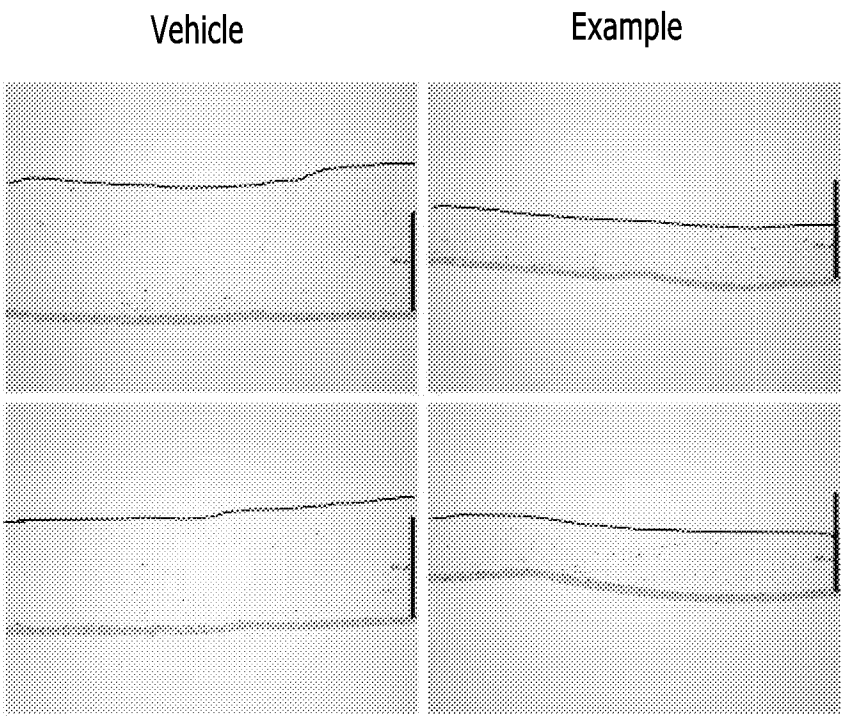
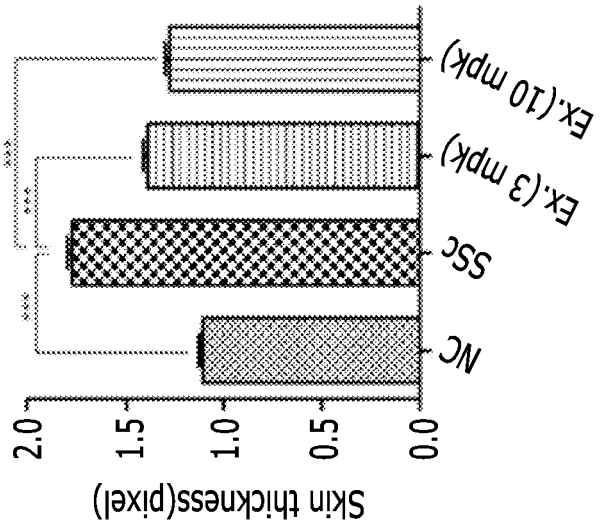
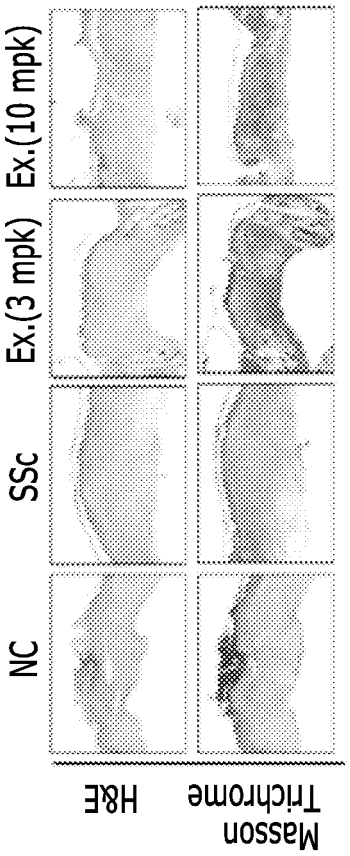
[DRAWING]

[FIG. 1]

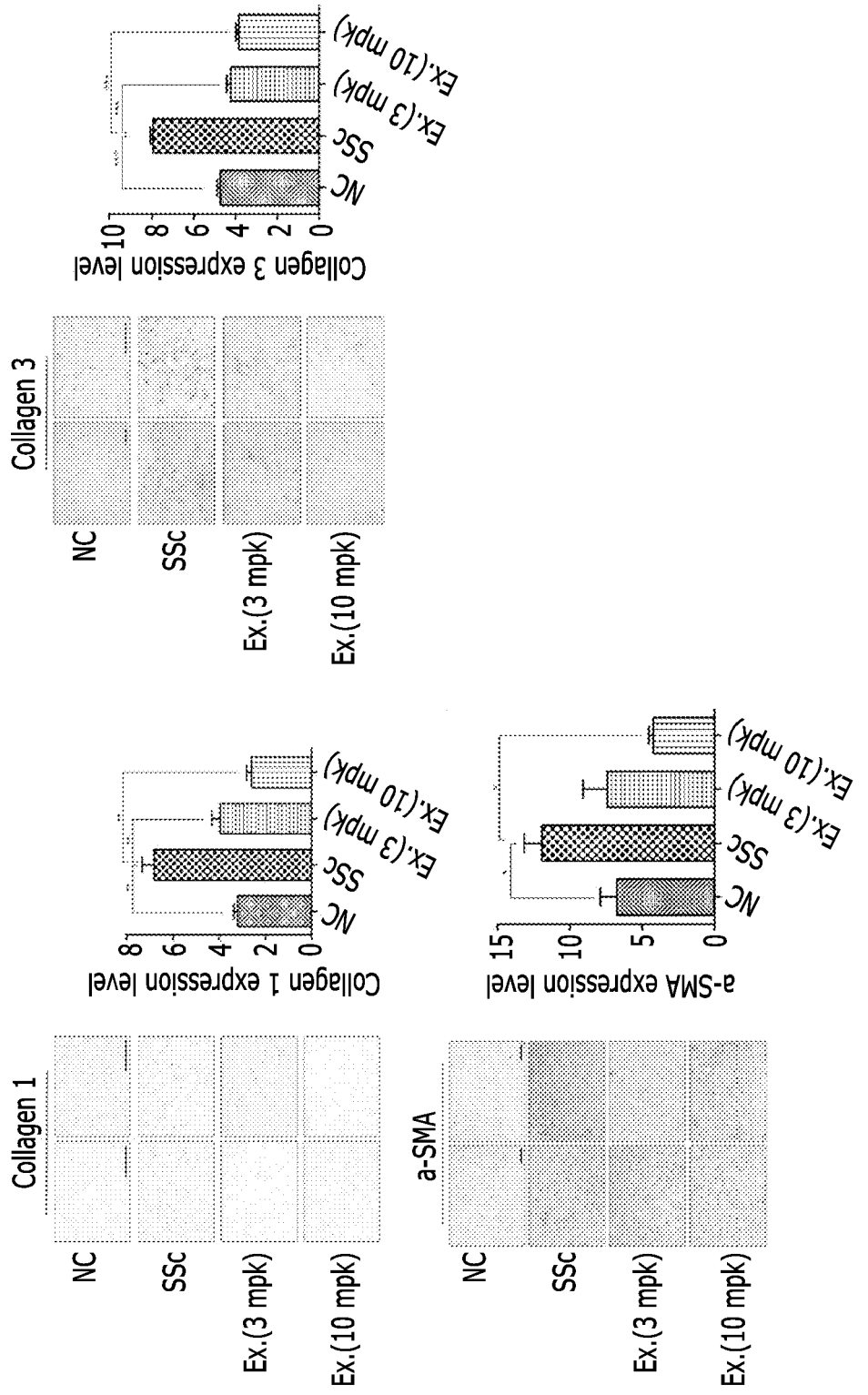


[FIG. 2]

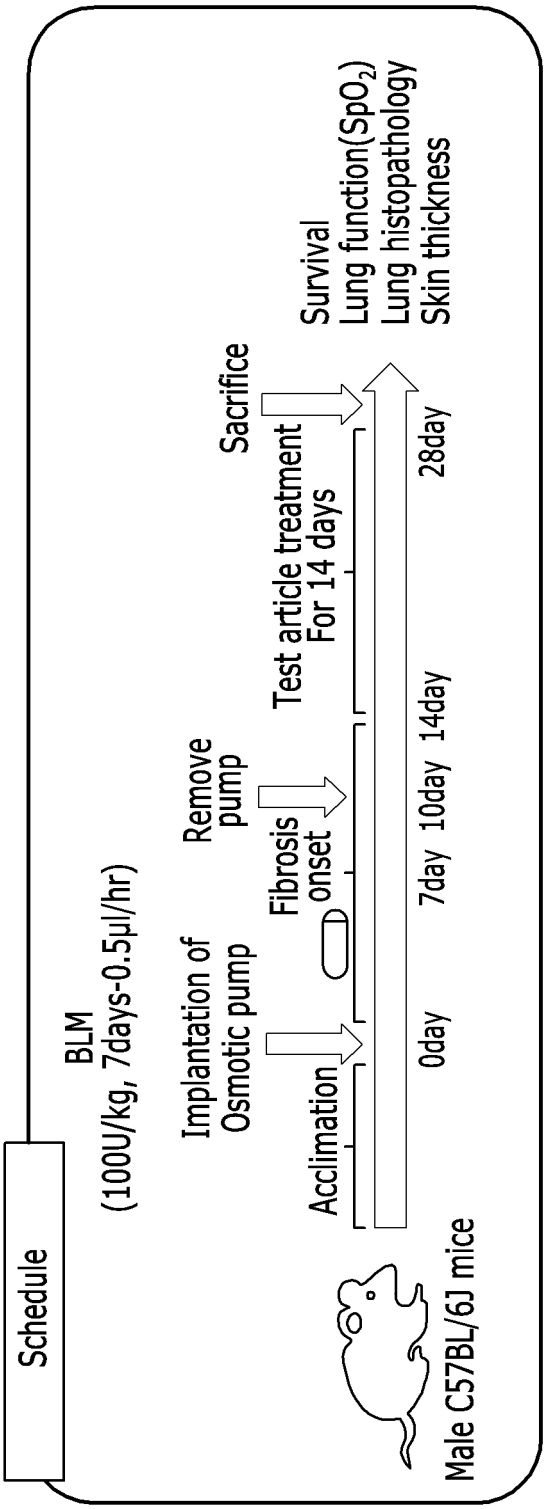

Skin thickness(pixel)
2.0
1.5
1.0
0.5
0.0
NC
SSc
Ex.(3 mpk)
Ex.(10 mpk)
***
***
***


NC
SSc
Ex.(3 mpk)
Ex.(10 mpk)
H&E
Masson Trichrome

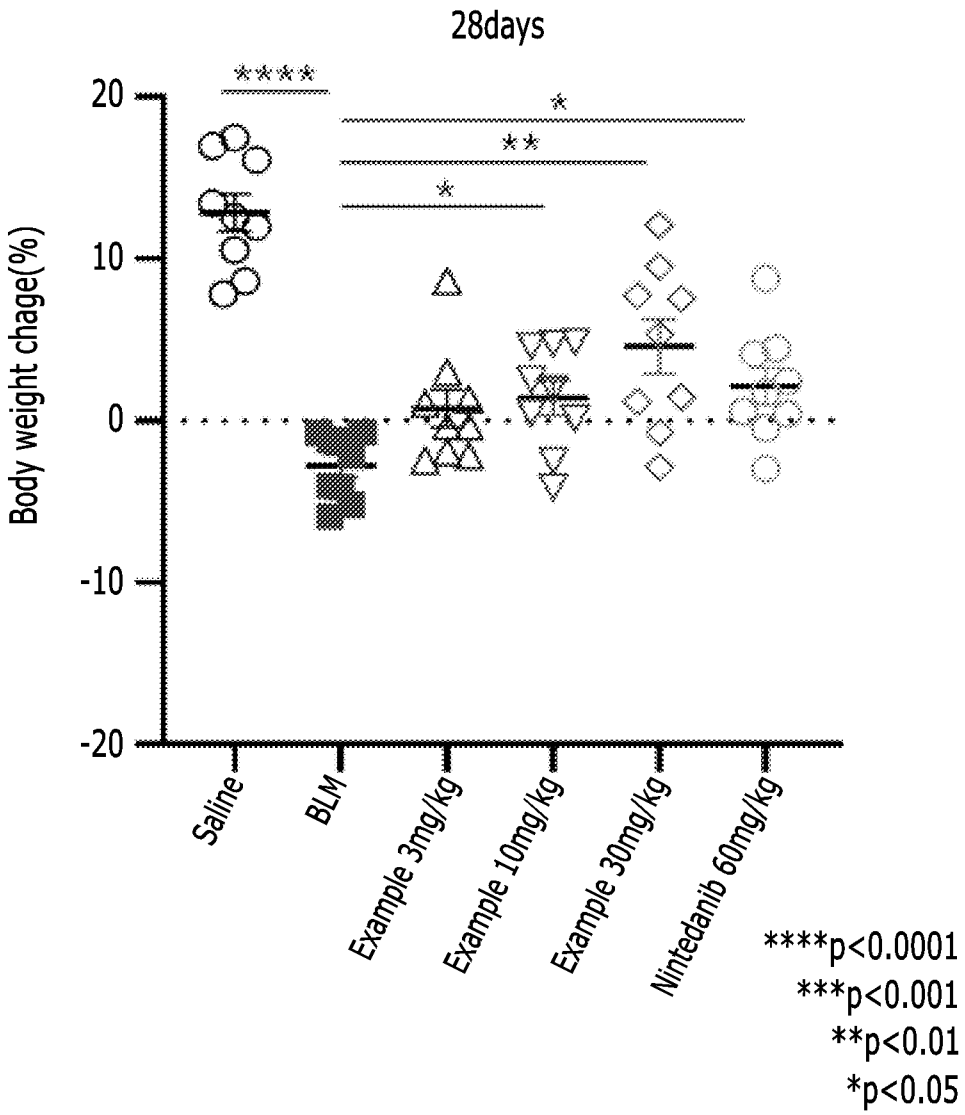
[FIG. 3]


Collagen 1
Collagen 1 expression level
Collagen 3
Collagen 3 expression level
a-SMA
a-SMA expression level
NC
SSc
Ex.(3 mpk)
Ex.(10 mpk)

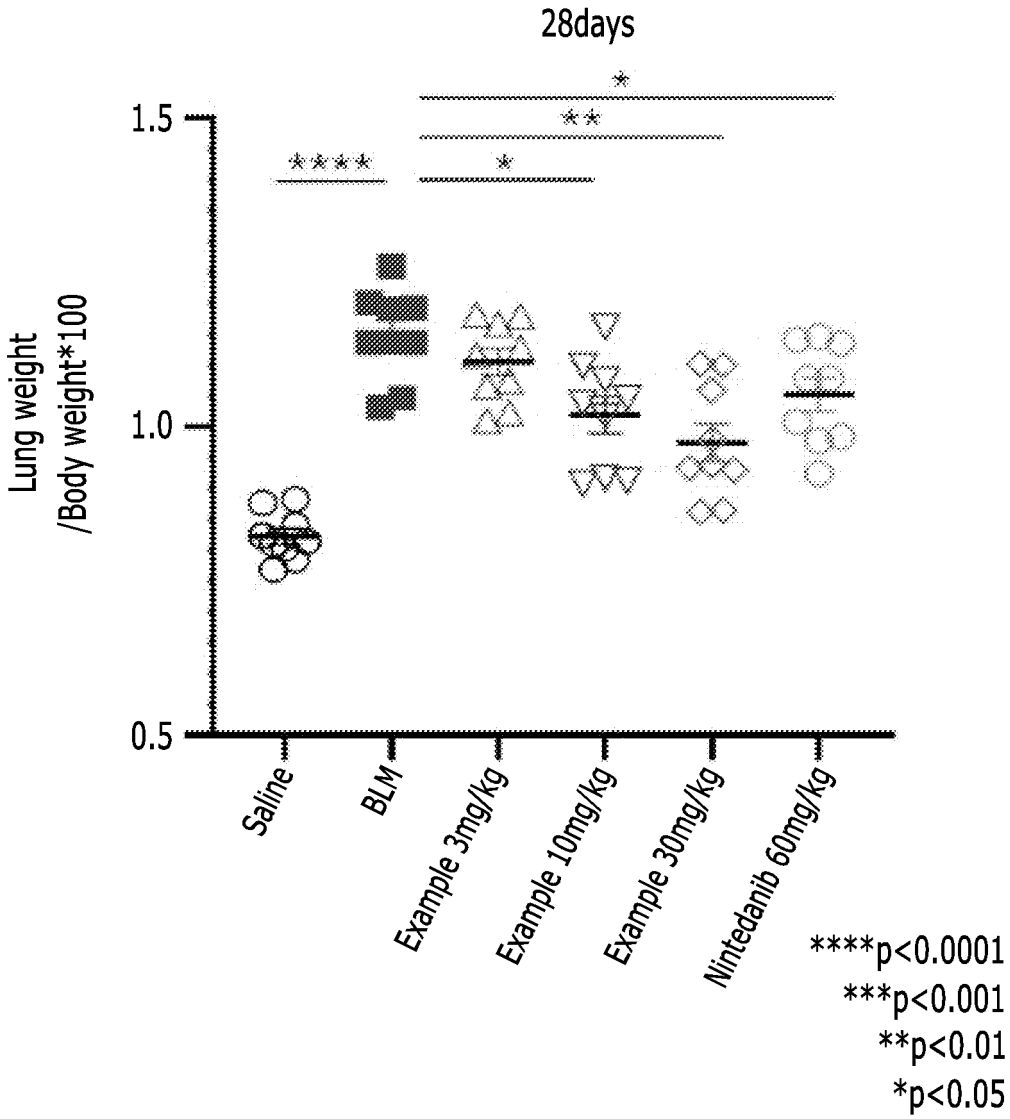
[FIG. 4]


Schedule
BLM
(100U/kg, 7days-0.5μl/hr)
Implantation of
Osmotic pump
Remove
pump
Fibrosis
onset
Test article treatment
For 14 days
Sacrifice
Survival
Lung function(SpO_2)
Lung histopathology
Skin thickness
Acclimation
0day
7day
10day
14day
28day
Male C57BL/6J mice
• Dosing : Example = 3 - 30 mg/kg, QD, once a day (N=9)
Nintedanib 60 mg/kg, QD, once a day
• Inducing agent : Bleomycin (BLM)

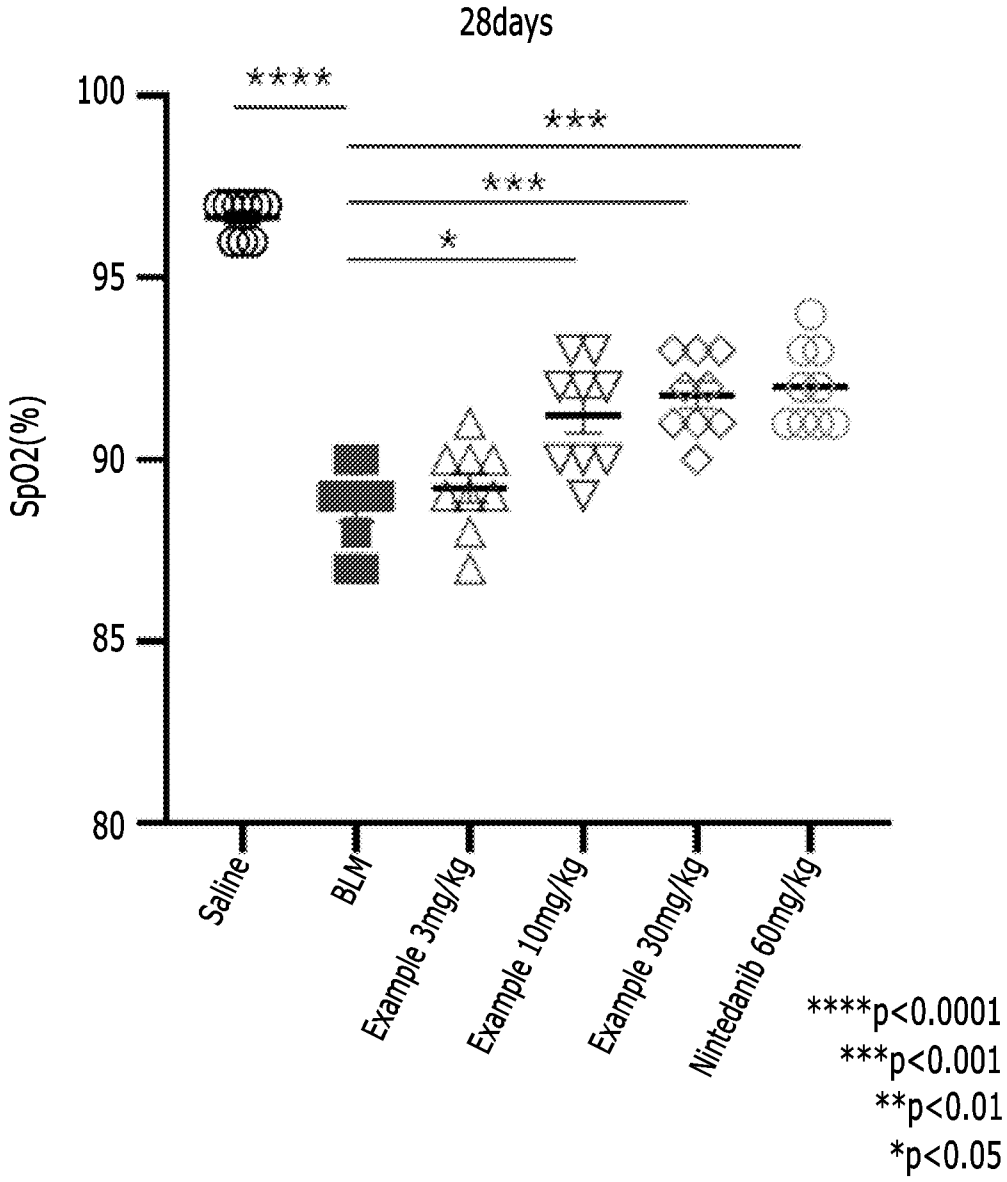
[FIG. 5]


28days
Body weight chage(%)
20
10
0
-10
-20
****
*
**
*
Saline
BLM
Example 3mg/kg
Example 10mg/kg
Example 30mg/kg
Nintedanib 60mg/kg
****p<0.0001
***p<0.001
**p<0.01
*p<0.05

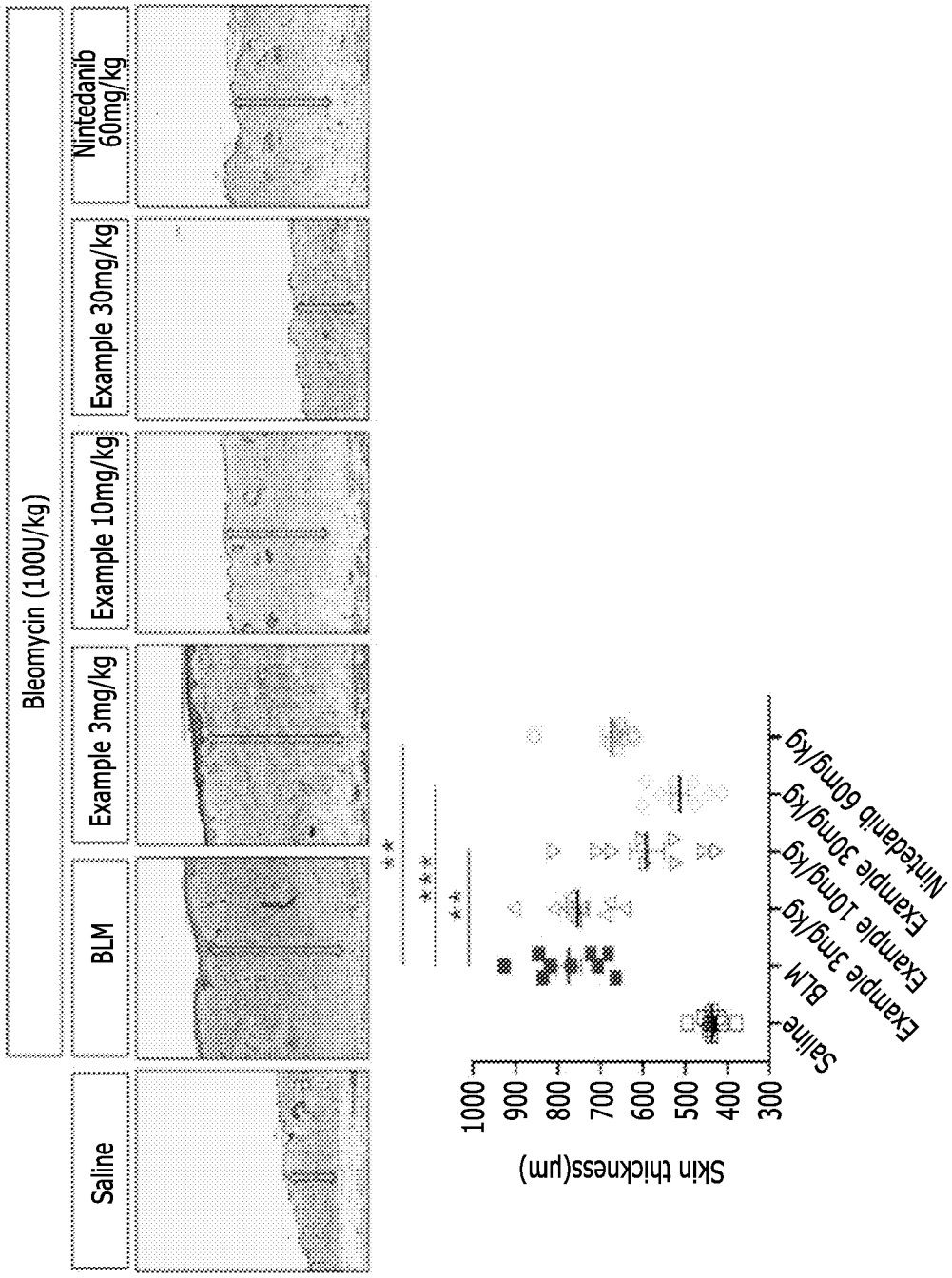
[FIG. 6]


28days
Lung weight
/Body weight*100
1.5
1.0
0.5
****
*
**
*
Saline
BLM
Example 3mg/kg
Example 10mg/kg
Example 30mg/kg
Nintedanib 60mg/kg
****p<0.0001
***p<0.001
**p<0.01
*p<0.05

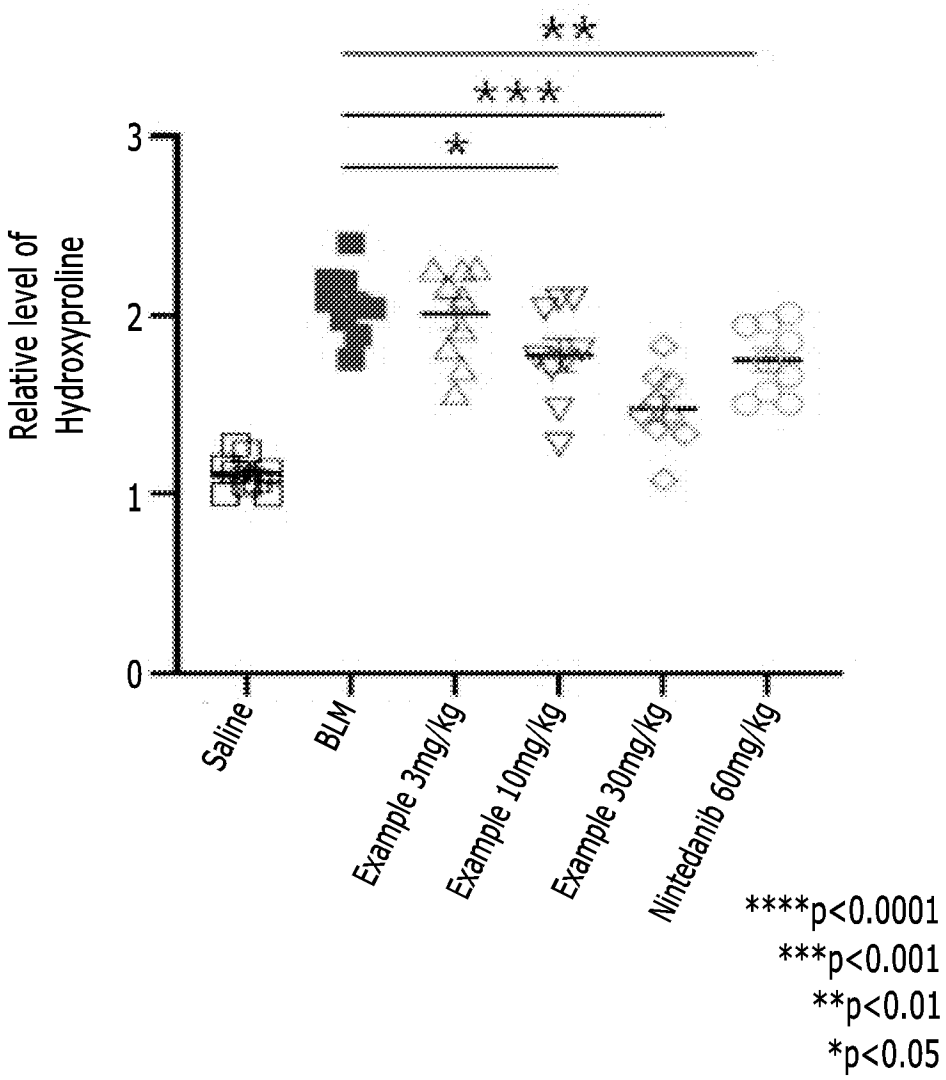
[FIG. 7]


28days
SpO2(%)
100
95
90
85
80
****
***
***
*
Saline
BLM
Example 3mg/kg
Example 10mg/kg
Example 30mg/kg
Nintedanib 60mg/kg
****p<0.0001
***p<0.001
**p<0.01
*p<0.05

[FIG. 8]


Bleomycin (100U/kg)
Saline
BLM
Example 3mg/kg
Example 10mg/kg
Example 30mg/kg
Nintedanib 60mg/kg
**
***
**
Skin thickness(μm)
1000
900
800
700
600
500
400
300
Saline
BLM
Example 3mg/kg
Example 10mg/kg
Example 30mg/kg
Nintedanib 60mg/kg

[FIG. 9]


Relative level of Hydroxyproline
0
1
2
3
*
***
**
Saline
BLM
Example 3mg/kg
Example 10mg/kg
Example 30mg/kg
Nintedanib 60mg/kg
****p<0.0001
***p<0.001
**p<0.01
*p<0.05