Challenges of Biomarker Development

(in Europe)
Disclaimer

• I work for industry (diagnostics)
• We have worked with over 30 biopharma companies in the arena of biomarkers
• The presentation is my own and does not necessarily reflect the views of Biodesix nor those of our partners
• My biases come from working in oncology, particularly lung cancer
Biomarkers in general

• Lots of them
  – a naturally occurring molecule, gene, or characteristic by which a particular pathological or physiological process, disease, etc. can be identified

• But what we are interested in are those that can be used in clinical practice...which I will call ‘tests’

• Why do we need clinically useful tests?
  – Giving the right therapy to the right patient
    • Maximizing outcomes, minimizing side effects and suffering
Global Oncology Costs - Financial Toxicity

Costs are increasing faster than the growth of our economies

Source: Global Oncology Trends Report 2017 (QuintilesIMS)
Diagnostic/Biomarker Trends

• Targeted therapies are giving way to the next wave of treatments: immunotherapy
  – Where there are many biological factors to consider
• Liquid biopsy is gaining traction
• Available tools
  – Better & better; still dominated by sequencing
    • But the approaches are diversifying
• Significant investment in ‘screening’ and ‘wellness’
  – Large markets attract large amounts of risk capital
  – Though not particularly in Europe
• Movement towards multivariate versus univariate
  – Which increases the complexity of the development process
• Machine learning / AI is finally coming to biomarker development
  – Though there is resistance to the ‘black box’
General Challenges

• Discovery
  – Tools and reagents are expensive
  – Samples & data
    • As you tease out more complex biology you naturally need larger sample sets in order to effectively stratify
    • Sample curation is not uniform, particularly for post-hoc analysis
    • Well curated data is always a challenge
    • Having a biomarker strategy ‘early’ is not always an option
  – Managing variability / reproducibility
    • Batch effects; variable readouts; test variability; clinical annotation
General Challenges

• Development
  – Can be difficult to move from discovery to a logistically viable test
  – Regulatory requirements can be demanding
• Commercialization
  – Validation
    • Costs are high
  – Reimbursement
    • Very difficult
  – Market Penetration
    • Relatively slow, complex, and expensive
  – Competition, in many cases, can ride on the back of other’s validation work
Challenges by Sector

- Many constituencies are involved in developing tests
  - each providing a unique benefit (or having a role to play)
  - each providing their own bias / challenge
Biomarker Constituencies

• Academics/researchers (purpose/biases)
  – Understanding biology in general to improve the understanding of disease etiology and progression
  – Biases / Challenges
    • Start from a biological hypothesis; known markers of relevance
    • Biased by the tool-set and approach they currently use
    • Herd effects
  – Counter trends:
    • Increasing amounts of biological data are leading to the use of machine (unsupervised/semi-supervised) learning
Biomarker Constituencies

• Biopharma/industry
  • Major force in driving the development of biomarkers
  • Facilitating the understanding of drug MOA & patient interactions
  • Bias towards the largest applicable population
  • Biased by the “in-place” infrastructure that enables testing
    – Novel / proprietary is the enemy of rapid adoption
  • Don’t like black box (machine learning) solutions
    – Introduces risk at the regulators and for adoption
  • Very careful control over clinical samples / data
Biomarker Constituencies

• Clinicians
  • Prognostic, predictive and monitoring tools
    – Informing prognosis, guiding treatment; monitoring resistance; dosing
  • Bias
    – Bias to treat
      » “well tolerated”
    – Resistance to novel approaches
      » Bias as to presumed causation (they are experts)
      » Simply don’t believe black boxes; particularly ones developed independently of biopharma
Biomarker Constituencies

• Payers / Society
  • Containing costs (overall) and improving health
  • Inherent bias against paying
    – Use of institutional barriers hinders novel tests
  • Naturally risk averse
  • Historically diagnostics is a cost+ business
    – Very significant resistance from pretty much all constituencies to change this....
Biomarker Constituencies

- Patients
  - Ultimately the main beneficiaries of precision medicine
    - But often lack a voice
    - Patient advocacy is not well developed in Europe
  - Patient pay is rising
    - Genetic profiling (risk assessment, prenatal screening)
    - Wellness & monitoring
    - In certain geographies
Biomarker Constituencies

• Diagnostic Industry
  – Dominated by ‘logistics’ companies
    • Commodity business driven by margin considerations...not research (akin to generics)
  – Discovery industry is small
    • Miniscule funding compared to drugs
    • VC’s stay away because the path to commercialization is so difficult
      – Even when you can demonstrate proof of principle
    • But this is where innovation can happen
Global Costs for Cancer Drugs vs. Molecular Diagnostics

Source: Combined (and calculated) data from Seo 2018 and Quintiles Global Oncology Trends (2017)
Discovery/Development is more important than ever

- It takes substantial focus and resources to create truly useful tests, particularly multivariate tests
  - So the focus is often on the largest markets given the constraints on pricing and reimbursement
  - But that may not be where the most value is
- We need champions focused on specific unmet needs
Finally: Benefits of Europe

• Access to samples
  – Better rules and willingness to work with companies
    • Often keep control of samples from pharma studies
    • Can more easily share their own samples
  – Current regulatory hurdles are lower
    • But this may be changing
Drawbacks of Europe

• From Bench top to bedside?
  – Getting reimbursed is very hard...
    • Fragmented markets
    • Major resistance to value-based pricing
  – Locals dominate access and testing
    • And typically only want to add commodity products to their menus
    • Pharma wants companion diagnostics that are widely available
Opportunities

• Lower the costs
  • For discovery, validation
  • Broader support for funded clinical studies
    – Competition from pharma; reduce reliance on pharma $$s
    – More pressure on pharma to share samples/data
  • Unified approvals with broad support for reimbursement across geographies

• Improve the pricing for clinically useful and cost-effective products
  – Reward risk and innovation when successful
Summary

• The tools we have for probing biology are rapidly improving and provide fantastic promise
  – Improve patient outcomes; manage costs & toxicities

• *Useful* biomarkers are getting more complex (and better) and are more needed than ever

• But the hurdles from discovery through to delivery to the clinic are very high

• You need dedicated champions to make it happen
  – and they need mechanisms of support to overcome the hurdles