TRINITY

WHITE PAPER

Empowering the Next-Generation Launch Model

Leslie Sandberg Orne • Krista Perry • Chris Barger • Jenna Fritz
Susheel Sukhtankar • Amid Zand • Curtis Staab

June 2022

Introduction

Sixty-two percent of the products that launched since September 2019 through December 2021 underperformed expectations, including a whopping **24 out of 28** non-rare, non-oncology products.

The pharma industry has seen dramatic shifts in scientific innovation over the last decade with a trend toward orphan markets, personalized medicine, higher priced products and new modalities including cell and gene therapies, oligonucleotides and others. COVID served to further accelerate scientific innovation, driving a near record-breaking number of FDA approvals, astronomical venture capital funding and remarkably rapid development and rollout of ground-breaking products (including anti-virals, novel antibodies and mRNA vaccines). **However, as Trinity Life Sciences discussed one year ago, the commercial models employed by companies that launched new products during 2020 and 2021 were largely based on traditional sales and marketing approaches, despite the massive shifts in the pharmaceutical industry and the healthcare environment at large.** We explore in this paper how industry players can elevate and evolve their commercialization approaches to better match the flourishing scientific innovation and enable those scientific breakthroughs to be accessed by the right patients at the right time.

Starting with what we know: The COVID-19 pandemic exposed and exacerbated challenges on the road to launch that had been emerging prior, including fundamentally changing the way we engage and access treatments. Launches have clearly been impacted; notably, **62% of the products that launched since September 2019 through December 2021 underperformed expectations, including a whopping 24 out of 28 non-rare, non-oncology products.** Other groups have noted declining performance by new drugs in the last two years relative to historical averages in terms of first-year sales.[1]

[1] McClellan, W., Muñoz, E., & Lasky, B. (2022, May). IQVIA U.S. Launch Quarterly.

Performance of Product Launches by Therapeutic Area

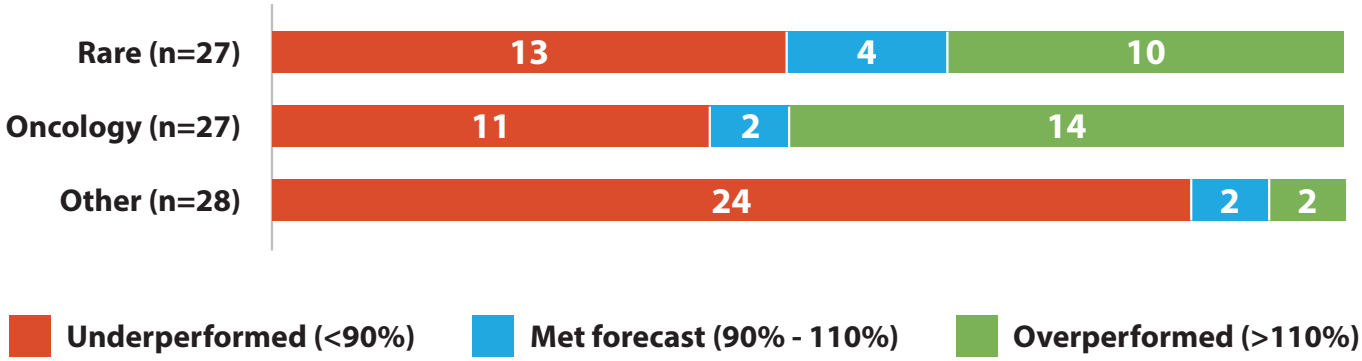


Figure 1: Launch performance (first year sales relative to pre-launch consensus forecast) by therapeutic area, for launches between September 2019 and December 2021.

The underperformance can be attributed to many factors and reflect a failure to employ innovative strategies to effectively engage patients, providers and payers throughout both clinical development and commercialization. First, we must consider that some of the wrong drugs have been developed and launched, without adequate early commercial insight into development plans and go/no-go decisions. Next, many companies forecast (pre-launch) unrealistic expectations for both peak and, more often, rate of uptake, leading to a sequela of bad decision-making around resourcing and spend levels. Then, execution in achieving access and engagement has yet to be optimized to meet new market realities. Recent launches have failed so predictably that the street is now betting against a successful launch – with 5 of the top 10 most-shorted stocks being biotech companies, at quarter end Q1 2021.[2]

Recently, we have seen meaningful trends emerge within the industry data we collect:

- 57% of companies believe their field has permanently lost at least 10% of their access to HCPs
- Virtual calls now make up ~30% of all call volume
- 90% of companies have deployed new or evolved current customer facing roles in the past year
- 73% of companies have plans to or already launched new pilots/innovations in digital marketing this year

While these market challenges have undeniably strained companies – a fact made all too apparent by **at least 52 pharmaceutical companies reporting layoffs thus far in 2022**[3] – it does not have to be so in perpetuity. We know that the shift to new roles and approaches will continue, but how do we optimize it and create a new approach to commercialization that is more rational, flexible and modern?

---

[2] Brian Sheid (2021). Biotech companies now most-shorted US stocks as tougher federal scrutiny looms. S&P Global Market Intelligence.

[3] Analee Armstrong (2022). Fierce Biotech Layoff Tracker

For years, the ingrained conventional wisdom that the overall success of a new drug launch is determined in the six months following approval has shaped stakeholders' expectations. Investors, boards and C-suite leadership have internalized this conventional wisdom and applied pressure to commercial teams to ensure strong performance at the six-month mark by building big at the outset of launch.

Here, we question whether this mantra remains applicable in 2022 and beyond: in a new age of product launches, can commercial teams afford NOT to take a more gradual, stepwise approach? Rather than fighting a losing battle against market forces that will elongate the uptake curves for new products, we make the case herein that in many circumstances it is only prudent to plan for a longer uptake and develop a go-to-market strategy that recognizes an extended (and more sustainable) initial period of sales growth. In fact, companies who make a clear-eyed assessment of the pace at which new drugs will enter markets can plan for long-term success and use the slower uptake to their advantage.

Optimizing a shift away from this conventional wisdom requires an innovative mindset and new strategies. **Regulatory approval can no longer be equated with success and launch performance should be measured against long-term profitability, rather than predicated on hitting first-year revenue expectations at any cost.** Balancing upfront spend with realistic near-term revenue will increasingly become essential to launch success and require leadership teams to set rational, data-driven expectations with investors ahead of launch. Many troubled launches – see below table for a few notable examples – can be attributed at least in part to spending and organizational expansion pre-approval that outpaced realistic post-approval revenue targets.

Company	Product	Indication	Approval Date	Outcome	Driver
Acacia	BARHEMSYS	Post-Operative Nausea and Vomiting	February 2020	March 2022 - Acquisition at 30% of stock value by Eagle Pharmaceuticals	Poor uptake due to physical access limitations attributable to COVID
Esperion	NEXLETOL / NEXLIZET	Hyper-cholesterolemia	February 2020	October 2021 – 40% workforce reduction, shift to focus on digital / virtual promotion	Poor sales performance due to stiffer-than-expected access barriers and competition from PCSK9s and generics
Epizyme	TAZVERIK	Epithelioid sarcoma and relapsed/ refractory follicular lymphoma	February 2020	March 2022 – 12% workforce reduction and withdrawn clinical studies to cut costs	Stunted sales due to lack of physician access during COVID and failure to capture broader market with narrow patient focus
Biogen	ADUHELM	Alzheimer's Disease	June 2021	March 2022 – workforce and cost reduction, 50% price cut for Aduhelm	Questions over efficacy with controversial FDA approval (and outright EMA rejection), limited CMS coverage and very poor access/uptake

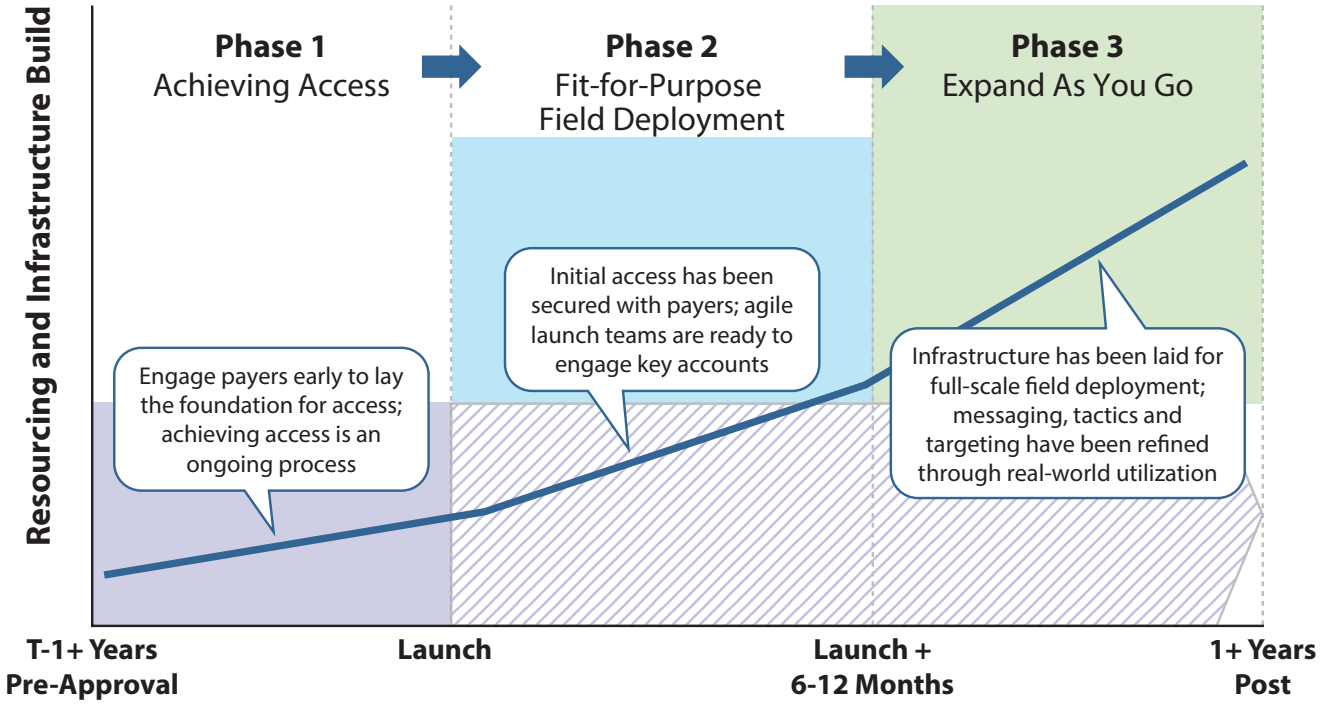
Table 1. Notable recent examples of companies facing poor outcomes and uncertain futures following highly anticipated launches.

How can commercial leaders developing their go-to-market model envision an approach built around a more gradual uptake and less emphasis on hitting a high six-month mark? Clinical research, founded on the principle of incremental analyses to minimize confounding variables, may provide a useful roadmap. We believe tomorrow's commercialization model will consist of three key "phases":

1. **Achieving Access:** Building **evidence and access** to ensure product gets to patients seamlessly
2. **Fit-for-Purpose Field Development:** Developing a **customer engagement model** that optimizes demand without breaking the bank
3. **Expand as You Go:** **Adjusting and expanding** as launch progresses – rather than going "all-in" from day one

By planning for a phased approach to commercialization, leaders can still ensure an excellent customer experience on day 1, then build the infrastructure to support growing demand over time. Below, we explore these three "phases" of a rationalized commercial launch through the lens of several recent launches that exemplify the innovation (and challenges) inherent in today's market.

Illustrative Phased Commercial Launch



Phase 1: Achieving Access

Access is foundational, just as safety is paramount in phase 1 of a clinical trial – table stakes

A robust, proactive approach to evidence generation and payer engagement is more important today than it has ever been. Gone are the days of assuming access will come automatically for innovative products with high patient and HCP demand. Diligent commercial teams must ensure that the necessary groundwork has been laid with payers prior to and immediately following approval, as no amount of field force planning and operational excellence can overcome poor formulary coverage and onerous reimbursement processes.

Gone are the days of assuming access will come automatically for innovative products with high patient and HCP demand.

Take Ascendis' launch of SKYTROFA for example, which launched into several markets in October 2021. Despite delivering robust clinical data, a clear improvement in patient quality of life (weekly vs daily injections) and its key competitor (Pfizer / OPKO's NGLENA) suffering a CRL, the stock continues to fare comparatively worse than the S&P Pharma index, and its US sales (~$1M in Q4 '21) were only a fraction of its consensus forecast for the same time period ($25M). SKYTROFA is a likely casualty of a challenging access landscape. As of the time of this writing, ~8 months after its launch, nearly half (42%) of commercially insured lives do not have coverage, including the vast majority of lives on CVS Health (82%) and ExpressScripts (96%) plans.[4] While this is not inherently surprising given the abundance of daily alternatives, it highlights the potential for access to complicate an otherwise successful launch.

Alternatively, an early focus on access can pave the road to long-term success, despite challenges in other areas. The COVID-19 pandemic delayed Bristol Myers Squibb's launch of ZEPOSIA for two months following the drug's approval. During this delay period, BMS focused on negotiating favorable access in a competitive market for the third-to-market S1P receptor modulator for multiple sclerosis. ZEPOSIA garnered a 20% prescriber base in the first two months after launch and now has preferred status on almost half of plans.[5] Even though ZEPOSIA did not meet early analyst forecasts, sales of the product in the U.S. increased from $10M in 2020 to $99M for the full year 2021; capturing favorable access laid the groundwork for accelerating uptake even with two prior agents launched in-class.

When Alnylam launched their second product GIVLAARI for acute hepatic porphyria (AHP) in November 2019, the company leveraged the capabilities they had built for their first product ONPATTRO which launched the year prior, as well as their partnership with Ironwood as a way to defer costs and hit the ground running. Nevertheless, the challenges to diagnosing AHP and identifying patients presented challenges to rapid adoption of GIVLAARI. Key to their access strategy was utilizing an innovative prevalence-based reimbursement strategy with a plan-by-plan negotiation approach to enable rapid reimbursement once patients were diagnosed. Alnylam was therefore able to drive diagnosis and genetic testing in the early period and ensure patients who were identified were able to quickly access treatment. GIVLAARI generated over $42 million in the first full year of sales, edging past analyst reports of $37 million.

With ZEPOSIA and GIVLAARI, both products faced headwinds that curbed initial adoption – in one case, a competitive environment with two in-class agents, in the other, a rare disease where patient identification is critical – the focus on access early and building evidence ultimately positioned the brands to optimize demand. However, challenges with initial access can also devastate launches that seem to be positioned well for success.

[4] Source: Managed Markets Insight & Technology Formulary Lookup

[5] Source: Managed Markets Insight & Technology Formulary Lookup

Phase 2: Fit-for-Purpose Field Deployment

Agile "test and control" mentality akin to dose-finding studies in clinical Phase II – what works??

After achieving adequate access (even if only in certain geographic regions or segments of the population initially), companies can then progress to a targeted sales approach to likely early adopters, identified via a data-driven method and approached with a range of potential sales strategies to optimize the engagement model. This trial-and-error phase often involves trialing novel field roles, unique engagement strategies and/or marketing tactics, and ultimately the right messages in order to find the right chemistry for success.

This trial-and-error phase often involves trialing novel field roles, unique engagement strategies and/or marketing tactics, and ultimately the right messages in order to find the right chemistry for success.

As an example, Ascendis employed a phased deployment of its sales team, among other strategies, to soften the blow (and allow for recovery) of their less-than-stellar access for SKYTROFA as detailed above. SKYTROFA launched with about 10 sales reps, but planned for and executed on a post-approval expansion to double its sales force size to 20 as access improved. Doing so allowed a small cadre of experienced reps to hit the ground on day 1 and start priming key accounts without the financial risk that comes with onboarding an entire sales team months before approval. Ascendis also developed unique roles to support the environment in pediatric growth hormone deficiency. Acknowledging the challenging access environment, a dedicated field team was deployed to develop tailored strategic plans with health systems and IDNs to increase provider access and sales, and a team focused on medical outcomes was brought on to navigate the complex clinical and health economics of the space. These tactics have clearly instilled analyst confidence in Ascendis' ability to right the ship, as current peak sales forecasts, which come in well over $1B, are largely the same as forecasts made before SKYTROFA's slower-than-expected start ($1.38B vs $1.41B, respectively).

Incyte provides another relevant example. Rather than standing up a dedicated specialty oncology sales force for PEMAZYRE's launch in ultra-rare cholangiocarcinoma (April 2020), Incyte expanded the scope of its already-in-field JAKAFI sales force (that was promoting myelofibrosis and polycythemia vera at the time). If Incyte had followed a typical launch playbook, they might have focused heavily on COEs and academic institutions specializing in cholangiocarcinoma first. Instead, by targeting the community hematologists / oncologists that treat both JAKAFI's approved indications and cholangiocarcinoma, PEMAZYRE beat analyst expectations for its first year on market ($26M actual vs. $8M pre-launch forecast) and continues to show strong performance.

For Oyster Point's launch of TYRVAYA in the dry eye disease market, the company was diligent about field deployment from the start. They developed a robust, data-driven launch forecast to assess the team's return on investment as well as capture market access constraints to assess the true addressable market potential, contributing significantly to right-sizing the team at launch. The company initially planned for 150 – 200 sales reps, with the first hires coming live three to four months before launch to begin training, on-boarding and account profiling. As of the end of 2021, Oyster Point had built their sales force team to 162 reps. While their field-based sales team covered the majority of high and medium potential prescribers, a small team of virtual specialists was also hired to cover low potential prescribers

and begin profiling and activating prescribers for inclusion in future target lists. TYRVAYA has maintained a consistent sales force size with no significant changes in their structure since launch, while driving modest uptake in a large market with potential to gain share and new patients. Oyster Point is also poised to build upon their first launch with additional indications for the varenicline solution behind TYRVAYA and multiple ophthalmic therapies in the pipeline.

To allow for more agile field deployment (and future scaling – see Phase 3 below), companies will need to adopt an intensely data-driven launch approach.

Takeda's launch of EXKIVITY provides a particularly salient example of anticipating the potentially noisy digital environment HCPs will face and in which companies will operate. They built an in-house digital content team to create high-quality content reflective of real-world data, planning proactively for what we believe to be a permanent decrease of in-office physician access. Additionally, the team has built AI into its non-personal targeting approach to ensure this content gets to the right HCPs at the right time, while recognizing the potential for HCPs to tune out incoming information as the volume of digital communication increases. We expect digital and data-centric approaches such as this will become differentiators going forward and allow for successful optimization and expansion of your launch.

These examples underscore the importance of:

- A robust ROI assessment to prioritize customer targets and right-size your field team. Understanding promotional factors along with market access dynamics that will drive uptake is more crucial than ever. This feeds into a forecast that will serve as a reliable foundation for planning commercial activities and that will allow leadership teams to set realistic expectations with investors ahead of launch
- Deploying customer-centric roles with clear responsibilities and allowing agility for those roles to evolve and adapt
- Taking a leaner approach heading into approval may also require heavier outsourcing of internal operations functions. This affords the organization greater flexibility to adapt to shifting financial environments and minimizes the bad press and investor skepticism that comes with mass layoffs

To allow for more agile field deployment (and future scaling – see Phase 3 below), companies will need to adopt an intensely data-driven launch approach. By incorporating robust live analytics into performance tracking, companies can maintain a nimbler go-to-market model that is easily adapted to shifting market dynamics (for example, evolving demand sub-nationally or improving payer coverage). Sales ops should leverage real-time integrated feedback via the plethora of data available (field activity, customer-level sales and market access, patient-level claims), allowing them to test which HCPs to target and which messages to provide via next-best-action guidance. Synthesizing these data and using these insights to adapt and refine your model will be critical for an effective phased approach.

Phase 3: Expand as You Go

Scaling up based on learnings from the prior two phases akin to a pivotal Phase III clinical study – prove the hypothesis

As brands position themselves to gain coverage and establish a foothold in new markets, such as in the example of BMS' ZEPOSIA above, commercial leaders can embrace an attitude of starting small (or leveraging existing infrastructure) and then expanding post-launch. This phased approach seems counterintuitive to the traditional attitude to hit the ground running aggressively on day 1 of launch, but in the case of the examples below (and several of the examples described above), this gradual build can drive commercial teams towards a more sustainable long-term growth strategy.

This phased approach seems counterintuitive to the traditional attitude to hit the ground running aggressively on day 1 of launch, but this gradual build can drive commercial teams towards a more sustainable long-term growth strategy.

Horizon's strong launch of TEPEZZA in Thyroid Eye Disease (TED – approved January 2020, $1.7B in sales in the US in 2021) provides a poignant example of allowing product demand and market feedback to inform the long-term go-to-market strategy. Launching into a poorly defined space during COVID, Horizon brought on a relatively lean field team and focused heavily on creating a robust network of COEs and driving disease awareness. With demand for TEPEZZA soaring and a larger addressable patient population than initially expected, Horizon announced plans to double the size of their existing sales force in late 2020. Add to this the hiring of dedicated roles for patient access support, site of care assistance and reimbursement support (among others), it is clear Horizon anticipated the complexities of launching into the TED space during COVID and built its customer engagement model accordingly.

Similar to Inctye's approach described above, Neurocrine leveraged their existing field force of 160 psychiatry and neurology specialty sales reps, in place since the 2017 launch of INGREZZA (for tardive dyskinesia), for the launch of ONGENTYS for Parkinson's disease in 2020. Neurocrine was able to employ this sales force to target specialists treating both diseases in the early days of the launch before eventually expanded their salesforce to 250. In 2021, Neurocrine announced an expansion and restructuring of their sales team to include 350 specialists for three dedicated teams: neurology, psychiatry and long-term care. While ONGENTYS has struggled with performance and uptake, in large part due to a challenging payer landscape limiting access to branded therapies (see above for the foundational nature of ensuring robust access), INGREZZA has shown steady growth with sales reaching $1.1 billion within the U.S. in 2021.

Perhaps the best example of tying each of the innovative approaches to commercialization together comes from Novo Nordisk's launch of RYBELSUS for type 2 diabetes, approved by the FDA in September 2019. If its long-term potential were determined by its first quarter on market alone, one would assume this product was doomed to fail. RYBELSUS generated just $7M in 2019, well under consensus pre-launch forecasts of $16M and a seemingly paltry sum for what was widely considered to be a gamechanger in a ~$50B market. However, few would say this launch has failed now: expectations for 2022 come in at well over $1B and all signs are pointing to revenues approaching $5B by 2026. In fact, the slow initial launch of RYBELSUS was part of an orchestrated effort that closely followed the three phases proposed above:

Phase 1

Achieving Access:

Anticipating the pivotal importance and complexity of securing access in the highly competitive diabetes market, Novo Nordisk utilized RYBELSUS' percentage of lives covered as a key metric in evaluating its launch timeline and progress. Clearly, this early effort paid off by not only ensuring a positive customer experience soon after launch, but also in securing present-day preferred coverage for nearly 90% of commercially insured patients.

Phase 2

Fit for Purpose Field Deployment:

As access was being secured with payers, Novo Nordisk began slowly rolling out RYBELSUS to a highly targeted group of specialists with a small group of super-reps. This pilot phase not only ensured that prescribers who were willing and able to handle early access and reimbursement issues were approached, but it also provided an opportunity to test RYBELSUS on the market and, importantly, get early insights into whether the company's ideal co-positioning of RYBELSUS and OZEMPIC stood up to real world prescribing practices.

Phase 3

Expand As You Go:

In August 2020, nearly a full year after Rybelsus' FDA approval, RYBELSUS hit the 70% access mark and the Novo team launched into "strike mode", deploying the full RYBELSUS sales team into the field and beginning promotional efforts in earnest. Notably, Novo Nordisk launched in full during the height of COVID, when many HCPs had already closed doors to reps and detailing had gone virtual. Where many other launches struggled to adapt to the new digital sales model, Novo Nordisk had already worked out the kinks during its pilot phase and had a sales team trained and ready to handle the challenge.

Conclusion

It is, undoubtedly, a challenging time to take a drug from the clinic and get it in the hands of patients, due both to the current market environment and the challenges noted herein. **In 2022, approval of a new drug is no guarantee of success – and the first six months post-approval are no longer a clear predictor of a drug's long-term trajectory.** Companies should not be dissuaded from pursuing opportunities that may require greater patience in the initial one to two years post-launch to reap substantial rewards in the many years that follow. **Moreover, investors should be prepared to fund a company well past the initial launch phase before profitability can be achieved.**

In 2022, approval of a new drug is no guarantee of success – and the first six months post-approval are no longer a clear predictor of a drug's long-term trajectory.

That in turn requires that companies – and especially emerging biotechs who have more riding on an individual launch – set appropriate pre-launch expectations both 1) internally regarding resourcing/investment as they build/scale and 2) externally with the investor community to avoid waning investor confidence following approval and eventually mass layoffs / restructuring. If getting to approval is no longer the end game and the six-month mark no longer dictates a drug's ultimate profitability, how can companies persuasively advocate for patience and communicate their long-term vision accurately?

With appropriate expectation setting informed by robust market research and analytics, and a well-articulated, data-driven commercialization model following the three phases above, tomorrow's commercial leaders can overcome many of the challenges today's leaders are facing. Teams must be willing and able to assert that launches which plan for a more gradual initial uptake are not "failed" launches nor a reflection of the company's confidence in their product. Rather, such launches should be seen as a valuable pilot phase, an opportunity to build access and validate the many hypotheses developed about the product in the years leading up to launch, before leaning in and launching fully. The waters of tomorrow's commercial landscape are both murky and uncharted – isn't it prudent to test them before diving in?

Strategic Advisory

At the heart of all we do, we advise. We understand how important every decision is along the continuum of getting a product to market, which in the life sciences industry can translate into getting a life-changing or lifesaving treatment to a patient. We have the experts and experience to bring in the right data, analysis and evidence to provide insights and recommendations to support your decisions. Our experts can help you with business development, corporate strategy, new product planning, brand strategy and dynamic market intelligence.

Launch Excellence

Trinity's Launch Excellence engagements help companies effectively and efficiently prepare for successful commercialization tailored to their market and situation. No matter where you are on the path to launch, Trinity works with you to define, execute and optimize your commercialization readiness. We directly support >30 companies annually in their launch journeys – strategy, planning and management – across dozens of therapeutic areas, from first-launch emerging biotech to the largest global pharma leaders.

Commercial Analytics

Trinity's Commercial Analytics offerings include forecasting, promotional analytics and analytics support. Our dedicated team of commercial operations experts have specialized skillsets and extensive industry experience in using and analyzing commercial data—their expertise facilitates a seamless integration of strategic and tactical planning. Trinity leverages primary, secondary and unparalleled benchmarking data powered by TGaS Advisors to enable success for all aspects of commercial operations and analytics.

TGaS Advisors

TGaS Advisors' benchmarking and advisory services offer access to industry experts and the TGaS Client Network, fact-based answers grounded in unbiased comparative information and practical, actionable advice to achieve operational excellence. TGaS Advisors helps clients answer the question, "How do/should other life sciences companies do it?" regarding organization structure, resources, processes, people, technology and vendors.

Authors

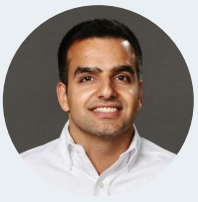
Leslie Sandberg Orne
President &
Chief Commercial Officer

Krista Perry
Partner &
Head of Launch Excellence

Chris Barger
Sr. Consultant,
Launch Excellence

Jenna Fritz
Sr. Consultant,
Launch Excellence

Susheel Sukhtankar
Partner &
Head of Commercial Analytics



Amid Zand
Associate Director,
Commercial Analytics

Curt Staab
Senior Vice President,
Emerging Life Sciences Network,
TGaS Advisors

About Trinity

Trinity is a trusted strategic commercialization partner, providing evidence-based solutions for the life sciences. With 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.