IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MARYLAND

THE JOHNS HOPKINS UNIVERSITY, Plaintiff, v. LABORATORY CORPORATION OF AMERICA HOLDINGS, Defendant.	Civil Action No.

COMPLAINT

Plaintiff The Johns Hopkins University ("JHU"), by and through its undersigned attorneys, brings this action for patent infringement and, in the alternative, breach of contract against Defendant Laboratory Corporation of America Holdings ("Labcorp") and hereby alleges as follows:

NATURE OF THE ACTION

1. This is an action for infringement of United States Patent No. 7,704,687 (the "'687 patent"), attached hereto as Exhibit 1, under 35 U.S.C. § 271, *et seq*. JHU also alleges, in the alternative to and in connection with the claim of infringement, breach of an Exclusive License Agreement by Labcorp.

2. JHU's genetics researchers invented digital karyotyping, a groundbreaking method of detecting chromosomal abnormalities in a patient's genomic profile that is claimed in the '687 patent. Labcorp performs and/or induces or contributes to others performing that patented method when it runs its MaterniT®- and GENOME-Flex-branded noninvasive prenatal tests. From 2016 to 2022, Labcorp performed the patented method without a license to the '687 patent. In 2022, Labcorp

assumed a license to the '687 patent when it acquired Personal Genome Diagnostics ("PGDx"), a JHU faculty start-up to which JHU had previously licensed the '687 patent. Even after assuming the DK License in 2022, however, Labcorp continued to perform the patented methods without paying royalties on the MaterniT® and GENOME-Flex tests due to JHU under the license, which is now terminated. Labcorp has performed, and continues to perform, the patented method without authorization since at least 2016, including after termination of the license, and JHU brings this action to remedy that infringement and unauthorized use.

THE PARTIES

3. JHU is a Maryland not-for-profit corporation having its principal place of business at 3400 N. Charles Street, Baltimore, Maryland 21218.

4. JHU is one of the world's preeminent research institutions and has been a leader in scientific discovery and innovation for nearly 150 years. Founded in 1876 as the first research university in the United States, JHU pioneered the modern model of the American research university, uniting advanced research with education and training generations of scientists, physicians, and engineers whose discoveries underlie the nation's health and quality of life. JHU is internationally recognized as a leader in medicine and biotechnology, and its faculty and researchers have been responsible for landmark advances, such as the discovery of the restriction enzymes that made modern genetic engineering possible. JHU is also responsible for foundational discoveries in human genetics, among them the work of the JHU scientists who invented the digital karyotyping method claimed in the '687 patent. JHU has led all universities in the United States in research and development spending every year since 1979. JHU devotes these substantial resources to research and development across a broad range of disciplines, and the resulting innovations are reflected in an extensive portfolio of patents, including the '687 patent.

5. Labcorp is a corporation organized and existing under the laws of the State of

Delaware with a principal place of business at 358 South Main Street, Burlington, North Carolina 27215. Ex. 2 at 1 (Labcorp's 10-K For Fiscal Year 2024). Labcorp maintains several places of business in this District, including diagnostic and testing facilities, laboratories, and office space for supporting and processing diagnostic tests, at 1420 Key Highway, Baltimore, MD 21230.

6. Labcorp, itself and/or through its subsidiaries and affiliates, makes, uses, and commercializes noninvasive prenatal tests ("NIPTs"), including MaterniT® 21 PLUS, MaterniT® GENOME, and GENOME-Flex (collectively, the "Accused Products"). For example, Labcorp, itself and/or through its subsidiaries, makes, uses, and commercializes NIPTs for karyotyping fetal genomes to detect chromosomal abnormalities, including the Accused Products. Labcorp offers and markets those tests throughout the United States, at least through its websites https://www.labcorp.com/ and https://womenshealth.labcorp.com *See, e.g.*, Ex. 3 (https://womenshealth.labcorp.com/providers/prenatal-screening/noninvasive-prenatal-testing/maternit-21-plus); Ex. 4 (https://womenshealth.labcorp.com/patients/pregnancy/maternit-genome); Ex. 5 (https://womenshealth.labcorp.com/providers/prenatal-screening/noninvasive-prenatal-testing/maternit-21-plus/maternit-genome-flex); Ex. 6 (https://womenshealth.labcorp.com/tests/451941/maternit-genome?utm_source=dl&utm_medium=rd&utm_campaign=ig).

JURISDICTION AND VENUE

7. This is an action for patent infringement arising under the patent laws of the United States, including § 271 *et seq*. The Court has subject matter jurisdiction over this action pursuant to 28 U.S.C. §§ 1331 and 1338(a).

8. Venue is proper in this District under 28 U.S.C. § 1400(b) and/or 28 U.S.C. §§ 1391(b) and (c) because Labcorp has a permanent and continuous presence in, has committed acts of infringement in, and maintains regular and established places of business in the District.

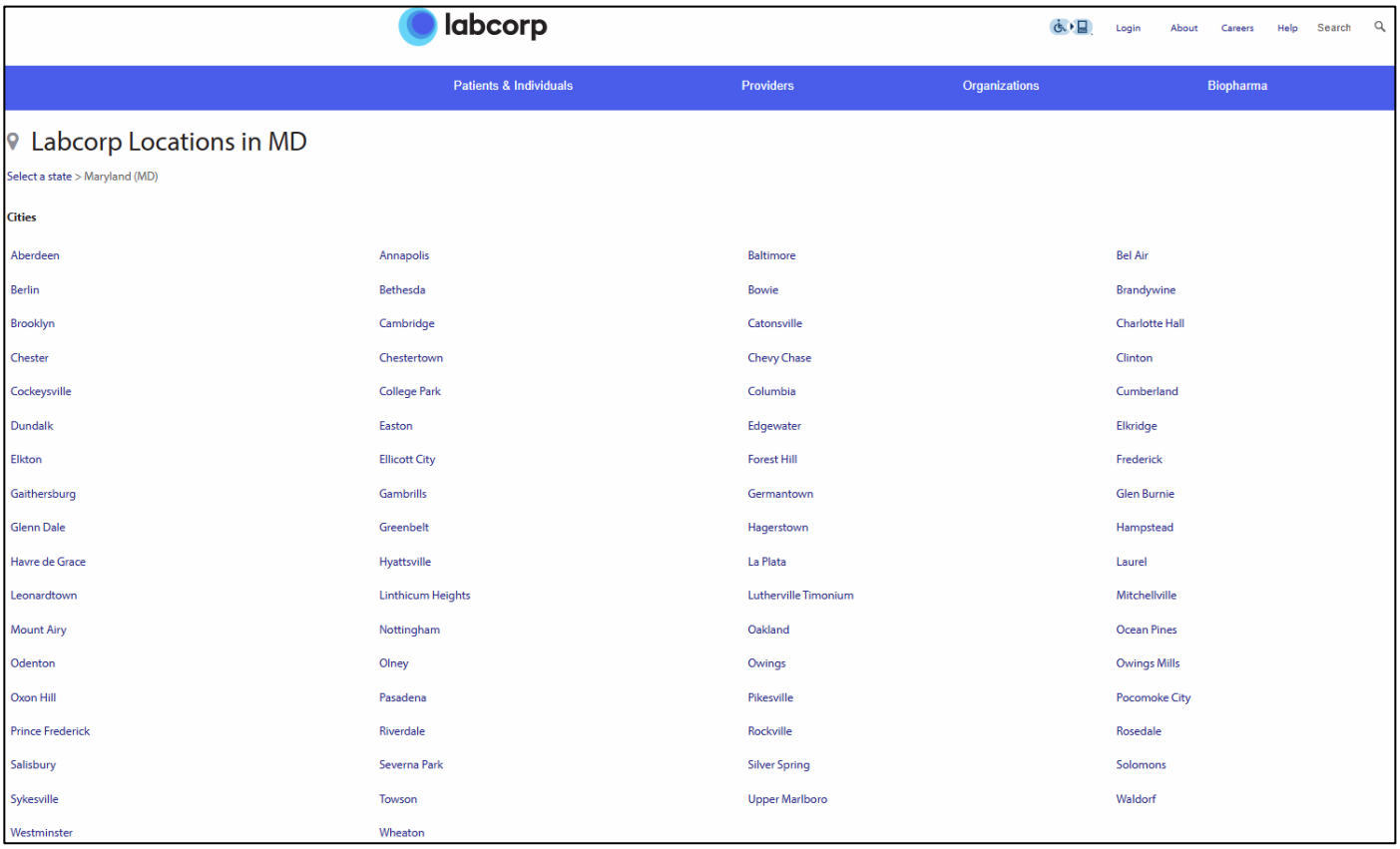
9. Labcorp, through its subsidiaries, is registered to conduct business in this District. Ex. 7. (Maryland Secretary of State Business Registration for Labcorp Bioanalytical Services LLC); *see also* Ex. 8 (Maryland Secretary of State Business Registration for Labcorp Employer Services, Inc.); Ex. 9 (Maryland Secretary of State Business Registration for Labcorp Genetics, Inc.). Labcorp has appointed Corporation Service Company (d/b/a CSC-Lawyers Incorporating Service Company) as its agent for service of process in Maryland. *Id.*

10. Labcorp maintains regular and established places of business in this District, including at least diagnostic testing facilities, laboratories, and office space for supporting and processing diagnostic tests, including the accused diagnostic tests (e.g., MaterniT® 21 PLUS, MaterniT® GENOME, and GENOME-Flex tests), at 1420 Key Hwy, Baltimore, MD 21230. Ex. 10 (https://locations.labcorp.com/md/baltimore/35192/); *see also* Ex. 11 (https://locations.labcorp.com/md/baltimore/); Ex. 12 at 5 (https://www.labcorp.com/assets/13731) ("Getting your blood drawn is easier than ever. As a Labcorp company, we have a nationwide network of patient service centers, allowing for convenient access to sample collection. Visit www.LabCorp.com to find your nearest location."); Ex. 13 (https://www.labcorp.com/assets/5886) (showing an example clinical questionnaire for noninvasive prenatal testing allowing a provider to request tests, including the MaterniT® 21 PLUS and MaterniT® GENOME tests).

11. Labcorp also maintains diagnostic testing facilities and laboratories throughout this District, including at the following exemplary locations in Baltimore, MD, as listed on its website:

- 3700 Fleet St., Baltimore, MD 21224
- 2700 Quarry Lake Dr., Baltimore, MD 21209
- 6821 Reisterstown Rd., Baltimore, MD 21215
- 733 West 40th St., Suite 225 PS, Baltimore, MD 21211
- 3449 Wilkens Ave., Baltimore, MD 21229
- 3407 Wilkens Ave., Baltimore, MD 21229
- 5525 Eastern Ave., Baltimore, MD 21224

Ex. 11 (https://locations.labcorp.com/md/baltimore/). In addition to facilities in Baltimore, Labcorp also maintains diagnostic testing facilities and laboratories at other locations throughout this District, as listed on its website:



Ex. 14. (https://locations.labcorp.com/md/).

12. Labcorp states on its website that "[a]ll LabCorp patient service centers offer routine specimen collections for adults, which can include blood and urine collection." Ex. 15 at 1 (https://www.labcorp.com/patients/labs-and-appointments).

13. Labcorp offers for sale and sells NIPT tests that employ the methods claimed in the '687 patent, including at least the Accused Products, throughout the United States, including at its facilities in this District and through its websites, which are accessible in this District. *See, e.g.*, Ex. 16 (https://www.labcorp.com/tests/451927/maternit21-plus-core-chr21-18-13-sex) (showing a button to order a MaterniT® 21 PLUS test); Ex. 6

(https://www.labcorp.com/tests/451941/maternit-genome) (showing a button to order a MateriT® GENOME test).

14. Labcorp has committed acts of direct infringement in this District. For example, on information and belief, Labcorp commits acts of infringement in this District by offering for sale and selling the service of performing the infringing methods at Labcorp's diagnostic testing facilities, such as at 1420 Key Highway, Baltimore, MD 21230. Specifically, as detailed further below, Labcorp performs the steps of the patented methods and induces and enables performance of the patented methods by, for example, using, offering for sale, and selling the Accused Products.

15. Labcorp is subject to this Court's jurisdiction under the Due Process Clause and/or the Maryland Long Arm Statute due at least to its substantial business in this State and District, including at least regularly doing and soliciting business at its facilities in this District, and engaging in persistent conduct and/or deriving substantial revenue from goods and services provided to customers in the State of Maryland. *See* Md. Cts. & Jud. Proc. Code. Ann. § 6-103.

16. This Court has personal jurisdiction over Labcorp due to, *inter alia*, its continuous presence in, and systematic contact with, this District. Labcorp has established minimum contacts within the forum such that the exercise of jurisdiction over Labcorp will not offend traditional notions of fair play and substantial justice.

17. Personal jurisdiction exists over Labcorp because Labcorp, directly and/or through subsidiaries or intermediaries, has committed acts of infringement in this District by, among other things, using, offering for sale, and selling products and/or services that infringe the '687 patent, which led to foreseeable harm and injury to JHU.

THE '687 PATENT

18. On April 27, 2010, the U.S. Patent and Trademark Office ("USPTO") duly and

legally issued the ’687 patent, entitled “Digital Karyotyping,” to Tian-Li Wang, Victor Velculescu, Kenneth Kinzler, and Bert Vogelstein. A true and correct copy of the ’687 patent is attached as Ex. 1.

19. JHU is the assignee of the entire right, title, and interest in and to the ’687 patent including the right to sue for and recover damages for infringement.

20. Independent claim 1 of the ’687 patent recites:

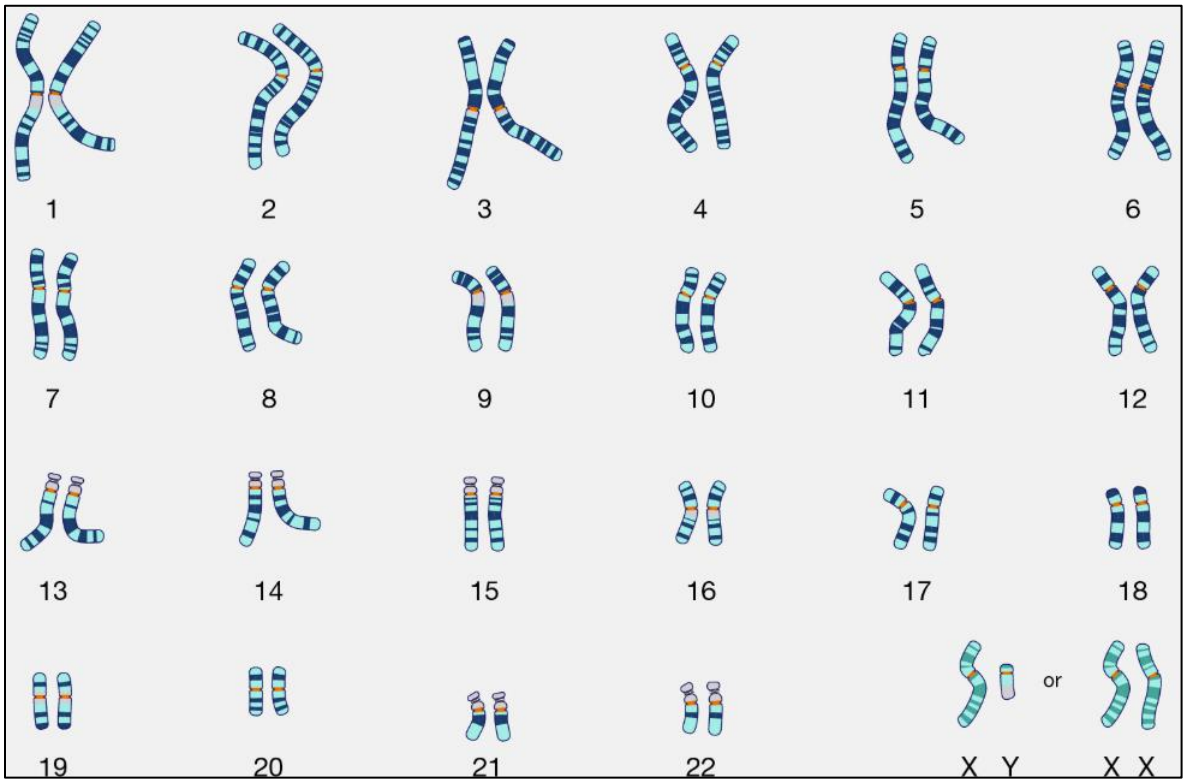
> A method of karyotyping a genome of a test eukaryotic cell, comprising:
>
> sequencing a population of pieces of the genome of the test eukaryotic cell to provide nucleotide sequence of said pieces;
>
> matching, in silico, pieces of the genome to genomic locations using the nucleotide sequence of said pieces;
>
> counting the pieces within windows of a selected size throughout the genome to determine number of pieces as a function of genomic location, wherein each window comprises a plurality of genomically clustered pieces;
>
> comparing the number of pieces enumerated within each window for the test eukaryotic cell to the average number of pieces in windows of the selected size throughout the genome to obtain piece densities per window, wherein the piece densities per window represent the karyotype of the genome of the test eukaryotic cell.

21. Dependent claim 23 depends from claim 1 or claim 9 and adds an additional step of comparing piece densities per window for the test eukaryotic cell to piece densities of a reference eukaryotic cell.

DIGITAL KARYOTYPING

22. The ’687 patent relates to a method of digital karyotyping. Karyotyping is the process of assessing the chromosomes of an individual, including the number of chromosomes and any structural abnormalities present on one or more chromosomes, such as the deletion or multiplication of a portion of a chromosome. Karyotyping enables the detection and diagnosis of certain genetic disorders by identifying an irregular chromosome number or chromosomal aberrations.

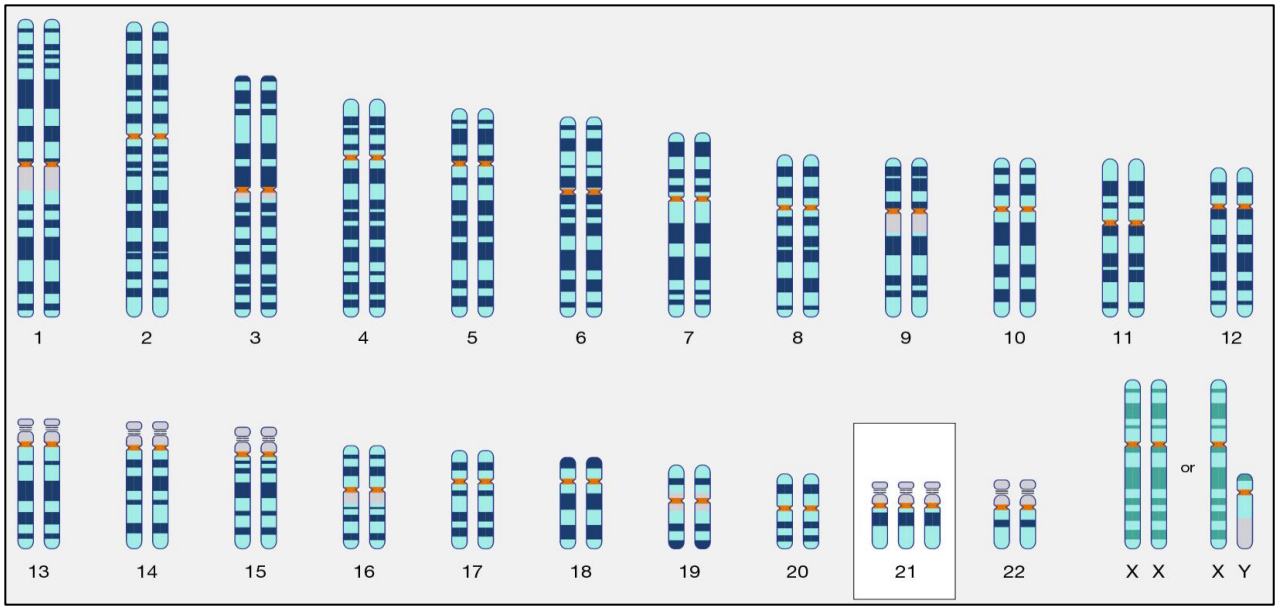
23. The human genome is made of structures called chromosomes, thread-like structures made of tightly wound DNA that store genetic information. A normal human genome consists of 46 chromosomes, comprising two copies of each of 23 distinct chromosomes. Each set of chromosomes has a pair of sex chromosomes, X and Y. Biological females have two X sex chromosomes, and biological males have one X and one Y sex chromosome. The DNA that makes up chromosomes is measured in units called base pairs (bp). One thousand base pairs is a kilobase (kb), while a million base pairs is a megabase (Mb). The figure below shows a normal human chromosomal profile, with 23 pairs of chromosomes total and the X and Y sex chromosomes.



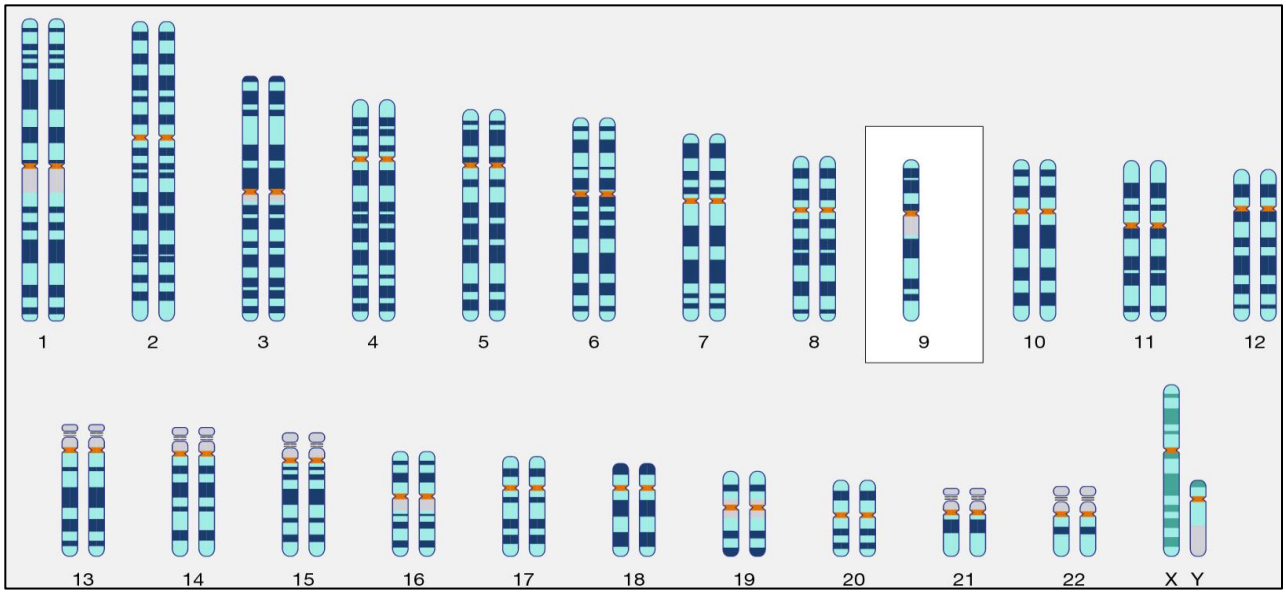
(NIH Human Genome Research Institute, Talking Glossary of Genomic and Genetic Terms-Karyotype, https://www.genome.gov/genetics-glossary/Karyotype)

24. Certain genetic disorders are caused by an abnormal chromosome number or by abnormalities within individual chromosomes. Some are caused by the presence of an additional chromosome (trisomy) or the absence of a chromosome (monosomy). Others are caused by the multiplication or deletion of part of a chromosome. For example, Down syndrome results from an

additional copy of Chromosome 21 (trisomy 21), while certain cancers result from deletions or amplifications within chromosomes. The figures below depict chromosomal profiles showing a trisomy at Chromosome 21 (Down syndrome) and a monosomy at Chromosome 9 (a rare chromosomal disorder that leads to intellectual disability and malformation of the skull):

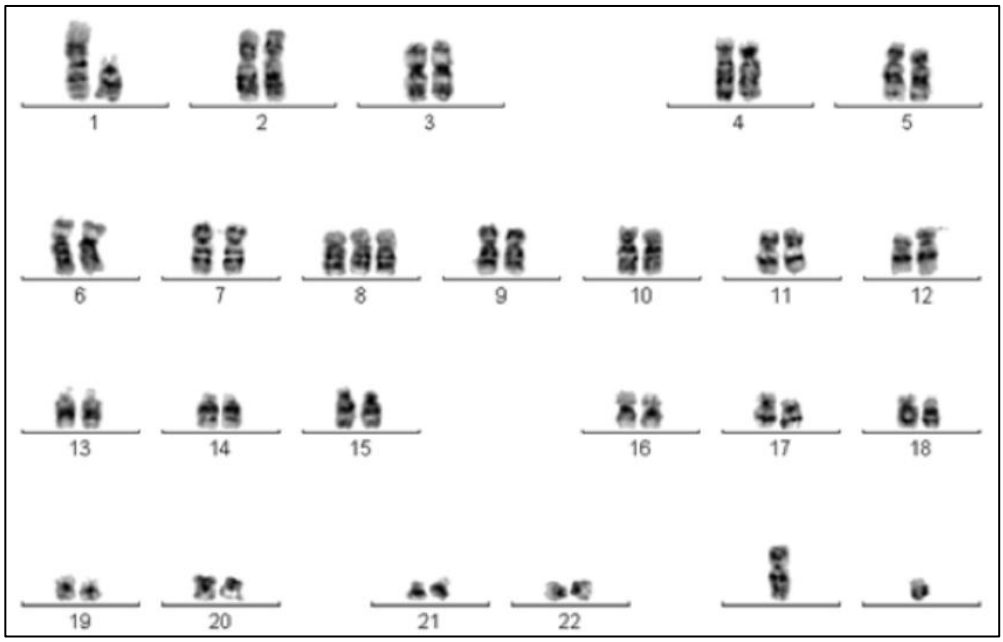


(NIH Human Genome Research Institute, Talking Glossary of Genomic and Genetic Terms- Down Syndrome (Trisomy 21), https://www.genome.gov/genetics-glossary/Down-Syndrome-Trisomy-21)

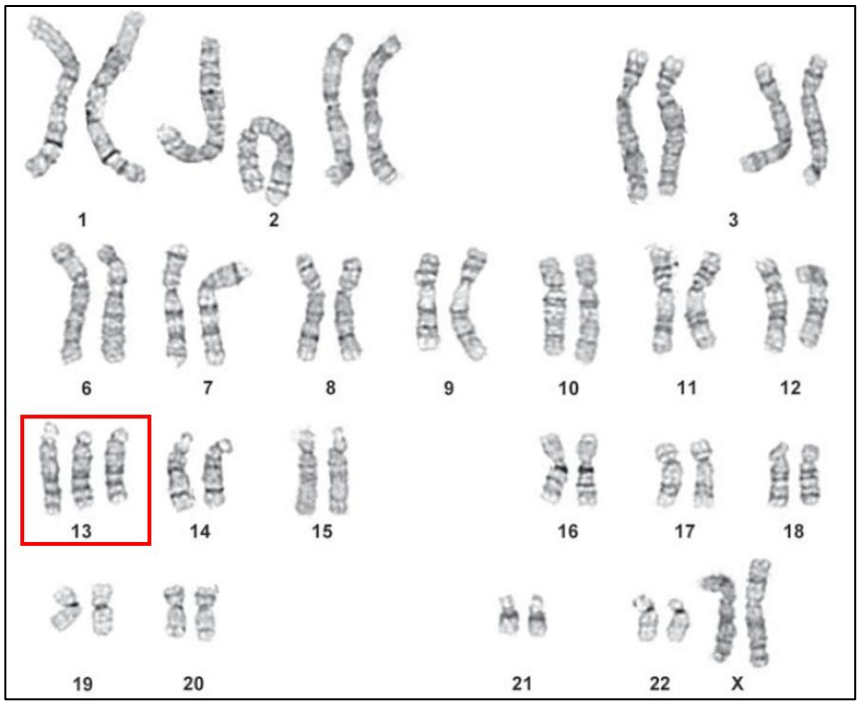


(NIH Human Genome Research Institute, Talking Glossary of Genomic and Genetic Terms- Monosomy, https://www.genome.gov/genetics-glossary/Monosomy)

25. For decades, karyotyping was performed by staining chromosomes and examining them under a microscope. In the most common staining method, called G-banding, chromosomes are stained with Giemsa dye to produce a pattern of light and dark bands that a trained technologist reads by eye. These staining-and-microscopy methods were for many years the conventional tools of cytogenetics.



Ex. 17 (Bayani, J. and J. Squire, Traditional banding of chromosomes for cytogenetic analysis, *Current Protocols in Cell Biology* 2004) at 22.3.2 (showing traditional G-banding technique for chromosome staining).



Ex. 18 (Jarmuz and Shaffer, Cytogenetic Analysis of Cardiovascular Disease, *Cardiovascular Disease, Methods and Protocols Vol. 1: Genetics*, pp. 1-9, Fig. 1) (showing trisomy at Chromosome 13) (annotations added).

Ex. 19 (Morrissette and Bagg, Acute Myeloid Leukemia: Conventional Cytogenetics, FISH, and Moleculocentric Methodologies, *Clin. Lab. Med*. 31 (2011), pp. 659-686, Fig. 4.) (showing monosomy at Chromosomes 5 and 11 and trisomy at Chromosome 7) (annotations added).

26. Conventional G-banded karyotyping has a fundamental limitation—it detects abnormalities only on the order of five to ten million base pairs (5–10 Mb) or larger, and cannot detect the many smaller deletions, duplications, and amplifications that cause disease. *See, e.g.,* Ex. 20 at 16156 (Wang et al., *Digital Karyotyping*, 99 PNAS 16156 (2002)) (describing the limited, approximately 20 Mb, mapping resolution of methods employing metaphase chromosomes); *see also* Ex. 21 at 2 (ASH Clinical News) (cytogenetics article describing the 5–10 Mb resolution limit of conventional G-banded karyotyping). These methods also require dividing cells and intact, well-formed chromosomes, are labor-intensive, and depend on subjective visual interpretation. As a result, conventional karyotyping routinely failed to detect clinically important, submicroscopic chromosomal abnormalities.

27. Researchers later introduced hybridization-based methods, which use a labeled DNA probe that binds to a matching sequence and is read from the signal it produces. Fluorescence in situ hybridization ("FISH") uses a probe directed to a specific target and can detect gains or losses at chromosomal regions. This method allows the identification of certain abnormalities too small to be seen by G-banded karyotyping, but only at the particular location a probe is designed to detect. Ex. 18 at 14-15 (Jarmuz and Shaffer). Another hybridization method, comparative genomic hybridization (CGH), compares a patient's DNA against reference DNA across the whole genome to reveal where DNA has been gained or lost. As the '687 patent explains, these hybridization methods are limited in ways digital karyotyping is not. Prior karyotyping methods "have a limited mapping resolution (~20 Mb) and therefore cannot be used to detect smaller alterations," and even the later microarray-based karyotyping techniques, though offering "improved resolution," remained "limited by the number of sequences that can be assessed" or "by the difficulty of detecting certain alterations." Ex. 1 at 1:25-50.

28. A team of JHU scientists at the Ludwig Center for Cancer Genetics and Therapeutics and the Sidney Kimmel Comprehensive Cancer Center—Bert Vogelstein, Kenneth Kinzler, Victor Velculescu, and Tian-Li Wang, among the world's foremost cancer-genetics researchers—invented a fundamentally new way to karyotype a genome, which they named digital karyotyping. The inventors published the method in the Proceedings of the National Academy of Sciences on December 10, 2002, and it is claimed in the '687 patent. Ex. 20 (Wang et al., *Digital Karyotyping*, 99 PNAS 16156 (2002)); Ex. 1.

29. Unlike the staining, microscopy, and hybridization methods that preceded it, digital karyotyping does not depend on imaging chromosomes or on measuring the intensity of a hybridization signal. It instead measures the copy number of DNA across the genome by a quantitative, sequencing- and counting-based technique.

30. One of the inventors' central insights was that a genome could be "sampled in groups of small pieces to determine karyotypic properties of an organism using a systematic and quantitative method." Ex. 1 at 3:49-51 (Detailed Description). Rather than attempting to read a genome in its entirety, digital karyotyping draws short, fixed-length pieces of DNA ("tags") from defined locations across the genome and treats each tag as a countable unit. Because a portion of the genome that carries an extra copy of a chromosome or portion of chromosome contributes proportionally more tags, and a portion that has a deleted copy of a chromosome or portion of chromosome contributes proportionally fewer, the number of tags mapping to a region is itself a direct, quantitative measure of that region's copy number. The inventors termed this "digital enumeration of tag observations," and used it to "quantitatively evaluate DNA content with high resolution." Ex. 20 at 16156 (Wang et al., *Digital Karyotyping*, 99 PNAS 16156 (2002)).

31. Digital karyotyping "reads" short DNA tags that are then used to identify the chromosomal region from which the tag was derived. *Id.* ("short sequence tags (21 bp each) can be

obtained from specific locations in the genome" and "contain sufficient information to uniquely identify the genomic loci from which they were derived"); Ex. 1 at 4:20-5:18. As such, digital karyotyping samples the genome rather than reading a patient's full genome. The '687 patent teaches that "far less than 100% of the sequence tags must be counted to obtain useful information," and that informative data can be obtained by reading only a small percentage of the tags present in the sample genome. Ex. 1 at 5:67-6:26.

32. The digital karyotyping method of the '687 patent generally proceeds in four steps. First, a population of DNA fragments is obtained by dividing a test cell genome into small pieces drawn from locations across the entire genome, i.e., all chromosomes. Second, the pieces are matched to a specific chromosomal location and grouped into "windows" along each chromosome. Ex. 1, claim 1; Ex. 20 at 16156 (Wang et al., *Digital Karyotyping*, 99 PNAS 16156 (2002)) ("populations of tags can be directly matched to the assembled genomic sequence, allowing observed tags to be sequentially ordered along each chromosome."). Third, the method counts the pieces that fall within "windows" of a selected size across a chromosome, and that count reflects how much DNA is present in that region. Ex. 1, claim 1; Ex. 22 at 1973 (Leary et al., *Digital Karyotyping*, 2 Nature Protocols 1973 (2007)) ("groups of tags are counted to quantify copy number along each chromosome"). Fourth, the method compares the number of pieces in each window to the average number of pieces per window across the genome, yielding a "piece density" for each window. A region with extra copies produces a proportionally higher density, and a region that has fewer copies produces a lower one; the resulting per-window densities represent the karyotype of the genome of the test eukaryotic cell. Ex. 1, claim 1. The claimed method may also include a further comparison of the test genome's per-window densities to those of a reference genome. Ex. 1, claim 23 and at 6:6-10.

33. Digital karyotyping was a breakthrough that overcame the limitations of the

previous karyotyping and hybridization methods. Where conventional karyotyping could resolve only changes spanning many millions of base pairs, digital karyotyping could detect alterations orders of magnitude smaller (theoretically a resolution of a few thousand base pairs) across the entire genome, without pre-designed probes and without the cell-culture and microscopy constraints of the older methods. Ex. 22 at 1973 (Leary et al., *Digital Karyotyping*, 2 Nature Protocols 1973 (2007)). Rather than reading a hybridization signal at pre-selected locations, digital karyotyping counts DNA tags sampled from across the genome. As such, digital karyotyping is not confined to particular probes or arrayed sequences and reaches far finer resolution. Applying digital karyotyping, the inventors detected amplifications smaller than half a megabase that conventional CGH "completely failed to identify" because they were "below the level of resolution achievable with [that] technique." Ex. 1 at 10:47-50 (Example 4); Ex. 20 at 16160 (Wang).

34. Using their new method, the JHU inventors identified in cancer cells not only gross chromosomal changes but also specific amplifications and deletions that "had not been previously described by comparative genomic hybridization (CGH) or other methods in any human cancer." Ex. 1 at 3:63-4:30. Digital karyotyping thereby unlocked new capabilities in cancer diagnosis and research. The inventors recognized that the method could also be used to identify the chromosomal abnormalities underlying hereditary and developmental disorders and could detect foreign DNA present in a sample. Ex. 1; Ex. 20 (Wang et al., *Digital Karyotyping*, 99 PNAS 16156 (2002)). For example, the '687 patent describes using digital karyotyping both to detect the copy-number changes characteristic of cancer and to identify the chromosomal abnormalities underlying hereditary and developmental disorders. Ex. 1 at 3:45-66; 4:20-37.

35. Because digital karyotyping analyzes all of the DNA present in a sample, whatever its source, it can provide a karyotype analysis of DNA from a mixed sample from multiple DNA sources. Ex. 22 at 1973 (Leary et al., *Digital Karyotyping*, 2 Nature Protocols 1973 (2007)) (digital

karyotyping "analyzes all sources of genomic DNA present in a sample" and "can also be employed to identify exogenous DNA sequences"). For example, cancer tests such as the PGDx elios™ plasma test, analyze mixtures of cell-free DNA from both normal and cancer cells. As another example, the '687 patent describes that digital karyotyping can be applied to a sample containing a mixture of human and non-human DNA. In analyzing human cells that also harbored Epstein-Barr virus, the inventors used digital karyotyping to detect and enumerate the viral DNA sequences intermixed with the human genomic DNA. Ex. 1 at Fig. 4; 11:49-12:6; Ex. 20 at 16161 (Wang et al., *Digital Karyotyping*, 99 PNAS 16156 (2002)) (identifying 2,368 sequence tags matching Epstein–Barr virus among the human tags); Ex. 1 at Abstract ("Foreign DNA sequences not present in the normal human genome could also be readily identified."). Digital karyotyping is thus well suited to analyzing samples in which DNA from more than one genome is present.

36. Years after the JHU inventors discovered digital karyotyping, Sequenom introduced the first commercial noninvasive prenatal tests, or NIPTs, to determine a fetus's karyotype from a sample of the mother's blood. Ex. 23 ("Sequenom Center for Molecular Medicine Announces Launch of MaterniT21™ Noninvasive Prenatal Test for Down Syndrome") (https://www.biospace.com/b-sequenom-center-for-molecular-medicine-b-announces-launch-of-maternit21-tm-noninvasive-prenatal-test-for-down-syndrome). A pregnant woman's blood contains cell-free DNA, including DNA shed from fetal and placental cells that reflects the fetal genome. The NIPTs determine the fetal karyotype using the same method described by the '687 patent, i.e., by dividing a genome into small DNA pieces drawn from across the genome, mapping those pieces to specific chromosomal locations, counting the pieces falling within windows across the genome, and comparing those counts to detect chromosomal gains and losses such as an extra copy of chromosome 21. *See, e.g.*, Ex. 24 (Palomaki 2011); Ex. 25 (Ehrich 2011); Ex. 26 (Chiu 2008); Ex. 27 (Lefkowitz); Ex. 28 (Jensen). As one Sequenom publication explains, a fetus with

trisomy 21 contributes additional genetic material, producing a larger share of sequence reads mapping to chromosome 21. Ex. 25 at 205.e3 (Ehrich).

37. In 2016, Labcorp acquired Sequenom. Labcorp now markets and sells Sequenom's NIPTs under the MaterniT® brand—including MaterniT® 21 PLUS, MaterniT® GENOME, and GENOME-Flex—and Labcorp employees perform the tests, for example, at its Sequenom Center for Molecular Medicine ("SCMM") laboratory. Each of these tests determines a fetal karyotype by performing the digital-karyotyping method claimed in the '687 patent.

THE DK LICENSE AND ITS TERMINATION

38. PGDx was a JHU faculty start-up, founded in Baltimore, MD, to commercialize the University's genomic technologies, including digital karyotyping, for cancer diagnostics.

39. On June 29, 2011, JHU and PGDx entered into an Exclusive License Agreement (the "DK License") granting PGDx an exclusive, royalty-bearing license to JHU's digital karyotyping patent rights, including the '687 patent. Ex. 29 at §§ 1.6-1.8, 2.1 (DK License). The DK License was amended twice. The first amendment occurred in 2015 and modified the consideration due to JHU for sublicensing under the agreement. Ex. 30 (2015 First Amendment to DK License). The second amendment occurred in 2021 and changed the royalty payment calculation with respect to the licensed products and services covered by the DK License. Ex. 31 (2021 Second Amendment to DK License). PGDx used the licensed technology in its cancer-diagnostic products, including its elio® cancer tests, and paid JHU royalties under the DK License, including a minimum annual royalty. *Id.* at §§ 3.2-3.3. Under the DK License, JHU's remedies are not limited to those provided by the agreement. *See* Ex. 29 at §§ 9.2 and 10.11 (DK License).

40. Labcorp acquired PGDx and, with it, the DK License on February 18, 2022. Ex. 32 at 1 (Vendor Letter for PGDx Acquisition). By acquiring PGDx, Labcorp assumed PDGx's obligations under the DK License, including the obligation to pay royalties to JHU for use of the

methods described by the '687 patent. Labcorp also assumed PGDx's obligations under the DK License by expressly or impliedly assuming them. Since the acquisition, Labcorp has administered the DK License and has continued to pay JHU the royalties due for PGDx's elio® cancer test, including for a cell-free-DNA (plasma) version of that test. On information and belief, PGDx no longer operates as a separate, independent business; its operations have been absorbed into Labcorp, and PGDx's former websites and product offerings now redirect to, and are provided through, Labcorp. Ex. 59 (Labcorp website for the PGDx elio® Kitted Solutions, https://www.labcorp.com/oncology/providers/testing-solutions/kitted-solutions); *see also* Ex. 32 at 1 (Vendor Letter for PGDx Acquisition) (stating that "[a]ny invoice not paid by PGDx as of October 1, 2022 should be sent to Labcorp Drug Development" and that invoices should be emailed to "APInvoice@labcorp.com").

41. By the time of the PGDx acquisition in 2022, on information and belief, Labcorp was also the largest provider of NIPTs in the United States, having previously acquired Sequenom and its MaterniT® tests in 2016. Labcorp's MaterniT® NIPTs rely on the digital-karyotyping method claimed in the '687 patent, yet Labcorp has never paid JHU any royalties on those tests.

42. In early 2023, in the wake of Labcorp's acquisition of PGDx and thus the license, JHU reached out to Labcorp to alert Labcorp that its NIPT products practiced JHU's licensed digital karyotyping patent rights. On July 21, 2023, Labcorp responded that, after reviewing its NIPT offerings, Labcorp did not believe JHU's licensed patents covered Labcorp's current or past NIPT tests. Ex. 33 (July 21, 2023 email from K. Watson (Labcorp)). Labcorp asked JHU to provide "a detailed analysis explaining how the [patents] read on" Labcorp's NIPT offerings, referring to the patents at issue as the "DK Pare Patents." *Id.*

43. On August 10, 2023, JHU responded and identified both the '687 patent and the specific Accused Products. JHU explained that the '687 patent covered the Accused Products. Ex.

34 (August 10, 2023 email from S. Kousouris (JHU)). JHU further explained that the '687 patent is directed to the identification of patient-specific copy number variants, such as those associated with Trisomy 21, Trisomy 18, and Trisomy 13, and that those chromosomal abnormalities are commonly tested for by NIPTs, including Labcorp's MaterniT® tests. *Id.* JHU proposed a call to discuss JHU's analysis of how the '687 patent reads on Labcorp's NIPTs and Labcorp's basis for contending that its NIPTs do not practice the patented method. *Id.* Labcorp has thus had knowledge of the '687 patent and of JHU's contention that Labcorp's NIPT products infringe it since at least August 10, 2023.

44. After August 10, 2023, Labcorp went silent regarding the DK patents. Finally, on December 16, 2024, Labcorp confirmed that it would meet via video on January 6, 2025, to discuss the dispute. Labcorp asked JHU to confirm that JHU would present claim charts comparing the claims of the '687 patent to Labcorp's accused NIPTs. Ex. 35 (December 16, 2024 email from J. Peterson (Labcorp)).

45. The parties' meeting was later rescheduled to February 5, 2025. In advance of that meeting, and in accordance with Labcorp's request, JHU provided Labcorp with a claim chart comparing the claims of the '687 patent to Labcorp's NIPTs.

46. During the ensuing February 5 meeting, counsel for JHU presented its infringement analysis to Labcorp, including citations to the MaterniT® test brochures and the underlying published references which explained the details of the tests.

47. In a follow up video meeting on February 28, Labcorp denied infringement and proposed that the parties bring their respective technical staff, including the JHU inventors, together for a call to discuss whether the technology claimed in the '687 patent covered the technology used in Labcorp's NIPTs.

48. On May 19, 2025, Labcorp abandoned that proposed call, writing that it "no longer

see[s] that 'education' approach as productive," and declined to proceed with further discussions. Ex. 36 (May 19, 2025 email from J. Peterson (Labcorp)).

49. Despite JHU's repeated notice that Labcorp's MaterniT® NIPTs practice the '687 patent, Labcorp has refused to pay any royalty on those tests.

50. Because Labcorp failed to pay royalties due under the DK License, JHU notified Labcorp of its intent to terminate the DK License for breach under Section 9.2 on September 17, 2026. Ex. 29 (DK License); Ex. 60 (September 17, 2026 Letter from JHU). On September 22, 2026, Labcorp notified JHU that it "does not believe its [NIPT products] practice the Digital Karyotyping patent" and disagreed that it had failed to perform any obligation under the DK License, effectively refusing to cure the breach under Section 9.2. Ex. 38 (September 22, 2026 Letter from Goldman). JHU thus formally terminated the license on October 5, 2026. Ex. 37 (October 5, 2026 Termination Letter). Since termination of the DK License, Labcorp has had no license or other authorization from JHU to practice any claim of the '687 patent.

51. Labcorp breached the DK License agreement despite Labcorp's full knowledge of its contractual obligations to JHU under the DK License, and continued its willful breach of the DK License up to and including October 5, 2026 when JHU terminated the DK License as it was permitted to do under Section 9.2.

LABCORP'S ACCUSED NIPT PRODUCTS

52. On or around October 17, 2011, Sequenom Inc. ("Sequenom") launched the MaterniT® 21 PLUS test, a commercial NIPT for detecting fetal genetic abnormalities. *See* Ex. 39 at 1 (A. Pollack, "*A Less Risky Down Syndrome Test Is Developed*," NEW YORK TIMES (October 17, 2011), https://www.nytimes.com/2011/10/18/business/sequenom-test-for-down-syndrome-raises-hopes-and-questions.html) ("The first new test, which analyzes fetal DNA in the mother's

blood, is being offered in 20 major cities starting [October 17, 2011] by Sequenom.).

53. On or around July 13, 2015, Sequenom launched the MaterniT® GENOME test, a commercial NIPT for detecting fetal genetic abnormalities. *See* Ex. 40 at 1 ("*Sequenom Laboratories Launches MaterniT™ GENOME,*" PR NEWSWIRE (July 13, 2015), https://www.prnewswire.com/news-releases/sequenom-laboratories-launches-maternit-genome-300111863.html) ("Sequenom Laboratories … announced today the upcoming launch of the MaterniT™ GENOME laboratory-developed test. This test is the first noninvasive prenatal test (NIPT) to provide karyotype-level insight into fetal chromosomal status prior to considering an invasive procedure."); Ex. 41 at 2 (https://womenshealth.labcorp.com/sites/default/files/2021-11/MaterniTGENOME_Negative_Female_SampleReport.pdf) ("The MaterniTTM GENOME test utilizes the same proprietary technology as the MaterniT21® PLUS test, with deeper sequencing.")

54. On or around July 27, 2016, Labcorp acquired Sequenom, including the MaterniT® 21 PLUS, MaterniT® GENOME, and GENOME-Flex tests (collectively, the "Accused Products"). *See* Ex. 43 at 1 ("*LabCorp Announces Agreement to Acquire Sequenom*," PR NEWSWIRE (July 27, 2016), https://www.prnewswire.com/news-releases/labcorp-announces-agreement-to-acquire-sequenom-300304676.html) ("Laboratory Corporation of America® Holdings (Labcorp®) (NYSE: LH), the world's leading healthcare diagnostics company, and Sequenom, Inc. (NASDAQ:SQNM), a pioneer in non-invasive prenatal testing (NIPT) for reproductive health, today announced that they have entered into a definitive agreement and plan of merger under which Labcorp would acquire all of the outstanding shares of Sequenom…").

55. Labcorp/Sequenom subsequently launched the GENOME-Flex test in 2019. Ex. 56 at 2 (MaterniT® 21 PLUS brochure citing Palomaki) ("Now offering more screening options and flexibility than other NIPTs, including GENOME-Flex – a new NIPT high risk pathway – MaterniT 21 PLUS will deliver more value to your practice, and more service to your patients."). Labcorp

describes the GENOME-Flex test as a high-risk pathway that rapidly re-sequences a previously run MaterniT® 21 PLUS sample using the deeper sequencing power of MaterniT® GENOME when anomalies are suspected later in the pregnancy, such as on ultrasound—typically without a redraw and with results in approximately 72 hours. Ex. 5 at 1 (https://womenshealth.labcorp.com/providers/prenatal-screening/noninvasive-prenatal-testing/maternit-21-plus/maternit-genome-flex). Labcorp offers GENOME-Flex only as an add-on to a previously performed MaterniT® 21 PLUS test, re-sequencing the saved MaterniT® 21 PLUS specimen through the same genome-wide MaterniT® GENOME analysis, i.e., reporting copy-number gains and losses of 7 Mb or larger across every chromosome, together with seven clinically relevant microdeletions smaller than 7 Mb. Ex. 42 at 1 (GENOME-Flex (Add On), Test No. 452104, https://womenshealth.labcorp.com/tests/452104/genome-flex-add-on).

56. Labcorp offers to sell and sells the Accused Products on its website and in its patient collection centers, including several patient collection centers in this District (such as 1420 Key Highway, Baltimore, MD 21230). Ex. 10 (https://locations.labcorp.com/md/baltimore/35192/; *see also* Ex. 11 (https://locations.labcorp.com/md/baltimore/); Ex. 12 at 5 (https://www.labcorp.com/assets/13731) ("Getting your blood drawn is easier than ever. As a Labcorp company, we have a nationwide network of patient service centers, allowing for convenient access to sample collection. Visit www.Labcorp.com to find your nearest location."); Ex. 13 (https://www.labcorp.com/assets/5886) (showing an example clinical questionnaire for noninvasive prenatal testing allowing a provider to request tests, including the MaterniT® 21 PLUS and MaterniT® GENOME tests); Ex. 5 (https://womenshealth.labcorp.com/providers/prenatal-screening/noninvasive-prenatal-testing/maternit-21-plus/maternit-genome-flex).

57. On information and belief, Labcorp's offer for sale and sale of the Accused Products includes subsequently performing the steps of the infringing methods. For example, when

a patient visits a patient collection center and purchases or agrees to pay in exchange for one of the Accused Products, Labcorp accepts the obligation, directly or through one or more subsidiaries and/or intermediaries, to perform a test pursuant to that test's protocol for the patient's sample(s). At these centers, Labcorp collects test samples from patients, including pregnant women, for the MaterniT® and GENOME-Flex tests. *See* Ex. 12 at 5 (https://www.labcorp.com/assets/13731) ("Getting your blood drawn is easier than ever. As a Labcorp company, we have a nationwide network of patient service centers, allowing for convenient access to sample collection. Visit www.Labcorp.com to find your nearest location"); Ex. 13 https://www.labcorp.com/assets/5886) (showing an example clinical questionnaire for noninvasive prenatal testing allowing a provider to request tests, including the MaterniT® tests). On information and belief, employees or other agents of Labcorp (e.g., Labcorp's employee or contracted lab assistants) collect test samples according to the Accused Products' test protocols. For example, Labcorp publishes and follows the instructions provided in the MaterniT® test specimen collection kit, which include instructions for collecting and transporting test samples. *See* Ex. 44 ("New MaterniT Specimen Collection Kit," https://womenshealth.labcorp.com/sites/default/files/2021-10/MaterniT_Kit_Flyer_rep-1356-v1-0619.pdf); Ex. 5 (https://womenshealth.labcorp.com/providers/prenatal-screening/noninvasive-prenatal-testing/maternit-21-plus/maternit-genome-flex). On information and belief, the published instructions are a part of the MaterniT® 21 PLUS test and MaterniT® GENOME test protocols, and Labcorp directs its employees and other agents to follow the MaterniT® 21 PLUS test, MaterniT® GENOME test, and the GENOME-Flex test protocols.

58. Labcorp directs and controls its wholly owned subsidiaries, Sequenom and Sequenom Center for Molecular Medicine, LLC. Ex. 45 (*Ravgen Inc. v. Laboratory Corporation of America Holdings,* Civil Action No. 6:20-CV-00969-ADA (W.D. Tex. Aug. 5, 2022), Dkt. No. 179, Joint Pretrial Order (Joint Statement of Uncontested Facts) at 2 ("For the purposes of this case,

Laboratory Corporation of America Holdings, as a parent entity, ***controls*** Sequenom Inc. and Sequenom Center for Molecular Medicine, LLC.") (emphasis added); *see also id*. ("Sequenom, Inc. is a wholly-owned subsidiary of Laboratory Corporation of America Holdings. Sequenom Center for Molecular Medicine, LLC is a wholly-owned subsidiary of Sequenom, Inc.").

59. Labcorp, either itself or through its wholly owned subsidiary Sequenom, processes the MaterniT® 21 PLUS, MaterniT® GENOME, and the GENOME-Flex test samples at its subsidiary laboratory, Sequenom Center for Molecular Medicine, LLC d/b/a Sequenom Laboratories ("SCMM"). *See* Ex. 12 at 6 (https://www.labcorp.com/assets/13731) (listing SCMM as the laboratory for the MaterniT® 21 PLUS test and describing it as a "(CLIA)-certified molecular diagnostics laboratory"); Ex. 46 at 1 (https://womenshealth.labcorp.com/sites/default/files/2023-01/DX_BRO_L17294-1122-6-2.pdf) (listing SCMM as the laboratory for the MaterniT® GENOME test and describing it as a "(CLIA)-certified molecular diagnostics laboratory"); Ex. 47 at 1 (https://womenshealth.labcorp.com/sites/default/files/2021-10/rep-1038-v4-1019.pdf) (Sequenom and Integrated Genetics are both brands of Labcorp); Ex. 48 at 6 (Sequenom Inc.'s Form 10-K For Fiscal Year 2014) ("Diagnostic services are provided through our wholly-owned subsidiary, Sequenom Center for Molecular Medicine LLC, or SCMM, doing business as Sequenom Laboratories. Sequenom Laboratories develops and validates its tests for use in, and solely by, Sequenom Laboratories, as a testing service to physicians."); *see also* Ex. 51. Labcorp employees perform and analyze the NIPTs at SCMM's laboratory. Ex. 49 at 3 (*Ravgen Inc. v. Laboratory Corporation of America Holdings*, Civil Action No. 6:20-CV-00969-ADA (W.D. Tex. November 23, 2021), Dkt. No. 72, Ex. A ¶ 6 (Declaration of Taylor Jensen, Ph.D)) ("All performance and analysis of the [MaterniT® 21 PLUS and MaterniT Genome tests] are conducted at Sequenom's laboratories in San Diego by Labcorp employees.").

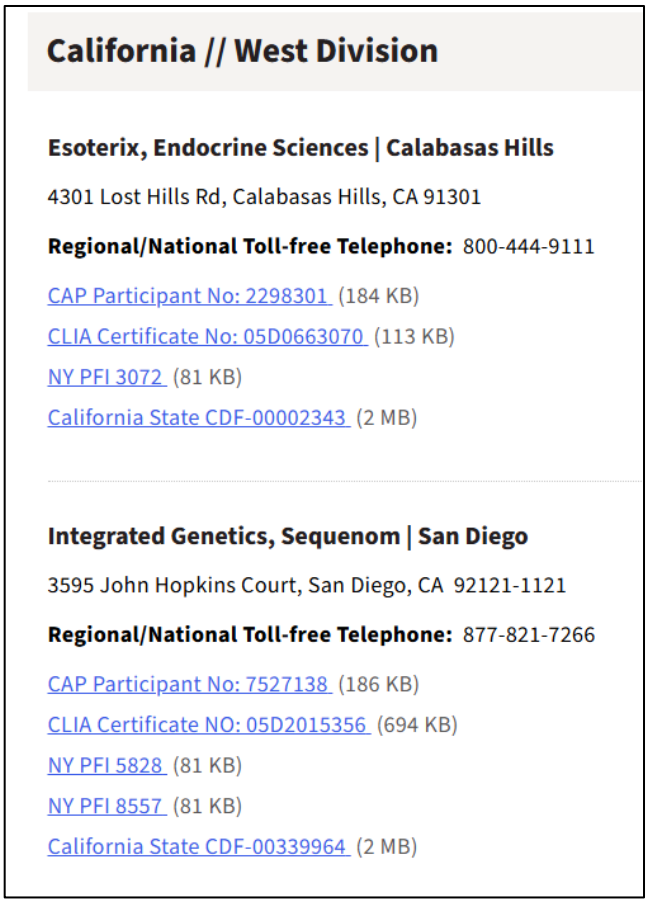
60. On information and belief, SCMM operates as Labcorp's laboratory and carries

out Labcorp's business, and Labcorp authorizes SCMM to act on its behalf. For example, as noted above, through SCMM, Labcorp develops and processes several of its diagnostic tests, including the MaterniT® 21 PLUS and MaterniT® GENOME tests. *See id.*; Ex. 50 at 1 (https://files.labcorp.com/labcorp-d8/2020-04/rep-1036-v7-1119.pdf) ("Sequenom Center for Molecular Medicine, LLC … is a CAP-accredited and Clinical Laboratory Improvement Amendment (CLIA)-certified molecular diagnostics laboratory dedicated to improving patient outcomes by offering revolutionary laboratory-developed tests for a variety of prenatal conditions."); Ex. 46 at 1 (https://womenshealth.labcorp.com/sites/default/files/2023-01/DX_BRO_L17294-1122-6-2.pdf) (same). Further, Labcorp's public statements, such as the portions quoted above, show that Labcorp intends for Sequenom and SCMM to act on Labcorp's behalf, including to perform tests on Labcorp's behalf and provide results to health care providers and/or patients on Labcorp's behalf. *See also* Ex. 51 (https://www.labcorp.com/node/80) (representing Sequenom as one of Labcorp's laboratories under its Integrated Genetics Specialty Testing Group).

61. Labcorp's SEC filings demonstrate that both Sequenom and SCMM are wholly-owned subsidiaries of Labcorp. *See, e.g.*, Ex. 52 at 7-8 (Laboratory Corporation of America Holdings' Form 10-K For Fiscal Year 2019 (List of Subsidiaries)) (listing "Sequenom, Inc." and "Sequenom Center for Molecular Medicine, LLC" as subsidiaries of Labcorp); *see also* Ex. 12 at 6 (https://www.labcorp.com/assets/13731) ("Sequenom Center for Molecular Medicine, LLC d/b/a Sequenom Laboratories, a wholly owned subsidiary of Sequenom, Inc. … Sequenom, Inc. is a wholly owned subsidiary of Laboratory Corporation of America Holdings."); Ex. 50 at 1 (https://files.labcorp.com/labcorp-d8/2020-04/rep-1036-v7-1119.pdf) (same). Labcorp's SEC filings further confirm that since Labcorp's acquisition of Sequenom in 2016, Labcorp has owned 100% of Sequenom and SCMM, and that Labcorp has the right and the ability to direct and control

the activities of SCMM. *E.g.*, Ex. 52 at 7-8 (Laboratory Corporation of America Holdings' Form 10-K For Fiscal Year 2019); Ex. 53 at 7-8 (Laboratory Corporation of America Holdings' Form 10-K For Fiscal Year 2016); Ex. 43 ("*LabCorp Announces Agreement to Acquire Sequenom*," PR NEWSWIRE (July 27, 2016), https://www.prnewswire.com/news-releases/labcorp-announces-agreement-to-acquire-sequenom-300304676.html).

62. On its website, Labcorp identifies the Sequenom and SCMM office as one of its California/West Division "Primary Testing and Specialty Labs":



California // West Division

Esoterix, Endocrine Sciences | Calabasas Hills

4301 Lost Hills Rd, Calabasas Hills, CA 91301

Regional/National Toll-free Telephone: 800-444-9111

CAP Participant No: 2298301 (184 KB)
CLIA Certificate No: 05D0663070 (113 KB)
NY PFI 3072 (81 KB)
California State CDF-00002343 (2 MB)

Integrated Genetics, Sequenom | San Diego

3595 John Hopkins Court, San Diego, CA 92121-1121

Regional/National Toll-free Telephone: 877-821-7266

CAP Participant No: 7527138 (186 KB)
CLIA Certificate NO: 05D2015356 (694 KB)
NY PFI 5828 (81 KB)
NY PFI 8557 (81 KB)
California State CDF-00339964 (2 MB)

Ex. 54 at 1-2 (https://www.labcorp.com/providers/resources/lab-certifications-accreditations)

63. Additionally, Labcorp represents in its brochures that Labcorp directs and controls the diagnostic test development and processing of SCMM, either directly or through Sequenom, such that SCMM is Labcorp's laboratory, and the three operate as one integrated business. For example, Labcorp brochures for the MaterniT® tests represent SCMM as the laboratory that developed and processes the tests. *E.g.*, Ex. 12 at 6 (https://www.labcorp.com/assets/13731) ("Sequenom Center for Molecular Medicine, LLC d/b/a Sequenom Laboratories … [is] dedicated to improving patient outcomes by offering revolutionary laboratory-developed tests for a variety of prenatal conditions."); Ex. 50 at 1 (https://files.labcorp.com/labcorp-d8/2020-04/rep-1036-v7-1119.pdf) (same).

64. Labcorp describes MaterniT® 21 PLUS as detecting chromosomal abnormalities including trisomy 21 (Down syndrome), trisomy 18 (Edwards syndrome), and trisomy 13 (Patau

syndrome), with optional screening for sex chromosome aneuploidies and clinically relevant microdeletions such as 22q (DiGeorge syndrome). Ex. 3 at 6-8 (https://womenshealth.labcorp.com/providers/prenatal-screening/noninvasive-prenatal-testing/maternit-21-plus).

65. Labcorp describes MaterniT® GENOME as reporting on every chromosome, including any trisomy or monosomy, sex chromosome abnormalities, and partial (subchromosomal) chromosome abnormalities. Labcorp markets it as its most comprehensive NIPT. Ex. 4 at 2 (https://womenshealth.labcorp.com/patients/pregnancy/maternit-genome). Labcorp describes GENOME-Flex as a high-risk pathway that rapidly re-sequences a previously run MaterniT® 21 PLUS sample using MaterniT® GENOME when later-stage anomalies are suspected. Ex. 3 at 2 (https://womenshealth.labcorp.com/providers/prenatal-screening/noninvasive-prenatal-testing/maternit-21-plus).

66. The Accused Products analyze cell-free DNA circulating in maternal plasma. *See* Ex. 4 (https://womenshealth.labcorp.com/patients/pregnancy/maternit-genome); Ex. 5 (https://womenshealth.labcorp.com/providers/prenatal-screening/noninvasive-prenatal-testing/maternit-21-plus/maternit-genome-flex); Ex. 6 (https://womenshealth.labcorp.com/tests/451941/maternit-genome?utm_source=dl&utm_medium=rd&utm_campaign=ig). That cell-free DNA includes DNA shed from fetal and placental cells, and the Accused Products analyze the fetal genome to screen for fetal chromosomal abnormalities.

67. MaterniT® 21 PLUS uses the karyotyping method described in Palomaki et al. (2011) ("Palomaki"), which reports the results of the MaterniT® 21 PLUS clinical validation study (ClinicalTrials.gov No. NCT00877292)), and further described in Ehrich et al. (2011) ("Ehrich") and Chiu et al. (2008) ("Chiu"). Ex. 56 at 8 (MaterniT® 21 PLUS brochure citing Palomaki); Ex.

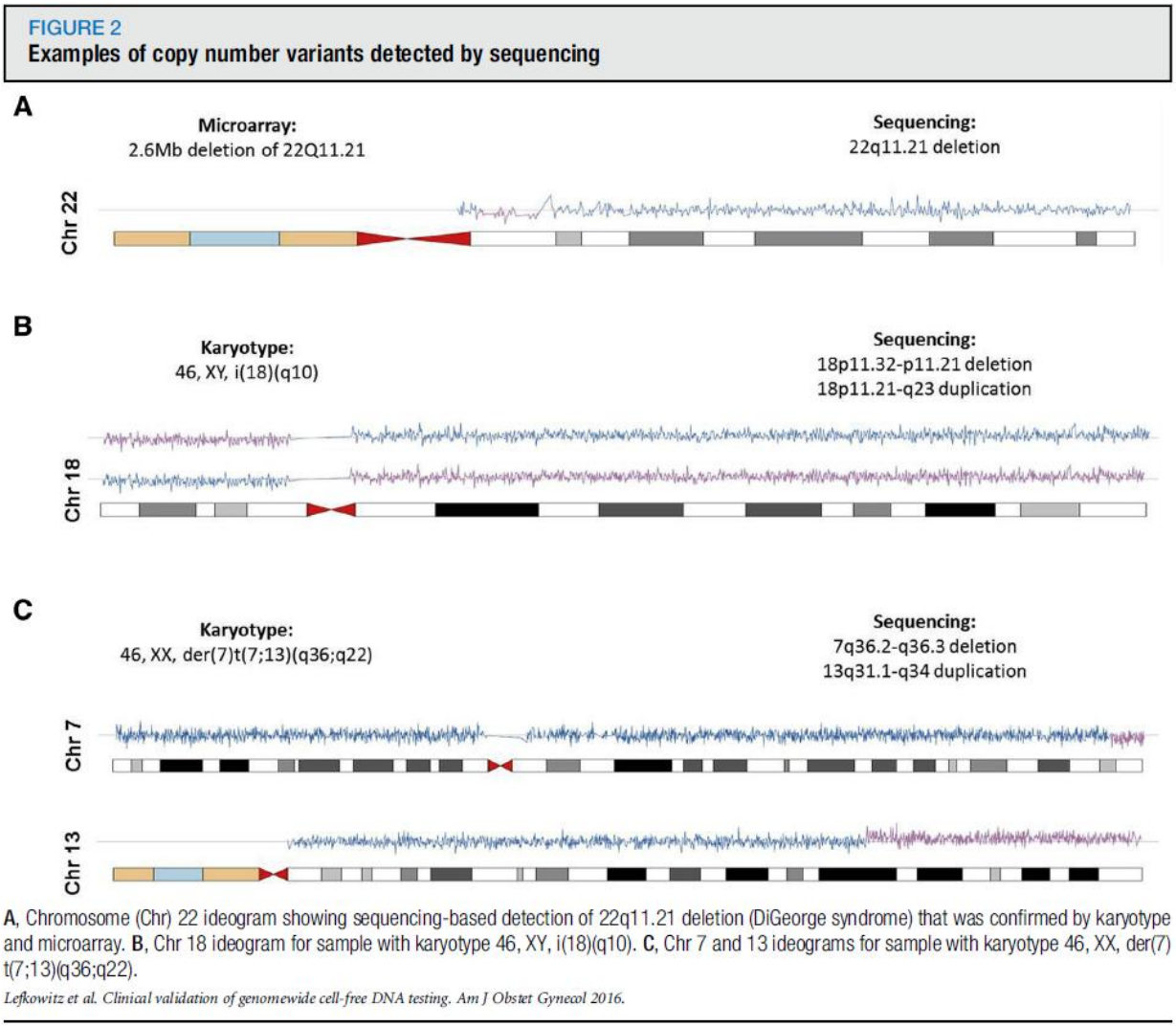
24 (Palomaki 2011); Ex. 25 (Ehrich 2011); Ex. 26 (Chiu 2008); *see also* Ex. 55 at 5-7 (Palomaki Supp. Mat.)

68. MaterniT® GENOME uses the karyotyping method described in Rafalko et al. (2021) ("Rafalko"). Ex. 46 at fn. 1 (citing Rafalko) (2022 MaterniT GENOME Brochure) (https://womenshealth.labcorp.com/sites/default/files/2023-01/DX_BRO_L17294-1122-6-2.pdf.) Rafalko, authored by Labcorp personnel, describes Labcorp's genome-wide MaterniT® GENOME test as a genome-wide NIPT that detects sub-chromosomal gains and losses across the genome. Ex. 57 at 1847 (Rafalko). According to Rafalko, maternal blood samples submitted to Sequenom Laboratories, a.k.a. SCMM, for MaterniT® GENOME testing are sequenced by genome-wide massively parallel sequencing as described in Jensen et al. (2013) ("Jensen") and are analyzed to detect aneuploidies and sub-chromosomal copy-number variants as described in Lefkowitz et al. (2016) ("Lefkowitz"). *Id.*

69. Sequenom personnel further described the sequencing and analytical method used in the MaterniT® GENOME test in Jensen. Ex. 28 (Jensen). Jensen describes preparing sequencing libraries from cell-free DNA, sequencing the fragments by massively parallel sequencing, aligning the reads to the genome, and, after normalization and genomic-segment filtering, calculating scores for the affected chromosomes relative to euploid (i.e., normal) reference samples. *Id.* at 1. Samples were classified as trisomic when the score exceeded a defined cutoff. *Id.* at 3.

70. MaterniT® GENOME additionally analyzes partial-chromosome (sub-chromosomal) abnormalities across the entire genome. Lefkowitz, a Sequenom clinical validation study of the genome-wide test authored by Sequenom personnel, describes the method by which the Accused Products sequence pieces of maternal and fetal DNA in maternal blood, align the sequence reads with the genome, which is divided into segments of a selected size (windows), count the aligned reads in each segment, and compare those counts to detect copy-number gains and losses

genome-wide and against a reference set of euploid samples. Ex. 27 (Lefkowitz).



Ex. 27 at 227.e5 (Lefkowitz).

COUNT I

INFRINGEMENT OF THE '687 PATENT

71. JHU realleges and incorporates by reference the allegations of the preceding paragraphs as though fully set forth herein.

72. The '687 patent was duly issued on April 27, 2010, in full compliance with Title 35 of the United States Code, and was valid and enforceable at all times prior to its expiration on October 11, 2026.

73. Labcorp has infringed one or more claims of the ’687 patent, including at least exemplary claims 1 and 23, under 35 U.S.C. § 271(a), either literally and/or under the doctrine of equivalents, by using and performing the MaterniT® 21 PLUS, MaterniT® GENOME and the GENOME-Flex tests, either itself or through its wholly-owned subsidiary and agent, Sequenom. For example, Labcorp assigns its Sequenom laboratories the task of using the MaterniT® 21 PLUS, MaterniT® GENOME, and the GENOME-Flex tests (by collecting samples and sending them to Sequenom for processing), and Labcorp gives interim instructions to control the means and details of the process by which Sequenom uses the MaterniT® 21 PLUS, MaterniT® GENOME and the GENOME-Flex tests (by establishing the MaterniT® 21 PLUS, MaterniT® GENOME, and the GENOME-Flex test protocols and requiring Sequenom to follow those protocols when processing tests).

74. Labcorp has infringed one or more claims of the ’687 patent, including at least exemplary claims 1 and 23, under 35 U.S.C. § 271(a), either literally and/or under the doctrine of equivalents, by directing and controlling the performance of the MaterniT® 21 PLUS, MaterniT® GENOME, and the GENOME-Flex tests, which includes performing the patented methods, by its Sequenom laboratory (including through its wholly-owned subsidiary Sequenom).

75. Labcorp has infringed one or more claims of the ’687 patent under 35 U.S.C. § 271(a), either literally and/or under the doctrine of equivalents, by offering for sale and selling products and services which include performance of infringing methods, such as by offering for sale and selling the MaterniT® 21 PLUS, MaterniT® GENOME, and the GENOME-Flex test. Labcorp’s offers for sale and sales of the MaterniT® 21 PLUS, MaterniT® GENOME, and GENOME-Flex tests include Labcorp (through its agents and subsidiaries) performing the steps of the patented methods, including at least the methods of exemplary claims 1 and 23.

76. Labcorp has induced infringement of one or more claims of the ’687 patent under

35 U.S.C. § 271(b). Labcorp has actively, knowingly, and intentionally induced infringement of the '687 patent by selling or otherwise supplying the MaterniT® 21 PLUS, MaterniT® GENOME, and the GENOME-Flex tests with the knowledge and intent that its wholly-owned and controlled subsidiary Sequenom will use the MaterniT® 21 PLUS, MaterniT® GENOME, and GENOME-Flex tests supplied by Labcorp, and the patient samples provided pursuant to the sales of those tests, to infringe the '687 patent; and with knowledge and intent to encourage and facilitate infringement through the dissemination of the MaterniT® 21 PLUS, MaterniT® GENOME, and GENOME-Flex tests and/or the creation and dissemination of promotional and marketing materials, supporting materials, instructions, product manuals, and/or technical information related to the MaterniT® 21 PLUS, MaterniT® GENOME, and GENOME-Flex tests.

77. Labcorp specifically intends and is aware that the ordinary and customary use of the MaterniT® 21 PLUS, MaterniT® GENOME, and GENOME-Flex tests would infringe the '687 patent. For example, Labcorp provides the MaterniT® 21 PLUS, MaterniT® GENOME, and GENOME-Flex tests, which, when used in their ordinary and customary manner as intended and instructed by Labcorp, infringe one or more claims of the '687 patent, including at least exemplary claims 1 and 23. Labcorp further provides product manuals and other instructional materials that cause Sequenom and/or SCMM to use the MaterniT® 21 PLUS, MaterniT® GENOME, and GENOME-Flex tests for their ordinary and customary use. Sequenom and/or SCMM have directly infringed the '687 patent, including at least exemplary claims 1 and 23, through the normal and customary use of the MaterniT® 21 PLUS, MaterniT® GENOME, and GENOME-Flex tests. Labcorp, accordingly, induced Sequenom and SCMM to use the MaterniT® 21 PLUS, MaterniT® GENOME, and GENOME-Flex tests in their ordinary and customary way to infringe the '687 patent, knowing, or at least being willfully blind to the fact, that such use constitutes infringement of the '687 patent.

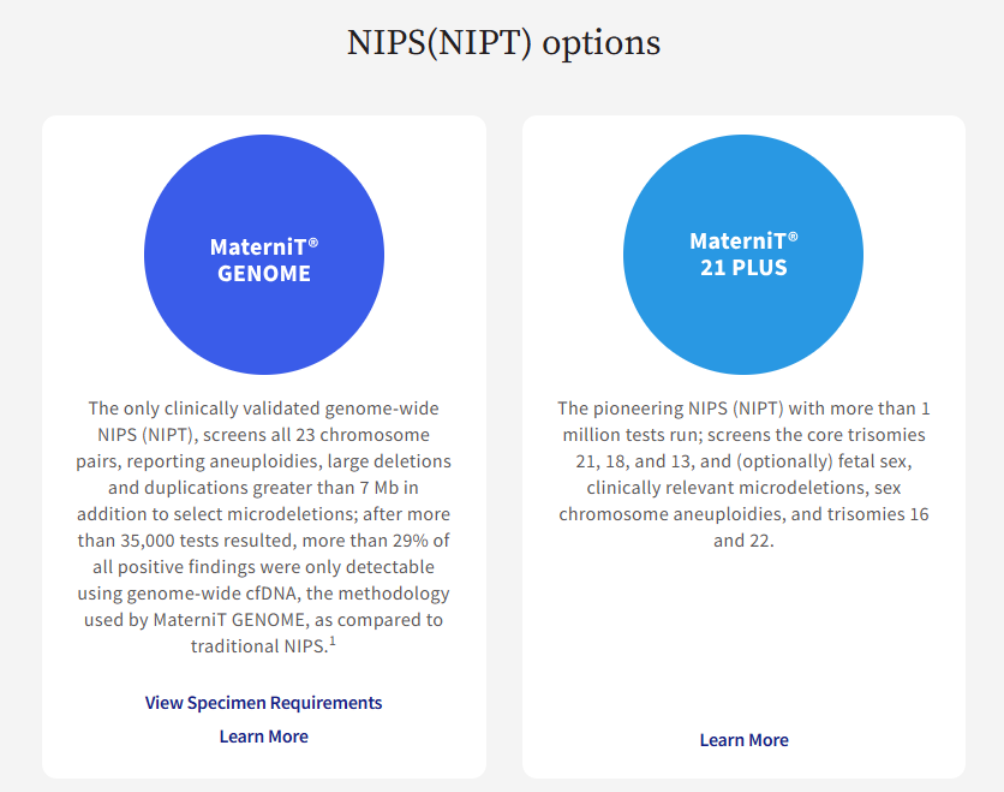
78. In addition, Labcorp has contributed to the infringement by others, including Sequenom and SCMM, of one or more claims of the ’687 patent under 35 U.S.C. § 271(c), including at least exemplary claims 1 and 23, by making, selling, and/or offering for sale in the United States, and/or importing into the United States, the MaterniT® 21 PLUS, MaterniT® GENOME, and GENOME-Flex tests, knowing that those products constitute a material part of the inventions of the ’687 patent, knowing that those products are especially made or adapted to infringe the ’687 patent, and knowing that those products are not staple articles of commerce suitable for substantial non-infringing use.

79. Labcorp has had actual or constructive knowledge of the ’687 patent since at least February 18, 2022, when Labcorp acquired PGDx and the DK License. Ex. 32 (Vendor Letter for PGDx Acquisition). At minimum, Labcorp has had actual knowledge of the ’687 patent since at least August 10, 2023, when JHU informed Labcorp that the ’687 patent covers the MaterniT® NIPTs as explained above.

80. Labcorp infringes, either literally or under the doctrine of equivalents, at least claim 1 of the ’687 patent, which recites in full:

> A method of karyotyping a genome of a test eukaryotic cell, comprising:
>
> sequencing a population of pieces of the genome of the test eukaryotic cell to provide nucleotide sequence of said pieces;
>
> matching, in silico, pieces of the genome to genomic locations using the nucleotide sequence of said pieces;
>
> counting the pieces within windows of a selected size throughout the genome to determine number of pieces as a function of genomic location, wherein each window comprises a plurality of genomically clustered pieces;
>
> comparing the number of pieces enumerated within each window for the test eukaryotic cell to the average number of pieces in windows of the selected size throughout the genome to obtain piece densities per window, wherein the piece densities per window represent the karyotype of the genome of the test eukaryotic cell.

81. When Labcorp performs the testing enabled by the Accused Products, it practices a method of karyotyping a genome of a test eukaryotic cell. *See* Exs. 3, 4, 5. The Accused Products analyze cell-free DNA circulating in maternal plasma. Ex. 56 at 3-5 (MaterniT® 21 PLUS brochure citing Palomaki); Ex. 46 at 1-2 (https://womenshealth.labcorp.com/sites/default/files/2023-01/DX_BRO_L17294-1122-6-2.pdf). That cell-free DNA includes DNA shed from fetal and placental cells, and the Accused Products analyze the fetal genome, i.e., the genome of a test eukaryotic cell, to screen for fetal chromosomal abnormalities. Ex. 56 at 3-5 (MaterniT® 21 PLUS brochure citing Palomaki); Ex. 46 at 2 (https://womenshealth.labcorp.com/sites/default/files/2023-01/DX_BRO_L17294-1122-6-2.pdf). The website for the Accused Products shows that MaterniT® 21 PLUS screens for trisomies (such as trisomy 21, Down syndrome) and other chromosomal disorders (such as DiGeorge syndrome). Ex. 3 at 3-4 (https://womenshealth.labcorp.com/providers/prenatal-screening/noninvasive-prenatal-testing/maternit-21-plus). The website describes the GENOME-Flex product as "rapidly re-sequenc[ing] previously run MaterniT® samples" when late stage anomalies are suspected. Ex. 5 at 1 (https://womenshealth.labcorp.com/providers/prenatal-screening/noninvasive-prenatal-testing/maternit-21-plus/maternit-genome-flex). The website describes MaterniT® GENOME as "report[ing] on all chromosomes" and screening for "trisomy 21 (Down syndrome), 18 (Edwards syndrome), and 13 (Patau syndrome)" in addition to "other chromosomal changes that may go undiagnosed at birth." Ex. 4 at 1-2 (https://womenshealth.labcorp.com/patients/pregnancy/maternit-genome).



https://womenshealth.labcorp.com/patients/pregnancy/noninvasive-prenatal-screening

82. Labcorp sequences a population of pieces of the genome of the test eukaryotic cell to provide a nucleotide sequence of those pieces. The Accused Products sequence a population of pieces of the fetal genome (derived from fetal DNA in maternal blood) to provide the nucleotide sequence of those pieces. For example, Palomaki (2011), reporting the MaterniT® 21 PLUS clinical validation study (ClinicalTrials.gov No. NCT00877292), states that circulating cell-free DNA fragments isolated from maternal plasma were sequenced on the Illumina HiSeq 2000 platform. Ex. 24 at 913–914; Ex. 55 at 5-7 (Palomaki Supp. Mat.). Ehrich describes the MaterniT® 21 PLUS as preparing DNA from maternal plasma and sequencing approximately five million 36-base fragments. Ex. 25 at 205.e3. (Ehrich). As another example, Rafalko (2021), explains that the MaterniT® GENOME samples are sequenced by massively parallel sequencing.[1] Ex. 57 at 1847,

[1] The MaterniT® GENOME analysis applies to the GENOME-Flex because GENOME-Flex re-sequences the sample using the MaterniT® GENOME method.

1851 (Rafalko). Jensen (2013) likewise describes that the cell-free DNA in the MaterniT® GENOME samples was extracted and sequenced on an Illumina HiSeq 2000 sequencer. Ex. 28 at 1–2 (Jensen).

83. Labcorp matches, in silico, the sequenced pieces to genomic locations using their nucleotide sequence. The Accused Products match the sequenced pieces of the fetal DNA to genomic locations in the human genome using their nucleotide sequence. For example, the MaterniT® 21 PLUS test, as described in Ehrich, matches the 36-base reads to a reference human genome to determine their chromosome origin. Ex. 25 at 205.e3. (Ehrich) ("[T]he 36-base reads [are] matched to a reference human genome to determine their chromosome origin."); *see also* Ex. 55 at 5 (Palomaki Supp. Mat.). With respect to the MaterniT® GENOME test, Jensen, Lefkowitz, and Rafalko also describe aligning the pieces to the reference genome. Ex. 28 at 3 (Jensen); Ex. 27 at 227.e2 (Lefkowitz); Ex. 57 at 1847, 1853 (Rafalko). Lefkowitz (2016) states that the sequencing reads were aligned to the reference human genome (hg19) using Bowtie 2. Ex. 27 at 227.e2 (Lefkowitz).

84. Labcorp counts the pieces within windows of a selected size throughout the genome to determine the number of pieces as a function of genomic location, each window comprising a plurality of genomically clustered pieces. The Accused Products partition the genome into windows or bins of a selected size that contain a plurality of genomically clustered sequences and count the aligned pieces within those windows across the genome. For example, for MaterniT® 21 PLUS, Palomaki describes counting the number of aligned reads within a 50 Kb bin. Ex. 55 at 9 (Palomaki Supp. Mat.). Third party researchers also noted for MaterniT®21 PLUS that "[a]fter isolation, sequencing, and alignment of cfDNA fragments…the reads are sorted into bins." Ex. 58 at 1640 (Snyder). As another example, for MaterniT® GENOME, Lefkowitz describes partitioning the genome into 50-kilobase-pair, non-overlapping segments and counting the number of aligned

reads in each segment. Ex. 27 at 227.e2-227.e3 (Lefkowitz). Rafalko confirms that the genome-wide MateriT® GENOME test detects copy-number changes across the genome using this analysis. Ex. 57 at 1852 (Rafalko). Each 50-kilobase segment or bin is a window of a selected size comprising a plurality of genomically clustered pieces. Lefkowitz further confirms this step and describes that after alignment, the genome was partitioned into 50-kbp non-overlapping segments and the total number of reads per segment was determined by counting the reads whose 5' ends overlap each segment. Ex. 27 at 227.e2-227.e3 (Lefkowitz).

85. Labcorp compares the number of pieces enumerated within each window to the average number of pieces in windows of the selected size throughout the genome, to obtain piece densities per window. The Accused Products perform intra-sample comparisons of the number of pieces in each bin to the average number of pieces in bins across the genome to obtain piece densities, with the resulting per-window densities representing the karyotype. For example, Lefkowitz describes an intra-sample comparison using circular binary segmentation made for MateriT® GENOME to identify copy number variations throughout the genome by segmenting each chromosome into contiguous regions of equal copy number. Ex. 27 at 227.e2-227.e3 (Lefkowitz). Lefkowitz also describes a bootstrapping analysis that calculates sample read count variability by calculating the median shift of segment fractions from the normal level across the chromosome. Ex. 27 at 227.e3 (Lefkowitz). As another example, for MateriT® 21 PLUS, Palomaki describes comparing counts for a given chromosome to counts on other chromosomes in a method similar to that used in Ehrich and Chiu. Ex. 55 at 7-8 (Palomaki Supp. Mat.); Ex. 26 at 20459, Fig. 1 (Chiu). In 2015, Snyder et al. identified maternal copy number variations as a source of false positive NIPT results and recommended the use of fixed genome bin sizes and the identification of region-specific outliers to avoid those false positives. Ex. 58 at 1644 (Snyder). On information and belief, Sequenom/Labcorp adopted this fixed genome bin size recommendation

including internal comparisons to the average number of pieces in windows of the selected size throughout the genome, to obtain piece densities per window, for the MateriniT® 21 PLUS.

86. Labcorp also infringes at least claim 23 of the '687 patent, which depends from claim 1 and adds the further step of "comparing piece densities per window for the test eukaryotic cell to piece densities of a reference eukaryotic cell." Ex. 1, claim 23. As alleged above, Labcorp performs every step of claim 1 when it uses the Accused Products.

87. Labcorp further compares the piece densities determined for the patient's (test) sample to the piece densities of reference eukaryotic cells. Each of the Accused Products compares the results of the counting analysis of the test sample to those of an external human reference to calculate a z-score, which is indicative of copy number variations, including trisomy and monosomy. For example, Palomaki describes MateriniT® 21 PLUS as comparing the normalized counts for a given chromosome to an external reference to calculate a z-score that reflects the number of standard deviations above a central estimate, with a z-score at or above 3 reflecting trisomy. Ex. 24 at 914 (Palomaki); Ex. 55 at 7-8 (Palomaki Supp. Mat.). Ehrich also describes comparing the test sample's normalized sequence counts to the mean normalized counts for the same regions in an external euploid control group, yielding a z-score that measures the deviation of the test sample from the euploid reference. Ex. 25 at 205.e5 (Ehrich). Chiu likewise describes calculating a z-score for the test sample by comparing the normalized count for a specific chromosome to the mean and standard deviation for the same chromosome in a euploid reference data set. Ex. 26 at 20459 (Chiu).

88. As another example, Jensen describes a similar external reference comparison for MateriniT® GENOME. After sequencing and normalization, z-scores are calculated for a given chromosome by comparing the sample results for the chromosome of interest to that of an external reference, and a sample is classified as trisomic when its z-score exceeds a defined cutoff (for example, $z = 3$ for chromosome 21). Ex. 28 at 3, 6 (Jensen). Lefkowitz also describes calculating

a z-score for both sub-chromosomal and whole chromosome variants by comparing the signal for a particular region with a reference set of samples in the same region to identify copy number variants. Ex. 27 at 227.e3, Fig. 2 (Lefkowitz).

89. By performing this additional comparison to reference eukaryotic cells, together with every step of claim 1, Labcorp infringes at least claim 23 of the '687 patent.

90. Labcorp's performance of the claimed method, with knowledge of the '687 patent and of JHU's infringement contentions, renders Labcorp's infringement willful and deliberate.

91. As a result of Labcorp's infringement of the '687 patent, JHU has been injured and has suffered damages.

92. Labcorp's conduct in infringing the '687 patent renders this case exceptional within the meaning of 35 U.S.C. § 285.

COUNT II

BREACH OF CONTRACT

93. JHU realleges and incorporates by reference the allegations of the preceding paragraphs as though fully set forth herein.

94. JHU asserts Count II for breach of contract in the alternative to, and in connection with, Count I. The allegations in this Count II are pleaded in the alternative and do not constitute an admission that the DK License remains in effect or that any Accused Product is licensed thereunder. *See* Fed. R. Civ. P.8(d)(2)-(3).

95. By acquiring PGDx, Labcorp assumed the obligations under the DK License, including the obligation to pay royalties to JHU for use of the methods described by the '687 patent. Labcorp assumed those obligations both as PGDx's successor by operation of law, *see* Md. Code Ann., Corps. & Ass'ns § 3-114, and by expressly or impliedly assuming them—including by administering the DK License and paying JHU royalties under it for other products.

96. Labcorp has breached the DK License agreement since at least February 18, 2022, including by failing to pay royalties to JHU under Article 3 of the DK License for the performance of the claimed DK methods by its MaterniT® 21 PLUS, MaterniT® GENOME, and GENOME-Flex NIPT tests.

97. Labcorp breached the DK License agreement despite Labcorp's full knowledge of its contractual obligations to JHU under the DK License and continued its willful breach of the DK License up to and including October 5, 2026 when JHU terminated the DK License as it was permitted to do under Section 9.2.

98. Labcorp's breach has deprived JHU of valuable benefits for which JHU bargained, for which Labcorp (through its predecessor PGDx) entered into a contract with JHU, and which JHU rightfully expected and which have been due under the DK License.

99. JHU has been directly and proximately injured by Labcorp's breach of the license including its royalty obligations to JHU.

100. As a result of Labcorp's breach, JHU has suffered damages in an amount to be determined at trial.

PRAYER FOR RELIEF

WHEREFORE, Plaintiff The Johns Hopkins University respectfully requests the following relief:

(A) That judgment be entered that Defendant has directly and/or indirectly infringed the '687 patent;

(B) That JHU be awarded damages adequate to compensate for Defendant's past infringement of the '687 patent, said damages being no less than a reasonable royalty together with

pre-judgment and post-judgment interest as allowed by law, costs, and other damages permitted by 35 U.S.C. § 284;

(C) A judgment that Defendant's infringement has been willful, and an award of enhanced damages pursuant to 35 U.S.C. § 284;

(D) That this case be declared exceptional under 35 U.S.C. § 285, and that JHU be awarded reasonable attorneys' fees and costs;

(E) That an accounting be performed to determine the damages to be awarded to JHU as a result of Defendant's infringing activities, including an accounting for infringing conduct not presented at trial and an award of additional damages for any such infringing activities;

(F) For any periods for which JHU is not awarded patent infringement damages, a judgment that Defendant has breached the DK License;

(G) For any periods for which JHU is not awarded patent infringement damages, that JHU be awarded contract damages adequate to compensate for Defendant's breach of contract, said damages being no less than the royalties owed to JHU under the DK License together with pre-judgment and post-judgment interest as allowed by law, costs, and other damages permitted by law;

(H) An award of costs and expenses incurred in prosecuting this action; and

(I) That this Court award such other and further relief as it may deem just and proper.

JURY TRIAL DEMAND

Pursuant to Rule 38 of the Federal Rules of Civil Procedure, JHU hereby respectfully demands a trial by jury on all issues so triable.

Respectfully submitted,

FISH & RICHARDSON P.C.

Dated: October 30, 2026

By: */s/ Ahmed J. Davis*

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