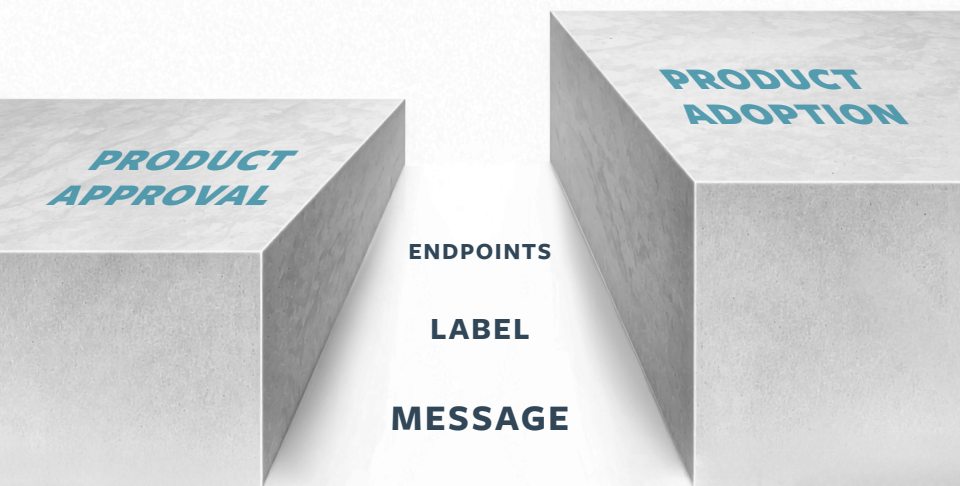


APPROVAL IS NOT ADOPTION

Measuring Adoption Risk Before
It Becomes Valuation Risk



HARRIS KAPLAN

APPROVAL IS NOT ADOPTION

Measuring Adoption Risk Before
It Becomes Valuation Risk

*For life sciences investors, CEOs, and boards who are serious
about investability and exit-ready company value creation.*

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Executive Summary

Life sciences has developed extraordinary discipline for managing scientific, clinical, regulatory, and manufacturing risk. Companies routinely invest hundreds of millions of dollars to answer:

- *Will the product work?*
- *Will regulators approve it?*
- *Can it be manufactured consistently?*

Yet the question that ultimately determines commercial success and future enterprise value is often not addressed as rigorously or is addressed much later, sometimes only after an NDA filing, or even after approval: ***Will the new product be adopted?***

Approval ≠ Adoption

Regulatory approval and commercial adoption are related but fundamentally different challenges. Regulators decide whether a product is safe and effective. Adoption is decided by everyone else: payers decide whether it justifies reimbursement, physicians decide whether it is worth changing prescribing habits, health systems decide

whether it fits existing workflows, and patients decide whether the benefits outweigh the cost, inconvenience, and uncertainty of switching therapies.

More than half of new products launched over the past fifteen years met every regulatory requirement yet failed to meet pre-launch forecasts because they did not satisfy the practical, economic, or behavioral requirements for broad adoption.

The commercial environment has made achieving future commercial success much more challenging. Payers exercise greater control over access. Physicians increasingly practice within large health systems where protocols, productivity pressures, and administrative burden shape treatment decisions. Therapeutic categories are crowded, and incremental innovation now competes against entrenched standards of care rather than unmet need alone.

Commercial success therefore depends on more than demonstrating clinical efficacy and safety. It requires demonstrating enough value to motivate multiple stakeholders to change established behavior. For each of them, before committing time to evaluate a new product, ***the juice has to be worth the squeeze.***

The High Cost of Asking Too Late

Most organizations recognize the challenge of driving new product adoption. Fewer evaluate future adoption potential systematically during early clinical development, while there is still time to influence decisions that shape a new product's revenue future. Adoption considerations are too often addressed only after the pivotal

trial design is finalized, when major investments have been committed and improving the product's profile has become limited, slow, and expensive.

The consequence of insufficient commercial input is rarely regulatory failure. It reveals itself post-approval: slower-than-expected uptake, restricted access, lower revenue vs. forecast, valuation discounts in partnering discussions, and acquisitions completed at lower multiples because commercial uncertainty remains unresolved.

Managing Adoption Risk Like Regulatory Risk

This book proposes that commercial adoption can be assessed early, with the same discipline that's applied to assessing regulatory risk. Adoption risk—the probability that physicians, payers, patients, and health systems will embrace a product rapidly enough to achieve its commercial potential—deserves the same rigor as clinical, regulatory, manufacturing, and financial risk.

Adoption risk is not random. It is driven by identifiable factors that can be evaluated and modeled years before launch, while product design, clinical endpoints, target populations, evidence generation, and positioning remain flexible.

To meet this need, Litmys has developed the **Realistic Assessment of Market Potential (RAMPx™)** framework. RAMPx brings commercial due diligence upstream into early product and clinical development, evaluating a product through the eyes of the stakeholders who determine its success across three dimensions:

- **Comparative Product Advantage:** Is the product sufficiently better than current practice to justify a change in their behavior?
- **Ease of Adoption:** How much clinical, operational, reimbursement, or workflow friction accompanies adoption?
- **Early Willingness to Adopt:** Which physicians, patients, and organizations will adopt first, and how quickly can broader adoption follow?

Together, these dimensions provide a customer-centric, evidence-based assessment of adoption readiness of a new product while development decisions are still actionable.

The RAMPx framework does not replace existing forecasting, market sizing, or regulatory planning tools; it is additive, measuring what those approaches often assume.

Why It Matters Now

Throughout this book, examples from pharmaceuticals, biotechnology, medical devices, and diagnostics show how adoption dynamics have shaped commercial outcomes; sometimes favorably, sometimes at considerable cost. The lesson is consistent: adoption challenges are rarely unpredictable. They are simply identified too late.

In today's commercial environment, you can't outspend a message that gives stakeholders insufficient reason to change their behavior.

Executive Summary

- Endpoints drive your new product's label.
- Label is the foundation of your differentiation and stakeholder message.
- Message drives a new product's revenue trajectory.

For investors, boards, and management teams, the financial stakes keep rising. When acquisition value depends on confidence in future commercial performance as much as scientific promise, understanding adoption risk early creates opportunities to improve development decisions, reduce commercial uncertainty, and strengthen enterprise value.

Regulatory approval creates the opportunity to compete. Commercial adoption determines what that opportunity is worth.

Most industry leaders and investors already know adoption matters. The purpose of this book is to offer a practical framework for measuring adoption risk early enough to influence the decisions that turn scientific innovation into commercially successful products.

CHAPTER 2

The High Cost of Managing Commercialization Too Late

Very early in Seroquel's development as a treatment for schizophrenia, the drug was presented to a group of KOLs at an advisory board as a three-times-a-day (TID) product. After reviewing the early clinical data, the KOLs spent almost two hours trying to rationalize how a TID product could work for a patient population notorious for poor compliance. As moderator, I finally said what no one wanted to say: "A TID drug for schizophrenia patients will never be used or be commercially successful."

There was a minute or so of silence. Then one of the physician attendees said, "He's right," and one by one nearly everyone converged on the need for twice-a-day (BID) dosing. When the clinical development team was asked by the VP of Zeneca's Global Marketing whether the drug could work BID, the answer was revealing: "We don't

know. We didn't try it because it worked, and we didn't realize it would be important."

A BID protocol was developed during that ad board. A larger quantitative study confirmed both the value of BID dosing and the unacceptability of TID. Zeneca implemented the change, the product remained highly effective, and Seroquel launched as a BID drug, eventually reaching nearly \$6 billion in peak sales.

One decision, made early, while the development path was still flexible, made all the difference.

Commercial Decisions Are Often Made by People Who Don't Realize They're Making Them

One of the most persistent misconceptions in life sciences is that commercialization begins after filing or approval. In reality, the most consequential commercial decisions are often made much earlier by people who either don't think of themselves as making commercial decisions or don't recognize the commercial consequences of the decisions they're making.

Discovery, clinical development, regulatory affairs, and manufacturing lead the product through development. Each function has leaders and budgets, and the sequence is logical—it mirrors the timing of development. When there's a clinical, financial, or manufacturing problem, CEOs know exactly who to call. But when prospective investors or acquirers push back on the market size or share projections in the pitch book, who gets that call? If the product does get approved and underperforms

forecasts, the commercial team gets blamed for poor execution when, in fact, the decisions leading to a new product's underperformance were made well before approval and launch.

Commercial organizations are typically assembled as pivotal trials near completion or once approval looks likely. By then, the decisions that determine commercial success have already been made:

- The target product profile has been defined.
- The endpoints, comparator, and patient population have been fixed.
- The route of administration has been selected.
- The evidence package is largely complete, and the label is taking shape.

At that point, commercial teams are not designing a product for adoption. They are building strategies to maximize adoption of a product whose fundamental characteristics can no longer change. And the clinical and regulatory teams that made those choices were focused on approval, often with no direct stake in the product's commercial future.

Development Decisions Are Really Adoption Decisions

Every major development decision shapes a new product's future commercial success:

- **Endpoint selection** does more than satisfy regulators; it determines the claims physicians will eventually see in the label and the messages

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a company's representatives and Medical Science Liaisons (MSLs) will deliver to convince them to prescribe the new product.

- **Comparator choice** frames how physicians evaluate the product against their current standard of care.
- **Study population definition** shapes the initial market and determines which patients physicians feel confident treating.
- Even seemingly operational decisions (**dosing schedule, route of administration, monitoring requirements, device design**) can impact adoption, as the Seroquel example demonstrates.

Viewed individually, each decision looks clinical or regulatory. Viewed collectively, they define the product's commercial potential years before launch. Commercialization does not begin when the chief commercial officer and sales force are hired. It begins with the earliest clinical development decisions and the development of a target product profile.

Clinical Development Flexibility Is Reduced Early

During discovery and early clinical development, nearly everything remains flexible: product characteristics, clinical development plans can still evolve, evidence generation strategies can be identified and modified, stakeholder feedback can still meaningfully shape the product. As development progresses, flexibility declines while regulatory commitments, manufacturing investments, and the cost of change all rise.

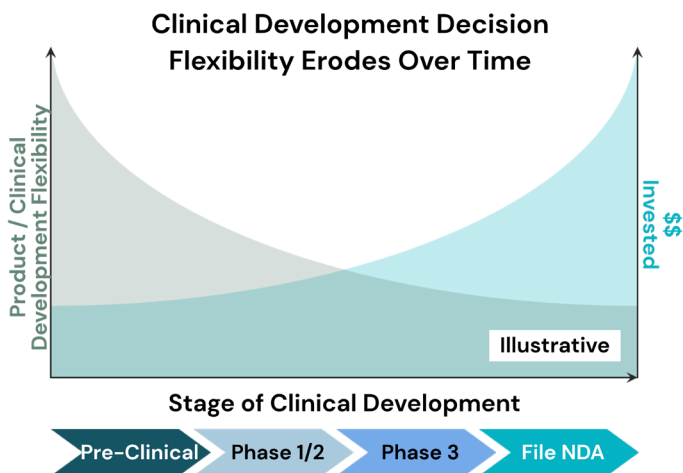


Figure 1: As clinical development progresses, the ability to influence a product declines while the cost of making changes rises dramatically.

Ironically, the point of minimum clinical flexibility is often when most organizations conduct their most comprehensive commercial planning.

The result is predictable: commercial teams identify important adoption barriers exactly when those barriers have become the most difficult and expensive to address. Managing adoption after pivotal decisions are locked is like redesigning a bridge after construction has begun, possible but guaranteed to be costly in both money and time.

Identified early, those same insights let a company modify its development program, reconfigure the product or delivery mode, add clinically meaningful endpoints, strengthen comparative evidence, or simplify the treatment experience—well before pivotal trials begin.

Which raises the questions this book aims to answer:

- What if adoption risk were evaluated with the same discipline and timing applied to regulatory risk?
- What if companies could identify adoption barriers while product design remained flexible?
- What if physicians, payers, patients, and health systems informed development decisions before pivotal trials rather than after approval?

CHAPTER 3

The RAMPx Model: A FICO-Type Score for Measuring Adoption Risk

If adoption risk can be managed, it must first be measured. That observation is the foundation of the RAMPx model (Realistic Assessment of Market Potential) and, after many years of providing this input informally to clients, the reason Litmys was formed.

Companies already conduct plenty of commercial assessments: market research, market sizing, forecasting, advisory boards, positioning, and pricing studies. But these activities are typically performed independently rather than as components of a unified assessment of adoption readiness, and they too often occur after the decisions that determine commercial success have been made.

The RAMPx model answers a different question: **How likely is this product to achieve broad adoption given the realities of today's healthcare environment?**

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Answering it requires understanding how each stakeholder views the product within the context of their existing practice patterns, administrative burdens, financial incentives, institutional policies, and personal willingness to change. Successful commercialization requires alignment across all of them. The RAMPx model measures those requirements while development decisions can still respond and adapt to them.

The framework functions much like a clinical risk assessment. Clinical development identifies the factors likely to prevent approval; RAMPx identifies the factors likely to prevent adoption. Both improve decision-making before outcomes become fixed. Rather than producing another forecast, RAMPx produces an assessment of adoption readiness: where barriers are likely to emerge, which matter most, and—critically—which can still be addressed through changes in clinical development, evidence generation, product design, or positioning.

A Common Language for CEOs, Clinical, and Investors

Product development spans clinical development, regulatory affairs, commercial strategy, medical affairs, health economics, business development, and executive leadership. Each evaluates success differently: clinical teams focus on endpoints, regulatory teams on approval, commercial teams on adoption, investors on return. Because these functions use different metrics, commercial implications become fragmented across the organization.

Like a FICO score, RAMPx gives all of the relevant stakeholders a shared number and a shared vocabulary. Instead of debating isolated research findings, leadership teams can evaluate how each development decision strengthens or weakens a new product's overall value proposition and its probability of future commercial success.

The Three Drivers of Adoption

Every new product's commercial success ultimately depends on one thing: Will someone change behavior? Decades of research in behavioral science, innovation diffusion, and healthcare decision-making point to a consistent answer. *People rarely change simply because something is new.* They change when the perceived value of changing exceeds the perceived cost, effort, and risk of abandoning what they know.

Regardless of therapeutic area, product type, or stakeholder, the decision to adopt a new product ultimately comes down to three questions:

- 1. Is the new product meaningfully better?**
- 2. How easy is the new product to adopt?**
- 3. How willing is someone to adopt the new product early?**

Product Advantages

How much better is the new product compared to what I'm currently using / taking?

Ease of Adoption

How accessible, affordable, or easy is the new product to adopt compared to what I'm currently using / taking?

Willingness to Adopt

How compelling is the data or what others are doing that makes me want to be an early adopter?



Figure 2: RAMPx evaluates adoption readiness through three dimensions: Product Advantage, Ease of Adoption, and Early Willingness to Adopt.

Driver One: Comparative Product Advantage

Is the product meaningfully better than the current standard of care?

The emphasis is on “meaningfully” and meaningful is defined by each stakeholder, not by statistics. Regulatory approval may require statistical superiority or non-inferiority; commercial adoption requires something different. Physicians rarely change prescribing habits for a statistically significant improvement with little practical relevance. Patients rarely switch for gains they can’t perceive. Payers rarely expand reimbursement for incremental benefits that don’t justify higher costs.

The threshold also varies by context. An oncologist treating a life-threatening cancer may adopt a therapy offering

a modest survival benefit. A primary care physician treating hypertension may require substantially greater differentiation before abandoning an effective, familiar therapy.

Predicting adoption means understanding which metrics stakeholders actually care about, how they weigh efficacy against safety and convenience, and how much differentiation is needed to change ingrained behavior.

Driver Two: Ease of Adoption

How much friction accompanies adoption?

Friction is the most underestimated variable in revenue forecasting. Every innovation introduces some: prior authorization, additional training, new diagnostic prerequisites, workflow disruption, monitoring requirements, dosing complexity. The greater the friction, the greater the clinical benefit required to overcome it.

Even highly differentiated and clinically superior new products meet resistance when adoption takes real effort. In our research, the highest-volume practices, the ones forecasts count on most, are frequently the least willing to change. And fewer time-pressured physicians will even meet with a sales representative to learn about a new product. As one specialist in a busy group practice told me, “If the new product isn’t clearly different, I don’t have the time or interest to learn about it.”

Ease of Adoption is not a secondary consideration; it is often one of the strongest determinants of real-world uptake. Products that fit seamlessly into existing clinical workflows require less evidence to overcome inertia than

products that ask physicians, patients, or health systems to work differently.

Bottom line:

Every new product asks stakeholders to do work in order to adopt it. The more work it asks them to do, the more value it must deliver.

Driver Three: Willingness to Adopt Early

Who will go first and who will wait?

My wife needed disc replacement surgery a number of years ago. When she met with the surgeon, she showed him an article describing a new disc material she'd read about, one that had demonstrated superiority in clinical trials to the product he planned to use. His response: "You're too young." She didn't understand. He continued: "I know the product I'm going to use will be buried with you when you die. No one knows how long this new product and disc material will last." End of discussion. He used the product he knew. And her back is fine.

Early adoption entails risk, and many physicians and patients prefer to wait until a new product is proven in real-world use. In the US, where the AMA reports one in three physicians has been sued for malpractice at least once, that caution is rational. I saw it firsthand when presenting a new product's clinical data to the department head of a major teaching hospital before launch. When

I mentioned the product's ability to address the unmet need, he cut me off: "There's no unmet need. How we treat this is perfectly satisfactory. This is likely better, but if a patient I treat with it has a severe adverse event, I don't want to be the first doctor on the stand explaining to a lawyer why I chose a new product over one with a long history of efficacy."

How compelling is the approval data? Who are the KOLs and what are they saying? How influential are patients, caregivers, and advocacy communities?

These differences in Willingness to Adopt are neither random nor temporary; they are predictable patterns documented across healthcare and virtually every other industry. Some physicians actively seek innovation; others want years of real-world evidence. Some health systems aggressively evaluate new technologies; others adopt only after peer institutions demonstrate success. Patients divide the same way.

Early adopter and adoption mapping is therefore more than commercial strategy. It is a proof-of-concept for the broader market's eventual behavior. If analysis reveals that the most influential or highest-volume practitioners have no incentive to go first—because they're tied to existing products, or because the therapeutic culture is conservative—that is a material signal about the asset's commercial trajectory.

A perfect example of this is publicly traded transplant molecular diagnostic company CareDx's introduction of AlloMap, a non-invasive gene expression-based blood

test used for heart transplant recipients that would quickly and more easily identify potential rejection of the donor heart. The company's goal was to position AlloMap so physicians would use it first during the period when they run a lot of diagnostic assessments and only biopsy the heart if AlloMap indicated there was a problem. The company was struggling to establish robust adoption of AlloMap at the time.

On my first visit to the company, on the lobby wall was painted: "AlloMap first, biopsy for cause." In speaking with transplant surgeons, they uniformly said they didn't trust AlloMap as a replacement for biopsy, particularly in the early period post-transplant. I thought Hospital CFOs would be interested in a less expensive and easier modality for assessing transplant risk, but the words of one stay with me even today, "We have over a million dollars invested in a heart transplant. It's not a moneymaker. It gives prestige to our hospital and the only things that matter are our success statistics and making sure the transplant surgeons are happy. I'm not going to push anything new on them. If they want it, they'll ask."

Because a heart biopsy is an invasive procedure, physicians typically limited their most intense surveillance to three or four months post-transplant. Following interviews with transplant cardiologists, we suggested that CareDx position AlloMap so it could be used to monitor patients longer. It's non-invasive and easier for the patient. Physicians liked that idea, and the company built a beachhead of trial and success that allowed AlloMap to comfortably be used earlier.

The company thought the superiority of a non-invasive diagnostic would easily and quickly win the hearts and minds of transplant physicians. Adoption took longer than anticipated, but the original hypothesis was validated, and CareDx is now a \$2 billion market cap company. “The insights gathered through primary market research of physicians about the use of AlloMap uncovered by Harris and his team led to a meaningful repositioning of the test, leading to its increased adoption,” said Matthew J. Meyer, former Chief Business Officer of CareDx.

Successful launches rarely try to change all clinicians at once. They begin with those most willing to change and use those early adopters to build confidence across the broader market.

Adoption Is an Integrated and Inter-Connected System

The three drivers interact continuously. A product with extraordinary clinical benefit may overcome considerable friction. A product offering modest differentiation must be exceptionally easy to adopt. Innovative physicians will accept a greater degree of uncertainty that conservative physicians reject. Even compelling and clinically superior new products struggle when administrative burden, reimbursement restrictions, or workflow disruption becomes excessive. Commercial success depends not on maximizing any single attribute but on achieving sufficiency across all three.

The entire chain of adoption is reasonably predictable even before the first patient is enrolled. RAMPx maps

it, quantifies it, and surfaces it as an input to program strategy, not a post hoc commercial plan, but upstream investment intelligence.

RAMPx: From Drivers to Measurement

For decades these drivers have been discussed qualitatively. Companies describe products as “highly differentiated,” “easy to use,” or “likely to appeal to innovators.”

Useful descriptions, but not measurements.

The central innovation of RAMPx is translating each driver into a structured, customer-centric assessment. Each is evaluated through measurable factors derived from interviews with physicians, payers, patients, and other stakeholders, producing an integrated view of adoption readiness that identifies commercial strengths, reveals hidden vulnerabilities, and allows opportunities to be compared on a common scale. Just as important, each driver maps directly to development decisions that are still open.

RAMPx driver	What it informs upstream
Comparative Product Advantage (Δ)	Trial endpoint selection Comparator choice Indication strategy Pricing and positioning
Ease of Adoption (γ)	Route of administration decisions Dosing regimen design Site-of-care strategy
Early Willingness to Adopt ($\star$)	KOL engagement strategy Patient advocacy investment Pre-launch access program design

Figure 3: Each RAMPx driver informs development decisions that influence future adoption and commercial performance.

What the RAMPx Model Reveals

RAMPx quantifies adoption readiness, identifies adoption barriers, predicts likely early adopters, and highlights the changes most likely to strengthen a new product's value proposition and future commercial success.

The chapters that follow examine each dimension in detail, demonstrate how they shape development decisions, and show why measuring adoption risk early has become a source of competitive advantage for management teams, investors, and acquirers alike.

CHAPTER 4

Measuring Adoption Risk: How RAMPx Works

A useful framework must do more than explain why products will succeed or underperform. It must allow companies to assess the strength of a new product's value proposition, adapt it to meet the requirements of the market, and evaluate future outcomes before those outcomes occur. That is the purpose of RAMPx. In addition to being predictive, it's prescriptive.

The framework translates the three drivers of adoption—Comparative Advantage, Ease of Adoption, and Willingness to Adopt—into a structured assessment of adoption readiness that can be applied at any stage of a new product's clinical development.

The Four Stages of a RAMPx Assessment

Although every product and therapeutic category is different, every RAMPx engagement follows four sequential stages.

Still Ahead In the Complete Book:

- The four stages of a RAMPx assessment, and what the result tells management **Chapter 4**
- The development decisions that measuring adoption risk can still change **Chapter 6**
- Four cases from the market, two of them assessed with RAMPx before the market returned its verdict **Chapter 7**
- Turning stakeholder enthusiasm into a realistic forecast **Chapter 8**
- The investment case, and adoption risk in due diligence **Chapters 9 and 10**

Read the complete book: ApprovalIsNotAdoption.com

About the Author



Harris Kaplan is Managing Partner of Litmys, a commercial strategy firm that brings clarity to life sciences innovators before the significant and irrevocable investments of Phase 3. Forty years, more than 125 products launched, more than fifty therapeutic categories.

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