EXECUTIVE INSIGHTS

Diagnostics and Research Tools: Outlook and Industry Trends in 2023

For the diagnostics and research tools industry, 2022 was a year of peaks and valleys. We witnessed a marketwide retreat from the all-time-high valuations seen in 2021, and a general resetting of expectations for the industry, as the wave of activity fueled by the COVID-19 pandemic subsided.

At the same time, fundamental megatrends and market drivers remained as strong as ever, with impressive clinical data reenforcing the promise of personalized medicines and advanced therapies. In this *Executive Insights*, L.E.K. Consulting reflects on key evolving trends that are likely to continue having significant impact throughout the industry this year:

- A challenging financial backdrop driving renewed focus on profitability
- Accelerating demand driven by continued growth in precision medicine and biotherapeutics
- The ongoing evolution of applications that leverage high-resolution advanced tools
- Intensifying competition in the battle for $100 whole genome sequencing

A challenging financial backdrop is driving renewed focus on profitability

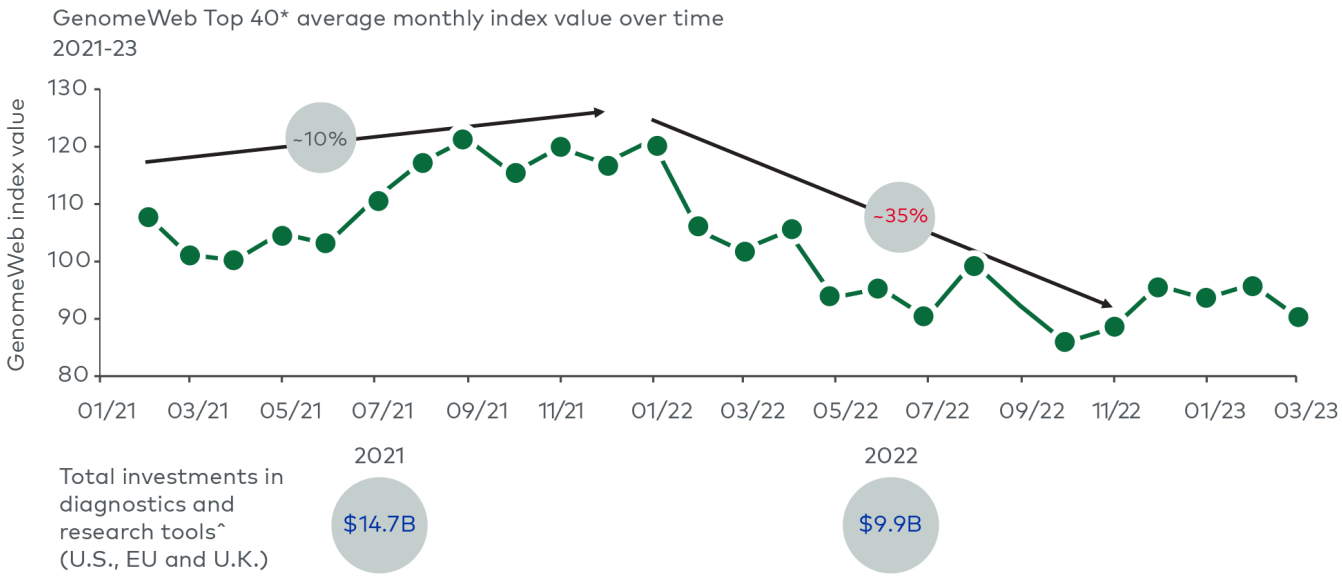
Driven by the challenging macroeconomic environment, companies are focusing on controlling cash burn and driving toward profitability.

Financial markets are creating near-term headwinds for the sector. Public market sentiment toward the sector has shifted as companies largely failed to meet the unrealistic expectations set by outsized performance during the COVID-19 pandemic.

The all-time-high valuations seen in 2021 continued to correct significantly throughout 2022; for example, GenomeWeb's index measurement of the top 40 tools and diagnostics companies declined by an average of roughly 35% in 2022 (compared with an approximately 18% loss for the S&P 500 and a roughly 9% decline in the Dow Jones Industrial Average), with half of tracked companies losing more than 50% of their market value (see Figure 1).[1]

Private financing also saw a significant decrease in 2022, with total dollars invested in research tools and diagnostics down from $14.7 billion in 2021 to $9.9 billion in 2022 (an approximately 35% year-over-year decrease).[2] However, seed/series A total investment dollars increased about 35% year over year, reaching $1.6 billion, indicating that investors may be focusing on early-stage opportunities while they wait for macro conditions to improve.

Figure 1
GenomeWeb Top 40 index versus diagnostics and research tools investment trend



*GenomeWeb top 40 includes the following companies: ADPT, A, BDX, BLI, BIO, BRKR, BNR, CDNA, CSTL, HLTH, DHR, EXAS, FLGT, DNA, GH, HOLX, ILMN, NVTA, VIVO, MYGN, NSTG, NTRA, NEO, PACB, PSNL, PKI, QGEN, QTRX, QSI, QDEL, SEER, SLGC, SOPH, TMO, TWST, VCYT, WAT, ME, TXG
^Diagnostics/tools includes diagnostic tests, diagnostic analytics and R&D tools (e.g., research equipment/services for biopharma)

As a result of these trends, companies have shifted from a growth-at-all-costs approach toward controlling opex and are striving for profitability. In recent years, when profitability was not a major focus, emerging companies focused on scaling topline revenues and could preserve their cash runway — with ample access to fundraising on the promise of disruptive technologies.

Now, financing is more challenging and expensive, market sentiment has shifted, and investors want proof that a business can scale toward sustainable operations. As a result, leading

players are touting significant strides toward profitability and have repeatedly touted profitability and expected timing as key goals to investors in quarterly earnings calls.

One example is Exact Sciences, which has advanced its timeline to profitability and now expects to reach this milestone by the end of 2023.[3] For players further away from profitability, however, restructuring and layoffs have increasingly been used as tools to trim opex and maximize their cash runway, given reduced access to financing. This shift has resulted in a broad set of companies across the diagnostics and research tools space (e.g., Adaptive Biotech, Personalis, Sema4, NanoString, TwinStrand, Illumina, Invitae, 10X Genomics and many others) reducing their workforce.

While the development of disruptive research tools and diagnostic technologies will continue, the financing trajectory and growth rate of small, early-stage private companies may differ significantly compared with the past five years because of these near-term economic headwinds.

Accelerating demand driven by continued growth in precision medicine and biotherapeutics

The success of molecular testing and corresponding maturation of precision oncology is beginning to drive precision medicine into new therapeutic areas. Molecular diagnostics (e.g., clinical next-generation sequencing (NGS)) have dramatically changed how oncology patients are managed. Molecular testing itself has also evolved from single tests looking at small panels of mutations to inform therapy selection for late-stage patients to a series of longitudinal diagnostics that inform management from presymptomatic (screening) through to initial diagnosis (prognosis and risk assessment), the adjuvant setting (testing for minimal residual disease), and monitoring for recurrence.

In parallel, molecularly defined patient subgroups have unlocked pan-cancer approvals (e.g., Viktravi for patients with NTRK mutations, regardless of tissue of origin) and challenged tumor site-specific treatment paradigms. With the growing evidence of the value of precision medicine in terms of total cost of care and patient outcomes, precision medicine principles are being applied in disease areas beyond oncology, including epilepsy, rheumatoid arthritis and depression, and will require entirely new molecular tests and predictive signatures to inform optimal patient management in these large, chronic indications.

Approvals of novel, disease-modifying therapies underscore the need for advanced diagnostics to effectively manage chronic diseases of large populations

The recent approvals of Biogen's Aduhelm[4] (aducanumab) and Eisai/Biogen's Leqembi[5] (lecanemab-irmb) gave patients the first potential therapies that may treat the root cause of

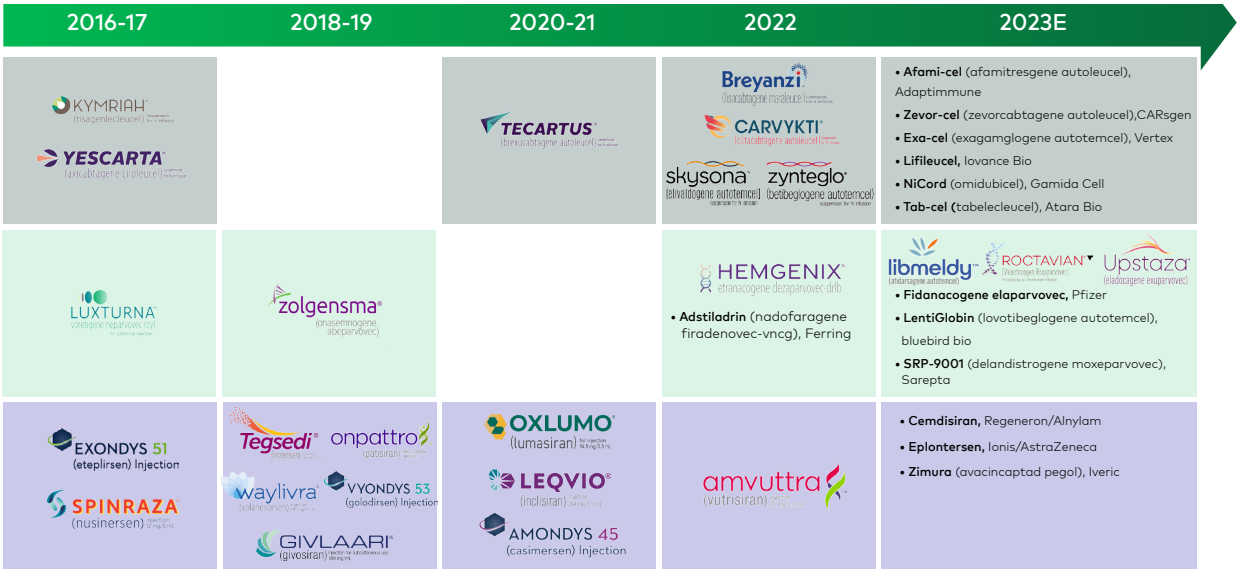
neurodegeneration observed in Alzheimer's patients. However, these approvals also underscored the significant need for better tools to identify patients early and stratify subpopulations,[6] both to identify patients most likely to respond to therapy and to identify those who may be at elevated risk of severe adverse events (e.g., amyloid-related imaging abnormalities.[7]

Continued acceleration of advanced modalities (cell, gene and nucleic acid therapies) will require novel bioproduction equipment and analytical tools

Advanced biologic therapies reached several milestones in 2022, with the first wave of CAR-T cell therapies gaining approval for second-line use in hematologic indications, approval of two new gene-modified cell therapies from bluebird bio, the approval of a new viral vector gene therapy (Hemgenix for hemophilia B) from uniQure, and compelling data from the RNA therapeutics pipeline (e.g., Moderna and Merck personalized cancer vaccine met the primary phase 2b efficacy endpoint).[8,9]

Advanced therapies are beginning to expand beyond the orphan and oncology indications (e.g., near-curative effect of autologous cell therapies in lupus),[10] and 2023 could see around 15 additional advanced therapeutic Food and Drug Administration (FDA) approvals (see Figure 2). To support development and commercialization of advanced therapies in larger patient populations, advances in tools and bioprocessing will need to significantly bend the cost curve of these complex and expensive-to-manufacture drugs.

Figure 2
Timeline of advanced therapy medicine launches in the US



*mRNA vaccines are excluded; launch dates are based on Food and Drug Administration (FDA) approval dates or expected FDA approval dates
Source: FDA; Evaluate Pharma; ARM State of the Industry Briefing 2023

Similarly, novel tools will be required to define and measure critical quality attributes of advanced biotherapeutics for quality control and release testing. Looking ahead, industry fundamentals are likely to continue to be as strong as ever, with accelerating demand driven by key megatrends in healthcare.

The ongoing evolution of novel applications leveraging high-resolution advanced tools

Rapid development and innovation in tools capabilities will continue to drive novel application development in the R&D, bioprocess testing and clinical diagnostic lab settings.

Tools innovators will continue to move beyond singleomic technologies toward multiomic approaches to better understand complex biology

This trend manifests in both the platform tools and the applications development side of the market. Research tools companies will continue to build flexibility and capabilities for multiomic integration on existing platforms. For example, 10X Genomics' Chromium platform was first adopted as a differentiated cell partitioning solution for single-cell RNA-seq analysis. Now, 10X Genomics has expanded the platform's capabilities to include adjacent workflow steps (e.g., library construction) as well as other "-omics analyses" (immune profiling, ATAC-seq, etc.).[11]

Similarly, diagnostics players are increasingly exploring multiomic approaches for developing more sensitive/specific tests. This is especially true in the multicancer early detection space, where players like Thrive (now part of Exact Sciences) and Freenome are pioneering tests that combine genomics, transcriptomics, proteomics and other biomarkers (e.g., methylation, fragmentomics) in conjunction with machine learning platforms to detect novel cancer signatures in blood.

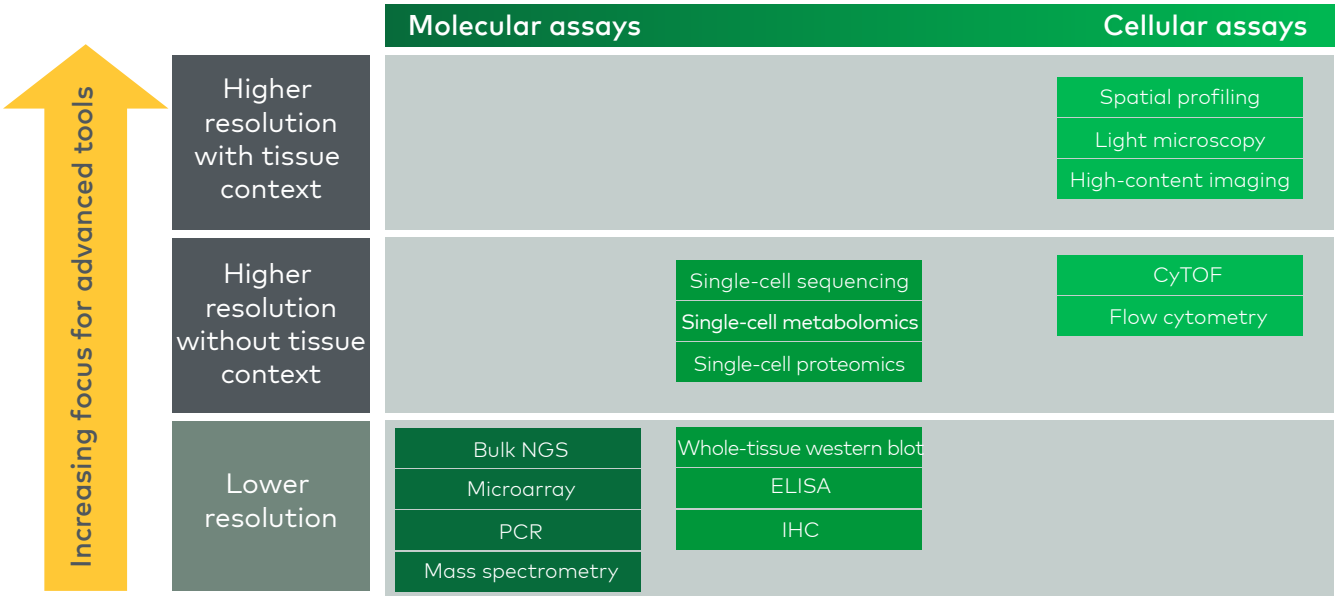
Spatial biology continues to bridge the gap between biomarkers and biological context and is beginning to demonstrate its potential in clinical applications

Historically, the spatial biology space has been segmented by transcriptomics-focused players (e.g., 10X Genomics and NanoString) and proteomics-focused players (e.g., Akoya, Standard BioTools). Now, both 10X Genomics and NanoString are launching "in situ" spatial imaging platforms (Xenium and CosMx SMI, respectively), with plans to combine both transcriptomics

and proteomics capabilities while promising improved resolution, higher throughput and greater plex for proteomics.

These platforms are being used to compare gene and protein expression with the added dimension of spatial resolution throughout a tissue sample, an approach with potential for generating actionable clinical signatures and representative of the broader trend toward higher-resolution outputs for analytical tools (see Figure 3). The leaders in spatial biology are actively pursuing development of clinical applications, with NanoString included in more than 100 sessions and presentations at the American Association for Cancer Research annual meeting in 2022, and Akoya announcing a partnership for developing a companion diagnostic (CDx) for Acrivon Therapeutics' candidate ACR-368.[12]

Figure 3
Map of advanced tools landscape



Note: ELISA=enzyme-linked immunoassay; IHC=immunohistochemistry; PCR=polymerase chain reaction; NGS=next generation-sequencing; CyTOF=cytometry by time of flight
Source: L.E.K. research and analysis

Going forward, multiomics technologies will increasingly seek to tie analytical findings to in vivo phenotype and, ultimately, biological function

The underlying need driving development of the -omics and spatial biology fields is a better understanding of biologic function, with the -omics analyses serving as surrogates for direct measurement of function/phenotype. Toward that end, analysis of live biological systems will become increasingly important, particularly as the FDA and other regulators begin to emphasize moving away from animal models for preclinical development.[13] As such, it's likely that custom cell-based disease models and 3D organoid model systems will be increasingly

important for biopharma R&D, with the market requiring better tools to create, monitor and analyze live biological systems. Further evidence for this trend can be seen in the recent combination of two players with significant capabilities in live cell -omics and functional cell characterization, with Berkeley Light's acquisition of IsoPlexis to form PhenomeX.

Going forward, we anticipate continued development of -omic technologies and acceleration of their uptake in biopharma R&D and clinical testing applications. However, these technologies generate large, complex, high-dimensional data sets, so the future winning players are likely to be those that can successfully reduce friction for data management and bioinformatics analysis and generate near "push button" solutions for higher-volume applications.

Intensifying competition in the battle for $100 whole genome sequencing

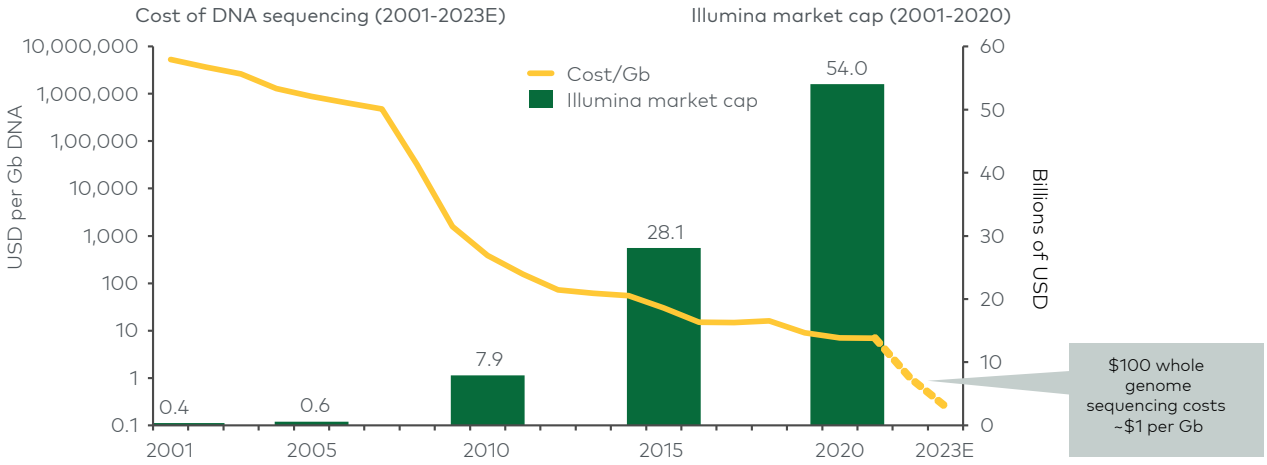
A new wave of competitors will attempt to erode Illumina's market-leading position in the core NGS workflow and further democratize NGS with lower-cost sequencing.

An emerging set of in-class (short-read sequencing) competition will attempt to push the boundaries of low-cost sequencing, as market leader Illumina faces potential patent cliffs for its core short-read sequencing by synthesis technology, whereby the genome is sectioned into small (50-300 base) fragments before massively multiplexed parallel sequencing is conducted by detection of light emitted from incorporation of a labeled base into a growing DNA strand.[14] Ultima Genomics launched from stealth in May 2022 with a flurry of headlines, on the strength of $600 million in funding and a widely touted claim to be "on the way to a $100 whole genome sequence."

Another potential competitor, Element Biosciences, launched its AVITI system in 2022 and emphasized its potential to democratize access to genomics with a low-cost, easy-to-use sequencing platform.[15] Most recently, Complete Genomics (a subsidiary of Chinese NGS player MGI Tech) announced DNBSeq-T20x2, an ultra-high throughput platform promising <$100 human genomes.[16] Illumina has not remained stagnant, however, and in 2022 unveiled its new sequencing chemistry while highlighting its near-term goal of achieving a $200 whole genome sequence.

A key question remains: "What novel applications will lower-cost sequencing unlock?" Historically, the cost of sequencing has been inversely proportional to the level of application development and valuation of genomics players (see Figure 4).

Figure 4
DNA sequencing cost per gigabase (Gb) over time



Note: Market capitalization value shown for last date of respective year
Source: National Institutes of Health (NIH) National Human Genome Research Institute (Wetterstrand KA. "DNA Sequencing Costs: Data from the NHGRI Genome Sequencing Program (GSP)"); S&P Capital IQ

Alternative approaches (e.g., long-read sequencing) may be starting to catch up on cost and accuracy

Long-read sequencing uses larger fragments of DNA to map genomes and benefits from fewer gaps in genome assemblies. Historically, long-read competitors have thrived in the area of de novo sequencing of complex genomes but have struggled to match short-read methods' costs and accuracy, which has tended to limit development of applied use cases for long-read technology (e.g., clinical diagnostics). However, PacBio recently unveiled its new Revio long-read sequencer, which utilizes "HiFi reads" capable of matching the accuracy of short-read methods.[17] PacBio anticipates a whole genome sequence could be generated at 30X coverage for approximately $1,000. Oxford Nanopore, leveraging nanopore sequencing technology, has experienced strong growth (approximately 50% year-over-year revenue increase during 2022), and researchers indicate that their direct measurement of nucleic acids may improve the fidelity of RNA sequencing (i.e., the method obviates the RNA synthesis workflow step) and may enable measurement of epigenic changes beyond today's commonly assessed cytosine methylation.[18]

In the future, the increase in competition may directly impact the economics of sequencing and potentially further democratize access to NGS technology — as well as drive more extensive use in clinical (e.g., genomics for universal newborn screening) and other applied markets (e.g., agricultural biotechnology).

Conclusion

Despite the near-term economic challenges, the core investment thesis for diagnostics and research tools remains as strong as ever. Development of advanced tools will continue, driven by needs underpinning megatrends in healthcare, such as precision medicine and advanced therapeutic modalities. Moving forward, we may see continued consolidation as many players still have significant cash reserves on the balance sheet to effect strategic M&A.

For more information, contact healthcare@lekinsights.com.

Endnotes

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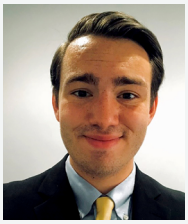
About the Authors

Jeff Holder
Jeff Holder, Ph.D., is a Managing Director and Partner in L.E.K. Consulting's San Francisco office and a member of the firm's Life Sciences practice. Jeff has expertise in the life science tools, bioprocessing, biopharma services and diagnostics space with a particular focus on growth strategy, portfolio planning, new product opportunities and business development support.

Adam Siebert
Adam Siebert is a Managing Director and Partner in L.E.K. Consulting's New York office and a member of the Life Sciences practice. Adam has been with L.E.K. for over eight years, and has experience across diagnostics and research tools, bioprocessing, and pharma services, as well as emerging, mid-cap and large pharma. He has helped a number of clients in the life sciences industry with growth strategy, life cycle management, portfolio optimization and M&A projects.

Tian Han
Tian Han is a Managing Director and Partner in L.E.K. Consulting's Los Angeles office. Tian joined L.E.K. in 2008 and is one of the leaders of the firm's Diagnostics and Research Tools practice, where he specializes in precision medicine, advanced diagnostics, life sciences research tools and advanced therapeutic bioprocessing. He advises clients on corporate and business strategy, product strategy, commercial planning, and transaction support.

Alex Vadas
Alex Vadas, Ph.D., is a Managing Director in L.E.K. Consulting's Los Angeles office, where he leads the firm's Diagnostics and Research Tools practice. Alex joined L.E.K. in 2000 and focuses on diagnostics, research tools and personalized medicine. Within those areas, he has worked with a range of established and emerging clients in the areas of corporate strategy, product strategy, commercial planning and transaction support.



Alex Masset
Alex Masset is a Senior Associate Consultant in L.E.K. Consulting's Boston office and a member of the Life Sciences Enablers practice. Alex has helped numerous clients across precision medicine, diagnostics, life science tools and bioprocessing. He has supported clients on a range of projects, including growth strategy, M&A, partnership strategy, and organization and planning.

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