Figure 1A XRPD Pattern of Free Form Pattern A (Compound A, Form A)

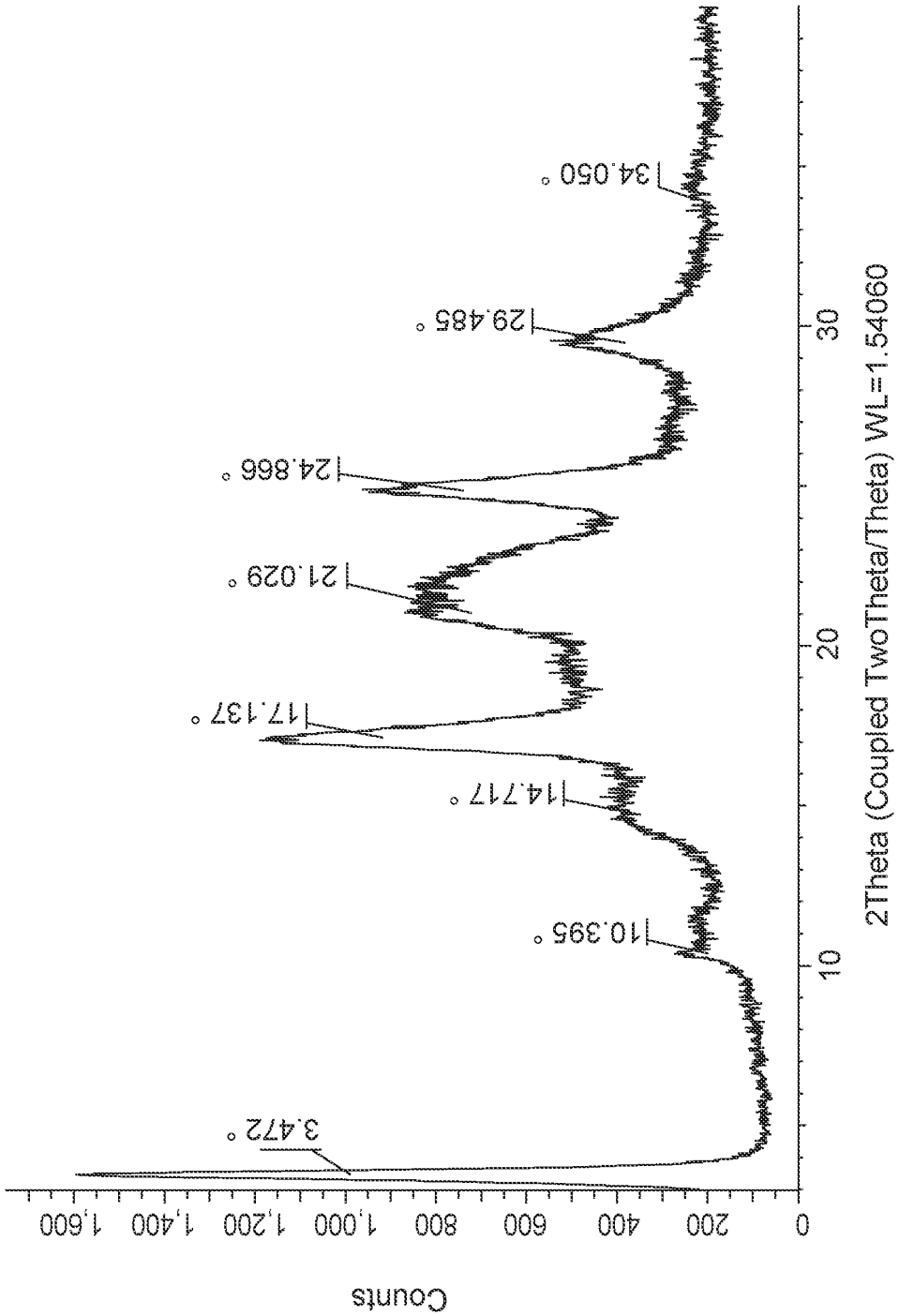
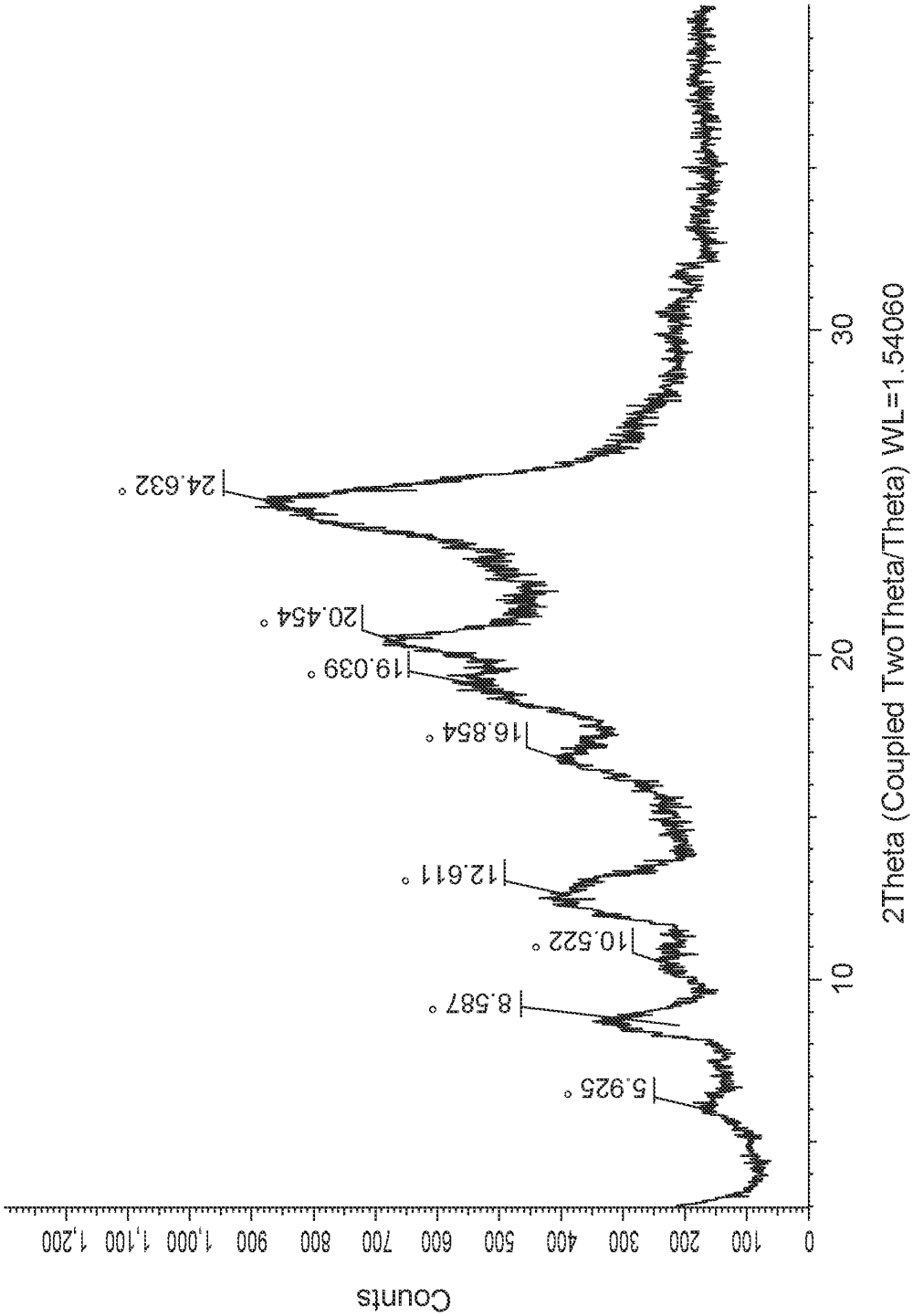


Figure 2A XRPD Pattern of Free Form Pattern B (Compound A, Form B)



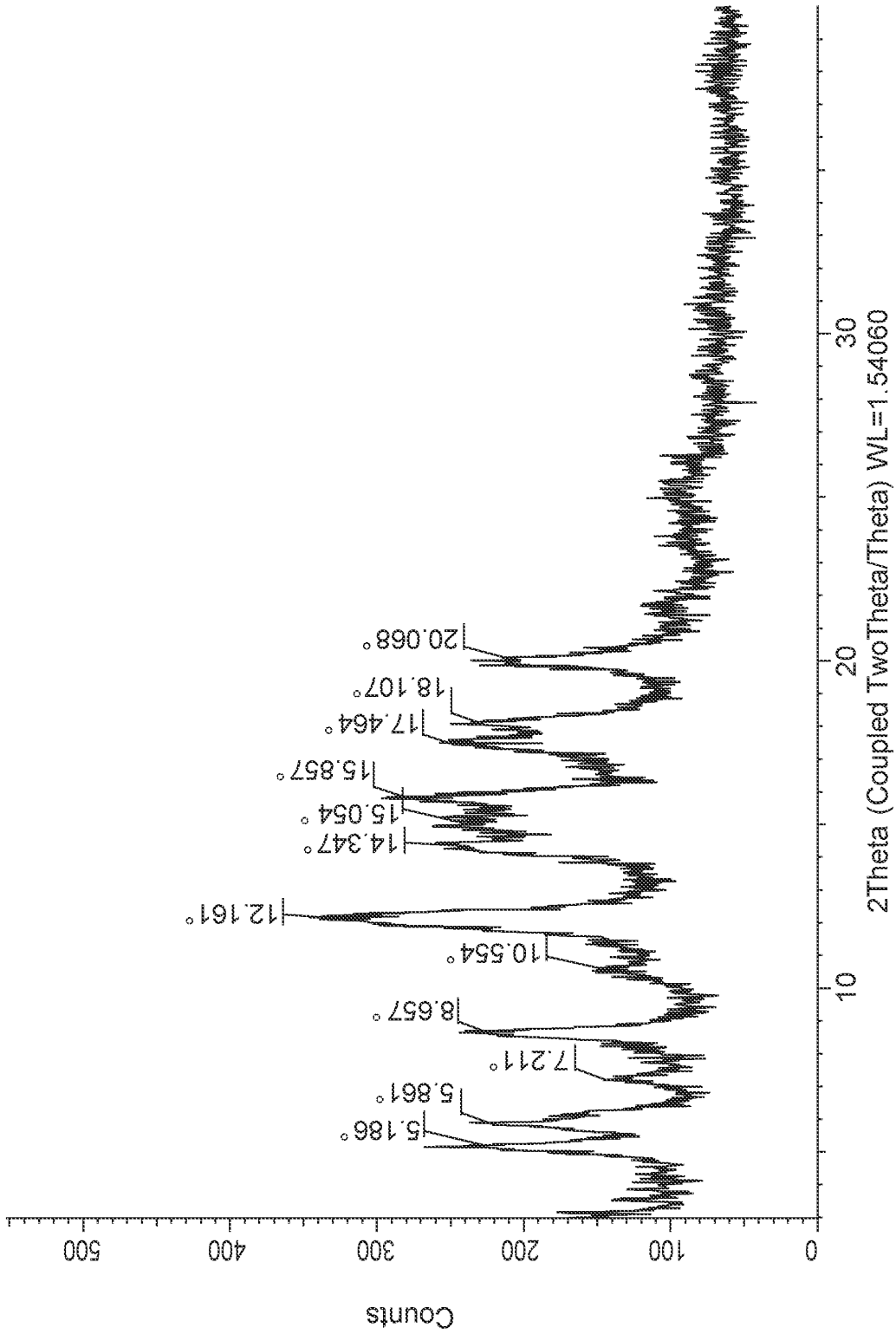


Figure 3A XRPD Pattern of Free Form Pattern C (Compound A, Form C)

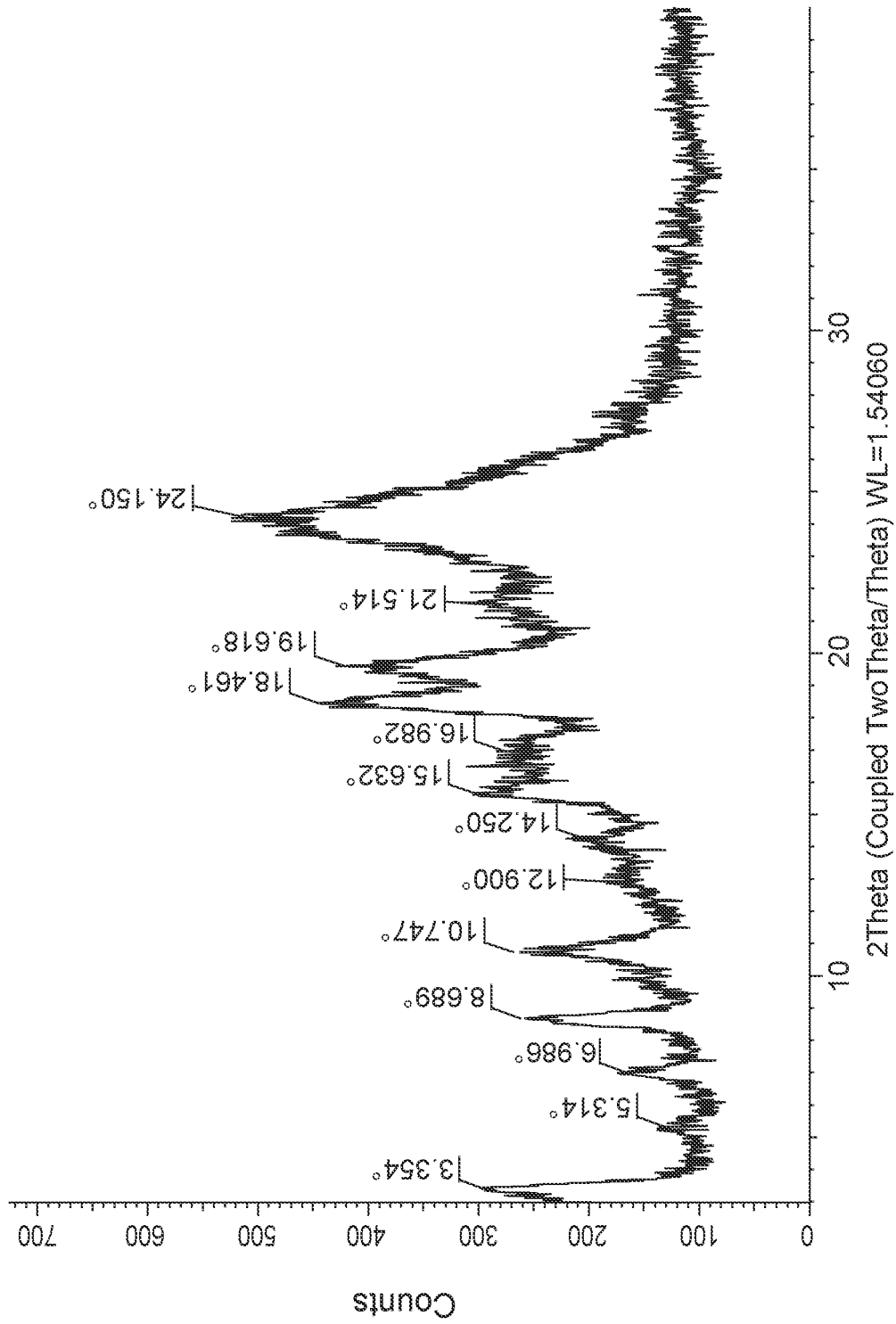


Figure 4A XRPD Pattern of Free Form Pattern D (Compound A, Form D)

Figure 5A XRPD Pattern of Free Form Pattern E (Compound A, Form E)

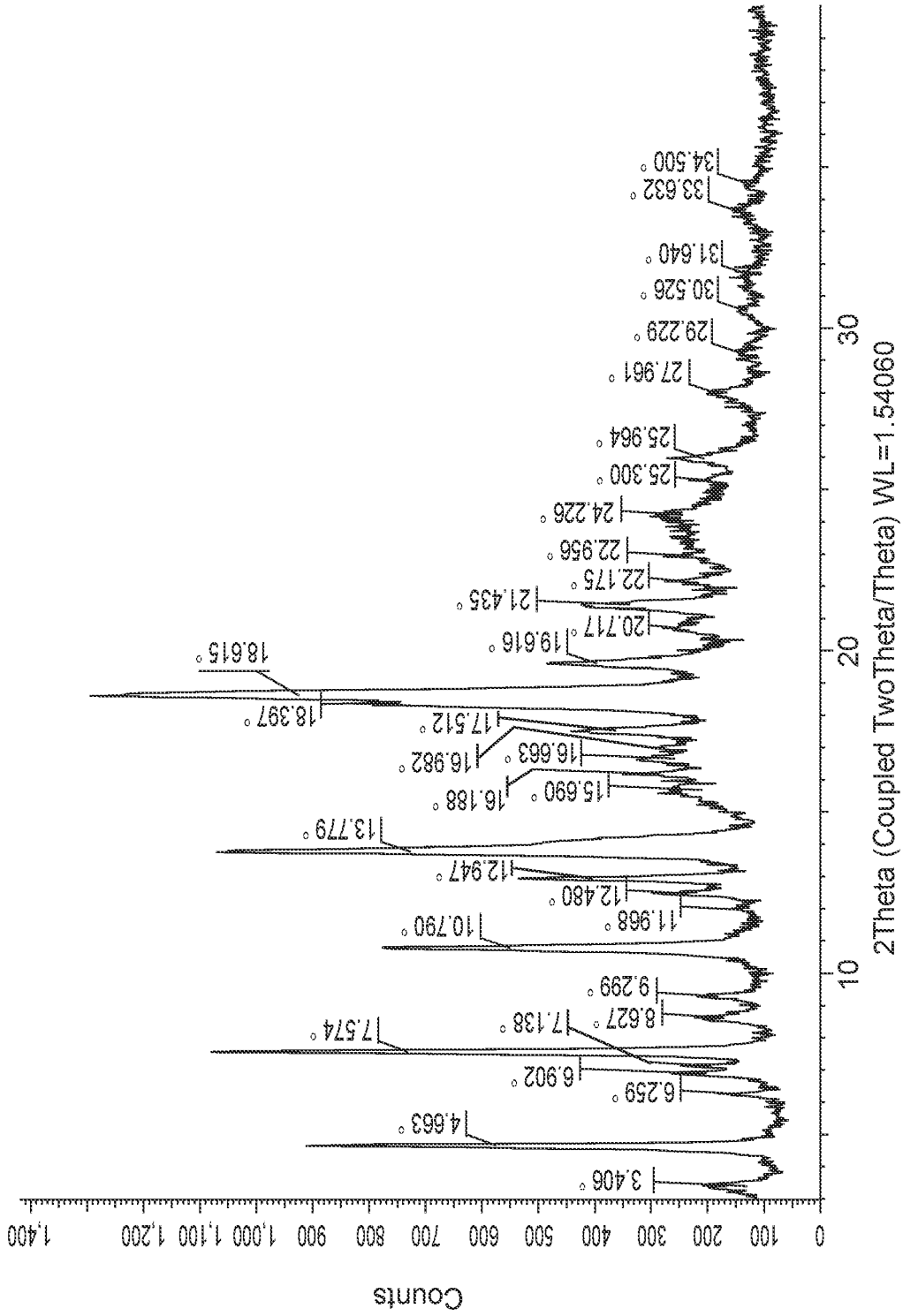


Figure 6A XRPD Pattern of Free Form Pattern F (Compound A, Form F)

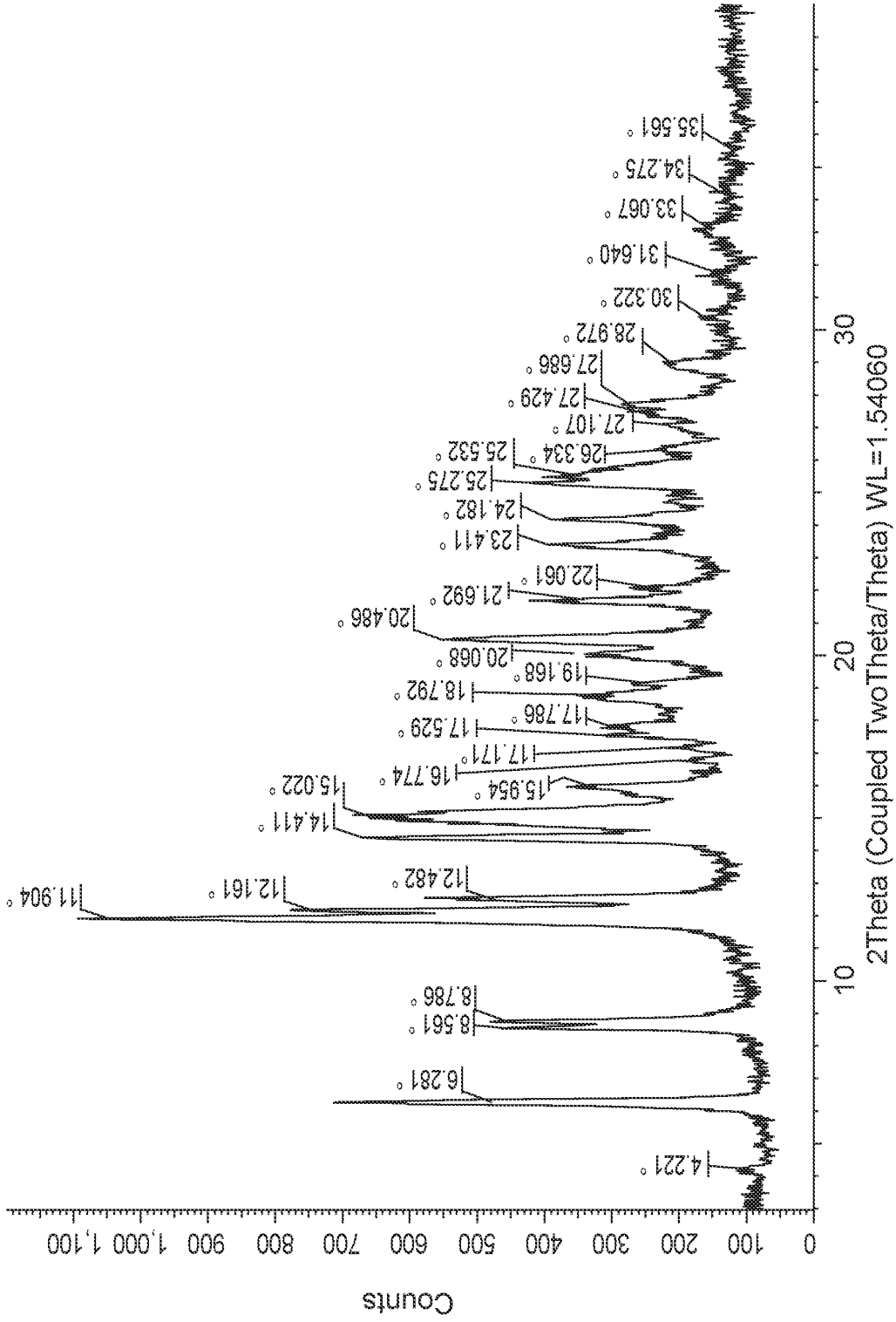


Figure 7A XRPD Pattern of Free Form Pattern G (Compound A, Form G)

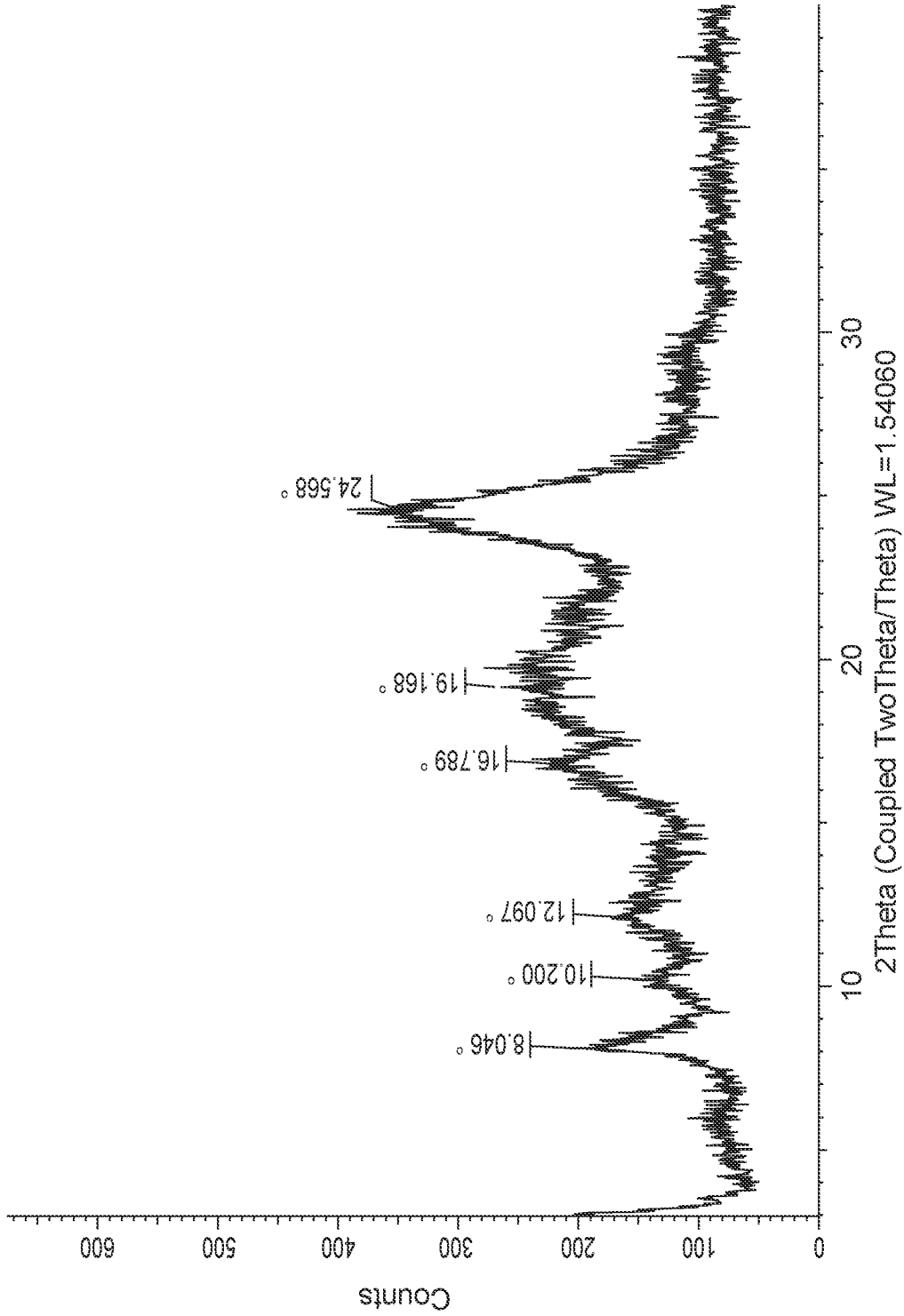


Figure 8A XRPD Pattern of Free Form Pattern J (Compound A, Form J)

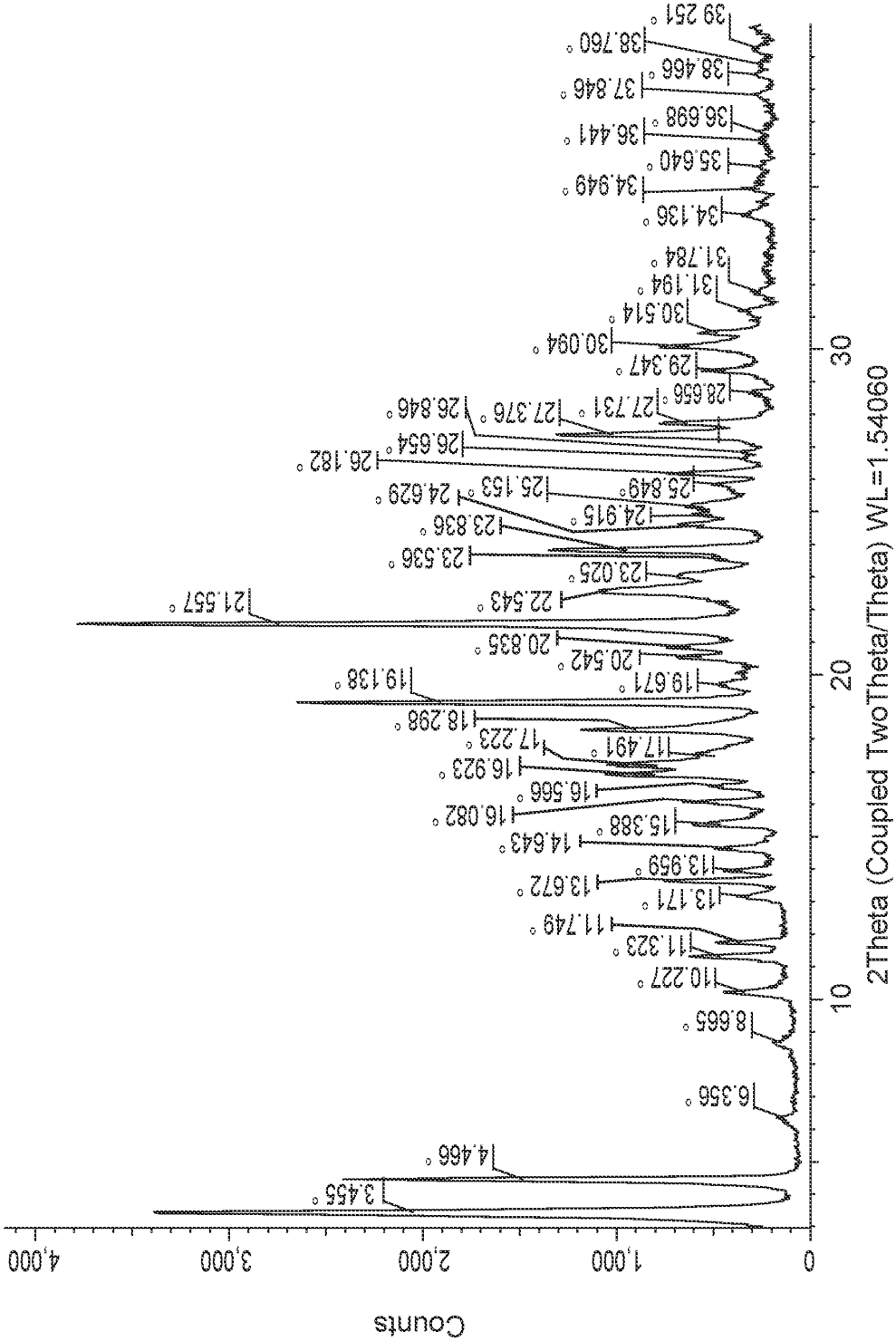
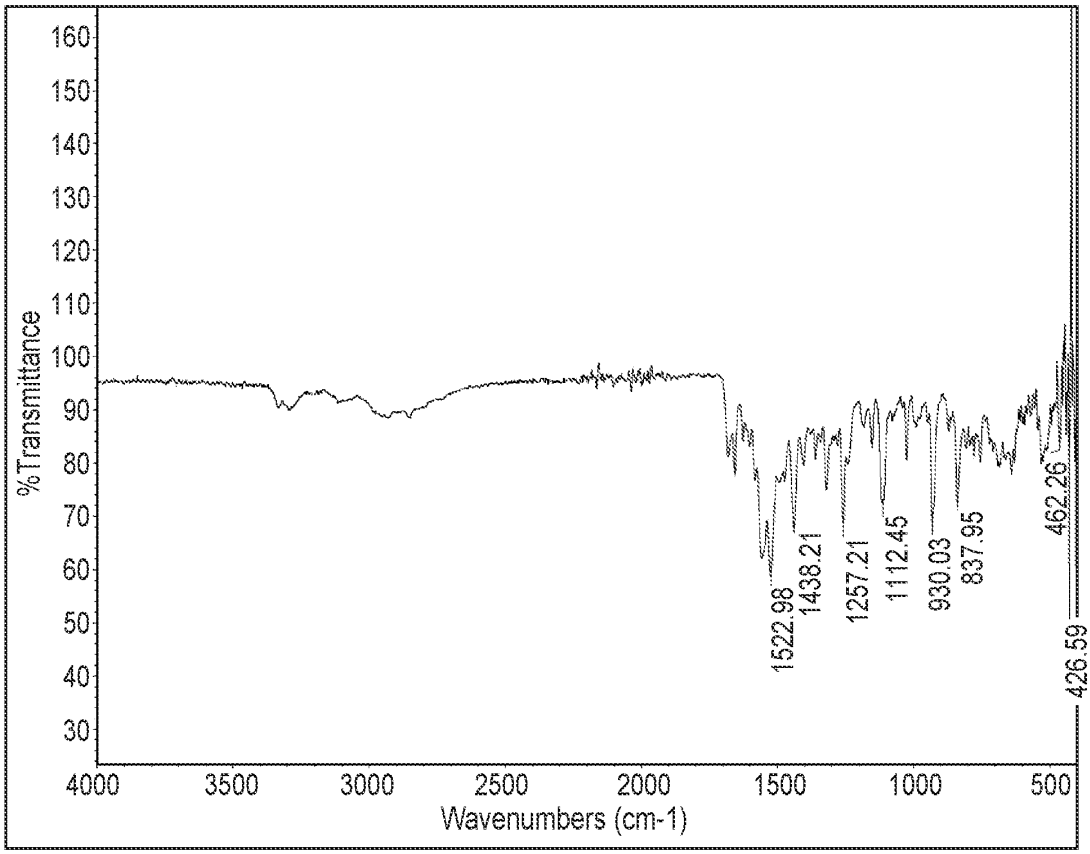


Figure 9A
IR Spectra of Free Form Pattern D (Compound A, Form D)



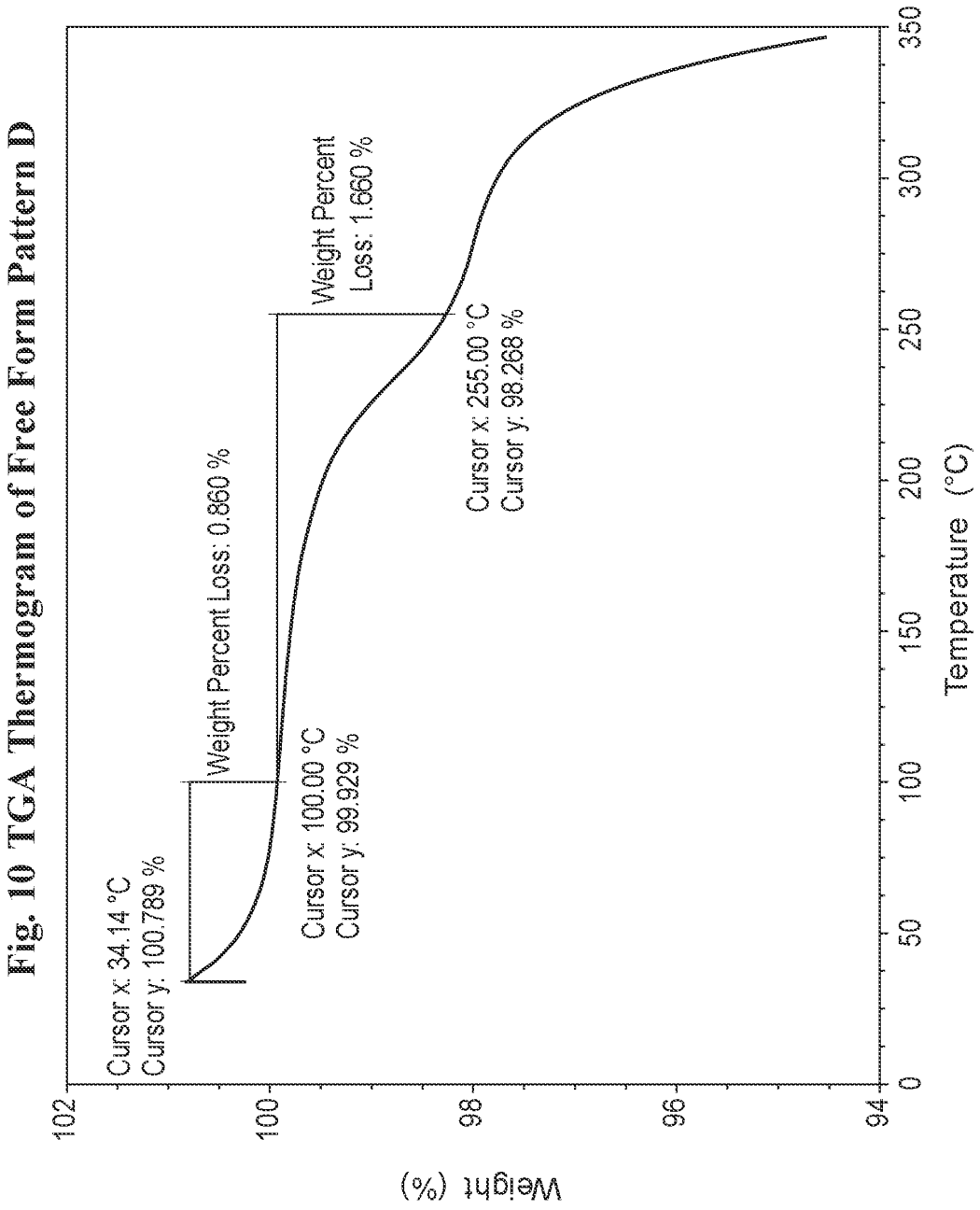


Fig. 10 TGA Thermogram of Free Form Pattern D

Fig. 11 DSC Thermogram of Free Form Pattern D

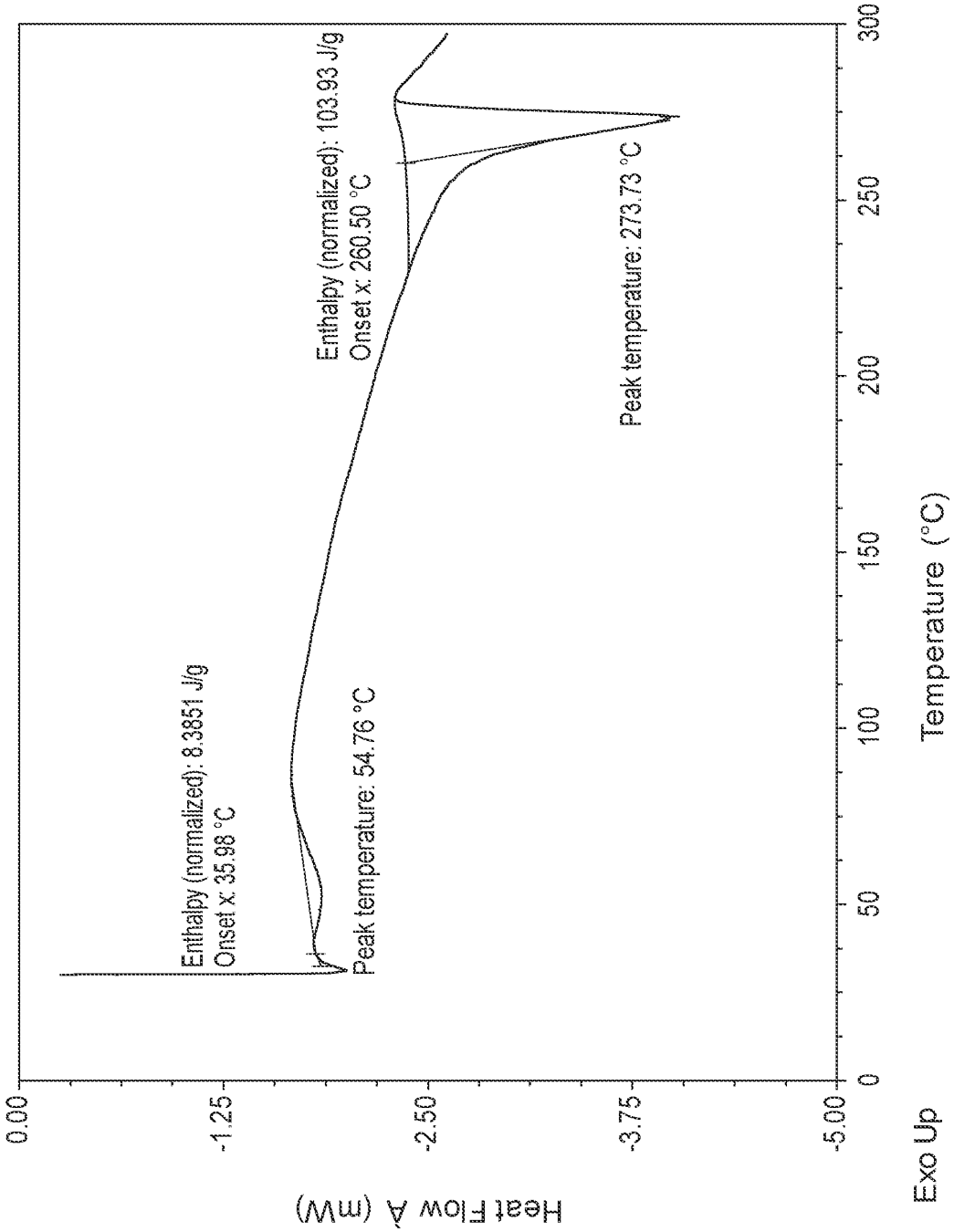


Fig. 12

^{1}H NMR Spectrum of Free Form Pattern D

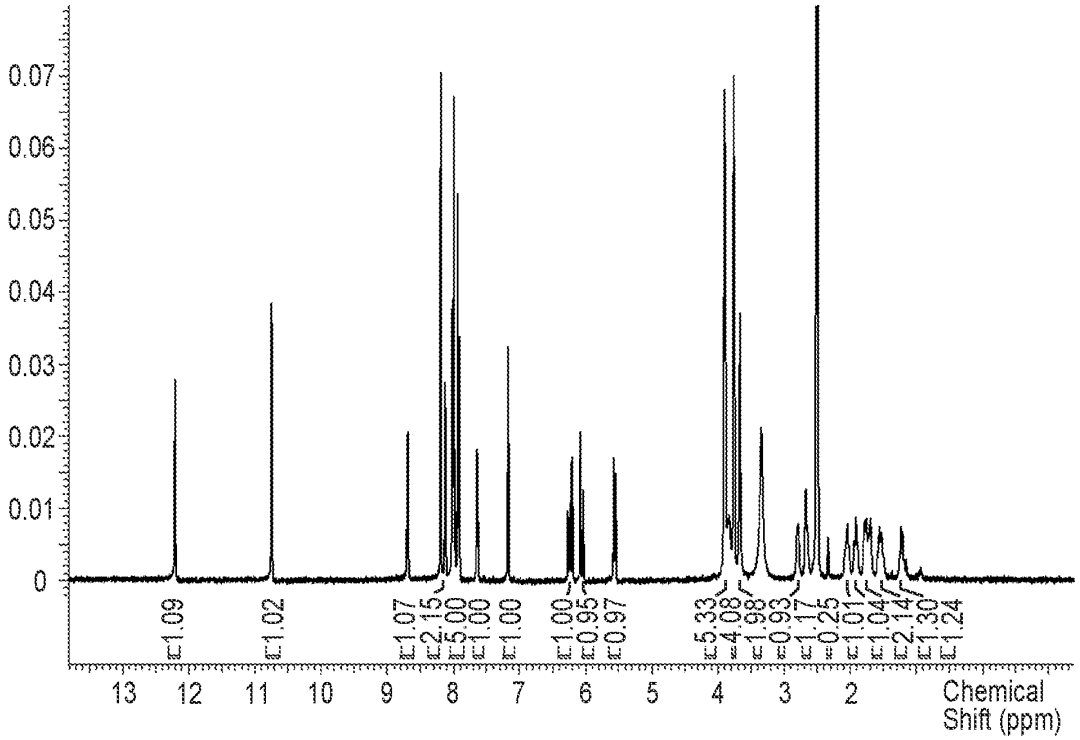


Fig. 13 XRPD Pattern of Pattern D, Sample ID FR01446-1-SU3-Pattern D

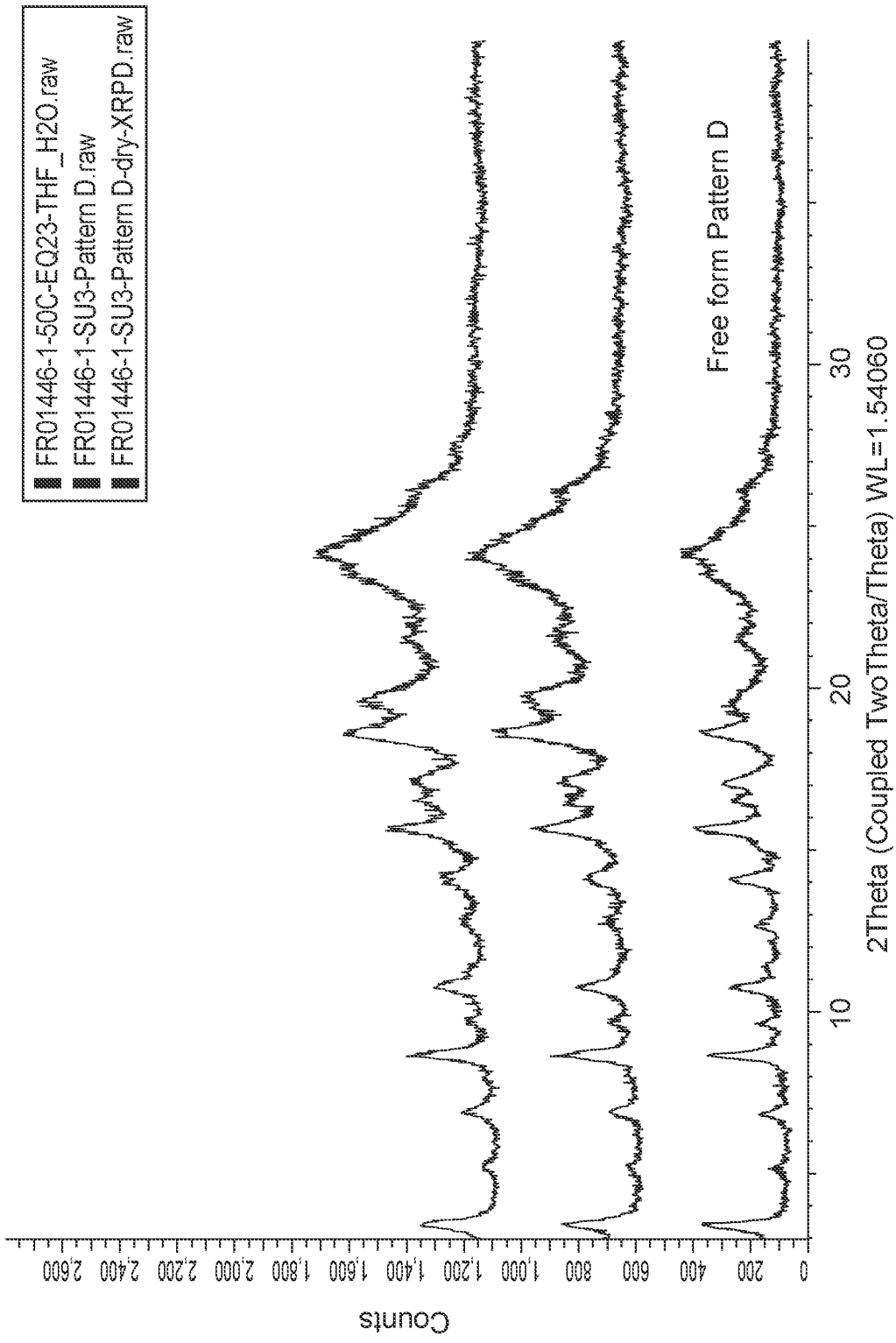


Figure 14 TGA Thermogram of Pattern D After Being Dried at 50°C for 3 h, Sample ID FR01446-1-SU3-Pattern D-dry

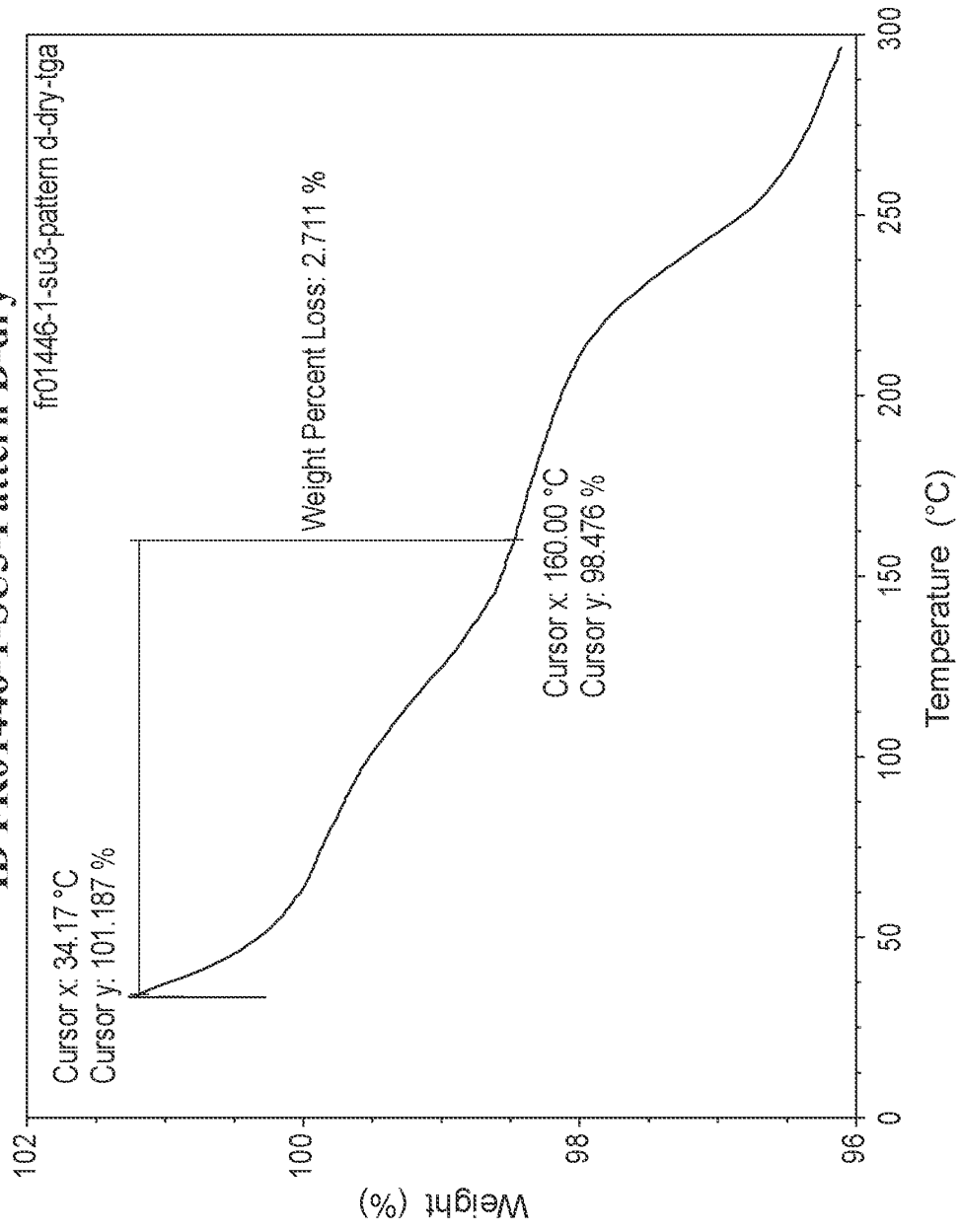


Fig. 15 DSC Thermogram of Pattern D After Being Dried at 50°C for 3 h, Sample ID FR01446-1-SU3-Pattern D-dry

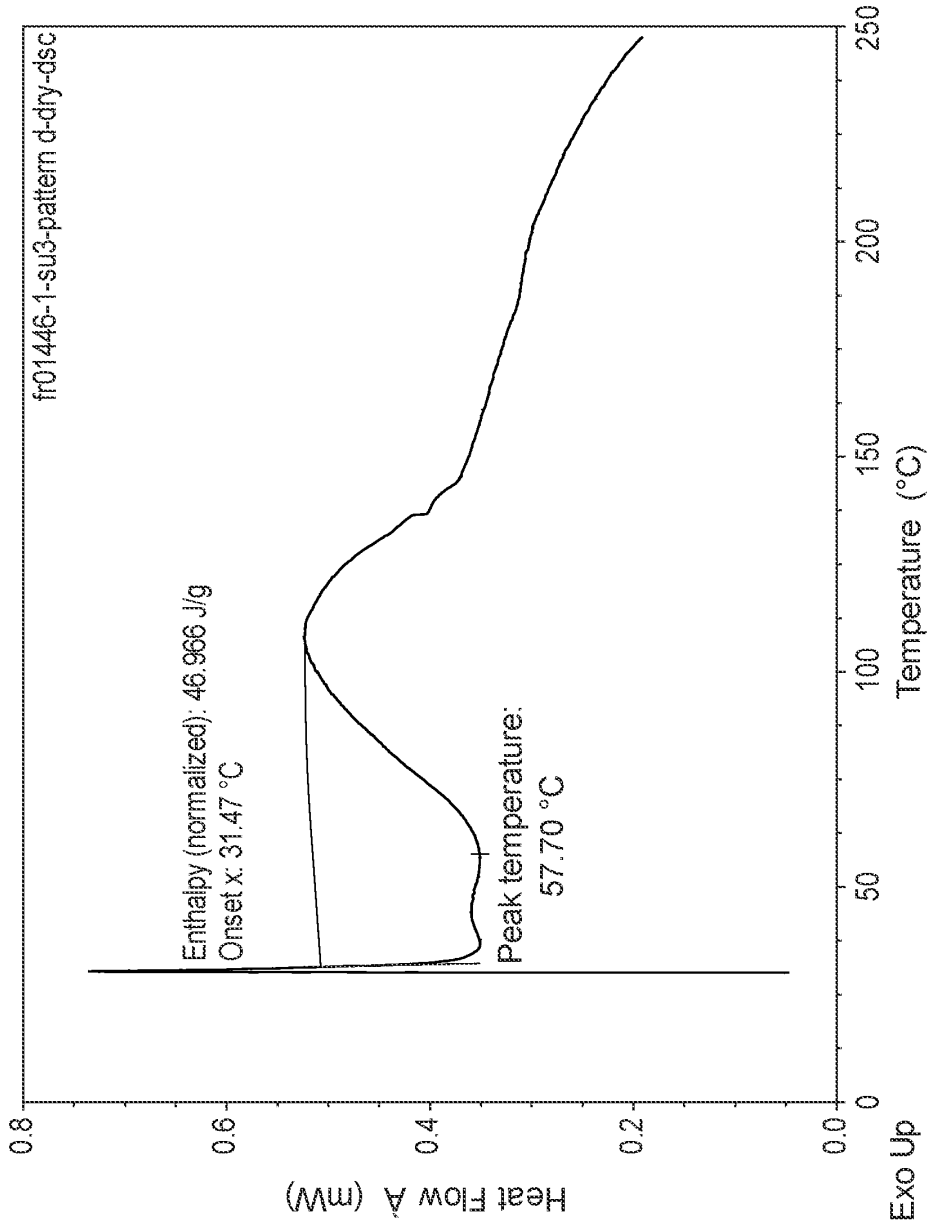


Fig. 16
^{1}H NMR Spectrum of Pattern D After Being Dried at 50°C for 3 h, Sample ID FR01446-1-SU3-Pattern D-dry

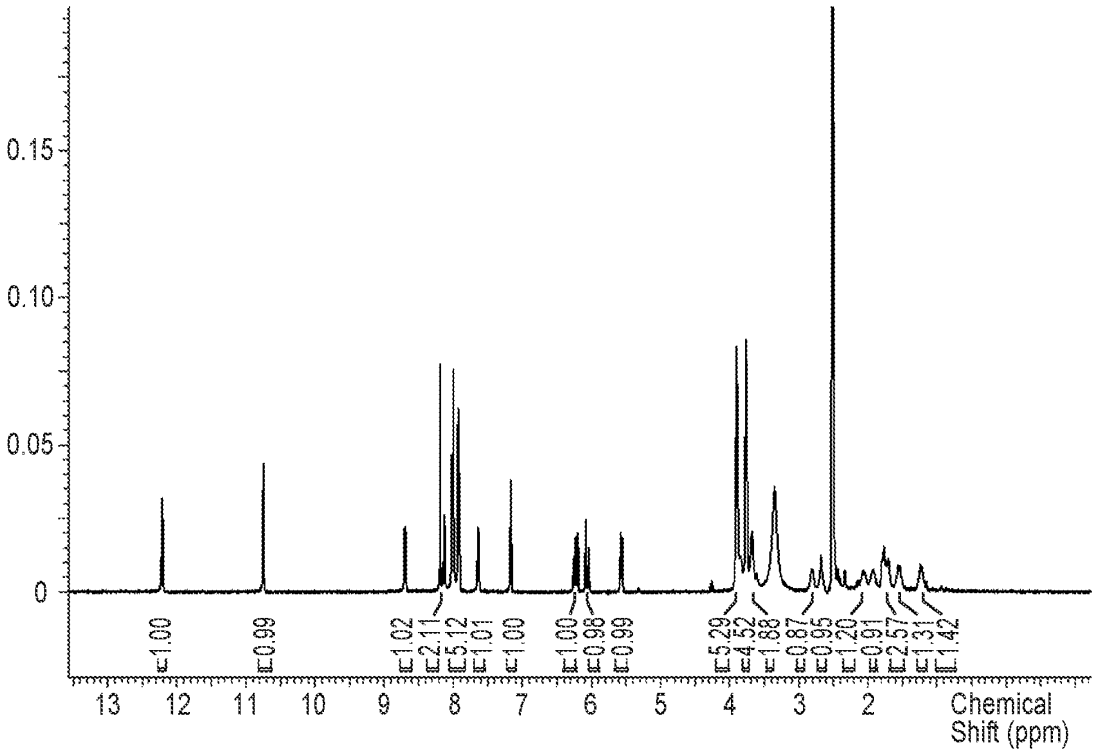


Fig. 17 PLM Photograph of Free Form Pattern D After Being Dried at 50°C for 3 h, Sample ID FR01446-1-SU3-Pattern D-dry

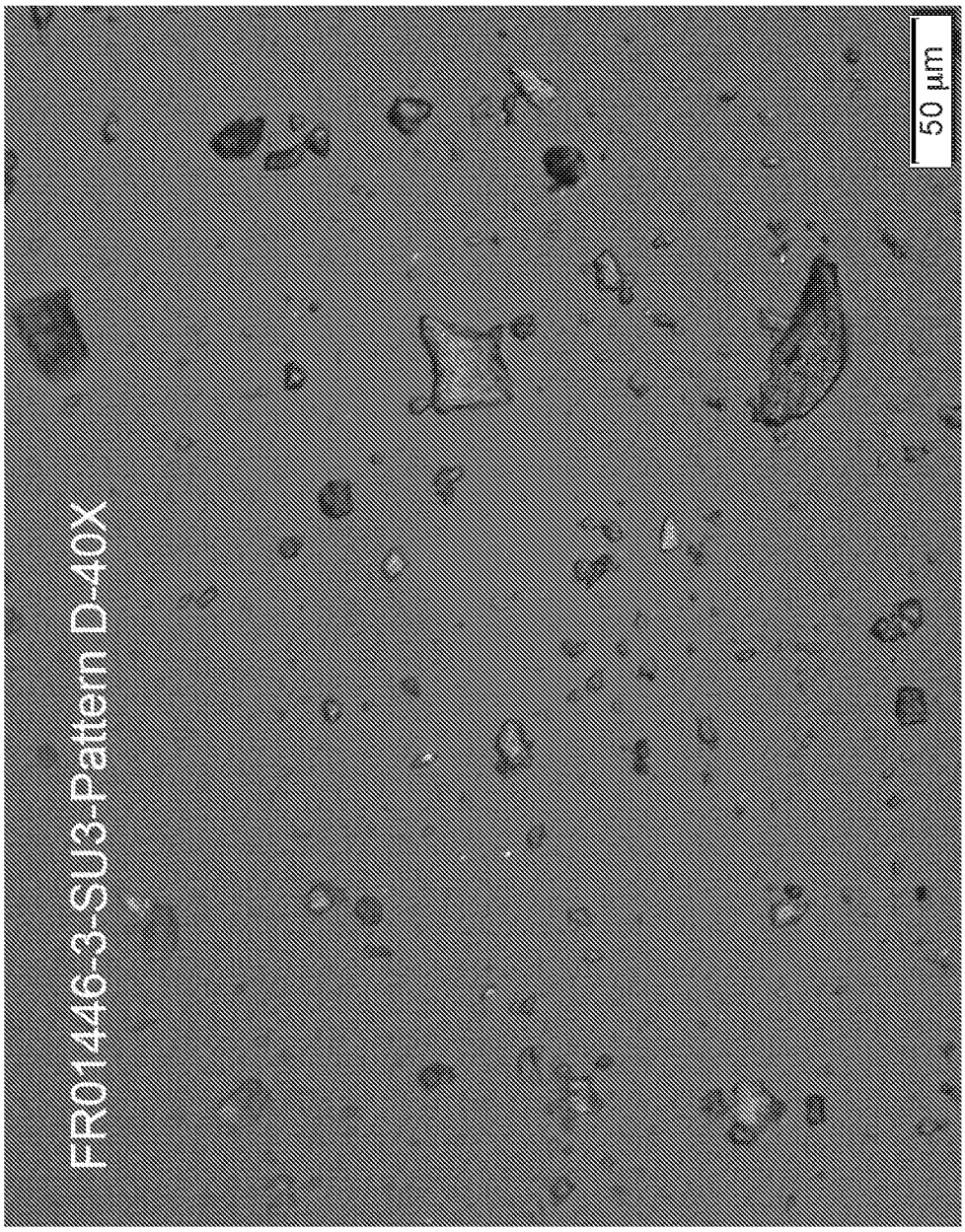
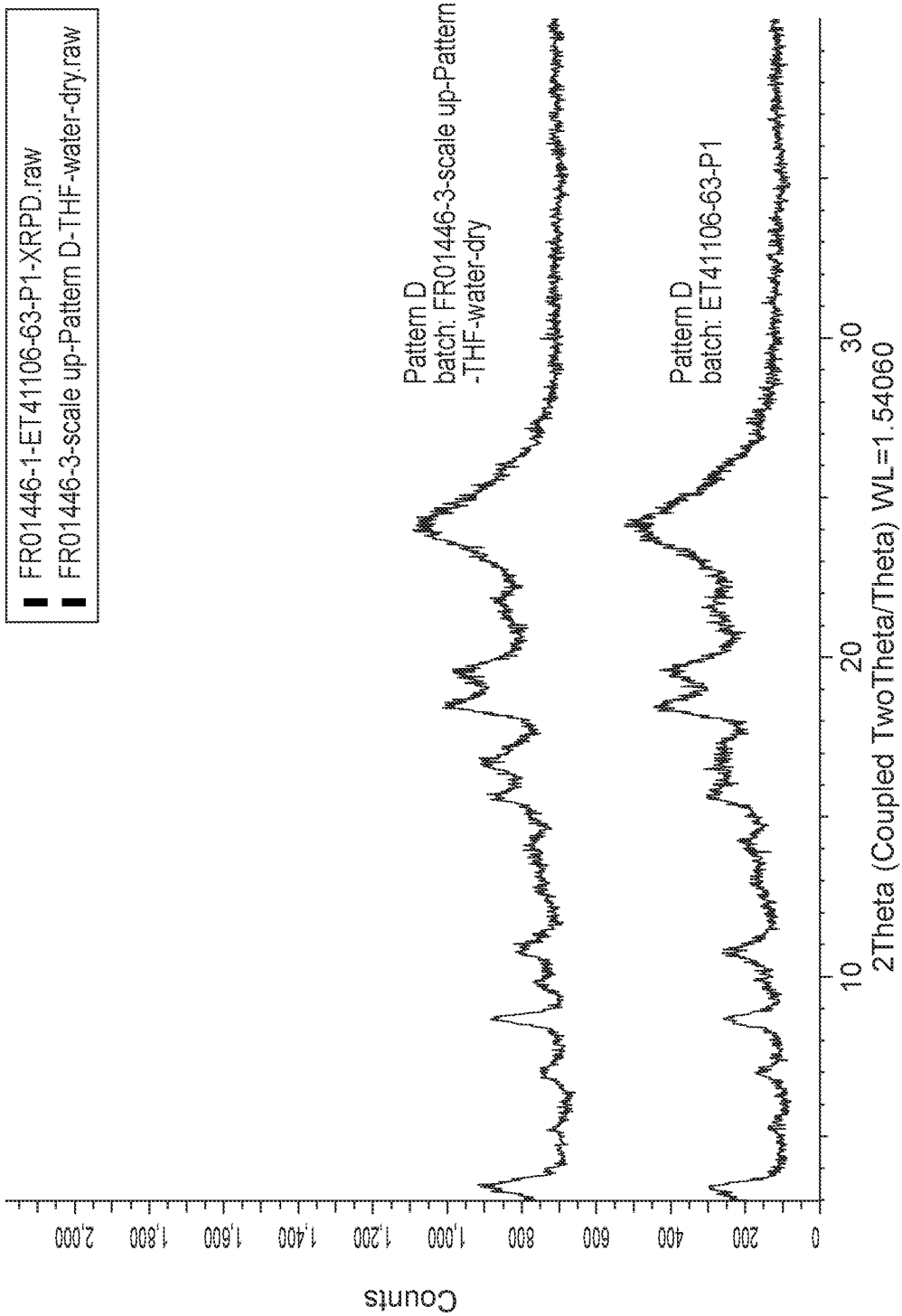


Fig. 18 XRPD Pattern of Pattern D, Sample ID FR01446-3-scale up-Pattern D-THF-water-dry



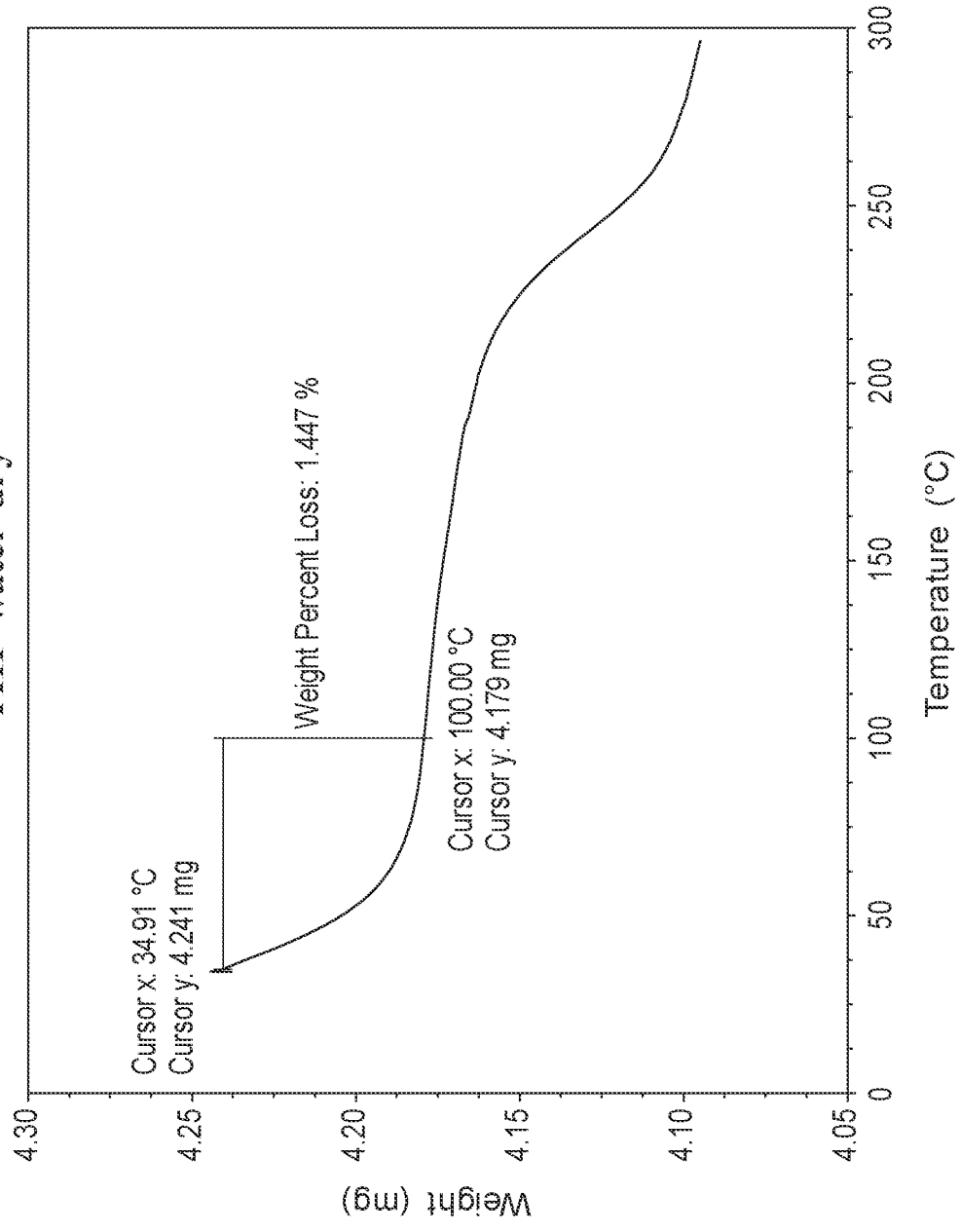


Fig. 19 TGA Thermogram of Pattern D, Sample ID FR01446-3-scale up-Pattern D-THF-water-dry

Fig. 20 DSC Thermogram of Pattern D, Sample ID FR01446-3-scale up-Pattern D-THF-water-dry

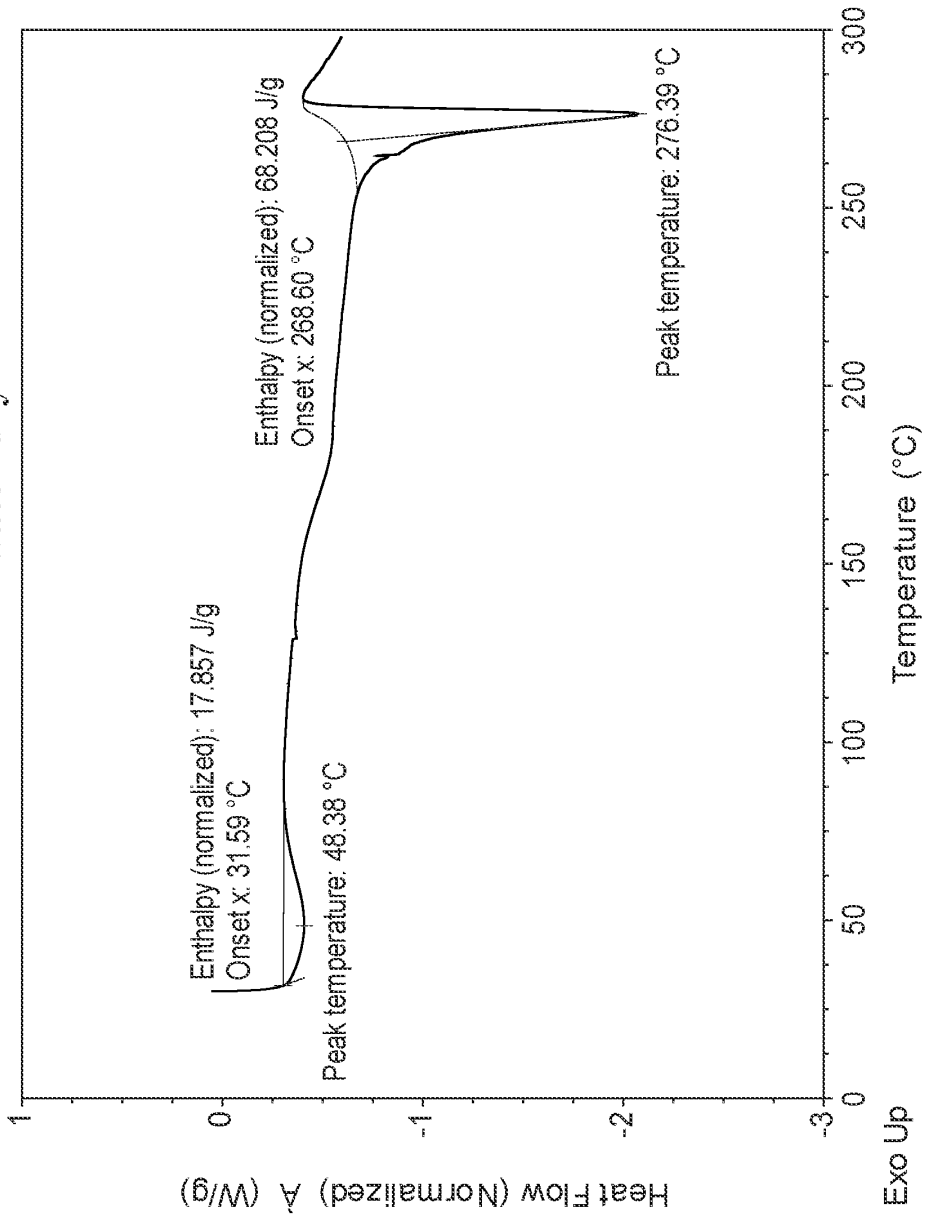


Fig. 21

^{1}H NMR Spectrum of Pattern D, Sample ID FR01446-3-scale up-Pattern D-THF-water-dry

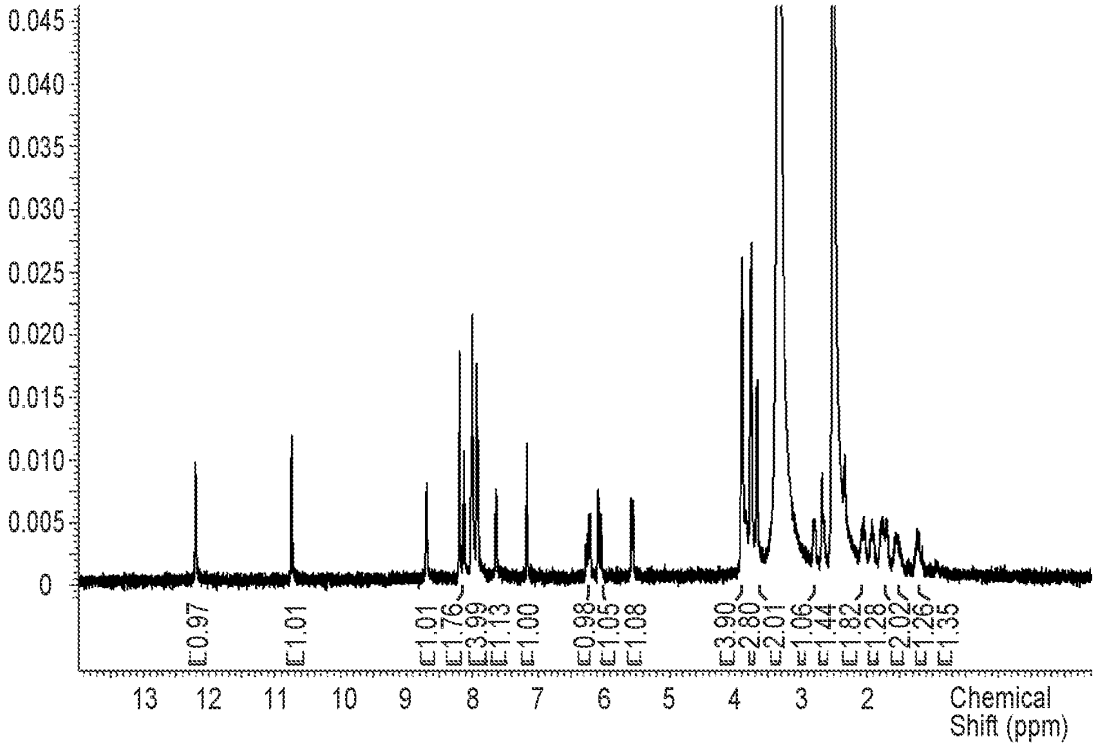
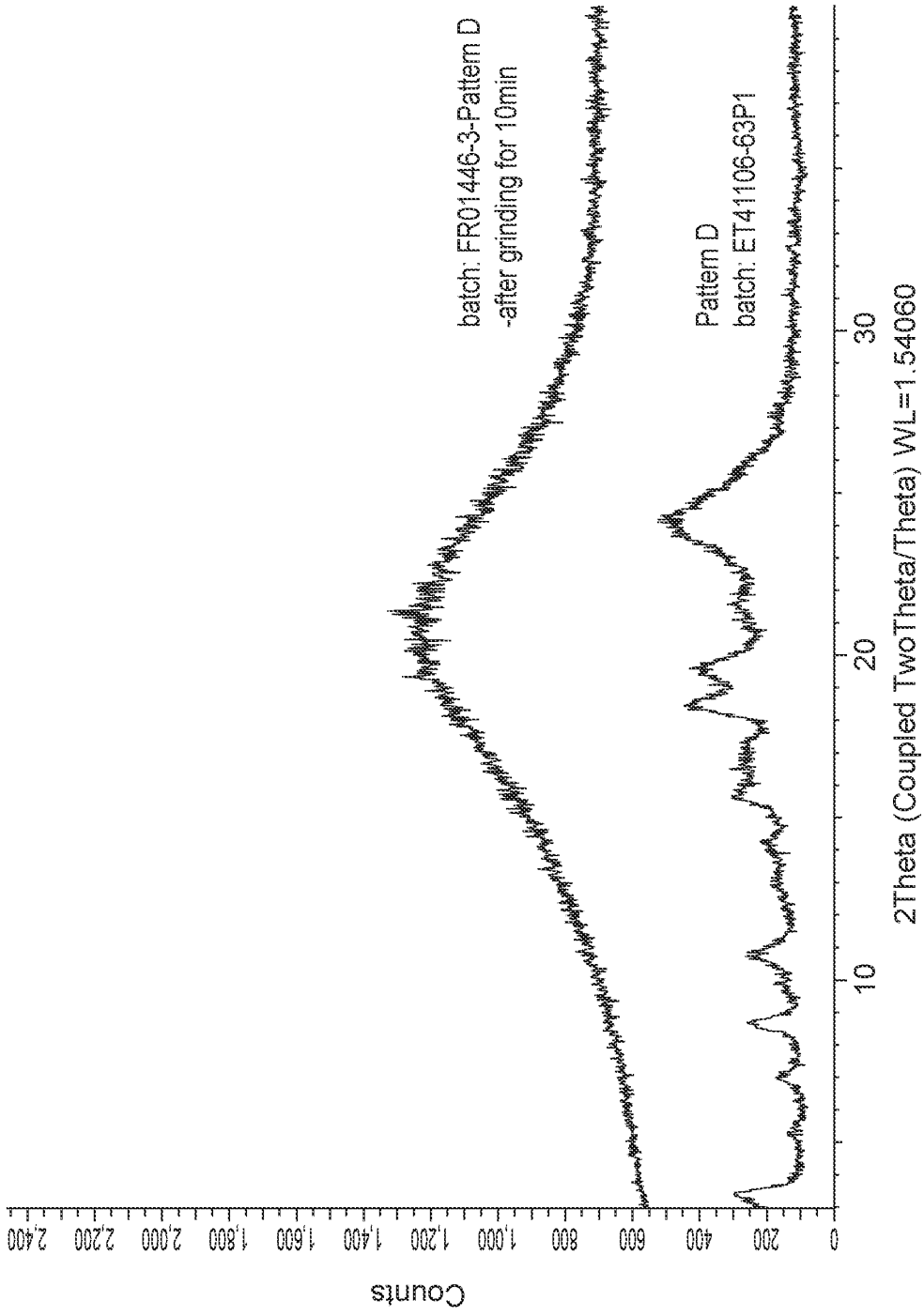


Fig. 22 XRPD Overlay of Pattern D (50 mg) After Grinding Simulation Experiment for 10 min



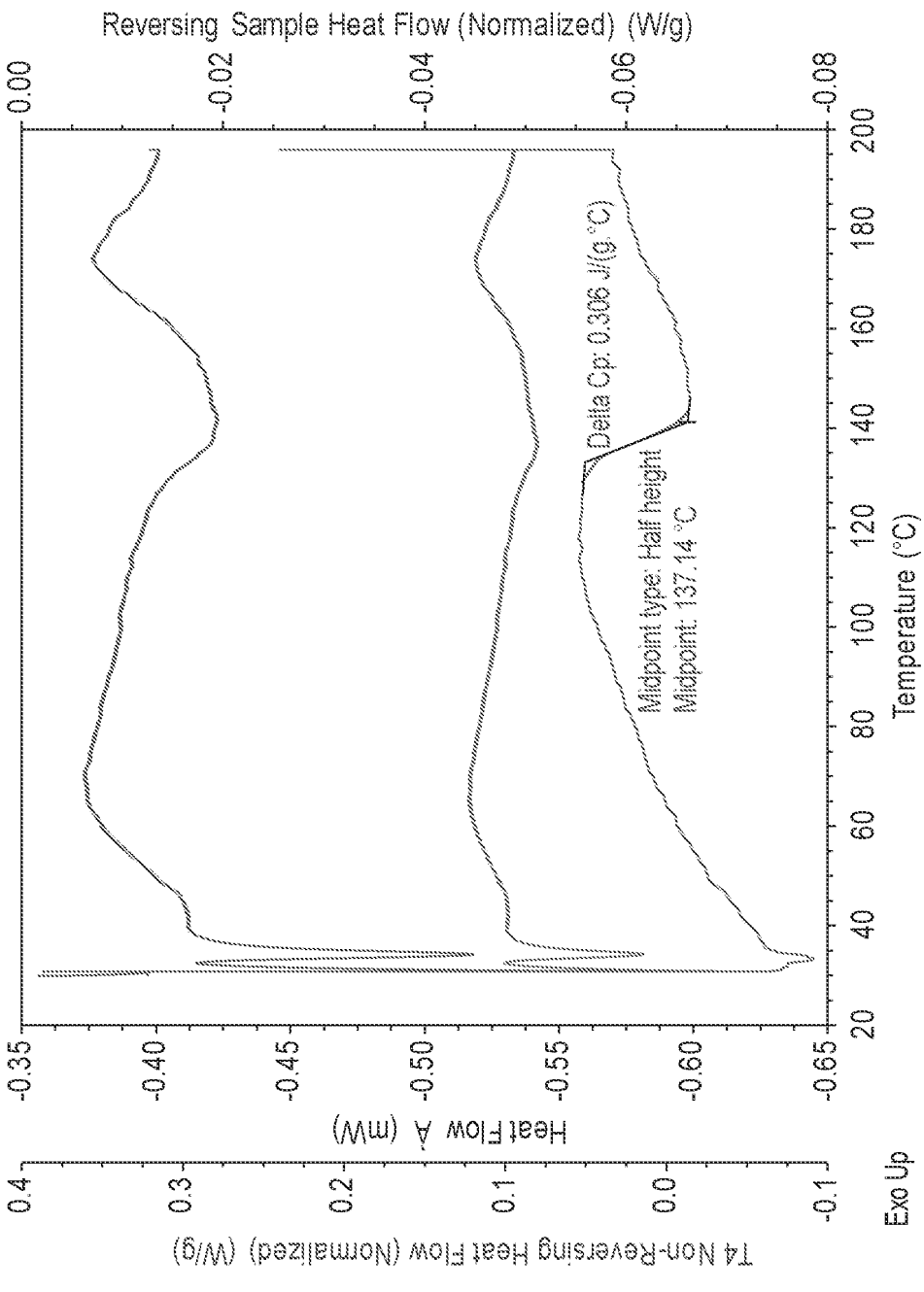
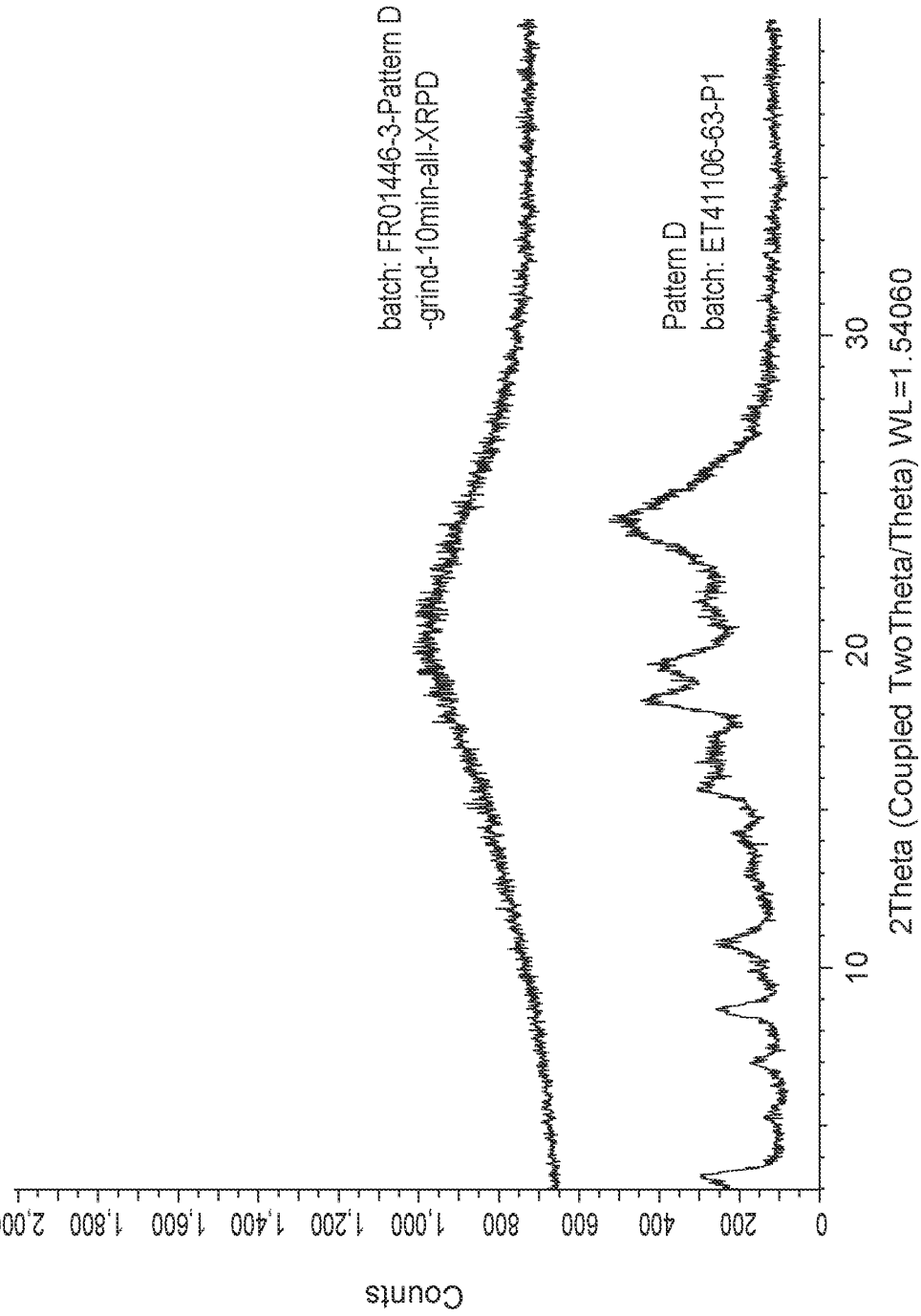


Fig. 23 mDSC Thermogram of Pattern D (50 mg) After Grinding Simulation Experiment for 10 min

Fig. 24 XRPD Overlay of Pattern D (600 mg) After Grinding Simulation Experiment for 10 min



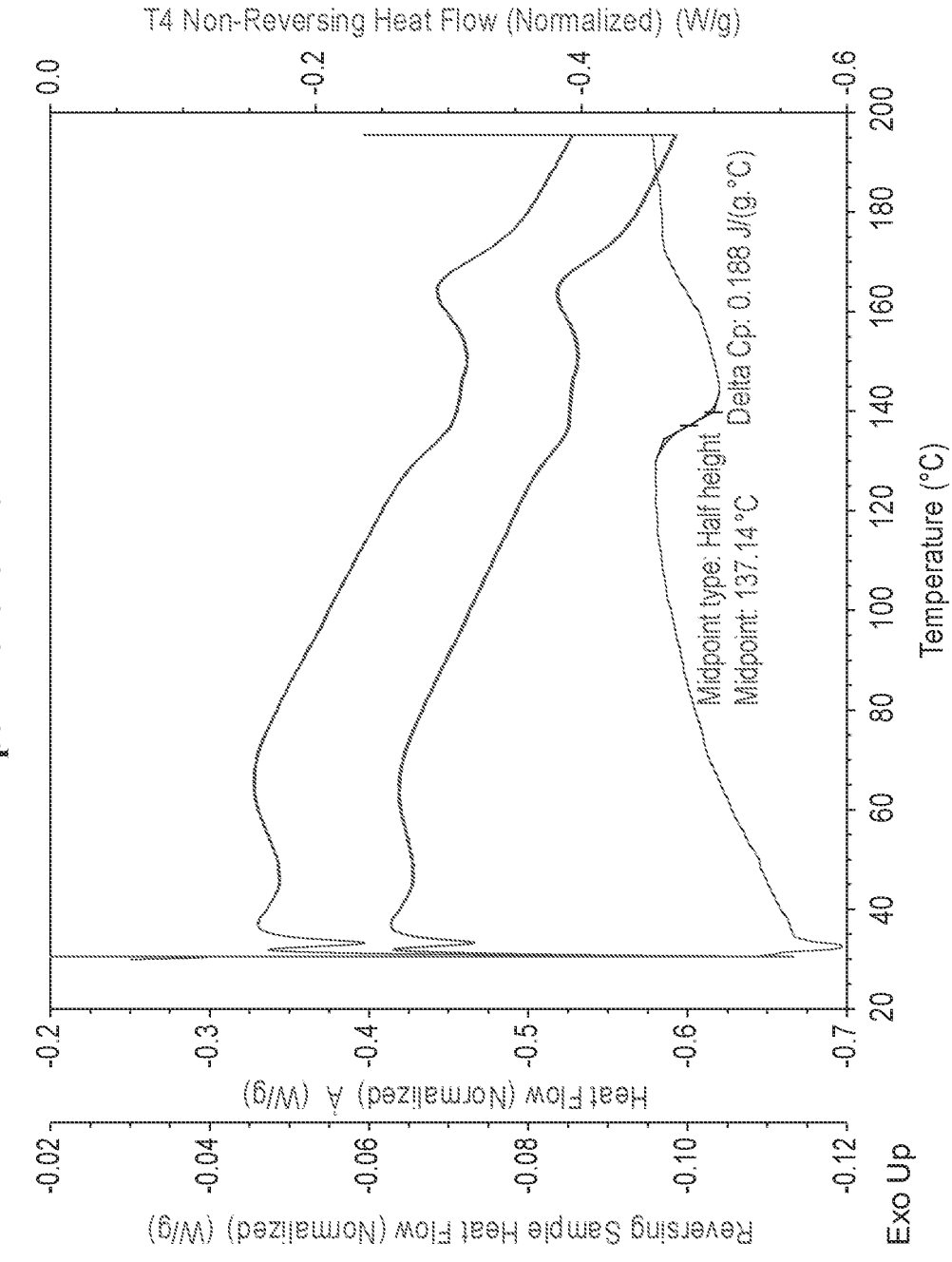


Fig. 25 mDSC Thermogram of Pattern D (600 mg) After Grinding Simulation Experiment for 10 min

Fig. 26 XRPD Overlay of Pattern D (2 g) After Grinding Simulation Experiment for 10 min

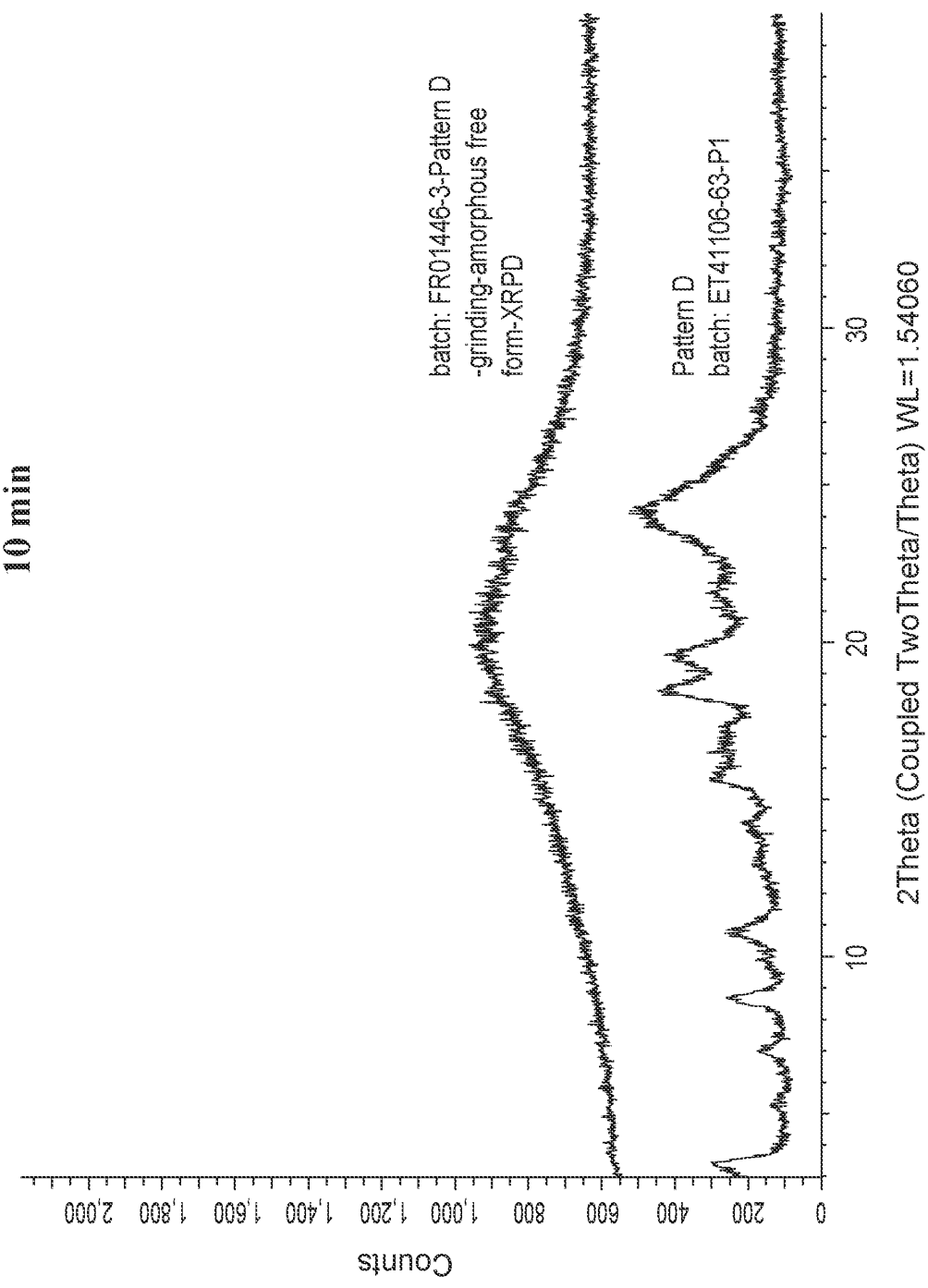


Fig. 27 mDSC Thermogram of Pattern D (2 g) After Grinding Simulation Experiment for 10 min

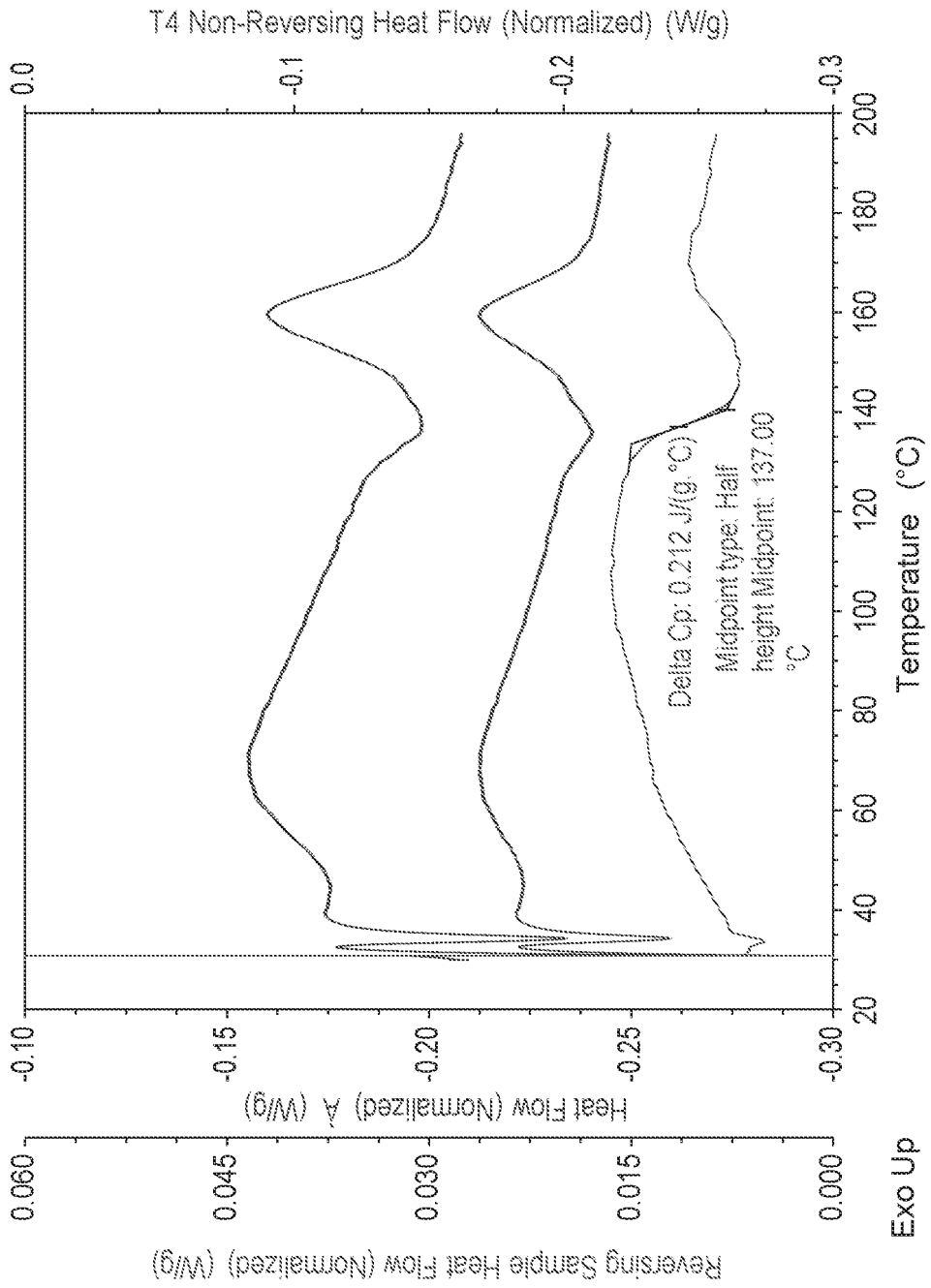


Fig. 28A

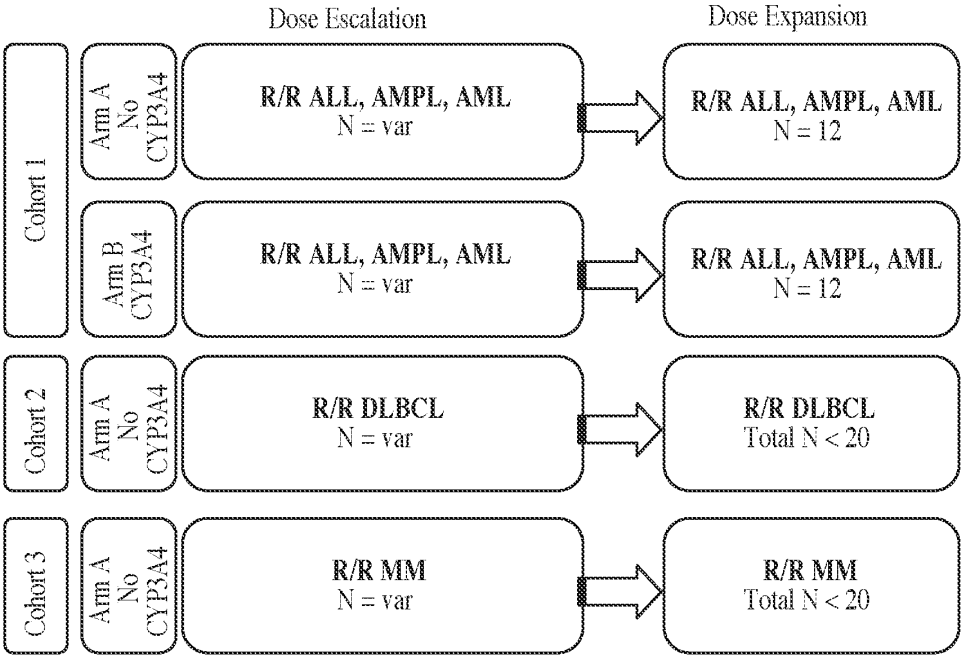

Dose Escalation
Dose Expansion
Cohort 1
Arm A No CYP3A4
R/R ALL, AMPL, AML
N = var
R/R ALL, AMPL, AML
N = 12
Arm B CYP3A4
R/R ALL, AMPL, AML
N = var
R/R ALL, AMPL, AML
N = 12
Cohort 2
Arm A No CYP3A4
R/R DLBCL
N = var
R/R DLBCL
Total N < 20
Cohort 3
Arm A No CYP3A4
R/R MM
N = var
R/R MM
Total N < 20

Fig. 28B

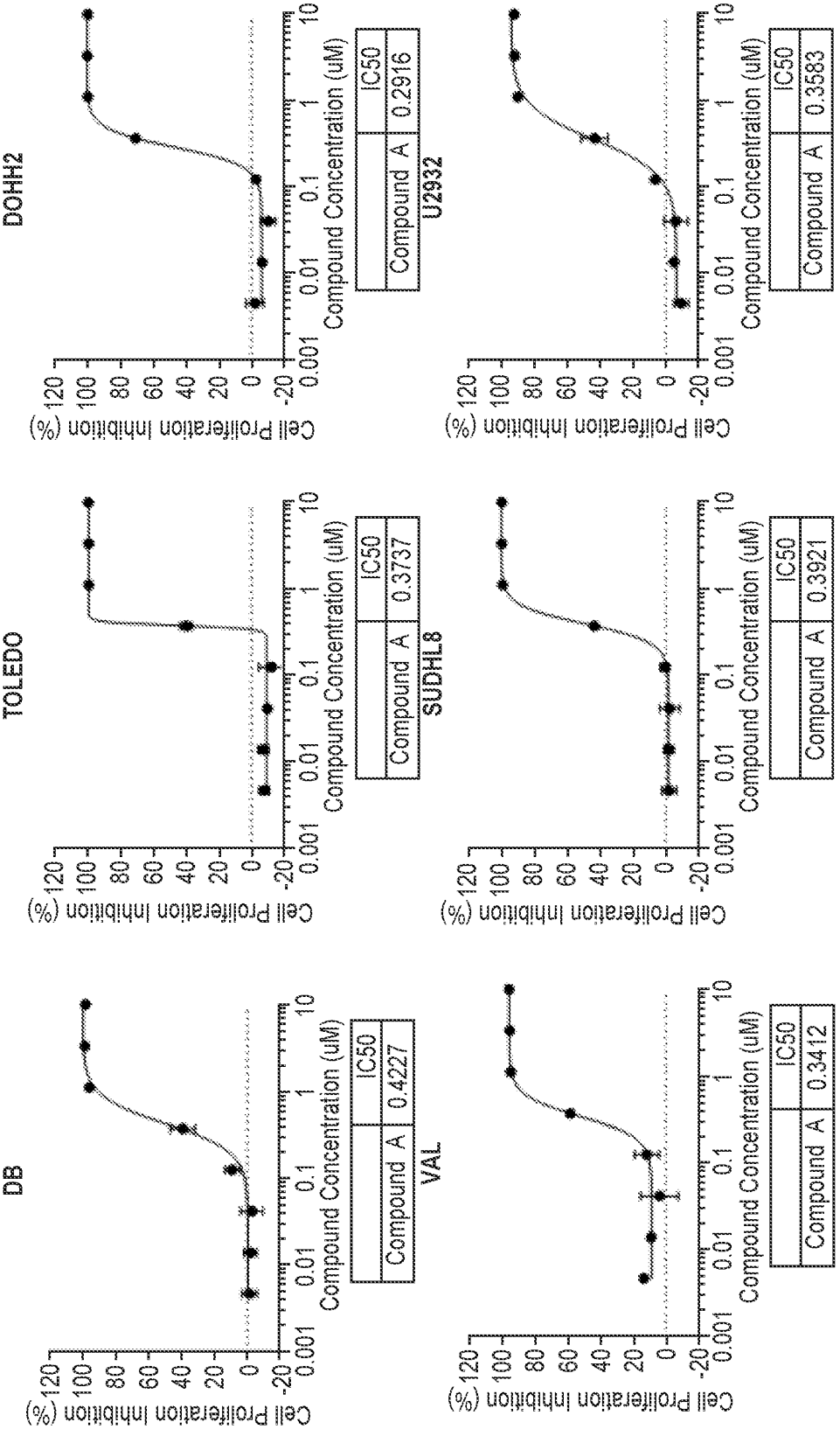
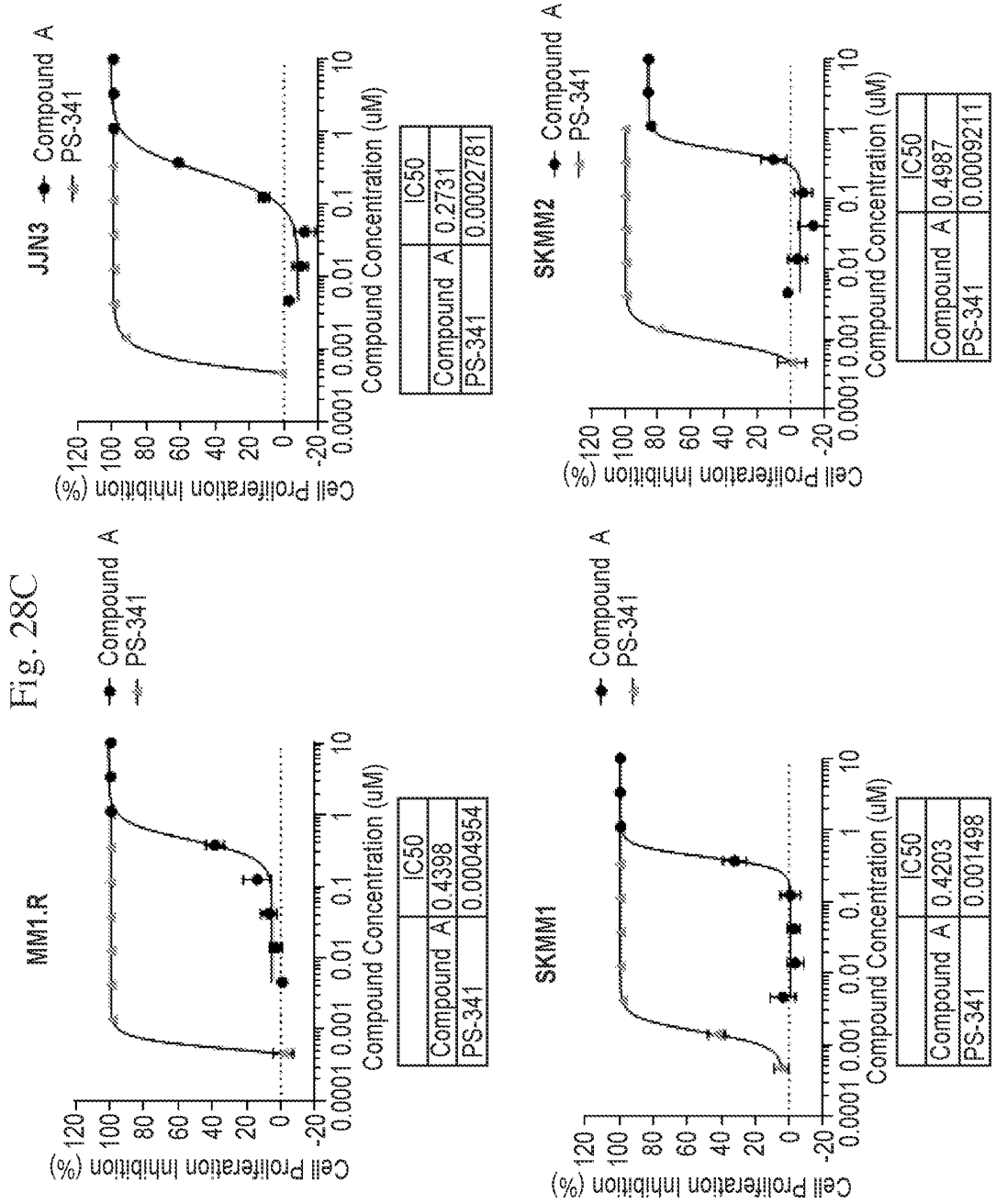

DB
Cell Proliferation Inhibition (%)
Compound Concentration (uM)
Compound A
IC50
0.4227
VAL
TOLEDO
Cell Proliferation Inhibition (%)
Compound Concentration (uM)
Compound A
IC50
0.3737
SUDHL8
DOHH2
Cell Proliferation Inhibition (%)
Compound Concentration (uM)
Compound A
IC50
0.2916
U2932
Cell Proliferation Inhibition (%)
Compound Concentration (uM)
Compound A
IC50
0.3412
Cell Proliferation Inhibition (%)
Compound Concentration (uM)
Compound A
IC50
0.3921
Cell Proliferation Inhibition (%)
Compound Concentration (uM)
Compound A
IC50
0.3583

Fig. 28C


JJN3
Compound A
PS-341
Cell Proliferation Inhibition (%)
Compound Concentration (uM)
IC50
Compound A 0.2731
PS-341 0.0002781
SKMM2
Compound A
PS-341
Cell Proliferation Inhibition (%)
Compound Concentration (uM)
IC50
Compound A 0.4987
PS-341 0.0009211
MM1.R
Compound A
PS-341
Cell Proliferation Inhibition (%)
Compound Concentration (uM)
IC50
Compound A 0.4398
PS-341 0.0004954
SKMM1
Compound A
PS-341
Cell Proliferation Inhibition (%)
Compound Concentration (uM)
IC50
Compound A 0.4203
PS-341 0.001498

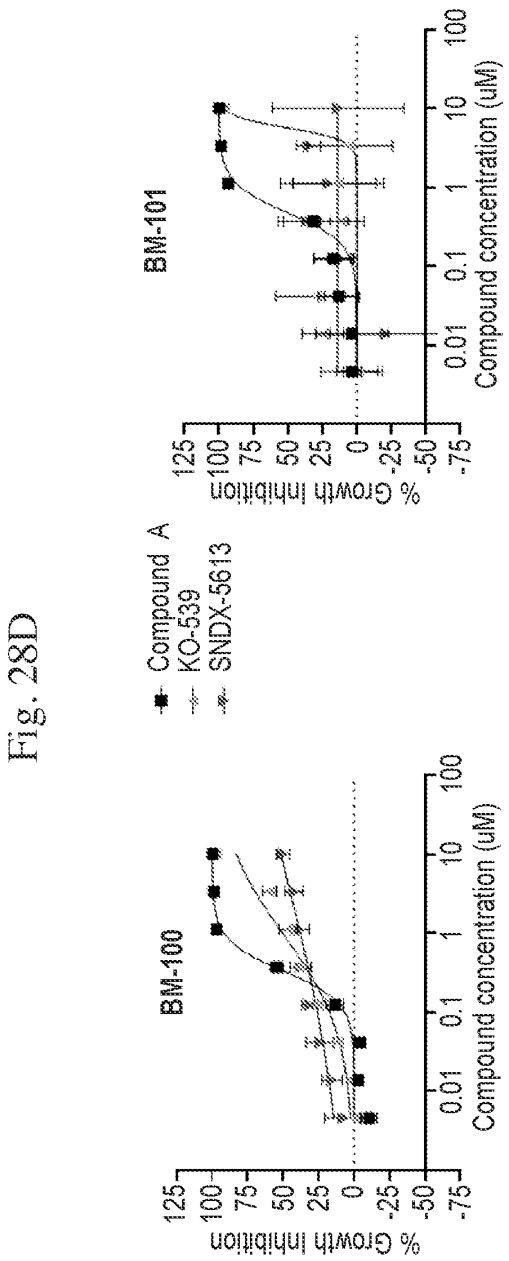

BM-100
BM-101
Compound A
KO-539
SNDX-5613
% Growth Inhibition
Compound concentration (uM)
125
100
75
50
25
0
-25
-50
-75
0.01
0.1
1
10
100

Fig. 28D

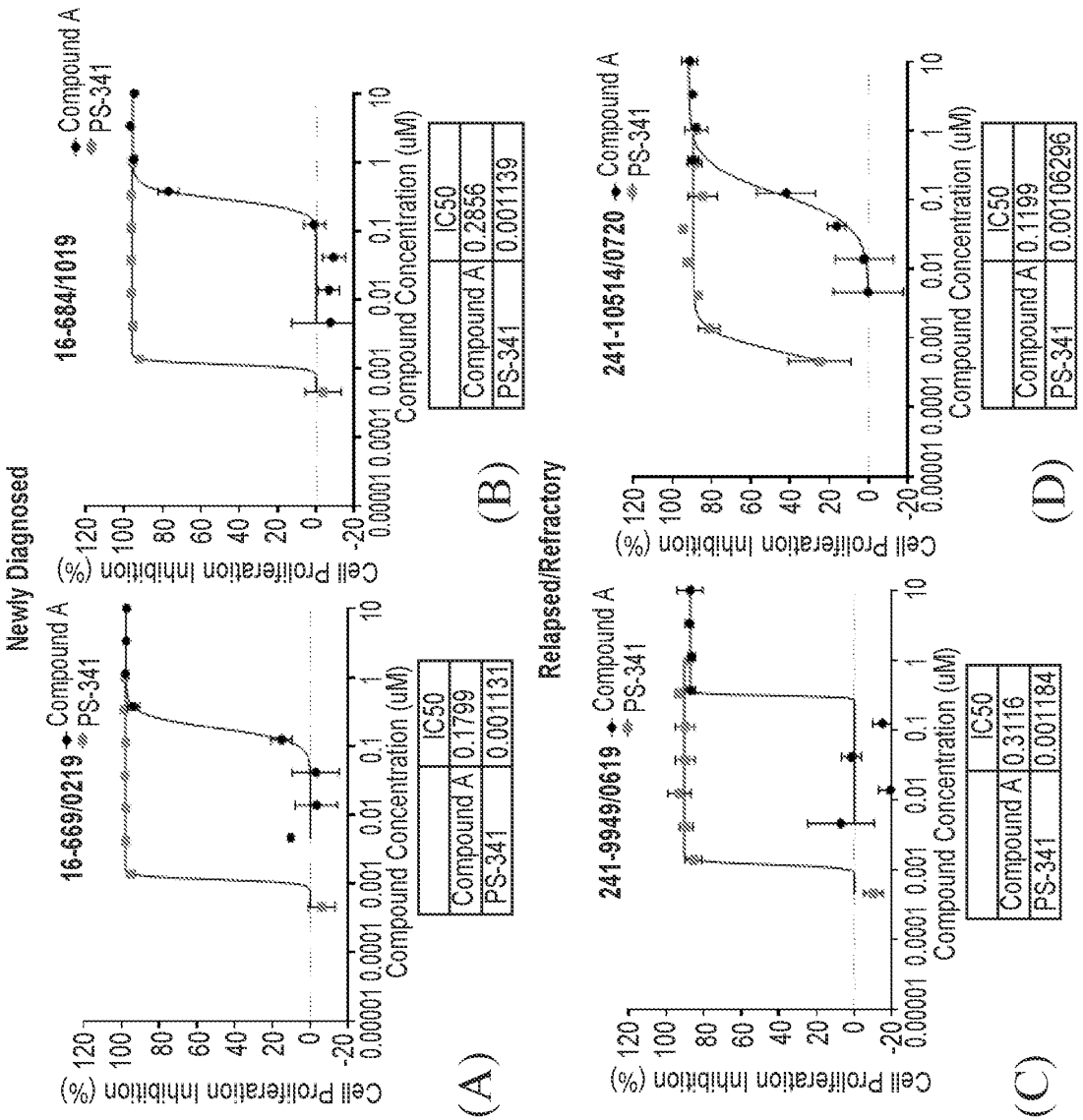

Newly Diagnosed
Relapsed/Refractory
16-669/0219
Compound A
PS-341
Cell Proliferation Inhibition (%)
Compound Concentration (uM)
IC50
Compound A 0.1799
PS-341 0.001131
(A)
16-684/1019
Compound A
PS-341
Cell Proliferation Inhibition (%)
Compound Concentration (uM)
IC50
Compound A 0.2856
PS-341 0.001139
(B)
241-9949/0619
Compound A
PS-341
Cell Proliferation Inhibition (%)
Compound Concentration (uM)
IC50
Compound A 0.3116
PS-341 0.001184
(C)
241-10514/0720
Compound A
PS-341
Cell Proliferation Inhibition (%)
Compound Concentration (uM)
IC50
Compound A 0.1199
PS-341 0.00106296
(D)

Fig. 28E

Fig. 28F

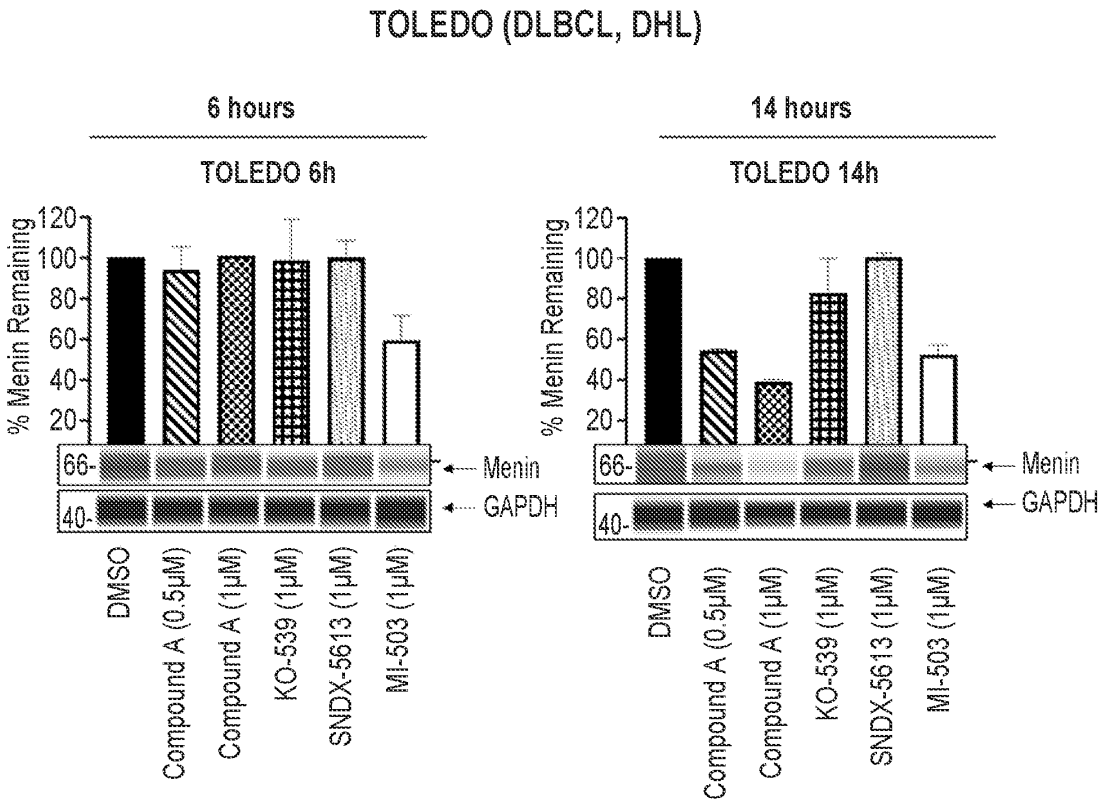

TOLEDO (DLBCL, DHL)
6 hours
14 hours
TOLEDO 6h
TOLEDO 14h
% Menin Remaining
120
100
80
60
40
20
66-
40-
Menin
GAPDH
DMSO
Compound A (0.5μM)
Compound A (1μM)
KO-539 (1μM)
SNDX-5613 (1μM)
MI-503 (1μM)

Fig. 29

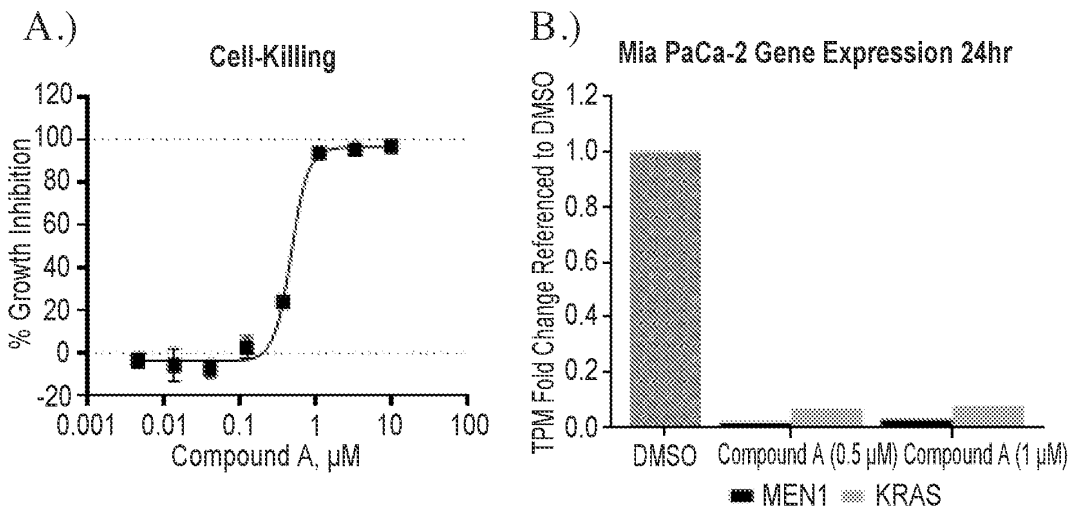

A.)
Cell-Killing
% Growth Inhibition
120
100
80
60
40
20
0
-20
0.001
0.01
0.1
1
10
100
Compound A, µM
B.)
Mia PaCa-2 Gene Expression 24hr
TPM Fold Change Referenced to DMSO
1.2
1.0
0.8
0.6
0.4
0.2
0.0
DMSO
Compound A (0.5 µM)
Compound A (1 µM)
MEN1
KRAS

Fig. 29

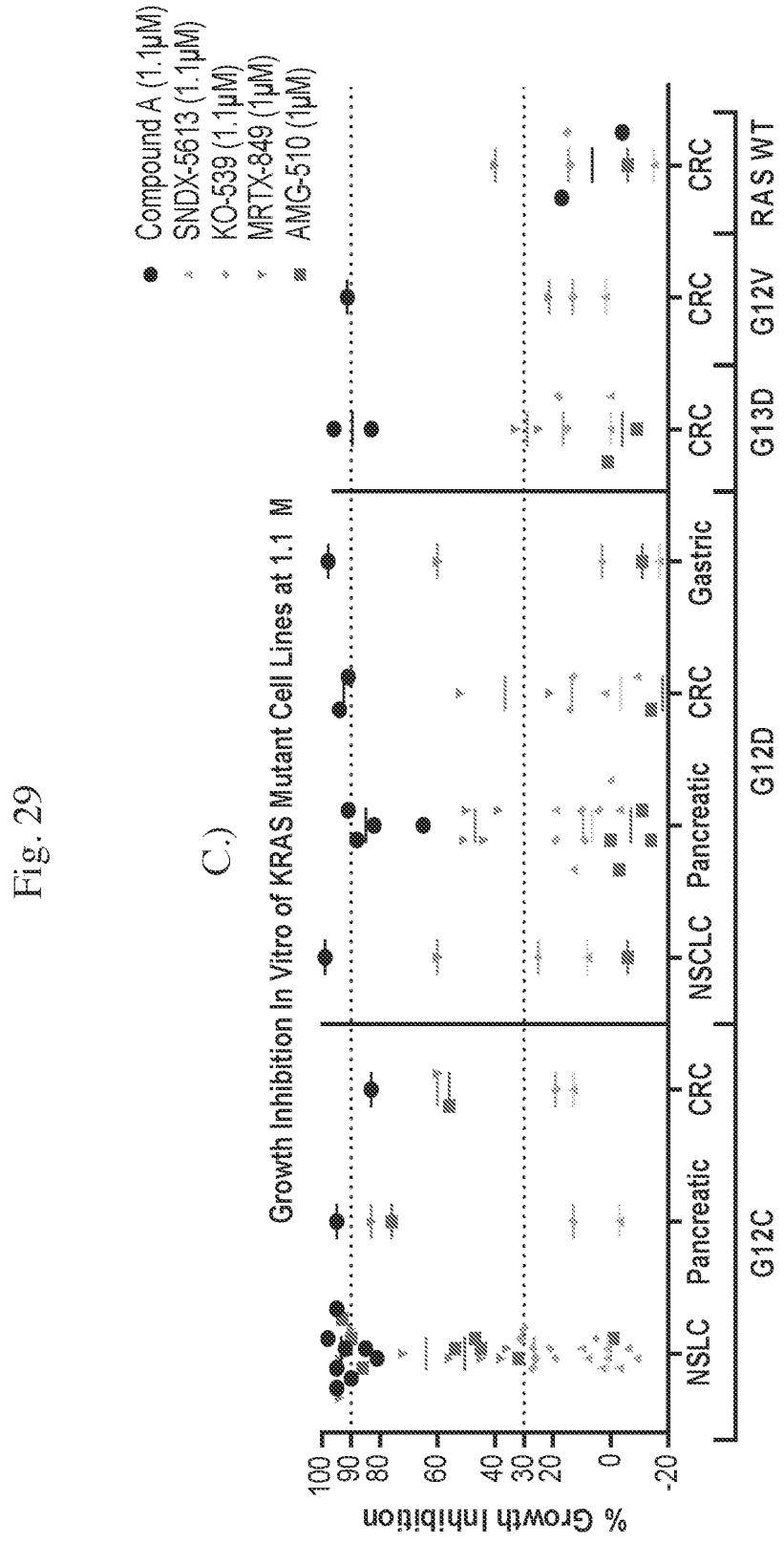

C.)
Growth Inhibition In Vitro of KRAS Mutant Cell Lines at 1.1 M
Compound A (1.1µM)
SNDX-5613 (1.1µM)
KO-539 (1.1µM)
MRTX-849 (1µM)
AMG-510 (1µM)
% Growth Inhibition
100
90
80
60
40
30
20
0
-20
NSLC
Pancreatic
CRC
NSCLC
Pancreatic
CRC
Gastric
CRC
CRC
CRC
G12C
G12D
G13D
G12V
RAS WT

Fig. 30A

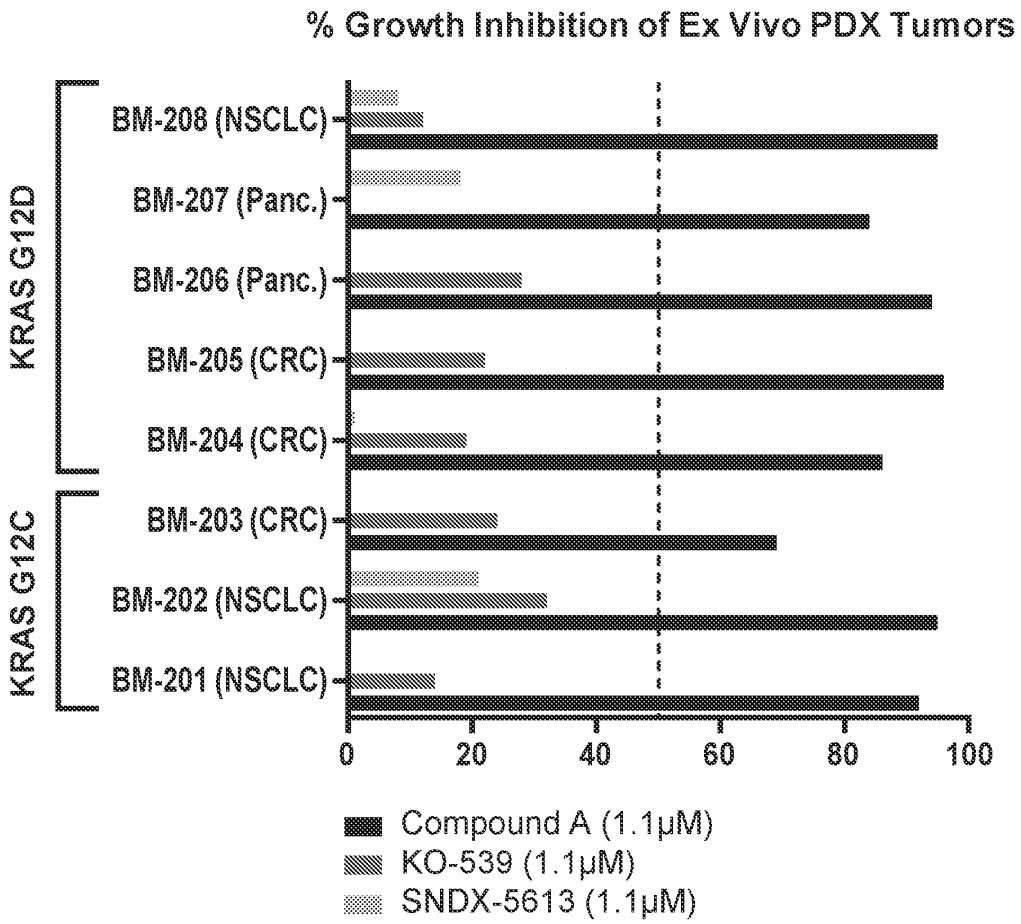

% Growth Inhibition of Ex Vivo PDX Tumors
KRAS G12D
KRAS G12C
BM-208 (NSCLC)
BM-207 (Panc.)
BM-206 (Panc.)
BM-205 (CRC)
BM-204 (CRC)
BM-203 (CRC)
BM-202 (NSCLC)
BM-201 (NSCLC)
0
20
40
60
80
100
Compound A (1.1μM)
KO-539 (1.1μM)
SNDX-5613 (1.1μM)

Fig. 30B

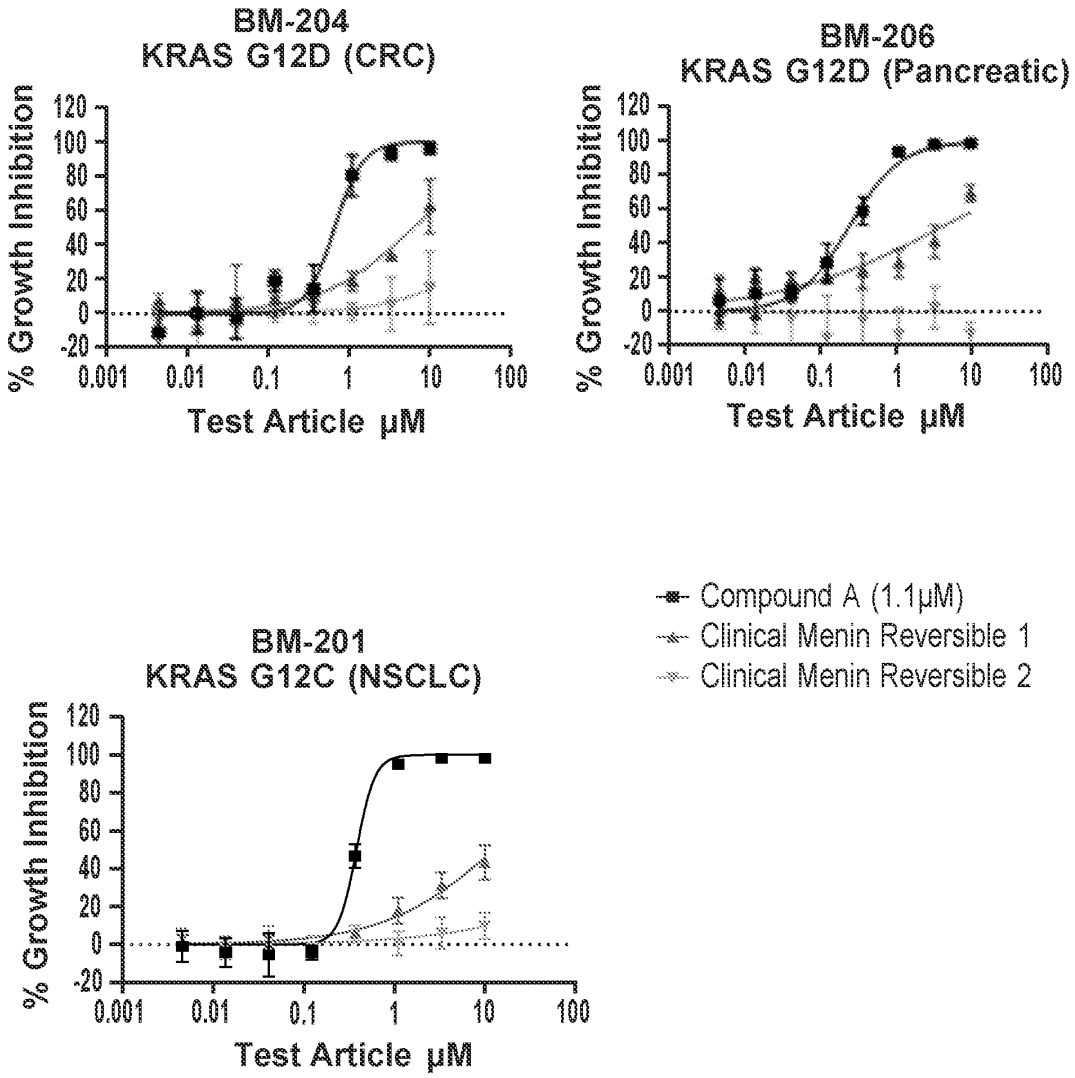

BM-204
KRAS G12D (CRC)
% Growth Inhibition
120
100
80
60
40
20
0
-20
0.001
0.01
0.1
1
10
100
Test Article µM
BM-206
KRAS G12D (Pancreatic)
% Growth Inhibition
Test Article µM
BM-201
KRAS G12C (NSCLC)
% Growth Inhibition
Test Article µM
Compound A (1.1µM)
Clinical Menin Reversible 1
Clinical Menin Reversible 2

Fig. 31
Relative Gene Expression - Compound A

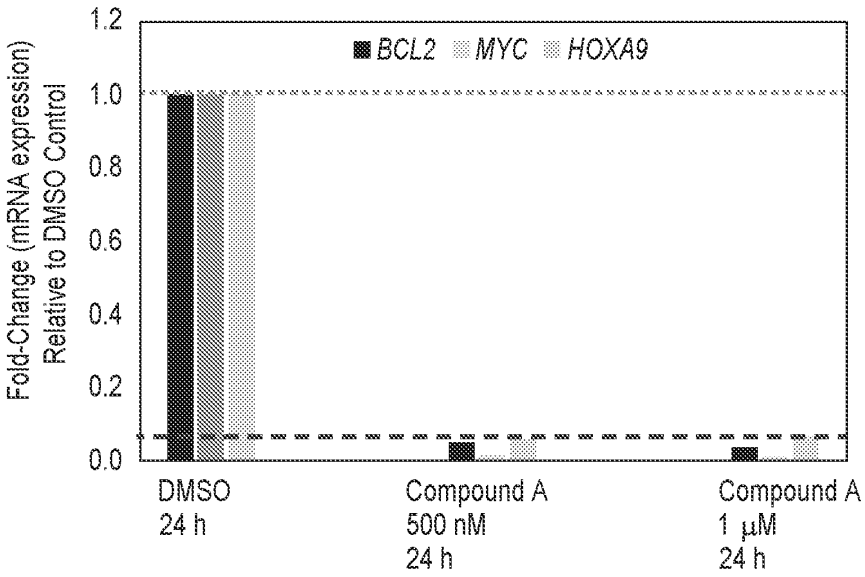


Fig. 32A and 32B

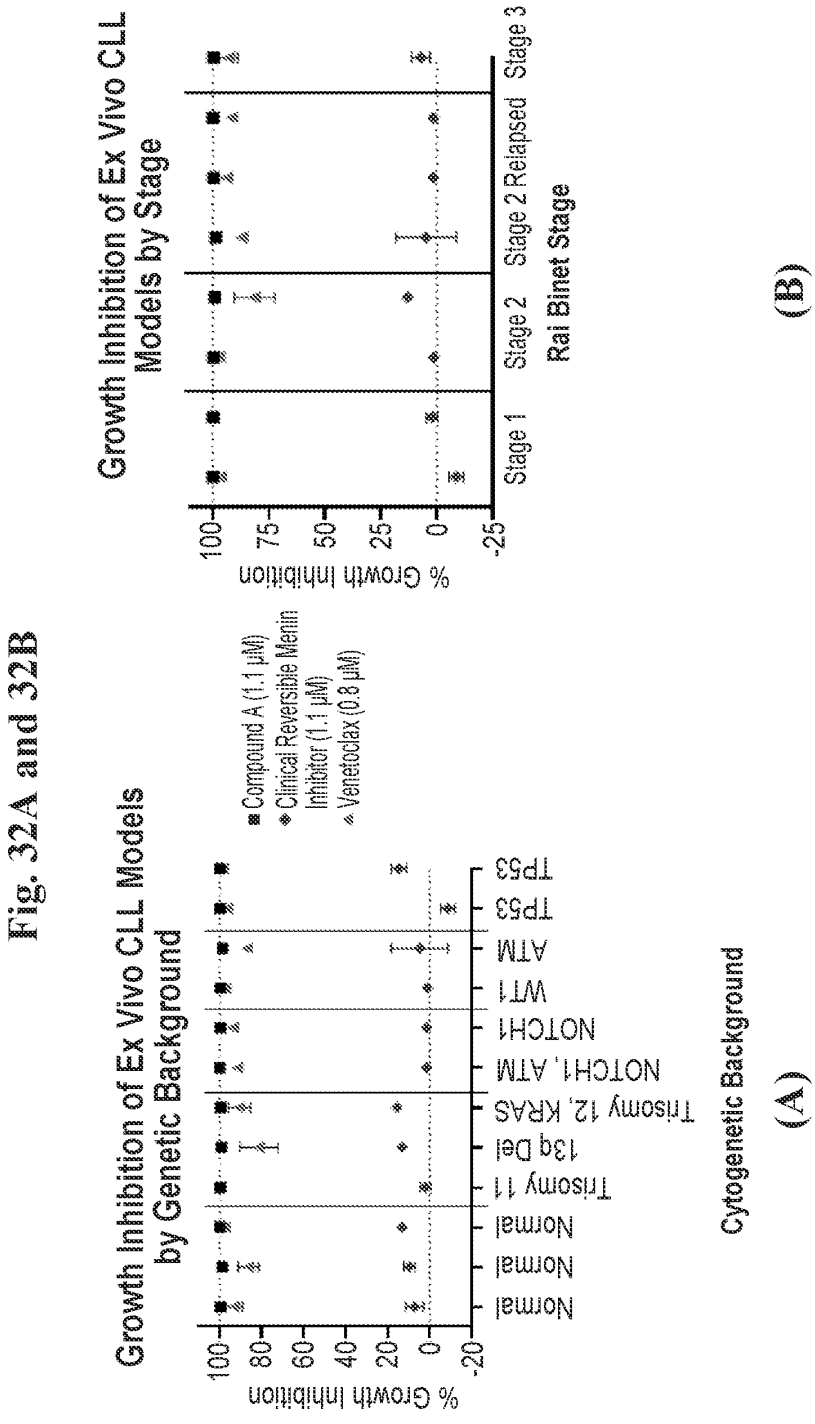


Fig. 32C, 32D, and 32E

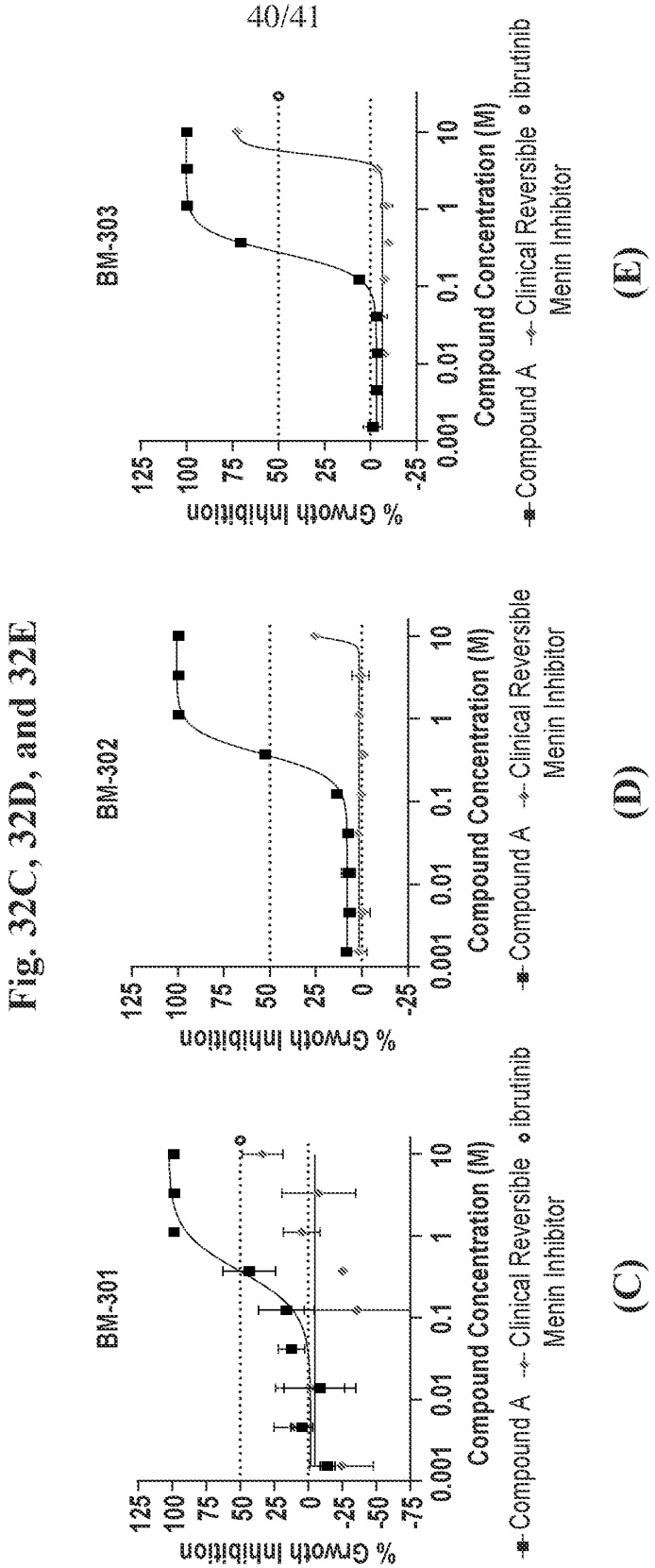
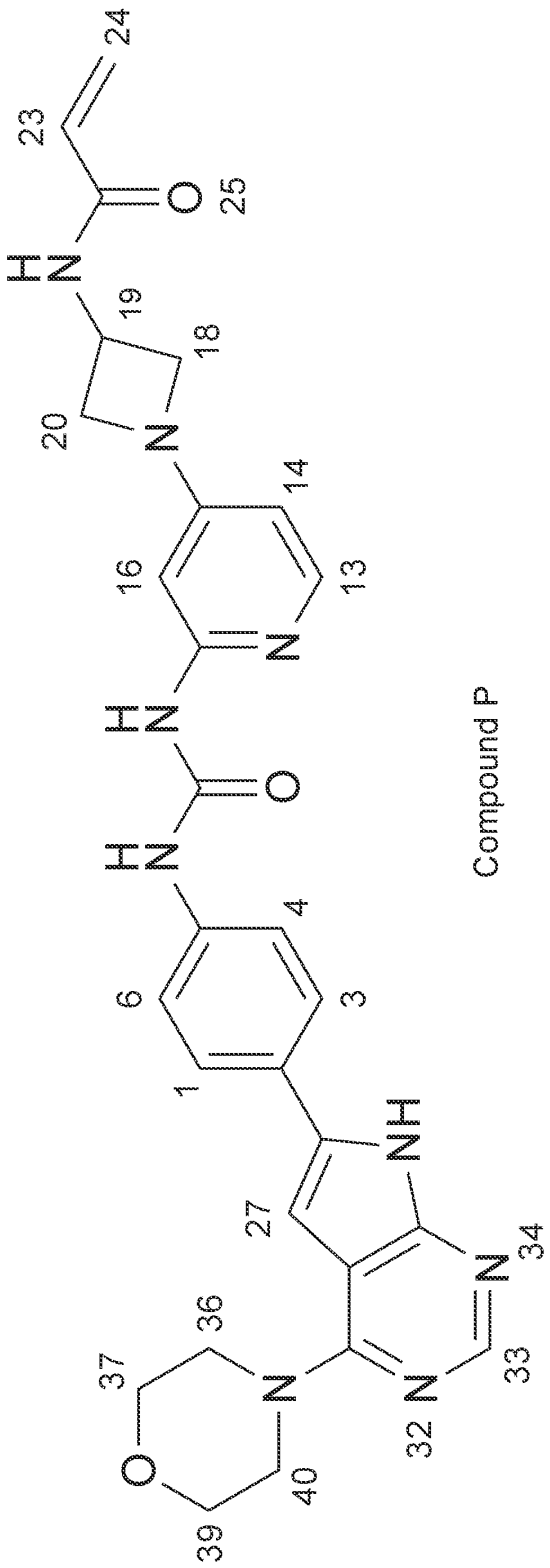


Fig. 33



Compound P