Wall Street Perspective Diagnostics

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Amanda Murphy, CFA, partner, joined William Blair in 2006. Ms. Murphy is a healthcare analyst with a focus on diagnostic services and life sciences. Previously, Ms. Murphy worked at Caremark as a business analyst and as a senior consultant within PricewaterhouseCoopers's strategy consulting division. She received a B.S. in biology from Boston College's honors program and holds an M.B.A. in finance, accounting, and economics from the Kellogg Graduate School of Management at Northwestern University.

Companies Under Coverage

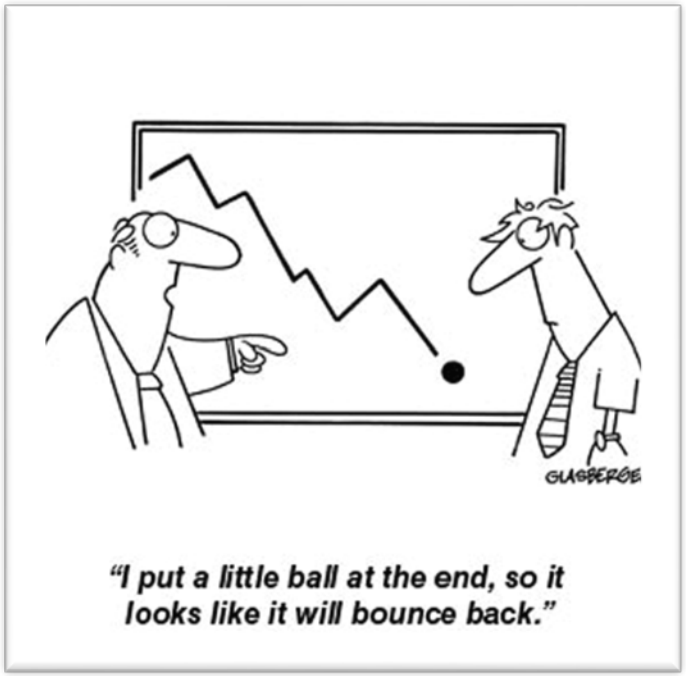
Diagnostic Services
Foundation Medicine, Inc. (FMI)
Genomic Health, Inc. (GHDX)
Invitae Corporation (NVTA)
Laboratory Corp. (LH)
Myriad Genetics, Inc. (MYGN)
NeoGenomics, Inc. (NEO)
Quest Diagnostics Inc. (DGX)
Veracyte, Inc. (VCYT)

Life Sciences
Bio-Techne Corporation (TECH)
Bruker Corporation (BRKR)
Illumina, Inc. (ILMN)
Pacific Biosciences, Inc. (PACB)
Repligen Corporation (RGEN)
Waters Corporation (WAT)

Stock Valuation – How Do Investors Think About Stocks?

Stock value equals the net present value of future cash flows

- Cash flow = volume of tests x what you **actually** get paid
- Discount rate = how much risk am I willing to take to hold this asset



$$\text{Equity value} = \sum_{t=1}^{\infty} \frac{\text{FCFE}_t}{(1+r)^t}$$

Sum of future free cash flows

Discounted back to present value

Diagnostics Investment Thesis

Demographic trends support increased usage (volume growth)

- Aging population
- Cancer incidence increases by age

Innovation in sequencing platforms

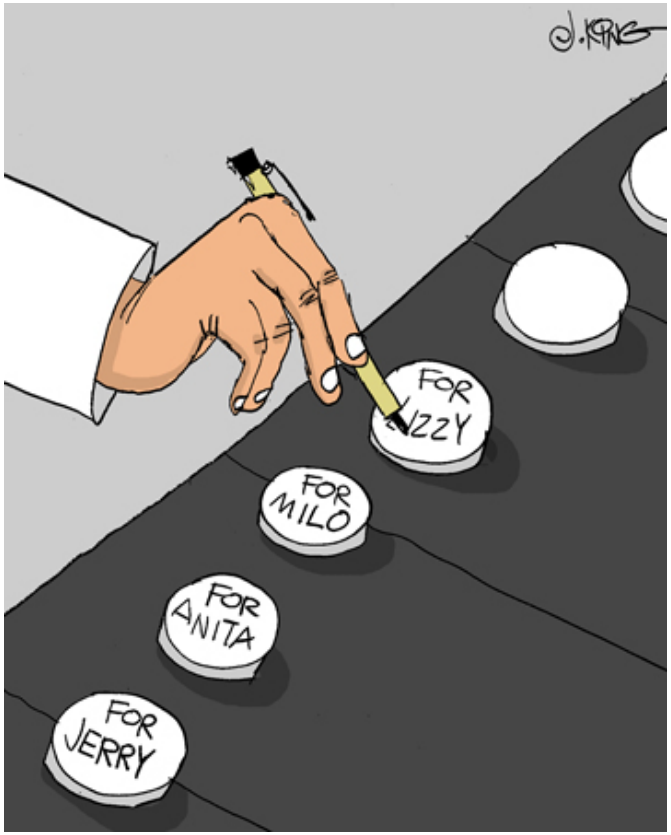
- Cost per base reductions faster than Moore's law
- Increase in sequencing tests on the market

Increased use of personalized medicine/targeted therapeutics

- Targeted therapeutics in pipeline
- Favorable regulatory environment

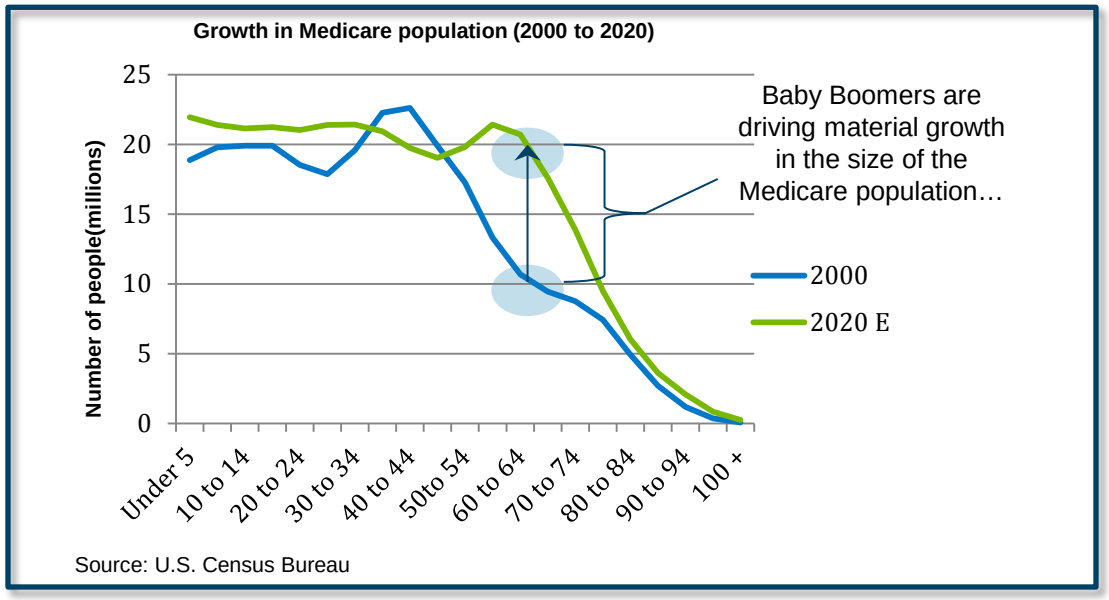
Transition to value-based care

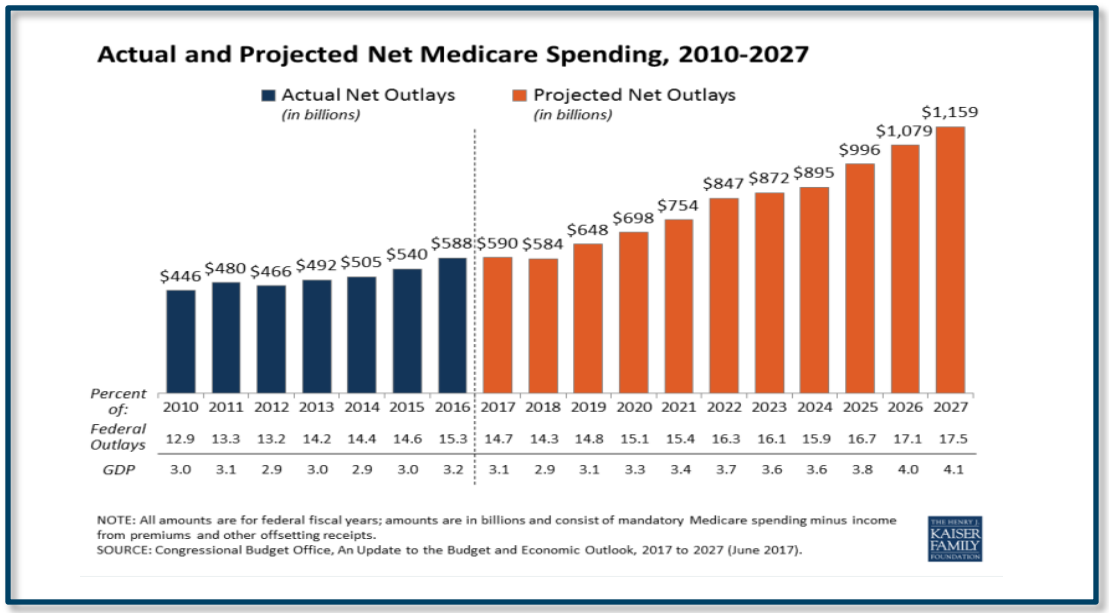
- Need to lower cost of cancer care
- Diagnostics mechanism to more appropriately guide treatment



Demographics Are a Major Factor in Driving Healthcare Usage

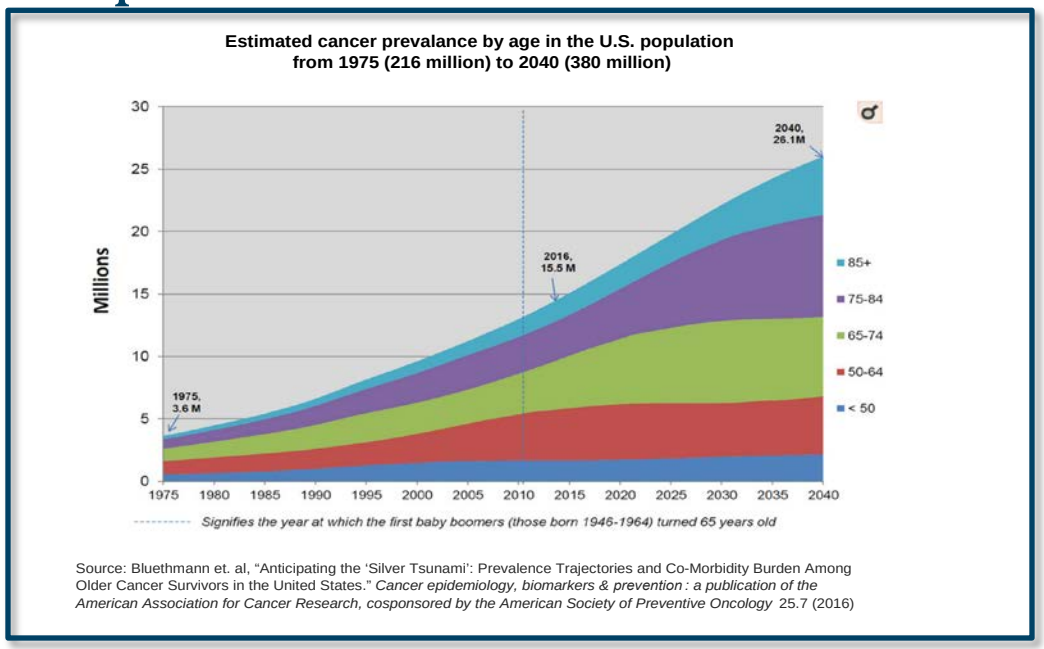
Demographics Are a Major Factor Affecting HC Spending Growth



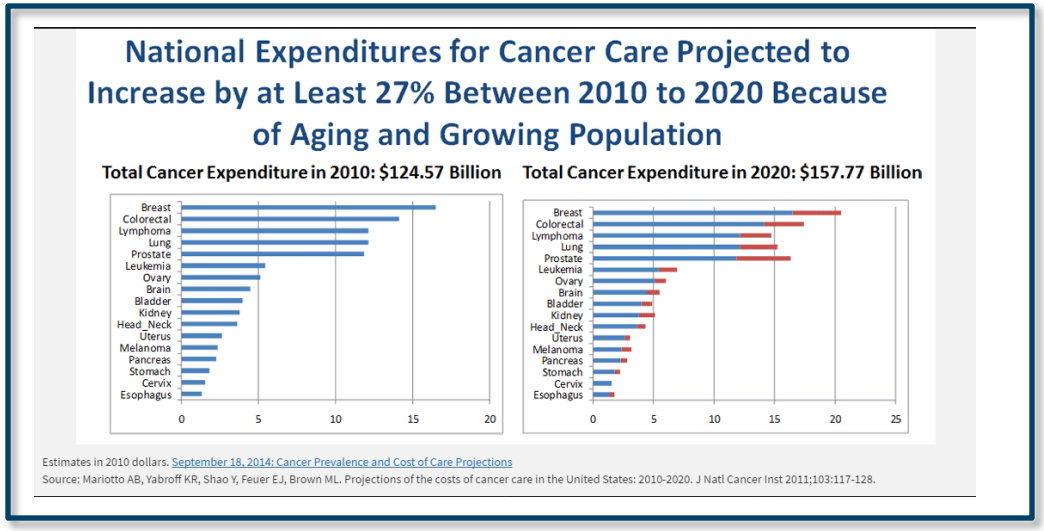


- Numbers of Medicare enrollment expected to surge with aging baby boomer population
- At the same time, the number of workers per beneficiary is expected to decline—creating a material funding challenge for the program
- Healthcare spending has slowed from recent levels but is still well in excess of GDP
- This situation is expected to become worse as the intensity of services and overall prices of Medicare are expected to accelerate
- This is expected to push healthcare to 20% of U.S. GDP ($5.5 trillion) by 2025

Cancer Prevalence/Cost to Treat Driven by Aging Population



Source: Bluethmann et. al, "Anticipating the 'Silver Tsunami': Prevalence Trajectories and Co-Morbidity Burden Among Older Cancer Survivors in the United States." *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology* 25.7 (2016)



- There are 1.74 million patients expected to be diagnosed with cancer a year—or 4,700 cases a day
- Mortality rates have declined and overall cancer incidence is down/stable, but the number of patients living with cancer is expected to grow from 15.5 million in 2016 to 26.1 million in 2040
- Average total treatment costs for patients in commercial insurance plans that were in active treatment for cancer reached $60K in 2014 (year-over-year growth of 19%)
- Over half of total costs are for outpatient services and the average combined cost of all drugs used by each patient represents 28% of the total cost of care
- Out-of-pocket costs are a major concern; average healthcare spending per patient increased from $2,000 in the month preceding diagnosis to as high as $25,000 in the month of diagnosis

Cost of Cancer Care – Key Focus of All Stakeholders

- Genentech's survey of five key stakeholder groups
- Control of cancer costs and cancer specialty drug costs one of top five issues

	MCOs (N=103)	SPs (N=28)	Oncologists (N=202)	OPMs (N=201)	Employers (N=200)
1	Control of cancer specialty drug costs: 90%	Control of cancer specialty drug costs: 82%	Control of overall cancer care costs: 63%	Control of overall cancer care costs: 54%	Control of overall cancer care costs: 60%
2	Control of overall cancer care costs: 67%	Balancing treatment *standardization*[b] with *personalization*[c]: 57%	Control of cancer specialty drug costs: 57%	Control of cancer specialty drug costs: 52%	Effective cancer therapies: 53%
3	Balancing treatment *standardization*[b] with *personalization*[c]: 65%	Control of overall cancer care costs: 57%	Effective cancer therapies: 57%	Escalation in patient OOP costs: 47%	Control of cancer specialty drug costs: 50%
4	Effective cancer therapies: 46%	Escalation in patient OOP costs: 57%	Escalation in patient OOP costs: 48%	Effective cancer therapies: 41%	Escalation in patient OOP costs: 46%
5	Advance care planning: 46%	Effective care coordination and patient navigation: 46%	Access to cancer care: 37%	Balancing treatment *standardization*[b] with *personalization*[c]: 40%	Developing better cancer diagnostics: 42%

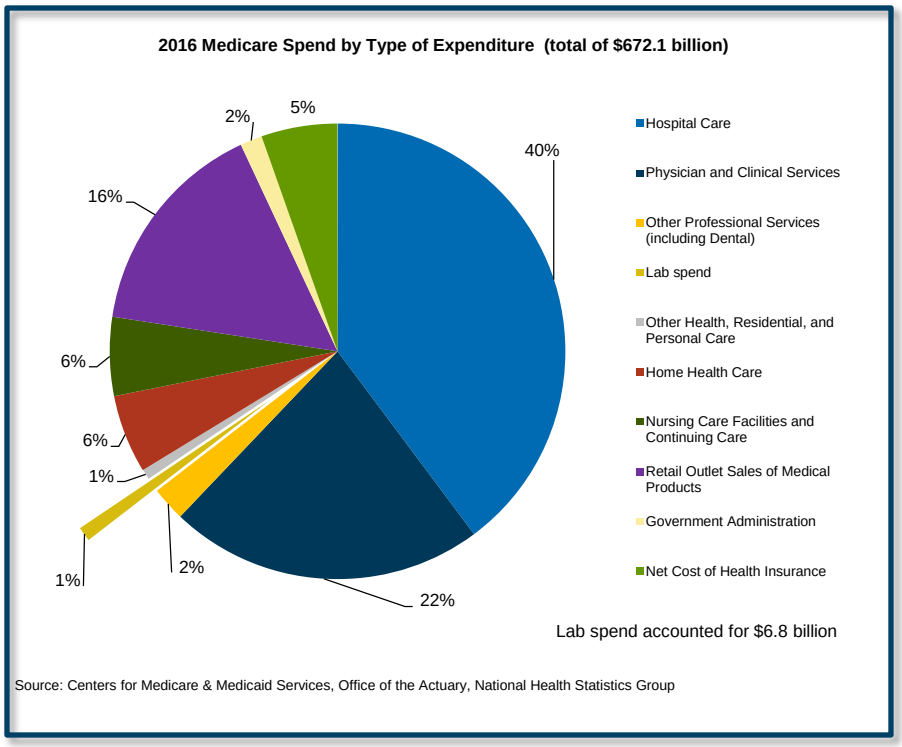
[a]List of 14 cancer care issues: Access to cancer care, advance care planning, balancing treatment standardization with personalization, control of cancer specialty drug costs, control of overall cancer care costs, developing an equitable provider alternative payment model, developing better cancer diagnostics, effective cancer therapies, effective care coordination and patient navigation, escalation in patient OOP costs, improving provider compliance with evidence-based treatment, increasing the availability of enhanced cancer clinical trials, patient engagement, and widespread adoption of interoperable health information technology to support quality improvements and outcomes measurement.

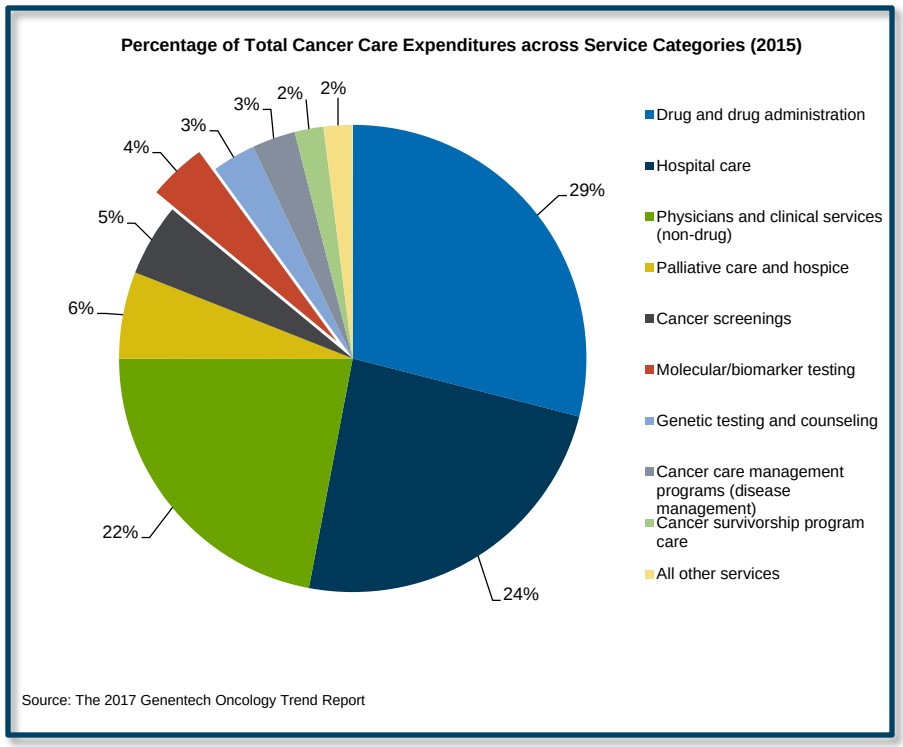
[b]Refers to treatment guidelines and pathways.

[c]Refers to molecular/biomarker testing.

Diagnostics as a Cost-Savings Mechanism

- Diagnostics are a small portion of the spending but drive meaningful treatment decisions
- Separation of pharma coverage and diagnostic coverage within payer decision making

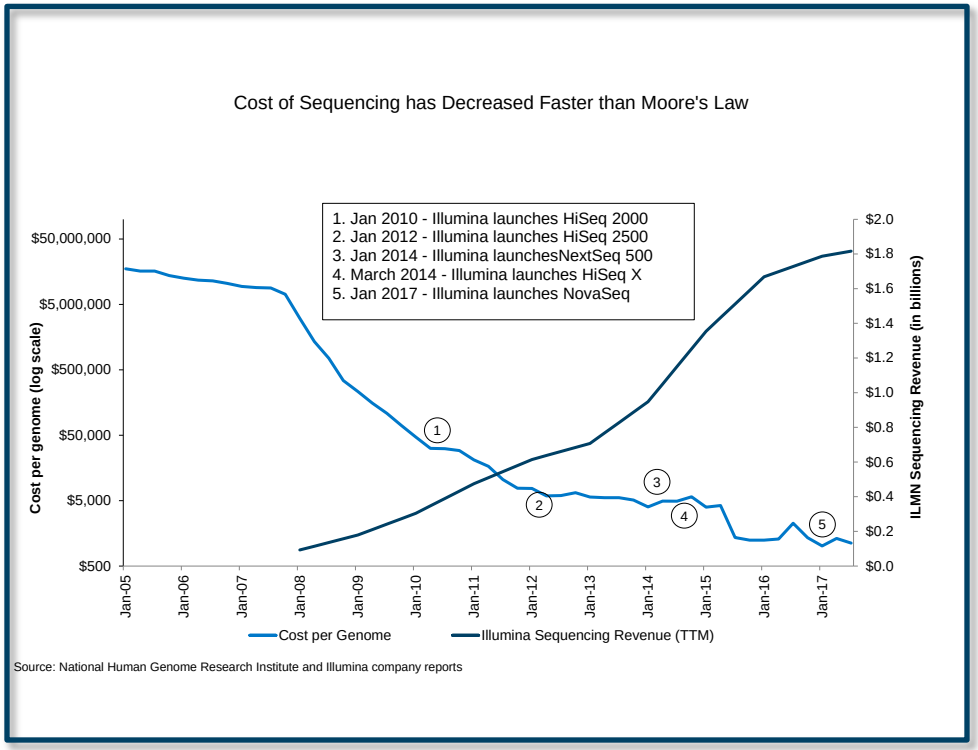


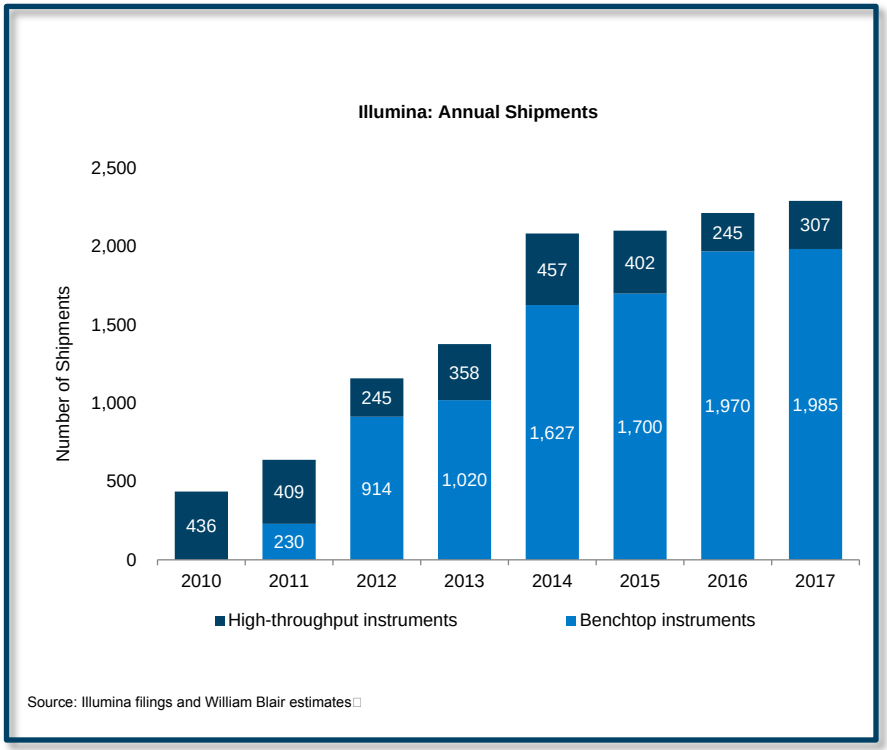


Innovation in Sequencing Has Been Astounding

Cost per Base Has Declined Faster Than Moore's Law

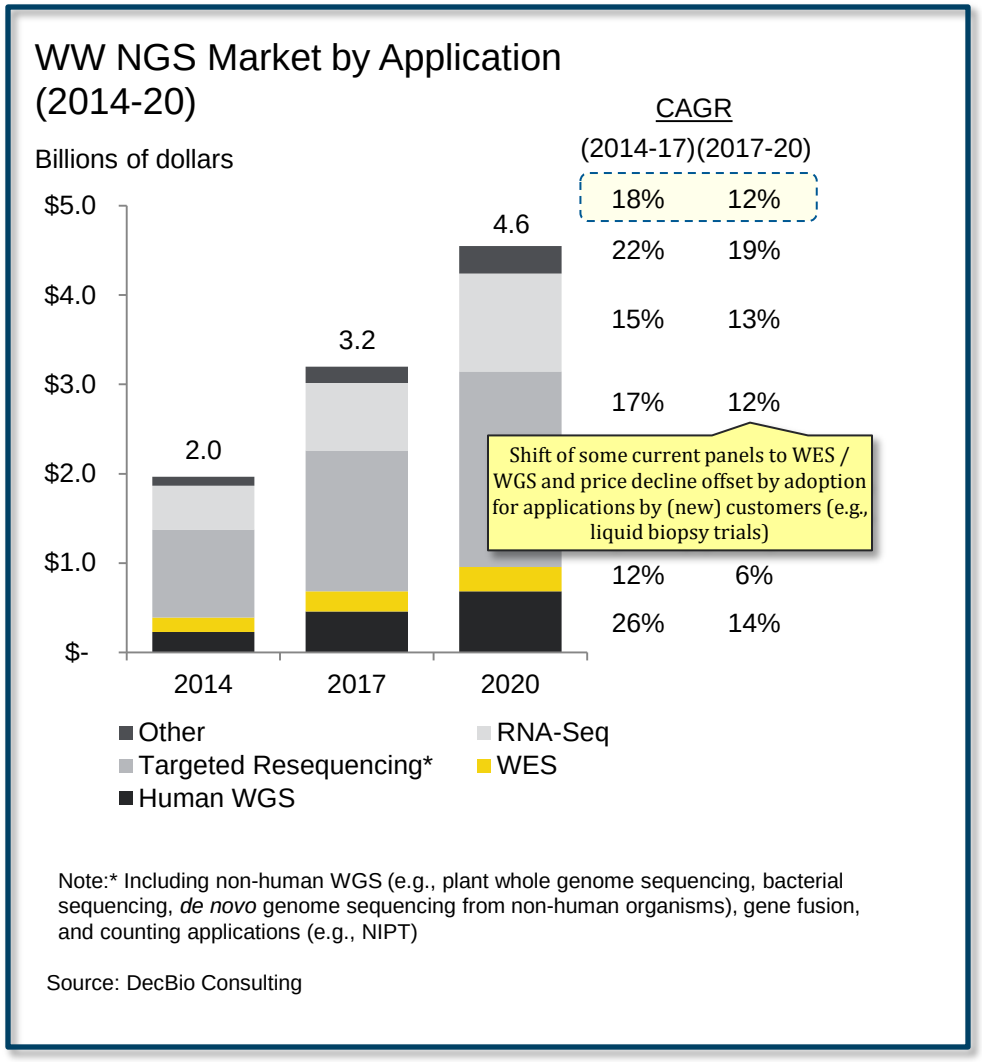
- Illumina has driven major reductions in cost per base since the HiSeq was first launched in 2010; the HiSeq X was a game changer lowering whole genome sequencing to $1,000 a genome
- At the same time, the company has focused on "democratizing" sequencing; the vast majority of the installed base is "benchtop platforms"





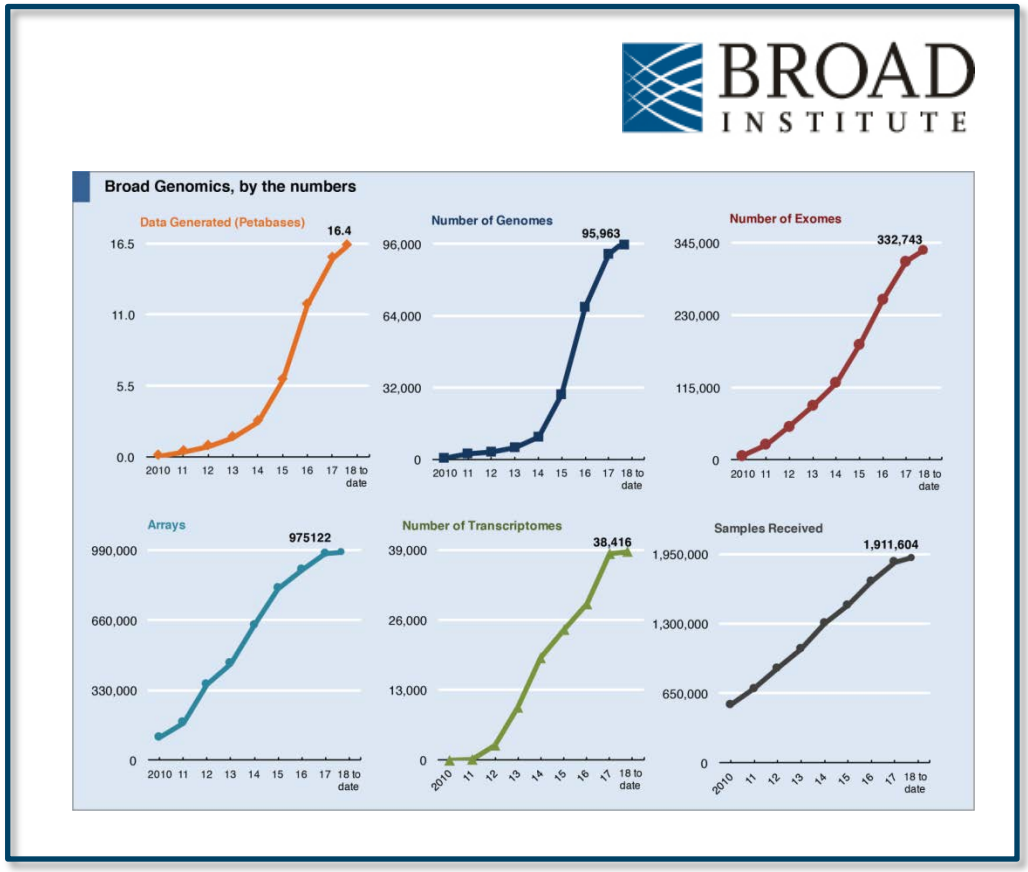
Growth in Sequencing Expected to Be Driven by Targeted Panels

- While WGS is now accessible at a cost of less than $1,000 per genome and declining, targeted sequencing is expected to drive the majority of market growth

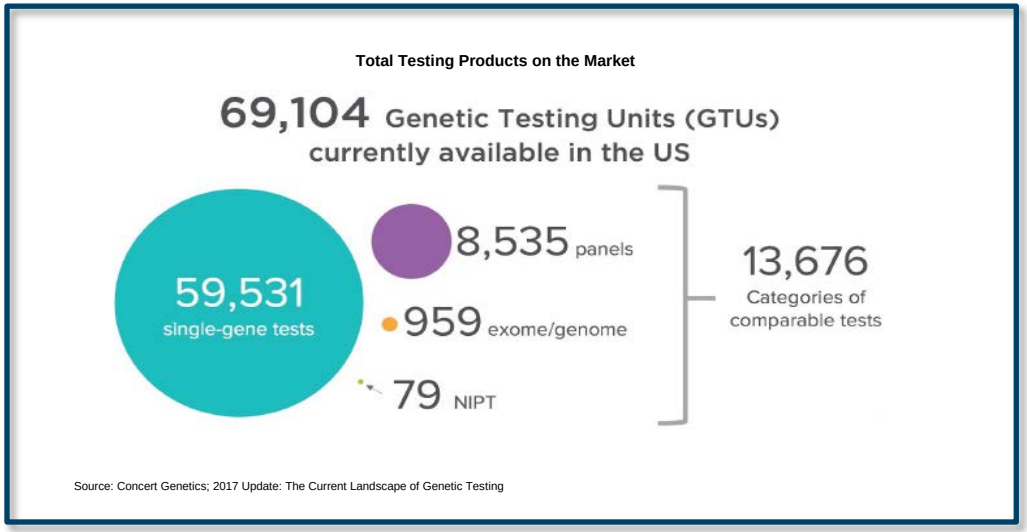


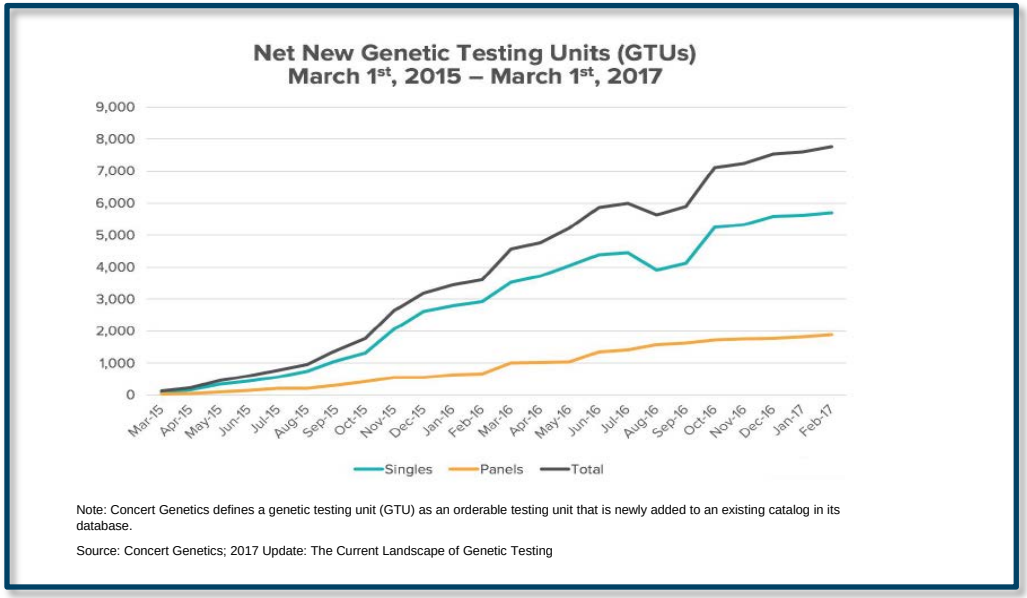
Innovation in Sequencing

- As an example, the Broad has generated over 16 petabases of sequencing data since the HiSeq was first launched in 2010
- A petabase is one thousand trillion base pairs, which is over 33,000 times as much sequence as was completed in the human genome project.



Proliferation of Genetic Testing





- Roche invests $1.2 billion in Foundation Medicine
- Tempus raised > $200 million
- Grail raised over $1 billion to bring a pre-screening liquid biopsy assay to market
- Genetic information company Invitae raised >$400 million
- Liquid-biopsy company Guardant raised >$550 million

FOUNDATION MEDICINE

INVITAE

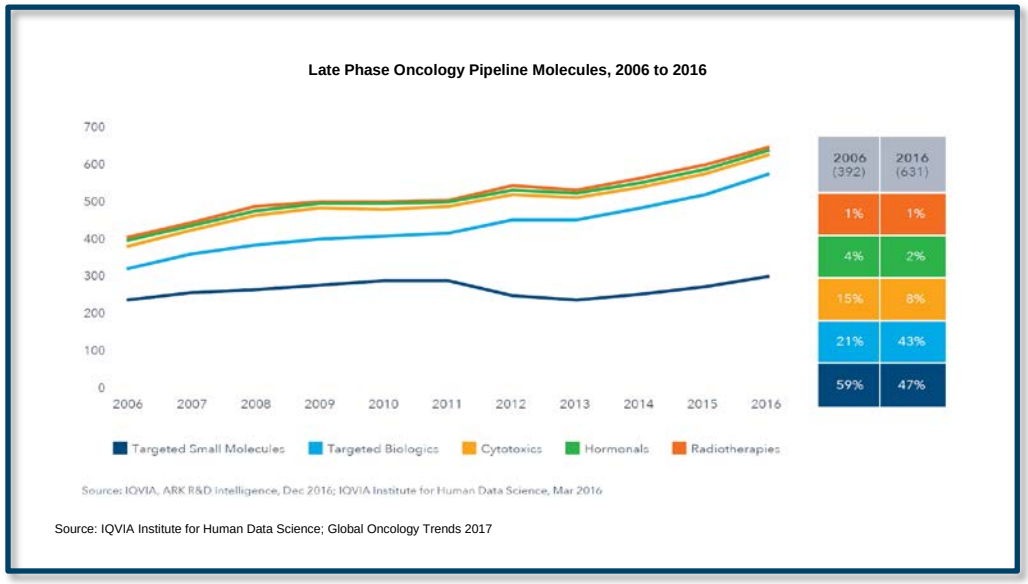
GRAIL

TEMPUS

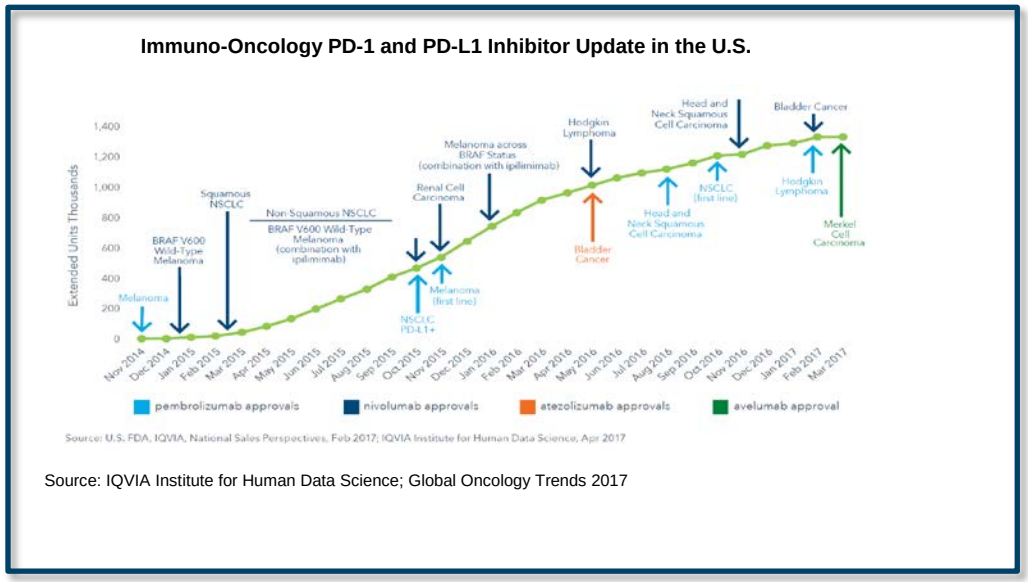
Guardant Health

Treatment Paradigms Becoming Only More Complex

Targeted Therapeutic Pipeline



Source: IQVIA Institute for Human Data Science; Global Oncology Trends 2017

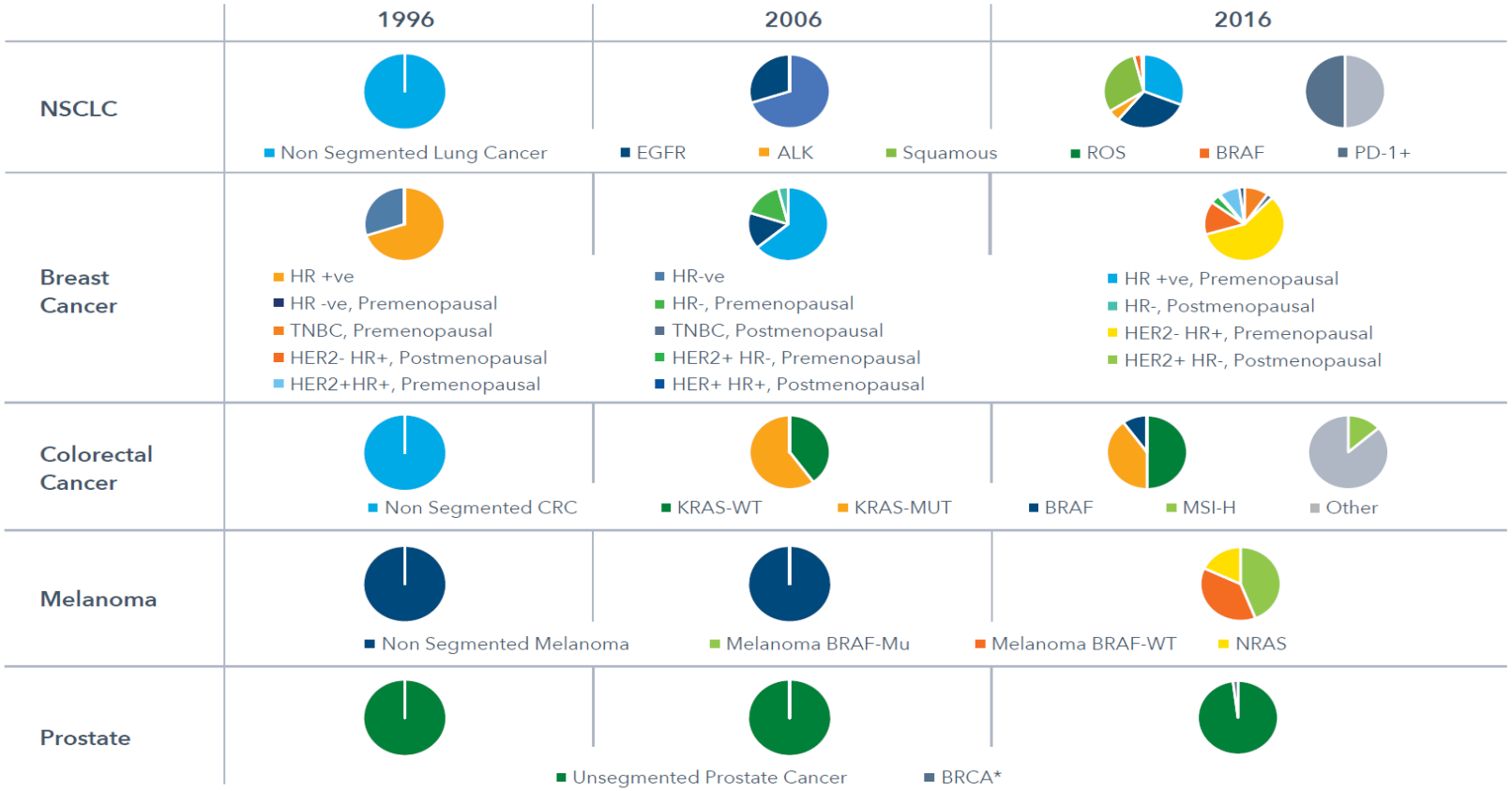


Source: IQVIA Institute for Human Data Science; Global Oncology Trends 2017

- Eighty-seven percent of the overall late stage pipeline are targeted therapeutics
- Almost all tumor types have seen increased segmentation based on biomarkers, age, and/or histology
- Biopharma pipeline is robust with over 1,100 number of therapies in phase III
- Ten percent of trials are currently using biomarker-based segmentation
- As an example, PD-1 and PD-L1 inhibitors have seen rapid uptake across cancers
- 728 trials using a PD-(L)1 inhibitor were posted to clinicaltrials.gov in 2017 with an additional 138 in 2018 to date; 140 of these are Phase III

Increased Complexity of Care

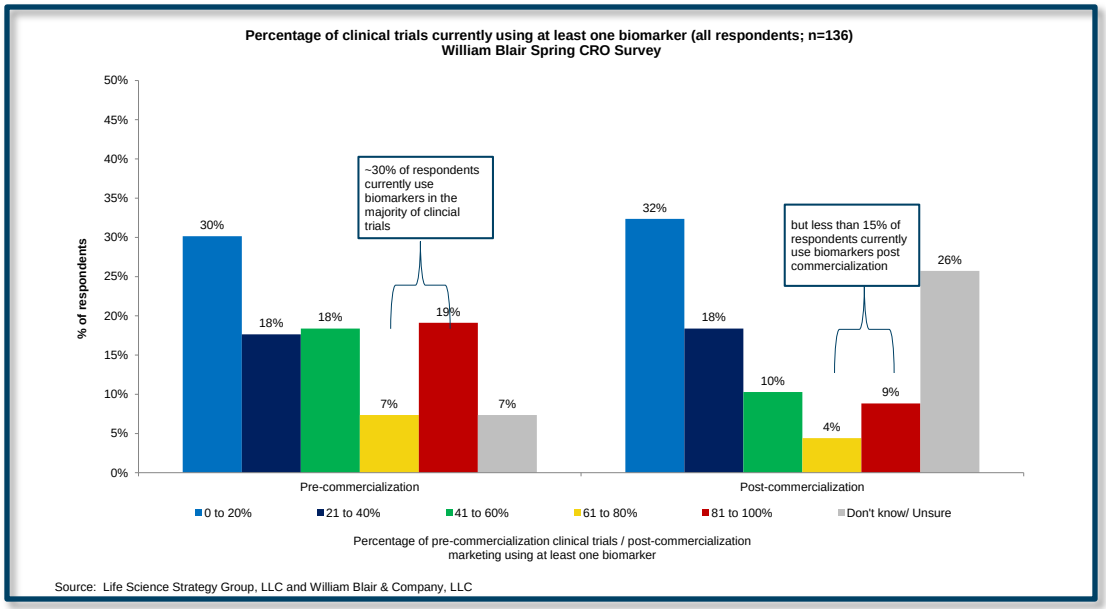
Percent of Biomarker-Based Segmentation in Selected Tumors



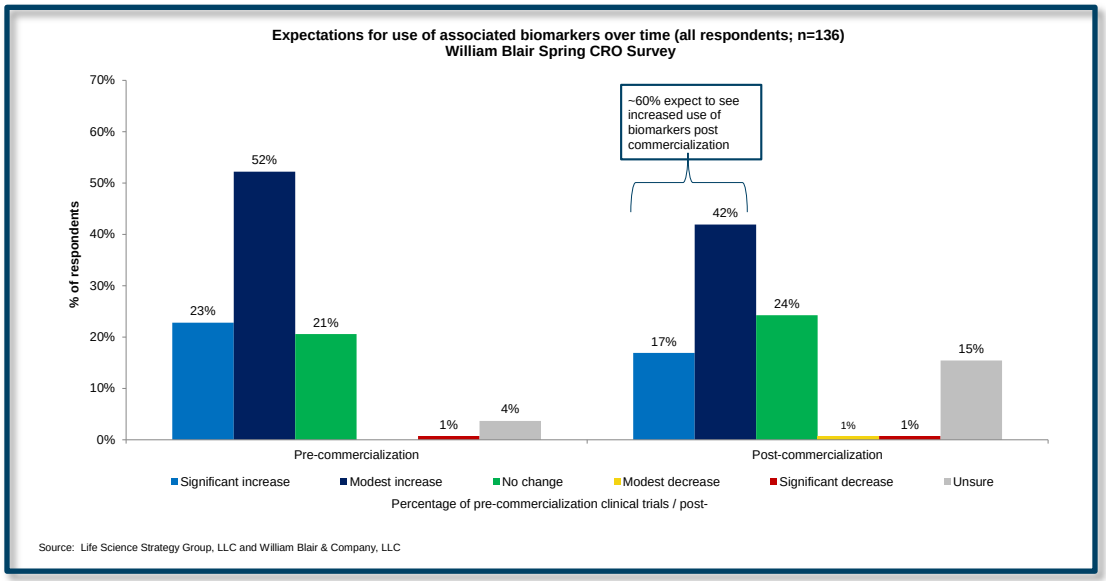
Source: FDA.gov and Drugs@FDA, Mar 2017; IQVIA, ARK R&D Intelligence, Feb 2017; IQVIA Institute for Human Data Science, Mar 2017

Source: IQVIA Institute for Human Data Science; Global Oncology Trends 2017

Increased Use of Biomarkers by Pharma



Source: Life Science Strategy Group, LLC and William Blair & Company, LLC

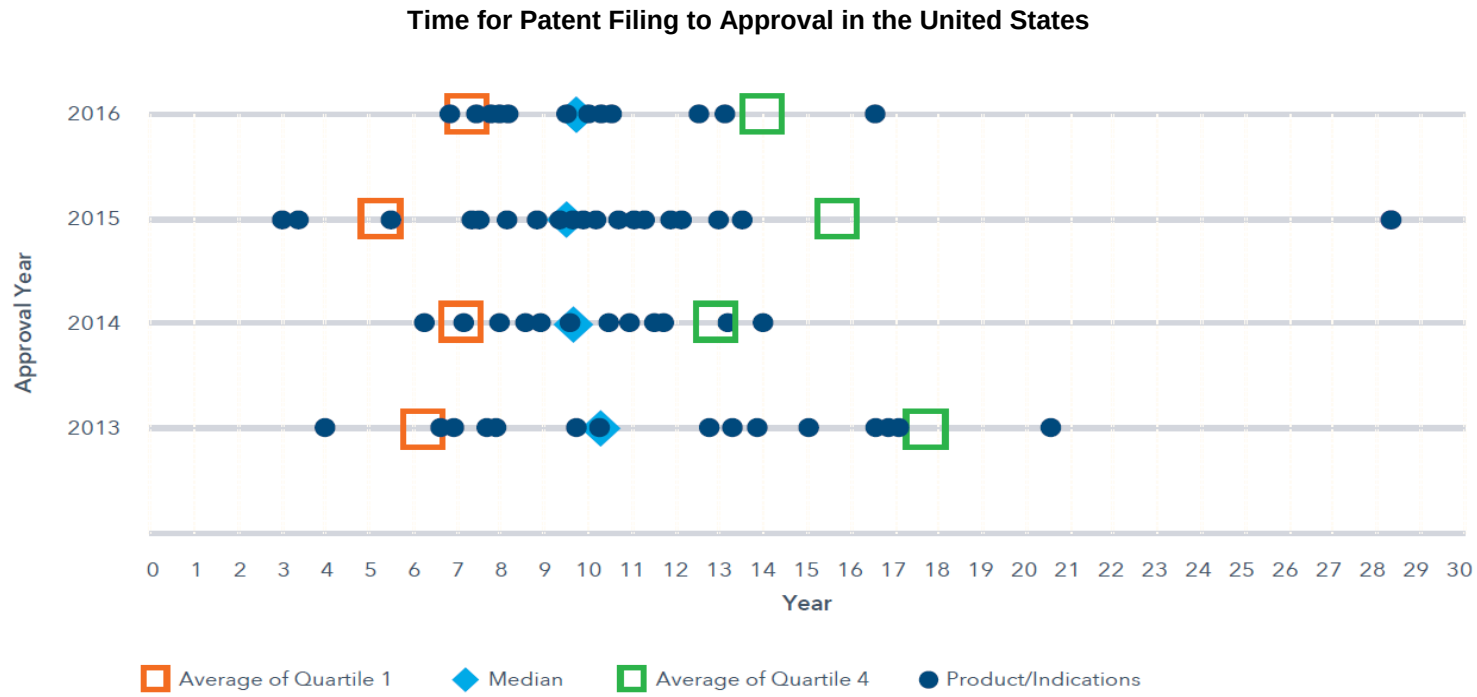


Source: Life Science Strategy Group, LLC and William Blair & Company, LLC

- William Blair's 20th bi-annual CRO survey (in collaboration with Life Science Strategy Group); n of 136 biopharma companies
- General responses indicate a healthy fundamental demand environment; most optimism since the recession
- Biopharma companies across the board expect a 1% to 2% greater percentage change in R&D in 2018 and 2019; overall expect midsingle-digit R&D budget growth, if not better, in the coming three years
- In another bullish indicator for 2018 demand, biotechnology funding in the first quarter was up 45% compared with a year ago; this comes on the heels of an increase of 37% during all of 2017
- Thirty percent use biomarkers currently in the majority of trials; over 60% expect to increase use of biomarkers post-commercialization

Favorable Regulatory Environment – Approvals

- Median time for drug approval has dropped from 10.25 years (2013) to 9.8 years in 2016 as the FDA has incorporated expedited review pathways (e.g., Breakthrough Therapy Designation)



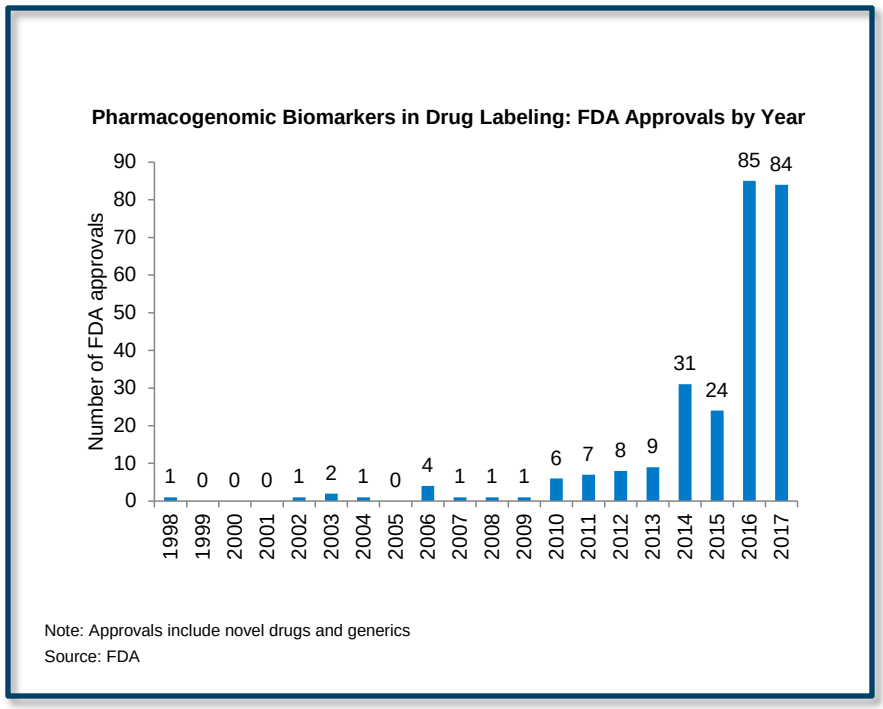
Source: IQVIA, ARK R&D Intelligence, Feb 2017, ARK Patent Intelligence, Mar 2017; Drugs@FDA, Feb 2017; IQVIA Institute for Human Data Science, Mar 2017

Source: Global Oncology Trends 2017; IQVIA Institute for Human Data Science

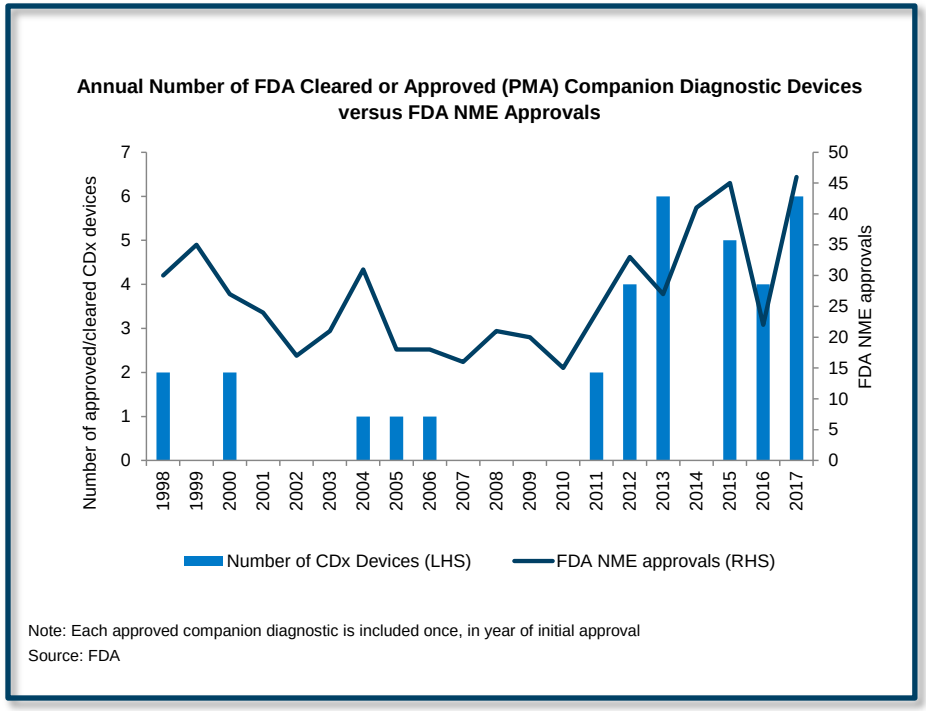
Favorable Regulatory Environment – Biomarkers

"By proposing streamlined approaches for our colleagues in the research and development communities, the FDA hopes to enable more efficient access to safe and effective, novel targeted therapies for the patients who need them."

– Scott Gottlieb, M.D., Commissioner of the FDA



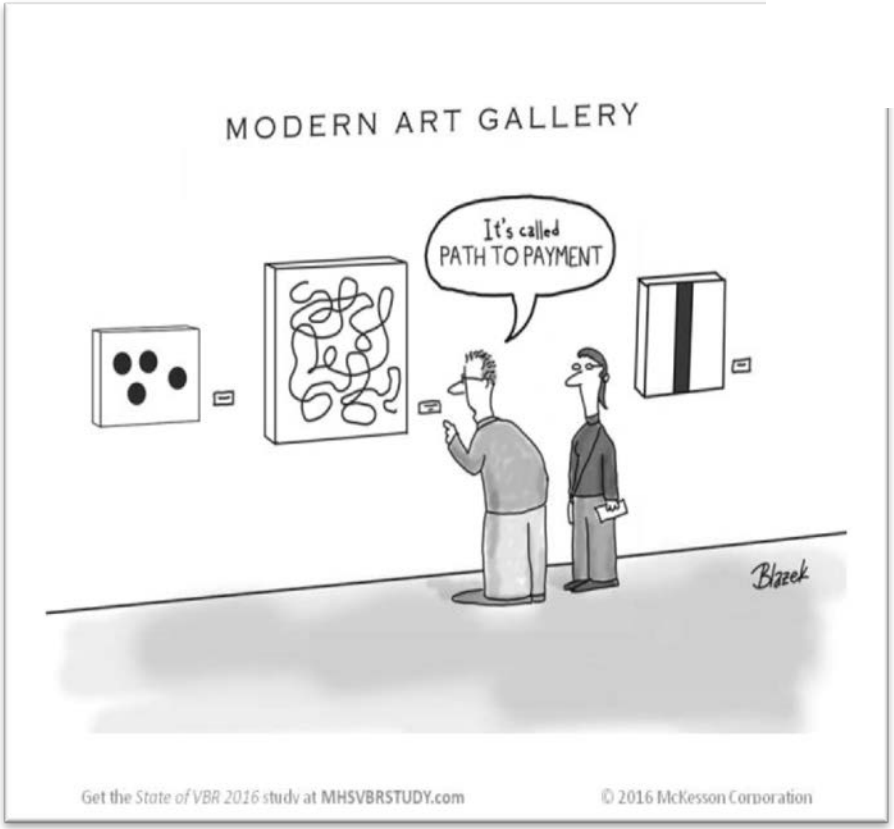
Note: Approvals include novel drugs and generics
Source: FDA



Note: Each approved companion diagnostic is included once, in year of initial approval
Source: FDA

What Are Investors Concerned About?

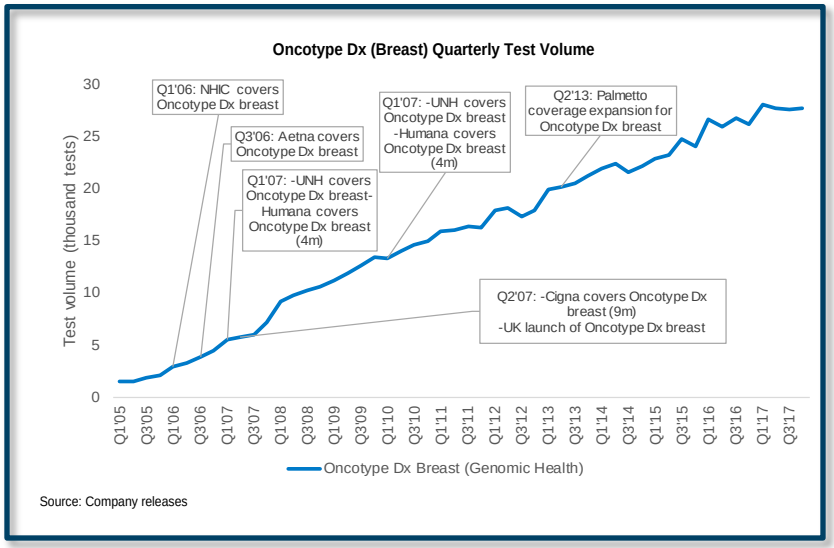
Reimbursement!



$$\text{Equity value} = \sum_{t=1}^{\infty} \frac{\text{FCFE}_t}{(1+r)^t}$$

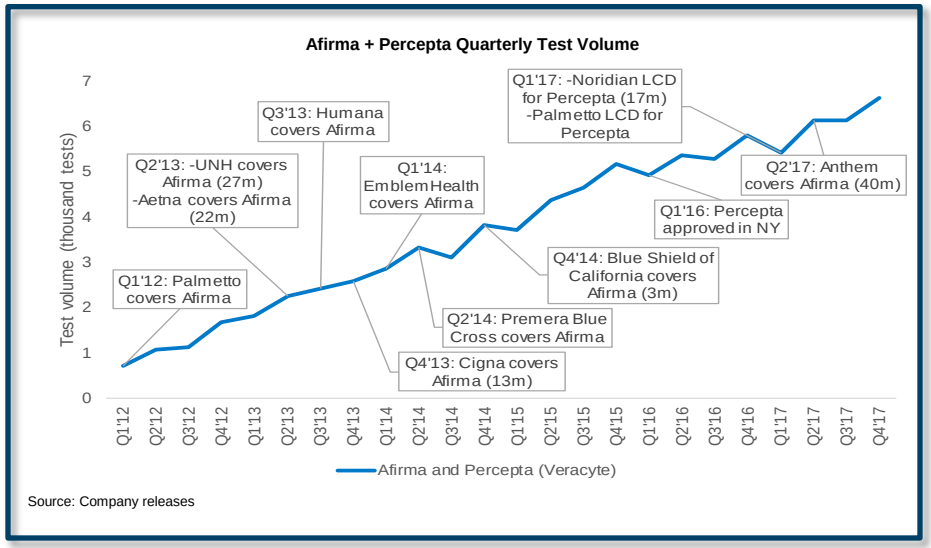
Reimbursement Success Stories

Genomic Health
LIFE, CHANGING.



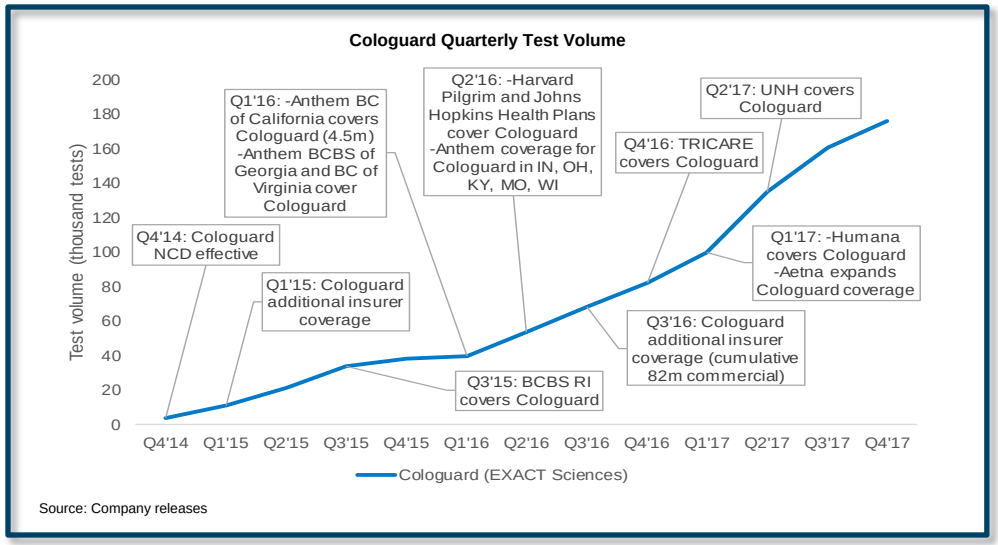
Source: Company releases

veracyte™



Source: Company releases

exact sciences



Source: Company releases

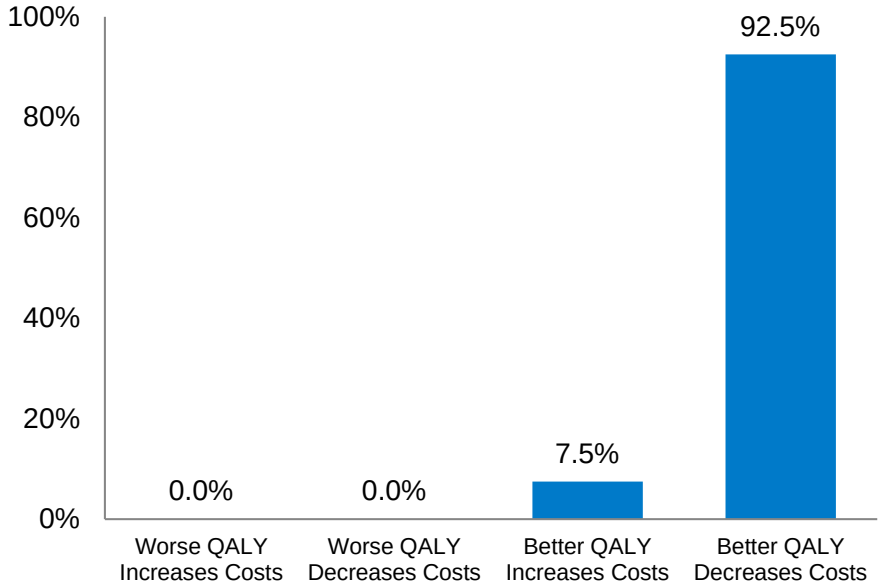
Reimbursement Success Stories – Case Study Afirma

Cost Savings and Quality of Life

Annual Cost Savings

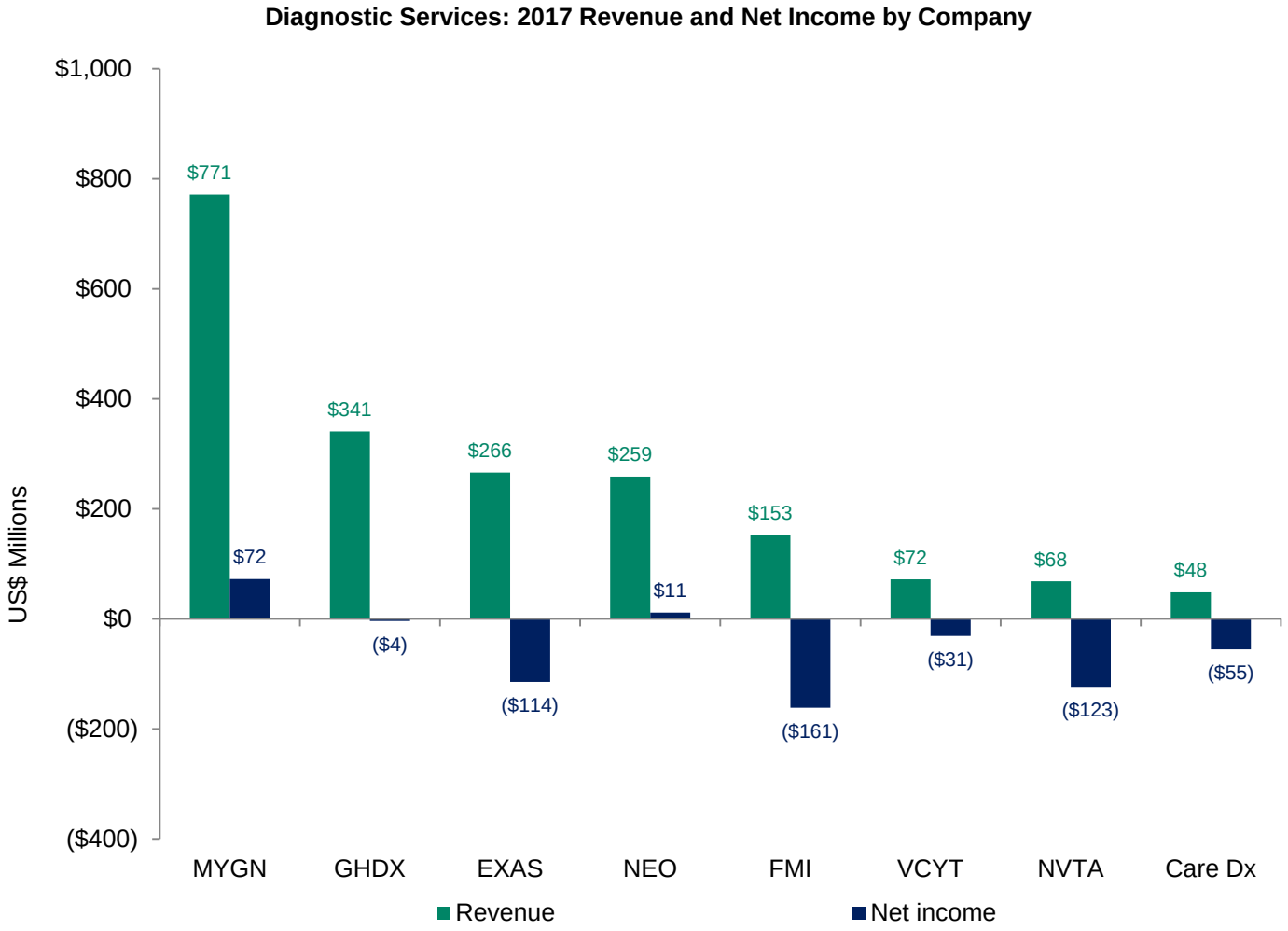
Without Afirma GEC	
Indeterminate Patients	94,000
Thyroid Surgery	$10,000
Total Cost	**$940,000,000**
With Afirma GEC	
Indeterminate Patients	94,000
Afirma GEC	$3,500
Cost	$329,000,000
Indeterminate Benign	47,000
Ultrasound (3 per year)	$900
Cost	$42,300,000
Indeterminate Suspicious	47,000
Thyroid Surgery	$10,000
Cost	$470,000,000
Total Cost	**$841,300,000**
Direct Annual Savings	**$98,700,000**

Lower Cost and Improved Quality-Adjusted Life



Sources: Company reports and William Blair & Company, L.L.C. estimates

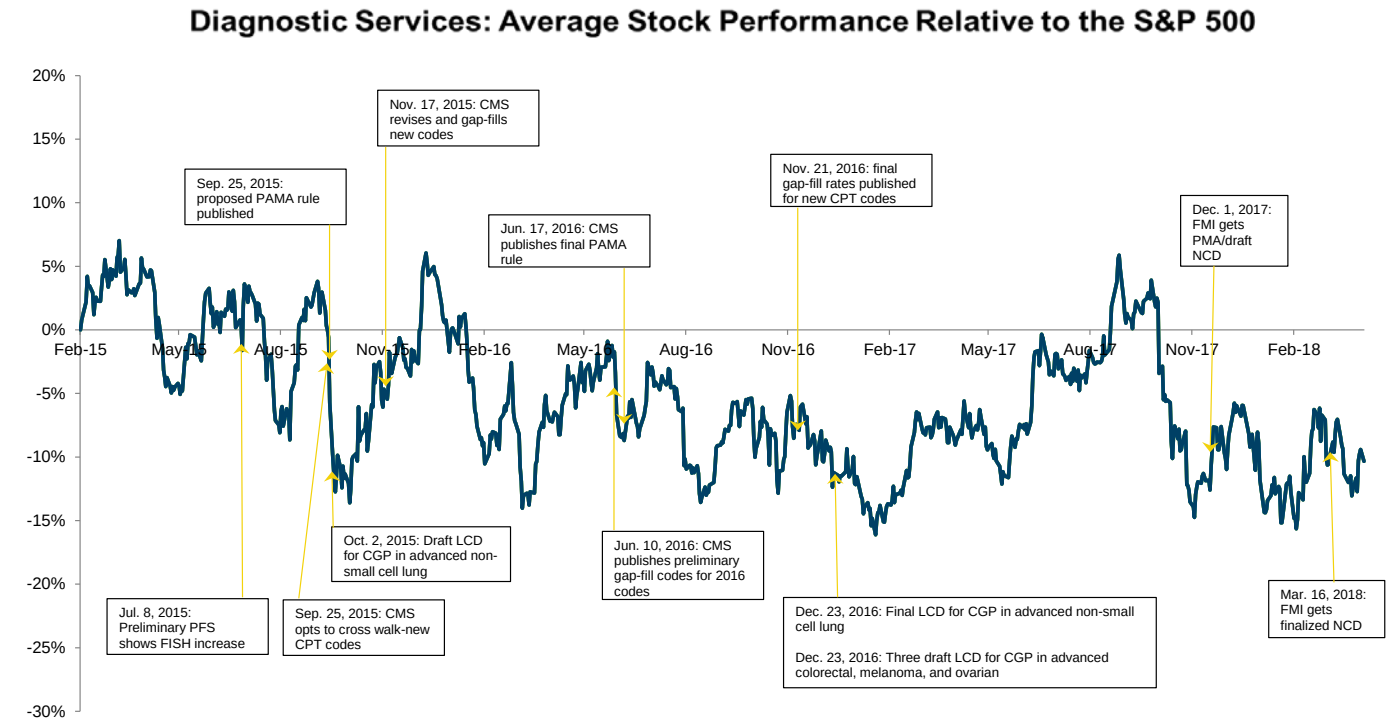
Companies/Investors Have Invested a Lot in Bringing Value-Added Tests to Market



Source: Company reports, William Blair estimates

Reimbursement – 2016/2017 Was "Depths of Despair"

- In late 2015, CMS opted to use the code-stack methodology for new 2016 CPT codes, which drove a market cap loss of $1.5 billion (almost 10%) for the space
- CMS reversed this decision two months later (opting to gapfill)
- Genomic Sequencing Procedure (GSP) codes priced below expectations (most at ~$600)
- PAMA pricing was published (worse than expected)



Note: Diagnostic Services average includes FMI, DGX, NEO, LH, GHDX, MYGN, NVTA, and VCYT

NGS Reimbursement Has Progressed Slowly

- Medicare via Palmetto and the CMS via most recent NCD has been "a more willing payer"
- Coverage polices for sequence-based tests/panels across private payers varies meaningfully, although we are seeing some progress
  - Cigna began covering whole exome sequencing in 2015 for certain indications
  - UNH began covering whole exome sequencing in 2017

Multigene test policy coverage by payer

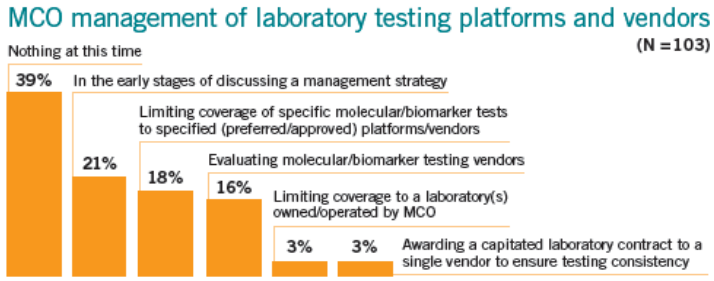
Payer[a]	Number of policies	Number of tests within policies	Percentage of policies covering all included tests	Percentage of policies covering none of included tests	Percentage of policies covering some but not all included tests
Payer no.1	7	48	43	29	29
Payer no. 2	15	116	13	60	27
Payer no. 3	4	40	25	25	50
Payer no. 4	15	54	13	73	13
Payer no. 5	14	55	29	36	36
Total	55	313	22	51	27

Source: Phillips, Kathryn A et al. "Payer Coverage Policies for Multigene Tests." Nature biotechnology 35.7 (2017): 614–617. PMC. Web. 13 Apr. 2018.

Increased Focus on "Lab Test Management"

- Increased payer focus on lab management programs
  - July 2017 - Anthem launched its "Genetic Testing Solution" via AIM Specialty Health for fully and self-insured members; required medical necessity review for all genetic tests
  - October 2017 – UnitedHealthcare targets national implementation of its prior authorization program for genetic tests

Most payers do not actively manage lab testing vendors/platforms



Source: 2017 Genentech Oncology Trend Report

Molecular/biomarker testing coverage policy

(N=103)

Requires companion diagnostic testing for approval of the associated drug therapy

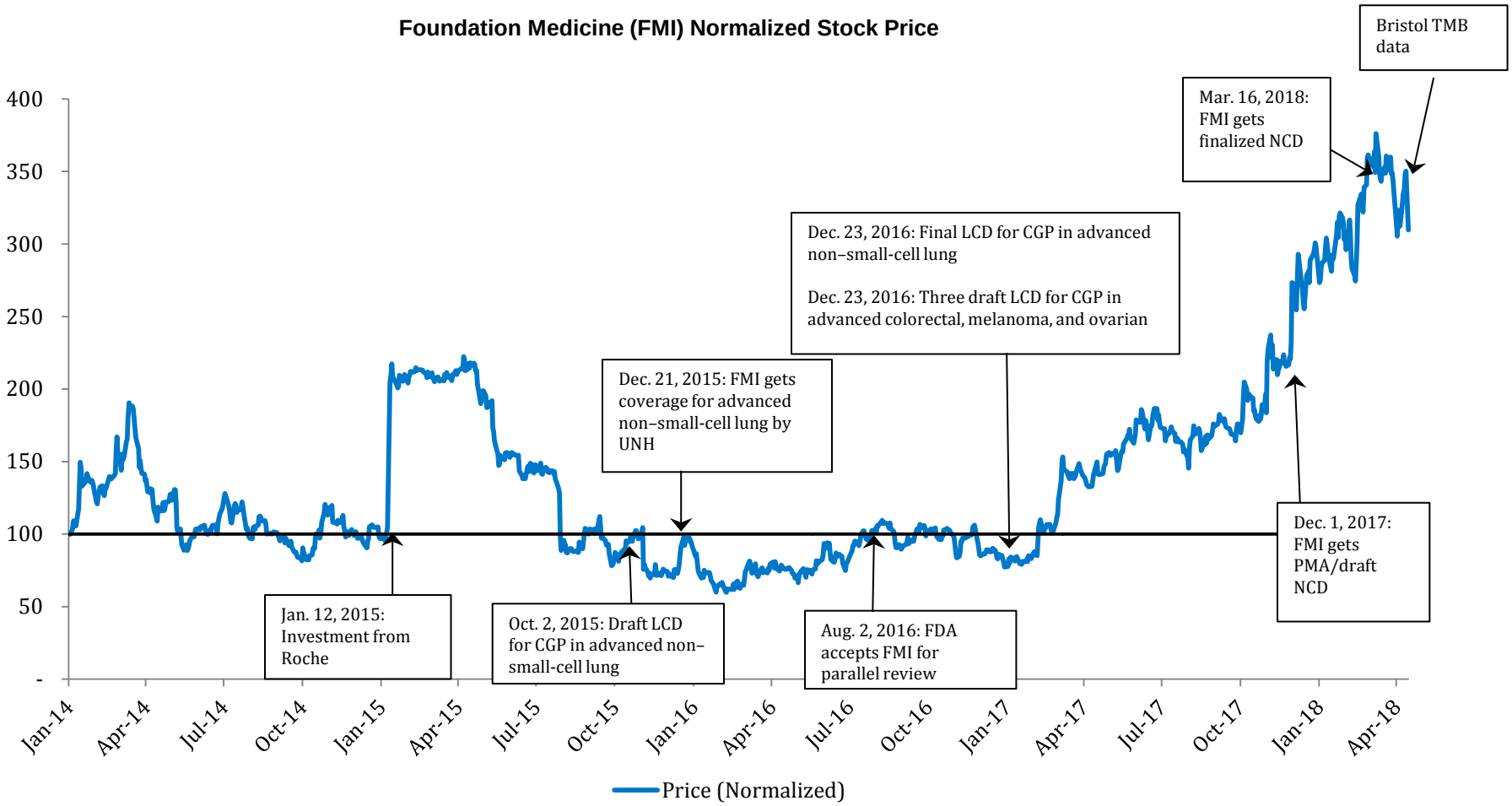
Only for FDA-approved tests	33%
With either FDA-approved tests or laboratory-developed tests	25%
Determined on a case-by-case basis	21%
No policy currently, but under review	13%
Unsure/do not know	8%

Includes coverage for complementary diagnostic testing

Yes	27%
Determined on a case-by-case basis	29%
No policy currently, but under review	21%
Unsure/do not know	23%

What Are Investor Hot Buttons?

New Medicare NGS National Coverage Determination



Sources: Company reports and FactSet

New Medicare NGS National Coverage Determination

Still a number of outstanding questions:

- Will there be a pathway for clearance for NGS-based assays for CDX indication?
- Does one, pan-cancer CDx indication imply coverage under the NCD?
- Will private payers follow suit?
- Do we even need biomarkers if pharma is successful with all-comers strategy?

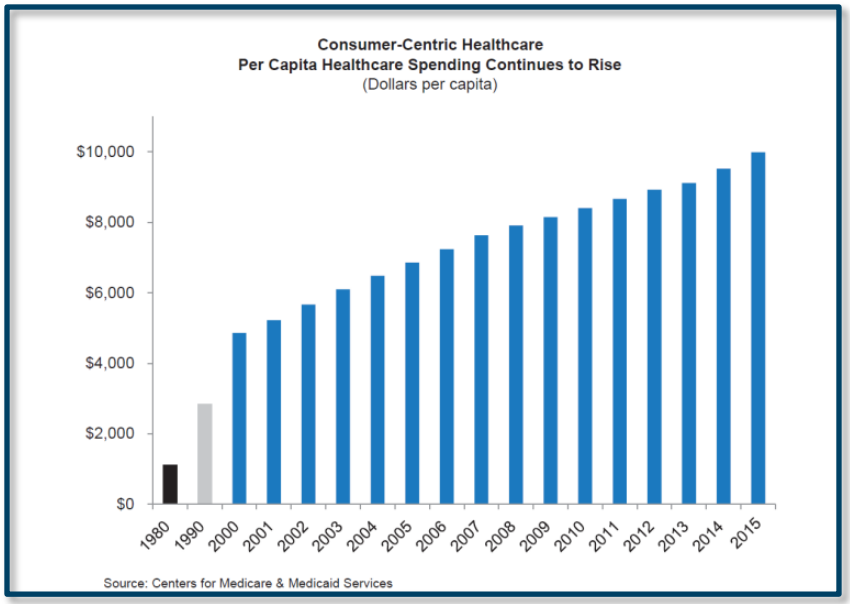
A number of companies have pointed to plans to pursue FDA approval/clearance:

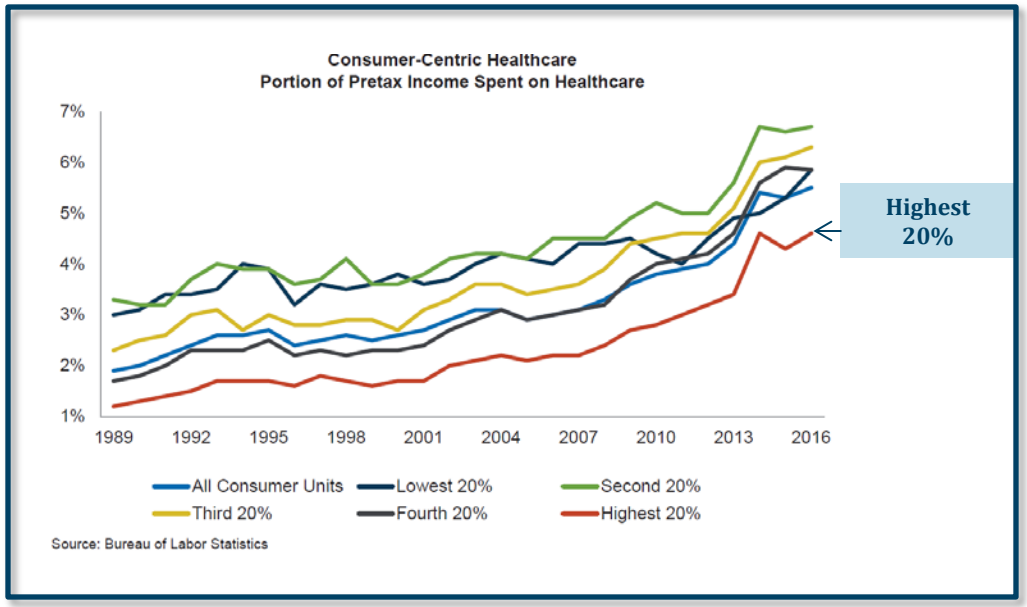
NEO

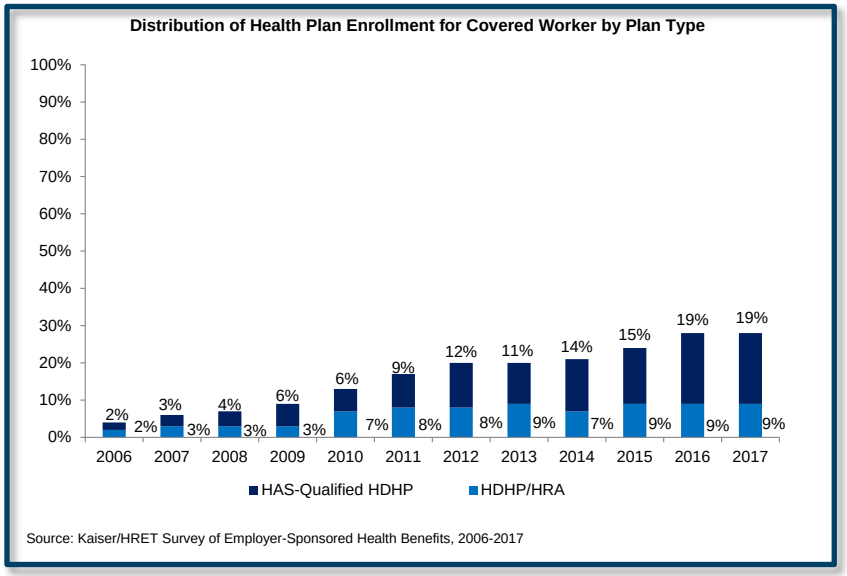
CARIS Dx

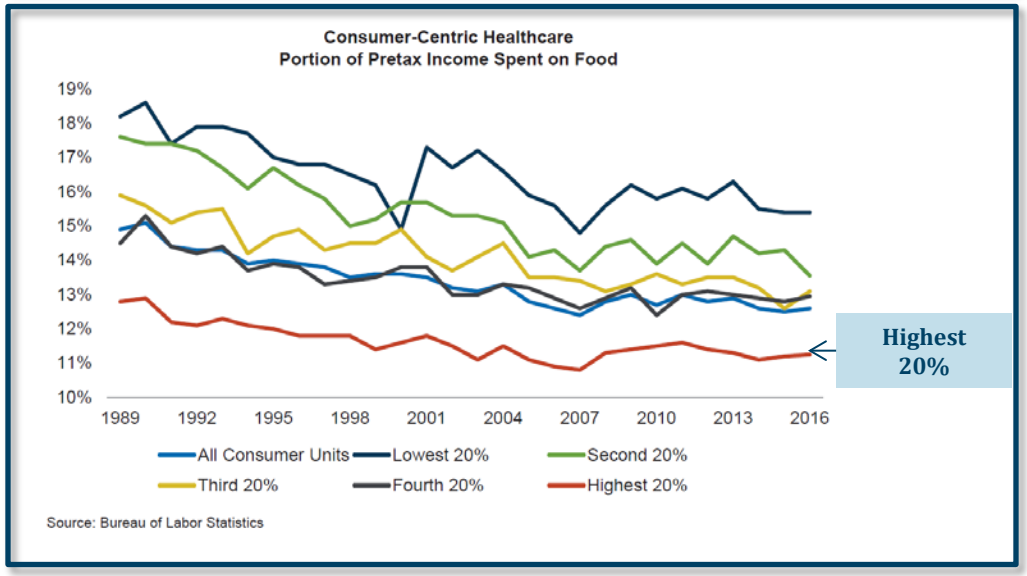
ONCOMINE power tools

Consumer Now a Key Buyer of Healthcare









Focus on Garnering Consumer "Mindshare"

Retail Clinics Expected to Grow

Clinics Drive Utilization, but Minimally Offset ED Utilization

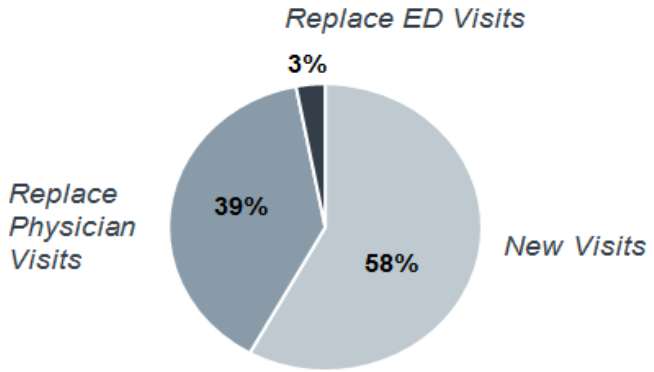
2800

Estimated total number of retail clinics[1] in the US.

2X

There are approximately double the number of retail clinics as there were in 2012.

Increased Utilization in Health Care Clinics Offsets Savings



Retailer	minute clinic	Walgreens healthcare clinic	The Little Clinic	RediClinic	Walmart Save money. Live better.
Operational Retail Clinics	1,105	400+	213	91	75[3]

1) Forecasted number of retail clinics in 2017, as of 2015.
2) Includes partner clinics operated in Walgreens' stores.
3) Includes 18 Walmart Care Clinics and 57 independently owned and operated Clinic at Walmart locations.

Source: Accenture, "Number of US Retail Clinics Will Surpass 2800 by 2017," 2015; Drug Channels Institute, "The 2017 Economic Report on U.S. Pharmacies and Pharmacy Benefit Managers," 2017; RAND Corporation, "The Evolving Role of Retail Clinics," 2016; Scott Ashwood et al., "Retail Clinic Visits for Low-Acuity Conditions Increase Utilization and Spending," 2016, Health Affairs; Walgreens, "Clinic Locations," 2017; Market Innovation Center interviews and analysis.

Source: The Advisory Board Company

Big Data – Use of AI and Machine Learning

THE 10 MOST ACTIVE APPLICATIONS* OF 2018 (YTD)

The **applications** (the use cases for the Company's technology) genomics, diagnostic/screening, and clinical decision support each raised in excess of $500M this quarter. Most notable is the disparity between the average and median deal size, with medians demonstrating 50% of the deal size. Entrepreneurs should take note of these new trends when structuring their capital campaigns and positioning.

	Application	Total Raised	Deal Count	Avg. Deal Size	Median Deal Size
1	Genomics	$565M	11	$51.4M	$40.0M
2	Diagnostic/Screening	$539M	25	$21.5M	$13.7M
3	Clinical Decision Support	$524M	16	$32.7M	$12.0M
4	Care Coordination	$340M	20	$17.0M	$7.8M
5	Employer Insurance	$228M	4	$57.2M	$31.4M
6	Operational Management	$206M	24	$8.6M	$3.5M
7	Personal Insurance	$168M	4	$42.0M	$1.5M
8	Remote/Continuous Monitoring	$166M	15	$11.1M	$7.3M
9	Care Pathway	$146M	7	$20.9M	$20.0M
10	Digital Treatment	$143M	8	$17.9M	$20.0M

Source: StartUp Health; Insights Digital Health Funding Report Q1 2018

IMPORTANT DISCLOSURES

Please contact us at +1 800 621 0687 or https://williamblair.bluematrix.com/sellside/Disclosures.action?ajax&page=ajax/williamblairDisclosures.jsp&firmId=18877 for all disclosures.

Q&A

https://www.genentech-forum.com/trend-reports.html

https://www.iqvia.com/institute/reports/global-oncology-trends-2017-advances-complexity-and-cost

Pharmaceutical Outsourcing & Services: CRO Industry Update: Results From Spring 2018 Survey of Biopharmaceutical Sponsors - 04/06/18 10:00AM

Life Sciences: Conclusions From NGS Survey Conducted in Collaboration With Genome Web (n=303) - 01/04/18 11:17PM