WHITE PAPER

LAUNCH EXCELLENCE: ONCE IN A LIFE CYCLE OPPORTUNITY

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HEALTH ADVANCES

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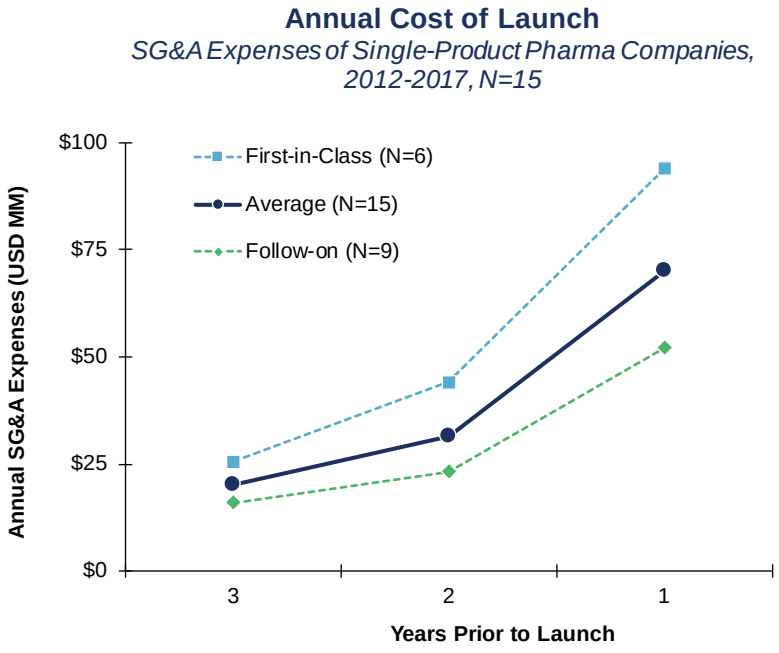
In business, we all know it is important to make a good first impression, but in pharma, that may be understating it: an effective commercial launch may swing cumulative revenue by billions of dollars.

Commercial launch is a hugely expensive endeavor. In the three years leading up to launch, the average single-product pharma company will spend over $125MM in SG&A (Figure 1), most of which will be dedicated to launching their product. This is not surprising when one considers the vast infrastructure required to launch a product: commercial salesforces; marketing; regulatory; pharmacovigilance; chemistry; manufacturing and controls; etc. Further, companies launching novel, first-in-class products spend even more, with three-year accumulated costs of approximately $160MM. This is because these products need to establish a market and because – generally speaking – the ultimate revenue opportunity is larger, and thus warrants a larger investment. Given the scale of these costs and complexity of the launch process, pharma companies need to create robust plans to ensure that they make informed and effective investments in their launches.

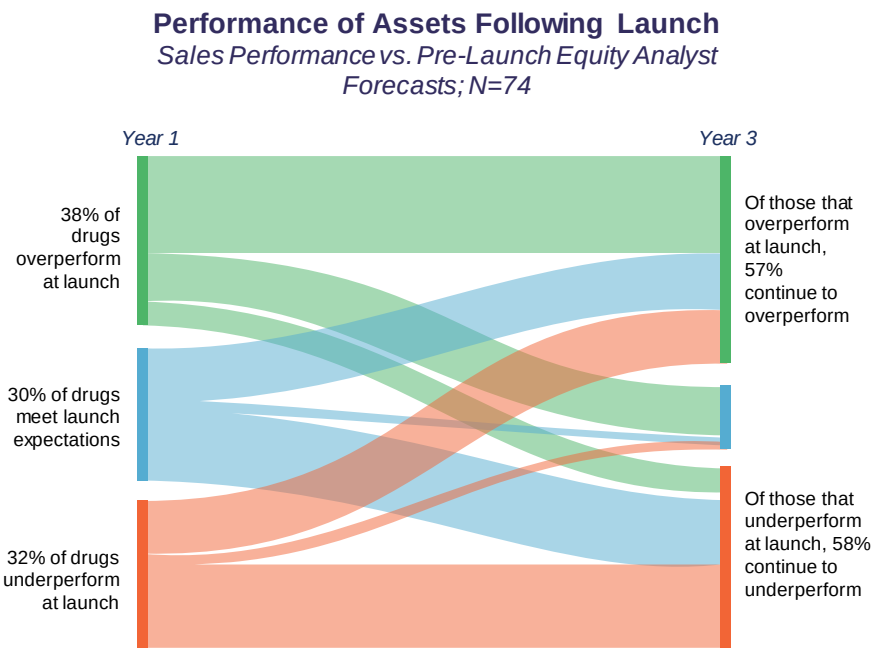


Note: Includes Acadia Pharmaceuticals, Amarin, Clovis Oncology, Collegium Pharmaceuticals, Corcept Therapeutics, Intercept Pharmaceuticals, Iroko Pharmaceuticals, Keryx Biopharmaceuticals, Lexicon Pharmaceuticals, NPS Pharma, Orexigen Therapeutics, Relypsa, Sarepta Therapeutics, Synergy Pharmaceuticals, and Tesaro. We recognize that companies have some baseline level of SG&A overhead that is included in the costs shown here. Nonetheless, it is fair to assume that these companies allocated most SG&A expenses to launch preparation for their lead product and that their pattern of increasing SG&A expense reflects the enormous commercial expense of launch. First-in-class products include NUPLAZID/Pimavanserin, RUBRACA/Rucaparib, OCALIVA/Obeticholic acid, XERMELO/Telotristat ethyl, GATTEX/Teduglutide, EXONDYS 51/Eteplirsen, VARUBI/Rolapitant. Follow-on products include VASCEPA/Ethyl eicosapentaenoic acid, XTAMPZA/Oxycodone, KORLYM/Mifepristone, ZORVOLEX/Diclofenac, AURYXIA/Ferric Citrate, CONTRAVE/Bupropion+naltrexone, VELTASSA/Patiromer, TRULANCE/Plecanatide. Source: Health Advances analysis, Thomson ONE, Company filings and press releases, company websites.

Figure 1: Cost of Launch: SG&A expenses of single-product biopharma companies in the three years prior to launch

However, launch planning is not simply about ensuring the efficient use of capital; a launch plan should also enable long-term commercial success. An effective launch cements a positive perception of the product in the eyes of customers and breeds future success. Conversely, pharma companies will struggle to recover from the wrong first impression. At Health Advances, we analyzed the actual sales performance of products versus pre-launch investor expectations, and found that 38% of products that overperformed in the first year following launch. Of those, 57% overperformed in subsequent years (Figure 2). Similarly, we found that 32% of drugs underperformed in the first year following launch. Of those, 58% underperformed in subsequent years. Overperforming drugs were defined as those in which actual sales exceed pre-launch equity analyst forecasts by: (a) ≥$10MM on an absolute basis, and (b) ≥10% on a relative basis. Similarly, we defined underperforming drugs as those in which actual sales fell short of pre-launch equity analyst forecasts by: (a) ≥$10MM on an absolute basis, and (b) ≥10% on a relative basis. The stickiness we observe here occurs because customer perceptions rapidly ossify following launch. Customers' perceptions are most malleable when products are new: they are more willing to invest time in learning about new products. However, this window in which pharma companies can create a favorable impression closes rapidly after launch as customers form their opinions. Customers are more recalcitrant about re-considering products with which they are already somewhat familiar.

Not surprisingly, our analysis shows that almost a third of launches underperformed relative to expectations (Figure 2).



Note: We evaluated 74 drugs launched between 2010-2014 using EvaluatePharma data to determine if the drug under- or overperformed based on actual sales performance compared to pre-launch equity analyst forecasts. Over/underperformance was defined as drugs with minimum absolute sales difference of $10MM and minimum relative sales difference of 10% between actual sales and pre-launch sales forecasts. Health Advances recognizes that equity analyst forecasts are imperfect for measuring underperformance and overperformance. Nonetheless, we feel they are the best metric for a large-scale analysis like this. Equity analysts, presumably, are incentivized to provide the most accurate forecasts to their customers to inform their investment decisions (although conflicts-of-interest with sell-side work can enter the picture). For this analysis, we selected the forecasts that most immediately preceded launch to minimize the effect of unexpected pivotal clinical trial data. For any one drug, our forecast data may incorporate one or multiple forecasts.
Source: Health Advances analysis, EvaluatePharma, SankeyMATIC.

Figure 2: Performance of assets following launch: comparison of actual vs. forecasted sales performance in years 1 and 3 following launch

We also note that our analysis is conservative in this regard: others have suggested that approximately two-thirds of launches underperform[1]. For any given launch, the reasons for underperformance are complex and manifold. However, we believe inadequate launch planning is a contributing factor in many of these launches. Too often, we see tired launch strategies that lack the nuance required to differentiate products in today's demanding market environments. Similarly, stumbles in execution reflect rote application of one-size-fits-all launch plans in which pharma companies complete activities perfunctorily rather than carefully orchestrating and prioritizing activities to serve broader strategic objectives.

[1] *It is hard to compare our analyses to others since the data and methods shared by others are typically limited. That said, we noted at least one important difference between our methodology and that of others: our analysis uses the latest possible pre-launch equity forecasts (i.e., those nearest to, without having exceeded, the launch date), where others have used pre-launch equity forecasts created a year prior to launch.*

LAUNCH PLANNING BEST PRACTICES

While launch is challenging, it is not a futile, thankless endeavor. Launches can and do overperform when they are underpinned by strategies that reflect and leverage the unique market and competitive circumstances and when launch teams have clear strategic direction and an actionable roadmap on which to execute. Several key market and competitive attributes vary considerably from product-to-product and underscore the importance of bespoke strategies and tactics:

Market and Competitive Dynamics Impacting Launch

Patient Population		Large indications benefit from broad awareness and well-understood diagnosis and treatment paradigms. Launch strategies for therapies serving large markets may seek to leverage or accommodate these existing paradigms to ease adoption. On the other hand, therapies for orphan indications may need to upend diagnosis and treatment paradigms by increasing provider awareness and/or diagnosis rates.
Competition		Therapies confronting direct competition such as in-class competitors often need to differentiate along a narrow and well-defined set of criteria (e.g., price, clinical endpoints, convenience). Alternatively, indirect competition for drug therapies such as surgical procedures may broaden the scope of trade-offs customers will consider. Launch strategies need to be sensitive to the axes of differentiation and support the transition of the treatment paradigm accordingly.
Customers		Launch teams must determine the differing needs and means of influence of all relevant customers (e.g., payers, providers, patients). This will vary from product-to-product, necessitating custom launch strategies to effectively communicate the product's value.
Therapeutic or Indication Complexity		Many of today's novel drugs are complex products that treat challenging indications (e.g., CAR-T therapies in oncology). These products require nuanced value propositions and sophisticated customer support solutions (e.g., patient and provider hubs) to ensure customers realize the full value of the therapy.

Figure 3: Market and competitive dynamics impacting launch

These market and competitive attributes necessitate unique launch strategies that reflect the environment. Those strategies should inform tactics that vary considerably in emphasis and focus from company-to-company. In Figure 4, we have illustrated in a simplified matrix how launch tactics can vary considerably for different market circumstances, covering some of the aforementioned issues.

Key Launch Tactics for Various Market and Competitive Circumstances

	Orphan Patient Population	Large Patient Population
Indirect or Limited Competition	• KOL engagement and buy-in • Disease awareness and diagnostic strategy • Patient advocacy and engagement	• Provider education and awareness • Salesforce readiness and mobilization
Direct Competition	• Payer contracting • Patient advocacy and engagement • Value-add product features (e.g., differentiated delivery device)	• DTC advertising • Payer contracting • Value-add product features (e.g., differentiated delivery device) • Salesforce readiness and mobilization

Figure 4: Variation in launch tactics according to competition and patient population size

Launch plans must also provide an actionable roadmap for the entire organization that enables rapid execution across hundreds of activities.

Several attributes of an effectively designed launch plan include:

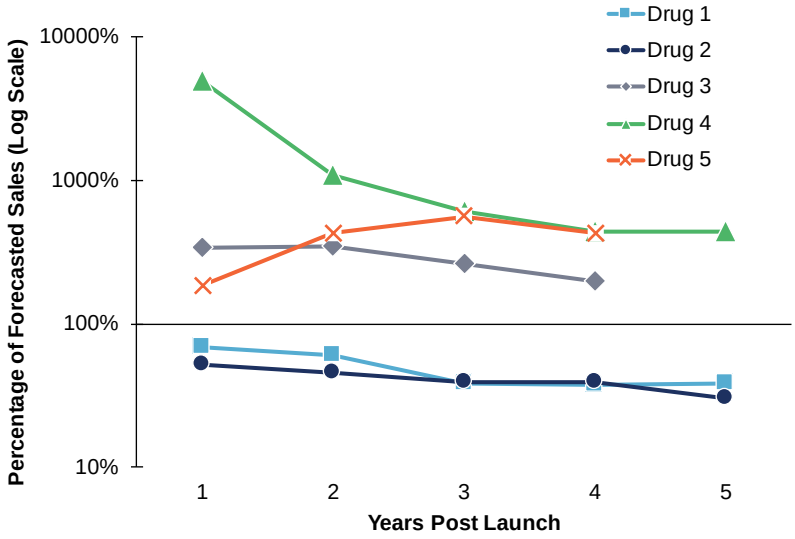
Key Attributes of Launch Plans

Alignment to Strategic Imperatives	Launch teams must rigorously align their activities with strategic imperatives so executing team members understand the broader purpose. This ensures customers receive consistent and complementary solutions and increases organizational efficiency by empowering team members to execute rapidly, confidently, and independently.
Prioritization	Relying on check-the-box launch solutions, launch teams can easily overinvest in activities that will not generate value for customers while underinvesting in activities that are more critical. Launch solutions must be customized to ensure that activities are appropriately prioritized for the specific company and market.
Clear Direction, Visibility, and Coordination	Launch teams must execute hundreds of interrelated activities (e.g., launching a patient services hub and preparing a payer dossier) to create the holistic solution. In order to do this, they must diligently plan their activities, identify these interdependencies, and remain coordinated as plans and timelines shift.
Flexibility	No plan survives first contact with the enemy, so launch teams must be prepared to rapidly adapt with flexible launch plans and careful scenario analysis.

Figure 5: Key attributes of launch plans

CASE STUDIES

We describe several underperforming and overperforming launches below. These case studies will underscore several of the best practices outlined in the preceding paragraphs. Figure 6 illustrates how those products performed relative to pre-launch expectations.



Note: EvaluatePharma data was used to determine if the launch of the drug underperformed/overperformed. Underperforming drugs' actual sales fell below (or rose above) pre-launch sales forecasts by a minimum absolute sales difference of $10MM and a minimum relative sales difference of 10%. We selected two examples of underperforming drugs and three examples of overperforming drugs that met these criteria for additional secondary research to understand the market and launch planning factors that may have impacted launch success.
Source: Health Advances analysis, EvaluatePharma, LexisNexis, company websites.

Figure 6 Performance of Case Study Drugs: Actual sales vs. pre-launch equity analyst forecasted

Underperformance Case Study: Drug 1

Circumstances

- Drug 1 was a first-in-class agent in a large indication launched by a large, multinational pharmaceutical company with a large portfolio of drugs in that therapeutic area. Initial expectations for Drug 1 were high because it is safer and more effective at reducing acute events than standard of care.
- Drug 1's challenges emerged with its FDA approval. Drug 1 was initially slated to launch well before its primary competitor had lost market exclusivity. However, FDA delayed approval and this meant Drug 1 had a shorter window in which to convert patients and providers from a high-priced branded rival (versus generics). Unsurprisingly, market access quickly emerged as a key challenge that frustrated potential customers.
- FDA also took a conservative view with respect to the drug label, adding restrictions, which made it more complex to use Drug 1 (i.e., contraindications and requirements for concomitant therapy).

Key Takeaways

- Drug 1's delayed launch meant that payers became a more significant customer group who needed to be courted with aggressive pricing and contracting tactics, as well as a compelling dossier highlighting long-term economic benefits (if any) and clinical differentiation.
- Though this had not been the most complex indication historically, Drug 1's label restrictions meant the company needed to invest more into provider support and education to drive adoption.
- The company did not adequately adapt to the changed circumstances: it was two years after launch that the company significantly increased promotional resources for the drug, but this was likely too little, too late.

Underperformance Case Study: Drug 2

Circumstances

- Drug 2 was a fifth-generation antibiotic launched by a mid-sized, multinational pharmaceutical company with limited experience in the infectious disease market.
- Drug 2 demonstrated higher cure rates and broader activity against resistant bacteria strains than competitors. The company rapidly grew its salesforce following launch, and priced at a discount to other branded competitors.
- Drug 2 launched into the hospital antibiotic market and struggled to gain traction with hospitals' cross-functional pharmacy and therapeutics (P&T) committees, who control the hospital formulary. It is important to note that because hospitals are reimbursed via a bundled payment system (i.e., DRG or diagnosis related groups), they cover the cost of inpatient drugs. Thus, P&T committees consider both clinical and economic incentives when designing formularies.

Key Takeaways

- Given the challenges surrounding antibiotic use and efforts to preserve novel antibiotics for later lines of therapy, the company needed to articulate specific patient populations where Drug 2 could be deployed readily. The company may have been well-served to promote diagnostic technologies/techniques that would rapidly identify particularly aggressive and antibiotic-resistant bacteria strains where it made sense to use Drug 2 more aggressively.
- In addition to articulating the most compelling clinical cases, the company needed to make an economic case to hospitals who have many generic antibiotics available to them. This economic case could examine readmission rates, for example.

Overperformance Case Study: Drug 3

Circumstances

- Drug 3 introduced a new mechanism into a crowded neurology market with about a dozen competitive alternatives. The company, a large multi-national biopharmaceutical company, was already a leader in this market.
- Drug 3 provides a compelling efficacy-safety profile (though it is neither the most efficacious, nor the safest drug for this indication) and an oral formulation (most MS drugs are injectable).

Key Takeaways

- Drug 3 was effectively positioned as a first-line therapy, which is safe and convenient for patients (i.e., oral). The company started early, generating awareness and enthusiasm in the lead-up to launch in its clinical program by highlighting the drug's safety profile. Early engagement was important, because this indication, though not orphan, is treated largely by a set of sub-specialist neurologists.
- The company also enabled broad market access: rather than stake out the highest price point, the company priced Drug 3 in line with key competitors. The manufacturer also offered a robust patient support program that provided a year's worth of free drug to patients in the US who had to wait more than two weeks for reimbursement.
- Finally, the company demonstrated flexibility in its approach to rapidly overcome obstacles: An initial DTC TV campaign was scrapped after some patients claimed the company had misrepresented the experience of the disease and treatment. The company revised its DTC approach and focused on a patient website and local events featuring celebrity spokespeople

Overperformance Case Study: Drug 4

Circumstances

- Drug 4 was a second-in-class specialty biologic for an ophthalmology indication marketed by a large, multinational biopharmaceutical company with limited experience in this market.

Key Takeaways

- The company also segmented and targeted key stakeholders early: it focused intensive pre-launch market development efforts with KOLs at a national / regional / local level one year before launch.
- Once launched, the company provided a positive prescribing and reimbursement experience for both patients and prescribers. Given that it was a second-to-market product, the company ensured that the product was similar in logistics and reimbursement to the existing therapy, and therefore convenient to prescribe and administer.
- Finally, the company clearly defined the appropriate patient candidate for therapy, which helped speed adoption among prescribers and lower barriers among payers.

Overperformance Case Study: Drug 5

Circumstances

- Drug 5 was a first-in-class oral agent approved for the treatment of Type II diabetes launched by a large multinational biopharmaceutical company with limited pharma experience in this space.
- Though safety concerns necessitated post-marketing studies, efficacy in pivotal trials was compelling.

Key Takeaways

- The company engaged multiple customer groups simultaneously with targeted tactics for each group. These tactics were developed in partnership with the company's non-pharma business unit, which had significant experience in diabetes:
  - Pre-launch, the company generated awareness and excitement among endocrinologists. Following launch, they engaged the broader prescriber community via a robust salesforce and by advertising in prominent medical journals. The company rapidly deployed a 2,000-strong salesforce following FDA approval. This rapid salesforce ramp-up was made possible due in part to an innovative e-learning program that allowed reps to be trained quickly.
  - The company generated patient interest with a large >$10MM DTC campaign.
  - Finally, the company aggressively engaged payers to ensure favorable coverage and reimbursement and prevent any market access issues for physicians and patients.

CONCLUSION

In conclusion, launch is a large investment and a key opportunity to set a therapeutic on the path to long-term success. During launch, companies have the unique opportunity to set lasting impressions of their product with customers, which (for better or worse) can be difficult to dislodge. Our experience is that launch excellence is truly a once in a life cycle opportunity and we suggest several best practices:

- Start Early. Effective launch planning takes two to three years.
- Know your market. Capture nuanced market insights to enable a compelling value proposition and effective launch strategy.
  - Understand how your product will affect treatment paradigms and patient journeys.
  - Understand all customer groups, including the magnitude and means of their influence.
  - Invest in robust competitive intelligence.
  - Understand processes and potential barriers related to logistics, reimbursement and market access.
- Develop a strategy that provides direction to the organization and clearly outlines critical success factors.
  - Create a strategy that reflects the unique market and competitive dynamics and the organizational experience and capabilities.
  - Ensure the strategy is relevant to and speaks to the challenges facing all key internal stakeholders.
- Develop a flexible and detailed tactical plan that executes on the strategy.
  - Prioritize tactics according to unique strategic objectives, and design timelines around organizational capabilities. Avoid check-the-box and one-size-fits all solutions.
  - Identify key cross-functional and interdependent activities and ensure relevant internal stakeholders are aligned on goals, timelines, and accountability.
  - Ensure flexibility with robust scenario planning

SOURCES AND METHODS

Cost of Launch Analysis:

- Identified companies that had products launching from 2012 to March 2017 via IQVIA product usage data.
- Focused on public, single product companies by removing large companies with multiple products and private companies.
  - We determined the number of marketed products and when the first product was launched by reviewing company websites, press releases, and FDA.gov.
- Determined Selling, General and Administrative (SG&A) expenses using Thomson ONE and company SEC filings for each of these companies in the three years prior to launch (as available) of their first commercial product.
  - Removed companies with significantly higher or lower SG&A costs due to unique company or drug-specific circumstances that did not allow for direct comparison across company SG&A costs. For example, one drug was removed due to additional costs associated with a companion diagnostic development.
- Averaged SG&A costs from the remaining 15 companies for each year prior to launch (up to three years).
- Companies include Acadia Pharmaceuticals, Amarin, Clovis Oncology, Collegium Pharmaceuticals, Corcept Therapeutics, Intercept Pharmaceuticals, Iroko Pharmaceuticals, Keryx Biopharmaceuticals, Lexicon Pharmaceuticals, NPS Pharma, Orexigen Therapeutics, Relypsa, Sarepta Therapeutics, Synergy Pharmaceuticals, and Tesaro.
- First-in-class products include NUPLAZID/Pimavanserin, RUBRACA/Rucaparib, OCALIVA/Obeticholic acid, XERMELO/Telotristat ethyl, GATTEX/Teduglutide, EXONDYS 51/Eteplirsen, and VARUBI/Rolapitant.
- Follow-on products include VASCEPA/Ethyl eicosapentaenoic acid, XTAMPZA/Oxycodone, KORLYM/Mifepristone, ZORVOLEX/Diclofenac, AURYXIA/Ferric Citrate, CONTRAVE/Bupropion+naltrexone, VELTASSA/Patiromer, and TRULANCE/Plecanatide.

Launch Performance Analysis:

- Data for actual sales and equity analyst forecasts for products launched worldwide between 2010 and 2014 were from EvaluatePharma.
  - Removed drugs that did not have actual sales data and/or pre-launch equity analyst forecasts available in EvaluatePharma.
- Forecasts used for comparison were those that most immediately preceded launch to minimize the effect of unexpected pivotal clinical trial data, as available in EvaluatePharma.
  - For any one drug, our forecast data may incorporate one or multiple forecasts.
- Calculated the absolute difference between actual and forecast sales as well as the relative percentage difference between actual and forecast sales using the forecasted sales as the point of reference.
  - We define overperforming drugs as those in which actual sales exceed pre-launch equity analyst forecasts by: (a) ≥$10MM on an absolute basis, AND (b) ≥10% on a relative basis.
- We define underperforming drugs as those in which actual sales fell short of pre-launch equity analyst forecasts by: (a) ≥$10MM on an absolute basis, AND (b) ≥10% on a relative basis

ABOUT HEALTH ADVANCES

Health Advances https://www.healthadvances.com is a global strategy-consulting firm that focuses exclusively on the healthcare industry. We have unique capabilities to provide launch planning services founded on actionable, nuanced market insights and flexible launch planning solutions. These capabilities include:

- Deep experience turning technological insight, clinical understanding, market knowledge, and competitive intelligence into compelling strategies.
  - Clients include top-five pharma as well as preclinical and clinical-stage start-ups.
  - Broad project experience in all areas related to launch (e.g., product positioning, stakeholder mapping, etc.).
- Robust primary and secondary market research capabilities to develop critical market insights.
  - Primary research experience includes in-depth interviews, focus groups, and surveys. We leverage a proprietary database of >45,000 expert contacts from all major markets.
  - o Secondary research capabilities include access to a knowledge management center with research experts; numerous databases and publications; and prior work.
- Proprietary, Microsoft Excel-based customizable launch excellence toolbox to enable rapid and efficient launch planning. Our tool details activities (including interdependencies, timelines, and costs) for each function in a user-friendly interface.

ABOUT THE AUTHORS

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