Natera, Inc.

Investor presentation

JPM 2022

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 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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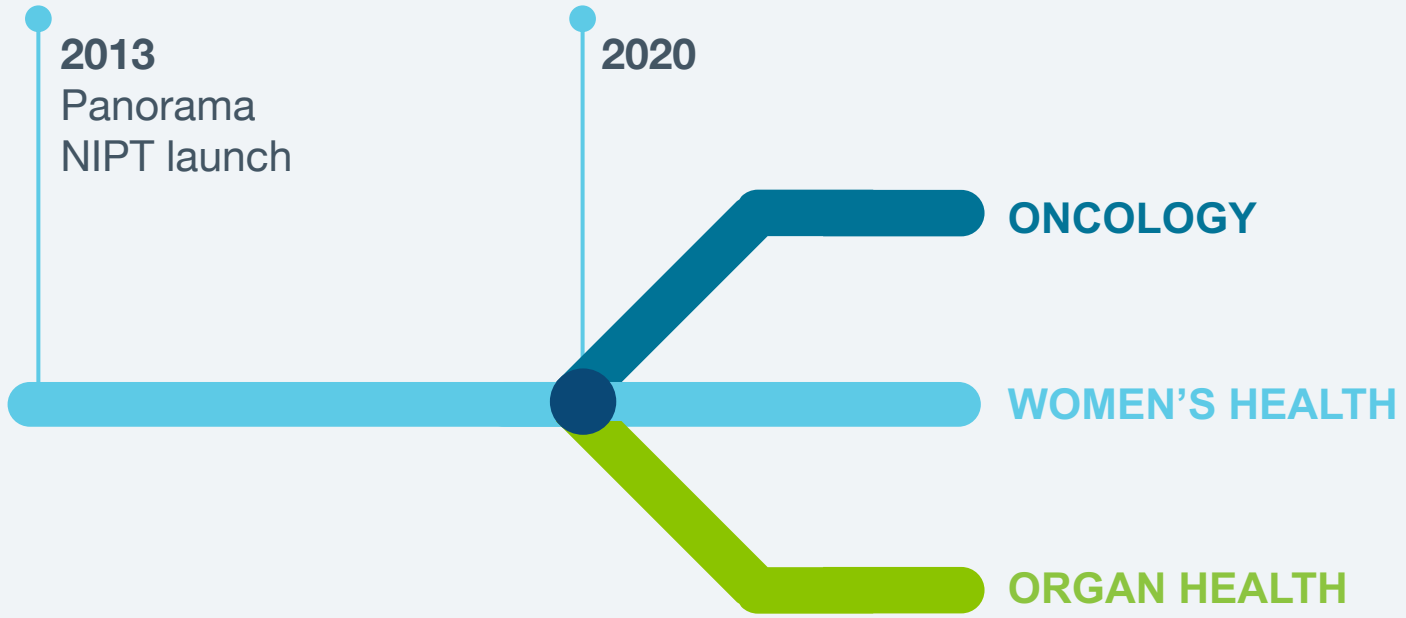
Leader in cell-free DNA technology

- **>3 million** tests performed
- Leader in published data across cell-free DNA applications
- **300+** technology patents filed, >100 issued



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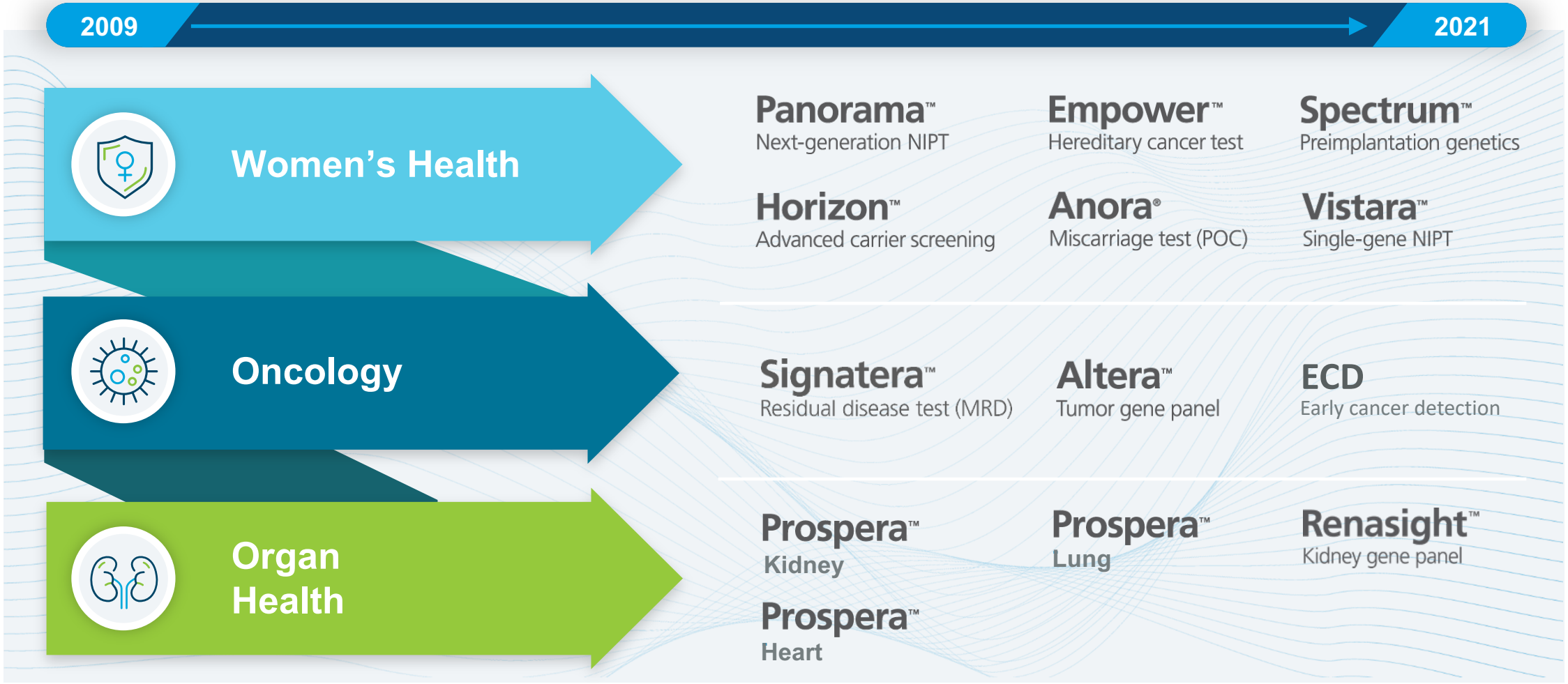
Rapid innovation and growth



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Driven by real world data

Leader in published data across cell-free DNA applications

69+
Women's Health peer-reviewed publications

15+
Oncology peer-reviewed publications

12+
Organ Health peer-reviewed publications



Clinical Cancer Research

Journal of Clinical Oncology

Contemporary OB/GYN

JAMA Oncology

AJOG American Journal of Obstetrics & Gynecology

Science

>1.3M patients studied

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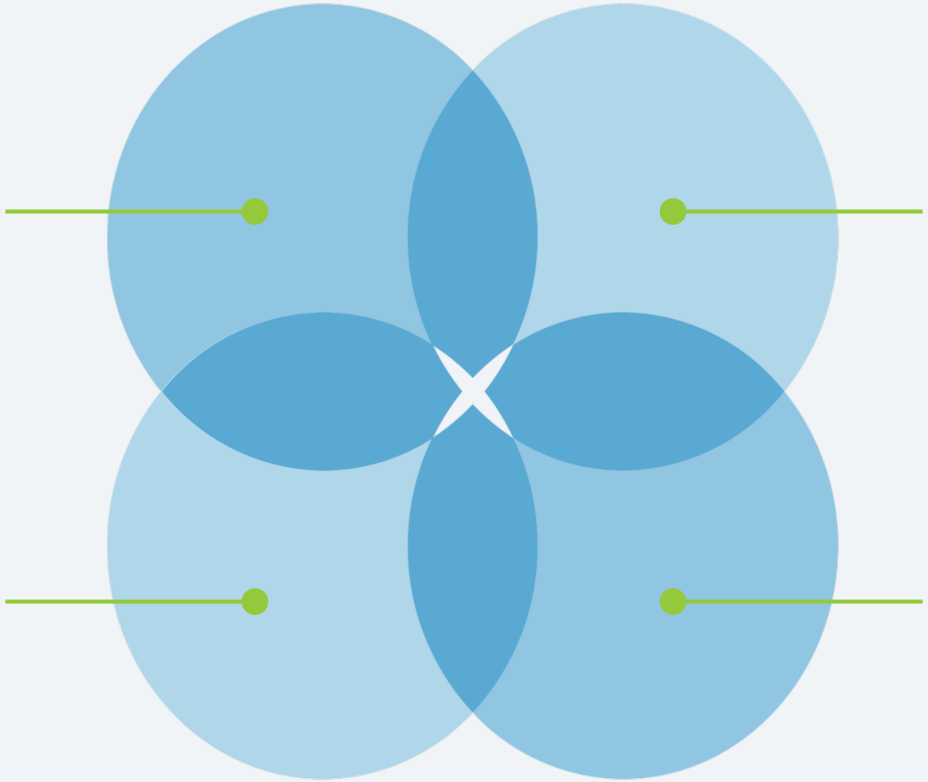
Our formula for success

Leading-edge technology + constant innovation

Broad + talented commercial teams



Extreme focus on customer experience + support services

#1 in clinical data + expert clinical teams

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Transformational 2021

- >1.5M total tests processed; ~52% growth vs 2020
- Consolidated market share in women's health even as the market expanded significantly
- Raised revenue guide by >$100M through the course of the year
- Groundbreaking new cancer data: phase 3 data in bladder cancer, landmark 6 month follow up data on ~800 patients in CIRCULATE trial
- Major reimbursement milestones for Signatera: ADLT awarded, umbrella LCD published
- Announced expansion into early cancer detection (ECD)
- SMART study readout in NIPT and microdeletions: landmark 5-year, 20,000 patient trial
- Achieved cash flow break-even in women's health
- Commercial launch of Prospera Kidney with quantification, Prospera Heart and Prospera Lung
- Successful readout of Trifecta study – largest prospective fully biopsy matched kidney data

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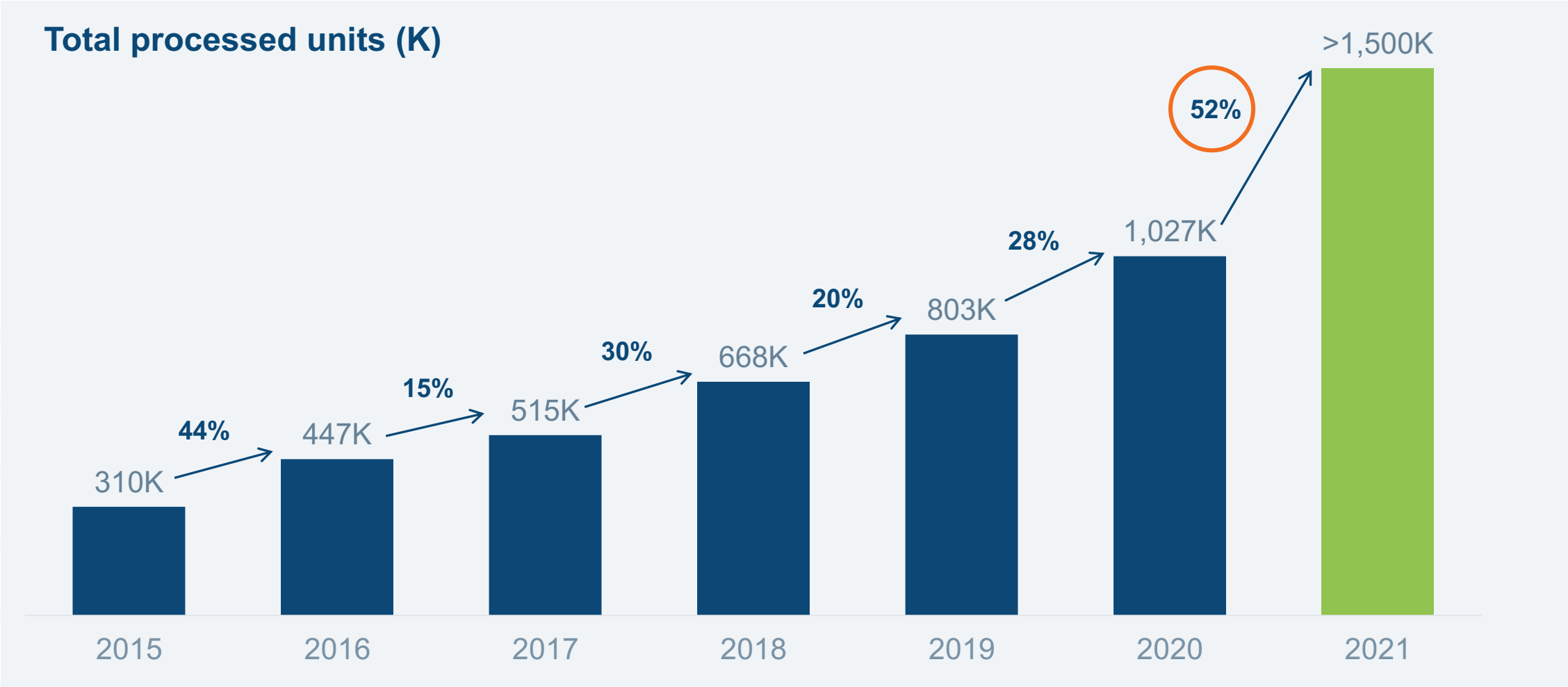
Volume acceleration in 2021



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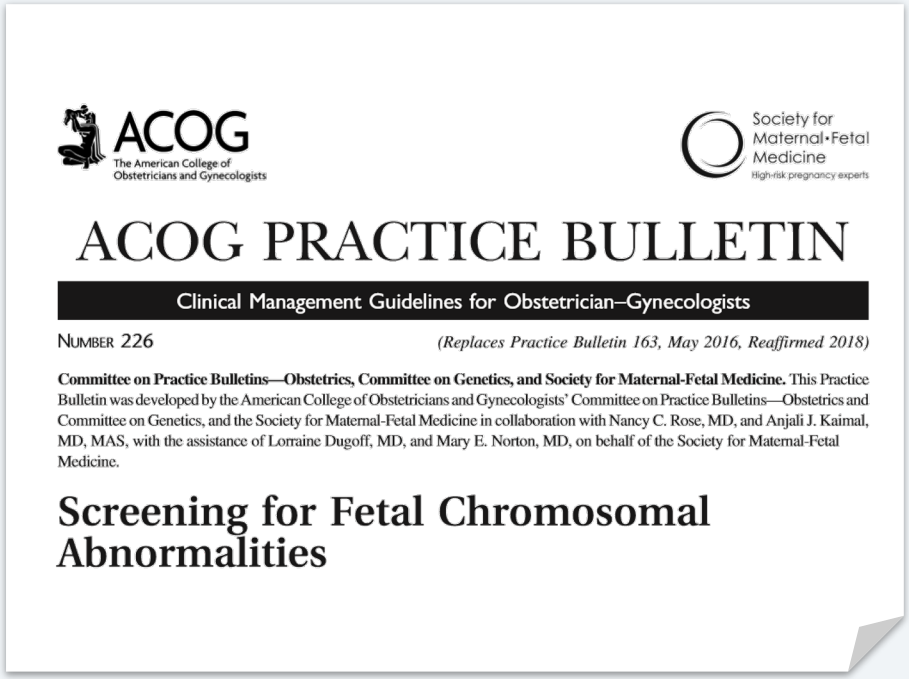
Average risk NIPT will help millions of patients per year

ACOG/SMFM support



ACOG
The American College of Obstetricians and Gynecologists

Society for Maternal-Fetal Medicine
High-risk pregnancy experts

ACOG PRACTICE BULLETIN

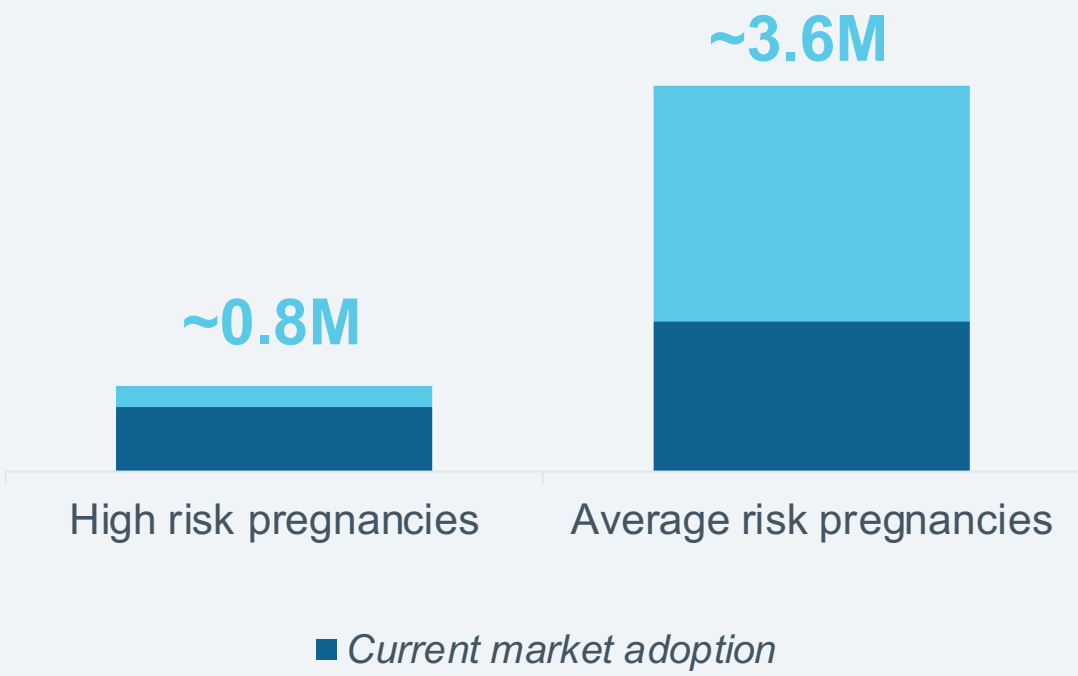
Clinical Management Guidelines for Obstetrician–Gynecologists

NUMBER 226 *(Replaces Practice Bulletin 163, May 2016, Reaffirmed 2018)*

Committee on Practice Bulletins—Obstetrics, Committee on Genetics, and Society for Maternal-Fetal Medicine. This Practice Bulletin was developed by the American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics and Committee on Genetics, and the Society for Maternal-Fetal Medicine in collaboration with Nancy C. Rose, MD, and Anjali J. Kaimal, MD, MAS, with the assistance of Lorraine Dugoff, MD, and Mary E. Norton, MD, on behalf of the Society for Maternal-Fetal Medicine.

Screening for Fetal Chromosomal Abnormalities

~4.4M pregnancies in U.S.[1]



1. 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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The value of prenatal screening

Identifies a high-risk cohort of patients who may benefit from diagnostic testing

Historical method

Serum test

Trisomy 21
(1 in 700)

Low risk	High risk
1 in 1870	1 in 29

Natera's approach

Panorama test

Trisomy 21
(1 in 700)

Low risk	High risk
<1 in 10,000	9 in 10

22q11.2
(1 in 2000)

Low risk	High risk
1 in 9000	1 in 2

Responsible approach:

- NPV and PPV on every report
- Free information sessions with licensed genetic counselor pre and post test
- Test only available through licensed physician with patient consent
- Results reported as high risk/low risk vs. positive or negative
- Extensive peer reviewed data validating test performance

References:

- Snijders et al. Ultrasound Obstet Gynecol 1999;13:167–170
- Gross et al. Prenatal Diagnosis 2011; 31, 259-266
- Norton et al. N Engl J Med 2015;372:1589-97
- Dar et al. Multicenter prospective study of SNP-based cfDNA screening for aneuploidy with genetic confirmation in 18,497 pregnancies. Society of Maternal-Fetal Medicine, SMFM Virtual Meeting. Oral Presentation. Jan 25-30, 2021
- Dar et al. Multicenter prospective study of SNP-based cfDNA for 22q11.2 deletion in 18,290 pregnancies with genetic confirmation. Society of Maternal-Fetal Medicine, SMFM. Virtual Meeting. Oral Presentation. Jan 25-30, 2021

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FINAL RESULTS SUMMARY

Result	*Fetal Sex*	*Fetal Fraction*
HIGH RISK for 22q11.2 deletion syndrome	**Male**	**8.3%**

This is a screening test only. Genetic counseling and diagnostic testing with a microarray should be offered to further evaluate these findings.

Panorama analyzes DNA from the placenta. In some cases placental DNA can differ from that of the fetus. Therefore, even with high risk results, the fetus may be unaffected.

RESULT DETAILS: ANEUPLOIDIES

Condition tested[1]	*Result*	*Risk Before Test*[2]	*Risk After Test*[3]
Trisomy 21	Low Risk	1/152	<1/10,000
Trisomy 18	Low Risk	1/354	<1/10,000
Trisomy 13	Low Risk	1/1,116	<1/10,000
Monosomy X	Low Risk	1/255	<1/10,000
Triploidy	Low Risk		

RESULT DETAILS: MICRODELETIONS

Condition tested[1]	*Result*	*Risk Before Test*[2]	*Risk After Test*[4]
22q11.2 deletion syndrome	High Risk	1/2,000	1/2

Definitive SMART trial highlights NIPT accuracy

Society for Maternal-Fetal Medicine

Study results

Aneuploidies (Trisomy 21):

- 99% sensitivity / 99.97% specificity
- Accuracy of 99.97% (results correct 99.97% of time)
- Positive predictive value 95.1% (9/10) vs. 3.5% (1/29) with maternal serum screening

Microdeletions (22q11.2 Deletion Syndrome):

- Incidence 1/1,524 – 2nd most common genetic disease – more common than Trisomy 21 for women under age 27
- Accuracy of 99.94% (results correct 99.94% of time)
- 22q clinical PPV of 53% (1/2) - algorithm in production since March 2021

Comments

Clinical utility of testing for 22q:

- Avoid diagnostic odyssey: average of 4.7 years to diagnosis
- Early interventions improve outcomes, e.g. calcium-level monitoring, correction of cardiac defects, delay of live vaccines, palatal eval. for speech & feeding issues
- Supported by the 22q11.2 foundation and The American College of Medical Genetics

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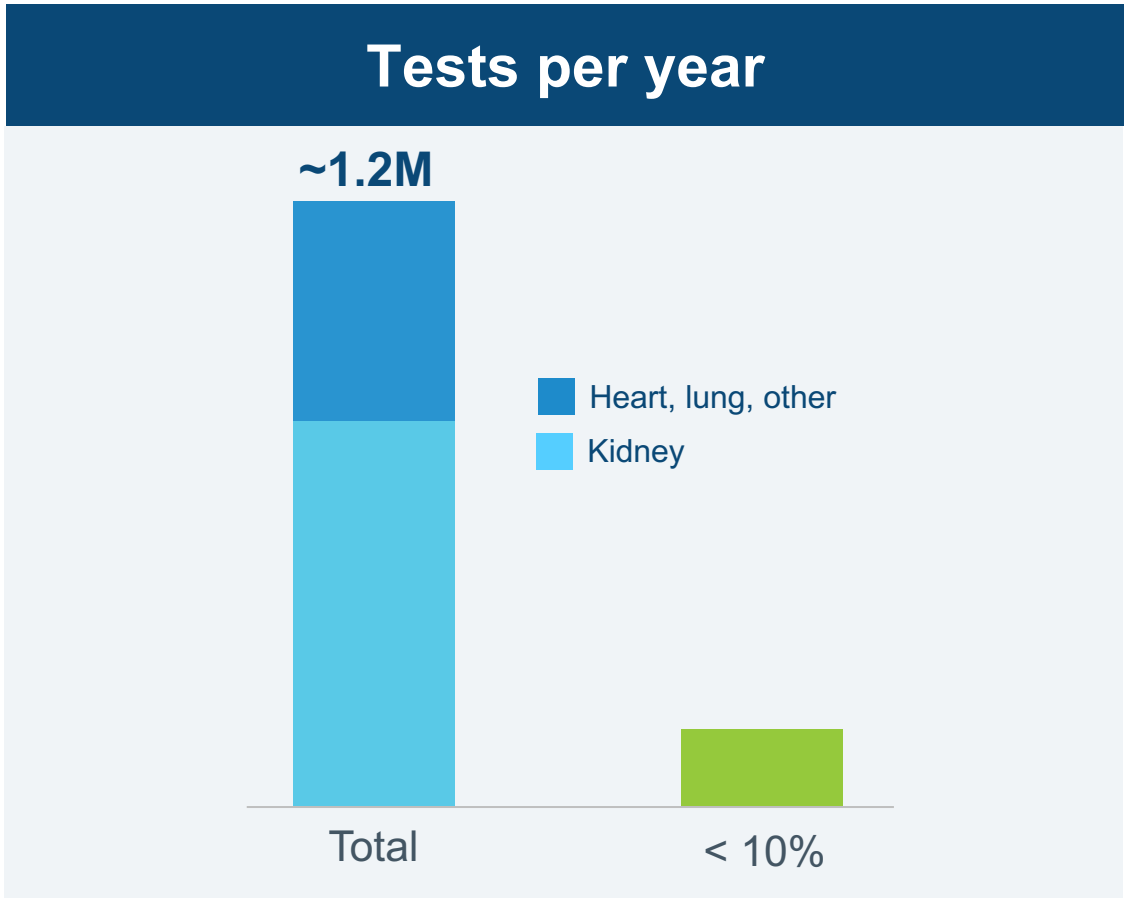
Transplant: significant opportunity to help patients

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



Source: internal company estimates

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Only Prospera Kidney offers quantification

$$\frac{\text{Absolute quantity of dd-cfDNA (copies per mL)}}{\text{Total quantity of cfDNA (copies per mL)}} = \left(\text{\% dd-cfDNA} \right)$$

Factors that may influence total cfDNA[1-9]

- High body mass index
- Infection
- Age
- Surgery
- Shipment & storage
- Chemotherapy
- Normal variation
- Myocardial infarction
- Hemodialysis
- Rejection

1. Vora N., et al. (2012). Prenat Diagn., 32(9):912–914. doi:10.1002/pd.3919
2. Ahmed A., et al. (2016). Clin Lab., 62(12):2395-2404.
3. Anker, P., et al. (2000). Medicina (B Aires), 60, 99–702.
4. Qi, Y., et al. (2016). Anesthesiology Research and Practice Volume 2016:2794364.
5. Page, K., et al. (2013). PLoS One 8(10):e77963. doi: 10.1371/journal.pone.0077963
6. Swystun, L. et al. (2011). Journal of Thrombosis and Haemostasis, 9:2313–2321.
7. Stroun, M., et al. (2001). Clin Chim Acta, 313(1-2): 139–142.
8. Chang, R., et al. Chimica Acta, 327(1-2):95-101.
9. Tovbin, N., et al. (2012). Nephrology Dialysis Transplantation, 27(10), 3929-3935

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Initial results from Trifecta study further validates Prospera with quantification

Largest prospective fully biopsy-matched, multi-site cohort of dd-cfDNA for kidney transplant recipients[1]

Details of study

- More than 300 biopsy-matched samples
- Over 100 biopsy-confirmed rejections
- From more than 20 US & international sites



Philip Halloran, MD, PhD
Distinguished University Professor
Department of Medicine,
Division of Nephrology and Transplant Immunology, University of Alberta

Initial results:

	Area under the curve
Rejection from non-rejection using BANFF 2019 as truth	**0.81**
Rejection from non-rejection using molecular pathology as truth	**0.89**
Rejection from 'quiescence' using BANFF 2019 as truth[2]	**0.91**

1. Halloran, et al. Manuscript in preparation, 2021
2. Quiescence: No signs of rejection on pathology or DSA

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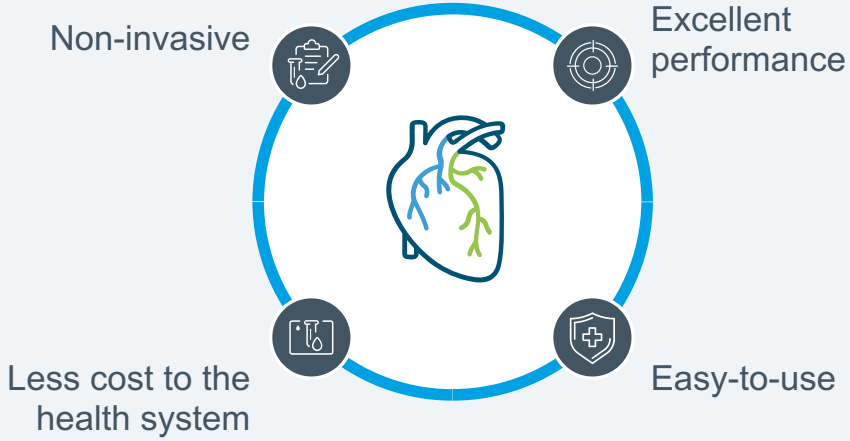
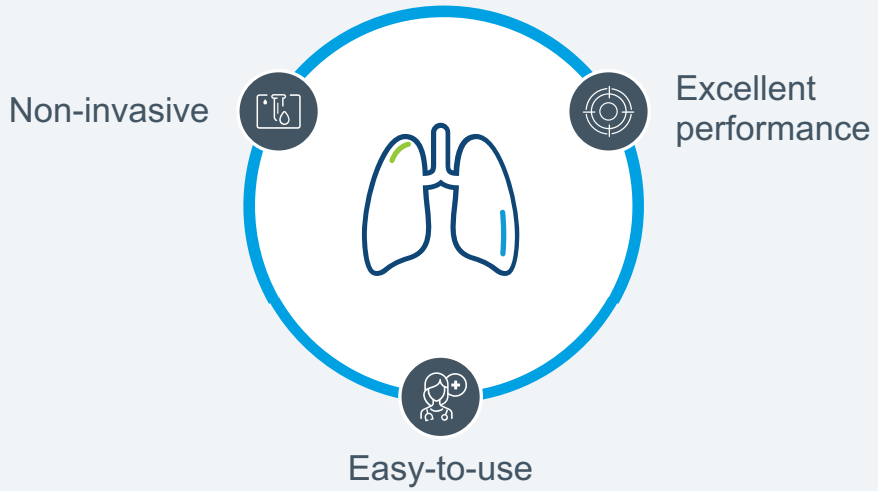
Commercial launch of Prospera Heart and Prospera Lung

Prospera Heart	
Heart Transplants/Yr[1]	3,952
Patients living with a transplant[2]	40,921
Tests per year	>190,000
Area Under the Curve (AUC)	0.844



Prospera Lung	
Lung Transplants/Yr[1]	2,940
Patients living with a transplant[2]	17,798
Tests per year	>90,000
Area Under the Curve (AUC)	0.91[3]



1. Year 2022. Assumes avg. of 5yr & 10yr rolling CAGR per UNOS database
2. Year 2022. Based on OPTN survival rates
3. AUC was calculated using trapezoidal rule and bootstrap method

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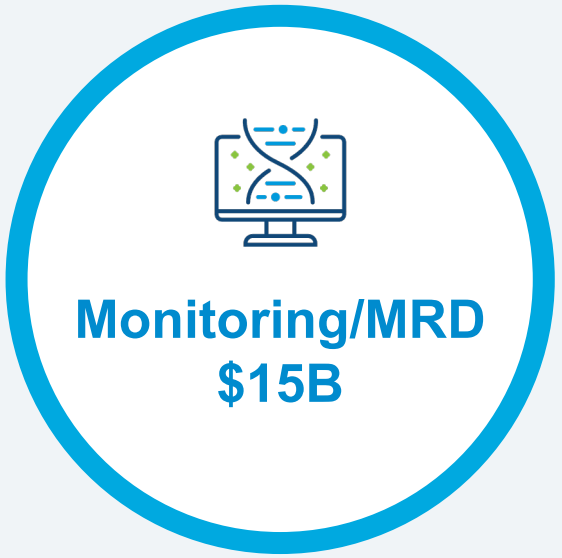
Expanding Oncology TAM opportunity

ctDNA / liquid biopsy







Source: internal company estimates

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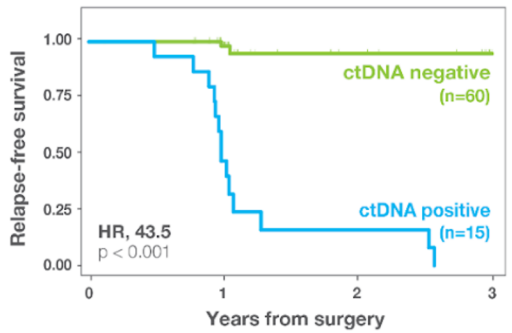
Consistent MRD results validated across multiple tumor types

JAMA ONCOLOGY

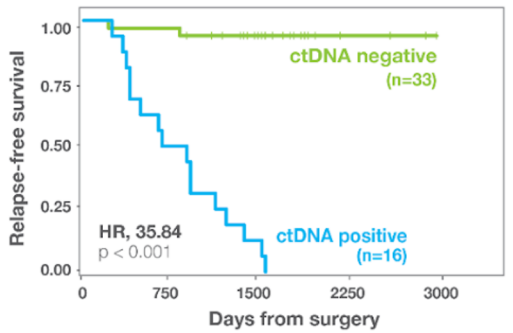
Colon[1]



88% sensitivity to relapse
Average lead time 8.7 mos

CLINICAL CANCER RESEARCH

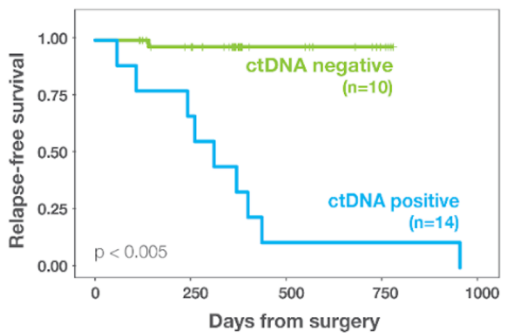
Breast[2]



89% sensitivity to relapse
Average lead time 9.5 mos

NATURE

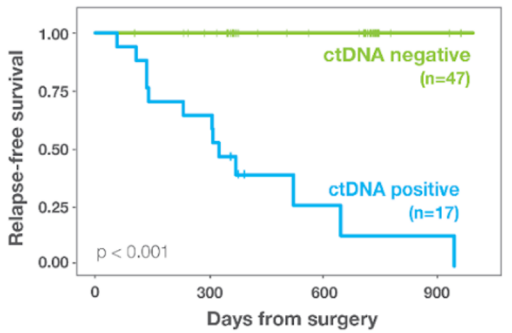
Lung[3]



92% sensitivity to relapse
Average lead time 4.0 mos

JOURNAL OF CLINICAL ONCOLOGY

Bladder[4]



100% sensitivity to relapse
Average lead time 2.8 mos

Positive Signatera result, without further treatment, has predicted relapse with overall PPV > 98%[1-4]

1. Reinert T, Henriksen TV, Christensen E, et al. Analysis of Plasma Cell-Free DNA by Ultradeep Sequencing in Patients With Stages I to III Colorectal Cancer. JAMA Oncol. 2019.
2. Coombes RC, Page K, Salari R, et al. Personalized Detection of Circulating Tumor DNA Antedates Breast Cancer Metastatic Recurrence. Clin Cancer Res. 2019;25(14):4255-4263.
3. Abbosh C, Birkbak NJ, Wilson GA, et al. Phylogenetic ctDNA analysis depicts early-stage lung cancer evolution. Nature. 2017;545(7655):446-451.
4. Christensen E, Birkenkamp-Demtroder K, Sethi H, et al. Early Detection of Metastatic Relapse and Monitoring of Therapeutic Efficacy by Ultra-Deep Sequencing of Plasma Cell-Free DNA in Patients With Urothelial Bladder Carcinoma. J Clin Oncol. 2019;37(18):1547-1557.

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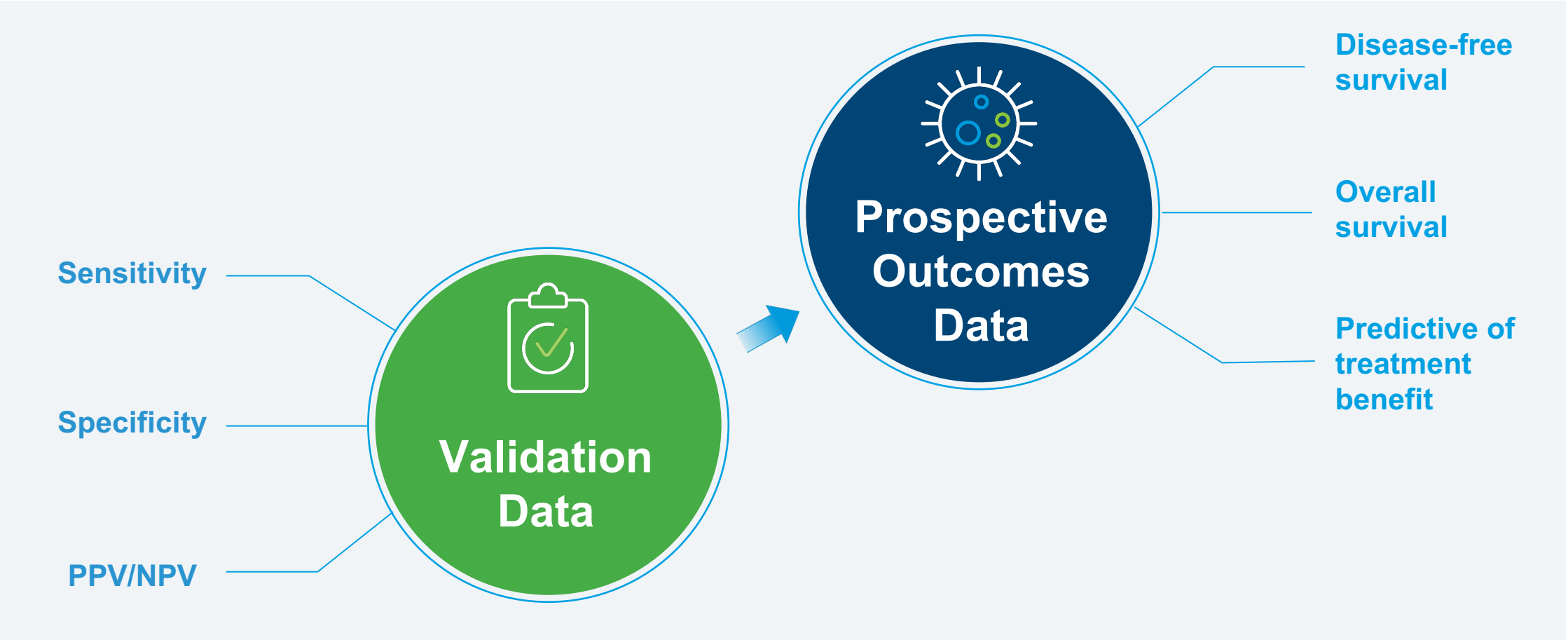
Oncology evidence generation advancing



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Circulate-IDEA Japan: largest prospective MRD study

ASCO, ESMO IO 2021

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

Upcoming 2022

- ~1600 patients enrolled
- ~1000 patients analyzed
- Disease free survival stratified by ctDNA result:
  - Mean ~ 12 months
  - Max ~20 months

Building evidence that could change society practice guidelines

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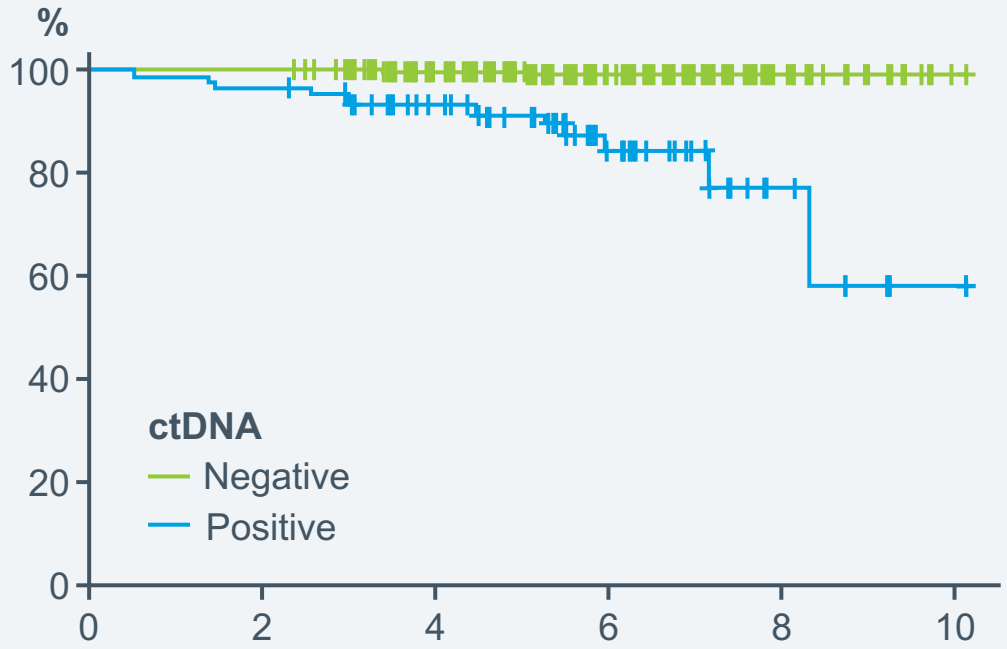
Leading in clinical data development

ASCO, ESMO IO 2021[1]

Prognostic



Upcoming 2022

Predictive

- Do MRD positive patients benefit from chemotherapy?
  - is the benefit present across stages?
- Are ctDNA dynamics predictive of adjuvant chemotherapy benefit?
- Do MRD negative patients benefit from adjuvant chemotherapy?

1. Shirasu H, Taniguchi H, Watanabe J, et al. Monitoring molecular residual disease by circulating tumor DNA in resectable colorectal cancer: Molecular subgroup analyses of a prospective observational study GALAXY in CIRCULATE-Japan. ESMO GI, June 30-July 4, 2021.

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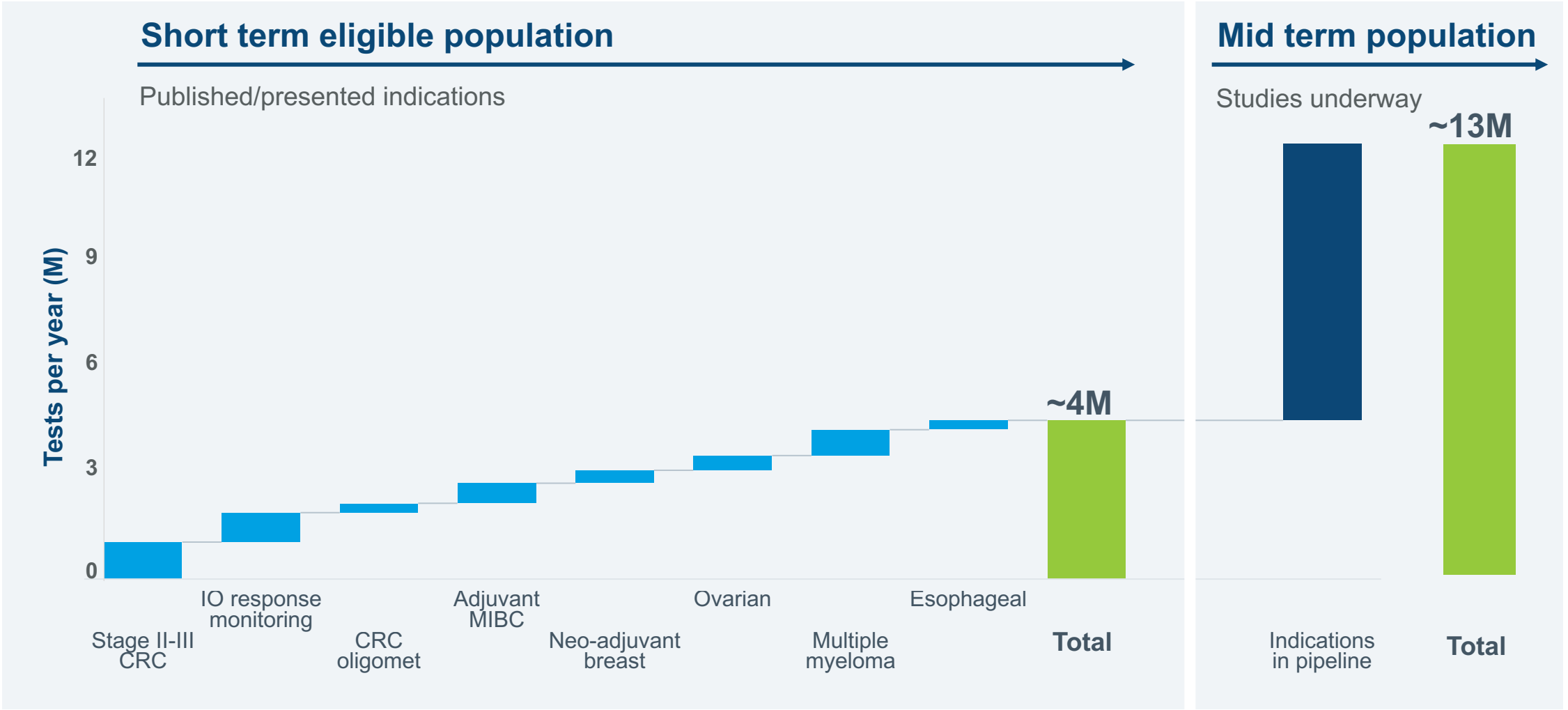
Significant unmet need served by one technology platform and one commercial team



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 in > 3,500 patients, >15 peer-reviewed publications

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

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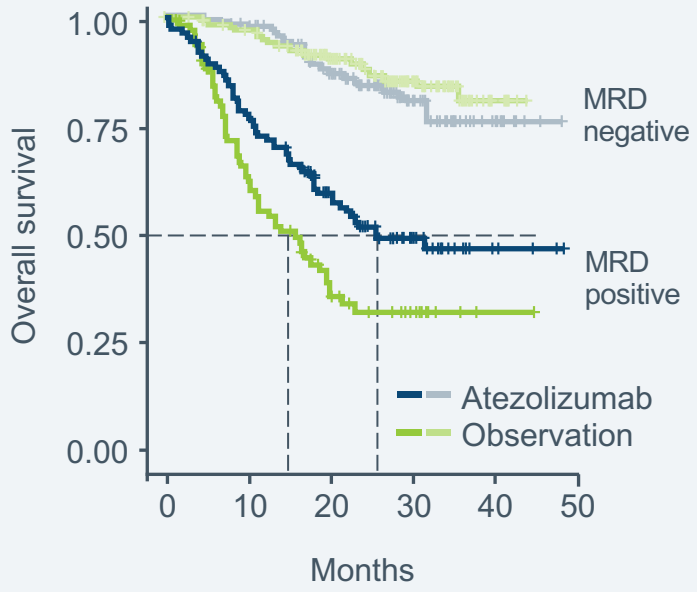
Pharma business yielding major phase III wins

IMvigor 010[1]



Phase III trials enrolling

Zest[2]

- Phase III trial evaluating niraparib (Zejula) in early-stage breast cancer patients

Imvigor 011[3]

- Phase III trial, evaluating adjuvant immunotherapy with atezolizumab in high-risk muscle-invasive bladder cancer patients

Why we win

- Product performance
- Regulatory capability
- Commercial and reimbursement leadership

1. Powles T, Assaf ZJ, Davarpanah N, et al. Clinical outcomes in post-operative ctDNA (+) muscle-invasive urothelial carcinoma patients after atezolizumab adjuvant therapy. ESMO IO, Dec 2020
2. https://clinicaltrials.gov/ct2/show/NCT04915755
3. https://clinicaltrials.gov/ct2/show/NCT04660344?term=imvigor+011&draw=2&rank=1

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Potential 2022 catalysts

- Continued adoption of NIPT
- SMART trial publication early 2022
- CIRCULATE-IDEA data in colorectal cancer
- BESPOKE data early readout 2H 2022
- Data and publications in multiple different cancer types
- Additional reimbursement for Signatera in new tumor types
- Suite of significant organ health publications
- Year 2 of commercialization in organ health and oncology
- Product enhancements and launches

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