

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE**

CLINICAL GENOMICS PTY LTD,	)	
CLINICAL GENOMICS TECHNOLOGIES	)	
PTY LTD, and CLINICAL GENOMICS, INC.,	)	C.A. No. _____
	)	
Plaintiffs,	)	Jury Trial Demanded
	)	
v.	)	
	)	
GRAIL, INC.,	)	
	)	
Defendant.	)	

COMPLAINT FOR PATENT INFRINGEMENT

Clinical Genomics Pty Ltd, Clinical Genomics Technologies Pty Ltd, and Clinical Genomics, Inc. (collectively “Clinical Genomics” or “Plaintiff”) brings this Complaint for patent infringement against Defendant GRAIL, Inc. (“Grail” or “Defendant”), and alleges as follows:

INTRODUCTION

1. In 2022, worldwide, there were approximately 20 million new cases of cancer reported and 10 million cancer-related deaths.¹ Cancer kills more than 600,000 Americans each year.² Cancer is more treatable, and sometimes curable, if it is detected early.³ To detect cancer early, a doctor needs to know where to look, what to look for, and how to look for it.

2. A blood-based test capable of detecting multiple cancers from a single sample would enable detection of many cancers earlier, when treatment is more likely to be effective. The science underlying such a test includes the analysis of cell-free DNA (cfDNA), the identification

¹ *Cancer Statistics*, Nat’l Cancer Inst., <https://www.cancer.gov/about-cancer/understanding/statistics> (last visited Aug. 14, 2026).

² Rebecca L. Siegel et al., *Cancer Statistics, 2025*, 75(1) CA Cancer J. Clin. 10, 13 tbl. 1 (2025) (hereinafter “Siegel 2025”).

³ Sameen Zafar et al., *Emerging biomarkers for early cancer detection and diagnosis: challenges, innovations, and clinical perspectives*, 30 Eur. J. Med. Rsch. 760 (2025).

of patterns of DNA modifications (such as methylation) that can distinguish cancerous from healthy tissue, and the locations within the genome to look for those modifications. This science was the product of decades of work in academic and biotechnology laboratories.

3. Plaintiff Clinical Genomics is a biotechnology company that pioneered novel methods of analyzing the methylation status of DNA for blood-based diagnosis of colorectal cancer. Over more than a decade of research, scientists at Clinical Genomics identified specific gene-region methylation markers that reliably distinguish cancerous tissue from healthy tissue, developed methods to detect those markers in cfDNA isolated from blood plasma, and reduced those discoveries to practice, including by developing and launching Colvera®, a commercial testing product to detect colorectal cancer.

4. In December 2016, Clinical Genomics launched Colvera®, a blood test for colorectal cancer that detected methylation at the sites of the *BCAT1* and *IKZF1* genes in cfDNA isolated from blood plasma. Colvera® was the first commercial test to apply Clinical Genomics' methylation-based circulating tumor DNA detection methods in a clinical setting.⁴ In addition to colorectal cancer, abnormal methylation of *BCAT1* and *IKZF1* genes has been correlated with lung cancer.⁵

5. The methylation-based detection methods that Clinical Genomics developed are protected by multiple United States patents, two of which are at issue in this action: U.S. Patent No. 10,590,468 (the “468 patent”) and U.S. Patent No. 10,941,449 (the “449 patent”)

⁴ Press Release, Clinical Genomics Pty Ltd, *Clinical Genomics Announces the Launch of Colvera™ for Colorectal Cancer Recurrence Monitoring*, GlobeNewswire (Dec. 20, 2016), <https://www.globenewswire.com/news-release/2016/12/20/899154/0/en/Clinical-Genomics-Announces-the-Launch-of-Colvera-for-Colorectal-Cancer-Recurrence-Monitoring.html> (hereinafter “Clinical Genomics Press Release 2016”).

⁵ Faridh Raja Mohamed et al., *A blood test measuring DNA methylation of BCAT1 and IKZF1 for detection of lung adenocarcinoma*, 40 Cancer Treatment Rsch. Commc'ns 100838 (2024).

(collectively, the “Asserted Patents”). Each of the Asserted Patents claims methods involving the bisulfite conversion (a technique to identify locations of methylation) of cfDNA from a blood-derived sample, followed by application of novel methods to detect methylation status of the cfDNA at specific regions to identify or screen for cancer.

6. Defendant GRAIL, Inc. (“Grail”) is a Delaware corporation that develops and commercializes a blood-based multi-cancer early detection test called Galleri. Grail introduced Galleri commercially in June 2021.⁶ Like the methods Clinical Genomics developed, commercialized, and patented, the Galleri test analyzes methylation patterns of cfDNA isolated from blood plasma, using bisulfite conversion and methylation-specific sequencing, to detect cancer signals.⁷

7. Grail markets the Galleri test as capable of detecting cancer signals across more than 50 cancer types, including colorectal cancer.⁸ The Galleri test is administered to a patient population that includes individuals who have or are suspected of having a colorectal neoplasm (an abnormal growth of tissue in the colon). Three of the cancer classes for which Galleri has “high

⁶ Press Release, GRAIL, Inc., *GRAIL Presents Interventional PATHFINDER Study Data at 2021 ASCO Annual Meeting and Introduces Galleri, a Groundbreaking Multi-Cancer Early Detection Blood Test* (June 4, 2021), <https://grail.com/press-releases/grail-presents-interventional-pathfinder-study-data-at-2021-asco-annual-meeting-and-introduces-galleri-a-groundbreaking-multi-cancer-early-detection-blood-test/> (hereinafter “GRAIL Galleri Press Release 2021”).

⁷ Eric A. Klein et al., *Clinical validation of a targeted methylation-based multi-cancer early detection test using an independent validation set*, 32(9) *Annals of Oncology* 1167, 1169 fig. 1 (2021) (hereinafter “Klein 2021”).

⁸ *Healthcare Providers: The Galleri Test*, GRAIL, Inc., <https://www.galleri.com/hcp/the-galleri-test-2> (last visited Aug. 14, 2026) (Galleri “screen[s] for a signal shared by more than 50 types of cancer,” including colorectal cancer); *see also* GRAIL Galleri Press Release 2021 (Galleri “has demonstrated the ability to detect more than 50 types of cancer”).

sensitivity” are colorectal, esophageal, and anal.⁹ Each time Grail performs the Galleri test on a sample from a patient, Grail practices the methods claimed in the Asserted Patents.

8. On information and belief, Grail has sold the Galleri test to a substantial number of patients in the United States since June 2021 and has generated substantial revenue from sales of the Galleri test. For example, Grail has disclosed that its full-year 2024 U.S. Galleri revenue was \$108.6 million, and its full-year 2025 U.S. Galleri revenue was \$136.8 million.¹⁰

9. On information and belief, Grail has had knowledge of the Asserted Patents since prior to the commercial launch of the Galleri test, or at the latest sometime prior to the filing of this Complaint, and Grail has continued to commercialize the Galleri test with knowledge of the Asserted Patents and despite an objectively high risk that the Galleri test infringes the Asserted Patents. Grail’s infringement of the Asserted Patents is willful and deliberate.

10. Clinical Genomics therefore seeks damages for Grail’s ongoing infringement of the Asserted Patents. Clinical Genomics does not seek injunctive relief.

PARTIES

11. Clinical Genomics Technologies Pty Ltd is a company organized under the laws of Australia. Its principal place of business is c/o OneVentures Pty Ltd, 179 Elizabeth Street Suite 13, Sydney NSW 2000, Australia.

12. Clinical Genomics Pty Ltd and Clinical Genomics, Inc. are wholly owned subsidiaries of Clinical Genomics Technologies Pty Ltd.

⁹ *Healthcare Providers: Test Performance*, GRAIL, Inc., <https://www.galleri.com/hcp/galleri-test-performance> (last visited Aug. 14, 2026).

¹⁰ Press Release, GRAIL, Inc., *GRAIL Reports Fourth Quarter and Full Year 2024 Financial Results* (Feb. 20, 2025), <https://grail.com/press-releases/grail-reports-fourth-quarter-and-full-year-2024-financial-results/>; Press Release, GRAIL, Inc., *GRAIL Reports Fourth Quarter and Full Year 2025 Financial Results* (Feb. 19, 2026), <https://grail.com/press-releases/grail-reports-fourth-quarter-and-full-year-2025-financial-results/>.

13. Clinical Genomics Pty Ltd is a company organized under the laws of Australia. Its principal place of business is c/o OneVentures Pty Ltd, 179 Elizabeth Street Suite 13, Sydney NSW 2000, Australia.

14. Clinical Genomics Pty Ltd is the owner and assignee of the Asserted Patents.

15. Clinical Genomics, Inc. is a company organized under the laws of the State of Delaware. Its principal place of business is c/o Corporation Service Company, 251 Little Falls Dr., Wilmington, DE 19808.

16. Clinical Genomics, Inc. holds an exclusive license to practice, sublicense, and enforce the Asserted Patents in the United States.

17. On information and belief, Grail is a company organized under the laws of the State of Delaware with its principal place of business at 1525 O'Brien Drive, Menlo Park, CA 94025.

JURISDICTION AND VENUE

18. This suit is an action for patent infringement arising under 35 U.S.C. § 1, *et seq.*

19. This Court has subject matter jurisdiction under 28 U.S.C. §§ 1331 and 1338(a) because this is an action for infringement under the patent laws of the United States.

20. This Court has personal jurisdiction over Grail because the company was formed and incorporated in Delaware. Further, Grail has, directly or through its agents and/or intermediaries, committed acts within Delaware giving rise to this action, including the offer for sale and sale of infringing Galleri tests. Further, Grail established minimum contacts with Delaware such that the exercise of jurisdiction would not offend traditional notions of fair play and substantial justice. For example, Grail has purposefully availed itself of the benefits and protections of Delaware's laws, including its laws of incorporation, such that it should reasonably anticipate litigation in Delaware.

21. On information and belief, Grail, directly or through its agents and/or intermediaries, makes, uses, imports, offers for sale, sells, and/or advertises the Galleri test in Delaware. Further, on information and belief, Grail has placed and continues to place infringing products into the stream of commerce through an established distribution channel and with the knowledge and/or understanding that such products are sold in the United States, including in Delaware.

22. On information and belief, Grail has derived substantial revenue from its infringing activity occurring in this District and/or should reasonably expect its infringing actions to have consequences and subject Grail to suit in this District. Further, Grail has committed patent infringement in this District that has led to foreseeable harm and injury to Clinical Genomics.

23. Under 28 U.S.C. § 1400(b), venue is proper in Delaware because Grail is a Delaware corporation.

BACKGROUND

I. Cancer Screening Saves Lives

24. Cancer is among the leading causes of death in the world. In the United States alone, the American Cancer Society projected that 2,041,910 Americans would be diagnosed with cancer in 2025, and 618,120 would die from the disease that same year.¹¹ Further, the typical age at which a cancer patient receives a first diagnosis is getting younger. Between 1995 and 2021, the proportion of adults aged 50–64 years in the cancer patient population increased from 25% to 29%.¹²

¹¹ Siegel 2025 at 13 tbl. 1.

¹² *Id.* at 12.

25. The stage of cancer at diagnosis is the most important determinant of treatment outcomes. For cancer types that are typically discovered only after they have spread, including lung and pancreatic cancers, the overall five-year relative survival rate remains below 30%.¹³ Colorectal cancer is the third leading cause of cancer deaths in men and fourth in women, responsible for 9% and 8% of cancer deaths, respectively.¹⁴ In the United States in 2026, the American Cancer Society projects approximately 160,000 new cases of colorectal cancer and approximately 55,000 deaths attributable to colorectal cancer.¹⁵ Detecting cancer early, before symptoms emerge and before metastasis, is therefore among the most consequential interventions in oncology.

26. Despite the proven value of early detection, patient adoption and coverage remain incomplete. And until recently, there was no established screening paradigm for many types of cancer (and thus no way to stay up to date on screening). In 2023, an estimated 80.0% of American adults were up to date on recommended breast cancer screening, but just 67.4% were up to date on recommended colorectal cancer screening.¹⁶ Certain characteristics are associated with an even lower screening prevalence, such as being uninsured (25%) and having less than a high school education (51%).¹⁷ Blood-based screening tests provide advantages in improving this situation—

¹³ *Id.* at 22 (reporting overall five-year relative survival of 27% for lung cancer and 13% for pancreatic cancer).

¹⁴ *Id.* at 18 fig. 1.

¹⁵ Rebecca L. Siegel et al., *Colorectal cancer statistics, 2026*, CA Cancer J. Clin. e70067, 3 (2026) (hereinafter “Siegel 2026”).

¹⁶ Susan A. Sabatino et al., *Use of Cancer Screening Tests, United States, 2023*, 22(E52) Preventing Chronic Disease 250139 (2025) (reporting age-standardized estimates of adults up to date with screening test use in 2023).

¹⁷ Siegel 2026.

when presented with the option, patients who had declined colorectal cancer screening to date strongly preferred a blood-based screening test to fecal testing.¹⁸

27. A blood-based screening test capable of detecting multiple cancers from a single sample would dramatically expand the population of cancers reachable by routine screening and thereby substantially improve cancer treatment outcomes. The scientists at Clinical Genomics dedicated decades of research into the biology of tumor-derived cfDNA and the chemical modifications that distinguish cancerous from healthy tissue, including novel methods to detect and characterize those chemical modifications, to make that goal a reality.

II. Cell-Free DNA and DNA Methylation Enable Blood-Based Cancer Detection

28. Human blood contains fragments of DNA not encapsulated within cells, called cell-free DNA (cfDNA), shed by cells throughout the body. In a person with cancer, the cfDNA in circulation includes a small fraction derived from tumor cells, often called circulating tumor DNA. Multiple studies have shown that this tumor-derived cfDNA can be isolated from a blood plasma sample and analyzed to detect the presence of cancer and to identify the tissue where the cancer originated.¹⁹ One of the ways scientists detect and identify cancer DNA is by using molecular modifications to the cancer DNA, called methylation.

29. Methylation is a chemical modification of a DNA molecule in which a methyl group (-CH₃) is added to a cytosine residue in a strand of DNA. Methylation is a chemical modification to a cytosine residue, and thus does not change the sequence of base pairs in the DNA molecule. Instead, methylation typically impacts gene expression. Such a modification is referred

¹⁸ Elizabeth G. Liles et al., *Uptake of a colorectal cancer screening blood test is higher than of a fecal test offered in clinic: A randomized trial*, 10 Cancer Treatment & Rsch. Commc'ns 27, 30 (2017).

¹⁹ See, e.g., Klein 2021.

to as an “epigenetic” modification. Methylation typically represses gene expression (turns a gene “off”) and demethylation promotes gene expression (turns a gene “on”). In cancer cells, methylation patterns change in characteristic ways. For example, regions of the genome that are unmethylated in healthy tissue often become hypermethylated in tumors. This hypermethylation often allows for unchecked cell growth. Because these methylation changes are both tissue-specific and disease-specific, the methylation pattern of tumor-derived cfDNA can be used both to detect the presence of cancer and to identify the tissue from which it originated.²⁰

30. Therefore, DNA methylation patterns provide one of the most informative biological signals to distinguish tumor-derived cfDNA from cfDNA shed by healthy cells. Because the patterns of methylation are often tissue-specific, these molecular signatures can be used to determine the tissue of origin for the DNA with a particular methylation pattern. This information allows doctors to determine the origin of the cancer signal.

31. Standard DNA sequencing techniques do not differentiate between methylated and unmethylated cytosine residues. In other words, the output of standard sequencing approaches cannot indicate which sequenced cytosine residues are methylated and which are not.

32. But DNA sequencing techniques may be used to detect methylation patterns by first chemically modifying the DNA molecule to convert unmethylated cytosine into uracil by a chemical reaction called deamination (removing an amine group), while leaving methylated cytosine (i.e., 5-methylcytosine) unchanged. In the resulting sequence output, the presence of a cytosine indicates the presence of a methylated cytosine at that position in the original molecule,

²⁰ *Id.*; Minetta C. Liu et al., *Sensitive and specific multi-cancer detection and localization using methylation signatures in cell-free DNA*, 31(6) *Annals of Oncology* 745 (2020) (hereinafter “Liu 2020”).

and the presence of a uracil indicates the presence of an unmethylated cytosine. This allows scientists to “see” the methylation pattern of a gene in the sequencing results.

33. One chemical method to perform this conversion is bisulfite conversion (or bisulfite treatment). The use of bisulfite conversion as the basis for a sequencing-based method to determine DNA methylation patterns was first published in a landmark 1992 study.²¹ Bisulfite treatment chemically converts unmethylated cytosines (C) into uracil (U) while leaving 5-methylcytosines unchanged.

34. After bisulfite conversion, a DNA sample is typically amplified (via polymerase chain reaction (PCR) or other methods) to create many additional copies of the DNA. The sample is then subjected to sequencing (which identifies the order of nucleotides in a DNA strand) and/or other analytical methods which allow discrimination between methylated and unmethylated cytosines.

35. Since Dr. Frommer and her colleagues first published their method for bisulfite treatment, other equivalent techniques have been developed to perform this chemical modification of unmethylated cytosine residues in order to detect methylation via sequencing. For example, at least one enzymatic technique to perform the deamination of unmethylated cytosine residues has been reported.²²

²¹ Marianne Frommer et al., *A genomic sequencing protocol that yields a positive display of 5-methylcytosine residues in individual DNA strands*, 89(5) PNAS 1827 (1992) (hereinafter “Frommer 1992”).

²² Twist Bioscience Corp., *Tech Note: Highly Sensitive Methylation Detection Using Enzymatic Methyl-seq and Twist Target Enrichment* (2021), https://www.twistbioscience.com/content/dam/twistbioscience/resources/2021-11/TechNote_NGS_HighlySensitiveMethylationDetectionUsingEnzymaticMethyl-seqandTwistTE_11NOV21_Rev2.0.pdf (discussing NEBNext[®] Enzymatic Methyl-seq (EM-seq[™])).

36. The chemical conversion of unmethylated cytosine residues to uracil is the underlying chemical processing step in essentially every modern DNA methylation assay, including the methods claimed in the Asserted Patents and the accused Galleri test.²³ But that conversion alone does not allow the detection of cancer—useful application of this chemical conversion depends on its application within specific methods for interrogating the methylation status of DNA regions, and the identification of relevant targets of analysis within the genome.

37. The successful performance of a method for detecting cancer that is based on analysis of methylation patterns is fundamentally dependent on the development and use of reliable, sensitive, repeatable methods of detecting subtle differences in methylation patterns of a DNA sample, including various states of partial methylation.

38. The successful performance of a methylation-based cancer detection method also depends on which regions in the genome are interrogated. Identifying which methylation changes in cfDNA reliably distinguish cancer from healthy tissue, and developing methods to measure those changes from the minute quantities of tumor-derived cfDNA in a blood sample, required years of laboratory research. Multi-cancer early detection (“MCED”) tests are built on this science, including the accused Galleri test. Those tests use targeted bisulfite sequencing and/or methylation-specific amplification across panels of informative methylation regions to detect

²³ Klein 2021 at 1169 fig. 1 (“Plasma cfDNA underwent bisulfite sequencing targeting a panel of >100 000 informative methylation regions.”); *see also* Ex. A, U.S. Patent No. 10,590,468, claim 1 (reciting that the method comprises “contacting a nucleic acid sample with an agent which modifies unmethylated cytosine residues”).

cancer signals across many cancer types from a single blood draw.²⁴ One of the key innovations made by Clinical Genomics was identification of certain regions within the genome where application of these methods leads to a reliable indicator about the presence of cancer.

III. Clinical Genomics Developed the Methylation-Based Cancer Detection Technology Claimed in the Asserted Patents and Identified Particular Hypermethylation Patterns Indicative of Cancer

39. Plaintiff Clinical Genomics is an Australian biotechnology company. It was founded in 2006 after Quest Diagnostics spun out certain assets from its purchase of Enterix, a colorectal cancer screening company. From its founding, Clinical Genomics worked in close collaboration with the Commonwealth Scientific and Industrial Research Organisation (“CSIRO”), Australia’s national science agency, and Flinders University on the development of molecular biomarkers for the detection of colorectal cancer.²⁵

A. Discovery of Genes with Elevated Methylation in Cancer Tissue

40. The Clinical Genomics research program focused on identifying DNA methylation targets that reliably distinguish colorectal cancer tissue from healthy tissue, and on developing methods to detect those markers in plasma cell-free DNA. One of the lead scientists in that program was Dr. Peter L. Molloy of CSIRO. Earlier in his career, Dr. Molloy was a co-author of the 1992

²⁴ Klein 2021; Liu 2020; *see also* Susanne K. Pedersen et al., CAHM, *a long non-coding RNA gene hypermethylated in colorectal neoplasia*, 9(8) Epigenetics 1071 (2014) (hereinafter “Pedersen 2014”) (analyzing plasma cfDNA using “quantitative methylation-specific PCR (qMSP)” on bisulfite-converted DNA); Graeme P. Young et al., *Evaluation of a panel of tumor-specific differentially-methylated DNA regions in IRF4, IKZF1 and BCAT1 for blood-based detection of colorectal cancer*, 13 Clinical Epigenetics 14 (2021) (hereinafter “Young 2021”) (analyzing plasma cell-free DNA via a “multiplexed real-time PCR assay targeting DMRs [differentially-methylated regions]” on bisulfite-converted DNA).

²⁵ Susan M. Mitchell et al., *A panel of genes methylated with high frequency in colorectal cancer*, 14 BMC Cancer 54 (2014) (hereinafter “Mitchell 2014”); Susan M. Mitchell et al., *Evaluation of Methylation Biomarkers for Detection of Circulating Tumor DNA and Application to Colorectal Cancer*, 7(125) Genes (2016).

study that established bisulfite genomic sequencing, the chemical method that is now the foundation for DNA methylation analyses.²⁶

41. Over more than a decade, scientists at Clinical Genomics, in collaboration with scientists at CSIRO and Flinders University, including Clinical Genomics' founder Lawrence C. LaPointe, chief research scientist Susanne K. Pedersen, Susan M. Mitchell, Rohan Baker, and Professor Graeme Young, published a series of peer-reviewed papers describing methylation biomarkers in colorectal cancer. That early work led to the team's 2012 publication on validating the use of molecular biomarkers for detecting colon cancer through blood testing.²⁷

42. The team continued its work and identified additional biomarkers related to colorectal cancer. In 2014, the team published a comprehensive analysis of 23 genes with elevated methylation in colorectal cancer tissue, identifying *BCAT1*, *IKZF1*, *IRF4*, *GRASP*, and other genes as suitable targets of methylation analysis for blood-based cancer detection.²⁸

43. Also in 2014, the team published the discovery and characterization of *CAHM* (Colorectal Adenocarcinoma HyperMethylated), a long non-coding RNA gene that is hypermethylated in colorectal cancer tissue, with the amount of methylated *CAHM* in cfDNA increasing with cancer stage.²⁹

44. Clinical Genomics' research continued in the years that followed. In 2021, scientists from Clinical Genomics and collaborating institutions published a clinical evaluation of

²⁶ Frommer 1992 (listing Peter L. Molloy among the co-authors).

²⁷ Lawrence C. LaPointe et al., *Discovery and Validation of Molecular Biomarkers for Colorectal Adenomas and Cancer with Application to Blood Testing*, 7(1) PLoS ONE e29059 (2012).

²⁸ Mitchell 2014.

²⁹ Pedersen 2014.

a multi-gene methylation panel targeting differentially methylated regions in *IRF4*, *IKZF1*, and *BCAT1* for the blood-based detection of colorectal cancer.³⁰

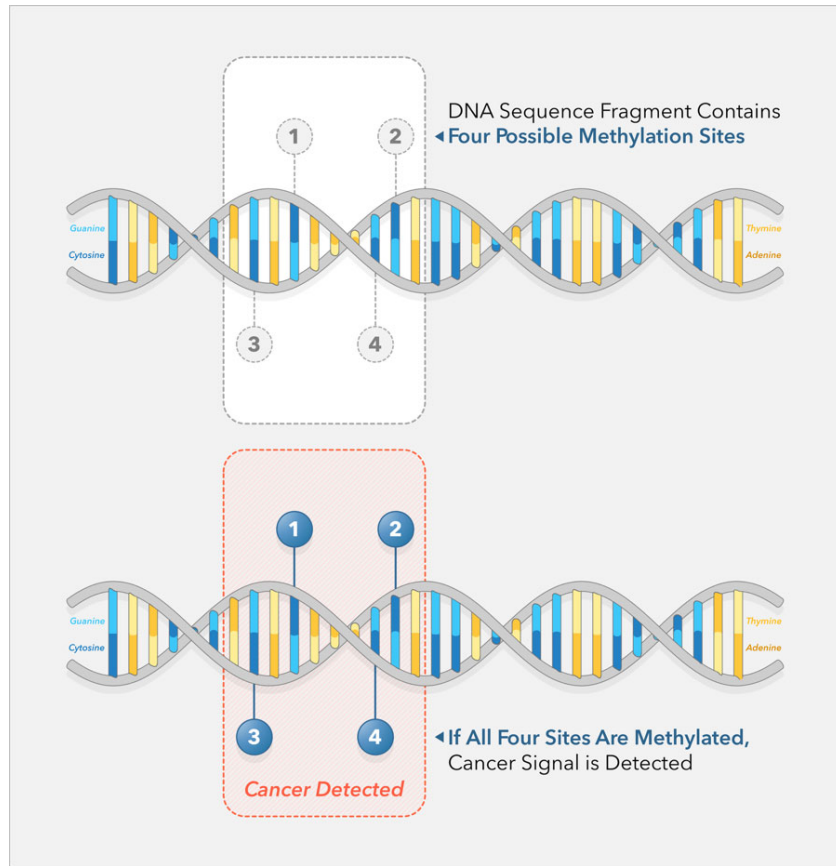
45. Clinical Genomics filed for and was granted patents on the methylation biomarker panels and methods developed through its research program, including the Asserted Patents in this action. The Asserted Patents are described in further detail in Section IV below.

B. Clinical Genomics Discovers Significance of Partial Methylation and Develops Novel Methods to Characterize It

46. The scientists at Clinical Genomics did not only discover important cancer biomarkers. They also identified that multiple patterns of methylation are indicative of cancer and developed a method for harnessing that discovery.

47. Abnormal methylation patterns in certain genes had previously been identified as useful for the detection of cancer. But in the early 2010s, methylation was thought to be an all-or-nothing signal. For example, the illustration below shows a sample fragment of a DNA sequence that contains four possible methylation sites. Prior analytical methods detected whether a DNA sample contained copies of this sequence with all four sites methylated.

³⁰ Young 2021.



48. In contrast to the prior all-or-nothing techniques, the scientists at Clinical Genomics made innovations that allow for detection of cancer signals through patterns of methylation, including partial methylation. For example, the scientists at Clinical Genomics invented novel methods of using methylation-specific primers in an amplification step followed by one or more methylation-sensitive probes to analyze methylation state. These novel methods allowed scientists to obtain accurate results regarding the methylation state (including partial methylation state) of the genomic region of interest. These innovations allow for the more nuanced detection of cancer.

49. The innovations made by the scientists at Clinical Genomics were initially driven by their observations of the melting behavior of DNA samples. The “melting” temperature of a double-stranded DNA sample is the temperature at which the molecule unzips from its double-stranded form such that half of the DNA strands are in a random coil or single-stranded state (also

called “denaturation”). The melting temperature depends on the length of the DNA molecule and on the specific nucleotide sequence.

50. Different base pairs and sequences of bases have different impacts on the melting temperature of a DNA sample. In general, a higher proportion of adenine-thymine (A-T) base pairs is associated with a lower melting temperature. Bisulfite (or equivalent) treatment converts unmethylated cytosine (C) residues to uracil (U) residues. Uracil is a base that is not typically present in biological samples of DNA, so subsequent DNA-based amplification steps then encode U as T. As a result, bisulfite (or equivalent) conversion causes the proportion of A-T base pairs to increase relative to an untreated sample, in proportion to the extent of methylation present. So if a given DNA molecule has regions which are methylated, it is expected to have a lower melting temperature after bisulfite (or equivalent) treatment as compared to an untreated copy of the same molecule.

51. Beginning in 2012, Clinical Genomics scientists observed that a cancer-derived DNA sample associated with the gene *IKZF1* had a melting temperature roughly 1.5 °C lower than a control sample. As discussed above, in methylation-specific analysis, the melt temperature of a sample depends on how many sites on the DNA were methylated.

52. By May 2012, further analysis by Clinical Genomics scientists showed that certain cancer-derived *IKZF1* samples exhibited two distinct melt peaks (i.e., two different melting temperature values for the same sample).

53. Scientists at Clinical Genomics hypothesized that the two-melt peak phenomenon was caused by partial methylation in DNA regions with repeating pairs of the nucleotide sequence CG (called CpG sites). In other words, some of the cytosines in the cancer DNA had been methylated, but not all of them. The team eventually confirmed their hypothesis that DNA that

was only partially methylated could be indicative of cancer. They then designed a new method to detect both full and partial methylation states of the DNA—allowing detection of cancer cases that prior tests would have missed. These new methods include nonconventional applications of laboratory techniques and analytical techniques which confer specific improvements that were previously unknown.

C. Colvera®

54. In December 2016, Clinical Genomics launched its commercial product, Colvera®, a blood test for the detection of methylated *BCAT1* and *IKZF1* DNA from circulating tumor DNA in patients with colorectal cancer. *BCAT1* and *IKZF1* are hypermethylated in approximately 95% of colorectal cancer cases. Analysis of Colvera® samples was performed in Clinical Genomics' CLIA-registered clinical laboratory in Bridgewater, New Jersey, with Quest Diagnostics providing specimen collection and logistics services.³¹

55. Although Clinical Genomics is no longer engaged in commercial operations, the methods for detection and analysis of methylation patterns that it developed in collaboration with CSIRO and Flinders University remain the core science underlying methylation-based circulating tumor DNA cancer detection, and the Asserted Patents that protect those methods remain in force.

IV. The Asserted Patents

56. Clinical Genomics is the owner of two United States patents that claim methods and associated diagnostic kits for the detection of DNA methylation relevant to the detection of cancer: U.S. Patent Nos. 10,590,468 and 10,941,449 (collectively, the “Asserted Patents”).

³¹ Clinical Genomics Press Release 2016.

A. U.S. Patent No. 10,590,468

57. The United States Patent and Trademark Office lawfully issued U.S. Patent No. 10,590,468 (the “’468 patent”) on March 17, 2020. The ’468 patent is titled “Method for Methylation Analysis.” The inventors of the ’468 patent are Susanne Pedersen and Rohan Baker. A true and correct copy of the ’468 patent is attached hereto as Exhibit A.

58. The ’468 patent issued from U.S. Patent App. No. 15/315,931.

59. The ’468 patent claims priority to Australian Patent App. No. 2014902155, filed on June 5, 2014. The ’468 patent is therefore entitled to a priority date of no later than June 5, 2014.

60. The ’468 patent claims, among other things, novel and unconventional methods for detecting cytosine methylation of a nucleic acid target of interest by contacting a nucleic acid sample with an agent which modifies unmethylated cytosine residues, followed by measurement, in a single reaction, of regions of partial methylation using primer sets and probes capable of collectively hybridizing to at least two differing methylation patterns at the target region.

61. The claimed methods of the ’468 patent comprise specific, unconventional sequences of laboratory techniques, not dictated by any natural phenomenon, for detecting cytosine methylation of a nucleic acid target of interest.

62. Clinical Genomics is the assignee of the ’468 patent and is the sole owner of all right, title, and interest in and to the ’468 patent.

B. U.S. Patent No. 10,941,449

63. The United States Patent and Trademark Office lawfully issued U.S. Patent No. 10,941,449 (the “’449 patent”) on March 9, 2021. The ’449 patent is titled “Method of Screening for Colorectal Cancer.” The inventors of the ’449 patent are Lawrence Charles LaPointe, Susanne K. Pedersen, Rohan Baker, Snigdha Gaur, and Melissa Thomas. A true and correct copy of the ’449 patent is attached hereto as Exhibit B.

64. The '449 patent issued from U.S. Patent App. No. 14/401,157.

65. The '449 patent claims priority to U.S. Provisional Patent App. No. 61/648,821, filed on May 18, 2012. The '449 patent is therefore entitled to a priority date of no later than May 18, 2012.

66. The '449 patent claims, among other things, novel and unconventional methods comprising measuring a methylation level of a DNA region of a sample from an individual having or suspected of having a large intestine neoplasm, comprising selecting a patient known to have or suspected of having a large intestine neoplasm, obtaining a blood-derived sample of cfDNA, bisulfite converting the cfDNA, and detecting a level of methylation in the bisulfite-converted cfDNA in a region comprising specified locations in the human genome.

67. The claimed methods of the '449 patent comprise specific, unconventional sequences of laboratory techniques, not dictated by any natural phenomenon, for measuring a methylation level of a DNA region of a sample from an individual having or suspected of having a large intestine neoplasm.

68. Clinical Genomics is the assignee of the '449 patent and is the sole owner of all right, title, and interest in and to the '449 patent.

V. Grail's Galleri Test Infringes the Asserted Patents

69. Grail develops and commercializes the Galleri test, a blood-based multi-cancer early detection test that uses targeted methylation analysis of circulating cell-free DNA to detect cancer signals across multiple cancer types from a single blood sample.³²

70. Grail introduced the Galleri test commercially on June 4, 2021, in conjunction with the presentation of data from its PATHFINDER study at the 2021 American Society of Clinical

³² Klein 2021; *Galleri*, GRAIL, Inc., <https://www.galleri.com> (last visited Aug. 14, 2026).

Oncology Annual Meeting. Grail markets and sells the Galleri test in the United States as a laboratory-developed test, available by prescription.³³

71. Grail markets the Galleri test as capable of detecting cancer signals across more than 50 cancer types, including colorectal cancer.³⁴

72. The Galleri test operates by analyzing circulating cell-free DNA isolated from a blood plasma sample. As Grail and its collaborators have published in peer-reviewed scientific journals, plasma cell-free DNA processed by the Galleri test undergoes bisulfite sequencing (i.e., bisulfite treatment followed by sequencing) targeting a panel of more than 100,000 informative methylation regions. Machine-learning classifiers then process the bisulfite-sequencing data to detect a cancer signal and to predict the cancer signal origin (the tissue of origin of the detected cancer).³⁵

73. Each time the Galleri test is administered to a patient, Defendant GRAIL, Inc. carries out the steps required by the methods claimed in the Asserted Patents. In particular, the Galleri test: obtains a blood-derived sample comprising circulating cell-free DNA from an individual; isolates and extracts the cell-free DNA from the sample; subjects the cell-free DNA to chemical conversion to convert unmethylated cytosine residues to uracil, such as bisulfite

³³ GRAIL Galleri Press Release 2021.

³⁴ *Id.* (“Galleri has demonstrated the ability to detect more than 50 types of cancer”); Klein 2021 (reporting detection of cancer signals across more than 50 cancer types, including colorectal cancer).

³⁵ Klein 2021 at 1169 fig. 1 (“Plasma cfDNA underwent bisulfite sequencing targeting a panel of >100 000 informative methylation regions.”); Liu 2020; W.H. Wilson Tang et al., *Performance of a targeted methylation-based multi-cancer early detection test by race and ethnicity*, 167 Preventive Med. 107384 (2023).

conversion; and detects the methylation status of DNA regions of the bisulfite-converted DNA by sequencing and amplification with methylation-specific primers and probes.³⁶

74. Galleri is marketed for use in adults at elevated risk for cancer, including adults aged 50 and older. The intended-use population for the Galleri test includes individuals who have or are suspected of having a colorectal neoplasm, and Galleri is marketed and used to screen those individuals for, among other cancer types, colorectal cancer. The Galleri test is therefore administered to, and performs methylation analysis on, cell-free DNA from a population that includes individuals having or suspected of having a large intestine neoplasm.³⁷

75. On information and belief, Grail has sold the Galleri test to a substantial number of patients in the United States since its commercial launch in June 2021, and Grail continues to make, use, sell, and offer for sale the Galleri test in this District and throughout the United States.

76. Grail's making, use, sale, and offer for sale of the Galleri test infringes each of the Asserted Patents, as set forth more fully in Counts I and II below.

VI. Grail Has Known of the Asserted Patents and Has Infringed Willfully

77. On information and belief, Grail has had knowledge of the Asserted Patents since prior to the commercial launch of the Galleri test in June 2021.

78. On information and belief, Grail and its scientists have long monitored the published scientific literature and the issued patent portfolio in the field of methylation-based circulating tumor DNA cancer detection, including the work of Clinical Genomics, CSIRO, and other entities active in that field.

³⁶ Klein 2021; Liu 2020.

³⁷ GRAIL Galleri Press Release 2021; Klein 2021 (reporting detection of cancer signals in colorectal cancer cases).

79. Notwithstanding its knowledge of the Asserted Patents and the high risk that the Galleri test infringes the Asserted Patents, Grail has continued, and continues, to make, use, sell, and offer for sale the Galleri test in the United States. Grail's continuing infringement of the Asserted Patents is willful and deliberate.

80. At the latest, Grail has had actual notice of the Asserted Patents and of its infringement of the Asserted Patents upon service of this Complaint. Grail's ongoing infringement of the Asserted Patents following service of this Complaint is willful.

COUNT I

Patent Infringement of U.S. Patent No. 10,590,468

81. Clinical Genomics incorporates paragraphs 1 through 80 of this Complaint as if fully set forth herein.

82. On March 17, 2020, the United States Patent and Trademark Office lawfully issued the '468 patent, entitled "Method for Methylation Analysis." Clinical Genomics is the sole owner of all right, title, and interest in and to the '468 patent. The '468 patent is valid and enforceable.

83. The invention of the '468 patent is directed to, among other things, methods for detecting cytosine methylation of a nucleic acid target of interest by contacting a nucleic acid sample with an agent which modifies unmethylated cytosine residues followed by measurement, in a single reaction, of regions of partial methylation using primer sets and probes capable of collectively hybridizing to at least two differing methylation patterns at the target region.

84. Grail has infringed, and continues to infringe, one or more claims of the '468 patent, including without limitation claim 1, in violation of 35 U.S.C. § 271(a), literally or under the doctrine of equivalents, by making, using, selling, offering for sale, and/or importing the Galleri test in the United States without authority. For example, each time Grail performs the Galleri test on a blood-derived sample, it practices each step of the methods claimed in the '468 patent.

85. Grail has also infringed, and continues to infringe, the '468 patent in violation of 35 U.S.C. § 271(b) by actively inducing infringement of the '468 patent by others, including healthcare providers who prescribe the Galleri test, patients who submit blood samples for analysis, and Grail's laboratory personnel and contractors. Grail has provided and continues to provide the Galleri test, instructions, marketing materials, and laboratory infrastructure necessary to practice the methods claimed in the '468 patent, with knowledge of the '468 patent and with the specific intent that those methods be practiced.

86. Grail has also infringed, and continues to infringe, the '468 patent in violation of 35 U.S.C. §§ 271(c) and 271(f) by selling, offering for sale, or causing to be supplied in or from the United States the components of the Galleri test, knowing that those components are specially made or specially adapted for practicing the methods claimed in the '468 patent and are not staple articles or commodities of commerce suitable for substantial non-infringing use.

87. Grail had pre-suit knowledge of the '468 patent as alleged in Section VI of the Background above, and at the latest had actual notice of the '468 patent upon service of this Complaint. Grail's infringement of the '468 patent is and has been willful and deliberate.

88. Grail's infringement has damaged Clinical Genomics, and Clinical Genomics is entitled to recover damages adequate to compensate for Grail's infringement of the '468 patent, but in no event less than a reasonable royalty.

COUNT II

Patent Infringement of U.S. Patent No. 10,941,449

89. Clinical Genomics incorporates paragraphs 1 through 88 of this Complaint as if fully set forth herein.

90. On March 9, 2021, the United States Patent and Trademark Office lawfully issued the '449 patent, entitled "Method of Screening for Colorectal Cancer." Clinical Genomics is the

sole owner of all right, title, and interest in and to the '449 patent. The '449 patent is valid and enforceable.

91. The invention of the '449 patent is directed to, among other things, methods comprising measuring a methylation level of a DNA region of a sample from an individual having or suspected of having a large intestine neoplasm, comprising selecting a patient known to have or suspected of having a large intestine neoplasm, obtaining a blood-derived sample of cfDNA, bisulfite converting the cfDNA, and detecting a level of methylation in the bisulfite-converted cfDNA in a region comprising specified locations in the human genome.

92. Grail has infringed, and continues to infringe, one or more claims of the '449 patent, including without limitation claim 1, in violation of 35 U.S.C. § 271(a), literally or under the doctrine of equivalents, by making, using, selling, offering for sale, and/or importing the Galleri test in the United States without authority. For example, each time Grail performs the Galleri test on a blood-derived sample from a patient having or suspected of having a colorectal neoplasm, it practices each step of the methods claimed in the '449 patent.

93. Grail has also infringed, and continues to infringe, the '449 patent in violation of 35 U.S.C. § 271(b) by actively inducing infringement of the '449 patent by others, including healthcare providers who prescribe the Galleri test, patients who submit blood samples for analysis, and Grail's laboratory personnel and contractors. Grail has provided and continues to provide the Galleri test, instructions, marketing materials, and laboratory infrastructure necessary to practice the methods claimed in the '449 patent, with knowledge of the '449 patent and with the specific intent that those methods be practiced.

94. Grail has also infringed, and continues to infringe, the '449 patent in violation of 35 U.S.C. §§ 271(c) and 271(f) by selling, offering for sale, or causing to be supplied in or from

the United States the components of the Galleri test, knowing that those components are specially made or specially adapted for practicing the methods claimed in the '449 patent and are not staple articles or commodities of commerce suitable for substantial non-infringing use.

95. Grail had pre-suit knowledge of the '449 patent as alleged in Section VI of the Background above, and at the latest had actual notice of the '449 patent upon service of this Complaint. Grail's infringement of the '449 patent is and has been willful and deliberate.

96. Grail's infringement has damaged Clinical Genomics, and Clinical Genomics is entitled to recover damages adequate to compensate for Grail's infringement of the '449 patent, but in no event less than a reasonable royalty.

PRAYER FOR RELIEF

WHEREFORE, Clinical Genomics respectfully requests that the Court:

- A. Enter a judgment that Grail infringes each of the Asserted Patents;
- B. Order an award of damages to Clinical Genomics in an amount adequate to compensate Clinical Genomics for Grail's acts of infringement, no less than a reasonable royalty;
- C. Enter a judgment that the infringement was willful and award treble damages under 35 U.S.C. § 284;
- D. Order an accounting to determine the damages to be awarded to Clinical Genomics as a result of Grail's acts of infringement, including an accounting for infringing sales not presented at trial and award additional damages for any such infringing sales;
- E. Assess pre-judgment and post-judgment interest against Grail, together with an award of such interest and costs under 35 U.S.C. § 284;
- F. Enter a finding that this case is exceptional and award Clinical Genomics its costs, expenses, reasonable attorneys' fees, and such other relief as the Court deems just and proper pursuant to 35 U.S.C. § 285; and

G. Grant any such other and further relief as the Court may deem just and proper.

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