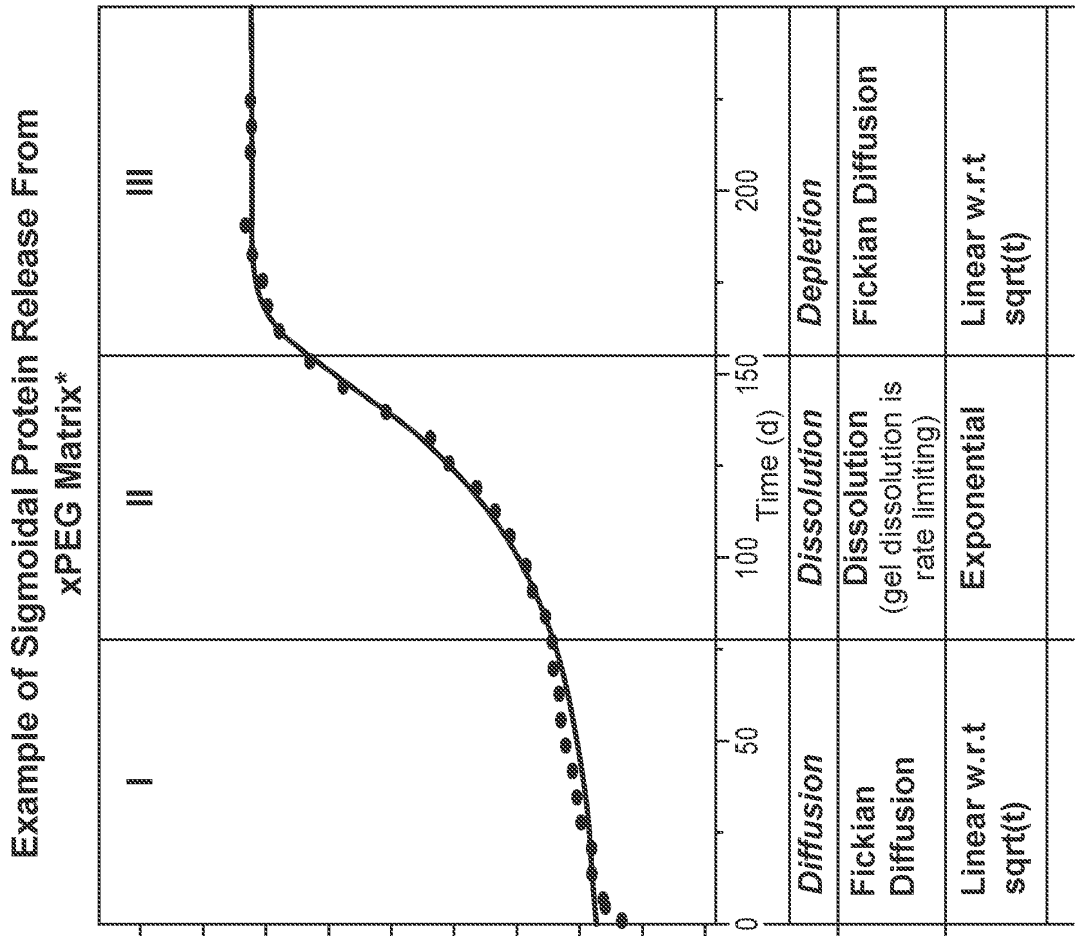
FIG. 1



"Phase"	*Diffusion*	*Dissolution*	*Depletion*
Mechanism governing protein release**	Fickian Diffusion	Dissolution (gel dissolution is rate limiting)	Fickian Diffusion
Release profile fundamentally associated with release mechanism	Linear w.r.t sqrt(t)	Exponential	Linear w.r.t sqrt(t)

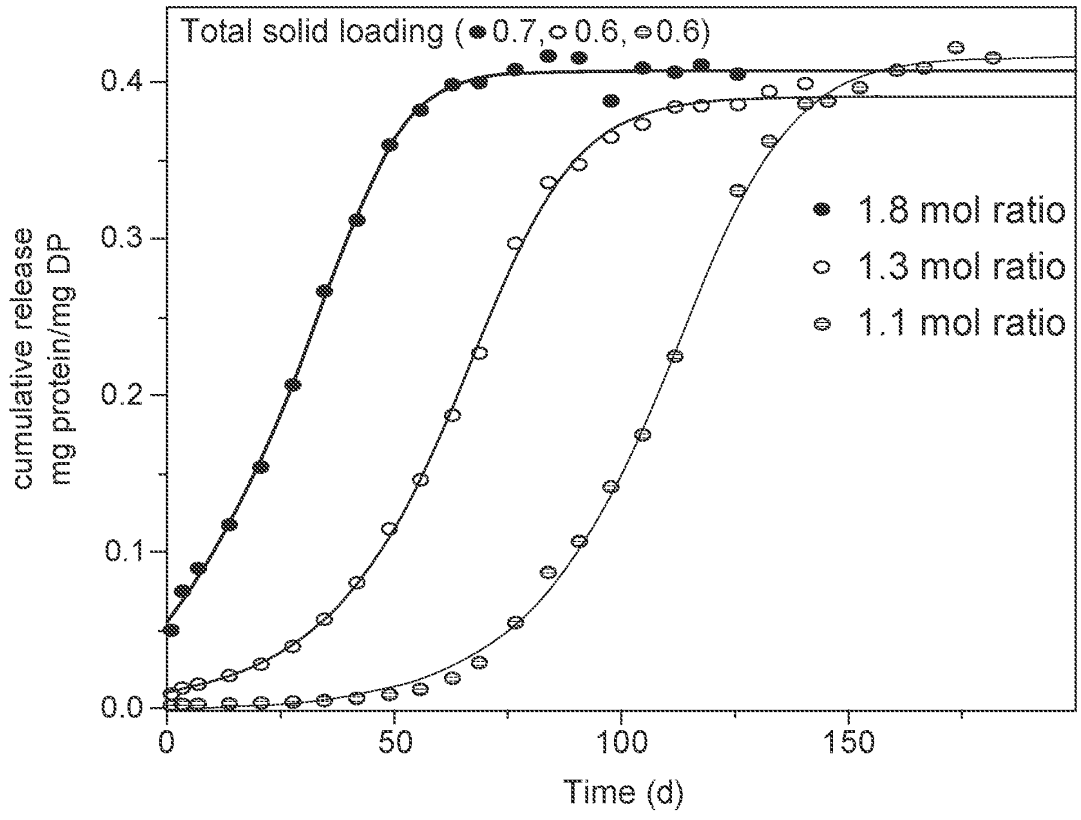
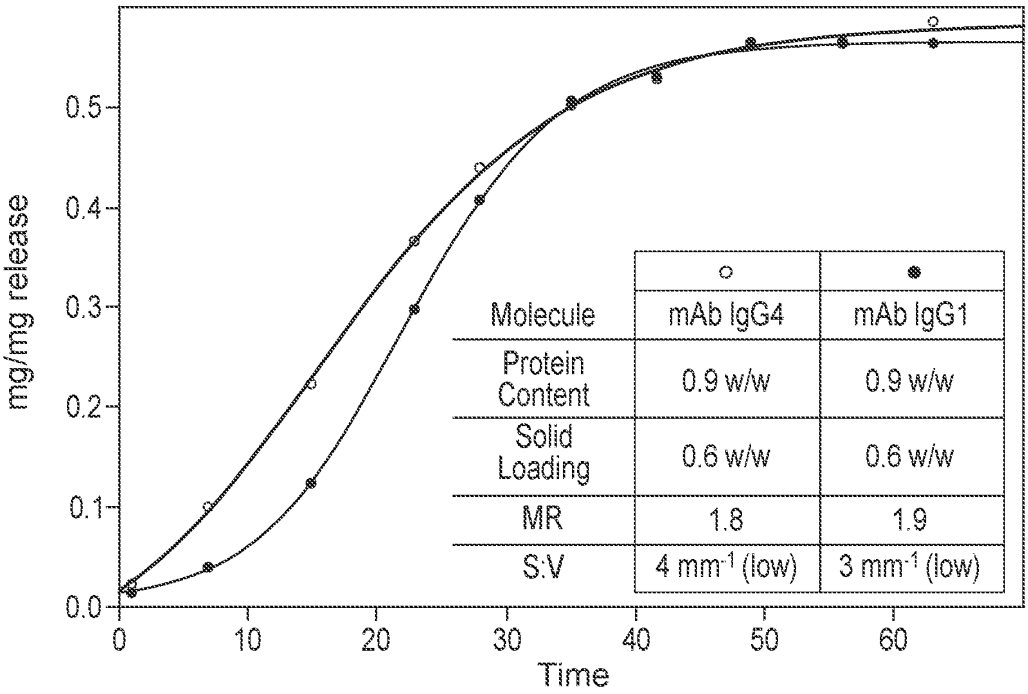
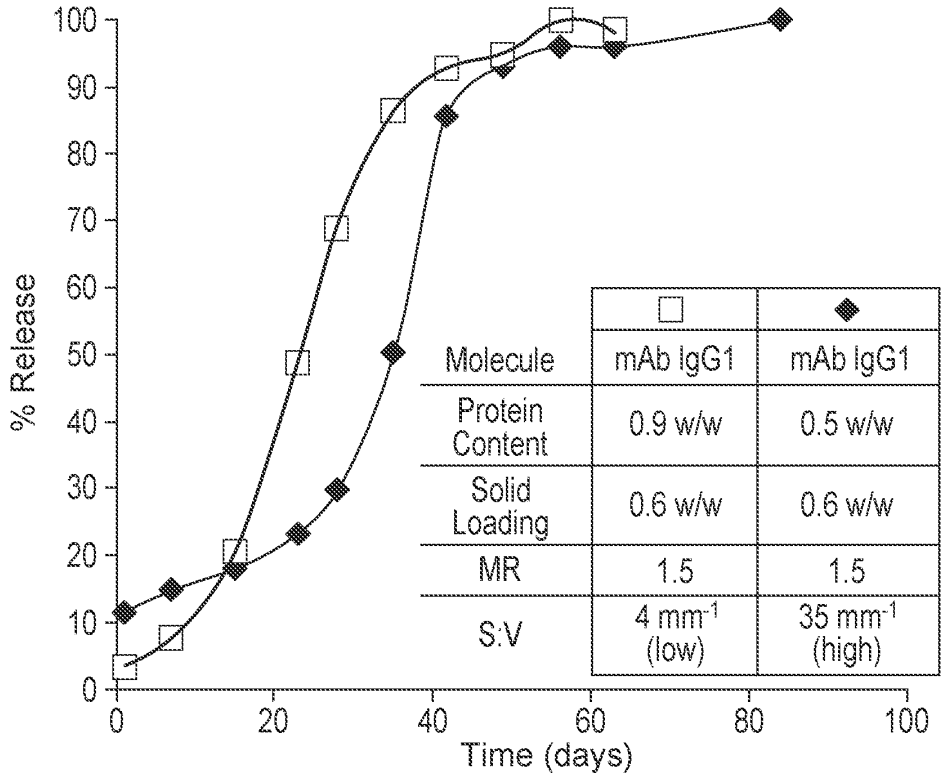

Total solid loading (0.7, 0.6, 0.6)
cumulative release
mg protein/mg DP
0.0
0.1
0.2
0.3
0.4
0
50
100
150
Time (d)
1.8 mol ratio
1.3 mol ratio
1.1 mol ratio

FIG. 2



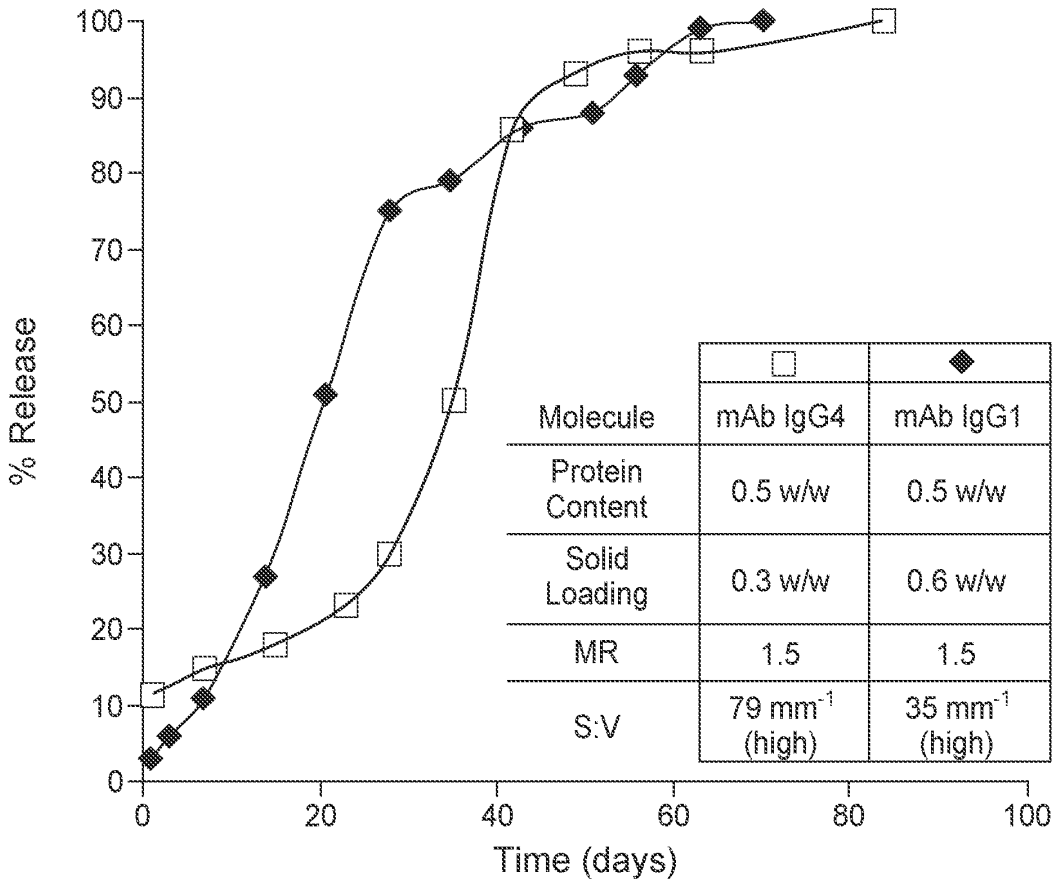
Molecule	○ mAb IgG4	● mAb IgG1
Protein Content	0.9 w/w	0.9 w/w
Solid Loading	0.6 w/w	0.6 w/w
MR	1.8	1.9
S:V	4 mm^{-1} (low)	3 mm^{-1} (low)

FIG. 3



Molecule	□ mAb IgG1	◆ mAb IgG1
Protein Content	0.9 w/w	0.5 w/w
Solid Loading	0.6 w/w	0.6 w/w
MR	1.5	1.5
S:V	4 mm^{-1} (low)	35 mm^{-1} (high)

FIG. 4



Molecule	mAb IgG4	mAb IgG1
Protein Content	0.5 w/w	0.5 w/w
Solid Loading	0.3 w/w	0.6 w/w
MR	1.5	1.5
S:V	79 mm^{-1} (high)	35 mm^{-1} (high)

FIG. 5

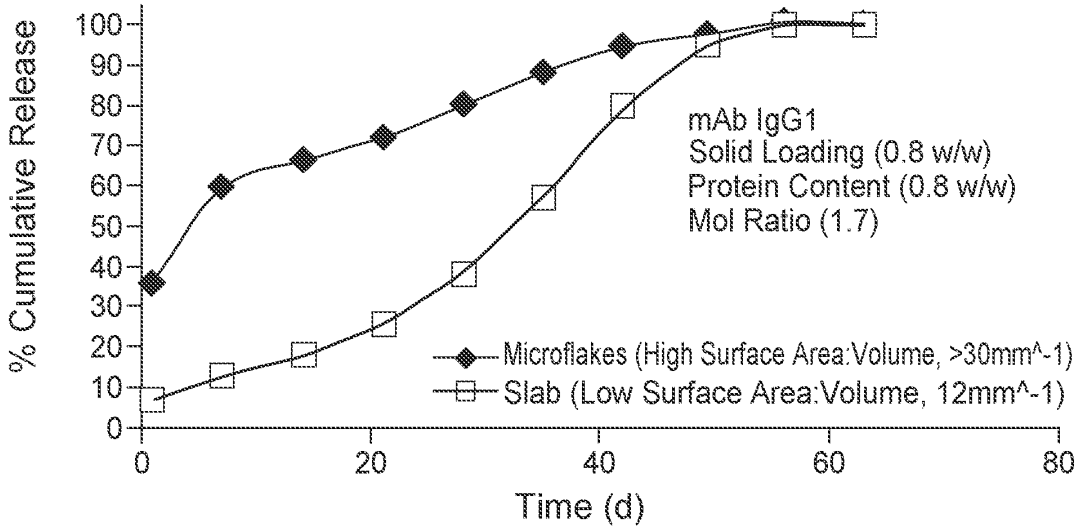


FIG. 6

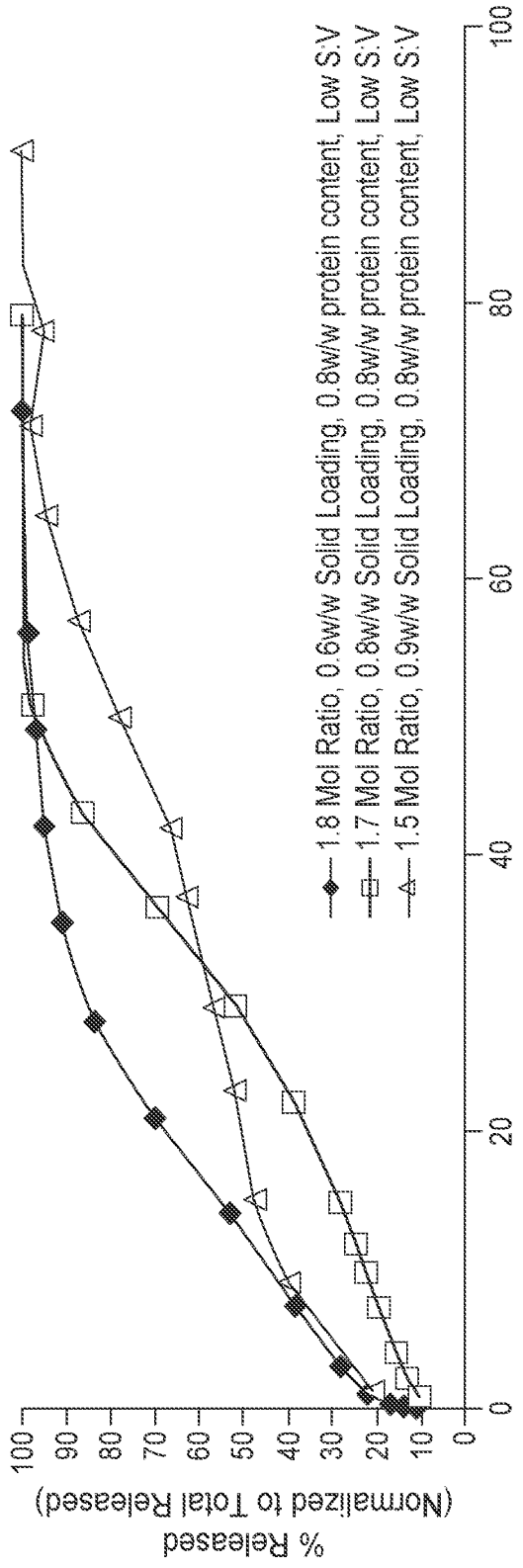
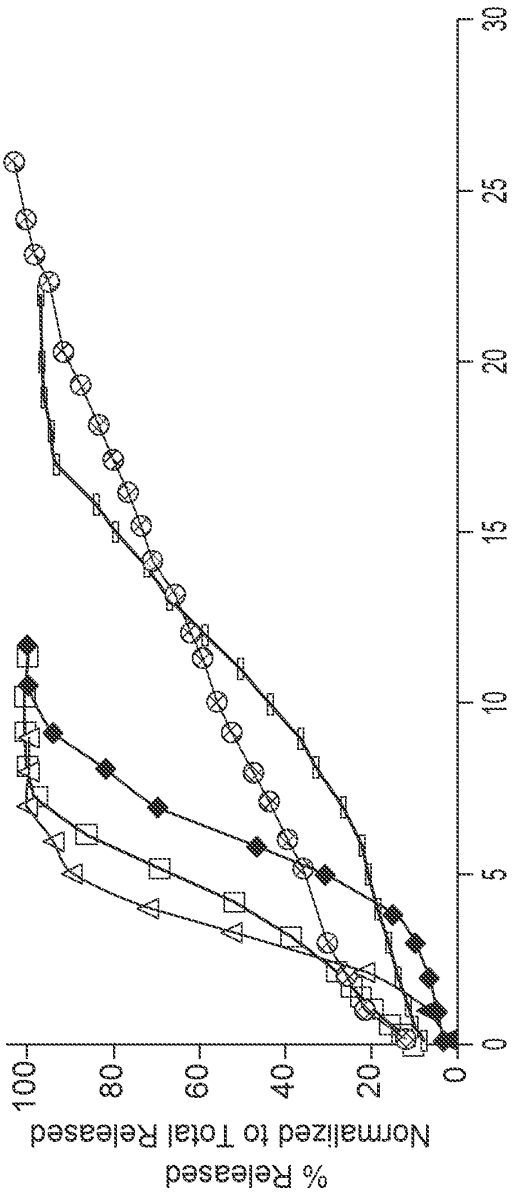
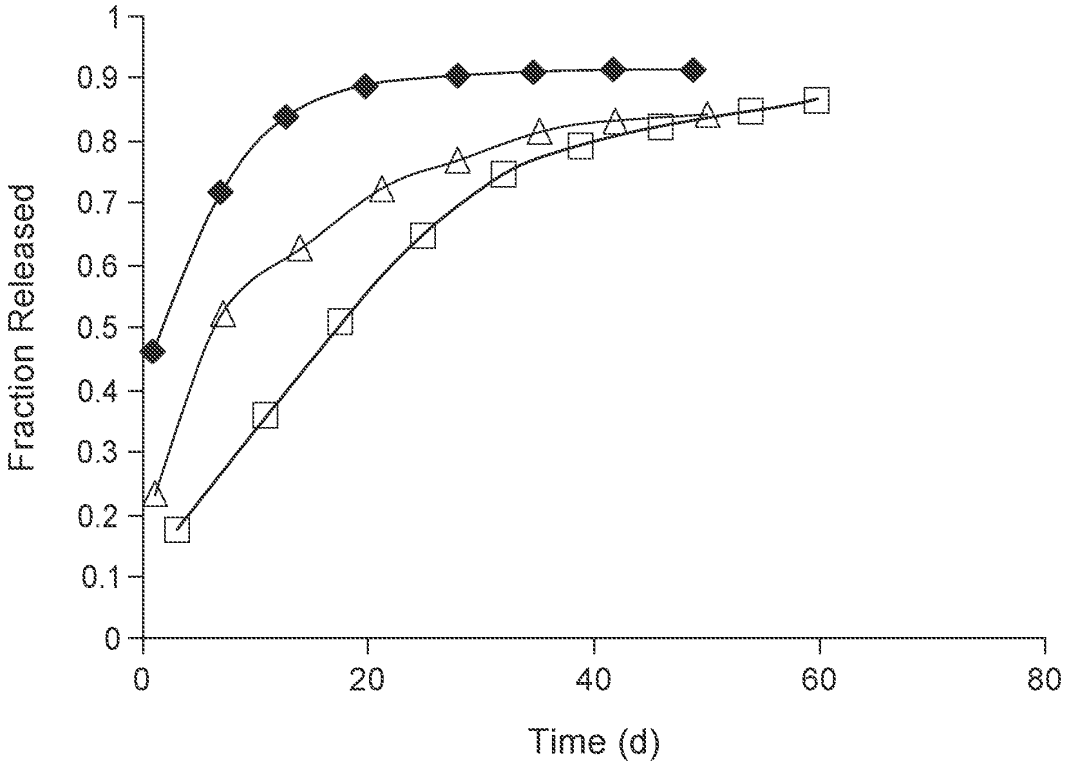

% Released
(Normalized to Total Released)
100
90
80
70
60
50
40
30
20
10
0
0
20
40
60
80
100
Time (d)
1.8 Mol Ratio, 0.6w/w Solid Loading, 0.8w/w protein content, Low S:V
1.7 Mol Ratio, 0.8w/w Solid Loading, 0.8w/w protein content, Low S:V
1.5 Mol Ratio, 0.9w/w Solid Loading, 0.8w/w protein content, Low S:V

FIG. 7



	Molecule	Mol Ratio (NH:NHS)	Solid Loading (w/w)	Protein Content (w/w)	Protein Loading (w/w)	Form
□	mAb IgG1	1.7	0.8	0.8	0.6	Film (high S:V)
△	mAb IgG1	1.9	0.6	0.9	0.5	Slab (low S:V)
▭	mAb IgG4	1.6	0.8	0.8	0.6	Slab (low S:V)
⊗	mAb bispecific	1.5	0.5	0.8	0.4	Slab (low S:V)
◆	Trap Protein	1.0	0.5	0.7	0.4	Film (high S:V)

FIG. 8



Mol Ratio (NH:NHS)	Solid Loading (w/w)	Protein Content (w/w)	Estimated S:V (microparticles)
△ 1.6	0.7	0.8	High >60 mm^{-1}
◆ 1.6	0.8	0.8	High >60 mm^{-1}
□ 1.8	0.7	0.9	High >60 mm^{-1}

FIG. 9

Power Analysis	
Significance Level	0.05
Anticipated RMSE	1

Term	Anticipated Coefficient	Power
Intercept	1	0.896
Mol Ratio	2	1.000
PEG NH Reagent (4-arm) 1	2	0.971
PEG NH Reagent (4-arm) 2	2	0.971
PEG NH Reagent (4-arm) 3	2	0.971
PEG NHS Reagent (4-arm) 1	2	0.971
PEG NHS Reagent (4-arm) 2	2	0.971
PEG NHS Reagent (4-arm) 3	2	0.971

Effect	Power
PEG NH Reagent (4-arm)	1
PEG NHS Reagent (4-arm)	1

FIG. 10

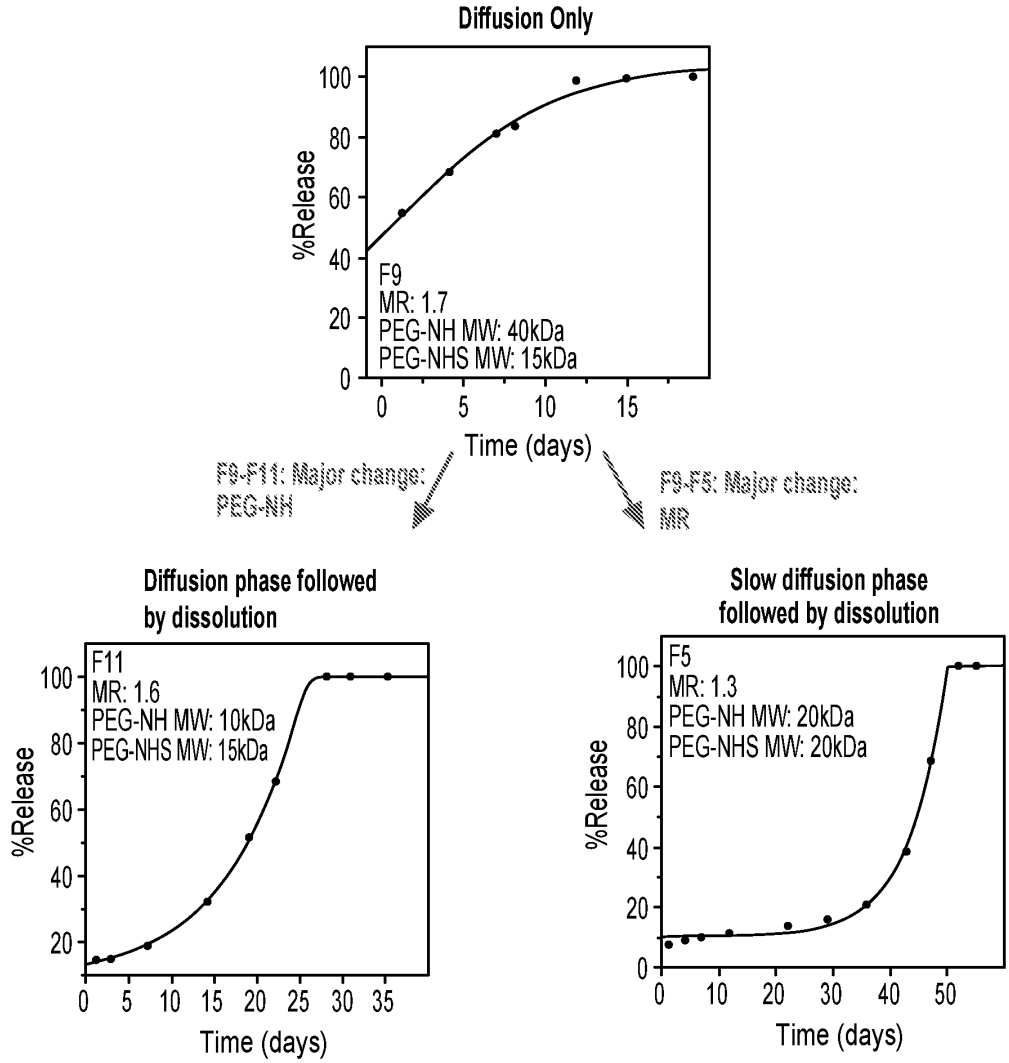
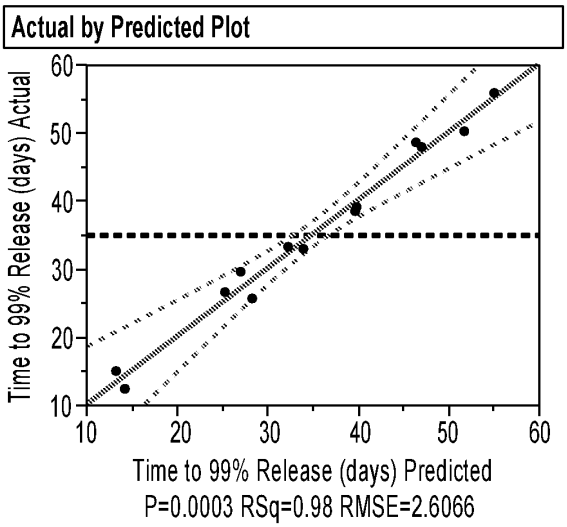

Diffusion Only
%Release
Time (days)
F9
MR: 1.7
PEG-NH MW: 40kDa
PEG-NHS MW: 15kDa
F9-F11: Major change: PEG-NH
F9-F5: Major change: MR
Diffusion phase followed by dissolution
F11
MR: 1.6
PEG-NH MW: 10kDa
PEG-NHS MW: 15kDa
Slow diffusion phase followed by dissolution
F5
MR: 1.3
PEG-NH MW: 20kDa
PEG-NHS MW: 20kDa

FIG. 11



Summary of Fit	
RSquare	0.984224
RSquare Adj	0.962137
Root Mean Square Error	2.6066
Mean of Response	34.98908
Observations (or Sum Wgts)	13

FIG. 12

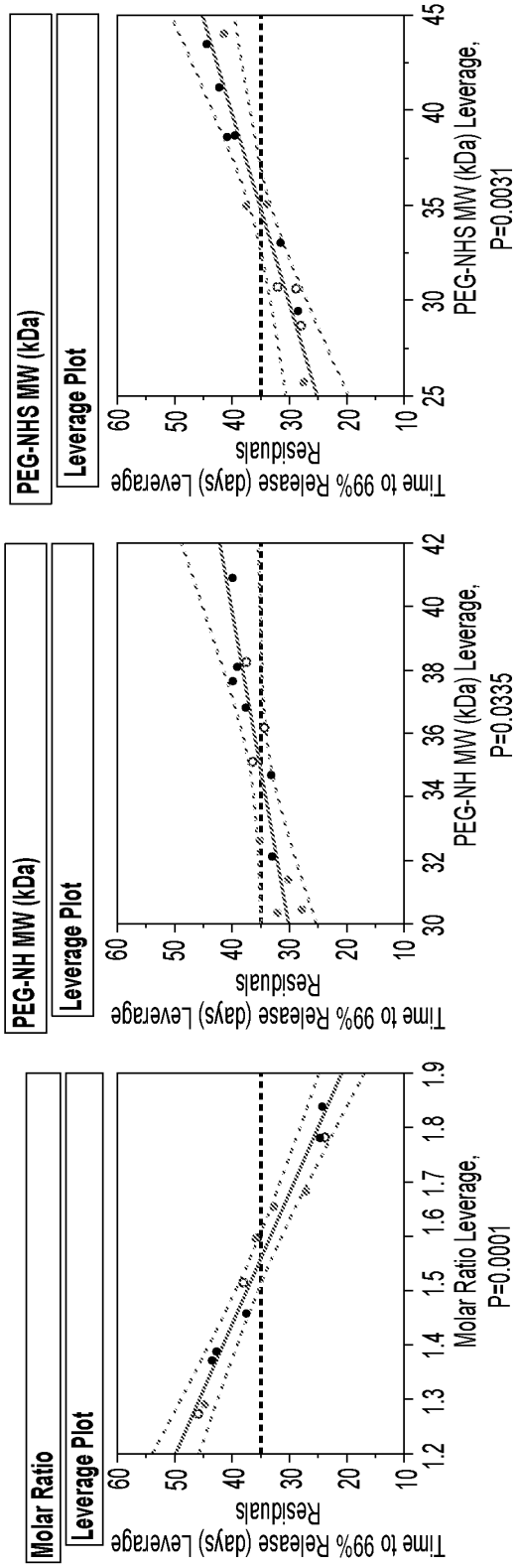

Molar Ratio
Leverage Plot
Time to 99% Release (days) Leverage Residuals
Molar Ratio Leverage, P=0.0001
PEG-NH MW (kDa)
Leverage Plot
Time to 99% Release (days) Leverage Residuals
PEG-NH MW (kDa) Leverage, P=0.0335
PEG-NHS MW (kDa)
Leverage Plot
Time to 99% Release (days) Leverage Residuals
PEG-NHS MW (kDa) Leverage, P=0.0031

FIG. 13

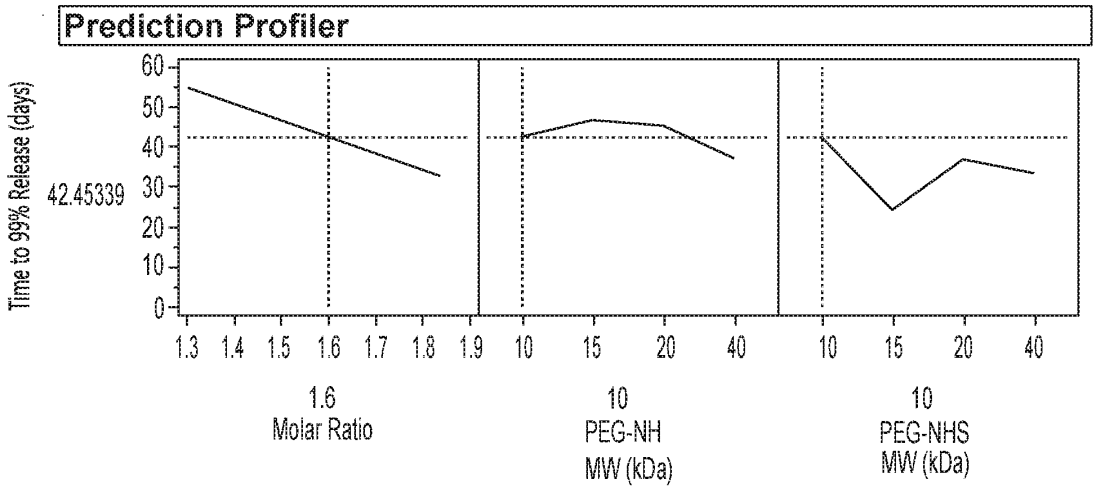

Prediction Profiler
Time to 99% Release (days)
42.45339
60
50
40
30
20
10
0
1.3 1.4 1.5 1.6 1.7 1.8 1.9 10 15 20 40 10 15 20 40
1.6
Molar Ratio
10
PEG-NH
MW (kDa)
10
PEG-NHS
MW (kDa)

FIG. 14

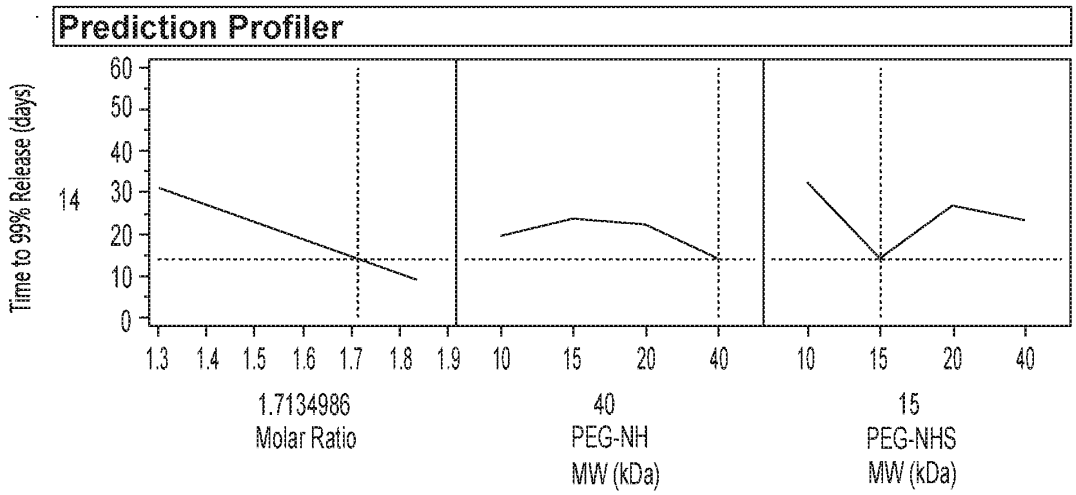

Prediction Profiler
Time to 99% Release (days)
14
60
50
40
30
20
10
0
1.3 1.4 1.5 1.6 1.7 1.8 1.9 10 15 20 40 10 15 20 40
1.7134986
Molar Ratio
40
PEG-NH
MW (kDa)
15
PEG-NHS
MW (kDa)

FIG. 15

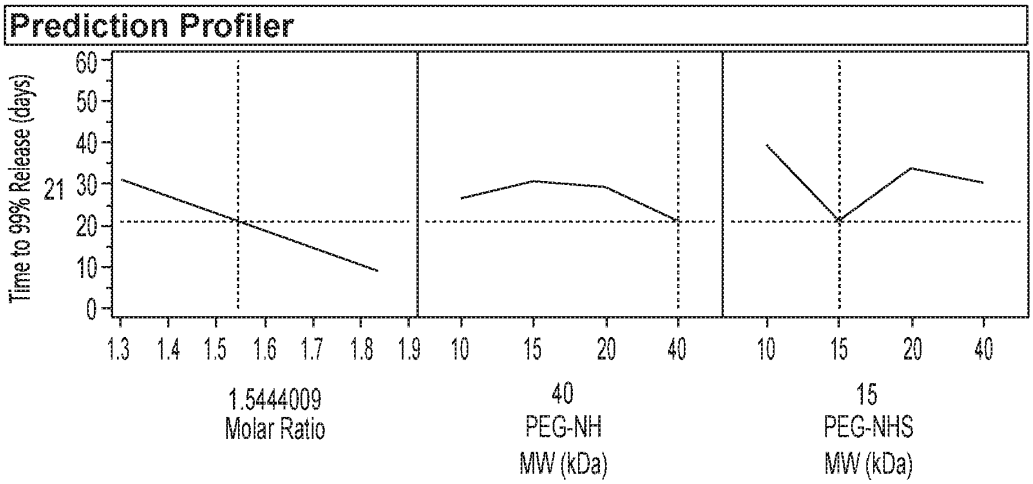

Prediction Profiler
Time to 99% Release (days)
60
50
40
21 30
20
10
0
1.3 1.4 1.5 1.6 1.7 1.8 1.9 10 15 20 40 10 15 20 40
1.5444009
Molar Ratio
40
PEG-NH
MW (kDa)
15
PEG-NHS
MW (kDa)

FIG. 16

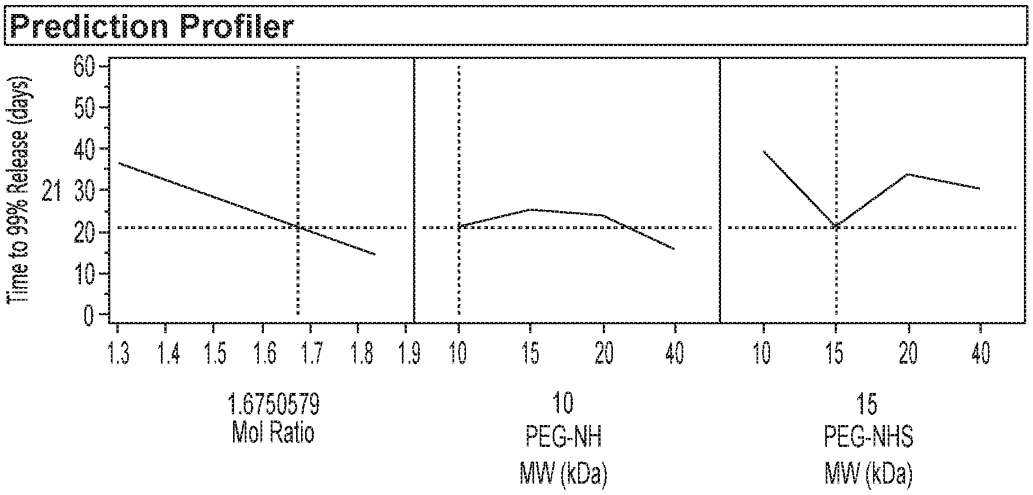

Prediction Profiler
Time to 99% Release (days)
60
50
40
21 30
20
10
0
1.3 1.4 1.5 1.6 1.7 1.8 1.9 10 15 20 40 10 15 20 40
1.6750579
Mol Ratio
10
PEG-NH
MW (kDa)
15
PEG-NHS
MW (kDa)

FIG. 17

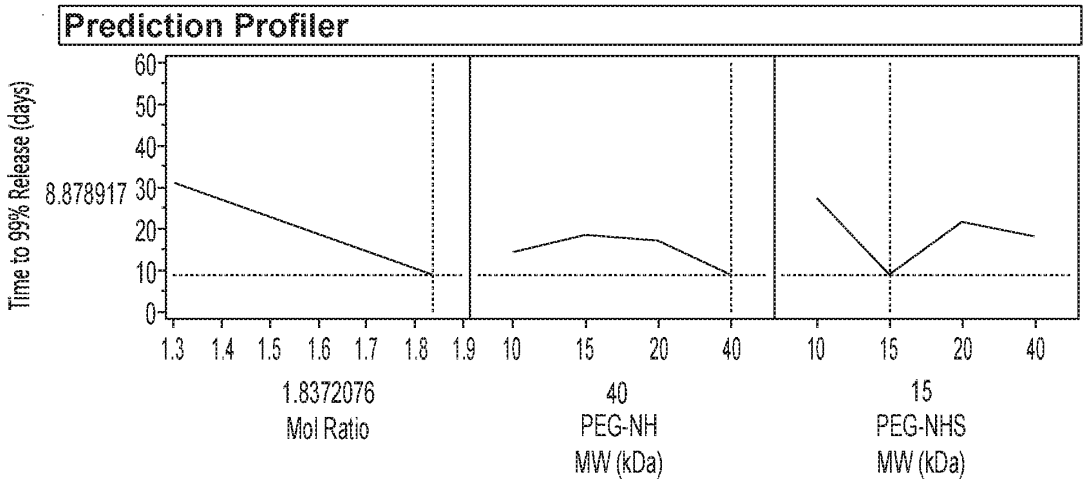

Prediction Profiler
Time to 99% Release (days)
8.878917
60
50
40
30
20
10
0
1.3 1.4 1.5 1.6 1.7 1.8 1.9 10 15 20 40 10 15 20 40
1.8372076
Mol Ratio
40
PEG-NH
MW (kDa)
15
PEG-NHS
MW (kDa)

FIG. 18

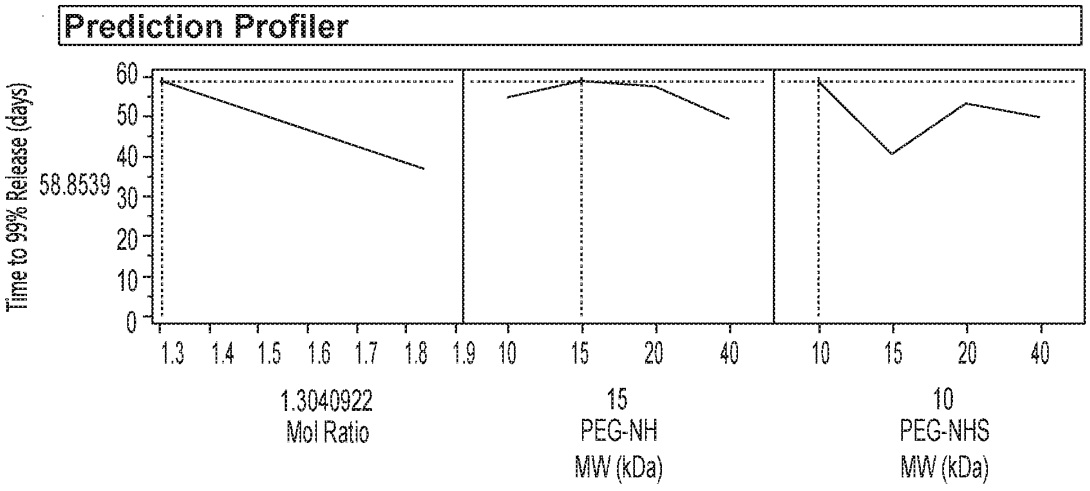

Prediction Profiler
Time to 99% Release (days)
58.8539
60
50
40
30
20
10
0
1.3 1.4 1.5 1.6 1.7 1.8 1.9 10 15 20 40 10 15 20 40
1.3040922
Mol Ratio
15
PEG-NH
MW (kDa)
10
PEG-NHS
MW (kDa)

FIG. 19

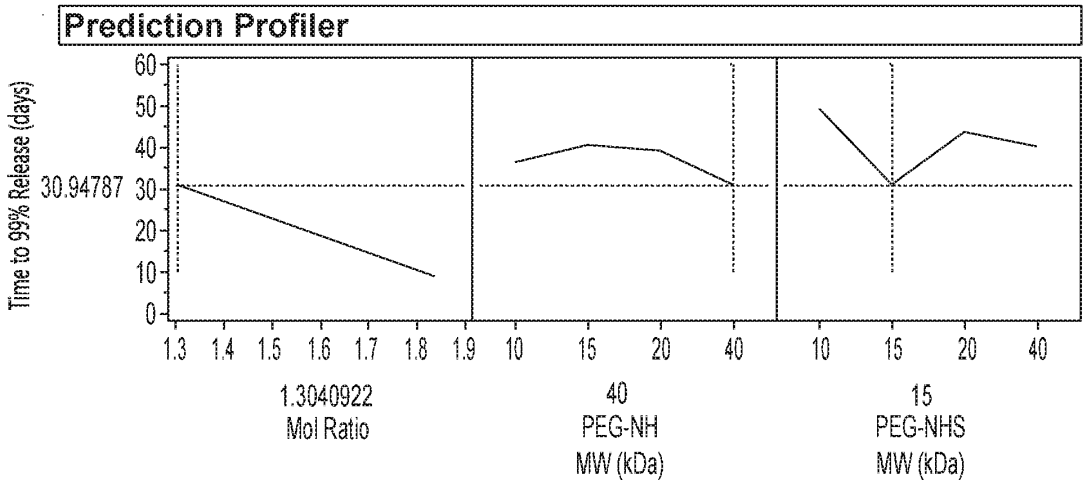

Prediction Profiler
Time to 99% Release (days)
30.94787
60
50
40
30
20
10
0
1.3 1.4 1.5 1.6 1.7 1.8 1.9
10 15 20 40
10 15 20 40
1.3040922
Mol Ratio
40
PEG-NH
MW (kDa)
15
PEG-NHS
MW (kDa)

FIG. 20

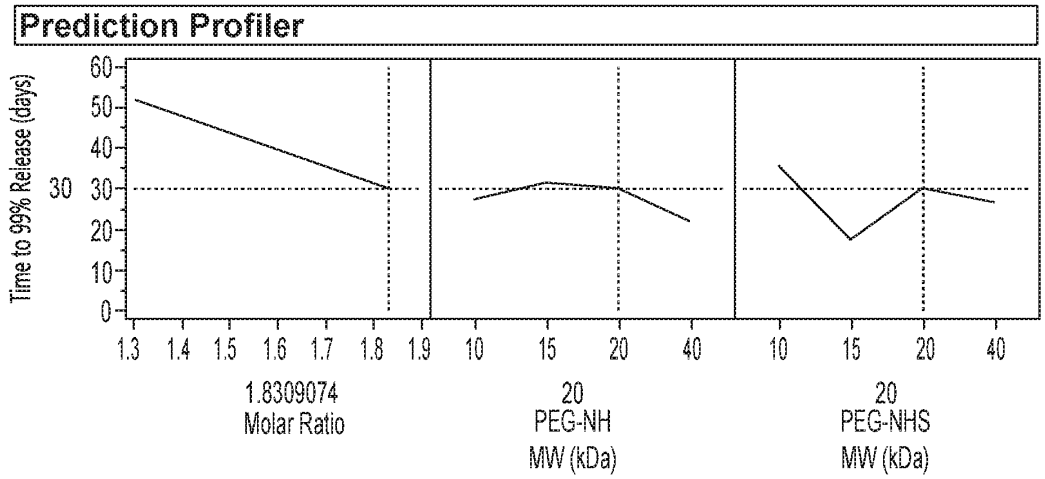

Prediction Profiler
Time to 99% Release (days)
60
50
40
30
20
10
0
30
1.3 1.4 1.5 1.6 1.7 1.8 1.9
10 15 20 40
10 15 20 40
1.8309074
Molar Ratio
20
PEG-NH
MW (kDa)
20
PEG-NHS
MW (kDa)

FIG. 21

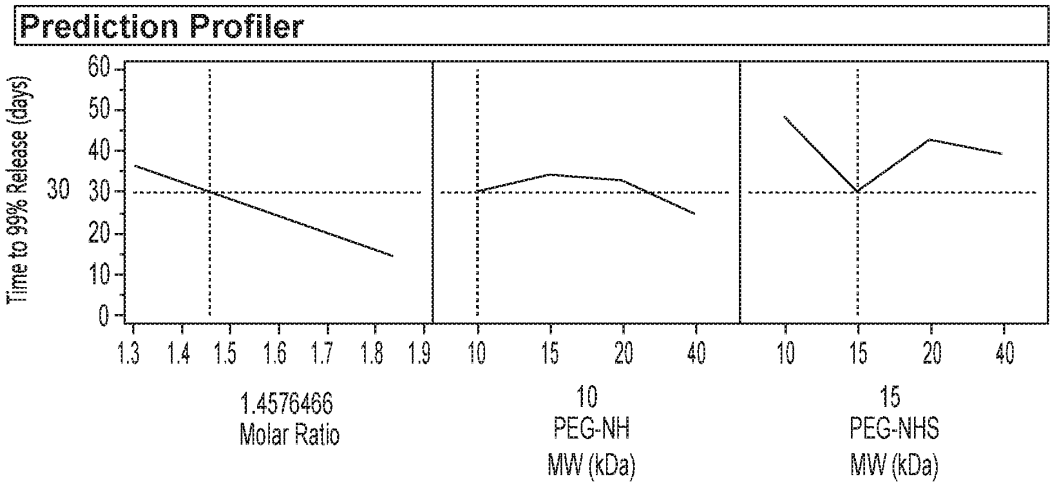

Prediction Profiler
Time to 99% Release (days)
60
50
40
30
20
10
0
30
1.3 1.4 1.5 1.6 1.7 1.8 1.9
10 15 20 40
10 15 20 40
1.4576466
Molar Ratio
10
PEG-NH
MW (kDa)
15
PEG-NHS
MW (kDa)

FIG. 22