EXECUTIVE INSIGHTS

Research Tools and Diagnostics: Outlook and Industry Trends in 2024

For the research tools and diagnostics industry, 2023 was a challenging year given the confluence of factors that impacted business performance such as macroeconomic headwinds, continued softness in biopharma funding and the resulting shift in spend patterns for key customers. While many industry players are forecasting limited market growth for 2024,[1] the mix of "green shoots" (e.g., stabilizing the biopharma funding environment, returning optimism in biotech, reversion to typical spending patterns for biopharma customers)[2] and continued headwinds (e.g., persistent high interest rates, continued economic challenges in key geographies such as China) creates uncertainty.

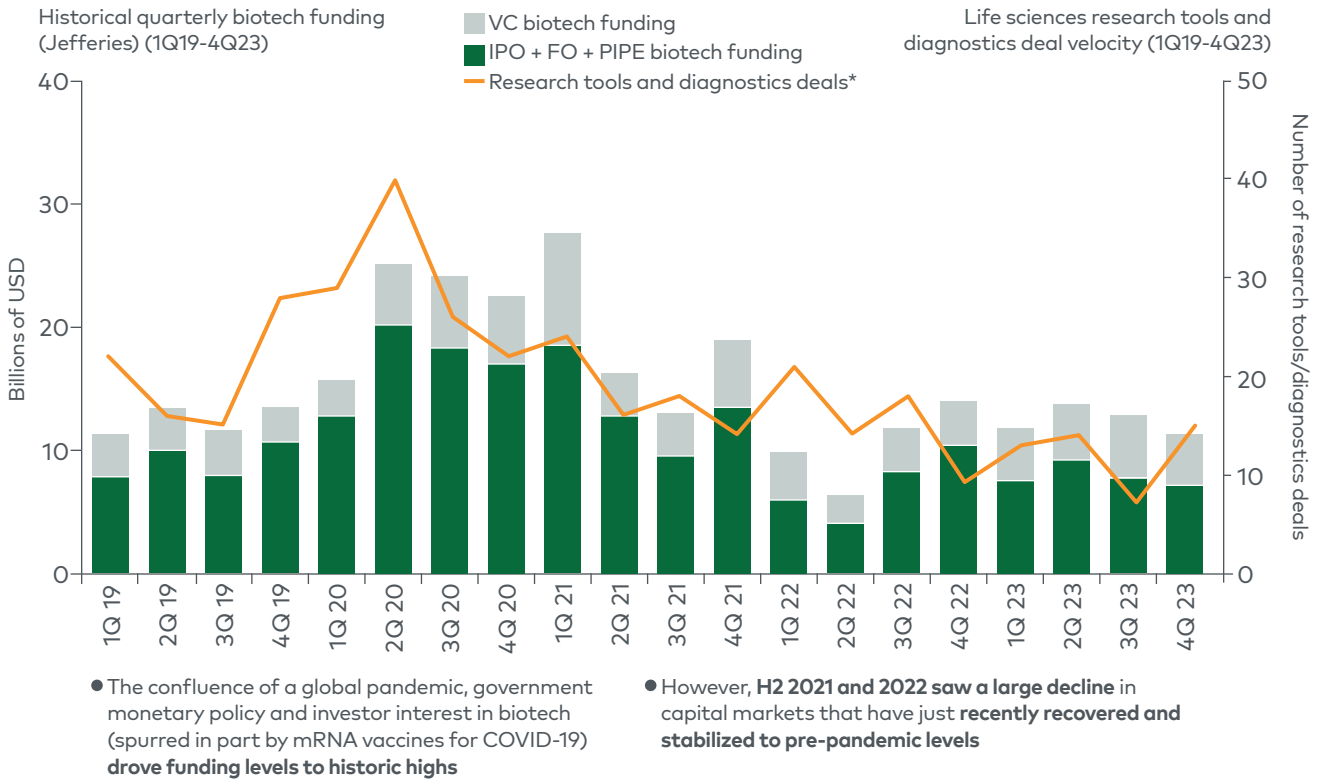
While the short-term outlook is impossible to predict, it is critical to remember that the key megatrends underpinning the long-term outlook for the industry remain extremely strong, with more clinical data and continued application growth supporting the promise of precision medicine and advanced therapeutic modalities. In this edition of *Executive Insights*, L.E.K. Consulting reflects on the key trends that are likely to continue to impact the research tools and diagnostics industry throughout 2024:

- Shift in the research tools and diagnostics deal themes driven by economic and funding trends
- Continued inflection of proteomics driven by scaling precision medicine applications within and beyond oncology
- Scaling of novel applications in the oncology precision medicine playbook
- Expansion of the precision medicine tool kit beyond oncology into neurology, autoimmune diseases and inflammatory diseases
- Evolving needs for fit-for-purpose R&D and manufacturing solutions driven by the "next wave" of advanced modality pipeline candidates

Shift in the research tools and diagnostics deal themes driven by economic and funding trends

Softness in biopharma funding has had a moderating effect on downstream biopharma spend on research tools, diagnostics and pharma services over the past 18 months; the ramifications of this headwind are continuing to impact both the nature and velocity of deals in research tools and diagnostics (see Figure 1).

Figure 1
Biopharma funding and research tools/diagnostics deal velocity



*Deals are limited to tools/Dx pharma and biotech deals (e.g., M&A, research, licensing); they do not include grants, settlements, etc.
Note: VC=venture capital; IPO=initial public offering; FO=follow on funding; PIPE=private investment in public equity; mRNA=messenger ribonucleic acid; H2=second half of the year; Dx=diagnostics
Source: Evaluate Pharma; Cortelis database; L.E.K. research and analysis of Jefferies

Following a spike in funding at the outset of the COVID-19 pandemic, the market witnessed a multi-quarter decline in funding from Q1 2021 through Q2 2022. While funding has stabilized — the past six quarters observed funding in line with 2019 levels — the rapid funding decline and resulting uncertainty drove a shift in biopharma spending that prioritized achieving regulatory milestones and driving toward value inflection points (e.g., clinical trial readouts) and deprioritized expansive spend on discovery efforts and paused clinical development for lower-priority programs.[3] The net effect has been a challenging market for research tools and diagnostics selling into early R&D and a significant shift in the nature of deals in the space.

While 2023 did witness several high-value acquisitions (see next section), M&A activity remained concentrated in a small number of large strategic acquirers. Because of this dynamic, the recycling of capital — where investors redeploy funds into the market ecosystem following windfall returns — has yet to materialize in the research tools and diagnostics segments (this contrasts with the recent acceleration of biopharma M&A, with returns distributed across a larger number of specialist funds). As a result, research tools and diagnostics deal themes have evolved from initial public offerings and special purpose acquisition companies, with all-time-high valuations, toward themes of cash preservation and alternative financing. Example deal archetypes include:

- Merger of equals to preserve capital (e.g., the merger of Standard BioTools and SomaLogic and Berkeley Lights' acquisition of IsoPlexis)
- Reverse mergers as an alternative route to access funding and public markets (e.g., Theralink Technologies merging to become a wholly owned subsidiary of IMAC Holdings Inc.)
- Consolidation of distressed assets (e.g., Pfizer's acquisition of Lucira Health for $36 million through a bankruptcy auction and Bruker's acquisition of PhenomeX for $108 million[4])

In 2024, it is likely that more deals of the above archetypes may come to fruition. In particular, savvy investors and strategics will continue to parse the landscape for inorganic opportunities in research tools players with attractive assets whose valuations have been overly impacted by the broader sector pullback. In parallel, the trend toward company profitability (highlighted in last year's "What to Watch For" industry outlook)[5] will likely continue as scaling research tools and diagnostics players continue to address cash burn to create attractive return on invested capital for strategic acquirers or to prepare for financing events in 2025 and beyond.

Continued inflection of proteomics driven by scaling precision medicine applications within and beyond oncology

Proteomics continues to be an active area of investment and high-growth applications for the research tools sector, evidenced by two high-profile, multibillion-dollar proteomics acquisitions in 2023 (Danaher's acquisition of Abcam for $5.7 billion[6] and Thermo Fisher's acquisition of Olink for $3.1 billion[7]). We anticipate continued acceleration and investment in the segment,[8] driven by global mega trends such as a) the massive parallelization of biology given scaling data outputs, bioinformatics capabilities and the maturation of artificial intelligence (AI)/ machine learning algorithms, and b) the continued convergence of -omic technologies (e.g., DNA barcodes used for proteomics readouts). These trends, in turn, catalyze application development and will continue to drive the expansion of precision medicine within and beyond oncology.

Scaling of novel applications in the oncology precision medicine playbook

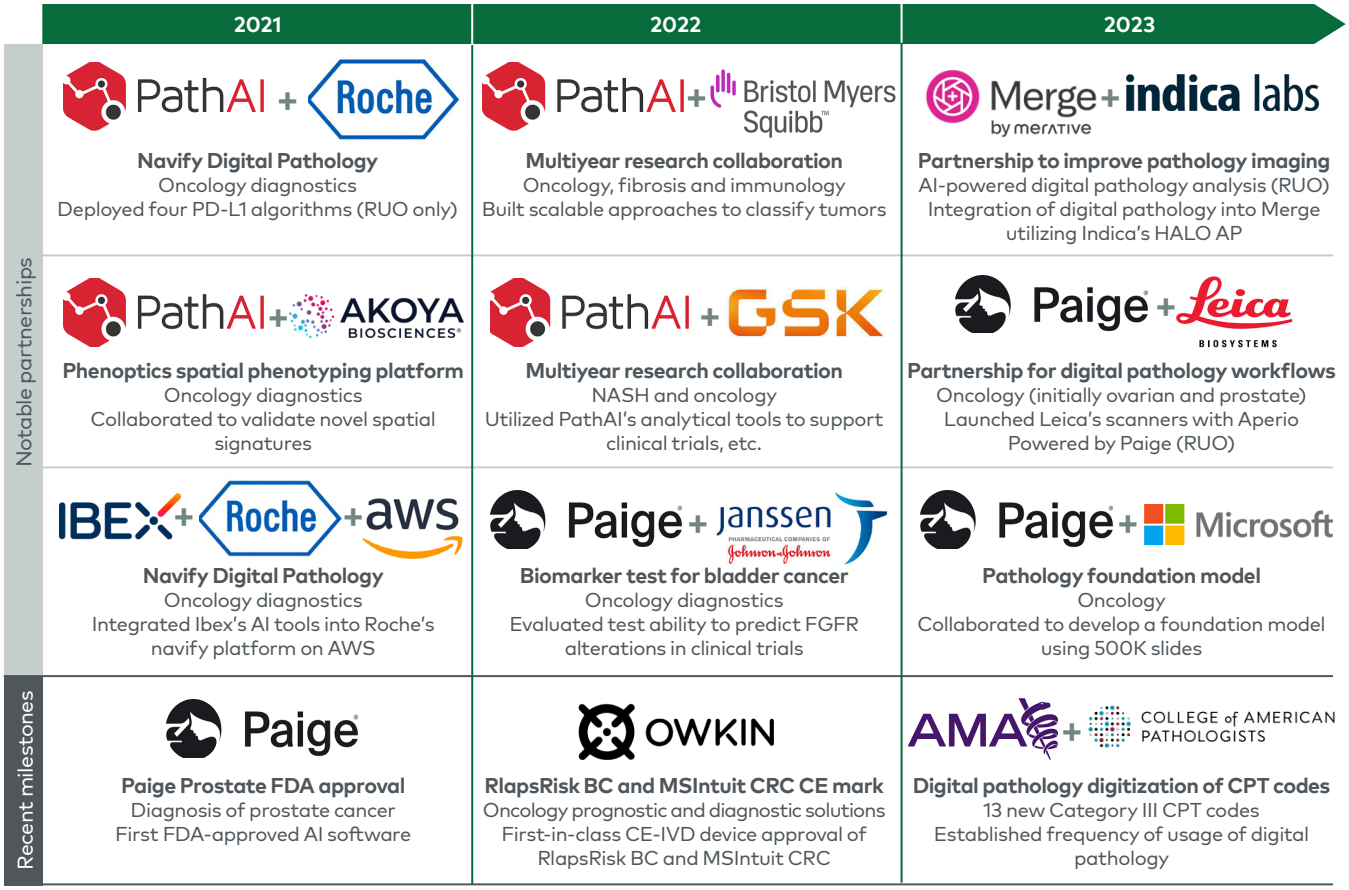
In prior years' editions of this outlook and industry trends report, we have discussed the role of next-generation sequencing in advanced oncology diagnostics and highlighted key advances in applications including minimal residual disease efforts toward multi-cancer early

detection. Recently, the other cornerstone technique of oncology diagnostics — pathology — has seen dramatic acceleration in digital and computational techniques. Though the U.S. Food and Drug Administration (FDA) first approved an AI-informed in vitro diagnostic device in 2021 (Paige Prostate for the diagnosis of prostate cancer),[9] efforts continue toward building a more expansive set of AI-based oncology diagnostic solutions across tumor types, with a number of landmark partnerships in 2023 (e.g., Microsoft and Paige, Owkin and MSD).

This emerging application reflects the maturation of AI tools in generating novel insights as well as a growing desire for researchers to understand the heterogeneity of biomarker expression at the (sub) cellular level. Early-adopter labs are using these tools to automate and standardize pathologist workflows, driving efficiency and creating cost savings for scaled pathology labs given the lack of additional reimbursement available for digital pathology Current Procedural Terminology codes. However, as algorithms improve and precision medicines increasingly require assessment of quantitative biomarkers (e.g., AstraZeneca's Enhertu indicated for HER2-low breast cancer, a newly defined subtype) or of novel morphological biomarkers, use cases may develop where the pathological analysis required is beyond the capabilities of human slide interpretation (see Figure 2).

Figure 2

Timeline of milestones and notable deals in digital pathology NONEXHAUSTIVE



Note: RUO=research use only; AI=artificial intelligence; FDA=Food and Drug Administration; NASH=nonalcoholic steatohepatitis; FGFR=fibroblast growth factor receptor; BC=breast cancer; CRC=colorectal cancer; CE=Conformité Européenne; IVD=in vitro diagnostic; CPT=Current Procedural Terminology
Source: L.E.K. research and analysis

Expansion of the precision medicine tool kit beyond oncology into neurology, autoimmune diseases and inflammatory diseases

As the oncology precision medicine tool kit diversifies beyond genomic analysis of oncogenic driver mutations, including the growing utilization of quantitative readouts rather than binary test results (e.g., circulating tumor DNA parts per million versus yes/no estimated glomerular filtration rate mutation), this tool kit can increasingly be applied to understand disease pathophysiology and inform patient management in disease areas where genetic drivers are less prevalent. In neurology and immunology, deriving clinically relevant insights from complex, noisy, interconnected protein or gene networks will require quantitative measurements of analytes over time. In many cases, it may be necessary to leverage ratios (e.g., amyloid beta 40:42 ratio for Alzheimer's disease), multi-analyte signatures (e.g., type I interferon gene signatures for lupus) or integration of other data (e.g., genotype, age).

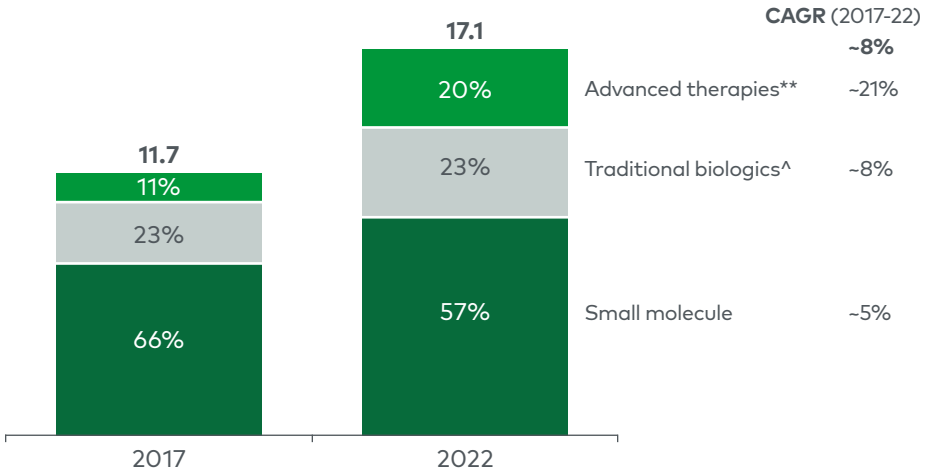
In the neurology space, Octave Biosciences published clinical validation data and initiated a real-world evidence study in 2023, as it continues to work toward establishing payor coverage for its multi-analyte multiple sclerosis disease activity test (based on Olink technology). There are also indications that pharma is increasingly seeing value in precision approaches outside oncology, as illustrated in the ulcerative colitis space by Merck's $10.8 billion acquisition of the precision therapeutics biotech Prometheus Biosciences and Roche's definitive agreement to acquire Telavant for $7.1 billion following a Phase 2b readout showing best-in-class remission rates for RVT-3101 in biomarker-positive patients.

Evolving needs for fit-for-purpose R&D and manufacturing solutions driven by the "next wave" of advanced modality pipeline candidates

The clinical and regulatory success of the "first wave" of cell, gene and nucleic acid therapies catalyzed significant investment (nearly $100 billion from 2017 to 2023) and concomitant rapid growth of the early-stage pipelines exploring these modalities. From 2017 through 2022, the overall pipeline grew at approximately 8% compound annual growth rate, with the small molecule pipeline growing about 5% annually and traditional biologics (e.g., monoclonal antibodies, recombinant protein therapies) growing around 8% annually, while the advanced modalities grew more than 20% annually, driving both overall pipeline growth and a modality mix shift away from the legacy modalities and toward the advanced modalities (see Figure 3).

By the end of 2022, more than 20% of the pipeline was focused on advanced modality drugs, compared to only about 10% just five years prior. In turn, this paradigm shift gave rise to critical modality-specific workflow solutions for the research and manufacturing of these novel medicines, including inputs (e.g., plasmid, novel cell lines), reagents (e.g., capping for messenger ribonucleic acid (mRNA), transfection reagents), equipment (e.g., novel bioreactors, chromatography columns and resins) and more.

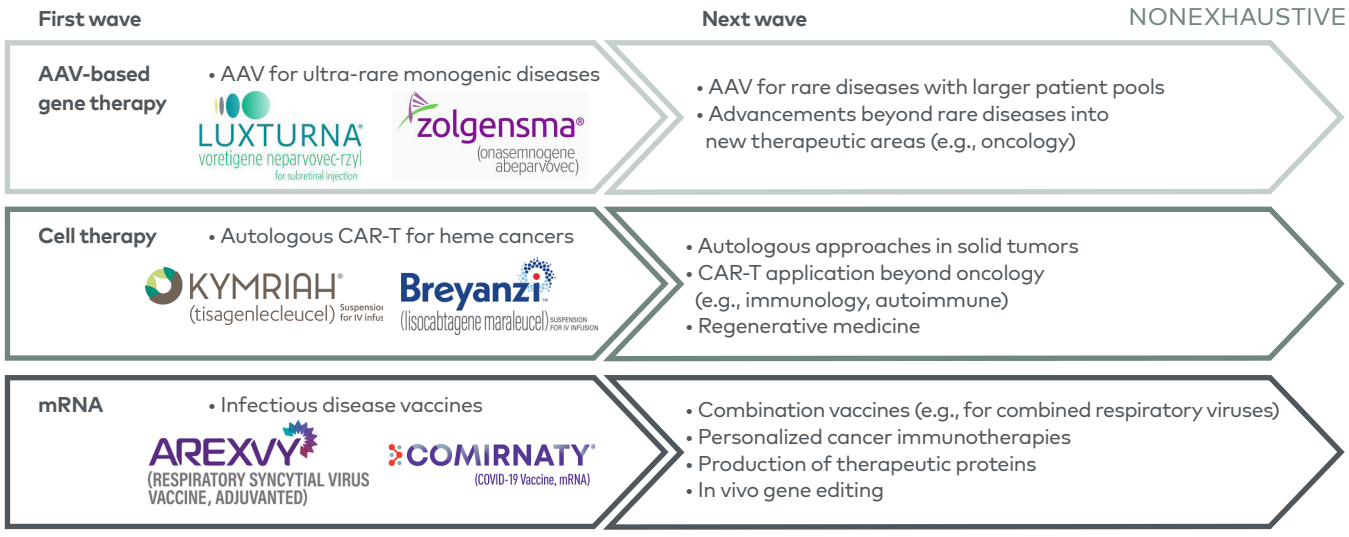
Figure 3
Global pharmaceutical pipeline mix shift toward advanced modalities



*Pipeline assets are in all stages, from preclinical to registration (excluding launched assets)
**Advanced therapies include NAT, GTx and CTx
^Biologics include mAbs, multispecific antibodies, ADCs and recombinant proteins
Note: WW=worldwide; CAGR=compound annual growth rate; NAT=nucleic acid therapeutics; GTx=gene therapies; CTx=cell therapies; mAbs=monoclonal antibodies; ADCs=antibody drug conjugates
Source: L.E.K. research and analysis of PharmaProjects

Now, with a number of first-wave programs approved across advanced modalities, the market is looking for proof of commercial traction, with participants closely monitoring for the next blockbuster advanced therapy drug that might join Zolgensma (Novartis) and Yescarta (Kite) with more than $1 billion in revenues. Looking ahead at the pipeline, developers are focusing on next-wave applications that, if successful, could catalyze subsequent inflows of investment into the advanced modality space and would trigger incremental workflow needs for fit-for-purpose solutions that address these emerging applications (see Figure 4).

Figure 4
Emerging "next wave" of advanced therapy applications driving future bioprocessing needs



Note: AAV=adeno-associated viruses; chimeric antigen receptor technology mRNA=messenger ribonucleic acid
Source: FDA.gov; ClinicalTrials.gov; company websites and press releases; L.E.K. research and analysis

Viral vector gene therapies (approximately seven scheduled or possible regulatory decisions in 2024 per approved reporting mechanism (ARM))

The pioneering viral vector gene therapies focused on gene addition to address ultra-rare monogenic diseases (e.g., Luxturna, Zolgensma). Recent approvals continue to leverage the gene addition manifold and apply the solution toward addressing larger (but still rare) indications such as hemophilia A (BioMarin's Roctavian). The next wave of pipeline therapies continues to explore gene addition in larger indications, including looking beyond rare diseases (e.g., Bayer and congestive heart failure, Candel Therapeutics' viral-based immunotherapies) and potentially in polygenic diseases (e.g., wet age-related macular degeneration, Parkinson's disease, frontotemporal dementia), where adeno-associated viruses can deliver a gene to express a therapeutic protein.

As the addressable indications scale, developers continue to seek solutions to selectively deliver vectors to target organs safely and reduce cost of goods. In a previous piece,[10] we outlined these key viral vector workflow needs and reviewed the emerging potential bioprocessing solutions.

Gene-edited cell therapies (approximately four scheduled or possible regulatory decisions in 2024 per ARM)

The first approved gene-edited cell therapies addressed hematologic cancers with autologous chimeric antigen receptor (CAR-T) cell therapy approaches. These six FDA-approved CAR-T therapies continue to scale,[11] including by winning approval in earlier lines of therapy and through clinical trials or compassionate use programs. The next wave of cell therapies includes expanded application of autologous CAR-T as well as both new approaches and new indications. Solid tumors remain a significant area of focus, with developers exploring a range of other autologous approaches (e.g., Iovance's recently approved tumor-infiltrating lymphocyte therapy[12] for melanoma, Adaptimmune's T-cell receptor therapy for synovial sarcoma).

Autologous CAR-T therapies are also being trialed in immunologic diseases beyond oncology, where early data has been extremely promising (e.g., Cabaletta Bio/ImmPACT Bio and lupus, Sonoma Biotherapeutics and rheumatoid arthritis). Cell therapies are also key in pioneering efforts in regenerative medicine, where stem cell-derived therapies are being trialed for metabolic (e.g., Vertex and type 1 diabetes) and neurologic (e.g., Bayer/Blue Rock and Parkinson's) disorders. With many expansion vectors under examination, the market continues to seek solutions to identify, isolate, engineer and expand the most promising cells to produce the most effective therapies. In a recent article,[13] we outlined in detail the key pain points and unmet needs in the autologous cell therapy manufacturing workflow and discussed emerging potential bioprocessing solutions.

Nucleic acid therapies (approximately three expected potential regulatory decisions in 2024 per Biomedtracker)

While early efforts in nucleic acid therapies focused on antisense oligonucleotides (ASO) and RNA-mediated interference (RNAi) approaches to knock down the expression of gene targets in rare disease (e.g., Alnylam's Onpattro), the COVID-19 pandemic saw mRNA medicines leap to the forefront through vaccine efforts from Moderna and Pfizer/BioNTech (BNT). Now, the next wave of mRNA medicines is targeting further respiratory infectious diseases (e.g., mRNA-1083 for COVID-19 and flu) as well as expanding to explore oncology with personalized cancer immunotherapies[14] (e.g., mRNA-4157 for melanoma, BNT122 for pancreatic cancer), where a patient-specific combination of neoantigens is expressed via mRNA to modulate immune response to checkpoint inhibitors. mRNA is also being explored to deliver therapeutic proteins (e.g., mRNA-3927 for propionic acidemia) and for in vivo delivery of gene-editing nucleases such as CRISPR-Cas9 (e.g., Verve's PCSK9-targeted base editor).

Evolving needs in mRNA include improved tools for in silico screening and sequence optimization, discovery and process support for novel mRNA types (e.g., circular RNA, self-amplifying RNA), and an expanded tool kit of drug delivery solutions to enable selective mRNA delivery to more organ types. Beyond mRNA, the ASO and RNAi pipelines continue to scale and address larger indications, as evidenced by approval of Novartis' Leqvio for low-density lipoprotein cholesterol reduction in patients with an increased risk of heart disease. Key needs as the oligonucleotide therapeutics space targets larger indications include improved scalability, reduced cost and organic solvent use, and improved yield and synthetic efficiency for longer (e.g., more than 50 base pairs) oligonucleotide sequences.

Conclusion

Despite near-term life sciences research tools and diagnostics market uncertainty owing to macro conditions, the scientific promise and transformational potential of precision medicine and advanced therapies continue to substantiate the core investment thesis for the space. Today's golden age of biotechnology continues to catalyze the engineering of novel advanced research tools and the concomitant development of high-value research and clinical applications. It is still early in the life cycle for many innovative companies that formed during the COVID-19-era funding boom, and moving forward this next wave of companies is anticipated to mature commercially and achieve scale, which may set the stage for future strategic business development activity into 2025 and beyond as consolidators seek to leverage M&A to drive topline growth and inorganically accelerate entry into emerging high-growth areas.

For more information, please contact lifesciences@lekinsights.com

Endnotes

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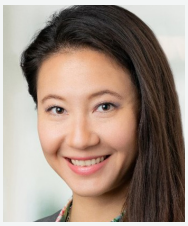

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