[0031] The ability to adjust biological production of energy has applications beyond the diseases described above. Various other disorders can result in suboptimal levels of energy biomarkers (sometimes also referred to as indicators of energetic function), such as ATP levels. Treatments for these disorders are also needed, in order to modulate one or more energy biomarkers to improve the health of the patient. In other applications, it can be desirable to modulate certain energy biomarkers away from their normal values in an individual that is not suffering from disease. For example, if an individual is undergoing an extremely strenuous undertaking, it can be desirable to raise the level of ATP in that individual.

[0032] Certain polymorphic or amorphous forms of a drug can have advantageous characteristics versus other forms; for example, increased stability, increased solubility, better handling properties, lack of associated toxic solvents, and increased purity.

[0033] Example 16 of PCT Application No. PCT/US2008/082374, published as WO 2009/061744 on May 14, 2009, describes a synthesis for racemic 2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide; this Example does not specifically describe the synthesis of any particular polymorphic or amorphous form for (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide or any particular stereoisomer thereof.

BRIEF SUMMARY OF THE INVENTION

[0034] ~~In one aspect of t~~The ~~invention~~ disclosure provides ~~is~~ a polymorph of an anhydrate, a hydrate, or a solvate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide, wherein the polymorph is selected from the group consisting of Form I, Form II, Form III, Form IV, Form V, and Form VI as described herein.

[0034a] In one aspect of the disclosure is an polymorph of an anhydrate, a hydrate, or a solvate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide, wherein the polymorph is selected from the group consisting of Forms II and III; wherein a powder X-ray diffraction pattern for polymorph Form II comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.63, 10.85, 11.33, and 19.33; wherein a powder X-ray diffraction pattern for polymorph Form III comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.16, 14.02, 15.23, and 21.10; and wherein the XRPD pattern is generated at 25 °C.

[0035] ~~In another aspect of t~~The ~~invention~~ disclosure also provides ~~is~~ a polymorph of an anhydrate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide, wherein the polymorph is Form I as described herein. In some ~~embodiments~~examples, the polymorph has a powder x-ray diffraction pattern substantially as shown in Figure 10. In some examples~~embodiments~~, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 12.06, 17.03, and 17.26. In some examples~~embodiments~~, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 12.06, 17.03, and 17.26. In some examples~~embodiments~~, a powder X-ray diffraction pattern for the

polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 12.06, 15.33, 17.03, and 17.26. In some examples~~embodiments~~, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 12.06, 15.33, 17.03, 17.26, and 18,72. In some examples~~embodiments~~, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, where in the angular positions may vary by ± 0.2: 12.06, 15.33, 17.03, 17.26, and 18.72. In some examples~~embodiments~~, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 7.67, 10.75, 12.06, 15.33, 16.41, 17.03, 17.26,~~-~~ 18.72, 20.04, and 23.92. In some examples~~embodiments~~, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 7.67, 10.75, 12.06, 15.33, 16.41, 17.03, 17.26, 18.72, 20.04, 20.64, 20.91, 21.14, 22.58, 23.13, 23.92, 24.19, 24.53, 27.21, and 27.56. In some embodiments, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 5.48, 7.67, 10.75, 12.06, 15.33, 16.41, 17.03, 17.26, 17.71, 17.94, 18.40, 18.72, 19.51, 20.04, 20.64, 20.91, 21.14, 21.55, 21.91, 22.25, 22.58, 23.13, 23.41, 23.92, 24.19, 24.53, 25.64, 26.13, 26.34, 27.21, 27.56, 28.01, 29.04, and 29.46. In some examples~~embodiments~~, including any of the foregoing examples~~embodiments~~, the angular positions may vary by ± 0.1. In some examples~~embodiments~~, including any of the foregoing examples~~embodiments~~, the angular positions may vary by ± 0.05. In some examples~~embodiments~~, including any of the foregoing examples~~embodiments~~, the angular positions may vary by ± 0.02. In some embodiments, including any of the foregoing examples~~embodiments~~, the polymorph is isolated. In some examples~~embodiments~~, including any of the foregoing examples~~embodiments~~, the polymorph is present in a composition, wherein the composition is essentially free of Forms II-VI, wherein Forms II-VI are described in Table A or Tables 3-7 respectively. In some examples~~embodiments~~, including any of the foregoing embodiments, the polymorph is present in a composition, wherein at least about 95% of the composition is the polymorph, exclusive of any solvents, carriers or excipients.

[0036] ~~In another aspect of t~~The ~~invention~~ disclosure also provides ~~is~~ a polymorph of an anhydrate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide, wherein the polymorph is Form V as described herein. In some examples~~embodiments~~, the polymorph has a powder x-ray diffraction pattern substantially as shown in a) or b) of Figure 30. In some examples~~embodiments~~, a

powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.61, 11.49, and 15.45. In some examples~~embodiments~~, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.61, 11.49, and 15.45. In some examples~~embodiments~~, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.61, 11.49, 15.45, and 23.96. In some examples~~embodiments~~, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.61, 11.49, 14.80, 15.45, 23.96. In some examples~~embodiments~~, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.61, 11.49, 12.93, 15.45, and 26.05. In some examples~~embodiments~~, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.61, 11.49, 12.93, 14.80, 15.45, 16.53, 23.96, 24.54, and 26.05. In some examples~~embodiments~~, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.61, 11.49, 12.93, 14.80, 15.45, 16.10, 16.34, 16.53, 20.18, 22.52, 22.86, 23.96, 24.54, and 26.05. In some examples~~embodiments~~, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 6.91, 7.72, 9.61, 11.49, 11.86, 12.93, 13.19, 13.87, 14.80, 15.45, 16.10, 16.34, 16.53, 17.14, 17.85, 19.12, 19.85, 20.18, 21.00, 22.06, 22.52, 22.86, 23.09, 23.96, 24.54, 25.26, 26.05, and 26.90. In some examples~~embodiments~~, including any of the foregoing examples~~embodiments~~, the angular positions may vary by ± 0.1. In some examples~~embodiments~~, including any of the foregoing examples~~embodiments~~, the angular positions may vary by ± 0.05. In some examples~~embodiments~~, including any of the foregoing examples~~embodiments~~, the angular positions may vary by ± 0.02. In some examples~~embodiments~~, including any of the foregoing examples~~embodiments~~, the polymorph is isolated. In some examples~~embodiments~~, including any of the foregoing examples~~embodiments~~, the polymorph is present in a composition, wherein the composition is essentially free of Forms I-IV and-VI, wherein Forms I-IV and-VI are described in Table A or Tables 2, or 4-7 respectively. In some examples~~embodiments~~, including any of the foregoing examples~~embodiments~~, the polymorph is present in a composition, wherein at least about 95% of the composition is the polymorph, exclusive of any solvents, carriers or excipients.

[0037] ~~In another aspect of t~~The ~~invention~~ disclosure also provides ~~is~~ a polymorph of a hydrate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide, wherein the polymorph is Form III as described herein. In some examples~~embodiments~~, the polymorph has a powder x-ray diffraction pattern substantially as shown in a) or b) of Figure 20. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 14.02, 15.23, and 21.10. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 14.02, 15.23, and 21.10. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.16, 14.02, 15.23, and 21.10. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.16, 13.74, 14.02, 15.23, and 21.10. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.16, 14.02, 15.23, 21.10, and 22.69. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.16, 11.81, 13.74, 14.02, 15.23, 21.10, 22.69, and 23.90. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.16, 11.81, 13.74, 14.02, 15.23, 17.35, 21.10, 22.69, 23.15, 23.90, and 26.10. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.16, 11.53, 11.81, 12.68, 12.93, 13.74, 14.02, 15.23, 16.53, 17.35, 17.98, 18.54, 19.09, 20.23, 21.10, 21.93, 22.69, 23.15, 23.50, 23.90, 24.65, 25.09, 25.46, 25.79, 26.10, 27.79, 28.22, 28.93, and 29.33. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the angular positions may vary by ± 0.1. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the angular positions may vary by ± 0.05. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the angular positions may vary by ± 0.02. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the polymorph is isolated. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the polymorph is present in a composition, wherein the composition

is essentially free of Forms I, II, IV, V, and VI, wherein Forms I, II, IV, V, and VI are described in Table A or Tables 2-3 and 5-7 respectively. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the polymorph is present in a composition, wherein at least about 95% of the composition is the polymorph, exclusive of any solvents, carriers or excipients.

[0038] ~~In another aspect of t~~The disclosure also provides ~~invention is~~ a polymorph of a solvate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide, wherein the polymorph is Form II as described herein. In some ~~embodiment~~examples, the polymorph has a powder x-ray diffraction pattern substantially as shown in a) or b) of Figure 15. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.63, 11.33, and 19.33. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.63, 11.33, 19.33. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.63, 11.33, 10.85, and 19.33. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: . 9.63, 11.33, 10.85, 19.33, and 17.3. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.63, 10.85, 11.33, 13.47, and 19.33. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 5.76, 8.04, 9.63, 10.85, 11.33, 11.97, 13.47, 14.75, 17.37, 17.71, and 19.33. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 5.76, 8.04, 9.63, 10.85, 11.33, 11.97, 13.47, 14.75, 16.42, 16.89, 17.37, 17.71, 19.33, 22.89, and 24.59. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 5.76, 6.72, 7.57, 8.04, 9.63, 10.85, 11.33, 11.97, 12.38, 13.13, 13.47, 14.75, 15.28, 16.42, 16.89, 17.37, 17.71, 18.17, 18.66, 19.33, 20.01, 20.29, 20.67, 20.90, 21.36, 21.54, 21.80, 22.55, 22.89, 23.27, 23.54, 23.87, 24.35, 24.59, 24.87, 25.29, 25.55, 25.89, 26.44, 27.49, 28.01, 28.39, and 29.17. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the

angular positions may vary by ± 0.1. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the angular positions may vary by ± 0.05. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the angular positions may vary by ± 0.02. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the polymorph is isolated. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the polymorph is present in a composition, wherein the composition is essentially free of Forms I, and III-VI, wherein Forms I, and III-VI are described in Table A or Tables 2-4 and 6-7 respectively. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the polymorph is present in a composition, wherein at least about 95% of the composition is the polymorph, exclusive of any solvents, carriers or excipients.

[0039] ~~In another aspect of t~~The disclosure also provides ~~invention is~~ a polymorph of a solvate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide, wherein the polymorph is Form IV as described herein. In some ~~embodiment~~examples, the polymorph has a powder x-ray diffraction pattern substantially as shown in a), b), or c) of Figure 25. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 4.31, 12.97, and 13.20. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 4.31, 12.97, 13.20. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 4.31, 8.76, 12.97, and 13.20. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 0.2: 4.31, 8.76, 12.97, 13.20, 16.66. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 4.31, 8.76, 12.97, 13.20, and 16.66. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 4.31, 7.94, 8.76, 12.97, 13.20, 16.66, 17.33, and 20.57. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 4.31, 7.94, 8.76, 12.97, 13.20, 15.08, 16.66, 17.33, 19.09, 20.57, and 21.58. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular

positions, wherein the angular positions may vary by ± 0.2: 4.31, 5.77, 6.28, 7.53, 7.94, 8.76, 9.39, 9.87, 10.54, 11.07, 11.68, 12.02, 12.28, 12.97, 13.20, 13.52, 14.40, 15.08, 15.90, 16.66, 16.96, 17.33, 17.59, 18.77, 19.09, 19.74, 20.27, 20.57, 21.09, 21.58, 22.81, 23.23, 24.01, 24.65, and 25.60. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the angular positions may vary by ± 0.1. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the angular positions may vary by ± 0.05. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the angular positions may vary by ± 0.02. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the polymorph is isolated. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the polymorph is present in a composition, wherein the composition is essentially free of Forms I-III and V-VI, wherein Forms I-III and V-VI are described in Table A or Tables 2-5 and 7 respectively. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the polymorph is present in a composition, wherein at least about 95% of the composition is the polymorph, exclusive of any solvents, carriers or excipients.

[0040] ~~In another aspect of t~~The disclosure also provides ~~invention is~~ a polymorph of a solvate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide, wherein the polymorph is Form VI as described herein. In some ~~embodiment~~examples, the polymorph has a powder x-ray diffraction pattern substantially as shown in a) of Figure 33. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 6.27, 9.91, and 12.94. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 6.27, 9.91, and 12.94. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 6.27, 9.91, 12.94, and 15.71. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 6.27, 9.91, 12.94, 15.71, and 19.13. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 6.27, 9.41, 9.91, 12.94, and 13.29. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 6.27, 8.85, 9.41, 9.91, 12.94, 13.29, 16.67, and 19.13. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph

comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 4.39, 6.27, 8.85, 9.41, 9.91, 11.32, 12.94, 13.29, 14.03, 16.67, 19.13, 20.76, and 22.06. In some ~~embodiment~~examples, a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 4.39, 6.27, 7.00, 8.62, 8.85, 9.41, 9.91, 11.32, 11.50, 12.25, 12.56, 12.94, 13.29, 14.03, 14.82, 15.10, 15.44, 15.71, 16.01, 16.67, 16.91, 17.33, 17.59, 18.33, 18.75, 19.13, 20.25, 20.76, 21.68, 22.06, 22.27, 22.61, 22.94, 24.01, 24.33, 24.65, 25.48, 26.05, 28.63, and 29.18. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the angular positions may vary by ± 0.1. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the angular positions may vary by ± 0.05. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the angular positions may vary by ± 0.02. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the polymorph is isolated. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the polymorph is present in a composition, wherein the composition is essentially free of Forms I-V, wherein Forms I-V are described in Table A or Tables 2-6 respectively. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the polymorph is present in a composition, wherein at least about 95% of the composition is the polymorph, exclusive of any solvents, carriers or excipients.

[0041] ~~In another aspect of t~~The ~~invention~~ disclosure also provides ~~is~~ a composition comprising amorphous (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide. In some ~~embodiment~~examples, the amorphous form is isolated. In some ~~embodiment~~examples, the composition is essentially free of Forms I-VI, wherein Forms I-VI are described in Table A or Tables 2-7 respectively. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, at least about 95% of the composition is amorphous (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide, exclusive of any solvents, carriers or excipients.

[0041a] In another aspect of the disclosure is a composition comprising the polymorph as defined herein, wherein the composition is essentially free of Forms I, II, IV, V, and VI, wherein a powder X-ray diffraction pattern for polymorph Form I comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 12.06, 15.33 17.03, and 17.26; wherein a powder X-ray diffraction pattern for polymorph Form II comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.63, 10.85, 11.33, and 19.33; wherein a powder X-ray diffraction pattern for polymorph Form IV comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 8.76, 12.97, 13.20, and 16.66; wherein a powder X-ray diffraction pattern for polymorph Form V comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.61, 11.49, 12.93, and 15.45; and wherein a powder X-ray diffraction pattern for polymorph Form

VI comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 6.27, 9.91, 12.94, and 15.71.

[0041b] In another aspect of the disclosure is a composition comprising the polymorph as defined herein, wherein at least about 95% by mole of the composition is the polymorph Form III, exclusive of any solvents, carriers or excipients.

[0041c] In another aspect of the disclosure is a composition comprising the polymorph as defined herein, wherein the composition is essentially free of Forms I, III-VI, wherein a powder X-ray diffraction pattern for polymorph Form I comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 12.06, 15.33 17.03, and 17.26; wherein a powder X-ray diffraction pattern for polymorph Form III comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.16, 14.02, 15.23, and 21.10; wherein a powder X-ray diffraction pattern for polymorph Form IV comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 8.76, 12.97, 13.20, and 16.66; wherein a powder X-ray diffraction pattern for polymorph Form V comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.61, 11.49, 12.93, and 15.45; and wherein a powder X-ray diffraction pattern for polymorph Form VI comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 6.27, 9.91, 12.94, and 15.71.

[0041d] In another aspect of the disclosure is a composition comprising the polymorph as defined herein, wherein at least about 95% by mole of the composition is the polymorph Form II, exclusive of any solvents, carriers or excipients.

[0042] ~~In another aspect of t~~The disclosure also provides ~~invention is~~ a pharmaceutical composition comprising a polymorphic or amorphous form of an anhydrate, a hydrate, or a solvate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide, or composition comprising such form, as described herein, including any of the foregoing or hereafter ~~embodiment~~examples, and a pharmaceutically acceptable carrier. In some ~~embodiment~~examples, the form is polymorph Form I. In some ~~embodiment~~examples, the form is polymorph Form II. In some ~~embodiment~~examples, the form is polymorph Form III. In some ~~embodiment~~examples, the form is polymorph Form IV. In some ~~embodiment~~examples, the form is polymorph Form V. In some ~~embodiment~~examples, the

form is polymorph Form VI. In some ~~embodiment~~examples, the form is amorphous. In some ~~embodiment~~examples, the pharmaceutical composition has an HPLC purity of more than about 95% for the anhydrate, hydrate, or solvate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide, exclusive of any solvents, carriers or excipients. In some ~~embodiment~~examples, the pharmaceutical composition has an HPLC purity of more than about 99% for the anhydrate, hydrate, or solvate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide, exclusive of any solvents, carriers or excipients. In some ~~embodiment~~examples, the pharmaceutical composition has an HPLC purity of more than about 99.9% for the anhydrate, hydrate, or solvate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide, exclusive of any solvents, carriers or excipients. HPLC purity % refers to the proportional area of a given compound's HPLC peak with respect to the area of all peaks in a given HPLC spectrum. HPLC % is calculated by dividing the area of a compound peak by the area of all peaks, in a HPLC spectrum, and multiplying this quotient by one-hundred.

[0043] ~~In another aspect of t~~The disclosure also provides ~~invention is~~ a pharmaceutical composition comprising an active agent and a pharmaceutically acceptable carrier, wherein the active agent consists of, or consists essentially of, a polymorphic or amorphous form of an anhydrate, a hydrate, or a solvate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide as described herein. In some ~~embodiment~~examples, the form is polymorph Form I. In some ~~embodiment~~examples, the form is polymorph Form II. In some ~~embodiment~~examples, the form is polymorph Form III. In some ~~embodiment~~examples, the form is polymorph Form IV. In some ~~embodiment~~examples, the form is polymorph Form V. In some ~~embodiment~~examples, the form is polymorph Form VI. In some ~~embodiment~~examples, the form is amorphous.

[0043a] In another aspect of the disclosure is a pharmaceutical composition comprising the polymorph as defined herein, or the composition as defined herein, and a pharmaceutically acceptable carrier.

[0044] ~~In another aspect of the~~The disclosure also provides ~~invention is~~ a method of treating or suppressing an oxidative stress disorder, modulating one or more energy biomarkers, normalizing one or more energy biomarkers, or enhancing one or more energy biomarkers, comprising administering to an individual in need thereof a therapeutically effective amount or effective amount of a polymorphic or amorphous form of an anhydrate, a hydrate, or a solvate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide, or composition comprising such form, as described herein, including any of the foregoing or hereafter ~~embodiment~~examples. The method can use any individual polymorphic or amorphous form of the invention as described herein, or a combination of such. In some ~~embodiment~~examples, the form is

polymorph Form I. In some ~~embodiment~~examples, the form is polymorph Form II. In some ~~embodiment~~examples, the form is polymorph Form III. In some ~~embodiment~~examples, the form is polymorph Form IV. In some ~~embodiment~~examples, the form is polymorph Form V. In some ~~embodiment~~examples, the form is polymorph Form VI. In some ~~embodiment~~examples, the form is amorphous. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the anhydrate, hydrate, or solvate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide is administered in a pharmaceutical composition comprising the polymorphic or amorphous form and a pharmaceutically acceptable carrier. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the pharmaceutical composition comprises an active agent consisting essentially of the polymorphic or amorphous form of the anhydrate, hydrate, or solvate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the method is a method of treating or suppressing an oxidative stress disorder. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the method is a method of treating an oxidative stress disorder. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the method is a method of suppressing an oxidative stress disorder. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the oxidative stress disorder is selected from the group consisting of: a mitochondrial disorder; an inherited mitochondrial disease; Alpers Disease; Barth syndrome; a Beta-oxidation Defect; Carnitine-Acyl-Carnitine Deficiency; Carnitine Deficiency; a Creatine Deficiency Syndrome; Co-Enzyme Q10 Deficiency; Complex I Deficiency; Complex II Deficiency; Complex III Deficiency; Complex IV Deficiency; Complex V Deficiency; COX Deficiency; chronic progressive external ophthalmoplegia (CPEO); CPT I Deficiency; CPT II Deficiency; Friedreich's Ataxia (FA); Glutaric Aciduria Type II; Kearns-Sayre Syndrome (KSS); Lactic Acidosis; Long-Chain Acyl-CoA Dehydrogenase Deficiency (LCAD); LCHAD; Leigh's syndrome; Leigh-like Syndrome; Leber's Hereditary Optic Neuropathy (LHON); Lethal Infantile Cardiomyopathy (LIC); Luft Disease; Multiple Acyl-CoA Dehydrogenase Deficiency (MAD); Medium-Chain Acyl-CoA Dehydrogenase Deficiency (MCAD); Mitochondrial Myopathy, Encephalopathy, Lactacidosis, Stroke (MELAS); Myoclonic Epilepsy with Ragged Red Fibers (MERRF); Mitochondrial Recessive Ataxia Syndrome (MIRAS); Mitochondrial Cytopathy, Mitochondrial DNA Depletion; Mitochondrial Encephalopathy; Mitochondrial Myopathy; Myoneurogastrointestina Disorder and Encephalopathy (MNGIE); Neuropathy, Ataxia, and Retinitis Pigmentosa (NARP); Pearson Syndrome; Pyruvate Carboxylase Deficiency; Pyruvate Dehydrogenase Deficiency; a

POLG Mutation; a Respiratory Chain Disorder; Short-Chain Acyl-CoA Dehydrogenase Deficiency (SCAD); SCHAD; Very Long-Chain Acyl-CoA Dehydrogenase Deficiency (VLCAD); a myopathy; cardiomyopathy; encephalomyopathy; a neurodegenerative disease; Parkinson's disease; Alzheimer's disease; amyotrophic lateral sclerosis (ALS); a motor neuron disease; a neurological disease; epilepsy; an age-associated disease; macular degeneration; diabetes; metabolic syndrome; cancer; brain cancer; a genetic disease; Huntington's Disease; a mood disorder; schizophrenia; bipolar disorder; a pervasive developmental disorder; autistic disorder; Asperger's syndrome; childhood disintegrative disorder (CDD); Rett's disorder; PDD-not otherwise specified (PDD-NOS); a cerebrovascular accident; stroke; a vision impairment; optic neuropathy; dominant inherited juvenile optic atrophy; optic neuropathy caused by a toxic agent; glaucoma; Stargardt's macular dystrophy; diabetic retinopathy; diabetic maculopathy; retinopathy of prematurity; ischemic reperfusion-related retinal injury; oxygen poisoning; a haemoglobinopathy; thalassemia; sickle cell anemia; seizures; ischemia; renal tubular acidosis; attention deficit/hyperactivity disorder (ADHD); a neurodegenerative disorder resulting in hearing or balance impairment; Dominant Optic Atrophy (DOA); Maternally inherited diabetes and deafness (MIDD); chronic fatigue; contrast-induced kidney damage; contrast-induced retinopathy damage; Abetalipoproteinemia; retinitis pigmentosum; Wolfram's disease; Tourette syndrome; cobalamin c defect; methylmalonic aciduria; glioblastoma; Down's syndrome; acute tubular necrosis; a muscular dystrophy; a leukodystrophy; Progressive Supranuclear Palsy; spinal muscular atrophy; hearing loss; noise induced hearing loss; traumatic brain injury; Juvenile Huntington's Disease; Multiple Sclerosis; NGLY1; Multiple System Atrophy; Adrenoleukodystrophy; and Adrenomyeloneuropathy. In some ~~embodiment~~examples, the oxidative stress disorder is Multiple System Atrophy. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the oxidative stress disorder is cancer. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the oxidative stress disorder is bipolar disorder. In some ~~embodiment~~examples, the oxidative stress disorder is schizophrenia. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the oxidative stress disorder is an age-associated disease. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the oxidative stress disorder is Huntington's Disease. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the oxidative stress disorder is Alzheimer's disease. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the oxidative stress disorder is amyotrophic lateral sclerosis (ALS). In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the oxidative stress disorder is

epilepsy. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the oxidative stress disorder is Parkinson's disease. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the oxidative stress disorder is seizures. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the oxidative stress disorder is stroke. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the oxidative stress disorder is a mitochondrial disorder. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the oxidative stress disorder is an inherited mitochondrial disease. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the oxidative stress disorder is Friedreich's Ataxia (FA). In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the oxidative stress disorder is Kearns-Sayre Syndrome (KSS). In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the oxidative stress disorder is Leigh Syndrome or Leigh-like Syndrome. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the oxidative stress disorder is Leber's Hereditary Optic Neuropathy (LHON). In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the oxidative stress disorder is Mitochondrial Myopathy, Encephalopathy, Lactacidosis, Stroke (MELAS). In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the oxidative stress disorder is Myoclonic Epilepsy with Ragged Red Fibers (MERRF). In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the oxidative stress disorder is macular degeneration. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the oxidative stress disorder is brain cancer. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the oxidative stress disorder is autistic disorder. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the oxidative stress disorder is Rett's disorder. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the oxidative stress disorder is Maternally inherited diabetes and deafness (MIDD). In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the oxidative stress disorder is chronic fatigue. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the oxidative stress disorder is contrast-induced kidney damage. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the oxidative stress disorder is contrast-induced retinopathy damage. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the oxidative stress disorder is cobalamin c defect. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the method is a method for modulating one or more energy biomarkers, normalizing one or more energy biomarkers, or enhancing one or more energy biomarkers, wherein the one or more energy biomarkers are selected from the group consisting of: lactic

acid (lactate) levels, either in whole blood, plasma, cerebrospinal fluid, or cerebral ventricular fluid; pyruvic acid (pyruvate) levels, either in whole blood, plasma, cerebrospinal fluid, or cerebral ventricular fluid; lactate/pyruvate ratios, either in whole blood, plasma, cerebrospinal fluid, or cerebral ventricular fluid; total, reduced or oxidized glutathione levels, or reduced/oxidized glutathione ratio either in whole blood, plasma, lymphocytes, cerebrospinal fluid, or cerebral ventricular fluid; total, reduced or oxidized cysteine levels, or reduced/oxidized cysteine ratio either in whole blood, plasma, lymphocytes, cerebrospinal fluid, or cerebral ventricular fluid; phosphocreatine levels, NADH (NADH +H+) levels; NADPH (NADPH+H+) levels; NAD levels; NADP levels; ATP levels; reduced coenzyme Q (CoQ_{red}) levels; oxidized coenzyme Q (CoQ_{ox}) levels; total coenzyme Q (CoQ_{tot}) levels; oxidized cytochrome C levels; reduced cytochrome C levels; oxidized cytochrome C/reduced cytochrome C ratio; acetoacetate levels, β hydroxy butyrate levels, acetoacetate/β hydroxy butyrate ratio, 8-hydroxy-2'-deoxyguanosine (8-OHdG) levels; levels of reactive oxygen species; levels of oxygen consumption (VO2); levels of carbon dioxide output (VCO2); respiratory quotient (VCO2/VO2); exercise tolerance; and anaerobic threshold. Energy biomarkers can be measured in whole blood, plasma, cerebrospinal fluid, cerebroventricular fluid, arterial blood, venous blood, or any other body fluid, body gas, or other biological sample useful for such measurement. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the levels are modulated to a value within about 2 standard deviations of the value in a healthy subject. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the levels are modulated to a value within about 1 standard deviation of the value in a healthy subject. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the levels in a subject are changed by at least about 10% above or below the level in the subject prior to modulation. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the levels are changed by at least about 20% above or below the level in the subject prior to modulation. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the levels are changed by at least about 30% above or below the level in the subject prior to modulation. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the levels are changed by at least about 40% above or below the level in the subject prior to modulation. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the levels are changed by at least about 50% above or below the level in the subject prior to modulation. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the levels are changed by at least about 75% above or below the level in the

subject prior to modulation. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the levels are changed by at least about 100% above or at least about 90% below the level in the subject prior to modulation. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the subject or subjects in which a method of treating or suppressing an oxidative stress disorder, modulating one or more energy biomarkers, normalizing one or more energy biomarkers, or enhancing one or more energy biomarkers is performed is/are selected from the group consisting of subjects undergoing strenuous or prolonged physical activity; subjects with chronic energy problems; subjects with chronic respiratory problems; pregnant females; pregnant females in labor; neonates; premature neonates; subjects exposed to extreme environments; subjects exposed to hot environments; subjects exposed to cold environments; subjects exposed to environments with lower-than-average oxygen content; subjects exposed to environments with higher-than-average carbon dioxide content; subjects exposed to environments with higher-than-average levels of air pollution; airline travelers; flight attendants; subjects at elevated altitudes; subjects living in cities with lower-than-average air quality; subjects working in enclosed environments where air quality is degraded; subjects with lung diseases; subjects with lower-than-average lung capacity; tubercular patients; lung cancer patients; emphysema patients; cystic fibrosis patients; subjects recovering from surgery; subjects recovering from illness; elderly subjects; elderly subjects experiencing decreased energy; subjects suffering from chronic fatigue; subjects suffering from chronic fatigue syndrome; subjects undergoing acute trauma; subjects in shock; subjects requiring acute oxygen administration; subjects requiring chronic oxygen administration; subjects requiring organ visualization via contrast solution; or other subjects with acute, chronic, or ongoing energy demands who can benefit from enhancement of energy biomarkers.

[0045] ~~In another aspect of the~~The disclosure also provides ~~invention is the~~ use of a polymorphic or amorphous form of an anhydrate, a hydrate, or a solvate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide as described herein, including any of the foregoing or hereafter described ~~embodiment~~examples, for treating or suppressing an oxidative stress disorder. In another aspect of the disclosure is use of a therapeutically effective amount of the polymorph as defined herein, the composition as defined herein, or the pharmaceutical composition as defined herein in the manufacture of a medicament for the treatment or suppression of an oxidative stress disorder. In some ~~embodiment~~examples, the form is polymorph Form I. In some ~~embodiment~~examples, the form is polymorph Form II. In some ~~embodiment~~examples, the form is polymorph Form III. In some ~~embodiment~~examples, the form is polymorph Form IV. In some ~~embodiment~~examples, the form is polymorph Form V. In some ~~embodiment~~examples, the form is polymorph Form VI. In some ~~embodiment~~examples, the form is amorphous. ~~In another aspect of the invention~~ The disclosure also provides ~~is the~~ use of a polymorphic or amorphous

form of an anhydrate, a hydrate, or a solvate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide as described herein, including any of the foregoing or hereafter described ~~embodiment~~examples, in the manufacture of a medicament for use in treating or suppressing an oxidative stress disorder. In some ~~embodiment~~examples, the form is polymorph Form I. In some ~~embodiment~~examples, the form is polymorph Form II. In some ~~embodiment~~examples, the form is polymorph Form III. In some ~~embodiment~~examples, the form is polymorph Form IV. In some ~~embodiment~~examples, the form is polymorph Form V. In some ~~embodiment~~examples, the form is polymorph Form VI. In some ~~embodiment~~examples, the form is amorphous.

[0046] For all compositions described herein, and all methods using a composition described herein, the compositions can either comprise the listed components or steps, or can "consist essentially of" the listed components or steps. When a composition is described as "consisting essentially of" the listed components, the composition contains the components listed, and may contain other components which do not substantially affect the condition being treated, but do not contain any other components which substantially affect the condition being treated other than those components expressly listed; or, if the composition does contain extra components other than those listed which substantially affect the condition being treated, the composition does not contain a sufficient concentration or amount of the extra components to substantially affect the condition being treated. When a method is described as "consisting essentially of" the listed steps, the method contains the steps listed, and may contain other steps that do not substantially affect the condition being treated, but the method does not contain any other steps which substantially affect the condition being treated other than those steps expressly listed. As a non-limiting specific example, when a composition is described as 'consisting essentially of' a component, the composition may additionally contain any amount of pharmaceutically acceptable carriers, vehicles, or diluents and other such components which do not substantially affect the condition being treated.

[0047] ~~In another aspect of t~~The ~~invention~~ disclosure also provides ~~is~~ a process for the preparation of polymorph Form I of an anhydrate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide, wherein the process comprises the steps: (a) contacting (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide with a liquid comprising IPA; and (b) removing the liquid. In some ~~embodiment~~examples, step (a) comprises dissolving the (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide in the liquid. In some ~~embodiment~~examples, step (a) comprises slurrying the (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-

3,6-dioxocyclohexa-1,4-dienyl)butanamide in the liquid. In some ~~embodiment~~examples, the slurrying in step (a) may be performed for at least about 24 hours. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the liquid is 100% IPA In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the liquid is 98% IPA/2% water (v/v). In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the process further comprises step (a)(i): adding heptane to the liquid. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, step (b) comprises filtering the (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the mixture in step (a) or step (a)(i) may be seeded with Form I crystals. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide in step (a) is at least about 95% pure. In various ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide in step (a) is at least about 96%, at least about 97%, at least about 98%, at least about 99%, at least about 99.5%, at least about 99.9% pure. ~~In another aspect of t~~The ~~invention~~ disclosure also provides ~~is~~ an anhydrate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide prepared by the above described process.

[0048] ~~In another aspect of t~~The ~~invention~~ disclosure also provides ~~is~~ a process for the preparation of polymorph Form II of an anhydrate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide, wherein the process comprises the steps: (a) dissolving the (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide in EtOAc, (b) rapidly cooling the mixture from (a), and (c) isolating the (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide. In some ~~embodiment~~examples, the initial (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide is Form I. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, step (a) is at about 60°C. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, step (b) comprises rapidly cooling the mixture in an ice bath. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the mixture in step (b) may be seeded with Form II crystals. The disclosure also provides ~~In another aspect of the invention is~~ an anhydrate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide prepared by the above described process.

[0049] ~~In another aspect of the~~The disclosure also provides ~~invention is~~ a process for the preparation of polymorph Form III of a solvate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-

dienyl)butanamide, wherein the process comprises the steps: (a) combining (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide and 0.5% MC/2%Tween 80 in water to create a slurry; (b) slurrying the mixture from (a), and (c) removing the 0.5% MC/2%Tween 80 in water. As used herein "MC" refers to methyl cellulose and "Tween 80" refers to a commercially available polysorbate nonionic surfactant In some ~~embodiment~~examples, the initial (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide is Form I. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, step (b) is performed for at least about 24 hours. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, step (b) is at room temperature. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the mixture in step (b) may be seeded with Form III crystals. The disclosure also provides ~~In another aspect of the invention is~~ a solvate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide prepared by the above described process.

[0050] ~~In another aspect of the~~ The disclosure also provides ~~invention is~~ a process for the preparation of polymorph Form III of a solvate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide, wherein the process comprises the steps: (a) combining (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide and 0.5% MC in water to create a slurry; (b) slurrying the mixture from (a), and (c) removing the 0.5% MC in water. In some ~~embodiment~~examples, the initial (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide is Form I, II, IV, V or VI. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, step (b) is performed at room temperature. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, step (b) may be performed for at least about 7 days. In some ~~embodiment~~examples, including any of the foregoing ~~embodiment~~examples, the mixture in step (b) may be seeded with Form III crystals. The disclosure also provides ~~In another aspect of the invention is~~ a solvate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide prepared by the above described process.

BRIEF DESCRIPTION OF THE FIGURES

[0051] Figure 1 shows a XRPD stack plot of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide short term slurry experiments, a) Pattern C, from slurry in 0.5% Methyl Cellulose/2% Tween 80, b) Pattern B, from slurry in tetrahydrofuran (THF), and c) starting material, Pattern A.

CLAIMS

What is claimed is:

1. An polymorph of an anhydrate, a hydrate, or a solvate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide, wherein the polymorph is selected from the group consisting of Forms II and III;~~I-VI as described in Table A or Tables 2-7 respectively~~

wherein a powder X-ray diffraction pattern for polymorph Form II comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.63, 10.85, 11.33, and 19.33;

wherein a powder X-ray diffraction pattern for polymorph Form III comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.16, 14.02, 15.23, and 21.10; and

wherein the XRPD pattern is generated at 25 °C.

~~2. The polymorph of claim 1, wherein the polymorph is Form I, wherein a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 12.06, 17.03, and 17.26.~~

~~3. The polymorph of claim 1, wherein the polymorph is Form I, wherein a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 12.06, 15.33, 17.03, 17.26, and 18.72.~~

~~4. The polymorph of claim 1, wherein the polymorph is Form I, wherein the polymorph has a powder x-ray diffraction pattern substantially as shown in Figure 10.~~

~~5. A composition comprising the polymorph of any one of claims 2-4, wherein the composition is essentially free of Forms II-VI, wherein Forms II-VI are described in Table A or Tables 3-7 respectively.~~

~~6. A composition comprising the polymorph of any one of claims 2-4, wherein at least about 95% by mole of the composition is the polymorph Form I, exclusive of any solvents, carriers or excipients.~~

~~7. The polymorph of claim 1, wherein the polymorph is Form V, wherein a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.61, 11.49, 15.45.~~

~~8. The polymorph of claim 1, wherein the polymorph is Form V, wherein a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.61, 11.49, 12.93, 15.45, and 26.05.~~

~~9. The polymorph of claim 1, wherein the polymorph is Form V, wherein the polymorph has a powder x-ray diffraction pattern substantially as shown in a), b), or c) of Figure 30.~~

~~10. A composition comprising the polymorph of any one of claims 7-9, wherein the composition is essentially free of Forms I-IV and VI, wherein Forms I-IV and VI are described in Table A or Tables 2 and 4-7 respectively.~~

~~11. A composition comprising the polymorph of any one of claims 7-9, wherein at least about 95% by mole of the composition is the polymorph Form V, exclusive of any solvents, carriers or excipients.~~

~~12. The polymorph of claim 1, wherein the polymorph is Form III, wherein a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 14.02, 15.23, and 21.10.~~

~~13~~2. The polymorph of claim 1, wherein the polymorph is Form III, wherein a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the

following angular positions, wherein the angular positions may vary by ± 0.2: 9.16, 14.02, 15.23, 21.10, and 22.69.

~~14. The polymorph of claim 1, wherein the polymorph is Form III, wherein the polymorph has a powder x-ray diffraction pattern substantially as shown in a) or b) of Figure 20.~~

3. The polymorph of claim 1, wherein the polymorph is Form III, having a DSC thermogram comprising three endothermic peaks at about 72.0 and 150.7 °C.

~~15~~4. A composition comprising the polymorph of any one of claims ~~12~~2-~~14~~3, wherein the composition is essentially free of Forms I, II, IV, V, and VI,

wherein a powder X-ray diffraction pattern for polymorph Form I comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 12.06, 15.33 17.03, and 17.26;

wherein a powder X-ray diffraction pattern for polymorph Form II comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.63, 10.85, 11.33, and 19.33;

wherein a powder X-ray diffraction pattern for polymorph Form IV comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 8.76, 12.97, 13.20, and 16.66;

wherein a powder X-ray diffraction pattern for polymorph Form V comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.61, 11.49, 12.93, and 15.45; and

wherein a powder X-ray diffraction pattern for polymorph Form VI comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 6.27, 9.91, 12.94, and 15.71.

~~wherein Forms I, II, IV, V, and VI are described in Table A or Tables 2-3 and 5-7 respectively.~~

~~16~~5. A composition comprising the polymorph of any one of claims ~~12~~2-~~14~~3, wherein at least about 95% by mole of the composition is the polymorph Form III, exclusive of any solvents, carriers or excipients.

~~17. The polymorph of claim 1, wherein the polymorph is Form II, wherein a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.63, 11.33, and 19.33.~~

~~18~~6. The polymorph of claim 1, wherein the polymorph is Form II, a solvate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide, wherein a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.63, 10.85, 11.33, 13.47, and 19.33.

7. The polymorph of claim 1, wherein the polymorph is Form II, having a DSC thermogram comprises two endothermic peaks at about 133.9 and 151.3°C.

~~19. The polymorph of claim 1, wherein the polymorph is Form II, wherein the polymorph has a powder x-ray diffraction pattern substantially as shown in a) of Figure 15.~~

~~20~~8. A composition comprising the polymorph of any one of claims ~~17~~6-~~19~~7, wherein the composition is essentially free of Forms I, III-VI,

wherein a powder X-ray diffraction pattern for polymorph Form I comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 12.06, 15.33 17.03, and 17.26;

wherein a powder X-ray diffraction pattern for polymorph Form III comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.16, 14.02, 15.23, and 21.10;

wherein a powder X-ray diffraction pattern for polymorph Form IV comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 8.76, 12.97, 13.20, and 16.66;

wherein a powder X-ray diffraction pattern for polymorph Form V comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.61, 11.49, 12.93, and 15.45; and

wherein a powder X-ray diffraction pattern for polymorph Form VI comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 6.27, 9.91, 12.94, and 15.71.

~~wherein Forms I, III–VI are described in Table A or Tables 2-4, and 6-7 respectively.~~

~~21~~9. A composition comprising the polymorph of any one of claims ~~17~~6-~~19~~7, wherein at least about 95% by mole of the composition is the polymorph Form II, exclusive of any solvents, carriers or excipients.

~~22. The polymorph of claim 1, wherein the polymorph is Form IV, wherein a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 4.31, 12.97, and 13.20.~~

~~23. The polymorph of claim 1, wherein the polymorph is Form IV, wherein a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 4.31, 8.76, 12.97, 13.20, and 16.66.~~

~~24. The polymorph of claim 1, wherein the polymorph is Form IV, wherein the polymorph has a powder x-ray diffraction pattern substantially as shown in a) or b) of Figure 25.~~

~~25. A composition comprising the polymorph of any one of claims 22-24, wherein the composition is essentially free of Forms I-III and V-VI, wherein Forms I-III and V-VI are described in Table A or Tables 2-5 and 7 respectively.~~

~~26. A composition comprising the polymorph of any one of claims 22-24, wherein at least about 95% by mole of the composition is the polymorph Form IV, exclusive of any solvents, carriers or excipients.~~

~~27. The polymorph of claim 1, wherein the polymorph is Form VI, wherein a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 6.27, 9.91, and 12.94.~~

~~28. The polymorph of claim 1, wherein the polymorph is Form VI, wherein a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at the following angular positions, wherein the angular positions may vary by ± 0.2: 6.27, 9.41, 9.91, 12.94, and 13.29.~~

~~29. The polymorph of claim 1, wherein the polymorph is Form VI, wherein the polymorph has a powder x-ray diffraction pattern substantially as shown in a) of Figure 33.~~

~~30. A composition comprising the polymorph of any one of claims 27-29, wherein the composition is essentially free of Forms I-V, wherein Forms I-V are described in Table A or Tables 2-6 respectively.~~

~~31. A composition comprising the polymorph of any one of claims 27-29, wherein at least about 95% by mole of the composition is the polymorph Form VI, exclusive of any solvents, carriers or excipients.~~

~~32. A composition comprising amorphous (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide.~~

~~33. The composition of claim 32, wherein the composition is essentially free of Forms I-VI, wherein Forms I-VI are described in Table A or Tables 2-7 respectively.~~

~~34. The composition of claim 32, wherein at least about 95% by mole of the composition is amorphous (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide, exclusive of any solvents, carriers or excipients.~~

~~35~~10. A pharmaceutical composition comprising the polymorph of any one of claims 1-~~4~~3, 6, and ~~7~~7-9, 12-14, 17-19, 22-24, and 27-29, or the composition of any one of claims 4, 5, 8, and ~~9~~5-6, 10-11, 15-16, 20-21, 25-26, and 30-34, and a pharmaceutically acceptable carrier.

~~36~~11. The pharmaceutical composition of claim ~~35~~10, wherein the pharmaceutical composition has an HPLC purity of more than about 95% for the anhydrate, hydrate, or solvate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide, exclusive of any solvents, carriers or excipients.

~~37~~12. The pharmaceutical composition of claim ~~35~~10, wherein the pharmaceutical composition has an HPLC purity of more than about 99% for the anhydrate, hydrate, or solvate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide, exclusive of any solvents, carriers or excipients.

~~38~~13. The pharmaceutical composition of claim ~~35~~11, wherein the pharmaceutical composition has an HPLC purity of more than about 99.9% for the anhydrate, hydrate, or solvate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide, exclusive of any solvents, carriers or excipients.

~~39~~14. Use of ~~A method of treating or suppressing an oxidative stress disorder, modulating one or more energy biomarkers, normalizing one or more energy biomarkers, or enhancing one or more energy biomarkers, comprising administering to an individual in need thereof~~ a therapeutically effective amount ~~or effective amount~~ of the polymorph of any one of claims 1-~~4~~3, 6, and ~~7~~7-9, ~~12-14, 17-19, 22-24, and 27-29~~, the composition of any one of claims 4, 5, 8, and 9~~5-6, 10-11, 15-16, 20-21, 25-26, and 30-34~~, or the pharmaceutical composition of any one of claims ~~35~~10-~~38~~13 in the manufacture of a medicament for the treatment or suppression of an oxidative stress disorder.

~~40~~15. The ~~method~~ use of claim ~~39~~14, wherein the ~~method is a method of treating or suppressing an~~ oxidative stress disorder is selected from the group consisting of: a mitochondrial disorder; an inherited mitochondrial disease; Alpers Disease; Barth syndrome; a Beta-oxidation Defect; Carnitine-Acyl-Carnitine Deficiency; Carnitine Deficiency; a Creatine Deficiency Syndrome; Co-Enzyme Q10 Deficiency; Complex I Deficiency; Complex II Deficiency; Complex III Deficiency; Complex IV Deficiency; Complex V Deficiency; COX Deficiency; chronic progressive external ophthalmoplegia (CPEO); CPT I Deficiency; CPT II Deficiency; Friedreich's Ataxia (FA); Glutaric Aciduria Type II; Kearns-Sayre Syndrome (KSS); Lactic

Acidosis; Long-Chain Acyl-CoA Dehydrogenase Deficiency (LCAD); LCHAD; Leigh Syndrome; Leigh-like Syndrome; Leber's Hereditary Optic Neuropathy (LHON); Lethal Infantile Cardiomyopathy (LIC); Luft Disease; Multiple Acyl-CoA Dehydrogenase Deficiency (MAD); Medium-Chain Acyl-CoA Dehydrogenase Deficiency (MCAD); Mitochondrial Myopathy, Encephalopathy, Lactacidosis, Stroke (MELAS); Myoclonic Epilepsy with Ragged Red Fibers (MERRF); Mitochondrial Recessive Ataxia Syndrome (MIRAS); Mitochondrial Cytopathy, Mitochondrial DNA Depletion; Mitochondrial Encephalopathy; Mitochondrial Myopathy; Myoneurogastrointestinal Disorder and Encephalopathy (MNGIE); Neuropathy, Ataxia, and Retinitis Pigmentosa (NARP); Pearson Syndrome; Pyruvate Carboxylase Deficiency; Pyruvate Dehydrogenase Deficiency; ~~a POLG Mutation;~~ a Respiratory Chain Disorder; Short-Chain Acyl-CoA Dehydrogenase Deficiency (SCAD); SCHAD; Very Long-Chain Acyl-CoA Dehydrogenase Deficiency (VLCAD); a myopathy; cardiomyopathy; encephalomyopathy; a neurodegenerative disease; Parkinson's disease; Alzheimer's disease; amyotrophic lateral sclerosis (ALS); a motor neuron disease; a neurological disease; epilepsy; an age-associated disease; macular degeneration; diabetes; metabolic syndrome; cancer; brain cancer; a genetic disease; Huntington's Disease; a mood disorder; schizophrenia; bipolar disorder; a pervasive developmental disorder; autistic disorder; Asperger's syndrome; childhood disintegrative disorder (CDD); Rett's disorder; PDD-not otherwise specified (PDD-NOS); a cerebrovascular accident; stroke; a vision impairment; optic neuropathy; dominant inherited juvenile optic atrophy; optic neuropathy caused by a toxic agent; glaucoma; Stargardt's macular dystrophy; diabetic retinopathy; diabetic maculopathy; retinopathy of prematurity; ischemic reperfusion-related retinal injury; oxygen poisoning; a haemoglobinopathy; thalassemia; sickle cell anemia; seizures; ischemia; renal tubular acidosis; attention deficit/hyperactivity disorder (ADHD); a neurodegenerative disorder resulting in hearing or balance impairment; Dominant Optic Atrophy (DOA); Maternally inherited diabetes and deafness (MIDD); chronic fatigue; contrast-induced kidney damage; contrast-induced retinopathy damage; Abetalipoproteinemia; retinitis pigmentosum; Wolfram's disease; Tourette syndrome; cobalamin c defect; methylmalonic aciduria; glioblastoma; Down's syndrome; acute tubular necrosis; a muscular dystrophy; a leukodystrophy; Progressive Supranuclear Palsy; spinal muscular atrophy; hearing loss; noise induced hearing loss; traumatic brain injury; Juvenile Huntington's Disease; Multiple Sclerosis; NGLY1; Multiple System Atrophy; Adrenoleukodystrophy; and Adrenomyeloneuropathy.

~~41. The method of claim 40, wherein the oxidative stress disorder is Multiple System Atrophy.~~

~~42. The method of claim 40, wherein the oxidative stress disorder is cancer.~~

~~43. The method of claim 40, wherein the oxidative stress disorder is bipolar disorder.~~

~~44. The method of claim 40, wherein the oxidative stress disorder is schizophrenia.~~

~~45. The method of claim 40, wherein the oxidative stress disorder is an age-associated disease.~~

~~46~~16. The ~~method~~ use of claim ~~40~~15, wherein the oxidative stress disorder is Huntington's Disease.

~~47. The method of claim 40, wherein the oxidative stress disorder is Alzheimer's disease.~~

~~48~~17. The ~~method~~ use of claim ~~40~~15, wherein the oxidative stress disorder is amyotrophic lateral sclerosis (ALS).

~~49. The method of claim 40, wherein the oxidative stress disorder is epilepsy.~~

~~50~~18. The ~~method~~ use of claim ~~40~~15, wherein the oxidative stress disorder is Parkinson's disease.

19. The use of claim 15, wherein the oxidative stress disorder is Multiple Sclerosis.

~~51. The method of claim 40, wherein the oxidative stress disorder is seizures.~~

~~52. The method of claim 40, wherein the oxidative stress disorder is stroke.~~

~~53. A process for the preparation of a polymorph of anhydrous (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide, wherein the process comprises the steps: (a) contacting (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide with a liquid comprising IPA; and (b) removing the liquid.~~

~~54. The process of claim 53, wherein the liquid is 100% IPA.~~

~~55. The process of claim 53, wherein the liquid is 98% IPA/2% water (v/v).~~

~~56. The process of any one of claims 53-55, wherein step (a) comprises dissolving the (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide in the liquid.~~

~~57. The process of any one of claims 53-55, wherein step (a) comprises slurrying the (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide in the liquid.~~

~~58. The process of any one of claims 53-57, wherein the process further comprises step (a)(i): adding heptane to the liquid.~~

~~59. The process of any one of claims 53-58, wherein step (b) comprises filtering the (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide.~~

~~60. The process of any one of claims 53-58, wherein the (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide in step (a) is at least 95% pure, exclusive of solvents.~~

~~61. A process for the preparation of a polymorph of anhydrous (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide, wherein the process comprises the steps: (a) dissolving (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-~~

dioxocyclohexa-1,4-dienyl)butanamide in EtOAc, (b) rapidly cooling the mixture from (a), and (c) isolating the (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide.

62. The process of claim 61, wherein the initial (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide in step (a) is Form I, as described in Table A or Table 2.

63. A process for the preparation of a polymorph of a solvate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide, wherein the process comprises the steps: (a) combining (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide and 0.5% MC/2%Tween 80 in water to create a slurry; (b) slurrying the mixture from (a), and (c) removing the 0.5% MC/2%Tween 80 in water.

64. The process of claim 63, wherein the initial (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide in step (a) is Form I, as described in Table A or Table 2.

65. The process of claim 63 or 64, wherein step (b) is performed for at least about 24 hours.

66. A process for the preparation of a polymorph of a solvate of (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide, wherein the process comprises the steps: (a) combining (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide and 0.5% MC in water to create a slurry; (b) slurrying the mixture from (a) for at least about 7 days, and (c) removing the 0.5% MC in water.

67. The process of claim 66, wherein the initial (R)-2-hydroxy-2-methyl-4-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dienyl)butanamide in step (a) is Form I, II, IV, V or VI, as described in Table A or Tables 2-3 or 5-7 respectively.

~~68. The polymorph of claim 1, wherein the polymorph is Form I, wherein a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 12.06, 17.03, and 17.26.~~

~~69. The polymorph of claim 1, wherein the polymorph is Form I, having a differential scanning calorimetry (DSC) thermogram substantially as shown in Figure 12.~~

~~70. The polymorph of claim 69, wherein the DSC thermogram has a single endothermic peak at about 152.9 °C.~~

~~71. The polymorph of claim 1, wherein the polymorph is Form I, having a thermogravimetric analysis (TGA) thermogram substantially as shown in 13.~~

~~72. The polymorph of claim 1, wherein the polymorph is Form I, having a ^{1}H NMR spectrum substantially as shown in Figure 40.~~

~~73. A composition comprising the polymorph of any one of claims 68-72, wherein the composition is essentially free of Forms II-VI, wherein Forms II-VI are described in Table A or Tables 3-7 respectively.~~

~~74. A composition comprising the polymorph of any one of claims 68-72, wherein at least about 95% by mole of the composition is the polymorph Form I, exclusive of any solvents, carriers or excipients.~~

~~75. The polymorph of claim 1, wherein the polymorph is Form V, wherein a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.61, 11.49, and 15.45.~~

~~76. The polymorph of claim 1, wherein the polymorph is Form V, having a differential scanning calorimetry (DSC) thermogram substantially as shown in Figure 31.~~

77. The polymorph of claim 76, wherein the DSC thermogram comprises three endothermic peaks at about 67.2, 92.2, and 150.6°C.

78. The polymorph of claim 1, wherein the polymorph is Form V, having a thermogravimetric analysis (TGA) thermogram substantially as shown in 32.

79. The polymorph of claim 1, wherein the polymorph is Form V, having a ^{1}H NMR spectrum substantially as shown in Figure 43.

80. A composition comprising the polymorph of any one of claims 75-79, wherein the composition is essentially free of Forms I-IV and VI, wherein Forms I-IV and VI are described in Table A or Tables 2 and 4-7, respectively.

81. A composition comprising the polymorph of any one of claims 75-79, wherein at least about 95% by mole of the composition is the polymorph Form V, exclusive of any solvents, carriers or excipients.

82. The polymorph of claim 1, wherein the polymorph is Form III, wherein a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 14.02, 15.23, and 21.10.

83. The polymorph of claim 1, wherein the polymorph is Form III, having a differential scanning calorimetry (DSC) thermogram substantially as shown in Figure 22.

84. The polymorph of claim 83, wherein the DSC thermogram comprises three endothermic peaks at about 72.0 and 150.7°C.

85. The polymorph of claim 1, wherein the polymorph is Form III, having a thermogravimetric analysis (TGA) thermogram substantially as shown in 23.

86. The polymorph of claim 1, wherein the polymorph is Form III, having a ^{1}H NMR spectrum substantially as shown in Figure 42.

87. A composition comprising the polymorph of any one of claims 82-86, wherein the composition is essentially free of Forms I-II and IV-VI, wherein Forms I-II and IV-VI are described in Table A or Tables 2-3 and 5-7 respectively.

88. A composition comprising the polymorph of any one of claims 82-86, wherein at least about 95% by mole of the composition is the polymorph Form III, exclusive of any solvents, carriers or excipients.

89. The polymorph of claim 1, wherein the polymorph is Form II, wherein a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 9.63, 11.33, and 19.33.

90. The polymorph of claim 1, wherein the polymorph is Form II, having a differential scanning calorimetry (DSC) thermogram substantially as shown in Figure 17.

91. The polymorph of claim 90, wherein the DSC thermogram comprises two endothermic peaks at about 133.9 and 151.3°C.

92. The polymorph of claim 1, wherein the polymorph is Form II, having a thermogravimetric analysis (TGA) thermogram substantially as shown in 18.

93. The polymorph of claim 1, wherein the polymorph is Form II, having a ^{1}H NMR spectrum substantially as shown in Figure 44.

94. A composition comprising the polymorph of any one of claims 89-93, wherein the composition is essentially free of Forms I, and III-VI, wherein Forms I, and III-VI are described in Table A or Tables 2-4 and 6-7 respectively.

95. A composition comprising the polymorph of any one of claims 82-86, wherein at least about 95% by mole of the composition is the polymorph Form II, exclusive of any solvents, carriers or excipients.

96. The polymorph of claim 1, wherein the polymorph is Form IV, wherein a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the following angular positions, wherein the angular positions may vary by ± 0.2: 4.31, 12.97, and 13.20.

97. The polymorph of claim 1, wherein the polymorph is Form IV, having a differential scanning calorimetry (DSC) thermogram substantially as shown in Figure 27.

98. The polymorph of claim 97, wherein the DSC thermogram comprises three endothermic peaks at about 70.5, 89.1, and 149.7°C.

99. The polymorph of claim 1, wherein the polymorph is Form IV, having a thermogravimetric analysis (TGA) thermogram substantially as shown in 28.

100. The polymorph of claim 1, wherein the polymorph is Form IV, having a ^{1}H NMR spectrum substantially as shown in Figure 41.

101. A composition comprising the polymorph of any one of claims 96-100, wherein the composition is essentially free of Forms I-III and V-VI, wherein Forms I-III and V-VI are described in Table A or Tables 2-5 and 7 respectively.

102. A composition comprising the polymorph of any one of claims 96-100, wherein at least about 95% by mole of the composition is the polymorph Form IV, exclusive of any solvents, carriers or excipients.

103. The polymorph of claim 1, wherein the polymorph is Form VI, wherein a powder X-ray diffraction pattern for the polymorph comprises characteristic peaks at least at the

following angular positions, wherein the angular positions may vary by ± 0.2: 6.27, 9.91, and 12.94.

104. The polymorph of claim 1, wherein the polymorph is Form VI, having a differential scanning calorimetry (DSC) thermogram substantially as shown in Figure 35.

105. The polymorph of claim 104, wherein the DSC thermogram comprises three endothermic peaks at about 93.2, 135.2, and 151.0°C.

106. The polymorph of claim 1, wherein the polymorph is Form VI, having a thermogravimetric analysis (TGA) thermogram substantially as shown in 36.

107. The polymorph of claim 1, wherein the polymorph is Form VI, having a ^{1}H NMR spectrum substantially as shown in Figure 45.

108. A composition comprising the polymorph of any one of claims 103-107, wherein the composition is essentially free of Forms I-V, wherein Forms I-V are described in Table A or Tables 2-6 respectively.

109. A composition comprising the polymorph of any one of claims 103-107, wherein at least about 95% of the composition is the polymorph Form VI, exclusive of any solvents, carriers or excipients.

110. A composition comprising a polymorph of claim 1, wherein the composition comprises Form I and II.

111. A composition comprising a polymorph of claim 1, wherein the composition comprises Form I and III.

112. A composition comprising a polymorph of claim 1, wherein the composition comprises Form I and IV.

~~113. A composition comprising a polymorph of claim 1, wherein the composition comprises Form I and V.~~

~~114. A composition comprising a polymorph of claim 1, wherein the composition comprises Form I and VI.~~

~~115. A composition comprising a polymorph of claim 1, wherein the composition comprises Form II and III.~~

~~116. A composition comprising a polymorph of claim 1, wherein the composition comprises Form II and IV.~~

~~117. A composition comprising a polymorph of claim 1, wherein the composition comprises Form II and V.~~

~~118. A composition comprising a polymorph of claim 1, wherein the composition comprises Form II and VI.~~

~~119. A composition comprising a polymorph of claim 1, wherein the composition comprises Form III and IV.~~

~~120. A composition comprising a polymorph of claim 1, wherein the composition comprises Form III and V.~~

~~121. A composition comprising a polymorph of claim 1, wherein the composition comprises Form III and VI.~~

~~122. A composition comprising a polymorph of claim 1, wherein the composition comprises Form IV and V.~~

~~123. A composition comprising a polymorph of claim 1, wherein the composition comprises Form IV and VI.~~

~~124. A composition comprising a polymorph of claim 1, wherein the composition comprises Form V and VI.~~

~~125. A composition comprising the polymorph of any one of claims 110-124, wherein at least about 95% by mole of the composition is the polymorph Form VI, exclusive of any solvents, carriers or excipients.~~