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34, chemin des Colombettes
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THE COUNTRY CODE AND NUMBER OF YOUR PRIORITY APPLICATION, TO BE USED FOR FILING ABROAD UNDER THE PARIS CONVENTION, IS *US61/562,176*

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Approved for use through 09/30/2010 OMB 0651-0032
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Provisional Application for Patent Cover Sheet

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c)

Inventor(s)

Inventor 1 — Remove

Given Name	Middle Name	Family Name	City	State	Country
Barry		Bernstein	Mequon	WI	US

Inventor 2 — Remove

Given Name	Middle Name	Family Name	City	State	Country
Daniel		Cohen	Wilmette	IL	US

Inventor 3 — Remove

Given Name	Middle Name	Family Name	City	State	Country
Scott	C	Brun	Green Oaks	IL	US

Inventor 4 — Remove

Given Name	Middle Name	Family Name	City	State	Country
Thomas		Podsadecki	Chicago	IL	US

Inventor 5 — Remove

Given Name	Middle Name	Family Name	City	State	Country
Rajeev		Menon	Buffalo Grove	IL	US

All Inventors Must Be Listed – Additional Inventor Information blocks may be generated within this form by selecting the **Add** button. Add

Title of Invention	METHODS FOR TREATING HCV
Attorney Docket Number (if applicable)	24704US02

Correspondence Address

Direct all correspondence to (select one):

◉ The address corresponding to Customer Number	○ Firm or Individual Name
Customer Number	23446

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The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.
◉ No.
◯ Yes, the name of the U.S. Government agency and the Government contract number are:

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Entity Status

Applicant claims small entity status under 37 CFR 1.27

◯ Yes, applicant qualifies for small entity status under 37 CFR 1.27

◉ No

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Signature	/Michael B. Harlin/			Date (YYYY-MM-DD)	2011-11-21
First Name	Michael	Last Name	Harlin	Registration Number (If appropriate)	43658

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METHODS FOR TREATING HCV

FIELD OF THE INVENTION

[0001] The present invention relates to interferon-free and ribavirin-free treatment for hepatitis C virus (HCV).

BACKGROUND OF THE INVENTION

[0002] The HCV is an RNA virus belonging to the Hepacivirus genus in the Flaviviridae family. The enveloped HCV virion contains a positive stranded RNA genome encoding all known virus-specific proteins in a single, uninterrupted, open reading frame. The open reading frame comprises approximately 9500 nucleotides and encodes a single large polyprotein of about 3000 amino acids. The polyprotein comprises a core protein, envelope proteins E1 and E2, a membrane bound protein p7, and the non-structural proteins NS2, NS3, NS4A, NS4B, NS5A and NS5B.

[0003] Chronic HCV infection is associated with progressive liver pathology, including cirrhosis and hepatocellular carcinoma. Chronic hepatitis C may be treated with peginterferon-alpha in combination with ribavirin. Substantial limitations to efficacy and tolerability remain as many users suffer from side effects, and viral elimination from the body is often incomplete. Therefore, there is a need for new therapies to treat HCV infection.

BRIEF SUMMARY OF THE INVENTION

[0004] As one aspect of the present invention, methods for treating HCV infection in a subject are provided. The methods comprise administering at least two direct acting antiviral agents (DAAs) for a duration of no more than twelve weeks, or for another duration as set forth herein. Preferably, the duration of the treatment is for no more than eight weeks. Preferably, the two or more direct acting antiviral agents (DAAs) are administered in amounts effective to provide a sustained virological response (SVR) or achieve another desired measure of effectiveness in a subject. The subject is not administered ribavirin during the duration of administering the at least two DAAs. Put another way, the methods

exclude the administration of ribavirin to the subject. The subject is also not administered interferon during the treatment regimen. Put another way, the methods exclude the administration of interferon to the subject, thereby avoiding the side effects associated with interferon. In some embodiments, the methods further comprise administering an inhibitor of cytochrome P-450 (such as ritonavir) to the subject to improve the pharmacokinetics or bioavailability of one or more of the DAAs.

[0005] As another aspect, methods for treating HCV infection in a subject are provided. The methods comprise administering (a) therapeutic agent 1, (b) at least one polymerase inhibitor selected from the group consisting of therapeutic agent 2, therapeutic agent 3, and combinations thereof, (c) an inhibitor of cytochrome P-450 for a duration of no more than twelve weeks, or for another duration as set forth herein (e.g., the treatment regimen can last for no more than 8 weeks). Preferably, therapeutic agent 1, the polymerase inhibitor(s), and the inhibitor of cytochrome P-450 are administered in amounts effective to provide high rates of SVR or another measure of effectiveness in the subject.

[0006] As still another aspect, methods for treating a population of subjects having HCV infection are provided. The methods comprise administering at least two DAAs to the subjects for a duration of no more than 12 weeks. Preferably, the at least two DAAs are administered to the subjects in amounts effective to result in SVR or another measure of effectiveness in at least about 50% of the population, preferably at least about 70% of the population.

[0007] In the foregoing methods as well as methods described hereinbelow, the DAAs can be selected from the group consisting of protease inhibitors, nucleoside or nucleotide polymerase inhibitors, non-nucleoside polymerase inhibitors, NS3B inhibitors, NS4A inhibitors, NS5A inhibitors, NS5B inhibitors, cyclophilin inhibitors, and combinations of any of the foregoing. For example, in some embodiments, the DAAs used in the present methods comprise or consist of at least one HCV protease inhibitor and at least one HCV polymerase inhibitor. The HCV polymerase inhibitor can be a nucleotide or nucleoside polymerase inhibitor or a non-nucleoside polymerase inhibitor.

[0008] In some embodiments, the HCV protease inhibitor is therapeutic agent 1 (described below) and the HCV polymerase inhibitor is therapeutic agent 2 and/or therapeutic agent 3

(also described below). By way of example, therapeutic agent 1 is administered a total daily dose of from about 5 mg to about 250 mg, alternatively from about 25 mg to about 250 mg, alternatively from about 100 mg to about 250 mg, or administered at least once daily at a dose of from about 5 mg to about 100 mg or from about 150 mg to about 250 mg, and therapeutic agent 2 is administered in a total daily dose of from about 100 mg to about 800 mg, alternatively from about 300 mg to about 1800 mg or administered at least twice daily at doses from about 200 mg to about 400 mg. For some embodiments, the HCV protease inhibitor is therapeutic agent 1 and the non-nucleoside HCV polymerase inhibitor is therapeutic agent 3. By way of example, therapeutic agent 1 can be administered in a total daily dose of from about 25 mg to about 250 mg and therapeutic agent 3 can be administered in a daily dose of from about 50 mg to about 1000 mg. Preferably, therapeutic agent 1 is administered at a total daily dose of about 100 mg, alternatively about 200 mg, alternatively about 250 mg and therapeutic agent 3 is administered at a total daily dose of about 50 mg, alternatively about 100 mg, alternatively about 200 mg, alternatively about 400 mg. Ritonavir (or another cytochrome P-450 3A4 inhibitor) can be co-administered with therapeutic agent 1 to improve the pharmacokinetics and bioavailability of therapeutic agent 1.

[0009] In some embodiments, the at least two DAAs comprise at least one HCV protease inhibitor and at least one NS5A inhibitor. Preferably, the HCV protease inhibitor is therapeutic agent 1 and the NS5A inhibitor is therapeutic agent 4. By way of example, therapeutic agent 1 can be administered at a total daily dosage from about 5 mg to about 250 mg, alternatively from about 25 mg to about 250 mg, and therapeutic agent 4 can be administered in a total daily dose from about 5 mg to about 200 mg, alternatively from about 25 mg to about 200 mg. Ritonavir (or another cytochrome P-450 3A4 inhibitor) can be co-administered with therapeutic agent 1 to improve the pharmacokinetics and bioavailability of therapeutic agent 1.

[0010] In the foregoing methods as well as methods described herein, the DAAs can be administered in any effective dosing schemes and/or frequencies, for example, they can each be administered daily. Each DAA can be administered either separately or in combination, and each DAA can be administered at least once a day, at least twice a day, or at least three

times a day. In some preferred embodiments, therapeutic agent 3 is administered once daily (QD) or twice daily (BID), and therapeutic agent 1 is administered once daily.

[0011] In some aspects, the present technology provides a method for treating HCV infection comprising administering to a subject in need thereof at least two DAAs for a duration of no more than twelve weeks, wherein the subject is not administered interferon or ribavirin during said duration. In some aspects, the at least two DAAs are administered in an amount effective to result in SVR. Some methods further comprise administering an inhibitor of cytochrome P450 to the subject. In some aspects, the duration is no more than eight weeks.

[0012] In some aspects of the present technology, the at least two direct acting antiviral agents comprise compound 1 or a pharmaceutically acceptable salt thereof, compound 2 or a pharmaceutically acceptable salt thereof, and ritonavir.

[0013] In other aspects, the at least two direct acting antiviral agents comprise compound 1 or a pharmaceutically acceptable salt thereof, compound 3 or a pharmaceutically acceptable salt thereof, and ritonavir.

[0014] In yet another aspect, the at least two direct acting antiviral agents comprise compound 1 or a pharmaceutically acceptable salt thereof, compound 4 or a pharmaceutically acceptable salt thereof, and ritonavir.

[0015] In yet a further aspect, the at least two direct acting antiviral agents comprise compound 1 or a pharmaceutically acceptable salt thereof, compound 2 or a pharmaceutically acceptable salt thereof, compound 4 or a pharmaceutically acceptable salt thereof, and ritonavir.

[0016] In yet another aspect, the at least two direct acting antiviral agents comprises a drug combination selected from the group consisting of: a combination of PSI-7977 and PSI-938, a combination of BMS-790052 and BMS-650032, a combination of GS-5885 and GS-9451, a combination of GS-5885, GS-9190 and GS-9451, a combination of BI-201335 and BI-27127, a combination of telaprevir and VX-222, a combination of PSI-7977 and TMC-435, and a combination of danoprevir and R7128.

[0017] In other aspects, the present technology provides a method for treating HCV infection in a subject comprising administering (a) therapeutic agent 1, (b) at least one

polymerase inhibitor selected from the group consisting of therapeutic agent 2, therapeutic agent 3 and combinations thereof, (c) an inhibitor of cytochrome P450 for a duration of no more than twelve weeks, wherein the therapeutic agent 1, the at least one polymerase inhibitor, and the inhibitor of cytochrome P450 are administered in amounts effective to result in SVR in the subject.

[0018] In yet another aspect, the present technology provides a method for treating a population of subjects having HCV infection, the method comprising administering at least two DAAs to the subjects for a duration of no more than 12 weeks, wherein the at least two DAAs are administered to the subjects in amounts and for a duration effective to provide a SVR in at least about 70% of the population.

[0019] In another aspect, the present technology features a combination of at least two DAAs for use in treating HCV infection, wherein the duration of the treatment regimen is no more than twelve weeks (e.g., the duration being 12 weeks; or the duration being 11, 10, 9, 8, 7, 6, 5, 4, or 3 weeks). Preferably, the duration of the treatment regimen is no more than eight weeks (e.g., the duration being 8 weeks; or the duration being 7, 6, 5, 4, or 3 weeks). The treatment does not include administering interferon or ribavirin. The treatment may include administering ritonavir or another CYP3A4 inhibitor (e.g., cobicistat) if one of the DAAs requires pharmacokinetic enhancement. The at least two DAAs can be administered concurrently or sequentially. For example, one DAA can be administered once daily, and another DAA can be administered twice daily. For another example, the two DAAs are administered once daily. For yet another example, the two DAAs are co-formulated in a single composition and administered concurrently (e.g, once daily). As a non-limiting example, the patient being treated can be infected with HCV genotype 1, such as genotype 1a or 1b. As another non-limiting example, the patient can be infected with HCV genotype 2 or 3. As yet another non-limiting example, the patient can be a HCV-treatment naïve patient, a HCV-treatment experienced patient, an interferon non-responder, or not a candidate for interferon treatment.

[0020] In another aspect, the present technology features a combination of compound 1 (or a pharmaceutically acceptable salt thereof) and compound 2 (or a pharmaceutically acceptable salt thereof) for use in treating HCV infection, wherein the duration of the treatment regimen

is no more than twelve weeks (e.g., the duration being 12 weeks; or the duration being 11, 10, 9, 8, 7, 6, 5, 4, or 3 weeks). Preferably, the duration of the treatment regimen is no more than eight weeks (e.g., the duration being 8 weeks; or the duration being 7, 6, 5, 4, or 3 weeks). The treatment does not include administering interferon or ribavirin. Ritonavir or another CYP3A4 inhibitor (e.g., cobicistat) is administered with compound 1 (or the salt thereof) to improve the pharmacokinetic of the latter. Compound 1 (or the salt thereof) and compound 2 (or the salt thereof) can be administered concurrently or sequentially. For example, compound 1 (or the salt thereof) can be administered once daily, together with ritonavir or another CYP3A4 inhibitor (e.g., cobicistat), and compound 2 (or the salt thereof) can be administered twice daily. For another example, compound 1 (or the salt thereof) and compound 2 (or the salt thereof) are administered once daily. For yet another example, compound 1 (or the salt thereof) and ritonavir (or another CYP3A4 inhibitor, e.g., cobicistat) are co-formulated in a single composition and administered concurrently (e.g, once daily). For yet another example, compound 1 (or the salt thereof), ritonavir (or another CYP3A4 inhibitor, e.g., cobicistat), and compound 2 (or the salt thereof) are co-formulated in a single composition and administered concurrently (e.g, once daily). As a non-limiting example, the patient being treated can be infected with HCV genotype 1, such as genotype 1a or 1b. As another non-limiting example, the patient can be infected with HCV genotype 2 or 3. As yet another non-limiting example, the patient can be a HCV-treatment naïve patient, a HCV-treatment experienced patient, an interferon non-responder, or not a candidate for interferon treatment.

[0021] In another aspect, the present technology features a combination of compound 1 (or a pharmaceutically acceptable salt thereof) and compound 3 (or a pharmaceutically acceptable salt thereof) for use in treating HCV infection, wherein the duration of the treatment regimen is no more than twelve weeks (e.g., the duration being 12 weeks; or the duration being 11, 10, 9, 8, 7, 6, 5, 4, or 3 weeks). Preferably, the duration of the treatment regimen is no more than eight weeks (e.g., the duration being 8 weeks; or the duration being 7, 6, 5, 4, or 3 weeks). The treatment does not include administering interferon or ribavirin. Ritonavir or another CYP3A4 inhibitor (e.g., cobicistat) is administered with compound 1 (or the salt thereof) to improve the pharmacokinetic of the latter. Compound 1 (or the salt thereof) and compound 3 (or the salt thereof) can be administered concurrently or sequentially. For

example, compound 1 (or the salt thereof) can be administered once daily, together with ritonavir or another CYP3A4 inhibitor (e.g., cobicistat), and compound 3 (or the salt thereof) can be administered twice daily. For another example, compound 1 (or the salt thereof) and compound 3 (or the salt thereof) are administered once daily. For yet another example, compound 1 (or the salt thereof) and ritonavir (or another CYP3A4 inhibitor, e.g., cobicistat) are co-formulated in a single composition and administered concurrently (e.g, once daily). For yet another example, compound 1 (or the salt thereof), ritonavir (or another CYP3A4 inhibitor, e.g., cobicistat), and compound 3 (or the salt thereof) are co-formulated in a single composition and administered concurrently (e.g, once daily). As a non-limiting example, the patient being treated can be infected with HCV genotype 1, such as genotype 1a or 1b. As another non-limiting example, the patient can be infected with HCV genotype 2 or 3. As yet another non-limiting example, the patient can be a HCV-treatment naïve patient, a HCV-treatment experienced patient, an interferon non-responder, or not a candidate for interferon treatment.

[0022] In another aspect, the present technology features a combination of compound 1 (or a pharmaceutically acceptable salt thereof) and compound 4 (or a pharmaceutically acceptable salt thereof) for use in treating HCV infection, wherein the duration of the treatment regimen is no more than twelve weeks (e.g., the duration being 12 weeks; or the duration being 11, 10, 9, 8, 7, 6, 5, 4, or 3 weeks). Preferably, the duration of the treatment regimen is no more than eight weeks (e.g., the duration being 8 weeks; or the duration being 7, 6, 5, 4, or 3 weeks). The treatment does not include administering interferon or ribavirin. Ritonavir or another CYP3A4 inhibitor (e.g., cobicistat) is administered with compound 1 (or the salt thereof) to improve the pharmacokinetic of the latter. Compound 1 (or the salt thereof) and compound 4 (or the salt thereof) can be administered concurrently or sequentially. For example, compound 1 (or the salt thereof) can be administered once daily, together with ritonavir or another CYP3A4 inhibitor (e.g., cobicistat), and compound 4 (or the salt thereof) can be administered twice daily. For another example, compound 1 (or the salt thereof) and compound 4 (or the salt thereof) are administered once daily. For yet another example, compound 1 (or the salt thereof) and ritonavir (or another CYP3A4 inhibitor, e.g., cobicistat) are co-formulated in a single composition and administered concurrently (e.g, once daily). For yet another example, compound 1 (or the salt thereof), ritonavir (or another CYP3A4

inhibitor, e.g., cobicistat), and compound 4 (or the salt thereof) are co-formulated in a single composition and administered concurrently (e.g, once daily). As a non-limiting example, the patient being treated can be infected with HCV genotype 1, such as genotype 1a or 1b. As another non-limiting example, the patient can be infected with HCV genotype 2 or 3. As yet another non-limiting example, the patient can be a HCV-treatment naïve patient, a HCV-treatment experienced patient, an interferon non-responder, or not a candidate for interferon treatment.

[0023] In another aspect, the present technology features a combination of compound 1 (or a pharmaceutically acceptable salt thereof), compound 2 (or a pharmaceutically acceptable salt thereof), and compound 4 (or a pharmaceutically acceptable salt thereof) for use in treating HCV infection, wherein the duration of the treatment regimen is no more than twelve weeks (e.g., the duration being 12 weeks; or the duration being 11, 10, 9, 8, 7, 6, 5, 4, or 3 weeks). Preferably, the duration of the treatment regimen is no more than eight weeks (e.g., the duration being 8 weeks; or the duration being 7, 6, 5, 4, or 3 weeks). The treatment does not include administering interferon or ribavirin. Ritonavir or another CYP3A4 inhibitor (e.g., cobicistat) is administered with compound 1 (or the salt thereof) to improve the pharmacokinetic of the latter. Compound 1 (or the salt thereof), compound 2 (or the salt thereof), and compound 4 (or the salt thereof) can be administered concurrently or sequentially. For example, compound 1 (or the salt thereof) can be administered once daily, together with ritonavir or another CYP3A4 inhibitor (e.g., cobicistat), and compound 4 (or the salt thereof) can be administered once daily, and compound 2 (or the salt thereof) can be administered twice daily. For another example, compound 1 (or the salt thereof), compound 2 (or the salt thereof), and compound 4 (or the salt thereof) are administered once daily. For yet another example, compound 1 (or the salt thereof), compound 4 (or the salt thereof), and ritonavir (or another CYP3A4 inhibitor, e.g., cobicistat) are co-formulated in a single composition and administered concurrently (e.g, once daily). For yet another example, compound 1 (or the salt thereof), ritonavir (or another CYP3A4 inhibitor, e.g., cobicistat), compound 2 (or the salt thereof), and compound 4 (or the salt thereof) are co-formulated in a single composition and administered concurrently (e.g, once daily). As a non-limiting example, the patient being treated can be infected with HCV genotype 1, such as genotype 1a or 1b. As another non-limiting example, the patient can be infected with HCV genotype 2 or

3. As yet another non-limiting example, the patient can be a HCV-treatment naïve patient, a HCV-treatment experienced patient, an interferon non-responder, or not a candidate for interferon treatment.

[0024] In another aspect, the present technology features a combination of at least two DAAs for use in treating HCV infection, wherein said combination comprises a combination selected from:

a combination of PSI-7977 and PSI-938,

a combination of BMS-790052 and BMS-650032,

a combination of GS-5885 and GS-9451,

a combination of GS-5885, GS-9190 and GS-9451,

a combination of BI-201335 and BI-27127,

a combination of telaprevir and VX-222,

a combination of PSI-7977 and TMC-435, and

a combination of danoprevir and R7128;

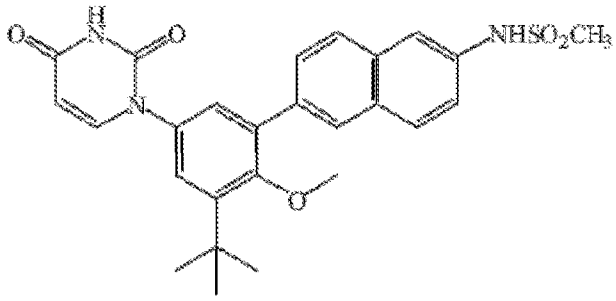
and wherein the duration of the treatment regimen is no more than twelve weeks (e.g., the duration being 12 weeks; or the duration being 11, 10, 9, 8, 7, 6, 5, 4, or 3 weeks). Preferably, the duration of the treatment regimen is no more than eight weeks (e.g., the duration being 8 weeks; or the duration being 7, 6, 5, 4, or 3 weeks). The treatment does not include administering interferon or ribavirin. The treatment may include administering ritonavir or another CYP3A4 inhibitor (e.g., cobicistat) if one of the DAAs requires pharmacokinetic enhancement. The at least two DAAs can be administered concurrently or sequentially. For example, one DAA can be administered once daily, and another DAA can be administered twice daily. For another example, the two DAAs are administered once daily. For yet another example, the two DAAs are co-formulated in a single composition and administered concurrently (e.g, once daily). As a non-limiting example, the patient being treated can be infected with HCV genotype 1, such as genotype 1a or 1b. As another non-limiting example, the patient can be infected with HCV genotype 2 or 3. As yet another non-limiting example, the patient can be a HCV-treatment naïve patient, a HCV-treatment experienced patient, an interferon non-responder, or not a candidate for interferon treatment.

DETAILED DESCRIPTION OF THE INVENTION

[0025] The present methods can include administering therapeutic agent 1 to a subject. Therapeutic agent 1 is compound 1 or a pharmaceutically acceptable salt thereof. Compound 1 is also known as (2R,6S,13aS,14aR,16aS,Z)-N-(cyclopropylsulfonyl)-6-(5-methylpyrazine-2-carboxamido)-5,16-dioxo-2-(phenanthridin-6-yloxy)-1,2,3,5,6,7,8,9,10,11,13a,14,14a,15,16,16a-hexadecahydrocyclopropa[e]pyrrolo[1,2-a][1,4]diazacyclopentadecine-14a-carboxamide. Compound 1 is a potent HCV protease inhibitor. The synthesis and formulation of Compound 1 are described in U.S. Patent Application Publication No. 2010/0144608, U.S. Provisional Application Serial No. 61/339,964 filed on March 10, 2010, and U.S. Patent Application Serial No. 13/042,805 filed on March 8, 2011. All of these applications are incorporated herein by reference in their entireties. Therapeutic agent 1 includes various salts of compound 1. Therapeutic agent 1 may be administered in any suitable amount such as, for example, in doses of from about 0.01 to about 50 mg/kg body weight, alternatively from about 0.1 to about 25 mg/kg body weight. As non-limiting examples, therapeutic agent 1 may be administered in a total daily dose amount of from about 50 mg to about 250 mg, preferably from about 100 mg to about 250 mg, and includes, but is not limited to, for example, about 50 mg, about 75 mg, about 100 mg, about 125 mg, about 150 mg, about 175 mg, about 200 mg, about 225 mg, about 250 mg and suitable amounts there between.

[0026] In preferred embodiments, ritonavir or another inhibitor of cytochrome P-450 is co-administered with therapeutic agent 1 to improve the pharmacokinetics of Compound 1.

[0027] The present methods can include administering therapeutic agent 2 to a subject. Therapeutic agent 2 is compound 2 or a salt thereof.

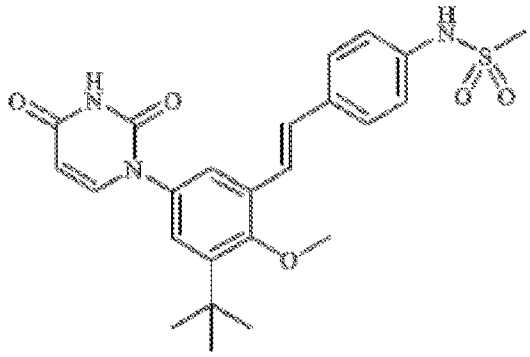


Compound 2

[0028] Compound 2 is also known N-(6-(3-tert-butyl-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2-methoxyphenyl)naphthalen-2-yl)methanesulfonamide as described in, for example, International Publication No. WO2009/039127, therapeutic agent 2 includes various salts of compound 2, such as sodium salts, potassium salts, and choline salts. Therapeutic agent 2 also includes crystalline forms of compound 2 and its salts such as solvate, hydrate, and solvent-free crystalline forms of compound 2 and its salts. Compositions comprising therapeutic agent 2 can be prepared as described in, for example, International Publication No. WO2009/039127 which is incorporated by reference herein.

[0029] Therapeutic agent 2 may be administered as a free acid, salt or particular crystalline form of compound 2. In some embodiments, therapeutic agent 2 is administered as a sodium salt. Therapeutic agent 2 may be administered in any suitable amount such as, for example, in doses of from about 5 mg/kg to about 30 mg/kg. As non-limiting examples, therapeutic agent 2 may be administered in a total daily dose amount of from about 300 mg to about 1800 mg, or from about 400 mg to about 1600 mg, or from about 600 mg to about 1800 mg, or from about 800 mg to about 1600 mg or any amounts there between. In some embodiments, therapeutic agent 2 may be administered in a total daily dose amount from about 100 mg to about 800 mg, preferably form about 200 mg to about 800 mg. In some embodiments, the total daily dosage amount for therapeutic agent 2 is about 100 mg. In some embodiments, the total daily dosage amount for therapeutic agent 2 is about 200 mg. In some embodiments, the total daily dosage amount for therapeutic agent 2 is about 300 mg. In some embodiments, the total daily dosage amount for compound 2 is about 400 mg. In some embodiments, the total daily dosage amount for therapeutic agent 2 is about 600 mg. In some embodiments, the total daily dosage amount for therapeutic agent 2 is about 800 mg. In some embodiments, the total daily dosage amount for therapeutic agent 2 is about 1200 mg. In some embodiments, the total daily dosage amount for therapeutic agent 2 is about 1600 mg.

[0030] The present methods can include administering therapeutic agent 3 or a salt thereof to a subject. Therapeutic agent 3 is compound 3 or a salt thereof.

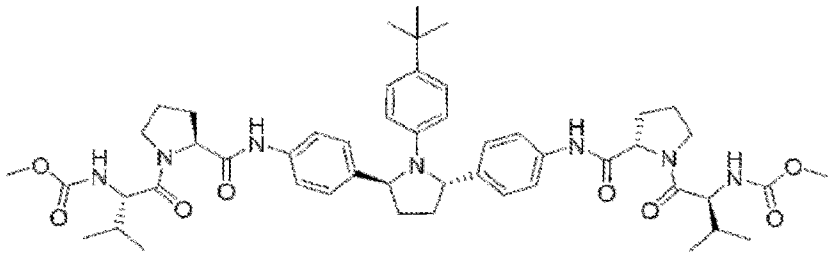


Compound 3

[0031] Compound 3 is also known as (E)-N-(4-(3-tert-butyl-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2-methoxystyryl)phenyl)methanesulfonamide. As described in, for example, International Publication No. WO2009/039127, therapeutic agent 3 includes various salts of compound 3, such as sodium salts, potassium salts, and choline salts. Therapeutic agent 3 also includes crystalline forms of compound 3 and its salts such as solvate, hydrate, and solvent-free crystalline forms of compound 3 and its salts. Compositions comprising therapeutic agent 3 can be prepared as described in, for example, International Publication No. WO2009/039127 which is incorporated by reference herein.

[0032] Therapeutic agent 3 may be administered as a free acid, salt or particular crystalline form of compound 3. In some embodiments, compound 3 is administered as a potassium salt. Therapeutic agent 3 may be administered in any suitable amount such as, for example, in doses of from about 0.5 mg/kg to about 15 mg/kg or from about 1 mg/kg to about 10 mg/kg. As non-limiting examples, therapeutic agent 3 may be administered in a total daily dose amount of from about 50 mg to about 1000 mg or from about 100 mg to about 600 mg or from about 80 mg to about 320 mg or any amounts there between. In some embodiments, the total daily dosage amount for therapeutic agent 3 is about 50 mg. In some embodiments, the total daily dosage amount for therapeutic agent 3 is about 80 mg. In some embodiments, the total daily dosage amount for therapeutic agent 3 is about 100 mg. In some embodiments, the total daily dosage amount for therapeutic agent 3 is about 160 mg. In some embodiments, the total daily dosage amount for therapeutic agent 3 is about 300 mg. In some embodiments, the total daily dosage amount for therapeutic agent 3 is about 320 mg. In some embodiments, the total daily dosage amount for therapeutic agent 3 is about 600 mg.

[0033] The present methods can include administering therapeutic agent 4 or a salt thereof to a subject. Therapeutic agent 4 is compound 4 or a salt thereof.



Compound 4

[0034] Compound 4 is also known as dimethyl (2S,2'S)-1,1'-((2S,2'S)-2,2'-(4,4'-((2S,5S)-1-(4-tert-butylphenyl)pyrrolidine-2,5,diyl)bis(4,1-phenylene))bis(azanediyl)bis(oxomethylene)bis(pyrrolidine-2,1-diyl)bis(3-methyl-1-oxobutane-2,1-diyl)dicarbamate. Compound 4 can be prepared as described in, for example, U.S. Publication No. 2010/0317568, which is incorporated herein by reference.

[0035] Therapeutic agent 4 may be administered as a free acid, or a salt form. Therapeutic agent 4 may be administered in any suitable amount such as, for example, in doses of from about 0.1 mg/kg to about 200 mg/kg body weight, or from about 0.25 mg/kg to about 100 mg/kg, or from about 0.3 mg/kg to about 30 mg/kg. As non-limiting examples, therapeutic agent 4 may be administered in a total daily dose amount of from about 5 mg to about 300 mg, or from about 25 mg to about 200 mg, or from about 25 mg to about 50 mg or any amounts there between. In some embodiments, the total daily dosage amount for therapeutic agent 4 is about 25 mg. In some embodiments, the total daily dosage amount for therapeutic agent 4 is about 5mg, alternatively about 10 mg, alternatively about 20 mg, alternatively about 25 mg, alternatively about 30 mg, alternatively about 35 mg, alternatively about 40 mg, or alternatively about 50 mg.

[0036] The current standard of care (SOC) for the treatment of HCV includes a course of treatment of interferon, e.g. pegylated interferon (e.g., pegylated interferon-alpha-2a or pegylated interferon-alpha-2b, such as PEGASYS by Roche, or Peg-Intron by Schering-Plough) and the antiviral drug ribavirin (e.g., COPEGUS by Roche, Rebetol by Schering-Plough, or RIBASPHERE by Three Rivers Pharmaceuticals). The treatment often lasts for

24-48 weeks, depending on hepatitis C virus genotype. Other interferons include, but are not limited to, inferferon-alpha-2a (e.g., Roferon-A by Roche), interferon-alpha-2b (e.g., Intron-A by Schering-Plough), and interferon alfacon-1 (consensus interferon) (e.g., Infergen by Valeant). Less than 50% of patients with chronic HCV infection with genotype 1 virus respond to this therapy. Further, interferon therapy has many side effects that hinder patient compliance and results in premature discontinuation of the treatment.

[0037] The interferon/ribavirin-based treatment may be physically demanding, and can lead to temporary disability in some cases. A substantial proportion of patients will experience a panoply of side effects ranging from a "flu-like" syndrome (the most common, experienced for a few days after the weekly injection of interferon) to severe adverse events including anemia, cardiovascular events and psychiatric problems such as suicide or suicidal ideation. The latter are exacerbated by the general physiological stress experienced by the patients. Ribavirin also has a number of side effects, including, anemia, high pill burden (e.g. 5-6 pills a day split BID) and teratogenicity restricting use in women of childbearing age.

[0038] The present methods provide effective treatment of HCV infection without the use of interferon or ribavirin and for a shorter period of time, specifically a treatment duration of no more than twelve weeks, alternatively no more than eleven weeks, alternatively no more than ten weeks, alternatively no more than nine weeks, alternatively no more than eight weeks, alternatively no more than seven weeks, alternatively no more than six weeks, alternatively no more than five weeks, alternatively no more than four weeks, or alternatively, no more than three weeks.

[0039] In some embodiments, the present technology provides methods for treating HCV infection in a subject comprising administering at least two DAAs in the absence of interferon and ribavirin for a duration of no more than twelve weeks, alternatively no more than eight weeks. Put another way, the present methods exclude interferon and ribavirin, or the subject does not receive interferon or ribavirin for the duration of the treatment. The at least two DAAs can be co-administered or can be administered independently (with the same or different dosing frequencies) and can be administered once a day, alternatively twice a day, alternatively three times a day.

[0040] In some embodiments, the methods of treatment comprise daily administration of two or more DAAs, wherein a first DAA may be administered once a day, twice a day, or three times a day, and a second DAA may be administered once a day, twice a day, or three times a day. In some embodiments, a third DAA may be administered once a day, twice a day, or three times a day. The DAAs may be co-administered or administered at different times or frequencies. Preferably, in the methods, at least two DAAs are administered in effective amounts to provide a desired measure of effectiveness in the subject. Preferably, the treatment has reduced side effects as compared with interferon-containing treatments.

[0041] Various measures may be used to express the effectiveness of the present methods of HCV treatment. One such measure is rapid virological response (RVR), meaning that HCV is undetectable in the subject after 4 weeks of treatment, for example, after 4 weeks of administration of two or more of DAAs. Another measure is early virological response (EVR), meaning that the subject has $>2\log_{10}$ reduction in viral load after 12 weeks of treatment. Another measure is complete EVR (cEVR), meaning the HCV is undetectable in the serum of the subject after 12 weeks of treatment. Another measure is extended RVR (eRVR), meaning achievement of RVR and cEVR, that is, HCV is undetectable at week 4 and 12. Another measure is the presence or absence of detectable virus at the end of therapy (EOT). Another measure is SVR, which, as used herein, means that the virus is undetectable at the end of therapy and for at least 8 weeks after the end of therapy (SVR8); preferably, the virus is undetectable at the end of therapy and for at least 12 weeks after the end of therapy (SVR12); more preferably, the virus is undetectable at the end of therapy and for at least 16 weeks after the end of therapy (SVR16); and highly preferably, the virus is undetectable at the end of therapy and for at least 24 weeks after the end of therapy (SVR24). SVR24 is often considered as a functional definition of cure; and a high rate of SVR at less than 24 week post-treatment (e.g., SVR12) can be predictive of a high rate of SVR24.

[0042] In some embodiments, the amounts of the two or more DAAs, and/or the duration of the treatment regimen of the two or more DAAs, are effective to provide an RVR in a subject, or an EVR in a subject, or a cEVR in a subject, or an eRVR in a subject, or an absence of detectable virus at EOT in a subject. In some embodiments, the present methods comprise treating a population of subjects having HCV infection (e.g. treatment naïve subjects), and the methods comprise administering at least two DAAs to the subjects for a

duration of no more than 12 weeks, or for another duration disclosed herein, wherein the at least two DAAs are administered to the subjects in amounts effective to provide an SVR (e.g., SVR after 8 weeks post-treatment, or SVR after 24 weeks post-treatment) in at least about 70% of the population, alternatively at least about 75% of the population, alternatively at least about 80% of the population, alternatively at least about 85% of the population, alternatively at least about 90% of the population, alternatively at least about 95% of the population, alternatively about 100% of the population. In some embodiments, the present methods comprise treating a population of IFN experienced subjects (e.g. interferon non-responder) having HCV infection, and the methods comprise administering at least two DAAs to the subjects for a duration of no more than 12 weeks, or for another duration disclosed herein, wherein the at least two DAAs are administered to the subjects in amounts effective to provide an SVR (e.g., SVR after 8 weeks post-treatment, or SVR after 24 weeks post-treatment) in at least about 50% of the population, alternatively at least about 55% of the population, alternatively at least about 60% of the population, alternatively at least about 65% of the population. In other embodiments, the amount of DAAs and the duration of the treatment are effective to provide one or more of an SVR (e.g., SVR after 8 weeks post-treatment, or SVR after 24 weeks post-treatment), an RVR, an EVR, a cEVR, an eRVR, or an absence of detectable virus at EOT, in at least about 50% of the population, alternatively at least about 55%, in at least about 60% of the population, alternatively at least about 65% of the population, alternatively at least about 70% of the population, alternatively at least about 75% of the population, alternatively at least about 80% of the population, alternatively at least about 85% of the population, alternatively at least about 90% of the population, alternatively at least about 95% of the population, alternatively about 100% of the population. For example, the present methods comprise administering at least two DAAs in amounts and for durations effective to provide an SVR (e.g., SVR after 8 weeks post-treatment, or SVR after 24 weeks post-treatment) in a subject. In some embodiments, the present technology provides for an SVR (e.g., SVR after 8 weeks post-treatment, or SVR after 24 weeks post-treatment) in at least about 50% of the population, alternatively at least about 55% of the population, in at least about 60% of the population, preferably in at least about 65% of the population, preferably in at least about 70% of the population, preferably at least about 75% of the patients treated by such methods herein described, more preferably

in at least 80% of the population, and highly preferably in at least about 90% of the patients being treated. In some embodiments, a treatment of the present technology provides an RVR or undetectable level of HCV RNA in the bloodstream at four (4) weeks of treatment (preferably in addition to a SVR).

[0043] A DAA of the present technology includes, but is not limited to, a protease inhibitor, a HCV polymerase inhibitor, an HCV NS5A inhibitor, an HCV N53B inhibitor, an HCV NS4A inhibitor, an HCV NS5B inhibitor, an HCV entry inhibitor, a cyclophilin inhibitor, a CD81 inhibitor, or an internal ribosome entry site inhibitor. The HCV polymerase inhibitors may be a nucleoside polymerase inhibitor or a non-nucleoside polymerase inhibitor.

[0044] In yet another example of this aspect of the technology, the combination of two or more DAAs comprises PSI-7977 and PSI-938. In yet another example, the combination of two or more DAAs comprises PSI-7977 and TMC-435. In yet another example, the combination of two or more DAAs comprises BMS-790052 and BMS-650032. In yet another example, the combination of two or more DAAs comprises GS-5885, GS-9190, and GS-9451. In yet another example, the combination of two or more DAAs comprises BI-201335 and BI-207127. In yet another example, the combination of two or more DAAs comprises telaprevir and VX-222. In another example, the combination of two or more DAAs comprises GS-5885 and GS-9451. In yet another example, the combination of two or more DAAs includes danoprevir (with ritonavir) and R7128.

[0045] Accordingly, in one aspect, the present technology features a method of treating HCV infection, comprising administering to a patient in need thereof an effective amount of a combination of two or more DAAs. The treatment lasts 8 weeks and does not include administration of any interferon or ribavirin. The DAAs can be administered at the same or different dosing frequencies. The patient being treated can be a treatment naïve patient, a treatment experienced patient, including, but not limited to, a relapser, an interferon partial responder, or an interferon non-responder; or a patient unable to take interferon. The patient may be infected with, for example and without limitation, HCV genotype 1, such as HCV genotype 1a or HCV genotype 1b; or HCV genotype 2 or 3. The treatment according to this aspect of the technology may also be effective against other HCV genotypes. The DAAs can be administered around the same time or at different times, and can be co-formulated in a

single formulation or formulated in different compositions. Each DAA can be selected from HCV protease inhibitors, HCV polymerase inhibitors, or HCV NS5A inhibitors. For instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor and at least one HCV polymerase inhibitor (e.g., a combination of at least one HCV protease inhibitor and at least one non-nucleoside polymerase inhibitor, or a combination of at least one HCV protease inhibitor and at least one nucleoside polymerase inhibitor, or a combination of at least one HCV protease inhibitor, at least one nucleoside polymerase inhibitor and at least one non-nucleoside inhibitor). For another instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor and at least one HCV NS5A inhibitor. For still another instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor, at least one HCV polymerase inhibitor, and at least one HCV NS5A inhibitor. For another instance, the combination of two or more DAAs can be a combination of at least two HCV polymerase inhibitors (e.g., a combination of at least two nucleoside polymerase inhibitors, or a combination of at least one nucleoside polymerase inhibitor and at least one non- nucleoside polymerase inhibitor, or a combination of at least two non- nucleoside polymerase inhibitors). For another instance, the combination of two or more DAAs can be a combination of at least two HCV protease inhibitors. For another instance, the combination of two or more DAAs can be a combination of at least two HCV NS5A inhibitors. For another instance, the combination of two or more DAAs can be a combination of at least one HCV polymerase inhibitor and at least one NS5A inhibitor (e.g., a combination of at least one HCV NS5A inhibitor and at least one non-nucleoside polymerase inhibitor, or a combination of at least one HCV NS5A inhibitor and at least one nucleoside polymerase inhibitor, or a combination of at least one HCV NS5A inhibitor, at least one nucleoside polymerase inhibitor and at least one non-nucleoside inhibitor). In one example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof) and Compound 2 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In another example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof) and Compound 3 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In still another example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof) and Compound 4 (or a

salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In a further example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof), Compound 2 (or a salt thereof) and Compound 4 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In yet another example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof), Compound 3 (or a salt thereof) and Compound 4 (or a salt thereof). Compound 1 can be co-formulated with ritonavir. Other DAA(s) can also be included in a treatment regimen according to this aspect of the technology. In yet another example of this aspect of the technology, the combination of two or more DAAs comprises PSI-7977 and PSI-938. In yet another example, the combination of two or more DAAs comprises PSI-7977 and TMC-435. In yet another example, the combination of two or more DAAs comprises BMS-790052 and BMS-650032. In yet another example, the combination of two or more DAAs comprises GS-5885, GS-9190, and GS-9451. In yet another example, the combination of two or more DAAs comprises BI-201335 and BI-207127. In yet another example, the combination of two or more DAAs comprises telaprevir and VX-222. In another example, the combination of two or more DAAs comprises GS-5885 and GS-9451. In yet another example, the combination of two or more DAAs includes danoprevir with ritonavir and R7128.

[0046] In another aspect, the present technology features a method of treating HCV, comprising administering to a patient in need thereof an effective amount of a combination of two or more DAAs. The treatment lasts 7 weeks and does not include administration of any interferonor any ribavirin. The DAAs can be administered at the same or different dosing frequency. The patient being treated can be a treatment naïve patient, a treatment experienced patient, including, but not limited to, a relapser, an interferon partial responder, an interferon non-responder, or a patient unable to take interferon. The patient can be infected with, for example and without limitation, HCV genotype 1, such as HCV genotype 1a or HCV genotype 1b; or HCV genotype 2 or 3. The treatment according to this aspect of the technology can also be effective against other HCV genotypes. The DAAs can be administered around the same time or at different times, and can be co-formulated in a single formulation or formulated in different compositions. Each DAA can be selected from HCV protease inhibitors, HCV polymerase inhibitors, or HCV NS5A inhibitors. For instance, the combination of two or more DAAs can be a combination of at least one HCV protease

inhibitor and at least one HCV polymerase inhibitor (e.g., a combination of at least one HCV protease inhibitor and at least one non-nucleoside polymerase inhibitor, or a combination of at least one HCV protease inhibitor and at least one nucleoside polymerase inhibitor, or a combination of at least one HCV protease inhibitor, at least one nucleoside polymerase inhibitor and at least one non-nucleoside inhibitor). For another instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor and at least one HCV NS5A inhibitor. For still another instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor, at least one HCV polymerase inhibitor, and at least one HCV NS5A inhibitor. . For another instance, the combination of two or more DAAs can be a combination of at least two HCV polymerase inhibitors (e.g., a combination of at least two nucleoside polymerase inhibitors, or a combination of at least one nucleoside polymerase inhibitor and at least one non- nucleoside polymerase inhibitor, or a combination of at least two non- nucleoside polymerase inhibitors). For another instance, the combination of two or more DAAs can be a combination of at least two HCV protease inhibitors. For another instance, the combination of two or more DAAs can be a combination of at least two HCV NS5A inhibitors. For another instance, the combination of two or more DAAs can be a combination of at least one HCV polymerase inhibitor and at least one NS5A inhibitor (e.g., a combination of at least one HCV NS5A inhibitor and at least one non-nucleoside polymerase inhibitor, or a combination of at least one HCV NS5A inhibitor and at least one nucleoside polymerase inhibitor, or a combination of at least one HCV NS5A inhibitor, at least one nucleoside polymerase inhibitor and at least one non-nucleoside inhibitor). In one example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof) and Compound 2 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In another example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof) and Compound 3 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated or co-administered with ritonavir. In still another example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof) and Compound 4 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In a further example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof), Compound 2 (or a salt thereof) and Compound 4 (or a salt thereof). Compound 1 (or a salt

thereof) can be co-formulated with ritonavir. In yet another example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof), Compound 3 (or a salt thereof) and Compound 4 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. Other DAA(s) can also be included in a treatment regimen according to this aspect of the technology. In yet another example, the combination of two or more DAAs comprises PSI-7977 and PSI-938. In yet another example, the combination of two or more DAAs comprises PSI-7977 and TMC-435. In yet another example, the combination of two or more DAAs comprises BMS-790052 and BMS-650032. In yet another example, the combination of two or more DAAs comprises GS-5885, GS-9190, and GS-9451. In yet another example, the combination of two or more DAAs comprises BI-201335 and BI-207127. In yet another example, the combination of two or more DAAs comprises telprevir and VX-222. In another example, the combination of two or more DAAs comprises GS-5885 and GS-9451. In yet another example, the combination of two or more DAAs includes danoprevir (with ritonavir) and R7128.

[0047] In yet another aspect, the present technology features a method of treating HCV, comprising administering to a patient in need thereof an effective amount of a combination of two or more DAAs. The treatment lasts 6 weeks and does not include administration of any interferon or any ribavirin. The patient being treated can be a treatment naïve patient, a treatment experienced patient, including, but not limited to, a relapser, an interferon partial responder, an interferon non-responder, or a patient unable to take interferon. The patient can be infected with, for example and without limitation, HCV genotype 1, such as HCV genotype 1a or HCV genotype 1b; or HCV genotype 2 or 3. The treatment according to this aspect of the technology can also be effective against other HCV genotypes. The DAAs can be administered around the same time or at different times, and can be co-formulated in a single formulation or formulated in different compositions. Each DAA can be selected from HCV protease inhibitors, HCV polymerase inhibitors, or HCV NS5A inhibitors. For instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor and at least one HCV polymerase inhibitor (e.g., a combination of at least one HCV protease inhibitor and at least one non-nucleoside polymerase inhibitor, or a combination of at least one HCV protease inhibitor and at least one nucleoside polymerase inhibitor, or a combination of at least one HCV protease inhibitor, at least one nucleoside

polymerase inhibitor and at least one non-nucleoside inhibitor). For another instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor and at least one HCV NS5A inhibitor. For still another instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor, at least one HCV polymerase inhibitor, and at least one HCV NS5A inhibitor. For another instance, the combination of two or more DAAs can be a combination of at least two HCV polymerase inhibitors (e.g., a combination of at least two nucleoside polymerase inhibitors, or a combination of at least one nucleoside polymerase inhibitor and at least one non- nucleoside polymerase inhibitor, or a combination of at least two non- nucleoside polymerase inhibitors). For another instance, the combination of two or more DAAs can be a combination of at least two HCV protease inhibitors. For another instance, the combination of two or more DAAs can be a combination of at least two HCV NS5A inhibitors. For another instance, the combination of two or more DAAs can be a combination of at least one HCV polymerase inhibitor and at least one NS5A inhibitor (e.g., a combination of at least one HCV NS5A inhibitor and at least one non-nucleoside polymerase inhibitor, or a combination of at least one HCV NS5A inhibitor and at least one nucleoside polymerase inhibitor, or a combination of at least one HCV NS5A inhibitor, at least one nucleoside polymerase inhibitor and at least one non-nucleoside inhibitor). In one example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof) and Compound 2 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In another example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof) and Compound 3 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In still another example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof) and Compound 4 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In a further example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof), Compound 2 (or a salt thereof) and Compound 4 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In yet another example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof), Compound 3 (or a salt thereof) and Compound 4 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. Other DAA(s) can also be included in a

treatment regimen according to this aspect of the technology. In yet another example, the combination of two or more DAAs comprises PSI-7977 and PSI-938. In yet another example, the combination of two or more DAAs comprises PSI-7977 and TMC-435. In yet another example, the combination of two or more DAAs comprises BMS-790052 and BMS-650032. In yet another example, the combination of two or more DAAs comprises GS-5885, GS-9190, and GS-9451. In yet another example, the combination of two or more DAAs comprises BI-201335 and BI-207127. In yet another example, the combination of two or more DAAs comprises telprevir and VX-222. In another example, the combination of two or more DAAs comprises GS-5885 and GS-9451. In yet another example, the combination of two or more DAAs includes danoprevir (with ritonavir) and R7128. In yet another example, the combination of two or more DAAs includes PSI-7977 and BMS-79002.

[0048] In yet another aspect, the present technology features a method of treating HCV, comprising administering to a patient in need thereof an effective amount of a combination of two or more DAAsThe treatment lasts 5 weeks and does not include administration of any interferon or any ribavirin. The DAAs can be administered at the same or different dosing frequency. The patient being treated can be a treatment naïve patient, a treatment experienced patient, including, but not limited to, a relapser, an interferon partial responder, or an interferon non-responder, or a patient unable to take interferon. The patient can be infected with, for example and without limitation, HCV genotype 1, such as HCV genotype 1a or HCV genotype 1b; or HCV genotype 2 or 3. The treatment according to this aspect of the technology can also be effective against other HCV genotypes. The DAAs can be administered around the same time or at different times, and can be co-formulated in a single formulation or formulated in different compositions. Each DAA can be selected from HCV protease inhibitors, HCV polymerase inhibitors, or HCV NS5A inhibitors. For instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor and at least one HCV polymerase inhibitor (e.g., a combination of at least one HCV protease inhibitor and at least one non-nucleoside polymerase inhibitor, or a combination of at least one HCV protease inhibitor and at least one nucleoside polymerase inhibitor, or a combination of at least one HCV protease inhibitor, at least one nucleoside polymerase inhibitor and at least one non-nucleoside inhibitor). For another instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor and at least

one HCV NS5A inhibitor. For still another instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor, at least one HCV polymerase inhibitor, and at least one HCV NS5A inhibitor. For another instance, the combination of two or more DAAs can be a combination of at least two HCV polymerase inhibitors (e.g., a combination of at least two nucleoside polymerase inhibitors, or a combination of at least one nucleoside polymerase inhibitor and at least one non- nucleoside polymerase inhibitor, or a combination of at least two non- nucleoside polymerase inhibitors). For another instance, the combination of two or more DAAs can be a combination of at least two HCV protease inhibitors. For another instance, the combination of two or more DAAs can be a combination of at least two HCV NS5A inhibitors. For another instance, the combination of two or more DAAs can be a combination of at least one HCV polymerase inhibitor and at least one NS5A inhibitor (e.g., a combination of at least one HCV NS5A inhibitor and at least one non-nucleoside polymerase inhibitor, or a combination of at least one HCV NS5A inhibitor and at least one nucleoside polymerase inhibitor, or a combination of at least one HCV NS5A inhibitor, at least one nucleoside polymerase inhibitor and at least one non-nucleoside inhibitor). In one example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof) and Compound 2 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In another example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof) and Compound 3 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In still another example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof) and Compound 4 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In a further example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof), Compound 2 (or a salt thereof) and Compound 4 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In yet another example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof), Compound 3 (or a salt thereof) and Compound 4 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. Other DAA(s) can also be included in a treatment regimen according to this aspect of the technology. In yet another example, the combination of two or more DAAs comprises PSI-7977 and PSI-938. In yet another example, the combination of two or more DAAs

comprises PSI-7977 and TMC-435. In yet another example, the combination of two or more DAAs comprises BMS-790052 and BMS-650032. In yet another example, the combination of two or more DAAs comprises GS-5885, GS-9190, and GS-9451. In yet another example, the combination of two or more DAAs comprises BI-201335 and BI-207127. In yet another example, the combination of two or more DAAs comprises telprevir and VX-222. In another example, the combination of two or more DAAs comprises GS-5885 and GS-9451. In yet another example, the combination of two or more DAAs includes danoprevir (with ritonavir) and R7128. In yet another example, the combination of two or more DAAs includes PSI-7977 and BMS-79002.

[0049] In yet another aspect, the present technology features a method of treating HCV, comprising administering to a patient in need thereof an effective amount of a combination of two or more DAAs. The treatment lasts 4 weeks and does not include administration of any interferon or ribavirin. The DAAs can be administered at the same or different dosing frequency. The patient being treated can be a treatment naïve patient, a treatment experienced patient, including, but not limited to, a relapser, an interferon partial responder, or an interferon non-responder, or a patient unable to take interferon. The patient can be infected with, for example and without limitation, HCV genotype 1, such as HCV genotype 1a or HCV genotype 1b; or HCV genotype 2 or 3. The treatment according to this aspect of the technology can also be effective against other HCV genotypes. The DAAs can be administered around the same time or at different times, and can be co-formulated in a single formulation or formulated in different compositions. Each DAA can be selected from HCV protease inhibitors, HCV polymerase inhibitors, or HCV NS5A inhibitors. For instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor and at least one HCV polymerase inhibitor (e.g., a combination of at least one HCV protease inhibitor and at least one non-nucleoside polymerase inhibitor, or a combination of at least one HCV protease inhibitor and at least one nucleoside polymerase inhibitor, or a combination of at least one HCV protease inhibitor, at least one nucleoside polymerase inhibitor and at least one non-nucleoside inhibitor). For another instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor and at least one HCV NS5A inhibitor. For still another instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor, at least one HCV polymerase

inhibitor, and at least one HCV NS5A inhibitor. For another instance, the combination of two or more DAAs can be a combination of at least two HCV polymerase inhibitors (e.g., a combination of at least two nucleoside polymerase inhibitors, or a combination of at least one nucleoside polymerase inhibitor and at least one non- nucleoside polymerase inhibitor, or a combination of at least two non- nucleoside polymerase inhibitors). For another instance, the combination of two or more DAAs can be a combination of at least two HCV protease inhibitors. For another instance, the combination of two or more DAAs can be a combination of at least two HCV NS5A inhibitors. For another instance, the combination of two or more DAAs can be a combination of at least one HCV polymerase inhibitor and at least one NS5A inhibitor (e.g., a combination of at least one HCV NS5A inhibitor and at least one non-nucleoside polymerase inhibitor, or a combination of at least one HCV NS5A inhibitor and at least one nucleoside polymerase inhibitor, or a combination of at least one HCV NS5A inhibitor, at least one nucleoside polymerase inhibitor and at least one non-nucleoside inhibitor). In one example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof) and Compound 2 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In another example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof) and Compound 3 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In still another example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof) and Compound 4 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In a further example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof), Compound 2 (or a salt thereof) and Compound 4 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In yet another example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof), Compound 3 (or a salt thereof) and Compound 4 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. Other DAA(s) can also be included in a treatment regimen according to this aspect of the technology. In yet another example, the combination of two or more DAAs comprises PSI-7977 and PSI-938. In yet another example, the combination of two or more DAAs comprises PSI-7977 and TMC-435. In yet another example, the combination of two or more DAAs comprises BMS-790052 and BMS-650032. In yet another example, the combination

of two or more DAAs comprises GS-5885, GS-9190, and GS-9451. In yet another example, the combination of two or more DAAs comprises BI-201335 and BI-207127. In yet another example, the combination of two or more DAAs comprises telprevir and VX-222. In another example, the combination of two or more DAAs comprises GS-5885 and GS-9451. In yet another example, the combination of two or more DAAs includes danoprevir with ritonavir and R7128. In yet another example, the combination of two or more DAAs includes PSI-7977 and BMS-79002.

[0050] In yet another aspect, the present technology features a method of treating HCV, comprising administering to a patient in need thereof an effective amount of a combination of two or more DAAs. The treatment lasts 3 weeks (or even less, depending on the patient's condition) and does not include administration of any interferon or ribavirin. The DAAs can be administered at the same or different dosing frequency. The patient being treated can be a treatment naïve patient, a treatment experienced patient, including, but not limited to, a relapser, an interferon partial responder, or an interferon non-responder, or a patient unable to take interferon.. The patient can be infected with, for example and without limitation, HCV genotype 1, such as HCV genotype 1a or HCV genotype 1b; or HCV genotype 2 or 3. The treatment according to this aspect of the technology can also be effective against other HCV genotypes. The DAAs can be administered around the same time or at different times, and can be co-formulated in a single formulation or formulated in different compositions. Each DAA can be selected from HCV protease inhibitors, HCV polymerase inhibitors, or HCV NS5A inhibitors. For instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor and at least one HCV polymerase inhibitor (e.g., a combination of at least one HCV protease inhibitor and at least one non-nucleoside polymerase inhibitor, or a combination of at least one HCV protease inhibitor and at least one nucleoside polymerase inhibitor, or a combination of at least one HCV protease inhibitor, at least one nucleoside polymerase inhibitor and at least one non-nucleoside inhibitor). For another instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor and at least one HCV NS5A inhibitor. For still another instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor, at least one HCV polymerase inhibitor, and at least one HCV NS5A inhibitor. For another instance, the combination of two or more DAAs can be a combination of at least two

HCV polymerase inhibitors (e.g., a combination of at least two nucleoside polymerase inhibitors, or a combination of at least one nucleoside polymerase inhibitor and at least one non- nucleoside polymerase inhibitor, or a combination of at least two non- nucleoside polymerase inhibitors). For another instance, the combination of two or more DAAs can be a combination of at least two HCV protease inhibitors. For another instance, the combination of two or more DAAs can be a combination of at least two HCV NS5A inhibitors. For another instance, the combination of two or more DAAs can be a combination of at least one HCV polymerase inhibitor and at least one NS5A inhibitor (e.g., a combination of at least one HCV NS5A inhibitor and at least one non-nucleoside polymerase inhibitor, or a combination of at least one HCV NS5A inhibitor and at least one nucleoside polymerase inhibitor, or a combination of at least one HCV NS5A inhibitor, at least one nucleoside polymerase inhibitor and at least one non-nucleoside inhibitor). In one example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof) and Compound 2 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In another example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof) and Compound 3 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In still another example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof) and Compound 4 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In a further example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof), Compound 2 (or a salt thereof) and Compound 4 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In yet another example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof), Compound 3 (or a salt thereof) and Compound 4 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. Other DAA(s) can also be included in a treatment regimen according to this aspect of the technology. In yet another example, the combination of two or more DAAs comprises PSI-7977 and PSI-938. In yet another example, the combination of two or more DAAs comprises PSI-7977 and TMC-435. In yet another example, the combination of two or more DAAs comprises BMS-790052 and BMS-650032. In yet another example, the combination of two or more DAAs comprises GS-5885, GS-9190, and GS-9451. In yet another example, the combination of two or more DAAs

comprises BI-201335 and BI-207127. In yet another example, the combination of two or more DAAs comprises telprevir and VX-222. In another example, the combination of two or more DAAs comprises GS-5885 and GS-9451. In yet another example, the combination of two or more DAAs includes danoprevir with ritonavir and R7128. In yet another example, the combination of two or more DAAs includes PSI-7977 and BMS-79002.

[0051] In yet another aspect, the present technology features a method of treating HCV, comprising administering to a patient in need thereof an effective amount of a combination of two or more DAAs. The treatment lasts 12 weeks and does not include administration of any interferon or ribavirin. The DAAs can be administered at the same or different dosing frequency. The patient being treated can be a treatment naïve patient, a treatment experienced patient, including, but not limited to, a relapser, an interferon partial responder, or an interferon non-responder, or a patient unable to take interferon. The patient can be infected with, for example and without limitation, HCV genotype 1, such as HCV genotype 1a or HCV genotype 1b; or HCV genotype 2 or 3. The treatment according to this aspect of the technology can also be effective against other HCV genotypes. The DAAs can be administered around the same time or at different times, and can be co-formulated in a single formulation or formulated in different compositions. Each DAA can be selected from HCV protease inhibitors, HCV polymerase inhibitors, or HCV NS5A inhibitors. For instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor and at least one HCV polymerase inhibitor (e.g., a combination of at least one HCV protease inhibitor and at least one non-nucleoside polymerase inhibitor, or a combination of at least one HCV protease inhibitor and at least one nucleoside polymerase inhibitor, or a combination of at least one HCV protease inhibitor, at least one nucleoside polymerase inhibitor and at least one non-nucleoside inhibitor). For another instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor and at least one HCV NS5A inhibitor. For still another instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor, at least one HCV polymerase inhibitor, and at least one HCV NS5A inhibitor. For another instance, the combination of two or more DAAs can be a combination of at least two HCV polymerase inhibitors (e.g., a combination of at least two nucleoside polymerase inhibitors, or a combination of at least one nucleoside polymerase inhibitor and at least one non- nucleoside polymerase inhibitor, or a

combination of at least two non- nucleoside polymerase inhibitors). For another instance, the combination of two or more DAAs can be a combination of at least two HCV protease inhibitors. For another instance, the combination of two or more DAAs can be a combination of at least two HCV NS5A inhibitors. For another instance, the combination of two or more DAAs can be a combination of at least one HCV polymerase inhibitor and at least one NS5A inhibitor (e.g., a combination of at least one HCV NS5A inhibitor and at least one non-nucleoside polymerase inhibitor, or a combination of at least one HCV NS5A inhibitor and at least one nucleoside polymerase inhibitor, or a combination of at least one HCV NS5A inhibitor, at least one nucleoside polymerase inhibitor and at least one non-nucleoside inhibitor). In one example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof) and Compound 2 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In another example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof) and Compound 3 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In still another example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof) and Compound 4 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In a further example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof), Compound 2 (or a salt thereof) and Compound 4 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In yet another example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof), Compound 3 (or a salt thereof) and Compound 4 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. Other DAA(s) can also be included in a treatment regimen according to this aspect of the technology. In yet another example, the combination of two or more DAAs comprises PSI-7977 and PSI-938. In yet another example, the combination of two or more DAAs comprises PSI-7977 and TMC-435. In yet another example, the combination of two or more DAAs comprises BMS-790052 and BMS-650032. In yet another example, the combination of two or more DAAs comprises GS-5885, GS-9190, and GS-9451. In yet another example, the combination of two or more DAAs comprises BI-201335 and BI-207127. In yet another example, the combination of two or more DAAs comprises telprevir and VX-222. In another example, the combination of two or more DAAs comprises GS-5885 and GS-9451. In yet

another example, the combination of two or more DAAs includes danoprevir with ritonavir and R7128.

[0052] In yet another aspect, the present technology features a method of treating HCV, comprising administering to a patient in need thereof an effective amount of a combination of two or more DAAs. The treatment lasts 11 weeks and does not include administration of any interferonor any ribavirin. The DAAs can be administered at the same or different dosing frequency. The patient being treated can be a treatment naïve patient, a treatment experienced patient, including, but not limited to, a relapser, an interferon partial responder, or an interferon non-responder, or a patient unable to take interferon. The patient can be infected with, for example and without limitation, HCV genotype 1, such as HCV genotype 1a or HCV genotype 1b; or HCV genotype 2 or 3. The treatment according to this aspect of the technology can also be effective against other HCV genotypes. The DAAs can be administered around the same time or at different times, and can be co-formulated in a single formulation or formulated in different compositions. Each DAA can be selected from HCV protease inhibitors, HCV polymerase inhibitors, or HCV NS5A inhibitors. For instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor and at least one HCV polymerase inhibitor (e.g., a combination of at least one HCV protease inhibitor and at least one non-nucleoside polymerase inhibitor, or a combination of at least one HCV protease inhibitor and at least one nucleoside polymerase inhibitor, or a combination of at least one HCV protease inhibitor, at least one nucleoside polymerase inhibitor and at least one non-nucleoside inhibitor). For another instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor and at least one HCV NS5A inhibitor. For still another instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor, at least one HCV polymerase inhibitor, and at least one HCV NS5A inhibitor with ritonavir. Other DAA(s) can also be included in a treatment regimen according to this aspect of the technology. In yet another example, the combination of two or more DAAs comprises PSI-7977 and PSI-938. In yet another example, the combination of two or more DAAs comprises PSI-7977 and TMC-435. In yet another example, the combination of two or more DAAs comprises BMS-790052 and BMS-650032. In yet another example, the combination of two or more DAAs comprises GS-5885, GS-9190, and GS-9451. In yet another example, the combination of two or more

DAAs comprises BI-201335 and BI-207127. In yet another example, the combination of two or more DAAs comprises telprevir and VX-222. In another example, the combination of two or more DAAs comprises GS-5885 and GS-9451. In yet another example, the combination of two or more DAAs includes danoprevir with ritonavir and R7128. In yet another example, the combination of two or more DAAs includes PSI-7977 and BMS-79002.

[0053] In yet another aspect, the present technology features a method of treating HCV, comprising administering to a patient in need thereof an effective amount of a combination of two or more DAAs. The treatment lasts 10 weeks and does not include administration of any interferon or ribavirin. The DAAs can be administered at the same or different dosing frequency. The patient being treated can be a treatment naïve patient, a treatment experienced patient, including, but not limited to, a relapser, an interferon partial responder, or an interferon non-responder, or a patient unable to take interferon. The patient can be infected with, for example and without limitation, HCV genotype 1, such as HCV genotype 1a or HCV genotype 1b; or HCV genotype 2 or 3. The treatment according to this aspect of the technology can also be effective against other HCV genotypes. The DAAs can be administered around the same time or at different times, and can be co-formulated in a single formulation or formulated in different compositions. Each DAA can be selected from HCV protease inhibitors, HCV polymerase inhibitors, or HCV NS5A inhibitors. For instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor and at least one HCV polymerase inhibitor (e.g., a combination of at least one HCV protease inhibitor and at least one non-nucleoside polymerase inhibitor, or a combination of at least one HCV protease inhibitor and at least one nucleoside polymerase inhibitor, or a combination of at least one HCV protease inhibitor, at least one nucleoside polymerase inhibitor and at least one non-nucleoside inhibitor). For another instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor and at least one HCV NS5A inhibitor. For still another instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor, at least one HCV polymerase inhibitor, and at least one HCV NS5A inhibitor. For another instance, the combination of two or more DAAs can be a combination of at least two HCV polymerase inhibitors (e.g., a combination of at least two nucleoside polymerase inhibitors, or a combination of at least one nucleoside polymerase inhibitor and at least one non- nucleoside polymerase inhibitor, or a

combination of at least two non- nucleoside polymerase inhibitors). For another instance, the combination of two or more DAAs can be a combination of at least two HCV protease inhibitors. For another instance, the combination of two or more DAAs can be a combination of at least two HCV NS5A inhibitors. For another instance, the combination of two or more DAAs can be a combination of at least one HCV polymerase inhibitor and at least one NS5A inhibitor (e.g., a combination of at least one HCV NS5A inhibitor and at least one non-nucleoside polymerase inhibitor, or a combination of at least one HCV NS5A inhibitor and at least one nucleoside polymerase inhibitor, or a combination of at least one HCV NS5A inhibitor, at least one nucleoside polymerase inhibitor and at least one non-nucleoside inhibitor). In one example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof) and Compound 2 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In another example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof) and Compound 3 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In still another example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof) and Compound 4 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In a further example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof), Compound 2 (or a salt thereof) and Compound 4 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In yet another example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof), Compound 3 (or a salt thereof) and Compound 4 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. Other DAA(s) can also be included in a treatment regimen according to this aspect of the technology. In yet another example, the combination of two or more DAAs comprises PSI-7977 and PSI-938. In yet another example, the combination of two or more DAAs comprises PSI-7977 and TMC-435. In yet another example, the combination of two or more DAAs comprises BMS-790052 and BMS-650032. In yet another example, the combination of two or more DAAs comprises GS-5885, GS-9190, and GS-9451. In yet another example, the combination of two or more DAAs comprises BI-201335 and BI-207127. In yet another example, the combination of two or more DAAs comprises telprevir and VX-222. In another example, the combination of two or more DAAs comprises GS-5885 and GS-9451. In yet

another example, the combination of two or more DAAs includes danoprevir with ritonavir and R7128. In yet another example, the combination of two or more DAAs includes PSI-7977 and BMS-79002.

[0054] In yet another aspect, the present technology features a method of treating HCV, comprising administering to a patient in need thereof an effective amount of a combination of two or more DAAs. The treatment lasts 9 weeks and does not include administration of any interferon. The DAAs can be administered at the same or different dosing frequency. The patient being treated can be an interferon naïve patient, a treatment experienced patient, including, but not limited to, a relapser, or an interferon partial responder, or an interferon non-responder, or a patient unable to take interferon.. The patient can be infected with, for example and without limitation, HCV genotype 1, such as HCV genotype 1a or HCV genotype 1b; or HCV genotype 2 or 3. The treatment according to this aspect of the technology can also be effective against other HCV genotypes. The DAAs can be administered around the same time or at different times, and can be co-formulated in a single formulation or formulated in different compositions. Each DAA can be selected from HCV protease inhibitors, HCV polymerase inhibitors, or HCV NS5A inhibitors. For instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor and at least one HCV polymerase inhibitor (e.g., a combination of at least one HCV protease inhibitor and at least one non-nucleoside polymerase inhibitor, or a combination of at least one HCV protease inhibitor and at least one nucleoside polymerase inhibitor, or a combination of at least one HCV protease inhibitor, at least one nucleoside polymerase inhibitor and at least one non-nucleoside inhibitor). For another instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor and at least one HCV NS5A inhibitor. For still another instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor, at least one HCV polymerase inhibitor, and at least one HCV NS5A inhibitor. For another instance, the combination of two or more DAAs can be a combination of at least two HCV polymerase inhibitors (e.g., a combination of at least two nucleoside polymerase inhibitors, or a combination of at least one nucleoside polymerase inhibitor and at least one non- nucleoside polymerase inhibitor, or a combination of at least two non- nucleoside polymerase inhibitors). For another instance, the combination of two or more DAAs can be a combination of at least two HCV protease

inhibitors. For another instance, the combination of two or more DAAs can be a combination of at least two HCV NS5A inhibitors. For another instance, the combination of two or more DAAs can be a combination of at least one HCV polymerase inhibitor and at least one NS5A inhibitor (e.g., a combination of at least one HCV NS5A inhibitor and at least one non-nucleoside polymerase inhibitor, or a combination of at least one HCV NS5A inhibitor and at least one nucleoside polymerase inhibitor, or a combination of at least one HCV NS5A inhibitor, at least one nucleoside polymerase inhibitor and at least one non-nucleoside inhibitor). In one example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof) and Compound 2 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In another example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof) and Compound 3 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In still another example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof) and Compound 4 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In a further example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof), Compound 2 (or a salt thereof) and Compound 4 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. In yet another example, the combination of two or more DAAs is a combination of Compound 1 (or a salt thereof), Compound 3 (or a salt thereof) and Compound 4 (or a salt thereof). Compound 1 (or a salt thereof) can be co-formulated with ritonavir. Other DAA(s) can also be included in a treatment regimen according to this aspect of the technology. In yet another example, the combination of two or more DAAs comprises PSI-7977 and PSI-938. In yet another example, the combination of two or more DAAs comprises PSI-7977 and TMC-435. In yet another example, the combination of two or more DAAs comprises BMS-790052 and BMS-650032. In yet another example, the combination of two or more DAAs comprises GS-5885, GS-9190, and GS-9451. In yet another example, the combination of two or more DAAs comprises BI-201335 and BI-207127. In yet another example, the combination of two or more DAAs comprises telprevir and VX-222. In another example, the combination of two or more DAAs comprises GS-5885 and GS-9451. In yet another example, the combination of two or more DAAs includes danoprevir with ritonavir

and R7128 In yet another example, the combination of two or more DAAs includes PSI-7977 and BMS-79002.

[0055] In another embodiment, the present technology provides interferon-free treatment comprising administering daily two DAAs, where the two DAAs include a HCV polymerase inhibitor, for example PSI-7977 and a NS5a inhibitor, for example PMS-790052 for a duration of no more than eleven weeks, preferably no more than eight weeks.

[0056] In some embodiments, the present technology provides a method of treating Hepatitis C virus infection in a subject comprising administering daily a HCV protease inhibitor and a HCV polymerase inhibitor to the subject in the absence of interferon for a duration of no more than twelve weeks, preferably no more than eight weeks. In some embodiments, ritonavir (or an equivalent thereof) is co-administered with one or more protease inhibitors to improve the pharmacokinetics of the protease inhibitor(s). The treatment excludes administering ribavirin to the patient. In some embodiments, the HCV polymerase inhibitor is at least one nucleoside polymerase inhibitor or at least one non-nucleoside polymerase inhibitor. In some embodiments, both a nucleoside polymerase inhibitors and a non-nucleoside polymerase inhibitor may be administered.

[0057] The methods of the present technology as described herein may be used to treat a naïve patient or a treatment experienced patient. Treatment experienced patients include interferon non-responders, partial responders (patients whose HCV RNA levels declined but never became undetectable), and relapsers (patients who achieved undetectable levels of HCV RNA during therapy but rebound). Methods of the present technology may also be used to treat patients who are not candidates for interferon treatment. Patients who are not candidates for interferon treatment include, but are not limited to, one or more of the following groups, patients intolerant to interferon, patients who refuse to take interferon treatment, patients with medical conditions which preclude them from taking interferon, and patients who have an increased risk of side effects or infection by taking interferon.

[0058] In some embodiments, a cytochrome P-450 inhibitor, e.g. ritonavir, is administered either in the same or separate pharmaceutical composition with the protease inhibitor (e.g. Compound 1 (or a pharmaceutically acceptable salt thereof)) to improve the pharmacokinetics. A cytochrome P450 inhibitor reduces the metabolism of some protease

inhibitors, such as Compound 1, thereby improving the pharmacokinetic and bioavailability of the protease inhibitor, for example Compound 1. More preferably, Compound 1 (or a pharmaceutically acceptable salt thereof) is co-formulated with ritonavir in the same dosage form. Other cytochrome P450 inhibitors, such as cobicistat, may also be administered in lieu of ritonavir, to enhance the pharmacokinetics of Compound 1 (or a pharmaceutically acceptable salt thereof).

[0059] Inhibitors of cytochrome P450, such as ritonavir, may be co-administered with the DAAs, either sequentially or simultaneously, in the same or different compositions. In some embodiments, the cytochrome P450 inhibitors are administered in order to improve the pharmacokinetics of at least one of the DAAs. Not to be bound by any theory, but a cytochrome P450 inhibitor may also reduce the development of resistant strains of HCV when co-administered with a DAA, thus providing the effectiveness in a shorter treatment. In some embodiments, ritonavir is co-administered with therapeutic agent 1. In some embodiments, ritonavir is co-administered with therapeutic agent 1 in the same compositions.

[0060] In some embodiments, the present technology provides a method of treating HCV infection comprising administering at least one protease inhibitor and at least one HCV polymerase inhibitor in a course of treatment of less than eight weeks in the absence of interferon. In some embodiments, the HCV polymerase inhibitor is Compound 1 (or a pharmaceutically acceptable salt thereof).

[0061] In some embodiments, the present technology provides a method of treating HCV infection comprising administering at least two DAAs to a patient in need thereof, wherein the at least two DAAs include at least one protease inhibitor and at least one HCV polymerase inhibitor. In some embodiments, the at least two DAAs includes therapeutic agent 1 with at least one HCV polymerase inhibitor. In some embodiments, the HCV polymerase inhibitor is at least one non-nucleoside polymerase inhibitor. In some embodiments, the non-nucleoside polymerase inhibitor is therapeutic agent 2 or therapeutic agent 3 or a combination thereof.

[0062] In some embodiments, the present technology provides a method of treating HCV infection comprising administering a HCV protease inhibitor, preferably therapeutic agent 1,

with at least one HCV NS5A inhibitor to a patient in need thereof. In some embodiments, the NS5A inhibitor is therapeutic agent 4.

[0063] In some embodiments of the present technology, a method of treating HCV infection comprises administering at least three DAAs to a subject for no more than 8 weeks without administering interferon or ribavirin. The at least three DAAs can be at least one protease inhibitor, at least one HCV polymerase inhibitor, and at least one NS5A inhibitors. In a preferred embodiment, the at least one protease inhibitor is therapeutic agent 1, the at least one polymerase inhibitor is therapeutic agent 2 or therapeutic agent 3, and the at least one NS5A inhibitor is therapeutic agent 4.

[0064] Preferred HCV protease inhibitors include, but are not limited to, therapeutic agent 1, telaprevir (Vertex), boceprevir (Merck), BI-201335 (Boehringer Ingelheim), GS-9451 (Gilead), and BMS-650032 (BMS). Other suitable protease inhibitors include, but are not limited to, ACH-1095 (Achillion), ACH-1625 (Achillion), ACH-2684 (Achillion), AVL-181 (Avila), AVL-192 (Avila), BMS-650032 (BMS), danoprevir (RG7227/ITMN-191, Roche), GS-9132 (Gilead), GS-9256 (Gilead), IDX-136 (Idenix), IDX-316 (Idenix), IDX-320 (Idenix), MK-5172 (Merck), narlaprevir (Schering-Plough Corp), PHX-1766 (Phenomix), TMC-435 (Tibotec), vaniprevir (MK-7009, Merck), VBY708 (Virobay), VX-500 (Vertex), VX-813 (Vertex), VX-985 (Vertex), or a combination thereof.

[0065] Preferred non-nucleoside HCV polymerase inhibitors for use in the present technology include, but are not limited to, therapeutic agent 2, therapeutic agent 3, GS-9190 (Gilead), BI-207127 (Boehringer Ingelheim), and VX-222 (VCH-222) (Vertex & ViraChem). Preferred nucleoside HCV polymerase inhibitors include, but are not limited to, PSI- 7977 (Pharmasset), and PSI-938 (Pharmasset). Other suitable and non-limiting examples of suitable HCV polymerase inhibitors include ANA-598 (Anadys), BI-207127 (Boehringer Ingelheim), BILB-1941 (Boehringer Ingelheim), BMS-791325 (BMS), filibuvir, GL59728 (Glaxo), GL60667 (Glaxo), GS-9669 (Gilead), IDX-375 (Idenix), MK-3281 (Merck), tegobuvir, TMC-647055 (Tibotec), VCH-759 (Vertex & ViraChem), VCH-916 (ViraChem), VX-759 (Vertex), GS-6620 (Gilead), IDX-102 (Idenix), IDX-184 (Idenix), INX-189 (Inhibitex), MK-0608 (Merck), RG7128 (Roche), TMC64912 (Medivir), GSK625433 (GlaxoSmithKline), BCX-4678 (BioCryst), ALS-2200 (Alios

BioPharma/Vertex), ALS-2158 (Alios BioPharma/Vertex), or a combination thereof. A polymerase inhibitor may be a nucleoside polymerase inhibitor, such as GS-6620 (Gilead), IDX-102 (Idenix), IDX-184 (Idenix), INX-189 (Inhibitex), MK-0608 (Merck), PSI-7977 (Pharmasset), PSI-938 (Pharmasset), RG7128 (Roche), TMC64912 (Medivir), ALS-2200 (Alios BioPharma/Vertex), ALS-2158 (Alios BioPharma/Vertex), or a combination therefore. A polymerase inhibitor may also be a non-nucleoside polymerase inhibitor, such as PF-00868554 (Pfizer), ANA-598 (Anadys), BI-207127 (Boehringer Ingelheim), BILB-1941 (Boehringer Ingelheim), BMS-791325 (BMS), filibuvir, GL59728 (Glaxo), GL60667 (Glaxo), GS-9669 (Gilead), IDX-375 (Idenix), MK-3281 (Merck), tegobuvir (Gilead),, TMC-647055 (Tibotec), VCH-759 (Vertex & ViraChem), VCH-916 (ViraChem), VX-222 (VCH-222) (Vertex & ViraChem), VX-759 (Vertex), or a combination thereof.

[0066] Preferred NS5A inhibitors include, but are not limited to, therapeutic agent 4, BMS-790052 (BMS) and GS-5885 (Gilead). Non-limiting examples of suitable NS5A inhibitors include GSK62336805 (GlaxoSmithKline), ACH-2928 (Achillion), AZD2836 (Astra-Zeneca), AZD7295 (Astra-Zeneca), BMS-790052 (BMS), BMS-824393 (BMS), GS-5885 (Gilead), PPI-1301 (Presidio), PPI-461 (Presidio) A-831 (Arrow Therapeutics), A-689 (Arrow Therapeutics) or a combination thereof.

[0067] Non-limiting examples of suitable cyclophilin inhibitors include alisporovir (Novartis & Debiopharm), NM-811 (Novartis), SCY-635 (Scynexis), or a combination thereof.

[0068] Non-limiting examples of suitable HCV entry inhibitors include ITX-4520 (iTherx), ITX-5061 (iTherx), or a combination thereof.

[0069] Specific examples of other DAA agents that are suitable for the present methods include, but are not limited to, AP-H005, A-831 (Arrow Therapeutics) (NS5A inhibitor), A-689 (Arrow Therapeutics) (NS5A inhibitor), INX08189 (Inhibitex) (polymerase inhibitor), ITMN-191 (Intermune/Roche) (NS3/4A Protease inhibitor), VBY-376 (Protease Inhibitor) (Virobay), ACH-1625 (Achillion, Protease inhibitor), IDX136 (Idinex, Protease Inhibitor), IDX316 (Idinex, Protease inhibitor), VX-813 (Vertex), SCH 900518 (Schering-Plough), TMC-435 (Tibotec), ITMN-191 (Intermune, Roche), MK-7009 (Merck), IDX-PI (Novartis), R7128 (Roche), PF-868554 (Pfizer) (non-nucleoside polymerase inhibitor), PF-4878691 (Pfizer), IDX-184 (Novartis), IDX-375 (Idenix, NS5B polymerase inhibitor), PPI-461

(Presidio), BILB-1941 (Boehringer Ingelheim), GS-9190 (Gilead), BMS-790052 (BMS), CTS-1027 (Conatus), GS-9620 (Gilead), PF-4878691 (Pfizer), RO5303253 (Roche), ALS-2200 (Alios BioPharma/Vertex), ALS-2158 (Alios BioPharma/Vertex), GSK62336805 (GlaxoSmithKline), or any combinations thereof.

[0070] In some embodiments, the compositions and methods of the present technology can be used to treat patients with genotype 1a HCV infection for no more than 12 weeks, preferably no more than 8 weeks. Patients with genotype 1a infection can be treated with a combination of at least 2 DAAs without interferon and without ribavirin where the at least two DAAs include therapeutic agent 1 and therapeutic agent 2. Therapeutic agent 1 and therapeutic agent 2 can be administered in therapeutically effective amounts to provide a SVR after a treatment duration of no more than 12 weeks, preferably no more than 8 weeks. The patients may be treatment naïve patients or treatment experienced HCV patients. The treatment duration can be no more than 12 weeks, including but not limited to, no more than 11 weeks, no more than 10 weeks, no more than 9 weeks, but preferably no more than 8 weeks, no more than 7 weeks, no more than 6 weeks, no more than 5 weeks, no more than 4 weeks, or no more than 3 weeks. Therapeutic agent 1 can be provided in a total daily dosage of an amount from about 5 mg to about 300 mg, alternatively from about 5 mg to about 250 mg, alternatively from about 25 mg to about 100 mg. The total daily dosage of therapeutic agent 1 can be, but is not limited to, for example, about 5 mg, about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 70 mg, about 80 mg, about 90 mg, about 100 mg, about 110 mg, about 120 mg, about 125 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220 mg, about 230 mg, about 240 mg, about 250 mg, about 260 mg, about 270 mg, or about 300 mg. Therapeutic agent 2 can be administered with therapeutic agent 1 in any of the dosages of therapeutic agent 1 described above. Therapeutic agent 2 can be provided in combination with therapeutic agent 1 in a total daily dose of therapeutic agent 2 of an amount from about 100 mg to about 1800 mg, preferably from about 100 mg to about 800 mg, more preferably about 200 mg to about 800 mg. The total daily dosage of therapeutic agent 2 can be, but is not limited to, for example, about 100 mg, about 200 mg, about 250 mg, about 300 mg, about 400 mg, about 500 mg, about 600 mg, about 700 mg, about 800 mg, about 900 mg, about 1000 mg, about 1500 mg,

or 1800 mg. Some suitable examples include, but are not limited to, therapeutic 1 provided in a total daily dose of from about 5 mg to about 250 mg and therapeutic agent 2 provided in a total daily dose of from about 100 mg to about 600 mg. In some embodiments, therapeutic 1 is provided in a total daily dose from 25 mg to about 200 mg, and therapeutic agent 2 is provided in an amount of about 100 mg to about 600 mg. In one embodiment, the total daily dose of therapeutic agent 1 is 50 mg. In some embodiments, ritonavir can be either co-administered or administered separately with therapeutic agent 1. Suitable dosages of ritonavir include, but are not limited to, from about 50 mg to about 400 mg per day, preferably about 100 mg per day. In some embodiments, if the treatment regimen of the present technology does not provide the desired SVR after treatments of no more than 12 weeks, the patient may be treated with interferon-containing regimen, a ribavirin-containing regimen, or a combination thereof.

[0071] In some embodiments, the compositions and methods of the present technology can be used to treat patients with genotype 2 or 3 HCV infection with a treatment duration of no more than 12 weeks, preferably no more than 8 weeks. Patients with genotype 2 or 3 HCV infection can be treated with a combination of at least 2 DAAs without interferon and without ribavirin where the at least two DAAs include therapeutic agent 1 and therapeutic agent 2. Therapeutic agent 1 and therapeutic agent 2 can be administered in therapeutically effective amounts to provide a SVR with a treatment duration of no more than 12 weeks, preferably no more than 8 weeks. The patients may be treatment naïve HCV patients or treatment experienced HCV patients. The treatment duration can be no more than 12 weeks, including but not limited to, no more than 11 weeks, no more than 10 weeks, no more than 9 weeks, but preferably no more than 8 weeks, no more than 7 weeks, no more than 6 weeks, no more than 5 weeks, no more than 4 weeks, or no more than 3 weeks. Therapeutic agent 1 can be provided in a total daily dosage of an amount from about 5 mg to about 300 mg, alternatively from about 5 mg to about 250 mg, alternatively from about 25 mg to about 100 mg. The total daily dosage of therapeutic agent 1 can be, but is not limited to, for example, about 5 mg, about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 70 mg, about 80 mg, about 90 mg, about 100 mg, about 110 mg, about 120 mg, about 125 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220

mg, about 230 mg, about 240 mg, about 250 mg, about 260 mg, about 270 mg, about 300 mg. Therapeutic agent 2 can be administered in connection with therapeutic agent 1 in any of the dosages of therapeutic agent 1 described above. Therapeutic agent 2 can be provided in combination with therapeutic agent 1 in a total daily dose of therapeutic agent 2 of an amount from about 100 mg to about 1800 mg, preferably from about 100 mg to about 800 mg, more preferably about 200 mg to about 800 mg. The total daily dosage of therapeutic agent 2 can be, but is not limited to, for example, about 100 mg, about 200 mg, about 250 mg, about 300 mg, about 400 mg, about 500 mg, about 600 mg, about 700 mg, about 800 mg, about 900 mg, about 1000 mg, about 1500 mg, or 1800 mg. Some suitable examples include, but are not limited to, for example, therapeutic 1 provided in a total daily dose from about 5 mg to about 250 mg and therapeutic agent 2 provided in a total daily dose of from about 100 mg to about 600 mg. In some embodiments, therapeutic 1 is provided in a total daily dose from about 25 mg to about 200 mg, and therapeutic agent 2 is provided in an amount of about 100 mg to about 600 mg. In one embodiment, the total daily dose of therapeutic agent 1 is 50 mg. In some embodiments, ritonavir can be either co-administered or administered separately with therapeutic agent 1. Suitable dosages of ritonavir include, from about 50 mg to about 400 mg per day, preferably about 100 mg per day. In some embodiments, if the treatment regimen of the present technology does not provide the desired SVR after treatments of no more than 12 weeks, the patient may be treated with interferon-containing regimen, a ribavirin-containing regimen or a combination thereof.

[0072] In some embodiments, the compositions and methods of the present technology can be used to treat patients with HCV infection comprising administration of at least two DAAs to a patient comprising therapeutic agent 1 and therapeutic agent 2 for no more than 12 weeks, preferably no more than 8 weeks in the absence of interferon and in the absence of ribavirin. Suitably, the patient may be a treatment naïve patient, a treatment experienced patient or an interferon nonresponder. In some embodiments, the patient is infected with HCV genotype 1, such as genotype 1a. In some embodiments, the patient is infected with HCV genotype 1b. In some embodiments, the patient is infected with HCV genotype 2 or 3, such as 2a or 2b. In some other embodiments, the patient is infected with HCV genotype 3a. The treatment according to this aspect of the technology can also be effective against other HCV genotypes. The treatment duration can be for no more than 12 weeks, preferably no

more than 8 weeks, including but not limited to, no more than 11 weeks, no more than 10 weeks, no more than 9 weeks, but preferably no more than 8 weeks, no more than 7 weeks, no more than 6 weeks, no more than 5 weeks, no more than 4 weeks, or no more than 3 weeks. Therapeutic agent 1 and therapeutic agent 2 can be administered in therapeutically effective amounts to provide a SVR after treatment duration of no more than 12 weeks, preferably no more than 8 weeks. Therapeutic agent 1 can be provided in a total daily dosage of an amount from about 5 mg to about 300 mg, alternatively from about 5 mg to about 250 mg, alternatively from about 25 mg to about 100 mg. The total daily dosage of therapeutic agent 1 can be, but is not limited to, for example, about 5 mg, about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 70 mg, about 80 mg, about 90 mg, about 100 mg, about 110 mg, about 120 mg, about 125 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220 mg, about 230 mg, about 240 mg, about 250 mg, about 260 mg, about 270 mg, or about 300 mg. Therapeutic agent 2 can be administered with therapeutic agent 1 in any of the dosages described above. Therapeutic agent 2 can be provided in combination with therapeutic agent 1 in a total daily dosage of an amount of from about 100 mg to about 1800 mg, preferably from about 100 mg to about 800 mg, more preferably about 200 mg to about 800 mg. The total daily dosage of therapeutic agent 2 can be, but is not limited to, for example, about 100 mg, about 200 mg, about 250 mg, about 300 mg, about 400 mg, about 500 mg, about 600 mg, about 700 mg, about 800 mg, about 900 mg, about 1000 mg. Some suitable examples include, but are not limited to, therapeutic 1 provided in a total daily dose from about 5 mg to about 250 mg and therapeutic agent 2 provided in a total daily dose of from about 100 mg to about 600 mg. In some embodiments, therapeutic 1 is provided in a total daily dose from 25 mg to about 200 mg, and therapeutic agent 2 is provided in an amount of about 100 mg to about 600 mg. In one embodiment, the total daily dose of therapeutic agent 1 is 50 mg. In some embodiments, ritonavir can be either co-administered or administered separately with therapeutic agent 1. Suitable dosages of ritonavir include, from about 50 mg to about 400 mg per day, preferably about 100 mg per day. In some embodiments, if the treatment regimen of the present technology does not provide the desired SVR after a treatment duration of no more than 12

weeks, the patient may be treated with interferon-containing regimen, a ribavirin-containing regimen, or a combination thereof.

[0073] In some embodiments, the compositions and methods of the present technology can be used to treat patients with HCV infection who are not candidates for interferon treatment. Patients who are not candidates for interferon treatment include, but is not limited to, one or more of the following groups, patients intolerant to interferon, patients who refuse to take interferon treatment, patients with medical conditions which preclude them from taking interferon, and patients who have an increased risk of side effects or infection by taking interferon. A non-candidate for interferon treatment can be infected with HCV genotype 1 or 2, for example, genotype 1a or 1b. A non-candidate for interferon treatment can be infected with HCV genotype 2, for example, genotype 2a or 2b. The treatment according to this aspect of the technology can also be effective against other HCV genotypes. In some embodiments, non-candidate for interferon treatment patients can be treated with a combination of at least 2 DAAs without interferon and without ribavirin for a treatment duration of no more than 12 weeks, including but not limited to, no more than 11 weeks, no more than 10 weeks, no more than 9 weeks, but preferably no more than 8 weeks, no more than 7 weeks, no more than 6 weeks, no more than 5 weeks, no more than 4 weeks, or no more than 3 weeks. The at least two DAAs include at least one HCV protease inhibitor and at least one HCV polymerase inhibitor. Suitably, the at least one HCV protease inhibitor can be therapeutic agent 1 and the at least one HCV polymerase inhibitor can be therapeutic agent 2. Therapeutic agent 1 and therapeutic agent 2 can be administered in therapeutically effective amounts to provide a SVR after a treatment duration of no more than 12 weeks, preferably no more than 8 weeks. Therapeutic agent 1 can be provided in a total daily dosage amount from about 5 mg to about 300 mg, alternatively from about 5 mg to about 250 mg, alternatively from about 25 mg to about 100 mg. The total daily dosage of therapeutic agent 1 can be, but is not limited to, for example, about 5 mg, about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 70 mg, about 80 mg, about 90 mg, about 100 mg, about 110 mg, about 120 mg, about 125 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220 mg, about 230 mg, about 240 mg, about 250 mg, about 260 mg, about 270 mg, or about 300 mg. Therapeutic agent 2 can be administered

with therapeutic agent 1 with therapeutic agent 1 administered at any of the dosages described above. Therapeutic agent 2 can be provided in combination with therapeutic agent 1 in a total daily dosage of an amount of therapeutic agent 2 from about 100 mg to about 1800 mg, preferably from about 100 mg to about 800 mg, more preferably about 200 mg to about 800 mg. The total daily dosage of therapeutic agent 2 can be, but is not limited to, for example, about 100 mg, about 200 mg, about 250 mg, about 300 mg, about 400 mg, about 500 mg, about 600 mg, about 700 mg, about 800 mg, about 900 mg, or about 1000 mg. Some suitable examples include, but are not limited to, therapeutic 1 provided in a total daily dose from about 5 mg to about 250 mg and therapeutic agent 2 is provided in a total daily dose of from about 100 mg to about 600 mg. In some embodiments, therapeutic 1 is provided in a total daily dose from 25 mg to about 200 mg, and therapeutic agent 2 is provided in an amount from about 100 mg to about 600 mg. In one embodiment, the total daily dose of therapeutic agent 1 is 50 mg. In some embodiments, if the treatment regimen of the present technology does not provide the desired SVR after treatments of no more than 12 weeks, the patient may be treated with a ribavirin-containing regimen.

[0074] In some embodiments, the compositions and methods of the present technology can be used to treat patients with HCV infection comprising administration of at least three DAAs to a patient comprising therapeutic agent 1, therapeutic agent 2 and therapeutic agent 4 for a treatment duration of no more than 12 weeks, preferably no more than 8 weeks without interferon and without ribavirin. In some embodiments, the patient is infected with HCV genotype 1, such as genotype 1a. The treatment according to this aspect of the technology can also be effective against other HCV genotypes. The treatment duration can be no more than 12 weeks, including but not limited to, no more than 11 weeks, no more than 10 weeks, no more than 9 weeks, but preferably no more than 8 weeks, no more than 7 weeks, no more than 6 weeks, no more than 5 weeks, no more than 4 weeks, or no more than 3 weeks. Therapeutic agent 1, therapeutic agent 2, and therapeutic agent 3 can be provided in effective amounts to provide a SVR after a treatment duration of no more than 12 weeks, preferably no more than 8 weeks. Therapeutic agent 1 can be provided in a total daily dosage of from about 5 mg to about 300 mg, alternatively from about 5 mg to about 250 mg, alternatively from about 25 mg to about 100 mg. The total daily dosage of therapeutic agent 1 can be, but is not limited to, for example, about 5 mg, about 10 mg, about 15 mg, about 20

mg, about 25 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 70 mg, about 80 mg, about 90 mg, about 100 mg, about 110 mg, about 120 mg, about 125 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220 mg, about 230 mg, about 240 mg, about 250 mg, about 260 mg, about 270 mg, about 300 mg. Therapeutic agent 2 can be administered with therapeutic agent 1 with therapeutic agent 1 being administered in any of the dosages described above. Therapeutic agent 2 can be provided in combination with therapeutic agent 1 in a total daily dosage of therapeutic agent 2 from about 100 mg to about 1800 mg, preferably from about 100 mg to about 800 mg, more preferably about 200 mg to about 800 mg. The total daily dosage of therapeutic agent 2 can be, but is not limited to, for example, about 100 mg, about 200 mg, about 250 mg, about 300 mg, about 400 mg, about 500 mg, about 600 mg, about 700 mg, about 800 mg, about 900 mg, or about 1000 mg. Therapeutic agent 4 can be provided in combination with therapeutic agent 1 and therapeutic agent 2 in which therapeutic agent 1 and therapeutic agent 2 are administered in any combination of the dosages for therapeutic agent 1 and therapeutic agent 2 described above. Therapeutic agent 4 can be provided in combination with therapeutic agent 1 and therapeutic agent 2 in a total daily dose of therapeutic agent 4 of an amount from about 5 mg to about 350 mg, preferably about 5 mg to about 300 mg, more preferably about 25 mg to about 200 mg. The total daily dosage of therapeutic agent 4 can be, but are not limited to, for example, about 5 mg, about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 70 mg, about 75 mg, about 80 mg, about 90 mg, about 100 mg, about 110 mg, about 120 mg, about 120 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220 mg, about 230 mg, about 240 mg, about 250 mg, about 260 mg, about 270 mg, about 280 mg, about 290 mg, about 300 mg, about 310 mg, about 320 mg, about 330 mg, about 340 mg, or about 350 mg. In some embodiments, ritonavir can be either co-administered or administered separately with therapeutic agent 1. Suitable dosages of ritonavir include, from about 50 mg to about 400 mg per day, preferably about 100 mg per day. Some suitable examples include, but are not limited to, therapeutic 1 provided in a total daily dose from about 5 mg to about 250 mg, therapeutic agent 2 provided in a total daily dose of from about 100 mg to about 600 mg, and therapeutic agent 4 provided in a total daily dose from about 5

mg to about 200 mg. In some embodiments, therapeutic 1 is provided in a total daily dose from 25 mg to about 200 mg, therapeutic agent 2 is provided in a total daily dose from about 100 mg to about 600 mg, and therapeutic agent 4 is provided in a total daily dose from about 25 mg to about 200 mg. In one embodiment, the total daily dose of therapeutic agent 1 is 50 mg. Suitably, in some embodiments, the patient may be a treatment naïve patient, a treatment experienced patient, or an interferon nonresponder. In some embodiments, if the treatment regimen of the present technology does not provide the desired SVR after treatments of 12 weeks, the patient may be treated with interferon-containing regimen, a ribavirin-containing regimen, or a combination thereof.

[0075] In some embodiments, the compositions and methods of the present technology can be used to treat patients with genotype 1, such as genotype 1a or 1b HCV infection for a treatment duration of no more than 12 weeks, preferably no more than 8 weeks with a combination of therapeutic agent 1 and therapeutic agent 3 without interferon and without ribavirin. The treatment duration may be no more than 12 weeks, including but not limited to, no more than 11 weeks, no more than 10 weeks, no more than 9 weeks, but preferably no more than 8 weeks, no more than 7 weeks, no more than 6 weeks, no more than 5 weeks, no more than 4 weeks, or no more than 3 weeks. In some embodiments, therapeutic agent 1 can be provided in a total daily dosage of from about 5 mg to about 300 mg, alternatively from about 5 mg to about 250 mg, alternatively from about 25 mg to about 100 mg. The total daily dosage of therapeutic agent 1 can be, but is not limited to, for example, about 5 mg, about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 70 mg, about 80 mg, about 90 mg, about 100 mg, about 110 mg, about 120 mg, about 125 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220 mg, about 230 mg, about 240 mg, about 250 mg, about 260 mg, about 270 mg, or about 300 mg. Therapeutic agent 3 can be administered in connection with therapeutic agent 1 with therapeutic agent 1 being administered at any of the dosages of described above. Therapeutic agent 3 can be provided in combination with therapeutic agent 1, wherein therapeutic agent 3 is administered in a total daily dosage from about 50 mg to about 1000 mg, preferably from about 50 mg to about 600 mg, alternatively from about 100 mg to about 600 mg. The total daily dosage of therapeutic agent 3 can be, but is not limited to, for example, about 50 mg,

about 60 mg, about 70 mg, about 80 mg, about 90 mg, about 100 mg, about 120 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220 mg, about 230 mg, about 240 mg, about 250 mg, about 260 mg, about 270 mg, about 280 mg, about 290 mg, about 300 mg, about 310 mg, about 320 mg, about 330 mg, about 340 mg, about 350 mg, about 360 mg, about 370 mg, about 380 mg, about 390 mg, about 400 mg, about 410 mg, about 420 mg, about 430 mg, about 440 mg, about 450 mg, about 460 mg, about 470 mg, about 480 mg, about 490 mg, about 500 mg, about 510 mg, about 520 mg, about 530 mg, about 540 mg, about 550 mg, about 560 mg, about 570 mg, about 580 mg, about 590 mg, about 600 mg, about 610 mg, about 620 mg, about 630 mg, about 650 mg, about 700 mg, about 750 mg, about 800 mg, about 850 mg, about 900 mg, about 950 mg, or about 1000 mg. Therapeutic agent 1 and therapeutic agent 3 can be administered in any of the suitable dosages of therapeutic agent 1 or therapeutic agent 3 recited above. In some embodiments, ritonavir can be either co-administered or administered separately with therapeutic agent 1. Suitable dosages of ritonavir include, from about 50 mg to about 400 mg per day, preferably about 100 mg per day. In some embodiments, if the treatment regimen of the present technology does not provide the desired SVR after treatments of no more than 12 weeks, the patient may be treated with interferon-containing regimen, a ribavirin-containing regimen, or a combination thereof.

[0076] In some embodiments, the compositions and methods of the present technology can be used to treat patients with genotype 2 or 3, such as genotype 2a, 2b or 3a HCV infection for a treatment duration of no more than 12 weeks, preferably no more than 8 weeks with a combination of therapeutic agent 1 and therapeutic agent 3 without interferon and without ribavirin. The treatment duration can be no more than 12 weeks, including but not limited to, no more than 11 weeks, no more than 10 weeks, no more than 9 weeks, but preferably no more than 8 weeks, no more than 7 weeks, no more than 6 weeks, no more than 5 weeks, no more than 4 weeks, or no more than 3 weeks. Therapeutic agent 1 and therapeutic agent 3 can be administered in therapeutically effective amounts to provide a SVR in a treatment duration of no more than 12 weeks, preferably no more than 8 weeks. In some embodiments, therapeutic agent 1 can be provided in a total daily dosage of an amount from about 5 mg to about 300 mg, alternatively from about 5 mg to about 250 mg,

alternatively from about 25 mg to about 100 mg. The total daily dosage of therapeutic agent 1 can be, but is not limited to, for example, about 5 mg, about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 70 mg, about 80 mg, about 90 mg, about 100 mg, about 110 mg, about 120 mg, about 125 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220 mg, about 230 mg, about 240 mg, about 250 mg, about 260 mg, about 270 mg, or about 300 mg. Therapeutic agent 3 can be administered with therapeutic agent 1 with therapeutic agent 1 being administered at any of the dosages described above. Therapeutic agent 3 can be provided in combination with therapeutic agent 1, wherein therapeutic agent 3 is administered in a total daily dosage of therapeutic agent 3 from about 50 mg to about 1000 mg, preferably from about 50 mg to about 600 mg, alternatively from about 100 mg to about 600 mg. The total daily dosage of therapeutic agent 3 can be, but is not limited to, for example, about 50 mg, about 60 mg, about 70 mg, about 80 mg, about 90 mg, about 100 mg, about 120 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220 mg, about 230 mg, about 240 mg, about 250 mg, about 260 mg, about 270 mg, about 280 mg, about 290 mg, about 300 mg, about 310 mg, about 320 mg, about 330 mg, about 340 mg, about 350 mg, about 360 mg, about 370 mg, about 380 mg, about 390 mg, about 400 mg, about 410 mg, about 420 mg, about 430 mg, about 440 mg, about 450 mg, about 460 mg, about 470 mg, about 480 mg, about 490 mg, about 500 mg, about 510 mg, about 520 mg, about 530 mg, about 540 mg, about 550 mg, about 560 mg, about 570 mg, about 580 mg, about 590 mg, about 600 mg, about 610 mg, about 620 mg, about 630 mg, about 650 mg, about 700 mg, about 750 mg, about 800 mg, about 850 mg, about 900 mg, about 950 mg, or about 1000 mg. Therapeutic agent 1 and therapeutic agent 3 can be administered in any combination of dosage of therapeutic agent 1 or therapeutic agent 3 recited above. In some embodiments, ritonavir can be either co-administered or administered separately with therapeutic agent 1. Suitable dosages of ritonavir include, from about 50 mg to about 400 mg per day, preferably about 100 mg per day. In some embodiments, if the treatment regimen of the present technology does not provide the desired SVR after treatments of no more than 12 weeks, the patient may be treated with interferon-containing regimen, a ribavirin-containing regime, or a combination thereof.

[0077] In some embodiments, the compositions and methods of the present technology can be used to treat patients with HCV infection for a treatment duration of no more than 12 weeks, preferably no more than 8 weeks with a combination of therapeutic agent 1 and therapeutic agent 3 without interferon and without ribavirin. Suitably, the patient may be a treatment naïve patient, a treatment experienced patient or an interferon nonresponder. In some embodiments, the patient is infected with HCV genotype 1, such as genotype 1a. In some embodiments, the patient is infected with HCV genotype 1b. In some other embodiments, the patient is infected with HCV genotype 2 or 3, such as 2a or 2b. In some other embodiments, the patent is infected with HCV genotype 3a. The treatment according to this aspect of the technology can also be effective against other HCV genotypes. The treatment duration can be no more than 12 weeks, including but not limited to, no more than 11 weeks, no more than 10 weeks, no more than 9 weeks, but preferably no more than 8 weeks, no more than 7 weeks, no more than 6 weeks, no more than 5 weeks, no more than 4 weeks, or no more than 3 weeks. In some embodiments, therapeutic agent 1 can be provided in a total daily dosage from about 5 mg to about 300 mg, alternatively from about 5 mg to about 250 mg, alternatively from about 25 mg to about 100 mg. The total daily dosage of therapeutic agent 1 can be, but is not limited to, for example, about 5 mg, about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 70 mg, about 80 mg, about 90 mg, about 100 mg, about 110 mg, about 120 mg, about 125 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220 mg, about 230 mg, about 240 mg, about 250 mg, about 260 mg, about 270 mg, or about 300 mg. Therapeutic agent 3 can be administered in connection with therapeutic agent 1 with therapeutic agent 1 being administered at any of the dosages described above. Therapeutic agent 3 can be provided in combination with therapeutic agent 1, wherein therapeutic agent 3 is administered in a total daily dosage from about 50 mg to about 1000 mg, preferably from about 50 mg to about 600 mg, alternatively from about 100 mg to about 600 mg. The total daily dosage of therapeutic agent 3 can be, but is not limited to, for example, about 50 mg, about 60 mg, about 70 mg, about 80 mg, about 90 mg, about 100 mg, about 120 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220 mg, about 230 mg, about 240 mg, about 250 mg, about 260 mg, about 270

mg, about 280 mg, about 290 mg, about 300 mg, about 310 mg, about 320 mg, about 330 mg, about 340 mg, about 350 mg, about 360 mg, about 370 mg, about 380 mg, about 390 mg, about 400 mg, about 410 mg, about 420 mg, about 430 mg, about 440 mg, about 450 mg, about 460 mg, about 470 mg, about 480 mg, about 490 mg, about 500 mg, about 510 mg, about 520 mg, about 530 mg, about 540 mg, about 550 mg, about 560 mg, about 570 mg, about 580 mg, about 590 mg, about 600 mg, about 610 mg, about 620 mg, about 630 mg, about 650 mg, about 700 mg, about 750 mg, about 800 mg, about 850 mg, about 900 mg, about 950 mg, or about 1000 mg. In some embodiments, ritonavir can be either co-administered or administered separately with therapeutic agent 1. Suitable dosages of ritonavir include, from about 50 mg to about 400 mg per day, preferably about 100 mg per day. In some embodiments, if the treatment regimen of the present technology does not provide the desired SVR after treatments of no more than 12 weeks, the patient may be treated with interferon-containing regimen, a ribavirin-containing regimen, or a combination thereof.

[0078] In some embodiments, the compositions and methods of the present technology can be used to treat patients with HCV infection who are not candidates for interferon treatment for a treatment duration of no more than 12 weeks, preferably no more than 8 weeks with a combination of therapeutic agent 1 and therapeutic agent 3 without interferon and without ribavirin. Patients who are not candidates for interferon treatment include, but is not limited to, one or more of the following groups, patients intolerant to interferon, patients who refuse to take interferon treatment, patients with medical conditions which preclude them from taking interferon, and patients who have an increased risk of side effects or infection by taking interferon. In some embodiments, the patient is infected with HCV genotype 1, such as genotype 1a. In some embodiments, the patient is infected with HCV genotype 1b. In some other embodiments, the patient is infected with HCV genotype 2 or 3, such as 2a or 2b. In some other embodiments, the patent is infected with HCV genotype 3a. The treatment according to this aspect of the technology can also be effective against other HCV genotypes. The treatment duration can be no more than 12 weeks, including but not limited to, no more than t 11 weeks, no more than 10 weeks, no more than 9 weeks, but preferably no more than 8 weeks, no more than 7 weeks, no more than 6 weeks, no more than 5 weeks, no more than 4 weeks, or no more than 3 weeks. In some embodiments, therapeutic agent 1 can be

provided in a total daily dosage of an amount from about 5 mg to about 300 mg, alternatively from about 5 mg to about 250 mg, alternatively from about 25 mg to about 100 mg. The total daily dosage of therapeutic agent 1 can be, but is not limited to, for example, about 5 mg, about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 70 mg, about 80 mg, about 90 mg, about 100 mg, about 110 mg, about 120 mg, about 125 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220 mg, about 230 mg, about 240 mg, about 250 mg, about 260 mg, about 270 mg, or about 300 mg. Therapeutic agent 3 can be administered with therapeutic agent 1 with therapeutic agent 1 being administered at any of the dosages described above. Therapeutic agent 3 can be provided in combination with therapeutic agent 1, wherein therapeutic agent 3 is administered in a total daily dosage of therapeutic agent 3 from about 50 mg to about 1000 mg, preferably from about 50 mg to about 600 mg, alternatively from about 100 mg to about 600 mg. The total daily dosage of therapeutic agent 3 can be, but is not limited to, for example, about 50 mg, about 60 mg, about 70 mg, about 80 mg, about 90 mg, about 100 mg, about 120 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220 mg, about 230 mg, about 240 mg, about 250 mg, about 260 mg, about 270 mg, about 280 mg, about 290 mg, about 300 mg, about 310 mg, about 320 mg, about 330 mg, about 340 mg, about 350 mg, about 360 mg, about 370 mg, about 380 mg, about 390 mg, about 400 mg, about 410 mg, about 420 mg, about 430 mg, about 440 mg, about 450 mg, about 460 mg, about 470 mg, about 480 mg, about 490 mg, about 500 mg, about 510 mg, about 520 mg, about 530 mg, about 540 mg, about 550 mg, about 560 mg, about 570 mg, about 580 mg, about 590 mg, about 600 mg, about 610 mg, about 620 mg, about 630 mg, about 650 mg, about 700 mg, about 750 mg, about 800 mg, about 850 mg, about 900 mg, about 950 mg, or about 1000 mg. In some embodiments, ritonavir can be either co-administered or administered separately with therapeutic agent 1. Suitable dosages of ritonavir include, from about 50 mg to about 400 mg per day, preferably about 100 mg per day.

[0079] In some embodiments, the compositions and methods of the present technology can be used to treat patients with HCV genotype 1b for a treatment duration of no more than 12 weeks, preferably in no more than 8 weeks. Patients with genotype 1b infection can be

treated with a combination of at least 2 DAAs without interferon and without ribavirin in which the at least two DAAs include therapeutic agent 1 and therapeutic agent 4. Therapeutic agent 1 and therapeutic agent 4 can be administered in therapeutically effective amounts to provide a SVR in a treatment duration of no more than 12 weeks, preferably no more than 8 weeks. The patients may be treatment naïve patients or treatment experienced patients. The treatment duration can be no more than 12 weeks, including but not limited to, no more than t 11 weeks, no more than 10 weeks, no more than 9 weeks, but preferably no more than 8 weeks, no more than 7 weeks, no more than 6 weeks, no more than 5 weeks, no more than 4 weeks, or no more than 3 weeks. Therapeutic agent 1 can be provided in a total daily dosage from about 5 mg to about 300 mg, alternatively from about 5 mg to about 250 mg, alternatively from about 25 mg to about 100 mg. The total daily dosage of therapeutic agent 1 can be, but is not limited to, for example, about 5 mg, about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 70 mg, about 80 mg, about 90 mg, about 100 mg, about 110 mg, about 120 mg, about 125 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220 mg, about 230 mg, about 240 mg, about 250 mg, about 260 mg, about 270 mg, or about 300 mg. Therapeutic agent 4 can be administered in connection with therapeutic agent 1 where therapeutic agent 1 is administered in any of the dosages described above. Therapeutic agent 4 can be provided in combination with therapeutic agent 1 in a total daily dose of therapeutic agent 4 of from about 5 mg to about 350 mg, preferably about 5 mg to about 350 mg, more preferably about 25 mg to about 200 mg. The total daily dosage of therapeutic agent 4 can be, but is not limited to, for example, about 5 mg, about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 70 mg, about 75 mg, about 80 mg, about 90 mg, about 100 mg, about 110 mg, about 120 mg, about 120 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220 mg, about 230 mg, about 240 mg, about 250 mg, about 260 mg, about 270 mg, about 280 mg, about 290 mg, about 300 mg, about 310 mg, about 320 mg, about 330 mg, about 340 mg, or about 350 mg. In some embodiments, ritonavir can be either co-administered or administered separately with therapeutic agent 1. Suitable dosages of ritonavir include, from about 50 mg to about 400 mg per day, preferably

about 100 mg per day. In suitable embodiments, therapeutic agent 1 and therapeutic agent 4 are administered once a day.

[0080] In some embodiments, the compositions and methods of the present technology can be used to treat patients with HCV infection with a treatment duration of less than 12 weeks, preferably no more than 8 weeks with a combination of at least 2 DAAs without interferon and without ribavirin in which the at least two DAAs include therapeutic agent 1 and therapeutic agent 4. The patients may be treatment naïve patients or treatment experienced patients. The treatment can be administered for a duration of no more than 12 weeks, including but not limited to, no more than 11 weeks, no more than 10 weeks, no more than 9 weeks, but preferably no more than 8 weeks, no more than 7 weeks, no more than 6 weeks, no more than 5 weeks, no more than 4 weeks, or no more than 3 weeks. The patient can have HCV genotype 1, such as HCV genotype 1b. In other embodiments, the patient may have HCV genotype 1b. In some embodiments, it is contemplated to treat other HCV genotypes. Therapeutic agent 1 can be provided in a total daily dosage from about 5 mg to about 300 mg, alternatively from about 5 mg to about 250 mg, alternatively from about 25 mg to about 100 mg. The total daily dosage of therapeutic agent 1 can be, but is not limited to, for example, about 5 mg, about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 70 mg, about 80 mg, about 90 mg, about 100 mg, about 110 mg, about 120 mg, about 125 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220 mg, about 230 mg, about 240 mg, about 250 mg, about 260 mg, about 270 mg, or about 300 mg. Therapeutic agent 4 can be administered in connection with therapeutic agent 1 in any of the dosages described above. Therapeutic agent 4 can be provided alone or in combination with therapeutic agent 1 in a total daily dose of therapeutic agent 4 of an amount from about 5 mg to about 350 mg, preferably about 5 mg to about 300 mg, more preferably about 25 mg to about 200 mg. The total daily dosage of therapeutic agent 4 can be, but is not limited to, for example, about 5 mg, about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 70 mg, about 75 mg, about 80 mg, about 90 mg, about 100 mg, about 110 mg, about 120 mg, about 120 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220 mg, about 230 mg,

about 240 mg, about 250 mg, about 260 mg, about 270 mg, about 280 mg, about 290 mg, about 300 mg, about 310 mg, about 320 mg, about 330 mg, about 340 mg, or about 350 mg. In some embodiments, ritonavir can be either co-administered or administered separately with therapeutic agent 1. Suitable dosages of ritonavir include, from about 50 mg to about 400 mg per day, preferably about 100 mg per day. In suitable embodiments, therapeutic agent 1 and therapeutic agent 4 are administered once a day.

[0081] In some embodiments, the compositions and methods of the present technology can be used to treat patients with HCV infection for a treatment duration of no more than 12 weeks, preferably no more than 8 weeks with a combination of at least 2 DAAs without interferon and without ribavirin, where the at least two DAAs include therapeutic agent 1 and therapeutic agent 4. The patients may be treatment naïve patients or treatment experienced patients. The treatment can be administered for a duration of no more than 12 weeks, including but not limited to, no more than 11 weeks, no more than 10 weeks, no more than 9 weeks, but preferably no more than 8 weeks, no more than 7 weeks, no more than 6 weeks, no more than 5 weeks, no more than 4 weeks, or no more than 3 weeks. The patient can have HCV genotype 2 or 3, such as HCV genotype 2a. In some embodiments, the patient may have HCV genotype 2b. In other embodiments the patient may have HCV genotype 3a. Therapeutic agent 1 can be provided in a total daily dosage of an amount from about 5 mg to about 300 mg, alternatively from about 5 mg to about 250 mg, alternatively from about 25 mg to about 100 mg. The total daily dosage of therapeutic agent 1 can be, but is not limited to, for example, about 5 mg, about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 70 mg, about 80 mg, about 90 mg, about 100 mg, about 110 mg, about 120 mg, about 125 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220 mg, about 230 mg, about 240 mg, about 250 mg, about 260 mg, about 270 mg, or about 300 mg. Therapeutic agent 4 can be administered in connection with therapeutic agent 1 in which therapeutic agent 1 is administered in any of the dosages described above. Therapeutic agent 4 can be provided in combination with therapeutic agent 1 in a total daily dose of therapeutic agent 4 of from about 5 mg to about 350 mg, preferably about 5 mg to about 300 mg, more preferably about 25 mg to about 200 mg. The total daily dosage of therapeutic agent 4 can be, but is not limited to, for example, about 5 mg, about 10

mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 70 mg, about 75 mg, about 80 mg, about 90 mg, about 100 mg, about 110 mg, about 120 mg, about 120 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220 mg, about 230 mg, about 240 mg, about 250 mg, about 260 mg, about 270 mg, about 280 mg, about 290 mg, about 300 mg, about 310 mg, about 320 mg, about 330 mg, about 340 mg, or about 350 mg. In some embodiments, ritonavir can be either co-administered or administered separately with therapeutic agent 1. Suitable dosages of ritonavir include, from about 50 mg to about 400 mg per day, preferably about 100 mg per day. In suitable embodiments, therapeutic agent 1 and therapeutic agent 4 are administered once a day. In some embodiments, if the treatment regimen of the present technology does not provide the desired SVR after treatments of no more than 12 weeks, the patient may be treated with interferon-containing regimen, a ribavirin-containing regimen, or a combination thereof.

[0082] In some embodiments, the compositions and methods of the present technology can be used to treat patients with HCV infection who are not candidates for interferon treatment with a treatment duration of no more than 12 weeks, preferably no more than 8 weeks with a combination of therapeutic agent 1 and therapeutic agent 3 without interferon and without ribavirin. Patients who are not candidates for interferon treatment include, but is not limited to, one or more of the following groups, patients intolerant to interferon, patients who refuse to take interferon treatment, patients with medical conditions which preclude them from taking interferon, and patients who have an increased risk of side effects or infection by taking interferon. In some embodiments, the patient is infected with HCV genotype 1, such as genotype 1a. In some embodiments, the patient is infected with HCV genotype 1b. In some other embodiments, the patient is infected with HCV genotype 2 or 3, such as 2a or 2b. In some other embodiments, the patent is infected with HCV genotype 3a. The treatment according to this aspect of the technology can also be effective against other HCV genotypes. Therapeutic agent 1 and therapeutic agent 4 can be administered in therapeutically effective amounts to provide a SVR after treatment of no more than 12 weeks, preferably no more than 8 weeks. The interferon non-responder patients include partial interferon responders and interferon rebound patients. The treatment can be administered for a duration of no more than 12 weeks, including but not limited to, no more than 11 weeks, no more than 10 weeks,

no more than 9 weeks, but preferably no more than 8 weeks, no more than 7 weeks, no more than 6 weeks, no more than 5 weeks, no more than 4 weeks, or no more than 3 weeks. Therapeutic agent 1 can be provided in a total daily dosage of an amount from about 5 mg to about 300 mg, alternatively from about 5 mg to about 250 mg, alternatively from about 25 mg to about 100 mg. The total daily dosage of therapeutic agent 1 can be, but is not limited to, for example, about 5 mg, about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 70 mg, about 80 mg, about 90 mg, about 100 mg, about 110 mg, about 120 mg, about 125 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220 mg, about 230 mg, about 240 mg, about 250 mg, about 260 mg, about 270 mg, or about 300 mg. Therapeutic agent 4 can be administered with therapeutic agent 1 where therapeutic agent 1 is administered in any of the dosages described above. Therapeutic agent 4 can be provided in combination with therapeutic agent 1 in a total daily dose of therapeutic agent 4 of from about 5 mg to about 350 mg, preferably from about 5 mg to about 350 mg, more preferably from about 25 mg to about 200 mg. The total daily dosage of therapeutic agent 4 can be, but is not limited to, for example, about 5 mg, about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 70 mg, about 75 mg, about 80 mg, about 90 mg, about 100 mg, about 110 mg, about 120 mg, about 120 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220 mg, about 230 mg, about 240 mg, about 250 mg, about 260 mg, about 270 mg, about 280 mg, about 290 mg, about 300 mg, about 310 mg, about 320 mg, about 330 mg, about 340 mg, or about 350 mg. In some embodiments, ritonavir can be either co-administered or administered separately with therapeutic agent 1. Suitable dosages of ritonavir include, from about 50 mg to about 400 mg per day, preferably about 100 mg per day. In suitable embodiments, therapeutic agent 1 and therapeutic agent 4 are administered once a day. In some embodiments, if the treatment regimen of the present technology does not provide the desired SVR after treatments of no more than 12 weeks, the patient may be treated with a ribavirin-containing regimen.

[0083] In some embodiments, the compositions and methods of the present technology can be used to treat interferon non-responder patients with HCV infection with a treatment

duration of no more than 12 weeks, preferably in no more than 8 weeks. Interferon nonresponder patients can be treated with a combination of at least 2 DAAs without interferon and without ribavirin wherein the two DAAs include therapeutic agent 1 and therapeutic agent 4. Therapeutic agent 1 and therapeutic agent 4 can be administered in therapeutically effective amounts to provide a SVR after treatment duration of no more than 12 weeks, preferably no more than 8 weeks. The interferon non-responder patients include partial interferon responders and interferon rebound patients. The interferon nonresponder patient may have HCV genotype 1, such as 1a. The interferon nonresponder patient may have HCV genotype 1b. The interferon nonresponder patient can have HCV genotype 2 or 3, such as HCV genotype 2a. In some embodiments, the patient may have HCV genotype 2b. In other embodiments the patient may have HCV genotype 3a. In some embodiments, it is contemplated to treat other HCV genotypes. The treatment can be administered for a duration of no more than 12 weeks, including but not limited to, no more than 11 weeks, no more than 10 weeks, no more than 9 weeks, but preferably no more than 8 weeks, no more than 7 weeks, no more than 6 weeks, no more than 5 weeks, no more than 4 weeks, or no more than 3 weeks. Therapeutic agent 1 can be provided in a total daily dosage of an amount from about 5 mg to about 300 mg, alternatively from about 5 mg to about 250 mg, alternatively from about 25 mg to about 100 mg. The total daily dosage of therapeutic agent 1 can be, but is not limited to, for example, about 5 mg, about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 70 mg, about 80 mg, about 90 mg, about 100 mg, about 110 mg, about 120 mg, about 125 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220 mg, about 230 mg, about 240 mg, about 250 mg, about 260 mg, about 270 mg, or about 300 mg. Therapeutic agent 4 can be administered with therapeutic agent 1 wherein therapeutic agent 1 is administered in any of the dosages described above. Therapeutic agent 4 can be provided in combination with therapeutic agent 1 in a total daily dose of therapeutic agent 4 of from about 5 mg to about 350 mg, preferably from about 5 mg to about 350 mg, more preferably from about 25 mg to about 200 mg. The total daily dosage of therapeutic agent 4 can be, but is not limited to, for example, about 5 mg, about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 70 mg, about 75 mg, about 80 mg, about 90 mg, about 100 mg,

about 110 mg, about 120 mg, about 120 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220 mg, about 230 mg, about 240 mg, about 250 mg, about 260 mg, about 270 mg, about 280 mg, about 290 mg, about 300 mg, about 310 mg, about 320 mg, about 330 mg, about 340 mg, or about 350 mg. In some embodiments, ritonavir can be either co-administered or administered separately with therapeutic agent 1. Suitable dosages of ritonavir include, from about 50 mg to about 400 mg per day, preferably about 100 mg per day. In suitable embodiments, therapeutic agent 1 and therapeutic agent 4 are administered once a day. Therapeutic agent 1 and therapeutic agent 4 can be administered in any combination of suitable dosages as described above. In some embodiments, if the treatment regimen of the present technology does not provide the desired SVR after treatments of no more than about 12 weeks, the patient may be treated with ribavirin-containing regimen.

[0084] Accordingly, in some embodiments, the present technology features a method of treating HCV infection, comprising administering to a patient in need thereof an effective amount of a combination of two or more DAAs without ribavirin.. The treatment lasts no more than 12 weeks, alternatively no more than 11 weeks, alternatively no more than 10 weeks, alternatively no more than 9 weeks, preferably no more than 8 weeks, alternatively no more than 7 weeks, alternatively no more than 6 weeks, alternatively no more than 5 weeks, alternatively no more than 4 weeks, alternatively no more than 3 weeks and does not include administration of any interferon or ribavirin. The DAAs can be administered at the same or different dosing frequencies. The patient being treated can be an HCV-treatment naïve patient or HCV-treatment experienced patient, including, interferon non-responders, interferon partial responders (patients whose HCV RNA levels declined but never became undetectable when treated with interferon), or relapsers (patients who achieved undetectable levels of HCV RNA during therapy but rebound) or a patient unable to take interferon. The patient can be infected with, for example and without limitation, HCV genotypes 1 or 2. In some embodiments are preferably genotypes 1a or 1b. In other embodiments, the HCV genotype is 2 or 3. Each DAA can be selected from HCV protease inhibitors, HCV polymerase inhibitors, or HCV NS5A inhibitors.

[0085] For instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor and at least one HCV polymerase inhibitor (e.g., a combination

of at least one HCV protease inhibitor and at least one non-nucleoside polymerase inhibitor, or a combination of at least one HCV protease inhibitor and at least one nucleoside polymerase inhibitor, or a combination of at least one HCV protease inhibitor, at least one nucleoside polymerase inhibitor and at least one non-nucleoside inhibitor).

[0086] For another instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor and at least one HCV NS5A inhibitor. In an example, the combination of two or more DAAs comprises GS-5885 (an NS5A inhibitor), and GS-9451 (a protease inhibitor, specifically a NS3 protease inhibitor). In some examples, GS-5885 is provided in a daily dose from about 3 mg to about 200 mg, alternatively from about 3 mg to about 100 mg, alternatively from about 30 mg to about 90 mg, including, but not limited to, for example, about 3 mg, about 5 mg, about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 70 mg, about 80 mg, about 90 mg, about 100 mg, about 110 mg, about 120 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, or about 200mg. GS-9451 can be administered in combination with any of the daily dosages of GS-5885 described above. GS-9451 can be administered in a total daily dose from about 100 mg to about 500 mg, alternatively from about 200 mg to about 400 mg, including, but not limited to, for example, about 100 mg, about 150 mg, about 200 mg, about 250 mg, about 300 mg, about 400 mg, or about 500 mg. Suitably examples include total daily dosages of about 30 mg GS-5885 and about 200 mg GS-9451; alternatively about 60 mg GS-5885 and about 200 mg GS-9451; alternatively about 90 mg GS-5885 and about 200 mg GS-9451.

[0087] In another instance, the present technology provides the at least two DAAs comprise at least two HCV polymerase inhibitors. In some embodiments, the at least two HCV polymerase inhibitors comprise at least one nucleoside or nucleotide analog polymerase inhibitor. In some embodiments, the at least two HCV polymerase inhibitors comprise at least two nucleoside or nucleotide analog polymerase inhibitors. A suitable nucleoside analog polymerase inhibitor includes PSI-7977 (Pharmasset) and a suitable nucleotide analog polymerase inhibitor includes PSI-938 (Pharmasset). Suitable daily dosages of the at least one nucleoside or nucleotide analog polymerase inhibitor include from about 100mg to about 500 mg, alternatively from about 200 mg to about 400 mg, including, but not limited to, for example, about 100 mg, about 150 mg, about 200mg, about 250 mg, about 300 mg, about

350 mg, about 400 mg, about 450 mg, or about 500 mg. For example, a suitable combination includes a total daily dose of PSI-7977 of about 400 mg and a total daily of PSI-938 of about 300 mg, alternatively a total daily dose of about 200 mg PSI-7977 and a total daily dose of about 300 mg PSI-938. In yet another instance, the combination of two or more DAAs comprises at least one HCV protease inhibitor and at least one HCV polymerase inhibitor. In some embodiments, the at least one protease inhibitor is TMC-435 (Medivir) and the at least one polymerase inhibitor is a nucleotide/nucleoside analog polymerase inhibitor, for example PSI-7977. Suitably, the at least one protease inhibitor, e.g. TMC-435, is provided in a total daily dosage from about 25 mg to about 250 mg, alternatively from about 25 mg to about 200 mg, alternatively from about 50 mg to about 200 mg, alternatively from about 75 mg to about 150 mg, for example, about 25 mg, about 50 mg, about 75 mg, about 100 mg, about 125 mg, about 150mg, about 175 mg, or about 200 mg; and the at least one polymerase inhibitor (e.g. PSI-7977) is provided in a total daily dose from about 100mg to about 500 mg, alternatively rom about 200 mg to about 400 mg, including, but not limited to, for example, about 100 mg, about 150 mg, about 200mg, about 250 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, or about 500 mg. For example, a combination can be a total daily dosage of about 75 mg TMC-435 and about 400 mg PSI-7977, alternatively about 100 mg TMC-435 and about 400 mg PSI-7977, alternatively about 150 mg TMC-435 and about 400 mg PSI-7977, alternatively about 100 mg TMC-435 and about 400 mg PSI-7977, alternatively about 75 mg TMC-435 and about 200 mg PSI-7977, alternatively about 150 mg TMC-435 and about 200 mg PSI-7977, alternatively about 100 mg TMC-435 and about 200 mg PSI-7977, alternatively about 75 mg TMC-435 and about 100 mg PSI-7977, alternatively about 100 mg TMC-435 and about 100 mg PSI-7977, alternatively about 150 mg TMC-435 and about 100 mg PSI-7977, and can include other suitable combinations. Suitably, in some embodiments, ritonavir or a suitably equivalent can be added to the at least two DAAs comprising at least one protease inhibitor, suitably in an amount from about 100mg to about 400 mg per day, preferably about 100 mg per day. In alternative embodiments, the at least one protease is BI-201335 (NS3/4A protease inhibitor) and the at least one HCV polymerase inhibitor is a non-nucleoside polymerase inhibitor, e.g. BI-207127. In some examples, the BI-201335 is provided in a total daily dose from about 100 mg to about 400 mg, alternatively from about 120 mg to about 240 mg, including about 100 mg, about 120 mg, about 125 mg, about 130

mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220 mg, about 230 mg, about 240 mg, about 250 mg, about 275 mg, about 300 mg, about 320 mg, about 330 mg, about 350 mg, about 360 mg, about 370 mg, about 380 mg, or about 400 mg; and BI-207127 can be administered in a total daily dose from about 300 mg to about 3600 mg, preferably from about 1200 mg to about 2100 mg, including, but not limited to, for example, about 300 mg, about 400 mg, about 500 mg, about 600 mg, about 700 mg, about 750 mg, about 800 mg, about 900 mg, about 1000 mg, about 1100, about 1200 mg, about 1300 mg, about 1400 mg, about 1500 mg, about 1600 mg, about 1700 mg, about 1800 mg, about 1900 mg, about 2000 mg, about 2100 mg, about 2200 mg, about 2400 mg, about 2500 mg, about 2600 mg, about 2700 mg, about 2800 mg, about 3000 mg, about 3200 mg, about 3400 mg, or about 3600 mg. Suitable examples, include, but are not limited to, a combination of a total daily dose of about 120 mg BI-201335 and about 1200 mg BI-207127, alternatively about 120 mg BI-201335 and about 1500 mg BI-207127, alternatively about 120 mg BI-201335 and about 1800 mg BI-207127, alternatively about 120 mg BI-201335 and about 2100 mg BI-207127, alternatively about 240 mg BI-201335 and about 1200 mg BI-207127, alternatively about 240 mg BI-201335 and about 1500 mg BI-207127, alternatively about 240 mg BI-201335 and about 1800 mg BI-207127, alternatively about 240 mg BI-201335 and about 2100 mg BI-207127. Suitably, in some embodiments, ritonavir or a suitably equivalent can be added to the at least two DAAs comprising at least one protease inhibitor, suitably in an amount of about 100mg per day. Suitably, in some embodiments, ritonavir or a suitably equivalent can be added to the at least two DAAs comprising at least one protease inhibitor, suitably in an amount from about 100 mg to about 400 mg per day, preferably about 100 mg per day. In yet another example, the combination of two or more DAAs comprises telaprevir (VX-950, protease inhibitor) and VX-222 (non-nucleoside polymerase inhibitor). In some examples, the telaprevir is provided in total daily doses from about 1000 mg to about 2500 mg, alternatively from about 2000 mg to about 2500 mg, including, but not limited to, for example, about 1000 mg, about 1200 mg, about 1300 mg, about 1500 mg, about 1700 mg, about 1800 mg, about 1900 mg, about 2000 mg, about 2100 mg, about 2200 mg, about 2250 mg, about 2300 mg, about 2400 mg, about 2500 mg. VX-222 can be administered with telaprevir in any combination with the dosage amounts of telaprevir provided above. VX-222 can be provided in a total daily dosage from

about 100 mg to about 1000 mg, alternatively from about 200 mg to about 800 mg, including, but not limited to, for example, about 100 mg, about 200 mg, about 300 mg, about 400 mg, about 500 mg, about 600 mg, about 700 mg, about 800 mg, about 900 mg, or about 1000 mg. In some examples, telaprevir can be a total daily dose of about 2250 mg and VX-222 can be a total daily dose of about 100 mg, alternatively telaprevir can be a total daily dose of about 2250 mg and VX-222 can be a total daily dose of about 200 mg, alternatively telaprevir can be a total daily dose of about 2250 mg and VX-222 can be a total daily dose of about 400 mg, alternatively telaprevir can be a total daily dose of about 2250 mg and VX-222 can be a total daily dose of about 600 mg, alternatively telaprevir can be a total daily dose of about 2250 mg and VX-222 can be a total daily dose of about 800 mg, alternatively telaprevir can be a total daily dose of about 1500 mg and VX-222 can be a total daily dose of about 200 mg, alternatively telaprevir can be a total daily dose of about 1500 mg and VX-222 can be a total daily dose of about 400 mg, alternatively telaprevir can be a total daily dose of about 1500 mg and VX-222 can be a total daily dose of about 800 mg. Suitably, telaprevir can be administered three times a day (TID), for example 3 times a day with 750 mg per dose. Other suitable daily dosage of telaprevir is 1125 mg twice a day (BID). Suitably, in some embodiments, ritonavir or a suitably equivalent can be added to the at least two DAAs comprising at least one protease inhibitor, suitably in an amount of about 100mg to about 400 mg per day, preferably about 100 mg per day.

[0088] In yet another example, the combination of two or more DAAs includes danoprevir (protease inhibitor) and R7128 (nucleoside polymerase inhibitor). In some embodiments, danoprevir can be administered in a total daily dosage from about 100 mg to about 2000 mg, alternatively from about 200 mg to about 1800 mg, alternatively from about 400 mg to about 1800 mg, including, but not limited to, for example, about 100 mg, about 200 mg, about 300 mg, about 400 mg, about 500 mg, about 600 mg, about 700 mg, about 800 mg, about 900 mg, about 1000 mg, about 1100 mg, about 1200 mg, about 1300 mg, about 1400 mg, about 1500 mg, about 1600 mg, about 1700 mg, about 1800 mg, and other amounts therebetween. R7128 can be administered in a total daily dose from about 100 mg to about 2000 mg, alternatively from about 200 mg to about 2000 mg, alternatively from about 1000 mg to about 2000 mg, including, but not limited to, for example, about 150 mg, about 200 mg, about 400 mg, about 500 mg, about 600 mg, about 700 mg, about 800 mg, about 900 mg,

about 1000 mg, about 1200 mg, about 1300 mg, about 1400 mg, about 1500 mg, about 1600 mg, about 1700 mg, about 1800 mg, about 1900 mg, or about 2000 mg. In some examples, the total daily doses of the danoprevir is about 200 mg and the total daily dose of R7128 at about 200 mg, alternatively the total daily doses of the danoprevir is about 400mg and the total daily dose of R7128 at about 200 mg, alternatively, the total daily doses of the danoprevir is about 1000 mg and the total daily dose of R7128 at about 200 mg, alternatively the total daily doses of the danoprevir is about 1800 mg and the total daily dose of R7128 at about 200 mg, alternatively the total daily doses of the danoprevir is about 2000 mg and the total daily dose of R7128 at about 200 mg, alternatively the total daily doses of the danoprevir is about 400mg and the total daily dose of R7128 at about 400 mg, alternatively, the total daily doses of the danoprevir is about 1000 mg and the total daily dose of R7128 at about 400 mg, alternatively the total daily doses of the danoprevir is about 2000 mg and the total daily dose of R7128 at about 400 mg, alternatively the total daily doses of the danoprevir is about 1800 mg and the total daily dose of R7128 at about 400 mg, alternatively the total daily doses of the danoprevir is about 400mg and the total daily dose of R7128 at about 1000 mg, alternatively, the total daily doses of the danoprevir is about 1000 mg and the total daily dose of R7128 at about 1000 mg, alternatively the total daily doses of the danoprevir is about 2000 mg and the total daily dose of R7128 at about 1000 mg, alternatively the total daily doses of the danoprevir is about 1800 mg and the total daily dose of R7128 at about 1000 mg, alternatively the total daily doses of the danoprevir is about 400mg and the total daily dose of R7128 at about 2000 mg, alternatively, the total daily doses of the danoprevir is about 1000 mg and the total daily dose of R7128 at about 2000 mg, alternatively the total daily doses of the danoprevir is about 2000 mg and the total daily dose of R7128 at about 2000 mg, alternatively the total daily doses of the danoprevir is about 1800 mg and the total daily dose of R7128 at about 2000 mg. In suitable embodiments, danoprevir and R7128 can be administered with ritonavir, suitably in an amount of about 100mg to about 400 mg per day, preferably about 100 mg per day.

[0089] In some other instances of the present technology, the combinations of two or more DAAs may be at least one protease inhibitor and at least one NS5A inhibitor. In some examples, the at least one protease inhibitor is an NS3 protease inhibitor. In some embodiments, the at least one proteases inhibitor and at least one NS5A inhibitor comprises

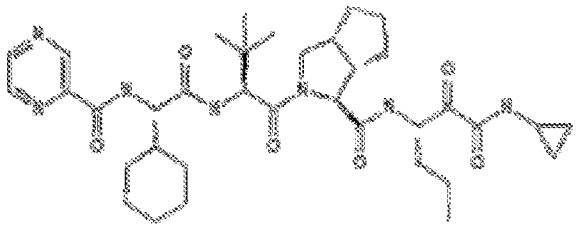
BMS-650032 (BMS) and BMS-790052 (BMS) respectively. In suitable embodiments, BMS-650032 can be administered in a total daily dose from about 300 mg to about 1500 mg, alternatively from about 500 mg to about 1500 mg, including, but not limited to, for example, about 300 mg, about 400 mg, about 500 mg, about 600 mg, about 700 mg, about 800 mg, about 900 mg, about 1000 mg, about 1100 mg, about 1200 mg, about 1300 mg, about 1400 mg, and about 1500 mg, and BMS-790052 (BMS) can have a total daily dose from about 10 mg to about 200 mg, alternatively from about 50 mg to about 100mg, including, but not limited to, for example, about 10 mg, about 20 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 75 mg, about 100 mg, about 125 mg, about 150 mg, or about 200 mg. In suitable examples, BMS-650032 (BMS) total daily dose is about 1200 mg and BMS-790052 (BMS) total daily dose is about 60 mg, alternatively BMS-650032 (BMS) total daily dose is about 300 mg and BMS-790052 (BMS) total daily dose is about 60 mg.

[0090] For still another instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor, at least one HCV polymerase inhibitor, and at least one HCV NS5A inhibitor. In an example, the combination of two or more DAAs comprises GS-5885 (an NS5A inhibitor), GS-9190 (tegobuvir, a non-nucleoside polymerase inhibitor), and GS-9451 (a protease inhibitor, specifically a NS3 protease inhibitor). In some examples, GS-5885 is provided in a daily dose from about 3 mg to about 200 mg, alternatively from about 3 mg to about 100 mg, alternatively from about 30 mg to about 90 mg, including, but not limited to, for example, about 3 mg, about 5 mg, about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 70 mg, about 80 mg, about 90 mg, about 100 mg, about 110 mg, about 120 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 170 mg, about 180 mg, about 190 mg, or about 200mg, and GS-9190 is provided in a daily dose from about 10 mg to about 100 mg, alternatively from about 30 mg to about 90 mg, including, but not limited to, for example, about 10 mg, about 20 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 70 mg, about 80 mg, about 90 mg, or about 100 mg; and GS-9451 can be administered in a daily dose from about 100 mg to about 500 mg, alternatively from about 200 mg to about 400 mg, including, but not limited to, about 100 mg, about 150 mg, about 200 mg, about 250 mg, about 300 mg, about 400 mg, or about 500 mg. Suitably examples include about daily amounts of about 30 mg GS-5885, about 60 mg GS-9190 and about 200 mg GS-9451;

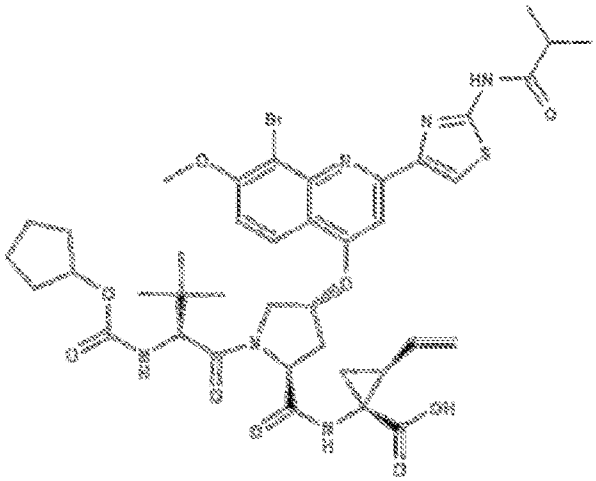
alternatively about 60 mg GS-5885, about 60 mg GS-9190, and about 200 mg GS-9451; alternatively about 90 mg GS-5885, about 60 mg GS-9190, and about 200 mg GS-9451. In some embodiments the GS-9190, GS-9451, and GS-5885 is administered with ritonavir or a suitably equivalent, suitably in an amount of about 100mg to about 400 mg per day, preferably about 100 mg per day. For still another instance, the combination of two or more DAAs can be a combination of at least one HCV protease inhibitor, at least one HCV polymerase inhibitor, and at least one HCV NS5A inhibitor.

[0091] In another embodiment, the present technology provides interferon-free treatment comprising administering daily two DAAs without ribavirin, where the two DAAs include a HCV polymerase inhibitor, for example PSI-7977 and a NS5a inhibitor, for example BMS-790052 for a duration of no more than eleven weeks, preferably no more than eight weeks. PSI-7977 and BMS-790052 are administered in an effective amount to provide an SVR with a treatment duration of no more than eleven weeks, no more than ten weeks, no more than nine weeks, no more than eight weeks, no more than seven weeks, no more than six weeks, no more than five weeks, no more than four weeks or no more than three weeks. The patients can be treatment naïve patients or treatment experienced patients. In some embodiments, the patients can have HCV genotype 1, such as 1a or 1b. In some embodiments, the patients can have genotype 2 or 3, such as 2a, 2b or 3a. PSI-7977 can be provided in a total daily dose of from about 100 mg to about 500 mg, alternatively from about 200 mg to about 400 mg, including, but not limited to, for example, about 100 mg, about 150 mg, about 200mg, about 250 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg. BMS-790052 can be administered in combination with PSI-7977 at any daily dose of PSI-7977 provided above. BMS-790052 (BMS) can have a total daily dose of from about 10 mg to about 200 mg, alternatively from about 50 mg to about 100mg, including, but not limited to, about 10 mg, about 20 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 75 mg, about 100 mg, about 125 mg, about 150 mg, or about 200 mg. In one suitable example, PSI-7977 is administered in a total daily dose of 400 mg and BMS-790052 is administered in a total daily dose of 60 mg.

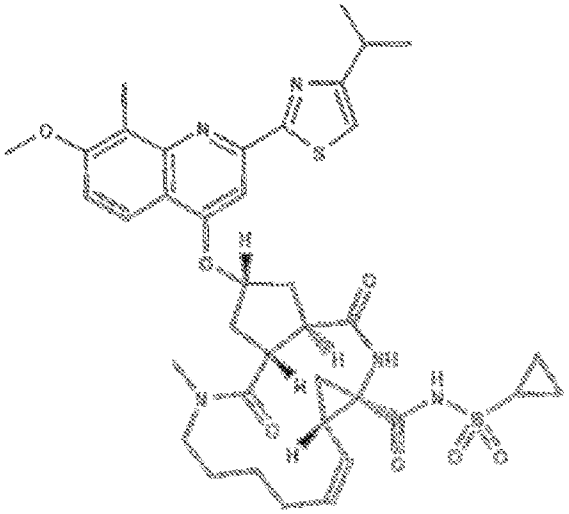
[0092] The chemical structures of some of these HCV inhibitors are provided below:



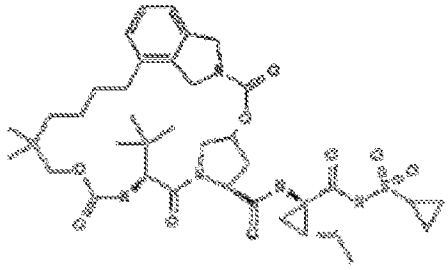
Telaprevir



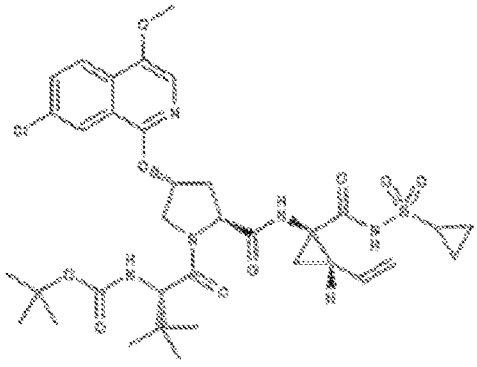
BI-201335



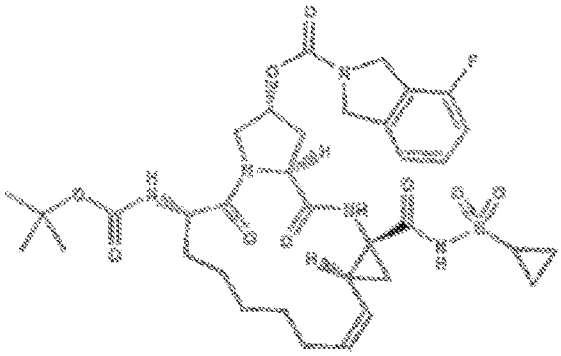
TMC-435 (TMC-435350)



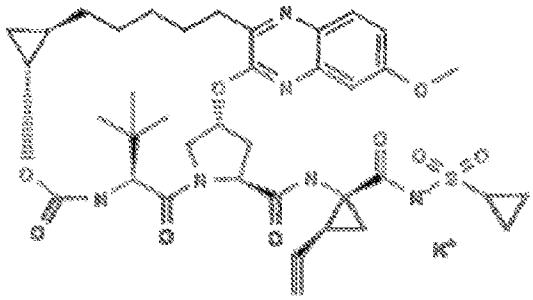
Vaniprevir, MK-7009



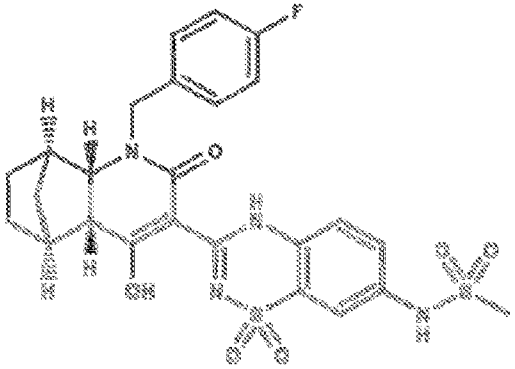
BMS-650032 (Asunaprevir)



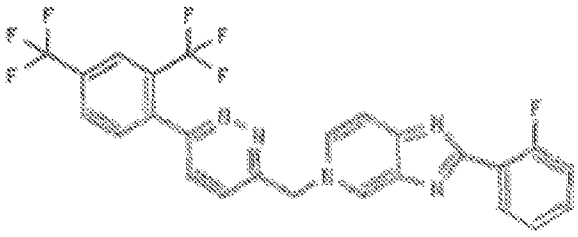
danoprevir



MK-5172

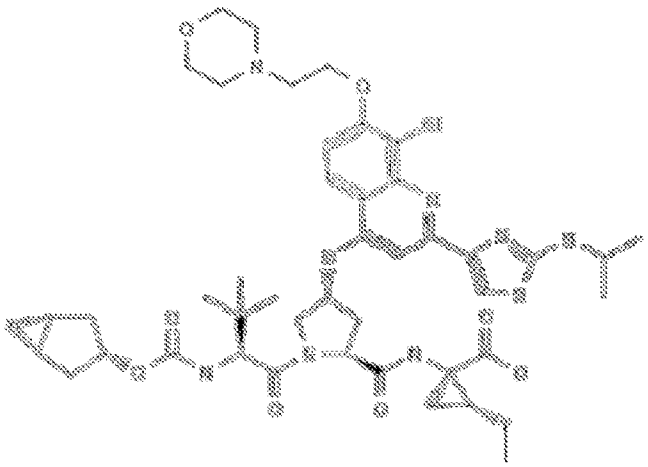


ANA-598 (Setrobuvir)



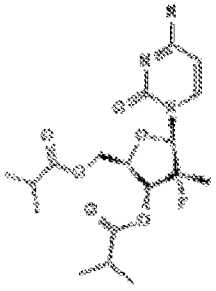
Tegobuvir

GS-333126 (GS-9190 or tegobuvir)

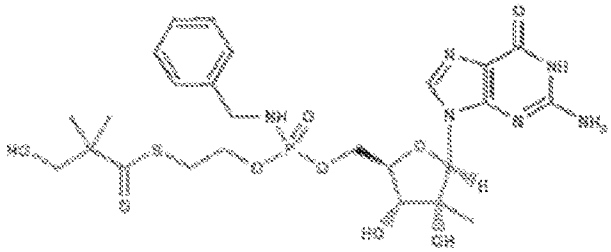


GS-9451

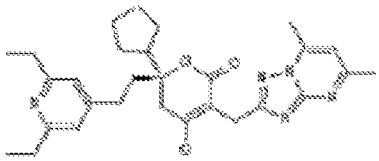
GS-9451



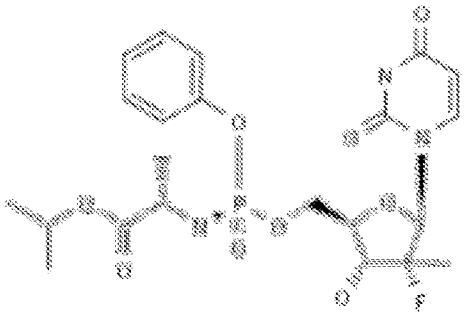
Mericitabine (R-4048)



IDX-184

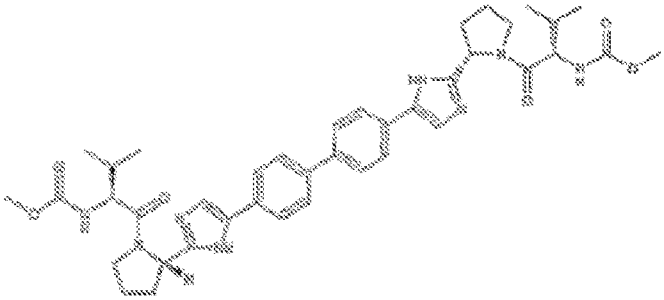


filibuvir (PF-00868554)

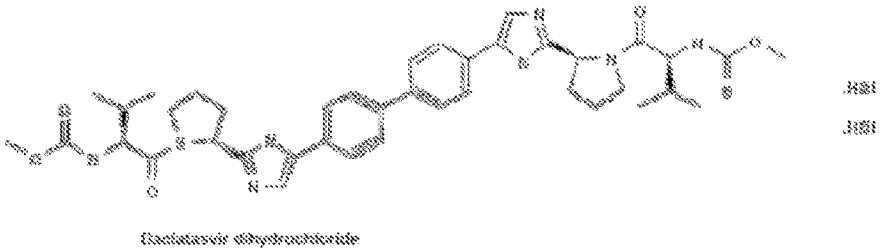


PSI-7977

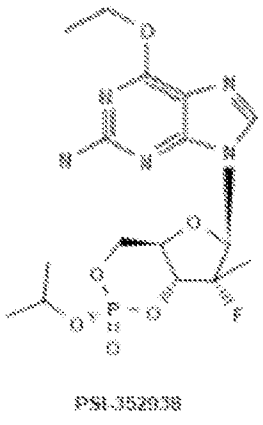
PSI-7977



BMS-790052 (daclatasvir)



BIT-225



PSI-352938

[0093] The following table lists non-limiting examples of the treatment regimens of the present technology. In each treatment regimen, the at least two DAA with or without ritonavir, are administered daily to an HCV patient under such treatment. Each treatment is

interferon-free and. ribavirin-free. Each treatment regimen may also optionally comprise administering one or more other additional DAAs to the patient. The duration of each treatment regimen may last, for example and without limitation, no more than 12 weeks, no more than 11 weeks, no more than 10 weeks, no more than 9 weeks, no more than 8 weeks, alternatively no more than 7 weeks, alternatively no more than 6 weeks, alternatively no more than 5 weeks, alternatively no more than 4 weeks and may depend on the patient's response. In any given regimen described below, the drugs can be, for example and without limitation, co-formulated in a single solid dosage form.

[0094] For instance, all drugs used in a regimen can be co-formulated in amorphous forms or molecularly dispersed in a matrix comprising a water-soluble polymer and optionally a surfactant; for another instance, therapeutic agent 1 and ritonavir (RTV) are formulated in an amorphous form or molecularly dispersed in a matrix comprising a water-soluble polymer and optionally a surfactant, and the other drug(s) are in crystalline form(s) and combined with amorphous Compound 1 and RTV in a single solid dosage form. For yet another instance, Compound 1 and RTV are formulated in a different dosage form than the other drug(s).

Non-Limiting Examples of Interferon-free Treatment Regimens with two or more DAAs (without ribavirin and with or without ritonavir)

Regime	Drugs Used in Treatment	Suitable total daily dosages
1	Therapeutic Agent 1* +	150 to 250 mg (250 mg)
	Therapeutic Agent 4	5 mg to 300mg (pref. 25 mg)
2	Therapeutic Agent 1* +	150 to 250 mg (250 mg)
	Therapeutic Agent 4	5 mg to 300mg (pref. 200 mg)
3	Therapeutic Agent 1* +	5 mg to 200 mg (pref. 50 mg)
	Therapeutic Agent 4	5 mg to 300mg (pref. 25 mg)
4	Therapeutic Agent 1* +	5 mg to 150 mg (pref. 5 mg, 25 mg, 50 mg, or 100 mg)
	Therapeutic Agent 4	5-300 mg (pref. 25 mg)
5	Therapeutic Agent 1* +	5 mg to 150 mg (pref. 5 mg, 25 mg, 50 mg, 100 mg)
	Therapeutic Agent 4	5 mg to 300 mg (pref. 200 mg)
6	Therapeutic Agent 1* +	5 mg to 150 mg (pref. 50 mg)
	Therapeutic Agent 4	5 mg to 200 mg (pref. 25 mg)
7	Therapeutic Agent 1* +	5 mg to 150 mg (pref. 50 mg)
	Therapeutic Agent 4	5 mg to 200 mg (pref. 5 mg)
8	Therapeutic Agent 1* +	150 to 250 mg (pref. 150 or 250 mg)
	Therapeutic Agent 4 +	5 mg to 300 mg (pref. 25 to 200 mg)
	Therapeutic Agent 2	300 to 1800 mg (pref. 400 mg)
9	Therapeutic Agent 1* +	5 mg to 250 mg (pref. 50 mg or 100 mg)
	Therapeutic Agent 4+	5 mg to 200 mg (pref. 25 mg)
	Therapeutic Agent 2	200mg to 800 mg (pref. 400 mg)
10	Therapeutic Agent 1* +	5 mg to 200 mg (pref. 5 mg, 25 mg, 50 mg, 100 mg)
	Therapeutic Agent 4+	5 mg to 200 mg (pref. 25 mg or 100 mg)
	Therapeutic Agent 2	200 mg- 800 mg (pref. 400 mg)
11	Therapeutic Agent 1* +	150-250 mg (pref. 150 mg or 250 mg)

	Therapeutic Agent 3 +	50 mg-1000 mg (pref. 400 mg)
	Therapeutic Agent 4	5 mg-300 mg (pref. 25 mg-200 mg, more pref. 25 mg)
12	Therapeutic Agent 1* +	5 mg to 150 mg (pref. 5 mg, 25 mg, 50 mg, or 100 mg)
	Therapeutic Agent 3 +	100 mg -600 mg (pref. 400 mg)
	Therapeutic Agent 4	5 mg-300 mg (pref. 25 mg to 200 mg, more pref. 25 mg)
13	Therapeutic Agent 1* +	150-250 mg (150 mg, 200 mg or 250 mg)
	Therapeutic Agent 2	300-1800 mg (pref. 800 mg)
14	Therapeutic Agent 1* +	150-250 mg (pref. 200 mg or 250 mg)
	Therapeutic Agent 2	300-1800 mg (pref. 200 mg)
15	Therapeutic Agent 1* +	5 mg to 150 mg (pref. 5 mg, 25 mg, 50 mg, 100 mg)
	Therapeutic Agent 2	200-800 mg
16	Therapeutic Agent 1* +	5 mg to 150 mg (pref. 50 mg)
	Therapeutic Agent 2	200-800 mg
17	Therapeutic Agent 1* +	50 mg to 250 mg (pref. 50 mg or 250 mg)
	Therapeutic Agent 3	50 mg to 1000 mg (pref. 400 mg to 800 mg)
18	Therapeutic Agent 1* +	50 mg to250 mg (pref. 50 mg or 200 mg)
	Therapeutic Agent 3	50 mg to 1000 mg (pref. 100 mg to 200 mg)
19	Therapeutic Agent 1* +	5 mg to 150 mg (pref. 5 mg, 25 mg, 50 mg, 100 mg)
	Therapeutic Agent 3	100 mg to 600 mg
20	Therapeutic Agent 1* +	5 mg to 150 mg (50 mg)
	Therapeutic Agent 3	100 mg to 600 mg
21	PSI-7977 +	100 mg to 500 mg (pref. 200 mg)
	PSI-938	100 mg to 500 mg (pref. 300 mg)
22	PSI-7977 +	100 mg to 500 mg (pref. 400 mg)
	PSI-938	100 to 500 mg (pref. 300 mg)
23	BMS-790052 +	10 mg to 200 mg (pref. 60 mg)

	BMS-650032	300 mg to 1500 mg (pref. 1200 mg)
24	GS-5885+	3 mg to 200 mg (pref. 30 mg to 90 mg)
	GS-9190+	30 mg to 90 mg (pref. 60 mg)
	GS-9451	100 mg to 500 mg (pref. 200 mg)
25	GS-5885+	3 mg to 200 mg (pref. 30 to 90 mg)
	GS-9451	100 mg to 500 mg (pref. 200 mg)
26	BI-201335 +	100 mg to 400 mg (pref. 120 mg or 240 mg)
	BI-207127	300 mg to 3600 mg (pref. 1200 mg to 2100 mg)
27	PSI-7977+	100 mg to 500 mg (pref. 400 mg)
	TMC-435	25 mg to 200 mg (pref. 75 mg to 150 mg)
28	telaprevir +	1000 mg to 2500 mg (pref. 2250 mg)
	VX-222	200 mg to 800 mg
29	Therapeutic Agent 1* +	5 mg to 150 mg (pref. 5 mg)
	Therapeutic Agent 4	5-200mg (pref. 25 mg)
30	Therapeutic Agent 1* +	5 mg to 150 mg (pref. 25 mg)
	Therapeutic Agent 4	5-300 mg (pref. 25 mg)
31	BMS-790052 +	10-200 mg (pref. 60 mg)
	BMS-650032	300-1500 mg (pref. 1200 mg)
32	GS-5885+	3-200 mg (pref. 30-90 mg)
	GS-9190+	30-90 mg (pref. 60 mg)
	GS-9451	100-500 mg (pref. 200 mg)
33	GS-5885+	3 mg to 200 mg (pref. 30mg)
	GS-9451	100 mg to 500 mg (pref. 200 mg)
34	GS-5885+	3 mg to 200 mg (pref. 60mg)
	GS-9451	100 mg to 500 mg (pref. 200 mg)
35	GS-5885+	3 mg to 200 mg (pref. 90mg)
	GS-9451	100 mg to 500 mg (pref. 200 mg)
36	BI-201335 +	100 mg to 400 mg (pref. 120 mg)
	BI-207127	300 mg to 3600 mg (pref. 1200 or 1500 mg)

37	BI-201335 +	100 mg to 400 mg (pref. 120 mg)
	BI-207127	300 mg to 3600 mg (pref. 1800 mg or 2100 mg)
38	BI-201335 +	100 mg to 400 mg (pref. 240 mg)
	BI-207127	300 mg to 3600 mg (pref. 1200 mg or 1500 mg)
39	BI-201335 +	100 mg to 400 mg (pref. 240 mg)
	BI-207127	300-3600 mg (pref. 1800 mg or 2100 mg)
40	PSI-7977+	100 mg to-500 mg (pref. 200 mg)
	TMC-435	25 mg to 200 mg (pref. 75 mg, 100 mg, or 150 mg)
41	PSI-7977+	100 mg to 500 mg (pref. 100 mg)
	TMC-435	25 mg to 200 mg (pref. 75 mg, 100 mg, or 150 mg)
42	telaprevir +	1000-2500 mg (pref. 2250 mg)
	VX-222	200-800 mg (pref. 100 mg)
43	telaprevir +	1000-2500 mg (pref. 2250 mg)
	VX-222	100 mg to 800 mg (pref. 200 mg or 400 mg)
44	telaprevir +	1000 mg to 2500 mg (pref. 2250 mg)
	VX-222	100 mg to 800 mg (pref. 600 mg or 800 mg)
45	telaprevir +	1000 mg to2500 mg (pref. 1500 mg)
	VX-222	100 mg to 800 mg (pref. 200 mg or 400 mg)
46	telaprevir +	1000 mg to 2500 mg (pref. 1500 mg)
	VX-222	100 mg to 800 mg (pref. 600 mg or 800 mg)
47	Danoprevir +	100 mg to 2000 mg (pref. 200 mg or 400 mg)
	R7122	100 mg to 2000 mg (pref. 200 mg)
48	Danoprevir +	100 mg to 2000 mg (pref. 800 mg or 1000mg)
	R7128	100 mg to 2000 mg (pref. 200 mg)

49	Danoprevir +	100 mg to 2000 mg (pref. 1800 mg or 2000 mg)
	R7128	100 mg to 2000 mg (pref. 200 mg)
50	Danoprevir +	100 mg to 2000 mg (pref. 200 mg or 400 mg)
	R7128	100 mg to 2000 mg (pref. 400 mg)
51	Danoprevir +	100 mg to 2000 mg (pref. 800 mg or 1000 mg)
	R7128	100 mg to 2000 mg (pref. 400 mg)
52	Danoprevir +	100 mg to 2000 mg (pref. 1800 mg or 2000 mg)
	R7128	100 mg to 2000 mg (pref. 400 mg)
53	Danoprevir +	100 mg to 2000 mg (pref. 200 mg or 400 mg)
	R7128	100 mg to 2000 mg (pref. 1000 mg)
54	Danoprevir +	100 mg to 2000 mg (pref. 800 mg or 1000 mg)
	R7128	100 mg to 2000 mg (pref. 1000 mg)
55	Danoprevir +	100 mg to 2000 mg (pref. 1800 mg or 2000 mg)
	R7128	100 mg to 2000 mg (pref. 1000 mg)
56	Danoprevir +	100 mg to 2000 mg (pref. 200 mg or 400 mg)
	R7128	100 mg to 2000 mg (pref. 2000 mg)
57	Danoprevir +	100 mg to 2000 mg (pref. 800 mg or 1000 mg)
	R7128	100 mg to 2000 mg (pref. 2000 mg)
58	Danoprevir +	100 mg to 2000 mg (pref. 1800 mg or 2000 mg)
	R7128	100 mg to 2000 mg (pref. 2000 mg)

* ritonavir or a suitable equivalent can be added to any one of these treatments as described and may be added to any of these treatments at a daily total dosage as described in the present technology; preferably ritonavir is co-formulated with therapeutic agent 1. Pref. = preferred

[0095] The treatments of the present technology may be effective in treating HCV infection against HCV genotypes 1, 2, 3, 4, 5, 6, including subgenotypes, such as 1a, 1b, 2a, and 3a.

[0096] In general and depending on patients' conditions, the total daily dose of the DAAs of the present technology may be administered (either as a single or divided dose) in amounts from about 0.001 mg/kg to about 200 mg/kg, or from about 0.001 mg/kg to about 30 mg/kg, or from about 0.001 mg/kg to about 30 mg/kg, or from about 0.01 mg/kg, to about 10 mg/kg (i.e. mg of the compound or salt per kg body weight), and include any amounts or ranges there between, including, but not limited to increments of 0.001 mg/kg, 0.005 mg/kg, 0.01 mg/kg, 0.05 mg/kg, and multiple factors thereof (e.g. 0.25x, 0.5x, 1x, 2x, 3x, 5x, 10x, 100x, etc.). Suitable dosages of the DAAs of the present technology include, but are not limited to, from about 25 mg to about 2000 mg, from about 25 mg to about 1500 mg, from about 25 mg to about 1600 mg, from about 25 mg to about 1000 mg, from about 25 mg to about 800 mg, from about 25 mg to about 500 mg, from about 25 mg to about 250 mg, from about 50 mg to about 2000 mg, from about 50 mg to about 1500 mg, from about 50 mg to about 1600 mg, from about 50 mg to about 1000 mg, from about 50 mg to about 800 mg, from about 50 mg to about 500 mg, from about 50 mg to about 250 mg, and include, but is not limited to, for example, about 25 mg, about 30 mg, about 35 mg, about 40 mg, about 45 mg, about 50 mg, about 55 mg, about 60 mg, about 65 mg, about 70 mg, about 80 mg, about 90 mg, about 95 mg, about 100 mg, about 110 mg, about 120 mg, about 130 mg, about 140 mg, about 150 mg, about 160 mg, about 165 mg, about 170 mg, about 180 mg, about 190 mg, about 200 mg, about 210 mg, about 220 mg, about 230 mg, about 250 mg, and includes any increments there between, including increments of about 1 mg, about 2 mg, about 3 mg, about 4 mg, about 5 mg, about 6 mg, about 10 mg, about 15 mg, about 20 mg, about 25, and multiples thereof (e.g. 0.25x, 0.5x, 1x, 2x, 3x, 5x, 10x, 100x, etc.). It will be understood, however, that the specific dose level for any particular patient will depend upon a variety of factors including the activity of the specific compound employed, the age, body weight, general health, sex, diet, time of administration, route of administration, rate of excretion, drug combination, and the severity of the disease undergoing therapy.

[0097] The cytochrome P-450 inhibitor may be administered in any suitable amount such as, for example, in doses of from about 0.3 mg/kg to about 2 mg/kg or from about 0.6 mg/kg to about 1.5 mg/kg. As non-limiting examples, the cytochrome P-450 inhibitor may be administered in a total daily dose amount of from about 25 mg to about 300 mg, or from about 50 mg to about 250 mg, or from about 100 mg to about 200 mg. In some embodiments,

the cytochrome P-450 inhibitor is administered in a total daily dose of about 100 mg to about 400 mg, preferably about 100 mg. In some embodiments, the cytochrome P-450 inhibitor is administered in a total daily dose amount of about 25 mg. In some embodiments, the cytochrome P-450 inhibitor is administered in a total daily dose amount of about 50 mg. In some embodiments, the cytochrome P-450 inhibitor is administered in a total daily dose amount of about 75 mg. In some embodiments, the cytochrome P-450 inhibitor is administered in a total daily dose amount of about 100 mg. In some embodiments, the cytochrome P-450 inhibitor is administered in a total daily dose amount of about 125 mg.

[0098] The one or more DAAs can be administered, for example and without limitation, concurrently or sequentially, and at the same or different frequencies. For instance, For example, one DAA can be administered immediately before or after the administration of another DAA. A short delay or time gap may exist between the administration of one DAA and that of another DAA. The frequency of administration may also be different. For example, a first DAA may be administered once a day and a second DAA may be administered twice or three times a day. For example, a first DAA with or without ritonavir may be administered once daily, and a second DAA may be administered twice daily.

[0099] The DAAs of the present technology can be co-formulated in a single dosage form. Non-limiting examples of suitable dosage forms include liquid or solid dosage forms. For example, a dosage form of compound 1 as a solid dosage form is described in U.S. Patent Application Serial No. 13/042,805, filed March 8, 2011 and entitled "Solid Compositions", the entire content of which is incorporated herein by reference. More preferably, the dosage form is a solid dosage form in which at least one of the DAAs is in an amorphous form, or highly preferably molecularly dispersed, in a matrix which comprises a pharmaceutically acceptable water-soluble polymer and a pharmaceutically acceptable surfactant. The other DAAs can also be in an amorphous form or molecularly dispersed in the matrix, or formulated in different form(s) (e.g., in a crystalline form).

[00100] The DAAs of the present technology can be formulated in different dosage forms. It will be understood that the total daily usage of the compounds and compositions to be administered will be decided by the attending physician within the scope of sound medical judgment.

[00101] In one embodiment, a method for treating a naïve subject comprises administering Therapeutic agent 1 at a dose of 150 mg, Therapeutic agent 2 at a dose of 400 mg or 800 mg, ritonavir at a dose of 100 mg, once a day for 12 weeks. At the end of treatment, the subject has no detectable virus.

[00102] In one embodiment, a method for treating a naïve subject comprises administering Therapeutic agent 1 at a dose of 50 mg, Therapeutic agent 2 at a dose of 400 mg or 800 mg, and ritonavir at a dose of 100 mg, once a day for 12 weeks. At the end of treatment, the subject has no detectable virus.

[00103] In one embodiment, a method for treating a naïve subject comprises administering Therapeutic agent 1 at a dose of 250 mg, Therapeutic agent 2 at a dose of 400 mg BID, ritonavir at a dose of 100 mg, once a day for 12 weeks. At the end of treatment, the subject has no detectable virus.

[00104] In another embodiment, a method for treating a naïve subject comprises administering Therapeutic agent 1 at a dose of 150 mg, Therapeutic agent 2 at a dose of 400 mg BID, and ritonavir at a dose of 100 mg, once a day for 12 weeks. At the end of treatment, the subject has no detectable virus.

[00105] In yet another embodiment, a method for treating a peginterferon + ribavirin (P/RBV) non-responder comprises administering Therapeutic agent 1 at a dose of 150 mg, Therapeutic agent 2 at a dose of 400 mg BID, ritonavir at a dose of 100 mg, once a day for 12 weeks.

[00106] In yet another embodiment, a method for treating a peginterferon + ribavirin (P/RBV) non-responder comprises administering Therapeutic agent 1 at a dose of 50 mg, Therapeutic agent 2 at a dose of 400 mg BID, ritonavir at a dose of 100 mg, once a day for 12 weeks.

CLAIMS

1. A method for treating Hepatitis C Virus (HCV) infection comprising administering to a subject in need thereof at least two direct acting antiviral agents (DAAs) for a duration of no more than twelve weeks,

wherein the subject is not administered with interferon or ribavirin during said duration..

2. The method of claim 1, wherein the at least two direct acting antiviral agents (DAAs) are administered in an amount effective to result in sustained virological response (SVR).

3. The method of claim 1, wherein the method further comprises administering an inhibitor of cytochrome P450 to the subject.

4. The method of claim 1, wherein the at least two DAAs are administered daily.

5. The method of claim 1, wherein each DAA is administered either separately or in combination, and wherein each DAA is administered once a day, twice a day, or three times a day.

6. The method of claim 1, wherein the at least two DAAs are administered once a day.

7. The method of claim 1, wherein the duration is no more than eight weeks.

8. The method of claim 1, wherein the at least two DAAs is selected from the group consisting of protease inhibitors, nucleotide or nucleoside polymerase inhibitors, non-nucleotide polymerase inhibitors, NS3B inhibitors, NS4A inhibitors, NS5A inhibitors, NS5B inhibitors, and cyclophilin inhibitors.

9. The method of claim 1, wherein the at least two DAAs comprise at least one HCV protease inhibitor and at least one HCV polymerase inhibitor.

10. The method of claim 9, wherein the at least one HCV protease inhibitor is selected from the group consisting of therapeutic agent 1, telaprevir, boceprevir, BI-201335, GS-9451, BMS-650032, and combinations thereof.

11. The method of claim 9, wherein the at least one HCV polymerase inhibitor is at least one nucleotide polymerase inhibitor or at least one non-nucleotide polymerase inhibitor.

12. The method of claim 11, wherein the at least one nucleotide or nucleoside polymerase inhibitor is selected from the group consisting of PSI-7977, PSI-938, and combinations thereof.

13. The method of claim 11, wherein the at least one non-nucleotide polymerase inhibitor is selected from the group consisting of therapeutic agent 2, therapeutic agent 3, GS-9190, BI-207127, VX-222 and combinations thereof.

14. The method of claim 10, wherein the HCV polymerase inhibitor is therapeutic agent 1 and the at least one HCV polymerase inhibitor is therapeutic agent 2.

15. The method of claim 14, wherein therapeutic agent 1 is administered a total daily dose of about 25 mg to about 250 mg and wherein therapeutic agent 2 is administered a total daily dose from about 100 mg to about 800 mg.

16. The method of claim 15, wherein therapeutic agent 1 is administered at least once daily at about 50 mg to about 250 mg and therapeutic agent 2 is administered at least twice daily at about 200 mg to about 400 mg.

17. The method of any of claims 14-16, wherein ritonavir is administered at least once a day at about 50 mg to about 100 mg.

18. The method of claim 11, wherein the HCV protease inhibitor is therapeutic agent 1 and the non-nucleoside HCV polymerase inhibitor is therapeutic agent 3.

19. The method of claim 18, wherein therapeutic agent 1 is administered in a total daily dose of from about 25 mg to about 250 mg and wherein therapeutic agent 3 is administered in a daily dose of about 50 mg to about 1000 mg.

20. The method of claim 19, wherein therapeutic agent 1 is administered at a total daily dose of about 50 mg and therapeutic agent 3 is administered at a total daily dose of about 400 mg.

21. The method of claim 19, wherein therapeutic agent 3 is administered in a daily dose of 50 mg.

22. The method of claim 21, wherein therapeutic agent 3 is administered once daily or twice daily.

23. The method of any of claims 19-22, wherein therapeutic agent 1 is administered at a daily dose of about 50 mg.

24. The method of claim 23, wherein therapeutic agent 1 is administered once daily.

25. The method of claim 1, wherein the at least two DAAs comprise at least one HCV protease inhibitor and at least one NS5A inhibitor.

26. The method of claim 25, wherein the at least one HCV protease inhibitor is therapeutic agent 1 and the at least one NS5A inhibitor is therapeutic agent 4.

27. The method of claim 26, wherein therapeutic agent 1 is administered at a total daily dosage of about 25 mg to about 250 mg.

28. The method of claim 26, wherein therapeutic agent 4 is administered in a total daily dose of about 5 mg to about 200 mg.

29. A method for treating Hepatitis C Virus (HCV) infection in a subject comprising administering

(a) therapeutic agent 1,

(b) at least one polymerase inhibitor selected from the group consisting of therapeutic agent 2, therapeutic agent 3 and combinations thereof,

(c) an inhibitor of cytochrome P450 for a duration of no more than twelve weeks,

wherein the therapeutic agent 1, the at least one polymerase inhibitor, and the inhibitor of cytochrome P450 are administered in amounts effective to result in sustained virological response (SVR) in the subject.

30. A method for treating a population of subjects having Hepatitis C Virus (HCV) infection, the method comprising administering at least two direct acting antiviral agents (DAAs) to the subjects for a duration of no more than 12 weeks, wherein the at least two direct acting antiviral agents (DAAs) are administered to the subjects in amounts and for a duration effective to provide a sustained virological response (SVR) in at least about 70% of the population.

31. The method of claim 1, wherein said at least two direct acting antiviral agents comprise:

compound 1 or a pharmaceutically acceptable salt thereof,

compound 2 or a pharmaceutically acceptable salt thereof, and

ritonavir.

32. The method of claim 31, wherein said duration is no more than 8 weeks.

33. The method of claim 32, wherein said subject is infected with HCV genotype 1.

34. The method of claim 32, wherein said subject is infected with HCV genotype 1a.

35. The method of claim 32, wherein said subject is infected with HCV genotype 1b.

36. The method of claim 32, wherein said subject is infected with HCV genotype 2 or 3.

37. The method of claim 32, wherein said subject is a HCV-treatment naïve patient.

38. The method of claim 32, wherein said subject is a HCV-treatment experienced patient.

39. The method of claim 32, wherein said subject is an interferon non-responder.

40. The method of claim 32, wherein said subject is not a candidate for interferon treatment.

41. The method of claim 32, wherein said compound 1 or pharmaceutically acceptable salt thereof is administered once daily and in combination with ritonavir.

42. The method of claim 1, wherein said at least two direct acting antiviral agents comprise:

compound 1 or a pharmaceutically acceptable salt thereof,

compound 3 or a pharmaceutically acceptable salt thereof, and

ritonavir.

43. The method of claim 41, wherein said duration is no more than 8 weeks.

44. The method of claim 43, wherein said subject is infected with HCV genotype 1.

45. The method of claim 43, wherein said subject is infected with HCV genotype 1a.

46. The method of claim 43, wherein said subject is infected with HCV genotype 1b.

47. The method of claim 43, wherein said subject is infected with HCV genotype 2 or 3.

48. The method of claim 43, wherein said subject is a HCV-treatment naïve patient.

49. The method of claim 43, wherein said subject is a HCV-treatment experienced patient.

50. The method of claim 43, wherein said subject is an interferon non-responder.

51. The method of claim 43, wherein said subject is not a candidate for interferon treatment.

52. The method of claim 43, wherein said compound 1 or pharmaceutically acceptable salt thereof is administered once daily and in combination with ritonavir.

53. The method of claim 1, wherein said at least two direct acting antiviral agents comprise:

compound 1 or a pharmaceutically acceptable salt thereof,

compound 4 or a pharmaceutically acceptable salt thereof, and

ritonavir.

54. The method of claim 53, wherein said duration is no more than 8 weeks.

55. The method of claim 54, wherein said subject is infected with HCV genotype 1.

56. The method of claim 54, wherein said subject is infected with HCV genotype 1a.

57. The method of claim 54, wherein said subject is infected with HCV genotype 1b.

58. The method of claim 54, wherein said subject is infected with HCV genotype 2 or 3.

59. The method of claim 54, wherein said subject is a HCV-treatment naïve patient.

60. The method of claim 54, wherein said subject is a HCV-treatment experienced patient.

61. The method of claim 54, wherein said subject is an interferon non-responder.

62. The method of claim 54, wherein said subject is not a candidate for interferon treatment.

63. The method of claim 54, wherein said compound 1 or pharmaceutically acceptable salt thereof is administered once daily and in combination with ritonavir.

64. The method of claim 1, wherein said at least two direct acting antiviral agents comprise:

compound 1 or a pharmaceutically acceptable salt thereof,

compound 2 or a pharmaceutically acceptable salt thereof,

compound 4 or a pharmaceutically acceptable salt thereof, and

ritonavir.

65. The method of claim 64, wherein said duration is no more than 8 weeks.

66. The method of claim 65, wherein said subject is infected with HCV genotype 1.

67. The method of claim 65, wherein said subject is infected with HCV genotype 1a.

68. The method of claim 65, wherein said subject is infected with HCV genotype 1b.

69. The method of claim 65, wherein said subject is infected with HCV genotype 2 or 3.

70. The method of claim 65, wherein said subject is a HCV-treatment naïve patient.

71. The method of claim 65, wherein said subject is a HCV-treatment experienced patient.

72. The method of claim 65, wherein said subject is an interferon non-responder.

73. The method of claim 65, wherein said subject is not a candidate for interferon treatment.

74. The method of claim 65, wherein said compound 1 or pharmaceutically acceptable salt thereof is administered once daily and in combination with ritonavir.

75. The method of claim 1, wherein said at least two direct acting antiviral agents comprises a drug combination selected from the group consisting of:

a combination of PSI-7977 and PSI-938,
a combination of BMS-790052 and BMS-650032,
a combination of GS-5885 and GS-9451,
a combination of GS-5885, GS-9190 and GS-9451,
a combination of BI-201335 and BI-27127,
a combination of telaprevir and VX-222,
a combination of PSI-7977 and TMC-435, and
a combination of danoprevir and R7128.

76. The method of claim 75, wherein said duration is no more than 8 weeks.

77. The method of claim 76, wherein said subject is infected with HCV genotype 1.

78. The method of claim 76, wherein said subject is infected with HCV genotype 1a.

79. The method of claim 76, wherein said subject is infected with HCV genotype 1b.

80. The method of claim 76, wherein said subject is infected with HCV genotype 2 or 3.

81. The method of claim 76, wherein said subject is a HCV-treatment naïve patient.

82. The method of claim 76, wherein said subject is a HCV-treatment experienced patient.

83. The method of claim 76, wherein said subject is an interferon non-responder.

84. The method of claim 76, wherein said subject is not a candidate for interferon treatment.

85. The method of claim 76, wherein at least one of said DAAs is therapeutic agent1, and wherein said therapeutic agent 1 is administered once daily and in combination with ritonavir.

ABSTRACT OF THE DISCLOSURE

The present invention features interferon-free therapies for the treatment of HCV over a shorter duration of treatment, such as no more than 12 weeks, which preferably result in undetectable virus at the end of treatment and afterward, or preferably cure the patient of HCV infection and thereby avoids the untoward long term consequences of the infection. The therapies comprise administering at least two direct acting antiviral agents without ribavirin to a subject. For example, the therapies comprise administering to a subject an effective amounts of therapeutic agent 1, therapeutic agent 2 (or therapeutic agent 3), an inhibitor of cytochrome P450 (e.g., ritonavir).

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Customer Number:	23446
Filer:	Micheal Bernard Harlin/Angeline R. Babel/ Angela Kubicki
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Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Provisional Cover Sheet (SB16)	24704US02_Pro_Cover.pdf	1059715 a650801ea97b0ed226f286e8059fb403505d8352	no	4
Warnings:					
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2		24704US02_Spec.pdf	1258385 e0b8b916167c73ff2d7908092ecfccb04d7e0798	yes	92

Multipart Description/PDF files in .zip description

Document Description	Start	End
Specification	1	81
Claims	82	91
Abstract	92	92

Warnings:					
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3	Fee Worksheet (SB06)	fee-info.pdf	29300 88b32f256ae925d506d847168e636f765c9648a8	no	2
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