McKinsey & Company

Pharmaceuticals & Medical Products

The pursuit of excellence in new-drug development

Innovations in biomedical sciences and technology fuel the opportunity to transform R&D for new-drug development holistically—500 days faster, better tailored to patient needs, and 25 percent cheaper.

by Gaurav Agrawal, Harriet Keane, Maha Prabhakaran, and Michael Steinmann

October 2019

We are living in a time of enormous scientific innovation and promise for improved human health. Our understanding of biology is expanding enormously alongside increased identification of novel targets and their associated modalities. Still, drug-development costs and timelines continue to rise, and the likelihood of success continues to fall. Collectively, the top 20 pharmaceutical companies spend approximately $60 billion on drug development each year, and the estimated average cost of bringing a drug to market (including drug failures) is now $2.6 billion—a 140 percent increase in the past ten years.[1]

The opportunity

We believe the time is right for a true step change in drug development. To make this a reality, holistic transformation is necessary. While there is no silver bullet, drug developers can make a concerted effort to apply and integrate multiple innovations that can transform development. In our estimation, it should be possible to bring medicines to the market 500 days faster, which would create a competitive advantage within increasingly crowded asset classes and bring much-needed therapies to patients sooner. To transform drug development, this acceleration can be combined with improved quality and compliance, enhanced patient and healthcare-professional experience, better insights and decision making, and a reduction in development costs of up to 25 percent.

Development excellence: The framework

Reimagining R&D demands transformation of the traditional approach to drug development to allow medicines to reach patients faster, reduce development costs, and improve insights and decision making. Five pillars form the basis of development excellence:

- patient- and healthcare-professional-centered design thinking, incorporated end-to-end from program and trial design to trial execution, approval, and launch
- process redesign, both cross-functionally and within R&D groups, that improves speed of development and builds on research insights
- digital and technology enablement that allows automation of highly repetitive processes alongside generation of new insights and data
- advanced analytics (including predictive modeling), informed through internal and external data sources, that improves decision-making quality and speed
- agile ways of working, with a working model optimized for speed and decision making across the portfolio

A transformed drug-development journey

We use the journey of an asset from investigational new drug to optimized portfolio resource to illustrate how the five pillars can accelerate drug development.

1. Investigational-new-drug accelerator

The space from candidate nomination to investigational new drug presents a unique opportunity for accelerated drug development. Compared with early discovery stages, in this stage, research groups and their work—for example, in animal toxicology; biomarkers; chemistry, manufacturing, and control (CMC); discovery sciences; drug metabolism and pharmacokinetics; protein and cell engineering; and regulatory—are highly cross-functional and less exploratory. This space is thus highly amenable to process redesign that may help reduce the time to the clinic without taking undue

[1] Joseph A. DiMasi, Henry G. Grabowski, and Ronald W. Hansen, "Innovation in the pharmaceutical industry: New estimates of R&D costs," *Journal of Health Economics*, May 2016, Volume 47, pp. 20–33, sciencedirect.com.

risk or compromising insight generation. Potential process improvements include the following:

— seamless transfer of materials, information, and work products across research groups to avoid delays

— clear visibility of the critical path to becoming an investigational new drug and of the contributing activities

— calibration of risk tolerance and agreement on a concrete set of options to execute at-risk steps along the critical path

— use of technology in areas that could benefit from faster analysis and decision making

— detailed examination of processes to identify opportunities for time-saving simplifications

— alignment on the data and activities necessary to develop before the investigational-new-drug stage and those that can wait until further down the pathway

Many of these redesigned processes can become part of the standard manual of operating, while others are project specific or depend on the probability of technical and regulatory success. The calibration of risk tolerance and the alignment on key activity prioritizations depend on both the overall organizational attitude to risk and the specific project (for instance, the level of prior validation and competitive intensity).

2. Agile development

Asset development is highly cross-functional, with many pharmaceutical companies adopting some variation of a core program team. Small, functionally oriented subteams (for example, clinical and CMC teams) typically act independently to prepare deliverables for overall governance discussions. We envisage several changes to an asset's team structure to harness the benefits of agile development:

— formation of thematic and cross-functional subteams assembled and disbanded based on the deliverable—for example, a presentation, delivery, and dosing subteam would not make CMC decisions in isolation but coordinate with a broader team on the implications of the decision on the program timeline, project competitiveness, regulatory pathways, and pricing

— increased empowerment of subteams and the core program team, with each subteam positioned as the primary decision maker for the asset on a specific deliverable, although major decisions will require the core program team's participation for endorsement, recommendations, trade-offs, and the connecting of dots among deliverables

— a cultural shift to iterations based on a minimum viable product—one that includes all critical elements without insisting upon perfection or extended chain of approvals—to accelerate development of key deliverables (for example, a clinical-development plan) and maximize outcomes for the overall project

— early input from internal stakeholders (for example, clinical-operations and regulatory subteams) and external stakeholders (for example, investigators and patients) to embed patient-centricity throughout development plans

— an increased focus on deploying agile methodologies for co-locational and cross-functional teams in areas such as scrum, backlog, "stand-up," and retrospective

— an assessment and incentive model oriented around overall asset performance alongside consistent, 360-degree review feedback that incorporates insights from the core program team and cross-functional subteams

An agile approach has beneficial implications for the program strategy, including indication selection and trial sequencing. It combines inputs from internal

stakeholders (for example, subteams in commercial and therapy area strategy, market access, competitive intelligence, regulatory, and clinical operations) and external stakeholders (for example, patients, payers, and investigators).

3. Asset optimization and risk strategy

Essential to program strategy are asset optimization and risk management. They will inevitably involve trade-offs—particularly given competitive environmental dynamics, including competitor-product profiles and asset positioning. It is imperative that decision-making and trade-off discussions consider all available data, which may lead to nonintuitive outcomes (for example, a quicker launch involving a narrow patient population with eventual stepwise expansion of the cohort).

Derived from these strategic choices is the integrated-evidence plan (IEP), developed and updated by its associated subteam. This plan threads the anticipated commercial and medical positioning of the asset with accompanying strategies from teams in clinical evidence, medical evidence, epidemiological evidence, health-economics and -outcomes research, and real-world evidence. As asset pathways become increasingly divergent, the development plans for assets will become more varied. Leaders must emphasize that there is no "one size fits all" approach: teams should tailor evidence-generation activities and timelines for individual programs according to data, risk, and competitive environment.

4. Protocol design and patient segmentation

The clinical subteam is responsible for an evolving, multiscenario approach to trial design and patient stratification (for example, end-point selection and criteria for inclusion and exclusion), with cross-functional input sought as required. The driver of the design choices is a clear plan of anticipated medical and commercial positioning, as assembled in the IEP.

The IEP undergoes refinement through the asset's life. For example, while the IEP may not be highly detailed at the beginning of Phase II trial, it will contain clear and strategic insight into planned achievements and ambitions at different stages of drug development. This is an important step, ensuring that a clear direction is evident to allow faster proceedings. The IEP will evolve in granularity and specificity as proof-of-concept and pivotal data become available. This helps avoid commonly observed Phase II and III trial problems, including the "everything under the sun" mentality that can make trials unwieldy and unviable. For example, if an asset is the fourth to market with a superior efficacy and safety profile, it is likely to be second or third in line behind cheaper available alternatives. Hence, organizations can deprioritize a trial involving treatment-naive patients for registration purposes but incorporate it into postapproval, real-world-evidence plans.

Innovative approaches from a patient-centric standpoint could be key accelerants, and pharmaceutical companies are beginning to realize their benefits—for example, in the switch of placebo arms to synthetic-control arms, seamless design for Phase IIB and III trials, and incorporation of digital technology (such as monitoring at home by app). Such innovations can help ease patient and physician burden while simplifying drug-development complexity and reducing cost. An R&D organization that systematically embeds digital and patient-centered design thinking will ensure that all trials are framed to focus on patient benefits and time savings.

The clinical subteam should closely coordinate with the clinical-operations subteam to simulate, via predictive algorithms, the operational feasibility of design options alongside cost, time, and quality dimensions. This would also include simulation of trial parameters to predict patient and physician experiences in addition to impact on patient recruitment and adherence. By approaching trial design from this cross-functional perspective, it is possible to streamline clinical trials and support a robust evidence-generation strategy.

5. Country and site selection for clinical trials

Country and site selection, particularly within a highly competitive indication, can significantly affect development costs and timelines. While some

pharmaceutical companies use historic recruitment data to determine selection strategy, the performance of a site does not necessarily correlate with its previous recruitment success.

Most pharmaceutical companies can achieve a new level of performance by linking internal and external data sets to build a predictive machine-learning model with a higher degree of precision in predicting drivers of site performance (for example, site congestion, protocol parameters, and excitement around the target). Applying these algorithms allows identification of ideal sites and the attainment of recruitment ambitions with fewer activated sites. At this stage, the subteam may benefit from developing a small number of scenarios (for example, one with or without trial sites in Japan and one with a regulatory request for local-population inclusion). The use of predictive models can sometimes help achieve a three- to six-month faster enrollment and a reduced default rate.

6. Chemistry, manufacturing, and control acceleration

With long lead times, CMC can often become the bottleneck in the path to drug launch. This is particularly relevant in early project stages or in situations involving program acceleration. A cross-functional engagement model that involves a CMC subteam and encourages participation from subteams in clinical development, regulatory, devices, and supply chain—and, in some situations, commercial—can enable identification of critical path activities. This iterative, agile operating model can support rapid resolution of open questions to align on appropriate trade-offs (for example, development of back-up strategies, transition to standard platforms, timing of final cell lines with the consideration of bridging studies, and up-front at-risk investment).

Organizations can consider combining new ways of working with digitization and application of advanced-analytics techniques (for example, predictive modeling of formulation lock using in silico prototyping and real-time batch monitoring). This approach has the potential to improve quality through proactive identification of delays and deviations (for example, reduction in deviations by 50 to 80 percent and increase in deviation-closure rates to more than 50 percent) and accelerated timelines (for example, from up to six months to one year).

7. Supervision and quality control by a control tower

A cross-functional control tower typically focuses on the planning and execution of pivotal studies. It also works to provide live data across multiple sites and studies, monitoring trial screening, recruitment, dropout, feedback from patients and physicians, and competitive intelligence. In addition, the subteam accumulates longitudinal data, ensuring transparency within the recruitment process (for example, during monitor visits, protocol-amendment rollouts, and medical interactions with principal investigators).

The control tower amasses a series of initiatives, refined over several trials, to accelerate recruitment. For example, upon identifying trial-recruitment challenges, the subteam rapidly explores a set of levers, including creating a site-specific platinum, gold, and silver engagement model based on predictive analytics of site potential; removing bottlenecks through systematic feedback; streamlining the site-contracting process; leveraging cross-industry tools and data sources to create “referral networks” around trial sites; using data-driven media campaigns; and ensuring clear communication of medical conversations with investigators. It can implement more intensive measures, including opening backup sites and simplifying trial protocols, as needed. Collectively, an effective control tower can improve the recruitment rate for pivotal studies by 30 to 50 percent.

8. Complete redesign of patient and investigator experience

Clinical-trial conduct, from design and site selection to start-up and execution, has evolved over the past decade. Although pharmaceutical companies have tried to build new patient- and site-engagement technologies (for example, patient-engagement and -reimbursement apps, e-consent, and protocol-burden measures) into existing trial processes, this

approach is not necessarily effective. In fact, it is likely a key contributor to low satisfaction among investigators and patients, as it requires multiple interfaces and additional trial steps.

Taking a cleansheet approach to trial design and execution can yield tremendous benefits, such as increasing recruitment and retention rates by improving patient and investigator experiences. Primary research and ethnographic surveys can be used to assess patient centricity and investigator centricity by both identifying challenges in their experiences and serving as benchmarks for future improvements. Solutions can vary, depending on the cause of challenges, and may include the following:

— linking patients with research staff and principal investigators via telemedicine

— using portals to connect investigators and to resolve process bottlenecks (for example, through "just in time" contracting)

— flagging patients with high risk of dropout based on preexisting parameters and then providing physician-appropriate talking points and tools

— replacing additional study visits with home-based visits or remote monitoring (for example, through wearable devices)

— allowing real-time, app-based payment for expenses rather than retrospective reimbursement

9. Submission excellence

Efficient processes for preparation of product-dossier submissions are critical to maximizing the probability of label success. It is possible to deliver consistently on a timeline of ten weeks after the database lock, although this is ambitious.

Achieving an accelerated-timeline goal requires embedding a host of solutions and platforms in dossier-filings teams that span both technology solutions and knowledge-driven assets. Technology solutions could include automated hyperlinking, artificial-intelligence-based writing of dossier sections (especially sections that require less interpretive writing), and a structured-content-management approach to writing. Knowledge-driven assets could include archetype-based filing timelines and a framework for defining the minimum viable dossier.

Changes to working methods are also critical. The core of the filing team should operate as a war room that is led by the regulatory subteam but closely involves multiple other functions (for example, clinical science, CMC, nonclinical, pharmacokinetics, pharmacodynamics, medical writing, and clinical operations). Prior to the start of major dossier-preparation activities, this war-room team will align on a single timeline, critical paths, and cross-functional initiatives to be implemented. The most common cross-functional initiatives could include prewriting portions of the dossier prior to the availability of pivotal data, using a systematic reviewer matrix to accelerate review, and agreeing on key messages based on a number of data scenarios. As the dossier preparation progresses, the team can adjust critical paths in real time to create and integrate "priority lanes" that guide the entire team on prioritization during heavy periods of review—always optimizing for overall timelines while retaining a high level of quality for the review.

10. Portfolio-resource optimization

At the above-asset level, the R&D leadership employs digitally informed governance to review consolidated readouts (from ongoing studies and competitor information) in real time, readjusting priorities and resources accordingly. Upon identification of high-priority projects—such as accelerating the filing of high-potential drugs and reauditing a high-risk site—reassignment of the talent and costs to support them can occur within days or weeks. This often involves a willingness to deprioritize programs, even before asset failure, and a readiness to concentrate a considerable proportion of company resources behind a single asset when justified.

It is critical that leadership incentives align with the company's development-excellence goals, with performances (and bonuses) closely tied to the metrics of time, cost, and quality in portfolio development. Tough decisions may be necessary to ensure that leaders have the requisite skills and mind-set to succeed in an increasingly agile and digitally enabled environment.

The consolidated impact

The relative impact of the development-transformation levers depends on the specific situation, starting point, and objectives of individual companies. It is important to realize that there is no instant solution that can optimize the time to market, cost, or quality for every company. The majority of these levers are highly effective, and R&D organizations can amalgamate them into their approach across the portfolio (as opposed to a one-off model for an individual asset). Some of these decisions, and the intensity of the levers applied, could accelerate prioritized programs (for example, CMC acceleration with at-risk investment and energy directed toward trial-recruitment acceleration).

Across the board, we have seen that a holistic approach can achieve a 500-day acceleration in the overall drug-development timeline in addition to improved quality and compliance, enhanced user experience for patients and healthcare professionals, better insights and decision making, and a reduction in costs of up to 25 percent. However, this approach requires a commitment from leadership and the implementation of several difficult decisions throughout the development process.

Implementing the change

Achieving a transformation of the drug-development process relies in equal measure on the specific initiatives previously described and on managerial skill and discipline in implementation. Pharmaceutical organizations embarking on the change need to consider several success factors.

Aspiration

It is often useful to set an aspiration for impact on a specific asset in the portfolio and use this as a flagship for broader change. Before transformation of the drug-development journey, it is essential that all stakeholders align on the overall vision for the asset, including on a "from/to" perspective at the individual function level.

Talent

Transforming and driving new ways of thinking and working requires a new set of skills. Capabilities that often go amiss include design thinking, patient- and physician-experience analyses, advanced analytics, digitization, and automation. Hiring or building on existing capabilities or employing capabilities beyond the organization's walls can fill the gaps.

Technology

At the heart of transformation is the use of technology. Over time, technological skills should go beyond an analytics center of excellence and deploy across the entire organization, establishing an integrated (and secure) data architecture and supporting capability growth.

Data

The explosion in quantity of available data means that the map of ownership is becoming increasingly complex. It is no longer possible for a pharmaceutical company to own all the data associated with its assets, and the linking of multiple data sets and types is just as valuable as the data themselves. R&D leaders must decide which data they will bring in house, which data they will access through partnerships, and which data are less relevant. Drug-development organizations will see a need to create a data strategy alongside their technology strategy to ensure secure, compliant access to the correct data.

Culture

A core part of transformation—in both scale and shape—is the desired cultural change. Working in agile and cross-functional ways can help break down silos, facilitate decision making based on ambiguous data, and create ambitions for rapidly iterative work.

Further, decision makers must be open to a more data-driven way of working, accepting potentially nonintuitive conclusions and being comfortable taking calculated risks. These changes can only happen with full leadership buy-in, empowered teams, and aligned evaluation and incentive models.

Lessons from development-excellence transformations

As several players explore the potential of development excellence to transform their R&D engines, we see a few common success factors:

— **End-to-end view of scaling across a capability, function, or asset—and eventually across the R&D function.** When designing an end state, organizations with the most successful efforts have a clear, value-backed business case to ensure organizational buy-in that acts as a North Star for decision making throughout the company.

— **Patient-centric view to provide a clear vision of what the future organization will look and feel like.** When implementing a transformation, an agile approach to rollout can maintain momentum through sprints, quickly gaining input from users and developing a rapid blueprint of the future state of the organization.[2]

— **Focus on engagement and skill development.** It is crucial for companies to recognize the importance of organizational engagement (at all levels) and investment in the appropriate capability building.

— **Ability to leverage innovation from beyond the pharmaceutical industry.** The skill of applying lessons from other sectors is particularly relevant in the space of analytics and digital (for example, analytical techniques and data storage). But it also applies to themes such as patient centricity: pharmaceutical companies can learn much from other highly customer-centric industries on creating a seamless user experience.

Getting started with development transformation

There are multiple ways to begin a development-transformation journey:

— **Asset-led acceleration.** Select an asset (or program) anticipated to deliver outsize mid- to long-term value. Then deploy transformational initiatives against the asset—throughout R&D functions and across all capabilities (such as agile, design thinking, and advanced analytics). Demonstrate tangible results with one high-priority asset and create near-term value and a desire for an approach that can span the portfolio.

— **Functional reinvention.** Choose a priority function and deploy all development-excellence pillars (patient-centric design, process redesign, digital, analytics, and agility) to deliver something truly exceptional. For example, a company could seek to achieve excellence in trial delivery across multiple elements, including reinvention of the patient journey, advanced analytics to inform site selection, and a control tower to manage real-time quality risks.

— **Capability engine.** Identify one flagship capability to embed across all areas—for example, an end-to-end, agile transformation to change the methods for asset team formation, material development, and decision making across an entire R&D organization. Further, use digital as a catalyst for growth by investing in associated capabilities across all aspects of R&D (for example, automation, artificial intelligence, and digital patient engagement).

— **Fast-track implementation of a proven use case.** Use known, high-priority use cases within

[2] Aliza Apple, Harriet Keane, Rachel Moss, and Valentina Sartori, "Designing an agile transformation in pharma R&D," July 2019, McKinsey.com.

a function to drive change and capture quick wins. Such an approach is the least transformative but may act as a pilot for broader transformation.

— **Holistic R&D transformation.** Drive a holistic transformation across all functions and capabilities—a multistep journey for the entire R&D organization to drive top-down change throughout all aspects of development. This requires both support from the CEO and R&D leadership and a belief that the transformation is important to the future of the company.

The approaches we described represent different levels of ambition and appetites for change. Pharmaceutical companies with new energy spurred by recent leadership changes could be amenable to adapt the holistic R&D transformation, the capability-engine approach, or the functional-reinvention approach. Those with a pipeline-asset-driving, disproportionate potential value could use it as the burning platform to take an asset-driven approach. Those that have invested many years in building a specific capability could opt for a more targeted use-case implementation. Whatever the specific approach, adopting a transformative development journey will help achieve the core ambition of the pharmaceutical industry: the development of effective and innovative medicines brought to patients with efficiency and timeliness.

Gaurav Agrawal is a partner in McKinsey's New York office, where **Harriet Keane** is an associate partner; **Maha Prabhakaran** is an associate partner in the Silicon Valley office; and **Michael Steinmann** is a senior partner in the Zurich office.

The authors wish to thank Matthias Evers, Edd Fleming, Peter Kristensen, and Martin Møller for their contributions to this article.

Designed by Global Editorial Services