IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NATERA, INC.,	)	
	)	
Plaintiff,	)	
	)	
v.	)	C.A. No. _____
	)	
CAREDX, INC.,	)	**JURY TRIAL DEMANDED**
	)	
Defendant.	)	

COMPLAINT

Natera, Inc. ("Natera") submits this Complaint against CareDx, Inc. ("CareDx"). Natera hereby alleges as follows:

NATURE OF THE ACTION

1. Natera brings this claim for patent infringement to compel CareDx to stop infringing Natera's patent and to compensate Natera for CareDx's infringement of Natera's patented technology.

2. Founded in 2004, Natera (f.k.a Gene Security Network) is a pioneering genetics and bioinformatics company with industry-leading diagnostics products. Natera is dedicated to improving disease management for reproductive health, oncology, and organ transplantation. For well over a decade, Natera has been researching, developing, and commercializing non-invasive methods for analyzing DNA in order to help patients and doctors manage diseases. These ongoing efforts have given rise to a number of novel and proprietary genetic testing services to assist with life-saving health management.

3. Natera's pioneering and ongoing innovation is especially evident in the area of cell-free DNA ("cfDNA")-based testing. In the cfDNA field, Natera has developed unique and highly optimized cfDNA-based diagnostic methods that can be used to non-invasively test for a

range of conditions. Natera developed an industry-leading cfDNA test, Panorama, which showcases its mastery of cfDNA in the field of non-invasive prenatal diagnostics. It is considered the industry leading test in this space, with about four million tests performed commercially, and with more than twenty-six peer-reviewed publications. Natera has also applied its cfDNA platform to the challenge of assessing organ transplant rejection. Natera's cfDNA testing methods are simpler and less invasive than traditional biopsy methods used to evaluate transplant health, and also are more sensitive and specific, and less variable, than biomarkers such as serum creatine across all types of kidney transplant rejection. Natera has developed its cfDNA technology for approval in the clinical setting in order to provide patients with tools for early, clinically meaningful rejection assessment. As such, Natera was awarded approval for coverage by Medicare.

4. Natera's cfDNA platform is the product of well over a decade of hard work and investment of, on average, more than fifty million dollars per year in research and development. Natera has expended substantial resources researching and developing its technologies and establishing its reputation among physicians, insurers, and regulators as a company committed to sound science and consistently accurate, reliable results. This research, and the resulting technological innovations therefrom, are protected by a substantial patent portfolio, with over 330 patents issued or pending worldwide.

5. Among these patented inventions is U.S. Patent No. 11,111,544 (the "'544 patent"), which CareDx infringes. In its efforts to improve upon the standard of care in the transplant space, Natera has leveraged its own technologies such as the inventions disclosed and claimed in the '544 patent. By contrast, CareDx has used Natera's patented cfDNA technology without permission and in violation of the patent laws, while asserting only the patents of others

(*e.g.*, Stanford) to create the false impression that it is a true innovator. CareDx must be held accountable for its infringement.

6. Natera is the legal owner by assignment of the '544 patent, which was duly and legally issued by the United States Patent and Trademark Office ("USPTO") on September 7, 2021.

7. Natera seeks monetary damages and injunctive relief to address ongoing infringement by CareDx of its valuable patent.

THE PARTIES

8. Natera is a Delaware corporation with its principal place of business at 201 Industrial Road, Suite 410, San Carlos, California 94070.

9. CareDx is a Delaware corporation with its principal place of business at 3260 Bayshore Boulevard, Brisbane, California 94005.

JURISDICTION AND VENUE

10. This is a civil action for patent infringement arising under the patent laws of the United States, 35 U.S.C. § 1 *et seq.*

11. This Court has subject matter jurisdiction over the matters asserted herein under 28 U.S.C. §§ 1331 and 1338(a).

12. CareDx is subject to this Court's personal jurisdiction at least because CareDx is a Delaware corporation, and because CareDx filed its own actions against Natera, Case Nos. 19-cv-00567-CFC-CJB and 19-cv-00662-CFC-CJB, in this District.

13. In addition, CareDx is subject to this Court's personal jurisdiction because, on information and belief, CareDx, directly or indirectly, uses, induces others to use, contributes to the use by others, offers for sale, and/or sells the products accused of infringement throughout the United States and within this District. CareDx has infringed and continues to infringe

Natera's patent in this District by, among other things, engaging in infringing conduct within and directed at or from this District and purposely and voluntarily placing its infringing products, including AlloSure, AlloSeq, KidneyCare, HeartCare, and any other CareDx products that use similar technologies (the "Accused Products"), into the stream of commerce with the expectation that the Accused Products will be used in this District.

14. Venue is proper in this District pursuant to 28 U.S.C. §§ 1391 and 1400(b). As discussed above, CareDx is incorporated in this District and thus resides in this District.

FACTUAL BACKGROUND

Natera's History of Innovation

15. Since 2004, Natera has been a global leader in genetic testing, diagnostics, and DNA testing, including cfDNA testing. Natera's mission is to improve the management of disease worldwide and focuses on reproductive health, oncology, and organ transplantation. To improve the management of these conditions, Natera has developed novel technologies to make significant and accurate clinical assessments from the miniscule amounts of cfDNA present in a single blood sample. These technologies include methods to manipulate cfDNA in unconventional ways in order to capture information about genetic variations ("polymorphisms") in cfDNA and usefully transform that information for noninvasive testing. Natera develops and commercializes its own innovative, non-traditional methods for manipulating, preparing samples of, and analyzing cfDNA, and offers a host of proprietary cfDNA genetic testing services to the public to assist patients and doctors to evaluate and track critical health concerns.

16. Since its founding, Natera has researched, developed, and released ten molecular tests with applications in prenatal diagnostics, cancer, and organ transplants, many of which are available through major health plans, or covered by Medicare or Medicaid, and therefore available to most patients in need of those tests. Natera's tests have helped more than four

million individuals to date. Natera's robust laboratory now processes around 130,000 tests per month from the United States and internationally, improving the ability of physicians to monitor and manage crucial health issues and patients to prosper around the world.

17. Building on these innovations, in 2019, Natera launched its patented next-generation cfDNA diagnostic test for evaluating organ transplant health called "Prospera." Prospera is designed to be the most precise medical testing regime for early, clinically meaningful transplant rejection assessment. Prospera was created to help physicians improve transplant survival by enabling them to optimally suppress immune-system-mediated rejection in transplant recipients while avoiding unnecessary and invasive biopsies of the transplanted organ itself.

18. Prospera's validation led Medicare to issue a draft Local Coverage Determination ("LCD") for Prospera in March 2019. In its draft LCD, Medicare determined that "[t]he evidence is sufficient to support that Prospera provides a non-invasive assessment tool to assess for the presence of active allograft rejection." Furthermore, the LCD established that the "evidence also supports that Prospera identifies both ABMR [antibody-mediated rejection] and TCMR [T-cell mediated rejection], and it is validated to detect subclinical AR [active rejection]." The LCD was finalized after receiving overwhelming public support, with the vast majority of public comments being positive. Natera received nearly four times as many supportive letters than not. In fact, the only three letters submitted which did not support the coverage were submitted either by CareDx itself, by self-identified paid advocates of CareDx or, on information and belief, by known CareDx advisors—all in an attempt by CareDx to interfere with Natera's commercialization efforts.

19. Natera's history of and dedication to innovation in the analysis and testing of cfDNA has resulted in a world-class patent portfolio, with over 133 patents issued to date. Natera has an additional 205 pending patent applications currently under review before various patent offices around the world, and of those 18 have been allowed.

CareDx

20. CareDx is a molecular diagnostics company that develops and commercializes testing products for transplant recipients.

21. CareDx markets and sells its own transplant diagnostic testing products, including the Accused Products.

22. On information and belief, the Accused Products infringe the '544 patent. The '544 patent covers an innovative, unconventional method for preparing preparations of amplified DNA from biological samples and manipulating and measuring DNA from a first individual in a biological sample of a second individual. As set forth below, CareDx's infringing Accused Products incorporate or use technology that is protected by the '544 patent owned by Natera. CareDx has used Natera's patented technology without payment or permission.

The '544 Patent

23. The '544 patent, issued on September 7, 2021, is titled "System and Method for Cleaning Noisy Genetic Data and Determining Chromosome Copy Number." Matthew Rabinowitz, Milena Banjevic, Zachary Demko, David Johnson, Dusan Kijacic, Dimitri Petrov, Joshua Sweetkind-Singer, and Jing Xu are the named inventors. Natera is the original and current owner by assignment of the '544 patent. A true and correct copy of the '544 patent is attached hereto as Exhibit B.

24. Claim 1 of the '544 patent recites:

1. A method for determining genetic data for DNA from a first individual in a biological sample of a second individual, the method comprising:

amplifying a plurality of target loci on cell-free DNA extracted from the biological sample to generate amplified products;

sequencing the amplified products by sequencing-by-synthesis to obtain genetic data of the plurality of target loci;

determining the most likely genetic data for DNA from the first individual based on allele frequencies in the genetic data at the plurality of target loci.

25. Claim 18 of the ’544 patent recites:

18. A method for determining genetic data for DNA from a first individual in a blood sample of a second individual, the method comprising:

performing targeted PCR to amplify a plurality of SNP loci on cell-free DNA extracted from the blood sample to generate amplified products, wherein the SNP loci are on a plurality of chromosomes;

sequencing the amplified products by sequencing-by-synthesis to obtain genetic data of the plurality of SNP loci, wherein the sequencing-by-synthesis comprises clonal amplification of the amplified products and measurement of sequences of the clonally amplified DNA;

determining the most likely genetic data for DNA from the first individual based on allele frequencies in the genetic data at the plurality of SNP loci.

26. Claim 21 of the ’544 patent recites:

21. A method for preparing a preparation of amplified DNA derived from a biological sample of a second individual useful for determining genetic data for DNA from a first individual in the biological sample, the method comprising:

extracting cell-free DNA from the biological sample;

preparing a preparation of amplified DNA by amplifying a plurality of target loci on the cell-free DNA extracted from the biological sample to generate amplified DNA;

analyzing the preparation of amplified DNA by sequencing the amplified DNA using sequencing-by-synthesis to obtain genetic data of the plurality of target loci, and determining the most likely genetic data for DNA from the first individual based on allele frequencies in the genetic data at the plurality of target loci.

27. Claim 38 of the ’544 patent recites:

38. A method for preparing a preparation of amplified DNA derived from a biological sample of a second individual useful for determining genetic data for DNA from a first individual in the blood sample, the method comprising:

extracting cell-free DNA from the biological sample;

preparing a preparation of amplified DNA by performing targeted PCR to amplify a plurality of SNP loci on the cell-free DNA extracted from the blood sample to generate amplified DNA, wherein the SNP loci are on a plurality of chromosomes;

analyzing the preparation of amplified DNA by sequencing the amplified DNA using sequencing-by-synthesis to obtain genetic data of the plurality

of SNP loci, wherein the sequencing-by-synthesis comprises clonal amplification of the amplified DNA and measurement of sequences of the clonally amplified DNA, and determining the most likely genetic data for DNA from the first individual based on allele frequencies in the genetic data at the plurality of SNP loci.

28. The claims of the ’544 patent are not directed to a natural law or natural phenomenon. Rather, they are directed to preparing preparations of amplified DNA derived from a biological sample and measuring DNA in a biological sample using synthetic pieces of DNA, including amplification products, which are produced using synthetic tools such as primers, to provide a novel and innovative solution to problems peculiar to the particular problem of amplifying and measuring small amounts of DNA from one individual or organism in a biological sample of another individual or organism. The ’544 patent claims are directed to specific, unconventional, non-routine methods for overcoming previously unresolved problems in this area.

CareDx’s Infringing Acts

29. The allegations provided below are exemplary and without prejudice to Natera’s infringement contentions. In providing these allegations, Natera does not convey or imply any particular claim constructions or the precise scope of the claims. Natera’s claim construction contentions regarding the meaning and scope of the claim terms will be provided under the Court’s scheduling order and local rules.

30. The infringing products include, but are not limited to, the Accused Products and any other infringing method, product, device, or test developed by CareDx.

31. As provided in more detail below, each element of at least one claim of the ’544 patent is literally present in the Accused Products or is literally practiced by the processes

through which the Accused Products are practiced. To the extent that any element is not literally present or practiced, each such element is present or practiced under the doctrine of equivalents.

32. On information and belief, CareDx released its AlloSure product for kidney transplant recipients to the public in 2017. On information and belief, CareDx released its AlloSeq product to the public in 2019. On information and belief, CareDx released its KidneyCare and HeartCare products to the public in 2021.

33. Performance of CareDx's Accused Products infringe at least one claim of the '544 patent as set forth in Exhibit A, which is a preliminary and exemplary claim chart detailing CareDx's infringement of the '544 patent. Exhibit A is not intended to limit Natera's right to modify this chart or any other claim chart or allege that other activities of CareDx infringe the identified claims or any other claims of the '544 patent or any other patents.

34. CareDx has made extensive use of Natera's patented technology, including the technology described and claimed in the '544 patent. Natera must defend its proprietary and patented technology, and thus requests that this Court award it damages sufficient to compensate for CareDx's infringement of the '544 patent, find this case exceptional and award Natera its attorneys' fees and costs, and grant an injunction against CareDx to prevent ongoing infringement of the '544 patent.

COUNT I: INFRINGEMENT OF U.S. PATENT NO. 11,111,544

35. Natera incorporates by reference and re-alleges the foregoing paragraphs as if fully set forth herein.

36. On information and belief, CareDx has infringed and continues to infringe the '544 patent pursuant to 35 U.S.C. § 271(a), literally or under the doctrine of equivalents, by making, using, selling, or offering to sell the Accused Products within the United States without authority.

37. Attached as Exhibit A is a preliminary and exemplary claim chart detailing CareDx's infringement of the '544 patent. This chart is not intended to limit Natera's right to modify the chart or allege that other activities of CareDx infringe the identified claims or any other claims of the '544 patent or any other patents. Exhibit A is hereby incorporated by reference in its entirety. Each claim element in Exhibit A that is mapped to the Accused Products is an allegation within the meaning of the Federal Rules of Civil Procedure and therefore a response to each allegation is required.

PRAYER FOR RELIEF

WHEREFORE, Natera respectfully requests the following relief:

1. A judgment that CareDx has infringed the '544 patent literally or under the doctrine of equivalents;

2. An order preliminarily and permanently enjoining CareDx and its officers, directors, agents, servants, affiliates, employees, divisions, branches, subsidiaries, parents, and all others acting on behalf of or in active concert or participation therewith, from further infringement of the '544 patent;

3. An award of damages sufficient to compensate Natera for CareDx's infringement under 35 U.S.C. § 284;

4. A determination that this is an exceptional case under 35 U.S.C. § 285 and that Natera be awarded attorneys' fees;

5. Costs and expenses in this action;

6. An award of prejudgment and post-judgment interest; and

7. Such other and further relief as the Court may deem just and proper.

DEMAND FOR JURY TRIAL

Pursuant to Rule 38(b) of the Federal Rules of Civil Procedure, Natera respectfully demands a trial by jury on all triable issues.

MORRIS, NICHOLS, ARSHT & TUNNELL LLP

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