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# Beyond fragmented strategy choices: a systemic approach to support R&D investment in pharma and biotech companies

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## Abstract

**Purpose** – This paper develops a systemic framework for investment decision-making in pharmaceutical and biotech companies, addressing growing complexity driven by regulatory uncertainty, technological disruption, and evolving market needs. It seeks to move beyond traditional, fragmented approaches toward more integrated and viable innovation strategies.

**Design/methodology/approach** – The study adopts a systemic perspective that combines risk management, strategic partnerships and technological enablers such as artificial intelligence and predictive analytics. Drawing on case studies from AstraZeneca and Eli Lilly, as well as on notable failures such as Pfizer's torcetrapib and repeated setbacks in Alzheimer's research, the analysis illustrates how systemic approaches enhance portfolio resilience and decision quality through cross-functional governance.

**Findings** – The findings demonstrate that a systemic model built around four interrelated pillars – scientific merit, regulatory feasibility, commercial viability and competitive positioning – supports better risk-adjusted decisions and stronger alignment between R&D, financial, and strategic functions. By integrating these dimensions, organizations can improve the robustness of their investment portfolios and foster long-term innovation capability.

**Originality/value** – This study contributes a novel conceptual and practical framework that links strategic intelligence, technological tools and governance mechanisms in the investment decision-making process. It offers actionable insights for managers, investors, and policymakers seeking to align capital allocation with sustainable innovation. By adopting systemic approaches, pharmaceutical and biotech firms can transition from reactive, fragmented decision-making toward proactive, evidence-based strategies that optimize risk-adjusted returns and accelerate the delivery of transformative therapies.

**Keywords** Systemic decision-making, Pharmaceutical and biotechnology investments, R&D portfolio management, Artificial intelligence and predictive analytics, Innovation ecosystems

**Paper type** Research article

## 1. Introduction

Investment in pharmaceutical and biotechnology firms is among the most capital-intensive and high-risk endeavors in the global economy (Işık and Orhangazi, 2022). Bringing a new drug to market can cost more than $2 billion in development and span more than a decade (DiMasi *et al*., 2016). Despite these costs, attrition rates remain high: only a fraction of drug candidates entering clinical trials ultimately achieve regulatory approval (Wouters *et al*.,



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2020). The consequence is a paradoxical environment: extraordinary opportunities for scientific and financial breakthroughs coexist with devastating risks of failure.

The central problem this paper addresses is how decision-makers in pharma and biotech companies can allocate scarce resources across competing projects under conditions of high uncertainty (Javanmardi *et al*., 2024). Investment failures erode shareholder value, stall scientific progress, and reduce patient access to critical therapies. Conversely, informed systemic approaches can enhance portfolio resilience, attract investors, and accelerate time-to-market.

Existing literature has emphasized discrete components of decision-making - such as market analysis (Pisano, 2006), R&D productivity (Paul *et al*., 2010), or collaboration networks (Powell *et al*., 1996). Yet, few frameworks integrate these dimensions into a holistic model. This fragmentation is problematic because investment choices in the pharmaceutical and biotechnology sectors are inherently systemic, involving interconnected risks, regulatory dependencies, competitive dynamics, and evolving scientific frontiers.

The contribution of this study is to advance an integrated systemic framework that balances financial, scientific, regulatory, and strategic perspectives in investment decision-making. Three motivations inform our approach. First, the industry's structural challenges–declining R&D productivity, pricing pressures, and capital constraints–necessitate more structured frameworks (Munos, 2009). Second, digital technologies such as Artificial Intelligence, machine learning, and predictive analytics are transforming the way firms assess risks and forecast returns (Mak and Pichika, 2019). Third, collaborative ecosystems–spanning biotech startups, academic institutions, and big pharma–demand governance mechanisms that integrate external innovation while managing uncertainty (Pisano and Teece, 2007).

By analyzing both successful turnarounds (e.g. AstraZeneca's "5 R" framework and Eli Lilly's focused differentiation) and notable failures (e.g. Pfizer's torcetrapib and Alzheimer's trials), this paper demonstrates the consequences of systemic versus fragmented approaches. Building on these insights, we propose a practical, evidence-based framework for managers and investors to navigate uncertainty.

The paper is structured as follows. Section 2 reviews the theoretical foundations of investment decision-making in the pharmaceutical and biotechnology industries. Section 3 develops the systemic approach framework. Section 4 applies the framework through case studies. Section 5 discusses tools and techniques–including AI-driven portfolio management and decision tree analysis–that enhance decision-making capacity. Section 6 outlines implications for managers and academics. Section 7 concludes by summarizing contributions and highlighting avenues for future research.

### *1.1 Conceptual framework: a systemic approach to support investment decision-making in pharma and biotech companies*

The complexity of pharma and biotech investment decisions requires moving beyond traditional linear models toward systemic frameworks. Our proposed model is based on four interdependent pillars – i.e. scientific merit, commercial viability, regulatory feasibility, and competitive positioning–encompassed within a cross-functional governance framework (Figure 1).

*Scientific merit:* Scientific validity remains the cornerstone of any R&D investment, especially in these industries (Schlander *et al*., 2021). This includes robust preclinical data, biomarker validation, and a clear understanding of mechanisms of action. Failures such as torcetrapib underscore the consequences of advancing projects without sufficient biological validation (Kola and Landis, 2004).

*Commercial viability:* Even scientifically sound candidates must align with market demand, pricing dynamics, and reimbursement potential. The rise of precision medicine illustrates the challenge of balancing smaller patient populations with high-value therapies (Garrison and Towse, 2017).

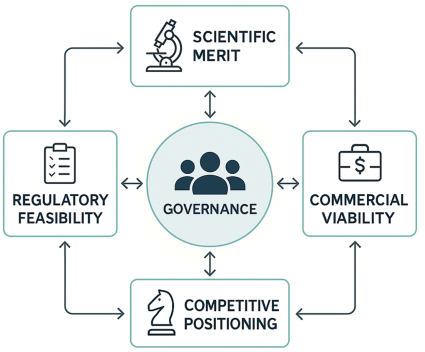


**Figure 1.** Systemic approach to investment decision-making in pharma and biotech organizations

*Regulatory feasibility*: Regulatory approval remains a critical bottleneck. Effective engagement with regulatory agencies, combined with adaptive trial designs, increases the likelihood of success (Downing *et al*., 2017).

*Competitive positioning*: Competitor monitoring allows firms to assess market entry timing, potential first-mover advantages, and patent landscapes (Cockburn and Henderson, 2001).

These four pillars are interdependent; in fact, scientific breakthroughs without commercial markets are unsustainable, drugs with strong commercial potential will falter if they cannot clear regulatory hurdles, and even solid science can deliver weak returns if it lacks a clear competitive position. Importantly, each pillar includes both an intra-firm assessment and an ecosystem-embedded assessment. Scientific merit depends not only on internal validation but also on access to external knowledge and complementary expertise; commercial viability is shaped by value networks, reimbursement regimes and distribution infrastructures; regulatory feasibility is co-produced through early and sustained engagement with regulators and clinical communities; and competitive positioning increasingly reflects ecosystem positioning, i.e. the focal firm's ability to orchestrate partnerships, secure complementary assets, and build platforms that can be leveraged across multiple projects over time. This ecosystem-embedded reading is consistent with the view that strategic criteria for portfolio decisions are partially co-determined by the broader innovation system and the governance arrangements that enable collaboration and long-horizon learning. To bring these elements together, the systemic framework relies on cross-functional governance teams that unite expertise from R&D, regulatory affairs, commercial strategy, and financial experts.

This framework is designed to operationalize systemic decision-making by embedding structured evaluation criteria at every stage of the investment process. It encourages portfolio managers to balance high-risk/high-reward projects with lower-risk investments, enhancing resilience while preserving innovation potential.

## 2. Theoretical background

Investment decision-making in pharmaceutical and biotechnology firms differs fundamentally from that in other industries due to exceptionally high levels of uncertainty, capital intensity, and regulatory complexity. Research has documented that the probability of a new drug reaching the market from preclinical stages remains below 12%, reflecting the inherent unpredictability of biological systems, stringent regulatory requirements, and lengthy timelines associated with clinical development (Wong *et al*., 2019; Işık and Orhangazi, 2022). This high attrition rate necessitates sophisticated frameworks for evaluating and selecting R&D projects, particularly as firms must transition from assessing individual

projects in isolation to managing interdependent portfolios that collectively build strategic competencies and enhance organizational resilience.

Traditional financial tools, such as discounted cash flow (DCF) or net present value (NPV), remain widely used but often fail to capture the systemic complexity of pharmaceutical R&D activities. These methods rely on assumptions of predictable cash flows and success probabilities that rarely hold in practice, particularly in the context of radical innovation where uncertainty pervades both technical and market dimensions (Munos, 2009; Pisano, 2006). To better navigate this complexity, investment frameworks need to integrate dynamic factors such as evolving regulatory requirements, competitive actions, and technological breakthroughs that reshape risk-return profiles over time. Moreover, the evaluation of individual projects must be complemented by portfolio-level considerations that account for interdependencies, resource constraints, and strategic alignment across multiple concurrent initiatives.

Real options theory has provided valuable insights by framing R&D investments as staged options that can be exercised or abandoned as evidence emerges (Trigeorgis and Reuer, 2017). This approach allows managers to value flexibility in investment decisions, thereby reducing exposure to downside risks while preserving upside potential. However, real options valuation often remains constrained by data availability and subjective probability assessments, underscoring the need for systemic approaches that integrate multiple evaluative perspectives. Furthermore, while real options theory addresses the sequencing of decisions within individual projects, it provides limited guidance on managing portfolios of interdependent projects, where decisions about one asset may fundamentally alter the value and risk profiles of others.

The challenge of pharmaceutical R&D productivity is further compounded by the long-term decline captured in "Eroom's Law", which observes that the number of new drugs approved per billion dollars invested in R&D has roughly halved every nine years (Scannell *et al*., 2012). Scholars have linked this trend to increasing scientific complexity, more stringent regulatory scrutiny, and the depletion of low-hanging therapeutic opportunities (Pammolli *et al*., 2011). This decline in productivity has forced firms to fundamentally reassess their investment strategies and decision-making frameworks. While portfolio diversification across multiple therapeutic areas and development stages is often recommended to mitigate risk (Paul *et al*., 2010), focused differentiation in specific therapeutic domains or technologies can strengthen expertise and competitive advantage (Pisano, 2006). Both strategies carry inherent trade-offs: over-diversification may dilute resources and organizational capabilities, while over-specialization may expose firms to catastrophic failure if scientific breakthroughs fail or markets shift unexpectedly.

The literature on project evaluation and portfolio management offers critical insights into how firms can navigate these tensions through structured assessment frameworks. Research on evaluation criteria in new product development has demonstrated that successful innovation requires the systematic application of multiple criteria dimensions throughout the development process (Carbonell-Foulquié *et al*., 2004; Martinsuo and Poskela, 2011). Carbonell-Foulquié *et al*. (2004) identified five key dimensions of go/no-go decision criteria for highly innovative products: strategic fit, technical feasibility, customer acceptance, market opportunity, and financial performance. Their empirical analysis revealed that the usage and relative importance of these criteria vary significantly across different stages of the development process, with strategic fit criteria being predominantly applied in approving new product concepts, technical feasibility criteria proving crucial during concept and prototype development, and financial performance criteria gaining prominence near the end of the development cycle. This staged approach to evaluation reflects the reality that different types of information become available and relevant at different points in the innovation process, and that premature application of certain criteria may lead to the rejection of potentially transformative innovations.

Building on this foundation, Martinsuo and Poskela (2011) examined how the use of evaluation criteria and formal assessment systems relates to innovation performance in the front end of innovation. Their study revealed nuanced relationships between different types of criteria and distinct dimensions of strategic opportunity. Specifically, they found that while formal assessment systems showed a negative or nonsignificant association with innovative performance, the use of specific evaluation criteria demonstrated significant positive associations with competitive potential and future business potential. Market and technical criteria were strongly associated with competitive potential, whereas strategic and technical criteria were linked to future business potential. These findings highlight an important tension: excessive formalization of evaluation processes may stifle creativity and flexibility in the front end of innovation, yet structured criteria provide essential guidance for decision-making and resource allocation. The study also revealed that concept complexity and novelty mediated the relationship between evaluation criteria and strategic opportunity, suggesting that the value of structured evaluation frameworks depends critically on the nature of the innovation being pursued.

These insights from the project evaluation literature underscore several fundamental principles that inform systemic investment decision-making in pharmaceutical and biotech organizations. First, evaluation frameworks must be multidimensional, incorporating scientific, commercial, regulatory, and strategic perspectives rather than relying solely on financial metrics. Second, the application of evaluation criteria must be adapted to the stage of development and the nature of the project, with different criteria gaining salience as projects progress through the innovation pipeline. Third, while structured evaluation systems provide necessary discipline and consistency, excessive formalization may undermine the flexibility and iterative learning required for radical innovation. Fourth, the evaluation of individual projects cannot be divorced from portfolio-level considerations, as the strategic value of any single project depends in part on its relationship to other initiatives and its contribution to building organizational capabilities.

A systemic approach to investment decision-making must reconcile these tensions by embedding structured portfolio governance that evaluates projects not in isolation, but in terms of their contribution to overall pipeline resilience and strategic alignment. This requires incorporating scientific, regulatory, commercial, and competitive perspectives at each decision point while maintaining sufficient flexibility to adapt to emerging evidence. Portfolio management frameworks must address not only project selection and prioritization but also the sequencing of investments, the allocation of shared resources, and the development of dynamic capabilities that enable the organization to respond to technological and market shifts (Teece *et al*., 1997).

Investment decisions are also increasingly shaped by the broader innovation ecosystem within which pharmaceutical and biotech firms operate (Wu and He, 2020). Building on the ecosystem view, we clarify that "strategic" criteria in portfolio decision-making cannot be treated as purely intra-firm constructs (e.g. alignment with internally defined priorities or resource availability). In complex, science-based innovation settings, the strategic value of an R&D project is partially co-determined by the external system in which the focal firm operates, because relevant knowledge, complementary assets, and legitimacy are distributed across multiple actors and institutions. Following Dougherty's perspective on complex innovation eco-systems (Dougherty, 2017), strategizing is less about optimizing a closed set of internal choices and more about continuously formulating and revising hypotheses about future value-creating opportunities grounded in learning events that emerge across the system. These opportunities are articulated as configurations of interdependencies among knowledge resources, partners, infrastructures, and rules that make certain development trajectories feasible and others impracticable. In this sense, the externally contextual dimension of strategic criteria concerns "fit" with internal capabilities, and ecosystem feasibility and capability-building: whether a project strengthens a platform of competencies and partnerships that can be mobilized repeatedly, whether it secures access to complementary

assets (e.g. specialized clinical networks, manufacturing or supply-chain capabilities, diagnostic or data infrastructures), and whether it is supported by viable governance structures for collaboration. Dougherty's emphasis on the coupled strategic and institutional cycles highlights that portfolio choices simultaneously select projects and shape the governance arrangements (collaborative commons, partnering rules, accountability mechanisms) required to persist, learn, and capture value over long and uncertain innovation horizons (Dougherty, 2017). In addition, research on open innovation and networks has highlighted the growing interdependence of large pharmaceutical firms, biotech startups, universities, and contract research organizations (Chesbrough, 2003; Powell *et al*., 1996). Ecosystem perspectives suggest that no single firm can master all scientific domains required for innovation. Instead, competitive advantage emerges from the ability to access, integrate, and orchestrate knowledge and resources across organizational boundaries (Autio and Thomas, 2014). For investment decision-making, this implies that firms must evaluate both the internal feasibility of projects and their potential to leverage external collaborations, licensing opportunities, and strategic alliances. Empirical research confirms the value of partnerships: collaborations with biotech firms have been shown to significantly increase the likelihood of successful drug approvals, while alliances with academic institutions enhance early-stage innovation (Rothaermel and Hess, 2007). However, partnerships also introduce coordination risks, intellectual property concerns, and cultural clashes. Systemic investment frameworks must therefore incorporate mechanisms for partnership evaluation and governance to ensure that collaborations enhance rather than erode portfolio value.

The regulatory environment further shapes strategic decision-making in profound ways. The pharmaceutical industry is among the most heavily regulated sectors worldwide, with approval processes governed by agencies such as the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA). Regulatory requirements shape investment decisions by influencing both costs and probabilities of success (Downing *et al*., 2017). The literature emphasizes that regulatory engagement should not be treated as a downstream activity but as an integral component of early-stage investment decisions. Adaptive trial designs, patient-centric endpoints, and real-world evidence are increasingly recognized as regulatory enablers that can accelerate approval and reduce uncertainty (Sherman *et al*., 2016). Investments in regulatory expertise thus become critical assets for strengthening portfolio resilience. Furthermore, global regulatory heterogeneity complicates decision-making. While accelerated approval pathways may exist in some jurisdictions, divergent standards across regions can delay launches and increase costs (Pepermans and Maertens, 2020). Systemic frameworks must therefore embed regulatory intelligence and scenario planning into the investment process, ensuring that projects are evaluated not only on their scientific and commercial merits but also on their regulatory feasibility across target markets.

Recent scholarship has highlighted the transformative role of digital technologies in pharmaceutical investment decision-making. Miozza *et al*. (2024) argue that the pharmaceutical sector has approached digital transformation in a fragmented manner, with research largely focused on single technologies rather than systemic frameworks. Their systematic review highlights the lack of managerial studies on how AI, big data, and IoT can support integrated governance, a gap this paper helps fill by embedding these technologies within a systemic decision-making approach. These technologies enable firms to analyze vast datasets – from genomic profiles to clinical trial outcomes – to identify promising targets and forecast probabilities of success (Mak and Pichika, 2019). Predictive analytics further supports decision-making by modeling market demand, pricing potential, and competitive dynamics (Gupta and George, 2016). The application of AI in portfolio management has been demonstrated to reduce attrition rates, enhance trial design, and expedite time-to-market (Zhavoronkov *et al*., 2019). However, reliance on algorithms also introduces risks, such as bias in training data or overreliance on model outputs without adequate expert oversight. Recent empirical evidence further substantiates AI's transformative potential across the drug

development continuum. Zhang *et al*. (2025) provide a comprehensive analysis demonstrating that AI technologies, particularly emerging large language models and generative AI, are fundamentally redefining traditional paradigms in pharmaceutical innovation. Their systematic review reveals that AI applications now span the entire drug development workflow, from disease target identification through post-market surveillance, with particularly notable advances in virtual screening, *de novo* molecular design, and ADMET property prediction. Critically, the authors emphasize that AI's capacity to process vast datasets – encompassing genomics, transcriptomics, clinical trial outcomes, and real-world evidence – enables the identification of patterns and correlations that would remain obscure through conventional analytical approaches. However, Zhang *et al*. (2025) also highlight persistent challenges, including data scarcity, limitations in model interpretability, and the absence of standardized evaluation frameworks, underscoring the need to embed AI tools within systemic governance structures that preserve human expertise and cross-functional judgment rather than pursuing purely algorithmic decision-making. A systemic approach requires blending computational insights with cross-functional judgment, ensuring that technology augments rather than replaces human expertise.

Ultimately, investment decision-making in pharmaceutical and biotech firms is defined by strategic trade-offs across multiple dimensions. No firm possesses unlimited financial or human resources and thus must prioritize competing projects while balancing short-term revenue needs against long-term innovation imperatives (Loch and Bode-Greuel, 2008). Case studies illustrate the risks of misaligned trade-offs: excessive focus on blockbuster drugs can expose firms to significant losses if those projects fail. At the same time, overly conservative strategies may yield incremental innovations but fail to capture market leadership (Cockburn and Henderson, 2001). Systemic approaches address these challenges by embedding structured evaluation criteria that enable assessment of financial returns, strategic fit, ecosystem positioning, and long-term resilience. By drawing on the extensive literature on portfolio management, evaluation criteria, and innovation ecosystems, firms can develop holistic frameworks that navigate uncertainty with an adaptive, evidence-based mindset while building the strategic competencies necessary for sustained competitive advantage.

## 3. Research method

This research draws on the use of illustrative cases of successes and failures in investment decision-making by pharma and biotech companies, as a method to explore specific features and issues characterizing these domains. The use of illustrative case studies as a research method has long been recognized as a valuable approach for advancing theoretical understanding while generating actionable insights for practitioners, particularly in contexts characterized by complexity and ambiguity (Eisenhardt, 1989; Yin, 2018). In the pharmaceutical and biotechnology sectors, where investment decisions unfold across lengthy timeframes, involve multiple interdependent stakeholders, and are shaped by scientific, regulatory, and market uncertainties, case-based inquiry offers distinct advantages over purely quantitative or survey-based methods (Siggelkow, 2007). Unlike large-scale statistical analyses that seek to establish generalizable patterns across populations, illustrative cases enable researchers to examine the nuanced interplay of contextual factors, strategic choices, and organizational processes that shape outcomes in specific settings (Flyvbjerg, 2006). This depth of analysis is particularly valuable when investigating systemic phenomena, as it allows scholars to trace causal mechanisms and identify how different dimensions of decision-making interact in practice (George and Bennett, 2005).

Illustrative cases serve multiple purposes within scholarly inquiry. First, they function as powerful instruments for theory building by revealing patterns, relationships, and mechanisms that may not be evident through abstract theorizing alone (Siggelkow, 2007; Ketokivi and Choi, 2014). By grounding theoretical propositions in empirical detail, cases enhance the plausibility and relevance of conceptual frameworks, ensuring that scholarly models reflect

the lived realities of organizational actors rather than idealized assumptions. Second, cases provide rich empirical grounding that bridges the persistent gap between academic rigor and managerial relevance (Bartunek and Rynes, 2014). Executives and policymakers often find case narratives more accessible and compelling than statistical abstractions, as they illustrate how theoretical principles operate in recognizable contexts and highlight the consequences of specific strategic choices.

The deliberate selection of contrasting cases – comparing successes with failures, or systemic approaches with fragmented ones – enables scholars to engage in what Eisenhardt and Graebner (2007) describe as replication logic. By demonstrating that similar mechanisms produce consistent outcomes across different organizational settings, or that divergent approaches yield predictably different results, researchers strengthen the internal validity of their theoretical claims. In the context of pharmaceutical investment decision-making, comparing firms that have successfully implemented systemic frameworks with those that have suffered high-profile failures highlights not only what works but also why it works, thereby offering deeper insights into the underlying logic of effective governance (Langley, 1999). Furthermore, cases facilitate what Tsang (2014) terms analytical generalization, wherein findings are generalized not to populations but to theoretical propositions, thereby extending the applicability of insights beyond the immediate empirical setting. Through this methodological lens, the following case analyses are positioned not merely as descriptive accounts but as theoretically informed examinations that advance scholarly understanding while informing managerial practice.

### *3.1 Case studies: successes and failures in systemic investment decision-making*

Case studies provide a powerful means to illustrate the consequences of systemic versus fragmented approaches to investment decision-making in pharma and biotech companies (Schünemann *et al.*, 2022). In line with the ecosystem-embedded perspective developed above, the illustrative cases are interpreted as examples of internal governance quality, showing also how portfolio criteria and project prioritization are shaped by configurations of external interdependencies (partners, infrastructures, regulatory and clinical communities, and complementary assets). We therefore highlight, for each case, how systemic decision-making involves both selecting projects and enabling the institutional and partnering arrangements required to learn and create value under long-horizon uncertainty. By examining firms that have successfully re-engineered their R&D decision-making processes alongside those that have suffered high-profile failures, we can distill key lessons for managers and investors.

*3.1.1 AstraZeneca's "5 R" framework: building systemic rigor.* In the early 2000s, AstraZeneca faced mounting criticism over declining R&D productivity and several costly late-stage failures. In response, the company developed its now well-known "5 R" framework, which reoriented portfolio decision-making around five guiding principles: the right target, the right tissue, the right safety, the right patient, and the right commercial potential (Cook *et al.*, 2014).

The 5 R model exemplifies a systemic approach. Instead of evaluating projects through isolated criteria–such as market size or early biological signals–AstraZeneca embedded a cross-functional governance process that required each project to demonstrate strength across all five pillars. Importantly, this framework integrated scientific rigor (e.g. validated targets), translational medicine (e.g. patient selection strategies), and commercial foresight (e.g. payer acceptability).

The 5 R criteria can be read as more than an internal checklist: they operationalize a strategic hypothesis about which external interdependencies must be mobilized to make a candidate viable. For instance, "right patient" and translational requirements implicitly depend on access to clinical networks, biomarker and diagnostic capabilities, and sustained engagement with regulators and external scientific communities. Thus, the strategic criterion is not only internal fit, but the feasibility of building and leveraging a platform of

complementary assets and collaborative arrangements that support repeated learning across projects.

Empirical outcomes suggest the framework's effectiveness. Following the adoption of 5 R, AstraZeneca reported a near-doubling of its clinical success rates from Phase II to Phase III, bringing them in line with or above industry averages (Morgan *et al*., 2018). Moreover, the company's late-stage pipeline stabilized, supporting the launches of blockbuster therapies in oncology and respiratory diseases.

From an investment decision-making perspective, the 5 R framework illustrates how systemic evaluation criteria can mitigate risks by preventing the premature advancement of weak assets, while enabling a more confident allocation of capital to promising candidates.

*3.1.2 Eli Lilly's focused differentiation strategy.* While AstraZeneca pursued systemic evaluation across multiple dimensions, Eli Lilly adopted a focused differentiation strategy. In the early 2010s, Lilly faced declining revenues due to patent expirations on blockbusters such as Zyprexa and Cymbalta. Rather than attempting broad diversification, the company concentrated resources on therapeutic areas where it held distinctive capabilities, including oncology, diabetes, and immunology (DrugPatentWatch, 2025).

Eli Lilly's strategy illustrates a different application of systemic thinking: rather than spreading resources thinly across multiple therapeutic bets, the company aligned its investment decisions with its organizational strengths, external partnerships, and regulatory expertise. This alignment enabled Lilly to deliver targeted innovations, such as Trulicity (for diabetes) and Verzenio (for oncology), both of which achieved strong commercial performance. Similarly, focused differentiation can be interpreted as a portfolio-level capability-building strategy contingent on external context. Concentrating investments in selected therapeutic domains is viable when the focal firm can reliably access and orchestrate complementary assets outside its boundaries, such as specialized research partners, trial infrastructures, and supply-chain and manufacturing capabilities aligned with the targeted modalities. In this view, the "strategic" criterion behind project selection captures not only internal strengths but also the ecosystem conditions that enable scaling, learning, and appropriating value from those strengths.

However, focused differentiation carries risks. A concentration of investment in select therapeutic areas exposes firms to sector-specific scientific uncertainties, as evidenced by Lilly's repeated failures in Alzheimer's disease programs. Still, by embedding systemic alignment between corporate strategy and R&D investment, Lilly reduced portfolio fragmentation and enhanced resilience in its chosen domains.

*3.1.3 The torcetrapib failure: the cost of fragmented decisions.* Not all firms have successfully applied systemic approaches. Pfizer's torcetrapib program, once heralded as a potential blockbuster for cardiovascular disease, provides a cautionary tale of fragmented decision-making.

Torcetrapib, a cholesteryl ester transfer protein (CETP) inhibitor, was designed to raise HDL cholesterol levels and thereby reduce cardiovascular risk. Despite accumulating evidence of biological complexity and early safety signals, Pfizer advanced the drug into large-scale Phase III trials without sufficient systemic evaluation of its mechanism of action and translational validity (Barter *et al*., 2007).

The outcome was catastrophic: the ILLUMINATE trial revealed on one side a lack of cardiovascular benefit, on the other side an increased risk of mortality among patients taking torcetrapib (Nissen *et al*., 2007). Pfizer terminated the program in 2006 after investing over $800 million, and the failure significantly damaged its pipeline and investor confidence.

Analysts have since argued that systemic gaps–particularly the insufficient integration of preclinical safety data, translational insights, and mechanistic plausibility–contributed to the flawed investment decision (Kola and Landis, 2004). Unlike AstraZeneca's 5 R framework, Pfizer's governance process allowed commercial optimism and market projections to overshadow scientific rigor.

The torcetrapib case underscores the risks of siloed decision-making, where financial enthusiasm and strategic aspirations advance projects without adequate systemic scrutiny.

*3.1.4 Alzheimer's disease: the "graveyard" of pharma investment.* Perhaps no therapeutic domain better illustrates the challenges of systemic investment decision-making than Alzheimer's disease (AD). Over the past 2 decades, more than 200 clinical trials targeting AD have failed, with estimated R&D expenditures exceeding $40 billion (Cummings *et al.*, 2018).

The persistent failures of AD programs reflect several systemic challenges. First, the underlying biology of Alzheimer's remains poorly understood, and the amyloid hypothesis–long the dominant scientific paradigm–has repeatedly failed to translate into clinical benefit (Hardy and Selkoe, 2002). Second, patient heterogeneity complicates trial design and endpoint measurement, while regulatory requirements for demonstrating disease modification remain stringent (Cummings *et al.*, 2021). Third, commercial pressures have driven firms to aggressively advance candidates, despite limited translational evidence.

The consequences have been profound. High-profile failures, such as Eli Lilly's solanezumab and Roche's crenezumab, have eroded investor confidence in the AD field, leading many firms to scale back or exit AD research altogether. Only recently, with the controversial accelerated approval of aducanumab and the subsequent debate over its clinical efficacy, has the field regained cautious interest (Knopman *et al.*, 2021).

From a systemic perspective, Alzheimer's represents a "perfect storm" of risks: scientific uncertainty, regulatory stringency, commercial desperation, and societal pressure. Fragmented decision-making - advancing candidates based on weak mechanistic validation or surrogate endpoints–has repeatedly led to costly failures. The lesson is clear: without systemic integration of scientific merit, regulatory feasibility, commercial viability, and competitive positioning, investment in such high-risk domains is likely to falter.

The four cases–AstraZeneca, Eli Lilly, Pfizer's torcetrapib, and Alzheimer's–offer valuable contrasts in how systemic versus fragmented approaches shape outcomes (Table 1).

This comparison highlights three insights. First, systemic frameworks (e.g., AstraZeneca's 5 R) enhance decision quality by embedding structured, multidimensional evaluation. Second, strategic alignment (e.g., Eli Lilly) can substitute for broad diversification, provided systemic coherence is maintained. Third, fragmented approaches–whether firm-specific (torcetrapib) or industry-wide (Alzheimer's) - expose companies to catastrophic failures.

The case studies confirm that investment decision-making in pharma and biotech organizations is not simply about financial projections or isolated scientific hypotheses. Rather, it requires systemic governance that integrates multiple perspectives.

Key implications include:

**Table 1.** Systemic vs fragmented investment decision-making: case comparisons

| Case | Approach | Key features | Outcome | Lessons learned |
|---|---|---|---|---|
| AstraZeneca (5R) | Systemic | Cross-functional evaluation across five pillars | Improved R&D productivity; successful launches | Systemic evaluation improves success rates |
| Eli Lilly | Semi-Systemic | Strategic alignment with organizational strengths | Strong launches; Alzheimer's failures persist | Alignment enhances resilience but risks concentration |
| Pfizer (Torcetrapib) | Fragmented | Overreliance on market projections; weak integration of safety data | Catastrophic failure; $800 m loss | Lack of systemic scrutiny led to failure |
| Alzheimer's Disease | Fragmented (Industry-wide) | Weak biological understanding; aggressive advancement | >200 failed trials; billions lost | High-risk domains require systemic integration |

(1) Cross-functional integration is critical. Projects must be evaluated simultaneously on scientific, regulatory, commercial, and competitive dimensions.

(2) Disciplined frameworks (e.g. AstraZeneca's 5 R) improve attrition rates by preventing weak assets from advancing.

(3) Strategic alignment enhances resilience, though it requires diversification across modalities or risk-adjusted balancing to avoid overexposure.

(4) High-risk domains such as Alzheimer's demand caution: without systemic integration of weak science, regulatory uncertainty, and commercial pressures, investment will repeatedly fail.

Together, these cases highlight the need for systemic frameworks to enhance investment decision-making.

## 4. Tools and techniques for systemic investment decision-making

Systemic approaches to investment decision-making in pharma and biotech require conceptual frameworks and concrete tools that can operationalize them. In recent years, advances in data analytics, AI, and decision science have reshaped how companies handle uncertainty, balancing risk, and optimizing resource allocation (Stephen, 2025; Yingngam *et al*., 2024). Based on the above cases, this section provides a report on contemporary practices and challenges that can support and complement the proposed systemic approach to investment decision-making in pharma and biotech organizations. Namely, it explores five categories of tools and techniques that enable systemic approaches, moving from established techniques – such as decision tree analysis, and market and product intelligence – to more novel methods – such as AI-driven portfolio management, predictive analytics, and virtual pipelines.

### *4.1 Decision tree analysis for R&D investments*

Decision tree analysis is a well-established technique in decision science that is particularly relevant for operationalizing systemic investment frameworks in pharmaceutical and biotechnology contexts. By mapping sequential choices as branching pathways and assigning probabilities and economic payoffs to each potential outcome, decision trees enable firms to quantify expected values, visualize trade-offs, and evaluate alternative strategies under conditions of uncertainty. This structured approach addresses the challenge of fragmented decision-making evident in Pfizer's torcetrapib program, where the absence of systematic mechanisms for weighing scientific risks against commercial aspirations led to optimism overriding cautionary signals.

A decision tree constructed for evaluating a Phase II oncology trial, for instance, might illustrate multiple potential trajectories: technical success leading to Phase III advancement with a probability-weighted net present value of five hundred million dollars; failure resulting in program termination with sunk costs of one hundred million dollars; or conditional outcomes dependent on biomarker-defined subgroup responses that might support accelerated regulatory pathways. By incorporating conditional probabilities that reflect real-world complexities such as patient heterogeneity, competitive dynamics, and regulatory contingencies, decision trees move beyond simplistic go/no-go binaries toward nuanced assessments that acknowledge multiple possible futures (Loch and Bode-Greuel, 2008). Had Pfizer employed rigorous decision tree analysis during torcetrapib development, explicitly modeling the probability and consequences of mechanistic failures alongside optimistic commercial projections, the unfavorable risk-return profile might have become apparent before committing resources to the ill-fated ILLUMINATE trial.

Decision tree analysis also facilitates risk-adjusted portfolio optimization by aggregating individual asset evaluations into comprehensive portfolio assessments. By constructing and

integrating decision trees across multiple concurrent projects, firms can evaluate systemic portfolio exposure to risk categories such as technical uncertainty, regulatory contingencies, commercial volatility, and competitive displacement. This portfolio-level perspective enables managers to pursue intelligent diversification strategies that balance high-risk breakthrough opportunities with more predictable incremental innovations, thereby achieving the resilience that AstraZeneca built through its systematic 5 R evaluation process. The approach also surfaces dependencies between projects that share common platforms, manufacturing capabilities, or market channels, revealing opportunities for strategic interactions alongside potential concentration risks.

While decision trees provide valuable clarity and analytical rigor, they can become unwieldy when projects involve dozens of uncertain variables interacting in complex ways across extended time horizons. Integration with predictive analytics and simulation modeling becomes essential for maintaining analytical tractability while preserving systemic completeness. Monte Carlo simulation techniques, for instance, can complement decision tree frameworks by modeling probability distributions around key assumptions rather than relying on point estimates, thereby providing more comprehensive characterizations of risk-return profiles that support robust decision-making even under deep uncertainty.

### *4.2 Market and product intelligence*

Systemic investment decision-making requires continuous monitoring of external market dynamics alongside internal scientific and operational assessments, as emphasized in the tools discussed previously. Market and product intelligence encompasses systematic tracking of competitor pipelines, pricing and reimbursement trends, patent landscapes, regulatory policy shifts, and evolving standards of care within therapeutic domains (Cockburn and Henderson, 2001). This external orientation addresses a blind spot evident in many pharmaceutical failures: the tendency to become so focused on internal development activities that organizations miss crucial signals about changing competitive contexts or shifting payer requirements that fundamentally alter the commercial viability of projects in development.

Competitor pipeline tracking has become particularly critical as therapeutic spaces grow increasingly crowded and product differentiation becomes more challenging. By monitoring ongoing clinical trials, regulatory submissions, patent expirations, and commercial launches, firms can anticipate competitive threats and identify strategic opportunities that might inform portfolio decisions. If intelligence reveals that a competitor's drug targeting the same indication is likely to launch two years earlier than a firm's own candidate, investing substantial resources in a late follower position may require demonstrable differentiation through superior efficacy, improved safety, more convenient administration, or cost advantages to remain commercially viable. The Alzheimer's disease experience illustrates this dynamic starkly: numerous firms pursued similar amyloid-targeting strategies simultaneously, yet the collective failure of these programs suggests that competitive intelligence focused solely on rival pipelines proved insufficient without deeper interrogation of shared mechanistic assumptions underlying the entire therapeutic approach.

Market intelligence extends beyond competitor tracking to encompass payer behavior, health technology assessment trends, and evolving reimbursement frameworks that increasingly emphasize demonstrated value rather than regulatory approval alone. With mounting pressures on healthcare budgets globally, reimbursement decisions depend progressively on cost-effectiveness evidence and real-world performance data that extend beyond the controlled efficacy demonstrations required for regulatory authorization (Neumann *et al.*, 2014). Investment frameworks must therefore evaluate how potential assets align with value-based healthcare models and anticipate payer expectations regarding pricing, comparative effectiveness, and budget impact. Eli Lilly's successful launches of Trulicity and Verzenio reflected not only scientific and regulatory achievements but also careful attention to commercial positioning within reimbursement environments that favored differentiated value propositions in diabetes and oncology, respectively.

Finally, market and product intelligence support geographic strategy development by surfacing regional variations in regulatory requirements, reimbursement mechanisms, and clinical practice patterns that shape market entry decisions. Regulatory approval timelines, evidentiary standards, and pricing frameworks vary significantly across jurisdictions, creating complex optimization challenges for firms seeking to maximize global commercial potential (Pepermans and Maertens, 2020). Organizations with systemic frameworks integrate these geographic considerations early in investment processes, ensuring that development programs generate the data required for successful launches across priority markets rather than discovering misalignments only after costly clinical programs have concluded. This geographic intelligence proved crucial for companies navigating the fragmented regulatory landscape during COVID-19 vaccine development, where success required simultaneous engagement with multiple regulatory authorities operating under different evidentiary frameworks and authorization mechanisms.

### *4.3 Virtual pipelines and resource allocation*

Virtual pipeline modeling extends predictive analytics by enabling firms to simulate entire research and development portfolios as dynamic, interconnected systems rather than collections of independent projects. Instead of relying on static spreadsheet projections that treat each asset in isolation, managers can construct digital representations of their pipelines and model how projects will compete for shared resources under various assumptions about technical success rates, funding availability, regulatory milestone timing, and manufacturing capacity constraints (Hughes *et al*., 2017). This systemic perspective addresses a critical gap evident in many pharmaceutical failures: the tendency to evaluate projects individually without considering portfolio-level interdependencies that may amplify risks or constrain opportunities.

Virtual pipeline capabilities enable the prospective identification of potential bottlenecks and the testing of alternative strategies before resource conflicts materialize as operational crises. For example, if scenario modeling reveals that two late-stage oncology programs following the focused differentiation logic employed by Eli Lilly might reach Phase III development simultaneously, virtual pipeline analysis can assess whether manufacturing capacity, clinical operations staffing, or regulatory affairs bandwidth would become constraining factors. Armed with these insights, firms can proactively adjust development timelines, establish outsourcing arrangements, or stagger trial initiations to prevent delays that might undermine commercial value. Such forward-looking resource planning stands in sharp contrast to the reactive crisis management that often characterizes organizations lacking systemic portfolio oversight.

Virtual pipelines also enhance transparency and credibility for external stakeholders, particularly investors seeking assurance that management teams employ disciplined, evidence-based approaches to capital allocation. By presenting scenario-based portfolio forecasts that explicitly model uncertainty and demonstrate resilience across plausible future states, firms can differentiate themselves from competitors still relying on deterministic projections and optimistic assumptions. This transparency is especially valuable in contexts such as Alzheimer's disease research, where repeated high-profile failures have eroded investor confidence and heightened scrutiny of firms' risk management capabilities. Organizations that can credibly demonstrate systemic approaches to portfolio construction and resource allocation may find it easier to attract capital for ambitious but well-reasoned innovation strategies.

### *4.4 AI-driven portfolio management*

AI has emerged as one of the most significant enablers of systemic investment decision-making in life sciences, fundamentally altering how organizations process information, identify patterns, and forecast outcomes. By combining machine learning algorithms with

natural language processing capabilities, AI systems can analyze enormous volumes of heterogeneous data spanning genomic databases, clinical trial registries, electronic health records, regulatory filings, and scientific literature (Stephen, 2025; Yingngam *et al*., 2024). This analytical capacity addresses a core challenge evident in the Alzheimer's disease failures documented earlier: the inability of traditional assessment methods to integrate complex biological insights with translational validity signals that might have cautioned against aggressive advancement of candidates built on questionable mechanistic foundations.

One of AI's most significant contributions lies in portfolio prioritization, where traditional methods have historically relied on expert judgment operating within constrained information boundaries. AstraZeneca's 5 R framework, while conceptually sophisticated, required substantial analytical support to assess whether candidates met criteria such as "right target" and "right safety" across diverse therapeutic contexts. AI augments this evaluation process by predicting probabilities of technical success, identifying previously unrecognized correlations in biological pathways, estimating likely regulatory trajectories, and highlighting potential safety liabilities that might escape conventional review (Mak and Pichika, 2019). Platforms such as BenevolentAI and Insilico Medicine exemplify these capabilities in practice by applying machine learning to discover novel therapeutic targets and identify repurposed opportunities for existing compounds, thereby reducing attrition rates during early research and development (Zhavoronkov *et al*., 2019).

The practical implementation of AI-driven portfolio management has yielded demonstrable advances in pharmaceutical discovery efficiency, as evidenced by recent breakthrough applications. Zhang *et al*. (2025) document how these platforms have successfully applied machine learning and natural language processing to discover novel therapeutic targets and repurpose existing compounds, thereby reducing attrition rates in early research and development. Their analysis reveals that AI technologies excel at analyzing complex biological systems, identifying disease biomarkers, simulating drug-target interactions, and predicting the safety and efficacy profiles of drug candidates. Notably, integrating multi-omics data with scientific literature via knowledge graph construction has enabled AI systems to discern previously unrecognized relationships among genes, disease pathways, and potential therapeutic interventions. The PandaOmics platform exemplifies this capability, having successfully identified TRAF2- and NCK-interacting kinase as a viable anti-fibrotic therapy target through multi-omics network analysis, ultimately leading to the development of a specific inhibitor validated in preclinical models (Zhang *et al*., 2025).

Importantly, AI-driven portfolio management also facilitates systemic integration by establishing linkages between scientific validation and commercial viability that might otherwise remain disconnected. Algorithms can evaluate how specific biomarker-based patient stratification strategies align with potential reimbursement environments, ensuring that scientific merit and commercial sustainability are considered jointly rather than sequentially. Had such capabilities been available and properly integrated into Pfizer's governance processes during torcetrapib development, the disconnect between mechanistic plausibility and clinical benefit might have been surfaced earlier, potentially preventing the advancement of a fundamentally flawed candidate into expensive late-stage trials.

Yet AI is not without inherent risks and limitations that must be acknowledged and managed within systemic frameworks. Overreliance on algorithmic outputs may obscure underlying uncertainties or create false confidence in predictions generated from incomplete or biased training datasets. The Alzheimer's disease experience offers a cautionary perspective: even the most sophisticated AI systems cannot compensate for fundamental gaps in biological understanding or validate hypotheses built on questionable scientific foundations. To ensure systemic rigor, firms must embed AI outputs within cross-functional governance structures where domain experts validate algorithmic insights, contextualize findings within broader scientific understanding, and maintain appropriate skepticism toward model predictions. In this sense, AI should be conceptualized as an enabler that augments rather than replaces human judgment in systemic decision-making processes.

*4.5 Predictive analytics for strategic decision-making*

Alongside AI, predictive analytics provides another essential layer of systemic foresight by applying statistical modeling techniques to forecast future outcomes from historical patterns and real-time data flows (Stephen, 2025). While AI focuses primarily on pattern recognition and relationship discovery within complex datasets, predictive analytics emphasizes probabilistic forecasting of specific events and trends relevant to portfolio management. In pharmaceutical and biotechnology organizations, this translates into capabilities for anticipating how clinical, commercial, and competitive dynamics will interact across extended development timelines, thereby enabling more informed resource allocation decisions.

Companies employing predictive analytics can estimate patient recruitment rates and protocol feasibility for planned clinical trials (Getz *et al.*, 2016), forecast market uptake trajectories and pricing elasticity under alternative commercialization scenarios (Garrison and Towse, 2017), and anticipate the timing and implications of competitors' regulatory approvals within contested therapeutic spaces. These forecasting capabilities are particularly valuable for scenario-planning exercises that test portfolio resilience under varying regulatory, market, and macroeconomic conditions (Courtney *et al.*, 1997). Eli Lilly's focused differentiation strategy, for instance, benefited from predictive insights that enabled the company to concentrate resources in therapeutic domains where market dynamics, competitive positioning, and organizational capabilities aligned favorably, even as the firm struggled to generate similar insights in the scientifically uncertain Alzheimer's landscape.

The integration of predictive analytics within systemic frameworks enables organizations to move beyond static evaluations of individual projects toward dynamic assessments that account for temporal dependencies and evolving contexts. Rather than simply asking whether a candidate satisfies evaluation criteria at a single decision point, firms can model how changing conditions might alter risk-return profiles over multi-year development horizons. This temporal dimension proves essential for understanding whether projects that appear attractive under current assumptions will maintain their value proposition as competitive landscapes shift, regulatory requirements evolve, or market preferences change. When these predictive insights are embedded within cross-functional decision-making structures similar to those employed in AstraZeneca's 5 R framework, organizations can more readily identify which projects combine strong intrinsic potential with sufficient resilience to sustain long-term strategic value.

Table 2 summarizes how the tools for systemic decision-making work and contribute to the systemic framework.

Individually, decision trees, market intelligence, AI, predictive analytics, and virtual pipelines offer powerful capabilities. However, their true value emerges when integrated into a systemic governance framework. In fact, AI provides early-stage insights into scientific and translational validity, predictive analytics can project clinical, commercial, and competitive outcomes, and virtual pipelines may simulate interdependencies and resource constraints. At the same time, decision trees allow for quantifying trade-offs and risk-adjusted returns, and, finally, market intelligence can contextualize decisions within payer, competitor, and regulatory landscapes.

Together, these tools operationalize the four systemic pillars – i.e. scientific merit, commercial viability, regulatory feasibility, and competitive positioning–by embedding evidence-based methods into decision-making. Importantly, cross-functional governance bodies must interpret and balance these tools, ensuring that systemic integration prevails over fragmented reliance on any single technique.

To illustrate integration, consider a company evaluating three oncology assets: (1) a targeted therapy in Phase II, (2) an immunotherapy in Phase I, and (3) a companion diagnostic platform in development.

(1) AI algorithms analyze genomic and clinical trial datasets to validate biomarkers for patient stratification.

**Table 2.** Tools and techniques for systemic decision-making in pharma and biotech companies

| Tool/Technique | Function | Contribution to systemic framework |
|---|---|---|
| AI-driven Portfolio Management | Analyzes large datasets, predicts success probabilities | Links science with commercial and regulatory projections |
| Predictive Analytics | Forecasts trial performance, market uptake, competitor moves | Supports scenario planning and foresight |
| Virtual Pipelines | Simulates interdependencies and resource allocation | Improves portfolio resilience and transparency |
| Decision Tree Analysis | Quantifies trade-offs and risk-adjusted NPVs | Operationalizes diversification and strategic balance |
| Market Intelligence | Monitors competitors, payers, and regulatory environments | Ensures strategic alignment and market readiness |

(2) Predictive analytics forecast patient uptake and reimbursement potential under different pricing scenarios.

(3) Virtual pipelines simulate the impact of advancing all three assets simultaneously on manufacturing and staffing capacity.

(4) Decision trees calculate expected NPVs based on regulatory contingencies, such as breakthrough designation.

(5) Market intelligence assesses competitor timelines and payer attitudes toward combination therapies.

By integrating these insights within a cross-functional governance structure, the company can decide whether to prioritize the targeted therapy (high short-term potential), immunotherapy (long-term disruptive innovation), or the diagnostic platform (strategic enabler). This systemic approach balances risk and return while aligning with corporate strategy.

Despite their promise, these tools face limitations. AI models may overfit data; predictive analytics rely on historical patterns that may not hold in novel scientific domains; virtual pipelines demand high-quality inputs that are often scarce; decision trees may oversimplify complex interdependencies; and information asymmetries can distort market intelligence.

Moreover, integration across tools requires substantial organizational capabilities, including data governance, IT infrastructure, and cross-functional expertise. Smaller biotech firms may lack these resources, while larger pharmaceutical companies face bureaucratic inertia. Policymakers and investors must therefore recognize that systemic frameworks are not universally accessible, and may require external partnerships or industry consortia to realize their full potential.

## 5. Discussion

The preceding sections have highlighted how systemic approaches, supported by tools and techniques, can reshape investment decision-making in pharmaceutical and biotechnology firms. The theoretical foundations emphasize the inadequacy of siloed decision-making, the case studies illustrate both successes and failures, and the tools demonstrate how to operationalize systemic integration. The discussion synthesizes these insights into broader themes relevant to both academics and practitioners: ecosystem orchestration, partnerships and alliances, resilience and agility, and the role of digital technologies.

In particular, pharma and biotech innovation increasingly depends on ecosystem dynamics (Wu and He, 2020). No firm possesses the scientific, regulatory, and commercial capabilities to innovate independently. Investment decisions must therefore account for the systemic interdependencies across universities, biotech startups, contract research organizations, regulators, and payers (Powell *et al*., 1996).

AstraZeneca's adoption of the 5 R framework illustrates how firms can orchestrate internal decision-making processes to better align with external networks. By emphasizing translational medicine and patient stratification, AstraZeneca positioned itself to collaborate effectively with academic partners and regulators. Conversely, Pfizer's torcetrapib failure illustrates how weak ecosystem integration–such as insufficient consultation with external scientific evidence–can amplify risks.

From a systemic perspective, investment decisions should be evaluated in terms of internal portfolio metrics ab of their fit within broader innovation ecosystems (Wu and He, 2020; Chesbrough, 2003). This requires mechanisms for absorptive capacity–the ability of firms to recognize, assimilate, and apply external knowledge (Cohen and Levinthal, 1990). Firms with strong absorptive capacity are better positioned to integrate external partnerships into systemic frameworks, thereby enhancing resilience. Dougherty's framework helps specify the mechanism through which ecosystem conditions enter strategic portfolio criteria (Dougherty, 2017). In complex innovation eco-systems, strategizing is a continuous abductive process that maps a portfolio of value-creating opportunities far into the future, using learning events generated across projects, partners and institutions. Portfolio decisions therefore evaluate projects not only by expected returns or internal alignment, but by the plausibility of the underlying configuration of interdependencies required for value creation, including the governance structures that sustain collaboration, accountability, and long-term learning. This view strengthens the link between external context, capability building and competitive advantage, and explains why "strategic" criteria in portfolio decision-making are inherently ecosystem-embedded rather than solely internally derived.

Additionally, strategic partnerships have become central to informed systemic investment decision-making. Large pharmaceutical firms increasingly rely on biotech startups for early-stage innovation, while biotech firms depend on big pharma for financial resources, regulatory expertise, and commercialization capabilities (Rothaermel and Deeds, 2004).

Partnerships mitigate risks by spreading costs and sharing knowledge, but they also introduce coordination challenges. Misaligned incentives, cultural clashes, and disputes over intellectual property can undermine value creation. Systemic frameworks must therefore incorporate partnership governance mechanisms–such as clear milestone-based financing, joint steering committees, and transparent data-sharing arrangements (Pisano, 2006).

Eli Lilly's focused strategy provides an example of effective partnership alignment. By focusing on therapeutic areas of strength, Lilly selectively partnered with biotech firms and academic centers, leveraging complementary expertise to enhance its portfolio value. Conversely, in Alzheimer's disease, the widespread failures across the industry reveal gaps in scientific foundations and show how fragmented collaboration structures have struggled to bring together patient perspectives, advances in biomarkers, and regulatory dialog within cohesive systemic frameworks. Partnerships also extend to co-investment models, where venture capital, governments, and public-private partnerships share the risks of early-stage development. For example, the Coalition for Epidemic Preparedness Innovations (CEPI) co-financed COVID-19 vaccine R&D, demonstrating how systemic collaboration can accelerate innovation under uncertainty (Gouglas *et al.*, 2018). Such models suggest that systemic investment frameworks must evolve beyond firm-level decision-making toward multi-stakeholder orchestration.

On the one hand, resilience – conceived as the capacity to absorb shocks and adapt to disruptions – is a critical outcome of systemic investment decision-making. Pharma and biotech firms face numerous external shocks, including regulatory rejections, trial failures, competitive disruptions, and macroeconomic crises.

Resilience requires portfolio diversification, but not in a simplistic sense. Excessive diversification can dilute expertise and increase coordination costs, while excessive concentration amplifies exposure to single-point failures (Scannell *et al.*, 2012). Systemic approaches enable firms to achieve portfolio balance, combining high-risk/high-reward projects with lower-risk, incremental innovations. Decision tree analysis and virtual pipelines

are particularly useful in operationalizing this balance, enabling firms to visualize systemic risk exposure across multiple projects.

Case evidence supports this point. AstraZeneca enhanced its resilience by systematically applying the 5 R framework, ensuring that its portfolio composition reflected rigorous evaluation across multiple key pillars. By contrast, Pfizer's torcetrapib failure weakened resilience because it represented an outsized bet on a single asset without adequate systemic safeguards.

From an academic perspective, resilience aligns with theories of real options and dynamic capabilities (Teece *et al*., 1997). Real options enable firms to maintain flexibility under uncertainty, while dynamic capabilities emphasize the ability to reconfigure portfolios in response to changing environments. Systemic investment frameworks operationalize these theories by embedding evaluation processes that sustain adaptability.

On the other hand, resilience addresses the ability to withstand shocks, while agility concerns the speed and flexibility of response. In pharma and biotech organizations, agility is particularly critical given the long timelines and high costs of development. Firms that cannot adapt quickly to emerging scientific evidence or regulatory signals risk compounding sunk costs.

Systemic frameworks enhance agility by ensuring that governance bodies receive real-time data from AI, predictive analytics, and market intelligence. For example, adaptive clinical trial designs allow firms to adjust sample sizes or patient stratification strategies mid-trial, thereby reducing the risk of costly late-stage failures (Sherman *et al*., 2016). Similarly, predictive analytics enables firms to reallocate resources rapidly in response to competitor developments or shifting payer requirements.

The development of the COVID-19 vaccine provides a striking example of agility. Companies like Moderna and BioNTech demonstrated systemic agility by leveraging mRNA platforms, AI-driven design, and global regulatory engagement to move from sequencing to authorization in under a year (Dolgin, 2021). These cases suggest that systemic frameworks should emphasize structured evaluation and institutionalize rapid learning and adaptation. In addition, research on the pandemic response reveals that approximately one-third of vaccine candidates emerged from collaborative partnerships, which were more likely to employ next-generation vaccine platforms than solo development efforts (Druedahl *et al*., 2021). More importantly, the analysis distinguishes between partnerships focused on knowledge-sharing – where partners engage in ongoing exchange of expertise and capabilities – and those centered on materials transfer, where innovation proceeds serially through distinct development stages (Druedahl *et al*., 2021). The former approach proved particularly valuable during the urgency of the pandemic, as organizations with robust prior knowledge bases in related scientific and technological domains, combined with established collaborative networks, exhibited significantly superior research and development performance (Laufs *et al*., 2024). This evidence underscores how the systemic integration of internal knowledge resources with diverse external partnerships enables organizations to rapidly mobilize capabilities under time-critical conditions. The findings reinforce that sustained investment in both fundamental research capabilities and cross-institutional relationships constitutes essential preparation for future innovation challenges, whether in pandemic response or other domains requiring accelerated development timelines.

The work highlights how digital transformation has moved from a peripheral concern to a central enabler of systemic investment decision-making. AI, predictive analytics, and virtual pipelines are not merely technical tools but strategic assets that reshape competitive advantage (Gupta and George, 2016).

The integration of digital tools into systemic governance structures is essential to avoid digital fragmentation, in which isolated algorithms or dashboards remain disconnected from strategic choices. This insight aligns with Miozza *et al*. (2024), who stress that digital transformation in pharma should be understood primarily as a managerial challenge, requiring organizational alignment, cultural adaptation, and stakeholder integration. By proposing a systemic framework

that links digital technologies with governance processes, our study addresses the call for more robust managerial perspectives in the field. The true value of digital technologies emerges when they are orchestrated within a cross-functional governance framework that links scientific insights with commercial, regulatory, and competitive considerations.

Importantly, digital transformation also creates new competitive asymmetries. Firms that master AI-driven portfolio management and real-world evidence analytics gain an advantage in both speed and quality of decision-making. Conversely, firms that underinvest in digital capabilities risk systemic disadvantages, as they are unable to match their competitors' foresight and agility.

This raises broader strategic questions for the industry. Should digital transformation be pursued primarily in-house, or through partnerships with specialized technology firms? Should companies share digital infrastructures (e.g. trial recruitment platforms) through consortia, or compete individually? These questions reflect the broader challenge of balancing co-opetition - simultaneous collaboration and competition – within systemic frameworks (Brandenburger and Nalebuff, 1996).

While systemic frameworks provide clear advantages, they also impose trade-offs. Cross-functional governance structures may slow decision-making compared to streamlined, siloed processes. Similarly, reliance on sophisticated tools such as AI and virtual pipelines demands significant investment in infrastructure and expertise.

Managers must therefore balance the costs of systemic integration against the benefits of improved decision quality. The challenge is not whether to adopt systemic frameworks but how to calibrate them to organizational size, strategy, and capabilities. Large pharmaceutical firms may benefit from highly formalized systemic governance, while smaller biotech companies may adopt lighter systemic processes supplemented by partnerships with external experts or consortia.

Academically, this reflects the tension between exploration and exploitation (March, 1991). Systemic approaches support exploration by enabling firms to rigorously evaluate novel opportunities, but they also risk bureaucratic inertia if overly rigid. The optimal balance lies in designing systemic frameworks that preserve flexibility while embedding discipline.

Finally, systemic approaches also have implications beyond firm-level decision-making. Policymakers and regulators influence systemic investment frameworks by shaping incentives, approval pathways, and data-sharing norms. For instance, adaptive trial regulations and accelerated approval pathways reduce uncertainty and encourage systemic agility (Downing *et al.*, 2017). Conversely, fragmented global regulatory requirements increase costs and reduce efficiency.

Public-private partnerships and shared infrastructures can enhance systemic resilience across the industry. Initiatives such as the European Innovative Medicines Initiative (IMI) illustrate how collaborative governance structures can accelerate translational research and reduce systemic risks (Khanna, 2012). Future policy directions should therefore focus on enabling systemic integration across firms and regulators to foster industry-wide resilience.

## 6. Future trends in systemic investment decision-making

Pharmaceutical and biotechnology industries are entering an era of unprecedented transformation (Stephen, 2025; Yingngam *et al.*, 2024). Systemic frameworks for investment decision-making will need to evolve in response to scientific advances, technological disruptions, and shifting socio-economic landscapes. Several trends are likely to redefine the way firms allocate capital and manage uncertainty.

Probably, the rise of precision medicine–tailoring therapies to genetic and molecular profiles–will profoundly affect investment decisions. Unlike traditional "blockbuster" models that target large populations, precision medicine often involves smaller patient segments, necessitating a careful balance of commercial viability with therapeutic innovation (Garrison and Towse, 2017).

Systemic frameworks must therefore incorporate genomic and real-world data into investment evaluations. Companies will increasingly rely on biomarker validation, patient stratification models, and companion diagnostics to reduce attrition and enhance their prospects for regulatory approval. Investments in integrated data platforms and partnerships with diagnostic firms will become essential for systemic decision-making.

The precision medicine paradigm paradoxically reveals both the promise and limitations of big data approaches in pharmaceutical investment decision-making. While large-scale genomic and phenotypic databases enable pattern recognition across populations, rare disease drug development necessitates what Ette *et al*. (2023) term a "small data paradigm"—rigorous analytical frameworks designed to extract maximum knowledge from necessarily limited patient populations. Their work on blarcamesine for Rett syndrome demonstrates how model-informed drug development methodologies, particularly item response theory modeling combined with Bayesian statistical approaches, can transform small clinical trials ($N = 6$ to $N = 25$) into powerful learning systems that characterize drug efficacy with appropriate strength of evidence. This integration of precision medicine principles with advanced pharmacometric modeling represents a critical evolution in systemic investment frameworks, enabling firms to balance the population-level insights of big data with the individualized, mechanism-based understanding required for rare disease therapeutics, thereby expanding the strategic opportunity space while managing inherent uncertainties.

Also, cell and gene therapies present a unique challenge for systemic investment frameworks. These therapies often promise transformative clinical benefits but come with high upfront costs, complex manufacturing, and uncertain long-term safety profiles (Challener, 2017).

Systemic approaches must be adapted by integrating manufacturing scalability, reimbursement models, and long-term follow-up requirements into investment decisions. Virtual pipelines and predictive analytics will be critical for modeling the unique risk-return profiles of these therapies. Furthermore, novel payment models–such as outcomes-based reimbursement–will need to be incorporated into systemic evaluations of commercial viability.

As AI continues to mature, its role in systemic frameworks will expand from supportive analytics to semi-autonomous decision support. Already, AI is being used to design novel molecules, optimize clinical trial design, and predict regulatory outcomes (Zhavoronkov *et al*., 2019).

The next frontier involves integrating AI into real-time portfolio governance. AI systems may continuously update probabilities of success for each asset based on new publications, clinical trial updates, or competitor moves. The convergence of AI-driven analytics with small-data methodologies offers particular promise for investment decisions in rare diseases, where traditional large-scale randomized controlled trials are often infeasible. As Ette *et al*. (2023) demonstrate, combining exposure-outcome modeling with Bayes factor analysis enables decision-makers to quantify the strength of evidence for therapeutic efficacy even in genetically stratified subpopulations of fewer than fifteen patients. Systemic frameworks must therefore evolve to incorporate hybrid analytical architectures that leverage big data for target identification and patient stratification, while employing sophisticated small-data techniques–including N-of-1 trials, basket trials, and pharmacometric modeling–for efficacy characterization. This dual-paradigm approach aligns with the precision medicine imperative to understand individual variability while maintaining the rigor necessary to support regulatory approval and investment confidence in rare disease programs. As such, this would enable governance bodies to make dynamic, data-driven adjustments to portfolio allocation.

The challenge will be striking a balance between algorithmic efficiency and human judgment. Systemic frameworks must institutionalize safeguards against algorithmic bias, ensure transparency, and preserve accountability in investment decisions.

In this context, societal expectations are increasingly shaping pharma and biotech investment priorities. Issues such as equitable access, environmental sustainability, and social responsibility are no longer peripheral but central to long-term legitimacy and value creation.

Systemic investment frameworks must therefore broaden their criteria to incorporate environmental, social, and governance (ESG) factors. For example, companies may prioritize projects that address underserved populations, reduce supply chain carbon footprints, or align with global health priorities. Investors, particularly institutional funds, are already pressuring firms to demonstrate ESG integration in their decision-making (Eccles and Klimenko, 2019).

This trend suggests that systemic frameworks will need to evolve beyond purely financial and scientific metrics to include societal value creation as a formal dimension of investment evaluation.

In this era, the globalization of clinical development introduces both opportunities and risks for systemic investment decision-making. Decentralized clinical trials, accelerated by the COVID-19 pandemic, enable faster recruitment and broader patient representation but also raise challenges in data integrity, regulatory harmonization, and logistics.

Systemic frameworks must integrate geopolitical risk assessment, regional regulatory intelligence, and decentralized data governance into portfolio decisions. Investments in digital trial platforms and patient engagement technologies will increasingly determine systemic resilience in globalized R&D environments.

In addition, a final trend concerns the convergence of therapeutics, diagnostics, and digital health. Digital biomarkers, wearables, and remote monitoring tools are increasingly integrated into clinical development, enabling continuous patient data collection (Topol, 2019).

From a systemic perspective, this convergence demands multi-modal investment frameworks. Firms need to assess the drug candidate alongside the diagnostic tools and digital platforms that will support its effective deployment. This implies new forms of partnership with technology firms, as well as cross-sector governance that bridges traditional silos between the pharmaceutical, biotech, and digital health sectors.

## 7. Managerial and theoretical implications

The systemic framework developed in this study yields significant contributions for both managerial practice and theoretical advancement in pharmaceutical and biotechnology innovation management. These implications arise from integrating multidimensional evaluation criteria, cross-functional governance mechanisms, and digital-enabling technologies within a coherent decision-making architecture designed to navigate the extreme uncertainty characteristic of drug development.

### *7.1 Implications for practice*

For managers navigating the complex landscape of pharmaceutical and biotechnology investment decisions, this research offers a structured yet adaptable approach to portfolio governance that addresses longstanding challenges in resource allocation under uncertainty. The framework's emphasis on systemic integration represents a fundamental departure from conventional linear decision models that evaluate projects sequentially through isolated functional lenses. Instead, managers are encouraged to institutionalize cross-functional evaluation processes wherein scientific merit, commercial viability, regulatory feasibility, and competitive positioning are assessed simultaneously and interdependently (Cooper, 2008; Chao and Kavadias, 2008). This concurrent evaluation approach enables earlier identification of fundamental incompatibilities between dimensions, thereby preventing the costly advancement of projects that appear promising from one perspective yet harbor fatal weaknesses in others.

The implementation of such systemic governance structures requires deliberate organizational design choices. Managers must establish decision-making bodies that

transcend traditional departmental boundaries, bringing together expertise from research and development, regulatory affairs, commercial strategy, manufacturing operations, and financial management (Martinsuo and Poskela, 2011). These cross-functional teams should operate not merely as advisory committees but as empowered governance entities with clear authority to advance, modify, or terminate projects based on holistic assessment. The composition and operating protocols of these bodies significantly influence their effectiveness, with research suggesting that cognitive diversity, psychological safety, and structured decision protocols enhance judgment quality in high-uncertainty contexts (Eisenhardt, 1989; Milliken and Martins, 1996).

Beyond governance structure, managers must strategically integrate digital technologies into decision-making processes while maintaining appropriate skepticism regarding algorithmic outputs. The framework positions artificial intelligence, predictive analytics, and virtual pipeline simulations as augmentative tools that enhance rather than replace human judgment (Agrawal *et al*., 2018). This distinction carries practical significance: while AI-driven portfolio management can process vast datasets to identify patterns imperceptible to individual decision-makers, the interpretation and strategic application of these insights require domain expertise, contextual understanding, and ethical judgment that remain fundamentally human capabilities (Davenport and Ronanki, 2018). Managers should therefore invest in building organizational competencies that enable productive human-machine collaboration, including data literacy among decision-makers, explainable AI systems that reveal the basis for algorithmic recommendations, and governance protocols that mandate human validation of machine-generated insights before they inform major investment decisions.

The framework also highlights the necessity of ecosystem-oriented thinking in portfolio strategy. Contemporary pharmaceutical innovation increasingly depends on orchestrating knowledge flows and resource complementarities across organizational boundaries, encompassing biotech startups, academic research institutions, contract research organizations, and regulatory agencies (Chesbrough, 2003; Autio and Thomas, 2014). Managers must develop capabilities for partnership evaluation and governance that extend beyond traditional alliance management practices. This includes implementing milestone-based financing mechanisms that preserve flexibility while ensuring accountability, establishing transparent intellectual property arrangements that incentivize collaboration without creating future conflicts, and building absorptive capacity to enable the effective integration of externally sourced knowledge (Cohen and Levinthal, 1990; Rothaermel and Hess, 2007).

Furthermore, incorporating environmental, social, and governance considerations into investment evaluation frameworks represents an emerging managerial imperative driven by both institutional investor expectations and societal legitimacy concerns (Eccles and Klimenko, 2019). Managers should develop methodologies for systematically assessing how portfolio decisions align with sustainability objectives, health equity goals, and broader stakeholder value creation beyond narrow shareholder returns. This expanded evaluative lens need not conflict with financial performance objectives; rather, it acknowledges that long-term value creation increasingly depends on organizational legitimacy and social license to operate (Porter and Kramer, 2011).

### *7.2 Implications for theory*

From a theoretical perspective, this study makes several distinctive contributions to scholarly discourse on innovation management, strategic decision-making, and healthcare economics. Most fundamentally, it advances conceptual understanding of systemic decision-making in high-uncertainty environments by synthesizing previously fragmented theoretical perspectives into an integrated framework. While real options theory illuminates the value of staged investment and flexibility (Trigeorgis and Reuer, 2017), dynamic capabilities theory

emphasizes organizational adaptation and resource reconfiguration (Teece *et al*., 1997), and ecosystem theory highlights interorganizational dependencies (Autio and Thomas, 2014), these perspectives have typically been examined in isolation. This research demonstrates that their integration yields deeper insight into pharmaceutical investment decision-making than any single theoretical lens alone.

The framework also contributes to ongoing scholarly debates regarding the appropriate balance between formal evaluation systems and flexibility in innovation management (Martinsuo and Poskela, 2011; Carbonell-Foulquié *et al*., 2004). The case evidence presented suggests that excessive formalization risks stifling radical innovation by prematurely applying conventional success criteria. At the same time, insufficient structure enables cognitive biases and organizational politics to distort resource allocation decisions. The systemic approach proposed here navigates this tension through stage-appropriate evaluation criteria, in which different dimensions gain prominence as projects progress through the development pipeline, coupled with governance mechanisms that preserve adaptability while embedding disciplined assessment.

Moreover, the study extends theoretical understanding of how digital technologies reshape strategic decision-making capabilities. While existing research has examined AI applications in specific functional domains such as drug discovery or clinical trial design (Zhang *et al*., 2025; Zhavoronkov *et al*., 2019), this framework positions digital technologies as integral components of a broader organizational decision-making architecture rather than standalone technical solutions. This conceptualization aligns with emerging perspectives on digital transformation as fundamentally an organizational and managerial challenge requiring systemic integration rather than merely a technological adoption question (Miozza *et al*., 2024; Vial, 2019).

The framework's emphasis on multidimensional evaluation criteria throughout the innovation process also contributes to project portfolio management theory by demonstrating how evaluation dimensions interact dynamically across development stages. Building on Carbonell-Foulquié *et al*. (2004) and Martinsuo and Poskela (2011), this research shows how scientific, regulatory, commercial, and competitive considerations must be continuously reassessed and reweighted as new evidence emerges, rather than applied as static filters at predetermined decision gates. This dynamic perspective better captures the reality of pharmaceutical innovation, wherein early-stage scientific promise must ultimately translate into regulatory approval and commercial viability, requiring ongoing recalibration of investment priorities as uncertainties resolve.

Finally, the study invites scholarly attention to the broader institutional and policy contexts that enable or constrain systemic investment decision-making. The framework demonstrates that organizational-level governance mechanisms operate within and are shaped by regulatory environments, reimbursement systems, intellectual property regimes, and public research funding patterns (Downing *et al*., 2017; Gouglas *et al*., 2018). Future theoretical development should examine these multi-level interactions more systematically, exploring how macro-level institutional arrangements influence micro-level organizational decision processes and vice versa.

## 8. Conclusions

This paper argued that investment decision-making in pharmaceutical and biotechnology companies requires a systemic approach that transcends traditional, fragmented methods. The stakes in this industry are exceptionally high: development costs often exceed $2 billion per drug, timelines stretch over a decade, and attrition rates remain dauntingly high (DiMasi *et al*., 2016; Wouters *et al*., 2020). In such an environment, reliance on siloed financial projections or narrow scientific assessments is inadequate.

We began by identifying the core problem: how to allocate scarce resources across multiple projects under conditions of high uncertainty. The theoretical review showed that while real options theory, ecosystem perspectives, and dynamic capabilities offer important insights, the

literature lacks a comprehensive integration across scientific, regulatory, commercial, and competitive domains. Our systemic framework addressed this gap by proposing four interdependent pillars – i.e., scientific merit, commercial viability, regulatory feasibility, and competitive positioning–embedded within a cross-functional governance framework.

The case studies reinforced this argument. AstraZeneca's adoption of the "5 R" framework demonstrated how systemic evaluation criteria can double clinical success rates and restore pipeline resilience. Eli Lilly's focused differentiation highlighted the benefits of aligning investment decisions with organizational strengths, while also revealing the risks associated with therapeutic concentration. Pfizer's torcetrapib debacle illustrated the catastrophic consequences of fragmented decision-making, where commercial optimism overshadowed scientific plausibility. The Alzheimer's "graveyard" exemplified systemic failure at an industry-wide level, showing how billions of dollars were lost due to weak scientific paradigms and fragmented collaboration structures.

We then examined the tools and techniques that operationalize systemic approaches. AI-driven portfolio management, predictive analytics, virtual pipelines, decision tree analysis, and market intelligence each address distinct uncertainties. Their integration within governance structures ensures that decisions are both evidence-based and informed by multidimensional perspectives. Yet tools alone are insufficient; their value lies in orchestration, not in isolation.

The discussion synthesized these insights into broader themes, such as (1) ecosystem orchestration is vital, as no firm innovates in isolation; (2) partnerships and alliances spread risks and enhance knowledge flows, but require governance mechanisms; (3) resilience emerges from portfolio balance, while agility enables rapid adaptation to shocks; (4) digital technologies are strategic enablers that can either strengthen systemic integration or fragment it further if poorly embedded; (5) managerial trade-offs highlight the need to calibrate systemic frameworks to organizational scale and strategy; (6) policy and regulation play an enabling role by shaping incentives, pathways, and collaborative infrastructures.

Looking forward, systemic frameworks must evolve to accommodate emerging trends. Precision medicine, cell and gene therapies, AI-enabled decision support, sustainability imperatives, decentralized clinical trials, and the convergence of therapeutics, diagnostics, and digital health all demand new forms of systemic evaluation. Importantly, the growing emphasis on ESG considerations means that investment frameworks must incorporate societal value creation alongside financial returns. More broadly, our findings contribute to the research agenda outlined by Miozza *et al*. (2024), who urge scholars to develop theory-driven and empirically grounded approaches to pharmaceutical digital transformation. While their work maps existing contributions and identifies research gaps, our systemic framework provides a practical response, demonstrating how digital tools can be orchestrated within governance structures to improve resilience, agility, and portfolio performance.

For managers and practitioners, the key message is that systemic governance and digital integration are not optional luxuries but strategic necessities. Firms that embed systemic decision-making will reduce costly failures, attract investor confidence, and accelerate the delivery of transformative therapies. For academics, this study contributes to innovation management, strategic decision-making, and healthcare economics by offering a holistic framework grounded in both theory and practice. It also opens avenues for research into metrics, policy engagement, and cross-sector applications.

Ultimately, the systemic framework deepens scholarly understanding while offering practical guidance for decision-makers. In an industry shaped by uncertainty, complexity, and interdependence, systemic approaches are essential for aligning investment decisions with long-term innovation and societal impact.

By adopting systemic approaches, pharmaceutical and biotech firms can transition from reactive, fragmented decision-making toward proactive, evidence-based strategies. This transformation is not merely a managerial choice but a strategic imperative–one that

determines whether companies will thrive or falter in delivering the next generation of life-saving therapies.



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