Oncology Disruption Demands Strategic Transformation

BY TROY NORRIS, KEYURI SHAH AND KRISTIN POTHIER

Developing the first or best molecule in a class is no longer enough to sustain a differentiated market position in oncology. Pharmas must create patient-centric strategies, often combining medicines produced by different companies.

Creative partnerships with a network of collaborators are essential in this new marketplace, particularly given the advent of immuno-oncology and targeted therapies, both of which are exponentially increasing competitive intensity and the number of possible therapeutic combinations.

So what? Facing market disruption, oncology-focused pharma companies must rethink their approach to leadership. Strategic transformation of portfolios, partnership networks and organizational dynamics will be critical. Organizations that don’t transform rapidly risk obsolescence.

With multiple modalities of care for cancer patients, oncology treatment decision-making has always been complex, but accelerating innovation is driving exponential growth in treatment complexity. Genomic advances continue to enable development of new targeted therapies and immunotherapy agents have demonstrated promising outcome improvements across multiple tumor types. These new treatments are being overlaid upon the more traditional chemotherapies and hormone therapies, producing a wide variety of possible treatment pathways.

The pace of new drug development continues to accelerate: there are more than 650 cancer treatment candidates in late-stage clinical development (Phases II and III). Based on historical success rates, these could potentially lead to the launch of nearly 100 new treatments across roughly 30 clinical indications over the next five to seven years. This accelerating pace has shortened the window for breakthrough drugs to capture value before facing therapeutic substitution, diminishing financial returns for pharma companies. In response, these companies are aggressively broadening the number of molecules, mechanisms and tumor indications for development, creating even more complexity. (See Exhibit 1.)

In particular, large pharma companies are placing their bets on the new class of promising immunotherapies. Although there are only a handful of drugs currently marketed in this segment, more than 200 immunotherapies are under study, including cell therapies and cancer vaccines. (See Exhibit 2.) Primary checkpoint inhibitors are the most advanced mechanistic category, with five drugs approved or in registration, and another eight drugs in Phase II or Phase III. Together, these checkpoint inhibitors are expected to become the backbone of combination therapy going forward.
The plethora of new molecules with complementary treatment mechanisms is driving further complexity through proliferation of possible combination regimens. Liz Barrett, global president and general manager, oncology, at Pfizer Inc., emphasized at the UBS Global Healthcare Conference that “PD-1 will always be a backbone of immuno-oncology,” adding that “the winning formulation for patients will ultimately be in the combinations of multiple immuno-oncology medicines and also in combination with targeted therapies.” Consequently, more than 750 clinical studies, according to Informa’s Trialtrove, are ongoing – testing the eight PD-1/PD-L1 inhibitor drugs in Phase III or later in combination with other therapies. (See Exhibit 3.) More than a quarter of these experimental regimens are testing combinations of three or more drugs. Many of these trials are exploratory, with small sample sizes, which will make interpretation of results challenging.

The sheer number of potential treatment combinations that these trials are expected to create across tumor types and stages promises to make treatment decision-making even more challenging for care providers. Adding to the challenge, some combination trials have seen mixed results, with little or no improvement to progression-free survival rates or even an increase in fatalities. This proliferation of treatment combinations, coupled with the unpredictability of combination trial outcomes, makes it ever more difficult for a drug to separate from the pack, while making it ever more imperative to establish a role in standard-of-care regimens.

**Value Shift Toward Treatment Decisions**

With so many similar compounds and combinations competing for a role in the standard-of-care treatment path, patient selection and optimization of the overall treatment regimen are paramount for success. The experiences of Merck & Co. Inc.’s Keytruda (pembrolizumab) and Bristol-Myers Squibb Co.’s Opdivo (nivolumab) are prime examples of the impact of patient selection on clinical outcomes and product positioning across tumor types and treatment lines.

Effective competitive differentiation therefore depends critically on designing the optimal clinical program for a molecule – targeting the right patients, with the appropriate treatment regimens, and using the best diagnostics. In addition to very strong clinical and molecular science, deciding upon the appropriate patients and regimens requires access to complex data, which are controlled by providers and payers. Treatment decisions at the clinic can no longer rely on package inserts, nor even standard clinical guidelines. Robust predictive treatment algorithms are needed to make clinical decisions using advanced data mining capabilities, analytics tools and statistical methods.

Driving toward optimal outcomes, major cancer centers and industry consortia are combining their clinical expertise and access to patient data to develop advanced clinical decision support systems. (Also see “Free And Open: The Next Wave In Clinical Trial Data?” - In Vivo, May 2017.)

**Transforming Portfolios, Partnerships And Organizations**

Differentiating within this shifting paradigm toward personalized combination therapy requires pharma companies to rethink their approach to market leadership. Traditional approaches to product development and operational management will no longer ensure success. This strategic transformation of oncology manufacturers requires coordination on
three dimensions: 1) refocused portfolio management, 2) innovative partnership networks and 3) dynamic organizational decision processes. (See Exhibit 4.)

**A SHIFT IN INVESTMENT FOCUS**

Accelerating complexity and personalization of care requires increased investment across the care continuum to establish leadership. As having the first or best molecule in a class becomes a more short-lived differentiator, market leaders need a portfolio of complementary mechanisms with a central role in combination regimens across tumor types. Consequently, innovators must balance the need to pursue complementary mechanisms and combination regimens against the greater intensity of investment required to develop and position each molecule. Discussing their oncology strategy on an earnings call, Vasant Narasimhan, global head of drug development and chief medical officer of **Novartis AG**, pointed out: “We continue to evaluate a range of different options, whether it’s in IO-IO combination or in combination with our targeted therapies ... the key is going to be for us to prioritize amongst all of these opportunities.”

Portfolio decision-making has traditionally aimed to identify the highest-value individual assets and to diversify risk through investment across multiple unrelated mechanisms. Going forward, portfolio strategy needs to optimize the collective value of a franchise within and across tumor types – evaluating different asset combinations to optimize the risk-reward balance and maximize overall portfolio value under a range of scenarios. Minimizing asset overlap and facilitating co-positioning of compounds may require delaying or deprioritizing otherwise attractive clinical candidates, or focusing specific molecules on a narrower set of indications and patient populations.

Companies also need to decide whether to co-develop combinations of candidates in their own pipeline or to partner, to access either promising clinical candidates or compounds already established as standard of care. Portfolio decision-makers must make complex trade-offs among achieving the best clinical profile in the broadest population, enabling creative outcomes-based premium pricing strategies and capturing a fair share of the economic value realized. (See Exhibit 5.)

The move toward expensive combination regimens will exacerbate reimbursement challenges. Payers are likely to demand lower pricing for new therapies when used as part of a combination rather than monotherapy. Companies with multiple effective and complementary therapies, especially including back-bone immune checkpoint inhibitors, will be well-positioned to pursue premium pricing through aggressive outcomes-based contracting for their combination regimens. Without this portfolio scope and scale, partnering to create the most effective combination therapies will be critical to capture value.

To support portfolio decision-making with this complex set of potential partners, development paths and clinical outcomes scenarios, more sophisticated scenario modeling and simulation tools are needed. Data analytics companies are developing tools, such as **InveniAl Corp.**’s **PharmGPS**, that can assess competitive gaming and potential partnering scenarios, as well as the commercial value across indications considering complementarity and cannibalization. These tools aim to determine the optimal development paths for individual
oncology treatment candidates that will collectively maximize overall portfolio value across indications, patient populations and treatment regimens. To help providers and patients grapple with the flood of new clinical findings, pharma companies are creating digital solutions to support their portfolio strategies. For example, Boehringer Ingelheim GmbH is developing an online portal to connect key opinion leaders and provide online resources for healthcare professionals, journalists, and patients. And companies such as AstraZeneca PLC and Eli Lilly & Co. have developed mobile applications to provide easy access to educational resources. These digital educational channels can create crucial dialogue with clinicians that enhances a company’s portfolio position.

**CREATIVE, COORDINATED AND PURPOSEFUL COLLABORATION**

To succeed in this new environment, biopharma companies need to create a vibrant network of partnerships. (See Exhibit 6.) Oncology innovators and marketers can no longer drive growth solely through traditional compound licensing and acquisitions. Partnerships with other companies will increasingly be needed to access compounds for combination regimens, co-develop diagnostics to identify the right patient populations and use real-world data to maximize therapeutic value and patient outcomes.

For each partnership category, companies must clearly define the objectives and role in achieving the target market position amid the emerging collaboration network. These partnerships will need to be carefully coordinated to assure alignment to support the portfolio as a whole, specific brands and potentially new revenue streams.

**Companion Diagnostics**

For immuno-oncology and targeted therapies alike, pharma companies will need to continue to partner with diagnostic companies to identify subsets of high responders. Testing technologies continue to advance quickly, enabling more rapid and robust treatment response prediction.

For example, researchers at companies such as PerkinElmer Inc., NanoString Technologies Inc. and Genoptix Inc. are developing more quantitative multiplexed immunohistochemistry (IHC) protein expression assays. Continued advances in nucleic acid testing methods are enabling routine analysis of comprehensive gene panels and overall tumor mutation burden. And new modalities that enable less invasive, more rapid treatment response and recurrence monitoring are emerging, such as liquid biopsy and advanced imaging techniques.
Assuring access to these new technologies, and anticipating future diagnostic pathways, will continue to be critical for successfully positioning products in the treatment path to drive rapid uptake into clinical practice.

**“Coopetition” Among Pharmas**

Companies with novel targeted and immuno-oncology therapies increasingly need to consider which other molecule and mechanism combinations will be optimal for which tumor types. The many companies with multiple compounds on the market and under development can no longer rely solely on compounds in their own portfolio, and instead must choose to partner with others with the aim to develop the best and broadest standard-of-care regimen.

Cooperation among pharma companies, forced by the clinical science to work together to secure a position in treatment pathways by creating best-in-class combination regimens, has risen dramatically. Within immuno-oncology, the growth in combination drug partnerships has outpaced growth in single drug agreements (e.g., traditional in-and-out-licensing). According to an April 2017 report, “Immuno-Oncology Deal Trends, 2012–16,” from Informa Pharma Intelligence’s Datamonitor Healthcare, combination deals recently outnumbered single asset deals by two-fold. (See Exhibit 7.)

More than half of these immuno-oncology combination agreements involve PD-1 and PD-L1 inhibitors, with 137 of these deals occurring over the past five years. For example, Merck has partnered with Pfizer and AstraZeneca to combine selected immuno-oncology and targeted

As the available diagnostic and therapeutic options expand, pharma product, portfolio and partnering decisions have become highly complex

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**Future**

Companies are forging relationships without pharma that are shifting the value equation

Therapeutic companies must actively establish themselves as hubs within a value network of cross-sector collaborative partnerships

![Diagram](https://via.placeholder.com/150)

- Access to targeted or immuno-therapies for development of combination regimens
- Partnerships to accelerate trials and/or co-market treatments
- Co-development or access to diagnostic tests to advance the development and marketing of drugs
- Licensing or acquisitions of analytics tools to accelerate trials, advance personalized medicine or enhance patient care
- Development of clinical decision tools and/or research studies for evidence-based care
- Cancer centers and integrated health systems

Companies are forging relationships without pharma that are shifting the value equation

(See Exhibit 7.)
medicines. BMS has entered into a wide range of co-development partnerships for Opdivo across tumor types. With a full portfolio of immuno-oncology and targeted medicines for solid tumors, AstraZeneca chose to license its checkpoint inhibitor and other immuno-oncology candidates to Celgene Corp. to develop for hematological malignancies.

Data Analytics

Increasingly, complex treatment choices and new diagnostic methods are catalyzing efforts to harness “big data” to guide translational programs, patient selection, health economics and outcomes research, market access and treatment algorithms.

These data analytics collaborations are expected to lead to improved therapies and more effective positioning and use of these drugs, while helping secure a place in future treatment algorithms and potentially enabling new revenue models derived from the clinical value of the analytics solutions. (See sidebar, “Pharma’s Big Data Deals.”)

Health Care Providers

As the oncology landscape becomes more competitive and complex, capturing full value for innovative products will require real-world evidence of a therapy’s ability to improve outcomes in specific patient populations. Pharma companies are thus partnering with cancer centers and health systems to access and analyze real-world data. For example, AstraZeneca has begun an initiative to collect and analyze real-world data to combine patient experience insights with molecular and clinical data from electronic health records.

As data technologies advance, some medical products companies are thinking even more holistically about the use of real-world data. For example, Partners HealthCare System Inc. and GE Healthcare recently announced a clinical data science collaboration to leverage clinical data sets and artificial intelligence to improve the entire continuum of cancer care, from reducing unnecessary biopsies to optimizing treatment. In its press release, Keith Dreyer, chief data science officer, Departments of Radiology and MGH and BWH, Partners Healthcare, emphasized the criticality of partnerships between hospitals and the industry for the advancement of clinical data science: “We’re evolving the health care system to be able to take advantage of the benefits of deep learning, bringing together hospitals, data sets and clinical and technical minds unlike ever before.”

Leveraging real-world evidence to identify novel approaches to patient care can also identify new treatment populations and reduce clinical program risk. For example, Celgene has recently partnered with Dana-Farber Cancer Institute and the University of Arkansas to compile a large data set of genomic and clinical information, to identify distinct molecular disease segments within multiple myeloma to be leveraged for future treatment development.

DYNAMIC ORGANIZATIONAL MODELS AND DECISION PROCESSES

The rapid pace of market and technology disruption coupled with the increasing complexity of decision-making is stressing the organizations of large multinational oncology businesses. The standard matrixed model of molecule-centric global R&D and brand teams with geographically focused sales and marketing organizations, typically coordinated centrally, needs to shift toward more agile, dynamic, delegated decision processes.

To support the responsive coordination needed to succeed in oncology,
companies such as AstraZeneca, Bayer AG and Novartis have separated their oncology business units from their broader pharma businesses. In Bayer’s annual news conference in 2017, Dieter Weinand, head of Bayer’s pharmaceutical division, defended his company’s decision to reorganize, reiterating the need for agility in oncology: “The unit will enable us to get to market first and fast with our oncology products. It is very important to be first to market, otherwise the standard of therapy is changed and your studies were against the old standard of therapy.” More nimble resource allocation and clinical progression decisions are expected to speed development and repositioning of pipeline agents in the quickly evolving cancer market.

Development and partnering decisions, especially regarding combination regimens and companion diagnostics, will require substantial clinical and commercial involvement, coordinated globally across brands and tumor types. To make more responsive decisions for their programs, brands and deals, functional teams across R&D, commercial and business development need greater coordination with predefined decision criteria and real-time competitive intelligence.

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To manage increasingly complex collaboration networks, organizations need to revisit how they are structured and resourced to effectively identify, evaluate, transact and manage these alliances. For example, effective coordination of data partnerships often requires centers of technology expertise with governance aligned to the organizational matrix to activate data across a wide range of clinical development, market access and commercial applications.

The need for rapid decision-making based on accurate and timely information will require dynamic, anticipatory decision processes that incorporate and integrate diverse inputs from across the organization to drive rapid, adaptive, coordinated decision-making and implementation. Companies will need to deploy more sophisticated decision tools to manage complexity and uncertainty while supporting less centralized decision-making processes. Those that successfully design and align a more dynamic organizational model will have a critical source of competitive advantage in oncology.

**Implications For Oncology Innovators And Marketers**

As the future oncology landscape becomes increasingly competitive, complex and data-driven, businesses that move confidently to adapt to and capitalize on this rapid disruption will have a strong competitive advantage and are more likely to achieve a profitable and growing market position. Transformation will require a shift in portfolio focus and scope, partnering creatively and purposefully with a wide range of stakeholders, and a more dynamic organizational model that enables rapid evaluation of strategic options and real-time decision-making. Innovators and established players alike must proactively adapt to secure a sustainable position in the future oncology ecosystem.

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**PHARMA’S BIG DATA DEALS**

Several biopharmas, such as Celgene Corp. and Pfizer Inc., have partnered with IBM Watson Health to speed the identification of new targets and patient selection strategies for immunotherapies.

Novartis AG has also partnered with IBM Watson Health to develop a cognitive solution that uses real-world data to predict response to breast cancer treatments, which follows on Novartis’ collaboration with COTA Inc. to apply its evidence-based analytics platform to improve outcomes and costs for breast cancer patients.

Celgene has invested in NantHealth LLC to support the creation of evidence-based personalized health tools across diagnoses, treatment decision support, monitoring and patient care.

And oncology developers are partnering with data analytics firms, such as GNS Healthcare, to discover new biological pathways, identify target populations and predict patient outcomes, or MediData Solutions Inc., to develop improved targeted therapies and evaluate new oncology indications.

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