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Spectra™ Target Discovery Platform De-Risks Investment Decisions by Predicting Avoidable Clinical Trial Failures

White Paper

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The Problem: High Failure Rates, Patient Impact, and Capital Drain

Drug discovery and development remains one of the most challenging and resource-intensive processes in modern medicine. With development timelines spanning 10-15 years and costs exceeding $1-3 billion per approved drug[1], the need for more efficient target identification methods has never been more critical. Traditional approaches, heavily reliant on expensive *in vitro* and *in vivo* experiments, face substantial failure rates, with about 90% of drug candidates failing during clinical trials.[1] An improved capability for identifying likely efficacious and nonefficacious novel targets could increase the odds of clinical trial success, bringing successful treatments to patients more quickly and effectively.

Investing in clinical trials is a high-stakes endeavor. While the potential for transformative medical breakthroughs and substantial financial rewards exists, the reality is that a significant portion of trials fail. These failures result in devastating financial losses, eroding investor confidence and delaying the development of life-saving therapies for patients world-wide.

According to a 2024 report by the IQVIA Institute for Human Data Science, the overall success rate for drug candidates progressing from Phase I clinical trials to FDA approval was **10.8%** in 2023. This indicates that approximately **89%** of **clinical development programs result in failure**—a staggering figure that translates directly into financial loss. The average cost of bringing a drug to market is estimated at **$1.3 to $2.8 billion,** with **Phase III trials alone often costing $250+ million** per indication.

Failures at later stages are particularly costly (JAMA Network, 2020):

- **Phase I failure:** $25 million average sunk cost
- **Phase II failure:** $60–80 million lost
- **Phase III failure: $250 million+** in unrecoverable expenses

The Opportunity: Financial Upside and Faster Patient Impact Through Better Predictive Insight

Our predictive analytics platform empowers decision makers to navigate this complex landscape with unprecedented clarity, significantly reducing the risk of costly failures and optimizing investment decisions.

Here, we present a comprehensive validation of the Spectra™ platform target ranking algorithm, based on our previously developed multi-omic, network-based approach to target discovery.[2]

By analyzing clinical trial outcomes across multiple diseases, we demonstrate that our target rankings predict the likelihood of clinical trial failures with high accuracy, demonstrating the platform's power as a tool for de-risking assets in the pharmaceutical development process and optimizing investment decisions.

Our predictive analytics platform helps investors and pharmaceutical company decision makers avoid predictable failures, thereby avoiding substantial wasted time and money, by flagging high-risk trials before large sums are committed.

Case Simulation from top Pharma:

- From our target ranking validation data (**Figure 1**), we evaluated the ability of our target ranking algorithm to predict asset failure from the top 10 pharmaceutical companies
- We ranked each identified asset using Scipher's Spectra™ platform for each indication the asset had been tested for, and we chose the 50th percentile target rank as a threshold for predicting high likelihood of failure of the asset for the indication (**Figure 2**)
- A total of 159 asset-indication pairs with worse than median target ranks were identified from the top 10 pharmaceutical companies, and none were successful
- Assets failed at stages ranging from preclinical testing onward, implying varying amounts of sunk costs

- Assuming average costs of $40 million for preclinical validation, $25 million for Phase I clinical trials, $60 million for Phase II clinical trials, and $250 million for Phase III clinical trials, using Scipher's target rankings to avoid investment in these predicted failures would have saved ~$12 billion in wasted investment with no loss of a successfully developed drug. With our platform flagging high-risk trials, decision makers can reallocate capital to higher-probability assets, increasing overall success rates and ultimate patient impact

Net impact:

- Using the same estimates of clinical trial costs by phase, we estimated the total amount spent on all successful and failed drugs in our target ranking validation data. We excluded from our analysis all assets that failed if they targeted the same target for the same indication as a successful asset, under the assumption the asset failed due to reasons other than efficacy of the target for the indication
- We estimate a total of $634 billion spent on 748 successes and 4523 failures, leading to an average cost per success of $847.5 million
- We performed the same analysis but restricted it to only drugs with targets ranked in the top 0.6th percentile of our ranking, resulting in an estimated $124 billion spent on 180 successes and 482 failures, leading to an average cost per success of $689.5 million
- Redirecting the avoided $12 billion in failed drug development investment towards top ranked targets would result in an estimated 17 additional success, compared to the 14 additional successes predicted without top-target prioritization
- Assuming a value of $1.6 billion for each additional launched drug, this amounts to an excess return across the top 10 pharma companies of $22.2 billion if Spectra target ranking had been used to avoid predicted failures and an **excess return of $27.3 billion** if Spectra target ranking had been additionally used to redirect investment towards only top-ranked targets[3]

Strategic Advantage

Our clients use the platform to:

- **Identify red flags** early to limit/eliminate high risk spending
- **Prioritize high-quality companies and assets** for investment or acquisition
- **Divest or renegotiate terms** for high-risk trials before incurring substantial losses
- **De-risk assets** in the portfolio for ongoing budgeting and funding

By embedding our predictive tool into investment due diligence processes, beyond just risk mitigation, new value is unlocked through compressed decision timelines and more consistent market-beating performance.

Spectra's Distinct Advantage: Addressing the Shortcomings of Traditional Drug Discovery and the Limitations of Standard AI/ML Approaches

The complexity of human biology presents a fundamental challenge to drug development. Traditional target discovery methods frequently fail to predict clinical success. This is evidenced by the very low success rates in drug development: approximately 90% of drug candidates fail during clinical trials, with lack of clinical efficacy (40-50%) and unmanageable toxicity (30%) being the primary causes of failure.[1] These challenges stem in part from the complexity of the underlying biology, and particularly the immense complexity of the human interactome—the network of protein-protein interactions within human cells. A therapy targeting one protein inevitably affects a broader network of proteins, which can impact both safety and efficacy. However, this same network complexity can be leveraged as an advantage when drug discovery is approached from a network medicine perspective.

Scipher's Spectra™ platform succeeds at novel target discovery by combining knowledge of

the underlying biological networks with disease-specific multi-omic data to reveal insights into the underlying network biology of the disease. This biology-first approach stands in contrast to standard artificial intelligence and machine learning (AI/ML) approaches which struggle in the domain of novel target discovery due to their reliance on well-labeled training data to perform effectively. While AI/ML approaches have revolutionized many aspects of drug discovery, their application to target identification faces the twin challenges of abundant false negatives (only a tiny fraction of possible targets are tested in clinical trials for a given indication) and variable signal quality in true positives (across indications, some approved therapies are highly effective while others have limited effectiveness and low response rates).

Real-world Clinical Validation of the Spectra™ Target Ranking Algorithm Across Indications

Our target discovery algorithm represents a novel approach to target discovery that combines multiple layers of biological data, including genetic disease associations, disease-specific gene expression profiles, experimentally validated drug response signatures, and protein-protein interaction networks. This integrated approach allows us to rank all proteins in the human interactome based on their potential as drug targets for specific diseases. The ranking considers both functional similarity to known treatment responses and topological proximity to disease-associated genes. Since publishing our target discovery algorithm in Voitalov et al. (2022)[2], we have performed target ranking on a range of diseases across several disease areas.

Using the Pharmaprojects database from Citeline[4], we evaluated our rankings against real-world clinical trial outcomes for drugs tested in four neurological indications, five autoimmune indications, three metabolic indications, and two respiratory indications (**Figure 1**). For all fourteen indications, we identified all drugs that had been either discontinued ("Ceased") or successfully passed clinical testing ("Successful"). For each drug, we identified its targets and determined the targets' Spectra™ rankings for the tested indication, using the highest-ranked target as representative of the drug's potential. Comparison of target rankings between successful and ceased drugs revealed that successful drugs target proteins that received better rankings from our platform.

Implications for the Future of Novel Target Discovery and Drug Development

The validation approach presented here, while confirming the algorithm's predictive power, has

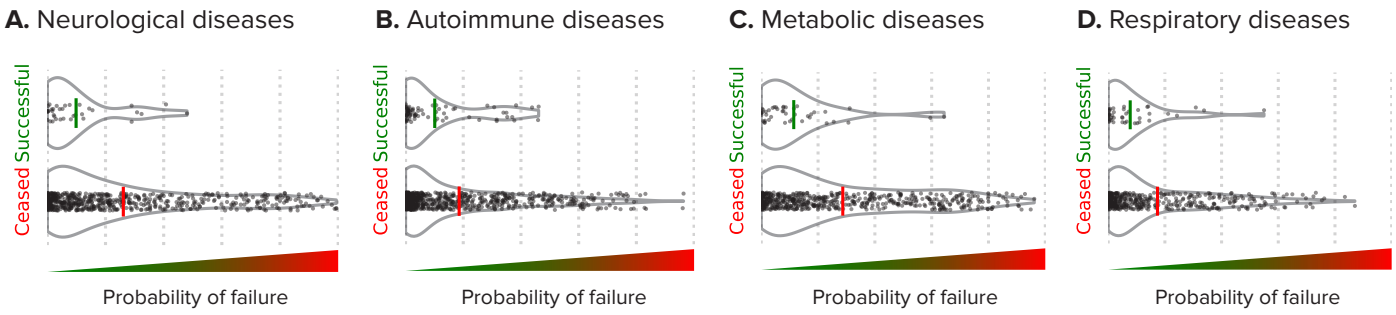

Figure 1. Distribution of Spectra™ target ranks of drugs evaluated for four neurological indications (**A.**), five autoimmune indications (**B.**), three metabolic indications (**C.**), and two respiratory indications (**D.**). Drugs that failed at any stage of testing or whose development was ceased are labeled "Ceased".

Drugs that successfully passed clinical testing (including those at the pre-registration, registered, and launched phases) are labeled "Successful". The range of the x-axis spans the ranks of all nodes of the human interactome, with positions to the right indicating worse Spectra™ ranking, corresponding to higher probability of failure. Black dots show individual drug target ranks for a particular indication, and the vertical lines indicate mean ranks for the two categories.

Spectra™ target ranks for the four indication groups are significantly different (Mann-Whiteny U test; neurological $p=1.10^{-4}$, autoimmune $p=5.91^{-4}$, metabolic $p=1.11^{-5}$, respiratory $p=2.93^{-4}$, combining all 12 indications $p=4.44^{-15}$), showing its predictive utility.

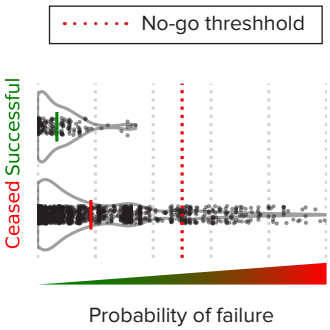

Figure 2: Distribution of all Spectra™ target ranks of all drug-indication pairs from the ten pharmaceutical companies included in the case study. Same as **Figure 1**, but each point corresponds to a particular asset-indication pair rather than a target-indication pair. From the top ten pharmaceutical companies there are 159 asset-indication pairs ranked worse than the 50th percentile, all of which failed.

inherent limitations in demonstrating the full utility of our target rankings. In the Successful category, poorly ranked targets may represent marginally effective drugs that are nonetheless classified as true positives.

In the Ceased category, some highly ranked targets may be efficacious but have failed testing due to drug toxicity or business-related events such as reprioritization or lack of funding. While the validation analysis presented in **Figure 1** focuses solely on validating efficacy predictions, the complete Spectra™ target discovery pipeline includes critical feasibility assessments that evaluate factors such as drugability, toxicity concerns, and tissue and cell-level expression patterns of the candidate targets. These feasibility metrics, though not included in this validation, play an essential role in identifying the most promising targets for drug development.

Our findings demonstrate that network-based target discovery methods provide valuable insights for drug development programs. By identifying targets more likely to succeed in clinical trials, this approach reduces development costs, accelerates the discovery timeline, and improves clinical success rates. The validation of the Spectra™ platform against clinical trial outcomes establishes its value as a powerful tool for drug target discovery. By leveraging biological network complexity to predict successful therapeutic targets, this approach represents a significant advance in making drug development more efficient and effective.

The network biology insights generated by the Spectra™ platform extend beyond single-indication target discovery to enable systematic drug repurposing strategies. For compounds that proved safe but ineffective in clinical trials, our platform can identify alternative indications where the same target ranks highly, offering a path to rescue these assets—reducing both the timeline and cost of bringing new treatments to patients. Similarly, for successfully launched drugs, our platform can identify additional therapeutic opportunities in diseases with related underlying network biology.

Our ongoing work demonstrates that cross-disease target ranking analysis can systematically identify both rescue opportunities for failed compounds and expansion opportunities for successful ones, maximizing the therapeutic potential of existing drug development investments.

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