

WHAT IS CLAIMED IS:

- 1 **1.** A crystalline form of 1-benzyl-N-(4-carbamimidoylbenzyl)-1H-pyrazole-
2 4-carboxamide acetate, substantially free of other polymorphic forms of 1-benzyl-N-(4-
3 carbamimidoylbenzyl)-1H-pyrazole-4-carboxamide acetate.
- 1 **2.** The crystalline form of claim **1**, wherein said crystalline form is anhydrous
2 1-benzyl-N-(4-carbamimidoylbenzyl)-1H-pyrazole-4-carboxamide acetate, and characterized by
3 having a melting point of about 253°C, and an aqueous solubility of about 8.3 mg/mL at 25°C
4 (“Form I”).
- 1 **3.** The crystalline form of claim **2**, wherein Form I is characterized by an X-
2 ray powder diffraction (XRPD) pattern that comprises peaks at 10.0, 18.1, 18.6, 20.1, and 23.9
3 degrees, ± 0.5 degrees, 2θ , wherein said XRPD is made using Cu K α radiation.
- 1 **4.** The crystalline form of claim **3**, wherein the XRPD pattern further
2 comprises a peak at 20.5 degrees, ± 0.5 degrees, 2θ .
- 1 **5.** The crystalline form of claim **3** or **4**, wherein the XRPD pattern is
2 substantially similar to the pattern of Fig. 1.
- 1 **6.** The crystalline form of claim **1**, wherein said 1-benzyl-N-(4-
2 carbamimidoylbenzyl)-1H-pyrazole-4-carboxamide acetate is hydrated, and characterized by
3 having a melting point of about 253°C and an aqueous solubility of about 5.5 mg/mL at 25°C
4 (“Form II”).
- 1 **7.** The crystalline form of claim **6**, wherein said Form II is characterized by
2 an XRPD pattern that comprises peaks at 4.2, 5.6, 8.4, 17.8, and 19.8 degrees, ± 0.5 degrees, 2θ ,
3 wherein said XRPD is made using Cu K α radiation.
- 1 **8.** The crystalline form of claim **7**, wherein the XRPD pattern further
2 comprises a peak at 12.7 degrees, ± 0.5 degrees, 2θ .
- 1 **9.** The crystalline form of claim **7** or **8**, wherein the XRPD pattern is
2 substantially similar to the pattern of Fig. 2.

1 **10.** The crystalline form of claim **1**, wherein said 1-benzyl-N-(4-
2 carbamimidoylbenzyl)-1H-pyrazole-4-carboxamide acetate is anhydrous, and is characterized by
3 having a melting point of about 249°C, and an aqueous solubility of about 7.2 mg/mL at 25°C
4 (“Form III”).

1 **11.** The crystalline form of claim **10**, wherein said Form III is characterized by
2 XRPD pattern that comprises peaks at 7.7, 10.7, 20.1, 23.7, and 24.3 degrees, ± 0.5 degrees, 2θ ,
3 wherein said XRPD is made using Cu K α radiation.

1 **12.** The crystalline form of claim **11**, wherein the XRPD pattern further
2 comprises peaks at 18.5 and 26.5 degrees, ± 0.5 degrees, 2θ .

1 **13.** The crystalline form of claim **11** or **12**, wherein the XRPD pattern is
2 substantially similar to the pattern of Fig. 3.

1 **14.** The crystalline form of claim **1**, wherein said form is 1-benzyl-N-(4-
2 carbamimidoylbenzyl)-1H-pyrazole-4-carboxamide acetate, characterized by having a melting
3 point of about 251°C, and characterized by an XRPD pattern that comprises peaks at 18.5, 19.6,
4 and 23.7 degrees, ± 0.5 degrees, 2θ , wherein said XRPD is made using Cu K α radiation (“Form
5 IV”).

1 **15.** The crystalline form of claim **14**, wherein the XRPD pattern further
2 comprises a peak at 24.6 degrees, ± 0.5 degrees, 2θ .

1 **16.** The crystalline form of claim **14** or **15**, wherein the XRPD pattern is
2 substantially similar to the pattern of Fig. 4.

1 **17.** An amorphous form of 1-benzyl-N-(4-carbamimidoylbenzyl)-1H-
2 pyrazole-4-carboxamide acetate, characterized by having a melting point of about 240°C, and an
3 aqueous solubility of about 7.1 mg/mL in water at 25°C (“Form V”).

1 **18.** A pharmaceutical composition for the treatment of a plasma kallikrein-
2 dependent disease or condition, comprising a therapeutically effective amount of the solid form
3 of any one of claims **1** to **17**, and a pharmaceutically acceptable carrier.

1 **19.** The pharmaceutical composition of claim **18**, wherein the solid form is the
2 Form I of any one of claims **2** to **5**, and a pharmaceutically acceptable carrier.

1 **20.** The pharmaceutical composition of claim **18**, wherein the solid form is the
2 Form II of any one of claims **6** to **9**, and a pharmaceutically acceptable carrier.

1 **21.** The pharmaceutical composition of claim **18**, wherein the solid form is the
2 Form III of any one of claims **10** to **13**, and a pharmaceutically acceptable carrier.

1 **22.** The pharmaceutical composition of claim **18**, wherein the solid form is the
2 Form IV of any one of claims **14** to **16**, and a pharmaceutically acceptable carrier.

1 **23.** The pharmaceutical composition of claim **18**, wherein the solid form is the
2 Form V of claim **17**, and a pharmaceutically acceptable carrier.

1 **24.** A method for making the Form I of any one of claims **2** to **5**, comprising:
2 contacting a solid form of 1-benzyl-N-(4-carbamimidoylbenzyl)-1H-pyrazole-4-
3 carboxamide acetate with a solvent selected from the group consisting of methanol, ethanol,
4 isopropanol, tetrahydrofuran, 2-methyl-tetrahydrofuran, anhydrous acetone, dichloromethane,
5 diethyl ether, 3-methyl-1-butanol, and nitromethane, or a mixture thereof, for a period of time
6 sufficient to produce Form I.

1 **25.** The method of claim **24**, wherein the solvent is methanol.

1 **26.** The method of claim **24** or **25**, wherein the solvent further comprises a
2 solvent selected from the group consisting of tetrahydrofuran, t-butyl-methyl ether, and heptane.

1 **27.** A method for making the Form II of any one of claims **6** to **9**, comprising:
2 contacting a solid form of 1-benzyl-N-(4-carbamimidoylbenzyl)-1H-pyrazole-4-
3 carboxamide acetate with a mixture of water and a solvent selected from the group consisting of
4 isopropanol, tetrahydrofuran, acetone, and ethyl acetate, or a combination thereof, for a period of
5 time sufficient to produce Form II.

- 1 **28.** The method of claim **27**, wherein the mixture comprises at least about
2 10% water.
- 1 **29.** The method of claim **27** or **28**, wherein said solvent is ethyl acetate.
- 1 **30.** A method for making the Form V of claim **17**, comprising:
2 (a) dissolving a solid form of 1-benzyl-N-(4-carbamimidoylbenzyl)-1H-pyrazole-
3 4-carboxamide acetate in a sufficient quantity of water to form a solution;
4 (b) freezing the solution; and
5 (c) lyophilizing the product of step (b).
- 1 **31.** A method for making the Form III of any one of claims **10** to **13**,
2 comprising:
3 contacting a solid form of 1-benzyl-N-(4-carbamimidoylbenzyl)-1H-pyrazole-4-
4 carboxamide acetate with acetonitrile for a period of time sufficient to produce Form III.
- 1 **32.** The crystalline form of claim **1**, having less than 10% by weight of any
2 other polymorphic form.
- 1 **33.** The crystalline form of claim **32**, having less than 5% by weight of any
2 other polymorphic form.
- 1 **34.** The crystalline form of claim **32** or **33**, having less than 1% by weight of
2 any other polymorphic form.
- 1 **35.** A method for treating of a plasma kallikrein-dependent disease or
2 condition, comprising:
3 administering an effective amount of the crystalline form of any one of claims **1**
4 to **17**, or the pharmaceutical composition of any one of claims **18** to **23** to a subject in need
5 thereof.

1 **36.** The method of claim **35**, wherein the plasma kallikrein-dependent disease
2 or condition is selected from the group consisting of:

3 diabetic macular edema, diabetic retinopathy, hereditary angioedema with C1
4 inhibitor deficiency, acute liver injury, inflammation, anaphylaxis, chemical-sensitized renal
5 damage, ischemic stroke, hemorrhagic stroke, hypertension, vascular complications of
6 hypertension, retinopathy, nephropathy, cerebrovascular edema, pulmonary hypertension,
7 inflammation, pain, acute myocardial infarction, deep vein thrombosis, complications from
8 fibrinolytic treatment, angina, angioedema, sepsis, arthritis, complications of cardiopulmonary
9 bypass surgery, capillary leak syndrome, inflammatory bowel disease, diabetes, diabetic
10 retinopathy, diabetic macular edema, diabetic nephropathy, diabetic neuropathy, age-related
11 macular degeneration, retinal vein occlusions, brain edema, ischemia-reperfusion injury, cancer-
12 related angiogenesis, asthma, anaphylaxis, and cerebrovascular complications of Alzheimer's
13 Disease, Parkinson's Disease, multiple sclerosis, Central Nervous System infections, and
14 glioblastoma multiforme.

1 **37.** The use of a solid form of 1-benzyl-N-(4-carbamimidoylbenzyl)-1H-
2 pyrazole-4-carboxamide acetate, substantially free of other polymorphic forms of 1-benzyl-N-(4-
3 carbamimidoylbenzyl)-1H-pyrazole-4-carboxamide acetate, for the treatment of a plasma
4 kallikrein-dependent disease or condition.

1 **38.** The use of claim **37**, wherein the solid form is the form of any one of
2 claims **1** to **17**.

1 **39.** The use of a solid form of 1-benzyl-N-(4-carbamimidoylbenzyl)-1H-
2 pyrazole-4-carboxamide acetate, substantially free of other polymorphic forms of 1-benzyl-N-(4-
3 carbamimidoylbenzyl)-1H-pyrazole-4-carboxamide acetate, for the manufacture of a
4 medicament for the treatment of a plasma kallikrein-dependent disease or condition.

1 **40.** The use of claim **39**, wherein the solid form is the form of any one of
2 claims **1** to **17**.

3 **41.** The crystalline form of any one of claims **3, 4, 7, 8, 11, 12, 14, 15,**
4 **wherein the XRPD peaks are within ± 0.2 degrees 2θ of the stated peak position.**

1 **42.** The crystalline form of claim **41**, wherein the XRPD peaks are within $\pm$
2 **0.1 degrees 2θ of the stated peak position.**