Proposed Acquisition by Illumina, Inc. of GRAIL, Inc.

Non-Invasive Prenatal Testing ("NIPT") Market Analysis

December 31, 2020

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Introduction

This white paper addresses Illumina's February 2013 acquisition of Verinata Health, Inc. ("Verinata") and subsequent developments relating to non-invasive prenatal testing ("NIPT") in the United States. In particular, the FTC has referred to concerns of past foreclosure in NIPT; this paper demonstrates those concerns are unfounded and lack merit.

NIPT is a non-invasive screening test for pregnant women to identify chromosomal abnormalities without the risks of miscarriage and other complications associated with invasive prenatal tests like Chorionic Villus Sampling ("CVS") and amniocentesis. NIPT allows for safe screening of fetal genetic abnormalities by testing the cell-free fetal DNA ("cffDNA") in a blood sample of a pregnant woman. Through NIPT technology, the DNA in a maternal blood sample may be sequenced to determine whether the fetus has known genetic abnormalities. NIPT is non-invasive, has no risk of miscarriage, can detect cffDNA as early as [redacted] weeks, is highly accurate, and allows for detection of the most frequently observed birth defects that are associated with chromosomal abnormalities.

In contrast to NIPT, the other options for prenatal testing are either invasive and risky for the fetus, or non-invasive but prone to a high error rate, which leads to an increased need for an invasive test. For example, CVS utilizes either a catheter or needle to biopsy placental cells that are derived from the same fertilized egg as the fetus.[1] Similarly, amniocentesis uses either a catheter or needle to take a small sample of the amniotic fluid that surrounds the fetus, which contains fetal cells.[2] Both CVS and amniocentesis are invasive, and thus increase the risk for miscarriage.[3] Serum screening, or the maternal serum multiple marker test, is a non-invasive procedure that has higher false positives and lower accuracy than NIPT, [redacted].[4] The higher error rate of serum screening requires the use of more invasive procedures to confirm a diagnosis.

According to Staff, certain complainants have claimed that, following its acquisition of Verinata, Illumina attempted to or did foreclose competition in the U.S.

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[1] Centers for Disease Control and Prevention, *Chorionic Villus Sampling and Amniocentesis: Recommendations for Prenatal Counseling*, Morbidity and Mortality Weekly Report (July 21, 1995), https://www.cdc.gov/mmwr/preview/mmwrhtml/00038393.htm, ILMN-NIPTPUBLIC-0000239.

[2] *Id.*

[3] *Id.*

[4] *See Diagnosis of Birth Defects*, Centers for Disease Control and Prevention, https://www.cdc.gov/ncbddd/birthdefects/diagnosis.html (last updated Oct. 27, 2020), ILMN-NIPTPUBLIC-0000236; *Maternal Serum Screening, Screening for Down Syndrome and Trisomies 13 & 18*, Johns Hopkins University Maternal-Fetal Medicine & Obstetric Services, https://www.hopkinsmedicine.org/gynecology_obstetrics/specialty_areas/maternal_fetal_medicine/services/fetal_diagnostic_procedures/down_syndrome_screening_information.html (last visited Dec. 31, 2020), ILMN-NIPTPUBLIC-0000325.

NIPT market. The evidence described below and in the accompanying production make clear that these claims are unfounded. In particular, Illumina's ordinary course data show that, since the Verinata acquisition:

- Verinata's share of downstream NIPT has generally declined, while the share of other providers, including Natera, has collectively increased, a fact that renders any foreclosure claim implausible;

- the prices Illumina charges its NIPT customers, including all-in prices taking into account any field of use or patent pool test fees, have decreased since the acquisition, which contradicts any claim that Illumina has raised rivals' costs;

- output of NIPT offerings from all providers has exploded; and

- NIPT has grown more competitive, with substantial new entry.

We would like to make clear at the outset that the "test fees" mentioned by Staff are ***not*** a form of raising rivals' costs. As discussed below, Illumina has charged two forms of test fees—a field of use fee and the patent pool agreement fee. Customers pay only one or the other fee, not both, and the patent pool fee has largely supplanted the field of use fee. Illumina charged a field of use fee to customers who used its sequencing consumables and related intellectual property ("IP") for clinical purposes in NIPT. Illumina started charging this fee for NIPT clinical testing when NIPT was first introduced commercially in the United States in the 2011-2012 timeframe, ***before*** the Verinata acquisition. In doing so, Illumina was following market practice. It is common practice for technology platform providers to charge field of use fees for using their platforms in clinical settings, as distinguished from research use only applications. As one example, Roche historically charged a fee for the use of its PCR platform in clinical applications.

The patent pool agreement fee relates to the NIPT patent pool agreement ("PPA") that Illumina entered into in 2014 with Sequenom (now part of Laboratory Corporation of America, or LabCorp). At the time, Sequenom was the leading NIPT innovator, and had a history of aggressively enforcing its patent rights, including against Verinata and its other competitors. As described more fully *infra* Section II, all of the NIPT providers were enmeshed in lawsuits filed by Verinata and Sequenom (and [redacted], another patent holder) seeking to enjoin their rivals, and each other, from practicing their respective NIPT patents. The patent disputes were restricting growth and competition in the NIPT field. Following its acquisition of Verinata, Illumina resolved the litigations by settling with Sequenom and executing the PPA, under which NIPT providers can secure patent peace from five different entities by paying a single patent pool test fee to practice NIPT-related patents ("Patent Pool Test Fee"). Under the PPA, Illumina is required to charge test fees to customers who use PPA patents. The fees are

set pursuant to volume-based fee tables established by the PPA.[5] [redacted] As shown below, NIPT dramatically expanded after execution of the PPA, and, importantly, since the execution of the PPA, Verinata's rivals' all-in NIPT costs also have fallen.[6]

That some Illumina customers might prefer not to pay Patent Pool Test Fee does not make the test fee an anticompetitive vertical effect of the Verinata acquisition—it plainly is not. Any argument that the test fees are a vertical effect of the Verinata acquisition would have to assume that—in the counterfactual world where Illumina had not acquired Verinata—Verinata and Sequenom (and the other NIPT IP holders) would have turned a blind eye to infringers of their IP, and there would be no royalties or patent litigation against infringers of PPA patents. Given the facts, this assumption is untenable. The reality is that Illumina's acquisition of Verinata and the formation of the PPA opened a field that the patent holders at the time had constrained.[7] Before the acquisition, industry observers expressed concerns that the conduct of Sequenom and Verinata could result in a "monopolized market",[8] which would cause NIPT competition and innovation to be diminished. Today, with the PPA, the field instead is flourishing. That is not vertical foreclosure; it is procompetitive.

The evidence also makes clear that Illumina has encouraged and enabled this NIPT growth. This is consistent with Illumina's mission. Illumina's incentives are to support and promote sequencing applications like NIPT, as increased growth and competition in sequencing applications increase the use of Illumina's sequencing platform. Indeed, catalyzing widespread adoption of NIPT was Illumina's core rationale

[5] If the customer is practicing IP included in the PPA, which is the vast majority of Illumina's NIPT customers, the customer pays the Patent Pool Test Fee. For the few customers that do not practice IP included in the PPA, but are using Illumina core consumables for NIPT testing, they pay Illumina the field of use fee to use NGS products and sequencing IP for NIPT.

[6] As described *infra* in Section I.B(iii), the field of use fee was introduced first by Illumina before the Verinata acquisition to grant NIPT providers the right to use NGS products and sequencing IP for clinical use in NIPT. A few years later when Illumina and Sequenom entered the Patent Pool Agreement, many NIPT providers paid a Patent Pool Test Fee to obtain access to the patent pool patents. In its supply agreements with NIPT providers thereafter, Illumina charged the Patent Pool Test Fee and granted the expanded field of use for use of NGS products for NIPT but did not charge any additional field of use fees. Consequently, since the PPA came into effect, there are very few customers paying the field of use fee.

[7] At the time, Illumina's CEO announced that "[t]he patent pool established through this agreement eliminates confusion over intellectual property rights and provides a single point of contact for those wishing to license this intellectual property for NIPT", and Sequenom's CEO stated that "[t]his settlement will allow for easier access to both parties' NIPT technology by healthcare providers and their patients". *See* Illumina, *Press Release*: *Illumina and Sequenom Pool Noninvasive Prenatal Testing Intellectual Property and End Outstanding Patent Disputes* (Dec. 3, 2014), https://www.illumina.com/company/news-center/press-releases/press-release-details.html?newsid=e4ce64dc-f0b3-4aa1-b02b-283b211d6ecc, ILMN-NIPTPUBLIC-0000323.

[8] *See, e.g.*, Lauren C. Sayres et al., *In the Public Interest?*, Sci. Translational Med., July 2012, at 2, https://stm.sciencemag.org/content/4/144/144fs23.full.pdf, ILMN-NIPTPUBLIC-0000330.

for the Verinata acquisition. Illumina has continued to invest significant resources to further that goal, to the benefit of all NIPT providers. Most importantly, expecting mothers now have expanded and cheaper access to quick, safe and more accurate non-invasive tests as an alternative to invasive procedures or serum screening. The procompetitive impact of Illumina's Verinata acquisition and successful efforts to encourage the widespread adoption of NIPT are described in more detail below, and demonstrated in the accompanying documents and data.

Section I of this submission sets forth key facts about NIPT and Illumina's prices since the Verinata acquisition, based on empirical analysis of Illumina data by Compass Lexecon. The data confirm that, over time, Verinata's share has remained low, and has generally decreased since Illumina's acquisition. Meanwhile, the shares of other NIPT providers have increased, including the shares of new entrants since the Verinata acquisition. Natera has been the market leader since shortly after it entered the market, and maintains its leading position today with significantly greater share than Verinata and others in the field. The data also show that the all-in per-test price Illumina charges to its NIPT customers has decreased, while NIPT has grown more competitive, demonstrating conclusively that there is no merit to claims that Illumina foreclosed downstream NIPT competition or raised NIPT providers' costs.

Section II discusses Illumina's efforts to catalyze NIPT growth by creating the patent pool; to pursue FDA approvals for an in-vitro diagnostic ("IVD") NIPT test that will enable more third-party lab competition[9]; and to expand reimbursement of NIPT, eliminating a critical barrier to its adoption. While the empirical data alone demonstrate that any allegations of NIPT foreclosure or raising rivals' costs are unfounded, the evidence from Illumina's ordinary course documents makes clear that Illumina's acquisition of Verinata and its actions since have made NIPT more competitive and broadened access to NIPT solutions. The evidence thus refutes any claim that Illumina's acquisition of Verinata led to anticompetitive vertical effects, or that the Verinata acquisition provides any basis for a tortured analogous concern relating to Illumina's proposed re-acquisition of GRAIL.

Finally, Section III explains one important connection between Illumina's Verinata acquisition and its proposed re-acquisition of GRAIL that has relevance to the FTC's investigation—specifically, that in studying clinical data it acquired from the Verinata acquisition, Illumina discovered the potential to use deep sequencing to detect cancer in the blood. It is from that discovery, arising from R&D synergies created as a result of the Verinata acquisition, that Illumina formed GRAIL.

[9] Illumina refers to an IVD product as one that has received FDA approval in the United States.

I. Empirical Data Demonstrate Increased NIPT Competition Since Illumina's Acquisition of Verinata.

As shown below, empirical evidence of the respective shares of NIPT providers in the U.S., Illumina's all-in prices charged to its NIPT customers, and the significant growth and new entry in NIPT make clear that there is no basis to claim that Illumina engaged in any foreclosure or raising rivals' costs strategy after it acquired Verinata in 2013.

A. **Since Illumina Acquired Verinata, Its Share of U.S. NIPT Has Generally Decreased, While Other Providers' Shares Have Stayed the Same or Have Increased.**

If Illumina had successfully pursued a vertical foreclosure or raising rivals' cost strategy (which it has not), other NIPT providers who were adversely affected by that strategy would have seen their share of test samples diverted to Illumina/Verinata over time (for ease of reference, we refer to Verinata's share of tests both before and after the acquisition). The data conclusively show that such diversion has not occurred. Figures 1 and 2 below provide share data for Verinata and for Illumina's top NIPT customers from 2015 through 2019. The share data is based on test samples run on Illumina's next-generation sequencing ("NGS") platform, which Illumina is required to track in connection with the PPA.[10]

Illumina does not have share data for providers that run tests on other platforms, and therefore Figures 1 and 2 overstate Verinata's actual shares.[11] Even so, as shown in Figure 1, Illumina's share has decreased since 2015, and has remained under 10% since 2016.[12] As shown in Figure 2, over that same time period, there have been many new entrants into the market, and the shares of several other NIPT providers in the U.S. have either remained steady or grown. [redacted] Industry sources, and Natera alike, describe Natera as the market leader.[13] Figure 2 also shows the entry and growth of new

[10] Under the PPA, NIPT providers that run on Illumina's NGS platform provide to Illumina the number of samples run and total revenue per quarter. [redacted]

[11] Because the share data in Figures 1 and 2 are based on information Illumina is required to track for the PPA, Illumina does not have comparable data pre-dating December 2014, when the PPA was executed. Although the data is not available for an apples-to-apples comparison, Illumina has no reason to believe—and it is highly unlikely given the amount of entry over the last several years—that Illumina/Verinata's share of the samples run on Illumina's platform has increased from the 2013 Verinata acquisition to the execution of the PPA.

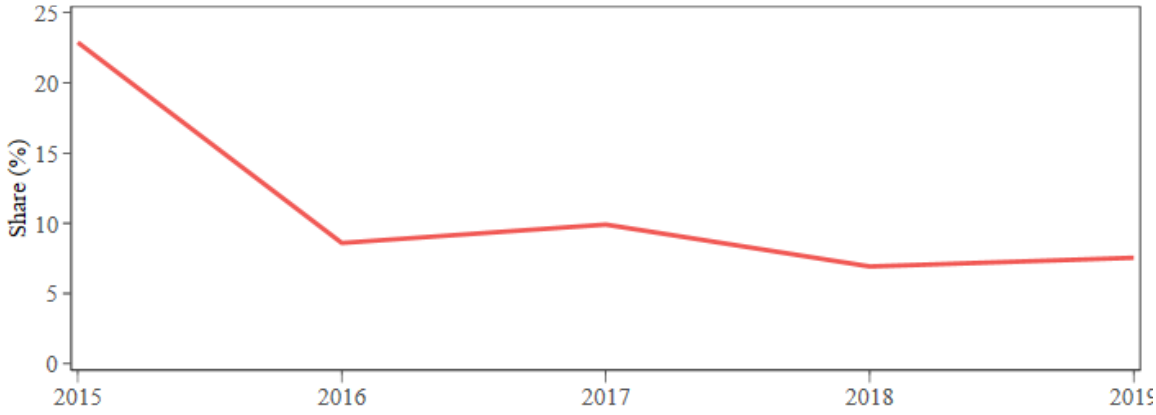
[12] The data used to create Figures 1 and 2 are not yet available for full year 2020, but Illumina's SAP shipment data indicates that Illumina's share will be under 10% for 2020 as well.

[13] For example, in a recent press release, the General Manager of Natera's Women's Health business described Natera as "the market leader" in the space. *See* Natera, *Largest U.S. Health Plan Now Covers*

providers in the market since the Verinata acquisition (additional entry data is provided in Figure 11 below).

The share data alone prove any claims of vertical anticompetitive effects from the Verinata acquisition are false. To the extent Natera or others have made such claims, the data showing Natera's consistent position as a market leader since the Verinata acquisition demonstrate that such claims have been squarely repudiated.

Figure 1: Verinata NIPT Shares in the United States



[redacted]

Non-Invasive Prenatal Testing (NIPT) For All Pregnancies (Dec. 1, 2020), www.natera.com/press-releases/largest-us-health-plan-now-covers-non-invasive-prenatal-testing-nipt-all-pregnancies, ILMN-NIPTPUBLIC-0000327. Similarly, GenomeWeb recently described Natera's NIPT screening tests as holding a "leading position" in the reproductive health market. *See* GenomeWeb, *SVB Leerink Initiates Coverage of Natera with Outperform Rating* (Sept. 17, 2020), https://www.genomeweb.com/molecular-diagnostics/svb-leerink-initiates-coverage-natera-outperform-rating#.X-1H9DSSlPY, ILMN-NIPTPUBLIC-0000318.

Figure 2: Supplier (Illumina Customer) NIPT Shares in the United States[14]

It is worth repeating that because Illumina does not have share data for tests run on non-Illumina platforms, Figures 1 and 2 do not show shares for all competitors in the field, resulting in an overstatement of Verinata's share and an understatement of the full amount of U.S. NIPT competition. For example, Ariosa decided to move its NIPT tests to Thermo Fisher's PCR and microarray-based Affymetrix system in late 2014 and, as a result, Illumina does not have reliable share estimates for Ariosa after that year. However, Ariosa—a subsidiary of Roche, one of the leading global molecular diagnostics companies—has remained a strong competitor in NIPT following its switch to the Affymetrix system, and Illumina is not aware of any diversion from Ariosa to Verinata at any point.[15]

The absence of any diversion of NIPT sales to Verinata from any NIPT provider shows that any claim that Illumina engaged in a foreclosure strategy[16] after the Verinata acquisition has been refuted. Indeed, far from showing market foreclosure, the data suggests that Illumina has been successful in its goal of enabling greater NIPT competition. Such NIPT growth benefits Illumina in multiple ways, including by increasing its opportunity to compete for sales of next-generation sequencing ("NGS") products to new entrants in the field and to existing NIPT providers who are already Illumina customers. It also benefits expecting mothers who use NIPT, as more providers compete on price, service and innovation.

B. Since the Verinata Acquisition, Illumina Customers' NIPT Test Costs Have Decreased.

If Illumina had implemented a raising rivals' costs strategy after the Verinata acquisition (which it has not), the data would show that the prices Illumina charges its customers in NIPT increased after the acquisition.[17] Empirical analysis of Illumina data shows the opposite. Figures 3-5 show the cost per NIPT test both overall and by customer. Like the share data, these cost data start in 2015 because Illumina only started to track NIPT-specific costs in December 2014 to calculate fees owed to Sequenom and other licensors of the NIPT IP under the PPA. In addition, Figure 7 shows that, for Sequenom, Natera and Ariosa (which were Illumina's only NIPT customers at the time of the Verinata acquisition, other than Verinata), the prices Illumina charged for consumables were lower ***after*** the Verinata acquisition, which is consistent with no evidence of raising rivals' costs.

The blue line in Figure 3 below shows that the weighted average all-in cost per test paid by all NIPT suppliers who use Illumina NGS products has consistently decreased. This figure reflects both types of costs that Illumina's NGS customers incur. First, NIPT providers pay Illumina for the costs of the sequencing consumables that they use to perform their tests on Illumina's instruments. Second, NIPT providers pay a test fee to Illumina to obtain access to relevant IP (including, for most customers, the IP of third parties whose patents are included in the patent pool, as discussed further *infra*).

[16] To engage in foreclosure, Illumina would have had to use its upstream sequencing platform to divert sales from other NIPT providers to Verinata's downstream product; no evidence of such foreclosure exists.

[17] The shares attributed to Verinata in Figures 1 and 2 above reflect both Illumina's own lab-run tests ([redacted] and tests run by third-party labs using Illumina VeriSeq kits. Thus, Illumina's declining share does not reflect share moving to Illumina tests sold by its third-party lab partners: even with those lab partner sales attributed to Verinata, the data indicate there has been no diversion from other NIPT providers to Verinata's tests.

Figure 3: Weighted Average Cost (Fees and Consumables) per NIPT Test

Figure 4 examines the same all-in cost per test, but at a customer level, for each of Illumina's largest customers in NIPT. It shows that Illumina's all-in prices have generally declined or stayed low for each such customer (including subsequent entrants such as Progenity) since 2015. The decrease in Illumina's all-in price per test squarely contradicts the notion that Illumina attempted to diminish competition from NIPT providers by raising their costs.

Figure 4: NIPT Customer Cost (Fees and Consumables) per Test

The all-in price is the relevant metric for assessing changes in the price Illumina charges its NIPT customers over time. However, analyzing the separate

components of the all-in price—Illumina's consumables prices and the test fees—also makes clear that Illumina has not raised rivals' costs following the Verinata acquisition. These components are examined below.

i. *Illumina's consumables prices have declined.*

If Illumina had used consumables prices to pursue a raising rivals' cost strategy (it has not), the data would show an increase in the prices Illumina charges for consumables to its NIPT customers for NIPT applications, either in absolute terms or relative to non-NIPT customers who purchase the same consumables for a non-NIPT use. The pricing evidence shows precisely the opposite.

In absolute terms, the weighted average of cost of consumables per NIPT test (in blue below as shown in Figure 5) has consistently decreased.

Figure 5: Weighted Average Cost of Consumables per NIPT Test

Illumina's ordinary course pricing analyses reflect a similar decline in consumables prices charged to NIPT customers, for example, as shown in Figure 6, which is a review of average sales price up to the first financial quarter of 2019.

Figure 6: Illumina Pricing Analysis[18]

Figure 7 calculates the change in consumables prices for Illumina's top NIPT customers ( ) at the time of the Verinata acquisition, comparing their prices one year before the acquisition to the prices both one year and two years after the acquisition. The data show declining consumables prices for each such comparison. As stated above, since Illumina did not track NIPT-specific sales before the PPA, Figure 7 looks at all consumables sales to three NIPT providers pre- and post-acquisition as a proxy. That analysis shows that, from before the acquisition to afterward, Illumina's consumables prices to NIPT providers decreased.

Figure 7: Customer-Level NIPT Consumables Price Comparison

ii. *There is no evidence of price discrimination against NIPT customers.*

Illumina's data show that it did not price discriminate between NIPT and non-NIPT customers. For Illumina to implement an effective raising rivals' costs strategy using the price of consumables, it would have to target its price increase to customers using those consumables for NIPT applications. For a number of reasons, including that Illumina has been focused on lowering costs to grow the market (to grow NGS sales), such a strategy would be neither practical nor profitable to attempt. That aside, the data show unequivocally that Illumina has not in fact implemented such a strategy. Figure 8 compares the price paid by NIPT customers to the price paid by non-NIPT customers for the same consumable in each year since the Verinata acquisition—specifically, the most purchased consumable by NIPT customers in each year. The comparison shows that, in every year since the Verinata acquisition, NIPT customers have paid less for that consumable than non-NIPT customers. The analysis indicates that Illumina has not discriminated against NIPT customers in the prices it charges for core consumables. The lack of price discrimination undercuts any claim that Illumina has used its position as a supplier of NGS products to harm downstream NIPT rivals.

Figure 8: Relative Price of Consumables for NIPT and Non-NIPT Customers

iii. *Illumina's test fees have not increased.*

Staff has also suggested that the test fees charged to NIPT providers could be an anticompetitive vertical effect of the Verinata acquisition. The evidence demonstrates clearly that they are not. First, Figures 1 and 2 above conclusively confirm there has been no competitive foreclosure. Verinata's competitors have expanded, NIPT has attracted new entrants, and Verinata has lost share in NIPT [redacted] Second, as

discussed below, contemporaneous evidence relating to the genesis of the fees confirms that they do not raise rivals costs.

Before the commercial launch of NIPT tests in the 2011-2012 time frame, sequencing was not widely used for clinical testing, and NIPT was emerging as one of the first NGS clinical applications. In accordance with the standard practice used by other platforms with clinical applications (*e.g.*, PCR), in the 2011 time frame—long before the Verinata acquisition—Illumina began to charge a field of use fee for the use of its core consumables (and related sequencing IP) for clinical NIPT testing. [redacted] Illumina continued to charge field of use fees for a small number of customers after the Verinata acquisition, though such fees were largely supplanted by the Patent Pool Test Fee.[20] Given that Illumina started charging field of use fees for NIPT ***before*** the Verinata acquisition, and was following standard practice, those fees are not a vertical effect of the Verinata acquisition.

Similarly, the Patent Pool Test Fee is not a vertical effect of the Verinata acquisition. Before the acquisition, the major NIPT providers—Verinata, Natera, Sequenom and Ariosa—were embroiled in patent litigation over the NIPT patents. As discussed in greater detail in Section II, in December 2014, Illumina settled the cases with Sequenom and entered into the PPA. This brought patent peace to the NIPT field held back by litigation and a thicket of blocking patents. The PPA established the Patent Pool Test Fee, under which NIPT providers obtain access to the key NIPT IP owned by ***five*** different entities by paying a ***single*** fee. As noted, after the creation of the patent pool, Illumina eliminated the field of use fee for NIPT customers who paid the Patent Pool Fee, such that no customer pays both the Patent Pool Test Fee and a field of use fee.[21] The Patent Pool Test Fee is a royalty for a license to a pool of patents: NIPT IP that Illumina acquired as part of the Verinata acquisition (including rights to IP that Verinata had exclusively licensed from other IP holders, for which Illumina owes royalties) and Sequenom's NIPT IP (including IP that Sequenom had exclusively

[redacted]

licensed).[22] The FTC has recognized such pools as procompetitive.[23] Of course, simply acquiring IP and charging for it is not a form of vertical foreclosure or raising rivals' costs.[24] Neither is suing those who infringe on IP and do not pay for a license. Illumina has the contractual right to enforce the PPA against infringers to protect the patent pool IP, and it has successfully done so.

Furthermore, as shown in Figure 9, the empirical data show that the Patent Pool Test Fee has come down over time, which independently destroys any claim that Illumina used the Patent Pool Test Fee to raise rivals' costs.[25] [redacted]

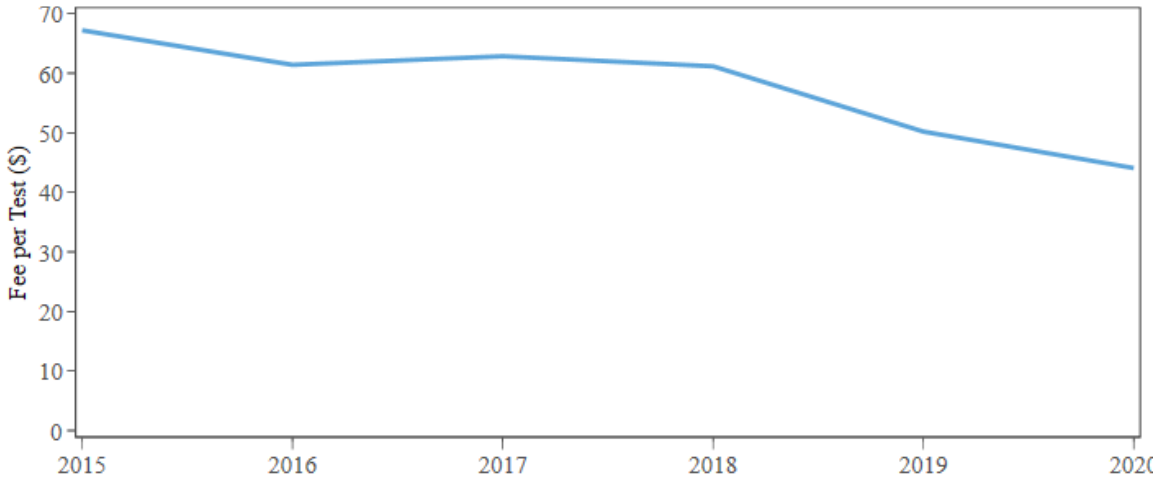
[22] There is no legacy Illumina IP—*i.e.*, patents or patent applications that Illumina owned before the acquisition—in the patent pool.

[23] *See* U.S. Dep't of Justice & Fed. Trade Comm'n, *Antitrust Guidelines for the Licensing of Intellectual Property* § 2.3 (2017), https://www.ftc.gov/system/files/documents/public_statements/1049793/ip_guidelines_2017.pdf, ILMN-NIPTPUBLIC-0000280.

[24] *See, e.g.*, *Dawson Chem. Co. v. Rohm & Haas Co.*, 448 U.S. 176, 215 (1980) (noting that a patent grants "the right to exclude others from profiting by the patented invention"), ILMN-NIPTPUBLIC-0000250; *Walker Process Equip., Inc. v. Food Mach. & Chem. Corp.*, 382 U.S. 172, 177 (1965) ("'A patent . . . is an exception to the general rule against monopolies. . . .'"), ILMN-NIPTPUBLIC-0000334; *see also* U.S. Dep't of Justice & Fed. Trade Comm'n, *supra* note 23, § 2.3 ("Field-of-use, territorial, and other limitations on intellectual property licenses may serve procompetitive ends by allowing the licensor to exploit its property as efficiently and effectively as possible.").

[redacted]

Figure 9: Weighted Average Patent Pool Test Fee Paid by U.S. Customers[26]



Notes: [1] Plotted Patent Pool Test Fees are the volume-weighted average over Illumina U.S. customers.
[2] Sequenom test fees are gross fees from ILMN-COMPASSBACKUP_00000013.

Source: ILMN-COMPASSBACKUP_00000013; ILMN-COMPASSBACKUP_00000004 - ILMN-COMPASSBACKUP_00000011.

[redacted]

[redacted]

In light of the foregoing, we submit that there is no basis to characterize either of the test fees Illumina has charged as a form of raising rivals' costs. [redacted] Natera and Illumina's commercial relationship has continued in the ordinary course both before, during and after the patent litigation, and the empirical evidence shows that Illumina's supply of sequencing instruments and consumables to Natera has continued uninterrupted throughout that period (see Figure 4). [redacted]

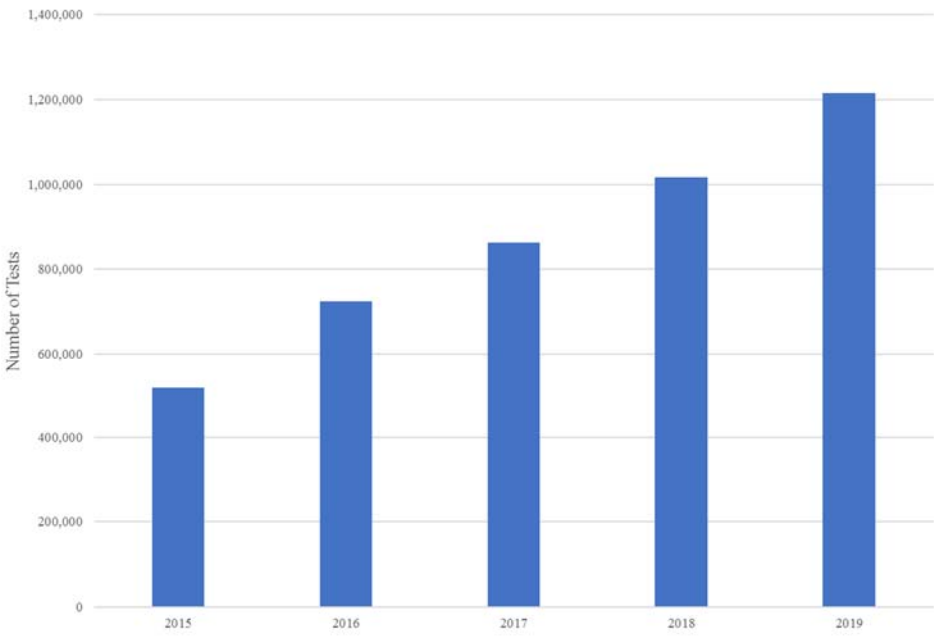
[redacted]

[redacted]

C. Output in NIPT Has Grown Significantly Since the Verinata Acquisition.

If Illumina had pursued a successful foreclosure strategy in NIPT (it has not), one would expect to see diminished competition and, therefore, lower output by other NIPT providers using the Illumina sequencing platform. The data show the opposite. Since the Verinata acquisition, the number of NIPT tests performed by Illumina customers has grown significantly. Figure 10 demonstrates this rapid growth. Specifically, based only on data from Illumina's sequencing customers—a conservative estimate of total NIPT tests performed, there were 518,000 performed in 2015, and just four years later, the number of tests more than doubled to 1,214,000 in 2019. That substantial increase in NIPT output is likely due to a variety of factors, but it is inconsistent with the claim that Illumina diminished NIPT competition through a foreclosure strategy, particularly when paired with the data above and below showing new entrants supplying the NIPT tests.

Figure 10: Number of NIPT Tests Performed by Illumina U.S. Customers



Notes: Tests are identified based on Patent Pool Test Fees and field of use test fees paid to Illumina. Verinata tests and NIPT tests that use non-Illumina platforms are not accounted for.
Source: ILMN-COMPASSBACKUP_00000012; ILMN-COMPASSBACKUP_00000013.

D. There Has Been Substantial New Entry in NIPT Since the Verinata Acquisition.

When a vertically integrated firm raises the costs of downstream rivals, potential entrants face higher entry costs than they would in the absence of such conduct, making entry less attractive and less likely to occur. Conversely, significant entry is a sign that a market is healthy and likely not constrained by anticompetitive foreclosure tactics. Here, in the years following Illumina's acquisition of Verinata, there has been significant entry in U.S. NIPT, contradicting the claim that Illumina has engaged in anticompetitive vertical foreclosure.

Figure 11 identifies notable new entrants to the U.S. NIPT market in each year since the Verinata acquisition. A firm is identified as offering the test in a given year if it paid test fees to Illumina during that year. Thus it does not show all new entrants into NIPT. Firms that entered on non-Illumina platforms are not captured by the data. [redacted] Indeed, many customers who enter using Illumina's Verifi test subsequently gain the knowhow to develop their own NIPT and become independent competitors. [redacted] ven with those limitations, the data show that, since the acquisition, the number of customers offering NIPT tests on an Illumina platform in the U.S. has more than doubled. That new firms continue to enter and provide NIPT tests is additional evidence that Illumina has not foreclosed other NIPT providers in favor of Verinata.

Figure 11: Number of Illumina U.S. Customers Performing NIPT Tests

II. Contemporaneous Evidence Confirms that Illumina Has Facilitated Growth in NGS-Based NIPT.

The empirical data in Section I refute any notion that Illumina has engaged in vertical foreclosure or raising rivals' costs in NIPT. Illumina's ordinary course documents are in accord with the data. The ordinary course documents—consistent with Illumina's incentive to facilitate widespread adoption of applications using its sequencing platform—demonstrate that Illumina has consistently worked to facilitate the growth of NGS-based NIPT. These efforts began with its acquisition of Verinata and continue today as Illumina invests in obtaining FDA approval for an IVD version of Verinata's test and pushes to expand payer coverage for all NGS-based NIPT tests.

Illumina's strategy in NIPT has been driven by Illumina's core goal and financial incentives to catalyze and accelerate the adoption of NGS applications. Illumina acquired Verinata to pursue that goal. At the time, NIPT was an emerging NGS application with the potential to become the first major clinical diagnostic use case for NGS. However, there were significant obstacles in its path.

First, the field was limited by a confusing and uncertain intellectual property landscape. There were a number of entities that held key NIPT patents, including Verinata, Sequenom, [redacted], Massachusetts General Hospital and Chinese University of Hong Kong. Between 2011 and 2012, Verinata (with [redacted] and Sequenom each filed lawsuits seeking to enjoin their rivals from practicing their

respective NIPT patents: Verinata and [redacted] sued Sequenom for alleged infringement, and separately sued Ariosa and LabCorp. (as the then exclusive distributor of Ariosa's NIPT test); Sequenom counterclaimed against Verinata for alleged infringement and separately sued Ariosa; and both Ariosa and Natera sued Sequenom and sought declaratory judgments of non-infringement and invalidity of Sequenom's NIPT patent.

The uncertain patent landscape both in the U.S. and globally created a chill over the field, and the growth of NIPT was impeded. In the U.S., Sequenom was the first to launch an NIPT test, in 2011, followed by Verinata, then Ariosa and then Natera. Natera was the last entrant before Illumina's acquisition of Verinata. In acquiring Verinata, including its IP, Illumina sought to broadly license the NIPT IP and open the field. To that end, it settled Verinata's litigation with Sequenom, and as part of that settlement, in December 2014, the parties entered into the PPA. Illumina's goal with the PPA was to usher in a new era of "one stop shop" NIPT licensing, where NIPT competitors could pay a single test fee and practice the key IP for NIPT from five different entities. This would, in turn, increase competition in the downstream NIPT application market, which would result in increased use of Illumina's instruments and consumables.

Under the PPA, Illumina is responsible for licensing the pooled patents and collecting royalties in the form of test fees, of which Illumina is required to pay [redacted] to Sequenom. Illumina also remits some of the test fee to the other IP-holders whose patents are included in the pool.[37] The PPA gives Illumina the right to sue infringers of PPA patents who refuse to pay the PPA test fee, and Illumina has done so.[38] For example:

- Illumina joined Verinata in its lawsuit against Ariosa, which Illumina won in 2018 after a jury trial.
- [redacted]

Overall, the PPA achieved its aim. It eliminated confusion by providing a single point of contact for anyone wishing to license the PPA patents, which include foundational

[redacted]

patents for NIPT applications. As a result, today many companies have obtained PPA licenses and are active in the NIPT field.

Second, at the time of the acquisition, none of the four companies with commercially available tests operated primarily using a distributable kit model, which limited the ability of third-party labs to participate in NIPT. Rather, each company primarily sold their respective tests directly to physicians or did so through an exclusive partnership (Verinata partnered with PerkinElmer, Natera partnered with Quest and Ariosa partnered with LabCorp.). In evaluating its strategic options shortly after the Verinata acquisition, Illumina examined a handful of potential business models.

Under Illumina's model, the majority of its NIPT sales in the U.S. come from third-party labs purchasing kits ( ) to develop in-house tests that they can run in their own labs. That has benefitted the third-party labs by facilitating their entry into an attractive clinical diagnostic segment,[43] as well as Illumina, by providing Illumina an opportunity to sell sequencers and consumables to those labs. Other NIPT providers, including Natera, operate using

[40] *Id.* at -794.

[41] *Id.* at -791; *see also* dated

similar models, further expanding the opportunities for third-party labs to participate in the field.[44]

Illumina's efforts to gain FDA approval for an IVD NIPT offering will further decentralize NIPT by making available a turn-key option to enable [redacted] laboratory—not just the highly sophisticated CLIA-certified labs who currently perform LDTs—to run tests themselves. [redacted][45] Reducing the up-front costs to run such tests (*e.g.*, removing the need to set up a CLIA-certified lab) will enable many more smaller players to enter and compete in NIPT.[46] Obtaining FDA approval of an IVD test is a time-consuming and expensive task, involving numerous prospective studies and a multi-year development and clinical validation process.[47] Illumina continues to push for FDA approval and hopes to obtain it in [redacted].

Third, the patient base for NIPT was limited because of the lack of payer coverage and because of the historically high costs for the NIPT offerings. Insurers have traditionally covered NIPT for nearly all high risk patients—*e.g.*, pregnant women of advanced maternal age, or those with a family history of birth defects—but only reimbursed NIPT services for about half of average risk patients.[48] Recently, the American College of Obstetricians and Gynecologists (ACOG) recommended that NIPT be made available to all pregnant women, regardless of maternal age or baseline risk, and some of the country's largest health care insurers look to the ACOG guidelines to determine coverage.[49] Due to broadening payer coverage and adoption in average risk patients, the number of patients in the United States receiving NIPT is expected to grow from about 1.4 million to 1.8 million by 2022.[50] Indeed, by 2022, more than 65% of

[redacted]

[49] Illumina, *New Guidelines Recommend Non-Invasive Prenatal Testing for All* (Aug. 19, 2020), https://www.illumina.com/company/news-center/feature-articles/nipt-for-all.html, ILMN-NIPTPUBLIC-0000320.

[redacted]

average risk U.S. pregnancies will be covered for NIPT, a significant improvement from 47% in 2019.[51] Currently, private payers reimburse from $700 to $1,000 per sample analyzed using a basic panel to in-network labs, while Medicaid payments range from $400 to $1,100.[52] As more NIPT providers compete in the market, different tiers of tests are becoming available to patients, including ultra-low cost NIPT (*e.g.*, Invitae's microassay) which is marketed for $99.[53]

Illumina has devoted resources to expanding reimbursement coverage to average-risk patients. Together with the other players in the NIPT space, Illumina formed the Coalition for Access to Prenatal Screening (CAPS), which works to promote public awareness about the value of NIPT.[54] CAPS has worked to educate patients, healthcare providers and insurers about NIPT and has advocated for legislative and reimbursement coverage policy changes.[55] As part of its efforts with CAPs, Illumina partnered with insurer Harvard Pilgrim Health Care to undertake a two-year study of the overall costs and outcomes of NIPT to develop further evidence to support insurance coverage of NIPT for average-risk patients.[56] The expanded coverage that Illumina is pushing for will benefit all NIPT test providers, and in turn, further Illumina's core strategic objective: enabling the work and growth of its NGS customers so as to expand Illumina's opportunities to sell profitable NGS instruments and consumables.

III. GRAIL

As we previously noted, Illumina formed GRAIL as a direct result of scientific discoveries that were made possible by its acquisition of Verinata. When Illumina acquired Verinata, over 100,000 women had taken Verinata's Verifi NIPT test. In a handful of cases, a signal was detected in the mother's blood that was initially believed to be a false signal indicating a genetic abnormality in the fetus. Researchers at Illumina analyzed that data and discovered that the NIPT test had detected circulating tumor DNA (ctDNA) fragments present in the mother's bloodstream.[57] Verinata's NIPT test had, incidentally, detected cancer in the blood, albeit at a late stage. From there, Illumina set out to achieve one of the most critical goals of cancer care—detecting cancer

[51] *Id.* at -413.

[redacted]

[53] *Id.*

[redacted]

[55] *Id.*

[redacted]

[57] *See* Diana W. Bianchi et al., *Noninvasive Prenatal Testing and Incidental Detection of Occult Maternal Malignancies*, 314 J. Am. Med. Ass'n 162 (2015), ILMN-NIPTPUBLIC-0000228.

in the blood at its earliest stages. A few years later, it formed GRAIL to pursue that moonshot objective.

We submit it is this chapter from Verinata's history that has relevance to the FTC's investigation of Illumina's proposed re-acquisition of GRAIL. As we have explained, the proposed transaction will create a number of merger-specific efficiencies arising from GRAIL having immediate access to Illumina's commercial infrastructure, back-up lab space, regulatory expertise, payer relationships and other resources that GRAIL, as a fairly new pre-commercial entity, has only begun developing itself. Building these resources is extremely costly and risky, yet they are critical to Galleri's prospects. On top of those important efficiencies, the proposed transaction also will create R&D synergies to increase the chance for innovative discoveries. Combining GRAIL's methylation expertise and rich clinical data with Illumina's deep sequencing and bioinformatics expertise enhances the likelihood of new breakthroughs in the war on cancer and possibly beyond oncology, just as the Verinata acquisition provided the foundations for Illumina's formation of GRAIL.

Conclusion

There is no basis to assert that Illumina foreclosed competition or raised rivals' costs in NIPT following its acquisition of Verinata. Illumina's sales data demonstrate that, since the Verinata acquisition, Illumina's share has declined, its prices to NIPT customers have come down, and NIPT has grown more competitive. Contemporaneous evidence makes clear that Illumina has sought to foster the growth of NIPT in line with its incentives to expand NGS usage.