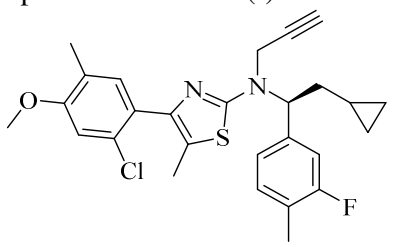
Provided herein is a compound of Formula (I):



(I),

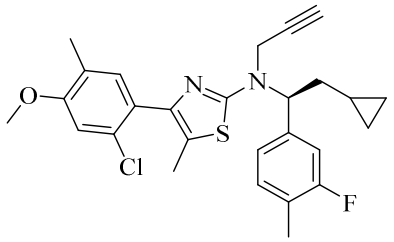
or a pharmaceutically acceptable salt thereof;

for use in a method of treating congenital adrenal hyperplasia in a subject,

wherein the compound of Formula (I), or a pharmaceutically acceptable salt thereof, is administered at a frequency of not less than twice daily; and

wherein the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the first administration is less than the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the second and any subsequent administrations.

In one aspect, the present disclosure refers to use of a compound of Formula (I):



(I),

or a pharmaceutically acceptable salt thereof;

in the manufacture of a medicament for treating congenital adrenal hyperplasia in a subject,

wherein the compound of Formula (I), or a pharmaceutically acceptable salt thereof, is to be administered at a frequency of not less than twice daily; and

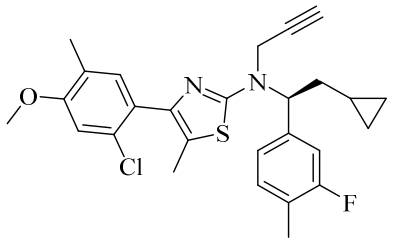
wherein the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the first administration is less than the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the second and any subsequent administrations.

Provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof for use in a method of treating congenital adrenal hyperplasia in a subject,

wherein the compound of Formula (I), or a pharmaceutically acceptable salt thereof, is administered at a frequency of not less than twice daily; and

wherein the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, administered daily is greater than 200 mg based on the weight of the free base.

In one aspect, the present disclosure refers to use of a compound of Formula (I):



(I),

or a pharmaceutically acceptable salt thereof;

in the manufacture of a medicament for treating congenital adrenal hyperplasia in a subject,

wherein the compound of Formula (I), or a pharmaceutically acceptable salt thereof, is to be administered at a frequency of not less than twice daily; and

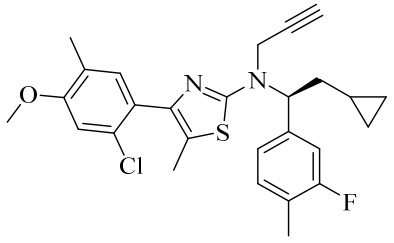
wherein the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, to be administered daily is greater than 200 mg based on the weight of the free base.

Provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, for use in a method of reducing the severity of one or more symptoms selected from hirsutism, precocious puberty, fertility problems, acne, and growth impairment in a subject having classic congenital adrenal hyperplasia,

wherein the compound of Formula (I), or a pharmaceutically acceptable salt thereof, is administered at a frequency of not less than twice daily; and

wherein the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the first administration is less than the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the second and any subsequent administrations.

In one aspect, the present disclosure refers to use of a compound of Formula (I):



(I)

or a pharmaceutically acceptable salt thereof;

in the manufacture of a medicament for reducing the severity of one or more symptoms selected from hirsutism, precocious puberty, fertility problems, acne, and growth impairment in a subject having classic congenital adrenal hyperplasia,

wherein the compound of Formula (I), or a pharmaceutically acceptable salt thereof, is to be administered at a frequency of not less than twice daily; and

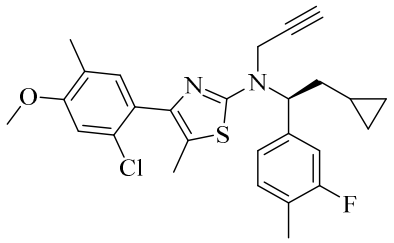
wherein the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the first administration is less than the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the second and any subsequent administrations.

Provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, for use in method of reducing the level of one or more biomarkers of congenital adrenal hyperplasia in a subject having congenital adrenal hyperplasia,

wherein the compound of Formula (I), or a pharmaceutically acceptable salt thereof, is administered at a frequency of not less than twice daily; and

wherein the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the first administration is less than the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the second and any subsequent administrations.

In one aspect, the present disclosure refers to use of a compound of Formula (I):



(I),

or a pharmaceutically acceptable salt thereof,

in the manufacture of a medicament for reducing the level of one or more biomarkers of congenital adrenal hyperplasia in a subject having congenital adrenal hyperplasia,

wherein the compound of Formula (I), or a pharmaceutically acceptable salt thereof, is to be administered at a frequency of not less than twice daily; and

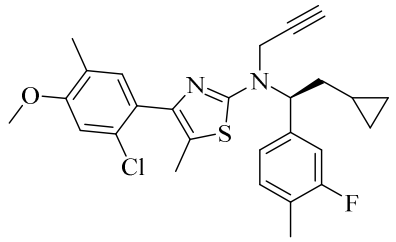
wherein the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the first administration is less than the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the second and any subsequent administrations.

Provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, for use in a method of reducing the dosage of corticosteroid administered to a subject having congenital adrenal hyperplasia for controlling congenital adrenal hyperplasia,

wherein the compound of Formula (I), or a pharmaceutically acceptable salt thereof, is administered at a frequency of not less than twice daily; and

wherein the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the first administration is less than the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the second and any subsequent administrations.

In one aspect, the present disclosure refers to use of a compound of Formula (I):



(I),

or a pharmaceutically acceptable salt thereof;

in the manufacture of a medicament for reducing the dosage of corticosteroid administered to a subject having congenital adrenal hyperplasia for controlling congenital adrenal hyperplasia,

wherein the compound of Formula (I), or a pharmaceutically acceptable salt thereof, is to be administered at a frequency of not less than twice daily; and

wherein the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the first administration is less than the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the second and any subsequent administrations.

Provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, for use in a method of reducing the severity of one or more side effects of glucocorticoid treatment in a subject having congenital adrenal hyperplasia,

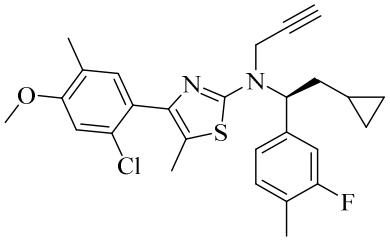
wherein the compound of Formula (I), or a pharmaceutically acceptable salt thereof, is administered at a frequency of not less than twice daily;

wherein the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the first administration is less than the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the second and any subsequent administrations; and

wherein the side effect is selected from osteoporosis, avascular necrosis of bone, myopathy, hyperglycemia, diabetes mellitus, dyslipidemia, weight gain, Cushing syndrome, Cushingoid features, growth suppression, adrenal suppression, gastritis, peptic ulcer, gastrointestinal bleeding, visceral perforation, hepatic steatosis, pancreatitis, hypertension, coronary heart disease, ischemic heart disease, heart failure, dermatoprosis, skin atrophy, ecchymosis, purpura, erosions, striae, delayed wound healing, easy bruising, acne, hirsutism, hair loss, mood changes, depression, euphoria, mood lability, irritability, akathisia, anxiety,

cognitive impairment, psychosis, dementia, delirium, cataract, glaucoma, ptosis, mydriasis, opportunistic ocular infections, central serous chorioretinopathy, suppression of cell-mediated immunity, predisposition to infections, and reactivation of latent infections.

In one aspect, the present disclosure refers to use of a compound of Formula (I):



(I),

or a pharmaceutically acceptable salt thereof,

in the manufacture of a medicament for reducing the severity of one or more side effects of glucocorticoid treatment in a subject having congenital adrenal hyperplasia,

wherein the compound of Formula (I), or a pharmaceutically acceptable salt thereof, is to be administered at a frequency of not less than twice daily;

wherein the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the first administration is less than the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the second and any subsequent administrations; and

wherein the side effect is selected from osteoporosis, avascular necrosis of bone, myopathy, hyperglycemia, diabetes mellitus, dyslipidemia, weight gain, Cushing syndrome, Cushingoid features, growth suppression, adrenal suppression, gastritis, peptic ulcer, gastrointestinal bleeding, visceral perforation, hepatic steatosis, pancreatitis, hypertension, coronary heart disease, ischemic heart disease, heart failure, dermatoprosis, skin atrophy, ecchymosis, purpura, erosions, striae, delayed wound healing, easy bruising, acne, hirsutism, hair loss, mood changes, depression, euphoria, mood lability, irritability, akathisia, anxiety, cognitive impairment, psychosis, dementia, delirium, cataract, glaucoma, ptosis, mydriasis, opportunistic ocular infections, central serous chorioretinopathy, suppression of cell-mediated immunity, predisposition to infections, and reactivation of latent infections.

Provided herein is a compound of Formula (I), or a pharmaceutically acceptable salt thereof, for use in a method of treating congenital adrenal hyperplasia in a subject, the method comprising:

(a) selecting a subject who has a glucocorticoid dose of greater than 11 mg/m^2/day after a time period of being administered a compound of Formula (I), or a pharmaceutically acceptable thereof, at an amount of about 100 mg twice daily based on the weight of the free base;

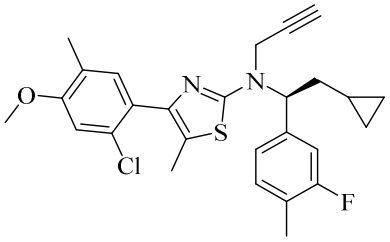
and

(b) administering to the subject the compound of Formula (I), or a pharmaceutically acceptable salt thereof, at a frequency of twice daily;

wherein the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the first administration is less than the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the second administration;

and wherein the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, administered daily is greater than or equal to about 200 mg based on the weight of the free base.

In one aspect, the present disclosure refers to use of a compound of Formula (I):



(I)

or a pharmaceutically acceptable thereof,

in the manufacture of a medicament for treating congenital adrenal hyperplasia in a subject, the use comprising:

selecting a subject who has a glucocorticoid dose of greater than 11 mg/m^2/day after a time period of being administered a compound of Formula (I), or a pharmaceutically acceptable thereof, at an amount of about 100 mg twice daily based on the weight of the free base;

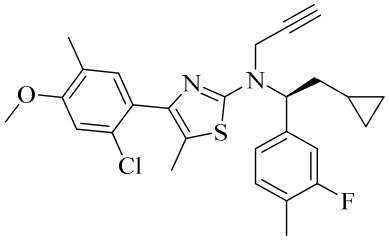
wherein

the subject is to be administered the compound of Formula (I), or a pharmaceutically acceptable salt thereof, at a frequency of twice daily;

wherein the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the first administration is less than the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the second administration;

and wherein the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, to be administered daily is greater than or equal to about 200 mg based on the weight of the free base.

Provided herein is a method of treating congenital adrenal hyperplasia in a subject in need thereof comprising administering to the subject a compound of Formula (I):



(I),

or a pharmaceutically acceptable salt thereof;

wherein the compound of Formula (I), or a pharmaceutically acceptable salt thereof, is administered at a frequency of not less than twice daily; and

wherein the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the first administration is less than the amount of the compound of Formula (I), or a pharmaceutically acceptable salt thereof, in the second and any subsequent administrations.