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UNITED STATES DISTRICT COURT

FOR THE NORTHERN DISTRICT OF CALIFORNIA

ABBVIE INC.

Plaintiff,

v.

NOVARTIS VACCINES & DIAGNOSTICS, INC. and GRIFOLS WORLDWIDE OPERATIONS LTD.

Defendants.

CASE NO. _____

**COMPLAINT**

**FILED UNDER SEAL**

**REDACTED VERSION OF DOCUMENT SOUGHT TO BE SEALED**

Plaintiff AbbVie Inc. ("AbbVie") brings this action against Novartis Vaccines and Diagnostics, Inc. ("Novartis") and Grifols Worldwide Operations Ltd. ("Grifols") (collectively, "Defendants") for a declaratory judgment that the claims of the patents at issue are invalid.

## INTRODUCTION

1. In 2001, AbbVie embarked on a program to develop novel therapies to treat Hepatitis C Virus ("HCV") infection. HCV infects millions of people in the United States and around the world, causing liver disease, liver cancer, and even death.

2. Historically, treatments for HCV were unsatisfactory. They involved lengthy regimens including a drug called interferon, which has serious and debilitating side effects, including nausea, fatigue, and depression, and which can therefore result in poor patient compliance. Interferon therapy is also only about 50% effective against so-called HCV Genotype 1, the form of HCV that is the most common in the U.S. and also the most challenging to treat. In sum, nearly half of patients suffering from HCV infection were left without a viable treatment option at all, while the other half faced a grueling and debilitating interferon-containing regimen.

3. Over more than a decade, AbbVie invested immense resources to develop multi-drug combination regimens capable of treating even the most difficult form of HCV in a period of just weeks, without interferon and its side effects. In clinical trials, AbbVie's novel combination therapies have demonstrated extraordinary efficacy, with cure rates in excess of 95%, even among difficult-to-treat patient groups.

4. AbbVie's investment in the research and development ("R&D") of interferon-free combination regimens led to the submission of New Drug Applications ("NDA") to the United States Food and Drug Administration ("FDA"). In particular, AbbVie submitted a NDA in April 2014 for permission to market its HCV therapy, available today as VIEKIRA PAK™. The FDA approved VIEKIRA PAK on December 19, 2014, and it is currently being sold in the U.S. On July 25, 2016, the FDA also approved VIEKIRA XR™, a once-daily, extended-release co-formulation of the active ingredients in VIEKIRA PAK, which is also currently being sold in the U.S.

5. AbbVie also submitted a NDA to the FDA in February 2015 for permission to market another HCV therapy, called TECHNIVIE™, for certain patients suffering from HCV genotype 4 infection. The FDA approved TECHNIVIE on July 24, 2015, and it is currently being sold in the U.S.

6. In addition, as part of its continued leading research in HCV therapeutics, in December 2016, AbbVie submitted a NDA to the FDA for an investigational, pan-genotypic combination regimen of Glecaprevir and Pibrentasvir for the treatment of HCV ("G/P"). Regulatory approval is currently pending.

7. In 2001, AbbVie was aware that Novartis (then Chiron Corporation or "Chiron") was engaged in an aggressive licensing program, demanding that any company seeking to undertake research in the area of HCV therapies obtain a license to a portfolio of HCV-related patents. Those patents purported to claim various naturally occurring proteins and nucleic acids that make up HCV viral particles, along with various routine and conventional molecular biology methods and reagents that were well known by scientists at the time for the manipulation and study of such natural "building blocks." Indeed, as it has admitted in prior litigation, Novartis's sole allegedly inventive contribution was the identification of the genomic sequence of naturally occurring HCV. In Novartis's own words regarding three patents at issue in this case, which are representative of those in its portfolio: "**The novel aspect of the invention of these three patents *is* the genomic sequence of HCV**." (*See* Ex. 1, *Chiron Corp. v. F. Hoffman-La Roche Ltd. et al.*, No. C98-0315, ECF No. 676, Chiron's Opening Brief on Claim Construction at 3 (N.D. Cal. Mar. 10, 2000) ("*Chiron v. Roche* Claim Construction Brief") (emphasis added).) As discussed below, however, under controlling Supreme Court precedent, that is not a patentable discovery under 35 U.S.C. § 101.

8. As announced in a press release on July 10, 2002, AbbVie (then Abbott Laboratories) entered into a license agreement with Novartis (then Chiron) (the "Agreement"). ("Chiron Grants Non-Exclusive HCV License to Abbott Laboratories," PR NEWSWIRE, http://www.prnewswire.com/news-releases/chiron-grants-non-exclusive-hcv-license-to-abbott-laboratories-76115947.html.)

9. REDACTED

10. REDACTED

These patents do not disclose or claim HCV therapies. None of the claims cover VIEKIRA PAK, VIEKIRA XR, TECHNIVIE, or G/P, including the use of these regimens. Instead, the claims of these patents purport to cover only aspects of the genomic sequence of HCV, and conventional variations and applications thereof.

11. At the time that AbbVie entered into the Agreement, the United States Patent and Trademark Office's ("PTO") practice was to grant patents covering naturally occurring protein and nucleic acid sequences, and conventional methods for working with them. Recent Supreme Court decisions regarding patent-eligible subject matter under 35 U.S.C. § 101, however, have clarified that the PTO erred in granting such patents. The Supreme Court opinions exclude from patent-eligible subject matter claims that are directed to "natural laws" (including products of nature) because these discoveries are not patentable inventions. They are instead basic tools of scientific and technological work. Allowing patents on such natural products would discourage the very scientific activity that the patent laws are meant to encourage.

Under the Supreme Court's analysis, the patents at issue are invalid under § 101 (as well as other provisions and patent law doctrines). The patents purport to claim natural laws, natural products, as well as conventional methods of using the same. The claims add no meaningful "inventive concept" to the patent-ineligible subject matter. To the contrary, as Novartis has admitted repeatedly in its patents, during prosecution, and in prior litigation, the claims add at most routine, conventional, and well-understood minor variations of these natural products that were well known in the art at the relevant time.

12. AbbVie brings this action to REDACTED These patents are exactly the type criticized and invalidated by the U.S. Supreme Court, the Court of Appeals for the Federal Circuit, and various

U.S. District Courts, because they claim natural laws and products, and minor variations or conventional applications thereof.

13. AbbVie invested in, and advanced, progress in the useful arts by inventing new drugs and breakthrough methods to treat a devastating infectious disease. Novartis's patents exclude the public from using basic tools for scientific research and are an improper tax on AbbVie (and others) that impedes scientific progress.

## NATURE OF THE ACTION

14. This action arises under the patent laws of the United States, 35 U.S.C. § 100 *et seq.*, and the Declaratory Judgment Act, 28 U.S.C. §§ 2201-2202.

## THE PARTIES

15. Plaintiff AbbVie is a corporation organized and existing under the laws of Delaware with its corporate headquarters at 1 North Waukegan Road, North Chicago, Illinois 60064. AbbVie is a global biopharmaceutical company engaged in the business of research, development, manufacture, and sale of pharmaceutical products throughout the world.

16. On information and belief, Defendant Novartis is a corporation organized and existing under the laws of the State of Delaware and has a principal place of business at 4560 Horton St., Emeryville, CA 94608-2916. Novartis is a wholly owned subsidiary of Novartis AG, a corporation organized and existing under the laws of Switzerland with its principal place of business at Lichtstrasse 35, Basel V8 CH 4056, Switzerland.

17. On information and belief, Defendant Grifols is a corporation organized and existing under the laws of Ireland with its principal place of business at Embassy House, Herbert Park Lane, Ballsbridge, Dublin 4, Ireland. On information and belief, Grifols is a wholly owned subsidiary of Grifols, S.A., a corporation organized and existing under the laws of Spain with its principal place of business at Avinguda de la Generalitat, 152-158 Parc de Negocis Can Sant Joan Sant Cugat del Vallès, Barcelona 08174, Spain. On information and belief, Grifols is the parent of Grifols Worldwide Operations USA, Inc., a Delaware company with a principal place of business in California.

18. On information and belief, Defendant Novartis is an owner of the following United States patents (collectively, the "Novartis Patents"): U.S. Patent No. 6,472,180 ("the '180 patent," a true and correct copy of which is attached as Exhibit 2); U.S. Patent No. 5,712,088 ("the '088 patent," a true and correct copy of which is attached as Exhibit 3); U.S. Patent No. 5,714,596 ("the '596 patent," a true and correct copy of which is attached as Exhibit 4); U.S. Patent No. 5,863,719 ("the '719 patent," a true and correct copy of which is attached as Exhibit 5); U.S. Patent No. 6,074,816 ("the '816 patent," a true and correct copy of which is attached as Exhibit 6); U.S. Patent No. 6,096,541 ("the '541 patent," a true and correct copy of which is attached as Exhibit 7); U.S. Patent No. 6,171,782 ("the '782 patent," a true and correct copy of which is attached as Exhibit 8); U.S. Patent No. 6,027,729 ("the '729 patent," a true and correct copy of which is attached as Exhibit 9); U.S. Patent No. 7,790,366 ("the '366 patent," a true and correct copy of which is attached as Exhibit 10); U.S. Patent No. 5,922,857 ("the '857 patent," a true and correct copy of which is attached as Exhibit 11); and U.S. Patent No. 6,057,093 ("the '093 patent," a true and correct copy of which is attached as Exhibit 12); (collectively, the "Novartis Patents").

19. On information and belief, all of the patents listed in the preceding paragraph are co-owned by Novartis and Grifols, other than the '180 patent, which, is owned only by Novartis.

20. REDACTED

Thus, AbbVie is only including the Novartis Patents in this Complaint, but reserves the right to add or remove patents in this case by amendment at a later time, as may be necessary or appropriate.

**SUBJECT MATTER JURISDICTION AND VENUE**

21. This Court has subject matter jurisdiction under 28 U.S.C. §§ 1331, 1338(a), and 2201(a).

22. Venue is proper in this judicial district under 28 U.S.C. § 1391.

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24. REDACTED

25. REDACTED

26. Under the totality of the circumstances, an actual controversy sufficient to establish declaratory judgment jurisdiction exists between AbbVie, Novartis, and Grifols.

**PERSONAL JURISDICTION**

27. The Court has personal jurisdiction over Novartis.

28. On information and belief, Novartis regularly and continuously transacts business within the State of California, and Novartis has a principal place of business at 4560 Horton St, Emeryville, CA 94608-2916, which is located in the jurisdiction of the Northern District of California.

29. On information and belief, Novartis is registered with the California Secretary of State as a corporation that may conduct business in the State of California.

30. On information and belief, Novartis has availed itself of the privilege of conducting business within the State of California, including by marketing and selling biological products throughout the United States, including in the State of California. On information and belief, Novartis derives substantial revenue from such sales in California.

31. On information and belief, Novartis's products are purchased by customers in the State of California and are administered to individuals in the State of California.

32. In addition, on information and belief, the activity leading to the filing of the Novartis Patents took place in California, the Novartis entity that entered into the Agreement with AbbVie (Chiron) had its principal place of business in California, all of the Novartis Patents were originally assigned to that Novartis entity (Chiron), REDACTED

33. The Court has personal jurisdiction over Grifols.

34. On information and belief, Grifols entered into a transaction with Novartis in which it purchased rights to all of the Novartis Patents other than the '180 patent. As announced in a press release on November 11, 2013, Grifols, S.A., the parent corporation of Grifols, acquired a Novartis diagnostics business unit, explaining that "[t]he assets acquired include patents, brands, licenses and royalties, together with the production plant at Emeryville (California, United States)." ("Grifols to acquire a Novartis diagnostics business unit for US$1,675 million," PR NEWSWIRE, http://www.prnewswire.com/news-releases/grifols-to-acquire-a-novartis-diagnostics-business-unit-for-us1675-million-231393111.html#.) The press release also describes the Novartis Diagnostics products as including instruments and assays that are used to test blood donations "for pathogens such as HIV (the AIDS virus,) hepatitis B and hepatitis C." (*Id.*) The press release explains that purchase of the Novartis diagnostics business unit "will be structured through Grifols' Diagnostic Division and a newly created 100% Grifols-owned subsidiary." (*Id.*) On information and belief, Grifols Worldwide Operations USA, Inc., a wholly-owned subsidiary of Grifols, was incorporated in Delaware on January 27, 2014, just over two months after this press release issued. On information and belief, the transaction between Grifols and Novartis involved correspondence with principals based in California. On information and belief, the filing of the Novartis Patents purchased by Grifols is based on activity that occurred in California. On information and belief, at the time of the transaction between Grifols and Novartis, Novartis had its principal place of business in California.

35. In the alternative, and to the extent that Grifols contends that it is not subject to jurisdiction in any state's courts of general jurisdiction, the Court also has personal jurisdiction over Grifols under Fed. R. Civ. P. 4(k)(2).

36. On information and belief, the Court's exercise of jurisdiction over Grifols is consistent with the Constitution and laws of the United States. On information and belief, Grifols has availed itself of the benefits and protections of the United States at least because it is (1) an assignee of patent rights created by the laws of the United States, including the Novartis Patents with the exception of the '180 patent, and the filing of those patent applications were related to activities in the United States (including in California); (2) an issuer with the Securities and Exchange Commission and offeror of exchange notes for sale in the United States; and (3) the parent of Grifols Worldwide Operations USA, Inc., a Delaware company with a principal place of business in California.

## FACTUAL BACKGROUND

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### The Supreme Court's Recent Recasting of Patent Eligibility

40. In a series of controlling recent decisions, the Supreme Court has clarified what constitutes patent subject matter eligibility under 35 U.S.C. § 101. Under cases such as *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. 66 (2012) ("*Mayo*"), *Association for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107 (2013)

("*Myriad*"), and *Alice Corp. v. CLS Bank International*, 134 S. Ct. 2347 (2014) ("*Alice*"), it has become clear that the Novartis Patents are directed to ineligible subject matter and are therefore invalid under § 101.

41. In *Mayo*, the Supreme Court held that a method claim is patent-ineligible under § 101 if it merely recites a law of nature. 566 U.S. at 71-72. Moreover, such claims cannot be salvaged by the addition of method steps consisting of well-understood, routine, conventional activity already known by the scientific community at the time of the purported invention. *Id.* at 72-73, 79-80, The Court explained that a process reciting a law of nature is not patentable, unless the claimed process has "additional features that provide practical assurance that the process is more than a drafting effort designed to monopolize the law of nature itself." *Id.* at 77.

42. The Supreme Court next addressed the natural law exception in *Myriad*, which held that isolated genomic DNA is not patent eligible under § 101. 133 S. Ct. at 2111. The Supreme Court found that isolated DNA is a product of nature and embodies a law of nature because isolating DNA is not an act of invention where the encoded information is the same as in the body. *Id.* at 2111, 2118. The decision addressed patents based on Myriad's discovery of genes associated with breast cancer, called "BRCA1" and "BRCA2." The Court explained that Myriad did not create or alter any of the genetic information encoded in the BRCA1 and BRCA2 genes or the genetic structure of the DNA and that Myriad's "principal contribution was uncovering the precise location and genetic sequence of the BRCA1 and BRCA2 genes." *Id.* at 2116.

43. Most recently in *Alice*, the Supreme Court further explained why certain subject matter is excluded from patent eligibility: "Laws of nature, natural phenomena, and abstract ideas are the basic tools of scientific and technological work." 134 S. Ct. at 2354 (citation and quotation marks omitted). Consequently, "[m]onopolization of those tools through the grant of a patent might tend to impede innovation more than it would tend to promote it, thereby thwarting the primary objective of the patent laws." *Id.* (citation and internal quotation marks omitted). The Court further explained that "in applying the § 101 exception, we must distinguish between patents that claim the building blocks of human ingenuity and those that integrate the building

blocks into something more, thereby transforming them into a patent eligible invention. The former would risk disproportionately tying up the use of the underlying ideas, and are therefore ineligible for patent protection. The latter pose no comparable risk of pre-emption, and therefore remain eligible for the monopoly granted under our patent laws." *Id.* at 2354-55 (internal citations, quotation marks and alterations omitted).

44. *Alice* set forth a framework for distinguishing "patents that claim laws of nature, natural phenomena, and abstract ideas from those that claim patent-eligible applications of those concepts." 134 S. Ct. at 2355. The first step is to "determine whether the claims at issue are directed to [a] patent-ineligible concept[]." *Id.* The second step is a search for an "'inventive concept'—i.e., an element or combination of elements that is sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the ineligible concept itself." *Id.* (quotation marks omitted).

45. The Court explained that "[s]imply appending conventional steps, specified at a high level of generality," to a claim that otherwise claims an abstract idea, natural phenomena or law of nature is "not enough to supply an inventive concept." 134 S. Ct. at 2357 (internal quotation marks omitted).

46. The Supreme Court's recent explication of the standard for patent eligibility under § 101 reveals that the PTO has been applying the wrong standard for decades, with the result that many patents have issued that claim patent-ineligible laws of nature and natural products. These patents, including the Novartis Patents, are invalid.

47. While such improperly issued patents are still subject to a statutory presumption of validity, that presumption is easier to overcome where, as here, the PTO did not examine the patents under the proper standard.

**The Novartis Patents Claim Ineligible "Discoveries" Based On A Naturally Occurring HCV Sequence, Not Patent-Eligible Applications Of Those Discoveries**

48. The Novartis Patents are based on Novartis's sequencing of certain naturally occurring nucleotides from HCV.

49. In prior litigation, Novartis characterized the '596, '088, '719 patents, which are at issue in this case and are representative of the ineligible subject matter purportedly claimed in the Novartis Patents, as "aris[ing] out of Chiron's [Novartis's] . . . identification and cloning of the virus that is now known as hepatitis C." (*See* Ex. 1, *Chiron v. Roche* Claim Construction Brief at 1.) Novartis further stated: "Methods of nucleic acid testing for detecting viruses other than HCV, including the 'PCR' amplification and detection methods referenced in the patents, were known before Chiron [Novartis] filed its first patent application." (*Id.* at 2.) "Once Chiron [Novartis] determined the sequence of HCV, those of skill in the art could readily design a nucleic acid test for detecting HCV." (*Id.* at 2-3.)

50. According to Novartis, "A simplified, but nonetheless accurate, way to describe the claims of the patents in suit is that the method patents (the '088 and '719 patents) claim nucleic acid test methods (including previously known methods) employing the nucleic acid sequence from the HCV genome to test for the presence or absence of HCV. The composition patent ('596) claims nucleotide sequences which are used in nucleic acid testing for HCV. The steps used in the method for nucleic acid testing for HCV are not themselves new. ***The novel aspect of the invention of these three patents is the genomic sequences of HCV***." (*Id.* at 3 (emphasis added).) Thus, Novartis admitted in prior judicial proceedings that the only alleged novelty of patents representative of those at issue in this case is the identification of a naturally occurring genomic sequence.

51. Similarly, Novartis previously described the contribution of certain patents related to those at issue here as follows: "Chiron [Novartis] scientists used recombinant DNA technology to successfully identify, clone and express the NS3 protease gene sequence. The pioneering work of Chiron's [Novartis's] scientists in the HCV protease field has been rewarded with [the related patents]." (*See* Ex. 14, *Chiron Corp. v. Gilead Scis., Inc.*, No. 98-2994, ECF No. 1, Complaint ¶ 8 (N.D. Cal. July 31, 1998); Ex. 15, *Chiron Corp. v. Eli Lilly & Co. et al.*, No. 98-2974, ECF No. 1, Complaint ¶ 9, (N.D. Cal. July 30, 1998).)

52. The Supreme Court's decisions in *Myriad*, *Mayo*, and *Alice*, however, prohibit the patenting of products found in nature (or minor and insignificant variations thereof). Under

those decisions, the claims of the Novartis Patents directed to nucleotide or protein sequences that mirror the natural genomic sequence of HCV are patent ineligible subject matter under § 101.

53. To the extent that Novartis contends that certain of the Novartis Patents recite minor variations that somehow make the claimed subject matter "markedly different" from what exists in nature, Supreme Court and Federal Circuit precedent establishes that is false. Indeed, the heart of every claim of the Novartis Patents is directed to the naturally occurring genomic sequence of HCV. The mere recitation of routine and conventional techniques or research tools that were widely known at the time does not avoid that analysis, let alone establish patent-eligibility under § 101.

54. For example, Novartis has specifically admitted that the claims of the '596 patent would cover "the HCV virus as it existed in nature" but for its inclusion of language specifying that the claimed oligonucleotide was "purified." (Ex. 1, *Chiron v. Roche* Claim Construction Brief at 24). But Supreme Court precedent—including the *Myriad* decision invalidating claims to isolated DNA sequences—has made clear that "isolation" is irrelevant to patent eligibility, and that such claims are invalid. *See Myriad*, 133 S. Ct. at 2118.

55. Similarly, claims of the Novartis Patents directed to routine laboratory techniques involving these HCV sequences, such as methods for assaying compounds for activity against HCV, adding labels to polynucleotide sequences, or making fusion proteins, are also invalid under the *Mayo*, *Myriad*, and *Alice* decisions (as well as decisions by the Federal Circuit and district courts). That precedent confirms that the mere presence of such claim elements does not change the basic and fundamental analysis – namely, the heart of the Novartis Patent claims is directed to a natural product. And, as the Federal Circuit has confirmed, conventional and routine methods are "not new and useful." *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1377 (Fed. Cir. 2015).

56. In fact, Novartis has admitted that "[t]he novel aspect of the invention of these three patents [the '719, '088, and '596 patents] ***is the genomic sequence of HCV***." (Ex. 1, *Chiron v. Roche* Claim Construction Brief at 3) (emphasis added). The Supreme Court has since

made clear that the identification of such naturally-occurring sequences is *per se* patent-ineligible. In essence, Novartis has sought to patent the Hepatitis C Virus, itself, so that anyone seeking to use or study the virus in order to invent new therapies must license the Novartis Patents.

57. To the extent that Defendants contend that any claims of the Novartis Patents recite anything more than natural products, the Novartis Patents, themselves, admit that such claims recite at most conventional variations and applications thereof.

58. The specifications of all of the Novartis Patents admit that the inventions utilize conventional techniques of scientific research that were routine and well known at the time the applications were filed.

59. For example, the specification of the '180 patent[1] states: "The practice of the present invention generally employs ***conventional techniques*** of molecular biology, microbiology, recombinant DNA, and immunology, ***which are within the skill of the art***. Such techniques are ***explained fully*** in the literature." (Ex. 2,'180 patent col. 7, ll. 28-51 (emphasis added); *see also* Ex. 6, '816 patent col. 20, l. 42 – col. 21., l. 3; Ex. 4, '596 patent col. 12, ll. 23-28; Ex. 7, '541 patent col. 20, ll. 9-37.)

60. Likewise, the specification of the '857 patent states: "The practice of the present invention will employ, unless otherwise indicated, ***conventional techniques*** of chemistry, molecular biology, microbiology, recombinant DNA, and immunology, ***which are within the skill of the art***. Such techniques are ***explained fully*** in the literature." (Ex. 11,'857 patent col. 4, ll. 5-15 (emphasis added); *see also* Ex. 3, '088 patent co. 12, ll. 13-28; Ex. 5, '719 patent col. 12, ll. 13-28; Ex. 4 '596 patent col. 12, ll. 23-38; Ex. 12, '093 patent col. 4, ll. 4-14.) The "literature" cited in the Novartis Patents includes numerous standard scientific texts and laboratory manuals that were widely known by those of ordinary skill in the art at the relevant times. This literature disclosed the use of conventional research techniques, including, for example, making and using fusion proteins, vectors, molecular cloning, synthesizing oligonucleotides, making labeled

[1] For purposes of this Complaint, AbbVie cites exemplary passages from select specifications.

polynucleotide sequences, and cellular transformation. (*See, e.g.*, Ex. 2, '180 patent col. 7, ll. 32-51; Ex. 6, '816 patent col. 20, l. 42 – col. 21, l. 3; Ex. 11, '857 patent col. 4, ll. 5-15.)

61. In still other portions of the specifications, the Novartis Patents further acknowledge that various techniques and methods in molecular and cell biology were routine and conventional at the relevant times.

62. For example, the Novartis Patents admit that the use of vectors was well known. (*See, e.g.*, Ex. 2, '180 patent col. 9, ll. 30-50 ("Vectors suitable for replication in mammalian cells are known in the art . . . :"); col. 9, l. 60 – col. 10, l. 24 ("May [sic] other vectors known to those of skill in the art have also been designed for improved expression[.]"); col. 11, ll. 6-18 ("Vector construction employs techniques which are known in the art."); col. 12, ll. 23-39 (describing routine vector construction)).

63. Additionally, the Novartis Patents disclose many other standard techniques, such as cellular transformation, labeling, hybridization techniques, insertion of particular polynucleotide sequences into expression vectors, determining whether polypeptide sequences have immunoreactivity, and fusion proteins. (*See, e.g.*, Ex. 2, '180 patent col. 10, ll. 50 – col. 11, l. 5 ("Transformation may be by any known method for introducing polynucleotides into a host cell, including, for example . . . ."); col. 11, ll. 39-44 (Synthetic oligonucleotides may be prepared using an automated oligonucleotide synthesizer as described by Warner, DNA (1984) 3:401. If desired, the synthetic strands may be labeled with $^{32}$P by treatment with polynucleotide kinase in the presence of $^{32}$P-ATP under standard reaction conditions."); Ex. 6, '816 patent col. 12, ll. 52-58 ("Information on several different strains/isolates of HCV is disclosed herein, particularly strain or isolate CDC/HCVI (also called HCV1). Information from one strain or isolate, such as a partial genomic sequence, is sufficient to allow those skilled in the art using standard techniques to isolate new strains/isolates and to identify whether such new strains/isolates are HCV."); col. 14, ll. 18-22 ("Methods for determining immunological reactivity are known in the art, for example, by radioimmunoassay, by Elisa assay, by hemagglutination, and several examples of suitable techniques for assays are provided herein."); col. 14, ll. 57-64 ("The techniques for determining amino acid sequence homology are known in

the art. For example, the amino acid sequence may be determined directly and compared to the sequences provided herein. Alternatively the nucleotide sequence of the genomic material of the putative HCV may be determined (usually via a cDNA intermediate), the amino acid sequence encoded therein can be determined, and the corresponding regions compared."); col. 17, ll. 49-51 ("The techniques for determining whether a polypeptide is immunologically reactive with an antibody are known in the art."); col. 33, ll. 48-52 (polynucleotide "probes are usually labeled. Suitable labels, and methods for labeling probes are known in the art, and include, for example, radioactive labels incorporated by nick translation or kinasing, biotin, fluorescent probes, and chemiluminescent probes."); col. 44, ll. 19-22 ("Vectors suitable for replication in mammalian cells are known in the art."); col. 46, ll. 11-12 ("Vector construction employs techniques which are known in the art."); Ex. 11, '857 patent at col. 5, l. 52 – col. 6, l. 12 ("Preferably, the antisense nucleic acid of this invention is RNA, DNA or a modified nucleic acid. Examples, without limitation, of modified nucleic acids are degradation-resistant sulfurized and thiophosphate derivatives of nucleic acids, and polynucleoside amides . . . . Many such modifications are known in the art . . . ."); col. 7, ll. 23-34 ("A particularly preferred moiety to increase uptake is a cholesteryl group. Cholesteryl-like groups may be attached through an activated cholesteryl chloroformate, for example, or cholic acid, by means known in the art as reflected in [the art].)").

64. Additionally, during prosecution of Novartis Patents, the Patentees admitted, among other things, that: "Once the nucleotide sequence of HCV was provided by Applicants' discovery, the use of these nucleotide sequences for both the expression of HCV polypeptides and HCV probes became obvious, and therefore not patentably distinct." *See, e.g.*, '816 patent 11/28/1995 Response to Restriction Requirement at 2.

**Novartis Patent Family 1**

65. The Novartis Patents can be grouped into three patent families based on their claims of priority to common patent applications. Patent Family 1 includes the '180 patent.

66. The '180 patent includes claims directed to protein sequences of naturally occurring HCV helicases, as well as naturally occurring polynucleotide sequences corresponding

to the naturally occurring HCV NS3 region of the HCV genome. (*See* Ex. 2,'180 patent claims 1-2, 5-7, 14-15). For example, claim 1 of the '180 patent recites "An isolated polynucleotide wherein said polynucleotide encodes a truncated fragment of the hepatitis C virus (HCV) NS3 helicase fragment, said truncated fragment retaining helicase activity." This claim is directed to a naturally occurring polynucleotide sequence within the HCV genome that has been "isolated." As the Supreme Court made clear in *Myriad*, mere isolation of a polynucleotide sequence that occurs in nature does not confer patent eligibility.

67. Other claims of the '180 patent are directed to natural products manipulated using laboratory techniques that were routine and conventional at the time the applications were filed, including fusion proteins and expression vectors. (*See* Ex. 2,'180 patent claims 3-4, 8-13). For example, claim 3 of the '180 patent recites "An isolated polynucleotide wherein said polynucleotide encodes a fusion protein comprising a truncated fragment of the HCV NS3 helicase fragment, said truncated fragment retaining helicase activity, and a fusion partner." This claim recites a naturally occurring polynucleotide sequence (i.e., that of an HCV NS3 helicase fragment), and adds to it a fusion partner, which the '180 patent discloses can be well-known enzymes such as β-galactosidase, horseradish peroxidase, or human superoxide dismutase, and the like. (Ex. 2, '180 patent col. 6, ll. 62 – col. 7, ll. 26). Adding a fusion partner like one of these enzymes to a polynucleotide sequence of interest was a routine and conventional scientific technique at the time the application for the '180 patent was filed—a fact essentially admitted in the '180 patent where it explains that "[t]he practice of the present invention generally employs conventional techniques of molecular biology, microbiology, recombinant DNA, and immunology, which are within the skill of the art. Such techniques are explained fully in the literature. [Citing 15 references]." (Ex. 2,'180 patent col. 7, ll. 28-51). Indeed, one of these cited references discusses routine methods of making fusion proteins that were widely known at the time. (*See Molecular Cloning: A Laboratory Manual* (1989)).

68. Still other claims of Patent Family 1 are directed to laboratory techniques that were routine and conventional at the time the applications were filed, and involve naturally occurring HCV protein and polynucleotide sequences, including methods of making HCV

proteins. (*See* Ex. 2,'180 patent claims 16-27). For example, claim 16 of the '180 patent recites "[a] method of making a purified truncated fragment of the Hepatitis C Virus (HCV) NS3 helicase fragment" that involves transfecting a host cell with an expression vector that contains the polynucleotide sequence encoding a truncated fragment of the HCV NS3 helicase fragment, incubating the transfected cell so that the helicase fragment is expressed, and then purifying the expressed fragment. As confirmed in texts that are expressly referenced in the '180 patent, using expression vectors and transfected host cells so as to obtain purified proteins was a routine and conventional technique at the at the time the application for the '180 patent was filed. (*See Molecular Cloning: A Laboratory Manual* (1989)).

69. As with the genomic DNA claims in *Myriad*, the claims in Patent Family 1 directed to naturally occurring HCV protein and nucleotide sequences are invalid under § 101.

70. Similarly, the claims in Patent Family 1 directed to natural products manipulated using laboratory techniques that were routine and conventional at the time the applications were filed, including claims directed to fusion proteins and expression vectors, are invalid under §101. As in *Mayo* and *Alice*, these claims contain no "inventive concept" that transforms them from ineligible natural products and phenomena to patent eligible applications of the natural products and phenomena.

71. Indeed, the patentees admit they relied on such routine and conventional laboratory techniques, describing them as "within the skill of the art" or "known in the art." (*See, e.g.*, Ex. 2,'180 patent col. 7, ll. 28-51 ("The practice of the present invention generally employs conventional techniques of molecular biology, microbiology, recombinant DNA, and immunology, which are within the skill of the art. Such techniques are explained fully in the literature."); col. 9, ll. 30-34 ("Vectors suitable for replication in mammalian cells are known in the art . . . :"); col. 9, l. 60 – col. 10, l. 24 ("May [sic] other vectors known to those of skill in the art have also been designed for improved expression[.]"); col. 10, ll. 50 – col. 11, l. 5 ("Transformation may be by any known method for introducing polynucleotides into a host cell, including, for example . . . ."); col. 11, ll. 6-18 ("Vector construction employs techniques which are known in the art."); col. 11, ll. 39-44 (Synthetic oligonucleotides may be prepared using an

automated oligonucleotide synthesizer as described by Warner, DNA (1984) 3:401. If desired, the synthetic strands may be labeled with $^{32}$P by treatment with polynucleotide kinase in the presence of $^{32}$P-ATP under standard reaction conditions."); col. 12, ll. 23-39 (describing routine vector construction).) Moreover, the claims do not add any "inventive concept" to the unpatentable natural products and phenomena and would preempt virtually all efforts to produce and study HCV nucleotide and protein sequences.

72. Claims in the '180 patent directed to routine and conventional laboratory techniques involving naturally occurring HCV protein and polynucleotide sequences, such as claims to methods of making HCV proteins, are also invalid under § 101. As in *Mayo* and *Alice*, these claims are directed to natural products, laws of nature and natural phenomena, and the addition of routine and conventional steps, recited at a high level of generality, and they cannot supply an "inventive concept" that would transform the claims from ineligible natural products and phenomena to patent eligible applications of natural products and phenomena.

73. To the extent that any claims of Patent Family 1 are found to be not invalid under § 101, they are invalid under § 112 and/or the doctrine of obviousness-type double patenting.

74. Numerous claims of the '180 patent purport to recite subject matter that a person of ordinary skill, in light of the respective specifications, would conclude that the respective named inventors did not possess at the relevant time. For instance, some claims of the '180 patent purport to encompass any and all of the at least seven major genetic types of HCV (so-called "genotypes,"), its numerous additional subtypes and quasi-species, as well as individual variants, and viral particles of any of those. (*See, e.g.*, Ex. 2, '180 patent claims 1, 3-4, 8-10, 14-18, 20-23, 25, and 27.) The respective specifications, however, disclose only a single form of HCV.

75. Numerous claims of the '180 patent are also invalid under the doctrine of obviousness-type double patenting. For instance, certain claims of the '180 patent recite isolated polynucleotide sequences encoding truncated HCV NS3 helicase fragments and methods of making purified truncated HCV NS3 helicase fragments. (Ex. 2, '180 patent claims 1-7 and 16-20.) However, the parent patent to the '180 patent, U.S. Patent No. 6,194,140 ("the '140

patent"), claims purified truncated HCV NS3 helicase fragments, which can be produced through use of recombinant polynucleotide sequences. At the time the patents were filed, skilled artisans could use conventional techniques of molecular biology to generate isolated polynucleotide sequences from known protein sequences, like that of the purified truncated HCV NS3 helicase fragments, and vice versa. (*See, e.g.*, '140 patent col. 7, ll. 38-61 (explaining that the claimed "invention generally employs conventional techniques of molecular biology, microbiology, recombinant DNA [i.e., polynucleotide], and immunology, which are within the skill of the art" and that "[s]uch techniques are explained fully in the literature. [Citing references]"); Ex. 2, '180 patent col. 7 ll. 28-51 (same).) No terminal disclaimer to the '140 patent was filed in the application for the '180 patent, and the expiration date of the '140 patent is earlier than that of the '180 patent.

**Novartis Patent Family 2**

76. Patent Family 2 includes the '088, '596, '719, '816, '541, '782, '729, and '366 patents.

77. Patent Family 2 differs from Patent Family 1 mainly in that it purportedly discloses more of the naturally occurring sequence of the HCV genome.

78. Patent Family 2 includes claims directed to naturally occurring HCV proteins and claims to sequences that correspond to the naturally occurring HCV genome, including naturally occurring HCV polypeptides, oligonucleotides capable of "selectively hybridizing" to the genome of HCV, the use of those nucleotides in detecting HCV, and kits containing those nucleotides. (*See* Ex. 9, '729 patent claims 1-27; Ex. 4, '596 patent claims 1-27; Ex. 6, '816 patent claims 1-36; Ex. 10, '366 patent claims 1-49, 86-103, 121-128, 131, 139-176).

79. For example, claim 1 of the '729 patent recites "[a]n isolated polypeptide comprising an amino acid sequence of at least 12 contiguous amino acids encoded by a hepatitis C virus (HCV) genome." This claim is directed to a naturally occurring polypeptide sequence within the HCV genome that has been "isolated." Similarly, claim 1 of the '596 patent recites "[a] purified preparation of an oligonucleotide" that is at least 10 nucleotides long and that is "capable of selectively hybridizing to the genome of a hepatitis C virus (HCV) or its

complement." This claim recites nothing more than a "purified" short, naturally occurring polynucleotide sequence. Indeed, the HCV polynucleotide itself, by definition, is capable of selectively hybridizing to its own complement. As the Supreme Court made clear in *Myriad*, mere isolation or purification of a polynucleotide or polypeptide sequence that occurs in nature does not confer patent eligibility. Claim 1 of the '816 patent is similar, reciting "[a] purified preparation of an oligonucleotide" that is at least 8 nucleotides long and that "is present in an amount capable of selectively and detectably hybridizing to the genome of a hepatitis C virus (HCV) or its complement." Likewise, the polynucleotide of claim 1 of the '366 patent is at least 12 and no more than 353 nucleotides long and has a sequence that corresponds to an HCV sequence that is recited in one of three figures in the '366 patent.

80. Other claims of Patent Family 2 are directed to natural products manipulated using laboratory techniques that were routine and conventional at the time the applications were filed, including labeled polynucleotides, anti-HCV antibodies and methods for making them in general terms, and cell cultures or cell lines for replicating HCV. (*See* Ex. 6, '816 patent claims 37-42; Ex. 7, '541 patent claims 1-3, 5; Ex. 10, '366 patent claims 50-85, 104-120, 129-130, 132-138, 299; Ex. 8, '782 patent claims 1-21).

81. For example, claim 37 of the '816 patent recites a polynucleotide vector that comprises an HCV polynucleotide sequence that encodes a polypeptide sequence that is at least 10 amino acids long and a polypeptide sequence that is an antigenic determinant (i.e., a sequence recognized by an antibody). This claim recites a short, naturally occurring polynucleotide sequence that encodes a short, naturally occurring polypeptide sequence, which has been included in a vector. The '816 patent explains that such vectors are known. (Ex. 6, '816 patent col. 44, ll. 19-22 ("Vectors suitable for replication in mammalian cells are known in the art, . . . ."). And at least one of the references incorporated into the '816 patent includes an entire chapter explaining how polynucleotides can be cloned into plasmid vectors, and an appendix section devoted to the pBR322 vector that the '816 patent explains may be used as part of its claims. (*Molecular Cloning: A Laboratory Manual* (1982); Ex. 6, '816 patent col. 43, ll. 17-40). Likewise, claim 50 of the '366 patent recites an HCV polynucleotide sequence that "is labeled."

The '366 patent explains that polynucleotide labels, commonly used on nucleotide probes, were known in the art. (Ex. 10, '366 patent col. 32, ll. 40-44). Claim 1 of the '541 patent recites a "hepatocyte cell culture infected with hepatitis C virus (HCV), wherein the culture replicates HCV." This claim does nothing more than recite infection of a particular cell line with a naturally occurring HCV virus. As the '541 patent explains, hepatocyte cell cultures were already known to support infection and replication of a related virus family, the Flavivirus family. (Ex. 7, '541 patent col. 39, l. 58 – col. 40, l. 6; col. 12, ll. 28-31). Claim 1 of the '782 patent recites an "anti-HCV antibody composition comprising isolated anti-HCV antibodies that are immunologically reactive with an HCV polypeptide, wherein said polypeptide comprises an amino acid sequence of at least 8 contiguous amino acids encoded by an HCV genome." This claim merely recites an anti-HCV antibody that has been made using a naturally occurring portion of an HCV protein. The '782 patent explains that "[t]he term 'antibody' includes, for example, vertebrate antibodies," and that "[v]ertebrate antibodies typicalily [sic] include native antibodies, for example, purified polyclonal antibodies and monoclonal antibodies." (Ex. 8, '782 patent col. 17, ll. 29-33, col. 17, ll. 55-57.) As such this claim covers antibodies that would naturally arise when an animal is infected with HCV. The specification indicates precisely this: "polyclonal antibodies may be isolated from a mammal which has been previously infected with HCV." (Ex. 8, '782 patent col. 31, ll. 52-53.)

82. Finally, certain claims of Patent Family 2 are directed to laboratory techniques that were routine and conventional at the time the applications were filed involving naturally occurring HCV protein and polynucleotide sequences, and anti-HCV antibodies, including methods for detecting HCV. (*See* Ex. 3, '088 patent claims 1-13; Ex. 5, '719 patent claims 1-6; Ex. 7, '541 patent claims 4, 6; Ex. 10, '366 patent claims 177-298; Ex. 8, '782 patent claims 22-27).

83. For example, claim 1 of the '088 patent recites "[a] method for detecting an HCV sequence in a test sample" by providing an oligonucleotide primer set, amplifying a target region identified by those primers using a polymerase chain reaction ("PCR") method, incubating the amplified target region with a test sample, detecting whether the amplified target region

hybridizes with another oligonucleotide that hybridizes to an HCV sequence, and determining that HCV is present if hybrids are formed. The '088 patent explains that both PCR and hybridization assays were known in the art. (Ex. 3, '088 patent col. 21, ll. 35–39 ("The amplification may be accomplished, for example, by the polymerase chain reactions (PCR) technique described by Saiki et al. (1986), by Mullis, U.S. Pat. No. 4,683,195, and by Mullis et al. U.S. Patent No. 4,683,202."); col. 4, ll. 35–36 ("Methods for detecting specific polynucleotides by hybridization assays are known in the art."); col. 28, ll. 51–52 ("Methods to detect hybrids formed between a probe and a nucleic acid sequence are known in the art."); *see also*, *id.* at col. 9, ll. 14–16 ("[h]ybridization techniques for determining the complementarity of nucleic acid sequences are known in the art")). As such, this claim, at its core, instructs that these well-known techniques should be used to detect HCV. Claim 1 of the '719 patent is similar, reciting "[a] method for detecting an HCV sequence in a test sample" by providing an oligonucleotide that is capable of hybridizing to an HCV sequence to a sample, incubating the sample, detecting whether any hybrids form, and determining that HCV is present if hybrids are formed. The only difference from claim 1 of the '088 patent is that no amplification step is required. Claim 4 of the '541 patent recites "[a] method of producing a hepatocyte cell culture that replicates HCV" by introducing a polynucleotide that encodes an HCV protein into cultured hepatocytes and then incubating those hepatocytes. As the '541 patent explains, methods for introducing polynucleotides into cell lines were known at the time the patent was filed. (Ex. 7, '541 patent col. 45, ll. 5–25 ("Transformation may be by any known method for introducing polynucleotides into a host cell, including . . . by direct uptake of the polynucleotide. . . . Mammalian transformation by direct uptake may be conducted using the calcium phosphate precipitation method of Graham and Van der Eb (1978), . . . ."). Claim 177 of the '366 recites "[a] method of selecting biological samples from a supply of human biological samples" by selecting those samples that have a "detectable polynucleotide" of a particular HCV sequence. The '366 patent explains that these selection methods can include introducing labeled polynucleotide probes to a biological sample and then detecting any hybridization of the probes with portions of the HCV genome present in the sample. (Ex. 10, '366 patent col. 33, l. 19 –

col. 34, l. 52). The probe labels and hybridization procedure, as explained in the '366 patent, were known in the art. (Ex. 10, '366 patent col. 32, ll. 41-42 ("Suitable labels, and methods for labeling probes are known in the art, . . . ."); *see id.* at col. 32, ll. 53-58 ("The stringency of hybridization is determined by a number of factors during hybridization and during the washing procedure, . . . . These factors are outlined in, for example, Maniatis, T. (1982).")). Claim 22 of the '782 patent recites "[a]n immunoassay method" using anti-HCV antibody, which can be a naturally occurring antibody, incubating it with a test sample, and detecting if any antigen-antibody complexes are formed. The '782 patent explains that such immunoassay techniques are well known in the art. (Ex. 8, '782 patent col. 33, ll. 64-66 ("Design of the immunoassays is subject to a great deal of variation, and many formats are known in the art."); col. 35, ll. 1-14 ("In immunoassays where HCV polypeptides are the analyte, the test sample, typically a biological sample, is incubated with anti-HCV antibodies under conditions that allow the formation of antigen-antibody complexes. Various formats can be employed. . . . These and other formats are well known in the art.").)

84. As with the genomic DNA sequences in *Myriad*, the claims in Patent Family 2 directed to HCV proteins and polynucleotide sequences that mirror those found in nature are invalid under § 101.

85. Similarly, the claims in Patent Family 2 directed to natural products manipulated using laboratory techniques that were routine and conventional at the time the applications were filed, including claims directed to labeled polynucleotides, anti-HCV antibodies, and cell cultures for replicating HCV, are invalid under §101. As in *Mayo* and *Alice Corp.*, these claims involve merely routine and conventional techniques and tools. At their core, these claims contain no "inventive concept" that transforms them from ineligible natural products and phenomena to patent eligible applications of the natural products and phenomena. *See also Ariosa*, 788 F.3d at 1378 ("[A]ppending routine, conventional steps to a natural phenomenon, specified at a high level of generality, is not enough to supply an inventive concept."). The patentees did not invent labeled polynucleotides, methods of making antibodies, or cell cultures; all were well known and routine in the art, and these modifications were equally and routinely

applicable to non-HCV viral sequences, and the claims do not add any "inventive" concept to the unpatentable natural products and phenomena.

86. Finally, the claims in Patent Family 2 directed to laboratory techniques that were routine and conventional at the time the applications were filed involving naturally occurring HCV protein and polynucleotide sequences, such as methods for detecting HCV are invalid under § 101. As in *Mayo* and *Alice Corp.*, these claims are recited at a high level of generality and do not contain any "inventive concept" or any meaningful limitations in addition to the natural products and phenomena.

87. To the extent that any claims of Patent Family 2 are found to be not invalid under § 101, they are invalid under § 112 and/or the doctrine of obviousness-type double patenting.

88. Numerous claims of Patent Family 2 purport to recite subject matter that a person of ordinary skill, in light of the respective specifications, would conclude that the respective named inventors did not possess at the relevant time. For instance, some claims of Patent Family 2 seek to encompass any and all of the at least seven genetic types of HCV (so-called "genotypes,"), its numerous additional subtypes and quasi-species, as well as individual variants, but in contrast, the specification discloses only a single form of HCV. (*See, e.g.*, Ex. 9, '729 patent claims 1, 3, and 6-27; Ex. 3, '088 patent claims 1-5, 7-10, and 12; Ex. 5, '719 patent claims 1-4; Ex. 7, '541 patent claims 1-6; Ex. 6, '816 patent claims 1-11, 15-25, 29-31, and 33-42.) Other claims of Patent Family 2 recite "selectively . . . hybridizing" and a person of ordinary skill in the art would not understand the scope of this claim limitation with reasonable certainty. (*See, e.g.*, Ex. 4, '596 patent claims 1-27; Ex. 3, '088 patent claims 1-13; Ex. 5, '719 patent claims 1-4; Ex. 6, '816 patent claims 7-11 and 15-28.)

89. Numerous claims of Patent Family 2 are also invalid under the doctrine of obviousness-type double patenting. For instance, some of the earlier expiring patents that name the same or overlapping inventors as those in Patent Family 2 and were also originally assigned to the same Novartis entity recite compositions comprising purified or isolated preparations of polynucleotides or polypeptides. Other, later expiring Family 2 patents in , where no terminal disclaimer was filed, recite purified or isolated preparations of polynucleotides or polypeptides

and methods that use such polynucleotides or polypeptides in laboratory techniques that were routine and conventional at the time the applications were filed. For example, certain claims of the '816 patent recite purified polynucleotide sequences encoding polypeptides that are encoded by the HCV genome, including polynucleotide sequences that encode non-structural HCV proteins such as the HCV protease. (*See, e.g.,* Ex. 6, '816 patent claims 29-35.) However, another patent that names the same inventors, was also originally assigned to the same Novartis entity (Chiron), but is in a separate patent family, U.S. Patent No. 5,371,017 ("the '017 patent"), claims isolated polynucleotides that encode the HCV protease. No terminal disclaimer to the '017 patent was filed in the application for the '816 patent, and the expiration date of the '017 patent is earlier than that of the '816 patent. Similarly, certain claims of the '729 patent recite isolated polypeptide sequences that are encoded by an HCV genome. (*See, e.g.,* Ex. 9, '729 patent claims 1-5, 7-27.) However, another patent that names overlapping inventors, was also originally assigned to the same Novartis entity (Chiron), but is in a separate patent family, the '140 patent, claims purified HCV NS3 helicase fragments, which are polypeptide sequences encoded by an HCV genome. No terminal disclaimer was filed in the application for the '729 patent, and the expiration date of the '140 patent is earlier than that of the '729 patent. The claims of these patents cover the same subject matter and would have been obvious in view of each other.

**Novartis Patent Family 3**

90. Patent Family 3 includes the '857 and '093 patents.

91. Patent Family 3 includes claims directed to compositions for enhancing or controlling the translation of a nucleic acid using naturally occurring HCV sequences and claims to related methods. (*See* Ex. 11, '857 patent claims 1-11; Ex. 12,'093 patent claim 1). For example, claim 1 of the '857 patent recites a composition comprising a nucleic acid having a sequence corresponding to a particular sequence disclosed in the patent (a "pestivirus homology box IV area") and another nucleic acid sequence. Naturally occurring sequences, such as HCV sequences, are included in this claim. For example, the HCV genome itself includes a nucleic acid sequence that comprises both a pestivirus homology box IV area sequence and a nucleic

acid sequence to be translated. The sole claim of the '093 patent recites "[a] method of enhancing the translation of a coding region" by making an RNA molecule made up of a coding region of interest and a 5' untranslated region that includes a particular sequence disclosed in the patent (i.e., a "pestivirus homology box IV" sequence), and then translating the RNA molecule. Like the '857 patent claim 1, the '093 patent claim 1 includes a naturally occurring nucleic acid sequence—specifically the HCV genome itself. HCV is an RNA molecule that comprises a coding region and a 5' untranslated region that includes a pestivirus homology box IV sequence. And, as part of the naturally occurring replication process for HCV, the HCV RNA molecule is translated.

92. As were the genomic DNA in *Myriad*, the claims in Patent Family 3 directed to nucleotide sequences that mirror those found in nature are invalid under § 101.

93. Similarly, claims to modified nucleic acid sequences made using laboratory techniques that were routine and conventional at the time the applications were filed are not patent eligible under *Mayo* and *Alice*. (*See, e.g.*, Ex. 11, '857 patent col. 4, ll. 5-15 ("The practice of the present invention will employ, unless otherwise indicated, conventional techniques of chemistry, molecular biology, microbiology, recombinant DNA, and immunology, which are within the skill of the art. Such techniques are explained fully in the literature."); col. 5, l. 52 – col. 6, l. 12 ("Preferably, the antisense nucleic acid of this invention is RNA, DNA or a modified nucleic acid. Examples, without limitation, of modified nucleic acids are degradation-resistant sulfurized and thiophosphate derivatives of nucleic acids, and polynucleoside amides . . . . Many such modifications are known in the art . . . ."); col. 7, ll. 23-34 ("A particularly preferred moiety to increase uptake is a cholesteryl group. Cholesteryl-like groups may be attached through an activated cholesteryl chloroformate, for example, or cholic acid, by means known in the art as reflected in [the art].")).

94. The claims in Patent Family 3 directed to methods of using nucleic acid sequences that mirror naturally occurring HCV sequences to enhance or control the translation of a nucleic acid are invalid under § 101 in view of *Mayo* and *Alice Corp.* The claimed sequences operate in the claimed method according to the same principles and in the same manner as in

nature. As in *Mayo* and *Alice Corp.*, these claims are recited at a high level of generality and do not contain any "inventive concept" or contain any meaningful limitations in addition to the natural products and phenomena.

95. To the extent that any claims of Patent Family 3 are found to be not invalid under § 101, they are invalid under § 112. Some claims of Patent Family 3 purport to recite subject matter that a person of ordinary skill, in light of the respective specifications, would conclude that the named inventors did not possess at the relevant time. For instance, some claims of Patent Family 3 seek to encompass any and all of the seven genetic types of HCV (so-called "genotypes,") (*see, e.g.*, Ex. 11, '857 patent claims 1-2), but in contrast, the specification discloses only a single isolate of HCV – namely, HCV-1.

**COUNT I FOR DECLARATORY JUDGMENT**
**(Invalidity of the '180 Patent)**

96. Plaintiff incorporates by reference and realleges Paragraphs 1-95 above as though fully restated herein.

97. This declaratory judgment claim arises under the United States Patent Laws, 35 U.S.C. § 100 et seq., including 35 U.S.C. § 271(a)-(c), and the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202. Subject matter jurisdiction is proper under 28 U.S.C. §§ 1331 and 1338(a).

98. As a result of the totality of circumstances detailed above, there is an actual, immediate, and justiciable controversy that exists between AbbVie and Novartis and Grifols concerning the validity of the '180 patent.

99. Any claims of the '180 patent REDACTED

are invalid for failing to satisfy the requirements of Title 35 of the United States Code, including one or more of 35 U.S.C. §§ 101, 112, and/or the doctrine of obviousness-type double patenting.

100. In addition, all other claims of the '180 patent are also invalid for failing to satisfy the requirements of Title 35 of the United States Code, including one or more of 35 U.S.C. §§ 101, 112, and/or the doctrine of obviousness-type double patenting.

101. AbbVie is entitled to a declaratory judgment that any claims of the '180 patent REDACTED are invalid, and that any other claims of these patents are also invalid.

**COUNT II FOR DECLARATORY JUDGMENT**
**(Invalidity of the '088 patent)**

102. Plaintiff incorporates by reference and realleges Paragraphs 1-95 above as though fully restated herein.

103. This declaratory judgment claim arises under the United States Patent Laws, 35 U.S.C. § 100 et seq., including 35 U.S.C. § 271(a)-(c), and the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202. Subject matter jurisdiction is proper under 28 U.S.C. §§ 1331 and 1338(a).

104. As a result of the totality of circumstances detailed above, there is an actual, immediate, and justiciable controversy that exists between AbbVie and Novartis and Grifols concerning the validity of the '088 patent.

105. Any claims of the '088 patent REDACTED are invalid for failing to satisfy the requirements of Title 35 of the United States Code, including one or more of 35 U.S.C. §§ 101, 112, and/or the doctrine of obviousness-type double patenting.

106. In addition, all other claims of the '088 patent are also invalid for failing to satisfy the requirements of Title 35 of the United States Code, including one or more of 35 U.S.C. §§ 101, 112, and/or the doctrine of obviousness-type double patenting.

107. AbbVie is entitled to a declaratory judgment that the claims of the '088 patent REDACTE

REDACTED are invalid, and that any other claims of these patents are also invalid.

**COUNT III FOR DECLARATORY JUDGMENT**
**(Invalidity of the '596 patent)**

108. Plaintiff incorporates by reference and realleges Paragraphs 1-95 above as though fully restated herein. This declaratory judgment claim arises under the United States Patent Laws, 35 U.S.C. § 100 et seq., including 35 U.S.C. § 271(a)-(c), and the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202. Subject matter jurisdiction is proper under 28 U.S.C. §§ 1331 and 1338(a).

109. As a result of the totality of circumstances detailed above, there is an actual, immediate, and justiciable controversy that exists between AbbVie and Novartis and Grifols concerning the validity of the '596 patent.

110. Any claims of the '596 patent REDACTED

are invalid for failing to satisfy the requirements of Title 35 of the United States Code, including one or more of 35 U.S.C. §§ 101, 112, and/or the doctrine of obviousness-type double patenting.

111. In addition, all other claims of the '596 patent are also invalid for failing to satisfy the requirements of Title 35 of the United States Code, including one or more of 35 U.S.C. §§ 101, 112, and/or the doctrine of obviousness-type double patenting.

112. AbbVie is entitled to a declaratory judgment that the claims of the '596 patent

REDACTED

are invalid, and that any other claims of these patents are also invalid.

**COUNT IV FOR DECLARATORY JUDGMENT**
**(Invalidity of the '719 patent)**

113. Plaintiff incorporates by reference and realleges Paragraphs 1-95 above as though fully restated herein.

114. This declaratory judgment claim arises under the United States Patent Laws, 35 U.S.C. § 100 et seq., including 35 U.S.C. § 271(a)-(c), and the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202. Subject matter jurisdiction is proper under 28 U.S.C. §§ 1331 and 1338(a).

115. As a result of the totality of circumstances detailed above, there is an actual, immediate, and justiciable controversy that exists between AbbVie and Novartis and Grifols concerning the validity of the '719 patent.

116. Any claims of the '719 patent REDACTED

are invalid for failing to satisfy the requirements of Title 35 of the United States Code, including one or more of 35 U.S.C. §§ 101, 112, and/or the doctrine of obviousness-type double patenting.

117. In addition, all other claims of the '719 patent are also invalid for failing to satisfy the requirements of Title 35 of the United States Code, including one or more of 35 U.S.C. §§ 101, 112, and/or the doctrine of obviousness-type double patenting.

118. AbbVie is entitled to a declaratory judgment that any claims of the '719 patent REDACTED are invalid, and that any other claims of these patents are also invalid.

**COUNT V FOR DECLARATORY JUDGMENT**
**(Invalidity of the '816 patent)**

119. Plaintiff incorporates by reference and realleges Paragraphs 1-95 above as though fully restated herein.

120. This declaratory judgment claim arises under the United States Patent Laws, 35 U.S.C. § 100 et seq., including 35 U.S.C. § 271(a)-(c), and the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202. Subject matter jurisdiction is proper under 28 U.S.C. §§ 1331 and 1338(a).

121. As a result of the totality of circumstances detailed above, there is an actual, immediate, and justiciable controversy that exists between AbbVie and Novartis and Grifols concerning the validity of the '816 patent.

122. Any claims of the '816 patent REDACTED

are invalid for failing to satisfy the requirements of Title 35 of the United States Code, including one or more of 35 U.S.C. §§ 101, 112, and/or the doctrine of obviousness-type double patenting.

123. In addition, all other claims of the '816 patent are also invalid for failing to satisfy the requirements of Title 35 of the United States Code, including one or more of 35 U.S.C. §§ 101, 112, and/or the doctrine of obviousness-type double patenting.

124. AbbVie is entitled to a declaratory judgment that any claims of the '816 patent REDACTED are invalid, and that any other claims of these patents are also invalid.

**COUNT VI FOR DECLARATORY JUDGMENT**
**(Invalidity of the '541 patent)**

125. Plaintiff incorporates by reference and realleges Paragraphs 1-95 above as though fully restated herein.

126. This declaratory judgment claim arises under the United States Patent Laws, 35 U.S.C. § 100 et seq., including 35 U.S.C. § 271(a)-(c), and the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202. Subject matter jurisdiction is proper under 28 U.S.C. §§ 1331 and 1338(a).

127. As a result of the totality of circumstances detailed above, there is an actual, immediate, and justiciable controversy that exists between AbbVie and Novartis and Grifols concerning the validity of the '541 patent.

128. Any claims of the '541 patent REDACTED

REDACTEI are invalid for failing to satisfy the requirements of Title 35 of the United States Code, including one or more of 35 U.S.C. §§ 101, 112, and/or the doctrine of obviousness-type double patenting.

129. In addition, all other claims of the '541 patent are also invalid for failing to satisfy the requirements of Title 35 of the United States Code, including one or more of 35 U.S.C. §§ 101, 112, and/or the doctrine of obviousness-type double patenting.

130. AbbVie is entitled to a declaratory judgment that any claims of the '541 patent REDACTED are invalid, and that any other claims of these patents are also invalid.

**COUNT VII FOR DECLARATORY JUDGMENT**
**(Invalidity of the '782 patent)**

131. Plaintiff incorporates by reference and realleges Paragraphs 1-95 above as though fully restated herein.

132. This declaratory judgment claim arises under the United States Patent Laws, 35 U.S.C. § 100 et seq., including 35 U.S.C. § 271(a)-(c), and the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202. Subject matter jurisdiction is proper under 28 U.S.C. §§ 1331 and 1338(a).

133. As a result of the totality of circumstances detailed above, there is an actual, immediate, and justiciable controversy that exists between AbbVie and Novartis and Grifols concerning the validity of the '782 patent.

134. Any claims of the '782 patent REDACTED are invalid for failing to satisfy the requirements of Title 35 of the United States Code, including one or more of 35 U.S.C. §§ 101, 112, and/or the doctrine of obviousness-type double patenting.

135. In addition, all other claims of the '782 patent are also invalid for failing to satisfy the requirements of Title 35 of the United States Code, including one or more of 35 U.S.C. §§ 101, 112, and/or the doctrine of obviousness-type double patenting.

136. AbbVie is entitled to a declaratory judgment that any claims of the '782 patent REDACTED are invalid, and that any other claims of these patents are also invalid.

**COUNT VIII FOR DECLARATORY JUDGMENT**
**(Invalidity of '729 Patent)**

137. Plaintiff incorporates by reference and realleges Paragraphs 1-95 above as though fully restated herein.

138. This declaratory judgment claim arises under the United States Patent Laws, 35 U.S.C. § 100 et seq., including 35 U.S.C. § 271(a)-(c), and the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202. Subject matter jurisdiction is proper under 28 U.S.C. §§ 1331 and 1338(a).

139. As a result of the totality of circumstances detailed above, there is an actual, immediate, and justiciable controversy that exists between AbbVie and Novartis and Grifols concerning the validity of the '729 patent.

140. Any claims of the '729 patent REDACTED are invalid for failing to satisfy the requirements of Title 35 of the United States Code, including one or more of 35 U.S.C. §§ 101, 112, and/or the doctrine of obviousness-type double patenting.

141. In addition, all other claims of the '729 patent are also invalid for failing to satisfy the requirements of Title 35 of the United States Code, including one or more of 35 U.S.C. §§ 101, 112, and/or the doctrine of obviousness-type double patenting.

142. AbbVie is entitled to a declaratory judgment that any claims of the '729 patent REDACTED

REDACTED are invalid, and that any other claims of these patents are also invalid.

**COUNT IX FOR DECLARATORY JUDGMENT**
**(Invalidity of '366 Patent)**

143. Plaintiff incorporates by reference and realleges Paragraphs 1-95 above as though fully restated herein.

144. This declaratory judgment claim arises under the United States Patent Laws, 35 U.S.C. § 100 et seq., including 35 U.S.C. § 271(a)-(c), and the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202. Subject matter jurisdiction is proper under 28 U.S.C. §§ 1331 and 1338(a).

145. As a result of the totality of circumstances detailed above, there is an actual, immediate, and justiciable controversy that exists between AbbVie and Novartis and Grifols concerning the validity of the '366 patent.

146. Any claims of the '366 patent REDACTED

are invalid for failing to satisfy the requirements of Title 35 of the United States Code, including one or more of 35 U.S.C. §§ 101, 112, and/or the doctrine of obviousness-type double patenting.

147. In addition, all other claims of the '366 patent are also invalid for failing to satisfy the requirements of Title 35 of the United States Code, including one or more of 35 U.S.C. §§ 101, 112, and/or the doctrine of obviousness-type double patenting.

148. AbbVie is entitled to a declaratory judgment that any claims of the '366 patent REDACTED are invalid, and that any other claims of these patents are also invalid.

**COUNT X FOR DECLARATORY JUDGMENT**
**(Invalidity of the '857 patent)**

149. Plaintiff incorporates by reference and realleges Paragraphs 1-95 above as though fully restated herein.

150. This declaratory judgment claim arises under the United States Patent Laws, 35 U.S.C. § 100 et seq., including 35 U.S.C. § 271(a)-(c), and the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202. Subject matter jurisdiction is proper under 28 U.S.C. §§ 1331 and 1338(a).

151. As a result of the totality of circumstances detailed above, there is an actual, immediate, and justiciable controversy that exists between AbbVie and Novartis and Grifols concerning the validity of the '857 patent.

152. Any claims of the '857 patent REDACTED

are invalid for failing to satisfy the requirements of Title 35 of the United States Code, including one or more of 35 U.S.C. §§ 101 and/or 112.

153. In addition, all other claims of the '857 patent are also invalid for failing to satisfy the requirements of Title 35 of the United States Code, including one or more of 35 U.S.C. §§ 101 and/or 112.

154. AbbVie is entitled to a declaratory judgment that the claims of the '857 patent

REDACTED

are invalid, and that any other claims of these patents are also invalid.

**COUNT XI FOR DECLARATORY JUDGMENT**
**(Invalidity of the '093 patent)**

155. Plaintiff incorporates by reference and realleges Paragraphs 1-95 above as though fully restated herein.

156. This declaratory judgment claim arises under the United States Patent Laws, 35 U.S.C. § 100 et seq., including 35 U.S.C. § 271(a)-(c), and the Declaratory Judgment Act, 28

U.S.C. §§ 2201 and 2202. Subject matter jurisdiction is proper under 28 U.S.C. §§ 1331 and 1338(a).

157. As a result of the totality of circumstances detailed above, there is an actual, immediate, and justiciable controversy that exists between AbbVie and Novartis and Grifols concerning the validity of the '093 patent.

158. Any claims of the '093 patent REDACTED

are invalid for failing to satisfy the requirements of Title 35 of the United States Code, including one or more of 35 U.S.C. §§ 101, 112, and/or the doctrine of obviousness-type double patenting.

159. In addition, all other claims of the '093 patent are also invalid for failing to satisfy the requirements of Title 35 of the United States Code, including one or more of 35 U.S.C. §§ 101, 112, and/or the doctrine of obviousness-type double patenting.

160. AbbVie is entitled to a declaratory judgment that any claims of the '093 patent REDACTED are invalid, and that any other claims of these patents are also invalid.

**PRAYER FOR RELIEF**

161. WHEREFORE, Plaintiff respectfully requests that this Court enter judgment in their favor as follows:

a) A declaration that any claims of U.S. Patent Nos. 6,472,180; 5,712,088; 5,714,596; 5,863,719; 6,074,816; 6,096,541; 6,171,782; 6,027,729; 7,790,366; 5,922,857; and 6,057,093 REDACTED are invalid for failure to comply with one or more of the provisions of 35 U.S.C. §§ 100 et seq., including §§ 101, 112, and/or the doctrine of obviousness-type double patenting;

b) A declaration that any other claims of U.S. Patent Nos. 6,472,180; 5,712,088; 5,714,596; 5,863,719; 6,074,816; 6,096,541; 6,171,782; 6,027,729; 7,790,366; 5,922,857; and 6,057,093 are also invalid for failure to comply with one or more of the provisions of 35 U.S.C. §§ 100 et seq., including §§ 101, 112, and/or the doctrine of obviousness-type double patenting;

c) A finding that this is an exceptional case warranting imposition of attorney fees against Defendants and an award to AbbVie of its reasonable costs and attorneys' fees incurred in bringing this action pursuant to 35 U.S.C. § 285; and

d) An award of such other and further relief as the Court may deem just and proper.

Dated: March 31, 2017

Respectfully submitted,

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By */s/ Gregory K. Sobolski*

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