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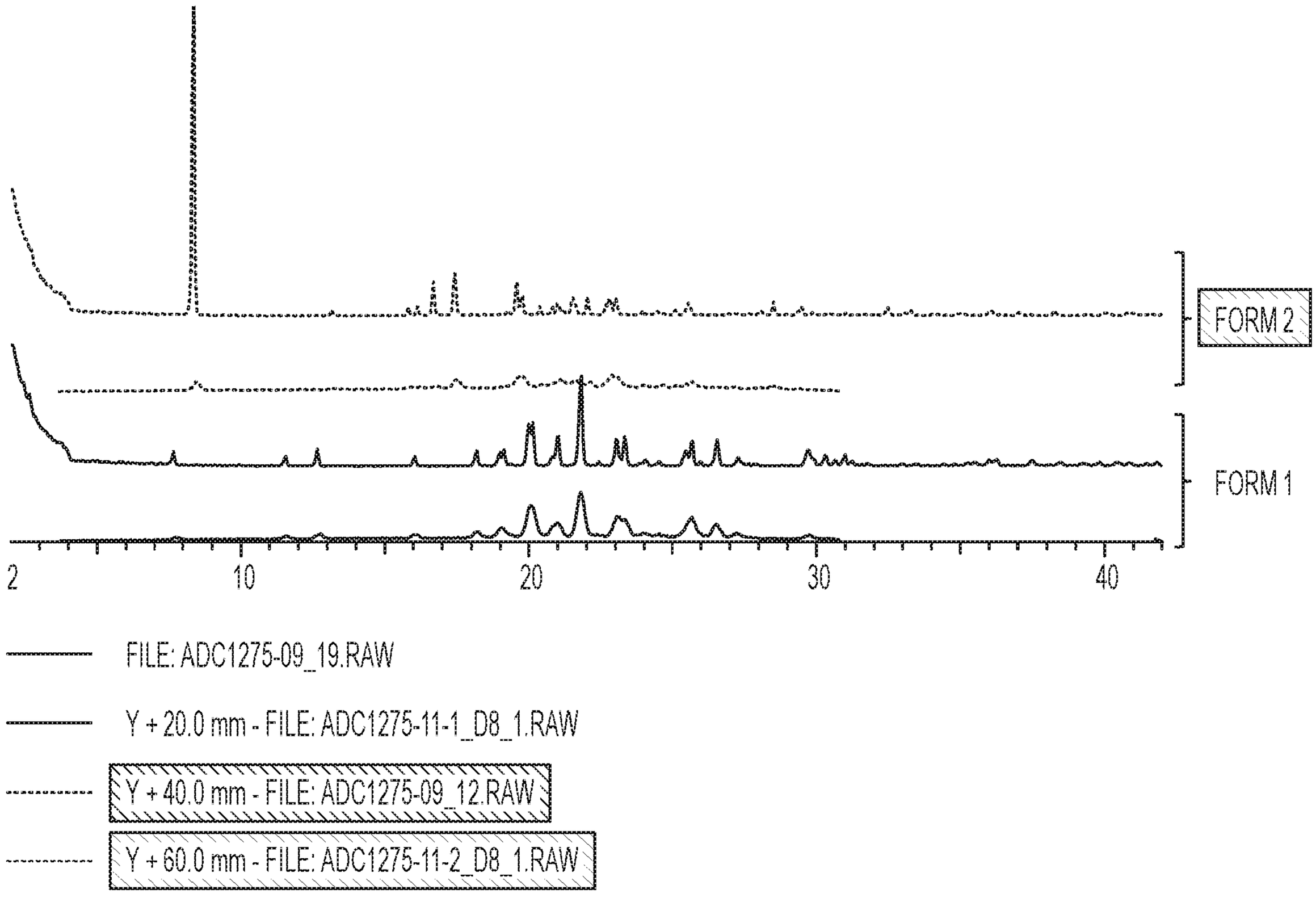
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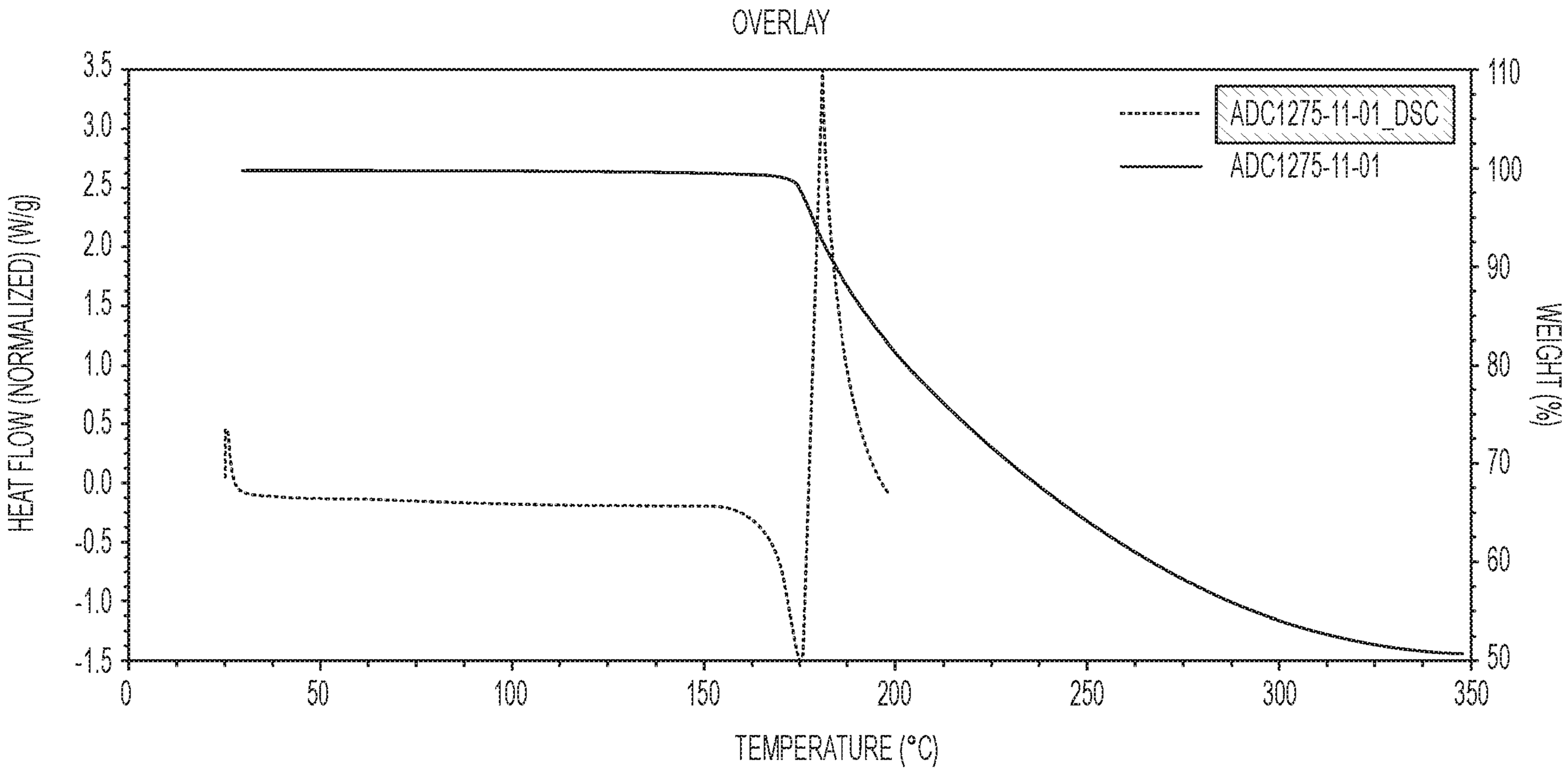
Figure 1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ADC1275-11-01
HEAT FLOW (NORMALIZED) (W/g)
WEIGHT (%)
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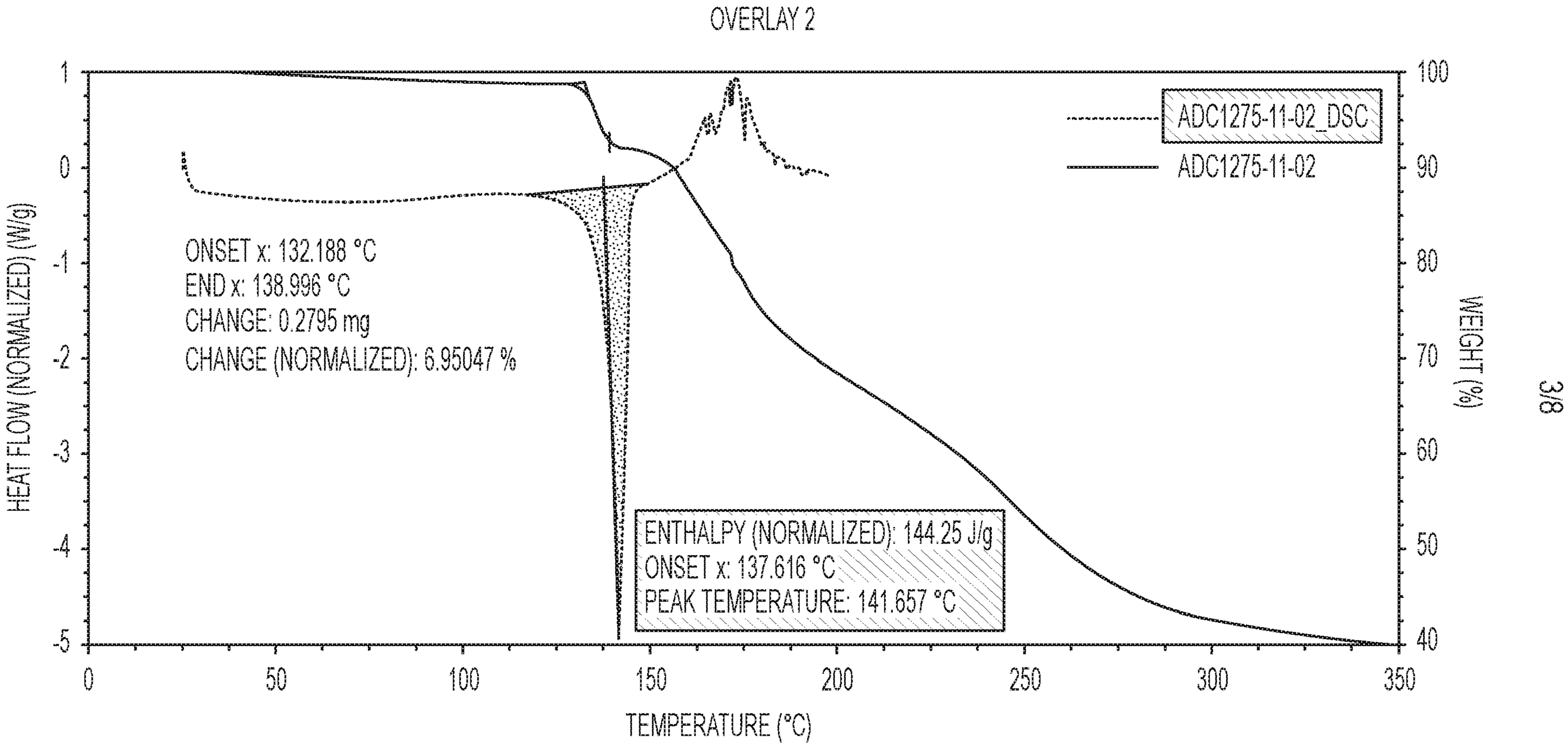
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
110
100
90
80
70
60
50
0
50
100
150
200
250
300
350

Figure 2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ADC1275-11-02
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END x: 138.996 °C
CHANGE: 0.2795 mg
CHANGE (NORMALIZED): 6.95047 %
ENTHALPY (NORMALIZED): 144.25 J/g
ONSET x: 137.616 °C
PEAK TEMPERATURE: 141.657 °C
HEAT FLOW (NORMALIZED) (W/g)
WEIGHT (%)
TEMPERATURE (°C)
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0
-1
-2
-3
-4
-5
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50
40
0
50
100
150
200
250
300
350

Figure 3

19 12 16

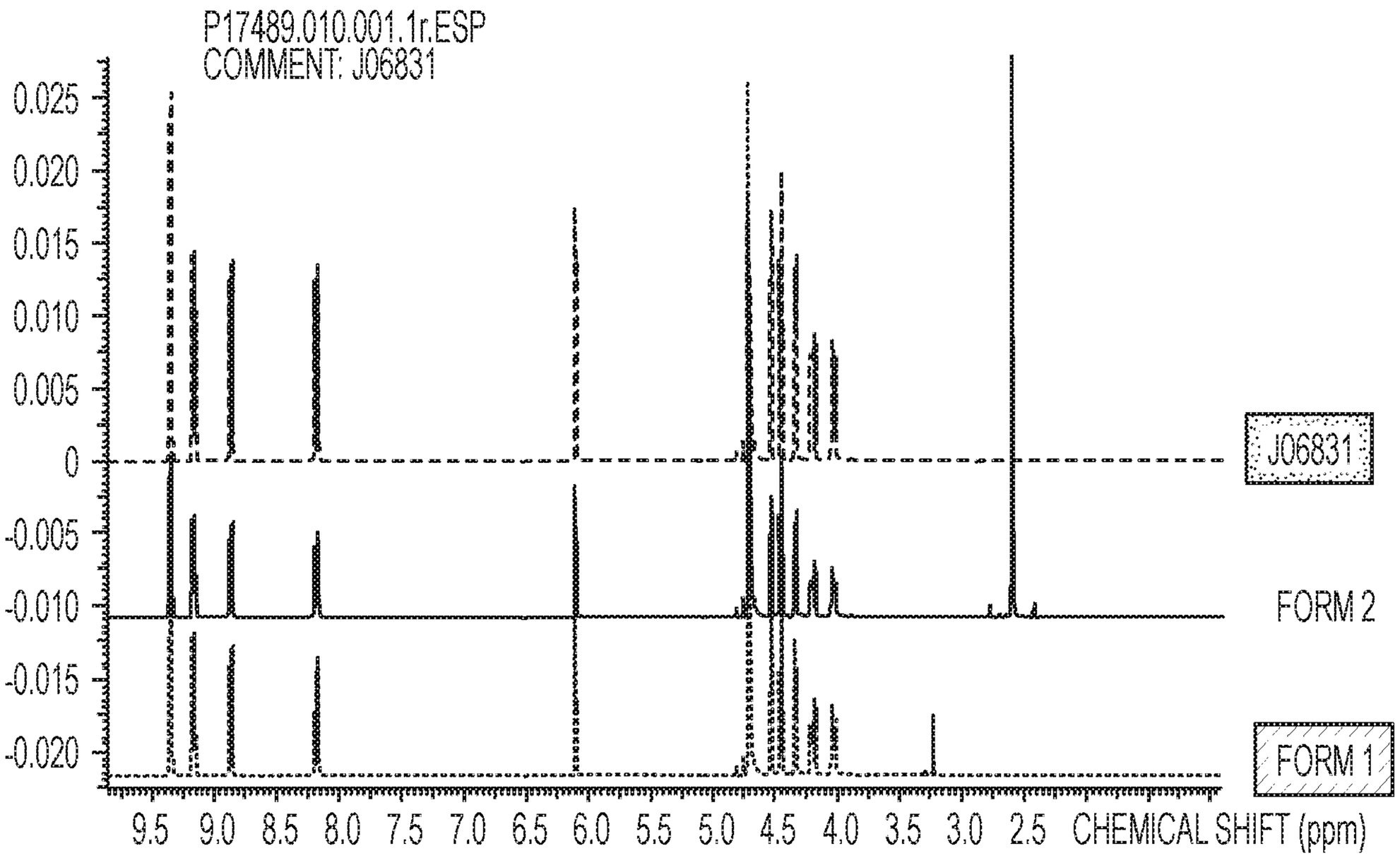

Figure 4

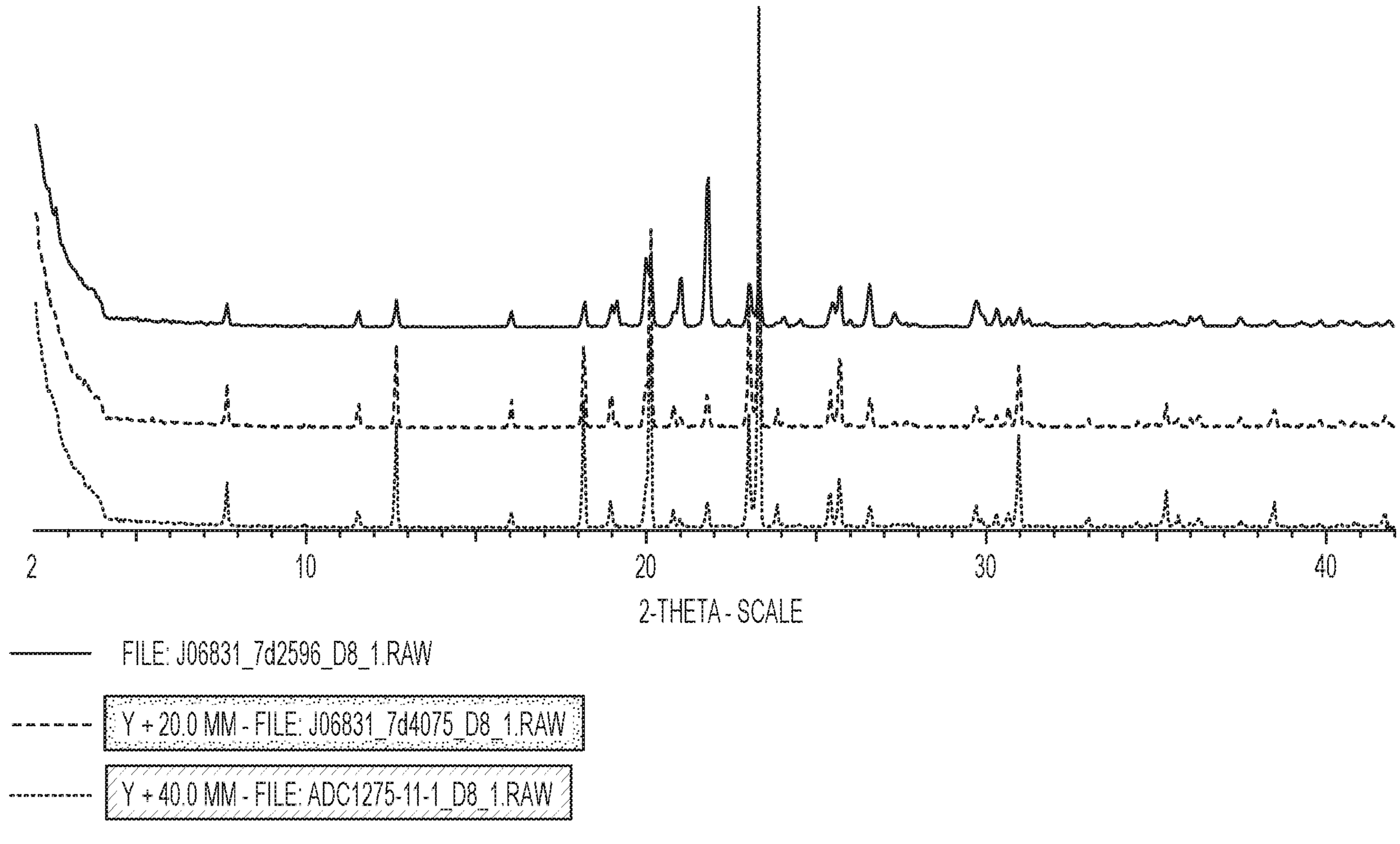
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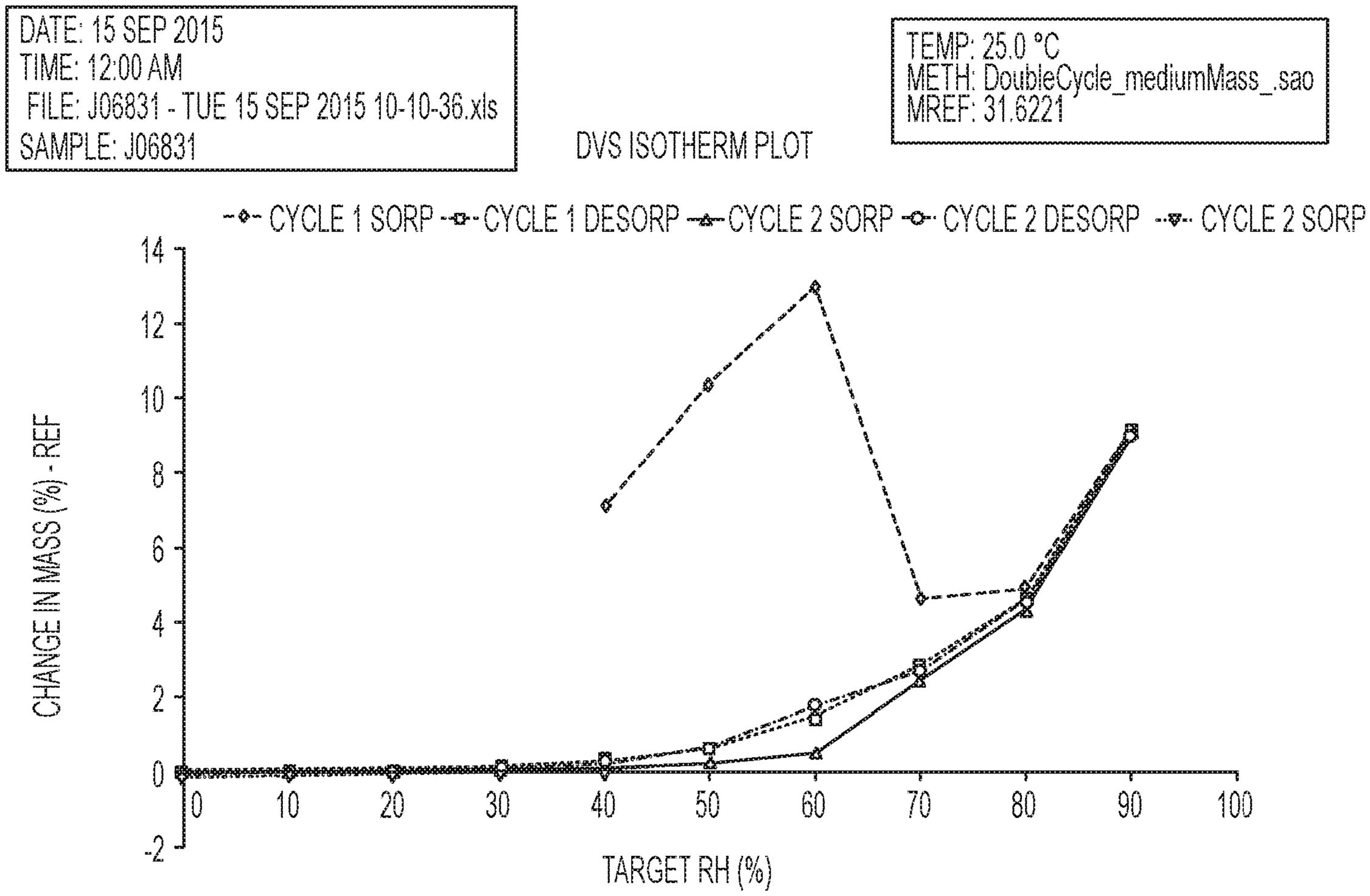
Figure 5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CYCLE 1 DESORP
CYCLE 2 SORP
CYCLE 2 DESORP
CYCLE 2 SORP
CHANGE IN MASS (%) - REF
TARGET RH (%)
14
12
10
8
6
4
2
0
-2
0
10
20
30
40
50
60
70
80
90
100

Figure 6

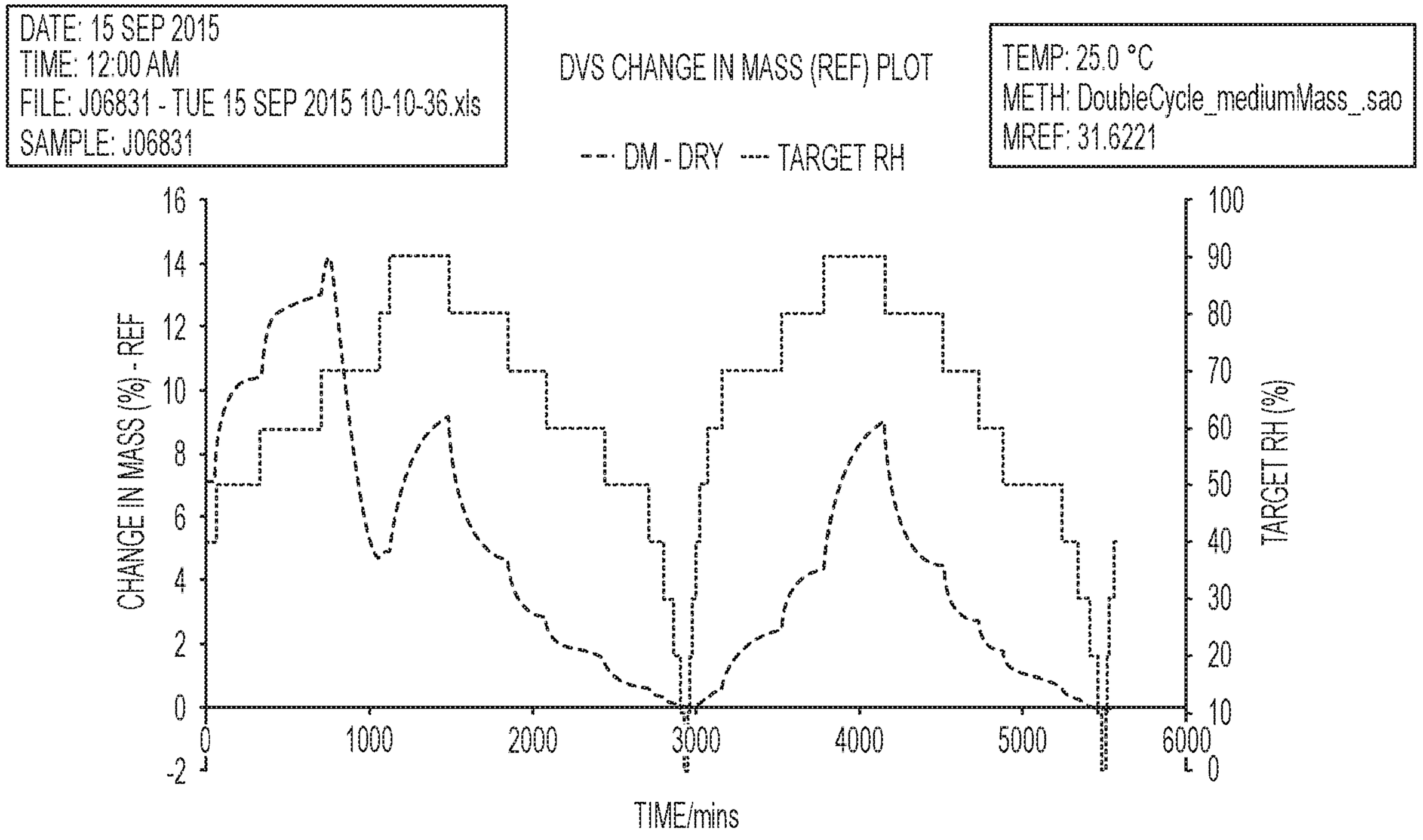
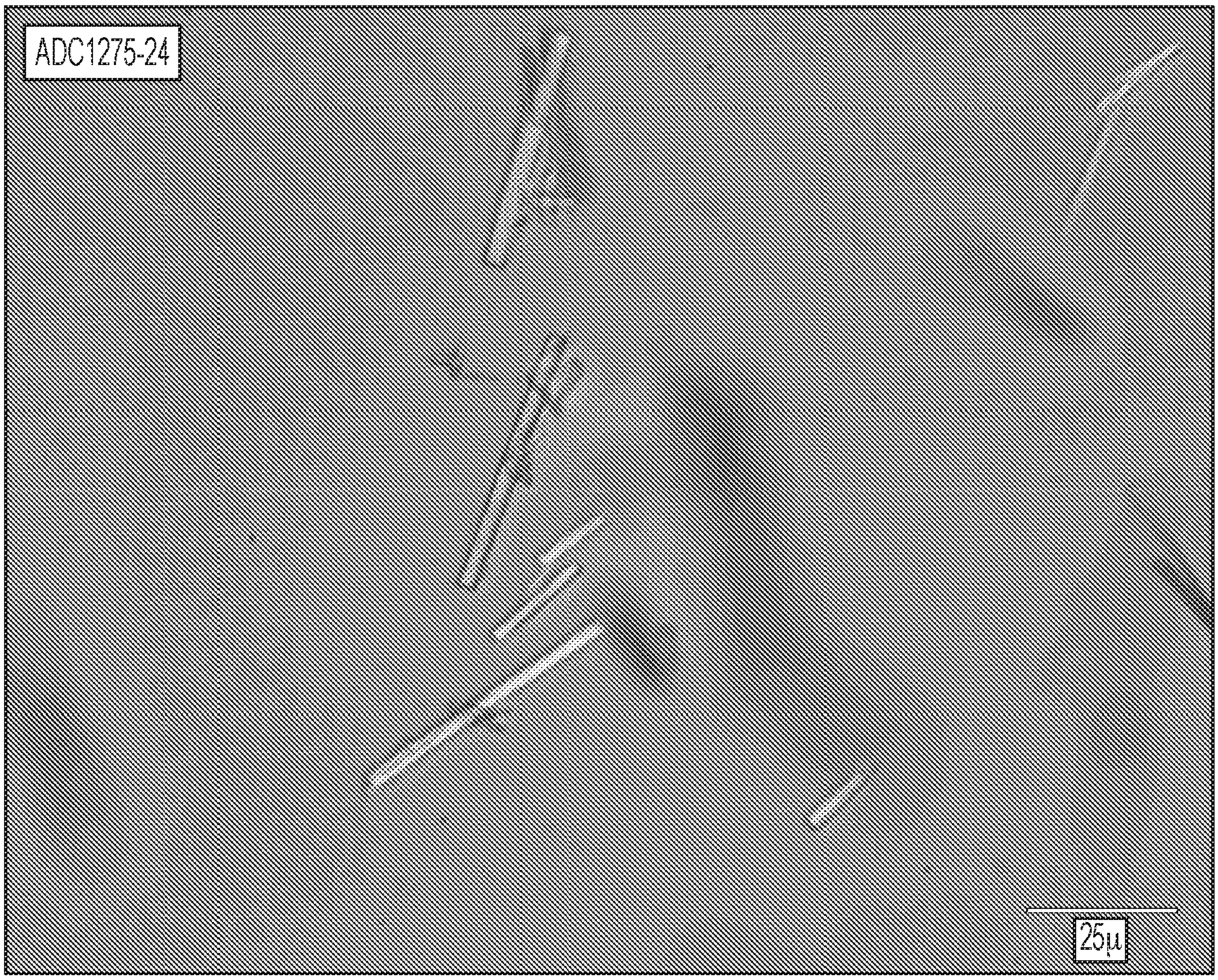

DATE: 15 SEP 2015
TIME: 12:00 AM
FILE: J06831 - TUE 15 SEP 2015 10-10-36.xls
SAMPLE: J06831
DVS CHANGE IN MASS (REF) PLOT
--- DM - DRY ---- TARGET RH
TEMP: 25.0 °C
METH: DoubleCycle_mediumMass_.sao
MREF: 31.6221
CHANGE IN MASS (%) - REF
TARGET RH (%)
TIME/mins
16
14
12
10
8
6
4
2
0
-2
100
90
80
70
60
50
40
30
20
10
0
0
1000
2000
3000
4000
5000
6000

Figure 7



12 16

19 1

Figure 8

Crystal Forms of β-Nicotinamide Mononucleotide

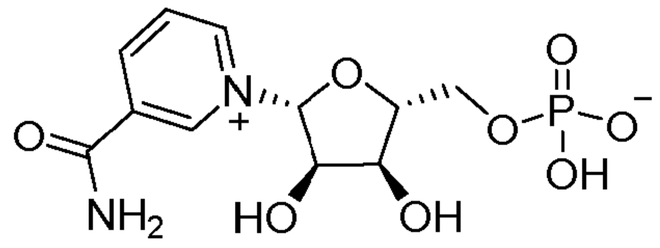
Background

β-Nicotinamide mononucleotide (NMN) has recently garned attention for its use in the treatment, amelioration, mitigation, slowing, arrest, prevention and/ or reversal of age-associated degenerative changes, such as age-related obesity, age-related increases in blood lipid levels, age-related decreases in insulin sensitivity, age-related decreases in memory function, and age-related changes in eye function such as macular degeneration.

Given the therapeutic benefits associated with this compound, there is a need for improved compositions of NMN that provide better product functionality. Further, there is a need for improved methods for preparing and formulating β-nicotinamide mononucleotide.

Summary of Invention

One aspect of the invention relates to a crystalline compound of Form 1 having the structure of formula (I),



(I).

Another aspect of the invention relates to methods for preparing the crystalline compound of Form 1 having the structure of formula (I).

In one aspect, the present invention provides a pharmaceutical composition suitable for use in a human patient, comprising a crystalline compound of Form 1 having the structure of formula (I), and one or more pharmaceutically acceptable excipients. In certain embodiments, the pharmaceutical compositions may be for use in treating or preventing a condition or disease as described herein. In certain embodiments, the pharmaceutical compositions have a low enough pyrogen activity to be suitable for intravenous use in a human patient.

Detailed Description of the Drawings

Figure 1 shows the XRPD patterns of β-nicotinamide mononucleotide (NMN) forms 1 and 2.

Figure 2 shows the differential scanning calorimetry thermogram of Form 1.

Figure 3 shows the differential scanning calorimetry thermogram of Form 2.

Figure 4 shows ^{1}H NMR spectra of the amorphous NMN, NMN Form 1, and NMN Form 2 after drying under vacuum. As shown in the spectra, Form 1 is substantially anhydrous, and Form 2 has about 1.1-1.2 DMSO molecules per molecule NMN.

Figure 5 shows a comparison of XRPD patterns of amorphous NMN, amorphous NMN post-storage, and NMN Form 1.

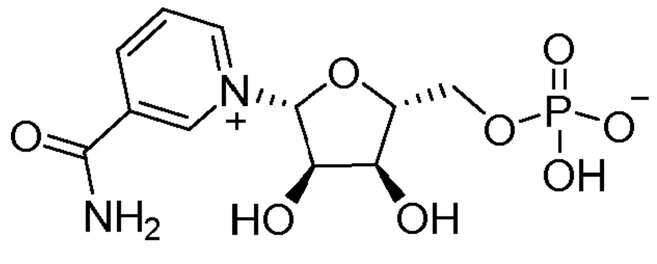
Figure 6 shows a dynamic vapor sorption isotherm for amorphous NMN.

Figure 7 shows a dynamic vapor sorption change in mass plot for amorphous NMN. When a sample of amorphous NMN is exposed to atmospheric humidity, the sample goes through phases. **Figure** 7 shows the mass change over time. The amorphous sample is hygroscopic until it deliquesces and starts crystallizing. The weight loss below 1000 min shows a crystallisation event. Once crystallised, the material remains crystalline, retaining the same XRPD pattern after a double cycle, but still shows the ability to pick up mass reversibly (up to 9% w/w change).

Figure 8 is an image showing single crystals of NMN Form 1, observed under a polarized microscope.

Detailed Description of the Invention

In one aspect, the invention provides a crystalline compound of Form 1 having the structure of formula (I),



(I).

In certain embodiments, a crystalline compound of formula (I) is not solvated (e.g., the crystal lattice does not comprise molecules of a solvent). In certain embodiments, the crystalline compound of formula (I) is anhydrous, or substantially anhydrous. In certain alternative embodiments, a crystalline compound of formula (I) is solvated. In certain such disclosures, the crystalline compound of formula (I) is a dimethylsulfoxide (DMSO) solvate.

Any crystalline compound described herein may be used in the manufacture of a medicament for the treatment of any diseases or conditions disclosed herein.

In certain embodiments, the compounds of the present invention can assemble into more than one crystal formation. In an exemplary embodiment, the crystalline compound

having the structure of formula (I) exists as "form I" and "form II", as described in detail below. These different forms are understood as "polymorphs" herein.

In certain embodiments, the polymorph of the crystalline compound is characterized by powder X-ray diffraction (XRD). θ represents the diffraction angle, measured in degrees. In certain embodiments, the diffractometer used in XRD measures the diffraction angle as two times the diffraction angle θ. Thus, in certain embodiments, the diffraction patterns described herein refer to X-ray intensity measured against angle 2θ.

In certain embodiments, an anhydrous crystalline compound of formula (I) has 2θ values 20.03; 20.14; 21.83; and 25.73. In further embodiments, the anhydrous crystalline compound has 2θ values 20.03; 20.14; 21.03; 21.83; 23.08; 23.39; 25.73; and 26.59. In yet further embodiments, the anhydrous crystalline compound has 2θ values 7.70; 11.54; 12.64; 16.03; 18.99; 20.03; 20.14; 20.83; 21.03; 21.83; 23.08; 23.39; 25.48; 25.73; 26.59; and 29.78. In still yet further embodiments, the anhydrous crystalline compound has 2θ values 7.70; 9.95; 11.54; 12.64; 16.03; 18.18; 18.99; 19.16; 19.44; 20.03; 20.14; 20.83; 21.03; 21.83; 22.44; 23.08; 23.39; 23.89; 24.08; 24.53; 24.68; 25.05; 25.48; 25.73; 26.08; 26.59; 27.33; 27.67; 29.78; and 29.92.

In certain embodiments, an anhydrous crystalline compound of formula (I) has an XRD pattern substantially as shown in FIG. 1, labeled Form 1.

In certain embodiments, a crystalline compound of formula (I) is not solvated (e.g., the crystal lattice does not comprise molecules of a solvent). In certain alternative embodiments, a crystalline compound of formula (I) is solvated.

In certain disclosures, a crystalline DMSO solvate of the compound of formula (I) has 2θ values 8.29; 17.39; 19.54; 22.78; and 22.98. In further disclosures, the crystalline DMSO solvate has 2θ values 8.29; 17.39; 19.54; 19.74; 20.98; 21.58; 22.03; 22.78; 22.98; and 25.53. In yet further disclosures, the crystalline DMSO solvate has 2θ values 8.29; 16.10; 17.39; 19.24; 19.54; 19.74; 20.33; 20.78; 20.98; 21.18; 21.58; 22.03; 22.78; 22.98; 25.53; 28.48; and 29.48. In further disclosures, the crystalline DMSO solvate has 2θ values 8.29; 13.12; 15.79; 16.10; 16.69; 17.39; 19.03; 19.24; 19.54; 19.74; 20.33; 20.78; 20.98; 21.18; 21.58; 22.03; 22.78; 22.98; 23.95; 24.14; 24.48; 24.64; 25.14; 25.53; 25.87; 26.89; 27.18; 27.67; 28.02; 28.13; 28.48; 28.98; 29.34; 29.48; and 29.92.

In one disclosure, a crystalline DMSO solvate of the compound of formula (I) has an XRD pattern substantially as shown in FIG. 1, labeled Form 2.

In certain disclosures, the crystalline DMSO solvate of the compound of formula (I) contains about 1.0, about 1.1, or about 1.2 molecules of DMSO to one molecule of NMN.

In one aspect, the invention relates to a pharmaceutical composition comprising a crystalline compound of formula (I) and one or more pharmaceutically acceptable excipients. In one aspect, the pharmaceutical composition is selected from tablets, capsules, and suspensions.

The term "substantially pure" as used herein, refers to a crystalline polymorph that is greater than 90% pure, meaning that contains less than 10% of any other compound, including the corresponding amorphous compound or an alternative polymorph of the crystalline salt. Preferably, the crystalline polymorph is greater than 95% pure, or even greater than 98% pure.

Methods of making the crystalline forms of NMN

In one aspect, the invention relates to a method for the preparation of a crystalline compound of Form 1 having the structure of formula (I), comprising a) providing a mixture of a compound of formula (I) in a solvent selected from acetonitrile, N,N-dimethylacetamide (DMA), dimethylformamide (DMF), dimethylsulfoxide (DMSO), ethanol, ethyl acetate, heptanes, hexanes, isopropyl acetate, methanol, methylethyl ketone, N-methyl-2- pyrrolidone (NMP), tetrahydrofuran, toluene, 2-propanol, 1-butanol, water, or any combination thereof; and b) crystallizing the compound of formula (I) from the mixture comprising the compound of formula (I).

In certain embodiments, the mixture comprising the compound of formula (I) is a solution. In certain embodiments, the mixture is a slurry or a suspension.

In certain embodiments, the crystalline compound made by the methods of the invention is anhydrous.

In certain embodiments or disclosures, the crystalline compound made by the methods of the invention is a solvate, e.g., a DMSO solvate.

In certain embodiments, the mixture comprising the compound of formula (I) is a solution, and the step of crystallizing the compound from the mixture comprises bringing the solution to supersaturation to cause the compound of formula (I) to precipitate out of solution.

In certain embodiments, bringing the mixture comprising the compound of formula (I) to supersaturation comprises the slow addition of an anti-solvent, such as heptanes, hexanes, ethanol, or another polar or non-polar liquid miscible with the organic solvent,

allowing the solution to cool (with or without seeding the solution), reducing the volume of the solution, or any combination thereof. In certain embodiments, bringing the mixture comprising the compound of formula (I) to supersaturation comprises adding an anti-solvent, cooling the solution to ambient temperature or lower, and reducing the volume of the solution, e.g., by evaporating solvent from the solution. In certain embodiments, allowing the solution to cool may be passive (e.g., allowing the solution to stand at ambient temperature) or active (e.g., cooling the solution in an ice bath or freezer).

In certain embodiments, the preparation method further comprises isolating the crystals, e.g., by filtering the crystals, by decanting fluid from the crystals, or by any other suitable separation technique. In further embodiments, the preparation method further comprises washing the crystals.

In certain embodiments, the preparation method further comprises inducing crystallization. The method can also comprise drying the crystals, for example under reduced pressure. In certain embodiments, inducing precipitation or crystallization comprises secondary nucleation, wherein nucleation occurs in the presence of seed crystals or interactions with the environment (crystallizer walls, stirring impellers, sonication, etc.).

In certain embodiments, the solvent comprises acetonitrile, N,N-dimethylacetamide (DMA), dimethylformamide (DMF), dimethylsulfoxide (DMSO), ethanol, ethyl acetate, heptanes, hexanes, isopropyl acetate, methanol, methylethyl ketone, N-methyl-2-pyrrolidone (NMP), tetrahydrofuran, toluene, 2-propanol, 1-butanol, water, or any combination thereof. In certain preferred embodiments, for example to achieve Form 1, the solvent is methanol or water. In other preferred embodiments, for example to achieve Form 2, the solvent is dimethylsulfoxide.

In certain embodiments, washing the crystals comprises washing with a liquid selected from anti-solvent, acetonitrile, ethanol, heptanes, hexanes, methanol, tetrahydrofuran, toluene, water, or a combination thereof. As used herein, "anti-solvent" means a solvent in which the salt crystals are insoluble, minimally soluble, or partially soluble. In practice, the addition of an anti-solvent to a solution in which the salt crystals are dissolved reduces the solubility of the salt crystals in solution, thereby stimulating precipitation of the salt. In certain embodiments, the crystals are washed with a combination of anti-solvent and the organic solvent. In certain embodiments, the anti-solvent is water, while in other embodiments it is an alkane solvent, such as hexane or

pentane, or an aromatic hydrocarbon solvent, such as benzene, toluene, or xylene. In certain embodiments, the anti-solvent is methanol.

In certain embodiments, washing the crystals comprises washing the crystalline compound of formula (I) with a solvent or a mixture of one or more solvents, which are described above. In certain embodiments, the solvent or mixture of solvents is cooled prior to washing.

In certain embodiments, the methods of making the crystalline forms of NMN are used to remove one or more impurities from NMN. In certain embodiments, the crystallization methods described herein are used for purifying NMN, e.g., as a final purification step in the manufacture of the compound.

Uses of crystal forms of NMN

In certain embodiments, the crystal forms of β-nicotinamide mononucleotide (NMN) may be used for treating, ameliorating, mitigating, slowing, arresting, preventing or reversing age-associated obesity in a subject. In some embodiments, the invention relates to the crystal forms of β-nicotinamide mononucleotide (NMN) for use in treating, ameliorating, mitigating, slowing, arresting, preventing or reversing age-associated increases in blood lipid levels in a subject. In some embodiments, the invention relates to the crystal forms of β-nicotinamide mononucleotide (NMN) for use in treating, ameliorating, mitigating, slowing, arresting, preventing or reversing age-associated loss of insulin sensitivity in a subject. In some embodiments, the invention relates to the crystal forms of β-nicotinamide mononucleotide (NMN) for use in treating, ameliorating, mitigating, slowing, arresting, preventing or reversing age- associated impairment of memory function in a subject. In some embodiments, the invention relates to the crystal forms of β-nicotinamide mononucleotide (NMN) for use in treating, ameliorating, mitigating, slowing, arresting, preventing or reversing age-associated decline in eye function in a subject. In some embodiments, the invention relates to the crystal forms of β-nicotinamide mononucleotide (NMN) for use in treating, ameliorating, mitigating, slowing, arresting, preventing or reversing age-associated retinal degeneration in a subject. In some embodiments, the invention relates to the crystal forms of β-nicotinamide mononucleotide (NMN) for use in treating, ameliorating, mitigating, slowing, arresting, preventing or reversing dry eye. In some embodiments, the invention relates to the crystal forms of β-nicotinamide mononucleotide (NMN) for use in treating, ameliorating, mitigating, slowing, arresting, preventing or reversing age- associated dry eye.

In some embodiments, the invention provides the crystal forms of β-nicotinamide mononucleotide (NMN) for use in treating age-associated defects in neural stem/progenitor cell (NSPC) functionality in a subject. In some embodiments, the invention provides the crystal forms of β-nicotinamide mononucleotide (NMN) for use in reducing age-associated decrease in a NSPC population in a subject. In some embodiments, the invention provides the crystal forms of β-nicotinamide mononucleotide (NMN) for use in maintaining at least one NSPC in a subject. In some embodiments, the invention provides the crystal forms of β-nicotinamide mononucleotide (NMN) for use in enhancing NAD biosynthesis in a subject. In some embodiments, the invention provides the crystal forms of β-nicotinamide mononucleotide (NMN) for use in promoting NSPC proliferation in a subject. The uses of each of these embodiments can comprise, consist essentially of, or consist of administration of a therapeutically effective amount of a crystal form of NMN.

In some embodiments, the invention provides the crystal forms of β-nicotinamide mononucleotide (NMN) for use in increasing bone density levels in a subject. In some embodiments, the invention provides the crystal forms of β-nicotinamide mononucleotide (NMN) for use in treating aberrantly low bone density levels in a subject. In some embodiments, the invention provides the crystal forms of β-nicotinamide mononucleotide (NMN) for use in treating an age-associated bone density decrease in a subject. In some embodiments, the invention provides the crystal forms of β-nicotinamide mononucleotide (NMN) for use in treating osteoporosis in a subject. In some embodiments, the invention provides the crystal forms of β-nicotinamide mononucleotide (NMN) for use in preventing an age- associated bone density decrease in a subject. The uses of each of these embodiments can comprise, consist essentially of, or consist of administration of a therapeutically effective amount of a crystal form of NMN.

In certain embodiments, the invention relates to the crystal forms of β-nicotinamide mononucleotide (NMN) for use in preventing, reducing risk of, and treating various diseases associated with photoreceptor dysfunction, including, without limitation, age-related macular degeneration (AMD), inherited and acquired retinal diseases such as, without limitation, retinitis pigmentosa (RP), rod and cone dystrophism, and Leber's congenital amaurosis (LCA) by administration of NMN. In various embodiments, administration of an NMN crystal form can be an effective intervention for the prevention and/or treatment of orphan retinal degenerative diseases including but not limited to rod dystrophy, cone dystrophy, retinitis pigmentosa, other inherited retinal degenerations,

Leber's congenital amaurosis (LCA) and acquired retinal degenerations such as, but not limited to, age-related macular dengeration photoreceptor degeneration following retinal detachment. In various embodiments, a crystal form NMN can be administered by any administration route known to skilled artisans, such as, without limitation, oral, parenteral, intraocular, intraperitoneal, intravenous or intramuscular routes. In various embodiments, NMN can be administered with or without an excipient.

As used herein, a therapeutic that "prevents" a disorder or condition refers to a compound that, in a statistical sample, reduces the occurrence or frequency of the disorder or condition in the treated sample relative to an untreated control sample, or delays the onset or reduces the severity of one or more symptoms of the disorder or condition relative to the untreated control sample. Thus, prevention of cancer includes, for example, reducing the number of detectable cancerous growths in a population of patients receiving a prophylactic treatment relative to an untreated control population, and/or delaying the appearance of detectable cancerous growths in a treated population versus an untreated control population, e.g., by a statistically and/or clinically significant amount. Prevention of an infection includes, for example, reducing the number of diagnoses of the infection in a treated population versus an untreated control population, and/or delaying the onset of symptoms of the infection in a treated population versus an untreated control population. Prevention of pain includes, for example, reducing the magnitude of, or alternatively delaying, pain sensations experienced by subjects in a treated population versus an untreated control population.

The term "treating" includes prophylactic and/or therapeutic treatments. The term "prophylactic or therapeutic" treatment is art-recognized and includes administration to the host of one or more of the subject compositions. If it is administered prior to clinical manifestation of the unwanted condition (e.g., disease or other unwanted state of the host animal) then the treatment is prophylactic (i.e., it protects the host against developing the unwanted condition), whereas if it is administered after manifestation of the unwanted condition, the treatment is therapeutic (i.e., it is intended to diminish, ameliorate, or stabilize the existing unwanted condition or side effects thereof).

Pharmaceutical Compositions

In certain embodiments, the present invention relates to pharmaceutical compositions comprising a crystalline compound of formula (I) and one or more pharmaceutically acceptable excipients. In certain embodiments, the pharmaceutical

preparations may be for use in treating or preventing a condition or disease as described herein. In certain embodiments, the pharmaceutical preparations have a low enough pyrogen activity to be suitable for intravenous use in a human patient.

Exemplary pharmaceutically acceptable excipient are presented herein, and include, for example binders, disintegrating agents, lubricants, corrigents, solubilizing agents, suspension aids, emulsifying agents, coating agents, cyclodextrins, and/or buffers. Although the dosage will vary depending on the symptoms, age and body weight of the patient, the nature and severity of the disorder to be treated or prevented, the route of administration and the form of the drug, in general, a daily dosage of from 0.01 to 3000 mg of the compound is recommended for an adult human patient, and this may be administered in a single dose or in divided doses. The amount of active ingredient which can be combined with a carrier material to produce a single dosage form will generally be that amount of the compound which produces a therapeutic effect.

The precise time of administration and/or amount of the composition that will yield the most effective results in terms of efficacy of treatment in a given patient will depend upon the activity, pharmacokinetics, and bioavailability of a particular compound, physiological condition of the patient (including age, sex, disease type and stage, general physical condition, responsiveness to a given dosage, and type of medication), route of administration, etc. However, the above guidelines can be used as the basis for fine-tuning the treatment, e.g., determining the optimum time and/or amount of administration, which will require no more than routine experimentation consisting of monitoring the subject and adjusting the dosage and/or timing.

In certain embodiments, the individual to which the composition is administered is a mammal such as a human, or a non-human mammal. When administered to an animal, such as a human, the composition or the compound is preferably administered as a pharmaceutical composition comprising, for example, a compound of the invention and a pharmaceutically acceptable carrier. Pharmaceutically acceptable carriers are well known in the art and include, for example, aqueous solutions such as water or physiologically buffered saline or other solvents or vehicles such as glycols, glycerol, oils such as olive oil, or injectable organic esters. In a preferred embodiment, when such pharmaceutical compositions are for human administration, particularly for invasive routes of administration (i.e., routes, such as injection or implantation, that circumvent transport or diffusion through an epithelial barrier), the aqueous solution is pyrogen-free, or

substantially pyrogen-free. The excipients can be chosen, for example, to effect delayed release of an agent or to selectively target one or more cells, tissues or organs. The pharmaceutical composition can be in dosage unit form such as tablet, capsule (including sprinkle capsule and gelatin capsule), granule, lyophile for reconstitution, powder, solution, syrup, suppository, injection or the like. The composition can also be present in a transdermal delivery system, e.g., a skin patch. The composition can also be present in a solution suitable for topical administration, such as an eye drop, through ophthalmic mucous membrane administration.

A pharmaceutically acceptable carrier can contain physiologically acceptable agents that act, for example, to stabilize, increase solubility or to increase the absorption of a compound such as a compound of the invention. Such physiologically acceptable agents include, for example, carbohydrates, such as glucose, sucrose or dextrans, antioxidants, such as ascorbic acid or glutathione, chelating agents, low molecular weight proteins or other stabilizers or excipients. The choice of a pharmaceutically acceptable carrier, including a physiologically acceptable agent, depends, for example, on the route of administration of the composition. The preparation or pharmaceutical composition can be a selfemulsifying drug delivery system or a selfmicroemulsifying drug delivery system. The pharmaceutical composition (preparation) also can be a liposome or other polymer matrix, which can have incorporated therein, for example, a compound of the invention. Liposomes, for example, which comprise phospholipids or other lipids, are nontoxic, physiologically acceptable and metabolizable carriers that are relatively simple to make and administer.

The phrase "pharmaceutically acceptable" is employed herein to refer to those compounds, materials, compositions, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio.

The phrase "pharmaceutically acceptable carrier" as used herein means a pharmaceutically acceptable material, composition or vehicle, such as a liquid or solid filler, diluent, excipient, solvent or encapsulating material. Each carrier must be "acceptable" in the sense of being compatible with the other ingredients of the formulation and not injurious to the patient. Some examples of materials which can serve as pharmaceutically acceptable carriers include: (1) sugars, such as lactose, glucose and

sucrose; (2) starches, such as corn starch and potato starch; (3) cellulose, and its derivatives, such as sodium carboxymethyl cellulose, ethyl cellulose and cellulose acetate; (4) powdered tragacanth; (5) malt; (6) gelatin; (7) talc; (8) excipients, such as cocoa butter and suppository waxes; (9) oils, such as peanut oil, cottonseed oil, safflower oil, sesame oil, olive oil, corn oil and soybean oil; (10) glycols, such as propylene glycol; (11) polyols, such as glycerin, sorbitol, mannitol and polyethylene glycol; (12) esters, such as ethyl oleate and ethyl laurate; (13) agar; (14) buffering agents, such as magnesium hydroxide and aluminum hydroxide; (15) alginic acid; (16) pyrogen-free water; (17) isotonic saline; (18) Ringer's solution; (19) ethyl alcohol; (20) phosphate buffer solutions; and (21) other non-toxic compatible substances employed in pharmaceutical formulations. In certain embodiments, pharmaceutical compositions of the present invention are non-pyrogenic, i.e., do not induce significant temperature elevations when administered to a patient.

The term "pharmaceutically acceptable salt" refers to the relatively non-toxic, inorganic and organic acid addition salts of the compounds. These salts can be prepared in situ during the final isolation and purification of the compounds, or by separately reacting a purified compound in its free base form with a suitable organic or inorganic acid, and isolating the salt thus formed. Representative salts include the hydrobromide, hydrochloride, sulfate, bisulfate, phosphate, nitrate, acetate, valerate, oleate, palmitate, stearate, laurate, benzoate, lactate, phosphate, tosylate, citrate, maleate, fumarate, succinate, tartrate, naphthylate, mesylate, glucoheptonate, lactobionate, laurylsulphonate salts, and amino acid salts, and the like. Preparation of the crystalline salts is detailed in the Examples, below (See, for example, Berge et al. (1977) "Pharmaceutical Salts", J. Pharm. Sci. 66: 1-19.).

In other cases, the compounds useful in the present invention may contain one or more acidic functional groups and, thus, are capable of forming pharmaceutically acceptable salts with pharmaceutically acceptable bases. The term "pharmaceutically acceptable salts" in these instances refers to the relatively non-toxic inorganic and organic base addition salts of a compound. These salts can likewise be prepared in situ during the final isolation and purification of the compound, or by separately reacting the purified compound in its free acid form with a suitable base, such as the hydroxide, carbonate, or bicarbonate of a pharmaceutically acceptable metal cation, with ammonia, or with a pharmaceutically acceptable organic primary, secondary, or tertiary amine. Representative alkali or alkaline earth salts include the lithium, sodium, potassium, calcium, magnesium,

and aluminum salts, and the like. Representative organic amines useful for the formation of base addition salts include ethylamine, diethylamine, ethylenediamine, ethanolamine, diethanolamine, piperazine, and the like (see, for example, Berge et al., supra).

A pharmaceutical composition (preparation) can be administered to a subject by any of a number of routes of administration including, for example, orally (for example, drenches as in aqueous or non-aqueous solutions or suspensions, tablets, capsules (including sprinkle capsules and gelatin capsules), boluses, powders, granules, pastes for application to the tongue); absorption through the oral mucosa (e.g., sublingually); anally, rectally or vaginally (for example, as a pessary, cream or foam); parenterally (including intramuscularly, intravenously, subcutaneously or intrathecally as, for example, a sterile solution or suspension); nasally; intraperitoneally; subcutaneously; transdermally (for example as a patch applied to the skin); and topically (for example, as a cream, ointment or spray applied to the skin, or as an eye drop). The compound may also be formulated for inhalation. In certain embodiments, a compound may be simply dissolved or suspended in sterile water. Details of appropriate routes of administration and compositions suitable for same can be found in, for example, U.S. Pat. Nos. 6,110,973, 5,763,493, 5,731,000, 5,541,231, 5,427,798, 5,358,970 and 4,172,896, as well as in patents cited therein.

The formulations may conveniently be presented in unit dosage form and may be prepared by any methods well known in the art of pharmacy. The amount of active ingredient which can be combined with a carrier material to produce a single dosage form will vary depending upon the host being treated, the particular mode of administration. The amount of active ingredient that can be combined with a carrier material to produce a single dosage form will generally be that amount of the compound which produces a therapeutic effect. Generally, out of one hundred percent, this amount will range from about 1 percent to about ninety-nine percent of active ingredient, preferably from about 5 percent to about 70 percent, most preferably from about 10 percent to about 30 percent.

Methods of preparing these formulations or compositions include the step of bringing into association an active compound, such as a compound of the invention, with the carrier and, optionally, one or more accessory ingredients. In general, the formulations are prepared by uniformly and intimately bringing into association a compound of the present invention with liquid carriers, or finely divided solid carriers, or both, and then, if necessary, shaping the product.

Formulations of the invention suitable for oral administration may be in the form of capsules (including sprinkle capsules and gelatin capsules), cachets, pills, tablets, lozenges (using a flavored basis, usually sucrose and acacia or tragacanth), lyophile, powders, granules, or as a solution or a suspension in an aqueous or non-aqueous liquid, or as an oil-in-water or water-in-oil liquid emulsion, or as an elixir or syrup, or as pastilles (using an inert base, such as gelatin and glycerin, or sucrose and acacia) and/or as mouthwashes and the like, each containing a predetermined amount of a compound of the present invention as an active ingredient. Compositions or compounds may also be administered as a bolus, electuary or paste.

To prepare solid dosage forms for oral administration capsules (including sprinkle capsules and gelatin capsules), tablets, pills, dragees, powders, granules and the like), the active ingredient is mixed with one or more pharmaceutically acceptable carriers, such as sodium citrate or dicalcium phosphate, and/or any of the following: (1) fillers or extenders, such as starches, lactose, sucrose, glucose, mannitol, and/or silicic acid; (2) binders, such as, for example, carboxymethylcellulose, alginates, gelatin, polyvinyl pyrrolidone, sucrose and/or acacia; (3) humectants, such as glycerol; (4) disintegrating agents, such as agar-agar, calcium carbonate, potato or tapioca starch, alginic acid, certain silicates, and sodium carbonate; (5) solution retarding agents, such as paraffin; (6) absorption accelerators, such as quaternary ammonium compounds; (7) wetting agents, such as, for example, cetyl alcohol and glycerol monostearate; (8) absorbents, such as kaolin and bentonite clay; (9) lubricants, such a talc, calcium stearate, magnesium stearate, solid polyethylene glycols, sodium lauryl sulfate, and mixtures thereof; (10) complexing agents, such as, modified and unmodified cyclodextrins; and (11) coloring agents. In the case of capsules (including sprinkle capsules and gelatin capsules), tablets and pills, the pharmaceutical compositions may also comprise buffering agents. Solid compositions of a similar type may also be employed as fillers in soft and hard-filled gelatin capsules using such excipients as lactose or milk sugars, as well as high molecular weight polyethylene glycols and the like.

A tablet may be made by compression or molding, optionally with one or more accessory ingredients. Compressed tablets may be prepared using binder (for example, gelatin or hydroxypropylmethyl cellulose), lubricant, inert diluent, preservative, disintegrant (for example, sodium starch glycolate or cross-linked sodium carboxymethyl cellulose), surface-active or dispersing agent. Molded tablets may be made by molding in a

suitable machine a mixture of the powdered compound moistened with an inert liquid diluent.

The tablets, and other solid dosage forms of the pharmaceutical compositions, such as dragees, capsules (including sprinkle capsules and gelatin capsules), pills and granules, may optionally be scored or prepared with coatings and shells, such as enteric coatings and other coatings well known in the pharmaceutical-formulating art. They may also be formulated so as to provide slow or controlled release of the active ingredient therein using, for example, hydroxypropylmethyl cellulose in varying proportions to provide the desired release profile, other polymer matrices, liposomes and/or microspheres. They may be sterilized by, for example, filtration through a bacteria-retaining filter, or by incorporating sterilizing agents in the form of sterile solid compositions that can be dissolved in sterile water, or some other sterile injectable medium immediately before use. These compositions may also optionally contain opacifying agents and may be of a composition that they release the active ingredient(s) only, or preferentially, in a certain portion of the gastrointestinal tract, optionally, in a delayed manner. Examples of embedding compositions that can be used include polymeric substances and waxes. The active ingredient can also be in micro-encapsulated form, if appropriate, with one or more of the above-described excipients.

Liquid dosage forms useful for oral administration include pharmaceutically acceptable emulsions, lyophiles for reconstitution, microemulsions, solutions, suspensions, syrups and elixirs. In addition to the active ingredient, the liquid dosage forms may contain inert diluents commonly used in the art, such as, for example, water or other solvents, cyclodextrins and derivatives thereof, solubilizing agents and emulsifiers, such as ethyl alcohol, isopropyl alcohol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propylene glycol, 1,3-butylene glycol, oils (in particular, cottonseed, groundnut, corn, germ, olive, castor and sesame oils), glycerol, tetrahydrofuryl alcohol, polyethylene glycols and fatty acid esters of sorbitan, and mixtures thereof.

Besides inert diluents, the compositions of the present invention can also include adjuvants such as wetting agents, lubricants, emulsifying and suspending agents such as sodium lauryl sulfate and magnesium stearate, or sweetening, flavoring, coloring, perfuming, preservative, or anti-oxidant agents.

Suspensions, in addition to the active compounds, may contain suspending agents as, for example, ethoxylated isostearyl alcohols, polyoxyethylene sorbitol and sorbitan

esters, microcrystalline cellulose, aluminum metahydroxide, bentonite, agar-agar and tragacanth, and mixtures thereof.

Formulations of the pharmaceutical compositions for rectal, vaginal, or urethral administration may be presented as a suppository, which may be prepared by mixing one or more active compounds with one or more suitable nonirritating excipients or carriers comprising, for example, cocoa butter, polyethylene glycol, a suppository wax or a salicylate, and which is solid at room temperature, but liquid at body temperature and, therefore, will melt in the rectum or vaginal cavity and release the active compound.

Formulations of the pharmaceutical compositions for administration to the mouth may be presented as a mouthwash, or an oral spray, or an oral ointment.

Alternatively or additionally, compositions can be formulated for delivery via a catheter, stent, wire, or other intraluminal device. Delivery via such devices may be especially useful for delivery to the bladder, urethra, ureter, rectum, or intestine.

Formulations which are suitable for vaginal administration also include pessaries, tampons, creams, gels, pastes, foams or spray formulations containing such carriers as are known in the art to be appropriate.

Dosage forms for the topical or transdermal administration include powders, sprays, ointments, pastes, creams, lotions, gels, solutions, patches and inhalants. The active compound may be mixed under sterile conditions with a pharmaceutically acceptable carrier, and with any preservatives, buffers, or propellants that may be required.

The ointments, pastes, creams and gels may contain, in addition to an active compound, excipients, such as animal and vegetable fats, oils, waxes, paraffins, starch, tragacanth, cellulose derivatives, polyethylene glycols, silicones, bentonites, silicic acid, talc and zinc oxide, or mixtures thereof.

Powders and sprays can contain, in addition to an active compound, excipients such as lactose, talc, silicic acid, aluminum hydroxide, calcium silicates and polyamide powder, or mixtures of these substances. Sprays can additionally contain customary propellants, such as chlorofluorohydrocarbons and volatile unsubstituted hydrocarbons, such as butane and propane.

The compounds described herein can be alternatively administered by aerosol. This is accomplished by preparing an aqueous aerosol, liposomal preparation, or solid particles containing the composition. A nonaqueous (e.g., fluorocarbon propellant) suspension could

be used. Sonic nebulizers are preferred because they minimize exposing the agent to shear, which can result in degradation of the compound.

Ordinarily, an aqueous aerosol is made by formulating an aqueous solution or suspension of the agent together with conventional pharmaceutically acceptable carriers and stabilizers. The carriers and stabilizers vary with the requirements of the particular composition, but typically include nonionic surfactants (Tweens, Pluronics, sorbitan esters, lecithin, Cremophors), pharmaceutically acceptable co-solvents such as polyethylene glycol, innocuous proteins like serum albumin, oleic acid, amino acids such as glycine, buffers, salts, sugars, or sugar alcohols. Aerosols generally are prepared from isotonic solutions.

Transdermal patches have the added advantage of providing controlled delivery of a compound of the present invention to the body. Such dosage forms can be made by dissolving or dispersing the active compound in the proper medium. Absorption enhancers can also be used to increase the flux of the compound across the skin. The rate of such flux can be controlled by either providing a rate controlling membrane or dispersing the compound in a polymer matrix or gel.

Ophthalmic formulations, eye ointments, powders, solutions and the like, are also contemplated as being within the scope of this invention. Exemplary ophthalmic formulations are described in U.S. Publication Nos. 2005/0080056, 2005/0059744, 2005/0031697 and 2005/004074 and U.S. Patent No. 6,583,124, the contents of which are incorporated herein by reference. If desired, liquid ophthalmic formulations have properties similar to that of lacrimal fluids, aqueous humor or vitreous humor or are compatable with such fluids. A preferred route of administration is local administration (*e.g.*, topical administration, such as eye drops, or administration via an implant).

The phrases "parenteral administration" and "administered parenterally" as used herein means modes of administration other than enteral and topical administration, usually by injection, and includes, without limitation, intravenous, intramuscular, intraarterial, intrathecal, intracapsular, intraorbital, intracardiac, intradermal, intraperitoneal, transtracheal, subcutaneous, subcuticular, intraarticular, subcapsular, subarachnoid, intraspinal and intrasternal injection and infusion. Pharmaceutical compositions suitable for parenteral administration comprise one or more active compounds in combination with one or more pharmaceutically acceptable sterile isotonic aqueous or nonaqueous solutions, dispersions, suspensions or emulsions, or sterile powders which may be reconstituted into

sterile injectable solutions or dispersions just prior to use, which may contain antioxidants, buffers, bacteriostats, solutes which render the formulation isotonic with the blood of the intended recipient or suspending or thickening agents.

The phrases "systemic administration," "administered systemically," "peripheral administration" and "administered peripherally" as used herein mean the administration of a ligand, drug, or other material other than directly into the central nervous system, such that it enters the patient's system and thus, is subject to metabolism and other like processes, for example, subcutaneous administration.

Examples of suitable aqueous and nonaqueous carriers that may be employed in the pharmaceutical compositions of the invention include water, ethanol, polyols (such as glycerol, propylene glycol, polyethylene glycol, and the like), and suitable mixtures thereof, vegetable oils, such as olive oil, and injectable organic esters, such as ethyl oleate. Proper fluidity can be maintained, for example, by the use of coating materials, such as lecithin, by the maintenance of the required particle size in the case of dispersions, and by the use of surfactants.

These compositions may also contain adjuvants such as preservatives, wetting agents, emulsifying agents and dispersing agents. Prevention of the action of microorganisms may be ensured by the inclusion of various antibacterial and antifungal agents, for example, paraben, chlorobutanol, phenol sorbic acid, and the like. It may also be desirable to include isotonic agents, such as sugars, sodium chloride, and the like into the compositions. In addition, prolonged absorption of the injectable pharmaceutical form may be brought about by the inclusion of agents that delay absorption such as aluminum monostearate and gelatin.

In some cases, in order to prolong the effect of a drug, it is desirable to slow the absorption of the drug from subcutaneous or intramuscular injection. This may be accomplished by the use of a liquid suspension of crystalline or amorphous material having poor water solubility. The rate of absorption of the drug then depends upon its rate of dissolution, which, in turn, may depend upon crystal size and crystalline form. Alternatively, delayed absorption of a parenterally administered drug form is accomplished by dissolving or suspending the drug in an oil vehicle.

Injectable depot forms are made by forming microencapsulated matrices of the subject compounds in biodegradable polymers such as polylactide-polyglycolide. Depending on the ratio of drug to polymer, and the nature of the particular polymer

employed, the rate of drug release can be controlled. Examples of other biodegradable polymers include poly(orthoesters) and poly(anhydrides). Depot injectable formulations are also prepared by entrapping the drug in liposomes or microemulsions that are compatible with body tissue.

The preparations of agents may be given orally, parenterally, topically, or rectally. They are, of course, given by forms suitable for each administration route. For example, they are administered in tablets or capsule form, by injection, inhalation, eye lotion, ointment, suppository, infusion; topically by lotion or ointment; and rectally by suppositories. Oral administration is preferred.

For use in the invention, active compounds can be given per se or as a pharmaceutical composition containing, for example, 0.1 to 99.5% (more preferably, 0.5 to 90%) of active ingredient in combination with a pharmaceutically acceptable carrier.

Methods of introduction may also be provided by rechargeable or biodegradable devices. Various slow release polymeric devices have been developed and tested *in vivo* in recent years for the controlled delivery of drugs, including proteinacious biopharmaceuticals. A variety of biocompatible polymers (including hydrogels), including both biodegradable and non-degradable polymers, can be used to form an implant for the sustained release of a compound at a particular target site.

These compounds may be administered to humans and other animals for therapy by any suitable route of administration, including orally, nasally, as by, for example, a spray, rectally, intravaginally, parenterally, intracisternally, and topically, as by powders, ointments or drops, including buccally and sublingually.

Regardless of the route of administration selected, the compounds, which may be used in a suitable hydrated form, and/or the pharmaceutical compositions of the present invention, are formulated into pharmaceutically acceptable dosage forms by conventional methods known to those of skill in the art.

Actual dosage levels of the active ingredients in the pharmaceutical compositions may be varied so as to obtain an amount of the active ingredient that is effective to achieve the desired therapeutic response for a particular patient, composition, and mode of administration, without being toxic to the patient.

The selected dosage level will depend upon a variety of factors including the activity of the particular compound or combination of compounds employed, or the ester, salt or amide thereof, the route of administration, the time of administration, the rate of

excretion of the particular compound(s) being employed, the duration of the treatment, other drugs, compounds and/or materials used in combination with the particular compound(s) employed, the age, sex, weight, condition, general health and prior medical history of the patient being treated, and like factors well known in the medical arts. In general, the compositions of this invention may be provided in an aqueous solution containing about 0.1-10% w/v of a compound disclosed herein, among other substances, for parenteral administration. Typical dose ranges are from about 0.01 to about 50 mg/kg of body weight per day, given in 1 single or 2-4 divided doses. Each divided dose may contain the same or different compounds of the invention.

A physician or veterinarian having ordinary skill in the art can readily determine and prescribe the therapeutically effective amount of the pharmaceutical composition required. For example, the physician or veterinarian could start doses of the pharmaceutical composition or compound at levels lower than that required in order to achieve the desired therapeutic effect and gradually increase the dosage until the desired effect is achieved. A "therapeutically effective amount" of a compound with respect to the subject method of treatment, refers to an amount of the compound(s) in a preparation which, when administered as part of a desired dosage regimen (to a mammal, preferably a human) alleviates a symptom, ameliorates a condition, or slows the onset of disease conditions according to clinically acceptable standards for the disorder or condition to be treated or the cosmetic purpose, e.g., at a reasonable benefit/risk ratio applicable to any medical treatment. It is generally understood that the effective amount of the compound will vary according to the weight, sex, age, and medical history of the subject. Other factors which influence the effective amount may include, but are not limited to, the severity of the patient's condition, the disorder being treated, the stability of the compound, and, if desired, another type of therapeutic agent being administered with the compound of the invention. A larger total dose can be delivered by multiple administrations of the agent. Methods to determine efficacy and dosage are known to those skilled in the art (Isselbacher *et al.* (1996) Harrison's Principles of Internal Medicine 13 ed., 1814-1882, herein incorporated by reference).

In general, a suitable daily dose of an active compound used in the compositions and uses of the invention will be that amount of the compound that is the lowest dose effective to produce a therapeutic effect. Such an effective dose will generally depend upon the factors described above.

If desired, the effective daily dose of the active compound may be administered as one, two, three, four, five, six or more sub-doses administered separately at appropriate intervals throughout the day, optionally, in unit dosage forms. In certain embodiments of the present invention, the active compound may be administered two or three times daily. In preferred embodiments, the active compound will be administered once daily.

The patient receiving this treatment is any animal in need, including primates, in particular humans, and other mammals such as equines, cattle, swine and sheep; and poultry and pets in general.

In certain embodiments, compounds of the invention may be used alone or conjointly administered with another type of therapeutic agent. As used herein, the phrase "conjoint administration" refers to any form of administration of two or more different therapeutic compounds such that the second compound is administered while the previously administered therapeutic compound is still effective in the body (*e.g.*, the two compounds are simultaneously effective in the patient, which may include synergistic effects of the two compounds). For example, the different therapeutic compounds can be administered either in the same formulation or in a separate formulation, either concomitantly or sequentially. In certain embodiments, the different therapeutic compounds can be administered within one hour, 12 hours, 24 hours, 36 hours, 48 hours, 72 hours, or a week of one another. Thus, an individual who receives such treatment can benefit from a combined effect of different therapeutic compounds.

This invention includes the use of pharmaceutically acceptable salts of compounds of the invention in the compositions and uses of the present invention. In certain embodiments, contemplated salts of the invention include, but are not limited to, alkyl, dialkyl, trialkyl or tetra-alkyl ammonium salts. In certain embodiments, contemplated salts of the invention include, but are not limited to, L-arginine, benenthamine, benzathine, betaine, calcium hydroxide, choline, deanol, diethanolamine, diethylamine, 2-(diethylamino)ethanol, ethanolamine, ethylenediamine, N-methylglucamine, hydrabamine, 1H-imidazole, lithium, L-lysine, magnesium, 4-(2-hydroxyethyl)morpholine, piperazine, potassium, 1-(2-hydroxyethyl)pyrrolidine, sodium, triethanolamine, tromethamine, and zinc salts. In certain embodiments, contemplated salts of the invention include, but are not limited to, Na, Ca, K, Mg, Zn or other metal salts.

The pharmaceutically acceptable acid addition salts can also exist as various solvates, such as with water, methanol, ethanol, dimethylformamide, and the like. Mixtures

of such solvates can also be prepared. The source of such solvate can be from the solvent of crystallization, inherent in the solvent of preparation or crystallization, or adventitious to such solvent.

Wetting agents, emulsifiers and lubricants, such as sodium lauryl sulfate and magnesium stearate, as well as coloring agents, release agents, coating agents, sweetening, flavoring and perfuming agents, preservatives and antioxidants can also be present in the compositions.

Examples of pharmaceutically acceptable antioxidants include: (1) water-soluble antioxidants, such as ascorbic acid, cysteine hydrochloride, sodium bisulfate, sodium metabisulfite, sodium sulfite and the like; (2) oil-soluble antioxidants, such as ascorbyl palmitate, butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), lecithin, propyl gallate, alpha-tocopherol, and the like; and (3) metal-chelating agents, such as citric acid, ethylenediamine tetraacetic acid (EDTA), sorbitol, tartaric acid, phosphoric acid, and the like.

The invention now being generally described, it will be more readily understood by reference to the following examples which are included merely for purposes of illustration of certain aspects and embodiments of the present invention, and are not intended to limit the invention.

Examples

Example 1: Lot ADC1275-23-1 (Form 1)

Amorphous nicotinamide mononucleotide (565 mg) was weighed into a glass vial and methanol (10.0 mL) added. The resulting slurry was stirred at room temperature for 4 h and then a further portion of MeOH (10.0 mL) added. The white solid present was isolated by filtration and then dried under vacuum at room temperature for ca. 16 h to give crystalline beta nicotinamide mononucleotide Form 1 (459 mg, 81% recovery).

Example 2: Lot ADC1275-24 (Form 1, highly crystalline batch produced by crystallisation from water)

Amorphous beta nicotinamide mononucleotide (605 mg) was weighed into a glass vial and deionised water (600 µL) added. After brief vortexing, a clear solution was formed. A portion of this solution (ca. 200 µL) was dispensed into a separate vial and cooled to 5°C

for ca. 16h. An evolved white solid was isolated by filtration and shown by XRPD analysis to be crystalline beta nicotinamide mononucleotide Form 1 (yield not determined).

Example 3: Lot ADC1275-22-01 (Form 1, batch produced by vapour diffusion for SCXRD)

Amorphous beta nicotinamide mononucleotide (605 mg) was weighed into a glass vial and deionised water (600 µL) added. After brief vortexing, a clear solution was formed. A portion of this solution (100 µL) was dispensed into a separate vial, which itself was placed into a larger vial containing methanol (500 µL) such that vapour can diffuse freely between both vials. The larger vial was sealed and stored at RT for ca. 16h, after which time a white solid had evolved. This solid was sampled and shown by SCXRD to be crystalline beta nicotinamide mononucleotide Form 1.

Reference Example 4: Lot ADC1275-23-1 (Form 2)

Amorphous beta nicotinamide mononucleotide (568 mg) was weighed into a glass vial and DMSO (10.0 mL) added. The resulting slurry was stirred at room temperature for ca. 20 h. The white solid present was then isolated by filtration, washed with acetone (3 x 1 mL) and dried under vacuum at room temperature for ca. 16 h to give crystalline beta nicotinamide mononucleotide Form 2 (501 mg, 72% recovery*).

* based on assumption that material is a DMSO mono-solvate

Incorporation by Reference

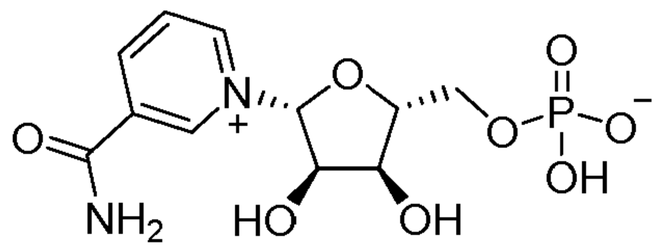
All publications and patents mentioned herein are hereby incorporated by reference in their entirety as if each individual publication or patent was specifically and individually indicated to be incorporated by reference. In case of conflict, the present application, including any definitions herein, will control.

Equivalents

While specific embodiments of the subject invention have been discussed, the above specification is illustrative and not restrictive. Many variations of the invention will become apparent to those skilled in the art upon review of this specification and the claims below. The full scope of the invention should be determined by reference to the claims, along with their full scope of equivalents, and the specification, along with such variations.

Claims:

1. A crystalline compound of Form 1 having the structure of formula (I),



(I).

2. The crystalline compound of claim 1, wherein the compound is anhydrous.

3. The crystalline compound of claim 2, having 2θ values 20.03; 20.14; 21.83; and 25.73.

4. The crystalline compound of claim 3, having 2θ values 20.03; 20.14; 21.03; 21.83; 23.08; 23.39; 25.73; and 26.59.

5. The crystalline compound of claim 4, having 2θ values 7.70; 11.54; 12.64; 16.03; 18.99; 20.03; 20.14; 20.83; 21.03; 21.83; 23.08; 23.39; 25.48; 25.73; 26.59; and 29.78.

6. The crystalline compound of claim 5, having 2θ values 7.70; 9.95; 11.54; 12.64; 16.03; 18.18; 18.99; 19.16; 19.44; 20.03; 20.14; 20.83; 21.03; 21.83; 22.44; 23.08; 23.39; 23.89; 24.08; 24.53; 24.68; 25.05; 25.48; 25.73; 26.08; 26.59; 27.33; 27.67; 29.78; and 29.92.

7. The crystalline compound of claim 6, having an XRD pattern substantially as shown in FIG. 1, labeled Form 1.

8. The crystalline compound of any one of claims 1-7, wherein the compound is at least 90% pure.

9. The crystalline compound of claim 8, wherein the compound is greater than 95% pure.

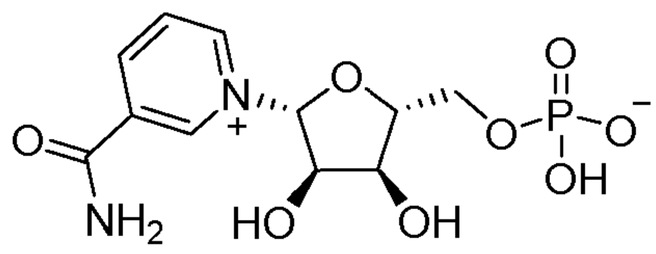
10. The crystalline compound of claim 9, wherein the compound is greater than 98% pure.

11. A composition comprising the crystalline compound of any one of claims 1-7, wherein the crystalline compound is at least 90% pure.

12. A pharmaceutical composition comprising the crystalline compound of any one of claims 1-10 and one or more pharmaceutically acceptable excipients.

13. The pharmaceutical composition of claim 12, wherein the compound is at least 90% pure.

14. A method for preparing a crystalline compound of Form 1 having the structure of formula (I):


(I);

comprising:

a) providing a mixture of a compound of formula (I) in a solvent selected from acetonitrile, N,N-dimethylacetamide (DMA), dimethylformamide (DMF), dimethylsulfoxide (DMSO), ethanol, ethyl acetate, heptanes, hexanes, isopropyl acetate, methanol, methylethyl ketone, N-methyl-2-pyrrolidone (NMP), tetrahydrofuran, toluene, 2-propanol, 1-butanol, water, or any combination thereof; and

b) crystallizing the compound of formula (I) from the mixture comprising the compound of formula (I).

15. The method of claim 14, wherein the crystalline compound is anhydrous.

16. The method of claim 14 or 15, wherein the solvent is methanol or water.

17. The method of any one of claims 14-16, wherein the mixture comprising the compound of formula (I) is a solution, and the step of crystallizing the compound of formula (I) from the mixture comprises bringing the solution to supersaturation to cause the compound of formula (I) to precipitate out of solution.

18. The method of claim 17, wherein the step of bringing the solution to supersaturation comprises slowly adding an anti-solvent, allowing the solution to cool, reducing the volume of the solution, or any combination thereof.

19. The method of claim 17, wherein the step of bringing the solution to supersaturation comprises cooling the solution to ambient temperature or lower.

20. The method of any one of claims 14-16, wherein the mixture comprising the compound of formula (I) is a slurry.

21. The method of any one of claims 14-16, further comprising isolating the crystalline compound.

22. The method of claim 21, wherein isolating the crystalline compound comprises filtering the crystallized compound from the mixture.

23. The method of claim 21 or claim 22, further comprising drying the crystalline compound under reduced pressure.

24. The method of any one of claims 14-23, wherein the crystalline compound is the crystalline compound of any one of claims 1-7.