Group	Drug	Dose (mg/kg)
1	No disease	-
2	Vehicle	QD
3	PRN1008	10, QD
4	PRN1008	20, QD
5	PRN1008	40, QD
6	Dex	1, QD
7	Vehicle	BID
8	PRN1008	20 BID

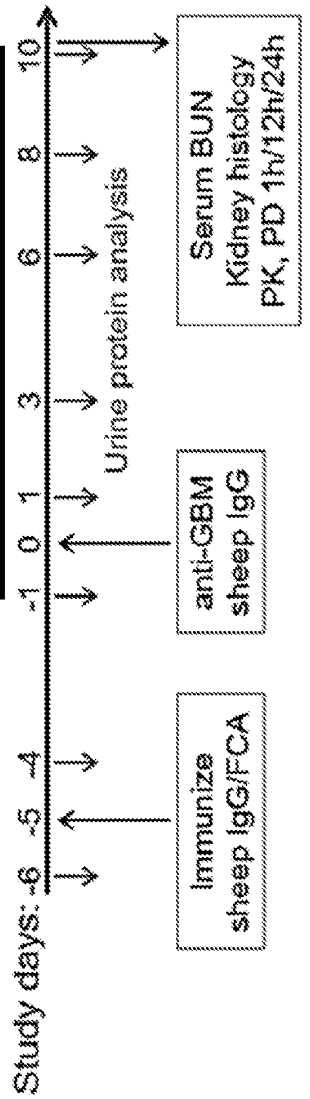


FIG. 1

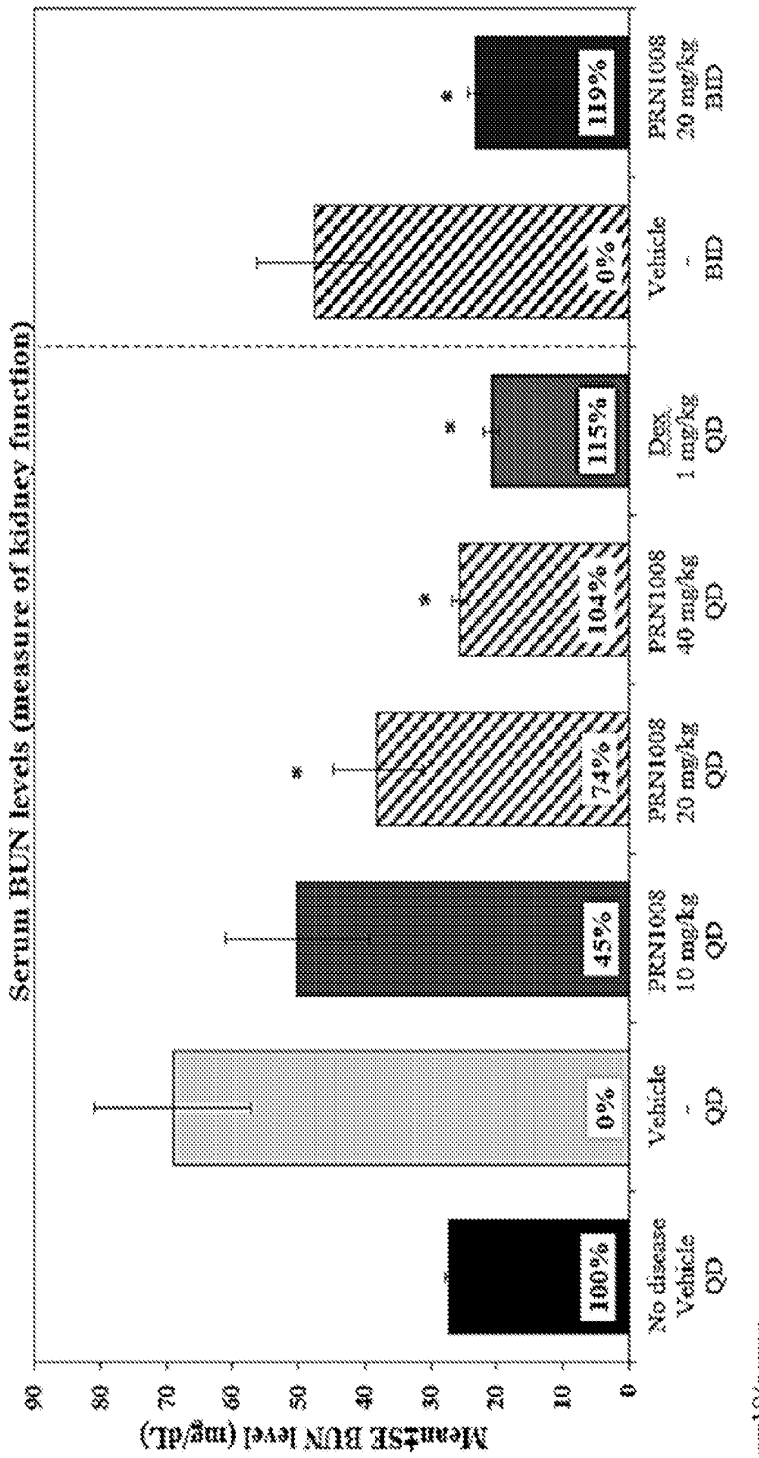

Serum BUN levels (measure of kidney function)
Mean±SE BUN level (mg/dL)
0
10
20
30
40
50
60
70
80
90
100%
0%
45%
74%
104%
115%
0%
119%
No disease
Vehicle
QD
Vehicle
-
QD
PRN1008
10 mg/kg
QD
PRN1008
20 mg/kg
QD
PRN1008
40 mg/kg
QD
Dex
1 mg/kg
QD
Vehicle
-
BID
PRN1008
20 mg/kg
BID
Treatment Group
n=10/group
* P≤0.05 T-test to Vehicle

FIG. 2

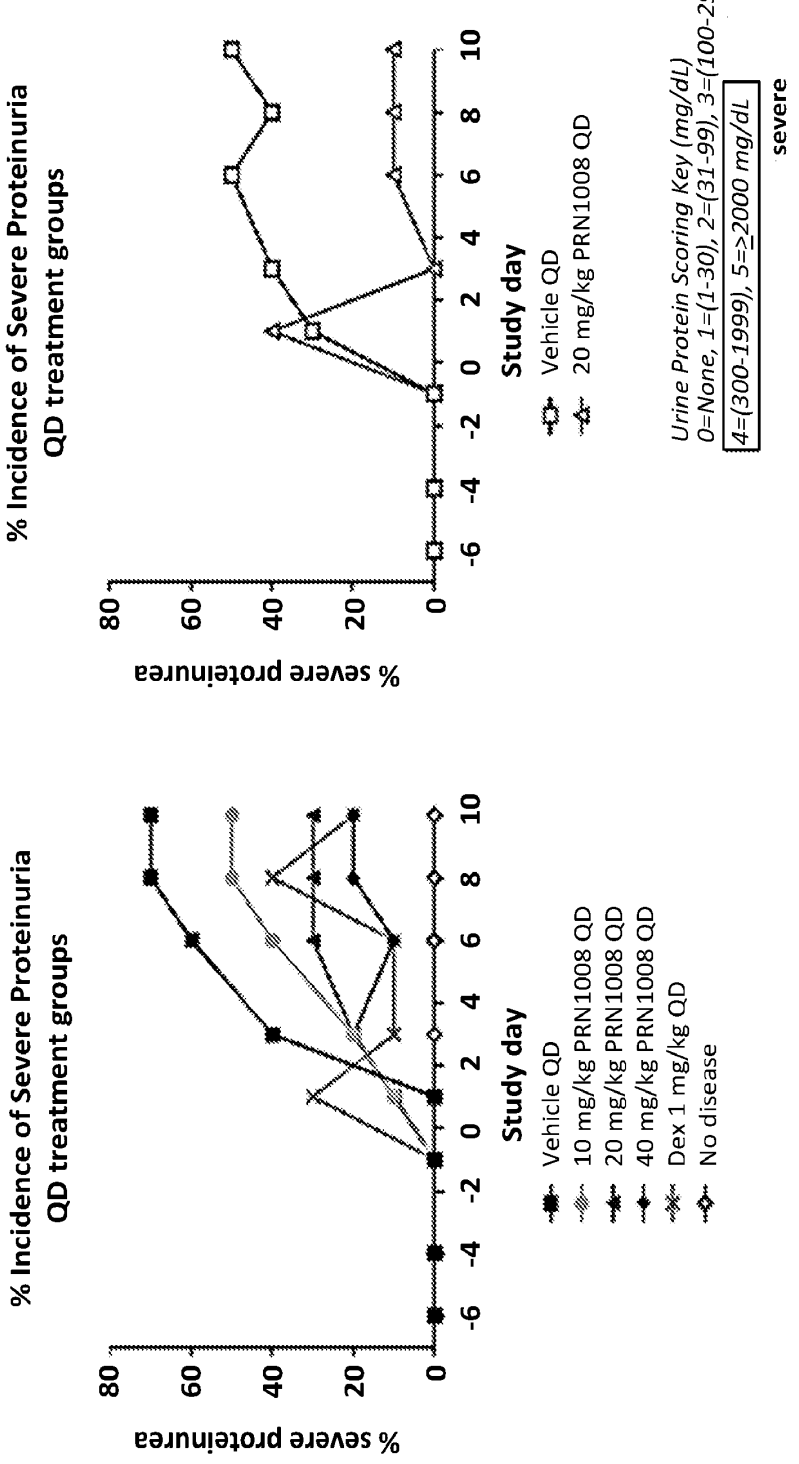

% Incidence of Severe Proteinuria
QD treatment groups
% severe proteinurea
80
60
40
20
0
-6
-4
-2
0
2
4
6
8
10
Study day
Vehicle QD
10 mg/kg PRN1008 QD
20 mg/kg PRN1008 QD
40 mg/kg PRN1008 QD
Dex 1 mg/kg QD
No disease
% Incidence of Severe Proteinuria
QD treatment groups
% severe proteinurea
Study day
Vehicle QD
20 mg/kg PRN1008 QD
Urine Protein Scoring Key (mg/dL)
0=None, 1=(1-30), 2=(31-99), 3=(100-299)
4=(300-1999), 5=≥2000 mg/dL
severe

FIG. 3

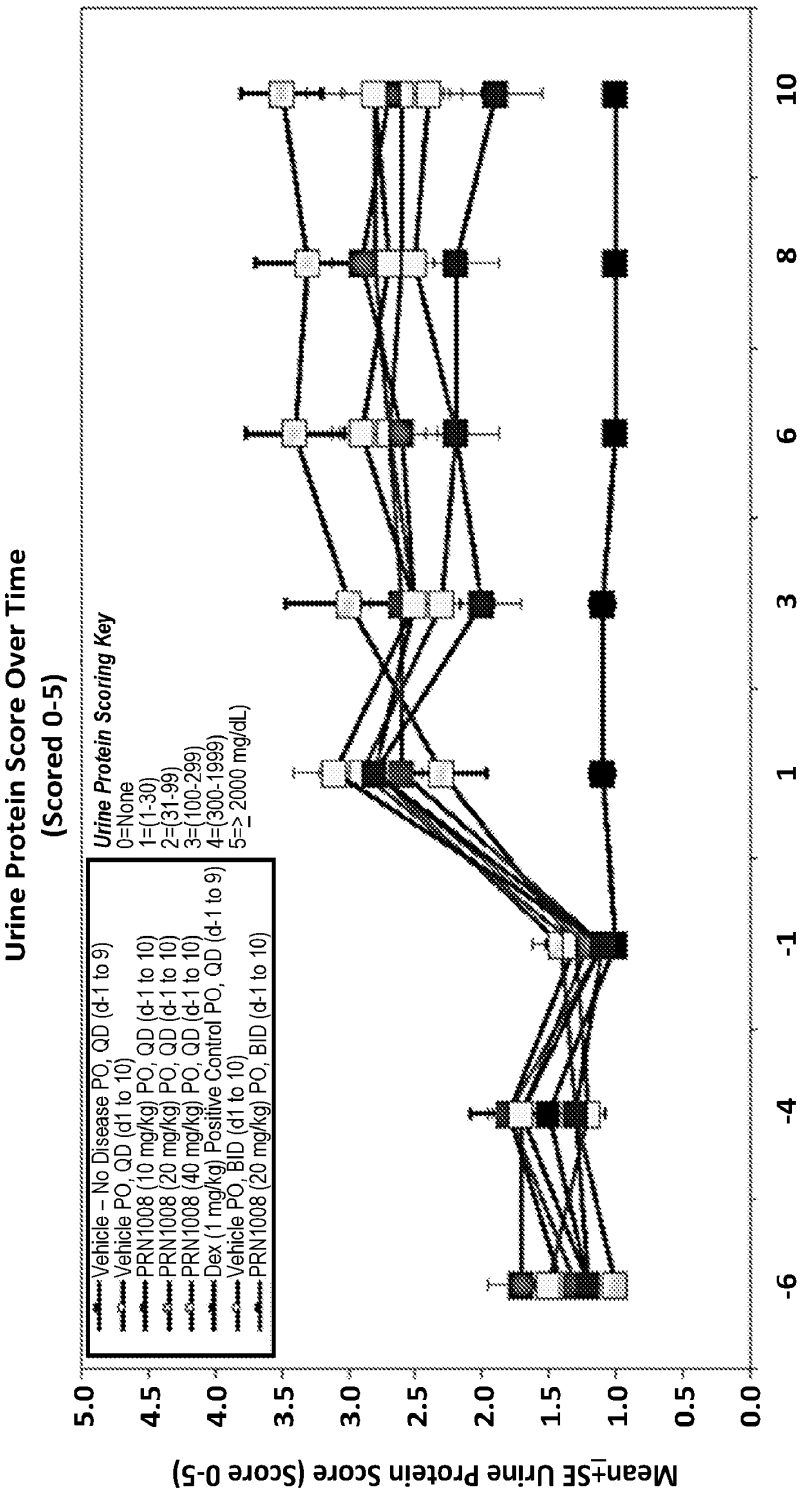

Urine Protein Score Over Time
(Scored 0-5)
Urine Protein Scoring Key
0=None
1=(1-30)
2=(31-99)
3=(100-299)
4=(300-1999)
5=≥ 2000 mg/dL
Vehicle – No Disease PO, QD (d-1 to 9)
Vehicle PO, QD (d1 to 10)
PRN1008 (10 mg/kg) PO, QD (d-1 to 10)
PRN1008 (20 mg/kg) PO, QD (d-1 to 10)
PRN1008 (40 mg/kg) PO, QD (d-1 to 10)
Dex (1 mg/kg) Positive Control PO, QD (d-1 to 9)
Vehicle PO, BID (d1 to 10)
PRN1008 (20 mg/kg) PO, BID (d-1 to 10)
Mean±SE Urine Protein Score (Score 0-5)
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-6
-4
-1
1
3
6
8
10
Study day

FIG. 4

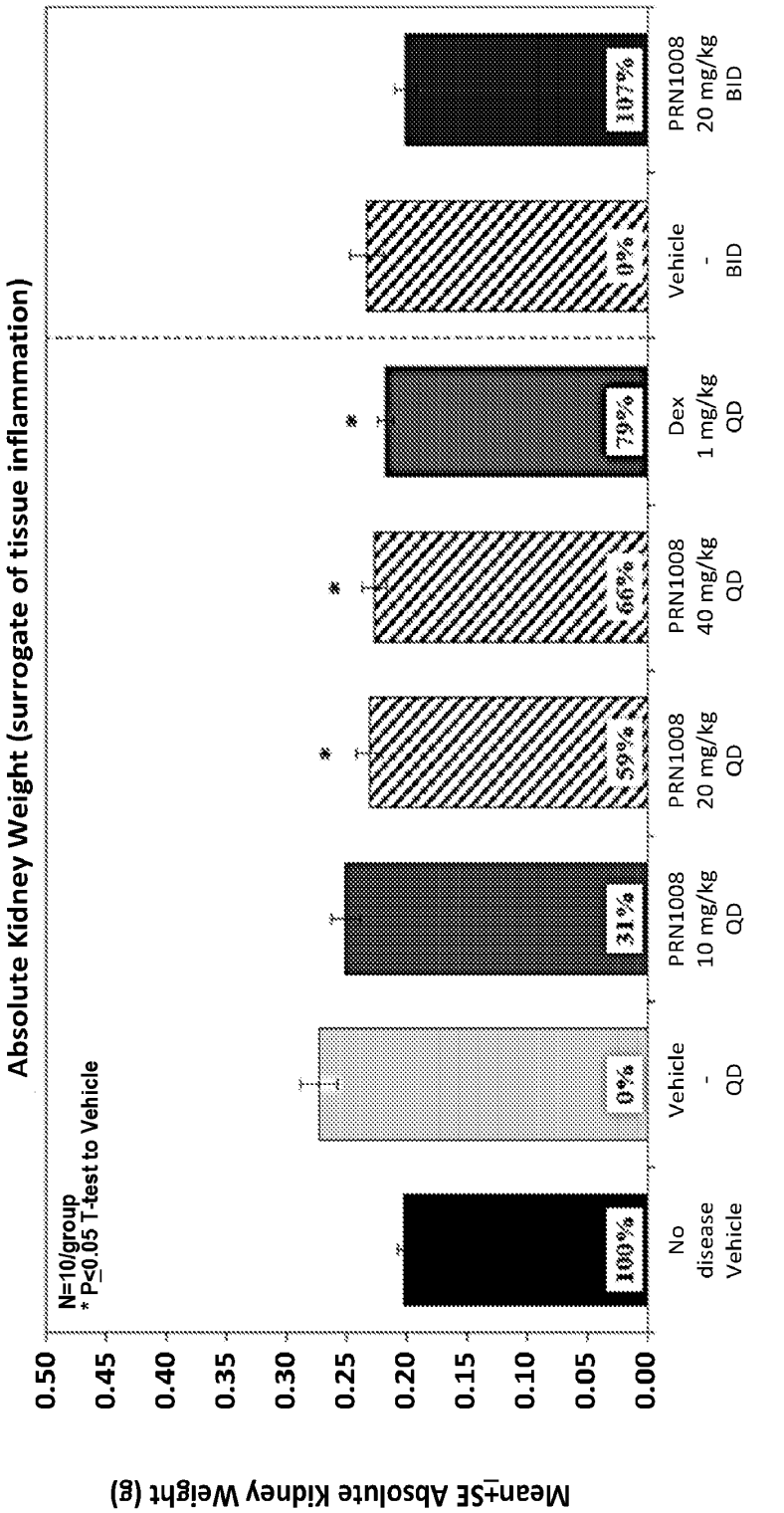

Absolute Kidney Weight (surrogate of tissue inflammation)
N=10/group
* P≤0.05 T-test to Vehicle
Mean±SE Absolute Kidney Weight (g)
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
100%
0%
31%
59%
66%
79%
0%
107%
*
*
*
No disease Vehicle
Vehicle - QD
PRN1008 10 mg/kg QD
PRN1008 20 mg/kg QD
PRN1008 40 mg/kg QD
Dex 1 mg/kg QD
Vehicle - BID
PRN1008 20 mg/kg BID

FIG. 5

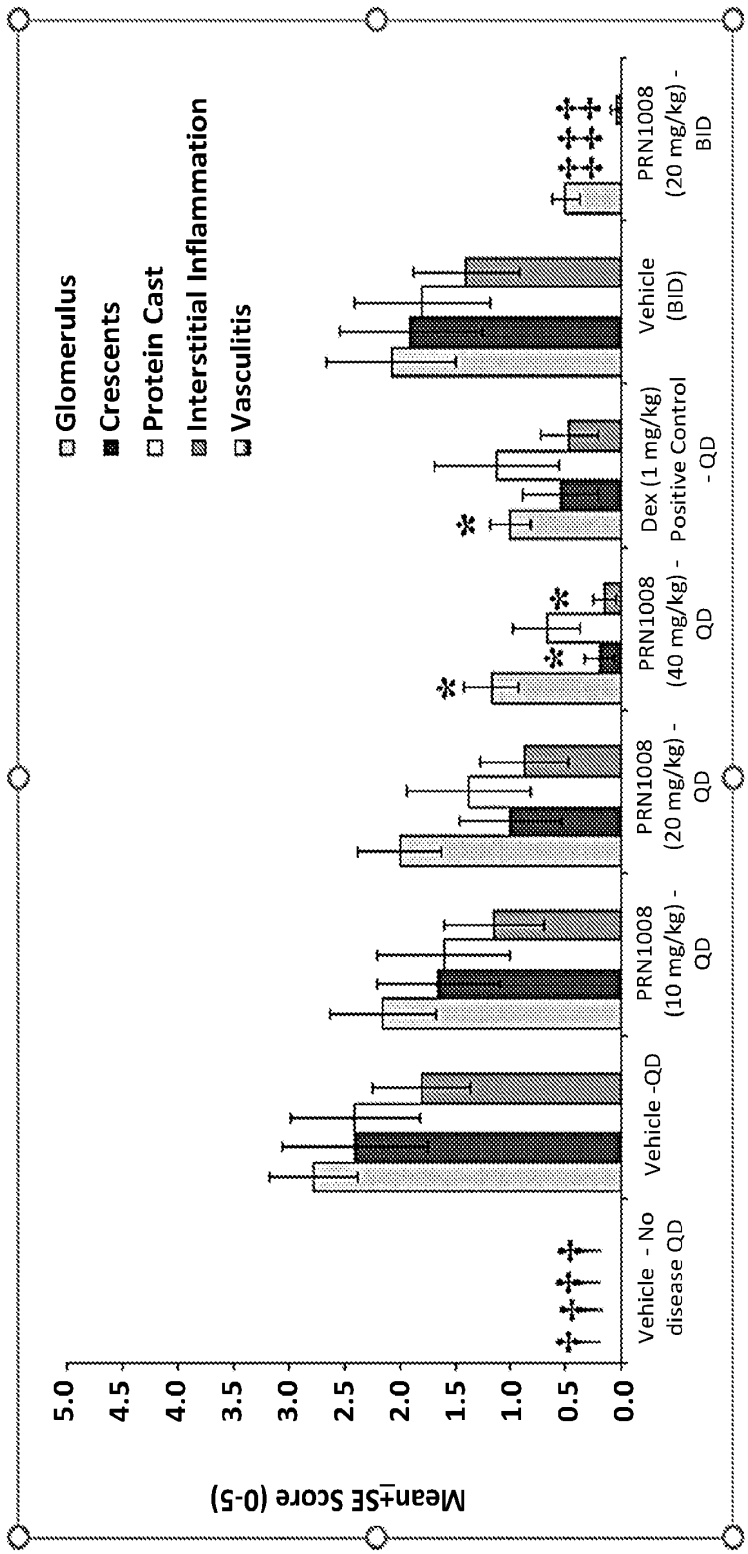

Glomerulus
Crescents
Protein Cast
Interstitial Inflammation
Vasculitis
Mean+SE Score (0-5)
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Vehicle - No disease QD
Vehicle -QD
PRN1008 (10 mg/kg) - QD
PRN1008 (20 mg/kg) - QD
PRN1008 (40 mg/kg) - QD
Dex (1 mg/kg) Positive Control - QD
Vehicle (BID)
PRN1008 (20 mg/kg) - BID

FIG. 6

System	Primary Human Cell Types	Disease/Tissue Relevance	Biomarkers Endpoints
3C	Venular endothelial cells	Cardiovascular Disease, Chronic Inflammation	MCP 1, VCAM 1, TM, TF, ICAM 1, E selection, uPAR, IL 8, MIG, IILA DR, Proliferation, SRB
4N	Venular endothelial cells	Asthma, Allergy, Oncology	MCP-1, t-otaxin-3, VCAM 1, P-selection, uPAR, SRB, VI-GI-RII
LPS	Preipheral blood mononuclear cells + Venular endothelial cells	Cardiovascular Disease, Chronic Inflammation	MCP-1, VCAM-1, TM, TF, CD40, E-selection, CD69, IL-8, IL-1α, M-CSF, sPEG2, SRB, sRNFα
SAg	Preipheral blood mononuclear cells + Venular endothelial cells	Autoimmune Disease, Chronic Inflammation	MCP-1, CD38, CD40, E-selection, CD69, IL-8, MIG, PBMC Cytotoxivity, Prolikeration, SRB
BT	B cells + Preipheral blood mononuclear cells	Asthma, Allergy, Oncology, Autoimmunity	B cell Proliferation, PBMC Cytotoxivity, Secreted IgG, sIL-17A, sIL-17F, sIL-2, sIL-6, sRNFα
BF4T	Bronchial epithelial cells + Dermal fibroblasts	Asthma, Allergy, Fibrosis, Lung	MCP-1, Eotaxin-3, VCAM-1, ICAM-1, CD90, IL-8, IL-1α,Keratin 8/18, MMP-1, MMP-3, MMP-9, PAI-1, SRB, tPA, uPA
BE3C	Bronchial epithelial cells	COPD, Lung Inflammation	ICAM-1, uPAR, IP-10, I-TAC, IL-8, MIG, EGFR, HLA-DR, IL-1α, Keratin 8/18, MMP-1, MMP-9, PAI-1, SRB, tPA, uPA
CASM3C	Coronary artery smooth muscle cells	Cardiovascular Inflammation, Restenosis	MCP-1, VCAM-1, TM, TF, uPAR, IL-8, MIG, HLA-DR, IL-6, LDLR, M-CSF, PAI-1, Proliferation, SAA, SRB
HDF3CGF	Dermal Fibroblasts	Fibrosis, Chronic Inflammation	MCP-1, VCAM-1, ICAM-1, Collagen I, Collagen III, IP-10, I-TAC, IL-8, MIG, EGFR, M-CSF, MMP-1, PAL-1, Proliferation_72hr, SRB, TIMP-1, TIMP-2
KF3CT	Keratinocytes + Dermal fibroblasts	Psoriasis, Dermatitis, Skin	MCP-1, ICAM-1, IP-10, IL-8, MIG, IL-1α, MMP-9, PAI-1, SRB, TIMP-2, uPA
MyoF	Lung fibroblasts	Fibrosis Chronic Inflammation	α-SMAction, bFGF, VCAM-1, Collagen I, Collagen III, Collagen IV, IL-8, Decorin, MMP 1, PAI-1, SRB, TIMP-1
SMphg	Venular epithelial cells + M1 macrophages	Cardiovascular Inflammation, Restenosis, Chronic Inflammation	MCP-1, MIP-1α, VCAM-1, CD40, E-selection, CD69, IL-8, IL-1α, M-CSF, sIL-10, SRB, SRB-Mphg

FIG. 7

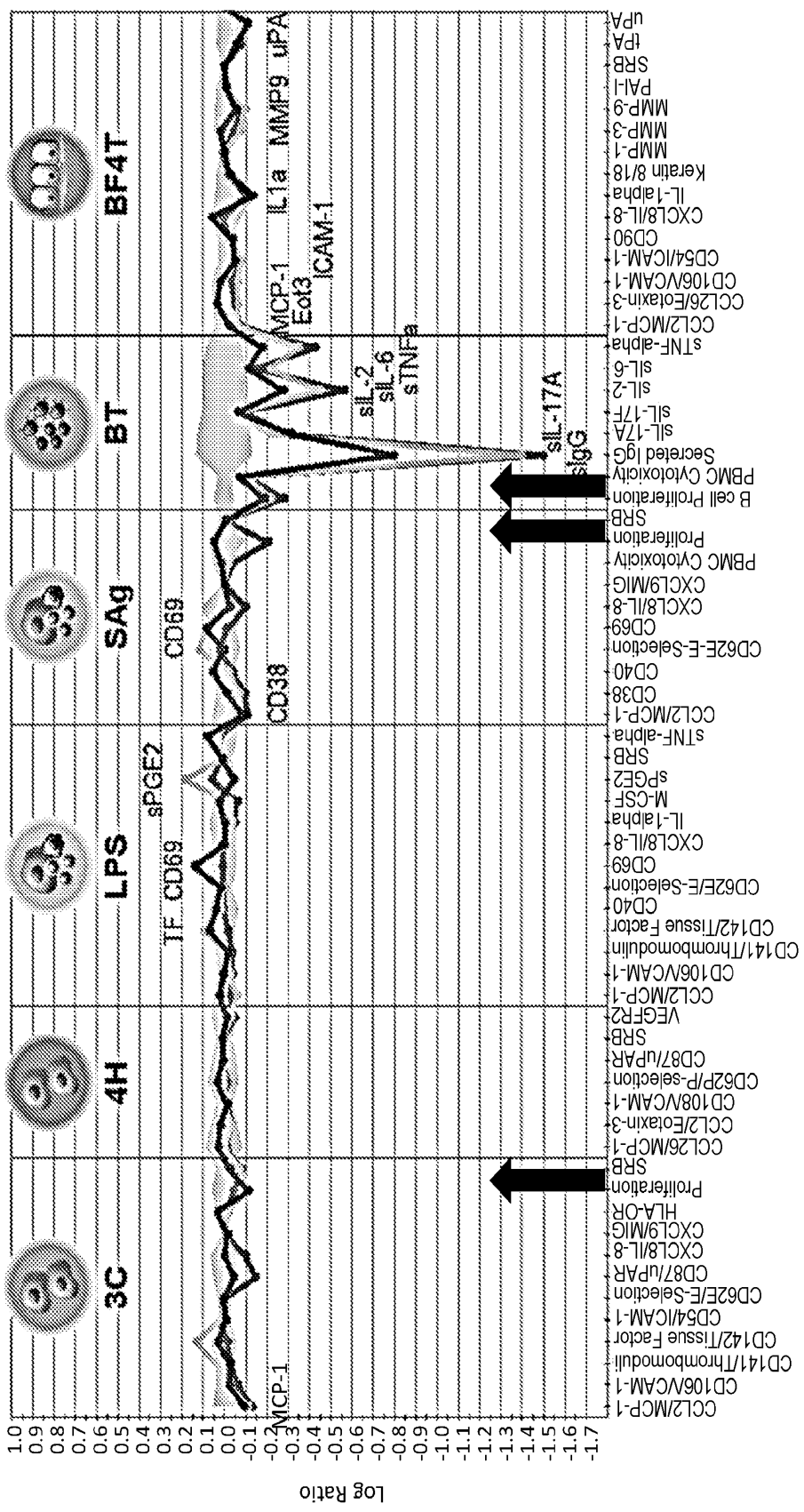

3C
4H
LPS
SAg
BT
BF4T
Log Ratio
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
-0.1
-0.2
-0.3
-0.4
-0.5
-0.6
-0.7
-0.8
-0.9
-1.0
-1.1
-1.2
-1.3
-1.4
-1.5
-1.6
-1.7
MCP-1
TF
CD69
sPGE2
CD69
CD38
MCP-1
Eot3
ICAM-1
IL1a
MMP9
uPA
sIL-2
sIL-6
sTNFa
sIL-17A
sIgG
CCL2/MCP-1
CD106/VCAM-1
CD141/Thrombomodulin
CD142/Tissue Factor
CD54/ICAM-1
CD62E/E-Selection
CD87/uPAR
CXCL8/IL-8
CXCL9/MIG
HLA-DR
Proliferation
CCL26/MCP-1
CCL2/Eotaxin-3
CD108/VCAM-1
CD62P/P-selection
CD87/uPAR
SRB
VEGFR2
CCL2/MCP-1
CD106/VCAM-1
CD141/Thrombomodulin
CD142/Tissue Factor
CD40
CD62E/E-Selection
CD69
CXCL8/IL-8
IL-1alpha
M-CSF
sPGE2
SRB
sTNF-alpha
CCL2/MCP-1
CD38
CD40
CD62E-E-Selection
CD69
CXCL8/IL-8
CXCL9/MIG
PBMC Cytotoxicity
Proliferation
SRB
B cell Proliferation
PBMC Cytotoxicity
Secreted IgG
sIL-17A
sIL-17F
sIL-2
sIL-6
sTNF-alpha
CCL2/MCP-1
CCL26/Eotaxin-3
CD106/VCAM-1
CD54/ICAM-1
CD90
CXCL8/IL-8
IL-1alpha
Keratin 8/18
MMP-1
MMP-3
MMP-9
PAI-I
SRB
tPA
uPA

FIG. 8

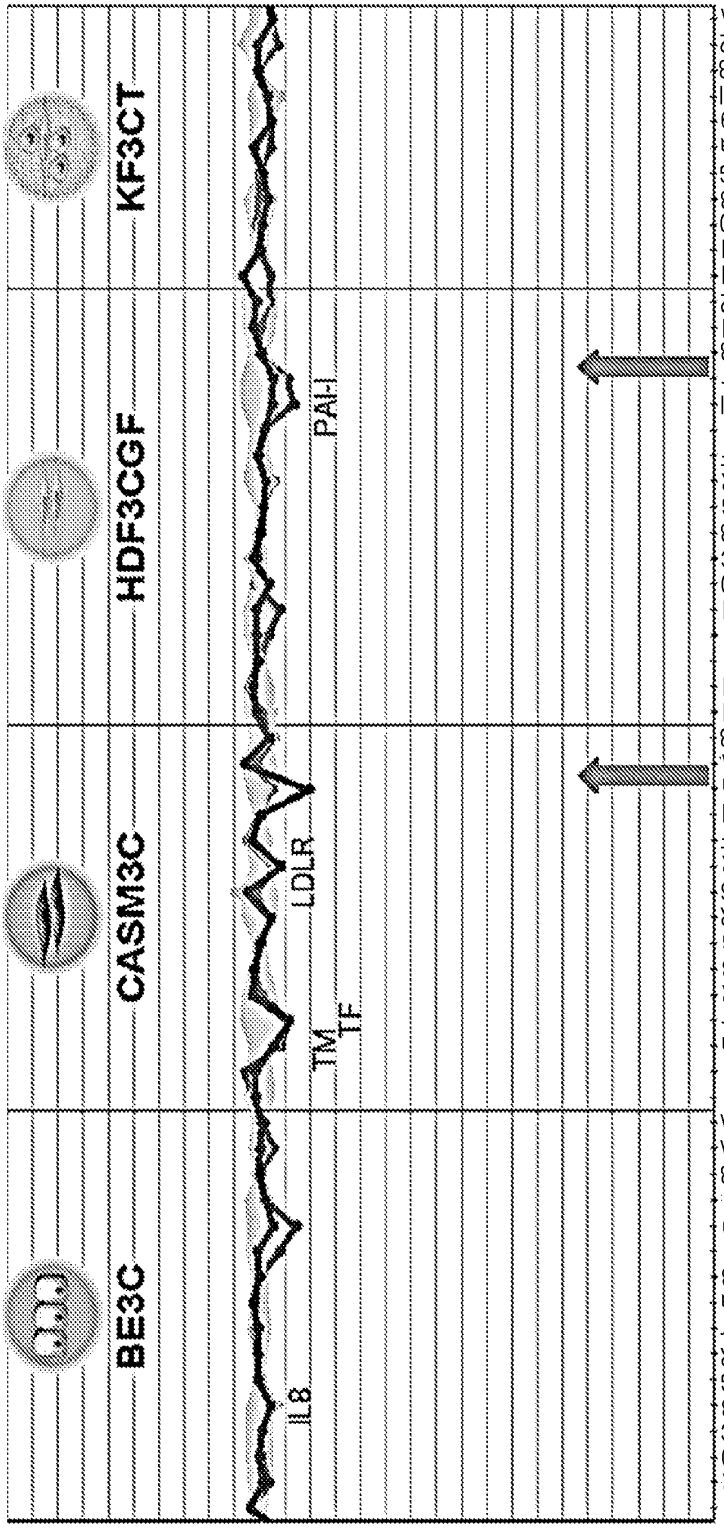

BE3C
CASM3C
HDF3CGF
KF3CT
IL8
LDLR
TM
TF
PAI-I
CD54/ICAM-1
CD87/uPAR
CXCL10/IP-10
CXCL11/I-TAC
CXCL8/IL-8
CXCL9/MIG
EGFR
HLA-Dr
IL-1alpha
Keratin 8/18
MMP-1
MMP-9
PAI-I
SRB
tPA
uPA
CCL2/MCP-1
CD106/VCAM-1
CD141/Thrombomodulin
CD142/Tissue Factor
CD87/uPAR
CXCL8/IL-8
CXCL9/MIG
HLA-DR
IL-6
LDLR
M-CSF
PAI-I
Proliferation
Serum Amyloid A
SRB
CCL2/MCP-1
CD106/VCAM-1
CD54/ICAM-1
Collagen I
Collagen III
CXCL10/IP-10
CXCL11/I-TAC
CXCL8/IL-8
CXCL9/MIG
EGFR
M-CSF
MMP-1
PAI-I
Proliferation_72hr
SRB
TIMP-1
TIMP-2
CCL2/MCP-1
CD54/ICAM-1
CXCL10/IP-10
CXCL8/IP-8
CXCL9/MIG
IL-1alpha
IMMP-9
PAI-I
SRB
TIMP-2
uPA

FIG. 8 (cont.)

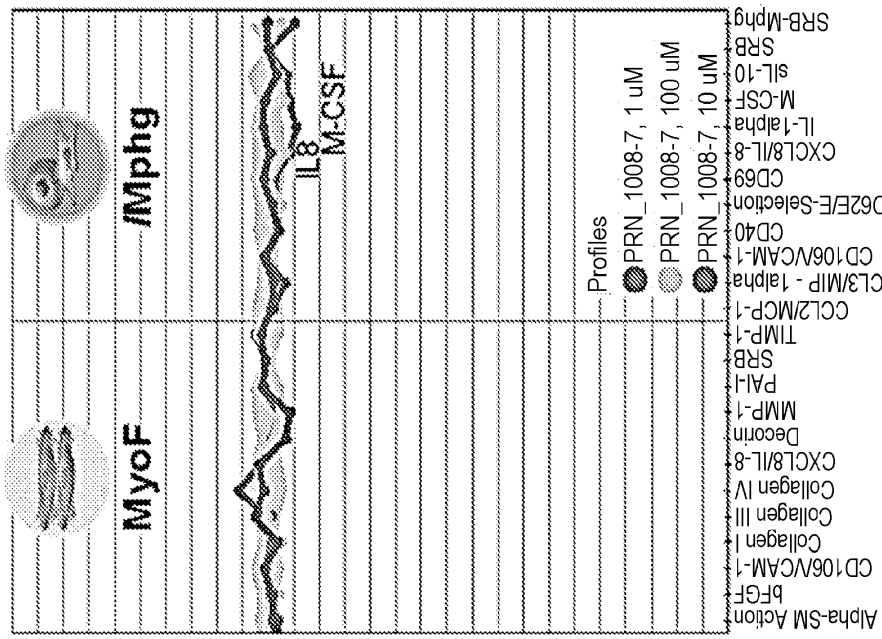

MyoF
/Mphg
IL8
M-CSF
Profiles
PRN_1008-7, 1 uM
PRN_1008-7, 100 uM
PRN_1008-7, 10 uM
Alpha-SM Actin
bFGF
CD106/VCAM-1
Collagen I
Collagen III
Collagen IV
CXCL8/IL-8
Decorin
MMP-1
PAI-1
SRB
TIMP-1
CCL2/MCP-1
CCL3/MIP - 1alpha
CD106/VCAM-1
CD40
CD62E/E-Selection
CD69
CXCL8/IL-8
IL-1alpha
M-CSF
sIL-10
SRB
SRB-Mphg

FIG. 8 (cont.)

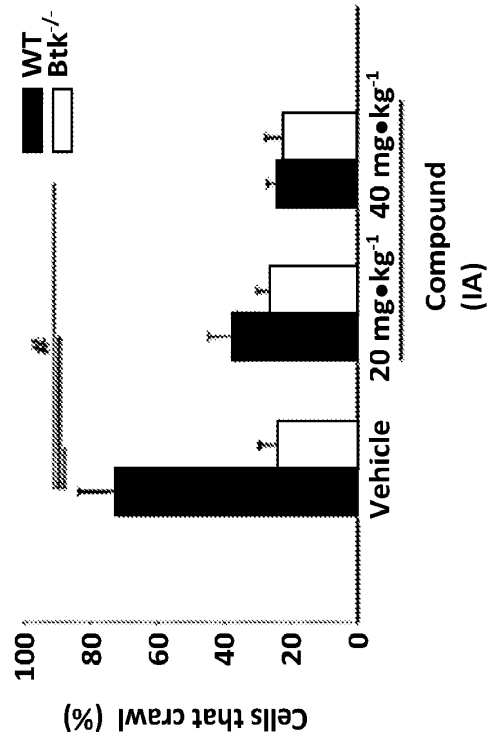

WT
Btk-/-
Cells that crawl (%)
100
80
60
40
20
0
Vehicle
20 mg•kg-1
40 mg•kg-1
Compound (IA)

FIG. 9A

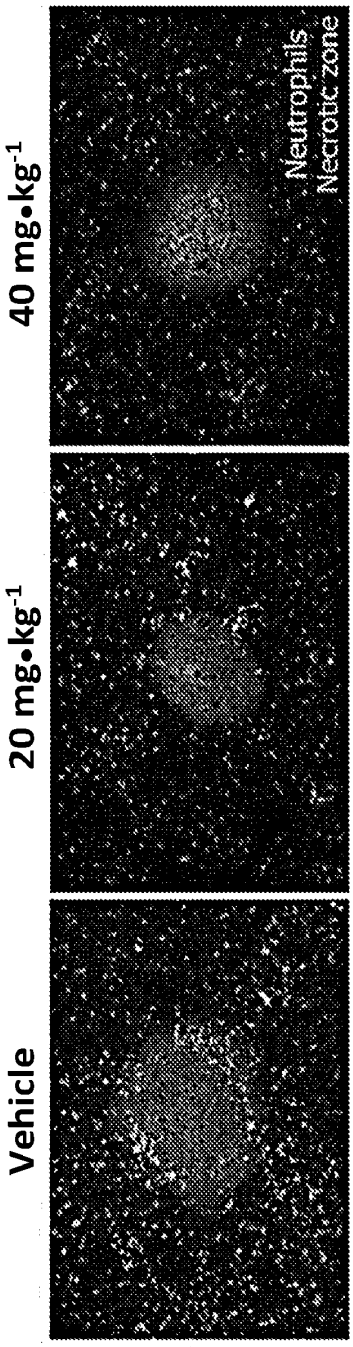

Vehicle
20 mg•kg-1
40 mg•kg-1
Neutrophils
Necrotic zone

FIG. 9B