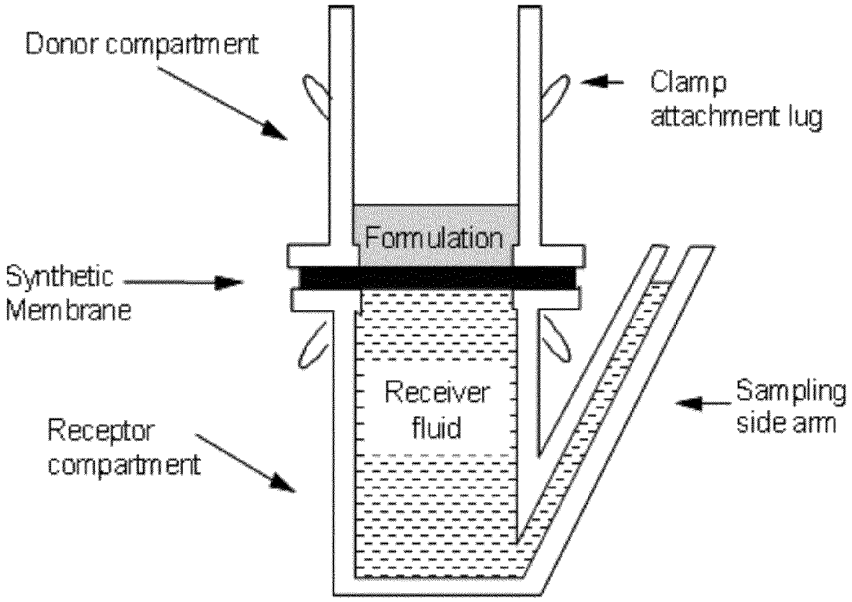

Donor compartment
Clamp attachment lug
Formulation
Synthetic Membrane
Receiver fluid
Sampling side arm
Receptor compartment

FIG 1

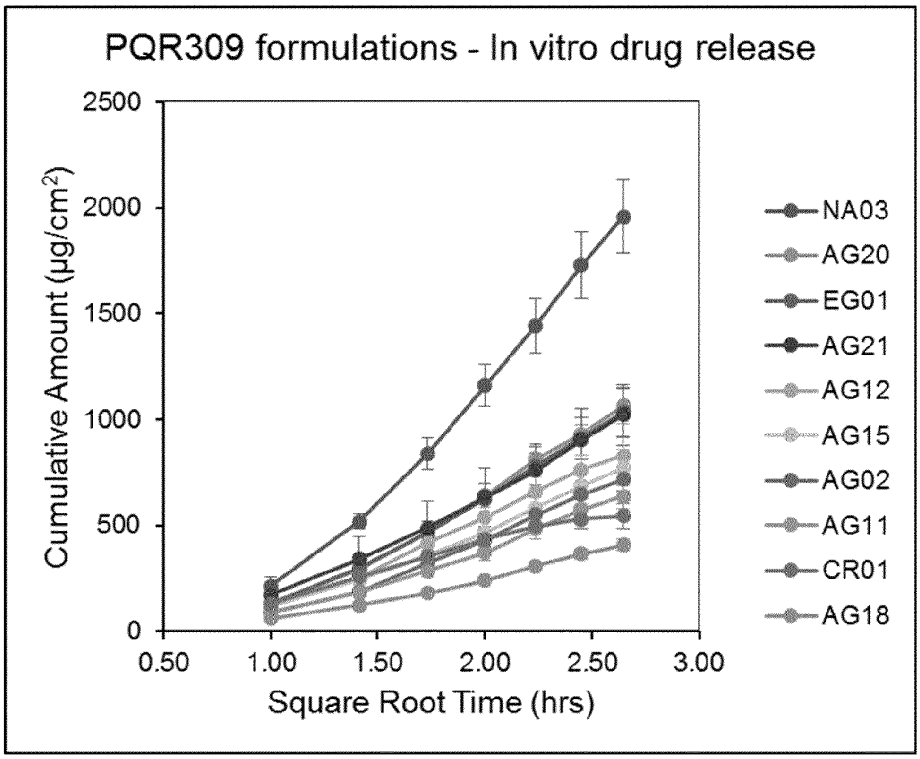

PQR309 formulations - In vitro drug release
Cumulative Amount (µg/cm²)
2500
2000
1500
1000
500
0
0.50
1.00
1.50
2.00
2.50
3.00
Square Root Time (hrs)
NA03
AG20
EG01
AG21
AG12
AG15
AG02
AG11
CR01
AG18

FIG 2

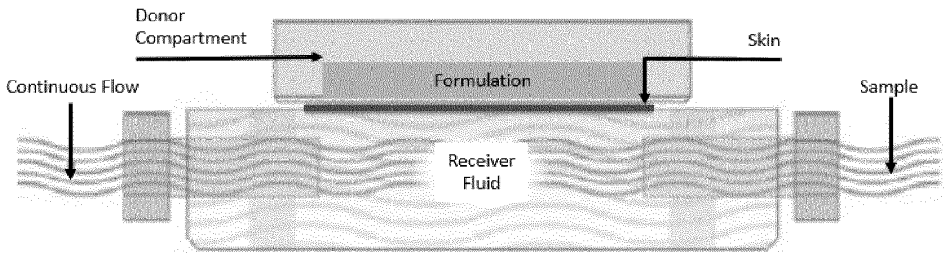

Donor Compartment
Skin
Continuous Flow
Formulation
Sample
Receiver Fluid

FIG 3

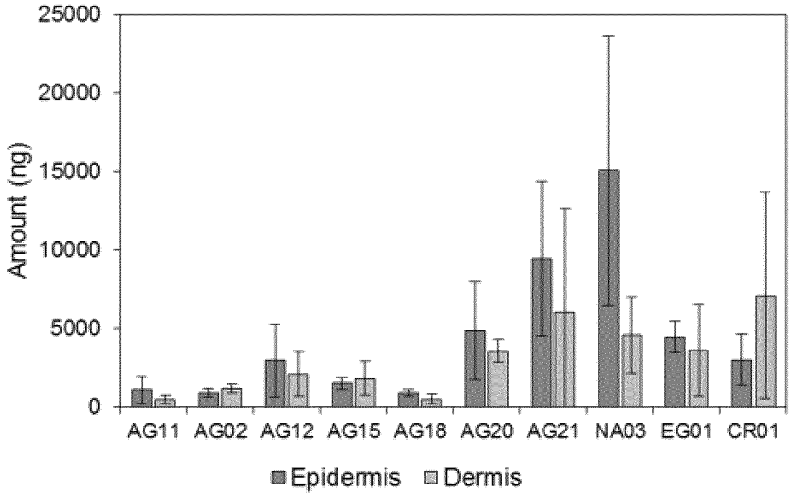

25000
20000
15000
10000
5000
0
Amount (ng)
AG11
AG02
AG12
AG15
AG18
AG20
AG21
NA03
EG01
CR01
Epidermis
Dermis

FIG 4

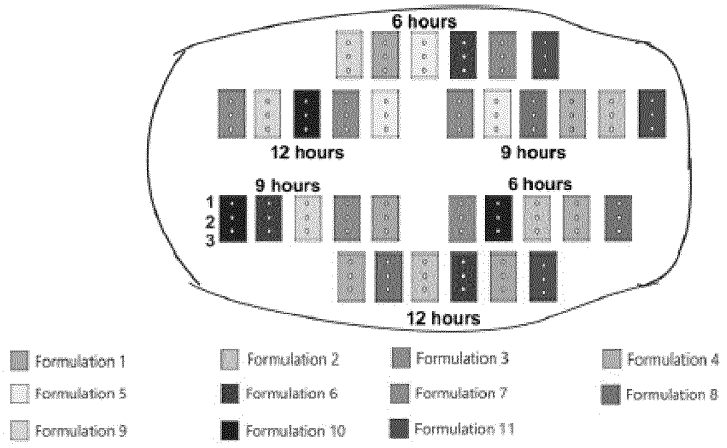

6 hours
12 hours
9 hours
9 hours
6 hours
1
2
3
12 hours
Formulation 1
Formulation 2
Formulation 3
Formulation 4
Formulation 5
Formulation 6
Formulation 7
Formulation 8
Formulation 9
Formulation 10
Formulation 11

FIG 5

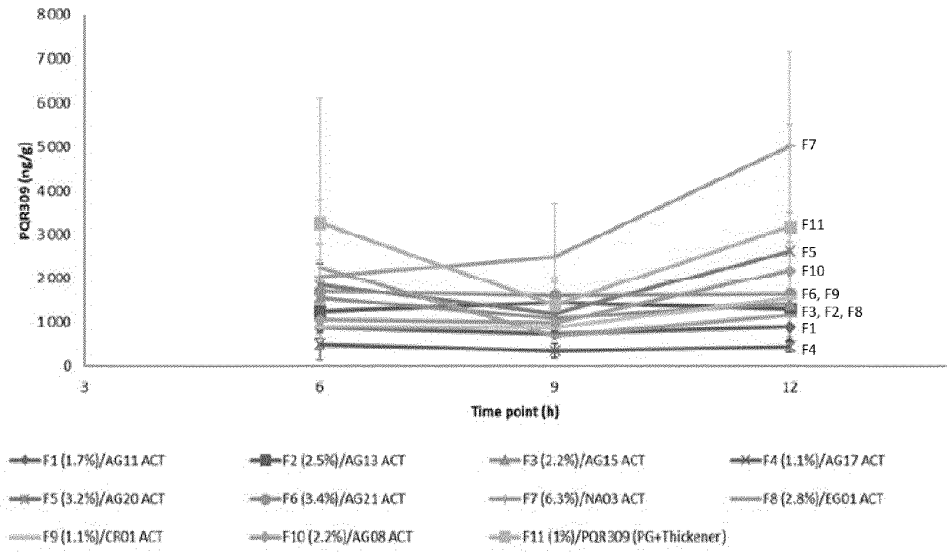

8000
7000
6000
5000
4000
3000
2000
1000
0
PQR309 (ng/g)
3
6
9
12
Time point (h)
F7
F11
F5
F10
F6, F9
F3, F2, F8
F1
F4
F1 (1.7%)/AG11 ACT
F2 (2.5%)/AG13 ACT
F3 (2.2%)/AG15 ACT
F4 (1.1%)/AG17 ACT
F5 (3.2%)/AG20 ACT
F6 (3.4%)/AG21 ACT
F7 (6.3%)/NA03 ACT
F8 (2.8%)/EG01 ACT
F9 (1.1%)/CR01 ACT
F10 (2.2%)/AG08 ACT
F11 (1%)/PQR309 (PG+Thickener)

FIG 6

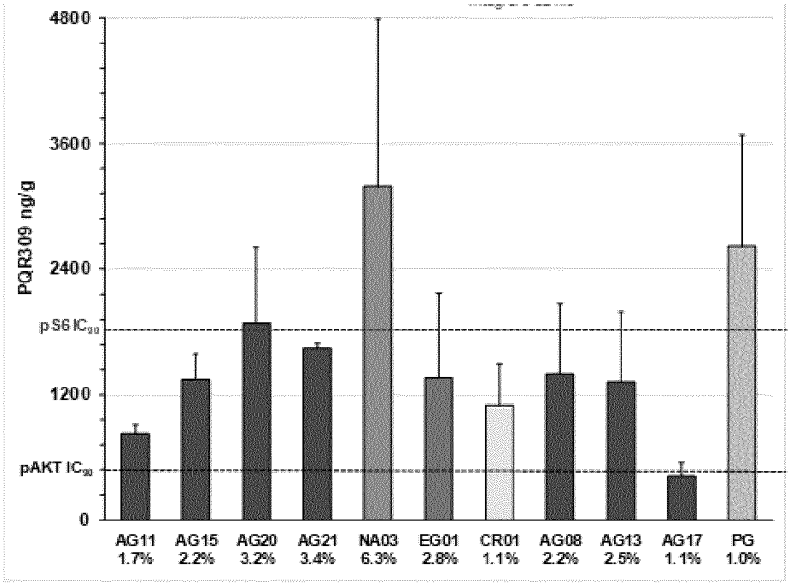

4800
3600
2400
1200
0
PQR309 ng/g
pS6 IC50
pAKT IC50
AG11 1.7%
AG15 2.2%
AG20 3.2%
AG21 3.4%
NA03 6.3%
EG01 2.8%
CR01 1.1%
AG08 2.2%
AG13 2.5%
AG17 1.1%
PG 1.0%

FIG 7

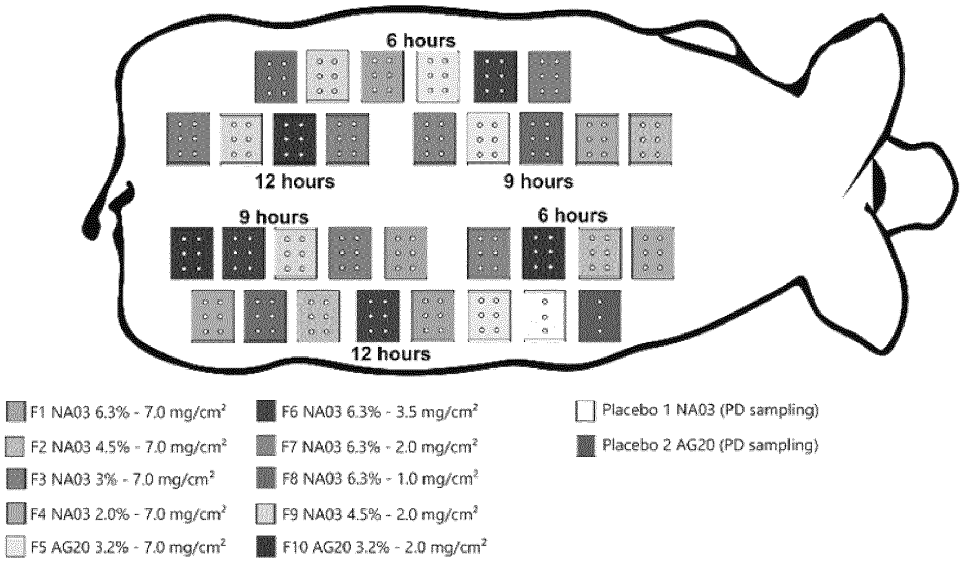

6 hours
12 hours
9 hours
9 hours
6 hours
12 hours
F1 NA03 6.3% - 7.0 mg/cm²
F2 NA03 4.5% - 7.0 mg/cm²
F3 NA03 3% - 7.0 mg/cm²
F4 NA03 2.0% - 7.0 mg/cm²
F5 AG20 3.2% - 7.0 mg/cm²
F6 NA03 6.3% - 3.5 mg/cm²
F7 NA03 6.3% - 2.0 mg/cm²
F8 NA03 6.3% - 1.0 mg/cm²
F9 NA03 4.5% - 2.0 mg/cm²
F10 AG20 3.2% - 2.0 mg/cm²
Placebo 1 NA03 (PD sampling)
Placebo 2 AG20 (PD sampling)

FIG 8

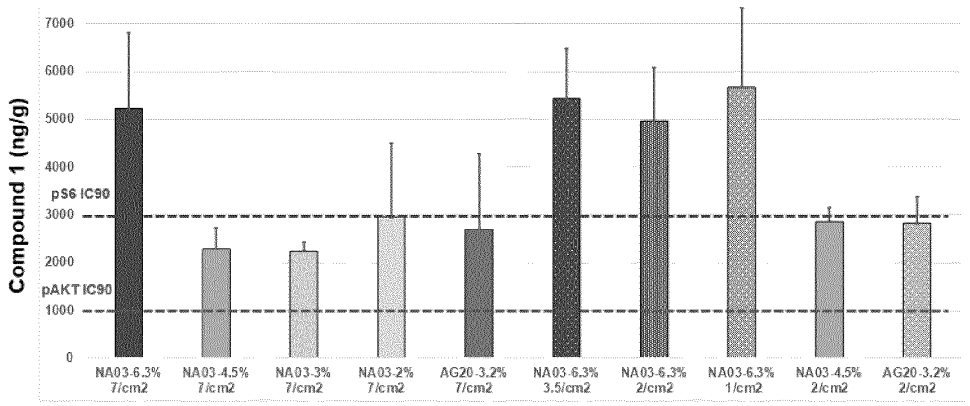

Compound 1 (ng/g)
7000
6000
5000
4000
3000
2000
1000
0
pS6 IC90
pAKT IC90
NA03-6.3% 7/cm2
NA03-4.5% 7/cm2
NA03-3% 7/cm2
NA03-2% 7/cm2
AG20-3.2% 7/cm2
NA03-6.3% 3.5/cm2
NA03-6.3% 2/cm2
NA03-6.3% 1/cm2
NA03-4.5% 2/cm2
AG20-3.2% 2/cm2

FIG 9

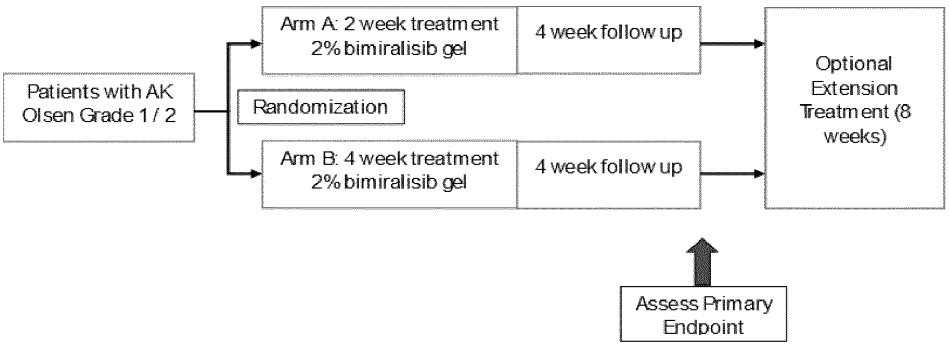

Patients with AK Olsen Grade 1 / 2
Randomization
Arm A: 2 week treatment 2% bimiralisib gel
4 week follow up
Arm B: 4 week treatment 2% bimiralisib gel
4 week follow up
Optional Extension Treatment (8 weeks)
Assess Primary Endpoint

FIG 10