



Veracyte R&D Day

Lung Cancer Portfolio Review and Data Update

December 16, 2020

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Veracyte Lung Cancer Portfolio R&D Day

Today's Agenda

Welcome Remarks	Tracy Morris VP Corp. Comms and IR Keith Kennedy CFO
Veracyte's Vision for Transforming Lung Cancer Care	Bonnie Anderson Chairman & CEO
Lung Cancer Diagnosis: Unmet Needs in the Patient Journey	Sonali Sethi, MD
Lung Cancer Portfolio Development Update	Giulia C. Kennedy, PhD CSO & CMO
A Lung Nodule Has Been Found: Now What?	Carla R. Lamb, MD
Barriers to Informing Treatment Decisions	Michael A. Bernstein, MD
KOL Roundtable Discussion: Vision for Solutions	Moderated by Bonnie Anderson
Q&A Session	All Speakers
Closing Remarks	Bonnie Anderson





Veracyte's Vision for Transforming Lung Cancer Care

Bonnie Anderson

Chairman and Chief Executive Officer

Veracyte



We are a global genomic diagnostics company transforming care throughout the patient journey.

Our foundational strategy drives our business

Relevant Questions

Integrated into current care pathway to change practice and reduce surgeries

Scientific Rigor

Build robust scientific and clinical evidence; inform guidelines

Value Creation

Clinical utility and economic value that change the standard of care

Successful Reimbursement

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Extensive coverage policies and contracted relationships pave way for additional tests

Our powerful science and technology

Enables innovation from large-scale clinical biorepositories



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Five clinical indications



Addressing unmet needs throughout the care continuum



>**\$40** billion TAM



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Lung Cancer

Unmet clinical needs throughout the care continuum



Veracyte's Lung Cancer Franchise

Genomic insights to drive care at each step of the patient's journey



NOBLE trial for future lung cancer early-detection tests

9000-patient, prospective, multicenter (~50 sites) study of people with lung nodules detected on CT scans

Includes smokers and nonsmokers, and those without cancer Collect nasal swab/other samples, CT imaging and other data

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Distinguish **lung cancer development and progression** for three years or until a lung cancer diagnosis Create **robust biorepository** of genomic, imaging, clinical and other data

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Develop potential tests that may help detect cancer at its earliest stages

Potential to identify and intercept lung cancer before it develops

Today's Goals:

Share our vision, discuss the unmet patient-care needs and share latest data on our pipeline tests

Sonali Sethi, MD, FCCP, DAABIP Associate Program Director for Procedural

Training, Interventional Pulmonology at the Cleveland Clinic





Bonnie Anderson Chairman and Chief Executive Officer

Carla R. Lamb, MD, FACP, FCCP

Director of Interventional Pulmonology Lahey Hospital & Medical Center Beth Israel Lahey Health





Giulia C. Kennedy, PhD Chief Scientific Officer and Chief Medical Officer

Michael A. Bernstein, MD, FCCP

Associate Director for Pulmonary and Critical Care at Stamford Health







Lung Cancer Diagnosis: Unmet Needs in the Patient Journey

Sonali Sethi MD, FCCP, DAABIP

Interventional Pulmonology

Associate Program Director for Procedural Training

Cleveland Clinic

Sonali Sethi MD, FCCP, DAABIP

Background and practice overview

Cleveland Clinic Cleveland, OH

- 14 years in practice
- Cleveland Clinic Interventional Pulmonologist and Associate Program Director for Procedural Training
- Lung nodule and Lung cancer clinic
- 16,000 Lung nodules a year
- 4000 Bronchoscopies per year
- 1200 EBUS cases
- 500 Navigational cases



Lung cancer: Many barriers on the road to diagnosis and treatment



Bottom line: Lung cancer remains a major medical problem

Lung cancer by the numbers

~135K

deaths in U.S. alone¹



of all cancer deaths¹ **59%** 5-year survival rate when detected early² 23%

lung cancers detected at early-stage²

We need to find more cancers early and ensure patients obtain the treatment they need

1 American Cancer Society, Cancer Facts & Figures 2020 ² American Lung Association, State of Lung Cancer Report 2020 Lung cancer diagnosis: Avoiding risky, costly procedures with Percepta GSC



Guidelines recommend a non-surgical biopsy for low/moderate risk of malignancy cases



Diagnostic modalities

		Diagnosis		Diagnosis + Staging	
MODALITY	TTNA	STANDARD BRONCHOSCOPY	ENB WITH RP- EBUS	EBUS	SURGERY
PROS	• High yield >92%	 Safer; <3% complication rate 	 Able to reach small peripheral nodules 	 Diagnosis + Staging 	 Gold Standard Therapy
CONS	 15-30% pneumotx rate 	 Low yield for small peripheral nodules 	 Variable diagnosis yield 	 Only targets adjacent to large airways 	 Invasive and 5% mortality
	F	OR SOLITARY PULMONAR NODULES, USE THESE	Y		

Bronchoscopy is the least invasive option for diagnosing suspicious lesions, but is often inconclusive



Percepta Genomic Sequencing Classifier

- Gene expression test that identifies genomic alterations in the epithelial lining of the respiratory airway ("field of injury"), which are associated with lung cancer in current and former smokers.
- Test relies on cells collected from the main airway during bronchoscopy
- Detects these genomic changes to determine the likelihood that a lung nodule is malignant

Test is used to help **RULE OUT** or **RULE IN** lung cancer



Spira A, et al. PNAS July 6, 2004 101 (27) 10143-10148 Billatos E, et al. Clin Cancer Res; 24(13) July 1, 2018 Silvestri GA, et al. N Engl J Med; 373:243-251, 2015

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Percepta GSC stratifies the risk of primary lung cancer when bronchoscopy is inconclusive



Silvestri GA, et al. N Engl J Med 2015; 373:243-251

Lee, H, et al. Bronchial Genomic Classifier Prospective Registry-Interim Analysis CHEST 2018

PATIENT BACKGROUND:

Age: 44 Gender: Male Current Smoker

CT SCAN: 12 mm spiculated nodule RUL

PET: RUL lung nodule SUV 2.0

PHYSICIAN ASSESSED PRE-TEST RISK: Intermediate Mayo calculator: 27.7% Risk



CBCT NAVIGATIONAL BRONCHOSCOPY W/ EBUS:

RUL lung nodule – Acute on chronic inflammatory cells, neutrophils, lymphocytes and macrophages



PATIENT BACKGROUND:

Age: 42 Gender: Male Current Smoker: 20 pack-years Other factors: History of Stage II COPD

CT SCAN:

12 mm, spiculated lung nodule RUL

PRE-TEST RISK LEVEL: Intermediate

NAVIGATIONAL BRONCHOSCOPY: Inflammation



NEXT STEPS:

DECISION:

Pursue CT surveillance

 Stable for 1 year and now has a calcified center consistent with a benign granuloma

The Percepta test saved the patient from an avoidable TTNA



Use of Percepta GSC at Cleveland Clinic



Silvestri GA, et al. N Engl J Med; 373:243-251, 2015





Lung Cancer Portfolio Development Update: Nasal Swab Test & Percepta Genomic Atlas

Giulia C. Kennedy, PhD

Chief Scientific Officer & Chief Medical Officer

Veracyte

Nasal Swab Test: For earlier lung cancer detection and diagnosis



and accelerate time to treatment for those with lung cancer

CHEST 2019: Preliminary data demonstrated novel test's feasibility

Data Presented at CHEST 2019				
Metric	Performance			
AUC	0.86			
High Risk Specificity	95%			
% Malignant Patients Called High Risk	50%			
Low Risk Sensitivity	97%			
% Benign Patients Called Low Risk	46%			

Demonstrated proof-of-concept for nasal swab test

- Conducted on single cohort, AEGIS, to investigate feasibility of the nasal swab
 - AEGIS is a highly specific cohort consisting primarily of high-risk patients
- AEGIS cohort data demonstrated high specificity and sensitivity of two-cutoff classifier

NEXT: Evolve models that perform in an expanded clinical setting representing "real world"

Numerous challenges needed to be addressed



Retrained algorithms with more patient samples

 Added two new cohorts, nearly doubling the training set

Built many models using a variety of structures, feature selection techniques and interaction terms

Built and refined genomic indexes to inform on technical factors and clinical features

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RNA Sequencing and Machine Learning: A powerful duet



DIAGNOSTIC ALGORITHMS

An "Algorithm of Algorithms" to tackle this complex problem



Evolving algorithms show consistent performance in cross-validation

Performance	CHEST 2019	Dolly	lzzy	Lacey	Layer Cake	Range
Evaluation Method	Independent Test Set N=411/261	Cross-Validation N=802	Cross-Validation N=896	Cross-Validation N=790	Cross-Validation N=802	
Comments	Single Pristine Cohort	Added 2 Cohorts	Clinical Data Cleaned	Optimized on 1 Cohort	Two-Layered Model	
AUC	0.86	0.84	0.80	0.82	0.85/0.82	0.80-0.85
High Risk Specificity (Goal: ≥90%)	95%	90%	90%	90%	91%	90-91%
% Malignant Patients Called High Risk	50%	54%	44%	52%	60%	44-60%
Low Risk Sensitivity (Goal: ≥90%)	97%	90%	93%	93%	94%	90-94%
% Benign Patients Called Low Risk	46%	57%	39%	56%	57%	39-57%

New risk assessment & diagnostic approach to improve standard-of-care



Next steps in developing the Nasal Swab Test for early lung cancer detection





Inform treatment decision at the time of diagnosis



TTNB: transthoracic needle biopsy SLB: surgical lung biopsy NCCN: National Comprehensive Cancer Network

Accurately detects known variants in lung cancer and is reproducible

Demonstrates that Percepta Genomic Atlas is a Sensitive and Reproducible assay



- In reference samples we detect >95% of SNV's at > 3% VAF
- >95% reproducible run to run

Percepta Genomic Atlas Detects all alteration types including SNV, indels, CNV, fusions and rearrangements



- EGFR SNV and indels
- KRAS SNV

- RET fusion
- MET exon14 skipping

Percepta Genomic Atlas can detect variants within bronchoscopy biopsies



Performs in bronchoscopy biopsies simply collected in RNAprotect

- Bronchoscopy biopsies collected into RNAprotect >95% pass DNA/RNA QC
- Concordance with reference assay >95%
- EGFR, KRAS, PIK3CA SNV detected

Potential impact of Percepta Genomic Atlas within lung cancer landscape

Faster, More Comprehensive Molecular Testing



Earlier, More Appropriate Treatment



More Efficient Healthcare Deliver

Improved Treatment Outcomes



Comprehensive Biorepository of ALL Stages of Lung Cancer

Biopharma Partnerships



Bringing Targeted Therapies to Earlier Stage Cancer Patients

Precision Medicine Advances

Next steps in developing Percepta Genomic Atlas







A Lung Nodule Has Been Found: Now What?

Carla R. Lamb, MD, FACP, FCCP

Director of Interventional Pulmonology

Lahey Hospital & Medical Center

Beth Israel Lahey Health

Background and practice overview

- Largest Lung Cancer Screening Program in the country outside of the NLST
- Director of Interventional Pulmonary Medicine and Interventional Pulmonary Fellowship Lahey Hospital & Medical Center
- Co-founder of the Lahey Multi-Disciplinary Thoracic Oncology Clinic
- Board Member of the Steering and Research Committee of Rescue Lung Rescue Life Society for Lung Screening
- Co-author of the American Thoracic Society/ American College of Chest Physicians policy statement on implementation of low-dose computed tomography CT lung screening programs in clinical practice
- 21 years in practice
- Mission of Lahey Screening program: implemented model throughout the country, patient advocates for CMS / third party coverage for evidence based broader range of qualified screened patients, smoking cessation, promoting lung health and responsible screening programs
- I see at least 15-20 lung nodule patients per week/ 60-80 month

Lahey Hospital & Medical Center Burlington, MA





A lung nodule has been found: Now what?



The Clinical Problem

The current evaluation of lung nodules needs improvement

The number of nodules found on CT is growing

- Annual rate of incidentally found nodules increased by 95% between 2006 and 2012¹
- ~10M people in the U.S. are now eligible for annual LDCT screening
- New USPSTF screening recommendations could double the number of eligible people

Too many patients undergo unnecessary procedures

- 35% of patients who underwent surgery had benign nodules²
- 44% of low-risk patients underwent one or more invasive procedures for a benign nodule²
- Other patients may not get the care they need or their cancer may be missed
 - Physicians often do not follow guidelines based on patient risk (likely due to lack of confidence in risk assessment)
 - In patients for whom surgery was recommended, physicians opted for lessaggressive management 75% of the time²





¹ Gould MK, et al. Am J of Resp and Critical Care Med 2015 192(10): 1208-1214. ² Tanner NT et al. *CHEST* 2015; 148(6):1405-1414.

Lung cancer screening saves lives AND increases the need for effective nodule management

Screening Saves Lives

- National Lung Screening Trial (NLST)
 - Large randomized trial of screening LDCT scan versus
 Chest radiograph in high-risk individuals
 - Showed a lung cancer mortality benefit of 20% and all cause mortality reduction of 6.7%

The NELSON Trial

- Large European randomized trial comparing LDCT with a control group with no screening
- Showed a 24% reduction in lung cancer deaths (10 year follow up)

Screening Expands Number of Nodules Found

- Current guidelines recommend annual lowdose CT screening based on age, smoking history and other risk factors.
 - USPSTF/NCCN/IELCAP
 - ~10M people in U.S. meet criteria
- New USPSTF recommendations proposed to save more lives and reduce disparities
 - Lower the age limit to 50-80 years (from 55-80)
 - Decrease smoking history to 20 pack years from 30

A better way to diagnose lung nodules will make screening more effective – and potentially more appealing to physicians

National Lung Screening Trial Research Team, Aberle DR et al. N Engl J Med. 2011 Aug 4;365(5):395-409. de Koning HJ et al. N Engl J Med. 2020 Feb 6;382(6):503-513. Moyer VA; U.S. Preventive Services Task Force. Ann Intern Med. 2014 Mar 4;160(5):330-8. doi: 10.7326/M13-2771.

Determining lung cancer risk in nodules found on CT is often challenging



Limitations of risk prediction model performance

- Risk prediction models have fair-moderate performance as they are too dependent upon the prevalence of malignancy
- Relying on a single prediction model reduces their overall effectiveness across populations
- Physician assessed risk (PAR) has been found to perform better than the validated prediction models but are limited
 - Subjective nature of risk assessment dependent upon experience, knowledge and intuition of the physician
 - Variability among different clinical practices



- Poor performance in classifying patients as high risk or low risk for lung cancer
- Inconsistent results between models

Tanner N et al. CHEST 2017 Balekian AA et al. Annals Am Thor Soc 2013 Tanner N et al. CHEST 2015 Yu D et al. A comparison of models predicting pretest probability of malignancy in patients undergoing diagnostic procedures for pulmonary nodules. Presented at CHEST 2019 New Orleans LA

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Case Study

- 77-year-old Caucasian male with former 20 pack / year tobacco history
- Frequent travel to Arizona to hunt and camp
- Evaluation for shoulder pain new lung nodule identified incidentally
- Chest CT / PET scan
- Coccidioidomycosis titer positive 1:8
- Sputum culture negative



An accurate, noninvasive genomic test could be a game changer



- Identify as many true cancer patients as possible so they can get complete diagnosis and treatment quickly
- Identify as many true benign patients as possible so they can be directed to CT surveillance
- Help solve the problem of unnecessary work-ups/ procedures and missed cancers that can occur today

Supports a Patient-Focused Approach





Informing Targeted Treatment Decisions in Lung Cancer: The Unmet Need

Michael A. Bernstein, MD, FCCP

Associate Director for Pulmonology

and Critical Care at Stamford Health

Michael A. Bernstein, MD, FCCP

Background and practice overview

- Undergraduate/Medical School: Duke University
- · Internship/Residency/Fellowship: Mount Sinai Medical Center, NY
- Board Certified in Internal Medicine, Pediatrics, Pulmonary Diseases, Critical Care, Hospice/Palliative Care, Interventional Pulmonary, COVID-19
- Associate Director of Pulmonary and Critical Care Stamford Health/Stamford Hospital
- Head, Interventional Pulmonary; Co-Director Lung Cancer Screening Program and Lung Nodule Clinic
- Teaching Faculty, Vagelos College of Physicians and Surgeons, Columbia University
- Blended Mix of "Academic" and "Private Practice" Pulmonary Medicine
- ~500 Lung Cancer Screening CTs annually
- Evaluate approximately 250 lung nodules annually
- Perform about 200 advanced bronchoscopies annually (EBUS and Navigational Bronchos)
- Multidisciplinary Tumor Board with Affiliation with Dana Farber Cancer Collaborative © Veracyte, Inc. All rights reserved. December 16, 2020.

Stamford Hospital Stamford, CT



Patient is diagnosed: How do we determine the right treatment?



Molecular testing is key to optimizing targeted therapy in lung cancer



- Up to 85% of lung cancers have potentially actionable driver mutations.²
- Use of targeted therapy prolongs survival 2-3 times more than chemotherapy₃₄
- Guidelines (NCCN/ASCO/IASLC) recommend testing for gene mutations to guide treatment
- The number of biomarkers continues to grow

¹ Seer.cancer.gov. ² Jordan EJ, et al. Cancer Discov. 2017;7(6):596-609.

³ Nadler E, et al. Clin Lung Cancer. 2018;19(4):360-370. ⁴ Gutierrez ME, et al. Clin Lung Cancer. 2017;18(6):651-659.

The Clinical Need

Patients are not getting the molecular testing they need

Example (study of 300 patients):

- Only 21% of patients with biomarker testing had results available at their initial oncology consultation
- Those with biomarker testing results had shorter times to treatment decision (0 vs. 22 days) and time to treatment initiation (16 vs. 29 days)
- 13% underwent repeat biopsy for molecular testing after the initial consultation
- Of those with EGFR+ or ALK+ results, 19% had already started chemotherapy

Example 2 (15-site study of >800 patients)²:

- Only 59% were tested for EGFR and ALK; only 8% were tested for all NCCN-recommended genes
- For patients tested for EGFR and ALK, time to results was 23 days
- 52% of those not tested for EGFR or ALK received chemotherapy
- Median overall survival was lower (12.7 months vs. 31.8 months for those with chemo vs. targeted therapy)

Leads to inappropriate or delayed therapy

¹ Lim C, et al. Ann Oncol 2015;26 (7):1415-1421. ² Gutierrez, ME, et al. Clin Lung Cancer. 2017;18(6):651-659.

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Molecular testing: The key barriers



Inadequate tissue

- Requires another biopsy (pulmonologist never knows if he/she has enough tissue)
- Pathologists hesitant to send out tissue (no standardization)
- Patient anxiety/distress/compliance may preclude getting more tissue sample

Rapidly Changing Biomarkers

- Difficult for pulmonologists to know which tests to order
- Need testing company to include current and future biomarkers

Logistical Challenges

- Too many different types of samples, collection tubes, biomarkers, etc.
- Lack of infrastructure for obtaining and sending samples

Delays

- Reflex single-gene testing (e.g., EGFR 3-5 days, ALK 3-5 days, etc.)
- Additional procedures to get more tissue
- Oncologist may start chemo if does not have molecular results

Lung cancer patient case study

78 year-old retired eighth grade teacher:

- 30 pack year smoker who quit 2 years ago
- presented with 2 weeks of shortness of breath

Evaluation revealed a 1.6 cm left lower lobe solitary lesion with mediastinal and hilar adenopathy



Lung cancer patient case study (Continued)

- Outpatient PET scan showed multiple hilar and mediastinal lymph nodes with an elevated SUV
- Navigational bronchoscopy with endobronchial ultrasound performed of the lymph nodes and to the mass
- Pathology report showed adenocarcinoma in the lung nodule and the lymph node
- Stage: T1b, N3, M0 IIIB Lung Cancer (incomplete molecular markers)
- INSUFFICIENT MATERIAL FOR MOLECULAR TESTING
- NEXT STEPS NEEDED:
 - Re-biopsy to get adequate tissue for molecular testing



Percepta Genomic Atlas could overcome many of today's challenges



Percepta Genomic Atlas could overcome many of today's challenges





KOL Vision for Solutions: A Round Table Talk



Michael Bernstein, MD, FCCP Stamford Health



Moderator Bonnie Anderson Chairman & CEO



Carla Lamb, MD, FACP, FCCP Beth Israel Lahey Health



Sonali Sethi MD, FCCP, DAABIP Cleveland Clinic



Giulia Kennedy, PhD Chief Scientific & Medical Officer

Investor Q&A



