Natera, Inc.

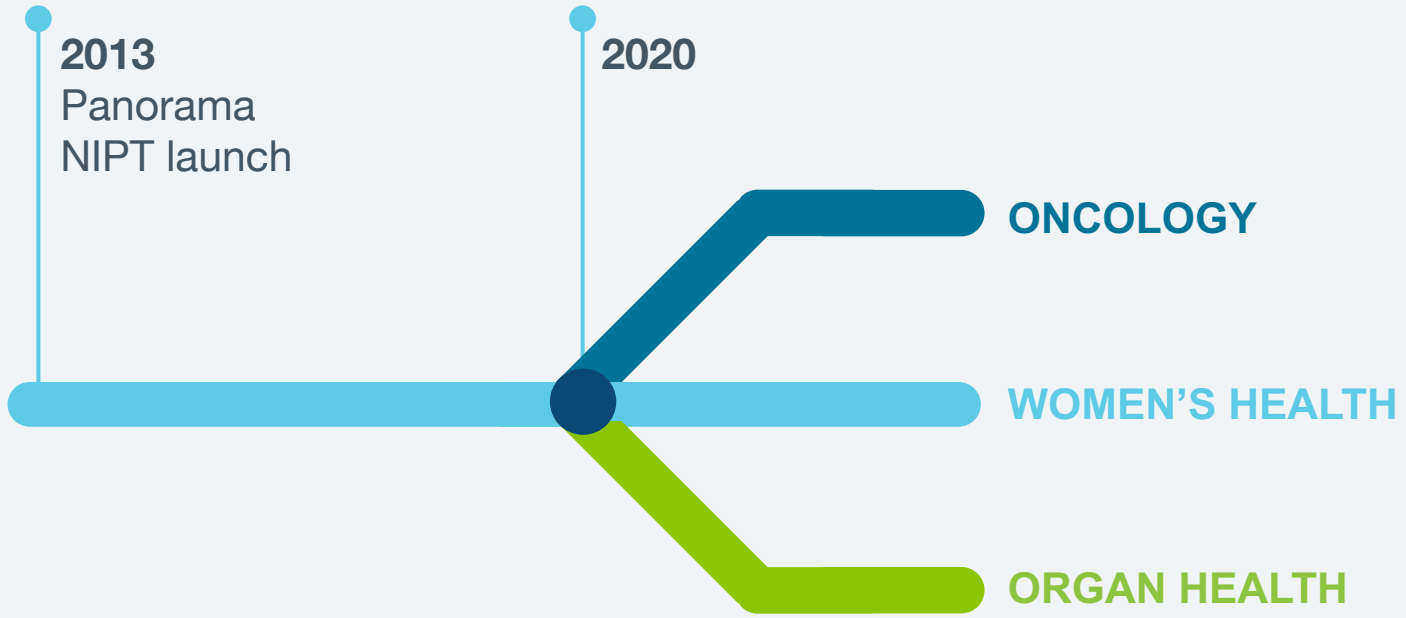
Investor presentation

January 2021

JP Morgan Conference

Leader in cell-free DNA technology

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



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We hit our goals in 2020

2020 Goals Achieved

1. **Extend** leadership position in reproductive health
2. **Change** patient care for transplant recipients
3. **Establish** Signatera™ as the new standard for cancer care

Well Positioned for 2021

- **~1 million tests processed,** momentum from average risk coverage and SMART study
- Pre-pandemic Prospera volume growth **targets exceeded**
- **Clinical launch and reimbursement,** drumbeat of new studies, pharma acceleration, sales team hired

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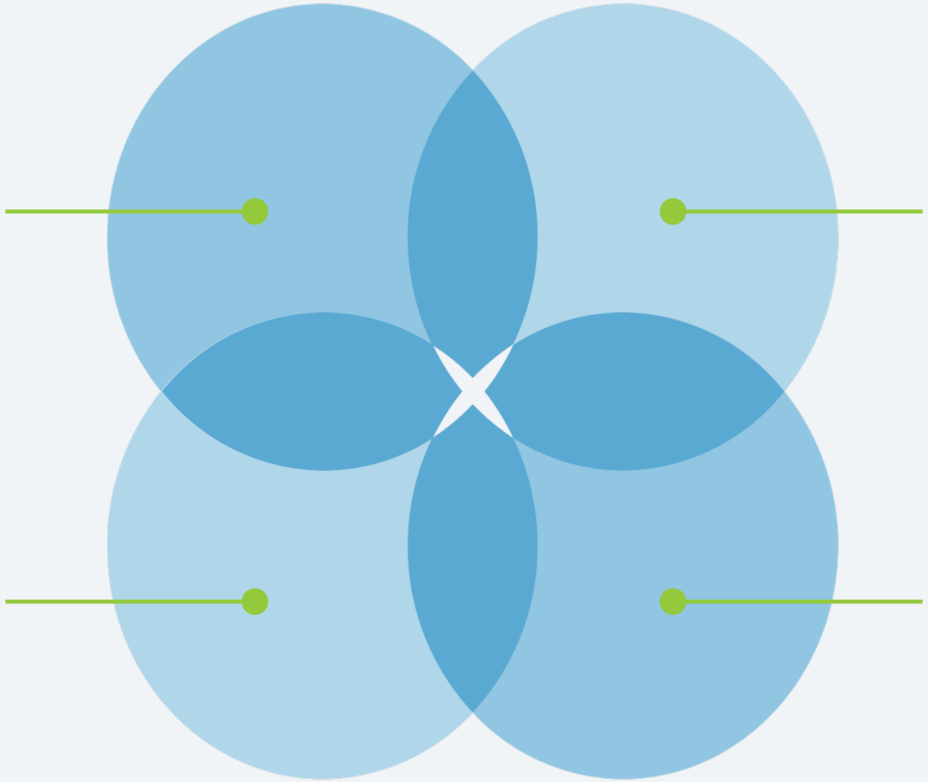
Our formula for success

Bleeding-edge technology + constant innovation

Extreme focus on user experience + support services



Broad + talented commercial teams

#1 in clinical data + expert clinical teams

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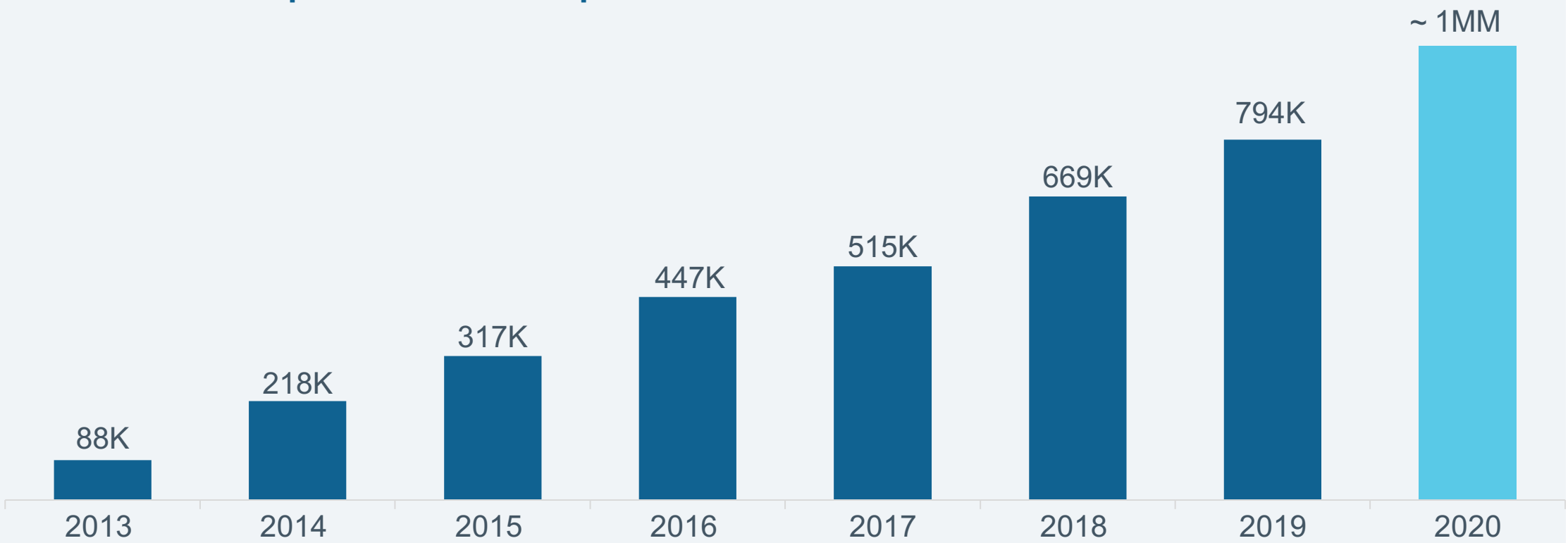
Leadership position in reproductive health

Test volumes – reproductive health products



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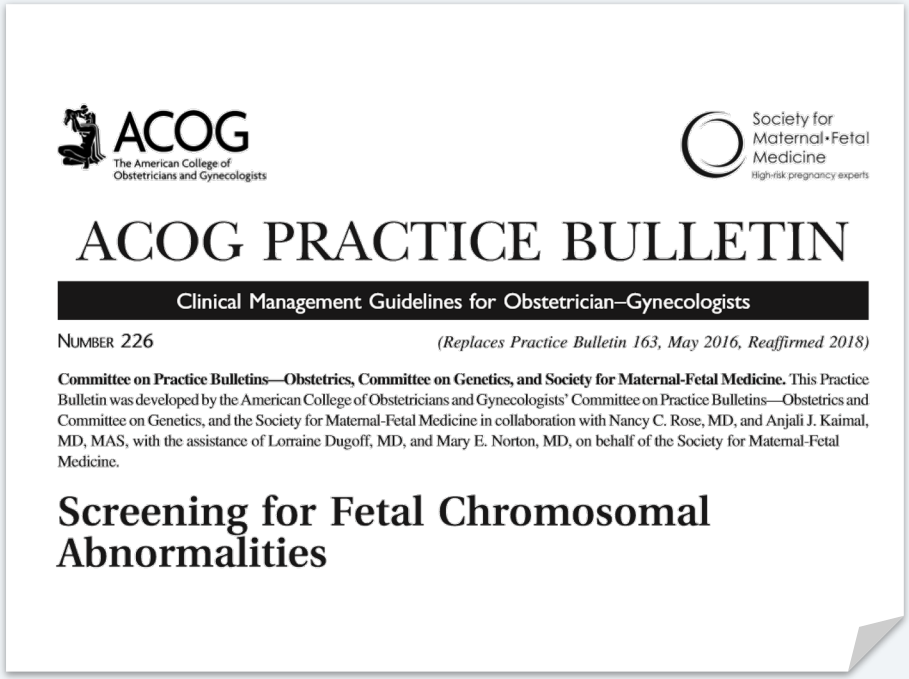
Average risk NIPT is just getting started

ACOG/SMFM support



ACOG
The American College of Obstetricians and Gynecologists

Society for Maternal-Fetal Medicine
High-risk pregnancy experts

ACOG PRACTICE BULLETIN

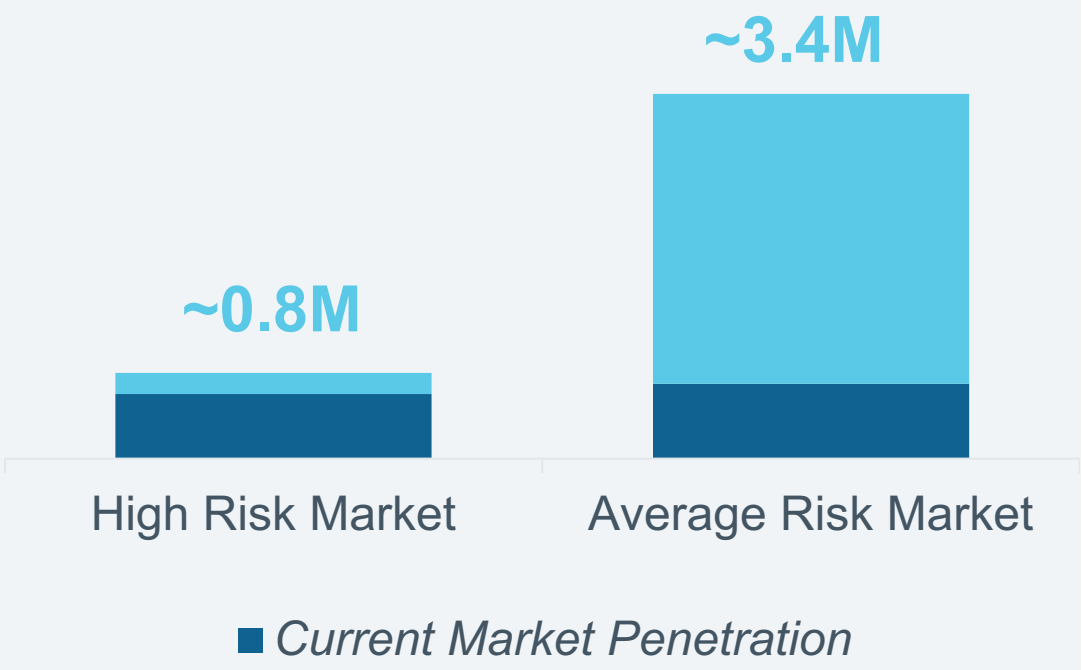
Clinical Management Guidelines for Obstetrician–Gynecologists

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

4.2 million births in U.S.



Source: internal company estimates

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SMART trial analysis complete, reading out in early ‘21

Study design

- 20,000 patient prospective clinical trial
- Two major publications expected in 2021:
  - Largest validation study in average risk NIPT
  - First large prospective trial showing microdeletions performance and incidence in the population
- Validation of Panorama AI platform

Future Impact

- Further differentiates Natera’s SNP-based approach; others use shotgun sequencing
- Market share: best in class performance, most extensively validated tests
- Reimbursement: Supports screening for NIPT and Microdeletions in all women
- CMS rate for microdeletions: $759
- >400K microdeletions tests run in 2020 by Natera

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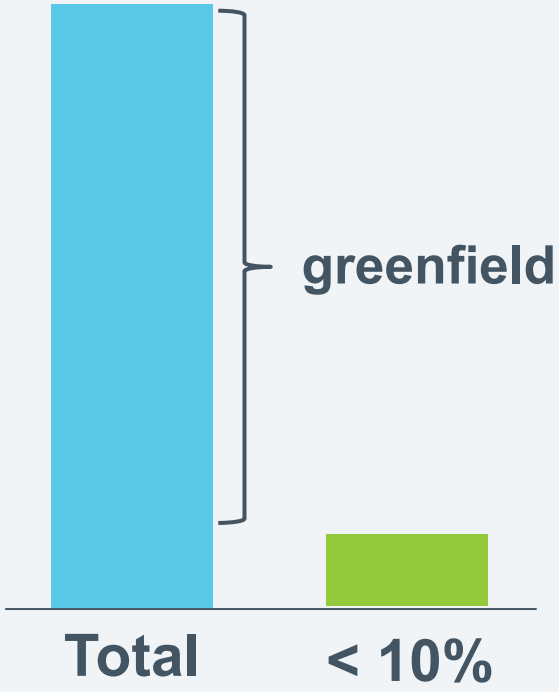
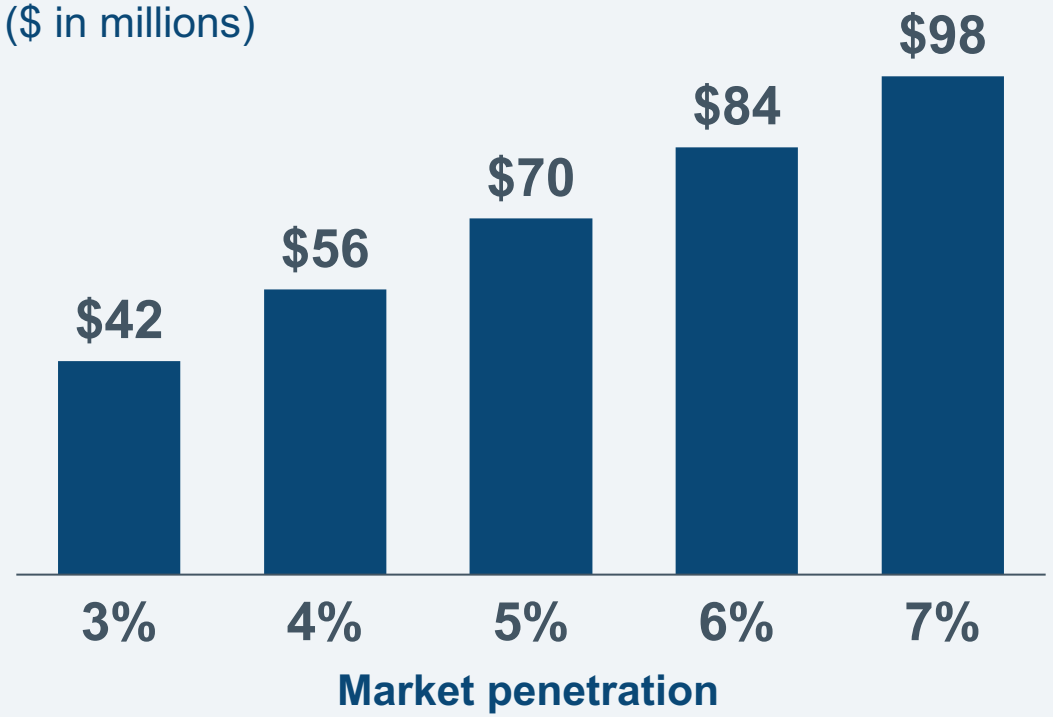
Transplant: Pathway to significant revenue opportunity

Total tests

- $2B market
- < 10% penetrated



Revenue sensitivity



Source: internal company estimates

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Background cf-DNA validation further differentiates Prospera

Background cf-DNA

- Launched at ATC, May 2020
- New real-world data presented at ASN showing clinical utility
- High levels of background cf-DNA impacted by viral infection, especially COVID, can mask rejection

COVID-19 studies

- Upcoming Natera publications studying background cf-DNA in transplant patients with COVID-19
  - COVID-19 case study submitted for publication
  - Study of ~25 COVID-19 patients completed

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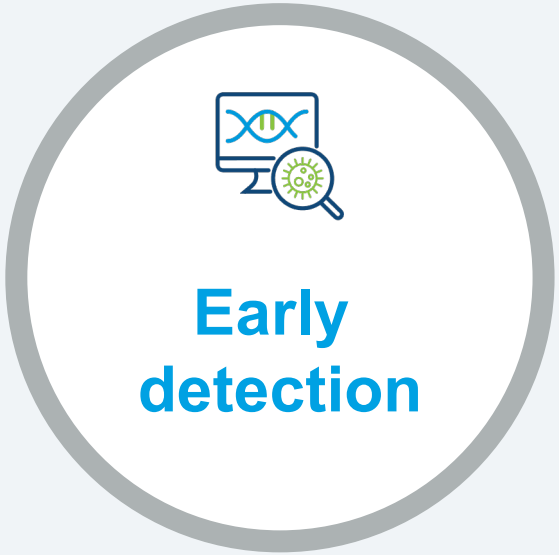
Oncology MRD market opportunity

ctDNA / Liquid biopsy







Source: internal company estimates

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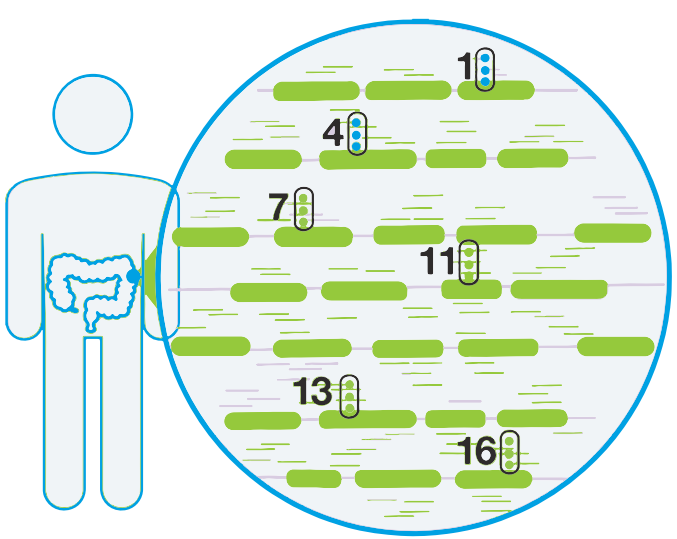
How Signatera works – personalized and tumor-informed MRD

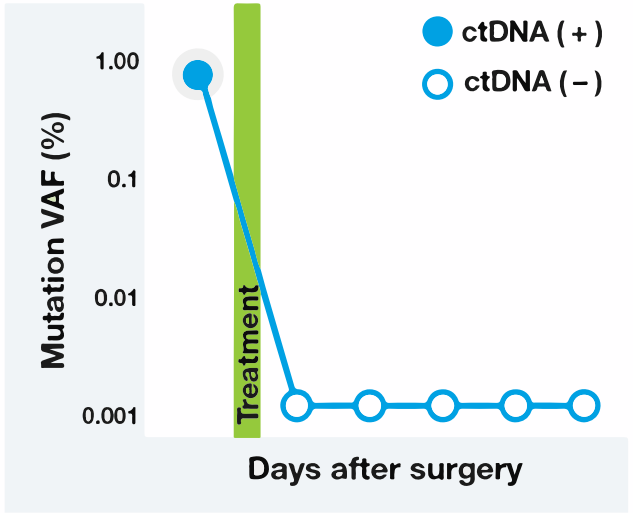
Sequencing of tumor tissue, to identify unique signature of tumor mutations

Custom design and manufacture of personalized mPCR assay for each patient, targeting the top 16 clonal mutations found in tumor

Use personalized assay to test patient's blood for presence of circulating tumor DNA (ctDNA)







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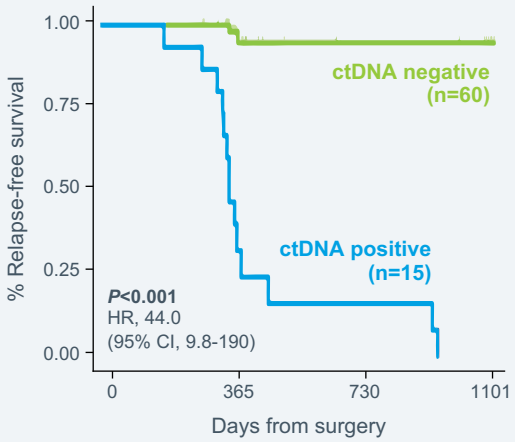
Signatera validated across multiple tumor types

JAMA Oncology

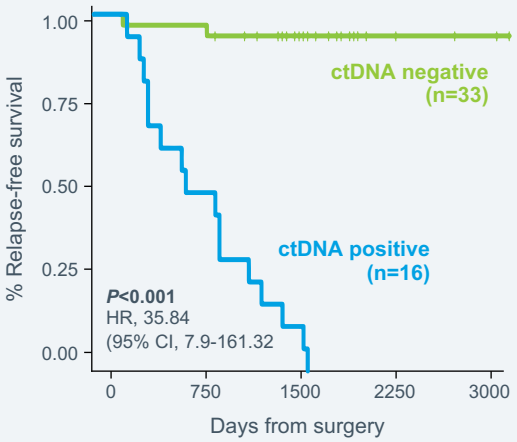
Colon[1]



88% sensitivity to relapse
Average lead time 8.7 mos

Clinical Cancer Research

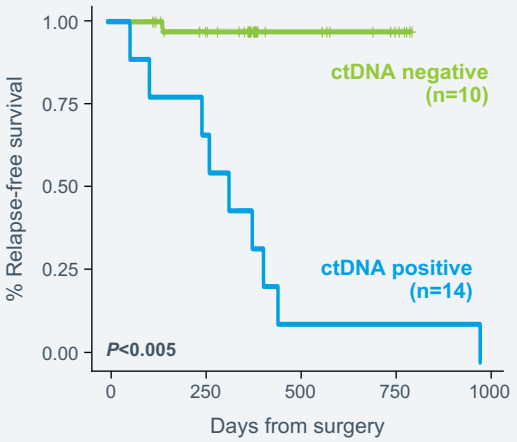
Breast[2]



89% sensitivity to relapse
Average lead time 9.5 mos

Nature

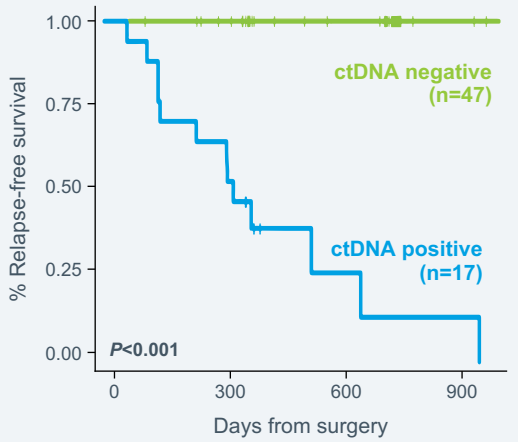
Lung[3]



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.[AMA Oncol. 2019. doi:10.1001/jamaoncol.2019.0528.
2. Coombes RC, Page K, Salari R, et al. Clin Cancer Res. 2019. doi: 10.1158/1078-0432.CCR-18-3663.
3. Abbosh C, Birkbak NJ, Wilson GA, et al. Phylogenetic ctDNA analysis depicts early-stage lung cancer evolution. Nature. 2017;545:446-451.
4. Christensen E, Birkenskamp-Demtroder K, Sethi H, et al. J Clin Oncol. 2019. doi: 10.1200/JCO.18.02052.

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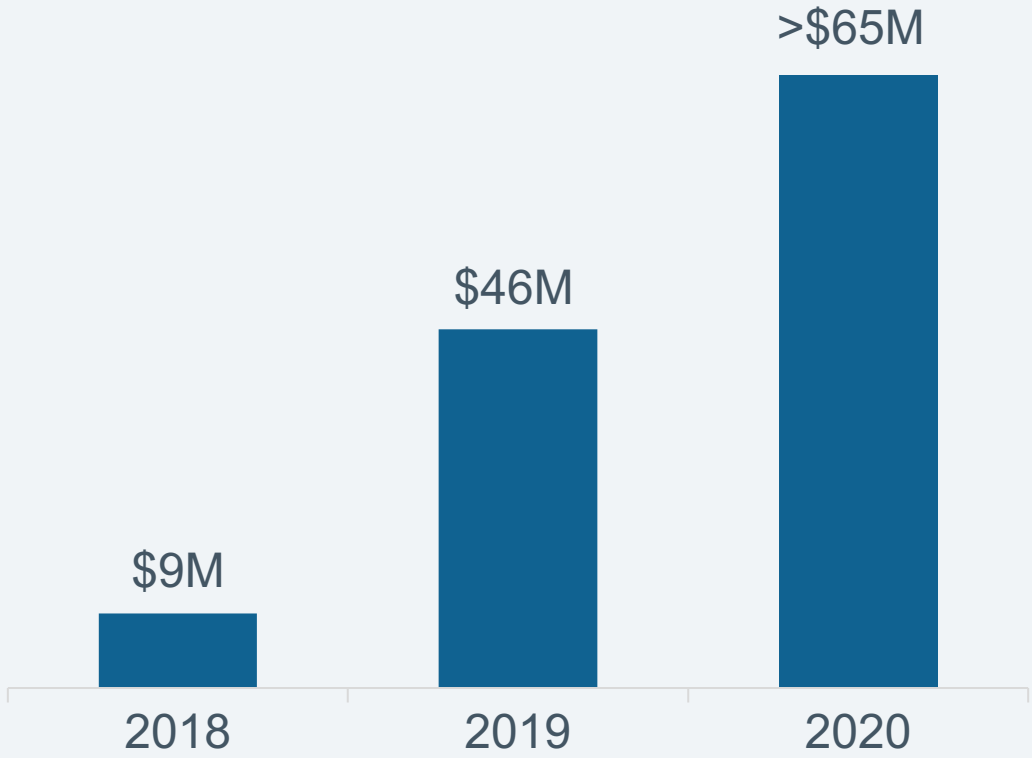
Acceleration in Pharma business, ~$120M signed to date

- Average deal size getting larger, including multiple phase 3 trials with patient volume and development fees
- Two key benefits for pharma:
  1. **Study enrichment:** treating only MRD-positive patients, for higher drug efficacy
  2. **Surrogate endpoint:** observing rates of MRD clearance, for faster study results

Value of new signed contracts



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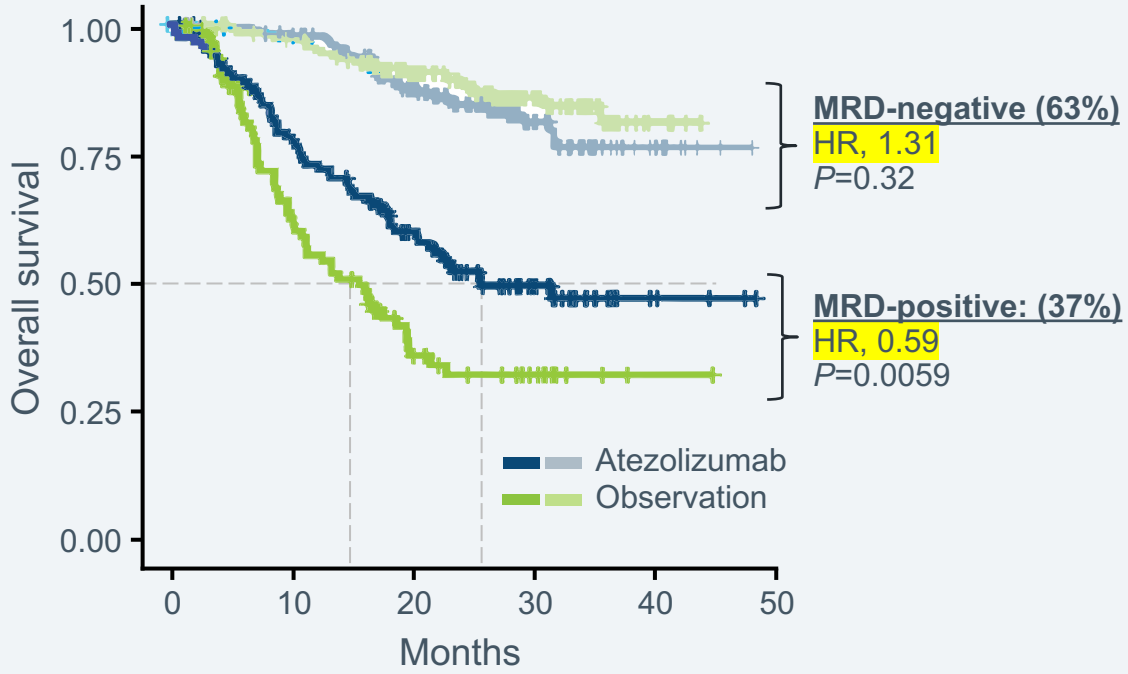
Phase 3 IMvigor study proved that Signatera is predictive of treatment benefit in the adjuvant setting

- **Background:**
  - GNE-sponsored, PhIII randomized controlled trial of atezo vs. obs in adjuvant bladder cancer. Pre-specified analysis with Signatera.
- **Results:**
  - 41% survival benefit in MRD-positive patients treated with atezo. Zero treatment benefit in MRD-negative population.
- **Significance:**
  1. Pharma: MRD stratification becomes a must-have for adjuvant trials
  2. Clinical: predictive evidence strengthens utility of Signatera in CRC

Overall survival in MIBC patients treated with adjuvant atezolizumab vs. observation[1]



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 9-12, 2020, Virtual Meeting, Oral Presentation #10 .

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Medicare final LCD and launch in colorectal cancer

- Est. opportunity ~1 million tests annually
- Over 85% of relapses caught **too late** for curative surgery[1-2]

Adjuvant MRD Program

Use Signatera after surgery to evaluate the need for adjuvant chemotherapy and avoid unnecessary treatment

For Stage II - III colon cancer, Stage IIA rectal cancer

Surveillance Program

Use Signatera alongside CEA to detect recurrence earlier while it may still be resectable, and reduce false positives

For Stage II - III colorectal cancer patients

1. Purandare NC, et al. The Indian journal of radiology & imaging. 2010;20(4):284-288. 2. Lapointe L. Laboratory, Advance Healthcare Network. 2016;25(9):14.
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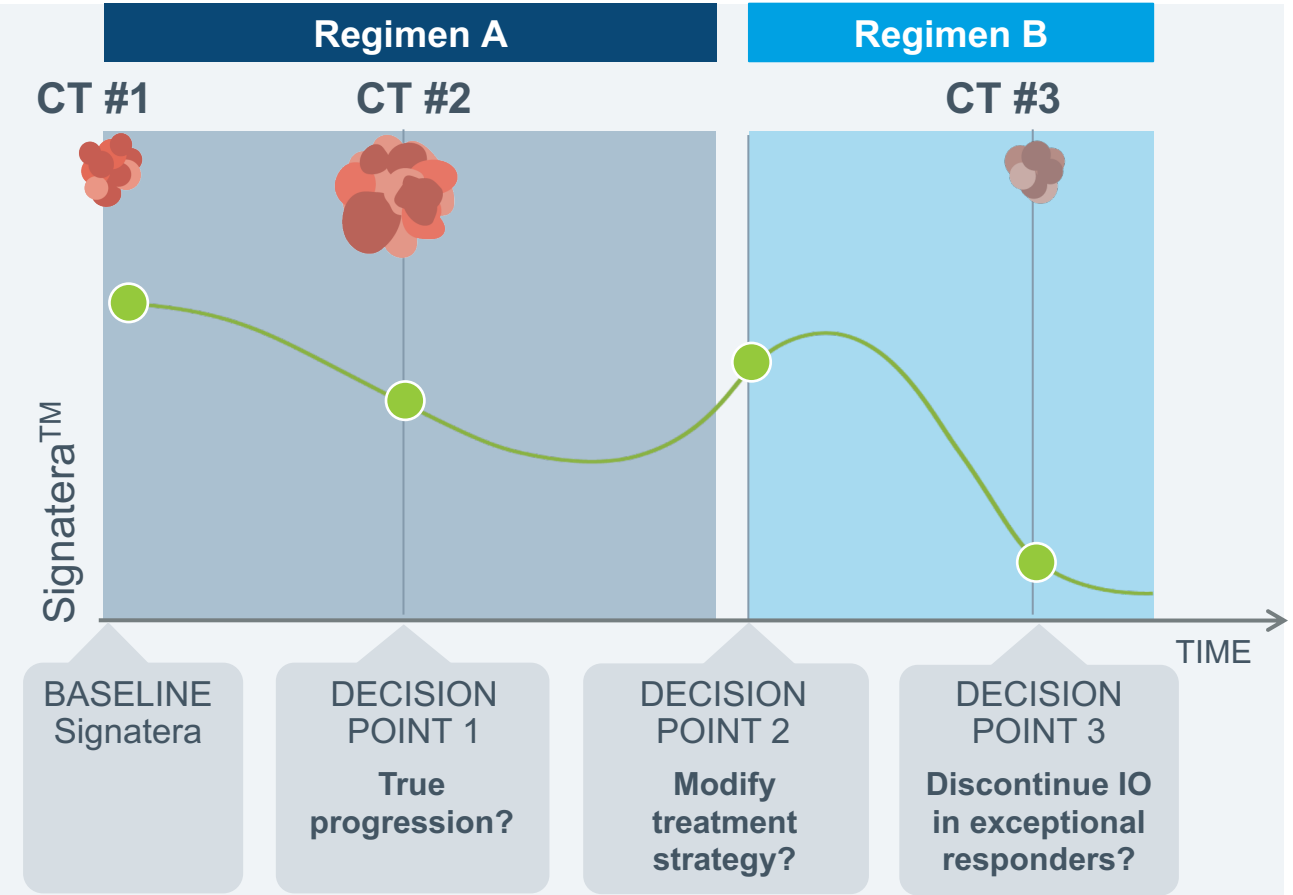
Medicare draft LCD in IO response monitoring

- > 200,000 patients treated with immunotherapy (IO) annually, most do not respond[1]
- Pseudo-progression delays identification of non-responders, Signatera combined with imaging shown to identify 100% of non-responders[2]
- Serial monitoring for secondary resistance or exceptional response, to inform timing of discontinuation



1. IQVIA™ Institute for Human Data Science Releases Global Oncology Trends 2019 Study: Record Number of Cancer Drugs Launched in 2018 across 17 Indications. IQVIA
2. Bratman SV, Yang SYC, Iafolla MAJ, et al. Personalized circulating tumor DNA analysis as a predictive biomarker in solid tumor patients treated with pembrolizumab. Nat. Cancer. 2020. doi: 10.1038/s43018-020-0096-5

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Extending our data leadership in MRD

7 clinical studies published

1. CRC – Reinert et al (JAMA Oncology)
2. IO pan-cancer – Bratman et al (Nature Cancer)
3. Lung – Abbosh et al (Nature)
4. Bladder – Christensen et al (JCO)
5. Breast – Coombes et al (CCR)
6. Breast – Magbanua et al (Annals)
7. Esophageal – Einstein et al (JCOPO)

50+ studies in pipeline

- Breast
- Melanoma
- Renal
- Pancreatic
- Liver
- Lymphoma
- Multiple myeloma
- Colorectal
- Lung
- Prostate
- Glioblastoma
- Ovarian
- Head & neck
- Gastro-esophageal

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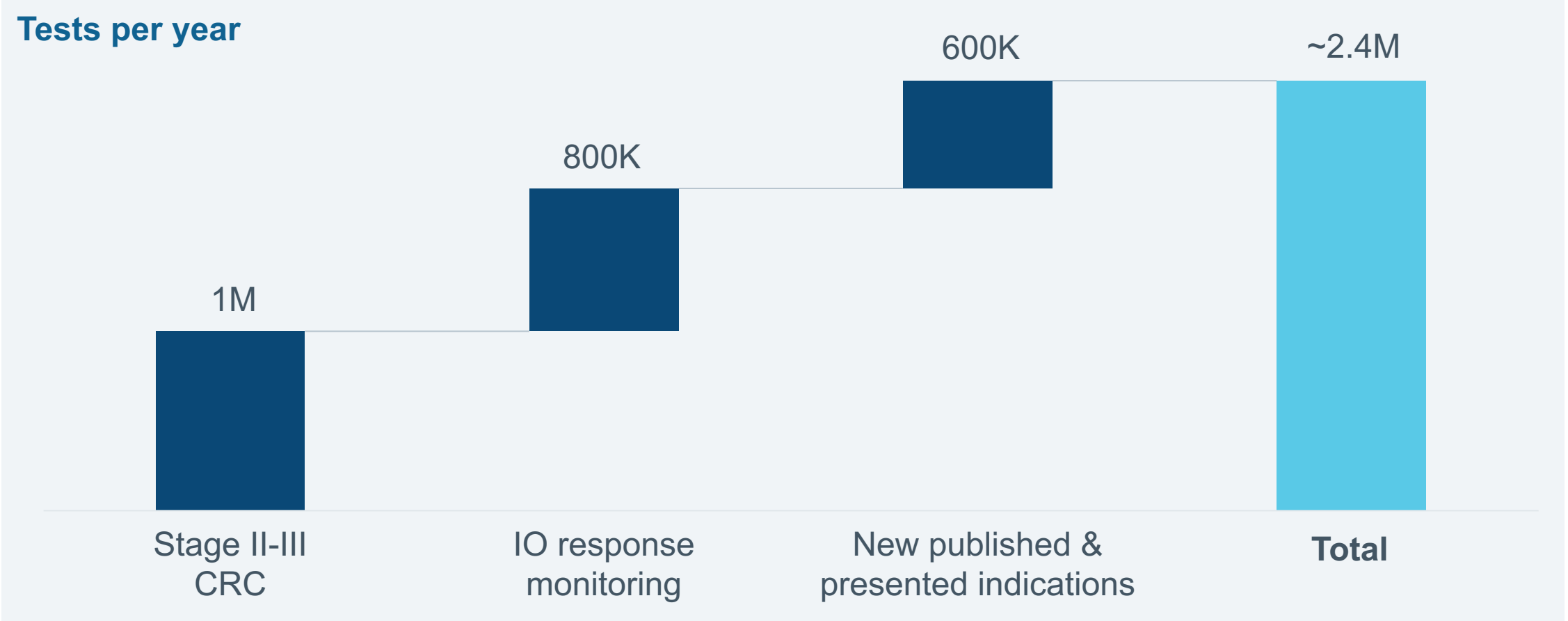
Oncology MRD market opportunity



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