CLAIMS

What is Claimed is:

1. Form HCl:SA-1 of crystalline (S,E)-4-(2-(3-(3-chloro-2-fluoro-6-(1H-tetrazol-1-yl)phenyl)acryloyl)-5-(4-methyl-2-oxopiperazin-1-yl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamido)benzoic acid, which is characterized by a powder X-ray diffraction pattern substantially in accordance with that shown in Figure 1.

2. Form HCl:SA-1 according to Claim 1 having a powder X-ray diffraction pattern comprising four or more 2θ values (CuKα λ= 1.5418 Å): 6.0, 8.3, 8.7, 12.3, 16.2, 16.7, 17.5, 19.9, and 20.4.

3. Form HCl:SA-1 of crystalline (S,E)-4-(2-(3-(3-chloro-2-fluoro-6-(1H-tetrazol-1-yl)phenyl)acryloyl)-5-(4-methyl-2-oxopiperazin-1-yl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamido)benzoic acid, which is characterized by unit cell parameters substantially equal to the following:

Cell dimensions:

a = 8.3746(2) Å

b= 20.2236(5) Å

c = 21.3099(6) Å

α = 90°

β = 90°

γ = 90°

Space group: P2(1)2(1)2(1)

Molecules/asymmetric unit: 1

wherein measurement of the crystalline form is at a temperature of about 23 ºC.

4. Form HCl:SA-1 according to Claim 3, which is characterized by fractional atomic coordinates substantially as listed in Table 2:

Table 2

Atomic Coordinates (x 10^4) and Equivalent Isotropic Displacement Parameters ($Å^2$x 10^3) for Compound (I) HCl:SA-1

	x	y	z	U(eq)*
Cl(2)	4183(3)	7590(1)	7388(1)	73(1)
C(1)	5350(8)	5357(3)	-5(3)	58(2)
C(2)	5189(9)	5113(3)	606(3)	62(2)
C(3)	6122(9)	4563(3)	743(3)	62(2)
C(4)	7131(8)	4259(3)	322(4)	63(2)
C(5)	7186(9)	4508(4)	-278(4)	71(2)
C(6)	6312(9)	5055(4)	-435(3)	72(2)
C(7)	3624(12)	6026(4)	-680(4)	87(2)
C(8)	4120(11)	5408(4)	1083(3)	76(2)
C(9)	3311(10)	5137(4)	1500(4)	78(2)
C(10)	2308(8)	5511(3)	1938(3)	57(2)
C(11)	481(11)	4538(3)	1991(4)	79(2)
C(12)	-331(9)	4186(3)	2541(4)	71(2)
C(13)	-1725(8)	4599(3)	2754(3)	56(2)
C(14)	-1568(8)	5294(3)	2755(3)	51(2)
C(15)	41(8)	5604(3)	2612(3)	50(2)
C(16)	-3161(9)	4326(3)	2946(3)	59(2)
C(17)	-4444(9)	4719(4)	3106(3)	69(2)
C(18)	-4286(9)	5400(4)	3088(4)	70(2)
C(19)	-2842(8)	5689(3)	2911(3)	60(2)
C(20)	938(8)	5679(3)	3244(3)	54(2)
C(21)	971(8)	6440(3)	4151(3)	53(2)
C(22)	2064(8)	6122(3)	4526(3)	61(2)
C(23)	2282(8)	6336(4)	5147(3)	62(2)
C(24)	1416(8)	6856(3)	5378(3)	54(2)
C(25)	315(9)	7169(3)	4999(3)	64(2)
C(26)	103(9)	6969(3)	4387(3)	62(2)
C(27)	1629(9)	7122(4)	6032(3)	67(2)
C(28)	-4232(14)	3275(4)	2493(4)	101(3)
C(29)	-3869(13)	2532(4)	2464(4)	96(3)

	x	y	z	U(eq)*
C(30)	-2699(9)	2550(3)	3483(3)	66(2)
C(31)	-2625(9)	3285(3)	3458(3)	60(2)
C(32)	-5588(10)	2286(4)	3384(5)	102(3)
Cl(1)	8255(3)	3595(1)	563(1)	95(1)
F(1)	6062(6)	4310(2)	1340(2)	93(1)
N(1)	4510(8)	5920(3)	-180(3)	71(2)
N(2)	4579(11)	6492(3)	148(3)	96(2)
N(3)	3701(14)	6911(4)	-149(5)	123(3)
N(4)	3089(12)	6638(4)	-679(4)	116(3)
N(5)	1037(7)	5207(2)	2179(2)	58(1)
N(6)	645(7)	6263(2)	3524(2)	58(1)
N(7)	-3312(7)	3606(2)	2977(3)	60(1)
N(8)	-3972(7)	2250(3)	3097(3)	68(2)
O(1)	2620(6)	6081(2)	2096(2)	70(1)
O(2)	1744(6)	5235(2)	3465(2)	63(1)
O(3)	971(7)	7602(3)	6233(2)	91(2)
O(4)	2705(7)	6777(2)	6357(2)	81(2)
O(5)	-1867(7)	3575(2)	3864(3)	80(2)
O(1S)	8222(7)	5981(2)	1227(2)	70(1)
O(2S)	489(6)	5435(3)	69(3)	103(2)
O(3SB)	9450(30)	6486(13)	631(17)	126(8)
O(3SA)	9170(30)	6463(11)	1022(13)	136(7)
O(3SC)	9560(30)	6237(13)	140(14)	137(8)

* U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

5. Form HCl:SA-1 of crystalline (S,E)-4-(2-(3-(3-chloro-2-fluoro-6-(1H-tetrazol-1-yl)phenyl)acryloyl)-5-(4-methyl-2-oxopiperazin-1-yl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamido)benzoic acid, which is characterized by unit cell parameters substantially as listed in Table 4:

Table 4

Cell Parameters for Single Crystal (Input) and Hybrid (Refined) for Form HCl: SA-1

Cell Parameter	Input	Refined
a (Å)	8.3746	8.2562
b(Å)	20.2236	20.2918
c(Å)	21.3099	21.2423
α°	90	90
β°	90	90
γ°	90	90
Volume ($Å^3$)	3609.14	3558.77

6. Form H.5-1 of crystalline (S,E)-4-(2-(3-(3-chloro-2-fluoro-6-(1H-tetrazol-1-yl)phenyl)acryloyl)-5-(4-methyl-2-oxopiperazin-1-yl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamido)benzoic acid, which is characterized by a powder X-ray diffraction pattern substantially in accordance with that shown in Figure 2.

7. Form H.5-1 according to Claim 6 having a powder X-ray diffraction pattern comprising four or more 2θ values (CuKα λ= 1.5418 Å): 5.9, 7.2, 12.0, 15.7, 17.2, 18.9, 20.3, 24.2, and 26.1.

8. Form H.5-1 of crystalline (S,E)-4-(2-(3-(3-chloro-2-fluoro-6-(1H-tetrazol-1-yl)phenyl)acryloyl)-5-(4-methyl-2-oxopiperazin-1-yl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamido)benzoic acid, which is characterized by unit cell parameters substantially equal to the following:

Cell dimensions:

a = 13.6547(3) Å

b= 18.7590(3) Å

c = 24.7370(5) Å

α = 90°

β = 90°

γ = 90°

Space group: I2(1)2(1)2(1)

Molecules/asymmetric unit: 1

Density (calculated): 1.401 Mg/m^3

wherein measurement of the crystalline form is at a temperature of about 23 ºC.

9. Form H.5-1 according to Claim 8, which is characterized by fractional atomic coordinates substantially as listed in Table 1:

Table 1

Atomic Coordinates (x 10^4) and Equivalent Isotropic Displacement Parameters ($Å^2$x 10^3) for Compound (I) H.5-1

	x	y	z	U(eq)*
Cl(1)	1142(1)	8638(1)	1383(1)	89(1)
F(1)	1133(2)	7271(1)	862(1)	67(1)
O(1)	1102(2)	5533(1)	-724(1)	52(1)
O(2)	-779(1)	4373(1)	15(1)	48(1)
O(3)	-4534(2)	4606(1)	-1807(1)	62(1)
O(4)	-3952(2)	3964(2)	-2477(1)	109(1)
O(5)	3532(2)	3748(1)	1408(1)	63(1)
N(1)	1127(2)	8164(1)	-968(1)	56(1)
N(2)	1654(2)	7703(2)	-1270(1)	73(1)
N(3)	1416(3)	7825(2)	-1768(2)	91(1)
N(4)	759(3)	8363(2)	-1810(1)	97(1)
N(5)	1100(2)	5019(1)	102(1)	35(1)
N(6)	-311(2)	4095(1)	-837(1)	46(1)
N(7)	2057(2)	3304(1)	1616(1)	43(1)
N(8)	2218(2)	3810(1)	2664(1)	57(1)
C(1)	1203(2)	8493(2)	699(1)	57(1)
C(2)	1257(2)	9049(2)	342(2)	59(1)
C(3)	1267(2)	8920(2)	-203(2)	54(1)
C(4)	1218(2)	8232(2)	-398(1)	46(1)
C(5)	1210(2)	7639(1)	-54(1)	41(1)
C(6)	1193(2)	7804(2)	496(1)	49(1)
C(7)	593(3)	8565(2)	-1310(2)	81(1)

	x	y	z	U(eq)*
C(8)	1150(2)	6900(1)	-250(1)	42(1)
C(9)	1279(2)	6305(1)	22(1)	45(1)
C(10)	1151(2)	5598(1)	-230(1)	38(1)
C(11)	947(2)	4321(1)	-154(1)	33(1)
C(12)	1229(2)	3707(1)	214(1)	36(1)
C(13)	1543(2)	3812(1)	746(1)	35(1)
C(14)	1604(2)	4554(1)	977(1)	38(1)
C(15)	912(2)	5043(1)	686(1)	39(1)
C(16)	1171(2)	3021(1)	5(1)	50(1)
C(17)	1412(2)	2438(2)	321(1)	59(1)
C(18)	1711(2)	2537(2)	845(1)	55(1)
C(19)	1785(2)	3214(1)	1053(1)	41(1)
C(20)	-134(2)	4263(1)	-318(1)	35(1)
C(21)	-1221(2)	4098(2)	-1108(1)	42(1)
C(22)	-1223(3)	3919(2)	-1650(1)	76(1)
C(23)	-2072(3)	3948(2)	-1947(1)	78(1)
C(24)	-2943(2)	4163(2)	-1711(1)	47(1)
C(25)	-2940(2)	4313(1)	-1170(1)	40(1)
C(26)	-2096(2)	4271(1)	-864(1)	42(1)
C(27)	-3846(3)	4228(2)	-2041(1)	57(1)
C(28)	2912(2)	3605(2)	1747(1)	45(1)
C(29)	3099(2)	3770(2)	2335(1)	56(1)
C(30)	1304(2)	3112(2)	2016(1)	59(1)
C(31)	1666(3)	3151(2)	2584(1)	67(1)
C(32)	2477(4)	3923(2)	3236(1)	90(1)
O(1S)	1006(2)	5000	2500	50(1)

* U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

10. Form P13 of crystalline (S,E)-4-(2-(3-(3-chloro-2-fluoro-6-(1H-tetrazol-1-yl)phenyl)acryloyl)-5-(4-methyl-2-oxopiperazin-1-yl)-1,2,3,4-tetrahydroisoquinoline-1-

carboxamido)benzoic acid, which is characterized by a powder X-ray diffraction pattern substantially in accordance with that shown in Figure 3.

11. Form P13 according to Claim 10 having a powder X-ray diffraction pattern comprising four or more 2θ values (CuKα λ= 1.5418 Å): 8.4, 8.9, 12.7, and 17.9.

12. The Form according to any of Claims 1, 6, and 10, in substantially pure form.

13. The Form according to Claim 12, wherein substantially pure is greater than 90 percent pure.

14. A pharmaceutical composition comprising a therapeutically effective amount of crystalline Form H.5-1 of (S,E)-4-(2-(3-(3-chloro-2-fluoro-6-(1H-tetrazol-1-yl)phenyl)acryloyl)-5-(4-methyl-2-oxopiperazin-1-yl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamido)benzoic acid and a pharmaceutically acceptable carrier.

15. A pharmaceutical composition comprising a therapeutically effective amount of crystalline Form P13 of (S,E)-4-(2-(3-(3-chloro-2-fluoro-6-(1H-tetrazol-1-yl)phenyl)acryloyl)-5-(4-methyl-2-oxopiperazin-1-yl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamido)benzoic acid and a pharmaceutically acceptable carrier.

16. A pharmaceutical composition comprising a therapeutically effective amount of crystalline Form HCl:SA-1 of (S,E)-4-(2-(3-(3-chloro-2-fluoro-6-(1H-tetrazol-1-yl)phenyl)acryloyl)-5-(4-methyl-2-oxopiperazin-1-yl)-1,2,3,4-tetrahydroisoquinoline-1-carboxamido)benzoic acid and a pharmaceutically acceptable carrier.