Translating Genomic Science into Clinical Practice: Time for Innovative Business Models

November 2012

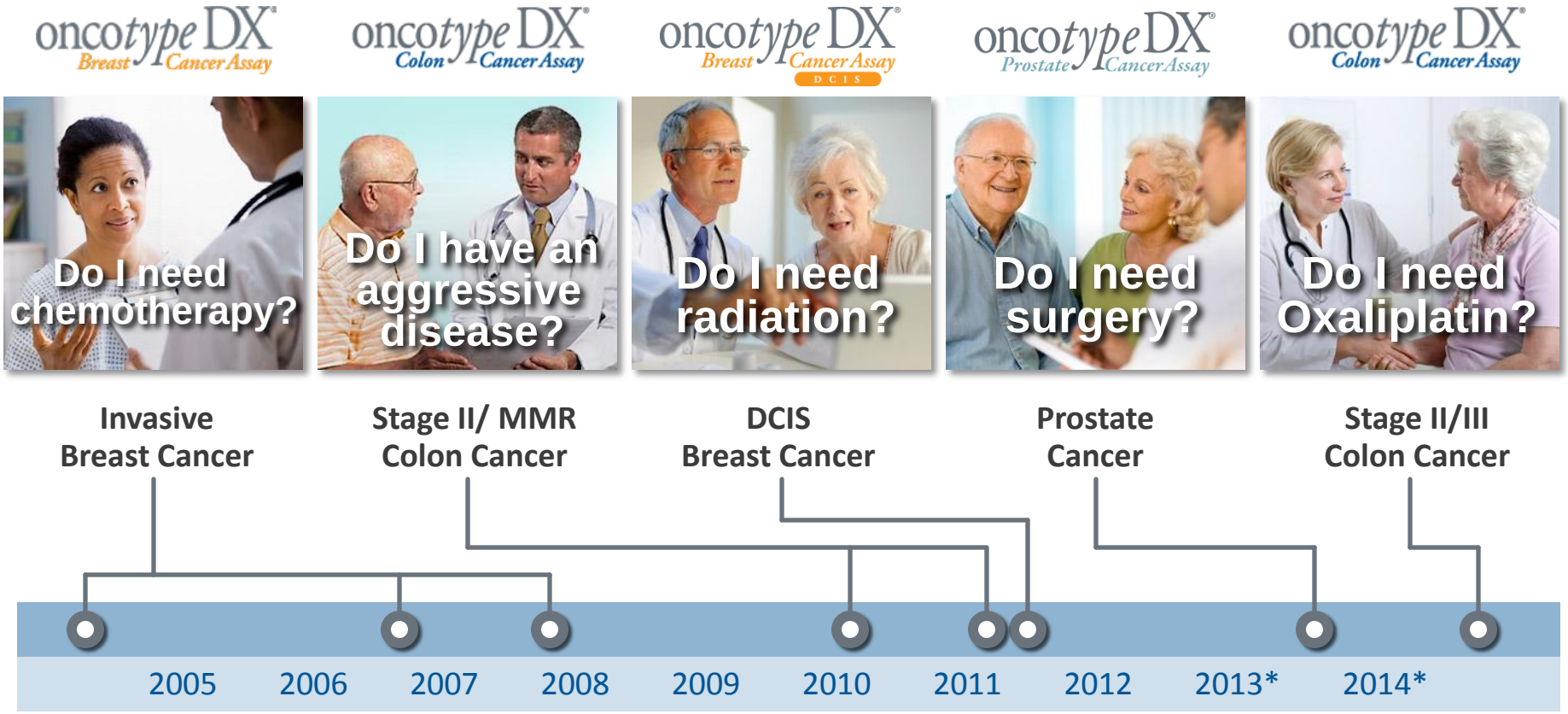
Topics

- Genomic Health as a successful business model for personalized medicine
  - Classical product development model
- Technology trends are driving us toward an inflection point – Moore's Law and Metcalfe's Law applied to healthcare
  - Disruption is on the horizon whether we like it or not – be careful what you ask for
- Invitae business model – Exploit Metcalfe's Law to build translational research into the medical system
  - Aggregate all genetic tests into a single assay and "free the data"

Genomic Health Business Model

- Start by asking the right clinical question
  - Focus on patients, patients, patients
  - Does this change treatment decisions
  - Does it make economic sense
- Do the right clinical trials, data, data, data…
  - Bulk of trials must be retrospective
  - Multiple large cohorts with key opinion leaders
  - Sophisticated statistical analysis and algorithm development
- Win over the physicians and advocates with data
  - Physicians will drive guidelines and reimbursement
  - Physician support will empower the advocacy community
- Reimbursement will reinforce adoption
  - All major payors in the US cover Oncotype DX for breast cancer

Asking the Right Clinical Questions



* Estimated

Genomic Health™

Contrasting Business Models

- Pharma Model
  - 10-15 year product development cycles
  - $1 billion cost of drug development
  - 80-90% failure rates

- Genomic Diagnostic Model
  - 3-4 year product development cycles (when using retrospective samples)
  - $100-$200 million cost of diagnostic development
  - 80-90% success rate

Business Model Comparison (2011)

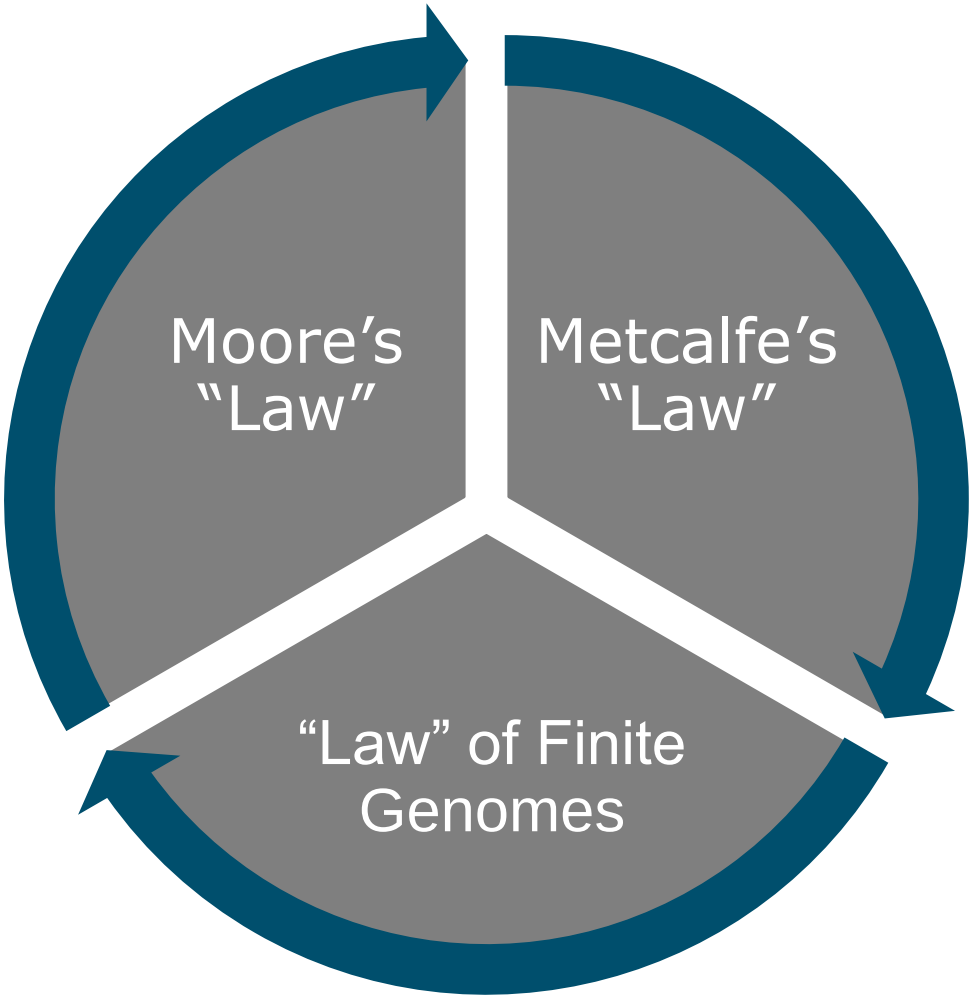
	Genomic Health		Labcorp			Amgen	Aetna
Revenue (millions)	$206.1	100%	$5,542	100%		100%	100%
Cost of Revenue	$33.8	16%	$3,267	59%		16%	70%
R&D	$39.8	19%	$0	0%		20%	0%
Selling, General & Administrative	$124.1	60%	$1,160	21%		34%	20%
Taxes	(Tax loss)		$333	6%			6%
Net Income	$7.8	4%	$519	9%		24%	6%

Lessons Learned From the Genomic Health Experience

- Despite Genomic Health success, the diagnostic industry is not yet financed at a scale that can support broad translational medicine
  - Largely a cost of capital and scale problem, not science or communication, or even reimbursement
- Pharmaceutical industry is not going to be a major driver
  - Pharma industry develops drugs not diagnostics
  - Companion Dx increases costs, time to market and probability of failure
- Reimbursement industry is not going to be a major driver
  - Payors are financial institutions not R&D institutions
    - They make money off the float between insurance premiums and payouts and struggle to define value

Technology to the Rescue

Driving Toward an Inflection Point



The New York Times ON THE WEB

"A Decade Later, Human Genomic Project Yields Few New Cures…" June 12, 2010

The New York Times

PERSONAL COMPUTERS; So Do You Need One? November 19, 1991

Whole Genome Sequencing Costs Will Drop Below Traditional Genetic Screening Within a Decade

NGS will be a disruptive force in diagnostics

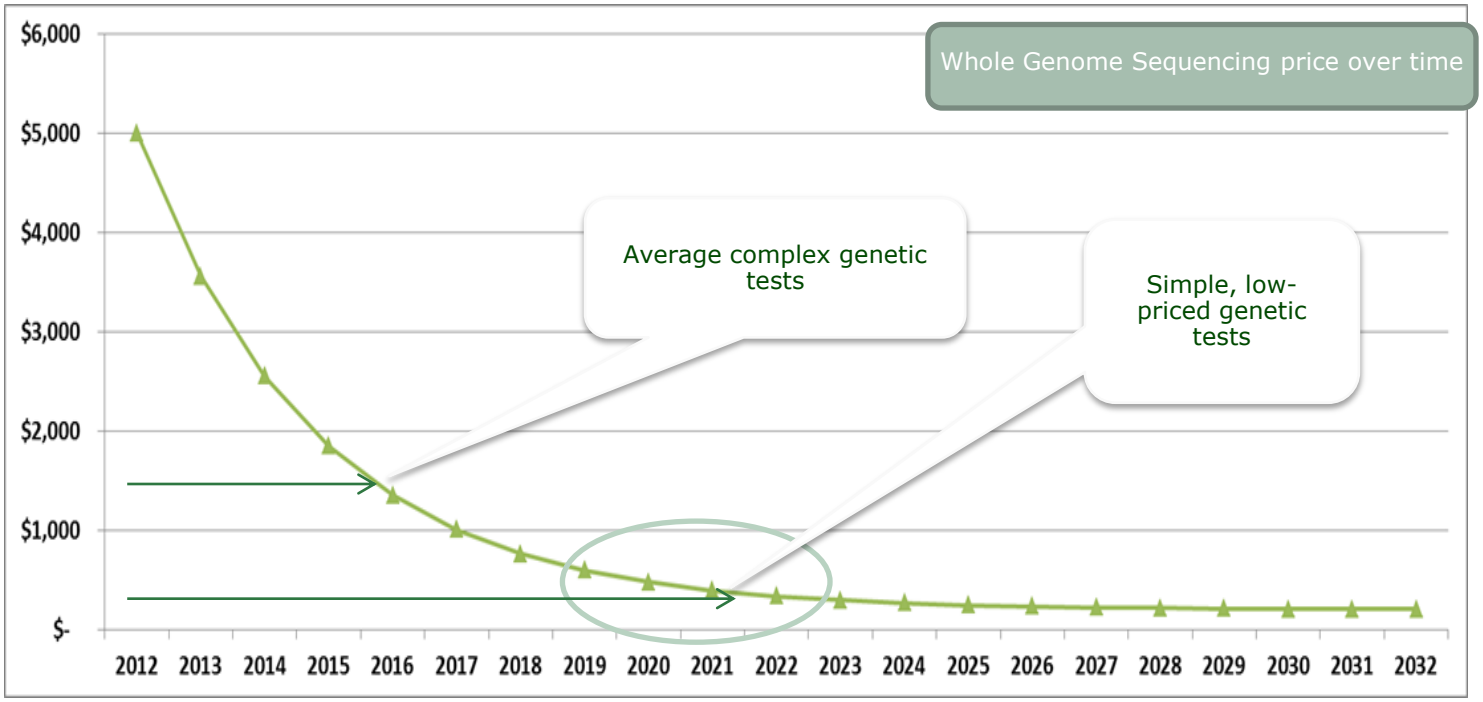


Figure 4: Falling price of whole genome sequencing (30% annual decrease modeled) and pending disruption

Genetic Testing is a $Billion Market and Growing Rapidly

Illustrative growth scenarios for molecular diagnostic and genetic testing spending, 2010 – 2021

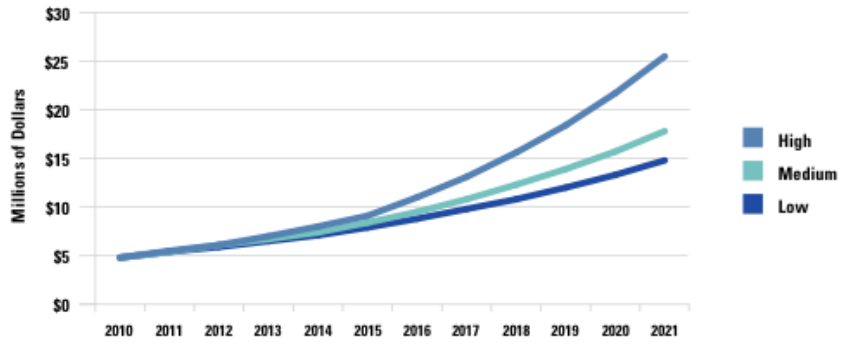


Figure 2.4; Source: UnitedHealth Center for Health Reform & Modernization, 2012

Do you believe that there are patients in your practice who have not yet had a genetic test but who would benefit from having one?

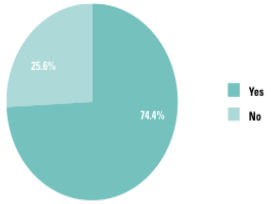
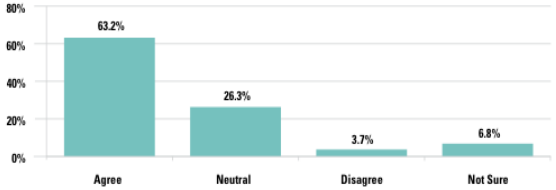


Figure 3.4; Source: UnitedHealth Center for Health Reform & Modernization/Harris Interactive survey of physicians, January 2012

Genetic testing gives me the ability to diagnose conditions that would otherwise be unknown.



Genetic testing gives me the ability to diagnose conditions that could be prevented.

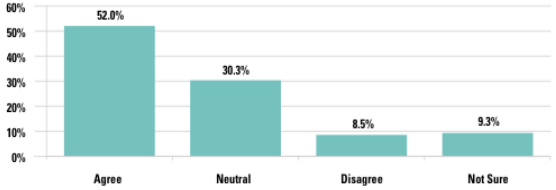


Figure 3.5; Source: UnitedHealth Center for Health Reform & Modernization/Harris Interactive survey of physicians, January 2012

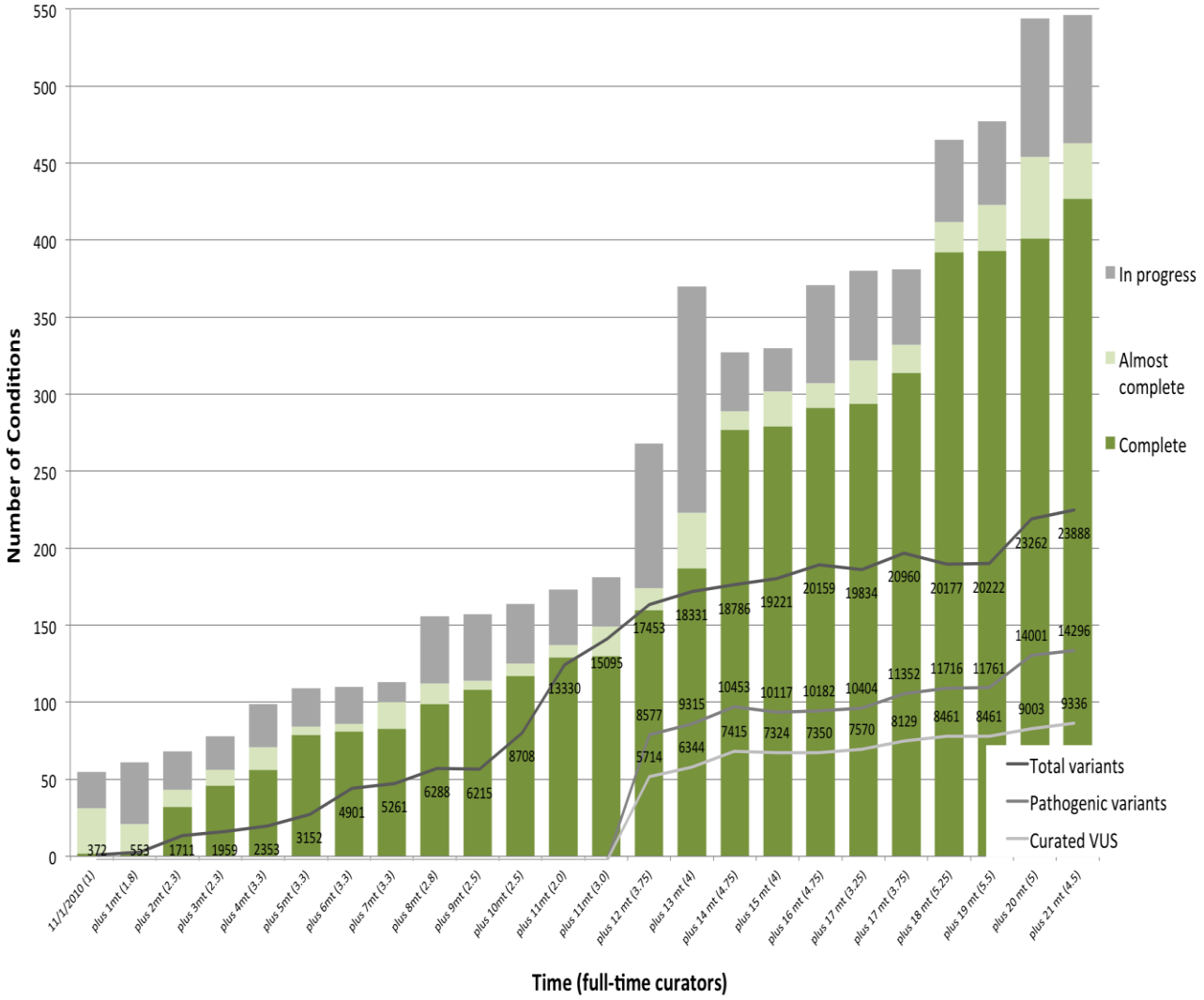
Invitae plans to aggregate all the world's genetic tests into a single assay with better quality at lower cost then most single gene assays today… and more…

InVitae Philosophy

- How would you design a company to take advantage of Metcalfe's Law?
  - Genetic testing must be broadly available to everyone
    - Make the value/price of genetic testing consumer friendly
    - Go global – beyond current regulatory/legal boundries
  - "Free the data" as a fundamental business principle
    - We don't patent genes… we set them free
    - Patient ownership and control over their data
    - Information, by its nature wants to be shared
  - Translational medicine becomes an integral part of the medical system
    - "Extra data" rides along for free
    - Data sharing within the network becomes the norm
    - New sources of revenue will pay for data generation

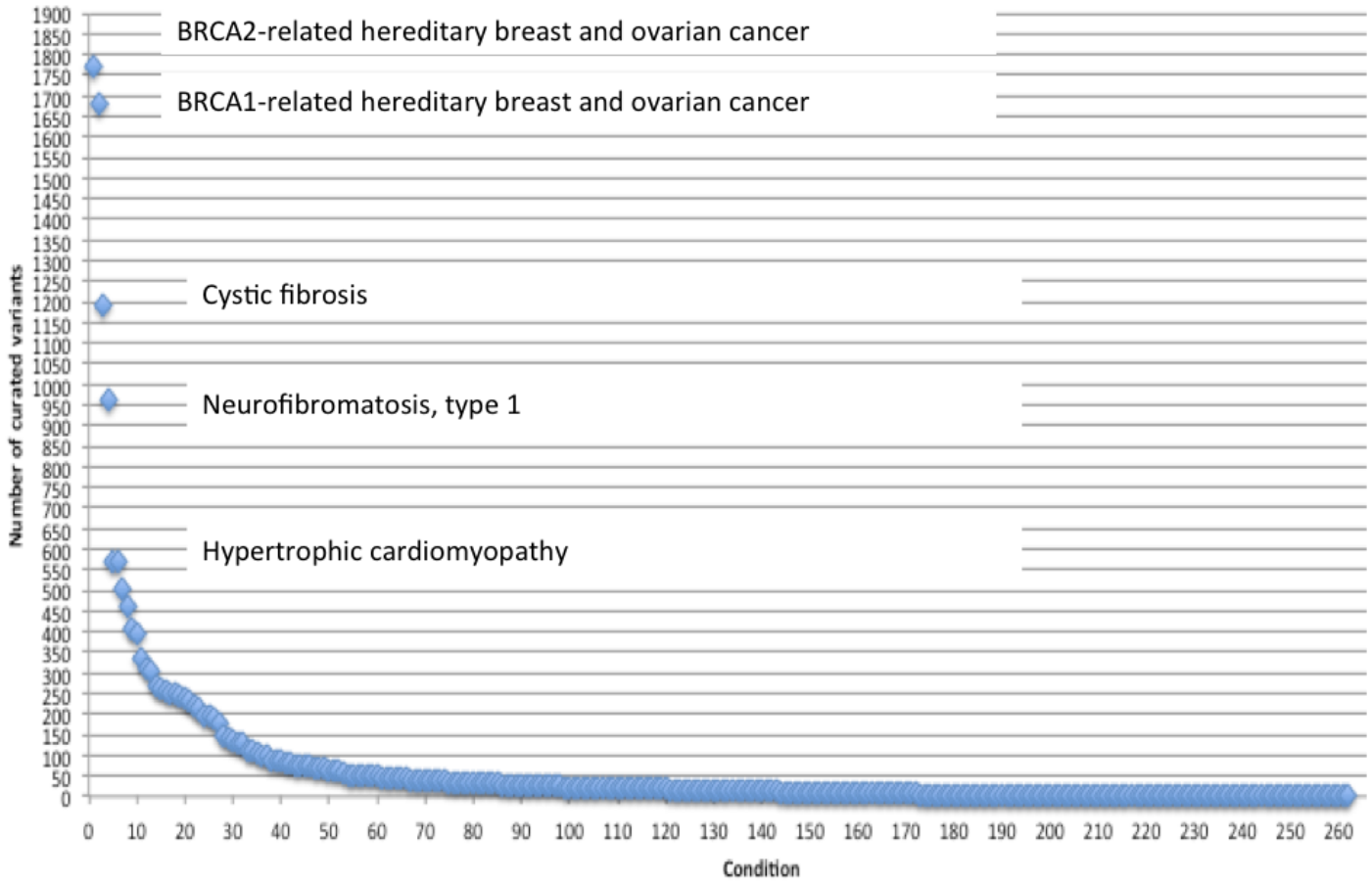

InVitæ

InVitae Database of Curated Genetic Variation



- 420 conditions curated with over 20,000 variants
- 50 conditions almost complete
- 80 conditions in progress

Massive Complexity Lends itself to Industrial-Scale Solutions



Designed to tackle the tough problems

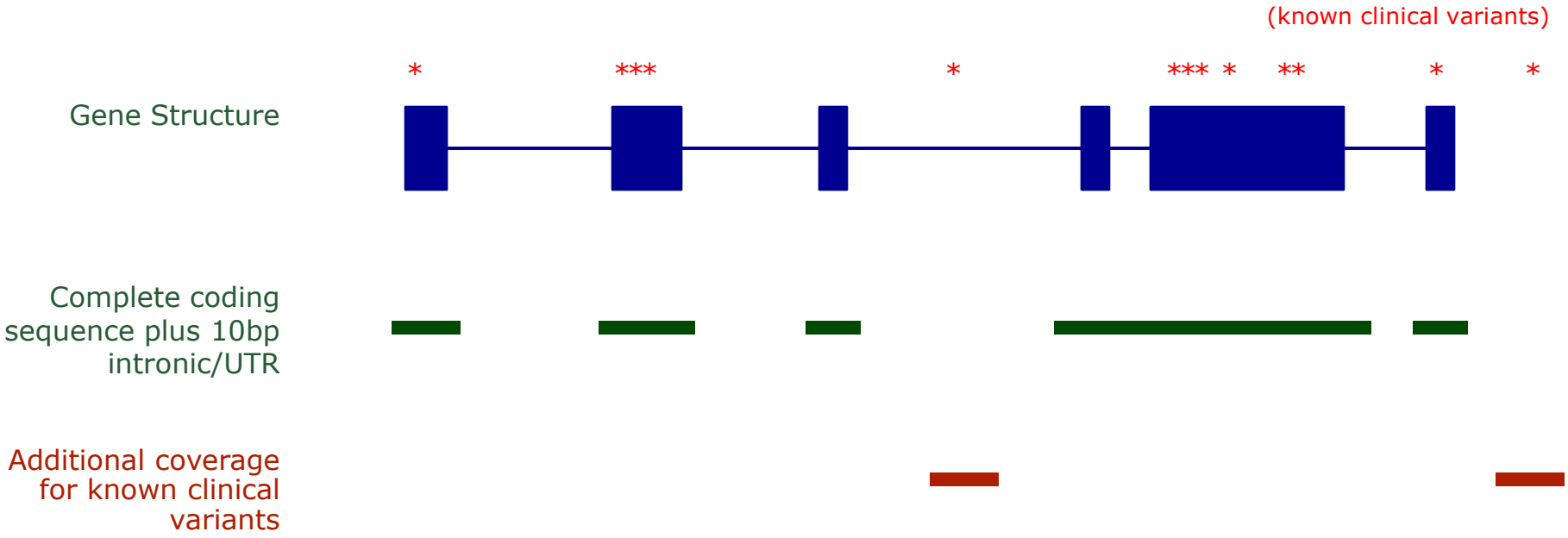
Difficult, clinical-grade 'must have' targets

- Read-through
- Insertions, deletions, inversions
- Copy number alterations
- Pseudogenes
- Tri/di-nucleotide repeats
- Homopolymers, high GC content regions of interest
- Diagnostic quality sensitivity and specificity
- Validation by second technology not required

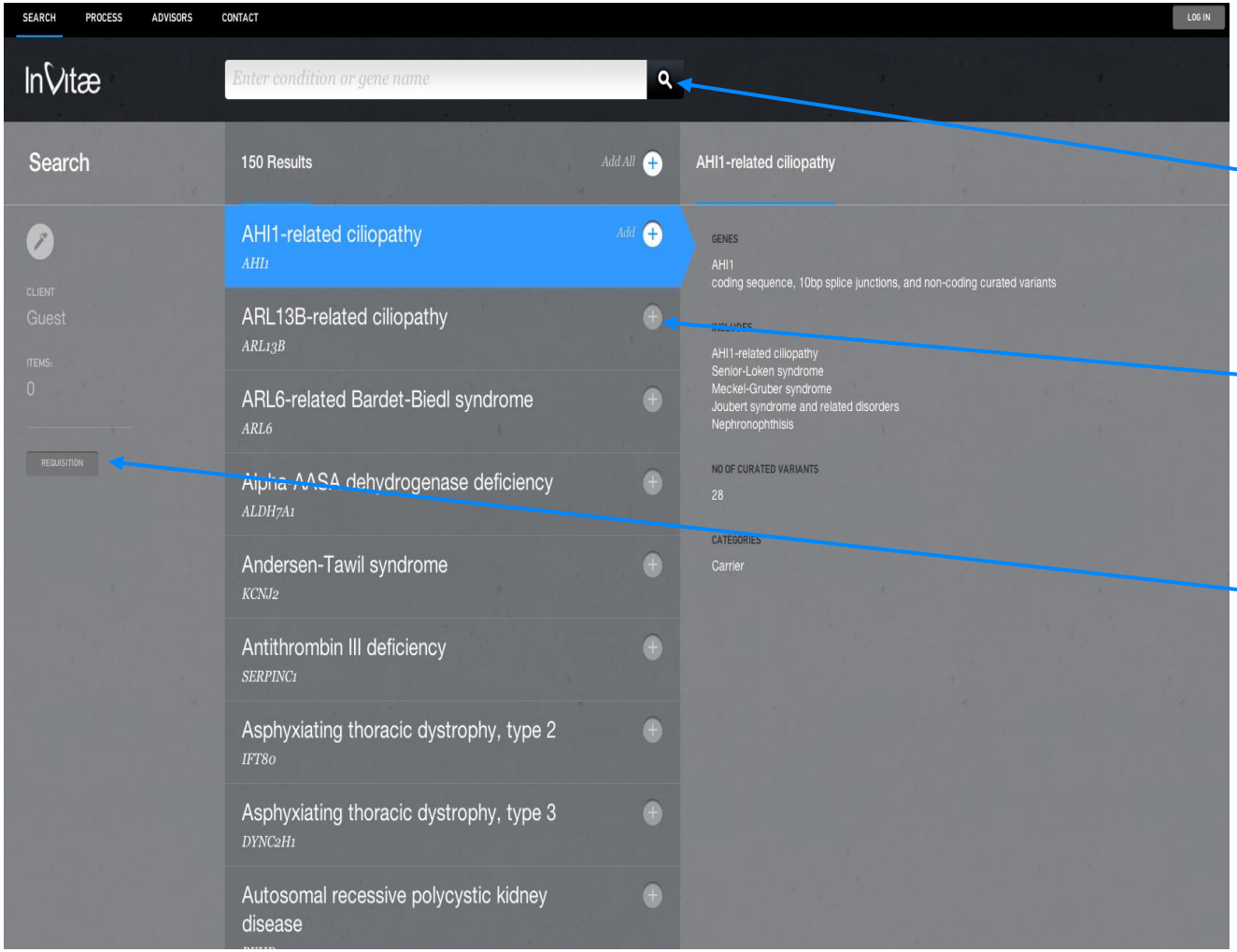
Disparate, non-standardized clinical annotation

- Incomplete databases
- 5-20% errors in databases and condition literature
- Unclear condition boundaries
- Multiple aliases
- Subjective pathological determination

Comprehensive clinical sequencing of exons and known variants



Current Beta Test Catalog Offers 150 Conditions



- Search
- Add one, more, or all conditions to the requisition
- Proceed to patient info and requisition