INDUSTRY IMPACT SERIES

TRINITY

WHITE PAPER

Picking Winners: Portfolio Management for a New Era

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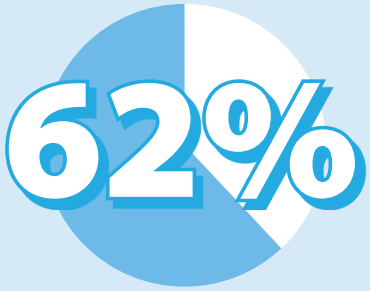
This is the first installment of Trinity's Industry Impact Series, a thought leadership series that identifies key issues that will revolutionize the way therapeutics are developed and commercialized in the years ahead. The focus of Trinity's Industry Impact Series in 2024 explores how biopharma can reimagine the blockbuster and translate scientific innovation to commercial success. The series is designed to leverage the totality of Trinity's background as a life sciences partner supporting strategy, insights and analytics across the product lifecycle.

The biopharmaceutical industry espouses the power of innovation to change lives and defeat disease, and indeed several major innovations have entirely transformed care paradigms in some indications. The immuno-oncology drugs used to treat diverse cancers and GLP-1 agonists now available to patients with diabetes and obesity are enabling improved health outcomes that are both clinically relevant and — equally as important — life-altering to patients. Such innovations are powered by major advances in our understanding of disease and therapeutic mechanisms, ability to leverage artificial intelligence to inform R&D and better target diseases, and massive technological innovations that allow patient needs to be addressed as never before.

With so many developmental assets facing substantial competitive headwinds, it is not surprising that a Trinity analysis found that **62% of products launched between September 2019 and December 2021 underperformed expectations in the first year of launch.** Despite the potential for true innovation, we still see many organizations continuing to advance the "wrong" therapies (those that deliver neither clinically meaningful benefit to patients nor value to shareholders) into the clinic. Companies continue to get it wrong because they fail to use early stage gates to quick-kill programs unlikely to succeed commercially given the current and evolving competitive environment. Evidence of this abounds throughout the industry.



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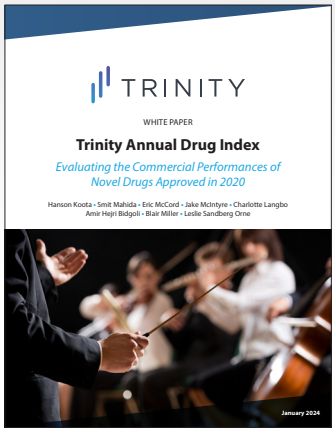

In Case You Missed It

Trinity Annual Drug Index

Evaluating the Commercial Performances of Novel Drugs Approved in 2020

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Notably, of the 55 therapeutics approved by the FDA in 2023, only 11 were the first FDA-approved drug for the approved indication, and 32 of the 44 remaining drugs were follow-on entrants of already approved indications. Drug development pipelines continue to reflect this concentration of activity on well-trodden ground: for example, five subcutaneous therapies targeting IL-17 for plaque psoriasis are in Phase 1-2 development, despite the fact that four such therapies are already FDA approved. This is a remarkable concentration of activity on an indication where marketed IL-23 and IL-17 inhibitors such as SKYRIZI®, COSENTYX® and others have already established a high bar for efficacy, safety and convenience, that additional clinically meaningful improvements are unlikely. The competitive market for new IL-17-targeted therapies for plaque psoriasis is further challenged by increasing global pricing pressures resulting from the market entrance of TNFa biosimilars. What value (clinical and commercial) can a fifth IL-17 targeted therapy provide in this indication?

Similarly, six assets are in Phase 1-2 development for neuromyelitis optica spectrum disorder (NMOSD), despite a U.S. addressable patient population of <10,000 and multiple FDA-approved treatment options. The concentration of activity on this small patient population appears to arise from companies whose assets in development for other indications are plausibly relevant to NMOSD, rather than focused innovation on NMOSD itself – resulting in a pipeline crowded from opportunistic lifecycle management. Yet, similar to psoriasis, current development-stage assets are unlikely to provide a compelling return on investment unless they provide superior efficacy — a seemingly insurmountable challenge given that UPLIZNA® has been shown to prevent relapse in greater than 90% of patients in its pivotal study.

Transforming patient outcomes (and achieving commercial success) demands more than "me too" drugs or new therapies that only provide incremental benefit compared with established treatment options. Additionally, as we look to the future of drug commercialization, policy changes such as the Inflation Reduction Act (IRA), global pricing constraints and increasingly tightening margins across several major pharmaceutical manufacturers, there is even more reason to be more thoughtful and selective about the drugs that are advanced into the clinic and market.

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What's going wrong?

With the biopharmaceutical industry focused on innovations that transform human health, when, why and how are so many companies going wrong in developing the right drugs? The issue isn't vision, commitment or capability, but how companies are organized and incentivized. With critical functions operating in silos and cross-functional collaboration strained with high workloads, decision-making processes (particularly within the early pipeline) too often fail to account for or prioritize long-term commercial considerations. Several factors contribute to this failure.

Misaligning incentives

Many R&D organizations are incentivized to meet clinical development goals, which encourages pursuit of "low-hanging fruit" opportunities for which proof-of-concept already exists or is easy to establish. By taking the road more traveled, this approach often selects for programs that are less innovative, have greater market competition and are less likely to demonstrate meaningful differentiation in the marketplace. While this mindset exists within large pharma companies, it also is embodied by a common venture capital mentality that values near- and mid-term attainment of clinical milestones over long-term clinical and commercial value. Pre-commercial companies continue to trade in this "clinical currency" to drive valuations in the absence of product revenue, but the pharma landscape is littered with failed late-stage trials and underperforming commercial products that demonstrate how quickly and severely this currency can be devalued.

Conflating scientific promise with clinical value

Too often, companies believe that scientific promise can support commercial success in the absence of evidence that demonstrates a compelling value proposition. Scientific advances — the identification of new pathways and targets or the development of novel therapeutic approaches — are necessary but not sufficient for pharmaceutical product innovation. Scientific promise can't be translated into true clinical innovation without robust data from clinical trials, real-world evidence, health economic studies or other evidence generation pathways that allow physicians, patients and payers to understand how the science improves safety, efficacy, ease of use or cost. If a company can't provide the facts that connect the science to an improved outcome (clinical, convenience or economic), it shouldn't expect key constituencies to do so. And it should stop investing in the asset unless or until it becomes feasible to demonstrate a compelling value proposition.

Novartis undertook this difficult but important step in 2018 when it announced it was culling 90 R&D programs out of 430 in an effort to focus on advancing to market only innovative medicines that could transform patient care. Key to this difficult but necessary decision was the ability to differentiate between exciting science and therapeutic relevance. As Jay Bradner, former head of the Novartis Institutes for BioMedical Research, commented to Bloomberg in October 2018, "The sadness about these 90 projects is there's some great science there…these are not bad ideas. Many of them have momentum, but they either are not likely to be transformative for patients or are ill-suited to the focused business ambitions of Novartis."

Failing to include commercial perspectives in early stage development

Many assets fail in the market because commercial perspectives were not considered early in their development. Such failure frequently results not from a lack of appreciation for the value such perspectives provide, but from a failure to scale up in resourcing, both from an FTE or budget standpoint to support integrating the commercial voice into early decision-making (i.e., pre-IND or IND-enabling). Commercial ownership of early assets is often the responsibility of New Products Planning (NPP) teams tasked with providing commercial perspectives and stewardship of 10-15 assets simultaneously, often with a lack of empowerment. Without sufficient staffing, commercial teams understandably focus more on supporting the larger decisions/investments for proof-of-concept (POC) or post-POC assets, creating a significant and ultimately detrimental commercial blind spot in decisions regarding earlier-stage assets, when fundamental development decisions are made. Scaling-up NPP personnel, resources and budgets (which typically allocate $1-5 million to a therapeutic area or subgroup inclusive of personnel, market research, and often business development and licensing activities as well) to enable more market-driven decision-making earlier in development will likely save companies money in the long term by enabling a more vigorous stage gate that limits downstream investment in assets unlikely to succeed commercially.

How can we get it right?

Given these factors, how can companies remove these self-imposed barriers to true innovation that yields clinical and commercial value? While going all-in on moonshot opportunities is great for innovation, it's not really in keeping with companies' fiduciary obligations to their shareholders. Additionally, with many commercial organizations facing near-term patent cliffs or gaps in near-to-mid-term revenue growth, radical risk-taking ignores financial reality. The solution lies in meaningfully changing how commercial organizations incentivize their teams, break down barriers to collaboration and define success. Taking new approaches in three key areas can create an evolved ecosystem that fosters and enables true clinical innovation.

Establish the "right" incentives

To start, R&D organizations need to redefine incentives to advance the "right" assets into the clinic, with a focus on quality rather than quantity. Additionally, assets should be prioritized with an eye toward populations with considerable unmet need, novel mechanisms of action and potential for competitive positioning – and focus on those assets that offer a clear and meaningful advantage over current and future competitors. Every aspect of prioritization should also be supported by the latest and most robust literature, and periodic portfolio reviews should be conducted to adapt priorities as information and the competitive landscape evolves. Objective, external perspectives are invaluable to ruthless, clear-eyed prioritization as they can provide a view of assets focused solely on commercial potential and detached from misaligned internal incentives.

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Develop an objective definition of innovation

It's also critical to define innovation in a way that can be objectively measured, enables a data-driven approach to pipeline prioritization and informs incentivization strategies. The proliferation of real-world data, increasing accessibility of customer insights, and advances in artificial intelligence (AI) and machine learning (ML) provide a deep trove of insights to guide innovation. For example, at Trinity we objectively identify areas of need and innovation using objective, AI-driven comparative intelligence. We leverage this approach to support internal decision-making around individual assets while guiding broader portfolio decision-making. Our Innovation Index leverages insights-based and AI-driven approaches to evaluating innovation across a company's portfolio, identifying areas of exposure and potential upside to guide portfolio decision-making. It provides a quantitative assessment of the level of innovation of individual assets, guiding decision-making for early pipeline assets and for objective adjudication of senior leadership incentives.

Trinity's Proprietary Portfolio Health Assessment

Trinity offers our Portfolio Health Assessment, a portfolio-level view of innovation and opportunity across all phases of development, which helps organizations understand potential portfolio risks and areas for optimization (see Exhibit A). This objective evaluation of innovation across the portfolio incorporates insights gained through the development of the Trinity Annual Drug Index, which evaluates the drivers of success and failure of recent launches across the biopharma industry. Based on a data-driven analysis of recent launches included in the Index, we derive the product- and market-factors essential for success in the marketplace. Our Portfolio Health Assessment applies this lens to an organization's portfolio to help identify areas for increased investment (e.g., accelerating clinical development to maximize competitiveness) or minimizing exposure to excessive risk for low-opportunity assets (e.g., "money pits") (see Exhibit B).

Exhibit A. Assessment for Assessing Portfolio Health

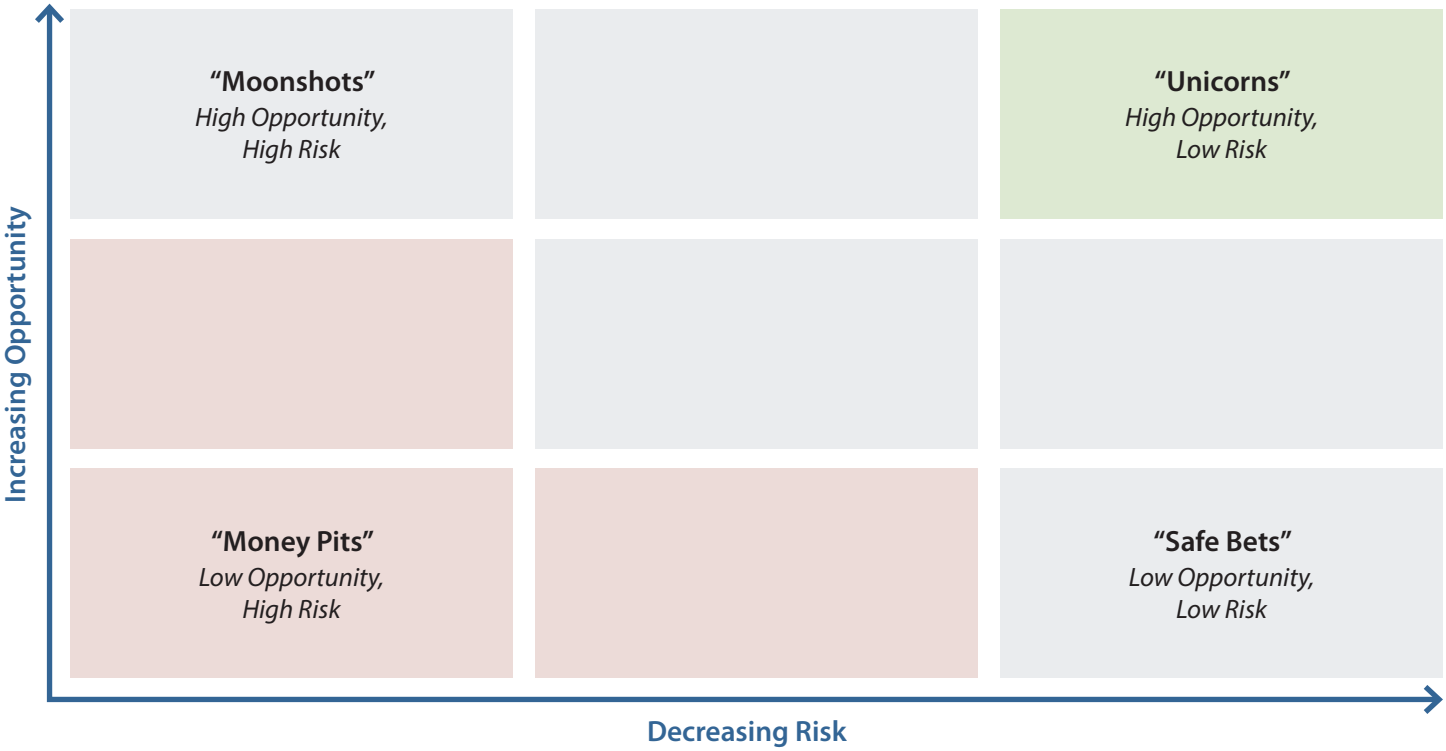
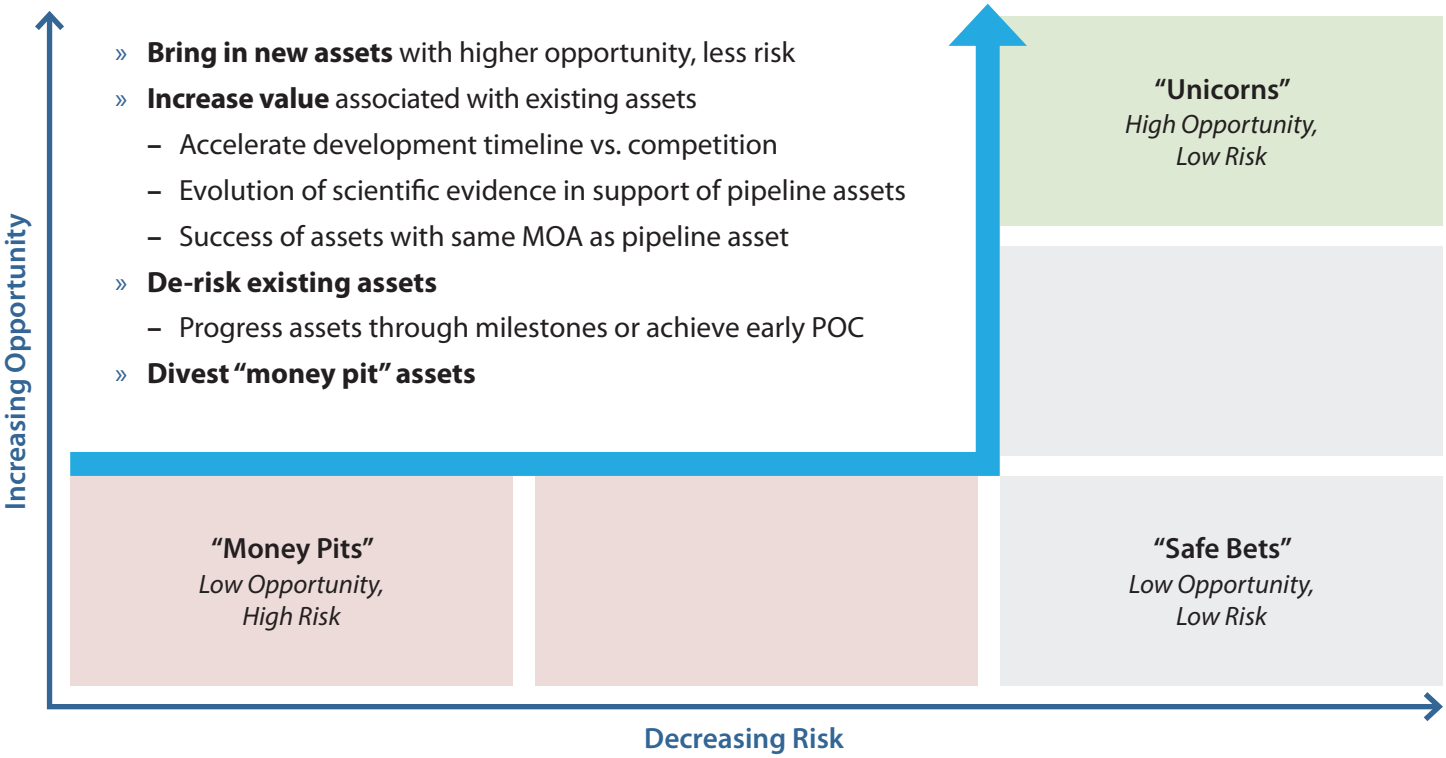


Exhibit B. Optimizing Portfolio Health through Innovation Index



Increase early commercial resourcing

Inclusion of commercial perspectives in decision-making around early assets can enable quick-kill of those with limited potential before considerable capital investments are made and also can drive optimized clinical development plans designed to better set up early assets for commercial success with differentiated data. But this is only feasible if these perspectives are provided when and where key decisions are made, given equal weight as R&D perspectives, and contextualized with compelling insights that provide meaningful input into the decision being made. This will require new resourcing mindsets and approaches.

One key change must be to limit the number of assets each member of an NPP group supports to ensure that the individual has bandwidth to provide meaningful insights across their portfolio rather than continually needing to deprioritize early programs to focus on later-stage assets nearing clinical milestones. Similarly, NPP resourcing needs to be increased to provide bandwidth to support early pipeline assets. This is especially important for assets focused on new patient populations or therapeutic modalities for which there may be less of an internal commercial foundation. Failure to do so forces teams to rely on outdated information and/or draw comparisons between irrelevant analogs when providing commercial input. Resources also need to be aligned to ensure that commercial and P&MA considerations are integrated in a manner yielding unified perspectives on opportunities and risks, as well as optimization opportunities to maximize potential for early stage assets.

Taken together, these changes have the potential to align an organization around a common vision, better facilitate collaboration and productivity, and optimize investment decisions. They also can set expectations for innovation in a manner that incentivizes investment that moves the organization forward. Innovation-oriented goals should:

- Increase the quality of assets in an organization's early pipeline
- Quickly identify opportunities for divestment, where necessary
- Accelerate quality assets into clinical development
- Increase overall portfolio value

It also is important to remember that your innovation metrics communicate what you value as a company to your employees and shareholders. Moreover, a data-driven approach to measuring innovation creates an objective assessment that can facilitate change management with internal stakeholders.

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Finally, these changes need to be taken holistically, strategically and consistently. We still see decisions made on a one-off basis, and/or late in an asset's development, long after considerable dollars have been invested in early development that ultimately will lead nowhere. Fortunately, there are examples of companies taking steps in the right direction. Sanofi CEO Paul Hudson began talking about focusing on "first in class, best in class" medicines within weeks over taking the helm at Sanofi, and we've seen a number of ways in which this strategy has guided decision-making across the company's portfolio. For example, Sanofi recently discontinued development of tolebrutinib in myasthenia gravis, citing the "emerging competitive landscape" as reason for the move. Similarly, earlier this year, Roche announced that it was implementing "stronger gates" for advancing assets into Phase 3 programs, citing declining success rates relative to their peers. As Roche CEO Thomas Schinecker acknowledged at the time of the announcement "We're putting too much risk into Phase 3…some of these projects should probably have stopped earlier in Phase 2." Other companies also have changed their "go/no-go" strategies in recent years, including significant adjustments to approaches for early pipeline prioritization, which have typically been subject to less commercial scrutiny and evaluation.

As we progress further into 2024, we look forward to applying our resources and expertise to help a growing number of companies shift focus to formalizing goals around innovation across their pipeline, as well as integrating data, analytics and AI into how organizations operate, make decisions and define success.

Authors

Leslie Sandberg Orne | President & Chief Executive Officer

Leslie oversees the delivery of integrated consulting, insights and analytic services to our customers. Since joining Trinity, she has been a critical advisor to hundreds of customers across thousands of projects, spanning an array of therapeutic areas and business models. Her support for billions of dollars in strategic transactions and the launches of dozens of products gives Leslie a unique vantage point on the industry, and her evidence-forward approach to strategic questions empowers customers to make smart, informed and timely decisions.

Leslie graduated summa cum laude and Phi Beta Kappa from Dartmouth College with a BS in Biology. While at Dartmouth, she was also an All-American and captain of the National Championship varsity sailing team. She spends her down time chasing around her two girls and spending as much time at the beach, ski slopes and horse barn as possible.

Chad Faulkner | Partner

Chad brings deep expertise to integrated research solutions, bridging elements of research, analytics and strategy to inform some of our clients' most complex and challenging issues. Chad's specialty lies at the nexus of corporate strategy and asset diligence, helping customers to decide how to invest in both internal and external development opportunities, but also shape larger franchises and portfolios in an ever-evolving and competitive landscape. Chad's work has touched billions of dollars of acquisitions over the years, both on the buy- and sell-side.

Chad earned an AB in Molecular Biology from Princeton University, where he also pole vaulted for the Track & Field team. Outside of Trinity, Chad enjoys trying a new cocktail, catching an old movie and raising his young pups.

Herman Sanchez | Chief Business Officer

Herman has been working in the life sciences industry for over 20 years in various positions including designing and running randomized trial research, optimizing of clinical administration of health services and working as a strategic consultant to the life sciences industry. He joined Trinity over a decade ago and has worked closely with clients to support strategic decision making across the product lifecycle. As a leader at Trinity, he has worked to build out Trinity's European offices and helps to run and build our centers of excellence in Market Access, Launch, and Health Economics and Outcomes Research (HEOR).

Herman earned an MBA from the Tuck School of Business at Dartmouth and an AB from Harvard University. At home, when he isn't reading, he enjoys jumping on the trampoline with his two kids and wife, and cooking various types of meals.

About Trinity

Trinity is a trusted strategic commercialization partner, providing evidence-based solutions for the life sciences. With over 25 years of experience, Trinity is revolutionizing the commercial model by providing exceptional levels of service, powerful tools and data-driven insights. Trinity's range of products and solutions includes industry-leading benchmarking solutions, powered by TGaS Advisors. To learn more about how Trinity is elevating life sciences and driving evidence to action, visit trinitylifesciences.com.

For more information, please contact us at info@trinitylifesciences.com.