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(54) **Title**: TREATMENT OF CHRONIC HEPATITIS C WITH IFN-A5 COMBINED WITH IFN-A2B IN A COHORT OF PATIENTS

(57) **Abstract**: The present invention relates to interferon alpha 5 (IFN-a5) combined with interferon alpha 2 (IFN-a2), for use as an anti-hepatitis C virus (HCV) drug in patients with chronic hepatitis C. Or in other words, the present invention relates to a method of treating patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-a5 combined with IFN-a2. In one embodiment, the present invention relates to a product containing IFN-a5 and IFN-a2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C.

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TREATMENT OF CHRONIC HEPATITIS C WITH IFN-A5 COMBINED WITH IFN-A2B IN A COHORT OF PATIENTS

Field of the invention

The field of the invention is in pharmacology and medical treatments, particularly in clinical uses or methods of treatment of Hepatitis C virus (HCV) infected patients.

Background of the invention

Hepatitis C virus (HCV), identified in 1989, is a member of the flaviviridae family of spherical, enveloped, positive-strand RNA viruses [1-2]. HCV has emerged as a major viral pandemic over the past two decades, with about 3% of the world's population chronically infected [3]. Chronic HCV infection is defined as persistent, detectable serum HCV RNA for a period greater than 6 months, with or without derangement in liver function tests. This is in contrast to acute HCV infection, in which serum HCV RNA clears within 6 months. Prospective studies have shown that 60–85% of HCV-infected people will develop chronic infection [2].

There are six distinct HCV genotypes, which prevail in different geographic regions, with genotype 1 being the predominant genotype (70%) in US and Europe and the most resistant to treatment [4], followed by genotypes 2 and 3 (10 and 20%) [5-7].

Current HCV antiviral drugs are associated with limited efficacy and significant toxicity. Treatment with pegylated Alpha interferon (PegIFNα) injections (once a week subcutaneously) combined with oral ribavirin (RBV) over 24 to 48 weeks represent the standard of care (SOC) and induce sustained virologic response (SVR, undetectable HCV RNA at 6 months following treatment discontinuation) in up to 80% of genotype-2 and -3 infected patients, but in only 50% of genotype-1 infected patients [8-11]. This treatment regimen is associated with a multitude of side effects including depression-related effects, neutropenia, thrombocytopenia, injection-site reactions, arthralgia, headache, fatigue, myalgia, insomnia, and nausea.

With each advance in antiviral therapy for chronic hepatitis C (CHC), patients who have failed to clear virus or relapsed following prior therapy have been retreated in the hope that the superior efficacy of newer therapies, as established in treatment-naïve patients, will extend to them as well. Thus patients who relapsed or failed to respond to 6 months of interferon (IFN)

monotherapy have been retreated with IFN in higher doses or over a longer duration [12,13], and subsequently with IFN in combination with RBV [14-17]. The latter studies established a rate of sustained virologic response (SVR) of 50% in prior IFN relapsers [16,17] and, in meta-analyses, 13 to 15% of prior non-responders to IFN [18,19]. Though PegIFN-α + RBV has demonstrated superior efficacy in treatment-naïve patients, in relapsers SVR is achieved in 32 to 55% of patients, and genotype 1 patients have lower SVR rates than others [20,21] leaving at least another 50% at risk of serious and life-threatening progression of their underlying disease. Also, recent trials have demonstrated that longer courses of low dose PegIFNα do not reduce the rate of disease progression in patients with CHC and advanced fibrosis, with or without cirrhosis, who had not had a response to SOC treatment [22].

For nonresponders to a previous course of standard IFN monotherapy, re-treatment with PEG-IFN plus ribavirin can increase the frequency of responsiveness to approximately 20%; for nonresponders to a previous course of standard IFN plus ribavirin, re-treatment with PEG-IFN plus ribavirin can increase the frequency of responsiveness to approximately 10%. Expectations for responsiveness to re-treatment are lower in patients with genotype 1, cirrhosis, high baseline HCV RNA levels, and black ethnicity.

Given the poor rates of SVR to current therapy of HCV genotype 1 infected naïve patients, given also the poor rates of SVR to current therapy of HCV infected relapsers and nonresponders, there is a need for more effective and less toxic therapy for these specific patients' populations.

Evidence-based practice aims to provide health care guided by a thoughtful integration of the best available scientific knowledge with clinical expertise. This approach allows the practitioner to critically assess research data, clinical guidelines, and other information resources in order to correctly identify the clinical problem, apply the most high-quality intervention, and re-evaluate the outcome for future improvement. In this respect, the results provided by randomised controlled trials as a means of reliably informing healthcare practice is fundamental.

In an attempt to provide treatments purported by evidenced-base medicine, the inventors designed and performed randomized controlled trials with IFN-α5, IFN-α2b, alone or in combination.

Type I interferons are a family of polypeptides with cytokine activity which were originally discovered by virtue of their inhibitory activity on the viral infection of cells lines in vitro (Pestka, et al., 2004). Human type I interferons include a multigene family of different IFN-α

subtypes and a single IFN-β. All type I IFNs are structurally related and share the same IFN receptor.

CastelRuiz et al. (Hepatology 1999; 29: 1900-1904) teach that IFN-α5 is the subtype mainly expressed in hepatic tissue and that IFN-α is decreased in the liver of patients with chronic HCV infection. From this statement, the authors speculate that IFN-α5 might have a role in the treatment of chronic hepatitis C (see page 1903 last column, last paragraph of the discussion).

Larrea et al. (J Viral Hepat. 2001; 8: 103-110) disclose that IFN-α5 is the major subtype expressed in PBMC from healthy controls and hepatitis C patients.

Patent EP1077068 (Instituto Científico y Tecnológico de Navarra) discloses uses of interferon alpha 5 in the treatment of viral hepatopathies, particularly chronic hepatitis C. The same patent disclosure submits on paragraph [0044] that no correlation was found between the expression of the IFNα or IFNβ genes in the liver or PBMC and C virus RNA levels in serum or the viral genotype.

Yanai et al. (J Interferon Cytokine Res. 2001 21(10), 835-41) disclose the antiviral effect of different IFN subtypes and subtype combinations on different cell lines cultures infected with vesicular stomatitis virus.

To the best of the inventors' knowledge, there is no prior art relating to organized clinical studies involving IFN-α5, IFN-α2b, or both combinedin an optimal proportion of 50 % IFN-α5 / 50 % IFN-α2b (w/w) or from a range of 10 % IFN-α5 / 90% IFN-α2b to 90% IFN-α5 / 10% IFN-α2b, let alone in the treatment of HCV infections, in patients with chronic hepatitis C, even less in treatment-experienced patients with chronic hepatitis C. Differently, all experiments disclosed in the prior art are performed onto infected laboratory cell lines or material biopsied from HCV infected patients. The prior art teachings relate to *in vitro* experiments that are non-conclusive studies performed on laboratory material eventually derived from unidentified patient sub-groups. Therefore, the tests described in the prior art do not allow any prediction to be made as to whether or not a treatment according to the present invention would bring about any therapeutic improvement in terms of viral response to SOC treatment-experienced patients.

As such, an object of the present invention is the provision of an evidence-based therapy for treating chronic hepatitis C in a defined patient cohort, thereby avoiding treating other patients for whom the therapy is not beneficial.

One of the technical teachings of the present invention demonstrates that patients where HCV-RNA detection occurs after SOC therapy is discontinued, or alternatively after IFN-α2 therapy is stopped, that is during the 6 months post-standard of care (post-SOC) treatment period, i.e. relapsing to a previous SOC treatment ("relapsers"), benefit most from a treatment with IFN-α5 in combination with IFN-α2b, as shown by an improved antiviral response, i.e., by a reduction of the viral load of the patients' serum in at least 0.5 log, or in at least around 1 log, respectively following 29 days of treatment, in comparison to the antiviral response of the same patient cohort treated with IFN-α5 or IFN-α2b, alone.

An additional technical teaching of the present invention demonstrates that relapsers who are infected with the hepatitis C genotype type 1 virus benefit most from a treatment with IFN-α5, in combination with IFN-α2b, as shown by an improved antiviral response, i.e., the diminishing of the viral load of the patients' serum in at least 0.5 log, or in at least around 1 log, respectively, following treatment discontinuation after 29 days) in comparison to the antiviral response of the same patient cohort treated with IFN-α5 or IFN-α2b, alone.

A further interesting technical teaching of the present invention demonstrates the synergic and beneficial effect of the combination of IFN-α5 with IFN-α2b in the above described cohort of patients, i.e. relapsers in general, and those relapsers infected with the hepatitis C genotype type 1 virus.

Summary of the invention

The present invention relates to a method of treating patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2.

In one embodiment of the invention, the patients are treatment-experienced patients.
In another embodiment, IFN-alpha2 is selected from IFN-alpha2a (IFN-α2a) and IFN-alpha2b (IFN-α2b).

The present invention also relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, in an optimal proportion of 50 % IFN-α5 / 50 % IFN-α2b (w/w) or from a range of 10 % IFN-α5 / 90% IFN-α2b to 90% IFN-α5 / 10% IFN-α2b.

In one embodiment of the invention, the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof.

In one embodiment of the invention, the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b.

In one embodiment of the invention, the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT.

In one embodiment of the invention, the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment of the invention, the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW.

Description of the invention

The present invention relates to a composition comprising IFN-α5 and IFN-alpha2 (IFN-α2), for use as an anti-hepatitis C virus (HCV) drug in patients with chronic hepatitis C. Or in other words, the present invention relates to a method of treating patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2.

Interferon alpha-5, abbreviated as IFN-alpha-5, IFN-α5, Hu-IFN-αG, Hu-IFN-α5, and a.k.a. Interferon alpha-61, Interferon alpha-G, or LeIF G, is a human protein naturally produced by macrophages and belongs to the alpha/beta interferon family. It has the following sequence of 189 amino acids long (SEQ ID NO. 1):

MALPFVLLMA LVVLNCKSIC SLGCDLPQTH SLSNRRTLMI MAQMGRISPF SCLKDRHDFG FPQEEFDGNQ FQKAQAISVL HEMIQQTFNL FSTKDSSATW DETLLDKFYT ELYQQLNDLE ACMMQEVGVE DTPLMNVDSI LTVRKYFQRI TLYLTEKKYS PCAWEVVRAE IMRSFSLSAN LQERLRRKE

Human interferon alpha-5 is disclosed for example in Uniprot database (www.uniprot.org) with Accession Number **P01569**. Amino acids 1 to 21 correspond to the signal peptide. Amino acids 22 to 189 correspond to the secreted protein (168 amino acids length, underlined sequence).

"Interferon alpha-2", abbreviated as IFN-alpha-2, IFN-alpha2 , IFN-α2 and LeIF A, is also a human protein naturally produced by macrophages and belongs to the alpha/beta interferon family. Human interferon alpha-2 is disclosed for example in Uniprot with Accession Number **P01563**. Complete human interferon alpha-2 is a 188 amino acids length protein: amino acids 1 to 23 correspond to the signal peptide. Amino acids 24 to 188 correspond to the secreted protein (165 amino acids length).

Several natural variations of Interferon alpha-2 have been disclosed as polymorphisms: Interferon alpha-2a, alpha-2b and alpha-2c. Interferon alpha-2 as used here in refers to any of these natural variations or recombinantly produced proteins with the same amino acid sequences than these natural variations.

Interferon alpha-2a, abbreviated as IFN-alpha-2a, IFN-α2a, has the sequence represented by SEQ ID NO. 4:

MALTFALLVALLVLSCKSSCSVGCDLPQTHSLGSRRTLMLLAQMRKISLFSCLKDRHDF GFPQEEFGNQFQKAETIPVLHEMIQQIFNLFSTKDSSAAWDETLLDKFYTELYQQLNDLE ACVIQGVGVTETPLMKEDSILAVRKYFQRITLYLKEKKYSPCAWEVVRAEIMRSFSLSTN LQESLRSKE

Underlined sequence corresponds to the secreted protein.

Interferon alpha-2b, abbreviated as IFN-alpha-2b, IFN-α2b, has the sequence represented by SEQ ID NO. 5:

MALTFALLVALLVLSCKSSCSVGCDLPQTHSLGSRRTLMLLAQMRRISLFSCLKDRHDFG FPQEEFGNQFQKAETIPVLHEMIQQIFNLFSTKDSSAAWDETLLDKFYTELYQQLNDLEA CVIQGVGVTETPLMKEDSILAVRKYFQRITLYLKEKKYSPCAWEVVRAEIMRSFSLSTNL QESLRSKE

Underlined sequence corresponds to the secreted protein.

Interferon alpha-2a is commercially available from Roche with the tradename Roferon-A®.

Interferon alpha-2b is commercially available from Schering Corporation with the tradename Intron A®, and formulations and preparations thereof are described in US5,935,566 and US6,610,830.

Typical suitable IFN-α5, IFN-α2a and IFN-α2b for the present invention include, but are not limited to human IFN-α5, IFN-α2a, or IFN-α2b, respectively, of natural origin or recombinant human IFN-α5, IFN-α2a, or IFN-α2b, available for example from R&D Systems. The present invention also includes bioequivalent forms and formulations of IFN-α5, IFN-α2a and IFN-α2b, also named biosimilars, as approved by the FDA (United States Food and Drug Administration), EMEA (European Medicines Agency), and other regulatory bodies.

Combinations of IFN-α5 and IFN-α2a in the present invention are preferably in an optimal proportion of 50 % IFN-α5 / 50 % IFN-α2a (w/w), or alternatively from a range of 10 % IFN-α5 / 90% IFN-α2a to 90% IFN-α5 / 10% IFN-α2a.

Combinations of IFN-α5 and IFN-α2b in the present invention are preferably in an optimal proportion of 50 % IFN-α5 / 50 % IFN-α2b (w/w), or alternatively from a range of 10 % IFN-α5 / 90% IFN-α2b to 90% IFN-α5 / 10% IFN-α2b.

Bioequivalence is defined by the FDA as the absence of a significant difference in the rate and extent to which the active ingredient or active moiety in pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site of drug action when administered at the same molar dose under similar conditions in an appropriately designed study.

IFN-α5, IFN-α2a, and IFN-α2b proteins may be obtained from a variety of cell sources that synthesize bioactive IFN-α5, IFN-α2a, or IFN-α2b proteins, respectively, including, for example, cells that naturally produce this protein, or cells transfected with recombinant DNA molecules capable of directing the synthesis or secretion of the protein. Alternatively, IFN-α5, IFN-α2a, and IFN-α2b proteins may be synthesized by chemical synthetic methods, including but not limited to, solid phase peptide synthesis.

The term "recombinant protein," as used in the present invention in relation to IFN-α5, IFN-α2a, or IFN-α2b refers to the protein as obtained by DNA recombinant techniques from prokaryotic or eukaryotic host cells as well as its salts, functional derivatives, variants, analogs, and fragments. Typically, recombinant IFN-α5, IFN-α2a, or IFN-α2b may be obtained from genetically

engineered Escherichia coli bacterium comprising DNA that codes for the human protein, followed by fermentation in a suitable nutrient medium.

The term "salts" herein refers to both salts of carboxyl groups and to acid addition salts of amino groups of the IFN-α5, IFN-α2a, and IFN-α2b molecule or analogs thereof. Salts of a carboxyl group may be formed by means known in the art and include inorganic salts, for example, sodium, calcium, ammonium, ferric, or zinc salts, and the like, and salts with organic bases as those formed, for example, with amines, such as triethanolamine, arginine, lysine, piperidine, procaine, and the like. Acid addition salts include, for example, salts with mineral acids, such as, for example, hydrochloric acid or sulfuric acid, and salts with organic acids, such as, for example, acetic acid or oxalic acid. Of course, any such salt must retain the biological activity of IFN-α5, IFN-α2a, or IFN-α2b. For therapeutic use, salts of IFN-α5, IFN-α2a, or IFN-α2b are those wherein the counter-ion is pharmaceutically acceptable. Non-pharmaceutically acceptable salts are also encompassed in the ambit of the present invention since they can be used in the production of pharmaceutically acceptable end products.

"Functional derivatives" as used herein covers derivatives which may be prepared from the functional groups which occur as side chains on the residues or the N- or C-terminal groups, by means known in the art, and are included in the invention as long as they remain pharmaceutically acceptable, i.e., they do not destroy the biological activity of the protein as described above, i.e., the ability to bind the corresponding receptor and initiate receptor signaling, and do not confer toxic properties on compositions containing it. Derivatives may have chemical moieties, such as carbohydrate or phosphate residues, provided such a derivative retains the biological activity of the protein and remains pharmaceutically acceptable.

For example, derivatives may include aliphatic esters of the carboxyl groups, amides of the carboxyl groups by reaction with ammonia or with primary or secondary amines, N-acyl derivatives or free amino groups of the amino acid residues formed with acyl moieties (e.g., alkanoyl or carbocyclic aroyl groups), or O-acyl derivatives of free hydroxyl group (e.g., that of seryl or threonyl residues) formed with acyl moieties. Such derivatives may also include for example, polyethylene glycol side-chains, which may mask antigenic sites and extend the residence of the molecule in body fluids.

Of particular importance is an IFN-α5, IFN-α2a, or IFN-α2b protein that has been derivatized or combined with a complexing agent to be long lasting. For example, pegylated versions, or those

genetically engineered to exhibit long lasting activity in the body, can be used according to the present invention.

A "variant" according to the present invention refers to a molecule, which is substantially similar to either the entire protein defined above or a fragment thereof. Variant proteins or peptides may be conveniently prepared by direct chemical synthesis of the variant molecule, using methods well known in the art. Of course, such variant would have similar receptor binding and signal initiating activity as the corresponding naturally occurring protein.

Variations in the protein primary structure, as well as variations in higher levels of structural organization, e.g. variation in the type of covalent bonds linking the amino acid residues or addition of groups to the terminal residues of the protein, are within the scope of the invention. Further, the protein molecules may include conservative or non-conservative alterations in the amino acid sequence that result in silent changes that preserve the functionality of the molecule including, for example, deletions, additions, and substitutions. Such altered molecules may be desirable where they provide certain advantages in their use. As used herein, conservative substitutions would involve the substitution of one or more amino acids within the sequence of the corresponding protein with another amino acid having similar polarity and hydrophobicity/hydrophilicity characteristics resulting in a functionally equivalent molecule. Such conservative substitutions include but are not limited to substitutions within the following groups of amino acids: glycine, alanine; valine, isoleucine, leucine; aspartic acid, glutamic acid; asparagine, glutamine; serine, threonine; lysine, arginine; phenylalanine, tyrosine; and methionine, norleucine.

Amino acid sequence variants of the IFN-α5, IFN-α2a, or IFN-α2b protein can be prepared by mutations in the DNAs, which encode the synthesized derivatives. Such variants include, for example, deletions from, or insertions or substitutions of, residues within the amino acid sequence. Any combination of deletion, insertion, and substitution may also be made to arrive at the final construct, provided that the final construct possesses the desired activity. Obviously, the mutations that will be made in the DNA encoding the variant protein must not alter the reading frame and preferably will not create complementary regions that could produce secondary mRNA structure.

At the genetic level, these variants ordinarily are prepared by site-directed mutagenesis of nucleotides in the DNA encoding the protein molecule, thereby producing DNA encoding the

variant, and thereafter expressing the DNA in recombinant cell culture. The variants typically exhibit the same qualitative biological activity as the non-variant protein.

An "analog" of the IFN-α5, IFN-α2a, or IFN-α2b protein according to the present invention refers to a non-natural molecule, which is substantially similar to either, the entire molecule or to an active fragment thereof. The similarity can be calculated in sequence similarity and is at least 70%, preferably at least 75%, 80%, 85%, 90%, or 95%. Such analog would exhibit the same activity as the corresponding naturally occurring protein.

A "fragment" according to the present invention refers to any subset of the IFN-α5, IFN-α2a, or IFN-α2b protein molecule, that is, a shorter peptide, which retains the desired biological activity. Fragments may readily be prepared by removing amino acids from either end of the molecule and testing the resultant for its properties as a receptor agonist. Proteases for removing one amino acid at a time from either the N-terminal or the C-terminal of a polypeptide are known in the art.

The term "treatment-experienced patient" as used herein refers to a patient having an HCV infection with viremia (HCV RNA measured by PCR) who has initiated some form of anti-HCV therapy, including but not limited to interferon-alpha, pegylated interferon alpha or ribavirin.

The term "treatment-naïve patient" refers to a patient having an HCV infection with viremia (HCV RNA measured by PCR) and who have not been previously treated with ribavirin or any interferon-based regimen including, but not limited to an interferon-alpha.

Treatment-experienced patients may be selected from non-responders, partial responders, relapsers, and breakthroughs.

The term "non-responder patient" as used herein refers to a patient having a HCV infection with viremia (HCV RNA measured by PCR) and who has previously been treated and fails to achieve sustained virologic response.

The terms "virological breakthroughs" or "breakthroughs" refer to the reappearance of HCV RNA while the patient is still on therapy.

The term "sustained virologic response" as used herein refers to undetectable HCV RNA levels for 6 months after completion of therapy.

The term "partial responder" refers to a patient having a HCV infection with viremia (HCV RNA measured by PCR) and who has previously been treated and fails to achieve 2 log drop versus baseline viral load despite at least twelve weeks of PEG-Intron (pegylated interferon) 1.5 mcg/kg/week plus weight based RBV (ribavirin) (>10.6 mg/kg/day). In practice, the application of this definition accommodates a 0.5 log variation of the definition, however, so that if an individual patient achieves as high as a 2.5 log drop versus baseline, or anywhere between 2 and 2.5 log drop versus baseline viral load despite at least twelve weeks of PEG-Intron (pegylated interferon) 1.5 mcg/kg/week plus weight based RBV (ribavirin) (>10.6 mg/kg/day), it would be within the discretion of the investigator to denominate the patient as a "non-responder" on a case by case basis.

Conversely, a responder is defined as a patient who completed the treatment phase of the study and reported SVR, i.e. for at least 6 months.

The term "relapse" refers to that patient, in which there is a return of a sign, symptom, or disease after a remission. More particularly, relapsers are those CHC patients who had achieved virologic response (HCV-RNA non-detectable) at any time during the standard care of treatment for CHC with IFN-α2 or PegIFN-α2 + ribavirin, and maintained it through the end of treatment at week 48 weeks, but HCV-RNA detection occurs before 6 months post-treatment.

The term "chronic" when relating to diseases, refers to diseases which have one or more of the following characteristics: they are permanent, leave residual disability, are caused by nonreversible pathological alteration, require special training of the patient for rehabilitation, or may be expected to require a long period of supervision, observation, or care. (Dictionary of Health Services Management, 2d ed). The acronym CHC refers to Chronic Hepatitis C.

By "chronic hepatitis C (CHC) infection" is meant those patients diagnosed by seropositivity for anti-HCV antibodies or detectable HCV-RNA, in an interval of at least 6 months. The diagnosis of chronic hepatitis C is based on the detection of HCV infection (positive anti-HCV antibodies and HCV RNA) in a patient with signs of chronic hepatitis.

A patient suffering from chronic hepatitis C infection may additionally exhibit, and without being limited to, one or more of the following signs or symptoms: elevated ALT, clinical stigmata of chronic liver disease, hepatocellular damage.

The term "no detectable HCV RNA" or "undetectable HCV RNA" in the present invention means that there is 50 IU/ml or less of HCV RNA levels in a patient serum as measured by quantitative, multi-cycle reverse transcriptase PCR methodology, ideally by a real-time PCR assay such as Abbott RealTime™ HCV and the like.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2a, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2a.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2a, for use as an anti-HCV drug in patients with chronic hepatitis C. Or in other words, the present invention relates to a method of treating patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2a.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in patients with chronic hepatitis C. Or in other words, the present invention relates to a method of treating patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2, for use as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof. Or in other

words, the present invention relates to a method of treating patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2 wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2a, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2a, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2a, for use as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof. Or in other words, the present invention relates to a method of treating patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2a, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof. Or in other words, the present invention relates to a method of treating patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2, for use as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b. Or in other words, the present invention relates to a method of treating patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2 wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2a, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2a, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b. Or in other words, the present invention relates to a method of treating treatment-experienced

patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2a, for use as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b. Or in other words, the present invention relates to a method of treating patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2a, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b. Or in other words, the present invention relates to a method of treating patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b.

Patients with CHC infection of genotype 1 (1a, 1b or mixed 1a/1b) may be confirmed by genotype testing at screening.

The genotypes 1a and 1b of HCV are both well known to one skilled in the art. As a non-limiting example, Holland, J. et al., "Hepatitis C Genotyping by Dire.0
ct Sequencing of the Product …," Pathology, vol. 30, pp.192-195 (1998), identify in Table 2 that the sequences of Genotype 1a and Genotype 1b of HCV are already well known as corroborated by the Genbank/EMBL identification provided for each genotype, respectively, namely, M62321 and D90208. Other literature provides comparable classification information regarding HCV genotypes 1a and 1b, including without limitation Simmonds, K A et al., J. Clin. Microbiol., 31(6), 1493-1503 (1993). Obviously, patients treated may also carry HCV of genotype 2, 3, 4, 5, 6, or any mixed genotype (1/2, 1/3, 1/4, 2/3, 3/4, 3/6), diagnosed by genotypic testing at screening; may also have Hepatitis B virus (HBV) infection based on the presence of HBsAg; may also have Hepatitis A virus (HAV) infection based on the presence of antiHAV-IgM; or may also be positive ELISA for HIV-1 or HIV-2. Also patients may present quasispecies variants of HCV.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2, for use as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT. Or in other words, the present invention relates to a method of treating patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2a, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2a, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients have a genotype of the single nucleotide

polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2a, for use as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT. Or in other words, the present invention relates to a method of treating patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2a, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT. Or in other words, the present invention relates to a method of treating patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2, for use as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT. Or in other words, the present invention relates to a method of treating patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the patients have a genotype of the single nucleotide polymorphism

rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2a, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2a, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2a, for use as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome

19q13 selected from CC, CT, and TT, preferably CT or TT. Or in other words, the present invention relates to a method of treating patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2a, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT. Or in other words, the present invention relates to a method of treating patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2, for use as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT. Or in other words, the present invention relates to a method of treating patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of

IFN-α5 and IFN-α2, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2a, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2a, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2a, for use as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT. Or in other words, the present invention relates to a method of treating patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2a,

wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT. Or in other words, the present invention relates to a method of treating patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

The treatments of the present invention are useful for treating patients for whom treatment for one or more symptoms associated with HCV genotype 1 (1a, 1b or mixed 1a/1b) is indicated, or patients for whom previous interferon therapy, meaning other than the composition comprising IFN-α5 and IFN-α2, has proved ineffective.

By "ineffective," in the context of patients having had previous interferon therapy, meaning other than the composition comprising IFN-α5 and IFN-α2, which proved to be ineffective, the definition of "ineffective" is failure to achieve at least about a 2 log drop versus baseline viral load despite at least twelve weeks of therapy including interferon alone or in combination with other active agents in which the interferon is administered at about 1.5 mcg/kg/week. This definition of "ineffective" further embraces that if the interferon(s) (i.e. IFN-α5 combined with IFN-α2) is or are given in combination therapy, the combination active agent may be ribavirin, or a wide variety of other agents, as well as either the presence or absence of viral rebound after the treatment period deemed to be "ineffective."

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2, wherein the

treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2a, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2a, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2a, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the treatment-experienced patients are selected from non-responders, partial

responders, relapsers, and breakthroughs. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2a, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2a, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2a,

wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients are infected with an HCV genotype selected 1 selected from 1a, 1b, and mixed 1a/1b, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2a, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2a, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13

selected from CC, CT, and TT, preferably CT or TT, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2a, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, and wherein the treatment-experienced patients are selected from non-responders, partial responders,

relapsers, and breakthroughs. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2a, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, and wherein the treatment-

experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2a, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2a, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to the composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to a composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in patients with chronic hepatitis C, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of

about 1.5 MIU, TIW. Or in other words, the present invention relates to a method of treating patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW.

In one embodiment, the present invention relates to a composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW.

In a further embodiment, the present invention relates to a composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1, 2, 3, 4, 5, 6, and mixes thereof, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW. Or in other words, the present invention relates to a method of treating patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients are infected with HCV genotype 1, 2, 3, 4, 5, 6, and mixes thereof, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW.

In a further embodiment, the present invention relates to a composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1, 2, 3, 4, 5, 6, and mixes thereof, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients are infected with HCV genotype 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW.

In a further embodiment, the present invention relates to a composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW. Or in other words, the present invention relates to a method of treating patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW.

In a further embodiment, the present invention relates to a composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW.

In a further embodiment, the present invention relates to a composition comprising IFN-α5 and IFN-α2b, for use as an anti-hepatitis C virus (HCV) drug patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW. Or in other words, the present invention relates to a method of treating patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW.

In a further embodiment, the present invention relates to a composition comprising IFN-α5 and IFN-α2b, for use as an anti-hepatitis C virus (HCV) drug in treatment-experienced patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW.

In a further embodiment, the present invention relates to a composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW. Or in other words, the present invention relates to a method of treating patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients are infected with HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW.

In a further embodiment, the present invention relates to a composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients

are infected with HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW.

In a further embodiment, the present invention relates to a composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW. Or in other words, the present invention relates to a method of treating patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW.

In a further embodiment, the present invention relates to a composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW.

In a further embodiment, the present invention relates to a composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW.

In a further embodiment, the present invention relates to a composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW.

In a further embodiment, the present invention relates to a composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients are infected with an HCV genotype selected

from 1, 2, 3, 4, 5, 6, and mixes thereof, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW.

In a further embodiment, the present invention relates to a composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW.

In a further embodiment, the present invention relates to a composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW.

In a further embodiment, the present invention relates to a composition comprising IFN-α5 and IFN-α2b, for use as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW. Or in other words, the present invention relates to a method of treating treatment-experienced patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2b, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C.

The term "product" is equivalent herein to a "composition", when interpreted under US patent law. The product or composition containing IFN-α5 and IFN-α2 form a functional unity or true combination through a purpose-directed application, i.e. as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C. Obviously, any formulation comprising the product or composition of the invention, may additionally comprises excipients, adjuvants, and any other convenient pharmaceutical ingredients, including other drugs.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in

patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug

in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients have a genotype of

the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the patients have a genotype of the

single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, and wherein

the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, and wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential
l use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof,

and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, and wherein

the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, wherein the patients have a

genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, and wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, and wherein the treatment-

experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV

life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

Anti-HCV drugs encompass compounds selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.
HCV polymerase inhibitors include, but are not limited to, NM283 (valopicitabine), R803, JTK-109, JTK-003, HCV-371, HCV-086, HCV-796 and R-1479.

Inhibitors of HCV proteases (NS2-NS3 inhibitors and NS3-NS4A inhibitors) include, but are not limited to, the compounds of WO02/18369 (see, e.g., page 273, lines 9-22 and page 274, line 4 to page 276, line 11); BILN-2061, VX-950, GS-9132 (ACH-806), SCH-503034, and SCH-6. Further agents that can be used are those disclosed in WO98/17679, WO00/056331 (Vertex); WO 98/22496 (Roche); WO 99/07734, (Boehringer Ingelheim), WO 2005/073216, WO 2005073195 (Medivir) and structurally similar agents.

Inhibitors of other targets in the HCV life cycle, including NS3 helicase; metallo-protease inhibitors; antisense oligonucleotide inhibitors, such as ISIS-14803, AVI-4065 and the like; siRNA's such as SIRPLEX-140-N and the like; vector-encoded short hairpin RNA (shRNA); DNAzymes; HCV specific ribozymes such as heptazyme, RPI.13919 and the like; entry inhibitors such as HepeX-C, HuMax-HepC and the like; alpha glucosidase inhibitors such as celgosivir, UT-231B and the like; KPE-02003002; and BIVN 401.

Immunomodulatory agents include, but are not limited to; natural and recombinant interferon isoform compounds, including IFN-α, IFN-β, IFN-γ, IFN-ω and the like, such as Roferon-A® (recombinant interferon alpha-2a), Canferon-A300®, Advaferon®, Infergen®, Humoferon®, Sumiferon MP®, Alfaferone®, IFN-beta®, Feron®, Berofor® (recombinant interferon alpha-2C), interferon alpha-n1, a purified blend of natural alpha interferons such as Sumiferon available from Sumitomo or as Wellferon interferon alpha-n1 (INS) available from Glaxo-Wellcome; or a

consensus interferon alpha such as those described in Patent Nos. US4897471 and US4695623 (especially Examples 7, 8 or 9 thereof), the specific product available from Amgen; or Alferon® (interferon alpha-n3) which is a mixture of natural interferon alphas. Further versions of interferon include polyethylene glycol derivatized (pegylated) interferon compounds, such as PEG interferon-α-2a (Pegasys®), PEG interferon-α-2b (PEG-Intron®), pegylated IFN-α-con1 and the like; long acting formulations and derivatizations of interferon compounds such as the albumin-fused interferon albuferon α and the like. Further interferons of the beta type include Avonex® or Rebif ® (interferon-beta-1a), Betaseron® (interferon-beta-1b). The IFN-beta-1a in Avonex® is the glycosylated, native human sequence whereas the IFN-beta-1b in Betaseron® is the unglycosylated, serine 17-substituted, native human sequence. Further examples of immunomodulatory agents include compounds that stimulate the synthesis of interferon in cells, such as resiquimod and the like; interleukins; compounds that enhance the development of type 1 helper T cell response, such as SCV-07 and the like; TOLL-like receptor agonists such as CpG-10101 (actilon), isatoribine and the like; thymosin α-1; ANA-245; ANA-246; histamine dihydrochloride; propagermanium; tetrachlorodecaoxide; ampligen; IMP-321; KRN-7000; antibodies, such as civacir, XTL-6865 and the like; and prophylactic and therapeutic vaccines such as InnoVac C, HCV E1E2/MF59 and the like.

Other antiviral agents include, but are not limited to, ribavirin, amantadine, viramidine, nitazoxanide; telbivudine; NOV-205; taribavirin; inhibitors of internal ribosome entry; broad-spectrum viral inhibitors, such as IMPDH inhibitors (e.g., compounds of U.S. Pat. No. 5,807,876, U.S. Pat. No. 6,498,178, U.S. Pat. No. 6,344,465, U.S. Pat. No. 6,054,472, WO97/40028, WO98/40381, WO00/56331, and mycophenolic acid and derivatives thereof, and including, but not limited to VX-950, merimepodib (VX-497), VX-148, and/or VX-944); or combinations of any of the above.

The term "cardiotrophin" refers to the cytokine cardiotrophin-1, a.k.a. CT-1, as well as to cardiotrophin-like cytokines.

The term "oncostatin M" refers to the cytokine a.k.a. OSM, as well as to OSM-like cytokines. OSM was originally isolated from medium conditioned by PMA-treated U-937 human histiocytic leukemia cells based on its ability to inhibit growth of A375 melanoma cells. The human OSM cDNA encodes a 252 amino acid pre-pro-OSM polypeptide with a 25 residue hydrophobic signal peptide and a hydrophilic C-terminal domain that are proteolytically processed to generate the 196 residue mature form of OSM. The listed accession number for this protein can be found in

the publicly available protein database at http://www.expasy.org/uniprot/P13725. The amino acid sequence of human OSM is the following represented by SEQ ID NO. 2:

MGVLLTQRTLLSLVLALLFPSMASMAAIGSCSKEYRVLLGQLQKQTDLMQDTSRLLDPY
IRIQGLDVPKLREHCRERPGAFPSEETLRGLGRRGFLQTLNATLGCVLHRLADLEQRLPK
AQDLERSGLNIEDLEKLQMARPNILGLRNNIYCMAQLLDNSDTAEPTKAGRGASQPPTPT
PASDAFQRKLEGCRFLHGYHRFMHSVGRVFSKWGESPNRSRRHSPHQALRKGVRRTRPS
RKGKRLMTRGQLPR

As used in the present invention, the cytokines CT-1 or OSM relate to the complete native form of said cytokine; or any active fraction of said cytokine, that is, any partial polypeptide sequence of said cytokine which maintains the physiological effects of the complete cytokine claimed in the present invention; and any polypeptide derivative of said cytokine, that is, any polypeptide sequence which has a sequence identity greater than 70% with said native cytokine and maintains the physiological effects of the complete cytokine claimed in the present invention.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, further comprising a third anti-HCV drug

selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 and the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b, further

comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-hepatitis C virus (HCV) drug in patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-hepatitis C virus (HCV) drug in treatment-experienced patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-hepatitis C virus (HCV) drug in patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-hepatitis C virus (HCV) drug in treatment-experienced patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, further comprising a third anti-HCV drug

selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-hepatitis C virus (HCV) drug in patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-hepatitis C virus (HCV) drug in treatment-experienced patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-hepatitis C virus (HCV) drug in patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-hepatitis C virus (HCV) drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, wherein the

patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-hepatitis C virus (HCV) drug in patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-hepatitis C virus (HCV) drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-hepatitis C virus (HCV) drug in patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-hepatitis C virus (HCV) drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-hepatitis C virus (HCV) drug in patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-hepatitis C virus (HCV) drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-hepatitis C virus (HCV) drug in patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, further comprising a third anti-HCV drug selected from an HCV

polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-hepatitis C virus (HCV) drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-hepatitis C virus (HCV) drug in patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b,, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-hepatitis C virus (HCV) drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in

treatment-experienced patients with chronic hepatitis C, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, wherein the treatment-

experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug

in treatment-experienced patients with chronic hepatitis C, wherein the patients are infected with HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in

treatment-experienced patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, wherein the patients are infected with HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, wherein the patients are infected with HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

In a further embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT, wherein the patients are infected with HCV genotype 1 selected from 1a, 1b, and mixed 1a/1b, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

Further embodiments of the present invention, are those mentioned above in respect to the product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C, further comprising a third anti-HCV drug selected from interferon alpha-2a, pegylated interferon alpha-2a, pegylated

interferon alpha-2b, a consensus interferon, a purified interferon alpha product, or a recombinant version thereof.

Further embodiments of the present invention, are those mentioned above in respect to the product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C, further comprising a third anti-HCV drug selected from interferon alpha-2a, pegylated interferon alpha-2a, pegylated interferon alpha-2b, a consensus interferon, a purified interferon alpha product, or a recombinant version thereof.

Further embodiments of the present invention, are those mentioned above in respect to the product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C, further comprising a third anti-HCV drug selected from interferon alpha-2a, pegylated interferon alpha-2a, pegylated interferon alpha-2b, a consensus interferon, a purified interferon alpha product, or a recombinant version thereof.

Further embodiments of the present invention, are those mentioned above in respect to the product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, further comprising a third anti-HCV drug selected from interferon alpha-2a, pegylated interferon alpha-2a, pegylated interferon alpha-2b, a consensus interferon, a purified interferon alpha product, or a recombinant version thereof.

Further embodiments of the present invention, are those mentioned above in respect to the product containing IFN-α5 and IFN-α2a as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, further comprising a third anti-HCV drug selected from interferon alpha-2a, pegylated interferon alpha-2a, pegylated interferon alpha-2b, a consensus interferon, a purified interferon alpha product, or a recombinant version thereof.

Further embodiments of the present invention, are those mentioned above in respect to the product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, further comprising a third anti-HCV drug selected from interferon alpha-2a, pegylated interferon

alpha-2a, pegylated interferon alpha-2b, a consensus interferon, a purified interferon alpha product, or a recombinant version thereof.

Preferred embodiments of the present invention are those mentioned above in respect to the product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in treatment-experienced patients with chronic hepatitis C, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the interferon alpha-2b is administered at a dosage of about 1.5 MIU, TIW.

In one embodiment, the present invention relates to a composition comprising IFN-α5 and IFN-α2b, for use in the treatment of patients infected with HCV, characterized in that the HCV is genotype 1.

In one embodiment, the present invention relates to a composition comprising IFN-α5 and IFN-α2b, for use in the treatment of patients infected with HCV, characterized in that patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

A further embodiment of the present invention relates to a composition comprising IFN-α5 and IFN-α2baccording to any one of the two preceding paragraphs, wherein the HCV infection is chronic.

A further embodiment of the present invention relates to a composition comprising IFN-α5 and IFN-α2b according to any one of the three preceding paragraphs, wherein the patients are treatment-experienced patients.

A further embodiment of the present invention relates to a composition comprising IFN-α5 and IFN-α2b according to the preceding paragraph, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

A further embodiment of the present invention relates to a composition comprising IFN-α5 and IFN-α2b according to any one of thefive preceding paragraphs, wherein the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b.

A further embodiment of the present invention relates to a composition comprising IFN-α5 and IFN-α2b according to any one of the six preceding paragraphs, wherein the IFN-α5 is

administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW).

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, in the treatment of patients infected with hepatitis C virus (HCV), characterized in that the HCV is genotype 1.

In one embodiment, the present invention relates to a product containing IFN-α5 and IFN-α2b as a combined preparation for simultaneous, separate, or sequential use, in the treatment of patients infected with hepatitis C virus (HCV), characterized in that patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT, preferably CT or TT.

A further embodiment of the present invention relates to the product according to any one of the two preceding paragraphs, wherein the HCV infection is chronic.

A further embodiment of the present invention relates to the product according to any one of the three preceding paragraphs, wherein the patients are treatment-experienced patients.

A further embodiment of the present invention relates to the product according to the preceding paragraph, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

A further embodiment of the present invention relates to the product according to any one of the five preceding paragraphs, wherein the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b.

A further embodiment of the present invention relates to the product according to any one of the six preceding paragraphs, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

A further embodiment of the present invention relates to the product according to the preceding paragraph, wherein the third anti-HCV drug is selected from interferon alpha-2a, pegylated

interferon alpha-2a, pegylated interferon alpha-2b, a consensus interferon, a purified interferon alpha product, and a recombinant version thereof..

A further embodiment of the present invention relates to the product according to any one of the eight preceding paragraphs, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the interferon alpha-2b is administered at a dosage of about 1.5 MIU, TIW.

To practice the invention, IFN-α5 with either IFN-α2a or IFN-α2b, preferably IFN-α2b, and optionally a third anti-HCV drug as mentioned above, are administered to the patient, as defined in any one of the embodiments above, in a sufficiently effective amount.

IFN-α5, IFN-α2a, and IFN-α2b may be formulated into various pharmaceutical forms for administration purposes. As appropriate compositions there may be cited all compositions usually employed for systemically administering drugs. To prepare the pharmaceutical compositions of this invention, effective amounts of IFN-α5, either IFN-α2a or IFN-α2b, preferably IFN-α2b, and optionally a third anti-HCV drug as mentioned above, as the active ingredients, are combined in intimate admixture with a pharmaceutically acceptable carrier, which carrier may take a wide variety of forms depending on the manner of preparation desired for administration. These pharmaceutical compositions are desirable in unitary dosage form suitable, particularly, for administration orally, rectally, transdermally, by inhalation, or by parenteral routes (i.e., subcutaneous, intravenous, intramuscular, or intraperitoneal). IFN-α5, either IFN-α2a or IFN-α2b, and optionally a third anti-HCV drug, can be administered by the oral route in solid dosage forms, such as tablets, capsules, and powders, or in liquid dosage forms, such as elixirs, syrups, and suspensions. The pharmaceutical compositions of this invention can also be administered parenterally, in sterile liquid dosage forms. Preferred routes of administration are those parenteral routes, particularly by intramuscular, intravenous, or subcutaneous injections.

Formulations for parenteral administration may be in the form of aqueous or non-aqueous isotonic sterile injection solutions or suspensions. Injectable solutions, for example, may be prepared, in which the carrier comprises saline solution, glucose solution or a mixture of saline and glucose solution. Injectable suspensions may also be prepared in which case appropriate liquid carriers, suspending agents and the like may be employed. Also included are solid form preparations that are intended to be converted, shortly before use, to liquid form preparations. In the compositions suitable for percutaneous administration, the carrier optionally comprises a penetration-enhancing agent and/or a suitable wetting agent, optionally combined with suitable

additives of any nature in minor proportions, which additives do not introduce a significant deleterious effect on the skin. These latter suitable additives may be anti-oxidants, preservatives, stabilizing agents, emulsifiers, salts for influencing the osmotic pressure, and/or buffer substances.

Alternatively, IFN-α5, either IFN-α2a or IFN-α2b, preferably IFN-α2b, and optionally a third anti-HCV drug, may be may be delivered to the epithelial cells formulated in liposomes. Liposomes can be prepared using conventional techniques including sonication, chelate dialysis, homogenization, solvent infusion coupled with extrusion, freeze-thaw extrusion, microemulsification, as well as others. Reagents used to crosslink a liposome or other lipid-containing agent to the proteins of the present invention comprise a phospholipid derivative to anchor one end of the crosslink in the lipid layer and a reactive group at the other end to provide a point of attachment to the target biomolecule. Polymerized liposomes or liposomes coated with polymer may as well be used. Such polymers may stabilize the liposome, reduce its clearance from the body, and/or reduce its immunogenicity. The liposome may be loaded with a functional moiety such as a diagnostic or therapeutic agent either during or after its formation. The agent may be contained in an aqueous core of the liposome or can be incorporated into or attached to its surrounding membrane.

It is especially advantageous to formulate the aforementioned pharmaceutical compositions in unit dosage form for ease of administration and uniformity of dosage. Unit dosage form as used herein refers to physically discrete units suitable as unitary dosages, each unit containing a predetermined quantity of active ingredient calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier. Examples of such unit dosage forms are tablets (including scored or coated tablets), capsules, pills, suppositories, powder packets, wafers, injectable solutions or suspensions and the like, and segregated multiples thereof.

The daily dosage of the compounds according to the invention shall vary with the mode of administration, the treatment desired, and the severity of the disorder.

In general it is contemplated that an effective amount of IFN-α5 would be from 1 to 10 MIU daily or three times a week, preferably from 1 to 5 MIU daily or three times a week, more preferably at a dosage of 3 MIU three times a week. When IFN-α5 is administered in combination with interferon alpha-2b, its preferred dosage is 1.5 MIU, TIW, and the interferon alpha-2b is administered at a dosage of about 1.5 MIU, TIW.

IFNα2a is usually administered at 11.1μg/0.5mL, 22.2μg/0.5mL, 33.3μg/0.5mL, daily or three times a week. IFNα2b is usually administered at 0.038mg/1mL, 0.069mg/1mL, 0.087mg/1.5mL, 0.144mg/1.5mL, 0.192mg/1mL, 0.288mg/1.5mL, by injection three or five times a week. IFNβ1a is usually administered at 8.8μg/0.5mL, 22μg/0.5mL, or 44μg/0.5mL injected subcutaneously three times per week. IFNβ1b is usually administered at 0.0625mg / 0.25mL and increased to 0.25mg/1mL injected subcutaneously every other day.

The recommended dosage of INTRON-A interferon alpha 2b (commercially available from Schering-Plough Corp.) as administered by subcutaneous injection at 3MIU(12 mcg)/0.5 mL/TIW is for 24 weeks or 48 weeks for first time treatment. The recommended dosage of PEG-INTRON interferon alpha 2b pegylated (commercially available from Schering-Plough Corp.) as administered by subcutaneous injection at 1.5 mcg/kg/week, within a range of 40 to 150 mcg/week, is for at least 24 weeks. The recommended dosage of ROFERON A interferon alpha 2a (commercially available from Hoffmann-La Roche) as administered by subcutaneous or intramuscular injection at 3MIU(11.1 mcg/mL)/TIW is for at least 48 to 52 weeks, or alternatively 6MIU/TIW for 12 weeks followed by 3MIU/TIW for 36 weeks. The recommended dosage of PEGASUS interferon alpha 2a pegylated (commercially available from Hoffmann-La Roche) as administered by subcutaneous injection at 180 mcg/1 mL or 180 mcg/0.5 mL is once a week for at least 24 weeks. The recommended dosage of INFERGEN interferon alphacon-1 (commercially available from Amgen) as administered by subcutaneous injection at 9 mcg/TIW is for 24 weeks for first time treatment and up to 15 mcg/TIW for 24 weeks for non-responsive or relapse treatment. Optionally, ribavirin, a synthetic nucleoside analogue with activity against a broad spectrum of viruses including HCV, can be included in combination with IFN-α5 and IFN-α2b. The recommended dosage of ribavirin is in a range from 600 to 1400 mg per day for at least 24 weeks (commercially available as Rebetol ribavirin from Schering-Plough or Copegus ribavirin from Hoffmann-La Roche).

It may be appropriate to administer the required dose as one, two, three, four or more sub-doses at appropriate intervals throughout the day. Furthermore, it is evident that said effective daily amount may be lowered or increased depending on the response of the treated subject and/or depending on the evaluation of the physician prescribing the compounds of the instant invention. The effective daily amount ranges mentioned hereinabove are therefore only guidelines.

The following examples are intended to illustrate the present invention and not to limit it thereto.

Examples

The following is an extract of a protocol and results of a human research study conducted according to international standards of Good Clinical Practice (International Conference on Harmonization Guidelines), applicable government regulations, local research policies and procedures, and in accordance with the Contract Research Organization (CRO) standard operating procedures (SOPs). Information about study subjects was kept confidential and managed according to local law requirement on subject data protection (Ley Orgánica 15/1999, de 13 de Diciembre, de Protección de Datos de Carácter Personal, Spain).

A randomised, open, active controlled, multicentre trial, phase I/II that included treatment-experienced relapser patients with CHC-infection of genotype 1 was performed. The clinical endpoints of the study where directed to compare the antiviral efficacy between three arms:

- Arm A: IFN-α5 for 29 days in monotherapy at an an initial dose of 3 MIU administered subcutaneously, 3 times a week;
- Arm B: IFN-α5 + IFN-α2b for 29 days in combined therapy at the same total dose of 3 MIU divided into equal doses of 1.5 MIU of IFN-α5 and 1.5 MIU of IFN-α2b, administered subcutaneously of each agent, 3 times a week; and
- Arm C (active-controlled group): IFN-α2b for 29 days in monotherapy at doses of 3 MIU administered subcutaneously, 3 times a week. IFN-α2b has proven efficacy in achieving SVR in CHC infected patients against placebo.

The selection of patients for the clinical study was based on the following inclusion criteria:

- Patients aged ≥18 years old.
- With chronic hepatitis C (CHC) infection diagnosed by seropositivity for anti-HCV antibodies or detectable HCV-RNA, at least 6 months prior to screening.
- Patients with CHC infection of genotype 1 (1a, 1b or mixed 1a/1b) confirmed by genotype testing at screening.
- Defined as relapsers: those CHC patients who had achieved viral response (HCV-RNA non-detectable) at any time during the standard care of treatment for CHC with IFN-α2 or PegIFN-α2 + ribavirin, and maintained it through the end of treatment at week 48 weeks, but HCV-RNA detection occured before 6 months post-treatment.
- In whom liver cirrhosis had been ruled out through fibro-scan or liver biopsy within 24 months prior to study enrolment.
- With a serum HCV viral load ≥ 100.000 IU/mL at screening.
- With alaninaminotransferase (ALT) and aspartate-aminotransferase (AST) serum measurements at screening less than 5 times of their upper limits of normal (ULN).
- With a body mass index (BMI) of at least 18 kg/m2, but not exceeding 36 kg/m2.

- For female subjects with childbearing potential: use of a known highly effective method of birth control, defined as those which results in a low failure rate: i.e. less 1% per year, (contraceptive pills, intrauterine contraceptive device, implants, vasectomized partner or sexual abstinence), for at least three consecutive months prior to the study, during the study and one month after the end of the study.
- For male subjects with partners of child bearing potential: use of appropriate contraceptive methods (vasectomy, condoms or sexual abstinence), for at least study period and one month after the end of the study.
- Was able to effectively communicate with the investigator and other testing center personnel.
- Was able to participate and willing to give written informed consent and comply with the study restrictions.

The withdrawal of patients for the clinical study was based on the following exclusion criteria:
- Hepatitis C infection of genotype 2, 3 or 4 or any mixed genotype (1/2, 1/3 and 1/4), diagnosed by genotypic testing at screening.
- A positive ELISA for HIV-1 or HIV-2.
- Hepatitis B virus (HBV) infection based on the presence of HBsAg.
- Descompensated liver disease, or history of decompensated liver disease, as evidenced by ascites, portal hypertension, jaundice or hepatic encephalopathy, coagulopathy, varices, history of variceal bleeding or any other clinical evidence of decompensation.
- History or other evidence of a medical condition associated with decompensated renal disease, immunologically mediated disease, chronic pulmonary disease, cardiac disease, thyroid disease, severe retinopathy, severe psychiatric disease, organ transplantation, cancer, seizure disorder or pancreatitis.
- An active or suspected malignancy or history of malignancy within the last 5 years (with the exception of appropriately treated basal cell carcinoma or in situ carcinoma of the uterine cervix).
- Patients with a documented drug and alcohol addiction free history of at least 12 months who were, in the opinion of the investigator unlikely to relapse, could be enrolled in the study.
- Positive results for drug abuse at screening.
- Haemoglobin <12.0g/dL for women, and <13.0g/dL for men at screening.
- White blood cell count <2000 cells/mm3 at screening.
- Absolute neutrophil count <1500 cells/mm3 at screening.
- Platelet count <100.000 cells/mm3 at screening.
- ALT and AST levels ≥ 5 xULN at screening.
- Prothrombin time INR (International Normalised Ratio) prolonged to 1.5xULN at screening.

- TSH an T4 outside normal limits and not adequately controlled thyroid function at screening; patients with TSH below the lower limit of normal could be enrolled if free T4 was normal and there was no clinical evidence of hyperthyroidism or hypothyroidism.
- Poorly controlled diabetes mellitus as evidenced by HbA1c >7.5% at screening.
- Alfa-fetoprotein value >100ng/mL at screening. If >20ng/mL and ≤100 ng/mL, patients could be included if there was no evidence of liver cancer in two congruent imaging studies (e.g. ultrasound, CT scan, MRI) within 6 months past from first visit.
- Total bilirrubin >1.5xULN with ratio of direct/indirect >1, at screening unless predominantly conjugated and reflecting Gilbert's disease.
- Estimated creatinine clearance of 30 mL/minute or less at screening.
- Women who were confirmed to be pregnant.
- People who had participated in another clinical trial in the last 4 weeks or with known hypersensitivity to any ingredient of the investigational agents.
- Patients who were at risk of bleeding (NSAIDs therapy, anticoagulant therapy, vitamin K deficienty, known coagulopathy, haemophilia).
- Haemoglobinopathy (e.g. thalassemia major or sickle cell anaemia).
- Screening ECG QTc value ≥ 450ms and/or clinically significant ECG findings.
- History of clinically significant drug allergies.
- Participation in a clinical study with an investigational drug, biologic, or device within 3 months prior to anticipated dose administration.
- Any chronic viral (including HSV), bacterial, mycobacterial, fungal, parasitic, or protozoal infection.
- Requirement for chronic systemic corticosteroids. Nasal or pulmonary steroids would be allowed.
- Receiving systemics antivirals, hematopoietic growth factor, or inmunomodulatory treatment within 30 days prior to enrolment.

The selected patients were administered Interferon-α5 as solution for subcutaneous injection was provided by study sponsor, Digna Biotech (Spain), and manufactured by Rentschler Biotechnologie GmbH (Germany), in a pre-filled syringe 1.0 mL. One syringe contained 9 MIU/0.6 ml solution for injection, which was 3 MIU in 0.2 mL.

The administered Interferon-α5 was a recombinant human protein IFN-α5, 167 amino acids long, and with the sequence (SEQ ID NO 3):

MCDLPQTHSLSNRRTLMIMAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLH
EMIQQTFNLFSTKDSSATWDETLLDKFYTELYQQLNDLEACMMQEVGVEDTPLMNVDS
ILTVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSLSANLQERLRRKE

Interferon-α2b (IntronA®), as solution for subcutaneous injection, was provided by study sponsor, Digna Biotech (Spain), and was obtained from Shering Plough (USA), in Multidose Pens for Injection 1.5 mL. One pen of Strength 3 MIU, contained 6 doses, 0.2 mL each. 3 MIU in 0.2 mL.

Eligible patients were randomised to one of the three treatment arms at Visit -1. The CRO was the provider of the randomization used in this trial. Patients were randomly assigned between the three available arms, depending on study phase.

In order to compare the antiviral efficacy of the three different treatments, a time-dependent decrease in viral load at day 29 versus day 1 was measured for each of the arms.

Viral load measurements were conducted in patients serum samples obtained at each visit. Detailed instructions for obtaining, handling, and shipping viral load measurement samples were duly provided. Samples were processed by Central Laboratory Services using an assay with a lower limit of quantification of 30 IU/mL.

The preliminary clinical data resulting from the human research study is exhibited in the following tables 1, 2, and 3.

Table 1. Per Protocol, patients, per treatment group.
Treatment Arm, patient number, result of nucleotide sequence (CC, CT or TT) near the gene encoding IL28B, HCV Log scale viral load on day 1 –before treatment- and day 29 of treatment, and viral load decrease per patient.

TREATMENT	Patient Number	IL28b	VL log Day 1	VL log Day 29	VL log change Day 29 vs Day 1
ARM A IFN-α5					
	1002	CC	5.73	3.65	-2.08
	3045	CT	6.07	6.27	0.20
	4062	TT	5.05	5.58	0.53
	4065	CT	6.07	5.91	-0.16
	5086	CC	5.36	3.70	-1.66

	14261	TT	5.69	4.71	-0.98
	13241	CT	6.51	6.07	-0.44
	13242	CC	6.46	5.09	-1.37
	4068	CT	5.61	5.12	-0.49
	10185	CT	6.96	6.97	0.01
	12224	CC	7.32	5.49	-1.83
	13245	CT	6.47	5.68	-0.79
	13246	CT	6.75	6.31	-0.44
ARM B **IFN-α5 + IFN-α2b**	1003	CC	6.38	5.23	-1.15
	3042	CT	6.74	5.82	-0.92
	3043	CT	5.61	5.55	-0.06
	4061	CC	6.49	5.20	-1.29
	4066	CT	5.86	5.76	-0.10
	5084	CC	6.31	4.25	-2.06
	16302	TT	5.53	3.68	-1.85
	14262	CT	7.52	6.95	-0.57
	4069	CT	5.61	4.63	-0.98
	10184	CT	6.69	6.83	0.14
	12223	CT	6.82	5.65	-1.17
	8141	CT	6.51	6.16	-0.35
	10186	CT	6.26	6.20	-0.06
	16307	CT	4.83	3.35	-1.48
ARM C **IFN-α2b**	2021	TT	5.23	4.88	-0.35
	2022	CT	5.81	5.85	0.04
	3041	CT	5.72	5.51	-0.21
	3044	CC	6.33	2.60	-3.73
	3046	CT	5.82	5.72	-0.10
	5087	CT	6.22	6.20	-0.02
	13243	CT	5.60	5.75	0.15
	6101	CC	6.97	4.29	-2.68
	9161	CC	5.86	2.39	-3.47
	10181	CT	6.31	6.49	0.18
	10182	CT	6.66	6.59	-0.07
	12222	CT	6.59	5.86	-0.73
	6102	CT	6.31	5.87	-0.44
	13244	CT	6.50	5.29	-1.21

Table 2. Per Protocol, CT and TT patients, per treatment group.

Treatment Arm, patient number, result of nucleotide sequence (CT or TT) near the gene encoding IL28B, HCV Log scale viral load on day 1 –before treatment- and day 29 of treatment, and viral load decrease per patient

TREATMENT	Patient Number	IL28b	VL log Day 1	VL log Day 29	VL log change Day 29 vs Day 1
ARM A IFN-α5	3045	CT	6.07	6.27	0.20
	4062	TT	5.05	5.58	0.53
	4065	CT	6.07	5.91	-0.16
	14261	TT	5.69	4.71	-0.98
	13241	CT	6.51	6.07	-0.44
	4068	CT	5.61	5.12	-0.49
	10185	CT	6.96	6.97	0.01
	13245	CT	6.47	5.68	-0.79
	13246	CT	6.75	6.31	-0.44
	Mean (SD)	6.13 (0.61)	5.85 (0.67)	-0.28 (0.48)	
ARM B IFN-α5 + IFN-α2b	3042	CT	6.74	5.82	-0.92
	3043	CT	5.61	5.55	-0.06
	4066	CT	5.86	5.76	-0.10
	16302	TT	5.53	3.68	-1.85
	14262	CT	7.52	6.95	-0.57
	4069	CT	5.61	4.63	-0.98
	10184	CT	6.69	6.83	0.14
	12223	CT	6.82	5.65	-1.17
	8141	CT	6.51	6.16	-0.35
	10186	CT	6.26	6.20	-0.06
	16307	CT	4.83	3.35	-1.48
	Mean (SD)	6,18 (0.77)	5,51 (1.17)	-0,67 (0.66)	
ARM C IFN-α2b	2021	TT	5.23	4.88	-0.35
	2022	CT	5.81	5.85	0.04
	3041	CT	5.72	5.51	-0.21
	3046	CT	5.82	5.72	-0.10
	5087	CT	6.22	6.20	-0.02
	13243	CT	5.60	5.75	0.15
	10181	CT	6.31	6.49	0.18
	10182	CT	6.66	6.59	-0.07
	12222	CT	6.59	5.86	-0.73

	6102	CT	6.31	5.87	-0.44
	13244	CT	6.50	5.29	-1.21
	Mean (SD)	6.07 (0.46)	5.82 (0.50)	-0.25 (0.42)	

Table 3. Per Protocol CT and TT patients grouped by monotherapy or combined therapy. Treatment Arm, patient number, result of nucleotide sequence (CT or TT) near the gene encoding IL28B, HCV Log scale viral load on day 1 –before treatment- and day 29 of treatment, and viral load decrease per patient.

TREATMENT	Patient Number	IL28b	VL log Day 1	VL log Day 29	VL log change Day 29 vs Day 1
Grouped	3045	CT	6.07	6.27	0.20
	4062	TT	5.05	5.58	0.53
ARM A	4065	CT	6.07	5.91	-0.16
IFN-α5	14261	TT	5.69	4.71	-0.98
and	13241	CT	6.51	6.07	-0.44
ARM C	4068	CT	5.61	5.12	-0.49
IFN-α2b	10185	CT	6.96	6.97	0.01
both as	13245	CT	6.47	5.68	-0.79
monotherapy	13246	CT	6.75	6.31	-0.44
	2021	TT	5.23	4.88	-0.35
	2022	CT	5.81	5.85	0.04
	3041	CT	5.72	5.51	-0.21
	3046	CT	5.82	5.72	-0.10
	5087	CT	6.22	6.20	-0.02
	13243	CT	5.60	5.75	0.15
	10181	CT	6.31	6.49	0.18
	10182	CT	6.66	6.59	-0.07
	12222	CT	6.59	5.86	-0.73
	6102	CT	6.31	5.87	-0.44
	13244	CT	6.50	5.29	-1.21
	Mean (SD)		6.10 (0.52)	5.83 (0.57)	-0.27 (0.43)
ARM B					
IFN-α5 + IFN-α2b	3042	CT	6.74	5.82	-0.92
	3043	CT	5.61	5.55	-0.06
	4066	CT	5.86	5.76	-0.10

	16302	TT	5.53	3.68	-1.85
	14262	CT	7.52	6.95	-0.57
	4069	CT	5.61	4.63	-0.98
	10184	CT	6.69	6.83	0.14
	12223	CT	6.82	5.65	-1.17
	8141	CT	6.51	6.16	-0.35
	10186	CT	6.26	6.20	-0.06
	16307	CT	4.83	3.35	-1.48
	Mean (SD)		6.18 (0.77)	5.51 (1.17)	-0.67 (0.66)

It was found, see Table 1, that in treatment Arm A, 6 out of 13 patients reached a viral load decreased ≥ 0.5 Log scale in treatment day 29 compared with day 1 -before treatment initiation-, 9 out of 14 patients in treatment Arm B, and 5 out of 14 patients in treatment Arm C, for patients with a CC, CT or TT nucleotide sequence in the polymorphism located in chromosome 19, close to the region coding for IL28B.

It was found, see Table 2, that in treatment Arm A, 2 out of 9 patients reached a viral load decreased ≥ 0.5 Log scale in treatment day 29 compared with day 1 -before treatment initiation-, 6 out of 11 patients in treatment Arm B, and 2 out of 11 patients in treatment Arm C, for patients with a CT or TT nucleotide sequence in the polymorphism located in chromosome 19, close to the region coding for IL28B.

It was found, see Table 3, that the combined therapy in Arm B, IFN-α5 plus IFN-α2b, results in 6 out of 11 patients reaching a viral load decreased ≥ 0.5 Log scale, in treatment day 29 compared with day 1, in comparison with 4 out of 20 patients in the grouped A and C monotherapy arms, for patients with a CT or TT nucleotide sequence in the polymorphism located in chromosome 19, close to the region coding for IL28B. Comparisons of response between treatments were performed estimating difference of proportions by means 95% confidence interval (Newcombe recommended method). The difference in proportions, 0.345, was significant at 0.05 level (95% confidence interval: 0 .0033, 0.615).

In Arm B, IFN-α5 plus IFN-α2b, see Table 3, the change in HCV viral load in Log scale, in treatment day 29 compared with day 1, was -0.67 (0.66) [mean (SD), n=11], in comparison with -0.27 (0.43) [mean (SD), n=20], in the grouped A and C monotherapy arms. Comparisons of mean values between treatments were made using Student-t test and difference of means were

estimated by means of 95% confidence intervals. A marginally significant statistical difference was found when comparing treatment means (P = 0.046).

All two-sided statistical tests were done at 0.05 level. All analyses were done with SAS 9.3.

It was concluded that treatment B (i.e. the combination of IFN-α5 + IFN-α2b) showed the best results in the rate of patients reaching more than 0.5 Log HCV viral load decrease in treatment at day 29, and also in the total decrease of viral load at day 29 of treatment, in patients with a CT or TT nucleotide sequence in the polymorphism located in chromosome 19, close to the region coding for IL28B.

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Claims

1. A composition comprising IFN-α5 and IFN-alpha2 (IFN-α2), for use as an anti-hepatitis C virus (HCV) drug in patients with chronic hepatitis C.

2. The composition according to claim 1, wherein the patients are treatment-experienced patients.

3. The composition according to any one of claims 1-2, wherein IFN-alpha2 is selected from IFN-alpha2a (IFN-α2a) and IFN-alpha2b (IFN-α2b).

4. The composition according to any one of claims 1-3, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof.

5. The composition according to claim 4, wherein the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b.

6. The composition according to any one of claims 1-5, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT.

7. The composition according to any one of claims 2-6, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

8. The composition according to any one of claims 3-7, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW).

9. A product containing IFN-α5 and IFN-α2 as a combined preparation for simultaneous, separate, or sequential use, as an anti-HCV drug in patients with chronic hepatitis C.

10. The product according to claim 9, wherein the patients are treatment-experienced patients.

11. The product according to any one of claims 9-10, wherein IFN-alpha2 is selected from IFN-alpha2a (IFN-α2a) and IFN-alpha2b (IFN-α2b).

12. The product according to any one of claims 9-11, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof.

13. The product according to claim 12, wherein the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b.

14. The product according to any one of claims 9-13, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT.

15. The product according to any one of claims 10-14, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

16. The product according to any one of claims 9-15, further comprising a third anti-HCV drug selected from an HCV polymerase inhibitor, an HCV protease inhibitor, an inhibitor of another target in the HCV life cycle, and immunomodulatory agent, an antiviral agent, cardiotrophin, oncostatin M, and combinations thereof.

17. The product according to claim 16, wherein the third anti-HCV drug is selected from interferon alpha-2a, pegylated interferon alpha-2a, pegylated interferon alpha-2b, a consensus interferon, a purified interferon alpha product, or a recombinant version thereof.

18. The product according to any one of claims 11-17, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW.

19. A method of treating patients with chronic hepatitis C, said method comprising the administration of a therapeutically effective amount of IFN-α5 and IFN-α2.

20. The method according to claim 19, wherein the patients are treatment-experienced patients.

21. The method according to any one of claims 19-20, wherein IFN-alpha2 is selected from IFN-alpha2a (IFN-α2a) and IFN-alpha2b (IFN-α2b).

22. The method according to any one of claims 19-21, wherein the patients are infected with an HCV genotype selected from 1, 2, 3, 4, 5, 6, and mixes thereof.

23. The method according to claim 22, wherein the HCV genotype 1 is selected from 1a, 1b, and mixed 1a/1b.

24. The method according to any one of claims 19-23, wherein the patients have a genotype of the single nucleotide polymorphism rs12979860 on chromosome 19q13 selected from CC, CT, and TT.

25. The method according to any one of claims 20-24, wherein the treatment-experienced patients are selected from non-responders, partial responders, relapsers, and breakthroughs.

26. The method according to any one of claims 21-25, wherein the IFN-α5 is administered at a dosage of about 1.5 MIU, TIW, and the IFN-α2b is administered at a dosage of about 1.5 MIU, TIW.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2012/062128

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K38/21
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, BIOSIS, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP 1 077 068 A1 (INST CIENTIFICO TECNOL NAVARRA [ES] FUNDACION PARA LA INVESTIGACIO [ES]) 21 February 2001 (2001-02-21) paragraph [0043]; claim 2	1-26
Y	US 2010/297080 A1 (BERTELSEN ARTHUR [US] ET AL) 25 November 2010 (2010-11-25) paragraph [0128]; claims 1,14,15	1-26
Y	US 2011/027229 A1 (VAN ANTWERP WILLIAM P [US] ET AL) 3 February 2011 (2011-02-03) paragraph [0106]; claims 1,2,7	1-26

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
21 August 2012	04/09/2012

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Bochelen, Damien

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	LARREA ESTHER ET AL: "IFN-alpha5 mediates stronger Tyk2-stat-dependent activation and higher expression of 2',5'-oligoadenylate synthetase than IFN-alpha2 in liver cells", JOURNAL OF INTERFERON AND CYTOKINE RESEARCH, vol. 24, no. 8, August 2004 (2004-08), pages 497-503, XP002682080, ISSN: 1079-9907 pages 499,502; figure 5 -----	1-26
Y	KOYAMA T ET AL: "Divergent activities of interferon-alpha subtypes against intracellular hepatitis C virus replication", HEPATOLOGY RESEARCH, AMSTERDAM, NL, vol. 34, no. 1, 1 January 2006 (2006-01-01), pages 41-49, XP028036682, ISSN: 1386-6346, DOI: 10.1016/J.HEPRES.2005.10.005 [retrieved on 2006-01-01] page 46; figures 2,3 -----	1-26

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2012/062128

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

   a. (means)

   [ ] on paper

   [X] in electronic form

   b. (time)

   [X] in the international application as filed

   [ ] together with the international application in electronic form

   [ ] subsequently to this Authority for the purpose of search

2. [ ] In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2012/062128

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