PATENT SITUATION OF KEY PRODUCTS
FOR TREATMENT OF HEPATITIS C

DACLATASVIR

WORKING PAPER

Prepared for the
World Health Organization (WHO) by
Thomson Reuters

Revised version October 2014

World Health Organization

This report was prepared for the WHO Department of Essential Medicines and Health Products by Thomson Reuters. It is available for free download: http://www.who.int/phi/en/. If you have questions or feedback, please write to phidepartment@who.int.

WHO/HIS/EMP/PHI/14.1

INTRODUCTION

The World Health Organization's (WHO) 2014 *Guidelines for the screening, care and treatment of persons with hepatitis C infection* state that worldwide more than 185 million people are infected with the hepatitis C virus (HCV). Of these people, 350 000 to 500 000 die each year. An estimated one third of those who become chronically infected develop liver cirrhosis or hepatocellular carcinoma. HCV infection can be cured, but most people infected with the virus are unaware of their infection and so do not seek timely treatment. Furthermore, treatment remains unavailable for many who have been diagnosed. Several medicines are available to treat HCV, including pegylated interferon and ribavirin but treatment duration is long, involves weekly injections, and side effects are considerable. With the development of new direct-acting antivirals, the treatment landscape is rapidly changing. These new antivirals are expected to reach cure rates of more than 90% in persons with HCV infection across different genotypes, with fewer side effects and a shorter duration of treatment.[1] Two new compounds, simeprevir and sofosbuvir, have recently been approved in the United States and Europe and are recommended by the new WHO treatment guidelines. Many others are in various stages of development.

Resolution WHA67.6 adopted by the Sixty-Seventh World Health Assembly, requested the Director-General "to work with national authorities, upon their request, to promote comprehensive, equitable access to prevention, diagnosis and treatment for viral hepatitis" and "to assist Member States to ensure equitable access to quality, effective, affordable and safe hepatitis B and HCV treatments and diagnostics, in particular in developing countries". Ensuring access to new treatments is a challenging task. In order for countries to identify ways of increasing access and affordability of new HCV medicines, they need clarity about patent status. To assess whether a medicine is patent protected in a certain country requires expert knowledge and access to specialized databases that are not easily available. The WHO Global strategy and plan of action on public health, innovation and intellectual property provides WHO with a mandate to support efforts to determine the patent status of health products (element 5.1c). Despite the possibility of filing patents under the World Intellectual Property Organization (WIPO) Patent Cooperation Treaty (PCT) in 148 jurisdictions, there is no such thing as a worldwide patent. Patents are granted individually under each jurisdiction, depending on the national patent law and the outcome of the examination process. National patents that relate to the same basic patent (i.e. the same invention) are called family members and together build a patent family. In the present study, patent families are based on the Derwent World Patent Index (DWPI).[2]

[1] Guidelines for the screening, care and treatment of persons with hepatitis C infection. Geneva: World Health Organization; 2014 (http://www.who.int/hiv/pub/hepatitis/hepatitis-c-guidelines/en, April 2014).

[2] The Derwent World Patents Index (or DWPI) is a database containing patent applications. Each patent family is grouped around a basic patent, which is usually the first published example of the invention.

The WHO Secretariat has mandated Thomson Reuters to carry out an analysis of the patent situation of seven new hepatitis treatments[3]:

International nonproprietary name	Sponsor
ABT-450	AbbVie Inc.
daclatasvir	Bristol-Myers Squibb Company
dasabuvir	AbbVie Inc.
ledipasvir	Gilead Sciences, Inc.
ombitasvir	AbbVie Inc.
simeprevir	Janssen Pharmaceutical Companies of Johnson & Johnson
sofosbuvir	Gilead Sciences Inc.

The draft reports were shared with the respective sponsor companies before publication.

OBJECTIVE

The objective of the patent working papers was to:

(1) identify the most relevant patents with respect to the medicines
(2) identify in which countries these patents have been filed and granted

One will often find numerous patents relating to one medicine. These patents will cover different aspects and innovations around the same product. Not all however are equally relevant, as many will cover variations or production processes but would not prevent somebody else to produce the medicine, e.g. by using a different process.

These patent working papers identify the most relevant patents for each medicine. The patents are categorized in primary and secondary patents. The patent publication covering the base compound is considered the “primary patent” and patents on specific pharmaceutical formulations, method of use, product derivatives, and processes are considered “secondary patents”. Secondary patents are generally easier to circumvent (“to invent around”), meaning to make the medicine without infringing the secondary patents. For example, a patent on the aqueous solution would not prevent competitors to produce a tablet, and a combination patent would not prevent competitors to produce the combined products separately.

[3] Initially two additional candidate medicines were included in the project (faldaprevir and deleobuvir), but development of these has been discontinued and thus the patent landscapes were not finalized.

The following are different types of patents:

Product patents claim the chemical molecule/the active pharmaceutical ingredient. Product patents are usually the strongest patents as the patent holder can use product claims to prevent others from making, selling, or importing the chemical product.

Product-by-process patents define the product by its process of preparation.

Process patents claim a (new) production process for an active pharmaceutical ingredient.

Formulation patents relate to the specific dosage form (e.g. coated tablet, soft gel capsule, syrup etc.).

Combination patents claim the combination of new or existing medicines.

Patents on product derivatives claim a specific form or derivative, e.g. a salt of an existing compound.

Patents containing Markush claims refer to a chemical structure with multiple alternatives in a format such as "chemical compound A wherein X^1 is selected from a group consisting of a, b and c".

This list is simplified and not exhaustive. Detailed explanations can be found in Philip Grubb, Peter Thomsen, *Patents for Chemicals, Pharmaceuticals, and Biotechnology*, 5th Edition Oxford 2010 as well as in the patenting guidelines of the respective national or regional patent offices.

Interpretation of patentability criteria varies, in particular with respect to the so-called secondary patents. Some jurisdictions are more restrictive to prevent a proliferation of secondary patents covering minor modifications of existing medicines. In those jurisdictions, for example India and Argentina, many of the secondary patents may not be granted as they do not fulfil their specific requirements. Further information can be found in the draft *Guidelines for the examination of pharmaceutical patents: developing a public health perspective* which provides detailed information on the different forms of patents in the pharmaceutical sector (www.who.int/phi/publications/category/en/).

HOW TO USE THIS WORKING PAPER?

The working papers identify the relevant patents and provide data where these patents have been filed or granted. They allow countries to carry out a first assessment on whether a medicine is patent protected and to assess their possibilities for rendering the new treatments more affordable. The data is also essential to allow WHO to fulfil its mandate under Resolution WHA67.6 which requests WHO to assist Member States in ensuring equitable access to quality, effective, affordable and safe HCV treatments. Assisting countries in accessing the new hepatitis treatments at an affordable price requires knowledge about the patent situation in the respective jurisdictions as this determines the various options countries have.

The working papers can also help other interested parties to negotiate transfer of technology or license agreements, research ways to enhance or improve the current drug or treatment modality, and facilitate the development of generics.

Although being public domain information, patent information in many countries is difficult to retrieve, as is reflected by the gaps in the Annex. N/A indicates that no information could be retrieved for the relevant patents in the databases that were used in this working paper. This can either mean that the information in the databases is not up-to-date or complete, or that the patents were not filed in these jurisdictions. While the latter may often be the case, certainty can only be achieved by checking the information with the local patent office. This can be done by using the patent numbers provided in this report, as they allow retrieval of information through national patent offices and/or national patent registries. The following WIPO page provides links to all national online patent search tools to search national patent registries:

http://www.wipo.int/branddb/portal/portal.jsp

LIMITATIONS

While endeavours have been made to make the content of this study accessible to the non-expert, the highly technical nature of the subject matter and the singularities of the patent system require a certain expertise to make full use of this study.

This study sets out relevant patents and patent applications in the countries included in this study as of March 2014 (see the Annex). Every effort has been made to obtain comprehensive and accurate information, including on the legal status of the patents. However, in many countries patent information is not readily available or not updated on a regular basis. In addition, some patent applications may have been published only after the searches were conducted and thus may not be included in this study. As this study endeavours to identify the most relevant patents, it does not include the many additional patents and application filed by various entities that may also relate to the compound.

It should also be noted that this study is not a freedom-to-operate analysis. The information provides useful guidance, but only reflects the situation at a particular point in time. Neither WHO nor Thomson Reuters accept any responsibility for the accuracy of data, nor guarantee that it is complete or up-to-date. Users are advised, before taking any investment or other legally relevant decision, to consult a local patent expert to provide a full assessment of the patent situation in a given country.

METHODOLOGY

Relevant patents and patent applications were identified by searching patent and non-patent databases, comprising Thomson Innovation, Newport, Thomson Pharma, Questel, Scientific Technology Network (STN) and Cortellis. Additional bibliographic details were collected from publicly available databases, comprising the United States Patent and Trademark Office

(USPTO), Espacenet and relevant national patent office websites. For Patent 1, the data was kindly complemented by the Sponsor Bristol-Myers Squibb.

Legal status and oppositions, if any, were retrieved from respective patent offices (to the extent that information was available). Patent Offices in Brazil, African Regional Intellectual Property Organization (ARIPO), India, Russian Federation, and Ukraine have been directly contacted.

Litigation data were retrieved from WestLaw, PACER, and pharma-related publicly available sources. The study differentiates between patents held by Sponsors and non-Sponsors. Sponsors are the entities developing the medicines and are filing for or already hold market authorization. Non-Sponsor entities include other pharmaceutical companies, public research institutes and other applicants. The patent position of the Sponsors is assessed. Patents of non-Sponsor entities are included in the complete data collection in form of an Excel file that can be made available on demand. Please send any requests to: phidepartment@who.int.

Wherever available, the application submitted under the WIPO PCT is used as a primary source, both because it is generally the favoured priority application for the pharmaceutical industry, and also because the WIPO International Search Report (ISR) include examiner references that are coded for relevance and for which initial rejections (an indicator of possible novelty issues) can be identified.

Thomson Reuters´ technical experts analysed the claims and determined whether the scope of each of the claims are broad or narrow. Where available, the outcome of the WIPO ISR on novelty and inventive step is described. It should be noted that quotes from the ISR are only examples and do not preclude objections or outcomes under national jurisdictions.

The expected time of expiration for all the patents was calculated and can be found in the respective Annexes.

GEOGRAPHIC SCOPE

Family members of the Sponsor patent collection have been searched for in the following jurisdictions. It would have been beyond the scope of this study to include patent information of all WHO Member States, thus a selection was made taking into account disease burden, local manufacturing capacities and regional representation:

Argentina (AR), African Regional Intellectual Property Organization (AP), Australia (AU), Brazil (BR), Canada (CA), Chile (CL), China (CN), China, Hong Kong SAR (HK), Colombia (CO), Costa Rica (CR), Ecuador (EC), Egypt (EG), European Patent Office (EPO), Ethiopia (ET), Eurasian Patent Office (EAPO), Georgia (GE), India (IN), Indonesia (ID), Iran (Islamic Republic of) (IR), Israel, (IL), Japan, Jordan (JO), Malaysia (MY), Mexico (MX), Morocco (MA), New Zealand (NZ), Nigeria (NG), African Intellectual Property Organization (OA), Pakistan (PK), Patent Office of the Cooperation Council for the Arab States of the Gulf (GCC), Peru (PE), Philippines (PH), Republic of Korea (KR), Russian Federation (RU), Singapore (SG), South Africa (ZA), Thailand (TH), Tunisia (TN), Ukraine (UA), the United States of America (US), Uruguay (UY), and Viet Nam (VN).

FURTHER RESOURCES

The WHO publication *How to Conduct Patent Searches for Medicines: A Step-by-Step Guide* provides guidance on how to identify the patent status of medicines.[4]

The draft *Guidelines for the examination of pharmaceutical patents: developing a public health perspective* provides detailed information on the different forms of patents in the pharmaceutical sector.[5]

Information on the relationship between public health and intellectual property can be found in the document *Promoting Access to Medical Technologies and Innovation. Intersections between public health, intellectual property and trade*.[6]

These publications as well as other relevant publications on issues related to public health and intellectual property can be found here:
www.who.int/phi/publications/category/en/

More information on HCV and the recommended treatments can be found here: www.who.int/topics/hepatitis/en/

[4] How to Conduct Patent Searches for Medicines: A Step-by-Step Guide. Delhi: World Health Organization; 2010 (http://www.wpro.who.int/publications/PUB_9789290223757/en/, April 2014).
[5] Guidelines for the examination of pharmaceutical patents: developing a public health perspective. Geneva: World Health Organization; 2006 (http://apps.who.int/medicinedocs/documents/s21419en/s21419en.pdf, April 2014).
[6] Promoting Access to Medical Technologies and Innovation. Intersections between public health, intellectual property and trade. Geneva: World Health Organization, World Trade Organization, World Intellectual Property Organization; 2013. (http://www.who.int/phi/promoting_access_medical_innovation/en/, April 2014)

DACLATASVIR

Daclatasvir (formerly BMS-790052; tradename: Daklinza) is an investigational drug candidate for the treatment of HCV. It is being developed by Bristol-Myers Squibb (hereby referred to as the 'Sponsor').

Daclatasvir belongs to a class of new directly acting antivirals that inhibit non-structural protein NS5A. It has been tested in combination regimens with pegylated interferon and ribavirin, as well as with other direct-acting antiviral agents including asunaprevir and sofosbuvir.[7] Bristol-Meyers Squibb filed for marketing approval for a combination therapy of daclatasvir and asunaprevir with the United States Food and Drug Administration (FDA) in early 2014. The FDA has granted the regimen Breakthrough Therapy Designation for use in the treatment of genotype 1b chronic HCV. Bristol-Meyers Squibb has also filed for marketing authorization in Europe for the use of daclatasvir in the treatment of adults with HCV. The European Medicines Agency approved daclatasvir in August 2014 in combination with other drugs for use across genotypes for the treatment of chronic hepatitis C virus infection in adults.[8]

CHEMICAL NAME

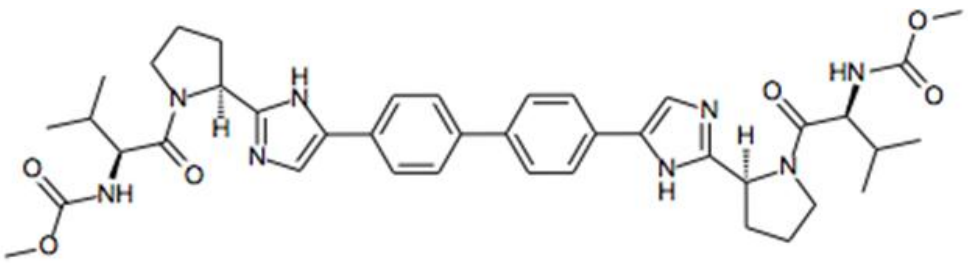
Systematic (IUPAC) name.

Methyl [(2*S*)-1-{(2*S*)-2-[4-(4'-{2-[(2*S*)-1-{(2*S*)-2-[(methoxycarbonyl)amino]-3-methylbutanoyl}-2-pyrrolidinyl]-1*H*-imidazol-4-yl}-4-biphenylyl)-1*H*-imidazol-2-yl]-1-pyrrolidinyl}-3-methyl-1-oxo-2-butanyl]carbamate

MOLECULAR FORMULA

$C_{40}H_{50}N_8O_6$

MOLECULAR STRUCTURE



[7] http://www.hivandhepatitis.com/hepatitis-c/hepatitis-c-topics/hcv-treatment/3378-aasld-Daclatasvir-with-pegylated-interferonribavirin-produces-high-rates-of-hcv-suppression

[8] http://www.firstwordpharma.com/node/1231982#axzz3CFzwqvbI

SUMMARY

The search revealed patents filed with respect to daclatasvir by the Sponsor.

The daclatasvir Sponsor patent collection comprises 8 different patents (patent families). The majority of these patent applications are still pending in the respective national and regional patent offices, 45 patents are granted, (see Patents 1 to 8 in the Annex).

Patent 1 is the primary patent claiming the base compound through a Markush claim, along with various substituents. Where granted, this patent can serve to prevent competitors from making daclatasvir.

Patent 2 is covering a process to make daclatasvir and thus if granted will require competitors to design around this patent and use other production processes. The chemical product itself is not protected.

Patent 3 claims specific derivatives of daclatasvir. Seeking subsequent patents on derivatives of existing drugs is a common strategy of companies (i.e., obtaining multiple patents that cover various aspects of the same product).

Patent 4 is a formulation patent, claiming the pharmaceutical dosage form (pharmaceutical composition).

Patents 5, 7 and 8 claim daclatasvir for the use in combination therapy with other HCV protease inhibitors. Co-administration of known drugs can have a synergistic effect in treating a disease and therefore provides an advantage over a single-agent therapy.

Patent 6 is a method patent for the screening of NS5A-targeting compounds to inhibit HCV replication.

There is competition and patents on daclatasvir have been filed by six non-Sponsor entities and one individual inventor.

Note: The search also revealed two patents that are relevant for all seven reports. Patent applications WO2013059630A1 and WO2013059638A1 inter alia claim the use of combinations of unnamed direct-acting antiviral agents for treating HCV, where the treatment does not include administration of interferon or ribavirin, and the treatment lasts between 8-12 weeks. The description and the dataset for these two patents can be found in the Working Paper on ombitasvir (Patents No 3 and 4). These patents are in litigation. Detailed information can be found in the Working Paper on sofosbuvir under Patent No 2.

DACLATASVIR PATENT SITUATION

SPONSOR PATENTS

Patent searches revealed eight Sponsor patents (referred to as Patent 1 to 8 in the following analysis section and in the Annex). For Patent 1, the data was kindly complemented by the Sponsor Bristol-Myers Squibb.

Patent 1 is the primary patent, claiming the base compound. Patents 2 to 8 are secondary patents, claiming formulation, method of use, process, product derivatives, or method for identifying NS5A-targeting compounds. All patents were filed and remain in the name of Sponsor entity Bristol-Myers Squibb.

PATENT 1

Patent application WO2008021927A2 discloses the base compound of daclatasvir (primary patent). The patent claims a general structural formula of the basic compound along with various substituents. This patent, if granted, serves as a blocking patent preventing competitors from making the product. Also disclosed are their salts, pharmaceutical compositions and combinations containing such compounds and methods for using these compounds in the treatment of HCV infection.

As per the WIPO ISR, the patent application is novel and not obvious in comparison to the closest prior art retrieved during the search. The application relates to biphenyl-imidazole compounds which inhibit HCV replication or inhibit the NS5A protein. According to the report, the novelty of the present invention resides in the saturated N-containing rings depicted in the claimed structure.

Prosecution at the USTPO

There are four patents granted in the United States: US8303944B2, US8329159B2, US8574563B2, and US8642025B2. US8303944B2 is a continuation-in-part of US8329159B2. It relates to substituted imidazole compounds and their salts. US8574563B2 is a divisional of US8303944B2 and continuation-in-part of US8329159B2. It relates to imidazole substituted biphenyl derivatives or their salts for the treatment of HCV infection. US8642025B2 is a continuation application of US8329159B2. It relates to biphenyl-imidazole compounds which inhibit HCV replication or inhibit the NS5A protein.

There are no litigation or opposition procedures reported.

PATENT 2

Patent application WO2009020825A1 is a process patent. The patent claims a process for the preparation of antiviral compounds or a pharmaceutically acceptable salt, describing a specific reaction and deprotection process of diacetylbiphenyl. The process is stated to

provide an efficient large-scale synthesis of the antiviral compounds. The claims are broad and cover a set of compounds specifically synthesized by the claimed process, therefore limiting the application of the process to these specific compounds only.

As per the WIPO ISR, the patent application is novel and not obvious in comparison to the closest prior art retrieved during the search.

As per the available legal status information (details available in the Annex):

- The patent has been granted in Australia, China, Hong Kong SAR, the EAPO, the EPO, Japan, and the United States.
- The patent (or a related patent thereof) is pending in Argentina, Canada, China, India, Japan, and Republic of Korea.
- Legal status is not available for Colombia and Mexico

There are no litigation or opposition procedures reported.

PATENT 3

Patent application WO2008021928A2 claims specific daclatasvir derivatives and their salts. The compounds include a core structure consisting of six directly linked systems. The claims are very broad, covering a Markush structure of the antiviral agents.

As per the WIPO ISR, the patent application is novel and not obvious in comparison to the closest prior art retrieved during the search. Though the prior art discloses similar compounds, the novelty lies in the core structure consisting of six directly linked core systems claimed.

As per the available information (details available in the Annex):

- The patent has been granted in Australia, China, Hong Kong SAR, the EAPO, the EPO, Israel, New Zealand, Singapore, and the United States.
- The patent is pending in Brazil, Canada, China, India, and Republic of Korea.
- Legal status is not available for Japan, and Mexico.

There are no litigation or opposition procedures reported.

PATENT 4

Patent application WO2009020828A1 claims new crystalline forms of substituted imidazole compounds, their composition and use in the treatment of HCV infection, comprising administration of a therapeutically-effective amount of a crystalline form of the compound to a patient. The claimed crystalline forms are subject to limitations of cell structure dimensions, temperature, and other structural parameters.

As per the WIPO ISR, the patent application is novel and not obvious in comparison to the closest prior art retrieved during the search. However, the report concludes that although it

claims compounds for HCV treatment, the specific compound claimed in the present application is not disclosed.

As per the available information (details available in the Annex):

- The patent has been granted in Australia, China, as well as China, Hong Kong SAR, the EAPO, New Zealand, Singapore, South Africa, and the United States.
- The patent is pending in Argentina, Canada, Israel, India, and Republic of Korea.
- An EPO patent EP2183244B1 ceased on 28 February 2014.
- Legal status is not available for Colombia, Egypt, Japan, Mexico, and Peru.

There are no litigation or opposition procedures reported.

PATENT 5

Patent application WO2011046811A1 is a formulation patent disclosing a combination of daclatasvir and a HCV NS3 protease inhibitor, asunaprevir. The application claims compositions thereof, exhibiting synergistic activity in the treatment of HCV infection. It is further claimed that the compositions may be administered in combination with an additional anti-HCV agent, preferably interferon or ribavirin.

As the composition claims a combination of two known compounds without claiming any substituent, the scope of the claims narrows down to only the combination of the claimed compounds.

As per the WIPO ISR, the patent application is novel but lacks an inventive step. Lack of inventive step relates to the synergetic combination claimed in the present invention, and according to the ISR, this is obvious from existing prior art.

As per the available information (details available in the Annex):

- The patent has been granted in New Zealand and the United States.
- The patent (or a related patent thereof) is pending in Australia, Canada, China, as well as China, Hong Kong SAR, the EPO, India, Israel, Japan, Republic of Korea, Singapore, South Africa, Thailand, and the United States.
- Legal status is not available for the EAPO, Mexico, Peru, Philippines, and Viet Nam.

There are no litigation or opposition procedures reported.

PATENT 6

Patent application WO2012009394A2 is a method patent for the screening of NS5A-targeting compounds to inhibit HCV replication. The invention is based on the finding that pairs of HCV NS5A-targeting inhibitors can be identified which display similar resistance profiles yet, when combined, exhibit synergistic inhibition of HCV wild type replicons and/or HCV replicons carrying mutations conferring resistance to the HCV NS5A-targeting inhibitor.

In addition, combinations of these molecules result in a higher genetic barrier to resistance, demonstrating their potential utility as novel combination therapies for treatment of HCV. As the application claims a general methodology of screening and testing the combinations, the claims have a broader scope.

As per the WIPO ISR, the invention is novel but lacks an inventive step. Thus the present invention is considered to be obvious over cited non-patent prior art.

As per the available information (details available in the Annex):

- The patent has not been granted yet, and is pending at the EPO and the United States.

There are no litigation or opposition procedures reported.

PATENT 7

Patent application WO2012018829A1 is another formulation patent, claiming a formulation comprising one or two HCV polymerase inhibitors and a pharmaceutically acceptable carrier. The composition shows synergistic effect, effectively inhibits HCV, achieves maximum efficacy, and potentially eradicates the HCV. Combinations comprise a HCV NS5A inhibitor, e.g. daclatasvir, a HCV NS3 inhibitor, e.g. asunaprevir, and a HCV NS5B inhibitor (compound of formula 3). As the claimed composition is a combination of one or two compounds without claiming any substituents in the claimed structure, the scope of the claims narrows down to only the claimed set of compounds.

As per the WIPO ISR, the patent application lacks novelty and is obvious in comparison to the closest prior art retrieved during the search.

As per the available information (details available in the Annex):

- The patent has not been granted yet, and is pending in Australia, Canada, China, as well as China, Hong Kong SAR, the EPO, Israel, Republic of Korea, Singapore, and the United States.
- Legal status is not available for the EAPO, Japan, and Mexico.

There are no litigation or opposition procedures reported.

PATENT 8

Patent application WO2013106520A1 is another formulation patent. The claimed formulation comprises a combination of an NS5A-targeting compound and a NS5A synergist, which provides synergistic anti-HCV activity against variants that contain mutation(s) conferring resistance to the NS5A-targeting compound alone. It is claimed that combinations may be used with additional compounds such as interferon or ribavirin.

As per the WIPO ISR, the patent application lacks novelty and is obvious in comparison to closest prior art retrieved during the search, including patent and non-patent publications which disclose combinations of compounds which can inhibit HCV.

As per the available information (details available in the Annex):

- The patent has not been granted yet, and is pending in the United States (ready for examination).
- Legal status is not available for Uruguay.

NON-SPONSOR PATENTS

There is competition, and patents on daclatasvir have been filed by six non-Sponsor entities and one individual inventor.

- AbbVie Inc.
- Boehringer Ingelheim GmbH
- Catabasis Pharmaceuticals
- INSERM
- Instituto di Ricerche di Biologia Molecolare Pietro Angeletti / Merck Sharp & Dohme Corp.
- Santaris Pharma

A total of eleven inventions (patent families) are counted, including method of use, formulation and product patents.

Patents of non-Sponsor entities are included in the complete data collection in form of an Excel file that can be made available on demand. Please send any requests to: phidepartment@who.int.

ANNEX - DACLATASVIR PATENT SITUATION

	Patent 1[9]	Patent 2	Patent 3	Patent 4	Patent 5	Patent 6	Patent 7	Patent 8
Subject Matter	Patent application WO2008021927 covers the base compound of daclatasvir.	Patent application WO2009020825 covers a process for synthesizing daclatasvir for the treatment of HCV.	Patent application WO2008021928 covers a novel HCV inhibitor or its salts useful for the treatment of HCV infection.	Patent application WO2009020828 covers crystalline forms of daclatasvir.	Patent application WO2011046811 covers a formulation comprising a combination of daclatasvir and asunaprevir.	Patent application WO2012009394 is related to the method of identifying NS5A-targeting compounds.	Patent application WO2012018829 covers a formulation comprising one or two HCV polymerase inhibitors.	Patent application WO2013106520 covers a formulation comprising a combination which provides synergistic anti-HCV activity.
Applicant	Bristol-Myers Squibb Co.	Bristol-Myers Squibb Co.	Bristol-Myers Squibb Co.	Bristol-Myers Squibb Co.	Bristol-Myers Squibb Co.	Bristol-Myers Squibb Co.	Bristol-Myers Squibb Co.	Bristol-Myers Squibb Co.
Int'l Patent Publication Number	WO2008021927	WO2009020825	WO2008021928	WO2009020828	WO2011046811	WO2012009394	WO2012018829	WO2013106520
Priority Number	US2006836996P	US2007954595P	US2006836999P	US2007954592P	US2009250648P	US2010364851P	US2010371399P	US2012586558P
Expected expiry[1]	8 Aug 2027	30 Jul 2028	8 Aug 2027	30 Jul 2028	7 Oct 2030	12 Jul 2031	1 Aug 2031	9 Jan 2033
PATENT STATUS								
ARIPO (AP)[2]	Not filed	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Argentina (AR)	Pending Pub No: AR63684A1	Pending Pub No: AR67896A1	N/A	Pending Pub No: AR070016A1	N/A	N/A	N/A	N/A

[9] For Patent 1, the data was kindly complemented by the Sponsor Bristol-Myers Squibb.

	Patent 1[9]	Patent 2	Patent 3	Patent 4	Patent 5	Patent 6	Patent 7	Patent 8
Australia (AU)	Granted Pub No: AU2007286222B2	Granted Pub No: AU2008284097B2	Granted Pub No: AU2007286223B2	Granted Pub No: AU2008284100B2	Pending Pub No: AU2010307144A1	N/A	Pending Pub No: AU2011285890A1	N/A
Brazil (BR)	Pending Pub No: PI0716483.1	N/A	Pending Pub No: BRPI0716220	N/A	N/A	N/A	N/A	N/A
Canada (CA)	Pending Pub No: CA2660520A1	Pending Pub No: CA2695711A1	Pending Pub No: CA2660628A1	Pending Pub No: CA2695729A1	Pending Pub No: CA2777560A1	N/A	Pending Pub No: CA2807589A1	N/A
Chile (CL)	Granted Pub No: CL49393	N/A	N/A	N/A	N/A	N/A	N/A	N/A
China (CN)	Granted Pub No: CN200780037723.7	Pending Pub No: CN101778841A	Pending Pub No: CN101528232A	Granted Pub No: CN101778840B	Pending Pub No: CN102655873A	N/A	Pending Pub No: CN103153280A	N/A
China, Hong Kong SAR (HK)	Pending Pub No: HK09105119.6	Granted Pub No: HK1137454A1	Granted Pub No: HK1125576A1	Granted Pub No: HK1144089A1	Pending Pub No: HK1172237A0	N/A	Pending Pub No: HK1180211A0	N/A
Colombia (CO)	Granted Pub No: CO6150171A2	Status: N/A Pub No: CO6251317A2	N/A	Status: N/A Pub No: CO6160327A2	N/A	N/A	N/A	N/A
Costa Rica (CR)	Not filed	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Ecuador (EC)	Not filed	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Egypt (EG)	Pending Pub No: EG174/2009	N/A	N/A	Status: N/A Pub No: EG2010020177	N/A	N/A	N/A	N/A
Ethiopia (ET)	Not filed	N/A	N/A	N/A	N/A	N/A	N/A	N/A
EAPO (EA)[3]	Granted Pub No: EA15756B1	Granted Pub No: EA17173B1	Granted Pub No: EA17348B1	Granted Pub No: EA018152B1	Status: N/A Pub No: EA201270555A1	N/A	Status: N/A Pub No: EA201390155A1	N/A
EPO (EP)[4]	Granted Pub No: EP2049522A2 Withdrawn Pub No: EP2385048A1 Pending Pub No: EP14168065.2	Granted Pub No: EP2178863B1	Granted Pub No: EP2049116B1	Ceased Pub No: EP2183244B1	Pending Pub No: EP2488192A1	Pending Pub No: EP2593565A2	Pending Pub No: EP2600835A1	N/A

	Patent 1[9]	Patent 2	Patent 3	Patent 4	Patent 5	Patent 6	Patent 7	Patent 8
GCC[5]	Pending Pub No: GC8874	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Georgia (GE)	Not filed	N/A	N/A	N/A	N/A	N/A	N/A	N/A
India (IN)	Pending Pub No: IN200900853P1 Indian National Patent Number: 853/DELNP/2009	Pending Pub No: IN201000854P1 Indian National Patent Number: 854/DELNP/2010	Pending Pub No: IN200900753P1 Indian National Patent Number: 753/DELNP/2009	Pending Pub No: IN201000806P1 Indian National Patent Number: 806DELNP/2010	Pending Pub No: IN201203372P1 Indian National Patent Number: 3372/CHENP/2012	N/A	N/A	N/A
Indonesia (ID)	Not filed	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Iran (Islamic Republic of) (IR)	Not filed	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Israel (IL)	Granted Pub No: IL196813A	N/A	Granted Pub No: IL196815A	Pending Pub No: IL203684	Pending Pub No: IL219123	N/A	Pending Pub No: IL224369	N/A
Japan (JP)	Granted Pub No: JP05235882B2 Pending Pub No: JP2013151535A Pending Pub No: JP2013064764	Granted Pub No: JP05324574B2 Pending Pub No: JP2013231072A	Status: N/A Pub No: JP05306203B2	Status: N/A Pub No: JP05244179B2	Pending Pub No: JP2013507439A	N/A	Status: N/A Pub No: JP2013535487A	N/A
Jordan (JO)	Not filed	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Lebanon (LB)	Granted Pub No: LB7962							
Malaysia (MY)	Not filed	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Mexico (MX)	Granted Pub No: MX287005	Status: N/A Pub No: MX290356B	Status: N/A Pub No: MX283096B	Status: N/A Pub No: MX307552B	Status: N/A Pub No: MX2012003835A	N/A	Status: N/A Pub No: MX2013001170A	N/A

	Patent 1[9]	Patent 2	Patent 3	Patent 4	Patent 5	Patent 6	Patent 7	Patent 8
Morocco (MA)	Not filed	N/A	N/A	N/A	N/A	N/A	N/A	N/A
New Zealand (NZ)	Granted Pub No: NZ574805A	N/A	Granted Pub No: NZ574769A	Granted Pub No: NZ583148A	Granted Pub No: NZ599284A	N/A	N/A	N/A
Nigeria (NG)	Not filed	N/A	N/A	N/A	N/A	N/A	N/A	N/A
OAPI[6]	Not filed	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Pakistan (PK)	Not filed	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Peru (PE)	Status: N/A Pub No: PE20080542A1 Granted Pub No: PE006425	N/A	N/A	Status: N/A Pub No: PE09402009A1	Status: N/A Pub No: PE14322012A1	N/A	N/A	N/A
Philippines (PH)	Not filed	N/A	N/A	N/A	Status: N/A Pub No: PH12012500571A1	N/A	N/A	N/A
Republic of Korea (KR)	Pending Pub No: KR20097004970 Pending Pub No: KR20147010437	Pending Pub No: KR2010045992A	Pending Pub No: KR2009040910A	Pending Pub No: KR20100042641A	Pending Pub No: KR2012088743A	N/A	Pending Pub No: KR2014002611A	N/A
Russian Federation (RU)	Granted Pub No: RU015756	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Singapore (SG)	Granted Pub No: SG150106	N/A	Granted Pub No: SG150105B	Granted Pub No: SG159059B	Pending Pub No: SG179814A1	N/A	Pending Pub No: SG187193A1	N/A
South Africa (ZA)	Granted Pub No: ZA200900962A	N/A	Granted Pub No: ZA200900935	Granted Pub No: ZA201000843A	Granted Pub No: ZA201203451A	N/A	N/A	N/A
Thailand (TH)	Pending Pub No: TH0701003997	N/A	N/A	N/A	Pending Pub No: TH1201001642	N/A	N/A	N/A
Tunisia (TN)	Not filed	N/A	N/A	N/A	N/A	N/A	N/A	N/A

	Patent 1[9]	Patent 2	Patent 3	Patent 4	Patent 5	Patent 6	Patent 7	Patent 8
Ukraine (UA)	Not filed	N/A	N/A	N/A	N/A	N/A	N/A	N/A
The United States (US)	Abandoned Pub No: US20100158862A1 Abandoned Pub No: US20110268697A1 Granted Pub No: US8303944B2 Granted Pub No: US8329159B2 Granted Pub No: US8574563B2 Granted Pub No: US8642025 Pending Pub No: US2014030199 Pending Pub No: US2014488990 Pending Pub No: US2006836996	Granted Pub No: US7728027B2	Granted Pub No: US7659270B2	Granted Pub No: US8629171B2	Pending Pub No: US20130259832A1 Granted Pub No: US8415374B2	Pending Pub No: US20130157894A1	Pending Pub No: US20120196794A1	Pending Pub No: US20130183269A1
Uruguay (UY)	Not filed	N/A	N/A	N/A	N/A	N/A	N/A	Status: N/A Pub No: UY34570A
Venezuela (VE)	Pending Pub No: VE20071726	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Viet Nam (VN)	Not filed	N/A	N/A	N/A	Status: N/A Pub No: VN31028A	N/A	N/A	N/A

[1] If granted and not subject to patent term extension.

[2] **The African Regional Intellectual Property Organization (ARIPO) includes the following countries:** Botswana, Ghana, Gambia, Kenya, Liberia, Lesotho, Malawi, Mozambique, Namibia, Sudan, Sierra Leone, Swaziland, the United Republic of Tanzania, Uganda, Zambia and Zimbabwe.

[3] **The Eurasian Patent Organization (EAPO) includes the following countries:** Armenia, Azerbaijan, Belarus, Kazakhstan, Kyrgyzstan, Russian Federation, Tajikistan and Turkmenistan.

[4] **The European Patent Office (EPO) includes the following countries:** Albania, Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Iceland, Italy, Liechtenstein, Lithuania, Luxemburg, Latvia, Malta, Monaco, Netherlands, Norway, Poland, Portugal, Romania, San Marino, Serbia, Slovenia, Slovakia, Spain, Sweden, Switzerland, The former Yugoslav Republic of Macedonia, Turkey and the United Kingdom.

[5] **The Patent Office of the Cooperation Council for the Arab States of the Gulf** (**Gulf Cooperation Council - GCC) includes the following countries**: Bahrain, Kuwait, Oman, Qatar, Saudi Arabia and United Arab Emirates.

[6] **The African Intellectual Property Organization (OAPI) includes the following countries:** Benin, Burkina Faso, Cameroon, Central African Republic, Chad, The Congo, Equatorial Guinea, Gabon, Guinea, Guinea Bissau, Côte d'Ivoire, Mali, Mauritania, Niger, Senegal and Togo.

GLOSSARY

INTERFERENCE PROCEEDING: An interference proceeding is a proceeding to determine the priority issues of multiple patent applications. Based on the (previous) first-to-invent system of the United States, a party which has failed to file a patent application on time is allowed to challenge the inventorship of another party which has a granted or pending patent.

N/A: Patent information was not available for this country at the time the patent searches were conducted, in March 2014.

NOTICE OF ALLOWANCE: During a USTPO examination, if it appears to the examiner that the applicant is entitled to a patent under the law, a notice of allowance is sent to the applicant. The notice of allowance specifies a sum constituting the issue fee which must be paid within a given time from the date of mailing of the notice of allowance to avoid abandonment of the application.

PATENT FAMILY MEMBER: All patent publications that relate to the same basic patent (that is, invention) are members of this patent family. In the present study patent families are based on the Derwent World Patent Index (DWPI).

PENDING or GRANTED: Indicates a patent´s legal status.

PRIORITY NO: Earliest application number.

PUB NO: Patent publication number.

SPONSOR: The term “Sponsor” refers to the entities that are developing the medicines and are holding or filing for market authorization. Note that a Sponsor is not necessarily the patent assignee or applicant.

THE WIPO INTERNATIONAL SEARCH REPORT (ISR): After an applicant files a PCT application with WIPO, a search is conducted by an authorised International Searching Authority (ISA) to find the most relevant prior art documents regarding the claimed subject matter. The search results in an International Search Report (ISR), together with a written opinion regarding patentability.