Natera, Inc.

Investor presentation

Fourth Quarter 2022 Earnings Call

February 28, 2023

Safe harbor statement

This presentation contains forward-looking statements under the meaning of the Private Securities Litigation Reform Act of 1995. All statements other than statements of historical facts contained in this presentation, including statements regarding our market opportunity, our proposed products and launch schedules, our reimbursement coverage and our product costs, our commercial partners and potential acquisitions, our user experience, our clinical trials and studies, our financial performance, our strategies, our anticipated revenue and financial outlook, our goals and general business and market conditions, are forward-looking statements.

These forward-looking statements are subject to known and unknown risks and uncertainties that may cause actual results to differ materially, including: we face numerous uncertainties and challenges in achieving our financial projections and goals; we may be unable to further increase the use and adoption of our products through our direct sales efforts or through our laboratory partners; we have incurred losses since our inception and we anticipate that we will continue to incur losses for the foreseeable future; our quarterly results may fluctuate from period to period; our estimates of market opportunity and forecasts of market growth may prove to be inaccurate; we may be unable to compete successfully with existing or future products or services offered by our competitors; we may engage in acquisitions, dispositions or other strategic transactions that may not achieve our anticipated benefits and could otherwise disrupt our business, cause dilution to our stockholders or reduce our financial resources; we may not be successful in commercializing our cloud-based distribution model; our products may not perform as expected;
the results of our clinical studies, including our SNP-based Microdeletion and Aneuploidy RegisTry, or SMART, Study, may not be compelling to professional societies or payors as supporting the use of our tests, particularly for microdeletions screening, or may not be able to be replicated in later studies required for regulatory approvals or clearances; if either of our primary CLIA-certified laboratories becomes inoperable, we will be unable to perform our tests and our business will be harmed; we rely on a limited number of suppliers or, in some cases, single suppliers, for some of our laboratory instruments and materials and may not be able to find replacements or immediately transition to alternative suppliers; if we are unable to successfully scale our operations, our business could suffer; the marketing, sale, and use of Panorama and our other products could result in substantial damages arising from product liability or professional liability claims that exceed our resources; we may be unable to expand, obtain or maintain third-party payer coverage and reimbursement for Panorama, Horizon and our other tests, and we may be required to refund reimbursements already received; third-party payers may withdraw coverage or provide lower levels of reimbursement due to changing policies, billing complexities or other factors; if the FDA were to begin actively regulating our tests, we could incur substantial costs and delays associated with trying to obtain premarket clearance or approval and incur costs associated with complying with post-market controls; litigation or other proceedings, resulting from either third party claims of intellectual property infringement or third party infringement of our technology, is costly, time- consuming and could limit our ability to commercialize our products or services; any inability to effectively protect our proprietary technology could harm our competitive position or our brand; and we cannot guarantee that we will be able to service and comply with our outstanding debt obligations or achieve our expectations regarding the conversion of our outstanding convertible notes. We discuss these and other risks and uncertainties in greater detail in the sections entitled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” in our periodic reports on Forms 10-K and 10-Q and in other filings we make with the SEC from time to time. Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statement. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this presentation may not occur and our actual results could differ materially and adversely from those anticipated or implied. As a result, you should not place undue reliance on our forward-looking statements. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation to conform these statements to actual results or to changes in our expectations. We file reports, proxy statements, and other information with the SEC. Such reports, proxy statements, and other information concerning us is available at http://www.sec.gov. Requests for copies of such documents should be directed to our Investor Relations department at Natera, Inc., 13011 McCallen Pass, Building A Suite 100, Austin, TX 78753. Our telephone number is (650) 980-9190.

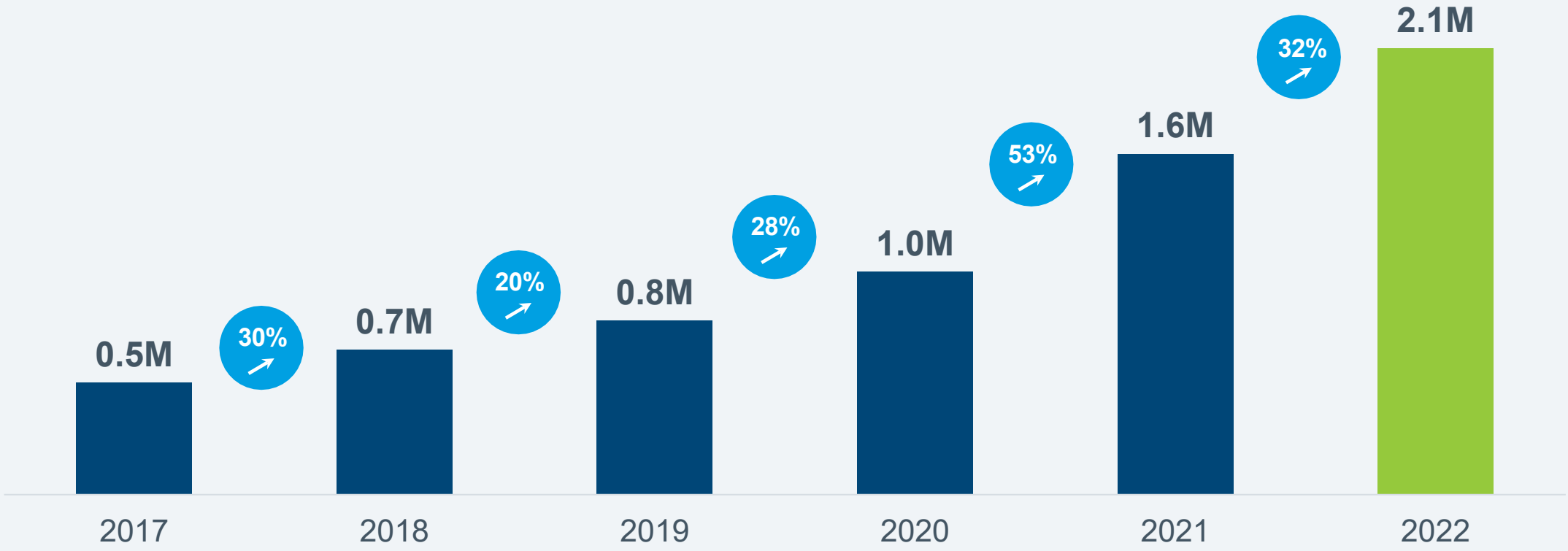
Recent highlights

- FY22 total revenues of $820.2M; ~37% growth[1] over 2021.
- 2.07M total tests processed in FY22; ~32% growth vs. 2021.
- Performed over 196K oncology tests in FY22, representing ~158% YoY growth, with 40 published peer-reviewed studies for Signatera to date.
- Guiding 2023 total revenue guidance of $980M – $1,000M, reducing cash burn by ~$150M in 2023.
- Secured Medicare coverage for breast cancer; representing fifth coverage decision for Signatera.
- Prospective, multi-site CIRCULATE study featured on the cover and as lead publication in the January 2023 issue of Nature Medicine, which demonstrated Signatera's ability to predict chemotherapy benefit in colorectal cancer with 18-months of clinical follow-up.
- New American College of Medical Genetics (ACMG) guideline supporting screening for 22q.11.2 deletion syndrome.
- National Society of Genetic Counselors (NSGC) guideline recommends expanded carrier screening be made available to all individuals considering reproduction and all pregnant pairs.
- Updated International Society for Heart and Lung Transplantation (ISHLT) published guidelines for heart transplant, including dd-cfDNA testing in a Class 1B recommendation.
- Seasoned healthcare executive Ruth Williams-Brinkley appointed to the Board, effective March 2, 2023.

1. Excluding non-recurring revenue of $28.6M from Qiagen arrangement in Q1 2021.

Strong volume growth at scale in 2022

Total processed units



Microdeletion guideline update by ACMG

SMART publication[1]

Only 22q test validated in real-world, multi-site prospective study:

- Robust validation with confirmed outcomes in >18,000 patients

22q results exceeded expectations:

- High incidence 1/1,524
- Excellent sensitivity and specificity:
  - Overall sensitivity of 83.3% (10 of 12 cases of 22q11.2 detected), when including the more difficult, smaller 22q deletions (41.6% of cases)
  - Sensitivity of 99.9% for deletions >2.5Mb
  - Specificity of 99.84%
- High PPV of 53% (>10X better than historically accepted screening tests)
- Prenatal ultrasound missed the majority of true positives

ACMG guideline update – 22q11.2 syndrome[2]

ACMG
American College of Medical Genetics and Genomics

Recommendation:

ACMG SUGGESTS THAT NIPS FOR 22q11.2 DELETION SYNDROME BE OFFERED TO ALL PATIENTS

1. Dar, Pe'er et al. "Cell-free DNA screening for prenatal detection of 22q11.2 deletion syndrome." American journal of obstetrics and gynecology vol. 227,1 (2022): 79.e1-79.e11. doi:10.1016/j.ajog.2022.01.002
2. Dungan JS, Klugman S, Darilek S, Malinowski J, Akkari YMN, Monaghan KG, Erwin A, Best RG; ACMG Board of Directors. Electronic address: documents@acmg.net. Noninvasive prenatal screening (NIPS) for fetal chromosome abnormalities in a general-risk population: An evidence-based clinical guideline of the American College of Medical Genetics and Genomics (ACMG). Genet Med. 2022 Dec 13:S1098-3600(22)01004-8. doi: 10.1016/j.gim.2022.11.004. Epub ahead of print. PMID: 36524989.

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Expanded Carrier Screening – NSGC guideline

Updated NSGC Expanded Carrier Screening (ECS) Guidelines[1]

The National Society of Genetic Counselors (NSGC) published an evidence-based (ECS) practice guideline stating:

"ECS is superior compared to ethnicity-based carrier screening in that it both identifies more carriers of AR and XL conditions as well as eliminates a single race-based medical practice."

National Society of Genetic Counselors

Recommendation:

"Based upon the current level of evidence, we recommend ECS be made available for all individuals considering reproduction and all pregnant reproductive pairs"

1. Sagaser, Katelynn G et al. "Expanded carrier screening for reproductive risk assessment: An evidence-based practice guideline from the National Society of Genetic Counselors." Journal of genetic counseling, 10.1002/jgc4.1676. 9 Feb. 2023, doi:10.1002/jgc4.1676

Prospera Heart – Updated ISHLT guideline for heart transplant includes the use of dd-cfDNA for surveillance

Prospera™ Transplant assessment

Updated ISHLT Heart Transplant Guidelines[1]

- Recent guideline update by ISHLT includes the use of donor-derived cfDNA (dd-cfDNA) testing for surveillance of heart transplant recipients
- ISHLT includes dd-cfDNA testing in a **Class I, Level B recommendation** covering the suggested components for ongoing rejection monitoring in heart transplant recipients
- The recommendation proposes monitoring for rejection (with noninvasive biomarkers or biopsy) monthly during the first six months post transplant, as well as testing in the 9th and 12th months post transplant (or 8 tests in the first year)

DTRT Study for Prospera Heart

- Independent, academically-led, prospective, multi-center, biopsy-matched study with >150 heart transplant recipients and >450 plasma samples followed up to 3.5 years post-transplant at 7 clinical sites
- Study submitted for publication
- Follows Prospera Heart clinical validation study (DEDUCE), published in April 2022[2]

1. Velleca A, Shullo MA, Dhital K, et al. The International Society for Heart and Lung Transplantation (ISHLT) Guidelines for the Care of Heart Transplant Recipients. J Heart Lung Transplant. 2022. https://doi.org/10.1016/j.healun.2022.10.015.
2. Kim PJ, Olymbios M, Siu A, et al. A novel donor-derived cell-free DNA assay for the detection of acute rejection in heart transplantation. J Heart Lung Transplant. 2022;41(7):919-927. doi:10.1016/j.healun.2022.04.002

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Renasight™
Kidney gene panel

Renasight – Key study readout coming in H1 23

RenaCARE Study for Renasight

- Real-world, prospective, multi-center study to assess clinical utility of the Renasight genetic testing panel for patients with chronic kidney disease (CKD)
- The study aims to demonstrate how Renasight genetic findings impact the clinical management of patient care and patient outcomes
- Completed enrollment in August with more than 1,600 patients across 30+ sites
- Publication expected in H1 23

Key Metrics for RenaCARE study

- **Diagnostic utility** – focused on the number of CKD cases with positive genetic findings
- **Clinical utility** – focused on the number of patients that had changes in clinical management and treatment

Source: internal company data

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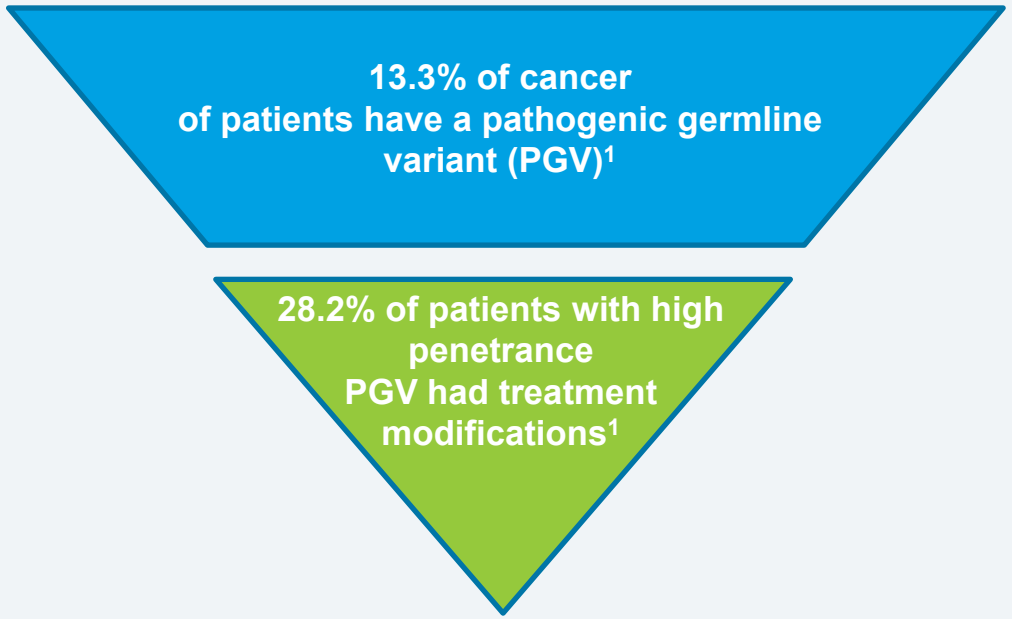
Renasight clinical actionability in CKD – comparison with hereditary cancer market

Renasight™
Kidney gene panel

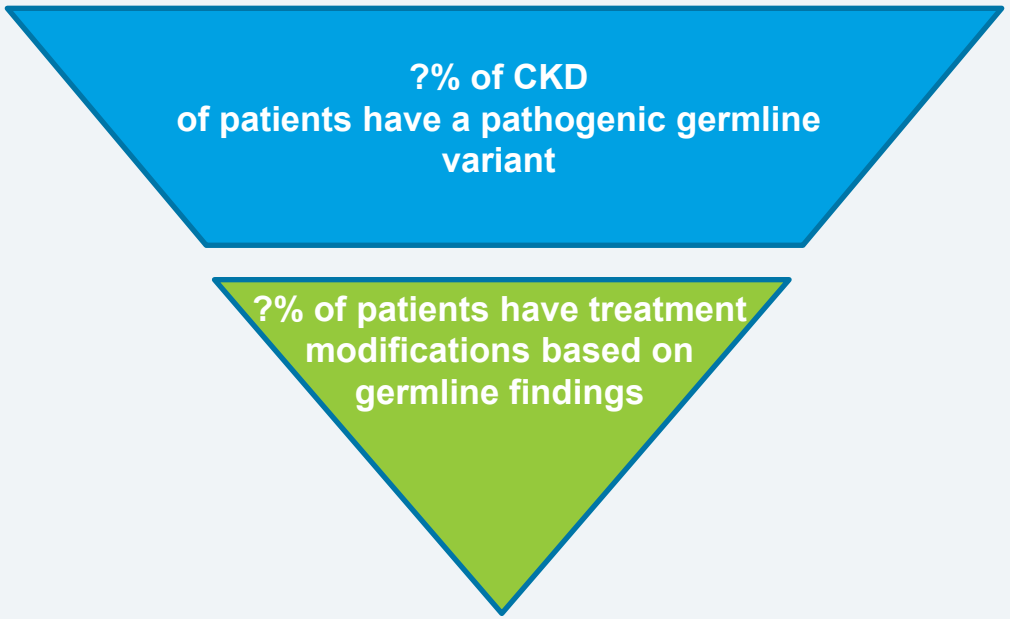
US Hereditary Cancer Market

Clinical Actionability



US CKD Market

Clinical Actionability



1. Samadder, N Jewel et al. “Comparison of Universal Genetic Testing vs Guideline-Directed Targeted Testing for Patients With Hereditary Cancer Syndrome.” JAMA oncology vol. 7,2 (2021): 230-237. doi:10.1001/jamaoncol.2020.6252

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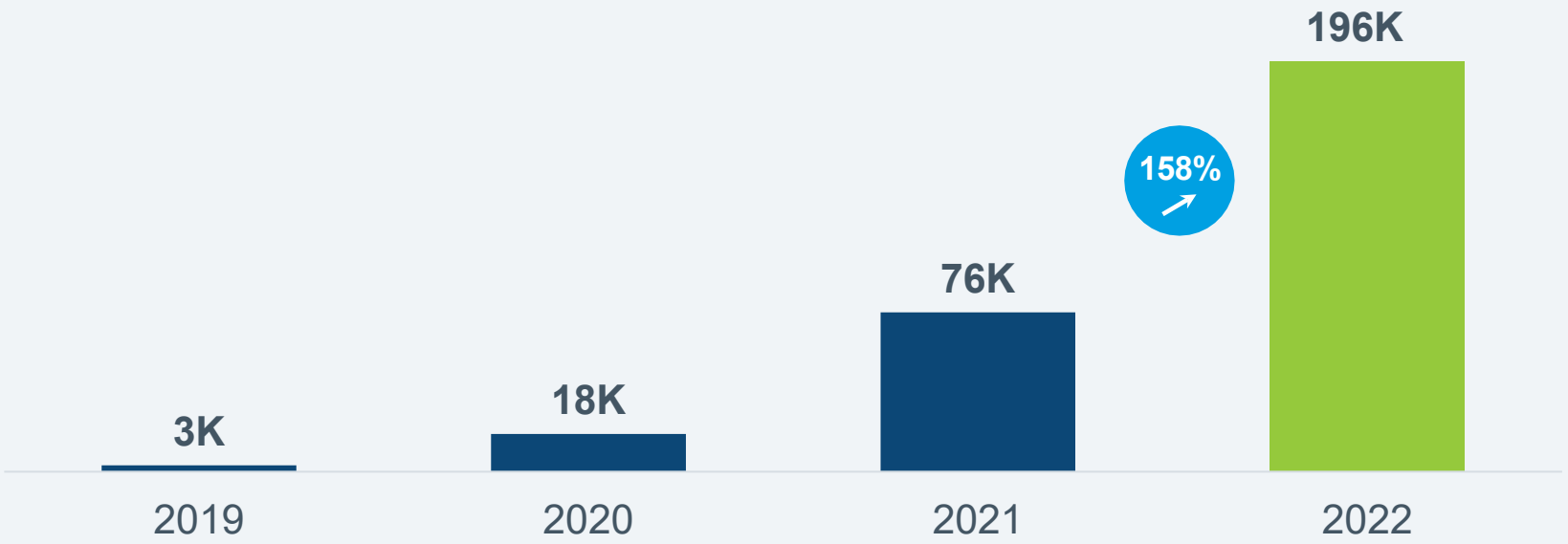
Oncology – Robust volume growth and commercial traction

Signatera™
Residual disease test (MRD)

- >30% of US oncologists ordered Signatera in the quarter with continued growth in new accounts
- Growth driven by both new patients and serial testing
- Increased utilization in CRC, bladder, breast, and IO monitoring

Total Oncology Unit Volumes



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Oncology commercial strengths

Commercial Team

Large, tenured pan-cancer sales and medical affairs team, with multiple physicians on staff, calling on community and academia

Market Access / Reimbursement

Broad Medicare coverage with CRC, bladder, breast, and pan-cancer IO monitoring

ADLT pricing >$3,500

User Experience

Mobile phlebotomy, physician portals, fast turnaround, EMR integration, easy to interpret results

Data Leadership

40 published peer-reviewed studies, covering thousands of patients and over 25 different cancer types

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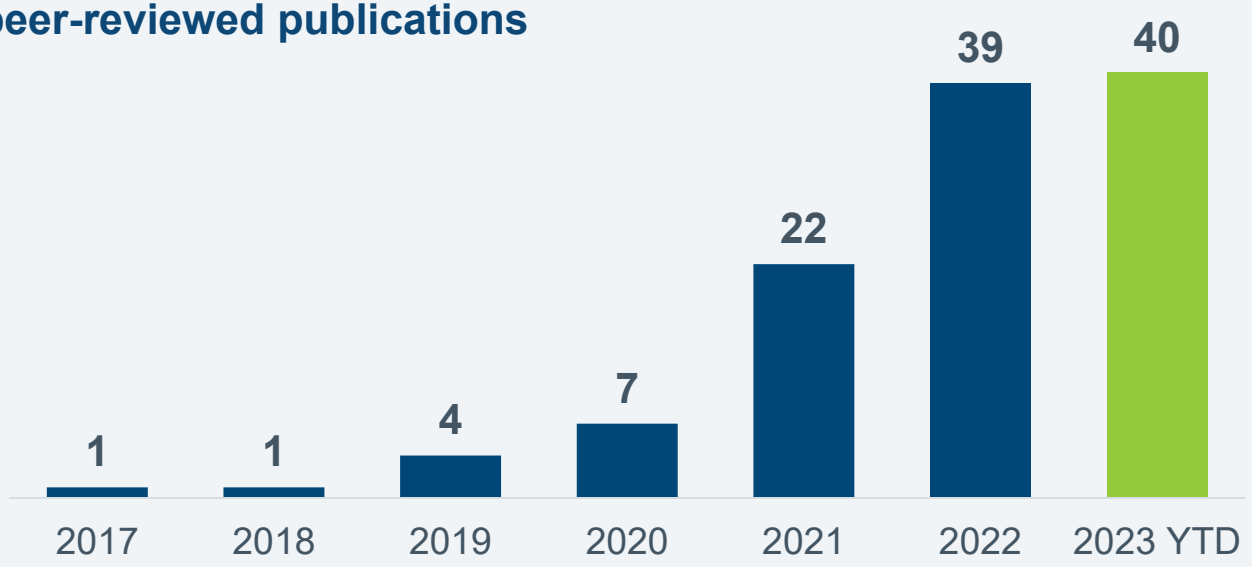
Building evidence for Signatera clinical validity and utility

Signatera™
Residual disease test (MRD)

Cumulative growth of Signatera peer-reviewed publications



Signatera published indications

CRC	Melanoma
Breast	Multiple Myeloma
Pan-cancer IO	Gastric
Bladder	Head & Neck
Lung	Pancreatic
Esophageal	Ovarian
Merkel Cell	Sarcoma

41 posters and 14 oral presentations at oncology conferences during 2022, in addition to the peer-reviewed publications

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CIRCULATE study published as lead article in *Nature Medicine*

Signatera™
Residual disease test (MRD)

- Outcomes analysis of 1,039 patients with Stage II-IV CRC, enrolled into the prospective, multi-site, observational GALAXY arm of CIRCULATE-Japan, with median clinical follow-up of **16.7** months, was published in *Nature Medicine*
- Pre-surgical detection rate of **95.9%** in patients with pathologic stage II-III disease and **93.1%** in patients with stage II-IV disease[1]
- Demonstrated both **prognostic** and **predictive** results in CRC
  - Post-surgery, Signatera-positive patients benefit significantly from adjuvant chemo
  - Signatera-negative patients do not significantly benefit from adjuvant chemo
  - Signatera ctDNA clearance is predictive of treatment response

1. Kotani D, Oki E, Nakamura Y, et al. Molecular residual disease and efficacy of adjuvant chemotherapy in patients with colorectal cancer. Nature Medicine. 2023; https://doi.org/10.1038/s41591-022-02115-4

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Signatera – Medicare coverage for Breast Cancer

Local Coverage Determination (LCD)

MolDX: Minimal Residual Disease for Cancer

- Received written confirmation from CMS MolDX for coverage of Signatera in breast cancer
- Indications include adjuvant and recurrence monitoring in patients with stage IIb or higher breast cancer across all subtypes (HR+, HER2+, and TNBC)

Stage IIB or higher estimated total test TAM of ~1M per year[1,2]

1. Cancer of the Breast (Female) - Cancer Stat Facts." SEER, seer.cancer.gov/statfacts/html/breast.html. Accessed 22 Feb. 2023.
2. Howlader, Nadia et al. "US incidence of breast cancer subtypes defined by joint hormone receptor and HER2 status." *Journal of the National Cancer Institute* vol. 106,5 dju055. 28 Apr. 2014, doi:10.1093/jnci/dju055

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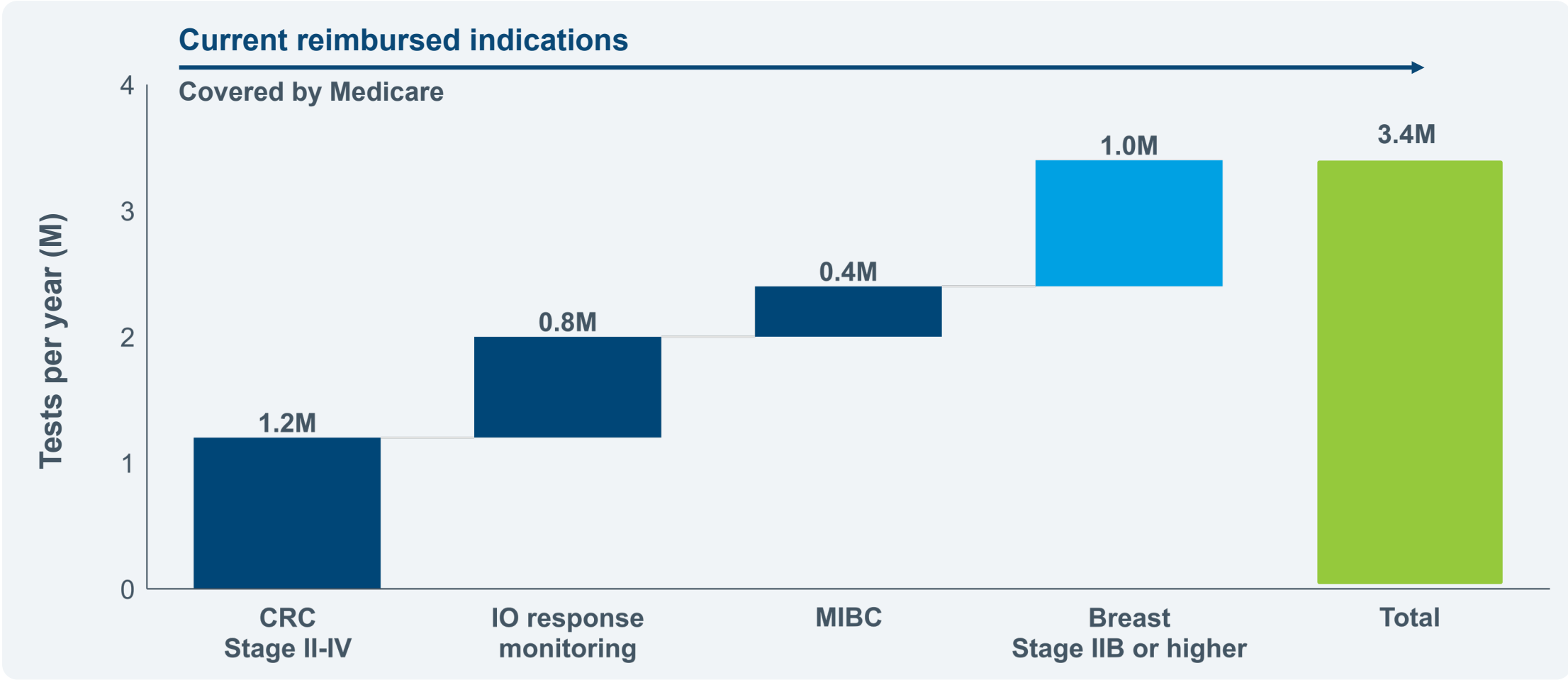
Significant unmet need served by one technology platform and one commercial team

Signatera™
Residual disease test (MRD)



Source: Internal estimates

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Signatera pan-cancer clinical pipeline

Anticipated near term publications

	Indication	Description	Patients	Plasma time points
✓	Gastroesophageal[1]	Multi center	295	943
✓	Anal[2]	Multi center	251	817
✓	CRC[3]	CIRCULATE GALAXY with 18m follow-up	>1,000	>7,000
Accepted	Melanoma	Single center	>50	>500
	CRC	Multi center	>300	>1,300
	Breast	EBLIS expanded cohort	>175	>1,200
	Breast	ISPY 2.0 expanded cohort	>275	>1,000
	Pancreatic	Multi center	>175	~500

Longer term definitive trials

- **Phase III CIRCULATE Japan (CRC)**
- **Phase III CIRCULATE US (CRC)**
- **Phase III CDx study (MIBC)**
- **Phase III CDx study (TNBC, mBRCA HR+)**

Phase III studies aim to drive Level 1A evidence

- Critical for guideline inclusion and broad clinical adoption in specific tumor types
- Investing in the product, evidence, and infrastructure needed for FDA approval

Building evidence to change practice guidelines

1. Huffman BM, Aushev VN, Budde GL, et al. Analysis of circulating tumor DNA to predict risk of recurrence in patients with esophageal and gastric cancers. JCO-Precision Oncology. 2022; 6:e2200420.
2. Azzi G, Tavallai M, Aushev VA, et al. Using Tumor-Informed Circulating Tumor DNA (ctDNA)-Based Testing for Patients with Anal Squamous Cell Carcinoma. The Oncologist. 2022; doi.org/10.1093/oncolo/oyac249
3. Kotani D, Oki E, Nakamura Y, et al. Molecular residual disease and efficacy of adjuvant chemotherapy in patients with colorectal cancer. Nature Medicine. 2023; https://doi.org/10.1038/s41591-022-02115-4
Source: internal company data

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FY22 financial overview

($ in millions, except for per share data)

P&L	FY22	FY21	Change
Product Revenues	$797.3	$580.1	$217.2
Licensing and Other Revenues[1]	$22.9	$45.4	($22.5)
Total Revenues	$820.2	$625.5	$194.7
Gross Margin%[2]	44.4%	49.1%	(472 bps)
R&D	$316.4	$264.2	$52.2
SG&A	$588.6	$511.0	$77.6
Net Loss Per Diluted Share	($5.57)	($5.21)	($0.36)

Balance sheet	Dec 31, 2022	Dec 31, 2021	Change Y/Y
Cash & Investments[3]	$898.4	$914.5	($16.1)
UBS Line of Credit	$80.4	$50.1	$30.3
Convertible Senior Notes[4]	$281.7	$280.4	$1.3

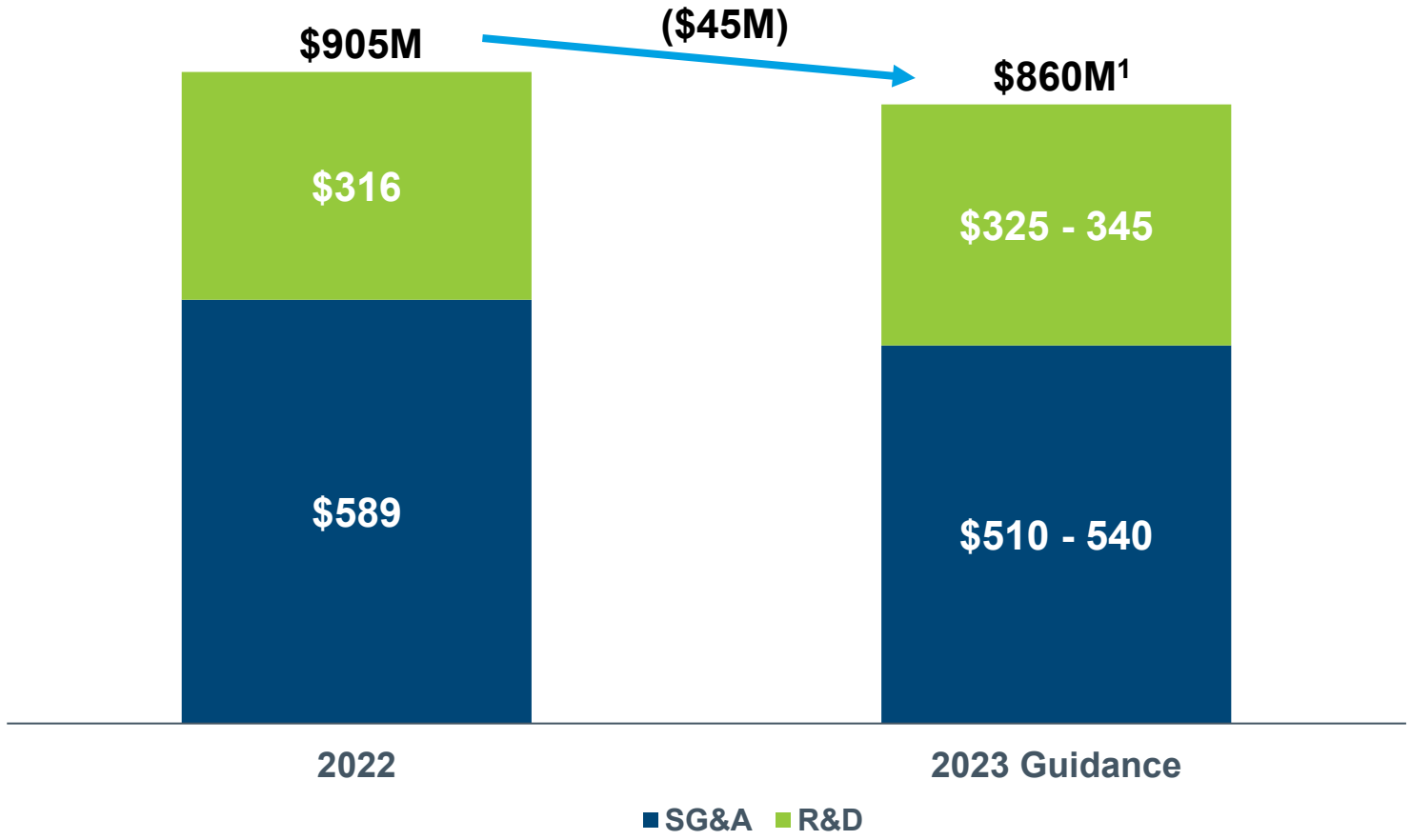
1. FY21 Licensing and Other Revenues includes non-recurring revenue of $28.6M from Qiagen arrangement in Q1 2021.
2. Gross margin is calculated as gross profit divided by GAAP total revenues. Gross profit is calculated as GAAP total revenues less GAAP cost of revenues.
3. Cash and investments includes cash and cash equivalents, restricted cash, and short-term investments.
4. This balance reflects net carrying value for the Convertible Senior Notes under ASC 470-20 while the gross principal amounts outstanding is $287.5 million as of December 31, 2022.

2023 annual guidance

Guide	$ (millions)	Key drivers
Revenue	$980 – $1,000	• Continued volume growth, conservative Women's Health ASPs, strong Oncology contribution
Gross margin % revenue	41% – 44%	• Conservative ASP assumptions, strong Oncology growth, completing key COGS improvement projects in 2023 for future leverage
SG&A	$510 – $540	• Modest reduction in spend vs. 2022 on mature commercial platforms
R&D	$325 – $345	• Focused investments in COGS reduction projects, clinical trials intended to drive guideline adoption
Cash burn	$300 – $325	• ~$150M reduction vs. 2022 cash burn

Continued revenue growth while reducing operating expenses

- **Expect cash burn reduction of ~$150M** on continued revenue growth and reduction in operating expenses.
- With the maturing buildout of our commercial infrastructure, we expect increasing productivity from our Oncology sales team.



1. Based on the midpoint of 2023 R&D and SG&A guidance.