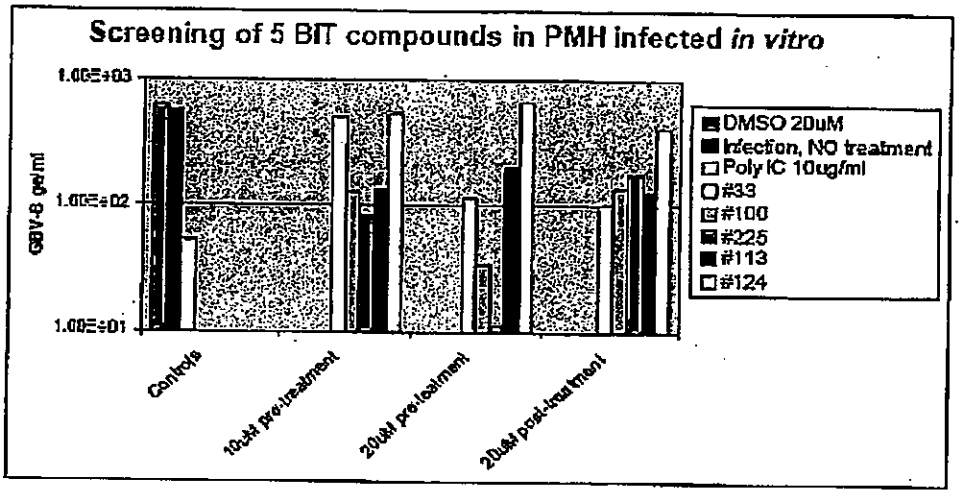

Screening of 5 BIT compounds in PMH infected in vitro
GBV-B ge/ml
1.00E+03
1.00E+02
1.00E+01
Controls
10uM pre-treatment
20uM pre-treatment
20uM post-treatment
DMSO 20uM
Infection, NO treatment
Poly IC 10ug/ml
#33
#100
#225
#113
#124

Figure 1

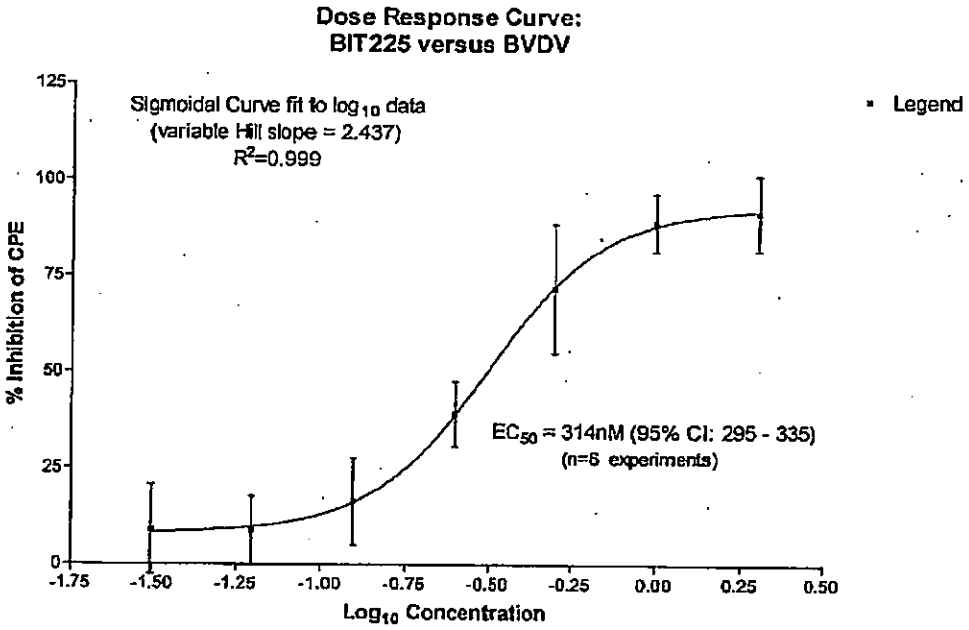

Dose Response Curve:
BIT225 versus BVDV
Sigmoidal Curve fit to log10 data
(variable Hill slope = 2.437)
R2=0.999
Legend
% Inhibition of CPE
125
100
75
50
25
0
-1.75
-1.50
-1.25
-1.00
-0.75
-0.50
-0.25
0.00
0.25
0.50
Log10 Concentration
EC50 = 314nM (95% CI: 295 - 335)
(n=6 experiments)

Figure 2

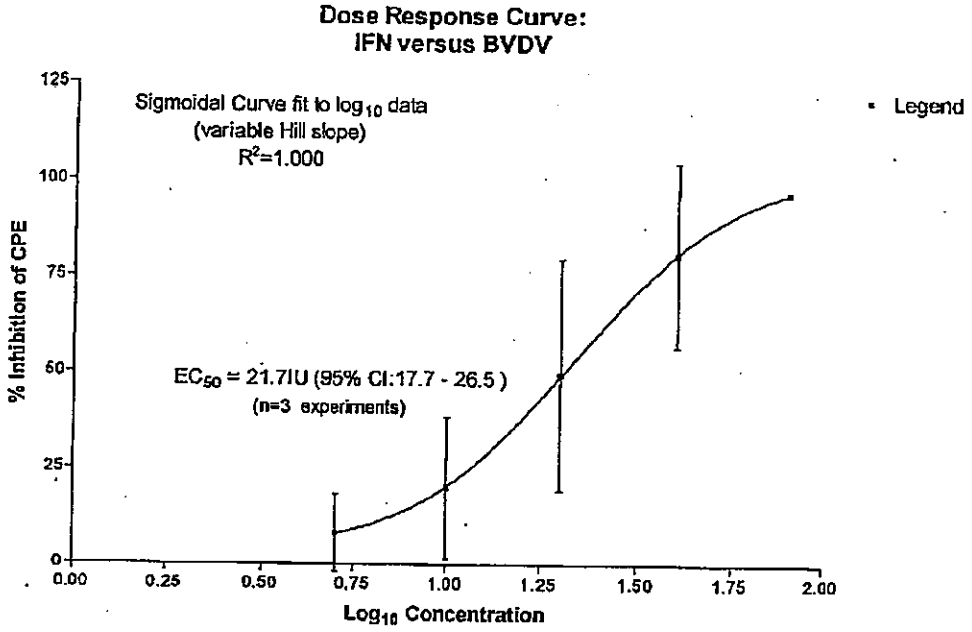

Dose Response Curve:
IFN versus BVDV
Sigmoidal Curve fit to log10 data
(variable Hill slope)
R2=1.000
EC50 = 21.7IU (95% CI:17.7 - 26.5)
(n=3 experiments)
Legend
% Inhibition of CPE
125
100
75
50
25
0
0.00
0.25
0.50
0.75
1.00
1.25
1.50
1.75
2.00
Log10 Concentration

Figure 3

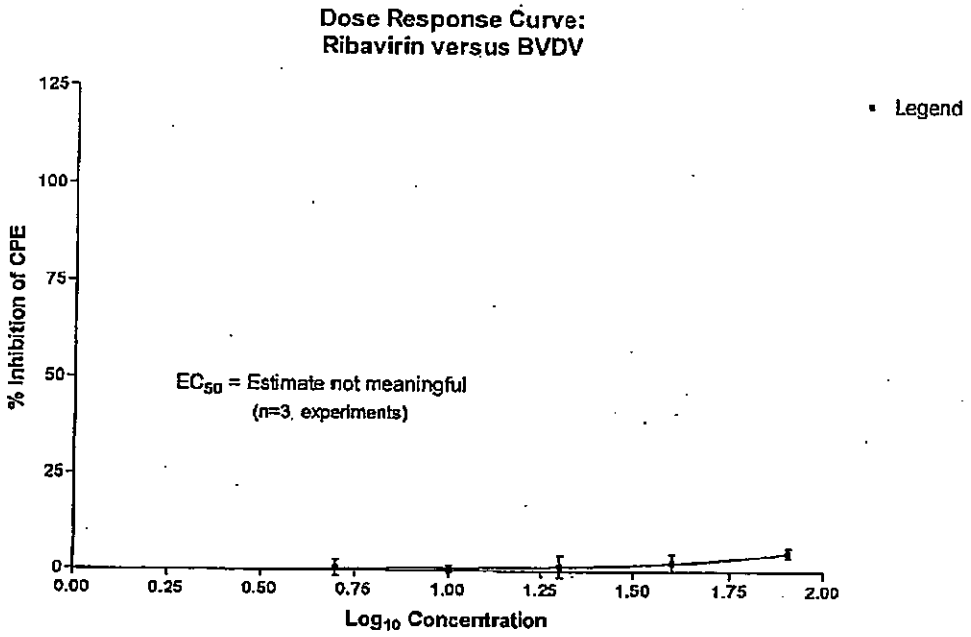

Dose Response Curve:
Ribavirin versus BVDV
Legend
% Inhibition of CPE
125
100
75
50
25
0
EC50 = Estimate not meaningful
(n=3, experiments)
0.00
0.25
0.50
0.75
1.00
1.25
1.50
1.75
2.00
Log10 Concentration

Figure 4

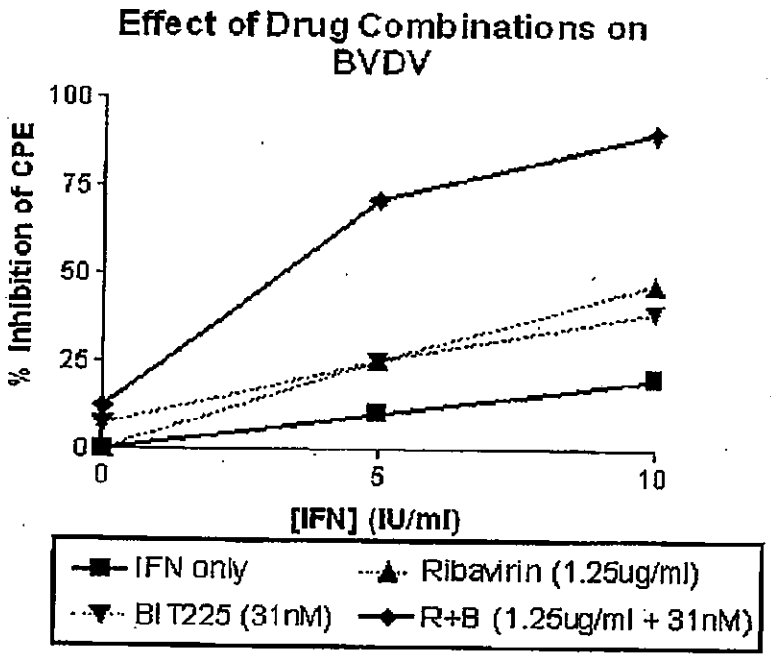

Effect of Drug Combinations on BVDV
% Inhibition of CPE
100
75
50
25
0
0
5
10
[IFN] (IU/ml)
IFN only
Ribavirin (1.25ug/ml)
BIT225 (31nM)
R+B (1.25ug/ml + 31nM)

Figure 5

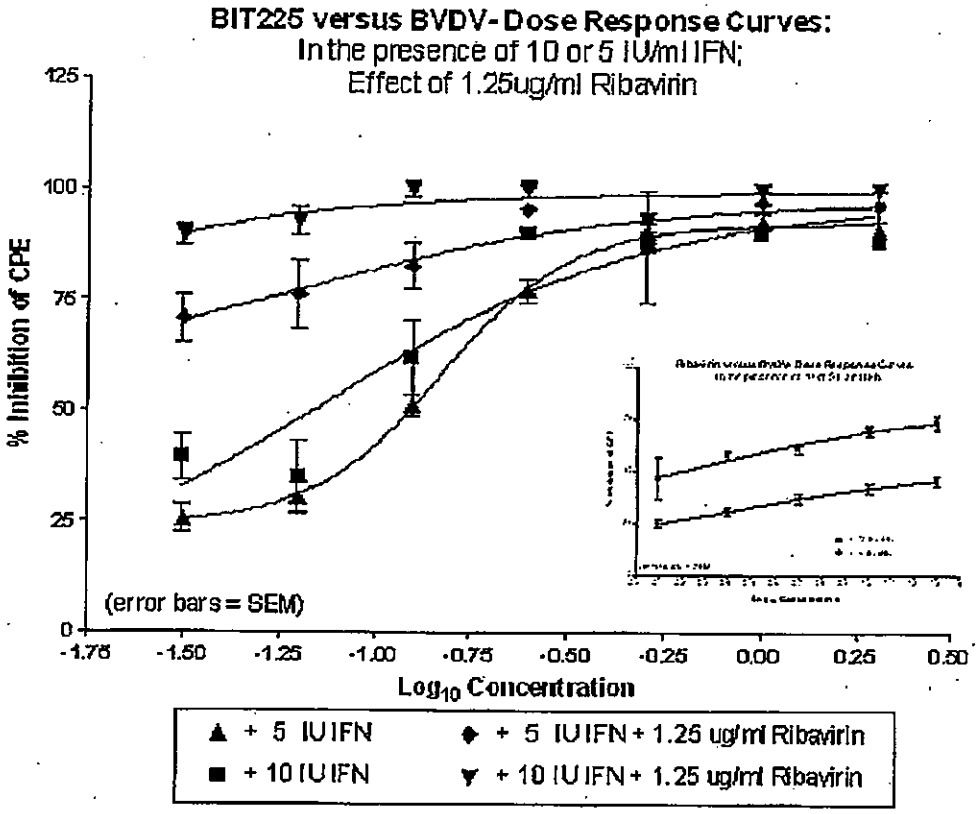

BIT225 versus BVDV - Dose Response Curves:
In the presence of 10 or 5 IU/ml IFN;
Effect of 1.25ug/ml Ribavirin
% Inhibition of CPE
125
100
75
50
25
0
(error bars = SEM)
-1.75
-1.50
-1.25
-1.00
-0.75
-0.50
-0.25
0.00
0.25
0.50
Log10 Concentration
+ 5 IU IFN
+ 10 IU IFN
+ 5 IU IFN + 1.25 ug/ml Ribavirin
+ 10 IU IFN + 1.25 ug/ml Ribavirin

Figure 6

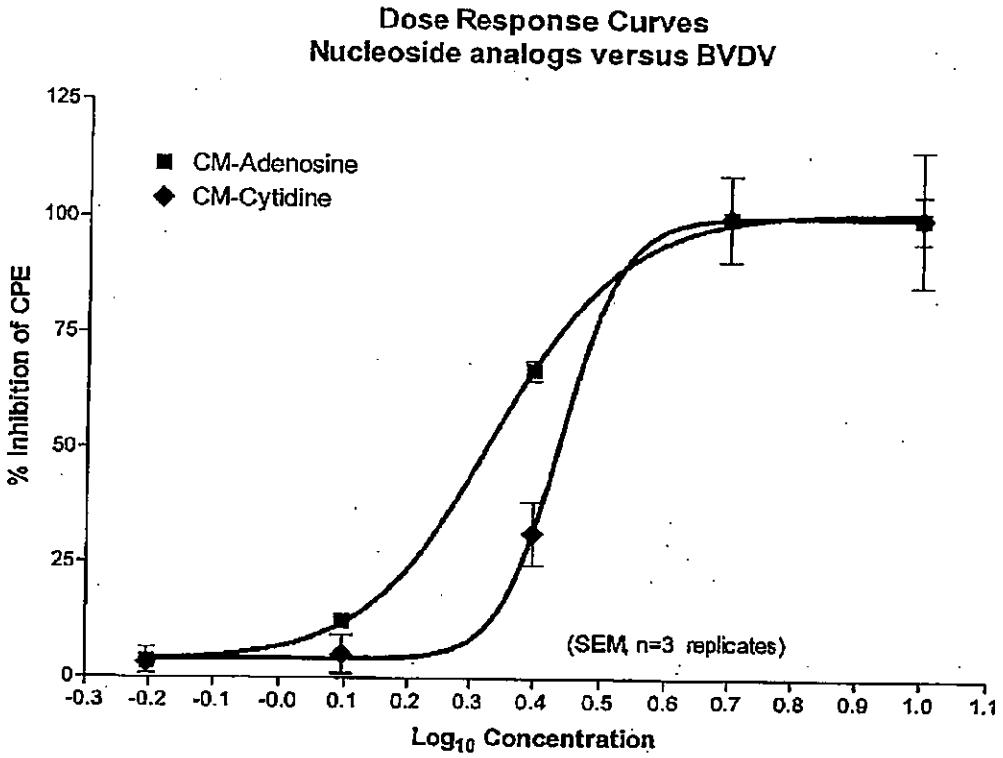

Dose Response Curves
Nucleoside analogs versus BVDV
CM-Adenosine
CM-Cytidine
% Inhibition of CPE
125
100
75
50
25
0
(SEM, n=3 replicates)
-0.3
-0.2
-0.1
-0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
1.1
Log10 Concentration

Figure 7

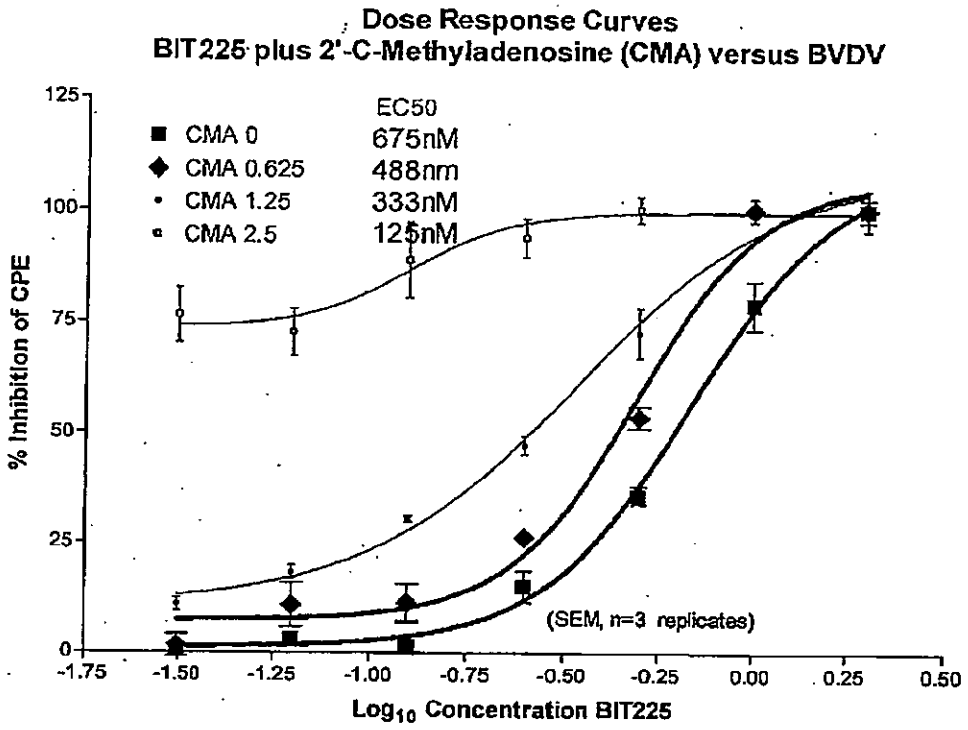

Dose Response Curves
BIT225 plus 2'-C-Methyladenosine (CMA) versus BVDV
EC50
CMA 0 675nM
CMA 0.625 488nm
CMA 1.25 333nM
CMA 2.5 125nM
% Inhibition of CPE
125
100
75
50
25
0
-1.75
-1.50
-1.25
-1.00
-0.75
-0.50
-0.25
0.00
0.25
0.50
(SEM, n=3 replicates)
Log10 Concentration BIT225

Figure 8

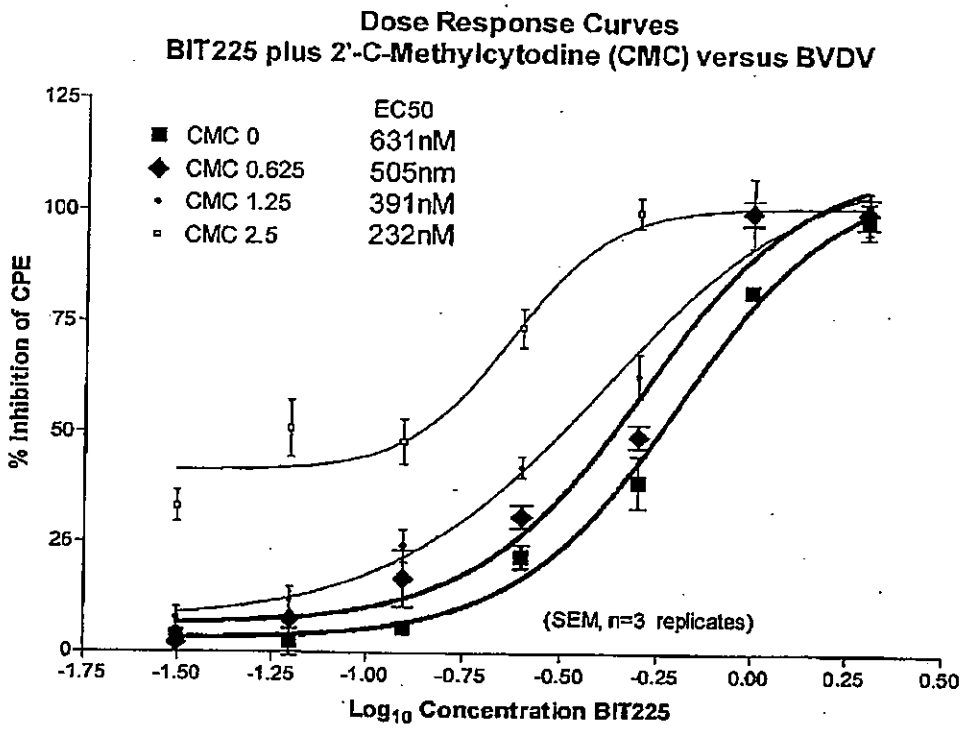

Dose Response Curves
BIT225 plus 2'-C-Methylcytodine (CMC) versus BVDV
EC50
CMC 0 631nM
CMC 0.625 505nm
CMC 1.25 391nM
CMC 2.5 232nM
% Inhibition of CPE
125
100
75
50
25
0
-1.75
-1.50
-1.25
-1.00
-0.75
-0.50
-0.25
0.00
0.25
0.50
(SEM, n=3 replicates)
Log10 Concentration BIT225

Figure 9

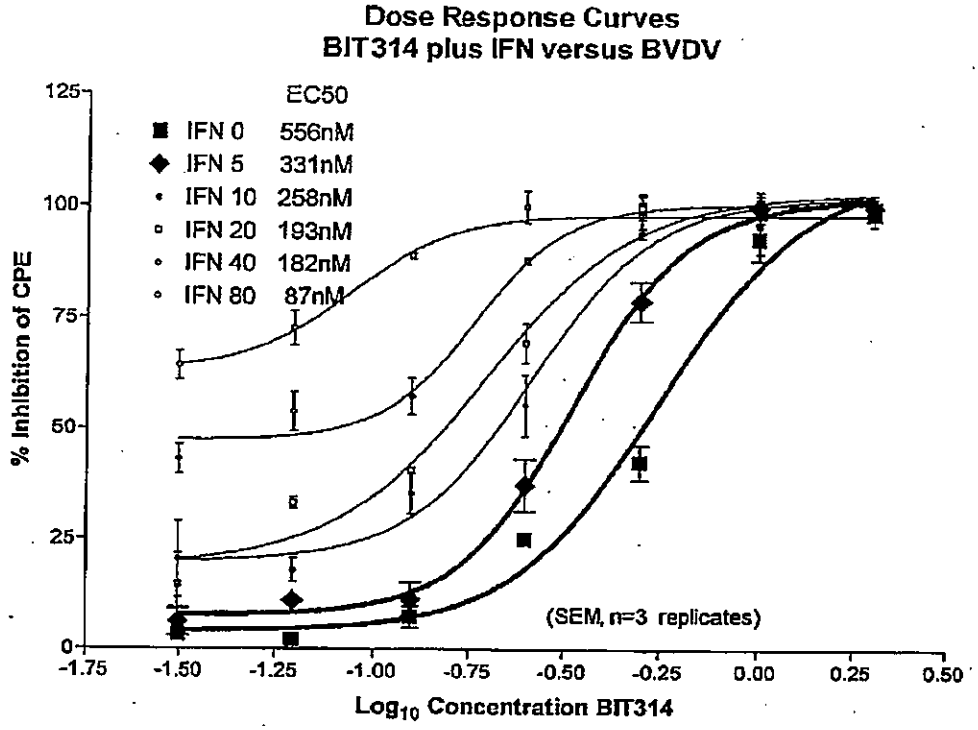

Dose Response Curves
BIT314 plus IFN versus BVDV
EC50
IFN 0 556nM
IFN 5 331nM
IFN 10 258nM
IFN 20 193nM
IFN 40 182nM
IFN 80 87nM
% Inhibition of CPE
125
100
75
50
25
0
-1.75
-1.50
-1.25
-1.00
-0.75
-0.50
-0.25
0.00
0.25
0.50
(SEM, n=3 replicates)
Log10 Concentration BIT314

Figure 10

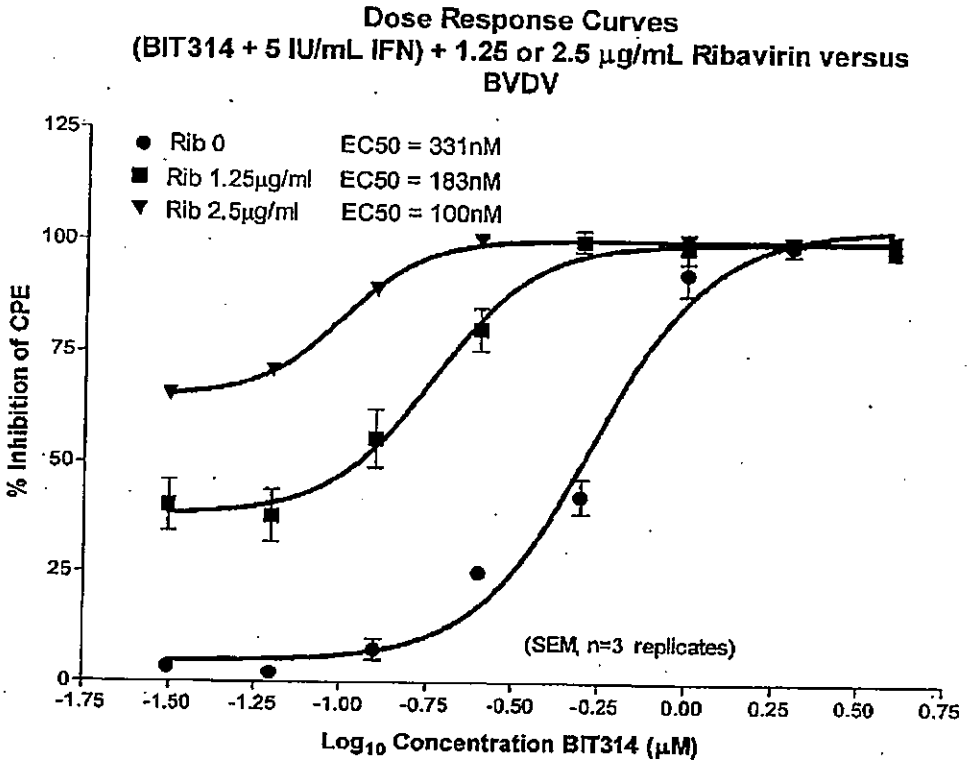

Dose Response Curves
(BIT314 + 5 IU/mL IFN) + 1.25 or 2.5 µg/mL Ribavirin versus BVDV
Rib 0 EC50 = 331nM
Rib 1.25µg/ml EC50 = 183nM
Rib 2.5µg/ml EC50 = 100nM
% Inhibition of CPE
125
100
75
50
25
0
(SEM, n=3 replicates)
-1.75
-1.50
-1.25
-1.00
-0.75
-0.50
-0.25
0.00
0.25
0.50
0.75
Log10 Concentration BIT314 (µM)

Figure 11