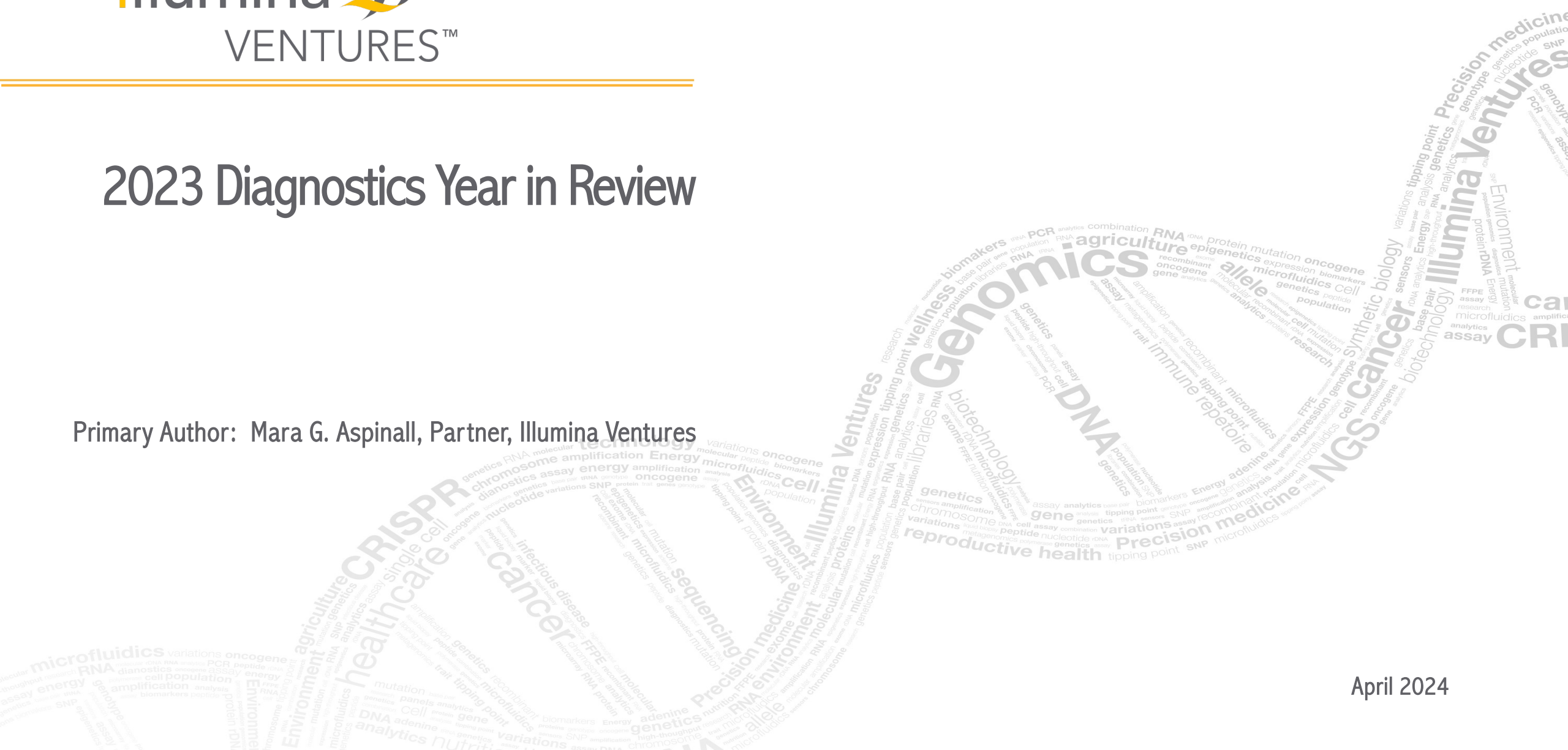




2023 Diagnostics Year in Review

Primary Author: Mara G. Aspinall, Partner, Illumina Ventures



Contents: Diagnostics Year in Review 2023

- Observations
- Financial Results
 - Stock Indices / M&A / IPO's / Capital Investments
- Operating Metrics
 - FDA approvals / Test Volumes / Biomarkers / CLIA labs
 - Regulatory Update
 - CEO Profiles
- Important Trends for Innovation in Diagnostics

Observations



Financial value of diagnostic companies (public & private) are down: at or below pre-pandemic values

- Stock prices / M & A / IPO / VC market – all at or below 2019 (2018 was the high water)
- Many distressed assets can't sustain operations & looking for new homes: especially COVID focused
- In contrast, biotech and pharma are above 2019 but below broader indices



Diagnostics' regulatory rules tighten significantly in the EU and at crossroad in the US

- US debating LDT into FDA again. Bi-partisan agreement for additional regulation but some industry opposition.
- US state biomarker mandates growing and may take power away from payors
- EU significantly tightening their diagnostics regulations



Diagnostic reimbursement continues as the “haves” and “have nots”

- Meaningful price increases for differentiated / well-published tests with strong market share
- Routine test volume remain flat to slightly down post pandemic except for molecular / genetic tests
- Pre-specified multiple test panels becoming more common reducing administrative burden for all



Omics beyond Genomics, Liquid Biopsy, MRD Testing, New Sample Types with AI leads innovation

- Increased use of new less invasive sample types making decentralization of testing easier / potentially cheaper
- Liquid biopsy and MRD tests maturing – increasing payer coverage
- AI will impact and improve all diagnostic areas



Knowledge about diagnostics is severely lacking in all sectors

- Lack of education for physicians / HCPs causing patient harm
- Lack of consumer educations causing confusion
- Burden of education remains with diagnostic companies - Broader healthcare community needs to embrace dx education

Contents: Diagnostics Year in Review 2023

- Observations

- Financial Results

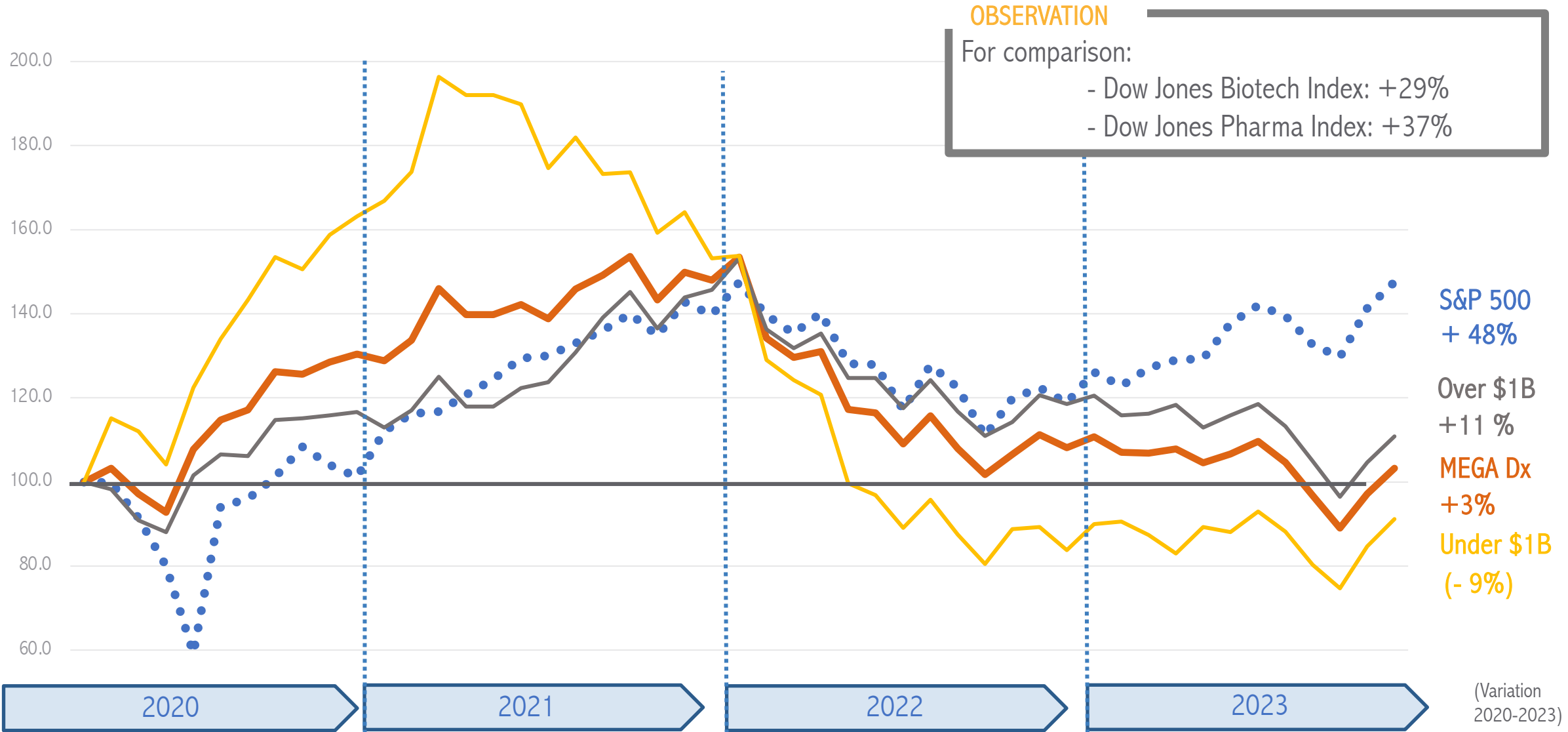
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- Operating Metrics

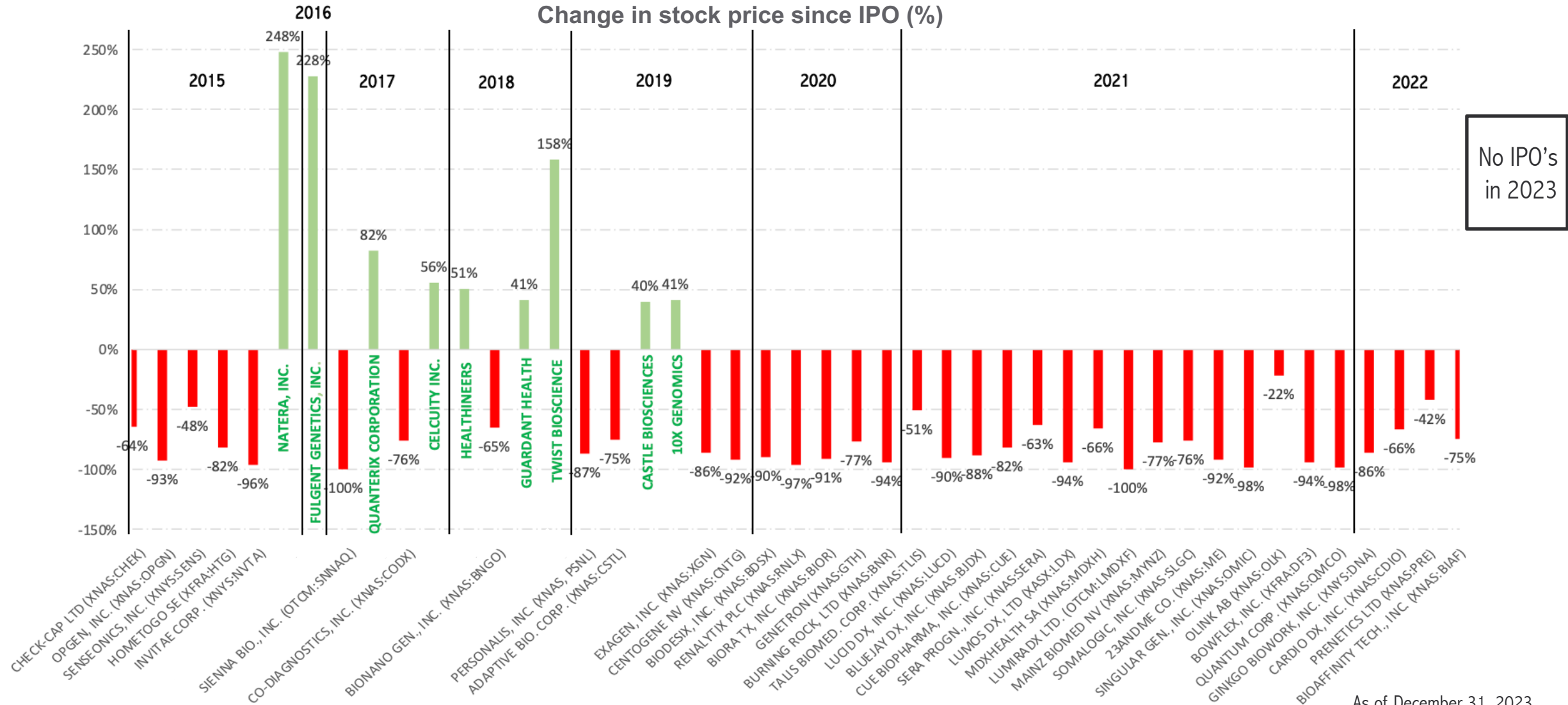
- FDA approvals / Test Volumes / Biomarkers / CLIA labs
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Diagnostics MEGA Dx Stock Index: 2020 - 2023

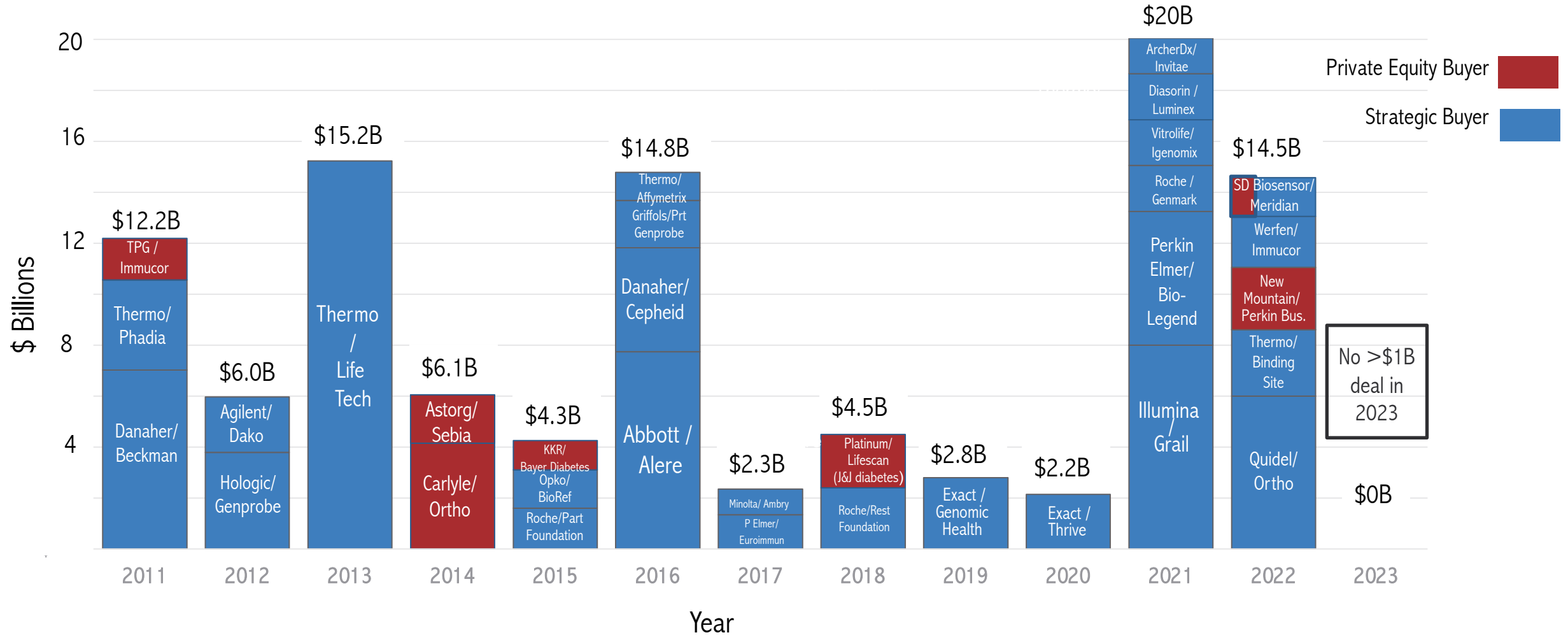


If You Bought \$1 of these Diagnostics Companies at their IPO Initial Price ...



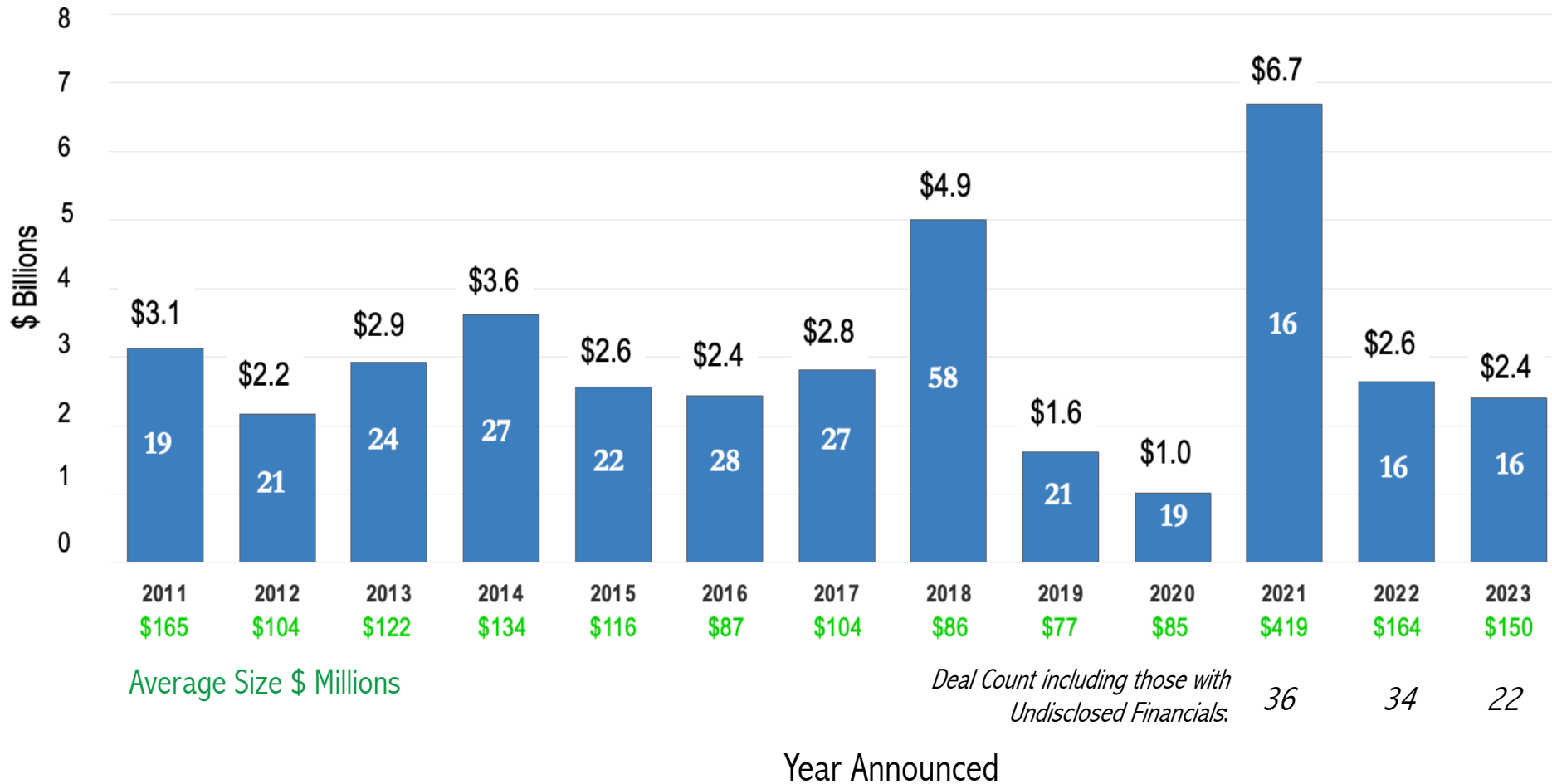
As of December 31, 2023

Diagnostic Industry Transforming Acquisitions (>\$1 Billion)



7 Data Source: Evercore and internal analysis of public filings

Smaller Diagnostic Acquisitions (<\$1 Billion)



Select 2023 Examples

Acquirer: Quest Diagnostics
Target: Haystack Oncology
Deal value: \$450m

Acquirer: Roche
Target: LumiraDx
Deal value: \$350m

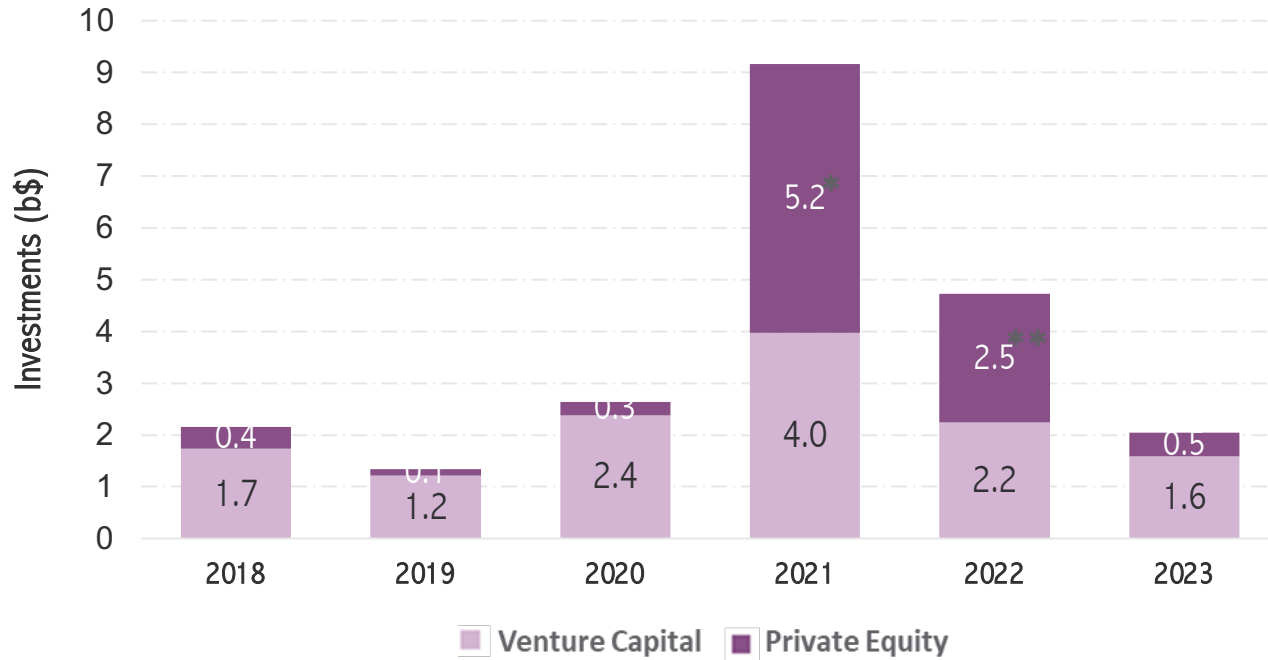
Acquirer: Sonic Healthcare
Target: Diagnosticum
Deal value: \$207m

Acquirer: Qiagen
Target: Verogen
Deal value: \$150m

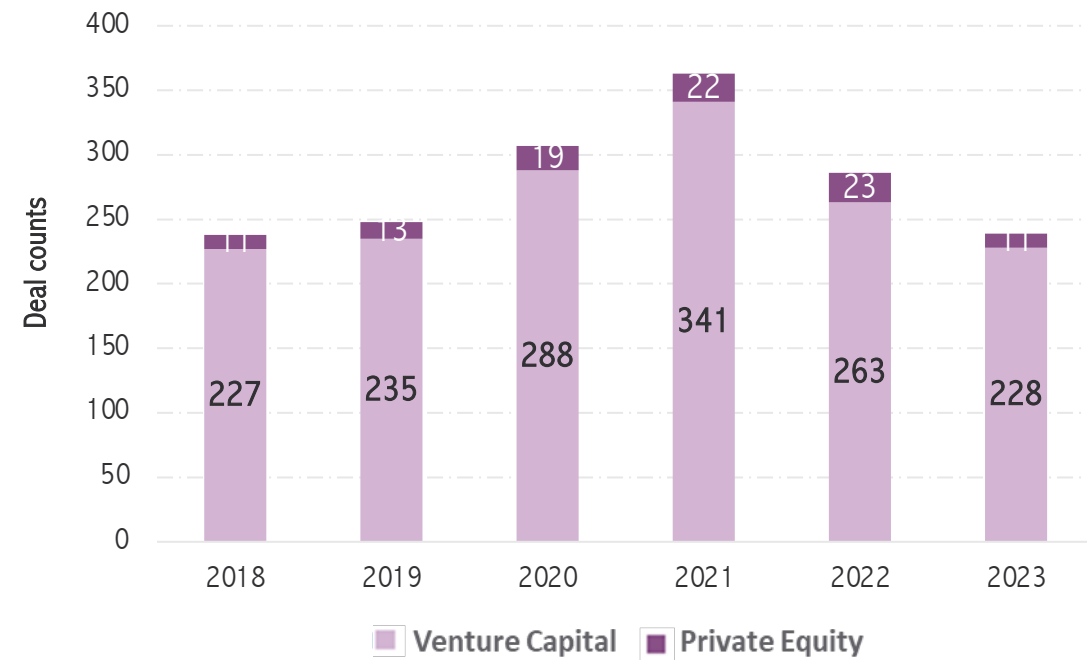
Acquirer: PAC Bio
Target: Apton Biosystems
Deal value: \$110m

Diagnostics Venture Capital & Private Equity Investments: 2018 - 2023

Diagnostics investments (amount)



Diagnostics investments (deal counts)



\$8	\$5	\$8	\$12	\$9	\$7	Average Deal Size (VC) \$M
\$39	\$10	\$13	\$236	\$108	\$42	Average Deal Size (PE) \$M

* Including Amedes Group (Buyout/LBO, \$1.66B) | Groupe Inovie (Buyout/LBO, \$2.3B)

** Including Affidea (Buyout/LBO, \$1.75B)

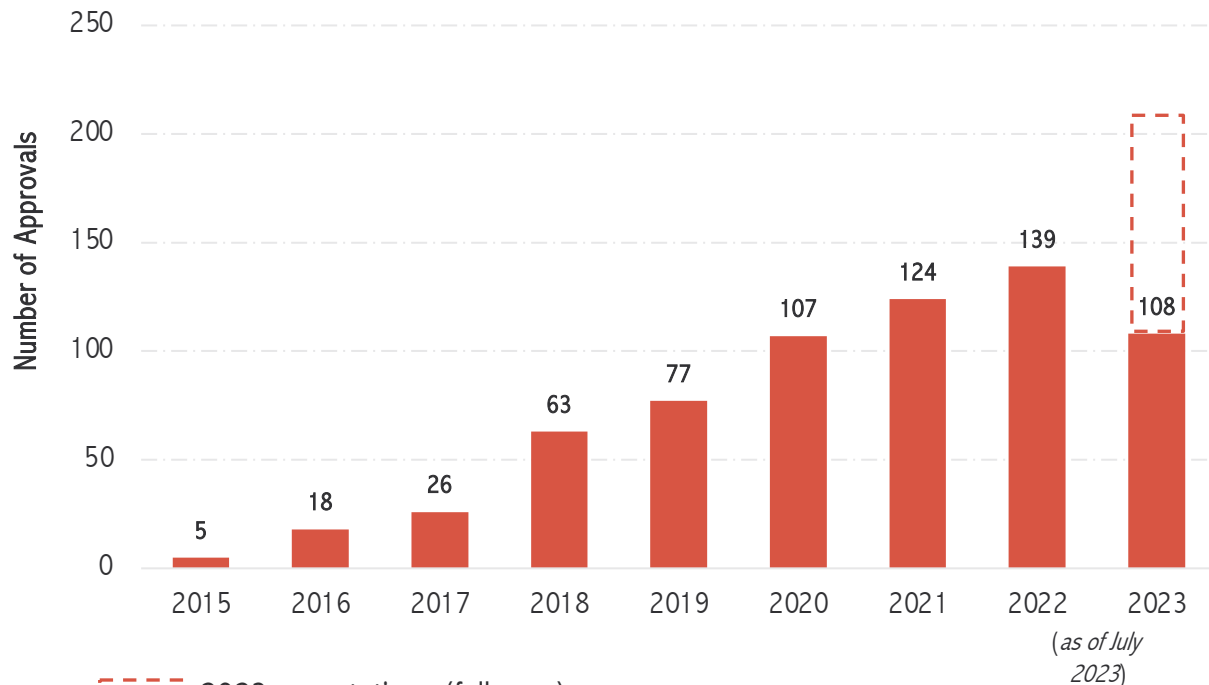
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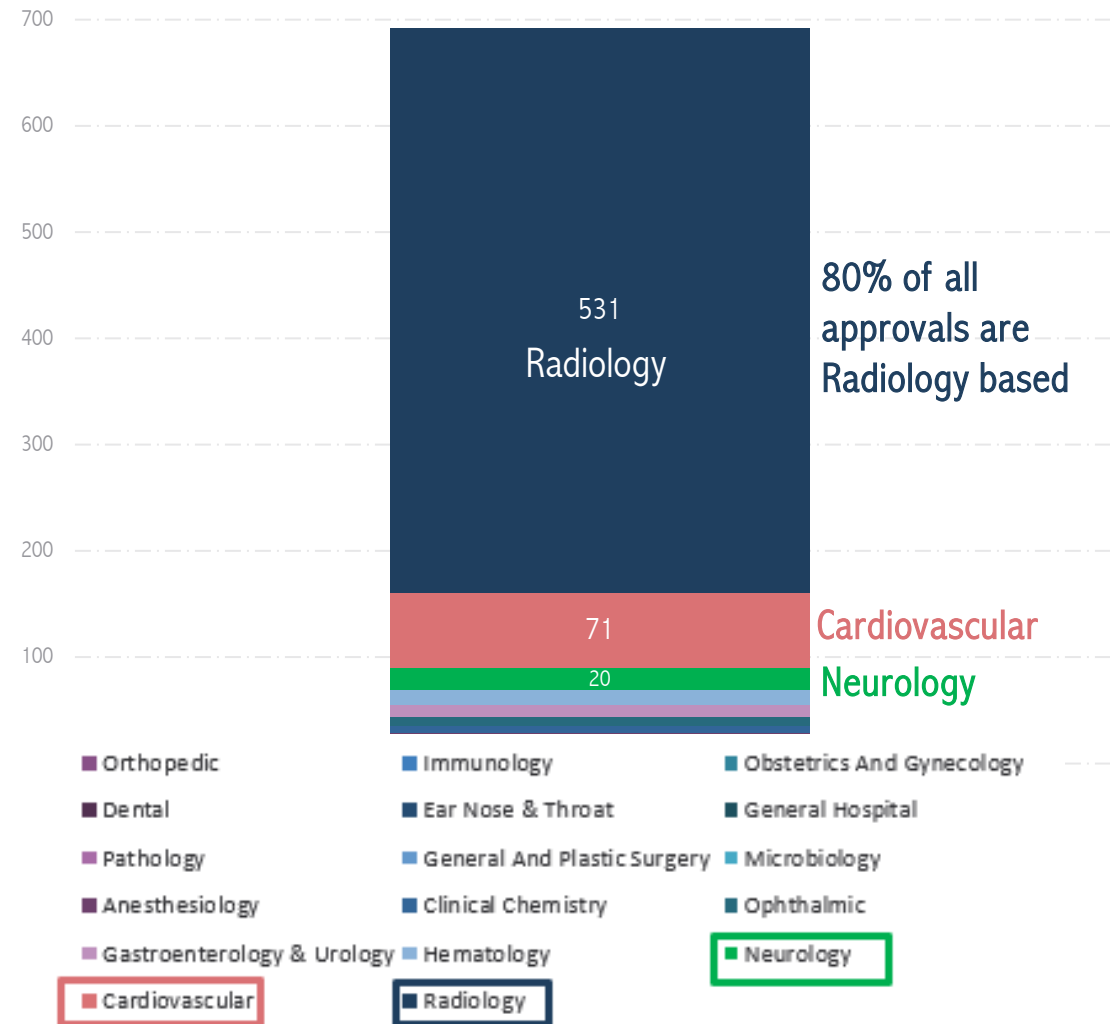
Artificial Intelligence / Machine Learning: Enabled Medical Devices



AI/ML FDA Approvals



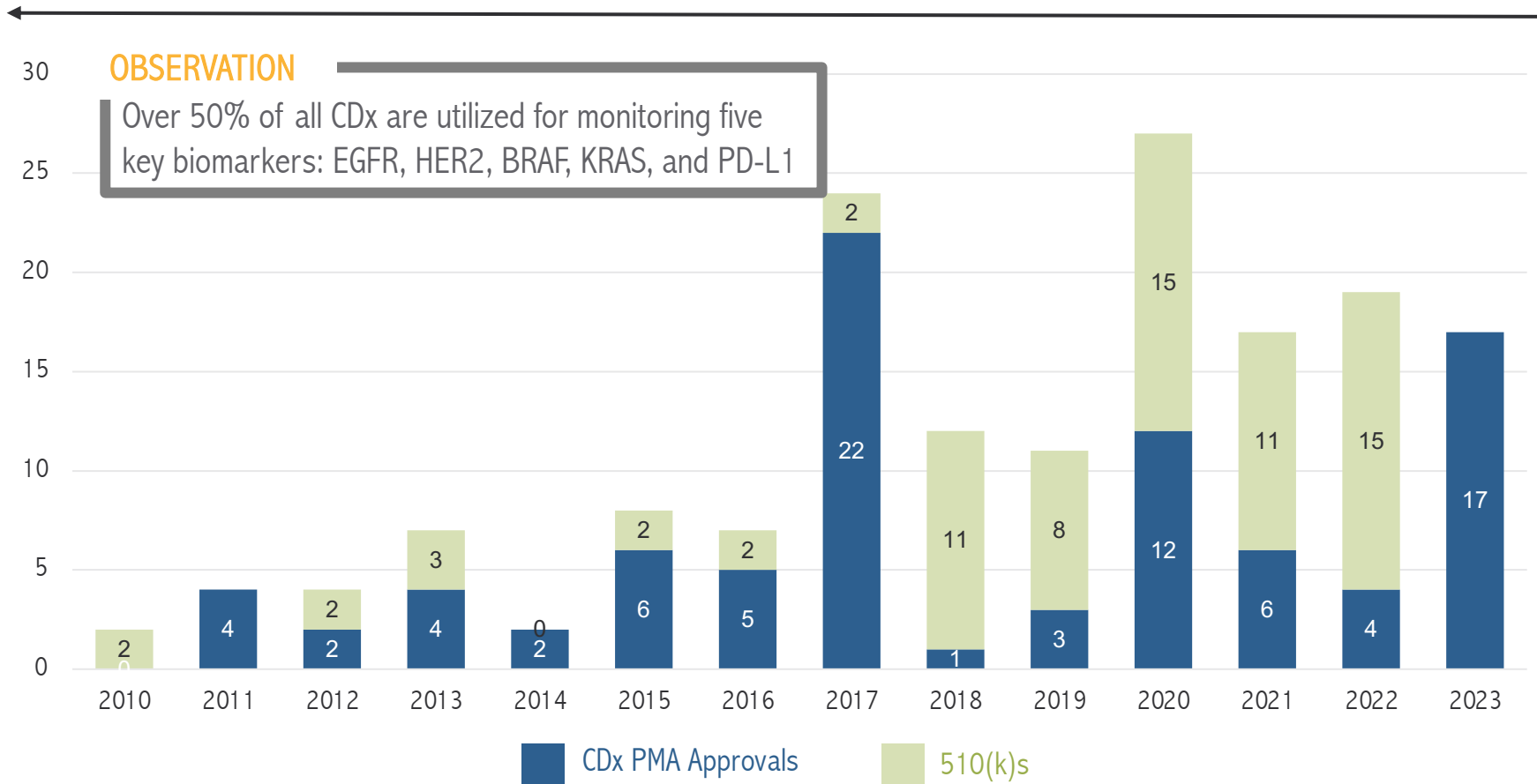
2023 expectations (full-year)



Companion Diagnostics with FDA Approval: 2010 - 2023



88 CDx PMA Approvals and 73 CDx 510(k)s



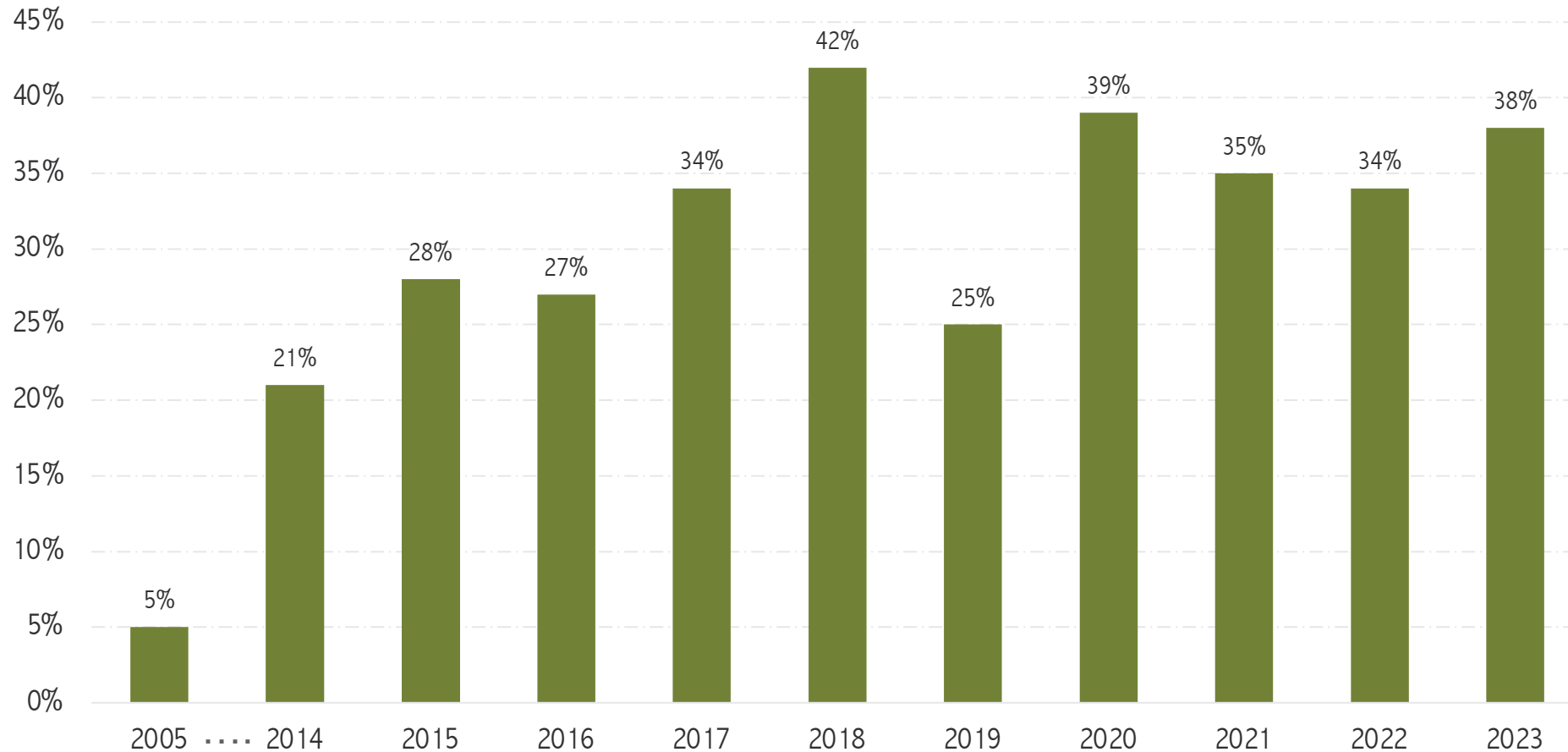
OBSERVATION

Over 50% of all CDx are utilized for monitoring five key biomarkers: EGFR, HER2, BRAF, KRAS, and PD-L1

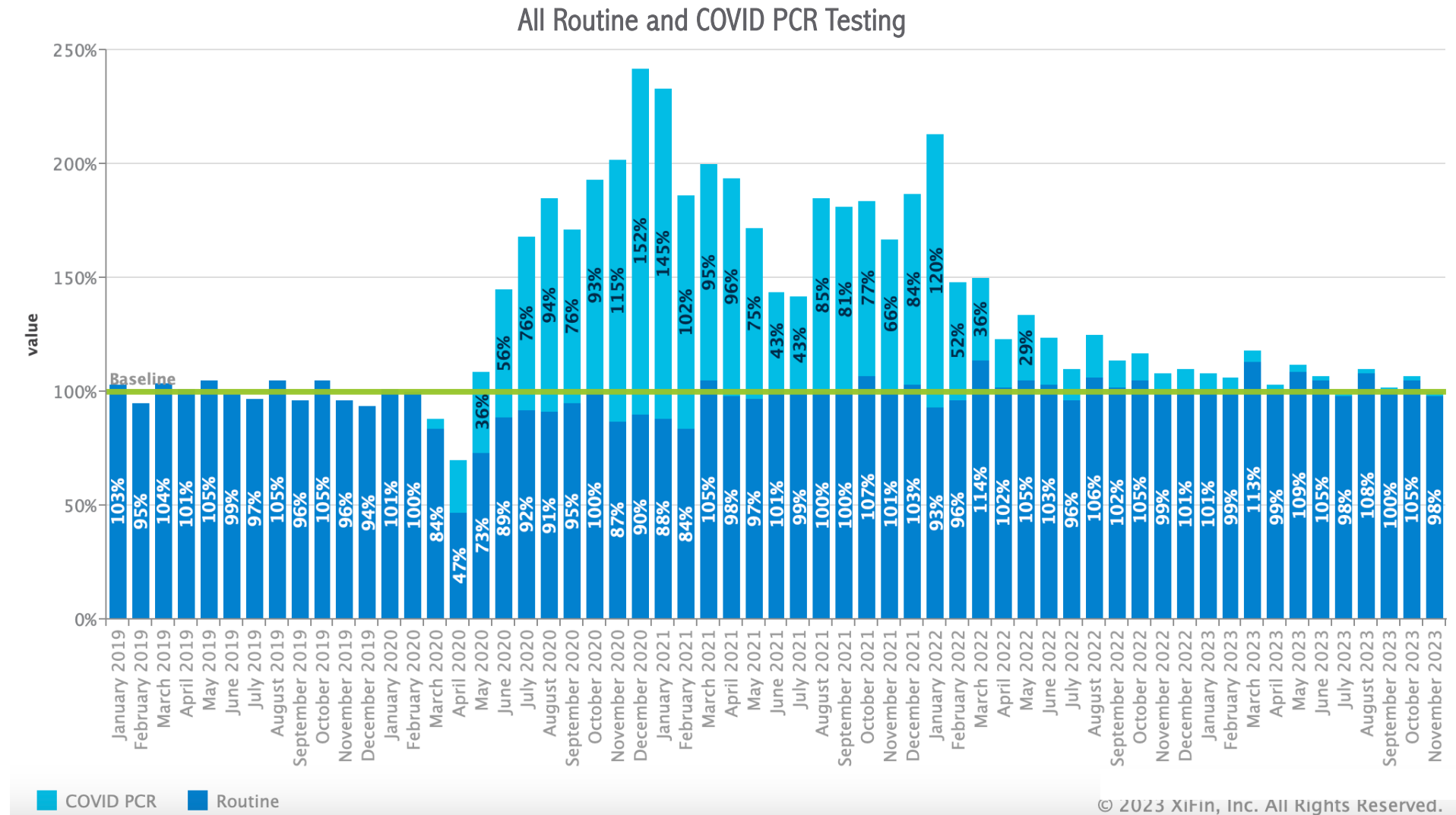
Select 2023 Examples

- AAV5 DetectCDx**
Assays to detect pre-existing antibodies to adeno-associated virus (AAV) viral vectors
ARUP Laboratories
Decision Date: June 29, 2023
- Abbott RealTime IDH1**
Somatic gene mutation detection system
Abbott Molecular, Inc.
Decision Date: October 24, 2023
- FoundationOne Liquid CDx**
Foundation Medicine, Inc.
Decision Date: May 3, 2023
- xT CDx**
Tempus Labs, Inc.
Decision Date: April 28, 2023

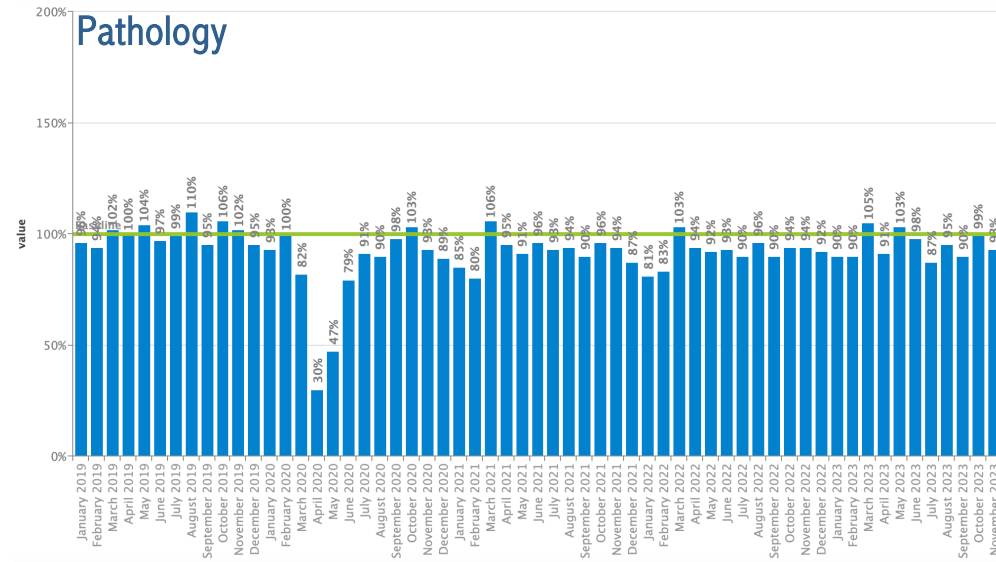
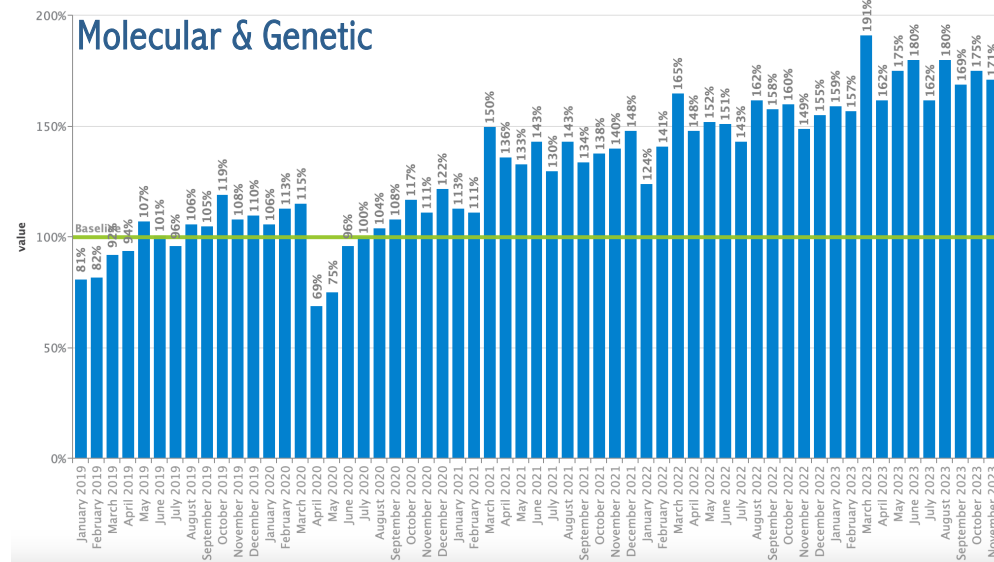
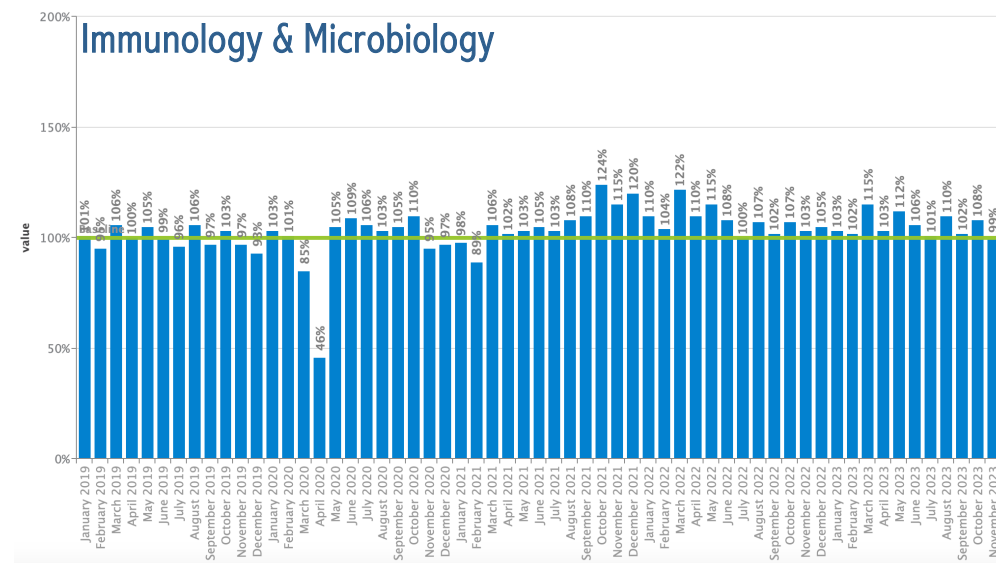
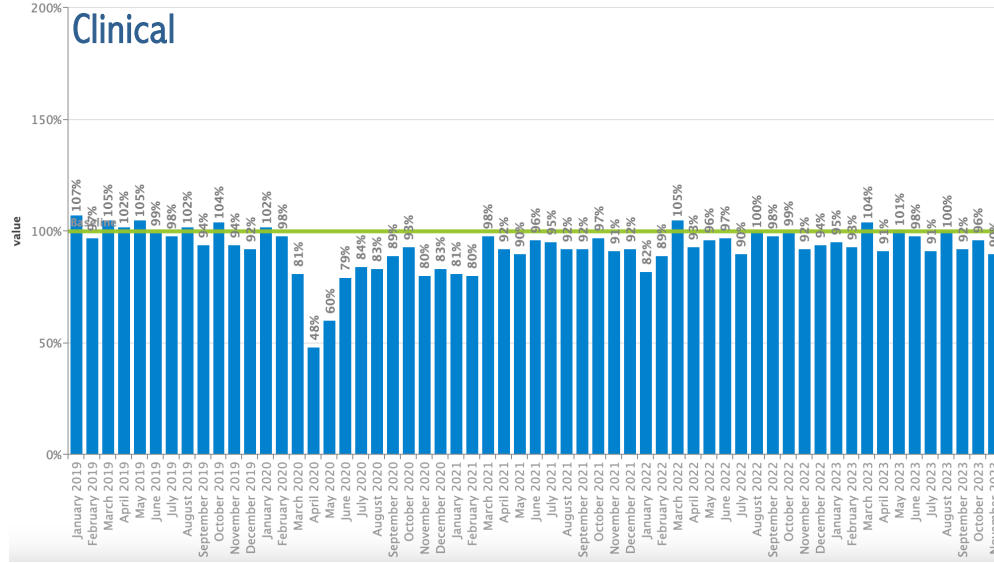
Biomarker-Dependent Drug Approvals as % of all Drug Approvals



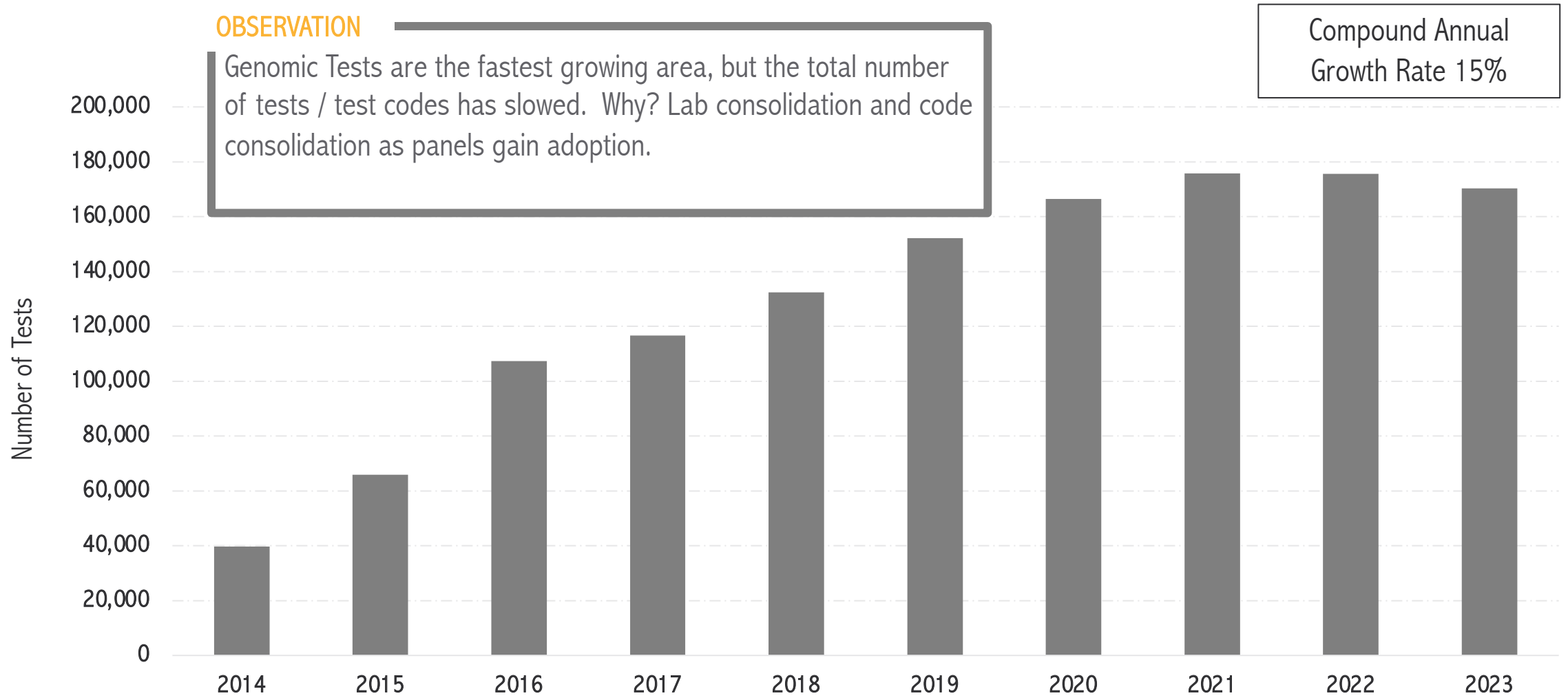
Laboratory Volume Index: Routine Lab Tests vs. COVID: 2019 - 2023



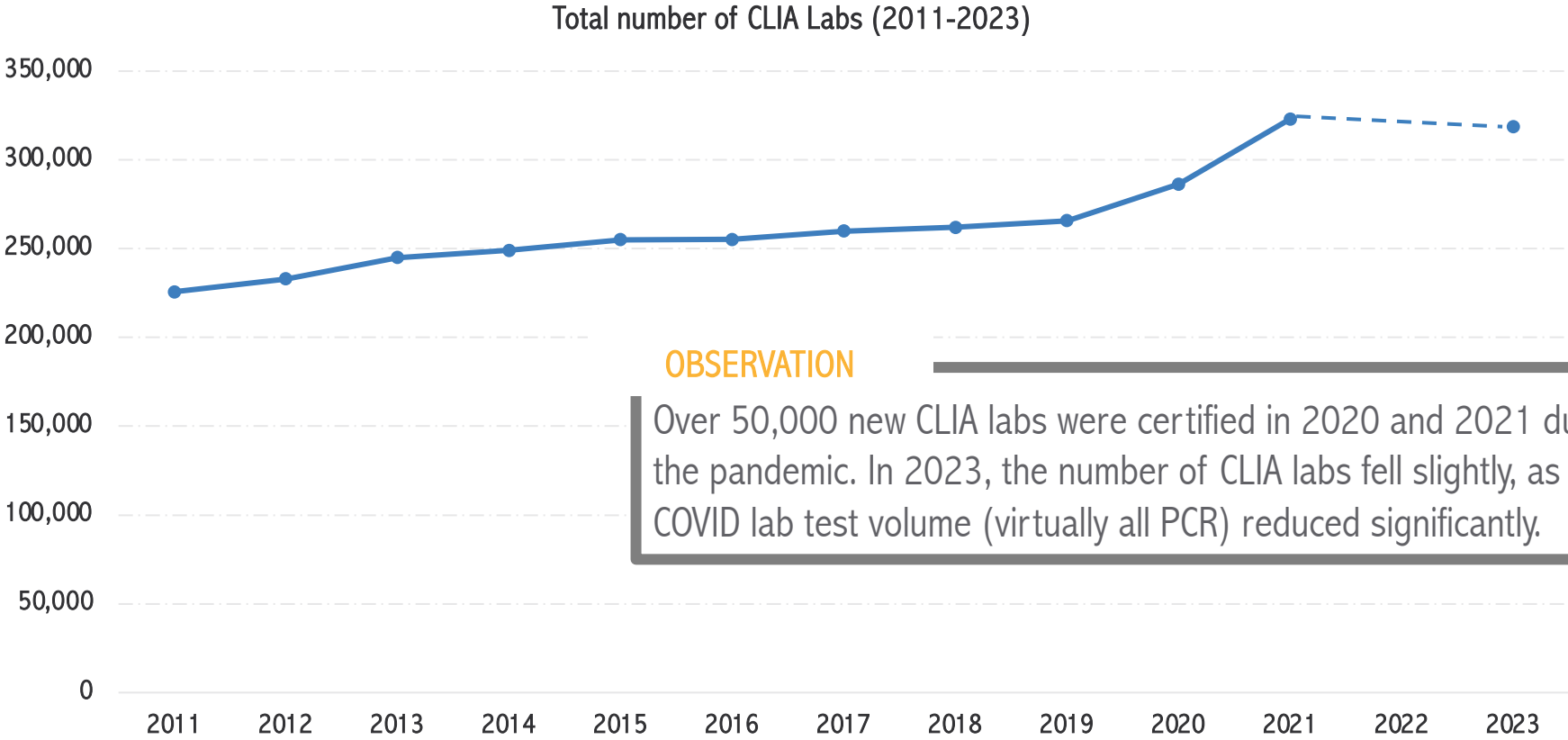
Laboratory Volume Index: 2019 - 2023



Clinically Available Genomic Tests



CLIA Laboratory Growth



OBSERVATION

Over 50,000 new CLIA labs were certified in 2020 and 2021 during the pandemic. In 2023, the number of CLIA labs fell slightly, as COVID lab test volume (virtually all PCR) reduced significantly.

2023 Regulatory and Legislative Update: US

Proposed Rule Aimed at Helping to Ensure Safety and Effectiveness of Laboratory Developed Tests

- *The proposed rule seeks to amend the FDA's regulations to make explicit that IVDs are devices under the Federal Food, Drug, and Cosmetic Act, including when the manufacturer of the IVD is a laboratory.*
- *Along with this amendment, the FDA is proposing a policy under which the agency intends to provide greater oversight of LDTs, through a phaseout of its general enforcement discretion approach to LDTs.*

New Approach to Provide Greater Transparency Regarding Minimum Performance Characteristics for Oncology Drug Tests

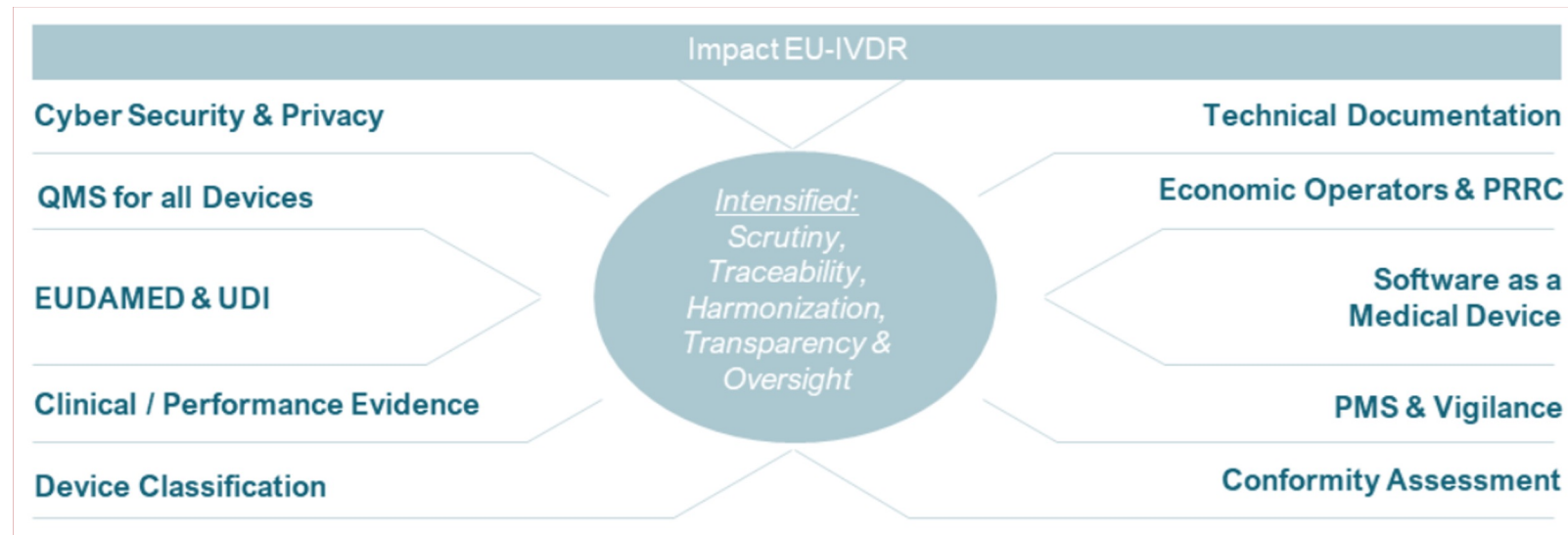
- *FDA is piloting a new approach to provide greater transparency regarding minimum performance characteristics that certain tests for certain oncology drugs should meet*
- *This pilot does not alter the standards for approval of the oncology drug products or for marketing authorization of the corresponding companion in vitro diagnostics*

Translational Coverage for Emerging Technology (TCET)

- *The proposed program updates and advances 2021's Medicare Coverage of Innovative Technology (TCIT) pathway that was repealed. It was meant to provide expedited access to innovative products through earlier coverage determination.*
- *Issue is whether diagnostics will be included in this initiative*

2023 Regulatory and Legislative Update – EUROPE

- The European In Vitro Diagnostic Medical Device Regulation (EU-IVDR) came into effect in May 2022, replacing the In Vitro Diagnostics Medical Device Directive. This regulation establishes the foundation for ensuring the safe market entry and maintenance of In Vitro Diagnostic Devices (IVDs)
- Navigating the entire certification process may extend over 18-24 months, and possibly longer.
 - 2023 revealed that the process of obtaining CE marking for IVDs can be lengthy and intricate
 - The duration hinges on: Current status / Assigned risk class / Maturity of technical documentation and more
 - Stricter requirements introduced affect many functions within an organisation, especially those related to:



EU IVDR Roll-Out Disrupting the Global IVD Industry



PLATOMICS

24,000 CE devices
certified by 2026

May 26th, 2022

May 26th, 2024

May 26th, 2026

May 26th, 2028

For Manufacturers CE Devices

IVDD
self-certification

IVDD self-certification valid

- Post Market Surveillance
- Vigilance
- Registration

IVDR in force for class C devices

For Diagnostic Labs LDT* Devices

(*Lab Developed Test)

self-certification

GSPRs
(General Safety and Performance
Requirements)

200,000 IH Tests
must comply

TECH DOC, QMS, PMS

Labs must prove
equivalence of
IH-tests

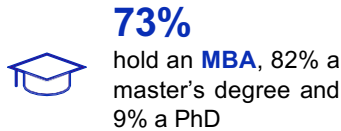
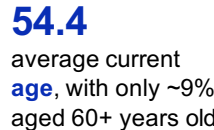
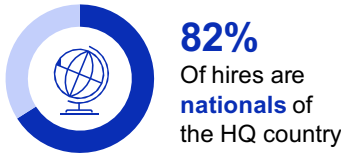
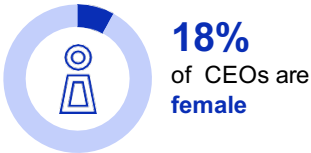
LDT's not conforming to
IVDR now banned

The Current Diagnostics *Private* Company CEO Landscape

Today's private company Diagnostics CEOs are typically external appointees with a commercial background and diagnostics background

Demographics & Appointment

There has been high turnover in the top role, and the majority were external appointments



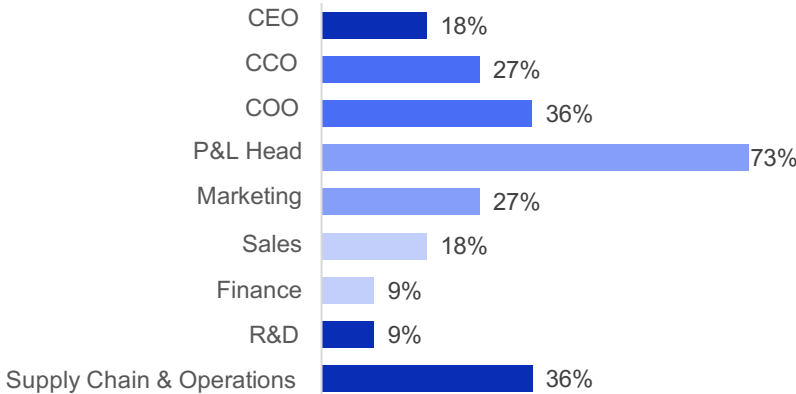
Private & Confidential

Experience

82% of CEOs have prior experience in Diagnostics and most commonly hail from a commercial background



Prior functional experience

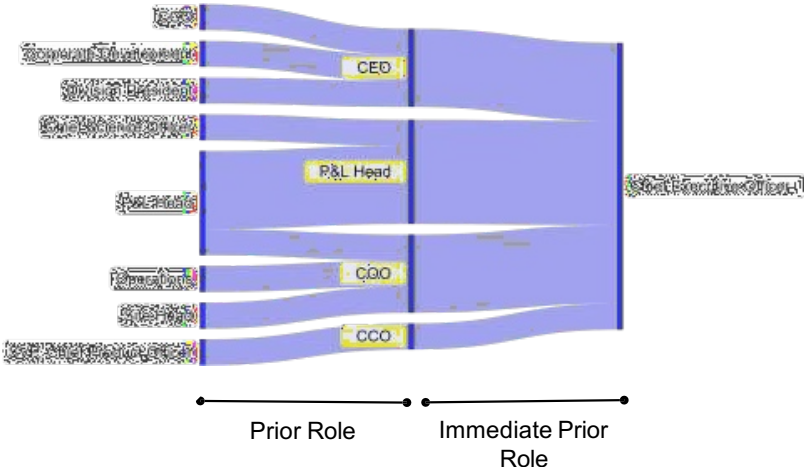


Career & Position

The majority of executives have a commercial background, with most serving as P&L leaders



Career pathway



Source: RRA analysis of CEOs at top 11 private Diagnostic companies (standalone and divisions) based on 2024 revenue headquartered in Europe and the US, Feb 2024

The Current Diagnostics *Public* Company CEO Landscape

Today's public company Diagnostics CEOs are typically internal successors with a commercial background

Demographics & Appointment

There is a lack of gender diversity in the top role, and over half of appointees were internal successors

Among the major public diagnostic companies there are **no female CEOs**



72% Of hires are **nationals** of the HQ country



52% were **internal successors** into the CEO position

55.1 average current **age**, with only ~14% aged 60+ years old

42% were **appointed** in the **last 2 years**, and **76%** in the last 5 years



33% hold an **MBA**, 38% a master's degree and 28% a PhD

Private & Confidential

Experience

91% of CEOs have **prior experience in Diagnostics** and most commonly hail from a commercial background



90% have **broader MedTech experience**

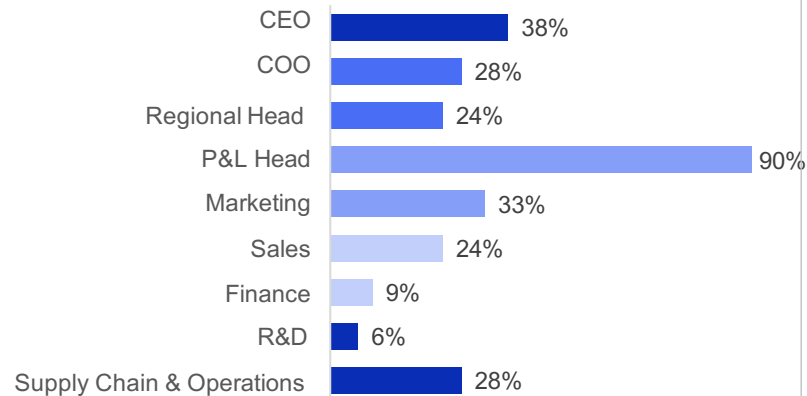


24% have a background in **biopharma**



6% have **industrial/natural resources experience**

Prior functional experience



Career & Position

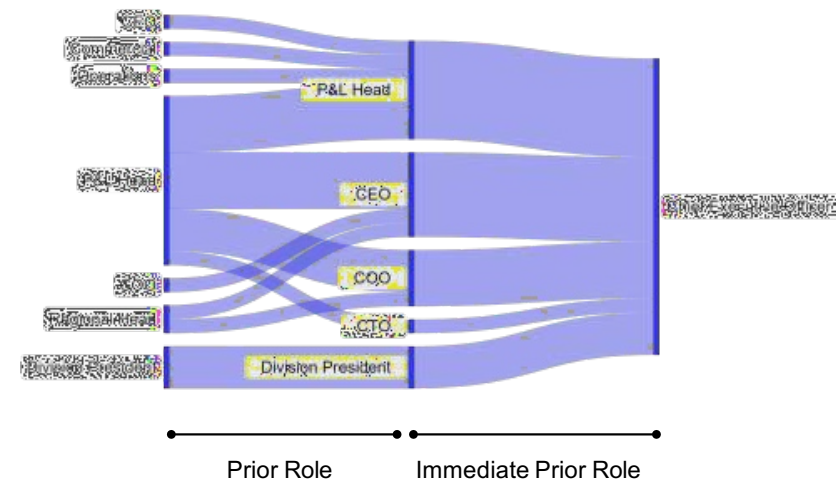
The majority of executives have a commercial background, with most serving as P&L leaders



4.2 years the average role **tenure**, with company career track of **8.5 years**

5% Are **lifers** who have been at their current company their entire career

Career pathway



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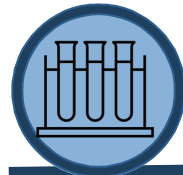
- Important Trends for Innovation in Diagnostics

Important Trends for Innovation in Diagnostics



AI in Diagnostics

As with all industries, 2023 was a critical year for the forward movement of AI in diagnostics. AI will enable the ability to combine data from multiple diverse sources / modes: the new pan-omics.



Liquid Biopsy

Liquid biopsy, slowly becoming standard of care in Minimal Residual Disease (MRD) and Multi-Cancer Early Diagnosis (MCED) tests will expand beyond blood and into non-oncology areas.



Multi-Omics

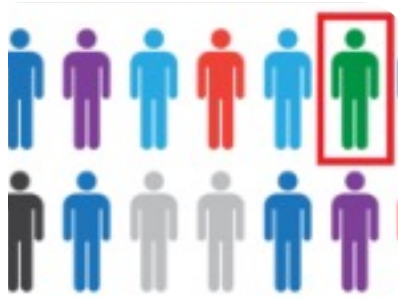
Multi-omics integrates diverse high-throughput technologies (genomics, transcriptomics, spatial biology, proteomics, etc.) for a comprehensive exploration of biological data dimensions.



New Sample types

A broader set of analytes continued to gain momentum, including tears, small-volume blood, sweat, gait, acoustics and other biometrics enabling future innovation and decentralization.

Artificial Intelligence: Moving from Imaging to All Diagnostics



Clinical Trial Patient Selection



Patient Recruitment



Pre-Analytic



Analytic



Patient Cohort Analysis



Integrating Multiple Data sources including wearables



Adverse Event Reporting



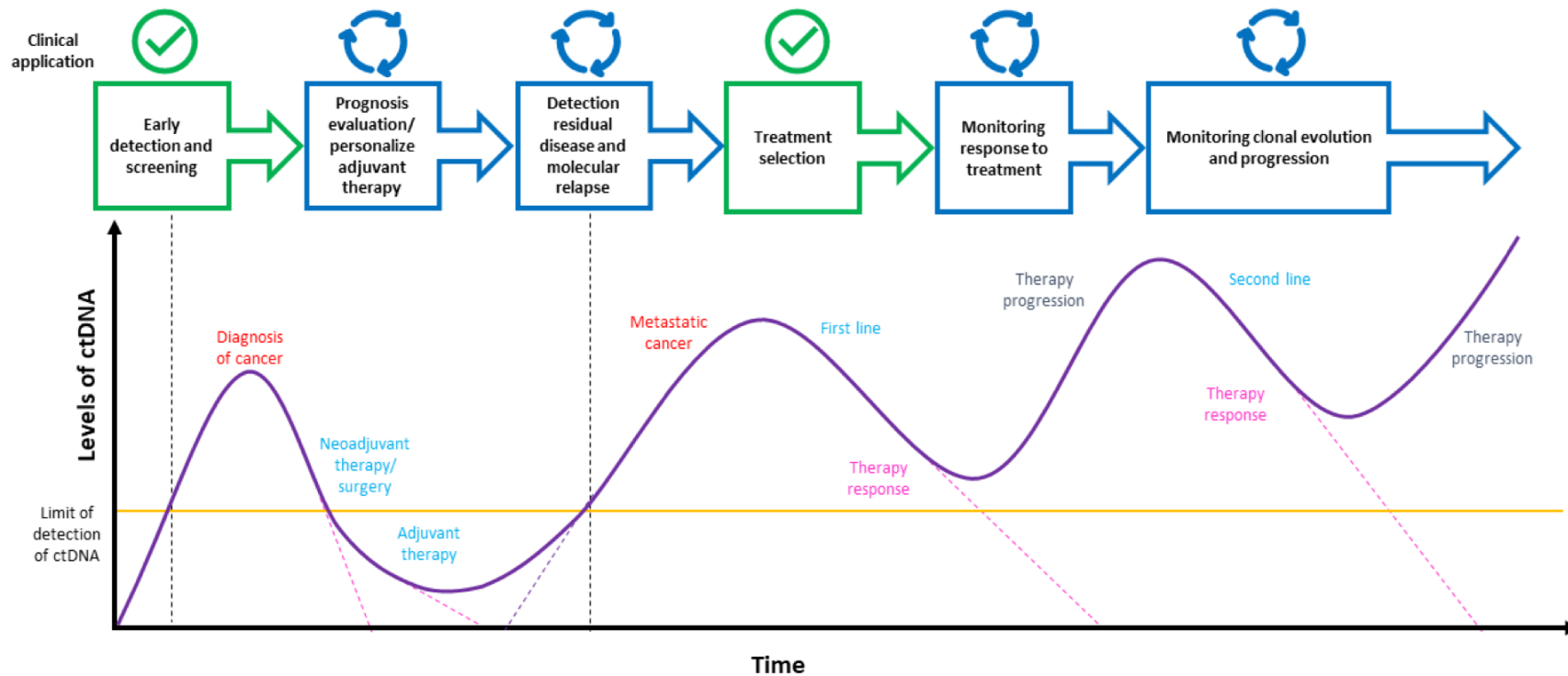
Report Generation

Liquid Biopsy: MRD and MCED

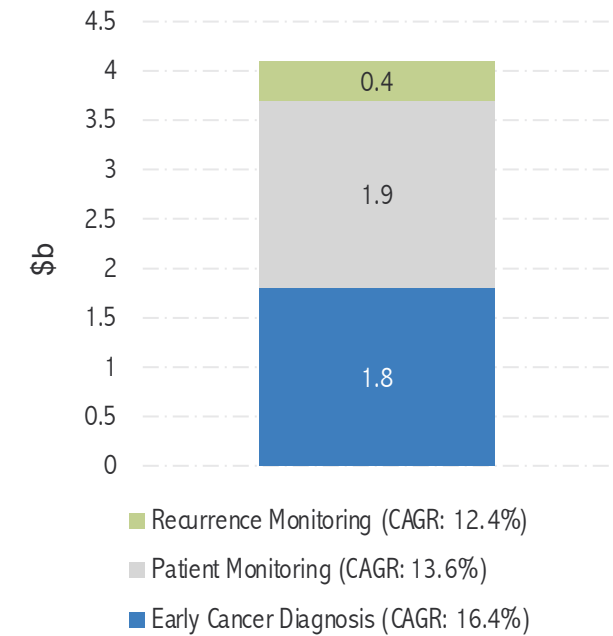
Today: Blood & Cancer. Tomorrow: New Sample Types & New Diseases



- Liquid biopsy emerged as powerful tool for real-time profiling of cancer genomes. Its minimal invasiveness: perfect for tailoring oncological decision-making
 - MRD: Disease Monitoring with Minimum Disease Testing
 - MCED: Multi-Cancer Early Diagnosis



Liquid Biopsy Market by Application (2023)

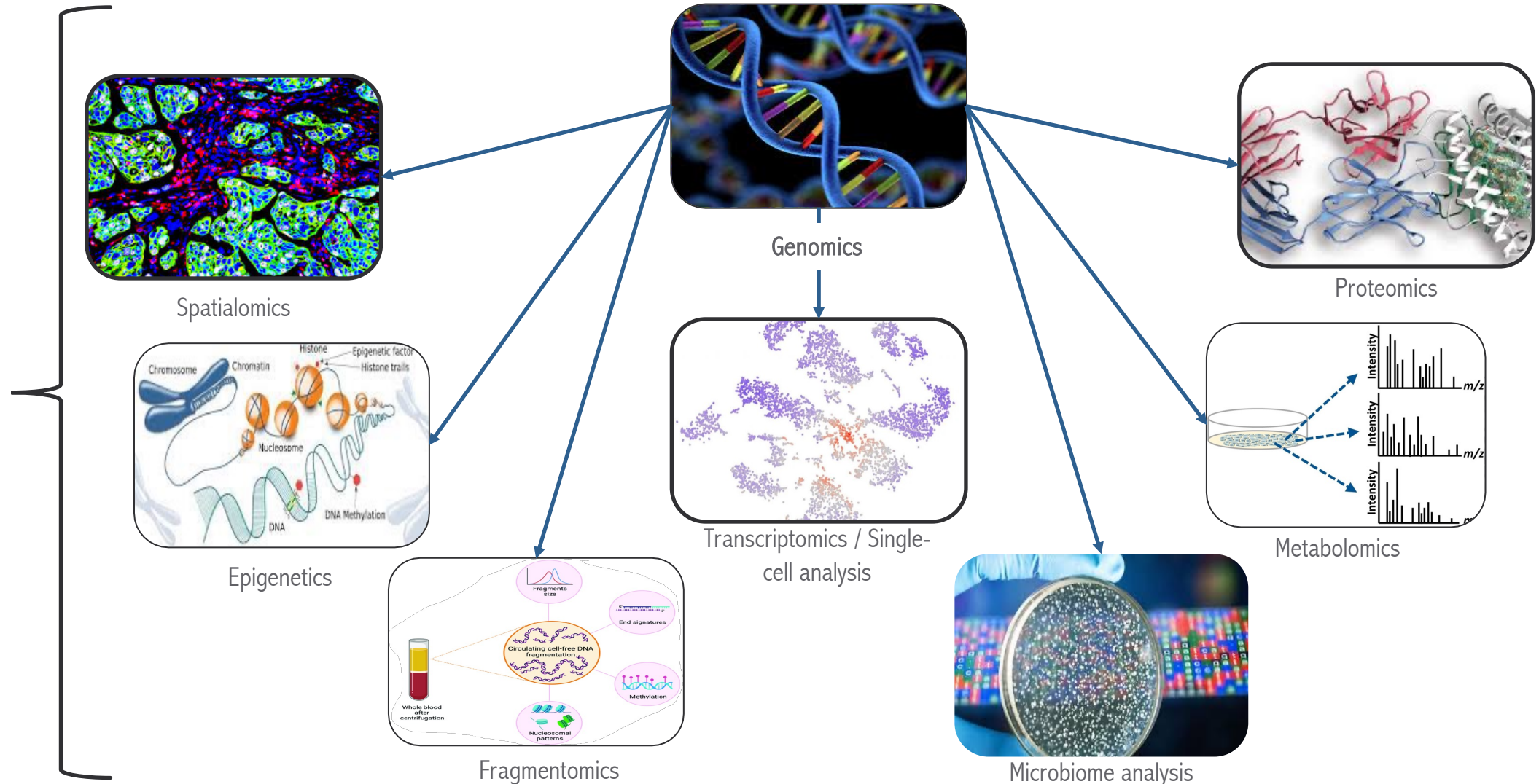


Multi-Omics: Genomics was just the start.

Multiple advanced technologies provide integrated approach

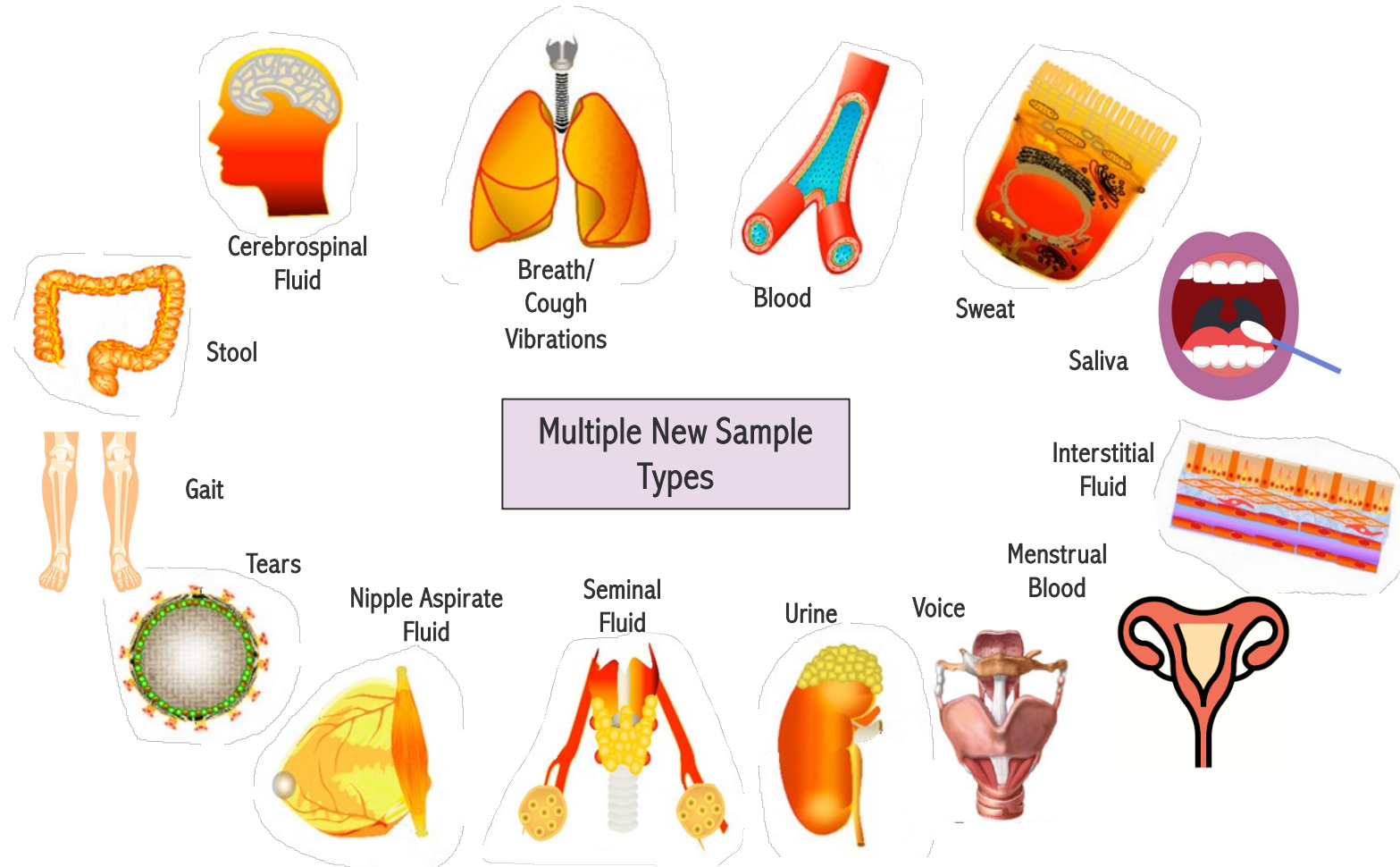


AI enhancement



New Less Invasive Sample Types:

Enabling Decentralization including home sampling & lowering cost



Acknowledgements: Thank you to the following for their insights and contributions

Illumina Ventures
Arnaud Autret, Nick Naclerio, Charles White



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Michael Donovan, Yassine Dguidegue, Samiha Sahraoui

Health Catalysts Group
Grace Gegenheimer



Concert Genetics
Gillian Hooker & Katri Gilbert

Leavitt Partners
Ralph Hall

EVERCORE



Deloitte
Rupal Desai, Chris Park, Erich Sachse

Personalized Medicine Coalition
Daryl Pritchard



Evercore
Bernhard Sakmann, Ashley Szporka

Russell Reynolds
Bob Brousseau



Greybird
Tom Miller

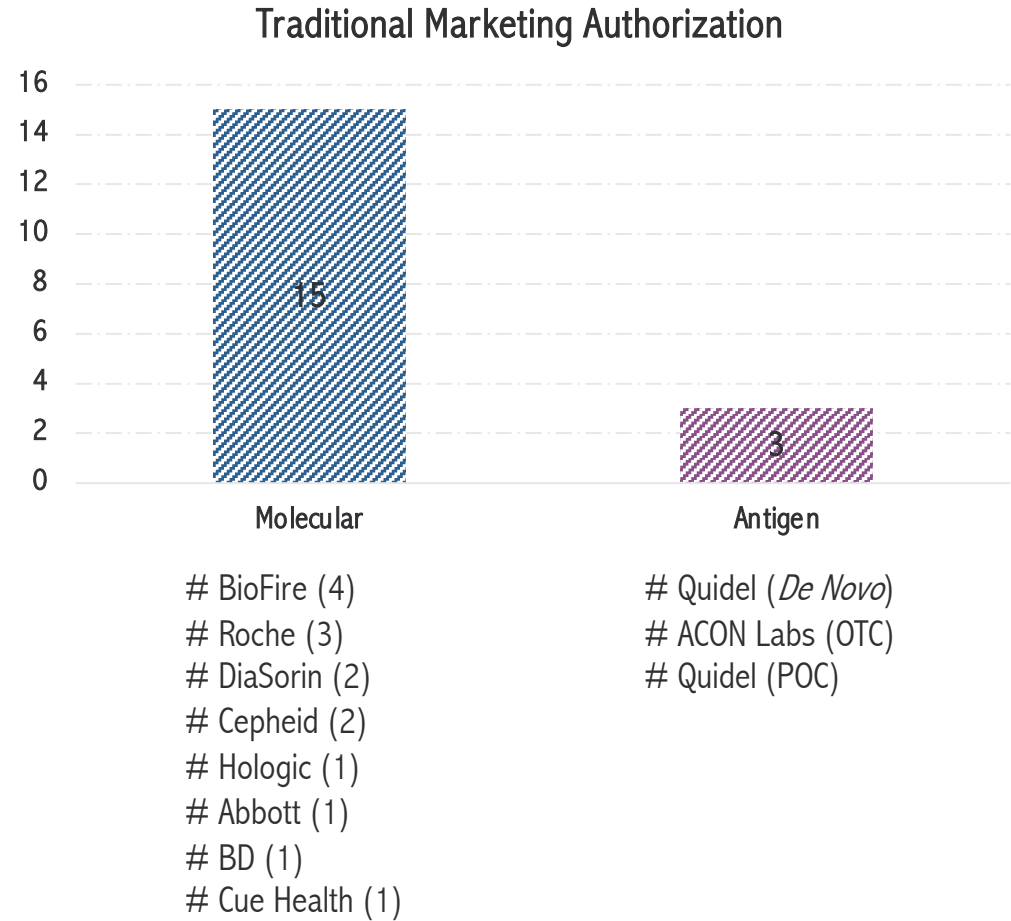
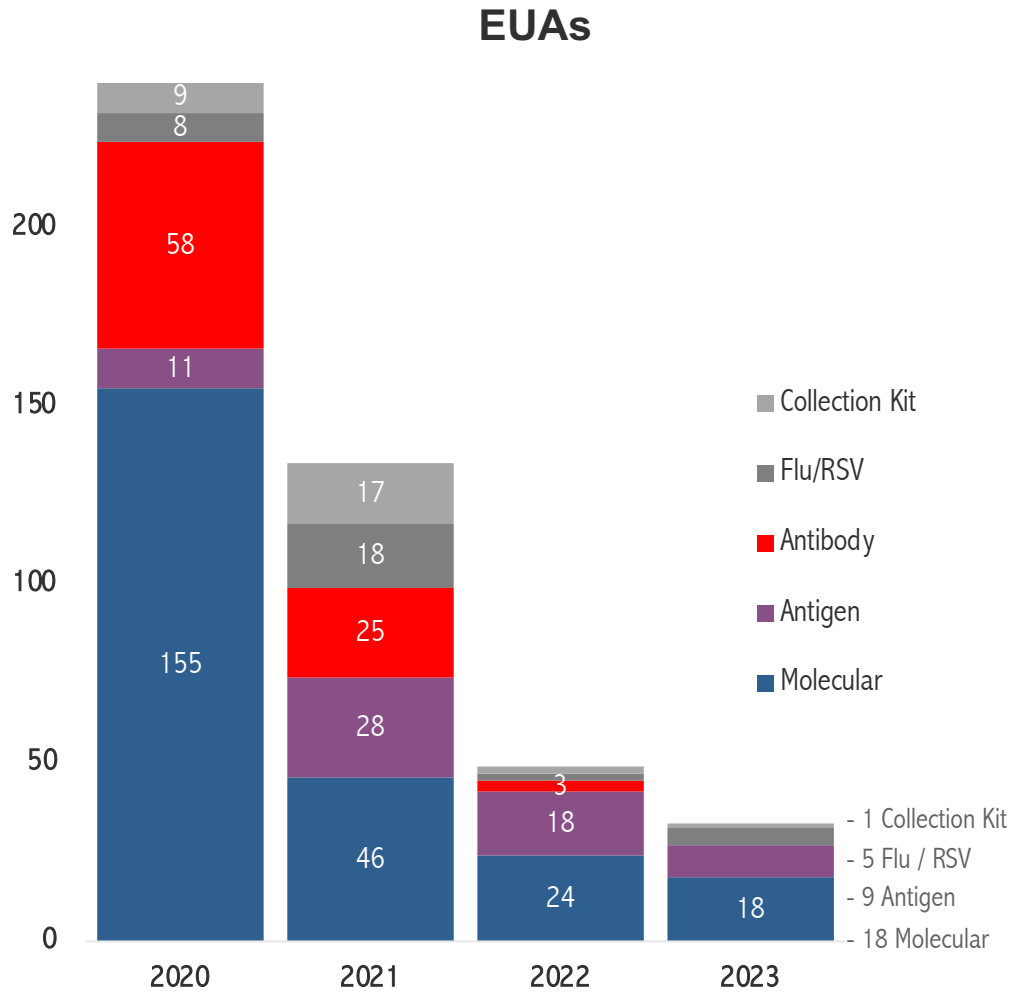
Xifin
Jeff Carmichael, Lale White



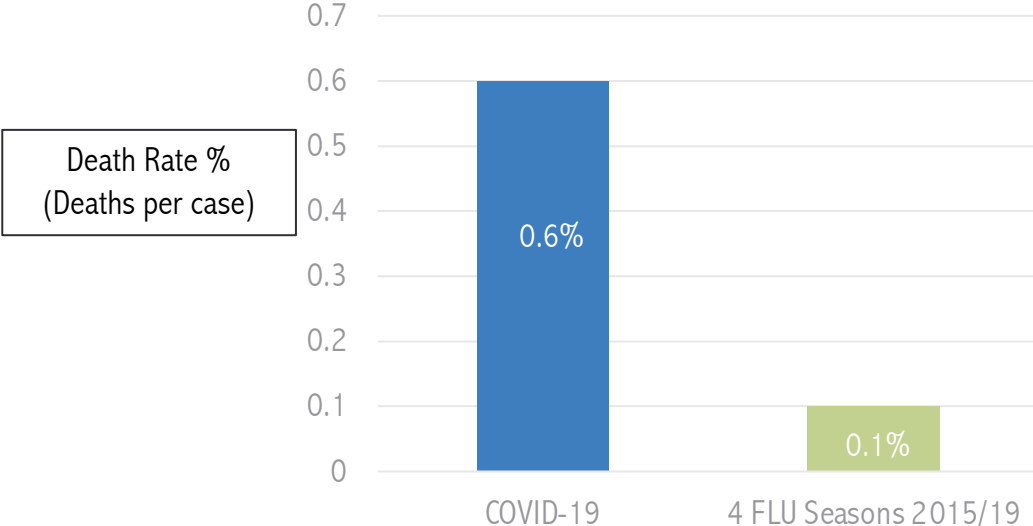
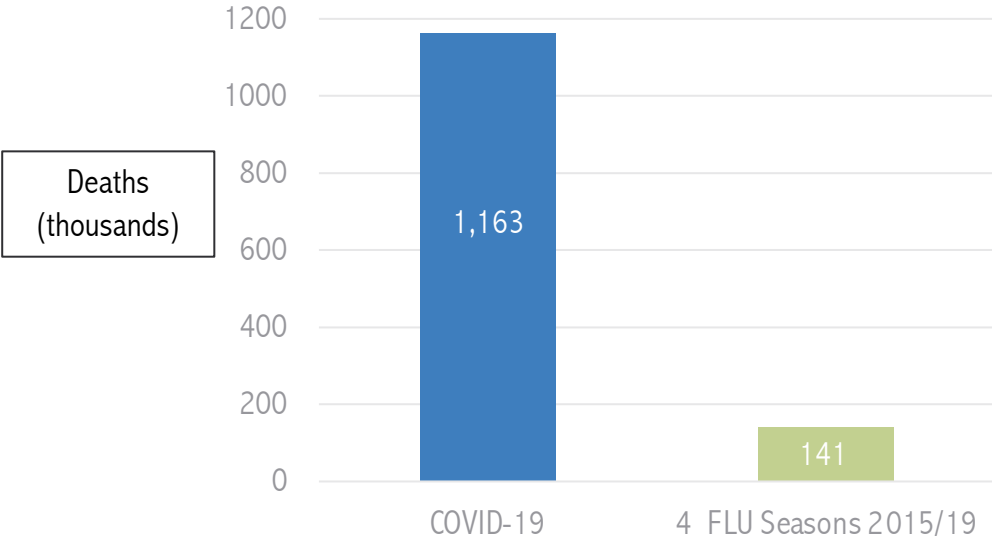
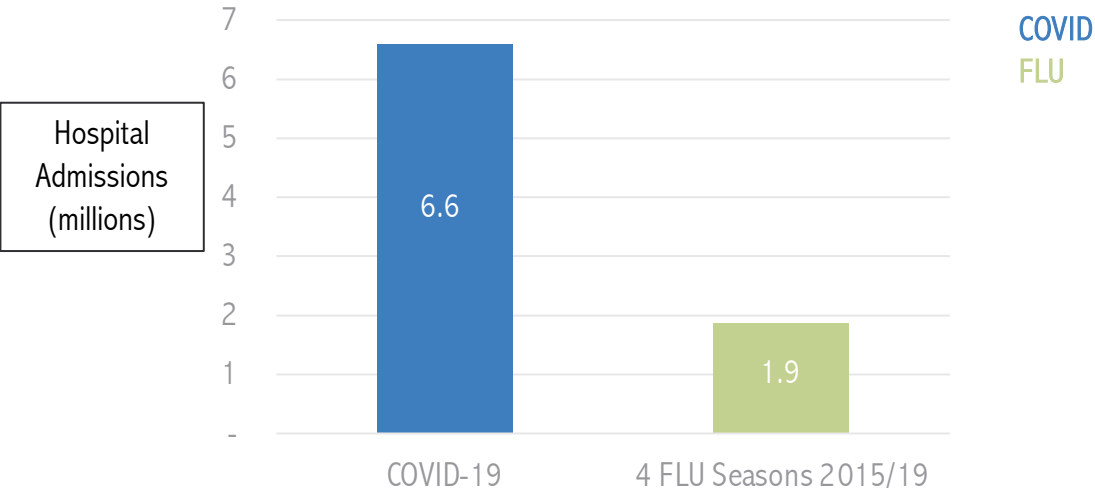
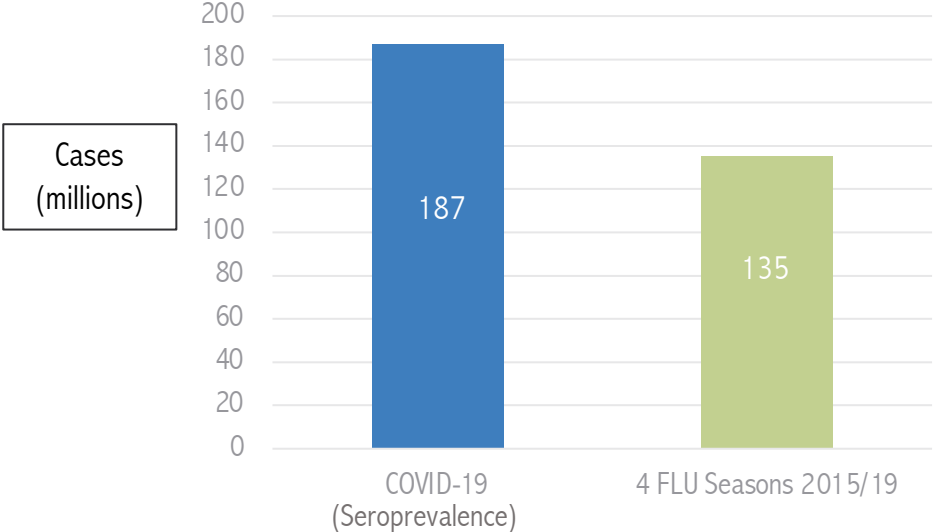
Appendix: COVID & Respiratory Diagnostics

MEGA Dx Index Companies

FDA COVID Test EUAs Issuances: 2019 - 2023

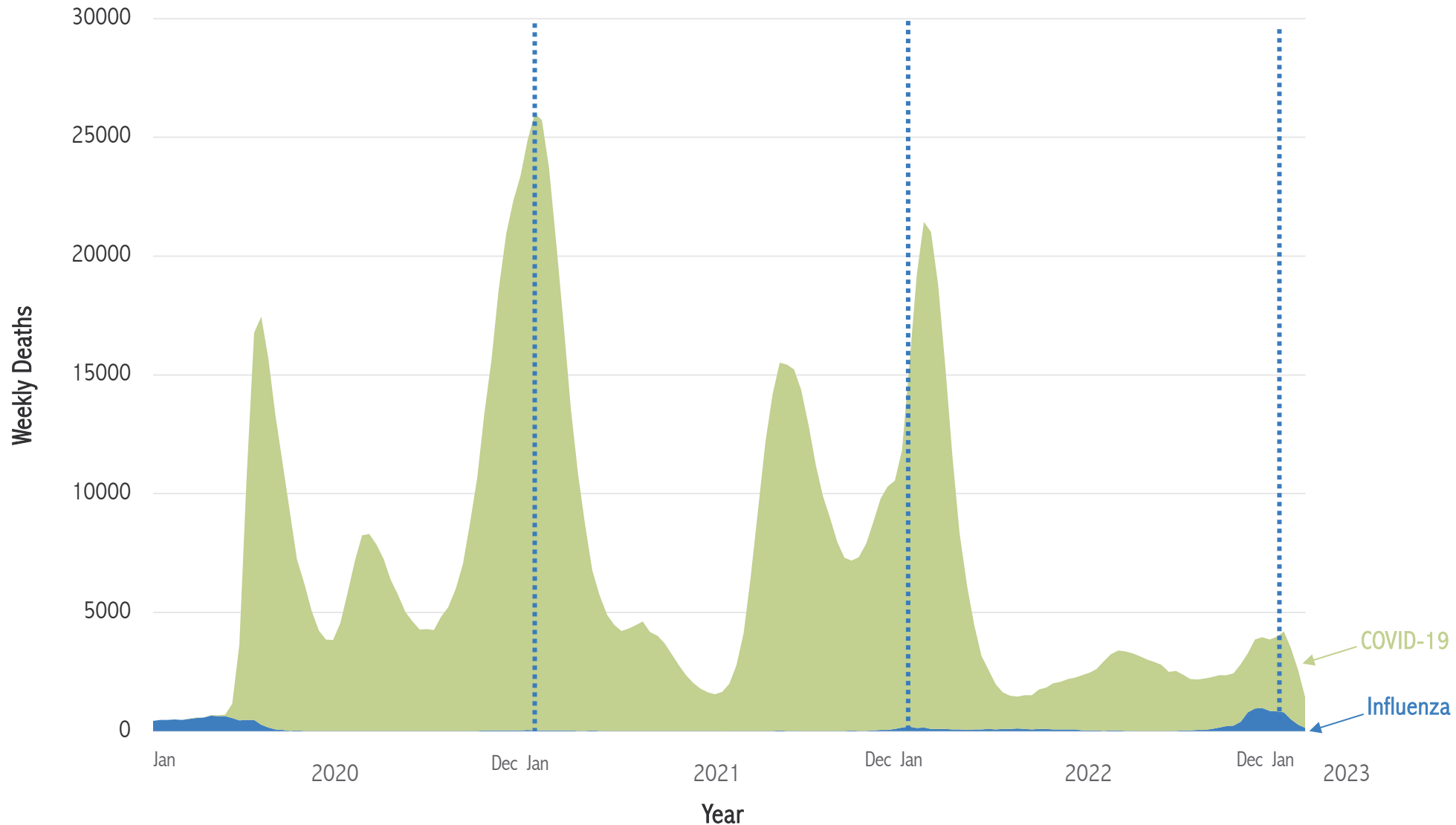


COVID -19 vs. Flu (Cumulative Four Flu Seasons: 2015 - 2019)



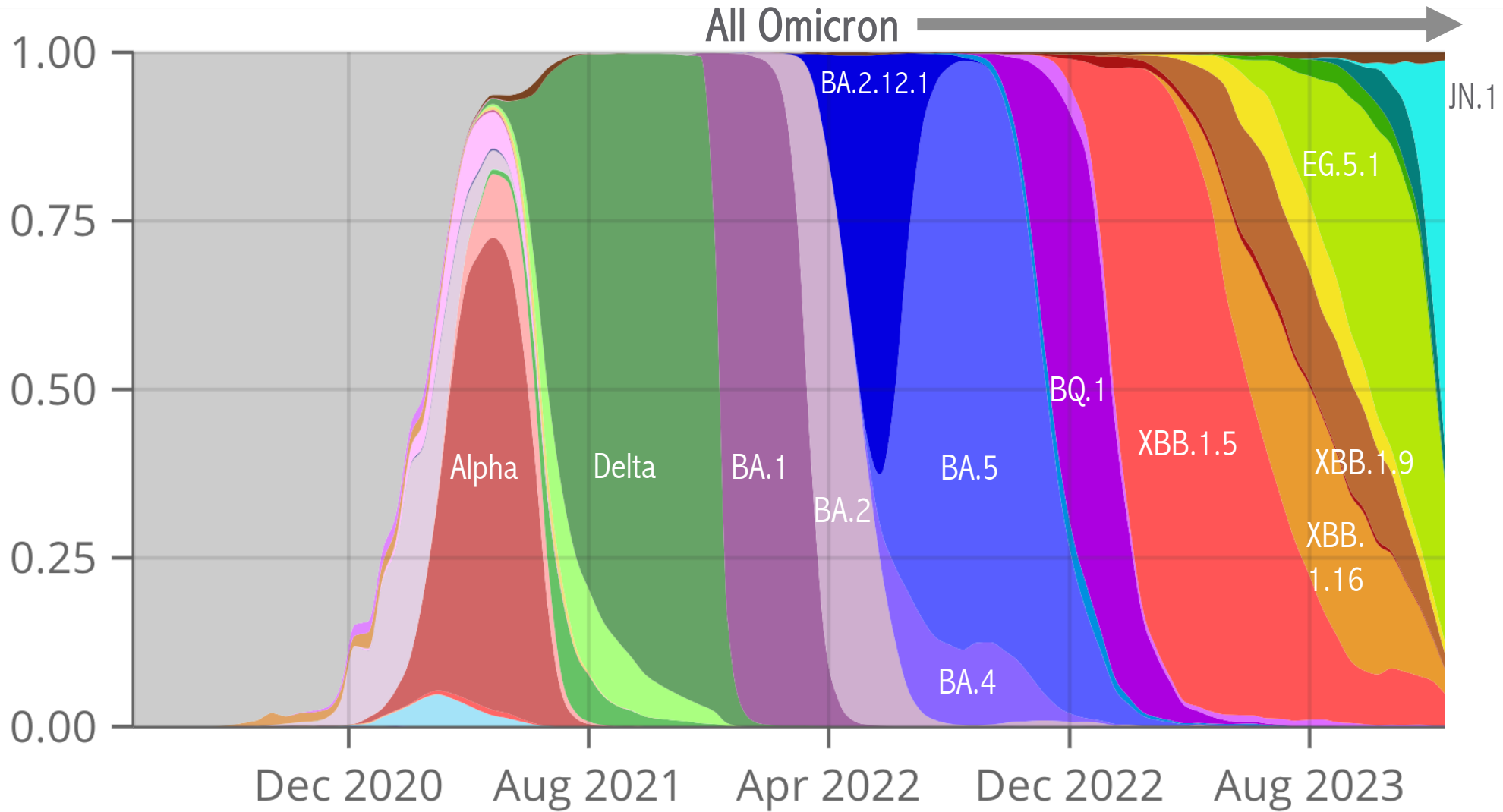
33 Source: COVID seroprevalence; CDC COVID data tracker; CDC flu seasons. Accessed 1/4/24

COVID -19 vs. Flu Deaths



34 Source: CDC FluView accessed 2/7/23

COVID Variant History of the US: 2020 - 2023



The MEGA Dx Index Explained

- MEGA Dx Index is a database and an associated index of changes in the market value of the most inclusive collection of public companies that participate in the clinical in-vitro diagnostic industry worldwide:
 - 135 public companies tracked during 2023: 81 headquartered in the US, 21 in China, and 33 elsewhere
 - Bias toward inclusion: many large Dx participants have most of their revenues outside clinical diagnostics.
 - The MEGA Dx index includes the proportion of their market value based on the proportion of diagnostics revenues to total revenues (e.g. 31% of Roche; 21% of Agilent). It does not value segments independently (due to circularity).
 - Companies are included for entire year if they were public for any month of that year (value introduced or revised for all public/private events: IPOs added (none in 2023); mergers and acquisitions; bankruptcy; etc.
 - Companies included in MEGA Dx index; diagnostic revenue proportion; and currency rates are revised at the beginning of each calendar year and held fixed for the full year.

MEGA Dx Index: Companies included in Index

More than \$1 billion in 2023 revenue

Abbott
Agilent
Beckton Dickinson
BioMerieux (Euro)
Bio-Rad
Da An Gene
Danaher (Cepheid, Beckman Coulter, Leica, Radiometer)
Dian Diagnostics Group
DiaSorin SpA(Italy)
Eurofins Scientific
Exact Sciences
Healthineers Siemens AG
Hologic
HU Group/Miraca Holdings/Fujirebio
Illumina
LabCorp
Perkin Elmer (now Revvity Inc.)
Qiagen
Quest
QuidelOrtho
Roche
Runda Medical Technology Co Ltd
SD BioSensor
Sonic Healthcare
SYNLAB
Sysmex
Thermo Fisher

10x Genomics
23andMe
Accelerate Dx
Adaptive Biotechnologies
amoy dx
Angle PLC
AnPac Bio-Medical Science Co Ltd
Autobio Dx
Beijing Strong Biotechnologies
BGI Genomics Co Ltd
Bioaffinity Technologies (2022 IPO)
Biocartis (Belgium)
Biocept, Inc.
Biodesix, Inc.
Biomerica inc
BioNano Diagnostics
BioSino Biotechnology and Science
Biosynex
Bio-Techne (was Techne)
Biovica
BluJay Diagnostics
Burning Rock Biotech Ltd
Cardio Diagnostics (2022 IPO)
CareDx Inc
Castle Biosciences
Cellavision AB
Centogene NV

Less than \$1 billion in 2023 revenue

Chembio DX
CoDiagnostics
Cue
DermTech
Diaceutics PLC
Dirui Industrial
Dr Lal PathLabs
EKF Diagnostics Holding PLC (UK)
Enzo Biochem
Epigenomics (Germany)
EuroBio Scientific (Diaxonhit)
Exagen
Fulgent Genetics
GeneDx (Sema4/CM Life SPAC)
Genetic Signatures
Genetic Technologies Ltd (Australia)
Genetron Health
Genomic Vision (France/Euro)
Getein Biotech
Ginkgo/Soaring Eagle (SPAC)
Grifols
Guardant
HTG Molecular Dx
Hyribio Biotech Co Ltd
Immunovia
Inoviq (Sienna IPO merged into Innoviq)
IntegraGen

Interpace Diagnostics
Invitae
Leadman Biochemistry Co Ltd
Lucid Diagnostics
Lucira Health
Lumira Dx
Lumos Diagnostics
Maccura Biotechnology
Mainz Biomed
MDX Health (Belgium) ADR
MedicalSystem Biotechnology
Medmira (Canada)
Myriad Genetics
Nanostring
Natera
Nautilus/Arya (SPAC)
Navidea Biopharmaceuticals, Inc
NeoGenomics
OncoCyte (Spin out of Biotime)
OpGen, Inc
Opko Health (incl. BioRef Labs)
OraSure Technologies
Oxford BioDynamics
Oxford Nanopore
Pacific Biosciences
Pacific Edge (New Zealand)
Personalis

Precipio (was TBIO)
Prenetics (2022 IPO)
ProMIS Neurosciences
ProPhase Labs
Proteomics International Laboratories Ltd
Psychemedics Corp
Quanterix
Renalytix AI
Senseonics
Sera Prognostics
Shanghai Kehua Bioengineering
Singular Genomic Systems, Inc
Sinocare (Shenzhen, China)
Snibe (Shenzhen New Industries Biomedical Engineer)
Somalogic
SurModics Inc.
T2 Biosystems
Talis Biomedical
Tellgen
Thalys Medical Technology Inc.
Theradiag
Trinity Biotech Plc (Ireland)
Universal Biosensors
Veracyte
VolitionRX Ltd (Belgium)
Wondfo Biotech
Youngene Health