

PEPTIDE INHIBITORS OF INTERLEUKIN-23 RECEPTOR AND PHARMACEUTICAL COMPOSITIONS THEREOF

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Patent Application No. 63/305,631, filed February 1, 2022, which is incorporated herein by reference in its entirety.

SEQUENCE LISTING

[0002] The contents of the electronic sequence listing (242272001440SEQLIST.xml; Size: 5,358 bytes; and Date of Creation: January 26, 2023) is herein incorporated by reference in its entirety.

FIELD OF THE INVENTION

[0003] The present invention relates to peptide inhibitor of the interleukin-23 receptor (IL-23R) or salt, solvates or forms thereof, corresponding pharmaceutical compositions, methods and/or uses for treatment of autoimmune inflammation diseases and related disorders.

BACKGROUND

[0004] The interleukin-23 (IL-23) cytokine has been implicated as playing a crucial role in the pathogenesis of autoimmune inflammation and related diseases and disorders, such as multiple sclerosis, asthma, rheumatoid arthritis, psoriasis, and inflammatory bowel diseases (IBDs), *e.g.*, ulcerative colitis and Crohn's disease. Studies in acute and chronic mouse models of IBD revealed a primary role of IL-23R and downstream effector cytokines in disease pathogenesis. IL-23R is expressed on various adaptive and innate immune cells including Th17 cells, $\gamma\delta$ T cells, natural killer (NK) cells, dendritic cells, macrophages, and innate lymphoid cells, which are found abundantly in the intestine. At the intestine mucosal surface, the gene expression and protein levels of IL-23R are found to be elevated in IBD patients. It is believed that IL-23 mediates this effect by promoting the development of a pathogenic CD4⁺ T cell population that produces IL-6, IL-17, and tumor necrosis factor (TNF).

[0005] Production of IL-23 is enriched in the intestine, where it is believed to play a key role in regulating the balance between tolerance and immunity through T-cell-dependent and T-cell-independent pathways of intestinal inflammation through effects on T-helper 1 (Th1) and Th17-

associated cytokines, as well as restraining regulatory T-cell responses in the gut, favoring inflammation. In addition, polymorphisms in the IL-23 receptor (IL-23R) have been associated with susceptibility to inflammatory bowel diseases (IBDs), further establishing the critical role of the IL-23 pathway in intestinal homeostasis.

[0006] Psoriasis (PsO), a chronic skin disease affecting about 2%-3% of the general population has been shown to be mediated by the body's T cell inflammatory response mechanisms. IL-23 has one of several interleukins implicated as a key player in the pathogenesis of psoriasis, purportedly by maintaining chronic autoimmune inflammation via the induction of interleukin-17, regulation of T memory cells, and activation of macrophages. Expression of IL-23 and IL-23R has been shown to be increased in tissues of patients with psoriasis, and antibodies that neutralize IL-23 showed IL-23-dependent inhibition of psoriasis development in animal models of psoriasis.

[0007] IL-23 is a heterodimer composed of a unique p19 subunit and the p40 subunit shared with IL-12, which is a cytokine involved in the development of interferon- γ (IFN- γ)-producing T helper 1 (T_H1) cells. Although IL-23 and IL-12 both contain the p40 subunit, they have different phenotypic properties. For example, animals deficient in IL-12 are susceptible to inflammatory autoimmune diseases, whereas IL-23 deficient animals are resistant, presumably due to a reduced number of CD4⁺ T cells producing IL-6, IL-17, and TNF in the CNS of IL-23-deficient animals. IL-23 binds to IL-23R, which is a heterodimeric receptor composed of IL-12R β 1 and IL-23R subunits. Binding of IL-23 to IL-23R activates the Jak-stat signaling molecules, Jak2, Tyk2, and Stat1, Stat 3, Stat 4, and Stat 5, although Stat4 activation is substantially weaker and different DNA-binding Stat complexes form in response to IL-23 as compared with IL-12. IL-23R associates constitutively with Jak2 and in a ligand-dependent manner with Stat3. In contrast to IL-12, which acts mainly on naive CD4(+) T cells, IL-23 preferentially acts on memory CD4(+) T cells.

[0008] Efforts have been made to identify therapeutic moieties that inhibit the IL-23 pathway, for use in treating IL-23-related diseases and disorders. A number of antibodies that bind to IL-23 or IL-23R have been identified, including ustekinumab, an antibody that binds the p40 subunit of IL-23, which has been approved for the treatment of moderate to severe plaque psoriasis, active psoriatic arthritis, moderately to severely active Crohn's disease and moderately to severely active ulcerative colitis. More recently, polypeptide inhibitors that bind to IL-23R and inhibit the binding of IL-23 to IL-23R have been identified (see, e.g., US Patent Application Publication No. US2013/0029907). Clinical trials in Crohn's Disease or psoriasis with briakinumab (which also target the common p40 subunit) and tildrakizumab, guselkumab, MEDI2070, and BI-655066 (which target the unique p19 subunit of IL-23) highlight the

potential of IL-23 signaling blockade in treatment of human inflammatory diseases. While these findings are promising, challenges remain with respect to successful delivery of such therapeutics to their target. Effective delivery can improve the treatment of intestinal inflammation, such as intestinal bowel diseases, including Crohn's disease, ulcerative colitis and related disorders.

[0009] An inhibitor of IL-23R was described as Peptide #104 in PCT publication WO 2021/146441 and US 2021/0261622, the disclosures of which are incorporated herein by reference in their entireties.

[0010] There remains a need in the art to develop effective pharmaceutical vehicles, such as pharmaceutical compositions, to deliver therapeutic agents to treat and prevent IL-23 and/or IL-23R associated diseases, especially those associated with autoimmune inflammation, such as in the intestinal tract, which may include, but are not limited to inflammatory bowel disease (IBD), ulcerative colitis, Crohn's Disease (CD), psoriasis, or psoriatic arthritis and the like.

[0011] The present invention addresses these needs by providing pharmaceutical compositions of peptide inhibitors or pharmaceutically acceptable salt or solvate forms thereof that: bind IL-23R to inhibit IL-23 binding, IL-23 signaling through IL-23 receptor and/or IL-23 Pathway, for treatment of inflammatory diseases or disorders (i.e., e.g., which may include, but is not limited to psoriasis, psoriatic arthritis, inflammatory bowel disease, ulcerative colitis, Crohn's disease and the like), which include, but not limited to aforementioned diseases or disorders that may be moderate to severe in degree and suitable for oral administration. In addition, pharmaceutical compositions and corresponding methods and/or uses for specific targeting of IL-23R from the luminal side of the gut can provide therapeutic benefit to IBD patients suffering from local inflammation of the intestinal tissue.

BRIEF SUMMARY

[0012] Provided herein are crystalline forms of a peptide inhibitor of the interleukin-23 receptor (IL-23R) as well as pharmaceutical compositions, methods and/or uses for treatment of autoimmune inflammation diseases and related disorders. Crystalline forms have advantageous properties such as ease of isolation, enhanced purity, and greater physical and chemical stability compared to analogous amorphous forms. These attributes can be particularly important for pharmaceutical agents where large-scale production, reproducibility, and compound purity are required. Crystalline forms of peptides may be uniquely advantageous as the corresponding amorphous forms are often unsuitable for formulating, such as tableting.

[0013] In general, the present invention relates to peptide inhibitor of the interleukin-23 receptor (IL-23R) or hydrochloride salt, solvates or forms thereof, corresponding pharmaceutical

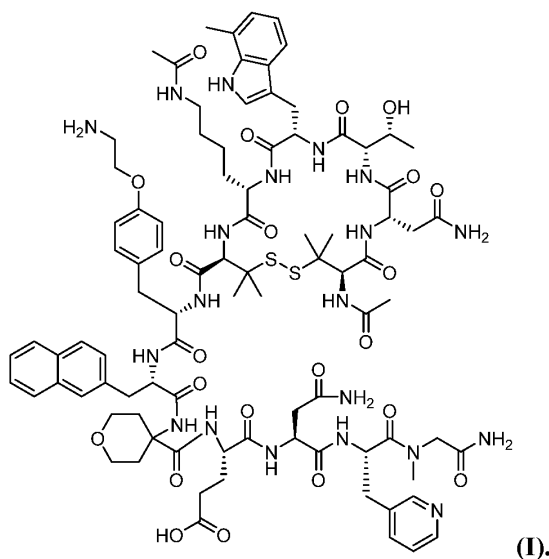
compositions, methods and/or uses for treatment of autoimmune inflammation diseases and related disorders.

[0014] In particular, the present invention relates to pharmaceutical compositions of peptide inhibitors of the interleukin-23 receptor (IL-23R) or hydrochloride salt, solvates or forms thereof, corresponding methods and/or uses for treatment of autoimmune inflammation and related diseases and disorders.

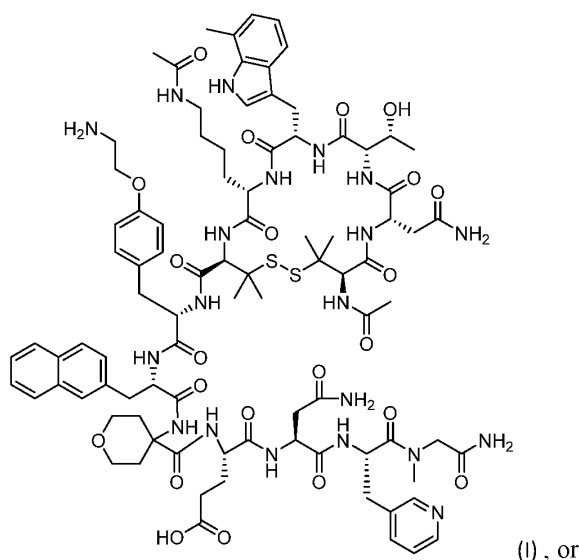
[0015] In particular, the present invention relates to pharmaceutical compositions of peptide inhibitors of the interleukin-23 receptor (IL-23R) or pharmaceutically acceptable salt, solvates or forms thereof, corresponding methods and/or uses for treatment of autoimmune inflammation and related diseases and disorders.

[0016] The present invention relates to pharmaceutical compositions as described herein, which comprises a crystalline form of the peptide of SEQ ID NO: 1:

Ac-[Pen]*-N-T-[W(7-Me)]-[Lys(Ac)]-[Pen]*-Phe[4-(2-aminoethoxy)]-[2-Nal]-[THP]-E-N-[3-Pal]-Sarc-NH₂ (in which [Pen]*-[Pen]* form a disulfide bond); or a pharmaceutically acceptable salt thereof, or a solvate of the foregoing, having the structure of Formula (I):



[0017] In particular, the present invention provides a crystalline hydrochloride salt form of a compound of Formula (I) that has the structure:



a solvate thereof.

[0018] The present invention also provides a crystalline form of a peptide of SEQ ID NO: 1, or a pharmaceutically acceptable salt thereof, or a solvate of the foregoing. The pharmaceutically acceptable salts of a peptide of SEQ ID NO: 1 provided herein include hydrochloride salts, bis-hydrochloride salts, acetate salts, fumarate salts, glutarate salts, glycolate salts, mesylate salts, sulfate salts, and citrate salts.

[0019] The present invention also provides a crystalline form of a compound of Formula (I), or a pharmaceutically acceptable salt thereof, or a solvate of the foregoing. The pharmaceutically acceptable salts of the compound of Formula (I) provided herein include hydrochloride salt, bis-hydrochloride salt, acetate salt, fumarate salt, glutarate salt, glycolate salt, mesylate salt, sulfate salt, and citrate salt.

[0020] Further provided herein is a crystalline form of a free base of a peptide of a compound of Formula (I), or a solvate thereof.

[0021] Further provided herein is a crystalline form of a free base of a compound of Formula (I) or a solvate thereof.

[0022] The present invention further provides pharmaceutical compositions that include the hydrochloride salt form of the peptide of a compound of Formula (I), or solvate thereof, wherein the hydrochloride salt form of peptide of SEQ ID NO: 1 is characterized by an XRPD pattern substantially as set forth in FIG. 1.

[0023] The present invention further provides pharmaceutical compositions that include the hydrochloride salt form of the compound of Formula (I) or solvate thereof, and a pharmaceutically acceptable excipient, characterized by an X-ray powder diffraction (XRPD) pattern substantially as set forth in FIG. 1.

[0024] The present invention further provides pharmaceutical compositions that include the hydrochloride salt form of the peptide of SEQ ID NO: 1 or solvate thereof, and one or more pharmaceutically acceptable excipients, wherein the hydrochloride salt form of peptide of SEQ ID NO: 1 is characterized by an XRPD pattern substantially as set forth in FIG. 2.

[0025] The present invention further provides pharmaceutical compositions that include the hydrochloride salt form of the peptide of SEQ ID NO: 1 or solvate thereof, and one or more pharmaceutically acceptable excipients, wherein the hydrochloride salt form of peptide of SEQ ID NO: 1 is characterized by an XRPD pattern substantially as set forth in FIG. 3.

[0026] The present invention further provides pharmaceutical compositions that include the acetate salt form of the peptide of SEQ ID NO: 1 or solvate thereof, and one or more pharmaceutically acceptable excipients, wherein the acetate salt form of the peptide of SEQ ID NO: 1 is characterized by an XRPD pattern substantially as set forth in FIG. 7.

[0027] The present invention further provides pharmaceutical compositions that include the fumarate salt form of the peptide of SEQ ID NO: 1 or solvate thereof, and one or more pharmaceutically acceptable excipients, wherein the fumarate salt form of the peptide of SEQ ID NO: 1 is characterized by an XRPD pattern substantially as set forth in FIG. 15.

[0028] The present invention further provides pharmaceutical compositions that include the glutarate salt form of the peptide of SEQ ID NO: 1 or solvate thereof, and one or more pharmaceutically acceptable excipients, wherein the glutarate salt form of the peptide of SEQ ID NO: 1 is characterized by an XRPD pattern substantially as set forth in FIG. 18.

[0029] The present invention further provides pharmaceutical compositions that include the glycolate salt form of the peptide of SEQ ID NO: 1 or solvate thereof, and one or more pharmaceutically acceptable excipients, wherein the glycolate salt form of the peptide of SEQ ID NO: 1 is characterized by an XRPD pattern substantially as set forth in FIG. 21.

[0030] The present invention further provides pharmaceutical compositions that include the mesylate salt form of the peptide of SEQ ID NO: 1 or solvate thereof, and one or more pharmaceutically acceptable excipients, wherein the mesylate salt form of the peptide of SEQ ID NO: 1 is characterized by an XRPD pattern substantially as set forth in FIG. 24.

[0031] The present invention further provides pharmaceutical compositions that include the sulfate salt form of the peptide of SEQ ID NO: 1 or solvate thereof, and one or more pharmaceutically acceptable excipients, wherein the sulfate salt form of the peptide of SEQ ID NO: 1 is characterized by an XRPD pattern substantially as set forth in FIG. 26.

[0032] The present invention further provides pharmaceutical compositions that include the citrate salt form of the peptide of SEQ ID NO: 1 or solvate thereof, and one or more

pharmaceutically acceptable excipients, wherein the citrate salt form of the peptide of SEQ ID NO: 1 is characterized by an XRPD pattern substantially as set forth in FIG. 28.

[0033] The present invention further provides pharmaceutical compositions that include the bis-hydrochloride salt form of the peptide of SEQ ID NO: 1 or solvate thereof, and one or more pharmaceutically acceptable excipients, wherein the bis-hydrochloride salt form of the peptide of SEQ ID NO: 1 is characterized by an XRPD pattern substantially as set forth in FIG. 29.

[0034] The present invention further provides pharmaceutical compositions that include the free base form of the peptide of SEQ ID NO: 1 or solvate thereof, and one or more pharmaceutically acceptable excipients, wherein the free base form of the peptide of SEQ ID NO: 1 is characterized by an XRPD pattern substantially as set forth in FIG. 11.

[0035] The present invention further provides pharmaceutical compositions that include the hydrochloride salt form of the compound of Formula (I) or solvate thereof, and a pharmaceutically acceptable excipient, wherein the hydrochloride salt form of the compound of Formula (I) is characterized by an XRPD pattern substantially as set forth in FIG. 3.

[0036] The present invention further provides pharmaceutical compositions that include the acetate salt form of the compound of Formula (I) or solvate thereof, and a pharmaceutically acceptable excipient, wherein the acetate salt form of the compound of Formula (I) is characterized by an XRPD pattern substantially as set forth in FIG. 7.

[0037] The present invention further provides pharmaceutical compositions that include the fumarate salt form of the compound of Formula (I) or solvate thereof, and a pharmaceutically acceptable excipient, wherein the fumarate salt form of the compound of Formula (I) is characterized by an XRPD pattern substantially as set forth in FIG. 15.

[0038] The present invention further provides pharmaceutical compositions that include the glutarate salt form of the compound of Formula (I) or solvate thereof, and a pharmaceutically acceptable excipient, wherein the glutarate salt form of the compound of Formula (I) is characterized by an XRPD pattern substantially as set forth in FIG. 18.

[0039] The present invention further provides pharmaceutical compositions that include the glycolate salt form of the compound of Formula (I) or solvate thereof, and a pharmaceutically acceptable excipient, wherein the glycolate salt form of the compound of Formula (I) is characterized by an XRPD pattern substantially as set forth in FIG. 21.

[0040] The present invention further provides pharmaceutical compositions that include the mesylate salt form of the compound of Formula (I) or solvate thereof, and a pharmaceutically acceptable excipient, wherein the mesylate salt form of the compound of Formula (I) is characterized by an XRPD pattern substantially as set forth in FIG. 24.

[0041] The present invention further provides pharmaceutical compositions that include the sulfate salt form of the compound of Formula (I) or solvate thereof, and a pharmaceutically acceptable excipient, wherein the sulfate salt form of the compound of Formula (I) is characterized by an XRPD pattern substantially as set forth in FIG. 26.

[0042] The present invention further provides pharmaceutical compositions that include the citrate salt form of the compound of Formula (I) or solvate thereof, and a pharmaceutically acceptable excipient, wherein the citrate salt form of the compound of Formula (I) is characterized by an XRPD pattern substantially as set forth in FIG. 28.

[0043] The present invention further provides pharmaceutical compositions that include the bis-hydrochloride salt form of the compound of Formula (I) or solvate thereof, and a pharmaceutically acceptable excipient, wherein the bis-hydrochloride salt form of the compound of Formula (I) is characterized by an XRPD pattern substantially as set forth in FIG. 28.

[0044] The present invention further provides pharmaceutical compositions that include the glycolate salt form of the compound of Formula (I) or solvate thereof, and a pharmaceutically acceptable excipient, wherein the glycolate salt form of the compound of Formula (I) is characterized by an XRPD pattern substantially as set forth in FIG. 21.

[0045] The present invention further provides pharmaceutical compositions that include the free base form of the compound of Formula (I) or solvate thereof, and a pharmaceutically acceptable excipient, wherein the free base form of the compound of Formula (I) is characterized by an XRPD pattern substantially as set forth in FIG. 11.

[0046] Also provided herein is a composition comprising a hydrochloride salt form of a peptide of the compound of Formula (I), or a solvate thereof, in an amount of from about 0.1% to about 15% (w/w) of the composition; and one or more pharmaceutically acceptable excipients.

[0047] Further provided herein is a composition comprising a crystalline form of a peptide of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, or a solvate of the foregoing, in an amount of from about 0.1% to about 60% (w/w) of the composition; and one or more pharmaceutically acceptable excipients.

[0048] Further provided herein is a composition comprising a hydrochloride salt form of a peptide of the compound of Formula (I), or a solvate thereof, in an amount of from about 0.1% to about 15% (w/w) of the composition; an absorption enhancer in an amount of from about 5% to about 50% (w/w) of the composition; and one or more pharmaceutically acceptable excipients.

[0049] Also provided herein is a composition comprising a crystalline form of a peptide of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, or a solvate of the

foregoing, in an amount of from about 0.1% to 60% (w/w), of the composition; an absorption enhancer in an amount of from about 5% to about 65% (w/w) of the composition; and one or more pharmaceutically acceptable excipients.

[0050] Provided herein is a method including: forming a mixture comprising a hydrochloride salt form of a peptide of the compound of Formula (I) , or a solvate thereof, a silicified microcrystalline cellulose, sorbitol, crospovidone, and a silica (e.g., Aerosil 200); adding magnesium stearate to the mixture; compressing the mixture; and applying a subcoating to the mixture, to form a tablet.

[0051] Also provided herein is a method including: forming a mixture comprising a hydrochloride salt form of a peptide of the compound of Formula (I) , or a solvate thereof, sodium caprate, a microcrystalline cellulose, sorbitol, a silica (e.g., Aerosil 200), a silicified microcrystalline cellulose and crospovidone to form a core tablet; applying a subcoating over the core tablet; and applying an enteric coating over the subcoating to form a tablet.

[0052] Further provided are tablets formed by the methods described herein.

[0053] The present invention provides a method of treating inflammatory disease, which comprises administering to the subject a therapeutically effective amount of a composition of the present invention to a subject or patient in need thereof as described herein.

[0054] The present invention provides a method of treating inflammatory bowel diseases (IBD), which comprises administering a therapeutically effective amount of a composition of the present invention to a subject or patient in need thereof.

[0055] The present invention provides use of the compositions of the present invention in the manufacture of a medicament for treating an inflammatory bowel disease (IBD).

[0056] The present invention provides a method of treating psoriasis or psoriatic arthritis in a subject that includes administering to the subject a therapeutically effective amount of a composition of the present invention described herein.

[0057] The present invention provides use of the compositions of the present invention, in the manufacture of a medicament for treating psoriasis or psoriatic arthritis.

BRIEF DESCRIPTION OF THE DRAWINGS

[0058] FIG. 1 shows an X-ray powder diffraction (XRPD) pattern of a crystalline form of a hydrochloride salt of a compound of Formula (I) .

[0059] FIG. 2 shows an XRPD pattern of a crystalline form of a hydrochloride salt of a compound of Formula (I) .

- [0060] FIG. 3 shows an XRPD pattern of a crystalline form of a hydrochloride salt of a compound of Formula (I) .
- [0061] FIG. 4 shows a thermogravimetric analysis (TGA) graph of a crystalline form of a hydrochloride salt of a compound of Formula (I) .
- [0062] FIG. 5 shows a differential scanning calorimetry (DSC) graph of a crystalline form of a hydrochloride salt of a peptide of a compound of Formula (I) .
- [0063] FIG. 6 shows a dynamic vapor sorption (DVS) curve of a crystalline form of a hydrochloride salt of a peptide of a compound of Formula (I) .
- [0064] FIG. 7 shows an XRPD pattern of a crystalline form of an acetate salt of a peptide of a compound of Formula (I) .
- [0065] FIG. 8 shows a TGA graph of a crystalline form of an acetate salt of a compound of Formula (I) .
- [0066] FIG. 9 shows a DSC graph of a crystalline form of an acetate salt of a compound of Formula (I) .
- [0067] FIG. 10 shows a DVS curve of a crystalline form of an acetate salt of a compound of Formula (I) .
- [0068] FIG. 11 shows an XRPD pattern of a crystalline form of a free base of a compound of Formula (I) .
- [0069] FIG. 12 shows a TGA graph of a crystalline form of a free base of a compound of Formula (I) .
- [0070] FIG. 13 shows a DSC graph of a crystalline form of a free base of a compound of Formula (I) .
- [0071] FIG. 14 shows a DVS curve of a crystalline form of a free base of a compound of Formula (I) .
- [0072] FIG. 15 shows an XRPD pattern of a crystalline form of a fumarate salt of a mesylate peptide of SEQ ID NO: 1.
- [0073] FIG. 16 shows a TGA graph of a crystalline form of a fumarate salt of a compound of Formula (I) .
- [0074] FIG. 17 shows a DSC graph of a crystalline form of a fumarate salt of a compound of Formula (I) .
- [0075] FIG. 18 shows an XRPD pattern of a crystalline form of a glutarate salt of a compound of Formula (I) .
- [0076] FIG. 19 shows a simultaneous thermal analysis (SDT) thermogram of a crystalline form of a glutarate salt of a compound of Formula (I) .

[0077] FIG. 20 shows a DVS curve of a crystalline form of a glutarate salt of a compound of Formula (I) .

[0078] FIG. 21 shows an XRPD pattern of a crystalline form of a glycolate salt of a compound of Formula (I) .

[0079] FIG. 22 shows a simultaneous thermal analysis (SDT) thermogram of a crystalline form of a glycolate salt of a compound of Formula (I) .

[0080] FIG. 23 shows a DVS curve of a crystalline form of a glycolate salt of a compound of Formula (I) .

[0081] FIG. 24 shows an XRPD pattern of a crystalline form of a mesylate salt of a compound of Formula (I) .

[0082] FIG. 25 shows a simultaneous thermal analysis (SDT) thermogram of a crystalline form of a mesylate salt of a compound of Formula (I) .

[0083] FIG. 26 shows an XRPD pattern of a crystalline form of a sulfate salt of a compound of Formula (I) .

[0084] FIG. 27 shows a simultaneous thermal analysis (SDT) thermogram of a crystalline form of a sulfate salt of a compound of Formula (I) .

[0085] FIG. 28 shows an XRPD pattern of a crystalline form of a citrate salt of a compound of Formula (I) .

[0086] FIG. 29 shows an XRPD pattern of a crystalline form of a bis-hydrochloride salt of a compound of Formula (I) .

[0087] FIG. 30 shows a TGA graph of a crystalline form of a bis-hydrochloride salt of a compound of Formula (I) .

[0088] FIG. 31 shows a DSC graph of a crystalline form of a bis-hydrochloride salt of a compound of Formula (I) .

[0089] FIG. 32 shows a DVS curve of a crystalline form of a bis-hydrochloride salt of a compound of Formula (I) .

DETAILED DESCRIPTION

I. GENERAL

[0090] The present invention relates to peptide inhibitors of the interleukin-23 receptor (IL-23R) or pharmaceutically acceptable salts thereof, or solvates of thereof, corresponding pharmaceutical compositions, methods and/or uses for treatment of autoimmune inflammation and related diseases and disorders. In particular, the present invention relates to crystalline forms of a peptide inhibitor of IL-23R and pharmaceutically acceptable compositions thereof.

[0091] In general, the present invention relates to hydrochloride salt compositions of peptide inhibitors of the interleukin-23 receptor (IL-23R) or solvates thereof, corresponding pharmaceutical compositions, methods and/or uses for treatment of autoimmune inflammation and related diseases and disorders.

II. DEFINITIONS

[0092] “A,” “an,” or “a(n),” is an indefinite article when used in reference to a group of substituents or “substituent group” herein, mean at least one.

[0093] “About” when referring to a value includes the stated value +/- 10% of the stated value. For example, about 50% includes a range of from 45% to 55%, while about 20 molar equivalents includes a range of from 18 to 22 molar equivalents. Accordingly, when referring to a range, “about” refers to each of the stated values +/- 10% of the stated value of each end of the range. For instance, a ratio of from about 1 to about 3 (weight/weight) includes a range of from 0.9 to 3.3. In some embodiments, reference to about a value or parameter includes a description of that value or parameter per se. For example, reference to about 20 molar equivalents includes and describes 20 molar equivalents per se.

[0094] “Absorption enhancer” refers to a component that improves or facilitates the mucosal absorption of a drug in the gastrointestinal tract, such as a permeation enhancer or intestinal permeation enhancer. As conventionally understood in the art, permeation enhancers (PEs) are agents aimed to improve oral delivery of therapeutic drugs with poor bioavailability. PEs are capable of increasing the paracellular and/or transcellular passage of drugs. Pharmaceutical excipients that can increase permeation have been termed ‘absorption modifying excipients’ (AMEs). AMEs may be used in oral compositions, for example, as wetting agents (sodium dodecyl sulfate), antioxidants (e.g. EDTA), and emulsifiers (e.g. macrogol glycerides), and may be specifically included in compositions as PEs to improve bioavailability. PEs can be categorized as to how they alter barrier integrity via paracellular or transcellular routes.

[0095] “Intestinal permeation enhancer (IPE)” refers to a component that improves the bioavailability of a component. Suitable representative IPEs for use in the present invention, include, but are not limited to, various surfactants, fatty acids, medium chain glycerides, steroidal detergents, acyl carnitine and alkanoylcholines, *N*-acetylated alpha-amino acids and *N*-acetylated non-alpha-amino acids, and chitosans, other mucoadhesive polymers and the like. For example, a suitable IPE for use in the present invention may be sodium caprate.

[0096] “Administering” refers to administration of the composition of the present invention to a subject.

[0097] “Composition” or “Pharmaceutical Composition” as used herein is intended to encompass an invention or product comprising the specified active product ingredient (API),

which may include pharmaceutically acceptable excipients, carriers or diluents as described herein, such as in specified amounts defined throughout the originally filed disclosure, which results from combination of specific components, such as specified ingredients in the specified amounts as described herein.

[0098] “Granulated mixture” refers to a mixture of two or more agents made by mixing the two or more agents and granulating them together in a particulate form. Such a mixture provides particulate material that is composed of two or more agents. For example, in the present invention, the compositions may include, but are not limited to granulated mixtures of a hydrochloride salt form of the peptide of SEQ ID NO: 1 or solvate thereof and absorption or permeation enhancer, such as sodium caprate. Such a granulated mixture is formed into a particle or tablet forms, which contain a hydrochloride salt form of a compound of Formula (I) or solvate thereof and sodium caprate. In some embodiments, the compositions may include granulated mixtures comprising sodium caprate.

[0099] “Disintegrant” refers to a pharmaceutical excipient that is incorporated into a composition to promote their disintegration when they come into contact with a liquid. For example, a disintegrant is a pharmaceutically acceptable agent, used in preparation of tablets, which causes tablets to disintegrate and release medicinal substances on contact with moisture. Examples of disintegrants include, without limitation, crosslinked polymers, including crosslinked polyvinylpyrrolidone (crospovidone), crosslinked sodium carboxymethyl cellulose (croscarmellose sodium), and modified starch sodium starch glycolate and the like.

Representative disintegrants for use in the present invention, may include, but are not limited to, agar-agar, alginic acid, calcium carbonate, microcrystalline cellulose, croscarmellose sodium, crospovidone, polacrilin potassium, sodium starch glycolate, potato or tapioca starch, other starches, pre-gelatinized starch, clays, other alginates, other celluloses, gums (like gellan), low-substituted hydroxypropyl cellulose, or mixtures thereof and the like. In some aspects, disintegrants for use in the present invention, may include, but are not limited to croscarmellose sodium. Additional representative disintegrants for use in the present invention, may include, but are not limited to microcrystalline cellulose, croscarmellose sodium, alginic acid, sodium alginate, crospovidone, cellulose, agar and related gums, sodium starch glycolate, corn starch, potato starch, sodium starch glycolate, Veegum HV, methylcellulose, agar, bentonite, carboxymethylcellulose, alginic acid, guar gum combinations thereof, and the like.

Representative disintegrants for use in the present invention, include, but are not limited to, starches, clays, celluloses, alginates and gums and crosslinked starches, celluloses and polymers, combinations thereof and the like.

[0100] “Disposed over” refers to the placement of one phase or coating on top of another phase or coating. Such placement can conform to the shape of the underlying phase or coating such that the layering of phases and coatings do not leave substantial gaps there between.

[0101] “Enteric coating” refers to any of the commonly applied polymeric coatings employed for delayed release of active ingredients. As conventionally understood in the art, an enteric coating generally is a polymer barrier applied to oral medication that prevents its dissolution or disintegration in the gastric environment. This helps by either protecting drugs from the acidity of the stomach, the stomach from the detrimental effects of the drug, or to release the drug after the stomach (usually in the upper tract of the intestine). Some drugs are unstable at the pH of gastric acid and need to be protected from degradation. An enteric coating is also an effective method to obtain drug targeting (such as gastro-resistant drugs). Such delayed release is typically pH dependent and allows for release of the active ingredient further in the intestinal tract where the pH differs from that in the stomach. In general, suitable materials used for enteric coatings may include, but is not limited to fatty acids, waxes, shellac, plastics, and plant fibers, where such enteric materials, may include, but is not limited to cellulose acetate phthalate, polyvinylalcohol phthalate, shellac, zein, hydroxypropylmethyl cellulose phthalate, cellulose acetate trimaleate, film resins, etc and the like. Additional examples of enteric coating for use in the present invention, may include, without limitation, those based on esters of aleuritic acid, cellulose acetate phthalate (CAP), poly(methacrylic acid-co-methyl methacrylate), poly(vinyl acetate phthalate) (PVAP), cellulose acetate trimellitate (CAT), hydroxypropyl methylcellulose phthalate (HPMCP) and the like. Other suitable materials used for enteric coatings may also include, but is not limited to methacrylic acid copolymers, poly(methacrylic acid ethyl acrylate) 1:1, poly(methacrylic acid methyl methacrylate) 1:2, poly(methacrylic acid ethyl acrylate) (L100D-55), combinations of methyl acrylate, methyl methacrylate, hydroxypropyl methylcellulose (HPMC), methacrylic acid (FS30D), Eudragit®, hydroxypropyl methylcellulose acetate succinate (HPMC-AS), and Type L, M or H of HPMC-AS. In some embodiments, the enteric coating is disposed over a subcoating.

[0102] “Glidant” refers to a substance that is added to a powder to improve its flowability and/or lubricity. Examples of glidants, may include, but is not limited to, magnesium stearate, fumed silica, starch, talc and the like.

[0103] “Silica” refers to a pharmaceutical excipient that can be employed as flow agent (anti-caking), adsorbent and desiccant in solid product forms. It can also be used to increase the mechanical stability and the disintegration rate of the compositions. The silica can be fumed, *i.e.*, referring to its production through a pyrogenic process to generate fine particles of silica. Particles of fumed silica can vary in size such as from 5 nm to 100 nm, or from 5 to 50 nm. The

particles can be non-porous and have a surface area from 50–1,000 m²/g or from 50–600 m²/g. Examples of silicas include Aerosil 200, having a specific surface area of about 200 m²/g. The silica can be hydrophilic. Examples of suitable silica materials include, but are not limited to SiO₂, colloidal silicon dioxide, aerosol, colloidal silica, fumed silica, silicon dioxide fumed, colloidal anhydrous silica, colloidal silicon dioxide, and the like.

[0104] “Lubricant” refers to a substance added to a formulation to reduce friction. Compounds that serve as lubricants can also have properties as glidants. Examples of lubricants may include, but are not limited to, talc, silica, and fats such as vegetable stearin, magnesium stearate or stearic acid and the like.

[0105] “Microcrystalline cellulose,” or “MCC,” refers to a pharmaceutical grade of cellulose manufactured from a refined wood pulp. The MCC can be unmodified or chemically modified, such as silicified microcrystalline cellulose (SMCC). MCC can serve the function of a bulking agent and aid in tablet formation due to its favorable compressibility characteristics.

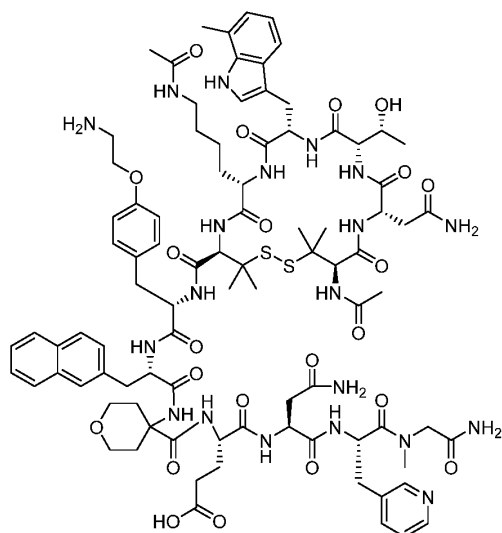
[0106] “Patient” or “subject” refers to a living organism, which includes, but is not limited to a human subject suffering from or prone to a disease or condition that can be treated by administration of a pharmaceutical composition as provided herein. Further non-limiting examples may include, but is not limited to humans, other mammals, bovines, rats, mice, dogs, monkeys, goat, sheep, cows, deer, horse, and other mammalian animals and the like. In some aspects, the patient is human.

[0107] By “pharmaceutically acceptable” it is meant the carrier(s), diluent(s) or excipient(s) must be compatible with the other components or ingredients of the compositions of the present invention, i.e., that which is useful, safe, non-toxic acceptable for pharmaceutical use. In accordance with the present invention pharmaceutically acceptable means approved or approvable as is listed in the U.S. Pharmacopoeia or other generally recognized pharmacopoeia for use in animals, and more particularly, in humans.

[0108] “Hemi” hydrochloride salts refer to salts having a substoichiometric amount of hydrochloride. For example, a hemi hydrochloride salt can have from about 0.1 to about 0.9 molar equivalents of hydrogen chloride associated with the peptide of SEQ ID NO: 1. Representative, non-limiting hemi hydrochloride salts, include, but are not limited to 0.2, 0.3, 0.4, 0.5 0.6 and 0.7 equivalents HCl associated with peptide of SEQ ID NO: 1. With regard to the present invention, the terms “hemi” hydrochloride salt shall be indistinguishable from the term “partial” hydrochloride. In some embodiments, “hemi” refers to other pharmaceutically acceptable salt forms of the peptide of SEQ ID NO: 1, such as an acetate salt of the peptide of SEQ ID NO: 1, a fumarate salt of the peptide of SEQ ID NO: 1, a glutarate salt of the peptide of SEQ ID NO: 1, a glycolate salt of the peptide of SEQ ID NO: 1, a mesylate salt of the peptide of

SEQ ID NO: 1, a bis-hydrochloride salt of the peptide of SEQ ID NO: 1, a citrate salt of the peptide of SEQ ID NO: 1, or a sulfate salt of the peptide of SEQ ID NO: 1.

[0109] “Free base” refers to the peptide of SEQ ID NO: 1 with the following structure:



in a salt-free form.

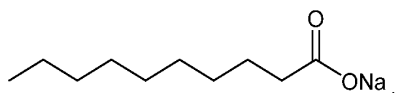
[0110] “Crystalline salt” refers to a crystalline form of a pharmaceutically acceptable salt of a compound of Formula (I), which may include, but is not limited to a crystalline acetate salt of a compound of Formula (I), a crystalline hydrochloride salt of a compound of Formula (I), a crystalline fumarate salt of a compound of Formula (I), a crystalline glutarate salt of a compound of Formula (I), a crystalline glycolate salt of a compound of Formula (I), a crystalline mesylate salt of the compound of Formula (I), a crystalline citrate salt of a compound of Formula (I), a crystalline bis-hydrochloride salt of a compound of Formula (I), or a crystalline sulfate salt of a compound of Formula (I).

[0111] Compositions or pharmaceutical compositions of the present invention may be in different pharmaceutically acceptable forms, which may include, but are not limited to a liquid composition, a tablet or matrix composition, a capsule composition, etc. and the like. When the composition is a tablet composition, the tablet may include, but is not limited to different layers. The tablet composition can also include, but is not limited to one or more coatings.

[0112] “Silicified microcrystalline cellulose,” or “SMCC,” refers to a particulate agglomerate of coprocessed microcrystalline cellulose and silicon dioxide. Suitable for use in the present invention, SMCC may include, but is not limited to amounts from about 0.1% to about 20% silicon dioxide, by weight of the microcrystalline cellulose, where the silicon dioxide can have a particle size from about 1 nanometer (nm) to about 100 microns (μm), based on average primary particle size. For example, the silicon dioxide can contain from about 0.5% to about 10% of the silicified microcrystalline cellulose, or from about 1.25% to about 5% by

weight relative to the microcrystalline cellulose. Moreover, the silicon dioxide can have a particle size from about 5 nm to about 40 μm , or from about 5 nm to about 50 μm . The silicon dioxide can have a surface area from about 10 m^2/g to about 500 m^2/g , or from about 50 m^2/g to about 500 m^2/g , or from about 175 m^2/g to about 350 m^2/g . Silicified microcrystalline cellulose is commercially available from a number of suppliers known to one of skill in the art, including Penwest Pharmaceuticals, Inc., under the trademark PROSOLV[®]. PROSOLV[®] is available in a number of grades, including, for example, PROSOLV[®] SMCC 50, PROSOLV[®] SMCC 90, and PROSOLV[®] HD. Other products include, without limitation, SMCC 50LD, SMCC HD90 and SMCC 90LM and the like.

[0113] “Sodium caprate” or “NaC10” refers to the IUPAC compound sodium decanoate having molecular formula $\text{C}_{10}\text{H}_{19}\text{NaO}_2$ and the structural formula:



[0114] In some embodiments, sodium caprate functions as either an absorption enhancer or an excipient in tablet formulation. Sodium caprate is approved by the European Union and Food and Drug Administration (FDA) as a direct food additive for human consumption.

[0115] “Solvate” as used herein, means a physical association of the peptide of SEQ ID NO: 1 of the present invention with one or more solvent molecules. This physical association involves varying degrees bonding, including hydrogen bonding. In certain instances, the solvate will be capable of isolation. The term “solvate” is intended to encompass both solution-phase and isolatable solvates. Non-limiting examples of suitable solvates include hydrates.

[0116] “Sorbitol” refers to the sugar alcohol D-glucitol and which may serve as a binder promoting adhesion of ingredients in tablet compositions.

[0117] “Sugar alcohol” as used herein refers to compounds derived from sugars and containing one or more hydroxyl groups. Sugar alcohol may contain multiple $-\text{OH}$ groups and be classified as polyols. Examples of sugar alcohol include but not limited to sorbitol, mannitol, xylitol.

[0118] “Subcoating” refers to any number of film layers disposed over the core tablet that can provide one or more benefits such as, providing a smooth tablet surface to ease swallowing of compositions, accommodate pigmentation to aid in pill identification, provide a moisture barrier, and provide a high tensile strength outer layer of the tablet. Such subcoatings can comprise, but is not limited to graft co-polymers of polyvinyl alcohol (PVA) and polyethylene glycol (PEG). Commercial products that provide subcoatings include the line of products under the trade names OPADRY[®], OPAGLOS[®], and the like. A subcoating may be further covered by one or more additional coatings.

[0119] In some embodiments, the subcoating refers to any number of film layers disposed over the core tablet. Examples of suitable materials for cosmetic subcoatings include a polyvinyl alcohol—polyethylene glycol (PVA-PEG) graft co-polymer (e.g., OPADRY® QX). Other coatings include, without limitation, HPMC, HPC, PVA, Eudragit E based coatings and the like.

[0120] In some embodiments, a subcoating may be further covered by one or more additional coatings, such as an enteric coating or a functional coating. In certain embodiments, a subcoating comprises one or more of a plasticizer, anti-tacking agent, coloring agent, HPMC, HPC, PVA, and Eudragit E based coatings. In some embodiments, a subcoating is covered with one or more additional coatings. In certain embodiments, the one or more additional coatings over the subcoating is an enteric coating. In other embodiments, the one or more additional coatings over the subcoating is a functional coating.

[0121] In some aspects, a subcoating is not covered by one or more additional coatings and is referred to as a cosmetic subcoating. For example, in certain embodiments, a core tablet is covered by a cosmetic coating and the cosmetic coating is not further covered with an enteric coating or a functional coating. In some embodiments, a cosmetic coating can serve as a smooth surface to aid in swallowing the tablet. In some embodiments, a cosmetic coating can provide a vehicle for pigmentation for tablet identification. serve as a smooth surface to aid in swallowing the tablet.

[0122] “Core tablet” refers to a mixture of the components of the core tablet. In some embodiments, the components are one or more of a crystalline form of the peptide of SEQ ID NO: 1, a pharmaceutically acceptable salt thereof, or a solvate of the foregoing, and suitable excipients. In some embodiments, the suitable excipient is one or more of the following, but not limited to, a filler, a disintegrant, a glidant, a lubricant, and an absorption enhancer. A subcoating, a cosmetic coating, an enteric coating, or any combination thereof may be disposed over the core tablet.

[0123] “Therapeutically effective amount” refers to an amount of a compound (i.e., a peptide of SEQ ID NO: 1) or of a pharmaceutical composition useful for treating or ameliorating an identified disease or condition, or for exhibiting a detectable therapeutic or inhibitory effect. “Therapeutically effective amount” further includes within its meaning a non-toxic but sufficient amount of the particular drug to which it is referring to provide the desired therapeutic effect. The exact amount required will vary from subject to subject depending on factors such as the patient’s general health, the patient’s age, etc. The exact amounts will depend on the purpose of the treatment, and will be ascertainable by one skilled in the art using known techniques (*see, e.g., Lieberman, Pharmaceutical Dosage Forms* (vols. 1-3, 1992); Lloyd, *The Art, Science and Technology of Pharmaceutical Compounding* (1999); Pickar, *Dosage Calculations* (1999); and

Remington: The Science and Practice of Pharmacy, 20th Edition, 2003, Gennaro, Ed., Lippincott, Williams & Wilkins).

[0124] “Treat”, “treating” and “treatment” refer to any indicia of success in the treatment or amelioration of an injury, pathology or condition, including any objective or subjective parameter such as abatement; remission; diminishing of symptoms or making the injury, pathology or condition more tolerable to the patient; slowing in the rate of degeneration or decline; making the final point of degeneration less debilitating; improving a patient’s physical or mental well-being. The treatment or amelioration of symptoms can be based on objective or subjective parameters; including the results of a physical examination, neuropsychiatric exams, and/or a psychiatric evaluation.

[0125] Abbreviation, “(V/V)” refers to the phrase “volume for volume”, i.e., the proportion of a particular substance within a mixture, as measured by volume or a volume amount of a component of the composition disclosed herein relative to the total volume amount of the composition. Accordingly, the quantity is unit less and represents a volume percentage amount of a component relative to the total volume of the composition. For example, a 2% (V/V) solvent mixture can indicate 2 mL of one solvent is present in 100 mL of the solvent mixture.

[0126] Abbreviation, “(w/w)” refers to the phrase “weight for weight”, i.e., the proportion of a particular substance within a mixture, as measured by weight or mass or a weight amount of a component of the composition disclosed herein relative to the total weight amount of the composition. Accordingly, the quantity is unit less and represents a weight percentage amount of a component relative to the total weight of the composition. For example, a 2% (w/w) solution can indicate 2 grams of solute is dissolved in 100 grams of solution.

[0127] Systemic routes of administration as conventionally understood in the medicinal or pharmaceutical arts, refer to or are defined as a route of administration of drug, a pharmaceutical composition or formulation, or other substance into the circulatory system so that various body tissues and organs are exposed to the drug, formulation or other substance. As conventionally understood in the art, administration can take place orally (where drug or oral preparations are taken by mouth, and absorbed via the gastrointestinal tract), via enteral administration (absorption of the drug also occurs through the gastrointestinal tract) or parenteral administration (generally injection, infusion, or implantation, etc).

[0128] “Systemically active” peptide drug therapy as it relates to the present invention generally refers to treatment by means of a pharmaceutical composition comprising a peptide active ingredient, wherein said peptide resists immediate metabolism and/or excretion resulting in its exposure in various body tissues and organs, such as the cardiovascular, respiratory, gastrointestinal, nervous or immune systems.

[0129] Systemic drug activity in the present invention also refers to treatment using substances that travel through the bloodstream, reaching and affecting cells in various body tissues and organs. Systemic active drugs are transported to their site of action and work throughout the body to attack the physiological processes that cause inflammatory diseases.

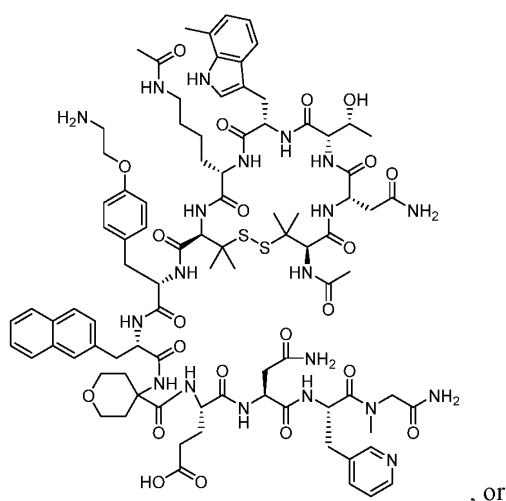
[0130] Bioavailability refers to the extent and rate at which the active moiety (drug or metabolite) enters systemic circulation, thereby accessing the site of action. Bioavailability of a drug is impacted by the properties of the dosage form, which depend partly on its design and manufacture.

[0131] “Digestive tract tissue” as used herein refers to all the tissues that comprise the organs of the alimentary canal. For example only, and without limitation, “digestive tract tissue” includes tissues of the mouth, esophagus, stomach, small intestine, large intestine, and anus.

III. CRYSTALLINE FORMS

[0132] Provided herein are crystalline forms of a peptide inhibitor of the interleukin-23 receptor (IL-23R). Crystalline forms of a compound of Formula (I) were unexpectedly obtained and isolated. Crystalline forms of pharmaceutically acceptable salts of a compound of Formula (I) were prepared, isolated, and found suitable for use in pharmaceutical formulations. As such, crystalline forms of peptides may be uniquely advantageous as the corresponding amorphous forms are often unsuitable for formulating, such as tableting.

[0133] In one aspect, the present invention relates to a pharmaceutical composition of a crystalline salt of a compound of Formula (I) :



a pharmaceutically acceptable salt thereof, or a solvate of the foregoing.

[0134] In another aspect, the present invention relates to a crystalline free base form of a compound of Formula (I) .

[0135] In one aspect, the present invention relates to a pharmaceutical composition of a hydrochloride salt of a peptide of SEQ ID NO: 1.

[0136] In one aspect, the present invention relates to a pharmaceutical composition of a hydrochloride salt of a compound of Formula (I).

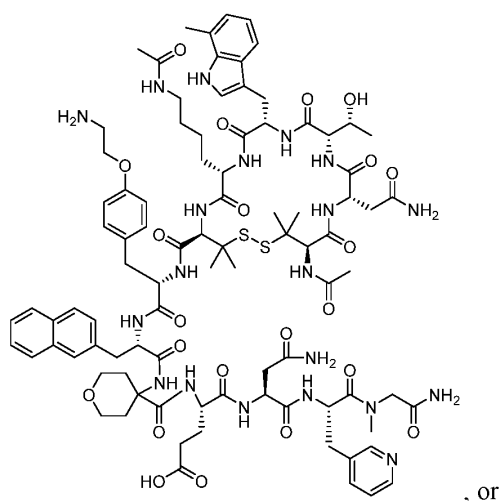
[0137] In another aspect, the present invention relates to a pharmaceutical composition of a crystalline form of the hydrochloride salt of a peptide of SEQ ID NO: 1.

[0138] In another aspect, the present invention relates to a pharmaceutical composition of a crystalline form of a pharmaceutically acceptable salt of a peptide of SEQ ID NO: 1. The crystalline form of a pharmaceutically acceptable salt of a peptide of SEQ ID NO: 1 may be a crystalline hydrochloride salt, a crystalline acetate salt, a crystalline fumarate salt, a crystalline glycolate salt, a crystalline glutarate salt, a crystalline mesylate salt, a crystalline sulfate salt, a crystalline bis-hydrochloride salt, and a crystalline citrate salt of a peptide of SEQ ID NO: 1.

[0139] In another aspect, the present invention relates to a pharmaceutical composition of a crystalline form of the hydrochloride salt of a compound of Formula (I).

[0140] In another aspect, the present invention relates to a pharmaceutical composition of a crystalline form of a pharmaceutically acceptable salt of a compound of Formula (I). The crystalline form of a pharmaceutically acceptable salt of a compound of Formula (I) may be a crystalline hydrochloride salt, a crystalline acetate salt, a crystalline fumarate salt, a crystalline glycolate salt, a crystalline glutarate salt, a crystalline mesylate salt, a crystalline sulfate salt, a crystalline bis-hydrochloride salt, and a crystalline citrate salt of a compound of Formula (I).

[0141] In some aspects, the crystalline hydrochloride salt form of a compound of Formula (I) has the structure:



a solvate thereof.

[0142] In other aspects, the crystalline hydrochloride salt form of a compound of Formula (I) is characterized by an X-ray powder diffraction (XRPD) pattern substantially as set forth in FIG. 1. In some aspects, the crystalline hydrochloride salt form or solvate thereof is a hemi hydrochloride salt. In some embodiments, the crystalline hydrochloride salt form of a compound of Formula (I) is characterized by an XRPD pattern substantially as set forth in FIG. 1 or FIG. 2.

[0143] In some aspects, the present invention relates to a pharmaceutical composition which comprises a therapeutically effective amount of a crystalline hydrochloride salt or solvate thereof described herein and one or more pharmaceutically acceptable excipients.

[0144] In other aspects, the present invention relates to a pharmaceutical composition which comprises a therapeutically effective amount of a crystalline salt or solvate thereof described herein and one or more pharmaceutically acceptable excipients.

Free Base Form

[0145] In some embodiments, the compound of Formula (I) is a free base of the compound of Formula (I). In some embodiments, the free base of the compound of Formula (I) is crystalline. In some embodiments, the free base of the compound of Formula (I) is in the form of a solvate. In certain embodiments, the solvate of the free base of the compound of Formula (I) is a hydrate. In some other embodiments, the free base of the compound of Formula (I) is crystalline and in the form of a solvate.

[0146] In some embodiments, the crystalline free base of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.3, 5.8, 7.7, 9.1, 9.6, and 13.3 $\pm$ 0.2 degrees two theta. In some embodiments, the crystalline free base of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.3, 5.8, 7.7, 9.1, 9.6, and 13.3 $\pm$ 0.3 degrees two theta. In some embodiments, the crystalline free base of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.3, 5.8, 7.7, 9.1, 9.6, and 13.3 $\pm$ 0.4 degrees two theta.

[0147] In certain embodiments, the crystalline free base of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.3, 5.8, 6.5, 6.8, 7.7, 8.3, 9.1, 9.6, 10.2, 11.1, 12.4, 12.9, 13.3, 14.0, 14.8, 15.4, 16.0, 17.3, 18.0, 18.5, 18.9, 19.4, 20.0, and 20.5 $\pm$ 0.2 degrees two theta. In certain embodiments, the crystalline free base of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.3, 5.8, 6.5, 6.8, 7.7, 8.3, 9.1, 9.6, 10.2, 11.1, 12.4, 12.9, 13.3, 14.0, 14.8, 15.4, 16.0, 17.3, 18.0, 18.5, 18.9, 19.4, 20.0, and 20.5 $\pm$ 0.3 degrees two theta. In certain embodiments, the crystalline free base of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.3, 5.8, 6.5, 6.8, 7.7, 8.3, 9.1, 9.6, 10.2, 11.1, 12.4, 12.9, 13.3, 14.0, 14.8, 15.4, 16.0, 17.3, 18.0, 18.5, 18.9, 19.4, 20.0, and 20.5 $\pm$ 0.4 degrees two theta.

[0148] In certain embodiments, the crystalline free base of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.3, 5.8, 6.5, 6.8, 7.7, 8.3, 9.1, 9.6, 10.2, 11.1, 12.4, 12.9, 13.3, 14.0, 14.8, 15.4, 16.0, 17.3, 18.0, 18.5, 18.9, 19.4, 20.0, and 20.5 $\pm$ 0.2 degrees two theta. In certain embodiments, the crystalline free base of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.3, 5.8, 6.5, 6.8, 7.7, 8.3, 9.1, 9.6, 10.2, 11.1, 12.4, 12.9, 13.3, 14.0, 14.8, 15.4, 16.0, 17.3, 18.0, 18.5, 18.9, 19.4, 20.0, and 20.5 $\pm$ 0.3 degrees two theta. In certain embodiments, the crystalline free base of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.3, 5.8, 6.5, 6.8, 7.7, 8.3, 9.1, 9.6, 10.2, 11.1, 12.4, 12.9, 13.3, 14.0, 14.8, 15.4, 16.0, 17.3, 18.0, 18.5, 18.9, 19.4, 20.0, and 20.5 $\pm$ 0.4 degrees two theta.

[0149] In certain embodiments, the crystalline free base of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks

at two theta angles selected from 3.3, 5.8, 6.5, 6.8, 7.7, 8.3, 9.1, 9.6, 10.2, 11.1, 12.4, 12.8, 13.3, 14.0, 14.8, 15.4, 16.0, 16.8, 17.3, 18.0, 18.5, 18.9, 19.4, 20.0, and 20.5 +/- 0.2 degrees two theta. In certain embodiments, the crystalline free base of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.3, 5.8, 6.5, 6.8, 7.7, 8.3, 9.1, 9.6, 10.2, 11.1, 12.4, 12.8, 13.3, 14.0, 14.8, 15.4, 16.0, 16.8, 17.3, 18.0, 18.5, 18.9, 19.4, 20.0, and 20.5 +/- 0.3 degrees two theta. In certain embodiments, the crystalline free base of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.3, 5.8, 6.5, 6.8, 7.7, 8.3, 9.1, 9.6, 10.2, 11.1, 12.4, 12.8, 13.3, 14.0, 14.8, 15.4, 16.0, 16.8, 17.3, 18.0, 18.5, 18.9, 19.4, 20.0, and 20.5 +/- 0.4 degrees two theta.

[0150] In certain embodiments, the crystalline free base of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.3, 5.8, 6.5, 6.8, 7.7, 8.3, 9.1, 9.6, 10.2, 11.1, 12.4, 12.8, 13.3, 14.0, 14.8, 15.4, 16.0, 16.8, 17.3, 18.0, 18.5, 18.9, 19.4, 20.0, and 20.5 +/- 0.2 degrees two theta. In certain embodiments, the crystalline free base of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.3, 5.8, 6.5, 6.8, 7.7, 8.3, 9.1, 9.6, 10.2, 11.1, 12.4, 12.8, 13.3, 14.0, 14.8, 15.4, 16.0, 16.8, 17.3, 18.0, 18.5, 18.9, 19.4, 20.0, and 20.5 +/- 0.3 degrees two theta. In certain embodiments, the crystalline free base of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.3, 5.8, 6.5, 6.8, 7.7, 8.3, 9.1, 9.6, 10.2, 11.1, 12.4, 12.8, 13.3, 14.0, 14.8, 15.4, 16.0, 16.8, 17.3, 18.0, 18.5, 18.9, 19.4, 20.0, and 20.5 +/- 0.4 degrees two theta. In some embodiments, the crystalline free base salt of the compound of Formula (I) or solvate thereof is characterized by an XRPD pattern substantially as set forth in FIG. 11.

[0151] In some embodiments, the crystalline free base of the compound of Formula (I) or solvate thereof is characterized as having endotherm peaks at about 71.0 °C and/or about 130.2 °C, as determined by DSC. In certain embodiments, the crystalline free base of the compound of Formula (I) or solvate thereof is characterized as having substantially a DSC curve as shown in FIG. 13.

[0152] In some embodiments, the crystalline free base of the compound of Formula (I) or solvate thereof is characterized as having a weight loss of about 3.7% from about 26.5 °C to about 70.0 °C and a weight loss of about 2.7% from 70.0 °C to about 170.0 °C, as determined by TGA. In certain embodiments, the crystalline free base of the compound of Formula (I) or solvate thereof is characterized as having a TGA graph substantially as shown in FIG. 12. In

some embodiments, the crystalline bis-hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having a DVS graph substantially as shown in FIG. 14.

[0153] In some aspects, the present invention relates to a pharmaceutical composition which comprises a therapeutically effective amount of the crystalline free base of the compound of Formula (I) or solvate thereof described herein and one or more pharmaceutically acceptable excipients.

Salt Ratios

[0154] In some embodiments, the compound of Formula (I) is in the form of a pharmaceutically acceptable salt. In certain embodiments, the pharmaceutically acceptable salt of the compound of Formula (I) is crystalline. In some embodiments, a crystalline pharmaceutically acceptable salt of a compound of Formula (I) comprises a cationic form of the compound of Formula (I) and a pharmaceutically acceptable anion. For example, a crystalline hydrochloride salt of a compound of Formula (I) comprises the compound of Formula (I) in its cationic form and a chloride anion. The salt compositions described herein include a salt of a compound of Formula (I) wherein the salt is a pharmaceutically acceptable salt chosen from an acetate salt, a fumarate salt, a glycolate salt, a glutarate salt, a mesylate salt, a sulfate salt, a citrate salt, a bis-hydrochloride salt, and the like.

[0155] In some embodiments, the pharmaceutically acceptable salt of a compound of Formula (I) is a hydrochloride salt and the anion is chloride. In some embodiments, the salt of a compound of Formula (I) is an acetate salt and the anion is acetate. In some embodiments, the salt of a compound of Formula (I) is a fumarate salt and the anion is fumarate. In some embodiments, the salt of a compound of Formula (I) is a glutarate salt and the anion is glutarate. In some embodiments, the salt of a compound of Formula (I) is a glycolate salt and the anion is glycolate. In some embodiments, the salt of a compound of Formula (I) is a mesylate salt and the anion is mesylate. In some embodiments, the salt of a compound of Formula (I) is a sulfate salt and the anion is sulfate. In some embodiments, the salt of a compound of Formula (I) is a citrate salt and the anion is citrate. In some embodiments, the salt of a compound of Formula (I) is a bis-hydrochloride salt and the anion is chloride.

[0156] In some embodiments, the molar equivalents of an anion of a crystalline salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 0.2 to about 2.0. In some embodiments, the molar equivalents of an anion of a salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is about 0.2, about 0.3, about 0.4, about 0.5, about 0.6, about 0.7, about 0.8, about 0.9, about 1.0, about 1.1, about 1.2, about

1.3, about 1.4, about 1.5, about 1.6, about 1.7, about 1.8, about 1.9, or about 2.0, including any amount in between and fractions thereof.

[0157] In some embodiments, the molar equivalents of a chloride anion of a crystalline hydrochloride salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 0.2 to about 2.0. In some embodiments, the molar equivalents of a chloride anion of a crystalline hydrochloride salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 0.4 to about 1.5. In other embodiments, the molar equivalents of a chloride anion of a crystalline hydrochloride salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 0.5 to about 1.0. In certain embodiments, the molar equivalents of a chloride anion of a crystalline hydrochloride salt of the compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 0.6 to about 0.7.

[0158] In some embodiments, the molar equivalents of an acetate anion of a crystalline acetate salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 0.2 to about 2.0. In some embodiments, the molar equivalents of an acetate anion of a crystalline acetate salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 0.4 to about 1.5. In other embodiments, the molar equivalents of an acetate anion of a crystalline acetate salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 0.5 to about 1.0. In certain embodiments, the molar equivalents of an acetate of a crystalline acetate salt of the compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 0.6 to about 0.7. In certain embodiments, the molar equivalents of an acetate of a crystalline acetate salt of the compound of Formula (I) relative to one mole of the compound of Formula (I) is about 0.65.

[0159] In some embodiments, the molar equivalents of a fumarate anion of a crystalline fumarate salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 0.2 to about 2.0. In some embodiments, the molar equivalents of a fumarate anion of a crystalline fumarate salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 0.4 to about 1.5. In other embodiments, the molar equivalents of a fumarate anion of a crystalline fumarate salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 0.5 to about 1.0. In other embodiments, the molar equivalents of a fumarate anion of a crystalline fumarate salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 1.0 to about 1.5. In other embodiments, the molar equivalents of a fumarate anion of a crystalline fumarate salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 1.5 to about 2.0.

[0160] In some embodiments, the molar equivalents of a glutarate anion of a crystalline glutarate salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 0.2 to about 2.0. In some embodiments, the molar equivalents of a glutarate anion of a crystalline glutarate salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 0.2 to about 1.0. In other embodiments, the molar equivalents of a glutarate anion of a crystalline glutarate salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 0.3 to about 0.6. In certain embodiments, the molar equivalents of a glutarate anion of a crystalline glutarate salt of the compound of Formula (I) relative to one mole of the compound of Formula (I) is about 0.5.

[0161] In some embodiments, the molar equivalents of a glycolate anion of a crystalline glycolate salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 0.2 to about 2.0. In some embodiments, the molar equivalents of a glycolate anion of a crystalline glycolate salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 0.2 to about 1.0. In other embodiments, the molar equivalents of a glycolate anion of a crystalline glycolate salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 0.3 to about 0.6. In certain embodiments, the molar equivalents of a glycolate anion of a crystalline glycolate salt of the compound of Formula (I) relative to one mole of the compound of Formula (I) is about 0.5.

[0162] In some embodiments, the molar equivalents of a mesylate anion of a crystalline mesylate salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 0.2 to about 2.0. In some embodiments, the molar equivalents of a mesylate anion of a crystalline mesylate salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 1.0 to about 2.0. In other embodiments, the molar equivalents of a mesylate anion of a crystalline mesylate salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 1.5 to about 2.0. In other embodiments, the molar equivalents of a mesylate anion of a crystalline mesylate salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 1.8 to about 1.9. In certain embodiments, the molar equivalents of a mesylate anion of a crystalline mesylate salt of the compound of Formula (I) relative to one mole of the compound of Formula (I) is about 1.8.

[0163] In some embodiments, the molar equivalents of a sulfate anion of a crystalline sulfate salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 0.2 to about 2.0. In some embodiments, the molar equivalents of a sulfate anion of a crystalline sulfate salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 1.0 to about 2.0. In other embodiments, the molar equivalents of a

sulfate anion of a crystalline sulfate salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 1.5 to about 2.0. In other embodiments, the molar equivalents of a sulfate anion of a crystalline sulfate salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 1.5 to about 1.7. In certain embodiments, the molar equivalents of a sulfate anion of a crystalline sulfate salt of the compound of Formula (I) relative to one mole of the compound of Formula (I) is about 1.6.

[0164] In some embodiments, the molar equivalents of a citrate anion of a crystalline citrate salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 0.2 to about 2.0. In some embodiments, the molar equivalents of a citrate anion of a crystalline citrate salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 0.4 to about 1.5. In other embodiments, the molar equivalents of a citrate anion of a crystalline citrate salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 0.5 to about 1.0. In other embodiments, the molar equivalents of a citrate anion of a crystalline citrate salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 1.0 to about 1.5. In other embodiments, the molar equivalents of a citrate anion of a crystalline citrate salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 1.5 to about 2.0.

[0165] In some embodiments, the molar equivalents of a chloride anion of a crystalline bis-hydrochloride salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 0.2 to about 2.0. In some embodiments, the molar equivalents of a chloride anion of a crystalline bis-hydrochloride salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 1.0 to about 2.0. In other embodiments, the molar equivalents of a chloride anion of a crystalline bis-hydrochloride salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 1.5 to about 2.0. In certain embodiments, the molar equivalents of a chloride anion of a crystalline hydrochloride salt of the compound of Formula (I) relative to one mole of the compound of Formula (I) is from about 1.9 to about 2.0. In certain embodiments, the molar equivalents of a chloride anion of a crystalline bis-hydrochloride salt of a compound of Formula (I) relative to one mole of the compound of Formula (I) is about 2.0.

Salt Forms

Hydrochloride Salt

[0166] In some embodiments, a pharmaceutically acceptable salt of a compound of Formula (I) is a hydrochloride salt. In some embodiments, a hydrochloride salt of the compound of

Formula (I) is crystalline. In some embodiments, the hydrochloride salt of the compound of Formula (I) is in the form of a solvate. In certain embodiments, the solvate of the hydrochloride salt of the compound of Formula (I) is a hydrate. In some other embodiments, the hydrochloride salt of the compound of Formula (I) is crystalline and in the form of a solvate.

[0167] In some embodiments, a pharmaceutically acceptable salt of a compound of Formula (I) is a hydrochloride salt. In some embodiments, a hydrochloride salt of the compound of Formula (I) is crystalline. In some embodiments, the hydrochloride salt of the compound of Formula (I) is in the form of a solvate. In certain embodiments, the solvate of the hydrochloride salt of the compound of Formula (I) is a hydrate. In some other embodiments, the hydrochloride salt of the compound of Formula (I) is crystalline and in the form of a solvate.

[0168] In some embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, and 9.2 $\pm$ 0.2 degrees two theta. In some embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, and 9.2 $\pm$ 0.3 degrees two theta. In some embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, and 9.2 $\pm$ 0.4 degrees two theta.

[0169] In some embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.8, 4.2, 6.9, 7.6, 8.5, 9.3, 10.0, 10.7, 12.2, 13.9, 15.7, or 17.1 $\pm$ 0.2 degrees two theta. In some embodiments, the crystalline hydrochloride salt of the compound of SEQ ID NO: 1 or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.8, 4.2, 6.9, 7.6, 8.5, 9.3, 10.0, 10.7, 12.2, 13.9, 15.8, or 17.1 $\pm$ 0.3 degrees two theta. In some embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.8, 4.2, 6.9, 7.6, 8.5, 9.3, 10.0, 10.7, 12.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 $\pm$ 0.3 degrees two theta. In some embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 $\pm$ 0.4 degrees two theta.

[0170] In other embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction

peaks at two theta angles selected from 4.3, 6.9, 7.7, 8.6, 9.3, 10.0, 10.7, 11.5, 12.0, 13.1, 13.3, 14.0, 14.8, 15.8, 17.1, 17.6, 18.1, 18.6, 19.3, 20.5, 20.7, or 21.8 $\pm$ 0.2 degrees two theta. In other embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.3, 6.9, 7.7, 8.6, 9.3, 10.0, 10.7, 11.5, 12.0, 13.1, 13.3, 14.0, 14.8, 15.8, 17.1, 17.6, 18.1, 18.6, 19.3, 20.5, 20.7, or 21.8 $\pm$ 0.3 degrees two theta. In other embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.3, 6.9, 7.7, 8.6, 9.3, 10.0, 10.7, 11.5, 12.0, 13.1, 13.3, 14.0, 14.8, 15.8, 17.1, 17.6, 18.1, 18.6, 19.3, 20.5, 20.7, or 21.8 $\pm$ 0.4 degrees two theta.

[0171] In some embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 4.3, 6.9, 7.7, 8.6, 9.3, 10.0, 10.7, 11.5, 12.0, 13.1, 13.3, 14.0, 14.8, 15.8, 17.1, 17.6, 18.1, 18.6, 19.3, 20.5, 20.7, or 21.8 $\pm$ 0.2 degrees two theta. In some embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 4.3, 6.9, 7.7, 8.6, 9.3, 10.0, 10.7, 11.5, 12.0, 13.1, 13.3, 14.0, 14.8, 15.8, 17.1, 17.6, 18.1, 18.6, 19.3, 20.5, 20.7, or 21.8 $\pm$ 0.3 degrees two theta. In some embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 4.3, 6.9, 7.7, 8.6, 9.3, 10.0, 10.7, 11.5, 12.0, 13.1, 13.3, 14.0, 14.8, 15.8, 17.1, 17.6, 18.1, 18.6, 19.3, 20.5, 20.7, or 21.8 $\pm$ 0.4 degrees two theta. In some embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized by an XRPD pattern substantially as set forth in FIG. 1. In some embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized by an XRPD pattern substantially as set forth in FIG. 2.

[0172] In some embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.8, 4.2, 6.9, 7.6, 8.5, 9.3, 9.4, 10.0, 10.8, 11.5, 12.0, 12.2, 12.8, 13.1, 13.3, 13.8, 13.9, 14.2, 14.4, 14.7, 15.3, 15.7, 16.2, 16.4, 17.2, 17.6, 18.2, 18.7, 19.2, 19.6, 19.9, 20.5, and 20.8 $\pm$ 0.2 degrees two theta. In some embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.8, 4.2, 6.9, 7.6, 8.5, 9.3, 9.4, 10.0, 10.8, 11.6, 12.0, 12.2, 12.8, 13.1, 13.3, 13.8, 13.9, 14.2, 14.4, 14.7, 15.3, 15.7, 16.2, 16.4, 17.2, 17.6, 18.2, 18.7, 19.2, 19.6, 19.9, 20.5, and 20.8 $\pm$ 0.3

degrees two theta. In some embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.8, 4.2, 6.9, 7.6, 8.5, 9.3, 9.4, 10.0, 10.8, 11.5, 12.0, 12.2, 12.8, 13.1, 13.3, 13.8, 13.9, 14.2, 14.4, 14.7, 15.3, 15.7, 16.2, 16.4, 17.2, 17.6, 18.2, 18.7, 19.2, 19.6, 19.9, 20.5, and 20.8 +/- 0.4 degrees two theta.

[0173] In some embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.2, 6.9, 7.6, 8.5, 9.3, 9.4, 10.0, 10.8, 11.5, 12.0, 12.2, 12.8, 13.1, 13.3, 13.8, 13.9, 14.2, 14.4, 14.7, 15.3, 15.7, 16.2, 16.4, 17.2, 17.6, 18.2, 18.7, 19.2, 19.6, 19.9, 20.5, and 20.8 +/- 0.2 degrees two theta. In some embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.2, 6.9, 7.6, 8.5, 9.3, 9.4, 10.0, 10.8, 11.5, 12.0, 12.2, 12.8, 13.1, 13.3, 13.8, 13.9, 14.2, 14.4, 14.7, 15.3, 15.7, 16.2, 16.4, 17.2, 17.6, 18.2, 18.7, 19.2, 19.6, 19.9, 20.5, and 20.8 +/- 0.3 degrees two theta. In some embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.2, 6.9, 7.6, 8.5, 9.3, 9.4, 10.0, 10.8, 11.5, 12.0, 12.2, 12.8, 13.1, 13.3, 13.8, 13.9, 14.2, 14.4, 14.7, 15.3, 15.7, 16.2, 16.4, 17.2, 17.6, 18.2, 18.7, 19.2, 19.6, 19.9, 20.5, and 20.8 +/- 0.4 degrees two theta. In some embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized by an XRPD pattern substantially as set forth in FIG. 3.

[0174] In some embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized by an XRPD pattern substantially as set forth in FIG. 1, FIG. 2, or FIG. 3.

[0175] In some embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having endotherm peaks at about 81.4 °C, as determined by differential scanning calorimetry (DSC). In certain embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having a DSC curve substantially as set forth in FIG. 5.

[0176] In some embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having a weight loss of about 5.6% from about 26.5 °C to about 160.0 °C, as determined by thermogravimetric analysis (TGA). In certain embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having a TGA graph substantially as set forth in FIG. 4. In some embodiments,

the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having a DVS graph substantially as shown in FIG. 6.

[0177] In some aspects, the present invention relates to a pharmaceutical composition which comprises a therapeutically effective amount of the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof described herein and one or more pharmaceutically acceptable excipients.

Acetate Salt

[0178] In some embodiments, a pharmaceutically acceptable salt of a compound of Formula (I) is an acetate salt. In some embodiments, the acetate salt of the compound of Formula (I) is crystalline. In some embodiments, the acetate salt of the compound of Formula (I) is in the form of a solvate. In certain embodiments, the solvate of the acetate salt of the compound of Formula (I) is a hydrate. In some other embodiments, the acetate salt of the compound of Formula (I) is crystalline and in the form of a solvate.

[0179] In some embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, and 9.2 $\pm$ 0.2 degrees two theta. In some embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, and 9.2 $\pm$ 0.3 degrees two theta. In some embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, and 9.2 $\pm$ 0.4 degrees two theta.

[0180] In some embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 $\pm$ 0.2 degrees two theta. In some embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 $\pm$ 0.3 degrees two theta. In some embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 $\pm$ 0.4 degrees two theta.

[0181] In some embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta

angles of at least 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 $\pm$ 0.2 degrees two theta. In some embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 $\pm$ 0.3 degrees two theta. In some embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 $\pm$ 0.4 degrees two theta.

[0182] In some embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having at least two diffraction peaks at two theta angles selected from 3.8, 4.3, 6.8, 7.0, 7.6, 7.7, 8.5, 8.6, 9.2, 9.9, 10.1, 10.4, 10.6, 10.7, 11.2, 11.4, 11.8, 12.1, 12.8, 13.1, 13.8, 14.3, 14.5, 15.2, 15.5, 15.9, 17.2, 17.4, 18.0, 18.4, 19.1, and 19.4 $\pm$ 0.2 degrees two theta. In some embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having at least two diffraction peaks at two theta angles selected from 3.8, 4.3, 6.8, 7.0, 7.6, 7.7, 8.5, 8.6, 9.2, 9.9, 10.1, 10.4, 10.6, 10.7, 11.2, 11.4, 11.8, 12.1, 12.8, 13.1, 13.8, 14.3, 14.5, 15.2, 15.5, 15.9, 17.2, 17.4, 18.0, 18.4, 19.1, and 19.4 $\pm$ 0.3 degrees two theta. In some embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having at least two diffraction peaks at two theta angles selected from 3.8, 4.3, 6.8, 7.0, 7.6, 7.7, 8.5, 8.6, 9.2, 9.9, 10.1, 10.4, 10.6, 10.7, 11.2, 11.4, 11.8, 12.1, 12.8, 13.1, 13.8, 14.3, 14.5, 15.2, 15.5, 15.9, 17.2, 17.4, 18.0, 18.4, 19.1, and 19.4 $\pm$ 0.4 degrees two theta.

[0183] In some embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having at least three diffraction peaks at two theta angles selected from 3.8, 4.3, 6.8, 7.0, 7.6, 7.7, 8.5, 8.6, 9.2, 9.9, 10.1, 10.4, 10.6, 10.7, 11.2, 11.4, 11.8, 12.1, 12.8, 13.1, 13.8, 14.3, 14.5, 15.2, 15.5, 15.9, 17.2, 17.4, 18.0, 18.4, 19.1, and 19.4 $\pm$ 0.2 degrees two theta. In some embodiments, the crystalline acetate salt of the peptide of SEQ ID NO: 1 or solvate thereof is characterized as having an XRPD pattern having at least three diffraction peaks at two theta angles selected from 3.8, 4.3, 6.8, 7.0, 7.6, 7.7, 8.5, 8.6, 9.2, 9.9, 10.1, 10.4, 10.6, 10.7, 11.2, 11.4, 11.8, 12.1, 12.8, 13.1, 13.8, 14.3, 14.5, 15.2, 15.5, 15.9, 17.2, 17.4, 18.0, 18.4, 19.1, and 19.4 $\pm$ 0.3 degrees two theta. In some embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having at least three diffraction peaks at two theta angles selected from 3.8, 4.3, 6.8, 7.0, 7.6, 7.7, 8.5, 8.6, 9.2, 9.9, 10.1, 10.4, 10.6, 10.7, 11.2,

11.4, 11.8, 12.1, 12.8, 13.1, 13.8, 14.3, 14.5, 15.2, 15.5, 15.9, 17.2, 17.4, 18.0, 18.4, 19.1, and 19.4 +/- 0.4 degrees two theta.

[0184] In some embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having at least two diffraction peaks at two theta angles selected from 3.8, 4.3, 6.8, 7.0, 7.6, 7.7, 8.5, 8.6, 9.2, 9.9, 10.1, 10.4, 10.6, 10.7, 11.2, 11.4, 11.8, 12.1, 12.8, 13.1, 13.8, 14.3, 14.5, 15.2, 15.5, 15.9, 17.2, 17.4, 18.0, 18.4, 19.1, 19.4, and 20.1 +/- 0.2 degrees two theta. In some embodiments, the crystalline acetate salt of the peptide of compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having at least two diffraction peaks at two theta angles selected from 3.8, 4.3, 6.8, 7.0, 7.6, 7.7, 8.5, 8.6, 9.2, 9.9, 10.1, 10.4, 10.6, 10.7, 11.2, 11.4, 11.8, 12.1, 12.8, 13.1, 13.8, 14.3, 14.5, 15.2, 15.5, 15.9, 17.2, 17.4, 18.0, 18.4, 19.1, 19.4, and 20.1 +/- 0.3 degrees two theta. In some embodiments, the crystalline acetate salt of compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having at least two diffraction peaks at two theta angles selected from 3.8, 4.3, 6.8, 7.0, 7.6, 7.7, 8.5, 8.6, 9.2, 9.9, 10.1, 10.4, 10.6, 10.7, 11.2, 11.4, 11.8, 12.1, 12.8, 13.1, 13.8, 14.3, 14.5, 15.2, 15.5, 15.9, 17.2, 17.4, 18.0, 18.4, 19.1, 19.4, and 20.1 +/- 0.4 degrees two theta.

[0185] In some embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having at least three diffraction peaks at two theta angles selected from 3.8, 4.3, 6.8, 7.0, 7.6, 7.7, 8.5, 8.6, 9.2, 9.9, 10.1, 10.4, 10.6, 10.7, 11.2, 11.4, 11.8, 12.1, 12.8, 13.1, 13.8, 14.3, 14.5, 15.2, 15.5, 15.9, 17.2, 17.4, 18.0, 18.4, 19.1, 19.4, and 20.1 +/- 0.2 degrees two theta. In some embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having at least two diffraction peaks at three theta angles selected from 3.8, 4.3, 6.8, 7.0, 7.6, 7.7, 8.5, 8.6, 9.2, 9.9, 10.1, 10.4, 10.6, 10.7, 11.2, 11.4, 11.8, 12.1, 12.8, 13.1, 13.8, 14.3, 14.5, 15.2, 15.5, 15.9, 17.2, 17.4, 18.0, 18.4, 19.1, 19.4, and 20.1 +/- 0.3 degrees two theta. In some embodiments, the crystalline acetate salt of the peptide of SEQ ID NO: 1 or solvate thereof is characterized as having an XRPD pattern having at least three diffraction peaks at two theta angles selected from 3.8, 4.3, 6.8, 7.0, 7.6, 7.7, 8.5, 8.6, 9.2, 9.9, 10.1, 10.4, 10.6, 10.7, 11.2, 11.4, 11.8, 12.1, 12.8, 13.1, 13.8, 14.3, 14.5, 15.2, 15.5, 15.9, 17.2, 17.4, 18.0, 18.4, 19.1, 19.4, and 20.1 +/- 0.4 degrees two theta.

[0186]

In some embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.3, 6.8, 7.0, 7.6, 7.7, 8.5, 8.6, 9.2, 9.9, 10.1, 10.4, 10.6, 10.7, 11.2, 11.4, 11.8, 12.1, 12.8, 13.1, 13.8, 14.3, 14.5, 15.2, 15.5, 15.9, 17.2, 17.4, 18.0, 18.4, 19.1, and 19.4 +/-

0.2 degrees two theta. In some embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.3, 6.8, 7.0, 7.6, 7.7, 8.5, 8.6, 9.2, 9.9, 10.1, 10.4, 10.6, 10.7, 11.2, 11.4, 11.8, 12.1, 12.8, 13.1, 13.8, 14.3, 14.5, 15.2, 15.5, 15.9, 17.2, 17.4, 18.0, 18.4, 19.1, and 19.4 +/- 0.3 degrees two theta. In some embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.3, 6.8, 7.0, 7.6, 7.7, 8.5, 8.6, 9.2, 9.9, 10.1, 10.4, 10.6, 10.7, 11.2, 11.4, 11.8, 12.1, 12.8, 13.1, 13.8, 14.3, 14.5, 15.2, 15.5, 15.9, 17.2, 17.4, 18.0, 18.4, 19.1, and 19.4 +/- 0.4 degrees two theta.

[0187] In some embodiments, the crystalline acetate salt of the peptide of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.3, 6.8, 7.0, 7.6, 7.7, 8.5, 8.6, 9.2, 9.9, 10.1, 10.4, 10.6, 10.7, 11.2, 11.4, 11.8, 12.1, 12.8, 13.1, 13.8, 14.3, 14.5, 15.2, 15.5, 15.9, 17.2, 17.4, 18.0, 18.4, 19.1, 19.4, and 20.1 +/- 0.2 degrees two theta. In some embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.3, 6.8, 7.0, 7.6, 7.7, 8.5, 8.6, 9.2, 9.9, 10.1, 10.4, 10.6, 10.7, 11.2, 11.4, 11.8, 12.1, 12.8, 13.1, 13.8, 14.3, 14.5, 15.2, 15.5, 15.9, 17.2, 17.4, 18.0, 18.4, 19.1, 19.4 and 20.1 +/- 0.3 degrees two theta. In some embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.3, 6.8, 7.0, 7.6, 7.7, 8.5, 8.6, 9.2, 9.9, 10.1, 10.4, 10.6, 10.7, 11.2, 11.4, 11.8, 12.1, 12.8, 13.1, 13.8, 14.3, 14.5, 15.2, 15.5, 15.9, 17.2, 17.4, 18.0, 18.4, 19.1, 19.4, and 20.1 +/- 0.4 degrees two theta. In some embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof is characterized by an XRPD pattern substantially as set forth in FIG. 7.

[0188] In some embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof is characterized as having endotherm peaks at about 80.7 °C and/or about 240.7 °C, as determined by DSC. In certain embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof is characterized as having a DSC curve substantially as set forth in FIG. 9.

[0189] In some embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof is characterized as having a weight loss of about 5.8% from about 26.5 °C to about 150.0 °C, as determined by TGA. In certain embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof is characterized as having a TGA graph substantially as set forth in FIG. 8. In some embodiments, the crystalline acetate salt of the

compound of Formula (I) or solvate thereof is characterized as having a DVS graph substantially as shown in FIG. 10.

[0190] In some aspects, the present invention relates to a pharmaceutical composition which comprises a therapeutically effective amount of the crystalline acetate salt of the compound of Formula (I) or solvate thereof described herein and a pharmaceutically acceptable excipient.

Fumarate Salt

[0191] In some embodiments, a pharmaceutically acceptable salt of a compound of Formula (I) is a fumarate salt. In some embodiments, the fumarate salt of the compound of Formula (I) is crystalline. In some embodiments, the fumarate salt of the compound of Formula (I) is in the form of a solvate. In certain embodiments, the solvate of the fumarate salt of the compound of Formula (I) is a hydrate. In some other embodiments, the fumarate salt of the compound of Formula (I) is crystalline and in the form of a solvate.

[0192] In some embodiments, the crystalline fumarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, and 9.2 $\pm$ 0.2 degrees two theta. In some embodiments, the crystalline fumarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, and 9.2 $\pm$ 0.3 degrees two theta. In some embodiments, the crystalline fumarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, and 9.2 $\pm$ 0.4 degrees two theta.

[0193] In some embodiments, the crystalline fumarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 $\pm$ 0.2 degrees two theta. In some embodiments, the crystalline fumarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 $\pm$ 0.3 degrees two theta. In some embodiments, the crystalline fumarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 $\pm$ 0.4 degrees two theta.

[0194] In some embodiments, the crystalline fumarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 $\pm$ 0.2

degrees two theta. In some embodiments, the crystalline fumarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 +/- 0.3 degrees two theta. In some embodiments, the crystalline fumarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 +/- 0.4 degrees two theta.

[0195] In some embodiments, the crystalline fumarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles of at least 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 11.5, 12.0, 12.8, 13.3, 14.0, 14.7, 15.7, 17.0, 17.6, 19.1, 20.4, 21.7, 23.1, 24.2, 25.4, and 27.1 +/- 0.2 degrees two theta. In some embodiments, the crystalline fumarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles of at least 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 11.5, 12.0, 12.8, 13.3, 14.0, 14.7, 15.7, 17.0, 17.6, 19.1, 20.4, 21.7, 23.1, 24.2, 25.4, and 27.1 +/- 0.3 degrees two theta. In some embodiments, the crystalline fumarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles of at least 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 11.5, 12.0, 12.8, 13.3, 14.0, 14.7, 15.7, 17.0, 17.6, 19.1, 20.4, 21.7, 23.1, 24.2, 25.4, and 27.1 +/- 0.4 degrees two theta.

[0196] In some embodiments, the crystalline fumarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 11.5, 12.0, 12.8, 13.3, 14.0, 14.7, 15.7, 17.0, 17.6, 19.1, 20.4, 21.7, 23.1, 24.2, 25.4, and 27.1 +/- 0.2 degrees two theta. In some embodiments, the crystalline fumarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 11.5, 12.0, 12.8, 13.3, 14.0, 14.7, 15.7, 17.0, 17.6, 19.1, 20.4, 21.7, 23.1, 24.2, 25.4, and 27.1 +/- 0.3 degrees two theta. In some embodiments, the crystalline fumarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 11.5, 12.0, 12.8, 13.3, 14.0, 14.7, 15.7, 17.0, 17.6, 19.1, 20.4, 21.7, 23.1, 24.2, 25.4, and 27.1 +/- 0.4 degrees two theta. In some embodiments, the crystalline fumarate salt of the compound of Formula (I) or solvate thereof is characterized by an XRPD pattern substantially as set forth in FIG. 15.

[0197] In some embodiments, the crystalline fumarate salt of the compound of Formula (I) or solvate thereof is characterized as having an endotherm peak at about 65.3 °C, as determined

by DSC. In certain embodiments, the crystalline fumarate salt of the compound of Formula (I) or solvate thereof is characterized as having a DSC curve substantially as set forth in FIG. 17. In some embodiments, the crystalline fumarate salt of the compound of Formula (I) or solvate thereof is characterized as having a weight loss of about 4.4% from about 26.5 °C to about 110.0 °C, as determined by TGA. In certain embodiments, the crystalline fumarate salt of the compound of Formula (I) or solvate thereof is characterized as having a TGA graph substantially as set forth in FIG. 16.

[0198] In some aspects, the present invention relates to a pharmaceutical composition which comprises a therapeutically effective amount of the crystalline fumarate salt of the compound of Formula (I) or solvate thereof described herein and a pharmaceutically acceptable excipient.

Glutarate Salt

[0199] In some embodiments, a pharmaceutically acceptable salt of a compound of Formula (I) is a glutarate salt. In some embodiments, the glutarate salt of the compound of Formula (I) is crystalline. In some embodiments, the glutarate salt of the compound of Formula (I) is in the form of a solvate. In certain embodiments, the solvate of the glutarate salt of the compound of Formula (I) is a hydrate. In some other embodiments, the glutarate salt of the compound of Formula (I) is crystalline and in the form of a solvate.

[0200] In some embodiments, the crystalline glutarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, and 9.2 +/- 0.2 degrees two theta. In some embodiments, the crystalline glutarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, and 9.2 +/- 0.3 degrees two theta. In some embodiments, the crystalline glutarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, and 9.2 +/- 0.4 degrees two theta.

[0201] In some embodiments, the crystalline glutarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 +/- 0.2 degrees two theta. In some embodiments, the crystalline glutarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 +/- 0.3 degrees two theta. In some embodiments, the crystalline glutarate salt of the compound of Formula (I) or solvate thereof is characterized as having an

XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 $\pm$ 0.4 degrees two theta.

[0202] In some embodiments, the crystalline glutarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 $\pm$ 0.2 degrees two theta. In some embodiments, the crystalline glutarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 $\pm$ 0.3 degrees two theta. In some embodiments, the crystalline glutarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 $\pm$ 0.4 degrees two theta.

[0203] In some embodiments, the crystalline glutarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.8, 4.3, 6.9, 7.6, 8.5, 9.2, 9.9, 10.8, 11.9, 13.0, 13.9, 15.7, 17.0, 17.6, 18.6, 19.2, 20.3, 20.7, 21.4, 23.3, and 25.3 $\pm$ 0.2 degrees two theta. In some embodiments, the crystalline glutarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles of selected from 3.8, 4.3, 6.9, 7.6, 8.5, 9.2, 9.9, 10.8, 11.9, 13.0, 13.9, 15.7, 17.0, 17.6, 18.6, 19.2, 20.3, 20.7, 21.4, 23.3, and 25.3 $\pm$ 0.3 degrees two theta. In some embodiments, the crystalline glutarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.8, 4.3, 6.9, 7.6, 8.5, 9.2, 9.9, 10.8, 11.9, 13.0, 13.9, 15.7, 17.0, 17.6, 18.6, 19.2, 20.3, 20.7, 21.4, 23.3, and 25.3 $\pm$ 0.4 degrees two theta.

[0204] In some embodiments, the crystalline glutarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.3, 6.9, 7.6, 8.5, 9.2, 9.9, 10.8, 11.9, 13.0, 13.9, 15.7, 17.0, 17.6, 18.6, 19.2, 20.3, 20.7, 21.4, 23.3, and 25.3 $\pm$ 0.2 degrees two theta. In some embodiments, the crystalline glutarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.3, 6.9, 7.6, 8.5, 9.2, 9.9, 10.8, 11.9, 13.0, 13.9, 15.7, 17.0, 17.6, 18.6, 19.2, 20.3, 20.7, 21.4, 23.3, and 25.3 $\pm$ 0.3 degrees two theta. In some embodiments, the crystalline glutarate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.3, 6.9, 7.6, 8.5, 9.2, 9.9, 10.8, 11.9, 13.0, 13.9, 15.7, 17.0, 17.6, 18.6, 19.2, 20.3, 20.7, 21.4, 23.3, and 25.3 $\pm$ 0.4 degrees two theta. In some

embodiments, the crystalline glutarate salt of the compound of Formula (I) or solvate thereof is characterized by an XRPD pattern substantially as set forth in FIG. 18.

[0205] In some embodiments, the crystalline glutarate salt of the compound of Formula (I) or solvate thereof is characterized as having an endotherm peak at about 224.0 °C, as determined by simultaneous thermal analysis (SDT). In certain embodiments, the crystalline glutarate salt of the compound of Formula (I) or solvate thereof is characterized as having an SDT thermogram substantially as set forth in FIG. 19. In some embodiments, the crystalline glutarate salt of the compound of Formula (I) or solvate thereof is characterized as having a weight loss of about 6.4% from about 26.5 °C to about 125.0 °C, as determined by SDT. In some embodiments, the crystalline glutarate salt of the compound of Formula (I) or solvate thereof is characterized as having a DVS graph substantially as shown in FIG. 20.

[0206] In some aspects, the present invention relates to a pharmaceutical composition which comprises a therapeutically effective amount of the crystalline glutarate salt of the compound of Formula (I) or solvate thereof described herein and a pharmaceutically acceptable excipient.

Glycolate Salt of a Peptide of SEQ ID NO: 1

[0207] In some embodiments, a pharmaceutically acceptable salt of a compound of Formula (I) is a glycolate salt. In some embodiments, the glycolate salt of the compound of Formula (I) is crystalline. In some embodiments, the glycolate salt of the compound of Formula (I) is in the form of a solvate. In certain embodiments, the solvate of the glycolate salt of the compound of Formula (I) is a hydrate. In some other embodiments, the glycolate salt of the compound of Formula (I) is crystalline and in the form of a solvate.

[0208] In some embodiments, the crystalline glycolate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, and 9.2 +/- 0.2 degrees two theta. In some embodiments, the crystalline glycolate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, and 9.2 +/- 0.3 degrees two theta. In some embodiments, the crystalline glycolate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, and 9.2 +/- 0.4 degrees two theta.

[0209] In some embodiments, the crystalline glycolate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 +/- 0.2 degrees two theta. In some embodiments, the crystalline glycolate salt of the

compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 $\pm$ 0.3 degrees two theta. In some embodiments, the crystalline glycolate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 $\pm$ 0.4 degrees two theta.

[0210] In some embodiments, the crystalline glycolate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 $\pm$ 0.2 degrees two theta. In some embodiments, the crystalline glycolate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 $\pm$ 0.3 degrees two theta. In some embodiments, the crystalline glycolate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 $\pm$ 0.4 degrees two theta.

[0211] In some embodiments, the crystalline glycolate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.8, 4.3, 6.9, 7.7, 8.5, 9.2, 10.0, 10.7, 11.5, 12.0, 13.1, 14.0, 15.8, 17.1, 17.7, 19.2, 20.2, 20.8, 21.6, 25.4, and 29.5 $\pm$ 0.2 degrees two theta. In some embodiments, the crystalline glycolate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.8, 4.3, 6.9, 7.7, 8.5, 9.2, 10.0, 10.7, 11.5, 12.0, 13.1, 14.0, 15.8, 17.1, 17.7, 19.2, 20.2, 20.8, 21.6, 25.4, and 29.5 $\pm$ 0.3 degrees two theta. In some embodiments, the crystalline glycolate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.8, 4.3, 6.9, 7.7, 8.5, 9.2, 10.0, 10.7, 11.5, 12.0, 13.1, 14.0, 15.8, 17.1, 17.7, 19.2, 20.2, 20.8, 21.6, 25.4, and 29.5 $\pm$ 0.4 degrees two theta.

[0212] In some embodiments, the crystalline glycolate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.3, 6.9, 7.7, 8.5, 9.2, 10.0, 10.7, 11.5, 12.0, 13.1, 14.0, 15.8, 17.1, 17.7, 19.2, 20.2, 20.8, 21.6, 25.4, and 29.5 $\pm$ 0.2 degrees two theta. In some embodiments, the crystalline glycolate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.3, 6.9, 7.7, 8.5, 9.2, 10.0, 10.7, 11.5, 12.0, 13.1, 14.0, 15.8, 17.1, 17.7, 19.2, 20.2, 20.8, 21.6, 25.4, and 29.5

+/- 0.3 degrees two theta. In some embodiments, the crystalline glycolate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.3, 6.9, 7.7, 8.5, 9.2, 10.0, 10.7, 11.5, 12.0, 13.1, 14.0, 15.8, 17.1, 17.7, 19.2, 20.2, 20.8, 21.6, 25.4, and 29.5 +/- 0.4 degrees two theta. In some embodiments, the crystalline glycolate salt of the compound of Formula (I) or solvate thereof is characterized by an XRPD pattern substantially as set forth in FIG. 21.

[0213] In some embodiments, the crystalline glycolate salt of the compound of Formula (I) or solvate thereof is characterized as having an endotherm peak at about 237.0 °C, as determined by SDT. In certain embodiments, the crystalline glycolate salt of the compound of Formula (I) or solvate thereof is characterized as having an SDT thermogram substantially as set forth in FIG. 22.

[0214] In some embodiments, the crystalline glycolate salt of the compound of Formula (I) or solvate thereof is characterized as having a weight loss of about 5.1% from about 26.5 °C to about 100.0 °C, as determined by SDT. In certain embodiments, the crystalline glycolate salt of the compound of Formula (I) or solvate thereof is characterized as having an SDT thermogram substantially as set forth in FIG. 22. In some embodiments, the crystalline glycolate salt of the compound of Formula (I) or solvate thereof is characterized as having a DVS graph substantially as shown in FIG. 23.

[0215] In some aspects, the present invention relates to a pharmaceutical composition which comprises a therapeutically effective amount of the crystalline glycolate salt of the compound of Formula (I) or solvate thereof described herein and one or more pharmaceutically acceptable excipients.

Sulfate Salt of a Peptide of SEQ ID NO: 1

[0216] In some embodiments, a pharmaceutically acceptable salt of a compound of Formula (I) is a sulfate salt. In some embodiments, the sulfate salt of the compound of Formula (I) is crystalline. In some embodiments, the sulfate salt of the compound of Formula (I) is in the form of a solvate. In certain embodiments, the solvate of the sulfate salt of the compound of Formula (I) is a hydrate. In some other embodiments, the sulfate salt of the compound of Formula (I) is crystalline and in the form of a solvate.

[0217] In some embodiments, the crystalline sulfate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, and 9.2 +/- 0.2 degrees two theta. In some embodiments, the crystalline sulfate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta

angles selected from 4.2, 6.9, 7.6, and 9.2 $\pm$ 0.3 degrees two theta. In some embodiments, the crystalline sulfate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, and 9.2 $\pm$ 0.4 degrees two theta.

[0218] In some embodiments, the crystalline sulfate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, 9.2, 9.6, 11.3, 12.5, 16.7, and 18.4 $\pm$ 0.2 degrees two theta. In some embodiments, the crystalline sulfate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, 9.2, 9.6, 11.3, 12.5, 16.7, and 18.4 $\pm$ 0.3 degrees two theta. In some embodiments, the crystalline sulfate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, 9.2, 9.6, 11.3, 12.5, 16.7, and 18.4 $\pm$ 0.4 degrees two theta.

[0219] In some embodiments, the crystalline sulfate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.1, 6.8, 7.6, 9.2, 9.6, 10.3, 11.3, 12.5, 13.7, 16.8, 17.9, 18.4, 19.8, 20.7, 21.3, and 22.7 $\pm$ 0.2 degrees two theta. In some embodiments, the crystalline sulfate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.1, 6.8, 7.6, 9.2, 9.6, 10.3, 11.3, 12.5, 13.7, 16.8, 17.9, 18.4, 19.8, 20.7, 21.3, and 22.7 $\pm$ 0.3 degrees two theta. In some embodiments, the crystalline sulfate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.1, 6.8, 7.6, 9.2, 9.6, 10.3, 11.3, 12.5, 13.7, 16.8, 17.9, 18.4, 19.8, 20.7, 21.3, and 22.7 $\pm$ 0.4 degrees two theta.

[0220] In some embodiments, the crystalline sulfate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 4.1, 6.8, 7.6, 9.2, 9.6, 10.3, 11.3, 12.5, 13.7, 16.8, 17.9, 18.4, 19.8, 20.7, 21.3, and 22.7 $\pm$ 0.2 degrees two theta. In some embodiments, the crystalline sulfate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 4.1, 6.8, 7.6, 9.2, 9.6, 10.3, 11.3, 12.5, 13.7, 16.8, 17.9, 18.4, 19.8, 20.7, 21.3, and 22.7 $\pm$ 0.3 degrees two theta. In some embodiments, the crystalline sulfate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 4.1, 6.8, 7.6, 9.2, 9.6, 10.3, 11.3, 12.5, 13.7, 16.8, 17.9, 18.4, 19.8, 20.7, 21.3, and 22.7 $\pm$ 0.4 degrees two theta.

In some embodiments, the crystalline sulfate salt of the compound of Formula (I) or solvate thereof is characterized by an XRPD pattern substantially as set forth in FIG. 26.

[0221] In some embodiments, the crystalline sulfate salt of the compound of Formula (I) or solvate thereof is characterized as having an endotherm peak at about 255.0 °C, as determined by SDT. In certain embodiments, the crystalline sulfate salt of the compound of Formula (I) or solvate thereof is characterized as having an SDT thermogram substantially as set forth in FIG. 27.

[0222] In some embodiments, the crystalline sulfate salt of the compound of Formula (I) or solvate thereof is characterized as having a weight loss of about 4.4% from about 26.5 °C to about 80.0 °C, as determined by SDT. In certain embodiments, the crystalline sulfate salt of the compound of Formula (I) or solvate thereof is characterized as having an SDT thermogram substantially as set forth in FIG. 27.

[0223] In some aspects, the present invention relates to a pharmaceutical composition which comprises a therapeutically effective amount of the crystalline sulfate salt of the compound of Formula (I) or solvate thereof described herein and a pharmaceutically acceptable excipient.

Mesylate Salt of a Peptide of SEQ ID NO: 1

[0224] In some embodiments, a pharmaceutically acceptable salt of a compound of Formula (I) is a mesylate salt. In some embodiments, the mesylate salt of the compound of Formula (I) is crystalline. In some embodiments, the mesylate salt of the compound of Formula (I) is in the form of a solvate. In certain embodiments, the solvate of the mesylate salt of the compound of Formula (I) is a hydrate. In some other embodiments, the mesylate salt of the compound of Formula (I) is crystalline and in the form of a solvate.

[0225] In some embodiments, the crystalline mesylate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, and 9.2 +/- 0.2 degrees two theta. In some embodiments, the crystalline mesylate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, and 9.2 +/- 0.3 degrees two theta. In some embodiments, the crystalline mesylate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, and 9.2 +/- 0.4 degrees two theta.

[0226] In some embodiments, the crystalline mesylate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, 9.2, 9.6, 11.3, 12.5, 16.7, and 18.4 +/- 0.2

degrees two theta. In some embodiments, the crystalline mesylate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, 9.2, 9.6, 11.3, 12.5, 16.7, and 18.4 +/- 0.3 degrees two theta. In some embodiments, the crystalline mesylate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, 9.2, 9.6, 11.3, 12.5, 16.7, and 18.4 +/- 0.4 degrees two theta.

[0227] In some embodiments, the crystalline mesylate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having at least two diffraction peaks at two theta angles selected from 4.1, 6.8, 7.6, 9.2, 9.6, 11.3, 12.5, 13.7, 15.5, 16.6, 18.4, 19.8, 20.6, 22.8 and 27.8 degrees two theta +/- 0.2 degrees two theta. In some embodiments, the crystalline mesylate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having at least two diffraction peaks at two theta angles selected from 4.1, 6.8, 7.6, 9.2, 9.6, 11.3, 12.5, 13.7, 15.5, 16.6, 18.4, 19.8, 20.6, 22.8 and 27.8 degrees two theta +/- 0.3 degrees two theta. In some embodiments, the crystalline mesylate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having at least two diffraction peaks at two theta angles selected from 4.1, 6.8, 7.6, 9.2, 9.6, 11.3, 12.5, 13.7, 15.5, 16.6, 18.4, 19.8, 20.6, 22.8 and 27.8 degrees two theta +/- 0.4 degrees two theta.

[0228] In some embodiments, the crystalline mesylate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 4.1, 6.8, 7.6, 9.2, 9.6, 11.3, 12.5, 13.7, 15.5, 16.6, 18.4, 19.8, 20.6, 22.8 and 27.8 degrees two theta +/- 0.2 degrees two theta. In some embodiments, the crystalline mesylate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 4.1, 6.8, 7.6, 9.2, 9.6, 11.3, 12.5, 13.7, 15.5, 16.6, 18.4, 19.8, 20.6, 22.8 and 27.8 degrees two theta +/- 0.3 degrees two theta. In some embodiments, the crystalline mesylate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 4.1, 6.8, 7.6, 9.2, 9.6, 11.3, 12.5, 13.7, 15.5, 16.6, 18.4, 19.8, 20.6, 22.8 and 27.8 degrees two theta +/- 0.4 degrees two theta. In some embodiments, the crystalline mesylate salt of the compound of Formula (I) or solvate thereof is characterized by an XRPD pattern substantially as set forth in FIG. 24.

[0229] In some embodiments, the crystalline mesylate salt of the compound of Formula (I) or solvate thereof is characterized as having an endotherm peak at about 242.1 °C, as determined by SDT. In certain embodiments, the crystalline mesylate salt of the compound of Formula (I) or solvate thereof is characterized as having an SDT thermogram substantially as set forth in FIG.

25. In some embodiments, the crystalline mesylate salt of the compound of Formula (I) or solvate thereof is characterized as having a weight loss of about 5.4% from about 26.5 °C to about 80.0 °C, as determined by SDT. In certain embodiments, the crystalline mesylate salt of the compound of Formula (I) or solvate thereof is characterized as having an SDT thermogram substantially as set forth in FIG. 25.

[0230] In some aspects, the present invention relates to a pharmaceutical composition which comprises a therapeutically effective amount of the crystalline mesylate salt of the compound of Formula (I) or solvate thereof described herein and a pharmaceutically acceptable excipient.

Citrate Salt of a Peptide of SEQ ID NO: 1

[0231] In some embodiments, a pharmaceutically acceptable salt of a compound of Formula (I) is a citrate salt. In some embodiments, the citrate salt of the compound of Formula (I) is crystalline. In some embodiments, the citrate salt of the compound of Formula (I) is in the form of a solvate. In certain embodiments, the solvate of the citrate salt of the compound of Formula (I) is a hydrate. In some other embodiments, the citrate salt of the compound of Formula (I) is crystalline and in the form of a solvate.

[0232] In some embodiments, the crystalline citrate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, and 9.2 +/- 0.2 degrees two theta. In some embodiments, the crystalline citrate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, and 9.2 +/- 0.3 degrees two theta. In some embodiments, the crystalline citrate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, and 9.2 +/- 0.4 degrees two theta.

[0233] In some embodiments, the crystalline citrate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, 9.2, 9.6, 11.3, 12.5, 16.7, and 18.4 +/- 0.2 degrees two theta. In some embodiments, the crystalline citrate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, 9.2, 9.6, 11.3, 12.5, 16.7, and 18.4 +/- 0.3 degrees two theta. In some embodiments, the crystalline citrate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, 9.2, 9.6, 11.3, 12.5, 16.7, and 18.4 +/- 0.4 degrees two theta.

[0234] In some embodiments, the crystalline citrate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having at least two diffraction peaks at two theta angles selected from 3.8, 4.3, 6.9, 7.0, 7.6, 8.4, 9.3, 10.0, 10.8, 12.2, 13.1, 13.9, 14.1, 15.3, 15.9, 16.3, 17.0, 17.4, 17.9, 19.0, 19.5, 19.8, 20.5, 22.0, 23.1, 24.4, 24.8, 25.2, 26.5, 29.1, 30.5, 32.1, 33.1, and 33.5 +/- 0.2 degrees two theta. In some embodiments, the crystalline citrate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having at least two diffraction peaks at two theta angles selected from 3.8, 4.3, 6.9, 7.0, 7.6, 8.4, 9.3, 10.0, 10.8, 12.2, 13.1, 13.9, 14.1, 15.3, 15.9, 16.3, 17.0, 17.4, 17.9, 19.0, 19.5, 19.8, 20.5, 22.0, 23.1, 24.4, 24.8, 25.2, 26.5, 29.1, 30.5, 32.1, 33.1, and 33.5 +/- 0.3 degrees two theta. In some embodiments, the crystalline citrate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having at least two diffraction peaks at two theta angles selected from 3.8, 4.3, 6.9, 7.0, 7.6, 8.4, 9.3, 10.0, 10.8, 12.2, 13.1, 13.9, 14.1, 15.3, 15.9, 16.3, 17.0, 17.4, 17.9, 19.0, 19.5, 19.8, 20.5, 22.0, 23.1, 24.4, 24.8, 25.2, 26.5, 29.1, 30.5, 32.1, 33.1, and 33.5 +/- 0.4 degrees two theta.

[0235] In some embodiments, the crystalline citrate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.3, 6.9, 7.0, 7.6, 8.4, 9.3, 10.0, 10.8, 12.2, 13.1, 13.9, 14.1, 15.3, 15.9, 16.3, 17.0, 17.4, 17.9, 19.0, 19.5, 19.8, 20.5, 22.0, 23.1, 24.4, 24.8, 25.2, 26.5, 29.1, 30.5, 32.1, 33.1, and 33.5 +/- 0.2 degrees two theta. In some embodiments, the crystalline citrate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.3, 6.9, 7.0, 7.6, 8.4, 9.3, 10.0, 10.8, 12.2, 13.1, 13.9, 14.1, 15.3, 15.9, 16.3, 17.0, 17.4, 17.9, 19.0, 19.5, 19.8, 20.5, 22.0, 23.1, 24.4, 24.8, 25.2, 26.5, 29.1, 30.5, 32.1, 33.1, and 33.5 +/- 0.3 degrees two theta. In some embodiments, the crystalline citrate salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.3, 6.9, 7.0, 7.6, 8.4, 9.3, 10.0, 10.8, 12.2, 13.1, 13.9, 14.1, 15.3, 15.9, 16.3, 17.0, 17.4, 17.9, 19.0, 19.5, 19.8, 20.5, 22.0, 23.1, 24.4, 24.8, 25.2, 26.5, 29.1, 30.5, 32.1, 33.1, and 33.5 +/- 0.4 degrees two theta. In some embodiments, the crystalline citrate salt of the compound of Formula (I) or solvate thereof is characterized by an XRPD pattern substantially as set forth in FIG. 28.

[0236] In some aspects, the present invention relates to a pharmaceutical composition which comprises a therapeutically effective amount of the crystalline citrate salt of the compound of Formula (I) or solvate thereof described herein and a pharmaceutically acceptable excipient.

Bis-Hydrochloride Salt of a Peptide of SEQ ID NO: 1

[0237] In some embodiments, a pharmaceutically acceptable salt of a compound of Formula (I) is a bis-hydrochloride salt. In some embodiments, the bis-hydrochloride salt of the compound of Formula (I) is crystalline. In some embodiments, the bis-hydrochloride salt of the compound of Formula (I) is in the form of a solvate. In certain embodiments, the solvate of the bis-hydrochloride salt of the compound of Formula (I) is a hydrate. In some other embodiments, the bis-hydrochloride salt of the compound of Formula (I) is crystalline and in the form of a solvate.

[0238] In some embodiments, the crystalline bis-hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, and 9.2 $\pm$ 0.2 degrees two theta. In some embodiments, the crystalline bis-hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, and 9.2 $\pm$ 0.3 degrees two theta. In some embodiments, the crystalline bis-hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 4.2, 6.9, 7.6, and 9.2 $\pm$ 0.4 degrees two theta.

[0239] In some embodiments, the crystalline bis-hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 $\pm$ 0.2 degrees two theta. In some embodiments, the crystalline bis-hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 $\pm$ 0.3 degrees two theta. In some embodiments, the crystalline bis-hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having two or more diffraction peaks at two theta angles selected from 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 $\pm$ 0.4 degrees two theta.

[0240] In some embodiments, the crystalline bis-hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 $\pm$ 0.2 degrees two theta. In some embodiments, the crystalline bis-hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 $\pm$ 0.3 degrees two theta. In some embodiments, the crystalline bis-hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having

an XRPD pattern having diffraction peaks at two theta angles of at least 3.8, 4.2, 6.9, 7.6, 8.5, 9.2, 10.0, 10.7, 12.1, 13.9, 15.8, or 17.1 $\pm$ 0.4 degrees two theta.

[0241] In some embodiments, the crystalline bis-hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having at least two diffraction peaks at two theta angles selected from 3.4, 4.6, 6.1, 8.3, 8.7, 9.1, 9.4, 9.8, 10.1, 11.1, 11.4, 12.0, 12.4, 13.6, 15.1, 15.9, 16.1, 16.7, 17.8, 18.4, 18.7, 19.4, 19.9, and 20.8 $\pm$ 0.2 degrees two theta. In some embodiments, the crystalline bis-hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having at least two diffraction peaks at two theta angles selected from 3.4, 4.6, 6.1, 8.3, 8.7, 9.1, 9.4, 9.8, 10.1, 11.1, 11.4, 12.0, 12.4, 13.6, 15.1, 15.9, 16.1, 16.7, 17.8, 18.4, 18.7, 19.4, 19.9, and 20.8 $\pm$ 0.3 degrees two theta. In some embodiments, the crystalline bis-hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having at least two diffraction peaks at two theta angles selected from 3.4, 4.6, 6.1, 8.3, 8.7, 9.1, 9.4, 9.8, 10.1, 11.1, 11.4, 12.0, 12.4, 13.6, 15.1, 15.9, 16.1, 16.7, 17.8, 18.4, 18.7, 19.4, 19.9, and 20.8 $\pm$ 0.4 degrees two theta.

[0242] In some embodiments, the crystalline bis-hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.4, 4.6, 6.1, 8.3, 8.7, 9.1, 9.4, 9.8, 10.1, 11.1, 11.4, 12.0, 12.4, 13.6, 15.1, 15.9, 16.1, 16.7, 17.8, 18.4, 18.7, 19.4, 19.9, and 20.8 $\pm$ 0.2 degrees two theta. In some embodiments, the crystalline bis-hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.4, 4.6, 6.1, 8.3, 8.7, 9.1, 9.4, 9.8, 10.1, 11.1, 11.4, 12.0, 12.4, 13.6, 15.1, 15.9, 16.1, 16.7, 17.8, 18.4, 18.7, 19.4, 19.9, and 20.8 $\pm$ 0.3 degrees two theta. In some embodiments, the crystalline bis-hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having an XRPD pattern having diffraction peaks at two theta angles of at least 3.4, 4.6, 6.1, 8.3, 8.7, 9.1, 9.4, 9.8, 10.1, 11.1, 11.4, 12.0, 12.4, 13.6, 15.1, 15.9, 16.1, 16.7, 17.8, 18.4, 18.7, 19.4, 19.9, and 20.8 $\pm$ 0.4 degrees two theta. In some embodiments, the crystalline bis-hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized by an XRPD pattern substantially as set forth in FIG. 29.

[0243] In some embodiments, the crystalline bis-hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having endotherm peaks at about 79.5 °C and/or about 235.3 °C, as determined by DSC. In certain embodiments, the crystalline bis-hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having a DSC curve as substantially set forth in FIG. 31.

[0244] In some embodiments, the crystalline bis-hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having a weight loss of about 11.3% from about 26.5 °C to about 190.0 °C, as determined by TGA. In certain embodiments, the crystalline bis-hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having a TGA graph substantially as set forth in FIG. 30.

[0245] In some embodiments, the crystalline bis-hydrochloride salt of the compound of Formula (I) or solvate thereof is characterized as having a DVS graph substantially as shown in FIG. 32.

[0246] In some aspects, the present invention relates to a pharmaceutical composition which comprises a therapeutically effective amount of the crystalline bis-hydrochloride salt of the compound of Formula (I) or solvate thereof described herein and a pharmaceutically acceptable excipient.

Purity

[0247] In some embodiments, the crystalline salt of the compound of Formula (I) or solvate thereof produced by the methods described herein has a purity level of at least about 85%, at least about 90%, at least about 91%, at least about 92%, at least about 93%, at least about 94%, at least about 95%, at least about 96%, at least about 97%, at least 98%, or at least about 99% as determined by ultra-performance liquid chromatography (UPLC), high-performance liquid chromatography (HPLC), or other appropriate methods. In some embodiments, the crystalline salt of the compound of Formula (I) or solvate thereof has a purity level of between about 90% and 100%. In some embodiments, the crystalline salt of the compound of Formula (I) or solvate thereof has a purity level of at least about 95.0%, about 96.0%, about 97.0%, about 98.0%, about 99.0%, about 99.1%, about 99.2%, about 99.3%, about 99.4%, about 99.5%, about 99.6%, about 99.7%, about 99.8%, or about 99.9%, including any amount in between and fractions thereof. In other embodiments, the crystalline salt of the compound of Formula (I) or solvate thereof has a purity level of between about 95.0% and 99.9%. In some embodiments, the crystalline salt of the compound of Formula (I) or solvate thereof has a purity level of at least 95%. In some embodiments, the crystalline salt of the compound of Formula (I) or solvate thereof has a purity level of at least 96%. In some embodiments, the crystalline salt of the compound of Formula (I) or solvate thereof has a purity level of at least 97%. In some embodiments, the crystalline salt of the compound of Formula (I) or solvate thereof has a purity level of at least 98%. In some embodiments, the crystalline salt of the compound of Formula (I) or solvate thereof has a purity level of at least 99%. In some embodiments, the crystalline salt of the compound of Formula (I) or solvate thereof has a purity level of at least 99.5%.

[0248] In some embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof has a purity level of at least about 95.0%, about 96.0%, about 97.0%, about 98.0%, about 99.0%, about 99.1%, about 99.2%, about 99.3%, about 99.4%, about 99.5%, about 99.6%, about 99.7%, about 99.8%, or about 99.9%, including any amount in between and fractions thereof. In other embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof has a purity level of between about 99.0% and 99.5%. In certain embodiments, the crystalline hydrochloride salt of the compound of Formula (I) or solvate thereof has a purity level of at least 99.0%.

[0249] In some embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof has a purity level of at least about 95.0%, about 96.0%, about 97.0%, about 98.0%, about 99.0%, about 99.1%, about 99.2%, about 99.3%, about 99.4%, about 99.5%, about 99.6%, about 99.7%, about 99.8%, or about 99.9%, including any amount in between and fractions thereof. In certain embodiments, the crystalline acetate salt of the compound of Formula (I) or solvate thereof has a purity level of at least 99.0%. In other embodiments, the crystalline salt of the compound of Formula (I) or solvate thereof has a purity level of between about 99.0% and 99.5%.

[0250] In some embodiments, the crystalline fumarate salt of the compound of Formula (I) or solvate thereof has a purity level of at least about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, or about 98%, or about 99%, including any amount in between and fractions thereof. In other embodiments, the crystalline fumarate salt of the compound of Formula (I) or solvate thereof has a purity level of between about 86% and 90%. In other embodiments, the crystalline fumarate salt of the compound of Formula (I) or solvate thereof has a purity level of between about 86% and 87%. In certain embodiments, the crystalline fumarate salt of the compound of Formula (I) or solvate thereof has a purity level of at least 86%.

[0251] In some embodiments, the crystalline glutarate salt of the compound of Formula (I) or solvate thereof has a purity level of at least about 95.0%, about 96.0%, about 97.0%, about 98.0%, about 99.0%, about 99.1%, about 99.2%, about 99.3%, about 99.4%, about 99.5%, about 99.6%, about 99.7%, about 99.8%, or about 99.9%, including any amount in between and fractions thereof. In some embodiments, the crystalline glutarate salt of the compound of Formula (I) or solvate thereof has a purity level of between about 85% and 90%. In some embodiments, the crystalline glutarate salt of the compound of Formula (I) or solvate thereof has a purity level of between about 90% and 95%. In some embodiments, the crystalline glutarate salt of the compound of Formula (I) or solvate thereof has a purity level of between about 95% and 99%. In some embodiments, the crystalline glutarate salt of the compound of Formula (I) or

solvate thereof has a purity level of between about 99.0% and 99.5%. In some embodiments, the crystalline glutarate salt of the compound of Formula (I) or solvate thereof has a purity level of at least 99.0%.

[0252] In some embodiments, the crystalline mesylate salt of the compound of Formula (I) or solvate thereof has a purity level of at least about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, or about 98%, or about 99%, including any amount in between and fractions thereof. In other embodiments, the crystalline mesylate salt of the compound of Formula (I) or solvate thereof has a purity level of between about 90% and 95%. In other embodiments, the crystalline mesylate salt of the compound of Formula (I) or solvate thereof has a purity level of between about 95% and 99%. In other embodiments, the crystalline mesylate salt of the compound of Formula (I) or solvate thereof has a purity level of between about 90% and 92%. In certain embodiments, the crystalline mesylate salt of the compound of Formula (I) or solvate thereof has a purity level of at least 90%.

[0253] In some embodiments, the crystalline sulfate salt of the compound of Formula (I) or solvate thereof has a purity level of at least about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, or about 98%, or about 99%, including any amount in between and fractions thereof. In other embodiments, the crystalline sulfate salt of the compound of Formula (I) or solvate thereof has a purity level of between about 90% and 95%. In other embodiments, the crystalline sulfate salt of the compound of Formula (I) or solvate thereof has a purity level of between about 95% and 99%. In other embodiments, the crystalline sulfate salt of the compound of Formula (I) or solvate thereof has a purity level of between about 90% and 92%. In certain embodiments, the crystalline sulfate salt of the compound of Formula (I) or solvate thereof has a purity level of at least 91%.

[0254] In some embodiments, the crystalline citrate salt of the compound of Formula (I) or solvate thereof has a purity level of at least about 95.0%, about 96.0%, about 97.0%, about 98.0%, about 99.0%, about 99.1%, about 99.2%, about 99.3%, about 99.4%, about 99.5%, about 99.6%, about 99.7%, about 99.8%, or about 99.9%, including any amount in between and fractions thereof. In other embodiments, the crystalline citrate salt of the compound of Formula (I) or solvate thereof has a purity level of between about 99.0% and 99.9%. In certain embodiments, the crystalline citrate salt of the compound of Formula (I) or solvate thereof has a purity level of at least 99.5%.

[0255] In some embodiments, the crystalline free base of the compound of Formula (I) or solvate thereof has a purity level of at least about 95.0%, about 96.0%, about 97.0%, about

98.0%, about 99.0%, about 99.1%, about 99.2%, about 99.3%, about 99.4%, about 99.5%, about 99.6%, about 99.7%, about 99.8%, or about 99.3%, including any amount in between and fractions thereof. In certain embodiments, the crystalline free base of the compound of Formula (I) or solvate thereof has a purity level of at least 97.0%. In certain embodiments, the crystalline free base of the compound of Formula (I) or solvate thereof has a purity level of at least 98.0%. In certain embodiments, the crystalline free base of the compound of Formula (I) or solvate thereof has a purity level of at least 99.0%. In other embodiments, the crystalline free base of the compound of Formula (I) or solvate thereof has a purity level of between about 97.0% and 98.0%. In other embodiments, the crystalline free base of the compound of Formula (I) or solvate thereof has a purity level of between about 98.0%. In other embodiments, the crystalline free base of the compound of Formula (I) or solvate thereof has a purity level of between about 99.0%.

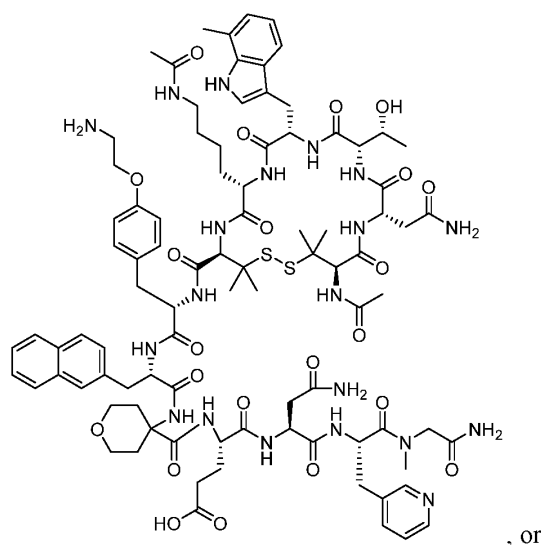
IV. PHARMACEUTICAL COMPOSITIONS

[0256] In general, the present invention relates to pharmaceutical hydrochloride salt forms and compositions of peptide inhibitors of the interleukin-23 receptor (IL-23R) or solvates thereof, corresponding pharmaceutical compositions, methods and/or uses for treatment of autoimmune inflammation and related diseases and disorders as defined herein.

[0257] Further, the present invention relates to pharmaceutical crystalline salt forms and compositions of peptide inhibitors of the interleukin-23 receptor (IL-23R) or solvates thereof, corresponding pharmaceutical compositions, methods and/or uses for treatment of autoimmune inflammation and related diseases and disorders as defined herein.

[0258] In one aspect, the present invention relates to a pharmaceutical composition of a hydrochloride salt of a compound of Formula (I):

Ac-[Pen]*-N-T-[W(7-Me)]-[Lys(Ac)]-[Pen]*-Phe[4-(2-aminoethoxy)]-[2-Nal]-[THP]-E-N-[3-Pal]-Sarc-NH₂ (in which ([Pen]*-[Pen]* form a disulfide bond); and having the chemical structure shown below:



a corresponding solvate thereof.

[0259] In some embodiments, the monocyclic peptide comprises an amino acid sequence of Ac-[Pen]-N-T-[W(7-Me)]-[Lys(Ac)]-[Pen]-[Phe(4-(2-aminoethoxy))]-[2-Nal]-[THP]-E-N-[3Pal]-[Sarc]-NH₂, wherein the monocyclic peptide is cyclized via a Pen-Pen disulfide bond; or a pharmaceutically acceptable salt thereof. In any of the foregoing embodiments, one or more amino acids is in the L configuration. In certain embodiments, all amino acids are in the L configuration.

[0260] In some embodiments, the crystalline form of a compound of formula (I) or solvate thereof has a moisture content in the range of about 0.1% to about 20%, 0.5% to about 15%, about 1% to about 10%, about 1% to about 5%, about 1% to about 4%, about 1% to about 3%, about 0.1% to about 5%, about 0.1% to about 4%, or about 0.1% to about 3% by weight. In some embodiments, the crystalline form of a compound of formula (I) or solvate thereof has a moisture content level of about 0.1%, 0.5%, 1%, 1.5%, 2%, 2.7%, 3%, 3.5%, 4%, 4.5%, 5%, 5.5%, 6%, 7%, 8%, 9%, or 10% by weight. In some embodiments, the crystalline form of a compound of formula (I) or solvate thereof has a moisture content level of greater than about 0.1%, 0.5%, 1%, 1.5%, 2%, 2.7%, 3%, 3.5%, 4%, 4.5%, 5%, or 5.5% by weight. In some embodiments, the crystalline form of a compound of formula (I) or solvate thereof has a moisture content level of lower than about 1%, 1.5%, 2%, 2.7%, 3%, 3.5%, 4%, 4.5%, 5%, 5.5%, 6%, 7%, 8%, 9%, or 10% by weight.

[0261] In some embodiments, the amount of a crystalline form of a compound of formula (I) or solvate thereof in the composition is in the range of about 0.1% to about 65%, about 0.1% to about 60%, about 0.1% to about 55%, about 0.1% to about 50%, about 0.1% to about 45%, about 0.1% to about 40%, about 0.1% to about 35%, about 0.1% to about 30%, about 0.1% to

about 25%, about 0.1% to about 20%, about 0.1% to about 15%, about 0.1% to about 10%, or about 0.1% to about 5% by weight. In some embodiments, the amount of a crystalline form of a compound of formula (I) or solvate thereof in the composition is in the range of about 1% to about 65%, about 1% to about 60%, about 1% to about 55%, about 1% to about 50%, about 1% to about 45%, about 1% to about 40%, about 1% to about 35%, about 1% to about 30%, about 1% to about 25%, about 1% to about 20%, about 1% to about 15%, about 1% to about 10%, or about 1% to about 5% by weight. In some embodiments, the amount of a crystalline form of a compound of formula (I) or solvate thereof in the composition is in the range of about 2% to about 65%, about 2% to about 60%, about 2% to about 55%, about 2% to about 50%, about 2% to about 45%, about 2% to about 40%, about 2% to about 35%, about 2% to about 30%, about 2% to about 25%, about 2% to about 20%, about 2% to about 15%, about 2% to about 10%, or about 2% to about 5% by weight. In some embodiments, the amount of a crystalline form of a compound of formula (I) or solvate thereof in the composition is in the range of about 5% to about 65%, about 5% to about 60%, about 5% to about 55%, about 5% to about 50%, about 5% to about 45%, about 5% to about 40%, about 5% to about 35%, about 5% to about 30%, about 5% to about 25%, about 5% to about 20%, about 5% to about 15%, or about 5% to about 10% by weight. In some embodiments, the amount of a crystalline form of a compound of formula (I) or solvate thereof in the composition is in the range of about 1%, 2%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, or 65% by weight.

[0262] In another aspect, the hydrochloride salt of a compound of Formula (I) or corresponding solvate thereof may be present in any form, such as a hydrate or other solvate. In some aspects, the hydrochloride salt of a compound of Formula (I) or solvate thereof may be provided in crystalline form, in an amorphous form, or a semi-crystalline form. In some aspects, the hydrochloride salt of a compound of Formula (I) or solvate thereof is a crystalline form. In some aspects, the hydrochloride salt of a compound of Formula (I) or solvate thereof is an amorphous form. In some aspects, the hydrochloride salt of a compound of Formula (I) or solvate thereof is a semi-crystalline form.

[0263] In one aspect, the composition of a hydrochloride salt of a compound of Formula (I) or solvate thereof is a hemi hydrochloride salt. In some aspects, the hemi hydrochloride salt has from about 0.1 to about 0.9, such as from about 0.2 to about 0.8 or from about 0.3 to about 0.7, molar equivalents of hydrogen chloride compared to the compound of Formula (I). In some aspects, the hemi hydrochloride salt has about 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, or about 0.9 molar equivalents of hydrogen chloride compared to the compound of Formula (I). In some aspects, the hemi hydrochloride salt has about 0.5 molar equivalents of hydrogen chloride compared to the compound of Formula (I).

[0264] In some aspects, the hydrochloride salt form of a compound of Formula (I) or solvate thereof may be a hydrate. In some aspects, the hydrate of the hydrochloride salt of a compound of Formula (I) has from about 0.2 to about 100 molar equivalents of water compared to the compound of Formula (I). In another aspect, the hydrate may be present in a range of about 2% w/w to about 10% w/w water compared to the hydrochloride salt of the compound of Formula (I). The present invention relates to hydrochloride salt compositions of the present invention, which may be in a liquid or a solid composition.

[0265] In some embodiments, the hydrochloride salt form of a compound of formula (I) or solvate thereof has a moisture content in the range of about 0.1% to about 20%, 0.5% to about 15%, about 1% to about 10%, about 1% to about 5%, about 1% to about 4%, about 1% to about 3%, about 0.1% to about 5%, about 0.1% to about 4%, or about 0.1% to about 3% by weight. In some embodiments, the hydrochloride salt form of a compound of formula (I) or solvate thereof has a moisture content level of about 0.1%, 0.5%, 1%, 1.5%, 2%, 2.7%, 3%, 3.5%, 4%, 4.5%, 5%, 5.5%, 6%, 7%, 8%, 9%, or 10% by weight. In some embodiments, the hydrochloride salt form of a compound of formula (I) or solvate thereof has a moisture content level of greater than about 0.1%, 0.5%, 1%, 1.5%, 2%, 2.7%, 3%, 3.5%, 4%, 4.5%, 5%, or 5.5% by weight. In some embodiments, the hydrochloride salt form of a compound of formula (I) or solvate thereof has a moisture content level of lower than about 1%, 1.5%, 2%, 2.7%, 3%, 3.5%, 4%, 4.5%, 5%, 5.5%, 6%, 7%, 8%, 9%, or 10% by weight.

[0266] The hydrochloride salt compositions of the present invention can be administered to a subject or patient by any means in accordance with therapeutic administration, which accomplishes intended purpose or pharmaceutical efficacy. Examples include administration by oral, parenteral, subcutaneous, intravenous, intramuscular, intraperitoneal, transdermal, topical, buccal or ocular routes. In some aspects, the administration of the hydrochloride salt composition of the present invention is adapted for oral administration.

[0267] In another aspect, the present invention provides a composition which comprises a hydrochloride salt of a compound of Formula (I) or solvate thereof in an amount of from about 0.1% to about 15% (w/w) of the composition and one or more pharmaceutically acceptable excipients.

[0268] In another aspect, the present invention provides a composition, which comprises: a hydrochloride salt of a compound of Formula (I) or solvate thereof; and about 50 mM pH 7.4 phosphate buffered aqueous solution.

[0269] In another aspect, the present invention relates to a composition, which comprises a hydrochloride salt of a compound of Formula (I) or solvate thereof in an amount of from about

0.1% to about 15% (w/w) of the composition; an absorption enhancer in an amount from about 10% to about 60% (w/w); and one or more pharmaceutically acceptable excipients.

[0270] [0001] In some embodiments, the amount of hydrochloride salt of a compound of formula (I) or solvate thereof in the composition is in the range of about 0.1% to about 65%, about 0.1% to about 60%, about 0.1% to about 55%, about 0.1% to about 50%, about 0.1% to about 45%, about 0.1% to about 40%, about 0.1% to about 35%, about 0.1% to about 30%, about 0.1% to about 25%, about 0.1% to about 20%, about 0.1% to about 15%, about 0.1% to about 10%, or about 0.1% to about 5% by weight. In some embodiments, the amount of hydrochloride salt of a compound of formula (I) or solvate thereof in the composition is in the range of about 1% to about 65%, about 1% to about 60%, about 1% to about 55%, about 1% to about 50%, about 1% to about 45%, about 1% to about 40%, about 1% to about 35%, about 1% to about 30%, about 1% to about 25%, about 1% to about 20%, about 1% to about 15%, about 1% to about 10%, or about 1% to about 5% by weight. In some embodiments, the amount of hydrochloride salt of a compound of formula (I) or solvate thereof in the composition is in the range of about 2% to about 65%, about 2% to about 60%, about 2% to about 55%, about 2% to about 50%, about 2% to about 45%, about 2% to about 40%, about 2% to about 35%, about 2% to about 30%, about 2% to about 25%, about 2% to about 20%, about 2% to about 15%, about 2% to about 10%, or about 2% to about 5% by weight. In some embodiments, the amount of hydrochloride salt of a compound of formula (I) or solvate thereof in the composition is in the range of about 5% to about 65%, about 5% to about 60%, about 5% to about 55%, about 5% to about 50%, about 5% to about 45%, about 5% to about 40%, about 5% to about 35%, about 5% to about 30%, about 5% to about 25%, about 5% to about 20%, about 5% to about 15%, or about 5% to about 10% by weight. In some embodiments, the amount of hydrochloride salt of a compound of formula (I) or solvate thereof in the composition is in the range of about 1%, 2%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, or 65% by weight.

[0271] In another aspect, the present invention provides a composition which comprises a hydrochloride salt of a compound of Formula (I) or solvate thereof in an amount of from about 0.1% to about 15% (w/w) of the composition, sodium caprate in an amount of from about 20% to about 45% (w/w) of the composition, and a microcrystalline cellulose.

[0272] In another aspect, the hydrochloride salt of a compound of Formula (I) or solvate thereof, may be present in any amount from about 0.1% to about 15% (w/w) of the composition. For example, the hydrochloride salt of a compound of Formula (I) or solvate thereof, may be present in an amount of from about 0.5% to about 15% (w/w), or from about 1% to about 10%, or from about 0.5% to about 5%, or from about 0.5% to about 3%, or from about 1% to about 3%, or from about 1.5% to about 2.5%, or from about 1.5% to about 2.0% (w/w) of the

composition. In another aspect, the hydrochloride salt of a compound of Formula (I) or solvate thereof is present in an amount of from about 1% to about 5% (w/w).

[0273] In another aspect, the hydrochloride salt of a compound of Formula (I) or solvate thereof may be present in an amount of from about 1 to about 5% (w/w). For example, the hydrochloride salt of a compound of Formula (I) or solvate thereof may be present in amounts including about 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 11%, 12%, 13%, 14%, or about 15% (w/w) of the composition, and any fractional amount in between. In another aspect, the hydrochloride salt of a compound of Formula (I) or solvate thereof may be present in an amount of about 1.8% (w/w).

[0274] In another aspect, the hydrochloride salt of a compound of Formula (I) or solvate thereof may be present in any amount, such as an amount of from about 1 mg to about 1000 mg, or from about 1 mg to about 500 mg, from about 1 mg to about 100 mg, from about 10 mg to about 50 mg, from about 20 mg to about 40 mg, or from about 20 mg to about 30 mg. In another aspect, the amount of the hydrochloride salt of a compound of Formula (I) or solvate thereof may be from about 1 mg to about 1000 mg. In another aspect, the amount of the hydrochloride salt of a compound of Formula (I) or solvate thereof may be from about 5 mg to about 300 mg. In another aspect, the amount of the hydrochloride salt of a compound of Formula (I) or solvate thereof is from about 25 mg to about 150 mg. In another aspect, the amount of the hydrochloride salt of a compound of Formula (I) or solvate thereof may be from about 25 mg to about 100 mg. In another aspect, the hydrochloride salt of a compound of Formula (I) or solvate thereof may be present in an amount of from about 1 mg to about 100 mg. In another aspect, the hydrochloride salt of a compound of Formula (I) or solvate thereof may be present in an amount of from about 20 mg to about 40 mg. In another aspect, the hydrochloride salt of a compound of Formula (I) or solvate thereof may be present in an amount of from about 20 mg to about 30 mg.

[0275] In yet another aspect, the hydrochloride salt of a compound of Formula (I) or solvate thereof may be present in an amount of about 5 mg, about 10 mg, about 25 mg, about 50 mg, about 75 mg, about 100 mg, or about 150 mg, including any amount in between and fractions thereof. In another aspect, an amount of the hydrochloride salt of a compound of Formula (I) or solvate thereof may be present in about 5 mg. In another aspect, an amount of the hydrochloride salt of a compound of Formula (I) or solvate thereof may be present in about 10 mg. In another aspect, an amount of the hydrochloride salt of a compound of Formula (I) or solvate thereof may be present in about 25 mg. In another aspect, an amount of the hydrochloride salt of a compound of Formula (I) or solvate thereof may be present in about 50 mg. In another aspect, an amount of the hydrochloride salt of a compound of Formula (I) or solvate thereof may be

present in about 75 mg. In another aspect, an amount of the hydrochloride salt of a compound of Formula (I) or solvate thereof may be present in about 100 mg. In another aspect, an amount of the hydrochloride salt of a compound of Formula (I) or solvate thereof may be present in about 150 mg.

[0276] In another aspect, the amount of the crystalline form of a pharmaceutically acceptable salt of a compound of Formula (I) or solvate thereof may be present in an amount of about 5 mg, about 10 mg, about 25 mg, about 50 mg, about 75 mg, about 100 mg, about 150 mg, about 200 mg, about 250 mg, about 300 mg, about 400 mg, about 500 mg, about 600 mg, about 700 mg, about 800 mg, about 900 mg, about 1000 mg, about 1100 mg, about 1200 mg, about 1300 mg, or about 1400 mg, including any amount in between and fractions thereof

[0277] In general, pharmaceutical compositions of the present invention may be formed into different dosage forms prepared using conventional materials and techniques known in the pharmaceutical and formulary arts, which may include, but is not limited to techniques, such as mixing, blending and the like and as set forth throughout the instant disclosure. Moreover, pharmaceutical composition used to form dosage forms may also include, but are not limited to, suitable adjuvants, carriers, excipients, or stabilizers, etc. and can be in solid or liquid form such as, solid or liquid dosage forms, which may include, but are not limited to tablets, capsules, powders, solutions, suspensions, or emulsions and the like, etc. In accordance with the present invention, solid unit dosage forms may be other conventional types known in the art.

[0278] Suitable compositions of the present invention may be in different forms, including, but are not limited to a liquid, a tablet, a capsule, etc. and the like. In some aspects, the composition may be a tablet composition or a capsule composition.

[0279] Further, suitable for use in the present invention are solutions, which may, but are not limited to, such as in water, saline, aqueous dextrose and related sugar solutions, and glycols such as, propylene glycol or polyethylene glycol, buffered solutions and the like, etc., are preferred liquid carriers, particularly for injectable solutions. Under ordinary conditions of storage and use, these preparations contain a preservative to prevent the growth of microorganisms.

[0280] The compositions of the present invention may include a variety of other pharmaceutically acceptable components or excipients, such as, including, but is not limited to, a glidant, a lubricant, a disintegrant, a binder, a desiccant, a filler, and other components or excipients and the like. These components are described within.

[0281] In accordance with the present invention, compositions as described herein may include at least one filler. In some aspects, a composition of the present invention may comprise a filler including, but is not limited to, one or more of alpha cellulose, beta cellulose, gamma

cellulose, starch, modified-starch, sorbitol, mannitol, lactose, dextrose, sucrose, dibasic calcium phosphate, tribasic calcium phosphate, or calcium carbonate and the like. In some aspects, a composition of the present invention may include mannitol. In other aspects, a composition of the present invention may include sorbitol.

[0282] Representative fillers for use in the compositions of the present invention may include, but are not limited to, starch, lactitol, lactose, an inorganic calcium salt, microcrystalline cellulose, sucrose, combinations thereof and the like. Additional fillers or diluents for use in the compositions of the present invention, may include, but are not limited to fillers or diluents conventionally known in the art, i.e., which are typically used in formulation of pharmaceutical compounds. Examples of such fillers or diluents for use in accordance with the present invention may include, but are not limited to sugars such as lactose, dextrose, glucose, sucrose, cellulose, starches and carbohydrate derivatives, polysaccharides (including dextrans and maltodextrin), polyols (including mannitol, xylitol, and sorbitol), cyclodextrins, calcium carbonates, magnesium carbonates, microcrystalline cellulose, combinations thereof, and the like. In some aspects, such fillers or diluents suitable for use in the present invention may include, but are not limited to lactose, microcrystalline cellulose, combinations thereof and the like.

[0283] Moreover, in another aspect, a filler for use in the present invention may be present in an amount of from about 1% to about 99% (w/w) of the composition, or from about 1% to about 50%, or from about 1% to about 25%, or from about 1% to about 20%, or from about 1% to about 10%, or from about 2% to about 8%, or from about 3% to about 5% (w/w) of a composition as defined in the instant specification. Moreover, such a filler may also be present in an amount of about 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, or about 10% (w/w) of the composition, which may include any fractional amount in between those as defined.

[0284] In some embodiments, the filler is present in an amount from about 10% to about 95% (w/w) of the composition as defined in the instant specification. In some embodiments, the filler is present in an amount from about 25% to about 95% (w/w) of the composition as defined in the instant specification. In some embodiments, the filler is present in an amount from about 30% to about 90% (w/w) of the composition as defined in the instant specification. In some embodiments, the filler is present in an amount from about 10% to about 50% (w/w) of the composition as defined in the instant specification. In some embodiments, the filler is present in an amount from about 10% to about 40% (w/w) of the composition as defined in the instant specification. In some embodiments, the filler is present in an amount from about 10% to about 30% (w/w) of the composition as defined in the instant specification. In some embodiments, the filler is present in an amount from about 10% to about 20% (w/w) of the composition as defined in the instant specification. In certain embodiments, the filler is present

in an amount from about 10% to about 15% (w/w). In certain embodiments, the filler is present in an amount of about 12% (w/w).

[0285] In some aspects, the composition further can include microcrystalline cellulose. Several types of microcrystalline cellulose may be suitable for use in compositions described herein, for example, microcrystalline cellulose may be selected from, but is not limited to MICROCEL® or AVICEL® types: PH101, PH102, PH103, PH105, PH 112, PH113, PH200, PH301, and the like and other types of microcrystalline cellulose, such as silicified microcrystalline cellulose. In one aspect, a composition for use in the present invention may include microcrystalline cellulose (AVICEL PH102). In another aspect, a composition suitable for use in the present invention may include microcrystalline cellulose (AVICEL PH101).

[0286] In another aspect, a microcrystalline cellulose may be present in an amount of from about 1% to about 99% (w/w) of the composition, or from about 1% to about 50%, or from about 1% to about 25%, or from about 1% to about 20%, or from about 1% to about 10%, or from about 2% to about 8%, or from about 3% to about 5% (w/w) of a composition as defined in the instant specification. In some aspects, a microcrystalline cellulose may also be present in an amount of about 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, or about 10% (w/w) of the composition, which may include any fractional amount in between those as defined. In some aspects, a microcrystalline cellulose may also be present in an amount of from about 3% to about 5% (w/w) of a composition.

[0287] In some aspects, the composition further can include a silicified microcrystalline cellulose. In some aspects, silicified microcrystalline cellulose may be, but is not limited to SMCC 50, SMCC 50LD, SMCC 90, SMCC HD90 or SMCC 90LM and the like. In some aspects, silicified microcrystalline cellulose may be SMCC 50, SMCC 50LD, SMCC 90, SMCC HD90 or SMCC 90LM. Without being bound by theory, the silicified microcrystalline cellulose is understood to protect an enteric coating from premature erosion by sodium caprate present in the composition. The silicified microcrystalline cellulose may be present in any suitable amount for use in the present invention. For example, the SMCC can be present in an amount of from about 1% to about 99% (w/w) of the composition, or from about 10% to about 50%, or from about 20% to about 50%, or from about 25% to about 45%, or from about 30% to about 40%, or from about 35% to about 37% (w/w) of the composition. In some aspects, the amount of the silicified microcrystalline cellulose is from about 30% to about 70% (w/w) of the composition. In some aspects, the amount of the silicified microcrystalline cellulose is from about 65% to about 85% (w/w) of the composition. In some aspects, the amount of the silicified microcrystalline cellulose is from about 66.5% to about 81.3% (w/w) of the composition. In some aspects, the amount of the silicified microcrystalline cellulose is about 31.3%, about

36.6%, about 37.7%, about 50.9%, about 52%, about 65.2%, about 71.5%, about 79%, or about 80.5% of the composition. The SMCC can be present in an amount of about 30% (w/w) of the composition, or about 31%, 32%, 33%, 34%, 35%, 36%, 36.1%, 36.2%, 36.3%, 36.4%, 36.5%, 36.6%, 36.7%, 36.8%, 36.9%, 37%, 38%, 39%, or about 40% (w/w) of the composition.

[0288] In some embodiments, SMCC is present in an amount of from about 20% to about 90% (w/w), which includes, but is not limited to any fractional amount in between. In some embodiments, SMCC is present in an amount of from about 25% to about 85% (w/w), which includes, but is not limited to any fractional amount in between. In some embodiments, SMCC is present in an amount of from about 25% to about 45% (w/w), which includes, but is not limited to any fractional amount in between. In some embodiments, SMCC is present in an amount of from about 30% to about 40% (w/w), which includes, but is not limited to any fractional amount in between. In some embodiments, SMCC is present in an amount of from about 65% to about 90% (w/w), which includes, but is not limited to any fractional amount in between. In some embodiments, SMCC is present in an amount of from about 70% to about 85% (w/w), which includes, but is not limited to any fractional amount in between. In some embodiments, SMCC is present in an amount of from about 70% to about 75% (w/w), which includes, but is not limited to any fractional amount in between. In some embodiments, SMCC is present in an amount of from about 80% to about 85% (w/w), which includes, but is not limited to any fractional amount in between. In some embodiments, SMCC is present in an amount of about 30%. In some embodiments, SMCC is present in an amount of about 40%, which includes, but is not limited to any fractional amount in between. In some embodiments, SMCC is present in an amount of about 50%, which includes, but is not limited to any fractional amount in between. In some embodiments, SMCC is present in an amount of about 60%, which includes, but is not limited to any fractional amount in between. In some embodiments, SMCC is present in an amount of about 70%, which includes, but is not limited to any fractional amount in between. In some embodiments, SMCC is present in an amount of about 80%, which includes, but is not limited to any fractional amount in between. In some embodiments, SMCC is present in an amount of about 90%, which includes, but is not limited to any fractional amount in between.

[0289] In some embodiments, SMCC is a mixture of microcrystalline cellulose and colloidal silicon dioxide.

[0290] In some aspects, the composition further can include one or more of alpha cellulose, beta cellulose, gamma cellulose, starch, modified-starch, sorbitol, mannitol, lactose, dextrose, sucrose, dibasic calcium phosphate, tribasic calcium phosphate, or calcium carbonate. In some aspects, the composition further can include mannitol.

[0291] In some aspects, a composition of the present invention may include sorbitol. For example, for use in the present invention, sorbitol may be present in an amount of from about 1% to about 99% (w/w) of the composition, or from about 1% to about 50%, or from about 1% to about 25%, or from about 5% to about 25%, or from about 5% to about 20%, or from about 5 to about 15%, or from about 8 to about 12% (w/w) of the composition. In another aspect, sorbitol can be present in an amount of about 5% (w/w) of the composition, or about 6%, 7%, 8%, 9%, 10%, 10.1%, 10.2%, 10.3%, 10.4%, 10.5%, 10.6%, 10.7%, 10.8%, 10.9%, 11%, 12%, 13%, 14%, or about 15% (w/w) of the composition. In some aspects, the composition also includes sorbitol in an amount of from about 5% to about 15% (w/w) of the composition. In some aspects, the amount of the sorbitol is from about 10% to about 15% (w/w) of the composition. In some aspects, the composition includes sorbitol in an amount of about 10.7% (w/w) of the composition.

[0292] In some embodiments, a composition of the present invention may include mannitol. For example, for use in the present invention, mannitol may be present in an amount of from about 1% to about 99% (w/w) of the composition, or from about 1% to about 50%, or from about 1% to about 25%, or from about 5% to about 25%, or from about 5% to about 20%, or from about 5 to about 15%, or from about 8 to about 12% (w/w) of the composition. In another embodiment, mannitol can be present in an amount of about 5% (w/w) of the composition, or about 6%, 7%, 8%, 9%, 10%, 10.1%, 10.2%, 10.3%, 10.4%, 10.5%, 10.6%, 10.7%, 10.8%, 10.9%, 11%, 12%, 13%, 14%, or about 15% (w/w) of the composition, which includes, but is not limited to any fractional amount in between. In some embodiments, the composition also includes mannitol in an amount of from about 5% to about 15% (w/w) of the composition. In some embodiments, the amount of the mannitol is from about 10% to about 15% (w/w) of the composition. In some embodiments, the composition includes mannitol in an amount of about 10.7% (w/w) of the composition.

[0293] In one embodiment, the amount of the sugar alcohol can be present in range from about 1% to about 50% (w/w) of the composition, or from about 5% to about 50%, or from about 5% to about 30%, or from about 10% to about 30% (w/w) of the composition. In some aspects, the amount of the sugar alcohol can be present in an amount of about 1%, 2.5%, 5%, 7.5%, 10%, 12.5%, 15%, 17.5%, or about 20% (w/w) of the composition. In some aspects, the amount of the sugar alcohol can be present in an amount higher than about 1%, 2.5%, 5%, 7.5%, 10%, 12.5%, 15%, 17.5%, or about 20% (w/w) of the composition. In some aspects, the amount of the sugar alcohol can be present in an amount lower than about 5%, 7.5%, 10%, 12.5%, 15%, 17.5%, or about 20% (w/w) of the composition.

[0294] In some embodiments, the pharmaceutical composition described herein does not include an sugar alcohol. In some embodiments, the pharmaceutical composition described herein does not include sorbitol. In some embodiments, the pharmaceutical composition described herein does not include mannitol.

[0295] The composition of the invention may include, but is not limited to at least one disintegrant in an effective therapeutic amount for use as determined in accordance with the present invention. Representative disintegrants for use in the present invention, include, but are not limited to, starches, clays, celluloses, alginates and gums and crosslinked starches, celluloses and polymers, combinations thereof and the like. Additional representative disintegrants for use in the present invention, may include, but are not limited to microcrystalline cellulose, croscarmellose sodium, alginic acid, sodium alginate, crospovidone, cellulose, agar and related gums, sodium starch glycolate, corn starch, potato starch, sodium starch glycolate, Veegum HV, methylcellulose, agar, bentonite, carboxymethylcellulose, alginic acid, guar gum combinations thereof, and the like.

[0296] In some aspects, the disintegrant is a cross-linked carboxymethyl cellulose (croscarmellose), a starch glycolate, a polyvinyl pyrrolidone, a sago starch, psyllium husk, a silicate, or a soy polysaccharide. In some aspects, the disintegrant is croscarmellose sodium or crospovidone. In some aspects, disintegrants for use in the present invention, may include, but are not limited to croscarmellose sodium. In some aspects, a disintegrant for use in the present invention can include crospovidone. In some aspects, a disintegrant may be present in an amount of from about 1% to about 99% (w/w) of a composition of the present invention, or from about 1% to about 50%, or from about 1% to about 25%, or from about 1% to about 20%, or from about 1% to about 10%, or from about 2% to about 8%, or from about 4% to about 6% (w/w) of the composition. Disintegrants for use in the present invention may also be present in an amount of about 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 11%, or about 12% (w/w) of the composition, which include, but is not limited to any fractional amount in between. In some aspects, an amount of the disintegrant may be present in from about 1% to about 10% (w/w) of a composition of the present invention. In some aspects, an amount of the disintegrant may be present in from about 8% to about 12% (w/w) of a composition of the present invention. In some aspects, an amount of the disintegrant may be present in from about 3% to about 8% (w/w) of a composition of the present invention.

[0297] In another aspect, a composition of the present invention may also include, but is not limited to silica in any amount for purposes of the present invention. In particular, silica is exemplified by Aerosil 200, having a specific surface area of about 200 m²/g. Alternatives to silica may include, but are not limited to talc, sodium ferrocyanide, potassium ferrocyanide,

calcium carbonate, magnesium carbonate, silicon dioxide, precipitated silica, sodium aluminosilicate, combinations thereof and the like.

[0298] In some aspects, a composition of the present invention may further comprise a silica. In one aspect, silica may be present in compositions of the present invention in an amount of from about 0.1% to about 10% (w/w) of the composition, or from about 0.1% to about 5%, or from about 0.1% to about 2%, or from about 0.1% to about 1.5%, or from about 0.1% to about 1.25%, or from about 0.5% to about 1.5%, or from about 1.0% to about 1.25%, or from about 0.1% to about 1%, or from about 0.3% to about 0.7% (w/w) of the composition of the present invention. For example, silica as used in the present invention may be present in an amount of about 0.1%, 0.2%, 0.3%, 0.4%, 0.5%, 0.6%, 0.7%, 0.8%, 0.9%, 1.0%, 1.1%, 1.2%, 1.3%, 1.4% or about 1.5% (w/w) of the composition, including any fraction amount in between as defined. In another aspect, a composition of the present invention may further include an amount of silica in from about 0.1% to about 1.5% (w/w) of the composition. In another aspect, a composition of the present invention may further include an amount of silica in from about 0.5% to about 2% (w/w) of the composition. In another aspect, a composition of the present invention may further include an amount of silica in from about 0.3% to about 0.7% (w/w) of the composition. In further aspects, a composition of the present invention may further include an amount of silica in about 0.5% (w/w) of the composition. In some aspects, the composition further may comprise silica in an amount of about 1% (w/w) of the composition. Examples of suitable silica materials include, but are not limited to colloidal silicon dioxide, aerosol, colloidal silica, fumed silica, silicon dioxide fumed, colloidal anhydrous silica, colloidal silicon dioxide, and the like. In some embodiments, the silica is colloidal silica.

[0299] The composition can also include a binder. Binders for use in the compositions of the present invention include binders commonly used in the formulation of pharmaceuticals. Examples of binders for use in the present invention include but are not limited to cellulose derivatives (including hydroxypropyl cellulose, hydroxypropyl methylcellulose, methylcellulose, and sodium carboxymethyl cellulose), glycol, sucrose, dextrose, corn syrup, polysaccharides (including acacia, targaranth, guar, alginates and starch), corn starch, pregelatinized starch, modified corn starch, gelatin, polyvinylpyrrolidone, polyethylene, polyethylene glycol, combinations thereof and the like.

[0300] In some embodiments, the binder is hydroxypropyl methylcellulose (HPMC). In some embodiments, binders for use in the present invention may also be present in an amount of about 0.25%, 0.5%, 0.75%, 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 11%, or about 12% (w/w) of the composition, which include, but is not limited to any fractional amount in between.

[0301] In the present invention, the composition may include a lubricant in any suitable amount for use as described herein. Examples of suitable lubricants for use in the present invention, may include, but are not limited to magnesium carbonate, magnesium lauryl sulphate, calcium silicate, talc, fumed silicon dioxide, combinations thereof, and the like. Other useful suitable lubricants, may include, but are not limited to magnesium stearate, calcium stearate, stearic acid, sodium stearyl fumarate, polyethylene glycol, sodium lauryl sulphate, magnesium lauryl sulphate, sodium benzoate, colloidal silicon dioxide, magnesium oxide, microcrystalline cellulose, starches, mineral oil, waxes, glyceryl behenate, polyethylene glycol, sodium acetate, sodium chloride, combinations thereof, and the like.

[0302] In some aspects, lubricant may include, but is not limited to magnesium stearate. In one aspect, an amount of the lubricant can be present in from about 0.1% to about 10% (w/w) of the composition, or from about 0.1% to about 5%, or from about 0.1% to about 2.5%, or from about 0.1% to about 1%, or from about 0.1% to about 0.5% (w/w) of the composition. In some aspects, an amount of the lubricant can be present in from about 0.5% to about 2.5% or about 0.5% to about 2.0% (w/w) of the composition. In some aspects, an amount of the lubricant can be present in from about 0.1% to about 0.5% (w/w) of the composition. In some aspects, the amount of the lubricant is from about 0.3% to about 0.7% (w/w) of the composition. In some aspects, the amount of the lubricant is about 0.5% (w/w) of the composition. The lubricant can also be present in an amount of about 0.10% (w/w) of the composition, or about 0.11%, 0.12%, 0.13%, 0.14%, 0.15%, 0.16%, 0.17%, 0.18%, 0.19%, 0.20%, 0.21%, 0.22%, 0.23%, 0.24%, 0.25%, 0.26%, 0.27%, 0.28%, 0.29%, or about 0.30% (w/w) of the composition. The lubricant can also be present in an amount of about 0.5% (w/w) of the composition, or about 0.75%, 1.0%, 1.25%, 1.5%, 1.75%, 2.0%, or about 2.5% (w/w) of the composition. In some aspects, the lubricant may be present in an amount of about 0.25% (w/w).

[0303] In some aspects, the composition includes: (i) the hydrochloride salt of the compound of Formula (I) or solvate thereof in an amount of from about 0.2% to about 15% (w/w) of the composition; (ii) a silicified microcrystalline cellulose in an amount of from about 66.5% to about 81.3% (w/w) of the composition; (iii) sorbitol in an amount of about 12.5% (w/w) of the composition; (iv) a disintegrant in an amount of about 5% (w/w) of the composition; (v) a silica in an amount of about 0.5% (w/w) of the composition; and (vi) a lubricant in an amount of about 0.5% (w/w) of the composition.

[0304] In some embodiments, the pharmaceutical composition includes: (i) the crystalline form of the pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, in an amount of from about 0.1% to about 60 % (w/w) of the composition; (ii) a silicified microcrystalline cellulose in an amount of from about 40% to about 85% (w/w) of the

composition; (iii) a disintegrant in an amount of about 5% to about 10% (w/w) of the composition; (iv) a silica in an amount of about 0.1% to about 1.0% (w/w) of the composition; and (v) a lubricant in an amount of about 0.5 % to about 1.5% (w/w) of the composition.

[0305] In some embodiments, the pharmaceutical composition includes: (i) the crystalline form of the pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, in an amount of from about 10% to about 20% (w/w) of the composition; (ii) the silicified microcrystalline cellulose in an amount of about 85% (w/w) of the composition; (iii) crospovidone in an amount of about 5% (w/w) of the composition; (iv) the silica in an amount of about 0.2% (w/w) of the composition; and (v) magnesium stearate in an amount of about 0.5% of the composition.

[0306] In some embodiments, the pharmaceutical composition includes: (i) an absorption enhancer in an amount of from about 5% to about 65% (w/w) of the composition; (ii) the crystalline form of the pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, in an amount of from about 0.1% to about 15% (w/w) of the composition, and (iii) a silicified microcrystalline cellulose in an amount of from about 10% to about 50% (w/w) of the composition.

[0307] In some embodiments, the pharmaceutical composition includes: (i) an absorption enhancer in an amount of from about 30% to about 45% (w/w) of the composition; (ii) a disintegrant in an amount of from about 5% to 10% (w/w) of the composition; and (iii) the crystalline form of the pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, in an amount of from about 0.5% to about 15% (w/w) of the composition; (iv) a silicified microcrystalline cellulose in an amount of from about 30% to about 40% (w/w) of the composition; (v) a silica in an amount of about 0.2% to about 1.5% (w/w) of the composition; (vi) a disintegrant in an amount of about 5% to about 10% (w/w) of the composition; (vii) a filler in an amount of about 7.5% to about 15% (w/w) of the composition; and (viii) a lubricant in an amount of about 0.2 % to about 1.5% (w/w) of the composition.

[0308] In some embodiments, the pharmaceutical composition includes: (i) a crystalline form of a pharmaceutically acceptable salt of a compound of Formula (I), or a solvate thereof, in an amount of from about 10% to about 20% (w/w) of the composition; (ii) an absorption enhancer in an amount of from about 30% to about 45% (w/w) of the composition; (iii) a disintegrant in an amount of from about 0.5% to about 1.0% (w/w) of the composition; (iv) crospovidone in an amount of about 5% (w/w) of the composition; (vi) a microcrystalline cellulose in an amount of about 1.3% (w/w) of the composition; (vii) a silicified microcrystalline cellulose in an amount of from about 34.8% to about 39.7% (w/w) of the composition; (viii) mannitol in an amount of about 10.7% (w/w) of the composition; (ix) crospovidone in an

amount of about 5% (w/w) of the composition; (x) a silica in an amount of about 1.0% (w/w) of the composition; and (xi) magnesium stearate in an amount of about 0.5% (w/w) of the composition.

[0309] In some embodiments, the pharmaceutical composition includes: (i) sodium caprate in an amount of about 38.5% (w/w) of the composition; (ii) hydroxypropyl methylcellulose in an amount of about 0.8% (w/w) of the composition; (iii) the crystalline form of the pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, in an amount of from about 3.9% (w/w) of the composition; (iv) a silicified microcrystalline cellulose in an amount of about 39.7% (w/w) of the composition; (v) mannitol in an amount of about 10.7% (w/w) of the composition; (vi) crospovidone in an amount of about 5% to about 7.5% (w/w) of the composition; (vii) a silica in an amount of from about 0.5% to about 1.0% (w/w) of the composition; and (viii) magnesium stearate in an amount of about 0.5% (w/w) of the composition.

[0310] In some embodiments, the pharmaceutical composition includes: (i) a crystalline form of a pharmaceutically acceptable salt of a compound of Formula (I), or a solvate thereof, in an amount of from about 10% to about 20% (w/w) of the composition; (ii) an absorption enhancer in an amount of from about 30% to about 45% (w/w) of the composition; (iii) a disintegrant in an amount of from about 0.5% to about 1.0% (w/w) of the composition; (iv) crospovidone in an amount of about 5% (w/w) of the composition; (v) a microcrystalline cellulose in an amount of about 1.3% (w/w) of the composition; (vi) a silicified microcrystalline cellulose in an amount of from about 34.8% to about 39.7% (w/w) of the composition; (vii) mannitol in an amount of about 10.7% (w/w) of the composition; (viii) crospovidone in an amount of about 5% (w/w) of the composition; (ix) a silica in an amount of about 1.0% (w/w) of the composition; and (x) magnesium stearate in an amount of about 0.5% (w/w) of the composition.

[0311] In some aspects, the composition includes: (i) the hydrochloride salt of the compound of Formula (I) or solvate thereof in an amount of about 1% (w/w) of the composition; (ii) a silicified microcrystalline cellulose in an amount of about 80.5% (w/w) of the composition; (iii) sorbitol in an amount of about 12.5% (w/w) of the composition; (iv) crospovidone in an amount of about 5% (w/w) of the composition; (v) a silica in an amount of about 0.5% (w/w) of the composition; and (vi) magnesium stearate in an amount of about 0.5% (w/w) of the composition.

[0312] In some aspects, the composition includes: (i) the hydrochloride salt of the compound of Formula (I) or solvate thereof in an amount of about 2.5% (w/w) of the composition; (ii) a silicified microcrystalline cellulose in an amount of about 79% (w/w) of the composition; (iii) sorbitol in an amount of about 12.5% (w/w) of the composition; (iv) crospovidone in an amount

of about 5% (w/w) of the composition; (v) a silica in an amount of about 0.5% (w/w) of the composition; and (vi) magnesium stearate in an amount of about 0.5% (w/w) of the composition.

[0313] In some aspects, the composition includes: (i) the hydrochloride salt of the compound of Formula (I) or solvate thereof in an amount of about 10% (w/w) of the composition; (ii) a silicified microcrystalline cellulose in an amount of about 71.5% (w/w) of the composition; (iii) sorbitol in an amount of about 12.5% (w/w) of the composition; (iv) crospovidone in an amount of about 5% (w/w) of the composition; (v) a silica in an amount of about 0.5% (w/w) of the composition; and (vi) magnesium stearate in an amount of about 0.5% (w/w) of the composition. The tablet composition can also include one or more coatings.

[0314] The composition described herein may include a variety of other pharmaceutically acceptable components or excipients, such as, including, but is not limited to, a glidant, a lubricant, a disintegrant, a binder, a desiccant, a filler, and other components or excipients and the like.

[0315] The composition described herein can include at least one disintegrant in any suitable amount in accordance with the present invention. Representative disintegrants for use in the present invention, may include, but are not limited to, agar-agar, alginic acid, calcium carbonate, microcrystalline cellulose, croscarmellose sodium, crospovidone, polacrillin potassium, sodium starch glycolate, potato or tapioca starch, other starches, pre-gelatinized starch, clays, other alginates, other celluloses, gums (like gellan), low-substituted hydroxypropyl cellulose, or mixtures thereof and the like. In one aspect, the disintegrant may include croscarmellose sodium. In one aspect, the disintegrant may include crospovidone. In another aspect, suitable disintegrant may be, but is not limited to being present in an amount of about 1% (w/w), 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, or about 10% (w/w) of the composition, including any fractional amount in between as defined in the present invention. In another aspects of the present invention, disintegrant may be, but is not limited to being present in an amount of about 1 to 10% (w/w) of the composition. In other aspects, the disintegrant may be present in an amount of about 5.0% (w/w) of the composition.

[0316] In some aspects, the microcrystalline cellulose can be present in an amount of from about 1% to about 10% (w/w) of the composition. In some aspects, the microcrystalline cellulose can be present in an amount of about 3.9% (w/w) of the composition.

[0317] In some aspects, the composition further may comprise silica. In some aspects, the composition further may comprise silica in an amount of from about 0.1% to about 1.5% (w/w) of the composition. For example, the silica can be present in an amount of about 0.1%, 0.2%, 0.25%, 0.3%, 0.4%, 0.5%, 0.6%, 0.7%, 0.75%, 0.8%, 0.9%, 1.0%, or about 1.5% (w/w) of the composition, including any fraction amount in between as defined herein. In some aspects, the

composition further may comprise silica in an amount of from about 0.3% to about 0.7% (w/w) of the composition. In some aspects, the composition further may comprise silica in an amount of from about 0.5% to about 2% (w/w) of the composition. In some aspects, the composition further may comprise silica in an amount of about 0.5% (w/w) of the composition.

[0318] In another aspect, the composition of the present invention may further comprise at least one of: a disintegrant in an amount from about 1% to about 10% (w/w) of the composition, a microcrystalline cellulose in an amount from about 1% to about 10% (w/w) of the composition, a silica in an amount from about 0.1% to about 1.5% (w/w) of the composition, or sorbitol in an amount from about 5% to about 15% (w/w) of the composition.

[0319] In yet another aspect, the composition further may comprise: a disintegrant in an amount from about 1% to about 10% (w/w) of the composition; a microcrystalline cellulose in an amount from about 1% to about 10% (w/w) of the composition; a silica in an amount from about 0.1% to about 1.5% (w/w) of the composition; and sorbitol in an amount from about 5% to about 15% (w/w) of the composition.

[0320] In some aspects, the compositions of the present invention further may comprise at least one of: a microcrystalline cellulose in an amount of about 3.9% (w/w); sorbitol in an amount of about 10.7% (w/w); a disintegrant in an amount of about 5.0% (w/w); and a silica in an amount of about 0.5% (w/w).

[0321] In some aspects, the compositions further may comprise: a microcrystalline cellulose in an amount of about 3.9% (w/w); sorbitol in an amount of about 10.7% (w/w); a disintegrant in an amount of about 5.0% (w/w); and a silica in an amount of about 0.5% (w/w).

[0322] In some aspects, the compositions further may comprise: Avicel PH101 in an amount of about 3.9% (w/w); sorbitol in an amount of about 10.7% (w/w); croscarmellose sodium in an amount of about 5.0% (w/w); and Aerosil 200 in an amount of about 0.5% (w/w).

[0323] The microcrystalline cellulose can include any microcrystalline cellulose known in the art. In some aspects, the microcrystalline cellulose may comprise a silicified microcrystalline cellulose (SMCC).

[0324] In some aspects, for use in the present invention, microcrystalline cellulose may be a silicified microcrystalline cellulose (SMCC) and may have any particle size. In some aspects, the composition includes silicified microcrystalline cellulose in an amount of from about 25% to about 45% (w/w) of the composition. In some aspects, the composition includes silicified microcrystalline cellulose in an amount of about 36.6% (w/w) of the composition.

[0325] The composition can include at least one disintegrant in any suitable amount in accordance with the present invention. Representative disintegrants for use in the present invention, may include, but are not limited to, agar-agar, alginic acid, calcium carbonate,

microcrystalline cellulose, croscarmellose sodium, crospovidone, polacrillin potassium, sodium starch glycolate, potato or tapioca starch, other starches, pre-gelatinized starch, clays, other alginates, other celluloses, gums (like gellan), low-substituted hydroxypropyl cellulose, or mixtures thereof and the like. In one aspect, the disintegrant may include croscarmellose sodium. In one aspect, the disintegrant may include crospovidone. The disintegrant for use in the present invention, may be, but is not limited to being present in an amount of from about 1% to about 99% (w/w) of the composition, or from about 1% to about 50%, or from about 1% to about 25%, or from about 1% to 20%, or from about 1% to about 10%, or from about 2% to about 8%, or from about 4% to about 6% (w/w) of the composition. In another aspect, suitable disintegrant may be, but is not limited to being present in an amount of about 1% (w/w), 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, or about 10% (w/w) of the composition, including any fractional amount in between as defined in the present invention. In another aspects of the present invention, disintegrant may be, but is not limited to being present in an amount of about 1% to about 10% (w/w) of the composition. In other aspects, the disintegrant may be present in an amount of about 5.0% (w/w) of the composition.

[0326] In another aspect, the composition may also include silica in any amount in accordance with the present invention. Silica is exemplified by Aerosil 200, having a specific surface area of about 200 m²/g. Alternatives to silica include, without limitation, talc, sodium ferrocyanide, potassium ferrocyanide, calcium carbonate, magnesium carbonate, silicon dioxide, precipitated silica, sodium aluminosilicate, and combinations thereof and the like. Silica (e.g., Aerosil 200) may be present in the compositions in an amount of from about 0.1 to 10% (w/w) of the composition, or from about 0.1 to 5%, or from about 0.1 to 2%, or from about 0.1 to 1.5%, or from about 0.1 to 1%, or from about 0.3 to 0.7% (w/w) of the composition. For example, the Aerosil 200 silica can be present in an amount of about 0.1%, 0.2%, 0.3%, 0.4%, 0.5%, 0.6%, 0.7%, 0.8%, 0.9%, 1.0%, or 1.5% (w/w) of the composition, including any fraction amount in between.

[0327] In some aspects, the composition further may comprise silica (e.g., Aerosil 200). In some aspects, the composition further may comprise silica (e.g., Aerosil 200) in an amount of from about 0.1% to about 1.5% (w/w) of the composition. For example, the silica can be present in an amount of about 0.1%, 0.2%, 0.25%, 0.3%, 0.4%, 0.5%, 0.6%, 0.7%, 0.75%, 0.8%, 0.9%, 1.0%, or about 1.5% (w/w) of the composition, including any fraction amount in between as defined herein. In some aspects, the composition further may comprise silica (e.g., Aerosil 200) in an amount of from about 0.3% to about 0.7% (w/w) of the composition. In some aspects, the composition further may comprise silica (e.g., Aerosil 200) in an amount of from about 0.5% to about 2% (w/w) of the composition. In some aspects, the composition further may comprise

silica in an amount of about 0.5% (w/w) of the composition. In some aspects, the composition further may comprise silica (e.g., Aerosil 200) in an amount of about 1% (w/w) of the composition.

[0328] The composition described herein can include a variety of other pharmaceutically excipients or components, which may include, but is not limited to a lubricant, a disintegrant, a binder, a desiccant, a filler, and other components and the like. For use in the present invention, a disintegrant may be present in the compositions in an amount of from about 0.1% to about 10% (w/w) of the composition, or from about 0.1% to about 5%, or from about 0.1% to about 2%, or from about 0.1% to about 1.5%, or from about 0.1% to about 1%, or from about 0.1% to about 0.4% (w/w) of the composition. In some aspects, the composition further may comprise a disintegrant. In some aspects, the composition further may comprise silica (e.g., Aerosil 200) in an amount of from about 0.1% to about 1.5% (w/w) of the composition. In some aspects, the composition further may comprise a disintegrant in an amount of about 0.25% (w/w) of the composition.

[0329] In some aspects, the compositions disclosed herein can further comprise at least one of: a lubricant in an amount from about 0.1% to about 0.5% by weight of the composition, a disintegrant in an amount from about 1% to about 10% by weight of the composition, or a silica (e.g., Aerosil 200) in an amount from about 0.1% to about 1.5% by weight of the composition.

[0330] In some aspects, the compositions further can include: a lubricant in an amount from about 0.1% to about 0.5% by weight of the composition; a disintegrant in an amount from about 1% to about 10% by weight of the composition; and a silica (e.g., Aerosil 200) in an amount from about 0.1% to about 1.5% by weight of the composition.

[0331] **[0021]** In some aspects the compositions disclosed herein can further comprise at least one of: a disintegrant in an amount of about 5.0% (w/w); a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w); and a lubricant in an amount of about 0.25% (w/w).

[0332] In some aspects, the compositions comprises: a silicified microcrystalline cellulose in an amount of about 36.6% (w/w); a disintegrant in an amount of about 5.0% (w/w); a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w); and a lubricant in an amount of about 0.25% (w/w).

[0333] In some aspects, the compositions can include: SMCC HD90 in an amount of about 36.6% (w/w); croscarmellose sodium in an amount of about 5.0% (w/w); Aerosil 200 in an amount of about 0.5% (w/w); and magnesium stearate in an amount of about 0.25% (w/w).

[0334] In some aspects, compositions of the present invention may not include or may exclude use of an absorption enhancer depending on the intended delivery or use thereof and/or for treatment of specific indications as defined in the present invention.

[0335] In some embodiments described herein, such as relating to pharmaceutical compositions, tablets, methods, processes, and the like, the absorption enhancer is excluded. In some embodiments described herein, such as relating to compositions, tablets, methods, processes, and the like, the absorption enhancer is included.

[0336] In other aspects, suitable compositions of the present invention may exhibit improved bioavailability when administered in conjunction with an absorption enhancer.

[0337] In some aspects, compositions of the present invention may include an absorption enhancer. When present, the absorption enhancer may be zwitterionic, cationic, anionic or non-ionic. In one aspect, the absorption enhancer is an intestinal permeation enhancer. In some aspects, the absorption enhancer may be selected from, but is not limited to medium-chain saturated fatty acids, such as a caprate, a caprylate, a myristate, a palmitate, or a stearate, including salt forms, such as sodium caprate, sodium caprylate, sodium myristate, sodium palmitate, or sodium stearate) and the like.

[0338] Other absorption enhancers may include, but is not limited to a citric acid or citrate salt, such as sodium citrate, tartaric acid or tartrate salt, a salicylic acid or a derivative thereof, or a salicylate salt, a fatty acid acylated amino acid, an alkylsaccharide, a C8-o-alkylpolysaccharide, n-octyl-beta-D-glucopyranoside, n-dodecyl-beta-D-maltoside, n-tetradecyl-beta-D-maltoside, tridecylbeta-D-maltoside, sucrose laurate, sucrose myristate, sucrose palmitate, sucrose cocoate, sucrose mono-dodecanoate, sucrose mono-tridecanoate, sucrose monotetradecanoate, a coco-glucoside, a cyclodextrins, alkanoyl carnitine such as lauroyl carnitine, myristoyl carnitine or palmitoyl carnitine, lauroyl carnitine chloride, myristoyl carnitine chloride or palmitoyl carnitine chloride, fatty acid acylated amino acids, including, without limitation, sodium lauroyl alaninate, N-dodecanoyl-L-alanine, sodium lauroyl asparaginate, N-dodecanoyl-L-asparagine, sodium lauroyl aspartic acid, N-dodecanoyl-L-aspartic acid, sodium lauroyl cysteinate, N-dodecanoyl-L-cysteine, sodium lauroyl glutamic acid, N-dodecanoyl-L-glutamic acid, sodium lauroyl glutamate, N-dodecanoyl-L-glutamine, sodium lauroyl glycinate, N-dodecanoyl-L-glycine, sodium lauroyl histidinate, N-dodecanoyl-L-histidine, sodium lauroyl isoleucinate, N-dodecanoyl-L-isoleucine, sodium lauroyl leucinate, N-dodecanoyl-L-leucine, sodium lauroyl methionate, N-dodecanoyl-L-methionine, sodium lauroyl phenylalaninate, N-dodecanoyl-L-phenylalanine, sodium lauroyl propionate, N-dodecanoyl-L-proline, sodium lauroyl serinate, N-dodecanoyl-L-serine, sodium lauroyl threoninate, N-dodecanoyl-L-threonine, sodium lauroyl tryptophanate, N-dodecanoyl-L-tryptophan, sodium lauroyl tyrosinate, N-dodecanoyl-L-tyrosine, sodium lauroyl valinate, N-dodecanoyl-L-valine, sodium lauroyl sarcosinate, N-dodecanoyl-L-sarcosine, sodium capric alaninate, N-decanoyl-L-alanine, sodium capric asparaginate, N-decanoyl-L-asparagine, sodium capric aspartic acid, N-

decanoyl-L-aspartic acid, sodium capric cysteinate, *N*-decanoyl-L-cysteine, sodium capric glutamic acid, *N*-decanoyl-L-glutamic acid, sodium capric glutamine, *N*-decanoyl-L-glutamine, sodium capric glycinate, *N*-decanoyl-L-glycine, sodium capric histidinate, *N*-decanoyl-L-histidine, sodium capric isoleucinate, *N*-decanoyl-L-isoleucine, sodium capric leucinate, *N*-decanoyl-L-leucine, sodium capric methioninate, *N*-decanoyl-L-methionine, sodium capric phenylalaninate, *N*-decanoyl-L-phenylalanine, sodium capric propionate, *N*-decanoyl-L-proline, sodium capric serinate, *N*-decanoyl-L-serine, sodium capric threoninate, *N*-decanoyl-L-threonine, sodium capric tryptophanate, *N*-decanoyl-L-tryptophan, sodium capric tyrosinate, *N*-decanoyl-L-tyrosine, sodium capric valinate, *N*-decanoyl-L-valine, sodium capric sarcosinate, *N*-decanoyl-L-sarcosine, sodium oleoyl sarcosinate, sodium *N*-decylleucine, sodium stearoyl glutamate (e.g., Amisoft HS-1 1 P), sodium myristoyl glutamate (e.g., Amisoft MS-1 1), sodium lauroyl glutamate (e.g., Amisoft LS-1 1), sodium cocoyl glutamate (e.g., Amisoft CS-1 1), sodium cocoyl glycinate (e.g., Am lite GCS-1 1), sodium *N*-decyl leucine, sodium cocoyl glycine and pharmaceutically acceptable salts of any of the aforementioned compounds; or an alkanoyl sarcosinate (e.g., a lauroyl sarcosinate, such as sodium lauroyl sarcosinate) or one of the 20 standard proteinogenic alpha-amino acids that is acylated with a C₈-C₂₀ alkanic acid), an alkylsaccharide (e.g., a C₁-C₂₀ alkylsaccharide, such as, Multitrope™ 1620-LQ-(MV); or, *n*-octyl-beta-D-glucopyranoside, *n*-dodecyl-beta-D-maltoside, *n*-tetradecyl-beta-D-maltoside, tridecyl-beta-D-maltoside, sucrose laurate, sucrose myristate, sucrose palmitate, sucrose cocoate, sucrose mono-dodecanoate, sucrose monotridecanoate, sucrose mono-tetradecanoate, a cocoglycoside, alkylsaccharides, a cyclodextrin (e.g., alpha-cyclodextrin, beta-cyclodextrin, gamma-cyclodextrin, methyl-beta-cyclodextrin, hydroxypropyl beta-cyclodextrin), *N*-[8-(2-hydroxybenzoyl)amino]caprylic acid, a *N*-[8-(2-hydroxybenzoyl)amino]caprylate, sodium *N*-[8-(2-hydroxybenzoyl)amino]caprylate, also referred to as "SNAC"), a calcium chelating compound (e.g., ethylenediaminetetraacetic acid (EDTA), cremophor EL (also referred to as "Kolliphor EL"; CAS no. 61791-12-6), chitosan, N,N,N-trimethyl chitosan, benzalkonium chloride, bestatin, or alkanols (e.g., ethanol, decanol), caprylocaproyl polyoxylglycerides (such as caprylocaproyl polyoxyl-8 glycerides; available as LABRASOL® or ACCONON® MC8-2), ethyl caprylate, glyceryl monolaurate, lysophosphatidylcholine, menthol, a C₈-C₂₀ alkylamine, a C₈-C₂₀ alkenylamine (e.g., oleylamine), phosphatidylcholine, a poloxamer, polyethylene glycol monolaurate, polyoxyethylene, polypropylene glycol monolaurate, a polysorbate (e.g., polysorbate 80), cholic acid (or a cholate salt, e.g., sodium chololate), a deoxycholate (e.g., sodium deoxycholate), sodium glycocholate, sodium glycodeoxycholate, sodium lauryl sulfate (SDS), sodium decyl sulfate, sodium octyl sulfate, sodium laureth sulfate, *N*-lauryl sarcosinate, decyltrimethyl ammonium bromide, benzyltrimethyl dodecyl ammonium chloride,

myristyltrimethyl ammonium chloride, dodecyl pyridinium chloride, or decyldimethyl ammonio propane sulfonate and the like.

[0339] In some aspects, the absorption enhancer may include, but is not limited to sodium caprate, sodium caprylate, sodium palmitate, sodium stearate, sodium citrate, sodium salicylate, sodium salcaprozate (SNAC), a polyethylene glycol (PEG)-modified medium chain fatty acid triglyceride of capric and caprylic acid (such as LABRASOL®, available from Gattefosse, USA), sucrose laurate, or lauroyl-L-carnitine (LC, such as PEPTELLIGENCE®, available from Enteris BioPharma, NJ, USA) and the like. In some aspects, the absorption enhancer is sodium caprate, sodium caprylate, sodium palmitate, sodium stearate, sodium citrate, sodium salicylate, sodium salcaprozate (SNAC), a polyethylene glycol (PEG)-modified medium chain fatty acid triglyceride of capric and caprylic acid, sucrose laurate, or lauroyl-L-carnitine (LC).

The absorption enhancer can be present in a composition in an amount of from about 1% to about 99% (w/w) of the composition, or from about 5% to about 50% (w/w), or from about 10% to about 50% (w/w), or from about 20% to about 50% (w/w), or from about 30% to about 50% (w/w), or from about 30% to about 40% (w/w), or from about 32% to about 38% (w/w), or from about 35% to about 36% (w/w) of the composition. In some aspects, an amount of the absorption enhancer is present in from about 5% to about 50% (w/w). In some aspects, an amount of the absorption enhancer is present in from about 5% to about 40% (w/w). In some aspects, an amount of the absorption enhancer is present in from about 30% to about 40% (w/w). For example, absorption enhancer can be present in an amount of about 30%, 31%, 32%, 33%, 34%, 35%, 36%, 37%, 38%, 39%, or about 40% (w/w) of the composition, including any fractional amounts in between. In some aspects, the absorption enhancer is present in an amount of from about 30% to about 40% (w/w). In some aspects, the absorption enhancer can be present in an amount from about 32% to about 38% (w/w). In some aspects, the absorption enhancer can be present in an amount of about 35.7% (w/w).

[0340] In some aspects, the absorption enhancer used in a composition of the present invention may be sodium caprate.

[0341] The sodium caprate can be present in a composition in an amount of from about 1% to about 99% (w/w) of the composition, or from about 5% to about 50% (w/w), or from about 10% to about 50% (w/w), or from about 20% to about 50% (w/w), or from about 30% to about 50% (w/w), or from about 30% to about 40% (w/w), or from about 32% to about 38% (w/w), or from about 35% to about 36% (w/w) of the composition. In some aspects, the sodium caprate is present in an amount of from about 5% to about 50% (w/w). In some aspects, the sodium caprate is present in an amount of from about 5% to about 40% (w/w). In some aspects, the sodium caprate is present in an amount of from about 30% to about 40% (w/w). For example, sodium

caprate can be present in an amount of about 30%, 31%, 32%, 33%, 34%, 35%, 36%, 37%, 38%, 39%, or about 40% (w/w) of the composition, including any fractional amounts in between. In some aspects, the sodium caprate is present in an amount of from about 30% to about 40% (w/w). In some aspects, the sodium caprate can be present in an amount from about 32% to about 38% (w/w). In some aspects, the sodium caprate can be present in an amount of about 35.7% (w/w).

[0342] In one aspect, for use in compositions of the present invention, sodium caprate may have a purity of at least about 98%, 98.2%, 98.4%, 98.6%, 98.8%, 99.0%, 99.5%, or at least about 99.9%. Without being bound by any theory, the higher degree of purity of the sodium caprate can provide improved bioavailability compared to lower technical grade sodium caprate, such about 90% or about 95% pure sodium caprate. In some aspects, sodium caprate for use in the present invention has a purity of at least about 98% for use in the present invention.

[0343] In another aspect, for use in the present invention, sodium caprate may have an average particle size of from about 10 nm to about 150 microns and sodium caprate may be in various particle sizes. In some aspects, sodium caprate particles suitable for use in the present invention may have an average diameter from about 1 micron to about 150 microns. In some aspects, such sodium caprate particles may have an average diameter from about 50 microns to about 150 microns. In other aspects, the sodium caprate particles may have an average diameter of from about 10 nm to about 5 microns. In some aspects, the sodium caprate particles may have an average diameter of from about 50 nm to about 1 micron. In some aspects, the sodium caprate particles may have an average diameter of from about 100 nm to about 800 nm.

[0344] In another aspect, sodium caprate may be present in crystalline form, amorphous form, or semi-crystalline form. In some aspects, the use of crystalline sodium caprate may enhance bioavailability of the hydrochloride salt of a compound of Formula (I) or solvate thereof. In some aspects, the use of amorphous sodium caprate may enhance bioavailability of the hydrochloride salt of a compound of Formula (I) or solvate thereof. In some aspects, the use of semi-crystalline sodium caprate may enhance bioavailability of the hydrochloride salt of a compound of Formula (I) or solvate thereof.

[0345] In another aspect, the hydrochloride salt of a compound of Formula (I) or solvate thereof and the sodium caprate may form a mixture or a granulated mixture. In some aspects, the hydrochloride salt of a compound of Formula (I) or solvate thereof and the sodium caprate form a mixture.

[0346] In some aspects, the hydrochloride salt of a compound of Formula (I) or solvate thereof and the sodium caprate form a granulated mixture. Accordingly, the hydrochloride salt of a compound of Formula (I) or solvate thereof and the sodium caprate can be mixed to form a

granulated mixture. The granulated mixture may be formed of particles having any average diameter suitable for use in compositions of the present invention. For example, the particles of the granulated mixture can have an average diameter of from about 100 nm to about 5 microns. The particles can also have an average diameter from about 1 micron to about 150 microns. In some aspects, the particles of the granulated mixture of the composition of the present invention may have an average diameter of from about 200 nanometers to about 1 micron.

[0347] In some aspects, the hydrochloride salt of a compound of Formula (I) or solvate thereof and the sodium caprate form a mixture or a granulated mixture.

[0348] In some aspects, the hydrochloride salt of a compound of Formula (I) or solvate thereof and the sodium caprate form a mixture. In some aspects, the hydrochloride salt of a compound of Formula (I) or solvate thereof and the sodium caprate form a granulated mixture.

[0349] In other aspects, the absorption enhancer used may be sodium salcaprozate. In some aspects, the absorption enhancer used may include, but is not limited to a polyethylene glycol (PEG)-modified medium chain fatty acid triglyceride of capric and caprylic acid and the like.

[0350] In some aspects, the composition can include a hydrochloride salt of a compound of Formula (I) or solvate thereof in an amount of from about 0.1% to about 15% (w/w) of the composition; an absorption enhancer in an amount from about 5% to about 50% (w/w); and one or more pharmaceutically acceptable excipients. In some aspects, the composition further can include microcrystalline cellulose.

[0351] In some aspects, the composition can include a hydrochloride salt of a compound of Formula (I) or solvate thereof in an amount of from about 0.1% to about 15% (w/w) of the composition; sodium caprate in an amount from about 5% to about 50% (w/w); and one or more pharmaceutically acceptable excipients. In some aspects, the composition further can include microcrystalline cellulose.

[0352] In another aspect, the composition described herein can include: the hydrochloride salt of a compound of Formula (I) or solvate thereof in an amount of about 1.8% (w/w); and sodium caprate in an amount of about 35.7% (w/w).

[0353] In some aspects, the present invention provides a composition which comprises a hydrochloride salt of a compound of Formula (I) or solvate thereof: in an amount of from about 0.1% to about 10% (w/w) of the composition, and an absorption enhancer in an amount of from about 20% to about 45% (w/w) of the composition.

[0354] In some aspects, the present invention provides a composition which comprises includes a hydrochloride salt of a compound of Formula (I) or solvate thereof: in an amount of from about 0.1% to about 15% (w/w) of the composition, and the absorption enhancer sodium

caprate in an amount of from about 5% to about 40% (w/w) of the composition, and a silicified microcrystalline cellulose.

[0355] In some aspects, the present invention provides a composition which comprises a hydrochloride salt of a compound of Formula (I) or solvate thereof in an amount of from about 0.1% to about 10% (w/w) of the composition, and sodium caprate in an amount of from about 20% to about 45% (w/w) of the composition, and a microcrystalline cellulose.

[0356] In some aspects, the present invention provides a composition includes: (i) the hydrochloride salt of the compound of Formula (I) or solvate thereof in an amount of from about 0.5% to about 10% (w/w) of the composition; (ii) the absorption enhancer sodium caprate in an amount of about 5% to about 40% (w/w) of the composition; (iii) a microcrystalline cellulose in an amount of about 3.9% (w/w) of the composition; (iv) sorbitol in an amount of about 10.7% (w/w) of the composition; (v) a disintegrant in an amount of about 5% (w/w) of the composition; and (vi) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; (vii) a silicified microcrystalline cellulose in an amount of from about 30% to about 70% (w/w) of the composition; (viii) a disintegrant in an amount of about 5% (w/w) of the composition; (ix) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; and (x) a lubricant in an amount of about 0.25% (w/w) of the composition.

[0357] In some aspects, the present invention provides a composition includes: (i) the hydrochloride salt of the compound of Formula (I) or solvate thereof in an amount of about 0.7% (w/w) of the composition; (ii) the absorption enhancer sodium caprate in an amount of about 35.7% (w/w) of the composition; (iii) a microcrystalline cellulose in an amount of about 3.9% (w/w) of the composition; (iv) sorbitol in an amount of about 10.7% (w/w) of the composition; (v) crospovidone in an amount of about 5% (w/w) of the composition; and (vi) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; (vii) a silicified microcrystalline cellulose in an amount of about 37.7% (w/w) of the composition; (viii) crospovidone in an amount of about 5% (w/w) of the composition; (ix) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; and (x) magnesium stearate in an amount of about 0.25% (w/w) of the composition.

[0358] In some aspects, the present invention provides a composition includes: (i) the hydrochloride salt of the compound of Formula (I) or solvate thereof in an amount of about 1.8% (w/w) of the composition; (ii) the absorption enhancer sodium caprate in an amount of about 35.7% (w/w) of the composition; (iii) a microcrystalline cellulose in an amount of about 3.9% (w/w) of the composition; (iv) sorbitol in an amount of about 10.7% (w/w) of the composition; (v) crospovidone in an amount of about 5% (w/w) of the composition; and (vi) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; (vii) a silicified

microcrystalline cellulose in an amount of about 36.6% (w/w) of the composition; (viii) crospovidone in an amount of about 5% (w/w) of the composition; (ix) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; and (x) magnesium stearate in an amount of about 0.25% (w/w) of the composition.

[0359] In some aspects, the present invention provides a composition includes: (i) the hydrochloride salt of the compound of Formula (I) or solvate thereof in an amount of about 0.7% (w/w) of the composition; (ii) the absorption enhancer sodium caprate in an amount of about 21.4% (w/w) of the composition; (iii) a microcrystalline cellulose in an amount of about 3.9% (w/w) of the composition; (iv) sorbitol in an amount of about 10.7% (w/w) of the composition; (v) crospovidone in an amount of about 5% (w/w) of the composition; and (vi) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; (vii) a silicified microcrystalline cellulose in an amount of about 52% (w/w) of the composition; (viii) crospovidone in an amount of about 5% (w/w) of the composition; (ix) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; and (x) magnesium stearate in an amount of about 0.25% (w/w) of the composition.

[0360] In some aspects, the present invention provides a composition includes: (i) the hydrochloride salt of the compound of Formula (I) or solvate thereof in an amount of about 1.8% (w/w) of the composition; (ii) the absorption enhancer sodium caprate in an amount of about 21.4% (w/w) of the composition; (iii) a microcrystalline cellulose in an amount of about 3.9% (w/w) of the composition; (iv) sorbitol in an amount of about 10.7% (w/w) of the composition; (v) crospovidone in an amount of about 5% (w/w) of the composition; and (vi) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; (vii) a silicified microcrystalline cellulose in an amount of about 50.9% (w/w) of the composition; (viii) crospovidone in an amount of about 5% (w/w) of the composition; (ix) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; and (x) magnesium stearate in an amount of about 0.25% (w/w) of the composition.

[0361] In some aspects, the present invention provides a composition wherein: (i) the hydrochloride salt of the compound of Formula (I) or solvate thereof in an amount of about 7.1% (w/w) of the composition; (ii) the absorption enhancer sodium caprate in an amount of about 35.7% (w/w) of the composition; (iii) a microcrystalline cellulose in an amount of about 3.9% (w/w) of the composition; (iv) sorbitol in an amount of about 10.7% (w/w) of the composition; (v) crospovidone in an amount of about 5% (w/w) of the composition; and (vi) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; (vii) a silicified microcrystalline cellulose in an amount of about 31.3% (w/w) of the composition; (viii) crospovidone in an amount of about 5% (w/w) of the composition; (ix) a silica (e.g., Aerosil

200) in an amount of about 0.5% (w/w) of the composition; and (x) magnesium stearate in an amount of about 0.25% (w/w) of the composition.

[0362] In some aspects, the present invention provides a composition includes: (i) the hydrochloride salt of the compound of Formula (I) or solvate thereof in an amount of about 1.8% (w/w) of the composition; (ii) the absorption enhancer sodium caprate in an amount of about 7.1% (w/w) of the composition; (iii) a microcrystalline cellulose in an amount of about 3.9% (w/w) of the composition; (iv) sorbitol in an amount of about 10.7% (w/w) of the composition; (v) crospovidone in an amount of about 5% (w/w) of the composition; and (vi) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; (vii) a silicified microcrystalline cellulose in an amount of about 65.2% (w/w) of the composition; (viii) crospovidone in an amount of about 5% (w/w) of the composition; (ix) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; and (x) magnesium stearate in an amount of about 0.25% (w/w) of the composition.

[0363] In some aspects, the present invention provides a composition includes: (i) the hydrochloride salt of the compound of Formula (I) or solvate thereof in an amount of about 1.8% (w/w) of the composition; (ii) the absorption enhancer sodium caprate in an amount of about 35.7% (w/w) of the composition; (iii) a microcrystalline cellulose in an amount of about 3.9% (w/w) of the composition; (iv) sorbitol in an amount of about 10.7% (w/w) of the composition; (v) crospovidone in an amount of about 5% (w/w) of the composition; and (vi) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; (vii) a silicified microcrystalline cellulose in an amount of about 36.6% (w/w) of the composition; (viii) crospovidone in an amount of about 5% (w/w) of the composition; (ix) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; and (x) magnesium stearate in an amount of about 0.25% (w/w) of the composition.

[0364] In some aspects, a composition of the present invention may be in a dosage form, which may be, but is not limited to a tablet or capsule dosage form. In some aspects, the composition may be a tablet or capsule composition. In some aspects, the composition can be a tablet composition. In some aspects, such as tablet composition may comprise a unit dose size in amounts which may include, but is not limited to amounts from about 25 mg to about 2000 mg, from about 500 mg to about 2000 mg. Compositions of the present invention, may be of any suitable size in accordance with the present invention, such as, but not limited tablets or capsules in doses or amounts of 25, 50, 75, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1050, 1100, 1150, 1200, 1250, 1300, 1350, 1400, 1450, 1500, 1550, 1600, 1650, 1700, 1750, 1800, 1850, 1900, 1950 or 2000 milligrams (mg) and the like. In one aspect, a composition of the present invention may be

as a 25 mg, 50 mg, 100 mg, 150 mg, 200 mg, 250 mg, 300 mg, 500 mg, 600 mg, 800 mg, 1000 mg, 1200 mg, or 1400 mg tablet, respectively, which may be administered, but is not limited to once or twice daily or as determined by medical necessity. In some aspects, the composition may be a unit dose size of from about 500 mg to about 2000 mg. In some aspects, the composition may be a unit dose size of about 1400 mg. In some aspects, the composition may be a unit dose size of about 1000 mg.

[0365] In some aspects, such as tablet composition may comprise a unit dose size from 500 mg to about 2000 mg. The tablet compositions may be of any suitable size in accordance with the present invention, such as, but not limited to 25, 50, 75, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1050, 1100, 1150, 1200, 1250, 1300, 1350, 1400, 1450, 1500, 1550, 1600, 1650, 1700, 1750, 1800, 1850, 1900, 1950 or 2000 mg tablets. In some aspects, the composition is a 1400 mg tablet.

[0366] Tablets formed from compositions of the present invention may be administered in single or multiple administrations depending on dosing and frequency as required and tolerated by the patient, where such tablets contain a sufficient quantity or amount of active agent to effectively treat specific disease state. Thus, in one aspect, the present invention relates to a composition for oral administration of the hydrochloride salt of a compound of Formula (I) or solvate thereof, which may be taken in a daily amount of from about 0.05 to about 30 mg per kg of body weight per day. In some aspects, dosages can be from about 0.1 mg to about 20 mg per kg of body weight per day. In another aspect, dosages can be from about 0.1 mg to about 5 mg per kg of body weight per day. In another aspect, dosages can be from about 0.1 mg to about 1 mg per kg of body weight per day.

Coatings

Cosmetic Subcoating

[0367] In some embodiments, the composition can further include a subcoating. In some embodiments, the subcoating is a cosmetic subcoating. In some embodiments, the cosmetic subcoating can also serve as a physical barrier. Cosmetic coatings can include polyethylene glycol-polyvinyl alcohol (PEG-PVA) graft copolymer, polyvinyl alcohol (PVA), hypromellose (HPMC), and hydroxypropyl cellulose (HPC). In some embodiments, the weight of the cosmetic subcoating is compared weight/weight to the weight of the composition prior to coating. In some embodiments, the cosmetic subcoating can be present in an amount from about 1% to about 10% (w/w). In some embodiments, the cosmetic subcoating is present in an amount from about 1% to about 5% (w/w). For example, the cosmetic subcoating can be present in amounts including about 1%, 1.5%, 2.0%, 2.5%, and about 3%, including any fractional amounts in

between and ranges thereof, such as between about 2.0% and 3.0%. In some embodiments, the cosmetic subcoating is present in an amount of about 3% (w/w). In some embodiments, the weight of the cosmetic subcoating is compared weight/weight to the weight of the composition, or to the weight of the core tablet, prior to coating.

[0368] In other embodiments, the cosmetic subcoating level is indicated in terms of weight (mg) of the cosmetic subcoating per the surface area of the core tablet. In some embodiments, the surface area is the surface area of the outer most layer of a coating covering the core tablet. For example, in some embodiments, the surface area for calculating the cosmetic subcoating level is the surface area of the core tablet. In other embodiments, the surface area is the surface area of the cosmetic subcoating, subcoating, or enteric coating disposed over the core tablet. For example, in some embodiments, more than one coating is disposed over the core tablet and the surface area refers to the surface area of the outermost coating.

[0369] In some embodiments, the cosmetic subcoating level is from about 6 mg/cm² to about 30 mg/cm². In some embodiments, the cosmetic subcoating level is from about 9 mg/cm² to about 30 mg/cm². In other embodiments, the cosmetic subcoating level is from about 12 mg/cm² to about 30 mg/cm². In some embodiments, the cosmetic subcoating level is from about 17 mg/cm² to about 30 mg/cm². In some embodiments, the cosmetic subcoating level is from about 20 mg/cm² to about 30 mg/cm². In some embodiments, the cosmetic subcoating level is from about 25 mg/cm² to about 30 mg/cm². For example, the cosmetic subcoating level is about 6 mg/cm², 7 mg/cm², 8 mg/cm², 9 mg/cm², 10 mg/cm², 11 mg/cm², 12 mg/cm², 13 mg/cm², 14 mg/cm², 15 mg/cm², 16 mg/cm², 17 mg/cm², 18 mg/cm², 19 mg/cm², 21 mg/cm², 22 mg/cm², 23 mg/cm², 24 mg/cm², 25 mg/cm², 26 mg/cm², 27 mg/cm², 28 mg/cm², 29 mg/cm², or 30 mg/cm². In some embodiments, the cosmetic subcoating level is about 6 mg/cm². In some embodiments, the cosmetic subcoating level is about 7 mg/cm². In some embodiments, the cosmetic subcoating level is about 8 mg/cm². In some embodiments, the cosmetic subcoating level is about 9 mg/cm². In some embodiments, the cosmetic subcoating level is about 10 mg/cm². In some embodiments, the cosmetic subcoating level is about 11 mg/cm². In some embodiments, the cosmetic subcoating level is about 12 mg/cm². In some embodiments, the cosmetic subcoating level is about 13 mg/cm². In some embodiments, the cosmetic subcoating level is about 14 mg/cm². In some embodiments, the cosmetic subcoating level is about 15 mg/cm². In some embodiments, the cosmetic subcoating level is about 16 mg/cm². In some embodiments, the cosmetic subcoating level is about 17 mg/cm². In some embodiments, the cosmetic subcoating level is about 18 mg/cm².

Subcoating

[0370] In some aspects, the composition further can include a subcoating of a PVA-PEG graft co-polymer disposed over the composition. In some aspects, compositions can comprise a subcoating of a PVA-PEG graft co-polymer disposed over the core tablet. This coating can serve as a smooth surface to aid in swallowing the tablet. It can also provide a platform for a further layer which can comprise an enteric coating disposed over the subcoating. In some aspects, the subcoating can also provide a vehicle for pigmentation for tablet identification. Other coatings include, without limitation, HPMC, HPC, PVA, Eudragit E based coatings and the like. In some aspects, the composition further can include a subcoating. This coating can serve as a barrier between the components of the core tablet and the enteric coating or functional coating. Subcoatings can include the OPADRY® class of products and can be present in any desired amounts. In some aspects, the weight of the subcoating is compared weight/weight to the weight of the composition prior to coating. In some aspects, the subcoating can be present in an amount from about 1% to about 10% (w/w). In some aspects, the subcoating is present in an amount from about 1% to about 5% (w/w). In some aspects, the subcoating can be present in an amount from about 1% to about 3% (w/w) relative to the core tablet prior to coating. For example, the subcoating can be present in amounts including about 1%, 1.5%, 2.0%, 2.5%, and about 3%, including any fractional amounts in between. In some aspects, the subcoating is present in an amount of about 3% (w/w). In some aspects, the weight of the subcoating is compared weight/weight to the weight of the composition, or to the weight of the core tablet, prior to coating.

[0371] In other embodiments, the subcoating level is measured in a coating weight gain (mg/cm^2). In some embodiments, the subcoating level is from about 6 mg/cm^2 to about 30 mg/cm^2 . In some embodiments, the subcoating level is from about 9 mg/cm^2 to about 30 mg/cm^2 . In other embodiments, the subcoating level is from about 12 mg/cm^2 to about 30 mg/cm^2 . In some embodiments, the subcoating level is from about 17 mg/cm^2 to about 30 mg/cm^2 . In some embodiments, the subcoating level is from about 20 mg/cm^2 to about 30 mg/cm^2 . In some embodiments, the subcoating level is from about 25 mg/cm^2 to about 30 mg/cm^2 . For example, the subcoating level is about 6 mg/cm^2 , 7 mg/cm^2 , 8 mg/cm^2 , 9 mg/cm^2 , 10 mg/cm^2 , 11 mg/cm^2 , 12 mg/cm^2 , 13 mg/cm^2 , 14 mg/cm^2 , 15 mg/cm^2 , 16 mg/cm^2 , 17 mg/cm^2 , 18 mg/cm^2 , 19 mg/cm^2 , 20 mg/cm^2 , 21 mg/cm^2 , 22 mg/cm^2 , 23 mg/cm^2 , 24 mg/cm^2 , 25 mg/cm^2 , 26 mg/cm^2 , 27 mg/cm^2 , 28 mg/cm^2 , 29 mg/cm^2 , or 30 mg/cm^2 . In some embodiments, the subcoating level is about 6 mg/cm^2 . In some embodiments, the subcoating level is about 7 mg/cm^2 . In some embodiments, the subcoating level is about 8 mg/cm^2 . In some embodiments, the subcoating level is about 9 mg/cm^2 . In some embodiments, the subcoating level is about 10 mg/cm^2 .

mg/cm². In some embodiments, the subcoating level is about 11 mg/cm². In some embodiments, the subcoating level is about 6 mg/cm². In some embodiments, the subcoating level is about 12 mg/cm². In some embodiments, the subcoating level is about 13 mg/cm². In some embodiments, the subcoating level is about 14 mg/cm². In some embodiments, the subcoating level is about 15 mg/cm². In some embodiments, the subcoating level is about 16 mg/cm². In some embodiments, the subcoating level is about 17 mg/cm². In some embodiments, the subcoating level is about 18 mg/cm².

Enteric Coating

[0372] In some aspects, the composition includes an enteric coating disposed over the subcoating. In some aspects, the enteric coating is selected to provide release of the tablet contents at a pH range from about 5 to about 8. In some aspects, the enteric coating is a pH 5.5 enteric coating. Enteric coating can include, without limitation, those based on cellulose acetate phthalate (CAP), poly(methacrylic acid-co-methyl methacrylate), cellulose acetate trimellitate (CAT), poly(vinyl acetate phthalate) (PVAP) or hydroxypropyl methylcellulose phthalate (HPMCP). In some aspects, the enteric coating can be a methacrylic acid co-polymer.

[0373] In some embodiments, the enteric coating can include, without limitation, poly(methacrylic acid ethyl acrylate) (L100D-55), a combination methyl acrylate, methyl methacrylate and methacrylic acid (FS30D), hydroxypropyl methylcellulose acetate succinate (HPMC-AS), Type L HPMC-AS, or a co-polymer of ethyl methacrylate acrylate (e.g., Acryl-eze®).

[0374] In some aspects, the weight of the enteric coating is compared weight/weight to the weight of the composition prior to coating. In some aspects, the enteric coating can be present in an amount from about 1% to about 15% (w/w). In some aspects, the enteric coating can be present in an amount from about 2% to about 15% (w/w). In some aspects, the enteric coating can make up from about 5% to about 15% (w/w) relative to the core tablet of the compositions. For example, the amounts of enteric coating can be in an amount of about 5%, 6%, 7%, 8%, 9%, 10%, 11%, 12%, 13%, 14%, or about 15% (w/w), including fractions thereof. In some aspects, the enteric coating can be present in an amount of about 6% (w/w). In some aspects, the enteric coating can be present in an amount of about 7% (w/w). In some aspects, the enteric coating can be present in an amount of about 8% (w/w). In some aspects, the weight of the enteric coating is compared weight/weight to the weight of the core tablet prior to coating.

[0375] In other embodiments, the enteric coating level is measured in a coating weight gain (mg/cm²). In some embodiments, the enteric coating level is from about 6 mg/cm² to about 30 mg/cm². In some embodiments, the enteric coating level is from about 9 mg/cm² to about 30 mg/cm². In other embodiments, the enteric coating level is from about 12 mg/cm² to about 30

mg/cm². In some embodiments, the enteric coating level is from about 17 mg/cm² to about 30 mg/cm². In some embodiments, the enteric coating level is from about 20 mg/cm² to about 30 mg/cm². In some embodiments, the enteric coating level is from about 25 mg/cm² to about 30 mg/cm². For example, the enteric coating level is about 6 mg/cm², 7 mg/cm², 8 mg/cm², 9 mg/cm², 10 mg/cm², 11 mg/cm², 12 mg/cm², 13 mg/cm², 14 mg/cm², 15 mg/cm², 16 mg/cm², 17 mg/cm², 18 mg/cm², 19 mg/cm², 21 mg/cm², 22 mg/cm², 23 mg/cm², 24 mg/cm², 25 mg/cm², 26 mg/cm², 27 mg/cm², 28 mg/cm², 29 mg/cm², or 30 mg/cm². In some embodiments, the enteric coating level is about 6 mg/cm². In some embodiments, the enteric coating level is about 7 mg/cm². In some embodiments, the enteric coating level is about 8 mg/cm². In some embodiments, the enteric coating level is about 9 mg/cm². In some embodiments, the enteric coating level is about 10 mg/cm². In some embodiments, the enteric coating level is about 11 mg/cm². In some embodiments, the enteric coating level is about 12 mg/cm². In some embodiments, the enteric coating level is about 13 mg/cm². In some embodiments, the enteric coating level is about 14 mg/cm². In some embodiments, the enteric coating level is about 15 mg/cm². In some embodiments, the enteric coating level is about 16 mg/cm². In some embodiments, the enteric coating level is about 17 mg/cm². In some embodiments, the enteric coating level is about 18 mg/cm².

[0376] In some aspects, the tablet compositions of the present invention may have a subcoating of OPADRY® QX yellow in an amount of about 3% (w/w) and an enteric coating of Acryl-eze® yellow of about 6% (w/w).

[0377] In some aspects, the tablet compositions of the present invention may have a subcoating of OPADRY® QX yellow in an amount of about 3% (w/w) and an enteric coating of Acryl-eze® yellow of about 7% (w/w).

[0378] In some aspects, the tablet compositions of the present invention may have a subcoating of OPADRY® QX yellow in an amount of about 3% (w/w) and an enteric coating of Acryl-eze® yellow of about 8% (w/w).

Order of Coatings

[0379] In some embodiments, the core tablet is covered by one or more of a cosmetic coating, a subcoating, an enteric coating, or any combination thereof. When more than one cosmetic coating, subcoating, and/or enteric coating covers the core tablet, such coatings may be applied in any order such that any of the cosmetic coating, subcoating, and/or enteric coating may be directly applied to the surface of the core tablet. In such instances, any additional cosmetic coating, subcoating, and/or enteric coating may be applied in any order subsequently.

[0380] In some embodiments, the core tablet is covered by a cosmetic subcoating. In some embodiments, the core tablet is covered by a cosmetic subcoating and then covered by an enteric coating. In some embodiments, the core tablet is covered by a cosmetic subcoating and then covered by a subcoating. In certain embodiments, the core tablet is covered by a cosmetic subcoating followed by a subcoating, and then followed by an enteric coating. In certain embodiments, the core tablet is covered by a cosmetic subcoating followed by an enteric coating, and then followed by a subcoating.

[0381] In other embodiments, the core tablet is covered by a subcoating. In some embodiments, the core tablet is covered by a subcoating and then covered by an enteric coating. In some embodiments, the core tablet is covered by a subcoating and then covered by a cosmetic subcoating. In certain embodiments, the core tablet is covered by a subcoating followed by an enteric coating and then covered by a cosmetic subcoating. In certain embodiments, the core tablet is covered by a subcoating followed by a cosmetic subcoating and then covered by an enteric coating.

[0382] In other embodiments, the core tablet is covered by an enteric coating. In other embodiments, the core tablet is covered by an enteric coating and then covered by a subcoating. In certain embodiments, the core tablet is covered by an enteric coating and then covered by a cosmetic subcoating. In other embodiments, the core tablet is covered by an enteric coating followed by a subcoating and then covered by a cosmetic coating. In certain embodiments, the core tablet is covered by an enteric coating followed by a cosmetic coating and then covered by a subcoating.

[0383] In some aspects, the tablet compositions of the present invention may have a bioavailability of from about 1% to about 10% (w/w). In some aspects, the tablet compositions of the present invention may have a bioavailability of from about 10% to about 50%. For example, bioavailability may be about 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, or about 10%. Bioavailability can be measured using area under curve (AUC) for oral dosing versus AUC by intravenous dosing.

[0384] In some aspects, the tablet compositions of the present invention may have a bioavailability of from about 0.01% to about 10% (w/w). In some aspects, the tablet compositions of the present invention may have a bioavailability of from about 0.1% to about 1% (w/w). For example, bioavailability may be about 0.01%, 0.1%, 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, or about 10%. Bioavailability can be measured using area under curve (AUC) for oral dosing versus AUC by intravenous dosing.

[0385]

[0386] A dose of a composition described herein may be administered according to a method and/or use of the present invention herein. In some aspects, a dose of a composition of the present invention can be administered once daily, twice daily, or three times daily. In some aspects, a dose of a composition of the present invention can be administered once daily. In some aspects, a dose of a composition of the present invention can be administered twice daily. In some aspects, a dose of a composition of the present invention can be administered three times daily.

[0387] In some embodiments described herein, such as relating to pharmaceutical compositions, tablets, methods, processes, and the like, the acetate salt of a compound of Formula (I) is excluded. In some embodiments described herein, such as relating to compositions, tablets, methods, processes, and the like, the acetate salt of a compound of Formula (I) is included.

V. METHODS OR PROCESSES OF MAKING TABLETS OR DOSAGE FORMS

[0388] In accordance with the present invention, pharmaceutical compositions are comprised of active principal ingredient (i.e., a hydrochloride salt of the compound of Formula (I) or solvate thereof) and at least one or more additional pharmaceutically acceptable ingredients (i.e., which may include, but is not limited to absorption enhancers) and adjuvants, carriers, excipients or stabilizers, etc., as defined throughout the instant disclosure.

[0389] In some embodiments, the active principal ingredient is a crystalline salt of a compound of Formula (I), or a pharmaceutically acceptable salt thereof, or a solvate of the foregoing, as described herein.

[0390] The percentage or amount of active principal ingredient (API) in compositions of the present invention, which may of course, be varied as amount of active compound in such therapeutically useful compositions is such that a suitable dosage for administration in a subject or patient will be obtained. It will be appreciated that the actual preferred dosages of API being used in the compositions of this invention will vary according to the particular composition formulated, the mode of administration, the particular site of administration and the host being treated. The choice of initial dosage most appropriate for the particular patient is determined by the practitioner using well-known medical principles, including, but is not limited to, body weight.

[0391] Moreover, an oral tablet dosage form of the present invention may have a surface layer is coated with an enteric coat, which may be, but is not limited to an enteric coating set forth in the Definition section of the instant specification. For example, an oral tablet dosage form may be formulated as with core components, separate sequential layers or combinations

thereof, where tablet components, such as core, other layers, may have different release-modifying component properties based upon gastrointestinal environment, pH or time. Hence, an oral tablet dosage form of the present invention may also be coated with a pH sensitive polymer.

[0392] Tablets including the compositions of the present invention may be prepared using conventional tablet forming equipment as conventionally known in the art, which may use compaction, rollers and the like. In some embodiments, the tablet forming technique is roller compaction.

VI. METHODS OF TREATMENT AND/OR USES

[0393] In one aspect, the present invention relates to a method and/or use for treating inflammatory disease in a subject which comprises administering to the subject a therapeutically effective amount of a crystalline hydrochloride salt of the compound of Formula (I) or solvate or composition thereof disclosed herein. In some aspects, the present invention provides a method of treating inflammatory disease in a subject which comprises administering to the subject a therapeutically effective amount of a crystalline hydrochloride salt of the compound of Formula (I) or solvate or composition thereof of the present invention. Suitable inflammatory diseases for treatment with compositions of the present invention, may include, but is not limited to inflammatory bowel disease (IBD), Crohn's disease (CD), ulcerative colitis (UC), psoriasis (PsO), or psoriatic arthritis (PsA) and the like. In some aspects, the inflammatory disease is moderate to severe in degree.

[0394] In any of the method of treatment and/or uses embodiments detailed herein, it is understood that such methods and uses may comprise any of the crystalline forms of a compound of Formula (I) and the pharmaceutical compositions as described herein the same as if each and every combination were specifically and individually listed. For example, any of the methods of treatment and/or uses may in some embodiments comprise administering to the subject a therapeutically effective amount of a crystalline form of a compound of Formula (I), a pharmaceutically acceptable salt thereof, or a solvate of the foregoing. In some embodiments, the crystalline form is selected from a hydrochloride salt of a compound of Formula (I), an acetate salt of a compound of Formula (I), a fumarate salt of a compound of Formula (I), a glutarate salt of a compound of Formula (I), a glycolate salt of a compound of Formula (I), a mesylate salt of a compound of Formula (I), a bis-hydrochloride salt of a compound of Formula (I), a citrate salt of a compound of Formula (I), and a sulfate salt of a compound of Formula (I).

[0395] In some aspects, the present invention provides methods and/or uses for treating a subject afflicted with a condition or indication associated with IL-21 or IL-23R (*e.g.*, activation

of the IL-23/IL-23R signaling pathway), where the method and/or use comprises administering to the subject the crystalline hydrochloride salt of the compound of Formula (I) or solvate or composition thereof of the present invention. In some aspects, a method and/or use is provided for treating a subject afflicted with a condition or indication characterized by inappropriate, deregulated, or increased IL-23 or IL-23R activity or signaling, which comprises administering to the individual a crystalline hydrochloride salt of the compound of Formula (I) or solvate or composition thereof of the present invention in an amount sufficient to inhibit (partially or fully) binding of IL-23 to IL-23R in the subject. In some aspects, the inhibition of IL-23 binding to IL-23R occurs in particular organs or tissues of the subject, *e.g.*, the stomach, small intestine, large intestine/colon, intestinal mucosa, lamina propria, Peyer's Patches, mesenteric lymph nodes, or lymphatic ducts.

[0396] In some aspects, methods and/or uses of the present invention can comprise administering a crystalline hydrochloride salt of the compound of Formula (I) or solvate or composition thereof of the present invention to a subject in need thereof. In some aspects, the subject in need thereof has been diagnosed with or has been determined to be at risk of developing a disease or disorder associated with IL-23/IL-23R. In some aspects, the subject is a mammal. In some aspect, the subject is a human.

[0397] In some aspects, the disease or disorder is autoimmune inflammation and related diseases and disorders, such as, which may include, but are not limited to multiple sclerosis, asthma, rheumatoid arthritis, inflammation of the gut, inflammatory bowel diseases (IBDs), juvenile IBD, adolescent IBD, Crohn's disease, ulcerative colitis, sarcoidosis, Systemic Lupus Erythematosus, ankylosing spondylitis (axial spondyloarthritis), psoriasis, or psoriatic arthritis. In some aspects, the disease or disorder is an inflammatory bowel disease (IBD). In some aspects, the disease or disorder is Crohn's disease. In some aspects, the disease or disorder is ulcerative colitis. In some aspects, the disease or disorder is psoriasis. In some aspects, the disease or disorder is psoriatic arthritis.

[0398] In some aspects, the disease or disorder is or may be selected from psoriasis (*e.g.*, plaque psoriasis, guttate psoriasis, inverse psoriasis, pustular psoriasis, Palmo-Plantar Pustulosis, psoriasis vulgaris, or erythrodermic psoriasis), atopic dermatitis, acne ectopica, ulcerative colitis, Crohn's disease, Celiac disease (nontropical Sprue), enteropathy associated with seronegative arthropathies, microscopic colitis, collagenous colitis, eosinophilic gastroenteritis/esophagitis, colitis associated with radio- or chemo-therapy, colitis associated with disorders of innate immunity as in leukocyte adhesion deficiency-1, chronic granulomatous disease, glycogen storage disease type 1b, Hermansky-Pudlak syndrome, Chediak-Higashi syndrome, Wiskott-Aldrich Syndrome, pouchitis, pouchitis resulting after proctocolectomy and ileoanal

anastomosis, gastrointestinal cancer, pancreatitis, insulin-dependent diabetes mellitus, mastitis, cholecystitis, cholangitis, primary biliary cirrhosis, viral-associated enteropathy, pericholangitis, chronic bronchitis, chronic sinusitis, asthma, uveitis, or graft versus host disease.

[0399] In one aspect, the present invention relates to methods and/or uses for treatment of autoimmune inflammation and related diseases and disorders, which may include, but is/are not limited to inflammatory bowel disease (IBD), Crohn's disease (CD), ulcerative colitis (UC), psoriasis (PsO), or psoriatic arthritis (PsA) and the like. In some aspects, the inflammatory disease is inflammatory bowel disease (IBD), Crohn's disease, ulcerative colitis, psoriasis, or psoriatic arthritis. In some aspects, the inflammatory disease is inflammatory bowel disease (IBD). In some aspects, the inflammatory disease is Crohn's disease. In some aspects, the inflammatory disease is ulcerative colitis. In some aspects, the inflammatory disease is psoriasis. In some aspects, the inflammatory disease is psoriatic arthritis.

[0400] In some aspects, the present invention relates to methods and/or uses for inhibiting IL-23 receptor for treatment of autoimmune inflammation and related diseases and disorders, that include administering a crystalline hydrochloride salt of the compound of Formula (I) or solvate or composition thereof of to a subject in need thereof. In some aspects, the IL-23 receptor is inhibited in blood, blood circulation, tissue, skin, or joints. In some aspects, the IL-23 receptor is inhibited in a tissue selected from blood, skin, cartilage, or synovial membrane. In some aspects, the IL-23 receptor is inhibited in blood. In some aspects, the IL-23 receptor is inhibited in skin. In some aspects, the IL-23 receptor is inhibited in cartilage. In some aspects, the IL-23 receptor is inhibited in synovial membrane.

[0401] In some aspects, the present invention relates to methods and/or uses for inhibiting IL-23 receptor in a digestive tract tissue for treatment of autoimmune inflammation and related diseases and disorders, that include administering a crystalline hydrochloride salt of the compound of Formula (I) or solvate or composition thereof of to a subject in need thereof.

[0402] In some aspects of the methods and/or uses of the present invention, the digestive tract tissue is selected from mouth, esophagus, stomach, small intestine, large intestine, duodenum, and anus. In some aspects, the digestive tract tissue is mouth. In some aspects, the digestive tract tissue is esophagus. In some aspects, the digestive tract tissue is stomach. In some aspects, the digestive tract tissue is small intestine. In some aspects, the digestive tract tissue is large intestine. In some aspects, the digestive tract tissue is duodenum. In some aspects, the digestive tract tissue is anus.

[0403] In some aspects, the present invention provides a method and/or use for treating an inflammatory bowel disease (IBD) in a subject in need thereof, which comprises administering to the subject a crystalline hydrochloride salt of the compound of Formula (I) or solvate or

composition thereof of the present invention. In some aspects, the present invention provides a method of treating an inflammatory bowel disease (IBD) in a subject comprising administering to the subject a therapeutically effective amount of a crystalline hydrochloride salt of the compound of Formula (I) or solvate or composition thereof of the present invention. In some aspects, the IBD is ulcerative colitis. In some aspects, the IBD is Crohn's disease.

[0404] In some aspects, the present invention provides methods or use of a crystalline hydrochloride salt of the compound of Formula (I) or solvate or composition thereof of the present invention in the manufacture of a medicament for treating an inflammatory bowel disease (IBD).

[0405] In another aspect, the present invention relates to a method of treating an inflammatory bowel disease (IBD) in a subject in need thereof which comprises administering to the subject a therapeutically effective amount of a crystalline hydrochloride salt of the compound of Formula (I) or solvate or composition thereof disclosed herein. In some aspects, the IBD is Crohn's disease or ulcerative colitis. In some aspects, the IBD is Crohn's disease. In some aspects, the IBD is ulcerative colitis.

[0406] In some aspects, the present invention provides for a use of a crystalline hydrochloride salt of the compound of Formula (I) or solvate or composition thereof disclosed herein in the manufacture of a medicament for treating an inflammatory bowel diseases (IBD).

[0407] In some aspects, the present invention relates to a method of treating psoriasis or psoriatic arthritis in a subject in need thereof which comprises administering to the subject a therapeutically effective amount of a crystalline hydrochloride salt of the compound of Formula (I) or solvate or composition thereof of the present invention. In some aspects, the present invention relates to a method that includes treating psoriasis. In some aspects, the present invention relates to a method that includes treating psoriatic arthritis.

[0408] In some aspects, the present invention provides for a use of a crystalline hydrochloride salt of the compound of Formula (I) or solvate or composition thereof disclosed herein, in the manufacture of a medicament for treating psoriasis or psoriatic arthritis. In some aspects, the present invention provides for a use for treating psoriasis. In some aspects, the present invention provides for a use for treating psoriatic arthritis.

[0409] In some aspects, the method and/or use includes orally administering the crystalline hydrochloride salt of the compound of Formula (I) or solvate or composition thereof of the present invention.

[0410] In some aspects, the present invention relates to methods and/or uses of treating inflammatory bowel diseases (IBD) in a subject, which comprises administering a therapeutically effective amount of a crystalline hydrochloride salt of the compound of Formula

(I) or solvate or composition thereof disclosed herein. In some aspects, the IBD is Crohn's disease or ulcerative colitis. In some aspects, the methods and/or uses of the present invention include administering a crystalline hydrochloride salt of the compound of Formula (I) or solvate or composition thereof in tablet form once, twice, or three times daily orally in accordance with patient treatment.

[0411] In some aspects, the present invention relates to methods and/or uses of treating psoriasis or psoriatic arthritis in a subject, which comprises administering a therapeutically effective amount of a crystalline hydrochloride salt of the compound of Formula (I) or solvate or composition thereof disclosed herein. In some aspects, the present invention relates to methods and/or uses of treating psoriasis. In some aspects, the present invention relates to methods and/or uses of treating psoriatic arthritis. In some aspects, the methods and/or uses of the present invention include administering a crystalline hydrochloride salt of the compound of Formula (I) or solvate or composition thereof in tablet form once, twice, or three times daily orally in accordance with patient treatment.

[0412] In some aspects, the methods and/or uses of the present invention include administering a dose of a crystalline hydrochloride salt of the compound of Formula (I) or solvate or composition thereof. In some aspects, the hydrochloride salt of a compound of Formula (I) or solvate thereof may be present in any dose range, such as a dose range of from about 1 mg to about 1000 mg, or from about 1 mg to about 500 mg, from about 1 mg to about 100 mg, from about 10 mg to about 50 mg, from about 20 mg to about 40 mg, or from about 20 mg to about 30 mg. In another aspect, the dose range of the hydrochloride salt of a compound of Formula (I) or solvate thereof may be from about 1 mg to about 1000 mg. In another aspect, the dose range of the hydrochloride salt of a compound of Formula (I) or solvate thereof may be from about 5 mg to about 300 mg. In another aspect, the dose range of the hydrochloride salt of a compound of Formula (I) or solvate thereof is from about 25 mg to about 150 mg. In another aspect, the dose range of the hydrochloride salt of a compound of Formula (I) or solvate thereof may be from about 25 mg to about 100 mg. In another aspect, the hydrochloride salt of a compound of Formula (I) or solvate thereof may be present in a dose range of from about 1 mg to about 100 mg. In another aspect, the hydrochloride salt of a compound of Formula (I) or solvate thereof may be present in a dose range of from about 20 mg to about 40 mg. In another aspect, the hydrochloride salt of a compound of Formula (I) or solvate thereof may be present in a dose range of from about 20 mg to about 30 mg.

[0413] In yet another aspect, the methods and/or uses of the present invention include administering a dose of a crystalline hydrochloride salt of the compound of Formula (I) or solvate or composition thereof in a dose of about 5 mg, about 10 mg, about 25 mg, about 50 mg,

about 75 mg, about 100 mg, or about 150 mg, including any amount in between and fractions thereof. In another aspect, a dose of the hydrochloride salt of a compound of Formula (I) or solvate thereof may be present in about 5 mg. In another aspect, a dose of the hydrochloride salt of a compound of Formula (I) or solvate thereof may be present in about 10 mg. In another aspect, a dose of the hydrochloride salt of a compound of Formula (I) or solvate thereof may be present in about 25 mg. In another aspect, a dose of the hydrochloride salt of a compound of Formula (I) or solvate thereof may be present in about 50 mg. In another aspect, a dose of the hydrochloride salt of a compound of Formula (I) or solvate thereof may be present in about 75 mg. In another aspect, a dose of the hydrochloride salt of a compound of Formula (I) or solvate thereof may be present in about 100 mg. In another aspect, a dose of the hydrochloride salt of a compound of Formula (I) or solvate thereof may be present in about 150 mg.

[0414] In some aspects, the methods and/or uses of the present invention include administering a dose of about 10 mg, about 25 mg, or about 50 mg of a crystalline hydrochloride salt of the compound of Formula (I) or solvate or composition thereof once daily or twice daily. In some aspects, the methods and/or uses of the present invention include administering a dose of about 10 mg of a crystalline hydrochloride salt of the compound of Formula (I) or solvate or composition thereof twice daily. In some aspects, the methods and/or uses of the present invention include administering a dose of about 25 mg of a crystalline hydrochloride salt of the compound of Formula (I) or solvate or composition thereof twice daily. In some aspects, the methods and/or uses of the present invention include administering a dose of about 50 mg of a crystalline hydrochloride salt of the compound of Formula (I) or solvate or composition thereof twice daily. In some aspects, the methods and/or uses of the present invention include administering a dose of about 10 mg of a crystalline hydrochloride salt of the compound of Formula (I) or solvate or composition thereof once daily. In some aspects, the methods and/or uses of the present invention include administering a dose of about 25 mg of a crystalline hydrochloride salt of the compound of Formula (I) or solvate or composition thereof once daily. In some aspects, the methods and/or uses of the present invention include administering a dose of about 50 mg of a crystalline hydrochloride salt of the compound of Formula (I) or solvate or composition thereof once daily.

[0415] In some embodiments described herein, such as relating to compositions, tablets, methods, processes, and the like, the acetate salt of a compound of Formula (I) is excluded. In some embodiments described herein, such as relating to compositions, tablets, methods, processes, and the like, the acetate salt of a compound of Formula (I) is included.

[0416] In some embodiments described herein, such as relating to compositions, tablets, methods, processes, and the like, the acetate salt of a compound of Formula (I) is excluded. In

some embodiments described herein, such as relating to compositions, tablets, methods, processes, and the like, the acetate salt of a compound of Formula (I) is included.

[0417] Each aspect of the present invention defined in this or in any other section may incorporate definitions and limitations, such as those set forth throughout the originally filed disclosure, specification and claims.

VII. EXAMPLES

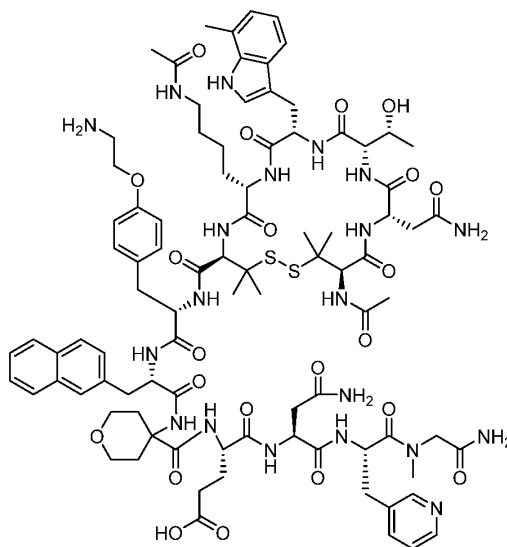
[0418] In describing the present invention, abbreviations and symbols utilized herein are in accordance with the common usage of such abbreviations and symbols by those skilled in the chemical and biological arts. Specifically, the following abbreviations may be used in the examples and throughout the specification:

List of Standard Chemical Definitions

Acronym or Abbreviation	Definition
Ac	acetate
ACN	acetonitrile
AEF	4-(2-aminoethoxy)-L-phenylalanine
Amt. or amt.	amount
amu	atomic mass unit(s)
Asn, N	L-asparagine
BOC or Boc	t-butoxy-
DIC	diisopropylcarbodiimide
DMF	dimethyl formamide
Equiv., equiv., or eq.	equivalents
Fmoc or Fmoc	fluorenylmethoxycarbonyl
Glu, E	L-glutamic acid
HPLC	high performance liquid chromatography
IPA	isopropanol
Lys	L-lysine
MBHA	4-methylbenzhydrylamine
2-Nal	2-naphthyl-L-alanine
3-Pal	3-(3-pyridyl)-L-alanine
Pen	penicillamine
Phe	L-phenylalanine
Sarc	sarcosine
SPPS	solid phase peptide synthesis
tBu	t-butyl
TFA	trifluoroacetic acid
THP	4-amino-tetrahydropyran-4-carboxylic acid
Thr, T	L-threonine
TIS	triisopropyl silane
Trp, W	L-tryptophan
Trt	trityl
UHPLC	ultra high performance liquid chromatography
UV	ultraviolet

Example 1. Preparation of a Crystalline Form of a Hydrochloride Salt of a Peptide of SEQ ID NO: 1

[0419] Ac-[Pen]*-N-T-[W(7-Me)]-[Lys(Ac)]-[Pen]*-Phe[4-(2-aminoethoxy)]-[2-Nal]-[THP]-E-N-[3-Pal]-Sarc-NH₂ (in which [Pen]*-[Pen]* form a disulfide bond) (SEQ ID NO: 1):



[0420] A synthesis of compounds of a compound of Formula (I) or a pharmaceutically acceptable salt thereof has been reported, i.e., which includes, Peptide #104 in U.S. Pat. Appln. Pub. No. 2021/0261622 ("U.S. '622 Pub."), Pub. Date: August 26, 2021, and which corresponds to WO 2021/146441 A1 ("WO '441 Appln."), Intern.'l Pub. Date: 22 July 2021, each of which respectively is incorporated herein by reference in its entirety.

[0421] The synthesis of the hydrochloride salt of the compound of Formula (I) was prepared using Fmoc solid phase peptide synthesis (SPPS) techniques as described herein in aforementioned U.S. '622 Pub. or WO '441 Appln. references.

[0422] The peptide was constructed on Rink Amide MBHA resin using standard Fmoc protection synthesis conditions reported in the literature. The constructed peptide was isolated from the resin and protecting groups by cleavage with strong acid followed by precipitation. Oxidation to form the disulfide bond was performed followed by purification.

[0423] During SPPS, the sequence of the desired compound (i.e., a compound of Formula (I)) was built up on a polymer support by sequential and repetitive addition of the chosen building blocks. Cross-linked polystyrene resins immobilized the growing peptide chains.

[0424] As building blocks (starting materials), suitably protected amino-acid derivatives were used (see, Table 1 below). Protection of the reactive α -amino groups relied on the Fmoc strategy. Necessary side-chain protection was achieved by use of other protecting groups that were stable toward the reagents used for Fmoc-cleavage.

[0425] The peptide chain was built up from the C-terminus to the N-terminus by repeated cycles until the resin carried the complete amino acid sequence: (i) N- α -deprotection with 20 % (V/V) piperidine in DMF to enable the coupling reaction (10 mL/g), (ii) coupling of protected building block (protected amino acid derivative) in the presence of DIC and Oxyma as suitable activating reagent(s) (solvent: DMF, 10 mL/g) (Table 2), systematic acetylation (capping) of remaining free amino groups using acetic anhydride and pyridine (solvent: DMF, 10 mL/g; c: DMF / Ac₂O / Pyridine 50:1:1). Each step consisted of the following operations: (i) addition of solvents/reagents to the resin; (ii) agitating of the reaction mixture, and (iii) removal of solvents/reagents by filtration and washing (solvents: DMF and/or IPA, 10 mL/g).

[0426] After cleavage of the N-terminal Fmoc group, a final acetylation was performed. Then, the peptide resin was washed alternatingly with dimethyl formamide (DMF) and isopropanol (IPA) and dried under reduced pressure. Batch size: 30.0 mol, yield (31.5 mol, 105%).

Table 1. Materials and Amounts for SPPS Synthesis

Cycle	Material	Coupling			Recoupling		
		Equiv.	Amt. [mol]	Amt. [kg]	Equiv.	Amt. [mol]	Amt. [kg]
0	Fmoc-Rink amide AM resin (100-200 mesh, 0.8-1.2 mmol/g)	1.0	30.0	⁽¹⁾	-	-	-
1	Fmoc-Sarc-OH	2.0	60.0	18.7	1.0	30.0	9.3
2	Fmoc- β -(3-pyridyl)-Ala-OH = Fmoc-3-Pal-OH	1.5	45.0	17.5	0.8	22.5	8.7
3	Fmoc-Asn(Trt)-OH	2.0	60.0	35.8	1.0	30.0	17.9
4	Fmoc-Glu(OtBu)-OH · H ₂ O	2.0	60.0	26.6	1.0	30.0	13.3
5	Fmoc-4-amino-tetrahydropyran-4-carboxylic acid = Fmoc-THP-OH	1.5	45.0	16.5	0.8	22.5	8.3
6	Fmoc-2-Nal-OH	1.5	45.0	19.7	0.8	22.5	9.8
7	Fmoc-Tyr(Boc-2-aminoethyl)-OH	1.5	45.0	⁽²⁾	0.8	22.5	⁽²⁾
8	Fmoc-Pen(Trt)-OH	2.0	60.0	⁽²⁾	1.0	30.0	⁽²⁾
9	Fmoc-Lys(Ac)-OH	2.0	60.0	24.6	1.0	30.0	12.3
10	Fmoc-7-Me-Trp-OH	1.8	54.0	⁽²⁾	0.9	27.0	⁽²⁾
11	Fmoc-Thr(tBu)-OH	2.0	60.0	23.9	1.0	30.0	11.9
12	Fmoc-Asn(Trt)-OH	2.0	60.0	35.8	1.0	30.0	17.9
13	Fmoc-Pen(Trt)-OH	2.0	60.0	⁽²⁾	1.0	30.0	⁽²⁾

⁽¹⁾ The amount was calculated taking into account the loading of the batch(es) used.

⁽²⁾ The amount was calculated taking into account the assay of the batch(es) used.

Table 2. Coupling Reagents for SPPS Synthesis

Reagent	Coupling			Recoupling		
	Equiv.	Amt. [mol]	Amt. [kg]	Equiv.	Amt. [mol]	Amt. [kg]
Cyano-hydroxyimino-acetic acid ethyl ester (Oxyma) (for couplings cycle 1, 3, 4, 8, 9, 11, 12, 13)	3.1	93.0	13.2	1.6	46.5	6.6
Cyano-hydroxyimino-acetic acid ethyl ester (Oxyma) (for couplings cycle 2, 5, 6, 7)	2.3	69.9	9.9	1.2	35.0	5.0

Reagent	Coupling			Recoupling		
	Equiv.	Amt. [mol]	Amt. [kg]	Equiv.	Amt. [mol]	Amt. [kg]
Cyano-hydroxyimino-acetic acid ethyl ester (Oxyma) (for couplings cycle 10)	2.8	83.7	11.9	1.4	41.9	6.0
N,N'-Diisopropylcarbodiimide (DIC), 1 st addition (for couplings cycle 1, 3, 4, 8, 9, 11, 12, 13)	2.6	78.0	9.8	1.3	39.0	4.9
N,N'-Diisopropylcarbodiimide (DIC), 2 nd addition (for couplings cycle 1, 3, 4, 8, 9, 11, 12, 13)	1.3	39.0	4.9	0.65	19.5	2.5
N,N'-Diisopropylcarbodiimide (DIC), 1 st addition (for couplings cycle 2, 5, 6, 7)	1.95	58.5	7.4	1.0	29.3	3.7
N,N'-Diisopropylcarbodiimide (DIC), 2 nd addition (for couplings cycle 2, 5, 6, 7)	1.0	29.3	3.7	0.49	14.6	1.85
N,N'-Diisopropylcarbodiimide (DIC), 1 st addition (for couplings cycle 10)	2.3	70.2	8.9	1.2	35.1	4.4
N,N'-Diisopropylcarbodiimide (DIC), 2 nd addition (for couplings cycle 10)	1.2	35.1	4.4	0.6	17.6	2.2

[0427] Cleavage of the peptide from the resin and simultaneous cleavage of the side-chain protecting groups were accomplished by treatment of the peptide resin with TFA (6.30 L/kg resin) in the presence of suitable scavengers: H₂O (0.175 L/kg resin), ethanedithiol (EDT) (0.175 L/kg resin) and triisopropylsilane (TIS) (0.27 kg/kg resin). After filtering off and washing the resin with TFA twice (in total 2.0 L/kg resin), the product was precipitated by the addition of cooled diisopropyl ether (40 L/kg resin). The product was filtered off, washed with diisopropyl ether three times (3.0 L/kg each), and dried under reduced pressure. Batch size: 5.16 mol; yield: 5.44 mol (105%).

[0428] The crude product was dissolved in aqueous AcOH solution (H₂O / AcOH 70:30, 100 g/L). The resulting peptide solution was treated with aqueous I₂/KI solution (52 mM I₂, 154 mM KI) to build the disulfide bond between the penicillamine residues by oxidation of the SH moieties. The reaction was quenched by addition of aqueous ascorbic acid solution (662 mM, 0.106 g ascorbic acid/ g crude, 1.35 equivalents). The cyclized peptide was purified by preparative HPLC on a reversed-phase column with ACN gradient elution and UV detection at 300 nm.

[0429] A NH₄HCO₃ system was employed for elution (eluent NH₄HCO₃ A: 15% ACN in 30 mM NH₄HCO₃; eluent NH₄HCO₃ B: 50% ACN in 10 mM NH₄HCO₃). The collected fractions were analyzed by HPLC and pooled accordingly (Target: ≥ 97.0%). The pH of the pooled main fractions was adjusted to 7.0 ± 0.2 with aqueous hydrochloric acid (5.5 M).

One-step Preparation of a Hydrochloride Salt of a Peptide of SEQ ID NO: 1

[0430] 12.0 kg of the of the compound of Formula (I) had been cyclized and purified by six prep. HPLC runs. Combination of all main cuts from the six purification runs resulted in a volume of the compound of Formula (I) solution of 202 L. To this solution, 67 L of side cuts

were added (volume ratio main cuts / side cuts = 3:1), obtaining in total 269 L. The pH was adjusted to 7.1 by adding 0.25 L of 5.5 N HCl aq. The solution was concentrated by evaporation *in vacuo* at 40°C jacket temperature down to the final volume of 60 L. The temperature of the concentrated turbid product solution was reduced to 23 °C. The pH was adjusted to 5.1 with 2.0 L of 1 N HCl aq., 12.0 L of IPA were added, and the solution was stirred for 19 hr. at 6°C. Further precipitation occurred during stirring of the solution. The suspension was transferred to the mobile filter dryer, allowed to sediment for 10 min, and filtered by applying overpressure (0.5 bar at the beginning, later increased up to 2 bar). A clear mother liquor was observed during filtration. The isolated product was dried *in vacuo* at 40°C, first at 65 mbar until solvent distillation ceased. Then, after approx. 8.5 hr. drying was continued at full vacuum, but the temperature was reduced to 25°C, as drying was performed over the weekend instead of overnight. After a total drying time of 62 hr. with a final vacuum of 6 mbar, the product was unloaded from the filter dryer.

[0431] Because of the aspect of the isolated material (coarse particles with agglomerates), the product was sieved (1.5 mm mesh size) applying a sieving mill. In total, 5.24 kg were obtained after sieving. A purity (HPLC) of 97.3% was determined with the QC HPLC release method. The chloride content was determined as 1.3% (theoretical chloride content of the mono hydrochloride salt is 1.9%.), and the isolated material was readily soluble in water (1 mg/mL) without any pH adjustment required.

Alternative two-step Preparation of Crystalline Form of a Hydrochloride Salt of a Peptide of SEQ ID NO: 1

Step 1:

[0432] 7.057 kg of the compound of Formula (I) had been cyclized and purified by four prep. HPLC runs. Combination of all main cuts from the four purification runs resulted in a solution volume of 100 L. The pH was adjusted by adding 0.2 L of 5.5 N HCl aq., resulting in pH 6.25 of the product solution. The solution was concentrated by evaporation *in vacuo* at 40 °C jacket temperature down to the final volume of 35 L (representing target volume of 10 vol. eq.). The temperature of the suspension was reduced to 26 °C and pH 5.1 was determined. As the pH of the suspension had already reached the target of pH 5.1 after evaporation, no further pH adjustment by addition of HCl aq. was performed. 7.0 L IPA were added, and the suspension was stirred for 20 hr. at 5 to 6 °C.

[0433] The suspension was transferred to the mobile filter dryer, allowed to sediment for 8 min, and filtered by applying overpressure (0.5 bar at the beginning, later increased up to 2 bar). The isolated product was dried *in vacuo* at 40 °C, first at 50 mbar until solvent distillation

ceased. Then, drying was continued at full vacuum. After a total drying time of 18 hr. with a final vacuum of 3 mbar, the product was unloaded from the filter dryer.

[0434] The product was sieved (1.5 mm mesh size) applying a sieving mill. In total, 2.43 kg of the compound of Formula (I) were obtained after sieving. The chloride content was determined as 0.5%.

Step 2:

[0435] The hydrochloride salt of the compound of Formula (I), as prepared in the previous step (2.13 kg) was suspended in 43 L of deionized water. A pH of 4.1 was determined for the suspension. By addition of 1.77 L of 1 N HCl aq. the pH was adjusted to 2.90. The resulting clear, slightly yellow solution was stirred for 1 h. By addition of 1.65 L of 1 M NH_4HCO_3 aq. the pH of the solution was increased from initially pH 2.87 to 5.09. To the slightly turbid solution 4.3 L of IPA was added. The resulting suspension was then stirred for 0.5 hr. at 25 °C and 19.5 hr. at 5 °C (pH 6.09 determined). The suspension was filtered on a mobile filter dryer and subsequently dried *in vacuo* for approx. 20 hr. at 40 °C (10 mbar final vacuum).

[0436] A sample was taken for IPC analysis, in particular determination of residual solvents and loss on drying. Drying was resumed at 25 °C until IPC results were available (6.5 hr., 3 mbar final vacuum). 602 mg/kg of residual IPA, a LOD of 1.57%, a chloride content of 1.0%, and a purity (HPLC) of 99.3% were determined. The product was unloaded from the filter dryer and sieved (1.5 mm mesh). In total, 1.82 kg of reworked hydrochloride salt of the compound of Formula (I) were obtained, a yield of 85.4% (w/w).

[0437] An X-ray powder diffraction (XRPD) pattern of the hydrochloride salt of the compound of Formula (I) confirmed its crystallinity (see, FIG. 1).

Example 2

[0438] 31.3 kg Rink amide AM resin (substitution: 0.96 mmol/g) were loaded into a 1000 L SPPS reactor and the SPPS was performed. Each SPPS cycle consists of Fmoc cleavage, coupling with the respective building block and obligatory capping. For Fmoc cleavage the resin was treated with 20% piperidine in DMF (10 ml/g resin each) for 5 ± 2 min and 10 ± 2 min at 25 °C. Couplings were performed using the building blocks, coupling reagents and conditions depicted in Table 3 with DMF as solvent (10 ml/g resin). For capping the resin was treated with acidic anhydride and pyridine in DMF (volumetric ratio DMF / Ac_2O /pyridine 50:1:1; DMF: 10 ml/g resin) for 20 min. Diisopropyl carbonate (DIC) was added in two portions, with the second portion was added after about 20 to 30 minutes after the first portion.

Table 3:

Cycle	Building block	Equivalents building block	Equivalents Oxyma	Equivalents DIC	Coupling duration	Coupling temp.
1	Fmoc-Sar-OH	1.50	2.30	2.00 + 1.00	10 h	25 °C
2	Fmoc-3-Pal-OH	1.50	2.30	2.00 + 1.00	13 h	25 °C
3	Fmoc-Asn(Trt)-OH	1.50	2.30	2.00 + 1.00	2 h	25 °C
4	Fmoc-Glu(OtBu)-OH · H ₂ O	1.50	2.30	2.00 + 1.00	14 h	25 °C
5	Fmoc-THP-OH	1.50	2.30	2.00 + 1.00	4 h	35 °C
6	Fmoc-2-Nal-OH	1.50	2.30	2.00 + 1.00	23 h	25 °C
7	Fmoc-Tyr(Boc-2-aminoethyl)-OH	1.50	2.30	2.00 + 1.00	3 h	35 °C
8	Fmoc-Pen(Trt)-OH	1.50	2.30	2.00 + 1.00	5 h	35 °C
9	Fmoc-Lys(Ac)-OH	1.50	2.30	2.00 + 1.00	5 h	35 °C
10	Fmoc-7-Me-Trp-OH	1.50	2.30	2.00 + 1.00	4 h	35 °C
11	Fmoc-Thr(tBu)-OH	1.50	2.30	2.00 + 1.00	10 h	35 °C
12	Fmoc-Asn(Trt)-OH	1.50	2.30	2.00 + 1.00	3 h	35 °C
13	Fmoc-Pen(Trt)-OH	1.50	2.30	2.00 + 1.00	4 h	35 °C

[0439] Final acetylation of the peptide resin was performed with acidic anhydride and pyridine in DMF (volumetric ratio DMF / Ac₂O/pyridine 10:1:1; DMF: 10 ml/g resin) for 20 min. After drying at 25 – 35 °C 123.7 kg linear peptide-Rink amide AM resin were obtained.

TFA cleavage

[0440] In a jacketed reactor 100 g of linear peptide-Rink amide AM resin were added at 20 °C to 700 mL of the cleavage cocktail, consisting of 630 mL TFA, 35 mL TIS, 17.5 mL EDT, and 17.5 mL water. The temperature increased to 34 °C upon addition of the resin, and the mixture was stirred for an additional 35 min at 30 °C. The mixture was cooled to 20 °C, and the resin was filtered off and washed two times with 100 mL TFA each. The filtrates were combined and cooled to -17 °C. For precipitation 4.0 L diisopropyl ether were added within 20 min maintaining the temperature of the solution / suspension at 5 °C. After complete addition of diisopropyl ether, the temperature was increased to 25 °C and the suspension stirred for 2.5 h. The suspension was then transferred to a filter dryer, and the precipitated crude product was filtered off at ambient temperature. The filter cake was subsequently washed three times with 300 mL of diisopropyl ether each and dried *in vacuo* at 30 °C over night. In total, 53.62 g of linear peptide was isolated as the TFA salt.

Oxidation and purification by preparative HPLC

[0441] 28 g cleaved linear peptide was dissolved in 280 mL 30% AcOH in water at ambient temperature. 3.71 g iodine and 7.17 g potassium iodide were dissolved in 280 mL water. Both the peptide and the iodine/iodide-solution were added in parallel to a vigorously stirred mixture of 2.2 L 30% AcOH in water at ambient temperature within 60 min. After complete addition of both solutions, a red-brown oxidation mixture was obtained. After stirring for 30 min at ambient temperature, IPC indicated nearly full conversion of starting material. 3.5 g Vitamin C were added, and the obtained yellow solution was stirred for 10 min. The oxidation mixture was filtrated over a fritted glass funnel before applying to the prep. RP-HPLC column. The chromatographic conditions are given in **Table 4**. All fractions were adjusted with 18% HCl in water to pH 7. The fractions collected during prep. RP-HPLC were analyzed by UHPLC. Fractions containing > 97% product were pooled for subsequent isolation.

Table 4: Chromatographic conditions

Column		ModCol 5 cm I.D.		
Column packaging		Kromasil C8, pore size 100 Å, particle size 10 µm		
Eluent A		15% ACN, 30 mM NH ₄ HCO ₃ in water		
Eluent B		50% ACN, 10 mM NH ₄ HCO ₃ in water		
Eluent C		5% ACN, 1% AcOH in water		
Gradient		0% – 1 min – 25% – 50 min – 75%B		
Detection wavelength		300 nm		
Fraction size		30 sec		
Process step	Flow [cm/h]	Flow [mL/min]	Duration	Solution
Equilibration	370	120	10	Eluent C
Product application	185	60	variable	Oxidation mixture
Column flush 1	185	60	10	Eluent C
Column flush 2	185	60	10	Eluent A
Gradient	185	60	50	Eluent A+B
Post gradient column flush	185	60	10	Eluent B

Isolation

[0442] In total, 1.87 g of the compound of Formula (I) (partial HCl salt) was isolated out of 60 mL of product pool, which calculates to 13.1 g of the compound of Formula (I) out of the entire 420 mL of product pool. From lyophilization of the mother liquor 0.17 g of residue was obtained.

[0443] 420 mL of product pool had been obtained after oxidation and preparative HPLC purification. By a test lyophilization the product concentration of this solution was determined as approx. 29 g/L, which corresponds to a theoretical yield of approx. 12.2 g.

[0444] From the overall pool volume, 120 mL were transferred to a round-bottom flask, and the initial pH of 7.01 was adjusted with 4.7 mL of 1 M HCl aq. to pH 2.98. Acetonitrile was evaporated from the product solution at 40 °C *in vacuo*, until water started to evaporate. After evaporation, 84 mL of aqueous product solution were remaining (pH 2.75), of which 42 mL were transferred to a reactor connected to a heating/cooling system and applied for the subsequent isolation.

[0445] The pH of the solution was then adjusted to pH 3.75 by addition of 1.1 mL of 0.5 M NH_4HCO_3 within 60 min. To the clear yellow solution 1% (w/w) compound of Formula (I) was added as seeding material and the formed thin suspension was stirred for 60 min at 25 °C. The pH of the suspension was then adjusted to pH 4.50 by addition of 2.6 mL of 0.5 M NH_4HCO_3 within 120 min. After stirring the suspension for 30 min at 25 °C the pH had dropped to pH 4.35. After stirring for 16 h at 25 °C a thick suspension was present, which was filtered (1 min filtration time) over a glass nutsche filter (G4) and washed without stirring with 1.74 mL of water (1 vol. eq.; 1 min filtration time). The washed filter cake was dried *in vacuo* at 40 °C for 16 h in a vacuum oven. The dried product was finally unloaded from the filter.

[0446] In total, 1.87 g of compound of Formula (I) (partial HCl salt) were isolated out of 60 mL of product pool, which calculates to 13.1 g compound of Formula (I) out of the entire 420 mL of product pool. For the isolated material a purity (HPLC) of 99.5%, a chloride content (titration) of 1.6%, and a water content (KF) of 3.2% was determined. The XRPD measurement confirmed the form of the partial HCl obtained was the same as that of Example 1.

Example 3: Alternative Synthetic Procedure for a Crystalline Hydrochloride Form of a Peptide of SEQ ID NO: 1

SPPS

[0447] 18.9 kg Rink amide AM resin (substitution: 0.95 mmol/g) were loaded into a 1000 L SPPS reactor and the SPPS was performed. Each SPPS cycle consists of Fmoc cleavage, coupling with the respective building block and obligatory capping. For Fmoc cleavage the resin was treated with 20% piperidine in DMF (10 ml/g resin each) for 5 ± 2 min and 10 ± 2 min at 25 °C. Couplings were performed using the building blocks, coupling reagents and conditions depicted in **Table 5**, with DMF as solvent (10 ml/g resin). For capping the resin was treated with acidic anhydride and pyridine in DMF (volumetric ratio DMF / Ac_2O /pyridine 50:1:1; DMF:

10 ml/g resin) for 20 min. Diisopropyl carbonate (DIC) was added in two portions, with the second portion was added after about 20 to 30 minutes after the first portion.

Table 5:

Cycle	Building block	Equivalents building block	Equivalents Oxyma	Equivalents DIC	Coupling duration	Coupling temp.
1	Fmoc-Sar-OH	2.00	3.10	2.60 + 1.30	3 h	25 °C
2	Fmoc-3-Pal-OH	1.50	2.33	1.95 + 0.975	7 h	25 °C
3	Fmoc-Asn(Trt)-OH	2.00	3.10	2.60 + 1.30	2 h	25 °C
4	Fmoc-Glu(OtBu)-OH · H ₂ O	2.00	3.10	2.60 + 1.30	14 h	25 °C
5	Fmoc-THP-OH	1.50	2.33	1.95 + 0.975	17 h	25 °C
6	Fmoc-2-Nal-OH	1.50	2.33	1.95 + 0.975	28 h	25 °C
7	Fmoc-Tyr(Boc-2-aminoethyl)-OH	1.50	2.33	1.95 + 0.975	6 h	25 °C
8	Fmoc-Pen(Trt)-OH	2.00	3.10	2.60 + 1.30	4 h	25 °C
9	Fmoc-Lys(Ac)-OH	2.00	3.10	2.60 + 1.30	2 h	25 °C
10	Fmoc-7-Me-Trp-OH	1.80	2.79	2.34 + 1.17	7 h	25 °C
11	Fmoc-Thr(tBu)-OH	2.00	3.10	2.60 + 1.30	2 h	25 °C
12	Fmoc-Asn(Trt)-OH	2.00	3.10	2.60 + 1.30	12 h	25 °C
13	Fmoc-Pen(Trt)-OH	2.00	3.10	2.60 + 1.30	4 h	25 °C

[0448] Final acetylation of the peptide resin was performed with acidic anhydride and pyridine in DMF (volumetric ratio DMF / Ac₂O/pyridine 10:1:1; DMF: 10 ml/g resin) for 20 min. After drying at 25 – 35 °C 72.8 kg linear peptide-Rink amide AM resin were obtained.

TFA cleavage

[0449] [In a jacketed reactor 100 g of PN21235-Rink amide AM resin (# 1000037885; 147841/1) were added at 18 °C to 700 mL of the cleavage cocktail, consisting of 630 mL TFA, 35 mL TIS, 17.5 mL EDT, and 17.5 mL water. The temperature increased to 30 °C upon addition of the resin, and the mixture was stirred for further 35 min at 30 °C. The mixture was cooled to 20 °C, and the resin was filtered off and washed two times with 100 mL TFA each. The filtrates were combined and cooled to -15 °C. For precipitation 4.0 L diisopropyl ether were added within 20 min maintaining the temperature of the solution / suspension at 7 °C. After complete addition of diisopropyl ether, the temperature was increased to 22 °C and the suspension stirred for 2.5 h.

[0450] The suspension was then transferred to a filter dryer, and the precipitated crude product was filtered off at ambient temperature. The filter cake was subsequently washed three times with 300 mL of diisopropyl ether each and dried *in vacuo* at 30 °C over night to yield 52.87 g of linear peptide as the TFA salt.

Oxidation and purification by preparative HPLC

[0451] 28 g of linear peptide as the TFA salt was dissolved in 280 mL 30% AcOH in water at ambient temperature. 3.71 g iodine and 7.17 g potassium iodide were dissolved in 280 mL water. Both the peptide and the iodine/iodide-solution were added in parallel to a vigorously stirred mixture of 2.2 L 30% AcOH in water at ambient temperature within 60 min. After complete addition of both solutions, a brown oxidation mixture was obtained. After stirring for 30 min at ambient temperature, IPC indicated nearly full conversion of starting material. 3.5 g Vitamin C were added 1.5 h after complete addition of the peptide and iodine solutions. The then obtained yellow solution was stirred for 10 min. The oxidation mixture was filtrated over a fritted glass funnel before applying to the prep. RP-HPLC column. The chromatographic conditions were the same as used in Example 2. All fractions were adjusted with 18% HCl in water to pH 7. The fractions collected during prep. RP-HPLC were analyzed by UHPLC. Fractions containing > 98% product were pooled for subsequent isolation.

Isolation

[0452] 420 mL of product pool had been obtained after oxidation and preparative HPLC purification. By a test lyophilization the product concentration of this solution was determined as approx. 29 g/L, which corresponds to a theoretical yield of approx. 12.2 g.

[0453] From the overall pool volume, 120 mL were transferred to a round-bottom flask, and the initial pH of 7.51 was adjusted with 4.5 mL of 1 M HCl aq. to pH 3.00. Acetonitrile was evaporated from the product solution at 40 °C *in vacuo*, until water started to evaporate. After evaporation, 80 mL of aqueous product solution were remaining (pH 2.54), of which 40 mL were transferred to a reactor connected to a heating/cooling system and applied for the subsequent isolation.

[0454] The pH of the solution was then adjusted to pH 3.75 by addition of 1.0 mL of 0.5 M NH_4HCO_3 within 65 min. To the clear yellow solution 1% (w/w) the compound of Formula (I) was added as seeding material and the formed thin suspension was stirred for 60 min at 25 °C. The pH of the suspension was then adjusted to pH 4.50 by addition of 2.9 mL of 0.5 M NH_4HCO_3 within 125 min. After stirring the suspension for 30 min at 25 °C the pH had dropped to pH 4.12. The pH was then re-adjusted to 4.50 by addition of 0.2 mL of 0.5 M NH_4HCO_3 . After stirring for 16 h at 25 °C a thick suspension was present, which was filtered (1 min filtration time) over a glass nutsche filter (G4) and washed without stirring with 1.59 mL of

water (1 vol. eq.; 1 min filtration time). The washed filter cake was dried *in vacuo* at 25 °C for 16 h in a vacuum oven. The dried product was finally unloaded from the filter.

[0455] In total, 1.77 g of the compound of Formula (I) (partial HCl salt) was isolated out of 60 mL of product pool, which calculates to 12.4 g of the compound of Formula (I) out of the entire 420 mL of product pool. For the isolated material a purity (HPLC) of 99.4%, a chloride content (titration) of 1.6%, a water content (KF) of 3.6%.

[0456] An X-ray powder diffraction (XRPD) pattern of the partial hydrochloride salt of the compound of Formula (I) confirmed its crystallinity (FIG. 2). The following two theta peaks were observed: 4.2920, 6.9201, 7.6600, 8.5693, 9.2667, 9.9817, 10.7256, 11.5429, 11.9937, 13.0633, 13.3317, 13.9650, 14.7879, 15.8430, 17.1481, 17.6468, 18.1402, 18.6158, 19.3291, 20.4899, 20.7090, or 21.7813 +/- 0.2 degrees two theta.

Example 4. Synthetic Procedure for Seeds of a Hydrochloride Salt of a Peptide of SEQ ID

NO: 1

[0457] Seeds of the hydrochloride salt of the compound of Formula (I) were prepared using an EasyMax 402 setup (100 mL scale). 3 g of HCl salt were dissolved in 21 mL MeOH and 9 mL water at 40 °C. 30 mL of H₂O were dosed into the reactor over 10 h. After 9 h of isotherm, the reactor was slowly cooled to 5 °C at a rate of 0.05 °C/min. After 2 h of isotherm, the reactor was heated to 40 °C at a rate of 1 °C/min, and after 1 h of isotherm at 40 °C, the reactor was cooled to 5 °C. The obtained filtrate was washed twice with 3 mL water, twice with 3 mL of isopropyl alcohol, and then dried atmospherically.

Example 5. Synthetic Procedure for a Crystalline Hydrochloride Salt of a Peptide of SEQ

ID NO: 1

[0458] Crystalline hydrochloride salt of the compound of Formula (I) (30 g) prepared according to Example 3 were dissolved in 120 mL of methanol and 51.4 mL of water. The dissolution was carried out in an EasyMax 402, under stirring at 40 °C. 57.1 mL of sodium chloride 1 M were dosed to the EasyMax reactor at over 1 h. The solution was then seeded with 300 mg of seeds of the hydrochloride salt of the compound of Formula (I) prepared according to Example 4. The slurry was then aged for 8 h under stirring at 40 °C. The slurry was cooled to 5 °C at a cooling rate of 0.1K/min. An extra 114.31 mL of sodium chloride 1 M were dosed to the EasyMax reactor over 4 h and the slurry was aged for extra 5 h. The solid was isolated by vacuum filtration and washed twice with 30 mL of water and twice with 30 mL of isopropanol. The solid was dried atmospherically.

[0459] The isolated solid of the crystalline hydrochloride form of the compound of Formula (I) had a purity (UPLC) of 99.3 area% and a water content (KF) of 6.33 w/w%. The chloride content of the isolated crystalline hydrochloride form of the compound of Formula (I) was assayed by ion chromatography and found to be 0.64 molar equivalents to the compound of Formula (I). An XRPD pattern of the crystalline hydrochloride form of the compound of Formula (I) confirmed its crystallinity (FIG. 3). The following two theta peaks were observed: 3.8, 4.2, 6.9, 7.6, 8.5, 9.3, 9.4, 10.0, 10.8, 11.6, 12.0, 12.2, 12.8, 13.1, 13.3, 13.8, 13.9, 14.2, 14.4, 14.7, 15.3, 15.7, 16.2, 16.4, 17.2, 17.6, 18.2, 18.7, 19.2, 19.6, 19.9, 20.5, and 20.8 degrees two theta +/- 0.2 degrees two theta.

[0460] A thermogravimetric analysis (TGA) of the isolated crystalline hydrochloride form of the compound of Formula (I) shows a 5.6% weight loss when heated to about 160°C, which is attributed to loss of solvent, mainly water (FIG. 4). The first endothermic event in the differential scanning calorimetry (DSC) profile of the isolated crystalline hydrochloride form of the compound of Formula (I) showing a maximum at 81.4 °C corresponds to the loss of solvent from the crystalline lattice, while the later event after 225 °C is attributed to decomposition of the solid (FIG. 5). A dynamic vapor sorption curve (DVS) of the isolated crystalline hydrochloride of the compound of Formula (I) showed a water intake of about 8.7% at 80% RH, indicating a hygroscopic material. (FIG. 6).

Example 6. Synthetic Procedure for Seeds of an Acetate Salt of a Peptide of SEQ ID NO: 1

[0461] Crystalline free base of the compound of Formula (I) (900mg) prepared according to Example 7 (900 mg) was dissolved in 4 mL of water. 1 mL of concentrated acetic acid was added to obtain a pH of 3.5. Then, 5 mL of ammonium acetate 1.6 M were dosed at 0.002 ml/min. After 2 days, the obtained slurry was filtered and the resulting solid was washed with 4 mL of water.

Example 7. Synthetic Procedure for a Crystalline Acetate Salt of a Peptide of SEQ ID NO: 1

[0462] Crystalline hydrochloride salt of the compound of Formula (I) (30 g) prepared according to Example 3 was dissolved in 120 mL of water and 30 mL of acetic acid concentrated. The dissolution was carried out in an EasyMax 402, under stirring at 25 °C. 150 mL of an ammonium acetate aqueous solution (2.4 M) were dosed to the EasyMax reactor over 2 h. The solution was then seeded with seeds of the acetate salt of the compound of Formula (I), prepared according to Example 6. The slurry was then aged for 12 h under stirring at 25 °C. An extra 150 mL of ammonium acetate aqueous solution (2.4 M) were dosed to the EasyMax

reactor over 4 h. The slurry was then aged for further 10 h under stirring at 25 °C. The solid was isolated by vacuum filtration and washed twice with 30 mL of water and twice with 30 mL of 2-propanol.

[0463] The isolated solid of the crystalline acetate form of the compound of Formula (I) had a purity (UPLC) of 99.3 area% and a water content (KF) of 6.39 w/w%. The acetate content of the isolated solid of the crystalline acetate form of the compound of Formula (I) was assayed by ion chromatography and found to be 0.61 molar equivalents to the compound of Formula (I). An XRPD pattern of the crystalline acetate form of the compound of Formula (I) confirmed its crystallinity (FIG. 7). The following two theta peaks were observed: 3.8, 4.3, 6.8, 7.0, 7.6, 7.7, 8.5, 8.6, 9.2, 9.9, 10.1, 10.4, 10.6, 10.7, 11.2, 11.4, 11.8, 12.1, 12.8, 13.1, 13.8, 14.3, 14.5, 15.2, 15.5, 15.9, 17.2, 17.4, 18.0, 18.4, 19.1, and 19.4 degrees two theta +/- 0.2 degrees two theta.

[0464] A TGA of the isolated crystalline acetate form of the compound of Formula (I) shows a 5.8% weight loss when heated to about 150 °C (FIG. 8). The first endothermic event in the DSC profile of the isolated crystalline acetate form of the compound of Formula (I) showing a maximum at 80.7 °C corresponds to the loss of solvent from the crystalline lattice, while the later event at 240.7 (228.2 °C (onset)) is attributed to melting/decomposition of the solid (FIG. 9). A dynamic vapor sorption curve (DVS) of the isolated crystalline acetate of the compound of Formula (I) indicated a hygroscopic material. (FIG. 10)

Example 8. Synthetic Procedure for a Crystalline Free Base of a Peptide of SEQ ID NO: 1

[0465] 150 mL of a phosphate buffer pH 8 at 1 M concentration were added to an EasyMax 402 reactor under stirring at 25 °C. In a separate reactor, crystalline hydrochloride salt of the compound of Formula (I) (30g) prepared according to Example 3 was dissolved under stirring at 25 °C in 150 mL of water/HCl solution (1.5 molar equivalents of HCl to the compound of Formula (I)). The solution was then dosed to the EasyMax 402 containing the buffer solution over 50 h. The solid was isolated by vacuum filtration and placed in a clean EasyMax 402 reactor. 400 mL of water were added to the reactor and the slurry was stirred at 25 °C for 24 h. The solid was isolated by vacuum filtration and washed twice with 30 mL of water. The solid was dried atmospherically.

[0466] The isolated solid of the crystalline free base of the compound of Formula (I) had a purity (UPLC) of 97.9% and a water content (KF) of 12.68 w/w%. The ionic content of the isolated crystalline solid was assayed by ion chromatography and found to be <0.02 w/w% chloride and <0.05 w/w% sodium. An XRPD pattern of that the crystalline free base of the compound of Formula (I) confirmed its crystallinity (FIG. 11). The following two theta peaks

were observed: 3.3, 5.8, 6.5, 6.8, 7.7, 8.3, 9.1, 9.6, 10.2, 11.1, 12.4, 12.9, 13.3, 14.0, 14.8, 15.4, 16.0, 17.3, 18.0, 18.5, 18.9, 19.4, 20.0, and 20.5 degrees two theta +/- 0.2 degrees two theta.

[0467] A TGA of the isolated crystalline free base of the compound of Formula (I) shows two step weight loss thermogram with the first one showing a 3.7% weight loss when heated to about 70°C and the second one showing a 2.7 % additional weight loss when heated to about to about 170°C, which is attributed to loss of solvent, mainly water (FIG. 12). The first and second endothermic events in the DSC profile of the isolated crystalline free base of the compound of Formula (I) showing a maximum at 71.0°C and 130.2°C respectively correspond to the loss of solvent from the crystalline lattice, while the later event at 180.5°C (onset) is attributed to melting/decomposition of the solid (FIG. 13). A dynamic vapor sorption curve (DVS) of the isolated crystalline free base of the compound of Formula (I) indicated a hygroscopic material (FIG. 14).

Example 9. Synthetic Procedure for a Crystalline Fumarate Salt of a Peptide of SEQ ID

NO: 1

[0468] Crystalline free base of the compound of Formula (I) (900 mg) prepared according to Example 8 was dissolved in MeOH (4.5 mL) to give a clear solution. This stock solution was partitioned into HPLC vials (150 µl per vial). 2 Mol eq. of a fumarate counterion stock solution was added to the vials at 25 °C. The samples were cooled from 25 °C to 5 °C at 1 °C/min. As solutions were obtained after cooling to 5 °C, 1 vol equivalent of tert-butyl methyl ether (TBME) (anti-solvent) is added. The samples were then stirred isothermally at 5 °C for ca. 16 h to obtain an amorphous suspension. The obtained suspensions were placed into a maturation chamber (RT – 50 °C, 4 h cycles) to encourage crystallisation. After 5 days, samples were removed, and suspensions analyzed.

[0469] The isolated solid of the crystalline fumarate salt of the compound of Formula (I) had a purity (UPLC) of 86.4 area%. An XRPD pattern of that the crystalline fumarate of the compound of Formula (I) confirmed its crystallinity (FIG. 15). The following two theta peaks were observed: 3.8, 4.2, 6.9, 7.6, 8.3, 8.4, 8.6, 9.2, 10.0, 10.7, 11.5, 12.0, 12.8, 13.3, 14.0, 14.7, 15.7, 17.0, 17.6, 19.1, 20.4, 21.7, 23.1, 24.2, 25.4, and 27.1 degrees two theta +/- 0.2 degrees two theta. A TGA of the isolated crystalline fumarate salt of the compound of Formula (I) shows a 4.4% weight loss when heated to about 110°C, which is attributed to loss of solvent, mainly water (FIG. 16). The first endothermic event in the DSC profile of the isolated crystalline fumarate salt of the compound of Formula (I) showing a maximum at 66.9°C corresponds to the loss of solvent from the crystalline lattice, while at higher temperature the solid decomposes (FIG. 17).

Example 10. Synthetic Procedure for a Crystalline Glutarate Salt of a Peptide of SEQ ID**NO: 1**

[0470] Crystalline free base of the compound of Formula (I) (200 mg) prepared according to Example 8 and 4.4 mol equivalents of glutaric acid were suspended in 1 mL of water, and stirred at 40°C for ca. 24 h until a clear solution was observed. 15 mL of anti-solvent (acetonitrile) was added to the solution, and precipitation of white solids was observed. The solids were isolated by Buchner filtration and air-dried at ambient prior to characterization.

[0471] The glutarate content of the isolated solid of the crystalline glutarate salt of the compound of Formula (I) was assayed by CAD analysis and found to be 0.5 molar equivalents to the compound of Formula (I). An XRPD pattern of the crystalline glutarate salt of the compound of Formula (I) confirmed its crystallinity (FIG. 18). The following two theta peaks were observed: 3.8, 4.3, 6.9, 7.6, 8.5, 9.2, 9.9, 10.8, 11.9, 13.0, 13.9, 15.7, 17.0, 17.6, 18.6, 19.2, 20.3, 20.7, 21.4, 23.3, and 25.3 degrees two theta +/- 0.2 degrees two theta.

[0472] A simultaneous thermal analysis (SDT) was used to obtain TGA and DSC data. The SDT thermogram of the isolated crystalline glutarate salt of the compound of Formula (I) shows a 6.4% weight loss when heated to about 125°C, which is attributed to loss of solvent, mainly water (FIG. 19). The first endothermic event in the SDT thermogram of the isolated crystalline glutarate salt of the compound of Formula (I) is wide and relates to the loss of solvent and continues until a maximum at 224°C is reached, corresponding to decomposition of the solid (FIG. 19). A dynamic vapor sorption curve (DVS) of the isolated crystalline glutarate salt of the compound of Formula (I) indicated a hygroscopic material (FIG. 20).

Example 11. Synthetic Procedure for a Crystalline Glycolate Salt of a Peptide of SEQ ID**NO: 1**

[0473] Crystalline free base of the compound of Formula (I) (200 mg) prepared according to Example 8 and 4.4 mol equivalents of glycolic acid were suspended in 1 mL of water and stirred at 40°C for ca. 24 h until a clear solution was observed. 15 mL of anti-solvent (acetonitrile) was added to the solution, and precipitation of white solids was observed. The solids were isolated by Buchner filtration and air-dried at ambient prior to characterization.

[0474] The glycolate content of the isolated solid of the crystalline glycolate salt of the compound of Formula (I) was assayed by CAD analysis and found to be 0.48 molar equivalents to the compound of Formula (I). An XRPD pattern of the crystalline glycolate salt of the compound of Formula (I) confirmed the crystallinity (FIG. 21). The following two theta peaks

were observed: 3.8, 4.3, 6.9, 7.7, 8.5, 9.2, 10.0, 10.7, 11.5, 12.0, 13.1, 14.0, 15.8, 17.1, 17.7, 19.2, 20.2, 20.8, 21.6, 25.4, and 29.5 degrees two theta +/- 0.2 degrees two theta.

[0475] A simultaneous thermal analysis (SDT) was used to obtain TGA and DSC data. The SDT thermogram of the isolated crystalline glycolate salt of the compound of Formula (I) shows a 5.1% weight loss when heated to about 100°C, which is attributed to loss of solvent, mainly water (FIG. 22). The first endothermic event in the SDT thermogram of the isolated crystalline glycolate salt of the compound of Formula (I) is wide and relates to the loss of solvent and continues until a maximum at 237°C is reached, corresponding to decomposition of the solid (FIG. 22). A dynamic vapor sorption curve (DVS) of the isolated crystalline glycolate form of the compound of Formula (I) indicated a hygroscopic material (FIG. 23).

Example 12. Synthetic Procedure for a Crystalline Mesylate Salt of a Peptide of SEQ ID

NO: 1

[0476] Crystalline free base of the compound of Formula (I) (100 mg) prepared according to Example 8 was added to a 20 mL scintillation vial. 3 mol equivalents of 1 M methanesulfonic acid with appropriate volume of water were added to the vial. The experiment was stirred at 25 °C for ca. 1 h until a clear solution was observed post-addition. Acetonitrile was added to the solution at 25 °C in 100 µL aliquots until maximum of 95 % v/v had been added. Stirring continued at 25 °C for ca. 72 h. The resulting slurry was vacuum filtered using What Grade 1 paper (ø 42.5 mm). The isolated solid was dried under reduced pressure at ambient (ca. 20 °C) for ca. 5 h.

[0477] The isolated solid of the crystalline mesylate salt of the compound of Formula (I) had a purity (UPLC) of 90.78 area%. The mesylate content of the isolated crystalline mesylate salt of the compound of Formula (I) solid was assayed by charged aerosol detected (CAD) analysis and found to be 1.8 molar equivalents to the compound of Formula (I). An XRPD pattern of the crystalline mesylate salt of the compound of Formula (I) confirmed the crystallinity (FIG. 24). The following two theta peaks were observed: 4.1, 6.8, 7.6, 9.2, 9.6, 11.3, 12.5, 13.7, 15.5, 16.6, 18.4, 19.8, 20.6, 22.8 and 27.8 degrees two theta +/- 0.2 degrees two theta.

[0478] A simultaneous thermal analysis (SDT) was used to obtain TGA and DSC data. The SDT thermogram of the isolated crystalline mesylate salt of the compound of Formula (I) shows a 5.4% weight loss when heated to about 80 °C, which is attributed to loss of solvent, mainly water (FIG. 25). The first endothermic event in the SDT thermogram of the isolated crystalline mesylate salt of the compound of Formula (I) is wide, relates to the loss of solvent and continues until a maximum at 242 °C is reached, corresponding to decomposition of the solid (FIG. 25).

Example 13. Synthetic Procedure for a Crystalline Sulfate Salt of a Peptide of SEQ ID NO:**1**

[0479] Crystalline free base of the compound of Formula (I) (100 mg) prepared according to Example 8 was added to a 20 mL scintillation vial. 3 mol equivalents of 1 M sulfuric acid with appropriate volume of water were added to the vial. The experiment was stirred at 25 °C for ca. 1 h until a clear solution was observed post-addition. Acetonitrile was added to the solution at 25 °C in 100 µL aliquots until maximum of 95 %v/v had been added. Stirring continued at 25 °C for ca. 72 h. The resulting slurry was vacuum filtered using What Grade 1 paper (ø 42.5 mm). The isolated solid was dried under reduced pressure at ambient (ca. 20 °C) for ca. 5 h.

[0480] The isolated solid of the crystalline sulfate salt of the compound of Formula (I) had a purity (HPLC) of 91.28 area%. The sulfate content of the isolated solid of the crystalline sulfate salt of the compound of Formula (I) was assayed by CAD analysis and found to be 1.6 molar equivalents to the compound of Formula (I). An XRPD pattern of the crystalline sulfate salt of the compound of Formula (I) confirmed the crystallinity (FIG. 26). The following two theta peaks were observed: 4.1, 6.8, 7.6, 9.2, 9.6, 10.3, 11.3, 12.5, 13.7, 16.8, 17.9, 18.4, 19.8, 20.7, 21.3, and 22.7 degrees two theta +/- 0.2 degrees two theta.

[0481] A simultaneous thermal analysis (SDT) was used to obtain TGA and DSC data. The SDT thermogram of the isolated crystalline sulfate salt of the compound of Formula (I) shows a 4.4% weight loss when heated to about 80 °C, which is attributed to loss of solvent, mainly water (FIG. 27). The first endothermic event in the SDT thermogram of the crystalline sulfate salt of the compound of Formula (I) is wide, relates to the loss of solvent and continues until a maximum at 255 °C is reached, corresponding to decomposition of the solid (FIG. 27).

Example 14. Synthetic Procedure for a Crystalline Citrate Salt of a Peptide of SEQ ID NO:**1**

[0482] Crystalline free base of the compound of Formula (I) (100 mg) prepared according to Example 8 was suspended in 0.2 mL of a 0.1 M citrate pH 5.5 buffer in a 2 mL glass vial. 3.3 mol equivalents of 1.2 M HCl was added to dissolve the solids at ca. 25°C. 2 mL of 2-propanol was added as anti-solvent in 100 µL aliquots, and precipitation of solids was observed. The resultant (thin) slurry was cooled to 5°C at 0.1 °C/min and aged at 5°C for ca. 18 h. The slurry was centrifuged (0.2 µm nylon filter) to isolate the solid.

[0483] The isolated solid of the crystalline citrate salt of the compound of Formula (I) had a purity (HPLC) of 99.59 area%. An XRPD pattern of the crystalline citrate salt of the compound of Formula (I) confirmed the crystallinity (FIG. 28). The following two theta peaks were observed: 3.8, 4.3, 6.9, 7.0, 7.6, 8.4, 9.3, 10.0, 10.8, 12.2, 13.1, 13.9, 14.1, 15.3, 15.9, 16.3, 17.0,

17.4, 17.9, 19.0, 19.5, 19.8, 20.5, 22.0, 23.1, 24.4, 24.8, 25.2, 26.5, 29.1, 30.5, 32.1, 33.1, and 33.5 degrees two theta +/- 0.2 degrees two theta.

Example 15. Synthetic Procedure for a Crystalline Bis-hydrochloride Salt of a Peptide of SEQ ID NO: 1

[0484] Crystalline hydrochloride salt of the compound of Formula (I) (12 g) prepared according to Example 3 was dissolved in 50.5 mL of water and 9.5 mL of hydrochloric acid 1 M. The dissolution was carried out in an EasyMax 102, under stirring at 20 °C. 60 mL of sodium chloride 0.6 M were dosed to the EasyMax reactor at 0.04 mL/min. The slurry was then aged for 2 h under stirring at 20 °C. The solid was isolated by vacuum filtration and washed twice with 3 mL of water. The solid was dried atmospherically.

[0485] The isolated solid had a purity of 99.7 area% measured by UPLC and a water content (KF) of 10.83 w/w%. The chloride content of the isolated crystalline solid of the bis-hydrochloride salt of the compound of Formula (I) was assayed by ion chromatography and found to be 1.97 molar equivalents to the compound of Formula (I). An XRPD pattern of the crystalline bis-hydrochloride salt of the compound of Formula (I) confirmed its crystallinity (FIG. 29). The following two theta peaks were observed: 3.4, 4.6, 6.1, 8.3, 8.7, 9.1, 9.4, 9.8, 10.1, 11.1, 11.4, 12.0, 12.4, 13.6, 15.1, 15.9, 16.1, 16.7, 17.8, 18.4, 18.7, 19.4, 19.9, and 20.8 degrees two theta +/- 0.2 degrees two theta.

[0486] A TGA of the isolated crystalline bis-hydrochloride salt of the compound of Formula (I) shows a 11.3 % weight loss when heated to about 190°C, which is attributed to loss of solvent, mainly water (FIG. 30). The first endothermic event in the DSC profile of the isolated crystalline bis-hydrochloride salt of the compound of Formula (I) showing a maximum at 79.5 °C corresponds to the loss of solvent from the crystalline lattice, while the later event at 235.3 °C (228.9°C (onset)) is attributed to melting/decomposition of the solid (FIG. 31). A dynamic vapor sorption curve (DVS) of the isolated crystalline bis-hydrochloride form of the compound of Formula (I) indicated a hygroscopic material (FIG. 32).

Example 16. Solubility of a Hydrochloride Salt of the Peptide of SEQ ID NO: 1

[0487] The hydrochloride salt of the compound of Formula (I) prepared in Example 2a was evaluated for solubility under various conditions. The results are shown in Table 6.

Table 6. Solubility of Hydrochloride Salt of the Peptide of SEQ ID NO: 1

Medium	HCl Salt of a Peptide of SEQ ID NO: 1 (mg/mL)
0.1 N HCl	130
0.01 N HCl	13

Medium	HCl Salt of a Peptide of SEQ ID NO: 1 (mg/mL)
Citrate buffer pH 2	53
Citrate buffer pH 5	0.70
phosphate buffer pH 7	0.031
Borate buffer pH 9	0.041
Phosphate buffer pH 12	6.0
0.1 N NaOH	42
Water	3.6

Example 17. Tablet Composition of a Hydrochloride Salt of the Peptide of SEQ ID NO: 1

Table 7. Summary of Tablet Compositions With & Without Absorption Enhancer

TC	Strength (mg)	Dosage form	AbE, (mg NaC10)	Core/coated tab wt (mg)	Disintegrant	Coating
1	50	FC	500	1400/1565.2	Crospovidone	3% QX Yellow + 8% Acryl-Eze Yellow
2	25	FC	500	1400/1565.2	Crospovidone	3% QX Yellow + 8% Acryl-Eze Yellow
3	10	FC	500	1400/1565.2	Crospovidone	3% QX Yellow + 8% Acryl-Eze Yellow
4	50	FC	300	1400/1565.2	Crospovidone	3% QX Yellow + 8% Acryl-Eze Yellow
5	25	FC	300	1400/1565.2	Crospovidone	3% QX Yellow + 8% Acryl-Eze Yellow
6	10	FC	300	1400/1565.2	Crospovidone	3% QX Yellow + 8% Acryl-Eze Yellow
7	25	FC	500	1400/1623.7	Croscarmellose Na	3% QX Pink + 11.8% Acryl-Eze White
8	25	FC	300	1400/1623.7	Croscarmellose Na	3% QX Pink + 11.8% Acryl-Eze White
9	25	FC	100	1400/1623.7	Croscarmellose Na	3% QX Pink + 11.8% Acryl-Eze White
10	100	FC	Non-AbE	1000/1030	Crospovidone	3% QX Yellow (cosmetic)
11	25	FC	Non-AbE	1000/1030	Crospovidone	3% QX Yellow (cosmetic)
12	10	FC	Non-AbE	400/412	Crospovidone	3% QX Yellow (cosmetic)
13	5	FC	Non-AbE	200/206	Crospovidone	3% QX Yellow (cosmetic)

Abbreviation: Tablet Composition (TC), Film-coated (FC), Absorption Enhancer (AbE), Sodium caprate (NaC10)

[0488] Tablet Compositions 1-3

Film-Coated Tablets with compositions of Tablet Compositions 1-3, which included 50 mg, 25 mg, and 10 mg (equivalent to free base), respectively, of the compound of Formula (I) hydrochloride (HCl) salt and 500 mg sodium caprate as an absorption enhancer, were prepared by following unit operations: milling & sieving, dry granulation, blending & compression, and film coating, described in Steps 1-4 below. The in-process control data of the core and coated tablets in representative stability or clinical batches were collected, as summarized in the tables below.

Step 1: Milling & Sieving

[0489] Teflon (PTFE) solid blocks were used to manually sieve the compound of Formula (I) through a 600 µm stainless-steel sieve. The collected powder was then sieved via the same procedure through stainless-steel sieves at 400 µm and 150 µm mesh size, sequentially.

Step 2: Dry Granulation

[0490] The resulting powder from Step 1 and all intragranular excipients, including functional excipients, comprising sodium caprate, microcrystalline cellulose, sorbitol, crospovidone and anhydrous colloidal silica listed in Composition of tablet compositions 1-3 were screened through a 1000 µm stainless-steel sieve and mixed for 10 minutes in a high-speed blender (such as Turbula). The blended dry powder was compacted into tablet-like solids through single-stage compression on a single-punch tablet press (such as Styl'One Evolution). Teflon (PTFE) solid blocks were used to manually break the resulting compact (i.e., "slugs") into granules which were screened through a 1000 µm stainless-steel sieve.

Step 3: Blending and Tableting

[0491] The resulting granulated powder from Step 2 and all extragranular excipients comprising silicified microcrystalline cellulose, crospovidone and anhydrous colloidal silica as listed in Composition of Ex 1-3 were screened through a 1000 µm stainless-steel sieve and mixed for 10 minutes in a high-speed blender (such as Turbula). To this mixture, extragranular magnesium stearate was screened through the same mesh, added to the above mixture, and further mixed for 5 minutes under the same conditions. The final blend was compressed into tablets through a two-stage (i.e., pre- and main-) compression cycle on a single-punch tablet press (such as Styl'One Evolution). The resulting core tablets were collected into appropriate containers (e.g., HDPE bottles) and packages (e.g., sealed in aluminum laminated bags) which were stored until the next step.

Step 4: Film Coating

Subcoat:

[0492] The coating suspension at approximately 30 wt% solid concentration was prepared by adding the coating powder of the subcoat (i.e., Opadry® QX 321A220063 Yellow) into the vortex of vigorously agitated purified water, which was stirred by an overhead stirrer. The suspension was further stirred for a sufficient time (e.g., at least 45 min) to achieve a homogenous dispersion without foam and remained stirred during the coating process.

[0493] The core tablets manufactured from Steps 1-3 were transferred to the pan of a semi-perforated tablet coating system such as Lödige. After warming up the uncoated tablets in the slowly rotating pre-warmed pan (e.g., at least 3 minutes at drum speed of 5 rpm), a pre-determined amount of coating suspension that was calculated to achieve the target weight gain

was then sprayed to the perforated coating pan. In a typical coating run of the subcoat using the 4L pan of Lödige, the process parameters were commonly optimized in following target values and ranges [min-max] – tablet bed temperature (indicated by the exhaust air temperature) at 40 °C [35-45 °C], inlet air flow rate and pressure at 105 [80-120] m³/hr and an atomizing air and pressure of 0.9 [0.6-1.2] bar, a drum rotation speed at 23 [10-30] rpm, and a feeding rate of coating suspension at 6.5-7 g/min [5-8] g/min. At the end of spraying, the coating pan continued to rotate at a reduced drum speed (e.g., 5 rpm) at approximately 45 °C to remove residual water of the coated tablets. The resulting subcoated tablets were collected from the pan and cooled to room temperature under ambient conditions.

Functional coat:

[0494] The coating suspension at approximately 20 wt% solid concentration was prepared by subsequently adding triethyl citrate (plasticizer) and Acryl-Eze® 93A220037 Yellow (coating powder), sequentially in this order, into the vortex of vigorously agitated purified water, which was stirred by an overhead stirrer. The suspension was further stirred for a sufficient time (e.g., at least 5 minutes after adding the plasticizer, at least 45 min after adding the coating powder) to achieve a homogenous dispersion free of agglomeration and free of foam. Prior to the coating, the coating suspension was passed through a 250 µm stainless-steel sieve and remained stirred during spraying.

[0495] The subcoated tablets were coated with the functional coat using the above coating and drying processes with modified parameters. In a typical semi-perforated coating run of the functional coat using the 4L pan of Lödige, the process parameters were commonly optimized in following target values and ranges [min-max] – the exhaust air temperature at 32 °C [28-38 °C], inlet air flow rate of 105 [80-120] m³/hr and an atomizing and pattern air pressure of 0.9 [0.6-1.2] bar, a drum rotation speed at 23 [10-30] rpm, and a feeding rate of coating suspension at 6.5 [5-8] g/min. At the end of spraying, the coating pan continued to rotate at a reduced drum speed (e.g., 5 rpm) at approximately 40-45 °C to remove residual water of the coated tablets. The coated tablets were removed from the coating pan and cooled to room temperature under ambient conditions. The film-coated tablets were finally collected into appropriate containers (e.g., HDPE bottles) and packages (e.g., sealed in aluminum laminated bags) and stored under appropriate conditions.

Table 8. Tablet Composition 1

Component	Function	Tablet Composition 1	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
<i>Intragranular Phase</i>			
Peptide of SEQ ID NO: 1 [A]	Active ingredient	50.0	3.58
Sodium caprate	Absorption enhancer	500.0	35.71
Microcrystalline cellulose [B]	Filler	55.0	3.93
Sorbitol	Filler	150.0	10.71
Crospovidone	Disintegrant	70.0	5.00
Anhydrous colloidal silica	Glidant	7.0	0.50
<i>Extragranular Phase</i>			
Silicified microcrystalline cellulose	Filler	487.5	34.82
Crospovidone	Disintegrant	70.0	5.00
Anhydrous colloidal silica	Glidant	7.0	0.50
Magnesium stearate	Lubricant	3.5	0.25
Core Tablet Weight:		1400.0	100.00
Coated Tablet			
<i>Subcoat</i>			
Coating powder Opadry® QX 321A220063 Yellow [C]	Subcoat coating layer	42.00	3.00
Purified water [D]	Process aid	q.s.	N/A
<i>Functional Coat</i>			
Coating powder Acryl-Eze® 93A220037 Yellow [E]	Functional coating layer	112.00	8.00
Triethyl citrate	Plasticizer	11.20	0.80
Purified water [D]	Process aid	q.s.	N/A
Coated Tablet Weight:		1565.2	111.80

[A] The dose (mg) is equivalent to the compound of Formula (I) free base and corrected for assay of the compound of Formula (I) (HCl salt) (assay= peptide content x purity by U/HPLC).

[B] The weight of this excipient was corrected based on the assay value of the API to maintain a fixed tablet weight.

[C] A typical coating suspension for subcoat contains approximately 30% wt% solids.

[D] The solvent of coating suspensions is removed during the coating processing.

[E] A typical coating suspension for the functional coat contains approximately 20% wt% solids without the plasticizer.

Table 9. Tablet Composition 2

Component	Function	Tablet Composition 2	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
<i>Intragranular Phase</i>			
Peptide of SEQ ID NO: 1 [A]	Active ingredient	25.0	1.79
Sodium caprate	Absorption enhancer	500.0	35.71
Microcrystalline cellulose [B]	Filler	55.0	3.93
Sorbitol	Filler	150.0	10.71
Crospovidone	Disintegrant	70.0	5.00
Anhydrous colloidal silica	Glidant	7.0	0.50
<i>Extragranular Phase</i>			
Silicified microcrystalline cellulose	Filler	512.5	36.61
Crospovidone	Disintegrant	70.0	5.00
Anhydrous colloidal silica	Glidant	7.0	0.50
Magnesium stearate	Lubricant	3.5	0.25
Core Tablet Weight:		1400.0	100.00
Coated Tablet			
<i>Subcoat</i>			
Coating powder Opadry® QX 321A220063 Yellow [C]	Subcoat coating layer	42.00	3.00
Purified water [D]	Process aid	q.s.	N/A
<i>Functional Coat</i>			
Coating powder Acryl-Eze® 93A220037 Yellow [E]	Functional coating layer	112.00	8.00
Triethyl citrate	Plasticizer	11.20	0.80
Purified water [D]	Process aid	q.s.	N/A
Coated Tablet Weight:		1565.2	111.80

[A] The dose (mg) is equivalent to the compound of Formula (I) free base and corrected for assay of the compound of Formula (I) (HCl salt) (assay= peptide content x purity by U/HPLC).

[B] The weight of this excipient was corrected based on the assay value of the API to maintain a fixed tablet weight.

[C] A typical coating suspension for subcoat contains approximately 30% wt% solids.

[D] The solvent of coating suspensions is removed during the coating processing.

[E] A typical coating suspension for the functional coat contains approximately 20% wt% solids.

Table 10. Tablet Composition 3

Component	Function	Tablet Composition 3	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Intragranular Phase			
Peptide of SEQ ID NO: 1[A]	Active ingredient	10.0	0.72
Sodium caprate	Absorption enhancer	500.0	35.71
Microcrystalline cellulose [B]	Filler	55.0	3.93
Sorbitol	Filler	150.0	10.71
Crospovidone	Disintegrant	70.0	5.00
Anhydrous colloidal silica	Glidant	7.0	0.50
Extragranular Phase			
Silicified microcrystalline cellulose	Filler	527.5	37.68
Crospovidone	Disintegrant	70.0	5.00
Anhydrous colloidal silica	Glidant	7.0	0.50
Magnesium stearate	Lubricant	3.5	0.25
Core Tablet Weight:		1400.0	100.00
Coated Tablet			
Subcoat			
Coating powder Opadry® QX 321A220063 Yellow [C]	Subcoat coating layer	42.00	3.00
Purified water [D]	Process aid	q.s.	N/A
Functional Coat			
Coating powder Acryl-Eze® 93A220037 Yellow [E]	Functional coating layer	112.00	8.00
Triethyl citrate	Plasticizer	11.20	0.80
Purified water [D]	Process aid	q.s.	N/A
Coated Tablet Weight:		1565.2	111.80

[A] The dose (mg) is equivalent to the compound of Formula (I) free base and corrected for assay of the compound of Formula (I) (HCl salt) (assay= peptide content x purity by U/HPLC).

[B] The weight of this excipient was corrected based on the assay value of the API to maintain a fixed tablet weight.

[C] A typical coating suspension for subcoat contains approximately 30% wt% solids.

[D] The solvent of coating suspensions is removed during the coating processing.

[E] A typical coating suspension for the functional coat contains approximately 20% wt% solids.

[0496] Table 11 shows properties of Tablet Compositions 1-3.

Table 11. Properties of Blends/Core/Coated Tablets – Tablet Compositions 1-3

	TC 1	TC 2	TC 3
Core Tablet [A]			
Blend size (=No. tablet [wt])	2500 tab [3.5 kg]	1750 tab [2.45 kg]	2500 tab [3.5 kg]
Punch size (length/width, mm)	20.5 x 10.25 mm	20.5 x 10.25 mm	20.5 x 10.25 mm
Pre-/main-compression forces (kN)	1/20	1/20	1/20
Weight (mg), avg (n=sample)	1395.6 (n=15)	1405.8 (n=80)	1400 (n=15)
Hardness (N) avg (n=sample)	211 (n=15)	224.7 (n=40)	195.1 (n=15)
Thickness (mm) avg (n=sample)	8.24 (n=15)	8.10 (n=40)	8.20 (n=15)
Disintegration time (min:sec) avg (n=sample)	12:25 (n=18)	12:54 (n=48)	11:06 (n=12)
Friability (%), 20 tablets	0.09%	0.02%	0.14%
Yield (No. tablet)	2250	1412	2150
Coated Tablet [A]			
Batch size of core tabs (No tab. [wt])	1750 tab [2.45 kg]	1000 tab [1.4 kg]	2030 tab [2.48 kg]
Coating pan size	4L (Lödige)	2L (Lödige)	4L (Lödige)
Appearance of subcoat	Yellowish orange to yellowish brown oval film-coated tablets	Yellowish orange to yellowish brown oval film-coated tablets	Yellowish orange to yellowish brown oval film-coated tablets
Coating layer of subcoat (wt% of core tablets) [B]	Target 42.0 mg [3.0%]		
	33.6 mg [2.4%]	34 mg [2.4%]	35.7 mg [2.5%]
Appearance of functional coat	Yellowish orange to yellowish brown oval film-coated tablets	Yellowish orange to yellowish brown oval tablets	Yellowish orange to yellowish brown oval film-coated tablets
Coating layer of functional coat (wt% of core tablets) [B]	Target 123.2 mg [8.8%]		
	117.9 mg [8.4%]	122 mg [8.7%]	122.8 mg [8.8%]

[A] Representative compression and coating batches such as stability or clinical batches were selected.

[B] Coating levels (wt%) of each coating layer were calculated based on the measured weight gain and core tablet weight of 50 tablets in the batch.

Tablet Compositions 4-6

[0497] Film-Coated Tablets with compositions of Tablet Compositions 1-3, which included 50 mg, 25 mg, and 10 mg (equivalent to free base), respectively, of the compound of Formula (I) hydrochloride (HCl) salt and 300 mg sodium caprate as an absorption enhancer, were prepared by following unit operations: milling & sieving, dry granulation, blending & compression, and film coating, described in Steps 1-4 in Tablet Compositions 1-3. The in-process control data of the core and coated tablets in representative stability or clinical batches were collected, as summarized in the tables below.

Table 12. Tablet Composition 4

Component	Function	Tablet Composition 4	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Intragranular Phase			
Peptide of SEQ ID NO: 1 [A]	Active ingredient	50.0	3.58
Sodium caprate	Absorption enhancer	300.0	21.43
Microcrystalline cellulose [B]	Filler	55.0	3.93
Sorbitol	Filler	150.0	10.71
Crospovidone	Disintegrant	70.0	5.00
Anhydrous colloidal silica	Glidant	7.0	0.50
Extragranular Phase			
Silicified microcrystalline cellulose	Filler	687.5	49.10
Crospovidone	Disintegrant	70.0	5.00
Anhydrous colloidal silica	Glidant	7.0	0.50
Magnesium stearate	Lubricant	3.5	0.25
Core Tablet Weight:		1400.0	100.00
Coated Tablet			
Subcoat			
Coating powder Opadry® QX 321A220063 Yellow [C]	Subcoat coating layer	42.00	3.00
Purified water [D]	Process aid	q.s.	N/A
Functional Coat			
Coating powder Acryl-Eze® 93A220037 Yellow [E]	Functional coating layer	112.00	8.00
Triethyl citrate	Plasticizer	11.20	0.80
Purified water [D]	Process aid	q.s.	N/A
Coated Tablet Weight:		1565.2	111.80

[A] The dose (mg) is equivalent to the compound of Formula (I) free base and corrected for assay of the compound of Formula (I) (HCl salt) (assay= peptide content x purity by U/HPLC).

[B] The weight of this excipient was corrected based on the assay value of the API to maintain a fixed tablet weight.

[C] A typical coating suspension for subcoat contains approximately 30% wt% solids.

[D] The solvent of coating suspensions is removed during the coating processing.

[E] A typical coating suspension for the functional coat contains approximately 20% wt% solids.

Table 13. Tablet Composition 5

Component	Function	Tablet Composition 5	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Intragranular Phase			
Peptide of SEQ ID NO: 1 [A]	Active ingredient	25.0	1.79
Sodium caprate	Absorption enhancer	300.0	21.43
Microcrystalline cellulose [B]	Filler	55.0	3.93
Sorbitol	Filler	150.0	10.71
Crospovidone	Disintegrant	70.0	5.00
Anhydrous colloidal silica	Glidant	7.0	0.50
Extragranular Phase			
Silicified microcrystalline cellulose	Filler	712.5	50.89
Crospovidone	Disintegrant	70.0	5.00
Anhydrous colloidal silica	Glidant	7.0	0.50
Magnesium stearate	Lubricant	3.5	0.25
Core Tablet Weight:		1400.0	100.00
Coated Tablet			
Subcoat			
Coating powder Opadry® QX 321A220063 Yellow [C]	Subcoat coating layer	42.00	3.00
Purified water [D]	Process aid	q.s.	N/A
Functional Coat			
Coating powder Acryl-Eze® 93A220037 Yellow [E]	Functional coating layer	112.00	8.00
Triethyl citrate	Plasticizer	11.20	0.80
Purified water [D]	Process aid	q.s.	N/A
Coated Tablet Weight:		1565.2	111.80

[A] The dose (mg) is equivalent to the compound of Formula (I) free base and corrected for assay of the compound of Formula (I) (HCl salt) (assay= peptide content x purity by U/HPLC).

[B] The weight of this excipient was corrected based on the assay value of the API to maintain a fixed tablet weight.

[C] A typical coating suspension for subcoat contains approximately 30% wt% solids.

[D] The solvent of coating suspensions is removed during the coating processing.

[E] A typical coating suspension for the functional coat contains approximately 20% wt% solids.

Table 14. Tablet Composition 6

Component	Function	Tablet Composition 6	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Intragranular Phase			
Peptide of SEQ ID NO: 1 [A]	Active ingredient	10.0	0.72
Sodium caprate	Absorption enhancer	300.0	21.43
Microcrystalline cellulose [B]	Filler	55.0	3.93
Sorbitol	Filler	150.0	10.71
Crospovidone	Disintegrant	70.0	5.00
Anhydrous colloidal silica	Glidant	7.0	0.50
Extragranular Phase			
Silicified microcrystalline cellulose	Filler	727.5	51.96
Crospovidone	Disintegrant	70.0	5.00
Anhydrous colloidal silica	Glidant	7.0	0.50
Magnesium stearate	Lubricant	3.5	0.25
Core Tablet Weight:		1400.0	100.00
Coated Tablet			
Subcoat			
Coating powder Opadry® QX 321A220063 Yellow [C]	Subcoat coating layer	42.00	3.00
Purified water [D]	Process aid	q.s.	N/A
Functional Coat			
Coating powder Acryl-Eze® 93A220037 Yellow [E]	Functional coating layer	112.00	8.00
Triethyl citrate	Plasticizer	11.20	0.80
Purified water [D]	Process aid	q.s.	N/A
Coated Tablet Weight:		1565.2	111.80

[A] The dose (mg) is equivalent to the compound of Formula (I) free base and corrected for assay of the compound of Formula (I) (HCl salt) (assay= peptide content x purity by U/HPLC).

[B] The weight of this excipient was corrected based on the assay value of the API to maintain a fixed tablet weight.

[C] A typical coating suspension for subcoat contains approximately 30% wt% solids.

[D] The solvent of coating suspensions is removed during the coating processing.

[E] A typical coating suspension for the functional coat contains approximately 20% wt% solids.

[0498] Table 15 shows properties of Tablet Compositions 4-6.

Table 15: Properties of Blends/Core/Coated Tablets – Tablet Compositions 4-6

	TC 4	TC 5	TC 6
Core Tablet [A]			
Blend size (=No. tablet [wt])	2500 tab [3.5 kg]	1750 tab [2.45 kg]	1750 tab [2.45 kg]
Punch size (length/width, mm)	20.5 x 10.25 mm	20.5 x 10.25 mm	20.5 x 10.25 mm
Pre-/main-compression forces (kN)	1/20	1/20	1/20
Weight (mg), avg (n=sample)	1404.8 (n=15)	1403.6 (n=70)	1401.0 (n=70)
Hardness (N) avg (n=sample)	260.4 (n=15)	282.7 (n=35)	285.2 (n=35)
Thickness (mm) avg (n=sample)	7.92 (n=14)	8.03 (n=35)	7.97 (n=35)
Disintegration time (min:sec) avg (n=sample)	09:41 (n=17)	11:07 (n=42)	10:18 (n=42)
Friability (%), 20 tablets	-0.15%	0.05%	-0.1%
Yield (No. tablet)	2200	1455	1463
Coated Tablet			
Batch size of core tabs (No tab. [wt])	1750 tab [2.45 kg]	1000 tab [1.4 kg]	1000 tab [1.4 kg]
Coating pan size	4L (Lödige)	2L (Lödige)	2L (Lödige)
Appearance of subcoat	Yellowish orange to yellowish brown oval film-coated tablets	Yellowish orange to yellowish brown oval film-coated tablets	Yellowish orange to yellowish brown oval film-coated tablets
Coating layer of subcoat (wt% of core tablets) [B]	<i>Target 42.0 mg [3.0%]</i>		
	34.0 mg [2.4%]	42.0 mg [3.0%]	29.9 mg [2.1%]
Appearance of functional coat	Yellowish orange to yellowish brown oval film-coated tablets	Yellowish orange to yellowish brown oval film-coated tablets	Yellowish orange to yellowish brown oval film-coated tablets
Coating layer of functional coat (wt% of core tablets) [B]	<i>Target 123.2 mg [8.8%]</i>		
	124.0 mg [8.8%]	96 mg [6.8%]	101.0 mg [7.1%]

[A] Representative compression and coating batches such as stability or clinical batches were selected.

[B] Coating levels (wt%) of each coating layer were calculated based on the measured weight gain and core tablet weight of 50 tablets in the batch.

Tablet Compositions 7-9

[0499] Film-Coated Tablets with compositions of Examples 7-9 at the strength of 25 mg (equivalent to free base) of the compound of Formula (I) hydrochloride (HCl) salt, which included 500 mg, 300 mg and 100 mg sodium caprate, respectively, as an absorption enhancer, were prepared by following unit operations: milling & sieving, dry granulation, blending & compression, and film coating, described in Steps 1-4 in Tablet Compositions 1-3.

[0500] In contrast to Tablet Compositions 1-6, Tablet Compositions 7-9 included croscarmellose sodium as the disintegrant in the core tablets and Opadry® QX 321A240072-CN Pink and Acryl-Eze® 93A18597 White (11.8% wt:wt with core tablets) in the coating layers. The in-process control data of the core and coated tablets in these batches were collected, as summarized in the tables below.

Table 16. Tablet Composition 7

Component	Function	Tablet Composition 7	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
<i>Intragranular Phase</i>			
Peptide of SEQ ID NO: 1 [A]	Active ingredient	25.00	5.00
Sodium caprate	Absorption enhancer	500.00	35.71
Microcrystalline cellulose [B]	Filler	55.00 ^b	3.93
Sorbitol	Filler	150.00	10.71
Croscarmellose sodium	Disintegrant	70.00	5.00
Anhydrous colloidal silica	Glidant	7.00	0.50
<i>Extragranular Phase</i>			
Silicified microcrystalline cellulose	Filler	512.50	65.18
Croscarmellose sodium	Disintegrant	70.00	5.00
Anhydrous colloidal silica	Glidant	7.00	0.50
Magnesium stearate	Lubricant	3.50	0.25
Core Tablet Weight:		1400.00	100.00
Coated Tablet			
<i>Subcoat</i>			
Coating powder Opadry® QX 321A240072-CN Pink [C]	Subcoat coating layer	42.00	3.00
Purified water [D]	Process aid	q.s.	NA
<i>Functional Coat</i>			
Coating powder Acryl-Eze® 93A18597 White [E]	Functional coating layer	165.20	11.80
Triethyl citrate	Plasticizer	16.5	1.18
Purified water [D]	Process aid	q.s.	NA
Coated Tablet Weight:		1623.70	115.98

[A] The dose (mg) is equivalent to Peptide of SEQ ID NO: 1 free base and corrected for assay of the Peptide of SEQ ID NO: 1 (HCl salt) (assay= peptide content x purity by U/HPLC).

[B] The weight of this excipient was corrected based on the assay value of the API to maintain a fixed tablet weight.

[C] The coating suspension for subcoat contains was prepared at a concentration of 20% wt% solids.

[D] The solvent of coating suspensions is removed during the coating processing.

[E] A typical coating suspension for the functional coat contains approximately 20% wt% solids.

Table 17. Tablet Composition 8

Component	Function	Tablet Composition 8	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Intragranular Phase			
Peptide of SEQ ID NO: 1 [A]	Active ingredient	25.00	5.00
Sodium caprate	Absorption enhancer	300.00	21.43
Microcrystalline cellulose [B]	Filler	55.00 ^b	3.93
Sorbitol	Filler	150.00	10.71
Croscarmellose sodium	Disintegrant	70.00	5.00
Anhydrous colloidal silica	Glidant	7.00	0.50
Extragranular Phase			
Silicified microcrystalline cellulose	Filler	712.50	50.89
Croscarmellose sodium	Disintegrant	70.00	5.00
Anhydrous colloidal silica	Glidant	7.00	0.50
Magnesium stearate	Lubricant	3.50	0.25
Core Tablet Weight:		1400.00	100.00
Coated Tablet			
Subcoat			
Coating powder Opadry® QX 321A240072-CN Pink [C]	Subcoat coating layer	42.00	3.00
Purified water [D]	Process aid	q.s.	NA
Functional Coat			
Coating powder Acryl-Eze® 93A18597 White [E]	Functional coating layer	165.20	11.80
Triethyl citrate	Plasticizer	16.5	1.18
Purified water [D]	Process aid	q.s.	NA
Coated Tablet Weight:		1623.70	115.98

[A] The dose (mg) is equivalent to Peptide of SEQ ID NO: 1 free base and corrected for assay of the Peptide of SEQ ID NO: 1 (HCl salt) (assay= peptide content x purity by U/HPLC).

[B] The weight of this excipient was corrected based on the assay value of the API to maintain a fixed tablet weight.

[C] The coating suspension for subcoat contains was prepared at a concentration of 20% wt% solids.

[D] The solvent of coating suspensions is removed during the coating processing.

[E] A typical coating suspension for the functional coat contains approximately 20% wt% solids.

Table 18. Tablet Composition 9

Component	Function	Tablet Composition 9	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
<i>Intragranular Phase</i>			
Peptide of SEQ ID NO: 1 [A]	Active ingredient	25.00	5.00
Sodium caprate	Absorption enhancer	100.00	7.14
Microcrystalline cellulose [B]	Filler	55.00 ^b	3.93
Sorbitol	Filler	150.00	10.71
Croscarmellose sodium	Disintegrant	70.00	5.00
Anhydrous colloidal silica	Glidant	7.00	0.50
<i>Extragranular Phase</i>			
Silicified microcrystalline cellulose	Filler	912.50	36.61
Croscarmellose sodium	Disintegrant	70.00	5.00
Anhydrous colloidal silica	Glidant	7.00	0.50
Magnesium stearate	Lubricant	3.50	0.25
Core Tablet Weight:		1400.00	100.00
Coated Tablet			
<i>Subcoat</i>			
Coating powder Opadry® QX 321A240072-CN Pink [C]	Subcoat coating layer	42.00	3.00
Purified water [D]	Process aid	q.s.	NA
<i>Functional Coat</i>			
Coating powder Acryl-Eze® 93A18597 White [E]	Functional coating layer	165.20	11.80
Triethyl citrate	Plasticizer	16.5	1.18
Purified water [D]	Process aid	q.s.	NA
Coated Tablet Weight:		1623.70	115.98

[A] The dose (mg) is equivalent to Peptide of SEQ ID NO: 1 free base and corrected for assay of the Peptide of SEQ ID NO: 1 (HCl salt) (assay= peptide content x purity by U/HPLC).

[B] The weight of this excipient was corrected based on the assay value of the API to maintain a fixed tablet weight.

[C] The coating suspension for subcoat contains was prepared at a concentration of 20% wt% solids.

[D] The solvent of coating suspensions is removed during the coating processing.

[E] A typical coating suspension for the functional coat contains approximately 20% wt% solids.

[0501] Table 19 shows properties of Tablet Compositions 7-9.

Table 19: Properties of Blends/Core/Coated Tablets – Tablet Compositions 7-9

	TC 7	TC 8	TC 9
Core Tablet			
Blend size (=No. tablet [wt])	150 tab [2.1 kg]	100 tab [1.4 kg]	100 tab [1.4 kg]
Punch size (tab length/width, mm)	20.5 x 10.25 mm	22 x 11 mm	21.08 x 10.54 mm
Pre-/main-compression forces (kN)	1/20	1/20	1/20
Weight (mg), avg (n=sample)	1411 (n=3)	1415 (n=2)	1414 (n=2)
Hardness (N) avg (n=sample)	7.91 (n=3)	7.17 (n=2)	7.93 (n=2)
Thickness (mm) avg (n=sample)	233 (n=3)	235 (n=2)	405 (n=2)
Disintegration time (min:sec) avg (n=sample)	12:48 (n=2)	7:12 (n=1)	03:01 (n=2)
Coated Tablet			
Batch size (No. tablet)	63 + backfills [1.6 kg]	48 + backfills [1.6 kg]	78 + backfills [1.6 kg]
Coating pan size	2L (Lödige)	2L (Lödige)	2L (Lödige)
Appearance of subcoat	Pink oval film-coated tablets	Pink oval film-coated tablets	Pink oval film-coated tablets
Coating layer of Subcoat (weight gain, mg [wt% of core tablets]) [A]	<i>Target 42.0 mg [3.0%]</i>		
	28.0 mg [2.0%]	31.2 mg [2.2%]	28.4 mg [2.0%]
Appearance of functional coat	White oval film-coated tablets	White oval film-coated tablets	White oval film-coated tablets
Coating layer of Func. Coat (weight gain, mg [wt% of core tablets]) [A]	<i>Target 181.7 mg [12.98%]</i>		
	189.6 mg [13.6%]	234.8 mg [16.7%]	223.4 mg [15.9%]

[A] Coating levels (wt%) of each coating layer were calculated based on the measured weight gain and core tablet weight of the target tablets (not including backfills).

Tablet Compositions 10 and 11

[0502] Film-Coated Tablets with compositions of Tablet Compositions 10 and 11 at the strengths of 100 mg and 25 mg (equivalent to free base) of the Peptide of SEQ ID NO: 1 hydrochloride (HCl) salt, respectively, were prepared by following unit operations: milling & sieving, blending & compression, and film coating, described in Steps 1-3 below. The in-process control data of the core and coated tablets in representative stability or clinical batches were collected, as summarized in the table below.

Step 1: Milling & Sieving

[0503] Teflon (PTFE) solid blocks were used to manually sieve the Peptide of SEQ ID NO: 1 through a 600 mm stainless-steel sieve. The collected powder was then sieved via the same procedure through stainless-steel sieves at 400 mm and 150 mm mesh size, sequentially.

Step 2: Blending and Tableting

[0504] The resulting powder from Step 1 and all excipients comprising silicified microcrystalline cellulose, sorbitol, crospovidone, and anhydrous colloidal silica as listed in Tablet Compositions 10 and 11 were screened through a 1000 mm stainless-steel sieve and mixed for 10 minutes in a high-speed blender (such as Turbula). To this mixture, magnesium

stearate was sieved through the same mesh, added to the above mixture, and further mixed for 5 minutes under the same conditions. The final blend was compressed into tablets through a two-stage (i.e., pre- and main-) compression cycle on a single-punch tablet press (such as Styl'One Evolution or rotary tablet press such as Modul S/P). The resulting core tablets were collected into appropriate containers and packages (e.g., sealed in aluminum laminated bags) which were stored until the next step.

Step 3: Film Coating

[0505] The core tablets manufactured from Steps 1-2 were transferred to the pan of a semi-perforated tablet coating system (such as Lödige or Bohle), depending on the batch size. After warming up the uncoated tablets in the slowly rotating pre-warmed pan, a pre-determined amount of coating suspension that was calculated to achieve the target weight gain was then sprayed to the perforated coating pan.

[0506] In a typical coating run using the Lödige coater (4L pan), the process parameters to coat the cosmetic coating layer listed in Tablet Compositions 10-11 were commonly optimized in following target values and ranges [min-max] – tablet bed temperature (indicated by the exhaust air temperature) at 40 °C [35-45 °C], inlet air flow rate of 105 [80-120] m³/hr and an atomizing and pattern air pressure of 0.9 [0.6-1.2] bar, a drum rotation speed at 25 [10-30] rpm, and a feeding rate of coating suspension at 6.5-7 [3-6] g/min. In the case of the Bohle coater (35L pan), the process parameters of a trial run coating 18k core tablets with Tablet Composition 10 were optimized as follow – exhaust air temp at 43.1 °C [41.8-44.8 °C], inlet air flow rate at 599.8 [578.3-616.5] m³/hr, a drum rotation speed at 19 rpm, and a feeding rate of coating suspension at 70.0 [69.2-70.9] g/min.

[0507] At the end of spraying, the coating pan continued to rotate at a reduced drum speed (e.g., 5 rpm) at approximately 45 °C to remove residual water of the coated tablets. For upscale coating in Bohle, the coated tablets remained in the slowly rotating pan (e.g., 2 rpm) with inlet cooling air for an additional cooling period until the exhaust air reached an adequate temperature (e.g., 38 °C) for collection. The resulting coated tablets were collected from the pan and cooled to room temperature under ambient conditions, before storing them in appropriate containers and packages (e.g., sealed in aluminum laminated bags) under appropriate conditions.

Table 20: Tablet Composition 10

Component	Function	Tablet Composition 10	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1 [A]	Active ingredient	100.00	10.00
Silicified microcrystalline cellulose [B]	Filler	715.00	71.50
Sorbitol	Filler	125.00	12.5
Crospovidone	Disintegrant	50.00	5.00
Anhydrous colloidal silica	Glidant	5.00	0.50
Magnesium stearate	Lubricant	5.00	0.50
Core Tablet Weight:		1000.00	100.00
Coated Tablet			
Coating powder Opadry® QX 321A220063 Yellow [C]	Cosmetic coating layer	30.00	3.00
Purified water [D]	Process aid	q.s.	NA
Coated Tablet Weight:		1030.00	103.00

[A] The dose (mg) is equivalent to Peptide of SEQ ID NO: 1 free base and corrected for assay of the Peptide of SEQ ID NO: 1 (HCl salt) (assay= peptide content x purity by U/HPLC).

[B] The weight of this excipient was corrected based on the assay value of the API to maintain a fixed tablet weight.

[C] A typical coating suspension contains approximately 30% wt% solids.

[D] The solvent of coating suspensions is removed during the coating processing.

Table 21: Tablet Composition 11

Component	Function	Tablet Composition 11	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1 [A]	Active ingredient	25.00	2.50
Silicified microcrystalline cellulose [B]	Filler	790.00	79.00
Sorbitol	Filler	125.00	12.5
Crospovidone	Disintegrant	50.00	5.00
Anhydrous colloidal silica	Glidant	5.00	0.50
Magnesium stearate	Lubricant	5.00	0.50
Core Tablet Weight:		1000.00	100.00
Coated Tablet			
Coating powder Opadry® QX 321A220063 Yellow [C]	Cosmetic coating layer	30.00	3.00
Purified water [D]	Process aid	q.s.	NA
Coated Tablet Weight:		1030.00	103.00

[A] The dose (mg) is equivalent to Peptide of SEQ ID NO: 1 free base and corrected for assay of the Peptide of SEQ ID NO: 1 (HCl salt) (assay= peptide content x purity by U/HPLC).

[B] The weight of this excipient was corrected based on the assay value of the API to maintain a fixed tablet weight.

[C] A typical coating suspension contains approximately 30% wt% solids.

[D] The solvent of coating suspensions is removed during the coating processing.

Table 22 shows properties of Tablet Compositions 10-11.

Table 22: Properties of Blends/Core/Coated Tablets – Tablet Compositions 10-11

	Tablet Composition 10	Tablet Composition 11
Blend		
Blend size (=No. tablet [wt])	45k tab [45 kg]	45k tab [45 kg]
Punch size (tab length/width, mm)	19 x 9.4 mm	19 x 9.4 mm
Pre-/main-compression forces (kN)	1.2/18	1.25/18
Weight (mg), avg (n=sample)	1008 (n=10)	1002.9 (n=60)
Hardness (N) avg (n=sample)	491 (n=10)	475.3 (n=30)
Thickness (mm) avg (n=sample)	6.47 (n=10)	6.46 (n=30)
Disintegration time (sec) avg (n=sample)	104.8 (n=6)	71 (n=36)
Friability (%), 20 tablets	-0.14%	-0.115%
Yield (No. tablet)	41k tab [41 kg]	43k tab [43 kg]
Coated Tablet		
Batch size (No tab. [nominal wt])	18k tab [18 kg]	42k tab [42 kg]
Coating pan size	35L (Bohle)	75L (Bohle)
Appearance	Yellowish orange to yellowish brown oval film-coated tablets	Yellowish orange to yellowish brown oval film-coated tablets
Coating layer (wt% of core tablets) [B]	Target 30.0 mg [3.0%]	
	30.2 mg [3.0%]	30 mg [3.0%]

[A] Representative compression and coating batches such as stability or clinical batches were selected.

[B] Coating levels (wt%) of each coating layer were calculated based on the measured weight gain and core tablet weight of 50 tablets in the batch.

Tablet Compositions 12 and 13

[0508] Film-Coated Tablets with compositions of Tablet Compositions 12 and 13 at the strength of 10 mg and 5 mg (equivalent to free base) of the compound of Formula (I) hydrochloride (HCl) salt, respectively, were prepared by following unit operations: milling & sieving, blending & compression, and film coating, described in Steps 1-3 in Tablet Compositions 10-11. The in-process control data of the core and coated tablets of selected batches were collected and summarized in the table below. It is understood that other salts of the compound of Formula (I) can also be used in forming the tablet compositions described herein.

Table 23: Tablet Compositions 12 and 13

Component	Function	Tablet Composition 12	Tablet Composition 13	TC 12/13 dose proportional to TC 11
		Quantity per Unit (mg)		% (w/w)
Core Tablet				
Peptide of SEQ ID NO: 1 [A]	Active ingredient	10.00	5.00	2.50
Silicified microcrystalline cellulose [B]	Filler	316.00	158.00	79.00
Sorbitol	Filler	50.00	25.00	12.5
Crospovidone	Disintegrant	25.00	10.00	5.00
Anhydrous colloidal silica	Glidant	2.00	1.00	0.50
Magnesium stearate	Lubricant	2.00	1.00	0.50
Core Tablet Weight:		400.0	200.0	100.00
Coated Tablet				
Coating powder Opadry® QX 321A220063 Yellow [C]	Cosmetic coating layer	12.00	6.00	3.00
Purified water [D]	Process aid	q.s.		NA
Coated Tablet Weight:		412.00	206.00	103.00

TC is Tablet Composition

[A] The dose (mg) is equivalent to Peptide of SEQ ID NO: 1 free base and corrected for assay of the Peptide of SEQ ID NO: 1 (HCl salt) (assay= peptide content x purity by U/HPLC).

[B] The weight of this excipient was corrected based on the assay value of the API to maintain a fixed tablet weight.

[C] A typical coating suspension contains approximately 30% wt% solids.

[D] The solvent of coating suspensions is removed during the coating processing.

[0509] Table 24 shows properties of Tablet Compositions 12-13.

Table 24: Properties of Blends/Core/Coated Tablets – Tablet Compositions 12 and 13

	Tablet Composition 12	Tablet Composition 13
Core Tablet [A]		
Blend size (=No. tablet [wt])	62.5k tab [25 kg]	8k tab [1.6 kg]
Punch size (tab diameter, mm)	9.91 mm, round	8 mm, round
Pre-/main-compression forces (kN)	1.2/12	1/10
Weight (mg), avg (n=sample)	404.6 (n=50)	201.2 (n=40)
Hardness (N) avg (n=sample)	273.4 (n=50)	146.3 (n=40)
Thickness (mm) avg (n=sample)	4.74 (n=50)	3.80 (n=40)
Disintegration time (sec) avg (n=sample)	78 (n=29)	119 (n=48)
Friability (%), 20 tablets	0.06%	0.02%
Yield (No. tablet)	52.9k tab [21.1 kg]	6.9k tab [1.38 kg]
Coated Tablet		
Batch size (No tab, [nominal wt])	25k tab [10 kg]	5.7k tab [1.14 kg]
Coating pan size	14L (Bohle)	2L (Lödige)
Appearance	Yellowish orange to yellowish brown round film-coated tablets	Yellowish orange to yellowish brown round film-coated tablets
Coating layer (wt% of core tablets) [B]	Target 30.0 mg [3.0%]	Target 6.0 mg [3.0%]
	11.1 mg [2.8%]	3.3 mg [1.7%]

[A] Representative batches were selected.

[B] Coating levels (wt%) of each coating layer were calculated based on the measured weight gain and core tablet weight of the entire coating batch for both Tablet Compositions 12 and 13.

Tablet Compositions 14-43

[0510] Tablets with compositions of Tablet Compositions 14 through 43 were prepared by blending together the components of the core tablet, such as a crystalline pharmaceutically acceptable salt of the compound of Formula (I), and various excipients, including on or more of a filler, a disintegrant, a glidant, and a lubricant. For certain tablet compositions, one or more of the components of the core tablet underwent a suitable granulation process before the blending procedure. After the blending procedure, the blended components were compressed into a core tablet employing a suitable tablet machine. A cosmetic subcoating was disposed over the core tablets of Compositions 17 through 28 and 30 through 43. The peptide of SEQ ID NO: 1 used in the compositions 14-43 is the crystalline form of HCl salt of the compound of Formula (I), but other crystalline forms of the compound of Formula (I) can also be used in forming the tablet compositions described herein.

Table 25: Tablet Compositions 14 and 15

Component	Function	Tablet Composition 14	Tablet Composition 15	
		Quantity per Unit (mg)		
Core Tablet				
Peptide of SEQ ID NO: 1	Active ingredient	25.00	150.00	3.13/18.75
Silicified microcrystalline cellulose	Filler	541.00	416.00	67.63/52.00
Sorbitol	Filler	150.00	150.00	18.75
Croscarmellose sodium	Disintegrant	70.00	70.00	8.75
Anhydrous colloidal silica	Glidant	7.0	7.0	0.88
Magnesium stearate	Lubricant	7.0	7.0	0.88
Core Tablet Weight:		800.00	800.00	100.00

Table 26: Tablet Composition 16

Component	Function	Tablet Composition 16	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	150.00	12.50
Silicified microcrystalline cellulose	Filler	978.00	81.50
Croscarmellose sodium	Disintegrant	60.00	5.00
Anhydrous colloidal silica	Glidant	6.0	0.50
Magnesium stearate	Lubricant	6.0	0.50
Core Tablet Weight:		1200.00	100.00

Table 27: Tablet Compositions 17 and 18

Component	Function	Tablet Composition 17	Tablet Composition 18	
		Quantity per Unit (mg)		% (w/w)
Core Tablet				
Peptide of SEQ ID NO: 1	Active ingredient	25.00	100.00	2.50/10.00
Silicified microcrystalline cellulose	Filler	790.00	715.00	79.00/71.50
Sorbitol	Filler	125.0	125.00	12.50
Croscarmellose	Disintegrant	50.00	50.00	5.00
Anhydrous colloidal silica	Glidant	5.00	5.00	0.50
Magnesium stearate	Lubricant	5.00	5.50	0.50
Core Tablet Weight:		1000.0	1000.0	100.00
Coated Tablet				
Coating powder Opadry® QX	Cosmetic coating layer	30.00	30.00	3.00
Purified water	Process aid	q.s.		NA
Coated Tablet Weight:		1030.00	1030.00	103.00

Table 28: Tablet Compositions 19 to 22

Component	Function	TC 19	TC 20	TC 21	TC 22	
		Quantity per Unit (mg)				% (w/w)
Core Tablet						
Peptide of SEQ ID NO: 1	Active ingredient	100.00	50.00	25.00	10.00	10.00/5.00/2.50/1.00
Silicified microcrystalline cellulose	Filler	715.00	765.00	790.00	805.00	71.5/76.5/79.0/80.5
Sorbitol	Filler	125.0	125.00	125.00	125.00	12.50
Crospovidone	Disintegrant	50.00	50.00	50.00	50.00	5.00
Anhydrous colloidal silica	Glidant	5.00	5.00	5.00	5.00	0.50
Magnesium stearate	Lubricant	5.00	5.00	5.00	5.00	0.50
Core Tablet Weight:		1000.0	1000.0	1000.0	1000.0	100.00
Coated Tablet						
Coating powder Opadry® QX	Cosmetic coating layer	30.00	30.00	30.00	30.00	3.00
Purified water	Process aid		q.s.			NA
Coated Tablet Weight:		1030.00	1030.00	1030.00	1030.00	103.00

Table 29: Tablet Compositions 23 and 24

Component	Function	Tablet Composition 23	Tablet Composition 24	% (w/w)
		Quantity per Unit (mg)		
Core Tablet				
Peptide of SEQ ID NO: 1	Active ingredient	10.00	5.00	2.50
Silicified microcrystalline cellulose	Filler	316.00	158.00	79.00
Sorbitol	Filler	125.00	25.00	12.50
Crospovidone	Disintegrant	20.00	10.00	5.00
Anhydrous colloidal silica	Glidant	2.00	1.00	0.50
Magnesium stearate	Lubricant	2.00	1.00	0.50
Core Tablet Weight:		400.0	200.0	100.00
Coated Tablet				
Coating powder Opadry®	Cosmetic coating layer	12.00	6.00	3.00
Purified water	Process aid	q.s.		NA
Coated Tablet Weight:		412.00	206.00	103.00

Table 30: Tablet Compositions 25 and 26

Component	Function	Tablet Composition 25	Tablet Composition 26	% (w/w)
		Quantity per Unit (mg)		
Core Tablet				
Peptide of SEQ ID NO: 1	Active ingredient	50.00	25.00	10.00
Silicified microcrystalline cellulose	Filler	357.50	178.75	71.50
Sorbitol	Filler	62.50	31.25	12.50
Crospovidone	Disintegrant	25.00	12.50	5.00
Anhydrous colloidal silica	Glidant	2.50	1.25	0.50
Magnesium stearate	Lubricant	2.50	1.25	0.50
Core Tablet Weight:		500.0	250.0	100.00
Coated Tablet				
Coating powder Opadry®	Cosmetic coating layer	15.00	7.50	3.00
Purified water	Process aid	q.s.		NA
Coated Tablet Weight:		515.00	257.50	103.00

Table 31: Tablet Compositions 27 and 28

Component	Function	Tablet Composition 27	Tablet Composition 28	
		Quantity per Unit (mg)		% (w/w)
Core Tablet				
Peptide of SEQ ID NO: 1	Active ingredient	50.00	25.00	10.00
Silicified microcrystalline cellulose	Filler	359.00	179.50	71.80
Sorbitol	Filler	62.50	31.25	12.50
Crospovidone	Disintegrant	25.00	12.50	5.00
Anhydrous colloidal silica	Glidant	0.50	0.50	0.20
Magnesium stearate	Lubricant	2.50	1.25	0.50
Core Tablet Weight:		500.0	250.0	100.00
Coated Tablet				
Coating powder Opadry®	Cosmetic coating layer	15.00	7.50	3.00
Purified water	Process aid	q.s.		NA
Coated Tablet Weight:		515.00	257.50	103.00

Table 32: Tablet Composition 29

Component	Function	Tablet Composition 29	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	25.00	10.00
Silicified microcrystalline cellulose	Filler	180.00	72.00
Sorbitol	Filler	31.25	12.50
Crospovidone	Disintegrant	12.50	5.00
Magnesium stearate	Lubricant	1.25	0.50
Core Tablet Weight:		250.0	100.00

Table 33: Tablet Compositions 30 to 33

Component	Function	TC 30	TC 31	TC 32	TC 33	
		Quantity per Unit (mg)				% (w/w)
Core Tablet						
Peptide of SEQ ID NO: 1	Active ingredient	50.00	50.00	50.00	25.00	10.00
Silicified microcrysta lline cellulose	Filler	359.0	356.5	354.0	177.00	71.80/72.3 0/ 72.80/72.8 0
Mannitol	Filler	62.50	62.50	62.50	31.25	12.50
Crospovidone	Disintegra nt	25.00	25.00	25.00	12.50	5.00
Anhydrous colloidal silica	Glidant	1.00	1.00	1.00	0.50	0.20
Magnesium stearate	Lubricant	2.50	5.00	7.00	3.75	0.50/1.00/ 1.50/1.50
Core Tablet Weight:		500.0	500.0	500.0	250.0	100.00
Coated Tablet						
Coating powder Opadry® QX	Cosmetic coating layer	15.00	15.00	15.00	30.00	3.00
Purified water	Process aid		q.s.			NA
Coated Tablet Weight:		515.00	515.00	257.50	1030.00	103.00

Table 34: Tablet Compositions 34 to 36

Component	Function	Tablet Composition 34	Tablet Composition 35	Tablet Composition 36	
		Quantity per Unit (mg)			% (w/w)
Core Tablet					
Peptide of SEQ ID NO: 1	Active ingredient	100.00	50.00	25.00	10.00
Silicified microcrystalline cellulose	Filler	718.00	359.00	179.50	71.80
Sorbitol	Filler	125.0	62.50	31.25	12.50
Crospovidone	Disintegrant	50.00	25.00	12.50	5.00
Anhydrous colloidal silica	Glidant	2.00	1.00	0.50	0.20
Magnesium stearate	Lubricant	5.00	2.50	1.25	0.50
Core Tablet Weight:		1000.0	500.0	250.0	100.00
Coated Tablet					
Coating powder Opadry® QX	Cosmetic coating layer	30.00	15.00	7.50	3.00
Purified water	Process aid	q.s.			NA
Coated Tablet Weight:		1030.00	515.00	257.50	103.00

Table 35: Tablet Compositions 37 and 38

Component	Function	Tablet Composition 37	Tablet Composition 38	
		Quantity per Unit (mg)		% (w/w)
Core Tablet				
Peptide of SEQ ID NO: 1	Active ingredient	100.00	200.00	10.00/20.00
Silicified microcrystalline cellulose	Filler	718.00	618.00	71.80/61.80
Sorbitol	Filler	125.0	125.0	12.50
Crospovidone	Disintegrant	50.00	50.00	5.00
Anhydrous colloidal silica	Glidant	2.00	2.00	0.20
Magnesium stearate	Lubricant	5.00	5.00	0.50
Core Tablet Weight:		1000.0	1000.0	100.00
Coated Tablet				
Coating powder Opadry®	Cosmetic coating layer	30.00	30.00	3.00
Purified water	Process aid	q.s.		NA
Coated Tablet Weight:		1030.00	1030.00	103.00

Table 36: Tablet Compositions 39 to 43

Component	Function	Tablet Composition					
		39	40	41	42	43	
				Quantity per Unit (mg)			
Core Tablet							
Peptide of SEQ ID NO: 1	Active ingredient	50.00	100.00	150.00	200.00	250.00	10.0/20.0/ 30.0/40.0/ 50.0
Silicified microcrystalline cellulose	Filler	417.50	367.50	317.50	267.50	217.50	83.5/73.5/ 63.5/53.5/ 43.5
Crospovidone	Disintegrant	25.00	25.00	25.00	25.00	25.00	5.00
Anhydrous colloidal silica	Glidant	5.00	5.00	5.00	5.00	5.00	1.00
Magnesium stearate	Lubricant	2.50	2.50	2.50	2.50	2.50	0.50
Core Tablet Weight:		500.0	500.0	500.0	500.0	500.0	100.00

Tablet Compositions 43-93

[0511] Tablets with compositions of Tablet Compositions 43 through 93 were prepared by blending together the components of the core tablet, such as a crystalline pharmaceutically acceptable salt of the compound of Formula (I), and various excipients, including on or more of a filler, a disintegrant, a glidant, and a lubricant. When relevant, one or more of the components of the core tablet underwent a suitable granulation process before the blending procedure. After the blending procedure, the blended components were compressed into a core tablet employing a suitable tablet machine. Two coatings, a subcoating followed by an enteric coating, were disposed over the core tablets in Compositions 43 through 55, 73, 74, 84 through 88, and 90 through 93. The peptide of SEQ ID NO: 1 used in the compositions 43-93 is the crystalline form of HCl salt of the compound of Formula (I), but other crystalline forms of the compound of Formula (I) can also be used in forming the tablet compositions described herein.

Table 37: Tablet Compositions 44 and 45

Component	Function	Tablet Composition 44	Tablet Composition 45		
		Quantity per Unit (mg)		% (w/w)	
Core Tablet					
Peptide of SEQ ID NO: 1	Active ingredient	25.0	150.0	3.58	10.71
Sodium caprate	Absorption enhancer	500.0		35.71	
Microcrystalline cellulose	Filler	55.0		3.93	
Sorbitol	Filler	150.0		10.71	
Croscarmellose Sodium	Disintegrant	140.0		10.00	
Anhydrous colloidal silica	Glidant	14.0		1.00	
Silicified microcrystalline cellulose	Filler	512.5	387.5	36.61	27.68
Magnesium stearate	Lubricant	3.5		0.25	
Core Tablet Weight:		1400.0		100.00	
Coated Tablet					
Subcoat					
Coating powder Opadry® QX	Subcoat coating layer	42.00		3.00	
Purified water	Process aid	q.s.		N/A	
Functional Coat					
Coating powder Acryl-Eze®	Functional coating layer	112.00		8.00	
Triethyl citrate	Plasticizer	11.20		0.80	
Purified water	Process aid	q.s.		N/A	
Coated Tablet Weight:		1565.2		111.80	

Table 38: Tablet Compositions 46 to 49

Component	Function	Tablet Composition 46 (47)	Tablet Composition 48	Tablet Composition 49			
		Quantity per Unit (mg)			% (w/w)		
Core Tablet							
Peptide of SEQ ID NO: 1	Active ingredient	50.0	25.0	10.0	3.58	1.79	0.72
Sodium caprate	Absorption enhancer	300.0			21.43		
Microcrystalline cellulose	Filler	55.0			3.93		
Sorbitol	Filler	150.0			10.71		
Crospovidone	Disintegrant	140.0			10.00		
Anhydrous colloidal silica	Glidant	14.0			1.00		
Silicified microcrystalline cellulose	Filler	687.5	712.5	727.5	49.10	50.89	51.96
Magnesium stearate	Lubricant	3.5			0.25		
Core Tablet Weight:		1400.0			100.00		
Coated Tablet							
Subcoat							
Coating powder Opadry® QX	Subcoat coating layer	42.00			3.00		
Purified water	Process aid	q.s.			N/A		
Functional Coat							
Coating powder Acryl-Eze®	Functional coating layer	112.00 (165.2)			8.00 (11.8)		
Triethyl citrate	Plasticizer	11.20 (16.5)			0.80 (1.18)		
Purified water	Process aid	q.s.			N/A		
Coated Tablet Weight:		1565.2 (1623.7)					

Table 39: Tablet Compositions 50 to 52

Component	Function	Tablet Composition 50	Tablet Composition 51	Tablet Composition 52			
		Quantity per Unit (mg)			% (w/w)		
Core Tablet							
Peptide of SEQ ID NO: 1	Active ingredient	50.0	25.0	10.0	3.58	1.79	0.72
Sodium caprate	Absorption enhancer	300.0			21.43		
Microcrystalline cellulose	Filler	55.0			3.93		
Sorbitol	Filler	150.0			10.71		
Crospovidone	Disintegrant	140.0			10.00		
Anhydrous colloidal silica	Glidant	14.0			1.00		
Silicified microcrystalline cellulose	Filler	687.5	712.5	727.5	49.10	50.89	51.96
Magnesium stearate	Lubricant	3.5			0.25		
Core Tablet Weight:		1400.0			100.00		
Coated Tablet							
Subcoat							
Coating powder Opadry® QX 321A220063 Yellow	Subcoat coating layer	42.00			3.00		
Purified water	Process aid	q.s.			N/A		
Functional Coat							
Coating powder Acryl-Eze® 93A220037 Yellow	Functional coating layer	112.00			8.00		
Triethyl citrate	Plasticizer	11.20			0.80		
Purified water	Process aid	q.s.			N/A		
Coated Tablet Weight:		1565.2					

Table 40: Tablet Compositions 53 to 55

Component	Function	Tablet Composition 53	Tablet Composition 54	Tablet Composition 55			
		Quantity per Unit (mg)			% (w/w)		
Core Tablet							
Peptide of SEQ ID NO: 1	Active ingredient	25.00			5.00		
Sodium caprate	Absorption enhancer	500.00	300.00	100.00	35.71	21.43	7.14
Microcrystalline cellulose	Filler	55.00 ^b			3.93		
Sorbitol	Filler	150.00			10.71		
Croscarmellose sodium	Disintegrant	140.00			10.00		
Anhydrous colloidal silica	Glidant	14.00			1.00		
Silicified microcrystalline cellulose	Filler	512.50	712.50	912.50	65.18	50.89	36.61
Magnesium stearate	Lubricant	3.50			0.25		
Core Tablet Weight:		1400.00			100.00		
Coated Tablet							
Subcoat							
Coating powder Opadry® QX 321A240072-CN Pink	Subcoat coating layer	42.00			3.00		
Purified water	Process aid	q.s.			NA		
Functional Coat							
Coating powder Acryl-Eze® 93A18597 White	Functional coating layer	165.20			11.80		
Triethyl citrate	Plasticizer	16.5			1.18		
Purified water	Process aid	q.s.			NA		
Coated Tablet Weight:		1623.70			115.98		

Table 41: Tablet Composition 56

Component	Function	Tablet Composition 56	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	25.00	1.79
Sodium caprate	Absorption enhancer	500.00	35.71
Microcrystalline cellulose Avicel PH101	Filler	55.00	3.93
Microcrystalline cellulose Ceolus KG-802	Filler	70.00	10.00
Sorbitol	Filler	150.00	10.71
Croscarmellose sodium	Disintegrant	140.00	10.00
Anhydrous colloidal silica	Glidant	14.00	1.00
Silicified microcrystalline cellulose	Filler	442.50	31.61
Magnesium stearate	Lubricant	3.50	0.25
Core Tablet Weight:		1400.00	100.00

Table 42: Tablet Composition 57

Component	Function	Tablet Composition 57	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	25.00	1.79
Sodium caprate	Absorption enhancer	500.00	35.71
Microcrystalline cellulose Avicel PH101	Filler	55.00	3.93
Microcrystalline cellulose Ceolus KG-802	Filler	70.00	10.00
Sorbitol	Filler	150.00	10.71
Croscarmellose sodium	Disintegrant	140.00	10.00
Anhydrous colloidal silica	Glidant	14.00	1.00
Silicified microcrystalline cellulose	Filler	342.50	26.35
Magnesium stearate	Lubricant	3.50	0.25
Core Tablet Weight:		1300.00	100.00

Table 43: Tablet Composition 58

Component	Function	Tablet Composition 58	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	25.00	1.79
Sodium caprate	Absorption enhancer	500.00	35.71
Microcrystalline cellulose Avicel PH101	Filler	55.00	3.93
Sorbitol	Filler	350.00	25.00
Croscarmellose sodium	Disintegrant	140.00	10.00
Anhydrous colloidal silica	Glidant	14.00	1.00
Silicified microcrystalline cellulose	Filler	312.50	22.32
Magnesium stearate	Lubricant	3.50	0.25
Core Tablet Weight:		1300.00	100.00

Table 44: Tablet Composition 59

Component	Function	Tablet Composition 59	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	25.00	1.79
Sodium caprate	Absorption enhancer	500.00	35.71
Microcrystalline cellulose Avicel PH101	Filler	55.00	3.93
Microcrystalline cellulose Ceolus KG-802	Filler	70.00	10.00
Sorbitol	Filler	350.00	25.00
Croscarmellose sodium	Disintegrant	140.00	10.00
Anhydrous colloidal silica	Glidant	14.00	1.00
Silicified microcrystalline cellulose	Filler	242.50	17.32
Magnesium stearate	Lubricant	3.50	0.25
Core Tablet Weight:		1400.00	100.00

Table 45: Tablet Composition 60

Component	Function	Tablet Composition 60	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	25.00	1.67
Sodium caprate	Absorption enhancer	500.00	33.33
Microcrystalline cellulose Avicel PH101	Filler	55.00	3.67
Microcrystalline cellulose Ceolus KG-802	Filler	70.00	4.67
Sorbitol	Filler	150.00	10.00
Croscarmellose sodium	Disintegrant	140.00	9.33
Anhydrous colloidal silica	Glidant	14.00	1.00
Silicified microcrystalline cellulose	Filler	612.50	40.83
Magnesium stearate	Lubricant	3.50	0.23
Core Tablet Weight:		1500.00	100.00

Table 46: Tablet Composition 61

Component	Function	Tablet Composition 61	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	25.0	1.79%
Sodium Caprate	Absorption enhancer	500.0	35.71%
Sorbitol	Filler	150.0	10.71%
SMCC HD90	Filler	644.5	46.04%
Crospovidone	Disintegrant	70.0	5.00%
Aerosil 200	Glidant	7.0	0.50%
Magnesium stearate	Lubricant	3.5	0.25%
Core Tablet Weight:		1400.00	100.00

Table 47: Tablet Composition 62

Component	Function	Tablet Composition 62	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	25.0	1.79%
Sodium Caprate	Absorption enhancer	500.0	35.71%
Sorbitol	Filler	214.3	15.31%
SMCC HD90	Filler	580.2	41.44%
Crospovidone	Disintegrant	70.0	5.00%
Aerosil 200	Glidant	7.0	0.50%
Magnesium stearate	Lubricant	3.5	0.25%
Core Tablet Weight:		1400.00	100.00

Table 48: Tablet Composition 63

Component	Function	Tablet Composition 63	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	25.0	1.79%
Sodium Caprate	Absorption enhancer	500.0	35.71%
Mannitol	Filler	214.3	15.31%
SMCC HD90	Filler	580.2	41.44%
Crospovidone	Disintegrant	70.0	5.00%
Aerosil 200	Glidant	7.0	0.50%
Magnesium stearate	Lubricant	3.5	0.25%
Core Tablet Weight:		1400.00	100.00

Table 49: Tablet Composition 64

Component	Function	Tablet Composition 64	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	25.0	1.79%
Sodium Caprate	Absorption enhancer	500.0	35.71%
MCC	Filler	214.3	15.31%
SMCC HD90	Filler	580.2	41.44%
Crospovidone	Disintegrant	70.0	5.00%
Aerosil 200	Glidant	7.0	0.50%
Magnesium stearate	Lubricant	3.5	0.25%
Core Tablet Weight:		1400.00	100.00

Table 50: Tablet Composition 65

Component	Function	Tablet Composition 65	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	25.0	1.79%
Sodium Caprate	Absorption enhancer	500.0	35.71%
Sorbitol	Filler	125.0	8.93%
SMCC HD90	Filler	669.5	47.82%
Crospovidone	Disintegrant	70.0	5.00%
Aerosil 200	Glidant	7.0	0.50%
Magnesium stearate	Lubricant	3.5	0.25%
Core Tablet Weight:		1400.00	100.00

Table 51: Tablet Composition 66

Component	Function	Tablet Composition 66	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	25.0	2.50%
Sodium Caprate	Absorption enhancer	500.0	50.00%
Sorbitol	Filler	150.0	15.00%
SMCC HD90	Filler	267.5	26.75%
Crospovidone	Disintegrant	50.0	5.00%
Aerosil 200	Glidant	5.0	0.50%
Magnesium stearate	Lubricant	2.5	0.25%
Core Tablet Weight:		1000.00	100.00

Table 52: Tablet Composition 67

Component	Function	Tablet Composition 67	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	25.0	2.50%
Sodium Caprate	Absorption enhancer	500.0	50.00%
Sorbitol	Filler	214.3	21.43%
SMCC HD90	Filler	203.2	20.32%
Crospovidone	Disintegrant	50.0	5.00%
Aerosil 200	Glidant	5.0	0.50%
Magnesium stearate	Lubricant	2.5	0.25%
Core Tablet Weight:		1000.00	100.00

Table 53: Tablet Composition 68

Component	Function	Tablet Composition 68	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	50.0	5.00%
Sodium Caprate	Absorption enhancer	500.0	50.00%
Sorbitol	Filler	214.3	21.43%
SMCC	Filler	178.2	17.82%
Crospovidone	Disintegrant	50.0	5.00%
Aerosil 200	Glidant	5.0	0.50%
Magnesium stearate	Lubricant	2.5	0.25%
Core Tablet Weight:		1000.00	100.00

Table 54: Tablet Composition 69

Component	Function	Tablet Composition 69	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	50.0	5.00%
Sodium Caprate	Absorption enhancer	500.0	50.00%
Sorbitol	Filler	125.0	12.50%
SMCC	Filler	267.5	26.75%
Crospovidone	Disintegrant	50.0	5.00%
Aerosil 200	Glidant	5.0	0.50%
Magnesium stearate	Lubricant	2.5	0.25%
Core Tablet Weight:		1000.00	100.00

Table 55: Tablet Composition 70

Component	Function	Tablet Composition 70	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	50.0	5.88%
Sodium Caprate	Absorption enhancer	500.0	59.00%
Sorbitol	Filler	125.0	14.71%
SMCC	Filler	126.1	14.84%
Crospovidone	Disintegrant	42.5	5.00%
Aerosil 200	Glidant	4.25	0.50%
Magnesium stearate	Lubricant	2.125	0.25%
Core Tablet Weight:		850.00	100.00

Table 56: Tablet Composition 71

Component	Function	Tablet Composition 71	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	50.0	6.25%
Sodium Caprate	Absorption enhancer	500.0	62.50%
Sorbitol	Filler	125.0	15.63%
SMCC	Filler	80.2	10.03%
Crospovidone	Disintegrant	40.0	5.00%
Aerosil 200	Glidant	4.0	0.50%
Magnesium stearate	Lubricant	0.8	0.10%
Core Tablet Weight:		800.00	100.00

Table 57: Tablet Composition 72

Component	Function	Tablet Composition 72	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	50.0	6.96%
Sodium Caprate	Absorption enhancer	500.0	62.50%
Sorbitol	Filler	125.0	15.63%
Crospovidone	Disintegrant	35.9	5.00%
Aerosil 200	Glidant	3.6	0.50%
Magnesium stearate	Lubricant	3.6	0.50%
Core Tablet Weight:		718.00	100.00

Table 58: Tablet Compositions 73 and 74

Component	Function	Tablet Composition 73 (74)	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	10.0 (50.0)	1.11% (5.56%)
Sodium Caprate	Absorption enhancer	500.0	55.56%
Sorbitol	Filler	125.0	69.44%
SMCC	Filler	215.3 (174.5)	23.92% (19.39%)
Crospovidone	Disintegrant	45.0	5.00%
Aerosil 200	Glidant	0.2 (1.0)	0.02% (0.11%)
Magnesium stearate	Lubricant	4.5	0.50%
Core Tablet Weight:		900.00	100.00
Coated Tablet			
Subcoat			
Coating powder Opadry® QX	Subcoat coating layer	27.00	3.00
Purified water	Process aid	q.s.	NA
Functional Coat			
Coating powder Acryl-Eze® Yellow	Functional coating layer	72.00	8.00
Triethyl citrate	Plasticizer	7.2	0.80
Purified water	Process aid	q.s.	NA
Coated Tablet Weight:		1006.2	

Table 59: Tablet Compositions 75 and 76

Component	Function	Tablet Composition 75		Tablet Composition 76	
		Quantity per Unit (mg)	Quantity per Unit (mg)	Quantity per Unit (mg)	% (w/w)
Core Tablet					
Peptide of SEQ ID NO: 1	Active ingredient	25.0	1.79%	25.0	2.08%
Sodium Caprate	Absorption enhancer	500.0	35.71%	300.0	25.00%
Crospovidone	Disintegrant	140.0	10.00%	120.0	10.00%
HPMC	Binder	10.4	0.74%	6.3	0.53%
Sorbitol	Filler	150.0	10.71%	150.0	12.50%
SMCC	Filler	553.6	39.54%	580.7	48.39%
Aerosil 200	Glidant	14.0	1.00%	12.0	1.00%
Magnesium stearate	Lubricant	7.0	0.50%	6.0	0.50%
Core Tablet Weight:		1400.00	100.00%	1200.00	100.00%

Table 60: Tablet Composition 77

Component	Function	Tablet Composition 77	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	25.0	1.79%
Sodium Caprate	Absorption enhancer	500.0	35.71%
HPMC	Binder	15.6	1.11%
SMCC	Filler	548.4	39.17%
Sorbitol	Filler	150.0	10.71%
Crospovidone	Disintegrant	140.0	10.00%
Aerosil 200	Glidant	14.0	1.00%
Magnesium stearate	Lubricant	7.0	0.50%
Core Tablet Weight:		1400.00	100.00

Table 61: Tablet Composition 78

Component	Function	Tablet Composition 78	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	25.0	1.79%
Sodium Caprate	Absorption enhancer	500.0	35.71%
HPMC	Binder	15.6	1.11%
Starch	Filler	250.0	17.86%
SMCC	Filler	298.4	21.31%
Sorbitol	Filler	150.0	10.71%
Crospovidone	Disintegrant	140.0	10.00%
Aerosil 200	Glidant	14.0	1.00%
Magnesium stearate	Lubricant	7.0	0.50%
Core Tablet Weight:		1400.00	100.00%

Table 62: Tablet Composition 79

Component	Function	Tablet Composition 79	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	25.0	1.79%
Sodium Caprate	Absorption enhancer	500.0	35.71%
HPMC	Binder	15.6	1.11%
Mannitol	Filler	250.0	17.86%
SMCC	Filler	298.4	21.31%
Sorbitol	Filler	150.0	10.71%
Crospovidone	Disintegrant	140.0	10.00%
Aerosil 200	Glidant	14.0	1.00%
Magnesium stearate	Lubricant	7.0	0.50%
Core Tablet Weight:		1400.00	100.00%

Table 63: Tablet Composition 80

Component	Function	Tablet Composition 80	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	25.0	1.79%
Sodium Caprate	Absorption enhancer	500.0	35.71%
HPMC	Binder	14.9	1.06%
Sorbitol	Filler	214.3	15.31%
SMCC	Filler	550.4	39.31%
Crospovidone	Disintegrant	84.9	6.06%
Aerosil 200	Glidant	7.0	0.50%
Magnesium stearate	Lubricant	3.5	0.25%
Core Tablet Weight:		1400.00	100.00%

Table 64: Tablet Composition 81

Component	Function	Tablet Composition 81	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	25.0	1.79%
Sodium Caprate	Absorption enhancer	500.0	35.71%
HPMC	Binder	13.0	0.93%
Sorbitol	Filler	125.0	8.93%
SMCC	Filler	643.5	45.96%
Crospovidone	Disintegrant	83.0	5.93%
Aerosil 200	Glidant	7.0	0.50%
Magnesium stearate	Lubricant	3.5	0.25%
Core Tablet Weight:		1400.00	100.00%

Table 65: Tablet Composition 82

Component	Function	Tablet Composition 82	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	25.0	1.79%
Sodium Caprate	Absorption enhancer	500.0	35.71%
HPMC	Binder	13.0	0.93%
Dicalcium phosphatre	Filler	125.0	8.93%
SMCC	Filler	643.5	45.96%
Crospovidone	Disintegrant	83.0	5.93%
Aerosil 200	Glidant	7.0	0.50%
Magnesium stearate	Lubricant	3.5	0.25%
Core Tablet Weight:		1400.00	100.00%

Table 66: Tablet Composition 83

Component	Function	Tablet Composition 83	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	25.0	2.08%
Sodium Caprate	Absorption enhancer	500.0	41.67%
HPMC	Binder	13.0	1.08%
Dicalcium phosphatre	Filler	125.0	10.42%
SMCC	Filler	443.5	36.96%
Crospovidone	Disintegrant	83.0	6.92%
Aerosil 200	Glidant	7.0	0.58%
Magnesium stearate	Lubricant	3.5	0.29%
Core Tablet Weight:		1200.00	100.00%

Table 67: Tablet Compositions 84 and 85

Component	Function	Tablet Composition 84		Tablet Composition 85	
		Quantity per Unit (mg)	% (w/w)	Quantity per Unit (mg)	% (w/w)
Core Tablet					
Peptide of SEQ ID NO: 1	Active ingredient	50.0	3.85%	10.0	0.77%
Sodium Caprate	Absorption enhancer	500.0	38.46%	500.0	38.46%
HPMC	Binder	10.2	0.78%	10.2	0.78%
Crospovidone	Disintegrant	65.0	5.00%	65.0	5.00%
Sorbitol	Filler	150.0	11.54%	150.0	11.54%
SMCC	Filler	517.3	39.79%	557.3	42.87%
Aerosil 200	Glidant	1.0	0.08%	1.0	0.08%
Magnesium stearate	Lubricant	6.5	0.50%	6.5	0.50%
Core Tablet Weight:		1300.00	100.00%	1300.00	100.00%
Coated Tablet					
Subcoat					
Coating powder Opadry® QX	Subcoat coating layer	39.00	3.00%	39.00	3.00%
Purified water	Process aid	q.s.		q.s.	
Functional Coat					
Coating powder Acryl-Eze® Yellow	Functional coating layer	104.0		104.0	
Triethyl citrate	Plasticizer	10.4		10.4	
Purified water	Process aid	q.s.	NA	q.s.	NA
Coated Tablet Weight:		1453.4		1453.4	

Table 68: Tablet Compositions 86 to 88

Component	Function	Tablet Composition 86 (87)		Tablet Composition 88	
		Quantity per Unit (mg)	% (w/w)	Quantity per Unit (mg)	% (w/w)
Core Tablet					
Peptide of SEQ ID NO: 1	Active ingredient	50.0	3.85%	10.0	0.77%
Sodium Caprate	Absorption enhancer	500.0	38.46%	500.0	38.46%
HPMC	Binder	10.2	0.78%	10.2	0.78%
Crospovidone	Disintegrant	65.0	5.00%	65.0	5.00%
Mannitol	Filler	139.0	10.69%	139.0	10.69%
SMCC	Filler	528.3	40.64%	568.3	43.72%
Aerosil 200	Glidant	1.0	0.08%	1.0	0.08%
Magnesium stearate	Lubricant	6.5	0.50%	6.5	0.50%
Core Tablet Weight:		1300.00	100.00%	1300.00	100.00%
Coated Tablet					
Subcoat					
Coating powder Opadry® QX	Subcoat coating layer	39.00	3.00%	39.00	3.00%
Purified water	Process aid	q.s.		q.s.	
Functional Coat					
Coating powder Acryl-Eze® Yellow	Functional coating layer	104.0 (153.4)	8.00% (11.80%)	104.0	8.00%
Triethyl citrate	Plasticizer	10.4 (15.3)	0.80% (1.12%)	10.4	0.80%
Purified water	Process aid	q.s.	NA	q.s.	NA
Coated Tablet Weight:		1453.4 (1507.7)		1453.4	

Table 69: Tablet Composition 89

Component	Function	Tablet Composition 89	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	50.0	3.85%
Sodium Caprate	Absorption enhancer	500.0	38.46%
HPMC	Binder	7.6	0.59%
Mannitol	Filler	139.0	10.69%
SMCC	Filler	518.9	39.91%
Crospovidone	Disintegrant	65.0	5.00%
Aerosil 200	Glidant	13.0	1.00%
Magnesium stearate	Lubricant	6.5	0.50%
Core Tablet Weight:		1300.00	100.00%

Table 70: Tablet Compositions 90 and 91

Component	Function	Tablet Composition 90 (91)	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	50.0	3.85%
Sodium Caprate	Absorption enhancer	500.0	38.46%
MCC	Filler	17.1	1.31%
HPMC	Binder	12.2	0.59%
Mannitol	Filler	139.0	10.69%
SMCC	Filler	466.7	35.90%
Crospovidone	Disintegrant	95.5	7.35%
Aerosil 200	Glidant	13.0	1.00%
Magnesium stearate	Lubricant	6.5	0.50%
Core Tablet Weight:		1300.00	100.00%
Coated Tablet			
Subcoat			
Coating powder Opadry® QX	Subcoat coating layer	39.00	3.00%
Purified water	Process aid	q.s.	
Functional Coat			
Coating powder Acryl-Eze® Yellow	Functional coating layer	104.0 (153.4)	8.00% (11.80%)
Triethyl citrate	Plasticizer	10.4 (15.3)	0.80% (1.12%)
Purified water	Process aid	q.s.	NA
Coated Tablet Weight:		1453.4 (1507.7)	

Table 71: Tablet Compositions 92 and 93

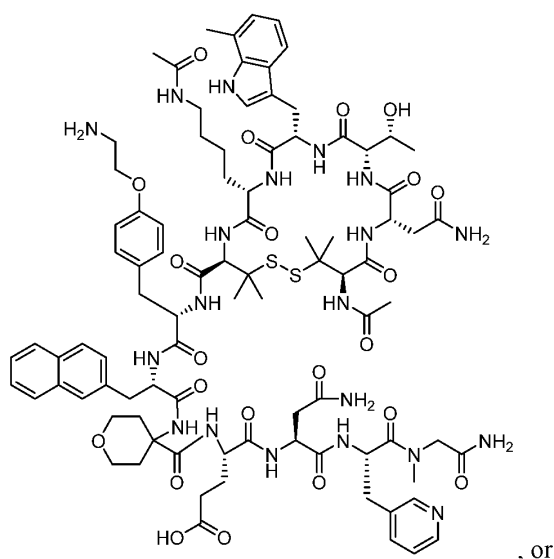
Component	Function	Tablet Composition 92 (93)	
		Quantity per Unit (mg)	% (w/w)
Core Tablet			
Peptide of SEQ ID NO: 1	Active ingredient	50.0	3.85%
Sodium Caprate	Absorption enhancer	500.0	38.46%
MCC	Filler	16.5	1.27%
HPMC	Binder	11.5	0.89%
Mannitol	Filler	139.0	10.69%
SMCC	Filler	498.5	38.35%
Crospovidone	Disintegrant	65.0	5.00%
Aerosil 200	Glidant	13.0	1.00%
Magnesium stearate	Lubricant	6.5	0.50%
Core Tablet Weight:		1300.00	100.00%
Coated Tablet			
Subcoat			
Coating powder Opadry® QX	Subcoat coating layer	39.00	3.00%
Purified water	Process aid	q.s.	
Functional Coat			
Coating powder Acryl-Eze® Yellow	Functional coating layer	104.0 (153.4)	8.00% (11.80%)
Triethyl citrate	Plasticizer	10.4 (15.3)	0.80% (1.12%)
Purified water	Process aid	q.s.	NA
Coated Tablet Weight:		1453.4 (1507.7)	

[0512] In addition, each reference, including all of the U.S. patents, U.S. patent application publications, U.S. patent applications, foreign patents, foreign patent applications and non-patent publications referred to in this specification are incorporated herein by reference, in their entirety, to the extent not inconsistent with the present description. Where a conflict exists between the instant application and a reference provided herein, the instant application shall dominate.

ASPECTS OF THE PRESENT INVENTION

[0513] In one aspect, the present invention relates to a crystalline form of a hydrochloride salt of a compound of Formula (I): Ac-[Pen]*-N-T-[W(7-Me)]-[Lys(Ac)]-[Pen]*-Phe[4-(2-

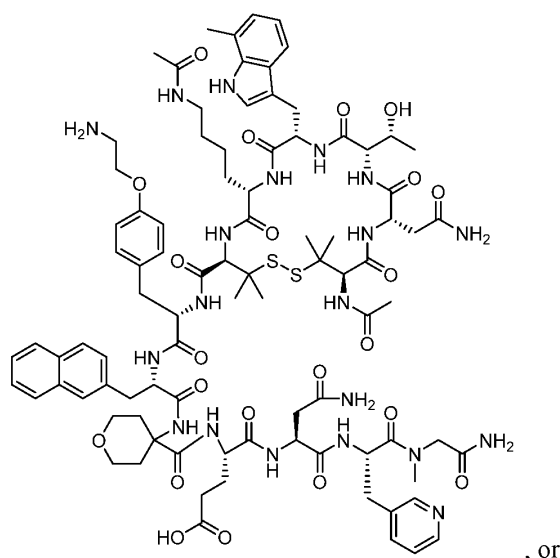
aminoethoxy)]-[2-Nal]-[THP]-E-N-[3-Pal]-Sarc-NH₂ (in which [Pen]*-[Pen]* form a disulfide bond), having the structure:



a solvate thereof.

[0514] In other aspects of the present invention, the crystalline hydrochloride salt is a hemi hydrochloride salt. In another aspects of the present invention, crystalline hydrochloride is further characterized by an X-ray powder diffraction pattern substantially as depicted in FIG. 2. In another aspect of the present invention, the X-ray powder diffraction pattern displays at least three measured 2 theta peaks from: 4.2920, 6.9201, 7.6600, 8.5693, 9.2667, 9.9817, 10.7256, 11.5429, 11.9937, 13.0633, 13.3317, 13.9650, 14.7879, 15.8430, 17.1481, 17.6468, 18.1402, 18.6158, 19.3291, 20.4899, 20.7090, or 21.7813 +/- 0.2 degrees two theta. In another aspect of the present invention, the X-ray powder diffraction pattern displays at least four measured 2 theta peaks from: 4.2920, 6.9201, 7.6600, 8.5693, 9.2667, 9.9817, 10.7256, 11.5429, 11.9937, 13.0633, 13.3317, 13.9650, 14.7879, 15.8430, 17.1481, 17.6468, 18.1402, 18.6158, 19.3291, 20.4899, 20.7090, or 21.7813 +/- 0.2 degrees two theta. In another aspect, the crystalline form produces an X-ray powder diffraction pattern which comprises peaks at 6.9, 7.7, and 9.3 degrees two theta +/- 0.2 degrees two theta. In another aspects of the invention, the crystalline form produces an X-ray powder diffraction pattern which comprises peaks at 6.9, 7.7, 8.6, and 9.3 degrees two theta +/- 0.2 degrees two theta.

[0515] In another aspect, the present invention relates to a crystalline form of a compound of Formula (I), which is Ac-[Pen]*-N-T-[W(7-Me)]-[Lys(Ac)]-[Pen]*-Phe[4-(2-aminoethoxy)]-[2-Nal]-[THP]-E-N-[3-Pal]-Sarc-NH₂ (in which [Pen]*-[Pen]* form a disulfide bond), having the structure:



a pharmaceutically acceptable salt thereof, or a solvate of the foregoing.

[0516] In some embodiments, the crystalline form is a crystalline form of the pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof. In some embodiments, the crystalline form is a crystalline form of the pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof. In some embodiments, the crystalline form of the pharmaceutically acceptable salt, or a solvate thereof, is characterized as having an X-ray powder diffraction (XRPD) pattern comprising peaks at angles two of 4.2, 6.9, 7.6, and 9.2 degrees two theta +/- 0.2 degrees two theta.

[0517] In some embodiments, the crystalline form of the pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, is a crystalline acetate salt of the compound of Formula (I) or a solvate thereof. In some embodiments, the crystalline form of the pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, is a crystalline hydrochloride salt of the compound of Formula (I) or a solvate thereof. In some embodiments, the crystalline form of the pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, is a crystalline glutarate salt of the compound of Formula (I) or a solvate thereof. In some embodiments, the crystalline form of the pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, is a crystalline glycolate salt of the compound of Formula (I) or a solvate thereof.

[0518] In some embodiments, the crystalline form of the pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, is

[0519] In some embodiments, the crystalline form of the pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, is a crystalline bis-hydrochloride salt of the compound of Formula (I) or a solvate thereof. In some embodiments, the crystalline form of the

pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, is a crystalline fumarate salt of the compound of Formula (I) or a solvate thereof. In some embodiments, the crystalline form of the pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, is a crystalline mesylate salt of the compound of Formula (I). In some embodiments, the crystalline form of the pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, is a crystalline sulfate salt of the compound of Formula (I) or a solvate thereof. In some embodiments, the crystalline form of the pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, is a crystalline citrate salt of the compound of Formula (I) or a solvate thereof.

[0520] In some embodiments, the crystalline pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, is characterized as having a XRPD pattern substantially as shown in FIG. 1, FIG. 2, FIG. 3, FIG. 7, FIG. 15, FIG. 18, FIG. 21, FIG. 24, FIG. 26, FIG. 28, or FIG. 29. In other embodiments, the crystalline pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, having a DSC graph or SDT thermogram substantially as shown in FIG. 5, FIG. 9, FIG. 17, FIG. 19, FIG. 22, FIG. 25, or FIG. 27. In some embodiments, the crystalline pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, is characterized as having: (i) endotherm peaks at about 80.7 °C and/or about 240.7 °C, as determined by DSC; (ii) endotherm peaks at about 81.4 °C as determined by DSC; (iii) endotherm peaks at about 79.5 °C and/or about 235.3 °C, as determined by DSC; (iv) an endotherm peak at about 65.3 °C, as determined by DSC; (v) an endotherm peak at about 224.1 °C, as determined by SDT; (vi) an endotherm peak at about 237.0 °C, as determined by SDT; (vii) an endotherm peak at about 242.0 °C, as determined by SDT; or (viii) an endotherm peak at about 255.0 °C, as determined by SDT.

[0521] In some embodiments, the crystalline pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, is characterized as having a TGA graph or SDT thermogram substantially as shown in FIG. 4, FIG. 8, FIG. 16, FIG. 19, FIG. 22, FIG. 25, FIG. 27, or FIG. 30.

[0522] In some embodiments, the crystalline pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, is characterized as having: (i) a weight loss of about 5.8% from about 26.5 °C to about 150.0 °C, as determined by TGA; (ii) a weight loss of about 5.6% from about 26.5 °C to about 160.0 °C, as determined by TGA; (iii) a weight loss of about 11.3% from about 26.5 °C to about 190.0 °C, as determined by TGA; (iv) a weight loss of about 4.4% from about 26.5 °C to about 110.0 °C, as determined by TGA; (v) a weight loss of about 6.4% from about 26.5 °C to about 125.0 °C, as determined by SDT; (vi) a weight loss of about 5.1% from about 26.5 °C to about 100.0 °C, as determined by SDT; (vii) a weight loss

of about 5.4% from about 26.5 °C to about 80.0 °C, as determined by SDT; or (viii) a weight loss of about 4.4% from about 26.5 °C to about 80.0 °C, as determined by SDT.

[0523] In some embodiments, the crystalline pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, the crystalline form is characterized as having a DVS graph substantially as shown in FIG. 6, FIG. 10, FIG. 20, FIG. 23, or FIG. 32.

[0524] In some embodiments, the crystalline pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, comprises a cationic form of the compound of Formula (I) and a pharmaceutically acceptable anion, wherein the molar equivalents of the pharmaceutically acceptable anion relative to one mole of the compound of Formula (I) is from about 0.2 to about 2.0.

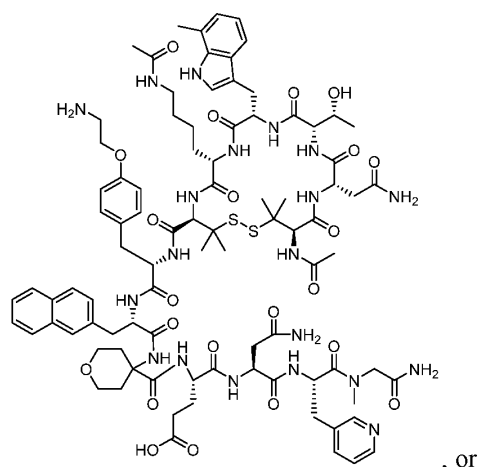
[0525] In some embodiments, the crystalline pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, is a crystalline form of a free base of the compound of Formula (I). In some embodiments, the crystalline form of a free base of the compound of Formula (I) is characterized as having an XRPD pattern comprising peaks at angles two theta of 3.3, 5.8, 6.5, 6.8, 7.7, 8.3, 9.1, 9.6, 10.2, 11.1, 12.4, 12.9, 13.3, 14.0, 14.8, 15.4, 16.0, 17.3, 18.0, 18.5, 18.9, 19.4, 20.0, and 20.5 degrees two theta +/- 0.2 degrees two theta. In certain embodiments, the crystalline form of a free base of the compound of Formula (I) is characterized as having an XRPD pattern substantially as shown in FIG. 11.

[0526] In some embodiments, the crystalline form of a free base of the compound of Formula (I) is characterized as having a DSC graph substantially as shown in FIG. 13.

[0527] In some embodiments, the crystalline form of a free base of the compound of Formula (I) is characterized as having endotherm peaks at about 71.0 °C and/or about 130.2 °C, as determined by DSC. In some embodiments, the crystalline form of a free base of the compound of Formula (I) is characterized as having a TGA graph substantially as shown in FIG. 12. In some embodiments, the crystalline form of a free base of the compound of Formula (I) is characterized as having a weight loss of about 3.7% from about 26.5 °C to about 70.0 °C and a weight loss of about 2.7% from 70.0 °C to about 170.0 °C, as determined by TGA. In some embodiments, the crystalline form of a free base of the compound of Formula (I) is characterized as having a DVS graph substantially as shown in FIG. 14.

[0528] In other aspects the present invention relates to a pharmaceutical composition which comprises a therapeutically effective amount of a crystalline hydrochloride salt or solvate thereof and a pharmaceutically acceptable excipient.

[0529] In other aspects the present invention relates to a pharmaceutical composition which comprises a hydrochloride salt of a compound of Formula (I) having the structure:



a solvate thereof, in an amount of from about 0.1% to about 15% (w/w) of the composition; and one or more pharmaceutically acceptable excipients.

[0530] In other aspects of the present invention, in the pharmaceutical composition: the hydrochloride salt of the compound of Formula (I) or solvate thereof is a crystalline hydrochloride salt. In another aspect of the present invention, the dose range of the hydrochloride salt of the compound of Formula (I) or solvate thereof is from about 1 mg to about 1000 mg, where the amount of HCl salt is defined in terms of an equivalent amount of a free base form of the compound of Formula (I). In another aspect of the present invention, a dose range of the hydrochloride salt of the compound of Formula (I) or solvate thereof is from about 5 mg to about 300 mg, where the amount of HCl salt is defined in terms of an equivalent amount of a free base form of the compound of Formula (I). In another aspect of the present invention, the dose of the hydrochloride salt of the compound of Formula (I) or solvate thereof is about 5 mg, about 10 mg, about 25 mg, about 50 mg, about 75 mg, about 100 mg, and the like.

[0531] In another aspect of the present invention, the pharmaceutical composition further comprises a silicified microcrystalline cellulose. In another aspect of the present invention, the amount of the silicified microcrystalline cellulose is from about 65% to about 85% (w/w) of the composition. In another aspect of the present invention, the pharmaceutical composition further comprises one or more of alpha cellulose, beta cellulose, gamma cellulose, starch, modified-starch, sorbitol, mannitol, lactose, dextrose, sucrose, dibasic calcium phosphate, tribasic calcium phosphate, or calcium carbonate. In another aspect of the present invention, the pharmaceutical composition further comprises sorbitol, where: the amount of the sorbitol is from about 10% to about 15% (w/w) of the composition. In another aspect of the present invention, the pharmaceutical composition further comprises a disintegrant, where: the disintegrant is a cross-linked carboxymethyl cellulose (croscarmellose), a starch glycolate, a polyvinyl pyrrolidone, a sago starch, psyllium husk, croscarmellose sodium or crospovidone a silicate, or a soy

polysaccharide; the amount of the disintegrant is from about 3% to about 8% (w/w) of the composition. In another aspect of the present invention, the pharmaceutical composition further comprises a silica (e.g., Aerosil 200), where the amount of the silica (e.g., Aerosil 200) is from about 0.3% to about 0.7% (w/w) of the composition. In another aspect of the present invention, the pharmaceutical composition further comprises a lubricant, where the amount of the lubricant is from about 0.3% to about 0.7% (w/w) of the composition.

[0532] In another aspect of the present invention, the composition is a tablet composition or a capsule composition.

[0533] In another aspect the pharmaceutical composition comprises: (i) the hydrochloride salt of the compound of Formula (I) or solvate thereof in an amount of from about 0.2% to about 15% (w/w) of the composition; (ii) a silicified microcrystalline cellulose in an amount of from about 66.5% to about 81.3% (w/w) of the composition; (iii) sorbitol in an amount of about 12.5% (w/w) of the composition; (iv) a disintegrant in an amount of about 5% (w/w) of the composition; (v) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; and (vi) a lubricant in an amount of about 0.5% (w/w) of the composition.

[0534] In another aspect the pharmaceutical composition comprises: (i) the hydrochloride salt of the compound of Formula (I) or solvate thereof in an amount of about 1% (w/w) of the composition; (ii) a silicified microcrystalline cellulose in an amount of about 80.5% (w/w) of the composition; (iii) sorbitol in an amount of about 12.5% (w/w) of the composition; (iv) crospovidone in an amount of about 5% (w/w) of the composition; (v) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; and (vi) magnesium stearate in an amount of about 0.5% (w/w) of the composition.

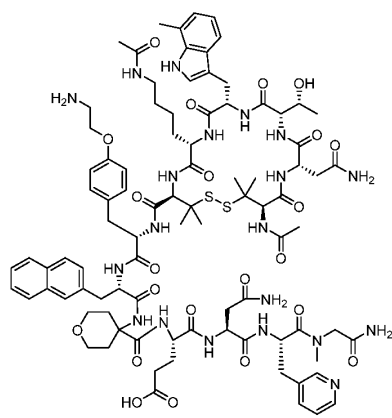
[0535] In another aspect the pharmaceutical composition comprises: (i) the hydrochloride salt of the compound of Formula (I) or solvate thereof in an amount of about 2.5% (w/w) of the composition; (ii) a silicified microcrystalline cellulose in an amount of about 79% (w/w) of the composition; (iii) sorbitol in an amount of about 12.5% (w/w) of the composition; (iv) crospovidone in an amount of about 5% (w/w) of the composition; (v) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; and (vi) magnesium stearate in an amount of about 0.5% (w/w) of the composition.

[0536] In another aspect the pharmaceutical composition comprises: (i) the hydrochloride salt of the compound of Formula (I) or solvate thereof in an amount of about 10% (w/w) of the composition; (ii) a silicified microcrystalline cellulose in an amount of about 71.5% (w/w) of the composition; (iii) sorbitol in an amount of about 12.5% (w/w) of the composition; (iv) crospovidone in an amount of about 5% (w/w) of the composition; (v) a silica (e.g., Aerosil 200)

in an amount of about 0.5% (w/w) of the composition; and (vi) magnesium stearate in an amount of about 0.5% (w/w) of the composition.

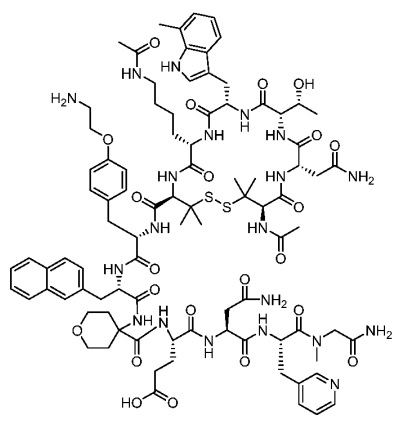
[0537] In another aspect the pharmaceutical composition comprises: A subcoating of a PVA-PEG graft co-polymer disposed over the composition, where the subcoating is present in an amount from about 1% to about 5% (w/w);

[0538] In another aspect the present invention relates to a tablet, capsule or dosage form which comprises: [1] a core or core tablet comprises: a hydrochloride salt form of a compound of Formula (I) having the structure:



or a solvate thereof; and pharmaceutically acceptable excipients; and [2] at least one overcoat over the core tablet formed from pharmaceutically acceptable excipients.

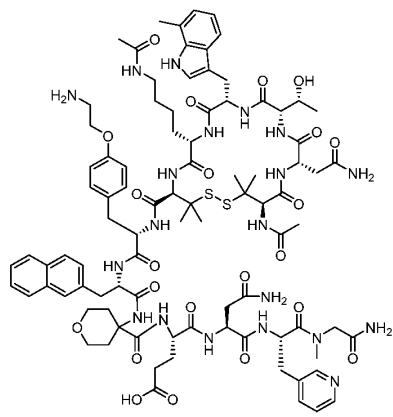
[0539] In another aspect the present invention relates to a tablet or dosage form comprises: [1] a core or core tablet comprises: a hydrochloride salt form of a compound of Formula (I) having the structure:



or a solvate thereof; and pharmaceutically acceptable excipients; and [2] at least one overcoat over the core tablet formed from pharmaceutically acceptable excipients.

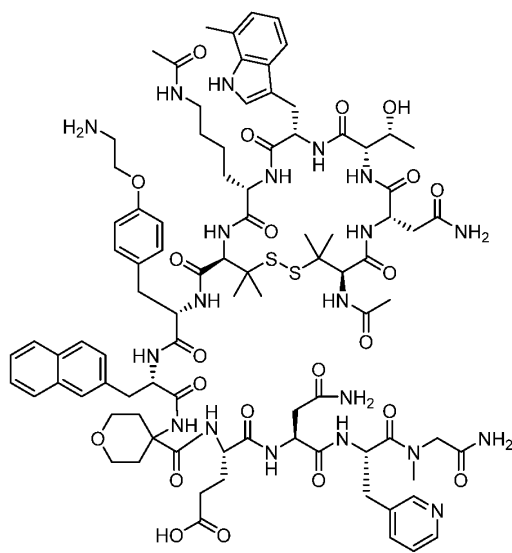
[0540] In another aspect, the tablet or dosage form where: the hydrochloride salt of a compound of Formula (I) is a crystalline form; and pharmaceutically acceptable excipients are selected from disintegrants, glidants, lubricants, film coatings or any combination thereof.

[0541] In another aspect, the present invention relates to a process of making a tablet or dosage form, comprises steps of: [1] forming a core or core tablet by blending and compressing a pharmaceutical composition mixture comprises: a hydrochloride salt form of a compound of Formula (I) having the structure:



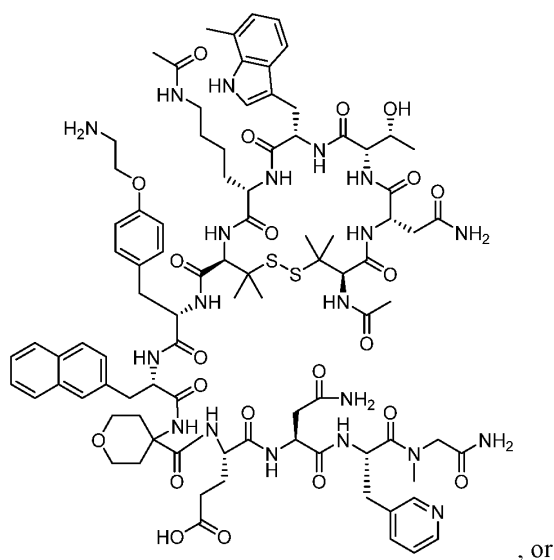
or a solvate thereof; and pharmaceutically acceptable excipients to form a tablet core composition; and [2] overcoating by applying at least one overcoat over the core tablet formed from pharmaceutically acceptable excipients.

[0542] In another aspect, the present invention relates to a tablet formed by the process of: forming a mixture which comprises a hydrochloride salt of a compound of Formula (I) having the structure:



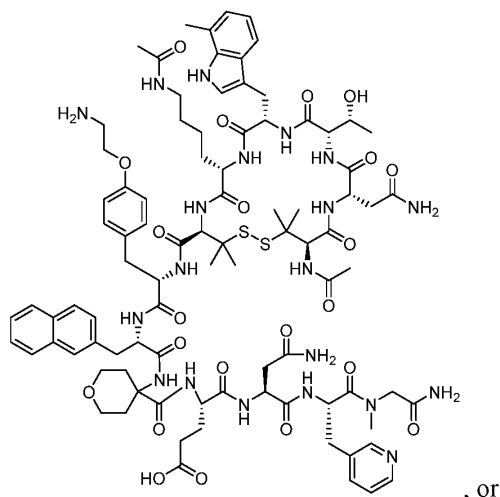
or a solvate thereof, a silicified microcrystalline cellulose, sorbitol, croscopvidone, and a silica (e.g., Aerosil 200); adding magnesium stearate to the mixture; compressing the mixture; and applying a subcoating to the mixture, to form the tablet.

[0543] In another aspect, the present invention relates to a method which comprises: forming a mixture which comprises a hydrochloride salt of a compound of Formula (I) having the structure:



a solvate thereof, a silicified microcrystalline cellulose, sorbitol, crospovidone, and a silica (e.g., Aerosil 200); adding magnesium stearate to the mixture; compressing the mixture; and applying a subcoating to the mixture, to form a tablet.

[0544] In another aspect, the present invention relates to a pharmaceutical composition which comprises a hydrochloride salt of a compound of Formula (I) having the structure:



a solvate thereof, in an amount of from about 0.1% to about 15% (w/w) of the composition; an absorption enhancer in an amount of from about 5% to about 50% (w/w) of the composition; and one or more pharmaceutically acceptable excipients.

[0545] In another aspect, the present invention relates to a pharmaceutical composition where: the hydrochloride salt of the compound of Formula (I) or solvate thereof is a crystalline hydrochloride salt. In another aspect, the present invention relates to a pharmaceutical composition where: the amount of the hydrochloride salt of the compound of Formula (I) or solvate thereof is from about 1 mg to about 1000 mg, where the amount of HCl salt is defined in terms of an equivalent amount of a free base form of the compound of Formula (I). In another aspect, the present invention relates to a pharmaceutical composition where: the amount of the hydrochloride salt of the compound of Formula (I) or solvate thereof is about 5 mg, about 10 mg, about 25 mg, about 50 mg, about 75 mg, about 100 mg. In another aspect, the present invention relates to a pharmaceutical composition where: absorption enhancer is sodium caprate, sodium caprylate, sodium palmitate, sodium stearate, sodium citrate, sodium salicylate, sodium salcaprozate (SNAC), a polyethylene glycol (PEG)-modified medium chain fatty acid triglyceride of capric and caprylic acid, sucrose laurate, or lauroyl-L-carnitine (LC).

[0546] In another aspect, the present invention relates to a pharmaceutical composition where: the amount of the absorption enhancer is from about 5% to about 40% (w/w) of the composition. In another aspect, the present invention relates to a pharmaceutical composition

where the pharmaceutical composition further comprises a microcrystalline cellulose. In another aspect, the present invention relates to a pharmaceutical composition where: the amount of the microcrystalline cellulose is from about 3% to about 5% (w/w) of the composition. In another aspect, the present invention relates to a pharmaceutical composition where the pharmaceutical composition further comprises sorbitol. In another aspect, the present invention relates to a pharmaceutical composition where: the amount of the sorbitol is from about 10% to about 15% (w/w) of the composition. In another aspect, the present invention relates to a pharmaceutical composition where the pharmaceutical composition further comprises a silicified microcrystalline cellulose. In another aspect, the present invention relates to a pharmaceutical composition where: the amount of the silicified microcrystalline cellulose is from about 30% to about 70% (w/w) of the composition.

[0547] In another aspect, the present invention relates to a pharmaceutical composition where the pharmaceutical composition further comprises a disintegrant, where the disintegrant is a cross-linked carboxymethyl cellulose (croscarmellose), a starch glycolate, a polyvinyl pyrrolidone, a sago starch, psyllium husk, croscarmellose sodium or crospovidone, a silicate, or a soy polysaccharide. In another aspect, the present invention relates to a pharmaceutical composition where: the amount of the disintegrant is from about 8% to about 12% (w/w) of the composition. In another aspect, the present invention relates to a pharmaceutical composition where: the amount of the disintegrant is from about 8% to about 15% (w/w) of the composition. In another aspect, the present invention relates to a pharmaceutical composition where: the amount of the disintegrant is about 8%, about 10%, about 12%, or about 15% (w/w) of the composition. In another aspect, the present invention relates to a pharmaceutical composition where: the composition further comprises a silica (e.g., Aerosil 200), where the amount of the silica (e.g., Aerosil 200) is from about 0.5% to about 2% (w/w) of the composition. In another aspect, the present invention relates to a pharmaceutical composition where: the composition further comprises a lubricant. In another aspect, the present invention relates to a pharmaceutical composition where: the amount of the lubricant is from about 0.1% to about 0.5% (w/w) of the composition. In another aspect, the present invention relates to a pharmaceutical composition where: the composition is a tablet composition or a capsule composition.

[0548] In another aspect the present invention relates to a pharmaceutical composition which comprises (i) the hydrochloride salt of the compound of Formula (I) or solvate thereof in an amount of from about 0.1% to about 15% (w/w) of the composition, and (ii) the absorption enhancer sodium caprate in an amount of from about 5% to about 40% (w/w) of the composition; and a silicified microcrystalline cellulose.

[0549] In another aspect the present invention relates to the composition which comprises: (i) the hydrochloride salt of the compound of Formula (I) or solvate thereof in an amount of from about 0.5% to about 10% (w/w) of the composition; (ii) the absorption enhancer sodium caprate in an amount of about 5% to about 40% (w/w) of the composition; (iii) a microcrystalline cellulose in an amount of about 3.9% (w/w) of the composition; (iv) sorbitol in an amount of about 10.7% (w/w) of the composition; (v) a disintegrant in an amount of about 5% (w/w) of the composition; and (vi) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; (vii) a silicified microcrystalline cellulose in an amount of from about 30% to about 70% (w/w) of the composition; (viii) a disintegrant in an amount of about 5% (w/w) of the composition; (ix) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; and (x) a lubricant in an amount of about 0.25% (w/w) of the composition.

[0550] In another aspect the present invention relates to the composition comprises: (i) the hydrochloride salt of the compound of Formula (I) or solvate thereof in an amount of about 0.7% (w/w) of the composition; (ii) the absorption enhancer sodium caprate in an amount of about 35.7% (w/w) of the composition; (iii) a microcrystalline cellulose in an amount of about 3.9% (w/w) of the composition; (iv) sorbitol in an amount of about 10.7% (w/w) of the composition; (v) crospovidone in an amount of about 5% (w/w) of the composition; and (vi) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; (vii) a silicified microcrystalline cellulose in an amount of about 37.7% (w/w) of the composition; (viii) crospovidone in an amount of about 5% (w/w) of the composition; (ix) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; and (x) magnesium stearate in an amount of about 0.25% (w/w) of the composition.

[0551] In another aspect the present invention relates to the composition comprises: (i) the hydrochloride salt of the compound of Formula (I) or solvate thereof in an amount of about 1.8% (w/w) of the composition; (ii) the absorption enhancer sodium caprate in an amount of about 35.7% (w/w) of the composition; (iii) a microcrystalline cellulose in an amount of about 3.9% (w/w) of the composition; (iv) sorbitol in an amount of about 10.7% (w/w) of the composition; (v) crospovidone in an amount of about 5% (w/w) of the composition; and (vi) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; (vii) a silicified microcrystalline cellulose in an amount of about 36.6% (w/w) of the composition; (viii) crospovidone in an amount of about 5% (w/w) of the composition; (ix) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; and (x) magnesium stearate in an amount of about 0.25% (w/w) of the composition.

[0552] In another aspect the present invention relates to the composition which comprises: (i) the hydrochloride salt of the compound of Formula (I) or solvate thereof in an amount of

about 0.7% (w/w) of the composition; (ii) the absorption enhancer sodium caprate in an amount of about 21.4% (w/w) of the composition; (iii) a microcrystalline cellulose in an amount of about 3.9% (w/w) of the composition; (iv) sorbitol in an amount of about 10.7% (w/w) of the composition; (v) crospovidone in an amount of about 5% (w/w) of the composition; and (vi) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; (vii) a silicified microcrystalline cellulose in an amount of about 52% (w/w) of the composition; (viii) crospovidone in an amount of about 5% (w/w) of the composition; (ix) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; and (x) magnesium stearate in an amount of about 0.25% (w/w) of the composition.

[0553] In another aspect the present invention relates to the composition which comprises: (i) the hydrochloride salt of the compound of Formula (I) or solvate thereof in an amount of about 1.8% (w/w) of the composition; (ii) the absorption enhancer sodium caprate in an amount of about 21.4% (w/w) of the composition; (iii) a microcrystalline cellulose in an amount of about 3.9% (w/w) of the composition; (iv) sorbitol in an amount of about 10.7% (w/w) of the composition; (v) crospovidone in an amount of about 5% (w/w) of the composition; and (vi) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; (vii) a silicified microcrystalline cellulose in an amount of about 50.9% (w/w) of the composition; (viii) crospovidone in an amount of about 5% (w/w) of the composition; (ix) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; and (x) magnesium stearate in an amount of about 0.25% (w/w) of the composition.

[0554] In another aspect the present invention relates to the composition which comprises: (i) the hydrochloride salt of the compound of Formula (I) or solvate thereof in an amount of about 7.1% (w/w) of the composition; (ii) the absorption enhancer sodium caprate in an amount of about 35.7% (w/w) of the composition; (iii) a microcrystalline cellulose in an amount of about 3.9% (w/w) of the composition; (iv) sorbitol in an amount of about 10.7% (w/w) of the composition; (v) crospovidone in an amount of about 5% (w/w) of the composition; and (vi) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; (vii) a silicified microcrystalline cellulose in an amount of about 31.3% (w/w) of the composition; (viii) crospovidone in an amount of about 5% (w/w) of the composition; (ix) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; and (x) magnesium stearate in an amount of about 0.25% (w/w) of the composition.

[0555] In another aspect the present invention relates to the composition which comprises: (i) the hydrochloride salt of the compound of Formula (I) or solvate thereof in an amount of about 1.8% (w/w) of the composition; (ii) the absorption enhancer sodium caprate in an amount of about 7.1% (w/w) of the composition; (iii) a microcrystalline cellulose in an amount of about

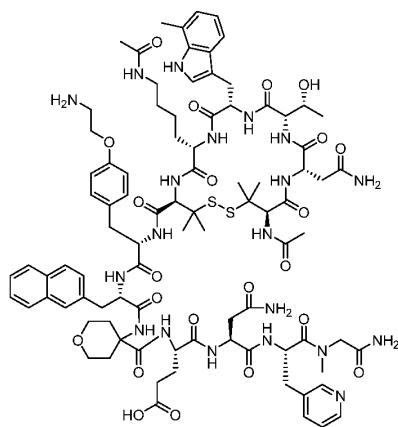
3.9% (w/w) of the composition; (iv) sorbitol in an amount of about 10.7% (w/w) of the composition; (v) crospovidone in an amount of about 5% (w/w) of the composition; and (vi) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; (vii) a silicified microcrystalline cellulose in an amount of about 65.2% (w/w) of the composition; (viii) crospovidone in an amount of about 5% (w/w) of the composition; (ix) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; and (x) magnesium stearate in an amount of about 0.25% (w/w) of the composition.

[0556] In another aspect the present invention relates to the composition which comprises: (i) the hydrochloride salt of the compound of Formula (I) or solvate thereof in an amount of about 1.8% (w/w) of the composition, (ii) the absorption enhancer sodium caprate in an amount of about 35.7% (w/w) of the composition; (iii) a microcrystalline cellulose in an amount of about 3.9% (w/w) of the composition; (iv) sorbitol in an amount of about 10.7% (w/w) of the composition; (v) crospovidone in an amount of about 5% (w/w) of the composition; and (vi) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; (vii) a silicified microcrystalline cellulose in an amount of about 36.6% (w/w) of the composition; (viii) crospovidone in an amount of about 5% (w/w) of the composition; (ix) a silica (e.g., Aerosil 200) in an amount of about 0.5% (w/w) of the composition; and (x) magnesium stearate in an amount of about 0.25% (w/w) of the composition.

[0557] In another aspect the present invention relates to a subcoating which comprises: PVA-PEG graft co-polymer disposed over the composition. In another aspect the invention, the subcoating is present in an amount from about 1% to about 5% (w/w).

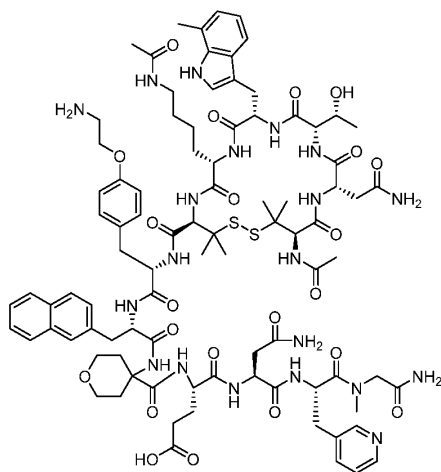
[0558] In another aspect the present invention relates to a subcoating which comprises: an enteric coating disposed over the subcoating. In another aspect of the invention, the enteric coating is a methacrylic acid co-polymer. In another aspect of the invention, the enteric coating is present in an amount from about 2% to about 15% (w/w).

[0559] In another aspect the present invention relates to a tablet, capsule or dosage form which comprises: [1] a core or core tablet which comprises: a granulated mixture formed from: (i) a hydrochloride salt form of a compound of Formula (I) having the structure:



or a solvate thereof, (ii) absorption enhancer; and (iii) optionally pharmaceutically acceptable excipients; wherein the mixture is blended and then compressed together to form a Core or Core Tablet; and [2] at least one overcoat over the core tablet formed from pharmaceutically acceptable excipients.

[0560] In another aspect the present invention relates to a tablet or dosage form which comprises: [1] a core or core tablet comprises: (i) a granule composition formed from: a hydrochloride salt form of a compound of Formula (I) having the structure:



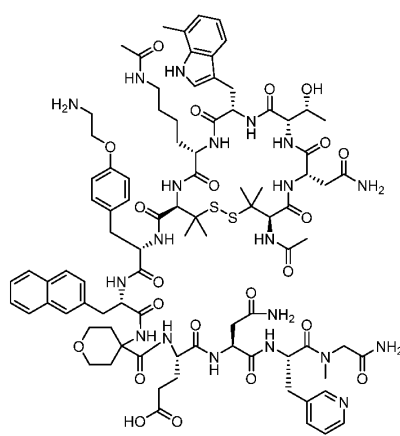
or a solvate thereof, (ii) absorption enhancer; and (iii) optionally pharmaceutically acceptable excipients; wherein the mixture is blended and then compressed together to form a Core or Core Tablet; and [2] at least one overcoat over the core tablet formed from pharmaceutically acceptable excipients.

[0561] In another aspect the present invention relates to tablet or dosage form where: the hydrochloride salt of a compound of Formula (I) is a crystalline form; the absorption enhancer is sodium caprate; the pharmaceutically acceptable excipients defined in 1[a] and 1[b],

respectively are selected from disintegrants, glidants, lubricants, film coatings or any combination thereof.

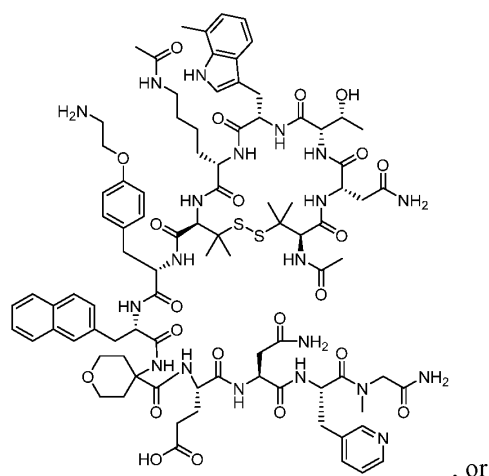
[0562] In another aspect the present invention relates to a tablet or dosage form where the at least one overcoat over the core tablet of [2] is comprised of: a sub coat over the core tablet to form a subcoated tablet; and an enteric coat is overcoated or coated over the subcoated tablet, where: each sub coat and function coat, respectively, are formed from pharmaceutically acceptable excipients.

[0563] In another aspect the present invention relates to a process of making a tablet or dosage form, which comprises steps of forming a core or core tablet which comprises: (1) a hydrochloride salt form of a compound of Formula (I) having the structure:



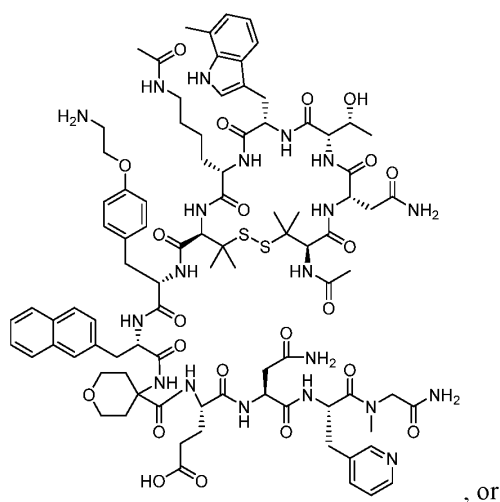
or a solvate thereof, (2) absorption enhancer; and (3) optionally pharmaceutically acceptable excipients; compressing the tablet core composition of step [2] to form a core or core tablet; overcoating by spraying or applying a subcoat to the core or core tablet to form a subcoated tablet; and finally applying another coating or over coating the subcoated tablet with a enteric coat; where: each sub coat and function coat, respectively, are formed from pharmaceutically acceptable excipients.

[0564] In another aspect the present invention relates to a tablet made by the process of: forming a mixture which comprises a hydrochloride salt of a compound of Formula (I) having the structure:



a solvate thereof, sodium caprate, a microcrystalline cellulose, sorbitol, crospovidone, and a silica (e.g., Aerosil 200), and a silicified microcrystalline cellulose and crospovidone to form a core tablet; applying a subcoating over the core tablet; and applying an enteric coating over the subcoating to form the tablet.

[0565] In another aspect the present invention relates to a method which comprises: forming a mixture which comprises a hydrochloride salt of a compound of Formula (I) having structure:



a solvate thereof, sodium caprate, a microcrystalline cellulose, sorbitol, crospovidone, and a silica (e.g., Aerosil 200); a silicified microcrystalline cellulose and crospovidone to form a core tablet; applying a subcoating over the core tablet; and applying an enteric coating over the subcoating to form a tablet.

[0566] Although the foregoing invention has been described in some detail by way of illustration and example for purposes of clarity of understanding, one of skill in the art will

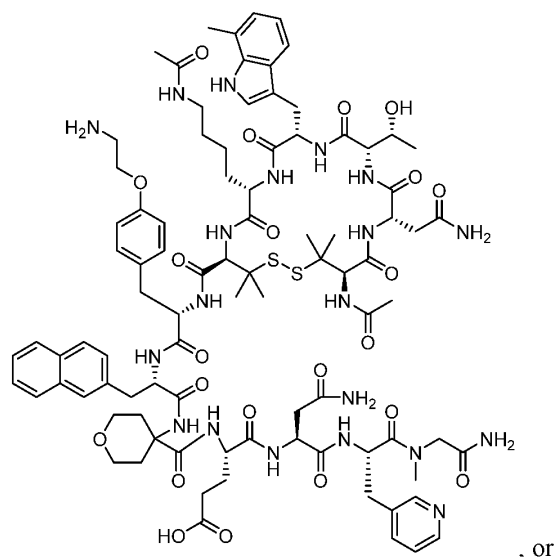
appreciate that certain changes and modifications can be practiced within the scope of the appended claims.

[0567] It is to be understood that the invention is not limited to the described aspects illustrated herein above and the right is reserved to the illustrated aspects and all modifications coming within the scope of the claims.

CLAIMS

What is claimed is:

1. A crystalline form of a compound of Formula (I) having the structure:



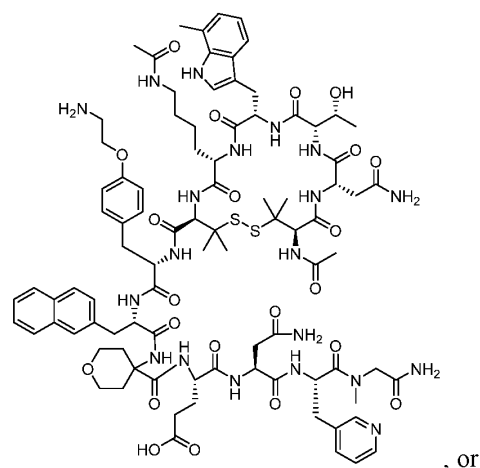
a pharmaceutically acceptable salt thereof, or a solvate of the foregoing.

2. The crystalline form of claim 1, wherein the crystalline form is a crystalline form of the pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof.
3. The crystalline form of claim 2, wherein the crystalline form of the pharmaceutically acceptable salt, or a solvate thereof, is characterized as having an X-ray powder diffraction (XRPD) pattern comprising peaks at angles two theta of 4.2, 6.9, 7.6, and 9.2 +/- 0.3 degrees two theta.
4. The crystalline form of claims 2 or 3, wherein the crystalline form is a crystalline acetate salt of the compound of Formula (I) or a solvate thereof.
5. The crystalline form of claims 2 or 3, wherein the crystalline form is a crystalline hydrochloride salt of the compound of Formula (I) or a solvate thereof.
6. The crystalline form of claims 2 or 3, wherein the crystalline form is a crystalline glutarate salt of the compound of Formula (I) or a solvate thereof.
7. The crystalline form of claims 2 or 3, wherein the crystalline form is a crystalline glycolate salt of the compound of Formula (I) or a solvate thereof.

8. The crystalline form of claims 2 or 3, wherein the crystalline form is a crystalline bis-hydrochloride salt of the compound of Formula (I) or a solvate thereof.
9. The crystalline form of claims 2 or 3, wherein the crystalline form is a crystalline fumarate salt of the compound of Formula (I) or a solvate thereof.
10. The crystalline form of claims 2 or 3, wherein the crystalline form is a crystalline mesylate salt of the compound of Formula (I).
11. The crystalline form of claims 2 or 3, wherein the crystalline form is a crystalline sulfate salt of the compound of Formula (I) or a solvate thereof.
12. The crystalline form of claims 2 or 3, wherein the crystalline form is a crystalline citrate salt of the compound of Formula (I) or a solvate thereof.
13. The crystalline form of any one of claims 2 to 12, wherein the crystalline form is characterized as having a XRPD pattern substantially as shown in FIG. 1, FIG. 2, FIG. 3, FIG. 7, FIG. 15, FIG. 18, FIG. 21, FIG. 24, FIG. 26, FIG. 28, or FIG. 29.
14. The crystalline form of any one of claims 2 to 11 or 13, wherein the crystalline form is characterized as having a DSC graph or SDT thermogram substantially as shown in FIG. 5, FIG. 9, FIG. 17, FIG. 19, FIG. 22, FIG. 25, or FIG. 27.
15. The crystalline form of any one of claims 2 to 11 or 13 to 14, wherein the crystalline form is characterized as having:
 - a. endotherm peaks at about 80.7 °C and/or about 240.7 °C, as determined by DSC;
 - b. endotherm peaks at about 81.4 °C as determined by DSC;
 - c. endotherm peaks at about 79.5 °C and/or about 235.3 °C, as determined by DSC;
 - d. an endotherm peak at about 65.3 °C, as determined by DSC;
 - e. an endotherm peak at about 224.0 °C, as determined by SDT;
 - f. an endotherm peak at about 237.0 °C, as determined by SDT;
 - g. an endotherm peak at about 242.1 °C, as determined by SDT; or
 - h. an endotherm peak at about 255.0 °C, as determined by SDT.
16. The crystalline form of any one of claims 2 to 11 or 13 to 15, wherein the crystalline form is characterized as having a TGA graph or SDT thermogram substantially as shown in FIG. 4, FIG. 8, FIG. 16, FIG. 19, FIG. 22, FIG. 25, FIG. 27, or FIG. 30.
17. The crystalline form of any one of claims 2 to 11 or 13 to 16, wherein the crystalline form is characterized as having:
 - a. a weight loss of about 5.8% from about 26.5 °C to about 150.0 °C, as determined by TGA;

- b. a weight loss of about 5.6% from about 26.5 °C to about 160.0 °C, as determined by TGA;
 - c. a weight loss of about 11.3% from about 26.5 °C to about 190.0 °C, as determined by TGA;
 - d. a weight loss of about 4.4% from about 26.5 °C to about 110.0 °C, as determined by TGA;
 - e. a weight loss of about 6.4% from about 26.5 °C to about 125.0 °C, as determined by SDT;
 - f. a weight loss of about 5.1% from about 26.5 °C to about 100.0 °C, as determined by SDT;
 - g. a weight loss of about 5.4% from about 26.5 °C to about 80.0 °C, as determined by SDT; or
 - h. a weight loss of about 4.4% from about 26.5 °C to about 80.0 °C, as determined by SDT.
18. The crystalline form of any one of claims 2 to 8 or 13 to 17, wherein the crystalline form is characterized as having a DVS graph substantially as shown in FIG. 6, FIG. 10, FIG. 20, FIG. 23, or FIG. 32.
19. The crystalline form of any one of claims 2 to 18, wherein the crystalline form of the pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, comprises a cationic form of the compound of Formula (I) and a pharmaceutically acceptable anion, wherein the molar equivalents of the pharmaceutically acceptable anion relative to one mole of the compound of Formula (I) is from about 0.2 to about 2.0.
20. The crystalline form of claim 1, wherein the crystalline form is a crystalline form of a free base of the compound of Formula (I).
21. The crystalline form of claim 20, wherein the crystalline form is characterized as having an XRPD pattern comprising two or more peaks at angles two theta selected from 3.3, 5.8, 6.5, 6.8, 7.7, 8.3, 9.1, 9.6, 10.2, 11.1, 12.4, 12.8, 13.3, 14.0, 14.8, 15.4, 16.0, 17.3, 18.0, 18.5, 18.9, 19.4, 20.0, and 20.5 +/- 0.2 degrees two theta.
22. The crystalline form of claim 20 or 21, wherein the crystalline form is characterized as having an XRPD pattern substantially as shown in FIG. 11.
23. The crystalline form of any one of claims 20 to 22, wherein the crystalline form is characterized as having a DSC graph substantially as shown in FIG. 13.

24. The crystalline form of any one of claims 20 to 23, wherein the crystalline form is characterized as having endotherm peaks at about 71.0 °C and/or about 130.2 °C, as determined by DSC.
25. The crystalline form of any one of claims 20 to 24, wherein the crystalline form is characterized as having a TGA graph substantially as shown in FIG. 12.
26. The crystalline form of any one of claims 20 to 25, wherein the crystalline form is characterized as having a weight loss of about 3.7% from about 26.5 °C to about 70.0 °C and a weight loss of about 2.7% from 70.0 °C to about 170.0 °C, as determined by TGA.
27. The crystalline form of any one of claims 20 to 26, wherein the crystalline form is characterized as having a DVS graph substantially as shown in FIG. 14.
28. A pharmaceutical composition comprising a crystalline form of a compound of Formula (I) having the structure:



a pharmaceutically acceptable salt thereof, or a solvate of the foregoing, and one or more pharmaceutically acceptable excipients.

29. The pharmaceutical composition of claim 28, wherein the crystalline form of the compound of Formula (I) or the pharmaceutically acceptable salt thereof, or a solvate thereof, is in an amount of from about 0.1% to about 60% (w/w) of the composition.
30. The pharmaceutical composition of claim 28 or 29, wherein the crystalline form of the compound of Formula (I) or the pharmaceutically acceptable salt thereof, or a solvate thereof, is in an amount of from about 0.1% to about 30% (w/w) of the composition.
31. The pharmaceutical composition of any one of claims 28 to 30, wherein the crystalline form of the compound of Formula (I) or the pharmaceutically acceptable salt thereof, or a solvate thereof, is characterized as having an XRPD pattern comprising peaks at angles two of 4.2, 6.9, 7.6, and 9.2 degrees two theta +/- 0.2 degrees two theta.

32. The pharmaceutical composition of any one of claims 28 to 31, wherein the crystalline form is a pharmaceutically acceptable salt of a compound of Formula (I), or a solvate thereof, and the pharmaceutically acceptable salt is selected from acetate salt, hydrochloride salt, fumarate salt, glutarate salt, glycolate salt, mesylate salt, sulfate salt, citrate salt, and bis-hydrochloride salt.
33. The pharmaceutical composition of claim 32, wherein the pharmaceutically acceptable salt of a compound of Formula (I) comprises a cationic form of the compound of Formula (I) and a pharmaceutically acceptable anion, wherein the molar equivalents of the pharmaceutically acceptable anion relative to one mole of the compound of Formula (I) is from about 0.2 to about 2.0.
34. The pharmaceutical composition of any one of claims 28 to 33, wherein the amount of the crystalline form of the compound of Formula (I) or the pharmaceutically acceptable salt, or a solvate thereof, is in a range of about 1 mg to about 1000 mg.
35. The pharmaceutical composition of any one of claims 28 to 34, wherein the amount of the crystalline pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, is in a range of about 25 mg to about 300 mg.
36. The pharmaceutical composition of claim 35, wherein the dose of the pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, is about 5 mg, about 10 mg, about 25 mg, about 50 mg, about 75 mg, about 100 mg, about 150 mg, about 200 mg, about 250 mg, or about 300 mg.
37. The pharmaceutical composition of any one of claims 28 to 36, wherein the composition further comprises a filler.
38. The pharmaceutical composition of claim 37, wherein the filler is silicified microcrystalline cellulose.
39. The pharmaceutical composition of claim 37 or 38, wherein the amount of filler is from about 25% to about 95% (w/w) of the composition, preferably about 30% to about 90% (w/w) of the composition.
40. The pharmaceutical composition of any one of claims 28 to 39, wherein the composition further comprises one or more of alpha cellulose, beta cellulose, gamma cellulose, starch, modified-starch, sorbitol, mannitol, lactose, dextrose, sucrose, dibasic calcium phosphate, tribasic calcium phosphate, or calcium carbonate.
41. The pharmaceutical composition of any one of claims 28 to 40, wherein the composition further comprises a binder.
42. The pharmaceutical composition of claim 41, wherein the binder is hydroxypropyl methylcellulose.

43. The pharmaceutical composition of claim 41 or 42, wherein the amount of the binder is from about 0.1% to about 85% (w/w) of the composition, preferably from about 0.1% to about 25% (w/w) of the composition.
44. The pharmaceutical composition of any one of claims 28 to 43, wherein the composition further comprises a disintegrant.
45. The pharmaceutical composition of claim 44, wherein the disintegrant is selected from one or more of a cross-linked carboxymethyl cellulose (croscarmellose), a starch glycolate, a polyvinyl pyrrolidone, a sago starch, psyllium husk, a silicate, a soy polysaccharide, croscarmellose sodium, or crospovidone.
46. The pharmaceutical composition of claim 44 or 45, wherein the total amount of the disintegrant is from about 3% to about 25% (w/w) of the composition, preferably from about 5% to about 15% (w/w) of the composition, and more preferably from about 5% to about 12% (w/w) of the composition.
47. The pharmaceutical composition of any one of claims 28 to 46, wherein the composition further comprises a lubricant.
48. The pharmaceutical composition of claim 47, wherein the amount of the lubricant is from about 0.1% to about 2.5%, preferably from about 0.3% to about 2% (w/w) of the composition.
49. The pharmaceutical composition of any one of claims 28 to 48, wherein the composition further comprises a sugar alcohol.
50. The pharmaceutical composition of claim 49, wherein the amount of the sugar alcohol is from about 5 % to about 40% (w/w) of the composition preferably from about 10% to about 30% (w/w) of the composition, and more preferably from about 10% to about 27.5% (w/w) of the composition.
51. The pharmaceutical composition of any one of claims 28 to 50, wherein the composition further comprises a silica.
52. The pharmaceutical composition of claim 51, wherein the amount of the silica is from about 0.1% to about 1.5% (w/w) of the composition.
53. The pharmaceutical composition of any one of claims 28 to 52, wherein the composition is a tablet composition or a capsule composition.
54. The pharmaceutical composition of any one of claims 28 to 53, comprising:
- a. the crystalline form of the pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, in an amount of from about 0.1% to about 60 % (w/w) of the composition;

- b. a silicified microcrystalline cellulose in an amount of from about 40% to about 85% (w/w) of the composition;
 - c. a disintegrant in an amount of about 5% to about 10% (w/w) of the composition;
 - d. a silica in an amount of about 0.1% to about 1.0% (w/w) of the composition; and
 - e. a lubricant in an amount of about 0.5 % to about 1.5% (w/w) of the composition.
55. The pharmaceutical composition of claim any one of claims 28 to 54, comprising:
- a. the crystalline form of the pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, in an amount of from about 10% to about 40% (w/w) of the composition;
 - b. the silicified microcrystalline cellulose in an amount in the range of about 60% to about 85% (w/w) of the composition;
 - c. crospovidone in an amount of about % to about 5% (w/w) of the composition;
 - d. the silica in an amount of about 0.1% to about 1% (w/w) of the composition; and
 - e. magnesium stearate in an amount of about 0.1% to about 1% of the composition.
56. The pharmaceutical composition of any one of claims 28 to 55, further comprising mannitol, wherein mannitol is present in an amount of about 10% to about 15% (w/w) of the composition.
57. The pharmaceutical composition of any one of claims 28 to 56, further comprising a cosmetic coating.
58. The pharmaceutical composition of claim 57, wherein the cosmetic coating is a film coating selected from formulations based on polyethylene glycol-polyvinyl alcohol (PEG-PVA) graft copolymer, polyvinyl alcohol (PVA), hypromellose (HPMC), hydroxypropyl cellulose (HPC), or any combination thereof.
59. The pharmaceutical composition of any one of claims 28 to 53, comprising:
- a. an absorption enhancer in an amount of from about 5% to about 65% (w/w) of the composition;
 - b. the crystalline form of the pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, in an amount of from about 0.1% to about 15% (w/w) of the composition, and

- c. a silicified microcrystalline cellulose in an amount of from about 10% to about 50% (w/w) of the composition.
60. The pharmaceutical composition of any one of claims 28 to 53, comprising:
- a. an absorption enhancer in an amount of from about 30% to about 45% (w/w) of the composition;
 - b. a disintegrant in an amount of from about 5% to 10% (w/w) of the composition;
 - c. the crystalline form of the pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, in an amount of from about 0.5% to about 15% (w/w) of the composition;
 - d. a silicified microcrystalline cellulose in an amount of from about 30% to about 40% (w/w) of the composition;
 - e. a silica in an amount of about 0.2% to about 1.5% (w/w) of the composition;
 - f. a disintegrant in an amount of about 5% to about 10% (w/w) of the composition;
 - g. a filler in an amount of about 7.5% to about 15% (w/w) of the composition; and
 - h. a lubricant in an amount of about 0.2 % to about 1.5% (w/w) of the composition.
61. The pharmaceutical composition of claim 60, wherein:
- a. the absorption enhancer in an amount of from about 30% to about 45% (w/w) of the composition;
 - b. the disintegrant in an amount of from about 5% to about 10% (w/w) of the composition;
 - c. the crystalline form of the pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, in an amount of from about 0.5% to about 5% (w/w) of the composition,
 - d. a silicified microcrystalline cellulose in an amount of from about 35% to about 40% (w/w) of the composition;
 - e. mannitol in an amount of about 5% to about 15% (w/w) of the composition;
 - f. crospovidone in an amount of about 1% to about 10% (w/w) of the composition;
 - g. a silica in an amount of about 0.1% to about 10% (w/w) of the composition; and

- h. magnesium stearate in an amount of about 0.1% to about 1% (w/w) of the composition.
62. The pharmaceutical composition of claim 58 or 59, wherein the absorption enhancer is sodium citrate, tartaric acid, tartrate salt, salicylic acid, sodium caprate, sodium caprylate, sodium palmitate, sodium stearate, sodium citrate, sodium salicylate, sodium salcaprozate (SNAC), a polyethylene glycol (PEG)-modified medium chain fatty acid triglyceride of capric and caprylic acid, sucrose laurate, or lauroyl-L-carnitine (LC).
63. The pharmaceutical composition of any one of claims 57 to 60, wherein:
- a. sodium caprate in an amount of about 38.5% (w/w) of the composition;
 - b. hydroxypropyl methylcellulose in an amount of about 0.8% (w/w) of the composition;
 - c. the crystalline form of the pharmaceutically acceptable salt of the compound of Formula (I), or a solvate thereof, in an amount of from about 3.9% (w/w) of the composition;
 - d. a silicified microcrystalline cellulose in an amount of about 39.7% (w/w) of the composition;
 - e. mannitol in an amount of about 10.7% (w/w) of the composition;
 - f. crospovidone in an amount of about 5% to about 7.5% (w/w) of the composition;
 - g. a silica in an amount of from about 0.5% to about 1.0% (w/w) of the composition; and
 - h. magnesium stearate in an amount of about 0.5% (w/w) of the composition.
64. The pharmaceutical composition of any one of claims 28 to 53, comprising:
- a. a crystalline form of a pharmaceutically acceptable salt of a compound of Formula (I), or a solvate thereof, in an amount of from about 10% to about 20% (w/w) of the composition;
 - b. an absorption enhancer in an amount of from about 30% to about 45% (w/w) of the composition;
 - c. a disintegrant in an amount of from about 0.5% to about 1.0% (w/w) of the composition;
 - d. crospovidone in an amount of about 5% (w/w) of the composition;
 - e. a microcrystalline cellulose in an amount of about 1.3% (w/w) of the composition;
 - f. a silicified microcrystalline cellulose in an amount of from about 34.8% to about 39.7% (w/w) of the composition;

- g. mannitol in an amount of about 10.7% (w/w) of the composition;
- h. crospovidone in an amount of about 5% (w/w) of the composition;
- i. a silica in an amount of about 1.0% (w/w) of the composition; and
- j. magnesium stearate in an amount of about 0.5% (w/w) of the composition.

65. The pharmaceutical composition of any one of claims 59 to 64, further comprising a subcoating.

66. The pharmaceutical composition of claim 65, wherein the subcoating is present in an amount from about 1% to about 5% (w/w).

67. The pharmaceutical composition of claim 65 or 66, further comprising an enteric coating.

68. The pharmaceutical composition of claim 67, wherein the enteric coating is present in an amount from about 2% to about 15% (w/w).

69. The pharmaceutical composition of claim 67 or 68, wherein the enteric coating is present in an amount of about 8% or about 12%.