IN THE UNITED STATES DISTRICT COURT
FOR THE WESTERN DISTRICT OF TEXAS
WACO DIVISION

Ravgen, Inc., Plaintiff, v. Laboratory Corporation of America Holdings, Defendant.	Civil Action No. _____ **JURY TRIAL DEMANDED**

COMPLAINT FOR PATENT INFRINGEMENT

Plaintiff Ravgen, Inc. ("Ravgen"), for its Complaint against Defendant Laboratory Corporation of America Holdings ("LabCorp"), hereby alleges as follows:

NATURE OF THE ACTION

1. This is a civil action for infringement of United States Patent Nos. 7,727,720 (the "'720 Patent") and 7,332,277 (the "'277 Patent") (collectively the "Patents-in-Suit"), arising under the Patent Laws of the United States, 35 U.S.C. §§ 271, *et seq.*

THE PARTIES

2. Plaintiff Ravgen is a Delaware corporation with its principal place of business at 9241 Rumsey Rd., Columbia, Maryland 21045. Ravgen is a pioneering diagnostics company that focuses on non-invasive prenatal testing. Ravgen has spent millions of dollars researching and developing novel methods for the detection of cell-free DNA to replace conventional, invasive procedures. Ravgen's innovative cell-free DNA technology has various applications, including non-invasive prenatal and other genetic testing. Those efforts have resulted in the issuance of several patents, including the Patents-in-Suit.

3. Defendant LabCorp is a Delaware corporation with its principal place of business at 358 South Main Street, Burlington, North Carolina, 27215. (Ex. 3 at 1 (Laboratory Corporation of America Holdings' Form 10-K For Fiscal Year 2019).) LabCorp is registered to do business in the state of Texas. (Ex. 4 (Texas Franchise Tax Account Status for Laboratory Corporation of America Holdings).) LabCorp has appointed Corporation Service Company (d/b/a CSC - Lawyers Incorporating Service Company) as its agent for service of process. (*Id.*) LabCorp maintains several places of business in this District, including diagnostic testing facilities, laboratories, and office space for supporting and processing diagnostic tests at 6603 First Park Ten Blvd, San Antonio, TX 78213. (Ex. 5 (https://www.labcorp.com/node/107).)

4. Defendant LabCorp, itself and/or through its subsidiaries and affiliates, makes, uses, and commercializes genetic tests using cell-free DNA, including the MateriT21 PLUS test, the MateriT Genome test, the informaSeq Non-invasive Prenatal Test (the "the informaSeq test"), and the Resolution ctDx Lung Assay (collectively the "Accused Tests"). For example, LabCorp, itself and/or through its subsidiaries, makes, uses, and commercializes tests for the detection of chromosomal abnormalities using cell-free fetal DNA, including the MateriT21 PLUS test, the MateriT Genome test, and the informaSeq test. For example, LabCorp, itself and/or through its subsidiaries and affiliates, commercializes assays for the extraction, processing, and detection of cell-free DNA, including Resolution ctDx Lung Assay test, a test for the detection of mutations using circulating tumor DNA. LabCorp offers and markets those tests throughout the United States, at least through its websites https://www.labcorp.com/, https://integratedgenetics.com/, and https://www.integratedoncology.com/. (*See, e.g.* Ex. 6 (https://www.labcorp.com/tests/451951/maternit21-plus-core-chr21-18-13-no-gender); Ex. 7 (https://www.integratedgenetics.com/tests/451927/maternit-21-plus-core-chr21-18-13-sex); Ex. 8

(https://www.labcorp.com/tests/451941/maternit-genome); Ex. 9 (https://www.integratedgenetics.com/tests/451941/maternit-genome); Ex. 10 (https://www.integratedgenetics.com/providers/tests/prenatal/nipt/informaseq); Ex. 11 (https://www.labcorp.com/tests/830697/resolution-ctdx-lung-assay-liquid-biopsy); Ex. 12 (https://www.integratedoncology.com/test-menu/46890/resolution-ctdx-lung-assay%E2%84%A2-liquid-biopsy).)

JURISDICTION AND VENUE

5. Ravgen incorporates by reference paragraphs 1–4.

6. This action arises under the patent laws of the United States, including 35 U.S.C. §§ 271 *et seq*. The jurisdiction of this Court over the subject matter of this action is proper under 28 U.S.C. §§ 1331 and 1338(a).

7. Venue is proper in this District pursuant to U.S.C. §§ 1391(b), (c), (d), and 1400(b) because LabCorp has a permanent and continuous presence in, have committed acts of infringement in, and maintain regular and established places of businesses in this District.

8. By registering to conduct business in Texas and by having facilities where they regularly conduct business in this District, LabCorp has a permanent and continuous presence and regular and established places of business in the Western District of Texas.

9. 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 (*e.g.*, the MaterniT21 PLUS, MaterniT Genome, informaSeq, and Resolution ctDx Lung Assay tests) at 6603 First Park Ten Blvd, San Antonio, TX 78213. (Ex. 5 (https://www.labcorp.com/node/107); *see also* Ex. 13 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. 14 (https://www.labcorp.com/assets/5886) (showing an example clinical questionnaire for noninvasive prenatal testing allowing a provider to request tests, including the informaSeq, MaterniT21 PLUS, and MaterniT Genome tests); Ex. 15 (https://www.dnatestingcenters.com/centers/texas/san-antonio/labcorp-first-park-ten-blvd/) (including as services offered at the LabCorp facility located at 6603 First Park Ten Blvd, San Antonio, TX "DNA Tests" and "Blood Work").)

(Ex. 16 (Google street view photo of 6603 First Park Ten Blvd, San Antonio, TX location).)

10. LabCorp also maintains diagnostic testing facilities and laboratories in this District at the following locations, as listed on its website:

- 1920 E. Riverside Dr, Austin TX 78741
- 711 W 38th St Suite B-2, Austin TX 78705
- 4207 James Casey St Ste 101, Austin TX 78745
- 9801 Manchaca, Austin TX 78748
- 11111 Research Blvd Suite 340, Austin TX 78759
- 2021 Pecan St W, Pflugerville TX 78660
- 2401 Ranch Road 620 S, Lakeway TX 78738
- 16030 Park Valley Suite 200, Round Rock TX 78681
- 5781 Kyle Parkway, Kyle TX 78640

- 1401 Medical Parkway Bl C 325, Cedar Park TX 78613
- 5317 Williams Dr, Georgetown TX 78633
- 1320 Wonder World Dr Suite 105, San Marcos TX 78666
- 2115 Stephen's Place 1200, New Braunfels TX 78130
- 12602 Toepperwein Rd Ste 220, Live Oak TX 78233
- 19016 Stone Oak Parkway 265, San Antonio TX 78258
- 8601 Village Dr Ste 202, San Antonio TX 78217
- 124 E Bandera Rd Ste 303, Boerne TX 78006
- 9618 Huebner Rd Suite 214, San Antonio TX 78240
- 8042 Wurzbach Rd Ste 140, San Antonio TX 78229
- 1303 McCullough Ave Ste 429, San Antonio TX 78212

(Ex. 17 (LabCorp Search Results in Texas, https://www.labcorp.com/labs-and-appointments/results?address_single=Austin%2C+TX&lat=30.2667&lon=-97.7428&geo_address=&address_street_1=&address_street_2=&city=Austin&state=TX&zip=&service=ROUTINE_PHLEBOTOMY&radius=100&op=Search&form_build_id=form-ZxDduvrY3KQCkcbiqplDY4e_v7C0uJvhg4ZWJO0fNTQ&form_id=psc-locator-advanced-form).) LabCorp states on its website that "[a]ll LabCorp patient service centers offer routine specimen collections for adults, which can include blood draws." (Ex. 18 (https://www.labcorp.com/labs-and-appointments/labcorp-services).) On information and belief, employees of LabCorp carry out LabCorp's business at places of business in this district. (*See, e.g.,* Ex. 19 (https://jobs.labcorp.com/job/san-antonio/lab-supervisor/668/1400668160) (including as duties of a Lab Supervisor at a LabCorp facility in San Antonio, TX "[m]anag[ing] the daily operations of assigned laboratory group to ensure that specimens are properly shipped and received, tests are performed accurately and efficiently, and results are reported in a timely manner").)

11. LabCorp offers for sale and sells cell-free DNA tests that employ methods claimed in the Patents-in-Suit, including at least the Accused Tests, throughout the United States, including at their facilities in this District and through their websites, which are accessible in this District.

(*See, e.g.*, Ex. 7 (https://www.labcorp.com/tests/451927/maternit21-plus-core-chr21-18-13-sex) (showing a button to order a MaterniT21 PLUS test); Ex. 8 (https://www.labcorp.com/tests/451941/maternit-genome) (showing a button to order a MaterniT Genome test); Ex. 11 (https://www.labcorp.com/tests/830697/resolution-ctdx-lung-assay-liquid-biopsy) (showing a button to order an Resolution ctDx Lung Assay test); Ex. 20 at 8 (https://www.labcorp.com/tests/related-documents/L13272) (providing instructions on how to order an informaSeq test).)

12. LabCorp has committed acts of direct infringement in this judicial District. For example, on information and belief, LabCorp commits acts infringement in this District by offering for sale and selling the performance of infringing methods at LabCorp's diagnostic testing facilities, such as at 6603 First Park Ten Blvd, San Antonio, TX 78213. Specifically, as detailed further below, LabCorp offers for sale and sells the obligation to perform the steps of the patented methods, by, for example, offering for sale and selling the Accused Tests.

13. LabCorp is subject to this Court's jurisdiction pursuant to due process and/or the Texas Long Arm Statute due at least to its substantial business in this State and judicial 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 Texas, including in the Western District of Texas. For example, LabCorp conducts business in the District, by at least offering for sale and selling products and services that comprise the performance of the claimed methods of the Patents-in-Suit, including at least the Accused Tests, including through its websites, which are accessible in this District. In addition, LabCorp leases and operates diagnostic testing facilities and laboratories

in this District that sell, offer for sale, and support products and services that comprise the performance of the claimed methods of the Patens-in-Suit, including at least the Accused Tests.

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

15. Personal jurisdiction exists over LabCorp because LabCorp, directly and/or through subsidiaries or intermediaries, has committed and continues to commit acts of infringement in this District by, among other things, using products and/or services that infringe the Patents-in-Suit, which led to foreseeable harm and injury to Ravgen.

BACKGROUND OF THE INVENTION

16. Dr. Ravinder S. Dhallan is the founder of Ravgen, Inc. and the inventor of several patents in the field of detection of genetic disorders, including chromosomal abnormalities and mutations. Ravgen's mission is to provide state of the art genetic testing that will enrich the lives of its patients. For example, through the use of its novel techniques in non-invasive prenatal diagnostic testing, Ravgen gives patients the knowledge they need to prepare for their pregnancies and treat diseases at an early stage.

17. Prior to founding Ravgen, Dr. Dhallan was a board-certified emergency room physician. During his time at medical school and his residency at Mass General (Harvard University School of Medicine), Dr. Dhallan and his wife suffered three miscarriages. At that time, the prenatal diagnostic testing procedures available included (a) non-invasive techniques with low sensitivity and specificity, and (b) tests with higher sensitivity and specificity that were highly invasive and therefore associated with a risk for loss of pregnancy. After discovering the

limitations on the available techniques for prenatal testing, Dr. Dhallan made it his mission to invent an improved prenatal diagnostic exam—one that was both non-invasive and accurate. In September of 2000, Dr. Dhallan founded Ravgen (which stands for "Rapid Analysis of Variations in the GENome") to pursue that goal.

18. Prior to Ravgen's inventions, scientists had recognized the need for a genetic testing technique that used "cell-free" or "free" fetal DNA circulating in maternal blood. A technique that relied on circulating free fetal DNA would require only a simple blood draw from the mother and would therefore be improvement over invasive diagnostic tests.

19. However, at that time, the use of free fetal DNA for detecting chromosomal abnormalities was limited by the low percentage of free fetal DNA that could be recovered from a sample of maternal blood using existing techniques. (*See, e.g.,* Ex. 21 (Y.M.D. Lo et al., *Presence of Fetal DNA in Maternal Plasma and Serum*, 350 THE LANCET 485-87 (1997), https://doi.org/10.1016/S0140-6736(97)02174-0.) Dr. Dhallan recognized that a method that could increase the percentage of free fetal DNA relative to the free maternal DNA in a sample was necessary to the development of an accurate, non-invasive prenatal diagnostic test.

20. After substantial research, Dr. Dhallan conceived that including an agent that impedes cell lysis (disruption of the cell membrane) if cells are present during sample collection, shipping, handling, and processing would permit the recovery of a larger percentage of cell-free fetal DNA (relative to the cell-free maternal DNA in a sample). Dr. Dhallan hypothesized that this new approach would decrease the amount of maternal cell lysis and therefore lower the amount of cell-free maternal DNA in the sample, thereby increasing the percentage of cell-free fetal DNA. He developed a novel method for processing cell-free fetal DNA that involved the addition of an agent that impedes cell lysis—for example, a membrane stabilizer, a cross-linker, and/or a cell

lysis inhibitor—to maternal blood samples coupled with careful processing protocols. With that novel method, Dr. Dhallan was able to increase the relative percentage of cell-free fetal DNA in the processed sample.

21. Having successfully increased the relative percentage of cell-free fetal DNA recovered, Dr. Dhallan next addressed the challenge of distinguishing between the cell-free maternal and cell-free fetal DNA in a sample in order to determine whether a chromosomal abnormality is present in the fetal DNA. Prior to Ravgen's inventions, known methods for detecting fetal chromosomal abnormalities were time-consuming and burdensome. Many required amplification of the entire sequence of a gene, or quantification of the total amount of a particular gene product in a sample. Dr. Dhallan developed an alternate method that greatly increased the efficiency of this process by taking advantage of the variation of base sequences among different individuals (including a mother and fetus) ("alleles") at particular positions ("loci") on chromosomes. The term "allele" refers to an alternate form of a gene, or a non-coding region of DNA that occurs at a particular loci on a chromosome. The alleles present at certain loci on chromosomes (including, for example, "single nucleotide polymorphisms" or "SNPs") vary between different individuals. At such a locus, a fetus may therefore inherit an allele from its father that differs from the alleles present at that locus on its mother's chromosome. Dr. Dhallan developed a novel method for quantifying the allelic ratio at such a locus (or loci) of interest in a sample comprising maternal and fetal cell-free DNA in order to detect whether a fetal chromosomal abnormality was present in the fetal DNA of the sample, without requiring physical separation of the fetal from the maternal cell-free DNA.

22. Dr. Dhallan understood that his breakthrough laid the foundation for the development of accurate non-invasive prenatal diagnostic tests. For example, he published a paper

in the Journal of the American Medical Association (JAMA) in 2004, explaining that "the methods described herein for increasing the percentage of cell-free fetal DNA provide a solid foundation for the development of a noninvasive prenatal diagnostic test." (Ex. 22 at 6 (R. Dhallan et al., *Methods to Increase the Percentage of Free Fetal DNA Recovered From the Maternal Circulation*, 291 JAMA 1114–19 (2004), https://doi.org/10.1001/jama.291.9.1114).)

23. JAMA also ran an editorial alongside Dr. Dhallan's article in 2004, recognizing the significance of his invention to applications in prenatal genetic diagnosis and cancer detection and surveillance:

> In this issue of THE JOURNAL, the findings reported in the study by Dhallan and colleagues on enhancing recovery of cell-free DNA in maternal blood have major clinical implications. Developing a reliable, transportable technology for cell-free DNA analysis impacts 2 crucial areas—prenatal genetic diagnosis and cancer detection and surveillance. In prenatal genetic diagnosis, detecting a fetal abnormality without an invasive procedure (or with fewer invasive procedures) is a major advantage. Likewise in cancer surveillance (e.g., in patients with leukemia), monitoring treatment without having to perform a bone marrow aspiration for karyotype also would be of great benefit
>
> * * *
>
> With prospective studies focusing on clinical applications of these findings, profound clinical implications could emerge for prenatal diagnosis and cancer surveillance.

(Ex. 23 at 1, 3 (J.L. Simpson & F. Bischoff, *Cell-Free Fetal DNA in Maternal Blood: Evolving Clinical Applications,* 291 JAMA 1135–37 (2004), https://doi.org/10.1001/jama.291.9.1135).)

24. In 2007, Dr. Dhallan published a second journal article in The Lancet that presented a study showcasing Ravgen's ability to use its novel technology to detect Down's syndrome using free fetal DNA in a maternal blood sample. (Ex. 24 (R. Dhallan et al., *A Non-Invasive Test for Prenatal Diagnosis Based on Fetal DNA Present in Maternal Blood: A Preliminary Study*, 369 THE LANCET 474-81 (2007), https://doi.org/10.1016/S0140-6736(07)60115-9).) Dr. Dhallan's

peers at the *Lancet* also recognized that his innovative test "opens a new era in prenatal screening." (*See* Ex. 25 (A. Benachi & J.M. Costa, *Non-Invasive Prenatal Diagnosis of Fetal Aneuploidies*, 369 THE LANCET 440–42 (2007), https://doi.org/10.1016/S0140-6736(07)60116-0).)

25. Dr. Dhallan's publications received worldwide press coverage, from outlets such as CNN, BBC, and Washington Post. (*See* Ex. 26 (L. Palmer, *"A Better Prenatal Test?"*, CNN MONEY (Sept. 12, 2007,) https://money.cnn.com/2007/09/07/smbusiness/amniocentesis.fsb/index.htm); Ex. 27 (*"Hope For Safe Prenatal Gene Test"*, BBC NEWS (Feb 2, 2007), http://news.bbc.co.uk/2/hi/health/6320273.stm); Ex. 28 (A. Gardner, *"Experimental Prenatal Test Helps Spot Birth Defects"*, WASHINGTON POST (Feb. 2, 2007), https://www.washingtonpost.com/wp-dyn/content/article/2007/02/02/AR2007020200914.html).)

26. The Patents-in-Suit resulted from Dr. Dhallan's years-long research at Ravgen to develop these innovative new methods for detecting genetic disorders.

PATENTS-IN-SUIT

27. Ravgen incorporates by reference paragraphs 1–26.

28. The '277 Patent, entitled "Methods For Detection Of Genetic Disorders," was duly and legally issued by the United States Patent and Trademark Office on February 19, 2008. The inventor of the patent is Ravinder S. Dhallan, and the patent is assigned to Ravgen. A copy of the '277 Patent is attached hereto as Exhibit 1.

29. Ravgen is the exclusive owner of all rights, title, and interest in the '277 Patent, and has the right to bring this suit to recover damages for any current or past infringement of the '277 Patent. (*See* Ex. 29.)

30. The '720 Patent, entitled "Methods For Detection Of Genetic Disorders," was duly and legally issued by the United States Patent and Trademark Office on June 1, 2010. The inventor

of the patent is Ravinder S. Dhallan, and the patent is assigned to Ravgen. A copy of the '720 Patent is attached hereto as Exhibit 2.

31. Ravgen is the exclusive owner of all rights, title, and interest in the '720 Patent, and has the right to bring this suit to recover damages for any current or past infringement of the '720 Patent. (*See* Ex. 30.)

32. The '277 Patent is directed to, among other things, novel methods used in the detection of genetic disorders. For example, claim 81 of the '277 Patent recites:

> A method for preparing a sample for analysis comprising isolating free fetal nucleic acid from a the sample, wherein said sample comprises an agent that inhibits lysis of cells, if cells are present, and wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor.

33. The '720 Patent is directed to novel methods for detecting a free nucleic acid in a sample. For example, claim 1 of the '720 Patent recites:

> A method for detecting a free nucleic acid, wherein said method comprises: (a) isolating free nucleic acid from a non-cellular fraction of a sample, wherein said sample comprises an agent that impedes cell lysis, if cells are present, and wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor; and (b) detecting the presence or absence of the free nucleic acid.

34. The Patents-in-Suit are directed to unconventional, non-routine techniques for preparing and analyzing extracellular circulatory DNA, including for the detection of genetic disorders. The Patents-in-Suit explain that, *inter alia*, the inventions claimed therein overcame problems in the field—for example, that the low percentage of fetal DNA in maternal plasma makes using the DNA for genotyping the fetus difficult—with a novel and innovative solution—the addition of cell lysis inhibitors, cell membrane stabilizers or cross-linkers to the maternal blood sample, which increase the percentage of cell-free DNA available for detection and analysis:

> The percentage of fetal DNA in maternal plasma is between 0.39-11.9% (Pertl, and Bianchi, *Obstetrics and Gynecology* 98: 483-490 (2001)). **The majority of the DNA in the plasma sample is maternal, which makes using the DNA for genotyping the fetus difficult**. However, methods that increase the percentage of fetal DNA in the maternal plasma allow the sequence of the fetal DNA to be determined, and allow for the detection of genetic disorders including mutations, insertions, deletions, and chromosomal abnormalities. **The addition of cell lysis inhibitors, cell membrane stabilizers or cross-linkers to the maternal blood sample can increase the relative percentage of fetal DNA.** While lysis of both maternal and fetal cells is inhibited, the vast majority of cells are maternal, and thus by reducing the lysis of maternal cells, there is a relative increase in the percentage of free fetal DNA.

(Ex. 1 ('277 Patent) at 32:24–39; Ex. 2 ('720 Patent) at 33:31–46 (emphasis added).)

35. The Patents-in-Suit teach that the benefit of Dr. Dhallan's discovery, an increase in the relative percentage of cell-free DNA, is realized by performance of the claimed method, including through the inclusion of an agent that inhibits the lysis of the cells in a sample:

> An overall increase in fetal DNA was achieved by reducing the maternal cell lysis, and thus, reducing the amount of maternal DNA present in the sample. In this example, formaldehyde was used to prevent lysis of the cells, however any agent that prevents the lysis of cells or increases the structural integrity of the cells can be used. The increase in fetal DNA in the maternal plasma allows the sequence of the fetal DNA to be determined, and provides for the rapid detection of abnormal DNA sequences or chromosomal abnormalities including but not limited to point mutation, reading frame shift, transition, transversion, addition, insertion, deletion, addition-deletion, frame-shift, missense, reverse mutation, and microsatellite alteration, trisomy, monosomy, other aneuploidies, amplification, rearrangement, translocation, transversion, deletion, addition, amplification, fragment, translocation, and rearrangement.

(Ex. 1 ('277 Patent) at 91:44–60; Ex. 2 ('720 Patent) at 92:10–26.)

36. For example, during the prosecution of the '720 Patent at the Patent and Trademark Office, Ravgen explained that the innovative concept of using agents that inhibit cell lysis during

cell-free DNA detection and analysis is recited by the claimed methods of the '720 Patent, including in claim 1:

> Applicant has discovered that the addition of a cell lysis inhibitor to a sample prior to detecting the presence of free nucleic acid can ***significantly and unexpectedly*** increase the proportion of free nucleic acid obtained from the non-cellular fraction of a sample.
>
> * * *
>
> The methods disclosed in claims 1-8, 21-23, and 26 serve a long-felt need in the medical community, and provide unexpected results, and are therefore non-obvious.

(Ex. 31 ('720 File History, June 2, 2009 Response to Office Action) at 12, 14 (emphasis added).)

37. The inventive concept of the Patents-in-Suit of including an agent that inhibits cell lysis—for example, a membrane stabilizer, a cross-linker, and/or a cell lysis inhibitor—with a sample represented a significant improvement in the preparation of samples used for non-invasive testing, including non-invasive prenatal testing to unmask previously undetectable fetal genetic traits. At the time of the invention, it would not have been routine or conventional to add an agent that inhibits cell lysis to a sample to increase the proportion of free nucleic acid obtained from the non-cellular fraction of a sample. In fact, as described above, that inventive concept was recognized by Dr. Dhallan's peers as "an important step in improving detection of cell-free DNA." (Ex. 23 at 3.)

38. The '277 Patent is further directed to an unconventional, non-routine method of detecting fetal chromosomal abnormalities which involves "quantitating a ratio of the relative amount of alleles in a mixture of maternal DNA and fetal DNA." (Ex. 32 ('277 File History, May 30, 2007 Response to Office Action) at 30.) For example, claim 1 of the '277 Patent recites:

> A method for detecting the presence or absence of a fetal chromosomal abnormality, said method comprising: quantitating a ratio of the relative amounts of alleles at a heterozygous locus of

> interest in a mixture of template DNA, wherein said mixture comprises maternal DNA and fetal DNA, and wherein said mixture of maternal DNA and fetal DNA has been obtained from a sample from a pregnant female, and further wherein said heterozygous locus of interest has been identified by determining the sequence of alleles at the locus of interest, and wherein said ratio indicates the presence or absence of a fetal chromosomal abnormality.

39. The '277 Patent explains that this claimed method represented a significant improvement over prior art methods of detecting fetal chromosomal abnormalities, many of which were costly, time-consuming, and burdensome because they either required the amplification of the entire sequence of a gene, or quantification of the total amount of a particular gene product. (Ex. 1 at 66:14-20.) By contrast, the claimed "ratio" method of the '277 Patent only requires sequencing of discrete "loci of interest" (such as "single nucleotide polymorphisms," or "SNPs") from the collected DNA sample. (*Id.* at 34:63-35:38 ("In fact, it is an advantage of the invention that primers that copy an entire gene sequence need not be utilized. . . . There is no advantage to sequencing the entire gene as this can increase cost and delay results. Sequencing only the desired bases or loci of interest maximizes the overall efficiency of the method because it allows for the sequence of the maximum number of loci of interest to be determined in the fastest amount of time and with minimal cost.").)

40. During the prosecution of the '277 Patent at the Patent and Trademark Office, Ravgen gave the following example of an implementation of the claimed "ratio" method:

> Applicants have invented a method for detecting the presence or absence of a fetal chromosomal abnormality, wherein the method comprises, inter alia, quantitating a ratio of the relative amount of alleles in a mixture of maternal DNA and fetal DNA.
>
> ***
>
> [R]atios were calculated at both chromosomes 13 and 21 in a heterogeneous mixture of 75% Down syndrome DNA and 25% maternal DNA. Single nucleotide polymorphisms were analyzed

> wherein the maternal genome was homozygous for one allele at a specific genetic site and the Down syndrome DNA was heterozygous at the same genetic site. If at a certain site, the maternal genome contains an adenine at both copies of chromosome 13, and the Down syndrome genome is comprised of one chromosome with an adenine nucleotide and one chromosome with a guanine nucleotide, then the ratio of G:A is 0.60 (0.75 (Down syndrome G allele)/(0.75 Down syndrome A allele + 0.25 + 0.25 maternal A alleles).
>
> ***
>
> On the other hand, if at a certain genetic site on chromosome 21, the maternal genome contains an adenine at both copies of chromosome 21, and the Down syndrome genome is comprised of two chromosome with an adenine nucleotide and one chromosome with a guanine nucleotide, then the ratio of G:A is 0.375 (0.75 (Down syndrome G allele)/(0.75 Down syndrome A allele + 0.75 Down syndrome A allele + 0.25 + 0.25 (maternal A alleles). Thus, the methods described in the present application detect chromosomal abnormalities using a method that comprises, inter alia, quantitating a ratio of alleles in a heterogeneous mixture of DNA, wherein the ratio represents alleles from more than one individual.

(Ex. 32 ('277 File History, May 30, 2007 Response to Office Action) at 30.)

DEFENDANT'S INFRINGING ACTIVITIES

41. Ravgen incorporates by reference paragraphs 1–40.

A. The MateniT Tests

42. On October 17, 2011, Sequenom, Inc. ("Sequenom") launched the MateniT21 PLUS test, a commercial non-invasive prenatal test for detecting fetal genetic abnormalities. (*See* Ex. 33 at 1 (A. Pollack, "*A Less Risky Down Syndrome Test Is Developed*," NEW YORK TIMES (October 18, 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.").)

43. On July 13, 2015, Sequenom launched the MateniT Genome test, a commercial non-invasive prenatal test for detecting fetal genetic abnormalities that uses the same technology

as the MateriniT21 PLUS test. (*See* Ex. 34 at 1 ("*Sequenom Laboratories Launches MateriniT™ 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 MateriniT™ 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. 35 at 1 (http://www.sequenca.nz/nipt/assets/mtgenome-validation-brochure.pdf) (describing the MateriniT21 PLUS test as "the foundation for the new MateriniT GENOME assay"); *see also id.* at 2 ("The **MateriniT GENOME test utilizes proprietary technology similar to the MateriniT21 PLUS test, however with deeper sequencing**. In a clinical study using 448 patient samples, the MateriniT GENOME test was equivalent in performance to the MateriniT21 PLUS test for the analysis of trisomy 21, trisomy 18, trisomy 13, sex chromosome aneuploidies (SCA) and fetal sex classification."); Ex. 36 at 3 (https://www.integratedgenetics.com/sites/default/files/2020-04/GENOME_Positive%20T18_Sample%20Report.pdf) ("**The MateriniT™ GENOME test utilizes the same proprietary technology as the MateriniT21® PLUS test,** with deeper sequencing.").)

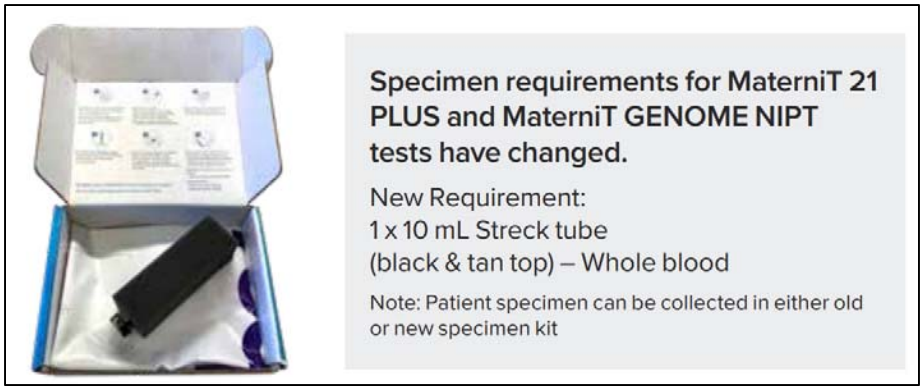
44. On July 27, 2016, LabCorp acquired Sequenom including the MateriniT21 PLUS test and the MateriniT Genome test (collectively "the MateriniT tests"). (*See* Ex. 37 at 1 ("*LabCorp Announces Agreement to Acquire Sequenom*," PR NEWSWIRE (July 27, 2016), https://www.prnewswire.com/news-releases/labcorp-announces-agreement-to-acquire-sequenom-300304676.html) ("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…").)

1. The Accused MaterniT21 PLUS Test

45. The MaterniT21 PLUS test is a commercial non-invasive prenatal test for detecting fetal genetic abnormalities from a maternal blood sample. (*See* Ex. 33 at 1 (A. Pollack, "*A Less Risky Down Syndrome Test Is Developed*," NEW YORK TIMES (October 18, 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."). Performance of the MaterniT21 PLUS test involves extracting cell-free DNA from maternal blood. (*Id.* at 3 ("The test counts small fragments of DNA in the mother's blood. While most of this DNA is from the mother, some is from the fetus.)"; *see also* Ex. 38 (https://sema4.com/products/test-catalog/noninvasive-prenatal-testing-nipt-sequenom/#) ("Sequenom noninvasive prenatal testing (NIPT) is a chromosome counting method that analyzes genetic information in fetal cell-free DNA in maternal blood."); Ex. 39 (A. Mazloom et. al., *Sample Specific Fetal Fraction Threshold for Non-Invasive Prenatal Testing*, LABCORP (2017), https://files.labcorp.com/labcorp-d8/Mazloom-ACMG-2017-SampleSpecificFetalFraction.pdf).)

46. The MaterniT21 PLUS test requires a sample containing an agent that inhibits cell lysis. For example, LabCorp lists as a requirement for the MaterniT21 PLUS test "[o]ne 10 mL BCT Streck tube" for collecting a whole blood specimen from the patient (mother). (Ex. 38 (https://sema4.com/products/test-catalog/noninvasive-prenatal-testing-nipt-sequenom/#).)

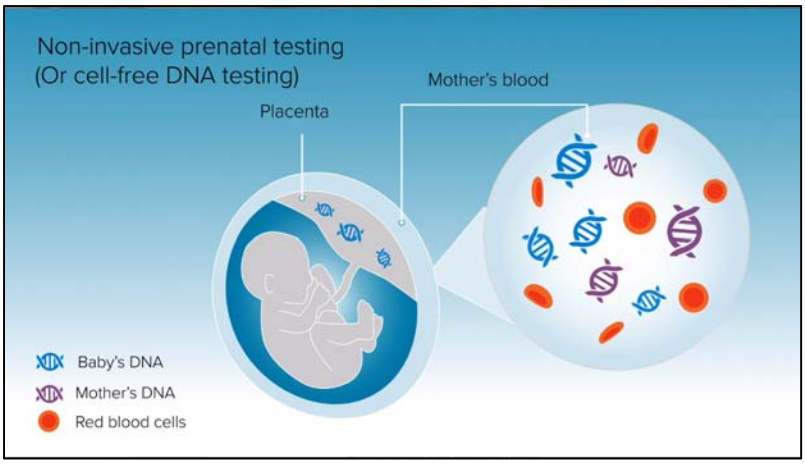


(Ex. 40 ("New MateriT Specimen Collection Kit," https://www.integratedgenetics.com/sites/default/files/2020-04/MateriT_Kit_Flyer_rep-1356-v1-0619.pdf).)

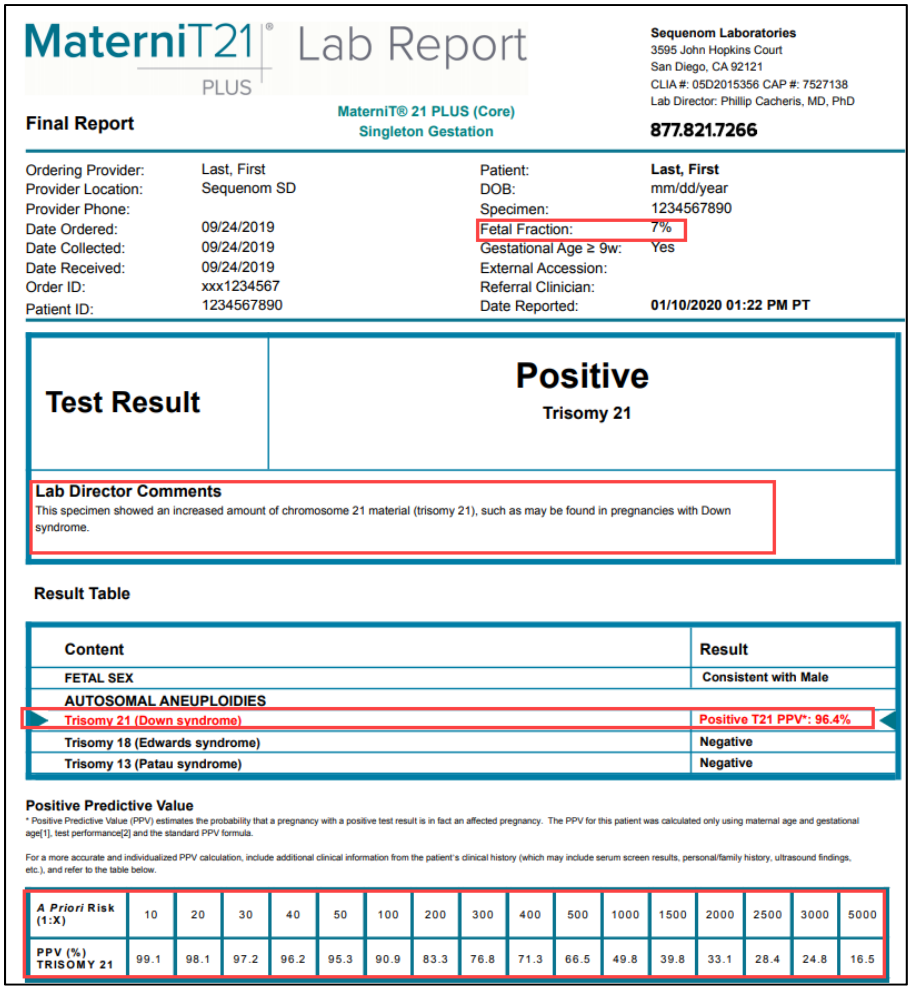
47. The "BCT Streck tube," or Streck Cell-Free DNA Blood Collection Tube ("BCT") includes an agent that inhibits cell lysis. For example, a Streck Cell-Free DNA BCT "stabilizes nucleated blood cells. The unique preservative ***limits the release of genomic DNA, allowing isolation of high-quality cell-free DNA***. Cell-Free DNA BCT has also been demonstrated to minimize the degradation of circulating tumor cells (CTCs). By ***limiting cell lysis***, the specialized chemistry provides sample integrity during storage, shipping and handling of blood samples. Cell-free DNA and gDNA are stable for up to 14 days at 6 °C to 37 °C. CTCs are stable for up to 7

days at 15 °C to 30 °C." (Ex. 41 at 2 (https://www.streck.com/products/stabilization/cell-free-dna-bct/#resources).)

48. Processing of the MateriT21 PLUS test involves isolating cell-free DNA from a sample of maternal blood collected in a Streck Cell-Free DNA BCT and analyzing the isolated cell-free DNA to detect chromosomal abnormalities as shown below:



(https://www.integratedgenetics.com/videos (displaying video entitled "Understanding your MateriT results") at 0:50).)



MaterniT21® PLUS Lab Report

Sequenom Laboratories
3595 John Hopkins Court
San Diego, CA 92121
CLIA #: 05D2015356 CAP #: 7527138
Lab Director: Phillip Cacheris, MD, PhD
877.821.7266

Final Report

MaterniT® 21 PLUS (Core)
Singleton Gestation

Ordering Provider:	Last, First	Patient:	**Last, First**
Provider Location:	Sequenom SD	DOB:	mm/dd/year
Provider Phone:		Specimen:	1234567890
Date Ordered:	09/24/2019	Fetal Fraction:	7%
Date Collected:	09/24/2019	Gestational Age ≥ 9w:	Yes
Date Received:	09/24/2019	External Accession:	
Order ID:	xxx1234567	Referral Clinician:	
Patient ID:	1234567890	Date Reported:	**01/10/2020 01:22 PM PT**

Test Result

Positive
Trisomy 21

Lab Director Comments
This specimen showed an increased amount of chromosome 21 material (trisomy 21), such as may be found in pregnancies with Down syndrome.

Result Table

Content	Result
FETAL SEX	Consistent with Male
AUTOSOMAL ANEUPLOIDIES	
Trisomy 21 (Down syndrome)	Positive T21 PPV*: 96.4%
Trisomy 18 (Edwards syndrome)	Negative
Trisomy 13 (Patau syndrome)	Negative

Positive Predictive Value

* Positive Predictive Value (PPV) estimates the probability that a pregnancy with a positive test result is in fact an affected pregnancy. The PPV for this patient was calculated only using maternal age and gestational age[1], test performance[2] and the standard PPV formula.

For a more accurate and individualized PPV calculation, include additional clinical information from the patient's clinical history (which may include serum screen results, personal/family history, ultrasound findings, etc.), and refer to the table below.

A Priori Risk (1:X)	10	20	30	40	50	100	200	300	400	500	1000	1500	2000	2500	3000	5000
PPV (%) TRISOMY 21	99.1	98.1	97.2	96.2	95.3	90.9	83.3	76.8	71.3	66.5	49.8	39.8	33.1	28.4	24.8	16.5

Ex. 42 at 3 (https://www.integratedgenetics.com/sites/default/files/2020-04/rep-1355-v1-0320_MT21%20Sample%20report%20booklet.pdf) (showing the use of the MaterniT21 PLUS test to determine the fetal fraction and amount of chromosome 21 in a blood sample) (annotation added); *see also, e.g.*, https://www.integratedgenetics.com/videos (displaying video entitled "Understanding your MaterniT results) at 0:33-0:52 ("MaterniT is a non-invasive prenatal test, also known as NIPT or cell-free DNA testing, which looks at DNA that can be found in the mother's bloodstream that usually represents the baby's chromosomes. The test determines the chance that a pregnancy is affected with certain chromosome disorders"); https://www.youtube.com/watch?v=fpEnZJmqF20 (displaying video entitled "MaterniT® 21 PLUS Noninvasive Prenatal Test") at 1:06-1:21 ("The MaterniT 21 PLUS Test analyzes placental

DNA fragments circulating in your bloodstream. It can tell you if you're having a boy or a girl and screen for chromosomal abnormalities such as trisomy 21, which is associated with Down Syndome."); Ex. 38 (https://sema4.com/products/test-catalog/noninvasive-prenatal-testing-nipt-sequenom/#) ("Sequenom noninvasive prenatal testing (NIPT) is a chromosome counting method that analyzes genetic information in fetal cell-free DNA in maternal blood to determine risk for specific fetal chromosomal and subchromosomal abnormalities."); Ex. 43 at 4 (C.K. Ellison et. al., *Using Targeted Sequencing of Paralogous Sequences for Noninvasive Detection of Selected Fetal Aneuploidies*, 62 CLINICAL CHEMISTRY 1621-29 (2016), https://academic.oup.com/clinchem/article/62/12/1621/5612069) ("Fetal fraction estimates for each sample were compared to data from the MaterniT21 PLUS laboratory developed test (LDT), which uses a distinct method based on genome-wide sequencing coverage for fetal fraction estimation."); Ex. 42 at 3 (https://www.integratedgenetics.com/sites/default/files/2020-04/rep-1355-v1-0320_MT21%20Sample%20report%20booklet.pdf) ("The MaterniT® 21 PLUS laboratory-developed test (LDT) analyzes circulating cell-free DNA from a maternal blood sample. The test is indicated for use in pregnant women with increased risk for fetal chromosomal aneuploidy"); Ex. 44 at 2 (B. Dyr et al., *A New Era in Aneuploidy Screening: cfDNA Testing in >30,000 Multifetal Gestations: Experience at One Clinical Laboratory*, 14 PLOS ONE (2019), https://doi.org/10.1371/journal.pone.0220979) ("This study [of MaterniT21 PLUS samples] analyzed extracted cfDNA fragments from maternal plasma, which were then subjected to genome-wide sequencing and algorithmic analysis for chromosomal aneuploidies and subchromosomal under-representation in specified regions, when requested. Both fetal (placental) and maternal fragments were sequenced and mapped to unique regions of the genome. The unique reads were assigned to a 50 kb bin, normalized across the genome, and counted. An under- or over-

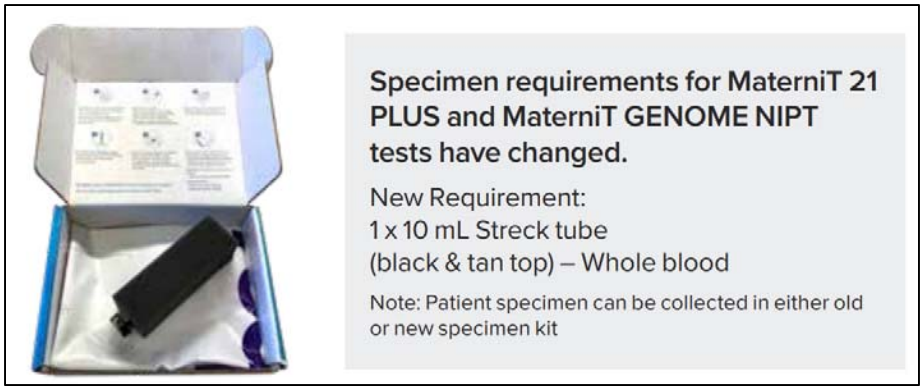
representation of fragments in a 50 kb bin are indicative of a loss or gain in the genome profile respectively."); Ex. 45 (S. Caldwell et. al., *MaterniT® 21 PLUS Performance in Lower Fetal Fraction Samples*, LABCORP (2019), https://files.labcorp.com/labcorp-d8/rep_1315_Caldwell_0.pdf) ("Maternal blood samples submitted to Sequenom Laboratories for MaterniT® 21 PLUS testing were subjected to DNA extraction, library preparation, and genome-wide massively parallel sequencing as described by **Jensen et al**. Fetal fraction calculation is described in **Kim et. al**."); Ex. 46 at 2-3 (T.J. Jensen et. al., *High-Throughput Massively Parallel Sequencing for Fetal Aneuploidy Detection from Maternal Plasma*, 8 PLOS ONE (2013), https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0057381) (describing the protocol used by Sequenom to analyze MaterniT21 PLUS samples, including extracting "ccfDNA [] from maternal plasma using the QIAamp Circulating Nucleic Acid Kit (Qiagen)," preparing "sequencing libraries," performing massively parallel sequencing using an "Illumina HiSeq2000 sequence," and comparing the output files from the HiSeq2000 to a baseline to "calculate the fraction of aligned reads derived from each chromosome"); Ex. 47 at 1-2 (S.K. Kim et. al., *Determination of Fetal DNA Fraction from the Plasma of Pregnant Women Using Sequence Read Counts*, 35 PRENATAL DIAGNOSIS 810-15 (2015)) (describing the SeqFF method for determining fetal fraction by comparing "the fragment length dissimilarities between maternal and fetal ccfDNA" in "a large cohort of well-characterized samples" to "infer discrete regions in the genome to be overrepresented in fetal DNA" and then "quantify[ing] the proportion of fetal ccfDNA in plasma" in those regions); *see generally* Ex. 48 (https://www.integratedgenetics.com/providers/tests/prenatal/nipt/maternit21plus).)

2. The Accused MaterniT Genome Test

49. The MaterniT Genome test is a commercial non-invasive prenatal test for detecting fetal genetic abnormalities from a maternal blood sample. (*See* Ex. 34 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) ("[The Materni GENOME test] is the first noninvasive prenatal test (NIPT) to provide karyotype-level insight into fetal chromosomal status prior to considering an invasive procedure.").)

50. Performance of the MaterniT Genome test involves extracting cell-free DNA from maternal blood. (Ex. 38 (https://sema4.com/products/test-catalog/noninvasive-prenatal-testing-nipt-sequenom/#) ("Sequenom noninvasive prenatal testing (NIPT) is a chromosome counting method that analyzes genetic information in fetal cell-free DNA in maternal blood."); *see also* Ex. 36 at 3 (https://www.integratedgenetics.com/sites/default/files/2020-04/GENOME_Positive%20T18_Sample%20Report.pdf) (sample MaterniT Genome report stating that the test "analyzes the relative amount of chromosomal material across the genome in circulating cell-free DNA from a maternal sample").)

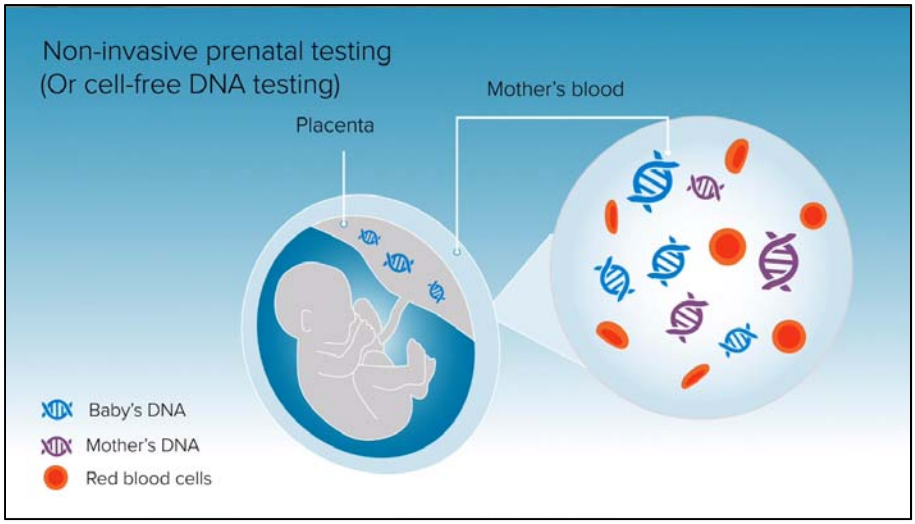
51. The MaterniT Genome test require a sample containing an agent that inhibits cell lysis. For example, LabCorp lists as a requirement for the MaterniT Genome test "[o]ne 10 mL BCT Streck tube" for collecting a whole blood specimen from the patient (mother). (Ex. 38 (https://sema4.com/products/test-catalog/noninvasive-prenatal-testing-nipt-sequenom/#).)



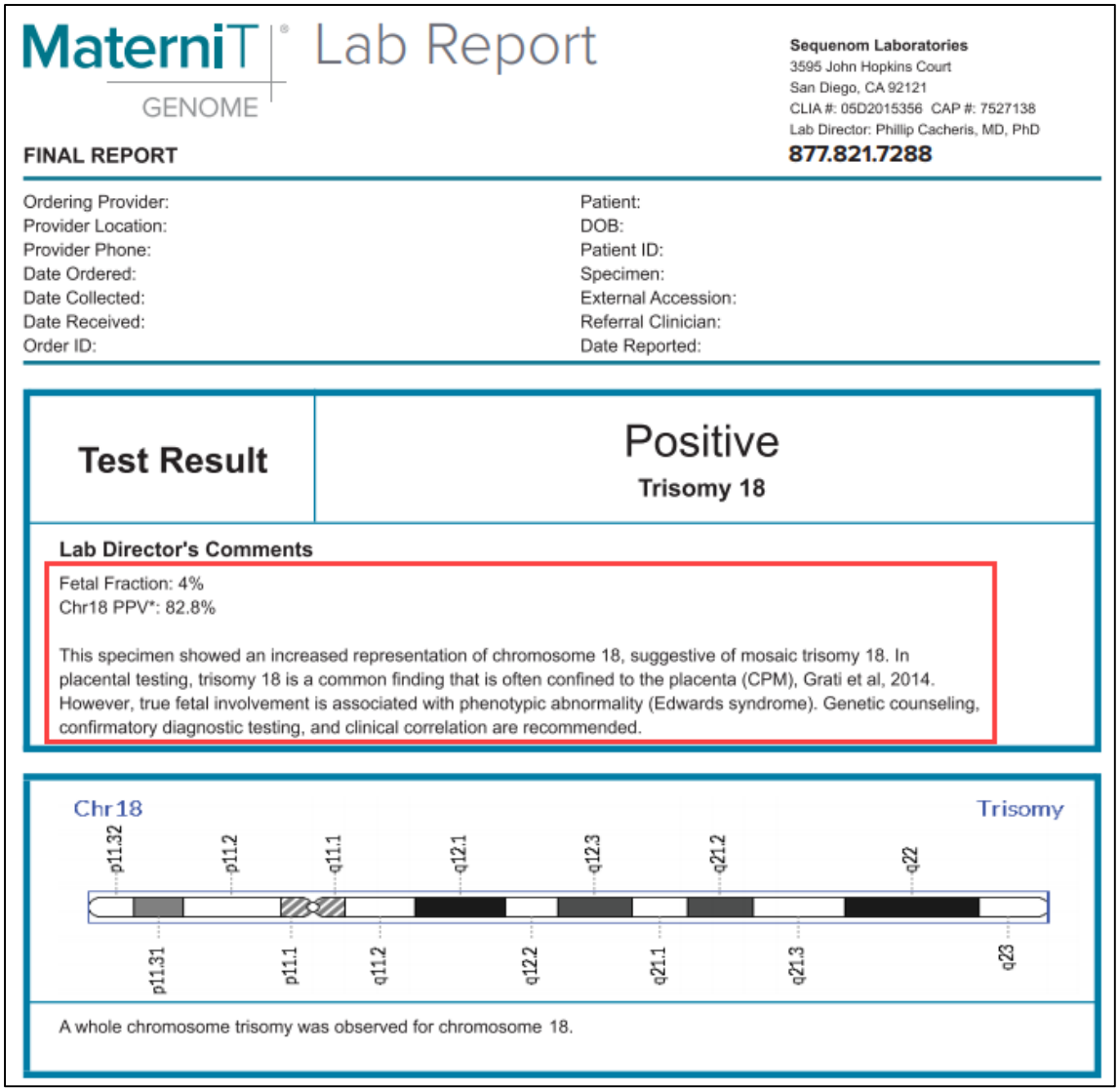
(Ex. 40 ("New MateriT Specimen Collection Kit," https://www.integratedgenetics.com/sites/default/files/2020-04/MateriT_Kit_Flyer_rep-1356-v1-0619.pdf).)

52. As described above, samples collected in Streck Cell-Free DNA BCT tubes, including MateriT Genome blood samples, contain an agent that inhibits cell lysis. (*See* Ex. 41 at 2) (https://www.streck.com/products/stabilization/cell-free-dna-bct/#resources).)

53. Processing the MateriT Genome test involves isolating cell-free DNA from a sample of maternal blood collected in a Streck Cell-Free DNA BCT and analyzing the cell-free DNA to detect chromosomal abnormalities as shown below:



(https://www.integratedgenetics.com/videos (displaying video entitled "Understanding your MaterniT results") at 0:50).)



MaterniT® GENOME Lab Report

Sequenom Laboratories
3595 John Hopkins Court
San Diego, CA 92121
CLIA #: 05D2015356 CAP #: 7527138
Lab Director: Phillip Cacheris, MD, PhD
877.821.7288

FINAL REPORT

Ordering Provider:	Patient:
Provider Location:	DOB:
Provider Phone:	Patient ID:
Date Ordered:	Specimen:
Date Collected:	External Accession:
Date Received:	Referral Clinician:
Order ID:	Date Reported:

Test Result	**Positive** **Trisomy 18**

Lab Director's Comments

Fetal Fraction: 4%
Chr18 PPV*: 82.8%

This specimen showed an increased representation of chromosome 18, suggestive of mosaic trisomy 18. In placental testing, trisomy 18 is a common finding that is often confined to the placenta (CPM), Grati et al, 2014. However, true fetal involvement is associated with phenotypic abnormality (Edwards syndrome). Genetic counseling, confirmatory diagnostic testing, and clinical correlation are recommended.

Chr 18 Trisomy

p11.32 p11.2 q11.1 q12.1 q12.3 q21.2 q22
p11.31 p11.1 q11.2 q12.2 q21.1 q21.3 q23

A whole chromosome trisomy was observed for chromosome 18.

Positive Predictive Value

* Positive Predictive Value (PPV) estimates the probability that a pregnancy with a positive test result is in fact an affected pregnancy. The PPV for this patient was calculated only using maternal age and gestational age[7], test performance[3] and the standard PPV formula.

For a more accurate and individualized PPV calculation, include additional clinical information from the patient's clinical history (which may include serum screen results, personal/family history, ultrasound findings, etc.), and refer to the table below.

***A Priori* Risk (1:X)**	10	20	30	40	50	100	200	300	400	500	1000	1500	2000	2500	3000	5000
PPV (%) TRISOMY 18	96.5	92.9	89.6	86.5	83.6	71.6	55.7	45.5	38.5	33.4	20.0	14.3	11.1	9.1	7.7	4.8

(Ex. 36 at 1-2 (https://www.integratedgenetics.com/sites/default/files/2020-04/GENOME_Positive%20T18_Sample%20Report.pdf) (showing the use of the MaterniT Genome test to determine the fetal fraction and amount of chromosome 18 in a blood sample)

(annotation added); *see also, e.g.*, https://www.integratedgenetics.com/videos (displaying video entitled "Understanding your MaterniT results") at 0:33-0:52 ("MaterniT is a non-invasive prenatal test, also known as NIPT or cell-free DNA testing, which looks at DNA that can be found in the mother's bloodstream that usually represents the baby's chromosomes. The test determines the chance that a pregnancy is affected with certain chromosome disorders"); Ex. 38 (https://sema4.com/products/test-catalog/noninvasive-prenatal-testing-nipt-sequenom/#) ("Sequenom noninvasive prenatal testing (NIPT) is a chromosome counting method that analyzes genetic information in fetal cell-free DNA in maternal blood to determine risk for specific fetal chromosomal and subchromosomal abnormalities."); Ex. 49 at 2 (M. Ehrich, *Genome-Wide cfDNA Screening: Clinical Laboratory Experience with the First 10,000 Cases*, 19 GENETICS IN MEDICINE 1332-37 (2017) (https://www.nature.com/articles/gim201756) (explaining that during the MaterniT Genome laboratory processing, "cfDNA was extracted from plasma … Plasma DNA was used to create indexed sequencing libraries as described by **Tynan et al**. Sequencing libraries were multiplexed, clustered, and sequenced on HiSeq 2000 or HiSeq 2500 instruments (Illumina, San Diego, CA), as described by Lefkowitz et al. Sequencing results were normalized and analyzed for fetal fraction; chromosome 21, 18, and 13 trisomy; sex chromosome aneuploidies; and other genome-wide whole-chromosome and subchromosome copy-number variants, using bioinformatics algorithms as previously described."); Ex. 50 at 2-3 (J.A. Tynan et. al., *Application of Risk Score Analysis to Low-Coverage Whole Genome Sequencing Data for the Noninvasive Detection of Trisomy 21, Trisomy 18, and Trisomy 13*, 36 PRENATAL DIAGNOSIS 56-62 (2016)) (explaining that sample processing includes extracting ccfDNA "from 4 mL of maternal plasma using [Qiagen]," preparing sequencing libraries using "[f]orty microliters of extracted ccf DNA," "multiplex[ing] and sequenc[ing] [the libraries] on either the HiSeq 2000 or HiSeq 2500," and

aligning the sequencing reads to a baseline, and further explaining that "[f]etal fraction was determined from sequencing reads as described by **Kim et. al.**"); Ex. 47 at 1-2 (S.K. Kim et. al., *Determination of Fetal DNA Fraction from the Plasma of Pregnant Women Using Sequence Read Counts*, 35 PRENATAL DIAGNOSIS 810-15 (2015)) (describing the SeqFF method for determining fetal fraction by comparing "the fragment length dissimilarities between maternal and fetal ccfDNA" in "a large cohort of well-characterized samples" to "infer discrete regions in the genome to be overrepresented in fetal DNA" and then "quantify[ing] the proportion of fetal ccfDNA in plasma" in those regions); Ex. 36 at 3 (https://www.integratedgenetics.com/sites/default/files/2020-04/GENOME_Positive%20T18_Sample%20Report.pdf) ("The MaterniT GENOME laboratory-developed test analyzes the relative amount of chromosomal material across the genome in circulating cell-free DNA from a maternal sample. The test is indicated for use in pregnant women with singleton pregnancies at risk of fetal chromosomal and/or subchromosomal abnormalities… Circulating cell-free DNA was purified from the plasma component of anti-coagulated maternal whole blood… **The MaterniT™ GENOME test utilizes the same proprietary technology as the MaterniT21® PLUS test,** with deeper sequencing."); *see generally* Ex. 51 (https://www.integratedgenetics.com/providers/tests/prenatal/nipt/maternitgenome).)

3. LabCorp's Infringing Activities Relating To The Accused MaterniT Tests

54. LabCorp offers to sell and sells the MaterniT tests on its website and at its patient collection centers, including several patient collection centers in this District (such as at 6603 First Park Ten Blvd, San Antonio, TX 78213). (*See* Ex. 5 (https://www.labcorp.com/node/107); *see also* Ex. 13 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. 14 (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); Ex. 15 (https://www.dnatestingcenters.com/centers/texas/san-antonio/labcorp-first-park-ten-blvd/) (including as services offered at the LabCorp facility located at 6603 First Park Ten Blvd, San Antonio, TX "DNA Tests" and "Blood Work").)

55. On information and belief, LabCorp's offers for sale and sales of the MaterniT tests comprise the obligation to perform 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 MaterniT tests, 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 tests. (*See* Ex. 13 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. 52 at 5 (https://www.integratedgenetics.com/sites/default/files/2020-04/rep-1038-v4-1019.pdf) ("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. 14 (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).)

56. On information and belief, employees or other agents of LabCorp (*e.g.*, LabCorp's lab assistants) collect test samples according to the MaterniT 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. 40 ("New MaterniT Specimen Collection Kit," https://www.integratedgenetics.com/sites/default/files/2020-04/MaterniT_Kit_Flyer_rep-1356-v1-0619.pdf).) On information and belief, the published instructions are a part of the MaterniT21 PLUS test and MaterniT Genome test protocols, and LabCorp directs its employees and other agents to follow the MaterniT21 PLUS test and MaterniT Genome test protocols.

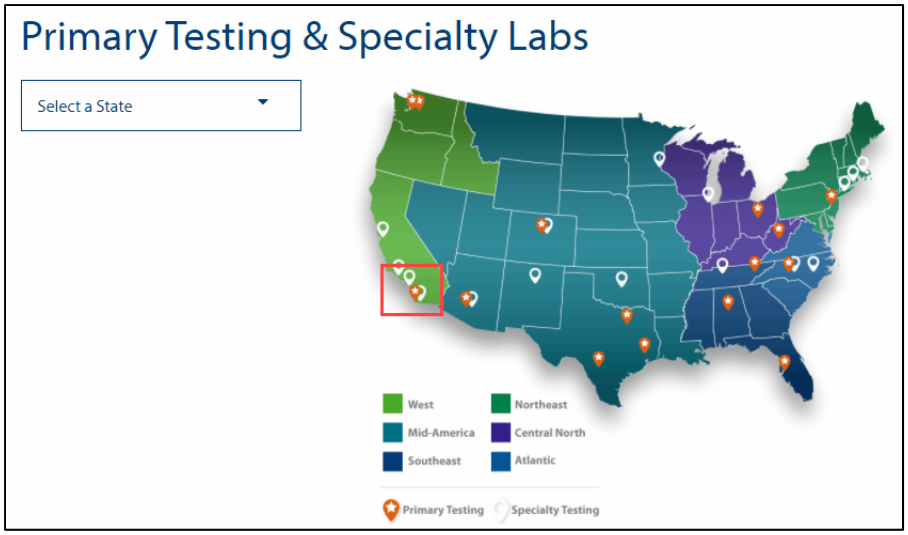
57. LabCorp, either itself or through its wholly-owned subsidiary Sequenom, processes the MaterniT21 PLUS and MaterniT Genome test samples at its subsidiary laboratory, Sequenom Center for Molecular Medicine, LLC d/b/a Sequenom Laboratories ("Sequenom Center"). (*See* Ex. 13 at 6 (https://www.labcorp.com/assets/13731) (listing Sequenom Center as the laboratory for the MaterniT21 PLUS test and describing it as a "(CLIA)-certified molecular diagnostics laboratory"); Ex. 52 at 1 (https://www.integratedgenetics.com/sites/default/files/2020-04/rep-1038-v4-1019.pdf) (listing Sequenom Center as the laboratory for the MaterniT Genome test and describing it as a "(CLIA)-certified molecular diagnostics laboratory"); Ex. 53 at 7 (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.").) On information and belief, LabCorp, either itself or through its wholly-owned subsidiary Sequenom, instructs Sequenom Center to process the collected samples in accordance with the established MaterniT21 and MaterniT Genome test protocols. (*See, e.g.*, Ex. 54 at 8 (*Verinata Health, Inc. v. Sequenom, Inc.*, Case No. 4:12-cv-00865-SI (N.D. Cal. July 16, 2012), Dkt. No. 38) ("Sequenom admits that

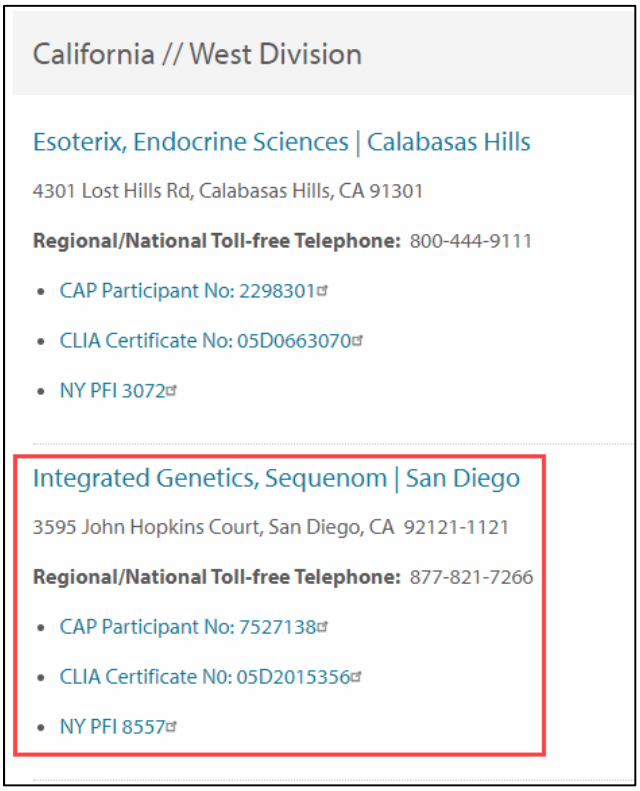
it has encouraged and continues to encourage the Sequenom Center for Molecular Medicine, LLC to perform the MaterniT21™ and MaterniT21™ PLUS tests.").) On information and belief, LabCorp conditions participation in an activity or receipt of a benefit (such as continued funding, status as LabCorp's laboratory, and payments related to discrete tests performed) on Sequenom Center's processing of the MaterniT test samples.

58. On information and belief, Sequenom Center operates as LabCorp's laboratory and carries out LabCorp's business, and LabCorp authorizes the Sequenom Center to act on its behalf. For example, through Sequenom Center, LabCorp develops and processes several of its diagnostic tests, including the MaterniT21 PLUS and MaterniT Genome tests. (*See id.*; Ex. 55 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. 52 at 1 (https://www.integratedgenetics.com/sites/default/files/2020-04/rep-1038-v4-1019.pdf) (same).) Further, LabCorp's public statements, such as the portions quoted above, show that LabCorp consents for Sequenom Center 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. 56 at 2 (https://www.labcorp.com/about-us/primary-testing-specialty-labs) (representing Sequenom Center as one of LabCorp's laboratories under its Integrated Genetics Specialty Testing Group); Ex. 57 (https://www.integratedgenetics.com/about/labs-and-offices) (identifying Sequenom Center's laboratory as one of LabCorp's Integrated Genetics Specialty Testing Group laboratories).)

59. LabCorp's SEC filings demonstrate that both Sequenom and Sequenom Center are both wholly-owned subsidiaries of LabCorp. (*See, e.g.*, Ex. 3 at 153 (Laboratory Corporation of America Holdings' Form 10-K For Fiscal Year 2019) (listing "Sequenom, Inc." and "Sequenom Center for Molecular Medicine, LLC" as subsidiaries of LabCorp); *see also* Ex. 13 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. 55 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 Sequenom Center, and that LabCorp has the right and the ability to direct and control the activities of the Sequenom Center. (*E.g.*, Ex. 3 at 153 (Laboratory Corporation of America Holdings' Form 10-K For Fiscal Year 2019); Ex. 58 at 129 (Laboratory Corporation of America Holdings' Form 10-K For Fiscal Year 2016); Ex. 37 ("*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).)

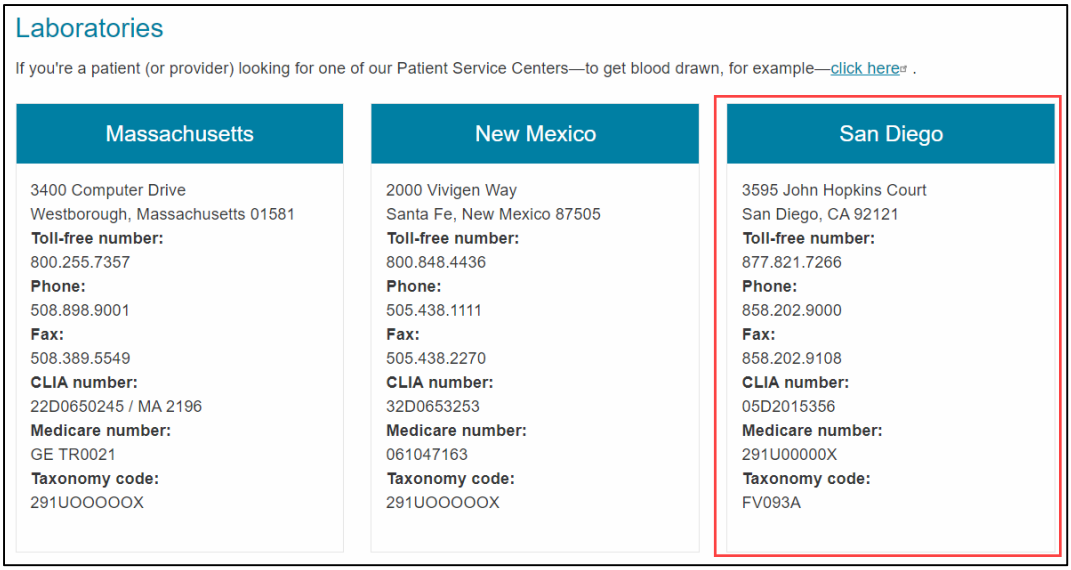
60. On its website, LabCorp identifies the Sequenom and Sequenom Center office as one of its California/West Division "Primary Testing and Specialty Labs":





(Ex. 56 (https://www.labcorp.com/about-us/primary-testing-specialty-labs) (annotation added).)

61. Additionally, on LabCorp's Integrated Genetics Website, LabCorp identifies the address of Sequenom and Sequenom Center as one of its laboratories:



Laboratories

If you're a patient (or provider) looking for one of our Patient Service Centers—to get blood drawn, for example—click here .

Massachusetts	New Mexico	San Diego
3400 Computer Drive Westborough, Massachusetts 01581 **Toll-free number:** 800.255.7357 **Phone:** 508.898.9001 **Fax:** 508.389.5549 **CLIA number:** 22D0650245 / MA 2196 **Medicare number:** GE TR0021 **Taxonomy code:** 291UOOOOOX	2000 Vivigen Way Santa Fe, New Mexico 87505 **Toll-free number:** 800.848.4436 **Phone:** 505.438.1111 **Fax:** 505.438.2270 **CLIA number:** 32D0653253 **Medicare number:** 061047163 **Taxonomy code:** 291UOOOOOX	3595 John Hopkins Court San Diego, CA 92121 **Toll-free number:** 877.821.7266 **Phone:** 858.202.9000 **Fax:** 858.202.9108 **CLIA number:** 05D2015356 **Medicare number:** 291U00000X **Taxonomy code:** FV093A

(Ex. 57 (https://www.integratedgenetics.com/about/labs-and-offices) (annotation added).)

62. Additionally, LabCorp represents in its brochures that LabCorp directs and controls the diagnostic test development and processing of Sequenom Center, either directly or through Sequenom, such that Sequenom Center is LabCorp's laboratory, and the three operate as one integrated business. For example, LabCorp brochures for the MaterniT tests represent Sequenom Center as the laboratory that developed and processes the tests. (*E.g.*, Ex. 13 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. 55 at 1 (https://files.labcorp.com/labcorp-d8/2020-04/rep-1036-v7-1119.pdf) (same); Ex. 52 at 1 (https://www.integratedgenetics.com/sites/default/files/2020-04/rep-1038-v4-1019.pdf) (same).)

63. Furthermore, LabCorp hosts advertisements for job postings at Sequenom. (*See, e.g.*, Ex. 59 (Lead Technician Job Posting) (https://jobs.labcorp.com/job/san-diego/lead-technician-molecular-sequenom/668/1050009600) (including as part of the description for the "Lead Technician – Molecular (***Sequenom***)" posting "Lab Corp is seeking a Lead Technician to

join ***our*** team in San Diego, Ca"); Ex. 60 (Medical Technologist Job Posting) (https://jobs.labcorp.com/job/san-diego/medical-technologist-clinical-laboratory-scientist-sequenom/668/626838688) (including as part of the description for the "Medical Technologist/Clinical Laboratory Scientist – ***Sequenom***" posting "LabCorp wants to speak with you about exciting opportunities to join ***our*** team in San Diego, CA" and "[t]he role focuses primarily on COVID-19 PCR testing in the Molecular department of ***our*** Clinical Laboratory"); Ex. 61 (Lab Assistant Job Posting) (https://jobs.labcorp.com/job/san-diego/lab-assistant-molecular-sequenom/668/886369536) (including as part of the description for the "Lab Assistant – Molecular (***Sequenom***)" posting "LabCorp is seeking a Lab Assistant to join ***our*** team in San Diego, CA").)

64. The officers of Sequenom Center are also officers of LabCorp. For example, Sandra D. van der Vaart is LabCorp's Executive Vice President, Chief Legal Officer, Chief Compliance Officer, and Corporate Secretary. (Ex. 62 (https://ir.labcorp.com/corporate-governance/management).) Sandra D. van der Vaart is also Sequenom Center's Manager and the signatory on its annual statement filed with the Michigan Department of Licensing and Regulatory Affairs. (Ex. 63 (Michigan Department of Licensing and Regulatory Affairs 2020 Annual Statement for Sequenom Center for Molecular Medicine, LLC).) On information and belief, Ms. van der Vaart is an employee and/or officer of LabCorp, whose leadership position at Sequenom Center further enables LabCorp to exercise direction and control over the activities of its fully owned subsidiary, Sequenom Center.

B. <u>The Accused informaSeq Test</u>

65. On August 19, 2014, LabCorp launched the informaSeq test, a commercial non-invasive prenatal test for detecting fetal genetic abnormalities from a maternal blood sample. (*See*

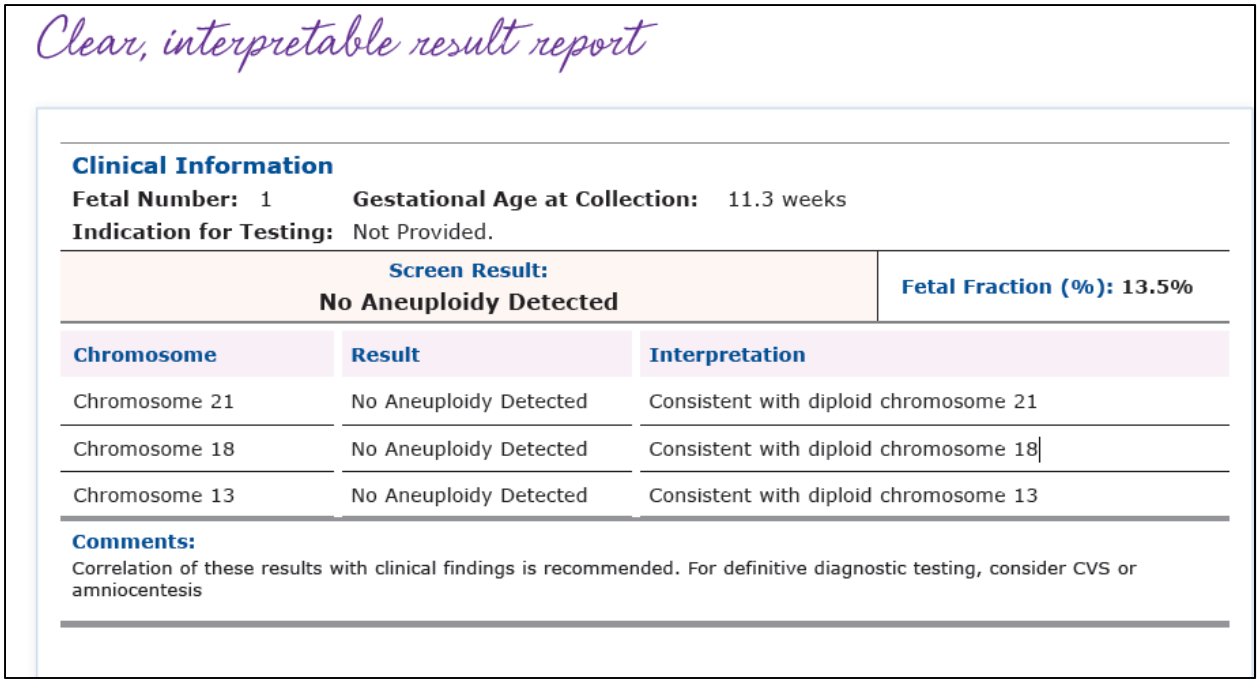
Ex. 64 at 1 (Press Release, "*LabCorp Announces the Availability of InformaSeq*^{SM} *Non-Invasive Prenatal Test*" (August 19, 2014), https://ir.labcorp.com/news-releases/news-release-details/labcorp-announces-availability-informaseqsm-non-invasive) ("Laboratory Corporation of America® Holdings (LabCorp®) (NYSE: LH) announced today [August 19, 2014] the availability of the informaSeq Prenatal Test.").)

66. Performance of the informaSeq test involves extracting cell-free DNA from maternal blood. (*See id.* ("The informaSeq Prenatal Test is an advanced, non-invasive, next-generation prenatal screening assay that can assess risk for multiple fetal chromosomal aneuploidies, or abnormalities in the number of chromosomes, from a single maternal blood draw.").)

67. The informaSeq test requires a sample containing an agent that inhibits cell lysis. For example, LabCorp instructs that the blood sample for the informsaSeq test be collected in "[o]ne Streck tube, minimum 7 mL." (Ex. 20 at 3 (https://www.labcorp.com/tests/related-documents/L13272).)

68. As described above, samples collected in Streck Cell-Free DNA BCT tubes, including informaSeq blood samples, contain an agent that inhibits cell lysis. (*See* Ex. 41 at 2 (https://www.streck.com/products/stabilization/cell-free-dna-bct/#resources).)

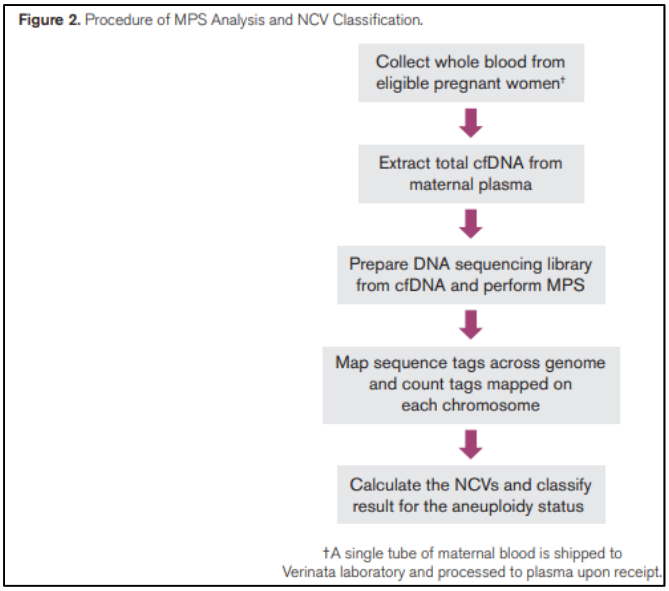
69. Processing the informaSeq test involves isolating cell-free DNA from a sample of maternal blood collected in a Streck Cell-Free DNA BCT and analyzing the cell-free DNA to detect chromosomal abnormalities:



(Ex. 20 at 5 (https://www.labcorp.com/tests/related-documents/L13272) (showing the use of the informaSeq test to determine the fetal fraction and any aneuploidy in a blood sample); *see also, e.g., id.* at 2 ("Provide your patients with a precise, non-invasive test that can assess risk for multiple fetal chromosomal aneuploidies from a single blood draw."); *id.* at 8 ("Testing performed via deep sequencing, which increases detection, even in samples with a lower fraction of fetal DNA fragments); Ex. 64 at 1 (Press Release, "*LabCorp Announces the Availability of InformaSeq*^{SM} *Non-Invasive Prenatal Test*" (August 19, 2014), https://ir.labcorp.com/news-releases/news-release-details/labcorp-announces-availability-informaseqsm-non-invasive ("The informaSeq Prenatal Test is an advanced, non-invasive, next-generation prenatal screening assay that can assess risk for multiple fetal chromosomal aneuploidies, or abnormalities in the number of chromosomes, from a single maternal blood draw."); Ex. 65 (C.D. Eversley et. al., *Clinical Performance of informaSeq Non-Invasive Prenatal Screening*, LABCORP (2016), https://www.integratedgenetics.com/sites/default/files/ACMG%20Poster%202016%20Final_3.6.

16.pdf) (explaining that the informaSeq test uses "a laboratory developed assay utilizing massively parallel sequencing").)

70. On information and belief, the informaSeq test uses "massively parallel sequencing (MPS) of total cell free DNA (cfDNA) extracted from maternal plasma … to detect fetal chromosome aneuploidies" and "a [calculated] Normalized Chromosome Value (NCV) … [to] remove[] variation within and between sequencing runs…." (Ex. 66 at 1 (*Analytical Validation of the verifi® Prenatal Test; Enhanced Test Performance for Detecting Trisomies 21, 18, 13 and the Option for Classification of Sex Chromosome Status*, VERINATA HEALTH (2012), https://www.prenatalsafe.it/pdf/bibliografia/10_verifi_white_paper_Letter-Size_11-16-2012.pdf)); *see also* Ex. 20 at 4-5 (https://www.labcorp.com/tests/related-documents/L13272) (LabCorp brochure for informaSeq test citing to "Verinata Health, Inc. (2012) analytical validation of the verifi® Prenatal Test; Enhanced Test Performance for Detecting Trisomies 21, 18, 13 and the Option for Classification of Sex Chromosome Status" to explain the testing performance of the informaSeq test).) The "MPS [is] performed on the Illumina Hi-Seq 2000 instrument" and "[s]equence tags from MPS were mapped to the human genome and NCVs were calculated for chromosomes 21, 18, 13, X, and Y." (Ex. 66 at 3.) The procedure is summarized in the following chart:



(*id.* at 2.)

71. LabCorp offers to sell and sells the informaSeq test on its website and at its patient collection centers, including several patient collection centers in this District (such as at 6603 First Park Ten Blvd, San Antonio, TX 78213). (*See* Ex. 5 (https://www.labcorp.com/node/107); *see also* Ex. 14 (https://www.labcorp.com/assets/5886) (showing an example clinical questionnaire for noninvasive prenatal testing allowing a provider to request tests. including the informaSeq test); Ex. 15 (https://www.dnatestingcenters.com/centers/texas/san-antonio/labcorp-first-park-ten-blvd/) (including as services offered at the LabCorp facility located at 6603 First Park Ten Blvd, San Antonio, TX "DNA Tests" and "Blood Work").) On information and belief, LabCorp's offers for sale and sales of the informaSeq test comprise the obligation to perform 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 the informaSeq test, LabCorp accepts the obligation, directly or through one or more subsidiaries and/or intermediaries, to perform a test pursuant to the informaSeq test protocol for the patient's sample(s). At these centers, LabCorp collects test samples from patients, including pregnant women, for the informaSeq test. (*See* Ex. 14

(https://www.labcorp.com/assets/5886) (showing an example clinical questionnaire for noninvasive prenatal testing allowing a provider to request tests, including the informaSeq test).) On information and belief, employees or other agents of LabCorp (*e.g.*, LabCorp's lab assistants) collect test samples according to the informaSeq test protocol.

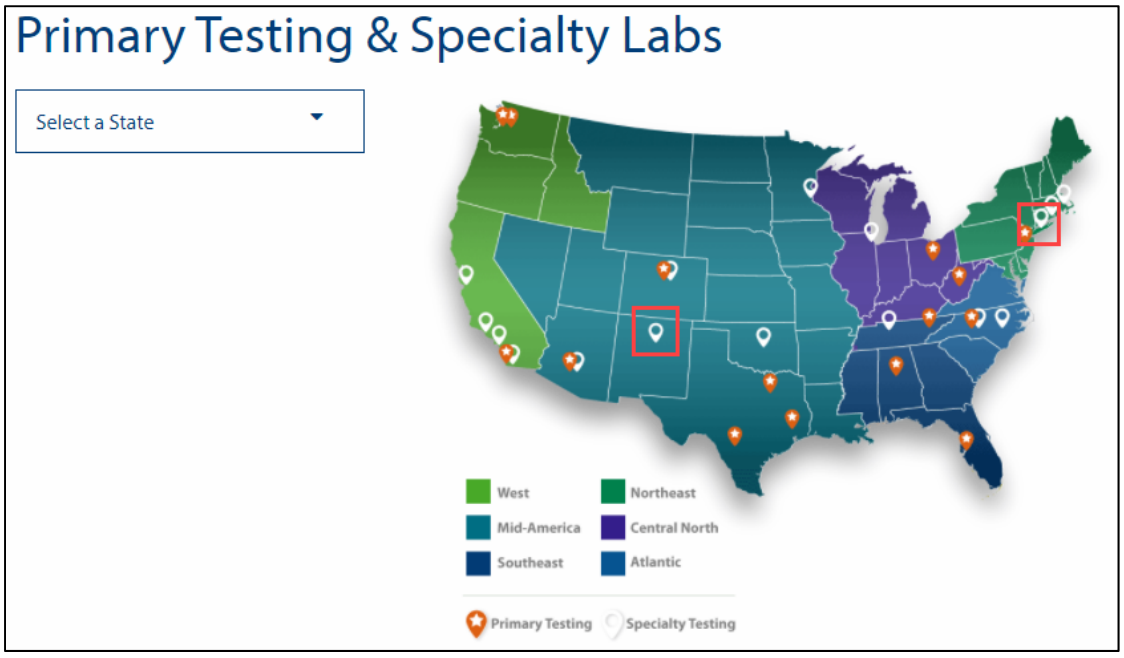
72. On information and belief, LabCorp publishes and follows instructions for collecting and transporting informaSeq test samples. (*See, e.g.* Ex. 20 at 3 (https://www.labcorp.com/tests/related-documents/L13272) (explaining that requirements of the test include "[u]s[ing] only the black and tan capped blood collection tube from the informaSeq kit," which is "[o]ne Streck tube, minimum 7 mL" and "[s]tor[ing] samples at room temperature and transport at ambient temperature in the informaSeq kit").) On information and belief, the published instructions are a part of the informaSeq test protocol, and LabCorp direct its employees and other agents to follow the informaSeq test protocol.

73. LabCorp processes the informaSeq test samples at its Integrated Genetics laboratories, one of LabCorp's Specialty Testing Groups. (*See, e.g.*, Ex. 20 at 8 (https://www.labcorp.com/tests/related-documents/L13272) (showing that the informaSeq test is provided and performed by Integrated Genetics); Ex. 67 (https://www.healthlabtesting.com/Test%20Directory/Test%20Directory%20Item.aspx?itemGuid=ed610c85-4355-40b5-b705-3eb5e3aef0dc) (listing LabCorp as the "Performing Lab"); *see also* Ex. 20 at 1, 8 (https://www.labcorp.com/tests/related-documents/L13272) (including on the informaSeq test brochure "Integrated Genetics LabCorp Specialty Testing Group").) On information and belief, Integrated Genetics laboratories operate as LabCorp's laboratories and carries out LabCorp's business. Through the Integrated Genetics laboratories, LabCorp develops and processes several of its diagnostic tests, including the informaSeq test. On information and

belief, LabCorp instructs the Integrated Genetics laboratories to process the collected samples in accordance with the established informaSeq test protocol.

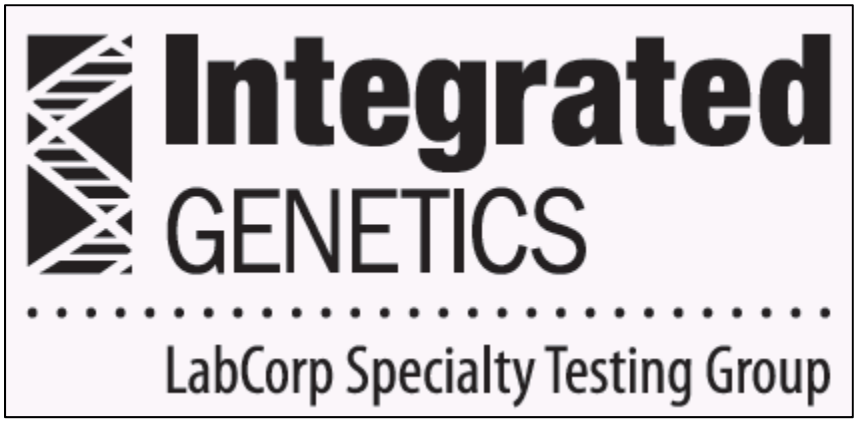
74. LabCorp's website demonstrate that the Integrated Genetics laboratories operate as LabCorp's laboratory, and that LabCorp authorizes the Integrated Genetics laboratories to act on its behalf. For example, LabCorp describes Integrated Genetics as one of LabCorp's specialized laboratories and "a premier reproductive genetics laboratory with an expansive menu of complex tests. Integrated Genetics' testing spans the continuum of care, ranging from maternal serum screening and prenatal diagnostics to carrier screening and postnatal testing services." (Ex. 68 at 2 (https://www.labcorp.com/about-us/our-businesses).)

75. As another example, LabCorp identifies the Integrated Genetics laboratories (located in Santa Fe, New Mexico and Westborough, Massachusetts) as two of its "Primary Testing & Specialty Labs":



(Ex. 56 (https://www.labcorp.com/about-us/primary-testing-specialty-labs) (annotation added).)

76. Additionally, in its marketing materials, LabCorp identifies Integrated Genetics as a "LabCorp Specialty Testing Group."



(Ex. 20 at 1 (https://www.labcorp.com/tests/related-documents/L13272).)

77. Additionally, LabCorp represents in its press releases that LabCorp directs and controls the diagnostic test development and processing of the Integrated Genetics laboratories, such that the Integrated Genetics laboratories are LabCorp's laboratories, and the laboratories and LabCorp operate as one integrated business. For example, press releases related to the launch of the informaSeq test represent that LabCorp developed the test, but it will be "offered through Integrated Genetics, part of the LabCorp Specialty Testing Group of laboratories." (Ex. 64 at 1 (Press Release, "*LabCorp Announces the Availability of InformaSeq℠ Non-Invasive Prenatal Test*" (August 19, 2014), https://ir.labcorp.com/news-releases/news-release-details/labcorp-announces-availability-informaseqsm-non-invasive).)

C. The Accused Resolution ctDx Lung Assay Test

78. On February 24, 2020, Resolution Bioscience, Inc. ("Resolution Bioscience") and LabCorp announced an agreement "to make the Resolution ctDx Lung assay available to clinicians and patients." (Ex. 69 at 1 (Press Release, "*Resolution Bioscience and LabCorp Will Collaborate to Commercialize the Resolution ctDx Lung™ Liquid Biopsy Assay*" (February 24, 2020),

http://www.resolutionbio.com/company/press/2020.02.24_resolution_ctdx_lung_lca.html).) The Resolution ctDx Lung Assay test is used "to detect actionable mutations in non-small cell lung cancer genes" and is analyzed using a "cell-free DNA (cfDNA) analysis platform." (*Id.*).

79. On September 24, 2020, LabCorp began offering the Resolution ctDx Lung Assay test to patients. (*See* Ex. 70 at 1 ("*LabCorp Resolution ctDx Lung Assay*," GENOMEWEB (September 24, 2020), https://www.genomeweb.com/resources/new-product/labcorp-resolution-ctdx-lung-assay) ("LabCorp has launched the Resolution ctDx Lung assay for patients with non-small cell lung cancer (NSCLC).").)

80. Performance of the Resolution ctDx Lung assay involves analyzing "circulating tumor DNA (CtDNA) from a plasma sample in patients with non-small cell lung cancer." (Ex. 11 at 1 (https://www.labcorp.com/tests/830697/resolution-ctdx-lung-assay-liquid-biopsy).)

81. The Resolution ctDx Lung Assay test requires samples containing an agent that inhibits cell lysis. For example, LabCorp requires that the blood sample for the Resolution ctDx Lung Assay be collected in Streck Cell-Free DNA tubes. (*See* Ex. 11 at 1 (https://www.labcorp.com/tests/830697/resolution-ctdx-lung-assay-liquid-biopsy) ("Collect 10 mL of whole blood into each of 2 Streck BCT tubes.").)

82. As described above, samples collected in Streck Cell-Free DNA BCT tubes, including Resolution ctDx Lung Assay blood samples, contain an agent that inhibits cell lysis. (*See* Ex. 41 at 2 (https://www.streck.com/products/stabilization/cell-free-dna-bct/#resources).)

83. Processing the Resolution ctDx Lung Assay involves isolating and sequencing cell-free DNA from the blood sample:

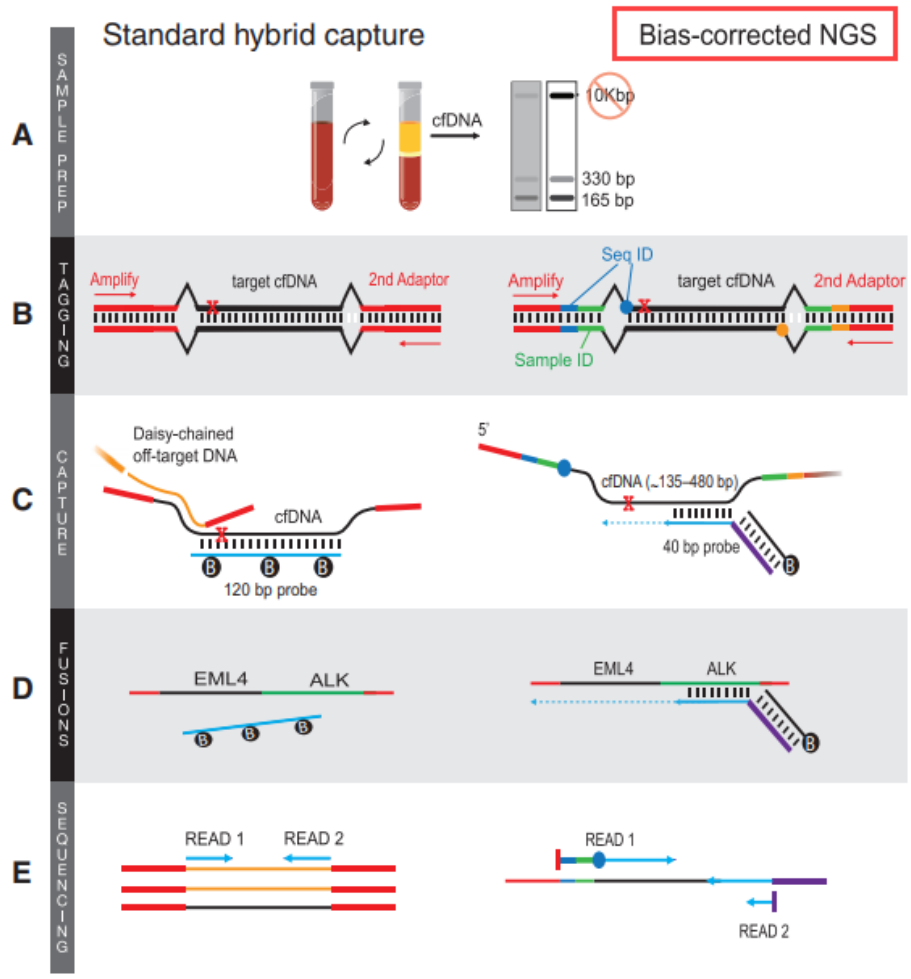


Figure 1.
Key differences between standard hybrid capture (left) and bias-corrected NGS (right). A, mono-, di-, and trimeric nucleosome cfDNA fragments ranging from 130 to 480 basepairs are isolated. B, in standard hybrid capture, cfDNA fragments are end-repaired and ligated with single primers. In contrast, bias-corrected NGS uses multifunctional adaptors that include sequences for single-primer amplification (red), tags for sample identification (green), and sequence identification tags (blue) that, in conjunction with the fragmentation site (blue dot) identify unique sequence clones. C, in standard hybridization cfDNA fragments are captured with large capture probes (up to 120 bp) that span the genetic region of interest and may result in off-target fragments being isolated (e.g., daisy-chaining off-target DNA). Bias-corrected NGS uses small capture probes (~40 bp) that are designed to be adjacent to the region of interest. Primer extension of fragments copies genomic and adaptor sequences. Finally, amplification with tailed PCR primers creates sequencing ready clones. D, although both approaches allow sequencing of gene rearrangements, large capture probes designed to target one gene will inefficiently target fragments containing a large amount of fusion partner gene sequence, resulting in poor sensitivity. In bias-corrected NGS, gene junction and partner gene sequence is replicated during primer extension. E, in standard hybrid capture all pulled-down cfDNA (specific and nonspecific) is amplified and sequenced without knowing the exact read or probe which captured the fragment. In bias-corrected NGS, READ_1 identifies the sample ID and the unique sequence identifiers, whereas READ_2 identifies the probe that pulled down each clone, facilitating read analysis, and probe optimization.

(Ex. 71 at 3 (C.P. Paweletz et. al., *Bias-Corrected Targeted Next-Generation Sequencing for Rapid, Multiplexed Detection of Actionable Alterations in Cell-Free DNA from Advanced Lung Cancer Patients*, 22 CLINICAL CANCER RESEARCH 915-22 (2016), https://clincancerres.aacrjournals.org/content/clincanres/22/4/915.full.pdf) (describing the bias-corrected Next Generation-Sequencing process of Resolution ctDx Lung Assay) (annotation

added); *see also, e.g.,* Ex. 72 at 1-2 (https://clincancerres.aacrjournals.org/highwire/filestream/132417/field_highwire_adjunct_files/4/152484_1_supp_3149955_nff3kj.docx) (describing in detail the methodology of the Next Generation-Sequencing process of Resolution ctDx Lung Assay shown in the figure above); Ex. 73 at 2-3 (J.K. Sabari et. al., *A Prospective Study of Circulating Tumor DNA to Guide Matched Targeted Therapy in Lung Cancers*, 111 J. NAT'L CANCER INST. 575-83 (2018), doi: 10.1093/jnci/djy156) (describing the methodology of the Resolution ctDx Lung Assay test, including extracting DNA from a blood sample and performing "targeted plasma [Next-Generation Sequencing] [] using a validated, bias-corrected, hybrid-capture 21-gene assay, ResBio ctDx-Lung" to determine point mutations and copy number alterations); Ex. 11 at 1 (https://www.labcorp.com/tests/830697/resolution-ctdx-lung-assay-liquid-biopsy) ("The test is a NGS multi-gene panel that assesses circulating tumor DNA (CtDNA) from a plasma sample in patients with non-small cell lung cancer."); Ex. 74 at 1 (http://www.resolutionbio.com/science/) ("The cfDNA is extracted from the plasma for analysis. Through a series of proprietary biochemical steps, we amplify the cfDNA and using very small probes, target and capture strands of ctDNA… The Resolution platform can find SNPs, insertion and deletions, copy number variations (CNVs) / amplifications, and fusions / translocations."); Ex. 75 at 2 (J.G. Supplee et. al., *"Sensitivity of Next-Generation Sequencing Assays Detecting Oncogenic Fusions in Plasma Cell-Free DNA*," 134 LUNG CANCER 96-99 (2016), https://doi.org/10.1016/j.lungcan.2019.06.004 ("Libraries were prepared and sequenced at DFCI using a pre-production ctDx-Lung kit (Resolution Bioscience, Redmond, WA) spanning exons and some introns of 20 NSCLC-associated genes. Importantly, libraries are hybridized with 40 nt targeting probes with each probe possessing an additional tail sequence that is complementary to a biotinylated pull-down

oligonucleotide. Following hybridization and purification of probe-clone complexes, primer extension of the probe is then used to copy the genomic sequence and tag information, allowing for high on-target rates as well as the association of each read with the identity of its cognate probe. Sequencing was performed on an Illumina NextSeq500 followed by cloud-based, bioinformatic variant calling.").)

84. LabCorp offers to sell and sells the Resolution ctDx Lung Assay test on its website and at its patient collection centers, including several patient collection centers in this District (such as at 6603 First Park Ten Blvd, San Antonio, TX 78213). (*See* Ex. 5 (https://www.labcorp.com/node/107); *see also* Ex. 76 (C. Hale, "*LabCorp to Roll Out Resolution Bio's Lung Cancer Liquid Biopsy Test*," FIERCE BIOTECH (September 23, 2020), https://www.fiercebiotech.com/medtech/labcorp-to-market-resolution-bio-s-lung-cancer-liquid-biopsy-test ("After **collecting samples through LabCorp's patient service centers**, the test will be performed within Resolution's certified laboratory as a lab-developed test.").) On information and belief, LabCorp's offers for sale and sales of the Resolution ctDx Lung Assay test comprise the obligation to perform 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 the Resolution ctDx Lung Assay test, LabCorp accepts the obligation, directly or through one or more subsidiaries and/or intermediaries, to perform a test pursuant to the Resolution ctDx Lung Assay test protocol for the patient's sample(s). At these centers, LabCorp collects test samples from patients for the Resolution ctDx Lung Assay test. (*See id.* ("After collecting samples through LabCorp's patient service centers, the test will be performed within Resolution's certified laboratory as a lab-developed test.").)

85. On information and belief, employees or other agents of LabCorp (*e.g.*, LabCorp's lab assistants) collect test samples according to the Resolution ctDx Lung Assay test protocol. For example, on information and belief, LabCorp publishes and follows instructions for collecting and transporting Resolution ctDx Lung Assay test samples. (*See, e.g.,* Ex. 11 at 1 (https://www.labcorp.com/tests/830697/resolution-ctdx-lung-assay-liquid-biopsy) ("Specimen must be submitted using the Integrated Oncology Liquid Biopsy kit and the Integrated Oncology Gene Profiling Assays test request form (ONC-793).").) On information and belief, the published instructions are a part of the Resolution ctDx Lung Assay test protocol, and LabCorp directs its employees and third parties, including Resolution Bioscience, to follow the Resolution ctDx Lung Assay test protocol in collecting and processing the Resolution ctDx Lung Assay test samples. LabCorp directs the blood samples it collects for the Resolution ctDx Lung Assay test at its patient service centers to Resolution Bioscience's certified laboratory for processing. (*See* Ex. 76 (C. Hale, "*LabCorp to Roll Out Resolution Bio's Lung Cancer Liquid Biopsy Test*," FIERCE BIOTECH (September 23, 2020), https://www.fiercebiotech.com/medtech/labcorp-to-market-resolution-bio-s-lung-cancer-liquid-biopsy-test ("After collecting samples through LabCorp's patient service centers, the test will be performed within Resolution's certified laboratory as a lab-developed test.").) On information and belief, LabCorp, either itself or through or through its subsidiaries or affiliates, instructs Resolution Biosience to process the collected samples in accordance with the established Resolution ctDx Lung Assay test protocols. On information and belief, conditions participation in an activity or receipt of a benefit (such as a continued commercial partnership with LabCorp) on Resolution Biosience's processing of the Resolution ctDx Lung Assay test samples. (*See id.* (including a statement from Resolution Bioscience's CEO describing the "commercial

partnership with LabCorp" as "an important step in our quest to enable broad access to our lung cancer test.").)

86. On information and belief, LabCorp sends blood samples to Resolution BioScience with the specific intent that Resolution BioScience perform the Resolution ctDx Lung Assay tests on the samples according to established protocols. On information and belief, Resolution Bioscience commercially performs the Resolution ctDx Lung Assay test exclusively on blood samples collected and provided by LabCorp. (*See, e.g.*, Ex. 69 (Press Release, "*Resolution Bioscience and LabCorp Will Collaborate to Commercialize the Resolution ctDx Lung™ Liquid Biopsy Assay*" (February 24, 2020), http://www.resolutionbio.com/company/press/2020.02.24_resolution_ctdx_lung_lca.html) (stating that the agreement between LabCorp and Resolution Bioscience is "to make Resolution ctDx™ Lung assay available to clinicians and patients" and referencing a study that concluded "the assay has the potential to be implemented broadly for patient care."); Ex. 76 (C. Hale, "*LabCorp to Roll Out Resolution Bio's Lung Cancer Liquid Biopsy Test*," FIERCE BIOTECH (September 23, 2020), https://www.fiercebiotech.com/medtech/labcorp-to-market-resolution-bio-s-lung-cancer-liquid-biopsy-test ("This commercial partnership with LabCorp is an important step in our quest to enable broad access to our lung cancer test … After collecting samples through LabCorp's patient service centers, the test will be performed within Resolution's certified laboratory as a lab-developed test.").)

D. LabCorp's Knowledge Of The Ravgen Patents

87. On information and belief, LabCorp has been aware of the Patents-in-Suit and the fact that performance of the Accused Tests practice the claimed inventions of the Patents-in-Suit at least since each of the Accused Tests was first used, made, offered for sale, and/or sold.

88. On information and belief, LabCorp became aware of the Patents-in-Suit at least through its acquisition of Genzyme Genetics in December 2010.

89. In September 2009, Kellie Watson, former Director of Business Development at Genzyme Corporation ("Genzyme"), communicated with Dr. Dhallan regarding Genzyme's interest in the NIPD space and Ravgen's technology relating to the Patents-in-Suit. (*See, e.g.*, Ex. 77 (September 30, 2009 email from Kellie Watson to Dr. Dhallan).) In February and March of 2010, Dr. Watson continued to communicate with Dr. Dhallan, including arranging an in-person visit to Ravgen for herself and Thomas Scholl, the then-Vice President of Research & Development at Genzyme's Genzyme Genetics division. (*See* Ex. 78 (Emails from February 15, 2020 to March 5, 2010 between Kellie Watson and Dr. Dhallan).) Those communications included discussions regarding Ravgen's technology covered by the Patents-in-Suit.

90. In December of 2010, LabCorp completed its purchase of Genzyme Genetics from Genzyme. (*See* Ex. 79 (Press Release, "*Genzyme Completes Sale of Genetic Testing Business to LabCorp*," SANOFI GENZYME (December 1, 2010), https://www.sanofigenzyme.com/en/about-us/newsroom/archive/2010/2010-12-01-08-00-00).) On information and belief, LabCorp became aware of the Patents-in-Suit at least through that acquisition of Genzyme Genetics. Further, on information and belief, as a result of LabCorp's acquisition of Genzyme Genetics, Thomas Scholl became a Vice President of Research & Development at LabCorp. (*See* Ex. 80 (https://www.linkedin.com/in/tom-scholl-7693596/) (showing Thomas Scholl as the "VP R&D" at LabCorp after the Genzyme Genetics acquisition).) On information and belief, LabCorp became aware of the Patents-in-Suit at least through its hiring of Thomas Scholl as Vice President of Research & Development.

91. In 2011 and 2012, LabCorp continued to communicate with Dr. Dhallan about Ravgen's technology and its patent portfolio. The Ravgen patent portfolio—both at that time and today—is composed of seven issued U.S. Patents, including the two Patents-in-Suit.

92. For example, on December 19, 2011, LabCorp, through Thomas Scholl, reached out to Dr. Dhallan via email and expressed LabCorp's interest in speaking with Dr. Dhallan regarding Ravgen's technology after "hear[ing] from their IP attorney on [Ravgen's] patents." (Ex. 81 (December 19, 2011 email from Thomas Scholl to Dr. Dhallan).) In another email that day, Mr. Scholl introduced Dr. Dhallan to Jonathan Meltzer, former Vice President of LabCorp's Corporate Development department and current Vice President of LabCorp's Esoteric Businesses, in order to facilitate discussions to "assess opportunities around Ravgen's technologies." (Ex. 82 at 3 (Emails from December 19, 2011 to December 22, 2011 between Thomas Scholl, Jonathan Meltzer, and Dr. Dhallan).) On December 23, 2011, Thomas Scholl and Jonathan Meltzer communicated with Dr. Dhallan via phone to discuss Ravgen's technology. (*Id.* at 1.)

93. In 2012, LabCorp, through Mr. Scholl and Mr. Meltzer, continued to communicate with Dr. Dhallan about Ravgen's technology through email correspondence, phone calls, and an in-person meeting. For example, according email correspondence from Mr. Scholl on March 16, 2012, discussions between Mr. Meltzer and Dr. Dhallan "around partnering ha[d] progressed to a point where additional conversations around the science of your testing are warranted." (*See* Ex. 83 at 1-2 (Emails from March 16, 2012 to March 21, 2012 between Thomas Scholl and Dr. Dhallan)).) On March 29, 2012, Mr. Scholl visited Ravgen to meet Dr. Dhallan for a "detailed discussion regarding [Ravgen's] methods and assays." (*Id.* at 1-2.)

94. Additionally, on information and belief, LabCorp obtained knowledge of the Patents-in-Suit and its infringement through its acquisition of Sequenom and Sequenom Center.

For example, in 2011 and 2012, Sequenom communicated with Dr. Dhallan about Ravgen's technology and the Patents-in-Suit through email correspondence, phone calls, and an in-person meeting.

95. For example, in August of 2011, Harry Hixson, Sequenom's Chief Executive Officer at the time, had a conversation with Dr. Dhallan regarding a potential collaboration between Ravgen and Sequenom. (*See* Ex. 84 (August 8, 2011 Email from Harry Hixon to Dr. Dhallan).) On March 20, 2012, Harry Hixson, on behalf of Sequenom, sent an email to Dr. Dhallan with a proposal for a relationship between Sequenom and Ravgen. Mr. Hixon proposed that Ravgen grant Sequenom an "exclusive license" to two of Ravgen's patents, and in exchange Sequenom "would make an upfront licensing payment to Ravgen" and "would pay Ravgen an annual royalty (or minimum) for the use of the Ravgen IP." (*See* Ex. 85 (March 20, 2012 Email from Harry Hixon to Dr. Dhallan).) On April 19, 2012, Mr. Hixson and Ronald Lindsay, then Executive Vice President of Research & Development at Sequenom, visited Ravgen to meet the staff and tour Ravgen's laboratory. (Ex. 86 (May 10, 2012 Letter from Harry Hixson to Dr. Dhallan).) On May 11, 2012, Harry Hixson sent a letter to Dr. Dhallan stating that Sequenom was "interested in acquiring exclusive rights to your **issued patents – 7,332,277**, 7,442,506 and **7,727,720**." (*Id.* (emphasis added).) U.S. Patent Nos. 7,332,277 and 7,727,720 are the Patents-in-Suit.

96. In 2015, Sequenom and Ravgen continued discussions regarding Ravgen's patent portfolio, including the Patents-in-Suit. For example, on June 29, 2015, then-President and Chief Executive Officer of Sequenom, Bill Welch, spoke with Dr. Dhallan by phone and, on July 6, 2015, Dr. Dhallan visited Mr. Welch at Sequenom's offices and discussed the applications of the '720 Patent in the oncology field. (Ex. 87 at 1-2 (Emails from June 29, 2015 to July 22, 2015

between Bill Welch and Dr. Dhallan) ("Our oncology patent that we talked about is US Patent No. 7,727,720.").) In an email dated July 22, 2015, Bill Welch, the then-President and Chief Executive Officer of Sequenom, acknowledged that Sequenom had taken a "*deeper dive* into the claims and descriptions of the US Patent No. 7,727,720." (*Id.* at 1.)

97. Additionally, Sequenom identified one of the Patents-in-Suit, the ''277 patent, as prior art to Sequenom's own patent applications in the field. For example, on December 23, 2012, Sequenom filed an Information Disclosure Statement ("IDS"), identifying U.S. Patent Publication No. 2004/0137470, which ultimately issued as the '277 patent, as prior art to Sequenom's patent application that subsequently issued as United States Patent No. 8,962,247 ("the '247 patent," attached hereto as Ex. 88). On January 13, 2013, Sequenom filed an IDS with the PTO identifying U.S. Patent Publication No. 2004/0137470 (the '277 patent as issued) as prior art to Sequenom's patent application that subsequently issued as United States Patent No. 8,476,013 ("the '013 patent," attached hereto as Ex. 89). The '013 patent is the parent patent of the '247 and both patents relate to compositions and processes for isolating fetal nucleic acid from a maternal sample for the purpose of non-invasive prenatal diagnostics. (*See* Ex. 88 at Abstract ("Provided are compositions and processes that utilize genomic regions that are differentially methylated between a mother and her fetus to separate, isolate or enrich fetal nucleic acid from a maternal sample. The compositions and processes described herein are particularly useful for non-invasive prenatal diagnostics, including the detection of chromosomal aneuplodies."); Ex. 89 at Abstract ("Provided are compositions and processes that utilize genomic regions that are differentially methylated between a mother and her fetus to separate, isolate or enrich fetal nucleic acid from a maternal sample. The compositions and processes described herein are particularly useful for non-invasive prenatal diagnostics, including the detection of chromosomal aneuplodies.").)

98. On May 28, 2013, Sequenom also filed an IDS with the PTO identifying U.S. Patent Publication No. 2004/0137470 as prior art to Sequenom's patent application that subsequently issued as United States Patent No. 9,920,361 ("the '361 patent," attached hereto as Ex. 90). The '361 patent relates to methods and compositions for analyzing nucleic acid, including for detecting the presence of genetic variations. *See* Ex. 90 at 155 ("Provided in some aspects are methods for analyzing one or more polynucleotide species in a nucleic acid mixture … In some embodiments, a method comprises detecting the presence or absence of a genetic variation.").

99. On January 20, 2016, Sequenom also filed an IDS with the PTO identifying U.S. Patent Publication No. 2004/0137470 as prior art to Sequenom's patent application that subsequently issued as United States Patent No. 9,367,663 ("the '663 patent," attached hereto as Ex. 91). The '663 patent relates to "methods, processes, and apparatuses for non-invasive assessment of genetic variations." (Ex. 91 at Abstract.) The types of genetic variations assessed include "segmental chromosomal aberration" and "fetal aneuploidy." (*Id.* at 135.)

100. On February 2, 2016, Sequenom also filed an IDS with the PTO identifying U.S. Patent Publication No. 2004/0137470 as prior art to Sequenom's patent application that subsequently issued as United States Patent No. 10,504,613 ("the '613 patent," attached hereto as Ex. 92). The '613 patent relates to "methods, processes, and apparatuses for non-invasive assessment of genetic variations." (Ex. 92 at Abstract.) The assessment method includes comparing the differences in nucleic acid fragments. (*Id.* at 141.)

101. On February 16, 2016, Sequenom also filed an IDS with the PTO identifying U.S. Patent Publication No. 2004/0137470 as prior art to Sequenom's patent application that subsequently issued as United States Patent No. 10,196,681 ("the '681 patent," attached hereto as Ex. 93). The '681 patent relates to methods and processes for "determining the fraction of fetal

nucleic acid [] derived from a pregnant female" and "the presence or absence of a genetic variation in a fetus" using "fetal fraction measurements." (Ex. 93 at Abstract.)

102. On February 17, 2016, Sequenom also filed an IDS with the PTO identifying U.S. Patent Publication No. 2004/0137470 as prior art to Sequenom's patent application that subsequently issued as United States Patent No. 10,424,394 ("the '394 patent," attached hereto as Ex. 94). The '394 patent relates to "methods, processes, and apparatuses for non-invasive assessment of genetic variations." (Ex. 94 at Abstract.) The assessment method includes determining the fetal fraction of a blood sample in order to determine fetal ploidy. (*Id.* at 196.)

103. On February 19, 2016, Sequenom also filed an IDS with the PTO identifying U.S. Patent Publication No. 2004/0137470 as prior art to Sequenom's patent application that subsequently issued as United States Patent No. 10,497,461 ("the '461 patent," attached hereto as Ex. 95). The '461 patent relates to "methods, processes, and apparatuses for non-invasive assessment of genetic variations." (Ex. 95 at Abstract.) The assessment method includes identifying the presence of "sex chromosome aneuploidy in a fetus." (*Id.* at 164.)

104. On February 22, 2016, Sequenom also filed an IDS with the PTO identifying U.S. Patent Publication No. 2004/0137470 as prior art to Sequenom's patent application that subsequently issued as United States Patent No. 9,984,198 ("the '198 patent," attached hereto as Ex. 96). The '198 patent relates to "methods, processes, and apparatuses for non-invasive assessment of genetic variations." (Ex. 96 at Abstract.) The assessment method includes "determining the presence or absence of a chromosome aneuploidy." (*Id.* at 151.)

105. On March 10, 2016, Sequenom also filed an IDS with the PTO identifying U.S. Patent Publication No. 2004/0137470 as prior art to Sequenom's patent application that subsequently issued as United States Patent No. 10,482,994 ("the '994 patent," attached hereto as

Ex. 97). The '994 patent relates to "methods, processes, and apparatuses for non-invasive assessment of genetic variations." (Ex. 97 at Abstract.) The patent includes methods for measuring the fetal fraction from pregnant females. (*Id.* at 135.)

106. On July 27, 2016, LabCorp completed its purchase of Sequenom. (*See* Ex. 37 ("*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).)

107. LabCorp has been aware of the Patents-in-Suit and aware of, or willfully blind to, its infringement of those patents since it began making, using, offering for sale, and/or selling each of the Accused Tests. For example, despite its knowledge of the Patents-in-Suit at least by December 2010, LabCorp launched the informaSeq test, which is built on and includes the claimed inventions, on August 19, 2014. Further, despite both LabCorp's and Sequenom's knowledge of the Patents-in-Suit and of the fact that performance of the MaterniT tests practice the claimed inventions of those patents, LabCorp acquired Sequenom and Sequenom Center on July 27, 2016 and began making, using, offering for sale, and selling the MaterniT tests. Additionally, despite LabCorp's knowledge of the '720 Patent and of its application to the oncology field, LabCorp began commercializing the infringing Resolution ctDx Lung Assay test on September 24, 2020.

108. Despite its knowledge of the Patents-in-Suit and of its infringement of those patents, LabCorp has continued to willfully infringe the Patents-in-Suit so as to obtain the significant benefits of Ravgen's innovations without paying compensation to Ravgen. For example, after becoming aware of the Patents-in-Suit, LabCorp began commercializing the Accused Tests, which are built on and include the claimed inventions. Further, on information

and belief, LabCorp has continued to use the claimed methods in Accused Tests without a license, generating hundreds of millions of dollars in revenue.

COUNT I

(Infringement Of The '277 Patent)

109. Ravgen incorporates by reference paragraphs 1–108.

110. The '277 Patent is valid and enforceable.

111. LabCorp has infringed, and continues to infringe, one or more claims of the '277 Patent under 35 U.S.C. § 271, either literally and/or under the doctrine of equivalents, by making, using, selling, and/or offering for sale in the United States, and/or importing into the United States, products and/or methods encompassed by those claims, including LabCorp's MaterniT21 PLUS, MaterniT Genome, and informaSeq tests.

112. For example, LabCorp infringes at least exemplary claim 81 of the '277 Patent by using the MaterniT21 PLUS test. For example, use of the MaterniT21 PLUS test requires using a method for preparing a sample for analysis, wherein said method comprises:

a. isolating free fetal nucleic acid (such as cell-free fetal DNA) from a sample (such as a maternal blood sample) (*see, e.g.*, Ex. 38 (https://sema4.com/products/testcatalog/noninvasive-prenatal-testing-nipt-sequenom/#) ("Sequenom noninvasive prenatal testing (NIPT) is a chromosome counting method that analyzes genetic information in fetal cell-free DNA in maternal blood to determine risk for specific fetal chromosomal and subchromosomal abnormalities."); Ex. 46 at 2-3 (T.J. Jensen et. al., *High-Throughput Massively Parallel Sequencing for Fetal Aneuploidy Detection from Maternal Plasma*, 8 PLOS ONE (2013),

https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0057381) (describing the protocol used by Sequenom to analyze MaterniT21 PLUS samples, including extracting "ccfDNA [] from maternal plasma")),

b. wherein said sample comprises an agent that inhibits lysis of cells, if cells are present, and wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor (such as cell-free DNA Streck tubes filled with at least 10mL of blood) (*see, e.g.*, Ex. 38 (https://sema4.com/products/test-catalog/noninvasive-prenatal-testing-nipt-sequenom/#) (listing as a requirement for the MaterniT21 PLUS test "[o]ne 10 mL BCT Streck tube"; Ex. 41 at 2 (https://www.streck.com/products/stabilization/cell-free-dna-bct/#resources) (describing Streck cell-free DNA tubes as containing a "unique preservative [which] limits the release of genomic DNA, allowing isolation of high-quality cell-free DNA" and "specialized chemistry" that "***limit[s] cell lysis***")).

113. For example, LabCorp infringes at least exemplary claim 81 of the '277 Patent by using the MaterniT Genome test. For example, use of the MaterniT Genome test requires using a method for preparing a sample for analysis, wherein said method comprises:

a. isolating free fetal nucleic acid (such as cell-free fetal DNA) from a sample (such as a maternal blood sample) (*see, e.g.*, Ex. 36 at 2 (https://www.integratedgenetics.com/sites/default/files/2020-04/GENOME_Positive%20T18_Sample%20Report.pdf) ("The MaterniT GENOME laboratory-developed test analyzes the relative amount of chromosomal material across the genome in circulating cell-free DNA from a maternal sample.");

Ex. 38 (https://sema4.com/products/test-catalog/noninvasive-prenatal-testing-nipt-sequenom/#) ("Sequenom noninvasive prenatal testing (NIPT) is a chromosome counting method that analyzes genetic information in fetal cell-free DNA in maternal blood to determine risk for specific fetal chromosomal and subchromosomal abnormalities."); Ex. 49 at 2 (M. Ehrich et al., *Genome-Wide cfDNA Screening: Clinical Laboratory Experience with the First 10,000 Cases*, 19 GENETICS IN MEDICINE 1332-37 (2017) (https://www.nature.com/articles/gim201756) (explaining that during the MaterniT Genome laboratory processing, "cfDNA was extracted from plasma")),

b. wherein said sample comprises an agent that inhibits lysis of cells, if cells are present, and wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor (such as cell-free DNA Streck tubes filled with at least 10mL of blood) (*see, e.g.*, Ex. 38 (https://sema4.com/products/test-catalog/noninvasive-prenatal-testing-nipt-sequenom/#) (listing as a requirement for the MaterniT Genome test "[o]ne 10 mL BCT Streck tube"; Ex. 41 at 2 (https://www.streck.com/products/stabilization/cell-free-dna-bct/#resources) (describing Streck cell-free DNA tubes as containing a "unique preservative [which] limits the release of genomic DNA, allowing isolation of high-quality cell-free DNA" and "specialized chemistry" that "***limit[s] cell lysis***")).

114. For example, LabCorp infringes at least exemplary claim 81 of the '277 Patent by using the informaSeq test. For example, use of the informaSeq test requires using a method for preparing a sample for analysis, wherein said method comprises:

a. isolating free fetal nucleic acid (such as cell-free fetal DNA) from a sample (such as a maternal blood sample) (*see, e.g.*, Ex. 64 at 1 (Press Release, "*LabCorp Announces the Availability of InformaSeq^{SM} Non-Invasive Prenatal Test*" (August 19, 2014), https://ir.labcorp.com/news-releases/news-release-details/labcorp-announces-availability-informaseqsm-non-invasive ("The informaSeq Prenatal Test is an advanced, non-invasive, next-generation prenatal screening assay that can assess risk for multiple fetal chromosomal aneuploidies, or abnormalities in the number of chromosomes, from a single maternal blood draw."); Ex. 20 at 5 (https://www.labcorp.com/tests/related-documents/L13272) (showing the use of the informaSeq test to determine the fetal fraction and any aneuploidy in a blood sample)),

b. wherein said sample comprises an agent that inhibits lysis of cells, if cells are present, and wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor (such as cell-free DNA Streck tubes filled with at least 10mL of blood) (*see, e.g.*, Ex. 20 at 3 (https://www.labcorp.com/tests/related-documents/L13272) (listing as a requirement for the MaterniT Genome test "[o]ne 10 mL BCT Streck tube"); Ex. 41 at 2 (https://www.streck.com/products/stabilization/cell-free-dna-bct/#resources) (describing Streck cell-free DNA tubes as containing a "unique preservative [which] limits the release of genomic DNA, allowing isolation of high-quality cell-free DNA" and "specialized chemistry" that "***limit[s] cell lysis***")).

115. LabCorp has infringed, and continue to infringe, one or more claims of the '277 Patent under 35 U.S.C. § 271(a), either literally and/or under the doctrine of equivalents, by using

the informaSeq tests, either itself or through its subsidiaries. For example, LabCorp uses the informaSeq tests by processing the informaSeq test samples at its Integrated Genetics laboratories according to the informaSeq test protocols. LabCorp assigns its Integrated Genetics laboratories the task of using the informaSeq tests (by collecting samples and sending them to the Integrated Genetics laboratories for processing), and LabCorp gives interim instructions to control the means and details of the process by which the Integrated Genetics laboratories uses the informaSeq test (by establishing the informaSeq test protocols and requiring the Integrated Genetics laboratories to follow that protocol when processing tests). Integrated Genetics is one of LabCorp's Specialty Testing Groups and LabCorp has the right and the ability to direct and control the activities of the Integrated Genetics laboratories in several ways, including through LabCorp's ownership of the Integrated Genetics laboratories, through instituting programs and measures (such as policies or protocols) at the Integrated Genetics laboratories, and through interim instructions via at least LabCorp's employees at the Integrated Genetics laboratories. Further, the Integrated Genetics laboratories act on behalf of LabCorp, including when the Integrated Genetics laboratories perform tests on LabCorp's behalf for LabCorp's patients, or provides test results to health care providers and/or patients on LabCorp's behalf.

116. LabCorp has infringed, and continues to infringe, one or more claims of the '277 Patent under 35 U.S.C. § 271(a), either literally and/or under the doctrine of equivalents, by directing and controlling the performance of the informaSeq test, comprising the performance of the patented methods, by its Integrated Genetics laboratories. For example, LabCorp conditions participation in an activity or receipt of a benefit (such as continued funding and status as LabCorp's laboratory) on the Integrated Genetics laboratories' performance of the steps of the patented method (such as the processing of the informaSeq test samples). Further, LabCorp

establishes the manner or timing of the performance of the steps of the patented method (such as the Integrated Genetics laboratories' processing of the informaSeqtest samples), including by collecting test samples and sending them to the Integrated Genetics laboratories with instructions to be processed according to the informaSeq test protocols, which include details regarding how the sample is to be collected. On information and belief, employees or other agents of LabCorp (*e.g.*, LabCorp's lab assistants) collect test samples according to the informaSeq test protocols, and the Integrated Genetics laboratories process the test samples according to the informaSeq test protocols.

117. LabCorp has infringed, and continues to infringe, one or more claims of the '277 Patent under 35 U.S.C. § 271(a), either literally and/or under the doctrine of equivalents, by using the MaterniT21 PLUS and MaterniT Genome tests, either itself or through its agent, Sequenom Center. For example, LabCorp assigns its laboratory Sequenom Center the task of using the MaterniT21 PLUS and MaterniT Genome tests (by collecting samples and sending them to Sequenom Center for processing), and LabCorp gives interim instructions to control the means and details of the process by which Sequenom Center uses the MaterniT21 PLUS and MaterniT Genome tests (by establishing the MaterniT21 PLUS and MaterniT Genome test protocols and requiring Sequenom Center to follow those protocols when processing the tests). LabCorp has the right and the ability to direct and control the activities of Sequenom Center in several ways, including through LabCorp's 100% ownership of Sequenom Center, through instituting programs and measures (such as policies or protocols) at Sequenom Center, and through interim instructions via at least LabCorp's employees and/or officers who hold leadership roles at Sequenom Center. Further, Sequenom Center acts on behalf of LabCorp, including when Sequenom Center performs

tests on LabCorp's behalf for LabCorp's patients, or provides test results to health care providers and/or patients on LabCorp's behalf.

118. LabCorp has infringed, and continues to infringe, one or more claims of the '277 Patent under 35 U.S.C. § 271(a), either literally and/or under the doctrine of equivalents, by directing and controlling the performance of the MaterniT21 PLUS and MaterniT Genome tests, comprising the performance of the patented methods, by its laboratory Sequenom Center (including through its wholly-owned subsidiary Sequenom). For example, LabCorp conditions participation in an activity or receipt of a benefit (such as continued funding, status as LabCorp's laboratory, and payments related to discrete tests performed) on Sequenom Center's performance of the steps of the patented method (such as the processing of the MaterniT21 PLUS and MaterniT Genome test samples). Further, LabCorp establishes the manner or timing of the performance of the steps of the patented method (such as the Sequenom Center's processing of the MaterniT21 PLUS and MaterniT Genome test samples), including by collecting test samples and sending them to Sequenom Center with instructions to be processed according to the MaterniT21 PLUS and MaterniT Genome test protocols, which include details regarding how the sample is to be collected. On information and belief, employees or other agents of LabCorp (*e.g.*, LabCorp's lab assistants) collect test samples according to the MaterniT21 PLUS and MaterniT Genome test protocols, and Sequenom Center processes the test samples according to the MaterniT21 PLUS and MaterniT Genome test protocols.

119. LabCorp has infringed, and continues to infringe, one or more claims of the '277 Patent under 35 U.S.C. § 271(a), either literally and/or under the doctrine of equivalents, by offering for sale and selling the performance of infringing methods, such as by offering for sale and selling the MaterniT21 PLUS, MaterniT Genome, and informaSeq tests. LabCorp's offers for

sale and sales of the MaterniT21 PLUS, MaterniT Genome, and informaSeq tests comprise the obligation to perform the steps of the patented methods. For example, when a patient agrees to pay (or for her insurer to pay) in exchange for the MaterniT21 PLUS, MaterniT Genome, or informaSeq tests, on information and belief, LabCorp accepts the obligation, directly or through one or more subsidiaries and/or intermediaries, to perform a test pursuant to the MaterniT21 PLUS, MaterniT Genome, or informaSeq test protocols for the patient's sample(s), including the acts of collecting a patient sample according to the MaterniT21 PLUS, MaterniT Genome, or informaSeq test protocols, preparing such sample for analysis so that it comprises an agent that inhibits lysis of cells, if cells are present, isolating free fetal nucleic acid from the sample, and reporting results to a health care provider and/or the patient.

120. In addition or in the alternative, LabCorp has induced infringement, and continues to induce infringement, of one or more claims of the '277 Patent under 35 U.S.C. § 271(b). LabCorp has actively, knowingly, and intentionally induced, and continues to actively, knowingly, and intentionally induce, infringement of the '277 Patent by selling or otherwise supplying the MaterniT21 PLUS and MaterniT Genome tests with the knowledge and intent that Sequenom Center will use the MaterniT21 PLUS and MaterniT Genome tests supplied by LabCorp to infringe the '277 Patent; and with the knowledge and intent to encourage and facilitate third-party infringement through the dissemination of the MaterniT21 PLUS and MaterniT Genome tests and/or the creation and dissemination of promotional and marketing materials, supporting materials, instructions, product manuals, and/or technical information related to the MaterniT21 PLUS and MaterniT Genome tests.

121. LabCorp specifically intends and is aware that the ordinary and customary use of the MaterniT21 PLUS and MaterniT Genome tests would infringe the '277 Patent. For example,

LabCorp provides the MaterniT21 PLUS and MaterniT Genome tests, which, when used in their ordinary and customary manner intended and instructed by LabCorp, infringe one or more claims of the '277 Patent, including at least exemplary claim 81. LabCorp further provides product manuals and other instructional materials that cause Sequenom Center to use the MaterniT21 PLUS and MaterniT Genome tests for their ordinary and customary use. Sequenom Center has directly infringed the '277 Patent, including at least exemplary claim 81, through the normal and customary use of the MaterniT21 PLUS and MaterniT Genome tests. LabCorp, accordingly, has induced and continues to induce Sequenom Center to use the MaterniT21 PLUS and MaterniT Genome tests in their ordinary and customary way to infringe the '277 Patent, knowing, or at least being willfully blind to the fact, that such use constitutes infringement of the '277 Patent.

122. In addition or in the alternative, LabCorp has contributed and continues to contribute to the infringement by third parties, including Sequenom Center, of one or more claims of the '277 Patent under 35 U.S.C. § 271(c), by making, selling and/or offering for sale in the United States, and/or importing into the United States, the MaterniT21 PLUS and MaterniT Genome tests, knowing that those products constitute a material part of the inventions of the '277 Patent, knowing that those products are especially made or adapted to infringe the '277 Patent, and knowing that those products are not staple articles of commerce suitable for substantial non-infringing use.

123. On information and belief, Defendants LabCorp has had knowledge of and notice of the '277 Patent at least since December 2010, as evidenced by communications between Ravgen and LabCorp and/or its subsidiaries. On information and belief, Defendant LabCorp has had knowledge of and notice of its infringement of the '277 Patent at least since it began making, using,

selling, and offering for sale each of the accused MateriT21 PLUS, MateriT Genome, and/or informaSeq tests.

124. LabCorp's infringement of the '277 Patent continues to be willful and deliberate at least since it began making, using, selling, and offering for sale the accused MateriT21 PLUS, MateriT Genome, and/or informaSeq tests.

125. Ravgen has been and continues to be damaged by LabCorp's infringement of the '277 Patent, and will suffer irreparable injury unless the infringement is enjoined by this Court.

126. LabCorp's conduct in infringing the '277 Patent renders this case exceptional within the meaning of 35 U.S.C. § 285.

COUNT II

Infringement Of The '720 Patent

127. Ravgen incorporates by reference paragraphs 1–126.

128. The '720 Patent is valid and enforceable.

129. LabCorp has infringed, and continues to infringe, one or more claims of the '720 Patent under 35 U.S.C. § 271, either literally and/or under the doctrine of equivalents, by making, using, selling, and/or offering for sale in the United States, and/or importing into the United States, products and/or methods encompassed by those claims, including LabCorp's MateriT21 PLUS, MateriT Genome, informaSeq, and Resolution ctDx Lung Assay tests.

130. For example, LabCorp infringes at least exemplary claim 1 of the '720 patent by using the MateriT21 PLUS test. For example, use of the MateriT21 PLUS test requires using a method for detecting a free nucleic acid, wherein said method comprises:

a. isolating free nucleic acid (such as cell-free DNA) from a non-cellular fraction of a sample (such as a maternal blood sample) (*see, e.g.*, Ex. 38

(https://sema4.com/products/test-catalog/noninvasive-prenatal-testing-nipt-sequenom/#) ("Sequenom noninvasive prenatal testing (NIPT) is a chromosome counting method that analyzes genetic information in fetal cell-free DNA in maternal blood to determine risk for specific fetal chromosomal and subchromosomal abnormalities."); Ex. 46 at 2-3 (T.J. Jensen et. al., *High-Throughput Massively Parallel Sequencing for Fetal Aneuploidy Detection from Maternal Plasma*, 8 PLOS ONE (2013), https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0057381) (describing the protocol used by Sequenom to analyze MaterniT21 PLUS samples, including extracting "ccfDNA [] from maternal plasma"); Ex. 44 at 3 (B. Dyr et al., *A New Era in Aneuploidy Screening: cfDNA Testing in >30,000 Multifetal Gestations: Experience at One Clinical Laboratory*, 14 PLOS ONE (2019), https://doi.org/10.1371/journal.pone.0220979) ("This study [of MaterniT21 PLUS samples] analyzed extracted cfDNA fragments from maternal plasma")),

b. wherein said sample comprises an agent that impedes cell lysis, if cells are present, and wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor (such as cell-free DNA Streck tubes filled with at least 10mL of maternal blood) (*see, e.g.*, Ex. 38 (https://sema4.com/products/test-catalog/noninvasive-prenatal-testing-nipt-sequenom/#) (listing as a requirement for the MaterniT21 PLUS test "One 10 mL BCT Streck tube"; Ex. 41 at 2 (https://www.streck.com/products/stabilization/cell-free-dna-bct/#resources) (describing Streck cell-free DNA tubes as containing a "unique preservative [which] limits the release of genomic DNA, allowing isolation

of high-quality cell-free DNA" and "specialized chemistry" that "limit[s] cell lysis")),

c. detecting the presence or absence of the free nucleic acid (*see, e.g.*, Ex. 44 at 3 (B. Dyr et al., *A New Era in Aneuploidy Screening: cfDNA Testing in >30,000 Multifetal Gestations: Experience at One Clinical Laboratory*, 14 PLOS ONE (2019), https://doi.org/10.1371/journal.pone.0220979) ("This study [of MaterniT21 PLUS samples] analyzed extracted cfDNA fragments from maternal plasma, which were then subjected to genome-wide sequencing and algorithmic analysis for chromosomal aneuploidies and subchromosomal under-representation in specified regions, when requested … An under- or over-representation of fragments in a 50 kb bin are indicative of a loss or gain in the genome profile respectively."); Ex. 38 (https://sema4.com/products/test-catalog/noninvasive-prenatal-testing-nipt-sequenom/#) ("Sequenom noninvasive prenatal testing (NIPT) is a chromosome counting method that analyzes genetic information in fetal cell-free DNA in maternal blood to determine risk for specific fetal chromosomal and subchromosomal abnormalities.").)

131. For example, LabCorp infringes at least exemplary claim 1 of the '720 patent by using the MaterniT Genome test. For example, use of the MaterniT Genome test requires using a method for detecting a free nucleic acid, wherein said method comprises:

a. isolating free nucleic acid (such as cell-free DNA) from a non-cellular fraction of a sample (such as a maternal blood sample) (*see, e.g.*, Ex. 36 at 2 (https://www.integratedgenetics.com/sites/default/files/2020-04/GENOME_Positive%20T18_Sample%20Report.pdf) ("The MaterniT

GENOME laboratory-developed test analyzes the relative amount of chromosomal material across the genome in circulating cell-free DNA from a maternal sample."); Ex. 38 (https://sema4.com/products/test-catalog/noninvasive-prenatal-testing-nipt-sequenom/#) ("Sequenom noninvasive prenatal testing (NIPT) is a chromosome counting method that analyzes genetic information in fetal cell-free DNA in maternal blood to determine risk for specific fetal chromosomal and subchromosomal abnormalities."); Ex. 49 at 2 (M. Ehrich et al., *Genome-Wide cfDNA Screening: Clinical Laboratory Experience with the First 10,000 Cases*, 19 GENETICS IN MEDICINE 1332-37 (2017) (https://www.nature.com/articles/gim201756) (explaining that during the MaterniT Genome laboratory processing, "cfDNA was extracted from plasma")),

b. wherein said sample comprises an agent that impedes cell lysis, if cells are present, and wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor (such as cell-free DNA Streck tubes filled with at least 10mL of maternal blood) (*see, e.g.*, Ex. 38 (https://sema4.com/products/test-catalog/noninvasive-prenatal-testing-nipt-sequenom/#) (listing as a requirement for the MaterniT Genome test "One 10 mL BCT Streck tube"; Ex. 41 at 2 (https://www.streck.com/products/stabilization/cell-free-dna-bct/#resources) (describing Streck cell-free DNA tubes as containing a "unique preservative [which] limits the release of genomic DNA, allowing isolation of high-quality cell-free DNA" and "specialized chemistry" that "limit[s] cell lysis")),

c. detecting the presence or absence of the free nucleic acid (*see, e.g.*, Ex. 49 at 2 (M. Ehrich et al., *Genome-Wide cfDNA Screening: Clinical Laboratory Experience with the First 10,000 Cases*, 19 GENETICS IN MEDICINE 1332-37 (2017) (https://www.nature.com/articles/gim201756) (explaining that during the MaterniT Genome laboratory processing, "[s]equencing results were normalized and analyzed for fetal fraction; chromosome 21, 18, and 13 trisomy; sex chromosome aneuploidies; and other genome-wide whole-chromosome and subchromosome copy-number variants … "); Ex. 38 (https://sema4.com/products/test-catalog/noninvasive-prenatal-testing-nipt-sequenom/#) ("Sequenom noninvasive prenatal testing (NIPT) is a chromosome counting method that analyzes genetic information in fetal cell-free DNA in maternal blood to determine risk for specific fetal chromosomal and subchromosomal abnormalities.").)

132. For example, LabCorp infringes at least exemplary claim 1 of the '720 patent by using the informaSeq test. For example, use of the informaSeq test requires using a method for detecting a free nucleic acid, wherein said method comprises:

a. isolating free nucleic acid (such as cell-free DNA) from a non-cellular fraction of a sample (such as a blood sample) (*see, e.g.*, Ex. 64 at 1 (Press Release, "*LabCorp Announces the Availability of InformaSeq^{SM} Non-Invasive Prenatal Test*" (August 19, 2014), https://ir.labcorp.com/news-releases/news-release-details/labcorp-announces-availability-informaseqsm-non-invasive ("The informaSeq Prenatal Test is an advanced, non-invasive, next-generation prenatal screening assay that can assess risk for multiple fetal chromosomal aneuploidies, or abnormalities in the number of chromosomes, from a single maternal blood draw."); Ex. 20 at 5

(https://www.labcorp.com/tests/related-documents/L13272) (showing the use of the informaSeq test to determine the fetal fraction and any aneuploidy in a blood sample),

b. wherein said sample comprises an agent that impedes cell lysis, if cells are present, and wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor (such as cell-free DNA Streck tubes filled with blood) (*see, e.g.*, Ex. 20 at 3 (https://www.labcorp.com/tests/related-documents/L13272) (listing as a requirement for the MateriT Genome test "[o]ne 10 mL BCT Streck tube"); Ex. 41 at 2 (https://www.streck.com/products/stabilization/cell-free-dna-bct/#resources) (describing Streck cell-free DNA tubes as containing a "unique preservative [which] limits the release of genomic DNA, allowing isolation of high-quality cell-free DNA" and "specialized chemistry" that "limit[s] cell lysis")),

c. detecting the presence or absence of the free nucleic acid (*see, e.g.*, Ex. 20 at 5 (https://www.labcorp.com/tests/related-documents/L13272) (showing the use of the informaSeq test to determine the fetal fraction and any aneuploidy in a blood sample).).

133. For example, LabCorp infringes at least claim 1 of the '720 patent by using the Resolution ctDx Lung Assay test. For example, use of the Resolution ctDx Lung Assay test requires using a method for detecting a free nucleic acid, wherein said method comprises:

a. isolating free nucleic acid (such as circulating tumor DNA) from a non-cellular fraction of a sample (such as a plasma sample) (*see, e.g.*, Ex. 11 at 1 (https://www.labcorp.com/tests/830697/resolution-ctdx-lung-assay-liquid-biopsy)

("The test is a NGS multi-gene panel that assesses circulating tumor DNA (CtDNA) from a plasma sample in patients with non-small cell lung cancer."); Ex. 74 at 2 (http://www.resolutionbio.com/science/) ("The cfDNA is extracted from the plasma for analysis. Through a series of proprietary biochemical steps, we amplify the cfDNA and using very small probes, target and capture strands of ctDNA.")),

b. wherein said sample comprises an agent that impedes cell lysis, if cells are present, and wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor (such as cell-free DNA Streck tubes filled with at least 10mL of blood) (*see, e.g.*, Ex. 11 at 1 (https://www.labcorp.com/tests/830697/resolution-ctdx-lung-assay-liquid-biopsy) (requiring clinicians to "[c]ollect 10 mL of whole blood into each of 2 Streck BCT tubes."); Ex. 41 at 2 (https://www.streck.com/products/stabilization/cell-free-dna-bct/#resources) (describing Streck cell-free DNA tubes as containing a "unique preservative [which] limits the release of genomic DNA, allowing isolation of high-quality cell-free DNA" and "specialized chemistry" that "limit[s] cell lysis")),

c. detecting the presence or absence of the free nucleic acid (*see, e.g.*, Ex. 73 at 1-2 (J.K. Sabari et. al., *A Prospective Study of Circulating Tumor DNA to Guide Matched Targeted Therapy in Lung Cancers*, 111 J. NAT'L CANCER INST. 575-83 (2018), doi: 10.1093/jnci/djy156) (describing the methodology of the Resolution ctDx Lung Assay test, including extracting DNA from a blood sample and performing "targeted plasma [Next-Generation Sequencing] [] using a validated, bias-corrected, hybrid-capture 21-gene assay, ResBio ctDx-Lung" to determine point mutations and copy number alterations); Ex. 11 at 1

(https://www.labcorp.com/tests/830697/resolution-ctdx-lung-assay-liquid-biopsy) ("The test is a NGS multi-gene panel that assesses circulating tumor DNA (CtDNA) from a plasma sample in patients with non-small cell lung cancer.").)

134. LabCorp has infringed, and continues to infringe, one or more claims of the '720 Patent under 35 U.S.C. § 271(a), either literally and/or under the doctrine of equivalents, by using the informaSeq tests, either itself or through its subsidiaries. For example, LabCorp uses the informaSeq tests by processing the informaSeq test samples at its Integrated Genetics laboratories according to the informaSeq test protocols. LabCorp assigns its Integrated Genetics laboratories the task of using the informaSeq tests (by collecting samples and sending them to the Integrated Genetics laboratories for processing), and LabCorp gives interim instructions to control the means and details of the process by which the Integrated Genetics laboratories uses the informaSeq test (by establishing the informaSeq test protocols and requiring the Integrated Genetics laboratories to follow that protocol when processing tests). Integrated Genetics is one of LabCorp's Specialty Testing Groups and LabCorp has the right and the ability to direct and control the activities of the Integrated Genetics laboratories in several ways, including through LabCorp's ownership of the Integrated Genetics laboratories, through instituting programs and measures (such as policies or protocols) at the Integrated Genetics laboratories, and through interim instructions via at least LabCorp's employees at the Integrated Genetics laboratories. Further, the Integrated Genetics laboratories act on behalf of LabCorp, including when the Integrated Genetics laboratories perform tests on LabCorp's behalf for LabCorp's patients, or provides test results to health care providers and/or patients on LabCorp's behalf.

135. LabCorp has infringed, and continues to infringe, one or more claims of the '720 Patent under 35 U.S.C. § 271(a), either literally and/or under the doctrine of equivalents, by

directing and controlling the performance of the informaSeq test, comprising the performance of the patented methods, by its Integrated Genetics laboratories. For example, LabCorp conditions participation in an activity or receipt of a benefit (such as continued funding and status as LabCorp's laboratory) on the Integrated Genetics laboratories' performance of the steps of the patented method (such as the processing of the informaSeq test samples). Further, LabCorp establishes the manner or timing of the performance of the steps of the patented method (such as the Integrated Genetics laboratories' processing of the informaSeqtest samples), including by collecting test samples and sending them to the Integrated Genetics laboratories with instructions to be processed according to the informaSeq test protocols, which include details regarding how the sample is to be collected. On information and belief, employees or other agents of LabCorp (*e.g.*, LabCorp's lab assistants) collect test samples according to the informaSeq test protocols, and the Integrated Genetics laboratories process the test samples according to the informaSeq test protocols.

136. LabCorp has infringed, and continues to infringe, one or more claims of the '720 Patent under 35 U.S.C. § 271(a), either literally and/or under the doctrine of equivalents, by using the MaterniT21 PLUS and MaterniT Genome tests, either itself or through its agent, Sequenom Center. For example, LabCorp assigns its laboratory Sequenom Center the task of using the MaterniT21 PLUS and MaterniT Genome tests (by collecting samples and sending them to Sequenom Center for processing), and LabCorp gives interim instructions to control the means and details of the process by which Sequenom Center uses the MaterniT21 PLUS and MaterniT Genome tests (by establishing the MaterniT21 PLUS and MaterniT Genome test protocols and requiring Sequenom Center to follow those protocols when processing tests). LabCorp has the right and the ability to direct and control the activities of Sequenom Center in several ways,

including through LabCorp's 100% ownership of Sequenom Center, through instituting programs and measures (such as policies or protocols) at Sequenom Center, and through interim instructions via at least LabCorp's employees and/or officers who hold leadership roles at Sequenom Center. Further, Sequenom Center acts on behalf of LabCorp, including when Sequenom Center performs tests on LabCorp's behalf for LabCorp's patients, or provides test results to health care providers and/or patients on LabCorp's behalf.

137. LabCorp has infringed, and continues to infringe, one or more claims of the '720 Patent under 35 U.S.C. § 271(a), either literally and/or under the doctrine of equivalents, by directing and controlling the performance of the MaterniT21 PLUS and MaterniT Genome tests, comprising the performance of the patented methods, by its laboratory Sequenom Center, either directly or through its wholly-owned subsidiary Sequenom. For example, LabCorp conditions participation in an activity or receipt of a benefit (such as continued funding, status as LabCorp's laboratory, and payments related to discrete tests performed) on Sequenom Center's performance of the steps of the patented method (such as the processing of the MaterniT21 PLUS and MaterniT Genome test samples). Further, LabCorp establishes the manner or timing of the performance of the steps of the patented method (such as the Sequenom Center's processing of the MaterniT21 PLUS and MaterniT Genome test samples), including by collecting test samples and sending them to Sequenom Center with instructions to be processed according to the MaterniT21 PLUS and MaterniT Genome test protocols, which includes details regarding how the sample is to be collected. On information and belief, employees or other agents of LabCorp (*e.g.*, LabCorp's lab assistants) collect test samples according to the MaterniT21 PLUS and MaterniT Genome test protocols, and Sequenom Center processes the test samples according to the MaterniT21 PLUS and MaterniT Genome test protocols.

138. LabCorp has infringed, and continue to infringe, one or more claims of the '720 Patent under 35 U.S.C. § 271(a), either literally and/or under the doctrine of equivalents, by directing and controlling the performance of the Resolution ctDx Lung Assay tests, comprising the performance of the patented methods, by Resolution Bioscience. For example, LabCorp conditions participation in an activity or receipt of a benefit (such as such as a continued commercial partnership with LabCorp) on Resolution Bioscience's performance of the steps of the patented method (such as the processing of the Resolution ctDx Lung Assaytest samples). Further, LabCorp establishes the manner or timing of the performance of the steps of the patented method (such as the Resolution Bioscience's processing of the Resolution ctDx Lung Assay test samples), including by collecting test samples and sending them to Resolution Bioscience with instructions to be processed according to the Resolution ctDx Lung Assay test protocol, which includes details regarding how the sample is to be collected. On information and belief, employees or other agents of LabCorp (*e.g.*, LabCorp's lab assistants) collect test samples according to Resolution ctDx Lung Assay test protocols, and Resolution Bioscience processes the test samples according to the Resolution ctDx Lung Assay test protocols.

139. LabCorp has infringed, and continues to infringe, one or more claims of the '720 Patent under 35 U.S.C. § 271(a), either literally and/or under the doctrine of equivalents, by offering for sale and selling the performance of infringing methods, such as by offering for sale and selling the MaterniT21 PLUS, MaterniT Genome, informaSeq, and Resolution ctDx Lung Assay tests. LabCorp's offers for sale and sales of the MaterniT21 PLUS, MaterniT Genome, informaSeq, and Resolution ctDx Lung Assay tests comprise the obligation to perform the steps of the patented methods. For example, when a patient agrees to pay (or for her insurer to pay) in exchange for the MaterniT21 PLUS, MaterniT Genome, informaSeq, or Resolution ctDx Lung

Assay tests, on information and belief, LabCorp accepts the obligation, directly or through one or more subsidiaries and/or intermediaries, to perform a test pursuant to the MaterniT21 PLUS, MaterniT Genome, informaSeq, or Resolution ctDx Lung Assay test protocols for the patient's sample(s), including the acts of collecting a patient sample according to the MaterniT21 PLUS, MaterniT Genome, informaSeq, or Resolution ctDx Lung Assay test protocols, preparing such sample for analysis so that it comprises an agent that impedes cell lysis, if cells are present, wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor; isolating free nucleic acid from a non-cellular fraction of a sample; detecting the presence or absence of the free nucleic acid; and reporting results to a health care provider and/or the patient.

140. In addition or in the alternative, LabCorp induces infringement, and continues to induce infringement, of one or more claims of the '720 Patent under 35 U.S.C. § 271(b). LabCorp actively, knowingly, and intentionally induced, and continues to actively, knowingly, and intentionally induce, infringement of the '720 Patent by supplying the MaterniT21 PLUS and MaterniT Genome tests with the knowledge and intent that Sequenom Center will use the MaterniT21 PLUS and MaterniT Genome tests supplied by LabCorp to infringe the '720 Patent; and with the knowledge and intent to encourage and facilitate third-party infringement through the dissemination of the MaterniT21 PLUS and MaterniT Genome tests and/or the creation and dissemination of promotional and marketing materials, supporting materials, instructions, product manuals, and/or technical information related to the MaterniT21 PLUS and MaterniT Genome tests.

141. LabCorp specifically intends and is aware that the ordinary and customary use of the MaterniT21 PLUS and MaterniT Genome tests would infringe the '720 Patent. For example, LabCorp provides the MaterniT21 PLUS and MaterniT Genome tests, which when used in their

ordinary and customary manner intended and instructed by LabCorp, infringe one or more claims of the '720 Patent, including at least exemplary claim 1. LabCorp further provides product manuals and other instructional materials that cause Sequenom Center to use the MaterniT21 PLUS and MaterniT Genome tests for their ordinary and customary use. Sequenom Center has directly infringed the '720 Patent, including at least exemplary claim 1, through the normal and customary use of the MaterniT21 PLUS and MaterniT Genome tests. LabCorp accordingly has induced and continues to induce Sequenom Center to use the MaterniT21 PLUS and MaterniT Genome tests in their ordinary and customary way to infringe the '720 Patent, knowing, or at least being willfully blind to the fact, that such use constitutes infringement of the '720 Patent.

142. Additionally, Labcorp actively, knowingly, and intentionally induced, and continues to actively, knowingly, and intentionally induce, infringement of the '720 Patent by supplying the Resolution ctDx Lung Assay test with the knowledge and intent that Resolution Bioscience will use the Resolution ctDx Lung Assay tests supplied by LabCorp to infringe the '720 Patent; and with the knowledge and intent to encourage and facilitate third-party infringement through the dissemination of the Resolution ctDx Lung Assay tests and/or the creation and dissemination of promotional and marketing materials, supporting materials, instructions, product manuals, and/or technical information related to the Resolution ctDx Lung Assay tests.

143. LabCorp specifically intends and is aware that the ordinary and customary use of the Resolution ctDx Lung Assay tests would infringe the '720 Patent. For example, LabCorp provides the Resolution ctDx Lung Assay tests, which when used in their ordinary and customary manner intended and instructed by LabCorp, infringe one or more claims of the '720 Patent, including at least exemplary claim 1. LabCorp further provides product manuals and other instructional materials that cause Resolution Bioscience to operate the Resolution ctDx Lung

Assay tests for their ordinary and customary use. Resolution Bioscience has directly infringed the '720 Patent, including at least exemplary claim 1, through the normal and customary use of the Resolution ctDx Lung Assay test. LabCorp accordingly has induced and continues to induce Resolution Bioscience to use the Resolution ctDx Lung Assay test in their ordinary and customary way to infringe the '720 Patent, knowing, or at least being willfully blind to the fact, that such use constitutes infringement of the '720 Patent.

144. In addition or in the alternative, LabCorp has contributed and continues to contribute to the infringement by third parties, including Sequenom Center and Resolution Bioscience, of one or more claims of the '720 Patent under 35 U.S.C. § 271(c), by making, selling and/or offering for sale in the United States, and/or importing into the United States, the MateriT21 PLUS, MateriT Genome, and Resolution ctDx Lung Assay tests, knowing that those products constitute a material part of the inventions of the '720 Patent, knowing that those products are especially made or adapted to infringe the '720 Patent, and knowing that those products are not staple articles of commerce suitable for substantial non-infringing use.

145. On information and belief, LabCorp has had knowledge of and notice of the '720 Patent at least since December 2010, as evidenced by communications between Ravgen and LabCorp and/or its subsidiaries. On information and belief, LabCorp has had knowledge of and notice of its infringement of the '720 Patent at least since it began making, using, selling, and offering for sale each of the accused MateriT21 PLUS, MateriT Genome, informaSeq tests, and/or Resolution ctDx Lung Assay tests.

146. LabCorp's infringement of the '720 Patent continues to be willful and deliberate at least since it began making, using, selling, and offering for sale each of the accused MateriT21 PLUS, MateriT Genome, informaSeq tests, and/or Resolution ctDx Lung Assay tests.

147. Ravgen has been and continues to be damaged by LabCorp's infringement of the '720 Patent, and will suffer irreparable injury unless the infringement is enjoined by this Court.

148. LabCorp's conduct in infringing the '720 Patent renders this case exceptional within the meaning of 35 U.S.C. § 285.

PRAYER FOR RELIEF

WHEREFORE, Ravgen prays for judgment as follows:

A. That Defendant has infringed each of the Patents-in-Suit;

B. That Defendant's infringement of each of the Patents-in-Suit has been willful;

C. That Ravgen be awarded all damages adequate to compensate it for Defendant's past infringement and any continuing or future infringement of the Patents-in-Suit up until the date such judgment is entered, including pre- and post-judgment interest, costs, and disbursements as justified under 35 U.S.C. § 284;

D. That any award of damages be enhanced under 35 U.S.C. § 284 as result of Defendant's willful infringement;

E. That this case by declared an exceptional case within the meaning of 35 U.S.C. § 285 and that Ravgen be awarded the attorney fees, costs, and expenses incurred in connection with this action;

F. That Ravgen be awarded either a permanent injunction, or, at least, a compulsory ongoing licensing fee; and

F. That Ravgen be awarded such other and further relief at law or equity as this Court deems just and proper.

DEMAND FOR JURY TRIAL

Plaintiff Ravgen hereby demands a trial by jury on all issues so triable.

Dated: October 16, 2020

Respectfully submitted,

/s/ Deron R. Dacus

Deron R. Dacus
State Bar No. 00790553
The Dacus Firm, P.C.
821 ESE Loop 323, Suite 430
Tyler, TX 75701
Phone: (903) 705-1117
Fax: (903) 581-2543
ddacus@dacusfirm.com

Of Counsel:

John M. Desmarais
Kerri-Ann Limbeek
Kyle Petrie
Frederick J. Ding
Jun Tong
Email: jdesmarais@desmaraisllp.com
Email: klimbeek@desmaraisllp.com
Email: kpetrie@desmaraisllp.com
Email: fding@desmaraisllp.com
Email: jtong@desmaraisllp.com

DESMARAIS LLP
230 Park Avenue
New York, NY 10169
Telephone: 212-351-3400
Facsimile: 212-351-3401

Attorneys for Plaintiff Ravgen, Inc.