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McKinsey Cancer Center
Launches in oncology: The elements of success

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Cancers figure among the leading causes of morbidity and mortality worldwide, with approximately 14 million new cases and 8.2 million cancer related deaths in 2012 alone (an estimated 13 percent of deaths worldwide). Today, the number is on the rise: it is expected that annual cancer cases will rise by nearly 70 percent, from 14 million in 2012 to 22 million within the next two decades.[1]

As the prevalence and severity has increased, significant continuous investments have been made by the pharmaceutical and broader healthcare industries to help patients and to provide a cure to the over 100 types of cancer known today[2] that each require unique diagnosis and treatment. This has also been reflected in the rise of healthcare costs with global healthcare spend related to cancer reaching north of $300 billion.

As pharmaceutical companies have invested an ever-increasing amount in oncology research with more than $200 billion since the 1970s[2] a growing number of available drugs and medications have become available making what was once a sparse therapeutic area one of the most complex and competitive in the industry. Today around 40 percent of trials conducted are oncology-related trials.[3]

The effect has been that, over the last few years alone, the drug landscape has dramatically changed, and by extension also the importance of a successful launch in oncology. With Novartis' launch of Kymriah and Gilead/Kite's Yescarta, gene therapy has now become a reality within oncology, evidence that the innovation bar is being raised, the complexity of therapies are increasing, and the criticality of a successful launch is more important than ever.

The changing launch environment can be illustrated with lung cancer (NSCLC). At the beginning of 2010, most companies would have launched a drug in lung cancer indicated broadly for NSCLC (for example, first-line therapy, chemotherapy Alimta), while in 2017 the same company would launch only in a NSCLC subpopulation (for example, large-cell carcinomas, squamous cell carcinomas, adenocarcinomas, and most likely further mutation-based stratification around ALK-1, EGFR, BRAF, RAS, and others; with immuno-oncology being the notable exception) in which there may already be two to three competitors. This would also require the drug to prove clinical benefit over an ever-changing standard of care and the large number of competitors. This has led to product life cycles shortening over the years, sometimes down to only one to two years before a new therapy enters the market given the large oncology R&D pipelines of pharmaceutical companies (for example, recent PD-(L)1 and PARPi wave of launches). Companies thus have less time to maximize the impact of their medicines on improving patients' lives as well as their topline.

The importance of the first few months of launch performance has thus dramatically increased to ensure the drug is successful and to maximize the time of drug on market. Launching a drug successfully in oncology has thereby become the critical basis of success. To be successful, a different approach from the standard launch framework is required. Even if similarities across therapeutic areas exist, they need to be placed in the context of oncology. This paper aims to provide a structure for the specificities and what it takes to be successful.

1 *World Cancer Report*, World Health Organization, 2014, who.int.

2 Amanda Chan, "The 10 deadliest cancers and why there's no cure," *Live Science*, September 10, 2010, livescience.com.

3 Top 10 drugs – trials TrialTrove (2016).

Four elements of success for an oncology drug launch

Our experience shows that companies who launch oncology drugs successfully excel in four areas.

1. Agility, speed, and competitive mind-set
They operate in an agile governing model allowing for competitive entry and faster approvals.

2. Distinctive product strategy
They have a clearly defined product strategy underscored by strong product planning.

3. Mastering market access
They know how to demonstrate value, are braced for increasingly difficult access negotiations, and effectively manage the evolving stakeholder landscape.

4. Go-to-market models
They develop new approaches to maximize their launch opportunity.

Area 1: Agility, speed, and competitive mind-set

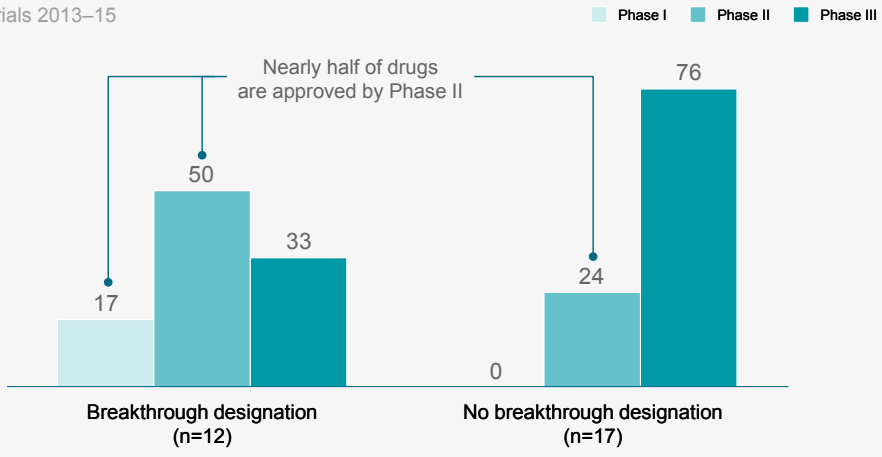
Agility and the right organization principles form the foundation of successful oncology launches given the complexity and intensity of the market environment.

As background, given the pace of innovation within this therapeutic area, companies must often respond to shortened approval time lines, rapid follow-on competitive entries, varying results on market access negotiations as well as success and failure in follow-on clinical programs. For example, oncology drug development programs between 2006 and 2015 accounted for 31 percent of the 9,985 efforts in total. This underscores a continuously large and continuously moving therapeutic area that through its relatively lower approval rate (5.1 percent Phase I to approval versus 11.9 percent for non-oncology) mandates agility and adaptability from its players.[4]

Additionally, time to approval has remained steady at 8.8 years between 2010 and 2015, however, oncology has seen the fastest filing to approval across all therapeutic areas. While neurology drugs took the longest to approve on average, at two years, oncology drugs were approved almost twice as fast at 1.1 years.[4] Many oncology drugs for unmet medical need may have benefited from expedited approval pathways from the FDA that include Breakthrough Therapy Designation and Accelerated Approval.[5] In FDA trials from 2013–15, nearly half of the drugs were approved by Phase II driven by breakthrough designation status.[5] Recent product approvals (for example, Keytruda, Tagrisso) suggest even more compressed timelines. This means a few years of additional data collection and launch preparation are simply not available any longer, requiring an agile launch set-up.

Exhibit 1: Nearly half of drugs are approved by Phase II given the high number with breakthrough designation.

%, FDA trials 2013–15

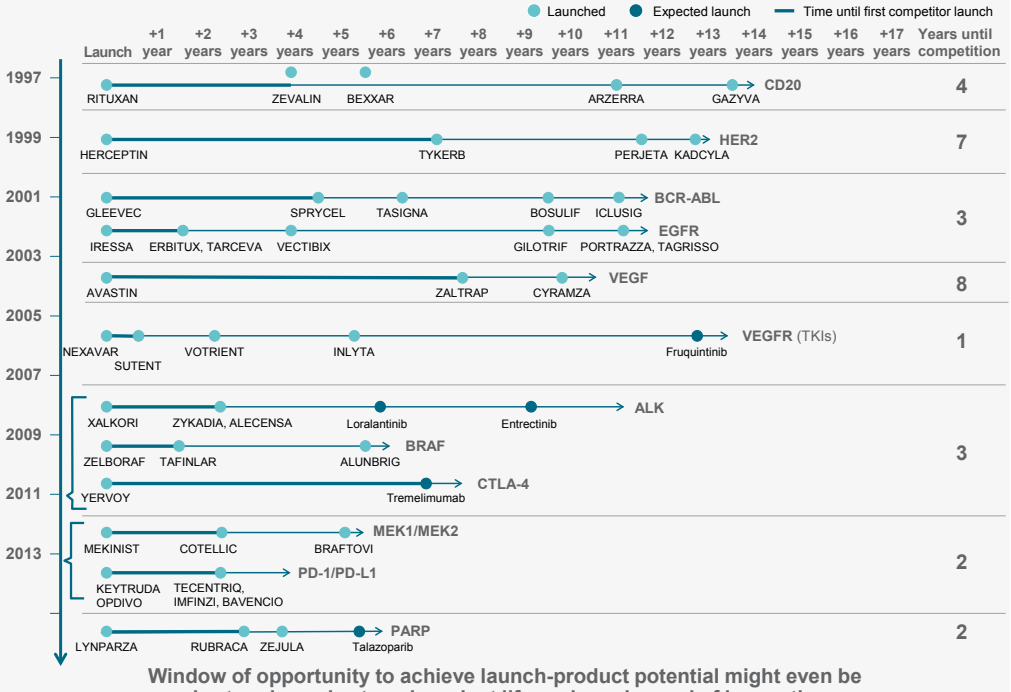


4 Clinical Development Success Rates 2006-2015: BIO, Biomedtracker, Amplion 2016

5 Richard K. Harrison, "Phase II and phase III failures: 2013-2015," *Nature Reviews Drug Discovery*, December 15, 2016, nature.com.

Finally, product life cycles are shortening generally, but particularly in oncology, with the number of years until competitive follow-on launches compressed dramatically. Time without competition may now be as short as one to two years (Mekinist, Keytruda, and Lynparza all had two years until competition), whereas products like Herceptin and Avastin enjoyed six to seven years on the market before entry of other compounds with similar modes of action even if not in the same tumor type or line of therapy (for example, Tykerb, Zaltrap) (see exhibit 2). There is an increasing focus on subsegments of drugs, where generally more competitive freedom can be seen than for a larger indication. The race around first-to-market entry into the immuno-oncology space is the most striking example of parallel development at this time. Achieving launch product potential in oncology therefore is increasingly difficult.[6]

Product life cycles shortened between 1997 and 2014.



Window of opportunity to achieve launch-product potential might even be shorter given shortened product life cycle and speed of innovation

For pharmaceuticals in this area to not become a victim of the situation, but proactively drive excellence, “agile” organizational principles must be maintained.

Generally, being agile requires an organization to make more informed decisions earlier to avoid a string of iterations, as well as being able to autocorrect quickly when it does happen. In oncology with fast innovation cycles and large data this is even more critical.

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This requires two things. First, advances in data and advanced analytics need to be leveraged to enable faster and more focused decision making, allowing the organization to be more agile at launch. Second, pharmaceuticals need to keep complexity to a minimum in oncology launch situations. They can ensure this by having launch leaders effectively engage across functional boundaries and by remaining flexible enough to rapidly steer-correct their launch especially in the first six months.

A different organization of the launch team is needed to ensure agility: while a project management team ensures completeness as a stable backbone, dynamic capabilities are needed to solve tough challenges quickly and effectively. Cross-functional teams can contribute to solving critical decisions more dynamically, while short timelines allow for arriving at a minimum viable product quickly to prevent "better becoming the enemy of good enough." This can be effectively achieved by running teams in four-to-six week "sprint" work cycles that must produce concrete outputs and workable products rather than partial answers. A senior leadership team with focus on high-priority deliverables ensures arriving at a "working answer" quickly, which can then be refined continuously.

Leadership therefore is critical, not only to appropriately deal with biases but also to effectively coordinate the teams and bridge organizational siloes. A vision, the ability to identify what really matters paired with decisiveness under uncertainty and a drive for focused execution are characteristics of seasoned leaders required in launches. Given the high value at stake and the importance of "first time right," targeted development of "launch leaders" comes at a significant return on investment.

Governance mechanisms like a control tower/situation room have been implemented by most companies and are deemed best practice today in allowing to proactively manage the launch and course corrections quickly. Innovation here has come mostly in the tools that are becoming available to allow members of the launch to drive a more effective launch, for example advanced analytics employed on customer data support for example, live market tests and A/B testing at launch. Exploiting the potential of CRM data for quick and robust decision making supports maximizing the launch curves against the background of shortening product life cycles is one of those tools.

The latest oncology launches will be measured how well they launch and how agile they are in their set-up to master this critical stage.

Area 2: Distinctive product strategy

In oncology, a set of key decisions around the launch and the product strategy in general can determine a high share of the value, because competition has stiffened and timelines have been compressed. Thus, launch decisions need to be considered in the broader context of a product strategy, which needs to be distinctive.

A set of key questions from early planning stages to leadership and implementation needs to be mastered. To create a distinctive product strategy, you will need to answer a set of strategic questions and plan accordingly. They are as follows:

- Do you understand healthcare providers and patient journeys, and does your launch strategy lead to unmatched experiences?
- Are the brand access and scientific stories compelling to the respective audiences? Are they mutually consistent and reinforcing?
- Do you have a clear, outcome-based value proposition to anticipate payer constraints?
- Do you use agile teams for make-or-break topics, and combine them with a reliable "machine" to execute standard launch plans?
- Do you prepare launch leaders at all levels for the challenges they will face?
- Do you incentivize these leaders in alignment with the overall strategy, and reward them adequately?
- Do you de-bias the critical launch decision?
- Do you leverage advanced analytics to develop hypotheses and design your strategy?
- Do you prepare an adequate data monitoring to be able to steer correctively after the launch?

Perhaps even more important than what is how you answer them. For example, to take decisions increasing the odds for a successful launch, a solid fact-based foundation can be built leveraging new analytics tools. For improved clinical trial enrollment, predictive algorithms can forecast site-level patient recruitment and through site optimization reduce enrollment time by 10–30 percent.[7] Such data-driven approaches allow choosing sites within regulatory boundaries while optimizing expected performance. During trials, real-time performance monitoring augmented with scenario tools to plan interventions can leverage information to sense and counter quality issues early.

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Area 3: Mastering market access

As outlined in the first chapter, faster access is central for a successful oncology launch and to maximize the product life cycle. However, faster access comes at the cost of increased uncertainty and complexity. With best practice data generation both aspects can be tackled, achieving faster approval while mitigating uncertainty risks. Merck (Keytruda) and AstraZeneca (Tagrisso) have shown that a well-executed seamless expansion of a single trial can lead quickly to launch. This faster access in turn makes postlaunch data generation ever more important for two reasons, to strengthen the early data and to potentially expand the label. In both cases, additional data generates a competitive edge compared to future entrants. Janssen has successfully employed this strategy with Darzalex and Pfizer with Ibrance, for which the vast amount of clinical trials was performed post launch. This increases the need for (field) medical to be able to coordinate the large number of investigator-initiated studies and other post authorization studies.

Exhibit 3: Seamless expansion trials can lead to launch with a single trial.

Drug	MERCK KEYTRUDA® (pembrolizumab)	AstraZeneca TAGRISSO® osimertinib
Time to approval (FIH to first approval)	3 years, 6 months	2 years, 9 months
Number of patients at submission	411	411
First indication approved	Advanced or unresectable melanoma	EGFR positive metastatic NSCLC

SOURCE: Source: Clinicaltrials.gov; FDA; TrialTrove

Complexity is added in this space as patient populations get fragmented and the treatment paradigms become increasingly complex, with various drugs used in different lines, for different subtypes and indications. This increases the need for subtype and indication specific data to guide payers and physicians to bring the best treatment to the patients. Decisions are becoming more difficult as complexity continues to increase, and simplifying the story become a must have.

In addition to the complexities of data for a single product, the rise of combination therapies for which multiple drugs, potentially from competitors, are combined, further add to the increasing complexity. The main driver for combination therapies are immuno-oncology drugs, whose market is expected to grow from about $5 billion today to over $35 billion by 2022.[8] However, given that the reimbursement of combination therapies at monotherapy price is difficult (see below), this trend demands better clinical trial data. With precise outcome data, the added value of a combination compared to the monotherapy can be proven and arguments for reimbursement are strengthened, enabling a successful launch. Further, this data can serve as the foundation for the value split negotiations with the partner company and hence further improves the likelihood of success.

8 Citi Analyst Report 2013, https://www.nature.com/news/immunotherapy-s-cancer-remit-widens-1.13079

As oncology drugs command some of the highest prices in the industry, health authorities are further scrutinizing them. Three themes of payer behavior to reduce oncology costs have emerged over the last years that need to be addressed in anticipation of launch, namely:

- **Higher HTA bar in Europe.** Increasing rates of negative/restrictive decisions in health technology assessments, limiting target population or the number of incremental therapies that are reimbursed.
- **Increased pressure.** As companies have expanded the patient pools with additional clinical trials, so has the scrutiny increased.
- **Shifting outcomes risk to pharmacos.** Drugs only receive a conditional reimbursement during which additional real-world evidence or clinical data must be collected to prove the additional benefit of the treatment and individual patient costs are only reimbursed in case of treatment success.

This increased pressure poses challenges for future oncology drug launches, but it also presents an opportunity for pharmaceutical companies and payers to work more closely together. To realize this opportunity, companies need to excel at understanding payers' needs and the available opportunities, as wells as on generating additional real-word evidence, to provide the underlying data for innovative pricing and contracting models, such as risk-sharing or outcome-based contracts. Hence, pharmaceutical companies that excel at oncology launches tend to invest into generating such evidence in the real world for several years before negotiating with payers.

As such, outcome-focused payer collaboration models will require an oncology player to adapt a holistic view of the patient journey and the payers' interests. A seven-step process can be employed to uncover common ground for collaboration:[9]

1. **Map end-to-end disease pathways**
2. **Prioritize untapped value pools for health systems**
3. **Identify and prioritize solutions ideas to improve outcomes**
4. **Assess potential of solution ideas in countries**
5. **Determine implication for data generation**
6. **Determine directional pricing and business case**
7. **Create an implementation plan**

This approach can generate win-win outcomes that benefit both sides.

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Area 4: Go-to-market models

The go-to-market models employed by pharmaceutical companies evolved significantly over the past years and the rapidly changing oncology market makes go-to-market models for oncology drugs particularly important.

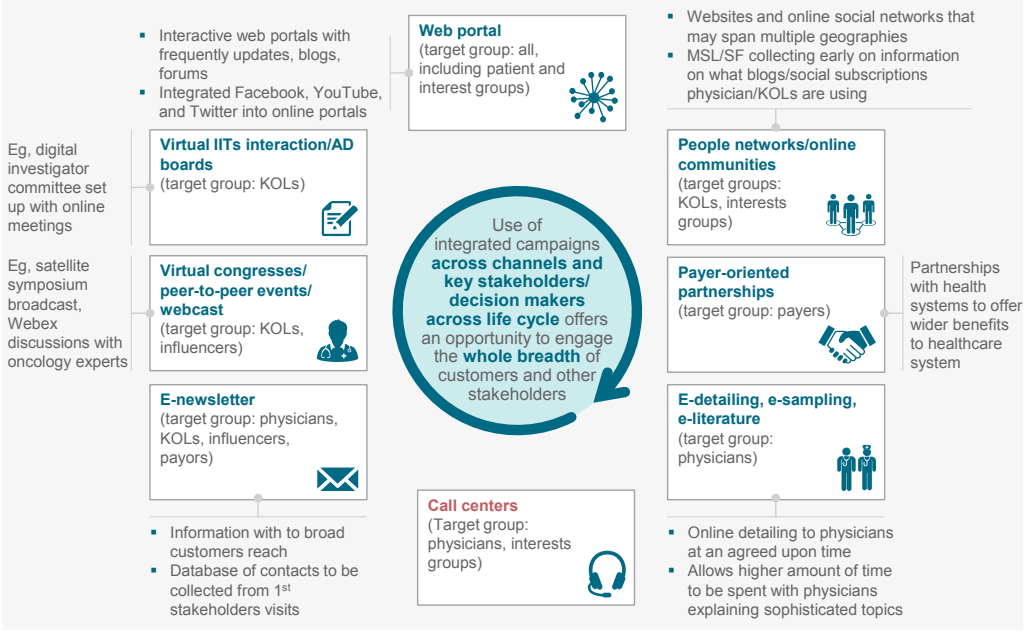
Plus, oncology differs as a therapeutic area in that its stakeholders are cross-cutting across other disease areas. A prescriber will not only be an oncologist, depending on the type of cancer, but could for example be a urologist or gynecologist. For example, 88 percent of the key prescribers for ovarian cancer are at the same time also key lung prescribers, creating commercial synergies between the prescriber bases. Yet, these groups have been deproritized in many launches we have observed, which can lead to underwhelming uptake. To avoid this, oncology players need to use the full range of channels available in innovative ways (see below). By leveraging the dynamically evolving mix of channels based on customer preferences and availability of new media, pharmaceuticals can set themselves up for launch success in oncology.

Especially two aspects are critical for success in future oncology launches:

- Channel mix. Shorter life cycles, complex products and an evolving stakeholder landscape increase the need for targeted, high-quality communications. A sophisticated channel mix of new, digital engagements and traditional sales-rep-based detailing is therefore at the heart of every successfully executed launch.
- Partnering for combination indications. Launch and marketing of combination therapies demands some form of collaboration between the involved companies. Finding the right framework for the partnership is therefore key to ensure success.

A successful channel strategy needs to leverage a diverse mix of channels, find the right balance for interactions and coordinate the activities across all channels. The most sophisticated players excel across these factors. From the bouquet of alternative channels, (for an overview, see exhibit 4) the appropriate ones are selected for each stakeholder and deployed in innovate ways.

Exhibit 4: Examples illustrate some alternative channels.



For example, e-detailing activities differentiate between different levels of physicians. HCPs that are also visited in person get additional material and personalized invites following up on the visit, while lower-tier physicians are targeted to participate in online webinars where the information is shared with a broader audience. Further, the frequency of interactions with each stakeholder is adjusted to its preferred level through opt-ins and advanced analytics. Interactions are being tracked and success is regularly monitored with KPIs. Further, the different departments with key stakeholder interactions, that is, marketing, sales, medical and access, coordinate their activities within the legal framework to ensure a seamless and coherent experience.

Combination indications, in which the combined drugs are from different companies are the second field, for which go-to-market models have the highest impact. The two companies need to find a partner agreement that optimizes for both of their assets. Given divergent long-term strategies and potential competition in other fields, this can be a challenging task. Specifically, two key questions need to be answered in these cases. First, how should the two companies work together on a day-to-day basis and on a functional level, and second, how should the value between the two companies be split.

To resolve the former question a dedicated agreement is necessary based on a strong partner management. In this agreement, incentives and guidelines should be placed that ensure the appropriate marketing of the combination as well as the monotherapy, for each indication to maximize patient benefit. Further, the roles, responsibilities and accountabilities for the marketing, sales and medical departments of both companies should be specified, for example, territories for sales and MSL should be defined and the ownership of medical information answering and pharmacovigilance reporting and liability should be assigned.

Different degrees of separation/sharing between the two companies are possible. However, learnings from other industries suggest that clear and simple rules minimize distraction and maximize overall value.

For the latter question, other industries can serve as learning models. These suggest three main models. In the first "flexible solution" model players are free to decide on how to interact and mainly outside market forces define the efficiency of the solutions, for example, in case of monetary caps such as a patient flat fee, a deal might fail as both parties are better off separately, leading to lower patient benefit. In the second and third more regulated models such as industry "guidelines" or "fixed formulas," both can lead to better outcomes, for example, a third party can own the revenue split formula and each party has the right to opt out. Applied to the budget-cap situation the third party could find a revenue maximizing strategy that when split appropriately, benefits both players more as when they would market the monotherapy only.

In general, four key learnings can be drawn from other industries. First, simple metrics are difficult to find but reduce the complexity and increase the stability of the partnership on the long run. Second, collaboration models can reduce the control for each company, but can be very successful (for example, IATA). Third, price negotiations should be separated from the revenue split mechanism and fourth, most collaboration models are evolutions from simpler systems and needed time to find the right balance.

Conclusions

The number of annual cancer cases is expected to rise by almost 70 percent within the next two decades, making launch excellence the fundament of success for oncology players. As such, launch success in oncology is driven by four main elements: an agile government model, a focus on data, a clear value demonstration with strong access capabilities, and a deep understanding of the changing stakeholder landscape and a tailored go-to-market model:

- The level of agility exhibited by a pharmaceutical's government model is determined by five organizational principles: leveraging of advances in data and advanced analytics, an evolution of medical-access commercial models, a strong product positioning with sufficient real-world evidence, the use of cross-functional global teams, and the reduction of complexity.
- The oncology drug space is facing increasing complexity due to shorter time to market, higher activity with niche focus, and the rise of combination therapies. To overcome these complexities and to successfully launch companies must focus on data generation to support their access and value claims and partnership negotiations.
- To demonstrate value and ensure access in light of increasing cost pressure from payers in oncology, pharmaceuticals have to collaborate more closely with payers, excel at tendering and truly understand their stakeholders.
- Two main factors should be considered for the go-to-market model: the channel mix should enable a tailored offering to each stakeholder with a coordinated and coherent message from sales, marketing, and medical and for drug combinations a suitable partnership model with clear governance should be established.

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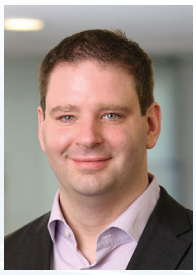

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