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Silicon Valley Bank

Technology Advancements Redefine Promise of Dx/Tools

Next-Gen Sequencing and Artificial Intelligence Drive
Moonshot Investments

NOVEMBER 2017

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Key Highlights for Dx/Tools

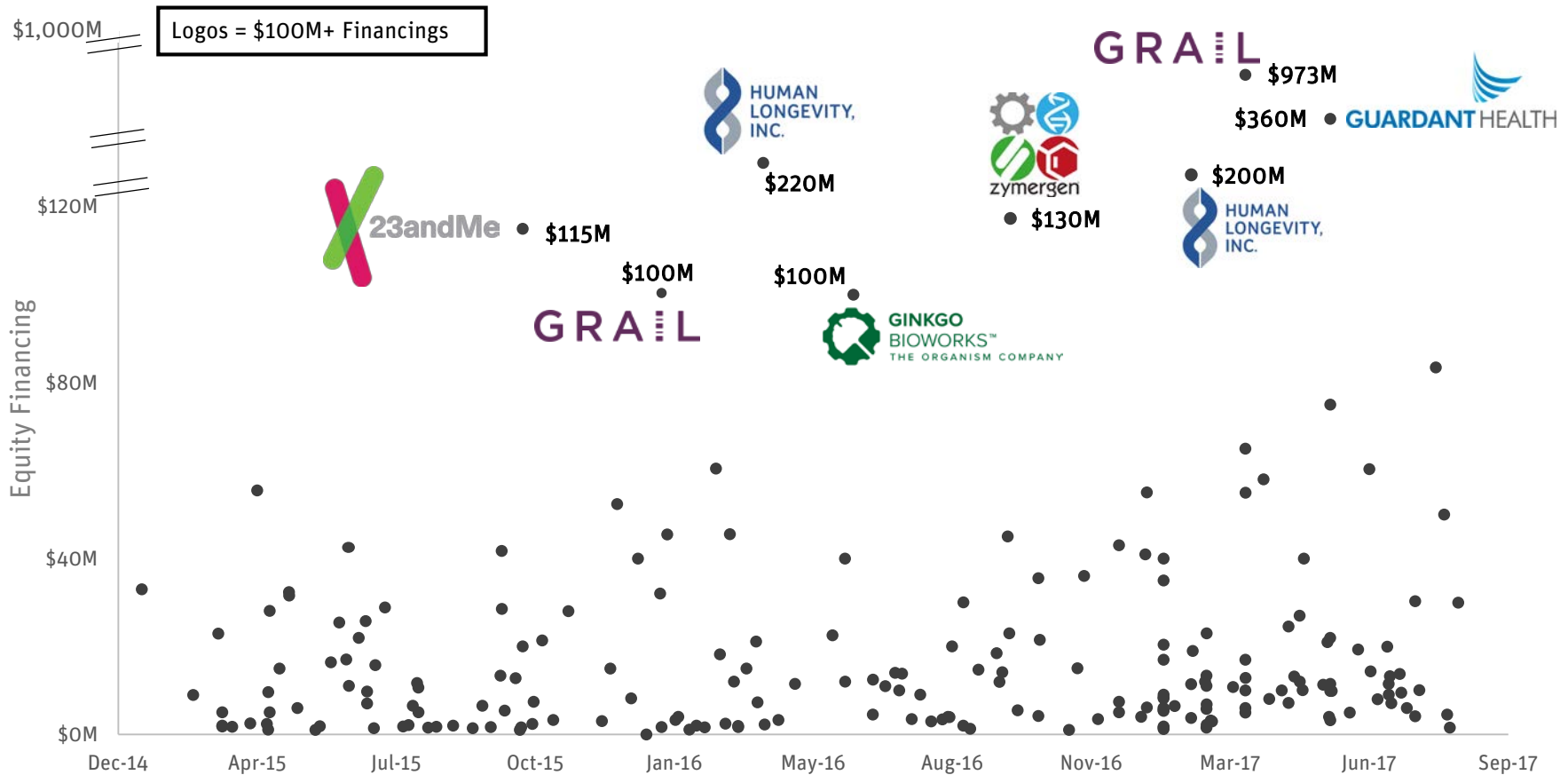
- Underscoring the intense interest in Dx/Tools innovations, investment in these companies in 1H 2017 reached \$2.6B – more than double the amount raised in any previous six-month period.
- Generalist investors, in contrast to healthcare-focused investors, have quickly become the most active players. They see the promise of an emerging ecosystem of companies that are focused on leveraging artificial intelligence (AI) with genomic data to drive new diagnostic and treatment options.
- This exuberant investment activity has led to record valuation levels. The subsector includes three unicorns (post-money valuations of at least \$1B) and 10 additional companies with post-money valuations exceeding \$250M.
- At the same time, these lofty valuations are making it difficult for traditional Dx/Tools investors to generate high-multiple returns. As of mid November, there has not been a single venture-backed Dx/Tools big exit* in 2017.
- Additionally, Dx/Tools investors now include the largest tech companies like Amazon and Google. They are increasing their investments as they learn how to integrate and leverage technological advancements in the enormous healthcare industry. We think this investment activity may be a precursor to acquisitions and lead to a land grab that could provide significant exit upsides and end the current Dx/Tools exit drought.
- The Dx/Tools sector includes several different technologies that are seeing unprecedented investment. Among areas gaining the most investor attention:
 - **Next-Generation Sequencing (NGS) companies** have significantly improved the speed, accuracy and cost of gene sequencing, leading to advancements in diagnostics and treatments. As a result, NGS companies are reaching unprecedented valuations.
 - **Liquid biopsy companies** enable clinicians to detect diseases with a blood test instead of surgical biopsy or other invasive methods. Three oncology-focused companies - GRAIL, Guardant Health and Human Longevity - have each raised more than \$400M since 2015.
 - **Software-based analytics companies** are building tools to interpret genomic and imaging data. The tools from these digital health companies advance clinical discovery and decision-making. Therefore, we include them in our Dx/Tools analysis.



Dx/Tools Investment Trends

Dx/Tools Companies See a Flood of New Investments

Dx/Tools Investments 2015 – 1H 2017



- Since 2015, investors have been stepping up their Dx/Tools activity, leveraging a spectrum of new technologies emerging in this sector. Each dot represents a single financing. Eight financings exceeding \$100M have occurred since 2015.
- In a nutshell, the true driver of value lies in drawing actionable results to either guide clinical development or help determine/direct treatment. Gene sequencing companies are drawing the most investor attention by providing tools to clinicians and researchers. These tools help develop new methods to prevent, diagnose and treat some of the most devastating diseases.

SVB Creates Proprietary System for Categorizing Dx/Tools Technologies

Subsectors

Dx Tests: Proprietary Yes/No Tests

Dx Analytics: Actionable Data Analytics to Help Determine/Direct Treatment

R&D Tools: Research Equipment/Services for Biopharma and Academia

Clinical Indication Tags

Cardiovascular

Gastrointestinal

Hepatic/Biliary

Immunologic

Infectious Disease

Metabolic/Endocrine

Neurology/Psychiatry

Oncology

Ophthalmic

Other

Renal/Urinary

Respiratory

Reproductive Health

Technology Tags

Liquid Biopsy

Artificial Intelligence

Imaging/Monitoring

Connected Health

Next-Gen Sequencing (NGS)

Gene Editing

Detection Analyte Tags

Protein

Metabolite/Small Molecule

Nucleic Acids

Detection Method Tags

Imaging/Optics

Electrochemical

The Dx/Tools investment landscape is rapidly evolving as new technologies redefine innovation in the sector. As a result, new investors have emerged. To help companies and investors clearly identify trends and opportunities in Dx/Tools, SVB has created a proprietary classification system that tracks innovation and investor activity.

Historically, the Dx/Tools sector included companies developing technologies that did not fit in biopharma or medical devices. The category's identity is now focused around technologies like NGS and AI. With this new categorization system, we can separately analyze technological innovations and underlying clinical indications.

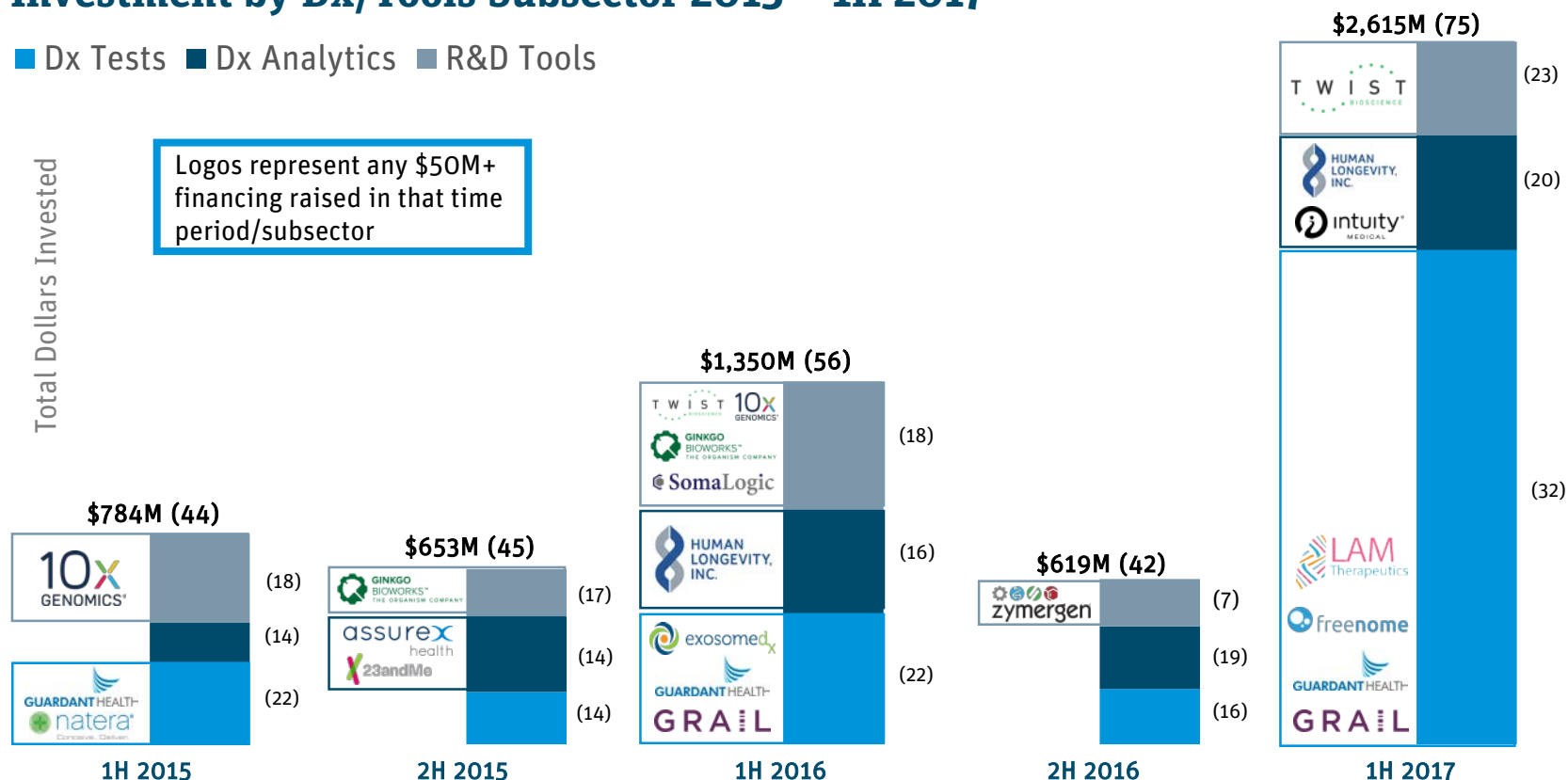
In this report, we are breaking Dx/Tools into three major subsectors:

- **Dx Tests:** proprietary yes/no tests
- **Dx Analytics:** AI-based analytics that help clinicians evaluate and direct treatment
- **R&D Tools:** tools and services for biopharma and academic researchers

New Technologies Fuel Investment Explosion

Investment by Dx/Tools Subsector 2015 – 1H 2017

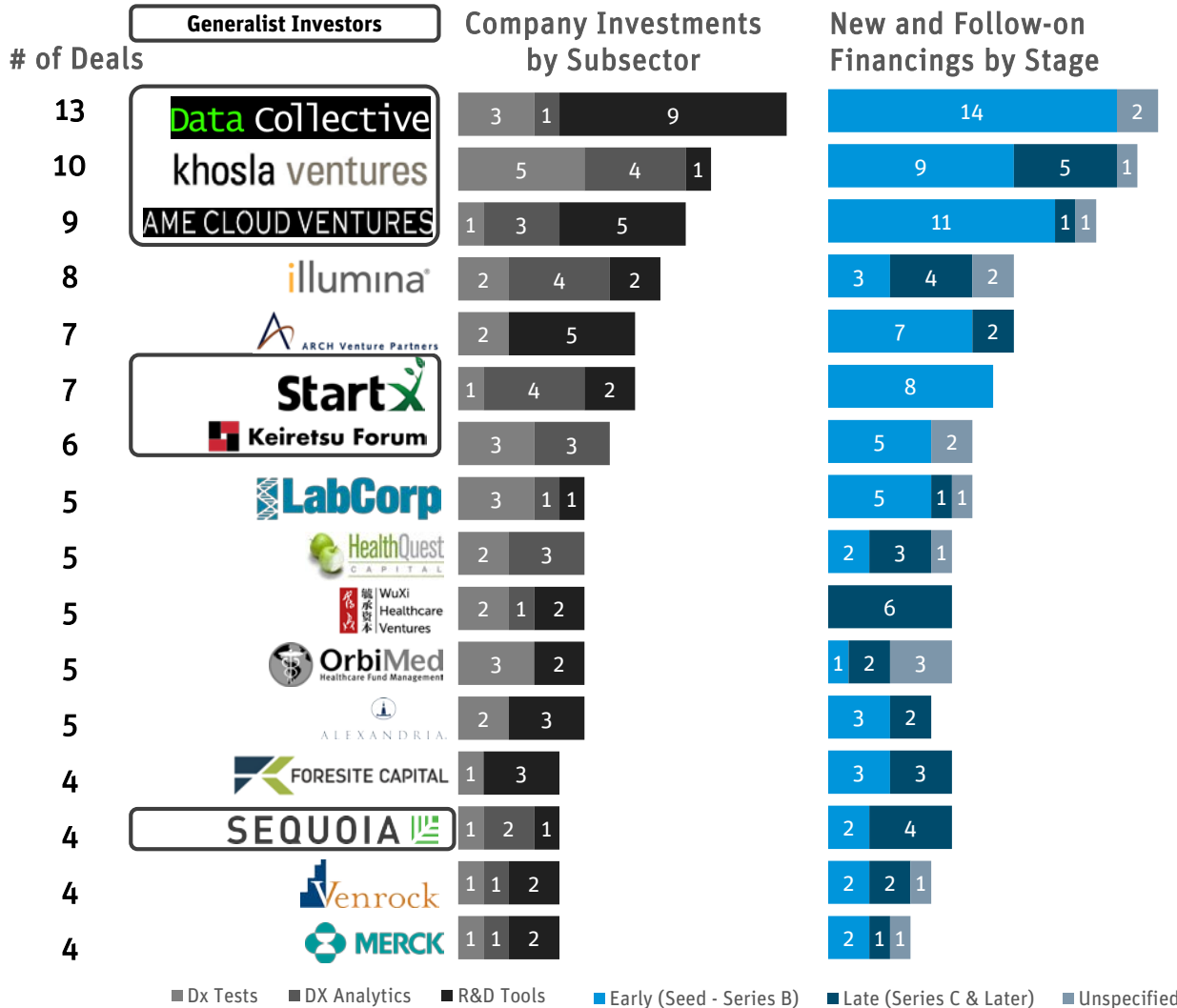
■ Dx Tests ■ Dx Analytics ■ R&D Tools



- 1H 2017 investments in Dx/Tools companies reached \$2.6B – a 33 percent increase over full year 2016. Mega-investments in GRAIL and Guardant Health alone accounted for \$1.3B.
- **Dx Tests** investments, led by GRAIL and Guardant Health, reached \$1.8B in 1H 2017. Point-of-care Dx Tests companies saw increased investments, especially in infectious diseases, highlighting optimism for clinical adoption in the short term.
- **Dx Analytics** investments were mostly early rounds for commercial-stage companies. Analytics technologies typically do not require regulatory approval before commercial rollout. Corporate venture investors were active, including Smith & Nephew (2), GE, Illumina, Pfizer and Samsung.
- **R&D Tools** investments were mostly in commercial-stage companies. Several companies, including Twist, Recursion and Synthego, have secured significant revenue-generating partnerships with large biopharma, tech and tools companies.

Generalist Firms Lead Dx/Tools Investment Rush

Most Active Investors in Dx/Tools Deals 2015 – 1H 2017



Starting in 2015, generalist investors began making larger investments in Dx/Tools, as adoption of AI made these companies more attractive. These investors include well-known names in the tech industry: Data Collective, Khosla Ventures and AME Cloud Ventures.

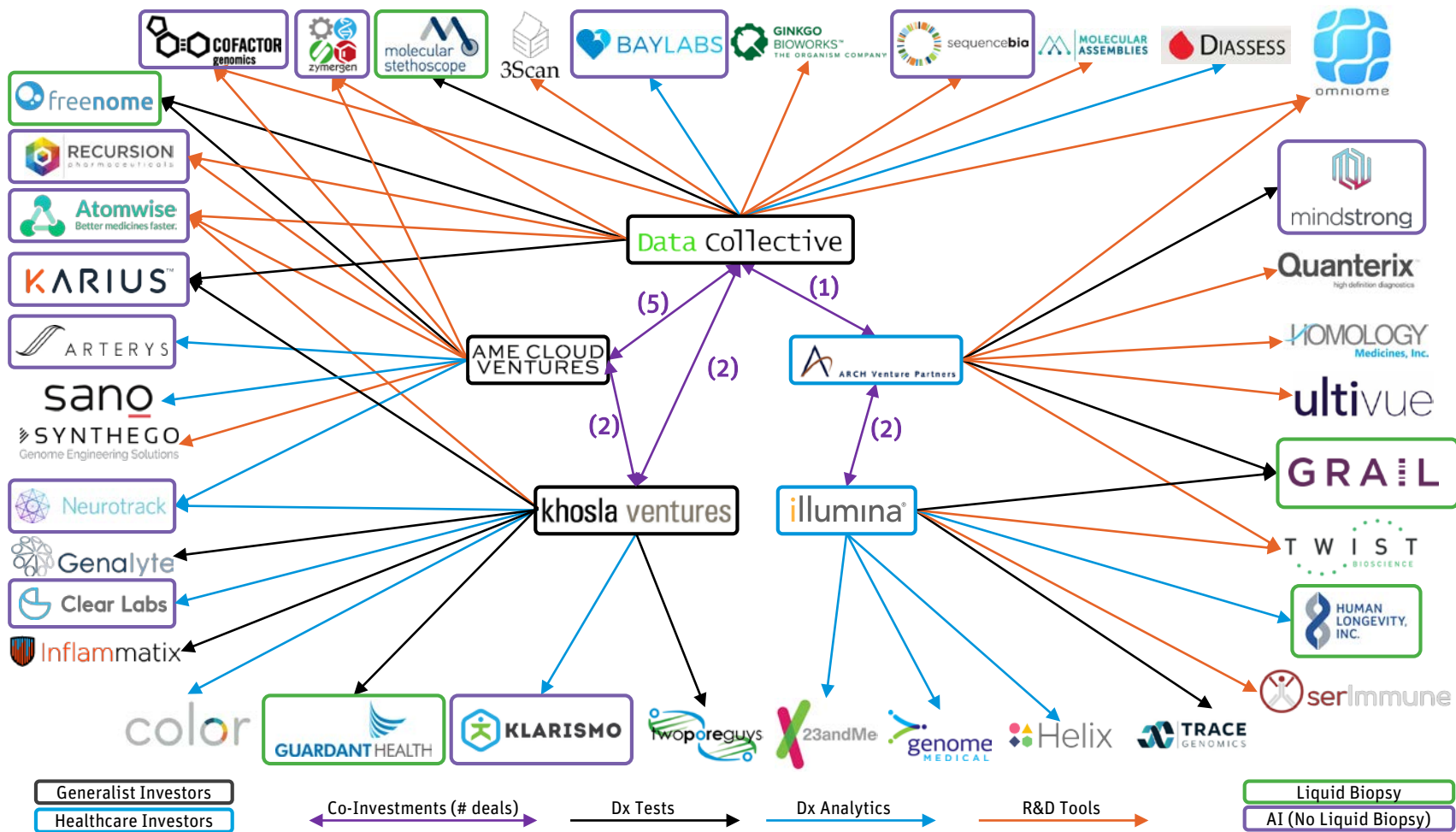
These generalist investors, when compared to healthcare-focused investors, are more likely to invest earlier (through Series B) and across many companies.

Challenge: Generalist investors have grown tech companies that don't have long development and commercialization timelines. These investors will need to adjust their growth strategies as they guide Dx/Tools companies through regulatory and commercial milestones.

Sources: PitchBook and SVB proprietary data.

Most Active Investors is defined as most active venture and corporate (including direct and venture arm) investors in unique deals between 2015 – 1H 2017

Top 5 Investors: AI Draws Generalist Activity



- Familiarity with artificial intelligence drives top generalist investor activity in Dx/Tools. These investors appear to prefer generalist-heavy syndicates. They have made most of their investments in liquid biopsy, synthetic biology and personalized medicine.
- These generalists appear to be more risk-tolerant than top healthcare investors, investing in early-stage companies that face regulatory and reimbursement hurdles. Healthcare investors, relying on previous experience, appear less bullish and more likely to invest in R&D Tools.

Healthcare Investors Bet on Dx/Tools Unicorns

Top Dx/Tools Companies by Post-Money Valuations 2015 – 1H 2017

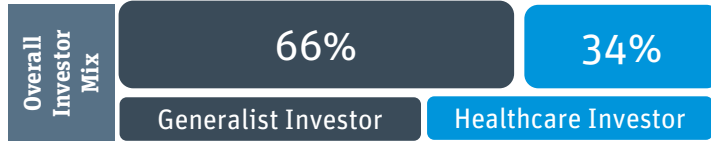
Unicorns

(\$1B+ Valuation)



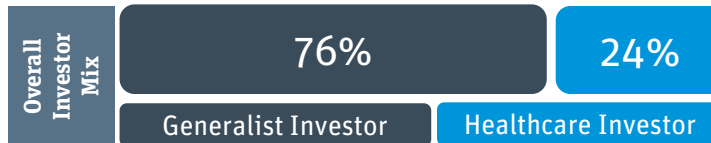
Breakouts

(\$500M - \$1B Valuation)



Standouts

(\$250M - \$500M Valuation)



Healthcare investors have shown major activity in Dx/Tools unicorns due to their potential to disrupt and dominate big clinical markets.

Breakout/standout companies include those in liquid biopsy, synthetic biology and personalized medicine. These companies typically leverage AI's predictive power to build their technologies and are preferred by generalist investors.

Among the unicorns and breakouts, only Ginkgo Bioworks is in the R&D Tools subsector. However, R&D Tools companies dominate the standout category. These companies are creating the foundation for the next generation of Dx Tests and Dx Analytics companies.

Sources: PitchBook for post-money valuations and investor data and SVB proprietary data.

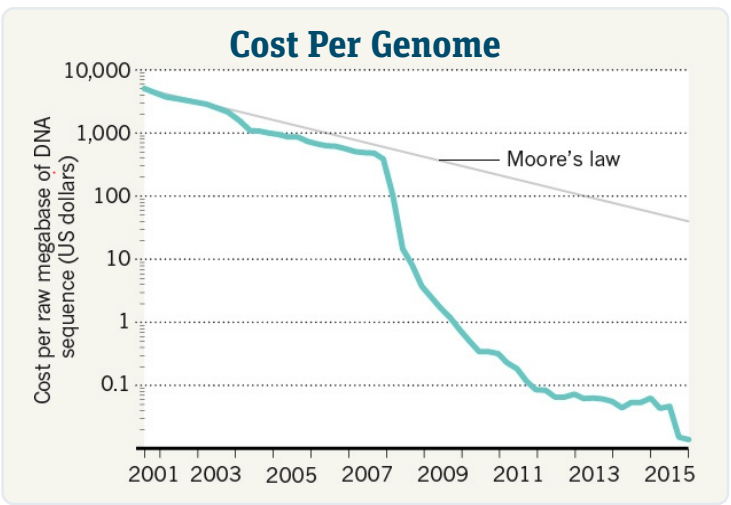
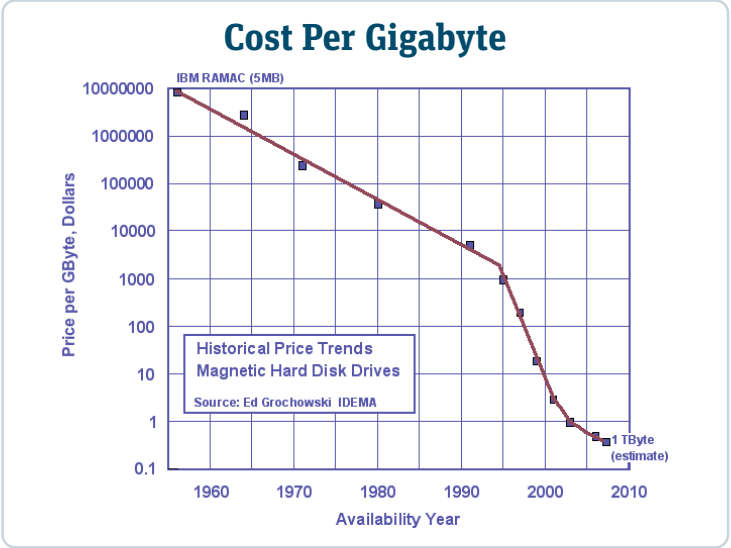
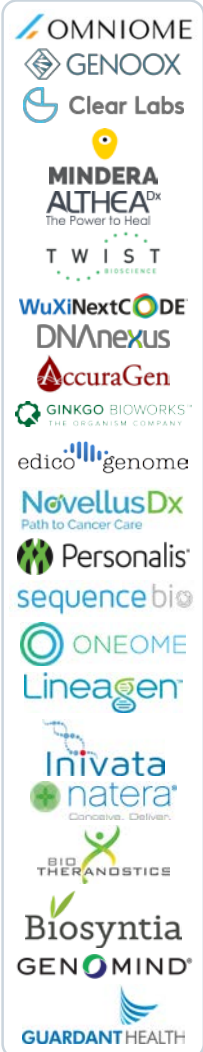
Generalist Investor: Investment that focus on multiple areas of interest. Healthcare Investor: Investment focus primarily on healthcare investments or dedicated healthcare team that has invested in healthcare over multiple funds.

Note: Natera IPO in June 2015; Assurex was acquired by Myriad Genetics in September 2016.



Dx/Tools Technology Trends

NGS: Decreasing Costs, Increasing Accuracy Enhance Investor Interest



Similar to the dramatic decrease in server storage cost of the past few decades, sequencing cost reductions in the last 10 years have led to widespread adoption and investment.

Between 2015 and 1H 2017, 50 NGS companies have seen nearly 70 separate financings. NGS technology is just starting to make the transition to clinical use.

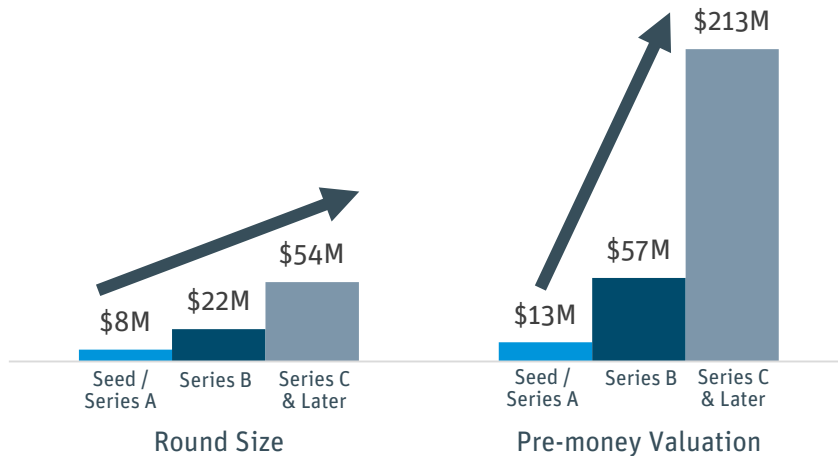
We predict that 2017 will close with more than 30 financing rounds for NGS companies – a tremendous boost for the subsector.



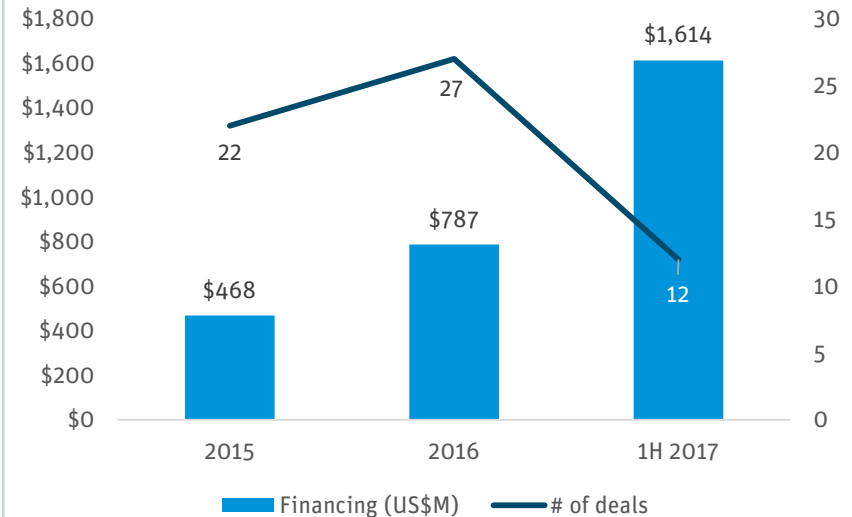
Valuations in NGS Companies Explode

Investments in Next-Generation Sequencing 2015 – 1H 2017

Explosion in NGS Valuations Median Round Size and Pre-Money Valuations



NGS Fundraising Surges in 1H 2017

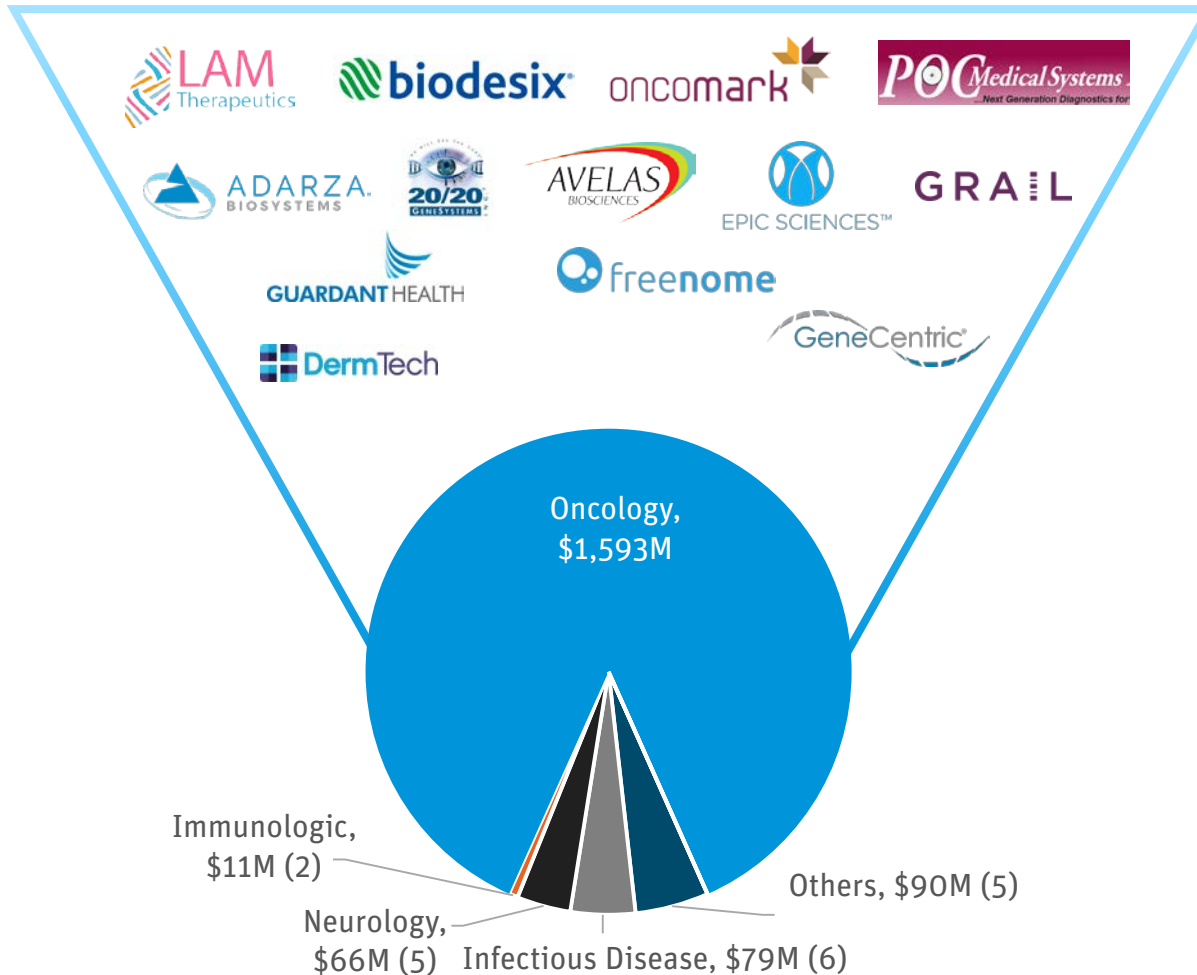


- Investors have flocked to NGS companies. Even in the face of early development and commercialization hurdles, investments (and valuations) have surged.
- Late-stage median pre-money valuations reached \$213M in 1H 2017, quadruple the valuations of non-NGS deals.
- However, NGS is just starting to prove itself in the market. It remains to be seen how sequencing analysis will impact patient diagnosis and treatment. How companies fare when seeking biopharma partnerships and ramping revenue will determine their success.

Oncology Dx Companies Attract Investment Dollars

Investments in Dx Tests Companies in 1H 2017

1H 2017: 32 Dx Tests Financings Raised \$1,943M



While fewer than half of 1H 2017 Dx Tests companies focused on oncology (13 of 32), this clinical area received 87% of \$1.9B raised. Oncology therapeutics investments also boosted this area, as these companies looked for diagnostics to pair with their drugs.

1H 2017 companies with technologies that use electrochemical detection outpaced those using imaging and optics detection in both deals and dollars (15 to 6; \$255M to \$58M). These funding amounts do not include GRAIL and Guardant Health.

AI-focused companies closed 12 financings in 1H 2017 alone, outpacing the 11 financings in all of 2016. Going forward, we think that AI will often be integrated into Dx Tests companies, prompting continued interest by generalist investors.

Liquid Biopsy Companies Hold Big Promise for Cancer Diagnostics

Investments in Liquid Biopsy Companies 2015 – 2016

Liquid Biopsy Process



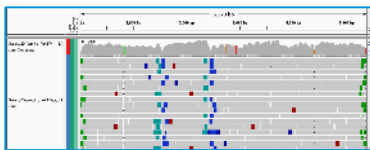
Collect Blood Sample



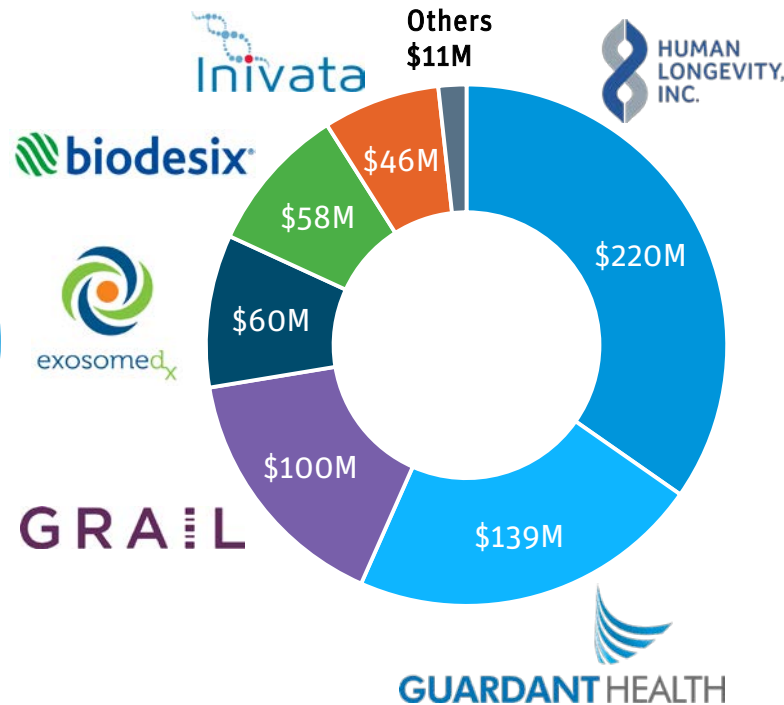
Process for Cell-Free DNA (cfDNA) and Exosomes



Next-Gen Sequencing for cfDNA, RNA and/or Exosomes



Analyze Sequencing Data for Cancer Mutations using AI



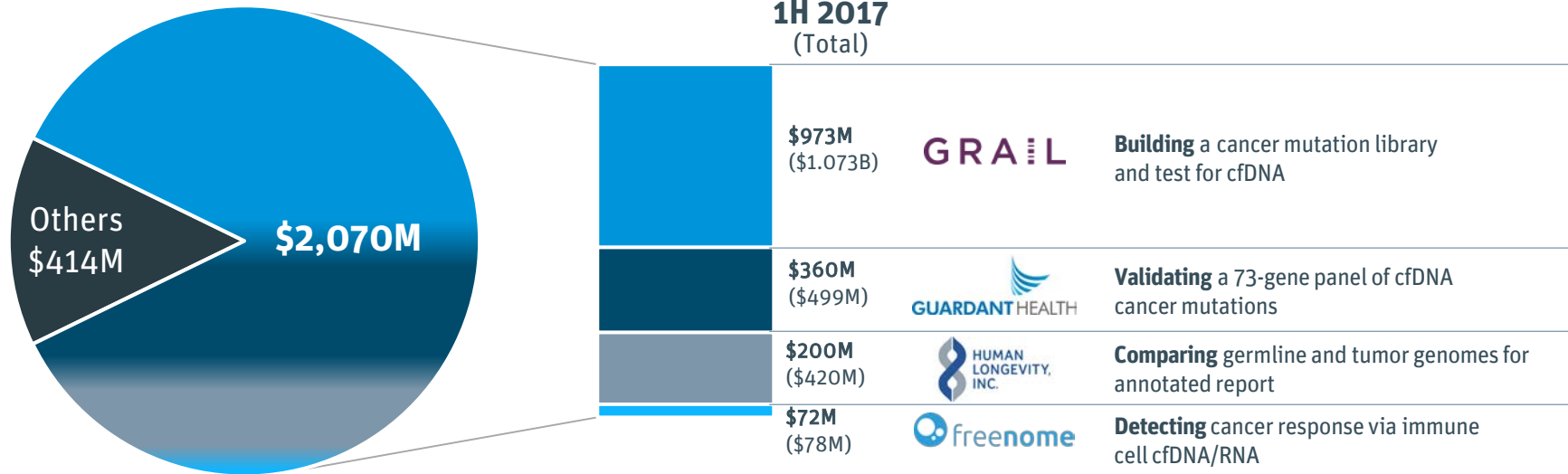
NGS enables patient DNA analysis at a resolution of singular bases. Adopted by Stanford University researchers, the technology has been used to analyze genetic markers for birth defects and more recently has jump-started liquid biopsy.

Cancer detection currently requires radioactive imaging and invasive biopsies. Liquid biopsies only use blood, allowing for minimally invasive early cancer detection.

Large 2015 and 2016 investments were made in Human Longevity, GRAIL and Guardant Health, which comprise two-thirds of total liquid biopsy funding. These companies were either optimizing blood collection/processing, improving their cancer DNA alignment and analytics tools or beginning to validate their test(s).

1H 2017 Liquid Biopsy Investments Centered on Four Companies

Investments in Liquid Biopsy Companies 2015 – 1H 2017



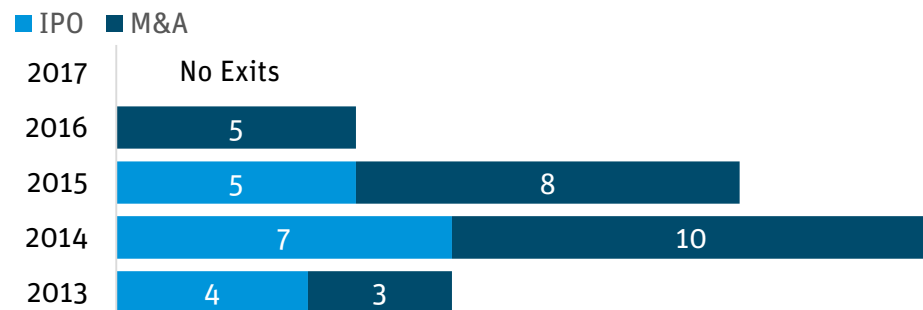
- Encouraged by the companies' progress in the past two years, investors doubled down on GRAIL, Guardant Health, Human Longevity and Freenome. These four companies dominated the 1H 2017 investment landscape, raising more than \$1.6B. Total investment in these companies represents 83% of Dx Tests funding since 2015.
- The companies have a mixed investor base. Generalist investors make up at least half the syndicate of Guardant, Human Longevity and Freenome. Healthcare investors predominately support GRAIL.
- Like any other diagnostic technology, liquid biopsy will require insurance coverage. Widespread insurance adoption will require multiyear cost-benefit analyses. Early-stage cancer diagnoses reduce personal and financial burden, and we predict that the majority of insurers will cover these tests within the next five years.



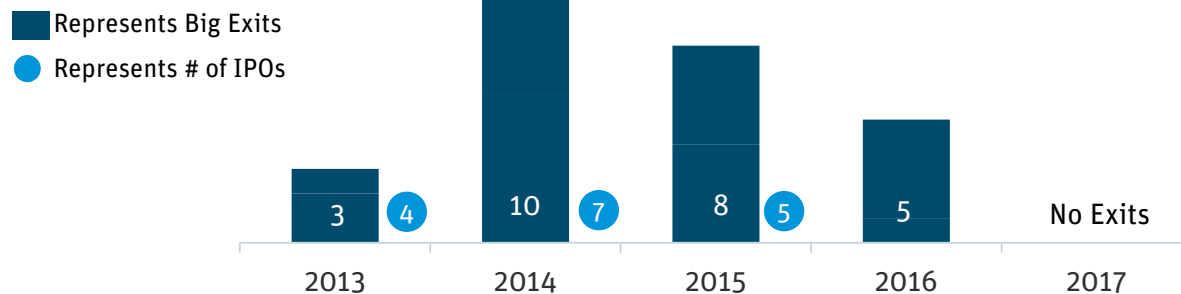
Exit Trends and Forecast

Will Lack of Dx/Tools Exits Cast a Shadow on Funding?

VC-backed Dx/Tools Big Exits* 2013 – 1H 2017



of Big Exits



	2013	2014	2015	2016	2017
Median Upfront (\$M)	350	133	164	225	N/A
Median Total Deal (\$M)	450	239	164	325	N/A
Median Years to Exit**	8.2	6.0	3.6	8.5	N/A

In some ways, 2017 seems like a contradiction, but we think it is the prelude to big Dx/Tools exits in the next few years.

Despite record Dx/Tools fundraising, there have been no big exit M&A or IPOs by mid November. In comparison, 2013 - 2016 had 42 exits (26 M&A and 16 IPOs). Major acquirers since 2013 were Roche (3), Bio-Techne (3) and Myriad (2).

Historically, the majority of Dx/Tools exits have been based on commercial revenue multiples rather than enterprise values typically seen in biopharma M&A.

Dx/Tools median upfront and total deal M&A values (\$150M/\$204M) significantly lag behind those of biopharma (\$200M/\$500M). A main reason for this: Biopharma companies are typically acquired faster (with early-stage clinical data) and via a robust bidding process.

The lack of exits could signal that these companies would have to ramp up revenue on their own with an IPO on the horizon. Fortunately, there is ample private capital to support continued financing.

Sources: PitchBook, press releases and SVB proprietary data.

*A Big Exit is defined as a private, venture-backed M&A with an upfront payment of at least \$50M.

**Median years to exit is defined as time to exit from close of Series A financing.

SVB's Forecast for Dx/Tools

GENERALIST INVESTMENTS WILL SURGE

- Generalist investors have often invested in Dx/Tools companies along side other generalist investors. These investors appear to be drawn to companies leveraging big data sets to create technologies for biopharma R&D and diagnostics.
- In a small number of follow-ons raised to date, the new lead investors have been other generalists and large tech companies. We expect this trend to continue. Healthcare investors will likely reengage further down the road as these companies grow.
- The driver of value is the data's ability to provide actionable results or guide clinical development. The next few years will prove out the actual value of these technologies, as determined by key healthcare stakeholders (i.e., payers).

NGS NEEDS TO PROVE ITS LOFTY VALUATIONS

- NGS was initially developed as an R&D Tool to expand our understanding of genomic data for research and drug discovery. Genomic databases have grown to the point that this information can be applied to the clinic, especially for personalized medicine.
- There is significant excitement and growing valuations in NGS; however, NGS companies still need actionable data to prove the value of their technologies. We think NGS will influence the evolution of today's dominant diagnostic players – likely through an M&A strategy.

INTEREST IN LIQUID BIOPSY AND INFECTIOUS DISEASE WILL GROW

- Liquid biopsy has dominated diagnostics funding. Its suitability for early cancer detection will increase the frequency of testing. As a result, we think that its adoption will provide long-term personal and financial benefits.
- Clinical adoption of point-of-care diagnostics will continue to increase. Strong investor interest indicates that these tests will focus on the detection of infectious diseases.

NEW ACQUIRERS ARE SET TO EMERGE

- Historically, Dx/Tools M&A activity ran in the \$100M - 200M range. Based on current valuations, robust exit multiples will be difficult to achieve.
- Large Dx/Tools companies will adopt M&A strategies similar to biopharma. These companies will fuel their primary R&D by acquiring early-stage, venture-backed Dx/Tools companies.
- Large tech companies have significantly invested in Dx/Tools. While today's giants like Roche and Illumina should maintain their leadership position, expect Amazon, Apple and Alphabet to join their ranks.

HEALTHCARE AND TECH ARE CONVERGING AT DX/TOOLS

- Dx/Tools technologies are increasingly integrating tech innovations like AI.
- As a result, generalist investor and tech corporate investment activity in Dx/Tools has surged.
- We expect today's top tech companies to also become the next generation of top Dx/Tools companies. With dedicated Dx/Tools teams, these tech giants could drive sector growth for the next decade.

Glossary

Artificial Intelligence (AI): Diagnostics or tools that leverage big data and advanced statistical/computational techniques in order to carry out their function. These devices generally incorporate feedback loops that iteratively improve their operating algorithms and often include machine learning.

Corporate Investor: Corporate investor is defined as venture and parent company investments into venture-backed companies

Dx Tests: Companies focused on proprietary tests that produce a Yes/No result

Dx Analytics: Companies that use actionable data analytics to help direct treatment

Generalist Investors: Investors that focus on multiple areas of interest, not only healthcare

Healthcare Investors: Investors that focus primarily on healthcare investments or have a dedicated healthcare team that invests in healthcare through multiple funds

Liquid Biopsy: A liquid biopsy, also known as fluid biopsy or fluid phase biopsy, is the sampling and analysis of non-solid biological tissue, primarily blood

Most Active Investors: Most Active Investors are defined as most active investors in unique deals between 2015 and 1H 2017

Next-Generation Sequencing (NGS): A new method for sequencing genomes at high speed and at low cost. It is also known as second-generation sequencing (SGS), high-throughput sequencing or massively parallel sequencing (MPS).

Post-Money Valuation: Valuation of a company after an investment or funding. The post-money valuation equals a company's pre-money valuation plus the new equity raised in its most recent round.

Pre-Money Valuation: The valuation of a company prior to an equity investment or funding

R&D Tools: Companies that provide research equipment/services for biopharma and academia

About the Authors



Jonathan Norris
Managing Director
Silicon Valley Bank
jnorris@svb.com

As a Managing Director in SVB's Life Science and Healthcare Practice, Jonathan Norris oversees business development efforts for banking and lending opportunities and also spearheads strategic relationships with many healthcare venture capital firms. In addition, he helps SVB Capital make sourcing decisions and provides advice on limited partnership allocations.

Norris speaks at major investor and industry conferences and authors widely cited analyses of healthcare venture capital trends. He has more than 17 years of banking experience working with healthcare companies and venture capital firms. Norris earned a bachelor's degree in business administration from the University of California, Riverside, and a juris doctorate from Santa Clara University.



Thomas Joyce
Senior Associate
SVB Securities
tjoyce@svb.com

Thomas Joyce is a Life Science Senior Associate based in Boston, where he performs strategic advisory services with a focus on Dx/Tools mergers and acquisitions.

Joyce was previously a Senior Associate in SVB's commercial bank, focused on financial analysis, portfolio management, business development and underwriting of complex credit transactions for life science and healthcare companies. Prior to SVB, Joyce was responsible for originating and analyzing private equity transactions for Kamylon Capital, a principal investment firm. Joyce earned a bachelor's degree in finance with a minor in economics from Suffolk University's honors program, graduating summa cum laude and as a member of the Beta Gamma Sigma Honors Society.



Ritish Patnaik
Dx/Tools Consultant
rp2616@stanford.edu

As a Dx/Tools Consultant, Ritish Patnaik helped develop SVB's Dx/Tools classification system. In addition, he helped analyze the final data set for the investment trends presented in this report.

Patnaik is currently pursuing a Ph.D. in bioengineering at Stanford University, where he is developing a multi-target liver cancer diagnostic test using a magnetically tagged liquid biopsy approach. He is also co-founder of Luso Labs LLC, which is developing a point-of-care device that uses machine learning and mobile computing to address cervical cancer screening issues. Patnaik earned a bachelor's degree in biomedical engineering at Columbia University.



About Silicon Valley Bank

For more than 30 years, Silicon Valley Bank has helped innovative companies and their investors move bold ideas forward, fast. SVB provides targeted financial services and expertise through its offices in innovation centers around the world. With commercial, international and private banking services, SVB helps address the unique needs of innovators.

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