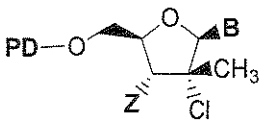
SUMMARY

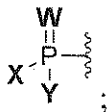
[0005][0001] Disclosed herein are compounds useful, for example, for the treatment of flavivirus infections such as HCV infections. The compounds are 2′-chloro nucleoside analogs. In certain examples the 2′-chloro nucleoside analogs display remarkable efficacy or bioavailability, or both, for the treatment of, for example, HCV infection in a human.

[0006] In one example, the present invention discloses a compound according to Formula 2001:



(2001);

or a pharmaceutically acceptable salt, or tautomeric form thereof, wherein:

PD is monophosphate, diphosphate, triphosphate, or 

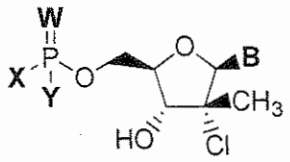
;

B is a nucleobase; **W** is S or O; **X** is an N-linked L-amino acid, or a derivative thereof;

and **Y** is $-OR^1$; **Z** is –OH;

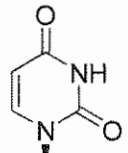
or, in the alternative, **Z** and **Y** join to form a six-membered heterocyclic ring wherein **Z** and **Y** together represent a single divalent –O–; and each R^1 is independently hydrogen, alkyl, cycloalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, alkylcarbonylthioalkyl, alkoxycarbonylalkyl, arylalkoxycarbonylalkyl, -alkoxy(–alkyl-aryl)-C(O)-alkyl, –alkoxyl-C(O)-cycloalkyl, alkoxycarbonylaminoalkylcarbonylthioalkyl, hydroxylalkylcarbonylthioalkyl, –alkoxyl-C(O)-alkyl, or–alkyl-S-C(O)-alkoxy-C(O)-alkyl-NH_2.

In certain examples, the compounds disclosed herein are useful in the prevention and treatment of *Flaviviridae* infections and other related conditions such as anti-*Flaviviridae* antibody positive and *Flaviviridae*-positive conditions, chronic liver inflammation caused by HCV, cirrhosis, fibrosis, acute hepatitis, fulminant hepatitis, chronic persistent hepatitis and fatigue. These compounds or formulations can also be used prophylactically to prevent or retard the progression of clinical illness in individuals who are anti-*Flaviviridae* antibody or *Flaviviridae*-antigen positive or who have been exposed to a *Flaviviridae*. In particular examples, the *Flaviviridae* is hepatitis C. In certain



(III);

or a pharmaceutically acceptable salt, or tautomeric form, wherein:



B is ; **W** is O; **X** is an N-linked L-amino acid ester; and **Y** is $-OR^1$ and R^1 is phenyl. In another aspect, the present invention refers to a pharmaceutical composition comprising the compound or a pharmaceutically acceptable salt, or tautomeric form thereof as disclosed herein, and a pharmaceutically acceptable carrier. In yet another aspect, the present invention refers to use of a compound or a pharmaceutically acceptable salt, or tautomeric form thereof of any one of claims 1-7 or composition of any one of claims 9-13 in the manufacture of a medicament for treating a host infected with a hepatitis C virus, wherein the host is a human.

[0014] *Flaviviridae* which can be treated are, *e.g.*, discussed generally in *Fields Virology*, Fifth Ed., Editors: Knipe, D. M., and Howley, P. M., Lippincott Williams & Wilkins Publishers, Philadelphia, PA, Chapters 33-35, 2006. In a particular example of the invention, the *Flaviviridae* is HCV. In an alternate example, the *Flaviviridae* is a flavivirus or pestivirus. In certain examples, the Flaviviridae can be from any class of *Flaviviridae*. In certain examples, the *Flaviviridae* is a mammalian tick-borne virus. In certain examples, the *Flaviviridae* is a seabird tick-borne virus. In certain examples, the *Flaviviridae* is a mosquito-borne virus. In certain examples, the *Flaviviridae* is an