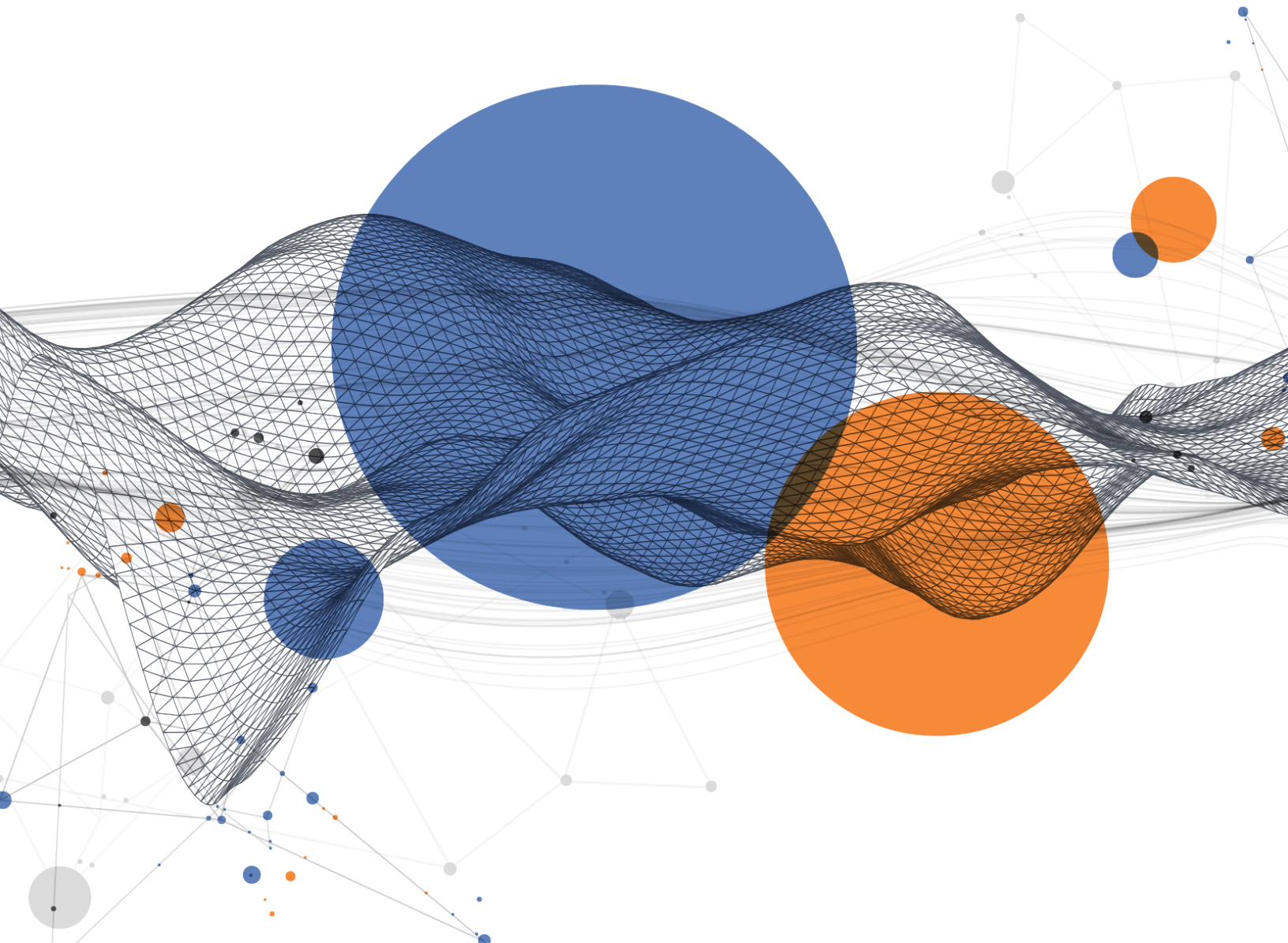# The Innovation Imperative: Pioneering New Modalities for Therapeutic Leadership

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Introduction

In the rapidly evolving landscape of pharmaceuticals and biotechnology, the emergence of multimodal drug discovery heralds a transformative era for drug discovery, where innovation and strategic foresight are paramount. This evolution is not just a scientific leap, but also requires a technological leap, transforming the competitive environment.
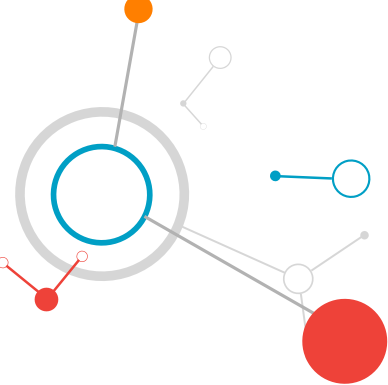
The new multimodal approaches – from monoclonal antibodies to RNA therapies, from small molecules to gene editing and cell therapies – offer entirely new therapeutic possibilities, turning formerly elusive targets into tangible opportunities for treatment.

This paradigm shift demands significant scientific and technological advances, in turn creating new commercial imperatives for pharmaceutical and biotech companies. In a competitive landscape, where innovation drives clinical success and market presence, embracing multimodal drug discovery will be critical. Rapid adaptation to the new landscape is pivotal in developing more effective, targeted, and personalized treatments, which will ultimately revolutionize patient care and enhance health outcomes.

In this article, we aim to investigate the nuanced layers of multimodal drug discovery:

- Explore multi-modality approaches in sculpting the future of drug discovery
- Strategic approaches: How collaborative technologies are essential to the scientific drug discovery pipeline
- Cast a forward gaze on the future of drug discovery, market conditions, and likely successful strategies

Contents

Understanding the New Drug Modalities Landscape

The landscape of new drug modalities is diverse and dynamic and signifies a radical departure from traditional pharmaceutical research practices.

Driven by a deeper understanding of disease mechanisms at the molecular and genetic levels, new targeted and personalized treatments are reshaping the future of drug development. The line between the possible and the impossible in drug therapy is increasingly blurred, as new therapeutic avenues are discovered, explored, and exploited.

However, the innovations also demonstrate how companies relying solely on traditional drug discovery paths are likely to be at a significant competitive disadvantage. Success in creating better drugs leading to improved patient outcomes now hinges on embracing diverse and multimodal strategies, which means adopting cross-functional, multi-team collaboration – a way of working that is often hindered by workflows and technical tools that were not designed with the new paradigm in mind.
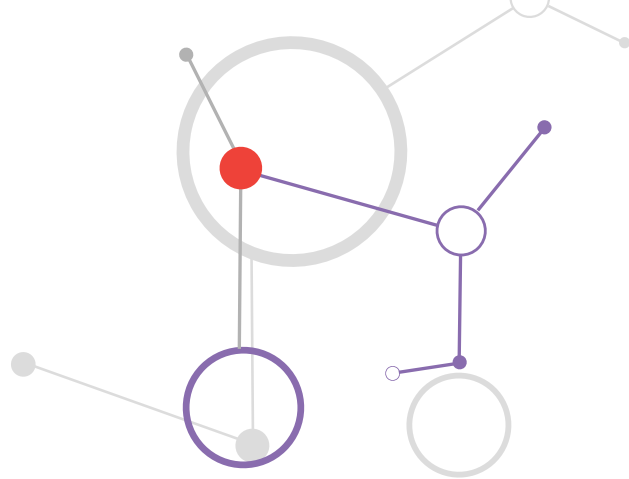
Specifically, the breadth of expertise required for effective multimodal drug discovery often exceeds the in-house capabilities across small-medium and large biotech/pharma companies. Bridging this gap creates a growing reliance on outsourcing, introducing novel challenges around data exchange and information delivery.

To leverage the full potential of multimodal drug discovery, success will rely on robust, reliable, and secure data capture, communication, and analysis across the extended partner ecosystem. Defining an effective data strategy will be a key factor in driving innovation in a landscape that is rapidly becoming more interconnected and technologically advanced.

Figure 1 - More than 17 New Drug Modalities Have Been Developed in the Past 20 Years

TECHNOLOGICAL MATURITY

Low   High

EMERGING
Proof of concept to demonstrate value for inital clinical applications

PROTACs
γδT therapies · TILs · Microbiome
mRNA
CAR-M · TCR-T · (therapeutics and vaccines) · Oncolytic virus · Stem Cell therapy
CAR-NK · Gene editing

ADVANCING
Technology advancing to cover different treatment areas and address wider clinical profiles

CAR-T
Bispecific antibodies · ADC
Gene therapy · RNAi and oligos
mRNA (prophylactic vaccine)

MATURE
Expanding to cover different mechanisms of action and improve convenience

Recombinant protein

Monoclonal antibodies

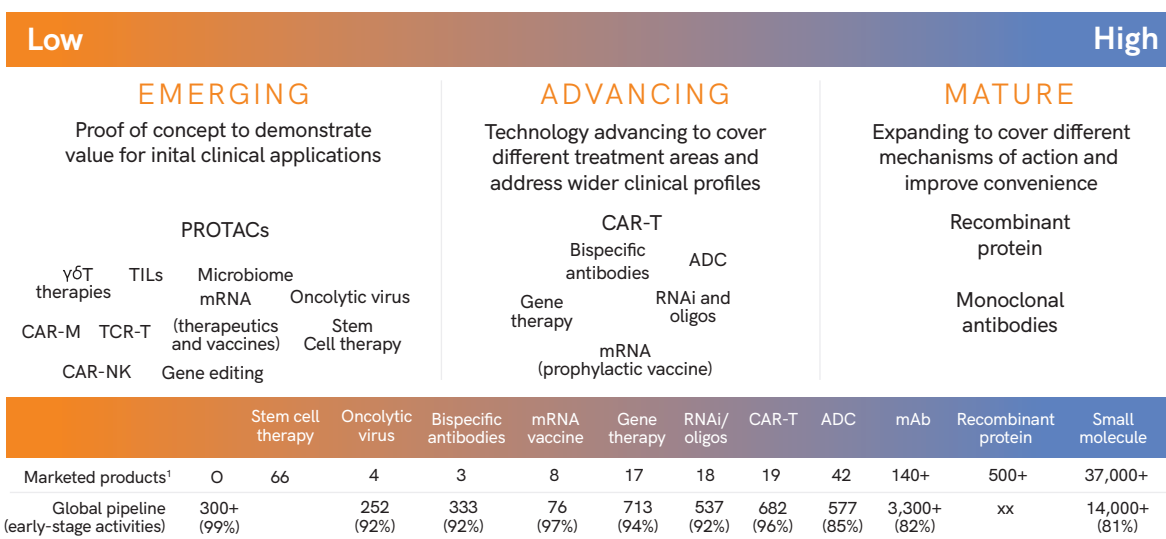|	Stem cell therapy	Oncolytic virus	Bispecific antibodies	mRNA vaccine	Gene therapy	RNAi/ oligos	CAR-T	ADC	mAb	Recombinant protein	Small molecule
Marketed products[1]	O	66	4	3	8	17	18	19	42	140+	500+	37,000+
Global pipeline (early-stage activities)	300+ (99%)		252 (92%)	333 (92%)	76 (97%)	713 (94%)	537 (92%)	682 (96%)	577 (85%)	3,300+ (82%)	xx	14,000+ (81%)

Figure 1: This is an adaptation of Exhibit 1 from the BCG article "Benefits and Risks of New Drug Modalities". It illustrates the technological maturity spectrum of over 17 new drug modalities developed in the past 20 years, ranging from emerging modalities in the proof-of-concept stage to mature modalities expanding to cover different mechanisms of action. The figure also shows the number of marketed products and global pipeline candidates (in early-stage and late-stage activities) for each modality as of October 2022.[1]

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Figure 2 - New Modalities Now Outpace Conventional Ones in Revenue Growth

FIVE-YEAR FORWARD-PROJECTED PIPELINE VALUE1 ($B)

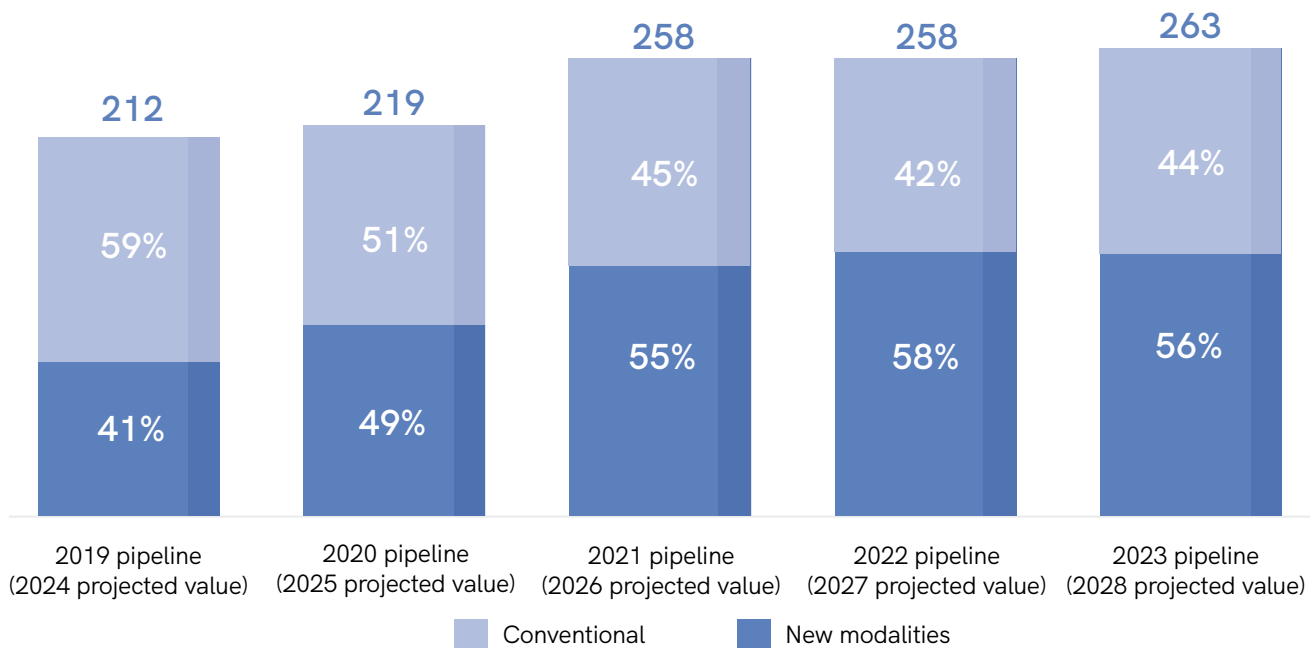|	2019 pipeline (2024 projected value)	2020 pipeline (2025 projected value)	2021 pipeline (2026 projected value)	2022 pipeline (2027 projected value)	2023 pipeline (2028 projected value)
Total	212	219	258	258	263
Conventional	59%	51%	45%	42%	44%
New modalities	41%	49%	55%	58%	56%

Figure 2: Is an adaption of Exhibit 1 from the BCG article "New Drug Modalities 2023", shows the five-year forward-projected pipeline value of conventional and new drug modalities from 2019 to 2023. The exhibit highlights the rapid growth of new modalities, which are expected to account for 56% of the total pipeline value by 2023, outpacing conventional modalities in terms of revenue growth potential.[2]
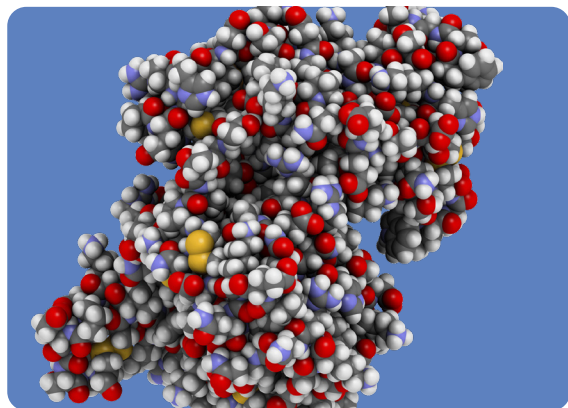
"The essence of multimodal drug discovery lies in its ability to harness the strengths of various therapeutic strategies…"

World of new modalities

In the rapidly evolving landscape of drug discovery and development, it is crucial for companies to avoid complacency and resist the temptation to rely solely on their current drug portfolios or even current drug modality strategies. While it may be comfortable to remain within a familiar modality and continue working on discovering disease targets until reaching candidate selection, this approach may not be sufficient to address the pressing need for novel and more effective treatments. The field of drug discovery is advancing at an unprecedented pace, and both new and established modalities must be continuously reexamined to identify potential combinatorial synergies or to explore entirely new modalities that can create once unattainable and more effective drugs.

New drug modalities encompass a broad spectrum of therapeutic strategies, each distinct in its action mechanism and target specificity. These span from monoclonal antibodies (mAbs) and RNA-based therapies to advanced gene editing techniques and cell therapies.[3] The classification of these modalities is multifaceted, considering both their therapeutic mechanics and stages of development. Established methods like mAbs coexist with emerging frontiers like CRISPR and CAR-T cell therapies, illustrating the breadth and depth of this field. [4,5,6]

Historically, the focus in pharmaceuticals has been on small molecules and/or antibodies targeting a relatively narrow scope of molecular structures. The evolution within of new drug modalities has revolutionized this paradigm, enabling the targeting of intricate molecular structures once considered 'undruggable.' This shift not only reflects the industry's deepening grasp of biological intricacies but also the technological strides enabling more precise medical interventions.[7] Furthermore, combinatorial strategies between new drug modalities has improved efficacy and safety creating a greater set of tools within the overall drug discovery process.

A noteworthy trend within the small-molecule-modality is the reemergence of PROteolysis TArgeting Chimeras (PROTAC) although they were first described in 2001. This class within small molecule therapeutics Targeted Protein Degraders (TPDs), along with covalent inhibitors, and macrocycles represent an exciting frontier in small molecule therapy.[8]

TPDs, for instance, are designed to harness the body's own protein disposal systems to eliminate disease-causing proteins, a strategy that could offer a new therapeutic angle for challenging targets.[9] Covalent inhibitors, with their ability to form permanent bonds with target proteins, offer enhanced specificity and potency.[10,11]

Macrocycles, characterized by their large, ring-shaped structures, present a unique balance of specificity and stability, enabling them to interact with complex protein surfaces that were previously inaccessible.[12]

To capitalize on these opportunities and stay at the forefront of drug discovery, companies should consider investing in creating a new toolset that incorporates cutting-edge modalities and technologies. This may involve combining the strengths of different modalities to create synergistic effects, such as using targeted drug delivery systems with novel therapeutic agents (ex: antibody drug conjugates). Additionally, exploring entirely new modalities, such as gene editing, RNA therapeutics, or cell therapies, has opened previously inaccessible therapeutic avenues and enabled the development of groundbreaking treatments for a wide range of diseases.

The Multimodal Approach in Drug Discovery

The essence of multimodal drug discovery lies in its ability to harness the strengths of various therapeutic strategies, creating a synergy that can address complex health challenges more effectively.

One of the primary benefits of the multimodal approach is its enhanced efficacy. By combining different modalities, each targeting different aspects of a disease, there is a higher probability of achieving a comprehensive therapeutic effect. This is particularly crucial in complex diseases like cancer, where a single treatment modality may not be sufficient, due to the heterogeneity of tumor cells. For instance, combining targeted therapies with immunotherapies has been shown to improve treatment outcomes significantly, as seen in some advanced oncology treatments.

For example, the use of combination therapies in oncology, where drugs targeting different pathways are prescribed in tandem, combats cancer significantly more effectively than single-therapy treatments. The use of BRAF inhibitors along with MEK inhibitors in the treatment of melanoma has been a landmark achievement in multimodal therapy, leading to significantly improved patient outcomes. BRAF and MEK Inhibitors: Use and Resistance in BRAF-Mutated Cancers - PMC (nih.gov)

Similarly, multimodal drug discovery allows for the tailoring of treatments to individual patients' needs, by considering their genetic makeup, disease progression, and other personal health factors. This personalized approach enhances treatment effectiveness and reduces the likelihood of adverse side effects.

Moreover, the multimodal approach is not confined to combining different drug types; it also encompasses the integration of diagnostics, drug delivery systems, and AI-driven digital tools capable of handling the resulting avalanche of data. The founding in 2021 and expansion in 2023 of the partnership between Evotec and Related Sciences[14] is a prime example of this type of approach.

Reinforcing the theme, a recent McKinsey report[15] advises pharmaceutical companies to address complex industry challenges through a long-term, transformative approach across four strategic domains. In particular, the report stresses the urgent need to accelerate and scale end-to-end adoption of digital and automation solutions across the value chain. Though digital implementation requires heavy investment, the rewards are significant, including cost savings, improved quality and resilience, and greater employee productivity. Companies that make digital a core strategic priority will be better positioned to navigate heavy industry headwinds.

In summary, multimodal drug discovery is more than just a passing trend; it is reshaping medical treatment, and making significant strides in developing more effective, safe, and personalized therapies.

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Strategic Considerations for Pharma and Biotech Companies

Larger companies with greater financial and personnel resources may have the luxury of deploying multiple research modalities targeting specific therapies; by comparison, smaller companies may find themselves at a competitive disadvantage, relying on a single modality.

In multimodal drug discovery, strategic considerations for large and small pharmaceutical and biotech companies are critical yet different. While larger companies may typically possess greater resources, their challenges concern how efficient they can be with internal work, how they manage outsourcing, and which partnerships would provide the greatest efficiency when adding to their portfolio of drugs. For smaller biotech companies, the focus is often on maximizing the impact of limited resources, making sometimes difficult choices on how to fund drug discovery, and weighing up the benefits of using multiple modalities against following a single drug development path with constrained budgets and manpower.
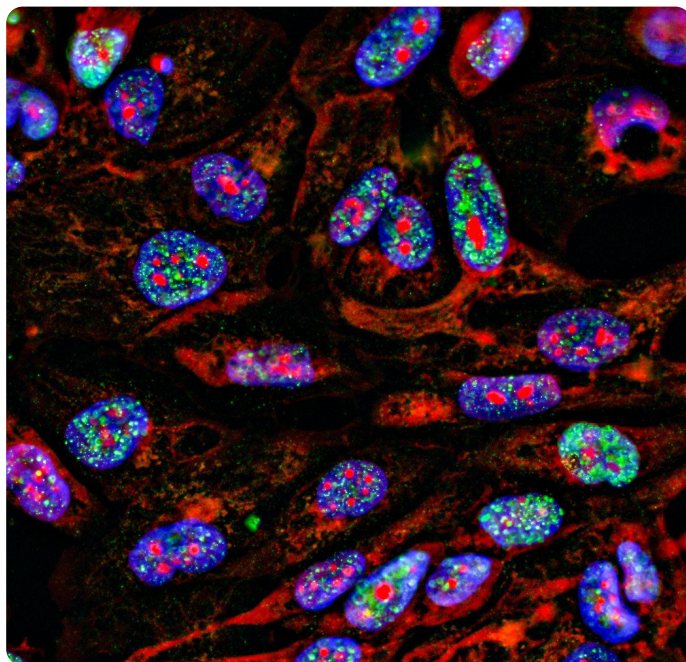
The investment strategy for smaller biotechs therefore often entails making pivotal decisions with limited capital. Choosing to invest in a particular drug modality requires a thorough analysis of potential ROI, considering both the scientific promise and the potential market reward. Boston Consulting Group[1,2] identified that these decisions can be make-or-break, determining the trajectory and sustainability of the company. Unlike larger firms that may spread risk by diversifying their portfolios across various modalities, smaller companies are compelled to concentrate on a few select areas where they can truly excel and differentiate themselves.

However, both large and smaller companies share challenges around how quickly they can generate, organize, and analyze data – iteratively, efficiently, and at scale. In addition, these processes rely on multiple teams to support the drug discovery pipeline, which adds to the complexity of communications. Overall success depends on a scalable and sustainable data strategy that reaches out beyond individual scientific teams and encompasses the whole organization.
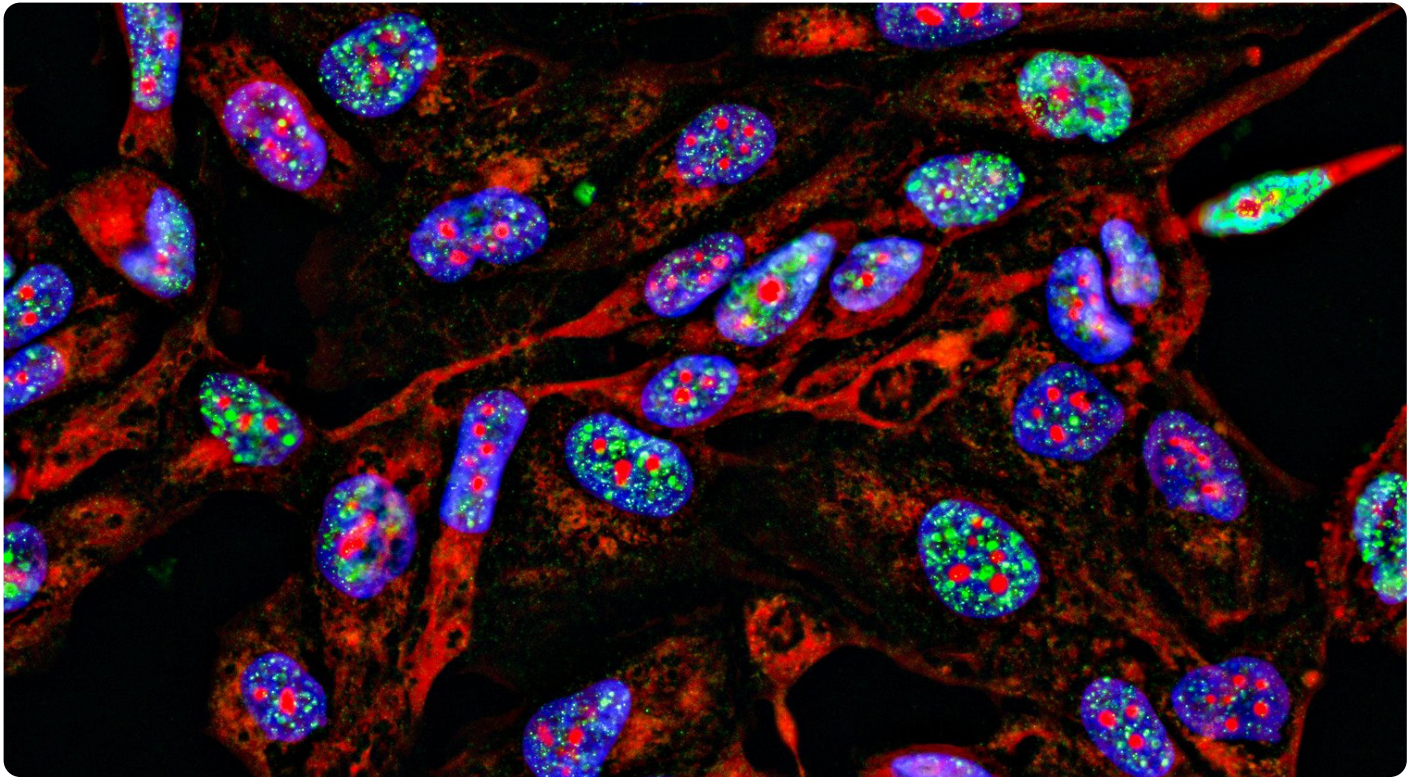
# Human Resources and Financial Capital

Resource allocation is not only about funding, but also about leveraging every asset, including human expertise, partnerships, and technology, and directing efforts where the potential for breakthroughs and commercial success is highest. Efficient project management and lean operational models are key to maximizing these resources.

The balance between groundbreaking innovation and practical market considerations is even more delicate when human and financial capital is comparatively limited. The potential for success will be considerably improved by aligning innovative efforts with clear, attainable market goals, to help ensure that groundbreaking work translates into viable, market-ready therapies.

Faced with resource constraints, smaller firms can instead use commercial agility to create a competitive advantage. New scientific insights and shifts in market demands can produce opportunities to build networks of partners and contractors, often faster than their larger counterparts, to seize the potential for multimodal development.

For C-level executives, these strategic considerations are essential when charting a viable path forward in a highly competitive and rapidly evolving industry.

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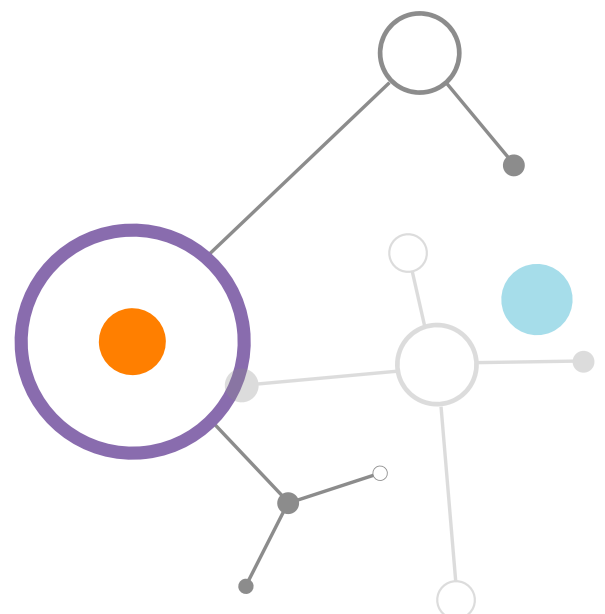
Navigating Risks and Opportunities

The journey through the landscape of multimodal drug discovery is marked by risks and opportunities. For companies in the pharma and biotech sectors, navigating this path requires a keen understanding of the inherent challenges and a strategic approach to capitalize on emerging opportunities. Some venture capitalists describe this as 'Outclassed: The Battle for Therapeutic Market Share.'[16]

One of the primary risks is the high degree of scientific and financial uncertainty. The process of developing new drug modalities often involves venturing into uncharted scientific territories, which can lead to unforeseen challenges and increased development costs. For example, novel modalities such as gene editing and RNA therapies present complex scientific questions that require substantial investment in research and development. Additionally, the regulatory landscape for these new modalities can be uncertain and evolving, posing another layer of risk.

"Companies that successfully develop new modalities can establish themselves as leaders in new therapeutic areas, creating strong – and possibly exclusive – competitive advantage"

However, despite the risks, the ability to address previously untreatable conditions or to provide more effective treatments for existing conditions opens vast potential markets. Companies that successfully develop new modalities can establish themselves as leaders in new therapeutic areas, creating strong – and possibly exclusive – competitive advantage. Advancements in these areas often lead to patentable innovations, providing valuable assets in a highly competitive pharmaceutical industry (see Table 1).

Table 1: Representative Companies developing new modalities in various disease areas

COMPANY	DRUG	DISEASE	MODALITY	YEAR	REFERENCE
IONIS	Nurinersen	spinal muscular	DNA/RNA atrophy	2016	FDA approves first drug for spinal muscular atrophy	FDA
Alnylam	Patisiran	Hereditary transthyretin-mediated amyloidosis	RNAi	2018	FDA approves first-of-its kind targeted RNA-based therapy to treat a rare disease	FDA
moderna	mRNA-1273	Covid-19	RNA	2023	Moderna Files for FDA Authorization of Its Updated COVID-19 Vaccine (modernatx.com)
ARVINAS	Vepdegestrant (ARV-471)	Breast cancer	Protein degraders (PROTACs)	2023	PROTAC Protein Degrader Pipeline	Arvinas
FireflyBio	$97 million in funding	Cancer and Immunotherapy	Antibody-drug conjugates with protein degraders	2024	Versant-backed Firefly Bio wants to make the next generation of ADCs	BioPharma Dive

Table 1: Highlights a diversity of modalities and diseases they treat. These representative companies are in no way the only companies that have shown success, but an example few that look to continue to do so within new modality drug research and development.

Collaborative Ecosystems and Sharing Risk

The development of new drug modalities in today's pharmaceutical and biotech landscape is increasingly characterized by collaborative ecosystems. Networks of partnerships and alliances are becoming essential in driving innovation, sharing risks, and accelerating the path to market for new therapies.[17]

Collaboration between different entities – biotech startups, big pharma companies, academic institutions, and even technology firms – brings together a diverse array of skills, knowledge, and resources. For instance, biotech startups often possess innovative ideas and novel approaches but may lack the resources or regulatory experience to bring a product to market. Conversely, large pharmaceutical companies have extensive resources and market access but may seek fresh perspectives or specific expertise found in smaller, more agile biotech firms or academic research labs.

To select just one example, a recent collaboration between Vertex and CRISPR Therapeutics led to the first CRISPR/Cas9 gene-edited therapy, CASGEVY™, for the treatment of sickle-cell disease and transfusion-dependent Beta Thalassemia.[18]

Drug development is an inherently risky business, with high rates of failure, substantial costs, and long development timelines. By working together, companies can share the financial and scientific risks associated with drug development, making it more feasible to pursue innovative projects. This risk-sharing is particularly crucial when exploring new drug modalities, where the paths to success are often unproven and the investment requirements substantial.

These ecosystems also foster a more integrated approach to drug development. By working closely with academic researchers, companies can gain deeper insights into disease mechanisms and patient needs, which can inform strategies for more effective and targeted therapies. Collaborations can also extend to patient advocacy groups and healthcare providers, ensuring that the end products align closely with patient needs and market demands.

While collaborative ecosystems offer numerous benefits, they also present distinct challenges that must be carefully navigated. Establishing partnerships, particularly with outsourcing entities, can be a time-intensive process fraught with legal and intellectual property considerations.

Precision not Proliferation of data

Collaboration complexities are often compounded by the logistical hurdles of data sharing and management. For instance, the transfer of research data, which is frequently in formats like PDFs, can be cumbersome and inefficient, requiring additional resources for data parsing and integration.

Success therefore also depends on data, with an increasing role in generating usable, large datasets and AI to accelerate discovery processes and offer predictive insights. However, managing and analyzing vast amounts of data requires sophisticated systems and expertise, posing a challenge for companies without these resources and around technical issues such as security and integration.

In addition, partnerships can lead to more efficient workflows, as different parties bring complementary skills and technologies to the table. For example, partnerships involving AI and data analytics firms have the potential to significantly speed up drug discovery, allowing for faster screening of compounds and more efficient clinical trial designs.

New drug modalities developed in partnerships not only hinges on the scientific synergy but also on the ability to streamline legal agreements and optimize data exchange methodologies. Overcoming these challenges is essential for maintaining the pace of innovation and ensuring that the collaborative efforts translate into tangible outcomes in drug development.

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Data: Strategy, Tactics, and Management

With a strategy in mind, thoughts inevitably turn to tactics – and the support necessary to turn plans into reality.

In research, particularly as AI capabilities continue to grow, data is now front-of mind. The days of paper notebooks are, or should be, long gone, and the importance of achieving digital transformation is now widely recognized.

Many technology initiatives in drug development and research fail because experimental data is too variable to be structured easily and data storage systems are not adaptable enough to store the data effectively. IT systems developed for the highly organized world of commercial transactions will not be well-suited for research data.
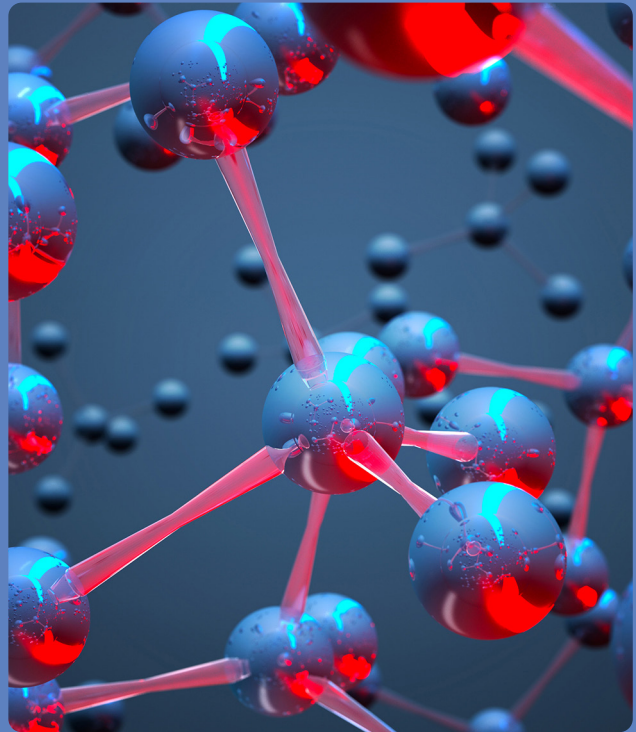
Revvity Signals recommends that the nonfunctional requirements – the 'how you do research' – are fully mapped and understood before embarking on a digital transformation project. Experience shows that capturing data from scientific instruments and turning it into structured output is the only way to realize the true benefits of digital transformation.

The sequence starts with capturing data from complex scientific instruments, then processes raw output into human-readable results, and then collates the output into datasets used for decision-making purposes. Core to digital transformation is the notion that these datasets are easily, if not automatically, assembled, and ready for sophisticated analysis, possibly by AI engines.

Revvity Signals offers a wide range of solutions designed for drug discovery, scientific research, and a host of specialist biotechnology use cases, helping global teams collaborate and innovate effectively and efficiently – and unlock new insights and opportunities for a better tomorrow.

Revvity Signals Research Suite

The Future of Drug Discovery

The future of drug discovery is poised to be shaped by a confluence of technological advancements, scientific breakthroughs, and evolving industry dynamics. The trajectory of drug development is increasingly being influenced both by emerging technologies and by a deeper understanding of biological systems, setting the stage for a new era of innovation and therapeutic solutions.

In particular, artificial intelligence (AI) and machine learning (ML) offer the potential to significantly accelerate the drug discovery process, from initial screening of compounds to the design of clinical trials. AI and ML algorithms are becoming increasingly adept at identifying potential therapeutic targets and predicting drug efficacy, dramatically reducing the time and cost of drug development.

Similarly, collaboration will enable access to specialized skills, novel technologies, and integrated perspectives from across different disciplines. The future success of drug discovery will rely heavily on navigating the technical, operational, and sometimes legal complexities of these cross-sector partnerships in order to fully harness their benefits. Companies that have a data strategy focus and find ways to streamline communication and data exchange within and between partners will gain a competitive advantage.

The enabling role of modern, accessible software technology cannot be overstated in shaping the future of drug discovery. These technological solutions are essential in managing the complex data and processes involved in drug development. Today's software platforms enable seamless integration of diverse research functions, facilitate collaboration across different teams and organizations, and ensure efficient data management and analysis. The speed of success in drug discovery hinges significantly on the adoption and optimization of such software technologies, which will empower researchers and developers to innovate more effectively and bring transformative drugs to market faster.

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Revvity Signals Perspective:

We aim to support multi-modal drug discovery with a single more connected software solution. We want scientists using less amount of software and for less time to provide greater quality time for greater quality science. Our Signals Research Suite aims to work for all modalities which we see is not just chemical or just biological but a balance of both requiring tools and workflows that fit the needs of individuals within a team as well as cross team collaboration.

Even outside organization for partnerships. Using the example of Antibody-Drug-Conjugates (ADC) as a common drug modality, what is hidden underneath are 3 smaller component modalities, small molecule (warhead), linker (peptide or chemical) and antibody (complex protein). Each of these components requires their own workflows that depend on clear scientific planning, documentation, data capture, and molecular or chemical tools. Also, teams need

tight communication software to manage each round of experiments while collaborating among teams in dependent stages that require samples and datasets before moving forward. Ultimately, each team and their data-streams need to have a holistic understanding of how each component and its respective datasets connect into the final product all in one scientific communication process. We see this as pulling results together across notebooks and disparate constituents that are all part of a final single construct and datasets and assembling all associated data into a single dashboard. There is an inherent challenge to visualize data over a highly multivariate space while having a single easy to manage dashboard for comparing and optimizing ADCs candidates and Signals aims to strike that balance.

Signals Research Suite is intended to make experimental planning, data capture, scientific workflow, and data analysis easy and faster for scientists and teams. With improved sustainable and efficient cycles of scientific iteration this will ultimately lead to faster discovery of better, new modality drugs for current and future diseases.
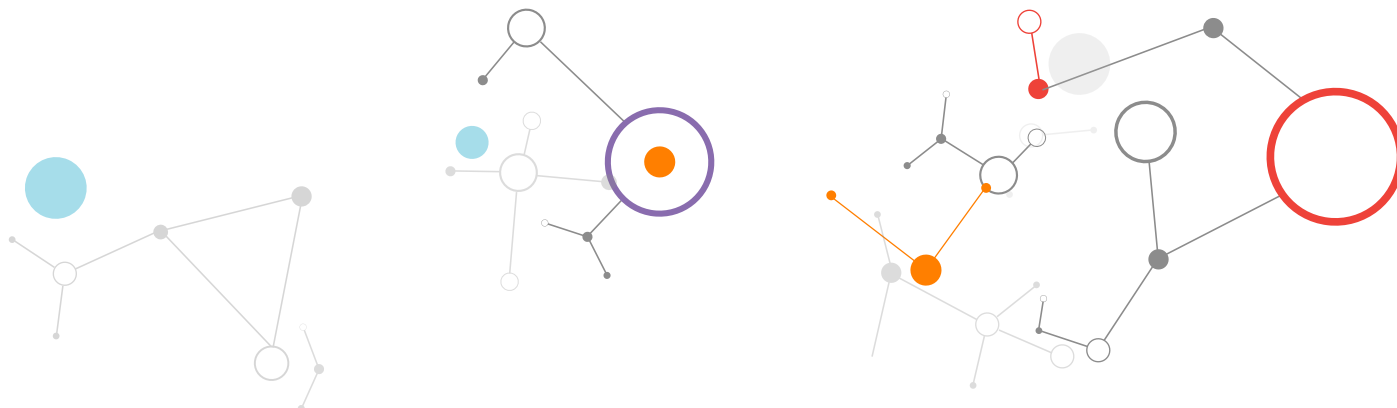
Revvity Drug Discovery

Conclusions

The future of drug discovery, while promising, will continue to face regulatory hurdles, ethical considerations, and the need for sustainable development practices. However, with the rapid pace of scientific and technological advancements, and the pivotal role of advanced software solutions, the industry has the capabilities and motivation to overcome these challenges and generate groundbreaking healthcare innovations.
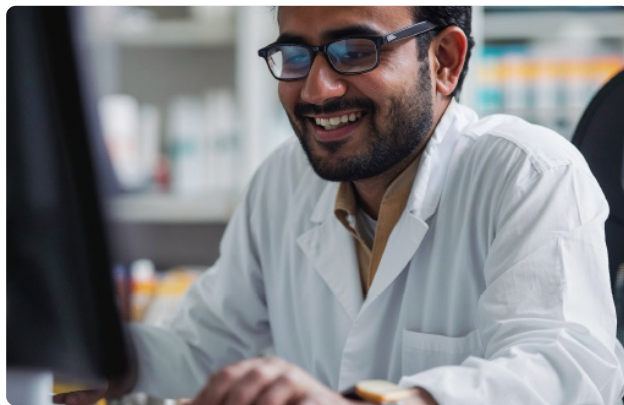
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