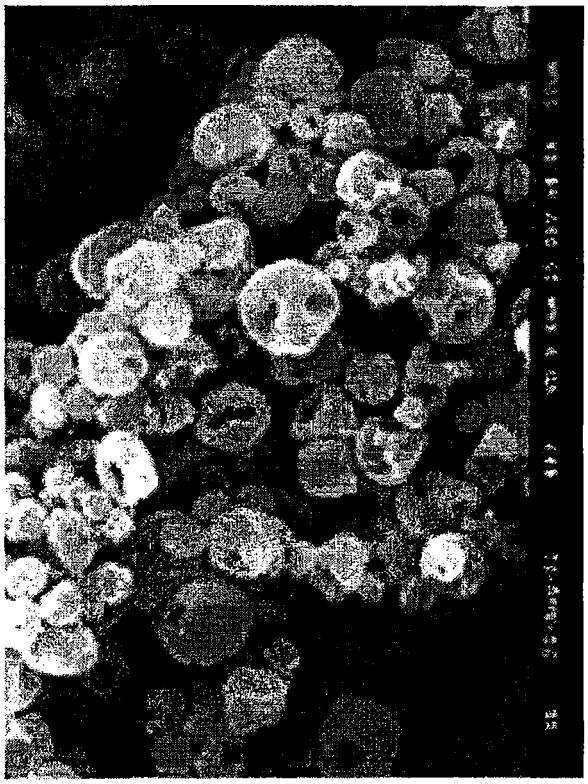
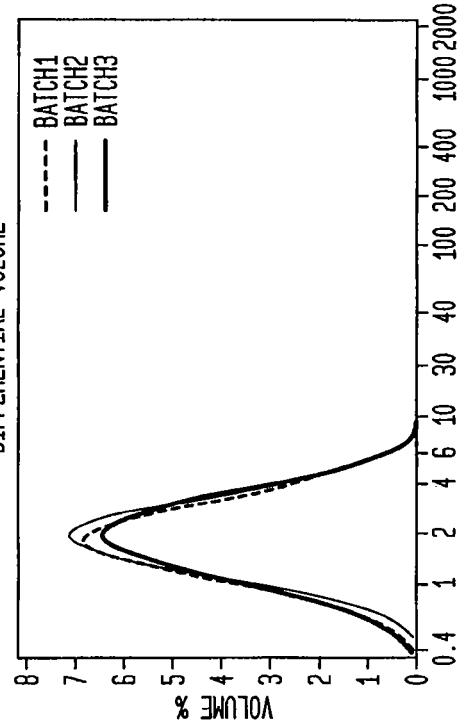
FIG. 1

NEAT SPRAY DRIED INSULIN

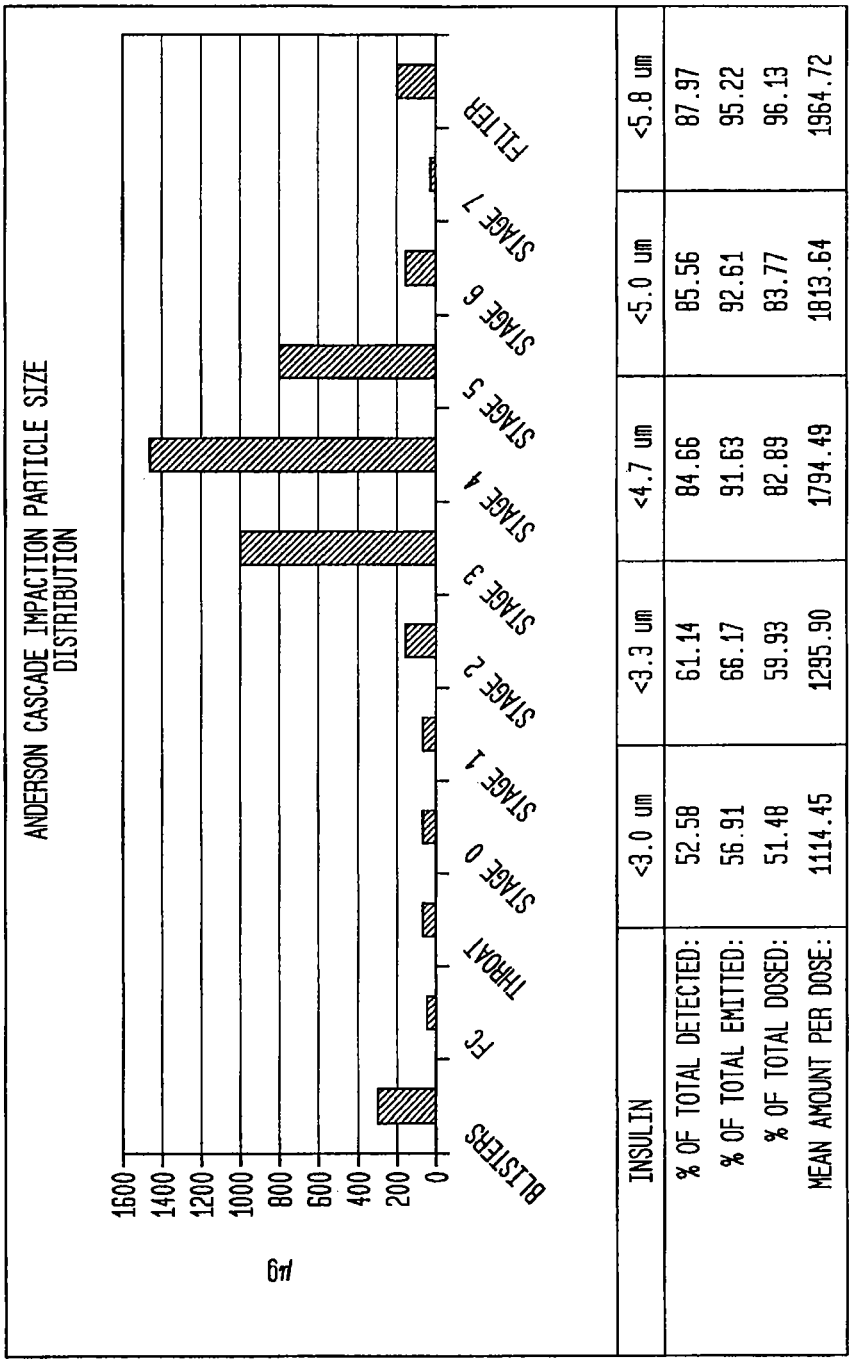




• MEAN PARTICLE SIZE
APPROXIMATELY 1.8 MICRONS

FIG. 2

PARTICLE SIZE DISTRIBUTION- INSULIN
2.4mg DOSE, ACI@28.3L/min



INSULIN	<3.0 um	<3.3 um	<4.7 um	<5.0 um	<5.8 um
% OF TOTAL DETECTED:	52.58	61.14	84.66	85.56	87.97
% OF TOTAL EMITTED:	56.91	66.17	91.63	92.61	95.22
% OF TOTAL DOSED:	51.48	59.93	82.89	83.77	96.13
MEAN AMOUNT PER DOSE:	1114.45	1295.90	1794.49	1813.64	1964.72

MEAN EMITTED DOSE = 93.76%

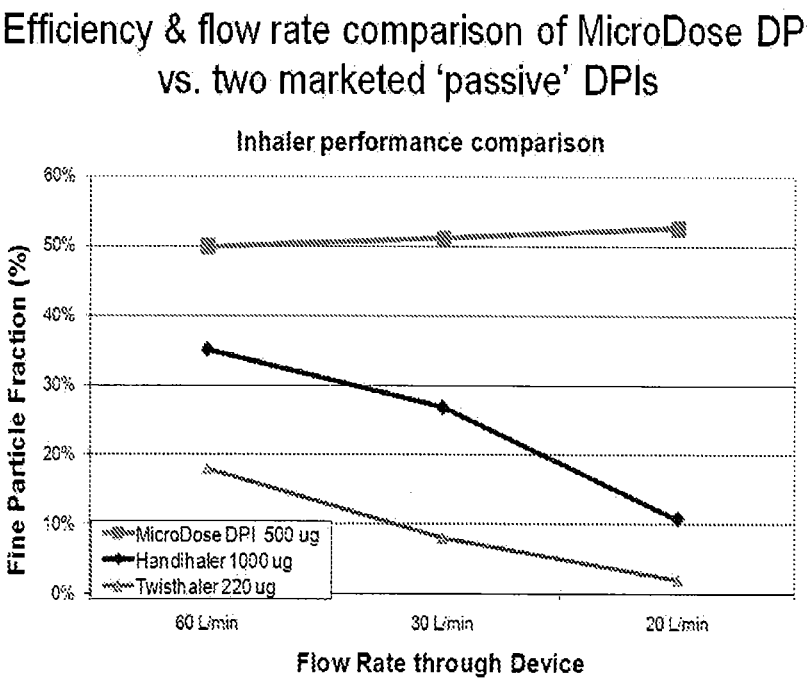
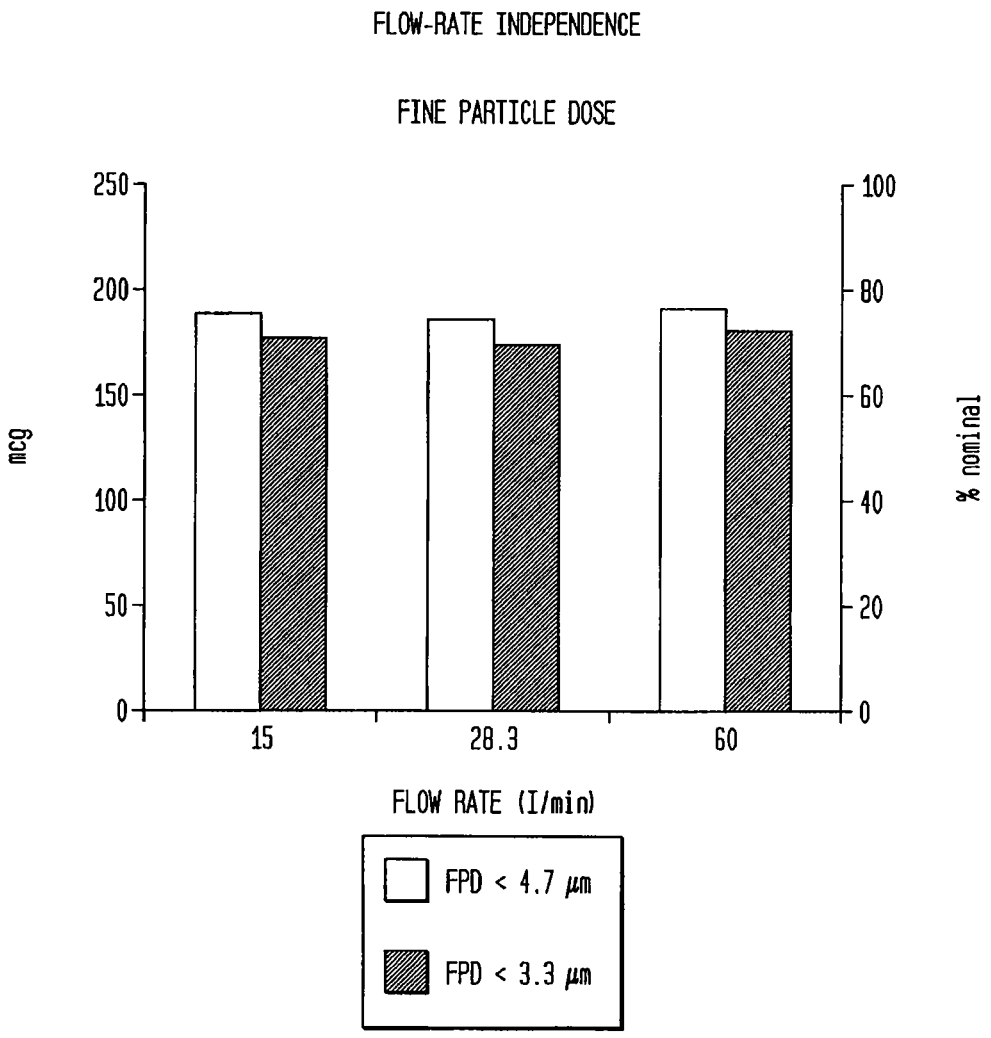

Efficiency & flow rate comparison of MicroDose DPI vs. two marketed 'passive' DPIs
Inhaler performance comparison
Fine Particle Fraction (%)
60%
50%
40%
30%
20%
10%
0%
MicroDose DPI 500 ug
Handihaler 1000 ug
Twisthaler 220 ug
60 L/min
30 L/min
20 L/min
Flow Rate through Device
Jet milled (micronized) corticosteroid w/lactose

FIGURE 3

FIG. 4



SPRAY-DRIED NEAT PEPTIDE 250 mcg

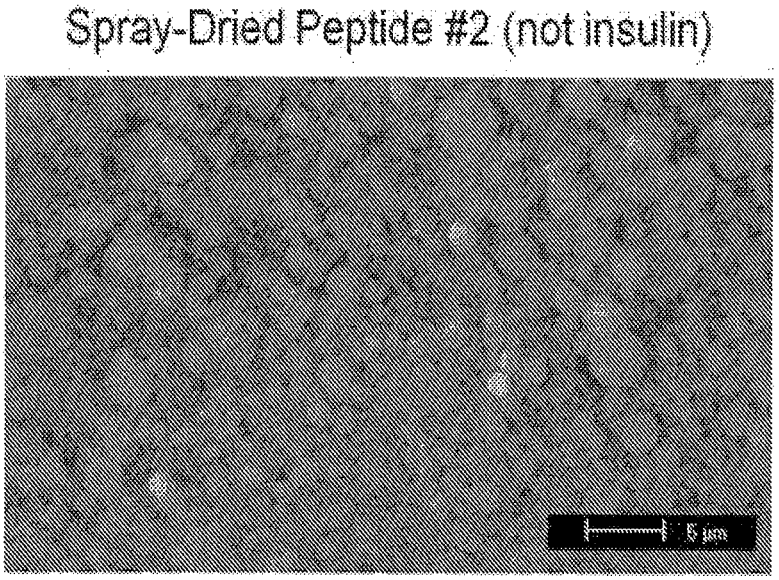


FIGURE 5

FIG. 6

PARTICLE SIZE DISTRIBUTION- PEPTIDE #2
250mcg DOSE, ACI@28.3L/min

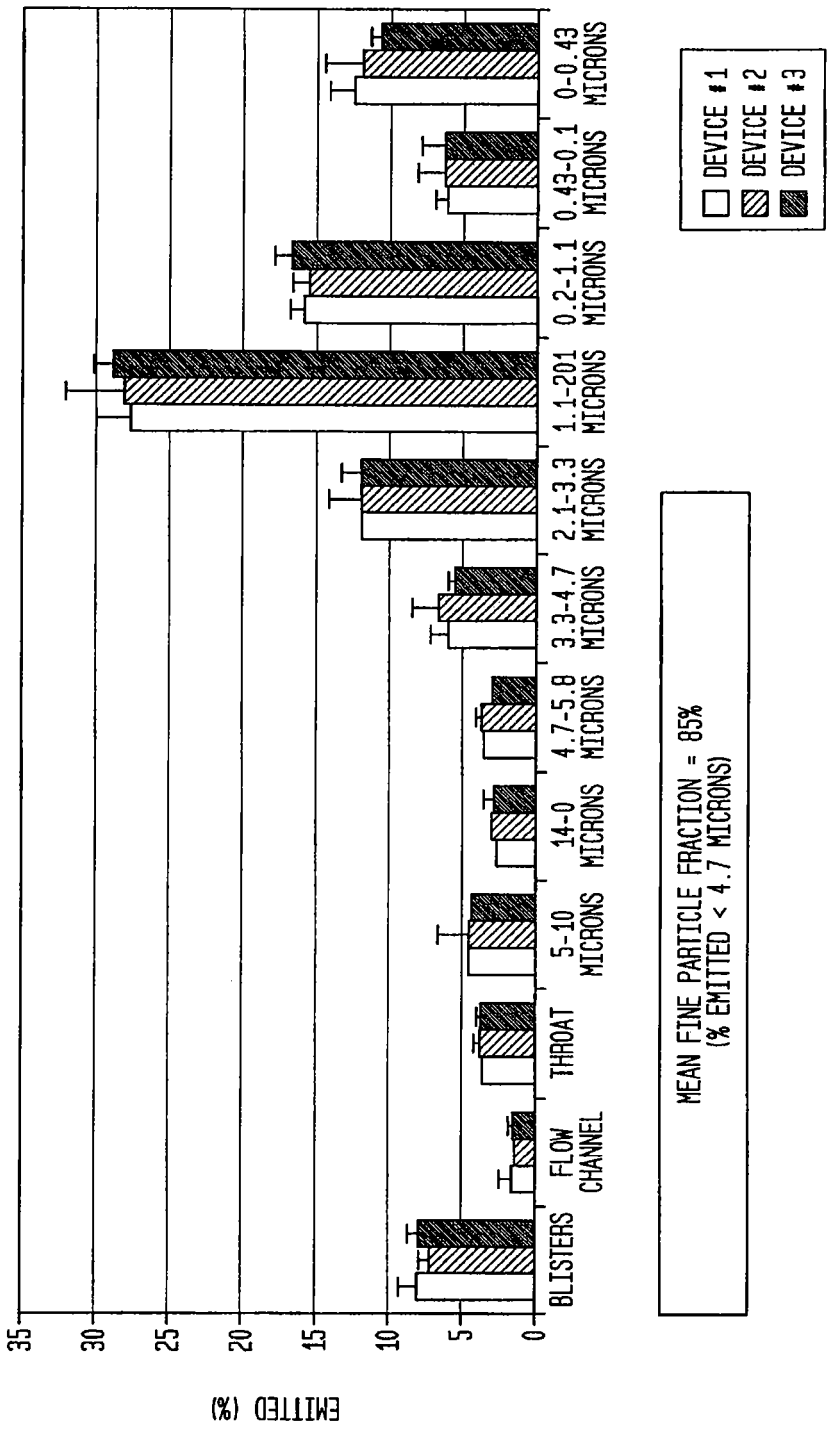
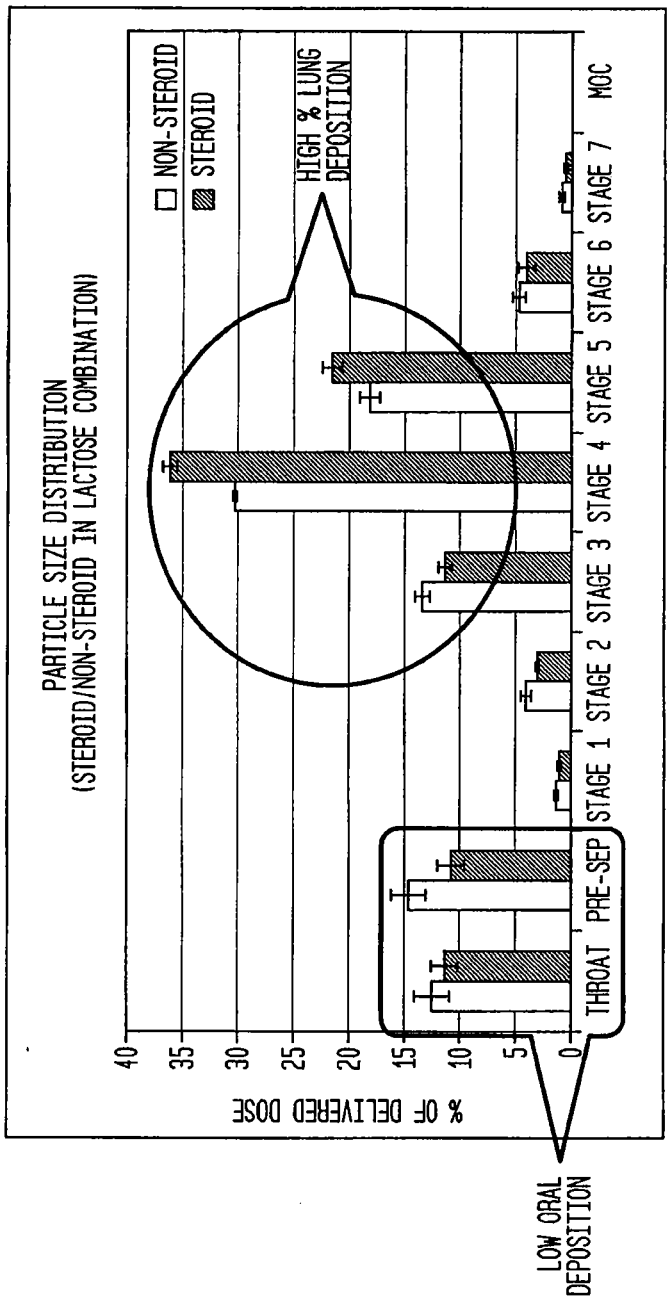


FIG. 7

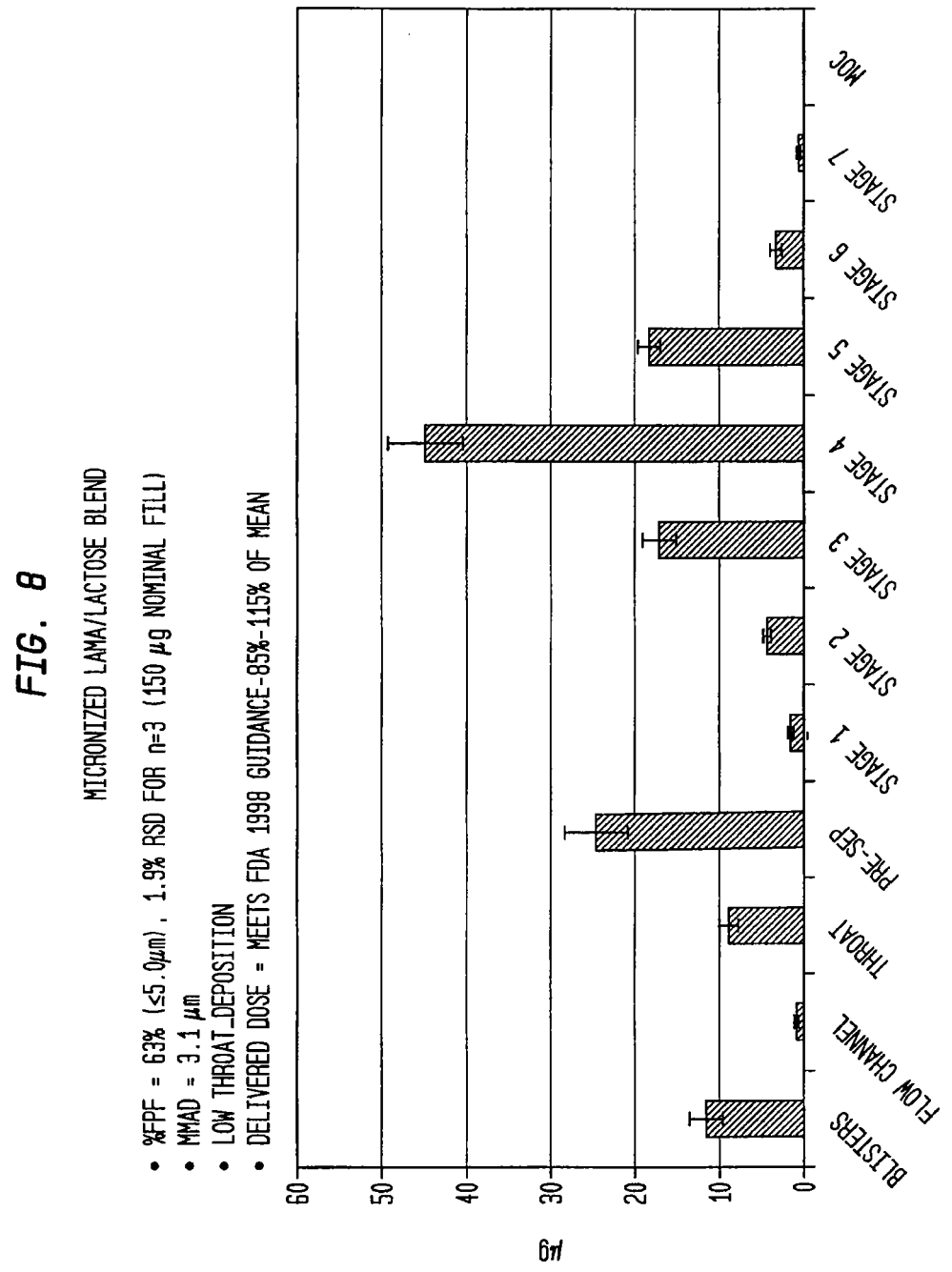
MICRONIZED/LACTOSE BLEND COMBINATION

PARTICLE SIZE DISTRIBUTION BY NGI
(3 RUNS @30L/min FLOW RATE /1mg FILL WT.



- 62% LUNG DOSE ≤5.0μm FOR 'OTHER' 1.95% RSD FOR n=5
- 70% LUNG DOSE ≤5.0μm FOR STEROID, 1.92% RSD FOR n=5

FIG. 8


MICRONIZED LAMA/LACTOSE BLEND
• %FPF = 63% (≤5.0μm), 1.9% RSD FOR n=3 (150 μg NOMINAL FILL)
• MMAD = 3.1 μm
• LOW THROAT_DEPOSITION
• DELIVERED DOSE = MEETS FDA 1998 GUIDANCE-85%-115% OF MEAN
μg
60
50
40
30
20
10
0
BLISTERS
FLOW CHANNEL
THROAT
PRE-SEP
STAGE 1
STAGE 2
STAGE 3
STAGE 4
STAGE 5
STAGE 6
STAGE 7
MOC

Activated MK2 Differentially Expressed in Human IPF vs. Normal Lung

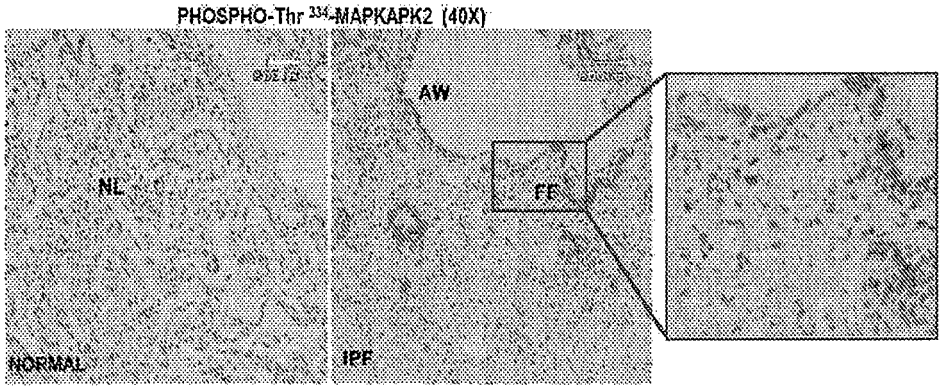
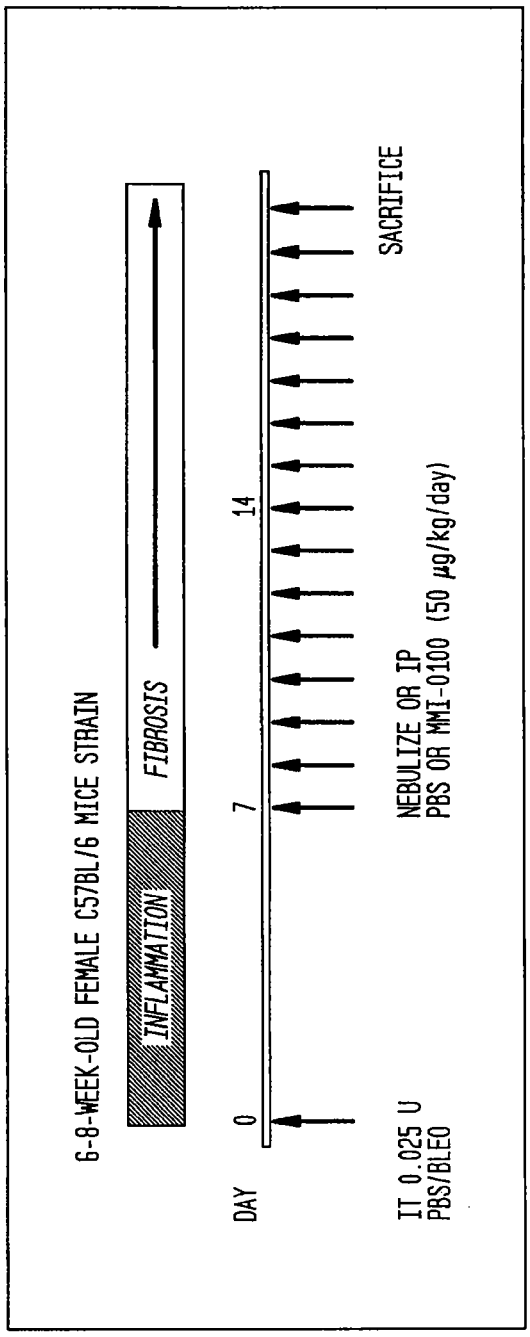


FIGURE 9

FIG. 10


BLEOMYCIN MODEL OF IDIOPATHIC PULMONARY FIBROSIS: PREVENTION MODEL
6-8-WEEK-OLD FEMALE C57BL/6 MICE STRAIN
INFLAMMATION
FIBROSIS
DAY
0
7
14
SACRIFICE
IT 0.025 U
PBS/BLEO
NEBULIZE OR IP
PBS OR MMI-0100 (50 μg/kg/day)

MMI-0100 Inhibits Development of Fibrosis in Idiopathic Pulmonary Fibrosis Prevention Model

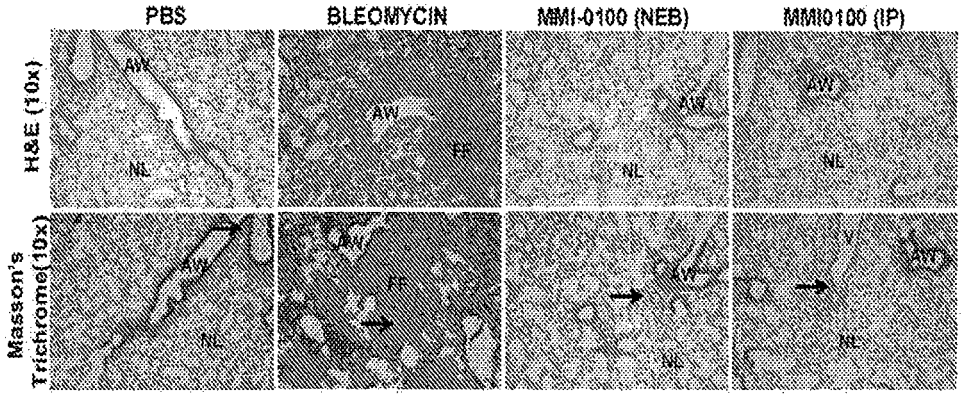


FIGURE 11

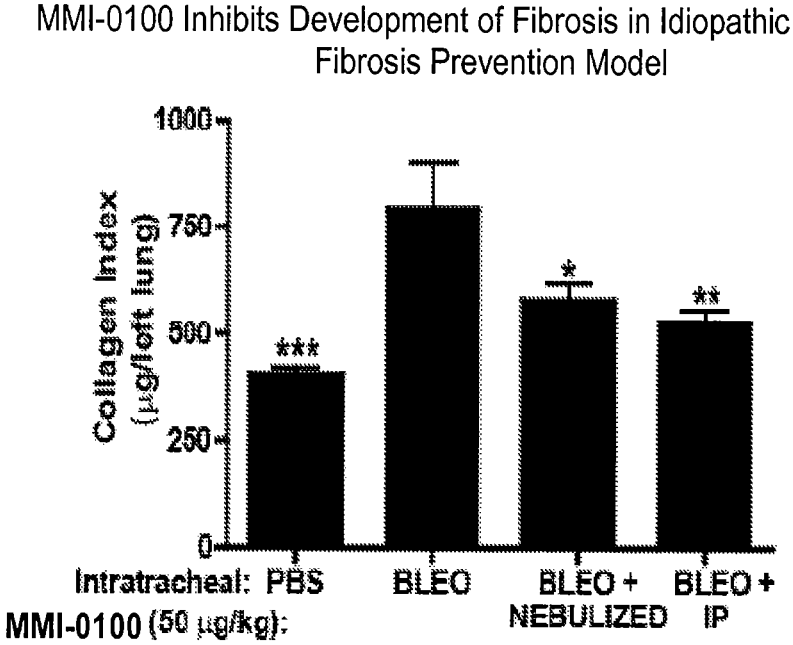

MMI-0100 Inhibits Development of Fibrosis in Idiopathic Pulmonary Fibrosis Prevention Model
Collagen Index (µg/left lung)
1000
750
500
250
0
***
*
**
Intratracheal: PBS
BLEO
BLEO + NEBULIZED
BLEO + IP
MMI-0100 (50 µg/kg):

FIGURE 12

MMI-0100 Dose-Response Data in Idiopathic Pulmonary Fibrosis Prevention Model

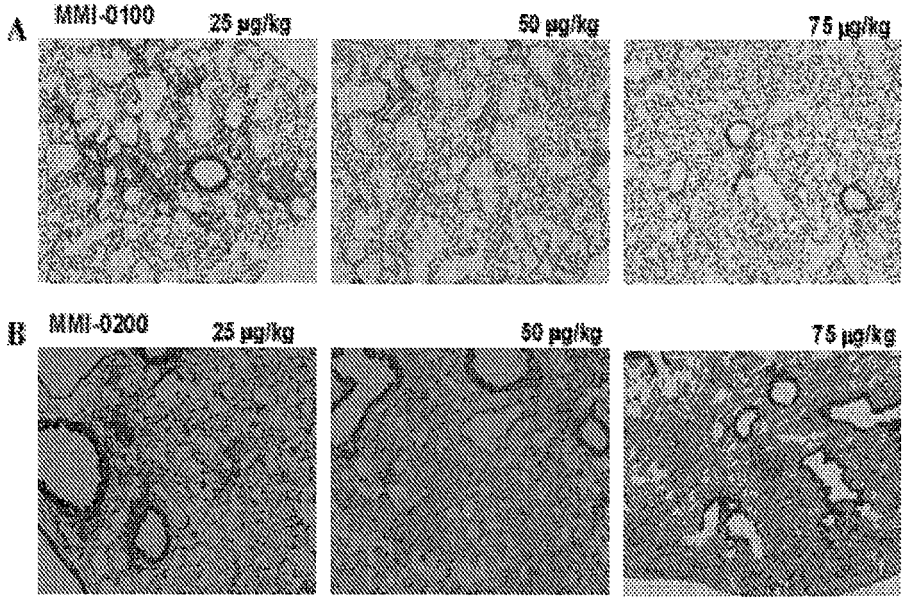


FIGURE 13

FIG. 14

MMI-0100 REDUCES SYSTEMIC T-CELL ACTIVATION IN IDIOPATHIC PULMONARY FIBROSIS PREVENTION MODEL

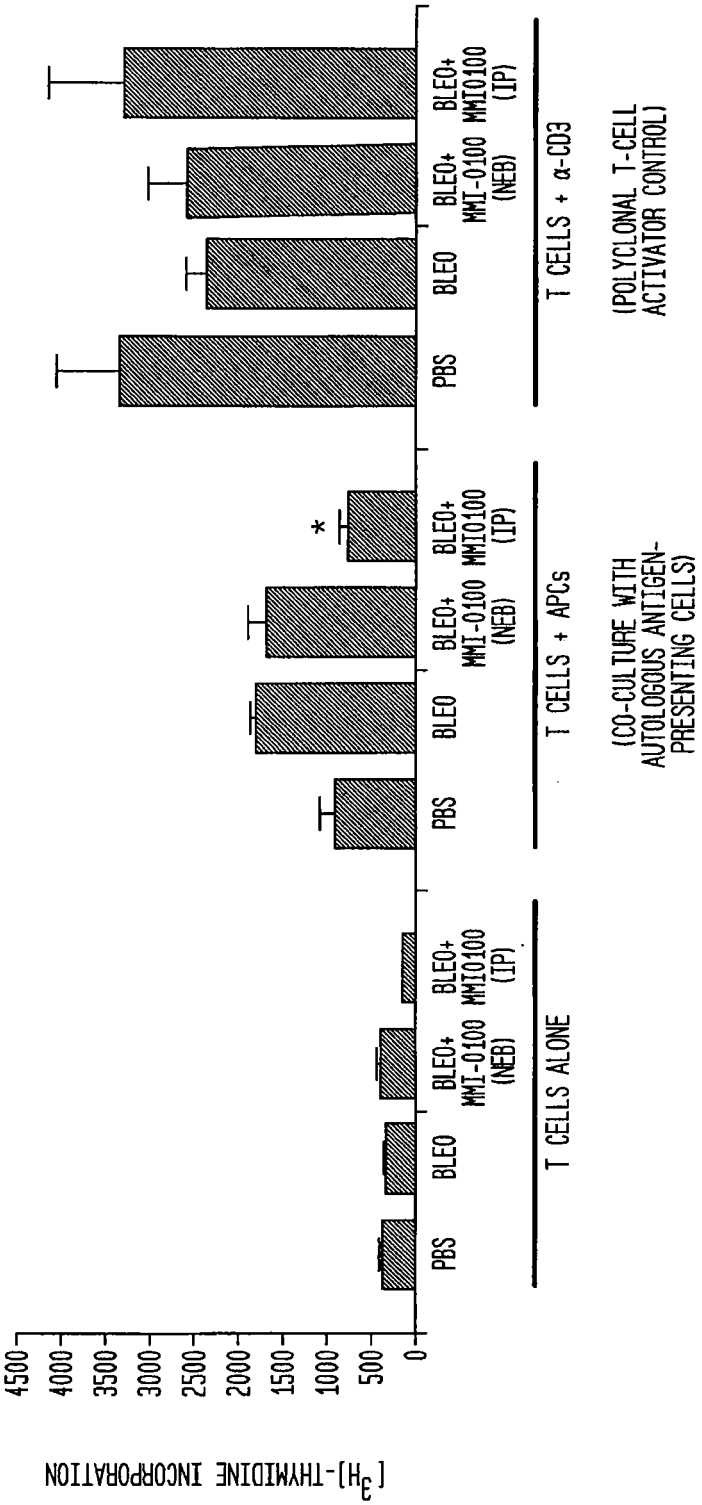
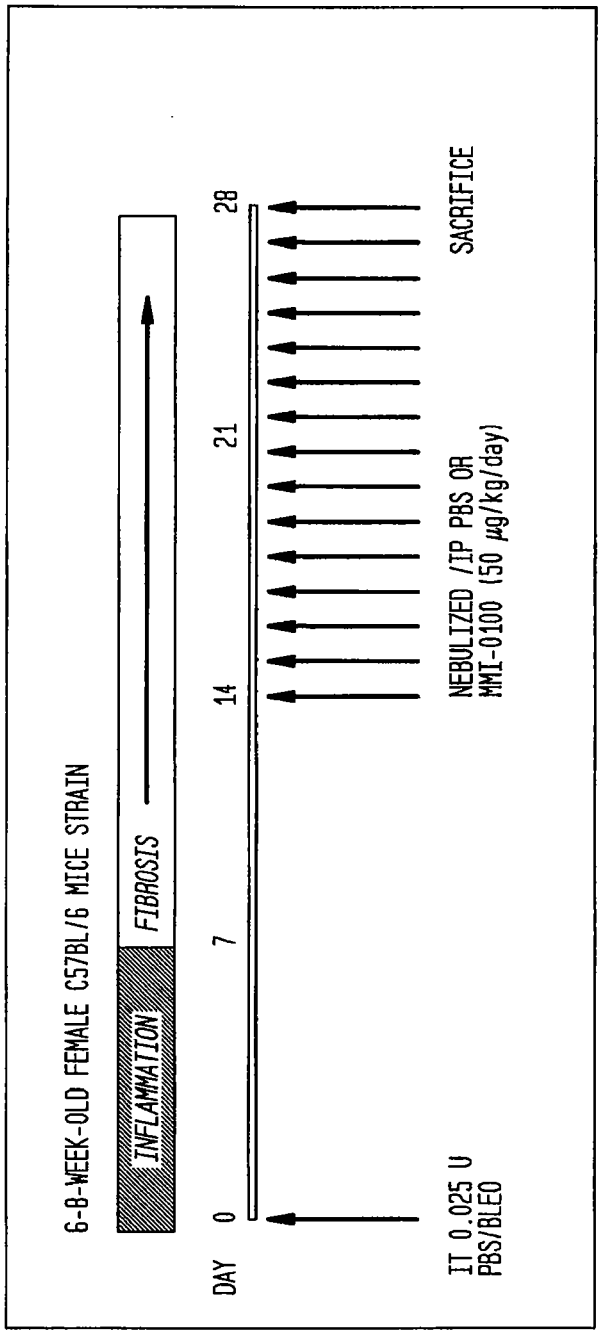


FIG. 15

BLEOMYCIN MODEL OF IDIOPATHIC PULMONARY FIBROSIS: TREATMENT MODEL



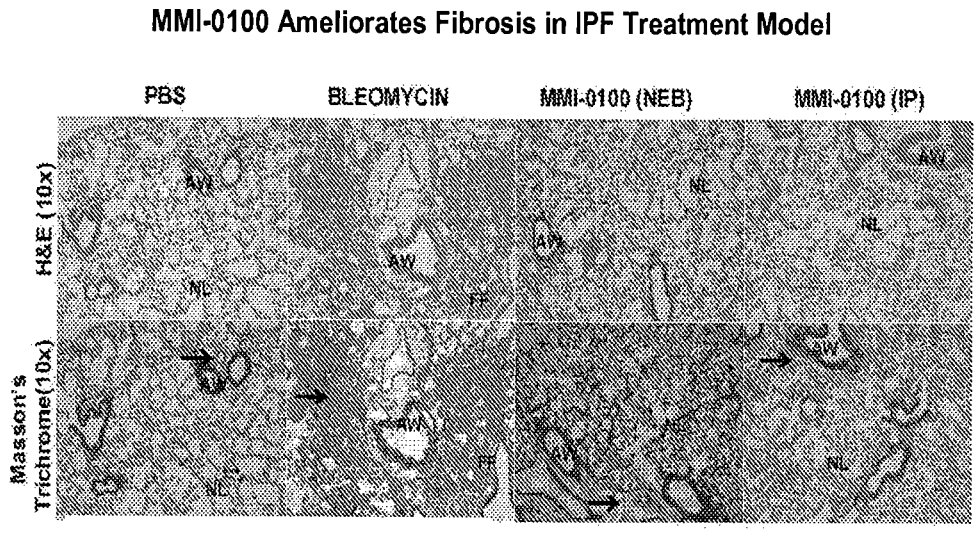

MMI-0100 Ameliorates Fibrosis in IPF Treatment Model
PBS
BLEOMYCIN
MMI-0100 (NEB)
MMI-0100 (IP)
H&E (10x)
Masson's Trichrome(10x)
AW
NL
FF

FIGURE 16

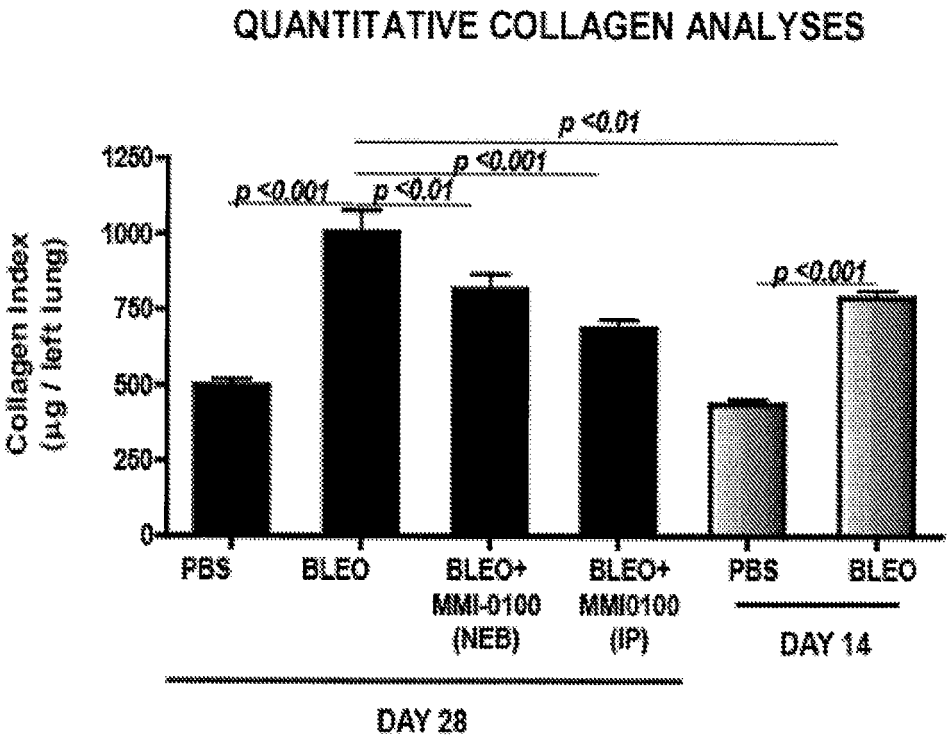

QUANTITATIVE COLLAGEN ANALYSES
p <0.01
p <0.001
p <0.001
p <0.01
p <0.001
Collagen Index (µg / left lung)
1250
1000
750
500
250
0
PBS
BLEO
BLEO+ MMI-0100 (NEB)
BLEO+ MMI0100 (IP)
PBS
BLEO
DAY 14
DAY 28

FIGURE 17

Reduced Activated MK2 with MMI-0100 in IPF Treatment Model

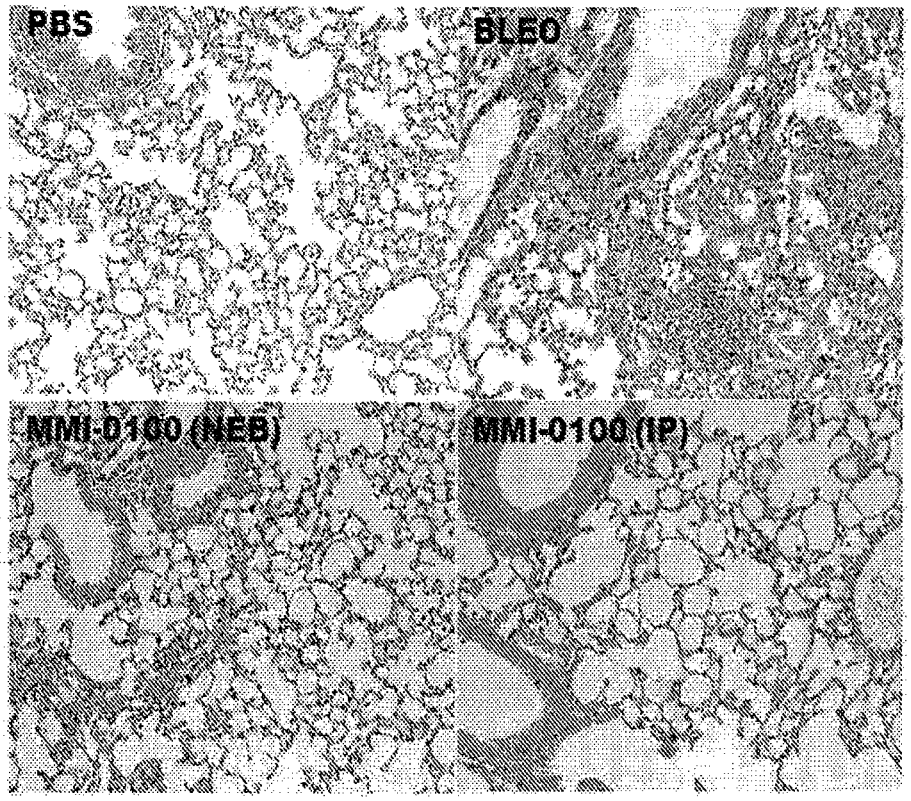


FIGURE 18

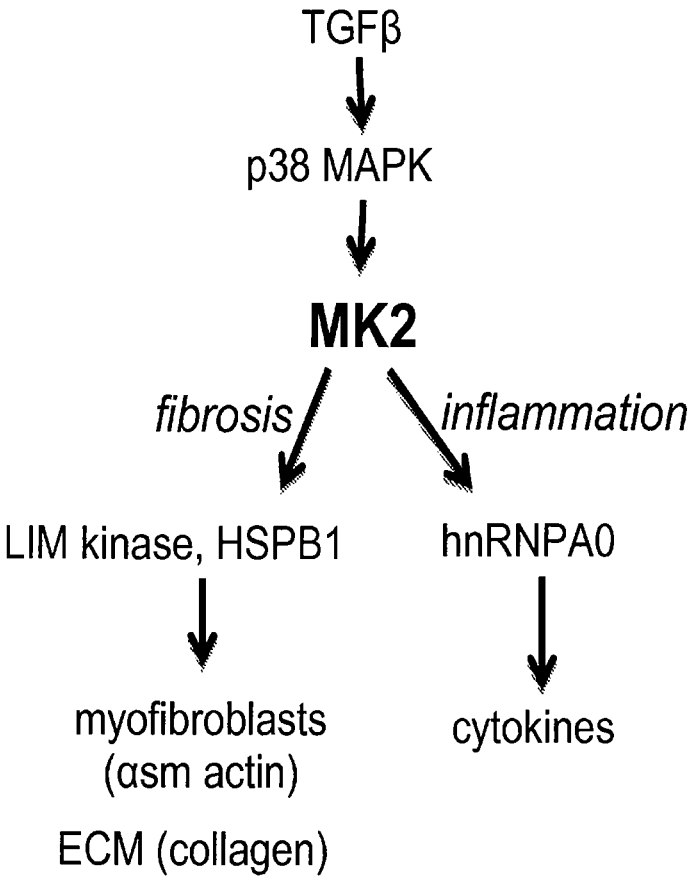

TGFβ
p38 MAPK
MK2
fibrosis
inflammation
LIM kinase, HSPB1
hnRNPA0
myofibroblasts
(αsm actin)
ECM (collagen)
cytokines

FIGURE 19

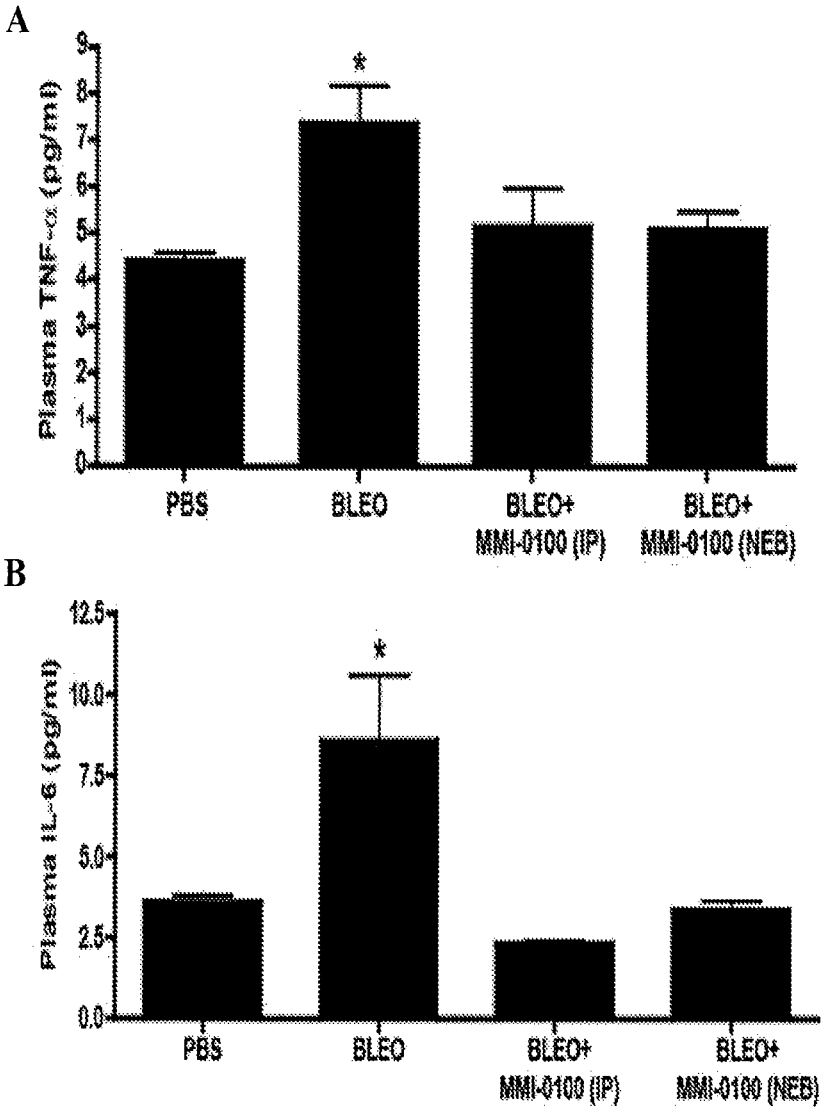

A
Plasma TNF-α (pg/ml)
*
PBS
BLEO
BLEO+ MMI-0100 (IP)
BLEO+ MMI-0100 (NEB)
B
Plasma IL-6 (pg/ml)
12.5
10.0
7.5
5.0
2.5
0.0
*
PBS
BLEO
BLEO+ MMI-0100 (IP)
BLEO+ MMI-0100 (NEB)

FIGURE 20

MMI-0100 Inhibits Myofibroblast (a-SMA) Activation in IPF Treatment Model

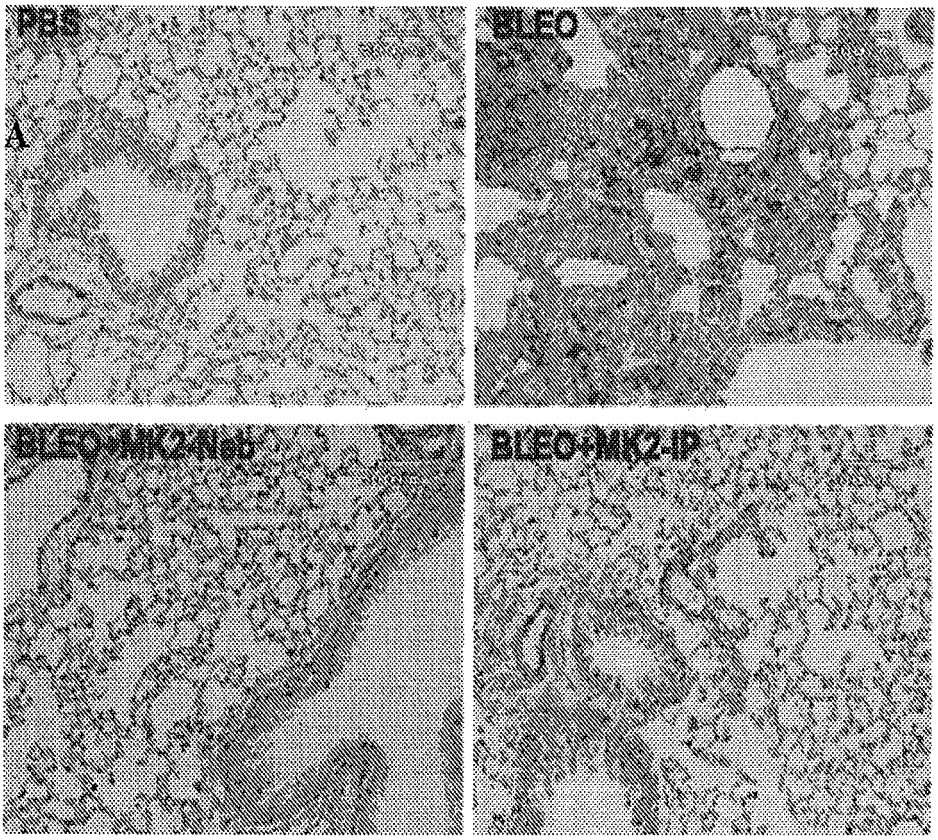


FIGURE 21

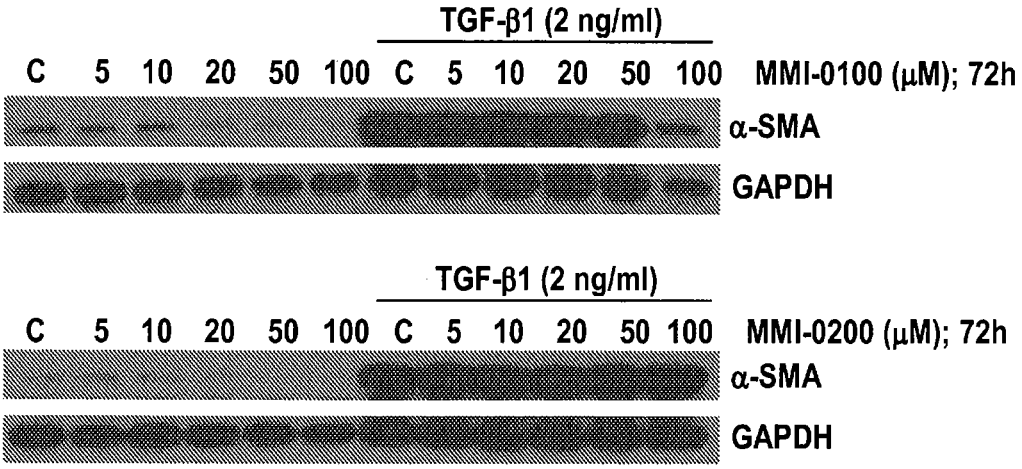

TGF-β1 (2 ng/ml)
C 5 10 20 50 100 C 5 10 20 50 100 MMI-0100 (μM); 72h
α-SMA
GAPDH
TGF-β1 (2 ng/ml)
C 5 10 20 50 100 C 5 10 20 50 100 MMI-0200 (μM); 72h
α-SMA
GAPDH

FIGURE 22

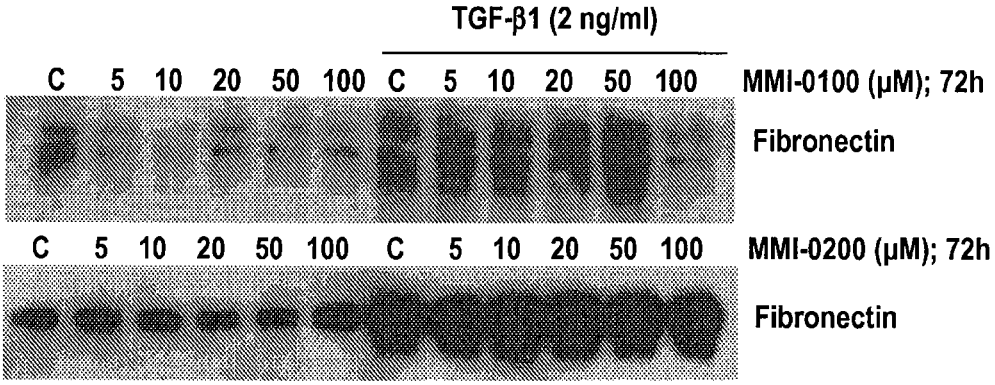

TGF-β1 (2 ng/ml)
C 5 10 20 50 100 C 5 10 20 50 100
MMI-0100 (μM); 72h
Fibronectin
C 5 10 20 50 100 C 5 10 20 50 100
MMI-0200 (μM); 72h
Fibronectin

FIGURE 23

MSC migration is regulated by fibronectin through α5β1-integrin-mediated activation of PDGFR-β

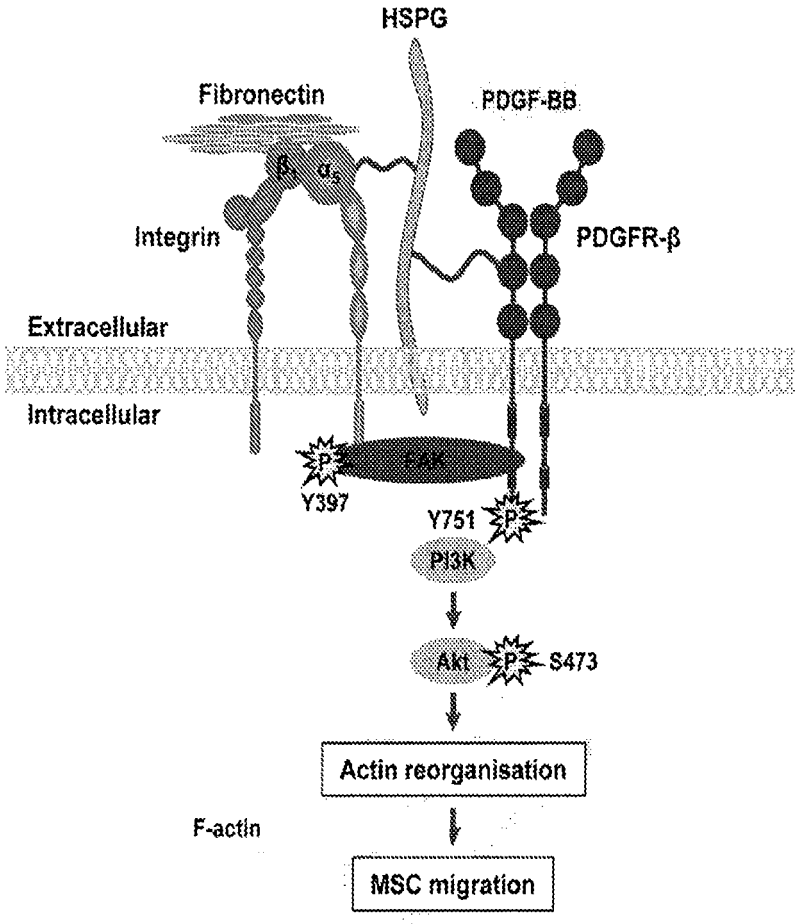
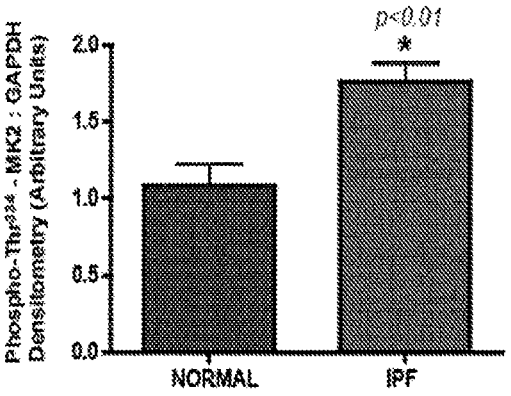


FIGURE 24

A



B

Correlation between Lung Function and MK2 Activation

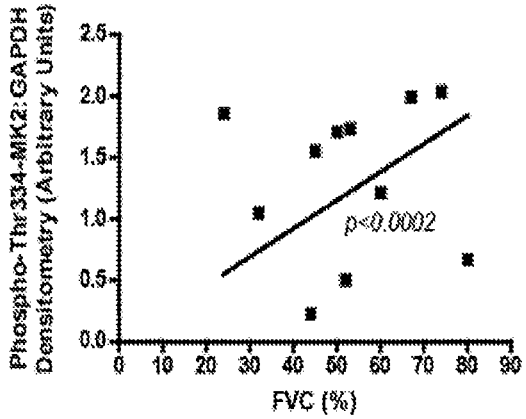


FIGURE 25

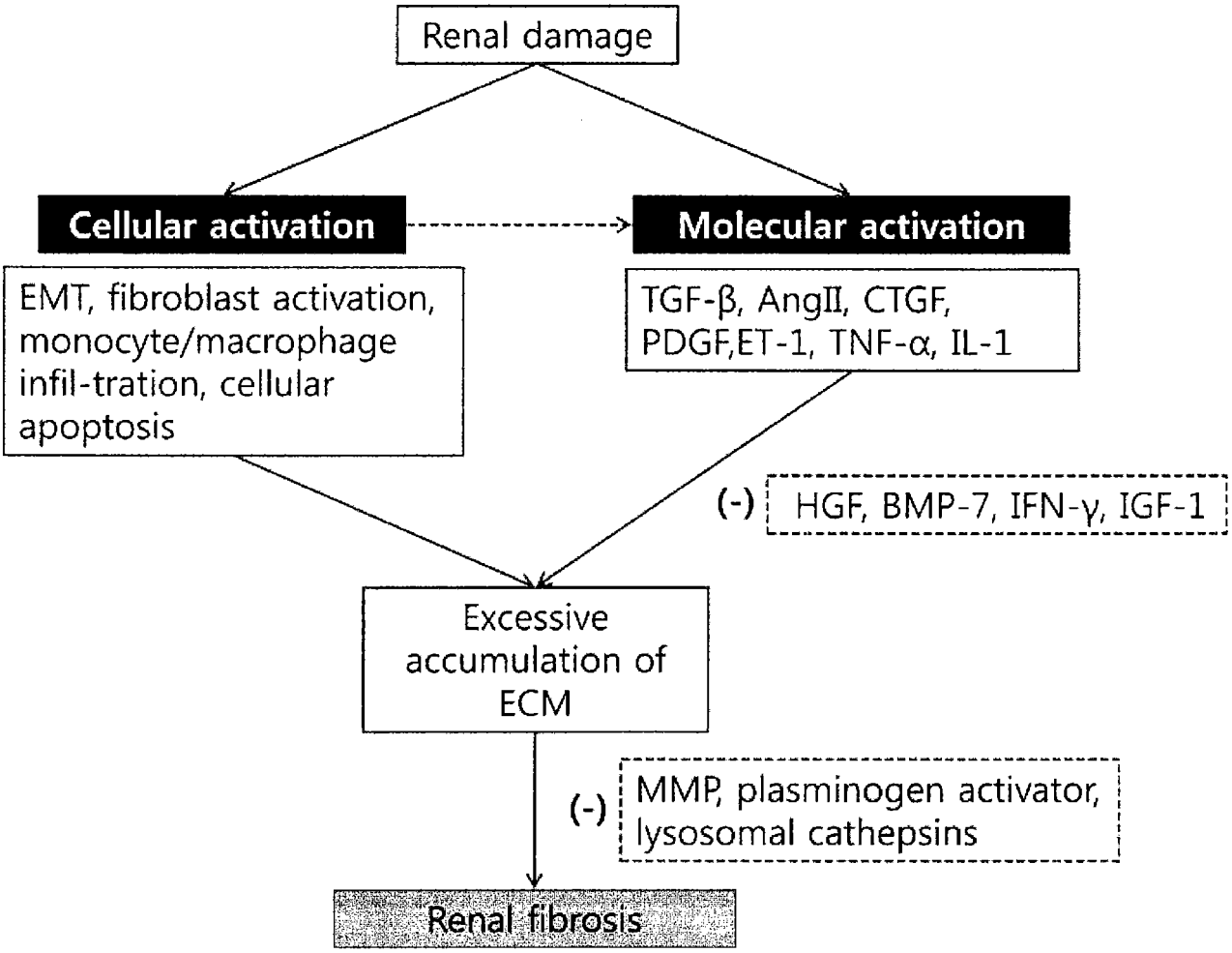

Renal damage
Cellular activation
Molecular activation
EMT, fibroblast activation, monocyte/macrophage infil-tration, cellular apoptosis
TGF-β, AngII, CTGF, PDGF,ET-1, TNF-α, IL-1
(-) HGF, BMP-7, IFN-γ, IGF-1
Excessive accumulation of ECM
(-) MMP, plasminogen activator, lysosomal cathepsins
Renal fibrosis

FIGURE 26