IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

CAREDX, INC. and THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY, Plaintiffs v. TAI DIAGNOSTICS, INC., Defendant.	C.A. No. _____ **JURY TRIAL DEMANDED**

COMPLAINT

Plaintiffs CareDx, Inc. ("CareDx") and The Board Of Trustees Of The Leland Stanford Junior University ("Stanford," and collectively with CareDx "Plaintiffs"), for their complaint against Defendant Tai Diagnostics, Inc. ("Tai"), hereby allege as follows:

NATURE OF THE ACTION

1. Years ago, researchers at Stanford University invented a method for determining organ transplant rejection. It allowed doctors to assess rejection through blood tests and without invasive biopsies. This method is intended to saves lives, minimize patient pain and stress, and cuts the healthcare costs of treating transplant patients.

2. Stanford University secured the patents to its researchers' invention and licensed the patents exclusively to CareDx. CareDx then brought this invention out of the lab and into the clinical setting, helping leading transplant centers around the country treat patients. CareDx has worked hard on this effort, investing substantially to make this technology widely available.

3. Now, years after Stanford researchers and CareDx put in the research and development work to invent this new method and bring it to the clinical setting, Tai uses CareDx's licensed technology without permission in violation of the patent laws. Tai must be held accountable.

4. Accordingly, this is an action for patent infringement arising under the patent laws of the United States, Title 35, United States Code, against Defendant Tai.

5. CareDx brings this action to halt Tai's infringement of CareDx's rights under the Patent Laws of the United States 35 U.S.C. § 1, et seq., which arise under U.S. Patent No. 10,494,669 ("the '669 patent") (attached as Exhibit 1).

PARTIES

6. CareDx is a corporation organized and existing under the laws of the state of Delaware, having its principal place of business at 3260 Bayshore Blvd., Brisbane, CA 94005.

7. CareDx was formed in 1998 by pioneers in molecular diagnostics. Since its inception, CareDx has focused its expertise on the discovery, development and commercialization of clinically differentiated, high-value solutions for organ transplant recipients. It was the first company to develop and commercialize non-invasive transplant surveillance testing to monitor transplant recipients' immune status with the aim to improve long-term patient outcomes.

8. Today, CareDx markets and sells AlloSure® ("AlloSure"). AlloSure uses advanced DNA sequencing methods to quantify donor-derived cell-free DNA (dd-cfDNA) in transplant recipients. Measuring dd-cfDNA in a transplant recipient's blood enables early detection of transplant rejection and facilitates personalized immunosuppressive treatment. AlloSure has helped numerous clinicians manage their patients' post-transplant care while avoiding the high costs and added risks of post-transplant biopsies.

9. Stanford is a trust possessing corporate powers that is organized under the laws of California, with a principal place of business at the Office of the President, Building 10 Main Quad, Stanford, California 94305. Stanford is the patent owner and licensor for the '669 patent and is joined in the infringement action for these patents because it is a necessary party.

10. On information and belief, Tai is a corporation organized and existing under the laws of the state of Delaware, having its principal place of business at 10101 Innovation Drive Suite 600, Wauwatosa, WI 53226. Tai markets and sells a non-invasive heart transplant rejection test called myTAIHEART, which it performs at its CLIA-certified laboratory in Wauwatosa, WI. Exhibit at 2 at 4-5.

JURISDICTION AND VENUE

11. This action arises under the patent laws of the United States, 35 U.S.C. §§ 100, *et seq.*, and this Court has jurisdiction over the subject matter of this action under 28 U.S.C. §§ 1331, 1338(a), 2201 and 2202.

12. Venue is proper in this Court under 28 U.S.C. §§ 1391 and 1400(b), since Tai is a Delaware corporation.

13. This Court has jurisdiction over Tai because Tai is a Delaware corporation.

14. This Court also has jurisdiction over Tai because, upon information and belief, Tai, directly or indirectly, uses, offers for sale, and/or sells its myTAIHEART test throughout the United States and in this judicial district.

BACKGROUND

15. Plaintiffs repeat and re-allege the foregoing paragraphs as if set forth specifically herein.

16. On January 13, 2020, scientists affiliated with Tai—including Tai's co-founders Michael E. Mitchell and Aoy Tomita-Mitchell—published a research article titled, "Cell-free DNA donor fraction analysis in pediatric and adult heart transplant patients by multiplexed allele-specific quantitative PCR: Validation of a rapid and highly sensitive clinical test for stratification of rejection probability" in the journal PLOS One. Exhibit 2 (hereafter the "PLOS Article"). A January 14, 2020 Tai press release states that the PLOS Article describes a "clinical validation study conducted by TAI Diagnostics and researchers at the Medical College of Wisconsin used the myTAIHEART® test to quantify changes in the cell-free DNA donor fraction (DF) of blood plasma samples." Exhibit 3. It goes on to state that "[t]he publication provides details of the development and use of the myTAIHEART test including parameters related to blood sample collection and preparation, automated cell-free DNA extraction and donor fraction (DF) calculation." *Id.* Thus, the PLOS Article describes the methodology of the myTAIHEART test.

17. According to a January 22, 2020 Tai press release, the myTAIHEART test "uses [the] fraction [of] cell-free donor DNA in a recipient's blood as a biomarker of heart transplant viability." Exhibit 4. According to this press release, "MyTAIHeart focuses on heart transplants. From initial donor and recipient samples, the firm takes a baseline signature of 94 SNPs in genomic DNA. It can then detect and quantify donor DNA in the transplant recipient's blood and calculate a donor fraction. cfDNA levels serve as a biomarker of viability, with rising donor fraction indicating a potential for transplant rejection."

18. On information and belief, Tai commercially launched its myTAIHEART test in 2019, and has already used it and sold it to customers. *See* Exhibit 5.

19. Tai infringes, literally or under the doctrine of equivalents, the ’669 patent through its activities connected to its sale, offer or sale, and use of the myTAIHEART test. For instance, representative claim 1 of the ’669 patent is listed below:

> 1. A method of detecting donor-specific circulating cell-free nucleic acids in a heart transplant recipient, the method comprising:
>
> (a) genotyping a heart transplant donor to obtain a single nucleotide polymorphism (SNP) profile of said heart transplant donor;
>
> (b) genotyping a heart transplant recipient to obtain a SNP profile of the heart transplant recipient;
>
> (c) obtaining a biological sample from said heart transplant recipient after said heart transplant recipient has received a heart transplant from said heart transplant donor, wherein said biological sample is selected from the group consisting of blood, serum and plasma, and wherein said biological sample comprises circulating cell-free nucleic acids from said heart transplant;
>
> (d) performing one or more quantitative polymerase chain reaction (PCR) reactions on said circulating cell-free deoxyribonucleic acid obtained from said biological sample from said heart transplant recipient, wherein said one or more quantitative PCR reactions amplify at least 10 different deoxyribonucleic acid targets, and wherein said at least 10 different deoxyribonucleic acid targets comprise at least 10 informative SNPs; and
>
> (e) quantifying an amount of heart transplant-derived circulating cell-free deoxyribonucleic acid from said heart transplant using markers distinguishable between said heart transplant recipient and said heart transplant donor, wherein said markers distinguishable between said heart transplant recipient and said heart transplant donor are said at least 10 informative SNPs, wherein said quantified amount of heart transplant-derived circulating cell-free deoxyribonucleic acid from said heart transplant using markers distinguishable between said heart transplant recipient and said donor comprises at least 0.03% of the total circulating cell free deoxyribonucleic acid from said biological sample from said heart transplant recipient.

20. Performance of the myTAIHEART test leads to infringement of this claim in at least the following way. Blood samples are collected from a heart transplant recipient and used to develop a single nucleotide polymorphism (“SNP”) profile of the donor and the recipient that focuses on 94 SNPs. *See* PLOS Article at 10 (“For each heart transplant recipient represented in the validation study set and for each volunteer blood donor providing samples for manufacture of

validation reference materials, one-time basic genotyping (bGT) of gDNA extracted from a blood sample was performed at each of the 94 highly informative target allelic sites (and 2 control sites) prior to qGT."); *id.* at 11-12 ("Preliminary random selections of candidate donor genotypes simulate what DFs a given qGT sample could represent. Statistical analyses provide evidence of the most probable donor genotypes. Secondary Monte Carlo simulations further explore these likely donor genotypes and yield a range of probable qGT outcomes."). Based on this information, the fraction of donor derived DNA in the recipient is determined. *See id.* at 11 ("DF was determined by multiplexed, high-fidelity amplification followed by allele-specific qPCR of 94 SNP targets and 2 control targets also targeted by one-time bGT of the recipient's native 'self' gDNA, but for qGT followed by algorithmic minor species determination of DF using the myTAIHEART software (see Calculation of cfDNA Donor Fraction below).").

21. As an example, attached hereto as Exhibit 6 is a preliminary and exemplary claim chart detailing Tai's infringement of multiple claims of the '669 patent. This chart is not intended to limit Plaintiffs' right to modify this chart or any other claim chart or allege that other Tai activities infringe the identified claims or any other claims of the '669 patent or any other patents.

22. Plaintiffs are entitled to past damages for Tai's infringement; the claims of the '669 patent are method claims to which the marking requirements of 35 U.S.C. § 287(a) do not apply.

23. The claims of the '669 patent are directed to an inventive method of detecting donor-specific cell-free nucleic acids that improves upon prior art methods, and are not directed to a natural law or natural phenomenon. The facts and analysis underlying Magistrate Judge Burke's attached opinion (Ex. 7) with respect to U.S. Patent Nos. 9,845,497 and 8,703,652, which share a common specification with the '669 patent, apply with equal force to the claims of the '669 patent, and Plaintiffs incorporate Magistrate Judge Burke's decision by reference.

COUNT I

(Infringement of U.S. Patent No. 10,494,669)

24. Plaintiffs repeat and re-allege the foregoing paragraphs as if set forth specifically herein.

25. On December 3, 2019, the United States Patent and Trademark Office duly and legally issued U.S. Patent No. 10,494,669 (the "'669 patent"), entitled "Non-Invasive Diagnosis of Graft Rejection in Organ Transplant Patients."

26. Stephen R. Quake, Ph.D., Thomas M. Snyder, Ph.D., and Hannah Valantine, M.D. are the sole and true inventors of the '669 patent. By operation of law and as a result of written assignment agreements, Stanford obtained the entire right, title, and interest to and in the '669 patent.

27. Pursuant to license agreements with Stanford, CareDx obtained an exclusive license to the '669 patent in the field of non-invasive monitoring of organ transplant rejection through cell-free DNA analysis.

28. On information and belief, Tai has infringed and continues to infringe the '669 patent pursuant to 35 U.S.C. § 271(a), literally or under the doctrine of equivalents, by performing within the United States without authority the myTAIHEART test. As an example, attached as Exhibit 6 is a preliminary and exemplary claim chart detailing Tai's infringement of the '669 patent. This chart is not intended to limit Plaintiffs' right to modify the chart or allege that other Tai activities infringe the identified claims or any other claims of the '669 patent or any other patents.

29. Exhibit 6 is hereby incorporated by reference in its entirety. Each claim element in Exhibit 6 that is mapped to the myTAIHEART test shall be considered an allegation within the

meaning of the Federal Rules of Civil Procedure and therefore a response to each allegation is required.

JURY DEMAND

30. CareDx and Stanford demand a jury trial on all issues so triable.

PRAYER FOR RELIEF

WHEREFORE, CareDx and Stanford pray that this Court grant the following relief:

A. A judgment that Tai has infringed the ’669 patent and that the ’669 patent is valid.

B. Damages or other monetary relief, including, but not limited to, costs and pre- and post-judgment interest, to Plaintiffs;

C. An order enjoining Tai and its officers, directors, agents, servants, affiliates, employees, divisions, branches, subsidiaries, parents, and all others acting in active concert therewith from further infringement of the ’669 patent;

D. Such further and other relief as this Court deems proper and just, including, but not limited to, a determination that this is an exceptional case under 35 U.S.C. § 285 and an award of attorneys’ fees and costs to Plaintiffs in this action.

Dated: April 8, 2020

Respectfully submitted,

Of Counsel:

FARNAN LLP

Edward R. Reines
Derek C. Walter
WEIL, GOTSHAL & MANGES LLP
201 Redwood Shores Parkway
Redwood Shores, CA 94065

/s/ Michael J. Farnan
Brian E. Farnan (Bar No. 4089)
Michael J. Farnan (Bar No. 5165)
919 N. Market St., 12th Floor
Wilmington, DE 19801

(650) 802-3000

Stephen Bosco
WEIL, GOTSHAL & MANGES LLP
2001 M St., NW
Suite 600
Washington, DC 20036
(202) 682-7000

(302) 777-0300
(302) 777-0301 (Fax)
bfarnan@farnanlaw.com
mfarnan@farnanlaw.com

Attorneys for Plaintiffs