WHITE PAPER

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# OPTIMIZING EARLY-STAGE COMMERCIAL ASSESSMENTS FOR EMERGING BIOPHARMA

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In recent years, small and emerging biopharma companies have become much more important in global drug development. Smaller companies now account for the bulk of clinical trial activity and originate the majority of drugs that launch, areas that have traditionally been dominated by large pharma. However, despite recent successes, smaller biopharmaceutical companies continue to experience challenges in design and implementation of clinical development programs that are associated with their size and scale, including limited resources and funding. Robust commercial assessments that provide solid evidence to help establish the value of assets at each stage of development play an important role in obtaining funding to support ongoing clinical and commercial development and fuel continued growth. In this white paper, we review approaches and some of the key success factors to optimize early-stage commercial assessments for emerging biopharma companies.

## Emerging Biopharma's Growing Importace in Drug Development

To get an idea of the impact of emerging biopharma companies on drug development and how it has changed over the past decade, it is useful to look at global clinical starts and drug launches by company size. For this analysis, emerging biopharma companies are defined as those companies spending less than $200M on research and development (R&D) and generating less than $500M in annual revenue, while large pharma is defined as those companies with greater than $10B in annual sales. Figure 1 demonstrates that emerging biopharma's share of clinical trial starts grew from 37% in 2014 to 62% in 2023, mostly at the expense of large pharma.[1] If we focus on the novel active substances that launch in Figure 2, we see a similar pattern; in 2013, the share of new drug launches originated by emerging pharma was 35%, increasing to 56% in 2023. Emerging pharma is now responsible for the lion's share of drug development, as illustrated by clinical trial activity and originations for drugs that launch. These smaller companies are also more likely to launch the products they originate; in 2023, a majority (53%) of drugs originated by an emerging biopharma were also launched by that company, an increase from 40% in 2013. Industry observers have attributed emerging pharma's growing importance in drug development to the absence of bureaucracy that often plagues larger companies, as well as their ability to attract scientific talent.[2] According to Naheed Kurja, CEO of Cylica, "We have started to witness a shift in the balance of power over the past decade, with a burst of innovation from the early-stage and emerging biotech companies. As the market landscape for drug discovery evolves, early-stage biotechs are increasingly entering the spotlight with a combination of subject-matter expertise in the science and the benefits of a lean organization conducive to rapid innovation."[3]

Figure 1. Share of Global Clinical Trial Starts[1]
By Company Segment (2014, 2023)

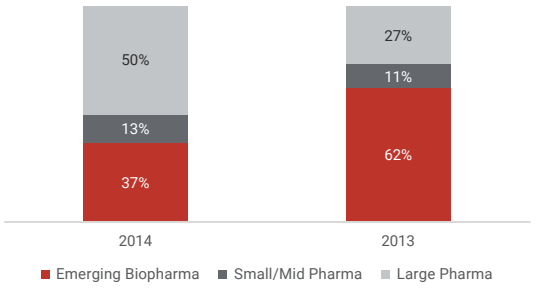
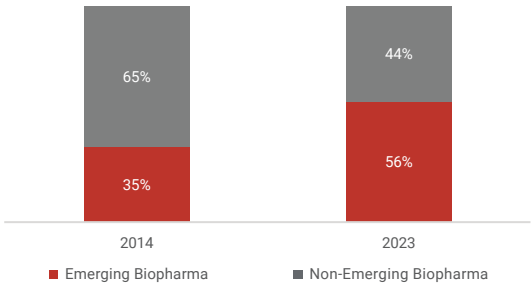



Figure 2. Novel Active Substance Originations[1]
By Company Segment and Launch Year




It is well known that drug development requires substantial capital to support R&D, clinical trials, and regulatory approvals, yet many startups have little or no commercial revenue. As a result, emerging biopharma's continually face the need to secure funding for their ongoing development endeavors. In this high-risk high-return environment it is not surprising that early commercial assessments – market research and forecasting to support prelaunch drug development – are essential for guiding strategies, mitigating risks, and providing evidence to support transactions and secure funding. Depending on the stage of clinical development and product situation, these commercial assessment projects range from focused due diligence and advisory opinions on go/no go decisions, to structured opportunity assessments including a high-level forecast, to detailed forecasts with comprehensive financial modeling and deal support.

## Commercial Assessment Research and Forecasting Requirements

Table 1 below outlines the business key questions that are addressed for different types of commercial assessment projects throughout the product lifecycle, along with the associated primary and secondary research requirements and forecast structures. Early exploration for preclinical and Phase I assets focuses on market opportunities for assets without clinical data. Research is based primarily on published and syndicated secondary sources, although a small number of qualitative interviews with key opinon leaders (KOLs) is sometimes included in therapeutic areas with limited data. Forecasts follow published epidemiology, use analogs for HCP prescribing shares, and typically focus on peak shares. With early product assessments for Phase I and Phase II assets where there is additional clinical data available, primary research (while still primarily qualitative) often includes healthcare professionals (HCPs) and payers in addition to KOLs. The forecast in this situation is more involved and may provide volumetrics and revenues over a ten-year period. For later stage products in Phase II or Phase III where more clinical data is available, research may include robust quantitative samples of HCPs and patients, and qualitative research with a diverse sample of payers. For assessments involving US markets, bespoke analysis of claims data sources is also increasingly being used for market sizing and landscape analyses.

**Table 1. Commercial Assessment Requirements**

| | Early Exploration<br>Preclinical/Phase I | Early Product Assessment<br>Phase I-II | Comprehensive Decision Modeling<br>Phase II-III |
|---|---|---|---|
| **Description** | › Market opportunity assessment | › Small scale new product forecast | › More comprehensive new product forecast |
| **Source of Uncertainty** | › No clinical data | › Limited clinical data (know potential endpoints but not performance) | › More clinical data, commercial uncertainty regarding label, pricing/access, competition |
| **Precision Needed** | › Low (rough estimate) | › Medium (to guide investments) | › High |
| **Research Inputs** | › Analogs, secondary data | › Analogs, secondary data, RWE<br>› Qualitative research using small sample of HCPs, KOLs, and payers | › Analogs, secondary data, RWE<br>› Quantitative research using robust sample of HCPs and possibly patents/caregivers, in depth qualitative research with payers |
| **Forecast Structure** | › Epi-based, long range<br>› Annual view | › Epi-based, long range<br>› Annual view | › Monthly, quarterly or annual view |
| **Key Outputs** | › Market size<br>› Peak volumetrics and revenues | › 10-year volumetrics and revenues | › 10-year volumetrics, revenue, SKU |
| **Potential Applications** | › Market potential for preclinical assets and early stage compounds<br>› In/out licensing decisions<br>› Go/no-go decisions | › Product and portfolio strategy<br>› Indication prioritization<br>› In/out licensing decisions<br>› Go/no-go decisions | › Product, portfolio and marketing strategy<br>› Indication prioritization<br>› Pricing strategy<br>› In/out licensing decisions |

A key feature of projects with primary research is an evaluation of the target product profile (TPP), a description of the product that outlines its intended use, target patient population and desired attributes including safety and efficacy. The TPP provides a strategic road map to guide product development and support communication between R&D and commercial functions. Obtaining customer reactions to a preliminary product profile is crucial for understanding what features drive interest in the product and why, as well as the characteristics that, if changed, might fundamentally influence the product's value proposition. TPP testing research provides the foundation for building a compelling commercial value proposition for the product, a vital component in any successful commercial assessment.

Regardless of the product's stage in development, it is very important to right-size investments in commercial assessments to properly reflect the amount of available information, the degree of precisio required, and the potential impact on the business. This does not mean the best approach is always the least expensive – but rather, understanding when and when not to go bigger to obtain additional rigor and precision is crucial for maximizing outcomes for the company. Major drivers of cost include the amount of primary research with customers and whether secondary analysis of claims data is included as part of the assessment.

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On the primary research side, small amounts of qualitative research can be very cost-effective, but costs can grow quickly for qualitative projects with a global scope, or when larger quantitative samples are required. In addition to the costs of developing and analyzing surveys, respondents are compensated for their time and honoraria for large projects can be substantial. Our clients sometimes question the utility and validity of early exploration and early product assessments because the primary research samples are small. However, it is important to recognize that uncertainty in a product's clinical profile is by far the most significant source of uncertainty in these early stages, and expending scarce resources on large primary research samples with HCPs, payers, and patients to obtain more statistical precision regarding a profile where there is limited information may not be warranted. Secondary sources and a small amount of primary research are often sufficient to accurately frame the market opportunity and provide a preliminary evaluation of product opportunity in these situations.

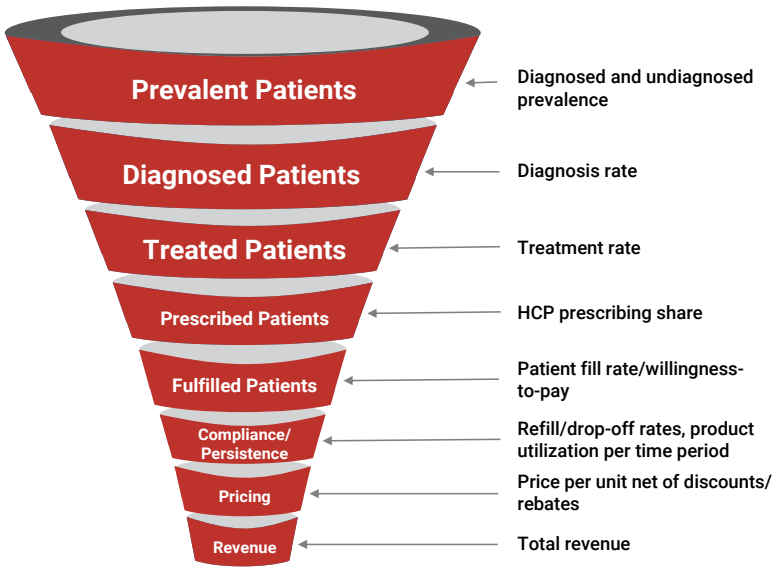
Sourcing and purchasing multiple datasets and building an in-house analytic platform for analyzing claims data is a complex and time-consuming task requiring significant expertise. As a result, claims analysis has historically been viewed as too costly to play a significant role in commercial assessment projects. However, this situation has recently changed as US claims datasets have matured and vendors have developed tools for quickly accessing and utilizing these data. Now, several third-party platforms have become available that integrate multiple data sources and streamline the development of business rules for claims analysis and reporting. Claims-based market analysis can now be initiated and completed in as little as a few weeks to a month, providing a timely and cost-effective solution for market sizing and landscape assessments in the US market.

## Forecast Structures

Forecasters often distinguish between "demand-based" vs. "patient-based" approaches when describing the overarching structure of pharmaceutical forecasts. "Demand-based" approaches are appropriate for mature markets with available unit data for existing treatment options. Market sizing is not an issue in these situations, and it is often possible to develop forecasts using historical data for existing products/analogs as the foundation. "Patient-based" approaches begin with epidemiology and often include more patient detail. The patient-based approach is more appropriate for novel or first-in-class therapies and often includes a more significant primary research component, although there is a role for primary research in both methodologies.

Figure 3 illustrates the general structure of a typical commercial assessment forecast. Some of the components in the funnel will vary in importance depending on the therapeutic area under consideration, and additional detail regarding lines of therapy, patient flows, and key patent segments can easily be incorporated into this structure. The patient-based forecast begins with epidemiology for the patient population of interest and factors in estimates of diagnosis and treatment rates to identity the target patient population, while demand-based methods use secondary data concerning treated patients to establish an estimate. In either case, estimates of peak prescribing share from HCP research or analogs provide an estimate of the peak opportunity for the specific product.

Figure 3. Forecast Funnel



Patient fill rates and estimates of compliance and persistence allow us to convert shares to utilization in each time period. Associated revenues are calculated using prices adjusted for any applicable discounts and rebates. It is often useful to develop a checklist from the funnel highlighting the available information sources for each element and any gaps that will require additional primary or secondary research. Regardless of the forecast structure, it is very important that it is well documented with clear assumptions and analyses that can be easily understood and verified by reviewers. These steps can go a long way to establishing credibility with funding sources and potential partners.

The structure outlined in Figure 3 produces a point forecast, or more generally, a time series of revenues over the forecast period for a given set of assumptions. It is important to realize that there is often considerable uncertainty surrounding these assumptions in early-stage assessments, and so providing an estimate of the range of potential revenues reflecting clinical risks and variability in other factors is also key for increasing confidence in the forecast. For example, in one of our recent projects a US claims analysis was used to size the market for a novel cardiovascular product, and the size of the prevalent population varied by 20% depending on relatively innocuous claims business rules and coding assumptions. Upside and downside scenarios or more formal risk analyses can be developed to reflect potential variability in forecast assumptions and to generate a relevant range for the forecast. The transactions supported by early-stage assessments are basically arrangements for sharing risks and rewards and developing a credible range for the forecast will influence how deals are structured and priced.

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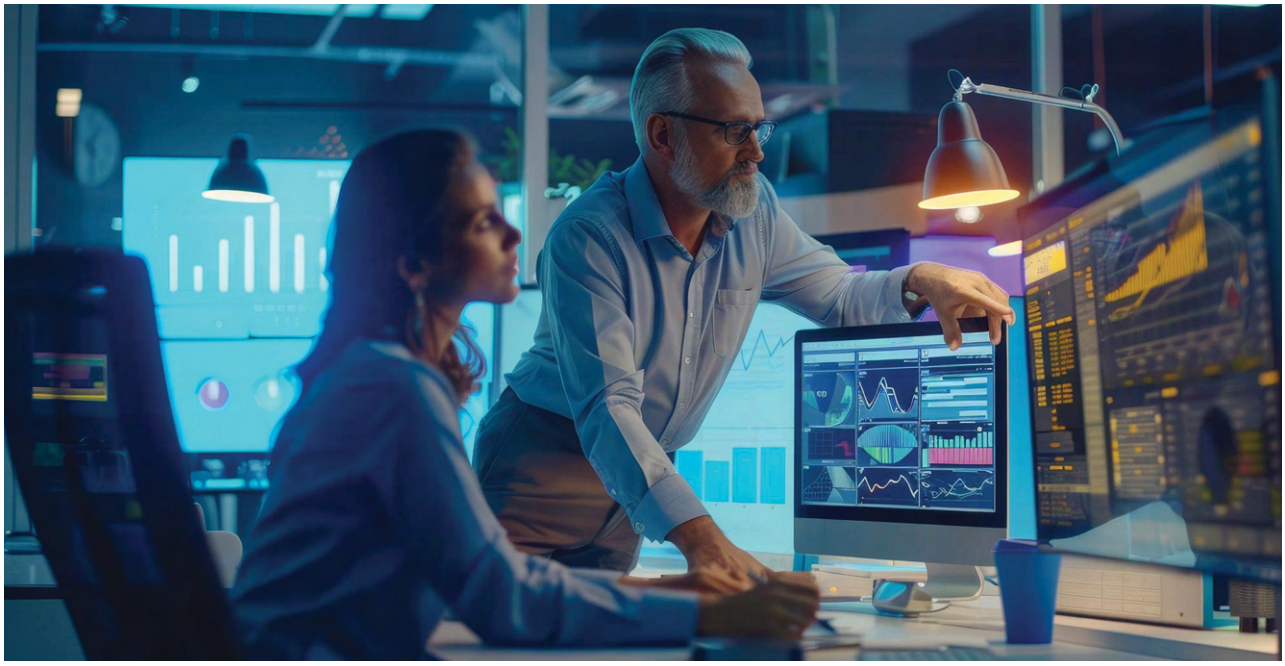

## Financial Modeling and Deal Support

A key characteristic of commercial assessments is the focus on financial valuation. The primary approach to valuation in pharmaceutical markets uses discounted cash flow analysis and the calculation of risk-adjusted net present value (rNPV). Net present value is the discounted value of cash inflows and outflows associated with an asset, including product sales on the revenue side and clinical development, cost-of-goods sold, and selling, general, and administrative expenses on the cost side. To get rNPV, cash flows are risk-adjusted across each phase of clinical development to reflect probabilities of success, so that the overall risk decreases as the product progresses through development and clinical risk is resolved.

Deals often involve a combination of upfront payments made immediately, milestone payments that are paid once goals in the development of the asset (i.e. Phase II or III clinical trial success) are achieved, and royalty payments once a product is marketed and sales are realized. Development-related milestone payments have increased across all stages of development in the past decade as they allow participants to share the increased cost of clinical development.[4]

Financial evaluation for each deal can be greatly aided with a deal modeling platform that links the forecast with all the deal-related cash flows. The platform provides flexibility in modeling the amount and timing of upfront, milestone, and royalty payments, and allows users to experiment with and optimize different deal terms and structures. Ideally, the platform should provide estimates for both sides of the deal, so that biopharmas can understand both what they are getting and what they are giving up in the transaction.

## Communicating the Value Story

Assessments should not focus exclusively on the numbers – it is equally important to clearly articulate a compelling commercial value proposition that will resonate with potential partners. Important elements of the value proposition include an explanation of the unmet need being addressed by the asset, a description of the market landscape, market sizing for the target patient population, and a revenue forecast that reflects assumptions about physician adoption and uptake for the product and relevant competitors. Decision makers will need a thorough understanding of all those factors to accurately determine an asset's potential value.

Different components of the commercial value proposition may be more or less important depending on the stage in the product lifecycle/type of commercial assessment. Preclinical and early-stage assessments necessarily focus on the potential of the science to address the unmet need and the preliminary landscape and market potential but are abbreviated on the commercial side because there is limited information about the product. Mid-stage assessments provide a balance of clinical and commercial information because there is more information about the product's potential and how it stacks up against current and pipeline competitors.

> Deals do not occur in a vacuum, and it is essential to understand the context and rationale for the deal and the expectations and preferences of potential partners.

In later stages, more detail is provided on the commercial opportunity, the product's position in the marketplace and how it is shaped by available clinical data, and pricing and market access considerations.

Regardless of stage, deals do not occur in a vacuum, and it is essential to understand the context and rationale for the deal and the expectations and preferences of potential partners. Some partners will require a rigorous analysis with considerable data and documentation, while others may prefer analysis with a broader brush and a more general description of potential risks and returns. Tailoring the description of the commercial value proposition and the analytics to the needs of the potential partner may ultimately be the most important factor for success.

## Conclusions

Industry observers believe that emerging biopharmas will continue to dominate early-stage drug development, and we expect commercial assessments to play an increasing role in supporting these companies for several reasons. Generative artificial intelligence (AI) is now being used extensively by commercial market intelligence services to streamline and improve market landscape analyses.[5] For our practice, our own research and applications suggest that some key tasks associated with creating the building blocks for these analyses can be streamlined with AI, but final analysis and reporting still requires significant guidance, expertise and experience. While machine learning has been successfully employed for estimating probabilities of success in clinical trials for over a decade, these tools have also recently been used to quantify clinical risks to be used in risk analyses underlying early-stage forecasts.[6,7] Nevertheless, there will still be a need for high quality primary research to fully articulate unmet needs, market opportunities and product perceptions, and to craft compelling commercial value propositions. Overall, these developments should reduce costs and timelines and improve the quality of commercial assessments across the product lifecycle.

[1] IQVIA Institute for Human Data Science. Global Trends in R&D 2024: Activity, Productivity, and Enablers, February 2024. 15, 37.

[2] Girvin G (2024). No contest: small pharma innovates better than big pharma. The Foundation for Research on Equal Opportunity (FREOPP). February 28.

[3] Robinson R (2020). Small pharma driving big pharma innovation. PharmaVoice. January 1.

[4] Edwards M (2019). Milestone payments in biopharma: negotiating an equitable value allocation. Nature Biopharma Dealmakers. News Briefing, May.

[5] For example, AlphaSense (https://www.alpha-sense.com/) advertises its service as "AI-powered research for consulting" where users can "spend less time searching for specific data points with our AI search technology and extensive universe of private and public content."

[6] Wong C, Wei Siah K, Lo A (2019). Estimation of clinical trial success rates and related parameters, Biostatistics. Volume 20, Issue 2, April, 273–286.

[7] See Willson D (2024). Incorporating risk in early-stage demand research and forecasting. Pharma Market Research Conference (PMRC) USA, Newark, NJ, February.