Natera, Inc.

Investor presentation

Fourth Quarter 2021 Earnings Call

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 maintain our business and operations as planned due to disruptions and economic uncertainty caused by the COVID-19 pandemic; we may be unable to further increase the use and adoption of Panorama and Horizon through our direct sales efforts or through our laboratory partners; we may be unable to develop and successfully commercialize new products, including Signatera and Prospera; 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 need to raise additional capital to support our business plans, which may not be available when necessary or on favorable terms; 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 in the average-risk pregnancy population or 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 laboratory facilities 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, such as the increased focus by third-party payers on requiring that prior authorization be obtained prior to conducting a test; 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) 249-9090.

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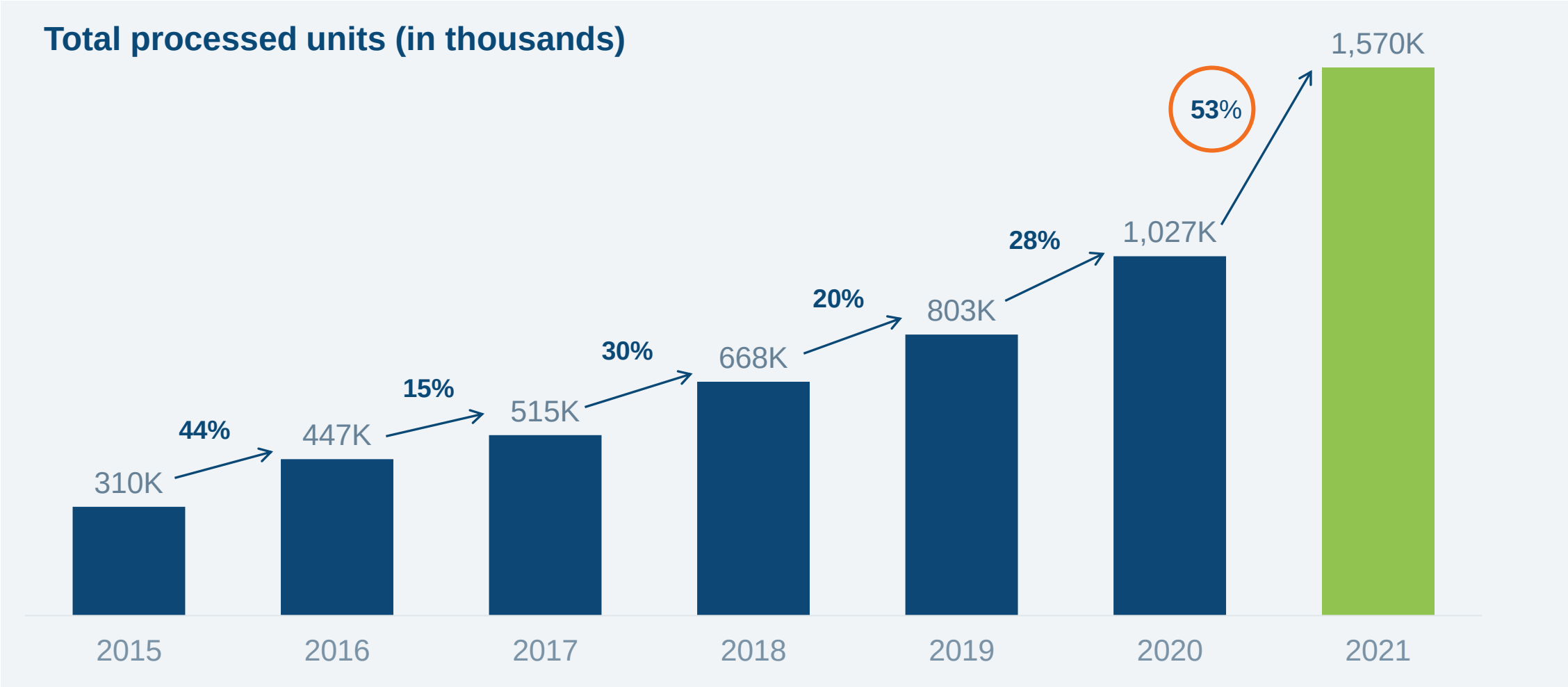
Recent highlights

- 1.57M total tests processed in FY 2021; ~53% growth vs 2020 and >5K more than preannounce
  - ~439K total tests processed in Q4 2021
- FY 2021 total revenue of $625.5M; ~60% growth vs 2020, and above top end of previous guidance range
  - Total revenue of $173M in Q4 2021
- Landmark CIRCULATE-Japan study shows Signatera™ MRD is predictive of chemotherapy benefit in colorectal cancer
- SMART 22q11.2 deletion study published in the *American Journal of Obstetrics and Gynecology*: landmark 5-year trial with 20,000 patients enrolled
- Successful readout of Trifecta study – largest prospective, fully biopsy-matched, kidney dataset to date
- Guiding 2022 total revenue of $770M to $790M; 31%[1] growth at the midpoint over 2021

1. Pro forma for the one-time Qiagen revenue recognition of $28.3M in 2021

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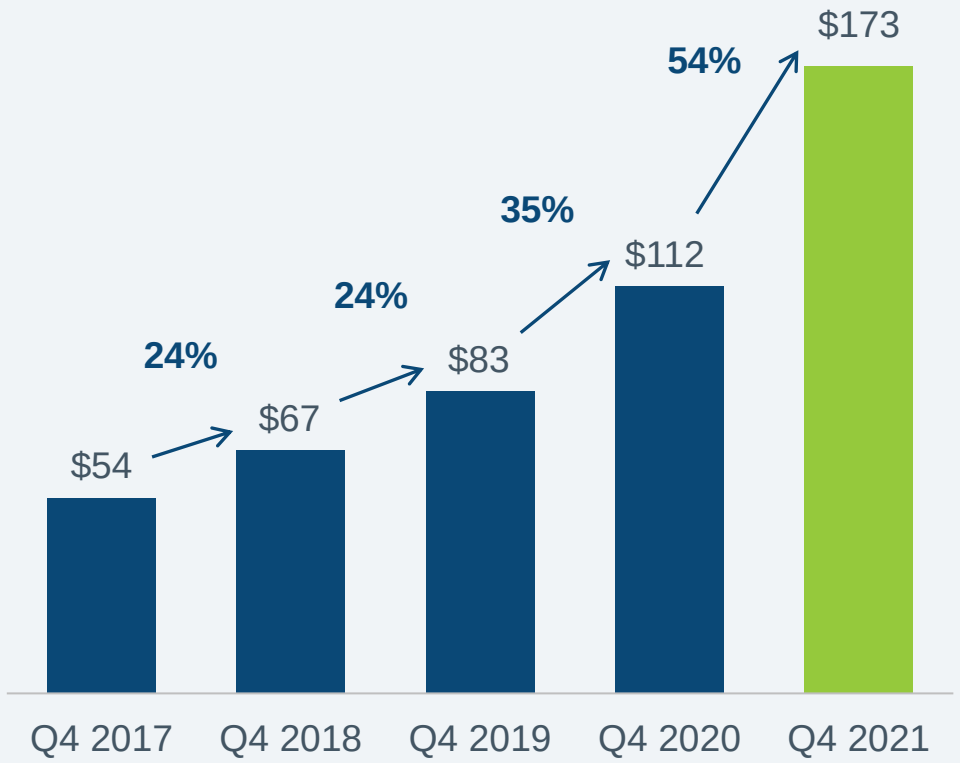
Volume acceleration in 2021



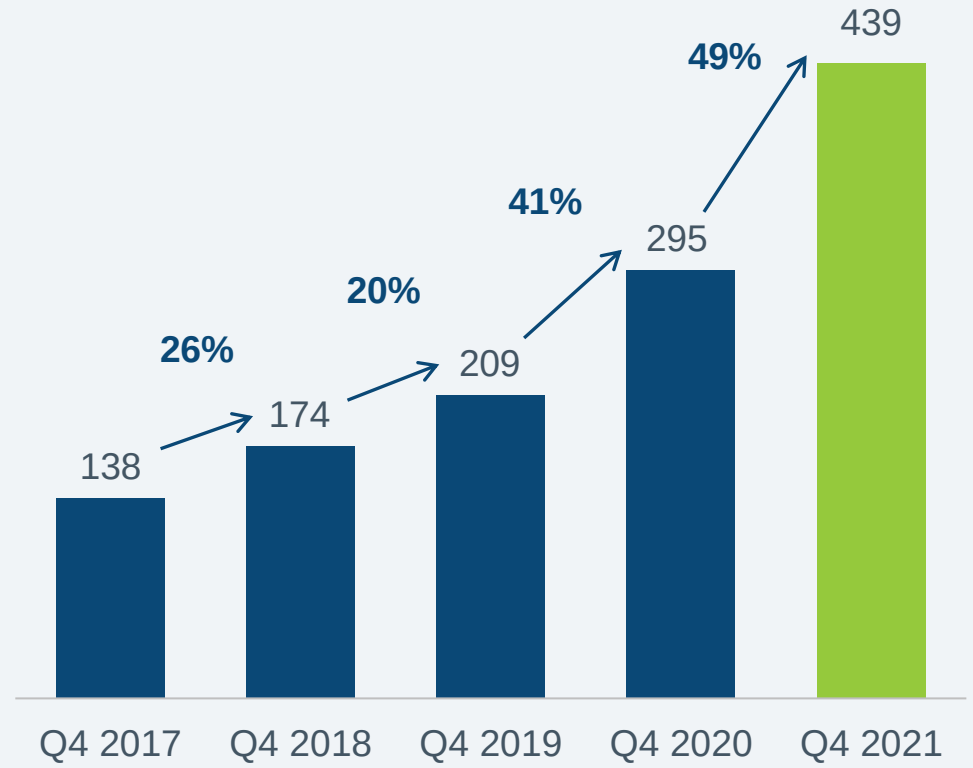
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Strong growth trends in Q4

Total revenues ($ in millions)



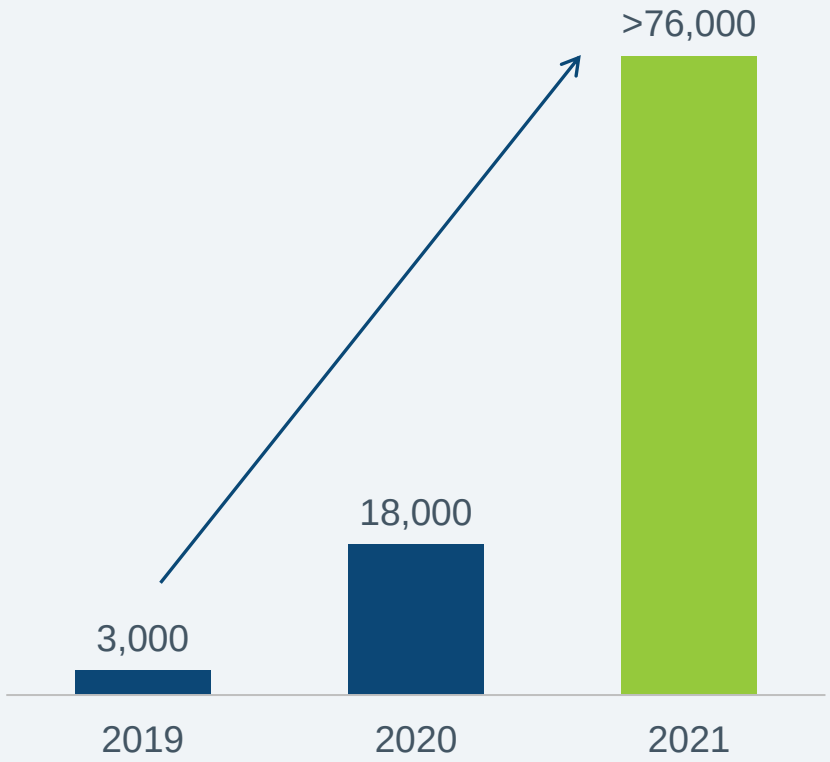
Tests processed (thousands)



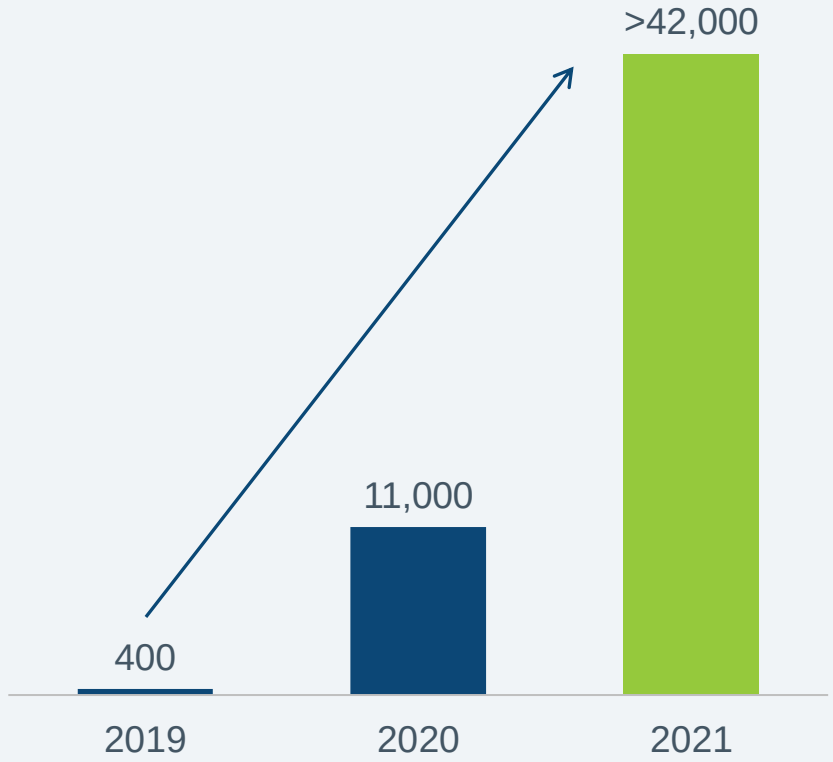
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New products contributing to growth trajectory

Signatera and Altera unit volumes



Prospera and Renasight unit volumes



Includes pharma and clinical units

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Rapid NIPT adoption, opportunity to help even more patients

Broad prenatal offering

Panorama NIPT:

- Robust validation in largest prospective NIPT trial
- Expanded share in 2021 even as market grew rapidly
- ACOG guideline in place

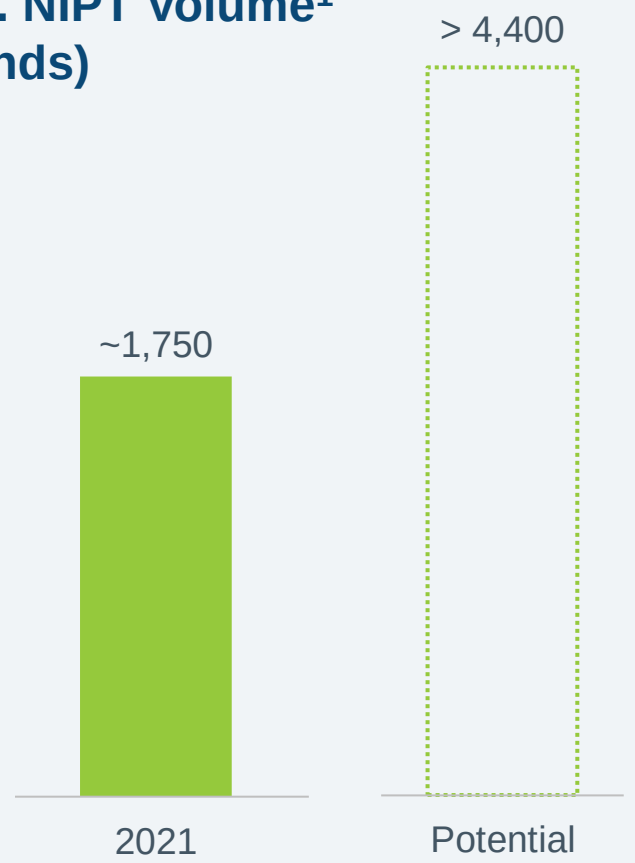
Panorama 22Q deletion:

- Only 22q NIPT validated in large prospective multi-site trial

Horizon Carrier Screening:

- Key conditions recommended by ACOG for all pregnancies

Est. U.S. NIPT Volume[1] (thousands)

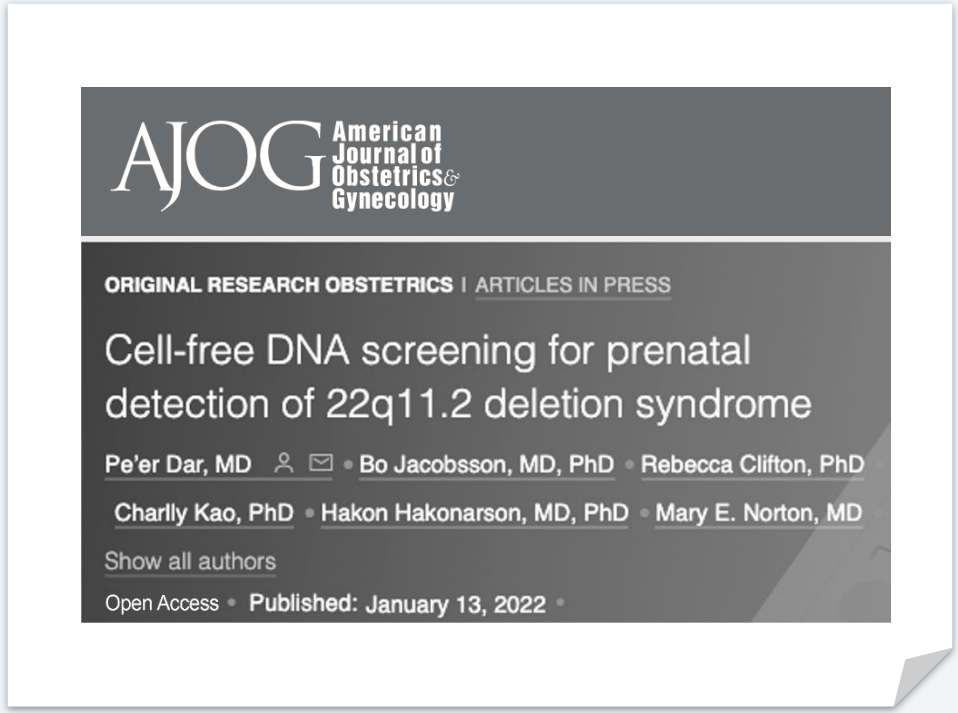


1. Internal estimates and CDC, National Vital Statistics Reports Volume 70, Number 2 March 23, 2021. Estimates based on number of pregnancies at week 5.

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Landmark SMART study published in AJOG

SMART publication



Key results

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
- High PPV of 53% (>10X better than historically accepted screening tests)

High clinical utility for 22q screening:

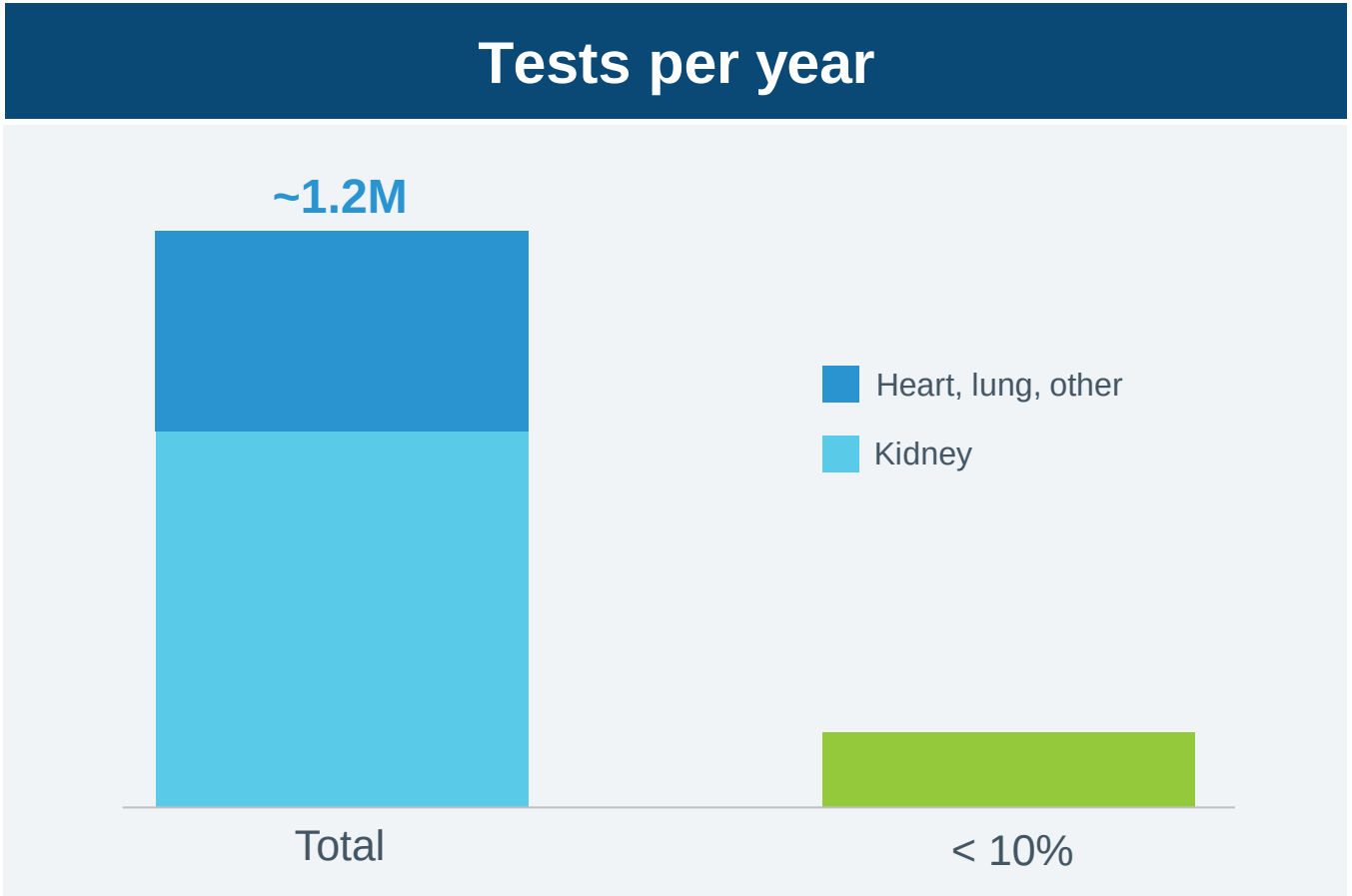
- One of the leading causes of congenital heart defects in the general population[1]
- Helps to avoid post-natal diagnostic odyssey – average of 4.7 years to diagnose
- Early interventions can improve outcomes

1. McDonald-McGinn et al. 22q11.2 deletion syndrome in Nature Reviews Disease Primers

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Transplant: Significant opportunity to help patients

- >1M tests per year
- < 10% of transplant recipients tested today



Source: Internal estimates

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Large clinical studies planned for 1H 2022 publication

Prospera Kidney with Quantification

Trifecta Study[1]

- Largest prospective, fully biopsy-matched, and multi-site study to date of dd-cfDNA for kidney transplant recipients[1]
- >300 biopsy-matched samples
  - Includes >100 biopsy-confirmed rejections
- 20+ US & international sites

Prospera Heart

Multi-Site Validation Trial[2]

- Includes >250 prospectively collected biopsy-matched samples
- Area Under the Curve (AUC): > 0.84
- Could eliminate the need for costly and cumbersome multi-modality testing

Prospera Lung

VALID Study[3]

- Largest prospective study in lung transplant recipients to date for commercially available dd-cfDNA assay
- AUC 0.91 for rejection vs stable
- 195 biopsy-matched samples

1. Halloran, et al. Manuscript submitted for publication, 2022. 2. Kim, et al. Manuscript submitted for publication, 2022. 3. Rosenheck, et al. Manuscript submitted for publication, 2022

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Expanding Oncology TAM opportunity

ctDNA / liquid biopsy



Early detection
$30B



Monitoring/MRD
$15B



Therapy selection
$6B

Source: Internal estimates

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Signatera staged for efficiency and growth



Commercial Reach

- Commercial footprint built – ready for future growth, currently at only 10% capacity



Robust Operations

- Median turnaround time 19 days for first test including tumor exome; 6 days for subsequent tests



Cutting-edge UX

- Online portals and EMR integration for easy test ordering and reporting
- Intuitive systems for recurring orders



Clinical Data

- >100 studies in the clinical pipeline
- >20 publications expected in 2022

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Circulate-IDEA Japan: Largest prospective MRD study

ASCO Gastrointestinal Cancers Symposium

2021: ASCO, ESMO IO

- ~1200 patients enrolled
- ~800 patients analyzed
- Disease free survival stratified by MRD status:
  - Mean ~6 months
  - Max ~10 months

2022: ASCO-GI

- ~3000 patients enrolled
- ~1000 patients analyzed
- Disease free-survival stratified by MRD status ***and by treatment status***:
  - Mean ~12 months
  - Max ~20 months

Building evidence that could change society practice guidelines

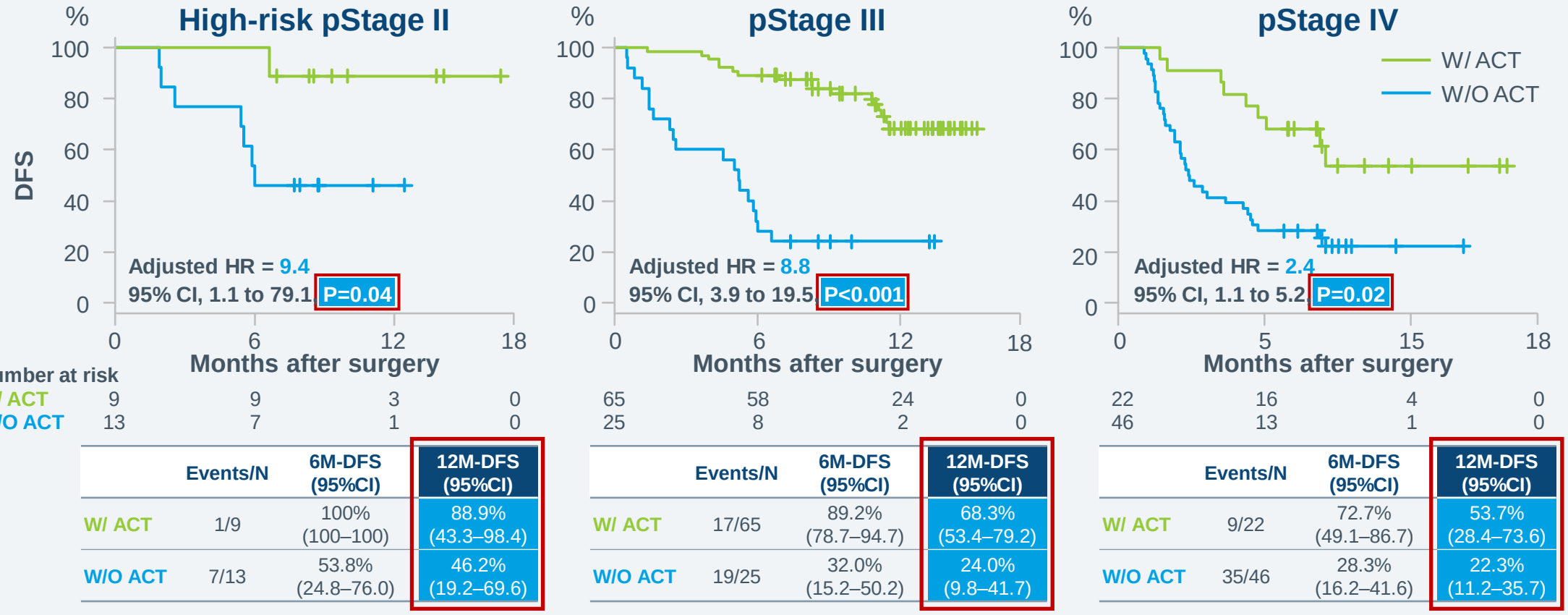
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MRD-positive patients benefit significantly from ACT

ASCO Gastrointestinal Cancers Symposium

DFS in post-op-4w MRD-positive population



	Events/N	6M-DFS (95%CI)	12M-DFS (95%CI)
W/ ACT	1/9	100% (100–100)	88.9% (43.3–98.4)
W/O ACT	7/13	53.8% (24.8–76.0)	46.2% (19.2–69.6)

	Events/N	6M-DFS (95%CI)	12M-DFS (95%CI)
W/ ACT	17/65	89.2% (78.7–94.7)	68.3% (53.4–79.2)
W/O ACT	19/25	32.0% (15.2–50.2)	24.0% (9.8–41.7)

	Events/N	6M-DFS (95%CI)	12M-DFS (95%CI)
W/ ACT	9/22	72.7% (49.1–86.7)	53.7% (28.4–73.6)
W/O ACT	35/46	28.3% (16.2–41.6)	22.3% (11.2–35.7)

HR was adjusted by sex, and performance status. ACT, adjuvant chemotherapy; DFS, disease-free survival; HR, hazard ratio; CI, confidential interval. DFS curve was estimated by the Kaplan-Meier method. HR and 95%CI were calculated by the Cox proportional hazard model.

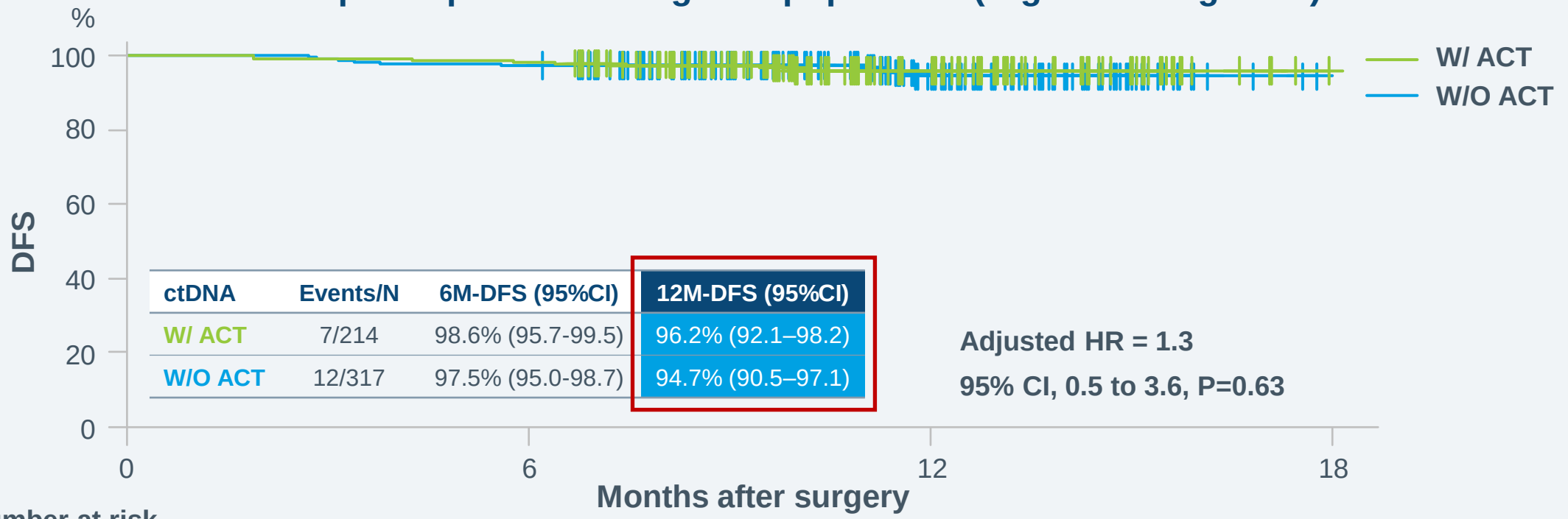
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No significant treatment benefit for MRD-negative patients

ASCO Gastrointestinal Cancers Symposium

DFS in post-op-4w MRD-negative population (High risk stage II-III)



ctDNA	Events/N	6M-DFS (95%CI)	12M-DFS (95%CI)
W/ ACT	7/214	98.6% (95.7-99.5)	96.2% (92.1–98.2)
W/O ACT	12/317	97.5% (95.0-98.7)	94.7% (90.5–97.1)

Adjusted HR = 1.3

95% CI, 0.5 to 3.6, P=0.63

Number at risk

W/ ACT	214	211	79	0
W/O ACT	317	309	117	0

Median follow-up time: 11.4 months. Data cutoff: Nov 19, 2021

HR was adjusted by age, performance status, pStage, and MSI status that are imbalanced between two groups.
ACT, adjuvant chemotherapy; DFS, disease-free survival; HR, hazard ratio; CI, confidential interval.
DFS curve was estimated by the Kaplan-Meier method. HR and 95%CI were calculated by the Cox proportional hazard model.

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Circulate Japan ASCO GI 22 key takeaways

Prognostic results

Circulate Japan ASCO GI 22[1]

12M-DFS for MRD-positives	**55.5%**
12M-DFS for MRD-negatives	**95.2%**
Hazard Ratio (HR) for MRD-positive vs. MRD-negative	**13.3**
Sensitivity at 4w post-op	**67.6%**

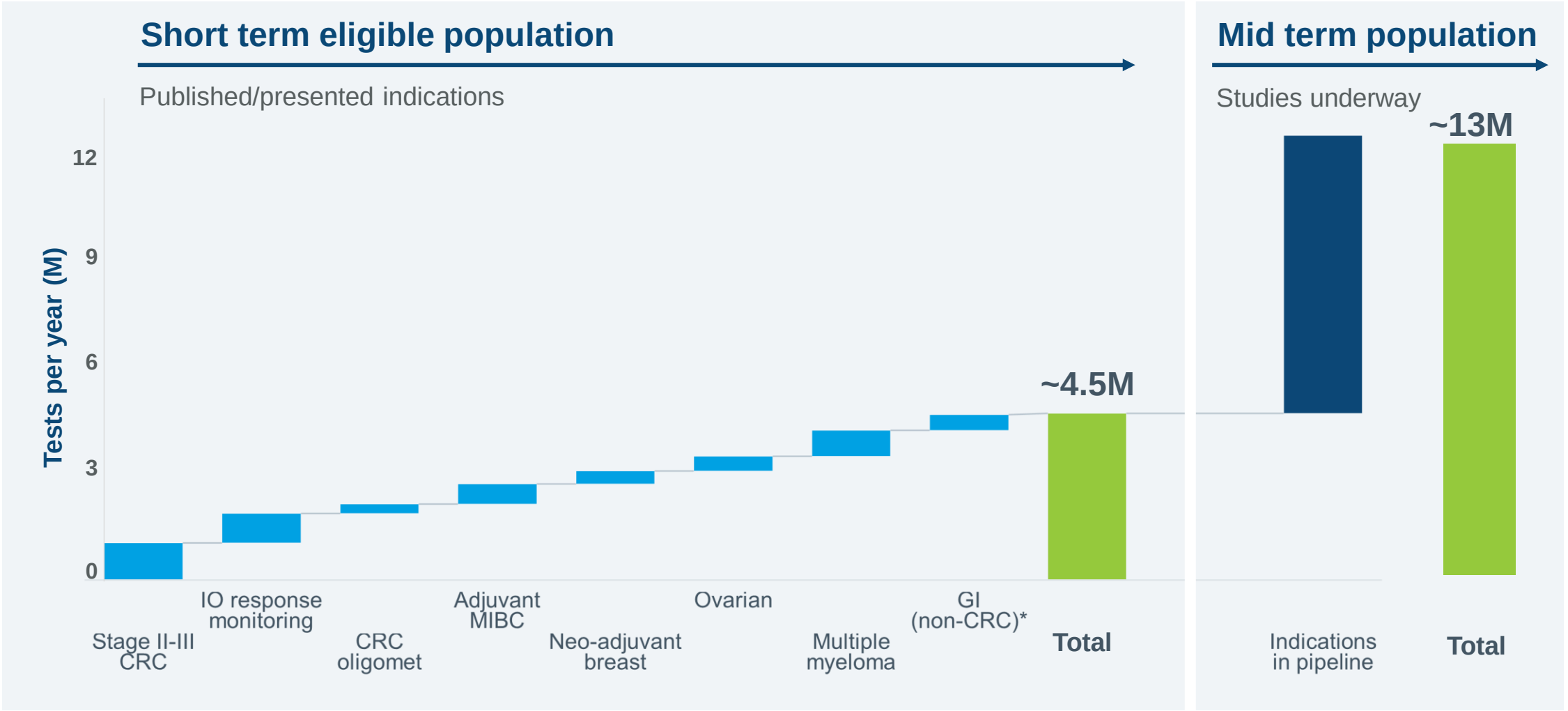
Predictive results

- **Signatera-positive post surgery:** benefit significantly from adjuvant chemo (HR 8.8-9.4 in high-risk Stage II or III)
- **Signatera-negative post surgery:** no significant benefit from adjuvant chemo (Absolute risk reduction of only 1.5% at 12 months DFS)
- **Signatera ctDNA clearance:** predictive of treatment efficacy (HR 15.8 clearance vs. no clearance)

1. Kotaka et al. Association of circulating tumor DNA dynamics with clinical outcomes in the adjuvant setting for patients with colorectal cancer from an observational GALAXY study in CIRCULATE-Japan. ASCO GI 2022.

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



*Esophageal, pancreatic, anal cancers

Source: Internal estimates

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Signatera coverage roadmap

2020 – 2021

- Colorectal, stages II-IV
- Immunotherapy response monitoring, pan-cancer
- ADLT status from CMS

2022 – 2023 goals

- NCCN guidelines in CRC
- Coverage for 5+ additional cancer types
- Private payor initial coverage

2024 onward

- Readouts from definitive, phase 3 studies
- Pan-cancer coverage

MRD leadership with data from > 3,500 patients, >15 peer-reviewed publications

100+ clinical studies in pipeline to drive coverage and practice guidelines

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FY21 financial overview

($ in millions, except for per share data)

P&L	FY21	FY20	Change
Product revenues	$567.1	$367.2	$199.9
Licensing and other revenues	$58.3	$23.8	$34.5
Total revenues	$625.5	$391.0	$234.5
Gross margin%[1]	49.1%	47.9%	117 bps
R&D	$264.2	$100.0	$164.2
SG&A	$511.0	$303.6	$207.4
Net loss per diluted share	($5.21)	($2.84)	($2.37)

Balance sheet	Dec 31, 2021	Dec 30, 2020	Change
Cash & investments[2]	$914.5	$737.5	$177.0
UBS line of credit	$50.1	$50.1	$ —
Convertible senior notes[3]	$280.4	$202.5	$77.9

1. 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.
2. Cash and investments also include cash equivalents and restricted cash.
3. 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, 2021.

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2022 annual guidance

Guide	$ (millions)	Key drivers
Revenue	$770 - $790	Continued volume growth, conservative ASPs, growing contribution from new products
Gross margin % revenue	46% – 48%	Conservative ASP assumptions, rapid growth in pan-cancer Signatera, new patients getting the upfront exome
SG&A	$560 – $590	Full commercial teams for Oncology, Organ Health in place
R&D	$340 - $360	Large clinical trials designed to drive broad adoption in oncology and transplant
Cash burn	$370 - $400	Maturing OpEx supporting multi-year revenue growth

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