SUMMARY

[0007] The present disclosure is based, in part, on the development of solid oral dosage forms of decitabine and cedazuridine, wherein the solid oral dosage form upon daily administration to a subject provides plasma levels of decitabine with a 5-day area under the curve (AUC) for decitabine that is equivalent to the 5-day AUC for a daily intravenous (IV) dose of decitabine of 20 mg/m^2 administered as a one hour infusion. In some examples, upon daily administration of such solid oral dosage form to a subject, the ratio of AUC for decitabine on day 2 versus day 1 is about 1.5:1 to about 2:1.

[0008] In one aspect, the present disclosure refers to a solid oral dosage form consisting of 100 mg of cedazuridine, 35 mg of decitabine, lactose monohydrate, hydroxypropyl methyl cellulose, croscarmellose sodium, colloidal silicon dioxide, and magnesium stearate, wherein composition of cedazuridine of the solid oral dosage form is 17-22 % w/w, composition of decitabine of the solid oral dosage form is 4-8 % w/w, composition of lactose monohydrate of the solid oral dosage form is 55-70 % w/w, composition of hydroxypropyl methyl cellulose of the solid oral dosage form is 1-3 % w/w, composition of croscarmellose sodium of the solid oral dosage form is 3-7 % w/w, composition of colloidal silicon dioxide of the solid oral dosage form is 0.5-2 % w/w, and composition of magnesium stearate of the solid oral dosage form is 0.1-2 % w/w. Another example of the disclosure refers to solid oral dosage forms comprising decitabine and cedazuridine wherein the solid oral dosage forms upon daily administration to a subject provide a pharmacodynamic effect that is equivalent to the pharmacodynamic effect for a daily intravenous dose of decitabine of 20 mg/m^2 administered as a one hour infusion. In particular examples, the pharmacodynamic effect is DNA demethylation.

[0009] An additional aspect of the disclosure refers to use of the solid oral dosage form disclosed herein in the manufacture of a medicament for treating hematological cancers which is selected from myelodysplastic syndromes (MDS), leukemia, and lymphoma in a subject in need thereof. In another example, there are described methods for treating a disorder in a subject in need thereof, comprising administering to the subject a solid oral dosage form disclosed herein, thereby treating cancer in the subject. In some examples, the disorder is cancer.

[0010] A further example of the disclosure refers to use of the solid oral dosage form disclosed herein in the manufacture of a medicament for inhibiting degradation of decitabine in a subject in need thereof. In another example, there are described methods for inhibiting degradation of decitabine in a subject in need thereof, comprising administering to the subject a solid oral dosage form disclosed herein, thereby inhibiting degradation of the decitabine in the subject.

[0011] Another example of the disclosure refers to use of the solid oral dosage form disclosed herein in the manufacture of a medicament for reducing DNA methylation in a subject in need thereof. In another example, there are described methods of reducing DNA methylation (*e.g.*, LINE-1 methylation) in a subject in need thereof, comprising administering to the subject a solid oral dosage form according to an embodiment of the invention, thereby reducing DNA methylation in the subject.

[0012] In another example, there is disclosed the use of a solid oral dosage form according to an embodiment of the invention in methods for treating a disorder, methods for inhibiting degradation of decitabine, and methods of reducing DNA methylation (*e.g.*, LINE-1 methylation).

[0013] These and other aspects of the invention are set forth in more detail in the description of the invention below.

What is claimed is:

1. A solid oral dosage form consisting of 100 mg of cedazuridine, 35 mg of decitabine, lactose monohydrate, hydroxypropyl methyl cellulose, croscarmellose sodium, colloidal silicon dioxide, and magnesium stearate,
wherein composition of cedazuridine of the solid oral dosage form is 17-22 % w/w, composition of decitabine of the solid oral dosage form is 4-8 % w/w, composition of lactose monohydrate of the solid oral dosage form is 55-70 % w/w, composition of hydroxypropyl methyl cellulose of the solid oral dosage form is 1-3 % w/w, composition of croscarmellose sodium of the solid oral dosage form is 3-7 % w/w, composition of colloidal silicon dioxide of the solid oral dosage form is 0.5-2 % w/w, and composition of magnesium stearate of the solid oral dosage form is 0.1-2 % w/w.

2. The solid oral dosage form according to claim 1, consisting of 100 mg cedazuridine, 35 mg decitabine, 322.5 mg lactose monohydrate, 10 mg hydroxypropyl methyl cellulose, 25 mg croscarmellose sodium, 5 mg colloidal silicon dioxide and 2.5 mg magnesium stearate.

3. The solid oral dosage form of claim 1 or 2, which is a tablet.

4. The solid oral dosage form of any one of claims 1-3, which is a capsule.

5. The solid oral dosage form of any one of claims 1-4, further comprising a coating.

6. The solid oral dosage form of claim 5, wherein the coating is a color coating.

7. Use of the solid oral dosage form of any one of claims 1-6 in the manufacture of a medicament for treating hematological cancers which is selected from myelodysplastic syndromes (MDS), leukemia, and lymphoma in a subject in need thereof.

8. The use of claim 7, wherein the leukemia is acute lymphocytic leukemia, acute myelogenous leukemia, chronic myelogenous leukemia, myeloproliferative neoplasms, or chronic myelomonocytic leukemia.

9. The use of claim 7, wherein the lymphoma is Hodgkin's Lymphoma, Non-Hodgkin lymphoma, or T-cell lymphoma.

10. The use of claim 7, wherein the myelodysplastic syndromes (MDS) is lower risk MDS (*e.g.*, IPSS low and/or IPSS intermediate 1).