The Business Model for Test Development

Perspective from a reference laboratory

National Cancer Policy Forum Workshop: Policy Issues in the Development and Adoption of Molecularly Targeted Therapies for Cancer

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INVITAE

Disclosures

- Former academic molecular pathologist who has crossed over to industry
- Invitae Corporation: employee & stock options
- Adjunct Pathology faculty at Baylor College of Medicine

Reference Laboratory Business

- Invitae is a genetics reference laboratory that provides genetic testing services to patients with inherited conditions, including cancer

- In the US there are two main types of labs that perform clinical testing.
  - Hospital (institutional) laboratories are attached to a hospital or healthcare provider (some are academic).
  - Reference laboratories receive samples from third party healthcare providers (practitioners, clinics, insurance companies and others).

- Large institutional laboratories often have outreach programs to offer laboratory services to smaller hospitals/clinics

Reference Laboratory Business

Institutional and reference laboratories are complementary, although at times they can compete for clinical specimens

Why have Reference Laboratories?

- Drivers:
  - Efficiency and cost reduction (high volume)
  - Quality
  - Provide access to small/medium size practices/institutions
  - Can offer testing for very specialized markets (esoteric tests)
- Cons:
  - Testing not done on site
  - Potential impact in turn-around-time (efficiency can balance)
  - Might impact communication with healthcare provider (can be solved with good customer service)

Reference Laboratory Business

- The clinical diagnostics market is a ~$50B+ (USD) global market, with the U.S. representing 40-50% and one of the most highly regulated.

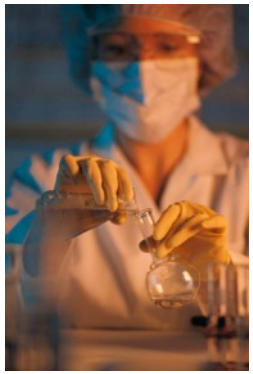
- Hospitals and large commercial reference labs represent the majority of the market (80%+), followed by point-of-care testing in clinics and physician office laboratories (~10%) and the home setting (~10%)
  - Molecular diagnostics (MDx) has been the fastest growing segment within the clinical diagnostics in the last decade
  - Next-generation sequencing (NGS) will play an increasingly important role in clinical diagnostics

- http://decibio.com/clinical-diagnostics.php
- JP Morgan Conference
- http://www.kaloramainformation.com/Worldwide-Vitro-Diagnostic-8326563/
- http://www.technologynetworks.com/Diagnostics/reports.aspx?id=162520

Academia: From Lab to Clinical Use

- Academic labs are a constant source of innovation
  - Discoveries made in research laboratories or clinical research environments can quickly be translated into tests performed in a CLIA environment
  - Diagnostic “conundrums” can be studied using infrastructure often not available in commercial laboratories
- Obstacles
  - Research funding for test development of biomarkers is limited and very competitive
  - Resources for validation and growth often face competition by other institutional priorities
  - Patient volume for specialized/esoteric tests might not be sufficient to support development and ongoing costs

Lab to Clinic – Bi-directional!!



Idea

Experimental, Biological
or Clinical Observations

Clinical
Utility

Testing Platform

Validation

Implementation

Reimbursement

Business Climate for Diagnostics

- Technology development
  - Sequencing platforms advances thanks to Human Genome Project (reduced costs / increased througput)
  - Other technologies: faster, cheaper. Better?
    - e.g. Theranos

- Increased competition
  - Low entry barrier for sequencing instrumentation
    - MiSeq, PGM
  - Increased interest from academic hospitals on tumor profiling
  - Increased availability of clinical trials with targeted agents
  - Ruling of SCOTUS on gene patents

Business Climate for Diagnostics

- Healthy trend on Investment

Invitae Completes $120 Million Series F Financing

Invitae Completes $120 Million Series F Financing

SAN FRANCISCO, October 13, 2014 – Invitae Corporation, a genetic information company, today announced the completion of a $120 million Series F financing. Invitae plans to use the proceeds to accelerate the build out of its infrastructure for its genetic information business, as well as to expand its global presence.

...erceptive Advisors, ...Capital, Genesys

Baylor, Miraca Holdings agree to joint venture on clinical genetic testing

2010

2021

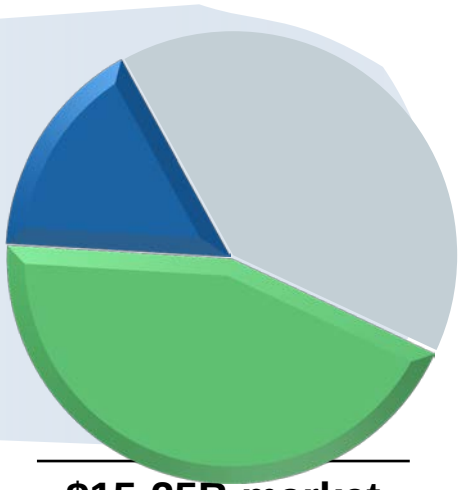
Oncology

Infectious Disease

Inherited Disorders

$3B TAM growing to $15B in near term

- 75% of physicians believe genetic testing allows for more personalized medicine and anticipate usage will nearly quadruple over next 5 years



$5B market

$15-25B market

United Healthcare, 2012

Business Climate for Diagnostics

- Downward pressure on reimbursement
  - With CMS pricing for new molecular codes in 2014, the median price dropped 15% compared to how CMS reimbursed molecular tests prior to the new codes, but many prices dropped by more than 50%.

- Uncertainty about the future of reimbursement
  - With new “Doc Fix” law, starting in 2017 Medicare will rely on an average of private payer rates to set Medicare’s fee schedule, and give special treatment to single-source proprietary tests.
  - The “Doc Fix” law limits how deep market-based rates can cut the current fee schedule for the first 6 years. For 2017–2019, CMS cannot reduce the payment for an individual test more than 10% per year, and for 2020–2022, not more than 15% per year.

Clinical Laboratory News

Business Climate for Diagnostics

- Threat of Increased Regulation

http://www.genomicslawreport.com/wp-content/uploads/2010/06/FDA-v-LDT.jpg

http://www.darkdaily.com/

FDA Pushes Forward with Plans to Regulate Laboratory-Developed Tests, in a Move that Will Impact Many Clinical Laboratory Companies and Pathology Groups

http://www.personalizedmedicinebulletin.com/

FDA Regulation of Laboratory Developed Tests: Benefit or Unnecessary Burden?

POSTED BY ANTOINETTE F. KONSKI ON 24 FEBRUARY 2013

POSTED IN COMPANION DIAGNOSTICS; DIAGNOSTIC METHODS; FDA; PERSONALIZED MEDICINE

FDA's Move to Regulate LDTs Could Reshape the Industry

Posted in IVD by MDDI Staff on September 19, 2014

Share

FDA has announced its intention to issue draft guidances on the regulation of laboratory-developed tests—a controversial decision that could increase the burden of compliance and stifle innovation.

By Allyson B. Mullen

http://www.mddionline.com/

Laboratory Developed Tests

- Large Majority of Oncology and Genetic tests are LDTs

- Genetic Tests in GTR

NIH thanks labs for registering over 24,000 tests for 5,000 conditions and 3,600 genes!

- Estimated >11,000 CLIA-certified labs perform high-complexity testing, including LDTs
- In New York, 565 labs submitted 9,800 LDTs for review in 2014.

- FDA Cleared/Approved Nucleid Acid Tests
  - 6 Oncology Disorders
  - 13 Tests

- FDA Cleared/Approved Companion Tests
  - HER2: 9
  - EGFR: 3
  - BRAF: 2
  - Other oncology: 3
  - Other: 1

www.ncbi.nlm.nih.gov/gtr/, www.fda.gov, www.captodayonline.com

Encourage innovation and development

- Many forecast that LDT regulation will lead to contraction of the field
  - Fewer laboratories will be able to support the added burden of regulation (Notification, MDR, QSR and PMA/510(k))
  - With added regulation, innovation in the diagnostic market will move to less regulated environments
  - Perception of laboratories as test manufacturers needs to change, laboratories are medical service providers

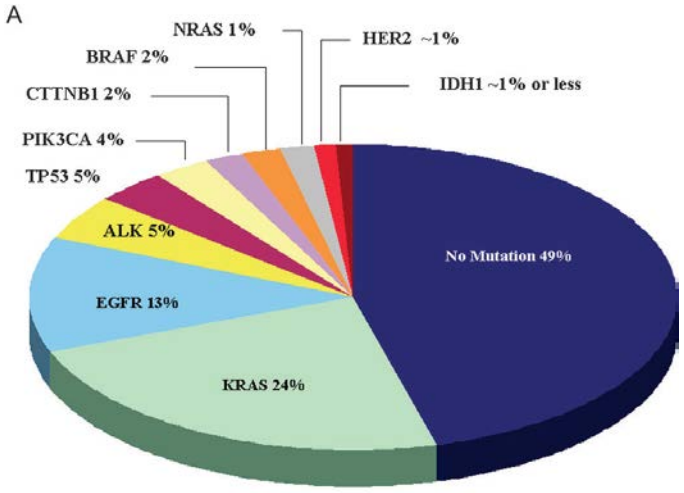
- Maintain LDT regulatory oversight with CMS (CLIA)
  - Improve CLIA to more stringent requirements for oversight, including review of clinical validity when appropriate
  - CLIA registry to become public and address needs for transparency and adverse event reporting

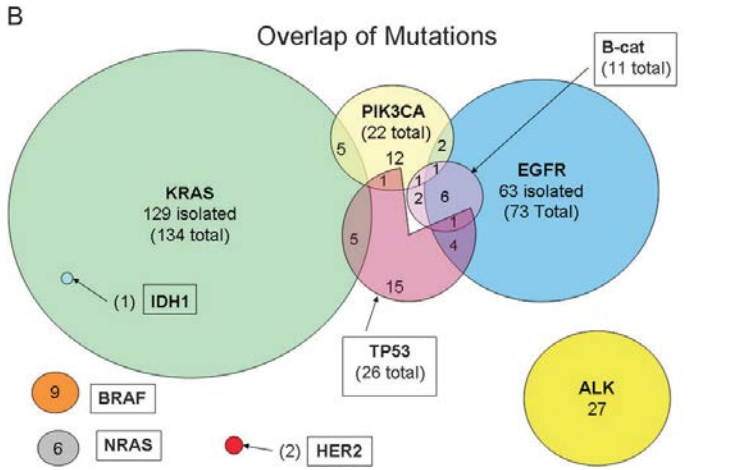
Ferreira-Gonzalez, et al. J Mol Diagn 2014, 16: 3e6.

Klein & Leib, AMP Webinar

Encourage innovation and development

- Companion Diagnostics
  - Specify molecular biomarker and not the specific platform to be used.
    - Should spell out performance characteristics for test
  - CDx model not sustainable in the era of multi-analyte tests (NGS)





original article

Annals of Oncology 22: 2616-2624, 2011
doi:10.1093/annonc/mdr489
Published online 9 November 2011

Implementing multiplexed genotyping of non-small-cell lung cancers into routine clinical practice

L. V. Sequist[1,2*], R. S. Heist[1,2], A. T. Shaw[1,2], P. Fidias[1,2], R. Rosovsky[1,2,3], J. S. Temel[1,2],

Encourage Clinical Diagnostic Development

- Need support 'post-test' research.
  - Support efforts for data harmonization and knowledgebase development in the somatic cancer arena, similar to those in the germline field (ClinGen)

http://www.clinicalgenome.org/

Encourage Clinical Diagnostic Development

- Need support 'post-test' research.
  - Encourage reporting and sharing of test performance and response to therapy data

- Address privacy concerns directly with patients
  - Multiple studies indicate that patients are less concerned about privacy issues than ELSI academics
  - Reduce barriers to data sharing in controlled-access databases

Leadership Position in Diagnostics

In Summary,

- U.S. patients have enjoyed access to cutting edge diagnostics in oncology
- Technologic advances open unprecedented opportunities to improve diagnostics and facilitate advances in cancer management
- Reimbursement and regulatory pressures could constrain our ability to remain in a leadership position in diagnostics development
- Need to develop policies that support data sharing among laboratories and healthcare providers to help advance clinical knowledgebase

Thank you!

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