EXACT SCIENCES

Making earlier cancer detection a routine part of medical care

Safe harbor and non-GAAP disclosures

This presentation contains forward-looking statements concerning our expectations, anticipations, intentions, beliefs or strategies regarding the future. These forward-looking statements are based on assumptions that we have made as of the date hereof and are subject to known and unknown risks and uncertainties that could cause actual results, conditions and events to differ materially from those anticipated. Therefore, you should not place undue reliance on forward-looking statements. Examples of forward-looking statements include, among others, statements we make regarding expected future operating results; expectations for development of new or improved products and services; our strategies, positioning, resources, capabilities and expectations for future events or performance; and the anticipated benefits of our acquisitions, including estimated synergies and other financial impacts.

In addition to the company's financial results determined in accordance with U.S. GAAP, the company provides non-GAAP measures that it determines to be useful in evaluating its operating performance. The company presents EBITDA, adjusted EBITDA, non-GAAP gross margin, non-GAAP gross profit, and normalized and constant currency growth rates in revenue. This presentation includes certain of these measures. Management believes that presentation of operating results using non-GAAP financial measures provides useful supplemental information to investors and facilitates the analysis of the Company’s core operating results and comparison of operating results across reporting periods. Management also uses non-GAAP financial measures to establish budgets and to manage the Company’s business. Please refer to our fourth quarter 2022 earnings release for discussion of non-GAAP financial measures and reconciliations to GAAP financial measures. Information reconciling forward-looking non-GAAP measures to U.S. GAAP measures is not available without unreasonable effort.

#1

cancer is the #1 cause of death under age 85

Source: Centers for Disease Control and Prevention

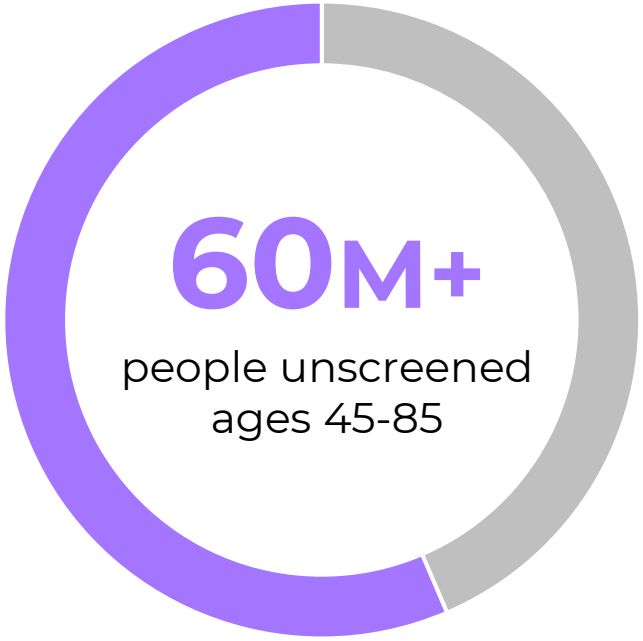
Exact Sciences helps detect cancer earlier and provide smarter answers at every step

HEREDITARY TESTING	SCREENING	EARLY-STAGE THERAPY	RECURRENCE TESTING	LATE-STAGE THERAPY
riskguard™	cologuard®	oncotype DX®	EXPECTED 2023	oncoExTra™

Addressing the persistent colorectal cancer problem

150K
new U.S. diagnoses

53K
U.S. deaths



Source: American Cancer Society Cancer Facts & Figures 2021, U.S. Census data,
Division of Cancer Prevention and Control, Centers for Disease Control and Prevention (2021),
Fisher D et al., ASCO Gastrointestinal Cancers Symposium abstract (2022), Exact Sciences estimates

Cologuard is an innovative solution

94%

early-stage cancer sensitivity*

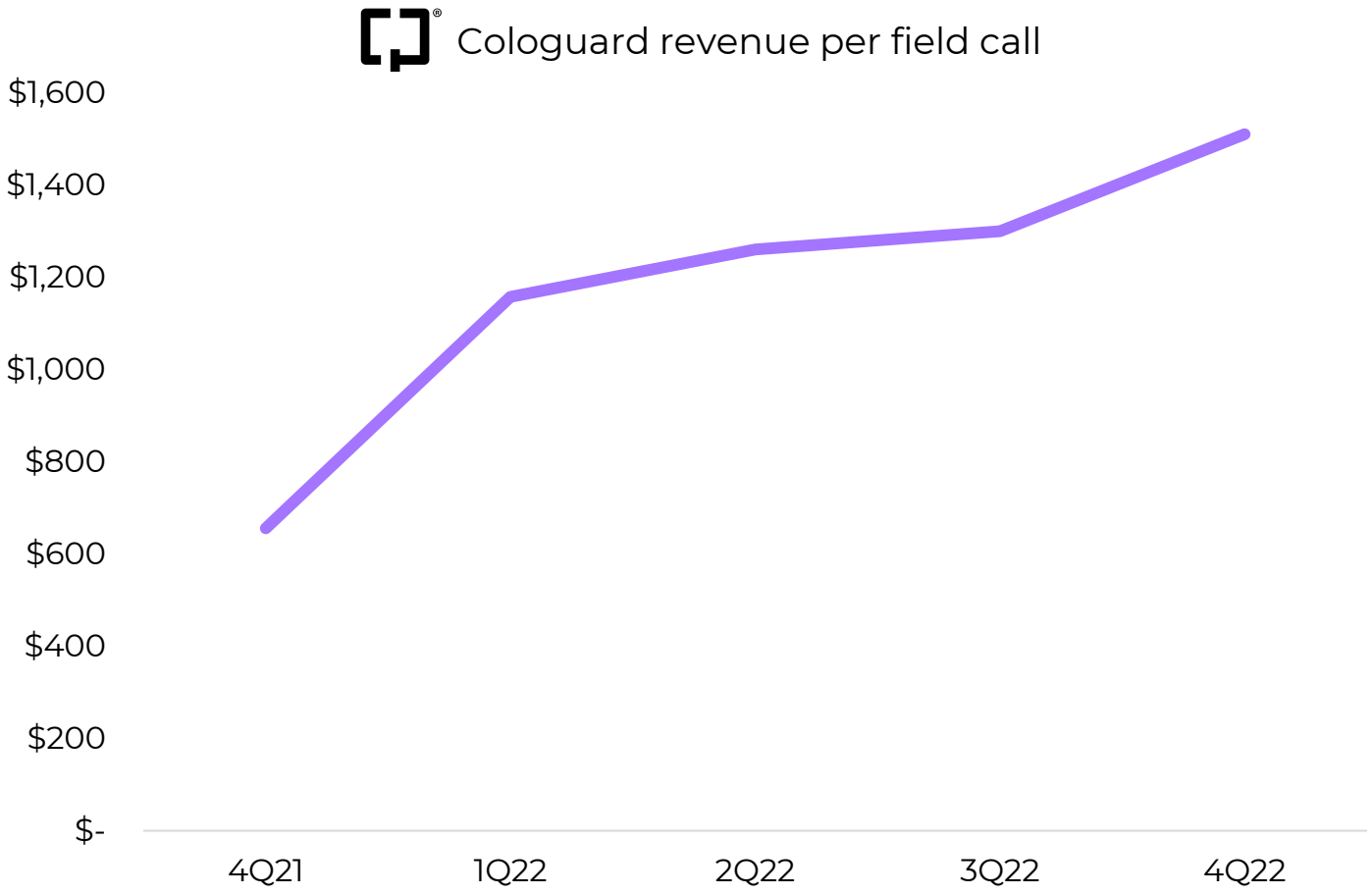
42%

precancer sensitivity

- Easy to use
- Non-invasive
- 24/7 support
- No sedation
- No time off work
- No preparation

*For stage I and II cancers;
92% sensitivity overall, 87% specificity
Source: Imperiale TF et al., N Engl J Med (2014)

Cologuard is becoming the preferred screening choice, supported by the most powerful commercial team in cancer diagnostics



10M+

total people screened

1M+

field calls each year

15B+

advertisement views each year

Using genomic information to personalize breast cancer treatment

oncotype DX®

Recurrence Score® (RS) Result

Range: 0-100

Decision on individual treatment especially around the RS 25 cutoff may consider other clinical factors.

Distant Recurrence Risk at 9 Years

With AI or TAM Alone

4%

TAILORx

AI = Aromatase Inhibitor / TAM = Tamoxifen

Group Average Absolute Chemotherapy (CT) Benefit

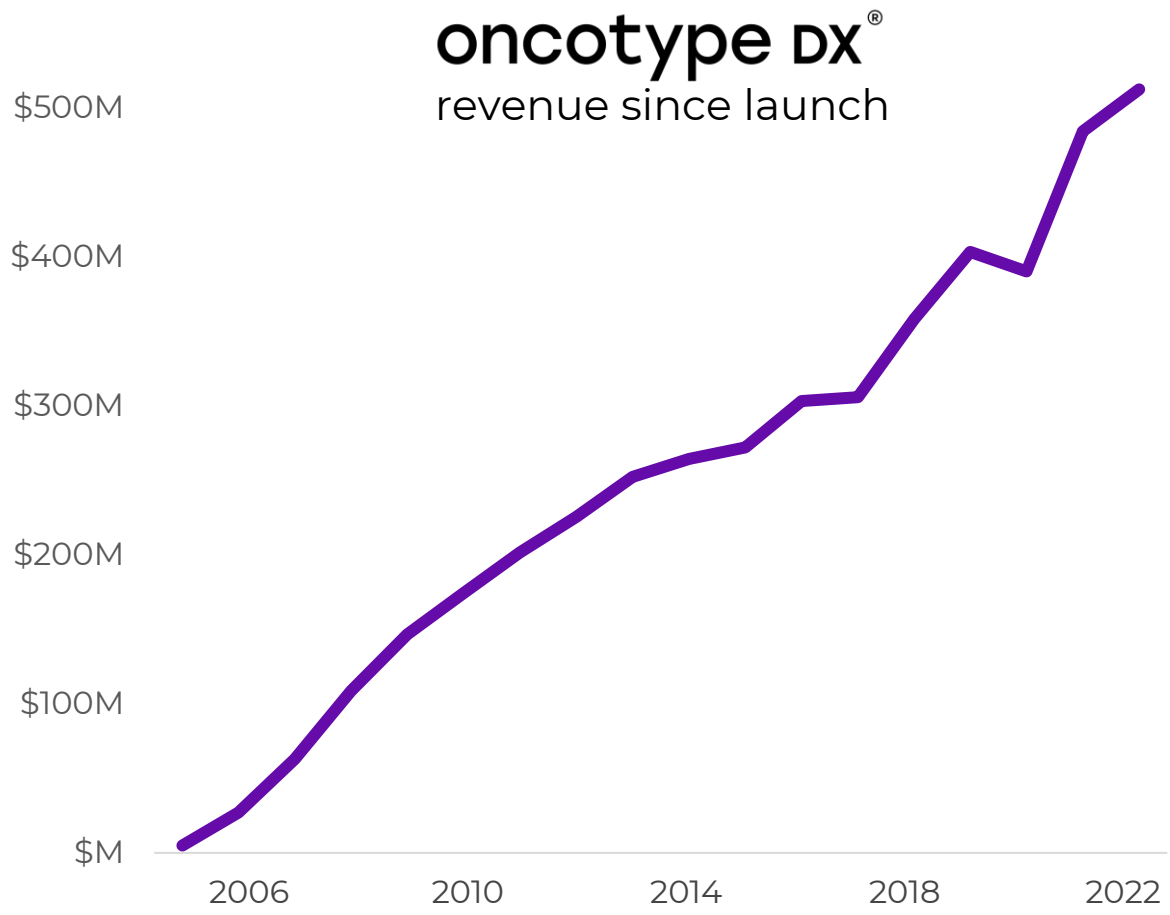
RS 11-25 All Ages

<1%

TAILORx

Source: Sparano et al., N Engl J Med (2018); Geyer et al., NPJ Breast Cancer (2018)

Oncotype DX is standard of care in early-stage breast cancer treatment



Note: chart includes revenue from Oncotype DX Breast Recurrence Score test only

$601M

2022 Precision Oncology revenue

1.7M+

people tested

98%

of U.S. oncologists have ordered

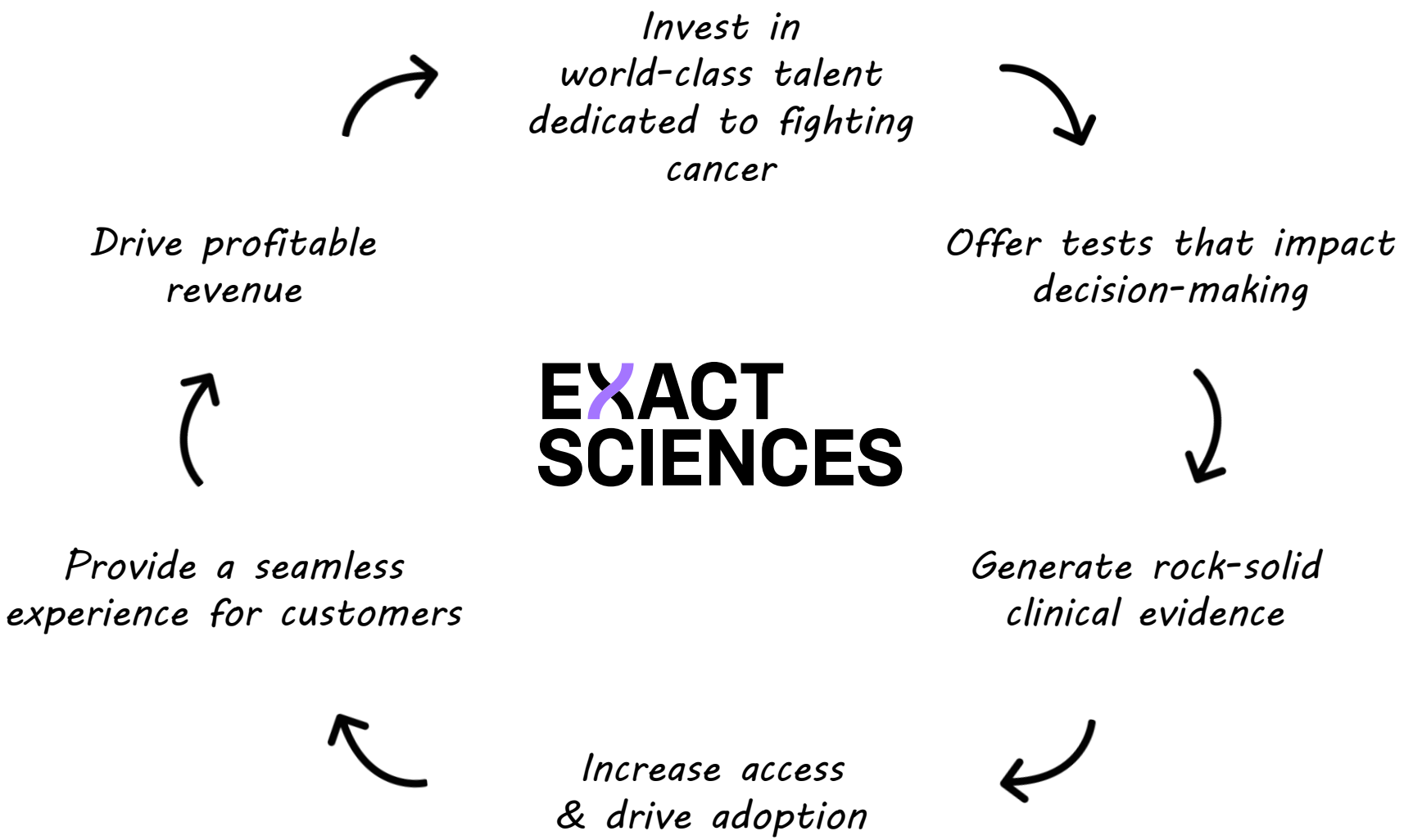
Powering better treatment decisions specific to each patient

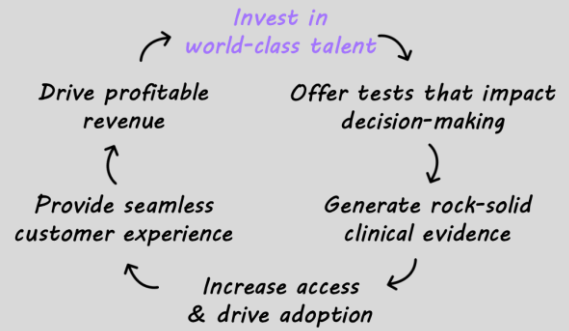
1,759,211

cumulative patients tested

HEREDITARY TESTING	EARLY-STAGE THERAPY	RECURRENCE TESTING	LATE-STAGE THERAPY
riskguard™	oncotype DX®	EXPECTED 2023	oncoExTra™

The Exact Sciences platform enables sustainable revenue growth and profitability improvement over time





Great Place To Work.® Certified MAY 2022-MAY 2023 USA™

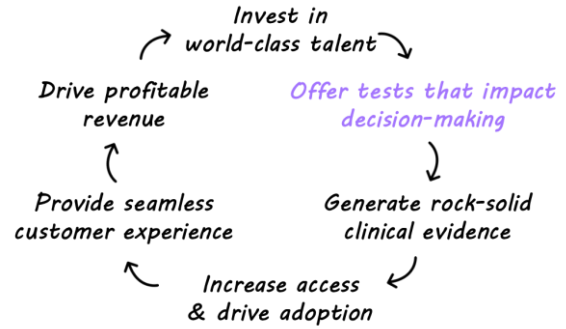
FORTUNE

Best Workplaces in Biopharma™

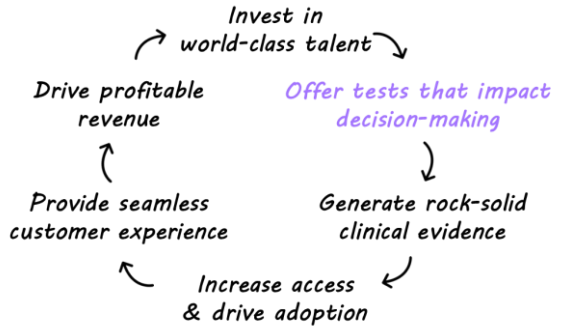
Forbes

Best-in-State Employer

Offer tests that impact decision-making



Advancing our pipeline of life-changing diagnostics



Colorectal cancer screening (CRC)

110M people in U.S.

Expected in 2023

Top-line next-generation **Cologuard BLUE-C data**

Multi-cancer early detection (MCED)

135M people in U.S.

Two studies further validating **multi-marker class approach**

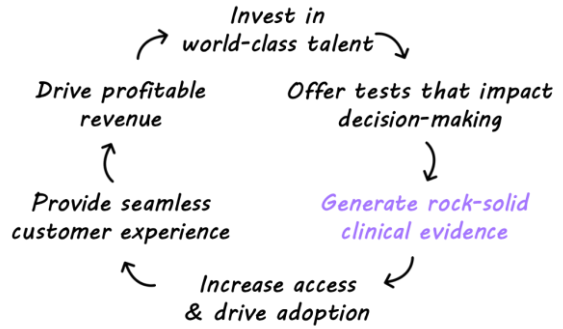
Molecular residual disease (MRD)

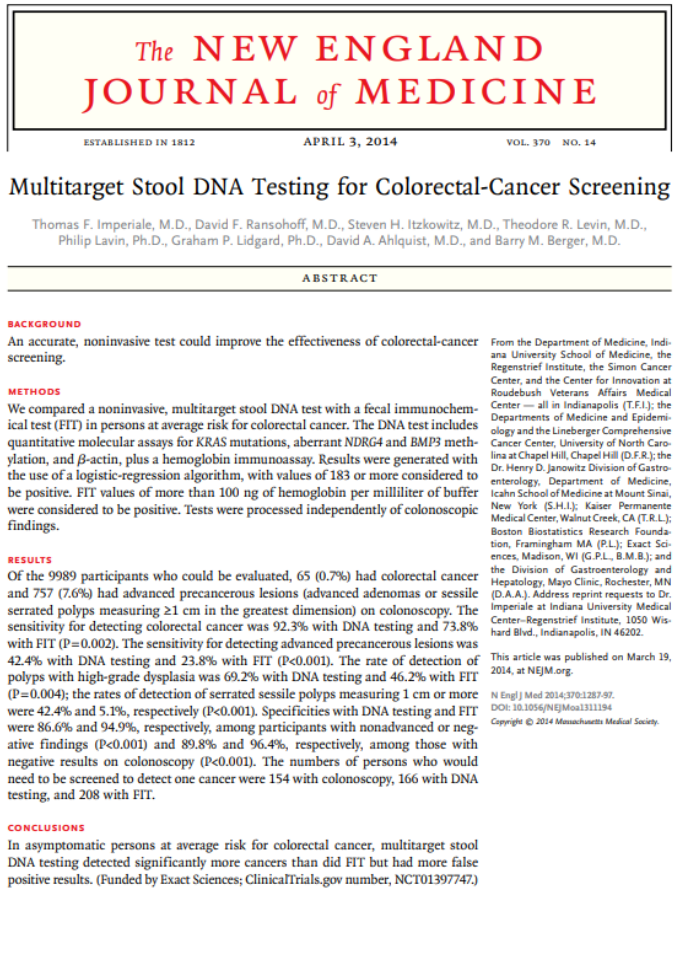
12M annual U.S. testing opportunities

Two additional studies, making **CRC tumor-informed test available**

Source: U.S. Census data, Exact Sciences estimates; includes U.S. markets only

Generate rock-solid clinical evidence





The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 3, 2014 VOL. 370 NO. 14

Multitarget Stool DNA Testing for Colorectal-Cancer Screening

Thomas F. Imperiale, M.D., David F. Ransohoff, M.D., Steven H. Itzkowitz, M.D., Theodore R. Levin, M.D., Philip Lavin, Ph.D., Graham P. Lidgard, Ph.D., David A. Ahlquist, M.D., and Barry M. Berger, M.D.

ABSTRACT

BACKGROUND

An accurate, noninvasive test could improve the effectiveness of colorectal-cancer screening.

METHODS

We compared a noninvasive, multitarget stool DNA test with a fecal immunochemical test (FIT) in persons at average risk for colorectal cancer. The DNA test includes quantitative molecular assays for *KRAS* mutations, aberrant *NDRG4* and *BMP3* methylation, and β-actin, plus a hemoglobin immunoassay. Results were generated with the use of a logistic-regression algorithm, with values of 183 or more considered to be positive. FIT values of more than 100 ng of hemoglobin per milliliter of buffer were considered to be positive. Tests were processed independently of colonoscopic findings.

RESULTS

Of the 9989 participants who could be evaluated, 65 (0.7%) had colorectal cancer and 757 (7.6%) had advanced precancerous lesions (advanced adenomas or sessile serrated polyps measuring ≥1 cm in the greatest dimension) on colonoscopy. The sensitivity for detecting colorectal cancer was 92.3% with DNA testing and 73.8% with FIT (P=0.002). The sensitivity for detecting advanced precancerous lesions was 42.4% with DNA testing and 23.8% with FIT (P<0.001). The rate of detection of polyps with high-grade dysplasia was 69.2% with DNA testing and 46.2% with FIT (P=0.004); the rates of detection of serrated sessile polyps measuring 1 cm or more were 42.4% and 5.1%, respectively (P<0.001). Specificities with DNA testing and FIT were 86.6% and 94.9%, respectively, among participants with nonadvanced or negative findings (P<0.001) and 89.8% and 96.4%, respectively, among those with negative results on colonoscopy (P<0.001). The numbers of persons who would need to be screened to detect one cancer were 154 with colonoscopy, 166 with DNA testing, and 208 with FIT.

CONCLUSIONS

In asymptomatic persons at average risk for colorectal cancer, multitarget stool DNA testing detected significantly more cancers than did FIT but had more false positive results. (Funded by Exact Sciences; ClinicalTrials.gov number, NCT01397747.)

From the Department of Medicine, Indiana University School of Medicine, the Regenstrief Institute, the Simon Cancer Center, and the Center for Innovation at Roudebush Veterans Affairs Medical Center — all in Indianapolis (T.F.I.); the Departments of Medicine and Epidemiology and the Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill, Chapel Hill (D.F.R.); the Dr. Henry D. Janowitz Division of Gastroenterology, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York (S.H.I.); Kaiser Permanente Medical Center, Walnut Creek, CA (T.R.L.); Boston Biostatistics Research Foundation, Framingham MA (P.L.); Exact Sciences, Madison, WI (G.P.L., B.M.B.); and the Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN (D.A.A.). Address reprint requests to Dr. Imperiale at Indiana University Medical Center–Regenstrief Institute, 1050 Wishard Blvd., Indianapolis, IN 46202.

This article was published on March 19, 2014, at NEJM.org.

N Engl J Med 2014;370:1287-97.
DOI: 10.1056/NEJMoa1311194

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 12, 2018 VOL. 379 NO. 2

Adjuvant Chemotherapy Guided by a 21-Gene Expression Assay in Breast Cancer

J.A. Sparano, R.J. Gray, D.F. Makower, K.I. Pritchard, K.S. Albain, D.F. Hayes, C.E. Geyer, Jr., E.C. Dees, M.P. Goetz, J.A. Olson, Jr., T. Lively, S.S. Badve, T.J. Saphner, L.I. Wagner, T.J. Whelan, M.J. Ellis, S. Paik, W.C. Wood, P.M. Ravdin, M.M. Keane, H.L. Gomez Moreno, P.S. Reddy, T.F. Goggins, I.A. Mayer, A.M. Brufsky, D.L. Toppmeyer, V.G. Kaklamani, J.L. Berenberg, J. Abrams, and G.W. Sledge, Jr.

ABSTRACT

BACKGROUND

The recurrence score based on the 21-gene breast cancer assay predicts chemotherapy benefit if it is high and a low risk of recurrence in the absence of chemotherapy if it is low; however, there is uncertainty about the benefit of chemotherapy for most patients, who have a midrange score.

METHODS

We performed a prospective trial involving 10,273 women with hormone-receptor–positive, human epidermal growth factor receptor 2 (HER2)–negative, axillary node–negative breast cancer. Of the 9719 eligible patients with follow-up information, 6711 (69%) had a midrange recurrence score of 11 to 25 and were randomly assigned to receive either chemoendocrine therapy or endocrine therapy alone. The trial was designed to show noninferiority of endocrine therapy alone for invasive disease–free survival (defined as freedom from invasive disease recurrence, second primary cancer, or death).

RESULTS

Endocrine therapy was noninferior to chemoendocrine therapy in the analysis of invasive disease–free survival (hazard ratio for invasive disease recurrence, second primary cancer, or death [endocrine vs. chemoendocrine therapy], 1.08; 95% confidence interval, 0.94 to 1.24; P=0.26). At 9 years, the two treatment groups had similar rates of invasive disease–free survival (83.3% in the endocrine-therapy group and 84.3% in the chemoendocrine-therapy group), freedom from disease recurrence at a distant site (94.5% and 95.0%) or at a distant or local–regional site (92.2% and 92.9%), and overall survival (93.9% and 93.8%). The chemotherapy benefit for invasive disease–free survival varied with the combination of recurrence score and age (P=0.004), with some benefit of chemotherapy found in women 50 years of age or younger with a recurrence score of 16 to 25.

CONCLUSIONS

Adjuvant endocrine therapy and chemoendocrine therapy had similar efficacy in women with hormone-receptor–positive, HER2-negative, axillary node–negative breast cancer who had a midrange 21-gene recurrence score, although some benefit of chemotherapy was found in some women 50 years of age or younger. (Funded by the National Cancer Institute and others; TAILORx ClinicalTrials.gov number, NCT00310180.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Sparano at Montefiore Medical Center, 1695 Eastchester Rd., Bronx, NY 10461, or at jsparano@montefiore.org.

A full list of the investigators in this trial is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on June 3, 2018, at NEJM.org.

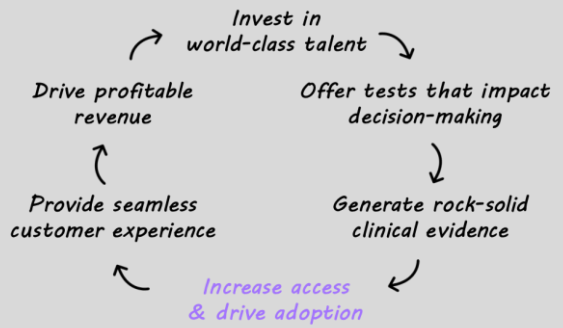
N Engl J Med 2018;379:111-21.
DOI: 10.1056/NEJMoa1804710

50

publications and abstracts presented in 2022

5

New England Journal of Medicine publications

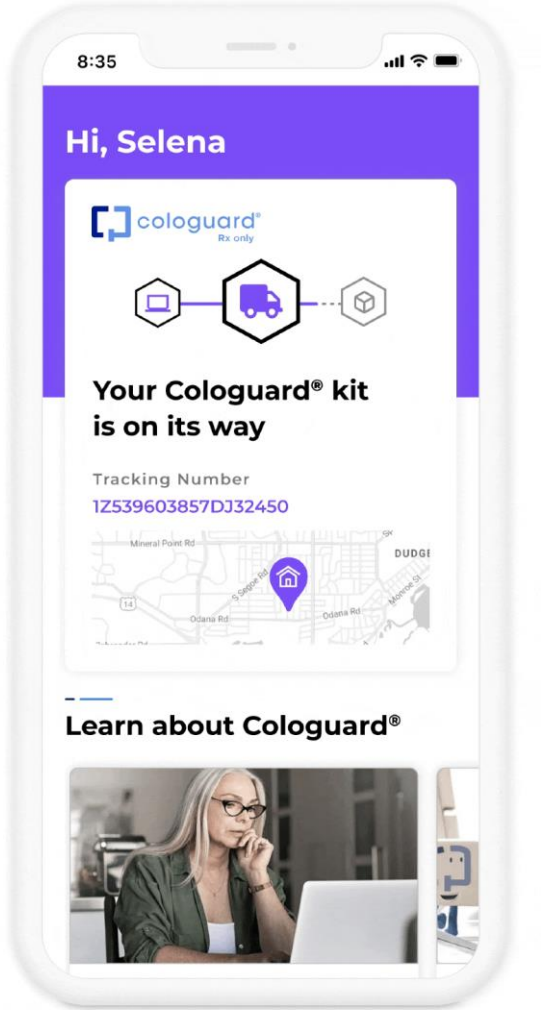


1,300
person commercial team

1,000
person primary care team

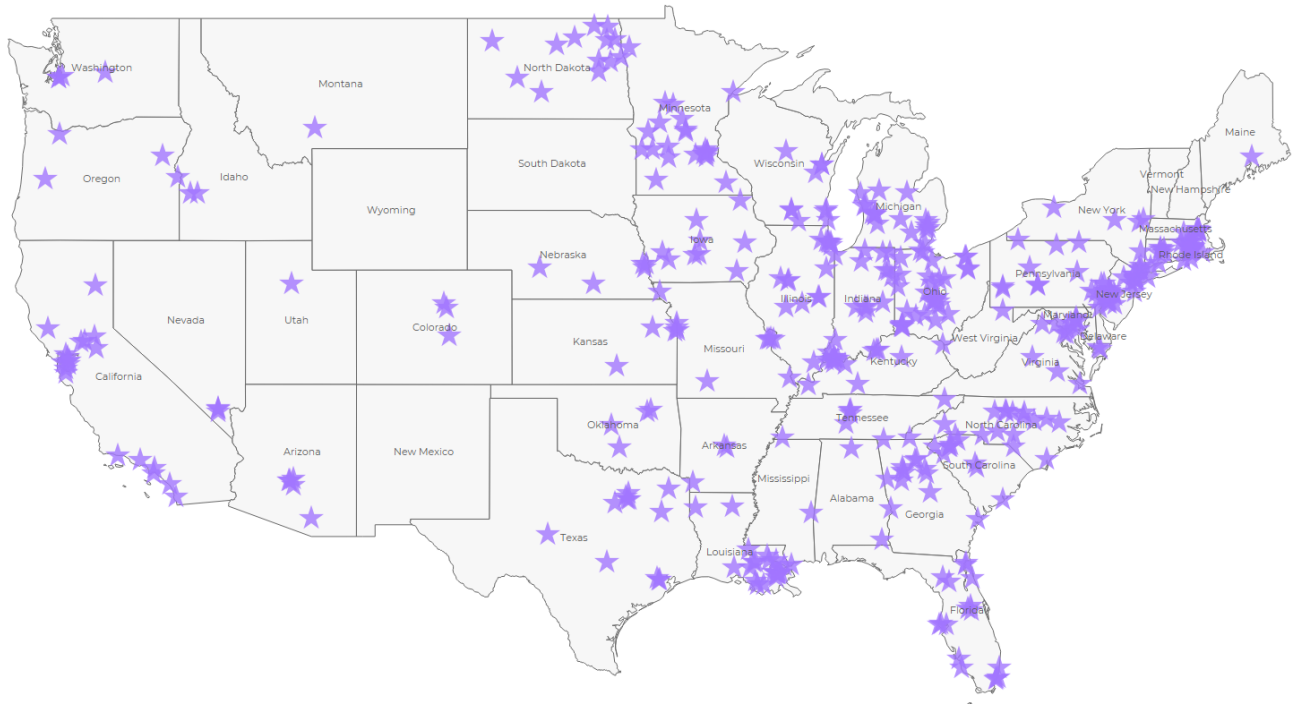
200
person global Precision Oncology team

Provide a seamless experience for customers



250+

health system connections



Invest in world-class talent

Drive profitable revenue

Offer tests that impact decision-making

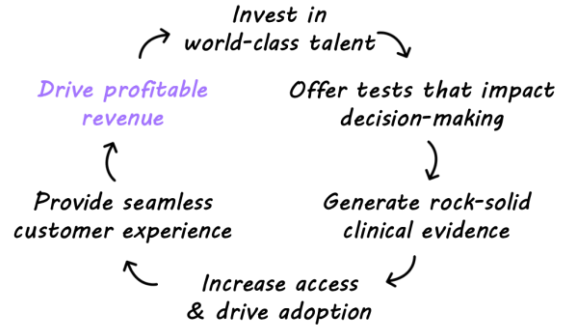
Provide seamless customer experience

Generate rock-solid clinical evidence

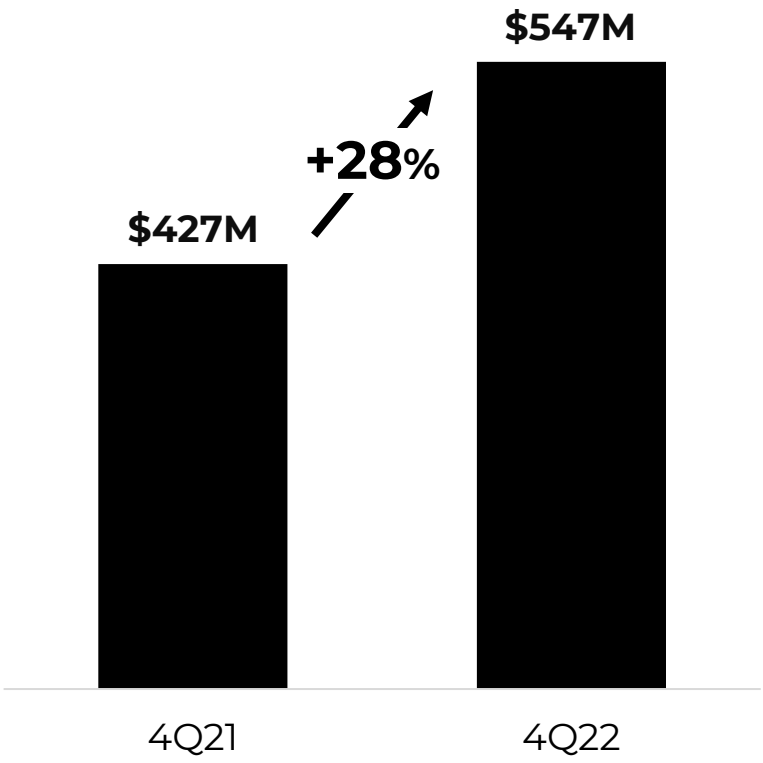
Increase access & drive adoption

Drive profitable revenue

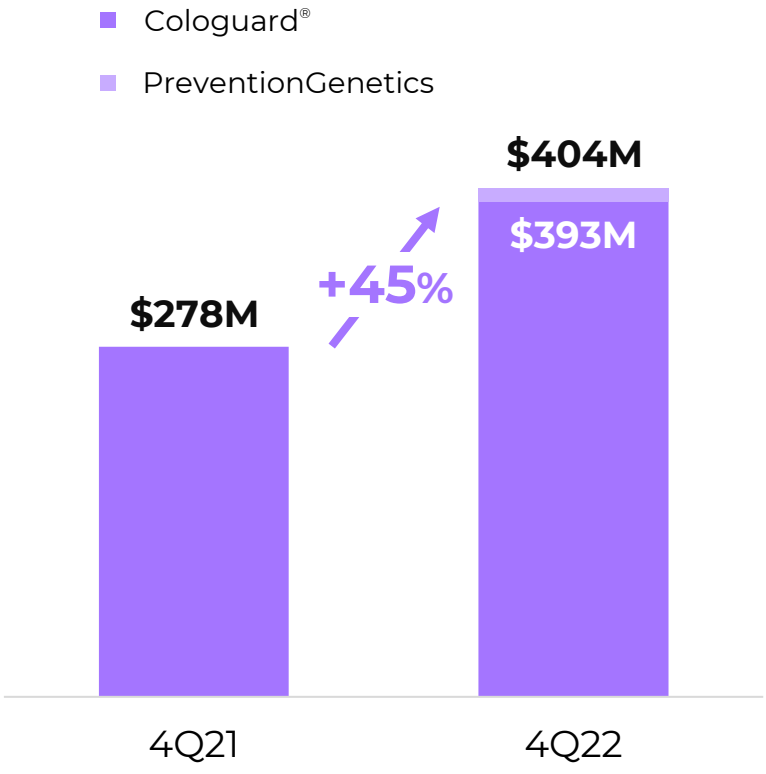
Total revenue excluding COVID testing grew 28% in 4Q22



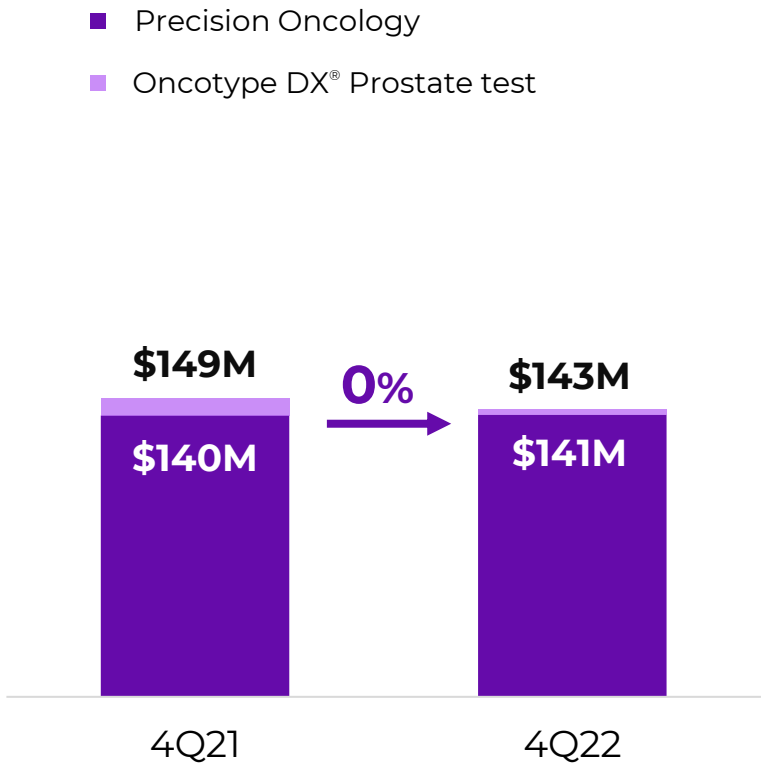
Total revenue
(excluding COVID testing)



Screening revenue

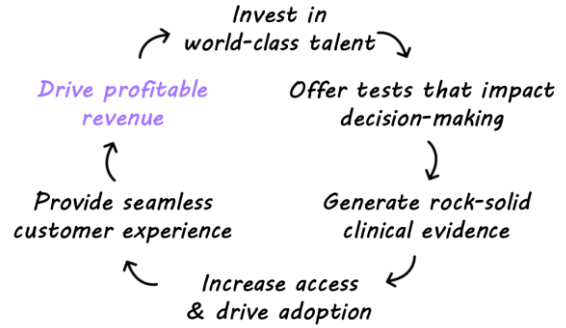


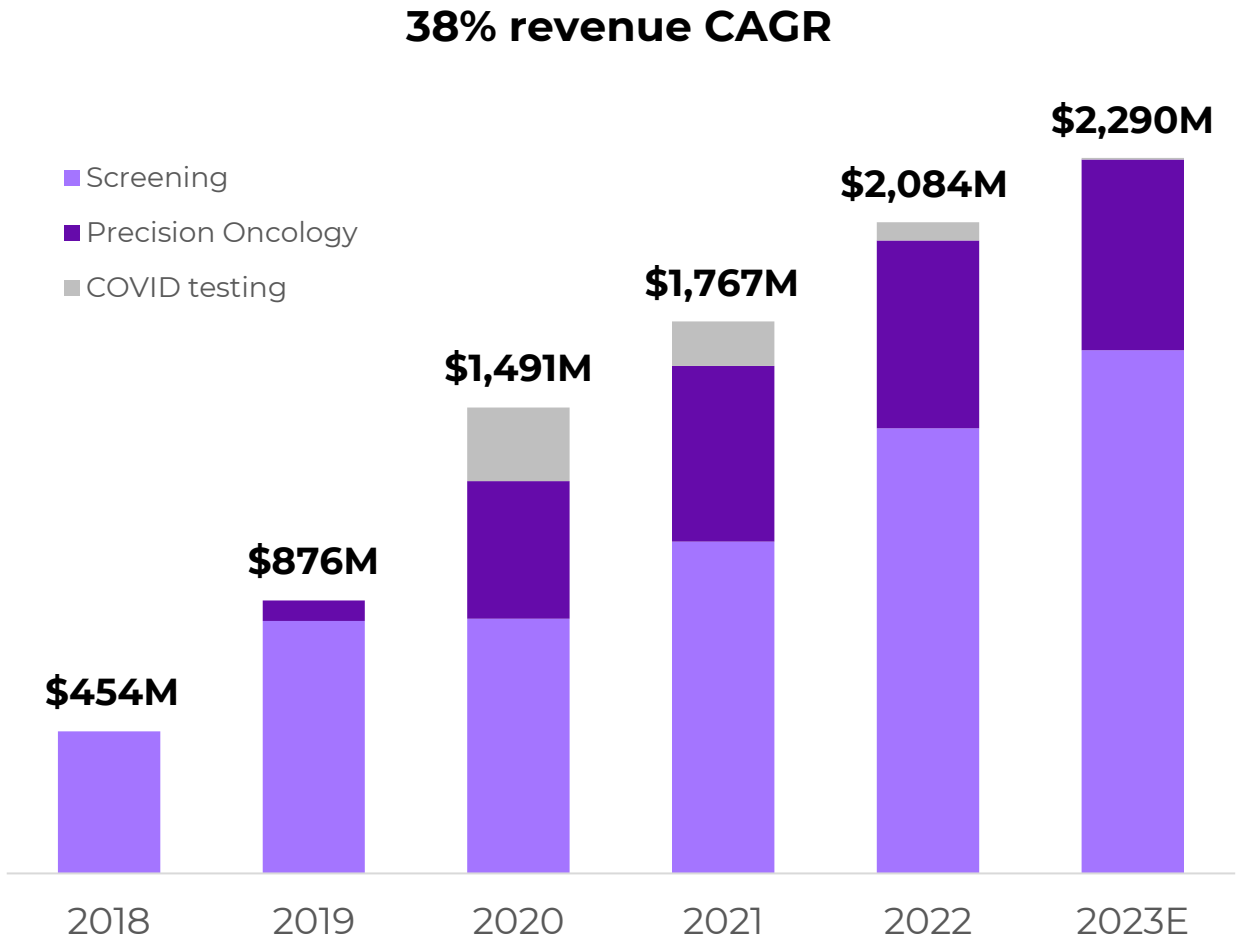
Precision Oncology revenue



Screening includes laboratory service revenue from Cologuard and PreventionGenetics
Precision Oncology includes laboratory service revenue from global Oncotype® products and therapy selection products
Precision Oncology revenue grew 1% excluding the divestiture of the Oncotype DX® Prostate test and a $2M FX headwind

Drive profitable revenue



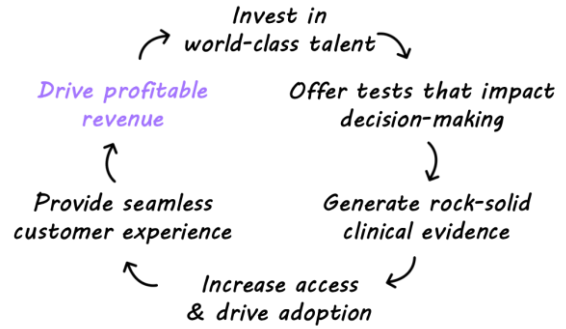


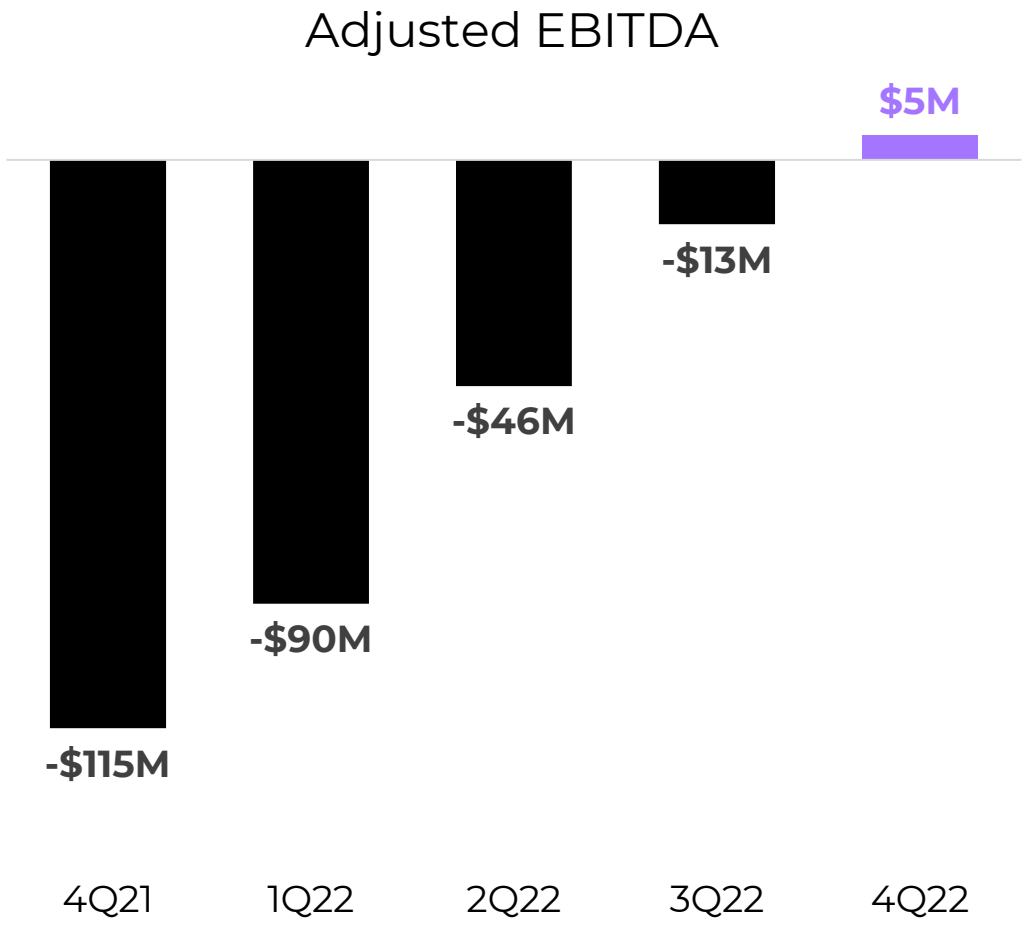
70%+

non-GAAP
gross margins

CAGR revenue calculated using GAAP figures and Exact Sciences guidance midpoint provided February 21, 2023

Drive profitable revenue





$0-25M

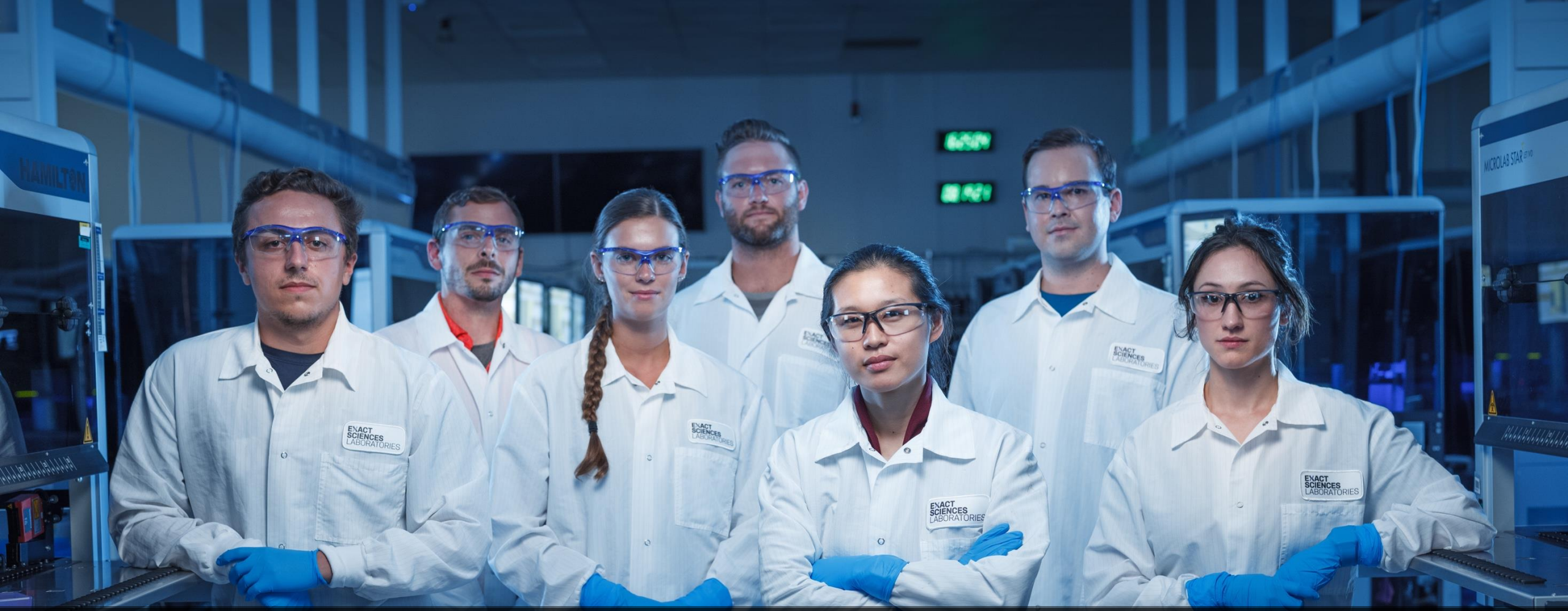
2023 adjusted EBITDA

Exact Sciences guidance provided February 21, 2023
Please refer to our fourth quarter 2022 earnings release for discussion of non-GAAP financial measures and reconciliations to GAAP financial measures

2023 guidance

	2022	2023	Δ at midpoint
Total revenue	**$2,084M**	**$2,265 - 2,315M**	**+$206M**
Screening	$1,425M	$1,660 - 1,690M	+$250M
Precision Oncology	**$601M**	**$600 - 620M**	**+$9M**
COVID testing	$58M	~$5M	-$53M
Adj. EBITDA	**-$143M**	**$0 - 25M**	**+$156M**
CapEx	**$214M**	**~$120M**	**-$94M**

Exact Sciences guidance provided February 21, 2023
Net loss was $624M in 2022
Please refer to our fourth quarter 2022 earnings release for discussion of non-GAAP financial measures and reconciliations to GAAP financial measures



Making earlier cancer detection a routine part of medical care