symptoms associated therewith, while reducing or avoiding adverse effects or unwanted effects. The invention further encompasses specific doses and unit dosage forms of 3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid or a pharmaceutically acceptable salt, solvate or hydrate thereof.

[0005a] In one aspect, there is provided the use of 3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid or a pharmaceutically acceptable salt, solvate or hydrate thereof in the manufacture of a medicament for treating, preventing or managing Cystic Fibrosis resulting from a premature stop codon in mRNA encoded by the *CFTR* gene in a human patient in need thereof or Duchenne Muscular Dystrophy resulting from a premature stop codon in mRNA encoded by the dystrophin gene in a human patient in need thereof, wherein said medicament is to be orally administered in three doses, wherein a first dose, a second dose and a third dose are administered in a 24 hour period according to the formula 1X, 1X, 2X, respectively, wherein X is 18-22 mg/kg and, wherein each dose maintains the plasma level of 3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid at greater than 2 μg/mL.

[0006] In one example~~embodiment~~, described are~~the invention relates to~~ methods for administering to a patient in need thereof an effective amount of 3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid or a pharmaceutically acceptable salt, solvate or hydrate thereof one, two or three times in the course of a 24 hour period. Also described are~~The invention also relates to~~ methods for administering to a patient in need thereof a pharmaceutical composition comprising an effective amount of 3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid or a pharmaceutically acceptable salt, solvate or hydrate thereof one, two or three times in the course of a 24 hour period. The dose at each administration during a 24 hour period can be the same or different. In one example~~embodiment~~, when administered three times in a 24 hour period, the dose at the first two administrations is the same and the third dose is twice the first dose. In another example~~embodiment~~, all three doses are the same.

[0007] In another example~~embodiment~~, the invention relates to methods for treating, preventing or managing a disease ameliorated by modulation of premature translation termination or nonsense-mediated mRNA decay comprising administering to a patient in need thereof an effective amount of 3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid or a pharmaceutically acceptable salt, solvate or hydrate thereof one, two or three times in the course of a 24 hour period. Preferably, the administration is made three times per day continuously, or with a rest period, for a number of days, weeks, months or years.

[0008] Also described herein are~~The invention also relates to~~ methods for treating, preventing or managing a disease ameliorated by modulation of premature translation termination or nonsense-mediated mRNA decay comprising administering to a patient in need thereof a pharmaceutical composition comprising an effective amount of 3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid or a pharmaceutically acceptable salt, solvate or hydrate thereof one, two or three times in the course of a 24 hour period. Preferably, the administration is made three times per day continuously, or with a rest period, for a number of days, weeks, months or years.

[0009] In one example it is described~~mbodiment, the invention relates to~~ a method of treating, preventing or reducing cough, comprising administering an effective amount of 3-[5-(2-fluoro-phenyl)-

[1,2,4]oxadiazol-3-yl]-benzoic acid or a pharmaceutically acceptable salt, solvate or hydrate thereof to a patient in need thereof.

[0010] In one example it is also referred to~~mbodiment, the invention relates to~~ a method of increasing dystrophin expression in muscle, comprising administering an effective amount of 3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid or a pharmaceutically acceptable salt, solvate or hydrate thereof to a patient in need thereof.

[0011] In one example it is also referred to~~mbodiment, the invention relates to~~ a method of administering 3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid or a pharmaceutically acceptable salt, solvate or hydrate thereof wherein the active agent is administered to a patient in need thereof one, two or three times in a 24 hour period, wherein each administration is preferably separated by about 4-14 hours. In a particular example~~mbodiment~~, the dose of active agent is escalated from the first to third dose.

[0012] In another example it is also described~~mbodiment, the invention relates~~ to continuous therapy wherein 3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid or a pharmaceutically acceptable salt, solvate or hydrate thereof is administered to a patient in need thereof for a certain period of time (*e.g.*, 5, 7, 10, 14, 20, 24, 28, 60 or 120 days or longer).

[0013] In another example it is also described~~mbodiment, the invention relates to~~ the administration of 3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid or a pharmaceutically acceptable salt, solvate or hydrate thereof in single or divided (*e.g.*, three times daily) doses between 0.1 mg/kg and 500 mg/kg, 1 mg/kg and 250 mg/kg, 1 mg/kg and 150 mg/kg, 1 mg/kg and 100 mg/kg, 1 mg/kg and 50 mg/kg, 1 mg/kg and 25 mg/kg, 1 mg/kg and 10 mg/kg or 2 mg/kg and 10 mg/kg to a patent in need thereof. In a particular example~~mbodiment~~, 3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid or a pharmaceutically acceptable salt, solvate or hydrate thereof is administered in a dose of about 4 mg/kg, about 7 mg/kg, about 8 mg/kg, about 10 mg/kg, about 14 mg/kg or about 20 mg/kg. In another example~~mbodiment~~, any dose of the 3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid or a pharmaceutically acceptable salt, solvate or hydrate described in the preceding example~~mbodiment~~ is administered one, two or three times in a 24 hour period.

[0014] In another example described are~~mbodiment, the invention relates to~~ unit dosage formulations that comprise between about 35 mg and about 1400 mg, about 125 mg and about 1000 mg, about 250 mg and about 1000 mg, or about 500 mg and about 1000 mg of 3-[5-(2-fluoro-phenyl)-

[1,2,4]oxadiazol-3-yl]-benzoic acid or a pharmaceutically acceptable salt, solvate or hydrate thereof.

[0015] In another example described are~~mbodiment, the invention relates to~~ unit dosage formulations that comprise 35 mg, 50 mg, 70 mg, 100 mg, 125 mg, 140 mg, 175 mg, 200 mg, 250 mg, 280 mg, 350 mg, 500 mg, 560 mg, 700 mg, 750 mg, 1000 mg or 1400 mg of 3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid or a pharmaceutically acceptable salt, solvate or hydrate thereof. In a preferred example described are~~mbodiment, the invention relates to~~ unit dosage formulations that comprise 125 mg, 250 mg or 1000 mg of 3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid or a pharmaceutically acceptable salt, solvate or hydrate thereof.

In another example it is described~~mbodiment, the invention relates to~~ a method of maintaining a plasma concentration of 3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid or a pharmaceutically acceptable salt, solvate or hydrate thereof of greater than about 0.1 μg/ml, 0.5 μg/ml, 1 μg/ml, 2 μg/ml, about 5 μg/ml, about 10 μg/ml, about 20 μg/ml, about 25 μg/ml, about 40 μg/ml, about 50 μg/ml, 100 μg/ml, 200 μg/ml, 300 μg/ml, 400 μg/ml, or 500 μg/ml in a patient for at least about 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 6, 8, 12 or 24 hours or longer, comprising administering an effective amount 3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid or a pharmaceutically acceptable salt, solvate or hydrate thereof to a patient in need thereof.

4. Detailed Description

4.1 Brief Description of the Drawings

[0016] **FIG. 1** provides the plasma 3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid concentration-time profiles and PK paramaters from 37 of 38 patients in a Phase 2 Duchenne muscular dystrophy study at 4-, 4-, and 8-mg/kg; 10-, 10-, and 20-mg/kg; and 20-, 20- and 40-mg/kg dose levels. The data from one patient was excluded from analysis due to insufficient data.

[0017] **FIG. 2** provides the effect on mean cough frequency over 24 hours by the administration of 3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid to a subject. This data indicates that the administration of 3-[5-(2-fluoro-phenyl)-[1,2,4]oxadiazol-3-yl]-benzoic acid provides an initial improvement in mean cough frequency, followed by temporary increase in mean cough frequency, followed by an overall improvement in mean cough frequency.