BIOMEDTRACKER
CITELINE COMMERCIAL

CITELINE

White Paper

Why Are Clinical Development Success Rates Falling?

Biomedtracker leads the way in collecting, analyzing, and publishing clinical development success rate data. This white paper uses these insights to explore the causes of declining rates, assess ROI on pipeline investment, and introduce our advanced likelihood of approval analysis tool to aid investment decision-making.

April 2024

Introduction

Daniel Chancellor
Thought Leadership and Consulting Director, Citeline

Biomedtracker has led the way in collecting, analyzing, and publishing clinical development success rate data for over a decade. The landmark peer-reviewed article in 2014 established the widely cited 10% benchmark (10.4%) for the likelihood of a new drug entering Phase I eventually reaching the market.[1] Since then, subsequent updates in 2016 and 2021 have showed that industry success rates have moderated, falling first to 9.6%[2] and later to 7.9%.[3]

This poses several questions. Is biopharma continuing to become less successful in clinical development? What are the underlying reasons dragging success rates down and can they be mitigated? What does this mean for R&D productivity and the return on investment on pipeline spend? What does all of this matter?

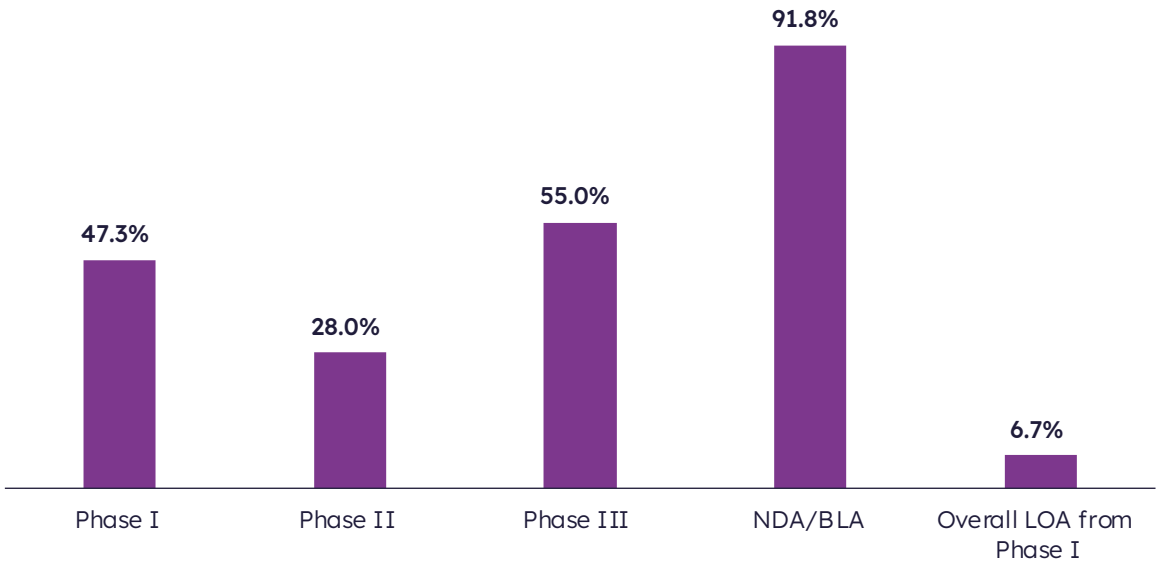
This white paper, which updates previous analyses with a fresh 10-year analysis window — the typical clinical development lifecycle of a drug before approval — can address some of these questions. New likelihood of approval (LOA) benchmarks are important as these metrics quantify risk and support investment decisions. Today's industry, which contains advanced genetic therapies, biomarker-defined patient populations, and expedited regulatory pathways, is very different to that analyzed by Hay et al. back in 2014.

The updated analysis also coincides with an enhancement to Biomedtracker, in which the ability to run custom, sophisticated LOA analyses is embedded. There are countless factors that influence a program's eventual success, from clinical features of a drug and the way its clinical trials are designed, through to the competitive landscape and regulatory interactions. Each drug development program is unique in its own right, and so the careful consideration of analogs and relevant variables can help to arrive at personalized estimates.

The LOA for new drugs entering Phase I is now just 6.7%

Biomedtracker's analysis of phase transitions between 2014 and 2023 suggests that success rates are continuing to fall. Overall LOA for new assets entering Phase I is now just 6.7%, down from 7.9% three years ago. The latest 10-year dataset contains 10,954 separate drug-indication development programs, which is the largest sample yet as industry pipelines have continued to grow. This expansion in the pipeline has been necessary to accommodate increasing attrition. As shown in Figure 1, Phase II remains the greatest hurdle with just a 28% probability of success, although the success rates at Phase I and III are also lower than previous analyses.

Figure 1. Probability of success and likelihood of approval, 2014–23



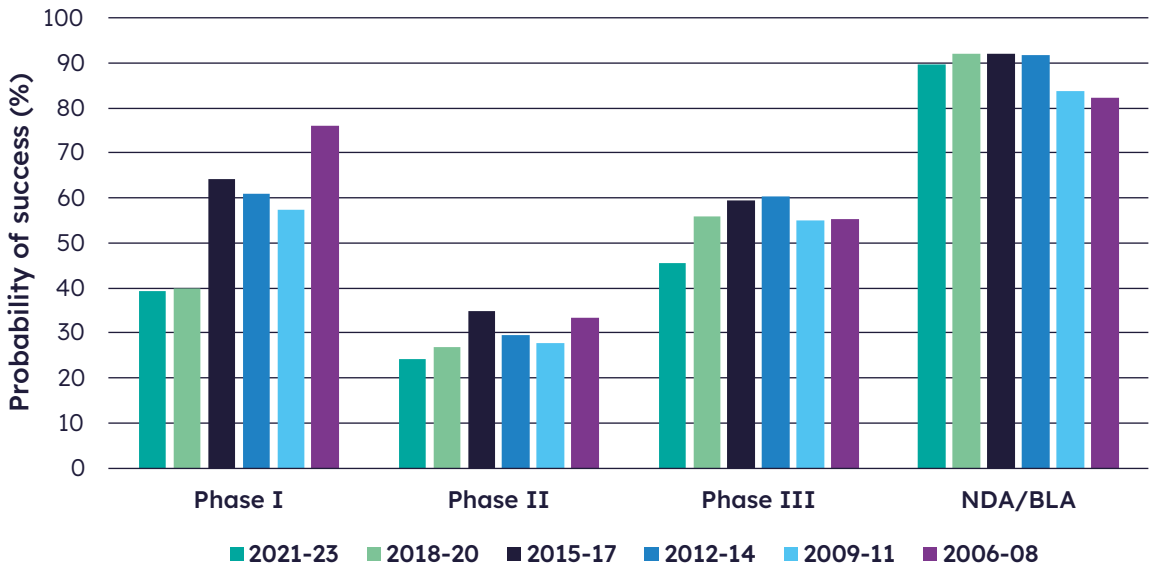
Source: Biomedtracker, Citeline, February 2024

Pharma is stopping more assets at early clinical stages

Success rates can be segmented in rolling time periods to judge how pharmaceutical companies have changed their approach to the various stage gates. Figure 2 below shows that the largest difference has been in Phase I, where a success rate of over 75% during 2006–08 has now dropped to below 40%. Whereas previously Phase I was considered to be a safety hurdle among healthy volunteers, drug companies are increasingly enrolling patients and evaluating efficacy surrogates. This allows for programs that are less likely to result in meaningful patient outcomes to be identified and discontinued at an early stage, thus avoiding the expense of larger trials.

Despite stricter criteria for go/no-go decisions at Phase I, the chart also shows that Phase II and Phase III success rates have also declined, albeit not to the same extent. Phase II remains the largest hurdle for drug development and it is often appropriate for this to be the stage when a program can be halted with confidence. It is worrying that Phase III success rates have dipped in tandem in the latest three-year window. Failures at this stage are the most expensive and catastrophic for R&D productivity measures. This will need to be carefully monitored as it is possible that Phase III success rates below 50% are not sustainable for long-term R&D investments. The continued 90% pass rate at the regulatory review stage mitigates this partially as the quality of NDA and BLA filings remains high.

Figure 2. Evolution of phase transition rates over time



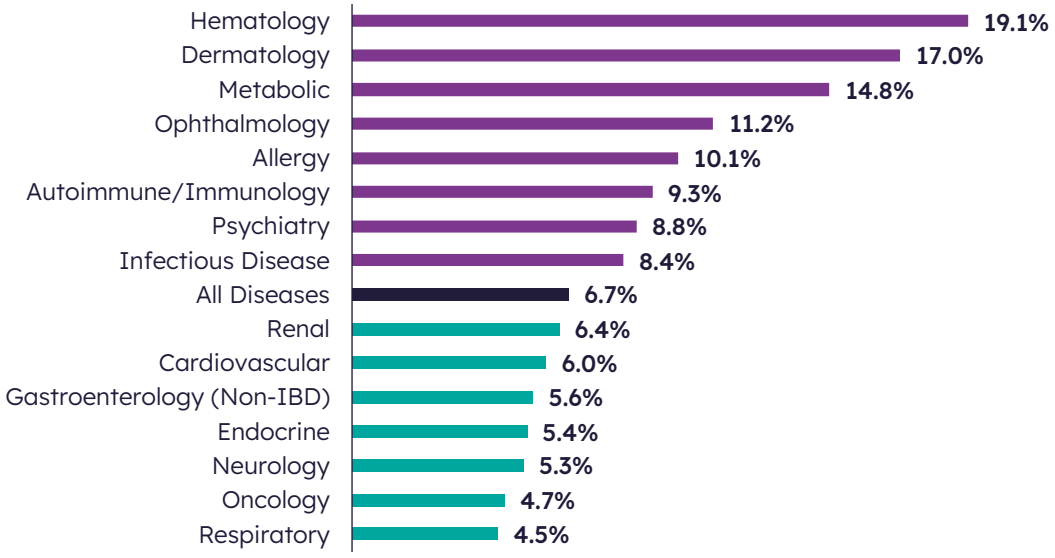
Source: Biomedtracker, Citeline, February 2024

Broad therapy area spread increases value of disease-specific benchmarks

Success rates are widely variable depending on the therapy area and disease under evaluation. Confidence in disease biology, validated clinical endpoints and trial designs, the competitive landscape, and regulatory pathways are all unique to each indication, and so it makes sense to apply disease-specific benchmarks for LOAs. Figure 3 shows the fourfold spread from the disease area with the highest success rates (hematology: 19.1%) down to the lowest (respiratory: 4.5%).

Portfolios are not static, and it is well established that an increasing proportion of drug development programs are targeted against oncology. With just a 4.7% likelihood of approval for new drugs in Phase I, the overall weighting of oncology within the broader industry is certainly dragging down trends. Furthermore, the competitive intensity in oncology itself will result in greater levels of attrition. The considerable amount of fast-follower R&D programs means that only the most differentiated assets have any reasonable commercial prospects once on the market. The lack of market potential is a leading cause for asset discontinuation.

Figure 3. Likelihood of approval by therapy area



Source: Biomedtracker, Citeline, February 2024

What does all of this mean?

It is perhaps inevitable that success rates decline over time as a natural consequence of "picking the low-hanging fruit first" — a common analogy for drug development. That leaves innovators with more complex drug targets to work with and a plethora of approved drug options that raise the barrier for viable new therapies. Nevertheless, optimists can point towards advances in our fundamental understanding of biology, chemistry, and data science that should unlock large untapped reserves of new drug potential. Certainly, drug development has become much more sophisticated with greater use of precision therapeutics, biomarkers, digital health, and regulatory innovation that all allow for greater R&D efficiency and raised success rates. There is no rule to say that these two competing forces should cancel each other out and LOAs remain at 10% indefinitely.

There is a school of thought that suggests optimization around LOA can come at the expense of risk taking and patient benefit. If all drug programs were designed to be successful, then we would only ever develop me-too drugs. Perhaps declining LOA should be embraced as a signal that biopharmaceutical companies are willing to take and invest in riskier bets, providing new treatment options for diseases such as obesity, Alzheimer's disease and non-alcoholic steatohepatitis (NASH). These are all indications where success rates are extremely unflattering and poor benchmarks have stifled investment.

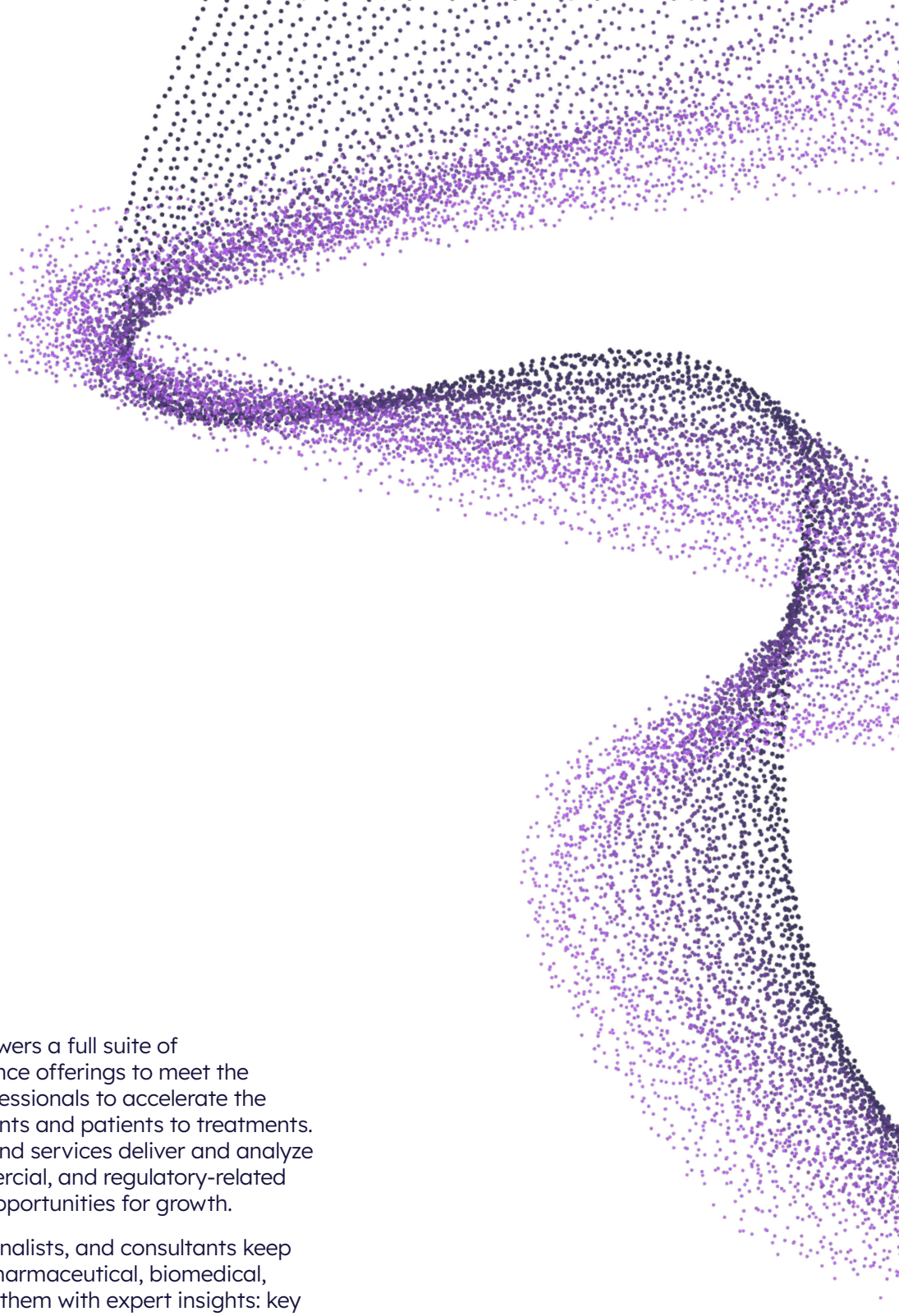
That does not mean drug companies should ignore success rates in their decision making. Quantifying risk and mitigating it against cost is essential to make informed investment and portfolio decisions. Frameworks such as AstraZeneca's 5R and 6R scrutinize each pipeline program against strict, objective criteria that increase probability of success.[4] It is no coincidence that AZ is enjoying a prolonged period of fruitful new approvals and revenue growth.

The ideal R&D strategy is one that identifies therapeutic and market potential as early as possible, allowing uncompetitive assets to be deprioritized. Risk should always be embraced, and early clinical development should be seen not just as a regulatory necessity but also to allocate precious later-stage resources as efficiently as possible. Just as each new drug approval is toasted, each effective early stage discontinuation should be heralded as a sign of progress.

References

1. Hay et al. (2014) Clinical development success rates for investigational drugs. Nat Biotechnol, 32(1), 40–51. Available from: https://www.nature.com/articles/nbt.2786
2. Citeline and BIO (2016) Clinical Development Success Rates 2006—2015. Available from: https://www.bio.org/sites/default/files/legacy/bioorg/docs/Clinical%20Development%20Success%20Rates%202006-2015%20-%20BIO,%20Biomedtracker,%20Amplion%202016.pdf
3. Citeline and BIO (2021) Clinical Development Success Rates and Contributing Factors 2011—2020. Available from: https://www.bio.org/clinical-development-success-rates-and-contributing-factors-2011-2020
4. Durán et al. (2023) Implementation of digital health technology in clinical trials: the 6R framework. Nat Med, 29(11), 2693–2697. Available at: https://www.nature.com/articles/s41591-023-02489-z

CITELINE
CLINICAL



Citeline, a Norstella company, powers a full suite of complementary business intelligence offerings to meet the evolving needs of life science professionals to accelerate the connection of treatments to patients and patients to treatments. These patient-focused solutions and services deliver and analyze data used to drive clinical, commercial, and regulatory-related decisions and create real-world opportunities for growth.

Our global teams of analysts, journalists, and consultants keep their fingers on the pulse of the pharmaceutical, biomedical, and medtech industries, covering them with expert insights: key diseases, clinical trials, drug R&D and approvals, market forecasts, and more. For more information on one of the world's most trusted life science partners, visit Citeline.com.