

**IN THE UNITED STATES DISTRICT COURT
FOR THE MIDDLE DISTRICT OF NORTH CAROLINA**

NATERA, INC.,

Plaintiff,

v.

NEOGENOMICS LABORATORIES,
INC.,

Defendant.

C.A. No. 1:23-cv-629

JOINT CLAIM CONSTRUCTION STATEMENT

Pursuant to Local Patent Rule 104.3 and the Court’s Scheduling Order (Doc. 213), Plaintiff Natera, Inc. (“Natera”) and Defendant NeoGenomics Laboratories, Inc. (“NeoGenomics”) (collectively, “the Parties”) hereby submit their Joint Claim Construction Statement with respect to the asserted claims of U.S. Patent Nos. 11,519,035 (the “’035 Patent”), and 11,530,454 (the “’454 Patent”).

I. L.P.R. 104.3 (A) – CONSTRUCTIONS OF CLAIMS, TERMS, PHRASES, OR CLAUSES ON WHICH THE PARTIES AGREE

The Parties have met-and-conferred and exchanged email correspondence in an effort to reduce the number of terms to be construed and to identify, narrow, and focus any areas of dispute. Natera and NeoGenomics have each withdrawn multiple terms for construction that were previously disclosed in the Parties’ respective Preliminary Identifications of Claim Terms served on March 1, 2024. The Parties may continue to meet and confer regarding the Parties’ claim constructions.

The Parties expressly reserve the right to rely on any evidence identified by the other party, and any evidence obtained, or that may be obtained, through claim construction discovery. The Parties expressly reserve the right to amend, correct, or supplement their claim construction positions and supporting or rebuttal evidence in response to any change of position by the other party, information received during claim construction discovery, supplementation to contentions (*e.g.*, infringement, invalidity) or for other good cause.

II. L.P.R. 104.3(B) – PROPOSED CONSTRUCTIONS OF EACH DISPUTED CLAIM TERM, PHRASE, OR CLAUSE, TOGETHER WITH AN IDENTIFICATION OF SUPPORTING INTRINSIC AND EXTRINSIC EVIDENCE

Natera’s and NeoGenomics’ proposed construction for each disputed claim term, phrase, or clause, along with citations to the intrinsic and extrinsic evidence each Party intends to rely upon is attached as Exhibit A.

III. L.P.R. 104.3(C) – THE ANTICIPATED LENGTH OF TIME NECESSARY FOR THE CLAIM CONSTRUCTION HEARING

A. Joint Agreement by the Parties

If the Court is to hold a Claim Construction Hearing, the Parties anticipate that a hearing will take no more than 3 hours, with the time divided equally per side. Subject to the Court’s preference, the Parties agree to present the disputed claim terms on a term-by-term basis. The Parties further agree that each Party may reserve time for rebuttal related to each term.

B. Natera's Position

Subject to the Court's preference, for each disputed term, Natera, as the patentee, proposes that it will present its position first, followed by NeoGenomics.

C. NeoGenomics' Position

Because NeoGenomics bears the burden of proof on indefiniteness, NeoGenomics proposes presenting its position first with respect to the terms it asserts are indefinite. NeoGenomics agrees with Natera's proposal for Natera to present its position first regarding the remaining terms.

IV. L.P.R. 104.3(D) – IDENTIFICATION OF WITNESSES AND SUMMARY OF OPINIONS

A. Natera's Position

(1) *Claim Construction Hearing*

Natera may offer live witness testimony at the hearing from Natera's technical expert, Dr. Michael Metzker, to explain, or respond to and rebut the opinions offered by Dr. Smith and evidence cited by NeoGenomics, regarding the constructions of any of the claim terms proposed for construction. Natera also may offer live testimony from Dr. Metzker regarding definiteness of the following claim terms from the '454 Patent: "clonal" (claims 3,5,17,19); "subclonal" (claims 4,5,18,19); "present in less than or equal to 0.015% of the cell-free DNA comprising the SNV locus" (claim 14); and "present in 0.005% to 0.015% of the cell-free DNA comprising the SNV locus" (claim 28). Natera further may offer Dr. Metzker to testify at the hearing in support of a plain and ordinary construction for each of the claim terms NeoGenomics argues are indefinite.

(2) *Claim Construction Briefing*

In support of its claim construction briefing, Natera may rely upon prior percipient and expert testimony offered during the Preliminary Injunction phase of this case, consistent with the identification of such testimony as set forth in Exhibit A.

Natera may also rely upon additional written and/or deposition testimony from Dr. Metzker offered as part of claim construction discovery consistent with the identification of such testimony as set forth in Exhibit A and as explained herein. Dr. Metzker may provide testimony in support of Natera's constructions for the claim terms at issue for both the '035 Patent and the '454 Patent. Dr. Metzker also may testify to rebut the constructions advanced by NeoGenomics and any opinions provided by its expert witness(es).

Regarding the '454 Patent claim terms that NeoGenomics alleges are indefinite and not amenable to construction, Dr. Metzker may opine that a person of ordinary skill in the art in could determine with reasonable certainty the meaning of the terms "clonal", "subclonal", "present in less than or equal to 0.015% of the cell-free DNA comprising the SNV locus", "present in 0.005% to 0.015% of the cell-free DNA comprising the SNV locus" based on the context provided by the surrounding claim language, the descriptions provided in the '454 Patent specifications, and the knowledge of a person of ordinary skill in the art. Dr. Metzker may further opine that, in light of the surrounding claim language and the specification of the '454 Patent, the aforementioned claim terms should each be construed according to their plain and ordinary meaning.

Dr. Metzker may modify his opinions, as well as the bases for his opinions, based upon the nature and content of the information that NeoGenomics or its expert witness(es) may produce or disclose.

B. NeoGenomics' Position

NeoGenomics intends to present written testimony from Dr. David I. Smith to show that the '454 Patent, read in light of the specification and the prosecution history, fails to inform those skilled in the art with reasonable certainty about the scope of the following claim terms: “clonal” (claims 3,5,17,19); “subclonal” (claims 4,5,18,19); “present in less than or equal to 0.015% of the cell-free DNA comprising the SNV locus” (claim 14); and “present in 0.005% to 0.015% of the cell-free DNA comprising the SNV locus” (claim 28). As an example, NeoGenomics intends to present written testimony from Dr. Smith that a person of ordinary skill in the art would not be able to determine whether a particular SNV mutation is “clonal” or “subclonal” with reasonable certainty. As another example, NeoGenomics intends to present written testimony from Dr. Smith that a person of ordinary skill in the art would not know with reasonable certainty which of multiple possible ways to use in order to determine whether a method is “capable of detecting an SNV mutation that is present in less than or equal to 0.015% of the cell-free DNA comprising the SNV locus” or “capable of detecting an SNV mutation that is present in 0.005% to 0.015% of the cell-free DNA comprising the SNV locus.”

NeoGenomics further reserves the right to rely on additional written or live testimony of David I. Smith to rebut any claim construction, or the testimony of any expert in support thereof, offered by Natera.

March 15, 2024

/s/ Robert C. Van Arnam

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Rule 83.1(d)*

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**Special Appearance under Local Civil
Rule 83.1(d)*

CERTIFICATE OF SERVICE

I hereby certify that I caused the foregoing document to be served via electronic mail on all counsel of record for Defendant.

Dated: March 15, 2024

/s/ Robert C. Van Arnam

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EXHIBIT A

No.	Patent Claim(s)	Proposed Term	Natera's Proposed Construction and Supporting Intrinsic and Extrinsic Evidence	NeoGenomics' Proposed Construction and Supporting Intrinsic and Extrinsic Evidence
1	'035 Patent, claim 1	"amplifying the tagged products . . . wherein one of the amplification steps comprises targeted amplification"	<u>Claim Construction:</u> Plain and ordinary meaning. <u>Intrinsic Evidence</u> <u>Claims/Specification</u> '035 Patent at 9:9-10:3; 19:62-21:53; 32:18-28; 42:4-33; 55:11-56:3; 63:60-64:29; 68:61-64; 71:53-61; 85:47-67; 87:11-17; 88:53-55; 90:38-91:18; 91:28-35; 94:13-95:23; 99:17-21; 101:28-104:67; 118:14-58; 119:30-44; 156:6-35; claims 1, 12, 13, 14, 15. <u>'035 Patent File History</u> 07/21/2020 Original claims in as-filed patent application 09/16/2020 Non-Final Office Action 12/02/2020 Applicant Response to Non-Final Office Action 03/03/2021 Applicant Response to Final Office Action	<u>Claim Construction:</u> This step is separate from and must occur after completion of (and therefore must use distinct PCR primers from) the step of "tagging . . . with one or more universal tail adapters to generate tagged products." <u>Intrinsic Evidence:</u> 6:6-22 7:9-22 9:33-35 9:44-50 10:4-6 10:16-23 15:52-60 20:27-33 21:12-27 32:18-23 32:52-65 33:12-21 34:10-13 37:31-42 42:4-33 55:41-47

No.	Patent Claim(s)	Proposed Term	Natera's Proposed Construction and Supporting Intrinsic and Extrinsic Evidence	NeoGenomics' Proposed Construction and Supporting Intrinsic and Extrinsic Evidence
			04/09/2021 Notice of Allowance 07/09/2021 Notice of Allowance 01/06/2022 Notice of Allowance 06/10/2022 Notice of Allowance 08/02/2022 Notice of Allowance <u>Extrinsic Evidence:</u> • Opening Declaration of Dr. Michael Metzker in support of Natera's Preliminary Injunction ("PI") Motion dated July 31, 2023 • Rebuttal Declaration of Dr. Brian Van Ness in support of NeoGenomics' PI Opposition dated October 19, 2023 • Reply Declaration of Dr. Michael Metzker in support of Natera's PI Motion dated November 6, 2023	84:43–85:67 86:26-87:28 89:5-16 91:28-41 94:13-25 95:16-23 96:3-6 99:31-45 104:29-40 105:60-63 118:53-58 132:59-67 Example 4 Example 6 Example 7 Example 9 Example 14 Example 15 Example 27 Example 28 Claim 1 Claim 2 Claim 12 Claim 13 Claim 14 Figures 1-8

No.	Patent Claim(s)	Proposed Term	Natera's Proposed Construction and Supporting Intrinsic and Extrinsic Evidence	NeoGenomics' Proposed Construction and Supporting Intrinsic and Extrinsic Evidence
			- September 26, 2023 Deposition testimony of Dr. Metzker - October 4, 2023 Deposition testimony of Dr. Bernhard Zimmermann - October 25, 2023 Deposition testimony of Dr. Brian Van Ness - November 14, 2023 Deposition testimony of Dr. Metzker - November 27, 2023 PI Hearing testimony of Dr. Metzker - IPR2024-00346 (NeoGenomics' Petition for IPR of the '454 Patent and evidence cited in support of its Petition) - Additional written and/or live expert testimony regarding the meaning of this term as understood by a person of ordinary skill in the art.	'035 Patent File History: 09/16/2020 Non-Final Rejection 12/02/2020 Applicant Argument/Remarks Made in Amendment <u>File History of Related Patent US 10,731,220</u> 03/06/2020 Non-Final Rejection <u>File History of Related Patent US 10,538,814</u> 10/02/2019 Notice of Allowance <u>Extrinsic Evidence:</u> Written or live expert testimony regarding the meaning of the term “amplifying the tagged products . . . wherein one of the amplification steps comprises targeted amplification” read in light of the specification and the prosecution history Lela Buckingham & Maribeth L. Flaws, <i>Molecular Diagnostics Fundamentals Methods and Clinical Applications</i> (2007).

No.	Patent Claim(s)	Proposed Term	Natera's Proposed Construction and Supporting Intrinsic and Extrinsic Evidence	NeoGenomics' Proposed Construction and Supporting Intrinsic and Extrinsic Evidence
			- Metzker & Caskey, <i>Polymerase Chain Reaction</i>, ENCYCLOPEDIA OF MEDICAL DEVICES AND INSTRUMENTATION, Second Edition, Volume 5, pp. 380-387 (2006). - Meyer & Kircher, Illumina sequencing library preparation for highly multiplexed target capture and sequencing, COLD SPRING HARBOR PROTOCOLS, pdb.prot5448 pp. 1-10 (2010). - Glenn, <i>Field guide to next-generation DNA sequencers</i>, MOLECULAR ECOLOGY RESOURCES, 11:759–769 (2011).	
2	'035 Patent, claim 1	"SNP loci . . . associated with cancer"	<u>Claim Construction:</u> Plain and ordinary meaning. <u>Intrinsic Evidence</u> <u>Claims/Specification</u> '035 Patent at 7:34-43; 10:45-11:24; 18:29-55; 20:42-21:4; 26:53-67; 34:46-35:15; 45:58-63; 49:12-64; 56:9-41; 76; 3-14; 84:14-85:46; 90:5-24; 92:15-52;	<u>Claim Construction:</u> "A single nucleotide that may differ between the genomes of two members of the same species and is associated with cancer" <u>Intrinsic Evidence:</u> 8:38-43

No.	Patent Claim(s)	Proposed Term	Natera's Proposed Construction and Supporting Intrinsic and Extrinsic Evidence	NeoGenomics' Proposed Construction and Supporting Intrinsic and Extrinsic Evidence
			95:24-35; 109::43-111:9; 112:1-40; 114:49-62; 130:22-131:25; 131:38-65; 133:1-134:26; 204:1-29; 205:50-206:50; 207:33-44; Examples 23, 28, 29; References Cited at pp. 15 (Popova, T. <i>et al.</i>), pp. 18 (Zhao <i>et al.</i>), pp. 20 (Meyerson. M. <i>et al.</i>); Figs. 38, 39; claim 1. <u>File History</u> 12/02/2020 Applicant Response to Non-Final Office Action 03/03/2021 Applicant Response to Final Office Action 04/09/2021 Notice of Allowance 07/09/2021 Notice of Allowance 01/06/2022 Notice of Allowance 06/10/2022 Notice of Allowance <u>Extrinsic Evidence:</u> Same as above.	10:57-66 11:8-24 15:27-30 17:33-36 18:9-12 18:29-43 20:43-21:4 26:10-13 28:43-45 25:43-50 28:32-29:13 32:66-33:11 33:51-54 34:32-36 34:45-47 34:58-62 34:63-67 35:1-2 35:30-33 36:1-13 37:4-23 38:65-67 39:18-25 40:41-43 41:22-40 45:58-63 47:60-48:5

No.	Patent Claim(s)	Proposed Term	Natera's Proposed Construction and Supporting Intrinsic and Extrinsic Evidence	NeoGenomics' Proposed Construction and Supporting Intrinsic and Extrinsic Evidence
				48:48-50:38 54:26-61 55:3-10 56:11-22 64:48-66:61 71:10-25 75:27-59 76:3-9 84:25-42 86:2-10 90:5-37 91:48-92:3 93:5-12 93:29-40 103:45-57 107:3-108:25 109:43-110:53 112:1-40 113:32-36 115:18-20 116:53-117:10 117:66-118:13 119:15-29 121:38-123:7 123:28-124:10 124:50-125:4 124:57-61

No.	Patent Claim(s)	Proposed Term	Natera's Proposed Construction and Supporting Intrinsic and Extrinsic Evidence	NeoGenomics' Proposed Construction and Supporting Intrinsic and Extrinsic Evidence
				130:33-56 134:1-11 134:20-26 143:30-33 146:51-64 147:25-36 154:15-29 195:18-35 204:31-44 205:44-49 205:50-64 207:32-44 234:9 134:56-135:35 137:12-24 138:57-139:36 140:24-36 140:62-141:4 142:55-143:37 145:59-146:6 146:51-64 147:5-36 150:5-67 154:15-29 155:1-9 156:25-29 159:19-21

No.	Patent Claim(s)	Proposed Term	Natera's Proposed Construction and Supporting Intrinsic and Extrinsic Evidence	NeoGenomics' Proposed Construction and Supporting Intrinsic and Extrinsic Evidence
				161:18-43 162:33-165:39 166:41-167:22 167:49-168:32 168:46-65 169:8-170:35 180:13-22 180:41-181:64 185:47-66 192:37-46 194:5-32 195:5-196:62 198:14-199:42 219:17-25 222:5-17 229:15-45 230:22-37 238:4-37 242:5-27 Examples 4 and 7-13 Example 19 Example 21 Example 23 Example 24 Example 26 Example 27 Example 28

No.	Patent Claim(s)	Proposed Term	Natera's Proposed Construction and Supporting Intrinsic and Extrinsic Evidence	NeoGenomics' Proposed Construction and Supporting Intrinsic and Extrinsic Evidence
				Example 29 FIGs. 15, 16, 17A-17D, 31A-31G, 35, 40A-40B, 41A-41B; Claim 1 <u>'035 Patent File History:</u> 09/16/2020 Non-Final Rejection 12/02/2020 Applicant Argument/Remarks Made in Amendment 01/06/2021 Final Rejection 03/03/2021 Applicant Argument/Remarks Made in Amendment 04/09/2021 Notice of Allowance and Notice of Allowability 07/09/2021 Notice of Allowance and Notice of Allowability 01/06/2022 Notice of Allowance and Notice of Allowability 06/10/2022 Notice of Allowance and Notice of Allowability 08/02/2022 Notice of Allowance and Notice of Allowability <u>Extrinsic Evidence:</u> Written or live expert testimony regarding the meaning of the term "SNP loci . . .

No.	Patent Claim(s)	Proposed Term	Natera's Proposed Construction and Supporting Intrinsic and Extrinsic Evidence	NeoGenomics' Proposed Construction and Supporting Intrinsic and Extrinsic Evidence
				associated with cancer” read in light of the specification and the prosecution history Lela Buckingham & Maribeth L. Flaws, <i>Molecular Diagnostics Fundamentals Methods and Clinical Applications</i> (2007).
3	'454 Patent, claims 1, 14	“sequencing the amplicons”	<u>Claim Construction:</u> Plain and ordinary meaning. <u>Intrinsic Evidence</u> <u>Claims/Specification</u> '454 Patent at 31; 17-24; 58:33-46; 62:1-13; 92:57-9:37; 96:5-29; 99:66-100:45; Examples 1, 9, 13; claims 1, 11, 14, 25. <u>File History</u> 07/07/2022 Non-Final Office Action 07/28/2022 Applicant Response to Non-Final Office Action 11/08/2022 Notice of Allowance	<u>Claim Construction:</u> “Sequencing the amplicons obtained from the targeted multiplex amplification step” <u>Intrinsic Evidence:</u> <u>Specification/Claims</u> 20:2–8 20:26–28 33:61–63 58:33–40 62:1–11 98:28–33 125:36–40 152:44–48 156:4–8 157:24–29 159:25–27

No.	Patent Claim(s)	Proposed Term	Natera's Proposed Construction and Supporting Intrinsic and Extrinsic Evidence	NeoGenomics' Proposed Construction and Supporting Intrinsic and Extrinsic Evidence
			IPR2024-00346 (NeoGenomics' Petition for IPR of the '454 Patent and evidence cited in support of its Petition) <u>Extrinsic Evidence:</u> • Opening Declaration of Dr. Michael Metzker in support of Natera's Preliminary Injunction ("PI") Motion dated July 31, 2023 • Rebuttal Declaration of Dr. Brian Van Ness in support of NeoGenomics' PI Opposition dated October 19, 2023 • Reply Declaration of Dr. Michael Metzker in support of Natera's PI Motion dated November 6, 2023 • September 26, 2023 Deposition testimony of Dr. Metzker • October 4, 2023 Deposition testimony of Dr. Bernhard Zimmermann	163:16–29 163:30–51 163:52–59 168:62–67 Claims 1, 14 <u>'454 Patent File History</u> 10/07/2022 Applicant Argument/Remarks Made in an Amendment <u>File History of Related Patent US 11,486,008</u> 01/08/2021 Applicant Argument/Remarks Made in an Amendment 05/22/2020 Applicant Initiated Interview Summary <u>Extrinsic Evidence:</u> Written or live expert testimony regarding the meaning of the term “sequencing the amplicons” read in light of the specification and the prosecution history

No.	Patent Claim(s)	Proposed Term	Natera's Proposed Construction and Supporting Intrinsic and Extrinsic Evidence	NeoGenomics' Proposed Construction and Supporting Intrinsic and Extrinsic Evidence
			• October 25, 2023 Deposition testimony of Dr. Brian Van Ness • November 14, 2023 Deposition testimony of Dr. Metzker • November 27, 2023 PI Hearing testimony of Dr. Metzker • Additional written and/or live expert testimony regarding the meaning of this term as understood by a person of ordinary skill in the art. • Metzker & Caskey, <i>Polymerase Chain Reaction</i>, <i>ENCYCLOPEDIA OF MEDICAL DEVICES AND INSTRUMENTATION</i>, Second Edition, Volume 5, pp. 380-387 (2006). • Meyer & Kircher, Illumina sequencing library preparation for highly multiplexed target capture and sequencing, <i>COLD SPRING HARBOR PROTOCOLS</i>, pdb.prot5448 pp. 1-10 (2010).	

No.	Patent Claim(s)	Proposed Term	Natera's Proposed Construction and Supporting Intrinsic and Extrinsic Evidence	NeoGenomics' Proposed Construction and Supporting Intrinsic and Extrinsic Evidence
			Glenn, <i>Field guide to next-generation DNA sequencers</i>, MOLECULAR ECOLOGY RESOURCES, 11:759–769 (2011).	
4	'454 Patent, claims 1, 14	"sequencing the amplicons to obtain sequence reads, and detecting one or more of the tumor-specific SNV mutations present in the cell-free DNA from the sequence reads"	<u>Claim Construction:</u> The terms are part of one sequencing step. <u>Intrinsic Evidence</u> <u>Claims/Specification</u> '454 Patent at 31; 17-24; 58:33-46; 62:1-13; 92:57-9:37; 96:5-29; 99:66-100:45; Examples 1, 9, 13; claims 1, 11, 14, 25. <u>File History</u> 07/07/2022 Non-Final Office Action 07/28/2022 Applicant Response to Non-Final Office Action 11/08/2022 Notice of Allowance IPR2024-00346 (NeoGenomics' Petition for IPR of the '454 Patent and evidence cited in support of its Petition)	<u>Claim Construction:</u> Plain and ordinary meaning, which is that "detecting...from the sequence reads" is performed on the sequence reads generated by the claimed sequencing step, and not part of the claimed sequencing step. <u>Intrinsic Evidence:</u> <u>Specification/Claims</u> 5:63–67 6:7–12 20:2–8 20:26–28 33:61–63 43:15-35 & Figs. 69, 70 58:33–40 60:21–63:49 65:20–33

No.	Patent Claim(s)	Proposed Term	Natera's Proposed Construction and Supporting Intrinsic and Extrinsic Evidence	NeoGenomics' Proposed Construction and Supporting Intrinsic and Extrinsic Evidence
			<u>Extrinsic Evidence:</u> Same as above.	67:52–5698:28–33 125:36–40 147:49–151:42 152:44–48 156:4–8 157:24–29 159:25–27 163:16–29 163:30–51 163:52–59 168:62–67 Claims 1, 14 <u>'454 Patent File History</u> 10/07/2022 Applicant Argument/Remarks Made in an Amendment <u>File History of Related Patent US 11,486,008</u> 01/08/2021 Applicant Argument/Remarks Made in an Amendment 05/05/2022 Applicant Initiated Interview Summary <u>Extrinsic Evidence:</u>

No.	Patent Claim(s)	Proposed Term	Natera's Proposed Construction and Supporting Intrinsic and Extrinsic Evidence	NeoGenomics' Proposed Construction and Supporting Intrinsic and Extrinsic Evidence
				Written or live expert testimony regarding the meaning of the term “sequencing the amplicons to obtain sequence reads, and detecting one or more of the tumor-specific SNV mutations present in the cell-free DNA from the sequence reads” read in light of the specification and the prosecution history
5	'454 Patent, claims 3,5,17,19	“clonal”	<u>Claim Construction:</u>¹ Not indefinite; plain and ordinary meaning <u>Intrinsic Evidence</u> <u>Claims/Specification</u> '454 Patent at 41:57-61; Example 13; Fig. 51; claims 1, 3, 5, 14, 17, 19. <u>File History</u> 07/07/2022 Non-Final Office Action	<u>Claim Construction:</u> Claim is indefinite and not amenable to construction. <u>Intrinsic Evidence:</u> <u>Specification/Claims</u> 31:17-24; 41:57-64; 168:12–17

¹ To the extent that NeoGenomics identifies any claim term is indefinite, Natera does not believe indefiniteness is properly addressed during claim construction. Natera contends this invalidity defense is more appropriately raised during summary judgment and trial along with the other invalidity grounds after a more complete factual and expert record is available.

No.	Patent Claim(s)	Proposed Term	Natera's Proposed Construction and Supporting Intrinsic and Extrinsic Evidence	NeoGenomics' Proposed Construction and Supporting Intrinsic and Extrinsic Evidence
			07/28/2022 Applicant Response to Non-Final Office Action IPR2024-00346 (NeoGenomics' Petition for IPR of the '454 Patent and evidence cited in support of its Petition) <u>Extrinsic Evidence:</u> • Opening Declaration of Dr. Michael Metzker in support of Natera's Preliminary Injunction ("PI") Motion dated July 31, 2023 • Rebuttal Declaration of Dr. Brian Van Ness in support of NeoGenomics' PI Opposition dated October 19, 2023 • Reply Declaration of Dr. Michael Metzker in support of Natera's PI Motion dated November 6, 2023 • September 26, 2023 Deposition testimony of Dr. Metzker	168:20–26 168:46–54 Fig. 51A; Fig. 51B; Fig. 52; Claims 3, 4, 5, 7, 17, 18, 19, 21 <u>'454 Patent File History</u> 07/07/2022 Non-Final Rejection <u>Extrinsic Evidence:</u> Written or live expert testimony that the claim terms “clonal” and “subclonal,” read in light of the specification and the prosecution history, fail to inform with reasonable certainty those skilled in the art about the scope of invention Lela Buckingham & Maribeth L. Flaws, <i>Molecular Diagnostics Fundamentals Methods and Clinical Applications</i> (2007). McGranahan et al., <i>Clonal status of actionable driver events and the timing of mutational processes in cancer evolution</i>,

No.	Patent Claim(s)	Proposed Term	Natera's Proposed Construction and Supporting Intrinsic and Extrinsic Evidence	NeoGenomics' Proposed Construction and Supporting Intrinsic and Extrinsic Evidence
			- October 4, 2023 Deposition testimony of Dr. Bernhard Zimmermann - October 25, 2023 Deposition testimony of Dr. Brian Van Ness - November 14, 2023 Deposition testimony of Dr. Metzker - November 27, 2023 PI Hearing testimony of Dr. Metzker - Additional written and/or live testimony from Dr. Michael Metzker to rebut NeoGenomics' allegation of indefiniteness and to support a plain and ordinary meaning construction for this claim term.	Sci Transl Med. 7(283):283ra54 (April 15, 2015) Gerlinger et al., <i>Genomic architecture and evolution of clear cell renal cell carcinomas defined by multiregion sequencing</i>, Nat Genet. 46(3); 225–233 (Mar. 2014) de Bruin et al., <i>Spatial and temporal diversity in genomic instability processes defines lung cancer evolution</i>, Science 346(6206): 251–256 (Oct. 10, 2014)
6	'454 Patent, claims 4, 5, 18, 19	"subclonal"	<u>Claim Construction:</u>¹ Not indefinite; plain and ordinary meaning. <u>Intrinsic Evidence</u> <u>Claims/Specification</u>	<u>Claim Construction:</u> Claim is indefinite and not amenable to construction. <u>Intrinsic Evidence:</u>

No.	Patent Claim(s)	Proposed Term	Natera's Proposed Construction and Supporting Intrinsic and Extrinsic Evidence	NeoGenomics' Proposed Construction and Supporting Intrinsic and Extrinsic Evidence
			'454 Patent at 41:57-61; Example 13; Fig. 51; claims 1, 4, 5, 14, 18, 19. <u>File History</u> 07/07/2022 Non-Final Office Action 07/28/2022 Applicant Response to Non-Final Office Action IPR2024-00346 (NeoGenomics' Petition for IPR of the '454 Patent and evidence cited in support of its Petition) <u>Extrinsic Evidence:</u> Same as above.	<u>Specification/Claims</u> 31:17-24; 41:57-64; 168:12-17 168:20-26 168:46-54 Fig. 51A; Fig. 51B; Fig. 52; Claims 3, 4, 5, 7, 17, 18, 19, 21 <u>'454 Patent File History</u> 07/07/2022 Non-Final Rejection <u>Extrinsic Evidence:</u> Written or live expert testimony that the claim terms "clonal" and "subclonal," read in light of the specification and the prosecution history, fail to inform with reasonable certainty those skilled in the art about the scope of invention

No.	Patent Claim(s)	Proposed Term	Natera's Proposed Construction and Supporting Intrinsic and Extrinsic Evidence	NeoGenomics' Proposed Construction and Supporting Intrinsic and Extrinsic Evidence
				Lela Buckingham & Maribeth L. Flaws, <i>Molecular Diagnostics Fundamentals Methods and Clinical Applications</i> (2007). McGranahan et al., <i>Clonal status of actionable driver events and the timing of mutational processes in cancer evolution</i>, Sci Transl Med. 7(283):283ra54 (April 15, 2015) Gerlinger et al., <i>Genomic architecture and evolution of clear cell renal cell carcinomas defined by multiregion sequencing</i>, Nat Genet. 46(3); 225–233 (Mar. 2014) de Bruin et al., <i>Spatial and temporal diversity in genomic instability processes defines lung cancer evolution</i>, Science 346(6206): 251–256 (Oct. 10, 2014)
7	'454 Patent, claim 14	"present in less than or equal to 0.015% of the cell-free DNA	<u>Claim Construction:</u>¹ Not indefinite; plain and ordinary meaning.	<u>Claim Construction:</u> Claim is indefinite and not amenable to construction.

No.	Patent Claim(s)	Proposed Term	Natera's Proposed Construction and Supporting Intrinsic and Extrinsic Evidence	NeoGenomics' Proposed Construction and Supporting Intrinsic and Extrinsic Evidence
		comprising the SNV locus”	<u>Intrinsic Evidence</u> <u>Claims/Specification</u> '454 Patent at 92:57-9:37; 99:23-52; 135:9-22; Examples 6, 13, 14; Fig. 53; claim 14. <u>File History</u> 07/07/2022 Non-Final Office Action 07/28/2022 Applicant Response to Non-Final Office Action 11/08/2022 Notice of Allowance IPR2024-00346 (NeoGenomics' Petition for IPR of the '454 Patent and evidence cited in support of its Petition) <u>Extrinsic Evidence:</u> - Opening Declaration of Dr. Michael Metzker in support of Natera's Preliminary Injunction (“PI”) Motion dated July 31, 2023 - Rebuttal Declaration of Dr. Brian Van Ness in support of	<u>Intrinsic Evidence:</u> <u>Specification/Claims</u> 6:19–21 40:25-30 42:15–26 93:34–37 157:51–158:36 168:62–171:8 Figs 34, 35, 59, 60, 61 Claims 14, 28 <u>Extrinsic Evidence:</u> Written or live expert testimony that the claim terms “present in less than or equal to 0.015% of the cell-free DNA comprising the SNV locus” and “present in 0.005% to 0.015% of the cell-free DNA comprising the SNV locus,” read in light of the specification and the prosecution history, fail to inform with reasonable certainty, those skilled in the art about the scope of the invention.

No.	Patent Claim(s)	Proposed Term	Natera's Proposed Construction and Supporting Intrinsic and Extrinsic Evidence	NeoGenomics' Proposed Construction and Supporting Intrinsic and Extrinsic Evidence
			NeoGenomics' PI Opposition dated October 19, 2023 • Reply Declaration of Dr. Michael Metzker in support of Natera's PI Motion dated November 6, 2023 • September 26, 2023 Deposition testimony of Dr. Metzker • October 4, 2023 Deposition testimony of Dr. Bernhard Zimmermann • October 25, 2023 Deposition testimony of Dr. Brian Van Ness • November 14, 2023 Deposition testimony of Dr. Metzker • November 27, 2023 PI Hearing testimony of Dr. Metzker • Additional written and/or live testimony from Dr. Michael Metzker to rebut NeoGenomics' allegation of indefiniteness and to support a plain	Lela Buckingham & Maribeth L. Flaws, <i>Molecular Diagnostics Fundamentals Methods and Clinical Applications</i> (2007). Clinical and Laboratory Standards Institute, <i>Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline—Second Edition</i>, EP17-A2 (June 2012) Armbruster et al., Limit of Blank, <i>Limit of Detection and Limit of Quantitation</i>, Clin Biochem Rev Vol 29 Suppl (i) (Aug. 2008)

No.	Patent Claim(s)	Proposed Term	Natera's Proposed Construction and Supporting Intrinsic and Extrinsic Evidence	NeoGenomics' Proposed Construction and Supporting Intrinsic and Extrinsic Evidence
			and ordinary meaning construction for this claim term. • Metzker & Caskey, <i>Polymerase Chain Reaction</i>, ENCYCLOPEDIA OF MEDICAL DEVICES AND INSTRUMENTATION, Second Edition, Volume 5, pp. 380-387 (2006). • Meyer & Kircher, Illumina sequencing library preparation for highly multiplexed target capture and sequencing, COLD SPRING HARBOR PROTOCOLS, pdb.prot5448 pp. 1-10 (2010). • Glenn, <i>Field guide to next-generation DNA sequencers</i>, MOLECULAR ECOLOGY RESOURCES, 11:759–769 (2011).	
8	'454 Patent, claim 28	“present in 0.005% to 0.015% of the cell-free DNA comprising the SNV locus”	<u>Claim Construction:</u>¹ Not indefinite; plain and ordinary meaning. <u>Intrinsic Evidence</u> <u>Claims/Specification</u>	<u>Claim Construction:</u> Claim is indefinite and not amenable to construction. <u>Intrinsic Evidence:</u>

No.	Patent Claim(s)	Proposed Term	Natera's Proposed Construction and Supporting Intrinsic and Extrinsic Evidence	NeoGenomics' Proposed Construction and Supporting Intrinsic and Extrinsic Evidence
			'454 Patent at 92:57-9:37; 99:23-52; 135:9-22; Examples 6, 13, 14; Fig. 53; claims 14, 28. <u>File History</u> 07/07/2022 Non-Final Office Action 07/28/2022 Applicant Response to Non-Final Office Action 11/08/2022 Notice of Allowance IPR2024-00346 (NeoGenomics' Petition for IPR of the '454 Patent and evidence cited in support of its Petition) <u>Extrinsic Evidence:</u> Same as above.	<u>Specification/Claims</u> 6:19–21 40:25-30 42:15–26 93:34–37 157:51–158:36 168:62–171:8 Figs 34, 35, 59, 60, 61 Claims 14, 28 <u>Extrinsic Evidence:</u> Written or live expert testimony that the claim terms “present in less than or equal to 0.015% of the cell-free DNA comprising the SNV locus” and “present in 0.005% to 0.015% of the cell-free DNA comprising the SNV locus,” read in light of the specification and the prosecution history, fail to inform with reasonable certainty, those skilled in the art about the scope of the invention.

No.	Patent Claim(s)	Proposed Term	Natera's Proposed Construction and Supporting Intrinsic and Extrinsic Evidence	NeoGenomics' Proposed Construction and Supporting Intrinsic and Extrinsic Evidence
				Lela Buckingham & Maribeth L. Flaws, <i>Molecular Diagnostics Fundamentals Methods and Clinical Applications</i> (2007). Clinical and Laboratory Standards Institute, <i>Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline—Second Edition</i>, EP17-A2 (June 2012) Armbruster et al., Limit of Blank, <i>Limit of Detection and Limit of Quantitation</i>, Clin Biochem Rev Vol 29 Suppl (i) (Aug. 2008)