air driven nebulizer system with an adequate air flow and equipped with a mouthpiece or suitable face mask. While rhDNAse/ PULMOZYNE®, and has been effective in improving the lung function, reducing rate of infection and improving the quality of life for Cystic Fibrosis patients, it has not been approved for other muco-obstructive disease. Doctors do utilize it for other diseases on a case-by-case basis.

PULMOZYNE®, has several limitations. PULMOZYNE®, has low deposition efficiency, reported in the range between 7.8% and 31.2%. PULMOZYNE®, also has storage restrictions, including the need to be stored in a protective foil pouch under refrigeration. A dose of PULMOZYNE®, takes 20-40 minutes to administer. Further, the nebulizer cup must be rinsed with warm water, cleaned of excess liquid, and allowed to air dry following each use. Further cleaning may be required, such as washing the nebulizer cup, mouthpiece, and/or mask with soap and/or disinfectant. Further, while the drug may be safe at these doses in ICU, it is not suitable for chronic out-patient use. Therefore, it has never been utilized and approved for chronic out-patient use.

The disadvantages of PULMOZYNE®, reduce effectiveness and patient adherence to the treatment, jeopardizing the rhDNAse therapy. This molecule has the propensity to readily form dimers and lose its mucolytic activity. Therefore, without stabilizing the activity and using an appropriate delivery method, only a fraction of the dose makes it to the lung. Furthermore, the particle size, flight characteristics, and delivery method have impact on the level of penetration of the drug into the airways and lungs.

Therefore, it is important to formulate and deliver the molecule in a way to stabilize the active form and ensure deeper penetration into the lungs and convenient delivery of a significant percentage, e.g., 60%, of the dose to patient airways.

There is also a desire to protect some mucolytic from degradation or loss of activity before being delivered to the treatment site. Certain mucolytic agents can readily oxidize before reaching their target, which may diminish their efficacy. This may explain inconsistent results in clinical trials. The need exists to provide protection from degradation or loss of activity for a mucolytic in order to maximize its potency.

SUMMARY

Accordingly, it is an object of the present disclosure to overcome these and other drawbacks of the prior art by providing novel inhalable therapeutic agents that allow effective dissolution of mucus.

In an aspect, there is provided a composition comprising a population of inhalable particles, wherein the particles comprise a first mucolytic contained in a biodegradable lipid encapsulation, and wherein the composition is for delivery via a dry powder inhaler.

In another aspect, there is provided a composition comprising a first population of inhalable particles and a second population of inhalable particles, wherein the first inhalable particles comprises a first mucolytic contained within a first biodegradable encapsulation, the second population of inhalable particles comprises the first or a second mucolytic contained within a second biodegradable encapsulation.

In another aspect there is provided a method for preparing the composition as defined above, wherein the method comprises micronization, crystallization, freeze drying, spray freeze drying, or spray drying.

In another aspect, there is provided the composition as defined above for use in therapy.

In another aspect, there is provided the use of the composition as defined above in the manufacture of a medicament for treatment of a subject in need thereof, wherein the composition is to be delivered through the nose, mouth, trachea, or bronchia.

In another aspect, there is provided a composition comprising spray-dried sodium 2-mercaptoethane sulfonate particles having a median mass aerodynamic diameter between 1 and 7 μm.

In another aspect, there is provided the composition as defined above for use in therapy.

In another aspect, there is provided the use of the composition as defined above in the manufacture of a medicament for the treatment of a respiratory illness in a subject.

In another aspect, there is provided a method for preparing a dry-powder active ingredient, comprising:

(i) providing the active ingredient, a first excipient solution, and a second excipient solution;

(ii) microfluidizing the first excipient solution to render the first excipient solution translucent;

(iii) adding the active ingredient to the second excipient solution;

(v) adding the second excipient solution comprising the active ingredient to the first excipient solution to form a feed solution; and

(iv) spray-drying the feed solution.

It is another object of the present disclosure to provide novel inhalable therapeutic agents designed to provide effective treatment at lower doses of the drug so as to reduce possible side effects and allow for self-administration in repeated applications performed multiple times.

It is a further object of the present disclosure to provide novel inhalable therapeutic agents configured for administration either by a medical professional or self-administration so as to make such treatment suitable for out-patient delivery.

It is yet another object of the present disclosure to provide novel therapeutic agents configured to protect the active drug from degradation and prevent loss of mucolytic activity prior to its direct delivery at the target site of the airways, whereby preserving its potency until its immediate interaction at the target site. In the most basic form, the present disclosure may be described as at least one or several pluralities of inhalable particles. Each particle may include one or more mucolytic or another suitable active therapeutic agent contained within one or several different types of biodegradable encapsulations, desirably without the risk of pre-delivery interaction. The number and respective concentration of

therapeutic agents including at least one mucolytic, the type of biodegradable encapsulation selected for each therapeutic agent, and the size of inhalable particles may be adjusted depending on a particular type of airways disorder in order to deliver the intended medication to an intended location of the airways to effectively treat the underlying condition.

In examples, at least two types and/or sizes of inhalable particles may be enclosed in a single dispersing apparatus configured for self-administration by the subject in repeated applications based on a predetermined schedule. At least one of such inhalable particles may include a mucolytic within a biodegradable encapsulation, such as a liposomal formulation, microsphere, nanoparticles or engineered spray-dried particles. Another example includes two such inhalable particles of the same therapeutic, only of different sizes.

Exemplary examples of the disclosure are described in the enumerated paragraphs below.

E1. A composition comprising a population of inhalable particles, wherein the particles comprise a first mucolytic contained in a biodegradable lipid encapsulation, and wherein the composition is for delivery via a dispersing apparatus.

E2. The composition of E1, wherein the is selected from a group of compounds consisting of: sodium 2-mercaptoethane sulfonate, N-acetylcysteine, L-α-ureido-mercaptopropionic acid, Bromhexine, ascorbic acid, vitamin E, tris(2-carboxyethyl)phosphine hydrochloride, N-butylcysteine, reduced glutathione, N-derivatives and C-derivatives of amino acid cysteine, di-peptide of cysteine and glutamic acid, di-peptide of aspartic acid, Ambroxol Hydrochloride, DNAse, and a DNA cleaving agent.

E3. The composition as in E1, wherein the first mucolytic is 2-mercaptoethane sulfonate (e.g., sodium 2-mercaptoethane sulfonate).

E4. The composition as in E1, wherein the mucolytic is N-acetylcysteine.

E5. The composition as in E1, wherein the mucolytic is L-α-ureido-mercaptopropionic acid.

E6. The composition as in E1, wherein the mucolytic is Bromhexine.

E7. The composition as in E1, wherein the mucolytic is ascorbic acid.

E8. The composition as in E1, wherein the mucolytic is vitamin E.

E9. The composition as in E1, wherein the mucolytic is tris(2-carboxyethyl)phosphine hydrochloride.

E10. The composition as in E1, wherein the mucolytic is *N*-butylcysteine.

E11. The composition as in E1, wherein the mucolytic is reduced glutathione.

E12. The composition as in E1, wherein the mucolytic is a *N*-derivative of amino acid cysteine.

E13. The composition as in E1, wherein the mucolytic is a C-derivative of amino acid cysteine.

E14. The composition as in E1, wherein the mucolytic is a di-peptide of cysteine and glutamic acid.

E15. The composition as in E1, wherein the first mucolytic is a di-peptide of aspartic acid.

E16. The composition as in E1, wherein the mucolytic is Ambroxol Hydrochloride.

E17. The composition as in E1, wherein the mucolytic is a DNAse.

E18. The composition as in E1, wherein the mucolytic is a DNA cleaving agent.

E19. The composition as in any one of E1 to E18, wherein the population of inhalable particles are sized to be from about 0.01 microns to about 49 microns, whereby the population of inhalable particles are configured for absorption at a target location of the airways of a subject.

E20. The composition as in E19, wherein the target location of the airways of the subject is the upper respiratory tract or the lower respiratory tract.

CLAIMS

1. A composition comprising a population of inhalable particles, wherein the particles comprise a first mucolytic contained in a biodegradable lipid encapsulation, and wherein the composition is for delivery via a dry powder inhaler.

2. The composition of claim 1, wherein the population of inhalable particles are sized to be from about 0.01 microns to about 49 microns, whereby the population of inhalable particles are configured for predominant absorption at a target location of the airways of a subject.

3. The composition of claim 2, wherein the target location of the airways of the subject is the upper respiratory tract or the lower respiratory tract.

4. A composition comprising a first population of inhalable particles and a second population of inhalable particles, wherein the first inhalable particles comprises a first mucolytic contained within a first biodegradable encapsulation, the second population of inhalable particles comprises the first or a second mucolytic contained within a second biodegradable encapsulation.

5. The composition of claim 4, wherein the first mucolytic or the second mucolytic are selected from a group of compounds consisting of: sodium 2-mercaptoethane sulfonate, N-acetylcysteine, L-α-ureido-mercaptopropionic acid, Bromhexine, ascorbic acid, vitamin E, tris(2-carboxyethyl)phosphine hydrochloride, N-butylcysteine, reduced glutathione, N-derivatives and C-derivatives of amino acid cysteine, di-peptide of cysteine and glutamic acid, di-peptide of aspartic acid, Ambroxol Hydrochloride, DNAse, and a DNA cleaving agent.

6. The composition of any of claims 1-5, wherein the first mucolytic is sodium 2-mercaptoethane sulfonate.

7. The composition of any of claims 1-5, wherein the first mucolytic is a DNAse.

8. The composition of any of claims 1-5, wherein the first mucolytic is a DNA cleaving agent.

9. The composition of any one of claims 4 to 8, wherein the second mucolytic is sodium 2-mercaptoethane sulfonate.

10. The composition of any one of claims 4 to 8, wherein the second mucolytic is a DNAse.

11. The composition of any one of claims 4 to 8, wherein the second mucolytic is a DNA cleaving agent.

12. The composition of any one of claims 4 to 11, wherein the first population of inhalable particles are sized to be from about 5 microns to about 49 microns, the second population of inhalable particles are sized to be from about 0.01 microns to about 6 microns, whereby the first population of inhalable particles are configured for predominant absorption at a first target location of the airways of a subject and the second population of inhalable particles are configured for predominant absorption at a second target location of the airways of a subject.

13. The composition of claim 12, wherein the first target location of the airways of the subject is the upper respiratory tract and the second target location of the airways of the subject is the lower respiratory tract.

14. The composition of claim 12 or 13, further comprising additional particles of mucolytics contained within biodegradable encapsulations, the additional particles are sized for predominant absorption at additional locations of the airways upon inhalation of the composition by the subject.

15. The composition of any one of claims 13 to 14, wherein the first biodegradable encapsulation is configured to release the first mucolytic immediately upon inhalation of the composition by the subject, the second biodegradable encapsulation is configured to release the second mucolytic with a predetermined delay, whereby providing an extended time release mucolytic therapy to the subject.

16. The composition of claim 15, further comprising additional particles comprising a mucolytic contained within a biodegradable encapsulation configured to release the mucolytic with additional predetermined delays.

17. The composition of any one of claims 4 to 16, wherein the first inhalable particles and the second inhalable particles are stored in a solution form or a dry powder form.

18. The composition of any one of claims 4 to 17, wherein the dispersing apparatus is configured upon activation to provide each dose of the composition containing from about 5 mg to about 200 milligrams of the first mucolytic.

19. The composition of any one of claims 1 to 18 further comprising one or more short-acting beta-agonist, long-acting beta-agonist, short-acting muscarinic antagonist, long-acting muscarinic antagonist, immunosuppressant, antibiotic, antiviral, antifungal, corticosteroid, or additional anti-infective agent.

20. The composition of any one of claims 1 to 19, wherein the composition comprises an immunosuppressant.

21. The composition of claim 19 or 20, wherein the immunosuppressant is cyclosporin.

22. The composition of any one of claims 1 to 21, wherein the composition comprises an anti-infective agent selected from the group consisting of quinolone, nalidixic acid, ciprofloxacin, cinoxacin, sulfoamide, sulanilamide, sulfadiazine, sulfamethoxazole, sulfisoxazole, aminoglycoside, streptomycin, gentamicin, tobramycin, amikacin, netilmicin, Kanamycin, tetracycline, chlortetracycline, oxytetracycline, methacycline, doxycycline, minocycline, para-aminobenzoic acid, diaminopyrimidine, trimethoprim, beta-lactam, penicillin, penicillin G benzathine, penicillin VK, ampicillin, amoxicillin, bacampicillin, carbenicillin, carbenicillin indanyl, ticarcillin, azlocillin, mezlocillin, piperacillin, penicillinase resistant penicillin, methicillin, oxacillin, cloxacillin, dicloxacillin, nafcillin, cephalosporin, first-generation cephalosporin, cefadroxil, cephalexin, cephradine, cephalothin, cephapirin, cefazolin, second-generation cephalosporin, cefaclor, cefamandole, cefonicid, cefoxitin, cefotetan,

cefuroxime, aefuroxime axetil, cefinetazole, cefprozil, loracarbef, ceforanide, third-generation cephalosporin, cefepime, cefoperaZone, cefotaxime, ceftizoxime, ceftriaxone, ceftazidime, cefixime, cefpodoxime, ceftibuten, cefotaxime, imipenem, meropenem, aztreonam, clavulanic acid, sulbactam, tazobactam, beta-lactamase inhibitor, clavulanate, chloramphenicol, macrolide, erythromycin, azithromycin, clarithromycin, lincomycin, clindamycin, spectinomycin, polymyxin, polymyxin A, polymyxin B, polymyxin C, polymyxin D, polymyxin E, vancomycin, bacitracin, isoniazid, rifampin, ethambutol, ethionamide, aminosalicylic acid, cycloserine, capreomycin, sulfone, dapsone, sulfoxone sodium, clofazimine, and thalidomide.

23. The composition of any one of claims 1 to 22, wherein the composition comprises an antifungal agent selected from the group consisting of polyene, amphotericin B, nystatin, natamycin, flucytosine, imidazole, miconazole, clotrimazole, econazole, ketoconazole, triazole, itraconazole, fluconazole, griseofulvin, terconazole, butoconazole, ciclopirox, ciclopirox olamine, haloprogin, tolnaftate, naftifine, and terbinafine.

24. The composition of any one of claims 1 to 23, wherein the composition comprises a corticosteroid selected from the group consisting of flunisolide, fluticasone, fluocortolone, triamcinolone, beclomethasone, budesonide, mometasone, ciclesonide, prednisolone, betamethasone, dexamethasone, hydrocortisone, methylprednisolone, and deflazacort.

25. The composition of any one of claims 1 to 24, wherein the composition comprises a short-acting beta-agonist selected from the group consisting of bitolterol, fenoterol, isoprenaline, levosalbutamol, orciprenaline, pirbuterol, procaterol, ritodrine, salbutamol, terbutaline, albuterol, .

26. The composition of any one of claims 1 to 25, wherein the composition comprises a long-acting beta-agonist selecting from the group consisting of formoterol, bambuterol, clenbuterol, formoterol, salmeterol, indacaterol, olodaterol, and vilanterol.

27. The composition of any one of claims 1 to 26, wherein the composition comprises a short-acting muscarinic antagonist.

28. The composition of claim 19 or 27, wherein the short-acting muscarinic antagonist is ipratropium.

29. The composition of any one of claims 1 to 28, wherein the composition comprises a long-acting muscarinic antagonist selected from the group consisting of aclidinium, glycopyrronium, glycopyrrolate, tiotropium, and umeclidinium.

30. The composition of any one of claims 1 to 29, wherein the composition comprises a long-acting muscarinic antagonist and a long-acting beta-agonist.

31. The composition of claim 30, wherein the long-acting muscarinic antagonist is umeclidinium and the long-acting beta-agonist is vilanterol.

32. The composition of claim 30, wherein the long-acting muscarinic antagonist is tiotropium and the long-acting beta-agonist is olodaterol.

33. The composition of claim 30, wherein the long-acting muscarinic antagonist is glycopyrrolate and the long-acting beta-agonist is formoterol.

34. The composition of claim 30, wherein the long-acting muscarinic antagonist is glycopyrronium and the long-acting beta-agonist is indacaterol.

35. The composition of any one of claims 1 to 34, wherein the composition comprises a long-acting muscarinic antagonist and a short-acting muscarinic antagonist.

36. The composition of any one of claims 1 to 35, wherein the composition comprises a long-acting muscarinic antagonist, short-acting muscarinic antagonist, long-acting beta-agonist, and a corticosteroid.

37. The composition of claim 19 or 36, wherein the composition comprises an antiviral agent selected from the group consisting of remdesivir, abacavir, adefovir, delavirdine, descovy, didanosine, doravirine, efavirenz, emtricitabine, entecavir, etravirine, lamivudine, loviride, nevirapine, rilpivirine, stavudine, tenofovir alafenamide, tenofovir disoproxil, zalcitabine, zidovudine, acyclovir, cidofovir, penciclovir, famciclovir, foscarnet, ganciclovir, valganciclovir, idoxuridine, ribavirin, taribavirin, sofosbuvir, telbivudine, trifluridine, valaciclovir, vidarabine, boceprevir, atazanavir, darunavir, fosamprenavir, indinavir, lopinavir, nelfinavir, ritonavir, saquinavir, simeprevir, telaprevir, tipranavir, bictegravir, elvitegravir, dolutegravir, raltegravir, oseltamivir, zanamivir, laninamivir, peramivir, ledipasvir, amprenavir, amantadine, umifenovir, baloxavir marboxil, daclatasvir, docosanol, edoxudine, enfuvirtide, fomivirsen, ibacitabine, ibalizumab, letermovir, maraviroc, metisazone, moroxydine, nexavir, nitazoxanide, pleconaril, rimantadine, tromantadine, and vicriviroc.

38. The composition of any one of claims 1 to 37, wherein the composition comprises liposomes, microspheres, engineered spray-dried particles, or nanoparticles.

39. The composition of any one of claims 19 to 38, wherein the first mucolytic, second mucolytic, short-acting beta-agonist, long-acting beta-agonist, short-acting muscarinic antagonist, long-acting muscarinic antagonist, immunosuppressant, antibiotic, antiviral, antifungal, corticosteroid, and/or additional anti-infective agent compound are encapsulated in nanoparticles.

40. The composition of any one of claims 1 to 39, wherein the composition comprises microspheres.

41. The composition of any one of claims 19 to 40, wherein the first mucolytic, second mucolytic, short-acting beta-agonist, long-acting beta-agonist, short-acting muscarinic antagonist, long-acting muscarinic antagonist, immunosuppressant, antibiotic, antiviral, antifungal, corticosteroid, and/or additional anti-infective agent compound are encapsulated in microspheres.

42. The composition of any one of claims 1 to 41, wherein the composition comprises liposomes.

43. The composition of any one of claims 19 to 42, wherein the first mucolytic, second mucolytic, short-acting beta-agonist, long-acting beta-agonist, short-acting muscarinic antagonist, long-acting muscarinic antagonist, immunosuppressant, antiviral, antifungal, antibiotic, corticosteroid, and/or anti-infective compound are encapsulated in liposomes.

44. The composition of any one of claims 1 to 43, wherein the composition comprises engineered spray-dried particles.

45. The composition of any one of claims 19 to 44, wherein the first mucolytic, second mucolytic, short-acting beta-agonist, long-acting beta-agonist, short-acting muscarinic antagonist, long-acting muscarinic antagonist, immunosuppressant, antiviral, antifungal, antibiotic, corticosteroid, and/or anti-infective compound are engineered spray-dried particles.

46. A method for preparing the composition of any one of claims 1 to 45, wherein the method comprises micronization, crystallization, freeze drying, spray freeze drying, or spray drying.

47. The method of claim 46, wherein the micronization involves milling, crushing, grinding, or precipitation from supercritical fluids.

48. The method of any one of claims 46 or 47, wherein the composition is mixed with a sugar selected from the group consisting of lactose, maltodextrin, mannitol, and trehalose.

49. The method of any one of claims 46 to 48, wherein the method comprises spray drying.

50. The method of any one of claims 46 to 49, wherein the spray drying inlet temperature is between 80 and 90°C.

51. The method of any one of claims 46 to 50, wherein the spray drying outlet temperature is between 55 and 65°C.

52. The method of any one of claims 46 to 51, wherein the spray drying feed rate is between 1 and 3 g/min.

53. The method of any one of claims 46 to 52, wherein the spray drying pressure is between 3 and 5 bar.

54. The method of any one of claims 46 to 53, wherein the method comprises freeze drying.

55. The method of any one of claims 46 to 54, wherein the method comprises spray freeze drying.

56. The method of any one of claims 46 to 55 further comprising dissolving the composition.

57. The method of any one of claims 46 to 56, wherein the composition is mixed with one or more of sodium alginate, chitosan, trehalose, raffinose, leucine, hydroxypropylmethylcellulose, hydroxypropylbetacyclodextrin or a dispersing agent.

58. The method as 57, wherein the dispersing agent is Pluronic F-68.

59. The composition of any one of claims 1 to 45 for use in therapy.

60. Use of the composition of any one of claims 1 to 45 in the manufacture of a medicament for treatment of a subject in need thereof, wherein the composition is to be delivered through the nose, mouth, trachea, or bronchia.

61. The use of claim 60, wherein the composition is to be delivered through the nose, mouth, trachea, or bronchia.

62. The use of any one of claims 60 or 61, wherein the composition is to be delivered via nebulization or instillation.

63. The use of any one of claims 60 to 62, wherein the subject in need is diagnosed with a muco-obstructive, lung, sinus, ear, or airway disease.

64. The use of any one of claims 60 to 63, wherein the subject in need is diagnosed with primary ciliary dyskinesia, cystic fibrosis, sinusitis, rhinosinusitis, bronchiolitis obliterans, emphysema, bronchitis, bronchiectasis, pneumonitis, pneumonia, chronic obstructive pulmonary disease (COPD), chronic obstructive airway disease (COAD), acute respiratory distress syndrome (ARDS), chronic respiratory distress syndrome (CRDS), or COVID-19.

65. A composition comprising spray-dried sodium 2-mercaptoethane sulfonate particles having a median mass aerodynamic diameter between 1 and 7 µm

66. The composition of claim 65, wherein the median mass aerodynamic diameter is between 3 and 5 µm.

67. The composition of claim 65 or 66, wherein the particles comprise between 20 and 60% w/w sodium 2-mercaptoethane sulfonate.

68. The composition of any one of claims 65 to 67, wherein the composition comprises between 5 and 200 mg of sodium 2-mercaptoethane sulfonate.

69. The composition of any one of claims 65 to 68, wherein the bulk density of the composition is between 0.1 and 5 g/mL.

70. The composition of any one of claims 65 to 69, wherein the fine particle fraction of the composition less than or equal to a mass median aerodynamic diameter of 6 µm is between 10 and 90%.

71. The composition of any one of claims 65 to 70, wherein the fine particle fraction of the composition less than or equal to a mass median aerodynamic diameter of 5 µm is between 10 and 90%.

72. The composition of any one of claims 65 to 71, wherein the fine particle fraction of the composition less than or equal to a mass median aerodynamic diameter of 4 µm is between 10 and 90%.

73. The composition of any one of claims 65 to 72, further comprising mannitol, calcium chloride, magnesium stearate, sodium acetate, DPPC (dipalmitoylphosphatidylcholine), soy lecithin, egg lecithin, hydrogenated soybean phosphatidylcholine (HSPC), cholesterol, PEG

(polyethylene glycol); DSPE (distearoyl-sn-glycero-phosphoethanolamine); DSPC (distearoylphosphatidylcholine); DOPC (dioleoylphosphatidylcholine); EPC (egg phosphatidylcholine); DOPS (dioleoylphosphatidylserine); POPC (palmitoyloleoylphosphatidylcholine); SM (sphingomyelin); MPEG (methoxy polyethylene glycol); DMPC (dimyristoyl phosphatidylcholine); DMPG (dimyristoyl phosphatidylglycerol); DSPG (distearoylphosphatidylglycerol); DEPC (dierucoylphosphatidylcholine); DOPE (dioleoly-sn-glycero-phophoethanolamine), triolein, 1,2-distearoyl-sn-glycero-3-phosphoethanolamine sodium salt (MPEG-DSPE), or DPPG (1,2-Dipalmitoyl-sn-glycero-3-phosphorylglycerol sodium salt).

74. The composition of any one of claims 65-73 for use in therapy.

75. Use of the composition of any one of claims 65-74 in the manufacture of a medicament for the treatment of a respiratory illness in a subject.

76. The use of claim 75, wherein the subject is a mammal, e.g., a human.

77. The use of claim 75 or 76, wherein the subject in need is diagnosed with a muco-obstructive, lung, sinus, ear, or airway disease.

78. The use of any one of claims 75 to 77, wherein the subject in need is diagnosed with primary ciliary dyskinesia, cystic fibrosis, sinusitis, rhinosinusitis, bronchiolitis obliterans, emphysema, bronchitis, bronchiectasis, pneumonitis, pneumonia, COPD, COAD, ARDS, CRDS, or COVID-19.

79. The use of any one of claims 75 to 78, wherein the subject is to be treated more than once per month.

80. The use of any one of claims 75 to 79, wherein the subject is to be treated as an out-patient.

81. The use of any one of claims 75 to 80, wherein the subject is to be treated with a cotherapy.

82. The use of any one of claims 75 to 81, wherein the fine particle dose to be delivered to the subject is between 0.1 and 200 mg.

83. The use of any one of claims 75 to 82, wherein the subject is to be treated with between 0.1 and 200 mg of therapeutic.

84. A method for preparing a dry-powder active ingredient, comprising:

(i) providing the active ingredient, a first excipient solution, and a second excipient solution;

(ii) microfluidizing the first excipient solution to render the first excipient solution translucent;

(iii) adding the active ingredient to the second excipient solution;

(v) adding the second excipient solution comprising the active ingredient to the first excipient solution to form a feed solution; and

(iv) spray-drying the feed solution.

85. The method of claim 84, wherein the active ingredient is selected from a group of compounds consisting of: sodium 2-mercaptoethane sulfonate, N-acetylcysteine, L-α-ureido-mercaptopropionic acid, Bromhexine, ascorbic acid, vitamin E, tris(2-carboxyethyl)phosphine hydrochloride, N-butylcysteine, reduced glutathione, N-derivatives and C-derivatives of amino acid cysteine, di-peptide of cysteine and glutamic acid, di-peptide of aspartic acid, Ambroxol Hydrochloride, DNAse, and a DNA cleaving agent.

86. The method of claim 84 or 85, wherein the active ingredient is sodium 2-mercaptoethane sulfonate.

87. The method of claim 84 or 85, wherein the active ingredient is a DNAse.

88. The method of claim 84 or 85, wherein the active ingredient is a DNA cleaving agent.

89. The method of any of claims 84-88, wherein the first excipient is 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC).

90. The method of any of claims 84-89, wherein the second excipient is calcium chloride.

91. The method of any of claims 84-90, wherein nitrogen is used as a drying gas.

92. The method of any of claims 84-91, wherein the first and/or second excipient solutions comprise de-ionized water.

93. The method of any of claims 84-92, wherein the spray drying inlet temperature is between 50 and 70°C.

94. The method of any of claims 84-93, wherein the feed solution is spray-dried at a rate of 1-3 g/min.

95. The method of any of claims 84-94, wherein spray-drying inlet pressure is between 3-5 bar.

96. The method of any of claims 84-95, wherein the second excipient solution comprises sodium chloride (NaCl).

97. The method of claim 96, wherein the pH of the second excipient solution is adjusted with the NaCl to be 6-6.5.

98. The method of any of claims 84-97, wherein the spray drying inlet temperature is between 80 and 90°C.

99. The method of any of claims 84-98, wherein the feed solution is maintained at a temperature between 60 and 70°C.