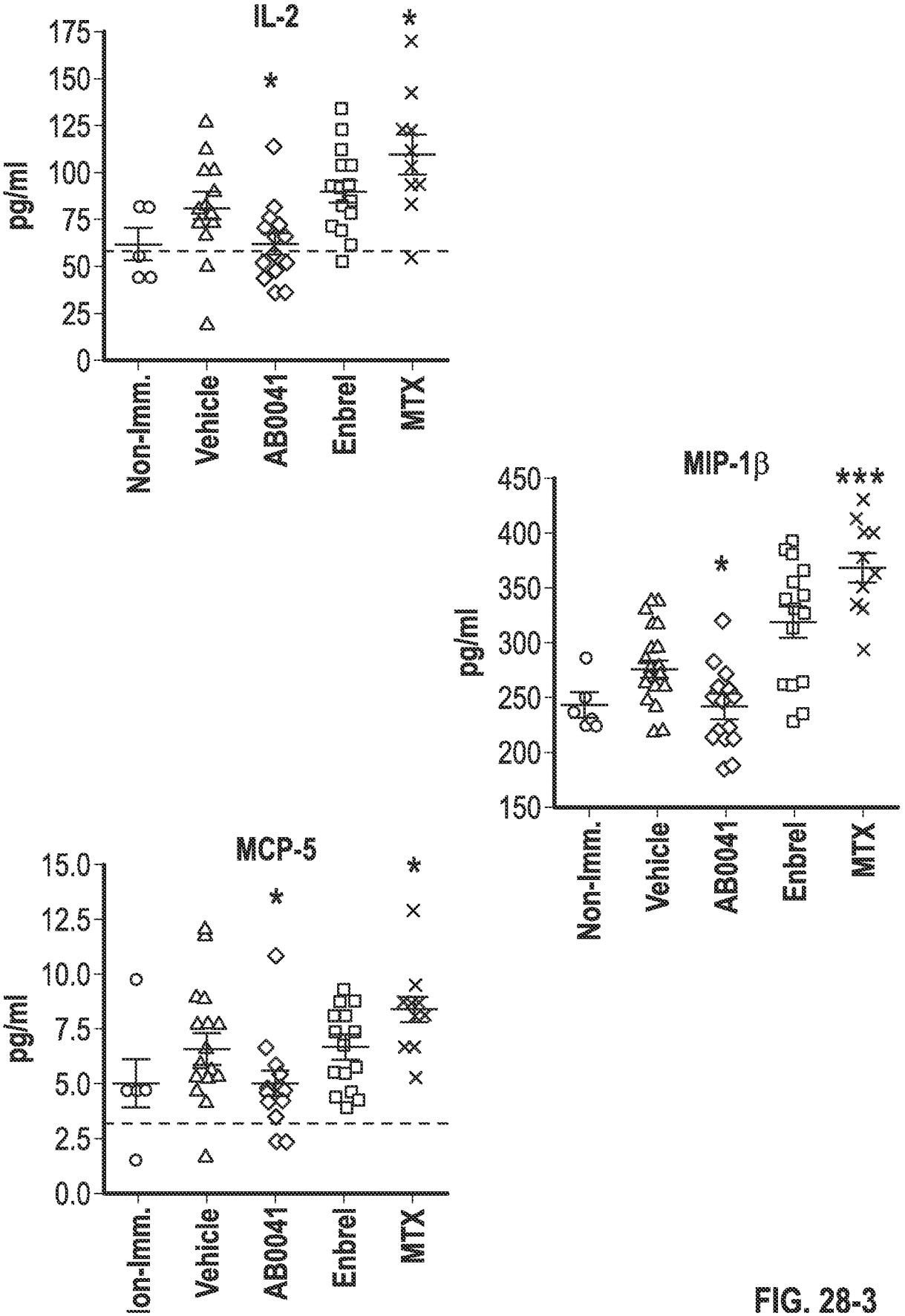



FIG. 28-3

Serum Markers Following Anti-MMP9
Treatment in Rat CIA Model of Rheumatoid Arthritis

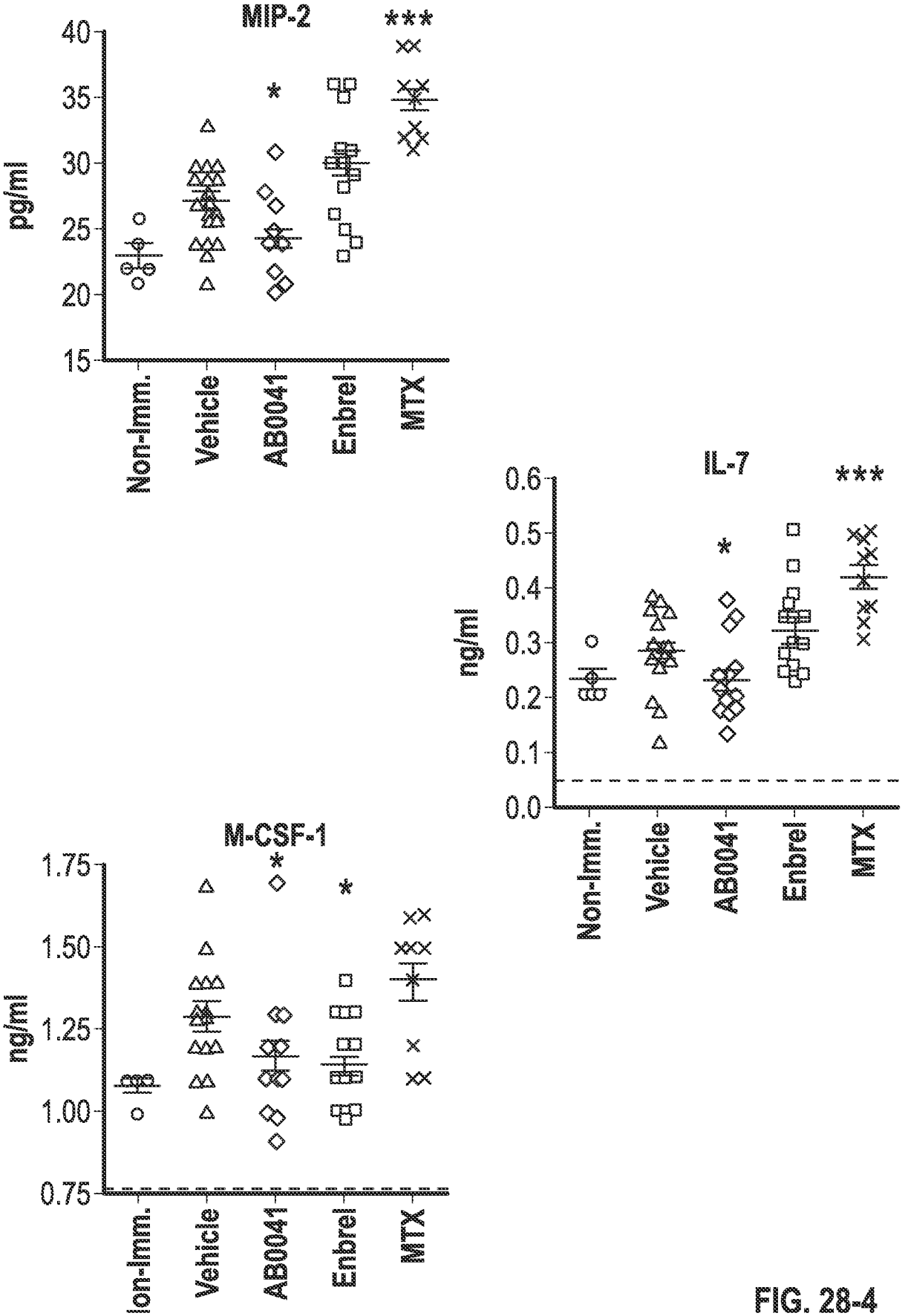



FIG. 28-4

Anti-MMP9 Antibody in Mouse CIA Model of Rheumatoid Arthritis

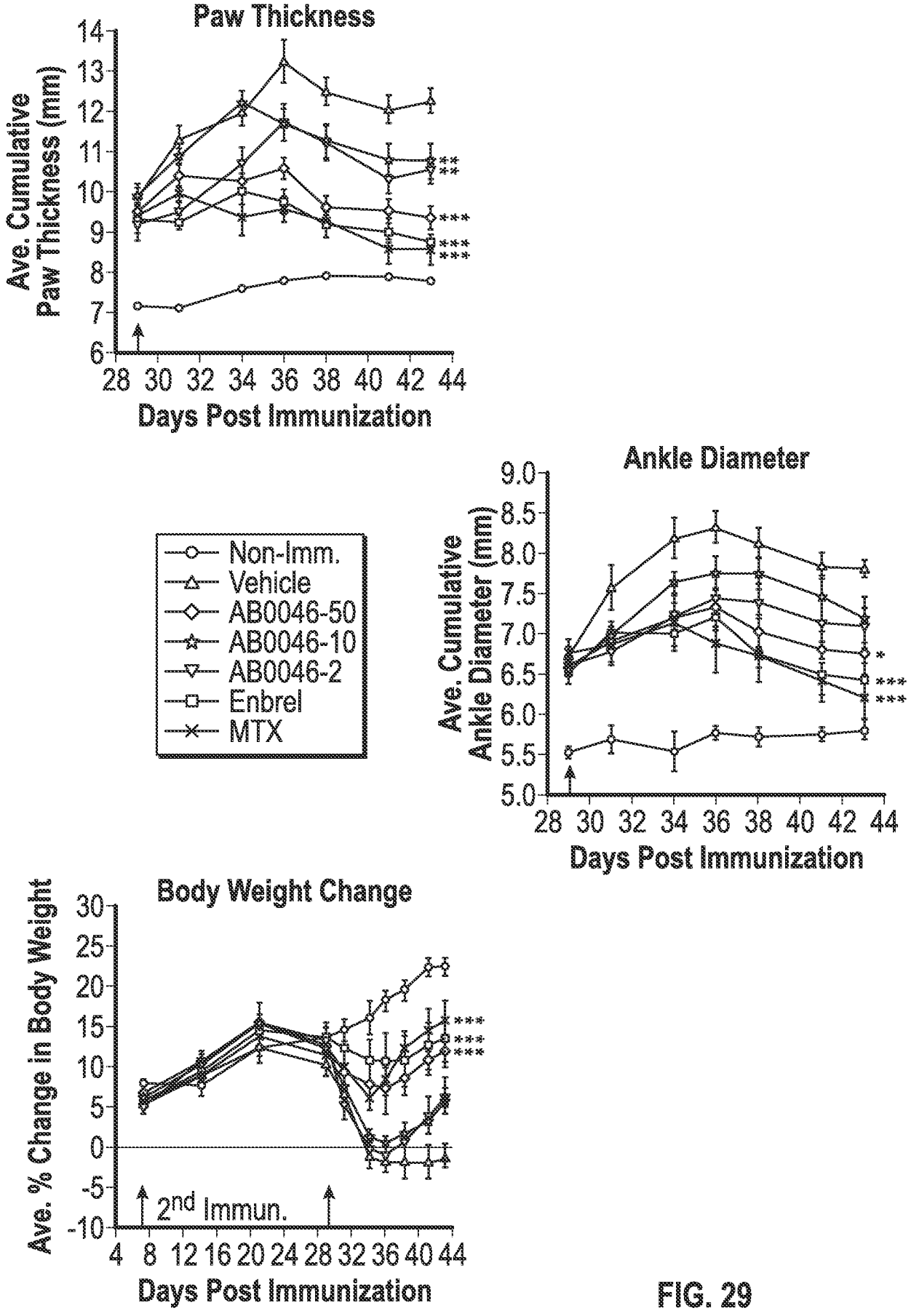



FIG. 29

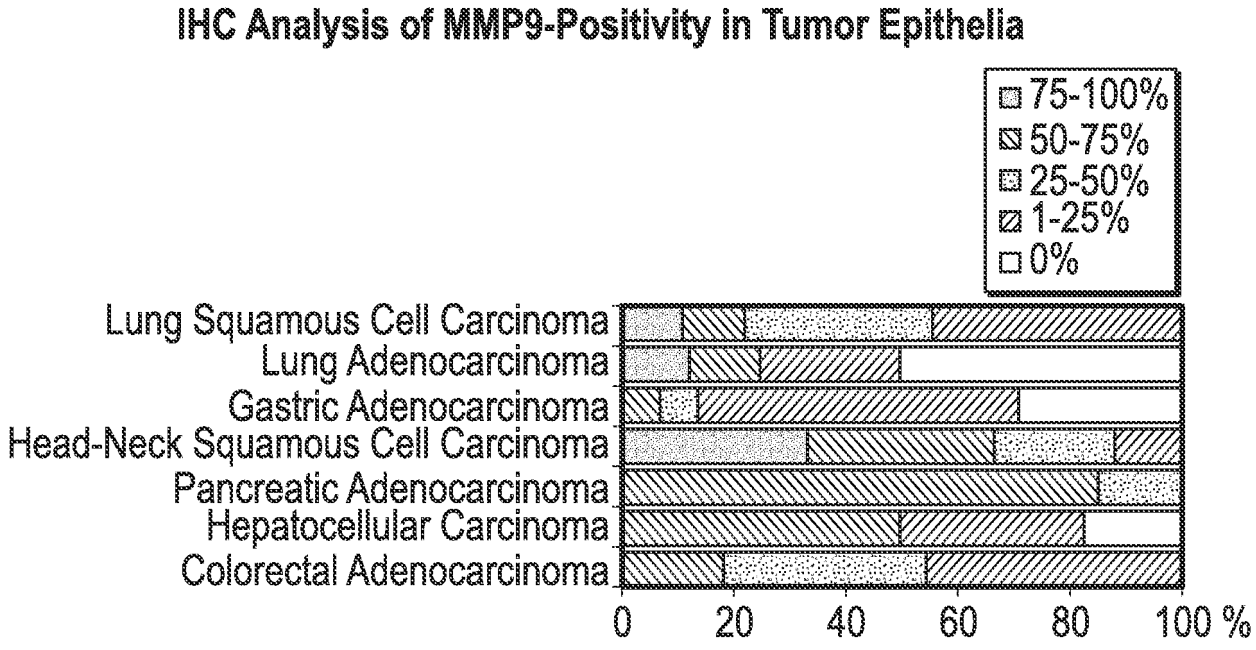

IHC Analysis of MMP9-Positivity in Tumor Epithelia
75-100%
50-75%
25-50%
1-25%
0%
Lung Squamous Cell Carcinoma
Lung Adenocarcinoma
Gastric Adenocarcinoma
Head-Neck Squamous Cell Carcinoma
Pancreatic Adenocarcinoma
Hepatocellular Carcinoma
Colorectal Adenocarcinoma
0
20
40
60
80
100 %

FIG. 30

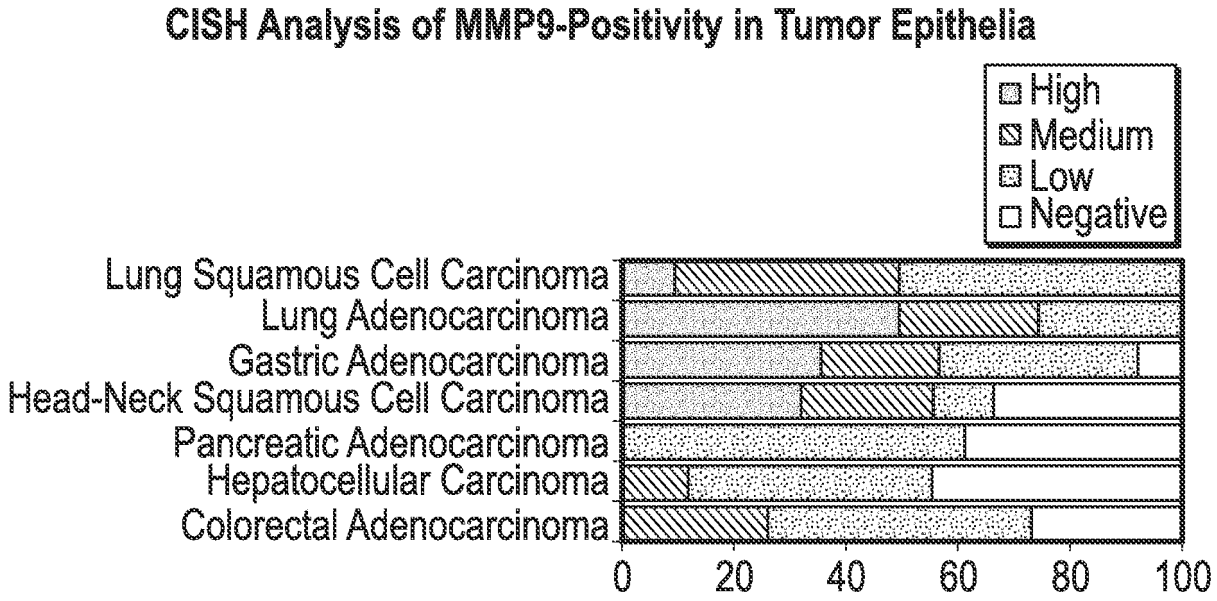

CISH Analysis of MMP9-Positivity in Tumor Epithelia
High
Medium
Low
Negative
Lung Squamous Cell Carcinoma
Lung Adenocarcinoma
Gastric Adenocarcinoma
Head-Neck Squamous Cell Carcinoma
Pancreatic Adenocarcinoma
Hepatocellular Carcinoma
Colorectal Adenocarcinoma
0
20
40
60
80
100

FIG. 31